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Computational simulations of respiratory-laryngeal interactions and their effects on lung volume termination during phonation: Considerations for hyperfunctional voice disorders

Maude Desjardins,[1,a)] Katherine Verdolini Abbott,[1] and Zhaoyan Zhang[2,b)]

[1]*Department of Communication Sciences and Disorders, University of Delaware, Tower at STAR 100 Discovery Boulevard, Newark, Delaware 19713-1325, USA*

[2]*Department of Head and Neck Surgery, University of California, Los Angeles, 31-24 Rehabilitation Center, 1000 Veteran Avenue, Los Angeles, California 90095-1794, USA*

ABSTRACT:

Glottal resistance plays an important role in airflow conservation, especially in the context of high vocal demands. However, it remains unclear if laryngeal strategies most effective in controlling airflow during phonation are consistent with clinical manifestations of vocal hyperfunction. This study used a previously validated three-dimensional computational model of the vocal folds coupled with a respiratory model to investigate which laryngeal strategies were the best predictors of lung volume termination (LVT) and how these strategies' effects were modulated by respiratory parameters. Results indicated that the initial glottal angle and vertical thickness of the vocal folds were the best predictors of LVT regardless of subglottal pressure, lung volume initiation, and breath group duration. The effect of vertical thickness on LVT increased with the subglottal pressure—highlighting the importance of monitoring loudness during voice therapy to avoid laryngeal compensation—and decreased with increasing vocal fold stiffness. A positive initial glottal angle required an increase in vertical thickness to complete a target utterance, especially when the respiratory system was taxed. Overall, findings support the hypothesis that laryngeal strategies consistent with hyperfunctional voice disorders are effective in increasing LVT, and that conservation of airflow and respiratory effort may represent underlying mechanisms in those disorders.

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I. INTRODUCTION

During phonation, the laryngeal and respiratory systems function as an integrated unit: a change in behavior in one part of the system induces compensatory changes in other coordinative structures such that specific respiratory or phonation goals (e.g., utterance duration or loudness)[1–3] are achieved. These interactions result in a constant trade-off between respiratory and laryngeal muscular activity based on the varying vocal demands. For example, when the expiratory pressure increases to meet a target subglottal pressure, glottal resistance increases simultaneously to keep the vocal folds from being blown apart while maintaining a small glottal opening.[4–6] This mechanism allows speakers to maintain a good vocal quality by limiting air turbulence, in addition to controlling airflow expenditure.[4]

As glottal resistance increases, mean glottal airflow is reduced and the potential duration of the expiratory phase of speech is lengthened. Consequently, the speaker can rely on strong relaxation pressures for a longer duration (by slowing the decline in lung volume) and end phonation at a higher lung volume, thus avoiding high expiratory effort. In a previous computational modeling study, Zhang[7] found that in conditions of normal speech, the need for airflow conservation [to complete an average 4-s breath group duration (BGD) without running out of air] does not impose a stricter constraint in terms of glottal resistance than that which would otherwise be required to meet phonation threshold pressure needs. However, when the context demands a greater intensity/subglottal pressure or a longer BGD, for example during singing or public speaking, the need for airflow conservation becomes greater.[7] In those cases, either the glottal resistance has to be increased or a change has to occur at the level of the respiratory system [e.g., a greater lung volume initiation (LVI)] to ensure sufficient airflow and subglottal pressure to meet vocal demands. Laryngeal strategies, such as vocal fry (also called "creak"), have been reported in healthy speakers and are thought to serve the purpose of lengthening a BGD, for example, when adding information in response to cues from a discussion partner.[8] Because vocal fry is produced with increased vocal fold thickness and associated with very low glottal airflow, it allows speakers to extend

[a)]Electronic mail: maude@udel.edu, ORCID: 0000-0003-4758-1968.
[b)]ORCID: 0000-0002-2379-6086.

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utterances beyond what they had planned by making economical use of the air available.[8]

Ideally, speakers manage to find a balance between respiratory and laryngeal involvement to meet phonation goals with no extraneous effort from either system. However, because a disruption or improper posturing in one system is expected to lead to compensations in the other system, inadequate lung volume planning could participate in the pathophysiology of voice disorders—specifically those involving vocal hyperfunction (VH). Hillman *et al.*[9] described two types of VH: phonotraumatic vocal hyperfunction (PVH), which is associated with the presence of benign vocal fold lesions, and nonphonotraumatic vocal hyperfunction (NPVH), which is associated with hyperfunction in the absence of structural changes to the vocal fold tissues. Among the factors involved in the pathophysiology of VH, altered biomechanics and sensorimotor deficits are thought to play a central role.[9] Importantly, these deficits are likely to disrupt the coordination of the laryngeal and respiratory systems in the attainment of phonation targets. In fact, the literature contains reports of atypical speech breathing patterns in patients with PVH and NPVH, who may speak at lung volumes that are abnormally low when compared to healthy speakers.[10–12] Additionally, a subset of patients with NPVH were found to use longer inspiratory durations when compared to healthy speakers, which, as suggested by the authors, may lead to unnecessarily elevated phonatory lung volumes in some instances.[13]

In this study, we focused on potential compensatory laryngeal adjustments in response to different respiratory conditions. Previous computational modeling simulations showed that increasing the glottal resistance plays a role in airflow conservation and reduction of respiratory effort,[7] but it is unclear which specific laryngeal parameters (initial glottal angle, medial surface vertical thickness, longitudinal or transverse stiffness) are the best predictors for lung volume termination (LVT), an important indicator of airflow conservation and respiratory effort. Additionally, whether or not the role of laryngeal strategies for airflow conservation is consistent with clinical manifestations of VH (PVH and/or NPVH[9]) remains to be investigated.

The aims of this study were to (1) investigate which specific laryngeal postures (in terms of initial glottal angle, medial surface vertical thickness, and stiffness) are the best predictors of LVT during phonation; and (2) assess how these effects are modulated by respiratory parameters (subglottal pressure, LVI, and BGD).

This study also aimed to consider the clinical implications of the findings, specifically, in terms of the pathophysiology of hyperfunctional voice disorders and indications for voice therapy. It is hoped that findings from this study will help us understand the underlying functions of different compensatory mechanisms used by speakers with VH and how they may be avoided by rebalancing the respective involvement of the respiratory and laryngeal systems.

II. METHODS

A. Model

The model used in this study included a three-dimensional vocal fold model and respiratory model (Fig. 1), coupled through the glottal volume flow rate.

The three-dimensional vocal fold model was developed by Zhang as reported in previous studies (see Zhang[4,15] for a detailed numerical description). The model assumes left-right symmetry about the glottal midline in both the geometry and vibration of the vocal folds so that one vocal fold is modeled and the other is an exact replication in terms of shape and movement. Constant parameters (length, depth, and density of the vocal fold) are shown in Table I, along with parameters that exhibited a range of values in the simulations [glottal angle α, medial surface vertical thickness T, body and cover anteroposterior (AP) shear modulus, respectively, G_{apb} and G_{apc}, and transverse Young's modulus E_t]. These parameters were chosen because they vary based on laryngeal muscle activation during phonation.[15] To limit the number of possible conditions, the AP Young's modulus (E_{ap}) was assumed to be equivalent to $4G_{ap}$ in all simulations. The lateral, anterior, and posterior ends of the vocal folds were fixed, and the medial surfaces (of vertical thickness T) formed an angle α [Fig. 1(A)], which determined the initial glottal opening, as well as the theoretical distance, between the vocal processes of the arytenoids. The vocal fold was modeled as a two-layer (body and cover) transversely isotropic, linear material. The body and cover sections were both modeled as an elastic layer with an isotropic plane perpendicular to the longitudinal axis. The model's ability to display essential human phonation features has been previously confirmed:[4] the vocal fold model, coupled with a one-dimensional glottal flow model, provides a valid representation of the glottal fluid-structure interactions during phonation and is suitable to assess laryngeal adjustment mechanisms. See Zhang[4] for the numerical details of the one-dimensional glottal flow model.

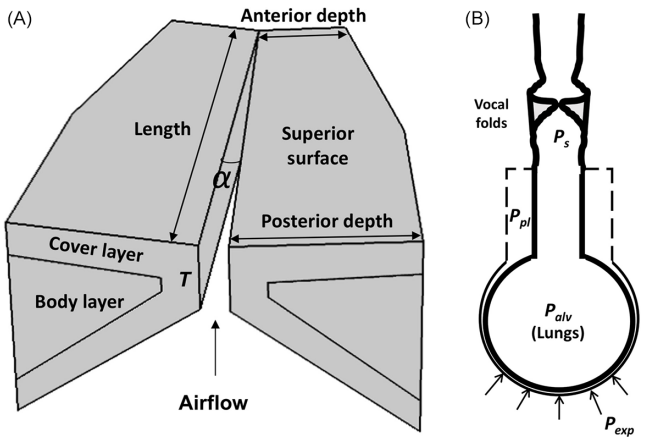

FIG. 1. (Color online) The three-dimensional vocal fold model (A) and respiratory model (B) [adapted from Zhang (Ref. 14)]. α = initial glottal angle; T = vertical thickness of the medial surface; P_s = subglottal pressure; P_{alv} = alveolar pressure; P_{exp} = net expiratory muscle pressure; P_{pl} = intrapleural pressure.

TABLE I. Simulation conditions, including constant and control vocal fold parameters. The values in bold represent the average phonation conditions as defined in this study. AP Poisson's ratio = 0.495 for all conditions.

	Unit	Value(s)
Constant parameters		
Length	mm	17
Posterior depth	mm	7.5
Anterior depth	mm	3.75
Density	kg/m^3	1030
Control parameters		
Initial glottal angle	°	$\alpha = \{-1.6, \mathbf{0}, 1.6, 4, 8\}$
Vertical thickness	mm	$T = \{1, 2, \mathbf{3}, 4.5\}$
Body stiffness (AP shear modulus)	kPa	$G_{apb} = \{1, 10, \mathbf{20}, 30, 40\}$
Cover stiffness (AP shear modulus)	kPa	$G_{apc} = \{1, 10, \mathbf{20}, 30, 40\}$
Transverse Young modulus	kPa	$E_t = \{1, 2, \mathbf{4}\}$
AP Young's modulus	kPa	$E_{ap} = 4G_{ap}$

Details of the respiratory model are described by Zhang.[7] As shown in Fig. 1(B), the alveolar pressure in the lungs (P_{alv}) is influenced by muscular action, generating expiratory muscle pressures (P_{exp}), and the elastic recoil of the lung-thorax unit, generating a relaxation pressure [P_{rlx}; Eq. (1)]

$$P_{alv} = P_{exp} + P_{rlx}. \tag{1}$$

Note that when the pressures generated by the inspiratory muscles are larger than those generated by the expiratory muscles, P_{exp} takes a negative value. The relationship between P_{rlx} and the lung volume (i.e., the relaxation pressure-volume curve) was described by a sigmoid function as demonstrated and used in previous studies.[7,16] In the present study, a target subglottal pressure P_s was established, which determined the required alveolar pressure while taking into account the lower and upper airway resistances (R_{law} and R_g, respectively), as shown in Eq. (2)

$$P_s = P_{alv}\frac{R_g}{R_{law} + R_g}. \tag{2}$$

Lung function parameters and respiratory system compliance were set at constant values. Manipulated parameters included the target subglottal pressure (P_s), BGD, and LVI expressed as a percentage of the vital capacity (VC; Table II).

B. Simulation conditions

Respiratory and vocal fold parameters are summarized in Tables I and II along with their respective value(s) used in the simulations. Values of the parametric conditions were based on previous studies: to model a pressed voice, the initial glottal angle was set at –1.6° (≈–0.5 mm between the vocal processes—a negative distance represents the medial compression of the vocal folds).[17,18] Initial glottal angles of 0° and 1.6° (≈0.0 and 0.5 mm of abduction) were modeled to simulate normal phonation, and initial glottal angles of 4° and 8° (≈1.2 and 2.4 mm of abduction) were modeled to simulate glottal insufficiency.[14] The vertical thickness T varied between 1 and 4.5 mm to model vocal folds ranging from thin to thick. A similar range of medial vertical thicknesses has been observed experimentally and used in previous computational studies, allowing for the generation of a broad range of vocal qualities (breathy, pressed, modal, falsetto, and irregular).[15,19–23] Longitudinal stiffness in the body layer and cover layer were independently controlled with values for the shear modulus varying between 1 and 40 kPa, and the transverse Young modulus was set at 1, 2, or 4 kPa.

TABLE II. Simulation conditions including constant and control respiratory parameters. Constant parameters were informed by Hoit and Hixon (1987)[30].

	Unit	Value(s)
Constant parameters		
System compliance	L/Pa	0.001
Total lung capacity	L	7
Resting volume	L	2
Functional residual capacity	L	3.5
Lower airway resistance	Pa.s/ml	0.1
Control parameters		
LVI	% of VC	LVI = {35, 55, 75}
Target subglottal pressure	Pa	P_s = 200–1800 (in 13 steps)
BGD	s	BGD = {4, 6.5}

As for the respiratory conditions, subglottal pressure in normal speech can vary between 200 and 1200 Pa in healthy speakers.[24] Higher subglottal pressure values (up to 1800 Pa) were also included in the simulations to model loud and potentially pathological phonation conditions.[25] Analyses were conducted for normal as well as low and high lung volume conditions (LVI = 55% of VC, LVI = 35% of VC, and LVI = 75% of VC, respectively). This range of LVIs is in line with the variation observed in human subjects when varying loudness cues.[26] Simulations were also conducted for normal and long BGDs (=4 s[27] and 6.5 s, respectively). The duration of 6.5 s was used in previous studies to represent a long BGD and corresponds to approximately one standard deviation above the average value for BGD during spontaneous speech in healthy speakers.[7,27] As for subglottal pressure, ranges were established for low, normal, and high values based on experimental studies.[24,28] The low subglottal pressure range varied from 200 to 600 Pa, the normal range varied between 800 and 1200 Pa, and the high range varied between 1400 and 1800 Pa.

The following values were used to represent "average" phonation conditions in the analysis (see Sec. II C): $\alpha = 0°$, $T = 3$ mm, $E_t = 4$ kPa, $G_{apb} = 20$ kPa, and $G_{apc} = 20$ kPa. Although normal voice production can occur with an initial glottal angle greater than 0°, α was set at 0° to model a fictitious patient with complete glottal closure and no air loss from a glottal gap. A vertical thickness T of 3 mm was chosen to represent normal modal phonation.[22] The transverse Young modulus was centered about the value of 4 kPa as in

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previous computational modeling studies in which this variable was held constant.[14,15,29] The longitudinal stiffness was centered about the intermediate value of 20 kPa for both G_{apb} and G_{apc}. These values are bold in Table I.

Constant parameters for the vocal fold and respiratory models were the same as those used by Zhang in 2016[7] and 2019[14] and are displayed in Tables I and II.

C. Data analysis

Only conditions that resulted in sustained phonation with the target subglottal pressure and BGD were included in the data analysis. Visual inspection of the data was conducted using MATLAB R2019b (The MathWorks, Natick, MA).

Regression models were selected using a best subsets regression approach in R (version 4.04, R Core Team, Vienna), which determined the best model for each number of predictors (from 1 up to 15, which included all main predictors and all two-way interaction terms). From these results, the number of predictors for the final regression models was chosen based on the adjusted R^2, Akaike information criterion (AIC), and Schwarz Bayesian information criteria (SBC). These data were plotted and a visual inspection was performed to identify the number of predictors at which the values for R^2, AIC, and SBC started to level off and reach a plateau. An evaluation of these criteria allowed for the selection of regression models that maximized the overall explained variance and minimized the prediction error while optimizing the balance between complexity (number of predictors) and goodness-of-fit. Results led to a high consistency between the models and, therefore, the same subset of seven predictors was used for all models to allow for comparison between different respiratory conditions.

Multiple linear regressions were conducted in IBM SPSS Statistics for Windows (version 25, released 2016, IBM Corp., Armonk, NY) to assess the predictive ability of each independent variable and their interaction effects on LVT (in % of VC) for different LVI, subglottal pressure, and BGD conditions. Only the predictors previously identified using the best subsets regression approach, as described above, were included in the regression models. Prior to fitting the models, the independent variables (α, T, G_{apb}, G_{apc}, and E_t) were centered about a chosen value (representing average phonation conditions as highlighted in bold in Table I) so that the intercept and regression coefficients would correspond to clinically meaningful values. When centering variables to a specific value, their regression coefficients represent the rate of change in the outcome (in this case, LVT) with respect to each given independent variable when all other predictors are held constant at the value chosen for centering. To form the interaction terms, the products of relevant combinations of independent variables were computed using the centered terms. Then, the change in R^2 was assessed when adding one predictor (and its interactions) to the model containing all of the other predictors. Note that a main predictor and its interaction effects had to be taken in and out of the model in a same block to assess the change in R^2 because otherwise the interaction effect would "absorb" the effect of the predictor.

Assumption testing for the regressions was performed by visually examining plots of the residuals to assess normality and homoscedasticity, by testing for multicollinearity (looking at the variance inflation factor, VIF), and by conducting the Cook's distance test to assess the presence of influential outliers. All assumptions were met, and no significantly influential outliers were identified.

III. RESULTS

A. Normal phonation conditions

The ability of the five laryngeal parameters to predict LVT was tested in a multilinear regression analysis. Together, the predictors explained 85.4% of the variance in LVT when LVI was set at 55% of VC and BGD was set at 4 s, for subglottal pressures between 800 and 1200 Pa (typical of normal phonation). The intercept of the model was 47.04, corresponding to the LVT value when all predictors were set at their typical values used for centering as described previously. Table III displays the regression coefficient for each variable. The initial glottal angle was the laryngeal strategy with the greatest associated change in R^2, closely followed by the vertical thickness. The regression coefficients for these two predictors indicate that as vertical thickness increases and initial glottal angle decreases, LVT increases as a result of greater airflow conservation (reduced airflow rate) via those laryngeal strategies, with all other predictors being held constant. For example, to give a clinical benchmark, a change in the initial glottal angle from 1.6° to –1.6° (from barely adducted/abducted to hyperadducted vocal folds) would allow a speaker to save approximately 12% of VC during a 4-s utterance. Importantly, the effect of the vertical thickness on LVT has to be interpreted in light of its interaction with transverse and longitudinal

TABLE III. Regression coefficients and the change in R^2 when adding a predictor and its associated interaction effects to the otherwise complete model for normal phonation conditions (LVI = 55% of VC; BGD = 4 s; P_s = 800–1200 Pa). Predictors include the initial glottal angle (α), vertical thickness (T), longitudinal body and cover stiffness (G_{apb} and G_{apc}, respectively), transverse stiffness (E_t), as well as the relevant interactions indicated by an asterisk. In bold, the p-value is significant at $p \leq 0.001$. The adjusted R^2 for the model = 0.854.

	Regression coefficient	Standard error	t	Change in R^2
(Intercept)	47.043	0.191	**245.675**	
α	−3.787	0.034	**−111.740**	0.544
T	4.749	0.165	**28.854**	0.376
E_t	1.562	0.081	**19.175**	0.039
G_{apb}	0.179	0.007	**25.307**	0.028
G_{apc}	0.046	0.008	**6.047**	0.014
T*E_t	−1.416	0.068	**−20.678**	
T*G_{apc}	−0.111	0.007	**−17.080**	

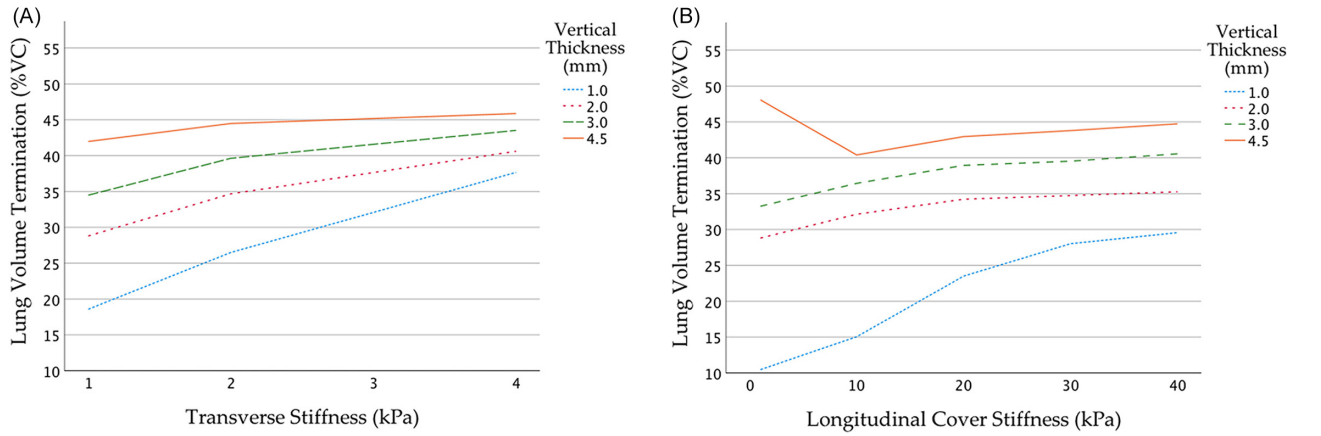

FIG. 2. (Color online) The interaction effect of vertical thickness and transverse stiffness (A) and longitudinal cover stiffness (B). Both graphs display the observed means for LVT in percent of VC for a LVI of 55% of VC, BGD of 4 s, and subglottal pressures between 800 and 1200 Pa.

stiffnesses, which is depicted in Fig. 2. Figure 2(A) shows that when the vocal folds have a low transverse stiffness, the impact of the vertical thickness on LVT is greater than when the vocal folds are stiffer. The clinical importance of this interaction will be discussed in Sec. IV. A similar interaction effect was found between the vertical thickness and longitudinal cover stiffness [Fig. 2(B)]. Note that the peak in LVT observed for thick vocal folds at very low cover stiffness is likely representative of a fry-like phonation mode in which the cover is very soft and airflow expenditure is low because of the large vertical thickness.

B. Effect of subglottal pressure

Table IV shows the regression model for high subglottal pressure values (1400–1800 Pa). When compared to typical subglottal pressure conditions (Table III), the intercept was reduced from 47.04 to 40.11, and regression coefficients for the main predictors were increased as a result of the greater airflow expenditure during phonation. Additionally, the relative importance of each predictor was not the same: vertical thickness became associated with the largest change in R^2 (0.565) when added to the model—indicating that of all predictors, its variation was the most highly correlated with the variance in LVT. Inversely, the change in R^2 associated with the parameter of the initial glottal angle was slightly reduced to 0.506. Transverse stiffness remained the third most important predictor, closely followed by longitudinal stiffness of the body layer: as stiffness increased, LVT also increased. Interactions between thickness and stiffness (transverse and longitudinal cover stiffness) followed a pattern similar to those pictured in Figs. 2(A) and 2(B), respectively. Refer to Table IV for details related to all predictors.

Figure 3 displays the mean LVT by subglottal pressure for each vertical thickness value. The graph shows that the effect of vertical thickness on LVT is amplified as the subglottal pressure increases, which could partly explain the increase in R^2 that is associated with vertical thickness at high subglottal pressures. These results indicate that a greater vocal fold thickness allows speakers to vary the subglottal pressure while limiting the impact on air loss and, thus, LVT. In fact, only the greatest vertical thickness value

TABLE IV. Regression coefficients and the change in R^2 when adding a predictor and its associated interaction effects to the otherwise complete model for conditions of high subglottal pressure (LVI = 55% of VC; BGD = 4 s; P_s = 1400–1800 Pa). Predictors include the initial glottal angle (α), vertical thickness (T), longitudinal body and cover stiffness (G_{apb} and G_{apc}, respectively), transverse stiffness (E_t), as well as the relevant interactions indicated by an asterisk. In bold, the p-value is significant at $p \leq 0.001$. The adjusted R^2 for the model = 0.819.

	Regression coefficient	Standard error	t	Change in R^2
(Intercept)	40.112	0.244	**164.110**	
T	8.655	0.206	**41.978**	0.565
α	−4.200	0.052	**−80.451**	0.506
E_t	2.666	0.111	**23.993**	0.061
G_{apb}	0.274	0.010	**26.441**	0.055
G_{apc}	0.099	0.011	**9.246**	0.020
$T * E_t$	−1.530	0.097	**−15.807**	
$T * G_{apc}$	−0.152	0.009	**−16.145**	

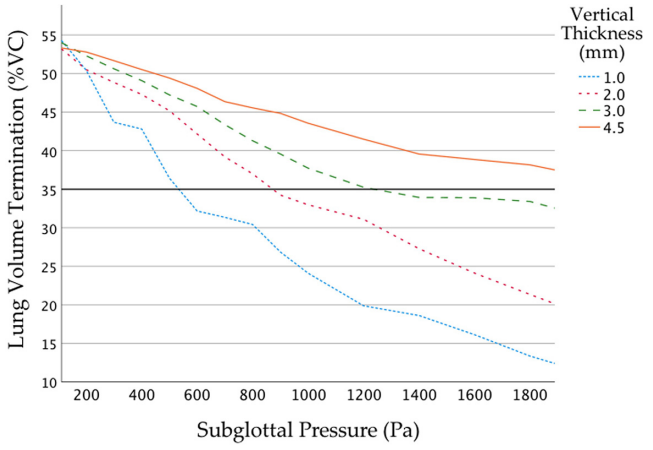

FIG. 3. (Color online) The observed LVT means (in percent of VC) for each vertical thickness value for a LVI set at 55% of VC and a BGD of 4 s. The line in bold at LVT = 35% indicates the REL typical in spontaneous speech.

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(4.5 mm) led to a mean LVT above the typical REL at 35% of VC[31] when the subglottal pressure value exceeded 1200 Pa (Fig. 3).

Table V shows the multilinear regression results for low subglottal pressures (200–600 Pa). The regression coefficients were all reduced when compared to normal and high subglottal pressure conditions, indicating that the rate of airflow expenditure is slower at a low subglottal pressure, as expected. This was manifested by the much higher intercept (52.23) when compared to high subglottal pressure conditions (40.11). Of note is also the relative contribution of the initial glottal angle to the model, which was greater at low subglottal pressures when compared to conditions of high and medium subglottal pressures, as shown by an associated change in R^2 of 0.582. This signifies that at low subglottal pressures, the variation in the initial glottal angle by itself accounts for almost 60% of the variance in LVT. On the other hand, the contribution of vertical thickness was greatly reduced when compared to higher subglottal pressure conditions and those of longitudinal and transverse stiffnesses were minimal. In fact, longitudinal and transverse stiffnesses exhibited behaviors similar to those of the vertical thickness (Fig. 3) in terms of their reduced impact on LVT at low subglottal pressures. Nonetheless, as was also the case with conditions of medium and high subglottal pressures, interaction effects were noted between vertical thickness and transverse and longitudinal stiffnesses, indicating that vocal fold thickness has a greater effect on LVT when the vocal folds are softer.

The different combinations of initial glottal angle, subglottal pressure, and vertical thickness and their resulting effects on LVT are further illustrated in Fig. 4(A). Figure 4(A) shows the combinations for which a speaker would be able to complete a 4-s utterance without running out of air (LVT ≅ 0% VC) as well as the resulting LVT. Figure 4(B) displays the maximum expiratory pressures associated with each condition. It is important to note that although some conditions may make an utterance theoretically achievable, those leading to a LVT below the REL (≅35% VC) require high expiratory effort and are, thus, undesirable. Figure 4 illustrates that it is possible to avoid such situations by modifying one or more of the parameters to minimize the airflow loss (i.e., by decreasing the subglottal pressure, increasing vertical thickness, and/or reducing initial glottal angle) and, therefore, increase LVT and reduce the maximum expiratory pressure. Figure 4 also shows that the effect of the vertical thickness became more dominant at high subglottal pressures.

TABLE V. Regression coefficients and the change in R^2 when adding a predictor and its associated interaction effects to the otherwise complete model for conditions of low subglottal pressure (LVI = 55% of VC; BGD = 4 s; P_s = 200–600 Pa). Predictors include the initial glottal angle (α), vertical thickness (T), longitudinal body and cover stiffness (G_{apb} and G_{apc}, respectively), transverse stiffness (E_t), as well as the relevant interactions indicated by an asterisk. In bold, the p-value is significant at $p \leq 0.001$. The adjusted R^2 for the model = 0.839.

	Regression coefficient	Standard error	T	Change in R^2
(Intercept)	52.234	0.174	**299.388**	
α	−3.147	0.033	**−95.157**	0.582
T	1.834	0.162	**11.320**	0.171
E_t	0.419	0.071	**5.885**	0.009
G_{apb}	0.063	0.006	**10.909**	0.008
G_{apc}	−0.007	0.006	−1.190	0.006
$T * E_t$	−0.661	0.064	**−10.276**	
$T * G_{apc}$	−0.054	0.005	**−9.781**	

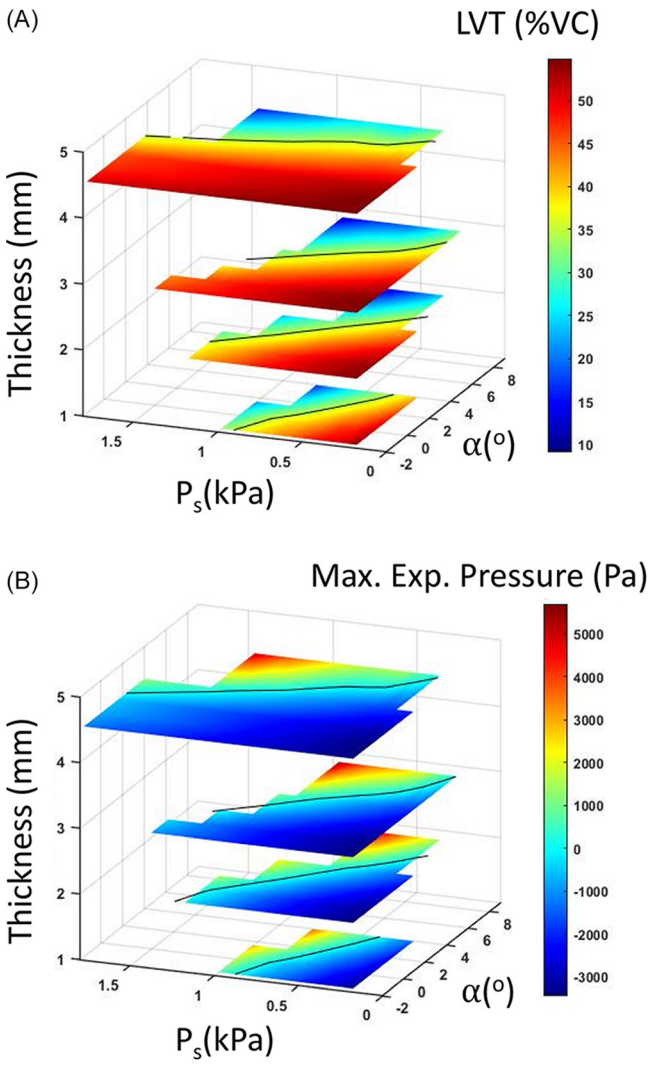

FIG. 4. (Color online) The LVT (in % of VC) (A) and maximum expiratory pressure (in Pa) (B) as a function of the vertical thickness (T), initial glottal angle (α), and subglottal pressure (P_s), averaged over all possible values of the remaining predictors, for a LVI set at 55% of VC and BGD of 4 s. The regions without data indicate conditions in which phonation cannot be sustained for the target BGD and subglottal pressure. The typical REL in spontaneous speech at 35% of VC is indicated by a black line.

C. Effect of LVI

Tables VI and VII show the results for conditions of high LVI (75% of VC) and low LVI (35% of VC) for a BGD of 4 s and normal subglottal pressures between 800 and 1200 Pa. The regression models for LVI =75% of VC and LVI = 35% of VC explained 87.4% and 80.5% of the

TABLE VI. Regression coefficients and the change in R^2 when adding a predictor and its associated interaction effects to the otherwise complete model for conditions of high LVI (=75% of VC; BGD = 4 s, P_s = 800–1200 Pa). Predictors include the initial glottal angle (α), vertical thickness (T), longitudinal body and cover stiffness (G_{apb} and G_{apc}, respectively), transverse stiffness (E_t), as well as the relevant interactions indicated by an asterisk. In bold, the p-value is significant at $p \leq 0.001$. The adjusted R^2 for the model 0.874.

	Regression coefficient	Standard error	t	Change in R^2
(Intercept)	67.089	0.210	**318.944**	
α	−4.112	0.034	**−120.784**	0.525
T	5.137	0.180	**28.510**	0.340
E_t	1.517	0.089	**16.977**	0.030
G_{apb}	0.183	0.008	**23.753**	0.020
G_{apc}	0.056	0.008	**6.816**	0.015
$T * E_t$	−1.569	0.074	**−21.088**	
$T * G_{apc}$	−0.132	0.007	**−19.037**	

variance in LVT, respectively. The relative importance of the predictors in terms of how much of their variance is correlated with the variance in LVT was similar for the low and high LVI conditions. However, the change in R^2 associated with adding the vertical thickness, transverse stiffness, and longitudinal body stiffness to the model were increased at low LVI when compared to high LVI by 39%, 56%, and 100%, respectively. The increase in R^2 associated with the initial glottal angle was trivial (2%), and no change was noted for cover stiffness.

R^2 is influenced by the range of possible values that the predictors can take as well as their different possible combinations. As a consequence, although similar rates of airflow expenditure are expected at both LVI conditions (for a given subglottal pressure and laryngeal configuration), the range of possible predictor combinations is likely to differ and induce discrepancies in their relative contributions to the variance in LVT. To demonstrate this point, Fig. 5 deconstructs the relationship between the initial glottal angle and vertical thickness and how it was impacted by LVI. It shows the mean vertical thickness as a function of the initial glottal angle. Because the mean vertical thickness was averaged over all conditions that resulted in sustained phonation for a given BGD, the relationship shown in Fig. 5 illustrates the necessary adjustments in vertical thickness in response to changes in the initial glottal angle to sustain phonation for a target utterance. An initial glottal angle of 1.6° required a greater mean vertical thickness when compared to no glottal gap in both LVI conditions. The high phonation threshold pressure and greater air loss resulting from the combination of a glottal gap and thin vocal folds reduced the number of conditions possible for a low vertical thickness, thus explaining the increased mean thickness with an initial glottal angle greater than 0°. As the initial glottal angle increased, a further increase in the vertical thickness was necessary for LVI = 35% of VC to maintain sufficient airflow during the whole BGD [Fig. 5(A)]. No further increase was observed for LVI = 75% of VC: BGD could be achieved without running out of air even with thinner folds [Fig. 5(b)]. Finally, note that the slightly higher mean vertical thickness observed at α= –1.6° for both LVI conditions could be explained by the possibility of phonating with a large vertical thickness and soft cover at low subglottal pressures when the folds are compressed such as in the case of vocal fry.

TABLE VII. Regression coefficients and the change in R^2 when adding a predictor and its associated interaction effects to the otherwise complete model for conditions of low LVI (=35% of VC; BGD = 4 s, P_s = 800–1200 Pa). Predictors include the initial glottal angle (α), vertical thickness (T), longitudinal body and cover stiffness (G_{apb} and G_{apc}, respectively), transverse stiffness (E_t), as well as the relevant interactions indicated by an asterisk. In bold, the p-value is significant at $p \leq 0.001$. The adjusted R^2 for the model = 0.805.

	Regression coefficient	Standard error	t	Change in R^2
(Intercept)	27.016	0.157	**172.308**	
α	−3.243	0.037	**−88.408**	0.536
T	4.436	0.136	**32.644**	0.474
E_t	1.319	0.067	**19.642**	0.047
G_{apb}	0.149	0.006	**24.253**	0.040
G_{apc}	0.029	0.007	**4.418**	0.015
$T*E_t$	−0.966	0.058	**−16.655**	
$T*G_{apc}$	−0.082	0.006	**−14.327**	

D. Effect of BGD

Table VIII displays the results for the conditions of long BGD and normal LVI and subglottal pressures (6.5 s; 55% of VC; P_s between 800 and 1200 Pa). Note that the resulting model was highly similar to the model for low LVI conditions (Table VII) in terms of the R^2 associated with each predictor.

The similarity of the models for long BGD and low LVI conditions is not surprising: in both cases, the conditions leading to greater airflow expenditure (specifically to an LVT below 0% of VC) were excluded from the analysis because they did not allow for completion of the utterance given the respiratory constraints. As explained previously, the exclusion of specific combinations of predictors impacts the regression model and R^2 associated with each predictor. As a result, the relationship between the vertical thickness and initial glottal angle depicted in Fig. 5(A)—showing an increase in the mean vertical thickness as the initial glottal angle increases—was also true for conditions of long BGD. Despite these similarities, the models for long BGD and low LVI differed in terms of the regression coefficients: as expected, coefficients were larger for the long BGD conditions, and the increase was generally proportional to the increase in BGD (from 4 to 6.5 s). For example, a change from thin vocal folds (T = 1 mm) to thick vocal folds (T = 4.5 mm) would allow a speaker to preserve approximately 16% of their VC during a 6.5-s utterance compared to approximately 25% of VC during a 4-s utterance (all other

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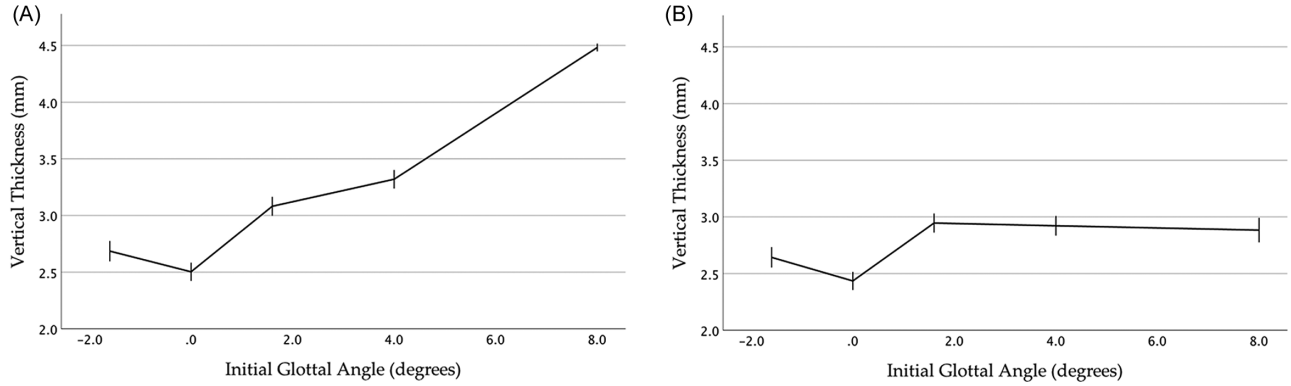

FIG. 5. The mean vertical thickness (T) by the initial glottal angle (α) for a BGD of 4 s and subglottal pressure between 800 and 1200 Pa at LVI = 35% of VC (A) and LVI = 75% of VC (B). The error bars indicate 95% confidence intervals.

predictors being held constant at typical values for speech). This proportionality speaks to the steadiness of the airflow rate for a given set of subglottal pressures and laryngeal parameters, regardless of LVI and BGD.

IV. DISCUSSION

A. Implications for normal voice production

In this computational modeling study, we assessed the contribution of specific laryngeal postures on LVT during phonation and how these relationships are modulated by changes in respiratory parameters. We found that respiratory conditions impact the relationships between laryngeal parameters and LVT in two main ways, either by affecting (1) the airflow rate for a given set of laryngeal parameters, or (2) the range of possible laryngeal condition combinations (i.e., those allowing for completion of the target utterance) for a given set of respiratory conditions.

The first case applies only to the subglottal pressure as it was the only respiratory condition in our study modulating the airflow rate for a given laryngeal configuration. A notable finding was that as the subglottal pressure increased, the effect of the vertical thickness on LVT also increased, considerably limiting the impact of the subglottal pressure on LVT. This suggests that as a speaker raises intensity via increased subglottal pressure, a simultaneous increase in the vocal fold thickness is a probable and effective mechanism to limit the airflow expenditure. By doing so, the speaker slows down the rate of decline in lung volume and can, thus, rely on greater natural expiratory pressures for longer durations.[7] This result is consistent with the finding that laryngeal resistance increases as the intensity increases in human subjects, leading to a stable glottal airflow.[32] It is also consistent with previous computational modeling findings showing that the effect of vocal fold bulging on the glottal flow resistance is amplified at high lung volume pressures.[33] Although increasing vertical thickness also participates in preserving lung volume at lower subglottal pressures, the effect on LVT is not as marked.

TABLE VIII. Regression coefficients and the change in R^2 when adding a predictor and its associated interaction effects to the otherwise complete model for conditions of long BGD (LVI = 55% of VC; BGD = 6.5 s, P_s = 800–1200 Pa). Predictors include the initial glottal angle (α), vertical thickness (T), longitudinal body and cover stiffness (G_{apb} and G_{apc}, respectively), transverse stiffness (E_t), as well as the relevant interactions indicated by an asterisk. In bold, the p-value is significant at $p \leq 0.001$. The adjusted R^2 for the model = 0.801.

	Regression coefficient	Standard error	t	Change in R^2
(Intercept)	42.020	0.251	**167.346**	
α	−5.176	0.060	**−86.453**	0.530
T	7.128	0.218	**32.715**	0.480
E_t	2.090	0.108	**19.412**	0.047
G_{apb}	0.237	0.010	**24.077**	0.041
G_{apc}	0.043	0.011	**4.079**	0.014
$T * E_t$	−1.528	0.093	**−16.397**	
$T * G_{apc}$	−0.128	0.009	**−13.777**	

The interaction effects between thickness and transverse stiffness and between thickness and longitudinal stiffness of the cover layer revealed that the impact of thickness on LVT was reduced as the stiffness increased and, therefore, stiffening the vocal folds allows to thin them while preserving the lung volume. This speaks to the airflow conservation role of vocal fold stiffness during phonation, which is consistent with findings from recent computational studies reporting a reduction in the mean glottal airflow with increasing vocal fold stiffness: using a three-dimensional continuum model of the vocal folds and a glottal flow model, Wang *et al*. found a decrease in the average flow rate with increasing transverse and longitudinal stiffnesses (for a constant subglottal pressure) in all vocal fold three layers, especially in the vocal ligament.[34] Similar results regarding longitudinal stiffness were found by Zhang in a previous study.[15] In our study, the role of the stiffness variation (transverse and longitudinal) in predicting the variance in LVT was especially important at high subglottal pressures, which corroborates results from a previous computational study.[4] Together, findings suggest that speakers can use different combinations of vertical thickness and stiffness to achieve a similar airflow rate and resulting LVT with all other respiratory and laryngeal parameters being kept

constant. Because both vertical thickness and stiffness are controlled primarily by the activation of the thyroarytenoid (TA) and cricoarytenoid muscles,[35,36] coordination between the activity of these muscles directly impacts the airflow conservation during phonation. To that effect, it is important to note that increasing the longitudinal stiffness through vocal fold elongation also affects the transverse stiffness (through a cross-axis coupling effect) and, therefore, both transverse and longitudinal stiffnesses can be modulated via laryngeal muscular control.[36]

Regarding the initial glottal angle, it was the main predictor of LVT in all of the respiratory conditions except for high subglottal pressures. This means that adduction of the vocal folds in terms of approximation of the arytenoids as controlled primarily by the lateral cricoarytenoid (LCA) and interarytenoid muscles[37] is a predominant laryngeal strategy for airflow conservation. The contribution of initial glottal angle to the variance in LVT was the largest at low subglottal pressure conditions when the vertical thickness' contribution was the lowest, and it was the lowest at high subglottal pressure conditions when the vertical thickness' contribution was the highest. This relationship speaks to the shared contributions of adduction and medial bulging of the vocal folds in controlling airflow during speech. These findings have implications for the pathophysiology and treatment of hyperfunctional voice disorders as discussed in Sec. IV B.

B. Implications for the pathophysiology of hyperfunctional voice disorders

There are reports in the literature suggesting that a disruption in speech breathing may contribute to the pathophysiology of phonotraumatic and nonphonotraumatic hyperfunctional voice disorders, specifically vocal fold nodules and related lesions and primary muscle tension dysphonia (MTD-1).[12,13,38] One of the aims of this study was to investigate whether the need for airflow conservation and reduction of respiratory effort could justify the use of laryngeal mechanisms potentially leading to a voice disorder.

1. PVH

Hyperadduction of the vocal folds leads to increased contact pressure and is thought to be associated with the formation of phonotraumatic lesions.[17] In "normal" phonation conditions as modeled in this study and with a LVI of 55% of VC, airflow conservation does not justify hyperadduction of the vocal folds: BGD would end at or above the resting lung volume even with vocal folds barely abducted/adducted. When the subglottal pressure is increased, LVI is reduced and/or BGD is increased, the necessity for increasing glottal resistance is heightened, driven by the need for airflow and respiratory effort conservation. These considerations are relevant to patients with vocal fold nodules who tend to end utterances at lower lung volumes when compared to healthy speakers—likely due to deficient laryngeal valving and, consequently, a large lung volume expenditure per syllable.[10,11] Whereas reducing the subglottal pressure would be the most effective way to slow down lung volume expenditure and preserve airflow (in addition to reducing contact pressure[39]), this strategy is counterproductive when trying to achieve a target sound pressure level (SPL)—that is, unless source-tract interactions can be improved to increase loudness while reducing subglottal pressure as is the goal in certain voice exercises.[40] Considering that patients with PVH already need to achieve greater subglottal pressures to meet a target SPL,[41] they might tend to rely on laryngeal strategies for airflow and respiratory effort conservation. The laryngeal strategy generally found to have the largest influence on LVT was the initial glottal angle: reducing the distance between the vocal processes of the arytenoids—a mechanism that is associated with a pressed voice[42]—was shown to significantly increase LVT in all of the respiratory conditions. Note that the effect of adduction on LVT is likely to be limited in the presence of vocal fold nodules, although speakers may continue to use this strategy out of habit. However, under the condition of vocal fold nodules, increasing the vertical thickness may become the primary mechanism to conserve airflow during speech, as described next.

Analyses indicated that the effect of the vertical thickness on LVT was amplified at high subglottal pressures. These results are particularly interesting in the context of recent findings:[39] using the same three-dimensional vocal fold model coupled with a vocal tract model, Zhang found that the vertical thickness was the best predictor for contact pressure at a high target SPL with an increase in thickness being associated with greater contact pressures likely because of greater subglottal pressure requirements.[39] Therefore, increasing the thickness to control airflow at high subglottal pressures could also be involved in the vicious circle of PVH. In fact, it has been suggested that patients with PVH increase their subglottal pressure to regain normal vocal quality and loudness, leaving them at risk of chronic benign lesions because of the increased maximum flow declination rate (MFDR), amplitude of the modulated flow component (AC-flow), and contact pressures.[41,43,44] A greater vertical thickness of the vocal folds could help compensate for the air loss from phonating at high subglottal pressures by modulating the impact of the subglottal pressure on LVT but at the cost of increased contact pressures. It is possible that patients with vocal fold nodules are increasing the vertical thickness simultaneously to the adduction of the arytenoids when trying to preserve the airflow, synchronizing a pattern of movements with the common goal of restraining the glottal opening and airflow escape. This would be consistent with the simultaneous activity of the TA and LCA muscles[39] and the increase in the glottal flow resistance associated with the resultant vocal fold bulging.[33] However, because of the methodological challenges involved in measuring the vertical thickness in human subjects, not much is known regarding the role of this parameter in the pathophysiology of PVH, and further experimental or computational studies would be required.

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2. NPVH

Findings with regard to vertical thickness also provide insights into the pathophysiology of NPVH, which is the etiological mechanism leading to MTD-1.[9] One of the hallmarks of some forms of MTD-1 is an incomplete adduction of the vocal folds, manifesting as a posterior glottal gap caused by a hypertonic posterior cricoarytenoid (PCA) muscle.[45] The results from our study showed that a positive initial glottal angle promotes an increase in vertical thickness to allow for completion of a whole BGD. Increasing vertical thickness involves the activation of the TA muscle and resulting inferomedial bulging of the membranous vocal folds[35] and is consistent with clinical manifestations of MTD-1, such as a reduced pitch range and a difficulty transiting between registers (from a TA-dominant to a cricothyroid-dominant posturing).[45,46] Whereas inferomedial bulging of the membranous vocal folds combined with superior bulging induced by the LCA muscles is necessary to achieve a rectangular glottal shape[35] and lower phonation threshold pressure,[47] excessive bulging can, on the other hand, increase the phonation threshold pressure and provoke irregular vibration patterns.[48] Bulging of the vocal folds is also associated with a greater closed quotient.[48] However, because patients with MTD-1 do not demonstrate abnormal increases in MFDR and AC-flow for a given SPL as do patients with PVH,[41] an increase in the vertical thickness is less likely to be associated with increased contact pressures.

The relationship between vertical thickness and initial glottal angle was even more pronounced at low LVI: as glottal angle increased, only conditions of larger vertical thickness were possible to finish the desired BGD. These observations are consistent with reports of patients with vocal fatigue (without lesions) speaking at low lung volumes[12] who could be experiencing fatigue because of increased TA activation. On the other hand, some patients with MTD-1 present with longer inspiration time, potentially associated with a greater LVI.[13] *A priori*, a high LVI would not be expected to require nor promote an increase in the glottal resistance because of the reduced risk of running out of air. Although the necessity for airflow conservation is not a concern, controlling subglottal pressure at higher lung volumes requires a sustained engagement of the inspiratory muscles, which, in turn, has an effect on the laryngeal posturing. The biomechanical coupling between the larynx and diaphragm induces an abducted vocal fold geometry (larger posterior glottal gap) when phonating at high lung volumes as compared to low lung volumes.[49,50] This abducted geometry is susceptible to triggering an increase in the vertical thickness of the vocal folds as shown by our results.

C. Implications for voice therapy

One of the main goals of voice therapy for hyperfunctional voice disorders is to establish a "resonant voice"—an easy voice produced with perceptible anterior oral vibrations[51]—generally achieved with barely adducted/abducted vocal folds.[18] In addition to modifying adduction (in terms of distance between the vocal processes of the arytenoids), resonant voice therapy may also act on the vocal fold thickness by reducing unwarranted TA and LCA activity.[39] Directly targeting laryngeal activity through voice therapy could also force the respiratory system to adapt should there be a disruption in speech breathing. For example, a speaker who speaks at low LVI and uses hyperadduction to conserve airflow may readjust their breathing pattern once adduction is rebalanced by increasing LVI or reducing the subglottal pressure or BGD.

However, *some patients might find it challenging to modify laryngeal posturing if disrupted respiratory parameters are not directly targeted during speech tasks*. Importantly, a low LVI, long BGD, and/or high subglottal pressure are likely to hinder the achievement of the resonant voice because of the airflow and respiratory effort conservation role played by the larynx. Additionally, the interaction observed between the subglottal pressure and vertical thickness indicates that lowering the subglottal pressure could prevent the increase in vertical thickness as a strategy to control airflow loss. This points to the relevance of reducing loudness during voice therapy until the vocal fold posturing is adjusted, prior to gradually increasing the SPL for functional needs. Further corroborating the relevance of gradually increasing the loudness, a study on canine larynges showed that an increase in SPL at a constant *F*0 as in *messa di voce*—a voice exercise involving a crescendo and decrescendo on a sustained vowel while maintaining a constant pitch[52,53]—required a decreased TA activation.[54] The concept of *messa di voce* is already present in some therapy programs such as the Lessac-Madsen Resonant Voice Therapy (LMRVT).[55] Maintaining a low thickness as the loudness increases is an economical mechanism because it allows for the attainment of the target SPL with minimal subglottal pressure, thus, minimizing contact pressures between the vocal folds.[39] In addition, because higher fundamental frequencies are primarily controlled by the cricothyroid muscles,[54] avoiding a reliance on strong TA activation to control airflow expenditure would likely facilitate the transition from low to high pitch (from TA-dominant to CT-dominant posturing) and, consequently, favor a smooth transition between registers.

Results from the present study suggest that therapies targeting lung volume may produce changes in laryngeal activity and be promising for patients with different types of VH. Preliminary evidence for the efficacy of targeting lung volumes has been demonstrated in patients with MTD-1 for whom voice and respiratory outcomes were improved following respiratory lung volume-based training.[38] Importantly, further clinical research is needed to understand how respiratory-laryngeal interactions can be targeted to improve the voice in patients with VH and other types of voice disorders.

D. Limitations and considerations for future studies

Computational modeling renders possible the study of parameters that could not be easily assessed in human

subjects, but they also present with limitations related to ecological validity. Importantly, mechanical and muscular couplings of the respiratory and laryngeal systems were not modeled in the simulations described here. Therefore, although the results provide information on how different laryngeal and respiratory parameters impact lung volume expenditure, the likelihood of those combinations occurring based on such mechanical or muscular couplings was not represented in the model. For example, the probability of a large initial glottal angle may be higher at high LVI because of the effect of the tracheal pull (the trachea exerting a downward force on the larynx as the diaphragm lowers during inspiration).[49,56] Moreover, the relationship between LVI and subglottal pressure was not represented in the findings because these two respiratory parameters were controlled independently in the simulations. Although LVI in itself does not impact airflow rate when subglottal pressure is being controlled for, it has a direct impact on the natural recoil of the lungs and, consequently, on the pulmonary pressure.

The type of phonation modeled in the simulations—sustained phonation—is also a limitation in terms of ecological validity. For a given set of respiratory and laryngeal conditions, LVT would be lower after a bout of speech production—containing voiced and voiceless portions—when compared to a sustained voiced segment of similar duration. Nonetheless, findings from the present study are applicable to a variety of voice exercises based on sustained vowels. One of the most common programs focused on sustained phonation is vocal function exercises (VFE)[57] in which patients are instructed to sustain facilitating vowels for as long as possible. Future computational modeling studies should explore the impact of laryngeal configurations on LVT in connected speech.

In the present simulations, glottic insufficiency was modeled as a given initial glottal angle (anterior), regulating the distance between the vocal processes of the arytenoids. This geometry is a gross representation of a posterior glottal gap but does not simulate the hourglass-shaped gap observed in patients with vocal fold nodules, which can occur regardless of the level of adduction of the vocal processes. The efficiency of different laryngeal configurations in controlling lung volume outflow in the presence of vocal fold nodules remains to be tested to further investigate airflow conservation in PVH.

Last, the vocal tract was not included in this study and, therefore, source-tract interactions were not considered. This limitation does not impact the outcomes of the present experiment, which focused on the efficacy of different laryngeal mechanisms to control LVT. However, a future study assessing the impact of these respiratory-laryngeal interactions on voice output (including acoustic and voice efficiency outcomes) should consider the modulating effect of the vocal tract.

V. CONCLUSION

Findings from this study provide preliminary evidence to support the hypothesis that an inadequate LVI, long BGD, or high subglottal pressure can promote laryngeal configurations consistent with VH. Specifically, requirements for airflow and respiratory effort conservation may trigger increased vocal fold adduction and/or vertical thickness, especially in conditions of low LVI, long BGD, and high subglottal pressure. Future studies should explore these relationships in the context of specific phonation goals (*F*0 and SPL) as well as in the context of patient-specific characteristics such as altered respiratory function and/or vocal fold viscoelastic properties due to disease processes or aging.

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