



## **Estimation of Subglottal Pressure, Vocal Fold Collision Pressure, and** Intrinsic Laryngeal Muscle Activation From Neck-Surface Vibration Using a **Neural Network Framework and a** Voice Production Model

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The ambulatory assessment of vocal function can be significantly enhanced by having access to physiologically based features that describe underlying pathophysiological mechanisms in individuals with voice disorders. This type of enhancement can improve methods for the prevention, diagnosis, and treatment of behaviorally based voice disorders. Unfortunately, the direct measurement of important vocal features such as subglottal pressure, vocal fold collision pressure, and laryngeal muscle activation is impractical in laboratory and ambulatory settings. In this study, we introduce a method to estimate these features during phonation from a neck-surface vibration signal through a framework that integrates a physiologically relevant model of voice production and machine learning tools. The signal from a neck-surface accelerometer is first processed using subglottal impedance-based inverse filtering to yield an estimate of the unsteady glottal airflow. Seven aerodynamic and acoustic features are extracted from the neck surface accelerometer and an optional microphone signal. A neural network architecture is selected to provide a mapping between the seven input features and subglottal pressure, vocal fold collision pressure, and cricothyroid and thyroarytenoid muscle activation. This non-linear mapping is trained solely with 13,000 Monte Carlo simulations of a voice production model that utilizes a symmetric triangular body-cover model of the vocal folds. The performance of the method was compared against laboratory data from synchronous recordings of oral airflow, intraoral pressure, microphone, and neck-surface vibration in 79 vocally healthy female participants uttering consecutive /pæ/ syllable strings at comfortable, loud, and soft levels. The mean absolute error and root-mean-square error for estimating the mean subglottal pressure were 191 Pa  $(1.95 \text{ cm H}_2\text{O})$  and 243 Pa (2.48 cm H<sub>2</sub>O), respectively, which are comparable with previous studies but with the key advantage of not requiring subject-specific training

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and yielding more output measures. The validation of vocal fold collision pressure and laryngeal muscle activation was performed with synthetic values as reference. These initial results provide valuable insight for further vocal fold model refinement and constitute a proof of concept that the proposed machine learning method is a feasible option for providing physiologically relevant measures for laboratory and ambulatory assessment of vocal function.

Keywords: ambulatory monitoring, neck-surface accelerometer, subglottal pressure estimation, voice production model, neural networks, clinical voice assessment

#### **1. INTRODUCTION**

Laryngeal voice disorders have been estimated to affect approximately 30% of the adult population in the United States at some point in their lives (Bhattacharyya, 2014). Voice disorders can disrupt or preclude normal oral communication and thus have far-reaching social, professional, economic, and personal consequences for those affected. The most common voice disorders are associated with detrimental patterns of daily vocal behavior and voice use (often classified as vocal hyperfunction) for which there is limited understanding of the underlying etiological and pathophysiological mechanisms. The paucity of such information serves to hinder the effective prevention, diagnosis and treatment of these common voice disorders.

Ambulatory voice monitoring using a neck-placed accelerometer (ACC) provides the capability to quantitatively assess daily vocal function and has also been shown to have the potential to assist in modifying vocal behaviors via ambulatory biofeedback (Popolo et al., 2005; Hillman and Mehta, 2011; Mehta et al., 2012; Andreassen et al., 2017; Van Stan et al., 2017a). Numerous features have been extracted from the ambulatory recording of the ACC signal, including phonation duration, sound pressure level (SPL), fundamental frequency  $(f_o)$  (Ghassemi et al., 2014), vocal vibration-dose measures (Titze et al., 2003; Titze and Hunter, 2015), spectral and cepstral measures (Mehta et al., 2015, 2019), and aerodynamic measures (Llico et al., 2015; Cortés et al., 2018). These measures have been used to differentiate the daily voice use of patients with vocal hyperfunction from matched controls (Ghassemi et al., 2014; Cortés et al., 2018; Van Stan et al., 2021) and to track changes related to surgical and voice therapy treatment of hyperfunctional voice disorders (Van Stan et al., 2017b, 2020). Current classification accuracy using these parameters is in the range of 0.7-0.85.

We argue that the extraction of additional physiological measures from ambulatory ACC recordings, such as subglottal pressure, vocal fold collision pressure, and laryngeal muscle activation, would provide critical additional insights into the etiologic and pathophysiological mechanisms that underlie hyperfunctional voice disorders and thus significantly enhance the capability to identify the detrimental daily patterns of vocal behavior associated with these disorders (Espinoza et al., 2017; Galindo et al., 2017; Hillman et al., 2020). There have been recent efforts to develop subject-specific representations that can capture such physiologically relevant measures (e.g.,

subglottal pressure, contact pressure, muscle activation, and material properties of the vocal folds) that are difficult to obtain directly (Deng et al., 2019; Hadwin et al., 2019; Alzamendi et al., 2020; Drioli and Foresti, 2020). These approaches take advantage of the physiological relevance of lumped and finite element models of voice production, which have been shown to be useful tools for the investigation, diagnosis, and treatment of voice disorders (Erath et al., 2013). The most recent *in vivo* approach uses a Bayesian framework to estimate lumped-element vocal fold model parameters to predict subglottal pressure, vocal fold collision pressure, and laryngeal muscle activation along with their corresponding confidence intervals from observations obtained in clinical recordings, i.e., high-speed videoendoscopy (HSV) and oral airflow (Alzamendi et al., 2020).

Direct application of Bayesian subject-specific estimation from the ACC signal remains unsolved. There are challenges associated with the current extended Kalman filter approach for processing ambulatory data and using the ACC as the solely observation that remain to be addressed, including the large computational cost for the volume of data to be processed, the need for data fusion from different recording sessions, the need for an online estimation of model covariance, and the incorporation of a time-domain neck skin model for the ACC sensor within the voice production model.

On the other hand, machine learning and artificial intelligence are becoming relevant tools in biomedical engineering, as they can provide accurate predictions and efficient implementations. Numerical models are attractive alternatives for training purposes, suitable representing a significant range of conditions and providing access to relevant measures that are difficult to obtain experimentally. Voice assessment is starting to make use of these modeling advantages, where machine learning methods have been trained using simulated data from physiological numerical models to predict clinical parameters of interest. This approach was utilized by Gómez et al. (2019) to predict subglottal pressure from HSV in excised porcine vocal folds and by Zhang (2020) to predict vocal fold (geometric and mechanical) properties and subglottal pressure from a microphone signal. No machine learning method trained with a voice production model has been devised for the ACC signal in a laboratory or ambulatory context.

Although there are ongoing efforts to address the challenges of the Bayesian framework for the ambulatory monitoring, we propose in this study a more direct solution for the estimation of ambulatory physiologically-based features from

the ACC that uses machine learning and voice modeling tools. Thus, we propose a method to obtain a non-linear optimal mapping between ACC features and subglottal pressure, vocal fold collision pressure, and laryngeal muscle activation. We propose using the impedance based inverse filtering (IBIF) algorithm (Zañartu et al., 2013; Cortés et al., 2018), which yields an unsteady glottal airflow signal from the ACC signal, to provide aerodynamic features that are used as inputs to the non-linear mapping. At the same time, we propose using a neural network (NN) regression architecture trained from a physiologically relevant muscle-controlled voice synthesizer with a triangular body-cover vocal fold model (Alzamendi et al., 2019, 2021) that takes the aerodynamic features as input and provides subglottal pressure, collision pressure, and laryngeal muscle activation as output. Predictions obtained with this scheme are validated against numerical simulations and laboratory measurements of subglottal pressure. The contributions of this work are twofold: First, the proposed scheme provides access, for the first time, to various physiologically relevant model-based features from a neck-surface accelerometer signal. Then, the approach provides a comprehensive contrast of the selected voice production model against laboratory data.

#### 2. MATERIALS AND METHODS

Figure 1 provides an overall schematic of the proposed method of estimating four vocal function measures from neck-surface vibration recorded using a neck-surface accelerometer (ACC) sensor. The first analysis block results in an estimate of the unsteady glottal airflow volume velocity signal using the IBIF model (Zañartu et al., 2013), which has been shown to provide aerodynamic features reliably for the classification of vocal hyperfunction in laboratory (Espinoza et al., 2020) and ambulatory (Cortés et al., 2018) settings. The second analysis block computes the following six features from the glottal airflow signal: amplitude of the unsteady glottal airflow (ACFL), maximum flow declination rate (MFDR), open quotient (OQ), speed quotient (SQ), spectral tilt measured as the log-magnitude difference between the first and second harmonics  $(H_1 - H_2)$ , and fundamental frequency  $(f_o)$ . A seventh feature—the sound pressure level (SPL)-can be estimated either directly using an acoustic microphone (MIC) in the laboratory setting or using a log-log mapping between the root-mean-square magnitude of the ACC signal and SPL (Švec et al., 2005). See Table 1 for descriptions of each feature. These seven features are used as input into a NN to estimate four desirable measures of vocal function: subglottal pressure  $(P_s)$ , vocal fold collision pressure  $(P_c)$ , and normalized activation levels of the cricothyroid  $(a_{CT})$ and thyroarytenoid  $(a_{TA})$  muscles.

The NN was trained using 13,000 Monte Carlo simulations of a numerical voice production model. The design of the network architecture and overall training description are provided in section 2.1, and the details of the numerical voice production model are found in section 2.2. Validation of the estimated output features were performed using *in vivo* laboratory reference measures of  $P_s$  or numerical simulations of phonation for reference measures of  $P_c$ ,  $a_{CT}$ , and  $a_{TA}$ . Details of the experimental validation are provided in section 2.3.

# 2.1. Neural Network Architecture and Training

A supervised machine learning framework for regression was implemented based on a multi-layer NN (Hagan et al., 2014). The network consisted of an input layer of the seven aerodynamic and acoustic features (ACFL, MFDR, OQ, SQ,  $H_1 - H_2$ ,  $f_o$ , and SPL), an output layer composed of the four target vocal function measures ( $P_s$ ,  $P_c$ ,  $a_{TA}$ , and  $a_{CT}$ ), and two interconnected hidden layers with a 10% dropout to avoid overfitting. Each neuron within the hidden layers had adjustable weight and bias parameters that combined with the outputs of the preceding layer to activate a rectified linear unit activation function; then, the resulting activation served as input for the next layer Bianco et al. (2019). The number of neurons for each layer was investigated as a function of the model performance against both numerical and experimental data. The training stage updates the weights and biases using the Adam optimization algorithm (Kingma and Ba, 2017) with a learning rate of 0.001. All the NNs involved in this work were implemented in a virtual machine from Google Colaboratory with two CPU models Intel(R) Xeon(R) CPU @ 2.00GHz, using Python 3.7.11. and the TensorFlow 2.5.0 library (Abadi et al., 2015). The runtime for the largest network (8 hidden layer with 128 neurons and 100 epoch) was less than 120 s.

The NN regression models were trained following the scheme shown in **Figure 2**. For this purpose, a synthetic voice dataset was obtained with a numerical voice production model described in section 2.2. Similar approaches were recently taken by other authors using different sensing modalities, i.e., high-speed videoendoscopy (Gómez et al., 2019) and MIC sensors (Zhang, 2020) in *ex vivo* experimental validation platforms (instead of *in vivo*). Using synthetic data for training helped addressing the lack of comprehensive and massive *in vivo* human datasets with thousands or even millions of conditions. Testing of the NN models was performed with both numerical and *in vivo* laboratory datasets. The laboratory dataset is described in section 2.3.

The voice production model described in section 2.2 was used to create 110,000 Monte Carlo simulations of sustained phonation. The simulations included a wide variation of the model control parameters such as lung pressure ( $P_L$ ), activation levels for the cricothyroid ( $a_{CT}$ ), thyroarytenoid ( $a_{TA}$ ), lateral cricoarytenoid ( $a_{LCA}$ ), interarytenoid ( $a_{IA}$ ), and posterior cricoarytenoid ( $a_{PCA}$ ) muscles. Control model parameters and their variation range are shown in **Table 2**. Each simulation lasted 800 ms, with the mean value of the seven input features taken for the last 50 ms to avoid transient artifacts. The glottal airflow was filtered using the same low- and high-pass filters utilized in the analysis of the laboratory recordings, as described in section 2.3.

As suggested by Gómez et al. (2019), the training data resembled the empirical distribution of the population-based aerodynamic and acoustic feature set. Thus, simulated data with ACFL less than 30 mL/s and  $f_o$  outside the range of 120–400 Hz were discarded, as these cases were not found in the



FIGURE 1 | A schematic of the proposed method for the ambulatory vocal assessment based on processing the neck skin acceleration signal and a regression neural network.

TABLE 1 | Description of aerodynamic features extracted from the glottal airflow signal and acoustic sound pressure level extracted from the microphone or accelerometer signal.

Feature	Description	Units
ACFL	The difference between the maximum and minimum amplitude of the AC glottal airflow (peak-to-peak) within each glottal cycle	mL/s
MFDR	Maximum flow declination rate: Negative peak of the first derivative of the glottal waveform	L/s <sup>2</sup>
OQ	Open quotient: Ratio of the open time of the glottal vibratory cycle to the corresponding cycle period. Computed as in Cortés et al. (2018)	%
SQ	Speed quotient: Ratio of the opening time of the glottis to the closing time. Computed as in Cortés et al. (2018)	_
$H_1 - H_2$	Difference between the magnitude of the first two harmonics	dB
f <sub>o</sub>	Fundamental frequency	Hz
SPL	Sound pressure level: dB from the RMS envelope of the acoustic signal	dB SPL

laboratory data used for testing the NN. As a result, the final synthetic dataset consisted of 13,000 samples. **Figure 3** shows the normalized histogram of features for the synthetic data (blue color) and laboratory data (red color).

Notice that feature ranges and distributions for both clinical and synthetic data sets agree, except for SPL and  $P_s$ , where ranges are noticeable dissimilar (see histograms for attenuated red color). Two bias corrections were considered for these components. First, as the SPL for the voice production model is obtained at the lips, the SPL value was corrected to match the 10 cm mouth-to-microphone recording distance considered in the clinical recordings, yielding a  $-28.5 \ dB$  correction factor (Švec and Granqvist, 2018). In addition, histograms of  $P_s$  suggest that the physiological voice synthesizer yields higher values for this measure. It is possible that sub and supra glottal tract propagation losses and the losses at the glottal boundary were not sufficiently high, thus amplifying source-filter interactions and raising up subglottal pressure. This bias has motivated subsequent exploration and model developments. However, to address the need to correct for the difference in  $P_s$  in this study,



Training data are produced from a numerical voice production model.

TABLE 2   Range and increment step for control parameters in the numerical
voice production model considered for building the synthetic dataset.

Parameter	Range	Step	Unit
a <sub>CT</sub>	0-1	0.1	_
<i>a</i> <sub>TA</sub>	0-1	0.1	-
a <sub>LCA</sub>	0.2-0.8	0.1	-
a <sub>PCA</sub>	0-0.1	0.1	-
a <sub>IA</sub>	0.2-0.8	0.1	-
$P_L$	500 - 2000	150	Pa

a bias correction was applied by taking the differences between the mean of clinical and synthetic  $P_s$  values, thus leading to a -3.37 cm H<sub>2</sub>O offset.

Synthetic training data were min-max normalized and selected randomly from 80% of the total simulations. Testing

was performed in the remaining 20% of synthetic data and in the clinical data in order to identify the models providing the best estimation of subglottal pressure. To assess the regression performance during both training and validation stages and to compare with prior studies (Gómez et al., 2018; Lin et al., 2020; Zhang, 2020), the mean absolute error (MAE) and the root-mean-squared error (RMSE) metrics were utilized.

Several NN architectures with different numbers of neurons in the hidden layers were trained for two cases. Case I included six glottal aerodynamic features, described in **Table 1** (ACFL, MFDR, OQ, SQ,  $f_o$ , and  $H_1 - H_2$ ) as input layer to the NNs, i.e., glottal measures extracted only from IBIF. Case II had the input layer of the NNs composed by all seven features in **Table 1**.

## 2.2. Voice Production Model

The selected voice production model for the training stage is a multi-physics scheme featuring a low-order model of the vocal



folds that allows for the coordinated activation of all five intrinsic laryngeal muscles (Alzamendi et al., 2019, 2021). The model was recently developed and was chosen due to its flexibility and physical and physiological relevant way to cover numerous (normal and disordered) phonatory conditions. The approach builds upon prior efforts that describe rules for controlling low-order models (Titze and Story, 2002), vocal fold posturing (Titze and Hunter, 2007), and a triangular body-cover vocal fold model (Galindo et al., 2017). The model also accounts for tissue-fluid-acoustic interactions at the glottis (Zañartu et al., 2014), sound wave propagation through the vocal tract followed by sound pressure radiated from mouth (Zañartu, 2006), and allows for describing sustained vowels and time-varying glottal gestures. Given that the model is fairly new, we describe its main components pertaining to the development of the NN regression model and training set.

The triangular body-cover model (TBCM) (Galindo et al., 2017) (see **Figure 2**) consists of paired three-mass bodycover systems interconnected with mechanical elements (Story and Titze, 1995) and configured in a triangular anatomical shape (Birkholz et al., 2011). Beside resembling the triangular glottis, the TBCM is physiologically relevant because it mimics the layered vocal fold structure and extends the vocal fold collision model with a gradual zipper-like incomplete glottal closure. The latter aided to describe the time-varying vocal fold collision pressure ( $P_c$ ) during phonation. Similar to Galindo et al. (2017), the parameterization of the TBCM followed the original body-cover description (Story and Titze, 1995) and applied the empirical rules to change geometrical and viscoelastic vocal fold parameters developed by Titze and Story (2002). However, the major difference with (Galindo et al., 2017) resided in the computation of both the internal tension and elongation in the vocal folds. The remaining rules in Titze and Story (2002) were taken as originally proposed for deriving the lumped-element dynamical parameters.

Given the interest in estimating intrinsic laryngeal activity with the proposed method, a comprehensive description of muscle activity on the laryngeal configuration was considered. For this purpose, the contributions of all five intrinsic muscles and the passive response of connective tissue (i.e., the vocal ligament and vocal fold mucosa) were included in the model. Hence, simulated laryngeal muscle activations were the control variables governing the phonatory posture and vocal fold elongation. The incorporation of this muscle-controlled model of the larynx allowed to dynamically modify the glottal function during phonation, e.g., the vocal fold oscillatory dynamics, time-varying glottal resistance, and aerodynamicacoustic coupling mechanisms. Following Titze and Hunter (2007), the five intrinsic muscles were modeled independently by using a modified Kelvin model (Hunter et al., 2004), which dynamically solves for the internal stress-strain response in onedimensional fibrous tissues by integrating both active and passive properties. Passive stress was described as a non-linear function of longitudinal strain. Additionally, the active stress resulted from the maximum isometric active stress and the normalized activation level, in the range  $0 \le a \le 1$ , mapping from relaxed to strong muscle tension. The simulated muscle activation for each intrinsic muscle was thus adjusted trough the corresponding activation levels { $a_{LCA}$ ,  $a_{IA}$ ,  $a_{PCA}$ ,  $a_{CT}$ ,  $a_{TA}$ }. In the TBCM, an adducted glottal configuration is critical for setting the system into self-sustained oscillations, thus requiring higher activation

of the adductory intrinsic (LCA and IA) musculature than the abductury intrinsic (PCA) musculature. For simplicity, we did not consider the effects of elevated antagonistic muscles (Alzamendi et al., 2021) and only explored a small range of PCA activation to secure self-sustained oscillations in the TBCM. This approach allowed us to reduce the number of simulations to be discarded and to optimize the computational load. Future investigations will involve further scenarios for muscle control in typical and disordered phonation. Models for the vocal ligament and vocal fold mucosa were similarly implemented, except that the active component was set to zero for these cases (Titze, 2006).

Beside controlling intrinsic muscle activation, the voice production model also allowed for the adjustment of the aerodynamic lung pressure,  $P_{I}$ . The aerodynamic forces acting over the vocal fold cover layer were then computed from the resulting subglottal pressure,  $P_s$ , and supraglottal pressure,  $P_e$ , according to Titze (2002). The three-way interaction at the glottal level between sound, flow, and vocal fold tissue was included, whereas the glottal airflow was computed from the acoustic driving pressures impinging on the glottal (membranous plus posterior portions) area following (Titze, 2006; Zañartu et al., 2014; Lucero and Schoentgen, 2015). Simulation of the timevarying acoustic wave propagation was achieved by applying the wave reflection analog scheme, where the subglottal and supraglottal tracts were modeled as a discrete concatenation of short uniform acoustic cylinders with variable cross-sectional areas. Effects due to the boundary condition at the lips was approximated by including an inertive radiation impedance, that produces the reflected pressure wave and the radiated sound wave, Pout. Losses due to viscosity, moving walls, and other losses are described by an exponential attenuation factor in the propagation through the cylindrical sections (Zañartu, 2006; Zañartu et al., 2007). Vocal tract area functions that resemble a typical male (Story, 2008) and female (Story et al., 1998) that could match the in vivo experimental data were selected, i.e., vowels /æ/ and /a, along with a representative subglottal tract (Zañartu et al., 2014).

# 2.3. Experimental Validation of NN-Estimated Subglottal Pressure

An *in vivo* laboratory dataset (Mehta et al., 2015; Espinoza et al., 2017, 2020) with synchronous recordings of intraoral pressure (IOP), oral airflow volume velocity (OVV), MIC, and ACC from vocally healthy subjects was utilized to provide a completely separate testing platform for the estimates obtained with the regression NN. This dataset was used to experimentally validate the NN estimates of subglottal pressure. Direct measurements of vocal fold collision pressure and laryngeal muscle activation are difficult to obtain in the laboratory and were not included in this experimental validation. Note that this dataset was not used to train the NN.

The data correspond to a group of participants composed of 79 adult females with no history of voice disorders. The mean (SD) age was 29.6 (13.0) years old. Their vocally healthy status was verified by a licensed speech-language pathologist via interview (subjects reported no difficulties with their voices in daily life), laryngeal videostroboscopic examination, and a clinician-administered Consensus Auditory-Perceptual Evaluation of Voice (CAPE-V) assessment (Kempster et al., 2009). Informed consent was obtained from all the participants in this study, and experimental and clinical protocols were approved by the institutional review board of Mass General Brigham (formerly Partners HealthCare) at the Massachusetts General Hospital. Data recordings were conducted in a sound-treated room where study staff instructed each participant to repeat strings of /pæ/ syllables in three loudness conditions (comfortable, loud, and soft). Although subjects were instructed to maintain a constant pitch and loudness within each syllable string, they were free to choose levels that were most natural for them without any prescribed levels of absolute pitch and loudness.

Recordings consisted of the simultaneous acquisition of acoustic pressure obtained with a condenser MIC (MKE104, Sennheiser, Electronic GmbH, Wedemark, Germany) placed 10 cm from the lips and having full bandwidth in the range of 0-6 kHz, OVV sensed by using a circumferentially vented pneumotachograph mask (PT-2E, Glottal Enterprises, Syracuse, NY) with a bandwidth of approximately 1.1 kHz, IOP measured with an oral catheter passed between the lips and connected to a low-bandwidth pressure sensor with an effective bandwidth of approximately 80 Hz (Espinoza et al., 2017), and ACC (BU-27135; Knowles Corp., Itasca, IL, USA) placed on the anterior neck surface halfway between the thyroid prominence and the suprasternal notch (Zañartu et al., 2013). All signals were sampled at 20 kHz/16 bits (Digidata 1440A, Axon Instruments, Inc.), low-pass filtered at 8-kHz cutoff frequency (CyberAmp Model 380, Axon Instruments, Inc.), and calibrated to physical units (Espinoza et al., 2017).

Signals obtained from the ACC and pneumotachograph mask were low-pass filtered at 1,100 Hz with a 10th-order Chebyshev Type II filter and decimated to 8,192 Hz. Then, a fourth-order Butterworth high-pass filter with cutoff frequency at 60 Hz was used to remove low-frequency components. The IOP signal was low-pass filtered at 80 Hz with a fifth-order Butterworth filter and then decimated to 256 Hz sample rate. All filters were applied with phase removal to avoid phase distortion (Perkell et al., 1994).

Reference values for subglottal pressure were obtained from IOP signals following (Espinoza et al., 2017). Driving pressure was extrapolated as the mean value of the two consecutive IOP plateaus produced by the combined lip closure and glottis opening prior to the /p/ sounds, that produced just before and after each vowel segment. The three middle syllables in each /pæ/ string were selected for the analysis, so that the initial and final portions were disregarded to avoid any evident transient dynamics. The estimated subglottal pressure was the average of these three-syllable values. Three reference measures per participant for comfortable, loud, and soft loudness conditions were obtained. Thus, a total of 237 /pæ/ tokens were used in this study.

The OVV-based glottal airflow was obtained through a common inverse filtering technique based on a single-notch filter with a conjugate pair of zeros and unity gain at DC at first vocal

tract resonance (Perkell et al., 1991; Cheyne, 2006). Each singlenotch filter was applied to a 50 ms stable portion of the middle /pæ/ string. The center frequency of the filter was determined following an optimization procedure developed by Espinoza et al. (2017).

The ACC-based glottal airflow was estimated using the IBIF scheme (Zañartu et al., 2013; Cortés et al., 2018). This method uses an acoustic transmission line model and a calibration step to obtain a set of subject-specific parameters corresponding to the neck-skin surface, length of the trachea, and accelerometer position (Zañartu, 2010; Zañartu et al., 2013; Cortés et al., 2018). These parameters are determined by minimizing the waveform error between the OVV-based glottal airflow (reference signal described previously) and the inverse filtered neck-skin ACC signal via a particle swarm optimization Kennedy and Eberhart (1995). The middle 50 ms of the glottal airflow signal estimated from IBIF was selected to compute the six acceleration-based aerodynamic feature (see Table 1). Even though SPL can be computed from the ACC signal using regression methods Švec et al. (2005), the synchronous microphone signal was used in this study to avoid introducing any additional estimation error at this point. Future work can be devoted to enhance current linear mapping between ACC and SPL.

Validation with human data is the gold standard to assess the ability of the NN regression scheme to represent *in vivo* data; but direct measurement of certain physiological measures of vocal function is not feasible. An advantage of using a voice production model to train a neural network is that we can estimate vocal function measures that are difficult to measure in practice, which is the case for vocal fold collision pressure and intrinsic muscle activation. Thus, the assessment of the estimates of subglottal pressure is described in terms of test sets from numerical simulations and laboratory data, whereas the estimates of vocal fold collision pressure and laryngeal muscle activation are only evaluated using a synthetic data test set.

#### 3. RESULTS

#### 3.1. Subglottal Pressure Estimation

The MAE and RMSE describing Ps estimates for the different architectures are reported in Table 3 for both synthetic and clinical test data. For both cases I and II, additional hidden layers and neurons per layer yielded an improvement in subglottal pressure estimation when tested against the synthetic data. For example, in case I, MAE decreased from 1.98 cm H<sub>2</sub>O to 0.93 cm H<sub>2</sub>O from the simplest (2 hidden layers with 4 neurons) to a more complex (4 hidden layers with 128 neurons) architecture, respectively. In case II, MAE decreased from 1.84 cm H<sub>2</sub>O to 0.78 cm H<sub>2</sub>O for the same prior complexity in the NN architecture. This represents a reduction of more than 50% in MAE in both cases. A similar trend is observed with RMSE. An explanation for the improvement comes from the fact that the training and testing data were obtained from the same voice production model. Therefore, more complex NN models appear to capture efficiently the non-linear mechanisms of the model, which has been suggested by Zhang (2020), when training and testing with synthetic data from the same model. However, for **TABLE 3** | MAE and RMSE between the estimated  $P_{\rm s}$  with the proposed NN regression model and the reference measures from synthetic and laboratory test data.

Neurons in	Number of	Synthe	Synthetic Data		Laboratory Data	
each hidden	hidden layers	MAE	RMSE	MAE	RMSE	
layer		(cm H <sub>2</sub> O)				
Case I:						
4	2	1.98	2.51	2.23	2.82	
8	2	1.81	2.34	2.28	2.86	
16	2	1.35	1.83	2.56	3.13	
32	2	1.18	1.64	2.82	3.43	
64	2	1.02	1.48	2.89	3.50	
128	2	0.99	1.68	2.94	3.58	
128	4	0.93	1.33	3.17	3.87	
128	6	0.97	1.38	3.14	3.85	
128	8	1.01	1.45	3.12	3.76	
Case II:						
4	2	1.84	2.42	1.95	2.48	
8	2	1.87	2.43	1.97	2.52	
16	2	1.27	1.74	2.42	2.98	
32	2	1.13	1.58	2.55	3.17	
64	2	0.99	1.42	2.88	3.45	
128	2	0.90	1.30	2.98	3.58	
128	4	0.78	1.12	3.23	3.87	
128	6	0.87	1.21	3.04	3.71	
128	8	1.00	1.38	3.08	3.70	

Errors are reported for different NN architecture (different number of neurons and hidden layers). Case I: Input aerodynamic features of ACFL, MFDR, OQ, SQ,  $f_0$ , and  $H_1 - H_2$ . Case II: Input aerodynamic features in Case I and acoustic SPL.

the NN architectures composed over the six hidden layer with 128 neurons, the MAE and RMSE for synthetic data increase, showing that a deeper NN does not improve the estimation of subglottal pressure in this context.

It is important to highlight that all NNs were trained using 100 epochs. This criterion was selected to ensure the convergence of models. Figure 4 shows mean squared error vs. the epochs for training and validation of the simplest and the most complex architecture models. The curves illustrate the convergence of the training procedure, where the simplest regression model exhibits a more rapid convergence. However, at around 100 epochs, the error remains constant, as the training progresses for both architectures. A similar trend was observed for all tested configurations. Another element to highlight is the absence of overfitting, since the training and validation error monotonically decrease at the same time. This shows that the network learns the structure of the observed data and is able to infer the validation data. An indication of overfitting would be a training error that decreases while the validation error remains the same or increases.

On the other hand, for the laboratory validation of subglottal pressure, we found the opposite trend for MAE as a function of the NN architecture complexity. In Case I, MAE increased from 2.23 cm  $H_2O$  to 3.17 cm  $H_2O$  for an increasing complexity



FIGURE 4 | Mean Squared Error (MSE) vs. epoch for training (blue color) and validation (red color) for two neural networks architectures. (Left) 2 hidden layers with 4 neurons. (Right) 8 hidden layers and 128 neurons.



from the 2 hidden layers with 4 neurons to 4 hidden layers with 128 neurons model. Case II also exhibited MAE increases from 1.95 cm  $H_2O$  to 3.23 cm  $H_2O$  for the same increasing complexity in the NN architecture. These results represented an increase of 42% and 66% in MAE for Case I and II, respectively, with similar trends for RMSE. Therefore, higher NN complexity was not adequate to represent sample distribution from the laboratory dataset.

**Table 3** also illustrates that the inclusion of SPL in the input feature vector improves the estimation of subglottal pressure for all tested NN architectures. Using the best architecture for the laboratory validation, we found a 12% reduction in MAE and RMSE. The best architecture for the synthetic validation exhibited a 16% reduction in MAE and RMSE when SPL was added. These results are in agreement with previous studies (Titze et al., 2003; Björklund and Sundberg, 2016; Espinoza et al., 2017) that reported a strong correlation between subglottal pressure and acoustic SPL. Although not reported, no significant error differences were observed when estimating SPL from either the MIC or ACC sensor.

Therefore, the NN model with lowest error in the validation set from the laboratory data was selected from 4 neurons in the hidden layers and all seven input features. **Figure 5** shows a scatter plot of the NN-estimated subglottal pressure vs. the reference subglottal pressure from the laboratory data. The dashed line represents a 1:1 correspondence between the estimated and reference subglottal pressure. The coefficient of determination  $R^2$  is 0.65 and the mean absolute percentage error is 24.9%. We highlight that even though the IOP data was used as ground truth for this assessment, differences in the subglottal pressure estimates from IOP and direct measurement of subglottal pressure via tracheal puncture has been reported in the range of 5% (Hertegård et al., 1995), although interpolation between the peaks of the pulses can lead to a 12% error (Rothenberg, 2013).

#### **3.2. Vocal Fold Collision Pressure and Laryngeal Muscle Activation Estimation**

**Table 4** reports the coefficient of determination  $R^2$ , MAE (in physical units and in percentage of range) using synthetic data for the four outputs ( $P_s$ ,  $P_c$ ,  $a_{CT}$ ,  $a_{TA}$ ) obtained using the NN for the 2 hidden layers with 4-neuron and 4 the hidden layers with

Parameters	Units	R <sup>2</sup>	MAE	MAE
			(Units)	(%)
2-HL and 4-N are	chitecture:			
Ps	$cm H_2O$	0.64	1.84	11.4
Pc	cm H <sub>2</sub> O	0.70	3.33	8.2
a <sub>TA</sub>	-	0.07	0.21	21.1
a <sub>CT</sub>	-	0.53	0.15	14.6
4-HL and 128-N	architecture:			
Ps	cm H <sub>2</sub> O	0.93	0.74	4.7
Pc	cm H <sub>2</sub> O	0.92	1.70	4.2
a <sub>TA</sub>	-	0.52	0.13	13.3
act	-	0.84	0.07	7.1

**TABLE 4** | Assessment of estimated vocal measures  $P_s$ ,  $P_c$ ,  $a_{TA}$ , and  $a_{CT}$  using the proposed NN regression method.

Reported values for R<sup>2</sup> and MAE (in physical units and in percentage of range) for two NN architectures with different hidden layers (HL) and neurons (N). The input vector includes the seven aerodynamic measures.

128-neuron architectures. The architectures with more layers exhibited the best performance for estimating subglottal pressure for the synthetic data.

As seen before for the synthetic validation of subglottal pressure, increasing the complexity of the NN architecture increases the accuracy of the estimates. This performance holds true for the estimates of vocal fold collision pressure and laryngeal muscle activation. However, there is a significantly smaller  $R^2$  of 0.52 for  $a_{TA}$  estimation when compared with  $R^2 > 0.8$  for estimation of the other measures using the 4 hidden layer with 128 neurons NN. This finding suggests that certain measures, such as  $a_{TA}$ , require deeper, more complex NN architectures to achieve similar performance.

#### 4. DISCUSSION

The purpose of this study was to explore the combination of neural network regression networks with a voice production model to estimate physiologically relevant vocal measures, i.e., subglottal pressure, vocal fold collision pressure, and (TA and CT) laryngeal muscle activation from a neck-surface vibration signal. Validation for this study was done both numerically and experimentally. Given that some of the predicted measures are difficult to obtain experimentally, only the estimates of subglottal pressure could be compared with reference estimates of mean subglottal pressure derived from the standard airflow interruption technique in the laboratory.

Both numerical and experimental validation experiments yielded reasonable accuracy. The robust and reliable estimates of the proposed method are dependent on the capacity of the selected voice production model to mimic the observed distributions in the laboratory data. As the architecture complexity of the NN increased, the estimation error decreased for the synthetic data but increases for the laboratory data. We argue that this is a result of the way the model was utilized, i.e., model parameters were swept across a large range of values, but no anatomical changes were considered; thus the model simply described a single subject for a range of conditions. This may be playing a role in the accuracy for the estimation of subglottal pressure because no inter-subject variability was considered. At the same time, we discarded cases that differed from the laboratory distributions during the training process and corrected for a bias in the estimation of subglottal pressure. In addition, it is possible that subglottal and supraglottal tract propagation losses and the losses at the glottal boundary were not high enough, thus amplifying the source-filter interactions and resulting subglottal pressure. Future efforts will be devoted to improve model development, better reflect population behaviors, and assess these effects in the predicted accuracy of the proposed approach. In spite of its simplicity and the aforementioned limitations, we still conclude that the triangular body cover model provides a good general representation of typical sustained phonation for a large range of subjects and conditions.

The predicted subglottal pressure in this study are comparable with those obtained in previous studies. Our lowest mean absolute error for estimated subglottal pressure from clinical data was 191 Pa (1.95 cm H<sub>2</sub>O), whereas two relevant studies reported mean absolute errors of 194 Pa (Gómez et al., 2019) and 115 Pa (Zhang, 2020). However, it is important to highlight that our predictions are obtained from a neck-surface accelerometer and that we tested our predictions against in vivo human data, whereas these studies used porcine and human excised larynx experiments. Lin et al. (2020) estimated subglottal pressure from a neck-surface accelerometer using a subject-specific stepwise factorial regression model in 26 normal subjects. The investigators obtained an average root-mean-square error in the range of 2.4-2.5 cm H<sub>2</sub>O, which is comparable with the root-mean-square error of 2.48 cm H<sub>2</sub>O in the current study. The linear regression models in Lin et al. (2020) included cepstral peak prominence and fundamental frequency, along with ACC-based aerodynamic measures and were constructed on an individual basis for every subject across multiple elicited voice qualities. The main advantages of the NN model approach are the fact that a single, general non-linear regression mapping is utilized and that our mapping also provides estimates of other clinically relevant measures of vocal function. It is acknowledged that future work is required to experimentally validate these other measures of vocal fold collision pressure and laryngeal muscle activation.

Titze et al. (2003) put forth a simple, empirically derived formula (Equation 15) that computed subglottal pressure using only measurements of SPL and  $f_o$ . Applying this formula to the laboratory data (237 tokens) in the current study to estimate subglottal pressure resulted in a root-mean-square error of 2.86 cm H<sub>2</sub>O and mean absolute error of 2.11 cm H<sub>2</sub>O. The relatively good performance for such a simple formula supports the idea that simple regression architectures are adequate for predicting subglottal pressure in vocally typical conditions; estimation accuracy of linear regression models reduces when non-modal voice qualities are included (Marks et al., 2019, 2020; Lin et al., 2020). The model-based approach of the current work allows for the estimation of additional measures of vocal function (e.g., vocal fold collision pressure, laryngeal muscle activation). On the other hand, the accuracy of estimates of muscle activation and collision pressure that was assessed against synthetic data was hampered by the simplicity of the rather shallow NN architecture that resulted from matching clinical data for subglottal pressure. When the complexity of the network is increased, the estimation of muscle activation and collision pressure improves. This result is encouraging to investigate the development of subject-specific models that can handle more complex neural network architectures without losing the ability to predict subglottal pressure.

These initial results constitute a proof of concept that the proposed NN method is a feasible option for estimating clinically relevant vocal measures that are difficult to directly measure in laboratory and ambulatory settings. Current results could be significantly improved by exploring different NN architectures, improving model development, training with ACC signal features directly (vs. model features), using subject-specific tuning with transfer learning instead of a generic training for all subjects, and including experimental validation of all predicted values. This study delineates a path for various subsequent research efforts in this direction.

The neck-surface accelerometer sensor can be worn by a speaker for laboratory, clinical, and ambulatory assessments of vocal function. The estimation of subglottal pressure was validated using sustained phonation datasets from numerical modeling and laboratory recordings. There is potential to translate this method into ambulatory settings due to the input of the network only needing accelerometer-based features for short-time windows of 50 ms in duration. We hypothesize that the physiologically relevant measures that are obtained with the proposed approach will yield salient measures of vocal function in real-world environments. We expect that the physiologically relevant measures that are obtained with the proposed approach will provide unique quantitatively based insights into the etiologic and pathophysiological mechanisms associated with daily voice use in patients with hyperfunctional voice disorders. The capability to link model outputs with clinical data is expected to produce more comprehensive and specific descriptions of aberrant phonatory mechanisms that will lead to better subclassification (phenotyping) of hyperfunctional voice disorders and ultimately improve the prevention, diagnosis, and treatment of these disorders.

## **5. CONCLUSION**

A framework to estimate subglottal pressure, collision pressure, and muscle activation from a neck surface accelerometer is developed integrating machine learning tools and a numerical model of voice production. Aerodynamic measures estimated from the neck surface accelerometer are combined with a sound pressure level estimate obtained from either an accelerometer or a microphone, and are selected as inputs to a neural regression network. The non-linear mapping is trained solely with a loworder voice production model featuring a symmetric triangular body-cover model of the vocal folds. When compared with clinical recordings from 79 female vocally healthy participants, the mean absolute error and root mean square error for the subglottal pressure were 1.95 cm H<sub>2</sub>O and 2.48 cm H<sub>2</sub>O. These results are comparable with previous studies but with the advantage of having a general mapping for all patients and providing simultaneous estimates of collision pressure and muscle activation. However, given that clinical validation for these latter features is cumbersome, only synthetic data were used for that purpose, and experimental validation is left for future efforts. At the same time, relevant insights are gained by comparing the numerical model with the clinical data that will lead to further model refinements. The initial results constitute a proof of concept that the proposed machine learning method is a feasible option for providing highly relevant physical measures for the ambulatory assessment of voice. Future efforts will be focused on creating individualized mappings for normal and disordered voices with transfer learning and validating all the estimated features with in vivo recordings.

## DATA AVAILABILITY STATEMENT

The datasets presented in this study can be found in online repositories. The names of the repository/repositories and accession number(s) can be found in the article/supplementary material.

## **ETHICS STATEMENT**

The studies involving human participants were reviewed and approved by Institutional Review Board of Mass General Brigham. The patients/participants provided their written informed consent to participate in this study.

## **AUTHOR CONTRIBUTIONS**

MZ conceived the study and contributed to data analysis and interpretation, supervision, and manuscript writing. EI and JP conducted numerical simulations, neural network design, training and testing, data analysis and interpretation, and manuscript writing. GA developed the triangular body-cover model and contributed to data analysis and interpretation, supervision, and manuscript writing. JC and VE contributed to data analysis and interpretation and manuscript writing. DM and RH contributed to laboratory data collection, results interpretation, clinical input, and review editing. All authors contributed to the article and approved submitted version.

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