To my children: Emilia, Patrick, and Alexandra
ACKNOWLEDGMENTS

I would like to thank my dissertation committee members for their support throughout the process of completing this project. First of all, I thank Dr. Christine Sapienza, my first mentor for her constant faith and encouragement of my efforts over the years and whom I admire for her knowledge, perseverance at work, and caring personality. Many thanks go to my current mentor, Dr. Karen Hegland for her excellent guidance, for sharing her scientific knowledge and experience, and for motivating me by her hard work and her professionalism. I also dedicate my sincere gratitude to Dr. Michelle Troche for her great support of my writings and her valuable input in the process of designing this project. I thank Dr. Neil Chheda who welcomed me to his clinic, dedicated his precious time and resources, and helped me tremendously in the process of data collection. Without his participation, this study would not be completed. My special thanks go to Dr. Donald Bolser who was willing to participate in my defense committee at the last moment. Finally, I would like to express my gratitude to Dr. Paul Davenport for participating in my academic advisory committee and for his support and guidance during my entire graduate program.

I thank God for blessing me with all the people who supported me on this journey. Especially, I thank my husband and my children for their love and patience, my friends, my clinic and lab colleagues for all the support, and, most of all, Kristin Drew for spending long hours in the lab to help me with data entry. Of course, the greatest appreciation goes to the study participants who made this project possible.
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<tr>
<td>ALM</td>
<td>Anterolateral muscle</td>
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<td>ALS</td>
<td>Amyotrophic lateral sclerosis</td>
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<td>AMM</td>
<td>Anteromedial muscle</td>
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<td>Böt-VRG</td>
<td>Bötzinger-ventral respiratory group</td>
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<td>BTVFI</td>
<td>Bilateral true vocal fold immobility</td>
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<tr>
<td>C1</td>
<td>Cough one</td>
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<tr>
<td>C2</td>
<td>Cough two</td>
</tr>
<tr>
<td>CIV</td>
<td>Cough inspired volume</td>
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<td>cmH$_2$O</td>
<td>Centimeters of water</td>
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<td>CPD</td>
<td>Compression phase</td>
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<td>CT</td>
<td>Cricothyroid</td>
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<td>CVA</td>
<td>Cough volume acceleration</td>
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<td>DRG</td>
<td>Dorsal respiratory group</td>
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<td>ENT</td>
<td>Ear nose and throat</td>
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<td>EPD</td>
<td>Expiratory phase durations</td>
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<td>FEV1</td>
<td>Forced expired volume within 1 second</td>
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<tr>
<td>fMRI</td>
<td>Functional magnetic resonance imaging</td>
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<tr>
<td>FVC</td>
<td>Forced vital capacity</td>
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<tr>
<td>FVF</td>
<td>False vocal fold</td>
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<td>IA</td>
<td>Interarytenoid</td>
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<td>IEMG</td>
<td>Integrated electromyography</td>
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<td>IPD</td>
<td>Inspiratory phase duration</td>
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<td>L</td>
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<td>LCA</td>
<td>Lateral cricoarytenoid</td>
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<td>LEMG</td>
<td>Laryngeal electromyography</td>
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<td>Laryngeal motor cortex</td>
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<td>LTF</td>
<td>Lateral tegmental field</td>
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<td>MCV</td>
<td>Maximal voluntary cough</td>
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<td>MEP</td>
<td>Maximum expiratory pressure</td>
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<tr>
<td>mmHg</td>
<td>Millimeter of mercury</td>
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<td>MND</td>
<td>Motor neuron disease</td>
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<tr>
<td>MS</td>
<td>Multiple sclerosis</td>
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<tr>
<td>msec</td>
<td>Millisecond</td>
</tr>
<tr>
<td>NA</td>
<td>Nucleus ambiguous</td>
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<tr>
<td>NRA</td>
<td>Nucleus retroambigualis</td>
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<tr>
<td>nTS</td>
<td>Nucleus tractus solitarius</td>
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<td>PCA</td>
<td>Posterior cricoarytenoid</td>
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<td>PD</td>
<td>Parkinson disease</td>
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<tr>
<td>PEF</td>
<td>Peak expiratory flow</td>
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<td>PEFR</td>
<td>Peak expiratory flow rate</td>
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<td>PEFRT</td>
<td>Peak expiratory flow rise time</td>
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<td>PGR</td>
<td>Pontine respiratory group</td>
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<td>PLM</td>
<td>Posterolateral muscle</td>
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<td>PSP</td>
<td>Progressive supranuclear palsy</td>
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<td>RLN</td>
<td>Recurrent laryngeal nerve</td>
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<td>RV</td>
<td>Residual volume</td>
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<td>SD</td>
<td>Standard deviation</td>
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<tr>
<td>sEMG</td>
<td>Surface electromyography</td>
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<td>SLN</td>
<td>Superior laryngeal nerve</td>
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<tr>
<td>Abbreviation</td>
<td>Description</td>
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<tr>
<td>TA</td>
<td>Thyroarytenoid</td>
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<td>TLC</td>
<td>Total lung capacity</td>
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<td>TVF</td>
<td>True vocal fold</td>
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<td>UTVFI</td>
<td>Unilateral true vocal fold immobility</td>
</tr>
<tr>
<td>VRC</td>
<td>Ventral respiratory column</td>
</tr>
<tr>
<td>VRG</td>
<td>Ventral respiratory group</td>
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The primary goal of this study was to determine the effects of glottal insufficiency on voluntary cough function and to examine the relationships between cough airflow parameters and true vocal fold (TVF) abduction and adduction angles in voluntary cough in individuals with reduced mobility of one TVF. This study also investigated the differences in cough airflow measures and TVF angles between single coughs and two first coughs (C1 and C2) of sequential coughs tasks in persons with glottal insufficiency. To achieve this goal, voluntary cough airflow and videolaryngoscopic images of the TVF abduction and adduction angles during single and sequential cough tasks were obtained simultaneously from 15 adults (9 females, 6 males) of ages 44-80 years with unilateral TVF paralysis or paresis. The degree of glottal closure was assessed during vowel phonation using the Glottal Closure Rating Scale (GCRS).

The study showed that the participants with greater severity of glottal insufficiency produced voluntary coughs with shorter compression phase durations, and greater pre-compression TVF adduction angles. There were direct relationships between pre-compression and post-compression abduction TVF angles and the durations of compression and expiratory phases of single coughs and first coughs (C1)
of cough sequences. Coughs produced with greater pre-compression TVF abduction angles and greater pre-compression TVF adduction angles were generated with longer expiratory phase durations but shorter compression phase durations. In addition, the first coughs (C1) of the cough sequences were produced with significantly higher values of pre-compression TVF abduction angles than the consecutive (C2) coughs of cough epochs.

This study results confirmed the hypothesis that glottal insufficiency can influence cough airflow parameters and TVF dynamics during voluntary cough in persons with reduced mobility of one TVF. Further studies should investigate the effect of glottal insufficiency on reflex cough function and test TVF medialization treatment outcomes related to cough.
Airway protection involves actions and mechanisms facilitating adequate ventilation, primarily by preventing foreign or endogenously produced materials from entering and remaining in the airway. One of those protective mechanisms is effective swallowing, which directs food, or/and liquids to the digestive tract. Other maneuvers such as glottal stops or throat clear involve glottal closure followed by forced exhalations produced in response to irritants or materials entering the larynx. When the preventive behaviors fail to protect the lower airways from aspiration or irritants, or when excessive secretions accumulate in the larger intrathoracic airways, ejection of those materials requires generation of high expiratory flow rates which may be achieved during a cough maneuver.\textsuperscript{1,2}

Effective cough requires coordinated action of respiratory and laryngeal muscles as well as adequate lung volumes and tracheal narrowing to produce high velocity flows.\textsuperscript{3} An impairment of one component in this mechanism may result in changes in the cough airflow dynamics and may subsequently reduce the ability to effectively clear the airway. For example, inability to modify laryngeal resistance and tracheal lumen during attempt to cough results in a less powerful ejective behavior resembling expiratory effort.\textsuperscript{4} Airway protection deficits associated with reduced effectiveness of airway clearance mechanisms have been reported in patients with neuromuscular diseases\textsuperscript{5-7} as well as head and neck cancer survivors,\textsuperscript{8} patients with stroke\textsuperscript{9,10} and/or aging populations.\textsuperscript{11} Although the laryngeal involvement in airway protection has been systematically studied, there is limited information regarding the impacts of laryngeal dysfunction on cough effectiveness.
Glottal insufficiency is a laryngeal dysfunction associated with inability to achieve an adequate glottal closure due to reduced true vocal fold (TVF) mobility or TVF immobility, vocal muscle atrophy, or true vocal fold tissue deficiency. This type of laryngeal dysfunction may cause dysphonia, disordered swallowing or dysphagia,\textsuperscript{12,13} and disordered cough or “dystussia”\textsuperscript{14} Because the TVF adduction and abduction properties are particularly important for modifications of laryngeal resistance and subglottal pressure build-up during cough, impaired TVF mobility may influence cough airflow parameters which depend on laryngeal functioning. To identify the impact of the TVFs on cough mechanism, observation of the TVF movement during cough is of importance.

**Cough Physiology**

**Cough Aerodynamics**

Cough is defined as a respiratory maneuver performed voluntarily, on command, or evoked by tussigenic stimulants. It’s function is to protect lungs from aspiration or to remove unwanted materials from the airway.\textsuperscript{15} A typical cough, either voluntary or reflex/evoked, consists of three distinct, consecutive phases: an inspiratory phase, compression phase, and expiratory phase (Figure 1-1).

**Inspiratory phase**

The cough inspiratory phase involves vocal fold abduction associated with contractions of intrinsic laryngeal muscles: posterior cricoarytenoids (PCA) and cricothyroid (CT). Simultaneously, the decrease in gastric pressure and esophageal pressure indicates reduction in laryngeal resistance. Contractions of inspiratory pump muscles, primarily diaphragm and external intercostal muscles promote inspiratory airflow and lung volume increase. In healthy individuals, the inspiratory phase duration
takes approximately 1 second to reach the average cough inspired volume of 1.50 liter (L).\textsuperscript{16}

The inspiratory volumes in voluntary coughs may vary according to the anticipated cough strength,\textsuperscript{17} but airflow modifications of the inspiratory phase prior to the reflex cough has not been fully explored. Hegland et al.\textsuperscript{18} compared voluntary and reflex cough airflow parameters in patients with Parkinson’s disease and found that inspiratory volumes in capsaicin-induced reflex coughs were slightly lower compared to voluntary coughs, but the differences were not statistically significant.\textsuperscript{18} Researchers speculate that the increased intensity of a stimulus causing cough could be a potential factor reducing the inspiratory volumes.\textsuperscript{15}

**Compression phase**

A cough compression phase is marked by glottal closure accomplished by adduction of the true and the ventricular vocal folds. The activation of intrinsic laryngeal muscles during compression phase begins with contractions of lateral cricoarytenoid (LCA), thyroarytenoid (TA), and interarytenoid (IA) which increase over approximately 400 milliseconds (msec); however, over the last 150 msec, overlapping activity of the adductors and abductors (PCA and CT) takes place.\textsuperscript{19} During this period, intrathoracic and subglottal pressure increase below closed glottis. At the end of the compression phase, subglottal pressure reaches its peak, but intrathoracic pressure keeps rising with simultaneous expiratory muscle contractions throughout the compression and the expiratory phases of cough. The main expiratory muscles that extend their activities from compression throughout expiratory phases are the internal intercostals and abdominal muscle group: the external and internal obliques, the tranversus abdominis, and the rectus abdominis.\textsuperscript{15,20,21}
**Expiratory phase**

The cough expiratory phase is characterized by rapid glottal opening and a burst of expiratory air reaching high flow rates through the opened airways. This phase of cough can be further subdivided according to the airflow characteristics and glottal resistance modifications. During the initial burst of air exiting through widely opened vocal folds the airflow rate rapidly increases, reaches its peak, and quickly decreases, but remains consistent for a period of time before complete termination. The drop in airflow rate is associated with the increase in airway resistance when the vocal folds are drawn back together, but allow the continuation of the expiratory flow. Tracheal lumen decreases to promote high airflow velocity. Subglottal pressure drops quickly after reaching its peak right before the expiratory airflow peak is reached. However, the intrathoracic pressure keeps rising and decreases after the cough peak flow is reached. Expiratory muscles generate isotonic contractions throughout the duration of the expiratory phase. In sequential cough, the expiratory phase of the first cough (C1) of a sequence is followed by a compression phase and another expulsion of air during a second cough (C2). This compression-expiration pattern repeats for the consecutive coughs of the cough sequence with significant decrease in lung volumes and continuously increased expiratory muscle force. During this activity, secretions and materials are transported by the increased sheering forces from the lower to the upper airways to be ejected.

**Cough Sensorimotor Pathways**

Cough is a mechanism which requires complex neuromuscular interactions; therefore, multiple brain regions responsible for sensory, motor, cognitive, and affective processes are activated during cough production. For cough to be produced as a
response to a stimulus, sensory information typically arises from laryngeal, trachea, and main stem bronchi. Sensory information received by laryngeal receptors is transmitted by the afferent fibers of the internal branch of the superior laryngeal nerve which terminate in nucleus tractus solitarius (nTS) and synapse on second-order neurons. Laryngeal second-order neurons are located in the commissural subnucleus of the nTS. Those neurons project to the other nTS subnuclei and other regions such as the medullary dorsal and ventral respiratory groups (DRG, VRG) and pontine respiratory group (PRG) responsible for control of breathing.

Generation of cough motor patterns in respiratory pump and laryngeal muscles is supported by rostral VRG neurons called Bötzinger-ventral respiratory group (Böt-VRG) which are components of the ventral respiratory column (VRC) and are located in ventrolateral medulla. These neurons form a “core” network with subpopulations of neurons creating excitatory and inhibitory connections with respiratory bulbospinal premotor neurons which drive spinal motoneurons and upper laryngeal motoneurons. The Böt-VRG interact with elements of the midline caudal medullary raphe nuclei (magnus, obscurus) which include cells that process sensory information influencing breathing and are responsible for expression of cough reflex.

Another network of neurons which interact with Böt-VRG to generate cough motor pattern is PRG found in the rostral lateral pons (medial parabranchial and Kolliker-Fuse nuclei and the lateral pons/mesencephalic junction). This group is responsible for normal breathing pattern and demonstrates complex changes in neural activity during cough. Those changes are potentially influenced by input from pulmonary
stretch receptors, but the mechanism of this interaction has not been established.  
Cough reflex is also modulated by the lateral tegmental field (LTF) in the medulla.

The impact of cerebellum on cough motor pattern has been reported based on the findings that cerebellectomy or lesions of the interposed nucleus in the experimental animal result in reduction in number of coughs generated by maximum stimulus and in reduction of peak discharge rate in abdominal expiratory motor nerves. It has been established that the deep cerebellar nuclei, such as fastigial, interposed, and intracerebellar/lateral, participate in modulation of breathing, especially during respiratory stress. In general, cerebellar role in cough production may be associated with its sensorimotor integration, coordination, and timing.

The central cough motor command for cough motor act is passed from the pre-motoneurones of the DRG and VRG to the spinal respiratory motoneurones and, via the phrenic, intercostals and lumbar nerves, to the respiratory pump muscles following the efferent pathways. This central motor command can be also transmitted via cranial motoneurones innervating the laryngeal intrinsic muscles, and via sympathetic and parasympathetic nerves supplying the airway smooth muscle and glands.

**Voluntary Control of Cough**

The foundation of our current knowledge of physiological mechanisms associated with cough has been provided by basic science experiments involving mechanical and chemical stimulation of airways of anesthetized animals. When relaying on the results of such experiments, it is important to consider the fact that anesthesia may cause altered cortical input and may also depress spinal reflexes in the experimental animals. Similar results may be observed in humans.
Based on the findings presented by Moulton and Pennycook, the cough reflex can be depressed in humans in deep coma caused by drugs or alcohol intoxication which potentially depresses entire brain including cough-control areas in the brainstem. However, coma caused by head injury often does not have an impact on reflex cough response to airway stimulation if the injury occurred in any other brain areas. The cough reflex may be also present under light surgical general anesthesia and during sleep but with the increased stimulus threshold. Interestingly, chronic cough in asthma is reduced and habit/psychogenic cough is absent in sleep. The absence of psychogenic cough indicates exclusive cortical control of this type of cough and suggests that the urge to produce psychogenic cough is not caused by an airway stimulus. There is still need for assessment methods that would provide information on neuromuscular events during cough in awake humans.

It has been reported that in awake humans, depending on the intensity of airway stimulation, reflex cough involves a certain degree of urge to cough which also indicates the level of awareness of an irritant in the airways, and this phenomenon is mediated on the cortical level of brain. According to Davenport, stimulation of the cough receptors in the upper and lower airways triggers the activation of the “urge” neural system. The “urge” signals are transferred into the limbic system via the thalamus. The limbic system projects the urge signal to the cortex, when the specific desire to cough is generated and the appropriate response is formulated. The response may include a motor action of cough, cough suppression, or a behavior modulation of cough act. The timing and intensity of cough response to a tussigenic agent reflects airway sensitivity as well as
the ability to initiate and execute cough motor act through coordination of respiratory and laryngeal system components responsible for airway protection.

Voluntary control of cough may be analyzed in two aspects: voluntary cough initiation and voluntary regulation of cough evoked by airway stimulation. Studies have shown that cough initiated voluntarily is controlled primarily by the suprapontine brain centers. Functional magnetic resonance imaging (fMRI) during voluntary cough in healthy humans revealed activation of the sensorimotor cortex, supplementary motor area, orbitofrontal, insula, mid-cingulate cortices, ventral and mediodorsal thalamus, caudate, putamen and cerebellum.\textsuperscript{25,33}

In the presence of airway stimulus, suprapontine control of cough-related processes involves at least two ascending airway sensory pathways.\textsuperscript{34} One of them includes projections from nuclei of medulla via the ventrobasal thalamus to the somatosensory cortices; another, thalamo-limbic pathway ascends through the mediodorsal thalamus and terminates in anterior insula, cingulate and orbital cortices. The involvement of these multiple cortical regions in perception and response to the airway stimulation suggests that cough requires coordination of sensory, motor, affective, and cognitive processing.

Cortical control of cough motor act was confirmed by the finding that cough response to airway stimulation with tussigenic agents such as capsaicin or citric acid can be voluntarily downregulated, upregulated, or completely suppressed.\textsuperscript{35,36} In addition, with the attempt to suppress cough response to the tussigenic agent challenge, other laryngeal behaviors, such as breath holding, swallowing, expiratory efforts, and throat clearing, can be present.\textsuperscript{35} In the study of Hegland et al.,\textsuperscript{35} voluntary
modification of capsaicin-evoked cough response included modulations of cough airflow parameters. Further, with the attempt to produce loud and long coughs, the surface electromyography (sEMG) signals durations from the respiratory muscles (rectus abdominis and the eighth internal intercostal) were significantly longer than the signals obtained during both baseline and short coughs. Prolonged expiratory muscle activation in long coughs was in synchrony with the increased post-peak plateau phase. This finding suggested that cortical control of the cough motor response to the sensory stimulation allows modification of physiologic and aerodynamic aspects of cough.35

Voluntary and reflex coughs have common aerodynamic parameters and require the same muscle involvement for cough motor output. However, there is evidence that generating voluntary and reflex cough involves different motor patterns of respiratory muscle activity engaged in expiratory phase.37 In healthy young adults, expiratory muscles (the internal intercostal, rectus abdominis, obliques) during voluntary cough demonstrate equal EMG activity which increases proportionally and linearly to the increases in cough flow rates. The increase in activity of accessory muscles (deltoid, pectoralis major, latissimus dorsi, and trapezius) in voluntary cough is exponentially proportional to the cough flow rates. In addition, expiratory muscle group activation is initiated earlier than activation of accessory muscles prior to the expiratory phase of cough. Finally, the duration of expiratory muscle activity exceeds the duration of activity of accessory muscles regardless of the voluntary cough flow rates. The principal difference between reflex and voluntary cough is the greater EMG activity with shorter EMG burst duration in expiratory and accessory muscles in reflex cough. Moreover, reflex cough involves expiratory and accessory muscle activation with simultaneous
onset and comparable burst durations.\textsuperscript{37} It has been speculated that the sensory inputs from airway afferents in the brainstem evoke synchronized efferent outputs to all expiratory and accessory muscles in order to generate maximum expiratory airflow at the initiation of reflex cough. In cough produced volitionally, the level and sequence of activation of different muscles can be modulated cortically to produce desired cough airflows. The level of the EMG activities of expiratory and accessory muscle may be influenced by lung volumes prior to cough initiation. Specifically, lung volume initiation tends to be lower for acid induced coughs than for voluntary cough.\textsuperscript{37}

Considering the ability of voluntary control of reflex cough, it is reasonable to study physiology and pathology of both cough types: cough produced exclusively voluntarily and cough evoked by airway irritant. Voluntary cough assessment allows for evaluation of maximum ability to initiate and execute cough, ability to recruit respiratory muscles, and for observation of laryngeal function maximal lung operating volumes. Further, the analysis of voluntary cough strength helps predict the maximum strength of cough motor response in the presence of an irritant in healthy individuals and in persons with dystussia. It has been reported that specific airflow parameters of both reflex and voluntary coughs become altered as a result of neurologic impairments. For example, stroke patients may demonstrate reduced expiratory airflow rate and volume in voluntary and reflex cough.\textsuperscript{38,39} Also, patients with motor neuron disease (MND) have shown significantly reduced peak expiratory rise time as compared to age matched healthy controls.\textsuperscript{14} Finally, decrease in peak expiratory airflow and prolonged CPD have been reported in voluntary cough in patients with Parkinson’s disease.\textsuperscript{6} The analysis of voluntary and reflex cough parameters, especially those requiring immediate changes in
laryngeal resistance may be useful in the assessment of the ability to protect the lower airways during swallow and to eject aspirate or penetrant materials from the airways.

**Laryngeal Contribution to Cough**

**Laryngeal Neurophysiology**

Non-impaired cough involves modifications of laryngeal resistance which requires laryngeal muscle contractions during the sequential cough phases. Laryngeal motor behaviors associated with voice production in humans are assumed to be controlled by the laryngeal motor cortex (LMC) in Broadman’s area 4 of the primary motor cortex, located within the vocalization area in the inferior portion of the precentral gyrus, above the area representing swallowing and below the face representations. Stimulation of the LMC region in humans evokes approximation or adduction of vocal folds, a mechanism necessary for laryngeal behaviors such as voice production, sneezing, the Valsalva maneuver, and cough. For voluntary voice production, motor output comes from the LMC which has projections to the parietal cortex, presumably allowing for sensorimotor integration for voluntary voice control. The LMC sends direct (monosynaptic) projections to reticular formation in the medulla and additionally, to the nucleus ambiguous (NA), found in the ventro-lateral part of the reticular formation.\(^{40}\) This direct connection between the LMC and the NA allows production of voluntary learned laryngeal behaviors and is unique for humans but not present in other species.\(^ {41}\)

Bilateral lesions to the LMC in humans results in the inability to control laryngeal function associated with modulation of pitch, intensity and quality of voice with preservation of involuntary vocal behaviors such as laughter and cry, which may be partially independently controlled by other cortical areas such as anterior cingulate
cortex and subcortical structures, e.g., periaqueductal gray.\textsuperscript{42} It can be speculated that the vocal fold activity during cough may be also mediated by those cortical and subcortical areas independent of the LMC.

The motor neurons of NA project large myelinated fibers in the bulbar rootlets of the accessory (XI) nerve, which join the vagus (X) nerve and innervate the muscles of larynx and pharynx.\textsuperscript{43} The axons from NA are sent to the following nerves: glossopharyngeal (IX), vagus, and accessory. Behind NA in a very close approximation, lies the nucleus retroambigualis (NRA) which is a part of the brainstem respiratory group and sends its axons to the spinal cord contralaterally.\textsuperscript{44} It is suggested that the close distance between the NA and the NRA may explain the impact of the respiratory pattern on the intrinsic laryngeal muscles, the palate, pharynx, and the stylopharyngeaus which may be observed in vocal fold movement with further abduction during inspiration and slight movement towards the midline with expiration. However, there is no evidence of direct synaptic connections between the NRA and the NA.\textsuperscript{43}

Muscles involved in laryngeal function are divided into groups: intrinsic and extrinsic laryngeal muscles. All the intrinsic laryngeal muscles except the CT receive their ipsilateral motor innervation from the recurrent laryngeal nerve (RLN) with its fibers descending from the vagus nerve traveling in the neck via the carotid sheath. The CT muscle is innervated ipsilaterally by the external branch of the superior laryngeal nerve (SLN) which fibers leave the brain via roots of the vagus nerve.\textsuperscript{45-47}

The right RLN descends inferiorly, loops the subclavian artery, and ascends posteriorly within the tracheoesophageal groove to enter the larynx. The left RLN descends to wrap under the aortic arch and ascends within the tracheoesophageal
groove toward the larynx. Due to its position in the area of mediastinum, the left RLN is at greater risk of damage during cardiac surgeries.\textsuperscript{48}

Intrinsic laryngeal muscles directly control vocal fold shape and movements. The adductors: LCA and IA muscles are responsible for glottal closure by tilting and rotating the arytenoid cartilages toward the midline. The TA muscle is a main component of the true vocal folds and a vocal fold tensor which shortens the TVFs and demonstrates synergistic activation with the CT muscle to modify the TVF vibration. Contractions of the CT muscle result in a decrease in anterior space between the cricoid and the thyroid cartilages and ultimately cause stretching of the TVFs. This action has been assigned to rectus portion of the CT.\textsuperscript{45} When the TVFs remain in the midline position during voice production, activation of the CT supports vocal pitch increase. In addition, the CT becomes active during inspiration and sniff.\textsuperscript{49} The role of the PCA muscles is supporting rocking movement of arytenoid cartilages for the TVF abduction.

The role of the false vocal folds (FVFs) also called the ventricular or vestibular vocal folds in laryngeal biomechanics cannot be ignored. The FVFs contain muscle fibers which contribute to modifying the glottal space in humans.\textsuperscript{50} Reidenbach\textsuperscript{51} described the muscular composition of the FVFs in human larynges of men and women of age range 44 to 87 years. She identified a separate muscular sheet at the posterolateral margin of the vestibular fold and named it the posterolateral muscular system (PLM). It was separated from the medial region of the vestibular fold with the fibers running in a sagittal direction. Some lateral muscle fibers of this portion of the FVFs connected to transverse arytenoid muscle. The muscle layers at the anterior half or third of the vestibular fold were called an anterolateral (ALM) and anteromedial
(AMM) layers. The structures of the PLM and the ALM appeared to be more consistent than the AMM which consisted of several isolated muscle fiber bundles scattered within the vestibular fold.\textsuperscript{51}

Reidenbach\textsuperscript{51} suggested that the FVF movement toward midline may be a result of the PLM and ALM contractions with some minor contribution from the AMM possibly containing fibers of ventricularis muscle. She also speculated that the fact that lesions of recurrent laryngeal nerve do not impact the adductor movement of the FVFs indicates their innervation by the internal branch of SLN which supplies the transverse IA muscle most likely connected to the PLM. According to Moon & Alipour,\textsuperscript{52} most of the muscle tissue, specifically thyroarytenoid and ventricularis muscle fibers, can be found in the posterior portion of the FVFs. Those muscle bundles run superiorly and medially through the upper half of the fold toward the lateral margin of the epiglottis. The majority of the FVFs mass, however, is composed of elastic, glandular, and adipose tissues.\textsuperscript{51,52}

The extrinsic laryngeal muscles: thyrohyoid, sternothyroid, sternohyoid, and mylohyoid support the intrinsic laryngeal muscle function in vocal pitch and loudness modification by stabilization of the thyroid cartilage and laryngeal elevation during phonation and swallowing.\textsuperscript{42,50} Motor innervation of the thyrohyoid and sternohyoid muscles comes from the ansa cervicalis which arises from the hypoglossal nerve and 1\textsuperscript{st} cervical spinal nerve with the origin in the hypoglossal nucleus. The 1\textsuperscript{st} spinal nerve and ansa cervicalis also innervate the sternothyroid muscle. Mylohyoid muscle is innervated by the mylohyoid nerve, a part of the mandibular branch of the trigeminal (V) nerve with the origin in the trigeminal motor nucleus.
Laryngeal Assessment during Cough Production

Electromyography (EMG) and manometry

The participation of larynx in cough motor act is demonstrated by the active involvement of the TVFs in all cough phases. The evidence of the TVF activities in cough has been shown based on EMG measures. For example, Poletto et al.\textsuperscript{49} reported activation patterns of all intrinsic laryngeal muscles: PCA, CT, TA, and LCA with respect to adduction and abduction angles of the TVFs. They observed that contractions of PCA were positively correlated with TVF opening, while TA and LCA contractions were correlated with TVF closure in cough. The study of Poletto et al.\textsuperscript{49} showed that in healthy persons, the TVF adductors and tensors are active during cough compression phase, which indicated that TVF adduction preceded the expulsive phase of cough, and PCA was active during the expiratory phase.\textsuperscript{49} This is in agreement with the observation of von Leden & Isshiki\textsuperscript{53} that the dilation of the glottis during the expiratory thrust of cough occurs with active abductor movement.

Further, Hillel\textsuperscript{19} provided a detailed description of EMG pattern of intrinsic laryngeal muscle activation during phonation, respiratory, and glottal tasks, including a single cough, throat clear, and the Valsalva maneuver. According to Hillel\textsuperscript{19}, cough is initiated by the TA, LCA, and IA sphincter-like contraction indicating TVF adduction builds gradually and abruptly stops a few milliseconds prior to the expulsion of air. Shortly before the inactivation of TVF adductors (about 150 msec), the PCA and CT activation results in brief co-contractions of the adductors and abductors. The authors explained that the co-contraction allows “spring loading” of the glottis, so it abruptly opens at the beginning of the expiratory phase when the adductors suddenly become inactive and a substantial amount of air passes through the wide glottal opening.
Following the initial air burst, the abductors’ EMGs become silent, and the adductors demonstrate immediate activation with a quick glottic closure. As a response, the high volume air flowing through the larynx increases its velocity and consequently assists in clearing secretions from the vocal fold surface by generating high shearing forces.\textsuperscript{19}

The degree of glottal closure and tracheal narrowing were investigated by Shaker et al.\textsuperscript{54} who measured intercordal and intratracheal pressures during cough, swallow, strain, and phonation. The average maximum pressure generated by TVF closure during compression phase of cough was 280±20 millimeter of mercury (mmHg), while average maximum intratracheal pressure produced simultaneously was 89±11 mmHg. As the intercordal pressure dropped at the end of compression phase, the intratracheal pressure increase extended to the expiratory phase, potentially throughout the acceleration of expiratory flow.\textsuperscript{54}

**Laryngeal imaging during cough**

Laryngeal contribution to cough, especially the role of the TVFs in modification of cough airflow dynamics, still requires investigation. Recently, laryngoscopy has become a method that allows observation of the TVF movement during inspiratory and expiratory phase in a maximal cough. However, the configuration of the TVFs during a compression phase of a maximal cough in a non-impaired larynx is difficult to detect due to ventricular fold compression and epiglottic occlusion above the TVFs. Observation of TVFs adduction can be possible only during a gentle cough production.\textsuperscript{53}

The study of Britton et al.\textsuperscript{55} was a first attempt to measure TVF kinematics during cough using endoscopic images in healthy individuals. The study analyses focused on glottal angles and TVF adduction and abduction velocities across the cough phases and included observations of the movement patterns of the supraglottic structures during the
compression phase and TVF closure after the expiratory phase for single coughs. Britton et al.\textsuperscript{55} reported that the maximum abduction angles of the TVFs during the expiratory phase were wider in moderate and hard coughs (mean angle = 54.9°, SD=12.9°) than in soft coughs (mean angle = 46.6°, SD=12.9°). Also, the maximum abduction TVF angles during inspiratory phase were wider in female (mean angle = 49.8°, SD=14.3°) than male participants (mean angle = 36.8°, SD=19.3°), however this difference was not statistically significant. The authors observed significantly higher and more variable TVF post-compression abduction velocities with a mean of 996°/s (SD=811°/s) in comparison to the pre-compression adduction velocities (mean velocity=541°/s, SD=309°/s). Although the study of Britton et al.\textsuperscript{55} lacked a consistent protocol for a type of scope (rigid vs flexible), uniform instructions for specific cough type, and a consistent number of trials performed by the participants, the findings provided normative data regarding TVFs kinematics during voluntary cough.\textsuperscript{55}

**Laryngeal interaction with respiratory system**

The phenomenon of glottal closure during cough has been discussed in literature;\textsuperscript{16,17,53} however, disagreements exist regarding its necessity for generating high intrathoracic pressures or airflow rates. For example, Young et al.\textsuperscript{56} observed inconsistency in the relationship between the onset of expiratory flow and the peak of intrathoracic or abdominal pressure in cough. In most analyzed coughs (single and sequential), the peak pressure followed the peak airflow; therefore, Young et al.\textsuperscript{56} speculated that the maximum linear velocity which coincides with peak pressure is generated during the post-peak flow phase (Figure 1-3) but *not* during glottal closure.
The analyses of cough mechanics in persons post-endotracheal intubation or laryngectomy demonstrate that glottal closure was not essential for productive cough.\textsuperscript{8} However, airflow dynamics in coughs with absent or impaired laryngeal activity appeared noticeably different from the coughs produced by healthy persons. For example, Fontana et al.\textsuperscript{8,17} showed that laryngectomized individuals demonstrated significantly lower values of cough volume acceleration (CVA) and longer peak expiratory flow rise time PEFRT compared to healthy controls in maximal voluntary cough (MVC) without significant differences in peak expiratory flow rate (PEFR) values between groups. The differences in the airflow dynamics of cough between groups could not be explained by variances in abdominal muscle activities since the integrated electromyography (IEMG) signals were relatively similar during MVC in controls and patients. Fontana at al.\textsuperscript{8} identified a correlation between PEFR and IEMG related variables within subjects, which indicated the significance of abdominal muscle involvement in generating high PEFRs. It suggests that laryngeal impact may be more significant in regulation of PEFRT, and subsequently CVA, versus the PEFR in voluntary cough.

Further, Ross et al.\textsuperscript{57} argued that glottal closure is a key mechanism for the induction of changes in tracheobronchial lumen size and that these diameter changes differentiate a cough from a forceful expiration. With glottal closure preceding the expiratory phase of the cough, a high initial expiratory pressure can be generated, and, once the glottis is opened, a high pressure gradient across the walls of the trachea and bronchi causes the rapid increase in airflow velocity. Ross et al.\textsuperscript{57} estimated that the linear air velocities in the human trachea with an average cross-section area of 1.5 cm\textsuperscript{2}
and cough volume flow rates of 7 L/sec will reach 46.5 meters/sec (equivalent to a hurricane velocity of 100 miles/hour). As Ross et al.\textsuperscript{57} investigated the effect of pressure applied to the outer wall of a section of human trachea, they found that a trans-wall pressure gradient of 40 cmH\textsubscript{2}O reduced the tracheal cross-section width to about 1/5 its original value. With such reduction of the tracheal lumen, the airflow velocities may reach 520 miles/hour at the narrowed area.\textsuperscript{57} According to von Leden & Isshiki,\textsuperscript{53} cough airflow velocities at the level of the larynx, with the cross-sectional glottal area much smaller than the trachea, are expected to be significantly higher.

Within the respiratory system, two major components identified by Knudson et al.,\textsuperscript{58} as cited in Fontana,\textsuperscript{3} contribute to the initial expiratory flow during cough and forced expiration. One of them is the pulmonary component which represents the flow from the lung parenchyma generated as alveolar pressure becomes greater that mouth pressure. Another, the airway component is defined as the flow produced by rapid displacement of gas volume in the central airways as they undergo dynamic compression due to the increase in pleural pressure acting on their collapsible walls.\textsuperscript{3,58} This airway component is depicted by the transient flow “spike”, a rapid increase, and decrease in expiratory flow. In contrast, cough expiratory dome-shaped flow patterns with absent spikes marking PEFRs may indicate severe laryngeal impairments. Such cough waveform shapes without spikes were also characteristic for patients with laryngectomy in voluntary coughs and coughs evoked by fog inhalation in the study of Fontana et al.\textsuperscript{8} Similar shapes of expiratory flow was observed in patients with motor neuron disease (MND) with bulbar involvement in the study of Chaudri et al.\textsuperscript{59} Neither group, of Fontana et al.\textsuperscript{8} (1999) nor Chaudri et al.\textsuperscript{59} (2002), examined the
airflow dynamics prior to the expulsive phase. Moreover, the study of Chaudri et al.\textsuperscript{59} lacked laryngeal assessment of the study participants to analyze a potential impact of glottal insufficiency on the airflow dynamics in the studied coughs. The absence of spikes in the cough airflow pattern may indicate deficiency of the airway component. It can be further speculated that without glottal closure, these transient spikes in airflow rate may be significantly reduced or even absent.

Modifications of the airway component can be observed in cough expiratory flow produced by persons with endotracheal intubation.\textsuperscript{17} The absence of glottal closure and inability to reduce tracheal lumen during cough reduces cough flow rates and changes the timing of transpulmonary peak pressure build-up. In the study of Gal,\textsuperscript{4} coughs produced by the intubated participants were characterized by the absence of compression phases. Although tracheal intubation did not affect the ability to generate high transpulmonary pressures, time to reach the peak flow rate was prolonged, and the PEFR was reduced. Endotracheal intubation significantly increased the duration of a sequence of three maximal voluntary coughs (from about 1.7 s in the control state to nearly 2.3 s with the tube in place) without significant changes in cough expired volumes. With a fixed tracheal diameter, the calculated velocities were significant lower in all three coughs in the sequence. Gal\textsuperscript{4} suggested that the cough produced by intubated participants resembled forced expiration, a maneuver less effective in airway clearance than cough. The assessment of changes in cough in persons with glottal insufficiency, but with intact ability of narrowing tracheal lumen, will provide evidence of the role of glottal closure in regulating flows rates and duration of maximal voluntary cough.\textsuperscript{4}
Cough airflow and velocities are modified with changes in laryngeal resistance.\textsuperscript{17} Such changes have been calculated by measuring subglottic pressure during cough phases. Yanagihara et al.\textsuperscript{17} obtained simultaneous recordings of flow rate, air volume, subglottic pressure, and acoustic signal of single coughs in healthy adults. Based on their observations, the positive subglottic pressure increased sharply during the compression phase, reached its maximum level (40-50 cmH\textsubscript{2}O) shortly prior to the PEFR, and decreased rapidly to about 0.5 cmH\textsubscript{2}O at the beginning of a post PEFR phase. This pressure increase was as important as the high flow velocity in generating the power to eliminate the foreign materials from the airways. Yanagihara et al.\textsuperscript{17} also argued that, for the effective airway clearance, the balance between the resistance at the level of glottis and the expulsive power is regulated by the larynx. A maximum glottal opening at the beginning of the expiratory phase provides minimum resistance to the airflow and increases power of expulsion. After the initial air burst, the glottis narrows to increase resistance which helps maintain high airflow velocity as the expiratory flow rate is reduced. This action prevents the expelled materials from reentering the lower airways. Yanagihara et al.\textsuperscript{17} suggested that inability to modify laryngeal resistance, especially after the initial air burst, leads to difficulty in expelling secretions, as it may be observed in laryngectomized patients.

Studies have shown that topical anesthesia applied to the upper airway can result in sensory deficits at the laryngeal level and can alter respiratory parameters due to increased laryngeal resistance. Ho et al.\textsuperscript{60} reported that upper airway anesthesia with 2\% and 1.5\% solution lidocaine significantly reduced the peak inspiratory flow rate (PIFR) and forced inspiratory flow between 20\% and 75\% of the maximum inhaled
volume (FIF 25-75) in healthy adults. The lidocaine solution was gurgled and intentionally aspirated by the study participants. Ho et al.\textsuperscript{60} argued that upper airway pressure is subatmospheric during inhalation; therefore, the pharynx and other upper airway soft tissue structures tend to collapse in proportion to the magnitude of the inspiratory effort. Typically, reflexive contractions of pharyngeal dilator muscles reduce collapsible forces and maintain airway stability; however, according to Ho et al.,\textsuperscript{60} these contractions are impaired with laryngeal anesthesia blocking mechanoreceptors in the larynx and pharynx.

Similarly, Liistro et al.\textsuperscript{61} claimed that the activity of upper airway receptors responsible for reducing upper airway collapsing forces are compromised during extensive topical laryngeal anesthesia in healthy adults. In their study, a 10\% lidocaine solution was sprayed four times in the oropharynx and the hypopharynx, and, additionally, 2 ml of a 4\% solution of lidocaine was applied over the vocal folds with a laryngeal syringe. The impact of the upper airway anesthesia was identified by significant reduction in maximum inspiratory flow at 25-75\% of forced vital capacity (FVC) (MIF25-75) and peak expiratory flow (PEF) for about 15 to 35 minutes following the application of the anesthesia.\textsuperscript{61} Moreover, the post-anesthesia flow-volume loop patterns suggested the presence of supraglottal or glottal obstruction. In contrast, Zemlin\textsuperscript{62} reported that topical laryngeal anesthesia did not significantly alter glottal parameters such as: maximum glottal width, glottal length, width of glottis spuria, duration of opening, closing, and closed phases of the vibratory cycle, and glottal area as a function of time during laryngeal motor behaviors including breathing and phonation. Similarly, Sulica et al.\textsuperscript{63} reported no changes in anatomy and gross vocal fold
motion after upper airway anesthesia including 1% lidocaine injections to the larynx bilaterally and to the thyroid notch, 2% lidocaine intratracheal injections, as well as perioral application of 4% lidocaine spray to the larynx and pharynx. Nevertheless, the study showed significant impairments in swallow function, especially premature spillage, pharyngeal residue, and laryngeal penetration of thin liquids and pure, as well as aspiration of thin liquids. According to Sulica et al., deep airway receptors which may serve as proprioceptors to control TVF position or tension are not affected by the topical anesthesia. Local topical anesthesia for the purpose of videolaryngoscopy is applied primarily to reduce discomfort associated with potential touch, pressure and irritation on the mucosal surface of the nasal cavity and nasopharynx. It is possible, that this type of anesthesia effects mainly mechanoreceptors controlling the responses to pressure changes, light touch, and vibration. However, it cannot be excluded that some other receptors are also impacted. The study of Beydon et al. showed an increase in respiratory resistance after 5% lidocaine solution sprayed in a nostril, on the posterior pharyngeal wall, the base of the tongue, the hypopharynx and the larynx and gargled for one minute. During videolaryngoscopic evaluation of two participants, they noticed that TVFs were drawn to the midline and showed vibrations during inspiration suggesting reduced TVF tension. Also, during maximal inspiration, the epiglottis dropped on the TVFs causing complete airway obstruction. However, complete glottal closure was achieved during phonation which was not altered. An important observation made by Beydon et al. was that the participants who demonstrated difficulties in gargling with lidocaine solution showed less effect of anesthesia on respiratory resistance.
Regardless of previous reports of significant effects of upper airway anesthesia on laryngeal function, it is important to highlight the differences in technique for local anesthesia between studies which may explain different results regarding changes in upper airway resistance. For example, Baier et al.\textsuperscript{65} did not find changes in respiratory resistance in healthy participants following an application of 2\% lidocaine sprayed in small amounts at the laryngeal and upper airway level, without gargling. There is no knowledge of the changes in motor behaviors such as voluntary cough and phonation or sensory responses to upper airway stimulation after the topical anesthesia in persons with reduced mobility of the TVFs; therefore, future studies should test an influence of upper airway topical anesthesia on cough and other airway protective behaviors in this patient population.

**Reduced True Vocal Fold Mobility**

**Overview, Etiologies, Symptoms**

Partial or complete limitations of the TVF movement may result from mechanical fixation of one or both TVFs or may occur due to neuropathy affecting the TVFs. Mechanical fixation can be caused by arytenoid dislocation, edema, inflammation, or neoplasm, while the potential neurogenic factors are lesions in the laryngeal motor cortex or the recurrent laryngeal nerve damage.\textsuperscript{66} Reduced or complete restrictions to the TVFs mobility may be unilateral or bilateral. While unilateral hypomobility or immobility of the TVF may cause dysphonia, dysphagia, and/or dyspnea (Klencher et al 1999), or may be asymptomatic due to contralateral TVF compensation, bilateral TVF immobility may result in severe airway obstruction which may require such interventions as intubation and/or tracheostomy.\textsuperscript{66}
Reduced TVF mobility may be caused by joint, muscle, and nerve dysfunction affecting laryngeal function. For example, inflammation developing in the cricoarytenoid joint space as a result of rheumatoid arthritis, gout, trauma, arytenoid cartilage dislocation during endotracheal intubation, laryngeal fracture, and surgical procedures performed in the area of the arytenoid cartilages leads to formation of scar tissue around the joint and reduces the mobility of the cartilage within the affected joint.\textsuperscript{67-71}

Laryngeal muscle dysfunction associated with an autoimmune disorder such as myasthenia gravis, may also cause TVF hypomobility. In this neuromuscular disease, the antibodies attack and destroy the receptors for acetylcholine at the neuromuscular junction.\textsuperscript{72} Consequently, the muscles do not receive signals from the nerves and are unable to produce full contractions. The TVF hypomobility can occur as a consequence of the damage to the muscle membrane from the inflammation which can disrupt the normal transmission of electrical impulses from the nerve through the muscle responsible for TVF movement. Muscle dystrophy occurring from abnormal muscle metabolism can affect the larynx and, if the muscle ultimately becomes atrophic, it becomes week and loses its mass. Atrophic vocal folds characterize in sluggish movement and bowed shape during the attempt to produce glottal closure.\textsuperscript{73-75}

Reduced mobility of the TVFs can be an indicator of vocal fold paresis due to unilateral or bilateral injuries to the RLN, SLN, or both. Those changes may occur also as a result of a neurologic disease such as multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), syringomyelia, GuillainBarre´, and Parkinson disease (PD) or as a consequence of neural injury to the LMC or its projection network to RLN during cerebrovascular accidents.\textsuperscript{76} In addition to laryngeal impairments in these types of
neurologic diseases, respiratory muscle weakness and/or chest wall rigidity impacts the ability to produce effective cough. Therefore, it is challenging to identify the impact of vocal fold dysfunction on cough effectiveness in isolation in these patients.

In the TVF paresis, the neuromuscular deficits are often undetected using videoostrobscopy, and laryngeal electromyography (LEMG) may be the only assessment method to confirm this type of impairment. The most common symptoms of vocal fold paresis are dysphonia, loss of the upper register of the voice, vocal fatigue, hoarseness, breathiness, diplophonia, odynophonia, and/or dysphagia. Laryngoscopic evaluation usually reveals asymmetric TVF (arytenoid) movement, especially hypomobile abduction, unilateral or bilateral TVF bowing, flaccidity of one vocal fold with pitch glides, and/or axial rotation of the larynx on high-pitch phonation, and pitch-locked, false vocal fold phonation. Vocal fold paresis often results in muscle tension dysphonia or vocal fold lesions, such as vocal nodules or contact ulcers/granulomas from compensatory hyperadduction. Instrumental voice assessment findings include abnormal electroglottography (prolonged open phase) and LEMG of the CT and TA muscles tested bilaterally indicating either the RLN or SLN neuropathy.

Vocal fold immobility due to paralysis indicates complete or partial damage to the RLN which may occur with concomitant SLN injury. According to the available reports, most cases (~40%) of the unilateral and bilateral TVF immobility are caused by surgical injuries. Within this etiology, thyroid surgeries cause one third of cases of unilateral TVF immobility (UTVFI) and two thirds of incidents of bilateral TVF immobility (BTVFI). About 20% incidents of UTVFI and 10% of BTVFI are idiopathic, and studies have shown an increase of such cases between 1970 and 2005. Idiopathic vocal fold paralyses often
are suspected to have a viral source, specifically an upper respiratory infection. The next most common etiologies of the TVF immobility are malignancies causing 18% occurrences of UTVFI with two thirds of cases caused by lung malignancies and 14% of BTVF with one third caused by lung malignancy. Intubation leads to BTVFI (13.2%) more frequently than to UTVFI (5.8%). The proportions of cases of UTVFI caused by the thyroid and non-thyroid surgeries have significantly increased between 1970 and 2005. Within the same period, the number of cases of the TVF immobility associated with lung and nonlung malignancies has decreased. The increase in number of idiopathic cases of both UTVFI and BTVFI and those following intubation have been also noted over the period between 1970 and 2005. A small percentage of cases of TVF paralysis occurs as a result of trauma, central nervous system disease, infections, inflammation, radiation therapy, stenosis, aortic aneurism, diabetes, Gerhard syndrome, laryngeal abductor paralysis that may be familial or acquired secondary to bulbar lesions or neurodegenerative disease.

**The Impact of Reduced Vocal Fold Mobility on Airway Protective Mechanisms**

Limited knowledge exists on the subject of the impact of reduced mobility of TVFs on cough effectiveness. Murty et al. measured peak expiratory flow rate (PEFR) and peak expiratory flow rise time (PEFRT) in voluntary cough produced by 10 patients with vocal cord paralysis and in 10 healthy controls. All the patients demonstrated the lateral (cadaveric) position of the paralyzed vocal fold as opposed to the paramedian position. They reported significantly higher PEFRT in the patient group which suggested that glottal insufficiency caused by unilateral TVF immobility influences the time to reach cough peak flow rate.
An injury to the RLN, either unilateral or bilateral, may have a great impact on respiration, phonation, and swallowing. In case of a combination of SLN and RLN damage, laryngeal dysfunction is more significant and results in more severe dysphagia with aspiration. A study of Flint et al. showed that 50% of 100 patients with UTVFI due to RLN or RLN/SLN damage demonstrated dysphagia ranged from mild, to very severe, requiring tube feeding. A prospective study of Bhattacharya et al. testing swallowing function in persons with UTVFI revealed that within the group of 64 participants, 31.3% demonstrated laryngeal penetration and 23.4% showed aspiration of thin liquid during videofluororoscopic swallow evaluation. Most of the laryngeal penetration occurrences were observed during swallow. However, about 50% of the patients demonstrated post-swallow aspiration of the bolus remaining in the hypopharynx. In their study, no evidence of decreased tongue base or reduced pharyngeal wall movement was found; therefore, dysphagia was most likely caused by incomplete glottal closure and consequently persistent open airways. The negative pressure necessary for pharyngeal clearance was insufficient and caused the residue in the vallecular and piriform recesses and aspiration immediately following post-swallow inhalation. It indicates that, with UVFP, the positive pressure generation for ejection of the aspirated or endogenous materials will be also reduced due to incomplete glottal closure, and expulsive force of expiratory flow in cough will be reduced.

**Specific Aims and Hypotheses**

Simultaneous measurements of cough airflow and vocal fold kinematics during voluntary cough are an emerging method of cough assessment with particular interest of on the laryngeal contribution to cough. However, no outcomes of laryngoscopic and
airflow assessment involving persons with unilaterally reduced TVF mobility have been reported to date.

The primary goal of this study was to examine the airflow parameters and TVF kinematics in voluntary cough in individuals with glottal insufficiency associated with reduced vocal fold mobility (Table 1-1)

**Specific Aim 1**

To determine the influence of the degree of the glottal closure measured by the Glottal Closure Rating Scale (GCRS) score on the TVF abduction and adduction angles and cough airflow measures in single and first two coughs (C1, C2) of sequential cough epochs.

**Hypothesis 1**

Coughs produced by patients with higher (more severe) GCRS scores will be produced with greater pre-compression adductor angles, shorter CPDs, lower values of PEFR, longer PEFRT, and lower values of CVA in all cough types.

**Specific Aim 2**

- 2a. To determine the relationships between cough airflow measures and TVF angles in single voluntary coughs and the first two (C1, C2) voluntary sequential coughs generated by participants with reduced vocal fold mobility.
- 2b. To examine the differences in the TVF angles and cough airflow parameters between single and sequential coughs and between C1 and C2 within one cough sequence.

**Hypothesis 2a**

The lower values of TVF abduction angles before the onset of the compression phase will be associated with longer inspiratory phase durations (IPD) of all each cough type. Coughs with greater values of maximum pre-compression TVF adduction angles will be produced with shorter compression phase durations (CPD). Coughs generated
with lower values of the maximum TVF abduction angles following the compression phase will show lower values of peak expiratory flow rate (PEFR), longer peak expiratory flow rise time (PEFRT), and lower cough volume acceleration (CVA). Such coughs will also be produced with longer expiratory phase durations (EPD) and lower cough expired volumes (CEV).

**Hypothesis 2b**

There will be significant differences between airflow measures of the second sequential cough (C2) as compared to the single cough, and first sequential cough (C1). Specifically, there will be reduced values of CPD, PEFR, CVA, and CEV and longer PEFRT in for the C2 coughs. As well, the TVF abduction and adduction angles will be significantly reduced in C2 of a sequential cough versus single cough and C1 of a sequential cough. There are no expected differences in airflow or TVF angles between the single cough and C1.
Figure 1-1. Cough phases marked on the cough waveform.
Figure 1-2. Cough expiratory flow and integrated electromyographic (IEMG) activities of abdominal muscles produced by a healthy control (left panels) and a laryngectomized patient (right panels) during maximal voluntary coughing (upper panels), reflex cough at threshold stimulus intensity (middle panels), and cough at suprathreshold stimulus intensity (lower panels).
Figure 1-3. Variable relationships between the rise in thoracic and abdominal pressures at the start of the main expulsive flow during single coughs in normal female subject. Traces from above: time in seconds, sound, flow (expiration upwards), thoracic (esophageal) pressure and abdominal pressure. Vertical lines identify equal time points.56
Table 1-1. Specific aims, outcome measures, and corresponding statistical tests.

<table>
<thead>
<tr>
<th>Aim</th>
<th>Primary Outcome Measures</th>
<th>Statistical test</th>
</tr>
</thead>
</table>
| 1. To determine the influence of the degree of the glottal closure measured on the abduction and adduction TVF angles and cough airflow measures in single and first two coughs (C1, C2) of sequential cough epochs. | 1. Dependent variable: Glottal Closure Rating Scale score  
   Angle measures: Pre-Compression abduction  
   Post-Compression Abduction  
   Cough airflow measures: IPD, CIV, CPD, PEFR, PEFRT, CVA, CEV, EPD | 1. Simple linear regression model |
| 2a. To determine the relationships between cough airflow measures and TVF angles in single voluntary coughs and the first two (C1, C2) voluntary sequential coughs generated by participants with reduced vocal fold mobility. | 2a. and 2b.  
   Angle measures: Pre-Compression abduction  
   Pre-Compression adduction  
   Post-Compression abduction  
   Cough airflow measures: IPD, CIV, CPD, PEFR, PEFRT, CVA, CEV, EPD | 2a. Pearson’s r correlation coefficients |
| 2b. To examine the differences in the TVF angles and cough airflow parameters between single and sequential coughs and between C1 and C2 within one cough sequence. | 2b. Repeated measure ANOVA (within subject cough type) |
CHAPTER 2
METHODS

Participants

The participant group consisted of 15 adult patients of the University of Florida Health ENT Clinic, Gainesville, FL diagnosed with vocal fold insufficiency due to reduced mobility of one true vocal fold.

Inclusion criteria:

1. Age between 18 and 85 years.
2. Glottal insufficiency secondary to reduced TVF mobility confirmed with the endoscopic evaluation performed by an otolaryngologist.
3. The ability to provide informed consent.
4. No history of severe chronic obstructive pulmonary disease, lung cancer, and/or lung transplant.
5. No history of neurodegenerative disease such as Parkinson’s disease (PD), multiple sclerosis (MS), amyotrophic lateral sclerosis (ALS), or progressive supranuclear palsy (PSP), Alzheimer’s disease, or dementia.
6. No chest infection within one month prior to the study participation.

The study was approved by the Institutional Review Board at the University of Florida (IRB201400733), and all participants provided verbal and written informed consent. The study was completed in the UF Health ear nose and throat (ENT) Clinic, Gainesville, FL. Participants’ demographic information included age, gender, race/ethnicity, height, weight, and a major complaint (dysphonia and/or dysphagia). Participant’s medical and surgical history as well as the diagnosis and the etiology of reduced vocal fold mobility were obtained from the participant’s medical record. Lastly, pulmonary function measures were obtained in order to rule out severe pulmonary dysfunction in these participants.
Procedures

Baseline Measures of Respiratory Function

Spirometry assessment

Pulmonary function testing was completed following the endoscopic evaluation using a pneumotachometer (ADInstruments, Inc.) connected with PowerLab 16/30 data acquisition hardware. Participants were seated upright, and a nose clip was used to prevent air escape through the nose. Flow volume flow-volume loop were obtained by directing participants to breathe through a filtered mouth piece attached to the pneumotachometer flow head. Participants performed normal tidal breathing into the mouthpiece connected to the spirometer for 5-10 seconds. After the tidal breathing period and at the end of a tidal expiration, the participant was instructed to inhale as deeply and as quickly as possible and then exhale as quickly as possible until they ran out of air. At least two but no more than five trials were completed.

The resulting flow-volume loop allowed for calculation of respiratory airflow in liters per second (L/s) as it relates to lung volume in liters (L) during maximal inhalation from complete exhalation to residual volume (RV) and during maximum exhalation from complete inhalation to total lung capacity (TLC).

The following measures were obtained: peak expiratory flow (PEF), forced vital capacity (FVC) in L, forced expired volume within 1 second (FEV1) in L, and the ratio FEV1/FVC in percent (%). The average value of the measurements was calculated for data analysis and was expressed in % predicted based on an individual's age, height, sex, and race/ethnicity. The spirometry airflow recordings were displayed, stored, and analyzed using LabChart software for Windows.
**Maximum expiratory pressure (MEP) and maximum inspiratory pressure (MIP) measurement**

Hand-held portable respiratory pressure meter (manometer) was used to assess the participant’s maximum expiratory pressure (MEP) and maximum inspiratory pressure (MIP). These are indirect measures of expiratory and inspiratory muscle strength respectively. The measurements were performed with a participant in the upright seated position. Nose clips were used to prevent air leak during the task.

During MEP measurement, a participant performed a deep inhalation to TLC, and then produced forceful exhalation into a filtered mouthpiece connected to the manometer tube. The participant was instructed to blow into the mouthpiece as fast and as hard as possible. The task was repeated at least three times, but no more than ten times. A mean of three highest MEP values differing by 5% or less was calculated and recorded for further analysis.

For MIP measurement, the participant exhaled to remove as much air from the lungs as possible and performed a forceful inhalation through the filtered mouthpiece of the manometer. The task was repeated at least three times, but no more than ten times. A mean of three highest MIP values differing by 5% or less was calculated and recorded for further analysis. MEP and MIP values were expressed in cmH2O.

**Laryngoscopic Procedure and Study Tasks**

Laryngoscopy and voluntary cough airflow recordings were completed in conjunction with a clinical evaluation visit. Videolaryngoscopy was performed as part of standard clinical care using the KayPentax EPK 700 digital work station. For the evaluation, the patient was seated in an examination chair. Following the clinical protocol, the nasal decongestant spray (Afrin) and topical anesthetic (4% Lidocaine
Hydrochloride solution) were applied to nasal cavities bilaterally. The flexible endoscope, connected to a light source and a video camera, was inserted into through the nostril and to the nasopharynx until the vocal folds were visible.

**Sniff-phonation**

With the flexible endoscope in nasopharynx, participants produced the vowel /i/ at a comfortable pitch and loudness level, and sustained it for three seconds. Next, the participant produced three repetitions of a sniff followed by a short /i/ vowel. The vocal fold image during a vowel and /i/-sniff pattern production was recorded for further analysis of the degree of glottal closure for phonation. The degree of glottal closure was assessed using Glottal Closure Rating Scale (GCRS) (Appendix). 84

**Cough assessment**

Vocal fold images and cough airflow were recorded simultaneously during voluntary cough production with the flexible endoscope in the nasopharynx. Cough airflow samples were obtained using a pneumotachometer (ADInstruments, Inc.) connected with PowerLab 16/30 data acquisition hardware. A disposable filtered mouthpiece attached to the pneumotachometer flow head was placed in the participant’s mouth with the lips sealed tightly around mouthpiece. Each participant produced 1) a single strong cough following the instruction to “take a deep breath and produce one hard cough” and 2) a strong cough bout following the instruction to “take a deep breath and cough hard a few times”. If a participant expressed difficulty with completing a sequential cough, the investigator demonstrated the cough pattern, and the participant was asked to repeat the task. Cough tasks was repeated up to four times to ensure an adequate view of vocal fold movements during cough.
Video images of the vocal fold movement during vowel phonation and cough production were recorded and stored on a CD for later analysis. The cough airflow recordings were displayed, stored, and analyzed using LabChart software for Windows.

Data Analysis and Outcome Measures

Cough Sample Selection Criteria

Among strong coughs completed by the participants, one single and one sequential cough were selected for the analysis. This approach was based on the method used by Britton et al.55 and allowed direct and specific comparison of the simultaneously produced cough airflows and TVF angles. These specific relationships would have been distorted had the data been averaged across trials. For the sequential coughs, regardless of the number of coughs in the sequence, two first coughs (C1, C2) were analyzed. If more than one cough of each type was produced, the primary criterion for selection was the highest PEFR value, and the secondary criterion was the adequate view of the TVFs during cough. If only sequential coughs were produced, C1 of the first available cough sequence which met the primary criteria was analyzed as a single cough. When a participant was not able to produce a cough sequence, a second single cough produced was analyzed as a C1 of a sequential cough and the measures of C2 for this participant was considered missing.

TVF Kinematic Measures

In order to assess TVF kinematics during cough tasks, the TVF abduction and adduction angles were measured. Prior to the TVF angles analysis, video clips containing the TVF images during selected coughs were prepared using Movie Maker software for Windows, stored as bitmap files, and converted to a sequence of frames with the rate of 30 frames per second. The duration of a cough video sample
corresponded to the duration of cough waveform which was determined by measuring the segment of the cough waveform between the onset of the inspiratory phase and the termination of the expiratory phase of cough. Matlab software was used for frame-by-frame image processing and computations using a customized algorithm following the method used by Britton et al. The TVF angle was marked between two segments connecting a vocal process on each TVF with one point on anterior commissure (Figure 2-1). The measurements were completed for each consecutive frame of cough. In cases when the view of anterior commissure was partially obscured by the epiglottis, but more than 50% of the TVF segments were visible, the angles were formed by the lines marking vocal processes of the TVFs and extending along the TVFs, down to the point of intersection. If more than 50% of the TVF image was obscured by the suprabglottic compression or inadequate lightning, the angles were not obtained and the note was provided to report the problem. The TVF angle values and corresponding notes for each analyzed frame were entered and stored in Excel file.

A maximal pre-compression TVF abduction angle corresponded to maximal TVF opening prior to compression phase of an analyzed cough. A maximal post-compression TVF abduction angle was equivalent to maximum abduction of the TVFs during the expiratory phase of a maximal cough. A pre-compression TVF adduction angle was measured during a maximal TVF adduction viewed prior to supraglottic compression which blocked the TVF view during compression phase of a maximal cough. The values of the TVF angles from one single and two first coughs (C1, C2) of one cough sequence were used for the analysis and these values are reported in degrees (°) (Table 2-1).
**Voluntary Cough Airflow Analysis**

All cough airflow recordings were displayed, stored, and analyzed using LabChart software. Cough airflow signals were low-pass filtered at 50 Hz. The following cough airflow parameters for each single cough and the first two coughs in the cough epoch (C1, C2) analyzed: inspiratory phase duration (IPD) in seconds (s), cough inspired volume (CIV) in liters (L), compression phase duration (CPD) in seconds (s), peak expiratory flow rate (PEFR) in liters per second (L/s), peak expiratory flow rise time (PEFRT) in seconds (s), expiratory phase duration (EPD) in seconds (s), and cough expired volume (CEV) in liters (L). Cough volume acceleration (CVA) was calculated from the ratio: PEFR/PEFRT and expressed in liters per second per second (L/s/s). The values of the airflow parameters used for the analysis were calculated separately for a single cough and C1 and C2 of a sequential cough (Figure 2-2).

**Inter-Rater and Intra-Rater Reliability**

For the assessment of inter-rater and intra-rater reliability, the values of the pre-compression TVF abduction angles, the pre-compression TVF adduction angles, and the TVF post-compression abduction angles were reported by the primary author and a student-assistant for three randomly selected participants (2, 3, and 13). The TVF angles were assessed for one single and two consecutive coughs (C1 and C2) of cough sequences. A total number of nine maximal pre-compression TVF abduction angles, nine maximal pre-compression TVF adduction angles, and eight post-compression TVF abduction angles were reevaluated. A post-compression TVF abduction angle of C1 of a sequential cough produced by participant 2 was not assessed due to inadequate view of the TVFs. The intra-rater reliability test was competed using ratings completed twice, with at least 24 hours between the rating sessions, by the primary author.
Statistical Analyses

All the statistical tests for the current study were performed using IBM SPSS Statistics 22.0 software. Descriptive statistics were used to report participants’ demographic characteristics, airflow parameters values, TVF angles, MEP, and pulmonary function assessment values. For the assessment of inter-rater and intra-rater reliability based on absolute agreement, the 2-way mixed model intraclass correlation coefficients were used. To examine the associations between the cough airflow measures and the maximum TVF angles, the authors employed Pearson’s correlation test. To examine differences between cough airflow parameters and maximum abduction and adduction TVF angles between the three cough types produced (single, C1, and C2), a repeated measure ANOVA was applied with within subjects factor cough type. To determine the relationship between degree of glottal insufficiency and the abduction and adduction TVF angles, a linear regression model was employed. The differences between subgroups were assessed with on-way ANOVA and Mann-Whitney U test for independent groups. The significance level was set at p<0.05.
Figure 2-1. True vocal fold (TVF) angle measured between a line segment connecting anterior commissure with a right TVF vocal process and a line segment connecting anterior commissure with a left TVF vocal process.
Figure 2-2. Cough airflow measures. IPD=inspiratory phase duration; CIV=cough inspired volume; CPD=compression phase duration; PEFR=peak expiratory flow rate; PEFRT= peak expiratory flow rise time; CEV=cough expired volume; C1, C2 = a first and a second cough in the epoch respectively; EPD = expiratory phase duration.
Table 2-1. The study outcome measures.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Name</th>
<th>Description</th>
<th>Unit</th>
</tr>
</thead>
<tbody>
<tr>
<td>Airflow</td>
<td>IPD</td>
<td>Inspiratory Phase Duration</td>
<td>seconds(s)</td>
</tr>
<tr>
<td>Airflow</td>
<td>CIV</td>
<td>Cough Inspired Volume</td>
<td>liters (L)</td>
</tr>
<tr>
<td>Airflow</td>
<td>CPD</td>
<td>Compression Phase Duration</td>
<td>s</td>
</tr>
<tr>
<td>Airflow</td>
<td>PEFR</td>
<td>Peak Expiratory Flow Rate</td>
<td>L/s</td>
</tr>
<tr>
<td>Airflow</td>
<td>PEFRT</td>
<td>Peak Expiratory Flow Rise Time</td>
<td>s</td>
</tr>
<tr>
<td>Airflow</td>
<td>EPD</td>
<td>Expiratory Phase Duration</td>
<td>s</td>
</tr>
<tr>
<td>Airflow</td>
<td>CEV</td>
<td>Cough Expired Volume</td>
<td>L</td>
</tr>
<tr>
<td>Airflow</td>
<td>CVA</td>
<td>Cough Volume Acceleration (PEFR/PEFRT)</td>
<td>L/s/s</td>
</tr>
<tr>
<td>TVF Angles</td>
<td>PreComAbd</td>
<td>Pre-Compression Maximum TVF Abduction Angle</td>
<td>degree (°)</td>
</tr>
<tr>
<td>TVF Angles</td>
<td>PreComAdd</td>
<td>Pre-Compression Maximum TVF Adduction Angle Prior To</td>
<td></td>
</tr>
<tr>
<td>TVF Angles</td>
<td></td>
<td>Supraglottal Compression</td>
<td></td>
</tr>
<tr>
<td>TVF Angles</td>
<td>PostComAbd</td>
<td>Post-Compression Maximum TVF Abduction Angle</td>
<td></td>
</tr>
</tbody>
</table>
CHAPTER 3
RESULTS

Demographic Characteristics

Fifteen participants (9 females, 6 males), ages 44-80 years with the diagnosis of reduced mobility or complete immobility of one TVF were recruited from the Ear, Nose, and Throat Clinic at the University of Florida, Gainesville, FL. Demographic information of each participant obtained from the medical record, clinical exam, and the questionnaire is in Table 3-1.

All the participants completed respiratory function test including maximum respiratory pressure measurements. Table 3-2 shows the percentages of the predicted normal values of respiratory function test outcomes. Seven participants had a FEV1/FVC ratio less than 0.80, indicating an obstructive pattern. Of those, five had a FEV1 % predicted below 50% and 2 were between 50 and 65%, indicating severe and moderate obstruction, respectively.

Primary Outcomes

TVF Angles and Airflow Parameters

Cough airflow and laryngeal images during cough were recorded simultaneously for all 15 participants. In 2 participants, it was not possible to view the TVFs during the cough tasks. Thus, this data is reported for 13 of 15 participants (Table 3-3). Two participants (4, 8) produced only single coughs and two participants (11, 12) produced only sequential coughs. Out of 13 participants who produced sequential coughs, 6 participants were able to generate cough sequences following single inhalations, and 7 produced bouts of coughs separated by short inhalations (Figures 3-1, 3-2). The
descriptive statistics for cough airflow parameters classified by the cough type (single, sequential) is presented in Table 3-4.

**Intra-Rater and Inter-Rater Reliability**

The inter-rater intraclass correlation coefficient for pre-compression TVF abduction angles was 0.99 with 95% confidence interval (CI) [0.96, 0.99], for pre-compression TVF adduction angles was 0.98, 95% CI [0.92, 0.96], and for post-compression TVF abduction angles was 0.99, 95% CI [0.99, 1.00].

The intra-class correlation coefficient for pre-compression TVF abduction angles was 0.97, 95% CI [0.87, 0.99], for pre-compression adduction angles was 0.97, 95% CI [0.87, 0.99], and for post-compression TVF abduction angles was 0.99, 95% CI [0.96, 0.99].

**The Effect of Glottal Insufficiency on Cough Airflow Measures and TVF Angles**

A simple linear regression was calculated to predict the influence of the degree of the glottal closure measured by the Glottal Closure Rating Scale (GCRS) score on the abduction and adduction TVF angles and cough airflow measures in single and first two coughs (C1, C2) of sequential cough epochs.

The degree of glottal closure was significantly associated with CPD in single coughs, F(1, 13)=15.20, p=0.002, B=-0.055, Beta=-0.73, with R²=0.73 (adjusted R²=.50). In addition, the results show a significant association between degree of glottal closure and the pre-compression maximum adduction TVF angles in C1 of sequential coughs, F(1, 10)=6.79, p=0.026, B=3.023, Beta=0.64, with R²=0.40 (adjusted R²=0.35). According to these results, the model explained 40% of the variance of the pre-compression maximum adduction TVF angles in C1 of sequential coughs. There was
not a significant relationship between adduction and abduction angles and degree of
glottal insufficiency for C2 coughs.

**Association between TVF Angles and Cough Airflow Parameters**

There was a significant, positive correlation between maximum pre-compression
TVF abduction angles and expiratory phase durations (EPD) \((r=0.56, p=0.047)\) and
between maximum post-compression TVF abduction angles and EPD in single coughs
\((r=0.76, p=0.003)\). In addition, there was a negative, significance approaching,
association between maximum pre-compression TVF abduction angles and
compression phase durations (CPD) \((r=-0.55, p=0.05)\) and significant, negative
correlation between maximum post-compression TVF abduction angles and CPD in C1
of sequential coughs \((r=-0.65, p=0.024)\). No significant correlations were identified
between the pre-compression maximum adduction TVF angles and cough airflow
parameters in any of the analyzed cough tasks.

**Differences between Cough Types**

Results of the RMANOVA showed that pre-compression TVF abduction angles
were significantly different in C1 and C2 of the sequential coughs, \(F(1, 9)=5.86, p=0.04\).
No significant differences in the maximum pre-compression TVF adduction and the
maximum post-compression abduction angles and cough airflow measures were
identified between the three cough types.

**Post-Hoc Analyses**

**Differences between Participants Grouped According To the Glottal Closure
Rating Score**

The post-hoc analysis was completed to further explore the effect of glottal
insufficiency on the cough airflow and TVF angles during cough. Based on the Glottal
Closure Rating Scale (GCRS) scores, 6 participants received score 1 which indicated the ability of complete glottal closure in phonation, and 9 participants demonstrated various degrees of glottal insufficiency during phonation with the GCRS scores between 2 and 6. The post-hoc analysis was performed to assess the differences in demographic characteristics, cough airflow parameters, and TVF angles between the group of participants who were able to complete glottal closure during phonation and the group of participants who demonstrated incomplete glottal closure during phonation. One-way ANOVA was employed to assess the differences between the two groups.

There were no significant differences between two groups in demographic characteristics. Significant differences were identified in cough airflow measures and TVF angles in single and sequential coughs. In single cough, there were significant differences in CPD (F(1) =18.72, p=0.001) with the mean values of CPD=0.376 s for the participants with the GCRS=1 and the mean CPD=0.132 s for the participants with the GCRS>1. There were differences in TVF angles in single coughs between groups which approached significance, specifically in the values of pre-compression TVF abduction angles (F(1) =4.52, p=0.057) and the values of pre-compression TVF adduction angles (F(1) =4.35, p=0.061) in single coughs. The mean values of the pre-compression TVF abduction angles and the pre-compression TVF adduction angles of single coughs in the group with the GCRS=1 were lower (29.91° and 3.60°) than the values of those angles for the group with the GCRS>1 (43.91° and 14.41°) respectively. Significant differences between groups were also found in pre-compression TVF adduction angles in C1 (F(1) =8.91, p=0.01) and C2 (F(1) =5.69, p=0.04) of a cough sequence. The mean values of the pre-compression TVF adduction angles for the group with the GCRS=1 in
C1 (4.33°) and C2 (2.92°) were lower than the mean values of the pre-compression TVF adduction angles for the group with the GCRS>1 in C1 (18.04°) and C2 (14.98°).

**Differences between Participants Grouped According To the Sequential Cough Production**

Within the group of 15 participants, there were 9 participants who did not generate the sequential cough as a single cough bout, but instead inhaled between C1 and C2 or produced one cough at the time (Figures 3-1, 3-2). As such, we completed a post-hoc analysis in order to determine whether this difference affected the TVF angles or the cough airflow in single and sequential coughs, and whether this difference was related to the degree of glottal insufficiency. A one-way ANOVA was used to compare the maximum abduction and adduction TVF angles and cough airflow parameters in single coughs and C1 and C2 of a cough sequence between the groups. There was significant differences between groups in IPD (F(1) =6.01, p=0.029), PEFR (F(1)=5.80, p=0.032), and PEFRT (F(1)=5.55, p=0.035) of a single cough. For sequential coughs, there was a significant difference in IPDs of C1 (F(1)=5.16, p=0.041) between the two groups. Mean values and standard deviations of IPDs of single coughs and of PEFR and PEFRT of C1 of a cough sequences are shown in Table 3-5.

Mann–Whitney U test was performed to assess the differences in the degree of glottal insufficiency between the groups with the 2 sequential cough patterns (no inhale, versus inhale, between C1 and C2). There was a significant difference in the median of the glottal insufficiency rating score ((GCRS), U= 8, p=0.019) between the two groups with the median GCRS=1 for a group producing cough sequence without additional inhalation and the median GCRS=5 for the group which produced coughs with additional inhalations between C1 and C2 of the sequential cough bouts.
Table 3-1. Demographic information of each participant obtained from the medical record, clinical exam, and the questionnaire completed by each participant.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (y)</th>
<th>Gender</th>
<th>Race</th>
<th>TVF Diagnosis</th>
<th>Etiology</th>
<th>Duration (y)</th>
<th>Glottal Closure</th>
<th>Affected TVF</th>
<th>Dysphagia</th>
<th>Dysphonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>64</td>
<td>F</td>
<td>W</td>
<td>paresis</td>
<td>idiopathic</td>
<td>&lt;1</td>
<td>5</td>
<td>R</td>
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<td>R</td>
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<td>Yes</td>
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<tr>
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<td>1</td>
<td>L</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Y=years, F=female; M=male; A-A=African-American, W=white; L=left, R=right
Table 3-2. The percentage of the predicted (%pred) of normal values respiratory function test outcomes.

<table>
<thead>
<tr>
<th>Participant Number</th>
<th>MIP (%pred)</th>
<th>MEP (%pred)</th>
<th>PEF (%pred)</th>
<th>FEV1/FVC (%pred)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>91</td>
<td>101</td>
<td>46.9</td>
<td>71.4</td>
</tr>
<tr>
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<td>80</td>
<td>79</td>
<td>82.7</td>
<td>108.1</td>
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<tr>
<td>3</td>
<td>72</td>
<td>143</td>
<td>46.1</td>
<td>66.3</td>
</tr>
<tr>
<td>4</td>
<td>303</td>
<td>101</td>
<td>68.6</td>
<td>72.4</td>
</tr>
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<td>86</td>
<td>53.9</td>
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</tr>
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<td>107</td>
<td>81</td>
<td>65.1</td>
<td>102.1</td>
</tr>
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<td>7</td>
<td>107</td>
<td>82</td>
<td>64.7</td>
<td>115.2</td>
</tr>
<tr>
<td>8</td>
<td>82</td>
<td>67</td>
<td>37.5</td>
<td>56</td>
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<td>9</td>
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</tr>
<tr>
<td>15</td>
<td>68</td>
<td>81</td>
<td>47.2</td>
<td>83.5</td>
</tr>
</tbody>
</table>

Mean 124.9  90.0  60.6  86.2
Median 107.0  86.0  58.0  83.5
Std. Deviation 61.6  20.7  24.3  22.8
Minimum 68.0  63.0  26.4  47.5
Maximum 303.0  143.0  114.8  118.9
Table 3-3. Maximum abduction and adduction true vocal fold (TVF) angles in single and the first (C1) and the second (C2) cough of a cough sequence.

<table>
<thead>
<tr>
<th>Cough Type</th>
<th>TVF Angle Degree(°)</th>
<th>Pre-compression Abduction Angle (°)</th>
<th>Pre-compression Adduction Angle (°)</th>
<th>Post-compression Abduction Angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>C1</td>
<td>C2</td>
<td>C1</td>
</tr>
<tr>
<td>Mean</td>
<td>38.53</td>
<td>39.25</td>
<td>32.75</td>
<td>10.25</td>
</tr>
<tr>
<td>Median</td>
<td>41.11</td>
<td>41.24</td>
<td>30.54</td>
<td>8.76</td>
</tr>
<tr>
<td>Minimum</td>
<td>16.04</td>
<td>14.23</td>
<td>13.36</td>
<td>0.00</td>
</tr>
<tr>
<td>Maximum</td>
<td>61.35</td>
<td>60.44</td>
<td>60.87</td>
<td>32.12</td>
</tr>
</tbody>
</table>
### Table 3-4. Cough airflow parameters.

<table>
<thead>
<tr>
<th>Cough Task</th>
<th>Single Cough</th>
<th>First Cough (C1) of a Cough Sequence</th>
<th>Second Cough (C2) of a Cough Sequence</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IPD</td>
<td>CIV</td>
<td>CPD</td>
</tr>
<tr>
<td>Mean</td>
<td>1.08</td>
<td>0.80</td>
<td>0.24</td>
</tr>
<tr>
<td>Median</td>
<td>0.90</td>
<td>0.55</td>
<td>0.27</td>
</tr>
<tr>
<td>Std. Deviation</td>
<td>0.69</td>
<td>0.70</td>
<td>0.16</td>
</tr>
<tr>
<td>Range</td>
<td>2.66</td>
<td>2.14</td>
<td>0.50</td>
</tr>
<tr>
<td>Minimum</td>
<td>0.25</td>
<td>0.02</td>
<td>0.00</td>
</tr>
<tr>
<td>Maximum</td>
<td>2.90</td>
<td>2.17</td>
<td>0.50</td>
</tr>
</tbody>
</table>
Table 3-5. Mean and standard deviation values of cough parameters produced by participants who generated sequential coughs without additional inhalations between C1 and C2 (Group 1) and participants who produced coughs with an additional inhalations between C1 and C2 of a cough sequence (Group 2).

<table>
<thead>
<tr>
<th>Airflow Measures</th>
<th>Group 1 Mean (SD)</th>
<th>Group 2 Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single Cough IPD (s)</td>
<td>0.59 (0.44)</td>
<td>1.38 (0.74)</td>
</tr>
<tr>
<td>PEFR (L/s)</td>
<td>2.16 (0.73)</td>
<td>3.81 (1.68)</td>
</tr>
<tr>
<td>PEFRT (s)</td>
<td>0.05 (0.03)</td>
<td>0.11 (0.05)</td>
</tr>
<tr>
<td>Sequential Cough (C1) IPD</td>
<td>0.87 (0.28)</td>
<td>1.34 (0.48)</td>
</tr>
</tbody>
</table>
Figure 3-1. An example of a waveform of a cough sequence produced without an additional inhalation between C1 and C2 (Subject 15).
Figure 3-2. An example of a waveform of a cough sequence produced with an additional inhalation between C1 and C2 (Subject 1).
CHAPTER 4
DISCUSSION

The current project was the first one to apply TVF imaging and cough aerodynamic measures to evaluate the impact of TVF incompetence on cough function in persons with reduced mobility of one true vocal fold (TVF).

Primary Findings

Glottal Closure

The study’s results showed that the degree of glottal closure assessed using glottal closure rating scale (GCRS) during phonation has significant effect on the pre-compression adduction angles in the first coughs of the cough sequence and CPD in single coughs. Specifically, the participants with greater glottal insufficiency initiated coughs with greater TVF adduction angles viewed immediately prior to supraglottic compression and had shorter CPDs in maximal coughs. This outcome supports the a priori hypothesis that degree of glottal insufficiency would influence pre-compression TVF adduction angles and CPD of cough. The impact of glottal insufficiency on cough function is partially in agreement with the observation reported by Chellini et al.\textsuperscript{85} in voluntary coughs produced by patients after partial laryngectomy. The comparison analysis of cough airflow produced by the group of 10 men pre and post supracricoid laryngectomy with cricohyoidopexy showed statistically significant changes including decreases in PEFR, CVA, CPD, and an increase in PEFRT two months after the surgery with no significant changes in maximum expiratory pressure (MEP). This report and our study findings suggest that laryngeal deficits have an impact on cough motor pattern despite no indication of impairment in expiratory muscle function.
Based on our study outcomes, it can be proposed that the assessment of the degree of glottal closure during phonation may provide important insight to the evaluation of cough function and overall assessment of airway protection in persons with glottal insufficiency.

**Relationship between Angles and Cough Airflow**

This study results support our hypothesis that the abduction TVF angles produced during cough in our participant group would be associated with cough compressive and expiratory durations. However, we did not identify direct relationships between the TVF kinematics and cough inspired and expired volumes, peak expiratory flow rate (PEFR), peak expiratory flow rise time (PEFRT), or cough volume acceleration (CVA). Single coughs and C1 of sequential coughs produced with greater pre-compression abduction angles were generated with longer EPDs but shorter CPDs. Similarly, the coughs produced with greater post-compression abduction angles were also produced with longer EPDs and shorter CPDs in both the single coughs and in C1 of sequential coughs. These outcomes suggest that the abduction TVF angles can influence the durations of compressive and expiratory phases of cough in persons with reduced mobility of one TVF. The TVF pre-compression adduction angles were not associated with cough-related airflow measures. It is not surprising since these angles were measured immediately prior to supraglottic occlusion which later obscured the view of the TVFs during compression phase. Cough compression phases observed during our study were initiated with either complete or incomplete adduction of the TVFs followed by ventricular vocal fold adduction with simultaneous epiglottic inversion and anteroposterior supraglottic compression in a sphincter-like fashion. It has been shown that the compression phase begins with activation of TVF adductors increasing over
approximately 400 milliseconds (msec) and it is followed by concurrent activity of the
adductors and abductors over the last 150 msec of the compression phase.\textsuperscript{19} During
this later period, subglottal pressure increases below the closed glottis. It is possible
that, in patients with reduced vocal fold mobility, regardless of the initial adduction of the
TVFs and ventricular vocal folds, adductor-abductor co-contractions do not occur in a
typical manner, leading to premature abduction of the TVFs and reduction of CPD.

Our findings also indicate that with a greater distance between the impaired and
the healthy TVF during abduction, an attempt of the TVFs adduction may be less
effective due to inability of the affected TVF to medialize, and consequently, a weaker
valving system may be produced by the TVF adduction during compression phase of
cough. To support this interpretation, it’s important to mention that there were 3
participants who produced at least one cough without supraglottic occlusion and these
coughs did not involve TVF closure. The values of CPDs of these coughs were between
0 s and 0.02 s and were the lowest in the entire participant group. Coughs produced
without glottal and supraglottal closure resemble forceful exhalations which are less
powerful airway clearing mechanisms. The impairment of supraglottic closure during
cough may suggest dysfunction of the false vocal folds (FVFs) adduction during cough.
It has been shown that lesions of recurrent laryngeal nerve do not impact the adductor
movement of the FVFs,\textsuperscript{51} therefore, other factors interrupting the adductory movement
of the FVFs during cough should be investigated.

Cough is a short but powerful respiratory behavior and involves complex
changes in respiratory and laryngeal subsystems, and modification of cough airflow
requires immediate changes in laryngeal resistance.\textsuperscript{19,54} In unilateral TVF
paralysis/paresis, those changes occur slower and are not as effective, especially for creating compressive phase of cough. As a result of impaired ability to modify laryngeal resistance, the expulsive forces of cough also become reduced.\textsuperscript{80} With reduced cough airflow rates, extending the expiratory phase of cough may become a compensatory behavior for successful ejection of secretions or aspirate/penetrant materials.

The lack of the compressive phase or significantly reduced compression phase potentially influences expiratory muscle contractions during cough and, consequently results in decreases of the expiratory flow rates and cough volume acceleration. According to Fontana et al.,\textsuperscript{8} the expiratory muscles develop isometric contractions during glottal closure, and, therefore, the tension developed with this type of contraction is higher than during the isotonic contractions. They argued that the lack of a compressive phase leads to reduction of expiratory muscle force generated during cough which consequently reduces cough volume acceleration during the initial burst of airflow during expiratory phase. Fontana et al.\textsuperscript{8} reported sustained activation of the expiratory muscles in voluntary coughs produced by patients with laryngectomy and suggested that these muscles contraction intensities were lower but of longer durations which could represent a compensatory mechanism to achieve optimal cough airflow rates and accelerations. Although their observation was made in voluntary coughs of laryngectomies, it can be related to coughs produced by patients with glottal insufficiency in the attempt to clear the airways. Based on the study of Harris and Lawson,\textsuperscript{22} the greater sheering forces are created during post-peak plateau phase of cough when the cough airflow is consistent and tracheal diameter becomes reduced. Therefore, maintaining longer post-peak plateau phases of cough may be a pattern of
successful airway clearance for persons who fail to create glottal and supraglottal
closure prior to expulsive phases of coughs.

**Within-Subject Differences between Cough Types**

Our analysis of the differences in abduction and adduction TVF angles and
cough airflow parameters between single and sequential coughs showed no significant
differences in cough airflow or the TVF kinematics between single cough and sequential
coughs. However, the first coughs (C1) of the cough sequences were produced with
significantly higher values of pre-compression TVF abduction angles than the
consecutive (C2) coughs of cough epochs with no significant differences in cough
airflow between C1 and C2. These analysis included cough sequences produced with
an additional inhalation between C1 and C2 and cough sequences produced without the
additional inhalations.

There is limited knowledge regarding the relationships between single and
sequential cough airflow parameters, especially in patient populations. Smith et al. investigated the effect of increasing operating volume, defined as the amount of air in
the lungs expressed as a percent of vital capacity at cough initiation, on trunk
movement, esophageal and gastric pressures, and PEFR and CEV change during
single and sequential voluntary coughs in healthy individuals. Although the differences
between the airflow parameters were not analyzed, their report showed similar values of
PEFR of single coughs and the first coughs of the cough epochs. They found that the
CIV prior to coughing was a significant predictor of both PEFR and CEV for both single
voluntary coughs and sequential voluntary coughs, and the changes in PEFR were
similar for both types of coughs as the operating volume decreased. In addition, the
EPDs of single coughs increased with operating volume increase, while the EPDs of
each cough of a cough sequence were considerably shorter than EPDs of single
coughs and did not vary significantly as the operating volume decreased.23

These data are in agreement with the lack of significant differences in cough
parameters, except for EPD, between single cough and the first coughs of the cough
epochs. However, the absence of significant differences in cough parameters between
single coughs and C2 or between C1 and C2 of a cough sequence may suggest
reduced strength of the single coughs and C1 of the cough sequences. According to
Harris and Lawson,22 CEV during the first cough in the cough epoch in healthy persons
comprises 53.2% of the volume of the first three coughs of the epoch combined as
compared to the second cough (28%) and the third cough (18.8%). Similarly, the first
cough efficacy is greater than the efficacy of the second and the third cough in the
sequence with the ratio of units: 1: 0.82: 0.67. Cough efficacy was defined as a quotient
of scrubbing action and cough airflow rate. These reports suggest significant decrease
in cough effectiveness from C1 to C2. Such a difference was not replicated in the airflow
parameters between C1 to C2 in our study, potentially due to overall reduced cough
strength which is reflected by relatively low PEFRs in single coughs and C1 of cough
sequences comparing to voluntary single coughs produced by healthy older adults
reported by Britton et al.14 and to the sequential coughs of young adults in the study of
Hegland et al.87 Significant decrease in pre-compression TVF abduction angles in C2 as
compared to C1 in our study participants is potentially associated with tracheal
narrowing at the end of the expiratory phase of C1.22 Whether the decrease of the TVF
angles during pre-compressive phase of C2 is typical for the non-impaired TVFs, it is
unknown due to lack of normative data of TVF kinematics in sequential coughs. Future
investigation of cough airflow and TVF angles in sequential coughs of healthy subjects may provide information for comparison.

**Post-Hoc Test Results**

Post-hoc analysis performed in this study identified differences in cough airflow measures and TVF kinematics between a subset of participants demonstrating complete glottal closure during phonation and the subset of participants demonstrating incomplete glottal closure of various degrees during phonation. Specifically, the group demonstrated glottal insufficiency during phonation produced single coughs with significantly shorter CPDs which indicated that glottal insufficiency primarily reduced the ability of expiratory air compression for creating high transient airflow rates. Moreover, participants who were unable to complete glottal closure during phonation produced coughs with greater pre-compression TVF abduction and pre-compression TVF adduction angles. It suggests that persons with reduced mobility or immobility of one TVF who are not able to complete glottal closure during phonation, are more likely to demonstrate reduced ability to increase laryngeal resistance in cough. The ability to produce complete glottal closure may be directly related to a more medial position of the paralyzed or paretic TVF as well as to compensatory adduction movements of the intact TVF. Therefore, TVF medialization procedures can not only improve glottal closure for phonation but can potentially improve cough function. An increase in CPD as a result of TVF medialization would allow building up higher subglottal pressure for greater expulsive power of cough and more effective airway clearance.

An interesting observation was made during the cough assessment, as a group of 9 participants did not generate the sequential cough as a single cough bout, but instead inhaled between C1 and C2 or produced one cough at the time. The group of
participants who did not produce the typical cough sequences was characterized with significantly higher IPDs in single coughs and significantly higher EPDs, PEFRs and PEFRTs in both types, single and C1 of sequential coughs. This group also demonstrated significantly higher ratings of the glottal closure during phonation. Six participants in this group demonstrated the highest (most severe) scores of the GCRS (5 and 6) associated with either incomplete closure of the posterior two-thirds of the TVFs or incomplete closure all along the TVFs. In contrast, only 2 participants in the group producing typical cough bouts received ratings of GCRS of 5 or 6. It can be argued that additional inhalation prior to C2 was performed as a result of low CIV prior to C1. However, our study results did not show significant differences in CIVs between the two groups. Average values of CIV produced in single and C1 of sequential coughs in all participants were relatively low (0.8 L) which was equivalent to 30% their forced vital capacity (FVC). The longer IPDs in both single and C1 of sequential coughs with no difference in CIV and no differences in pre-compression TVF abduction angles may indicate reduced inspiratory effort or can be associated with greater degree of upper airway obstruction, but this would require further assessments. The greater values of PEFRT in C1 of cough sequences in the group producing additional inhalations for the second cough indicate less robust TVF abduction for the initial expiratory expulsion during the first cough; however, the first coughs of cough sequences were produced with higher PEFRs in this group. It is possible that these coughs initiated with low percent of vital capacity and produced with high airflow rates, resulted in exhalation to residual volume and required an additional inhalation to continue a cough sequence.
A typical sequential cough is initiated with an inhalation followed by several airflow expulsions separated by compression phases and does not involve inhalations between consecutive coughs of the sequence. Several studies analyzed the differences in sequential cough airflow patterns in healthy adults and patients with neurologic disease such as Parkinson disease (PD).\textsuperscript{18,87} It has been shown that regardless of chest wall rigidity and laryngeal muscle weakness, patients with PD are able to produce sequential coughs without additional inhalations.\textsuperscript{18}

The presence of inspiratory phases between coughs in the group with a higher degree of glottal insufficiency may as well suggest alterations in the rhythmic cough reacceleration pattern related to certain types of laryngeal dysfunction such as TVF paralysis. It is possible that these modifications of sequential cough are not produced volitionally but occur on the level of brainstem and are controlled by central pattern generator.\textsuperscript{88} The underlying factors of modified patterns of sequential coughs in our study participants require further investigation.

**Clinical Implications of the Study Findings**

Airway defensive behaviors involve coordinated function of respiratory and laryngeal subsystems. There is growing interest in upper airway dysfunction and its impact on swallowing and cough effectiveness. This study adds to the airway protection literature by specifically identifying an effect of glottal insufficiency on cough motor function.

Our findings showed associations between pre- and post-compression TVF abduction during cough and compressive and expiratory phase durations in persons with reduced TVF mobility. Further, we determined significant effect for the degree of glottal insufficiency assessed in phonation on pre-compression TVF adduction angles
and compression phase duration in voluntary cough. This result indicates that the impairments in laryngeal subsystem primarily influences compression phase of cough. Therefore, studying the mechanisms impacting the ability to generate high tracheal pressures via modification of laryngeal resistance is an important aspect of cough studies.

Next step in the process of understanding the impact of glottal insufficiency on cough effectiveness may involve studying reflex cough in this patient population. Studies have shown that cortical control of the cough motor response to the sensory stimulation allows modification of physiologic and aerodynamic aspects of cough.\textsuperscript{25,35,89} Future research may involve testing cuing effects on modification of laryngeal resistance during cough and its associations with the cough airflow changes.

This study assessed the differences between single and sequential voluntary coughs produced by persons with glottal insufficiency. Whether the decrease of the TVF angles during pre-compressive phase of C2 is physiologically normal or distinctive for this particular study group, it cannot be assumed without further investigations. There is no existing normative data of TVF kinematics in sequential coughs. Therefore, further examination of cough airflow and TVF angles in sequential coughs of healthy subjects and patient populations may provide stronger evidence of normal and abnormal laryngeal behaviors during repetitive cough.

A valuable observation was made during the course of data collection and analysis. We identified a group of participants who produced atypical patterns of sequential coughs by inhaling between consecutive coughs in the sequence. This group demonstrated on average more severe glottal insufficiency than those who were able to
produce classical cough sequences. Based on the some aerodynamic differences in production of the first cough in the sequence between the two groups, it can be speculated that the cough pattern modifications are related to disproportions between cough inspired and expired volumes. It is possible, however, that modifications of the sequential cough patterns in this participant group occur involuntarily and are a result of neural mechanisms associated with unilateral peripheral nerve damage. Further studies of sequential cough in patients with EMG-confirmed unilateral and bilateral TVF paralysis involving larger participant samples will help understand the nature of this preliminary observation.

**Study Limitations**

This study had several limitations. First, the study included a small sample size of 15 participants which could increase a risk of interpreting random variations as a real effect and could cause overestimation of the magnitude of associations between variables of interest. However, due to strict inclusion/exclusion criteria and limited access to participant pool, this sample size was acceptable given the exploratory character of the study. The unequal number of male and female participants in the sample was disadvantageous, and the effect of gender on the outcome variables was difficult to determine. Some participants demonstrated respiratory function outcomes falling below standard norms for their age and gender; however, without the diagnosis of respiratory impairments, they were not excluded from the study. The future study should include more specific exclusion criteria for respiratory function in the process of participant selection.

Second, the lack of a control group with very limited access to the normative data in the literature influenced the process of interpretation of the outcomes obtained from
the patient group. There were study limitations related to the data collection procedure which could impact the quality of data recording. The nasal endoscopy coupled with cough airflow collection required coordinated action of two investigators and great cooperation of the participants. The participants were required to maintain stable head and trunk position, to produce a good lip seal around the mouthpiece of the pneumotachometer flow head during cough, and to produce maximum effort during study task. With the endoscope in the nasopharynx, the entire procedure had to be quick to avoid additional discomfort; therefore, controlling multiple aspects of the procedure was at times challenging. The factors that could have influenced the quality of data collected were potential: nasal airflow leak due to manual nose occlusion, oral airflow leak due to inadequate lip seal produced by the participant during cough airflow collection, and involuntary movements during cough producing undesirable movements of the pneumotach flow head causing signal distortion. The degree of participants’ discomfort, although not self-reported, could potentially influence their performance during cough tasks. An additional cough airflow sample recorded separately from endoscopic evaluation may reflect the participant’s maximum effort.

Another study limitation was inadequate viewing of the TVFs during compression phase of cough due to supraglottic compression obscuring the glottis. By analyzing the pre-compression adduction TVF angles during cough, the investigators provided information regarding TVF activity at the initiation of the compression phase, but the TVFs activity during supraglottic occlusion could not be viewed, except for three participants who did not produce supraglottic occlusions. Future study should be focused on developing a reliable method of assessment allowing observation of the
TVFs during compressive supraglottic activities for cough and other airway protective behaviors.

Finally, the application of topical upper airway anesthesia could have altered the study outcomes; however, low concentration of lidocaine applied only into the nasal cavity without additional gargling of the solution or without injecting the solution into the larynx, it is unlikely that significant changes in laryngeal sensory or motor function occurred. There is no available study assessing the changes in motor behaviors such as voluntary cough and phonation or sensory responses to upper airway stimulation after the topical anesthesia in persons with reduced mobility of the TVFs. If the upper airway anesthesia causes collapsibility of the TVFs during inspiration, it can be speculated that it could result in a decrease of pre-compression TVF angles during inspiratory phase of cough and, consequently, could cause prolonged inspiratory phase durations or reduced cough inspired volumes in coughs produced by our study participants. Since our study did not include reflex cough assessment, we did not expect an impact of the upper airway anesthesia on the study outcomes. Future studies should include an assessment of an effect of upper airway topical anesthesia on cough and other airway protective behaviors in persons with reduced TVF mobility.

**Future Research**

This study provided preliminary outcomes for larger group investigations of laryngeal contribution to cough. The following topics should be addressed in the future research related to the topic of this study:

- Assessing replicability of findings in larger groups of similar participant characteristics in voluntary and reflex cough tasks
- Providing normative data for comparison of the outcomes reported in this study and for the future investigations of patient groups
• Testing the effects of glottal insufficiency on cough in populations with bilateral TVF paralysis/paresis

• Evaluating reliability of TVF imaging for assessment of cough effectiveness

• Assessing the effects of available treatments for reduction of glottal insufficiency on cough airflow parameters and TVF kinematics

• Investigating single and sequential cough patterns to provide comparison outcomes for healthy adults and patients with glottal insufficiency related to unilateral or bilateral TVF paralysis/paresis.
APPENDIX
GLOTTAL CLOSURE RATING SCALE

1. Complete closure all along the vocal folds.

2. Indication of incomplete closure of the cartilaginous part.

3. Triangular incomplete closure reaching anterior to the vocal processes.

4. Triangular incomplete closure of the posterior third of the folds.

5. Incomplete closure of the posterior two-thirds of the folds.

6. Incomplete closure all along the folds.

A. Spindle-shaped incomplete closure, closure at the vocal processes.

B. Spindle-shaped incomplete closure at the posterior third of the membranous folds, closure at the vocal processes.

C. Spindle-shaped incomplete closure at the anterior third of the folds, closure at the vocal processes.

D. Spindle-shaped incomplete closure at the posterior and the anterior thirds of the folds, closure at the vocal processes and at the middle of the membranous portion ("hourglass").

LIST OF REFERENCES


BIOGRAPHICAL SKETCH

Helena Laciuga received her master’s degree in vocal performance from Stanislaw Moniuszko Academy of Music (Poland) in 1994, master’s degree in communication sciences and disorders from the University of Florida in 2011, and her PhD in communication sciences and disorders from the University of Florida in 2016. She currently works as a Speech-Language Pathologist in the UF Health Speech and Audiology Center. She sees patients with voice disorders and upper airway dysfunction. Her research interests include upper airway dysfunction and rehabilitation and respiratory muscle strength training. She plans to continue her research on airway protective mechanisms, her clinical practice in the area of voice disorders, and teaching courses related to voice and upper airway physiology and pathology.