Modeling Subglottic Stenosis Effects on Phonation Threshold Flow in the Porcine Larynx

Robin Michelle Smith
Brigham Young University

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Modeling Subglottic Stenosis Effects on Phonation Threshold Flow

in the Porcine Larynx

Robin Michelle Smith

A thesis submitted to the faculty of
Brigham Young University
in partial fulfillment of the requirements for the degree of

Master of Science

Kristine Tanner, Chair
Christopher Dromey
Scott L. Thomson

Department of Communication Disorders
Brigham Young University

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ABSTRACT

Modeling Subglottic Stenosis Effects on Phonation Threshold Flow in the Porcine Larynx

Robin Michelle Smith
Department of Communication Disorders, BYU
Master of Science

Subglottic stenosis (SGS) is an abnormal narrowing of the airway at the level of the cricoid cartilage, above the first tracheal ring and immediately beneath the vocal folds. Individuals with SGS experience a reduction in their ability to breathe as well as adverse effects on voice function. SGS can result from a variety of causes with the type of treatment depending on stenosis severity. Surgical techniques such as laryngotraheal and cricotracheal reconstruction are beneficial for airway maintenance; however, these procedures have resulted in negative effects on voice production. On the other hand, there are patients with SGS who do not require surgery and still experience voice problems. The purpose of this study was to quantify the effects of SGS on vocal fold vibration using an excised larynx benchtop mechanical model. Using a within-subjects repeated measures design, nine porcine larynges underwent experimental conditions including 0% (i.e., normal airway), 50% and 75% stenosed. The primary outcome measure was phonation threshold flow (PTF), which is the rate of flow observed at the onset of phonation. For all larynges, the normal and stenosed conditions were sampled three times each and averaged. Analysis of the results revealed no statistically significant differences in PTF; however, descriptive data showed decreases in PTF and increased variability in PTF values as percent stenosis increased. These findings lay important groundwork for future research in SGS, specifically those that employ ex vivo methodologies. PTF has emerged as a promising means of quantifying voice function in addition to the traditional onset pressure measures. Future studies should examine a broader range of stenosis conditions with a larger sample size to promote generalization to clinical populations including individuals with SGS.

Keywords: subglottic stenosis, voice disorders, larynx, bench model, phonation threshold flow
ACKNOWLEDGMENTS

With much gratitude and appreciation, I would like to thank Dr. Kristine Tanner for the knowledge and support she has bestowed upon me throughout the research and writing process. Additionally, I wish to express my appreciation to Benjamin Hilton for his part in developing the subglottic stenosis (SGS) device, as well as Mark Berardi for his knowledge and expertise with Matlab programming. I wish to express my sincerest gratitude to my data collection partner, Jessica Murphey, who has provided vast moral support, knowledge, and assistance in solving problems throughout this research. I would like to acknowledge the assistance provided by Amber Prigmore and Meg Hoggan, as data collection could not have been achieved, or been as successful, without their assistance. Lastly, I wish to thank my family and husband, Rocky Pratt, for the love and encouragement provided when needed and the means with which to succeed in my schooling and career. This study was supported by the grants 2R56DC009616-06 and 2R01DC009616-06A1 from the National Institute on Deafness and Other Communication Disorders and National Institutes of Health.
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DESCRIPTION OF THESIS STRUCTURE

The following thesis, *Modeling Subglottic Stenosis Effects on Phonation Threshold Flow in the Porcine Larynx*, is written in a hybrid format. As such, the format of this thesis is a combination of journal publication formats and classic thesis requirements. Additionally, this thesis is a part of a larger study on airway stenosis that aims to shed light on the relationship between voice disorders and stenosis severity. It also is a companion study to the 2019 thesis by Jessica Murphey, *Modeling Subglottic Stenosis Effects on Phonation Threshold Pressure in the Porcine Larynx*. A comprehensive annotated bibliography can be found in Appendix A. An experimental checklist can be found in Appendix B.
Introduction

Stenosis is an abnormal narrowing of a passage in the body and can occur in a variety of anatomical structures. In reference to voice and respiration, there are four distinct types of upper airway stenosis: supraglottic, glottic, subglottic, and tracheal stenosis. Upper airway stenosis is a condition that significantly impairs breathing and voice quality by affecting laryngeal soft tissue and cartilage support structures (Conley, 1953; Parrish & Miller, 1991). Stenoses affect women at a higher prevalence than men, which could indicate a possible relationship between estrogen and irritation response mechanisms in the airway (Damrose, 2008; Hseu, Benninger, Haffey, & Lorenz, 2014; Valdez & Shapshay, 2002). Stenoses can occur as a result of bacteria, trauma, radiation, prolonged orotracheal intubation, autoimmune disorders, or gastro-esophageal reflux disease (GERD). However, many cases of upper airway stenosis are idiopathic, meaning that there is no known cause for its development. The present study will examine subglottic stenosis (SGS) specifically.

Subglottic stenosis is a narrowing in the diameter or alteration in shape of the airway below the level of the vocal folds and above the first tracheal ring, more specifically at the level of the cricoid cartilage with a noticeable change in lumen diameter (Conley, 1953). SGS can be characterized as either an acquired disease or congenital, appearing at or near the time of the infant’s birth (Parrish & Miller, 1991). In cases where SGS is seen in infants, it is often in relation to a genetic syndrome or other genetic factors that result in the presence of the stenosis. As SGS is known to develop later in life, these instances are considered acquired and can occur as a result of prolonged orotracheal intubation, trauma to the airway, GERD, or from chronic illnesses and autoimmune diseases like Wegner’s granulomatosis or relapsing polychondritis (Dedo & Catten, 2001; Gelbard et al., 2015; Maldonado et al., 2014; Taylor, Clayburgh,
Rosenbaum, & Schindler, 2013; Valdez & Shapshay, 2002). Clinically, SGS is distinguishable from other upper airway stenoses such as supraglottic, glottic, and tracheal stenosis by the location of the narrowed lumen as identified during endoscopic evaluation. As previously mentioned, SGS occurs at the level of the cricoid cartilage directly below the vocal folds. Treatment for SGS is dependent on multiple factors such as the shape of the stenosis, level of severity in narrowing, as well as other patient health factors. Myer, O’Connor, and Cotton (1994) developed a scale as a means to classify stenosis severity that consists of four severity levels. The first grade (I) consists of narrowing up to 50% obstruction. Grade two (II) is from 51% stenosed to 70% stenosed. Grade three (III) is a stenosing of over 70% but with lumen detectible. Grade four (IV) indicates no clear lumen detectible (Hseu et al., 2014). For milder grades of SGS, nonsurgical methods such as pharmacological management are valid treatment options in an effort to target the underlying disease processes that are likely contributing to the development of the stenosis, such as with GERD or a rheumatologic disease. For more moderate cases of SGS, patients require medical management with the aim of reducing lumen narrowing by removing the excess tissue, such as with an endoscopic laser treatment or balloon dilation procedure. When SGS severity progresses to a level III or IV, treatment in the form of surgical management is required in an effort to restore an open airway. This can be accomplished by either a laryngotracheal or cricotracheal reconstruction surgery.

Prior to surgical management, the voices of individuals with SGS have been described as dysphonic, specifically characterized by breathiness and hoarseness, with the presence of audible breathing patterns such as wheezing or stridor, as well as dyspnea (Hseu et al., 2014). As a result, SGS may be mistaken for another type of breathing disorder such as asthma or paradoxical vocal fold dysfunction (Maldonado et al., 2014). Although laryngotracheal and cricotracheal
reconstruction are current surgical techniques used in the management of SGS and are found to be helpful in minimizing the occurrence of tracheostomies, there have been negative results in the form of disordered voice production as a result (Ettema, Tolejano, Thielkes, Toohill, & Merati, 2006; George & Monnier, 2010; Grillo, Mathisen, Wright, Ashiku, & Wain, 2003; Hseu et al., 2014; Nouraei, Chir, & Sandhu, 2013; Parrish & Miller, 1991; Smith, Roy, Stoddard, & Barton, 2008; Tanner et al., 2016; Valdez & Shapshay, 2002). Negative voice results that have been documented in the literature consist of breathiness, hoarseness, vocal strain, an inability to project one’s voice, reduced fundamental frequency (F₀) range, a lower mean habitual F₀, and an overall reduction in intensity. Currently, there is no standard of best practice for providing voice therapy to patients with these voice alterations as a result of SGS surgery. Additionally, there are people who have SGS who do not require surgery, but have deviant voice characteristics. To guide treatment planning and the development of specific therapeutic and surgical techniques, it is essential to determine the physiologic underpinnings of how SGS affects vocal fold vibration. For this purpose, the current preliminary study was undertaken.

Most of what is currently understood about SGS comes from imaging techniques such as laryngoscopy, intraoperative observations, as well as CT imaging; however, this approach has been limited due to the risks associated with radiation exposure (Costello, Cecava, Tucker, & Bau, 2013). There are a variety of research methodologies and models that may be used to better understand the effects of SGS on phonation. One potential approach is to use a computational model. Computational Modeling involves the use of computers to simulate the behavior of complex systems using mathematics, physics, and computer science in an effort to study a desired behavior (National Institute of Biomedical Imaging and Bioengineering, 2016). Another approach is a theoretical design. A theoretical framework is a conceptual model that provides the
rationale for investigating a particular research question. It establishes main theories and concepts, and includes variables intended to be measured and relationships to be understood (Secomb, Beard, Frisbee, Smith, & Pries, 2008). The research model used for the present study is an excised larynx model. This relies on physical simulations of processes to study the relationships between variables.

Excised larynx models, either animal or human, allow researchers to study the structures of the larynx as well as their function. With an excised larynx benchtop model, researchers are able to accurately control and manipulate the independent variables of a study (Berry, Herzel, Titze, & Story, 1996). This is a preferred model to examine the mechanics of vibration, vocal fold hydration, and the ability of the vocal folds to adduct and abduct. A study conducted by Hottinger, Tao, and Jiang (2007) compared how phonation threshold pressure (PTP) and phonation threshold flow (PTF) change with vocal fold abduction with an excised larynx model. Additionally, Alipour, Jaiswal, and Finnegan (2007) used an excised larynx model to study the effects that the epiglottis and false vocal folds would have on aerodynamic and acoustic voice measures. Researchers have also shown that some animal larynges have a similar structure and physiology to human larynges, which allows for a reliable supply of samples to use in an excised larynx benchtop model (Alipour & Jaiswal, 2008). Limitations do exist with this model, however. The excised larynx model requires dissection and preservation, each with multiple steps, which can introduce variability that can be difficult to control. However, this variability can be minimized by employing consistent procedures of operation.

An aerodynamic measure that has been traditionally used as a means to reflect vocal function is phonation threshold pressure (PTP), defined as the minimum amount of pressure needed to initiate phonation (Titze, 1994). In clinical usage, PTP can be used to assess laryngeal
function by discriminating pathologic phonation from typical phonation. While PTP has been frequently reported in the literature, phonation threshold flow (PTF) is another, less commonly used aerodynamic measure that might complement PTP in excised larynx studies (Hottinger et al., 2007; Jiang & Tao, 2007). PTF may be operationally defined as the rate of flow at the onset of phonation.

To establish PTF as a viable measure for laryngeal studies, research has been conducted using an excised larynx model to analyze the effects of different independent variables on PTF. A study conducted by Hottinger and colleagues (2007) determined that PTF decreases with the decrease of glottal area and tissue viscosity, as well as increasing the length of the glottal duct vertically. Additionally, to directly measure PTP in vivo, a tracheal puncture is required, whereas to measure PTF an external flow transducer or a pneumotachograph mask can be used. PTP can only be estimated in vivo on the basis of intraoral pressure. For this reason, PTF may be an appealing option for future research in voice function. It was used in the present study to examine phonatory differences across experimental conditions (Jiang & Tao, 2007).

Pressure and flow are aerodynamic measures that are interdependent. Ohm’s Law states that laryngeal resistance can be calculated by dividing subglottic pressure by airflow. In most situations, as pressure changes, so does the flow (Definition of ‘Ohm’s Law’, 2019). Due to this relationship, separating the two factors during in vivo phonation is difficult. To further understand the relationship between PTP and PTF, an ex vivo model is useful because it allows for individual variables to be manipulated and controlled. For example, researchers can change the level of adduction, keeping the driving pressure constant, and then observing the effects on flow. The present study capitalizes on the ability to manipulate several independent variables to examine their influence on PTF.
Statement of Purpose

Currently, there is no standardized quantitative rating scale for the measure of voice severity in patients with subglottic stenosis. The four-point grading scale developed by Myer et al. (1994) provides an overall estimation framework to classify obstruction severity; however, this is a flexible perceptual scale that does not address corresponding changes in voice function. Additionally, there are perceptual severity rating scales such as the GRBAS (grade, roughness, breathiness, asthenia, strain) and Voice Related Quality of Life (V-RQOL) that are used to describe voice severity in stenosis patients, but neither rating scale provides quantitative information as to the severity of voice disorders (Hirano, 1981; Kupfer, Hogikyan, & Hogikyan, 2014). To provide an accurate representation of SGS severity, it is important to quantify the effects of SGS on the function of the vocal folds in addition to any perceptual classification of severity. Therefore, more understanding needs to be gained in relation to how stenosis affects the vocal fold vibration. The purpose of the present study was to examine the effects of the percent of airway narrowing of the subglottis on PTF using a within-subjects experimental design. Specifically, this study documented onset PTF for vocal fold oscillation for each level of severity of stenosis in comparison to a 0% stenosed airway in the same excised porcine larynges. The goal was to establish preliminary aerodynamic data for the air flow required to initiate and sustain phonation for several diameters of stenosis as compared to a normal subglottis. Additionally, further anticipated outcomes are to gain a deeper insight into the sources of dysphonia in SGS patients, as well as into aerodynamic and acoustic changes associated with SGS. The outcome of the current work will lay an important foundation for further research in voice disorder treatments for patients with SGS.
Research Questions

The research question that guided this work was as follows: What is the effect of SGS on PTF in excised porcine larynges at 0%, 50%, and 75% stenosis?

Method

All procedures involved in this study were conducted in rooms 105 and 106 of the John Taylor Building, room 105 of the John Taylor Building Annex, and in room 126 of the Nicholes Building at Brigham Young University. This study was conducted in accordance with regulations from Brigham Young University Risk Management and the Institutional Animal Care and Use Committee. All excised porcine larynges used in this study were donated from Circle V Meats, a butcher shop in Spanish Fork, Utah.

Research Design

Our study employed a prospective within-subjects repeated measures experimental design. Thirteen porcine larynges were mounted on a benchtop setup and phonated three times each at 0% stenosed, 50% stenosed, and 75% stenosed. The order of stenosis conditions was randomly assigned, with the 0% normal condition being assigned either first or last due to the time required to dismount the larynx and place the stenosis mechanism. Isotonic saline was sprayed on the larynges throughout the experiment to prevent desiccation. For all larynges, PTP (cmH₂O) and PTF (L/min) were recorded at the onset of phonation. Each porcine larynx served as its own control, allowing a comparison of each degree of stenosis; this controlled for baseline variability between larynges. The independent variable was the percent stenosed. The dependent variables included PTP and PTF, the latter being the focus of the current work.
Larynges

For this study, 13 excised porcine larynges were collected from adult, food-grade pigs that were all at least 2 years of age. Following the collection of larynges from the slaughterhouse, the larynges were immediately brought back to room 106 of the John Taylor Building at Brigham Young University to be inspected and roughly dissected. All larynges were methodically inspected for any structural abnormalities or punctures of the trachea and were discarded if any abnormalities were found. Two larynges were found to be unsuitable for inclusion due to compromised anatomical structures or tears. Rough dissection consisted of removing excess muscle, tissue, fat, trachea exceeding 6 cm in length, and the esophagus. The dissected larynges were then lightly rinsed with tap water before being individually placed in gallon plastic zip seal freezer bags filled with 0.9% Sodium Chloride Irrigation USP fluid (isotonic saline, 0.9% Na\(^+\)Cl\(^-\)) to the point of complete submersion. All larynges were then taken to room 126 of the Nicholes Building to be flash frozen in liquid nitrogen for approximately seven minutes. Following this, the larynges were then stored in a freezer in room 108 of the John Taylor Building, set to -19 degrees Celsius until the time of fine dissection. The process from picking up the larynges at Circle V Meats to freezing and storing took roughly two hours to complete. Prior to being included in the study, larynges were removed from the freezer 72 hours in advance and placed in a refrigerator for thawing. The larynges were then finely dissected to reveal the true vocal folds. Fine dissection took place the day the experimental trials were performed and involved removing the cartilage and supraglottic tissues. This specifically included the false vocal folds and surrounding portion of the thyroid cartilage. Two different-sized scalpels were used to dissect each porcine larynx. A No. 21 stainless steel blade (larger scalpel) was used to dissect excess tissue, muscle, and cartilage. A No. 11 (smaller scalpel) was
used to carefully dissect away the false vocal folds without puncturing the true vocal folds. Dissection was accomplished with the help of metal hemostats that were used to abduct the false vocal folds and aid in the precise dissection. The arytenoid cartilage was left intact for additional support in adducting the vocal folds during experimentation. The thyroid cartilage was transected approximately 0.5 cm above the true vocal folds and the cartilage was trimmed at an upward angle from anterior to posterior to provide additional support during arytenoid adduction. The epiglottis was also removed. The tracheas of the porcine larynges were cut to be approximately 6 cm in length. Additionally, a suture was placed at the anterior commissure for the purpose of vocal fold elongation during experimentation. Following fine dissection, the larynges were placed in individual gallon sized bags with isotonic saline until removed and mounted for experimentation.

**Procedures**

**Benchtop setup.** Jiang and Titze (1993) reported using a benchtop mechanical model for experiments involving excised larynges. The present study used a similar model, which included an excised larynx mounted on a vertically positioned plastic tube that was projecting from a custom engineered pseudolung with foam insulation. The benchtop setup is shown in Figure 1. The plastic tubing was passed through a hole in a standard stainless-steel breadboard tabletop (Thorlabs, Ann Arbor, MI). In between the plastic tubing and porcine larynx was an artificial silicone subglottic stenosis mechanism, 3D printed by the Brigham Young University Department of Mechanical Engineering, that allowed for the simulation of a stenosis in the 50% and 75% stenosed trial and removed for the 0% stenosed control trial. This mechanism was held in place by hooking it onto two stainless steel bars that were fastened into the stainless-steel breadboard tabletop. The larynx was held in place by micropositioners (Model 1460, Kopf
Industries, Tujunga, CA), which were secured to the tabletop with ¼-20 headless screws by custom made bases. Two micropositioners with three custom prongs were used to help in adduction of the vocal folds by bilaterally piercing the arytenoid cartilages. The third micropositioner was located in front of the larynx. The larynx was secured to the micropositioner via an anteriorly sewn string in the thyroid cartilage. The micropositioners were used to adduct and lengthen the vocal folds until phonation occurred. Internal consistency with micropositioning of the larynges was maintained by having the same examiner operate the mechanism and precisely duplicating the adjustments for normal versus stenosed conditions. The trachea was attached to the SGS mechanism, which was affixed below to the vertical plastic tubing. To provide a tight seal from the SGS mechanism to the porcine larynx, an adjustable metal hose clamp was wrapped around the junction.
Figure 1. The benchtop setup utilized during research. This included the humidifier, pseudolung, vertically positioned plastic tubing, standard stainless-steel breadboard tabletop, pressure transducer, excised larynx, adjustable metal hose clamp, 3 micropositioners, compressed air tank, adjustable flow regulator, and in-line thermal flow meter.

**Percent stenosed using SGS device.** Each stenosis condition was computed using radius and created with an SGS simulation device that consisted of a silicone sleeve (Smooth On Dragon Skin 10, E=22 psi) that was narrowed via two perpendicular threads connected to two dials on the side of the subglottic stenosis mechanism for tightening as shown in Figures 2 through 6. The dials had been previously calibrated and marked so as to consistently achieve the diameter of narrowing desired and when twisted for tightening would result in the marks lining up and the silicone sleeve being narrowed in an elliptical shape on a perpendicular axis. When both dials were turned to narrow the silicone sleeve, a circular shape was achieved.
Figure 2. Manual subglottic stenosis (SGS) device secured in place on the vertical tubing of the optic table.

Figure 3. Superior view of the subglottic stenosis (SGS) silicone sleeve while looking through the trachea.
Figure 4. Dimensions of the subglottic stenosis (SGS) silicone sleeve developed by the Brigham Young University Department of Mechanical Engineering.

Figure 5. Manual subglottic stenosis (SGS) device presenting a 75% artificial narrowing of the subglottis.
Flow and pressure measurement. The mechanical benchtop model setup for the acquisition of flow and pressure measurements, following the direction of airflow, consisted of the following elements. A compressed air tank (<1% relative humidity) and adjustable flow regulator at 50 psi led to an in-line thermal flow meter that was secured to tubing which led to a Theraheat temperature-controlled humidifier (Model RC70000, Smiths Medical, Dublin, OH). The tubing was attached to another clear plastic tube that passed through a 20-cm aluminum pseudolung that was insulated with foam. The clear tubing then traveled up through the hole in the stainless-steel table top that had a subtracheal outlet that allowed for a pressure transducer (Model PT-25-S, Glottal Enterprises, Syracuse, NY) to be attached perpendicular to the direction of the flow.

Trials of phonation. Once mounted on the benchtop setup, the larynges underwent phonatory trials for 0%, 50%, and 75% stenosis, in varying orders. To begin phonation, compressed air was passed through the humidifier and pseudolung, then up through the

Figure 6. Porcine larynx mounted on top of the manual subglottic stenosis (SGS) device without optics table and micropositioners.
subglottis to the vocal folds. The length of the vocal folds was increased via the anteriorly sewn string attached to the anterior micropositioner until phonation began, at which point lengthening was then halted and the folds remained at a constant length. Air was supplied subglottally until phonation occurred for roughly three seconds, at which point the air was turned off.

**Signal acquisition.** An acoustic signal, indicating phonation onset, as well as pressure and airflow were obtained simultaneously following each onset of phonation using the DATAQ A/D (DI-720 Series) converter and WinDaq software (Series Di-720, Akron, OH) that was programmed to sample at 10 kHz per channel. The acoustic signal was collected using a dynamic microphone (Model SM-48, Shure, Niles, IL) that was positioned about 6 inches above the true vocal folds. An audio mixer (Samsung MIXPAD 4, New York, NY) was also used to preamplify the signal. The pressure transducer was calibrated to 0 and 10 cmH₂O using a pressure calibrator (PC-1H, Glottal Enterprises, Syracuse, NY) and the flow meter was calibrated as well at 0 and 15 L/min prior to the beginning of data collection. All Windaq files were event-marked and saved prior to PTP and PTF analysis. The onset of phonation was verified using the acoustic signal.

**Data analysis.** Following data collection, the WinDaq files were segmented and imported into a custom MatLab program for analysis (MathWorks, Natick, MA). All acoustic recordings that were taken during each trial were used as a means of audible discrimination of phonation onset. The PTP and PTF were computed by averaging the subglottal pressure and flow that occurred 10 ms before and after the onset of phonation. The PTP and PTF values were then exported for statistical analysis.

**Statistical analysis.** Data from each of the three conditions were assessed for central tendency and variability at baseline. Repeated measures analyses were undertaken to test for
changes in the dependent variables across the stenosis conditions, using an alpha level of .05. All statistical analyses were completed using SPSS, version 24 (IBM Corp., Armonk, NY).

Results

Among the excised larynges obtained for data collection, only 13 larynges completed experimentation; however, on the final day of data collection there was an equipment failure during the signal acquisition phase that rendered the data from those larynges unusable. Therefore, data from a total of 9 larynges were available for analysis. Anatomical dimensions of the vocal folds for each larynx are reported in Table 1. Anatomical dimensions of the thyroid cartilage for each larynx are reported in Table 2. Anatomical dimensions of the trachea are reported in Table 3. The weight for each larynx is reported in Table 4.

Descriptive Statistics

PTF summary data were analyzed for central tendency and variability. For each observation (i.e., each specimen at each percent stenosis), larynges were phonated three times and the data averaged, resulting in one data point for each observation. The range of PTF values for 0% stenosis was 4.88 to 20.00 L/min (median = 10.62 L/min, mean= 10.35 L/min, SD= 4.65 L/min). Ranges for the two stenosis conditions were 5.40 to 16.22 L/min (median = 8.02 L/min, mean= 9.35 L/min, SD= 3.82 L/min) for 50% stenosed and 6.59 to 12.31 L/min (median = 7.88 L/min, mean= 8.53 L/min, SD= 1.82 L/min) for 75% stenosed.

Inferential Statistics

Examination of the distribution for PTF indicated that the data were not normally distributed. The data were within acceptable limits for Mauchly’s test of Sphericity, Mauchly's W = .380, p = .641. However, due to potential violations of the assumptions for a parametric
Table 1

*Vocal Folds Anatomical Size and Dimensions*

<table>
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<th>Group</th>
<th>Session Date</th>
<th>Length of Vocal Folds (mm)</th>
<th>Width of Vocal Folds (mm)</th>
<th>Width from Vocal Folds to Thyroid Cartilage (mm)</th>
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<td>2.53</td>
<td>11.02</td>
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<tr>
<td>Pig 2</td>
<td>7/6/2018</td>
<td>16.05</td>
<td>2.09</td>
<td>11.03</td>
</tr>
<tr>
<td>Pig 4</td>
<td>7/12/2018</td>
<td>18.00</td>
<td>4.00</td>
<td>11.00</td>
</tr>
<tr>
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<td>7/12/2018</td>
<td>17.00</td>
<td>3.00</td>
<td>12.00</td>
</tr>
<tr>
<td>Pig 6</td>
<td>7/16/2018</td>
<td>19.37</td>
<td>2.37</td>
<td>10.64</td>
</tr>
<tr>
<td>Pig 7</td>
<td>7/16/2018</td>
<td>17.03</td>
<td>1.87</td>
<td>10.29</td>
</tr>
<tr>
<td>Pig 8</td>
<td>7/16/2018</td>
<td>20.51</td>
<td>2.12</td>
<td>13.28</td>
</tr>
<tr>
<td>Pig 10</td>
<td>8/9/2018</td>
<td>17.79</td>
<td>1.36</td>
<td>12.04</td>
</tr>
<tr>
<td>Pig 11</td>
<td>8/9/2018</td>
<td>19.46</td>
<td>1.62</td>
<td>10.33</td>
</tr>
<tr>
<td>Pig 13*</td>
<td>9/21/18</td>
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<td>9/21/18</td>
<td>19.42</td>
<td>1.87</td>
<td>10.28</td>
</tr>
<tr>
<td>Pig 15*</td>
<td>9/21/18</td>
<td>18.99</td>
<td>1.55</td>
<td>9.58</td>
</tr>
<tr>
<td>Pig 16*</td>
<td>9/21/18</td>
<td>15.78</td>
<td>1.86</td>
<td>8.90</td>
</tr>
</tbody>
</table>

*Note.* * = Pigs not included in the data analysis due to equipment malfunction.
Table 2

*Thyroid Cartilage Anatomical Dimensions*

<table>
<thead>
<tr>
<th>Group</th>
<th>Session Date</th>
<th>Height (protuberance to top) (mm)</th>
<th>Height (protuberance to bottom) (mm)</th>
<th>Width of Thyroid Cartilage (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pig 1</td>
<td>7/6/2018</td>
<td>51.24</td>
<td>35.56</td>
<td>43.12</td>
</tr>
<tr>
<td>Pig 2</td>
<td>7/6/2018</td>
<td>31.39</td>
<td>33.44</td>
<td>44.52</td>
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<tr>
<td>Pig 4</td>
<td>7/12/2018</td>
<td>38.37</td>
<td>12.59</td>
<td>43.00</td>
</tr>
<tr>
<td>Pig 5</td>
<td>7/12/2018</td>
<td>45.00</td>
<td>16.00</td>
<td>45.00</td>
</tr>
<tr>
<td>Pig 6</td>
<td>7/16/2018</td>
<td>57.97</td>
<td>31.03</td>
<td>48.04</td>
</tr>
<tr>
<td>Pig 7</td>
<td>7/16/2018</td>
<td>58.91</td>
<td>31.81</td>
<td>45.11</td>
</tr>
<tr>
<td>Pig 8</td>
<td>7/16/2018</td>
<td>46.65</td>
<td>25.05</td>
<td>48.22</td>
</tr>
<tr>
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<td>53.10</td>
<td>31.96</td>
<td>43.68</td>
</tr>
<tr>
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<td>8/9/2018</td>
<td>56.59</td>
<td>30.91</td>
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<tr>
<td>Pig 13*</td>
<td>9/21/18</td>
<td>52.00</td>
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<td>44.89</td>
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<tr>
<td>Pig 14*</td>
<td>9/21/18</td>
<td>49.95</td>
<td>26.96</td>
<td>45.85</td>
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<tr>
<td>Pig 15*</td>
<td>9/21/18</td>
<td>49.92</td>
<td>27.86</td>
<td>45.00</td>
</tr>
<tr>
<td>Pig 16*</td>
<td>9/21/18</td>
<td>49.71</td>
<td>28.38</td>
<td>46.75</td>
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</tbody>
</table>

*Note.* * = Pigs not included in the data analysis due to equipment malfunction.
Table 3

*Trachea Anatomical Dimensions*

<table>
<thead>
<tr>
<th>Group</th>
<th>Session Date</th>
<th>Trachea Length (mm)</th>
<th>Trachea Width (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pig 1</td>
<td>7/6/2018</td>
<td>19.00</td>
<td>20.49</td>
</tr>
<tr>
<td>Pig 2</td>
<td>7/6/2018</td>
<td>19.00</td>
<td>18.25</td>
</tr>
<tr>
<td>Pig 4</td>
<td>7/12/2018</td>
<td>12.72</td>
<td>22.24</td>
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<td>7/12/2018</td>
<td>19.00</td>
<td>22.00</td>
</tr>
<tr>
<td>Pig 6</td>
<td>7/16/2018</td>
<td>19.00</td>
<td>18.77</td>
</tr>
<tr>
<td>Pig 7</td>
<td>7/16/2018</td>
<td>19.00</td>
<td>17.42</td>
</tr>
<tr>
<td>Pig 8</td>
<td>7/16/2018</td>
<td>19.00</td>
<td>20.63</td>
</tr>
<tr>
<td>Pig 10</td>
<td>8/9/2018</td>
<td>19.00</td>
<td>21.95</td>
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<tr>
<td>Pig 11</td>
<td>8/9/2018</td>
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<td>19.00</td>
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<td>Pig 14*</td>
<td>9/21/18</td>
<td>19.00</td>
<td>19.35</td>
</tr>
<tr>
<td>Pig 15*</td>
<td>9/21/18</td>
<td>19.00</td>
<td>23.39</td>
</tr>
<tr>
<td>Pig 16*</td>
<td>9/21/18</td>
<td>19.00</td>
<td>20.84</td>
</tr>
</tbody>
</table>

*Note.* * = Pigs not included in the data analysis due to equipment malfunction.
### Table 4

**Larynx Weight**

<table>
<thead>
<tr>
<th>Group</th>
<th>Session Date</th>
<th>Pre Trachea Cut Without Thyroid Cartilage (oz)</th>
<th>Post Trachea Cut Without Thyroid Cartilage (oz)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pig 1</td>
<td>7/6/2018</td>
<td>4.66</td>
<td>3.99</td>
</tr>
<tr>
<td>Pig 2</td>
<td>7/6/2018</td>
<td>3.88</td>
<td>3.17</td>
</tr>
<tr>
<td>Pig 4</td>
<td>7/12/2018</td>
<td>3.32</td>
<td>2.43</td>
</tr>
<tr>
<td>Pig 5</td>
<td>7/12/2018</td>
<td>3.81</td>
<td>3.10</td>
</tr>
<tr>
<td>Pig 6</td>
<td>7/16/2018</td>
<td>3.70</td>
<td>2.89</td>
</tr>
<tr>
<td>Pig 7</td>
<td>7/16/2018</td>
<td>2.36</td>
<td>2.15</td>
</tr>
<tr>
<td>Pig 8</td>
<td>7/16/2018</td>
<td>3.49</td>
<td>2.61</td>
</tr>
<tr>
<td>Pig 10</td>
<td>8/9/2018</td>
<td>3.84</td>
<td>3.28</td>
</tr>
<tr>
<td>Pig 11</td>
<td>8/9/2018</td>
<td>3.74</td>
<td>3.42</td>
</tr>
<tr>
<td>Pig 13*</td>
<td>9/21/18</td>
<td>3.67</td>
<td>3.10</td>
</tr>
<tr>
<td>Pig 14*</td>
<td>9/21/18</td>
<td>3.81</td>
<td>3.10</td>
</tr>
<tr>
<td>Pig 15*</td>
<td>9/21/18</td>
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<td>2.86</td>
</tr>
<tr>
<td>Pig 16*</td>
<td>9/21/18</td>
<td>3.49</td>
<td>2.61</td>
</tr>
</tbody>
</table>

*Note.* * = Pigs not included in the data analysis due to equipment malfunction.
repeated measures test, the Friedman Analysis of Variance by Ranks was performed. The results from the Friedman test were not significant, \( p = .368 \). Data for PTF values for each percent stenosis for each porcine larynx are displayed in Figure 7.

![Figure 7. Phonation threshold flow (PTF) for each percent stenosed condition for each porcine larynx.](image)

**Discussion**

The aim of this study was to determine how progressive narrowing of the subglottic space impacts PTF in an excised porcine larynx benchtop mechanical model. The rationale for this work was that airflow differences could be studied independent of the myriad of physiological covariates that exist for voice function in vivo. As onset flow has been found to change with prephonatory glottal area changes and an appropriate measure for examining tissue mobility and stiffness (Jiang & Tao, 2007), this study explored PTF as a means to develop further insight into
vocal fold function with subglottal narrowing. The degrees of narrowing included 0%, 50%, and 75% stenosed, with each porcine larynx serving as its own control. There were no significant differences in PTF across conditions; however, descriptive interpretation of the data was undertaken for the purposes of refining the current study methodology for future research.

**Theoretical Framework**

In the present study, the hypothesis that PTF would change with the narrowing of the subglottis was based on several principles that served as a theoretical framework. The first law drawn upon was Ohm’s Law, and Ohm’s law indicates that for a constant pressure, the flow and the resistance are inversely related (Definition of 'Ohm's Law', 2019). The second principle is Bernoulli Principle which states that as flow increases, while keeping temperature constant, the pressure of the liquid or gas will decrease (Bernoulli’s Principle, 2018). The last principle utilized is Poiseuille’s Law which describes how the radius and tube length, viscosity of the liquid (i.e., assuming a liquid flow model), and the pressure of the current affect the flow through the tube. In the context of the present study, Poiseuille’s Law predicts that with the slightest narrowing of the tube, a resistance will be created that will result in a reduction in flow (Flow and Poiseuille's Law in Operation, 2019). As pertaining to SGS, these principles when combined provide a basis for how voice function is affected as airflow and air pressure interact.

**Airflow and Voice Function**

On the basis of the theoretical framework, PTF may be interpreted to reflect the efficiency and ease of vocal fold vibration. According to the results observed by Hottinger et al. (2007), PTF might be a more sensitive measure of detection for changes in posterior glottal width than PTP. Additionally, PTF is dependent on factors such as resistance of the glottis and pressure during phonation (Smith & Thomson, 2013). Theoretically, this relationship to flow can
be expressed by Ohm’s law as the ratio of subglottal pressure to glottal flow resistance (Herbst, 2017). In this formula, airflow and glottal resistance are inversely related, meaning that as the resistance increases, flow decreases. In terms of the present study this would mean that as the degree of subglottic stenosis narrowing increased from 0% stenosed, to 50%, and then 75% stenosed, the PTF would decrease. This is the general pattern that was observed in the results of the study. It should be noted, however, that this formula results in only an approximation as flow rate is a product of multiple factors such as human phonatory behavior that are not taken into consideration with this formula. Additionally, while these findings might be expected given a narrowing of the airway tube with resistance on the end, there was also variability among conditions and between larynges.

PTF Variability

In the current study, PTF in the nonstenosed, normal subglottis condition was characterized by greater larynx-to-larynx variability than the stenosed conditions. It is possible that there is slightly less variability at the greatest stenosis condition because with that much narrowing there is likely not much room for flow variation. It is important to consider this variability in light of the descriptive finding that PTF also decreased with percent stenosis. Generally, one would expect decreased PTF with a decreased amount of respiratory effort, which is a positive factor for voice function in many cases. But in the case of narrowing below the vocal folds, the reduced onset pressure might be a necessity with increased obstruction. On the other hand, with more obstruction the lungs may have to put forth greater effort to initiate vocal fold vibration. It is possible that each laryngeal mechanism might respond differently to this form of airflow obstruction, some with increased pressure at the glottis and some the opposite. This would also explain the significant variability among people with SGS with respect to voice
quality ranging from strained and hoarse on one end of the spectrum to weak and breathy on the other (Ettema et al., 2006; George & Monnier, 2010; Grillo et al., 2003; Hseu et al., 2014; Smith et al., 2008). That being said, it is also essential to be cautious when interpreting PTF as applied to clinical populations. Furthermore, future research should examine sustained flow values to further examine aerodynamic features of SGS within the theoretical framework for pressure-flow relationships.

**Methodological Considerations**

**SGS device.** An area of concern for this study that should be addressed in future studies that use an ex vivo larynx model and artificial silicone SGS mechanism was the design of the device. As the device required removal for 0% stenosing trials, this required a rearranging of the larynx, the micropositioners, the trachea device or tube junction, and the changing of the vertical placement of the glottis in relation to the transducers that may introduce variability into the study. It is recommended that the stenosis mechanism design be altered to allow for the device to remain on the benchtop setup for the duration of the procedure that would allow for a complete spectrum of narrowing (i.e. 0% stenosed up to 100% stenosed). This would help reduce the influence of these variables and help standardize the benchtop setup.

**Preservation of the porcine larynges.** Changes in histology may have resulted in variability in the study. In an experiment performed by Chan and Titze (2003), it was found that larger crystals formed on the vocal folds as a result of slow freezing and smaller crystals formed on the vocal folds as a result of being flash frozen. They concluded that the smaller crystals that formed as a result of flash freezing were less likely to alter the histology of the vocal folds. During the present study, the dissected larynges were submerged in liquid nitrogen for flash freezing for 7 minutes. Following the freezing and subsequent storage in the freezer, the larynges
were moved to a refrigerator for thawing. The first 10 larynges were left to thaw for 24 hours, however at the end of the 24 hours, the larynges were still significantly frozen. For the larynges included in the present study, they were submerged in liquid nitrogen for 7 minutes and then thawed in a refrigerator for 72 hours. A slower thawing process as described above has been documented in the literature to lead to larger ice crystals forming on the tissue (Young, Armitage, Bowerman, Cook, & Easty, 1994). The longer thawing time could have resulted in larger ice crystals forming on the larynges in the present study, thus impacting the pliability and histology of the vocal folds. As the changes in histological properties may vary from subject to subject, greater variability may have been introduced in the data as a result.

**Increasing number of trials.** Another consideration of this study is the need for larger trial sizes per observation. An original concern for the larynges was the possibility of dehydration the longer they were mounted and exposed to experimentation, and thus affecting PTF and PTP values. However, from the results it was shown that PTP did not increase after prolonged use in the study, and PTF trends aligned with what we were expecting to find. Therefore, in the future it would be beneficial to run a large quantity of trials, such as 10 to 15 per observation, and average the results as opposed to only three trials per observation. This would allow for the reduction in the influence of outliers and better reflect the impact SGS has on measures of PTF in an ex vivo porcine model.

**Increasing sample size.** Results of the study may have been impacted by having a small data set. Although researchers had 21 porcine larynges over the course of data collection, only 13 of those larynges were used in experimentation. Larynges were unable to complete experimental protocol for various reasons such as anatomical damage or anomalies, vocal folds not vibrating on any experimental condition, and software malfunction that required the disposal of already
thawed and dissected larynges. On the last day of the study computer failure during signal acquisition left only 9 larynges available for analysis. Given the small data set, we were unable to determine statistical significance using parametric statistics. With a larger data set, future studies will be able to more confidently infer the effects of SGS on measures of PTF.

**General Limitations**

As this is a pilot study, it does have several limitations that need to be discussed. One limitation of the study is the possible variability in procedural operations as there was a learning curve for the researchers with laryngeal dissection and trials of phonation. The skills of the researchers in dissecting larynges, mounting larynges on the benchtop, and overall use of equipment improved over the course of the study. With multiple steps of rough and fine dissection of the larynges, there are many opportunities for the integrity of the larynges to be affected. For example, a cut that is too large or made in a slightly different location could potentially result in altered data. Specifically, while trying to dissect away the false vocal folds and excess mucosal tissue, the true vocal folds could have been marginally damaged in the process which could have impacted measures of PTP and PTF. One way to minimize these limitations was to have trainings on how to perform the operational procedures of calibrating the equipment, dissecting larynges, mounting the larynges, and the process for vibrating the vocal folds for collection of data. Larynges that were unable to be used in the study were used as practice for dissection purposes. Additionally, to minimize researcher variability, having the same person perform the same task each day of experimentation allowed for increased accuracy in each step of procedural operations during data collection.

Another possible limitation of this study may have resulted from the process of flash freezing the larynges. Although the researchers standardized the time to 7 minutes for
submersion in the liquid nitrogen, the larynges differed in size and weight and may have required different submersion times. As the liquid became more opaque, severely hindering the ability of the researchers to see into the center of the bag, it was difficult to accurately determine if a larynx was entirely frozen or not. This limitation was minimized early on by determining beforehand which larynges may require more time to freeze and checking throughout the freezing process for moving liquid; however, variability may still occur in this process.

In this study, variability in the form of physical properties of pig larynges may have contributed to the results. The physical dimensions may have varied widely between ages and genders of the pigs. Although the researchers were able to thoroughly document dimensions and weights, we were not aware of the age or gender of the pigs the larynges came from. These differences in physical dimensions may have resulted in variations in the data. Additionally, although studies have shown that porcine larynges have many similar physical and structural properties as human larynges, the angle of the vocal folds are a major difference between them (Alipour & Jaiswal, 2008). Human vocal folds lie at a 0° angle, while porcine larynges lie at a 45° angle. This difference in angle may impact measures of PTF differently.

**Implications for Future Research**

Future studies aiming to explore PTF in the SGS population should utilize a larger sample size and increase the number of trials per observation to reduce the variability between stenosis groups and to reduce the effects of outliers. In the present study the results were in the direction that we would anticipate clinically; however, because there is going to be an inherently greater variability as the airway is increasingly constricted, the variability would need to be accounted for, which can be done by increasing the sample size and increasing the number of trials. Additionally, an increase in the sample size and number of trials would allow for the use
of parametric statistics, which offer more power in detecting significance. For studies involving an ex vivo porcine larynx model, it would be beneficial to gain information as to the gender and age of the larynges, so as to minimize variability between stenosis grades and trials. The most ideal larynges would be from male pigs, as their larynges are larger and more closely resemble the size of human larynges (Pipkin-Litster, 2018).

When considering future research that involves the use of an artificial stenosis mechanism, a device that would allow for adjustments from 0% to 100% stenosing would be ideal to standardize the benchtop setup and eliminate any variability introduced by having to remove the device, remount the larynges on the plastic tubing, and rearrange the micropositioners when adjusting before or after the 0% stenosed trials. This would also aid in standardizing the vertical placement of the glottis in reference to the transducers for collection of data measures.

**Implications for Practitioners**

Given the descriptive findings of this study, the results provide valuable clinical insight into voice treatment for patients with SGS. From this study it can be learned that with the increase in degree of stenosis, flow is slightly decreased. Although SGS is managed with medical intervention with high recurrence rates, this knowledge can help inform clinical management of these populations by supporting voice treatments that would facilitate optimal flow for phrase length and voicing such as: how deep a breath to take prior to speech, shorter phrases, pause intervals, more stable loudness levels, and maintaining as even a pitch as possible (Aronson & Bless, 2009; Boone, McFarlane, Von Berg, & Zraick, 2010; Dobres, Lee, Stemple, Kummer, & Kretschmer, 1990; Pannbacker, 1998; Stemple, Roy, & Klaben, 2014).
Conclusion

Results from the present study, when examined descriptively, indicate that PTF is reduced as the severity of subglottic stenosis increases. This information can help guide clinical practice by informing speech therapists of the needs of SGS patients when it comes to voice treatment for adequate airflow. Given the limitations previously discussed for the above pilot study, future work in this area should focus on addressing these concerns to reduce the presence of variability. Additionally, future research should examine sustained flow values to further examine aerodynamic features of SGS within the theoretical framework for pressure-flow relationships.
References

doi:10.1121/1.2908289


APPENDIX A

Annotated Bibliography


**Purpose of the study.** This study compared the properties of animal larynges, such as pig, sheep, and cow, with human larynges. By doing so, an additional purpose of this study was to identify alternative models of phonation for the human larynx.

**Method.** The study used eight pig larynges, eight sheep larynges, and six cow larynges that were purchased from a butcher shop. Each larynx was cleaned and slow frozen until the time of their use when they were thawed in 0.9% saline overnight and the epiglottis was removed. The excised larynges were then individually mounted onto a tapered tube providing air through the larynges that was humidified, pressurized, and heated. Researchers stimulated the lateral cricoarytenoid muscle to manipulate vocal fold adduction, where the levels of adduction were low, medium, and high, and the fundamental frequency was identified using an electroglottograph. All larynges were subjected to upward and downward pressure-flow sweeps, with each sweep including low, medium, and high levels of adduction. Variables measured consisted of subglottal pressure, sound pressure level, mean flow rate, audio signal, and electroglottograph.

**Results.** The results of the study found that the pig larynges, physically, were the most similar to human larynges partly as a result of them being the only animal larynges with ventricles. Additionally, the results show that the pig larynges had the largest fundamental frequency (F₀) range and produced the loudest sound. It was observed that in pig larynges, the false folds contributed to the production of sound which may have played a part in the loud noise produced. The use of false folds in sound production is a noted difference between human larynges and pig larynges. The larynges with the greatest maximum frequency range value was produced by the pig larynges while the lowest was produced by the cow larynges and it is speculated that it is due to the larger size of the cow larynx.

**Conclusions.** Out of the three animal larynges included in the study, the pig larynges were identified to be the most similar larynges to the human larynx.

**Relevance to the current work.** The results of this study support the use of pig larynges as a more accurate representation of human larynges compared to studies that involve different animal models.


**Review Article.** The purpose of this article is to provide a description of subglottic stenosis as well as potential treatment options. Six methods of treatment (dilation, free graft only, free graft and stent, direct approximation, utilization of mucoperichondrial flap, and reconstruction of the trachea) were described and illustrated. The author included the purpose of each technique, how they are to be performed, and their outcomes. To demonstrate each of the six treatment approaches, the author included six case studies. This article provides useful information for the
present study as it describes the vocal quality for each patient, for which we hope to find PTP and PTF measures to quantitatively define.


**Review Article.** The article begins with the description of idiopathic subglottic stenosis (SGS) and a list of the more common causes for SGS. It then goes on to discuss the demographic most affected by it and their hypothesis as to why. The author hypothesizes that the cause for idiopathic SGS are severe coughing events that begin a chain reaction. Severe coughing causes a rise in subglottic pressure which results in the constriction of the first tracheal ring and the telescoping up to the cricoid cartilage. As a result, mucosal edema, cricoid mucosa trauma, and a reduction in cricoid cartilage blood supply occurs. This results in inflammation to the area, as well as potentially ischemia, which leads to fibrosis and SGS that is then worsened by atypical reactions to estrogen receptors. This occurs until medical intervention is required. This hypothetical explanation as to the etiology of idiopathic SGS is significant because it demonstrates an alteration to the structural integrity of the larynx and subglottis, which may significantly alter the onset PTP and PTF required for phonation.


**Purpose of the study.** The purpose of the study is to conduct a chart review of the authors 52 patients with idiopathic progressive subglottic stenosis, making note of the characteristics found and to assess treatment outcomes.

**Method.** A retroactive chart review was conducted for 52 patients, each with idiopathic progressive subglottic stenosis (IPPS). Data collected across patients consisted of age of onset, gender, symptoms duration, previous surgery/trauma including type and number/frequency, and presence of GERD. Stenosis measurement at the time of the patients first and last surgery were obtained using a 2- or 4-mm outside diameter suction tip at the point of greatest severity at both the anterior-posterior and lateral planes. Additionally, tracheostomies were also recorded.

**Results.** It was found that age of presentation and treatment and follow-up durations varied significantly. All 52 patients had stenosis that were found to begin slightly below the inferior edge of the vocal folds. Preoperatively, the average measurements of width at the points of greatest severity were 4mm in the anterior-posterior plane and 5mm in the lateral plane. However, at last follow-up, the average measurements of width at the points of greatest severity were 6mm in the anterior-posterior plane and 7 mm in the lateral plane. Of the 52, 15 patients presented with a tracheotomy with another 10 patients with tracheotomies being performed.

**Conclusions.** From the chart review a cause for IPSS remains unknown. Repeated endoscopic laser submucosal resection as well as rotation mucosal flaps appears to be the least invasive method for airway maintenance without the need for a tracheotomy.

**Relevance to the current work.** This study may serve to help deliver the current study as it shows the age at which it occurs and affects people is vast and that there is a need for further research into the area of subglottic stenosis for further treatment development for at risk populations.
Purpose of the study. The purpose of this study was to characterize perceptual voice abnormalities and identify potential risk factors for perceptual voice abnormalities in patients with SGS.

Method. This study was a retrospective review that consisted of 31 patients and their medical records (22 females, 9 males) with SGS from a three-year period. At the initial visit, the GRBAS scale (Grade, Roughness, Breathiness, Asthenia, and Strain) was administered to each patient to identify possible relationships between patient characteristics. Additionally, an audio recording sample was acquired from patients, as well as from patients with benign vocal disorders, to allow for comparison and intra-rater reliability, which were also statistically analyzed.

Results. It was found that at the initial visit, the average baseline data for all patients was $G_{1.4}$ $R_{1.2}$ $B_{0.5}$ $A_{0.5}$ $S_{1.1}$. The average Grade scores for males were worse than those for females. Additionally, when it came to GRBAS values, patients who presented with multi-stenosis scored worse than patients with single-stenosis. For Grade, Roughness, and Breathiness scores in patients with prior airway surgery, their average scores were worse than for those patients without any prior airway surgery; and for those patients without having any previous surgery, they had perceptually better voices across all categories. In the categories of Grade, Breathiness, and Strain, there was a higher likelihood of moderate or extreme dysphonia in patients who had been affected by vocal fold motion impairment.

Conclusions. Based on the results of the GRBAS scale, as a whole the patients were perceived to have a mild to moderate dysphonia. There were significant voice quality differences between those patients with multiple-site stenosis and those patients with single-site stenosis. Additionally, patients who have had previous stenosis surgery had a worse voice quality than those patients who had not undergone any previous surgery. Patients who had not undergone any previous surgery also had normal vocal fold motion.

Relevance to the current work. The study above is relevant to the current study as the perceptual measurements collected in the above study sets a framework for the aerodynamic measurements of PTP and PTF that the current study will be collecting in an ex vivo setup with simulated stenosis. By collecting quantitative measures such as PTP and PTF to characterize SGS impact on phonation in conjunction with the perceptual GRBAS measures, speech pathologists and other health care professionals can have more information to guide the treatment process and measure treatment outcomes.


Purpose of the study. The purpose of this study was to determine the validity of the hypothesis that laryngotracheal stenosis (LTS) is heterogeneous in etiology, clinical outcome, and natural history.

Method. This study is a retrospective cohort study which included 150 adult patients with LTS from 1998 to 2013. Patient information such as age, gender, race, comorbidities, and follow-up duration were obtained and recorded. Additional information obtained included etiology of
stenosis, surgical dates, treatment approach, and if a tracheostomy was present at the time of the last follow-up.

**Results.** Data collected revealed that 54.7% of individuals had an iatrogenic etiology, 18.5% with idiopathic, 18.5% with autoimmune, and 8% with a traumatic etiology. Additionally, iatrogenic and autoimmune etiologies caused a significantly larger percentage of individuals to remain tracheostomy-dependent compared to traumatic or idiopathic etiologies.

**Conclusions.** Based on the data collected, LTS is indeed heterogeneous in nature and occurs from a variety of etiologies. The rates of long-term tracheostomy dependence vary based on the etiology of the disease.

**Relevance to the current work.** LTS affects similar anatomical structures as subglottic stenosis and this retrospective study provides valuable information as to the complex nature of stenosis in the respiratory tract from varying etiologies.


**Purpose of the study.** The purpose of this study was to examine the correlation between pre-surgical glottis involvement and post-operative outcome of the voice in children with SGS. The measurements were compared following a cricotracheal resection. The results of both pre- and post-operative voice were derived from voice questionnaires. In addition, the hypothesis of patients with vocal fold involvement in their SGS would have an impaired vocal quality following surgery and those without vocal fold involvement would have normal vocal quality following surgery was tested as well.

**Method.** This study compared endoscopic observations between two surgical ear, nose, and throat surgeons for 108 patients over a 30-year period who had undergone PCTR. The raters independently observed endoscopic images and dynamic functional airway assessment of the SGS in 108 patients and asked to rate their severity. The raters were blinded to one another’s ratings. Glottic involvement was rated and divided into the following four categories: A) SGS clear from vocal folds (3 to 4mm below) with normal function, B) SGS reaching the free border of vocal fold and/or posterior commissure with slightly limited abduction with no true posterior glottis stenosis, C) SGS with associated posterior glottal stenosis or vocal fold fusion without cricoarytenoid ankyloses, or D) Transglottic stenosis with/or without bilateral cricoarytenoid ankyloses. In addition, a questionnaire was also given to evaluate the functioning of patient vocal fold.

**Results.** Of the original 108 patients, only 77 were available for long-term follow-up. The 77 patients were divided into the four categories as follow, 31 patients were categorized as group A, 30 were in group B, 12 were in group C, and 4 were in group D. The questionnaires indicated 18% of patient’s voices were perceived to be normal following PCTR. The patient’s voices perceived as normal were in group A. Patients with mild dysphonia were from either group A or B. Those with moderate dysphonia belonged to group C. Patients with severe dysphonia were from group D.

**Conclusions.** From preoperative endoscopic imaging and dynamic assessment to determine the extent of glottis involvement, a patient’s voice outcome can be predicted. Additionally, if the patient presented with glottic involvement, there is a high likelihood of poor vocal quality following PCTR treatment.
Relevance to the current work. This study utilized dynamic functional airway assessment as a means to determine vocal fold functioning. Similarly, the current study is using aerodynamic measures of PTP and PTF to analyze vocal fold functioning with varying SGS severity.


Purpose of the study. The aim of this study was to look at the early and long-term effects of a single stage laryngotracheal resection and reconstruction on idiopathic laryngotracheal stenosis (ILTS).

Method. Researchers collected data from 73 patients, of which 71 were females, through chart reviews and questionnaires. The age of patients ranged from 13-74 years.

Results. Following roughly an eight-year period, good to excellent results were seen in 90% of the patients (66 patients). It was found that 26% of patients saw no difficulties in breathing while at rest or during exercise and no changes were reported in their voice. It was reported, however, that 64% of the patients noted difficulty with both singing and speaking louder as they were able to before, while 7% experienced dyspnea with moderate exertion, noisy breathing, and the need for occasional dilation.

Conclusions. The results of the study show that ILTS is able to be effectively treated with 1-stage laryngotracheal resection and reconstruction both early on and in the long-term.

Relevance to the current work. Although this study included idiopathic laryngotracheal stenosis, it is fairly closely related to idiopathic subglottic stenosis and the voice of patients can be impacted as was seen in the study above. With the addition of aerodynamic measurements of PTP and PTF, patients will be able to see how their voice is affected as a result of SGS, as well as the relative function of their vocal folds from treatment. Patients and care providers would be able to track vocal fold function and be able to determine how far from normal the vocal folds are functioning and be able to use that information help guide treatment and therapy practices.


Purpose of the study. The purpose of this study was to evaluate microlaryngoscopy with balloon dilation on patients voices in regard to the outcomes of quality of life and perceptual voice characteristics both preoperatively and postoperatively. Additionally, researchers looked at how the level of stenosis impacted voice quality, as well as how voice quality changed in regard to endoscopic dilation.

Method. The study was a retroactive chart review of patients with laryngotracheal stenosis that had been treated via balloon dilation from the years 2010 to 2013 at a tertiary-care academic hospital. The laryngotracheal stenosis patients were categorized into either 1) subglottic or tracheal stenosis and 2) multilevel stenosis occurring at the glottis, subglottis/trachea. Voice characteristics of grade, roughness, breathiness, asthenia, and strain (GRBAS) were compared preoperatively and postoperatively using V-RQOL. Additionally, the number of times a balloon
dilation procedure was performed and the frequency with which a patient received it were variables that were looked examined.

**Results.** The chart review identified 38 patients with LTS, 26 with subglottic/tracheal and 12 with multilevel stenosis. It was identified that 27 patients V-RQOL mean scores improved postoperatively. Additionally, it was identified that subglottic/tracheal stenosis preoperatively and postoperatively had higher V-RQOL means than the multilevel stenosis group did. GRBAS ratings were identified to have improved in 10 patients across all domains except for breathiness.

**Conclusions.** Patients in the MLS group with glottic involvement had a worse voice quality of life by a significant amount than those in the tracheal/subglottic stenosis group. V-RQOL improves preoperatively to postoperatively following endoscopic balloon dilation in the subglottic/tracheal stenosis population. Furthermore, it can be concluded that LTS has a direct association with dysphonia.

**Relevance to the current work.** Much like the study above, the current study will also look at the impact that subglottic stenosis will have on phonation. The study above may help predict the outcomes of the excised pig larynges breathiness during attempted phonation.


**Purpose of the study.** The purpose of this study was to quantify phonation instability flow as a means to assess when normal vocal fold vibration occurs. Phonation instability flow is defined as the point when vocal fold oscillation becomes irregular.

**Method.** This study is a control study where each ex vivo larynx serves as its own control. Seven canine larynges were acquired post-mortem and examined for damages prior to being frozen in a 0.9% saline solution. Prior to their use in experimentation, the larynges were finely dissected to expose the true vocal folds and then mounted on a bench apparatus with a metal hose clamp around the trachea and 2 lateral three-pronged holders in the larynx for stabilization. A suture was then placed anteriorly in the thyroid cartilage and attached to a device that could be adjusted for elongation trials. A pseudolung was used to send air through the larynx to initiate phonation. During experimentation, air pressure and flow were measured at both the onset of phonation as well as the onset of chaos under the following three conditions: 0% elongation with no glottal gap, 20% elongation without a glottal gap, and 20% elongation with a 3-mm posterior glottal gap. Airflow was continually increased until PTP and PTF were achieved and then increased until chaotic phonation was achieved. Following this, airflow as then reduced until phonation halted. Researchers then used a paired t-test to identify if there were any significant differences present between elongation and degrees of abduction.

**Results.** The findings show that both phonation instability flow and phonation flow range were significant for abduction and not elongation. Phonation instability pressure was not dependent on either of the parameters. It was also found that phonation instability flow and phonation flow range showed greater significant differences for abduction then compared to PTP and PTF.

**Conclusions.** The results of this study show that PIF and PFR could serve as useful parameters of evaluation in the clinical setting for vocal fold pathologies such as paralysis, presbylaryngis, vocal nodules, and vocal polyps.

**Relevance to the current work.** The study above utilizes a similar benchtop setup as the present study and provided greater insight into the use of aerodynamic measures such as PTF.
Additionally, as it was found in the above study that PTF is influenced by abduction, adequate vocal fold abduction will be highly monitored through each trial to ensure collection of best PTF measures.


**Purpose of the study.** Compare PTP and PTF following variations in prephonatory glottal width. PTP and PTF where observed and measured in terms of physiologic changes.

**Method.** Ten excised canine larynges with posterior glottal widths abducted using a metal shim to five different widths ranging from 0mm to 4mm. The pressures and airflow at onset were measured for each larynx.

**Results.** The results of PTP were not significant and did not increase with glottal width; however, PTF did increase in conjunction with glottal width. The results of the study were evaluated using a one-way analysis of variance.

**Conclusions.** The study showed that PTF is a more sensitive measure to changes in posterior glottal width than PTP and can be a helpful aerodynamic measure in detecting vocal fold pathologies of adduction.

**Relevance to the current work.** Measures of PTP and PTF were both collected in the present study. As PTF was observed to be a more sensitive measure of posterior glottal width in excised canine larynges, similar findings of PTF sensitivity may have been indicated in the current study with excised porcine larynges with variations in subglottal width.


**Purpose of the study.** This study looked at treatment outcomes for adult patients with SGS following endoscopic surgical management over the time span of 10 years.

**Method.** This study is a 10-year retrospective review of 92 adult patients (69 female, 23 male) medical charts diagnosed with SGS. Researchers examined case information such as age, gender, presenting symptoms, and comorbidities such as history of cardiac, pulmonary, and gastroesophageal reflux disease. Additionally, researchers looked at etiology, the grade of stenosis, and the dates of surgery for each patient. Voice Handicap Index (VHI) and maximum phonation time (MPT) were used for voice assessment. Statistical analysis was conducted using standard deviations, t-tests, Kaplan-Meier estimation, and log-rank test, and Cox regression.

**Results.** Of the 92 patients, 45% were due to granulomatosis with polyangiitis, 33% were idiopathic, and 25% were as a result of intubation. In total, the 92 adults had 247 endoscopic dilations and 55% of the patients required multiple surgeries. Further surgical management was determined based on severity of SGS, time post-surgery, and the surgical method used. Additionally, steroid injections during the first surgery did not increase the time in between additional surgeries. Except for one patient, all other patients had received voice assessments both pre-surgery and post-surgery. Voice assessment was conducted using VHI, MPT, and videostroboscopy with results indicating that 83 patients had mild to no complaints while 8 patients were considered to be dysphonic. For 44 patients, their results indicated improvement in VHI and MPT. For all patients, improvement in symptoms was reported postsurgery.
Conclusions. Endoscopic management of SGS results in symptom improvement in patients. However, while patients breathing improves, recurrence rates remain elevated. Neither etiology, injection of steroids, method of scar lysis, or application of mitomycin C made a difference in the need for multiple procedures or the time in between procedures.

Relevance to the current work. The study above relates to the current study as the researchers used an aerodynamic measurement of MPT to assess patient’s voice with SGS. Similarly, the current study aims to use other aerodynamic measures (PTP and PTF) to assess SGS impact on phonation which may help to develop additional parameters of measurement for clinical assessment and treatment outcomes for patients with SGS.


Purpose of the study. The purpose of this study was to observe the anatomical and physiological differences between the four larynges to identify the best animal model for the physiological study of phonation.

Method. The study included larynges from 3 pigs, 3 dogs, 3 white-tailed deer, and 2 humans. The excised larynges were then dissected of excess muscle and tissue to greater expose the vocal folds. The following measurements were taken: resting length of the vocal folds, vocal fold height, cricothyroid joint ROM, vocal fold stiffness, and glottal configurations.

Results. Results of the study indicate that all larynges studied had fairly similar vocal fold length. There was similar cricothyroid joint movement and more precise movement due to the cartilage framework in human, pig, and dog larynges, while the deer larynges had a more restricted movement. The study also found the vocal fold cover and stiffness to be the most similar between the human and pig larynges. Additionally, following acoustic analysis of the recordings of the natural phonation of each species, it was found that the F0 and phonation range are the closest between humans and pigs.

Conclusions. Given the anatomical structure and vocal physiology of the pig larynx, the pig may be the superior model for studying phonation in regard to the human larynx.

Relevance to the current work. This study validates the use of porcine larynges as a suitable means to represent and study phonation of the human larynx. Additionally, the similarities between pig and human laryngeal properties as described in this study may help in delivering the current study as it aims to analyze how excised porcine vocal folds function given a subglottic narrowing and its translation to human phonation under similar circumstances.


Purpose of the study. The purpose of this study was to identify the minimal amount of airflow required to initiate steady phonation. This study looked at PTF as a viable measure of assessment and compared it to PTP.

Method. The method of study used was a one mass model to study the minimal amount of air flow required to initiate vocal fold vibration.

Results. The study results showed that PTF was affected by the shape of the glottis and was varied depending on the tissue viscosity of the folds. Additionally, the amount of PTF required
could have been reduced with the decrease in resistance of the vocal tract.

**Conclusions.** This study showed that PTF is a viable and more reliable method of evaluating laryngeal dysfunction as a result of vocal pathologies than PTP.

**Relevance to the current work.** This study examined the effects of PTF and the factors that may result in PTF to change. The current study likewise will examine PTF and how PTF changes as a result of glottal narrowing.


**Purpose of the study.** This study observed hemilarynx phonation characteristics in comparison to phonation characteristics of a full larynx.

**Method.** This study utilized nine large excised mongrel dog larynges. The larynges were dissected and placed in 0.67% saline solution and refrigerated prior to use in the study. Prior to mounting for the initiation of the experiment, the larynges were removed and thawed. Data of whole larynx phonation was then collected. Following whole larynx phonation, the larynges were dissected, removing the left vocal fold and a 9-mm thick plexiglass plate with pressure transducers was used in its place. Each hemilarynx was then phonated again, recording PTP, sound pressure level, F0, and average glottal flow. To record the amplitude of each laryngeal vocal fold vibration, a stroboscope was used.

**Results.** Following data collection, researchers found that PTP and frequency ranges were similar for both hemilarynges and whole larynges. However, researchers found that full larynges were louder on average than hemilarynges. The full larynges also had a slightly lower phonation instability pressure than the hemilarynges. Additionally, the amplitude of vocal fold vibrations differed between hemilarynges and full larynges in that the hemilarynges appeared to vibrate at half the amplitude that the whole larynges did.

**Conclusions.** This research shows that a hemilarynx and full larynx are similar, which provides knowledge about phonation that can be beneficial to patients who have a partial laryngectomy in the vertical plane; as well as for SLP’s who provide therapy for such patients and may lead to enhancement in treatment techniques for this population.

**Relevance to the current work.** This study relates to the current study as they both include measures of PTP in data collection, which may lead to increased knowledge of PTP in pathological voices.


**Purpose of the study.** The purpose of this study was to examine the correlation between length of intubation and additional risk factors on the development of laryngeal lesions in children undergoing endotracheal intubation in the ICU. Additionally, this study aimed to identify the incidence of subglottic stenosis (SGS).

**Method.** This was a prospective study that looked at children at the ages from birth to no more than 5 years old who were admitted to the hospital and required an endotracheal intubation for at least 24 hours. This equated to 142 admitted children. Eligible children were examined using a flexible fiberoptic laryngoscopy (FFL) following the removal of the intubation tube. When
Results. It was found that of the 142 children included in the investigation, there were 58 in the first round of FFL that had moderate to severe abnormalities. This equaled out to be 40.8%. Additionally, it was found that 16 of the children had developed subglottic stenosis at some point. This equaled out to be 11.3%. The severity of SGS was as follows: two with Grade 1 SGS, five with Grade 2 SGS, six with grade 3 SGS, and three with grade 4 SGS. Following the use of a multivariate analysis, it was found that there was a 50.3% risk increase for SGS development for every 5 additional days a child was intubated. With each additional sedation doses per day, the multivariate analysis showed that there was a 12% increase for developing SGS.

Conclusions. Based off of the cases followed and data collected, the length of the intubation and doses of sedation were the primary causes for the development of SGS in these children who underwent endotracheal intubation.

Relevance to the current work. The above study demonstrates the frequency with which SGS occurs and supports the need for further research into SGS to develop clinical assessments for earlier identification in at risk populations. The current study begins to answer that need by examining aerodynamic measurements of PTP and PTF possible at varying degrees of stenosing.


Purpose of the study. This study identified PTP and PTF for excised human larynges and observed the effects of glottal area, posterior glottal width, and gender on PTP and PTF outcomes. Additionally, the research study aimed to determine the presence of hysteresis in excised human larynges during phonation.

Method. The study included nine human larynges that were harvested 24 hours or less after death and were then placed in a phosphate-buffered saline solution in a sealed beaker. The larynges were prepared for testing by removing extrinsic laryngeal musculature and any additional associated tissue prior to mounting on a benchtop setup for test initiation. Both PTP and PTF were measured at phonation onset and offset. To aid in maintaining consistency across trials, screws were used to secure laryngeal structures. During testing, desiccated and compressed airflow was passed through the larynges while the mean flow was measured via an inline flow meter. Additionally, electroglottograph was measured via electrode plates secured to the strap muscles and for additional experiments later on a sound level meter was attached. To test the effects of posterior glottal width on PTP and PTF, plastic shims with the following thicknesses of 0.5, 1, 2, 3 mm were placed between the arytenoid cartilages and five phonation trials were conducted per each posterior glottal width on all larynges used.

Results. The study results showed PTP and PTF onset measurements to have more variability than the offset measurements. Additionally, there was not a significant difference in aerodynamic measurements in posterior glottal width on PTP and PTF. When measuring prephonatory glottal area effects on PTP and PTF, a positive relationship was found between glottal area and PTF onset and offset, but there was no correlation observed between glottal area and PTP onset and
offset. In regard to gender difference on PTP and PTF, it was observed that PTP and PTF onset and offset were greater for males than females. Following the completion of the 197 trials, the PTP mean range was 0.783 ± 0.093 and the PTF mean range was 0.880 ± 0.087.

**Conclusions.** The results of this study confirmed hysteresis where offset and onset differed. Additionally, the results of smaller variability in offset measures indicates that PTP and PTF offset measures might be a more reliable value than onset measures. Furthermore, this study supports the use of canine larynges as a better model for measuring PTP and PTF rather than human larynges.

**Relevance to the current work.** This study provided relevant data from human larynges as to PTP and PTF; variables that were measured in the current study, as well as setting up an excised larynx model with secured laryngeal structures for consistency. This study also lays out benefits to using animal models for collecting data related to human vocal fold pathologies.


**Purpose of the study.** This study aims to evaluate how well a multimodality approach will treat idiopathic subglottic stenosis and identify any potential predicting factors that treatment will be successful. It also aims to better define limitations and roles of endoscopic and open surgery.

**Method.** The study included 54 females with subglottic stenosis who were treated either with an endoscopic approach or by an open surgical procedure between 2004 and 2012. The mean age of females in the study at the time of diagnosis was 47.8 years +/- 12.1 years. For 21 patients (39%) they received treatment prior to being involved in the study.

**Results.** For maintenance of 78% of those involved in the study, they could be treated endoscopically with a minimally invasive procedure. There was a five-year actuarial success rate of 87.5% for the endoscopic treatment of subglottic only disease as opposed to only 18.7% for concomitant glottis and subglottic diseases. It was found that open treatment reduced the rate of intervention from 5.44 +/- 5.8 to 1.14 +/- 1.61 a year. For those who had received a laryngectomy, the airway-dyspnea-voice-swallowing system (ADVS) indicated that all except one patient were able to maintain prosthesis-and stoma-free airways (A1) by the last follow-up. There were 26 patients who had D1 and D2 dysphonia grades, 41 patients received a V1 voice, 9 patients had V2 voices, 4 patients had V3 or V4 voices, and 51 patients had a normal swallow (S1). Additionally, the suboptimal voice outcomes were due to weak breathy dysphonia. There was only one variable that remained significantly and independently associated with dyspnea and voice outcomes on a multivariable regression analysis and that variable was if the glottis was involved or not.

**Conclusions.** ISGS is able to be effectively treated using a minimally invasive approach to treatment. The less severe the ISGS is the fewer endoscopic treatments are needed. Airway framework expansion with implantation of biological inhibitors of fibrosis is a viable treatment method for those who are unable to benefit from an endoscopic treatment. This approach is able to achieve long-term disease remission without causing vocal gender reassignment. At the time of presentation, glottis involvement was the only variable that was independently associated with dyspnea and suboptimal voice outcomes

**Relevance to the current work.** This study quantified ISGS patients voice outcomes. The current study is also looking to identify quantifiable measures of vocal fold vibration of SGS.

**Review Article.** This article provided valuable insight and knowledge about SGS including the etiology, clinical presentation, anatomy, and treatment of it. It addressed a variety of etiologies and the common symptoms such as stridor, dyspnea, hoarseness, aphonia, and cough. The article discussed anatomical abnormalities of both the trachea and larynx as a result of SGS. The article’s discussion of treatment varied across the board from the least to the most invasive medical procedures with benefits and disadvantages for each treatment option noted. A disadvantage of particular note that is relevant to the current study was permanent voice disorders. This article provides valuable supporting evidence for the effects SGS has on the voice; effects that the current study hopes to see when collecting PTP and PTF measures.


**Purpose of the study.** The purpose of this study was to measure PTF onset and offset in excised canine larynges.

**Method.** The study included ten excised canine larynges that were stored in a 0.9% saline solution and frozen until their time of use when they were thawed and mounted on a bench apparatus with a pseudolung attached inferiorly. During experimentation, subglottal flow was increased until the time of phonation. Following phonation, subglottal flow was decreased until phonation ended. Measurement of PTP and PTF were obtained for both onset and offset. Following collection of first measurements, the vocal folds were elongated and PTP and PTF were then recorded. This data was then compared to determine if similar PTP and PTF values would be attained for larynges with vocal fold pathologies.

**Results.** The results of the study showed a higher onset PTF than offset as well as ratios between 0.515 and 0.972; a larger range than what was expected.

**Conclusions.** The use of PTF as a diagnostic measurement could be valuable in the identification and treatment of the voice; helping to describe aerodynamics and laryngeal resistance in combination with PTP.

**Relevance to the current work.** Such as with this study, the current study includes excised animal larynges, previously frozen larynges, the use of a pseudolung, and data collection of both PTP and PTF. The setup of this study may be helpful with providing insight for the current study.


**Purpose of the study.** This thesis sought to examine the relationship between subglottic geometry and vocal fold vibration in both a computational and synthetic vocal fold model.

**Method.** The research was conducted using three separate studies. A self-oscillating two-dimensional vocal fold model was used for measuring the association between voice production and the surface angle of the inferior vocal fold. Then SGS was added with the shape manipulated to evaluate the effect SGS had on vocal fold vibration. A synthetic model was then used as a
means of studying SGS on vocal fold vibration. Both the computational and synthetic models used the 0%, 60%, and 95% stenosis severities as well as the pressures onset pressures of 1.25 and P1.5 cmH2O.

**Results.** This study found that by varying the inferior angle, there were significant changes in the glottal width, vibratory motion, energy transfer, and flow rate which occurred mainly as a result of structure changes as opposed to aerodynamic changes. Additionally, it was also found that the vocal fold vibration, vibration sequence, flow resistance, flow rate, and glottal width were most significantly affected by the 95% SGS severity only. The most change was seen in radiated acoustic sound, glottal efficiency, and subglottal pressure.

**Conclusions.** From both the computational and synthetic models, a subglottic stenosis of 90% and greater affected vocal fold model vibration. With significant decreases in the rate of maximum flow declination and the presence of more severe SGS, both the sound and power of the voice was affected. When the inferior angle of the model was differed, vocal fold vibration was significantly changed.

**Relevance to the current work.** As with the study above, the current study is looking at varied narrowing severity of subglottic stenosis and its effect on vocal fold oscillation. This study provides valuable information as to the possible PTP and PTF outcomes of the current study.


**Purpose of the study.** The purpose of this study is to compare presentation and surgical methods of treatment in granulomatosis-related SGS with polyangiitis (GPA-SGS) and idiopathic SGS (ISGS).

**Method.** A retrospective chart review of 39 patients from 2005 and 2010. The patients consisted of 15 individuals with granulomatosis-related SGS (both males and females) and 24 individuals with idiopathic SGS (females only). There was a median age of 36.3 years for the granulomatosis-related SGS individuals and a median age of 45.2 years for the idiopathic SGS individuals. The 39 patients included in the study were also described using the Myer-Cotton staging system (MCS) to classify stenosis severity, the presence of tracheostomy, if there is a need for endoscopic tracheal dilation procedures, and the presence of GERD.

**Results.** Patients with ISGS were found to have more severe stenosing while there was a tendency to see more circumferential stenosis in the GPA group. There was no additional need for further management for the ISGS group following surgical management involving operative section or reconstruction, while the individuals in the GPA-SGS group required more than one airway dilation. Likewise, no patients in the ISGS group required a tracheotomy procedure, while 40% of patients in the GPA-SGS group required a tracheotomy procedure.

**Conclusions.** From the study, ISGS presents almost exclusively in females, mostly who are middle aged, and results in a more severe stenosis. This type of SGS also is treated most effectively with open airway reconstruction. Contrastingly, GPA-SGS occurs in both males and females equally and has a greater occurrence of tracheotomy.
Relevance to the current work. This study relates to the current work as it provides further insight into the variability of SGS as a disease and shows that different etiologies of SGS affect populations differently. It supports the need for further research into the disease and its effects on the voice.


Purpose of the study. This study set out to examine the characteristics of idiopathic subglottic stenosis (ISS).

Method. A retrospective chart review was conducted on 16 qualifying patients (16 females, 2 males) ranging in ages from 13-73 years at time of diagnosis. Data collected consisted of age at presentation, gender, previous airway infections, GERD symptoms and treatment, previous endotracheal intubation or local trauma, number and type of surgical procedures, and any other possibly related systemic illnesses.

Results. Researchers found the average follow-up time to be 75.5 months. There were 14 patients that had a presentation of dyspnea. In 9 of the patients, there was a medical history of endotracheal intubation with an onset of roughly 4 years prior to onset symptoms. Surgical procedures were required in 14 of the patients for airway improvement due to symptoms severity. Endoscopic laser procedures were conducted in 8 patients, however the procedure failed in 5 of these patients. Laryngotraheal resection and reconstruction proved to be helpful in those patients where the endoscopic laser procedure failed.

Conclusions. Based off of the results found, researchers concluded that ISS is a diagnosis of exclusion. Patients with this disorder may present with symptom such as stridor, airway obstruction that can grow to be life threatening, and dyspnea. Endoscopic laser procedures are effective in treating non-complicated lesions that are thinner while laryngotraheal resection and reconstruction is an effective treatment for the more complex and thicker stenosis.

Relevance to the current work. This study relates to the current study as it collected data on percent of stenosing in each patient. The study examined voice effects as a result of the stenosis, however the current study can build on this study by providing qualitative measures of vocal fold function in regard to the percent of narrowing in the vocal folds as a means for comparison pre and postsurgical treatment.


Purpose of the study. This study aimed to determine how PTP is affected with the increase in exposure to dry air in excised canine larynges.

Method. Eleven excised canine larynges were obtained postmortem, examined for damage, and frozen in 0.9% saline solution until their time of use when the larynges were mounted on a benchtop setup. The experiment consisted of three groups: a desiccation group with 8 larynges, a control group with 2 larynges, and then 1 larynx that was used in both groups. The trials consisted of cycles with 10 seconds for phonation and then three seconds for rest. Dry air was presented subglottally until phononation was initiated. The control group received humidified air subglottally as well as a 0.9% saline applied to the vocal folds topically, supraglottally.
**Results.** It was found that PTF increased with the increase in exposure to dry air. This relationship was not seen in the control group. Additionally, a point did exist at which the vocal folds could no longer be initiated to vibrate.

**Conclusions.** A clear relationship exists between the level of vocal fold dehydration and PTF. This knowledge gained can help improve clinical assessment of vocal dehydration and preventing these effects in humans. However, further research will need to be conducted to evaluate the relationship between dehydration and vocal fold health, as well as research using an in vivo model, for further development of techniques for hydration therapy.

**Relevance to the current work.** The current study aims to assess PTF for larynges that serve as their own control, thus exposing them to prolonged air exposure. Knowing how dry air can impact the function of ex vivo vocal folds on a benchtop model, and thus PTF measures, allows us to be able to monitor for potential dryness and the necessity for maintaining hydration when switching between stenosis narrowing in between trials.


**Purpose of the study.** To uncover the dynamic mechanisms of phonation pressure range, PTP, and phonation instability pressure by utilizing bifurcation analysis. In addition, this study observed how phonation pressure range, PTP, and phonation instability pressure were affected by vocal fold lengthening.

**Method.** This experiment consisted of 10 canine larynges that were collected and run experimentally 48 hours after. The experiment setup was as follows: the larynges were mounted onto a pipe attached to a pseudolung, the larynges were fixed using a metal clamp around the trachea with 2 three pronged devices for better stabilization of the larynx. Researchers then began a regulated airflow stream through the larynges and vocal folds while researchers measured PTP and phonation instability pressure. The vocal folds were then elongated using a precise micrometer system to 5%, 10%, and 15% for each larynx while PTP and phonation instability pressure were tested again. The procedure for each percent of elongation was repeated three times for greater accuracy.

**Results.** Bifurcation analysis was an effective measurement for phonation pressure range, PTP, and phonation instability pressure. From the study, it was found that there was a significant increase in PTP with increased elongation, phonation instability pressure was not significantly affected, and a significant decrease in phonation pressure range with vocal fold elongation.

**Conclusions.** Phonation instability pressure and phonation pressure range may serve as a valuable clinical measurement for phonation instability in the assessment and treatment of laryngeal pathologies. Additionally, bifurcation analysis may also serve as a valuable tool for future research into vocal fold pathology investigations and identifying the mechanisms behind the three parameters.

**Relevance to the current work.** A similar benchtop setup was utilized in the present study. Additionally, this study supports the use of animal larynges in analyzing PTP when assessing constants and changes in human laryngeal pathologies.
APPENDIX B

Experimental Checklist

Materials for Dissection and Preservation:
1. scalpels (2 different types)
2. apron
3. gloves
4. green dissection paper (to be laid on the dissection table)
5. saline spray bottle
6. 1 Ziploc bag
7. hemostats
8. sutures (1 for each larynx)
9. dissection tables
10. red hazard box (rinse scalpels and then place them in this box)
11. Clorox wipes (for clean-up)
12. paper towels (to hold larynx steady)
13. Mini fridge
14. Freezer
15. 0.9% sodium chloride irrigation USP fluid (isotonic saline)
16. Styrofoam cooler (to place liquid nitrogen in)
17. Liquid nitrogen (from the Chemistry Central Stockroom located in room 126 of the Nicholes Building at Brigham Young University)

Additional Notes for Dissection:
- Remove all surrounding tissues of the larynx such as the esophagus, thyroid gland, fat, excess tendons, innervation, vascularization. Make sure the trachea and thyroid cartilage are intact and without any abnormal openings or damage.
- Use the largest tracheas—these are best for phonation and mounting onto custom tubing.
- Tracheas should be cut superiorly of the true vocal folds.
- The shape should be a smile formed from the anterior commissure to the lateral posterior ends of the thyroid cartilage.
- The true vocal folds should not be punctured (this will prevent air leakage).
- The arytenoid cartilages should be left intact (this will aid in adduction).
- The epiglottis should be removed by cutting a triangle posterior and in between the arytenoid cartilages.
- Remove false folds completely (may use a hemostat for better precision).
- Remove any leftover tissue superficial and superior to the vocal folds (this prevents flopping of tissue during vibration of true vocal folds).
- Trim the trachea leaving the trachea about 8-10 cm in length. (verify the inferior end of the trachea fits around the custom tubing connecting to the pseudolung).
- Suturing: should be placed above the anterior commissure on the thyroid cartilage. First tie the end of the string attached to the suture in a knot (make several knots in the same location in order to prevent the string from going through the cartilage). Hold the sharp end of the suture using a hemostat to provide support to puncture the anterior end of the
thyroid cartilage (located just above and in front of the anterior commissure) (repeat this 4 times) make sure suture is tight and tug at it to observe its strength

Materials for Quick Freezing:
1. dissected larynges in Ziploc bags filled with saline
2. extra saline
3. extra Ziploc bags
4. protective ear equipment
5. 2 styrofoam boxes
6. sharpie
7. cold resistant gloves
8. liquid nitrogen
9. freezer
10. refrigerator

Additional Notes
- Fill a styrofoam box with liquid nitrogen
- While wearing cold resistant gloves and ear protection, submerse 2 larynges in the bags with saline in the liquid nitrogen. Leave the Ziploc bags open
- Leave the larynges submersed for approximately 7 minutes. Check and make sure they are completely frozen by tipping the bag on its side and observing if any liquid is still moving
- Once frozen, place each larynx in a second Ziploc bag
- Write the date on each Ziploc bag
- Place each frozen larynx in the second styrofoam box to keep them from melting
- Once all the larynges are frozen, put them in a freezer until 48 hours before the experiment
- Move the larynges from the freezer to a refrigerator the night before the experiment to allow them to thaw. Ensure that they are in an enclosed space, such as a drawer, because the bags tend to leak as they thaw

Materials for Experiment:
1. 4 LED lights (make sure fresh batteries are in place)
2. artificial silicone subglottic stenosis mechanism
3. macropositioners
4. micropositioners
5. adjustable hose clamp (used to seal edges of trachea onto the stenosis device and custom tubing which is attached to the pseudolung)
6. Flow meter (Aalborg mass flow meter GFM-47)—flow should be calibrated at 0, 10 and 15 cmH₂O
7. Medical Flow Meter- attached directly to the air tank and to the Aalborg mass flow meter GFM
8. 2 Air tanks (one will attach to the flow meter and the humidifiers; the other will be for desiccated air)
9. Pressure transducer (should be plugged in from computer to inferior lateral portion of larynx or the custom tubing)
10. pressure calibrator box (should be used only to calibrate pressure transducer) calibration occurs at 0, 10 and 15 PSI
11. check all plugs
12. WinDaq should be turned on and 4 different waves should be showing (wave 1 measures: microphone signal; Wave 2: pressure; Wave 3: Flow; Wave 4: High Speed Trigger)
13. Humidifier (make sure tubing is plugged in to pseudolung and air tank)
14. High Speed video camera: Trigger should be on and plugged into the sound board
15. Microphone (SHURE SM-48) should be on and plugged in (before starting experiment make sure the wave shows up on WinDaq by tapping the mic lightly) (position microphone about 4 inches away from the larynx.)
16. High Speed-make sure trigger is plugged in
17. Clorox Wipes
18. Paper towels
19. Metal shim (diameter 5mm)

Measuring Flow
1. Make sure flow meter (Aalborg mass flow meter GFM) is plugged into outlet
2. Verify computer is turned on and the WinDaq window is opened
3. Verify flow signal is not peaking (max should be 100 liters/min)
4. Should be directly attached to WinDaq box which is attached to the computer
5. Record when flow is at 0 (mark exact number ~ -.6)
   a. Shift space-to make a comment
6. Record when flow is at 15 (mark exact number)
7. System is ready to record
   a. Hit F4 to record
   b. Hit shift F4 to standby
   c. Hit shift space to apply comment (comment does not appear until you hit enter)

Measuring Pressure
1. Make sure pressure transducer is plugged into the WinDaq box which is connected to the computer
2. PSI or cm H2O
3. Insert pressure transducer directly into PC-IH box
4. Verify WinDaq is picking up pressure signal by observing wave 2
5. Calibrate pressure at 0 and 10 PSI
   a. Record F4 at 0 PSI
   b. Hit shift space to apply the comment (insert press_cal_0)
   c. Do the same for 10 PSI
6. Remove pressure transducer from PC-IH box
   a. Press button before releasing syringe
   b. There should not be any tension when releasing the syringe
7. Insert pressure transducer into opening inferior to the mounted trachea
8. Ready to record
   a. Record F4
   b. Hit shift space to apply the comment (e.g., D3P01) (trial type and pig number along with trial number)
   c. Do the same for all trials

**Recording High Speed**
- Unit should be plugged in and on
- Verify all components are turned on in order (high-speed, computer, monitor)
- Login to computer, open Kay Pentax software
- Verify camera and waveform signals are on, and ensure settings are to record “END”
- Click record, wait for camera to lock
- Click trigger when ready to record (records 4 seconds prior to trigger)

**Microphone signal**
- SHURE SM-48
- Make sure the microphone is plugged into an outlet.
- The microphone should be about 4 inches away from the glottis
- Make sure there is not peak clipping in the recording. If there is, move the mic away from the larynx

**Procedure for Phonatory Trials**
- Use random number generator to determine order of trials (0%, 50%, 75%)
- Depending on order, either mount larynx directly onto plastic tubing protruding from the benchtop for 0% stenosing trials or mount stenosis device and then mount larynx onto device for 50% or 75% stenosing trials
- Mount larynx on stenosis device for 50% and 75% stenosed trials
- Allow vocal folds to vibrate for 2-3 seconds

**Humidifier**
- (Thera-Heat Heated Humidifier-Portex) by Smiths Medical:
  - Make sure this is plugged into an outlet
  - Use standard settings
  - Should be plugged in directly to the flow meter (clear tube) and into the custom tubing of the pseudo lung. (blue tube should be attached to the pseudolung)

**Flashlights:**
- UltraFire XML-T6
- Verify these have fresh batteries and are working prior to beginning the experiment
- Should be equidistant from the glottis.
- Position one directly anterior to the glottis
- 2 will be positioned laterally equidistant from the glottis
- 1 should be positioned posteriorly
- Use as many as are necessary (check prior to beginning experiment)