

**Maximum Glottal Angle in Patients with Functional and Organic Laryngeal Pathologies
Compared to Healthy Controls**

by

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Katherine Gold, M.S.

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Objectives: Currently, practitioners rely on visual judgments of glottal angle (viewed endoscopically) to determine whether maximum abduction is within normal limits on a repeated sniff maneuver. Investigators have previously examined maximum glottal angle of healthy individuals and patients with unilateral vocal fold paralysis during an “ee-sniff” maneuver. Others have compared maximum glottal angle in healthy individuals to those with paradoxical vocal fold movement disorder during inspiration at rest and during exercise. However, no one has yet systematically compared groups of patients with various voice and laryngeal breathing disorders to vocally healthy control participants to characterize the nature of differences in vocal fold mobility across groups.

Design: Via retrospective analysis of laryngoscopic exam videos obtained from a specialty voice center, we measured glottal angle in five groups: vocally healthy controls and patients with spasmodic dysphonia/essential tremor (SD/ET), lesions, atrophy, paradoxical vocal fold motion disorder (PVFMD), or muscle tension dysphonia (MTD). From each laryngoscopic exam video, we calculated maximum glottal angle (GA_{MAX}) and average glottal angle (GA_{AVG}) during three subsequent sniff maneuvers. Individual disorder groups (MTD, PVFMD, SD/ET, atrophy, lesion) and broader disorder types (functional and organic) were compared to healthy controls using simple linear regression analyses.

Results: No significant difference in vocal fold mobility was found between healthy individuals and individuals within a disorder subgroup or broader disorder type for neither GA_{MAX} nor GA_{AVG} . Follow-up analyses revealed statistically significant differences in variability magnitude of maximum glottal angle in both PVFMD (6.2° more variability ($p < 0.001$)) and SD/ET (5.8° more variability ($p < 0.001$)) compared to healthy controls.

Conclusion: Neither average nor maximum glottal angle derived from a sniff maneuver were useful in differentiating patients with voice disorders. However, the magnitude of glottal angle variance in SD/ET and PVFMD might be a useful objective measurement for laryngoscopy. Future research should probe the sensitivity of this measurement for identification and differential diagnosis of these patient populations in clinical or research settings.

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Preface

Starting my academic career at the University of Pittsburgh, I would never have imagined I would be here in this moment. Research always seemed like something that was far too out of my reach and that I was always meant to be a consumer of, not a creator. I have my mentor and thesis advisor, Dr. Leah Helou to thank for changing that perspective. Thank you for leading by example and showing me that doing research is not just exciting but also attainable. You have challenged me every step of the way and it has made this project what it is. Thank you most of all for believing in me and allowing me the independence I needed to not only make this project happen but to grow as a student, researcher, and clinician in the process. Thank you also to Brett Welch for all your knowledge, guidance, and support over the past two years. You have been unwavering in your patience with every question I've had, every zoom meeting you've hosted, and every additional analysis needed to get this project to the finish line, and I cannot thank you enough. Thank you to my undergraduate research assistant, Hannah Kramer for all your help on this project, you rock! To round out our little team, thank you to my thesis partner-in-crime, Sarah Hoch for being the best support system and sounding board I could ask for. Words can't describe how lucky and grateful I am to have gone through this journey with you. Lastly, thank you to the members of my thesis committee, Dr. Bernard Rousseau and Dr. Andrej Petrov and my clinical instructor at the UPMC Voice, Dr. Jackie Gartner-Schmidt for contributing your valuable insight, time, and experience to this project.

There are not enough words in the world to describe the love and appreciation I have for my friends and family that listened to me go on and on about this project, even when most of it sounded like another language to you. To my parents, thank you for reminding me time and time

again that I am smart and capable and that the finish line was getting closer every day. Thank you for every time you've picked up the phone in the middle of work or dinner or your favorite television show when I needed you. None of this would be possible without your support and encouragement every step of the way. To my friends, thank you for listening to me talk about this project for two years straight, for being a shoulder to cry on and bringing so much sunshine into my life even on the cloudiest Pittsburgh days. Lastly, to my partner Kenny Reilly, thank you for giving me the space I needed in our small apartment to get this project done, for talking things through with me even when you didn't fully understand them and for all around being my biggest support system. Most of all, thank you for convincing me that I was capable of doing a thesis in the first place. You have always been the first one to believe in me, even before I believe in myself, and I wouldn't be half the person I am today without you.

This project is the product of all the people who have supported my academic journey at Pitt the past six years, and I am eternally grateful for everyone that assisted in making this thesis a reality. Thank you.

1.0 Introduction

Voice disorders are a category of communication disorders specifically affecting a person's vocal quality or vocal characteristics such as pitch, loudness, or resonance (American Speech-Language-Hearing Association, 1993). In a survey of the general population, 29.9% of people reported experiencing some kind of voice disorder in their lifetime (Roy et al., 2005). Additionally, the prevalence is higher within high-risk populations who typically have a larger dose of vocal use. For example, in a population of teachers surveyed, 93.7% experienced at least one voice disorder symptom, with 42.3% of those individuals experiencing more than five symptoms (Roy et al., 2004.) Voice disorders not only impact a person's ability to communicate effectively, but also affect their social and professional life. The prevalence of anxiety and depression among those with voice disorders is significantly higher than in healthy populations (Merrill et al., 2011), demonstrating the emotional burden felt by these patients and impact of these conditions on quality of life.

For the purposes of this study, voice disorders can be broadly categorized in two ways: functional and organic laryngeal pathologies. *Organic voice disorders*, such as vocal fold lesions, spasmodic dysphonia (SD), essential tremor (ET), and paralysis, are those that result from some abnormality in the anatomical structures of the vocal mechanism or due to an underlying neurogenic condition (Naqvi and Gupta, 2021). *Functional voice disorders* in contrast, including muscle tension dysphonia (MTD) and paradoxical vocal fold movement disorder (PVFMD), are those that are considered “nonorganic” and allegedly stem from inefficient use of the vocal system but without an apparent underlying anatomical or physical cause (Baker, 2016).

1.1 Vocal Fold Mobility

The true vocal folds have multiple functions, including airway protection and vibration to produce voice (Stemple et al., 2020). When the vocal folds adduct, they move towards the midline which protects the trachea during swallowing and allows them to vibrate when air passes through them during phonation. The vocal folds are abducted away from midline during the inspiratory phase of quiet breathing. During speech, the vocal folds are arranged in a variety of configurations, cycling between abduction and adduction to produce voiced and voiceless phonemes. The term *vocal fold mobility* refers to these abduction and adduction movement patterns of the vocal folds (Rosen et al., 2016), and observing these movements can help clinicians characterize neuromuscular functioning (Dailey et al., 2005).

For the purposes of this paper, glottal angle is the quantitative measurement of the angle created by the two vocal folds during maximum abduction. This abduction angle is observed during laryngoscopy at the point of maximum abductory excursion during the “ee-sniff” maneuver, a standard part of the protocol for the instrument evaluation of voice disorders. The “ee-sniff” maneuver has been shown to be effective at producing repetitive cycles of maximum abduction and adduction of the vocal folds (Carroll et al., 2017; Poletto et al., 2008) and allows clinicians to better appreciate vocal fold mobility compared to typical cycles of phonation and respiration.

Previous research has utilized the “ee-sniff” maneuver to examine glottal angle of healthy individuals and patients with laryngeal impairments (unilateral vocal fold paralysis and PVFMD). Glottal angle varied greatly between healthy individuals during the maximally abducted portion of the “ee-sniff” task, ranging from 31° to 77° (Dailey et al., 2005) suggesting that range of vocal fold mobility is dependent on individual anatomy and physiology even within populations without dysfunction. Likewise, Adamian et al. (2021) compared glottal angle in healthy individuals to

those with unilateral vocal fold paralysis. Their healthy participants demonstrated a similar range of glottal angle from 35° to 84° with a mean angle of 66°. Patients with unilateral vocal fold paralysis demonstrated a glottal angle range of 27° to 65° with a mean of 47°. Unsurprisingly, glottal angle in individuals with unilateral vocal fold paralysis was significantly decreased compared to healthy individuals, with an overall difference of 19°. As these results exhibit, vocal fold mobility is directly impacted by unilateral vocal fold paralysis due to the lack of movement on one side of the glottis, thus producing a predictable decrease in glottal angle.

Glottal angle was also examined in patients with PVFMD, also known as exercise-induced laryngeal obstruction (EILO). Adrianna Shembel (2017) found that no significant difference existed in inspiratory glottal angle during quiet respiration in individuals with EILO (mean of 53.3°) compared to healthy controls (mean of 52.6°). Likewise, Shembel et al. (2018) examined glottal angle during exercise and again found that the glottal angle during inspiration in the EILO cohort did not significantly differ from the control group. However, this research indicated that glottal configuration and inspiratory laryngeal patterns were more variable both between subjects and within a single subject in the EILO group which potentially contributed to the null differences seen. This suggests that while the degree of maximum abduction generally may not be impacted by functional laryngeal breathing disorders, overall variability of inspiratory laryngeal response patterns may be greater in this population (Shembel et al., 2018).

While glottal angle for healthy individuals and populations of patients with unilateral vocal fold paralysis and PFVMD has been quantified, no one has yet examined whether glottal angle is significantly impacted in other kinds of organic and functional voice disorders. The present study aims to fill this gap in the literature by quantifying vocal fold mobility on the “ee-sniff” maneuver within and across healthy/normal and vocally-impaired patient groups to determine if glottal angle

derived from the “ee-sniff” maneuver differs as a function of laryngeal impairment and whether the nature of the impairment, functional or organic, impacts an individual’s maximum glottal angle.

1.2 Diagnosis of Voice Disorders

Although diagnostic protocols for voice disorders can differ based on setting, practice and location, the basic features of a clinical voice evaluation or voice diagnostic protocol are fairly standardized. This diagnostic protocol includes four main areas that contribute to the assessment and diagnosis of voice disorders: case history, perceptual analysis, indirect voice measures and direct voice measures. Indirect voice measures include the acoustic and aerodynamic evaluation of voice and direct measures include the visualization of the laryngeal structures, typically performed using laryngoscopy (Watts and Awan, 2019). These four areas contribute to the overall complete profile of the voice, depicted in Figure 1. Developing a complete profile of the voice then allows clinicians to make clinical decisions and differential voice diagnosis, ideally with input from a team of voice specialized speech language pathologists and medical professionals (laryngologists, physician assistants).

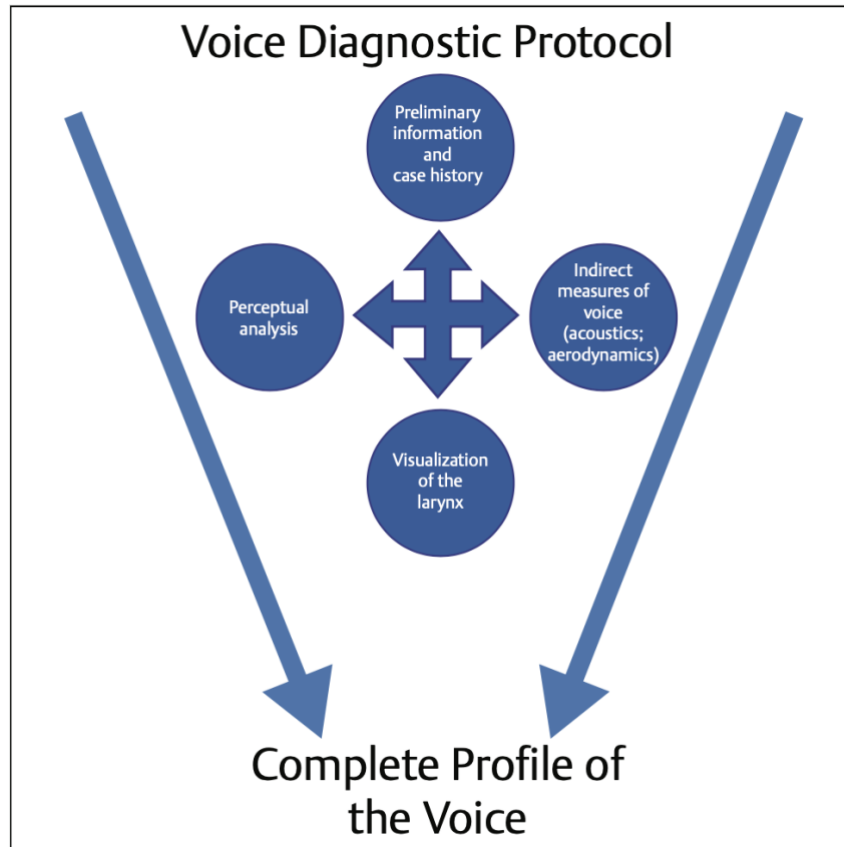


Figure 1 Voice Diagnostic Protocol (Watts and Awan, 2019)

The direct measures component of the voice diagnostic protocol is the focus of the current study, specifically clinician visualization of the larynx under laryngoscopy. Laryngoscopy is superior to a history and physical examination in the accuracy of voice disorder diagnosis (Paul et al., 2013) but has certain limitations. Clinicians rely most heavily on subjective judgments of the laryngeal structures to determine patient diagnosis, and few objective measurements are available in clinical settings. The lack of objective measures presents a challenge for differential diagnosis and patients with certain voice disorders can often be misdiagnosed. This leads to longer periods of time before proper diagnosis and improper treatment for patients. As previously mentioned, voice disorders can have a substantial impact on quality of life (Merrill et al., 2011) and the longer

patients wait to receive proper treatment, the longer they need to manage the emotional burden associated with voice disorders.

One such common occurrence of misdiagnosis is between MTD and SD. Because the symptomatology of MTD is like that of SD (Barkmeier and Case, 2000), SD is frequently misdiagnosed (Roy, 2007; Roy, 2010) especially in its early stages of presentation. In fact, patients with SD often go more than four years without a diagnosis from their first presentation with a physician and roughly a third of patients are prescribed ineffective medications/therapies (Creighton et. al, 2015). Objective evaluation such as aerodynamic measures paired with visual observation and analysis of vocal fold mobility can be useful in distinguishing SD from MTD (Barkmeier and Case, 2000) suggesting that objective measurements increase accuracy of diagnosis. But, no objective laryngoscopic measures have yet been identified that might aid in the differential diagnosis of these groups.

Likewise, paradoxical vocal fold movement disorder (PVFMD) can also present diagnostic challenges. PVFMD refers to the laryngeal obstruction of the airway through the intermittent adduction of the vocal folds that occurs during inspiration (Cukier-Blaj et al., 2008; Kenn and Hess, 2008). Most people diagnosed with PVFMD report primary symptoms of dyspnea, cough, and changes in their voice (Cukier-Blaj et al., 2008). Like SD, PVFMD can be misdiagnosed as other breathing disorders (e.g., asthma) and it can be both a lengthy and costly process to arrive at a proper diagnosis. In fact, 62% of patients eventually diagnosed with PVFMD have been misdiagnosed at some point in time with asthma (Traister et al., 2016). The average time for some patients between onset of dyspnea symptoms and proper diagnosis was 33 months with some patients going up to 60 months without diagnosis. The direct cost of office visits, prescriptions, and procedures for these patients during their pre-diagnosis period on average was \$8,625 (Lunga

et al., 2022). For patients misdiagnosed with asthma specifically, the estimated monthly cost of medication alone was up to \$136.40 –\$256.90 (Traister et al., 2016). Those with misdiagnosed PVFMD were also found to have higher rates of emergency department visits compared to those that were never misdiagnosed and therefore incur higher emergency healthcare associated costs as well (Traister et al., 2016).

In addition, some voice disorders cannot adequately be appreciated under laryngoscopy at the time of presentation in a clinical setting due to fluctuating symptoms. PVFMD is episodic in nature, often triggered by irritants or exercise (Røksund et. al, 2009; Chiang et. al, 2013; Marcinow et al., 2015). One problem with diagnosing patients with PVFMD through laryngoscopy is that patients are not often experiencing an episode at the moment of presentation in clinic, and the phenotypes vary. Therefore, the extent of their symptoms cannot typically be visually appreciated under laryngoscopy and clinicians must instead rely heavily on patient reports and case history information.

Misdiagnosis of voice disorders such as SD and PVFMD, carries a significant emotional and economic burden. As such, identifying clear and distinct differential diagnosis criteria is necessary to reduce the degree of misdiagnosis within this patient population. The present study seeks to determine if glottal angle has any utility as a contributing measurement to the differential diagnosis of voice disorders. If so, this can broaden the objective diagnostic toolbox available to clinicians, in turn allowing patients to potentially receive a voice disorder diagnosis closer to their onset of symptoms, provide them with quicker access to effective treatments and reduce the economic and emotional burden that comes with having a prolonged undiagnosed or misdiagnosed voice disorder.

2.0 Research Questions and Hypotheses

The current study aims to determine if differences in glottal angle exist between healthy controls and those with the following common functional and organic laryngeal pathologies: SD/ET, lesions, atrophy, PVFMD, and MTD.

Research Question 1: Do patients with voice and laryngeal breathing disorders differ in glottal angle during abduction on the sniff maneuver as compared to healthy controls?

Research Question 2: Do patients with functional voice and laryngeal breathing disorders (MTD and PVFMD) differ in glottal angle during abduction on the sniff maneuver as compared to patients with organic laryngeal pathologies (SD/ET, atrophy, and lesions)?

We hypothesized that a difference in glottal angle would be seen between the *healthy laryngeal anatomy and physiology control group* compared to *individual disorder groups* (MTD, PVFMD, SD/ET, atrophy, lesion). We also hypothesized that glottal angle would differ between the *healthy laryngeal anatomy and physiology control group* compared to *broader voice disorder types* (functional and organic).

3.0 Methods and Procedures

We used a retrospective, observational case-control design. This research was approved by the University of Pittsburgh Institutional Review Board. Research Question 1 involves a comparison of glottal angle (dependent variable) between vocally healthy controls and five populations of patients classified by *individual voice disorder*: SD/ET, lesions, atrophy, PVFMD, and MTD (independent variable). Research Question 2 involves a comparison of glottal angle (dependent variable) between vocally healthy controls and patient categorized by *broader disorder types*: functional and organic voice disorders (independent variable). Participants were instructed to perform three consecutive trials of the “ee-sniff” maneuver during their clinical visit. De-identified laryngoscopic exam videos were retrospectively accessed, and maximum glottal angle was determined through manual editing, annotation, and analysis of these videos.

Trials were analyzed to determine two variables of interest: the maximum glottal angle (GA_{MAX}) and the average glottal angle (GA_{AVG}). GA_{MAX} refers to the largest angle observed across three trials of the “ee-sniff” maneuver and GA_{AVG} refers to the average angle across three trials of the “ee-sniff” maneuver.

3.1 Participants

Participants were selected from a database of patients who presented at the UPMC Voice Center and received a laryngoscopy examination of their vocal fold function. Participants were assessed by a team including at least one voice-specialized Speech-Language Pathologist and

either a voice-specialized Physician Assistant or Laryngologist the UPMC Voice Center. Patients were included in the study if they were diagnosed with one of five voice disorders (MTD, PVFMD, mid-membranous vocal fold lesion, SD/ET, and atrophy) or confirmed to have healthy laryngeal function. SD and ET were classified as one patient population due to insufficient quantity of qualifying participants with an exclusive SD diagnosis. Patients were excluded from the study if they were diagnosed with more than one voice disorder or did not complete at least three trials of “ee-sniff” maneuver on laryngoscopy exam. In addition, videos in which quality was poor or vocal fold edge could not be adequately determined due to lack of visualization/obstruction were excluded from the present study to ensure that the final images had clearly defined vocal fold edges. Subsequently, ten participants were excluded due to insufficient video quality. 140 participants were used in the final data analysis.

3.2 Data Collection and Annotation

All participant videos were deidentified and stored in a UPMC-housed password-protected server before annotation and analysis was performed. A record of all personal identifying information was stored in a separate UPMC password protected database. For each video, the researcher captured still images of frame-by-frame maximum vocal fold abduction across three “ee-sniff” trials per participant. These stills were then annotated using the ImageJ (Schneider et al., 2012) processing program to determine the angle of maximal abduction for each of these three trials, and the mean was calculated from these measures. Data were then stored in a deidentified database categorized by disorder group/healthy control for analysis. Sample annotations are indicated in Figure 2 below.

The three images per participant were uploaded to ImageJ (Schneider et al., 2012) and annotated using the angle annotation tool. The researcher marked the origin of the angle on the superior surface of the vocal fold. Markers were then placed on the posterior end of each vocal fold, connecting at the origin to form an angle. Similar methods of annotation have been previously used in analysis of glottal angle (Dailey et al., 2005) and were found to be both effective and reliable in detection of vocal fold edge across groups of researchers.

Quality control was performed for questionable images as follows. Images were identified and discussed between primary researcher and research assistant to determine accurate identification of vocal fold edge and subsequently measured based on that determination. This angle was then recorded in the patient database.

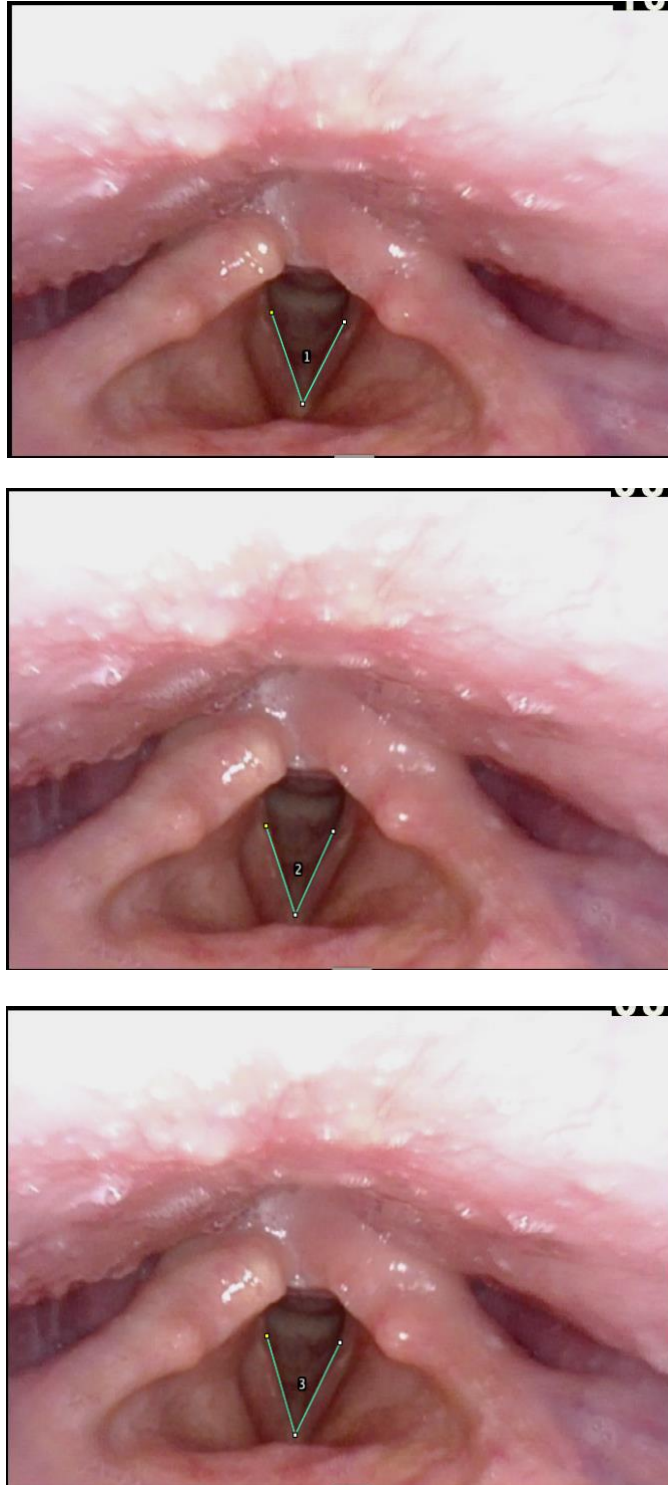


Figure 2 ImageJ Glottal Angle Annotation

Three annotated trials of glottal angle in Patient 29, a 41 year old male diagnosed with PVFMD.

3.3 Training and Reliability Testing

An undergraduate research assistant was trained and oriented to the project by the primary researcher across two 1-hour training sessions, one virtual and one in person. The research assistant was trained in video editing, annotation, and data collection methods by the primary researcher. Fifteen images (10% of the data) were randomly selected to test for both inter- and intra-rater reliability.

3.4 Data and Statistical Analysis

Analysis of maximum glottal angle was first performed using the ImageJ (Schneider et al., 2012) Analyze function, which measured glottal angle during each of three trials per participant. GA_{AVG} and GA_{MAX} were determined for each participant within a group. These measurements were then averaged with all participants' (per group) GA_{AVG} and GA_{MAX} measurements to produce an overall GA_{AVG} and GA_{MAX} for that group. The same procedures were used to determine GA_{AVG} and GA_{MAX} measurements by disorder type, functional and organic. The intraclass correlation coefficients were used to determine inter- and intra-rater reliability between and within the primary investigator and undergraduate research assistant. Data were analyzed using R Studio (R Core Team, 2020). A Shapiro-Wilk normality test indicated the data were normally distributed ($p = .09$). The healthy/normal control group served as the contrast against which data from all other groups were compared, and a simple linear regression was applied to compare whether glottal angles differed by disorder type. We applied the same analysis to also compare groups of patients with functional versus structural pathologies. All assumptions for linear regression were met. To

establish intra- and inter-rater reliability we applied intraclass correlation coefficients using the Psych package (Revelle, 2020).

4.0 Results

We quantified the glottal angle of vocally healthy individuals and those with functional voice disorders, MTD and PVFMD and organic pathologies, lesion, SD/ET, and atrophy. This study aimed to determine if differences exist in glottal angle as a function of those individual disorder groups or broader disorder types (functional vs organic) compared to individuals with healthy laryngeal anatomy and physiology.

Twenty-one adult participants were deemed vocally healthy and with normal laryngeal function. The remaining 119 participants comprised the group of patients with voice and laryngeal breathing disorders. Table 1 provides demographic information of participants.

Table 1 Demographic Information

Demographic Information	Healthy	Atrophy	Lesion	SD/ET	MTD	PVFMD
<i>n</i>	21	25	22	25	25	22
Gender						
Male (%)	10 (47%)	13 (52%)	11 (50%)	9 (36%)	14 (56%)	12 (54%)
Female (%)	11 (52%)	12 (48%)	11 (50%)	16 (64%)	11 (44%)	10 (45%)
Age						
Mean	47.1	71.1	46.3	59.2	39.4	47.3
SD	17.4	8.23	14.9	16.1	17.7	19.0
Min-Max	17-80	54-91	21-72	25-84	14-73	14-77

4.1 Research Question 1: Individual Disorder Groups

RQ1: Do patients with voice and laryngeal breathing disorders differ in glottal angle during abduction as compared to healthy controls?

To determine if significant differences existed between healthy controls and disorder populations, we performed a simple linear regression with the normal/healthy group serving as the contrast for the five disordered groups. For the model using GA_{AVG} , no significant differences were observed across individual disorder populations ($R^2 = .01$, $F(5, 134) = 0.30$, $p = .91$). See Table 2 for details. Likewise, no significant differences were observed across individual disorder populations for the model using GA_{MAX} ($R^2 = .01$, $F(5, 134) = 0.33$, $p = .90$). See Table 3 for details. Figure 3 and Figure 4 display these results organized by individual disorder group with each dot representing a single participant identified by their GA_{AVG} and by their GA_{MAX} respectively. These results indicate that patients with voice and laryngeal breathing disorders did not differ in glottal angle during abduction compared to patients with healthy laryngeal anatomy and physiology.

Table 2 GA_{AVG} by Individual Disorder Group

Disorder Group	GA_{AVG}	Standard Deviation	Standard Error	t-value	p-value	95% CI
Healthy	51.6	9.4	2.8			[46.1, 57.1]
Lesion	48.8	-2.8	3.9	-0.70	0.482	[38.3, 43.8]
Atrophy	49.6	-2.0	3.8	-0.53	0.600	[40.1, 44.1]
SD/ET	51.3	-0.3	4.0	-0.07	0.943	[43.5, 44.1]
MTD	52.7	1.2	4.0	0.30	0.763	[46.3, 44.0]
PVFMD	50.0	-1.6	3.9	-0.41	0.685	[40.7, 43.9]

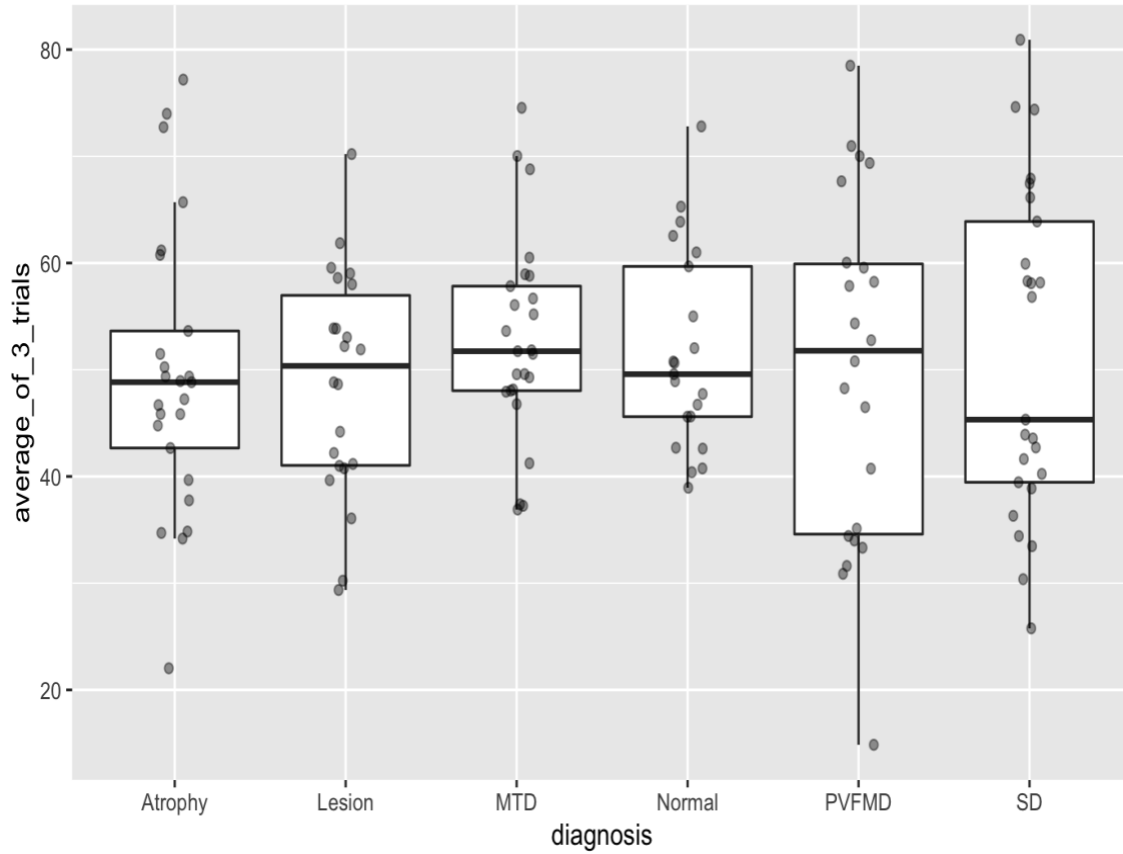


Figure 3 GA_{AVG} by Individual Disorder Group

Table 3 GA_{MAX} by Individual Disorder Group

Disorder Group	GA_{MAX}	Standard Deviation	Standard Error	t-value	p-value	95% CI
Healthy	54.2	9.6	2.9			[48.5, 59.9]
Lesion	52.4	-1.7	4.0	-0.43	0.666	[42.7, 58.6]
Atrophy	53.3	-0.9	3.9	-0.26	0.820	[44.7, 60.1]
SD/ET	54.9	0.7	3.9	0.18	0.861	[47.9, 63.3]
MTD	56.7	2.6	3.9	0.65	0.516	[51.5, 67.0]
PVFMD	53.1	-1.0	4.0	-0.26	0.797	[44.1, 60.0]

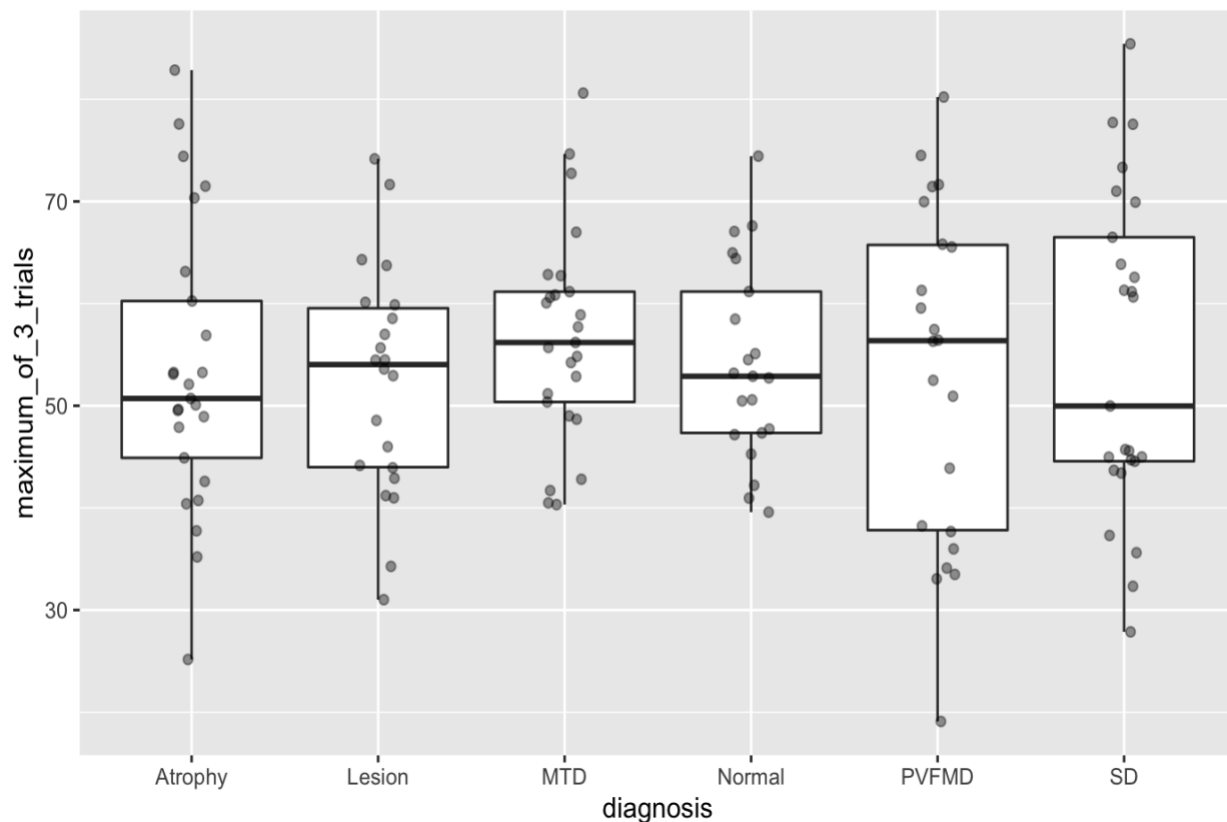


Figure 4 GA_{MAX} by Individual Disorder Groups

4.2 Research Question 2: Broad Voice Disorder Type

RQ2: Do patients with functional voice and laryngeal breathing disorders (i.e., MTD and PVFMD) differ in glottal angle during abduction as compared to patients with organic laryngeal pathologies (i.e., SD/ET, atrophy, and lesion)?

To determine if significant differences existed between healthy controls and broader disorder types (function and organic) we performed a simple linear regression with the normal/healthy group serving as the contrast for the two broader disorder groups. The GA_{AVG} and GA_{MAX} for atrophy, lesion and SD/ET were each averaged to produce a GA_{AVG} and a GA_{MAX} for

the organic voice disorder group and the GA_{AVG} and GA_{MAX} for MTD and PVFMD were each averaged to produce a GA_{AVG} and a GA_{MAX} for the functional voice disorder group. For the model using GA_{AVG} , no significant differences were observed across broad disorder types ($R^2 = .004$, $F(2, 137) = 0.26$, $p = .77$). See Table 4 for details. Likewise, no significant differences were observed across broad disorder types for the model using GA_{MAX} ($R^2 = .003$, $F(2, 137) = 0.18$, $p = .84$). See Table 5 for details. Figure 5 and Figure 6 display these results organized by broader disorder type with each dot representing a single participant identified by their GA_{AVG} and by their GA_{MAX} respectively. These results indicate that patients with functional voice and laryngeal breathing disorders and those with organic laryngeal pathologies do not differ in glottal angle during abduction compared to patients with healthy laryngeal anatomy and functioning.

Table 4 GA_{AVG} Across Functional and Organic Groups

Disorder Type	GA_{AVG}	Standard Deviation	Standard Error	t-value	p-value	95% CI
Healthy	51.9	9.9	2.9			[46.1, 57.1]
Organic	50.0	-1.6	3.6	-0.52	0.607	[42.1, 54.6]
Functional	51.4	-0.2	3.3	-0.04	0.968	[44.7, 56.0]

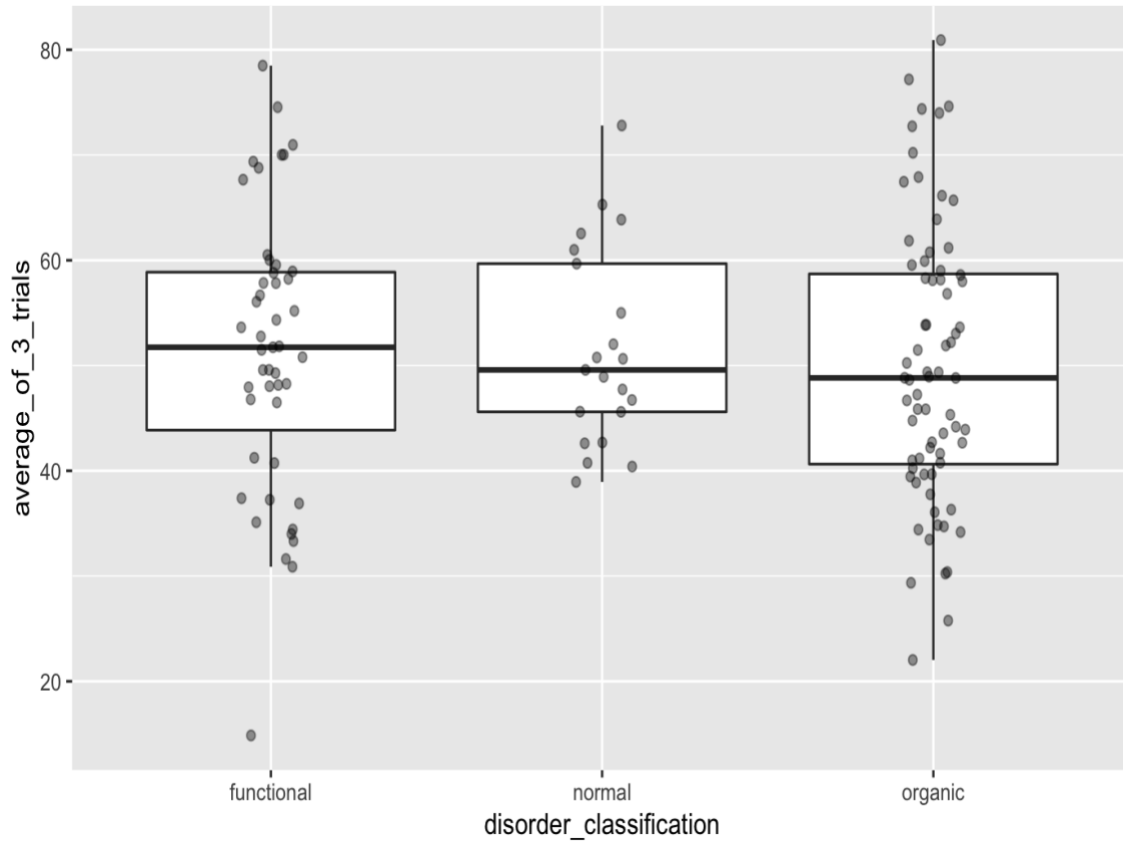


Figure 5 GA_{AVG} Across Functional and Organic Groups

Table 5 GA_{MAX} Across Functional and Organic Groups

Disorder Type	GA_{MAX}	Standard Deviation	Standard Error	t-value	<i>p</i> -value	95% CI
Healthy	54.2	9.6	2.9			[48.5, 59.9]
Organic	53.6	-0.6	3.3	-0.19	0.853	[46.6, 59.4]
Functional	55.0	0.9	3.5	0.25	0.801	[49.1, 62.7]

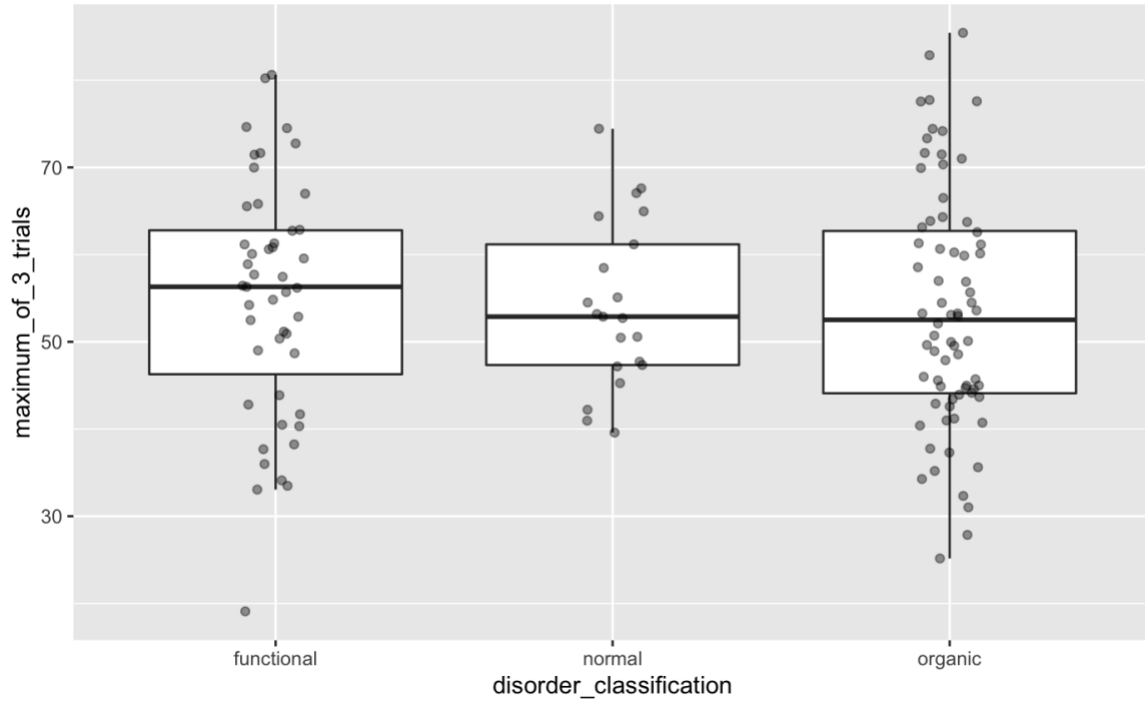


Figure 6 GA_{MAX} Across Functional and Organic Groups

4.3 Post Hoc Analysis: Average Variance of Angle

Upon reviewing the data, we noticed that the glottal angle measurements from the healthy controls seemed to vary less than that from the patient groups. The standard deviation of the healthy control group was 9.7° compared to 13.7° in atrophy, 11.0° in lesions, 15.7° in SD/ET, 10.3° in MTD and 16.6° in PVFMD. Likewise, the standard deviation of the functional voice disorder group was 13.6° and the standard deviation of the organic voice disorder group was 13.7° . Figure 7 displays the distribution of the data by broad disorder type. In this figure, each of the three sniff tokens is represented separately.

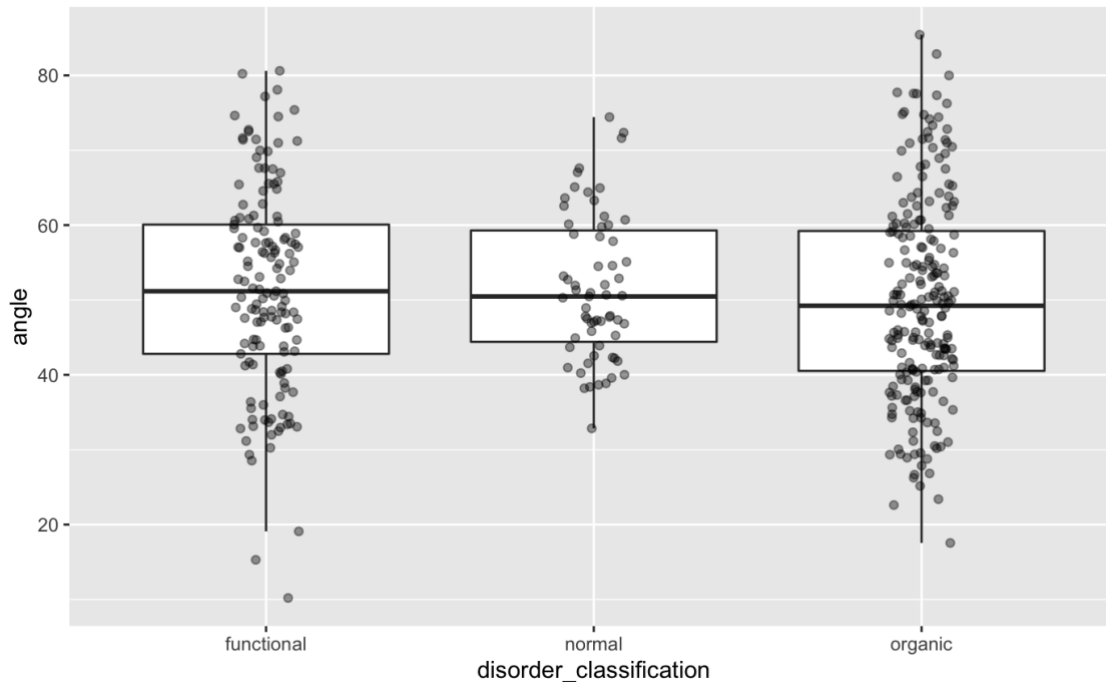


Figure 7 Distribution by Broad Disorder Type Based on Raw Data

To determine magnitude of variability by disorder type, we subtracted each angle measured from the mean glottal angle for the respective disorder type, functional and organic. We then used the absolute value of this measurement to measure the magnitude of variance, irrespective of direction. Absolute values were used examine the magnitude of variance but not directionality. The average variance of angle for each type was then determined and compared to the healthy controls using a simple linear regression. The same process was used to determine variance by individual disorder group.

The average variance of glottal angle for healthy controls was 7.9° . On average patients with a functional voice disorder display 3.1° more variability and those with an organic voice disorder display 3.8° more variability compared to healthy controls. Figure 8 displays these results organized by broad disorder type with each dot representing the magnitude of variance for each trial from the mean of that disorder type.

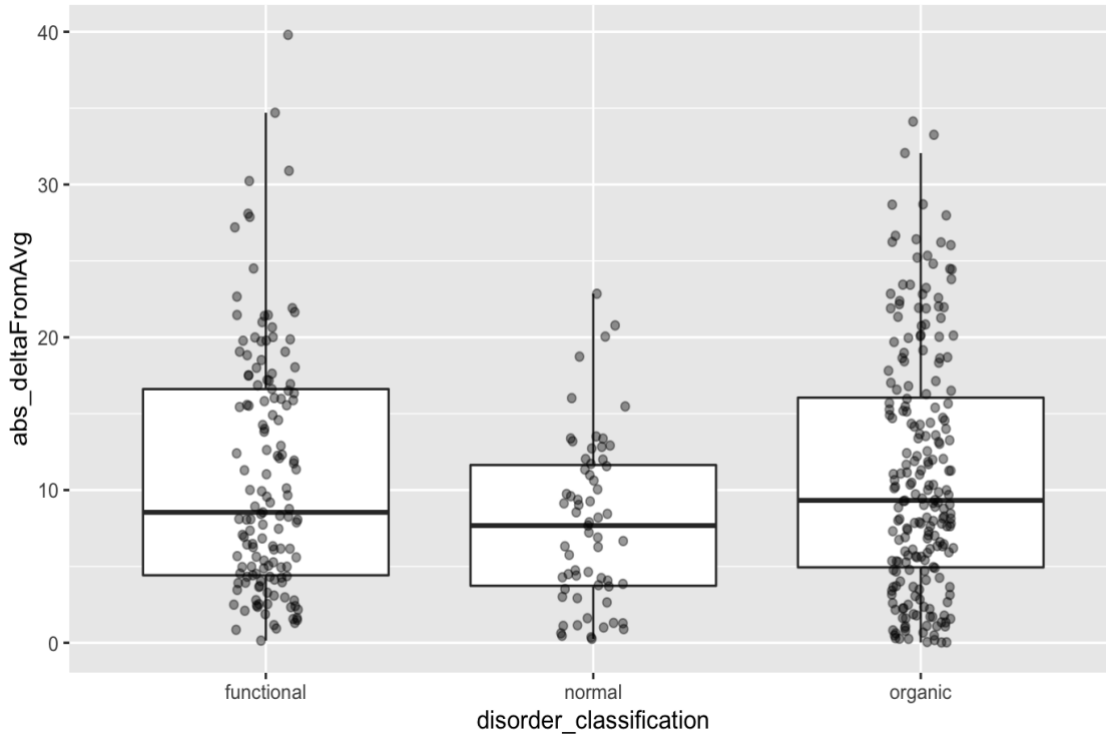


Figure 8 Average Variability of Angle Across Functional and Organic Groups

The magnitude of variability in both disorder types, functional ($p = .007$). and organic ($p = .004$) was statistically significant compared to healthy controls ($R^2 = .104$, $F(5, 414) = 9.608$, $p = .01$). This indicates that having either a functional or organic voice disorder is predicted by increased variability of glottal angle during “ee-sniff” maneuver. See Table 6 for details.

Table 6 Average Variability of Angle Across Functional and Organic Groups

Disorder Type	Average Variability of Angle	Standard Deviation	Standard Error	t-value	p-value	95% CI
Healthy	7.9	9.6	1.0			[6.0, 9.8]
Organic	11.1	13.7	1.1	2.92	0.004*	[11.9, 16.4]
Functional	11.0	13.6	1.2	2.69	0.007*	[12.0, 16.4]

However, differences in standard deviation by individual disorder group within these broad disorder types are still present. For example, MTD ($SD = 10.3$) showed the smallest difference in standard deviation compared to normal ($SD = 9.7$) while PVMD ($SD = 16.6$) showed the greatest

difference in standard deviation, even though both disorders are classified as functional. Figure 9 displays the distribution of the data by individual disorder group based on the total raw data. In this figure, each participant is represented by three unique dots, representing each of the three trials of “ee-sniff” maneuver measured.

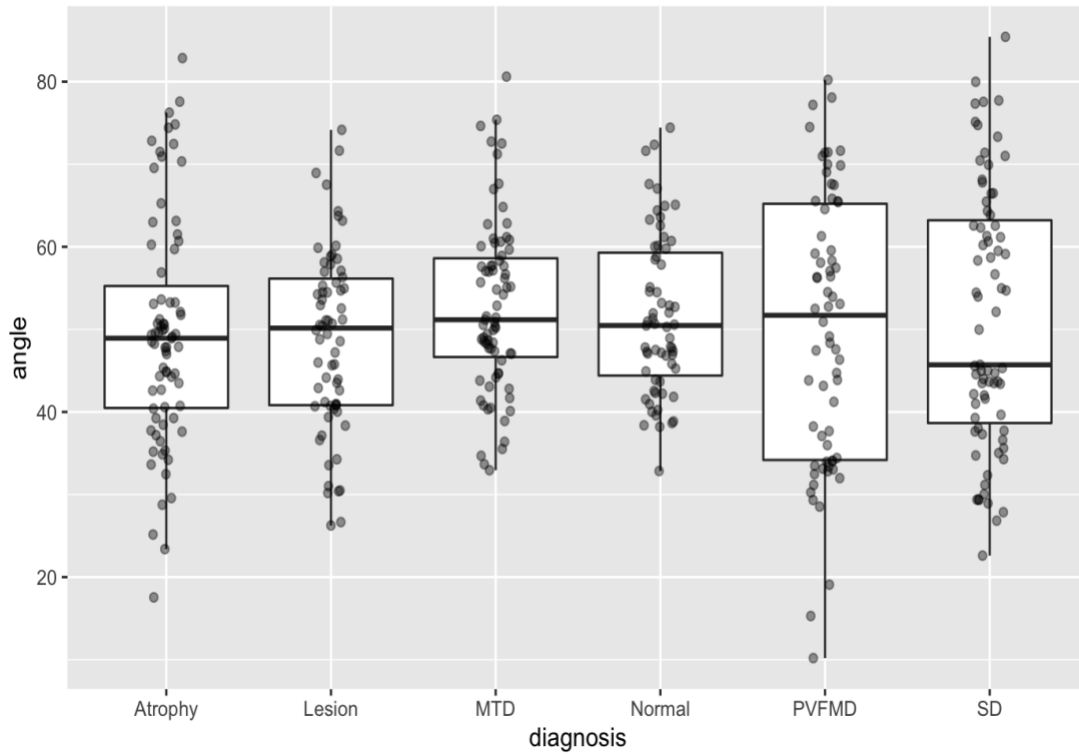


Figure 9 Distribution By Individual Disorder Group Based on Raw Data

Due to the differences observed in standard deviation within individual disorder groups, the individual magnitude of variability was defined to determine the influence of individual disorder variability on the results of the broad disorder types. On average, patients diagnosed with lesions display 1.1° more variability, those with atrophy display 2.5° more variability, those with MTD display 0.4° more variability, those with PVFMD display 6.2° more variability and those with SD/ET displays 5.8° more variability compared to healthy controls. Figure 10 displays these results organized by individual disorder group with each dot representing the magnitude of variance for each trial from the mean of that disorder type.

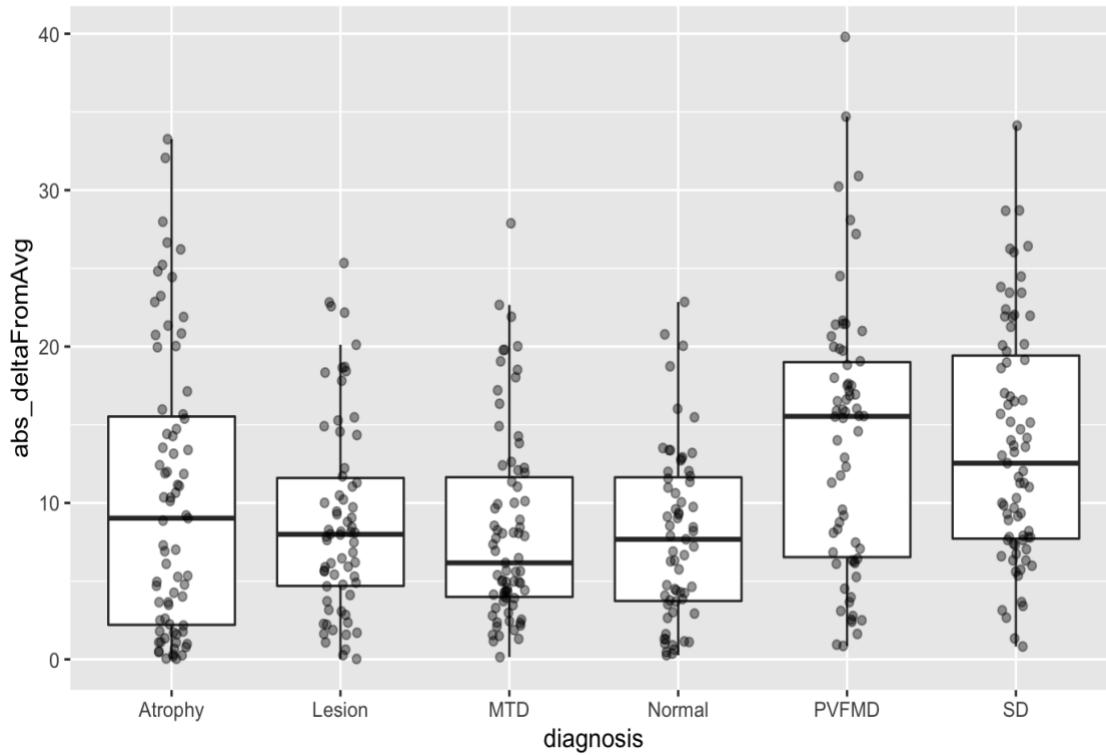


Figure 10 Average Variability of Angle by Individual Disorder Group

When analyzed using a simple linear regression, the magnitude of variability in the lesion, atrophy and MTD groups was not statistically significant from the healthy controls but that for SD/ET ($p < .001$) and PVFMD ($p < 0.01$) groups was ($R^2 = .02$, $F(2, 417) = 4.6$, $p < .001$). Overall, patients in these two voice disorder subgroups display more variability in their maximum glottal angle during the “ee-sniff” maneuver. Those diagnosed with lesions, atrophy or MTD performed nearly identically compared to the healthy controls in terms of angle variability. See Table 7 for details.

Table 7 Average Variability of Angle by Individual Disorder Group

Disorder Subgroup	Average Variability of Angle	Standard Deviation	Standard Error	t-value	p-value	95% CI
Healthy	7.9	9.7	0.9			[6.1, 9.7]
Lesion	8.9	11.0	1.3	0.81	.417	[7.4, 12.5]
Atrophy	10.3	13.7	1.3	1.96	.051	[10.3, 15.2]
SD/ET	13.7	15.7	1.3	4.64	<.001*	[10.3, 21.9]
MTD	8.3	10.3	1.3	0.32	.753	[6.2, 11.1]
PVFMD	14.1	16.6	1.3	4.81	<.001*	[10.4, 22.3]

4.4 Reliability

Inter-rater and intra-rater reliability data was analyzed to determine the fidelity of angle measurements between the two investigators. The intraclass correlation coefficient (ICC) for inter-rater reliability suggested excellent reliability (ICC = .989, 95% CI [.968, .996]), indicating that the two investigators behaved similarly to each other in their measurements of maximum glottal angle when measuring the videos. Intra-rater reliability of both investigators 1 and 2 was also excellent (Investigator 1 ICC = .98, 95% CI [.95, .99] and Investigator 2 ICC = .997, 95% CI [.99, .99]).

5.0 Discussion

When examining maximum glottal angle at face value, no significant differences exist across individual disorder groups (MTD, PVFMD, SD/ET, atrophy, and lesion) and broader disorder types (functional and organic). Therefore, maximum glottal angle will not likely be a useful tool in the identification and differential diagnosis of voice disorders. In general, glottal angle varied greatly between individuals, a finding demonstrated in previous research (Dailey et al., 2005). Similar to Dailey et al.'s (2005) findings of healthy glottal angle range from 31° to 77° , the current study shows similar results, with glottal angle in our healthy control group ranging from 32° to 74° . This again suggests that overall range of vocal fold mobility is dependent on individual anatomy and physiology. Likewise, the results of this study reflect Shembel et al.'s (2018) quantifications of mean glottal angle for PVFMD with a high degree of similarity. They found a mean glottal angle of 53.3° compared to our patient populations average glottal angle of 53.1° .

While maximum glottal angle may not be a meaningful tool for differential diagnosis, one objective measure that might have utility is the variability of glottal angle across several sniff tokens within a particular patient. Specifically, patients diagnosed with SD/ET and PVFMD both demonstrate significantly more variability in glottal angle compared to other disorder groups and healthy controls. Therefore, these patients are likely to have more variable trial-to-trial glottal angle measurements during a sniff maneuver compared to other populations. These observations align with previous PVFMD research (Shembel et al., 2018) that observed increased intrasubject and intrasubject variability of glottal angle.

As previously mentioned, SD/ET and PVFMD are often more nuanced in their presentation and differential diagnosis, which can lead to higher rates of undiagnosed and misdiagnosed disorders. The results of this study suggest that variability of maximum glottal angle on “ee-sniff” maneuver might serve as another diagnostic parameter that can be used in differential diagnosis of these two disorders. Knowing that SD/ET and PVFMD have a larger magnitude of variability in glottal angle compared to those with MTD, clinicians could evaluate the glottal angle performed by patients under laryngoscopy to utilize in their clinical decision making. If variability is a more consistently observable characteristic of these disorders and can be appreciated regardless of active symptomatology, clinicians may be able to make better, more accurate judgements when presented with challenging cases. Further research is warranted to replicate these findings with a larger clinical sample and to investigate the actual sensitivity of glottal angle variability for the differential diagnosis of PVFMD and SD.

5.1 Limitations and Future Research

Limitations of this study are as follows. The study relied on retrospective analysis of laryngoscopy videos, which did not allow researchers to control for variations in participant and clinician behaviors. For example, while a standardized procedure exists for the performance of laryngoscopy exam, variations in patient behavior and interactions in the examination room sometimes require deviations from the protocols which could lead to slight variations in patient performance. Additionally, due to lack of access to documentation, researchers could not determine whether patients with PVFMD were documented in an active attack upon presentation at the UPMC Voice Center. Informal review of examination videos was performed, and

researchers determined that evidence of an active attack could not be appreciated in PVFMD patient videos. Prevalence of patients who were examined under laryngoscopy during an active attack was discussed with UPMC Voice Center and determined to be very rare, even if attempts are made to trigger an attack, but without examination of documentation, presence of an attack could not be confirmed. Another limitation is that laryngoscopy images were not corrected for barrel distortion, which is known to warp the “true” degree of maximum glottal angle especially as the larynx is viewed off-of-midline. However, in a clinical setting, videos are always appreciated and analyzed with barrel distortion present, so the findings of this study are more representative of true clinical circumstances. Finally, measurement of glottal angle was also done manually using annotation markers. Other research (Zhang et al., 2010; Yousef et al., 2021; Adamian, et al., 2021) has utilized machine learning to identify vocal fold edge in order to increase accuracy of glottal measurements which may be a more effective method in performing measurements. While measurements were demonstrated to have high inter- and intra-rater reliability, data could still be impacted by small variations in the identification of vocal fold edge in a given image.

Future research should examine vocal fold variability as a potential diagnostic indicator for PVFMD and SD. This study also focused specifically on a single point of interest during an inspiratory cycle, maximum glottal angle. Future research should examine broader forms of vocal fold mobility classification like glottal area during similar vocal postures to determine if similar conclusions regarding vocal fold mobility can be drawn across different types of measurements, including ways to standardize the appreciation of glottal area based on distance from the tip of the scope. In addition, an experimental study may be warranted to analyze glottal angle variance before and after voice treatment in populations demonstrating a greater degree of variance to determine if variability persists after treatment. Lastly, the present study did not examine the impact of sex

or age on glottal angle performance. Future research may be warranted to examine differences in vocal fold mobility based on sex and age to determine if glottal angle is impacted by either of these two factors.

5.2 Clinical Significance

This project aimed to expand existing literature regarding maximum glottal angle across different organic and functional laryngeal pathologies. As previously mentioned, prior studies have compared glottal angle in healthy individuals to those with unilateral vocal fold paralysis and PVFMD, but this study compared and quantified vocal fold mobility across a range of disorder groups. Currently, vocal fold function is determined by way of visual judgements, but there is no previous data on average glottal angle within disorder groups for clinicians to compare patient mobility against. Data from this study suggest that objective measures of glottal angle variability might have utility in clinical research. In addition, this study is the first to highlight quantitative differences in glottal angle variability in both PVFMD and SD populations. These findings could contribute to the literature regarding possible diagnostic indicators to assist in the differential diagnosis of these patients, in turn reducing incidence of misdiagnosis, which has emotional and financial impacts on patients.

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