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Influence of glottal closure on the phonatory process in *ex vivo* porcine larynges

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Many cases of disturbed voice signals can be attributed to incomplete glottal closure, vocal fold oscillation asymmetries, and aperiodicity. Often these phenomena occur simultaneously and interact with each other, making a systematic, isolated investigation challenging. Therefore, *ex vivo* porcine experiments were performed which enable direct control of glottal configurations. Different pre-phonatory glottal gap sizes, adduction levels, and flow rates were adjusted. The resulting glottal closure types were identified in a post-processing step. Finally, the acoustic quality, aerodynamic parameters, and the characteristics of vocal fold oscillation were analyzed in reference to the glottal closure types. Results show that complete glottal closure stabilizes the phonation process indicated through a reduced left-right phase asymmetry, increased amplitude and time periodicity, and an increase in the acoustic quality. Although asymmetry and periodicity parameter variation covers only a small range of absolute values, these small variations have a remarkable influence on the acoustic quality. Due to the fact that these parameters cannot be influenced directly, the authors suggest that the (surgical) reduction of the glottal gap seems to be a promising method to stabilize the phonatory process, which has to be confirmed in future studies.

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I. INTRODUCTION

Voice is an important medium of human communication. Impairment of voice affects not only one's quality of life, but has also a massive impact on the economy, since more and more employees work in the service sector. At-risk individuals span many types of professions, e.g., teachers, telemarketers, vocalists, etc.[1] Hence, an effective diagnosis and treatment of voice disorders is of primary importance, which must be based on a fundamental understanding of voice production.

The primary signal of voice is produced in the larynx by a self-sustained oscillation of the vocal folds (e.g., phonation), which is driven by a constant airstream from the lungs. Subsequently, the primary signal is modulated by the vocal tract. Examination of the phonatory process is executed using *in vivo* experiments and by utilization of *ex vivo*, numeric, and synthetic larynx models.

Glottal closure (GC) plays an essential role in the phonatory process. In most cases, a complete closure of the vocal folds is desirable. Incomplete closure results in an increased broadband noise which is thought to be one of the main factors causing hoarseness.[2–5] Therefore, several techniques are applied for reducing the vocal fold gap and thereby improving voice quality, e.g., material injection and implantation or arytenoid adduction.[6–9] On the other hand, several publications contradict these findings by implying that a vocal fold gap does not necessarily lead to dysphonic or pathological voice production. Glottal gaps in the posterior glottis can be found in vocally healthy subjects, primarily in women[3,10–12] and children.[10]

Besides the closure of the vocal folds, their oscillation properties (e.g., left-right asymmetry and periodicity) are of interest due to their influence on the acoustic signal. Recording technologies like high-speed video endoscopy allows for a detailed investigation of these parameters.[13] Healthy voice is considered to be characterized by almost complete left-right symmetry and periodic vocal fold oscillations.[14] However, the reported effects of such conditions on the acoustic signal are inconsistent.

Regarding asymmetric vocal fold vibration, some *in vivo* investigations suggest that this property is related to a rough voice signal.[3,15,16] On others, it is reported that asymmetries were also observed in healthy patients.[17–19] Experiments with synthetic vocal fold models support the assumption that an asymmetric oscillation does not necessarily lead to a reduction in voice quality.[20] Numerical investigations report only little influence of asymmetry on objective acoustic measures.[21,22] Furthermore, *ex vivo* investigations suggest that glottal gap exerts more influence on jitter and shimmer than asymmetry.[4]

Due to the fact that quantitative analysis of high-speed video endoscopy is still not widely distributed in the clinical environment,[23] extensive investigations of periodicity in

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[a)] Electronic mail: veronika.birk@uk-erlangen.de phonation and the influence on acoustic are rare. Mehta *et al.*[24] reported a positive correlation between periodicity in vocal fold vibration and cepstral peak magnitude displaying the quality of the acoustic signal. In contrast, Biever and Bless[25] found aperiodicity in 30% of 20 healthy women. These diverse findings of the influence of phonation characteristics on the acoustic quality require further systematic investigations.

Ex vivo experiments offer the possibility of adjusting glottal settings through a systematic variation of parameters, such as the pre-phonatory glottal gap or glottal flow. When this is done, the measurement of fundamental data like subglottal pressure, high-speed video, and the acoustic signal provides a basis for a systematic investigation of relationships between the phonation characteristics and the acoustic outcome. Therefore, this study has the following goals:

Goal 1: Investigate the influence of different GC types on the phonatory process by inducing various pre-phonatory glottal gap sizes and vocal fold adduction levels in an *ex vivo* porcine larynx model. Objective measures displaying the acoustic quality [Cepstral Peak Prominence (CPP)], vocal fold oscillation characteristics [left-right phase asymmetry (PA), amplitude, and time aperiodicity (AP, TP)], and aerodynamic properties (glottal flow resistance) are analyzed to gain quantitative results.

Goal 2: Examine the impact of the different vocal fold oscillation characteristics and aerodynamic properties, resulting from different GC types, on the acoustic quality.

The aim of this study is to systematically investigate the different factors which may influence the phonatory process and/or the acoustic output through utilization of *ex vivo* experiments. Therefore, it is hoped that such information about the phonatory process will help improve the diagnosis and treatment of pathological voices.

II. METHODS

A. Experimental setup and measurement procedure

Nine *ex vivo* porcine larynges were obtained from the local slaughter house. This species has proven to be an adequate model for comparison with human phonation.[26,27] *Ex vivo* studies were utilized, despite the fact that the ventricular folds are active oscillators in normal phonation compared to human phonation.[26] After their dissection, the larynges were quick frozen with 2-methylbutan (−150 °C) and stored at −80 °C in order to preserve the tissue properties.[28] The larynx was slowly thawed in a refrigerator and soaked in a NaCl solution 15 min before the experiment. The supraglottal structures were removed to the level of the ventricular folds to gain an optimal view of their movement during phonation. Subsequently, the larynx was mounted on an artificial tracheal tube of stainless steel with a diameter of 20 mm.

Figure 1 shows the experimental setup including the larynx prepared for the experiment, the electro-mechanic devices for cartilage posturing, and the measurement equipment. The experiment was conducted using the setup described in Ref. 29 and is summarized below.

Vocal fold elongation was achieved using a 50 g weight fixed to the thyroid cartilage by a surgical suture according to *ex vivo* investigations with porcine larynges.[27] Two electro-mechanic devices were used to adjust variable vocal fold adduction levels by rotating the arytenoid cartilages simulating lateral cricoarytenoid muscle contraction. The induced torque T was measured by a TD70 (ME Meßsysteme GmbH, Hennigsdorf, Germany) sensor quantifying the adduction level. Several metal shims (from 0 up to 2, each 1 mm thick) were inserted between the two arytenoid cartilages to induce different pre-phonatory glottal gap sizes, see Fig. 1(b).

Mass flow Q was adjusted using a 4000B (MKS, Andover, MA) digital power supply driving a 1579A/B (MKS) mass flow controller. The air was physiologically heated and humidified by an Ultrasonat 810 (Hico, Hirtz & Co. KG, Köln, Germany) ultrasound nebulizer preventing tissue dehydration. The time resolved subglottal pressure signal P_s was captured by an XCS-93-5PSISG (Kulite Semiconductor Products, Inc., Leonia, NJ) pressure sensor driven by a PXIe-4330 (National Instruments, Austin, TX) bridge module and was flush-mounted to the internal wall of the artificial trachea. The acoustic signal was captured by a 4189 (Brüel&Kjaer, 2850 Nærum, Denmark) $^1/_2$-in free-field microphone mounted with an inclination of 45° and a

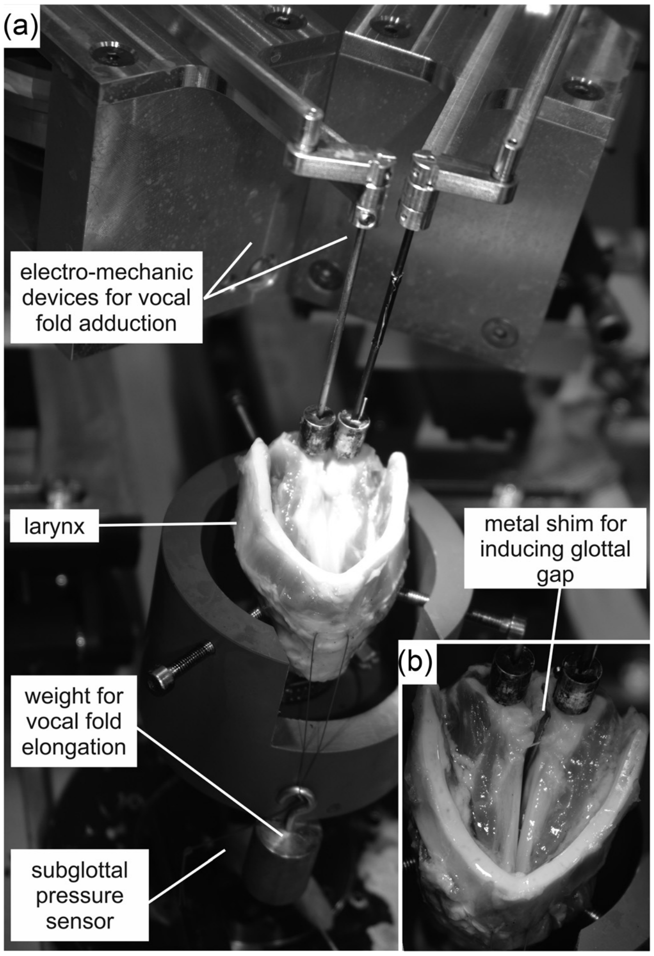


FIG. 1. (a) Experimental setup for inducing different vocal fold adduction levels, and (b) induced pre-phonatory glottal gap.

distance of 30 cm toward the glottis. The acoustic signal was amplified by a Nexus 2690 microphone conditioning amplifier (Brüel&Kjaer) and captured by a 4492 (National Instruments) dynamic signal acquisition module. Subglottal and acoustic pressure signals were recorded with a sampling rate of 96 kHz and duration of 2 s. The ventricular and vocal fold motion was captured by a Phantom V2511 (Vision Research, Wayne, NJ) high-speed camera with a frame rate of 4000 fps, a spatial resolution of 768 px × 768 px, and a duration of 600 ms. For the measurement series, three different pre-phonatory gap sizes ($g_1 = 0\,\text{mm}$, $g_2 = 1\,\text{mm}$, $g_3 = 2\,\text{mm}$) were adjusted in sequence. For each gap, three successive symmetric vocal fold adduction levels were applied ($T_1 = 5$ mNm, $T_2 = 15$ mNm, $T_3 = 25$ mNm). After adjusting the phonation posture, glottal airflow was increased manually until sustained phonation occurred. Afterward, glottal flow was increased stepwise 6 times by 5 standard liters per minute (slm). Nine different glottal configurations (3 gaps × 3 adduction levels = 9), each including 7 flow steps, were applied yielding 63 runs for each *ex vivo* larynx. In total, 567 runs were recorded, whereas 103 of them did not show proper or even absence of phonation. Due to the massive noise component, these data sets had to be removed from the study, since no fundamental frequency could be identified. Hence, 464 data sets were chosen to be suitable for further processing.

B. Data analysis

For analysis of the aerodynamic properties and the vocal fold oscillation characteristics, the following parameters were calculated.

Glottal flow resistance:

$$R = \frac{\bar{P}_s}{\bar{Q}}. \tag{1}$$

R was computed according to literature,[30] with mean glottal flow $\bar{Q}$ and mean subglottal pressure $\bar{P}_s$.

The high-speed videos were analyzed with our in-house software entitled, “Glottis Analysis Tools.” The analysis involved glottal segmentation and subsequently the computation of the glottal parameters on the basis of 50 sequential oscillation cycles from each high-speed video. This number of cycles has proven to be appropriate based on previous studies.[31–33] The following glottal parameters ranging from 0 to 1 were derived based on the glottal area (GA).

Glottis Gap Index (GGI) is the minimum GA divided by the maximum GA during one cycle:[32]

$$\mathrm{GGI} = \frac{1}{N}\sum_{i=1}^{N}\frac{\min(\mathrm{GA}_i)}{\max(\mathrm{GA}_i)}, \tag{2}$$

with N being the number of oscillation cycles and GA_i the glottal area for the ith cycle. GGI values close to 1 indicate small changes in GA during one vibrational cycle whereas values close to 0 indicate large movement of vocal folds. Complete closure of the glottis is expressed by $\mathrm{GGI} = 0$.

Open Quotient (OQ) is the duration of the glottis being open divided by the total cycle duration:[34]

$$\mathrm{OQ} = \frac{1}{N}\sum_{i=1}^{N}\frac{t_i^{\mathrm{open}}}{T_i}, \tag{3}$$

with t_i^{open} being the duration of glottis being open and T_i the total duration of the ith cycle. OQ values of 1 are assumed when the vocal folds do not close completely during one cycle (also indicated by $\mathrm{GGI} > 0$). Hence, the duration of GC can only be quantified by OQ if no gap remains. PA is the time difference between the left and right part of the GA reaching their maximum normalized by the total cycle duration:[35]

$$\mathrm{PA} = \frac{1}{N}\sum_{i=1}^{N}\frac{|t_i^{\mathrm{L(max)}} - t_i^{\mathrm{R(max)}}|}{T_i}, \tag{4}$$

with $t_i^{\mathrm{Side}}(\max)$ being the time at which the GA of the left/right side in the ith cycle is a maximum.

PA of 0 indicates total temporal left-right symmetric vocal fold oscillation, whereas the value 1 signifies a phase shift of 180° between the left and right vocal fold oscillation. Amplitude periodicity (AP) is the quotient of the minimal and maximum GA amplitude A_i between two successive cycles[35]

$$\mathrm{AP} = \frac{1}{N-1}\sum_{i=1}^{N-1}\frac{\min(A_i, A_{i+1})}{\max(A_i, A_{i+1})}, \tag{5}$$

with

$$A_i = \max(\mathrm{GA}_i) - \min(\mathrm{GA}_i). \tag{6}$$

Time Periodicity (TP) is the quotient of the minimal and the maximal cycle duration between two successive cycles[35]

$$TP = \frac{1}{N-1}\sum_{i=1}^{N-1}\frac{\min(T_i, T_{i+1})}{\max(T_i, T_{i+1})}. \tag{7}$$

Periodicity values close to 1 indicate a high cycle-to-cycle periodicity and 0 indicate large changes from one cycle to the next.

The acoustic signal is evaluated by CPP displaying the quality of voice. Besides CPP, further acoustic parameters have been established for the assessment of dysphonic voice, e.g., H1–H2.[36] As CPP has proven to be a reliable indicator for breathy voice[37] and seems to be sensitive to glottal noise generation, vocal fold oscillation periodicity,[24] and asymmetry,[38] CPP is used in this study to quantify the influence of glottal parameters on the acoustic signal quality. CPP was calculated based on the definition introduced by Hillenbrand *et al.*[39] with a rectangular window with a length of 2^{13} sample points (corresponding to 42.67 s).

Table I gives an overview of all calculated parameters, their value range, and the meaning of a minimum and maximum parameter value.

According to the formulated goals, the analysis contains two parts. First, the impact of GC on the phonatory process is investigated. Therefore, GC is categorized into four groups by

TABLE I. Overview of the calculated parameters, their value range, and meaning.

Parameter	Range	Meaning
GC	[0,4]	1: complete closure, 2: posterior gap 3: partial vocal fold contact, 4: no contact
R	no range provided	low-high flow resistance
GGI	[0,1]	0: glottis closes entirely 1: glottis does not move
OQ	[0,1]	0: glottis does not open 0.5: glottis is open half of the cycle duration 1: glottis does not close
PA	[0,1]	0: total temporal left-right symmetric vocal fold oscillation 1: phase shift of 180°
AP	[0,1]	0: large changes of maximum GA from one cycle to the next 1: complete cycle-to-cycle periodicity
TP	[0,1]	0: large changes of period duration from one cycle to the next 1: complete cycle-to-cycle periodicity
CPP	no range provided	low: low periodicity of the acoustic signal high: high periodicity of the acoustic signal

visually evaluating the video data. Second, the effect of aerodynamic and glottal dynamic parameters on the acoustic quality is examined. Therefore, an objective clustering method for partitioning the parameter values into three groups is applied. The detailed procedure is explained below.

1. Partitioning of GC types

For the investigation of GC, the high speed video data were assessed subjectively and partitioned into four types of GC on the basis of Inwald *et al.*[3] The resulting GC groups $GC_{1–4}$ and the procedure of classification of GC are described below. The number of data sets in each group is given in brackets.

GC_1: Complete GC (103).
GC_2: Glottal gap in the posterior part (one-third of the vocal fold length) (201).
GC_3: Partial vocal fold contact (less than two-thirds of the vocal fold length) (128).
GC_4: No vocal fold contact (32).

Figure 2 shows representative images of the four GC groups. GC_1 displays vocal fold contact with complete closure of the glottis which is associated with the phonation of healthy men. GC_2 shows a posterior gap up to one-third of the vocal fold length and is predominantly observed in healthy women. GC_3 shows partial vocal fold contact of less than two-thirds of the vocal fold length and can be located anterior or medial (in this case). It is predominantly observed in cases of dysphonia, but was also occasionally found in healthy women. GC_4 displays the case without vocal fold contact. Solely, the vocal fold edges vibrate with small amplitude. It is observed almost exclusively in women and men with dysphonia.[3]

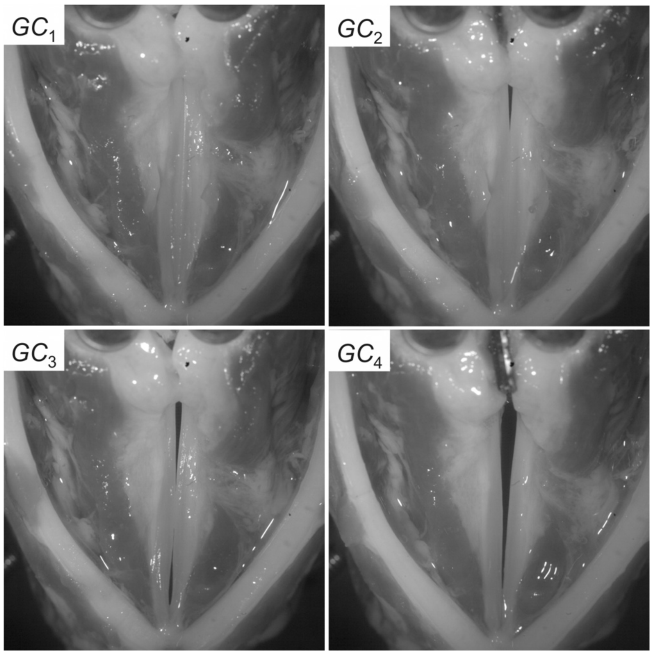


FIG. 2. Partitioning of GC types into 4 groups. GC_1: complete closure, GC_2: glottal gap in the posterior third. GC_3: partial vocal fold contact, GC_4: no vocal fold contact. Each figure shows the time point in the oscillation cycle at which the glottal gap reaches its minimum.

2. Partitioning of glottal and aerodynamic parameters

Although the classification of GC types is based on a visual evaluation method which can be assessed quickly in daily clinical practice, this procedure is very time consuming for comprehensive studies. Therefore, objective parameters (e.g., GGI, PA, AP) indicating glottal gap size or vocal fold oscillation characteristics should be established. To investigate the influence of these parameters, the computed values must be grouped. Unlike the case of GC partitioning, this procedure cannot be done subjectively. Hence, an objective clustering method, *K*-means, is used to subdivide the values into three groups. This enables a comparison between a low, medium, and high range of the parameter, although the variance of the values is small compared to the total range of the parameters. The cluster centers and the number of data sets per center are given in Table II.

Clustering of OQ was executed solely for cases in which $OQ \neq 1$. This was the case for complete closure of the vocal folds, i.e., GC_1. Furthermore, OQ_4 contains all cases of GC_2; OQ_5 all cases of GC_3 and GC_4. To arrange the parameter values according to its influence on phonation (mild…severe), we ordered the cluster centers as follows. Cluster centers of GGI, OQ, PA, and *R* are arranged in ascending order, AP and TP cluster centers in descending order.

3. Statistical analysis

Since the group values were not normally-distributed, the Kruskal-Wallis test was used for multiple group comparison. A significance level of $\alpha = 0.05$ was chosen. The Dunn-Bonferroni correction was applied for *post hoc* tests (Mann-Whitney-U). The correction factor was selected according to the number of tests $n = 3, 6, 10$ executed for the

TABLE II. Cluster centers (built with *K*-means) and number of runs per resulting group.

	1		2		3	
Cluster center	mean	#runs	mean	#runs	mean	#runs
Gap parameters						
GGI_{1-3}	0.04	276	0.20	130	0.43	58
OQ_{1-3}	0.32	41	0.56	33	0.82	29
Symmetry parameters						
PA_{1-3}	0.03	272	0.09	139	0.17	53
Periodicity parameters						
AP_{1-3}	0.97	359	0.83	75	0.59	30
TP_{1-3}	0.97	301	0.90	112	0.82	51
Aerodynamic parameter						
R_{1-3}	99.3	18	51.6	82	20.8	364

individual number of groups [3 (GGI, PA, AP, TP, R), 4 (GC), 5(OQ)]. The corrected significance levels $\alpha_c = \alpha/n$ are given in Table III in the Appendix.

The clustering and statistical analysis were performed using IBM SPSS Statistics 21 software (IBM, Armonk, NY). Detailed results are given in the Appendix.

III. RESULTS

A. Aerodynamic parameters

All larynges showed nearly linear dependence between $\bar{Q}$ and $\bar{P}_s$. Pearson's correlation coefficient was determined for each larynx for all 9 glottal configurations ($r = 0.99 \pm 0.03$). $\bar{Q}$ ranged from 8–155 slm and $\bar{P}_s$ from 0.2–4 kPa. Average fundamental frequency was $f_0 = 126 \pm 69$ Hz. Regarding the individual GC groups, a frequency jump from $GC_{1,2}$ to $GC_{3,4}$ is observable (see Fig. 3). Statistical analysis yielded significant differences except for the comparison of $GC_{1,2}$ and $GC_{3,4}$ (for details see Table IV in the Appendix).

B. Influence of GC

CPP decreases continuously for increasing GC groups (see Fig. 4). From cases with complete closure (GC_1) to cases with minimal vocal fold contact (GC_3), the CPP value decreases by one-third of its maximum, whereas the drop from GC_2 to GC_3 (approx. 22%) is more distinct than the decrease from GC_1 to GC_2 (approx. 10%). From GC_3 to GC_4, CPP remains largely constant. The Kruskal-Wallis test shows statistically significant differences between all groups, except for $GC_{3,4}$ (for details see Table IV in the Appendix).

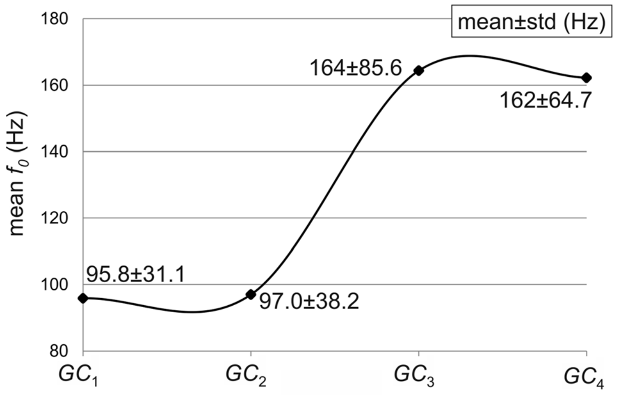


FIG. 3. Fundamental frequency f_0 as a function of the four GC groups GC_{1-4}.

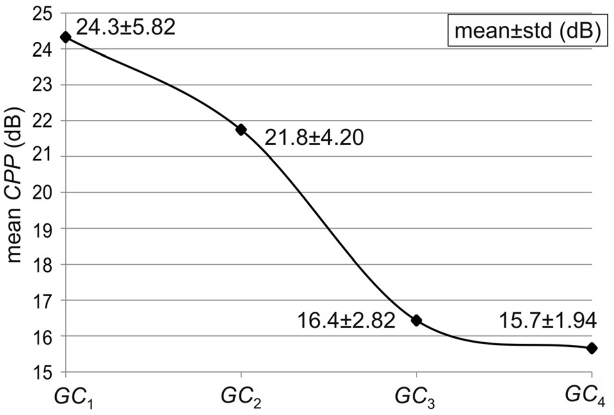


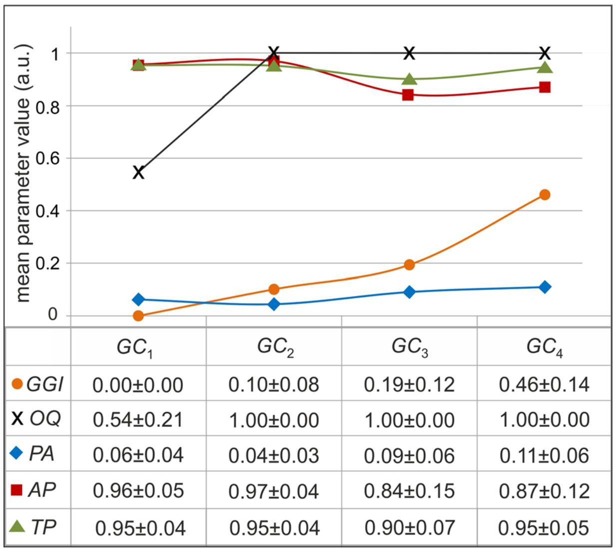
FIG. 4. CPP as a function of the four GC groups GC_{1-4}.

GGI increases with increasing GC group (see Fig. 5), whereas from GC_1 to GC_3, the increase covers 41% of the possibly attainable values. From GC_3 to GC_4, GGI increases steeper which makes up the greater part of change in value. Group comparison yields statistically significant differences between all GC groups.

OQ for complete closure (GC_1) is 0.54 and increases to 1 for GC_{2-4}. Comparisons between GC_1 and the remaining groups are significant ($p = 0.000$). All other comparisons yield a significance value of 1.

PA decreases slightly, but is statistically significant from GC_1 to GC_2 and increases distinctly from GC_2 to GC_3. PA does not increase significantly from GC_3 to GC_4. The Kruskal-Wallis test shows significant differences between all groups except for $GC_{3,4}$.

Regarding the periodicity parameters (AP, TP), the values for complete closure (GC_1) and posterior gap (GC_2) are not significantly different. A significant decrease to GC_3 is



	GC_1	GC_2	GC_3	GC_4
● GGI	0.00±0.00	0.10±0.08	0.19±0.12	0.46±0.14
X OQ	0.54±0.21	1.00±0.00	1.00±0.00	1.00±0.00
◆ PA	0.06±0.04	0.04±0.03	0.09±0.06	0.11±0.06
■ AP	0.96±0.05	0.97±0.04	0.84±0.15	0.87±0.12
▲ TP	0.95±0.04	0.95±0.04	0.90±0.07	0.95±0.05

FIG. 5. (Color online) Glottal parameters (GGI, PA, AP, TP) as a function of the four GC groups GC_{1-4}.

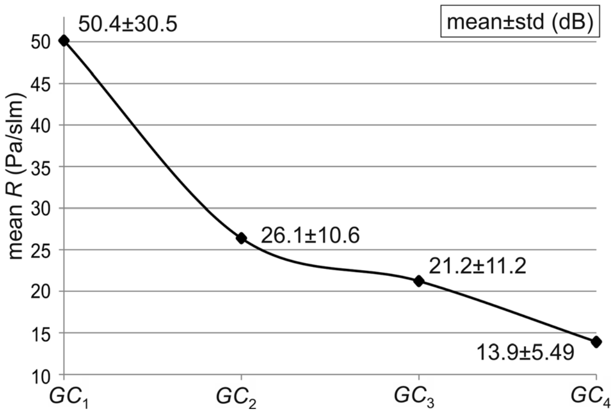


FIG. 6. Glottal flow resistance R as a function of the four GC groups GC_{1-4}.

observed for both periodicity parameters. For GC_3 to GC_4, the values increase slightly, whereas group differences are only significant for TP.

R decreases by approx. 48% from GC_1 to GC_2 (see Fig. 6) and further from GC_2 to GC_4, but less distinctly (by approx. 24%). The Kruskal-Wallis test shows significant differences between all groups.

C. Influence of glottal and aerodynamic parameters on acoustic quality

CPP shows a decreasing tendency for increasing OQ values (OQ_1–OQ_3) (see Fig. 7). The Kruskal-Wallis test does not show significant differences for $OQ_{1,2}$ or $OQ_{2,3}$. However, for comparison between OQ_1 and OQ_3, statistical analysis yields $p = 0.002$. From OQ_3 to OQ_4, the CPP value is almost constant and statistical testing does not show a significant difference. The decrease of CPP is more distinctive for OQ_4 to OQ_5 in which OQ has the value 1 and the groups differ in terms of the vocal fold contact area. OQ_5 differs from all remaining groups significantly ($p = 0.000$). For detailed results of group comparison, see Table V in the Appendix.

Influences of GGI, PA, AP, TP, and R groups on CPP are summarized in Fig. 8. The individual cluster centers of each parameter group are listed in Table II. All parameters exert a negative influence on CPP and thus on the acoustic quality. For the groups of GGI_{1-3} and R_{1-3}, CPP decreases almost linearly. CPP decreases slightly from PA_1 to PA_2 and drops more rapidly toward PA_3. The reduction of CPP is steeper for $AP_{1,2}$ and $TP_{1,2}$ than for $AP_{2,3}$ and $TP_{2,3}$.

All Kruskal-Wallis tests show significant differences between the groups, except for $PA_{1,2}$ and $AP_{2,3}$. For detailed results of statistical tests, see Table VI in the Appendix.

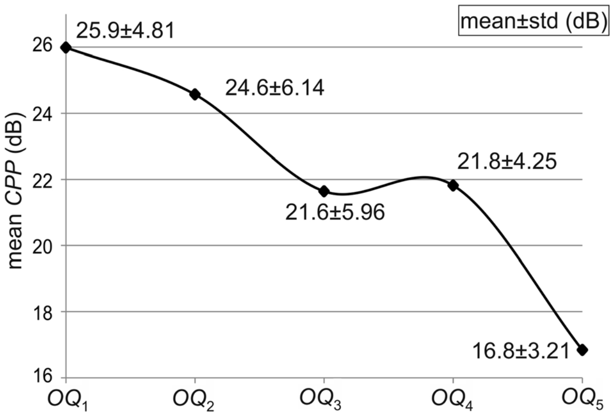


FIG. 7. CPP as a function of OQ.

IV. DISCUSSION

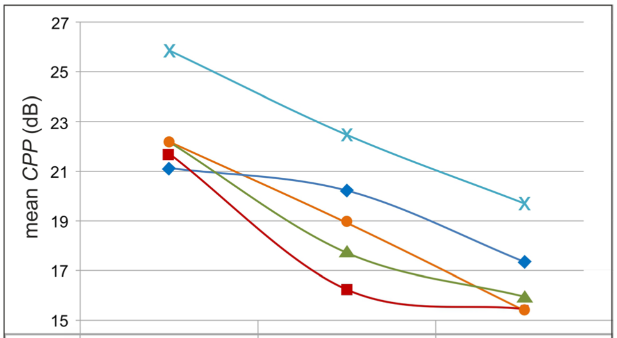
A. Phonatory parameter values

Results show a wider range of values in glottal flow rate ($\bar{Q} = 8\ldots155$ slm) and subglottal pressure ($\bar{P}_s = 0.2\ldots4\,\text{kPa}$) than other *ex vivo* porcine experiments. Alipour and Jaiswal[27] reported values of $\bar{Q} = 36\ldots78$ slm and $\bar{P}_s = 0.1\ldots2.5\,\text{kPa}$ using *ex vivo* porcine larynges at different vocal fold adduction levels. Furthermore, they reported a non-linear relationship between $\bar{Q}$ and $\bar{P}_s$ with some linear portions. Our results show an almost linear behavior with a Pearson correlation coefficient of $r = 0.99 \pm 0.03$. The fundamental frequency ($f_0 = 126 \pm 69$ Hz) lies below the findings of Alipour and Jaiswal ($f_0 = 194 \pm 105$ Hz;[27] $f_0 = 220 \pm 57$ Hz[26]).

This discrepancy could be due to the difference in the procedure of vocal fold adduction control. However, control of fundamental frequency is achieved primarily by vocal fold elongation (by cricothyroid muscle contraction) rather than by vocal fold adduction (through lateral cricoarytenoid and inter arytenoid muscle contraction), as reported in literature.[40]

Unfortunately, Alipour and Jaiswal[26,27] do not provide detailed information on the vocal fold elongation technique in their study. Therefore, this discrepancy cannot be further explained.

A significant increase in f_0 was found in comparing "healthy phonation" ($GC_{1,2}$) with "pathologic phonation" ($GC_{3,4}$) (see Fig. 3). Fundamental frequency is a function of the length, stress, and density of the vocal folds and is also dependent on the subglottal pressure.[41,42] These dependencies were reproduced in *ex vivo* investigations applying the present setup.[29] However, GC during phonation is a complex interplay of vocal fold adduction, elongation, pre-phonatory



	group1	group2	group3
● GGI	22.2±5.36	18.9±3.98	15.4±1.79
◆ PA	21.1±4.87	20.2±5.60	17.3±5.10
■ AP	21.7±5.14	16.2±2.55	15.5±2.41
▲ TP	22.2±5.18	17.7±3.84	16.0±2.44
× R	25.9±4.98	22.5±5.62	19.7±4.90

FIG. 8. (Color online) CPP as a function of glottal and aerodynamic parameter groups (GGI, PA, AP, TP, and R).

glottal gap, and the subglottal pressure, which has to be investigated in further studies.

Nonetheless, the relationship between GC and fundamental frequency was also reported by Yamauchi *et al.*[43] who investigated healthy subjects and patients with vocal fold paralysis (VFP). The authors reported more frequent incomplete closure combined with an increase in fundamental frequency in cases with VFP. Furthermore, they reported an increased oscillatory frequency of the atrophied vocal fold compared to the normal vocal fold, which could be an explanation for the computation of increased f_0.

Therefore, it is supposed that fundamental frequency can serve as an additional indicator for distinguishing between healthy and pathologic voice. This was reported by Wolfe *et al.*[44] who found an improved correlation between jitter and the degree of dysphonia by considering the mean fundamental frequency in a multiple regression analysis.

However, a detailed investigation of the correlation between fundamental frequency and the left-right separated oscillation frequencies of the vocal folds should be implemented to investigate the cause of frequency increase for reduced GC.

CPP values ($\Delta\text{CPP} = \text{CPP}(\text{GC}_1)–\text{CPP}(\text{GC}_4) = 8.6$ dB) cover the range of *in vivo* investigations of Hillenbrand *et al.*,[37,39] who examined breathy and non-breathy voices, and reported a resulting difference in ΔCPP of 8.5 dB.

Glottal gap was induced by inserting several metal shims between the arytenoid cartilages. GGI ranges from 0 for complete closure (GC_1) up to 0.46 ± 0.14 for the case without vocal fold contact (GC_4). For GC_2 (posterior glottal gap) which is associated with the phonation of healthy women, GGI is 0.1 ± 0.08. This lies within the range of Patel *et al.* and Kunduk *et al.*, who reported values for healthy women of 0.05 ± 0.07 (Ref. 32) and 0.17 ± 0.31.[45]

OQ was evaluated solely for GC_1 and was found to be 0.54 ± 0.21. For $\text{GC}_{2–4}$, the values were 1 due to no complete closure of the vocal folds. OQ values for healthy subjects were found to be 0.78 ± 0.18.[46] Disaggregated by gender, OQ values were reported for men: 0.70 ± 0.16,[47] 0.74 ± 0.19;[33] for women: 0.85 ± 0.13,[47] 0.86 ± 0.17.[33] Baken and Orlikoff[34] reported values for healthy subjects from 0.47 to 0.82 depending on f_0 (120 Hz…325 Hz) and vocal intensity (low…high). OQ values for GC_1 lie within the range of the findings in literature that are calculated on the basis of the GA.

Despite a symmetric stimulation of vocal fold adduction in our experiment, PA values up to 0.11 ± 0.06 for GC_4 are observed. The values lie within the range of normal phonation with a maximal asymmetry of 20% for healthy subjects reported by Bonilha *et al.*[48] and Mehta *et al.*[14]

Both periodicity values (AP, TP) lie in the range of the values for normal phonation reported in literature. Patel *et al.*[32] reported values for men ($\text{AP} = 0.99 \pm 0.003$, $\text{TP} = 0.97 \pm 0.01$) and women ($\text{AP} = 0.98 \pm 0.01$, $\text{TP} = 0.95 \pm 0.02$). Corresponding values of GC_1 ("healthy men") were $\text{AP} = 0.96 \pm 0.05$ and $\text{TP} = 0.95 \pm 0.04$, of GC_2 ("healthy women") values were $\text{AP} = 0.97 \pm 0.04$ and $\text{TP} = 0.95 \pm 0.04$. Due to the lack of high-speed investigations in the clinical environment, quantitative values for vocal fold periodicity, especially for pathological phonation, are rare.

In summary, the aerodynamic parameter values in this study cover a wider range than comparable investigations with *ex vivo* porcine larynges. Acoustic measures displayed the difference between healthy and pathological phonation according to *in vivo* investigations. Glottal gap and dynamic measures lie in the range of the values reported in literature of *in vivo* investigations. Despite the fact that the ventricular folds are active oscillators in normal phonation of the porcine larynx[26] this model seems to be suitable for the investigation of human phonation.

B. Influence of GC

With regard to goal number 1, the influence of GC on glottal and aerodynamic parameters and the acoustic output is discussed.

Vocal fold contact has a distinct influence on the acoustic output, see Fig. 4. CPP decreases from complete closure (GC_1) to cases with posterior gap (GC_2) and decreases further to cases exhibiting partial vocal fold contact (GC_3) and no contact (GC_4). This indicates that complete GC is most beneficial for the acoustic output.

The assigned GC groups are based on the classification of GC in Inwald *et al.*[3] The authors report that a subjective evaluation of GC is a valuable predictor for distinguishing between healthy and pathological subjects. This corresponds to the major decrease in CPP from "healthy men and women" ($\text{GC}_{1,2}$) to "pathological phonation" ($\text{GC}_{3,4}$). Mehta *et al.*[24] reported an increase in cepstral peak magnitude due to the reduction of glottal gap by phonomicrosurgical treatment of organic lesions. The authors assume the variation of turbulent noise to be the main factor of decrease in cepstral measures. This confirms the decrease of CPP from GC_1 to GC_2.

Despite the increased glottal gap from GC_3 to GC_4, CPP does not show significant differences. This indicates that the curve tends toward a limiting value, although the reason is not evident. Hence, a further evaluation of the factors affecting the acoustic output is executed in the following.

An increase in GGI and OQ for increasing GC groups confirm the visual classification of the GC types (see Fig. 5). For GC_1 the GGI value is 0 and OQ less than 1, which indicates a complete closure of the vocal folds during each oscillation cycle. For $\text{GC}_{2–4}$, the OQ value is 1 and GGI larger than 0 indicating a remaining gap during each cycle. A major increase in GGI is found for GC_3 to GC_4, since the minimal GA in one cycle increases dramatically for cases without vocal fold contact.

Comparing $\text{GC}_{1,2}$ (healthy) with $\text{GC}_{3,4}$ (dysphonic), a significant increase in PA is observed. The phonation seems to be destabilized by an increase in glottal gap. These findings are supported by Yamauchi *et al.*,[49] who reported that increased vocal fold asymmetries are combined with a poorer GC in *in vivo* investigations. Isshiki *et al.*[50] reported that a complete closure reduces vibrational vocal fold asymmetry in canine and human *ex vivo* larynges with induced asymmetrical vocal fold tension.

A slight but significant decrease of PA is observed for GC_1 ($\text{PA} = 0.06 \pm 0.04$) to GC_2 ($\text{PA} = 0.04 \pm 0.03$), which indicates a stabilization of the phonation for cases with posterior gap. This was also observed in Patel *et al.*,[32] who reported values for men of PA = 0.05 ± 0.04 and for women of PA = 0.03 ± 0.02 in vocally healthy subjects. This decrease is in the same range (2%) of the investigations in this study.

The destabilization from $GC_{1,2}$ to $GC_{3,4}$ is also indicated by a decrease of AP and TP values. This is confirmed by Kobayashi *et al.*,[51] who reported a stabilizing effect of reduced pre-phonatory glottal gap resulting in an increased periodicity at unilateral paralyzed vocal folds in *ex vivo* canine larynges. While the periodicity parameters do not change for GC_1 to GC_2, a slight increase from GC_3 to GC_4, which is only significant for TP, is observed. The results suggest that a partial contact decreases the oscillation periodicity of the vocal folds. The increased periodicity for cases without vocal fold contact was also observed by Isshiki *et al.*[50] in *ex vivo* canine and human larynx experiments supported by a theoretical model.

Generally, the variation of absolute values of PA, AP, and TP are small compared to the total value range of the parameters. Hence, it is questionable if these parameters are suitable for voice evaluation in the clinical environment.

Overall, the increase in R is significant, whereas major variation is present from GC_1 to GC_2. This was also reported in Döllinger *et al.*,[52] who investigated the dependency of R on the vocal fold adduction level, which also results in larger amplitudes of oscillation. Zañartu *et al.*[53] reported a reduction of energy transfer from the glottal airstream to the vocal folds up to 80% for an increase of glottal gap size to 0.1 cm in a numerical model. The results suggest that small gaps between the vocal folds decrease the glottal flow resistance dramatically and thus the energy transfer. Hence, a complete closure of the vocal folds yields to a large energy transfer since the maximum value of R was found for GC_1. Comparatively small changes in R for $GC_{2–4}$ indicate that variation in gap size does not lead to a considerable contribution to the energy transfer in cases with pre-phonatory glottal gap.

In summary, a complete GC (GC_1) but also cases with posterior gap (GC_2) stabilize the phonatory process indicated by decreased PA and increased AP and TP. The visual classification of GC was confirmed by the objective parameters quantifying the GC. The energy transfer from the glottal airstream to the vocal folds is strongly dependent on the glottal gap size. This fact and the destabilizing effect of the glottal gap are also reflected by the decrease of acoustic quality. The stagnation of CPP from cases with partial vocal fold contact (GC_3) to no contact (GC_4) raises questions which require further investigations. Increased periodicity values for GC_4 compared to GC_3 might provide an explanation for this phenomenon. Our hypothesis is that periodicity is a function of contact area between the vocal folds with a minimum value even lower than the periodicity for GC_4. Thus, at high GGI values, vocal fold contact seems to further destabilize the vocal fold oscillation compared to the commonly suggested worst case of no contact.

C. Influence of glottal and aerodynamic parameters on acoustic quality

With regard to goal number 2, the influence of the glottal and aerodynamic parameters on the acoustic quality is discussed.

GGI yields a negative influence on CPP (see Fig. 8). This is consistent with the findings of Chen *et al.*,[54] who reported that CPP is affected by glottal gap area in *in vivo* investigations. Being a valuable predictor for glottal gap, GGI can serve as indicator for proper phonation. However, the absolute value of GGI does not provide information about the location of the gap and the type of vocal fold contact.

OQ reflects the duration of complete GC. A decrease of CPP from OQ_1 to OQ_3 is observable (see Fig. 7), whereas solely the group comparison between OQ_1 and OQ_3 yields statistical significant results. This indicates that, besides the fact that closure is present, the duration of complete GC has an influence on the acoustic quality. OQ_3 and OQ_4 exhibit similar CPP values. This refers to the fact that a phonatory sample which includes a posterior gap may yield comparable acoustic output with cases involving complete closure, but a short period of vocal fold contact. It may be assumed that a posterior gap would not necessarily lead to a poor acoustic signal. This coincides with the findings of Kreiman *et al.*,[55] who reported that the cause of breathiness is dependent on the speaker. In fact, breathiness is the result of a combination of several factors and therefore cannot be inferred solely from OQ. The severe drop of the curve toward OQ_5 confirms the findings from above that partial and no vocal fold contact (corresponding to GC_3 and GC_4) decreases the acoustic quality significantly compared to cases with complete vocal fold contact and posterior gap (GC_1 and GC_2). Due to the fact that OQ assumes the value of 1 as soon as a gap remains during phonation (in this study about 78%), this parameter can only provide information when the glottis closes completely and is therewith limited in application.

Glottal dynamic parameters contain detailed information about vocal fold oscillation. Low PA as well as high AP and TP are indicators of a stable phonatory process. Despite the fact that the absolute values show a small variation and PA lies within the range of normal phonation,[48] a significant influence on the acoustic quality is still noticeable (see Fig. 8). For increasing PA, the CPP value decreases. This was also reported by Yamauchi *et al.*,[49] who found asymmetries of vocal fold vibration in patients with laryngeal pathologies. Samlan and Story[38] found an impact of different types of asymmetry on the acoustic quality in a numerical model.

Furthermore, a decreased periodicity (ascending AP and TP groups) of vocal fold oscillation leads to a reduced acoustic quality. This was also reported by Mehta *et al.*,[24] who attributes an increase in cepstral peak magnitude to an attenuation of vocal fold aperiodicity.

Despite the fact that the cluster centers of TP (see Table II) cover a smaller range than the ones for AP, the comparison between TP groups yields overall significant results whereas for AP only the comparisons between $AP_{1,2}$ and $AP_{1,3}$ are significant. This indicates that TP, in particular, plays an essential role in voice quality.

An increasing glottal flow resistance R (and thus a higher energy transfer from the glottal flow to the vocal folds) yields an improved acoustic quality, see Fig. 8, with overall significance for all group comparisons. This is supported by

Rosenthal *et al.*,[56] who reported an increase in CPP by increasing glottal flow resistance estimated in vocally healthy patients producing speech at minimal, medium, and maximum vocal effort. In *in vivo* investigations, R can only be measured directly using invasive methods or assumed using indirect measuring methods. Hence, integration in the clinical environment is a critical process.

In summary, glottal parameters confirmed that GC and the duration of closure are essential for proper phonation. Despite only a small variation of glottal oscillation parameters, their influence on CPP was very clear. Glottal flow resistance is strongly dependent on the glottal gap and correlates with acoustic quality. Thus, it is potentially a reliable predictor for healthy voice.

V. SUMMARY AND CONCLUSION

This study systematically investigates the factors impacting the phonatory process and the resulting acoustic quality. *Ex vivo* porcine larynx experiments were used, which offer the advantage of direct parameter control as compared to *in vivo* investigations.

The resulting absolute values of glottal parameters quantifying glottal gap and vocal fold oscillation characteristics lie in the range of the results reported in *in vivo* investigations.

With respect to goal number 1 (investigation of GC types on acoustic quality, vocal fold oscillation characteristics, and aerodynamic properties), the results indicate that complete GC (GC_1) but also cases with posterior gap (GC_2), stabilize the phonatory process. This was indicated by decreased PA and increased AP and TP. This stabilization was also observed in an increase of the acoustic quality indicated by CPP especially for complete closure (GC_1).

Further examination of asymmetry and periodicity parameters (goal number 2) showed that even small changes of absolute values exhibited a remarkable influence on the acoustic quality. Hence, detailed investigations of these parameters on the acoustic output would be desirable, e.g., by isolated variation of left-right asymmetry or AP and TP in numerical models. Furthermore, standard values regarding glottal dynamic parameters (especially periodicity) for healthy and pathological subjects need to be established. However, these small variations in dynamic parameter values question their applicability for diagnosis of voice disorders in the clinical environment. Furthermore, a direct influence of therapy on these parameters is doubtful. Therefore, it is suggested that the focus be on the optimization of surgical methods for reducing the glottal gap which have proven to be beneficial for voice quality.

Besides these main effects the following results were observed:

The energy transfer from the glottal airstream to the vocal folds, as indicated by the glottal resistance, was strongly dependent on GC and had an essential influence on the acoustic quality. This parameter seems to be a good predictor of a healthy voice, but is limited in the direct measurement in *in vivo* investigations.

Aside from the GC itself, the duration of complete closure, as indicated by the OQ was beneficial for the acoustic quality. However, this parameter is only applicable for cases with complete GC (in this study in only 22% of the data). A calculation using a combination of multiline kymogram and GA might help overcome this limitation.

Results indicated that the glottal gap size only exerts an influence on the acoustic quality up to a certain degree. For cases without vocal fold contact (GC_4) compared to cases with partial vocal fold contact (GC_3), CPP did not significantly change. A possible explanation could be found in the increased periodicity values for cases without vocal fold contact compared to cases with partial contact. To examine this effect, further studies have to be undertaken to investigate the influence of total glottal gap size and periodicity on acoustic quality.

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APPENDIX: STATISTICAL ANALYSIS

TABLE III. Corrected significance levels α_c (Dunn-Bonferroni) for *post hoc* tests (Mann-Whitney-U).

Parameter group	α_c
GC_{1-4}	0.008
OQ_{1-5}	0.005
$PA_{1-3}, AP_{1-3}, TP_{1-3}, GGI_{1-3}, R_{1-3}$	0.017

TABLE IV. P-values (Kruskal-Wallis test) for comparison of acoustic, glottal, and aerodynamic parameters between the four GC groups.

	post-hoc test ($p \le 0.008$)						Kruskal-Wallis
Parameters	$GC_{1,2}$	$GC_{2,3}$	$GC_{3,4}$	$GC_{1,3}$	$GC_{2,4}$	$GC_{1,4}$	($p \le 0.05$)
f_0	0.113	**0.000**	0.841	**0.000**	**0.000**	**0.000**	**0.000**
CPP	**0.000**	**0.000**	0.279	**0.000**	**0.000**	**0.000**	**0.000**
GGI	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**
OQ	**0.000**	1.000	1.000	**0.000**	1.000	**0.000**	**0.000**
PA	**0.000**	**0.000**	0.156	**0.000**	**0.000**	**0.000**	**0.000**
AP	0.012	**0.000**	0.415	**0.000**	**0.000**	**0.000**	**0.000**
TP	0.820	**0.000**	**0.002**	**0.000**	0.498	0.485	**0.000**
R	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**	**0.000**

TABLE V. P-values (Kruskal-Wallis test) for comparison of CPP between the five OQ groups.

Parameter	post-hoc test ($p \le 0.005$)					Kruskal-Wallis ($p \le 0.05$)
CPP	$OQ_{1,2}$	$OQ_{2,3}$	$OQ_{3,4}$	$OQ_{4,5}$	$OQ_{1,3}$	**0.000**
	0.461	0.046	0.536	**0.000**	**0.002**	
	$OQ_{1,4}$	$OQ_{1,5}$	$OQ_{2,4}$	$OQ_{2,5}$	$OQ_{3,5}$	
	0.000	**0.000**	0.013	**0.000**	**0.000**	

TABLE VI. P-values (Kruskal-Wallis test) for comparison of CPP between the three glottal and aerodynamic parameter groups.

Parameter	*post hoc* test ($p \leq 0.017$)			Kruskal-Wallis ($p \leq 0.05$)
CPP	$GGI_{1,2}$	$GGI_{2,3}$	$GGI_{1,3}$	GGI_{1-3}
	0.000	**0.000**	**0.000**	**0.000**
	$PA_{1,2}$	$PA_{2,3}$	$PA_{1,3}$	PA_{1-3}
	0.028	**0.000**	**0.000**	**0.000**
	$AP_{1,2}$	$AP_{2,3}$	$AP_{1,3}$	AP_{1-3}
	0.000	0.133	**0.000**	**0.000**
	$TP_{1,2}$	$TP_{2,3}$	$TP_{1,3}$	TP_{1-3}
	0.000	**0.004**	**0.000**	**0.000**
	$R_{1,2}$	$R_{2,3}$	$R_{1,3}$	R_{1-3}
	0.011	**0.000**	**0.000**	**0.000**

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