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**Research Article**

# An Asymmetric Animal Phonatory Model with the Unilateral High Stiffness Curved Surface Vocal Fold

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**Abstract**

**Aim:** Patients with glottic cancer usually undergo voice deterioration due to insufficient glottic closure after cordectomy. We aimed to develop a sizeable left-right mismatch asymmetric vibration animal model to reconstruct high stiffness and smooth material vocal fold match normal vocal fold oscillation, which can restore a near-normal voice after cordectomy.

**Methods:** Twelve larynges removed from adult mongrel dogs were first used for the control group in the excised larynges phonation model of canine. The unilateral vocal fold of animals was reconstructed for RHSCS (reconstructed high stiffness cambered surface) vocal fold by silicone column after cordectomy. The phonation threshold flow (PTF), phonation threshold pressure (PTP), acoustic signals, and ultra-high-speed video images were recorded in the larynges phonation models of the canine. The vocal fold vibration amplitude was measured for two groups separately.

**Results:** The RHSCS vocal fold asymmetric phonation models produced a voice whose parameters (PTF, F0, jitter, shimmer, HNR) had no significant differences compared to the symmetric bilateral regular vocal fold oscillation. An exception was the significant increase of PTP and PTW in the RHSCS vocal fold model compared to the symmetric phonation model.

**Conclusion:** Our study reveals that high stiffness, smooth, and curve surface reconstruction of asymmetric vocal folds model can produce a near-normal voice within a range of intensity.

## INTRODUCTION

Glottic cancer is a laryngeal cancer in the true vocal cords and anterior and posterior commissures. According to the estimation of the latest study, 12470 new individuals were diagnosed with laryngeal cancer, and 3980 cases of death were caused by laryngeal cancer in the United States in 2022 [1]. Almost half of the cases were diagnosed as early-stage cancer, which includes Tis, T1, and a part of T2 cancer [2]. Early-stage laryngeal cancer has a relatively higher 5-year survival rate (82% for T1 and 60% for T2) and can be managed by transoral cordectomy, which removes partial or whole of the vocal fold [3]. However, voice deterioration is a common complication for patients undergone transoral cordectomy.

Voice deterioration usually results from insufficient glottic closure after cordectomy. Patients may appear with dysphonia, vocal fatigue, and dysphagia [4,5]. The voice restoration after cordectomy negatively affects patients' voice recovery and quality of life. Surgical techniques such as medialization thyroplasty (MT) and injection laryngoplasty (IL) have been used to restore voice sometimes, including unilateral vocal fold paralysis, sulcus vocalis, vocal fold scarring, and atrophy [6,7]. In recent years, they have also been used to treat glottic incompetence caused by transoral cordectomy for early-stage glottic cancer [8]. However, the efficacy of MT and IL in post-cordectomy voice restoration is uncertain. Berthelsen et al. reviewed seven studies about voice outcomes after MT application to patients who have undergone cordectomy [9]. These studies reported varying degrees of improvement in different acoustic indexes, whereas no consistent effect has been revealed on all aspects of voice outcomes. Three studies reported voice reconstruction by IL after cordectomy [10-12]. Their results only showed some improvements in limited acoustic indexes. Very difficult is known about the satisfactory improvement of voice reconstruction by IL or MT in patients with cordectomy. We plan to develop a surgery to restore a near-normal voice by different glottic vibratory mechanisms in this study.

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Unilateral cordectomy for early-stage laryngeal tumors leads to fibrous healing and scar formation on the vocal fold in the operated side vocal fold, which presents more stiffness and insufficient glottis closure compared to the control side vocal fold. This asymmetric vibration can result in worse timbre and pitch [13]. However, the asymmetric vibration may produce a near-normal voice in exceptional conditions. Jiang et al. investigated the canine hemi laryngeal phonatory model consisting of rigid plexiglass on one side and regular vocal fold on the control side [14]. No significant difference in acoustic parameters was found between the hemi laryngeal model and the normal larynx, except for a slight decrease in sound pressure of the hemilarynx [14]. Jiang suggests that surgeons had two choices for treating a damaged vocal fold: 1. repair the damaged vocal fold to make it normal enough to cooperate with the opposite normal vocal fold, or 2. modify the damaged vocal fold to a wall-like structure that is stiff enough not to interfere with the vibration of the opposite vocal fold. Even if a vocal fold can be reconstructed grossly, the biomechanical and geometrical characteristics cannot be restored. Reconstruction of the rigid vertical wall in the glottis is still impossible. Zhang et al. studied a physical asymmetric oscillation model with a sizeable left-right stiffness mismatch for which vocal fold vibration was dominated by the soft vocal fold, determined phonation frequency and vibration amplitude [15]. Both studies have revealed that a large stiffness and smooth material to replace the damaged unilateral vocal fold and paired normal vocal fold vibration in the control side may have a close-normal phonation frequency and vibratory amplitude in an entire excised laryngeal model.

Therefore, we developed a large left-right mismatch asymmetric vibration animal model to reconstruct high stiffness, and smooth material vocal fold match normal vocal fold oscillation, which may restore a near-normal voice after cordectomy.

## METHODS

### Larynges

Twelve larynges were removed from adult mongrel dogs from another experiment without laryngeal surgery. Larynges with vocal fold diseases like nodules or polyps were excluded from this study. The vocal fold length of twelve larynges ranged from 14.8mm to 17.4mm, and the mean length was 15.8mm. Excised larynges were stored in a -80°C refrigerator. Every larynx was used for full-larynx vibration and then for reconstruction of vibration again.

Before experiments, larynges were carried out from the refrigerator and placed in 0.9% saline solution for unfreezing at room temperature. The following steps were used to expose the true vocal folds. Part of the lower trachea was removed, and the upper trachea closed to the cricoid cartilage was retained with a 3-5cm length. The lymphoid and connective tissue around the trachea was also removed. The epiglottis, plica aryepiglottica, ventricular vocal folds, the upper one-third of the thyroid cartilage, and attached mucosa were removed to expose the whole vocal folds. The corbiculae cartilage, cuneiform cartilage, and superior and inferior cornu of the thyroid cartilage were dissected.

### Preparation of the mismatch stiffness oscillation model

Twelve larynges were used for symmetric phonation as a full-larynx vibration group first. After data collection, larynges were immediately operated for silicone reconstruction as the RHSCS (reconstructed high stiffness curved surface vocal fold) group. The left vocal fold and partial vocalis muscle were removed with ophthalmic scissors. Meanwhile, the right vocal fold was carefully protected to avoid any damage.

The silicon column with a Shore hardness of $55^0$ was used to reconstruct the defection of the left vocal fold. The diameter of the silicone column was 1.2cm and was cut to a smaller size appropriate to the size of the defection. The cambered surface of the silicone column was oriented toward the right vocal fold, and the long axis was parallel with the glottic midline. The cambered surface could oscillate and match the right vocal fold during the phonation. The flat surface opposite the cambered surface was clipped onto the internal surface of the left thyroid cartilage. A trapezoid shape of the silicone could adapt to the curved surface of the thyroid cartilage. 3-0 sutures were used to stitch the silicone, thyroid cartilage, and soft tissue up. The glass glue and stitch were used to seal the remaining tiny gaps between the silicon and the left thyroid and arytenoid cartilage and to prevent air leakage from undesired gaps instead of the glottic gap, which could fail vocal fold oscillation. The RHSCS model is shown in Figure 1. The production of the RHSCS model was finished as soon as possible after the experiment of the self-control group in order to avoid dehydration and maintain the biological activity of the vocal fold.

### The Apparatus, Larynx Mounting

The entire apparatus used for experimentation was described in detail by Weijian and Jiang [16,17]. The excised larynges were then mounted on the in vitro larynx apparatus for initiating phonation. The apparatus comprised two parts: the dynamic airflow system and the oscillation system. An air compressor

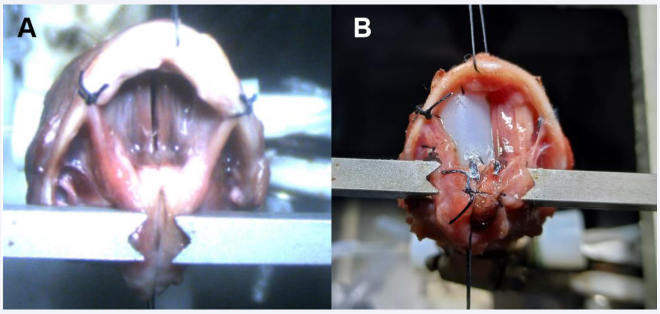

**Figure 1** Top views of a regular excised canine larynx (A) and a RHSCS larynx (B) mounted on the experimental apparatus.

was used to provide sustained and stable airflow. The trachea of the laryngeal was tightly clamped to the metal tube with a hose clamp. The airflow was supplied from the air compressor and controlled manually by a needle valve (Juba LD-1600W, Juba Machine Equipment Co, Ltd, Zhejiang, and China). A humidified air with a clarifier (SH300, Curative Medical Technology Inc, Beijing, China) maintains the vocal fold surface moisture and warmth. A suture and a four-pronged positioning device adduct the bilateral arytenoid cartilage. The anterior and posterior commissure sutures and suspending weights were used to keep the tension of the vocal fold.

### Data collection

The in vitro larynx apparatus was placed in a soundproofing room to avoid external noise interference. An analog airflow meter controlled and recorded the airflow, and an air manometer (PT-200S, Chengdu Tuchman Software Co Ltd, Chengdu, China) for subglottal pressure. The flowmeter and pressure transducer are connected to the pipe directly beneath the vocal folds. A microphone was used to record the acoustic signal and synchronously verify the subglottic pressure and airflow. The aerodynamic and acoustic signals were synchronously recorded using the Biological Signal Collection System (BL-420s, Chengdu Tuchman Software Co Ltd). Another condenser microphone and DiVAS Documentation System (XION GmBH, Berlin, and Germany) were used to collect and analyze the acoustic signals at 44000Hz. Before each experiment, the calibrations of aerodynamic and acoustic signals were performed.

A high-speed camera was placed 40cm above the glottis to directly capture images of vocal fold oscillation. After the airflow reached 20L/min and stable phonation was achieved, the spotlight was turned on to provide enough luminance, which was positioned 30cm above the glottis with an angle of 45 degrees from the vertical axis of the glottis. Videos of vocal fold oscillation were recorded by the high-speed camera and software (YVSION OSG030-815UMTZ, Yingshi Tech Co. Ltd, Shenzhen, China) with a resolution of 640X480 pixels at a rate of 3200 frames per second). The video contained at least three glottic periods of vocal fold vibration. The maximum abduction distance of the unilateral vocal fold away from the glottic midline was defined as the vibration amplitude in both groups.

### Data analysis

The minimum airflow needed for achieving stable phonation was recorded by the airflow meter and called phonation threshold flow (PTF). The minimum subglottal pressure needed to initiate phonation was termed phonation threshold pressure (PTP). Phonation threshold power (PTW) is the lowest aerodynamic power needed for voice phonation, equal to the product of PTF and PTP values [17,18]. Sample signals, including PTF, PTP, and PTW, that were collected by BL-420s were described previously by Weijian [17]. There is a 30-second interval between each process to reduce fatigue after vocal fold oscillation.

An airflow of 20L/min was chosen to produce acoustic signals in the control and RHSCS groups, in which stable phonation could be acquired during signal collection. The length of acoustic signals collected was more than 5 seconds. The stable 3-second portion of the acoustic waveform was analyzed using PRAAT 5.5.04 software for acoustic signal parameters assessment, including fundamental frequency(F0), percent jitter, percent shimmer, and HNR(harmonic to noise ratio). Each parameter was measured three times. The average value of them was used for the statistics.

Images of the vocal fold vibration amplitude were captured and analyzed by Photoshop (V13.2). The longitudinal length from endpoints at the anterior commissure to the posterior end of the glottis was measured manually using images of the glottal opening phase. The vibration amplitude of the following positions was selected and measured: the anterior quarter point, the middle point, the posterior quarter point, and the posterior eighth point, with 0 points set at the anterior commissure and 1 point at the posterior commissure [Figure 2]. In the control group, the vibration amplitude was half the distance between bilateral measured points. In the RHSCS group, the silicone's smooth cambered surface reached the glottic midline. Therefore, the vibration amplitude was the distance from the measured point to the silicone's surface. A metal fixation column beside the vocal fold was used as the length mark. Their relative length could be calculated by comparing pixels of the vibration amplitude to the mark width in images.

### Statistical analysis

A paired sample t-test was used to determine whether statistical significance existed between the acoustic, aerodynamic, and vibration videography parameters of the RHSCS group and those of the control group. Analysis was performed using SPSS 22.0(IBM Watson). A p-value smaller than 0.05 was considered as statistical significance.

## RESULTS

### Aerodynamics

The average value with standard deviation and statistical

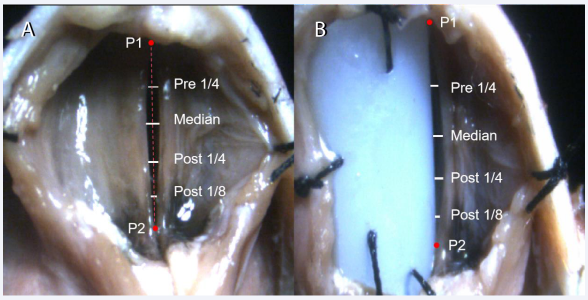

**Figure 2** Four points on the vocal fold were chosen: the anterior quarter point (pre 1/4), the middle point (median), the posterior quarter point (post 1/4), and the posterior eighth point (post 1/8). The distance between P1 and P2 was the longitudinal length. The red line signifies the glottic midline. The vibration amplitude was defined as the distance from the measured point to the glottic midline. In the control group, the vibration amplitude was half the distance between bilateral measured points (A). In the RHSCS group, the silicone's smooth cambered surface reached the glottic midline. Therefore, the distance from the measured point to the silicone's surface was the vibration amplitude

results for PTF, PTP, and PTW of the control and the RHSCS group is shown in Table 1. The RHSCS group showed a statistically significant increase in PTP and PTW compared with the control group (p<0.01). The mean PTP value of the control group was 11.55 cmH20 with a standard deviation (SD) of 3.27. The mean PTP value of the RHSCS group was 20.72 cmH20 (7.72 SD). The control group had a mean PTW value of 146.78 L*cmH20/min (78.04 SD). The RHSCS group had a mean PTW value of 287.17 L*cmH20/min (197.61 SD). No statistically significant difference was observed in PTF between the two groups. The mean PTF value of the control group was 12.32L/min (5.78 SD). The mean PTF value of the RHSCS group was 12.19L/min (6.18 SD).

### Acoustics

Statistical results of acoustic parameters, including percent jitter, percent shimmer, HNR, and F0, are shown in Table 2. The mean F0 was 279.63 Hz (114.44 SD) for the control group and 231.80 Hz (82.09 SD) for the RHSCS group. The mean percent jitter was 1.61% (1.41 SD) for the control group and 2.08% (1.36 SD) for the RHSCS group. The mean percent shimmer was 17.86% (3.66 SD) for the control group and 13.88% (4.59 SD) for the RHSCS group. The mean HNR was 7.20 dB (4.43 SD) for the control group and 5.53dB (2.37 SD) for the RHSCS group. There were no statistically significant differences in all acoustic parameters between the control and the RHSCS groups.

### Videography

Four different positions on the vocal fold were included in the statistics: the anterior quarter point (pre 1/4), the middle point (median), the posterior quarter point (post 1/4), and the posterior eighth point (post 1/8). The vibration amplitude was defined as the distance from the measured point to the glottic midline. The vibration amplitude values in the control group were listed below 0.522mm (pre 1/4), 0.679mm (median), 0.561mm (post 1/4), and 0.212mm (post 1/8). The vibration amplitude values in the RHSCS group were listed below 0.473mm (pre 1/4), 0.627mm (median), 0.481mm (post 1/4), and 0.218mm (post 1/8). The mean longitudinal length was 13.956mm (1.793 SD) for the control group and 13.552mm (2.107 SD) for the RHSCS group. Vibration amplitude values with standard deviation and statistic results are displayed in Table 3. For vibration amplitude, Statistical analysis showed no statistically significant differences in all positions and longitudinal length between the control and the RHSCS group [Table 3].

**Table 1**: Aerodynamic Parameters of the Control Group vs. RHSCS group

| | Control(M±SD) | RHSCS(M±SD) | T-value | P-value |
|---|---|---|---|---|
| PTF(L/min) | 12.32±5.78 | 12.19±6.18 | 0.110 | 0.914 |
| PTP(cmH20) | 11.55±3.27 | 20.72±7.72 | -4.334 | <0.001* |
| PTW(L*cmH20/min) | 146.78±78.04 | 287.17±197.61 | -3.298 | 0.007* |

**Table 2**: Acoustic Parameters of the Control Group vs. RHSCS Group

| | Control(M±SD) | RHSCS(M±SD) | T-value | P-value |
|---|---|---|---|---|
| F0(Hz) | 279.63±114.44 | 231.80±85.09 | 1.267 | 0.231 |
| Jitter(%) | 1.62±1.41 | 2.08±1.36 | -1.457 | 0.173 |
| Shimmer(%) | 17.86±3.66 | 13.88±4.59 | 2.168 | 0.053 |
| HNR(dB) | 7.20±4.43 | 5.53±2.37 | 1.967 | 0.075 |

**Table 3:** Vibration Amplitude of the Control Group vs. RHSCS Group

| | Control(M±SD) | RHSCS(M±SD) | T-value | P-value |
|---|---|---|---|---|
| Pre 1/4(mm) | 0.522±0.189 | 0.473±0.166 | 0.845 | 0.416 |
| Median(mm) | 0.679±0.256 | 0.627±0.211 | 0.65 | 0.529 |
| Post 1/4(mm) | 0.561±0.217 | 0.481±0.185 | 1.262 | 0.233 |
| Post 1/8(mm) | 0.212±0.066 | 0.218±0.167 | -0.113 | 0.912 |
| Longitudinal length(mm) | 13.956±1.793 | 13.552±2.107 | 1.333 | 0.209 |

## DISCUSSION

Deterioration in voice quality is the main complication of cordectomy in patients with early-stage glottic cancer [19]. It hurts patients' communication ability and working efficiency. Accordingly, voice reconstruction after cordectomy is crucial for patients' life quality improvement. However, current voice reconstruction strategies like MT and IL partially improved some aspects of voice outcomes [9]. Therefore, a voice reconstruction method that can restore a near-normal voice is needed up to now.

This study used the excised canine larynx model to restore voice in unilateral defective vocal folds. The rigid silicone with a smooth cambered surface reconstructs the defective left vocal fold that can oscillate with the regular right vocal fold. By silicone reconstruction, we built an asymmetric vocal oscillation model. In this study, the PTP and PTW of the RHSCS group significantly increased compared to the control group. Phonation threshold pressure (PTP) was defined, as the minimum pressure required initiating small amplitude vocal fold vibration. PTP can clinically assess abnormal voice function and vocal fold diseases. PTP is positively correlated with vocal fold viscosity damping, prephonatory glottal width, and mucosa wave velocity, while negatively correlated with vocal fold thickness [20]. In Jiang's study, there was no statistical difference between full larynges and hemi larynx counterparts. The range of PTP is 8.0-10cmH20 in Jiang's study [14]. Our study shows significantly higher PTP in RHSCS compared to normal vocal folds phonatory model. Increases in phonation threshold pressures affected the intensity range, especially by the loss of quiet phonation. PTW is the lowest aerodynamic power needed for voice phonation and is the product of PTF and PTP [18]. PTW reflects the threshold energy that vocal folds take in for phonation, which equals the energy lost in internal viscosity damping. It indicates the laryngeal efficiency in transferring energy in subglottal airflow into acoustic energy during phonation [18]. PTW also plays a role in the vocal intensity range in this study [16]. The increased PTP and PTW might be attributed to prephonatory glottal width and vibratory configuration changes.

F0 correlates with vocal fold length, tissue rigidity, and density [21]. Our study acquired the fundamental frequency from 20L/s airflow, which produced constant and stable phonation in each phonatory larynx. There was no significant difference in F0 between the RHSCS and control groups in our study. Commonly, the rigidity and density of the silicone were significantly higher than the normal vocal fold. The results of our study are cohere with Zhang's physical model. Zhang reported that the vocal fold vibration was dominated by the soft fold and had a phonation frequency determined by the properties of the soft fold alone on the conditions of significant left-right vocal stiffness mismatch [15]. In Jiang's study, the slope of fundamental frequency increase over subglottal pressure was no difference between hemi larynx and full larynx phonation. Our study did not measure the slope because the narrow airflow range elicited constant elongation phonatory.

The acoustic parameters, including jitter, shimmer, and HNR, in the RHSCS group showed no statistically significant differences compared with those in the control group when the voice was induced by stable and same airflow. The proper vocal vibration amplitude in the RHSCS group was not significantly different from the control group under the stable and same phonatory airflow. HNR is the ratio between the acoustic energy of the harmonic constituent and the noise constituent in a sustained vowel [22]. Inadequate vocal fold closure and excessive glottic air leakage lead to turbulent airflow that generates noise signals [22]. Jitter and shimmer are voice perturbation parameters that reflect the stability of vocal fold oscillation [23]. Irregular vocal fold vibration and property abnormality in vocal fold tissue give rise to higher values in jitter and shimmer [24]. This study, jitter, shimmer, and HNR showed no significant differences between the RHSCS and the control groups. The results indicated that the vocal fold oscillation of the RHSCS group had similar stability and irregular vibration to the control group in stable vocal airflow. It can be inferred that the voice produced by unilateral vocal fold paired with silicone oscillation had similar voice quality in hoarseness and roughness to regular symmetric vocal fold oscillation.

The high-speed camera provided a direct view of vocal fold vibration characteristics. Vocal fold pathology that alters vibration characteristics affects acoustic parameters like F0, jitter, shimmer, and HNR [25]. In this study, the following 4 points on the vocal fold were chosen and measured for vibration amplitude: the anterior quarter point, the middle point, the posterior quarter point, and the posterior eighth point. Compared to the control group, the vibration amplitude of each RHSCS group point showed no significant differences. The results suggested that the unilateral vocal fold of silicone reconstruction did not affect the vibration characteristics of the contralateral vocal fold. The similar vibration configuration of both groups supported that the acoustics parameters of the RHSCS group had no significant differences from the control group. From the high-speed camera, the vocal fold in the control group was not wholly closed but slightly abducted. The prephonatory glottal width was not 0 before the oscillation began. In the RHSCS group, due to the left vocal cord being substituted by rigid silicone, the silicone's smooth cambered surface reached the glottic midline, and the left part of the prephonatory glottal width disappeared. Therefore, the prephonatory glottal width of the RHSCS group is smaller than the control group. It seems to conflict with the above relationship because a smaller prephonatory glottal width should bring a smaller PTP. However, this can be explained by Title's study [26], in which they found that PTP increases with the prephonatory glottal width only if the prephonatory glottal width was larger than a specific value that they called the optimal glottal width. However, when the glottal width is smaller than this optimal value, PTP increases as the prephonatory glottal width decreases. The result of the RHSCS group suggested that the prephonatory glottal width is smaller than the optimal value, which brings a higher PTP.

### Suggestion for surgery

Reconstruction of the rigid vertical wall or normal enough vocal fold to cooperate with the opposite normal vocal fold is difficult. Reconstruction of high stiffness curve surface vocal fold to match the opposite normal vocal fold using implantation could be performed. It may produce a closely normal voice in a narrow intensity range.

## CONCLUSION

This study reconstructed the damaged unilateral vocal fold with smooth, rigid silicone in the excised canine larynx model. The asymmetrical vibration from reconstruction with silicone and paired normal vocal fold produced a voice whose parameters (F0, jitter, shimmer, HNR) were similar to symmetric bilateral regular vocal fold oscillation on the same phonatory subglottic airway. An exception was the significant increase of PTP and PTW in reconstructed glottis. According to the high-speed camera images, the vibratory amplitude of the normal side vocal fold in the reconstructed glottis was equal to either side of the vocal folds in the normal glottis. Our study reveals that high stiffness, smooth, and curved surface reconstruction of damaged vocal fold can produce near-normal voice within a range of intensity.

### Declaration of Conflicting Interests

All authors of this research declare that there are no conflicts of interest and contribution associated with this publication and no competing financial interests exist. The protection of the privacy of research participants has been ensured. The adequate level of confidentiality of the research data has been ensured.

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**Ethical Approval:** The study was approved by the Ethics Committee of Guangdong Provincial People's Hospital (S2023-077-01).

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