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Injection laryngoplasty using hyaluronic acid for Chinese patients with unilateral vocal fold paralysis - an acoustic, durational and perceptual study

Au Yat Chun, Andrew

A dissertation submitted in partial fulfillment of the requirements for the Bachelor of Science (Speech and Hearing Sciences), The University of Hong Kong, June 30, 2013.
Abstract

The study evaluated the surgical efficacy of injection laryngoplasty (IL) with respect to perceptual voice-related quality of life (QOL), acoustic and aerodynamic measurements in patients with unilateral vocal fold paralysis (UVFP). In a longitudinal and prospective clinical cohort study, 14 patients with UVFP who received injection laryngoplasty with hyaluronic acid (Restylane) were examined preoperatively, 1 week, 1 month, and 3 months postoperatively. The patients’ voice was evaluated by self-perception questionnaire (Voice Handicap Index, VHI) and objectively acoustical as well as durational measurements. Patients’ performance in Cantonese lexical tone production was also evaluated in terms of percent correct identification. Results of VHI showed significant improvement in vocal quality immediately after injection. IL yielded a significant decrease in percent jitter and shimmer in dB, and a significant increase in signal-to-noise ratio (SNR). Whereas discernible increment in the duration of maximum phonation time (MPT) was elicited, the procedure significantly improved UVFP patients’ ability to produce HL, HR and LR tones. The improvement observed in all vocal and QOL parameters was maintained for at least 3 months after injection. Results of this paper showed that the treatment effect of IL was immediate and sustainable. The study provides objective evidence for the application of IL on Cantonese-speaking patients with UVFP.

Key words: Injection laryngoplasty, Hyaluronic acid, Unilateral vocal fold paralysis, Voice handicap index, Jitter, Shimmer, Signal-to-noise ratio, Maximum phonation time, Cantonese lexical tone production
Unilateral vocal fold paralysis (UVFP), referring to a paralyzed vocal fold with impaired tension, mobility and/or bulk, is associated with an assorted variety of etiologies, including surgical trauma, compromise of recurrent laryngeal nerve (RLN) and superior laryngeal nerve (SLN) branches (Havas, Lowinger, & Priestley, 1999). Glottic insufficiency predominantly stems from UVFP (Crary & Glosask, 2000). Because of glottic incompetence, UVFP patients often report signs and symptoms of dysphonia and dysphagia, entailing persistent hoarseness, vocal fatigue and occasional liquid aspiration (Yumoto et al., 2002). The greater degree is the glottis incompetence, the more severe are the signs and symptoms of dysphonia and dysphagia (Kelchner et al., 1999). Functional use of voice for expressive communication and swallowing ability are hindered by glottic insufficiency. Many studies have reported the adverse effects on UVFP patients’ quality of life (QOL) due to persistent dysphonia (Benninger et al., 1998; Baba et al., 1999). UVFP patients’ QOL is significantly hampered by the presence of glottis incompetence (Kelchner et al., 1999). Since UVFP patients’ QOL is significantly implicated by glottic insufficiency, treatments for UVFP by otolaryngologists and voice therapists are deemed necessary (Havas, Lowinger, & Priestley, 1999).

Behavioral voice therapy techniques, such as Lessac Madsen Resonant Voice Therapy (LMRVT), have shown some improvement for UVFP, especially for those with mild signs and symptoms of dysphonia and dysphagia. Yet, it is widely regarded as an adjunct to surgical intervention. Phonosurgery has been documented as the major intervention to glottic incompetence due to UVFP (Yumoto et al., 2002). Percutaneous injection laryngoplasty and transcutaneous laryngeal framework surgery, which includes medialization thyroplasty and arytenoid adduction, are considered as the primary phonosurgical procedures to UVFP (Hoff & Hogikyan, 1996). Ng, Wong, Wei, Wong, and Lam (2008) reported that injection laryngoplasty is adopted by an increasing number of otolaryngologists as surgical treatment
for UVFP patients in Hong Kong. The procedure involves injection of an implant material to the medial edge of the paralyzed vocal fold (Brüning, 1911). It attempts to enhance the medial compression of the paralyzed vocal fold with the non-paralyzed one, and glottal closure during phonation. With advantages such as procedural simplicity, low post-surgical risks, operation costs, treatment efficacy, reversibility and outcome predictability, injection laryngoplasty is preferred over laryngeal framework surgery as a feasible surgical intervention option to UVFP (Carroll & Rosen, 2010).

Both injection laryngoplasty and medialization thyroplasty increase the vocal fold volume through injection or insertion of implant materials into a paralyzed vocal fold in an attempt to medialize the paralyzed fold. Yet, injection procedure appears to be less invasive and sophisticated with reduced technical demands and operation time. Furthermore, the procedure can be carried out under local anesthesia as an outpatient procedure (Rosen, 1998). UVFP patients can resume normal diets immediately after surgery.

The risks associated with injection laryngoplasty are much lower than that with medialization thyroplasty and arytenoids adduction. Permanent fibrosis in the paraglottic space, submucosal hemorrhage, implant extrusion and changes to cricoarytenoid joint are documented as possible ramifications of insertion of implant materials into vocal fold in medialization thyroplasty (Hoffman et al., 2010). Medialization thyroplasty using silicon may even result in suboptimal shaping of silicone implant, hindering performance in voicing, breathing and swallowing (Hoffman et al., 2010). The predicted outcome of medialization thyroplasty are complicated by their respective post-operation drawbacks.

Comparable to medialization thyroplasty, injection laryngoplasty has been proven to be effective in reducing glottal gap significantly. Hoffman et al. (2010) also evidenced the injection laryngoplasty was as effective as medialization thyroplasty in improving speech acoustically and aerodynamically. The findings by Hoffman et al. (2010) are consistent with
that reported by Morgan, Zraick, Griffin, Bowen, and Johnson (2007). Carroll and Rosen (2010) also reported that injection laryngoplasty was effective in improving UVFP patient's quality of life as indicated by reduced VHI scores.

That said, the controversies regarding injection procedure centers on the choice of implant materials. Teflon, autologous fat and collagen were previously used as implant materials for injection laryngoplasty (Lau et al., 2010). These implant materials were reported to be associated with limitations in bio-compatibility, durability, and bio-mechanical compatibility to vocal fold. Hyaluronic acid as an implant material has addressed the drawbacks of aforementioned implant materials for injection. It is concluded as a safe, sustainable and useful implant material for vocal fold augmentation. Unlike Teflon which has been documented to induce granuloma formation in vocal fold after injection, hyaluronic acid has been shown to be bio-compatible to augmentation without eliciting any adverse and acute immune response or allergic reaction (Dahlqvist et al., 2004; Lee, Son, Kim, Lee, Kim, & Koh, 2007).

According to Ford, Bless, and Loftus (1992), gradual absorption of implant materials by surrounding tissues has been documented to pose UVFP patients at an increased likelihood/risk of repeat injections. Collagen and fat were reported with high reabsorption rate into surrounding tissues, lasting for only three to six months only. In stark contrast to other implant materials, hyaluronic acid is resistant to absorption to surrounding tissues. Lee et al. (2007) proved the durability of hyaluronic acid as implant material since only 30% of hyaluronic acid was gradually reabsorbed over 9 months. Dahlqvist et al. (2004) also reported similar findings regarding the durability of hyaluronic acid and its ability to stimulate formation of new connective tissues in vocal fold. The maintenance effect of hyaluronic acid in vocal outcomes was also found to be comparatively better than other implant materials (Hertegård et al., 2002; Lim, Kim, Kim, Kim, & Choi, 2008).
The bio-mechanical incompatibility of implant materials such as Teflon and autologous fat has been reported by Gardner and Parnes (1991). They might alter vocal fold mucosal wave by decreasing mucosal wave amplitude as vocal fold stiffness is increased. An implant material with viscoelastic properties similar to that of vocal fold does not induce any alterations to the vocal fold’s biomechanical properties and is considered as a viable implant material for injection (Dahlqvist et al., 2004). Although the amplitude of mucosal wave slightly was decreased after injection, hyaluronic acid was reported to have viscoelastic properties most similar to that of normal vocal folds (Dahlqvist et al., 2004). From the perspective of vibratory biomechanics, injection laryngoplasty using hyaluronic acid can yield a vibratory behavior of a healthy vocal fold, with minimum vocal fold mucosal defects and lamina propria deficiencies which should constitute a good voice quality (Gärskog et al., 2004; Lau et al., 2010).

Despite most studies attesting to improvement of vocal characteristics after injection laryngoplasty, relatively few examined the efficacy of injection using hyaluronic acid and almost all of them were predominantly based on English-speaking patients. It remains unknown whether Chinese patients with UVFP will benefit equally in voice restoration from injection laryngoplasty using hyaluronic acid as the English-speaking counterparts. Therefore, this study aimed to investigate the efficacy of injection laryngoplasty using hyaluronic acid to Cantonese-speaking patients. The study attempted to reveal if there is any improvement in quality of life (QOL) in Cantonese-speaking patients with UVFP after injection procedure. Changes in voice quality were monitored by examining patients’ pre-operative and post-operative voice by means of objective acoustic and durational measurements. Since perceptual voice quality including breathiness and roughness was only investigated by in previous studies based on Cantonese-speaking patients, objective analysis of voice quality such as measuring maximum phonation time, jitter, shimmer and signal-to-
noise ratio was included in the study.

Unlike English which is a stress-timed language in which pitch serves for the purpose of intonation only, Cantonese is a tonal language and speech intelligibility is mainly predicated on a speaker’s ability to produce lexical tone contrasts effectively. Lexical tone contrast is an indispensable feature to distinguish Cantonese words which are segmentally identical and to differentiate word meanings. In Cantonese, there are six contrastive tones, namely high-level (HL), mid-level (ML), low-level (LL), low-falling (LF), high-rising (HR), and low-rising (LR) tone. Variations in voice pitch constitute contrasts in lexical tone and are essential at syllable and word level to convey different lexical meanings. In other words, the effectiveness of patients’ verbal communication depends largely on pitch variations. Therefore, the ability of Cantonese-speaking patients with UVFP to produce lexical tones contrasts to an extent for listener to perceive correctly is integral for effective communication in daily lives.

Pitch level and pitch contours are the most salient, primary and integral cues for tone identification (Gandour, 1981). Production of varying pitch level and contour hinges on a speaker’s ability to alter pitch, which is predicated on the control of vocal fold tension (Tucker, 1997). UVFP patients were reported to have limited improvement in pitch control due to the limitation of injection procedure in restoration of normal control of vocal fold tension (Rusnov & Tucker, 1981; Tucker, 1999). In view of the limited improvement in pitch control reported by Tucker (1997), it remains unknown whether injection using hyaluronic acid can help improve lexical tone production, which constitutes the effectiveness of daily communication. Therefore, the current study was undertaken as a pilot investigation to examine whether injection laryngoplasty leads to an improvement in the production of lexical tone contrasts in Cantonese, which is conducive to more effective communication.
Methods

Participants

Subjects. Fourteen adult patients (9 males and 5 females) with ages between 40 to 80 years were recruited to participate in the study. All of them were diagnosed with glottic insufficiency due to idiopathic/iatrogenic UVFP by otorhinolaryngologists. Patients with UVFP caused by laryngeal cancer were excluded from this study. Neither of them has received any phonosurgery before, nor any improvement in voice after completion of a course of speech therapy. They were referred by otorhinolaryngologists from the Queen Mary Hospital or Tung Wah Group Hospital to participate in this study in order to restore voice production from injection laryngoplasty using hyaluronic acid (Restylane).

Listeners. Forty native Cantonese speakers (20 males and 20 females) who have reported hearing ability within normal limits were recruited as listeners to participate in the Cantonese tone perceptual experiment of the study.

Injection Laryngoplasty Procedure

All patients were voluntary and were informed of the details of the study, including the purpose and procedures involved. All of them were arranged for injection laryngoplasty that was carried out in the Ear, Nose, and Throat Clinic of the Tung Wah Group Hospital, which was carried out under local anesthesia with hyaluronic acid (Restylane) by an experienced otorhinolaryngologist. A second experienced otorhinolaryngologist was also present who was responsible for monitoring the whole procedure with laryngeal endoscopy.

On the day of injection, the patient was instructed to fast for six hours prior to the procedure. To begin the procedure, local anesthesia was administered to nearby skin tissue. Hyaluronic acid (Restylane) of approximately 1 mL was slowly injected percutaneously by the otorhinolaryngologist to medialize the paralyzed fold, and to close the interglottal gap. The entire process was simultaneously monitored through a flexible laryngoscope held by
another otorhinolaryngologist who was also experienced in the procedure. The patient was discharged from the clinic approximately one hour after the procedure and feeding was resumed.

Recording Procedure

In the study, QOL, perceptual and acoustical measurements were obtained four times: once before the injection was carried out, then one week, one month and three months after injection procedure was administered. To avoid recording of extraneous noise, all recordings took place in a sound booth in the Department of Ear, Nose, and Throat of the Tung Wah Group Hospital. The speech samples were recorded via a high quality microphone (Shure, SM58) with a constant mouth-to-microphone distance of approximately 10 cm. Brief instructions of the recording procedure were provided before the recording took place. All participants were allowed to familiarize themselves with the speech stimuli and the recording environment by practicing the speech materials several times prior to the actual recording.

During the recording session, the subjects were instructed to produce the citation words embedded in the carrier phrase three times at a normal speaking rate and comfortable loudness level. The speakers were provided with a sheet of paper on which Chinese characters representing each citation word were printed.

Speech Tasks

In order to assess the voice quality, the participants were instructed to sustain the vowels /i/, /a/, and /u/. The recorded acoustic signals were used for later acoustic analysis. To examine production of Cantonese lexical tones, the participants were also asked to read aloud 48 tokens of printed Cantonese words. All printed stimuli corresponded to the six tones associated with two sets of isolated Cantonese monosyllables (/ji/ and /si/), yielding a total of 12 words (6 tones x 2 syllables). Each Cantonese monosyllable was minimally distinguished by tones and thus entailed different meanings. All patients were instructed to
read aloud all stimuli with each word embedded in a neutral carrier phrase “This one read _____” in order to eliminate possible contextual effect. In the Cantonese version of the carrier phrase, each citation word was preceded by a voiceless unreleased stop consonant (/k/). Each target monosyllable, preceded by a voiceless unreleased stop consonant, can be identified more clearly for later acoustic analysis and tone identification.

**Listening tasks**

The listening tasks took place in the Speech Science Laboratory of the University of Hong Kong. The presented stimuli were citation words produced by UVFP patients. Each stimulus corresponding to a Cantonese lexical tone was presented in isolation to all listeners. All listeners were instructed to mark down the citation word they heard in a blank space provided on the answer sheet. To ensure sufficient response time, an inter-stimulus pause of 5 seconds was included. A brief practice session was provided to the listeners prior to the actual experiment so as to familiarize them with the experimental setup and procedure.

**Measurements**

The present project is a multi-dimensional efficacy study of injection laryngoplasty using hyaluronic acid on Chinese UVFP patients. Self-perceived QOL, acoustic, perceptual and durational characteristics associated with the speech samples obtained during their hospital visits before, one week, one month, and three months after injection laryngoplasty.

**Voice Handicap Index (VHI).** The Cantonese version of voice handicap index (VHI-30) questionnaire was administered in order to examine any improvement in patient’s QOL after surgery. VHI-30 has been widely used as a self-administered, standardized questionnaire which assesses how participants perceive the degree of handicap in reference to their own voice (Jacobson et al., 1997). The questionnaire comprises 30 questions, with three subscales targeting the functional (VHI-F), physical (VHI-P) and emotional (VHI-E) aspects of patient’s voice problem (Jacobson et al., 1997). UVFP patients responded to the frequency
of occurrence of each experienced situation by rating from 0 to 4 on a Likert scale (Rosen & Murray, 2000). The higher are the VHI scores, the greater is the voice handicap perceived by patients.

VHI questionnaire is identified to be a psychometrically robust instrument to evaluate Quality of Life (QOL) (Lam, Chan, Ho, Kwong, Yiu, & Wei, 2006). The Cantonese version of VHI have been translated from the English version and documented to be useful to evaluate voice- related QOL of Cantonese- speaking population (Lam, Chan, Ho, Kwong, Yiu, & Wei, 2006). The VHI questionnaire has also been validated to strictly correlate with the vocal outcomes of UVFP treatments (Lau et al., 2010; Rosen et al., 2000).

**Acoustic characteristics.** In order to examine the changes in patient’s voice quality after the surgery, objective acoustic parameters including jitter (RAP, %), shimmer (in dB), and signal-to-noise ratio (SNR) were obtained from the sustained vowels. Jitter and shimmer refer to perturbation in fundamental frequency and amplitude of a sound wave respectively. Signal-to-noise ratio indicates the strength of the correlated component of a speech signal relative to the uncorrelated unpredictable noise component.

**Durational characteristics.** In order to investigate the glottic efficiency, maximum phonation time (MPT) was obtained from the sustained vowels. MPT (in seconds) refers to the maximum duration a person can sustain a vowel after maximum inspiration at a comfortable pitch and loudness level.

**Data and Statistical Analyses**

To assess changes in QOL, acoustic and durational characteristics of patients’ voice, repeated-measures analyses of variance (rmANOVAs) followed by necessary post-hoc multiple comparisons were carried out for each parameters. In order to determine the accuracy in identification of Cantonese tones, confusion matrices in terms of percent correct identification were constructed. A two-way ANOVA followed by necessary simple main
effect analyses were also carried out in order to examine any significant improvement in lexical tone production by UVFP patients.

Results

Self-reported quality of life - VHI

Average and standard deviation values of various aspects of VHI are shown in Table 1. From Table 1, a decreasing trend in average total and subscale VHI scores was observed before and after injection surgery.

The test of normality, examining standardized skewness and the Shapiro-Wilk test indicated the data were statistically normal. As the data of total VHI scores, $X^2(5) = 15.482$, $p = .009$, violated the assumption of sphericity, a Greenhouse-Geisser correction was used.

Results of repeated-measures ANOVA showed that total VHI scores (VHI-Total) were significantly different between time of measurement, $F(2.019, 26.250) = 13.428$, $p < .001$.

Post-hoc tests using Bonferroni correction revealed that total VHI scores at all post-treatment stages (for 1 week after treatment, $p = .011$; for 1 month after treatment, $p < .001$; for 3 months after treatment, $p = .003$) were significantly reduced from that in pre-treatment whereas no significant difference in total VHI scores was found between any two post-treatment stages.

Table 1

<table>
<thead>
<tr>
<th>Analysis of VHI scores before and after surgery</th>
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<tbody>
<tr>
<td>Time of measurement</td>
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<tr>
<td>---------------------</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Before Treatment</td>
</tr>
<tr>
<td>1 week after treatment</td>
</tr>
<tr>
<td>1 month after treatment</td>
</tr>
<tr>
<td>3 months after treatment</td>
</tr>
</tbody>
</table>
The test of normality, examining standardized skewness and the Shapiro-Wilks test indicated the data were statistically normal. As the data of emotional aspect of VHI, \( X^2(5) = 13.274, p = .021 \), violated the assumption of sphericity, a Greenhouse-Geisser correction was used. In addition, rmANOVAs also showed that the functional, \( F(3, 39) = 10.880, p < .001 \), physical, \( F(3, 39) = 7.360, p = .001 \), and emotional, \( F(2.178, 28.314) = 8.536, p = .001 \), aspect of VHI were significantly different between time of measurement. Post-hoc tests using Bonferroni correction revealed that functional (for 1 week after treatment, \( p = .036 \); for 1 month after treatment, \( p < .001 \); for 3 months after treatment, \( p = .004 \)) and emotional (for 1 week after treatment, \( p = .004 \); for 1 month after treatment, \( p = .002 \); for 3 months after treatment, \( p = .003 \)) aspect of VHI scores in all post-treatment were significantly reduced from that in pre-treatment whereas no significant difference in scores was found between each post-treatment stage. However, for physical aspect of VHI scores, only scores at the stage of 1 month after treatment were significantly lower than that in pre-treatment (\( p = .002 \)).

**Acoustic characteristics**

In order to describe acoustic characteristics of pre-operative and post-operative voices, mean jitter, shimmer and signal-to-noise ratio (SNR) were obtained from the production of vowels /a/, /i/, and /u/. Average and standard deviation values of jitter, shimmer and SNR are shown in the Table 2.

The test of normality, examining standardized skewness and the Shapiro-Wilks test indicated the data were statistically normal. As the data of jitter, \( X^2(5) = 48.850, p < .001 \) and shimmer, \( X^2(5) = 20.653, p = .001 \), violated the assumption of sphericity, a Greenhouse-Geisser correction was used. Results of rmANOVAs indicated that jitter, \( F(1.271, 16.521) = 8.167, p = .008 \), shimmer, \( F(1.535, 19.949) = 21.617, p < .001 \), and SNR, \( F(3, 39) = 9.250, p < .001 \), differed significantly between time of measurement. Post-hoc pairwise
comparisons revealed a significantly lower jitter (for 1 week after treatment, \( p = .039 \); for 1 month after treatment, \( p = .033 \)) and shimmer (for 1 week after treatment, \( p < .001 \); for 1 month after treatment, \( p < .001 \)), but greater SNR (for 1 week after treatment, \( p < .001 \); for 1 month after treatment, \( p = .020 \)) one week and one month after than before the injection procedure. At three month after treatment, only shimmer (\( p = .011 \)) and SNR (\( p = .040 \)) were significantly lower and greater than their counterparts in pretreatment respectively. No significant difference in jitter, shimmer and SNR was found between any other two post-treatment stages.

**Durational characteristics**

To describe the change in air usage before and after the procedure, average maximum phonation time (MPT) was obtained from the production of vowels /a/, /i/, and /u/. Average and standard deviation values of MPT are shown in the Table 2. From Table 2, an increasing trend in average MPT was observed before and after injection surgery.

**Table 2**

<table>
<thead>
<tr>
<th>Time of measurement</th>
<th>Jitter, %</th>
<th>Shimmer, dB</th>
<th>SNR</th>
<th>MPT, s</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Before treatment</td>
<td>1.4</td>
<td>1.4</td>
<td>1.3</td>
<td>0.6</td>
</tr>
<tr>
<td>1 week after treatment</td>
<td>0.2</td>
<td>0.2</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>1 month after treatment</td>
<td>0.2</td>
<td>0.1</td>
<td>0.3</td>
<td>0.2</td>
</tr>
<tr>
<td>3 months after treatment</td>
<td>0.4</td>
<td>0.5</td>
<td>0.5</td>
<td>0.4</td>
</tr>
</tbody>
</table>

The test of normality, examining standardized skewness and the Shapiro-Wilks test indicated the data were statistically normal. The assumption of sphericity was not violated. Results of rmANOVA revealed MPT differed significantly between time of measurement, \( F(3, 39) = 4.172, p = .012 \). Post-hoc multiple comparisons using Bonferroni correction reveal that injection procedure elicited a marked increase in MPT from pre-treatment to the stage of
1 week after treatment, which was not statistically significant ($p = .070$). No significant difference in MPT was found between each post-treatment stage.

**Subjective perceptual judgment of Cantonese tones contrast**

**Percent correct identification of lexical tones in isolation.** Confusion matrices were constructed for before, one week, one month and three months after the surgery. Data are summed over 19 listeners to obtain 4 matrices (see Tables 3 to 6). No treatment stage was associated with 100% correct identification for Cantonese lexical tones.

The test of normality, examining standardized skewness and the Kolmogorov-Smirnov test indicated the data were statistically normal. The test for homogeneity of variance was not significant, $Levene F (23, 432) = 1.062, p = .385$, indicating that his assumption underlying the application of the two-way ANOVA was met. Results of the two-way ANOVA revealed that there was a significant interaction between time of measurement and tone on the percent correct identification, $F (15, 432) = 5.959, p < .001$. There were significant main effect on percent correct identification for both time of measurement, $F (3, 432) = 21.807, p < .001$, and Cantonese lexical tones, $F (5, 432) = 69.099, p < .001$. Post-hoc multiple comparisons using Bonferroni correction showed that the percent correct identifications at pre-treatment differed significantly from that at any post-treatment stage (for 1 week after treatment, $p < .001$; for 1 month after treatment, $p = .007$; for 3 months after treatment, $p < .001$) while percent correct identifications for HL and HR tones were significantly better than other lexical tones ($p < .001$).

Relationship of time of measurement and lexical tones on the percent correct identification are shown in Figure 1. Simple main effect analyses showed that there was a significant difference among time of measurement for HR, $F (3, 75) = 26.359, p < .001$, HL, $F (3, 75) = 16.253, p < .001$ and LR tones, $F (3, 75) = 6.201, p = .001$. Follow-up pairwise comparisons showed that percent correct identification for HR tones at all post-treatment
stages was significantly greater than that in pre-treatment ($p < .001$), whereas percent correct identification for HL and LR tones at 1 week and 3 months after treatment was significantly greater than that in pre-treatment ($p < .001$). Furthermore, a slight decrease in percent correct identification for HR, HL and LR tones at the stage of 1 month after treatment was also observed. Percent correct identification for LF, ML and LL tones fluctuated but without significant differences throughout pre- and post-treatment stages.

Despite the fluctuations in performance, a general increasing trend in percent correct identification of lexical tones was observed, especially for HR, HL and LR tones. Simple main effect analysis also showed that there was a significant difference among time of measurement for 1 week, $F(5, 113) = 31.289, p < .001$, 1 month, $F(5, 113) = 13.947, p < .001$ and 3 months after treatment, $F(5, 113) = 28.055, p < .001$. The percent correct identification for all lexical tones did not differ significantly, except that ML tones markedly lower than other lexical tones. Follow-up pairwise comparisons showed that at any post-treatment stages, HR, HL and LR tones were identified significantly and consistently better than other lexical tones, with an accuracy of over 50%.

Table 3

<table>
<thead>
<tr>
<th>Listeners' Responses</th>
<th>Stimuli</th>
<th>HL</th>
<th>HR</th>
<th>ML</th>
<th>LF</th>
<th>LR</th>
<th>LL</th>
</tr>
</thead>
<tbody>
<tr>
<td>HL</td>
<td>42.5</td>
<td>1.2</td>
<td>18.0</td>
<td>19.3</td>
<td>4.2</td>
<td>14.8</td>
<td></td>
</tr>
<tr>
<td>HR</td>
<td>2.2</td>
<td>40.6</td>
<td>5.6</td>
<td>17.5</td>
<td>22.7</td>
<td>11.2</td>
<td></td>
</tr>
<tr>
<td>ML</td>
<td>17.4</td>
<td>2.7</td>
<td>23.9</td>
<td>18.2</td>
<td>14.6</td>
<td>23.1</td>
<td></td>
</tr>
<tr>
<td>LF</td>
<td>5.8</td>
<td>0.6</td>
<td>12.2</td>
<td>50.9</td>
<td>3.0</td>
<td>27.4</td>
<td></td>
</tr>
<tr>
<td>LR</td>
<td>5.5</td>
<td>14.6</td>
<td>10.4</td>
<td>16.1</td>
<td>41.0</td>
<td>12.3</td>
<td></td>
</tr>
<tr>
<td>LL</td>
<td>8.0</td>
<td>2.7</td>
<td>18.5</td>
<td>31.6</td>
<td>5.6</td>
<td>33.5</td>
<td></td>
</tr>
</tbody>
</table>

*Note.* Percent correct identification for each lexical tone is in boldface.
### Table 4

Mean confusion matrix of percent identification for tones 1 week after surgery

<table>
<thead>
<tr>
<th>Stimuli</th>
<th>HL</th>
<th>HR</th>
<th>ML</th>
<th>LF</th>
<th>LR</th>
<th>LL</th>
</tr>
</thead>
<tbody>
<tr>
<td>HL</td>
<td><strong>65.0</strong></td>
<td>1.3</td>
<td>23.2</td>
<td>1.47</td>
<td>3.6</td>
<td>5.4</td>
</tr>
<tr>
<td>HR</td>
<td>0.5</td>
<td><strong>70.5</strong></td>
<td>1.0</td>
<td>0.4</td>
<td>27.1</td>
<td>0.5</td>
</tr>
<tr>
<td>ML</td>
<td>13.8</td>
<td>11.5</td>
<td><strong>22.1</strong></td>
<td>5.0</td>
<td>27.0</td>
<td>20.7</td>
</tr>
<tr>
<td>LF</td>
<td>11.8</td>
<td>1.16</td>
<td>13.3</td>
<td><strong>44.8</strong></td>
<td>5.6</td>
<td>23.4</td>
</tr>
<tr>
<td>LR</td>
<td>5.2</td>
<td>29.1</td>
<td>5.7</td>
<td>0.6</td>
<td><strong>54.3</strong></td>
<td>5.1</td>
</tr>
<tr>
<td>LL</td>
<td>7.3</td>
<td>4.8</td>
<td>23.9</td>
<td>16.7</td>
<td>5.5</td>
<td><strong>41.9</strong></td>
</tr>
</tbody>
</table>

Note. Percent correct identification for each lexical tone is in boldface.

### Table 5

Mean confusion matrix of percent identification for tones 1 month after surgery

<table>
<thead>
<tr>
<th>Stimuli</th>
<th>HL</th>
<th>HR</th>
<th>ML</th>
<th>LF</th>
<th>LR</th>
<th>LL</th>
</tr>
</thead>
<tbody>
<tr>
<td>HL</td>
<td><strong>48.4</strong></td>
<td>0.6</td>
<td>26.5</td>
<td>3.4</td>
<td>6.4</td>
<td>14.8</td>
</tr>
<tr>
<td>HR</td>
<td>2.0</td>
<td><strong>55.4</strong></td>
<td>4.5</td>
<td>0.6</td>
<td>34.3</td>
<td>3.2</td>
</tr>
<tr>
<td>ML</td>
<td>24.7</td>
<td>1.9</td>
<td><strong>26.8</strong></td>
<td>5.9</td>
<td>16</td>
<td>24.7</td>
</tr>
<tr>
<td>LF</td>
<td>4.6</td>
<td>3.0</td>
<td>11.6</td>
<td><strong>48.7</strong></td>
<td>8.3</td>
<td>23.8</td>
</tr>
<tr>
<td>LR</td>
<td>7.3</td>
<td>21.9</td>
<td>9.9</td>
<td>3.8</td>
<td><strong>48.7</strong></td>
<td>8.4</td>
</tr>
<tr>
<td>LL</td>
<td>8.7</td>
<td>3.0</td>
<td>20.2</td>
<td>28.3</td>
<td>2.3</td>
<td><strong>37.6</strong></td>
</tr>
</tbody>
</table>

Note. Percent correct identification for each lexical tone is in boldface.

### Table 6

Mean confusion matrix of percent identification for tones 3 months after surgery

<table>
<thead>
<tr>
<th>Stimuli</th>
<th>HL</th>
<th>HR</th>
<th>ML</th>
<th>LF</th>
<th>LR</th>
<th>LL</th>
</tr>
</thead>
<tbody>
<tr>
<td>HL</td>
<td><strong>71.2</strong></td>
<td>2.2</td>
<td>15.1</td>
<td>2.0</td>
<td>5.4</td>
<td>4.1</td>
</tr>
<tr>
<td>HR</td>
<td>1.9</td>
<td><strong>67.9</strong></td>
<td>1.1</td>
<td>0.3</td>
<td>27.7</td>
<td>1.1</td>
</tr>
<tr>
<td>ML</td>
<td>27.1</td>
<td>1.1</td>
<td><strong>31.2</strong></td>
<td>2.7</td>
<td>18.5</td>
<td>19.5</td>
</tr>
<tr>
<td>LF</td>
<td>4.4</td>
<td>1.3</td>
<td>12.3</td>
<td><strong>41.6</strong></td>
<td>4.1</td>
<td>36.2</td>
</tr>
<tr>
<td>LR</td>
<td>5.9</td>
<td>23.2</td>
<td>7.9</td>
<td>0.4</td>
<td><strong>58.9</strong></td>
<td>3.7</td>
</tr>
<tr>
<td>LL</td>
<td>13.0</td>
<td>0.6</td>
<td>26.5</td>
<td>17.9</td>
<td>3.7</td>
<td><strong>38.0</strong></td>
</tr>
</tbody>
</table>

Note. Percent correct identification for each lexical tone is in boldface.
Figure 1. Percent correct identification of six Cantonese tones produced by UVFP patients before, 1 week after, 1 month after, and 3 months after injection laryngoplasty procedure.

Discussion

Injection laryngoplasty using hyaluronic acid is increasingly carried out as an intervention to glottic incompetence due to UVFP. The procedure attempts to restore the functional rather than anatomical integrity of vocal fold. The present study examined the overall efficacy of injection procedure to Cantonese-speaking patients with iatrogenic UVFP. Different outcome measures, including self-perceived QOL, acoustics and durational parameters and identification of lexical tones were investigated.

Self-reported quality of life - VHI

The VHI-30 questionnaire was designed to reveal changes in voice-related QOL with reference to the physical, functional, and emotional aspects of patients’ daily life. According to the present study, UVFP patients reported a significant and immediate improvement in voice and associated QOL after injection. The results are in line with the findings reported by Rosen et al. (1999), who concluded a significant change in VHI scores following
treatment for UVFP patients. UVFP patients perceived themselves with reduced handicap due to dysphonia immediately one week after injection procedure. Immediate treatment effects were reported and recognized by UVFP patients.

Furthermore, the treatment effect of injection laryngoplasty using hyaluronic acid was reported to be maintained and sustained consistently after three months, as evidenced by the consistently improving post-treatment total VHI scores. The sustained improvement in voice-associated QOL for at least three months after surgery is consistent with the findings of Lau et al. (2010), who reported progressive improvement in VHI six months after injection procedure. The present VHI data are also concurrent with what Borzacchiello, Mayol, Gärskog, Dahlqvist, and Ambrosio (2005), which suggested that injection using hyaluronic acid appears to be sustainable and improvement in vocal fold adduction should last for at least six months.

The lower are the subscale VHI scores, the more improvement is seen in different aspects of voice-related QOL. In the present study, a decreasing trend in all aspects of VHI scores was observed. Since injection procedure attempts to improve the functional rather than physical integrity of vocal folds, modest decrease found in physical aspect of VHI scores is expected. Yet, only functional and emotional aspects of VHI score drastically improved and remained consistently constant for at least three months after surgery whereas improvement in physical aspect of VHI in was not significant, except at one month after treatment. Nevertheless, the degree of reduction in emotional aspect of VHI scores was observed to be more than that in functional aspect. The degree of improvement in emotional aspect of VHI did not commensurate with that in functional aspect.

Findings in the pattern and degree of changes in functional, physical and emotional aspects of VHI revealed information about direction of further research. Despite limited improvement reported by UVFP patients in the physical aspect, UVFP patients experienced a
significant improvement in the functional use of voice due to enhanced glottic competence.
Yet, they were emotionally more satisfied with the outcomes of injection. The discrepancy in
the degree of improvement between emotional and functional aspect of QOL may imply the
presence of improvement in other functions, in addition to phonation. Apart from dysphonia,
UVFP patients also suffer from varying degrees of dysphagia, depending on the severity of
glottic incompetence (Kelchner et al., 1999). The significant improvement in emotional
aspect of VHI may be attributed to enhancement in swallowing ability of UVFP patients.
Changes in swallowing ability of UVFP patients should have to be taken into account in
order to faithfully describe the benefits from treatments on glottic insufficiency. Future
research on treatment efficacy of injection laryngoplasty may adopt a more holistic approach
by considering both voice and swallowing improvement.

From UVFP patients’ subjective perception, injection procedure was deemed effective
in treating dysphonia, as reflected by reduction in functional and emotional impact of their
voice problems in the context of daily living and functioning.

**Acoustic and durational characteristics**

In the current study, changes in voice quality after injection were depicted with the
use of objective measurements. Jitter, shimmer, signal-to-noise ratio (SNR) and maximum
phonation time (MPT) were obtained in the recorded voice samples. Injection using
hyaluronic acid led to significant decrease in jitter and shimmer, and significant increase in
SNR and MPT. These findings are consistent with that reported by Hoffman, Witt, Chapin,
McCulloch, and Jiang (2010), in which improvement in acoustic measurements after
injection laryngoplasty was found. Maintenance of improved jitter, shimmer, SNR and MPT
was also observed three months after surgery.

The reduction in perturbation in fundamental frequency and amplitude of sound wave
signifies improved control of vocal fold vibration, implying a better periodicity and
symmetry in glottal vibration. Significant increase in SNR can be attributed to a reduction in noise that may be associated with breathiness, accrediting to narrowed glottal gap.

Despite the existing controversies regarding the specific relationship and reliability between each parameter of objective and subjective voice measurements, jitter, shimmer and SNR are generally related to breathiness, hoarseness, roughness and harshness (Hartl, Hans, Vaissiere & Bransnu, 2003; Rabinov, Kreiman, Gerratt & Bielamowicz, 1995). An improvement in overall voice quality will exhibit a decrease in SNR (Eskenazi & Childers, 1990; Prosek et al., 1987). The greater the hoarseness and breathiness of UVFP patients’ voice exhibit, the greater the jitter and SNR are (Eskenazi & Childers, 1990; Prosek et al., 1987; Yumoto & Gould, 1982; Yumoto, Sasaki, & Okamura, 1984). Accordingly, it is expected that UVFP patients’ perceptual voice quality should have improved after injection using hyaluronic acid. Apparently, further studies focusing on the subjective voice parameters such as GRBAS (Grade, Roughness, Breathiness, Aesthenia, and Strain) and correlation between objective and subjective voice measurements of UVFP patients are needed.

UVFP patients demonstrated a discernible improvement in neuromuscular and aerodynamic control of voice, as reflected by the increasing trend observed in MPT. Injection procedure is effective in eliminating inter-glottal gap and increase glottis efficiency. Yet, the increase in MPT was not significant. There can be two reasons for this. The first is related to the use of a heterogeneous group of patients who have different co-morbidities and etiologies in the present study. Patients with different co-morbidities and etiologies may have varying vital capacity for the task of maximum phonation. The second suggested reason might be related to the fact that the UVFP patients did not have a significant improvement in terms of control of vocal fold and expiratory flow after injection laryngoplasty. In other words, supportive respiratory capacities compensate for poor membranous vocal fold closure.
Further research may investigate whether injection laryngoplasty leads to improvement in phonation quotient (PQ) (a ratio of vital capacity over MPT). Phonation threshold flow (PTF), phonation threshold pressure (PTP), and phonation threshold power (PTP) may also be investigated in future studies to more holistically document the efficacy of injection procedure on aerodynamic parameters.

Regardless, based on the objective voice measurements, the procedure of injection laryngoplasty appeared to be an effective treatment to dysphonia associated with UVFP which was characterized by Rudolf and Sibylle (2011) to be weak in intensity, hoarse and breathy. Significant improvement after injection in all objective parameters reflects the expected efficacy of injection laryngoplasty in reducing hoarseness and breathiness while enhancing the intensity of signals.

**Perception of Cantonese lexical tones**

In the present study, patients with UVFP patients’ production of lexical tone contrast after injection is investigated in term of percent correct identification. Before treatment, UVFP patients cannot produce any contrast in lexical tones, as indicated by the lack of significant difference in accurate tone identification. Nevertheless, after injection procedure, improved lexical tone production was found, with significant improvement in HL, HR and LR tones. The treatment effect of injection procedure in Cantonese lexical tone production can be maintained as reflected from the consistent performance in production of lexical tone contrast throughout three months after surgery.

Injection using Teflon, fat and collagen was reported not to restore vocal fold tension and hence pitch control, unless re-innervation coupled with medialization surgery were employed (Harvey, 1999). The significant improvement in the production of lexical tone contrast may be credited to the similarity of viscoelastic properties of hyaluronic acid to that of vocal folds. Injection using hyaluronic acid can render a vocal fold with similar vibratory
behavior to a healthy vocal fold, with minimum vocal fold mucosal defects and lamina propria deficiencies (Dahlqvist et al., 2004).

It is also noted that none of the six lexical tones has attained perfect tone identification. Injection procedures improved UVFP patients’ production of HL, HR and LR tones significantly whereas no significant treatment effect was observed for other lexical tones. The accuracy in identifying HL and HR tones after surgery was the best among all Cantonese lexical tones with post-treatment average around 60% to 70%, followed by LR tone around 50% to 60%. The identification of ML ad LL tones was the worst among all Cantonese lexical tones, with an average accuracy around 20% to 30%. The patterns of tone identification in this study are similar to the findings for normal adults reported by Ching (1981). HL, HR and LF tones were tones to be best identified even in difficult listening conditions whereas significant confusions arose for the perception of ML and LL tones. According to Ching (1981), this discrepancy in tone perception accuracy might be related to the different tone contours associated with different lexical tones.

The tone identification errors indicated by the confusion matrices can be explained in terms of a lack of salient information about pitch level, and/or pitch variation that might have led to confusion between tones of different pitch heights and pitch contours correspondingly. Error analyses revealed that HR tone was perceived mainly as LR tone; HL tone was perceived mainly as ML or LL tone; LR tone was perceived mainly as HR tone. Pitch contour did not appear to pose any difficulty for perceiving UVFP tones whereas pitch height was found to be the missing information in UVFP tones. The error pattern revealed that patients with UVFP were able to produce pitch contour significantly adequate for perception but failed to produce the difference in pitch level enough for correct perception on most occasions. Confusions among lexical tones also pointed to an inadequate contrast in pitch register of UVFP patients. This finding might imply the need for post-treatment adjunct
voice therapy for patients with UVFP in order to maximize the potential range of pitch variation for better production of tone contrast.

It is expected that more patients who do not benefit from spontaneous recovery and voice therapy may consider undergo this type of phonosurgical procedure. Not only should the choice of phonosurgical procedure be guided by considerations of efficacy, invasiveness and risks, factors that are linguistically and communicatively relevant to Cantonese speakers should also be taken into account. Findings from the present study prove that linguistic concerns may play an important role in rehabilitation of UVFP. The ability in producing high pitch level and rising pitch contour is conducive to more intelligible and useful communication for UVFP patients. Post-surgical voice therapy on pitch variation/gliding may also be suggested as an adjunct method to maximize the treatment effect of injection laryngoplasty. According to the tone perception experiment, it is clear that injection laryngoplasty can be effective in helping UVFP patients to produce contrast in lexical tones. Significant improvements in production of HL, HR and LR tones are evident after injection.

Yet, further research on maintenance effect of injection laryngoplasty using hyaluronic acid 6 months and 1 year post-operatively have to be carried out. The long-term effects on perceptual, acoustic and aerodynamic measurements, as well as lexical tone production by injection laryngoplasty remain to be examined further.

**Conclusion**

The present study assessed the use of injection laryngoplasty using hyaluronic acid in Cantonese-speaking patients with UVFP. Acoustical and durational findings before and after the procedure indicated that voice quality and glottic competence improved significantly and maintained consistently after the surgery. Production of lexical tone contrasts by Cantonese-speaking patients with UVFP also improved significantly and maintained consistently three months after the surgery. Treatment and maintenance effects were recognized by UVFP
perceptually in terms of QOL. These favorable results appear to point to the conclusion that injection laryngoplasty for Cantonese-speaking UVFP patients are immediate and sustainable for at least three months after injection. Long-term effect of injection of over six months post-surgery remains to be further studied.

Acknowledgement
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References


INJECTION LARYNGOPLASTY


