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Vocal Fold Injection: Review of Indications, Techniques, and Materials for Augmentation

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Abstract

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Vocal fold injection is a procedure that has over a 100 year history but was rarely done as short as 20 years ago. A renaissance has occurred with respect to vocal fold injection due to new technologies (visualization and materials) and new injection approaches. Awake, un-sedated vocal fold injection offers many distinct advantages for the treatment of glottal insufficiency (vocal fold paralysis, vocal fold paresis, vocal fold atrophy and vocal fold scar). A review of materials available and different vocal fold injection approaches is performed. A comparison of vocal fold injection to laryngeal framework surgery is also undertaken. With proper patient and material selection, vocal fold injection now plays a major role in the treatment of many patients with dysphonia.

Keywords: Vocal fold injection, Vocal fold insufficiency

INTRODUCTION

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In the past decade, vocal fold injection (VFI) has re-emerged as a valuable treatment modality for a variety of laryngeal disorders. Recent advances in injection materials have broadened the indications for this technique, while the increasing capabilities of endoscopic technology have increased the number of available approaches and precision of injection delivery. The basic indications for VFI have expanded to include treatment for vocal fold paralysis, paresis, atrophy, and scar or sulcus ([1](#)). However, the myriad of options in patient selection, injectable materials, and approach to injection has made utilizing this modality increasingly complex for the clinician.

In the broadest sense, VFI can include procedures that target the superficial (subepithelial space) aspect of the vocal fold. This procedure involves injection of a substance as a lamina propria replacement. Useful for mild-to-moderate vocal fold scar and lamina propria defects, superficial injection provides correction of vibratory defects rather than global augmentation.

In the stricter sense, VFI refers to deep or lateral injection, as a means for vocal fold augmentation. Typically, deep injection allows for placement of a filler substance in the lateral aspect of the thyroarytenoid/lateral cricoarytenoid muscle complex (medial aspect of the paraglottic space). The result is a medially displaced free edge of the vocal fold, akin to laryngeal framework surgery, or type I thyroplasty. The procedure allows for correction of glottal insufficiency from a variety of causes, and is

typically used to treat temporary or permanent mild-to-moderate glottal insufficiency (<1 to 3 mm glottal gaps). For the purposes of this review, VFI will refer to this latter method of deep vocal fold injection augmentation.

INJECTION APPROACHES

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Several approaches exist to perform vocal fold injection augmentation. With advancing technology, such as distal chip and flexible working channel laryngoscopes, awake in-office techniques have become viable alternatives to the traditional microsuspension laryngoscopy technique. Available technology, choice of materials, surgeon preference, and patient preference must all dictate the approach used for VFI.

Direct laryngoscopy provides the most direct approach to VFI. Traditionally, microscopic suspension laryngoscopy is performed under general anesthesia with a small endotracheal tube or under jet ventilation, and with an adequately sized laryngoscope in suspension. The degree of glottic incompetence is assessed through a combination of pre-operative awake stroboscopy and intra-operative visualization with microlaryngoscopy and zero-, thirty-, and seventy-degree angled telescopes. As an alternative, VFI may be done with a combination of conscious sedation and topical anesthesia, without endotracheal intubation, using a smaller slotted laryngoscope with 0-degree telescopic visualization endoscopic vocal fold injection (2). Both techniques provide direct access to the vocal fold, and allow for precise needle placement along the superior arcuate line with a direct, linear trajectory. Additionally, both provide the ability to directly monitor augmentation. These techniques prove especially valuable in the patient who is otherwise unable to tolerate an awake procedure. However, both techniques do not provide real time assessment of vocal fold closure or voice quality.

Though VFI in the awake patient was initially described over a century ago, VFI in an in-office setting has re-emerged in the past decade as an attractive alternative to microsuspension laryngoscopy. Pointing to the popularity of this technique, a recent multi-institutional review revealed that VFI was performed equally often in an awake patient as one under general anesthesia (3). VFI in the awake setting has the distinct advantages of providing direct feedback of vocal fold closure and voice outcome during the injection, avoiding limitations of difficult exposure, and avoiding general anesthesia with its inherent risks and increased cost (4). Technical successes, as well as voice outcomes, as measured by standardized patient-based voice surveys, are similar to injection performed under general anesthesia when performed by an experienced laryngologist (4, 5). Patient selection is critical when choosing VFI in an awake patient; a cooperative, calm patient without a strong gag reflex is required for successful completion. One concern about awake VFI lies in the relative decrease in needle control, leading to decrease in precision of injection. In fact, there is some evidence that minor complications are slightly increased in an in-office setting (5). In-office VFI encompasses percutaneous (trans-cricothyroid membrane, trans-thyroid cartilage, and trans-thyrohyoid membrane), per-oral, and trans-nasal endoscopic approaches. Typically the three approaches are performed with a flexible laryngoscope in place, visualizing the larynx for visualization and to monitor injection effects. In most cases, optimal visualization is provided with a distal chip laryngoscope with digital, high quality video image output.

The trans-cricothyroid membrane approach typically utilizes a submucosal path; a 25 g needle bent 45-degrees is inserted below the inferior border of the thyroid cartilage, 3-7 mm lateral to midline and subsequently passed cephalad and laterally. Applying gentle pressure medially transmits motion to the vocal fold, allows the surgeon to confirm submucosal location of the needle and thus prevents perforation of the mucosa by the needle. Alternatively, with adequate tracheal anesthesia, the needle can be inserted into the midline in the infra-glottis, and then directed superior and lateral, intraluminally, to the deep aspect of the vocal fold. Anatomic studies using multidetector array computed tomography has confirmed this approximate 45-degree cephalad angle from a typical injection point 7 mm off of the midline (6).

The trans-thyroid cartilage approach utilizes a percutaneous approach perpendicular to the thyroid cartilage ala. A 24- or 25 gauge needle is inserted 3 mm to 5 mm above the lower border of the thyroid cartilage and passed gently through the cartilage. Advancing the needle toward midline with gentle pressure transmits motion to the vocal fold, and allows the surgeon to estimate the location of the

needle tip. Inadvertent mucosal violation may occur secondary to excessive medial pressure. Occasional obstruction of the needle with cartilage may be overcome through pressure on the plunger, with care to avoid excessive pressure and possible overinjection of material. This technique is optimal for younger patients without extensively calcified cartilage. A trochar-based injection device has been made to assist trans-thyroid cartilage VFI (Casiano Needle, Medtronic Inc., Jacksonville, FL, USA).

The trans-thyrohyoid membrane approach utilizes an extramucosal route to the vocal fold. A straight 25-gauge needle is inserted into the skin overlying the thyroid cartilage notch. Once through the thyrohyoid membrane, the needle is directed sharply caudal and advanced; with this maneuver, the needle can be visualized entering the lumen at the petiole of the epiglottis. From this position, with direct visualization using the flexible laryngoscope, the needle can be directed toward the vocal fold for injection. Bending the needle, while improving the inferior angle, often makes directing the needle more difficult, and therefore is discouraged. Among the percutaneous techniques, the trans-thyrohyoid membrane approach offers the distinct advantage of direct needle placement, increasing precision of the injection (7, 8).

The per-oral vocal fold injection approach utilizes a direct approach and offers excellent precision and needle visualization. Topical anesthesia of the oropharynx and larynx is critical, as the needle is guided from the mouth to the vocal fold with a per-oral approach. Typically the patient is placed in a seated "sniffing position", with the neck flexed and the head slightly extended. A flexible laryngoscope is inserted through the nose while the patient protrudes and holds his or her own tongue. Topical anesthesia may be given via an Abrahms cannula passed per-oral to the base of tongue, epiglottis, and true vocal folds. Alternatively, topical anesthetic may be applied through a flexible catheter directed through the working channel of a flexible laryngoscope; the laryngoscope is used to drip anesthetic onto the base of tongue, epiglottis, and, while the patient is phonating, onto the true vocal folds. The route of the needle is typically a 90-degree path, though this varies from patient to patient, and may be approximated by comparing with the Abrahms cannula passage. Typically, the false vocal fold will be retracted with the shaft of the needle, allowing for a lateral injection. Several commercially available needles, length 220 mm to 250 mm, may be purchased separately or included with injectate materials for per-oral VFI.

A final injection approach is the trans-nasal endoscopic approach to the vocal fold. This approach utilizes a flexible working channel laryngoscope with a 23- or 25-gauge flexible needle introduced through the working channel. With the needle slightly from the tip of the endoscope, the needle can be guided to the appropriate lateral position under direct visualization. Advocates describe utilizing this technique as an alternative to other approaches for its ease of use, patient tolerance, and ability to overcome anatomic and patient limitations. However, it should be noted that the fine gauge injection needles only accommodate dilute preparations of most substances unless a mechanical injection device is used. This approach has been advocated using a dilute concentration of micronized deep dermal tissue (Cymetra®), mixed with 2.3 mL of 1% lidocaine for all cases (9). It should also be noted that due to the length and caliber of the injection needle, this approach requires more than the normal amount of injection material to accommodate the relatively large dead space in the needle.

INJECTION MATERIALS

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In the past 10 years material sciences have increased the number of injectables with increased safety profile and improved biomechanical profiles. Materials developed have sought to eliminate the deleterious foreign body and inflammatory reactions caused by some of the early injectable materials such as paraffin, silicone, and Teflon™. Recent efforts have focused on matching the biomechanical and viscoelastic properties of the superficial lamina propria.

Materials for deep augmentation injection are typically described as temporary, and permanent/long lasting. Long lasting, and sometimes, permanent injectable materials include autologous fat, calcium hydroxylapatite (Radiesse™), polydimethylsiloxane (PDMS or particulate silicone), and historically, and polytef paste (Teflon™). Temporary injection materials include bovine gelatin (Gelfoam™, Surgifoam™), collagen-based products (Cymetra™, Zyplast™, Cosmoplast/Cosmoderm™), hyaluronic acid (Restylane™, Hyalaform™), and carboxymethylcellulose (Radiesse Voice Gel™). The

materials vary in the duration of integration and are thought to vary in their specific viscoelastic properties and biocompatibility.

Autologous fat typically lasts from one to several years, and is considered a permanent injection by many. Though the material is autologous, may be generously injected, and is readily available, it is typically harvested in the operating suite under sterile conditions. Additionally, the survival is highly, which may be due to fat preparation techniques; indeed, many suggest substantial overinjection of due to this immediate variability. In addition to global augmentation, autologous lipoinjection has been described for vocal fold scar and vocal fold atrophy ([10](#), [11](#)).

Polydimethylsiloxane, or particulate silicone, has been advocated by some for global vocal fold augmentation. The duration of this substance is likely permanent, as alluded to in follow up of close to 10 years post-injection ([12](#)). Recent evidence points to safety and efficacy in both the short and long term, though complications of extrusion and foreign body reaction have been reported. In addition, recent studies comparing this directly to some of the more accepted materials do not exist ([13](#), [14](#)).

Polytetrafluoroethylene, or Teflon, is another permanent injectable that is of considerable historical significance but has fallen out of favor in the past 20 years. Long-term studies have revealed significant foreign-body inflammatory reactions to this substance, often requiring removal with subsequent significant vocal fold tissue loss. Presently, Teflon it is rarely used, with newer substances providing safer alternatives.

Calcium hydroxylapatite (CaHA), known by the trade name Radiesse Voice, is currently a FDA approved substance for potentially long-term vocal fold injection. Comprised of microspheres of CaHA in a carboxymethylcellulose carrier, this substance has been studied in both animal and human studies. In an in vivo canine vocal fold model, it has been shown that CaHA injection provided adequate medialization of the canine vocal fold up to 12 month follow up without migration or resorption, and a giant cell reaction without appreciable chronic inflammation ([15](#)). A recent multi-institutional clinical trial revealed excellent results of 80% improvement at 12 month follow-up ([16](#)). Long term clinical results show that persistent medialization after CaHA injection may be present up to 2 years and more, with an average duration of 18 months ([17](#)).

Bovine-based gelatin products, such as Gelfoam and Surgifoam, can be used for temporary vocal fold injection augmentation. An injectable version of this product may be prepared by mixing the powder with saline. The resulting substance is highly viscous, and may be used for injection by injecting with a pressurized syringe through a 18- or 19-gauge large bore needle. This has been used extensively for temporary augmentation, lasting 4-6 weeks and found to be very safe ([18](#)). Despite the excellent track record, this material has little utility due to development of new substances that are easier to use and last longer.

Bovine-based collagen products, such as Zyplast, have been used for longer injection. There is a very small potential for allergic response to this material. Thus, the FDA advocates skin hypersensitivity testing prior to using this substance. Despite this possibility, the rarity of this reaction in laryngeal injection augmentation has led some to question the need for testing ([19](#)). Atelocollagen, a water-soluble form of bovine dermal collagen, has been used in the past for injection augmentation and for scar and sulcus, though some evidence exists that this may impair normal mucosal wave when injected submucosally. Bovine cross-linked collagen typically lasts 3 to 4 months in duration.

Human based collagen injectables include micronized cadaveric dermis, such as Cymetra, and tissue engineered human collagen, such as Cosmoplast/Cosmoderm. The former has been used extensively and results have been positive for vocal fold immobility and presbylarynx ([20](#)). It has also been used sparingly for scar and sulcus, though this has not been studied extensively. Cymetra is clinically effective for 2 to 3 months, and radiographic evidence of the injectable up to 11 months has been reported ([21](#)). Because this is prepared from human cadaveric tissue, potential for infectious transmission exists, though this has not been documented to date. Cosmoplast/Cosmoderm has recent use as a dermal filler, though the experience as an augmentation filler for vocal folds is limited.

Hyaluronic acid gels, such as Restylane, Hyalaform, and Juvederm, are animal or bacterial derived variations of the naturally occurring extracellular matrix glycosaminoglycan found in various human

tissues, including the vocal fold lamina propria. Clinical studies have supported the safety and efficacy of this injectable for deep vocal fold augmentation ([22](#), [23](#)). Some clinical studies, supported by rheologic studies and animal model work suggest hyaluronic acid derivatives may be useful as a lamina propria replacement for vocal fold scar and sulcus. However, our clinical experience has been very disappointing and has even worsened vocal fold vibration when placed superficially ([23-25](#)). The substance is believed to last 4-6 months, though clinical effects may last up to 12 months ([22](#), [23](#)).

Carboxymethylcellulose, sold as Radiesse Voice Gel, is the carrier substance used in the longer lasting Radiesse Voice injectable. This has been utilized extensively for temporary vocal fold paralysis and for trial vocal fold injection augmentation for a variety of causes of glottic incompetence. This material requires no preparation and has no biologic infection transmission risk. The substance typically lasts 2-3 months after injection ([26](#)).

INDICATIONS

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Vocal fold injection is a surgical treatment alternative to laryngeal framework surgery. Though each approach has advantages and drawbacks, no formal algorithm exists in the considerable circumstances where either approach may be acceptable. In general, vocal fold augmentation is used for the temporary correction of incompetence due to unilateral vocal fold paralysis/paresis, permanent correction of mild-to-moderate glottic insufficiency, and glottic insufficiency from soft tissue loss of the vocal fold ([27](#)).

Temporary vocal fold injection is currently the treatment of choice for the treatment of glottic incompetence when prognosis for recovery is unclear. This is best illustrated in the case of acute unilateral vocal fold paralysis or paresis. During the time for potential recovery of function, usually up to 6-months post-onset, vocal fold injection with a shorter duration substance has been shown to alleviate voice symptoms and improve swallowing until function recovers or the patient is a candidate for a more permanent treatment option. In this setting, injection with collagen, HA, or Radiesse Voice Gel provides the best treatment option ([20](#), [26](#), [28](#)).

Vocal fold injection may also be used to treat permanent causes of mild-to-moderate glottic insufficiency. Specifically, this has been successfully used to treat vocal fold atrophy, paralysis, paresis, and augmentation after previous framework surgery. Specifically, results with calcium hydroxyapatite ([3](#), [29](#)) and autologous fat injections ([30](#)) have proven acceptable in the treatment of atrophy, paralysis, and paresis. Though some have reported inconsistent results with fat when compared to type I thyroplasty in cases of unilateral vocal fold paralysis ([10](#)), many may find better results with the ability to "fine tune" serial injections for progressive vocal fold atrophy and presbylarynx. Additionally, results are promising for those requiring injection augmentation for recalcitrant glottic insufficiency after type I thyroplasty with or without arytenoid adduction ([31](#)).

Though studies purport vocal fold injection is comparable to laryngeal framework surgery in many clinical scenarios, the former modality has several advantages over the latter. Patients with very mild forms of glottic gap (less than 1 mm) may be better suited for injection than framework surgery. Additionally, the ability to perform vocal fold injection in the awake setting has numerous distinct advantages over framework surgery; patient preference not to undergo an operation, and the ability to obtain direct voicing and vocal fold vibration feedback during the procedure are particularly desirable. Ease of performing the procedure with limited experience is greater in the case of vocal fold injection performed under general anesthesia, when compared with laryngeal framework surgery. Finally, significant cost benefit has been found in the case of in-office awake injection when compared to those performed in the operating room ([4](#)).

It is important to bear in mind that vocal fold injection has several limitations. It is generally considered feasible for a glottic gap up to 3 mm, after which the insufficiency becomes increasingly difficult to correct. In cases of posterior glottic gap or significantly foreshortened vocal fold, arytenoid adduction typically performed in conjunction with medialization laryngoplasty often provides better results. One limitation is the ability to permanently correct for glottic incompetence; autologous lipoinjection may be inconsistent due to the variability in viability within the first several weeks and calcium hydroxyapatite typically lasts 1 to 2 years, with an average of 18 months ([17](#)).

TIMING OF INJECTION

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Currently, three clinical scenarios exist to guide the timing of vocal fold injection augmentation. The options for trial injection, temporary injection, or permanent injection should guide the timing and material selection for injection. Specific laryngeal pathology, patient expectations, and adjunctive diagnostics will all aid in choosing the proper timing of injection when considering the type of injection performed.

Trial injection augmentation consists of injection of temporary substance in patients for whom injection benefits are unclear. In the case of bilateral vocal fold atrophy, voice results with injection may be unpredictable, and in these cases trial injection may reasonably predict the results of a more permanent augmentation (VFI or thyroplasty). In another subset, patients with dysphonia with a significant dysarthria component may undergo trial augmentation to predict if articulation difficulties do or do not preclude improved communication outcomes with permanent augmentation. Finally, in a subset of patients, apprehension or unrealistic expectations exist; in these patients, trial injection will give an idea of realistic expectations after injection ([32](#)).

A temporary vocal fold injection may be performed for acute unilateral vocal fold paralysis or paresis. In these cases of uncertain recovery, laryngeal electromyogram (LEMG) may aid in determining prognosis for recovery. Sensitivity for LEMG in predicting no recovery in the case of a "poor" or "fair" prognosis is 91%. Specificity for predicting adequate recovery in the case of "excellent" prognosis for recovery is only 44%, however ([33](#)). Recent evidence suggests that the presence of laryngeal synkinesis can effect the prognosis for recovery. Specificity of LEMG with synkinesis analysis increases to 64%, while accuracy is increased from 59% to 84% ([34](#)). Given this, LEMG with synkinesis testing can play a major role in assessing the prognosis for recovery.

Permanent vocal fold injections timing varies based on specific pathology. For vocal fold paralysis, early permanent injection may be considered in the LEMG-determined case of poor prognosis for recovery with or without synkinesis. Alternatively, it may be performed after 6-month duration in the case of persistent vocal fold immobility. As discussed previously, permanent injection can be considered after trial injection for atrophy or paresis.

FUTURE DIRECTIONS

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Many advances are expected with vocal fold injection. Currently, no optimal materials exist for superficial lamina propria replacements; injectable materials that improve or enhance mucosal wave would prove to be immensely useful in the treatment of vocal fold scar and sulcus vocalis. Improvements in the delivery methods or the viscosity of materials would allow for improved injection delivery through a trans-nasal endoscopic approach. Finally, improvements in instrumentation, such as articulating cannulas may aid in performing injections in the awake, in-office setting.

Currently, much research concentrates on optimizing the biomechanical matches of injectables with the host tissue. The thyroarytenoid/lateral cricoarytenoid muscle complex as well as the superficial lamina propria have specific rheologic properties affecting mucosal wave characteristics, vocal fold vibration, and ultimately voice quality. Studies examining the effects of injection on the viscoelastic properties of the specific host site exist. Future development of vocal fold injectable materials will likely focus on providing a product that is not only safe, but functionally matches host viscoelastic properties. This is important both in the short-term and in the long-term, where tissue incorporation may alter the typical characteristics of the material/vocal fold interactions.

CONCLUSION

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Vocal fold injection is a proven technique with favorable results for the treatment of mild-to-moderate glottic insufficiency due to a variety of causes. The technique has the advantages of ability to perform in an in-office, awake setting and may be easier to master than laryngeal framework surgery. In select cases of temporary paralysis or paralysis with uncertain prognosis, temporary vocal fold injection may be considered the standard of care for treating glottic insufficiency. Recent advances in material engineering and digital imaging technology have made this an attractive alternative to laryngeal framework surgery that must be considered in a variety of clinical scenarios.

Footnotes

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No potential conflict of interest relevant to this article was reported.

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