

Long-Term Results of Calcium Hydroxylapatite for Vocal Fold Augmentation

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Objectives/Hypothesis: Studies have shown excellent results for 12-month post-injection augmentation data for calcium hydroxylapatite (CaHA) for glottal incompetence; however, the longevity of the material past one year was unknown. Our objective was to report the long-term effectiveness of CaHA as a vocal fold injectable by assessing data from a cohort of patients who underwent injection for glottal insufficiency.

Study Design: Retrospective chart review.

Methods: Patients who underwent CaHA injection for glottal insufficiency of any etiology were considered for inclusion in the study. The change in Voice Handicap Index (VHI)-10 scores between preinjection scores and best postinjection scores as well as between the preinjection and the most recent VHI-10 scores were used as primary outcome measures to determine the persistence of benefit or the time to loss of benefit. Complications among the cohort were identified.

Results: Ninety patients who underwent 108 vocal fold injections with CaHA were evaluated for inclusion. Twenty patients with 22 injections met the criteria for inclusion. Fourteen of 22 (64%) subjects showed loss of benefit of the CaHA material. The average length of benefit was 18.6 months, with a range of 8 to 36 months. Three complications were identified among the original cohort of 108 injections.

Conclusions: CaHA remains a safe and effective long-term vocal fold injectable with an average length of benefit of 18.6 months. Three complications were seen among 108 CaHA injections. CaHA is a long-term injectable with an excellent track record that does not appear to warrant concern for permanent or late complications.

Key Words: Laryngology, vocal fold injection, injection augmentation, augmentation materials, voice, glottal insufficiency, injectables, quality of life.

Level of Evidence: 4

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INTRODUCTION

Glottal insufficiency (GI) that requires permanent true vocal fold (VF) augmentation is a common problem treated by otolaryngologists. GI may be gross or subtle based on the underlying disease processes such as VF atrophy, paresis, paralysis, scar, or sulcus vocalis.¹ Treatments for GI are based on symptoms and severity and range from voice therapy to VF injection augmentation and laryngeal framework surgery. Finding an ideal long-term injectable for VF augmentation has been a goal of those who treat GI since Brunings first offered

this treatment using paraffin nearly 100 years ago.² The ideal long-term VF injectable should be available “off the shelf” without the need for preparation; it should be biologically inert and should be a good rheologic match for the native VF. It also should be passable through a fine-gauge needle (≤ 22 gauge). Many currently available materials such as autologous fat, fascia, hyaluronic acid, and collagen-based products fall short of these requirements.³⁻⁷ Teflon and silicone have both been previously used as permanent VF augmentation materials; they were discontinued owing to the significant immunologic/granulomatous responses seen in numerous patients.^{8,9} The chemical make-up and track record of calcium hydroxylapatite (CaHA) in the VF and elsewhere in the body are well described in the literature.¹⁰⁻¹⁶ CaHA has been available commercially since 2003 as Radiesse Voice (Bioform Medical Inc., San Mateo, CA) and has met many of the requirements of the ideal VF injectable, including being readily available, biologically inert, and passable through a small-gauge needle; however, its rheologic properties and longevity remain uncertain.^{17,18} Rosen et al. prospectively evaluated the effectiveness of CaHA up to the 12-month time point.¹⁸ Eighty-one percent of patients in this study subjectively reported at least moderate improvement in voice at 12 months. Twenty-two percent of patients (14 of 63 patients) required further intervention before the 12-month time

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point for loss of initial injection benefit. There were no major complications and no superficial injections of CaHA reported in that study.

The study by Rosen et al. included only patients with unilateral VF paralysis (UVFP) and patients with GI but bilaterally mobile VFs (paresis and/or atrophy). Patients were excluded if they had scar or sulcus, prior external beam radiation to the larynx, or a history of prior laryngeal surgery with the exception of a temporary VF injection augmentation. A more recent study by Kwon et al. confirms the 12-month persistent benefit of CaHA specifically in GI patients with bilateral VF atrophy.¹⁹ Real world applications of CaHA often include patients who do not have straightforward UVFP or GI with mobile VFs. Patients often have had prior laryngeal framework surgery and need a small amount of additional bulk for optimal voice; they may have VF scar or sulcus present and may benefit from global VF augmentation; or they may have a history of external beam radiation or a terminal diagnosis. The longevity of CaHA and its potential as a permanent VF augmentation material have yet to be determined. The goal of this study was to look at a new cohort of patients from one institution who had received a deep VF augmentation with CaHA for any indication deemed appropriate by the surgeon and to examine the results for those patients by using the change in their Voice Handicap Index-10 (Delta VHI-10) for a period of longer than 12 months. Our intent was to determine the longevity of initial voice benefit from CaHA VF augmentation in this “real world” patient population and to report any complications from our institution’s cohort.

MATERIALS AND METHODS

After approval from the University of Pittsburgh Medical Center Institutional Review Board was received, data were accumulated by means of retrospective chart review. We then deidentified data for any adult subject (18 years or older) who had received a CaHA VF injection at least 24 months before the date of data extraction. Subject demographics including age, sex, and diagnosis were extracted along with the primary outcome measure of the study, the VHI-10 scores (the VHI-10 is a patient-based survey that quantifies a patient’s perception of his or her vocal handicap and is scored from 0 to 40, with 40 being the highest degree of perceived handicap). In addition, the dates of the CaHA injection(s), side of injection, amount of CaHA injected, and any preceding or subsequent laryngeal procedures and their dates were recorded.

Follow-up surveys were sent to all patients whose last available VHI-10 score showed persistence of benefit but whose chart lacked a post-24-month VHI-10 score (24 months or more from the date of injection). The survey included a VHI-10 and a subsequent question asking whether they had undergone any further laryngeal surgery since their last visit to our practice. This question was added to avoid VHI-10 scores worsening or improving based on further laryngeal surgery that was not performed at our institution.

Patients were excluded from analysis for the following reasons: 1) if they never showed improvement in VHI-10 from preinjection to postinjection (i.e., there was never a clinically meaningful improvement in VHI-10 and thus no way to track the long-term effectiveness of CaHA, which is the objective of this study); 2) if their chart lacked a preinjection VHI-10 score;

3) if their chart lacked at least two postinjection VHI-10 scores to establish a trend of improvement or decline in determining long-term results following the initial CaHA injection (to establish if and when they lost the benefit); or 4) if they had a terminal diagnosis and they died before final data collection was possible.

All injections were performed under the direction of the senior author (c.a.r.) and were performed using primarily a peroral approach in the office (transthyroid cartilage or transcricothyroid membrane approaches were used rarely) or via microsuspension laryngoscopy in the operating room based on the preference of the surgeon and patient.¹ The amount of material injected and the exact deep injection site(s) were determined based on the underlying diagnosis and the decision of the surgeon at the time of injection.

There is a subset of patients who receive a CaHA injection and lose their benefit fairly rapidly. This phenomenon is presumed to be caused by underaugmentation of the VF by the surgeon at the time of the first injection. As the carrier gel in the CaHA product wears off in an underaugmented VF, the remaining amount of CaHA is insufficient to give meaningful benefit to the patient and thus warrants reinjection. Subjects who received a subsequent CaHA injection less than or equal to 4 months after their first injection were presumed to have been underaugmented; the date of data collection for these subjects in the final analysis was thus started from the date of their repeat injection. Four months was chosen as the cutoff for possible underaugmentation, as it can take 2 to 3 months for the gel carrier of the CaHA to wear off and additional time to reschedule the repeat procedure.

Subjects who lost benefit after the 4-month underaugmentation window (i.e., had an acceptable benefit from the first injection) and went on to have a subsequent procedure (such as repeated CaHA injection, medialization laryngoplasty, or autologous fat injection) were deemed to have lost their benefit at the time of the last recorded VHI-10 preceding their surgery. Loss of benefit was defined as a return to within 4 points of their preinjection VHI-10 score or a score that was even higher (worse) than their preinjection score (see discussion).

As data were gathered, we realized that some subjects had received two or more CaHA injections and that each individual injection had an acceptable period of benefit before reinjection was performed (i.e., each injection lasted longer than the 4-month underaugmentation “window”). This finding is not surprising because CaHA is used this way in the clinical setting for patients who do not desire a trip to the operating room and prefer serial in-office procedures (when the benefit of CaHA wears off, an expected repeat procedure is performed). In an effort to extract as much long-term data from our population as possible, it was decided that patients could be used for two separate statistical subject data points if they had lost the benefit of their first injection after a period longer than the first 4-month time point and then went on to have a separate period of benefit from a subsequent injection that also lasted longer than 4 months. For example, a subject might have received an initial injection that gave him or her benefit for 10 months. Subsequently, that same subject might have lost the benefit of the first injection and then received a second CaHA injection with a resultant period of benefit of 18 months; both of those injections gave meaningful benefit and would be used as separate “subjects” (with individual data points) for the purpose of this study.

The Delta VHI-10 was used as the primary outcome measure for this study to determine when the benefit of the CaHA injection was lost; it was defined as the difference in two VHI-10 scores on two different dates (i.e., the preinjection VHI-10 score minus the postinjection VHI-10 score equals the Delta VHI-10

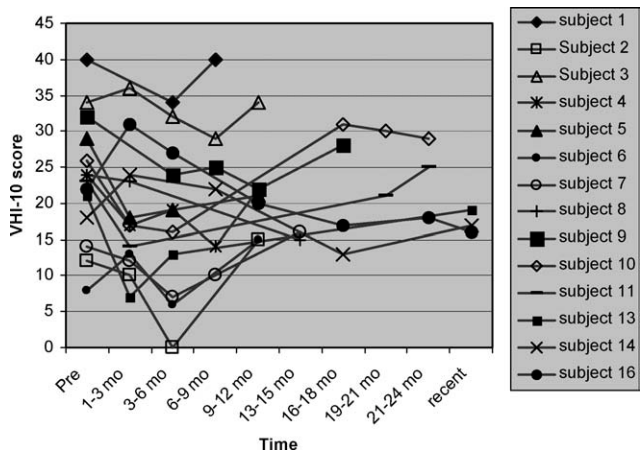


Fig. 1. Graphic representation of the change in Voice Handicap Index (VHI)-10 scores for subjects who lost the benefit of their calcium hydroxylapatite injection. Note the return of their VHI-10 scores to near or above their preinjection values.

for those two values). Paired two sample mean *t* tests (alpha level set at .05) were used to statistically compare the Delta VHI-10 values between 1) the preinjection VHI-10 score and the best postinjection VHI-10 score and 2) the preinjection VHI-10 score and either a) the VHI-10 score that showed evidence of loss of benefit at any time point after 4 months (i.e., return to near preinjection score or last score before a repeat augmentation procedure) or b) the most recent VHI-10 score showing maintenance of benefit. Readers should note that the best postinjection VHI-10 score and the most recent VHI-10 score showing benefit could be the same score in someone who was still benefitting from the injection at the time of this study and therefore would give the same Delta VHI-10 value. Mann-Whitney *U* tests (alpha equal to .05) were used for comparison of subject age and the amount of material injected between the groups with less than or greater than 36 months of time since their injection. This non-parametric test was chosen owing to the small and unequal sample sizes of these two groups (Table I).

RESULTS

A total of 20 patients fit the criteria to be included in the study. From these, 22 separate injections were appropriate for the study (hereafter called “subjects”). The average age of the subjects was 66.7 years (range, 47.7–86 years), and 12 subjects were male. The injections were unilateral in 11 of 22 subjects, and the average amount of total CaHA injected (unilateral or total bilateral) was 0.53 mL. The diagnoses treated were UVFP (11 of 22), unilateral VF paresis (4 of 22), bilateral VF atrophy (5 of 22), unilateral VF atrophy (1 of 22), and bilateral VF scar (1 of 22).

Of the 22 subjects, 16 (73%) had data up to the 36-month time point, and six (27%) had data beyond the 36-month time point (hereafter “long-term benefit” group). Data up to the 36-month time point were analyzed both separately from and as part of the overall cohort in an effort to avoid a potential reporting bias among the six subjects who all had long-term benefit and were the only subjects to return surveys (see discussion). The average duration of benefit for those 16 subjects with less than or equal to 36 months of data

was 18.6 months, with a range of 8 to 36 months. The amount of CaHA injected into the VFs was similar ($P = .5$) between the pre- and post-36-month time point groups. The ages of the subjects in the group who benefited longer than 36 months were significantly lower ($P = .02$).

Fourteen of the total 22 subjects (64%) demonstrated loss of CaHA benefit (3 evidenced by reinjection of CaHA, 3 by medialization laryngoplasty, and 8 by loss of benefit through VHI-10 criteria) (Table I). For the 14 subjects who lost their benefit, the average time to this loss was 16.9 months (Fig. 1). Six of 14 subjects lost their benefit by 12 months, six of 14 demonstrated loss of benefit by 24 months, and the two remaining lost their benefit by 36 months. For the eight subjects who maintained their benefit at the time of data collection, they were benefitting at an average of 45.3 months (range, 24–60 months) after the date of injection at the time of data collection (Fig. 2). When all 22 subjects (the 8 subjects who maintained benefit along with the 14 who lost benefit) were analyzed together, the average duration of benefit was 27.2 months, with a range of 8 to 60 months.

The average Delta VHI-10 for all subjects between preinjection VHI-10 scores to best postinjection VHI-10 scores was 10.7, and the Delta VHI-10 between preinjection VHI-10 scores to most recent VHI-10 scores was 5.1. This finding was statistically significant ($P < .00005$), demonstrating an overall loss of benefit of the CaHA injection. When only those with data up to 36 months were assessed, the average Delta VHI-10 between preinjection to best VHI-10 score was 10.2, and the Delta VHI-10 between preinjection to most recent VHI-10 score was 2.7. This finding also was statistically significant ($P < .00005$), demonstrating loss of benefit. Finally, when only those who lost benefit were examined, the average Delta VHI-10 between preinjection to best VHI-10 score was 8.6, and the Delta VHI-10 between preinjection to most recent VHI-10 score was 0.6 (a near return to their preinjection VHI-10 value). This finding showed a statistical difference as well ($P < .00005$), demonstrating significant loss (Fig. 3). Although not its purpose,

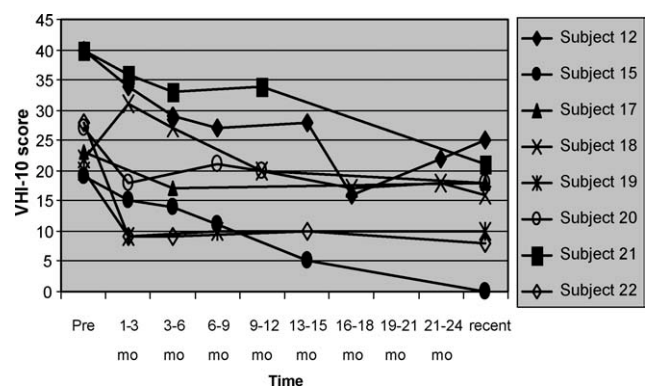


Fig. 2. Graphic representation of the change in Voice Handicap Index (VHI)-10 scores for subjects who had a long-term benefit from their calcium hydroxylapatite injection. Note the persistence of a lower (improved) VHI-10 score compared to their preinjection value.

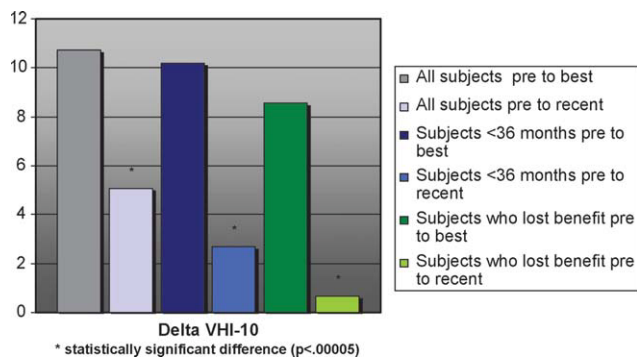


Fig. 3. A statistically significant difference ($P < .0005$) demonstrating loss of benefit of calcium hydroxylapatite injections over time exists among the 16 subjects with less than or equal to 36 months of data as well as among all 22 subjects who met inclusion criteria. The Delta Voice Handicap Index (VHI)-10 is the difference in VHI-10 scores between the two time periods (i.e., preinjection to best score postinjection). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

this paper adds to previous studies that demonstrate the effectiveness of CaHA.^{14–16,18} The average preinjection VHI-10 score was 24.5 for all subjects, and the average best postinjection VHI-10 score was 13.8 for all subjects, demonstrating a significant improvement ($P < .00005$).

Two subjects demonstrated significant worsening of their VHI-10 scores after their injection wore off, with a most recent VHI-10 score that was more than 4 points worse than their preinjection score (i.e., high negative Delta VHI-10 values). One of these subjects (subject 10) had a Delta VHI-10 score of -5 and had the complication of infraglottic migration requiring surgical excision. The other subject (subject 6) had Delta VHI-10 score of -7 and went on to have a subsequent CaHA injection 12 months after his first with longer term success. Subject 6 represents the first injection of a patient with two separate injections for two subject data points. Interestingly, his first injection lost its benefit by 9 months, but the benefit of his second injection persisted longer than 24 months (reported on Table I as subject 16).

We offer our institution's overall CaHA injection numbers to aid in the discussion of overall complications and method of CaHA delivery. Ninety patients received a total of 108 CaHA injections at the senior author's (c.a.r.) institution between April 2004 and July 2007. Fifty-one of these 108 (49%) were performed in the office with local anesthesia: 49 via the transoral route, one via the transthyroid cartilage route, and one via the transcricothyroid membrane route. Fifty-eight of 108 injections (54%) were bilateral. Twenty-two of 90 subjects (24%) were found to be deceased at the time of the review; however, only 18 of 90 (20%) had a terminal diagnosis at the time of their injection. Twelve of 90 patients (13%) were lost to follow-up, and the remainder (36 patients) did not have enough data points to be included in the study or did not return the survey to provide a recent VHI-10 score.

There were three complications for our 108 injections (2.8%; 1 of the 3 was from our 22 subjects): one superficial injection and two infraglottic submucosal col-

lections of CaHA. Although not life threatening, these complications did require surgical removal. One infraglottic collection was due to inadvertent placement during an in office transoral injection, and the second was from presumed CaHA migration, as the collection was not recognized during the injection that was performed under microscopic visualization via general anesthesia.

DISCUSSION

Many questions have been posed in regard to the longevity of CaHA and its potential for long-term complications. These questions are partly due to persistent concerns that remain following the use of Teflon; resultant granulomas continue to be seen a decade or so after Teflon stopped being used as a VF injection material. The potential for any permanent VF augmentation material to cause untoward long-term complications after placement would, obviously, not be known until the complication were to occur. In addition, it is not yet clear whether CaHA should be placed in the category of a permanent injectable and should therefore carry the concerns physicians have for long-term side effects. This study was meant to determine how long CaHA provided benefit for our patients and to review the long-term data at one institution in regard to any untoward complications of using CaHA as a VF augmentation material.

Our review affords evidence that, in the majority of cases, the benefit of CaHA as a VF augmentation material has worn off before the 24-month time point and, on average, lasts approximately 19 months. Statistical evaluation comparing the mean Delta VHI-10 of preinjection and best postinjection VHI-10 scores to the mean Delta VHI-10 of the preinjection and most recent VHI-10 scores confirmed the overall loss of benefit for our entire cohort, despite 36% of subjects demonstrating persistence of benefit on or after 24 months. Imaging studies such as computed tomography to confirm the presence of CaHA in the VF were not available or pursued in this study given that this testing is outside our routine clinical care. Without follow-up imaging, it is impossible to know whether all of the material is truly gone; however, the clinical picture suggests this may be the case.

Three complications were found on review of 108 CaHA injections, and all required operative excision; none was life threatening, and all were realized within a short time after the injection if not during the time of the injection procedure itself. The errors that caused these complications were technical in nature and by no means CaHA-specific complications or ones that could have been avoided with other VF-injectable materials.²⁰ Placement of CaHA into the superficial layer of the VF should obviously be avoided and is reported here and by others to cause significant vibratory stiffness and resultant dysphonia.²¹ Removal of a superficial injection by a microflap technique appears to be warranted when it inadvertently occurs, and many reports have emphasized the importance of a "deep" plane of injection when using CaHA to avoid this complication.^{1,18,21} A more recent paper by Gillespie et al. describes a 21% complication rate with CaHA, and the majority of the complications were

TABLE I.
Subject Data.

Subject No.	Age, yr	Diagnosis	Side	Total Volume (mL)	Pre-injection VHI	1-3 Month VHI	4-6 Month VHI	6-9 Month VHI	9-12 Month VHI	13-15 Month VHI	16-18 Month VHI	19-21 Month VHI	21-24 Month VHI	Recent VHI	No. of Months From Injection to Recent VHI	Best VHI	VHI Delta Pre to Best	VHI Delta Pre to Recent Or Post 24 Months
1M	63	Paralysis	Unilateral	NA	40		34	40						40	8	34	6	0
2F	56.8	Paralysis	Unilateral	0.5	12	10	0		15					15	11	0	12	-3
3M	86	Atrophy	Unilateral	0.35	34	36	32	29	34					34	11	29	5	0
4F	55.2	Paralysis	Unilateral	0.25	24	17	19	14	22	C				22	11	14	10	2
5F	69	Paralysis	Unilateral	NA	29	18	19	19	21	G				21	12	18	11	8
6M	62.7	Paresis	Bilateral	0.6	8	13	6		15	C				15	12	6	2	-7
7M	72	Atrophy	Bilateral	0.85	14	12	7	10		16				16	14	7	7	-2
8M	80	Atrophy	Bilateral	0.5	24	23				15	G			15	14	15	9	9
9M	84	Atrophy	Bilateral	0.4	32	17	24	25	22		28	C		28	17	22	10	4
10M	77.9	Atrophy	Unilateral	0.5	26	17	16			31	31	30	29	31	17	16	10	-5
11M	78	Scar	Bilateral	NA	23	14						21	25	25	20	14	9	-2
12M	71	Paresis	Unilateral	0.45	40	34	29	27		28	16		22	25	24	16	24	15
13F	48	Paralysis	Unilateral	0.4	21	7	13							19	24	7	14	2
14M	71.6	Paralysis	Bilateral	0.4	18	24					13			17	30	13	5	1
15M	81.7	Atrophy	Bilateral	1.45	19	15	14	11	5	5			7	0	36	0	19	19
16M	62.7	Paresis	Bilateral	0.6	15	12	7		5					17	36	5	10	-2
17F	53.4	Paralysis	Unilateral	0.3	23		17							18	37	17	6	5
18F	55.2	Paralysis	Bilateral	NA	22	31	27		20		17		18	16	44	14	8	6
19M	57.4	Paralysis	Unilateral	NA	20	9		10						10	50	9	11	10
20F	73.5	Paralysis	Bilateral	0.35	27	18		21	20					18	53	18	9	9
21F	60.3	Paresis	Bilateral	0.65	40	36	33		34					21	58	21	19	19
22F	47.7	Paralysis	Unilateral	0.25	28	9	9			10				8	60	8	20	20

Raw data are presented for the 22 subjects. Subjects 6 and 16 represent the course of two separate injections in one patient. Subjects 4 and 18 represent the course of two separate injections in another patient. Two injections in one patient independently met criteria for inclusion as separate study subjects.

VHI = VHI-10; M = male; NA = not available; F = female; C = calcium hydroxyapatite injection; G = Gore-Tex medialization laryngoplasty.

due to superficial injection of CaHA. The authors of that paper posit that CaHA should be placed in the controlled setting of general anesthesia.²² The current study and the previous studies by Rosen et al. and Kwon et al. support the idea that placement of CaHA in both the office and operative setting is safe and effective.^{18,19} Emphasis must be placed on the experience and comfort level of the physician performing the injection when deciding whether the in-office approach is appropriate to avoid untoward immediate complications (such as superficial injection, overinjection, underaugmentation, or placement in the subglottic area rather than lateral to or deep within the thyroarytenoid-lateral cricoarytenoid muscle complex).

The current study was not intended to evaluate the safety and satisfaction of patients after CaHA injection, as these findings have already been demonstrated in previous studies.^{14–16,18,22} However, our study did demonstrate a statistically significant improvement from preinjection to postinjection VHI-10 scores. More literature continues to emerge surrounding CaHA as a viable injection material for VF augmentation. A recent study by Kwon et al. demonstrated the effectiveness of CaHA for a period of 12 months in those with bilateral VF atrophy.¹⁹ Gillespie et al. demonstrated subjective effectiveness for 62% of their subjects after injection of CaHA for GI due to paresis and paralysis but also VF scar. Their lower than previously reported subjective satisfaction rates were concisely theorized to be due to inclusion of patients with glottic soft-tissue defects (i.e., cancer excision patients), longer average follow-up times, and voice care within the setting of a general otolaryngology clinic instead of a tertiary laryngology clinic.²²

As in the Gillespie study, this paper did not exclude those with diagnoses of scar when considering its outcomes. The use of CaHA to improve GI due to bad VF scar or previous cancer resection that has left a muscular defect of one or both VFs is often disappointing. A trial VF injection with a short-term augmentation material in the setting of scar and GI is often advised before proceeding to permanent augmentation.²³

Using a return to within 4 VHI-10 points of the preinjection value to demonstrate loss of benefit could possibly be better addressed by using a percentage of the original values; however, as is used clinically, it is the trend of VHI-10 scores that is more valuable rather than absolute values (all data are presented in Table I). Sixty-four percent of subjects in this study demonstrated loss of benefit after injection, leaving 36% with a persistent benefit at the time of data collection (Table I). Because two of the eight patients with persistent benefit were doing so at or less than 36 months postinjection (and were essentially within the range of our cohort who eventually lost their benefit), they should not be considered as part of the long-term benefit group. Additional consideration, though, is given to those six subjects with evidence of true benefit greater than 36 months (the long-term benefit group). They were all subjects who completed the survey and met criteria for inclusion and were uniformly subjects who remained satisfied with their voices for the longest periods of time. The reason none of these subjects

demonstrated loss of benefit after the 36-month time point may be explained by the likelihood that patients who had lost their benefit would have already returned to the laryngology clinic for further treatment and therefore would not have been contacted by survey for recent VHI-10 data. Thus, those who filled in the surveys may represent a smaller group of patients with persistent benefit who did not return for further evaluation. Regardless, in an effort to avoid any possibility of a reporting bias in the long-term benefit group, subjects with a benefit of less than 36 months were analyzed both as a separate group and as part of the entire cohort for the long-term average duration of benefit analysis.

Bias aside, why six of 22 subjects (27%) had a clear persistence of benefit past 36 months (more than 50 months in 4 cases and 60 months in 1 case) must be addressed. The postinjection VHI-10 scores clearly demonstrated an improvement over the pre-VHI-10 scores, and the most recent VHI-10 scores continued to demonstrate the benefit of augmentation. The number of subjects for statistical comparison between the group that had a benefit longer than 36 months and the group that had a benefit less than or equal to 36 months was small; however, some areas of explanation for the longer benefit can be addressed. The amount of CaHA injected into the VFs was similar ($P = .5$) for the pre- and post-36-month time point groups. The ages of the subjects, however, in the group that benefited longer than 36 months were statistically lower ($P = .02$). There may be a greater chance of reporting a long-term benefit in a younger population because a cohort of older subjects may have more deceased members and thus have less people responding to the follow-up survey. Five of the six subjects (83%) with a benefit greater than 36 months had a diagnosis of UVFP, as compared with only six of 16 (38%) with a loss of benefit or benefit less than or equal to 36 months. It is possible in the setting of UVFP that the position of the VF can migrate medially over time. If synkinesis of the recurrent nerve is present providing bulk to the thyroarytenoid-lateral cricoarytenoid muscle complex and the VF position migrates in a favorable fashion, the perceived long-term benefit of the CaHA injection may reflect this phenomenon despite the material being most likely resorbed. Alternatively, the nature of CaHA is to have resorption by the body's immune system with some fibrous ingrowth where the material was placed. In the report by Chhetri et al., a local foreign body reaction to the CaHA particles was present, but neither signs of inflammation in the larynx nor any evidence of CaHA in the regional cervical lymph nodes was seen.¹⁶ It is less likely, but theoretically possible, that some patients experience enough of this fibrous ingrowth to allow a long-term benefit.

Bilateral injections were seen in half of our subjects, and this finding should be emphasized. A unilateral diagnosis does not always warrant only a unilateral injection; the experience of the surgeon should determine whether or not to augment the mobile, opposite VF in the setting of a unilateral process to afford the best resolution of the underlying GI. In regard to the question of using CaHA in otherwise young and healthy

patients without a terminal diagnosis, only 20% of our population had a terminal diagnosis at the time of injection.

CONCLUSION

The benefit of CaHA as a VF augmentation material was found to last an average of 18.6 months in the majority of our patients. There were three complications identified among 108 injections performed at our institution since April 2004, and all required operative removal of the CaHA. No complication was due to the CaHA material itself, and the technical problems encountered could have been seen with other injectables. Attention should be paid to avoid superficial injection and subglottic injection. With appropriate experience and confidence by the injecting physician, CaHA is safe to inject in the office with use of local anesthesia. CaHA is a long-term injectable with an excellent track record that does not appear to warrant concern for permanent or late complications.

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