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ORIGINAL ARTICLE

A split-face, blind, randomized placebo-controlled clinical trial investigating the efficacy and safety of hyaluronic acid filler for the correction of atrophic facial scars

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Abstract

Background: Hyaluronic acid fillers have been studied extensively for facial wrinkles; however, their efficacy for atrophic facial scars has yet to be analyzed in a prospective placebo-controlled study.

Objective: To analyze the efficacy and safety of a hyaluronic acid filler for atrophic facial scars.

Methods & Materials: Fifteen subjects were randomized to receive up to 1 ml of VYC-17.5 L on one cheek and up to 1 ml of saline on the other side, with an optional touch-up treatment. Subjects were graded by a live blind evaluator using the Quantitative Global Scarring Grading System (QGSGS) (J Cosmet Dermatol. 2006;**5**:48), the Global Aesthetic Improvement Scale (GAIS), and Canfield photo-analysis.

Results: According to the blind evaluator, there was a significant reduction 90 days after the last treatment on the QGSGS for VYC-17.5L compared with saline (−6.6 VYC-17.5L vs −1.7 saline [$t(28) = -4.3196$, $p = 0.008$]). There was a smaller, but still significant reduction on the QGSGS for saline alone (10.4 to 8.6 [$t(14) = -3.453$, $p = 0.004$]). In addition, 93% (13/14) of subjects chose VYC-17.5L over saline treatment and reported an improvement on the GAIS. There were no serious side effects and all minor side effects resolved by Day 30.

Conclusion: VYC-17.5L achieved significant improvements in rolling atrophic scars as compared to saline, though saline also had modest improvements.

KEYWORDS
acne scarring, atrophic scar, hyaluronic acid, rolling scar, scar

Abbreviations: Er:YAG, erbium:yttrium–aluminum–garnet, FDA, federal Drug AdministrationGAIS, Global Aesthetic Improvement ScaleHA, Hyaluronic AcidIDE, Investigational Device ExemptionNS, normal salinePIH, Post-inflammatory HyperpigmentationPMMA, polymethylmethacrylateQGSGS, Quantitative Global Scarring Grading SystemVYC-17.5L, Juvederm Vollure.

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1 | INTRODUCTION

Atrophic scars have a myriad of etiologies including acne (most common), varicella, surgery, and trauma. Most adolescents and some adults experience acne, with many having some degree of secondary scarring. Atrophic scarring is an unfortunate permanent potential complication that can be difficult to treat and result in significant psychological distress. General and cosmetic dermatologists are often confronted with the challenge of treating these patients.

Current treatment options for atrophic scarring, include hyaluronic acid (HA)[1-7] or polymethylmethacrylate (PMMA) fillers,[8-10] chemical peels,[11] ablative or non-ablative laser treatments,[12-16] dermabrasion,[14] punch techniques,[17] microneedling[18-21] with or without radiofrequency,[22] fractional micro-plasma radiofrequency,[23] botox,[24] and subcision.[25-27] Most of these treatments have limited efficacy, possible side effects, and prolonged downtime.

There is a paucity of high-quality data to inform physicians and patients on the best approach to treating atrophic acne scars. A 2016 Cochrane Systematic Review on atrophic acne scarring concluded that most studies were "underpowered," employed "poor methodology," and "lacked standardized assessments."[28] While the authors mentioned there is "moderate quality evidence that injectable filler might be effective for treating atrophic acne scars," the "absence of studies that establish efficacy compared to placebo or sham interventions," was the reason they did not support first-line use of any intervention for the treatment of acne scars.[28] They recommended placebo trials to "to establish whether any of the active treatments produce meaningful patient benefits over the long term."[28]

The Federal Drug Administration (FDA) has approved many HA fillers which differ in cross-linking technology, percentage of cross-linking, hyaluronic acid concentration, particle size, viscosity, hardness, cohesivity, and ease of injection. These differences allow for tailored treatments. *Juvéderm* Vollure (VYC-17.5L; Allergan plc) was chosen for atrophic scars that have a thin dermis due to its particle size, cross-linking, and ability to spread and integrate into surrounding tissue. Therefore, it has the potential to create a smooth, long-lasting, volumized appearance and a natural look in a dynamic area such as the face. Hyaluronic acid can be reversed with hyaluronidase injection, so it has less risk of irreversible complications that come with the use of permanent fillers such as polymethylmethacrylate (PMMA), which is FDA approved for this condition.[10]

While there are no robust placebo-controlled clinical trials utilizing HA filler for atrophic scarring, smaller non-controlled studies have shown that HA fillers improve acne scarring through soft tissue augmentation and stimulation of collagen production. These trials of various hyaluronic acid fillers suggest high treatment satisfaction with minimal adverse effects such as transient and minimal erythema, bruising, swelling, and pain.[2,4,7,29]

The first placebo-controlled clinical trial utilizing a HA filler to treat atrophic facial scars is vital to assess the efficacy of HA filler because inserting the needle without injection[25,27,30] or with saline injection[31,32] is a stand-alone treatment for atrophic scarring. Since HA filler must be injected with a needle, it would be impossible to rule out the injection method alone as a contributing factor to the improvement in the atrophic scarring. This trial aimed to determine if the injection technique is effective with saline, and if so, how much in comparison to the injection with HA in the same subject.

2 | MATERIALS AND METHODS

A single-center study was performed at a private practice in Boynton Beach, Florida.

2.1 | Patient selection

Subjects 22 years of age and older with scores from 4–55 on the Quantitative Global Scarring Grading System (QGSGS)[33] in good general health were eligible to enroll. Exclusion criteria included the following: allergy to hyaluronic acid or lidocaine, neuromodulators in the previous 6 months or hyaluronic acid filler in the previous year in the treatment area, history of surgery or non-hyaluronic acid fillers in the treatment area, pregnancy or nursing, and the need to use anticoagulants, chemotherapy, immunosuppressive or immunomodulatory agents, diuretics, antihistamines, or anti-inflammatory drugs 2 weeks before or during the trial.

2.2 | Study design

The clinical research coordinator and investigator recruited, enrolled, consented, and assigned fifteen subjects (30 cheeks) over 6 months using random sorting with a computer-generated sequence into the following groups: (1) Up to 1Ml of VYC-17.5L on the right and saline on the left and (2) up to 1 ml of VYC-17.5L on the left and saline on the right.

Subjects were blind until the primary endpoint and the evaluator remained blind throughout the study. A touch-up with up to 1 ml on each side with the same group assignment was allowed on Day 30 if deemed appropriate by the primary investigator. Subjects were graded by a live blind evaluator, Canfield standardized photos were done with photo-analysis, and questionnaires and diaries were completed by subjects and analyzed. On Day 120, the side receiving saline was eligible to receive a crossover treatment with up to 2 cc of VYC-17.5L.

2.3 | Treatment

Topical anesthetic cream (benzocaine 20%, lidocaine 10%, and tetracaine 6%) was applied to the treated area for 30 min and wiped off with 70% isopropyl alcohol. A single dermatologist (Dr. Siperstein) performed the injections. The treatment area included atrophic scars in the area outlined in Figure 1. A 30-gauge co-packed needle was used to inject both in a parallel plane for broader lesions with an average of 0.005 ml per thread and in a perpendicular plane superficially in the dermis with small aliquots of 0.002 ml (50 injections per 0.1Ml of product) creating superficial dermal blebs for all lesions which were smoothed out with a q-tip. The total amount of

filler used was based on the number, width, and depth of the scars according to the primary investigator. After injection and massage, ice packs were applied for 15 min with pressure.

2.4 | Study end points

The primary endpoint was the mean change from baseline to 90 days after the last treatment on the QGSGS (sample shown in Figure 2) in the VYC-15 L group vs saline group according to a live blind evaluator. The primary endpoint was scored in 14 out of 15 subjects (one subject was lost to follow-up). Secondary endpoints included (1) the Global Aesthetic Improvement Scale (GAIS), (2) the number of atrophic rolling scars, (3) side effects the first 30 days after treatment, (4) patient preferred treatment side, and (5) the change in the QGSGS and number of atrophic rolling scars on the saline side.

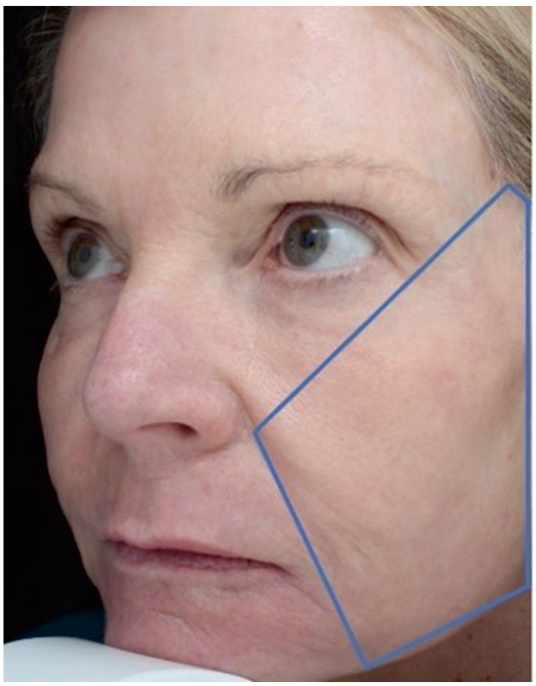


FIGURE 1 Outlined treatment area

2.5 | Safety assessments

Pain was self-assessed by subjects during, immediately after, and 30 min after injection. Vital signs and vision were tested both before and 30 min after the procedure. During all visits, including one 24–48 h after the treatment, the blind evaluator and investigator assessed the subject for any side effects. The subjects reported all side effects each day for 30 days after each treatment in their subject diaries and at every visit.

2.6 | Statistical analysis

When analyzing the mean change on the QGSGS or number of atrophic rolling scars, a dependent Student's *t*-test with a two-tailed hypothesis was used to verify VYC-15L's superiority over saline. Descriptive summaries of categorical outcomes include the types of side effects reported, skin types, and sex of the subjects, while descriptive summaries of continuous measures include the subject's age, and baseline scores on QGSGS which are reported with the number of subjects (*n*), mean, median, minimum, and maximum. The Chi-Square was used to test the difference in the incidence of side effects between the VYC-17.5L and saline group.

3 | RESULTS

3.1 | Demographics

All subjects' ages ranged from 26–59 (Mean 42.1, Median 39). There were 4 men and 11 women with at least two of each Fitzpatrick Skin Type. The average number of atrophic rolling scars at baseline according to the blind evaluator was 13 on both the left and right

Sample of QGSGS		Number of Lesions		
		1-10 Lesions	11-20 Lesions	>20
Milder Scarring		1 Point	2 Points	3 Points
	Mild atrophic dish-like	#3 (1 Point)		
Moderate Scarring		2 Points	4 Points	6 Points
	Moderate atrophic dish-Llke	#1 (2 Points)		
	Punched out with shallow base			
	Shallow but broad			
Severe Scarring		3 Points	6 Points	9 Points
	Punched out with deep but normal base			
	Punched out with deep abnormal base			
	Linear dermal scar	#1 (3 Points)		
	Deep broad atrophic area	#1 (3 Points)		
TOTAL		**#6 (9 Points)**		

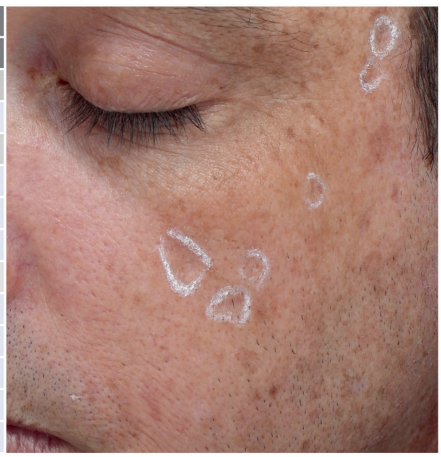


FIGURE 2 Sample Subject Scoring on the QGSGGS

(range 4–21, median 12). After randomization, according to the blind evaluator, the number of atrophic scars on the VYC-17.5L and saline assigned sides were 12.4 and 13.9, respectively, and the QGSGS score for the VYC-17.5L and saline assigned sides were 9.9 and 10.2, respectively.

3.2 | Product amount

All patients were treated twice, 30 days apart, with an average of 0.66 Ml of VYC-17.5L on the first treatment session on the assigned side and 0.61 Ml on the second treatment on that same side. The patient's opposite side served as the control and was injected with saline.

3.3 | Primary endpoint

The mean reduction in the QGSGS score as rated by the blind evaluator viewing live patients from baseline to 90 days after the last treatment was significantly lower in the VYC-L17.5 group (−6.6 reduction) as compared to the saline group (−1.7 reduction) [$t(28) = -4.320$, $p = 0.0008$]. Similarly, the investigator scores showed the same significant findings (−7.1 VYC-17.5L vs −1.4 saline [$t(28) = -5.043$ $p = 0.0002$), shown in Table 1.

3.4 | Secondary endpoints

There was a significant reduction in the number of rolling atrophic scars in the VY17.5L side vs saline side 90 days after treatment according to both the blind evaluator and the investigator, respectively, (−8.1 VYC-L17.5 vs −2.1 saline [$t(28) = -6.2825$, $p = 0.00003$] and −8.0 VYC-17.5L vs −1.5 saline [$t(28) = -5.643$ $p = 0.00008$) also shown in Table 1.

When analyzing only the effect of saline treatments, there was a smaller, but still significant reduction in the QGSGS score from baseline to 90 days after treatment according to the blinded evaluator (−1.7) [$t(14) = -3.453$, $p = 0.004$]) and investigator (−1.4) [$t(14) = -4.177$, $p = 0.001$]. In addition, there was a significant reduction in the number of atrophic scars according to both the blind evaluator (−2.1) [$t(14) = -4.707$, $p = 0.0004$] and investigator (−1.5) [$t(14) = -3.3045$, $p = 0.006$]). Ninety days after the last treatment, 93% (13/14) of blind subjects chose VYC-17.5L as their preferred treatment, with 93% also selecting an improvement on the GAIS scale (1–3) and 71% 10/14 stating it was much or very much improved (2–3 on GAIS).

3.5 | Safety

All side effects reported in the patient diaries are listed in Table 2. There were no serious or long-lasting side effects, such as a granulomas, infection, or vascular occlusion reported by either subjects, blind evaluator, or investigator. The only significant difference between the VYC-17.5L and Saline side 1 day after treatment was more bumps on the active side (χ^2 [1, $N = 30$] = 6.5, $p = 0.01059$). All side effects were resolved by Day 30.

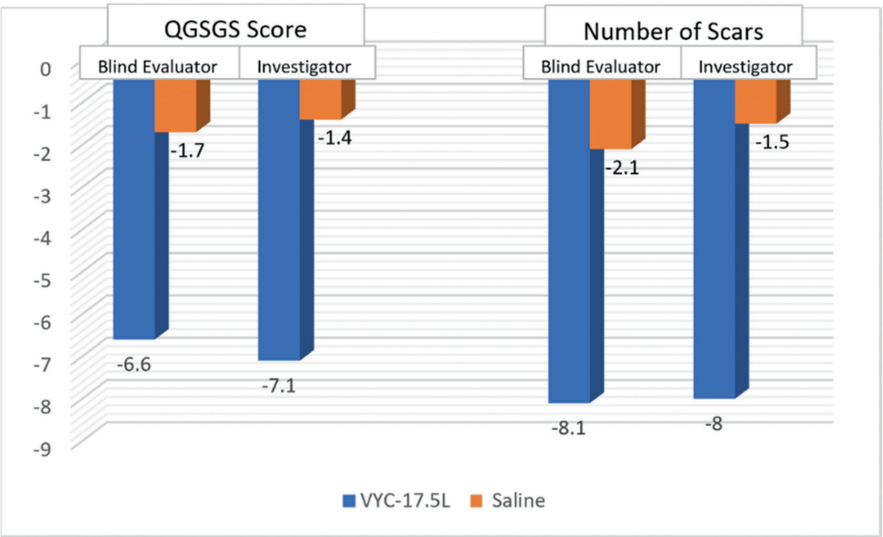
3.6 | Representative outcomes

Representative Outcomes from our trial can be seen in Figures 3–8.

4 | DISCUSSION

Atrophic facial scarring is a common condition that is difficult to treat and causes significant psychological distress. The most commonly described types of atrophic scars are ice pick, boxcar, and

TABLE 1 Reduction in QGSGS score and number



rolling,[34] of which rolling atrophic scars are the most amenable to treatment. While a variety of treatment options exist, outcomes are often sub-optimal, and a series of treatments are often necessary for modest improvement. There is a paucity of prospective, placebo-controlled clinical trials as well as limited comparative studies.

Subcision, microneedling, and fractional lasers are among the most popular treatment options for atrophic scars. First described in 1995,[25] subcision efficacy is based on the hypothesis that atrophic scars have an "anchor" "which is deep" and that "corrective measures must reach the deep dermis and subcutis."[4] Alam et al. reported in 40 patients with rolling acne scars there was improvement observed by both physicians and patients likely through skin remodeling. In addition, Balighi et al. reported efficacy in a study of Nokor subcision in the treatment of rolling acne scars in 20 patients. However, subcision takes a significant amount of healing time and potentially has considerable side effects such as pain,[26] swelling, scar formation, and infection.[27] In one study with 100 subjects, 18% of patients treated with needle subcision suffered from scar formation and 4% experienced skin infections.[27] In addition, the recurrence of the depression is a very common side effect,[27] particularly in the first 2–3 weeks after treatment, which is not corrected with repeated treatments or with placement of a subdermal implant.[35]

These temporary results from subcision are often secondary to inflammation during the post-procedural healing process. Ultimately, once the inflammation resolves, the recurrence of the depression is likely. This effect is also mirrored in microneedling studies. Geronemus and colleagues presented data in 2018[36] showing regression of effects following microneedling. Another study showed diminishing results at 6 months compared with 3 months.[37] Since the inflammatory response from the procedure can last 3 months in some patients, 30-day endpoints common in studies make it hard to determine if the improvement is a true long-lasting result or simply post-procedure inflammation. For this reason, waiting at least 90 days or longer after treatment for a primary endpoint analysis is vital. Microneedling, subcision, and fractional ablative or non-ablative resurfacing are all examples of treatments that cause post-treatment inflammation that can last months, especially when repeated treatments are recommended. In addition, these treatment modalities induce collagen broadly and moderately, often affecting both the scar and adjacent skin (blue area in Figure 9).

In contrast, filler offers more precise volumization only to the scar itself. Injection of atrophic scars with filler dates to the 1980's with bovine collagen. Since then, other long-lasting fillers have been used successfully such as autologous fat,[38] poly-l-lactic acid,[39] PMMA[8,37] and calcium hydroxylapatite[40]; however, any side effects with these cannot be easily treated since they are non-reversible. Currently, PMMA is the only injectable filler with an FDA indication for treating atrophic scars and requires a skin test since it contains bovine collagen. In a phase 3 trial with 147 subjects, success (2-point improvement on a 4-point scale) was achieved by 64% of subjects receiving PMMA and in 33% of those receiving saline. Interestingly, 91% and 76% of scars treated with PMMA and saline, respectively, achieved a 1-point improvement, and 84% and 52% of the subjects were satisfied with PMMA and saline treatment, respectively.[9]

TABLE 2 Patient-reported side effects

Side effect	% Patients day 1	Last day reported
Pain	46.6%	Day 8
Tenderness	60%	Day 12
Redness	60%	Day 11
Bruise	53.3%	Day 8
Swelling	60%	Day 8
Itching	26.6%	Day 21
Bumps	26.6%	Day 29

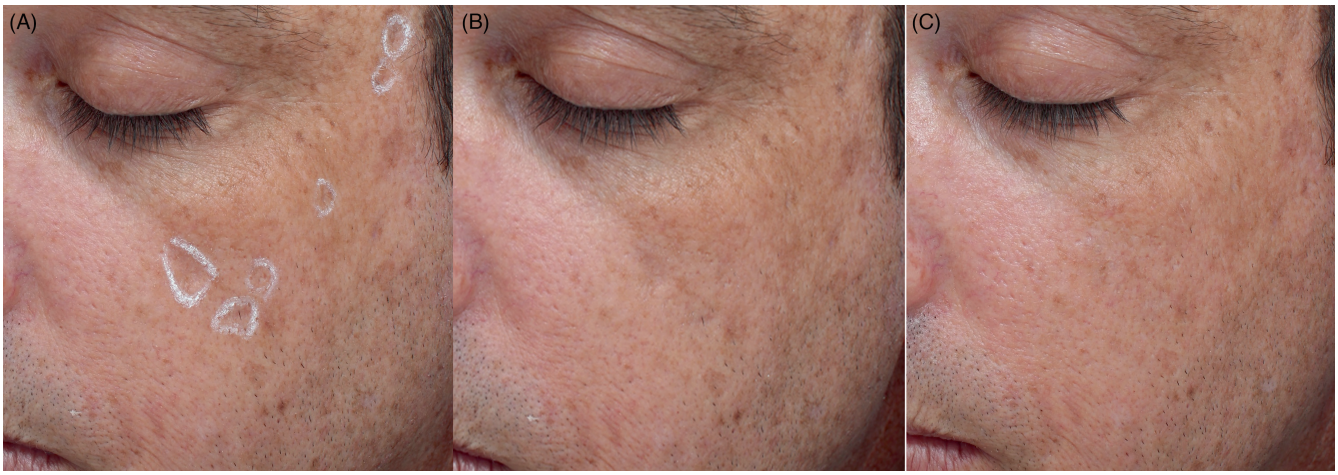
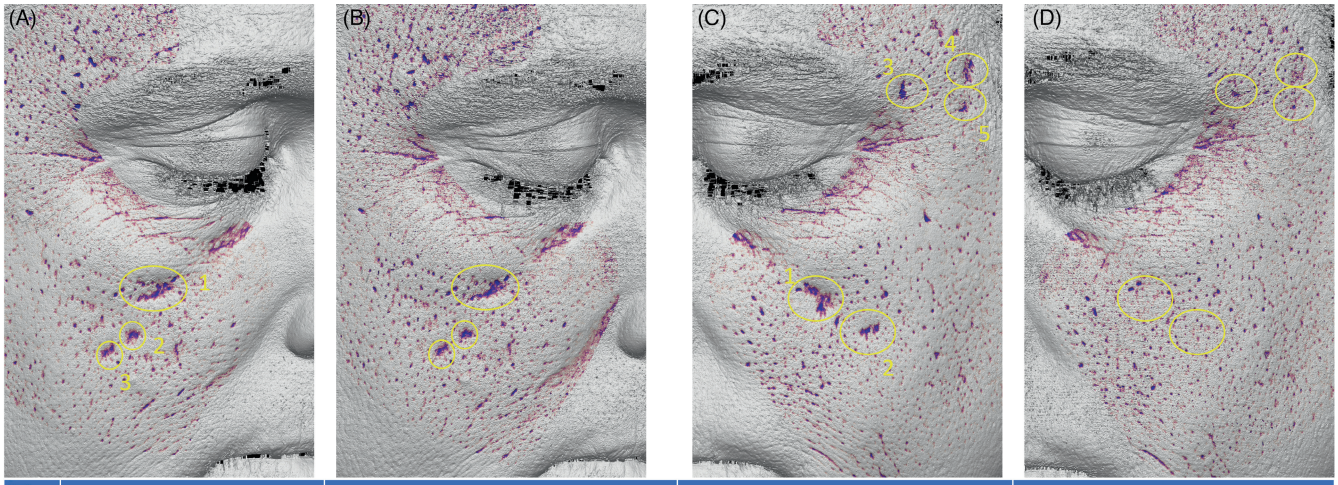


FIGURE 3 (A–C). Canfield Visia photographs showing 59-year-old man with (A) circled atrophic scars according to a live blind evaluator, (B) immediately before treatment, and (C) 90 days after treatment

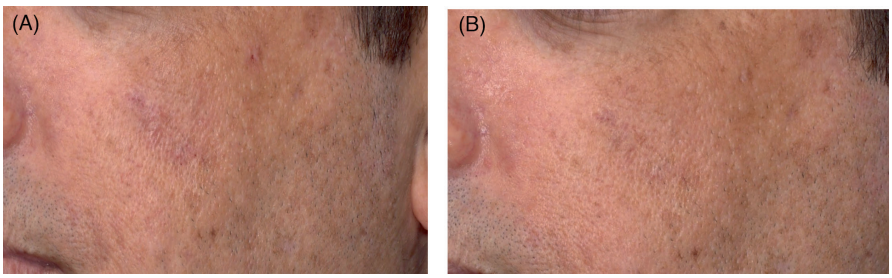


(E)

#	Baseline Right (mm3)	Day 120 Post Saline Tx Right (mm3)	Baseline Left (mm3)	Day 120 Post VYC-17.5L Tx Left (mm3)
1	15.25	15.75 | +3.23%	23.06	5.99 | -74.02%
2	4.97	4.13 | -16.95%	4.37	2.68 | -38.62%
3	3.59	4.04 | +12.77%	4.27	1.07 | -75.08%
4	-	-	10.51	3.93 | -62.61 %
5	-	-	2.49	2.25 | -9.73%

FIGURE 4 (A–D). Canfield Primos 3D Photo-analysis of 59-year-old male (A) before and (B) after treatment with saline on the right and (C) before and (D) after treatment with VYC-17.5L on the left with (E) 3D photo-analysis of areas circled in yellow

FIGURE 5 (A and B) 59-year-old male (A) immediately after treatment with mild erythema and (B) 1 day after treatment



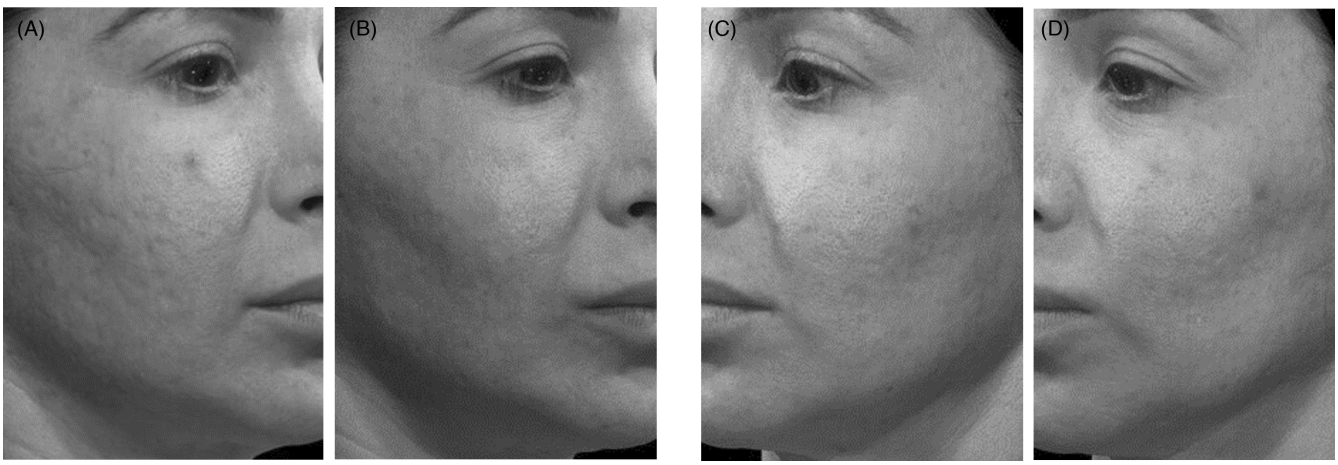


FIGURE 6 (A–D). 39-year-old female (A) before and (B) after treatment with VYC-17.5L on the right and (C) before and (D) after saline on the left

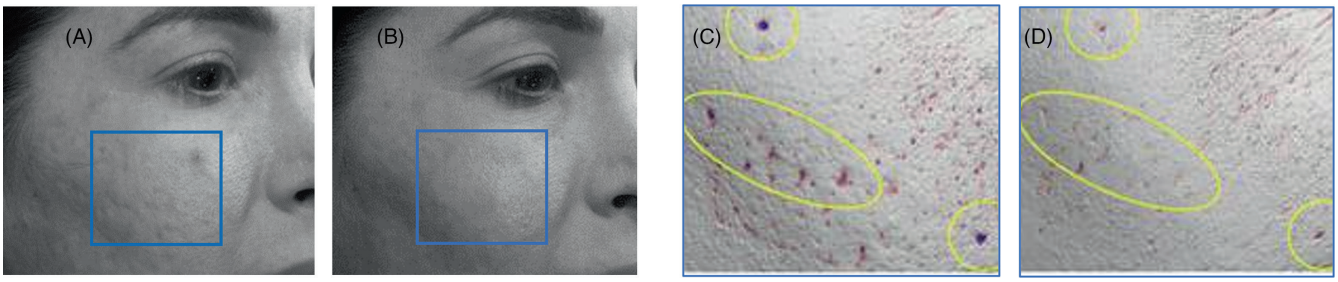


FIGURE 7 (A–D). 39-year-old female (A) before and (B) after treatment with close up 3D Primos color photo-analysis on the VYC-17.5L side (C) before and (D) after treatment

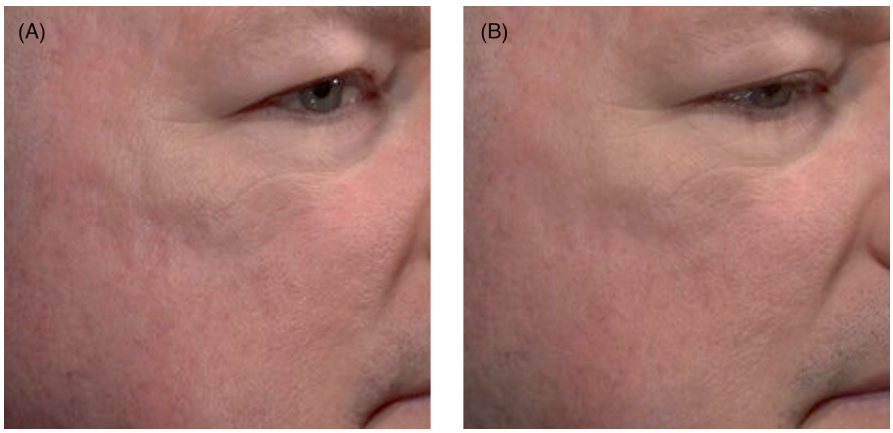


FIGURE 8 (A and B). 42-year-old male (A) before and (B) 90 days after saline treatment with modest improvement

A major limitation of PMMA is the concern of creating a visible permanent bump if too much is injected superficially, especially since optimal correction with atrophic scars often requires placing most of the filler in the superficial dermis to create maximum projection. HA's ability to be placed safely high in the dermis, along with its reversibility, gives it a more favorable risk profile than PMMA. Taken together, the efficacy of HA filler due to pinpoint volumization of the superficial dermis of the scar (Figure 9), its limited adverse event profile, minimal downtime (Figure 5), and ease of use without any testing before treatment, leads the authors to believe that HA fillers should be a first-line treatment in most patients with rolling distensible atrophic scars and in some distensible boxcar scars.

Hyaluronic acid is currently the leading dermal filler type for cosmetic use due to both its efficacy and improved safety (low allergenicity, longevity, and ability to be reversed). Hyaluronic acid filler in previous atrophic scar studies showed high treatment satisfaction with only mild transitory erythema, bruising, and mild to moderate pain during injection.[1-7] Goodman and Broek published the use of a modified tower technique, creating vertical posts through a retrograde injection bringing the HA up into the superficial dermis with resolution of over 70% of the scars.[2] This paper also noted the importance of injection of the superficial dermis to create blebs that could then be massaged out,[2] something that should not be done with PMMA. Artzi et al. and Hussain et al.[7,41] describe success using HA injections in both the subdermal and dermal plane, while another publication reports success with a micro-injector placing 0.01 ml of HA repeatedly in the superficial dermis until visible correction is noted.[4] While typically HAs are thought to last 3 to 12 months, they have recently been shown to last for over 10 years,[42] especially in areas with less movement.

When HA fillers are used for rhytids, the area continues to experience the motion originally causing the rhytid, likely pushing the filler away before it is completely metabolized. HA fillers last longer in atrophic scars since there is no continued trauma or inflammation which caused the previous damage. Patients who are concerned with using HA filler as first-line treatment due to longevity can be given the analogy of a folded shirt creating a crease. Once the crease has been ironed out (filled with filler), if the shirt is folded again (patient making expression that created the rhytid), the crease (wrinkle) will likely return. However, with atrophic scars, the ironed shirt stays unfolded (no continued trauma) resulting in long-lasting results. In this trial, all subjects received a second treatment to maximize efficacy as additional expansion of the dermis is often possible over time after inflammation from the first treatment is resolved. A 2-year study is currently underway to shed light on the exact longevity of this procedure; however, in the senior author's practice, this procedure lasts much longer than 2 years.

The potential for the appearance of bumps and a bluish discoloration with superficial HA filler needs to be addressed through the proper selection of both filler type and injection technique. Since the placement of HA filler in this trial was high in the dermis, small micro-droplets (0.002 cc) were injected. The HA filler (VYC-17.5L) chosen utilizes VYCROSS technology (developed by Allergan Inc.,

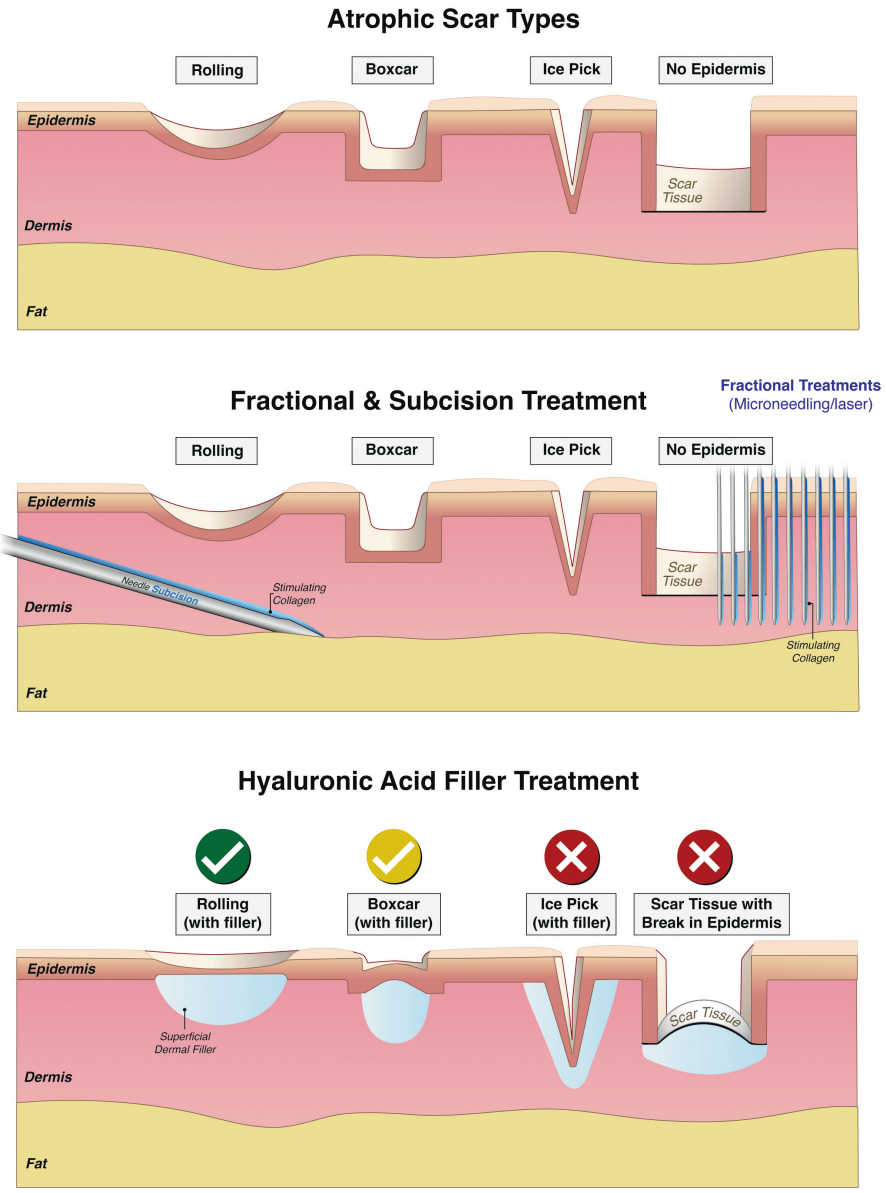


FIGURE 9 Atrophic scar types and common treatments

Irvine, CA, USA) with a high degree of cross-linking thought to be more resistant to enzymatic and free radical degradation increasing its longevity.[44] In addition, it is a viscoelastic, colorless, homogeneous soft HA gel with small particles, and a concentration of 17.5 mg/ml containing 3 mg/ml of lidocaine for patient comfort.[43] These properties were selected to create a long-lasting, smooth, and natural-appearing improvement. While this clinical study did not show any long-lasting side effects, this may not have been the case if a filler with different rheological properties or different technique was used.

Furthermore, the senior author believes most rolling atrophic scars are simply due to dermal atrophy rather than adherence to underlying tissue. With correct injection technique, the missing volume in rolling and some boxcar scars are easily and immediately replaced with HA filler. To determine if scars are good candidates for HA filler, the scar can be tested for the "Dimple Sign" by placing lateral inward pressure on the skin. If this pressure produces a depression (dimple) due to the attachment to the underlying subcutaneous tissue (positive dimple sign), then it likely will not be amenable to HA filler alone. In those cases, other treatments such as subcision, excision, or laser treatments may be helpful. If the dimple sign is absent and the skin pops up as in Figure 10, the scar is an excellent candidate for dermal fillers (See Video S1).

When assessing if a scar is amenable to HA filler, it is important to also analyze the epidermis. Atrophic scars with gentle sloping edges and fully intact normal epidermis (Figure 11 in green) will improve the most and complete resolution may be possible. Those in yellow will yield partial improvement (irregular edges/partially scarred base replacing some epidermis), and those in red will only have minimal improvement (deep edges/white scar tissue at the base with lack of normal epidermal connection). It is important to manage patient expectations based on these features.

For those with mixed scar types wanting the best results, erbium: yttrium–aluminum–garnet (Er:YAG) full ablative laser resurfacing

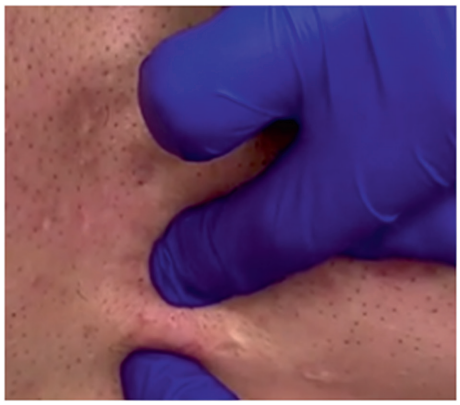


FIGURE 10 Negative dimple sign

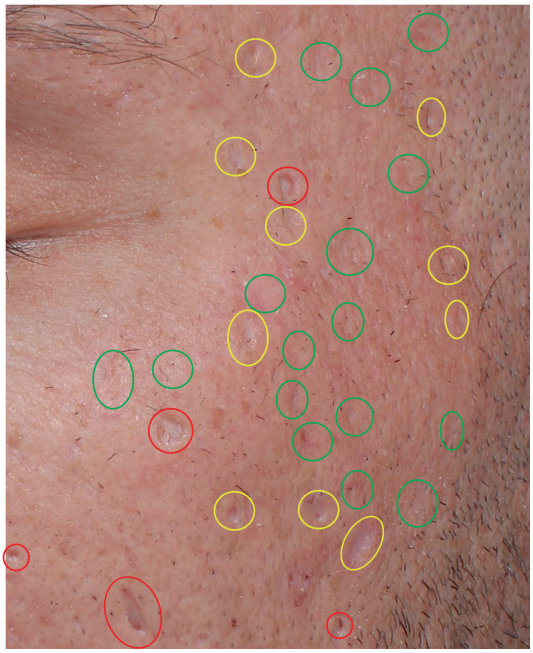


FIGURE 11 Multiple scar types

can correct some epidermal surface irregularities as a first step before HA filler. By targeting the edges and base of the scar to create smoother gentler sloping transitions, more difficult boxcar scars can often be transformed into rolling scars that are easier to treat with HA filler. Other resurfacing modalities such as carbon dioxide laser, deep chemical peels, and dermabrasion would also be effective for this purpose. However, it is important to note that several studies have shown HA filler destruction by energy devices[45,46] so it is best to treat with energy devices first.

If the HA filler has already been injected, an understanding of the depth of both the device and the HA filler is important. Due to the superficial nature of HA filler placement necessary for optimal results in atrophic scars, any treatment that extends into the dermis will likely interact with the filler. For example, microneedling with radiofrequency, deep fractional ablative laser, and deep nonablative lasers are not recommended after superfical HA is injected; however, ablative lasers, such as Er:YAG, used to treat the scar edges to contour the top layer of skin does not affect the filler. Darker skin types can experience post-inflammatory hyperpigmentation (PIH) with ablative lasers, though this condition is easily treated with topical hydroquinone and intense pulsed light in the author's practice. While PIH can occur from filler or saline injections alone, this was not seen in our trial likely due to the small 30-gauge needle and limited post-procedure erythema (Figure 5).

Since 2015, there have been several publications utilizing saline injections for atrophic acne scars showing significant improvement in scar severity and number, especially those with mild to moderate atrophic scars, as well as improvement in life quality index.[33,47] The hypothetical mechanism includes stimulating growth factor release from white blood cells and platelets to induce tissue growth,[47] stimulating collagen production and remodeling by fibroblasts, and subcision of collagen fibers and clot formation to elevate the skin and act as a lattice for extracellular matrix formation. In our study, both saline and HA showed a statistically significant improvement, but HA was superior at decreasing both number of atrophic scars (65% vs 15%) and QGSGS (62% vs 17%).

Normal saline (NS) is a 0.9% isotonic solution containing electrolytes (sodium and chloride ions). It is safe, inexpensive, as well as quick and easy to administer (takes only a few minutes to inject) with less side effects than most atrophic scar treatments. While saline injections are not commonly used in clinical practice, based on this study and previous studies in the literature, it should be considered for modest improvements in patients with mild to moderate atrophic scars who cannot afford HA filler or for those who do not have access to specialists. In fact, in the PMMA study, while saline was used only as a control, 76% of subjects experience a 1-grade improvement and more than half of the subjects were happy with saline treatment alone.[8] Further studies exploring the optimal amount of saline and frequency of injections to maximize results are needed. One comparative study of pneumatic injections of saline showed similar efficacy to subcision with less side effects.[26] Our study showed that HA filler was superior to saline, therefore based on this previously mentioned study, it can be inferred that is likely superior to subcision. A more recent study showed subcision with HA filler was superior to subcision with threads or subcision alone (improvements in 94.1%, 82.4%, and 67.3% of patients, respectively).[48] In our study, HA filler alone yielded a similar result in patient-rated improvement (93%) as the subcision with HA filler arm of that study[48] signifying that subcision may not be necessary. Therefore, we believe HA filler should be used as a first-line stand-alone treatment for distensible atrophic rolling scars.

Capturing photos of atrophic scars is challenging. Most standardized photo systems use direct illumination which causes scars to disappear, whereas tangential lighting can cause shadows, exaggerating the depth of these scars. Therefore, we not only had a live blind evaluator, but also used three different standardized photo systems. The Canfield Visia was used to capture 2D images under an array of different standardized lighting modalities. The Vectra

M4+ was used to capture full face 3D images and the Primos was used to capture half face, high-resolution 3D images able to accurately represent fine skin surface details. In addition, Canfield 3D Primos technology creates color height mapping (Figures 4 and 7), which shows an objective, measurable improvement in scar depth and volume. Since most scars improve without complete resolution, being able to objectively measure the volume of improvement in each scar instead of just reduction in the number of scars is invaluable.

The main study limitations include a small sample size, regional nature of a single-center study, and data up to 120 days. A longer 2-year extension of this trial is underway and will shed light on the longevity of HA filler for this condition. However, in this small short-term pilot study looking at subjects 90 days after their last treatment, there was a high degree of tolerability, safety, and effectiveness of HA filler for atrophic rolling scars. Future studies comparing the efficacy and longevity among different HA fillers would also be helpful but was beyond the scope of this trial.

5 | CONCLUSION

There are many treatment options for atrophic scars, however, few placebo-controlled, blinded, prospective studies analyzing efficacy. VYC-17.5L injected in the dermis with a needle micro-droplet technique achieved a significant reduction in the QGSGS and number of atrophic rolling scars as compared to saline without any significant side effects. In addition, when cost is a large consideration, saline alone was able to achieve an improvement though to a much lesser degree.

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CONFLICT OF INTEREST

Dr. Siperstein: Allergan - Consultant, Clinical Trial Investigator and Trainer.

AUTHOR CONTRIBUTIONS

Dr. Siperstein performed all the treatments and follow-up visits. Dr. Nestor and Dr. Meran were blinded evaluators and Dr. Grunebaum was the sub-investigor. The paper was original drafted by Dr. Siperstein, but significant written contributions to the paper were made by all four authors.

ETHICAL APPROVAL

The study was carried out in accordance with the ethical guidelines and principles of the 1975 Declaration of Helsinki and good clinical practice. The protocol received Investigational Device Exemption (IDE) approval on June 17, 2020, from The Food and Drug Administration (FDA), and was approved on August 10, 2020, by Sterling IRB (ID #8117).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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