Received: 28 March 2019 | Revised: 13 April 2019 | Accepted: 16 April 2019

DOI: 10.1111/jocd.12991

ORIGINAL CONTRIBUTION

JCD Journal of Cosmetic Dermatology WILEY

Dual-plane hyaluronic acid treatment for atrophic acne scars

Ofir Artzi MD[1] | Sarit Cohen MD[2] | Amir Koren MD[1,3] | Roni Niv MD[3] | Or Friedman MD[4]

[1]Department of Dermatology, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel

[2]Department of Plastic and Reconstructive Surgery, Assaf Harofeh Medical Center, Zeriffin, Israel

[3]Dr. Artzi Clinic and Research Center, Tel Aviv, Israel

[4]The Plastic and Reconstructive Surgery Department, Tel Aviv Sourasky Medical Center, affiliated with the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

Correspondence
Or Friedman, The Plastic and Reconstructive Surgery Department, Tel Aviv Medical Center, 6 Weizmann Street, Tel Aviv 6423906, Israel.
Emails: or.friedman@gmail.com; orfriedman@tauex.tau.ac.il

Abstract

Background: Acne is a common condition that affects up to 80% of all adolescents. Scarring may affect some 95% as a function of severity and delay before treatment. The pathogenesis includes enzymatic degradation of collagen fibers and subcutaneous fat.

Objective: This study aimed to treat atrophic acne scars using the Dual-Plane injection of Hyaluronic Acid.

Methods: A total of 12 patients with moderate-to-severe atrophic acne scars were treated with a novel NAHYCO™ based Hyaluronic Acid filler, using a dual-plane technique for two treatment sessions at a 4-week interval. Results were objectively assessed by two blinded Dermatologists and subjectively evaluated by the patients themselves.

Results: A total of 8 out of the 12 patients reported moderate improvement, two indicated marked improvement and two rated minimal improvement. Dermatologists' mean global evaluation score was 2.5 ± 0.43.

Limitations: The small sample size and regional nature of a single-center study. Nevertheless, both the expert dermatologists' and the patients' evaluations of standardized high-resolution medical photographs were consistent, suggesting that this inherent bias was negligible.

Conclusion: The treatment led to impressive improvement in the depth of the scars, suggesting that this technique can result in safe and rapid amelioration of atrophic acne scars in only two sessions.

KEYWORDS

acne scar, atrophic, hyaluronic acid, hybrid cooperative complexes

1 | INTRODUCTION

Acne is a common inflammatory condition that affects up to 80% of the adolescent population to varying degrees[1-8] and can result in permanent scars.[9] Scarring may affect some 95% of patients with this disease, as a function of its severity and the delay before treatment.[6]

Atrophic acne scars are the most common subtype.[1,3,10] The pathogenesis of atrophic acne scarring is most likely related to inflammatory mediators and enzymatic degradation of collagen fibers and subcutaneous fat.[1] The most basic and practical system divides atrophic acne scars into three main types known as ice pick, rolling, and boxcar.[11-13] Many types of treatment are available to reduce the appearance of these scars, but the treatment of acne scars needs to

be individually tailored for each patient depending on the types of scars present.

Different dermal and subcutaneous filling for scars is an attractive choice for both physicians and patients because it provides a simple and accurate nonsurgical correction of atrophic scars that produce immediate improvement.[14,15] The use of HA-based fillers in the treatment of acne scars is well established.[16,17] This retrospective case series describe a new technique using a novel patented (WO/2012/032151) NAHYCO™ technology based filler[18] commercially available as ProfHilo® for the treatment of acne scars.

2 | MATERIALS AND METHODS

Twelve patients aged 23-52 (mean 33.2 ± 9 years) with Fitzpatrick skin phototypes II to IV and moderate-to-severe atrophic acne scars were treated. Acne scars were graded using the Goodman and Baron qualitative scarring grading system.[6] The dominant scar type was rolling. Six patients had previously undergone laser treatment, four had undergone radiofrequency treatment, but none had been treated by injectables before the study. The average duration of scars was 8 (1-20) years. The baseline demographics are presented in Table 1.

Written-informed explanatory consent was obtained from all the patients before treatment. Patients with a history of active herpes, photosensitivity, pregnancy or lactation, a previous history of hypertrophic or keloidal scarring, a history of facial laser treatment, or surgical procedures in the area of acne scars within the last 6 months were excluded.

Before the procedure, the face was cleansed with a mild cleanser. Then, 5% lidocaine cream (EMLA; AstraZeneca) was applied to the treatment area and removed 1 hour later. Post-treatment care consisted of the application of antibiotic cream twice daily for a week and a broad-spectrum sunscreen with a sun protection factor of at least 30 SPF. Patients were instructed to avoid exfoliants, not to excoriate the healing lesions, and to avoid exposure to the sun. All patients received two treatment sessions at a 4-week interval. Patients were followed up 1, 3, and 6 months after the last treatment.

The dual-plane technique consists of filling the atrophic dermal component of the scar and then addressing the subdermal element by subcision and placement of a small amount of HA for regenerative stimulation. In the sample treated here, each marked scar was filled in the dermis with 0.02-0.1 mL of Hyaluronic Acid (HA) (Profhilo®, IBSA Farmaceutici Italia), using a 29G syringe (Figure 1A). The second injection pass was done immediately afterward using a 25g cannula inserted into the superficial hypodermis using the blunt cannula to disrupt the subcutaneous fat under the superficially injected scars (Figure 1B). Areas were massaged as required to flatten the filler and ensure correct placement.

Two dermatologists blind to the treatment assignment rated the degree of improvement by comparing random mixed side-by-side photographs taken at baseline before the first treatment and at 1, 3, and 6 months after treatment. The pictures were taken by VISIA® (Canfield Scientific, Inc). Grading scales were as follows: Grade 1 = 0%-25%, minimal to no improvement/unsatisfied; Grade 2 = 26%-50%, moderate improvement/slightly satisfied; Grade 3 = 51%-75%, marked improvement/satisfied; and Grade 4 = >75%, near total improvement/very satisfied (Table 2). Before each grading session, sample photographs from previous studies with a similar grading system were provided as training for the raters.

Each patient was provided with the same set of baseline, and 1, 3, and 6 months post-treatment digital photographs as those evaluated by the dermatologists. They were instructed to rate the changes using the same grading systems as those used by the expert dermatologists.

Immediately following each session, as well as before each treatment, patients were asked to report any adverse events. After each treatment, the patients rated their pain level on a visual analog scale (VAS 1-10).

Baseline characteristics and side effects were calculated using descriptive statistics (mean values with standard deviations or median with interquartile range). The degree of improvement as rated by the expert dermatologists and the patient evaluations are reported as medians. Objective measurements were calculated as the median percent change. All statistical analyses including inter-rater reliability implemented the SPSS program (Version 22, SPSS Inc, Chicago, IL, USA).

3 | RESULTS

Twelve patients with moderate-to-severe acne scars were treated in the senior author's private clinic from January through August 2018. Most patients had Fitzpatrick skin phototype III (II-IV) as shown in Figure 2.

Eight out of the 12 patients reported moderate improvement (Grade 2) at 6 months post-treatment. Two patients indicated marked improvement (Grade 4), whereas two patients rated minimal improvement (Grade 1). This corresponds to the dermatologists' mean global evaluation score at 6 months, which was 2.5 ± 0.43 (the experts' overall score at 1 month, after the second treatment was 3 ± 0.5; at 3 months was 2.5 ± 0.49 and at 6 months was 2.5 ± 0.43). The interclass correlation coefficient (inter-rater reliability) was 0.72. The mean pain scores (VAS) were 2.3 ± 1.3 and 3.3 ± 0.9 after the first and second sessions. The average amount of HA injected in the first and second treatments were 1.2 ± 0.2 mL and 0.9 ± 0.2 mL, respectively. Two patients had minor visible HA deposits following the injection that disappeared with manual pressure and waiting by the time of the last follow-up visit. No other complications were noted.

4 | DISCUSSION

Acne scarring is a common and persistent complication of acne vulgaris affecting a large proportion of the population. No single

TABLE 1 Demographics

#	Age	Fitzpatrick skin phototype	Goodman and Baron scar scale	Years from last scar	Main scar type	Previous treatments
1	41	3	2	20	Rolling	RF
2	29	3	2	10	Box	None
3	30	4	3	5	Rolling	LASER
4	24	3	2	1	Box	LASER
5	37	2	3	1	Box	RF
6	45	3	3	15	Rolling	LASER
7	25	3	2	4	Rolling	LASER
8	25	4	4	2	Box	LASER
9	23	2	3	2	Box	RF
10	25	3	2	6	Box	None
11	52	3	2	10	Box	LASER
12	43	4	3	20	Box	RF

Abbreviations: LASER, Light amplification by stimulated emission of radiation; RF, Radio frequency.

treatment modality has been shown to be universally effective, which poses a significant challenge to the treating physician. Due to the distressing nature of the condition and its psychological impact on patients, a quick and efficient treatment is highly sought after.

Atrophic acne scarring treatments include surgical techniques (punch graft, punch excision, and subcision), resurfacing procedures (dermabrasion, ablative laser treatment, and chemical peels), other energy-based device treatments, autologous fat transfer, and the injection of dermal fillers.[19]

The use of dermal fillers in atrophic acne scarring was first described in 1980[14] and is accepted as an effective treatment for rolling, dish and boxcar acne scars, whether used independently or in conjunction with other therapies. Different dermal and subcutaneous filling for scars is an attractive choice for both physicians and patients because it provides simple and accurate nonsurgical correction of atrophic scars that produce immediate improvement. Fillers raise the scar deficit to the level of the surrounding skin, thereby working to even out skin texture and enhance overall contour.[14,15]

Hyaluronic Acid is commonly used in aesthetic medicine as dermal fillers and for revitalization procedures. In the human dermis, the high percentage of HA enables hydration while maintaining the proper tissue volume which buffers skin cells from mechanical damage. Alone or in combination with other molecules, HA accelerates in vitro processes related to wound healing[20] and in vivo tissue regeneration (eg, burns, ulcers).[21] Furthermore, HA has an anti-inflammatory and bio-stimulating effect and is thought to activate other signaling pathways through its interactions with different cell membrane receptors.[22] A wide range of HA-based hydrogels are manufactured to provide minimally invasive treatments.[23] Intradermal HA formulations are classified by their composition such as bio-fermentative or

FIGURE 1 Dual-plane technique. A, First pass filling the scars in the dermis, using a 29G syringe. B, The second injection pass was done using a 25g cannula immediately under the dermis, using the blunt cannula to disrupt the subcutaneous fat under the superficially injected scars

Grade	Percent improvement	Description	Satisfaction
I	0%-25%	Minimal to no improvement	Unsatisfied
II	26%-50%	Moderate improvement	Slightly satisfied
III	51%-75%	Marked improvement	Satisfied
IV	>75%	Near total improvement	Very satisfied

TABLE 2 Expert dermatologist and patient rating scale

animal, cross-linked or not cross-linked, and even for the additional presence of other compounds (amino acids, vitamins, antioxidant compounds). The major drawback of linear HA is its short in vivo half-life, due to the rapid degradation from hyaluronidases enzymatic attacks as well as free radicals, dilution, and compression. For these reasons, HA derivates have been developed with a wide range of characteristics in terms of concentration and size of the molecule, type, cross-linking degree, chemical, and physical stability of the final product.[24-27] The use of HA-based fillers in the treatment of acne scars is well established.[16,17]

Here, we treated 12 atrophic acne scar patients with a novel patented (WO/2012/032151) NAHYCO™ technology based filler[18] commercially available as ProfHilo®. This hybrid cooperative complex (HCC) HA formation is characterized by a drop in dynamic viscosity which, in clinical practice, makes it possible to deliver and inject very high concentrations of HA. Furthermore, HCC HA was shown to exert a pro-collagenic effect on fibroblasts and keratinocytes, increase ECM protein synthesis (eg, collagen I and III vs Col IV and VII).[28-30] and potentiate ASC differentiation.[31]

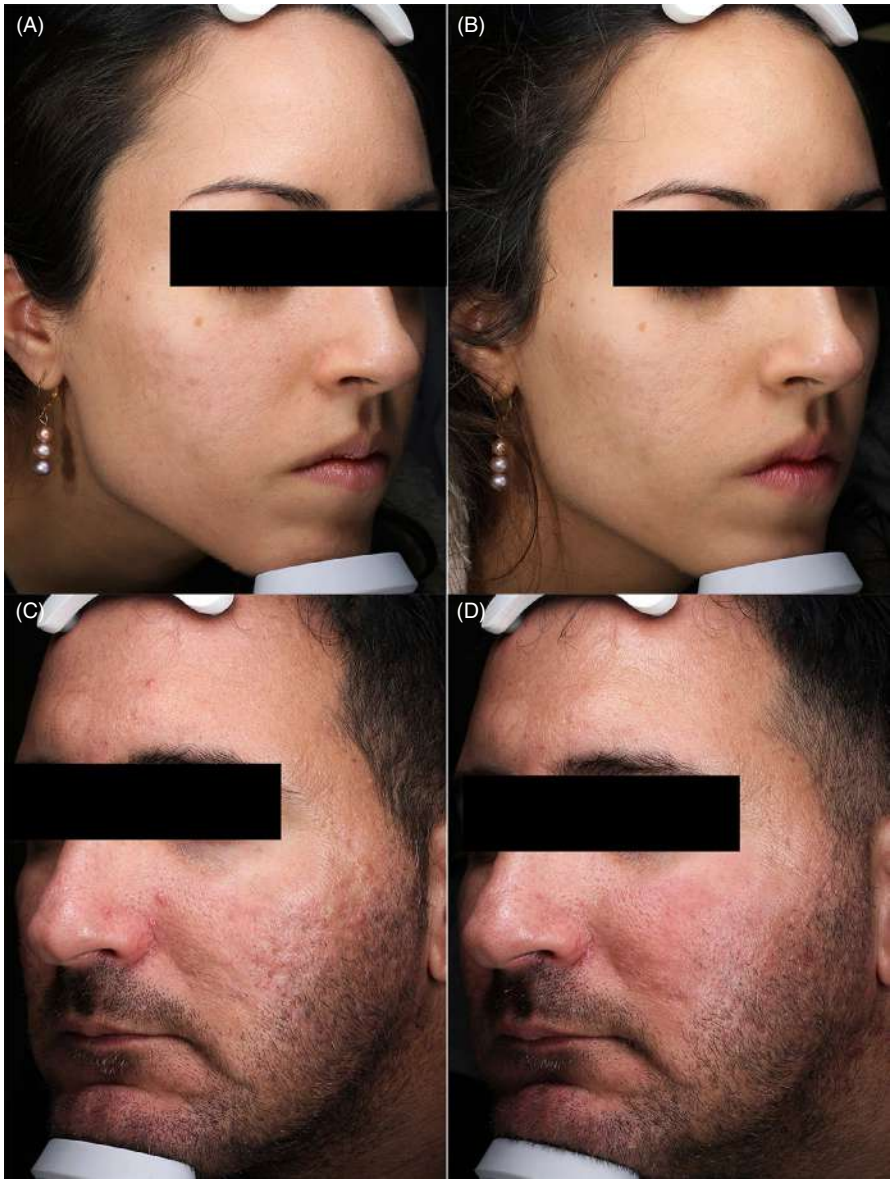

FIGURE 2 Baseline and outcome photographs of patients: A, Patient 9 at baseline exhibiting grade 3 Goodman and Baron scarring; note the significant rolling, shallow "box car" apparent at socially significant distances, not covered easily by makeup or 5 o'clock shadow. B, Patient 9 at 6 mo after treatment. Note the marked improvement in the texture of the cheek area, mainly the reduction in scar depth enabling better concealment with makeup. C, Patient 8 at baseline exhibiting grade 4 Goodman and Baron scarring; note the punched out atrophic "box car," gross atrophy, dystrophic scars. D, Patient 8 at 6 mo after treatment. Note the marked improvement in texture and transitions between the cheek and nasolabial fold, and temporal area to cheek

The dual-plane injection technique, using this gel for atrophic acne scars, led to impressive objective and subjective improvement in the depth of the scars at 1-month post-therapy (mean improvement grade 3 ± 0.5). At 3 months, probably due to natural HA degradation, only moderate improvement was observed (mean improvement grade 2.5 ± 0.49). However, surprisingly, the results were maintained at 6 months after treatment (mean improvement grade 2.5 ± 0.43). The treatment was well-tolerated by the patients and complications were minimal. The whole procedure takes <15 minutes using 0.5-2 mL of hyaluronic acid. As depicted in Figure 1, the dual-plane technique consists of seven steps:

1. Mark each appropriate scar, outlining where it is to be injected.
2. Assess the total volume likely to be required.
3. Evaluate what structures may lie beneath the scar to avoid injury.
4. Inject each scar intradermally using a 29g needle.
5. Manually mold small overfilled scars into position at the end of the injection if necessary.
6. Make an entry point adjacent to the scar or scarred area, insert a 25G cannula into the superficial hypodermis. Subcise the below the scar area and leave a small deposit of material.
7. Repeat at 4 weeks in a supplemental procedure usually requiring about 70% of the initial corrective volume.

5 | CONCLUSION

Dual-Plane atrophic acne scar treatment appears to be a safe and efficient way to treat facial atrophic acne scars. The benefits of HCC HA-based formulations may be related to their pro-collagenogenic and pro-adipogenic effects. ProfHilo® is currently available in Europe but has not yet been FDA approved for the use in the USA. Further research is needed on a larger and more heterogenic group of patients using proper controls.

6 | LIMITATIONS

This study has a number of limitations which future research could remedy. These include the small sample size, the lack of treatment controls, the potential bias of treating private patients who want to see a change, and the relatively short time to follow-up. In addition, this study was regional and treated a young Middle-Eastern population. It would be of value to test whether other skin types and ethnicities would benefit from this treatment. Nevertheless, both the expert dermatologists' and the patients' own evaluations of standardized high-resolution medical photographs were consistent, suggesting that this inherent bias was negligible.

CONFLICT OF INTEREST

None to declare.

ORCID

Or Friedman https://orcid.org/0000-0002-4362-7909

REFERENCES

1. Fife D. Practical evaluation and management of atrophic acne scars: tips for the general dermatologist. *J Clin Aesthet Dermatol*. 2011;4:50-57.
2. Jacob CI, Dover JS, Kaminer MS. Acne scarring: a classification system and review of treatment options. *J Am Acad Dermatol*. 2001;45:109-117.
3. Fife D, Zachary CB. Combining techniques for treating acne scars. *Curr Dermatol Rep*. 2012;1:82-88.
4. Fabbrocini G, Fardella N, Monfrecola A, Proietti I, Innocenzi D. Acne scarring treatment using skin needling. *Clin Exp Dermatol*. 2009;34:874-879.
5. Sadove R. Injectable poly-L lactic acid: a novel sculpting agent for the treatment of dermal fat atrophy after severe acne. *Aesthetic Plast Surg*. 2009;33:113-116.
6. Goodman GJ. Postacne scarring: a review of its pathophysiology and treatment. *Dermatol Surg*. 2000;26:857-871.
7. Fabbrocini G, Cacciapuoti S, Fardella N, Pastore F, Monfrecola G. CROSS technique: chemical reconstruction of skin scar method. *Dermatol Titer*. 2008;21:S29-S32.
8. Nouri K, Ballard CJ. Laser therapy for acne. *Clin Dermatol*. 2006;24:26-32.
9. Fabbrocini G, Annunziata MC, D'Arco V, et al. Acne scars: pathogenesis, classification and treatment. *Dermatol Res Pract*. 2010;2010:893080.
10. Thiboutot D, Gollnick H. New insights into the management of acne: an update from the Global Alliance to Improve Outcomes in Acne Group. *J Am Acad Dermatol*. 2009;60:S1-S50.
11. LaTowsky B, MacGregor JL, Dover JS, Arndt KA. Prevention and treatment of scars. In: Alam M ed. *Evidence-Based Procedural Dermatology*. New York, NY: Springer; 2012:149-177.
12. Bhatia N, David CV, Hazany S, Samrao A. Acne scarring. In: Zeichner JA, ed. *Acneiform Eruptions in Dermatology: A Differential Diagnosis*. New York, NY: Springer; 2014:237-243.
13. Beasley K, Dai JM, Brown P, Lenz B, Hivnor CM. Ablative fractional versus nonablative fractional lasers-where are we and how do we compare differing products? *Curr Dermatol Rep*. 2013;2:135-143.
14. Stegman SJ, Tromovitch TA. Implantation of collagen for depressed scars. *J Dermatol Surg Oncol*. 1980;6:450-453.
15. Smith KC. Repair of acne scars with dermicol-P35. *Aesthet Surg J*. 2009;29(3 Suppl.):S16-S18.
16. Goodman GJ, Van Den Broak A. The modified tower vertical filler technique for the treatment of post-acne scarring. *Australas J Dermatol*. 2016;57(1):19-23.
17. Baumann L. Skin ageing and its treatment. *J Pathol*. 2007;211(2):241-251.
18. De Rosa M, D'Agostino A, La Gatta A, Schiraldi C.Hybrid cooperative complexes of hyaluronic acid. WO Patent WO/2012/032,151.
19. Valeska GM, Zhou B, Lou D. Effective treatments of atrophic acne scars. *J Clin Aesthet Dermatol*. 2015;8(5):33-40.
20. D'Agostino A, Stellavato A, Busico T, et al. In vitroanalysis of the effects on wound healing of high- and low-molecular weight chains of hyaluronan and their hybrid H-HA/L-HA complexes. *BMC Cell Biol*. 2015;11(16):19.
21. Dicker KT, Gurski LA, Pradhan-Bhatt S, Witt RL, Farach-Carson MC, Jia X. Hyaluronan: a simple polysaccharide with diverse biological functions. *Acta Biomater*. 2014;10(4):1558-1570.
22. Vigetti D, Karousou E, Viola M, Deleonibus S, De Luca G, Passi A. Hyaluronan: biosynthesis and signaling. *Biochim Biophys Acta*. 2014;1840(8):2452-2459.

23. Girardeau-Hubert S, Teluob S, Pageon H, Asselineau D. The reconstructed skin model as a new tool for investigating in vitro dermal fillers: increased fibroblast activity by hyaluronic acid. *Eur J Dermatol*. 2015;25(4):312-322.
24. La Gatta A, Schiraldi C, Papa A, et al. Hyaluronan scaffolds via diglycidyl ether crosslinking: toward improvements in composition and performance. *Carbohyd Polym*. 2013;96:536-544.
25. La Gatta A, Papa A, Schiraldi C, De Rosa M. Hyaluronan dermal fillers via crosslinking with 1,4-butandiol diglycidyl ether: exploitation of heterogeneous reaction conditions. *J Biomed Mater Res B Appl Biomater*. 2016;104(1):9-18.
26. Paliwal S, Fagien S, Sun X, et al. Skin extracellular matrix stimulation following injection of a hyaluronic acid-based dermal filler in a rat model. *Plast Reconstr Surg*. 2014;134(6):1224-1233.
27. Kim ZH, Lee Y, Kim SM, Kim H, Yun CK, Choi YS. A composite dermal filler comprising cross-linked hyaluronic acid and human collagen for tissue reconstruction. *J Microbiol Biotechnol*. 2015;25(3):399-406.
28. Funt D, Pavicic T. Dermal fillers in aesthetics: an overview of adverse events and treatment approaches. *Clin Cosmet Investig Dermatol*. 2013;12(6):295-316.
29. Varma SR, Sivaprakasam TO, Mishra A, et al. Protective effects of triphala on dermal fibroblasts and human keratinocytes. *PLoS ONE*. 2016;11(1):e0145921.
30. La Gatta A, De Rosa M, Frezza MA, Catalano C, Meloni M, Schiraldi C. Biophysical and biological characterization of a new line of hyaluronan-based dermal fillers: a scientific rationale to specific clinical indications. *Mater Sci Eng C*. 2016;68:565-572.
31. Stellavato A, La Noce M, Corsuto L, et al. Hybrid complexes of high and low molecular weight hyaluronans highly enhance HASCs differentiation: implication for facial bioremodelling. *Cell Physiol Biochem*. 2017;44(3):1078-1092.

How to cite this article: Artzi O, Cohen S, Koren A, Niv R, Friedman O. Dual-plane hyaluronic acid treatment for atrophic acne scars. *J Cosmet Dermatol*. 2019;00:1–6. https://doi.org/10.1111/jocd.12991