Review Article Annals of Dermatology 2023;35(6):400-407 • https://doi.org/10.5021/ad.22.230

Dermal Fillers in the Treatment of Acne Scars: A Review

Eman Almukhadeb, Faisal Binkhonain, Abeer Alkahtani[1], Sarah Alhunaif[2], Feras Altukhaim, Khalid Alekrish

Department of Dermatology, College of Medicine, King Saud University, Riyadh, Saudi Arabia; [1]Department of Dermatology, King Faisal Specialist Hospital & Research Centre, Riyadh, Saudi Arabia; [2]Department of Dermatology, College of Medicine, King Saud Bin Abdulaziz University for Health Sciences, Riyadh, Saudi Arabia

Received January 12, 2023
Revised April 8, 2023
Accepted May 18, 2023

Corresponding Author
Khalid Alekrish
Department of Dermatology, College of Medicine, King Saud University, Riyadh 11564, Saudi Arabia
Tel: +966-592162977
Fax: +011-2033479
E-mail: khalidalekrish@gmail.com
https://orcid.org/0000-0002-0032-3980

Acne vulgaris (AV) is the eighth most common disease in the world. This condition can impair the affected patients' social and psychological functioning and lower their quality of life. In general, scar reduction, rather than complete scar removal, is the aim of AV treatment. Dermal abrasion, chemical peeling, laser resurfacing, subcision, punch methods, tissue-improving substances, and dermal fillers are the currently available therapeutic options. In this study, we focused on the rapidly developing field of dermal fillers used alone or in combination with other therapies to reconstruct skin affected by acne scars and to evaluate the improvement of facial appearance after using different types of dermal fillers.

Keywords: Acne, Cosmetics, Dermal fillers, Review

INTRODUCTION

Acne vulgaris (AV) is the eighth most common disease in the world. Over 10% of the population are affected by AV, with the highest prevalence in adolescents[1]. Among adolescents, the prevalence is up to 85%[2], while up to 12% of adults are affected[3,4]. In all ethnic groups, AV affects more than 90% of men and 80% of women[5,6]. Despite this, acne is neither physically dangerous nor life-threatening, but it can impair patients' social and psychological functioning and lower their quality of life (QOL). Moderate to severe acne lesions may leave atrophic scars or post-inflammatory hyperpigmentation that can impair a patient's QOL, lower self-esteem, and reduce social interactions[7]. Up to 95% of acne patients experience scarring as a typical long-term side effect, most frequently on the face[8]. The majority of acne scars are atrophic or marked by tissue loss. Although these lesions are typically divided into icepick, boxcar, rolling, keloidal, and hypertrophic scars, there is no universal agreement on the classification of atrophic scars[9]. Since there is no established standard of care in clinical practice, the treatment option must be customized for each patient.

Additionally, a combination of treatment approaches is typically necessary due to the variable nature of scarring among the patients in terms of both the scar types and the severity of the scars (as discussed in Sánchez Viera 2015)[10]. In general, scar reduction, rather than complete scar removal, is the aim of AV treatment[11]. Dermal abrasion, chemical peeling, laser resurfacing, subcision, punch methods, tissue-improving substances, and dermal fillers are the currently available therapeutic options[9-11]. In this study, we focused on the rapidly developing field of dermal fillers used alone or in combination with other therapies to reconstruct skin affected by acne scars and to evaluate the improvement of facial appearance after using different types of dermal fillers.

FILLER TYPES

Fillers can be categorized as either temporary (effects that endure for up to 18 months, with hyaluronic acid [HA] being one example), semi-permanent (results lasting for up to two years, with examples including calcium hydroxyapatite [CH] and poly-L-lactic acid [PLLA]), or long-lasting (effects lasting for more than three years, with examples including silicone,

polymethylmethacrylate [PMMA], polyacrylamide, and polyalkylimide). Several techniques are used to inject the fillers, such as droplet injection, linear threading, fanning, or three-dimensional volumization. The augmentation of dermal and subcutaneous tissue scaffolding, as well as the acceleration and enhancement of collagen and tissue synthesis, are the postulated mechanisms of action of these fillers[12,13]. Despite their use in the past, human-, bovine-, and porcine-collagen-based fillers have been replaced by longer-lasting alternatives due to their limited duration of action.

TEMPORARY FILLERS

Hyaluronic acid

HA is a temporary filler that was approved by the United States Food and Drug Administration (FDA) in 2003. It is a polysaccharide composed of repeating disaccharide units of N-acetylglucosamine and D-glucuronic acid[14]. Intradermal injections of HA fillers stimulate collagen synthesis by activating the dermal fibroblasts. They are commonly used to restore skin volume and improve the appearance of wrinkles and nasolabial folds[15]. There are multiple products containing HA fillers, and each has its own characteristics[16]. Seven studies have been performed to assess the effectiveness of different products containing HA fillers in the treatment acne scars, and all of them showed improvements in the appearance of acne scars, with no or minimal adverse events (AEs) (Table 1)[17-23]. In the most recent publication by Mahamoud et al. (2020)[23], the study incorporated a considerably larger patient population in comparison to earlier studies investigating the employment of HA for the treatment of acne scars. This study involved 30 participants who underwent three sessions of full-face fractional CO_2 laser, accompanied by intradermal HA injections or platelet-rich plasma injections on each facial side. Subsequently, the patients were monitored for a period of four weeks following each session. A significant reduction in acne scar severity was observed on both sides of the face, utilizing qualitative and quantitative assessment tools. Minimal AEs were reported in a few patients such as postprocedural pain, erythema, and edema.

SEMI-PERMANENT FILLERS (BIO-STIMULANTS)

Poly-L-lactic acid

PLLA is a semi-permanent filler that was approved for soft tissue augmentation in 1999. Currently, PLLA dermal filler is marketed under the brand name Sculptra. It is a synthetic biodegradable polymer that corrects volume loss by stimulating the fibroblasts and, therefore, collagen synthesis. The gradual effect of PLLA on dermal volume can last for up to 2~3 years from the time of treatment[24]. Five studies have been conducted from 2007 to 2015 to assess the efficacy and safety of PLLA for acne scars, with sample sizes varying from 1 to 80 patient. All studies demonstrated positive outcomes in enhancing the appearance of atrophic acne scars, despite the considerable variability in the number of sessions each patient received, which ranged from one to seven sessions. Additionally, the follow-up intervals in these investigations varied, extending from three months to four years after the final treatment sessions. With regard to AEs, the majority of patients in these studies exhibited minimal or no AEs. Examples of the AEs reported in these articles include mild pain, erythema, edema, swelling, and bruising. In one case, a non-visible palpable nodule and an epidermal inclusion cyst were observed (Table 1)[12,25-28].

Calcium hydroxylapatite

CH is a naturally occurring substance in the human body, especially in human bones and teeth. The injectable form is developed using uniform CH microspheres dissolved in an aqueous carboxymethylcellulose gel carrier. Since 2006, Radiesse has been the only FDA-approved CH filler[29]. It provides long-lasting deep dermal and subdermal soft tissue augmentation, as it can instantly create significant changes in volume and replenish lost volume[30]. In addition to their volumizing effects, CH fillers tend to stimulate neocollagenesis and, subsequently, tissue formation, and their effects can last for up to 18 months[29].

Although CH fillers are commonly used, only two studies have investigated their role in the treatment of atrophic acne scars, one of which was a clinical trial that showed a beneficial effect and improvement in all treated individuals after 12 months, with the exception of deep icepick scars[31]. A recent study was conducted in 2019 by Koren et al.[32] supported the use of CH fillers followed by fractional ablative CO_2 laser treatment in separate treatment sessions, as these products yielded better cosmetic outcomes compared with the other evaluated modalities (Table 1).

Table 1. Summary of studies conducted on the use of dermal fillers in the treatment of atrophic acne scars

Study	Indication	Aim	No. of patients	Finding
HA (temporary)				
Mahamoud et al. (2020)[23]	Patients with acne scars received HA injections, or PRP injections, on each face's side for comparison. Brand name: Viscoderm.	Patients underwent three sessions of full-face fractional CO_2 laser, immediately followed by intradermal HA injections or PRP injections on each side of the face with four weeks between sessions.	30	Using qualitative and quantitative Goodman and Baron, both sides had a significant reduction in the severity of acne scars. Collagen and elastic fiber content increased in both, but more in the PRP-treated side.
Kim et al. (2019)[22]	HA pneumatic injections were given to Fitzpatrick skin types IV~V patients with acne scars. Brand name: Unial.	Patients underwent a single treatment session. Follow-ups were given 1 and 2 months after treatment.	10	The mean scar volume values were 0.964, 0.741, and 0.566 mm^3, respectively, at baseline, one month, and two months after the injection. No adverse events were reported.
Dierickx et al. (2018)[21]	HA fillers were used to treat patients with moderate to severe acne scars. Brand name: Restylane.	Patients received three sessions of HA filler four weeks apart. Results were assessed up to 36 weeks after treatment.	12	Scar severity has improved in most patients (67%). Patient satisfaction with the overall facial appearance and with the sensation and perception of the skin improved in most patients. Patients' self-esteem and self-confidence also improved. AEs were redness, swelling, bumps, pain, and bruising (all resolved in 2 weeks).
Goodman and Van Den Broek (2016)[20]	HA fillers were used with the vertical modified tower technique. Brand name: Juvederm Voluma (Allergan).	Patients were treated twice with three months follow up after the second treatment.	5	The mean scar count reduced from 48.8 to 15.4 after the second session. The static objective grading scale demonstrated improvement from 3.2 prior to first treatment to 2.6 at the final review.
Patel and Tevet (2015)[19]	HA pneumatic injections were given to patients who had Fitzpatrick skin types IV~V with acne scars. Brand name: Belotero Balance.	Patients received two sessions at 4-week intervals of pneumatic, needleless injections of crosslinked HA. Follow up were given three months later.	2	Patient 1: acne scar grade improved from 2 to 1. Patient 2: acne scar grade improved from 3 to 2. No AEs were reported.
Halachmi et al. (2013)[18]	HA pneumatic injections were given to patients who had Fitzpatrick skin types IV~V with acne scars. Brand name: Unial.	20 mg/ml microinjections of HA were used, and follow-ups were given 1~2 months later, with one follow-up visit.	12	Immediate visual improvement was noticed in all scars. Pinpoint bleeding at the injection site was the only reported AE.
Hasson and Romero (2010)[17]	HA fillers were used to treat facial atrophic scars caused by acne vulgaris, dog bites, piercing, basal cell carcinoma, and leishmaniasis. Brand name: Esthelis.	The injection technique was linear threading, serial puncture, or both. Follow-ups for assessment of the injection were given immediately, one week, and one month after the injection.	12	The authors assessed the results immediately, one week, and one month after the injection. 27% had moderate improvement, 57% had good improvement, and 17% had excellent improvement. Mild erythema was the only reported AE.

Table 1. Continued

Study	Indication	Aim	No. of patients	Finding
PLLA (semi-permanent)				
Sapra et al. (2015)[25]	PLLA injections were given for the treatment of atrophic acne rolling scar. Brand name: Sculptra.	Single-arm, unblinded, open-label phase 2 study. Patients received 3 to 4 sessions if needed at four weeks intervals—follow-ups are given after six months from the first session.	22	45.5% to 68.2% of patients reported excellent improvement using photographs. Subject treatment satisfaction scores increased by 44%. AEs included one patient with a non-visible, palpable nodule.
Rkein et al. (2014)[26]	Ablative fractionated CO_2 laser and topical PLLA immediately after to improve atrophic scars. Brand name: Sculptra.	An uncontrolled, prospective study. Most of the patients had only one treatment session with laser and PLLA. The follow-up duration was three months after the laser and PLLA.	19	Patients had 95% scar improvement with minimal AEs, such as mild pain, erythema, and edema. One patient developed an epidermal inclusion cyst.
Sadick and Palmisano (2009)[27]	PLLA injections were given to a 60-year-old white woman who had previously been treated with CO_2 laser resurfacing without improvement on acne scars. Brand name: Sculptra.	Seven sessions of PLLA were given to individual acne scars. The patient was followed up twice; the first was six months after the last session, and the second 14 months after the previous session.	1	The patient reported a good improvement with minimal swelling and bruising at injection sites lasting 5~7 days.
Sadove (2009)[28]	PLLA to correct dermal fat loss in macular atrophic acne scarring Brand name: Newfill.	Both patients received three sessions over 12 weeks. The first follow-up was one year after the last session, and the second was four years after the previous session.	2	Both patients reported marked improvement with only minimal swelling and redness.
Beer (2007)[12]	PLLA fillers were used to treat patients with moderate to severe acne scars. Brand name: Sculptra.	Single-center, open-label, prospective study with seven sessions of PLLA. Injections were given at 1-month intervals. Patients were followed up after each treatment session.	20	A noticeable reduction in acne scar size.
CH (semi-permanent)				
Goldberg et al. (2006)[31]	Use of CH in acne scars. Brand name: Radiesse	Open study. Subjects underwent 1~2 injection sessions. Follow up duration was 12 months.	10	Depressed acne scars responded to treatment, but no response from icepick scars. No significant AEs.
Koren et al. (2019)[32]	Combination of CH and EBD in acne scars. Brand name: Radiesse	A single center retrospective study reviewed medical records of acne scar patients between 2013~2016 who were treated with one of four treatments: ablative fractional CO_2 laser, a radiofrequency bipolar device, a 1,540 nm non-ablative fractional laser, and injection of CH.	352	Injection of CH-based fillers 2~4 weeks prior to the treatment with ablative fractional CO_2 laser yields a better outcome and should be recommended for suitable patients.

PERMANENT FILLERS

Polymethylmethacrylate

PMMA is a synthetic, permanent filler that was approved for soft tissue augmentation in 2006[33]. In December 2014, the FDA also approved its use for moderate to severe atrophic acne scars[34]. Currently, collagen-PMMA dermal filler is marketed under the brand name Bellafil (Suneva Medical). This is the most recent formulation of collagen-PMMA, with its particles modified to obtain a diameter of 30 to 50 μm[35,36]. This

Table 1. Continued

Study	Indication	Aim	No. of patients	Finding
PMMA (permanent)				
Joseph et al. (2019)[34]	PMMA to treat acne scars over the entire face. Brand name: Bellafil	Open-label, multicenter, single-arm non-randomized study. Patients received two treatment sessions with one month in between. Patients were followed up for seven months.	42	Using the acne scar assessment scale (ASAS), lower face responders were 92% and 97% at the 4- and 7-month marks, respectively. Upper-face responders were 64% and 67% at the 4- and 7-month marks, respectively. Only two reported skin testing-related AEs, and no AEs were attributed to PMMA dermal filler.
Karnik et al. (2014)[39]	Treatment of atrophic acne scars over the cheeks using PMMA dermal fillers. Brand name: Artefill.	A double-blind, multicenter, randomized controlled trial. Patients received two treatment sessions with six months of follow-up.	147	Using Acne Scar Rating Scale, PMMA treatment improved 91% of the treated scars. In contrast, the investigators reported improvement in only 76% of the scars treated with saline. AEs were minimal.
Epstein and Spencer (2010)[40]	PMMA fillers were used for the treatment of atrophic acne scars. Brand name: Artefill.	Pilot study. Patients had only one injection session, with eight months of follow-up.	14	At the eight months mark, investigators reported that 96% of treated scars showed some improvement. No AEs were reported.
Carvalho Costa et al. (2009)[13]	PMMA fillers were used to determine their efficacy and safety as a facial filler. Brand name: Artefill.	Patients had 1∼4 sessions with a 2-month interval. They were followed up for up to 9 years, with follow-up visits at each session, at one month and six months, then yearly thereafter.	25*	Using physical examination and before-and-after photos at 1 and 6 months, then yearly to assess the improvement, more than 85% of subjects were satisfied with their results. Most patients experienced no AEs (80%), and mild, transient AEs were reported by 20% of patients.
Silicone (permanent)				
Barnett and Barnett (2005)[42]	Silicone liquid injections were used to assess the improvement of acne scars.	Monthly liquid silicone injections using a technique known as the microdroplet, multiple-injection approach. Patients were followed up for 30 years, with follow-up immediately and then at 10-, 15- and 30-years posttreatment.	5	Investigators noticed an improvement in acne scars with liquid silicone injection immediately after treatment, at 10, 15, and 30 years, although the improvement was not quantified. Only minor AEs were reported.

HA: hyaluronic acid, PLLA: poly-L-lactic acid, CH: calcium hydroxyapatite, EBD: energy-based device, PMMA: polymethylmethacrylate, AE: adverse event. *Total patient number with different diagnoses. Of those, 25 patients received PMMA dermal filler for atrophic acne scars.

diameter was shown to have a better tolerability and resulted in fewer cases of foreign body reactions[37]. In contrast to other biological filler materials, PMMA contains a bovine collagen carrier as well as microsphere particles that cannot be metabolized. These residual particles stimulate the replacement of the bovine collagen carrier by autologous collagen, and the induction of autologous collagen production is a unique advantage of PMMA fillers[38].

Four studies have been conducted to determine the efficacy of PMMA dermal filler in the treatment of atrophic acne scars, and all showed positive outcomes (Table 1)[13,34,39,40]. The most recent study was conducted in 2019 by Joseph et al.[34] where they used Bellafil® for full-face acne scar treatment. Participants underwent two treatment sessions with a one-month interval, followed by a seven-month follow-up period. The researchers employed the Acne Scar Assessment Scale to objectively evaluate the treatment outcomes. Scars on the lower face demonstrated a more substantial improvement compared to those on the upper face. The authors reported no filler-related AEs in their study.

Silicone

In 1983, the use of liquid silicone injection as a treatment for atrophic acne scars was first attempted[41], and since then, it has been used as an off-label filler substance[42]. Given its permanent nature, side effect profile, and the scarcity of data proving its safety, the FDA has not approved liquid silicone injections for tissue augmentation, regardless of the body site[43]. To date, a single study has been conducted to assess the efficacy and safety of liquid silicone injections in the treatment of atrophic acne scars, studied over 30 years. The investigators concluded that the treatment was effective and safe. However, only five patients were included, and the improvement was based solely on a photographic evaluation, with no objective scale employed to quantify the improvement (Table 1)[42].

Polyacrylamide and polyalkylimide

To this day, no research has substantiated the use of polyacrylamide and polyalkylimide in the treatment of atrophic acne scars (Table 1).

CONCLUSION

Today, an increasing number of patients are seeking medical solutions for their acne scars. Acne scarring is a prevalent and challenging pathology that leads to stress and anxiety. Dermatologists have used abrasion, chemical peeling, laser resurfacing, and subcision as therapeutic options, with varying degrees of efficacy. Although the use of fillers for facial tissue augmentation is widespread, their role in the management of acne scars is yet to be capitalized. Multiple studies have been conducted to assess the efficacy and safety of dermal fillers in the treatment of acne scars. While most of them were limited by a low number of participants, they all showed promising results, with no or minimal AEs. The continuation of such studies is critical in order to further ensure the efficacy and safety of dermal fillers in the management of acne scars and the development of appropriate therapeutic protocols.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

FUNDING SOURCE

None.

ORCID

Eman Almukhadeb, https://orcid.org/0000-0001-8296-0213
Faisal Binkhonain, https://orcid.org/0000-0003-4905-3819
Abeer Alkahtani, https://orcid.org/0000-0002-4150-2803
Sarah Alhunaif, https://orcid.org/0000-0002-3468-2682
Feras Altukhaim, https://orcid.org/0000-0001-7802-7914
Khalid Alekrish, https://orcid.org/0000-0002-0032-3980

REFERENCES

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2163-2196. Erratum in: Lancet 2013;381:628.
2. Prevalence, morbidity, and cost of dermatological diseases. J Invest Dermatol 1979;73(5 Pt 2):395-401.
3. Cunliffe WJ, Gould DJ. Prevalence of facial acne vulgaris in late adolescence and in adults. Br Med J 1979;1:1109-1110.
4. Goulden V, Stables GI, Cunliffe WJ. Prevalence of facial acne in adults. J Am Acad Dermatol 1999;41:577-580.
5. Yosipovitch G, Tang M, Dawn AG, Chen M, Goh CL, Huak Y, et al. Study of psychological stress, sebum production and acne vulgaris in adolescents. Acta Derm Venereol 2007;87:135-139.
6. Tan JK, Bhate K. A global perspective on the epidemiology of acne. Br J Dermatol 2015;172 Suppl 1:3-12.
7. Alajlan A, Al Turki YA, AlHazzani Y, Alhowaish N, AlEid N, Alhozaimi Z, et al. Prevalence, level of knowledge and lifestyle as-

sociation with acne vulgaris among medical students. J Dermatol Dermatol Surg 2017;21:58-61.
8. Layton AM, Henderson CA, Cunliffe WJ. A clinical evaluation of acne scarring and its incidence. Clin Exp Dermatol 1994;19:303-308.
9. Jacob CI, Dover JS, Kaminer MS. Acne scarring: a classification system and review of treatment options. J Am Acad Dermatol 2001;45:109-117.
10. Sánchez Viera M. Management of acne scars: fulfilling our duty of care for patients. Br J Dermatol 2015;172 Suppl 1:47-51.
11. Abdel Hay R, Shalaby K, Zaher H, Hafez V, Chi CC, Dimitri S, et al. Interventions for acne scars. Cochrane Database Syst Rev 2016;4:CD011946.
12. Beer K. A single-center, open-label study on the use of injectable poly-L-lactic acid for the treatment of moderate to severe scarring from acne or varicella. Dermatol Surg 2007;33 Suppl 2:S159-S167.
13. Carvalho Costa IM, Salaro CP, Costa MC. Polymethylmethacrylate facial implant: a successful personal experience in Brazil for more than 9 years. Dermatol Surg 2009;35:1221-1227.
14. Tezel A, Fredrickson GH. The science of hyaluronic acid dermal fillers. J Cosmet Laser Ther 2008;10:35-42. Erratum in: J Cosmet Laser Ther 2014;16:45.
15. Bukhari SNA, Roswandi NL, Waqas M, Habib H, Hussain F, Khan S, et al. Hyaluronic acid, a promising skin rejuvenating biomedicine: a review of recent updates and pre-clinical and clinical investigations on cosmetic and nutricosmetic effects. Int J Biol Macromol 2018;120(Pt B):1682-1695.
16. Kim JE, Sykes JM. Hyaluronic acid fillers: history and overview. Facial Plast Surg 2011;27:523-528.
17. Hasson A, Romero WA. Treatment of facial atrophic scars with Esthélis, a hyaluronic acid filler with polydense cohesive matrix (CPM). J Drugs Dermatol 2010;9:1507-1509.
18. Halachmi S, Ben Amitai D, Lapidoth M. Treatment of acne scars with hyaluronic acid: an improved approach. J Drugs Dermatol 2013;12:e121-123.
19. Patel T, Tevet O. Effective treatment of acne scars using pneumatic injection of hyaluronic acid. J Drugs Dermatol 2015;14:74-76.
20. Goodman GJ, Van Den Broek A. The modified tower vertical filler technique for the treatment of post-acne scarring. Australas J Dermatol 2016;57:19-23.
21. Dierickx C, Larsson MK, Blomster S. Effectiveness and safety of acne scar treatment with nonanimal stabilized hyaluronic acid gel. Dermatol Surg 2018;44 Suppl 1:S10-S18.
22. Kim BY, Chun SH, Park JH, Ryu SI, Kim IH. Prospective evaluation of atrophic acne scars on the face with needle-free high-pressure pneumatic injection: quantitative volumetric scar improvement. Dermatol Surg 2019;45:829-835.
23. Mahamoud WA, El Barbary RA, Ibrahim NF, Akmal EM, Ibrahim SM. Fractional carbon dioxide laser combined with intradermal injection of autologous platelet-rich plasma versus noncross-linked hyaluronic acid in the treatment of atrophic postacne scars: a split face study. J Cosmet Dermatol 2020;19:1341-1352.
24. Fitzgerald R, Bass LM, Goldberg DJ, Graivier MH, Lorenc ZP. Physiochemical characteristics of Poly-L-Lactic Acid (PLLA). Aesthet Surg J 2018;38(suppl_1):S13-S17.
25. Sapra S, Stewart JA, Mraud K, Schupp R. A Canadian study of the use of poly-L-lactic acid dermal implant for the treatment of hill and valley acne scarring. Dermatol Surg 2015;41:587-594.
26. Rkein A, Ozog D, Waibel JS. Treatment of atrophic scars with fractionated CO2 laser facilitating delivery of topically applied poly-L-lactic acid. Dermatol Surg 2014;40:624-631.
27. Sadick NS, Palmisano L. Case study involving use of injectable poly-L-lactic acid (PLLA) for acne scars. J Dermatolog Treat 2009;20:302-307.
28. 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.
29. Forbat E, Ali FR, Al-Niaimi F. The role of fillers in the management of acne scars. Clin Exp Dermatol 2017;42:374-380.
30. Pavicic T. Calcium hydroxylapatite filler: an overview of safety and tolerability. J Drugs Dermatol 2013;12:996-1002.
31. Goldberg DJ, Amin S, Hussain M. Acne scar correction using calcium hydroxylapatite in a carrier-based gel. J Cosmet Laser Ther 2006;8:134-136.
32. Koren A, Isman G, Cohen S, Bar Ilan E, Salameh F, Sprecher E, et al. Efficacy of a combination of diluted calcium hydroxylapatite-based filler and an energy-based device for the treatment of facial atrophic acne scars. Clin Exp Dermatol 2019;44:e171-e176.
33. Lemperle G, Knapp TR, Sadick NS, Lemperle SM. ArteFill permanent injectable for soft tissue augmentation: I. Mechanism of action and injection techniques. Aesthetic Plast Surg 2010;34:264-272.
34. Joseph JH, Shamban A, Eaton L, Lehman A, Cohen S, Spencer J, et al. Polymethylmethacrylate collagen gel-injectable dermal filler for full face atrophic acne scar correction. Dermatol Surg 2019;45:1558-1566.
35. Lemperle G, Morhenn VB, Pestonjamasp V, Gallo RL. Migration studies and histology of injectable microspheres of different sizes in mice. Plast Reconstr Surg 2004;113:1380-1390.
36. Lemperle G, Morhenn V, Charrier U. Human histology and persistence of various injectable filler substances for soft tissue augmenta-

tion. Aesthetic Plast Surg 2003;27:354-366; discussion 367.
37. Lemperle G, Gauthier-Hazan N, Wolters M, Eisemann-Klein M, Zimmermann U, Duffy DM. Foreign body granulomas after all injectable dermal fillers: part 1. Possible causes. Plast Reconstr Surg 2009;123:1842-1863.
38. Nicolau PJ. Long-lasting and permanent fillers: biomaterial influence over host tissue response. Plast Reconstr Surg 2007;119:2271-2286.
39. Karnik J, Baumann L, Bruce S, Callender V, Cohen S, Grimes P, et al. A double-blind, randomized, multicenter, controlled trial of suspended polymethylmethacrylate microspheres for the correction of atrophic facial acne scars. J Am Acad Dermatol 2014;71:77-83.
40. Epstein RE, Spencer JM. Correction of atrophic scars with artefill: an open-label pilot study. J Drugs Dermatol 2010;9:1062-1064.
41. Orentreich N, Durr NP. Rehabilitation of acne scarring. Dermatol Clin 1983;1:405-413.
42. Barnett JG, Barnett CR. Treatment of acne scars with liquid silicone injections: 30-year perspective. Dermatol Surg 2005;31(11 Pt 2):1542-1549.
43. U.S. Food and Drug Administration (FDA). FDA-Approved Dermal Fillers [Internet]. FDA; 2020 Sep 11 [cited 2023 Jan 1]. Available from: https://www.fda.gov/medical-devices/aesthetic-cosmetic-devices/fda-approved-dermal-fillers.