

Clinical results of skin remodeling using a novel pneumatic technology

Alex Levenberg¹, MD, Shlomit Halachmi², MD, PhD, Abigail Arad-Cohen³, MD, Dean Ad-El^{4,6}, MD, Daniel Cassuto⁵, MD, and Moshe Lapidot^{2,6}, MD, MPH

¹Beit Ha'rofeem Plastic Surgery Clinic, Tel Aviv, Israel, ²Laser Unit, Department of Dermatology, Rabin Medical Center, Petach Tikva, Israel, ³Ear, Nose and Throat Clinic, Beit Rof'im Dubnov, Tel Aviv, Israel, ⁴Department of Plastic Surgery, Rabin Medical Center, Petach Tikva, Israel, ⁵Department of Plastic Surgery, University of Catania, Catania, Italy, and ⁶Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel

Correspondence

Shlomit Halachmi, MD, PhD
Laser Unit
Department of Dermatology
Rabin Medical Center
Petach Tikva
Israel
E-mail: shlomitha2@clalit.org.il

Abstract

Background A myriad of technologies are available for the treatment of aging skin. These, however, still lack the ability to combine immediate, short-term and long-term aesthetic results with no downtime. Furthermore, the treatment of fine wrinkles on large surfaces remains challenging, as does the treatment of delicate regions, such as the dorsal hand, neck, and chest.

Objectives The aims of this study were to evaluate the short-term as well as the long-term efficacy and safety of a new skin remodeling device that pneumatically accelerates a jet of hyaluronic acid (HA) solution under high pressure into the dermis.

Methods Thirty-four participants at three clinical sites underwent treatments with the Airgent device on the face, neck, chest, and dorsal hands for a total of 69 sites. Safety and efficacy were evaluated in short-term (1–3 months) and long-term follow-up (up to 18 months) by photography, by an independent reviewer and by participant self-evaluation. Histology was assessed before and 4 months after the third treatment.

Results A total of 69 treatment areas were evaluable at 1–3 months follow-up. Photographic analysis demonstrated improvement in skin variables at all body sites treated. Treatment of the face and neck reduced the mean Fitzpatrick–Goldman Wrinkle Classification score by 39.4 and 30.4%, respectively, representing a full wrinkle class improvement. Treatments of the chest demonstrated significant visual improvement. Treatment of the dorsal hands produced good overall improvement (OI), with good improvement of protruding veins. Overall improvement increased with increasing number of treatments. A total of 56 treatment areas were evaluable for long-term follow-up. Treatment of the face and neck reduced the mean Fitzpatrick–Goldman Wrinkle Classification score by 27.6 and 21.2%, respectively. Improvement after treatment of the face represented a full wrinkle class reduction. Treatment of the chest and dorsal hands yielded significant visual improvement. Overall, 80% of subjects were satisfied with the treatment outcome and would recommend the treatment to friends and family. Histological analysis demonstrated increased dermal collagen III.

Conclusions Pneumatic injection of HA under high pressure provides a safe, well-tolerated and effective method for improving the appearance of wrinkles on the face, neck, chest, and dorsal hands. Improvement can be seen as early as 1 month and as long as 18 months after treatment.

Introduction

Wrinkles are the most prominent feature of the aging process and are the most difficult aspect to conceal. Chronological aging combined with photodamage leads to reduced skin volume caused by the loss of collagen in the dermis.^{1–3} A myriad of energy-based skin rejuvenation

technologies, such as lasers, radiofrequency, IPL (intense pulsed light), and photodynamic therapy, have been introduced and are aimed at triggering collagen remodeling in response to controlled thermal damage of the dermal skin layers.^{4–19} These technologies produce long-term effects, but they may have limited immediate visible effects. Immediate dermal thickening is more commonly achieved

by injection with dermal fillers.^{20–22} The main limitation of injections is that the effects are confined to small skin areas and focal defects.

Dermal fillers are thought to exert short- and long-term effects via distinct mechanisms. The immediate and temporary volumizing effect of the injections is derived directly from the introduction of volume, an effect that persists in relation to the longevity of the filler in the dermis.^{23,24} Furthermore, injection of hyaluronic acid (HA) into the dermis has been demonstrated to trigger changes in the activity of fibroblasts in recipient skin, with a consequent increase in collagen synthesis; this has been touted as the reason for its long-lasting effect in dermal thickening, which extends beyond the known longevity of the dermal filler.²⁵

We investigated a novel device which delivers an HA solution into the dermis via pneumatic needleless action.²⁶ The parameters of the high-pressure injection allow the focal introduction of the solution through the epidermis.²⁷ The mechanical properties of the dermis cause the solution to be distributed laterally in a radial fashion along the dermis, generating a field of approximately 1 cm in diameter in which the injected solution is distributed (Fig. 1a). The high-impact delivery of HA solution is proposed to effect two types of change in the dermis. In the short-term, the volume of dermal filler and its water-attracting effects produce immediate volume augmentation. In the longer term, the described HA-induced effects on fibroblasts, as well as the possible induction of a wound healing response by the mechanical micro-trauma of the pneumatic injection, are expected to produce longer-lasting changes in the dermis (Fig. 1a,b).

The use of the pneumatic acceleration of HA should provide a well-tolerated method for treating larger areas of skin, with minimal downtime and long-term improvement. We report short- and long-term clinical outcomes using the new device in the treatment of the aging hands, chest, neck, and face.

Materials and methods

Thirty-four participants with Fitzpatrick skin types I–IV and mild to moderate skin aging underwent 1–4 treatments per body area to evaluate the safety and efficacy of the Airgent system (PerfAction Ltd, Rehovot, Israel). Participants were treated at one or more body sites (Table 1), for a total of 69 treatment areas. Most participants completed three or four treatments at each site (1–4 treatments were performed on 2, 6, 44, and 17 participant sites, respectively). Informed consent was provided before treatment. Mean participant age was 53.2 years (range: 43–63 years). Treatment areas included the dorsal hands (38 cases), chest (7 cases), neck (13 cases), and face (11 cases). The study was conducted at three independent clinical sites. Exclusion criteria included pregnancy, connective tissue disease, history of herpes simplex in the treatment area, active infection of the skin in the treatment area, use of anticoagulants, clotting disorders, immunosuppressive therapy, prolonged systemic steroid therapy, or a tendency for hypertrophic scarring. Pre-treatment included cleaning the skin with 70% isopropyl alcohol. A granular scrub was used for mild exfoliation, after which a moisturizing cream was applied to hydrate the epidermis. A lidocaine-based topical anesthetic cream was applied for 30–40 min prior to treatment. At each treatment session, the needleless pneumatic injections of cross-linked, non-animal, HA solution were delivered in a grid-like distribution at 1 cm intervals to cover the treatment area homogeneously; approximately 2 mg HA are deposited in each 5 cm² treatment area. Contact time at each injection site was approximately 1 s. Treatments were performed at intervals of 3–4 weeks. The treatment area was gently massaged following treatment.

Short-term efficacy was evaluated 1–3 months after treatment. Long-term effects were evaluated 3–18 months after the conclusion of treatments. Prior to clinical studies, histological analysis was performed in the forearm skin of one participant, prior to treatment and at 4 months after the third treatment. Clinical efficacy outcomes were assessed by photographic analysis and by an independent medical reviewer.

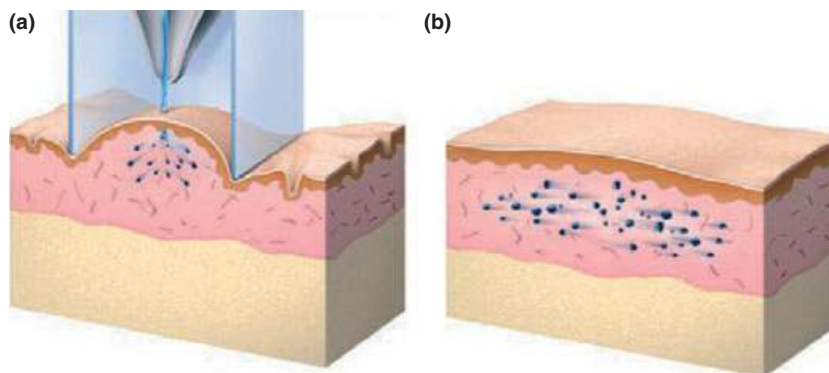


Figure 1 (a, b) The Airgent system uses a high-pressure jet to accelerate and disperse hyaluronic acid laterally at a controlled depth within the dermis

Table 1 Participant demographics

	Face n = 11	Neck n = 13	Chest n = 7	Dorsal hands n = 38
Mean age, years	56.6 ± 3.2	47.8 ± 6.8	51.1 ± 3.7	58.5 ± 4.4
Age range, years	48–61	43–63	47–55	48–63

Participant self-evaluation was also recorded. Before and after photographic images of the neck and face were scored according to the Fitzpatrick–Goldman classification of wrinkling and degree of elastosis (Table 2). Overall improvement was scored according to a predefined scale of 1–5 (0, worsening; 5, outstanding visual improvement; Table 3). Photographs of the dorsal hands were scored for improvement of protruding veins and OI according to the OI scale. Photographs of the chest were scored for OI according to the OI scale. Participant satisfaction was assessed using a three-category scale (unsatisfied, satisfied, very satisfied). Participants were also asked if they would recommend the treatment to others.

Results

The procedure was well tolerated by all participants, none of whom showed any serious adverse events. Immediately following treatment, the skin demonstrated focal elevations at the injection sites; these were fully resorbed within a few hours. The skin was then palpably thicker and visually more homogeneous in all treatment areas.

Table 2 Fitzpatrick–Goldman classification of wrinkling and degree of elastosis scale (1–9)

Class	Wrinkling	Score	Degree of elastosis
I	Fine wrinkles	1–3	<i>Mild</i> Fine textural changes with subtly accentuated skin lines
II	Fine to moderate depth wrinkles, moderate number of lines	4–6	<i>Moderate</i> Distinct papular elastosis
III	Fine to deep wrinkles, numerous lines, with or without redundant skin folds	7–9	<i>Severe</i> Multi-papular and confluent elastosis

Table 3 Protruding veins/overall improvement scale (OI scale)

0	Worsening
1	No visual effect
2	Mild visual improvement
3	Good visual improvement
4	Significant visual improvement
5	Outstanding visual improvement

Short-term results

A total of 69 body areas were treated.

Face

Eleven faces were treated. Figure 2 shows a representative result, with a notable reduction in facial wrinkles after a single treatment session. The Fitzpatrick–Goldman wrinkle severity scale score was reduced from 3.9 to 2.2 (39.4%; $P < 0.05$), representing a drop of an entire wrinkle class. The mean OI score was good (2.9; $P < 0.05$).

Neck

Thirteen neck areas were treated. Figure 3 shows a representative result. The Fitzpatrick–Goldman wrinkle severity scale score was reduced from 3.7 to 2.7 (30.4%; $P < 0.05$) representing a drop of an entire wrinkle class. The mean OI was good (2.4; $P < 0.05$).

Chest

Seven chest areas were treated. Figure 4 shows a representative result. Significant visual improvement was noticed following treatment (mean OI score 3.7; $P < 0.05$).

Dorsal hands

A total of 38 hands were treated. Overall improvement was good (mean OI score 2.8; $P < 0.05$). Improvement in vein prominence was also good (mean 2.8; $P < 0.05$). Figure 5 shows a representative result with reduced skin transparency and vein prominence.

Table 4 summarizes the results by treatment area, including OI in all areas treated and Fitzpatrick–Goldman scale scores for the neck and face.

Short-term participant satisfaction

Participants filled out a satisfaction questionnaire. Sixty of 69 body areas were evaluable. Overall, 80% of participants reported that they were satisfied or very satisfied, and 80% reported that they would recommend the treatment to others. After treatment of the face, 100% of participants (11/11) were very satisfied with results and would recommend the procedure to friends and family. The satisfaction and recommendation rates for treatment of the chest and dorsal hands were approximately 80%. The neck, which showed milder improvement in OI scores, yielded lower but still positive satisfaction reports (> 60%).

Long-term results

In total, 56 of 69 body areas were available for long-term follow-up (3–18 months). Of the 56 body areas, 50 underwent three or four treatments. The results seen in

Figure 2 Central region of the cheek in a 58-year-old woman at 1 month after treatment 2. (a) Before treatment; (b) after treatment

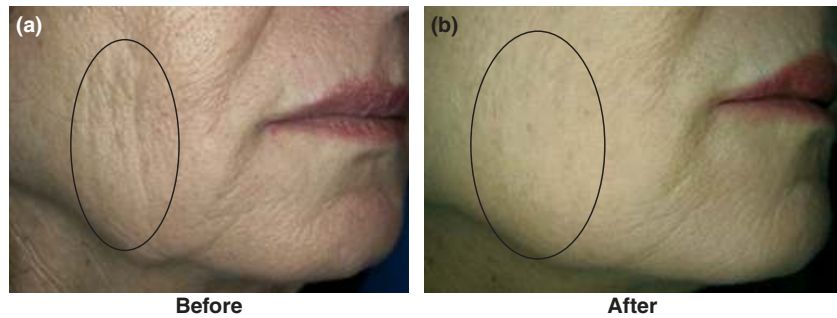


Figure 3 Neck in a 51-year-old woman at 1 month after treatment 2. (a) Before treatment; (b) after treatment

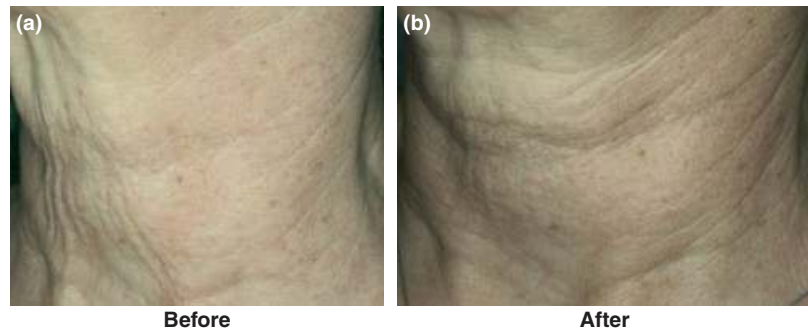
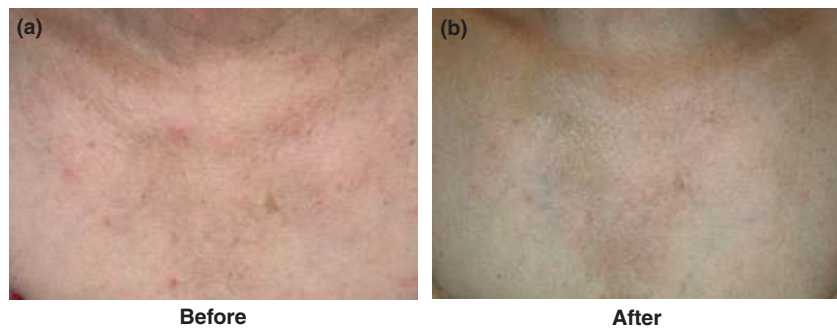


Figure 4 Chest in a 55-year-old woman, before and 1 month after treatment 2. (a) Before treatment; (b) after treatment



short-term evaluations persisted at long-term follow-up in all body areas.

Face

Nine faces were treated. Figure 6 shows a representative result, with a notable reduction in facial wrinkles. The Fitzpatrick–Goldman wrinkle severity scale was reduced from a baseline score of 4.3 to 3.1 (27.6%; $P < 0.05$), representing a drop of an entire wrinkle class. The mean OI score was significant (3.6; $P < 0.05$).

Neck

Seven neck areas were treated. Figure 7 shows a representative result. The Fitzpatrick–Goldman wrinkle severity score was reduced from a baseline score of 3.9 to a long-term follow-up score of 3.0, representing a 21.2%

decrease ($P < 0.05$). The mean OI was good (3.1; $P < 0.05$).

Chest

Five chest areas were treated. Figure 8 shows a representative result. Significant visual improvement was noticed (mean OI score 3.3; $P < 0.05$).

Dorsal hands

A total of 35 hands were treated. Overall improvement was significant (mean 3.6; $P < 0.05$). Improvement in vein prominence was good (mean 2.7; $P < 0.05$). Figure 9 shows a representative result with reduced skin transparency and vein prominence.

Table 5 summarizes the long-term results by treatment site, along with the OI for all treatment sites and the

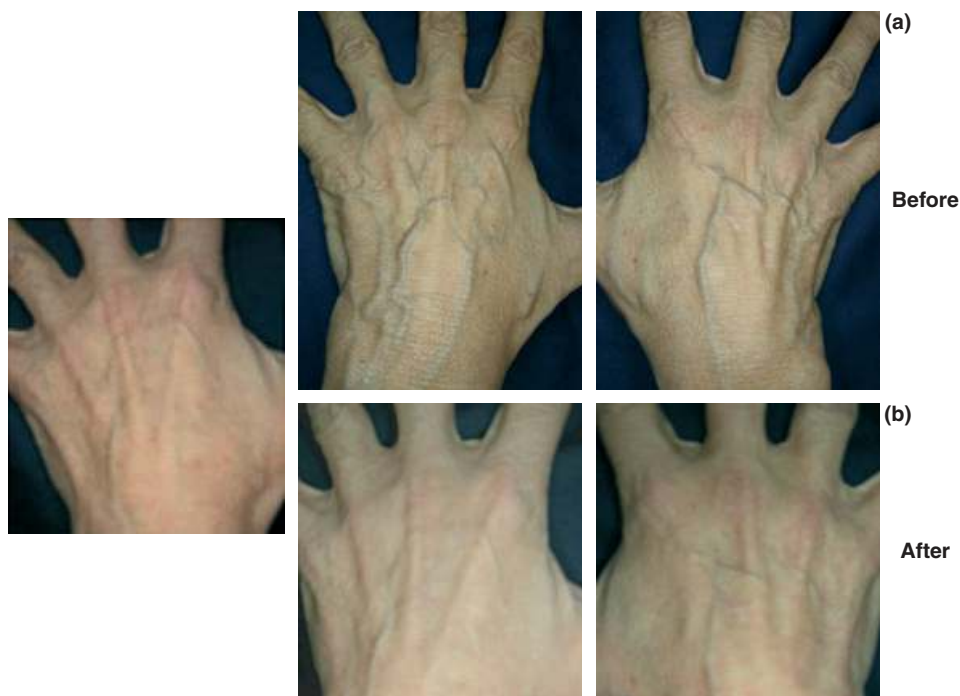


Figure 5 Dorsal hands in a 55-year-old woman, before and 1 month after treatment 2. (a) Before treatment; (b) after treatment

Table 4 Short-term results by treatment area

	Number of cases ^a	Overall improvement	Vein prominence	Fitzpatrick–Goldman scale		Change (%)
				Before ^b	After	
Face	11	Good (2.9) ^c		3.9	2.2 ^c	–39.4
Neck	13	Mild (2.4) ^c		3.8	2.7 ^c	–30.4
Chest	7	Significant (3.7) ^c				
Dorsal hands	38	Good (2.8) ^c	Good (2.8) ^c			

^aNumber of cases per area treated; some participants were treated on more than one body site; ^bMean “before” Fitzpatrick–Goldman scale scores were calculated for participants who completed the follow-up; ^c $P < 0.05$.

improvement in Fitzpatrick–Goldman scale scores for the face and neck.

Histological analysis

Histological analysis was performed in one volunteer. Biopsy specimens were obtained from treated and untreated skin of the forearm in a 39-year-old male 4 months after the third treatment. Comparison of the treated and untreated skin shows increased levels of collagen III in treated skin, confirmed by reticulin staining

(Fig. 10). The finding of increased collagen at 4 months after treatment supports the proposed mechanism of stimulation of neocollagenesis.

Adverse effects were mild and transient. Pinpoint bleeding, transient erythema, mild and transient edema, and focal tenderness were common and resolved within 24 h. A single case of focal post-inflammatory hyperpigmentation was reported. This case resolved almost completely within 6 months and completely within 12 months.

Discussion

Non-surgical rejuvenation of aging skin is expanding to “off-the-face” treatments to improve the appearance of aging skin in all visible areas. Laser and radiofrequency devices have been demonstrated to induce collagen remodeling and new collagen formation, both by thermal stimulation and in concert with a dermal wound healing response. Dermal fillers, such as HA, also induce neocollagenesis. The Airgent system was designed to combine the benefits of HA injections with those of mild dermal wound healing. The pneumatic delivery of the HA causes focal dermal trauma, and the needleless delivery mechanism improves the ability to treat extended planes of skin. The device is commercially available in North America, Europe, and Asia.

This study assessed the safety and efficacy of high-pressure, pneumatic, needleless injections on the face,

Figure 6 Central region of the cheek in the 58-year-old woman shown in Fig. 2, at 8 months after treatment 4. (a) Before treatment; (b) after treatment

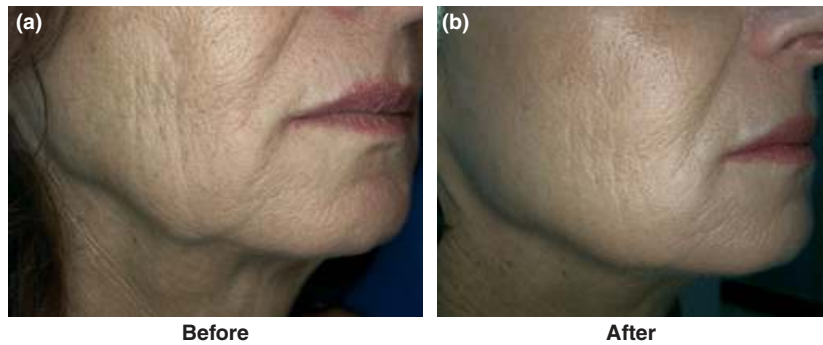


Figure 7 Neck in a 55-year-old woman at 18 months after treatment 2. (a) Before treatment; (b) after treatment

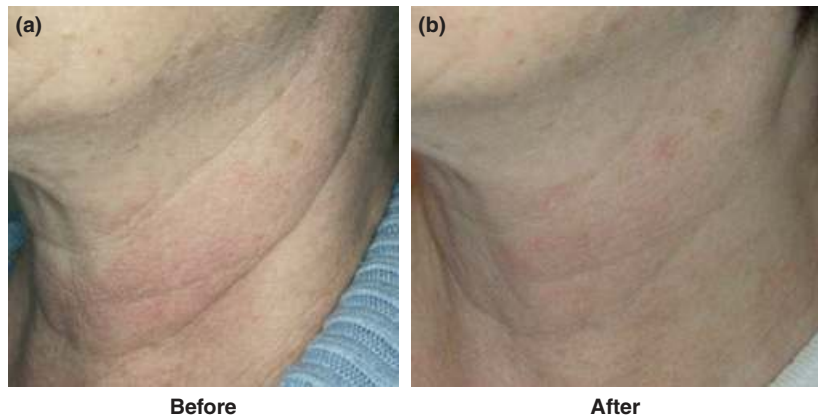


Figure 8 Chest in a 47-year-old woman, before and 8 months after treatment 3. (a) Before treatment; (b) after treatment

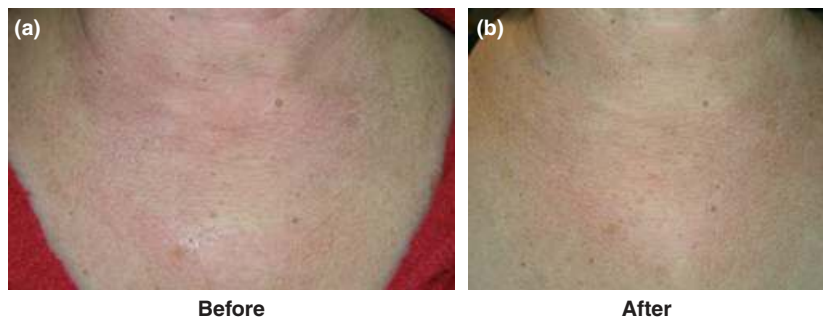
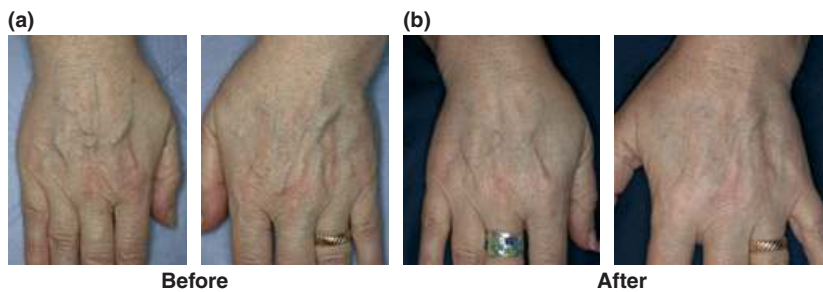


Figure 9 Dorsal hands in a 50-year-old woman, before and 5 months after treatment 4. (a) Before treatment; (b) after treatment



neck, chest, and dorsal hands. These areas are often sun-damaged and are not very well addressed by current filler-based technologies. The data demonstrate significant

short-term improvement, particularly on the face and neck, on which treatment reduced the mean Fitzpatrick–Goldman scale score by 30% in short-term evaluation

Table 5 Long-term results (up to 18 months) by treatment area

	Number of cases ^a	Overall improvement	Vein prominence	Fitzpatrick–Goldman scale		Change (%)
				Before ^b	After	
Face	9	Significant (3.6) ^c		4.3	3.1 ^c	-27.6 ^d
Neck	7	Good (3.1) ^c		3.9	3.0 ^c	-21.2 ^d
Chest	5	Significant (3.6) ^c				
Dorsal hands	35	Good (3.3) ^c	Good (2.7) ^c			

^aNumber of cases per area treated; some participants were treated on more than one body area; ^bMean “before” Fitzpatrick–Goldman scale scores were calculated for participants who completed the follow-up; ^c $P < 0.05$; ^d.

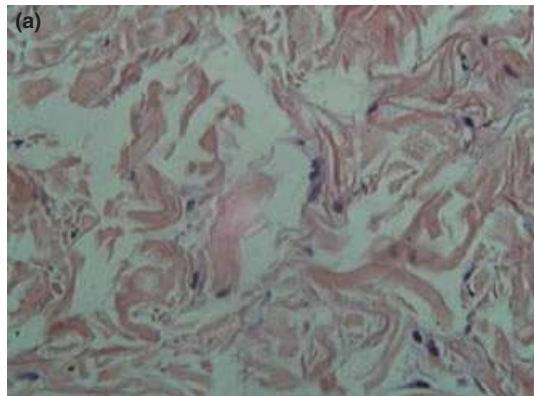
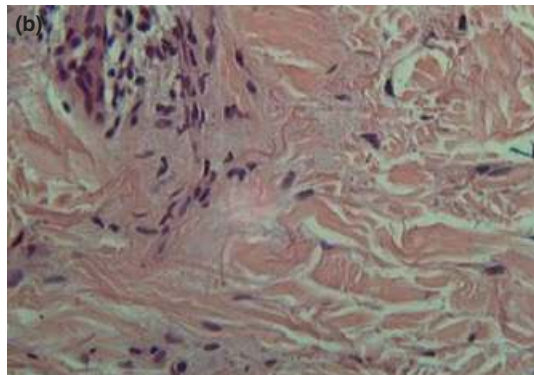
Control site**Treated site**

Figure 10 Histological analysis of (a) untreated and (b) treated skin from the arm of a 39-year-old man 4 months after treatment 3. Reticulin staining highlights an increased amount of collagen III fibers in the dermis of the treated area. (Hematoxylin and eosin stain; original magnification $\times 40$)

and by 21% in long-term evaluation (up to 18 months). Treatment of the dorsal hands and chest, for which there are no well-established treatments, showed good visible results and elicited high levels of satisfaction. The overall patient satisfaction rate of over 80% demonstrates the tolerability and effectiveness of the treatments.

Conclusions

Based on the results of this study, high-pressure, pneumatic, needleless injection of HA solution appears to be safe and effective for short- and long-term skin rejuvenation. The procedure can be performed on numerous body areas, particularly on the dorsal hands, chest, neck, and face. The low downtime and prolonged improvement provide an attractive treatment option for dermal restoration.

References

- 1 Fisher GJ, Varani J, Voorhees JJ. Looking older: fibroblast collapse and therapeutic implications. *Arch Dermatol* 2008; **144**: 666–672.
- 2 Uitto J, Bernstein EF. Molecular mechanisms of cutaneous aging: connective tissue alterations in the dermis. *J Invest Dermatol Symp Proc* 1998; **3**: 41–44.
- 3 Ramos-e-Silva M, da Silva Carneiro SC. Elderly skin and its rejuvenation: products and procedures for the aging skin. *J Cosmet Dermatol* 2007; **6**: 40–50.
- 4 Nelson JS, Majaron B, Kelly KM. What is non-ablative photorejuvenation of human skin? *Semin Cutan Med Surg* 2002; **21**: 238–250.
- 5 Hruza GJ. Rejuvenating the aging face. *Arch Dermatol* 2004; **140**: 1383–1386.
- 6 Herne KB, Zachary CB. New facial rejuvenation techniques. *Semin Cutan Med Surg* 2000; **19**: 221–231.
- 7 Dover JS, Zelickson B. Results of a survey of 5700 patient monopolar radiofrequency facial skin tightening treatments: assessment of a low-energy multiple-pass technique leading to a clinical endpoint algorithm. *Dermatol Surg* 2007; **33**: 900–907.
- 8 Weiss RA, Gold M, Bene N, et al. Prospective clinical evaluation of 1440-nm laser delivered by microarray for treatment of photoaging and scars. *J Drugs Dermatol* 2006; **5**: 740–744.
- 9 Alexiades-Armenakas M, Dover JS, Arndt KA. Unipolar versus bipolar radiofrequency treatment of rhytides and laxity using a mobile painless delivery method. *Lasers Surg Med* 2008; **40**: 446–453.
- 10 Grekin RC, Tope WD, Yarbrough JM Jr, et al. Electrosurgical facial resurfacing: a prospective multicenter study of efficacy and safety. *Arch Dermatol* 2000; **136**: 1309–1316.
- 11 Sadick NS. Combination radiofrequency and light energies: electro-optical synergy technology in esthetic

- medicine. *Dermatol Surg* 2005; 31: 1211-1217. Discussion 1217.
- 12 Yu CS, Yeung CK, Shek SY, et al. Combined infrared light and bipolar radiofrequency for skin tightening in Asians. *Lasers Surg Med* 2007; 39: 471-475.
- 13 Gold MH, Goldman MP, Rao J, et al. Treatment of wrinkles and elastosis using vacuum-assisted bipolar radiofrequency heating of the dermis. *Dermatol Surg* 2007; 33: 300-309.
- 14 Nestor MS, Gold MH, Kauvar AN, et al. The use of photodynamic therapy in dermatology: results of a consensus conference. *J Drugs Dermatol* 2006; 5: 140-154.
- 15 Gold MH. Photodynamic therapy update 2007. *J Drugs Dermatol* 2007; 6: 1131-1137.
- 16 Goldberg DJ. Photodynamic therapy in skin rejuvenation. *Clin Dermatol* 2008; 26: 608-613.
- 17 Dover JS, Bhatia AC, Stewart B, Arndt KA. Topical 5-aminolevulinic acid combined with intense pulsed light in the treatment of photoaging. *Arch Dermatol* 2005; 141: 1247-1252.
- 18 Weiss RA, Weiss MA, Munavalli G, Beasley KL. Monopolar radiofrequency facial tightening: a retrospective analysis of efficacy and safety in over 600 treatments. *J Drugs Dermatol* 2006; 5: 707-712.
- 19 Nouri K, Rivas MP, Bouzari N, Faghieh S. Non-ablative lasers. *J Cosmet Dermatol* 2006; 5: 107-114.
- 20 Kono T, Kinney BM, Groff WF, et al. Randomized, evaluator-blind, split-face comparison study of single cross-linked versus double cross-linked hyaluronic acid in the treatment of glabellar lines. *Dermatol Surg* 2008; 34(Suppl 1): 25-30.
- 21 Gold MH. What's new with hyaluronic acid fillers. *J Drugs Dermatol* 2007; 6: 1050-1053.
- 22 Gold MH. Use of hyaluronic acid fillers for the treatment of the aging face. *Clin Interv Aging* 2007; 2: 369-376.
- 23 Kelly PE. Injectable success: from fillers to botox. *Facial Plast Surg* 2007; 23: 7-18. Discussion 19-20.
- 24 Lupo MP. Hyaluronic acid fillers in facial rejuvenation. *Semin Cutan Med Surg* 2006; 25: 122-126.
- 25 Wang F, Garza LA, Kang S, et al. *In vivo* stimulation of *de novo* collagen production caused by cross-linked hyaluronic acid dermal filler injections in photodamaged human skin. *Arch Dermatol* 2007; 143: 155-163.
- 26 Mitragotri S. Current status and future prospects of needle-free liquid jet injectors. *Nat Rev Drug Discov* 2006; 5: 543-548.
- 27 Martin P. Wound healing – aiming for perfect skin regeneration. *Science* 1997; 276: 75-81.