Histologic Effects of Fractional Laser and Radiofrequency Devices on Hyaluronic Acid Filler

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BACKGROUND Hyaluronic acid fillers (HAFs) and energy-based devices are frequently used sequentially. However, the effect of using fractional devices directly over HAF is unclear.

OBJECTIVE To evaluate histologic changes after fractional laser and radiofrequency (RF) therapies applied over preinjected HAF.

MATERIALS AND METHODS Abdominoplasty skin samples were divided into 8 zones. Intradermal injections of HAF were performed to 7 zones with 1 zone as untreated control. Six of 7 HAF injected zones were then treated with the following devices: 1,540-, 1,550-, 1927-, and 10,600-nm fractional lasers, and fractional bipolar RF delivered through insulated and noninsulated microneedles. After treatment, biopsies were collected for H&E staining.

RESULTS Histology revealed HAF in the mid to deep dermis. Treatment with 1,540-, 1,550-, 1927-, and 10,600-nm lasers did not result in any morphologic changes of HAF, although thermal changes from 1,540- and 1,550-nm lasers were in very close proximity to the filler. The RF devices demonstrated thermal damage of HAF along the microneedle tracks.

CONCLUSION Hyaluronic acid filler is unaffected by fractional lasers in this model. Fractional RF devices, which produce deeper dermal penetrations, will cause thermal damage of HAF. Caution is advised in using microneedle RF over recently injected filler. Study limitations include use of nonfacial skin and lack of inflammatory response in an ex-vivo model.

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There is a growing demand for noninvasive and minimally invasive procedures for facial rejuvenation. These procedures include injectables such as fillers and neuromodulators, as well as energy-based devices including lasers or intense pulsed light, radiofrequency (RF), and ultrasound therapies.

In particular, fractional lasers, both nonablative and ablative, are becoming the preferred method for skin resurfacing. Fractional resurfacing is based on the concept of fractional photothermolysis and refers to the creation of arrays of microscopic thermal wounds in the skin, or microscopic treatment zones (MTZs).[1] As the tissue surrounding each wound is spared, the skin is able to heal more rapidly and with significantly reduced side effects as compared to traditional fully ablative lasers. Similar to the concept of fractional photothermolysis in laser therapy, fractional RF involves the formation of spatially confined zones of thermal injury. Furthermore, with the incorporation of microneedles, controlled, deeper dermal penetrations are able to be achieved. Fractional RF has been found to be particularly effective in stimulating collagen and elastin production, and is frequently used for the treatment of skin laxity, rhytides, and acne scars.

To obtain the optimal aesthetic result, a therapeutic plan involving multiple treatment modalities is often necessary. For examples, fillers may be used to address

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volume loss and deeper folds, whereas energy devices may be needed to address more superficial changes such as pigmentation and skin texture. Although same day treatments are generally preferred, there is apprehension toward concomitant treatments because the interaction between energy-based therapies and recently injected fillers is unclear. Among the various soft-tissue fillers, hyaluronic acid fillers (HAFs) tend to be placed more superficially and therefore may be at greater risk of alteration when an energy-based device is used to treat the overlying skin.

Several previous studies have examined the effect of energy devices on HAF and other soft-tissue fillers.[2–7] However, studies specifically examining the histologic effects of using fractional lasers and microneedle RF devices directly over HAF in human skin are lacking. Therefore, this study was conducted to evaluate whether the use of fractional lasers and RF therapies after implantation of HAF alters the integrity of the filler in human abdominal skin samples.

Methods

Fresh human skin samples were obtained from deidentified, discarded tissue during routine cosmetic abdominoplasty surgery. The tissue was divided into 8 zones, and intradermal injections of 0.1 mL of HAF (Juvederm Ultra; Allergan, Irvine, CA) were performed to 7 of the 8 zones. One of the zones was left untreated as normal control. Six of the 7 zones were additionally treated with a fractional laser or RF device. Treatment parameters commonly used in the clinical setting for acne scarring or rejuvenation were applied.

Detailed settings used were as follows:

(1) 1,540-nm Erbium:Glass Fractional Nonablative Laser (Starlux 1540; Palomar Medical Technologies, Burlington, MA): 50 mJ, 15 ms, and 5 stacked-pulses
(2) 1,550-nm Erbium:Glass Fractional Nonablative Laser (Fraxel DUAL; Solta Medical, Hayward, CA): 40 mJ, treatment level 6, set passes 6, and actual passes 6
(3) 1,927-nm Thulium Fiber Fractional Nonablative Laser (Fraxel DUAL; Solta Medical): 20 mJ, treatment level 4, set passes 6, and actual passes 6
(4) 10,600-nm CO_2 Fractional Ablative Laser (UltraPulse Encore; Lumenis, Santa Clara, CA): DeepFx, 30 mJ, density 5%, and 2 passes
(5) Fractional Bipolar RF with Insulated Microneedles (INFINI; Lutronic, Burlington, MA): 3 passes; first pass: 2.5 mm/level 3/300 ms, second pass: 2 mm/level 3/300 ms, and third pass: 1 mm/level 3/300 ms
(6) Fractional Bipolar RF with Non-insulated Microneedles (Intensif; EndyMed, Caesarea, Israel): 2.5 mm/14W/110 ms for 3 passes and 1 mm/14W/110 ms for 1 pass

A total of 4-mm punch biopsies were collected from each of the 8 zones and stained with hematoxylin and eosin (H&E) after vertical sectioning.

To obtain an accurate representation of the interaction between the fractional energy device and HAF in each sample, at least 80 sections of each specimen were processed. Histologic evaluation of all specimens was performed by a board-certified dermatopathologist (H.J.C.).

The distance from the granular layer and from the dermoepidermal junction (DEJ) to the most superficial portions of HAF was measured in all specimen. In addition, the distance from the granular layer and from the DEJ to the deepest portions of the MTZ was measured in each specimen treated with a laser or RF device. As even slight sectioning angles could dramatically affect the identification of the true depth of the MTZ, 3 of the deepest MTZs were identified in each specimen, and an average depth was obtained.

Results

In the 7 zones that were injected with HAF, H&E stains revealed amorphous basophilic deposition of HAF mainly in the mid to deep reticular dermis. Average distances from the granular layer and from the DEJ to the most superficial portions of the filler were 0.47 mm (range 0.24–0.83 mm) and 0.42 mm

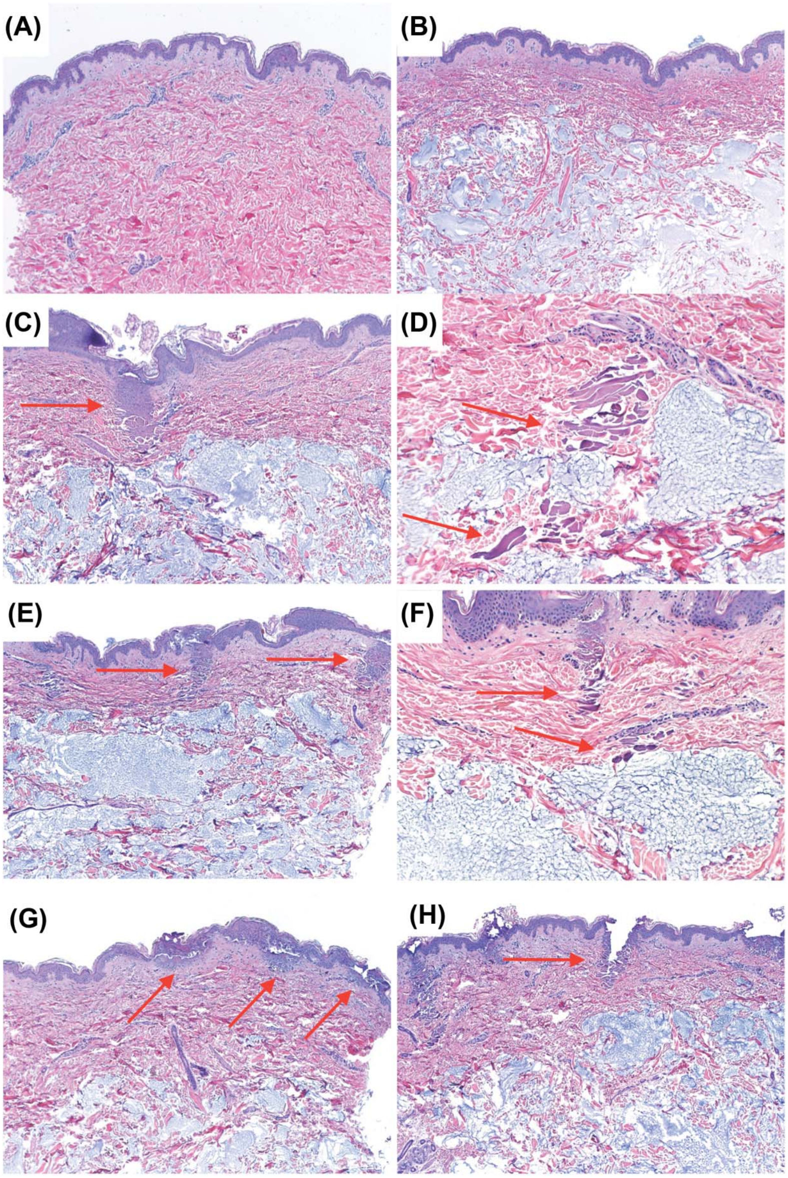

Figure 1. Histology of control skin (A), skin injected with HAF (B), skin injected with HAF followed by treatment with fractional 1,540-nm Er:glass (C and D), 1,550-nm Er:glass (E and F), 1,927-nm thulium (G), and 10,600-nm CO_2 lasers (H). Arrows indicate the zones of thermal changes induced by each laser treatment. (H&E stain; magnification: 4× for A–H, 10× for D and F). HAF, hyaluronic acid filler.

(range 0.20–0.79 mm), respectively, with normal skin in the control zone (Figure 1A,B).

The 1,540-nm Er:glass, 1,550-nm Er:glass, and 1,927-nm thulium fiber lasers created coagulated collagen columns with intact stratum corneum and separation of DEJ (Figure 1C–G). The 10,600-nm CO_2 fractional laser produced a conical-shaped evaporation of the dermis and epidermis with surrounding thermal damage, demonstrated by degenerated collagen bundles (Figure 1H). Depths of MTZs of the 1,540-, 1,550-, 1927-, and 10,600-nm fractional lasers were measured to be 0.85, 0.54, 0.21, and 0.58 mm from the granular layer, and 0.78, 0.44, 0.10, and 0.54 mm from the DEJ, respectively.

Damage induced by the 1,927- and 10,600-nm lasers did not penetrate deeply enough to come in direct contact with the filler (Figure 1G,H). Microcolumns of injury from the 1,540-nm laser abutted the superficial portions of the filler and did not reveal any significant collateral changes of HAF (Figure 1C,D). Thermal

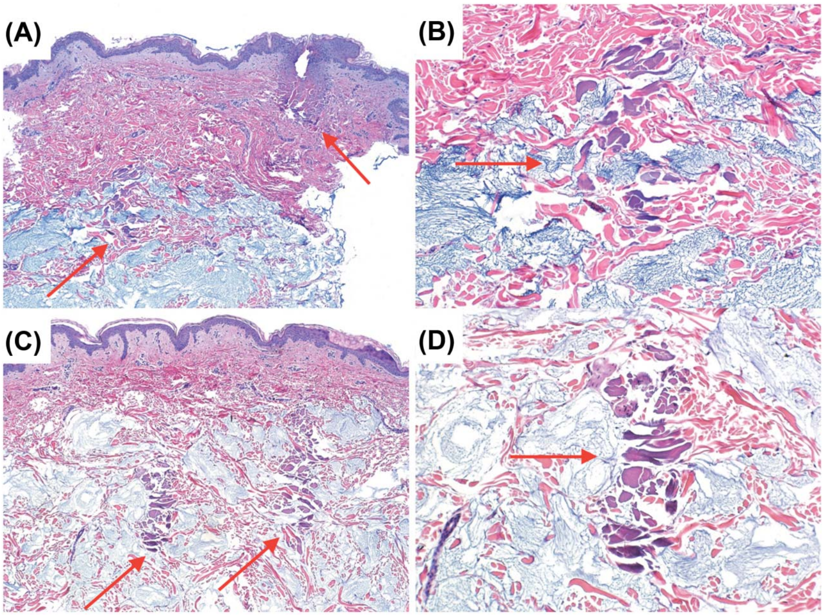

Figure 2. Histology of skin injected with HAF followed by treatment with fractional bipolar radiofrequency delivered through insulated microneedles (A and B) and noninsulated microneedles (C and D). Arrows indicate the zones of thermal changes induced by the radiofrequency device. (H&E stain; magnification: 4× for A and C, 10× for B and D). HAF, hyaluronic acid filler.

changes from the 1,550-nm laser were also found to be in very close proximity to the HAF, and there was no evidence of HAF changes in the areas adjacent to the MTZ (Figure 1E,F).

The 2 microneedle bipolar RF devices produced deeper dermal penetrations as compared to the lasers. The greatest depths of thermal damage were 1.92 mm with insulated microneedles (Figure 2A,B) and 1.38 mm with noninsulated microneedles (Figure 2C,D). At these depths, columns of injury induced by the RF devices penetrated into the preinjected HAF, with histologic evidence of thermal injury of the filler along the microneedles tracks. Evidence of thermal injury was demonstrated by decreased filler between the purplish degenerated collagen bundles as compared to the surrounding tissue. HAF in the areas immediately around the microneedle tracks seemed to be unaffected.

Conclusion

The use of fillers in combination with fractional lasers and RF devices has the potential to address various changes related to aging and photodamage. However, it has been theorized that the use of an energy-based device immediately after filler injection may reduce the clinical effect and/or longevity of the filler. This study demonstrates that treatment with a fractional non-ablative or ablative laser after implantation of HAF does not result in any significant morphologic changes of the filler.

It should be noted that none of the fractional lasers produced MTZs that penetrated through the pre-injected HAF, although thermal injuries from the 1,540- and 1,550-nm lasers were adjacent to or in very close proximity to the filler. Histologically, the HAF was identified in the mid to deep reticular dermis, while depth of injury from the fractional lasers was limited to the papillary to mid reticular dermis. This is not to say that thermal injury cannot penetrate deeper with these devices. The treatment parameters used in this study were intended to simulate what may be used in a clinical setting. However, more aggressive treatment parameters would have certainly increased the depth of thermal damage. It has been suggested that the depth of coagulation from a fractional laser increases roughly by a factor of 10 μm for each millijoule of increased energy.[8] A previous study on a porcine model used the fractional ablative CO_2 and erbium:YAG lasers to create dermal injuries that actually came in direct contact with the preinjected

HAF.[4] Histology revealed the filler within some of the ablated microchannels, but morphologic changes or denaturation of HAF was not demonstrated.

On the other hand, fractional microneedle RF devices, which involve deeper dermal penetrations, were found to cause thermal damage of the filler along the microneedle tracks. The target temperature of fractional RF devices is 60 to 75°C, which is the optimal dermal temperature for collagen contraction and neocollagenesis.[9,10] Although the temperature right at the surface of the microneedles may be higher, it is unlikely significantly greater. This study suggests that HAF may not be stable at these temperatures, as demonstrated by decreased HAF in the areas penetrated by microneedle RF as compared to adjacent areas. It is likely that the reduction in HAF represents evaporation of the filler from thermal damage. With regard to the use of nonablative RF devices over preinjected HAF, studies have previously demonstrated that the underlying filler is not affected.[2,3]

A significant limitation of this study was the use of abdominal skin, which is certainly not a perfect model for facial skin where combination treatments are typically administered. Facial skin has a higher density of hair follicles, sebaceous glands, and vessels, as well as a thinner epidermis and dermis,[11] and therefore may react differently to laser/RF therapies than abdominal skin. Furthermore, an ex vivo model does not capture the inflammatory response that follows treatment with an energy-based device, which may also affect the HAF.

Given these limitations, it still remains to be explored whether the histologic findings from this study translates to clinical outcomes. Overall, however, this study highlights the importance of understanding the level of penetration of energy-based therapies with respect to the depth of HAF injection. When the thermal energy penetrated through the filler, as was the case with the microneedle RF devices, there was evidence of significant changes of the surrounding HAF. When the thermal injury was superficial to the HAF, as with the fractional lasers, the HAF remained intact. Based on these findings, particular caution should be taken when using microneedle RF devices directly over HAF, especially when the filler is placed superficially.

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