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PUBLICATION INFORMATION

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- The Renuvion® APR Handpiece is intended for the delivery of radiofrequency energy and/or helium plasma for cutting, coagulation, and ablation of soft tissue during open surgical procedures.
- The Renuvion® APR Handpiece is indicated for use in subcutaneous dermatological and aesthetic procedures to improve the appearance of lax (loose) skin in the neck and submental region.
- The Renuvion® APR Handpiece is intended to be used with compatible electrosurgical generators owned by Apyx Medical (specifically BVX-200H, BVX-200P, APYX-200H, APYX-200P, APYX-RS3, and APYX-JS3).
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- The use of Renuvion with liposuction has not been approved or cleared by the FDA.

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- As with all energy devices there are inherent risks associated with its use. Risk associated with the use of the Renuvion APR may include: helium embolism into the surgical site due to inadvertent introduction into the venous or arterial blood supply system, unintended burns (deep or superficial), pneumothorax, temporary or permanent nerve injury, ischemia, fibrosis, infection, pain, discomfort, gas buildup resulting in temporary and transient crepitus or pain, bleeding, hematoma, seroma, subcutaneous induration, pigmentation changes, increased healing time, scarring, asymmetry and/or unacceptable cosmetic result.

As with any procedure, individual results may vary. As with all energy devices there are inherent risks associated with its use, refer to the IFU for further information.

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ORIGINAL CONTRIBUTION

Thermal effects of percutaneous application of plasma/radiofrequency energy on porcine dermis and fibroseptal network

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Abstract

Background: Skin laxity is one of the defining characteristics of aging and can be the result of various factors including intrinsic aging, genetics, diet, stress, lifestyle, sun exposure, weight fluctuations, and smoking. Recent reports suggest the ability of subdermal energy application to reduce skin laxity. Thermal energy can be delivered using different devices including lasers, radiofrequency (RF) monopolar and bipolar devices, and plasma/RF devices. Plasma-based energy platforms generate a plasma gas, allowing heat to be applied to the tissue. This study focused on the evaluation of thermal effect of plasma/RF compared to a monopolar RF device applied percutaneously to the subdermis and connective fibroseptal network in a porcine model.

Methods: The subdermal application of energy was conducted using a plasma/RF system and a monopolar RF system. Both low and high energy/temperature settings were evaluated in dynamic and stationary modes. Histomorphometry was used to determine the depth of thermal effect associated with each treatment setting.

Results: Both dermis and fibroseptal network tissue exhibited the presence of microscopically thermally treated zones. There were no significant differences in average and maximum depths of thermal effect between the different handpieces and electrosurgical systems used for all treatment settings.

Conclusions: No significant differences in the thermal effect between plasma/RF and monopolar RF systems were observed, suggesting that plasma/RF systems can be safely used for the percutaneous application of energy in the subcutaneous space.

KEYWORDS

comparative study, collagen, cosmetic surgery, helium plasma, nitrogen plasma, porcine model, radiofrequency

1 | INTRODUCTION

Thermally induced contraction of soft tissue due to the coagulation and denaturation of collagen has long been used to achieve therapeutic effects in ophthalmology, vascular surgery, treatment of varicose veins, and cosmetic and reconstructive surgery.[1-5] The reduction in volume and tissue surface area is the result of protein denaturation and collagen contraction after a thermal energy threshold has been transmitted to the tissue.[6,7]

In dermatology and cosmetic surgery, the noninvasive use of lasers, radiofrequency (RF), and plasma devices have been well established for the treatment of facial wrinkles and rhytides.[8-10] Recently, lasers and RF energy devices have also been used percutaneously for collagen coagulation to induce skin contraction and reduce laxity.[11] Laser-assisted liposuction and radiofrequency-assisted liposuction consist of the application of energy in conjuction with liposuction.[12,13] Percutaneous probes are placed in the same tissue plane where the suction is done to deliver energy to the underside of the dermis, fascia, and connective fibroseptal network. The coagulation of the subcutaneous tissue results in collagen/tissue contraction and thus reduces skin laxity.

More recently, the subdermal application of energy using plasma/RF devices to induce tissue contraction has been reported.[14,15] Plasma energy systems consist of an electrosurgical generator unit, a handpiece, and a supply of gas. A gas plasma is generated when the gas is passed over an energized electrode. Heat is generated both by the production of the plasma beam and when the current passed through the tissue.[14,15] Zamora and Roman reported a beneficial effect of plasma/RF for the reduction of laxity on the body, face, and neck in more than 700 cases.[15] Also, Gentile published case reports of successful treatment of submental and neck laxity following subcutaneous application of plasma/RF energy.[16]

Although Holcomb and Shucker have reported on the tissue effects of helium plasma on porcine epidermis,[17] the thermal effect of subcutaneous delivery of plasma/RF to the subcutaneous space and its impact on the reticular dermis and fibroseptal network (FSN) has not been well characterized. The purpose of this study was to quantify and compare the thermal effects of a plasma/RF system to a temperature-controlled RF system in a porcine model.

2 | MATERIALS AND METHODS

This study was conducted per Good Laboratory Practice (GLP) standards at the MedStar Health Research Institute (Washington DC) and approved by the MedStar's Institutional Animal Care and Use Committee (IACUC). In order to ensure appropriate study controls and data integrity, an independent GLP study director and quality assurance monitor conducted the study, gathered and reviewed the data, and prepared the study report. In addition, the histomorphometric analysis was performed per GLP standards by American Preclinical Services. The histopathologist who performed the depth measurements was blinded to the treatment modality and settings used for each of the treatment sites evaluated.

2.1 | Device descriptions

2.1.1 | Plasma/RF system

The plasma/RF system used in this study was the Renuvion system (Apyx Medical) that is indicated for cutting, coagulation, and ablation of soft tissue.[18] RF energy is delivered to the electrode which is used to energize a helium gas, thereby creating an electrically conductive plasma. The RF generator provides adjustable power up to 40 W expressed as 0%-100%, where 100% is 40 W. Two handpieces were used during this study. The first was the Renuvion Precise handpiece which is used for the delivery of helium plasma/RF for cutting, coagulation, and ablation of soft tissue. The second was the Renuvion Plasma/RF handpiece, a newly developed handpiece, designed to be inserted percutaneously into the subdermal space where it can be used to deliver plasma/RF energy to the underside of the dermis, fascia, and septal connective tissue.

2.1.2 | Temperature-controlled radiofrequency system

The temperature-controlled, monopolar RF system used in this study was the ThermiX (ThermiGen, LLC) which consists of a RF generator with an integrated temperature feedback loop that adjusts the energy delivery to maintain the set temperature.[19] It is operating with a set temperature range between 35°C and 90°C and allows the physician to control treatment temperature.[19]

2.2 | Treatment procedure

One female Yorkshire domestic cross swine (26.7 weeks of age, 68.8 kg) was sedated and intubated. The hair from both lateral flanks was clipped. In order to address the challenges associated with identification and harvesting of subcutaneous treatment locations, two skin flaps, one on the right side and one on the left side of the animal, were prepared. The u-shaped skin flaps were produced by making a 30-cm longitudinal incision along the dorsal plane just lateral to the teats and two 25-cm incisions perpendicular to the longitudinal incision (Figure 1). The dissection plane of the skin flap on the left flank was closer to the superficial dermis (Figure 2A), while the dissection plane of the skin flap on the right flank was in the deeper connective tissue/fibroseptal network (Figure 2B). Prior to treatment of the tissue, a loop of suture was placed through the skin so that it was visible on the underside of the flap. The tip of the handpiece being tested was then placed through the loop of suture, the flap of tissue was reapproximated to simulate percutaneous activation of the handpiece, and the device was activated while being pulled through the suture. This method ensured that energy was delivered to the tissue directly within the suture loop. During harvesting, enough tissue was taken to allow the suture to remain intact to serve as a marker for the histological evaluation.

The different treatment settings used in this study can be found in Table 1. The application of energy was conducted using either the plasma/RF system or the temperature-controlled RF system. For the plasma/RF system, the two handpieces described previously were evaluated. The application of energy was conducted both in a stationary and a dynamic mode using a 60% and 80% power generator

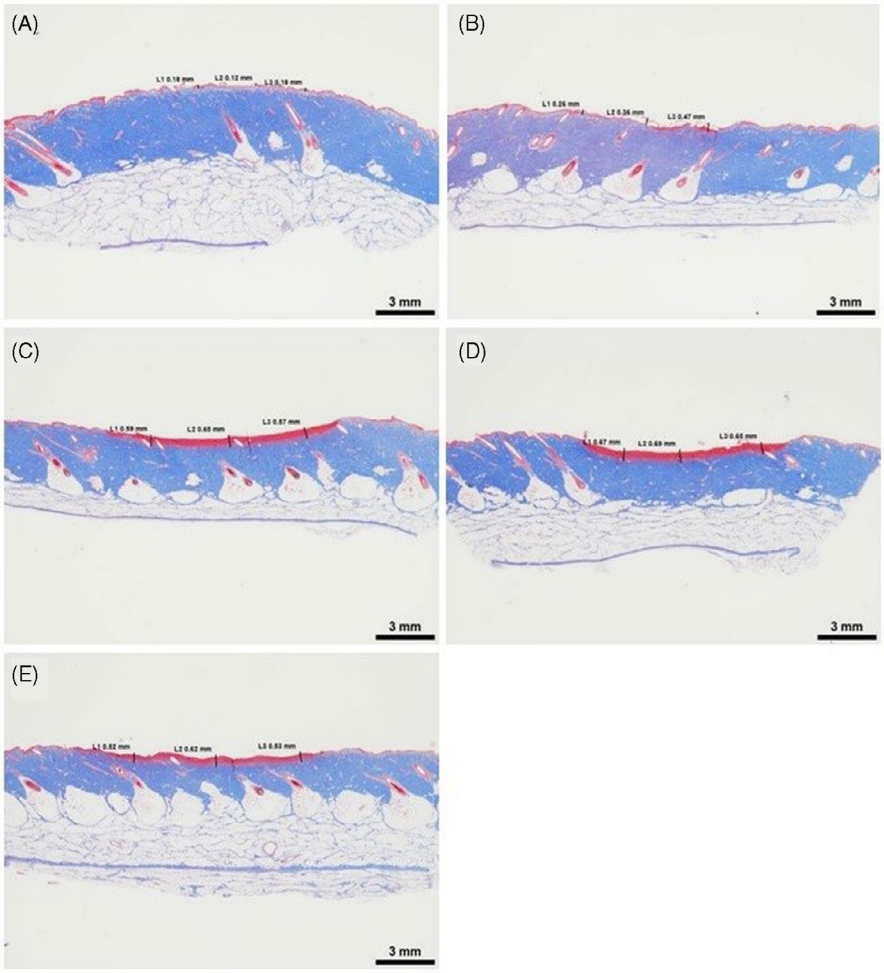

FIGURE 1 Schematic of skin flaps used on the right and left flanks. The cross marks indicate the treatment locations

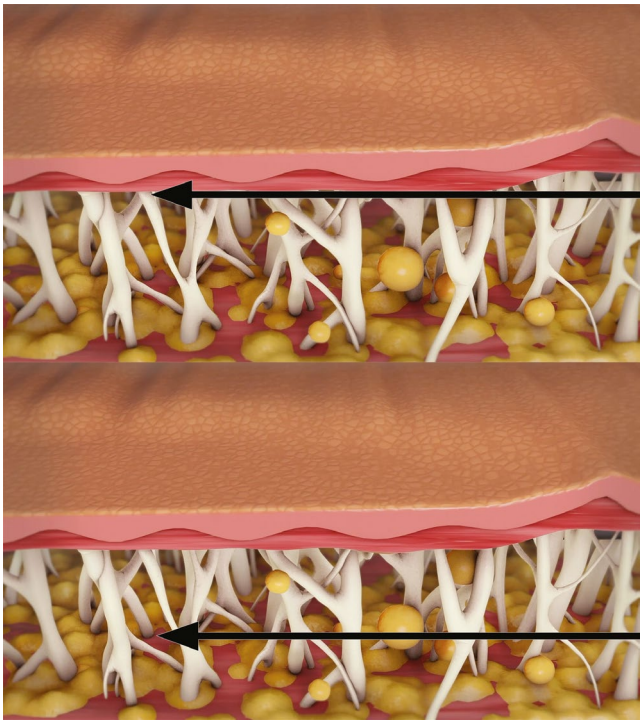

FIGURE 2 Skin flap dissection planes indicated by the black arrow. (A) Superficial dissection plane used on the left flank. (B) Deep dissection plane used on the right flank

setting for the plasma/RF system and a high and low energy/temperature setting (50°C and 75°C) for the temperature-controlled RF system, as these settings are consistent with the low and high settings for these devices commonly used in the clinical setting. For the plasma/RF system, the helium flow rate was set to 4 L/min.

For dynamic treatments, the handpiece was activated, and the tip of the device was pulled through the loop of suture at a speed of approximately 1 cm/s. For stationary treatments, the distal tip of the handpiece was placed directly within the loop of suture, and energy was delivered for 5 seconds is the same location. Each treatment condition was conducted in triplicates. The animal was euthanized immediately after completion of all treatments.

2.3 | Histological evaluation

Skin tissue samples, including a 5 mm area around the treatment site containing the suture, were harvested immediately after euthanasia. Following formalin fixation, each treatment site was sectioned through the center (4-6 μm) and processed routinely. Each section was stained with Haemotoxylin and Eosin, and Masson's trichrome. Three measurements of the depth of thermal effect were determined and recorded for each slide by measuring from

TABLE 1 Electrosurgical systems, handpieces, power settings, treatment modalities used in the study and maximum skin temperature recorded during the procedure

Electrosurgical system (generator & handpiece)	Generator power setting	Treatment modality	Maximum skin temperature (°C)
Plasma-radiofrequency generator with J-Plasma Precise handpiece	60%	Dynamic	38.4
		Static	57.5
	80%	Dynamic	38.7
		Static	46.2
Plasma-radiofrequency Generator with APR Plasma/RF handpiece	60%	Dynamic	38.7
		Static	45.8
	80%	Dynamic	39.4
		Static	47.1
Temperature-controlled radiofrequency system with percutaneous accessory	Low (55°C)	Dynamic	69.1
		Static	43.2
	High (70°C)	Dynamic	61.6
		Static	63.9

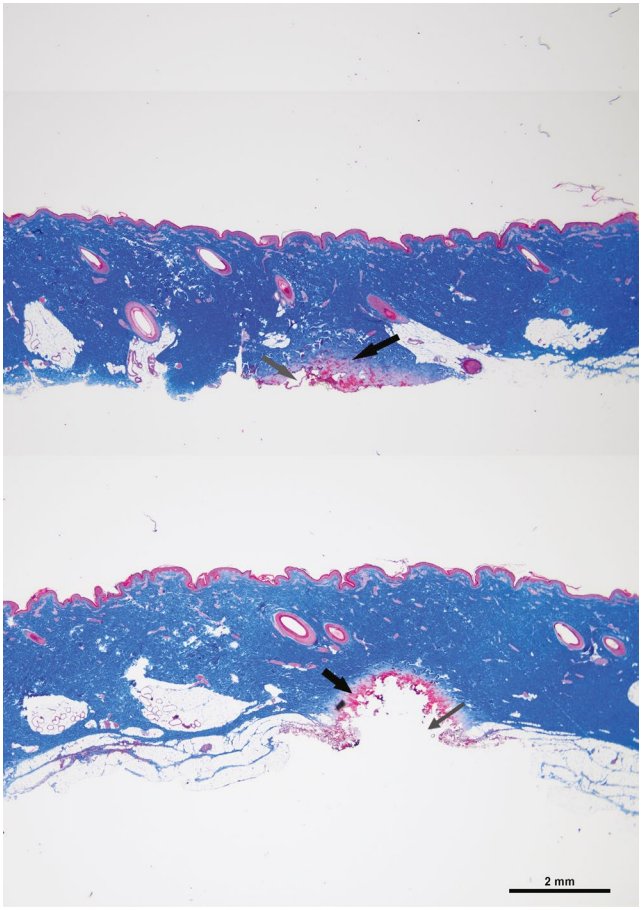

FIGURE 3 Mason trichrome stained reticular dermis treated using the plasma/RF system coupled with the J-Plasma Precise handpiece in stationary mode using (A) 60% generator power setting and (B) 80% generator power setting. The ablative zones are indicated by the gray arrows and the thermocoagulated zones indicated by the solid arrows

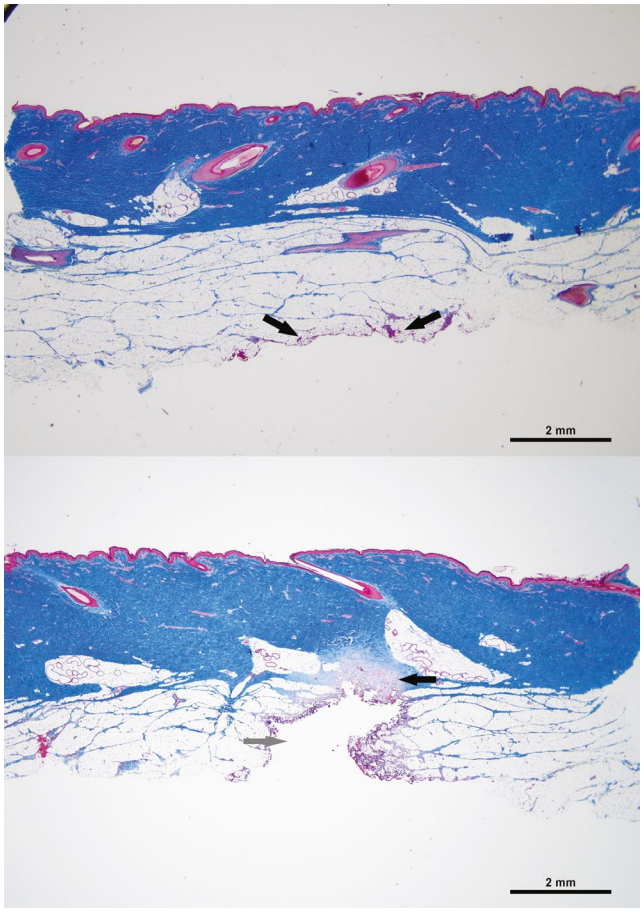

FIGURE 4 Mason trichrome stained fibroseptal network treated using the plasma/RF system coupled with the J-Plasma Precise handpiece in stationary mode using (A) 60% generator power setting and (B) 80% generator power setting. The ablative zones are indicated by the gray arrows and the thermocoagulated zones indicated by the solid arrows

the point of contact of the energy/device with the tissue to the deepest evidence of thermal change visible from the staining. Both the average and maximum depths of thermal effect, with standard deviations, were determined for each set of treatment conditions.

2.4 | Tissue temperature measurements

A FLIR A-615 Series thermal imaging camera was used to determine the external skin temperature associated with each treatment setting used. Following reapproximation of the skin flap but prior to device activation, the FLIR camera was focused on an object placed directly adjacent to the portion of the suture loop visible on the surface of the skin. A high-resolution thermal imaging video was captured before, during, and after device activation in order to capture the skin surface temperature directly above the treated area. Outside of the laboratory setting, each of the thermal imaging videos was analyzed to extract maximum tissue temperatures using the FLIR Tools+ Software, Version 6.4.17317.1002.

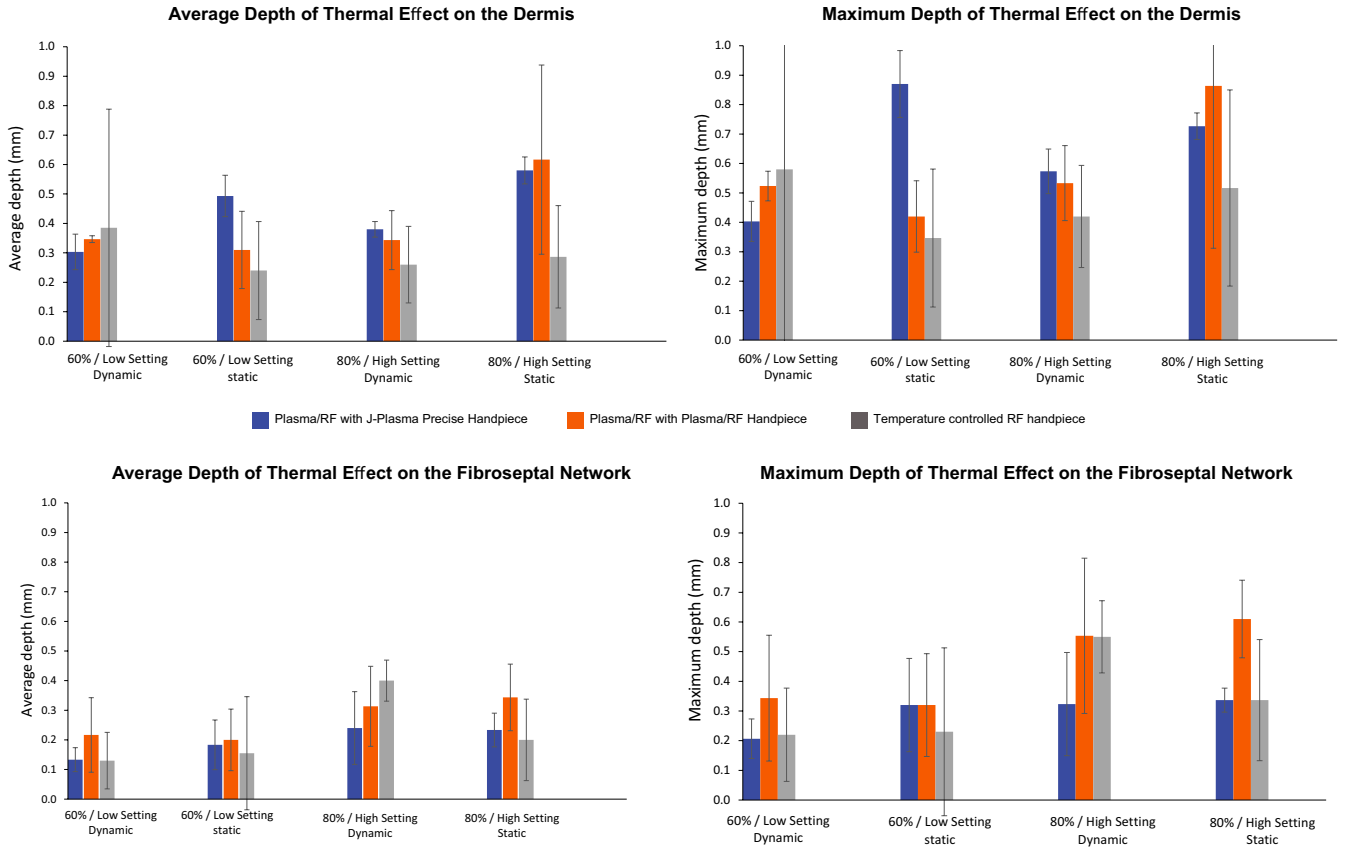

FIGURE 5 Average (A/C) and maximum (B/D) depths of thermal effect (with standard deviation) in the reticular dermis (A/B) and fibroseptal network (C/D) using various treatment settings. Plasma/RF system with J-Plasma Precise handpiece (blue), plasma/RF system with plasma/RF handpiece (orange), temperature-controlled RF system with a percutaneous accessory (gray)

3 | RESULTS

Both the plasma/RF and the temperature-controlled RF systems induced microscopic thermal effect in the reticular dermis and fibroseptal network of the porcine model at low and high energy settings in both the stationary and dynamic modes (Figures 3 and 4). These microscopic zones showed the presence of both ablative and thermocoagulated zones.

The average and maximum depths of thermal effect are presented in Figure 5 for all settings assessed (nine measurements per setting). Due to the sample size limitations of this study, it was not possible to determine statistically significant differences in average and maximum depths of thermal effect between the different handpieces and electrosurgical systems used for all the treatment settings assessed. However, there were a few general trends in the data. The depth of the effect tended to increase with increasing generator power setting in the fibroseptal network but not in the reticular dermis. There were no obvious differences between stationary and dynamic treatments except for a tendency of increased thermal effect in the reticular dermis with the stationary mode at the higher energy setting. Finally, the magnitude of the effect was generally higher in the reticular dermis than in the fibroseptal network.

The maximum external tissue temperature associated with each of the treatment settings used for this study is presented in Table 1. For most of the treatment settings used, the external tissue temperatures were higher in the static treatment mode when compared to the dynamic mode. There was no distinguishable relationship between energy setting (60% vs 80% and Low vs High) and external skin temperature.

4 | DISCUSSION

Successes in the treatment of skin laxity with percutaneous plasma generating devices have been reported, but no clinical studies using this technique have been published.[15,16] The aim of this study was to evaluate the thermal effect of helium plasma/RF energy on the reticular dermis and fibroseptal network in comparison with energy delivered using a monopolar temperature-controlled RF device with demonstrated efficacy in improvement of skin laxity.[20-22]

The histological findings suggest that, similar to the previously reported impact of laser and RF energy on the dermis, the percutaneous application of plasma/RF energy leads to the formation of ablative and thermocoagulated zones.[23,24] In the current study, no obvious

difference in average and maximum depth of the thermal injury was observed between the helium plasma/RF system and the temperature-controlled RF system.

An average 54.3% increase in the depth of the thermal effect was observed in the fibroseptal network when increasing generator power settings, and no such effect was observed in the reticular dermis. This correlates well with the observation made by Shin et al with noninvasive devices that, as opposed to fractional CO_2 laser for which the depth of the thermal injury increases when energy is increased, increasing the energy delivered by Er:glass or RF systems tends to increase the width of the injury instead of its depth.[23]

There were no obvious differences between stationary and dynamic treatments except for a tendency of increased thermal effect in the reticular dermis with the stationary mode at the higher energy setting.

For both devices, the depth of thermal effect was higher in the reticular dermis than in the fibroseptal network.

The major limitation of our study is the high variability of the depth measurement and a small sample size for each energy setting tested. Fibroseptal orientation, hydration level, and adipocyte concentration may have an unrecognized impact on thermal effect and, therefore, breadth of injury. Further studies evaluating the impedance impact of these variables may help bridge the gap between energy delivery and, ultimately, clinical effect.

5 | CONCLUSION

Globally, these results show that the depth of thermal effect induced by a plasma/RF system is not significantly different than the thermal effect created using a monopolar temperature-controlled RF device. Variability in depth measurement may be impacted by anatomy and hydration levels within the target tissues. These results and the published clinical cases suggest that plasma/RF system could be effective and safe for the treatment of submental laxity, but this needs to be confirmed in clinical studies.

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CONFLICT OF INTEREST

Dr Ruff is a paid consultant, speaker, investigator, and is on the advisory board for Apyx Medical.

AUTHOR CONTRIBUTIONS

Dr Ruff was responsible for study design, surgery procedure, data analysis, and critical review and final approval of the manuscript. These data were not presented at any conferences. This study was approved by the MedStar's Institutional Animal Care and Use Committee.

ETHICAL APPROVAL

This study was performed in compliance with the US Public Health Service Policy on Humane Care and Use of Laboratory Animals.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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REFERENCES

1. Palanker DV, Blumenkranz MS, Marmor MF. Fifty years of ophthalmic laser therapy. *Arch Ophthalmol*. 2011;129:1613-1619.
2. Belramman A, Bootun R, Lane TRA, Davies AH. Endovenous management of varicose veins. *Angiology*. 2019;70:388-396.
3. Poder TG, Fisette JF, Bedard SK, Despatis MA. Is radiofrequency ablation of varicose veins a valuable option? A systematic review of the literature with a cost analysis. *Can J Surg*. 2018;61:128-138.
4. Azadgoli B, Baker RY. Laser applications in surgery. *Ann Transl Med*. 2016;4:452.
5. Hainer BL. Electrosurgery for the skin. *Am Fam Physician*. 2002;66:1259-1266.
6. Chen SS, Wright NT, Humphrey JD. Heat-induced changes in the mechanics of a collagenous tissue: isothermal free shrinkage. *J Biomech Eng*. 1997;119:372-378.
7. Ross EV, McKinlay JR, Anderson RR. Why does carbon dioxide resurfacing work? A review. *Arch Dermatol*. 1999;135:444-454.
8. Dover JS, Hruza GJ, Arndt KA. Lasers in skin resurfacing. *Semin Cutan Med Surg*. 2000;19:207-220.
9. Preissig J, Hamilton K, Markus R. Current laser resurfacing technologies: a review that delves beneath the surface. *Semin Plast Surg*. 2012;26:109-116.
10. Sadick N, Rothaus KO. Minimally invasive radiofrequency devices. *Clin Plast Surg*. 2016;43:567-575.
11. Mulholland RS. Nonexcisional, minimally invasive rejuvenation of the neck. *Clin Plast Surg*. 2014;41:11-31.
12. Shridharani SM, Broyles JM, Matarasso A. Liposuction devices: technology update. *Med Devices (Auckl)*. 2014;7:241-251.
13. Bellini E, Grieco MP, Raposio E. A journey through liposuction and liposculture: review. *Ann Med Surg (Lond)*. 2017;24:53-60.
14. Duncan DI. Helium plasma-driven radiofrequency in body contouring. In: Salgado AA, ed. *The Art of Body Contouring*. London, UK: IntechOpen; 2019. https://www.intechopen.com/books/the-art-of-body-contouring/helium-plasma-driven-radiofrequency-in-body-contouring. Accessed May 11, 2020.
15. Zamora J, Roman S. Subcutaneous neck skin plasma tightening. *Advances in Cosmetic Surgery*. 2019;2:89-95.
16. Gentile RD. Cool atmospheric plasma (J-Plasma) and new options for facial contouring and skin rejuvenation of the heavy face and neck. *Facial Plast Surg*. 2018;34:66-74.
17. Holcomb JD, Schucker A. Helium plasma skin regeneration: evaluation of skin tissue effects in a porcine model and comparison to nitrogen plasma skin regeneration. *Lasers Surg Med*. 2020;52:23-32.
18. Food and Drug Administration. *Clearance Letter for the Apyx Plasma/RF Hanpiece*. Silver Spring, MD: Food and Drug Administration; 2019. https://www.accessdata.fda.gov/cdrh_docs/pdf19/K191542.pdf. Accessed April, 2020.
19. Food and Drug Administration. *Clearance Letter for Thermi Temperature-controlled Radiofrequency System*. Silver Spring, MD:

Food and Drug Administration; 2017. https://www.accessdata.fda.gov/cdrh_docs/pdf17/K173582.pdf. Accessed April, 2020.
20. Dendle J, Wu DC, Fabi SG, et al. A retrospective evaluation of subsurface monopolar radiofrequency for lifting of the face, neck, and jawline. *Dermatol Surg*. 2016;42:1261-1265.
21. Key DJ. Integration of thermal imaging with subsurface radiofrequency thermistor heating for the purpose of skin tightening and contour improvement: a retrospective review of clinical efficacy. *J Drugs Dermatol*. 2014;13:1485-1489.
22. Wu DC, Liolios A, Mahoney L, et al. Subdermal radiofrequency for skin tightening of the posterior upper arms. *Dermatol Surg*. 2016;42:1089-1093.
23. Shin MK, Choi JH, Ahn SB, Lee MH. Histologic comparison of microscopic treatment zones induced by fractional lasers and radiofrequency. *J Cosmet Laser Ther*. 2014;16:317-323.
24. Harth Y, Frank I. In vivo histological evaluation of non-insulated microneedle radiofrequency applicator with novel fractionated pulse mode. *J Drugs Dermatol*. 2013;12:1430-1433.

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