DERMATOLOGICA SINICA 33 (2015) 134–141

Contents lists available at ScienceDirect

Dermatologica Sinica

journal homepage: http://www.derm-sinica.com

ORIGINAL ARTICLE

A prospective clinical and histologic study of axillary osmidrosis treated with the microwave-based device

Yao-Yu Chang [1, 2], Chien-Hsun Chen [1, 2], Rosaline Chung-Yee Hui [1, 2], Shih-Ming Jung [2, 3], Chih-Hsun Yang [1, 2, *]

[1] Department of Dermatology, Chang Gung Memorial Hospital, Taipei, Taiwan
[2] College of Medicine, Chang Gung University, Taipei, Taiwan
[3] Department of Pathology, Chang Gung Memorial Hospital, Taipei, Taiwan

ARTICLE INFO

Article history:
Received: Dec 7, 2014
Revised: Dec 30, 2014
Accepted: Dec 30, 2014

Keywords:
bromhidrosis
microwave-based device
osmidrosis

ABSTRACT

Background/Objective: Microwave-based devices target sweat glands through energy delivery at the dermal–subcutaneous interface. These devices have been approved by the Food and Drug Administration as a noninvasive treatment for axillary hyperhidrosis. Treatment for osmidrosis has only been reported in one preliminary study. This study aimed to investigate the efficacy, safety, and histological changes of the microwave-based devices in treating axillary osmidrosis.

Methods: We conducted a prospective study in a tertiary referral center in Taiwan. Patients with axillary osmidrosis were recruited and received two consecutive treatment sessions with a 3-month interval. Skin biopsy was obtained to evaluate histological changes. The efficacy was determined by odor reduction using a patient reported 10-point odor scale. Responders were defined as participants with a reduction of at least 3 points of the Odor-10 score at their 90-day follow-up visit.

Results: Seven patients were enrolled. Mean reduction of odor was 61.8%. Six patients met the primary endpoint of odor reduction. Skin biopsy specimens reveled 93% reduction of apocrine glands. Histopathological changes include dermal fibrosis, necrosis of sweat glands, and subcutaneous fat necrosis. Transient swelling, bruise, numbness, lumps, and hypotrichosis were possible side effects. No patient reported disabling side effects.

Conclusion: Microwave-based devices are noninvasive and a potential alternative therapeutic modality for axillary osmidrosis treatment.

Introduction

Axillary osmidrosis refers to an offensive and unpleasant body odor from the axillary area. It is a very distressing issue impairing an individual's psychosocial well-being. Secretions from the apocrine glands of the axillae are responsible for the malodor. Thus, several surgical techniques have been developed to remove the glands, but the results and complication rates vary.[1–3] Microwave-based devices, approved by the United States Food and Drug Administration, have been developed to treat axillary hyperhidrosis by selectively heating the interface between the skin and underlying fat of the axilla.[4] However, treatment of axillary osmidrosis using this technique has only been reported in one preliminary study.[5]

The objectives of this study were to investigate the efficacy, safety, and histological changes of microwave-based devices in treating axillary osmidrosis.

Materials and methods

Patients

Seven adults with axillary osmidrosis (aged 22–53 years, 2 men and 5 women) were enrolled in a single-group unblinded study in a tertiary referral medical center in Taiwan. All patients were rated 3 or 4 on the hyperhidrosis disease severity scale (HDSS) and at least

Conflicts of interest: The authors declare that they have no financial or nonfinancial conflicts of interest related to the subject matter or materials discussed in this article.

* Corresponding author. Department of Dermatology, Chang Gung Memorial Hospital, 199, Dun-hua North Road, Taipei City, Taiwan.
E-mail address: dermadr@hotmail.com (C.-H. Yang).

http://dx.doi.org/10.1016/j.dsi.2014.12.008

5 on the Odor-10 scale. No patient had been treated with endoscopic thoracic sympathectomy, liposuction, or other surgeries for axillary osmidrosis or hyperhidrosis. They had no botulinum toxin injection within 1 year, and had not used any topical treatment within 14 days prior to treatment.

The study was approved by Chang Gung Memorial Hospital's institutional review board (103-4012C4), and informed consent was obtained prior to any study procedures.

Odor and sweat assessments

All participants were asked to record their own perception of their underarm odor using a 10-point scale (Odor-10), where 1 stands for completely no odor and 10 for severe odor.

The method of assessing the level of axillary sweat was patient-reported HDSS score. Table 1 provides the definition of the four scores respectively.

Treatment

Baseline evaluation including past medical history, physical examination, and sweat and odor self-assessment (HDSS and Odor-10) were performed on each patient. An incisional skin biopsy was taken from the left central axilla. The incision was 1.5-cm in length and depth to the deep subcutis. Treatment sessions began 1 month after the skin biopsy to avoid wound dehiscence during microwave treatment.

After being marked with a treatment template, the axillary area was anesthetized with 1% lidocaine with 1:100,000 epinephrine. Both axillary areas were fully treated by miraDry system (Miramar Labs, Santa Clara, CA, USA), which is a microwave-based device with integrated vacuum and cooling included. It allows different energy settings within a small range. Energy level 3 (the middle energy setting), which is the most commonly used setting in previous reports,[4] was used for the first treatment session. The second session was carried out 3 months after the first session. Energy level was increased to level 5 because there were no apparent side effects after the first treatment. The second session also covered the entire bilateral axilla region.

After completion of all sessions, all patients attended follow-up visits 30 days and 90 days after their last session. An additional skin biopsy was taken from a location 1 cm away from the previous biopsy site in the ipsilateral axilla to avoid scar tissue at their 30-day follow-up visits.

Study efficacy and patient satisfaction measurement

Efficacy of odor reduction was measured using the Odor-10 score. For the study's primary endpoint, responders were defined as a reduction of at least 3 points on the Odor-10 score at their 90-day follow-up visit. In addition, the HDSS score was used as a measurement of sweat reduction. Responders were defined as participants reporting a HDSS score of 1 or 2 at their 90-day follow-up visits.

All participants were asked about their satisfaction regarding the whole procedure at the 90-day follow-up visit. Patient satisfaction score was ranked on a scale of 1 to 5 (1 = very dissatisfied, 2 = somewhat dissatisfied 3 = no comment, 4 = very satisfied, and 5 = absolutely satisfied).

Histological evaluation

The skin biopsy specimens were stained with hematoxylin and eosin. All slides were reviewed by a dermatopathologist. Histological changes after the treatments were evaluated in terms of the reduction of apocrine glands, changes in hair follicles, nerves, and subcutaneous fat. Immunohistochemistry staining with CAM5.2 (BD Biosciences, Franklin Lakes, New Jersey, USA), which reacts with low molecular weight cytokeratin, was used to highlight apocrine sweat glands. All the immunohistochemistry slides were photographed and stored digitally. The total area of the tissue (TAT) and the area of the tissue containing apocrine sweat glands (AAG) were measured using computerized image processing software (Adobe Photoshop, San Jose, CA, USA) and subjected to statistical analysis.[6] Probability of error < 0.05 was set as the cut-point for level of significance.

Safety assessments

Postoperative pain was recorded using numeric pain rating scale from D0 to D6 after each treatment session. If there was discrepancy in pain between two sides of axilla, the higher pain score was recorded.

During each visit, patients were asked about adverse events. The degree to which the events were associated with the procedure was judged by the investigators. All events were monitored until they were adequately resolved.

Results

Demography

Demographic information and baseline sweat assessment values for all participants are shown in Table 2. All patients completed study visits up to 90 days of follow-up. Every patient underwent two procedure sessions and was skin biopsied twice.

Efficacy and patient satisfaction

The efficacy of odor and sweat reduction is shown in Table 2 and Figure 1. Six out of seven (85.7%) patients met the primary endpoint of odor reduction. The mean percentage of reduction in odor-10 scale was 76.4% and 61.8%, at 30-day and 90-day visits respectively. As for sweat reduction, six of seven (85.7%) patients

Table 1 Hyperhidrosis disease severity scale definition.

Score	How would you rate the severity of your hyperhidrosis?
1	My underarm sweating is never noticeable and never interferes with my daily activities
2	My underarm sweating is tolerable but sometimes interferes with my daily activities
3	My underarm sweating is barely tolerable and frequently interferes with my daily activities
4	My underarm sweating is intolerable and always interferes with my daily activities

Table 2 Demographic characteristics and the results of sweat reduction.

Patient	Age/Sex	BMI (kg/m^2)	Baseline Odor-10	Baseline HDSS Score	HDSS Score Day 30	HDSS Score Day 90
1	27/M	23.0	10	3	2	1
2	31/F	17.0	8	4	2	3
3	25/F	22.4	8	4	3	2
4	22/F	21.2	6	3	1	1
5	35/M	21.5	5	3	1	1
6	53/F	24.4	9	3	1	1
7	32/F	18.0	9	3	3	1

BMI = body mass index; HDSS = hyperhidrosis disease severity scale.

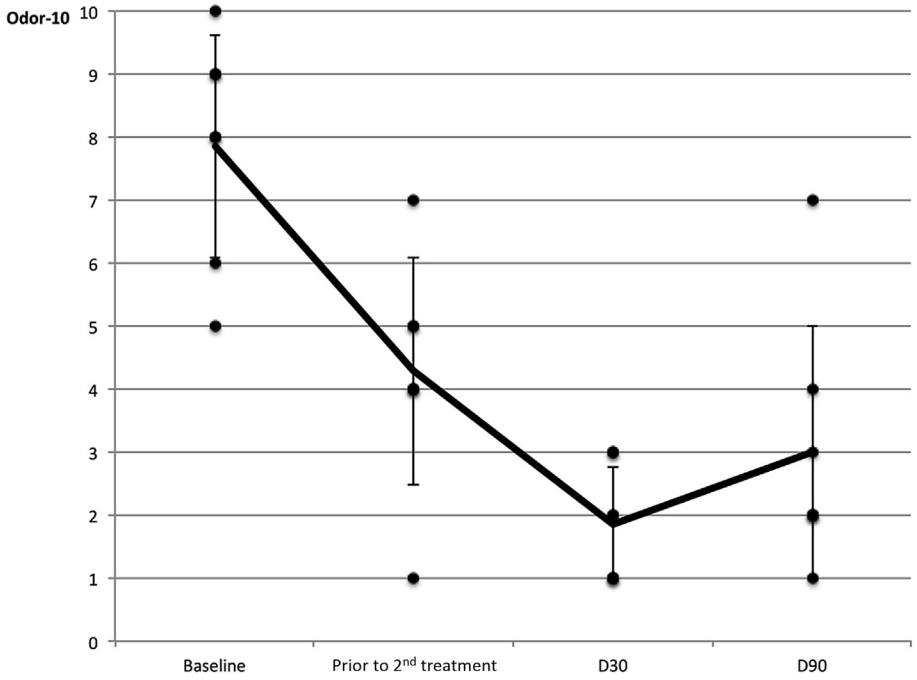

Figure 1 Results of odor reduction with mean Odor-10 scale ± 1 standard deviation.

met the primary endpoint of sweat reduction. However, Patient 3 had recurrent axillary odor and hyperhidrosis at their 90-day visit.

Four out of seven participants were very satisfied, two participants were satisfied, and only Patient 3 was somewhat dissatisfied with the procedure. Overall, 85.7% of participants were satisfied with the procedure.

Histological studies

Microscopic features of each postoperative specimen were recorded in terms of necrosis of sweat glands, fibrosis of deep dermis, hemorrhage, hair follicle changes, fat necrosis, and nerve changes, as shown in Table 3. The amount of eccrine and apocrine glands decreased tremendously after treatment in all patients, as shown in Figure 2. Moreover, necrosis of both eccrine and apocrine glands, lymphocytic infiltrates with giant cells around the sweat glands, fibrosis of deep dermis, as well as subcutaneous fat necrosis were found on high-power microscopy. The epidermis and upper dermis remained intact (Figure 3). Hair follicles were surrounded by inflammatory cells with dyskeratotic cells in the follicular epithelium. Perifollicular fibrosis and formation of keratin cysts all indicated damage to hair follicles (Figure 4A–C). Nerve injury was found in one specimen (Figure 4D).

Immunohistochemically, apocrine glands react strongly to CAM5.2 with heavy staining of the nucleus and cytoplasm whereas eccrine glands showed only little reactivity (Figure 5). The results of apocrine sweat glands reduction are shown in Table 4. Mean reduction in the area of apocrine sweat glands was 9.61 mm^2 (95% confidence interval, 6.35–12.87 mm^2) and 93% (95% confidence interval, 86.3–99.7%) in percentage. There were significant differences between pre- and postoperative AAG and AAG/TAT ratio ($p = 0.001$ and $p < 0.001$, respectively), which represented a substantial decrease of apocrine glands.

Adverse events and safety

Postoperative pain was recorded using numeric pain scale from Day 0 to Day 6, as shown in Figure 6. Pain score dropped dramatically and all patients reported only mild pain 3 days after the first treatment. However, after the second session in which energy level 5 was used, the pain was greater and lasted longer in all patients. Although all patients had to take diclofenac to relieve pain on the treatment day, all reported no disabling pain interfering with activities of daily living.

Other common adverse events included local erythema, bruise, local swelling, numbness, and hypotrichosis (Figure 7). Erythema and

Table 3 Microscopic features after the treatment of each patient with clinical correlation.

Patient	Hyalinization and necrosis of sweat glands	Fibrosis	Fat necrosis	Microscopic hemorrhage	Clinical bruise	Microscopic hair follicle damage	Hypotrichosis	Microscopic nerve injury	Numbness[a]
1	+	+	+	+	−	+	+	−	−
2	+	+	+	−	−	−	−	−	−
3	+	+	+	+	−	−	+	−	+
4	+	+	−	+	−	−	−	−	−
5	+	+	+	+	−	+	+	+	+
6	+	+	+	−	−	+	−	−	+
7	+	+	+	−	−	−	−	−	+

[a] Clinical findings at 30-day follow-up visit.

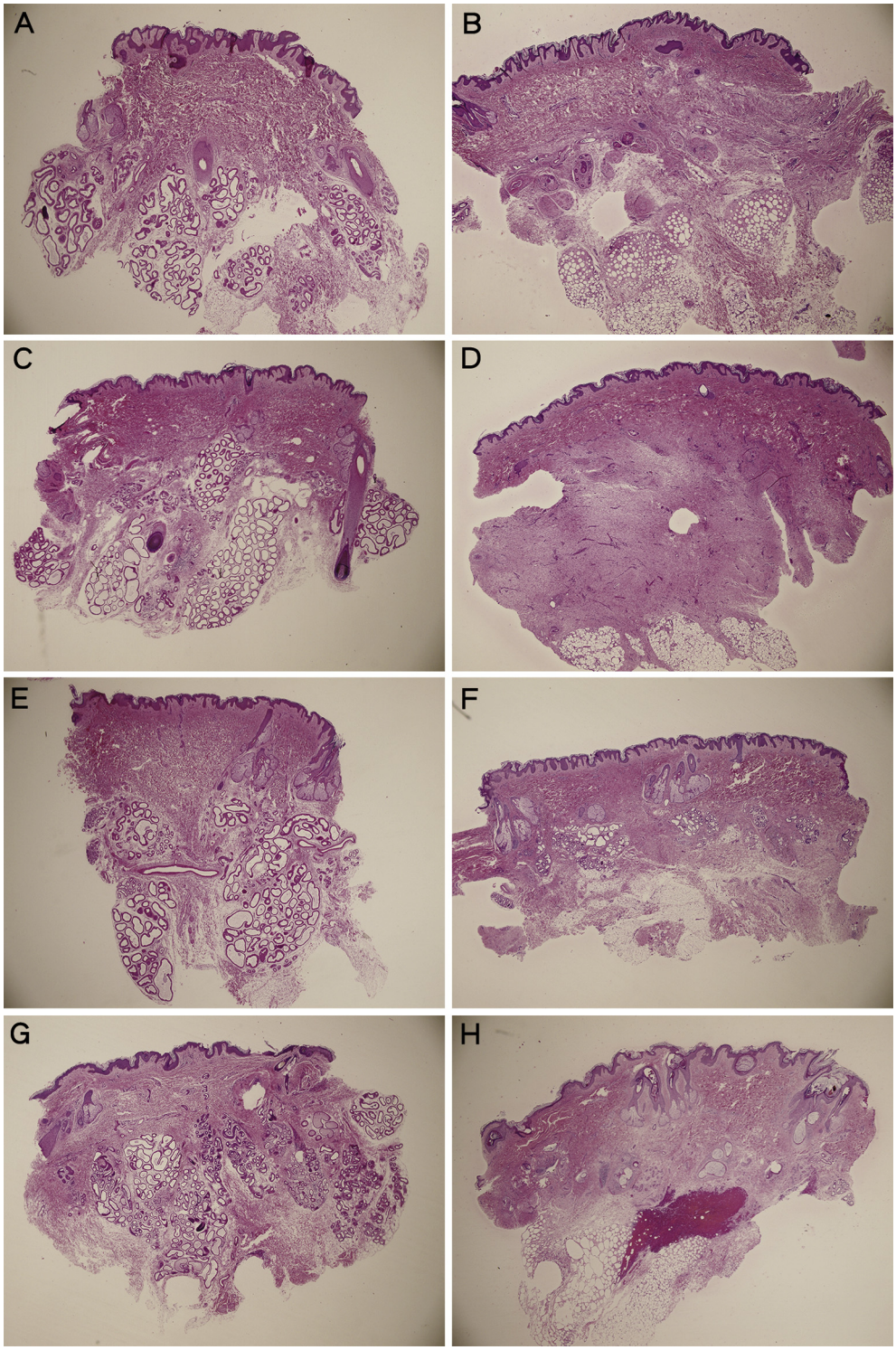

Figure 2 Histopathologic findings of four out of seven patients showing reduction of sweat glands. Histology: (A, C, E, G) before treatment and (B, D, F, H) after treatment in Patients 6, 7, 2, and 5, respectively (hematoxylin and eosin, 20×).

bruise were presented in all patients and resolved in a few days. Four out of seven had numbness that diminished in 1–3 months. Local swelling mostly went away in 1–2 weeks, but there were some small lumps remaining in all patients. Those lumps resolved gradually but could be still be palpated in five patients at 90-day follow-up visit. Three patients reported hypotrichosis and decelerated axillary hair growth rate, which existed up to their 90-day follow-up visit.

In summary, no severe and debilitating adverse effects were observed. All patients showed good tolerance during all treatment and follow-up visits.

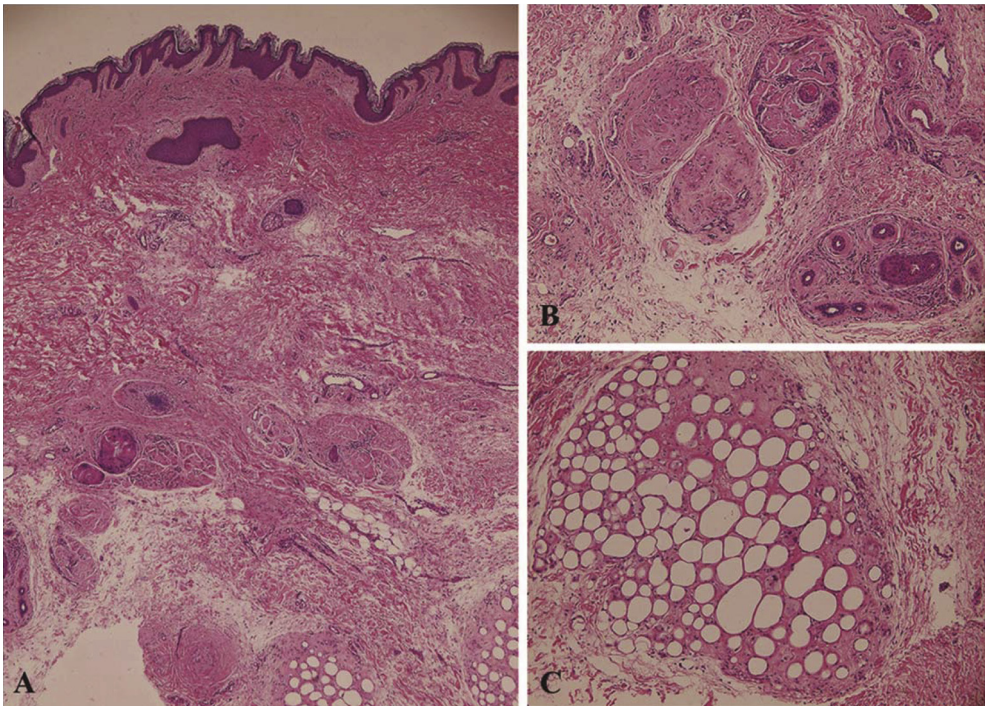

Figure 3 (A) Fibrosis of the deep dermis [hematoxylin and eosin (H&E), 100×]. (B) Hyalinization and necrosis of sweat glands (H&E, 400×). (C) Fat necrosis at superficial subcutis (H&E, 400×).

Discussion

There have been many reports showing good efficacy in sweat reduction using microwave-based devices. Hong et al[7] demonstrated that 90.3% patients had HDSS score of 1 or 2 at the 12-month follow-up visit. Glaser et al[8] conducted a randomized blinded sham-controlled trial and there was a significant difference regarding sweat reduction rate between the active treatment group (89%) and the sham group (54%). There is only one preliminary report evaluating the efficacy of microwave-based

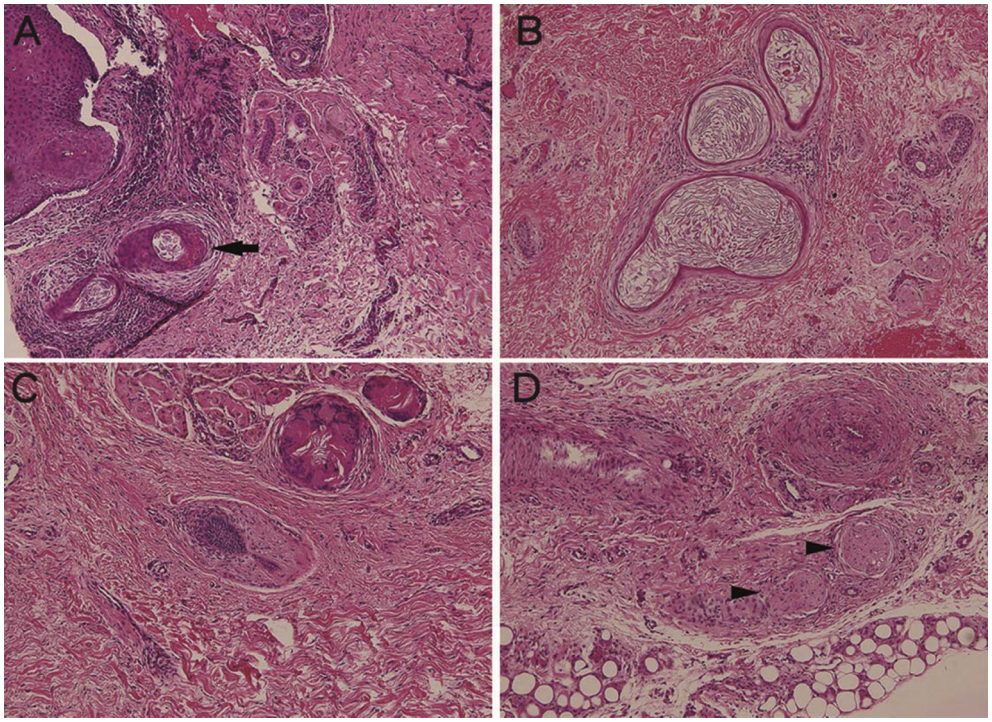

Figure 4 Damage to the hair follicles and nerves. (A) Dyskeratotic cells within the follicular epithelium surrounded by inflammatory cells (arrow). (B) Degenerated hair follicles with keratin cysts. (C) Fibrosis around the hair follicle (D) Nerve injury surrounded by inflammatory cells (arrowheads; hematoxylin and eosin, 200×).

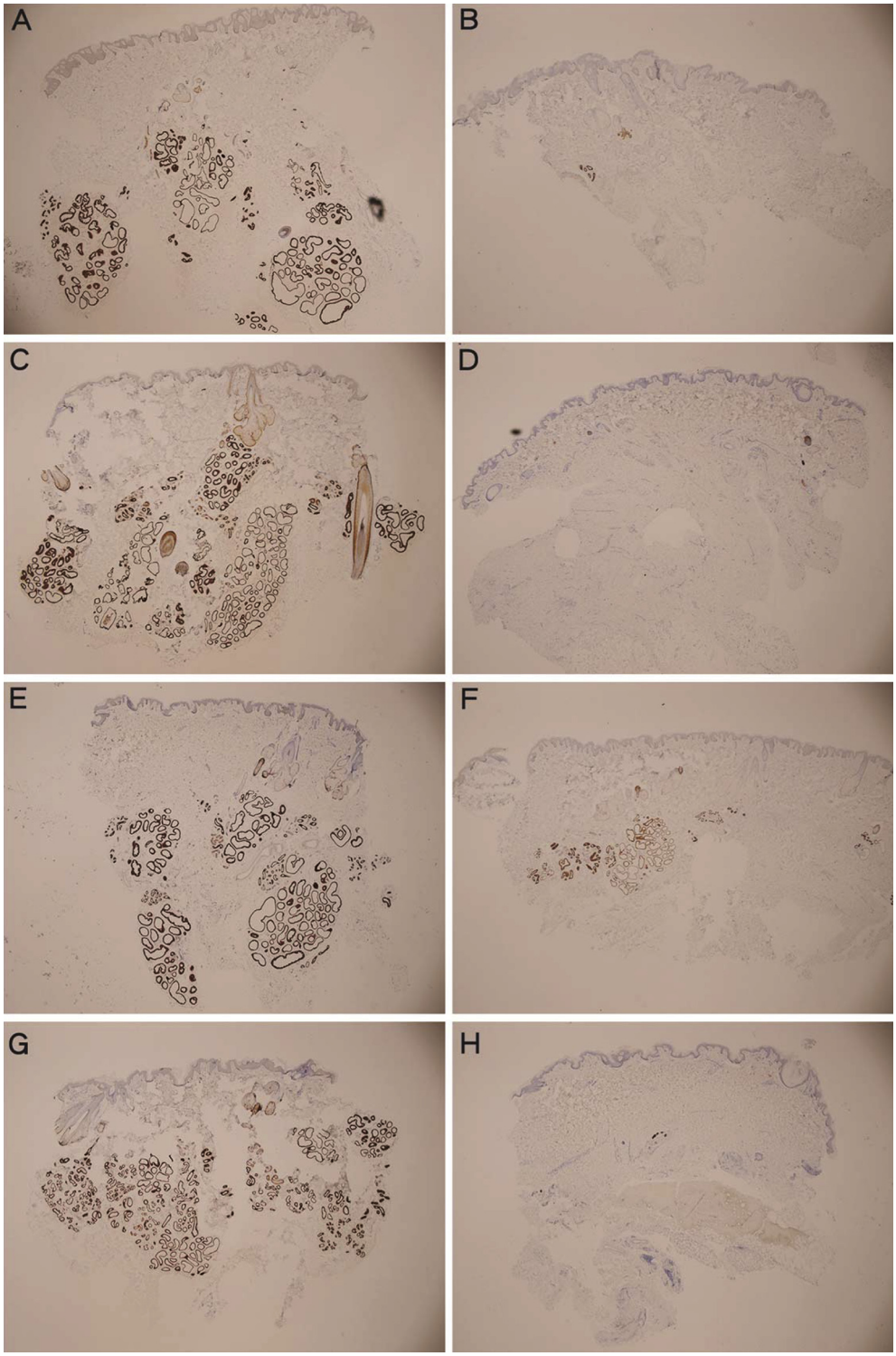

Figure 5 Immunohistochemistry staining using CAM5.2 to highlight apocrine sweat glands: (A, C, E, G) were from Patients 6, 7, 2, and 5, respectively, preoperatively, and (B, D, F, H) were from Patients 6, 7, 2, and 5, respectively, postoperatively. Note that only Patient 2 had residual sweat glands (F).

devices for axillary osmidrosis in Asians, which showed good efficacy (93.8%).[5] Our study further demonstrates good efficacy for axillary hyperhidrosis and osmidrosis. At the visits 30 days and 90 days after treatment series, 100% and 85.7%, respectively, of patients had achieved the primary end point of odor reduction. The mean reduction in odor-10 scale was 61.8% at 90-day follow-up visit.

The safety profile of the procedure showed low risk for all patients. Local swelling, erythema and pain were expected but last only about 1 week. The degree of pain seemed to be related to the energy level used during the treatment, since the second treatment session with higher energy level caused more pain. Ice packing and some anti-inflammatories could ameliorate these mild discomforts. Some side effects such as numbness and local lumps might last

Table 4 Results of reduction in apocrine glands.

Patient	TAT (mm^2)		AAG (mm^2)		AAG/TAT	
	Preop	Postop	Preop	Postop	Preop	Postop
1	28.19	22.59	7.60	0.17	0.27	0.01
2	29.86	27.83	9.46	2.41	0.32	0.09
3	34.42	41.15	20.08	1.68	0.58	0.04
4	20.01	19.27	4.80	0.35	0.24	0.02
5	27.77	29.63	9.82	0.00	0.35	0.00
6	34.88	20.85	9.97	0.07	0.29	0.00
7	34.33	36.18	10.24	0.00	0.30	0.00
p*	0.65		0.001		<0.001	

* Unpaired *t* test was used for the variable TAT and paired *t* test for AAG and AAG/TAT.
AAG = area of tissue containing apocrine glands; postop = postoperative data; preop = preoperative data; TAT = total area of the tissue.

longer but did not affect patients' daily activities. Even though there were nerve injuries microscopically, all patients with numbness recovered within 1–3 months, suggesting that nerve injuries were temporary and reversible. Hypotrichosis lasted longer, as there was hair follicle damage and reduction of hair follicles histologically. A longer follow-up period is required to elucidate the long-term effects on hair follicles.

Analysis of histological changes has further demonstrated that microwave energy reaches the interface of the deep dermis and subcutis. This results in destruction of the eccrine and apocrine glands without seriously damaging the surrounding tissue. Some clinical adverse events were compatible with histological findings (Table 3), such as numbness and nerve injury, hypotrichosis, and damage to hair follicles. Nerve injury was not found in some patients who experienced numbness, because the nerve could be destructed or not present in the histological section. No patient had clinically evident bruising at the 30-day follow-up visit, and thus microscopic hemorrhage may result from skin biopsy *per se*. Immunohistochemistry staining with CAM5.2 highlighted apocrine glands, providing a convenient way to evaluate the extent of sweat glands destruction.

There are many treatments for axillary osmidrosis reported in the literature, such as conservative treatments (topical agents, botulinum toxin) and surgical treatments (subcutaneous shaving, tumescent liposuction with or without curettage, thoracic sympathectomy).[1–3,9–14] Most of them are targeted at the axillary sweat glands. Surgical treatments have been proven to be definite and effective treatments while the effect of botulinum toxin was shown to be temporary and insignificant.[9] Subcutaneous shaving is the procedure most commonly performed in our institution.[10] Although different techniques have been proposed to reduce complications, such as hematoma, epidermal necrosis, and scarring, these complications are not uncommon.[3,9–13] Furthermore, this technique was associated with more postoperative pain, longer operation time, shoulder range of motion limitation, and approximately 10-day postoperative downtime, which may interfere with daily activities.[10] By contrast, we have shown that microwave-based device treatment has less postoperative pain, shorter recovery time, and minimal interference with daily activities. Patient satisfaction was also high (85.7%) and comparable with a previous study using subcutaneous shaving with a suction-assisted cartilage shaver.[11]

In conclusion, the miraDry system is a novel microwave energy device that can be used to treat not only axillary hyperhidrosis but also osmidrosis by heating the lower dermis and superficial subcutis, where the eccrine and apocrine glands are located. Patient satisfaction with the procedure is high, and adverse events are self-limited and well tolerated. This system provides a noninvasive and definite alternative therapeutic modality for patients with this common and distressing problem.

Nonetheless, the recurrence of odor and its relationship with the number of residual viable apocrine glands remains unknown, since no definite evidence of correlation was found in our study. Further studies to establish long-term efficacy, long-term histological changes, and recurrence rate are necessary.

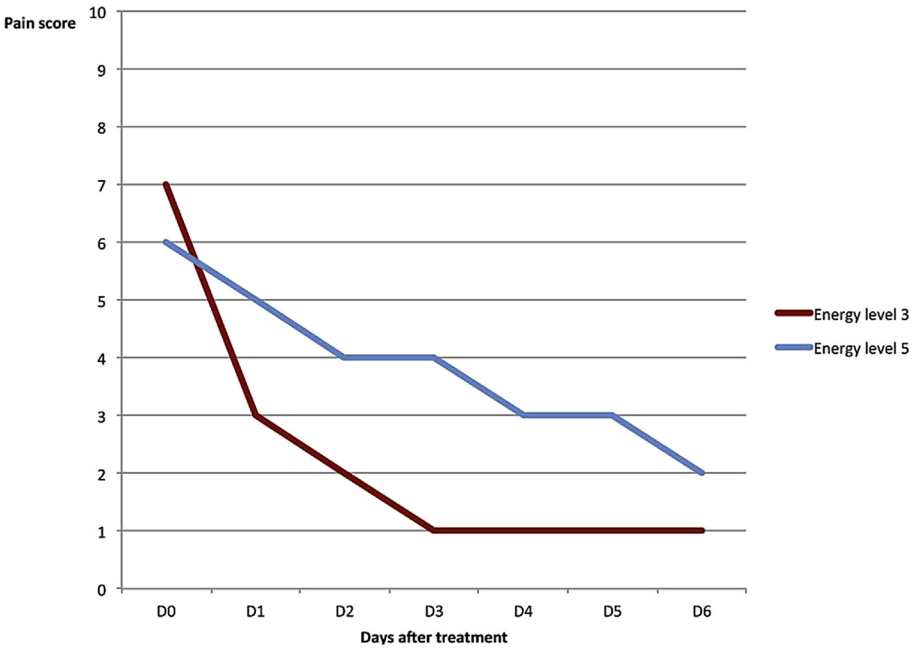

Figure 6 Postoperative median pain score using energy level 3 (red) and energy level 5 (blue). Note that the pain was greater and lasted longer using level 5.

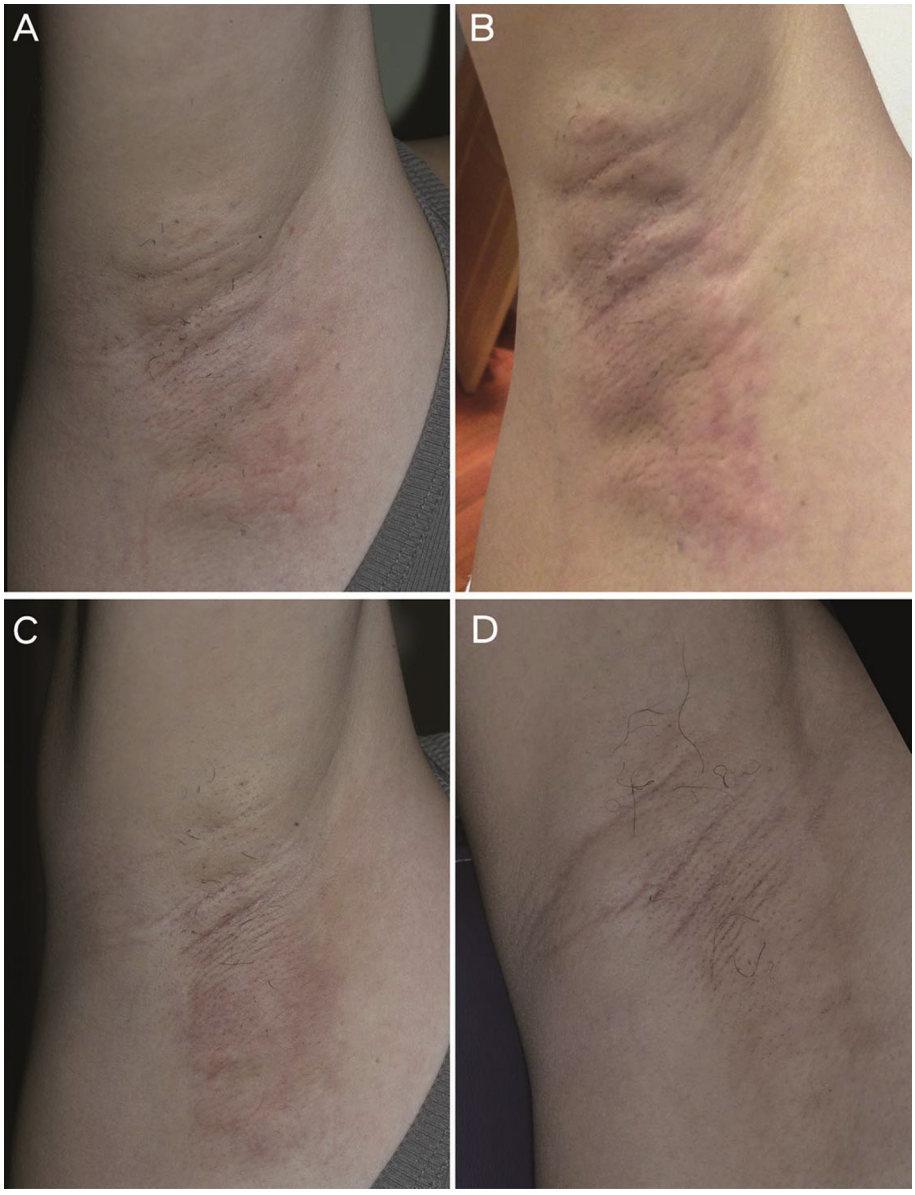

Figure 7 Common adverse effects. (A) Mild swelling immediately after treatment (D0). (B) Bruise and some lumps could be seen on D2. (C) Bruise and lumps subsided partially with some hyperpigmentation on D6. (D) All lumps and hyperpigmentation had resolved by the 90-day follow-up visit. Note the hypotrichosis.

Acknowledgments

We thank Dermacare Biomed Inc. (Taipei, Taiwan) for lending the device and providing treatment tips. No funds were provided.

References

1. Endo T, Nakayama Y. Surgical treatment of axillary osmidrosis. *Ann Plast Surg* 1993;**30**:136–9.
2. Tung TC, Wei FC. Excision of subcutaneous tissue for the treatment of axillary osmidrosis. *Br J Plast Surg* 1997;**50**:62–6.
3. Wu WH, Ma S, Lin JT, et al. Surgical treatment of axillary osmidrosis: an analysis of 343 cases. *Plast Reconstr Surg* 1994;**94**:288–94.
4. Johnson JE, O'Shaughnessy KF, Kim S. Microwave thermolysis of sweat glands. *Lasers Surg Med* 2012;**44**:20–5.
5. Lee SJ, Chang KY, Suh DH, Song KY, Ryu HJ. The efficacy of a microwave device for treating axillary hyperhidrosis and osmidrosis in Asians: a preliminary study. *J Cosmet Laser Ther* 2013;**15**:255–9.
6. Chu CH, Lin DJ, Lee JW. Quantitative assessment for the efficacy of the osmidrosis treatment using liposuction plus shaver. *J Plast Reconstr Aesthet Surg* 2011;**64**:972–4.
7. Hong CH, Lupin M, O'Shaughnessy KF. Clinical evaluation of a microwave device for treating axillary hyperhidrosis. *Dermatol Surg* 2012;**38**:728–35.
8. Glaser DA, Coleman WP, Fan LK, Kaminer MS, et al. A randomized, blinded clinical evaluation of a novel microwave device for treating axillary hyperhidrosis: the dermatologic reduction in underarm perspiration study. *Dermatol Surg* 2012;**38**:185–91.
9. Xie A, Nie L, Tan Q. Local injection of botulinum toxin A: an alternative therapy for axillary osmidrosis. *J Dermatol* 2014;**41**:153–6.
10. Lee JC, Kuo HW, Chen CH, Juan WH, Hong HS, Yang CH. Treatment for axillary osmidrosis with suction-assisted cartilage shaver. *Br J Plast Surg* 2005;**58**:223–7.
11. Huang YH, Yang CH, Chen YH, Chen CH, Lee SH. Reduction in osmidrosis using a suction-assisted cartilage shaver improves the quality of life. *Dermatol Surg* 2010;**36**:1573–7.
12. Qian JG, Wang XJ. Radical treatment of axillary osmidrosis by subdermal excision of apocrine glands: a prospective study in 31 cases. *J Plast Reconstr Aesthet Surg* 2006;**59**:860–4.
13. Seo SH, Jang BS, Oh CK, Kwon KS, Kim MB. Tumescent superficial liposuction with curettage for treatment of axillary bromhidrosis. *J Eur Acad Dermatol Venereol* 2008;**22**:30–5.
14. Wong LS, Chern E, Yen Y, Wu WM. Use of a purse-string suture method and blunt-ended dissector in arthroscopic surgery for axillary osmidrosis. *Dermatol Sinica* 2013;**31**:126–9.