

Non-Invasive Short-Wave Guided Radiofrequency Device for Long-Term Sweat Reduction in Patients with Primary Axillary Hyperhidrosis: A Preliminary Study

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ABSTRACT

Background. Patient demand for non-invasive, no-downtime aesthetic and medical procedures is growing steadily. Radiofrequency (RF) has become an adjunct non-invasive modality for improvement in the appearance of cellulite, reduction in excess fat deposits and skin tightening and is typically applied for deep skin heating without ablation of the epidermis and dermis. Since RF can cause skin hyperthermia (temperature >45°C) even in deep skin structures, non-invasive RF technology may be an attractive modality for sweat gland thermolysis in the case of primary axillary hyperhidrosis.

Material & Methods. Twenty patients (17 women, 3 men) diagnosed with primary axillary hyperhidrosis assessed by hyperhidrosis disease severity scale (HDSS) and positive iodine-starch test [8 patients (40%) HDSS = 4; 12 patients (60%) HDSS = 3] underwent 4 axillary (bilateral) treatments with high power, guided radiofrequency device (SweatXTM, Alma Lasers Ltd, Caesarea Israel).

Results. All 20 patients demonstrated sweat reduction at 1, 3 and 6 months after the last treatment as indicated by iodine-starch test and HDSS questionnaire. One month after the last treatment all patients shifted from HDSS 3 or 4 to HDSS 1 or 2. At 6-month follow-up, 11 patients (55%) reported HDSS=2 and 9 patients (45%) reported HDSS =1. In the control group, 80% of patients (8 patients) showed HDSS=2 and 2 patients HDSS=1 (no change from baseline).

Conclusion. The use of non-invasive bimodal RF technology is safe and effective for long-term (up to 6 months) sweat reduction in patients with primary axillary hyperhidrosis.

Recommendations. Since axillary hyperhidrosis is known to coexist with malodor originating from the apocrine sweat glands, the SweatX technology could potentially be effective for reduction in axillary osmidrosis.

INTRODUCTION

Patient demand for non-invasive, no-downtime procedures for the treatment of aesthetic and medical conditions is surging. Radiofrequency (RF) electromagnetic energy has become a common, non-invasive, safe and effective modality in the aesthetic market for skin imperfections such as improvement in cellulite, skin tightening and body contouring. In these conditions, the RF energy applicator comprises a monopolar or bipolar electrode configuration and is applied in a stationary mode for deep skin heating, without being absorbed in the skin's biological chromophores and without causing ablation of the epidermis and dermis. Since pathological and histological analysis in these indications revealed no irreversible damage to the upper skin layers or structures below the subcutaneous fat, RF technology may be an attractive non-invasive modality for sweat gland hyperthermia-induced thermolysis and thus compromising the sweat glands electro-chemical activity in primary axillary hyperhidrosis.

SWEAT GLANDS FUNCTION

Hyperhidrosis is a disorder of excessive sweating by the eccrine sweat glands, due to overactive cholinergic innervation, beyond what is physiologically necessary for thermoregulation. Primary hyperhidrosis is a disorder in which there is excess sweating of the hands, feet, face, and the axilla. Found in greatest density in the axillae, palms, and soles of the foot, the eccrine glands produce sweat to help maintain body temperature in response to exercise or exposure to heat. Axillary hyperhidrosis is believed to arise from

overstimulation of the eccrine glands by cholinergic nerve fibers of the sympathetic nervous system. The result is more sweat than is necessary for thermal regulation.

About 2 to 4 million sweat glands are dispersed over the human body. Sweat glands are classified according to morphology and function as eccrine and apocrine sweat glands. Eccrine sweat glands are innervated by postganglionic sympathetic fibers of unmyelinated class C type via acetylcholine. When acetylcholine binds to muscarinic receptors on the sweat gland, intracellular Ca²⁺ concentrations increase. This results in an increase in the permeability of K⁺ and Cl⁻ channels, which initiates the release of an isotonic precursor fluid from the secretory cells. Eccrine secretion is a clear fluid (pH 4.0-6.0) consisting of 99.0-99.5% water and 0.5-1.0% solids, a mixture of inorganics salts, largely sodium chloride, and organic substances which include lactic acid and traces of urea. Eccrine glands are distributed throughout the skin in a common anatomic pattern of 3-6mm depth (Fig 1).

Eccrine Glands	Apocrine Glands
Secrete a clear, non-odorous sweat	Secrete a milky sweat responsible for malodor
Distributed all over the body	Primarily in the axillae and genital
Reside in the lower dermis	Reside in the dermis-hypodermis
Controlled by sympathetic cholinergic nerves	Controlled by sympathetic adrenergic transmitters

Table 1. Sweat Glands Comparison.

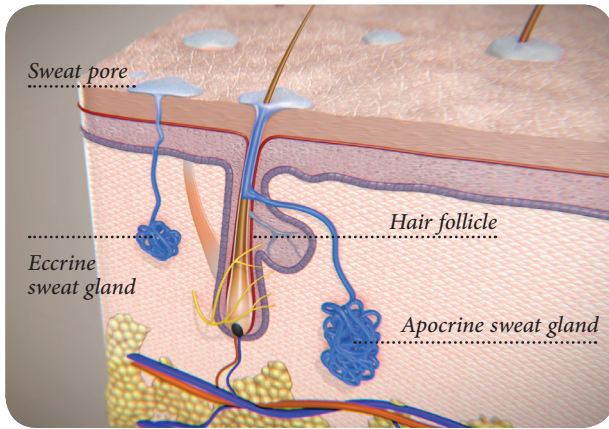


Figure 1. Anatomical view of the eccrine and apocrine glands.

The apocrine gland is relatively bigger than the eccrine. It is situated in the deep dermis or sub-cutaneous tissue at 6-8 mm depth (Fig 1). The apocrine gland secretion is a thick, milky, odorless fluid rich in proteins, ammonia, lipids and carbohydrates. Their secretion which fluoresces is a turbid fluid (pH 5.0-6.5) containing proteins, sugars, ferric iron, and ammonia. A characteristic smell is produced when bacteria residing on the skin decompose the produced fluid.

TECHNOLOGY

The SweatX system (Alma Lasers Ltd., Caesarea, Israel) is a high power, short-wave electromagnetic energy device operating at 40.68 MHz. The SweatX system employs two types of RF-induced heating of biological tissue: (1) Unipolar Pro handpiece – single electrode characterized by high RF-energy penetration depth and (2) Coaxipolar Pro handpiece – coaxial electrodes optimized for shallow treatment. The dominant heating mechanism in both cases is rotational movement of water molecules in the alternating electromagnetic fields (dielectric heating). The handpieces is operated by dynamic phase control of the RF electromagnetic field intensity and depth of penetration to accommodate the different depths and physical size of the eccrine and apocrine sweat glands, and impedance matching network which provides compensation of the reactance of the attached piece of the skin. Figure 2 depicts thermographs of the Unipolar Pro and Coaxipolar Pro handpieces with multi-level depths of tissue penetration: Unipolar-Pro: Shallow (5-8mm), medium (10-12mm) and deep (15-18mm), and Coaxipolar Pro: Shallow (1-2mm), medium (3-5mm) and deep (6-8mm), respectively.

MECHANISM OF ACTION

Water is a polar compound and is abundant in the human body. When radiant RF electromagnetic energy is absorbed in tissue, it provokes oscillation of the dipole water molecules, which leads to frictional heating. The amount of heating is proportional to the amount of radiation. Sweat gland water content is 99-99.5% whereas that of surrounding skin appendages (hair follicle, sebaceous gland) is significantly less.

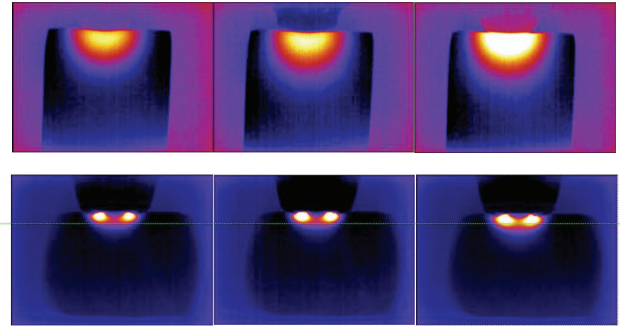


Figure 2. Unipolar-Pro (Upper) and Coaxipolar-Pro (Lower) dynamic phase control thermographs - Shallow (left), Medium, and Deep (right).

The rapidly oscillating electromagnetic RF field (40.68 MHz) emitted by the RF Unipolar Pro causes rapid rotation of the dielectric water molecules in the saturated hyperactive sweat glands and consequently greater friction and heat production in the glands in comparison with that induced in lower water-content adjacent skin structures, such as hair follicles. The Coaxipolar handpiece greater power density targets the more superficial eccrine glands and traps the caloric reservoir of the Unipolar-Pro volumetric deep heating to increase glands thermolysis. Thus, the RF heating by the Unipolar Pro and Coaxipolar handpieces is to induce irreversible thermal damage to the hyperactive water-targeted and to both eccrine and apocrine glands which are significantly different in their physical size and anatomical depths..

CLINICAL STUDY

Between December 2012 and March 2013 twenty patients (17 women and 3 men; age range 16-51 year-old) diagnosed with primary axillary hyperhidrosis were randomly recruited to the SweatX study conducted at a major dermatology clinic in Moscow. Study objectives, protocol (number of treatments and intervals) benefits and possible risks were delegated to the patient by the clinic medical staff. Patients screening for the study was done on the population routinely seeking dermatology services at the clinic. Each patient signed an informed consent. The following Inclusion/Exclusion criteria were applied to each prospective patient prior to the study enrollment. Inclusion criteria were: hyperhidrosis disease severity scale (HDSS) questionnaire between 3 and 4 (Fig. 3).

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- 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
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Figure 3. Hyperhidrosis Disease Severity Scale (HDSS).

In the iodine-starch test, a 10% povidone iodine antiseptic solution was applied to both axillae and allowed to dry for five minutes. Cornstarch powder was then spread on the area and any excess starch brushed away. After 15 minutes, the regions were photographed (Fig 4A). Exclusion criteria: iodine allergic reaction, active infection, pregnancy planning, pregnancy or lactation, prior surgery for axillary hyperhidrosis in the past 12 months, axillary injections of botulinum toxin A in the last 12 months, history of cancer, pacemaker or other electronic implant. At baseline 8 patients had HDSS level 4, and 12 patients had HDSS level 3. Forty eight hours prior to the iodine-starch test male patients were asked to shave both axillas and all patients to avoid any use of deodorants. All qualified patients exhibited positive iodine-starch test (Minor's test) on both axillas. Each patient underwent consecutive 4 treatments spaced one week apart. Baseline photography of each patient's axilla iodine – starch test was captured at baseline, 1, 3 and 6 months after the last treatment. Similarly, HDSS was recorded at baseline, 1, 3 and 6 months after the last treatment.

During each treatment, room ambient conditions – temperature and relative humidity were monitored and recorded. Prior to the application of the RF handpieces, each axilla was coated with water-free aromatic oil for lubrication to ease handpiece engagement with the axilla area. Both handpieces were applied in overlapping strokes across the treatment area. Axillary skin temperature was monitored by laser thermometer (Fig 4B) to keep the epidermis below 45°C. Each SweatX treatment comprised 2 treatment steps: Initially, the Unipolar-Pro was employed over the entire axilla area to increase the axilla temperature under 45 degrees Celsius to the therapeutic level by depositing 25kJ of dielectric RF energy at 70-80 Watts.

The Unipolar Pro enables efficient, safe volumetric deposition of RF energy to creating heat load on both eccrine and apocrine sweat glands, despite their differing anatomical structures and depths. Immediately upon conclusion of the first step, the Coaxial Pro handpiece is applied to the same, now heated, axilla area. The purpose of the second step is to maintain the axilla deep tissue temperature at a therapeutic level of 48-50 degrees Celsius by depositing and maintaining thermal load primarily at the eccrine gland level (4-6 mm in depth) by depositing 10kJ of dielectric RF energy at 50-60 Watts.

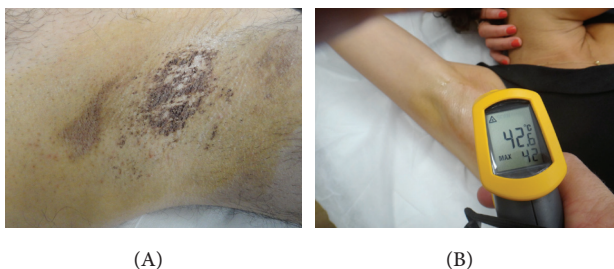


Figure 4. Positive axillary iodine-starch test (A); laser beam axillary skin temperature monitoring during SweatX treatment (B).

Treatment time for each axilla was 8-10 minutes (~20 minutes for both axillae). Clinical endpoints were transient tissue erythema and skin tenderness which last up to 1 hour. No pre-treatment local anesthesia or pain medications were needed and downtime is minimal. Post treatment care was cleaning and drying both axillae. Each patient underwent consecutive 4 treatments spaced one week apart. Baseline photography of each patient's axilla iodine-starch test was captured at baseline, 1, 3 and 6 months after the last treatment. Adverse side effect log was recorded for each patient and after each treatment and during each follow-up visit.

RESULTS

All 20 patients completed the study protocol. Expectedly, during the treatment the axillae become erythematous and tender which resolved up to 3-4 hours after the treatment. No adverse side effects were noted or recorded during the course of the study (between the study treatments and the follow-up visits). Before starting the SweatX treatment protocol, 8 patients (40%) reported sweating severity (HDSS) equal to HDSS 3, and 12 patients (60%) HDSS level 4. At 3 month follow-up visit, patient improvement (by iodine-starch and HDSS) was almost unchanged (with one patient exception) in comparison with 1 month follow-up visit. At the conclusion of the 6 month follow-up, 11 patients (55%) were evaluated for sweat intensity of HDSS level 2, and 9 patients (45%) reported sweat intensity of HDSS level 1 (Fig. 5). At 6 month follow-up visit, the control group patients showed no changes from baseline in their HDSS questionnaires.

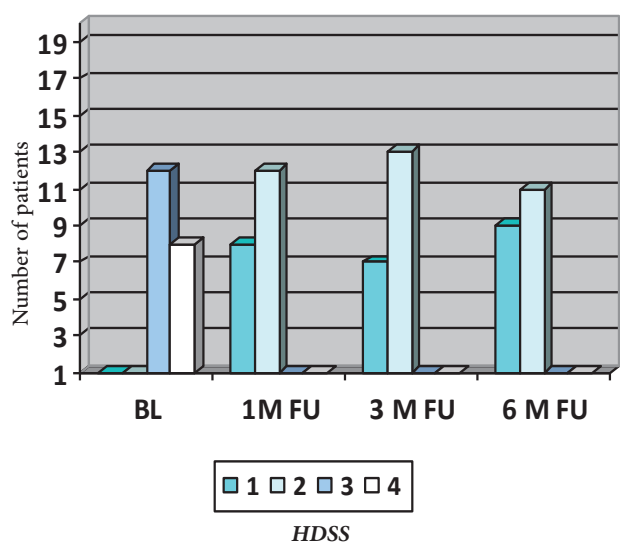


Figure 5. Patients HDSS (1-4) at baseline (BL), 1, 3 and 6 months (M) follow-up (FU)

Figure 6 below depicts the number of patients shifted from baseline HDSS (4 and 3) one month after the last treatment. From patient HDSS 4 group (n=8), 5 patients (63%) converted to HDSS 2 and 3 patients (37%) to HDSS 1. From patient HDSS 3 group (n=12), 9 patients (75%) converted to HDSS 2 and 3 patients (25%) to HDSS 1.

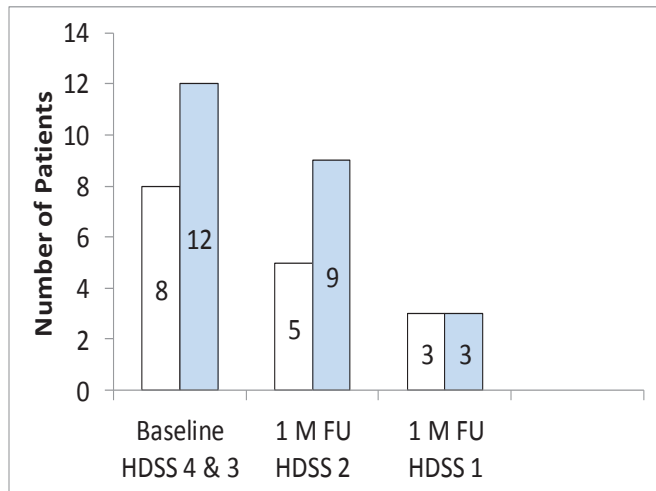


Figure 6. Patients HDSS 4 (white bar) and 3 (blue bar) at baseline and at 1 month (M) follow-up (FU).

DISCUSSION

This is the first study demonstrating the safety and long term efficacy (up to 6 months) of non-invasive short-wave guided dielectric radiofrequency technology for sweat reduction in patients with primary axillary hyperhidrosis. Interestingly, one month after the last treatment, all patients with HDSS 3 or 4 shifted to HDSS 1 or 2. This observation was in corresponded with improved in iodine-starch test results.

Although significant and similar improvement pattern was established 1 month after the last treatment in patients with HDSS 4 & 3 (Fig. 6), patients reported significant improvement in their daily sweat sensation already after their 3rd and 4th treatment. The clinical results were maintained unchanged in most patients up to 6 months where patients demonstrated significant sweat reduction (Fig. 7). In the absence of histological evidence, it is speculated that the sustained high power RF dielectric heating of the highly saturated eccrine glands at different levels in the dermis and hypodermis may deactivate the gland electrophysiology function (i.e., thermal shock) or/and damage the hyperactive water-targeted secretory ducts of the eccrine glands by shut down the electro-conductivity pathway of the glands and presumably deactivation or decay of pre-synaptic and post-synaptic excitation/activation of the gland cholinergic receptors. The current concept about axillary sweat glands differentiates between eccrine sweat glands producing abundant clear, non-odorous sweat and acrine sweat glands excreting small amounts of turbid, odorous milky sweat. Since axillary hyperhidrosis is known to coexist with malodor, the SweatX technology may potentially be effective

for the reduction in axillary osmidrosis (malodor).

In summary, the SweatX RF device provides safe and effective long term solution for patients with primary axillary hyperhidrosis.

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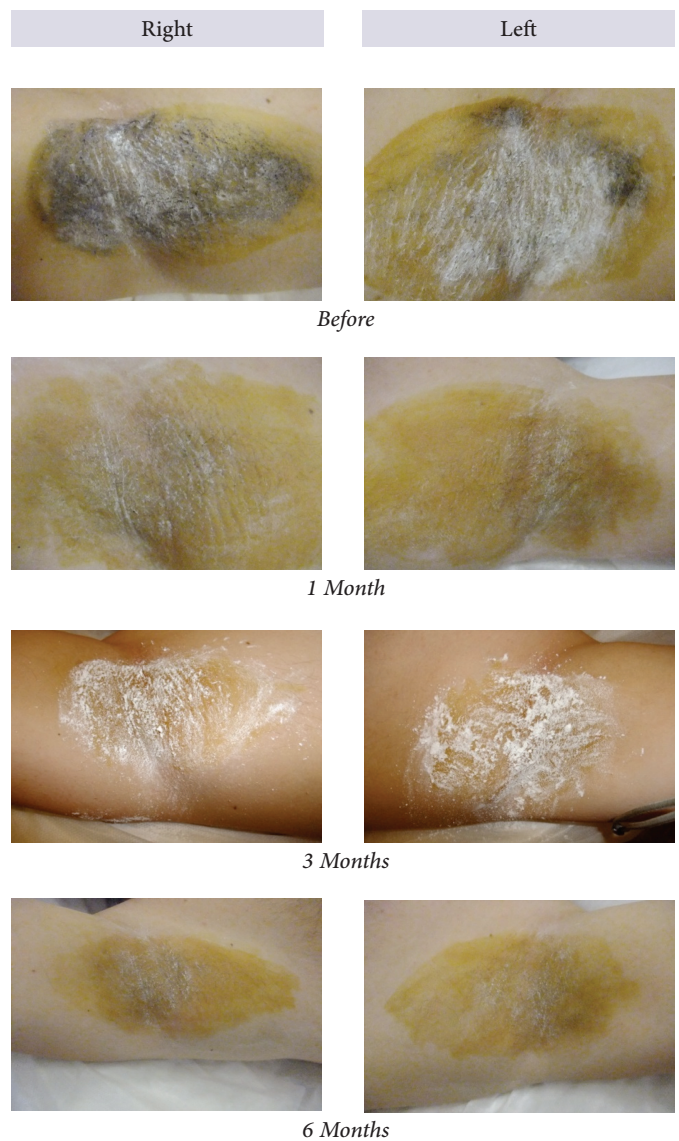


Figure 7. Right and left axillae before, 1, 3 & 6 months after 4 treatments.