First Clinical Use of a Novel Microwave Device for Treatment of Axillary Hyperhidrosis

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Introduction

Primary focal hyperhidrosis is a disorder of excessive, bilateral, and relatively symmetric sweating that can occur in focal areas of the body, very commonly in the underarms.[1] It is characterized by uncontrollable sweating that is more than is needed for thermal regulation of the body.

Hyperhidrosis can have significant psychological and social effects on patients and negatively impact their quality of life.[1]

Current therapy options include temporary over-the-counter treatments and prescription anti-perspirants, longer-lasting but still temporary botulinum toxin injections, as well as invasive sympathectomy and liposuction/curettage surgery. Although each has its merits, the potential for a long lasting, non-invasive, effective device holds promise.

A new non-invasive microwave device for treatment of primary axillary hyperhidrosis has been explored and tested in feasibility studies.

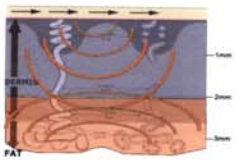
Objectives

The objectives of this study were to demonstrate a safe and effective local treatment for primary axillary hyperhidrosis with prototype devices, and develop a treatment protocol for full axillary treatment with demonstrated clinical benefit.

Methods

Device Description

The microwave devices being tested in this study were designed to focus microwave energy at the dermal/subdermal interface in the location of the apocrine and eccrine sweat glands. The sweat glands are especially susceptible to microwave energy due to their high ionic water content.



The molecular rotation of the sweat gland molecules in the presence of microwaves causes localized heating, which in turn leads to irreversible thermal necrosis of the sweat glands. The handpiece portion of the device incorporates a vacuum suction feature to lift and localize the treatment area and provide stability during the energy delivery phase. The vacuum lift feature along with the design of the microwave antenna (including the choice of an optimal frequency of operation) helps protect the deeper critical structures in the axilla. Additionally, an active hydro-ceramic cooling system integrated into the handpiece that is in direct thermal contact with the skin prevents damage to the upper and mid dermis. Local anesthesia injections were used for patient comfort, but the device itself is non-invasive.

The microwave system consists of four major components:

1. Generator: The Generator contains electric circuits, circuit boards and an ingrated control panel and provides generation of microwave energy at 5.8GHz, up to 100 Watts set by the user in 5 Watt increments, generation of vacuum set by the user, user settings of pre-cool, energy delivery, and post-cool durations in sub-second increments and display of the skin and coolant temperatures.
2. Chiller/Circulator: The Chiller/Circulator is a solid-state chiller designed to chill water in its reservoir and pump the water through inlet and outlet ports on the back of the unit. It is used to create fluid flow through the Applicator cooling chamber to protect the skin from thermal damage.
3. Isolation Transformer: This component provides isolation of the AC mains to the equipment as part of the patient safety system.
4. Applicator: The applicator includes a vacuum acquisition chamber, a surface cooling feature, four microwave antennas which can be activated sequentially, and thermocouple temperature sensors to monitor skin and cooling fluid temperatures. Not shown is the disposable snap-on head that provided a protective barrier between the patient and the Applicator.

Over the course of the study, adjustments were made to the power and time settings used and the extent of the axilla that was treated in a single session as one of the goals of the study was to determine appropriate device settings and treatment protocol for a larger study.

Pre-Clinical Experience

Many animal studies were performed to confirm the safety of the device and that the energy can be focused in the dermal-hypodermal interface. The animal model used was the Yorkshire pig. The belly/fore flank area of the pig where the dermal thickness is in the range of 1-2mm was utilized as the test area. Energy dosage studies were performed, with animal survival out to several time-points (1 wk, 1 month, and 3 months). A range of energy levels demonstrated consistent thermal damage to the tissue in the dermal-hypodermal interface and showed a high safety profile.

The conclusions made from the studies were that the therapy is safe and that it would be appropriate to initiate human clinical studies with the energy levels developed from the pre-clinical experience.

Study Design

This was a prospective, multi-center, non-randomized single-group feasibility study. IRB approval was obtained for this study and all subjects gave informed consent. The study was conducted in two stages.

The first stage used a prototype device (not shown) to treat small areas of the axilla in one treatment session. In this first stage, efficacy was qualitatively measured using the starch-iodine test and safety information was recorded.

The second stage used a device with the same technology as in the first step, modified to more easily treat larger areas of the axilla. Subjects' full axillae (hair bearing area) were treated in multiple sessions (ranging from one to four) with slightly different device settings. Local anesthetic injected throughout the axilla was used to provide pain management. Subjects were followed for a minimum of 90 days after their final treatment session to establish the safety and efficacy of the treatment. Efficacy was measured by Hyperhidrosis Disease Severity Scale and gravimetric assessments (standardized weighing of sweat produced) and safety information was recorded.

Hyperhidrosis Disease Severity Scale (HDSS) definition. The question asked is: How would you rate the severity of your hyperhidrosis?

HDSS Value	Definition
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

Subjects

For both steps of the study, subjects were males and females at least 18 years of age diagnosed with primary axillary hyperhidrosis, as evidenced by all of the following:

- Subjects were required to have an HDSS of 3 or 4
- Bilateral primary axillary hyperhidrosis

Subjects were excluded if they met any of the following conditions:

- Prior endoscopic thoracic sympathectomy, liposuction or other surgery for axillary hyperhidrosis
- Axillary injection of botulinum toxin within 180-days preceding the treatment
- Topical treatments for axillary hyperhidrosis within 14 days immediately preceding the treatment
- Oral anticholinergic medication use or cholinmimetic medication within the last 6 months or planned use during

Efficacy Outcomes

For the first stage of the study where only small areas were treated, efficacy was qualitatively determined from reviewing the starch-iodine photos.

For the second stage of the study, more global efficacy measures were used after the full axilla was treated. The primary efficacy measure was the Hyperhidrosis Disease Severity Scale (HDSS) questionnaire. A positive outcome was defined as a subject that rated themselves with an HDSS score of 1 or 2 at the 30-day follow-up visit (relative to the last treatment session). Last-observation-carry-forward was used to replace missing values for missed visits.

A gravimetric assessment was also used as a second, quantitative efficacy measure. The gravimetric assessment is a test that uses standard filter paper to absorb underarm sweat over a 5-minute period at room temperature while the patient is at rest. The filter paper is weighed before and after and the amount of sweat produced is measured in milligrams.

Safety Outcomes

Safety data was collected for all enrolled subjects throughout the study. These data included subject-rated pain ratings after each treatment session, evaluation of the axilla condition immediately post-treatment by the physician, and adverse events. Expected treatment effects that were minor in severity and in the treatment region were recorded separately from adverse events.

Results

First Stage Results – Local Efficacy

In the first stage of the study, fifteen subjects were enrolled at two sites. Small areas in the axilla ranging from size 1 to 3 cm^2 were treated in one treatment session. An example of the starch-iodine test from one subject shows the treated area has remained without sweat for 14 months after the one treatment session.

Second Stage Results – Full Axilla Treatment

In the second step of the study, thirty subjects were enrolled at six sites. Subject demographics are summarized in Table 1 below.

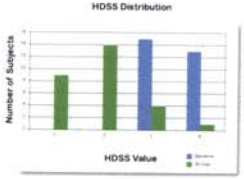
Patient Demographics and Characteristics

Age		**Ethnicity**	**N (%)**
Median	34 years old	Caucasian	23 (77%)
Range	19-49	Hispanic / Latino	6 (20%)
		African American	1 (3%)
Gender	**N (%)**	**Body Mass Index**	
Male	13 (43%)	Median	25.6
Female	17 (57%)	Range	20.2 – 40.8

Efficacy

There were 28 subjects that completed all treatments and were available for post-treatment follow-up HDSS efficacy measurements. Of these 28 subjects, 20 had baseline gravimetric values of at least 50 mg in each axilla, allowing a post-treatment evaluation of efficacy using the gravimetric assessments.

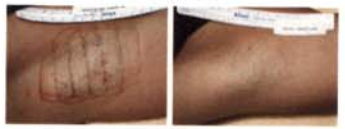
- For the primary efficacy analysis, 23/28=82% of the subjects were classified as responders (their HDSS scores dropped to 1 or 2 at the 30 day follow-up visit).
- The efficacy reduced slightly by the final 90-day visit; 18/28=64% had HDSS score of 1 or 2. Further investigation identified improvements that could be made to the procedure and the device to improve the long-term efficacy.
- The average HDSS score dropped from 3.5 at baseline to 1.9 at the 30-day follow-up visit and 2.1 at the 90-day follow-up visit.
- Gravimetric assessment values showed a similar trend. The median reduction in produced sweat was 83% at the 30-day follow-up visit and 74% at the 90-day final follow-up visit. If one defines success as achieving at least a 50% reduction in sweat, at the 30 day follow-up visit the efficacy was 80% (16/20); at the 90-day visit the efficacy was 75% (15/20).



Safety

Safety data showed that the treatments were well tolerated and that adverse events were generally mild. In the first stage of the study, where only small areas were treated, there were no adverse events recorded.

In the second stage, averaging over all subjects and treatment sessions, the average pain rating was 1.5 out of 10 on a scale of 0 to 10, with 0 being no pain at all and 10 being the worst pain the subjects could imagine. 88% of subjects experienced a pain rating of 3 or less during the procedure.



All subjects were evaluated immediately post-treatment by the investigator. The most common treatment effects noticeable in the axilla included: bruising (77%), soreness due to procedure position (49%), redness (25%) and edema in the treatment area (21%). These were all expected, relatively mild, transient effects. An example of a post-treatment subject's axilla is shown above, with the photo on the left taken immediately post-treatment and the one on the right taken four days later, showing that all the effects have healed.

There were no reports of device-related serious adverse events or unanticipated adverse device effects during the study. There were a total of 24 adverse events, where 6 were judged by the investigator as not being related to the device or procedure. Treatment-related adverse events included: numbness, tingling, or sensitivity in treatment limb (43% of subjects treated, n=13); altered sweating elsewhere (7%, n=2); blisters (3%, n=1), infection due to ingrown hair (3%, n=1) and decreased sensitivity in treatment area (3%n=1). All events resolved.

Conclusions

The study demonstrated a highly feasible microwave-based non-invasive treatment for primary axillary hyperhidrosis.

A larger study would need to be performed to determine predictable efficacy and the duration of such treatments. This study provided data for the appropriate device settings and treatment session optimization for such a study. Some improvements for the device and procedure were identified and have been implemented in the next generation device to increase the long-term efficacy.

References

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