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CLINICAL REPORTS

Impact of microwave thermolysis energy levels on patient-reported outcomes for axillary hyperhidrosis and osmidrosis

G. L. Grove MD[1] | K. Togsverd-Bo MD, PhD, DMSc[1] | J. F. B. Schwensen MD, PhD[1] | N. W. Andersson MD[2] | C. V. Nissen MD, PhD[1] | C. Zachariae MD, PhD, DMSc[2] | M. Haedersdal MD, PhD, DMSc[1]

[1]Department of Dermatology, Copenhagen University Hospital – Bispebjerg, Copenhagen, Denmark

[2]Department of Dermatology, Copenhagen University Hospital – Gentofte, Copenhagen, Denmark

Correspondence

G. L. Grove, MD, Department of Dermatology, Copenhagen University Hospital – Bispebjerg, Copenhagen, Denmark.
Email: ggro0013@regionh.dk

Abstract

Objective: Microwave thermolysis (MWT) is an emerging treatment for axillary hyperhidrosis reducing both sweat and odor. No prior studies have investigated and compared the different available energy settings of the MWT device. This study evaluated patient-reported outcome measures (PROMs) for axillary hyperhidrosis and osmidrosis following MWT treatment with two different energy levels.

Methods: Twenty adults with axillary hyperhidrosis and osmidrosis reported sweat on Hyperhidrosis Disease Severity scale (HDSS: 1–4) and odor on Odor scale (OS: 1–10), respectively, supplemented by overall Dermatology Life Quality Index (DLQI: 0–30). This was a prospective, randomized, patient-blinded and intraindividually controlled study with 3 months follow-up (FU). Randomization comprised MWT treatment of one axilla with a standard medium energy setting (energy level 3) and the contralateral axilla with a standard high energy setting (energy level 5).

Results: At baseline, patients reported substantial sweat and odor, negatively affecting their quality of life. At 3 months FU, PROMs showed improved quality of life with significantly reduced odor and sweat. Overall DLQI was reduced from a median of 10 to 4, with a median 6.5-point reduction ($p = 0.0002$). HDSS was reduced from a median of 4 to 2 on both sides, with a median reduction of 1 for medium energy level and 2 points for high energy level ($p = 0.014$). OS was reduced from a median of 8 to 3 for both energy levels, with a median reduction of 3.5 and 4.5 points for the medium and high energy level, respectively ($p = 0.017$). Local skin reactions were mild and transient, but slightly more pronounced following treatment with the high energy level.

Conclusion: MWT effectively improved patients' quality of life, axillary sweat, and odor 3 months after on baseline treatment. Treatment with the high energy level presented a subtle but significant increase of efficacy based on PROMs for both sweat and odor. Patients were willing to accept a higher amount of temporary local skin reactions from a higher energy setting when experiencing greater odor and sweat reduction.

KEYWORDS

bromhidrosis, DLQI, energy based device, HDSS, hyperhidrosis, microwave thermolysis, osmidrosis, patient reported outcome measures, PROMs, QoL

INTRODUCTION

Axillary hyperhidrosis is a primary skin condition significantly affecting patients' daily activities and quality of life.[1,2] Standard of care for axillary hyperhidrosis consists of temporary solutions such as topical and systemic treatment and especially botulinum toxin.[3] Surgical treatments have been limited due to long downtime and a higher risk of complications such as nerve damage, scarring, and compensatory hyperhidrosis. Patient demands are increasingly pushing toward noninvasive treatments with long-term efficacy as well as limited downtime and side effects.[4,5]

In many patients with axillary hyperhidrosis, the condition is accompanied by increased malodor, called osmidrosis. Odor is caused by the interaction of secretion from the apocrine glands and bacteria on the skin surface in the axillae. Current treatments generally target hyperhidrosis, which may simultaneously reduce odor, while osmidrosis, specifically, has proven more challenging to treat. The consequence of axillary osmidrosis has been shown to result in social and emotional distress and studies have presented osmidrosis to have a substantial impact on patients' Dermatology Life Quality Index (DLQI).[1,6]

While axillary hyperhidrosis is both visible and measurable, osmidrosis is challenging to clinically assess. Patient-reported outcome measures (PROMs) comprise a standardized method to assess both subjective sweat and odor, which allows the assessment of treatment effect to be based on patient satisfaction rather than purely objective measures.

Microwave thermolysis (MWT) has gained an increasingly significant position in the treatment of axillary hyperhidrosis and osmidrosis.[7–16] The MWT device delivers energy through the epidermis specifically targeting the sweat glands that do not regenerate.[17] The treatment is considered to target both the eccrine and apocrine glands in the axillae, and thus the treatment can provide long-term reduction of both sweat and odor.[7,18]

The MWT device has a range of standard energy settings (levels 1–5) with incremental total energy delivery with higher energy levels. In previous studies, a variety of energy settings for the device has been used, but none have directly compared two standard energy levels. Some studies have performed standardized treatments with a fixed energy level,[6,12,15] other studies have adjusted energy settings between visits,[9–11] while a few studies omitted to specify energy level.[1,14] Additionally, the number of treatments in studies has ranged from 1 to 3, minimizing the comparability between studies and energy levels utilized. Overall, it is assumed that treatment with a higher energy level can increase the efficacy but simultaneously increase the risk of side effects,[9] but this has not previously been investigated specifically.

This study aimed to evaluate PROMs on sweat and odor following MWT treatment with two different energy levels. The study also aimed to compare energy levels by side effects and patient satisfaction, while assessing the overall treatment effect on patient quality of life.

MATERIALS AND METHODS

Study design

A prospective, randomized, patient-blinded, and split-patient clinical trial was conducted where patients received one baseline treatment, followed by a telephone survey on day 2, and clinical follow-up visits 1 and 3 months after treatment.

The study was conducted at the Department of Dermatology, Bispebjerg Hospital, Copenhagen University Hospital, Denmark. Patient recruitment was carried out at two dermatologic departments, Gentofte and Bispebjerg, Copenhagen University Hospital.

The Danish Data Protection Agency and the Regional Committee on Health Research Ethics in Copenhagen approved this study (H-20013908), and it was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all subjects before study procedures.

Study population

The inclusion criteria comprised adults from 18 years of age with primary axillary hyperhidrosis with a positive gravimetric test at baseline as well as a subjective rating of 3 or 4 on the 4-point Hyperhidrosis Disease Severity scale (HDSS) *and* ≥5 on a 10-point Odor scale (OS).

The exclusion criteria included universal or secondary hyperhidrosis, a medical treatment known to affect sweat secretion (e.g., anticholinergics, antidepressants, antidiabetic drugs), pregnancy or lactation, previous axillary surgery and/or neurologic deficit in the upper limb, abnormal skin in the axillae (e.g., hidradenitis suppurativa, breast tissue), established contraindications for MWT including severe circulatory or respiratory disease (supplemental oxygen and/or electronic device implants, e.g., pacemaker), and history of intolerance to the utilized local anesthesia (LA), as well as other hyperhidrosis treatments before inclusion defined by time limits as follows:

Topical prescription medication (≤1.5 weeks), systemic treatment (≤1.5 weeks), iontophoresis (≤3 months), and botulinum toxin A (≤12 months).

Concomitant treatment during the study was not allowed except for over-the-counter deodorants or antiperspirants which were allowed except for 1–5 days (depending on the type) before study visits.

Study procedures

Treatment with MWT was performed with the miraDry® System (miraDry Inc.), which delivers energy to the dermal–subcutaneous interface, where eccrine and apocrine glands reside. With a built-in feature, the MWT device simultaneously protects the epidermis and upper dermis by constant surface cooling during and after energy delivery.

By randomization, one axilla received treatment with energy level 3 (5.8 GHz, 2.7 s) and the contralateral axilla with energy level 5 (5.8 GHz, 3.0 s), corresponding to medium and high energy settings. The randomization was computer generated an revealed at baseline to clinicians, only, while patients remained blinded throughout the study. Patient blinding during treatment was secured by manually covering the device screen.

All treatments were performed by the same two trained clinicians. Treatment areas were assessed individually by the hair-bearing areas in axillae supported by the starch iodine test. After defining the exact treatment area, the hair was removed with a shaver. The LA consisted of tumescent infiltration (70–124 ml per axilla based on area size) with lidocaine–adrenaline (50 ml; 10 mg/ml + 5 µg/ml) in a solution with sodium chloride (250 ml), which was injected in a standardized way in either axilla disregarding the following treatment energy level.

Data collection

Basic patient characteristics included age, gender, body weight and height. PROMs were collected using standardized scales for odor, sweat, and quality of life. Objective measures of sweat were collected as supporting data. Measures of sweat, odor, side effects, and patient satisfaction were collected from each axilla, respectively, to compare the specific impact of energy levels.

PROMs

Overview of the patient-reported outcome scales is presented in detail in Table 1.

The primary effect measure was the change in axillary odor on the OS from baseline to 3-months follow-up, comparing energy level 3 and 5. The OS is a PROM on a 10-point scale.

Secondary effect measure comprised change in sweat from baseline to 3-months follow-up comparing energy levels for change in sweat, assessed by HDSS, a standardized patient-reported 4-point scale.

The overall impact on quality of life was assessed by patients on the Dermatology Life Quality Index. The DLQI is a standardized subjective 10-item questionnaire,[19–21] each item assessed on a scale from 0 to 3: 0: "Not at all/Not relevant"; 1: "A little"; 2: "A lot"; 3: "Very much."

Objective measures

Sweat was objectively assessed by gravimetric test and visualized with starch iodine test. Gravimetric testing was conducted with standardized filter paper (Whatman ashless quantitative filter paper, 9.0 cm diameter,

TABLE 1 Assessment scales for PROMs

PROM scales	Best outcome → Worst outcome									
Odor Scale (OS)	No odor					Severe odor				
Score (1–10)	1	2	3	4	5	6	7	8	9	10
Hyperhidrosis Disease Severity Scale (HDSS)	Underarm sweating never noticeable and never interferes with daily activities		Underarm sweating is tolerable but sometimes interferes with daily activities			Underarm sweating is barely tolerable and frequently interferes with daily activities		Underarm sweating intolerable and always interferes with daily activities		
Score (1–4)	1		2			3		4		
Dermatology Life Quality Index (DLQI)	No effect at all on patient's life		Small effect on patient's life		Moderate effect on patient's life		Very large effect on patient's life		Extremely large effect on patient's life	
Score (0–30)	0 – 1		2 – 5		6 – 10		11 – 20		21 – 30	

Abbreviation: PROM, patient-reported outcome measure.

Grade 40), weighed before and 5 minutes after placement in the axilla. Patients did not use antiperspirants for a minimum of 24 hours before gravimetric testing and were placed in a resting position at normal room temperature for all tests. At least one axilla produced ≥50 mg/5 min for women and ≥100 mg/5 min for men for the gravimetric test to be considered positive. The contralateral axilla was not allowed to be more than 25% below the gender-specific threshold.

The starch iodine test was performed on each axilla, which is standard in both clinical and hyperhidrosis research settings as a visualization parameter. It is performed by application of iodine and corn starch in the axilla, which in contact with sweat will appear as purple-black coloration.[1] The test provided a momentaneous visualization of axillary sweat, supporting the definition of the treatment area, but was not utilized for quantitative assessments.

Side effects and local skin reactions (LSRs)

Side effects and LSRs were assessed and compared by energy level immediately after treatment, on day 2 (telephone survey), and at both 1- and 3-months follow-up. LSRs and side effects were evaluated and assessed on a scale from 0 to 3: 0: *None*; 1: Light; 2: Moderate; 3: Severe.

Patient satisfaction and treatment preference

Patient satisfaction and preferred treatment (energy level) were assessed at 3-months follow-up.

Overall satisfaction with treatments was assessed on a 3-statement Likert scale: "Satisfied, "Indecisive," and "Not satisfied."

Patients' preferred treatment was assessed with the patients still blinded and responding to their overall preferred treatment, considering both sweat, odor, and side effects, on a 3-statement Likert scale: "Prefer right side," "Indecisive," and "Prefer left side", with sides corresponding to energy level 3 and 5 according to the given randomization.

Statistics

Descriptive statistics reported patient characteristics and prevalence of side effects and LSRs accordingly. Effect measures were presented both with absolute values and by deltas between baseline and follow-up. Outcomes measures were not normally distributed, and non-parametric test of paired data was applied (Wilcoxon's signed-rank test), presented with medians and interquartile range (IQR). p values <0.05 were considered statistically significant. STATA v.14.2 (StataCorp LP) was used.

RESULTS

Patient characteristics

A total of 20 patients with primary axillary hyperhidrosis and concomitant osmidrosis were included. Fifteen (75%) were women and five (25%) were men. The median age was 30 years (IQR: 28–41), and the median Body Mass Index (BMI) was 24.9 (IQR: 22.2–28.0).

By randomization, 10 patients received MWT treatment with a medium energy level (3) in the right axilla and high energy level (5) in the left axilla, while the other 10 patients received the opposite.

All 20 patients completed the 1-month follow-up. Meanwhile, 18 patients completed the 3-months follow-up, with 2 patients lost to follow-up, both male but otherwise comparable to the study group at baseline and early follow-up.

PROMs

Osmidrosis

At baseline, patients bilaterally reported an OS score of median 8. Baseline and follow-up OS scores are presented in detail in Table 2.

At 1-month follow-up, OS scores were reduced to a median of 3.5 for energy level 3 and 5, both significantly reduced compared to baseline ($p = 0.0001$). The delta reduction was a median of 3.5 points for energy level 3 and 4 points for energy level 5, which was a nonsignificant difference between energy levels ($p = 0.471$).

At 3-months follow-up, OS scores were reduced to a median of 3 for both energy level 3 and 5 ($p = 0.0002$). However, the delta median reduction of 3.5 and 4.5 points for energy level 3 and 5, respectively, favored the high energy level ($p = 0.017$).

Hyperhidrosis

At baseline, patients bilaterally reported an HDSS score of median 4. Baseline and follow-up HDSS scores are presented in detail with IQRs in Table 2.

At 1-month follow-up, patients reported reduced HDSS scores at median 2 for both energy level 3 and 5, both significantly reduced compared to baseline ($p = 0.0001$). The delta reduction was a median of 1.5 points for energy level 3 and 2 points for energy level 5, representing a nonsignificant difference between energy levels ($p = 0.564$).

At 3-months follow-up, subjective sweat on HDSS remained at the reduced median 2 for both energy levels ($p = 0.0002$). However, compared to baseline, the delta for energy levels 3 and 5 differed with a median 1 and 2 points reduction, respectively, favoring the high energy level ($p = 0.014$).

Quality of life

The change in overall DLQI scores throughout the study is presented in Figure 1.

Overall, patients reported a substantial negative impact of axillary hyperhidrosis and osmidrosis on

TABLE 2 Patient-reported odor and sweat reduction compared by medium energy level (3) and high energy level (5)

Outcome assessment	Patient-reported odor OS (1–10)		Patient-reported sweat HDSS (1–4)	
	Energy level 3	Energy level 5	Energy level 3	Energy level 5
Baseline (n = 20)				
Baseline median score (IQR)	8 (7 – 8)	8 (7 – 8)	4 (3 – 4)	4 (3 – 4)
1-month follow-up (n = 20)				
1M FU median score (IQR) p value baseline versus 1M FU	3.5 (1.5– 6) **0.0001**	3.5 (1.5 – 6) **0.0001**	2 (2 – 2) **0.0001**	2 (1.5 – 2) **0.0001**
Delta median reduction (IQR) from baseline	3.5 (2 – 5.5)	4 (2 – 5.5)	1.5 (1 – 2)	2 (1 – 2)
p value energy level 3 versus 5 at 1M FU	0.471		0.564	
3-month follow-up (n = 18)				
3M FU median score (IQR) p value baseline versus 3M FU	3 (1 – 6) **0.0002**	3 (1 – 5) **0.0002**	2 (2 – 3) **0.0002**	2 (2 – 2) **0.0002**
Delta median reduction (IQR) from baseline	3.5 (2 – 5)	4.5 (3 – 6)	1 (1 – 2)	2 (1 – 2)
p value energy level 3 versus 5 at 3M FU	**0.017**		**0.014**	

Note: Bold values are statistically significant.

Abbreviations: 1M, 1-month; 3M, 3-months; FU, follow-up; OS, Odor scale; HDSS, Hyperhidrosis Disease Severity scale; IQR, interquartile range.

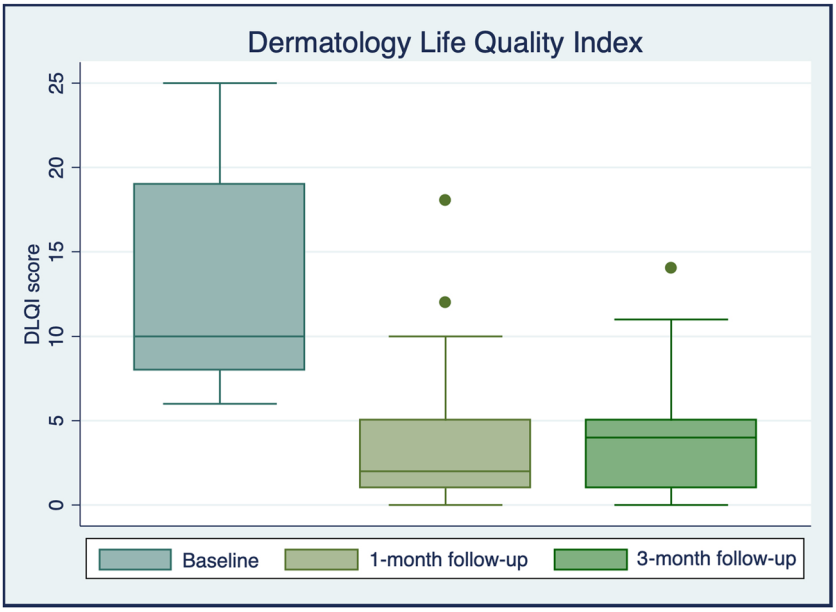

FIGURE 1 Overall quality of life at baseline and follow-up visits: From baseline DLQI score of median 10 to a median below 5 at 3-months follow-up, showing a significant improvement with median 6.5 points ($p = 0.0002$) reduction following MWT treatment. DLQI, Dermatology Life Quality Index; MWT, microwave thermolysis.

their quality of life with a baseline DLQI score of median 10 (IQR: 8–19) and a range between 6 and 25, spanning from moderate to extremely large effect on patient's life.

Following MWT treatment, the negative impact of axillary hyperhidrosis and osmidrosis was significantly improved, having no-to-small effect on patients' lifes. At 1-month follow-up, patients reported an improvement in quality of life compared to baseline with DLQI score median 2 (IQR: 1–5), ($p = 0.0001$). Quality of life remained significantly improved at 3-months follow-up compared to baseline with DLQI median 4 (IQR: 1–5) and a delta median of 6.5 points reduction ($p = 0.0002$).

Objective outcome measures

Gravimetric test changes throughout the study are presented in Figure 2.

Gravimetric tests at baseline presented a bilateral median of 121 mg/5 min (IQR: 82–154, 92–156) with no significant difference between men and women.

At 1- and 3-months follow-up, gravimetric tests presented significant sweat reduction. At the 3-months follow-up, gravimetric tests presented a median of 16 mg/5 min (IQR: 5–43) for energy level 3 and a median of 14 mg/5 min (IQR: 4–39) for energy level 5, corresponding to a percentual decrease of 89% (IQR: 74–93) and 90% (IQR: 75–95), respectively. Compared to baseline, sweat amount was significantly reduced on both sides ($p = 0.0002$), but with no detectable difference between energy levels ($p = 0.53$). Additionally, no gender-specific difference in efficacy was detected.

The individual %–sweat reductions at the 3-month follow-up compared to baseline are presented in Supporting Information: Material A.

The starch iodine test was a momentaneous visual tool and presented with a clear reduction in present axillary sweat at control visits as exemplified in Figure 3.

Side effects and LSRs

Pain during the procedure was low and comparable between energy levels; in both axillae, ≥80% of patients reported a light-to-moderate stinging/pain from injection of LA ($p = 0.71$), while 90% experienced none-to-light discomfort/pain from the actual microwave treatment despite LA ($p = 0.29$). Procedural pain measures are presented in detail in Table 3. No differences in immediate LSRs in axillae were detected between energy level 3 and 5.

Two days after baseline treatment, only patient-reported swelling and soreness of the treatment area differed significantly between energy levels, with a higher prevalence of moderate–to-severe swelling and soreness on the side treated with energy level 5 ($p = 0.011$ and $p = 0.026$).

At 1-month follow-up, LSRs had generally diminished. Only subjective altered sensation, mainly numbness, in the treatment area differed significantly between energy levels, with a higher prevalence of moderately altered sensation in the treatment area on the side treated with energy level 5 ($p = 0.046$).

At 3-months follow-up, most side effects had worn off partially or completely. Only hair reduction in axillae differed significantly between energy levels, with hair reduction seen in most patients, but with a higher prevalence of moderate-to–severe hair reduction after treatment with energy level 5 ($p = 0.025$).

No unexpected or serious adverse events were detected during the study.

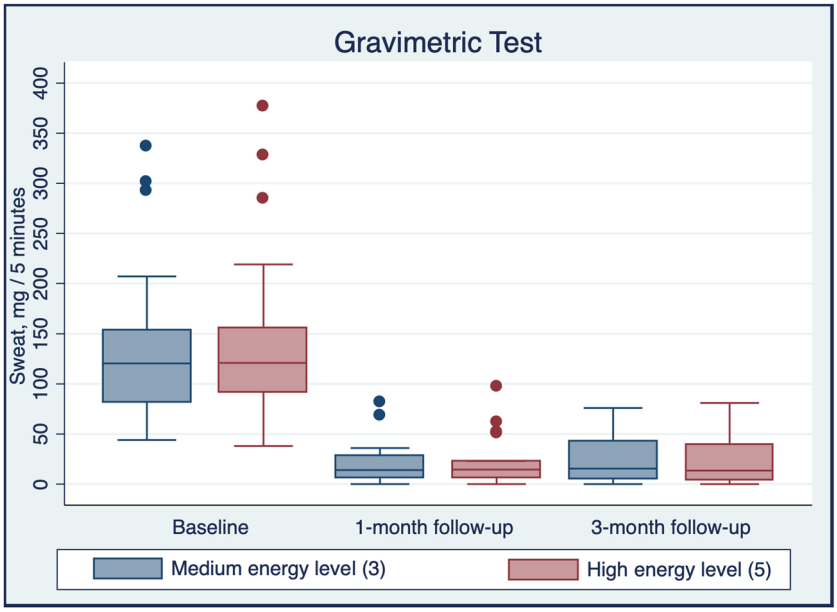

FIGURE 2 Gravimetric test from baseline and follow-up visits compared by medium energy level (3) and high energy level (5): Gravimetric test results from baseline are widespread with tests just around the standard threshold to tests up to several 100 mg/5 min. At 1-month follow-up, patients' tests were significantly reduced with some outliers between 50 and 100 mg/5 min. At 3-months follow-up, the tests had stabilized at a slightly higher level, but both median and interquartile range remained below the lower threshold of 50 mg/5 min.

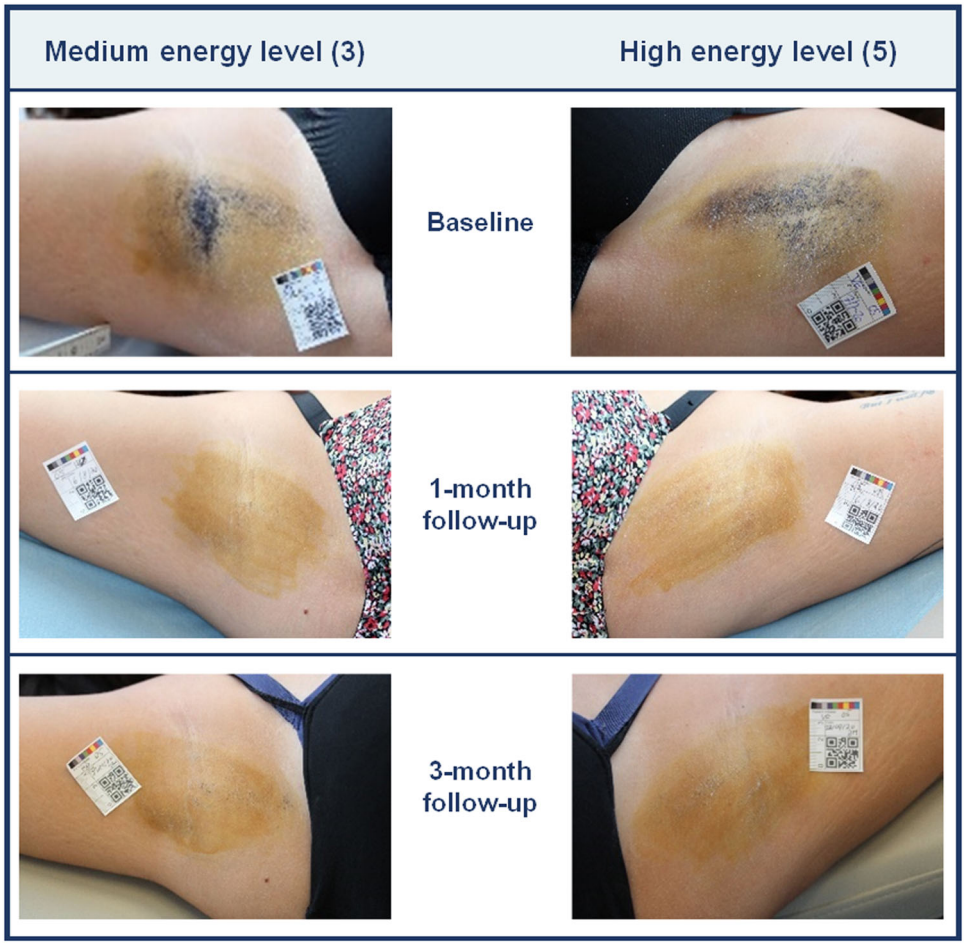

FIGURE 3 Starch iodine test: A visualization of momentaneous presence of axillary sweat. This patient was a good responder as sweat was neither measured nor visualized during 1- and 3-months follow-up. The test could not detect a visual difference between energy levels.

TABLE 3 Procedural pain during anesthesia and MWT treatment compared by medium energy level (3) and high energy level (5)

Pain measures	Baseline treatment (*n* = 20)		
	Energy level		
	3	5	3 versus 5
Assessment	Median (IQR) *Distribution*	Median (IQR) *Distribution*	***p* value**
Stinging or pain from injection of local anesthesia (0–3)	1 (1 – 2) *0: 0 (0%)* *1: 11 (55%)* *2: 5 (25%)* *3: 4 (20%)*	2 (1 – 2) *0: 1 (5%)* *1: 8 (40%)* *2: 9 (45%)* *3: 2 (10%)*	0.71
Discomfort or pain in axilla during MWT-treatment despite local anaesthesia (0–3)	1 (0 – 1) *0: 9 (45%)* *1: 9 (45%)* *2: 1 (5%)* *3: 1 (5%)*	0 (0 – 1) *0: 13 (65%)* *1: 5 (25%)* *2: 2 (10%)* *3: 0 (0%)*	0.29

Abbreviations: 0, none; 1, light, 2, moderate; 3, severe; MWT, microwave thermolysis; N/A, not applicable.

TABLE 4 Main side effects and local skin reactions compared by medium energy level (3) and high energy level (5)

LSR/side effect	2-day telephone survey (n = 20)			1-month follow-up (n = 20)			3-month follow-up (n = 18)		
	Energy level			Energy level			Energy level		
	3	5	3 vs. 5	3	5	3 vs. 5	3	5	3 vs. 5
Assessment	Median (IQR) *Distribution*	Median (IQR) *Distribution*	*p* value	Median (IQR) *Distribution*	Median (IQR) *Distribution*	*p* value	Median (IQR) *Distribution*	Median (IQR) *Distribution*	*p* value
Swelling in treatment area (0–3)	2 (1 – 2) ***0:*** *0 (0%)* ***1:*** *6 (30%)* ***2:*** *14 (70%)* ***3:*** *0 (0%)*	2 (2 – 2.5) ***0:*** *0 (0%)* ***1:*** *2 (10%)* ***2:*** *13 (65%)* ***3:*** *5 (25%)*	**0.011**	0 (0 – 0.5) ***0:*** *15 (75%)* ***1:*** *4 (20%)* ***2:*** *1 (5%)* ***3:*** *0 (0%)*	0 (0 – 1) ***0:*** *13 (65%)* ***1:*** *6 (30%)* ***2:*** *1 (5%)* ***3:*** *0 (0%)*	0.16	0 (0 – 0) ***0:*** *17 (94%)* ***1:*** *1 (6%)* ***2:*** *0 (0%)* ***3:*** *0 (0%)*	0 (0 – 0) ***0:*** *17 (94%)* ***1:*** *1 (6%)* ***2:*** *0 (0%)* ***3:*** *0 (0%)*	1.00
Soreness, discomfort or tenderness of treated area (0–3)	1 (1 – 2) ***0:*** *4 (20%)* ***1:*** *10 (50%)* ***2:*** *5 (25%)* ***3:*** *1 (5%)*	1.5 (1 – 2) ***0:*** *3 (15%)* ***1:*** *7 (35%)* ***2:*** *8 (40%)* ***3:*** *2 (10%)*	**0.026**	1 (0 – 1) ***0:*** *9 (45%)* ***1:*** *9 (45%)* ***2:*** *2 (10%)* ***3:*** *0 (0%)*	1 (0 – 1) ***0:*** *7 (35%)* ***1:*** *10 (50%)* ***2:*** *3 (15%)* ***3:*** *0 (0%)*	0.08	0 (0 – 0) ***0:*** *18 (100%)* ***1:*** *0 (0%)* ***2:*** *0 (0%)* ***3:*** *0 (0%)*	0 (0 – 0) ***0:*** *16 (89%)* ***1:*** *2 (11%)* ***2:*** *0 (0%)* ***3:*** *0 (0%)*	0.16
Altered sensation in or around treatment area (0–3)	1 (0 – 1.5) ***0:*** *7 (35%)* ***1:*** *8 (40%)* ***2:*** *5 (25%)* ***3:*** *0 (0%)*	1 (1 – 2) ***0:*** *9 (45%)* ***1:*** *5 (25%)* ***2:*** *5 (25%)* ***3:*** *1 (5%)*	0.98	1 (0 – 1) ***0:*** *9 (45%)* ***1:*** *11 (55%)* ***2:*** *0 (0%)* ***3:*** *0 (0%)*	1 (0 – 1) ***0:*** *8 (40%)* ***1:*** *9 (45%)* ***2:*** *3 (15%)* ***3:*** *0 (0%)*	**0.046**	0 (0 – 0) ***0:*** *14 (78%)* ***1:*** *4 (22%)* ***2:*** *0 (0%)* ***3:*** *0 (0%)*	0 (0 – 1) ***0:*** *13 (72%)* ***1:*** *5 (28%)* ***2:*** *0 (0%)* ***3:*** *0 (0%)*	0.32
Reduction or loss of hair in axilla (0–3)	N/A	N/A	N/A	1 (0 – 1.5) ***0:*** *8 (40%)* ***1:*** *7 (35%)* ***2:*** *5 (25%)* ***3:*** *0 (0%)*	1 (0 – 1.5) ***0:*** *7 (35%)* ***1:*** *8 (40%)* ***2:*** *5 (25%)* ***3:*** *0 (0%)*	0.56	1.5 (1 – 2) ***0:*** *4 (22%)* ***1:*** *5 (28%)* ***2:*** *7 (39%)* ***3:*** *2 (11%)*	2 (1 – 2) ***0:*** *2 (11%)* ***1:*** *5 (28%)* ***2:*** *8 (44%)* ***3:*** *3 (17%)*	**0.025**

Note: Bold values are statistically significant.

Abbreviations: 0, none; 1, light; 2, moderate; 3, severe; IQR, interquartile range; N/A: not applicable.

A detailed overview of the four LSRs that differed between energy levels throughout the study is presented in Table 4.

Patient satisfaction and treatment preference

At 3-months follow-up, patients assessed energy level preference regarding sweat and odor reduction, as well as side effects. Taking all into account, eight patients (45%) preferred high energy level (5), while four (22%) preferred medium energy level (3), and six patients (33%) remained indecisive. Figure 4 presents a patient case with a visible difference between axillae following MWT treatment, favoring high energy level (5).

Fourteen patients (78%), who completed the 3-months follow-up (n = 18), declared a satisfaction with their treatment, while one patient (6%) was not satisfied. Three patients (17%) were indecisive, mainly due to insufficient effect.

DISCUSSION

To our knowledge, this is the first study to present a direct patient-blinded comparison of two standard energy settings on the available MWT device in a randomized clinical trial.

The chosen energy levels were medium (level 3) and high (level 5) to assure a detectable effect on the standardized PROM scales. Odor is usually measured on a subjective scale (OS), which makes it a more challenging endpoint than sweat, which can be assessed both subjectively (HDSS) and objectively (gravimetric testing). However, previous studies[7,9,10] have successfully assessed odor with subjective scales, and a 10-point scale was chosen to detect smaller changes and differences. PROMs are gaining more and more focus as clinical endpoints since they correlate closely to patient satisfaction with treatments and may therefore assess the actual impact of the chosen therapies. However, PROMs cannot stand alone in the assessment of treatment of axillary hyperhidrosis and osmidrosis since current guidelines for treatment indication depend largely on objective findings such as positive gravimetric tests.

Overall, compared to baseline, a significant reduction of odor and sweat was detected for both energy levels, which corresponds well to the findings of other studies.[1,7,9,12,13] There was a difference between energy levels for HDSS and OS reduction at 3-months follow-up compared to baseline; however, the scales did not discriminate sufficiently to detect a great score difference with HDSS median 2 and OS median 3 for both sides. Likewise, for the objective gravimetric test, a significant difference could not be found. Many patients asked for a more elaborate scale than HDSS, since they found that

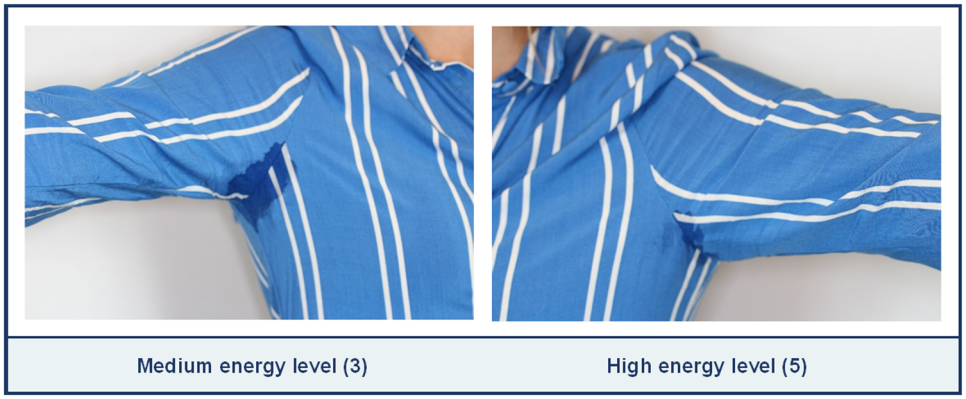

FIGURE 4 Patient's subjective assessment of sweat: A patient presenting unequal sweat patches on a shirt following treatment with medium energy level (3) and high energy level (5), respectively. Patients assess their axillary sweat highly based on the affection on clothing, which largely contributes to the daily challenges and stigmatization related to their condition. A second MWT treatment was indicated for this patient on both sides and the patient preferred the high energy level (5).

the four statements were too broad and did not allow for proper distinction between the two treatments. Additionally, it is worth noting that a gravimetric test is always a mere snapshot of a patient's sweat and thereby has incorporated limitations when assessing patients' everyday sweating issues. In the case of OS, the patients reported difficulty distinguishing daily odor between the two axillae. Since the difference between energy levels first appeared at 3-months follow-up, it is probable that a longer follow-up time could have detected an increased difference between energy levels for both subjective and objective measures.

Quality of life was assessed overall and confirmed the findings of previous studies[1,5,6] as MWT significantly improved patients' quality of life. We saw a small score increase from 1- to 3-months follow-up, but the median score remained <5, which was a >50% improvement from the baseline median of 10.

Overall, side effects and LSRs were mild and transient and corresponded well to findings in previous studies.[1,6,7,9,12,13] There were no serious or unexpected adverse reactions. Temporary side effects such as swelling, soreness, and altered sensation were slightly worse on the axilla treated with energy level 5. At 3-months follow-up, however, only the reduction of hair growth remained significantly different. Generally, patients did not consider this side effect problematic, but sufficient information should be prioritized to meet the patient expectations.

A total of 78% of patients were satisfied with the treatments overall. Dissatisfaction by patient (6%) was due to a change in subjective odor bilaterally. However, at a clinical outpatient visit 3 months after the end of the study, it had spontaneously resolved, and the patient had continued sweat reduction.

A total of five patients (28%) qualified for a second treatment due to insufficient objective (gravimetric test) and subjective treatment effect at 3-months follow-up. The proportion was in-between the findings of previous studies,[1,5,12] however, most other studies had a higher prevalence of second treatment, which may be connected to the chosen follow-up time. Overall, almost half of the patients preferred a high energy level, and all patients who received a second treatment preferred a high energy level (5). The blinded patients generally acknowledged that high energy level (5) was slightly more significant in regard to temporary local skin reactions, but were willing to accept these in exchange for subjectively better efficacy. Not surprisingly, patients who had a sufficient effect with the low energy level were satisfied with that and did not want to accept more side effects.

A few case reports[22,23] have suggested that patients with low BMI and thus a lower amount of fat tissue in the axillae are at higher risk of complications and nerve injury. Based on this, some researchers have suggested the use of a low energy level for thin patients. However, the treatments utilized in the given patient cases were energy levels 1 and 5, respectively, which implies that the risk of complications cannot be entirely eliminated even with the lowest energy level. In one case report,[23] a patient had severe numbness in the upper limb immediately after treatment, which persisted and required rehabilitation. None of the patients in our study experienced this. However rare, the risk of nerve injury requiring rehabilitation cannot be completely obliterated, which substantiates the importance of meticulous patient information before treatment. Finally, it is worth noting that conservative treatment with a lower energy level may increase the need of a second treatment, thus not reducing the patient's overall risk of experiencing side effects.

In this study, we did not find a higher risk of severe side effects between energy levels, but limitations could involve the size of the patient group, since rare side

effects may appear in <5% of cases. In addition to the limitations in sweat and odor assessment, sample size and follow-up time were the main limitations of this study. There were 2 patients lost to follow-up, both male, but otherwise comparable to the rest of the study population at baseline and at 1-month follow-up with no unexpected or serious side effects, and both with a significant odor and sweat reduction with bilateral gravimetric tests <10 mg/5 min.

The main strength of this study was the prospective design and randomization, and that patients were blinded when evaluating sweat, odor and side effects, as well as satisfaction and preferred treatment. The usage of PROMs allowed this study to evaluate the actual impact on patients' every day following treatments, supporting that objective measures, alone, are not sufficient in regard to optimal device settings and coveted clinical endpoints.

CONCLUSION

This study investigated MWT treatment in patients with axillary hyperhidrosis and osmidrosis, comparing two standard energy levels. PROMs on odor and sweat presented significant reductions following treatment with both energy levels at 3-months follow-up, and correspondingly, patients' quality of life improved significantly. The PROMs also showed a subtly increased reduction of both odor and sweat with the high energy level (5), but only with a nonsignificant tendency within the objective measures.

Treatment with high energy levels on t MWT device is safe, and patients were willing to accept increased temporary side effects and LSRs in exchange for a subjectively better efficacy on odor and sweat. Optimal device settings from a clinical perspective should consider the PROMs disclosing on subjective efficacy, treatment preference, and satisfaction.

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ORCID

G. L. Grove http://orcid.org/0000-0002-6954-4458
K. Togsverd-Bo http://orcid.org/0000-0002-4272-4889
J. F. B. Schwensen http://orcid.org/0000-0003-0418-1622
N. W. Andersson http://orcid.org/0000-0001-7622-6303
C. V. Nissen http://orcid.org/0000-0002-5961-9399
C. Zachariae http://orcid.org/0000-0001-5506-1319
M. Haedersdal http://orcid.org/0000-0003-1250-2035

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SUPPORTING INFORMATION

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