NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of transcutaneous microwave ablation for severe primary axillary hyperhidrosis

Axillary hyperhidrosis is excessive underarm sweating. In this procedure, a hand-held device sends microwaves to the sweat glands in the armpit to damage them. The aim is to destroy the glands and stop the sweating.

Introduction

The National Institute for Health and Care Excellence (NICE) has prepared this interventional procedure (IP) overview to help members of the interventional procedures advisory committee (IPAC) make recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This IP overview was prepared in March 2017.

Procedure name

- Transcutaneous microwave ablation for severe primary axillary hyperhidrosis

Specialist societies

- British Association of Dermatologists
- Royal College of Physicians.

Description

Indications and current treatment

Primary axillary hyperhidrosis typically begins during childhood or adolescence, but can happen at any age. It is usually life-long, although in a few people symptoms can spontaneously improve over time. Severe primary axillary hyperhidrosis can be defined as a score of 3 or 4 on the Hyperhidrosis Disease Severity Scale. Excessive sweating can have a profound effect on quality of life, interfering with daily activities and causing anxiety and embarrassment.

First-line management of primary axillary hyperhidrosis includes lifestyle measures such as avoiding known triggers and tight clothing, and using antiperspirants (including aluminium chloride hexahydrate). Other treatments include iontophoresis and botulinum-toxin A injection, and oral medications such as anticholinergics, antimuscarinics, beta-blockers, antihypertensives and anxiolytics. If these do not work, surgical options include local sweat-gland excision by subcutaneous curettage or tumescent liposuction, or thoracic sympathectomy.

What the procedure involves

Transcutaneous microwave ablation for severe primary axillary hyperhidrosis is done under local anaesthesia using a machine with a hand-piece that emits microwaves. After numbing the underarm area with several injections of local anaesthesia, the hand-piece is placed on the area where the sweat glands are and microwaves are applied with the intention of ablating the sweat glands. The machine has a cooling system that prevents damage to the superficial skin layers and a vacuum system that lifts the underlying skin to help isolate the target tissue from underlying structures. The procedure takes about 1 hour; patients typically have a second treatment session approximately 3 months later to attain the maximum benefit. Patients may need to take oral analgesics and apply ice packs to reduce swelling of the treated area for a few days after the procedure.

Outcome measures

The Hyperhidrosis Disease Severity Scale has a score from 1 to 4, depending on the patient's rating of severity:

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.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to transcutaneous microwave ablation for severe primary axillary hyperhidrosis. The following databases were searched, covering the period from their start to 12 December 2016: MEDLINE, PREMEDLINE, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches (see appendix C for details of search strategy). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection criteria could not be determined from the abstracts the full paper was retrieved.

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with severe primary axillary hyperhidrosis.
Intervention/test	Transcutaneous microwave ablation.
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the IP overview

This IP overview is based on 190 patients from 1 randomised controlled trial, 4 case series and 1 case report[1–6]. There is also a summary of safety events reported on the FDA Manufacturer and User Facility Device Experience (MAUDE) database[7].

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (table 2) have been listed in appendix A.

Table 2 Summary of key efficacy and safety findings on transcutaneous microwave ablation for severe primary axillary hyperhidrosis

Study 1 Glaser DA (2012)

Details

Study type	**Randomised controlled trial**
Country	US
Recruitment period	Not reported
Study population and number	**n=120 (81 microwave ablation versus 39 sham)** Adults with primary axillary hyperhidrosis
Age and sex	Median 31 years; 58% (69/120) female
Patient selection criteria	Hyperhidrosis Disease Severity Scale (HDSS) score of 3 or 4 (barely tolerable or intolerable sweating) and baseline axillary sweat production of more than 50 mg per 5 minutes as measured by gravimetric readings. Patients were excluded if they had ever had surgery for primary axillary hyperhidrosis or botulinum toxin injections in the past 12 months.
Technique	Each session included 3 steps: marking the axilla with a treatment template, injecting local anaesthesia throughout the indicated area, and applying the microwave treatment. Patients in the sham group had all steps of the procedure session, but microwave energy was not delivered. Patients typically had 2 treatment sessions, about 2 weeks apart. A third procedure was allowed within a 30-day window, if necessary. The microwave-based device included integrated vacuum and cooling (DTS G2 system; Miramar Labs, US). A fixed setting was used for energy delivery throughout the study.
Follow-up	**12 months (active treatment group); 6 months (sham group)**
Conflict of interest/source of funding	The study was funded by Miramar Labs. Three of the 8 authors are on the Scientific Advisory Board for Miramar Labs and have equity in the company.

Analysis

Follow-up issues: 84% (101/120) of patients completed the study as planned. 16% (13/81) of patients in the active group and 15% (6/39) of patients in the sham group exited the study early, none because of adverse events.

Study design issues: Patients were randomised to a treatment group at the first procedure session; the method of randomisation is not described. Patients were blinded to the treatment allocation and the paper states that 'procedures were put in place to protect blinding during the treatment period'. The primary endpoint defined responders as patients with a HDSS score of 1 or 2 at the 30-day follow-up visit. Gravimetric success was defined as more than a 50% reduction in weighed sweat from baseline data. The HDSS questionnaires and gravimetric assessments were administered by blinded study staff. In the first procedure session, the hair-bearing areas of both axillae were treated. 83% of patients had a second procedure session. An unblinded investigator determined the extent of the area to be treated based on a starch-iodine test and sweat assessments (active group) or a defined area based on axilla size (sham group). All patients and study staff were unblinded at the end of the 6-month study visit. An intention-to-treat analysis was done; the method of last observation carried forward was used to impute missing data.

Study population issues: There were no statistically significant differences between the groups, but the proportion of patients with a HDSS score of 3 was substantially higher in the sham group than the active treatment group (67% compared with 51%). This meant that more patients in the sham group could meet the definition of success according to the primary endpoint by dropping a single point (from 3 to 2).

Other issues: The authors noted that room conditions, such as temperature and humidity, were not strictly controlled and this could have contributed to variations in gravimetric measurements.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **120 (81 versus 39)**

Hyperhidrosis Disease Severity Scale (HDSS) score

	Proportion of patients with HDSS score 1 or 2			Proportion of patients with HDSS score reduced by 2 or more points		
Follow-up period	Active n=81	Sham n=39	p value	Active n=81	Sham n=39	p value
30 days	89% (n=72)	54% (n=21)	<0.001	67%	13%	<0.001
3 months	74%	44%	<0.001	57%	13%	<0.001
6 months	67%	44%	0.02	47%	13%	<0.001
9 months	69%	-	-	42%	-	-
12 months	69%	-	-	38%	-	-

Gravimetric efficacy results

	Proportion of patients with 50% or greater reduction from baseline			Proportion of patients with 75% or greater reduction from baseline		
Follow-up period	Active n=81	Sham n=39	p value	Active n=81	Sham n=39	p value
30 days	80%	67%	0.07	62%	39%	0.01
3 months	75%	64%	0.20	52%	44%	0.34
6 months	63%	59%	0.69	41%	36%	0.60

Safety

There were no serious procedure-related adverse events reported in the study.

Total procedure-related adverse events=45 (38 in the active group and 7 in the sham group)

Proportion of patients reporting an adverse event

- Active=28.4% (23/81)
- Sham=12.8% (5/39)

Altered sensation in the skin of the upper arm (change in sensitivity, tingling or numbness; average area 12 cm length at onset)

- Active=9.9% (8/81) (mean duration 67 days, range 4 to 225)
- Sham=2.6% (1/39) (duration 79 days)

All events resolved over time.

Pain or soreness

- Active=6.2% (5/81) (mean duration 22 days, range 1 to 74)
- Sham=5.1% (2/39) (duration 3 and 4 days respectively)

Swelling in the treated limb

- Active=4.9% (4/81) (mean duration 9 days, range 2 to 20)
- Sham=2.6% (1/39) (2 episodes in the same patient; duration 2 and 3 days respectively)

This event was rated mild in all but 1 event, where the patient stayed in bed over a weekend, which was rated as severe.

Blisters, burns, or ulcerations

- Active=4.9% (4/81) (mean duration 28 days, range 12 to 40)
- Sham=0% (0/39)

Skin: rash, irritation, or dermatitis

- Active=4.9% (4/81) (mean duration 27 days, range 3 to 87)
- Sham=0% (0/39)

Axillary bumps or nodules

- Active=2.5% (2/81) (mean duration 30 days, range 8 to 52)
- Sham=2.6% (1/39) (2 events in the same patient, duration 10 to 12 days)

Compensatory sweating

- Active=2.5% (2/81) (1 patient reported ongoing sweating of the face at study exit)
- Sham=0% (0/39)

Abbreviations used: HDSS, Hyperhidrosis Disease Severity Scale

Study 2 Scuderi S (2016)

Details

Study type	**Case series**
Country	Australia
Recruitment period	2014 to 2015
Study population and number	**n=20** Patients with severe axillary hyperhidrosis
Age and sex	Median 30 years (range 19 to 45); 45% (9/20) female
Patient selection criteria	Hyperhidrosis Disease Severity Scale (HDSS) score of 3 or 4. All patients had previous unsuccessful treatments with topical agents.
Technique	The starch iodine test was done to determine the treatment area. Tumescent anaesthesia was used and the microwave treatment was applied to both armpits. The energy levels were determined by the length of time for which the device was applied. Level 1 used a shorter period of application than the longer duration of level 5, which subsequently generated more heat. Most patients were treated with level 3 or 4 at the initial visit and level 4 or 5 at the final visit. Most patients had a second treatment around 3 months after the initial treatment.
Follow-up	**Mean 5 months (range 1 to 12)**
Conflict of interest/source of funding	None

Analysis

Follow-up issues: No patients were lost to follow-up.

Study design issues: Retrospective survey on treatment outcomes and complications conducted through telephone and email questionnaires as well as the analysis of clinical notes. The level of sweat reduction was based on the patient's estimation.

Other issues: At the time of the survey, 5 patients had not had a second treatment but they were still included in the study.

Key efficacy and safety findings

Efficacy	Safety
Number of patients analysed: **20** **Mean percentage sweat reduction=72.5% (±14.8)** **Mean Hyperhidrosis Disease Severity Scale (HDSS) score (range 1 to 4)** • Before treatment=3.75 (±0.44) • After treatment=1.75 (±0.55) Mean difference before and after treatment=2 HDSS points (95% CI 1.85 to 2.15, p<0.0001) 95% (19/20) of patients had a HDSS score of 2 or less at follow-up. Mean return to complete physical activity after the last treatment=8.75 days. Patients were asked, in retrospect, if they were satisfied and if they would have the treatment again. All patients responded that they would have the treatment again.	The most common short-term side effects were: • Pain=65% • Swelling=60% • Bruising=15% • Temporary numbness=20% The pain and swelling were mild and typically lasted 2 weeks. Longer-term side-effects included regional hair loss (25%) and nodule formation (25%). Nodule formation lasted up to 4 weeks and the hair loss was permanent.
Abbreviations used: CI, confidence interval; HDSS, Hyperhidrosis Disease Severity Scale	

Study 3 Hong H (2012)

Details

Study type	**Case series**
Country	Canada
Recruitment period	Not reported
Study population and number	**n=31** Adults with primary axillary hyperhidrosis
Age and sex	Median 33 years (range 18 to 65); 74% (23/31) female
Patient selection criteria	Hyperhidrosis Disease Severity Scale (HDSS) score of 3 or 4 and a gravimetric sweat assessment of at least 50 mg in 5 minutes in each axilla. Patients were excluded if they had had surgery for axillary hyperhidrosis or botulinum toxin injections in the axillae in the past 12 months.
Technique	Each session included 3 steps: marking the axilla with a treatment template, injecting local anaesthesia in a grid pattern throughout the indicated area, and applying the microwave treatment. The microwave-based device included integrated vacuum and cooling (miraDry system; Miramar Labs, US). There was a small range (±10%) of energy settings and some variation in energy settings was explored to determine the optimal parameters. At the first visit, the hair-bearing areas of both axillae were treated. Subsequent treatment sessions were done approximately 30 days later, if necessary, targeting the areas that were still sweating. A maximum of 3 procedure sessions were allowed, and all procedures had to be completed within 6 months.
Follow-up	**12 months**
Conflict of interest/source of funding	The study was funded by Miramar Labs, US. One of the authors is an employee of Miramar Labs.

Analysis

Follow-up issues: 84% (26/31) of patients completed the study visits through 12 months of follow-up. There is no discussion of patients lost to follow-up.

Study design issues: The primary method for assessing the level of underarm sweat at baseline was the patient-reported HDSS score. A gravimetric assessment of sweat was used as a secondary measure. A starch-iodine test was used in some treatment sessions to identify areas that still had active sweat glands. The primary overall efficacy measure was the proportion of patients with a HDSS score reduced from 3 or 4 at baseline to 1 or 2 at follow-up. A secondary assessment used the 10-question validated Dermatology Life Quality Index (DLQI; score ranges from 0 to 30 with higher scores indicating poorer quality of life).

Study population issues: 65% (20/31) of the patients scored 3 on the HDSS at baseline and 35% (11/31) had a score of 4.

Key efficacy and safety findings

<table>
<tr><td>Efficacy</td><td>Safety</td></tr>
<tr><td>Number of patients analysed: 31

12 patients had 2 treatment sessions and 15 had 3 treatment sessions within the allowed 6-month window. 4 patients had only 1 session (1 patient had full sweat reduction after 1 session, 2 patients declined further treatment because of side effects and 1 declined because of lack of efficacy).

Efficacy assessment results at follow-up visits
<table>
<tr><th>Efficacy measure</th><th>30 days</th><th>3 months</th><th>6 months</th><th>12 months</th></tr>
<tr><td>HDSS score reduction to 1 or 2, n (%) [95% CI]</td><td>28 (90.3)
[74.3 to 98.0]</td><td>29 (93.6)
[78.6 to 99.2]</td><td>28 (90.3)
[74.3 to 98.0]</td><td>28 (90.3)
[74.3 to 98.0]</td></tr>
<tr><td>≥50% reduction in sweat (gravimetric), n (%) [95% CI]</td><td>28 (90.3)
[74.3 to 98.0]</td><td>29 (93.6)
[78.6 to 99.2]</td><td>28 (90.3)
[74.3 to 98.0]</td><td>28 (90.3)
[74.3 to 98.0]</td></tr>
<tr><td>Mean reduction in sweat (gravimetric), % (n=31)</td><td>83.1</td><td>82.3</td><td>82.1</td><td>81.7</td></tr>
<tr><td>Mean DLQI score (n=31)</td><td>2.5</td><td>2.7</td><td>3.1</td><td>3.0</td></tr>
<tr><td>Reduction in DLQI score, mean [95% CI]*</td><td>10.4
[8.3 to 12.4]</td><td>10.2
[7.9 to 12.4]</td><td>9.6
[7.3 to 12.0]</td><td>9.9
[7.5 to 12.2]</td></tr>
<tr><td>Reduction of DLQI by ≥5 points, n (%) [95% CI]</td><td>26 (96.3)
[81.0 to 99.9]</td><td>24 (88.9)
[70.8 to 97.7]</td><td>24 (88.9)
[70.8 to 97.7]</td><td>23 (85.2)
[66.3 to 95.8]</td></tr>
</table>
*Included only patients with a baseline DLQI of ≥5 (n=27)

94% (29/31) of patients had at least a 1-point drop in HDSS at 12-month follow-up and 55% (17/31) had a 2-point drop or greater.

Patient satisfaction – proportion of patients reporting being very satisfied or somewhat satisfied
• 30 days=90.0% (27/30)
• 3 months=96.4% (27/28)
• 6 months=92.6% (25/27)
• 12 months=88.5% (23/26)

Proportion of patients with no noticeable underarm odour (self-reported)
• Baseline=12.9% (4/31)
• 30 days=67.7% (21/31)
• 3 months=71.0% (22/31)
• 6 months=74.2% (23/31)
• 12 months=61.3% (19/31), p<0.001 for all time points</td><td>Mild procedure effects lasting a few days to a week:
• Oedema=90%
• Redness and vacuum acquisition marks=87%
• Discomfort=84%

Longer term effects:
• Altered sensation in the skin of the axillae=65% (median duration 37 days, range 4 days to 4 months)
• Palpable bumps under the skin of the axillae=71% (median duration 41 days; 2 patients had the effect at study exit)
• Axillary hair loss=26%

Procedure effects that were rated to have even a remote chance of being procedure related that were evident outside the axillae:
• Altered sensation in the skin of the treated limb=38.7% (12/31) (median duration 50 days, range 6 days to 12 months; all resolved)
• Swelling outside the axilla, in the arm or chest=number of patients not reported (median duration 7 days, range 2 to 23 days)

One patient had transient neuropathy of the left arm with associated muscle weakness after the procedure; the prognosis from the consulting neurologist was complete resolution. The patient had improved at the 6 month follow-up, after which she was lost to follow-up.</td></tr>
<tr><td colspan="2">Abbreviations used: CI, confidence interval; DLQI, Dermatology Life Quality Index; HDSS, Hyperhidrosis Disease Severity Scale</td></tr>
</table>

Study 4 Lee SJ (2013)

Details

Study type	**Case series**
Country	Korea
Recruitment period	Not reported
Study population and number	**n=11** Patients with axillary hyperhidrosis or osmidrosis (3 patients had hyperhidrosis only, 3 had hyperhidrosis and osmidrosis, and 3 had osmidrosis only)
Age and sex	Mean 38 years (range 20 to 52); 73% (8/11) female
Patient selection criteria	Not reported
Technique	Patients had 1 microwave treatment on each axilla.
Follow-up	**7 months**
Conflict of interest/source of funding	None

Analysis

Study design issues: The self-reported Hyperhidrosis Disease Severity Scale (HDSS) score was used to assess the degree of hyperhidrosis. Patients, family members and close friends evaluated the degree of malodour and graded it as excellent (1), good (2), fair (3) or poor (4).

Study population issues: Before treatment, 3 of the 6 patients with hyperhidrosis reported a HDSS score of 3 and 3 patients had a score of 4. Of the 8 patients with osmidrosis, 1 patient had an odour grade of 3 and the other 7 patients had an odour grade of 4.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **11**

		HDSS		Odour grade	
Patient	**Diagnosis**	**Before treatment**	**After treatment**	**Before treatment**	**After treatment**
1	Hyperhidrosis/osmidrosis	3	1	3	2
2	Hyperhidrosis/osmidrosis	3	1	4	1
3	Hyperhidrosis/osmidrosis	4	1	4	2
4	Hyperhidrosis	4	2		
5	Hyperhidrosis	3	3		
6	Hyperhidrosis	4	1		
7	Osmidrosis			4	1 (right), 3 (left)
8	Osmidrosis			4	1
9	Osmidrosis			4	1
10	Osmidrosis			4	2
11	Osmidrosis			4	1

Of the 6 patients with hyperhidrosis, 83.3% (10/12) axillae had at least a 2-point drop in HDSS at follow-up.

Histological examination of axillary skin from a patient with both hyperhidrosis and osmidrosis showed increased size and number of eccrine and apocrine glands before the procedure. Six months after treatment, no sweat glands were noted in the lower dermis and a high-power view demonstrated deep dermal fibrosis.

Safety

One patient had loss of sensation at the lateral side of both forearms. This gradually improved, and she fully recovered within 3 months.

Transient adverse effects that resolved within 10 days of treatment:

- Pain, n=2
- Tension, n=2
- Oedema, n=3
- Nodules, n=1

One patient had skin tagging in both arms, which resolved after 2 months.

One patient had hyperpigmentation, which resolved after 2 months.

Abbreviations used: HDSS, Hyperhidrosis Disease Severity Scale

Study 5 Chang YY (2015)

Details

Study type	**Case series**
Country	Taiwan
Recruitment period	Not reported
Study population and number	**n=7** Adults with axillary osmidrosis
Age and sex	Age range 22 to 53 years; 5 women, 2 men
Patient selection criteria	All patients were rated 3 or 4 on the hyperhidrosis disease severity scale (HDSS) and at least 5 on the Odor-10 scale. No patient had been treated with endoscopic thoracic sympathectomy, liposuction, or other surgery for axillary osmidrosis or hyperhidrosis. They had no botulinum toxin injection within 1 year, and had not used any topical treatment in the 14 days before the microwave treatment.
Technique	An incisional skin biopsy was taken from the left central axilla 1 month before treatment sessions began. Both axillary areas were fully treated with the miraDry system (Miramar Labs, US). Energy level 3 (the middle energy level) was used for the first treatment session. The second treatment session was done 3 months after the first session, with energy level increased to level 5. The second session also covered the entire bilateral axilla region. 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 the 30-day follow-up visit.
Follow-up	**90 days**
Conflict of interest/source of funding	None

Analysis

Study design issues: Prospective case series. For the primary endpoint, responders were defined as patients reporting a reduction of at least 3 points on a 10-point odour scale (Odor-10) at the 90-day follow-up visit. For sweat reduction, responders were defined as patients reporting a HDSS score of 1 or 2 at follow-up.

Key efficacy and safety findings

Efficacy

Number of patients analysed: **7**

All patients had 2 treatment sessions, 3 months apart.

Patient	Baseline Odor-10 (range 0 to 10)	Baseline HDSS score (range 1 to 4)	HDSS Score day 30	HDSS score day 90
1	10	3	2	1
2	8	4	2	3
3	8	4	3	2
4	6	3	1	1
5	5	3	1	1
6	9	3	1	1
7	9	3	3	1

85.7% (6/7) of patients met the primary endpoint of sweat reduction. One patient had recurrent axillary odour and hyperhidrosis at the 90 day follow-up.

85.7% (6/7) of patients met the primary endpoint of odour reduction. The mean percentage of reduction in odor-10 scale was 76.4% at 30 days and 61.8% at 90 day follow-up.

Patient satisfaction

- Very satisfied, n=4
- Satisfied, n=2
- Somewhat dissatisfied, n=1

Skin biopsy specimens revealed 93% reduction of apocrine glands. Histopathological changes included dermal fibrosis, necrosis of sweat glands, and subcutaneous fat necrosis.

Safety

Postoperative pain – median score (range 0 to 10)

Days after treatment	Energy level 3 (first treatment session)	Energy level 5 (second treatment session)
0	7	6
1	3	5
2	2	4
3	1	4
4	1	3
5	1	3
6	1	2

All patients needed to take diclofenac to relieve pain on the treatment day.

Common adverse events:

- Local erythema, n=7 (resolved in a few days)
- Bruising, n=7 (resolved in a few days)
- Local swelling (mostly resolved within 2 weeks but some patients had small lumps remaining)
- Numbness, n=4 (diminished in 1 to 3 months)
- Hypotrichosis, n=3 (still present at 90 day follow-up)

Abbreviations used: HDSS, Hyperhidrosis Disease Severity Scale

Study 6 Suh D (2014)

Details

Study type	**Case report**
Country	Korea
Recruitment period	Not reported
Study population and number	**n=1** Patient with axillary hyperhidrosis
Age and sex	32-year-old man
Patient selection criteria	Not applicable
Technique	MiraDry system (Miramar Labs, US) was used, at the lowest energy level (level 1, 2.4 seconds) in each axilla.
Follow-up	**12 months**
Conflict of interest/source of funding	None

Key safety findings

Transient median and ulnar neuropathy

After treatment, the patient noticed numbness in his left first and second fingers. He could abduct his arm up to, but not above 90°. He recovered strength in left shoulder abduction 10 days after treatment but numbness in his fingers continued.

Nerve conduction study and electromyography revealed median neuropathy with moderate partial axonotmesis and ulnar neuropathy with mild partial axonotmesis in his left arm. The patient had physiotherapy twice daily, including neuromuscular electrical stimulation for the flexor muscles in the forearm and the thenar muscles and strengthening exercise of the finger flexors. After 6 months of rehabilitation, his motor power and sensory deficit improved but the thenar muscles remained atrophic.

The authors note that the patient was thin (body mass index 18.5 kg/m^2) and assumed that the microwave energy penetrated deep enough to damage some nerve fibres of the brachial plexus. They suggest that more caution is needed when treating thin, male patients.

Study 7 FDA Manufacturer and User Facility Device Experience (MAUDE)

Details

Study type	**Database of medical device reports submitted to the FDA by mandatory reporters (manufacturers, importers and device user facilities) and voluntary reporters such as health care professionals, patients and consumers.**
Country	US
Recruitment period	Page updated: 28 February 2017; accessed 30 March 2017
Study population and number	146 reports
Age and sex	Not available for all reports
Patient selection criteria	Not applicable
Technique	Device: MiraDry (Miramar Labs, US)
Follow-up	**Not available for all reports**
Conflict of interest/source of funding	Not applicable

Analysis

- The incidence or prevalence of an event cannot be determined from this reporting system alone because of potential under-reporting of events and lack of information about frequency of device use.
- There may be some duplicate reporting.
- A causal relationship between the event and the procedure has not necessarily been established.

Key safety findings

Number of patients analysed: unknown

The following events occurred between 1/1/2012 and 30/12/2016 (n=146)

Abscess	22
Blister	5
Burn	8
Cellulitis	6
Cysts	2
Haematoma	2
Infection	30
Nerve damage or numbness	39
Nodules	3
Skin or tissue necrosis	4
Swelling	3
Ulcer	11
Other/mixed	11

Efficacy

Symptom relief

In a randomised controlled trial of 120 patients who had active or sham microwave ablation for severe primary axillary hyperhidrosis, the proportion of patients with an Hyperhidrosis Disease Severity Scale (HDSS) score of 1 or 2 (unnoticeable or tolerable sweating) was 89% (72/81) and 54% (21/39) respectively at 30 day follow-up ($p<0.001$)[1]. At 6-month follow-up, 67% and 44% of patients had an HDSS score of 1 or 2 ($p=0.02$) respectively. In the active treatment group, 69% of patients had an HDSS score of 1 or 2 at the 9- and 12-month follow-up. The proportion of patients with an HDSS score reduced by 2 or more at 30-day follow-up was 67% in the active treatment group and 13% in the sham group ($p<0.0001$). At 6-month follow-up, the proportions were 47% and 13% respectively ($p<0.001$). The proportion of patients with an HDSS score reduced by 2 or more at the 9 and 12-month follow-up were 42% and 38% respectively. In a case series of 20 patients, the mean reduction in HDSS score at a mean follow-up of 5 months was 2 (95% CI 1.85 to 2.15, $p<0.0001$); the mean HDSS score was 3.75 (±0.44) before treatment and 1.75 (±0.55) after treatment[2]. At follow-up, 95% (19/20) of patients had a HDSS score of 2 or lower. The mean percentage sweat reduction, estimated by patients, was 73% (±14.8). In a case series of 31 patients, 90% (28/31) of patients had HDSS scores of 1 or 2 at 12-month follow-up; 94% (29/31) of patients had at least a 1-point drop in HDSS and 55% (17/31) had a 2-point drop or greater[3]. In the same study, 85% (23/31) of patients had a reduction of at least 5 points on the Dermatologic Life Quality Index at 12-month follow-up[3].

Gravimetric outcomes

In the randomised controlled trial of 120 patients who had active or sham microwave ablation for severe primary axillary hyperhidrosis, the proportion of patients with a 50% or more reduction in weighed sweat compared with baseline was 80% and 67% respectively at 30-day follow-up ($p=0.07$)[1]. At 6-month follow-up, 63% and 59% of patients respectively had a 50% or greater reduction ($p=0.69$). The proportion of patients with a 75% or more reduction was 62% in the active group and 39% in the sham group ($p=0.01$) at 30-day follow-up. By 6 months, the proportions were 41% and 36% respectively ($p=0.60$). In the case series of 31 patients, 90% (28/31) of patients had at least a 50% reduction in axillary sweat from baseline[3].

Recovery time

In the case series of 20 patients, the mean time to return to complete physical activity after the last treatment was 9 days.

Patient satisfaction

In the case series of 31 patients, 90% (27/30), 96% (27/28), 93% (25/27) and 89% (23/26) of patients were very or somewhat satisfied after 30 days, 3 months, 6 months and 12 months respectively[3]. In the case series of 20 patients, patients were asked if they were satisfied and if they would have the treatment again. All patients responded that they would have the treatment again[2].

Safety

Neuropathy

Transient neuropathy of the left arm with associated muscle weakness after the procedure was reported in 1 patient in a case series of 31 patients. The prognosis from the consulting neurologist was complete resolution. The patient had improved at the 6-month follow-up, after which she was lost to follow-up[3]. Transient median and ulnar neuropathy was described in 1 patient in a case report[6]. After 6 months of rehabilitation, the patient's motor power and sensory deficit had improved but the thenar muscles remained atrophic.

Altered sensation in the skin

Altered sensation in the skin of the upper arm (change in sensitivity, tingling or numbness) was reported in 10% (8/81) of patients who had active microwave ablation (mean duration 67 days) and 3% (1/39) of patients who had a sham treatment (duration 79 days) in a randomised controlled trial (RCT) of 120 patients[1]. Temporary numbness was reported in 20% of patients in a case series of 20 patients[2]. Altered sensation in the skin of the axillae was reported in 65% of patients in a case series of 31 patients (median duration 37 days, range 4 days to 4 months)[3]. Altered sensation in the skin of the treated limb was reported in 39% (12/31) of patients in the same study (median duration 50 days, range 6 days to 12 months). Loss of sensation at the lateral side of both forearms was reported in 1 patient in a case series of 11 patients[4]. This gradually improved, and she fully recovered within 3 months.

Pain

Pain or soreness was reported in 6% (5/81) of patients in the active treatment group (mean duration 22 days, range 1 to 74) and 5% (2/39) (duration 3 and 4 days respectively) of patients in the sham treatment group, in the RCT of 120 patients[1]. Pain was reported in 65% of patients in the case series of 20 patients; this was described as mild and typically lasted 2 weeks[2]. Mild discomfort, lasting a few days to a week, was reported in 84% of patients in a case series of 31 patients[3].

Swelling

Swelling in the treated limb was reported in 5% (4/81) of patients in the active treatment group (mean duration 9 days, range 2 to 20) and 3% (1/39) of patients in the sham treatment group (2 episodes; duration 2 and 3 days respectively) in the RCT of 120 patients[1]. All but 1 of the events were rated as mild. Swelling was reported in 60% of patients in the case series of 20 patients; this was described as mild and typically lasted 2 weeks[2]. Mild oedema, lasting a few days to a week, was reported in 90% of patients in the case series of 31 patients[3]. Swelling outside the axilla, in the arm or chest was also reported in the same study (number of patients affected not reported; median duration 7 days, range 2 to 23 days).

Blisters, burns or ulcerations

Blisters, burns or ulcerations were reported in 5% (4/81) of patients in the active treatment group (mean duration 28 days, range 12 to 40) and no patients in the sham treatment group in the RCT of 120 patients[1].

Skin rash, irritation, or dermatitis

Skin rash, irritation or dermatitis was reported in 5% (4/81) of patients in the active treatment group (mean duration 27 days, range 3 to 87) and no patients in the sham treatment group in the RCT of 120 patients[1].

Axillary bumps or nodules

Axillary bumps or nodules were reported in 3% (2/81) of patients in the active treatment group (mean duration 30 days, range 8 to 52) and 3% (1/39) of patients in the sham treatment group (2 episodes; duration 10 to 12 days)[1]. Nodule formation, lasting up to 4 weeks, was reported in 25% of patients in the case series of 20 patients[2]. Palpable bumps under the skin of the axillae was reported in 71% of patients in the case series of 31 patients (median duration 41 days; still present in 2 patients at study exit)[3].

Bruising

Bruising was reported in 15% of patients in the case series of 20 patients[2].

Compensatory sweating

Compensatory sweating was reported in 3% (2/81) of patients in the active treatment group and no patients in the sham treatment group in the RCT of 120 patients[1].

Regional hair loss

Permanent regional hair loss was reported in 25% of patients in the case series of 20 patients[2]. Axillary hair loss was reported in 26% of patients in the case series of 31 patients[3].

Hyperpigmentation

Hyperpigmentation was reported in 1 patient in the case series of 11 patients[4].

Other

There are a number of reports on the FDA Manufacturer and User Facility Device Experience (MAUDE) website, describing events that have occurred after treatment with microwave ablation for axillary hyperhidrosis. These include nerve damage, infection, abscesses, ulcers, burns, cellulitis, blisters and skin or tissue necrosis[7]. It is not possible to calculate the incidence of these events because the total number of procedures is unknown.

Validity and generalisability of the studies

- There are no data from the UK.
- None of the studies have followed patients up for longer than 12 months.
- Two studies include patients with osmidrosis, with or without hyperhidrosis[4,5].
- There are a number of adverse events associated with this procedure listed on the FDA MAUDE database – the denominator for these events is unknown.
- The technology used for this procedure has evolved.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

Below is a list of NICE guidance related to this procedure. Appendix B gives details of the recommendations made in each piece of guidance listed.

Interventional procedures

- Endoscopic thoracic sympathectomy for primary hyperhidrosis of the upper limb. Interventional Procedures Guidance 487 (2014). Available from http://www.nice.org.uk/guidance/IPG487

Specialist advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and is not intended to represent the view of the society. The advice provided by Specialist Advisers, in the form of the completed questionnaires, is normally published in full on the NICE website during public consultation, except in circumstances but not limited to, where comments are considered voluminous, or publication would be unlawful or inappropriate. One Specialist Advisor Questionnaires for transcutaneous microwave ablation for severe primary axillary hyperhidrosis was submitted and can be found on the NICE website.

Patient commentators' opinions

NICE's Public Involvement Programme will send questionnaires to NHS trusts for distribution to patients who had the procedure (or their carers). When NICE has received the completed questionnaires, these will be discussed by the committee.

Company engagement

A structured information request was sent to 2 companies who manufacture or distribute a potentially relevant device for use in this procedure. NICE received 1 completed submission. This was considered by the IP team and any relevant points have been taken into consideration when preparing this overview.

Issues for consideration by IPAC

Ongoing trials:

- Microwave Energy-induced Thermolysis of Axillary Apocrine Glands and Hair Follicles Will Result in Improvement of Secondary Psychopathology Related to Hyperhidrosis (NCT02295891); single group assignment; US; estimated enrolment 24; study start date November 2014; estimated study completion date January 2019.

References

1. Glaser DA, Coleman WP III, Fan LK et al. (2012) A randomized, blinded clinical evaluation of a novel microwave device for treating axillary hyperhidrosis: the dermatologic reduction in underarm perspiration study. Dermatologic Surgery 38: 185–91
2. Scuderi S, Manoharan P, Lim D et al. (2016) A survey of patient satisfaction with use of microwave device for axillary hyperhidrosis. Australasian Journal of Dermatology doi:10.1111/ajd.12448
3. Hong HC, Lupin M, O'Shaughnessy KF (2012) Clinical evaluation of a microwave device for treating axillary hyperhidrosis. Dermatologic Surgery 38: 728–35
4. Lee SJ, Chang KY, Suh DH et al. (2013) The efficacy of a microwave device for treating axillary hyperhidrosis and osmidrosis in Asians: a preliminary study. Journal of Cosmetic and Laser Therapy 15: 255–9
5. Chang YY, Chen CH, Hui RCY et al. (2015) A prospective clinical and histologic study of axillary osmidrosis treated with the microwave-based device. Dermatologica Sinica 33: 134–41
6. Suh DH, Lee SJ, Kim K et al. (2014) Transient median and ulnar neuropathy associated with a microwave device for treating axillary hyperhidrosis. Dermatologic Surgery 40: 482–5
7. Food and Drug Administration (FDA). Manufacturer and user facility device experience (MAUDE) database. Available from: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfmaude/textResults.cfm?q=bWlyYWRyeSBoeXBlcmhpZHJvc2lz&sc=&pf=&pn=500 [accessed 30 March 2017]

Appendix A: Additional papers on transcutaneous microwave ablation for severe primary axillary hyperhidrosis

The following table outlines the studies that are considered potentially relevant to the IP overview but were not included in the main data extraction table (table 2). It is by no means an exhaustive list of potentially relevant studies.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Brown AL, Gordon J, Hill S (2014) Hyperhidrosis: review of recent advances and new therapeutic options for primary hyperhidrosis. Current Opinion in Pediatrics 26: 460–65	Review	Hyperhidrosis affects millions of people and can be a source of tremendous social and psychological stress. There are currently no data regarding the use of microwave technology for hyperhidrosis in the paediatric population.	All the included studies are already described in table 2.
Glaser DA, Galperin TA (2014) Local procedural approaches for axillary hyperhidrosis. Dermatologic Clinics 32: 533–40	Review 1 RCT on microwave ablation	Surgical treatments are effective at reducing excessive sweating, but need time for recovery after the procedure are operator dependent and can have poor cosmetic outcomes. Treatment with microwave thermolysis is effective, minimally invasive, needs limited downtime, and has good cosmetic outcomes.	The single RCT on microwave ablation is already included in table 2.
Mordon SR, Trelles MA, Leclere M et al. (2014) New treatment techniques for axillary hyperhidrosis. Journal of Cosmetic and Laser Therapy 16: 230–35	Review 2 studies on microwave ablation (1 RCT and 1 abstract)	Techniques have recently appeared that make use of energy sources, in particular microwave devices and light. The aim is to obtain very long-lasting efficacy without notable side effects. The only microwave device available on the market is certainly interesting.	The single RCT on microwave ablation is already included in table 2.
Nasr M, Jabbour SF, Haber RN et al. (2017) Comparison of microwave ablation, botulinum toxin injection, and liposuction-curettage in the treatment of axillary hyperhidrosis: a systematic review. Journal of Cosmetic and Laser Therapy 19: 36–42	Systematic review 1 study on microwave ablation	All 3 treatments are safe and efficient minimally invasive alternatives for the treatment of axillary hyperhidrosis. Well-designed randomised controlled trials are needed to further compare the efficacy of these techniques.	Only 1 study on microwave ablation was included, which is already described in table 2 (Hong et al., 2012).
Singh S, Davis H, Wilson P. (2015) Axillary hyperhidrosis: a review of the extent of the problem and treatment modalities. The Surgeon 13: 279–85	Review 2 studies on microwave ablation	Further studies are needed to determine the efficacy of this treatment.	The included studies are already described in table 2.

Appendix B: Related NICE guidance for transcutaneous microwave ablation for severe primary axillary hyperhidrosis

Guidance	Recommendations
Interventional procedures	**Endoscopic thoracic sympathectomy for primary hyperhidrosis of the upper limb. NICE interventional procedure guidance 487 (2014).** 1.1 Current evidence on the efficacy and safety of endoscopic thoracic sympathectomy (ETS) for primary hyperhidrosis of the upper limb is adequate to support the use of this procedure with normal arrangements for clinical governance, consent and audit. 1.2 Clinicians wishing to undertake ETS for primary hyperhidrosis of the upper limb should ensure that patients understand the risks of the procedure. In particular they must explain that: • there is a risk of serious complications • hyperhidrosis elsewhere on the body is usual after the procedure: this can be severe and distressing and some patients regret having had the procedure (especially because of subsequent and persistent hyperhidrosis elsewhere) • the procedure sometimes does not reduce upper limb hyperhidrosis. Clinicians should also provide patients considering the procedure with clear written information. 1.3 In view of the risk of side effects this procedure should only be considered in patients suffering from severe and debilitating primary hyperhidrosis that has been refractory to other treatments. 1.4 This procedure should only be undertaken by clinicians trained and experienced in thoracic endoscopy, and there should be the capacity to deal with intraoperative complications. 1.5 Further research into ETS for primary hyperhidrosis of the upper limb should include clear information on patient selection and should seek to identify which patient characteristics might predict severe side effects. All complications should be reported. Outcomes should include measurements of efficacy, including quality of life and social functioning both in the short and long term and in particular the frequency and severity of compensatory hyperhidrosis.

Appendix C: Literature search for transcutaneous microwave ablation for severe primary axillary hyperhidrosis

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane)	12/12/2016	Issue 12 of 12, December 2016
HTA database (Cochrane)	12/12/2016	Issue 4 of 4, October 2016
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane)	12/12/2016	Issue 11 of 12, November 2016
MEDLINE (Ovid)	12/12/2016	1946 to November Week 5 2016
MEDLINE In-Process (Ovid)	12/12/2016	December 09, 2016
EMBASE (Ovid)	12/12/2016	1974 to 2016 Week 50
PubMed	12/12/2016	n/a
BLIC (British Library)	12/12/2016	n/a

Trial sources searched on 10/11/2016

- Clinicaltrials.gov
- ISRCTN
- WHO International Clinical Trials Registry

Websites searched on 10/11/2016

- National Institute for Health and Care Excellence (NICE)
- NHS England
- Food and Drug Administration (FDA) - MAUDE database
- Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP – S)
- Australia and New Zealand Horizon Scanning Network (ANZHSN)
- EuroScan
- General internet search

The following search strategy was used to identify papers in MEDLINE. A similar strategy was used to identify papers in other databases.

1	hyperhidrosis/
2	sweating/
3	eccrine glands/ or apocrine glands/ or sweat glands/
4	(hyperhidros* or hidrosis*).ti,ab.
5	((increas* or excess* or primary* or focal* or local*) adj4 (sweat* or perspir*)).ti,ab.
6	((eccrine* or apocrine* or sweat* or axilla*) adj4 gland*).ti,ab.

7	axilla/
8	((axilla* or underarm* or armpit* or arm pit*) adj4 (sweat* or perspir*)).ti,ab.
9	or/1-8
10	Ablation Techniques/
11	microwaves/
12	((microwave* or micro-wave*) adj4 (ablat* or coagulat* or therap* or thermotherap* or thermoablat*)).ti,ab.
13	(miradry or miramar).ti,ab.
14	or/10-13
15	9 and 14
16	animals/ not humans/
17	15 not 16