

Management of Palmar Hyperhidrosis With Hydrogel-based Iontophoresis  
NCT02854540  
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## STUDY PROTOCOL

Subjects will be recruited from referrals by Dermatologists at Stanford Hospital and clinics, via self-referrals from recruitment flyers and from the Stanford Dermatology Clinics Stanford Hospital and clinics hyperhidrosis patient population. Patients will be screened for eligibility either in person during a routine clinical visit or over the phone.

The study will consist of 3 treatment phases (daily treatment for 2 weeks, 3x/week treatment for 3 weeks and 2x/week treatment for 3 weeks) and a post-treatment evaluation.

During the daily treatment phase, the subject will perform sweat level assessments and deliver treatment during office visits (1 in person and 1 virtual in this phase) and daily at home. The sweat level assessments will include gravimetry (in-office), visual assessment, iodine imprint testing (at home and in-office), and a study diary (at home and in-office), all commonly used methods to assess sweat levels for research purposes. Treatment will consist of 30 -60 minutes of hydrogel-based iontophoresis. During the three-time per week and two-time per week phases, the patients will undergo the allocated amount of treatments per week, perform iodine imprints at home and complete a study diary. There will be one office visit at the start of the 3x/week phase. The post-treatment evaluation will take place as an office visit.

The first visit will be used to explain the study protocol, obtain informed consent, assess disease severity with baseline sweat level assessments, determine treatment settings, and provide training on performing the treatment and a study diary at home. Sweat level assessment will be obtained using gravimetry (quantitative measurement of sweat production by weight over a specified time period), iodine imprint testing (topical application of an iodine solution to qualitatively visualize sweat production after making an imprint on paper), and completion of a study diary. Study diary entries consist of a hyperhidrosis disease severity scale (HDSS) score (modified to reflect the severity of symptoms over a single day, visual pain assessment (Wong-Baker pain scale), and a prompt to specify general comments or any side effects related to the treatment. Treatment will consist of delivering a low level of direct electrical current to the palmar side of one hand.

In line with standard tap water iontophoresis, amperage will be increased manually by the patient until the tingling induced by the current is at the upper limit of comfort. The current level will not be increased beyond 20 mA regardless of patient's tolerance. The treatment may not be effective below a minimal therapeutic level (R.A. Fischer MD-2 manual). Therefore, if the subject finds low levels of current intolerable (e.g. below 6ma), the investigators may decide to exclude the subject from the study. The treatment duration will be up to 1 hour, consistent with

what commercial devices are able to sustain (Hidrex DVP1000 user manual).

During the various treatment phases, the subject will be asked to perform the following tasks independently at home: deliver treatments daily, triweekly or biweekly for a period of 2-3 weeks each, complete a daily questionnaire/study diary, and perform iodine imprint testing at least twice per week. Data will be collected through a REDCap survey. The patient will also be asked to photograph and store the paper imprints in a dedicated folder.

A second contact point will be scheduled virtually within 2-4 days of the first visit to ensure that the subject is correctly performing the treatment, and to provide any additional training needed.

After the end of the daily treatment phase (day 14, 15, 16 or 17), the subject will return to the office to perform treatment, complete gravimetry and iodine imprint sweat level assessments.

The subject then enters treatment phases with decreased treatment frequency to 3x/week for 3 weeks and 2x/week for 3 weeks. They will return to the office for a final evaluation visit and study wrap-up (day 56, 57, 58 or 59).

#### STATISTICAL ANALYSIS PLAN

We will be assessing the difference in sweat levels between the hands using gravimetry, iodine imprint testing, and symptom questionnaires. Gravimetry is commonly used in research settings to quantify sweat levels. Filter paper is weighed before and after application to the palmar surface of the hand for a fixed duration in time, e.g. 5 minutes. The weight difference quantifies the amount of sweat produced over a period of time (in mg/min). We will follow up changes in sweat levels based on data uploaded through REDCap. After the study the Student's t-test will be used to assess sweat levels between the treated and untreated hands.

Iodine paper imprint testing is a documented method to qualitatively assess sweat levels. The hands are cleaned and dried prior to application of iodine solution to the palmar sides of the hands. After the iodine solution has dried, subjects will apply steady pressure with their palms onto a sheet of paper. Sweat in contact with iodine and starch will produce a colorimetric change, with a purple-black color on the paper indicating the presence of sweat on the hands. The subject will take a photograph of this paper as a baseline qualitative measure of sweating and upload this onto the REDCap system through the survey diary. We will follow up changes in sweat levels on a daily basis based on data

uploaded through REDCap. Differences in iodine imprint testing results between the left and right hand, and changes over the course of the study, will be assessed visually by a member of the research staff. After the study we will try to quantify the difference in sweat levels between the hands using image analysis software (e.g. ImageJ).

Subjects will complete a survey diary with questions based on the Hyperhidrosis Disease Severity Scale (HDSS), a sweat assessment that is commonly used in hyperhidrosis studies. Modifications that we have made to the HDSS include distinguishing symptom severity of each hand and assessing overall symptom severity on a single day. Study diary responses will be reviewed by a member of the research staff on a daily basis