



[\[reviewer notes~\]](#)

Provide a short title for this study (200 characters or less):

Foot Neuromodulation for Nocturnal Enuresis in Children

T1.0

Select the type of application:

New Research Study

T2.0

Is the proposed research study limited to the inclusion of deceased individuals?

* No

T2.1

Are any research activities being conducted at the VA Pittsburgh Healthcare System or with VA funds?

* No

[\[reviewer notes~\]](#)

T3.0

What is the anticipated risk to the research participants?

Minimal Risk

T3.1

Why do you feel that all aspects of this research study, including screening and follow-up, involve no more than minimal risk to the research subjects?

Trans-cutaneous Electrical Nerve Stimulation (TENS) devices are FDA approved and commercially available to treat a variety of clinical conditions including pain (migraines, musculoskeletal pain and labor pain). The only reported side-effects are local irritation from electrode pads and minor cramping of stimulated muscles. Many studies have evaluated the use of TENS devices for parasacral neuromodulation in children with no serious adverse events reported.

The voltage used for the TENS device will be only as high as is required to stimulate an involuntary muscle contraction of at least two toes. In various trials in adults this voltage very rarely corresponds to any actual discomfort to the patient. If during the trial stimulation at the time of enrollment in the office, the child demonstrates an intolerance to this stimulation due to discomfort, he/she will be excluded from the study.

T4.0

Does the proposed study qualify for 'exempt' IRB review or for a determination of either 'not research' or 'no human subject' involvement?

* No

T5.0

Does the proposed research study qualify for 'expedited' IRB review status?

* No

[\[reviewer notes~\]](#)**CS1.0 What is the reason for this submission?**

New Research Protocol Submission

CS1.1 Has this research study been approved previously by the University of Pittsburgh IRB?

* No

CS1.1.1 Has this research study (or a substantially similar research study) been previously disapproved by the University of Pittsburgh IRB or, to your knowledge, by any other IRB?

* No

[\[reviewer notes~\]](#)**CS2.0 Title of Research Study:****Foot Neuromodulation for Nocturnal Enuresis in Children****CS2.0.1****Requested approval letter wording:****CS2.1 Research Protocol Abstract:**

Background: Previous animal model studies at the University of Pittsburgh have shown a significant impact on inhibiting bladder overactivity and increasing bladder capacity with neuromodulation techniques, specifically tibial nerve stimulation. This has been translated into adult clinical trials through the department of urology. Through the use of a commercially available subcutaneous nerve stimulator placed on the dorsum of the foot, we were able to demonstrate a significant increase in bladder capacity and the delay of voiding sensation for up to 5 hours after stimulation in eight healthy subjects. This prompted the clinical trial approved under IRB PRO13020474 which is currently enrolling patients.

The incidence of night-time overactive bladder leading to nocturnal enuresis (bedwetting) is very common in the pediatric and teenage population, particularly in patients without daytime bladder overactivity symptoms. When behavioral modification (i.e. refraining from night-time fluid consumption and bladder irritants, and bedwetting alarms for timed voiding) fails which it often does there is a paucity of effective and safe treatment options. Medications can be tried, but generally these are from the tricyclic antidepressant family and carry significant side effects limiting their use.

Aim: We aim to utilize the same technology currently being studied under IRB PRO13020474 for pediatric patients with nocturnal enuresis, taking advantage of the possible increase in bladder capacity and inhibited bladder activity to potentially help children stay dry at night. Electrical stimulation will be applied to the foot via skin surface electrodes for a minimum of 1

hour before bed for 2 weeks to 25 subjects. Subjects will be required to keep a daily log indicating the number of night-time incontinent voids. Subjects will also be asked to complete a validated questionnaire prior to treatment, during the two week treatment phase and two weeks after treatment. The primary outcomes of this study are improvement in the average number of night-time incontinent voids measured by daily log and subjective symptom improvement based on questionnaire comparison at the three phases of the study. Subjects who feel they are having a positive response to TENS treatment and would like to continue participation in the study for an additional 6 weeks may do so.

CS2.2 Select the category that best describes your research:

[\[reviewer notes~\]](#)

CS3.0 Name of the Principal Investigator:

[Heidi Stephany](#)

Note: Adjunct faculty of the University, including lecturers and instructors, are not permitted to serve as a PI or Faculty Mentor but may serve as co-investigators. Refer to [Chapter 4](#) on the HRPO website for more information.

CS3.1 Affiliation of Principal Investigator:

UPitt faculty member

If you chose any of the **Pitt options**, please indicate the specific campus:

[Main Campus - Pittsburgh](#)

If you chose the UPitt faculty member option, provide the PI's **University Faculty Title:**
Assistant Professor

CS3.2 Address of Principal Investigator:

One Children's Hospital Drive
4401 Penn Avenue
4th Floor Faculty Pavilion
Pittsburgh, Pa 15224

CS3.3 Recorded Primary Affiliation of the Principal Investigator:

U of Pgh | School of Medicine | Urology

CS3.4 Identify the School, Department, Division or Center which is responsible for oversight of this research study:

[U of Pgh | School of Medicine | Urology](#)

CS3.5 Telephone Number of Principal Investigator:

412-692-7984

CS3.6 Recorded Current E-mail Address of Principal Investigator to which all notifications will be sent:

heidi.stephany@chp.edu

CS3.7 Fax Number:

412-692-8614

CS3.8 Does this study include any personnel from Carnegie Mellon University, and/or use any CMU resources or facilities (e.g., Scientific Imaging and Brain Research Center (SIBR))?

* No

CS3.9 Is this your first submission, as PI, to the Pitt IRB?

* No

[\[reviewer notes~\]](#)

CS4.0 List of Co-Investigators:

Last	First	Organization
Cannon	Glenn	U of Pgh School of Medicine Urology
Chermansky	Christopher	U of Pgh School of Medicine Urology
Dwyer	Moir	U of Pgh School of Medicine Urology
Ferroni	Matthew	U of Pgh School of Medicine Urology
Ost	Michael	U of Pgh School of Medicine Urology
Reese	Jeremy	UPMC Hospital Divisions Presbyterian/Shadyside
Schneck	Francis	U of Pgh School of Medicine Urology
Tai	Changfeng	U of Pgh School of Medicine Urology

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CS5.0 Name of Primary Research Coordinator:

[Matthew Ferroni](#)

CS5.1 Address of Primary Research Coordinator:

One Children's Hospital Drive
4401 Penn Avenue
4th Floor Faculty Pavilion
Pittsburgh, Pa 15224

CS5.2 Telephone Number of Primary Research Coordinator:

617-270-3676

CS6.0 Name of Secondary Research Coordinator:

Jennifer Szczepaniak

CS6.1 Address of Secondary Research Coordinator:

4401 Penn Avenue
Pittsburgh, PA 15224

CS6.2 Telephone Number of Secondary Research Coordinator:

412-692-6203

CS6.3 Key Personnel/Support Staff (Only list those individuals who require access to OSIRIS):

Last	First	Organization
Chermansky	Christopher	U of Pgh School of Medicine Urology
Ferroni	Matthew	U of Pgh School of Medicine Urology
Reese	Jeremy	UPMC Hospital Divisions Presbyterian/Shadyside
Stephany	Heidi	U of Pgh School of Medicine Urology
Tai	Changfeng	U of Pgh School of Medicine Urology

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CS7.0 Will this research study use any [Pediatric PittNet](#) or Clinical and Translational Research Center (CTRC) resources?

No

[\[reviewer notes~\]](#)

CS8.0 Select the entity responsible for scientific review.

Department Review - (a dean, department chair, division chief, or center head)

Note: **DoD funded studies** require departmental review

CS8.1 Select the school, department or division which is responsible for scientific review of this submission.

[U of Pgh | School of Medicine | Urology](#)

[\[reviewer notes~\]](#)

CS9.0 Does this research study involve the administration of an investigational drug or an FDA-approved drug that will be used for research purposes?

* No

CS10.0 Is this research study being conducted under a University of Pittsburgh-based, sponsor-investigator IND or IDE application?

* No

If YES, you are required to submit the IND or IDE application and all subsequent FDA correspondence through the Office for Investigator-Sponsored IND and IDE Support

(O3IS). Refer to applicable University policies posted on the O3IS website (www.O3IS.pitt.edu).

[\[reviewer notes-\]](#)

CS11.0 Use the 'Add' button to upload one or more of the following:

- the sponsor protocol (including investigator initiated studies) and/or other brochures
- the multi-center protocol and consent form template, *if applicable*

Name Modified Date

Is this research study supported in whole or in part by industry? This includes the provision of products (drugs or devices).

* No

Is this a multi-centered study?

* No

[\[reviewer notes-\]](#)

CS12.0 Does your research protocol involve the evaluation or use of procedures that emit ionizing radiation?

* No

CS13.0 Does this research study involve the deliberate transfer of recombinant or synthetic nucleic acid molecules into human subjects?

* No

Upload Appendix M of NIH Guidelines:

Name Modified Date

CS14.0 Are you using UPMC facilities and/or UPMC patients during the conduct of your research study?

* Yes

If Yes, upload completed Research Fiscal Review Form:

Name Modified Date

[Fiscal Review](#) 8/26/2014 8:24 AM

[\[reviewer notes-\]](#)

CS15.0 Indicate the sites where research activities will be performed and/or private information will be obtained.

Choose all sites that apply and/or use **Other** to include sites not listed:

Sites:

UPMC

UPMC

Sites:

UPMC Children's Hospital

If you selected **School**, **International** or **Other**, list the sites:

***For research being conducted at non Pitt or UPMC sites, upload a site permission letter granting the researcher permission to conduct their research at each external site:**

Name Modified Date

CS15.1 Have you, Heidi Stephany, verified that all members of the research team have the appropriate expertise, credentials, and if applicable, hospital privileges to perform those research procedures that are their responsibility as outlined in the IRB protocol?

* Yes

CS15.2 Describe the availability of resources and the adequacy of the facilities to conduct this study:

* We have previously been awarded a \$25,000 grant from the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction (SUFU) which we will use for the purchase of equipment (neuromodulators and subcutaneous foot pads). Subjects will be enrolled in the urology outpatient clinics at the Children's Hospital of Pittsburgh. We anticipate have adequate resources to enroll subjects and perform all necessary study tasks.

[\[reviewer notes~\]](#)

CS16.0 Special Research Subject Populations:

Categories

Children (age < 18 years old)

[\[reviewer notes~\]](#)

CS17.0 Does your research involve the experimental use of any type of human stem cell?

* No

[\[reviewer notes~\]](#)

NIH Definition of a Clinical Trial

A research study¹ in which one or more human subjects² are prospectively assigned³ to one or more interventions⁴ (which may include placebo or other control) to evaluate the effects of those interventions on health related biomedical or behavioral outcomes.⁵

¹ See Common Rule definition of research at [45 CFR 46.102\(d\)](#) .

² See Common Rule definition of human subject at [45 CFR 46.102\(f\)](#) .

³ The term “prospectively assigned” refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.

⁴ An intervention is defined as a manipulation of the subject or subject’s environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.

⁵ Health-related biomedical or behavioral outcome is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects’ biomedical or behavioral status or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.

CS18.0 * Based on the above information, does this study meet the NIH definition of a clinical trial?

☐ Yes ☐ No

If Yes, click Save and then [Click Here For Study Team's CITI Training Records](#) . Please ensure all personnel's training is up to date

[\[reviewer notes~\]](#)

- 1.1 Objective: What is the overall purpose of this research study?** (Limit response to 1-2 sentences.)
To determine the effects of electrical stimulation of the nerves in the foot on the incidence of nocturnal enuresis (bedwetting) in children.
- 1.2 Specific Aims: List the goals of the proposed study (e.g., describe the relevant hypotheses or the specific problems or issues that will be addressed by the study).**
Aim #1: To determine if foot stimulation can decrease nocturnal enuresis in children as measured by daily night-time voiding log.

Aim #2: To determine if foot stimulation can improve quality of life questionnaire scores during a 6-week period, with foot stimulation applied during the third and fourth week, as measured by a validated quality of life survey.

Aim # 3: Subjects who feel they are having a positive response to TENS treatment and would like to continue participation in the study for an additional 6 weeks may do so. By collecting this data for an extended period of time we hope to prove long-term efficacy and sustainability in symptom relief, and to ensure no unanticipated adverse outcomes with continued usage
- 1.3 Background: Briefly describe previous findings or observations that provide the background leading to this proposal.**
Previous animal model studies at the University of Pittsburgh have shown a significant impact on inhibiting bladder overactivity and increasing bladder capacity with neuromodulation techniques, specifically tibial nerve stimulation (Tai et al, 2011). This has been translated into adult clinical trials through the department of urology. Through the use of a commercially available subcutaneous nerve stimulator placed on the dorsum of the foot, we were able to demonstrate a significant increase in bladder capacity and the delay of voiding sensation for up to 5 hours after stimulation in eight healthy subjects (Chen et al, 2014). This prompted the clinical trial approved under IRB PRO13020474 which is currently enrolling patients.

The incidence of night-time overactive bladder leading to nocturnal enuresis (bedwetting) is very common in the pediatric and teenage population, particularly in patients without daytime bladder overactivity symptoms. When behavioral modification (i.e. refraining from night-time fluid consumption and bladder irritants, and bedwetting alarms for timed voiding) fails which it often does there is a paucity of effective and safe treatment options. Medications can be tried, but generally these are from the tricyclic antidepressant family and carry significant side effects limiting their use.

Various clinical trials abroad have studied the impact of transcutaneous parasacral nerve stimulation as well as percutaneous tibial nerve stimulation for overactive bladder in children with promising results (Sillen et al, 2014; Barroso et al, 2013; DeGannaro et al 2011; Loredelo et al 2010; Malm-Buatsi et al 2007). These studies have shown good efficacy and child tolerability with nerve stimulation in a more invasive approach then we are attempting with transcutaneous foot stimulation.
- 1.4 Significance: Why is it important that this research be conducted? What gaps in existing information or knowledge is this research intended to fill?**
Nocturnal Enuresis is a very common and difficult to treat problem in the pediatric population which can have significant negative impact on a child's quality of life. Apart from medications which can have significant side effects limiting their use, there is a lack of effective and safe treatment options for children with frequent nocturnal enuresis. If foot

stimulation prior to bed does indeed improve the frequency of nocturnal enuresis, it may provide a safe and non-invasive therapeutic option.

For subjects the would like to continue participation in the study for an additional 6 weeks, we would like to explore how durable of a response we can achieve with a longer stimulation period

[\[reviewer notes→\]](#)

2.1 Does this research study involve the use or evaluation of a drug, biological, or nutritional (e.g., herbal or dietary) supplement?

* No

[\[reviewer notes→\]](#)

2.2 Will this research use or evaluate the safety and/or effectiveness of one or more devices?

* Yes

2.2.1 Does this research study involve an evaluation of the safety and/or effectiveness of one or more devices not currently approved by the FDA for general marketing?

* No

[\[reviewer notes→\]](#)

2.2.2 Does this research study involve the use or evaluation of the safety and/or effectiveness of one or more devices approved by the FDA for general marketing?

* Yes

2.2.2.1 Does this research study involve an evaluation of one or more FDA-approved devices for a clinical indication, subject population, and/or operational parameter that is not specified in the current FDA-approved product labeling for that device (i.e., for an "off-label" indication)?

* Yes

2.2.2.1.1 List each of the devices being evaluated for an "off-label" indication. Specify for each listed device the corresponding Investigational Device Exemption (IDE) number for this device/research study; or provide a justification for why you feel that this device and its "off-label" use, as proposed in this research study (i.e., to include potential failure of the device) constitute a non-significant risk to the involved research subjects.

*

Device	IDE #	Non-significant risk justification
View TRANSCUTANEOUS ELECTRICAL NERVE STIMULATOR (TENS)		The TRANSCUTANEOUS ELECTRICAL NERVE STIMULATOR (TENS) is a battery powered stimulator that is commercially available and FDA-approved for individual use at home to stimulate muscles/nerves. 1. It is not an implant. 2. It is not used in supporting or sustaining human life. 3. It does not aid in diagnosing, curing, mitigating, or treating disease. 4. It does not present a potential for serious risk to the health, safety, or welfare of a subject. TENS will be used in this study to deliver electrical stimulation via adhesive pad electrodes attached to the skin surface of the foot. The proposed use parallels the safety parameters of TENS already approved by the FDA. The investigators, Drs. Tai, Reese, and Ferroni, have many years of experience with electrical stimulation and neurophysiology. They are qualified in using the TENS stimulator correctly. Furthermore, the FDA approves of TENS use at home for muscle/back pain and neuropathy. Therefore, we believe this is a non-significant risk device.

[\[reviewer notes→\]](#)

2.3 Summarize the general classification (e.g., descriptive, experimental) and methodological design (e.g., observational, cross-sectional, longitudinal, randomized, open-label single-blind, double-blind, placebo-controlled, active treatment controlled, parallel arm, cross-over arm) of the proposed research study, as applicable.

This is an experimental, open-label study. Both the subject and the investigator will be informed about the foot stimulation. The results obtained before and after the treatment will be compared in the same subject.

2.3.1 Does this research study involve a placebo-controlled arm?

* No

[\[reviewer notes→\]](#)

2.4 Will any research subjects be withdrawn from known effective therapy for the purpose of participating in this research study?

* No

[\[reviewer notes→\]](#)

2.5 Will screening procedures (i.e., procedures to determine research subject eligibility) be performed specifically for the purpose of this research study?

* Yes

2.5.1 List the **screening procedures that will be performed for the purpose of this research study. Do NOT include the inclusion/exclusion criteria in this section as they will be addressed in section 3; questions 3.13 and 3.14.**

The screening procedure only includes a review of patient's medical records and performing an office based urinalysis to rule out concern for urinary tract infection. No other procedures will be performed. Patient's medical record has all the information we need to determine the idiopathic nocturnal enuresis condition. A urinalysis is normally done as part of standard of care for all office visits. The standard office visit questions, which is also available in the medical record and includes questions about neurological disorders, spinal cord injuries, and so forth will be used to rule out those who may have a neurological reason for nocturnal enuresis. Drs. Stephany, Ost, Schneck, and Cannon who have clinical responsibilities to the patient will review the medical records for eligibility. We also request a waiver of consent for this review on section 4.7.

[reviewer notes~]

2.6 Provide a detailed description of all research activities (e.g., all drugs or devices; psychosocial interventions or measures) that will be performed for the purpose of this research study.

This description of activities should be complete and of sufficient detail to permit an assessment of associated risks.

At a minimum the description should include:

- **all research activities**
- **personnel (by role) performing the procedures**
- **location of procedures**
- **duration of procedures**
- **timeline of study procedures**

Night-time voiding log:

The subject/parents will be instructed to record a night-time voiding log specifying the number of incontinent episodes per night. This log is included in the IRB application. Subjects/parents will fill out the log for a two week period prior to foot stimulation to determine a baseline average of nocturnal enuresis episodes, during the two week foot stimulation period to measure any acute effect on nocturnal enuresis episodes and finally during the two weeks after stimulation to evaluate any post-stimulation residual benefit.

Neuromodulation:

In the office to calibrate TENS device - skin surface electrodes will be attached to the bottom of one foot for electrical stimulation. The stimulator and electrodes are FDA-approved devices for TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) and are commercially available. The stimulation characteristics include a continuous frequency of 5 Hz, pulsewidth 0.2 ms, and intensity 2-4 times the threshold voltage required for inducing

toe twitching - or the intensity that the subject feels comfortable with. The subjects will also be instructed how to use the stimulator and where to attach the electrodes on the foot at the beginning of the study. The investigator will provide the stimulator and electrodes. The subjects will be asked to wear socks to prevent the electrodes from detachment and to stop the stimulation during walking or in any non-resting situation. Subjects will be provided a TENS device and disposable foot pads for two weeks of treatment. Subjects will be asked to use the stimulator for a MINIMUM of 60 minutes in the evening prior to bedtime at home for two weeks. They will be encouraged to use the stimulator for more time than the minimum as long as they accurately record the total duration. Stimulation will be performed during the second and third weeks of the study only.

TENS Unit Training:

The training session will take place in a patient room in the office of pediatric urology. The training will be conducted in person by Dr. Stephany with the parent(s) and child in the room. Dr. Stephany will explain the device, how it works and how to use it to the parent(s) along with a detailed user manual that is provided with the stimulator. The parent(s) will be instructed how to place the stimulation pads on the child's foot (most distal covering the planar bridge of the foot and more proximal pad over the medial edge of the foot). The parent(s) will then be instructed on how to connect the two electrode wires to the device and turn it on. The device settings are preprogrammed at time of sale, so no frequency change adjustments need to be made. The parent(s) will incrementally increase the voltage on the device until the child elicits a response of involuntary contraction of at least two toes of the foot including the great toe. Stimulation will be continuous for 5 minutes assessing the child's comfort level. If the child is obviously uncomfortable at the level of voltage required for involuntary motor movement and does not perceive they would be able to stimulate in this fashion at home for periods of up to one hour, they will not be eligible for the study.

Questionnaire:

Subjects will complete the quality of life questionnaire attached to this application at the start of the study (prior to week 1) to establish a baseline, after the second week of treatment period (week 4 of study) to determine a treatment effect, and after the sixth week to determine any residual post-treatment effect.

The subjects can call or email the investigators anytime during the 6-week at-home test for questions or any problems encountered. At the end of the 6-week study, the subjects are asked to return the stimulator and night-time voiding log to the investigator's office.

Subjects who feel they are having a positive response to TENS treatment and would like to continue participation in the study for an additional 6 weeks may do so. We will ask that they continue to keep their logs and answer the questionnaires

2.6.1 Will blood samples be obtained as part of this research study?

* No

*If submitting a protocol for expedited review, it should be clear that the planned blood draws are within the parameters described here: <http://www.hhs.gov/ohrp/policy/expedited98.html> (see Expedited Research Category #2)

If **Yes**, address the frequency, volume per withdrawal, the total volume per visit, and the qualifications of the individual performing the procedure:

Study Flow Chart:

Name	Modified Date
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[\[reviewer notes~\]](#)

- 2.7 Will follow-up procedures be performed specifically for research purposes? Follow-up procedures may include phone calls, interviews, biomedical tests or other monitoring procedures.**

* No

[\[reviewer notes~\]](#)

- 2.8 Does this research study involve the use of any questionnaires, interview or survey instruments?**

* Yes

Upload a copy of all materials except for the SCID or KSADS which are on file at the IRB. The use of all instruments must be addressed in question 2.6 and/or question 2.7 (except for an exempt submission where they should be addressed on the appropriate uploaded exempt form).

Name	Modified Date
Quality of Life Survey	8/12/2014 8:56 PM
Night-time Voiding Log	8/12/2014 8:53 PM

Previously the name and publisher for commercially available materials were listed in the textbox below but effective 9/1/2015, all materials (except for the SCID and KSADS) must be uploaded using the Add button above.

[\[reviewer notes~\]](#)

- 2.9 If subjects are also patients, will any clinical procedures that are being used for their conventional medical care also be used for research purposes?**

* yes

If **Yes**, describe the clinical procedures (and, if applicable, their frequency) that will be used for research purposes:

We will not perform a urinalysis specifically for this research project. However, the result of urinalysis as part of standard clinical care will be reviewed in the medical record and used to screen the patients for eligibility.

2.10 The blood sample question was moved to 2.6.1.

[\[reviewer notes→\]](#)

2.11 What is the total duration of the subject's participation in this research study across all visits, including follow-up surveillance?

* 6 to 12 weeks

[\[reviewer notes→\]](#)

2.12 Does this research study involve any type of planned deception?

If Yes, you are required to request an alteration of the informed consent process (question 4.7)

* No

[\[reviewer notes→\]](#)

2.13 Does this research study involve the use of UPMC/Pitt protected health information that will be de-identified by an IRB approved "honest broker" system?

* No

[\[reviewer notes→\]](#)

2.14 Will protected health information from a UPMC/Pitt HIPAA covered entity be accessed for research purposes or will research data be placed in the UPMC/Pitt medical record?

* Yes

If you answer **Yes**, you are required to submit this study to the Center for Assistance in Research using e-Record (CARE). Per UPMC Policy HS-RS0005, all research projects that access or involve UPMC electronic protected health information (e-PHI) must be submitted to CARE, with the exception of clinical trials that are contracted through the UPMC Office of Sponsored Programs and Research Support (OSPARS).

Complete the online submission form at <https://care.upmc.com/request.aspx>. After the study is submitted in OSIRIS, a CARE representative will conduct a review. You will be notified once your

CARE review is complete or if anything further is needed.

Studies that will access only paper-based medical records (not in combination with any electronic records) do not need to be submitted to CARE.

For additional information, please see <https://care.upmc.com>.

Describe the medical record information that will be collected from the UPMC/Pitt HIPAA covered entity and/or the research-derived information that will be placed in the medical records.

Medical records will be accessed for screening the patients for eligibility and information concerning the child's diagnosis, age, past medical history, and diagnostic procedures that were already done as part of their standard medical evaluations will be retained for this study. A urinalysis is normally done as part of standard of care and will be checked in the medical record for evidence of urinary tract infection. The standard office visit questions, which is also available in the medical record and includes questions about prior neurological disorders, spinal cord injuries, and so forth, will be reviewed to rule out those who may have a neurological reason for nocturnal enuresis. No research data will be placed in the medical record.

2.14.1 Will protected health information from a non-UPMC/Pitt HIPAA covered entity be obtained for research purposes or will research data be placed in the non-UPMC/Pitt medical record?

* No

I, Heidi Stephany, certify that any member of my research team accessing, reviewing and/or recording information from medical records have completed the CITI Privacy & Information Security course or, if completed within the past year, the Internet-Based Studies in Education and Research (ISER) HIPAA for Researchers (Formerly RPF Module 6). The HIPAA certificates must be available for review if audited but do not need to be uploaded into this OSIRIS application.

* Yes

2.14.2 Are you requesting a waiver of the requirement to obtain written HIPAA authorization for the collection of the PHI?

* No

[\[reviewer notes~\]](#)

2.15 Does this research study involve the long-term storage (banking) of biological specimens?

* No

[\[reviewer notes~\]](#)

2.16 Will research participants be asked to provide information about their family members or acquaintances?

* No

[\[reviewer notes~\]](#)

2.17 What are the main outcome variables that will be evaluated in this study?

1) Number of night-time incontinent episodes per two week period comparing baseline number of voids (first two weeks of study), number during two-week stimulation period (weeks 3-4), and number during two-week after-stimulation period (weeks 5-6).

2) Subjective quality of life measures as recorded by validated quality of life questionnaire prior to study start, after week 4 and after week 6 to evaluate for any differences.

3) For the subjects who continue participation for an additional 6 weeks, we hope to prove long-term efficacy and sustainability in symptom relief, and to ensure no unanticipated adverse outcomes with continued usage

2.18 Describe the statistical approaches that will be used to analyze the study data.

* Addressed below:

The data will be statistically analyzed using student t-test and ANOVA

[\[reviewer notes~\]](#)

2.19 Will this research be conducted in (a) a foreign country and/or (b) at a site (e.g., Navajo Nation) where the cultural background of the subject population differs substantially from that of Pittsburgh and its surrounding communities?

* No

Note that copies of training records, licenses, certificates should be maintained in the study regulatory binder and are subject to audit by the Research Conduct and Compliance Office (RCCO).

In addition, individuals planning to conduct human subject research outside the United States must complete an optional module on the CITI training website: International Studies. [Click here](#) to access the instruction sheet for accessing optional CITI modules.

[\[reviewer notes~\]](#)

2.21 Will this research study be conducted within a nursing home located in Pennsylvania?

* No

[\[reviewer notes~\]](#)

Section 3 - Human Subjects

3.1 What is the age range of the subject population?

5 to 18 years old

3.2 What is their gender?

* Both males and females

Provide a justification if single gender selected:

3.3 Will any racial or ethnic subgroups be explicitly excluded from participation?

* No

If **Yes**, identify subgroups and provide a justification:

3.4 For studies conducted in the U.S., do you expect that all subjects will be able to comprehend English?

* Yes

[\[reviewer notes~\]](#)

3.5 **Participation of Children:** Will children less than 18 years of age be studied?

* Yes

3.5.1 Specify the age range of the children to be studied.

(Check all that apply below:)

*

Choices

0-6 years of age

7-13 years of age

14-17 years of age

3.5.2 Provide a rationale for the specific age ranges of the children to be studied:

Child needs to be adequately potty trained with daytime dryness and be able to communicate quality of life subjective information to parents.

3.5.3 Describe the expertise of the study team for conducting research with children within this age range:

The study team has significant clinical experience in the pediatric population as Drs. Stephany, Cannon, Ost, and Schneck are board certified urologic pediatricians and have

facilitated a number of research studies through the Children's Hospital of Pittsburgh urology department.

- 3.5.3.1 Have you obtained the following clearances from all research staff who may have direct contact with children under the age of 18? Direct contact under the law includes face-to-face, and telephonic or electronic, contact with minors. Please see the [Child Clearances](#) guidance document for further explanation?**

**Pennsylvania Department of Public Welfare Child Abuse History Clearance;
Pennsylvania State Police Criminal Record Check; and
FBI Criminal Background Check**

Yes

Note: If No, once all clearances are obtained, a modification must be submitted.

If you selected N/A, please explain:

It is important to note that "direct contact" refers not only to face-to-face meetings but also extends to communication via phone (including text messaging), social media or internet. Direct contact also includes the care, guidance, supervision or control, or routine interaction with, minors. Conversely, a participating investigator or support staff member who does not have direct contact, either electronically or in person, with children does not need to obtain clearances (e.g., statistician, non-clinical laboratory personnel, etc.). If your research study provides babysitting services, the babysitters must have the required child clearances.

*** Note:** It is the **responsibility of the principal investigator** to ensure that all research staff have these clearances prior to any interaction with children. Contact Human Resources at 412-624-8150 for assistance with this process.

- 3.5.4 Describe the adequacy of the research facilities to accommodate children within this age range:***
Addressed below:

The department of urology at the Children's Hospital of Pittsburgh outpatient clinic has all of the necessary resources to implement this research study.

- 3.5.5 Permitted Categories of Research: The Federal Policy and FDA regulations governing human subject protections specify that research involving children must fall into one of the following permitted categories.**

*

The research does not involve greater than minimal risk [45 CFR 46.404/21 CFR 50.51].

45 CFR 46.406

- The risk represents only a minor increase over minimal risk.
- The research procedures present experiences to the subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.

- The research procedures are likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for understanding or amelioration of the subjects' disorder or condition.

45 CFR 46.407

- The risk is justified by the anticipated benefit to the subjects; and the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches.

Provide a justification which **must address all considerations** related to the designated category of research:

At stated prior we feel this study provided minimal risk based on the rarity and minority of side effects from previous TENS studies in adults. We will use a voltage only high enough to elicit an involuntary twitch of the toes, which is generally non-painful.

Although the electrical stimulation may help subjects with nocturnal enuresis, this benefit is not known or guaranteed. However, information learned from this study will help investigators learn how to better treat children with nocturnal enuresis in the future.

[\[reviewer notes→\]](#)

3.6 Does this research study involve prisoners, or is it anticipated that the research study may involve prisoners?

* No

[\[reviewer notes→\]](#)

3.7 Will pregnant women be knowingly and purposely included in this research study?

* No

[\[reviewer notes→\]](#)

3.8 Does this research study involve neonates of uncertain viability or nonviable neonates?

* No

[\[reviewer notes→\]](#)

3.9 Fetal Tissues: Does this research involve the use of fetal tissues or organs?

* No

[\[reviewer notes~\]](#)

--->

3.10 What is the total number of subjects to be studied at this site, including subjects to be screened for eligibility?

Note: The number below is calculated by summing the data entered in question 3.11. Any additions or changes to the values entered in 3.11 will be reflected in 3.10.

* 40

3.11 Identify each of the disease or condition specific subgroups (include healthy volunteers, if applicable) that will be studied.

Click on the "Add" button and specify for each subgroup:

1) how many subjects will undergo research related procedures at this site; and

2) if applicable, how many subjects will be required to undergo screening procedures (e.g., blood work, EKG, x-rays, etc.) to establish eligibility. **Do Not include subjects who will undergo preliminary telephone screening.**

*

Subgroup	Number to undergo research procedures	Number to undergo screening procedures
View Pilot study of tibial nerve stimulation	25	40

3.12 Provide a statistical justification for the total number of subjects to be enrolled into this research study at the multicenter sites or this site.

* Described below:

This is a pilot study to determine if foot stimulation has any effect on nocturnal enuresis. The study is designed through the use of an objective night-time voiding log and subjective quality of life questionnaires to determine the effect of foot stimulation. As the variations on these symptom parameters is unknown, it is difficult to to determine the total number of subjects based on statistical analysis. Therefore, we decided on 25 subjects in this pilot study. Once statistical significance is reached , we will stop recruiting additional subjects in order to maintain the subject number at a minimum.

[\[reviewer notes~\]](#)

3.13 Inclusion Criteria: List the specific criteria for inclusion of potential subjects.

1. Children ages 5 to 16 years old without any specific neurological disorder or urinary tract infection, clinically diagnosed as having nocturnal enuresis AT LEAST 4 episodes per month by history

2. Currently having no daytime overactive bladder symptoms, i.e. urinary frequency,

urgency, or daytime incontinence

3. Having been assessed for and treated if applicable for behavioral etiologies of nocturnal enuresis - consuming excess fluids or specific bladder irritants

4. Having been assessed for and treated if applicable for constipation

3.14 Exclusion Criteria: List the specific criteria for exclusion of potential subjects from participation.

1. Children with known neurological disorders which may be contributing to nocturnal enuresis episodes

2. Children found through history to have significant behavioral causes of nocturnal enuresis including consumption of excessive fluids or known bladder irritants

3. Children with chronic constipation who are non-compliant with previous pharmacologic efforts to treat.

4. Children who are not adequately potty trained

5. Children with significant daytime symptoms of overactive bladder including frequency, urgency, and daytime incontinence

5. Children who do not tolerate initial stimulation training session in the urology clinic upon enrollment

6. Children with any implantable medical devices such as a pacemaker will be excluded from the study

Note: Any patient currently taking medication such as an anti-muscarinic or a tricyclic antidepressant for overactive bladder at time of enrollment will be eligible to participate and will be continued on their usual medication and dosage throughout the study.

3.15 Will HIV serostatus be evaluated specifically for the purpose of participation in this research study?

* No

If **Yes**, provide a justification:

[\[reviewer notes~\]](#)

**4.1 Select all recruitment methods to be used to identify potential subjects:
Other Strategies: Described below**

4.2 Provide a detailed description of your recruitment methods, including identifying and initiating contact with participants:

Children will be assessed during clinic visit to department of pediatric urology for nocturnal enuresis for eligibility in this study. Medical record and detailed history will be reviewed to ensure no confirmed neurological diagnosis or other known etiologies of nocturnal enuresis including bladder irritants or constipation which would make child ineligible. Routine urinalysis will be reviewed to rule out any urinary tract infection.

Note: Questions jump from 4.2 to 4.6 as questions 4.3-4.5 have been removed and the information is now captured in 4.1

[\[reviewer notes-\]](#)

4.6 Are you requesting a waiver to document informed consent for any or all participants, for any or all procedures? (e.g., a verbal or computerized consent script will be used, but the subjects will not be required to sign a written informed consent document. *This is not a waiver to obtain consent.*

* No

[\[reviewer notes-\]](#)

4.7 Are you requesting a waiver to obtain informed consent or an alteration of the informed consent process for any of the following?

* Yes

4.7.1 If Yes, select the reason(s) for your request:

Medical record review for ONLY the identification of potential subjects

General Requirements: The Federal Policy **[45 CFR 46.116 (d)]** specifies in order for a waiver of consent to be approved, the request must meet four criteria. For each request, you will be asked to provide a justification addressing how each of these criterion is met.

Medical record review for the identification of potential subjects:

The research involves no more than minimal risk to the subjects;
[45 CFR 46.116 (d)(1)]

We will only review medical records to identify potential subjects. We will not extract or record any information from the medical record. This review procedure imposes no physical or psychological risks to the patients. Therefore, we believe it has no more than minimal risk.

The waiver or alteration will not adversely affect the rights and welfare of the subjects;
[45 CFR 46.116 (d)(2)]

The rights and welfare of these patients will not be negatively affected because this research team is comprised of pediatric urologists who already have legitimate access to the medical records by virtue of their clinical responsibilities.

The research could not practicably be carried out without the waiver or alteration;

[45 CFR 46.116 (d)(3)]

Whenever appropriate, the subjects will be provided with additional pertinent information after participation;

[45 CFR 46.116 (d)(4)]

It would not be practical to obtain the full consent of the urology patient without first reviewing the medical record. Medical record review is intended to determine whether or not the patient meets the eligibility criteria, which can not be used to replace the patient consent. A full consent will be conducted as described in this application.

We will not obtain any pertinent information from the medical record review.

4.7.2 Under what circumstances (if any) will you obtain consent from some of these subjects?

Under no circumstances will we obtain consent for medical record review. However, we will obtain a full consent from the patient's parent or guardian for the study to be performed.

[\[reviewer notes→\]](#)

4.8 Are you requesting an exception to the requirement to obtain informed consent for research involving the evaluation of an 'emergency' procedure?

Note: This exception allows research on life-threatening conditions for which available treatments are unproven or unsatisfactory and where it is not possible to obtain informed consent.

* No

[\[reviewer notes→\]](#)

4.9 Upload all consent documents for watermarking:

Draft Consent Forms for editing:

Name	Modified Date
New Consent	5/13/2015 12:01 PM

Approved Consent Form(s):

Name Modified Date

[\[reviewer notes→\]](#)

4.10 Will all potential adult subjects be capable of providing direct consent for study participation?

*

Not applicable

Indicate why direct consent is not possible:

Study participants will all be children < age 18 years old and therefore consent will be obtained from a parent or legal guardian.

[\[reviewer notes→\]](#)

4.11 At what point will you obtain the informed consent of potential research subjects or their authorized representative?

After performing certain of the screening procedures, but prior to performing any of the research interventions/interactions

4.11.1 Address why you feel that it is acceptable to defer obtaining written informed consent until after the screening procedures have been performed.

Our screening procedure only includes a review of patient medical record. We have a requested a waiver of consent for assessing medical record and provided the reasons for the waiver on section 4.7

4.11.2 Taking into account the nature of the study and subject population, indicate how the research team will ensure that subjects have sufficient time to decide whether to participate in this study. In addition, describe the steps that will be taken to minimize the possibility of coercion or undue influence.

The research study will be discussed in detail with the child's parent or guardian in the outpatient clinic by the pediatric urologist. If the parent is immediately interested in enrolling the child in the study, informed consent will take place during the clinic visit as will the providing of the TENS equipment will all necessary teaching on the use of the device. If the parent would like additional time to consider participation, we will wait for them to contact us at a later date. The intention for participation will always be initiated by the parent, thus we will make no attempts to call or email them if they do not contact us after the clinic visit.

[\[reviewer notes→\]](#)

4.12 Describe the process that you will employ to ensure the subjects are fully informed about this research study.

* Addressed below:

This description must include the following elements:

- who from the research team will be involved in the consent process (both the discussion and documentation);
- person who will provide consent or permission;
- information communicated; and
- any waiting period between informing the prospective participant about the study and obtaining consent

In addition, address the following if applicable based on your subject population:

- process for child assent and parental permission
 - continued participation if a child subject turns 18 during participation
- process for obtaining proxy consent and assent for decisionally impaired subjects
 - continued participation if subject regains capacity to consent

Drs. Stephany, Cannon, Ost, or Schneck will be involved in the consent process to discuss the study in detail with the parent including all of the potential risks. The consent form will be provided and the parent will be free to ask any questions related to the study. We will provide the parent with the option to sign the consent form at a later date if they choose to do so.

Legal guardians may provide consent only if they have a court order specifically indicating their authority.

4.13 Are you requesting an exception to either IRB policy related to the informed consent process?

- For studies involving a drug, device or surgical procedures, a listed physician investigator is required to obtain the written informed consent unless an exception to this policy has been approved by the IRB
- For all other studies, a listed investigator is required to obtain consent (Note: In order to request an exception to this policy, the study must be minimal risk)

* No

If **Yes**, provide a justification and describe the qualifications of the individual who will obtain consent:

4.14 Will you inform research subjects about the outcome of this research study following its completion?

* No

If **Yes**, describe the process to inform subjects of the results:

5.1 Describe potential risks (physical, psychological, social, legal, economic or other) associated with screening procedures, research interventions/interactions, and follow-up/monitoring procedures performed specifically for this study:

*

View	Research Activity:	Electrical Stimulation of the Foot
	Common Risks:	Common risks may include potential foot cramp, skin irritation, redness, or rash.
	Infrequent Risks:	N/A
	Other Risks:	N/A
View	Research Activity:	Medical Record Review
	Common Risks:	<i>No Value Entered</i>
	Infrequent Risks:	<i>No Value Entered</i>
	Other Risks:	Potential for breach of confidentiality

5.1.1 Describe the steps that will be taken to prevent or to minimize the severity of the potential risks:

To minimize foot cramping, the lowest threshold voltage required (to induce spontaneous movement of the toes) will be used for actual stimulation. To minimize the risks, the research procedures will be conducted by experienced personnel. The subjects will be appropriately trained on how to use the TENS stimulator and attach the electrodes. The subjects will also be told that they can call the investigators anytime with any questions or problems.

5.2 What steps will be taken in the event that a clinically significant, unexpected disease or condition is identified during the conduct of the study?

* **Addressed below:**

The study will be stopped immediately in the event that a clinically significant, unexpected condition is identified. The subject will also be referred to appropriate care for the unexpected condition.

5.3 All the risk questions (screening, intervention/interaction, follow-up) have been merged into one question (5.1).

[\[reviewer notes→\]](#)

5.4 Do any of the research procedures pose a physical or clinically significant psychological risk to women who are or may be pregnant or to a fetus?

* No

[\[reviewer notes→\]](#)

5.5 Do any of the research procedures pose a potential risk of causing genetic mutations that could lead to birth defects?

* No

[\[reviewer notes→\]](#)

5.6 Are there any alternative procedures or courses of treatment which may be of benefit to the subject if they choose not to participate in this study?

* Not applicable

If **Yes**, describe in detail:

[\[reviewer notes→\]](#)

5.7 Describe the specific endpoints (e.g., adverse reactions/events, failure to demonstrate effectiveness, disease progression) or other circumstances (e.g., subject's failure to follow study procedures) that will result in discontinuing a subject's participation?

* Describe below:

The study is expected to end when the six weeks have been completed with associated completion of weekly night-time voiding log and quality of life questionnaires. However, if the subject can not follow the study procedures such as an inability to tolerate foot stimulation or non-compliance with completing night-time voiding logs and/or quality of life questionnaires, the subject's participation will be discontinued and the study will be ended.

We expect some electrodes to detach from the foot. However, occasional unattached electrodes will not end the study, since the data will be collected in a week period and a few occurrences of detachment should not change the results. Also, if skin irritation is caused by the electrodes, the study will continue by using the other foot and giving the irritated foot a day or two to recover. However, if unexpected serious irritation occurs that cannot be avoided by changing feet, the study will be terminated for that subject.

[\[reviewer notes→\]](#)

5.8 Will any individuals other than the investigators/research staff involved in the conduct of this research study and authorized representatives of the University Research Conduct and Compliance Office (RCCO) be permitted access to research data/documents (including medical record information) associated with the conduct of this research study?

* No

5.9 Has or will a Federal Certificate of Confidentiality be obtained for this research study?

* No

5.10 Question has been moved to 5.17**5.11 Question has been moved to 5.16**[\[reviewer notes~\]](#)**5.12 Does participation in this research study offer the potential for direct benefit to the research subjects?**

No - Describe the general benefits to society (e.g., increased knowledge; improved safety; better health; technological advancement) that may result from the conduct of this research study.

Describe the benefit:

The subject may not receive direct benefit from participation in this research study. Although the electrical stimulation may help with nocturnal enuresis, this benefit is not known or guaranteed. However, information learned from this study will help investigators learn how to better manage the conditions of nocturnal enuresis.

5.13 Describe the data and safety monitoring plan associated with this study. If the research study involves multiple sites, the plan must address both a local and central review process.

11. Drs. Stephany, Tai and Ferroni will be responsible for the data and safety monitoring.

2. After the ADDITIONAL 3 WEEKS OF ONGOING stimulation, parents will be called on the telephone by either Dr. Stephany or Dr. Ferroni to inquire if any issues and assess the child's tolerability to continue treatments. All questions will be addressed as well. If no issues, the patient will continue the EXTENDED study and follow-up in clinic at the conclusion to submit their completed log and return the stimulation device. If during the monitoring telephone call an issue is detected, Drs. Ferroni or Stephany will attempt to troubleshoot issues related to device usage over the telephone. A follow-up phone call will be scheduled on an as needed basis (2-3 days later) if any adjustments are made to the parents' technique of providing the stimulation or adjustments to the device settings. If at the monitoring phone call it is determined that the child is not reasonably tolerating the stimulation and/or they have developed concerning side effects, a prompt clinic appointment will be made to assess the child in person and remove them from the study.

3. The investigators will monitor the progress of the study and the efficacy of the treatment after collecting data from the first 10 subjects. Any unexpected adverse effect will be addressed immediately and reported to the IRB committee. In addition to the monitoring of every 10 subjects, an annual review of the study will also be conducted to assure the experimental design, identify any unexpected adverse effects for reporting, and review the progress of subject recruitment

4. The data will be locked in the urology office by the investigators for safety and privacy. An annual review of the safety and privacy of the data will be performed. If any problem occurs, it will also be addressed immediately during any time of the year.

5. The following will be reported to IRB annually: a list of persons who monitored the data

and safety; the date when the monitoring/review occurs; a summary of any problems detected; final decisions about changes of the study based on the annual review.

6. The potential adverse events may be reported to IRB including:

Use of TENS stimulator: Foot skin irritation, redness, or rash, or foot cramp.

[reviewer notes~]

Section 5 - Potential Risks and Benefits of Study Participation

- 5.14 What precautions will be used to ensure subject privacy is respected?** (e.g. the research intervention will be conducted in a private room; the collection of sensitive information about subjects is limited to the amount necessary to achieve the aims of the research, so that no unneeded sensitive information is being collected, drapes or other barriers will be used for subjects who are required to disrobe)

The initial instruction of the TENS device will be conducted in a private examination room in the urology clinic. The 6 to 12-week voiding diaries and quality of life questionnaires will be conducted by the subjects/parents at home without privacy concerns.

- 5.15 What precautions will be used to maintain the confidentiality of identifiable information?** (e.g., paper-based records will be kept in a secure location and only be accessible to personnel involved in the study, computer-based files will only be made available to personnel involved in the study through the use of access privileges and passwords, prior to access to any study-related information, personnel will be required to sign statements agreeing to protect the security and confidentiality of identifiable information, whenever feasible, identifiers will be removed from study-related information, precautions are in place to ensure the data is secure by using passwords and encryption, because the research involves web-based surveys, audio and/or video recordings of subjects will be transcribed and then destroyed to eliminate audible identification of subjects)

The subject's name will only be used for screening and scheduling purposes. Once the subject enters the experiment, an ID number will be assigned to each subject in place of his/her name and only the subject's age and gender will be recorded for privacy reasons. Subject name will not appear on data collection forms.

The information linking the ID number with the subject's name will be stored in a separate secure location during the study, and will be destroyed at the end of the study. We will not keep any document to link the subject's name to the ID number. After the study is finished, we will have consent forms with subjects names and data forms with ID numbers. Since the link between names and ID numbers are not kept, there will be no identifiable information that could be released. However, the data on papers will still be locked for safety reasons and the electronic data will be stored in password-protected, fire-walled computers.

- 5.16 If the subject withdraws from the study, describe what, if anything, will happen to the subject's research data or biological specimens.**

If a subject requests withdrawal or is withdrawn by the PI, no further data should be collected, but all data obtained prior to withdraw will be retained and analyzed for the study purposes.

- 5.17 Following the required data retention period, describe the procedures utilized to protect subject confidentiality.** (e.g., destruction of research records; removal of identifiers; destruction of linkage code information; secured long-term retention)

After the required data retention period, all data and subject information will be destroyed.

[\[reviewer notes~\]](#)

6.1 Will research subjects or their insurance providers be charged for any of the procedures (e.g., screening procedures, research procedures, follow-up procedures) performed for the purpose of this research study?

*
No

[\[reviewer notes~\]](#)

6.2 Will subjects be compensated in any way for their participation in this research study?

* Yes

6.2.1 Describe the amount of payment or other remuneration offered for complete participation in this research study.

\$200 for complete participation involving the completion of 6-week night-time voiding log and quality of life questionnaires as well as the ability to tolerate foot stimulation during the third and fourth week of the study. Upon receipt of all completed forms and return of the TENS equipment, compensation will be distributed.
There will be no additional compensation for the subjects who wish to continue with the study for an additional 6 weeks

6.2.2 Describe the amount and term of payment or other remuneration that will be provided for partial completion of this research study.

\$50 for partial completion. Partial completion is defined as that the subject has signed the consent form and the study has begun, but the data collection is not finished.

[\[reviewer notes~\]](#)

7.1 Summarize the qualifications and expertise of the principal investigator and listed co-investigators to perform the procedures outlined in this research study.

Heidi A. Stephany, MD, is an assistant professor of urology at the University of Pittsburgh School of Medicine. She received her medical DEGREE from the University of Kansas School of Medicine, where she also completed a residency in urology. Dr. Stephany completed a fellowship in pediatric urology at Vanderbilt University in Nashville, Tenn., and specializes in pediatric urology.

Changfeng Tai, PhD, Assistant Professor Dr. Tai has many years of experience in electrical stimulation, neurophysiology, and urologic studies. The TENS stimulator is a FDA-approved device for routine use by individuals at home for muscle and back pain. Therefore, he is

qualified for performing the non-invasive electrical stimulation of the foot using skin surface electrodes and the TENS stimulator during the initial instruction period for the subjects.

Matthew C. Ferroni, MD, is a urologic surgery resident at the University of Pittsburgh School of Medicine. He received his medical DEGREE FROM Thomas Jefferson University in Philadelphia, PA. Prior to his current career in medicine, Dr. Ferroni spent five years working in financial services after graduating from Boston College in 2001. His interests within the field of urology center around minimally invasive surgery and oncology.

Michael C. Ost, MD, is an associate professor of urology and vice chairman of the Department of Urology, University of Pittsburgh School of Medicine and chief of the division of pediatric urology at Children's Hospital of Pittsburgh of UPMC. He is a graduate of the University of Michigan and earned his MEDICAL DEGREE at Mount Sinai School of Medicine. Following surgical and urologic residencies at Mount Sinai, Dr. Ost completed fellowship training in endourology at the North Shore — Long Island Jewish Medical Center and in pediatric urology at Children's Hospital of Pittsburgh of UPMC. Dr. Ost's clinical interests include adult and pediatric minimally-invasive urologic surgery, robotic treatment of urologic diseases and complex stone disease. He is a member of the American Urological Association and the Endourological Society.

Glenn M. Cannon, MD, is an assistant professor of urology at the University of Pittsburgh School of Medicine. A graduate from Thomas Jefferson University Medical College, Dr. Cannon completed residencies in urology at the University of Pittsburgh, and in surgery at Barnes-Jewish Hospital in St. Louis. He also completed a fellowship in pediatric urology at the Children's Hospital of Boston

Francis X. Schneck, MD, is an associate professor of urology at the University of Pittsburgh School of Medicine. He earned his medical DEGREE FROM the Georgetown University School of Medicine in 1987, and completed a residency in urology at the University of Pittsburgh School of Medicine in 1993 and a pediatric urology fellowship at the Harvard Medical School and Children's Hospital in 1995. He joined UPMC upon completion of his fellowship. He is the author of numerous articles and book chapters in the field of pediatric urology. Dr. Schneck is board certified by the American Board of Urology.

[\[reviewer notes~\]](#)

7.2 Indicate all sources of support for this research study.

*

Selections

Foundation: Upload a copy of the research plan that was submitted to the agency

If **Federal** support, provide the sponsor information:

Federal sponsor	Grant Title	Grant number	Awardee institution	Federal grant application
-----------------	-------------	--------------	---------------------	---------------------------

For projects not supported by a federal grant, upload the research plan that was submitted for funding:

Name	Modified	Date
------	----------	------

If **Industry** support, provide the sponsor information and level of support:

If **Foundation** support, provide the sponsor information:

A grant of \$25,000 was received by Dr. Tai from the Society of Urodynamics and Female Urology in order to proceed with research studies evaluating the clinical impact of neuromodulation. This grant will cover all equipment costs, and patient compensation required for completion.

If **Other** support, provide the support information and level of support:

[\[reviewer notes→\]](#)

7.3 Is this study funded in part or whole by a PHS Agency?

* No

Does any investigator* involved in this study (select all that apply):

Name
<input type="checkbox"/> A. Have equity in a publicly-traded entity that either sponsors** this research or owns the technology being evaluated or developed that exceeds a 5% ownership interest or a current value of \$10,000 ?
<input type="checkbox"/> B. Have equity in a non-publicly-traded entity that either sponsors this research or owns the technology being evaluated or developed?
<input type="checkbox"/> C. Receive salary, consulting fees, honoraria, royalties or other remuneration from an entity that either sponsors this research or owns the technology being evaluated or developed that is expected to exceed \$10,000 during the past or next 12 months?
<input type="checkbox"/> D. Have rights as either the author or inventor of intellectual property being evaluated or developed in this research that is the subject of an issued patent or has been optioned or licensed to an entity?
<input type="checkbox"/> E. Have an officer or management position**** with a Licensed Start-up Company overseen by the COI Committee that either sponsors this research or owns the technology being evaluated or developed?
<input type="checkbox"/> F. Receive compensation of any amount when the value of the compensation would be affected by the outcome of this research, such as compensation that is explicitly greater for a favorable outcome than for an unfavorable outcome or compensation in the form of an equity interest in the entity that either sponsors this research or owns the technology being evaluated or developed?
<input checked="" type="checkbox"/> None of the above options apply and there are no other financial conflicts of interest in the conduct of this research.

***Investigator** means the PI, co-investigators, and any other member of the study team, regardless of title, who participates in the design, conduct, or reporting of this research, as well as his/her spouse, registered domestic partner, dependents, or other members of

his/her household. **The PI is responsible for ensuring that s/he and all other relevant members of the study team review the above questions describing Significant Financial Interests.**

******through the provision of funds, drugs, devices, or other support for this research

********Such as serving on the Board of Directors or Board of Managers or a position that carries a fiduciary responsibility to the company (e.g., CEO, CFO, CTO, or CMO).

[\[reviewer notes~\]](#)

Supporting Documentation Section

References and Other Attachments

Additional documents:

Name	Modified Date	Version
Grant Approval Letter	8/26/2014 8:24 AM	0.01
Reference List	9/15/2014 12:15 PM	0.01

Please use the Add button to the left to upload additional documents if needed.

[\[reviewer notes~\]](#)

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world.

"[Applicable clinical trials](#)" are required **by [federal law](#)** to be registered in [ClinicalTrials.gov](#).

Applicable Clinical Trials (ACTs) are studies that meet the following criteria:

- The study is an interventional study AND
- The study intervention is a drug, biologic, medical device, radiation or genetic AND
- The Study is not Phase 0 or 1 AND
- The study has at least one site in the United States or is conducted under an investigational new drug application or investigational device exemption

NIH Policy

Effective January 18, 2017, revised [NIH](#) Policy requires that all [clinical trials](#) funded in whole or in part by the NIH be registered and results information posted on ClinicalTrials.gov.

As defined by the NIH, a [clinical trial](#) is:

A research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health related biomedical or behavioral outcomes.

The NIH Policy extends beyond the Food and Drug Administration Amendment Act (FDAAA 801) requirements in that it requires registration and results reporting of:

- clinical trials of behavioral, surgical and other types of health and medical interventions
- phase 1 studies of drugs and biological products
- small feasibility studies of device products

Failure to submit all required registration and results information requested on ClinicalTrials.gov can jeopardize University grant funding, the future funding of the grantee and subject the University of Pittsburgh to future monetary penalties.

In addition, to promote transparency of the clinical trials process, the [International Committee of Medical Journal Editors \(ICMJE\)](#) has established a policy requiring the entry of clinical trials in a public registry, such as ClinicalTrials.gov, prior to subject enrollment as a condition of consideration for publication of the trial results.

*** Based on the above information, will this study be registered in ClinicalTrials.gov?**