PROTOCOL NARRATIVE FOR EXPEDITED OR FULL COMMITTEE RESEARCH

University of California, Irvine
Institutional Review Board

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For IRB Office Use Only

Lead Researcher Name: Felicia Lane, MD
Study Title: Pilot Study of Percutaneous Posterior Tibial Nerve Stimulation for the Treatment of Interstitial Cystitis/Painful Bladder Syndrome

NON-TECHNICAL SUMMARY

Provide a non-technical summary of the proposed research project that can be understood by IRB members with varied research backgrounds, including non-scientists and community members. The summary should include a brief statement of the **purpose of the research** and **related theory/data supporting** the intent of the study as well as a brief description of the **procedure(s) involving human subjects**. ***This summary should not exceed ½ page.***

Painful Bladder Syndrome (previously known as Interstitial Cystitis) is a long-lasting condition with symptoms of bladder pain (particularly when the bladder is full) and other bladder symptoms, such as frequent urination. No one knows the exact cause of painful bladder syndrome, but there are many theories and there are likely multiple factors that can lead to the same symptoms. Unfortunately, no cure for painful bladder syndrome has been found and most current treatments simply focus on improving symptoms.

The American Urological Association represents urologists who treat bladder conditions, and this society has published guidelines for doctors who treat Painful Bladder Syndrome. The guidelines suggest sacral neuromodulation as a 4th line treatment; sacral neuromodulation involves a two stage surgical procedure and the implantation of a permanent electrode and battery. Although the guidelines note that we do not know exactly why sacral neuromodulation improves the symptoms of Painful Bladder Syndrome, it is thought to affect the way pain signals from the bladder are sent to the brain.

Percutanteous posterior tibial nerve stimulation (PTNS) has more recently been approved for neuromodulation aimed at the same targets as sacral neuromodulation, without the need to have surgery or a permanently implanted device. The purpose of our research is to determine if PTNS is potentially helpful in the treatment of Painful Bladder syndrome. If this study suggests that PTNS is effective in treating symptoms, we believe additional research in this area will be worthwhile.

Our study will involve enrolling patients with Painful Bladder Syndrome and urinary frequency or urgency symptoms to treatment with 12 weekly treatments of PTNS. Each PTNS session involves placing a small needle (like an acupuncture needle) behind the inside of the ankle and connecting it to a mild electrical stimulation for 30 minutes. We will assess symptoms and bladder function before and after the treatments. At the end of the trial, patients will be asked to enroll (if they want to) in a continuation of the study to find out the duration of symptom improvement, if any is found.

PTNS is an FDA-approved treatment, and this study will involve only using PTNS for approved indications. The patients who participate in the study would be eligible to receive PTNS therapy as part of routine care. The study will involve the collection of additional information (in the form of questionnaires and voiding diary) on the subset of Painful Bladder Syndrome patients to learn how PTNS treatment affects their symptoms.

SECTION 1: PURPOSE AND BACKGROUND OF THE RESEARCH

1. Describe **the purpose of the research** project and state the overall objectives, specific aims, hypotheses (or research question) and scientific or scholarly rationale for performing the study.
2. Provide the **relevant background information** on the aims/hypotheses (or research question) to be tested and the procedures/products/techniques under investigation.
3. Include a description of the **primary outcome variable(s), secondary outcome variables, and predictors** and/or comparison groups as appropriate for the stated study objectives.
4. Include a critical evaluation of **existing knowledge**, and specifically identify the information gaps that the project intends to address.
5. Describe **previous research** with animals and/or humans that provides a basis for the proposed research. **Include references/citations**, as applicable.
   This section should not exceed 4 pages.

1- Purpose of the research:

The objective of this prospective, pilot study is to determine if patients with urinary urgency, frequency and bladder pain also known as interstitial cystitis/painful bladder syndrome (IC/PBS) respond to percutaneous tibial nerve stimulation (PTNS) like patients with urinary frequency and urgency without pain. The specific aim is to evaluate how patients with IC/PBS respond to PTNS with regards to the reduction of symptoms in subjects with this disorder. Pre and post treatment questionnaires will be used to assess this endpoint.

The hypothesis is that subjects who receive PTNS will demonstrate a response to treatment through a reduction in symptoms similar to what has been described has been demonstrated in the literature with sacral neuromodulation (SNM) for IC/PBC. Though there is no uniform outcome measure for SNM studies, the majority use pain or symptom scales and have reported 55-80% response rates.[1] The study will assess response to PTNS treatment based on the variables described in section 3.

There is compelling scientific and scholarly rationale to perform this trial. Previous studies have found that PTNS may be helpful in chronic pelvic pain conditions but there are still many gaps in our knowledge regarding when and how effective this modality is. There are very few studies specifically examining PTNS in subjects with IC/PBS. Given how persistent and debilitating IC/PBS can be, even with the most thorough and advanced treatments, the potential to add another treatment modality with minimal morbidity to the treatment algorithm is significant.

2- Relevant background information:

IC/PBS is a chronic condition which is "characterized by an unpleasant sensation (pain, pressure, discomfort) perceived to be related to the urinary bladder, associated with lower urinary tract symptoms of more than six weeks duration, in the absence of infection or other identifiable causes."[2] The most common lower urinary tract symptom is urinary frequency, often consequent to pain associated with bladder filling. Treatment for IC/PBS is often multimodal with behavioral modifications recommended first, followed by oral or intravesical medications and directed physical therapy. As a chronic pain condition, patients often require trials of multiple treatment modalities to manage symptoms or require chronic pain medication. Given that the etiology of IC/PBS is unknown, treatment currently focuses on managing symptoms, predominantly the complaints of pain and urinary frequency. Current treatment for refractory IC is often surgical/procedural and associated with significant cost and morbidity. Considerable benefit could be derived from contributing an additional treatment modality to the algorithm for IC/PBS.

Sacral neuromodulation (SNM) is fourth line treatment as outlined in the algorithm in the guidelines for diagnosis and treatment published by the American Urological Association in June 2011[2]. The majority of the evidence supporting SNM in the treatment of PBS/IC comes from small case series of patients with refractory IC/PBS.[1] PTNS (under the brand name NURO™ System) is an FDA-

approved device for the treatment of urinary urgency, urinary frequency and urge incontinence. It is often described as a peripheral form of neuromodulation (as opposed to SNM which is central neuromodulation at the level of the nerve root). PTNS involves 12 weeks of weekly 30 minute office-based treatment sessions with a small electrode placed slightly above the ankle in order to stimulate the S2-4 nerve roots. If benefits are obtained, 12 weeks of treatment is followed by spaced maintenance sessions at timing of provider and patient discretion. In comparison, sacral neuromodulation (SNM) involves a two stage procedure, with both stages most often being performed under conscious sedation in the operating suite and leading to the implantation of a permanent device with consequent expense and risks. Because PTNS and SNM share some of the same mechanisms of action and are approved for treatment of some of the same indications, there has been interest in the utility of PTNS in the treatment algorithm of IC/PBS. Given that PTNS has FDA approval for the indication of urinary frequency, one of the most common complaints in IC/PBS, the majority of IC/PBS patients already qualify for PTNS. It is the objective of our trial to systematically study the utility of PTNS in IC/PBS.

Prior studies have examined PTNS for the treatment of a variety of pain syndromes. These studies have either been performed as single arm studies or with a comparison arm of routine care for IC/PBS.[3] During literature search, we found only a single study that examined PTNS for treatment of IC/PBS and it only evaluated a highly refractory population with longstanding disease.[4] Given the lack of literature and limited statistical information on which to base our estimates, it is beneficial to conduct a pilot study to collect additional information and direct future research.

3- Outcomes:

The primary outcome variable will be the percentage of subjects to report that they are moderately improved or markedly improved in overall symptoms compared to baseline on a 7-point global response assessment (GRA) scale. The GRA scale involves asking the question, “As compared to when you started the current study, how would you rate your overall symptoms now?”. There are 7 possible responses: markedly worse, moderately worse, slightly worse, the same, slightly improved, moderately improved and markedly improved. This scale is the current standard for outcome in studies that are evaluating treatments and interventions for IC/PBS.

There will be a number of secondary outcome variables including: changes in a 24 hour voiding diary during the course of the interventions, ratings for bladder pain, urinary urgency and urinary frequency on standardized scales, the score on O'Leary-Sant IC Symptom and Problem Index, scores validated questionnaires for pelvic floor, sexual dysfunction and general health and any reports of adverse events.

The study will also examine demographic data and information on the course of the disease in subjects.

4- Existing Knowledge:

There are few published studies looking at PTNS and IC/PBS. Literature review identified six studies that evaluated the effect of PTNS on pain syndromes. Four of these studies looked at chronic pelvic pain [5,6,7,8], one study evaluated chronic prostatitis/chronic pelvic pain in men[9] and only a single study examined PTNS in patients with IC/PBS[10]. However, in the study of IC/PBS, there was a nonstandard treatment course (10 instead of 12 sessions of PTNS), the subjects had severely refractory IC/PBS with multiple prior treatments attempted in all cases and often long-standing disease (up to 22 years). By only examining highly refractory subjects, the potential benefit of a minimally invasive intervention early in the disease process may have been missed.

The current literature leaves many questions about the potential utility of PTNS in patients with IC/PBS. With one, uncontrolled study in refractory patients examining the topic, it is still unclear if PTNS could be useful in reducing IC/PBS symptoms and if so, which symptoms in which patients and by how much. The goal of this study is to begin to answer these questions. If PTNS is not found to be effective in the treatment of IC/PBS, it provides additional information about the pathophysiology of IC/PBS and allows for focus of future research elsewhere.

[1]Marcelissen, T., et al. "Sacral neuromodulation as a treatment for chronic pelvic pain." The Journal of urology 186.2 (2011): 387-393.

[2]Hanno, Philip M., et al. "AUA guideline for the diagnosis and treatment of interstitial cystitis/bladder pain syndrome." The Journal of urology 185.6 (2011): 2162-2170.
[3]Gokyildiz S, Kizilkaya Beji N, Yalcin O, Istek A. Effects of percutaneous tibial nerve stimulation therapy on chronic pelvic pain.Gynecol Obstet Invest. 2012;73(2):99–105
[4]Zhao J, Nordling J: Posterior tibial nerve stimulation in patients with intractable interstitial cystitis. BJU Int 2004;94:101–104.
[5]van Balken, Michael R., et al. "Percutaneous tibial nerve stimulation as neuromodulative treatment of chron pelvic pain." European urology 43.2 (2003): 158-163.
[6]van Balken MR, Vergunst H, Bemelmans BL. Prognostic factors for successful percutaneous tibial nerve stimulation. Eur Urol 2006;49: 360– 5
[7]Kim, Soo Woong, J-S. Paick, and Ja Hyeon Ku. "Percutaneous posterior tibial nerve stimulation in patients chronic pelvic pain: a preliminary study."Urologia internationalis 78.1 (2007): 58-62.
[8]Gokyildiz S, Kizilkaya Beji N, Yalcin O, Istek A. Effects of percutaneous tibial nerve stimulation therapy o chronic pelvic pain.Gynecol Obstet Invest. 2012;73(2):99–105
[9]Kabay S, Kabay SC, Yucel M, Ozden M. Efficiency of posterior tibial nerve stimulation in category IIIB chronic prostatitis/chronic pelvic pain: a sham-controlled comparative study. Urol Int 2009;83:33–38.
[10]Zhao J, Nordling J: Posterior tibial nerve stimulation in patients with intractable interstitial cystitis. BJU Int 2004;94:101–104.

SECTION 2: ROLES AND EXPERTISE OF THE STUDY TEAM

List all study team members below.

1. Identify each **member's position** (e.g., Associate Professor, graduate or undergraduate student) and **department**, and describe his or her **qualifications, level of training and expertise.** Include information about relevant licenses/medical privileges, as applicable.
2. Describe each team member's **specific role and responsibility** on the study.
3. **Faculty Sponsors** - list as Co-Researchers and describe their role on the project; include oversight responsibilities for the research study.
4. Explain who will have **access to subject identifiable data**.
5. Indicate who will be **involved in recruitment, informed consent process, research procedures/interventions, and analysis of data.**

Lead Researcher:

Felicia Lane, MD: Dr. Felicia Lane is a fellowship trained Urogynecologist, an Associate Professor in the Department of Obstetrics and Gynecology at the University of California-Irvine, Division Director of Urogynecology, and the fellowship director of the Division of Female Pelvic Medicine and Reconstructive Surgery (FPMRS). In this study, she will be responsible for the mentorship of Dr. Emily Adams-Piper as well as the supervision of patient evaluation, selection of suitable candidates, and appropriate conduction of data collection and analysis. Dr. Lane has a large population of patients being treated with PTNS therapy and has considerable experience treating women with urinary incontinence. She will be responsible for identifying eligible patients, informed consent, analysis of data, follow-up, data collection analysis, and manuscript publication and presentation. Dr. Lane will have access to subject identifiable information.

Co-Researchers:

Emily Adams-Piper, MD: Dr. Emily Adams-Piper is a third-year fellow in FPMRS in the Department of Obstetrics and Gynecology at the University of California, Irvine. She will be responsible for all aspects of the study including patient recruitment, education, informed consent, analysis of data, follow-up, data collection analysis, and manuscript publication and presentation. Dr. Adams-Piper will have access to

subject identifiable information.

Sonia Dutta, MD: Dr. Sonia Dutta is a second-year fellow in FPMRS in the Department of Obstetrics and Gynecology at the University of California, Irvine. She will be identifying eligible patients and will be involved in the informed consent process. Dr. Dutta will have access to subject identifiable information.

Neha Talreja: MD: Dr. Talreja is a first-year fellow in FPMRS in the Department of Obstetrics and Gynecology at the University of California, Irvine. She will be involved with all aspects of the study including patient recruitment, education, informed consent, analysis of data, follow-up, data collection analysis, and manuscript publication and presentation. Dr. Talreja will have access to subject identifiable information.

Research Personnel:
Angie Contreras, LVN is a nurse in the division of Urogynecology, Department of Ob/Gyn. She will be involved in data collection and patient follow up. She will have access to subject identifiable information.

Phuong Linh Huynh is the new Assistant Clinical Research Coordinator for the division of Urogynecology, Department of Ob/Gyn. She will be involved in patient recruitment, education, analysis of data, follow-up, and data collection analysis. She will have access to subject identifiable information.

SECTION 3: RESEARCH METHODOLOGY/STUDY PROCEDURES

A. Study Design and Procedures

1. Provide a **detailed chronological description of all study activities** (e.g., pilot testing, screening, intervention/interaction/data collection, and follow-up) and **procedures**.
   a. Include an explanation of the study design (e.g., randomized placebo-controlled, cross-over, cross-sectional, longitudinal, etc.) and, if appropriate, describe stratification, randomization, and blinding scheme.
   b. Provide precise definitions of the study endpoints and criteria for evaluation; if the primary outcomes are derived from several measurements (i.e., composite variables) or if endpoints are based on composite variables, describe precisely how the composite variables are derived.
   c. Indicate how much **time will be required of the subjects**, per visit and in total for the study.
   d. Indicate the **setting where each procedure will take place**/be administered (e.g. via telephone, clinic setting, classroom, via email). ***Note:*** *If any of the procedures will take place at off-campus locations (e.g., educational institutions, businesses, organizations, etc.)* ***Letters of Permission*** *are required.*
   e. If a procedure will be completed more than once (e.g., multiple visits, pre and post survey), indicate **how many times** and the **time span** between administrations.
2. **For studies that involve routine (standard of care) medical procedures:**
   Make clear whether procedures are being done for clinical reasons or for study purposes, including whether the procedures are being done more often because of the study. Use the following guidelines to determine the extent to which standard procedures and their associated risks need to be described in protocol:
   a. If the standard procedure is not explicitly required by the study protocol, the protocol need not describe that procedure or its risks.
   b. If the standard procedure is a main focus of the study (e.g., one or more arms of a randomized study is standard) or is explicitly required by the study protocol, the protocol must include a full description of the procedure and its risks.]
3. It is **strongly recommended** that you include a table of visits, tests and procedures. Tables are easier to understand and may help to shorten long repeated paragraphs throughout the

narrative.

4. If study procedures include collecting **photographs, or audio/video recording**, specify whether any subject identifiable information will be collected and describe which identifiers will be collected, if any.
5. Describe how the **subject's privacy will be protected** during the research procedures. ***Note****: This is not the same as confidentiality (see the Privacy and Confidentiality web page).*
6. Be sure to submit **data collection instruments** for review with your e-IRB Application (e.g., measures, questionnaires, interview questions, observational tool, etc.).

1. Chronological description of all study activities and procedures
This is a single-arm pilot study designed to determine if and by how much percutaneous tibial nerve stimulation (PTNS) decreases the symptoms of interstitial cystitis/painful bladder syndrome (IC/PBS).

The chronological description of study activities is as follows:

Recruitment: This will be a routine visit to the UCI urogynecology division that the patient has scheduled to initiate or continue routine care for their complaints. If the provider identifies the patient as a candidate for PTNS the patient will be given information regarding the study and a consent to review. If desired, the patient will be provided with an informational handout about the study. Patients will have ample time to review the consent form and ask questions.
If the patient elects to proceed and a consent is signed, then the patient will proceed to screening.

Screening: Once consents have been signed, the patients will be assessed by the MD for participation and screened to confirm they meet inclusion and exclusion criteria.
The screening will take approximately 20 minutes, not including routine care.

Pre-treatment (Visit 0): This visit will follow the screening visit. The following materials will be given and tests will be administered:
a) demographic and history survey
b) 24 hour voiding diary
c) visual analog scale (VAS) for bladder pain
d) Pelvic Pain and Urgency/Frequency Patient Symptom Scale (PUF Questionnaire)
e) O'Leary-Sant IC Symptom and Problem Index
f) urine pregnancy test (for all premenopausal subjects)
Questionnaires will be provided and will take 20 minutes to complete. The 24 hour voiding diary will be sent home with the patient and will require approximately 20 minutes spread throughout 1 day.

Treatment (Visits 1-5): Prior to the start of first treatment visit, the subject will return the above forms/questionnaires. These visits will be conducted in the UCI urogynecology clinic. PTNS will be administered by a clinical nurse under physician supervision. This is standard of care in clinical practice. These treatments will occur weekly for 12 weeks total. Treatments will be administered per standard protocol. At all visits, the nurse will inquire regarding any noted adverse reactions to treatment and will have the subject complete a VAS.
Each treatment takes approximately 30 minutes.

Treatment (Visits 6): This treatment visit will be administered in the same fashion and with the same requirements at as all other treatment visits. Following this visit, the subject will be provided with the following forms/questionnaires to complete prior to the subsequent visit:
a) 7-point global response assessment (GRA) scale
b) 24 hour voiding diary
c) visual analog scale (VAS) for bladder pain
d) Pelvic Pain and Urgency/Frequency Patient Symptom Scale (PUF Questionnaire)

e) O'Leary-Sant IC Symptom and Problem Index
The time required for the treatment session and completion of the forms is 45 minutes.

Treatment (Visits 7-11): Prior to the start of seventh treatment visit, the subject will return the additional forms/questionnaires. These visits will continue to be conducted in the UCI urogynecology clinic. PTNS will be administered by a clinical nurse under physician supervision. This is standard of care in clinical practice. Treatments will be administered per standard protocol. At all visits, the nurse will inquire regarding any noted adverse reactions to treatment and will have the subject complete a VAS.
Each treatment takes approximately 30 minutes.

Final Treatment (Visit 12): This visit will be conducted per the routine protocol in visits 1-11, with any adverse reactions noted and a VAS collected. After completion of the visit, the patient will be given the following materials for completion within the subsequent two weeks.
a) 7-point global response assessment (GRA) scale
b) 24 hour voiding diary
c) visual analog scale (VAS) for bladder pain
d) Pelvic Pain and Urgency/Frequency Patient Symptom Scale (PUF Questionnaire)
e) O'Leary-Sant IC Symptom and Problem Index
The time required for the treatment session and completion of the forms is 45 minutes.

Follow-up (Visit 13): This visit will consist of a follow-up clinic visit with the subjects' provider per routine care. If not returned previously, the patient will submit the materials completed after Visit 12. The subject and her provider will review her current symptoms and complaints and create an individualized management plan. At this time, depending on their current symptoms and response to the treatment, the subjects will be offered to continue with PTNS treatments at a standard maintenance interval (typically every 4-6 weeks) or to pursue alternative care outside of the study protocol if no benefit was obtained from treatment. Any additional treatments (PTNS or otherwise) after the 12 sessions of PTNS are not considered part of the study and will be determined by provider and patient per clinical standard of care. At this time, we will offer patients to enroll in post-study follow up. If they choose to continue, they will have a visit 14.
This visit will require 30 minutes.

Post-study Follow-Up (Visit 14) - optional: This visit will occur 12-16 weeks after the last treatment visit and will consist of providing the subject with additional surveys to monitor progression of symptoms and maintenance of potential benefits. The subject will be encouraged to complete these materials through the method of contact she prefers. The following materials will be administered:
a) 7-point global response assessment (GRA) scale
b) 24 hour voiding diary
c) visual analog scale (VAS) for bladder pain
d) Pelvic Pain and Urgency/Freuqency Patient Symptom Scale (PUF Questionnaire)
e) O'Leary-Sant IC Symptom and Problem Index
f) Post-study follow-up survey
The forms will take 20 minutes to complete and the 24 hour voiding diary will require approximately 20 minutes spread throughout 1 day.

Study design-
This a single-arm pilot study.

Study endpoints-
The end point for initial evaluation of data is following 12 treatment weekly treatment sessions of PTNS and completion of a 24 hour voiding diary and repeat surveys. At this time, depending on their current symptoms and response to the treatment, the subjects will be offered to continue with PTNS at maintenance intervals or pursue care outside of the study protocol. We will offer patients to enroll in

post-study follow up as described previously.

All treatment visits will take place in the UCI urogynecology clinic. Enrollment and follow-up visits may take place in the clinic or over the phone if the subject prefers this method of contact.

2. Routine medical procedures:
This study involves a standard of care medical procedure/intervention that will be administered in the standard fashion and frequency as they are performed in non-research settings. The device will not be used concurrently with other medical monitoring equipment and that it will not be used in or around water.

PTNS involves the placement of a thin needle (similar to an acupuncture needle) inserted near the posterior ankle. The needle is then connected to an electrode stimulator and the stimulation is adjusted until appropriate response (toe flex or fan) is obtained without patient discomfort. When at the appropriate level, the electrode is stimulated for 30 minutes per treatment session. The most frequent adverse reaction to PTNS is a small, temporary local reaction (inflammation or pain) at or near the site of needle insertion. (See image below for location of needle insertion; arrow is pointing to device.)

An important point that will be thoroughly explained to subjects during the consent process is that PTNS has been demonstrated to be effective in the treatment of urinary urgency and urinary frequency (inclusion criteria for this study) but has not been studied in the context of the global complaints related to IC/PBS. This investigation is not aimed at providing a new FDA indication for PTNS. It is designed to assess if the subset of patients with urinary urgency, frequency and bladder pain benefit from PTNS therapy.

No photographs, video or audio recordings will be collected as part of this study.

During the consent process prior to participation in this research study, we will inform the subject of all planned contact episodes. We will also request from the subject the preferred method by which to reach them and the general times at which to reach them between the scheduled contact episodes that comprise the study visits. The timing of the contact episodes (i.e. appointment times for treatment and follow up) will be at their discretion, within the constraints of the study personnel and the clinic scheduling.

The subjects' privacy will be protected during PTNS treatment sessions through adherence to the routine protocol of the urogynecology division. PTNS is administered in private treatment rooms by the nurses.

See attached data collection instruments.

Visit #	Visit Name	Intervention	Information Obtained	Materials Provided

	Recruitment	consent for participation	per routine medical care	a) Study consent b) HIPAA consent c) informational handout
	Screening	review of inclusion/exclusion criteria	per routine medical care	
0	Pre-treatment	none	Urine pregnancy test (if patient is premenopausal)	a) demographic and history survey b) 24 hour voiding diary c) visual analog scale (VAS) for bladder pain d) Pelvic Pain and Urgency/Frequency Patient Symptom Scale (PUF Questionnaire) e) O'Leary-Sant IC Symptom and Problem Index
1	Treatment	PTNS	a) adverse reactions b) visual analog scale (VAS) for pain	
2	Treatment	PTNS	a) adverse reactions b) VAS	
3	Treatment	PTNS	a) adverse reactions b) VAS	
4	Treatment	PTNS	a) adverse reactions b) VAS	
5	Treatment	PTNS	a) adverse reactions b) VAS	
6	Treatment	PTNS	a) adverse reactions b) VA	a) 7-point global response assessment (GRA) scale b) 24 hour voiding diary c) visual analog scale (VAS) for bladder pain d) Pelvic Pain and Urgency/Freuqency Patient Symptom Scale (PUF Questionnaire) e) O'Leary-Sant IC Symptom and Problem Index
7	Treatment	PTNS	a) adverse reactions b) VAS	
8	Treatment	PTNS	a) adverse reactions b) VAS	
9	Treatment	PTNS	a) adverse reactions b) VAS	
10	Treatment	PTNS	a) adverse reactions b) VAS	
11	Treatment	PTNS	a) adverse reactions b) VAS	
12	Treatment	PTNS	a) adverse reactions b) VAS	a) 7-point global response assessment (GRA) scale b) 24 hour voiding diary c) visual analog scale (VAS) for bladder pain d) Pelvic Pain and Urgency/Frequency Patient Symptom Scale (PUF Questionnaire) e) O'Leary-Sant IC Symptom and Problem Index
13	Follow-up	None	per routine medical care	
14	Post-study Follow-up	None		a) 7-point GRA scale b) 24 hour voiding diary c) visual analog scale (VAS) for bladder pain d) Pelvic Pain and Urgency/Frequency Patient Symptom Scale (PUF Questionnaire)

				e) O'Leary-Sant IC Symptom and Problem Index f) Post-study follow-up survey

B. Statistical Considerations

1. **Statistical Analysis Plan:** Describe the statistical method(s) for the stated specific aims and hypotheses **described in Section 1**. ***Note:*** *Required for scientific review.*
2. **Explain how the overall target sample size was determined** (Provide power / sample size justification for the study).

If a statistical analysis plan is not appropriate for your study design, please describe a plan for assessing your study results.

This is a pilot study with primary aim to estimate the proportion of patients experiencing moderate or marked improvement in overall symptom score as measured by response to a 7-point global response assessment scale collected after the intervention period. Responders will be defined as those reporting a moderate or marked improvement in symptoms in global response score. We will estimate the proportion of responders with 95% confidence limits, as defined by a response of moderate or marked improvement on the GRA scale collected at follow-up. Pain response will be measured using the Pelvic Pain and Urgency/Frequency Patient Symptom Scale (score total range: 0-35). We will estimate mean (plus standard deviations and 95% CI) for pain score at baseline and follow-up and change in response to therapy, testing for change over time using a paired t-test.

Other secondary outcomes that we will be reviewing are: change in frequency of urinary collected in 24 hour voiding diaries, change in visual analog scale, and change in O'Leary-Sant IC Symptom and Problem Index. These data consist of continuous variables to be described using means, SDs and confidence intervals at baseline and follow-up. Change over time will also be estimated and tested for difference from zero using a paired t-test.

SECTION 4: SUBJECTS (PERSONS/CHARTS/RECORDS/SPECIMENS)

A. Number of Subjects (Charts/Records/Biospecimens)

1. Indicate the **maximum number of subjects to be recruited/consented** on this UCI protocol. This is the number of potential subjects you may need to recruit to obtain your target sample size. This number should include projected **screen failures and early withdrawals**. ***Note:*** *The IRB considers individuals who sign the consent form to be "enrolled" in the research.*
2. For **Mail/Internet surveys** include the number of people directly solicited.
3. If the study involves use of **existing charts, records, biospecimens**, specify the maximum number that will be reviewed/tested to compile the data or the sample population necessary to address the research question.

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4. Of the maximum number of subjects listed above, indicate the **target sample size** for the study. This is the number of subjects expected to complete the study or the number necessary to address the research question.

5. *For social/behavioral research*, the maximum sample size is often similar to the target sample size. If the **maximum sample size** is significantly greater (i.e., ≥ 1.5x) than the **target sample size** provide a justification.
6. For studies where multiple groups of subjects will be evaluated, **provide a breakdown per group** (e.g. controls vs. experimental subjects; children vs. adults; by age group).

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7. For **multi-center research**, indicate the overall sample size for the entire study (across all sites).

[X] Not applicable - This study is not a multi-center research study.

8. Demonstrate that the **target sample size will be sufficient** to achieve the study goal and should coincide with the statistical approach **described in Section 3B**. ***Note:*** *Required for scientific review.*
9. **Sources and information** of assumed group effects and variability should be supplied (e.g., pilot data; data from related literature). ***Note:*** *Required for scientific review.*

This is a pilot study with a primary aim to estimate the proportion of patients experiencing moderate or marked improvement in overall symptom score. With a target sample size of 24 patients, 95% confidence limits will extend ±0.2 from the estimate. If the estimated improvement rate is 60%, the 95% CI will extend from 40% to 80%, indicating that there is a 95% probability that the true percent experiencing moderate or marked improvement is ≥40%. This response rate would be of clinical importance.

The maximum number of subjects to be recruited was determined at 32, assuming a 33.3% rate of exclusion or withdrawal by subjects enrolled in the study that will allow for obtaining the target sample size.

B. Inclusion and Exclusion Criteria

1. Describe the **characteristics and provide justification** for inclusion of the proposed subject population. At a minimum include information about the age and gender of the study population.
2. Describe **different subject groups** (e.g., students and teachers; control group and treatment group(s), children and adults) separately.

University of California-Irvine urogynecology patients, who are exclusively female. In addition IC/PBS disproportionately affects women. The study population will be women 18 years of age and older to enable independent consenting and medical decision making. Our subject population will be most significantly defined by their diagnosis of IC/PBS with the related lower urinary tract symptoms of either urinary frequency or urinary urgency. Subjects will have had to attempt at least one prior treatment for their symptoms.

3. Provide the **inclusion and/or exclusion criteria** for the proposed subject population, as applicable.

[ ] Not applicable – This is not a clinical investigation and/or the characteristics of the population sufficiently describe the proposed subject population.

Inclusion Criteria
- clinical diagnosis of IC/PBS
- complaint of urinary urgency (sudden, compelling desire to pass urine which is difficult to defer) or urinary frequency (voiding >8 times per 24 hour period)
- female
- have undergone at least 1 course of a standard therapy for IC/PBS
- 18 years of age or older

Exclusion Criteria:
- not having undergone at least 1 course of a standard therapy for IC/PBS
- having a pacemaker or implantable defibrillator
- being prone to excessive bleeding
- having nerve damage that could impact the posterior tibial nerve
- pregnant or planning pregnancy during treatment course
- non-English speaking
- current malignancy

4. If **exclusion** is based on age, gender, pregnancy/childbearing potential, social/ethnic group, or language spoken (e.g., Non-English Speakers), **provide a scientific rationale**.

We will be including only women over 18 years of age in our study for the practical reason that subjects will be recruited from the UCIMC urogynecology clinic. We are excluding women who are pregnant or attempting pregnancy based on manufacturer recommendations for the PTNS device. We will be excluding non-English speaking patients given that our survey and validated questionnaires are only in English.

SECTION 5: RECRUITMENT METHODS AND PROCESS

A. Recruitment Methods

Please check **all** applicable recruitment methods that apply to the study. Place an "**X**" in the bracket **[ ]** next to the recruitment method.

[ ] This study involves no direct contact with subjects (i.e., use of existing records, charts, specimens)
- ***Skip to Section 6.***

[ ] UCI IRB approved advertisements, flyers, notices, and/or media will be used to recruit subjects. ***Submit advertisements for IRB approval.***
- Passive Recruitment - Potential subjects initiate contact with the study team.
- ***Complete Question 5B - Explain where recruitment materials will be posted.***

[ ] The study team will recruit potential subjects who are unknown to them (e.g., convenience

sampling, use of social networks, direct approach in public situations, random digit dialing, etc.)

- Active Recruitment – Researchers contact potential subjects.
- ***Complete Question 5B.***

[X] The UCIMC Clinical Trials web page will be used. ***Submit the UCIMC Standard Research Recruitment Advertisement for IRB approval.***

- Passive Recruitment - Potential subjects initiate contact with the study team.
- ***Skip to Section 6.***

[X] The study will be listed on **Clinicaltrials.gov**. ***Note:*** *This is required for all clinical trials.*

- Passive Recruitment - Potential subjects initiate contact with the study team.
- **Skip to Section 6.**

[ ] The UCI Social Sciences human subject pool will be used. ***Submit the Social Science Human Subject Pool Recruitment Advertisement for IRB approval.***

- Passive Recruitment - Potential subjects initiate contact with the study team.
- ***Skip to Section 6****.*

[ ] Study team members will contact potential subjects who have provided permission to be contacted for participation in future research studies.

- Active Recruitment – Researchers contact potential subjects.
- ***Complete Question 5B – Explain when and how these individuals granted permission for future contact; provide the IRB protocol numbers, if applicable.***

[X] Study team members will approach their own patients, students, employees for participation in the study.

- Active Recruitment – Researchers contact potential subjects.
- ***Complete Question 5B.***

[ ] Study team members will send UCI IRB approved recruitment materials (e.g., recruitment flyer, introductory letter) to colleagues asking for referral of eligible participants.*

- Passive Recruitment – Potential subjects initiate contact with the study team or
- Active Recruitment – Colleagues get permission from interested individuals to release contact information to researchers. Researchers contact potential subjects.
- ***For Active Recruitment, complete Question 5B.***

***Note:** Additional requirements for using this recruitment method are included in the Protocol Narrative instructions.*

[ ] Study team members will provide their colleagues with a UCI IRB approved introductory letter. The letter will be signed by the treating physician and sent to his/her patients to inform them about how to contact study team members.

- Passive Recruitment - Potential subjects initiate contact with the study team.
- The IRB approved letter must be sent by the treating physician.
- The study team does not have access to patient names and addresses for mailing.

- ***Skip to Section 6.***

[X] UCI study team members will screen UCIMC medical records to determine subject eligibility and approach patients directly about study participation.*
- Active Recruitment – Researchers contact potential subjects.
- ***Complete Appendix T to request a partial waiver of HIPAA Authorization.***
- ***Complete Question 5B.***

** **Note** Additional requirements for using this recruitment method are included in the Protocol Narrative instructions.*

[ ] Other Methods: <indicate the recruitment method(s) here>
- ***Complete Question 5B, as applicable.***

B. Recruitment Process

1. Based on the methods checked above, describe and provide **details of the recruitment process** (i.e. when, where, by whom and how potential subjects will be approached, e.g. screening medical charts, findings subjects during routine patient visits, etc.).
2. If you will recruit by mail, e-mail, or phone, explain how potential subjects' **contact information will be obtained**.
3. If active recruitment methods will be used (i.e., researchers will make direct contact with subjects for the purpose of recruitment), explain how the individual's **privacy will be protected**. ***Note:*** *This is not the same as confidentiality (see the Privacy and Confidentiality web page).*

Subjects will be recruited during routine patient care by study research personnel in the UCI urogynecology clinics and the UCIMC clinical trials website. If a patient in clinic is thought to be eligible for PTNS and the study, they will be asked if they are interested in learning more about the study, if they would like to discuss it then or at a later time and how they would like to be contacted. The review of the consent form with the subject will take place in a private patient area within the urogynecology clinic in order to maintain privacy of all potential subjects.

Additionally, one of the approved study investigators will pre-screen the physician clinic schedules for the Division of Urogynecology in the Department of Ob/Gyn and identify patients with Interstitial Cystitis/Painful Bladder syndrome who may qualify for the study. The treating physician will be alerted that she has a potential subject on her schedule and will review to see if she feels the patient qualifies. If yes, then the physician will ask the patient if they might be interested in the study and if so, an IRB approved researcher will review the study and consent with them to appropriately enroll the patient.

SECTION 6: INFORMED CONSENT PROCESS

1. Specify **how consent will be obtained** and describe the specific **steps for obtaining informed consent**.
2. Include information about **when and where** consent will take place and the **length of time**

subjects will be given to decide whether they wish to participate.
3. If study team members will approach their own patients, students, or employees for participation in the study, explain what precautions will be taken to **minimize potential undue influence or coercion**, and **how compromised objectivity will be avoided**.
4. If children are involved in this study, please describe the **parental permission** process and the **child assent** process.
5. Be sure to **submit the consent/assent document(s)** with your e-IRB Application (i.e. Study Information Sheet, Recruitment script, Consent Form, etc.).
6. If this study involves the creation, use, or disclosure of Protected Health Information (PHI), specify the process for **obtaining HIPAA Authorization**. Be sure to submit the HIPAA Research Authorization form with your e-IRB Application.

Check all that apply:

[X] Written (signed) informed consent will be obtained from subjects. Signed informed consent, parental permission, and/or child assent will be obtained from subjects, as applicable. ***Describe the informed consent process.***

[ ] Requesting a waiver of written (signed) informed consent (i.e., signed consent will not be obtained)**.** Informed consent, parental permission and/or child assent will be obtained from subjects, as applicable. **Explain how informed consent will be obtained.** ***Complete Appendix P.***

[ ] Requesting a waiver of informed consent (i.e., consent will not be obtained). ***Complete Appendix O. Skip to Section 7.***

The consent process will take place in the UCIMC urogynecology patient offices. Patients will given ample time to review the consent form and HIPAA Research Authorization. Patients will be given the option to take the consent form home for review if desired. Researchers will review with all potential subjects that the care they receive from their physician will not be affected by their decision to or to not participate in this study. All questions will be answered by the co-researchers.

7. **Non-English Speaking Participants:** In order to consent subjects who are unable to read and speak English, the English version of the consent form must be translated into appropriate languages once IRB approval is granted.

Check all that apply:

[X] Not applicable - Only individuals who can read and speak English are eligible for this study.

[ ] The English version of the consent form will be translated into appropriate languages for non-English speaking subjects once IRB approval is granted. An interpreter will be involved in the consenting process. ***Note:*** *The IRB must officially stamp the translated consent forms.*

[ ] Requesting a short form consent process. ***Complete Appendix Q.***
The short form process will be used for the following languages:
[ ] All non-English languages
[ ] All non-English languages except Spanish
[ ] Other languages (specify): <Type here>

SECTION 7: RISK ASSESSMENT AND POSSIBLE BENEFITS

Note: *Review of the instructions for this section is strongly recommended.*

A. Risk Assessment

Place an "**X**" in the bracket **[ ]** next to the level of review (based upon the investigator's risk assessment).

[ ] This study involves greater than minimal risk to subjects and requires **Full Committee review.**

[X] This study involves no more than minimal risk and qualifies as **Expedited research**.
Provide justification below for the level of review and for the applicable Expedited Category(ies) that you have chosen:

Category 9 – Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where Expedited review categories two through eight do not apply but the IRB has determined and documented at a convened meeting (during the initial review) that the research involves no greater than minimal risk and no additional risks have been identified.

B. Risks and Discomforts

1. Describe the **risks/potential discomforts** (e.g., physical, psychological, social, economic) associated with **each** intervention or research procedure.
2. Describe the expected frequency (i.e., **probability**) of a given side effect or harm and its severity (e.g., mild, moderate, severe).
3. If subjects are **restricted from receiving standard therapies** during the study, describe the risks of those restrictions.
4. If collecting identifiable private information, address the risk of a **potential breach of confidentiality**.

PTNS is typically very well tolerated with minimal side effects. The more common physical risks associated with PTNS treatment are low. The most common side-effects include:

- transient mild pain or discomfort at or near the stimulation site
- skin inflammation at or near the stimulation site.

In the experience of our clinic, the probability of this kind of mild reaction is low (<10% of the time). Subjects must be positioned before each treatment so as to minimize positional discomfort during the 30 minute treatment session.

Rare, but potentially serious risks as stated by the device manufacturer, include

- bleeding or hematoma at the needle site
- numbness of the toes
- stomach ache

Additional risks to be included in the consent form are:
Unknown risks: There may be risks related to the research that we don't know about yet. The subjects will

be informed of any additional risks to which they might be exposed, and any changes that are made to the study, as a result of any newly identified risks.
Reproductive Risks: Subjects will be informed that they should not get pregnant while in this study. The PTNS therapy used in this study has not been evaluated in pregnant women and while no specific risks are anticipated, it is not recommended to become pregnant while receiving PTNS therapy. It will be suggested that subjects check with the researchers about what types of birth control, or pregnancy prevention, to use while in this study.

While subjects will be restricted from receiving new additional standard therapies during the course of the study, there is very limited risk associated with this because they will only be restricted during the course of the study protocol. Patients will be permitted to continue standard of care oral medical therapies (such as pyridium, Elmiron, or other medications considered second line in the AUA guidelines for treatment of IC/PBS) if they had been receiving this medication prior to enrollment in the trial protocol. If they so choose, they will be able to receive any other additional indicated treatments immediately following conclusion of the trial protocol. If they choose to withdraw from the study in order to receive another indicated (standard) therapy that will be noted and included in our results. Any subject who withdraws will be offered an appointment with her physician.

PHI will be collected as part of this study. Breach of confidentiality is a theoretical risk.

5. Discuss what steps have been taken and/or will be taken to **prevent and minimize** any risks/ potential discomforts to subjects (address physical risks as well as other risks such as the potential for a breach of confidentiality). Examples include: designing the study to make use of procedures involving less risk when appropriate; minimizing study procedures by taking advantage of clinical procedures conducted on the subjects; mitigating risks by planning special monitoring or conducting supportive inventions for the study.

All subjects will be carefully monitored throughout the study protocol. They will have weekly visits with a trained, urogyneology practitioner who will be administering the PTNS treatments. This provider is qualified to assess and triage complaints related to the PTNS procedure and will contact the appropriate research physician if additional assessment is indicated. The practitioner administering the PTNS treatments will work with the subject, in the standard fashion for PTNS, to minimize any transient discomfort during the treatments.

Subjects may return to UCIMC urogynecology clinic for additional visits outside of the study protocol at their own discretion, if there are any complaints they feel need to be assessed by a physician. We will work to minimize inconvenience associated with study participation by allowing the subject to schedule the PTNS treatments at the time most convenient for them, within clinic scheduling ability.

We will prevent any possible risks to the subjects from breach of confidentiality through the methods outlined in Section 12.

C. Potential Benefits

1. Discuss the potential benefits that may accrue **directly to subjects.** ***Note:*** *Compensation is not a benefit. Do not include it in this section.*

[ ] There is no direct benefit anticipated for the subjects.

OR

There is no guarantee to subjects that they will benefit directly from participating in this study and all subjects will be informed of this during the consent process. The subject may experience an improvement in her IC/PBS symptoms because of the treatment intervention with PTNS. If the subject does experience improvement in symptoms, they may derive direct benefit by avoiding other, more invasive interventions for the treatment of this condition.

If the subject completes 12 treatment visits and returns the subsequent 24 hour voiding diary and questionnaires, they will receive a $50 check as a stipend.

2. Describe the **potential societal/scientific benefit(s)** that may be expected from this study.

Information obtained from this study will benefit the urogynecologic, urologic and medical communities in determining if additional studies investigating the use of PTNS for the treatment of symptoms related to IC/PBS is useful. If the study intervention is found to be efficacious, this could be a significant contribution to the management of this chronic disease. If the study intervention is not found to reduce symptoms, additional information about the pathophysiology of the disease and the mechanism of action of both PTNS and SNM may be obtained. This will also allow for future research to be better directed elsewhere.

D. Risk/Benefit Assessment

Explain why the study risks are reasonable in relation to the **potential benefits** to subjects and society.

This study has the potential to evaluate if a minimally invasive, rapid, outpatient treatment may be useful in the treatment of the complex disease of IC/PBS. There are few risks associated with the study. Procedure associated risks as outlined in section 7.B. are rare and typically mild and transient. These are the same possible treatment risks if the patient elected to undergo treatment with PTNS as standard of care for their symptoms. Study specific risks are minimal and related to possible breach of confidentiality. Given that few procedure and study risks (and very few serious risks) have been reported in studies examining our treatment intervention (PTNS) for other indications, the potential to add a new treatment to the armamentarium with which to approach IC/PBS has significant value to contribute to society while exposing the subjects to minimal risk. PTNS is a proven (and FDA-approved) treatment for the symptoms of urinary urgency and frequency, both of which are hallmarks of IC/PBS. Patients with urinary urgency or frequency and IC/PBS may benefit from the targeted treatment of such symptoms with PTNS. If PTNS is ultimately effective in treating these and other symptoms of IC/PBS, the subjects in the study will have benefited from receiving this intervention and society will benefit from added information to the scientific literature to guide future research.

SECTION 8: ALTERNATIVES TO PARTICIPATION

1. Describe the **standard or usual care** activities at UCI (or study site) that are available to prospective subjects who do not enroll in this study, as applicable.
2. Describe other **appropriate alternative procedures** to study participation that are available to prospective subjects.
3. If no alternatives exist, indicate that the only alternative is non-participation

[ ] No alternatives exist. The only alternative to subjects is not to participate in the study.

OR

Subjects will be informed that it is not necessary for subjects to participate in this study in order to treat their IC/PBS. Subjects will also be informed that there are other treatments available in the community including physical therapy techniques and pharmacotherapies with side effects and efficacy that may be equivalent to, better or worse than what the subject may experience in this study. This will be discussed prior to enrollment into the study. If patients choose not to enroll in this study but have symptoms for which PTNS is indicated, they may still receive this as a possible therapy.

SECTION 9: ADVERSE EVENT REPORTING/MANAGEMENT AND COMPENSATION FOR INJURY

A. Adverse Events and Unanticipated Problems

1. Indicate that you are familiar with **UCI's Adverse Events/Unanticipated Problems** reporting policy and procedures. See http://www.research.uci.edu/compliance/human-research-protections/researchers/reporting-of-adverse-events-unanticipated-problems-and-violations.html for details.

[ ] Although this study involves no interaction/intervention with research subjects (i.e., involves the use of records, charts, biospecimens) an unanticipated problem may still occur (e.g., a breach in confidentiality), the researchers are aware of UCI's Unanticipated Problems involving Risk to Participants or Others reporting policy and procedures and will comply with this policy.

[X] This study involves interaction/intervention with research subjects. The researchers are aware of UCI's Unanticipated Problems involving Risk to Participants or Others reporting policy and procedures and will comply with this policy.

2. **If this study involves interaction/intervention with research subjects,** explain how the research team will **manage adverse events and unanticipated problems** that may occur during the study or after completion of the study (i.e., provide a plan).

[ ] Not applicable - This study involves **no interaction/intervention** with research subjects (i.e., involves the use of records, charts, and/or biospecimens).

OR

If an adverse event occurs during the study, the steps are as follows:

1) Subject informs the physician, clinic nurse or another research team member of the possible adverse event.
2) Study physician determines if it is, in fact, an adverse event that is related to the study protocol.
3) Physician decides an appropriate medical response within a reasonable timeframe. This includes coordinating urgent care if indicated.
4) The adverse even is reported appropriately within the timeframe noted below depending on the nature of the adverse event.

Unexpected, related adverse events will be reported to the IRB via the electronic, online reporting process as soon as possible, but not later than 10 working days after the research team first learns of the event. Serious adverse events will be reported in the same manner as soon as possible but not later than 48 hours after the researcher first learns of the event, followed by any follow-up reports as applicable.

All adverse events will be followed to appropriate resolution. Where appropriate, medical tests and examinations are performed to document resolution of event(s).

B. Compensation for Injury

For **Full Committee protocols**, explain how costs of treatment for research related injury will be covered.

[ ] Not applicable - This study involves no more than minimum risk and qualifies as **Expedited research**.

[X] Researchers are familiar with and will follow UC policy regarding treatment and compensation for injury. If subjects are injured as a result of being in the study, UCI will provide necessary medical treatment. The costs of the treatment may be covered by the University of California, the study sponsor, or billed to subject or the subject's insurer just like other medical costs, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury.

[ ] Other: <Type here>

SECTION 10: PARTICIPANT COSTS

1. If subjects or their insurers will be charged for study procedures, **identify and describe those costs.**
2. Explain why it is **appropriate to charge those cost** to the subjects or their insurers. Provide supporting documentation as applicable (e.g., FDA Device letter supporting charges).

[ ] Not applicable - This study involves no interaction/intervention with research subjects (i.e., involves the use of records, charts, biospecimens).

[ ] There are no costs to subjects/insurers.

OR

PTNS is an FDA approved device for the treatment of "urinary urgency, urinary frequency and urge incontinence." It is typically a covered benefit of health insurance as a second line treatment for these complaints and all subjects will be required to qualify for PTNS based on the FDA approved indications of urinary frequency and urgency.

SECTION 11: PARTICIPANT COMPENSATION AND REIMBURSEMENT

1. If subjects will be compensated for their participation, explain **the method/terms of payment** (e.g., money; check; extra credit; gift certificate).
2. Describe the **schedule and amounts of compensation** (e.g., at end of study; after each session/visit) including the total amount subjects can receive for completing the study.
3. Specify whether subjects will be **reimbursed for out-of pocket expenses**. If so, describe any requirements for reimbursement (e.g., receipt).

Note: *Compensation should be offered on a prorated basis when the research involves multiple sessions.*

[ ] Not applicable - This study involves no interaction/intervention with research subjects (i.e., involves the use of records, charts, biospecimens).

[ ] No compensation will be provided to subjects.

[X] No reimbursement will be provided to subjects.

OR

If the subject completes 12 treatment visits and returns the subsequent 24 hour voiding diary and questionnaires, they will receive a $50 stipend (cash or gift card). No other compensation or stipends will be provided for in the study.

SECTION 12: CONFIDENTIALITY OF RESEARCH DATA

1. Indicate all identifiers that may be included in the research records for the study. Check all that apply:

   Note: *If this information is being derived from a medical record; added to a medical record; created or collected as part of health care, or used to make health care decisions it qualifies as PHI under HIPAA. The subject's HIPAA Research Authorization is required or a waiver of HIPAA Authorization must be requested (Appendix T).*

[ ] No subject identifiers are obtained (i.e., researchers will not collect information that can link the subjects to their data)

OR

[X] Names	**[ ]** Social Security Numbers	**[ ]** Device identifiers/Serial numbers
[X] Dates*	**[X]** Medical record numbers	**[ ]** Web URLs
[X] Postal address	**[ ]** Health plan numbers	**[ ]** IP address numbers
[X] Phone numbers	**[ ]** Account numbers	**[ ]** Biometric identifiers
[ ] Fax numbers	**[ ]** License/Certificate numbers	**[ ]** Facial Photos/Images
[ ] Email address	**[ ]** Vehicle id numbers	**[ ]** Any other unique identifier

[ ] Other (Specify all): <Type here>

* birth date, treatment/hospitalization dates

2. Explain how data will be **recorded.**

Check all that apply:

[X] Paper documents/records
[X] Electronic records/database
[ ] Audio recording
[ ] Video recording
[ ] Photographs
[ ] Biological specimens
[ ] Other(s) (specify): <Type here>

3. Indicate **how data will be stored, secured** including paper records, electronic files, audio/video tapes, biospecimens, etc.

Note: *If the research data includes subject identifiable private information and/or Protected Health Information, the storage devices or the electronic research files must be encrypted.*

Electronic Data (check all that apply):
[X] Coded data; code key is kept separate from data in secure location.
[ ] Data includes subject identifiable information. ***Note:*** *Encryption software is required.* (Provide rationale for maintaining subject identifiable info)**:** <Type here>
[X] Data will be stored on secure network server.
[ ] Data will be stored on stand alone desktop computer (not connected to network/internet)
[ ] Other (specify here): <Type here>

Hardcopy Data, Recordings and Biospecimens (check all that apply):
[ ] Coded data; code key is kept separate from data in secure location.
[ ] Data includes subject identifiable information (Provide rationale for maintaining subject identifiable info)**:** <Type here>
[X] Data will be stored in locked file cabinet or locked room at UCI/UCIMC.
[ ] Data will be stored locked lab/refrigerator/freezer at UCI/UCIMC.
[ ] Other (specify here): <Type here>

Data on Portable Devices:
4. Describe the **portable device(s) to be used** (e.g. laptop, PDA, iPod, portable hard drive including flash drives).
5. Specify whether **subject identifiable data** will be stored on the device. If so, **justify why** it is necessary to store subject identifiers on the device.

Note: *Only the "minimum data necessary" should be stored on portable devices as these devices are particularly susceptible to loss or theft. If there is a necessity to use portable devices for initial collection of identifiable private information, the portable storage devices or the research files* ***MUST BE ENCRYPTED****, and subject identifiers transferred to a secure system as soon as possible.*

[X] Not applicable – No study data will be maintained on portable devices.

Data Access:

6. Specify who, besides the entities listed below, will have **access to subject identifiable private data and records**.
7. If there is a **code key**, specify who on the research team will hold the key, and who will have access to the key.
8. If publications and/or presentations will include **subject identifiable information**, specify where the data will be **published and/or presented** and address how the study team will obtain permission from subjects.

Note: *Authorized UCI personnel such as the research team and the IRB, the study sponsor (if applicable), and regulatory entities such as the Food and Drug Administration (FDA) and the Office of Human Research Protections (OHRP), may have access to study records to protect subject safety and welfare. Any study data that identifies the subjects should not be voluntarily released or disclosed without the subjects' separate consent, except as specifically required by law. Publications and/or presentations that result from this study should not include subject identifiable information; unless the subject's separate consent has been obtained.*

[ ] Not applicable – No subject identifiers will be collected.
[X] Not applicable – Only the entities listed above will have access to subject identifiable private data and records.

<Type here>

Data Retention:

9. Explain **how long subject identifiable research data** will be **retained**. The data may include a code with a separate code key or the data may include subject identifiers.

Notes:

- ***If more than one of the options below is applicable*** *[e.g., the study involves children],* ***records should be kept for the longer period****.*
- *Research documentation involving Protected Health Information (PHI) should be retained for six years (e.g., IRB documentation, consent/assent forms –* ***NOT*** *the actual PHI). Investigators must destroy PHI at the earliest opportunity, consistent with the conduct of this study, unless there is an appropriate justification for retaining the identifiers or as required by law.*

[ ] Not applicable. No subject identifiable research data will be retained.

[ ] Destroy once data collection is completed

[ ] Destroy at the earliest opportunity, consistent with the conduct of this research. Specify timeframe: <Type here>

[X] Destroy after publication/presentation

[ ] Maintain for approximately <Type here> years. (e.g., 3 months, etc.)

[ ] Maintain in a repository indefinitely. Other researchers may have access to the data for future research. Any data shared with other researchers, will not include name or other personal identifying information. Note: ***Appendix M is required.***

[ ] Research records will be retained for seven years after all children enrolled in the study reach the age of majority [age 18 in California] as this study includes children .

[ ] Research records will be retained 25 years after study closure as this study involves in vitro fertilization studies or research involving pregnant women.

[ ] As this is a FDA regulated study, research records will be retained for two years after an approved marketing application. If approval is not received, the research records will be kept for 2 years after the investigation is discontinued and the FDA is notified.

[ ] Other: <Type here>

Data Destruction:

10. If audio or video recordings will be taken, specify the **timeframe for the transcription and/or destruction of the audio and video recordings.**
11. If photographs will be collected, specify the **timeframe destruction of photographs.**

[X] Not applicable – No audio/video recordings or photographs will be collected.
[ ] Audio or video recordings transcribed; specify time frame: <Type here>
[ ] Audio or video recordings destroyed; specify time frame: <Type here>
[ ] Audio or video recordings maintained indefinitely
[ ] Photographs destroyed; specify time frame: <Type here>
[ ] Photographs maintained indefinitely

Certificate of Confidentiality:

12. Specify whether a Certificate of Confidentiality (COC) has been or will be requested from the NIH. If yes, explain in what situations personally identifiable information protected by a COC will be disclosed by the UCI study team.

Note: *If the COC has been secured a copy of the COC Approval Letter should accompany the IRB application or be provided to the IRB upon receipt.*

[X] Not applicable – No COC has been requested for this study.