Optimal Frequency Used in Transcutaneous Electrical Nerve Stimulation (TENS) for Treating Pelvic Pain in Adults

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A. STUDY BACKGROUND AND PURPOSE

Pelvic pain can be a debilitating and often frustrating condition as its origin is not always known. Pelvic pain can present as interstitial cystitis/bladder pain syndrome, sexual pain syndrome, prostate pain syndrome, scrotal pain syndrome, urethral pain syndrome, vaginal and vulvar pain syndromes, myofascial pain syndromes, and prolapse/incontinence mesh pain. These conditions can be multidisciplinary in nature involving overlap of etiology: urologic, gynecologic, gastroenterological, neurologic and even psychiatric. There are dozens of etiologies of pelvic pain, and causes can be multiple or unknown (1).

Each different pain modality has potential treatment targets. Historically treatments have been differentiated, rather than on etiology, but with a blanket approach: anti-inflammatories such as steroids or NSAIDs if pain was of the "-itis" etiology and treated with antibiotics if presumed to be of an infectious nature (4). We currently know much more about pain as a disease state and as we continue to unravel more about chronic pelvic pain. Treatment modalities have likewise become more accurate in their scope. Currently the AUA/EAU has treatment specific guidelines for how to algorithmically approach each different lineage of pelvic pain based on its origin and likely nature of the primary cause. Some modalities of pain have more rigorous data then others for their treatment. However, one new emerging therapy for the treatment of pelvic pain across many etiologies is the use of the TENS unit and transcutaneous stimulation of the posterior tibial nerve (1,3,4). The literature on the use of this modality for pelvic pain is still emerging. Traditionally TENS units in chronic pain have been extensively studied to show benefit in conditions such as knee, back, shoulder and even menstrual pains. Less studied is the use of TENS units as a noninvasive and low risk modality to help alleviate chronic pelvic pain of heterogeneous etiologies. Importantly, it also puts control into the participants' hands, can be used as an adjunct to existing strategies, and expands the options for regaining quality of life.

A systematic review identified 8 Randomized controlled trials, 1 Crossover trial, 4 Randomized trials, 18 Prospective cohort studies, 5 Retrospective case series investigating neuromodulation for pelvic pain, including implanted sacral nerve stimulators, needle-based posterior tibial nerve stimulators, and transcutaneous TENS units. The 8 RCTs showed a significant reduction in pain following twelve weeks of treatment for pain conditions including dysmenorrhea and chronic pelvic pain by a variety of objective and subjective measures. However, there appeared to be conflicting evidence when it came to QoL measures. The beneficial effects specifically of a course of TENS may be sustained beyond 12 weeks; one study showed a persistent benefit at 43 months in 73% of men with chronic pelvic pain and another demonstrated a prolonged significant improvement in women with provoked vestibular pain at ten months post-trial for those who opted to continue therapy. Overall, there were few adverse events cited. In sum, neuromodulation in general and TENS in particular have been shown to be successful for chronic pelvic pain (3). Stronger data, however, is needed, in particular for the non-invasive transcutaneous electrical nerve stimulation as an option for participants with chronic pelvic pain. Its applications in general have not been explored fully and specifically the technical parameters – settings and placement sites - have not been delineated for optimal results.

Placement: The studies in the table below have used TENS or some other form of neuromodulation for chronic pelvic pain. One used the posterior tibial nerve transcutaneously, and many others used the sacral region or pelvic region (15,16,17). Based on a recent study in manuscript submission demonstrating superior outcomes for posterior tibial placement in bedwetting, we will study the tibial site of application.

Our proposal is to study pain outcomes with different frequencies of stimulation. We will employ the posterior tibial nerve location and by varying the frequency (pulse rate, Hz) will identify the most effective setting for pelvic pain modulation by application of a TENS Unit. We will use a fixed pulse width of 200 microseconds, with continuous rather than biphasic stimulation, based on expert input from 5 colleagues with experience in electrophysiology and usage of TENS. Frequencies and pulse widths previously studied are summarized as follows (3):

Study	Frequency (Pulse Rate, Hz)	Width (Pulse Width, Microseconds)	Amplitude	Comments	Effect
Bai	2–100			Transcutaneous Posterior Tibial, Dysmenorrhea, frequency not controlled or compared	Efficacious for Dysmenorrhea
Lauretti	85		variable	Transcutaneous Suprapubic, Dysmenorrhea	Efficacious for dysmenorrhea pain and QOL
Lee	100	100		TENS lower abdomen and thermotherapy for Dysmenorrhea	Efficacious for dysmenorrhea pain and QOL
Buffenoir	100-200	1.4-8.7		Implanted spinal cord stimulation for pudendal neuralgia	Efficacious for decreasing pain
Comiter	16	210		Sacral nerve stimulation, Interstitial cystitis	Effective to reduce pain
Ghazwani	14	200		Sacral nerve stimulation, Bladder pain syndrome	Effective to reduce pain

Kaplan	100	95	50	TENS, Dysmenorrhea,	Effective for pain
Kim	20		10	PTENS(Percutaneous electrical nerve stimulation), chronic pelvic pain	May be helpful for pain but was not statistically significant
Maher	15	210		Percutaneous S3 Sacral Nerve Stimulation, Interstitial Cystitis	Improved pelvic pain, nocturia
Schneider	80	150		Transcutaneous penile electrodes, pain scale and QOL	Reduced pain and increased QOL
Tugay	120	100		Transcutaneous Lower Back, Dysmenorrhea	Not statistically significant for dysmenorrhea
Vallinga	80	50-180		TENS (Location not specified), Vestibulodinia	Reduced Vulvar pain
Van Balken	20	200	0-10	Percutaneous, Posterior tibial nerve, Chronic pelvic pain	Reduced pain and improved QOL

The goal of the current study is to determine which pulse rate (Hz) is the most effective to use in posterior tibial transcutaneous electric nerve stimulation for treating pelvic pain given a set location (posterior tibial nerve) and Pulse Width (200 microseconds) on continuous stimulation.

Specific Aim: To determine if a low (Group 1, 20 Hz), medium (Group 2, 50Hz), or high (Group 3, 100 Hz) pulse rate (frequency) used in posterior tibial TENS is better in improving pelvic pain (as measured by decreased Visual Analog Scale (VAS) scores and improved pain, urinary and QOL scales on the validated Genitourinary Pain Index (GUPI).

Hypothesis: A high frequency (100 Hz) used in TENS will show the most improvement in pelvic pain compared to low and medium frequencies.

B. STUDY DESIGN

Adults ages 18-90 years old referred to the Urology and Multidisciplinary Pelvic Health clinics at Albany Medical Center for chronic refractory pelvic pain will be screened for enrollment and offered participation. Participants who have first been given the standard of care therapy

according to the AUA/EUA guidelines depending on their specific pain modality, first line treatments based on suspected etiology (for example pelvic floor physical therapy for high tone pelvic floor muscle dysfunction or amitriptyline for interstitial cystitis) without success will be defined as refractory. Participants who have plateaued on their response to current intervention strategies will be offered the TENS unit as an adjunct.

Participation will be offered by mail or in person. If by mail, we will send the consent with the letter and questionnaires asking participants to call or bring the material if they would like to enroll. If we speak to the subject over the phone, we will discuss the study as comprehensively as if they were in the clinic. This will include explaining the concept of the TENS unit, the study itself, and clarifying any questions the participant has. Subsequently if they are interested in the study, we will ask them to sign the consent and return it to us via mail or email. Once we receive the consent we will sign and document the reason for the difference in signature dates.

Those whose pain symptomatology is above a threshold and who choose TENS therapy will be included in the study (4). Participants who have recently initiated new pharmacologic treatment or alternative therapy for pelvic pain (or related urologic disorders) within the past 30 days, who cannot work a TENS unit, or who report prior use of a TENS unit or other neuromodulation for chronic pain, and those who have any contraindications to usage of a TENS unit (such as having a pacemaker or an adhesive allergy) will be excluded.

The participants will be randomized into three groups of 25 participants each. The randomization will occur in blocks so that if we need to terminate the study early there will be an equal number of participants in each group. The size of the blocks will also be kept secret for allocation concealment purposes. The randomization will be stratified by gender so that there is an equal number of participants from each gender in each group, reducing potential for gender as a confounding variable. Group 1 will be the low frequency set at 20 Hz. Group 2 will be the medium frequency set at 50 Hz. Group 3 will be the high frequency set 100 Hz. There is no sham group in this study as it has previously been found that posterior tibial TENS is effective and lasting. As such, all participants will be treated as a matter of routine medical care for pelvic pain. We will use a fixed pulse width of 200 microseconds (uS), with continuous rather than biphasic stimulation based on input from 5 colleagues with expertise in neurophysiology and TENS and on the above literature review. We will aim to recruit 25 participants per group for a total of 75 participants.

Study Procedures

Participants with chronic/persistent pain that has been continuous or recurrent for at least three months (in accordance with EAU Guideline definition) who have failed first line treatment will be advised of the study. All participants will be asked if they have an adhesive allergy and medical record reviewed for this allergy as this will exclude them from the study. A detailed explanation of the purpose of the study, along with the risks and benefits of TENS will be given to the participant by a provider prior to obtaining informed consent for enrollment into the study. After informed consent has been obtained, if the participant is of childbearing potential, a urine pregnancy test will be conducted. The participant will be excluded from participation if pregnant and referred for appropriate care.

Study Schedule Overview:

	Standard Visit Billed in Part to Insurance	Just a Study Visit	Virtual Phone or Video is an Option	In Person Only	Questionn-aires: 1-10 pain scores and GUPI	Usage Chart Completed (During phase when TENS being Used)	Treatment Map Completed / Updated with Dates	Adjusting TENS Settings Permitted	New Treatments outside of pre-existing treatment and TENS Permitted
Week 1 – Phone Call in Response to Mailer		√	√		√		√		
Week 1 – Occurring as Part of Regular Office Visit	√		√		√		√		
Week 2	√			√	√				
Week 3		√	√		√	√	√		
Week 4	√		√		√	√	√		
Optional Week 8		√	√		√	√	√	√	√
Optional Week 12		√	√		√	√	√	√	√
Optional Week 16	√		√		√	√	√	√	√

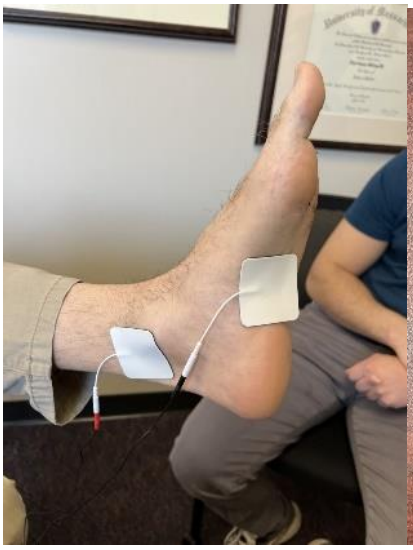
Screening Day 7/ Week 1 (in clinic or virtual): The first data points (Day 0) will take place in the clinic during the participant's routine visit or at the time of the participant's phone call seeking participation. If during a phone call seeking participation, this will be considered a study phone call, not a billable visit. The participant will fill out the VAS and GUPI. The participants will be taught how to fill out the pain assessment questionnaires (the VAS and GUPI, validated tools for measuring genitourinary pain and symptoms respectively). This can be done via paper to be brought into the office at their next checkup or via an emailed link through Qualtrics and uploaded to a spreadsheet in a protected AMC OneDrive. The baseline pain logs will be reviewed for sufficient severity of pain episodes and the participant will be randomized into the study if their pain is above the designated threshold: participants who record a pain scale of 4 or higher on any of the VAS scores or QOL score of 3 or higher on the GUPI question #9 will be eligible for the TENS study. Those who record lower scores will be ineligible for the TENS study but will be offered therapy in according to the AUA/EUA guidelines using the recommended second or third line therapies for their specific pain etiology, including a trial of a TENS unit.

The GUPI and VAS will be collected at this time; this will record the participant's pain 1 week prior to the study and will be considered Day 7/week 1. The week 1 of screening will be combined with the first week of baseline measurement (week 2) for a 2-week lead-in. Participants will be taught how to complete a usage log (stating if the TENS was used each day and for how long in minutes) and will be asked to repeat this weekly. Participants will complete

an inventory (the Treatment Map) of treatments tried prior to the TENS, throughout the study, and at the end.

Baseline Day 14/ Week 2: If the participant enrolls, they will be asked to continue logging pain (VAS and GUPI, on paper or via Qualtrics) for one week, with the week 1 screening and the week 2 baseline week totalling a 14-day control period. The control period will represent data (2 weeks of VAS and GUPI) with only baseline treatments and no TENS unit.

At week 2 (the end of the 2-week baseline, in person), participants will hand in scores and be randomized to a frequency. Part of this 60-minute visit will be considered standard of care, a level 3, 20-minute educational visit on a commonly used treatment option. They will be given a TENS unit and taught how to use the unit. Teaching will include positioning of electrodes, as well as what buttons they are allowed to manipulate. The TENS unit settings will be pre-determined at the clinic and measures will be taken to ensure that the settings cannot be altered at home. The participant will be instructed not to open the TENS unit during the 2 treatment weeks of the study to ensure the settings are maintained. They will be instructed to continue only their baseline treatments.



Settings: The TENS unit used is a Compass Health TENS 3000, 3 mode Analog Unit. The participants' TENS unit will be set at Normal Mode (N), a pulse width of 200 microseconds and an intensity to be determined in the office based upon when the participant feels sensitive to the TENS unit. Frequency (pulse rate) will be determined by randomization. The participant will place the electrodes along the posterior tibial nerve on the medial ankle with a ground on the inner arch, each day for 30 minutes for a total of 14 days at the time of day typically associated with the worst pain or at the first opportunity for rest after this time.

Group 1 will be the **low** frequency group. This means that the TENS therapy will use a frequency of 20 Hz.

Group 2 will be the **medium** frequency group. This means that the TENS therapy will use a frequency of 50 Hz.

Group 3 will be the **high** frequency group. This means that the TENS therapy will use a frequency of 100 Hz.

Participants will be provided the TENS unit, its manual, and enough patches to last the 2 weeks of the treatment period. Participants will be given a weekly usage log, weekly pain VAS and weekly GUPI questionnaire logs again for 2 weeks they are actively using the TENS, with the option of paper or Qualtrics. In this log, the rating of pain by VAS and GUPI, the rating of genitourinary symptoms by GUPI, duration of TENS therapy, usage for every day of the week and adverse reactions to the TENS unit (rash) will be recorded.

Participants may be called during the 14-day treatment period to keep on track, address any concerns, questions, or any adverse reactions to TENS therapy by the physician or research staff. Their phone numbers will be maintained in the master key associated with the deidentified database in the AMC Onedrive protected research file for this purpose.

At 7 days and the end of the 14-day treatment period the visit can be performed either virtually or in the office. The 7-day visit will be considered purely a study visit and the 14 day visit a standard of care visit.

The completed week 3 and 4 VAS and GUPI, treatment usage documents will be returned. The participants will also be asked the question “Will you continue using TENS therapy for your pelvic pain?” Any persistent issues will be addressed during these visits as well and further options discussed.

For those who would like to continue the TENS unit, participants will be taught how to adjust settings and sites at home. Participants will be given repeat VAS and GUPI at 1, 2, and 3 months post-initial phase and seen again at 3 months as part of standard care. Here we will review logs of what frequency patterns they developed with TENS usage on their own, if any. In this time participants may increase or decrease the frequency of their device anywhere in the range of 2 Hz to 150 Hz to see which they prefer most in this part of the trial. Participants will also be allowed to adjust pulse width (30 to 260 *u*S), mode (B N M), time (continuous, 15, 30 minutes), and intensity (1 to 8, 10-80mA) as desired. The only requests will be that they remove the device if any discomfort occurs and that they log their settings versus their response.

Note:
TREATMENT MODE (B, N, M):
Normal (Continuous, Conventional) TENS offers the practitioners complete control over all the various treatment parameters of the instrument. **Burst** Mode is analogous to the Low Rate TENS technique except the low frequency individual pulses are replaced by individual "bursts" of 7-10 individual pulses. It is thus a combination of Conventional TENS and Low Rate TENS. In Burst Mode, the treatment frequency is fixed by the instrument and is not adjustable with the Frequency Rate control. Participants will be educated about this. **Modulated** Mode attempts to

prevent nerve accommodation by continuously cycling the treatment intensity. When using Modulated Mode increase the intensity only when the unit is at the maximum intensity of the modulation cycle. If the intensity is increased during a low intensity period of the cycle, the participant may turn up the control very slowly, so that they may feel the intensity any higher.

In a future study we will want to look at Normal (more like massage) versus Modulated mode (more like acupuncture).

C. SUBJECT POPULATION (WHO, WHAT, WHERE)

Inclusion criteria for cases:

1. Age 18-90 years of age seen at Albany Medical Center Division of Urology
2. Presenting with chronic pelvic pain (chronic/persistent pain that has been continuous or recurrent for at least three months (in accordance with EAU Guidelines).
3. Unsuccessful initial interventions based on initial assessments
4. Ability to provide informed consent and complete study requirements
5. Ability to complete a comprehensive history (including with an interpreter)

Exclusion criteria for cases:

1. Participants who have previously tried a new pharmacologic treatment for pelvic pain, neuromodulation or other alternative therapy for urologic disorders within the past 30 days
2. Inability to work a TENS unit
3. Any contraindications to usage of a TENS unit (pacemaker or other implantable device, lymphedema, pregnancy, malignancy, bleeding or clotting disorders, unhealthy tissue, seizure disorders, impaired cognition)
4. Any history of electrophysiologic heart disease or complications
5. Source of pain being an obvious anatomic issue requiring alternative treatment – for example urethral diverticulum, distal ureteric stone.
6. Participant who is pregnant
7. Participant with adhesive allergy either reported by the participant or upon chart review

D. DATA ANALYSIS

The data collection list is attached to the protocol. The data will be collected on a deidentified excel spreadsheet by participant study number and the deidentified data will be entered into the database. The source documents and informed consents will be kept in the locked Urology Research Office. Qualtrics data will be downloaded onto a secure excel spreadsheet that will immediately be uploaded to the secure urology one drive. Paper responses will be entered to this spreadsheet manually.

The objective of this study is to evaluate which pulse rate (frequency) is the most efficacious in transcutaneous electric nerve stimulation (TENS) as a therapeutic option for pelvic pain. The

proposed study will be a randomized clinical trial. There will be three treatment arms with no sham or control:

- 1. Group1: TENS frequency is set to 20 Hz
- 2. Group2: TENS frequency is set to 50 Hz
- 3. Group3: TENS frequency is set to 100 Hz

The study will be conducted for a total of 4 weeks (28 days, including the data for the week prior to the initial consent, week 1), followed by a 90-day observational period.

1. Baseline Measurement of chronic pain using the VAS and GUPI with baseline treatment for 7 days [Week 1 (at first visit, data from week prior) then at Week 2 as a control period]

2. Active measurement of chronic pain using the VAS and GUPI as well as weekly usage logs during TENS treatment for 2 weeks [Week 3-4]

3. Durability: We will again collect data at 1, 2, and 3 months after the week visit for those who elect to continue, repeating the VAS and GUPI and treatment inventory, asking how much the TENS has been used and at what setting, to assess durability and observe participant-directed settings.

RANDOMIZATION

Subjects will be randomly assigned with equal probability to one of the three study groups. Randomization will utilize a web site (www.randomization.com) to provide randomization. Randomization will occur in blocks so that if the study needs to be terminated early there is an equal number of participants in each group at the time of termination. Also, we will stratify groups by gender so that there is an equal number of participants from each gender in each group to help limit this confounding variable. Allocation-concealment will be achieved by using sealed envelopes opened only after subjects are enrolled. Record keeping will be from participant responses via Qualtrics before and during TENS treatment. The scoring of the VAS and GPI scales, the compliance rate (used TENS or not), and any participant comments are recorded. Participant demographic will include age, gender, and pertinent urological history, if any.

BLINDING

There will be single blinding. Study participants/caretakers will not know which frequency has been assigned.

INTENTION-TO-TREAT

All subjects will be analyzed according to the intention-to-treat [ITT] principle. A participant will be considered evaluable and will be included in the intention-to-treat analysis if the participant has documented at least 8 sessions of their designated TENS treatment (about 4 times a week of TENS therapy). Analyses that take into account the actual treatment received (e.g., non-compliance, etc.) will be carried out as a secondary analysis (per protocol [PP] analysis).

Primary Statistical Objective:

The primary objective of the study is to compare the three TENS treatment groups after two weeks of active treatment, with respect to:

The change in VAS and GUPI pain questionnaires from baseline to after two weeks of

therapy.

The proportion of responders after two weeks of therapy.

Secondary Statistical Objectives:
Secondary objectives include comparison of the three treatment groups with respect to the rating of VAS and GUPI scores, separately, over time (by weekly diary entries). Analysis will be carried out to determine if there are time-dependent changes in questionnaire scores across the three TENS treatment groups. Urinary symptoms and individual pain site questions will be noted.
Pairwise comparisons of TENS groups will also be carried out to compare each arm with one another using Tukey's multiple comparison tests.
We will again collect data at 1,2-, and 3-months post-trial, asking how much the TENS has been used, to assess durability.

Outcome Variables and Schedule of Assessments:
The primary outcome variable of interest is participant's percentage change in VAS and GUPI from before treatment to the end of 2 weeks of active TENS. Also evaluated will be the response to treatment each week during the 14-day TENS therapy period and the 2 weeks of observation. A participant is said to have a favorable response to the treatment if he/she has a decrease of at least 2 points on the VAS or 1 point on the GUPI question #9 from baseline to after two weeks of TENS therapy. Change in outside interventions will not be permitted during the study but stable therapies will be maintained (e.g., medications).

Demographics and participant characteristics will be collected at baseline (age, gender, medical history, surgical history, current medications, site of pain, duration of chronic pelvic pain). The following outcomes will be measured at baseline, at each week, and at 3 months after the TENS therapy month:

- VAS Weekly Scores
- GUPI Weekly Scores

Statistical Methods
For the primary objectives:

- Analysis of variance with a fixed effect of treatment with Tukey's multiple comparison test will be used to test for differences in the reduction in genitourinary symptoms among the three treatment arms. Reduction will be parameterized as a relative change from baseline to after the two weeks of treatment. VAS pain response before and after treatment will be compared among the three groups using repeated measures ANOVA with Tukey's multiple comparison tests.
- The Chi-square test or Fisher's exact test, as appropriate, will be used to compare the rates of response among the three treatment arms at the end of the 14-day treatment period.

For the secondary objectives, a repeated measures analysis of variance will be used to analyze the outcomes of interest on a week-to-week basis (improvement in GUPI scores). A treatment-by-time interaction will be examined to determine if the patterns of change in GUPI and VAS scores over time differ across groups. Adjusted pairwise comparisons (Tukey or Bonferroni method) will be used to compare treatment groups to one another.
Data transformations may be applied, if necessary, in order to meet the required standard model assumptions.

Sample Size Considerations
Power: The number of participants needed was based on a power calculation (ANOVA with 2-tailed alpha of 0.05) assuming that the minimally important difference to detect among the three groups in the change in VAS score would be at least one within-group standard deviation of the change in score at 14 days. With 21 participants per group the power is estimated at 81%. We propose to randomize 25 per group assuming the dropout rate may be as high as 20%.

Based on investigator expertise and some published studies, we assume that the proportions of responders based on our criteria of a "favorable response" for each of the three TENS groups will be around 40 % (1,2,4,7,10). In our study we are aiming for at least a 40% response rate in our complex and refractory population.

Conduct of the study
The principal investigator, Elise De MD, is responsible for overall oversight of the data, monitoring the data, assuring protocol compliance, and conducting the safety reviews. The principal investigator will also be responsible for compiling the data sheets, day to day oversight of research and ensuring the integrity and privacy of the data. During the review process the principal investigator, along with the other investigators, will evaluate whether the study should continue unchanged, require modification/amendment, or close to enrollment. The principal investigators or the Institutional Review Board (IRB) have the authority to stop or suspend the study or require modifications.

The master key will house PHI relating to name, address, phone number, MR number and date of birth. The secure Qualtrics survey obtained weekly from participants will be securely downloaded as an excel spreadsheet into a protected AMC Onedrive file accessible only to study personnel. This spreadsheet will be uploaded directly to the secure one drive account to ensure participant confidently and security of PHI. Paper surveys will be entered into this database within Onedrive. The master key and database will be stores in separate protected Onedrive files.

Any worsening symptoms or adverse reactions will be reported to the examiners, by way of pain questionnaire, phone calls to participants, the 14-day clinic visits, or reported by participants aside from these instances. For participants with any severe or persistently worsening symptoms or adverse reactions, TENS therapy will be immediately discontinued, they will be removed from the study and considered to have failed treatment and receive medical treatment as necessary. Skin irritation is the most common adverse reaction to TENS units; however, this is mostly associated with allergy to the self-adhesive electrodes (12). While pain may be a

complication with TENS, studies have shown TENS is actually beneficial in treatment of pain over different areas of the body (12).

Participants with contraindications to TENS (eg, other electrical devices, pregnancy, bleeding or clotting disorders, unhealthy tissue, seizure disorders, malignancy, impaired cognition, adhesive allergy) will be excluded from the study. Participants will be taught safe practice with the use of a TENS unit, such as performing a sensory discrimination test in the office, checking and cleaning skin before starting a TENS session, monitoring skin for signs of irritation, changing adhesive on electrode pads after each use, securing electrodes with even pressure distribution and full contact, and watching for signs of TENS unit malfunction requiring maintenance [11].

Participants will be instructed to adjust the intensity to the level they can tolerate, so if the TENS intensity is too high then the participants will not be able to tolerate. Pain is the main issue with increased intensity (when it is not used to actually treat pain), therefore intensity will be minimized as per protocol to prevent this ("to the participant's perception and tolerance"). Increased intensity would be assumed to lead to skin break down, however, reports of this are exceedingly rare (13). Participant education will be comprehensive here.

While reports of dermatitis have been reported in the literature, in most of these cases the dermatitis is caused by an allergy to the adhesive on the TENS electrode pads and not the actual electrical stimulation. Skin irritation can occur, but this is mostly seen in cases where TENS therapy has been used for multiple hours in a row. There has been only one case report in the literature (and not even searchable in Pubmed) of an actual burn from a TENS unit (14). In contrast, TENS therapy is actually used for pain relief on burn participants. Therefore, the risk of being burned from TENS therapy is extraordinarily low.

The effects of prolonged TENS usage have been studied in the literature before.
The meta-analysis by Mark Johnson et al showed TENS units to be very safe with very few adverse effects seen even for more extended periods of use (10)

E. RISKS

The risks are minor and unanticipated. If there is any irritation to the participants skin due to the adhesive pads the participant will be treated and taken off the study.

Adverse reactions to the TENS units: The participants will be closely monitored and may be called during the treatment period to ensure that the participant is not experiencing any adverse reactions to TENS therapy. Risks can include pain, skin irritation, dermatitis, or burns. The most common reaction to the TENS unit is skin irritation related to an allergy to the self-adhesive electrodes.

Safe use of TENS units: The participants will be educated to safely use the TENS unit, including monitoring for signs of irritation, changing adhesive on the electrode pads after each

use and securing the electrodes appropriately and alternating the side of each electrode in terms of laterality (for example, place the electrode pads on the right foot on one day, then on the left foot on the next day, etc). Failure to adhere to safety guidelines could result in an adverse reaction to TENS therapy and dismissal from the study.

Malfunction of the TENS units: The participants will be taught how to monitor the TENS unit they are given for signs of malfunction that will require immediate maintenance.

F. BENEFITS

Participants enrolled into this study will have failed first-line conventional AUA/EAU treatment based on the modality of their pain. Participants will then be offered TENS therapy and thus enrollment into the study as a standard alternative to pharmacologic therapy for pelvic pain based on AUA/EAU guidelines and their etiology of pain after proper counseling of the risks and benefits by the provider and signing an informed consent. TENS units have been shown to be safe with very rare side effects reported in studies. Participants experiencing side effects or adverse reactions to TENS will terminate treatment and receive prompt medical attention. Follow up after treatment will determine if continuation of TENS therapy should resume as to avoid unnecessary treatment delay with other modalities.

G. CONFIDENTIALITY

All data will be kept in an excel database file on the secure AMC Onedrive network with access restricted to the study personnel which is HIPPAA compliant to protect the confidentiality of participants. Consents will be taken in private locations to ensure privacy is not invaded, and paper documents locked in the AMC Urology research office file room.

H. OPTIONS

Rather than participate in this study the subject can opt for standard assessment and care.

I. REFERENCES

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J. APPENDIX

VISUAL ANALOGUE SCALES

Please rate your pelvic pain:

Last 7 Days:	No Pain = 0 1 2 3 4 5 6 7 8 9 10 =	Max Pain
Pain Right Now:	No Pain = 0 1 2 3 4 5 6 7 8 9 10 =	Max Pain
Best this Week:	No Pain = 0 1 2 3 4 5 6 7 8 9 10 =	Max Pain
Worst Day this Week:	No Pain = 0 1 2 3 4 5 6 7 8 9 10 =	Max Pain

GUPI FEMALE

Name: _____

Date: _____

Pain or Discomfort

1. In the last week, have you experienced any pain or discomfort in the following areas?
   a. Entrance to vagina θ_1 Yes θ_0 No
   b. Vagina θ_1 Yes θ_0 No
   c. Urethra θ_1 Yes θ_0 No
   d. Below your waist, in your pubic or bladder area θ_1 Yes θ_0 No

2. In the last week, have you experienced:
   a. Pain or burning during urination? θ_1 Yes θ_0 No
   b. Pain or discomfort during or after sexual intercourse? θ_1 Yes θ_0 No
   c. Pain or discomfort as your bladder fills? θ_1 Yes θ_0 No
   d. Pain or discomfort relieved by voiding? θ_1 Yes θ_0 No

3. How often have you had pain or discomfort in any of these areas over the last week?
   θ_0 Never θ_1 Rarely θ_2 Sometimes θ_3 Often θ_4 Usually θ_5 Always

4. Which number best describes your AVERAGE pain or discomfort on the days you had it, over the last week?

θ	θ	θ	θ	θ	θ	θ	θ	θ	θ	θ
0	1	2	3	4	5	6	7	8	9	10

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No Pain — Pain as bad as you can imagine

Urination

5. How often have you had a sensation of not emptying your bladder completely after you finished urinating, over the last week?

θ_0 Not at all	θ_1 Less than 1 time in 5	θ_2 Less than half the time	θ_3 About half the time	θ_4 More than half the time	θ_5 Almost always

6. How often have you had to urinate again less than two hours after you finished urinating, over the last week?

θ_0 Not at all	θ_1 Less than 1 time in 5	θ_2 Less than half the time	θ_3 About half the time	θ_4 More than half the time	θ_5 Almost always

Quality of Life

7. How much have your symptoms kept you from doing the kinds of things you would usually do, over the last week?

θ_0 None θ_1 Only a little θ_2 Some θ_3 A lot

8. How much did you think about your symptoms, over the last week?

θ_0 None θ_1 Only a little θ_2 Some θ_3 A lot

9. If you were to spend the rest of your life with your symptoms just the way they have been during the last week, how would you feel about that?

θ_0 Delighted
θ_1 Pleased
θ_2 Mostly satisfied
θ_3 Mixed (about equally satisfied and dissatisfied)
θ_4 Mostly dissatisfied
θ_5 Unhappy
θ_6 Terrible

Scoring

Pain subscale: Total of items 1a, 1b, 1c, 1d, 2a, 2b, 2c, 2d, 3, and 4 = _____
Urinary subscale: Total of items 5 and 6 = _____
QOL Impact: Total of items 7, 8, and 9 = _____
Total score: Sum of subscale scores = _____

GUPI Male

Name: _____

Date: _____

Pain or Discomfort

1. In the last week, have you experienced any pain or discomfort in the following areas?

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a. Area between rectum and testicles (perineum) θ_1 Yes θ_0 No
b. Testicles θ_1 Yes θ_0 No
c. Tip of penis (not related to urination) θ_1 Yes θ_0 No
d. Below your waist, in your pubic or bladder area θ_1 Yes θ_0 No

2. In the last week, have you experienced:
a. Pain or burning during urination? θ_1 Yes θ_0 No
b. Pain or discomfort during or after sexual climax (ejaculation)? θ_1 Yes θ_0 No
c. Pain or discomfort as your bladder fills? θ_1 Yes θ_0 No
d. Pain or discomfort relieved by voiding? θ_1 Yes θ_0 No

3. How often have you had pain or discomfort in any of these areas over the last week?
θ_0 Never θ_1 Rarely θ_2 Sometimes θ_3 Often θ_4 Usually θ_5 Always

4. Which number best describes your AVERAGE pain or discomfort on the days you had it, over the last week?

θ	θ	θ	θ	θ	θ	θ	θ	θ	θ	θ
0	1	2	3	4	5	6	7	8	9	10
No Pain										Pain as bad as you can imagine

Urination

5. How often have you had a sensation of not emptying your bladder completely after you finished urinating, over the last week?

θ_0 Not at all θ_1 Less than 1 time in 5 θ_2 Less than half the time θ_3 About half the time θ_4 More than half the time θ_5 Almost always

6. How often have you had to urinate again less than two hours after you finished urinating, over the last week?

θ_0 Not at all θ_1 Less than 1 time in 5 θ_2 Less than half the time θ_3 About half the time θ_4 More than half the time θ_5 Almost always

Quality of Life

7. How much have your symptoms kept you from doing the kinds of things you would usually do, over the last week?

θ_0 None θ_1 Only a little θ_2 Some θ_3 A lot

8. How much did you think about your symptoms, over the last week?

θ_0 None θ_1 Only a little θ_2 Some θ_3 A lot

9. If you were to spend the rest of your life with your symptoms just the way they have been during the last week, how would you feel about that?

θ_0 Delighted
θ_1 Pleased
θ_2 Mostly satisfied
θ_3 Mixed (about equally satisfied and dissatisfied)
θ_4 Mostly dissatisfied
θ_5 Unhappy
θ_6 Terrible

Scoring
Pain subscale: Total of items 1a, 1b, 1c, 1d, 2a, 2b, 2c, 2d, 3, and 4 = _____
Urinary subscale: Total of items 5 and 6 = _____
QOL Impact: Total of items 7, 8, and 9 = _____
Total score: Sum of subscale scores = _____

Usage Chart Week 3-4, Month 1

Day	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Used (Y/N)							
Duration (Minutes)							

Usage Chart Extension Month 1,2,3

Date Range	No Use	Use (Minutes)	Patch location	Hertz (frequency, 2-150 cycles per second)	Pulse Width (30-260)	Mode (N, B, M)	Intensity (1-8)	Pain level at edn of session (1-10)

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