PROTOCOL TITLE:

Add-On Efficacy of Home-Based Transcutaneous Tibial Nerve Stimulation via the ZIDA Control Sock in Adults with Overactive Bladder on Preexisting Stable Pharmacotherapy

PRINCIPAL INVESTIGATOR:

- Dr. Connie Wang

1.0 Objectives / Specific Aims

- This is a prospective, single-arm, pre-post cohort study to look at the efficacy of the ZIDA Control Sock as an add-on therapy for patients with overactive bladder (OAB) and urgency urinary incontinence (UUI) who are already on preexisting stable OAB pharmacotherapy. The ZIDA sock is a new device, engineered as a wearable neuromodulation system in a sock, that provides transcutaneous tibial nerve stimulation to help relieve symptoms of OAB such as urinary urgency, urinary frequency, and urgency urinary incontinence. The device is non-invasive and has been well-tolerated overall in previous studies. A small number of studies have been conducted on this new device as primary therapy for OAB. We aim to study the effects of adding ZIDA onto the treatment plan of patients who are already on stable pharmacotherapy OAB with persistent symptoms.
- **Primary Objective:** To evaluate the mean change in total daily UUI episodes after addition of ZIDA therapy to patients on stable pharmacotherapy with OAB and persistent UUI. We will evaluate the mean change in episodes from baseline to weeks 1, 4, and 8 for interim analysis, and to week 12 for final analysis. Interim analyses will be descriptive and will not be used for stopping the study early or hypothesis testing.
- **Secondary Objectives:** (1) To assess change in daily urgency episodes (2) to assess change in daily urinary frequency; (3) To assess changes in patient-reported outcomes including a disease specific outcomes questionnaire (OAB-q Short Form (OAB-q SF) total score) (4) to assess a patient's impression of improvement (Patient Global Impression of Improvement (PGI-I)); (5) To assess usability, satisfaction, and adherence (with Device Use Log and Usability and Satisfaction Survey); and (6) To describe any device-related adverse events (with Adverse Event Log).
- We hypothesize that adding ZIDA therapy to the treatment regimen of OAB-wet patients already on stable pharmacotherapy will reduce their total daily urgency urinary incontinence episodes over 12 weeks.

2.0 Background

Overactive bladder (OAB) is a chronic condition characterized by urinary urgency, either with or without urgency urinary incontinence (UUI).[1-2] Those with UUI are classified as OAB-wet, and those without UUI are classified as OAB-dry. OAB patients also typically have increased daytime frequency and nocturia, which is not accounted for by another pathology. It is estimated that between 12-16% of the population has OAB, and this condition has significant negative impacts on patient's quality of life.[3-5] The conservative treatment options for OAB are lifestyle changes, pelvic floor muscle training, and pharmacotherapy.[6] The more invasive and expensive treatment choices include intravesical botulinum toxin injections and sacral neuromodulation.[6] Unfortunately, many OAB patients struggle to follow the lifestyle changes, while many others remain symptomatic despite pharmacotherapy. Some also discontinue their drug therapy due to cost or side effects such as dry mouth, constipation, and cognitive concerns.[7]

Neuromodulation for OAB is thought to work by stimulating afferent nerves to the sacral spinal cord, which suppresses abnormal afferent bladder signaling and promotes guarding reflexes. This stimulation also regulates other central nervous system pathways, such as the prefrontal cortex and limbic system, which play a role in urgency perception and bladder control.[8-10] Neuromodulation can be delivered in several ways; percutaneously, transcutaneously, or more centrally, just depending on the clinical setting.[11-13] Percutaneous tibial nerve stimulation (PTNS)

and transcutaneous tibial nerve stimulation (TTNS) both deliver electrical stimulation adjacent to the medial malleolus in the lower extremity. They target the tibial nerve and primarily stimulate the S2 to S3 pathways, as well as the L4 and L5 pathways.[11-13] Multiple studies have shown benefit between the different delivery methods.[12-14] Systematic reviews have shown that both PTNS and TTNS improve OAB symptoms, including urgency, frequency, and incontinence episodes.[15-16]

Recent studies have shown that TTNS can be used effectively and safely outside of the clinic. Wearable at-home TTNS devices offer comparable symptom improvement while reducing treatment burden for patients.[17] The ZIDA Control Sock is an FDA-cleared TTNS device that can be self-administered at home.[18] A recent study conducted on another wearable TTNS device found that it is safe, effective, and feasible for patients to use neuromodulation devices for at-home treatment sessions.[19] Prior randomized controlled trials conducted on the ZIDA sock have found statistically significant improvements in total daily incontinence episodes and OAB-related quality of life.[20]

Despite first and second line therapy such as pharmacotherapy, many patients with OAB continue to have urinary urgency incontinence episodes. Current pharmacotherapy for OAB includes agents which either antagonize muscarinic receptors or stimulate beta-3 receptors in the lower urinary tract. These agents are not completely effective and have dose-limiting adverse effects. Currently, it is unclear whether TTNS, which has a different mechanism of action as compared to medications, can be used as an add-on therapy in these OAB patients on pharmacotherapy to provide even more symptom relief.[21] TTNS is non-invasive and studies show that it does not have significant adverse events.[22-25] This study aims to evaluate whether the addition of the ZIDA device in patients with an incomplete response to pharmacotherapy will provide further relief of symptoms and improve quality of life.

3.0 Intervention to be studied

- The ZIDA device is a wearable, non-invasive sock, used for OAB treatment. This study will evaluate its use as an adjunct (add-on) therapy to standard pharmacologic treatment, which has not previously been studied. While studies have shown the efficacy of ZIDA as a stand-alone home therapy for OAB, it has not yet been evaluated in combination with ongoing OAB pharmacotherapy. This study will help us better understand whether adding TTNS to a patient's medication regimen is practical, safe, and helpful for symptom control.
- The ZIDA device has reported minimal adverse events. During prior studies it was found that two patients had mild cases of foot pain and two other patients had unrelated urinary tract infections. These events were minimal and self-resolved quickly without discontinuing treatment.
- The treatment sessions will be the participant wearing the ZIDA Control Sock (with conductive gel), attaching the small control unit device, and turning this on to administer electrical stimulation for 30 minutes. The stimulation is set to a comfortable level that may produce a mild tingling sensation or mild toe movement; this indicates the activation of the tibial nerve.
- The intervention will be once weekly 30-minute sessions using the ZIDA sock for 12 consecutive weeks. Each patient will serve as their own control.

4.0 Study Endpoints

- Our primary endpoint is to evaluate the mean change in total daily UUI episodes from baseline to week 12. Exploratory interim analyses at weeks 1, 4, and 8 will be descriptive. Our secondary endpoints include urgency episodes, total voiding frequency per day, QOL questionnaire Overactive Bladder Questionnaire (1-Week Recall) (OAB-Q SF 1W), Patient Global Impression of Improvement (PGI-I) responder, and any adverse events.
- Device usability and satisfaction will be measured at Week 12 using the Usability & Satisfaction Survey. This survey is a six-item questionnaire adapted from prior OAB studies. Five items are rated on a five-point Likert scale (1 = Strongly disagree to 5 = Strongly agree) to measure device ease of use, comfort, clearness of instructions, convenience, and patient willingness to continue therapy. There is also an open-ended feedback question. We'll summarize responses to get a sense of usability and patient experience.
- Adherence will be measured as the proportion of prescribed weekly sessions completed, based on the participant's Device Use Log. Study staff will review logs during remote check-ins (Weeks 1, 4, 8, and 12). Adherence will be expressed as both total number and percentage of completed sessions (out of 12).
- Safety related to usability will also be captured through the Adverse Event Log, reviewed by the principal investigator at each contact.

5.0 Inclusion and Exclusion Criteria/ Study Population

- Potential participants will be found through MUSC Urology clinic visits or electronic health-record (EHR) prescreening. Authorized study staff will identify adults with OAB-wet who are also on stable pharmacotherapy who may meet eligibility criteria.

Inclusion Criteria

- Age ≥ 18 years
- Diagnosis of OAB-wet (OAB with urgency urinary incontinence) documented by clinical diagnosis
- Baseline ≥1 UUI episode/day averaged over a 3-day diary
- Is on a stable pharmacotherapy for OAB (antimuscarinic or β3-agonist) for ≥4 weeks, with intent to remain on their medication regimen for the duration of this study
- Has the ability to complete bladder diaries, questionnaires, and attend follow-up visits
- Cognitively intact adult and able to understand study procedures and provide informed consent independently.
    - A study team member at the informed consent conversation will assess cognitive ability and the ability to provide informed consent. Assessment will be based on the participant's ability to understand the study procedures and accurately restate their study roles in their own words. No formal cognitive testing will be performed.

Exclusion Criteria

- Neurologic conditions that affect bladder function, such as multiple sclerosis, spinal cord injury, Parkinson's disease, or other neurogenic bladder conditions.
- Significant pelvic organ prolapses or other pelvic pathology that interferes with bladder emptying, neuromodulation efficacy, or study assessments
- Active urinary tract infection (UTI) or unexplained hematuria at screening
- Clinically significant post-void residual (PVR) volume above threshold (e.g., >100 mL)
- History of, failure of, or current use of neuromodulation therapies, including percutaneous or transcutaneous tibial nerve stimulation (PTNS/TTNS), sacral neuromodulation (InterStim), implantable tibial devices (eCoin)
- Intravesical botulinum toxin injections less than 9 months prior to entry into the study
- Pregnancy or plans to become pregnant during study participation, and women of childbearing age not using contraception. A urine pregnancy test will be performed for women of childbearing potential to confirm non-pregnant status prior to enrollment.
- Contraindications to electrical stimulation (cardiac pacemaker or implanted defibrillator without physician clearance, unhealed wounds near stimulation site, metal implants in the ankle region)
- Significant uncontrolled medical conditions, such as unstable cardiac disease, poorly controlled diabetes mellitus, severe peripheral edema, or severe peripheral neuropathy that may affect lower-limb sensation or response to stimulation in the opinion of the investigator
- Pelvic malignancy of GI, GU or GYN origin, or prior pelvic radiotherapy.
- Current participation in another investigational drug or device trial, or use of an investigational therapy within the last 30 days
- Known hypersensitivity or intolerance to materials used in the ZIDA device (electrode adhesives, conductive gels)

6.0 Number of Subjects

20

7.0 Setting

The study will be conducted at MUSC's Department of Urology. Participants will administer their treatment at home.

8.0 Recruitment Methods

Potential participants will be identified through MUSC Urology clinic visits or by using Epic EHR review to locate adults with a diagnosis of OAB-wet who are on stable pharmacotherapy and may meet eligibility criteria. Prescreening will be performed by authorized study staff through chart review only; no direct patient contact will occur at this stage. When a potentially eligible patient is identified through chart review, the study team will notify the treating clinician prior to the patient's upcoming appointment. The treating clinician will briefly introduce the study during the clinical encounter. If the patient is interested in participating in this study, the clinician will ask for permission from the patient for the research team to follow up with them. Study staff will only

contact potential participants after permission has been confirmed. The research coordinator will be present in clinic to come speak with the patient.

Some eligible patients may be missed during prescreening. Their treating clinician (including attending physicians, fellows, and PAs within the MUSC Urology clinic) also have the option to identify eligible patients during clinic. In these cases, clinicians may briefly inform the patient about the study and, if the patient is interested, get permission for the research team to follow up. The research coordinator will be present in clinic to come speak with the patient.

Recruitment will occur on a rolling basis over approximately 10 to 14 months, with an estimated enrollment rate of 1.5 to 2 participants per month.

9.0 Consent Process

Informed consent will be obtained from all participants before any study-related screening procedures are conducted. The consent process will take place in a private setting. Consent will be obtained by IRB-approved study personnel either in person during the participant's screening visit (which may coincide with a routine clinic appointment) or remotely via a secure HIPAA-compliant telehealth platform. Participants will be provided the consent form and given adequate time to review it and ask questions before signing. Individuals who wish to consider participation further will be offered at least 24 hours for reflection before providing consent. The study team will make sure that participants understand that their participation is voluntary and that their refusal or withdrawal at any time will not affect their clinical care. This consent form will explain that screening procedures to confirm final eligibility for enrollment will take place after consent. The participant will receive copy of their signed consent form.

10.0 Study Design / Methods

After providing informed consent, participants will complete a 14-week study consisting of a screening visit, baseline visit, 12 weeks of home treatment, remote check-ins, and a final in-person visit.

Screening Visit:

Participants may complete informed consent either remotely before the screening visit or in person at the time of screening, depending on preference. Once they have been consented, they will begin the screening visit, which may occur with a routine clinic appointment. At the screening visit a physical exam will occur. If a patient is already having the procedure or exam per standard of care for their clinic visit, we will not repeat the procedure but will instead review the medical record for the results. During this visit, the following will occur:

- medical history and medication review,
- physical examination,
- urinalysis (to assess for hematuria or UTI),
- urine dipstick pregnancy test for women of childbearing potential (the test will be done on the same urinalysis urine sample when possible),

- post-void residual (PRV) volume measurement. This will be conducted by using a non-invasive ultrasound scanner after voluntary voiding to assess for incomplete bladder emptying and rule out urinary retention.
- completion of baseline questionnaires, including the OAB-Q SF 1W and the PGI-S. The OAB-Q SF 1W is a validated 19-item questionnaire that is used to assess patient quality of life. The PGI-S is a single item scale that measures symptom severity. Study questionnaires may be completed on paper or electronically through REDCap, depending on participant preference.

After these screening procedures are done and eligibility is confirmed, the participants will be enrolled in the study. Study-related procedures will only be conducted by clinicians who are members of the study team.

Baseline Visit (same day or on a different day):

- Participants go over the screening results and confirm their enrollment in the study.
- Participants will be instructed that they should remain on stable OAB pharmacotherapy throughout the study.
- They will receive the ZIDA device and get device training based on the ZIDA manufacturer's IFU. They will be instructed to call the study team if, while using the device, they experience any pain, skin irritation, or technical problems.
- They will also be given a 3-day bladder diary and instructions on how to complete it at home over three consecutive days before starting device therapy. This diary records voiding time, urgency, and urgency-urinary-incontinence episodes.
- They will also receive the Device Use Logs, Adverse Event Logs, and Bladder Diaries for the entirety of the study.
- The baseline visit may occur on the same day as the screening visit or may be scheduled for a later date, depending on when all screening procedures are completed and eligibility is confirmed. If all screening assessments are finished during the initial clinic encounter and the participant has enough time to complete the baseline visit, then the baseline visit could be completed. Or, if preferred by the participant, the baseline visit may also be conducted remotely after the screening visit. If this is the case (once eligibility is confirmed) the participant will receive all of the required study materials; the ZIDA device, IFU, conductive gel, and all study logs (Device Use Log, Adverse Event Log, and bladder diaries). Then device training will be conducted either in person or remotely before the participant begins device use. Participants who do not have time to complete all screening and baseline activities in a single visit may return for one additional visit (combined Screening and Baseline visit) to finish any screening procedures and the baseline visit. In all scenarios, the participants will complete all screening procedures, then once they meet eligibility criteria, will receive device training, and receive all study materials before beginning the intervention period.

Intervention Period (Weeks 1–12):

- Participants will self-administer the ZIDA therapy once a week for 30 minutes. They choose a day of the week that works best for them. For each session, the participant will be seated comfortably, they will put conductive gel on the inside of the ZIDA sock, connect the control unit, and turn it on to begin electrical

stimulation. After 30 minutes, the device will automatically turn off. Participants take off the device, clean off any leftover gel. Participants will complete one session every week for 12 weeks (ideally on the same day ±24 hours). Reminders may be sent by telephone, secure email, or text message through a HIPAA-compliant system, depending on participant preference. Reminder messages will be brief and only related to the study (e.g., "Please remember to do your session this week").

- They will be asked to complete a Device Use Log after each session where they will write down the date, duration, and any notes about the session.
- Study staff will conduct remote study check ins at weeks 1, 4 and 8. Participants may choose to do these using a HIPAA-compliant telehealth platform or a phone call. During these check ins, the study team will confirm that patients are using and adhering to the session schedules by reviewing the Device Use Log. During remote visits, adherence will be confirmed either verbally by the participant reading their Device Use Log entries during the call, or through secure REDCap data entry if the participant prefers to complete their weekly log electronically. During these remote visits, the study team will record any adverse events or side effects. Adverse events and device-related complaints are documented on a standardized Adverse Event Log and reviewed by the study team and/or principal investigator. 3 Day Bladder Diaries: Participants will complete additional 3-day bladder diaries at Weeks 4, 8, and 12. Reminders may be sent by telephone, secure email, or text message through a HIPAA-compliant system, depending on participant preference. Reminder messages will only have neutral content that is relevant to the study (e.g., "Please remember to complete your bladder diary this week"). Participants may complete the 3-day bladder diaries on paper or electronically on REDCap given their preference. Paper diaries may instead be reviewed verbally during the telehealth check-in or collected at the final visit.

Final Visit (Week 12) In person study visit:

- Participants will return their bladder diaries
- Patients will again complete the OAB-Q SF 1W, PGI-S,
- Patients will complete a PGI-I, and Usability and Satisfaction Survey questionnaires. The PGI-I is a single item scale that measures symptom improvement.
- PVR measurement will be repeated using a bladder scanner
- All Device Use Logs will be collected and reviewed with the participant.
- Adverse events will be collected, and the Adverse Event Log will be reviewed with the participant.

The participant will return the device and any additional supplies they had received from the study team. Total participation is approximately 14 weeks.

11.0 Data Management

All data will be limited to clinical and patient-reported outcomes (e.g., bladder diaries, questionnaires, adverse event logs). Collected data will include demographic information

(age, sex), OAB history, current medications, baseline and follow-up diary metrics, and questionnaire scores. Research data will be coded. Identifiable patient information will be stored in a linking document and stored separately from the research data in a password-protected software accessible only to authorized study staff. All study staff will complete CITI training in human subjects research and will be HIPAA compliant. Only de-identified patient data will be removed from MUSC servers. Hard copy documentation (like consent forms and bladder diaries) will be stored in locked cabinets within MUSC Urology research offices. Any data collected electronically (eg. Electronic consents or questionnaires) will be stored in REDCap. Paper responses will be entered into REDCap by study staff, and hard copies stored as source documentation. If any participants complete electronic consent via REDCap's e-consent module, those signed forms will be stored securely within REDCap under MUSC's encrypted server.

- For this single arm pre/post study design, we plan to enroll a total of 20 participants. Since we expect no more than 20% drop-out, this will yield complete data on at least 16 participants. A sample size of n=16 provides 85% power to detect modest changes (effect sizes of 0.7) in study outcomes, including Total Daily Incontinence episodes). Earlier work by Cava & Orlin (2022) suggest that the device may yield an even larger decline in incontinence episodes (i.e. from 1.2 ± 0.8 at baseline down to 0.3 ± 0.3, at week 12, corresponding to an effect size of 1.4), meaning that we may likely have even greater statistical power. This sample size would also provide sufficient power (>80%) to detect changes in secondary outcomes, including Quality of Life (OAB-Q SF 1W total score). While primary analysis compares baseline to week 12, repeated-measures models will incorporate interim timepoints (weeks 1, 4, 8) descriptively.
- Initially, descriptive statistics will be used to characterize the study participants at baseline and at follow-up. Continuous outcomes (i.e. measures of incontinence and quality of life) will be compared pre- and post-use of the device using paired t-tests, or Wilcoxon signed rank tests (if necessary). The proportion of participants who have no incontinence at follow-up will be reported, and these percentages will be compared using McNemar's tests for paired binomial proportions. The results of this study will be vital for helping to design a larger, definitive 2-arm randomized controlled trial.

12.0 Withdrawal of Subjects

- Participants could be withdrawn from the study if they no longer meet eligibility criteria (like ceasing their medication use or are non-adherent to device use) or for safety concerns (like an adverse reaction).
- Participants can withdraw from the study at any time without penalty by notifying the Principal Investigator or a member of the study team. Data collected up to that point will be retained unless the participant requests their data be removed.
- If a participant withdrawals during the study, the reason for withdrawal will be documented in the study enrollment and tracking log maintained by the study team.

13.0 Risks to Subjects

- Possible risks of ZIDA use include mild tingling, warmth, or discomfort at the ankle during use, and mild self-resolving skin redness or irritation from electrode adhesive.

- Some of the study questionnaires will ask the patients about their urinary symptoms and its impact on their quality of life. This could cause mild embarrassment or emotional discomfort. Participants will be informed that they may skip any question they do not wish to answer.
- There is a risk of loss of confidentiality, but every effort will be made to mitigate that risk by coding the data and storing it securely.

14.0 Potential Benefits to Subjects or Others

- It is possible, but cannot be guaranteed, that the ZIDA device may result in a reduction in urgency, frequency, and incontinence episodes.
- More broadly, this study helps clarify how TTNS and medication might work together for patients with OAB.
- Risks are minimal and resolvable, as seen in prior studies.

15.0 Sharing of Results with Subjects

- De-identified study results will be available to participants after the study is completed, either via mailed summary or secure email. Individual-level results, such as each participant's own bladder diary summaries, questionnaire scores (e.g., OAB-Q SF or PGI-I), and clinical progress measures, can be reviewed with participants during follow-up visits in clinic or remotely if requested.

16.0 Drugs or Devices

- The ZIDA Control Sock is an FDA-cleared (Class II, K192731, product code NAM) at-home device for OAB treatment. It is cleared to treat OAB and associated symptoms of urinary urgency, urinary frequency, and urge incontinence. All device operation and safety procedures will follow the manufacturer's Instructions for Use (IFU). A copy will be included in the study binder and provided to participants.
- Devices will be stored at the MUSC Urology office in a locked room accessible only to authorized study staff. Devices will be logged, numbered, and dispensed only to enrolled participants.
- Only trained study staff will instruct participants in device operation. Participants will self-administer therapy according to IFU (one 30-minute session weekly for 12 weeks).

References

1. Wallace KM, Drake MJ. Overactive bladder. F1000Res. 2015;4:F1000 Faculty Rev-1406. Published 2015 Dec 7. PMID: 26918151.
2. Abrams P, et al. The standardisation of terminology in lower urinary tract function: report from the Standardisation Sub-committee of the International Continence Society. Neurourol Urodyn. 2002;21(2):167-178. PMID: 11979331.
3. Stewart WF, Van Rooyen JB, Cundiff GW, et al. Prevalence and burden of overactive bladder in the United States. World J Urol. 2003;20(6):327-336. PMID: 12811491.
4. Milsom I, Abrams P, Cardozo L, et al. How widespread are the symptoms of an overactive bladder and how are they managed? A population-based prevalence study. BJU Int. 2001;87(9):760-766. PMID: 11412210.
5. Coyne KS, Sexton CC, Irwin DE, Kopp ZS, Kelleher CJ, Milsom I. The impact of overactive bladder, incontinence and other lower urinary tract symptoms on quality of life, work productivity, sexuality and emotional well-being in men and women: results from the EPIC study. BJU Int. 2008;101(11):1388-1395. PMID: 18454794.
6. Gormley EA, Lightner DJ, Burgio KL, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU Guideline (2024 update). J Urol. 2024;211(3):645-659.
7. Cameron AP, Chung DE, Dielubanza EJ, et al. The AUA/SUFU Guideline on the Diagnosis and Treatment of Idiopathic Overactive Bladder. J Urol. 2024;212(1):11-20.
8. de Groat WC, Yoshimura N. Mechanisms underlying the recovery of lower urinary tract function following spinal cord injury. Prog Brain Res. 2006;152:59-84. PMID: 17027738.
9. Finazzi-Agrò E, Rocchi C, Pachatz C, et al. Percutaneous tibial nerve stimulation produces effects on brain activity: results from a functional magnetic resonance imaging study in humans. J Urol. 2009;182(6):2070-2076. PMID: 19836700.
10. Tai C, Roppolo JR, de Groat WC. Neuromodulation of bladder afferent pathway for the treatment of overactive bladder. Neurotherapeutics. 2007;4(2):215-223. PMID: 17514118.
11. Finazzi-Agrò E, Campagna A, Sciobica F, et al. Posterior tibial nerve stimulation: is the once-a-week protocol the best option? Eur Urol. 2005;48(1):181-185. PMID: 15953651.
12. Amarenco G, Ismael SS, Even-Schneider A, et al. Urodynamic effect of acute transcutaneous posterior tibial nerve stimulation in overactive bladder. J Urol. 2003;169(6):2210-2215. PMID: 12771763.
13. Peters KM, Macdiarmid SA, Wooldridge LS, et al. Randomized trial of percutaneous tibial nerve stimulation versus extended-release tolterodine: results from the overactive bladder innovative therapy trial. J Urol. 2009;182(3):1055-1061. PMID: 19616807.
14. Wang M, Jian Z, Ma Y, Jin X, Li H, Wang K. Percutaneous tibial nerve stimulation for overactive bladder syndrome: a systematic review and meta-analysis. Int Urogynecol J. 2020;31(12):2457-2471. PMID: 32681345.
15. Booth J, Connelly L, Dickson S, Duncan F, Lawrence M. The Effectiveness of Transcutaneous Tibial Nerve Stimulation (TTNS) for Adults With Overactive Bladder Syndrome: A Systematic Review. Neurourol Urodyn. 2018;37(2):528-541. PMID: 28731583.
16. Ghavidel-Sardsahra A, Ghojazadeh M, Rahnama'I MS, et al. Efficacy of Percutaneous and Transcutaneous Posterior Tibial Nerve Stimulation on Idiopathic Overactive Bladder and Interstitial Cystitis/Painful Bladder Syndrome: A Systematic Review and Meta-Analysis. Neurourol Urodyn. 2022;41(2):539-551. PMID: 35032328.
17. Vaca-Benavides DA, Ju W, Gonzalez C, et al. The Importance of Electrical Parameters on Transcutaneous Tibial Nerve Stimulation for Overactive Bladder Syndrome: A Systematic Review and Meta-Analysis. Age Ageing. 2025;54(7):afaf203.

18. U.S. Food and Drug Administration. 510(k) Summary K192731: ZIDA Control Sock (Exodus Innovations Ltd). Silver Spring, MD: FDA; 2020.
19. Liao L, Li X, Chong T, et al. Efficacy and Safety of Tibial Nerve Stimulation Using a Wearable Device for Overactive Bladder. BJU Int. 2024;133(6):760-769.
20. Cava JL, Orlin J, El-Haddad T, et al. Transcutaneous posterior tibial nerve stimulation using the ZIDA home-use device for overactive bladder: a randomized, double-blind, sham-controlled trial. Int Urol Nephrol. 2022;54(7):1623-1633. PMID: 35595844.
21. Lee UJ, MacDiarmid S, Matthews CA, Gillespie E, Peters KM. Tibial Nerve Stimulation for Urge Urinary Incontinence and Overactive Bladder: Narrative Review of Randomized Controlled Trials and Applicability to Implantable Devices. Adv Ther. 2024;41(7):2635-2654. PMID: 38748331.
22. Stanley RF, Meyer I, Blanchard CT, Richter HE. Posterior tibial nerve stimulation with versus without mirabegron: a randomized controlled trial. Int Urogynecol J. 2024;35(8):1709-1717. PMID: 38588590.
23. Peters KM, MacDiarmid SA, Wooldridge LS, et al. Efficacy and safety of the implantable eCoin tibial neuromodulation device for refractory urgency urinary incontinence: results of the pivotal randomized trial. J Urol. 2022;208(6):1353-1362. PMID: 36106697.
24. Vecchioli-Scaldazza C, Morosetti C, Berouz A, Giannubilo W, Ferrara V. Effectiveness and durability of solifenacin versus percutaneous tibial nerve stimulation versus their combination for the treatment of women with overactive bladder syndrome: a randomized controlled study with a ten-month follow-up. Int Braz J Urol. 2018;44(1):102-108. PMID: 23548260.
25. Chen G, Liao L. Transcutaneous tibial nerve stimulation in women with overactive bladder syndrome: a randomized controlled trial. Int Urogynecol J. 2021;32(2):297-304. PMID: 34161360.