# CLINICAL STUDY PROTOCOL

# TENS 2.0

## Transcutaneous Electrical Nerve Stimulation as an Adjunct to Local Anaesthesia During Transperineal MRI-Ultrasound Fusion-Guided Prostate Biopsy: A Randomized Triple-Blind Sham-Controlled Trial

| Item | Detail |
|---|---|
| **Brief title** | TENS During Transperineal Prostate Biopsy |
| **Acronym** | TENS 2.0 |
| **ClinicalTrials.gov Identifier** | NCT07578324 |
| **Unique Protocol ID** | TENS2-TPB-RCT-2026 |
| **Document type** | Study Protocol |
| **Protocol version** | Version 1.0 |
| **Version date** | 10 August 2026 |
| **Responsible party** | Principal Investigator |
| **Study site** | Department of Urology, Medical University of Gdansk / University Clinical Centre, Gdansk, Poland |
| **Ethics approval** | Bioethics Committee for Scientific Research, Medical University of Gdansk |
| **Approval number and date** | KB/326/2026, 9 July 2026 |

The trial will be conducted in accordance with this protocol, the Declaration of Helsinki (2013) and the principles of Good Clinical Practice:

## Protocol Synopsis

| Parameter | Detail |
|---|---|
| **Full title** | Transcutaneous Electrical Nerve Stimulation as an Adjunct to Local Anaesthesia During Transperineal MRI-Ultrasound Fusion-Guided Prostate Biopsy: A Randomized Triple-Blind Sham-Controlled Trial |
| **Short title** | TENS 2.0 |
| **Design** | Single-centre, prospective, randomized, sham-controlled, two-parallel-group superiority trial with blinding of participants, the operating urologist (who is also the Principal Investigator) and the trial statistician |
| **Blinding (plain description)** | Blinded: participants; the operating urologist, who is also the Principal Investigator; the independent statistician. All pain and post-procedural scores are self-recorded by the participant on a paper form, so the outcome assessor is the blinded participant and no member of staff asks for a score. Not blinded: one designated study nurse (Nurse A), who operates the device, records no outcome data and never handles the form. |
| **Blinding (label)** | Described conventionally as triple-blind (participant, care provider, outcome assessor); registered on ClinicalTrials.gov as quadruple-masked (Participant, Care Provider, Investigator, Outcomes Assessor). |
| **Primary outcome** | NRS pain score (0-10) during periprostatic nerve block (PNB) |
| **Key secondary outcomes** | NRS at three further procedural stages; procedural safety (Clavien-Dindo); patient satisfaction; operator satisfaction; willingness to repeat; blinding integrity in participants and in operators (James and Bang indices) |
| **Exploratory outcomes** | Pain catastrophizing (PCS-13); preoperative anxiety (STAI-S); NRS-anxiety and pre-to-post change; TENS amplitude versus procedural pain; procedure duration |
| **Population** | Men aged 40 years or older, PI-RADS >= 3, scheduled for transperineal MRI-US fusion biopsy under local anaesthesia |
| **Intervention** | Active TENS (80 Hz, 180 us, symmetrical biphasic compensated pulse, amplitude titrated to the highest comfortably tolerable level) plus standard local anaesthesia |
| **Comparator** | Sham TENS (identical electrode placement, identical activation ritual, no current delivered) plus standard local anaesthesia |
| **Local anaesthesia (both arms)** | 10 mL of 2% lignocaine gel transrectally, followed by 20 mL of 1% lignocaine in total (approximately 10 mL needle-path infiltration, 10 mL bilateral PNB) |
| **Allocation ratio** | 1:1 |
| **Sample size** | 60 evaluable participants per group (120); inflated by 15% for dropout and non-evaluable primary outcome, giving a recruitment target of 70 per group (140 in total) |
| **Randomization** | Computer-generated sequence, variable block sizes (4 and 6); allocation concealment by sequentially numbered, opaque, sealed envelopes (SNOSE) |
| **Primary outcome measurement** | Self-recorded by the participant on a paper form, cued by a fixed stage announcement from the blinded operator; no member of staff asks for a score |
| **Primary analysis** | Two-sided Mann-Whitney U test at alpha = 0.05, intention-to-treat; Hodges-Lehmann median difference with 95% CI |
| **Registration** | ClinicalTrials.gov NCT07578324, prospectively registered before first enrolment |
| **Ethics approval** | Bioethics Committee, Medical University of Gdansk, KB/326/2026, 9 July 2026 |
| **Duration** | Approximately 8 months recruitment plus 30-day follow-up per participant |

## Abbreviations

| Abbreviation | Definition |
|---|---|
| **AE / SAE** | Adverse event / serious adverse event |
| **ARE** | Asymptotic relative efficiency |
| **BI** | Blinding index |
| **CI** | Confidence interval |
| **eCRF** | Electronic case report form |
| **GCP** | Good Clinical Practice |
| **ITT** | Intention-to-treat |
| **LA** | Local anaesthesia |
| **MCID** | Minimum clinically important difference |
| **mpMRI** | Multiparametric magnetic resonance imaging |
| **NRS** | Numeric rating scale |
| **OSF** | Open Science Framework |
| **PCS-13** | Pain Catastrophizing Scale, 13 items |
| **PI** | Principal Investigator |
| **PI-RADS** | Prostate Imaging Reporting and Data System |
| **PNB** | Periprostatic nerve block |
| **PP** | Per-protocol |
| **PSA** | Prostate-specific antigen |
| **SAP** | Statistical analysis plan |
| **SNOSE** | Sequentially numbered, opaque, sealed envelopes |
| **STAI-S** | State-Trait Anxiety Inventory, State subscale |
| **TENS** | Transcutaneous electrical nerve stimulation |
| **TPB** | Transperineal prostate biopsy |
| **TRUS** | Transrectal ultrasound |

# 1. Background and Rationale

Transperineal prostate biopsy (TPB) has become the preferred diagnostic technique owing to a substantially lower rate of infectious complications compared with the transrectal approach. Performed under local anaesthesia (LA) in an outpatient setting, it offers a practical and cost-effective alternative to general or sedation-based anaesthesia and avoids the resource burden of theatre time. However, patients consistently report higher procedural pain with TPB than with the transrectal route, and pain is greatest during periprostatic nerve block (PNB) and during local anaesthetic infiltration of the needle path.

Non-pharmacological adjuncts to LA remain underexplored in this setting. Transcutaneous electrical nerve stimulation (TENS) is a non-invasive, low-cost modality with a well-established safety profile and no systemic effects. Its proposed mechanism involves activation of large-diameter A-beta afferent fibres, attenuating nociceptive transmission in a manner consistent with the gate control theory of pain; segmental inhibition at the level of the dorsal horn is the most plausible pathway for a perineally applied stimulus during transperineal instrumentation.

A preceding single-centre, randomized, sham-controlled pilot study conducted at this department (TENS 1.0; n = 84, 1:1:1 allocation to active TENS, sham TENS and LA alone) demonstrated significantly lower NRS pain scores in the active TENS group during PNB (median 4 versus 7; epsilon-squared 0.59) and during biopsy sampling (epsilon-squared 0.52), with no significant difference between the LA-alone and sham groups at any procedural stage. No device-related adverse events occurred. The pilot was retrospectively registered, was explicitly hypothesis-generating and was conducted without a formal power calculation.

The present confirmatory trial (TENS 2.0) addresses the principal limitations of TENS 1.0. It is prospectively registered, formally powered against a pre-specified minimum clinically important difference rather than against the inflated pilot effect estimate, and restricted to two parallel groups on the basis of the pilot finding that sham TENS is an adequate control condition and does not itself confer analgesia. The blinding procedures have been strengthened and are specified in operational detail in Section 7, together with a pre-specified assessment of blinding integrity in both participants and operators.

# 2. Objectives and Hypotheses

## 2.1 Primary objective

To determine whether TENS applied as an adjunct to standard local anaesthesia reduces pain intensity during periprostatic nerve block, compared with sham TENS plus standard local anaesthesia, in men undergoing transperineal MRI-US fusion-guided prostate biopsy.

## 2.2 Primary hypothesis

H0: there is no difference in the distribution of NRS pain scores during PNB between the active TENS and sham TENS groups.

H1: participants allocated to active TENS report lower NRS pain scores during PNB than participants allocated to sham TENS (superiority; two-sided alpha = 0.05).

## 2.3 Secondary objectives

- To compare NRS pain scores between groups at three further procedural stages: ultrasound probe insertion, perineal needle-path infiltration and fusion-targeted biopsy sampling.
- To compare procedural safety and tolerability through 30-day follow-up, classified according to the Clavien-Dindo system.

- To compare patient satisfaction with the procedure (Likert 1-5).
- To compare operator satisfaction with procedural conditions (Likert 1-5).
- To compare willingness to undergo the same procedure again in the future (yes / no / unsure) at the 30-day visit.
- To quantify the integrity of participant and operator blinding using the James and Bang blinding indices.

### 2.4 Exploratory objectives

- To examine the association between preoperative pain catastrophizing (PCS-13) and procedural pain intensity.
- To examine the association between preoperative anxiety (STAI-S and single-item NRS-anxiety) and procedural pain intensity.
- To describe the change in anxiety from before to immediately after the procedure (NRS-anxiety delta) and compare it between groups.
- To examine the association between the titrated TENS amplitude and procedural pain within the active group.
- To examine the association between procedure duration and procedural pain.

## 3. Trial Design

TENS 2.0 is a single-centre, prospective, randomized, sham-controlled, two-parallel-group superiority trial conducted at the Department of Urology of a tertiary academic centre. Participants are allocated 1:1 to active TENS or sham TENS, both in addition to an identical standard local anaesthesia protocol. Follow-up extends to 30 days after biopsy. No interim analysis is planned.

The single-centre design is deliberate. All biopsies are performed by experienced operators at the same institution following an identical standardised procedure, using the same MRI-US fusion platform, the same local anaesthesia technique and the same TENS protocol as in TENS 1.0. This minimises inter-operator and inter-centre variability and preserves direct methodological continuity with the pilot. The corresponding limitation for external validity is acknowledged in Section 21.

The trial is reported in accordance with CONSORT 2025, and this protocol has been prepared in accordance with the SPIRIT 2013 recommendations for interventional trial protocols.

## 4. Study Setting and Population

### 4.1 Setting

Department of Urology, Medical University of Gdansk / University Clinical Centre, Gdansk, Poland. All procedures are performed in the outpatient biopsy suite under local anaesthesia. No participant receives sedation or general anaesthesia as part of the standard procedure.

### 4.2 Inclusion criteria

- Male, aged 40 years or older.
- Indication for prostate biopsy: elevated serum PSA (per institutional protocol and EAU guidelines) or abnormal digital rectal examination.

- Suspicious lesion on multiparametric MRI classified as PI-RADS 3 or higher (version 2.1).
- Scheduled for transperineal MRI-US fusion-guided prostate biopsy under local anaesthesia.
- Able to provide written informed consent.

### 4.3 Exclusion criteria

- Prior treatment for prostate cancer (radical prostatectomy, radiotherapy, hormonal therapy or focal therapy).
- Contraindications to TENS: cutaneous damage or dermatological conditions at the electrode application sites; cardiac pacemaker or implantable cardioverter-defibrillator; uncontrolled cardiac arrhythmia or congestive heart failure; history of epilepsy or seizure disorder; metallic implants near the stimulation site; malignancy at or near the stimulation site.
- Contraindications to transperineal biopsy: active urinary tract infection; bleeding disorder or ongoing anticoagulation not amenable to bridging; anatomical abnormality preventing safe prostatic access.
- Known allergy or intolerance to local anaesthetic agents or to biopsy-related materials.
- Severe comorbidity or unstable medical condition compromising procedural safety.
- Inability to complete the study questionnaires, or inability to self-record scores on a paper form during the procedure, including uncorrected visual impairment, tremor or any motor impairment that would prevent marking a form while in the lithotomy position.
- Participation in another interventional clinical trial within 30 days before enrolment.

## 5. Recruitment, Screening and Informed Consent

### 5.1 Recruitment

Consecutive patients scheduled for transperineal MRI-US fusion biopsy at the study site are screened for eligibility from the biopsy scheduling list. No advertising is used. A screening log recording the number of patients assessed, the number excluded and the reason for each exclusion is maintained throughout the trial and is used to construct the CONSORT flow diagram.

### 5.2 Informed consent

Written informed consent is obtained by the Principal Investigator or by a delegated physician member of the study team who is trained in the protocol and listed on the delegation log. Consent is obtained before any study-specific procedure, including before any questionnaire is administered and before randomization.

Patients receive the participant information sheet at the time the biopsy is scheduled, which in routine practice at the study site is at least several days before the procedure, and are given the opportunity to ask questions and to consult family before signing. Where a patient is first identified on the day of the procedure, a minimum period of 60 minutes for consideration is documented. Participation is voluntary; refusal has no effect on the biopsy or on any aspect of subsequent care.

The information sheet and consent form state explicitly that participants may be allocated to a sham (inactive) device; that the stimulation they experience may be strong, weak or entirely imperceptible; that they will not be told their allocation until the trial analysis is complete; and that de-identified participant-level data will be made publicly available at the time of publication.

### 5.3 Participant withdrawal

Participants may withdraw at any time without giving a reason and without consequence for their clinical care. Data collected before withdrawal are retained and analysed unless the participant explicitly requests deletion, in which case the request is documented and honoured for data not yet included in a locked analysis dataset. Participants who withdraw are not replaced; the 15% inflation of the recruitment target accounts for this.

## 6. Randomization and Allocation Concealment

A computer-generated randomization sequence with a 1:1 allocation ratio and variable, randomly permuted block sizes of 4 and 6 is prepared by a research assistant who takes no other part in trial activity and who has no contact with participants. Variable block sizes are used to prevent prediction of allocation towards the end of a block. The sequence is not accessible to any member of the clinical team.

Allocation concealment is achieved using sequentially numbered, opaque, sealed envelopes (SNOSE). Envelopes are prepared and held by an independent researcher. Each envelope is opaque when held to strong light, is sealed with tamper-evident tape, is numbered sequentially on the outside and contains a carbon-copy sheet on which the participant identifier and the date and time of opening are recorded, so that the record of opening is reproduced on the enclosed allocation slip. Envelopes are opened strictly in sequence.

Nurse A opens the next envelope in sequence only after eligibility has been confirmed and written consent has been obtained, and immediately before the procedure. Nurse A does not communicate the allocation to the operating urologist or to the participant at any time before analysis lock. Any envelope opened in error, out of sequence, or found damaged is documented as a protocol deviation and reported to the Principal Investigator.

## 7. Blinding

This section specifies who is blinded, how blinding is achieved and maintained, and how its integrity is measured. In accordance with CONSORT 2025, the trial is described primarily by naming the blinded roles rather than by a numeric label; the relationship between that description and the labels used in the registry is set out in Section 7.6.

### 7.1 Summary of roles

| Role | Blinded? | Function and safeguards |
|---|---|---|
| **Participant (also the outcome assessor)** | Yes | Self-records every pain and post-procedural score on a paper form; identical electrode placement and identical titration ritual in both arms; device display not visible; device silent on activation; informed before consent that stimulation may be imperceptible |
| **Operating urologist, who is also the Principal Investigator (care provider and investigator)** | Yes | Enters the room only after amplitude titration is complete; opaque screen between device and operative field; participant instructed not to comment on device sensation; announces each stage in fixed wording and asks nothing about pain; records only his own satisfaction rating and blinding-index guess |
| **Independent statistician** | Yes | Receives a dataset coded A and B without the allocation key until the primary analysis is complete and locked |
| **Nurse A (device operator)** | NO | Opens the allocation envelope; applies electrodes; titrates and operates or simulates operation of the device; records amplitude, |

| Role | Blinded? | Function and safeguards |
|---|---|---|
| | | device events and procedure duration; records no outcome data, administers no questionnaire and never handles the participant form |
| **Research assistant** | NO (sequence) | Generates the randomization sequence and prepares the envelopes; no participant contact; no role in outcome assessment |

**Design principle.** Exactly one member of the study team who is present during the procedure knows the allocation (Nurse A), and that person is functionally isolated from every measurement. No member of staff asks the participant for a pain score at any point: the participant writes every score himself on a paper form, cued only by a fixed stage announcement from the blinded operator. Because the person giving the cue does not know the allocation, any residual influence of timing or manner on the reported score is non-differential between arms and cannot bias the treatment comparison. Because no one asks, the courtesy bias that arises when a participant is questioned by the clinician who has just performed the intervention is removed rather than merely reduced.

## 7.2 Participant blinding

In the sham group, electrodes are applied identically to the active group and the device is activated in an identical manner but delivers no electrical current. The device display is oriented away from the participant and the device produces no audible signal on activation in either group.

To equalise the pre-procedural experience, Nurse A performs an identical titration ritual in both arms, using the standardised script in Appendix A. In both arms Nurse A makes the same sequence of dial adjustments, pauses for the same interval between adjustments and asks the same two questions. In the active arm the titration endpoint is the highest comfortably tolerable amplitude, which is recorded in milliamperes. In the sham arm the same sequence is performed with no current delivered, the same questions are asked, and the amplitude is recorded as zero.

All participants are informed before consent that the intensity of stimulation may be strong, weak or entirely imperceptible, and that the absence of any sensation does not indicate which group they are in. This wording is reproduced verbatim in the participant information sheet.

Complete participant blinding cannot be guaranteed in TENS research, because participants receiving active stimulation at a suprathreshold amplitude may perceive paraesthesia. This is an acknowledged and unavoidable limitation of sham-controlled TENS trials.

## 7.3 Operator blinding

The operating urologist is blinded to group allocation throughout. Operator blinding is achieved by a standardised four-component procedure:

- Amplitude titration and device activation or sham activation by Nurse A are completed in full before the operating urologist enters the procedure room. The operator is not present at any point during this phase.
- An opaque physical screen is placed between the TENS device and the operative field for the entire duration of the procedure, preventing the operator from observing the device status, the electrode leads or any indicator light. In addition, the device display is covered with opaque tape as a redundant safeguard.

- Participants are instructed before the procedure not to comment on any device-related sensation, such as tingling, warmth or the absence of sensation. This instruction is delivered by Nurse A, before the operator enters the room.
- Neither Nurse A nor any other team member communicates the allocation to the operator before, during or after the procedure. Unblinding of the operator occurs only after the primary analysis has been completed and locked.

The operator announces the completion of each assessed stage aloud in the fixed wording given in Appendix A, which is the participant cue to mark the corresponding row of the form. The operator asks no question about pain, does not look at the form during the procedure, and does not comment on anything the participant writes. Because the operator is blinded, any effect of tone, timing or manner on the reported score is identical in expectation between the two arms.

## 7.4 Outcome assessment: participant self-report

The outcome assessor in this trial is the participant. All intra-procedural pain scores, the post-procedural anxiety item, the satisfaction rating and the blinding-index response are self-recorded by the participant on a single paper form, and no member of the study team asks the participant for a score at any point.

This arrangement is a deliberate response to the staffing structure of the trial. The operating urologist is also the Principal Investigator. Having the person who performs the periprostatic block also ask the participant to rate the pain of that block would introduce courtesy bias, which compresses reported scores towards lower values and reduces sensitivity to detect a treatment difference, and would place assessment of a subjective participant-reported outcome in the hands of the person delivering the intervention. Self-report removes both concerns without requiring a second blinded assessor, which is not available at the study site.

Operationally: the form is mounted on a clipboard rested on the participant chest, with one clearly labelled row per assessed stage and a wide-barrel marker. The standardised explanation of the NRS and of the form is delivered by Nurse A before the allocation envelope is opened, so that at the moment of explanation no person in the room knows the allocation. During the procedure the operator announces each completed stage in the fixed wording and the participant marks the corresponding row within 30 seconds. After the last core the participant completes the remaining items on the same form. The participant then places the form in an opaque envelope and seals it himself.

Nurse A never handles the form, sealed or unsealed. Data entry is performed by another team member, who is blinded to allocation.

The 30-day assessment is self-completed by the participant on a second paper form at the follow-up visit and returned in the same way. Adverse events at 30 days are abstracted from the clinical record by a blinded team member.

Because self-report replaces verbal assessment, the trial pre-specifies a data-completeness safeguard: for every participant a single field records whether each stage score was marked within the 30-second window. Scores marked outside the window are retained in the primary analysis and examined in a pre-specified sensitivity analysis restricted to in-window scores.

## 7.5 Blinding of the Principal Investigator and the statistician

The Principal Investigator remains blinded to individual allocation for the duration of recruitment and follow-up. Adverse events are reviewed by the Principal Investigator on a blinded basis; where a safety

question cannot be resolved without knowledge of allocation, the emergency unblinding procedure applies.

The independent statistician receives a dataset in which the groups are coded A and B, without access to the allocation key, until the primary analysis is complete and locked. The statistical analysis plan is finalised and locked before database lock and before unblinding. In accordance with good practice for blinded interpretation, the statistician records the principal conclusions under both possible directions of the coding before the key is released; this record is retained in the trial master file.

## 7.6 Masking terminology and alignment with the registry

This protocol defines blinding by naming the blinded roles wherever it is described. The label is retained only where an external data field requires one, and is always accompanied by the list of roles it denotes.

| Context | Wording used |
|---|---|
| **Official title** | A Randomized Triple-Blind Sham-Controlled Trial |
| **This protocol and the manuscript Methods** | Participants, the operating urologist, who was also the Principal Investigator, and the trial statistician were blinded to group allocation; all outcomes were self-recorded by the blinded participant |
| **Where a short label is required** | Triple-blind (participants, operating urologists and independent outcome assessors) |
| **ClinicalTrials.gov masking field** | Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor) |
| **Mapping to registry roles** | Participant = trial participant;<br>Care Provider = operating urologist;<br>Outcomes Assessor = the participant, who self-records every score;<br>Investigator = the Principal Investigator, who is also the operator;<br>Independent statistician |

The conventional label triple-blind, as used in the official title, denotes blinding of the participant, the care provider and the outcome assessor. The ClinicalTrials.gov masking data element counts the investigator as a separate masked role; because both the Principal Investigator and the independent statistician are blinded until analysis lock, the trial is registered as quadruple-masked. The two descriptions refer to the identical set of procedures specified in this section, and no discrepancy is intended. The official title is not amended, so that the registered title, the ethics approval and the eventual publication remain identical.

## 7.7 Assessment of blinding integrity

Blinding integrity is assessed in both participants and operators and is reported irrespective of the result.

Participants. Immediately after biopsy sampling and before any unblinding, the participant self-records on the same paper form which group he believes he was allocated to (active stimulation, sham stimulation, or no opinion), followed by a certainty rating from 1 (not at all certain) to 5 (completely certain).

Operators. Immediately after each procedure, and before leaving the procedure room, the operating urologist records the same guess (active, sham, or no opinion) and the same certainty rating for that participant.

Two indices are calculated and reported, because they answer different questions and are not interchangeable:

- The James blinding index is a single overall index for the trial, ranging from 0 to 1, in which 1 indicates complete blinding, 0.5 indicates responses consistent with random guessing and values below 0.5 indicate systematic unblinding. It is reported once for participants and once for operators, with a 95% confidence interval. Acceptable blinding is defined a priori as a James index greater than 0.5.
- The Bang blinding index is calculated separately for each arm, ranges from -1 to +1, and takes the value 0 when guesses within that arm are consistent with random guessing. It is reported per arm with 95% confidence intervals. Acceptable blinding within an arm is defined a priori as a Bang index whose 95% confidence interval includes 0. The Bang index is reported in addition to the James index because it detects the asymmetric unblinding that is expected in TENS trials, where participants receiving active stimulation may correctly identify their allocation while participants receiving sham do not.

The distribution of responses (active, sham, no opinion) is presented as a contingency table by arm, and certainty scores are summarised descriptively. Blinding indices are descriptive; the primary analysis is not conditioned on them and is reported unchanged whatever the indices show.

### 7.8 Emergency unblinding

Unblinding during the trial is expected to be unnecessary, since TENS delivers no systemic agent and can be discontinued instantly by removing the electrodes; discontinuation of stimulation is the appropriate response to any device-related concern and does not require knowledge of allocation. Should an event nevertheless arise in which knowledge of allocation would alter clinical management, the Principal Investigator may request unblinding for that participant from the independent researcher holding the sequence. The request, the reason, the date and time, and the identity of those unblinded are documented in the trial master file and reported to the ethics committee. Any unblinded participant is retained in the intention-to-treat analysis and is excluded from the per-protocol analysis.

## 8. Interventions

### 8.1 Standard procedure (both groups)

Participants are placed in the lithotomy position. 10 mL of 2% lignocaine gel is applied transrectally before insertion of the ultrasound probe. The perineum is prepared and draped according to institutional protocol.

Local anaesthesia consists of 20 mL of 1% lignocaine in total, administered as full needle-path infiltration under real-time ultrasound guidance with aspiration before each injection. The total volume is distributed as follows:

- Needle-path infiltration: approximately 10 mL infiltrated along the needle track, comprising perineal skin, subcutaneous tissue and pelvic floor musculature. This stage corresponds to the secondary outcome NRS during perineal infiltration.
- Periprostatic nerve block: 10 mL administered into the periprostatic space bilaterally as two injections of 5 mL, one per side. This stage corresponds to the primary outcome.

No local anaesthetic beyond the 20 mL total is administered as part of the standard procedure. Any additional anaesthetic or analgesic given at the participant request is recorded as rescue analgesia and constitutes a protocol deviation for the purposes of the per-protocol analysis.

Fusion-targeted biopsies are performed using the BK 5000 system (BK Medical) with a CIVCO stepper and an 18G x 25 cm needle; 3 to 6 cores are obtained per lesion. In accordance with current EAU Guidelines on

Prostate Cancer, only MRI-targeted cores are obtained and systematic biopsy is not performed. The number of cores obtained is recorded for each participant.

## 8.2 Active TENS group

Nurse A initiates TENS 3 to 5 minutes before local anaesthesia using a Cefar Rehab X2 device (Class II, Type BF; CE-marked and used within its intended purpose). Stimulation parameters are fixed for all participants: symmetrical biphasic compensated pulse; frequency 80 Hz; pulse duration 180 microseconds. Amplitude is individually titrated to the highest comfortably tolerable level using the script in Appendix A, and the resulting value is recorded in milliamperes.

Stimulation is delivered through a single channel using two self-adhesive 5 x 5 cm electrodes, one applied to each side of the perineum, so that the current path crosses the perineum transversely. The electrodes are placed on the paraperineal skin over the medial aspect of the upper thigh, bilaterally and symmetrically about the midline, at the craniocaudal level of the perineal grid template and clear of the biopsy field. This configuration delivers stimulation over the S2 to S4 dermatomes, corresponding to the pudendal innervation of the perineum and the periprostatic region. Placement replicates the TENS 1.0 protocol exactly and is specified, with a reference photograph and dermatome map, which Nurse A follows for every participant in both arms.

Stimulation continues at the titrated amplitude throughout all procedural stages and is discontinued after the last biopsy core has been obtained. If a participant reports that the stimulation has become uncomfortable at any point, Nurse A reduces the amplitude to the highest comfortable level and records both the adjustment and the timing; if stimulation is discontinued at the participant request, this is recorded as a protocol deviation and the participant is retained in the intention-to-treat analysis.

## 8.3 Sham TENS group

Nurse A places the electrodes identically to the active group, using the same placement guide, and activates the device in an identical manner, but no electrical current is delivered. The device display is not visible to the participant and the device produces no sound. The titration ritual described in Section 7.2 is performed in full, with the same dial movements, the same pauses and the same questions as in the active arm. The recorded amplitude is zero. The device is deactivated after biopsy sampling in a manner identical to the active group.

## 8.4 Device malfunction

If the device fails to activate, disconnects, or is found to have delivered no current in a participant allocated to the active arm, Nurse A records the event, the procedural stage at which it occurred and the duration of interruption. Such participants are retained in the intention-to-treat analysis and excluded from the per-protocol analysis. Device output is verified before each session using the manufacturer self-test, and the verification is logged.

## 8.5 Rescue analgesia and discontinuation of the procedure

No routine pre-procedural analgesics or anxiolytics are administered. If a participant requests additional analgesia or sedation during the procedure, the type, dose, timing and procedural stage are recorded. Rescue analgesia is classified as an adverse event (Clavien-Dindo Grade I unless otherwise indicated).

If a participant requests discontinuation of the procedure, the following rules apply:

- Discontinuation before PNB, so that the primary outcome has not yet been assessed: the participant is included in the intention-to-treat analysis and the missing primary outcome is handled by worst-

case imputation in the primary sensitivity analysis, with the value assigned being the highest observed NRS within that participant allocated group.

- Discontinuation after PNB but before biopsy sampling: the participant has a valid primary outcome and is included in the intention-to-treat analysis in the ordinary way. Missing secondary NRS scores are described narratively and excluded from the corresponding secondary analyses.
- In all cases the reason, the procedural stage and any rescue analgesia administered are documented. These participants are retained in the per-protocol sensitivity analysis only if discontinuation was unrelated to the study intervention.

## 9. Outcome Measures

### 9.1 Primary outcome

NRS pain score (0-10) during periprostatic nerve block.

PNB is defined as bilateral periprostatic infiltration comprising two injections of 5 mL of 1% lignocaine, one per side, under real-time ultrasound guidance. The participant self-records the score on the paper form within 30 seconds of the operator announcing completion of the second and final PNB injection in the fixed wording of Appendix A, and before the next procedural stage begins. This fixed window is standardised to prevent contamination of pain recall between stages.

Before the procedure, each participant receives a standardised explanation of the NRS and of the form from Nurse A (Appendix A): the participant is asked to rate pain on a scale from 0 to 10, where 0 means no pain at all and 10 means the worst pain imaginable, and to mark one number per row. The explanation is delivered after consent and before the allocation envelope is opened, so that no person present knows the allocation at that moment.

The minimum clinically important difference is defined a priori as 1.5 NRS points, consistent with established thresholds for procedural pain in urological and surgical settings.

### 9.2 Secondary outcomes

- NRS pain score during ultrasound probe insertion, assessed within 30 seconds of probe placement and before local anaesthesia begins.
- NRS pain score during perineal needle-path infiltration, assessed within 30 seconds of completion of that stage and before PNB begins.
- NRS pain score during fusion-targeted biopsy sampling, assessed within 30 seconds of the last biopsy core being obtained.
- Procedural safety: adverse events through 30-day follow-up, classified according to Clavien-Dindo.
- Patient satisfaction: single-item Likert scale (1 = very dissatisfied to 5 = very satisfied), self-recorded by the participant on the paper form immediately after the procedure.
- Operator satisfaction with procedural conditions: single-item Likert scale (1 = very dissatisfied to 5 = very satisfied), recorded by the operating urologist immediately after the procedure.
- Willingness to repeat the procedure: single question (yes / no / unsure) at the 30-day follow-up.
- Blinding integrity in participants and in operators: James index overall and Bang index per arm, assessed immediately after biopsy sampling and before unblinding (Section 7.7).

### 9.3 Exploratory outcomes

Pain Catastrophizing Scale (PCS-13). Thirteen-item self-report questionnaire; total score 0 to 52; three subscales (rumination, magnification, helplessness). Administered before the procedure using the licensed Polish version. Association with the primary outcome is assessed by Spearman correlation and as a covariate in sensitivity analysis.

Preoperative state anxiety (STAI-S). State subscale of the State-Trait Anxiety Inventory, validated Polish adaptation (Wrzesniewski, Sosnowski, Jaworowska and Fecenec; Pracownia Testow Psychologicznych). Twenty items rated 1 to 4; total score 20 to 80, higher scores indicating greater state anxiety. Administered once before the procedure and reported as the mean per arm. Association with the primary outcome explored by Spearman correlation.

NRS-anxiety. Single item (0 to 10; "How anxious are you right now?") administered before the procedure and immediately after biopsy sampling. Both the baseline value and the pre-to-post change (post minus baseline; range -10 to +10, negative values indicating reduced anxiety) are reported.

TENS amplitude and procedural pain. Within the active group only, the association between the titrated amplitude in milliamperes and the primary outcome NRS at PNB is assessed by Spearman correlation. No pre-procedural pain measurement is obtained in this trial; the analysis therefore uses the absolute NRS at PNB rather than a within-participant change score.

Procedure duration. Minutes from insertion of the ultrasound probe to acquisition of the last biopsy core, recorded by Nurse A from the procedure room clock. Association with the primary outcome is assessed by Spearman correlation and duration is compared between arms by Mann-Whitney U test.

## 10. Schedule of Enrolment, Interventions and Assessments

| Measure | Pre-procedure | Intra-procedure | Post-procedure | 30-day visit |
|---|---|---|---|---|
| Eligibility assessment and screening log | X | | | |
| Informed consent | X | | | |
| Baseline data (age, BMI, PSA, prostate volume, prior biopsies, TENS naivety) | X | | | |
| STAI-S | X | | | |
| PCS-13 | X | | | |
| NRS-anxiety (0-10) | X | | X | |
| Standardised NRS and form explanation (before envelope opened) | X | | | |
| Randomization (envelope opened by Nurse A) | X | | | |
| Electrode placement and titration ritual | X | | | |
| TENS amplitude, mA | | X | | |
| Procedure duration | | X | | |
| NRS - probe insertion | | X | | |
| NRS - perineal infiltration | | X | | |

| Measure | Pre-procedure | Intra-procedure | Post-procedure | 30-day visit |
|---|---|---|---|---|
| NRS - periprostatic nerve block (PRIMARY) | | X | | |
| NRS - biopsy sampling | | X | | |
| Form sealed by participant in opaque envelope | | | X | |
| Blinding index - participant (self-recorded on form) | | X | | |
| Blinding index - operator | | | X | |
| Number of biopsy cores obtained | | X | | |
| Intra-procedural adverse events | | X | | |
| Patient satisfaction (self-recorded on form) | | | X | |
| Operator satisfaction (Likert) | | | X | |
| Post-procedural adverse events | | | | X |
| Willingness to repeat | | | | X |
| Biopsy histopathology result | | | | X |

## 11. Sample Size

The sample size is based on the primary outcome, NRS during PNB. The TENS 1.0 pilot observed a median difference of 3.0 points with an epsilon-squared of 0.59, corresponding to a very large standardised effect. Because effect estimates from small pilot trials are systematically inflated, the trial is deliberately not powered on the pilot estimate. The planning scenario instead uses the pre-specified MCID of 1.5 NRS points with an assumed standard deviation of 2.0, giving a Cohen d of 0.75, and robustness is examined across smaller effects.

Calculations assume a two-sided alpha of 0.05 and a Mann-Whitney U test, applying an asymptotic relative efficiency adjustment of 0.955 relative to the two-sample t-test under a normal shift alternative.

| Scenario | Cohen d | n per group for 80% power | Power at 60 evaluable per group |
|---|---|---|---|
| Planning scenario (MCID 1.5, SD 2.0) | 0.75 | 29 | 98% |
| Intermediate effect | 0.60 | 46 | 89% |
| Conservative robustness scenario | 0.50 | 66 | 76% |

To retain adequate power against effects appreciably smaller than the planning scenario, the trial adopts 60 evaluable participants per group. This provides 80% power for effects of d = 0.52 or larger, 89% power at d = 0.60 and 98% power at the planning scenario of d = 0.75. Inflating by 15% for dropout and non-evaluable primary outcomes yields a recruitment target of 70 per group, that is 140 participants in total. If dropout is lower than anticipated and all 70 participants per group are evaluable, power reaches 82% even in the conservative robustness scenario of d = 0.50.

No interim analysis is planned and no alpha spending is required. Recruitment stops when 140 participants have been randomized, irrespective of the number evaluable; the trial is not extended on the basis of accumulating outcome data.

## 11. Data Collection, Management and Confidentiality

Outcome data are recorded by the participant on the paper form, which is the source document; procedural data are recorded by Nurse A and by the operator on the procedure record. Completed participant forms are sealed by the participant in an opaque envelope labelled only with the study identifier and are opened for data entry by a blinded team member. Each participant is assigned a sequential study identifier; the linking log between study identifiers and patient identifiers is held separately, in a locked location accessible only to the Principal Investigator, and is destroyed after publication.

Data entry is performed by personnel blinded to allocation; Nurse A takes no part in data entry and never handles the participant form. A second blinded team member verifies 100% of primary outcome entries and 10% of all other fields against the source form; discrepancies are resolved against the source and logged. Range and consistency checks are applied to all NRS fields before database lock. Forms with an ambiguous mark are adjudicated independently by two blinded team members against the following pre-specified rules, and every adjudication is logged with both readings and the resolved value: a mark falling between two integers is resolved to the nearer integer, and to the higher integer if it falls exactly midway; a mark spanning more than two integers is recorded as missing; two or more marks in one row are recorded as missing; a row left blank is recorded as missing; a mark placed in a row that does not correspond to the announced stage is recorded as missing for both rows. Disagreement between the two readers is resolved by the Principal Investigator, who remains blinded.

Backups are performed daily to institutional storage. Access is restricted to authorised study personnel listed on the delegation log. Data are retained for 10 years after publication in accordance with institutional policy. Processing complies with the General Data Protection Regulation and with institutional data protection procedures.

The database is locked after the last 30-day follow-up is complete, all queries are resolved and the statistical analysis plan is signed. Unblinding follows database lock; no data field may be altered after lock other than by a documented and justified amendment recorded in the audit trail.

## 12. Statistical Analysis

A separate Statistical Analysis Plan specifies all analyses in full, including derived variables, estimator and confidence interval methods, handling of ties in discrete NRS data, table and figure shells, and reproducibility requirements. The plan is finalised and locked before database lock and before unblinding, and is made publicly available. The summary below is consistent with the locked plan; in the event of any discrepancy, the locked plan takes precedence.

### 13.1 Analysis populations

The primary analysis population is intention-to-treat, comprising all randomized participants analysed in the group to which they were allocated, irrespective of the intervention actually received. A per-protocol sensitivity analysis excludes participants with major deviations, defined as device failure, inadvertent unblinding, discontinuation of stimulation at participant request, or deviation from the 20 mL local anaesthetic protocol in volume or technique.

## 13.2 Primary analysis

The primary comparison is a two-sided Mann-Whitney U test at alpha = 0.05. The effect size is reported as the Hodges-Lehmann estimate of the median difference with a 95% confidence interval, together with the rank-biserial correlation and epsilon-squared, the latter for direct comparability with TENS 1.0. Exact p-values are used where the sample size and the tie structure permit; otherwise the normal approximation with a continuity correction is applied and this is stated. No adjustment for covariates is made in the primary analysis.

The distribution of NRS scores is described by group with medians, interquartile ranges and full frequency distributions, and displayed as a stacked bar chart of the complete score distribution rather than only as summary statistics, so that ceiling and floor effects are visible.

## 13.3 Secondary analyses

NRS at the three secondary stages, patient satisfaction and operator satisfaction are compared by Mann-Whitney U test with Hodges-Lehmann estimates and 95% confidence intervals. Adverse event rates and willingness to repeat are compared by the chi-square or Fisher exact test as appropriate. Secondary p-values are presented without multiplicity correction and interpreted as supportive rather than confirmatory; this is stated explicitly in the publication. Clinical significance for secondary NRS outcomes uses the same MCID of 1.5 points, and a statistically significant difference below that threshold is interpreted as statistically but not clinically meaningful.

## 13.4 Blinding integrity

The James index is calculated overall for participants and for operators, with 95% confidence intervals. The Bang index is calculated separately for each arm, for participants and for operators, with 95% confidence intervals. Response distributions are presented as contingency tables by arm and certainty ratings are summarised descriptively. These analyses are descriptive and do not modify the primary analysis.

## 13.5 Exploratory analyses

PCS-13, STAI-S and NRS-anxiety are related to the primary outcome by Spearman correlation, with a sensitivity analysis using ANCOVA on the rank-transformed primary NRS with STAI-S and PCS-13 as continuous covariates. The pre-to-post change in NRS-anxiety is analysed by the Wilcoxon signed-rank test within each group and by the Mann-Whitney U test between groups. TENS amplitude is related to NRS at PNB by Spearman correlation within the active group only. Procedure duration is related to the primary outcome by Spearman correlation and compared between arms by Mann-Whitney U test. All exploratory analyses are pre-specified and are labelled as hypothesis-generating in the publication.

## 13.6 Missing data

A primary outcome missing because of discontinuation before PNB is handled by worst-case imputation in the primary sensitivity analysis, with best-case imputation reported as a secondary sensitivity analysis; such participants are retained in the intention-to-treat population. A primary outcome missing for any other reason is described narratively, with no imputation if overall missingness is 5% or less, and with both best-case and worst-case sensitivity analyses if it exceeds 5%. Missing secondary and exploratory data are analysed as complete cases, and the number of observations contributing to each analysis is reported. Because scores are self-recorded, the proportion of stage scores that are missing, illegible or adjudicated is reported for each arm, together with the pre-specified sensitivity analysis restricted to scores marked within the 30-second window.

### 13.7 Independence

Analyses are performed by an independent statistician/

## 14. Safety Monitoring and Adverse Event Reporting

### 14.1 Definitions

An adverse event is any untoward medical occurrence in a participant after enrolment, whether or not related to the trial intervention. A serious adverse event is any event that results in death, is life-threatening, requires hospitalisation or prolongation of hospitalisation, results in persistent disability, or is judged medically important. A device-related adverse event is any event assessed by the Principal Investigator as having a reasonable possibility of being caused by the TENS device or its application, including cutaneous reactions at the electrode sites.

### 14.2 Collection and grading

Adverse events are collected from randomization through the 30-day follow-up. Intra-procedural events are recorded contemporaneously by Nurse A and by the operator; post-procedural events are abstracted from the clinical record at the 30-day assessment and from any unscheduled contact by the Principal Investigator, who remains blinded. All events are graded according to the Clavien-Dindo classification. Expected post-biopsy events, including haematuria, haematospermia, perineal pain and transient voiding difficulty, are recorded systematically rather than only on spontaneous report.

### 14.3 Reporting

No formal data and safety monitoring board is constituted, given the established safety profile of TENS, the absence of any systemic agent and the low-risk nature of the procedure; this decision was reviewed and accepted by the ethics committee. The Principal Investigator reviews all adverse events on an ongoing and blinded basis. Any event of Clavien-Dindo Grade III or higher is reported to the ethics committee within 24 hours and triggers immediate review.

### 14.4 Stopping rules

Recruitment is suspended pending ethics committee review if either of the following occurs: two or more device-related serious adverse events; or an unexpected harm signal judged by the Principal Investigator and the ethics committee to outweigh the anticipated benefit. There are no efficacy stopping rules, since no interim efficacy analysis is performed.

## 15. Ethics and Regulatory

The trial is conducted in accordance with the Declaration of Helsinki (2013) and the principles of Good Clinical Practice. Ethics approval was granted by the Bioethics Committee for Scientific Research of the Medical University of Gdansk (KB/326/2026, 9 July 2026) before first enrolment. The trial was prospectively registered at ClinicalTrials.gov (NCT07578324) before first enrolment.

The TENS device used is CE-marked and is applied within its intended purpose. The trial does not evaluate the performance or safety of the device itself for regulatory purposes and is not a clinical investigation of a medical device within the meaning of the Medical Device Regulation. The trial does not study a US FDA-regulated drug or device.

Participants receive no financial compensation. There is no anticipated harm arising from participation beyond the risks of the biopsy itself, which are unchanged by the trial; both arms receive the full standard local anaesthesia protocol and no participant is deprived of standard care. Participants are covered by the institutional civil liability insurance held by the sponsor, which extends to research activity conducted at the site. Post-trial care is standard clinical care, unchanged by participation. Participants are informed of their allocation on request after the primary analysis has been locked.

## 16. Protocol Deviations and Amendments

A protocol deviation is any departure from the procedures specified in this document. Deviations are recorded in a deviation log with the date, the nature of the departure, the participant identifier and the action taken. Major deviations, defined in Section 13.1, exclude a participant from the per-protocol population but never from the intention-to-treat population.

Substantive amendments to this protocol are submitted to the ethics committee and reflected in the ClinicalTrials.gov record before implementation. Amendments affecting eligibility, the intervention, the primary outcome, the sample size or the blinding procedures are always treated as substantive. Every amendment is entered in the amendment log in Appendix B, and the version number and date on the title page are incremented. Where an amendment is made after recruitment has begun, the publication states what was changed, when and why.

## 17. Data Sharing and Dissemination

De-identified individual participant data underlying the reported results, together with the study protocol, the locked statistical analysis plan, the informed consent form and the analytic code, are made publicly available without restriction at the Open Science Framework at the time of publication, with no end date. Participants are informed of this in the consent form.

Results are submitted for publication in a peer-reviewed urology journal irrespective of the direction of the findings, and are reported in accordance with CONSORT 2025 with a completed checklist and flow diagram. The registry record is updated with results within 12 months of primary completion. Authorship follows the ICMJE criteria; no professional medical writers are used. The pilot trial (TENS 1.0) is cited in every report of this trial so that the relationship between the two studies is transparent.

## 18. Roles and Responsibilities

| Role | Responsibility |
|---|---|
| **Principal Investigator, who is also the operating urologist** | Overall oversight; protocol development; ethics and registry submissions; consent; conduct of the procedure and standardised stage announcements; own satisfaction rating and blinding-index guess; blinded review of adverse events; blinded data entry; data integrity; unblinding after analysis lock |
| **Participant** | Self-records all pain scores, post-procedural anxiety, satisfaction and blinding-index response on the paper form; seals the completed form |
| **Nurse A (allocation and device)** | Delivers the standardised NRS and form explanation BEFORE opening the envelope; opens the randomization envelope; applies electrodes; performs the titration ritual; operates or simulates operation of the device; records amplitude, device events and procedure duration; records NO outcome data and NEVER handles the participant form; NOT blinded |

| Role | Responsibility |
|---|---|
| **Research assistant** | Generates the randomization sequence; prepares and holds the SNOSE envelopes; eCRF management; no participant contact |
| **Radiologist** | Multiparametric MRI interpretation; PI-RADS scoring; lesion delineation |
| **Independent statistician** | Statistical analysis plan; primary, secondary and exploratory analyses; blinded until analysis lock |

## 19. Funding

The trial receives no external commercial funding. Costs are met from departmental resources; the TENS devices, electrodes and consumables are provided by the department. No manufacturer of any device used in the trial has any role in the design, conduct, analysis, interpretation or reporting of the trial, and no manufacturer has any right of review before publication.

The investigators declare no competing interests; any interest arising during the conduct of the trial is declared to the ethics committee and in the publication.

## 20. Timeline and Trial Status

| Milestone | Status or estimated timing |
|---|---|
| **Ethics committee submission** | Completed - May 2026 |
| **Ethics approval (KB/326/2026)** | Completed - 9 July 2026 |
| **ClinicalTrials.gov registration** | Completed - first posted 11 May 2026; NCT07578324 |
| **First participant enrolled** | 12.08.2026 |
| **Recruitment complete (n = 140)** | Month 8 |
| **30-day follow-up complete** | Month 9 |
| **Database lock, unblinding and analysis complete** | Month 10 |
| **Manuscript submission** | Month 11 |

## 21. Anticipated Limitations

The single-centre design limits external validity, although it maximises procedural standardisation and continuity with the pilot trial. Generalisability to centres using different local anaesthesia volumes, different needle-path techniques or systematic in addition to targeted sampling is not established by this trial.

The primary outcome is participant-reported and therefore subjective. This is inherent to procedural pain research and is mitigated by self-report rather than verbal questioning, a standardised explanation of the form delivered before the allocation is known to anyone present, fixed stage-announcement wording, and a fixed 30-second window at each stage.

The mode of measurement differs from the pilot. TENS 1.0 collected scores verbally, whereas the present trial uses participant self-report on a paper form. The change is deliberate and is made because the operating urologist is also the Principal Investigator, so verbal questioning by the operator would place assessment of a subjective outcome in the hands of the person delivering the intervention. The

consequence is that effect sizes are not strictly comparable between the two studies, and the comparison of epsilon-squared values with the pilot is presented as indicative rather than as a formal replication.

Complete participant blinding cannot be guaranteed in TENS research, because participants receiving active stimulation may perceive paraesthesia while participants receiving sham perceive nothing. This is mitigated by excluding TENS-experienced participants, by equalising the activation ritual across arms and by pre-procedural wording that normalises the absence of sensation, and it is quantified by the Bang index within each arm rather than concealed. Asymmetric unblinding, if observed, is reported and discussed as a constraint on interpretation.

The trial is powered for the primary outcome only. Secondary and exploratory analyses are not powered, are not corrected for multiplicity and are interpreted as supportive or hypothesis-generating.

Finally, the trial compares active TENS against sham TENS only. The pilot found no difference between sham and local anaesthesia alone, which justifies the omission of a third arm, but the present design cannot itself re-examine that question.

## Appendix A. Standardised Scripts and Form Wording

All wording below is fixed. Personnel do not paraphrase, expand, soften or repeat these statements, and no member of staff asks the participant for a pain score at any point. The Polish wording used at the site is the authoritative version, both for what is spoken and for what is printed on the participant form; the English rendering is provided for the registry submission and for publication. Scripts are laminated and available in the procedure room.

### A1. NRS and form explanation - delivered by Nurse A before the allocation envelope is opened

*"During the procedure you will write down your own pain scores on this form. Each row is one stage of the procedure. The doctor will say out loud when a stage is finished, and that is your signal to mark that row. Please use the scale from 0 to 10, where 0 means no pain at all and 10 means the worst pain you can imagine, and mark one number in the row. Nobody will ask you for a number, so please mark it yourself each time."*

### A2. Titration ritual - delivered by Nurse A, identical in both arms

Nurse A performs the same sequence of dial adjustments, with the same pauses, and asks the following two questions at the same points in both arms. In the sham arm no current is delivered and the recorded amplitude is zero.

*"I am now going to turn the device up gradually. Please tell me when you first feel anything - it may be a tingling, or you may feel nothing at all. Both are normal."*

*"Is this still comfortable for you?"*

### A3. Non-verbalisation instruction - delivered by Nurse A before the operator enters the room

*"During the procedure, please do not comment on what you feel from the device - whether that is tingling, warmth, or no sensation at all. The doctor must not know which group you are in. If anything from the device becomes uncomfortable, please say the word 'device' and I will adjust it."*

### A4. Stage announcement - spoken by the operating urologist

The operator announces the completion of each assessed stage in fixed wording. The announcement is the participant cue to mark the corresponding row, and it names the row so that the participant cannot mark in the wrong place. The operator asks nothing about pain and does not look at the form.

*"Probe in - row one." / "Path infiltration complete - row two." / "Block complete - row three." / "Last core - row four."*

### A5. Items printed on the participant form

The form carries the following items in fixed wording. Rows 1 to 4 are marked during the procedure at the cue; the remaining items are completed by the participant immediately after the last core, before the drapes are taken down.

- Rows 1 to 4, one per stage: "How much pain did you feel during this stage?" with the numbers 0 to 10 printed and the anchors "no pain at all" and "worst pain imaginable".
- Anxiety after the procedure: "How anxious are you right now?" 0 to 10, anchored "not at all anxious" and "the most anxious I can imagine". The same item is completed before the procedure on the baseline form.

- Satisfaction: "Overall, how satisfied are you with the procedure?" 1 to 5, anchored "very dissatisfied" and "very satisfied".
- Blinding index: "Which group do you think you were in?" with three boxes - real electrical stimulation, inactive stimulation, no opinion - followed by "How certain are you?" 1 to 5, anchored "not at all certain" and "completely certain".

The participant then places the form in the opaque envelope provided and seals it. Nurse A does not handle the form or the envelope at any stage.

### A6. Operator blinding-index question - self-recorded by the operating urologist after each procedure

*"Which group do you think this participant was in - active stimulation, sham stimulation, or no opinion?" followed by a certainty rating from 1 to 5.*

### A7. Operator satisfaction - self-recorded immediately after the procedure

*"Overall, how satisfied are you with the procedural conditions during this biopsy, from 1 meaning very dissatisfied to 5 meaning very satisfied?"*

### A8. Thirty-day form - self-completed by the participant at the follow-up visit

*"If it were necessary in the future, would you be willing to undergo the same procedure again?" with three boxes - yes, no, unsure.*

## Appendix B. Electrode Placement Guide

This guide reproduces the electrode configuration used in TENS 1.0 and is applied without modification to every participant in both arms of TENS 2.0. Nurse A follows it for each procedure. A laminated copy is kept in the procedure room.

### B1. Anatomical placement

A single stimulation channel is used, comprising two self-adhesive 5 x 5 cm electrodes (Dura-Stick or equivalent), one applied to each side of the perineum, so that the current path crosses the perineum transversely between them. No further electrodes are applied. Each electrode is placed on the paraperineal skin over the medial aspect of the upper thigh, immediately lateral to the perineum and symmetrically about the midline, with the distance from the midline matched between sides for each participant. The craniocaudal position corresponds to the level of the perineal grid template, so that the electrodes lie immediately lateral to the template and clear of the biopsy field.

This configuration delivers stimulation over the S2 to S4 dermatomes, which correspond to the pudendal innervation of the perineum and the periprostatic region, as shown in the dermatome panel of the figure below. The stimulation field therefore overlaps the segmental territory carrying nociceptive input from the needle path and from the periprostatic space.

### B2. Application procedure

- Electrodes are applied after the participant is positioned in lithotomy and before skin preparation and draping, so that placement can be verified against this guide without interrupting the sterile field.
- The skin is dry and free of gel, hair at the electrode site is not shaved, and full adhesive contact across the whole electrode surface is confirmed by palpation before connection.
- Lead wires are routed laterally and caudally, away from the operative field, the stepper and the template mount, and are secured to the drape. The leads are connected identically in both arms.
- Electrode placement is verified against the photograph in B3 before the titration ritual begins, and adherence to the guide is recorded as a single yes or no field in the eCRF for every participant.
- At the end of the procedure the electrodes are removed by Nurse A after the drapes are taken down, and the skin at each site is inspected for erythema or reaction; any finding is recorded as an adverse event.

## B3. Reference photograph and dermatome map

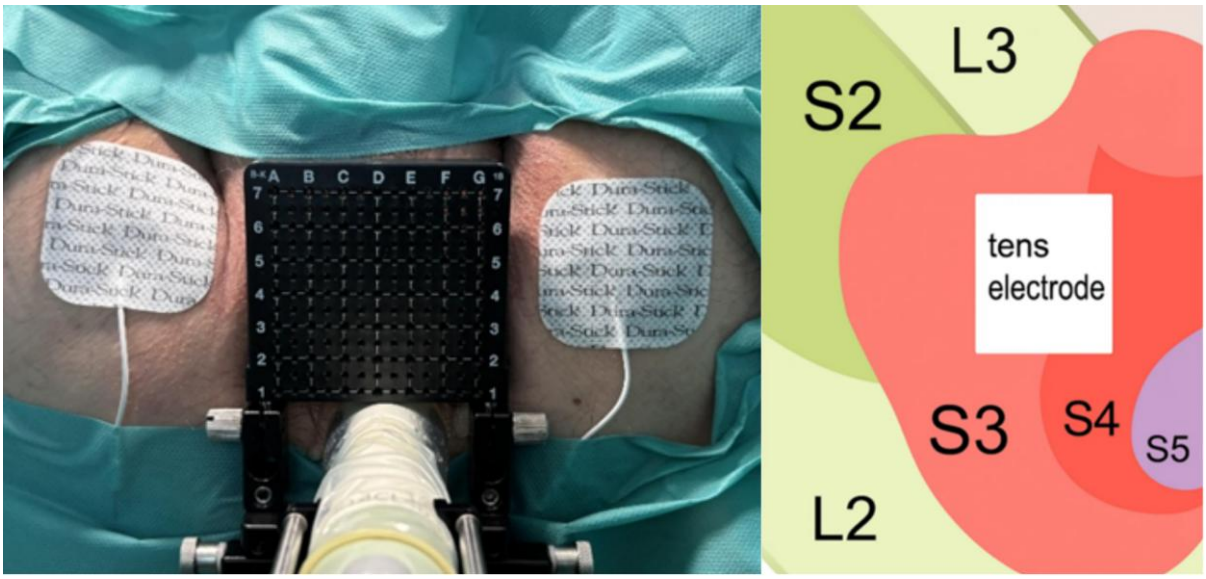



**Figure B1.** Left: intraprocedural photograph showing bilateral paraperineal electrode placement in the lithotomy position, with the perineal grid template and stepper-mounted transrectal probe between the electrodes. Right: corresponding dermatome map, with the electrode position lying within the S3 territory adjacent to S2 and S4.