Clinical Trial Protocol

Based on SPIRIT 2013 checklist (https://doi.org/10.7326/0003-4819-158-3-201302050-00583)

Study Title (English):

A randomized controlled trial comparing fractional bipolar radiofrequency therapy Vs sham for treatment of vaginal laxity in premenopausal women.

Sponsor or planned sponsor, grant, scholarship <if applicable>:

- The budget proposal includes a plan to seek funding from the Faculty of Medicine, Ramathibodi Hospital, Mahidol University
- The fractional radiofrequency devices and the sham applicators will be provided through sponsorship by Morpheus8V (InMode) company

Conflict of Interest:

- No

Study sites (list all as planned):

- Outpatient department – Female Pelvic Medicine and Reconstructive Surgery clinic (FPMRS clinic), Department of Obstetrics & Gynaecology, Faculty of Medicine Ramathibodi Hospital

Trial registration:

- The trial is intended to be registered on www.clinicaltrials.gov.

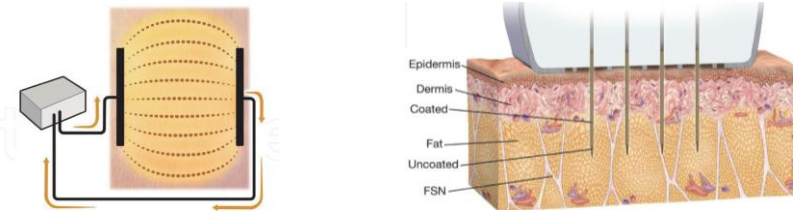
Background and Significance:

Vaginal laxity is a prevalent concern among premenopausal women today. A retrospective cohort study found that 24% of women reported experiencing vaginal laxity.[1] According to the IUGA/ICS 2018 definition, vaginal laxity is characterized by a sensation of looseness in the vagina.[2] The relationship between vaginal laxity (VL) and childbirth is not entirely clear, but it is increasingly recognized that vaginal

delivery can contribute to trauma in the pelvic floor. Symptoms of vaginal laxity include loose vaginal tissue and other organs that are not displaced or pressing against the vagina, which differ from those associated with pelvic organ prolapse.[3] The laxity of vulvovaginal tissue can arise from several factors, including natural aging, childbirth, genetic predispositions, and trauma. These factors can result in common symptoms such as stress urinary incontinence, atrophic vaginitis, dyspareunia, or dissatisfaction with appearance.[4] Therefore, this condition should not be overlooked, as it can have a substantial impact on a woman's quality of life, resulting in discomfort, diminished sexual satisfaction, and emotional distress.[5]

There are several management modalities for the treatment of vaginal laxity, such as pelvic floor muscle training, energy-based devices, and surgical management. As of now, no studies have specifically assessed the application of pelvic floor muscle training (PFMT) for the treatment of vaginal laxity.[1] Moreover until now, there are no standard treatment for vaginal laxity in the current guidelines. However, energy-based devices are common modalities for improving vaginal laxity nowadays, which can be categorized into ablative fractional laser therapies, such as the ablative CO2 laser, and non-ablative therapies like Erbium-doped yttrium-aluminum-garnet (Er:YAG) and radiofrequency therapy.[3]

Principle of bipolar radiofrequency therapy



Bipolar technology refers to an electrosurgical device in which the electrical current flows between two active electrodes positioned closely together. In bipolar devices, both electrodes produce a similar thermal effect and are applied to the area of tissue being treated. These devices generate larger thermal zones and are commonly utilized in electro-coagulators. The advantage of bipolar systems is the localization of all RF energy in the treatment zone.[6]

Fractional bipolar radiofrequency therapy has emerged as a promising minimally invasive treatment modality. This non-ablative approach uses fractional RF technology with microneedles to deliver thermal injury to the subdermis, stimulating collagen production, promoting tissue remodeling and improving tissue tightening, potentially addressing symptoms associated with vaginal laxity.[7] Recent advancements in RF technology have led to its increasing use in aesthetic and gynecological applications. Evidence suggests that RF microneedling effectively remodels subdermal fat and improves skin firmness.[13] However, no previous study has been conducted on the treatment of vaginal laxity using fractional bipolar

radiofrequency (with microneedling), highlighting the need for rigorous scientific evaluation to provide conclusive evidence on its effectiveness, including improvements in sexual function and safety.[3]

Additionally, the use of 3D transvaginal ultrasound to measure vaginal wall thickness is still limited in clinical studies. It is necessary to investigate whether fractional bipolar radiofrequency can improve vaginal wall thickness and explore the association between vaginal wall thickness and the clinical presentation of vaginal laxity in patients.

This study aims to address this gap by conducting a first randomized controlled trial to compare the efficacy of fractional bipolar radiofrequency therapy with a sham treatment in premenopausal women. By employing a methodological approach, this research seeks to contribute valuable insights into the clinical benefits of fractional bipolar radiofrequency therapy, ultimately guiding future treatment strategies for vaginal laxity.

Review literatures:

1. **The efficacy and safety of a combined multipolar radiofrequency with pulsed electromagnetic field technology for the treatment of vaginal laxity: a double-blinded, randomized, sham-controlled trial**[8] *(Lasers in Medical Science, 2022)*

This study aimed to evaluate the efficacy and safety of a multipolar RF and pulsed electromagnetic field-based device (PEMF) compared to a sham treatment for vaginal laxity. Thirty-two premenopausal women with self-reported vaginal laxity and at least one vaginal delivery were randomized into two groups: active (RF + PEMF) and sham. Both groups underwent three vaginal treatments at three-week intervals. Outcomes were assessed using the Vaginal Laxity Questionnaire (VLQ), perineometer measurements, and Brink score at baseline, 4 weeks, and 12 weeks post-treatment. Additionally, vaginal histology, Female Sexual Function Index (FSFI), patient satisfaction, pain, and adverse events were evaluated.

Results showed that the active group had significantly improved VLQ scores compared to the sham group ($p < 0.001$), with **50% of the active group reporting no vaginal laxity at the final follow-up, compared to 12% in the sham group ($p = 0.054$)**. The active group also demonstrated significant improvements in perineometer measurements, Brink scores ($p < 0.001$), FSFI scores ($p < 0.05$), and patient satisfaction ($p < 0.001$). Mild adverse effects such as pain and burning were similar between groups, but itching was significantly more frequent in the sham group ($p = 0.014$). Six participants consented to undergo pre- and post-treatment vaginal wall biopsies for histological analysis. Punch biopsies (3 mm.) were

collected two weeks prior to the initial treatment and 12 weeks after completing the third session. The formalin-fixed vaginal tissue samples were stained with hematoxylin and eosin (H&E) and further processed with Verhoeff-van Gieson stain to evaluate elastic fibers.

Histological analysis after RF + PEMF treatment showed neocollagenesis, neoelastogenesis, and neoangiogenesis. In conclusion, RF + PEMF therapy was safe and effective in improving vaginal laxity, enhancing pelvic floor muscle strength, and boosting female sexual function for at least 12 weeks post-treatment, with confirmed histological improvements.

Similarity: This randomized controlled trial (RCT) investigates premenopausal women with vaginal laxity in Thailand.

Difference: This RCT compares the effectiveness of a multipolar radiofrequency (RF) device with a pulsed electromagnetic field-based device (PEMF), whereas my research utilizes a fractional bipolar radiofrequency device. This distinction highlights the use of two different types of radiofrequency therapies.

Importance: This finding is significant for estimating the improvement in vaginal laxity within the sham group in the study, which demonstrated that 12% of participants reported no vaginal laxity three months post-treatment. This contrasts with the active group, where 50% reported no vaginal laxity at the final follow-up ($p = 0.054$). This study also performed vaginal biopsies on volunteer participants for histological analysis at the study center located in Ramathibodi Hospital, with no significant complications reported.

2. **Radiofrequency Treatment of Vaginal Laxity after Vaginal Delivery: Nonsurgical Vaginal Tightening**[9] *(J Sex Med, 2010)*

This pilot study aimed to evaluate the safety and tolerability of nonsurgical radiofrequency (RF) thermal therapy for treating vaginal introitus laxity post-delivery and to assess the utility of self-report questionnaires in evaluating the device's subjective effectiveness. The study involved treating 24 women once with reverse gradient RF energy (75–90 joules/cm²) delivered through the vaginal mucosa. Follow-up assessments were conducted at 10 days, 1 month, 3 months, and 6 months. Safety was assessed through pelvic examinations and adverse event reports. Effectiveness was evaluated using modified Female Sexual Function Index (mv-FSFI), Female Sexual Distress Scale-Revised (FSDS-R), and newly designed Vaginal Laxity and Sexual Satisfaction Questionnaires, as well as the Global Response Assessment.

The RF treatment was well-tolerated, with no reported adverse events or need for topical anesthetics. Self-reported vaginal tightness improved in 67% of participants at one month and 87% at six

months (P < 0.001). Mean sexual function scores increased significantly from 27.6 ± 3.6 before treatment to 32.0 ± 3.0 at six months (P < 0.001), and FSDS-R scores decreased from 13.6 ± 8.7 to 4.3 ± 5.0 (P < 0.001). Among 12 women who initially reported reduced sexual satisfaction, all showed sustained improvements on the Sexual Satisfaction Questionnaire at six months (P = 0.002). To conclude, RF treatment was well-tolerated and demonstrated a strong safety profile over six months. Subjective improvements in vaginal tightness, sexual function, and reduced sexual distress were reported, suggesting that further studies are warranted.

Similarity: This incorporates subjective assessments, including self-reported vaginal tightness and questionnaires evaluating sexual function, such as the Female Sexual Function Index (FSFI), the Female Sexual Distress Scale - Revised (FSDS-R), and a sexual satisfaction questionnaire.

Difference: This procedure is conducted using a different type of radiofrequency technology from my research proposal.

3. **Safety, tolerability and short‐term efficacy of transvaginal fractional bipolar radiofrequency therapy for symptoms of stress and or mixed incontinence in conjunction with genitourinary syndrome of menopause**[10] *(Neurourol Urodyn. 2023)*

The study introduces the application of radiofrequency (RF) energy through microneedling as a method to enhance collagen and elastin remodeling in the superficial vaginal mucosa, with the aim of restoring elasticity and moisture. This research is unique as it reports the use of microneedling to deliver RF energy directly to the vaginal canal, following a novel approach where needles penetrate at depths of 1, 2, or 3 mm. The objective was to evaluate the safety and short-term outcomes of a single fractional RF treatment on a cohort of twenty women experiencing stress urinary incontinence (SUI) or mixed urinary incontinence (MUI) alongside genitourinary syndrome of menopause (GSM). Using the EmpowerRF platform with the Morpheus8V applicator, RF energy was applied via 24 microneedles, and various outcomes were assessed through clinical tests and questionnaires at 1, 3, and 6 months post-treatment. Results showed significant improvements across all eight measured outcomes, including various urinary symptoms, at each follow-up compared to baseline.

Five biopsies were conducted, revealing that histological examination of the vaginal mucosa three months after treatment showed an increase in the density of elastic fibers compared to baseline samples. Both superficial and deeper layers of elastic fibers were identified. Additionally, the biopsies indicated no

damage to the submucosal collagen layer and no evidence of scar tissue formation following the treatment, confirming that fractional RF treatment did not have any adverse effects

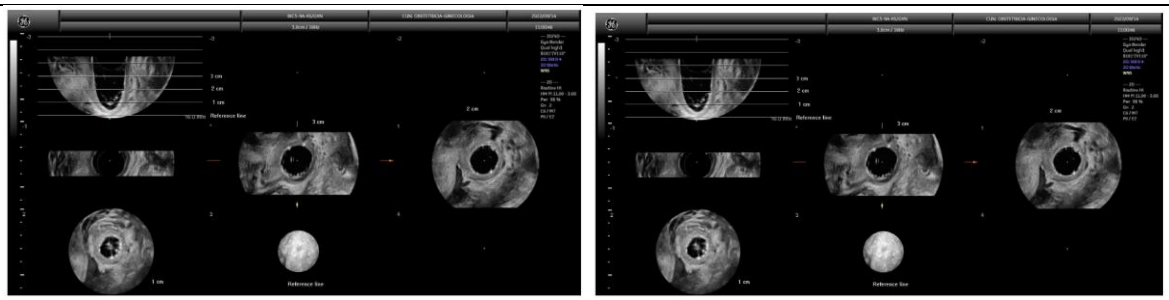
The study concludes that fractional RF energy treatment delivered vaginally is safe, well tolerated, and offers short-term benefits for women suffering from SUI and/or MUI in conjunction with GSM.

Similarity: This study represents the first randomized controlled trial (RCT) utilizing a fractional bipolar radiofrequency device combined with microneedling for intravaginal treatment, a methodology that aligns with the radiofrequency treatment employed in my research. In this trial, the protocol involves administering **a single session** with the fractional bipolar radiofrequency device, followed by an evaluation of the outcomes.

Difference: The population in the RCT study consists of women with coexisting stress or mixed urinary incontinence (MUI) and genitourinary syndrome of menopause. In contrast, my RCT focuses on premenopausal women with vaginal laxity, so the main difference lies in the objective of the study and the outcome measurements.

4. **Vaginal wall thickness as potential biomarker of vaginal health. A proposal for standardized ultrasound measurement using three-dimensional transvaginal ultrasound**[11] *(J Clin Ultrasound, 2023)*

The pilot study in ten patients from Spain proposes a standardized method utilizing three-dimensional (3D) transvaginal ultrasound to measure vaginal wall thickness as a biomarker of vaginal health. The methodology is outlined as follows: First, the vagina is filled with gel. An endovaginal transducer is then inserted into the vagina, reaching up to the mid-third. In the sagittal plane, the cervix and vaginal fornices are visualized, and a 3D volume of the upper third of the vagina is captured. Using the tomographic ultrasound imaging function in the sagittal plane, with the posterior vaginal fornix as the reference point, at least three axial planes of the vagina are obtained, spaced 1 cm apart. Vaginal wall thickness is measured at a distance of 2 cm from the posterior vaginal fornix at the 12, 3, 6, and 9 o'clock positions. The study demonstrates high reproducibility of these measurements, establishing that assessments of vaginal wall thickness can be performed reliably.



Similarity: This pilot study proposes a reliable method for measuring vaginal wall thickness, demonstrating high reproducibility of measurements.

Limitations of this study: The study is limited by the small number of cases (only 10 patients) and the lack of correlation with patients' clinical data.

Objectives:

Primary Objective:

- To evaluate and compare the efficacy of fractional bipolar radiofrequency therapy versus a sham treatment for vaginal laxity in premenopausal women.

Secondary Objectives (if any):

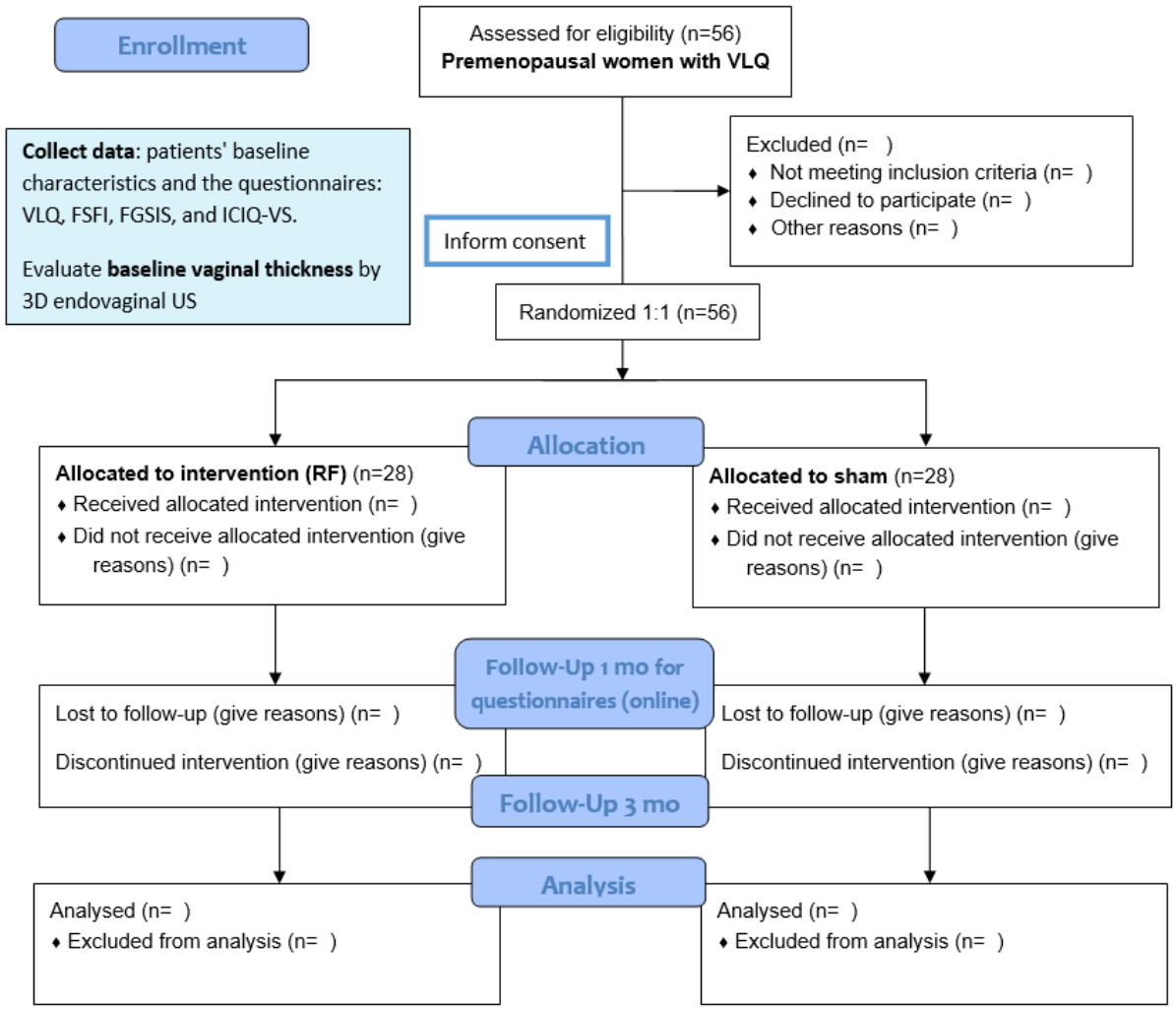
- To evaluate patient satisfaction and changes in sexual function before and after fractional bipolar radiofrequency therapy Vs sham treatment.
- To assess alterations in vaginal thickness based on 3D transvaginal ultrasound before and after fractional bipolar radiofrequency therapy Vs sham treatment.
- To evaluate any potential side effects or adverse events associated with intravaginal fractional bipolar radiofrequency therapy.

Study design/methodology:

Study design: A double-blind, randomized controlled trial

Study flow diagram

CONSORT Flow Diagram



Study Population:

- Premenopausal women with clinically diagnosed vaginal laxity who are sexually active.

Inclusion Criteria:

- Premenopausal women
- Age 20-55 years
- Reported symptoms of vaginal looseness with a score of at least 1 on The Vaginal Laxity Questionnaire (VLQ)
- Sexually active (≥1 time/month)
- Willing to undergo vaginal energy-based treatment and attend follow-up visits 3 months after treatment

Exclusion criteria

- Presence of sexually transmitted diseases or active genital lesions
- Currently pregnant or planning for conception during study period
- Pelvic organ prolapse (POP ≥ Stage II)
- Previous treatment for vaginal laxity with modalities other than pelvic floor muscle training
- Currently using intrauterine devices for contraception
- Presence of any active electrical implant such as pacemaker, internal defibrillator
- Current condition of genital cancer

Treatment allocation and concealment:

Patients who meet the inclusion criteria will be randomly assigned to treatment group and sham group using a block randomization method with a 1:1 treatment ratio. The sequence generation will be provided by a senior statistician from the Clinical Epidemiology and Biostatistics section at Ramathibodi Hospital. Random sequences will be created using Stata version 18, an automated process without investigator involvement. One research team member from the FPMRS department will be responsible for allocation but will not participate in the treatment procedure or the evaluation process.

Blinding (masking):

This study employs a double-blind design to minimize bias by blinding both the patients and evaluators. All patients, regardless of group, will remain blinded. The sham group will receive treatment with a specialized sham device that mimics the treatment group's equipment. There are no differences in the design of the tip device, the auditory signal (beeping), or the pulse count display. The physician managing the allocation, will not be involved in the treatment procedures or the assessment process. Subjective outcomes, such as questionnaires (VLQ, FSFI, FGSIS, ICIG-VS, PGI-I), will be assessed by a research assistant from the urogynecology clinic who is blinded to the group assignments, ensuring she is unaware of which patients received the actual treatment and which received the sham.

Participant timeline and Procedures:

Time	Visit	Procedure
Week 0	Screening and enrollment	Eligibility screening, Inform consent, General advice for PFMT

	Baseline assessment	Demographic data, Questionnaires (VLQ, FSFI, FGSIS, ICIQ-VS)
	Physical examination 3D endovaginal US	PV: Evaluate genital hiatus (Gh), vaginal caliber (fingerbreadth) Evaluate baseline vaginal thickness
Week 1	Intervention *	Radiofrequency therapy Vs Sham
72 hours Post-intervention	Telemedicine	Inquire with the patients about any adverse events they may have experienced following the intervention
Week 4 (1 month Post-intervention)	Telemedicine/questionnaires by mail	Questionnaires (VLQ, FSFI, FGSIS, ICIQ-VS), Assessment for any adverse events The Patient Global Impression of Improvement (PGI-I)
Week 13 (3 months Post-intervention)	Follow-up visit	Questionnaires (VLQ, FSFI, FGSIS, ICIQ-VS) Assessment for any adverse events The Patient Global Impression of Improvement (PGI-I)
	Physical examination 3D endovaginal US	PV: Evaluate genital hiatus (Gh), vaginal caliber (fingerbreadth) Evaluate vaginal thickness post-RF treatment

Outcomes/endpoints:

Primary outcomes

- **Subjective outcomes**

- The Vaginal Laxity Questionnaire (VLQ) will be utilized to assess patient-reported levels of vaginal laxity.

Secondary outcomes

- **Subjective outcomes**

- The Thai version of the Female Sexual Function Index (FSFI) will be administered to evaluate sexual function.
- The Thai version of the Female Genital Self-Image Scale (FGSIS) will be employed to assess patients' perceptions of their genital self-image.

- The International Consultation on Incontinence Questionnaire-Vaginal Symptoms (ICIQ-VS), validated in Thai, will be used for symptom evaluation.
- The Patient Global Impression of Improvement (PGI-I) will measure overall patient satisfaction with treatment outcomes.
- Patients will report any side effects or adverse events experienced during the study.

- **Objective outcomes**

- Vaginal wall thickness will be assessed using 3D transvaginal ultrasound imaging, following the standardized protocol established in previous studies.

Discontinuation/withdrawal criteria:

- **Adverse Events:** Development of serious adverse effects or complications related to the therapy, such as severe pain, infection, or significant bleeding. Or any signs or concerns that the participant might not be safe to continue, as determined by the investigator.
- **Pregnancy:** If a participant becomes pregnant during the study, they may need to withdraw to ensure safety for both the mother and the fetus.
- **Medical Conditions:** Emergence of new medical conditions or exacerbation of existing conditions that could complicate participation or the study's objectives such as active genital infection.
- **Patient Preference**: Participant's decision to withdraw from the study for personal reasons, including dissatisfaction with the treatment or its effects.

Adverse Event Reporting:

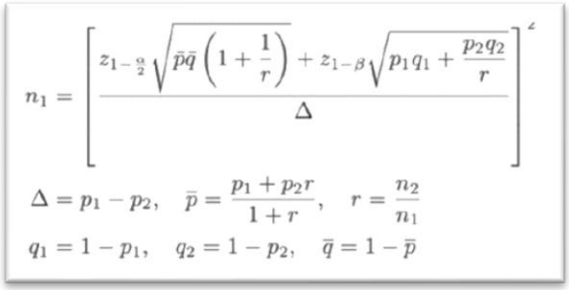
- Pain, discomfort, or a burning sensation during or after the procedure.
- Worsening of urinary symptoms
- The presence of vaginal burn
- Vaginal discharge
- The presence of abnormal vaginal bleeding (spotting).
- Swelling and bruising: Mild to moderate swelling and bruising at the treatment site
- Infection: There is a small risk of infection at the site of microneedling if proper post-treatment care is not followed.

Statistical Analysis Plan:

- **Software:** Stata version 14 for sample size calculation and statistical data analysis.
- **Data analysis:** calculate relevant statistics to summarize range, means, medians, and variability of numerical data, 95% confidence intervals for means, geometric means, and proportions
- **Comparative Analysis:** use t-tests and chi-square tests to evaluate statistical significance of differences in means (possibly log-transformed) or proportions
- Use Intention to treat for data analysis

Sample size determination:

- Calculate with "Two independent population proportions formula (without continuity correction)"



$$n_1 = \left[\frac{z_{1-\frac{\alpha}{2}} \sqrt{\bar{p}\bar{q}\left(1+\frac{1}{r}\right)} + z_{1-\beta}\sqrt{p_1 q_1 + \frac{p_2 q_2}{r}}}{\Delta} \right]^2$$

$$\Delta = p_1 - p_2, \quad \bar{p} = \frac{p_1 + p_2 r}{1+r}, \quad r = \frac{n_2}{n_1}$$

$$q_1 = 1 - p_1, \quad q_2 = 1 - p_2, \quad \bar{q} = 1 - \bar{p}$$

Proportion in group1 (Treatment group) (p1) = 0.5*

Proportion in group2 (Sham group) (p2) = 0.12**

alpha(α) = 0.05, Beta(β) = 0.2

*Sample size (N) = 23 / groups

Add dropout 20% = 28 / groups

Total sample size (N) = 56 participants

- Proportion in group1 (Treatment group) (p1) = 0.5 **>>** Predicted % improvement in treatment group (Fractional bipolar radiofrequency) = 50%
- Proportion in group2 (Sham group) (p1) = 0.12 **>>** % improvement in sham group (base on VLQ) = 12% *(Wattanakrai, P, et al., 2022)*

Recruitment procedure:

1. **Collaboration with Healthcare Providers:**

- Pre-menopausal women with complaints of vaginal laxity or vaginal looseness will be recruited from the outpatient department—FPMRS clinic at Ramathibodi Hospital
- Collaborate with obstetrician, gynecologists, or primary care providers who may refer eligible patients to the study. Provide them with study materials they can share with potential participants.

2. Advertising:

- Poster and Brochures: Distribute in relevant clinics in the hospital.

Informed Consent Process:

- Preparation of Informed Consent Document: The study's purpose, objectives, and significance, a clear explanation of the procedures involved, including the randomization process and treatment assignments, potential risks and benefits of participation, the confidentiality and security measures for managing personal data, information about the right to withdraw from the study at any time without penalty. >> By principal investigator
- In-Person Discussion: when the patient feels interested, a member of the research team will schedule a one-on-one meeting to explain the study verbally. This meeting will allow participants to ask questions and clarify any concerns.
- Assessment of Understanding: The research team will assess participants' comprehension of the information presented by asking follow-up questions to ensure they fully understood the study and their rights as participants.
- Voluntary Participation Assurance: Emphasize that participation in the study is entirely voluntary and that individuals can withdraw at any time without affecting their future care or treatment.
- Obtaining Written Consent: After ensuring that potential participants have all their questions answered and understand the study, they will be provided with the informed consent document to review and sign. The principal investigator or a designated team member will also sign the document to confirm that the informed consent process was appropriately conducted.
- Documenting Consent: Copies of the signed informed consent documents will be securely stored and participants will receive their own copy for reference.

Privacy and confidentiality (Data Management Plan):

1. The researcher and their collaborators are responsible for data management and ensuring patient confidentiality.
2. Each participant will be assigned an ID to anonymize data and samples; identifiable information like hospital numbers or names will be documented in a codebook maintained exclusively by the lead researcher.
3. Physical copies of data (such as paper forms and consent documents) will be securely stored in locked cabinets, with access restricted to authorized individuals.

4. All electronic data will be maintained in encrypted databases, and data transfers will occur over secure, encrypted networks. Regular backups will be executed to prevent data loss, and data will be retained for a minimum of five years.

Ethical consideration:

- ***Risks to participants and how to minimize the risks:***

  There are no significant physical or mental risks associated with the study, as the Morpheus8V device is specifically designed for vaginal treatments and the research protocol adheres to established treatment standards. Additionally, participants have voluntarily consented to take part in the study.

- ***Direct Benefits to Participants***

  Participants in the treatment group will receive this energy-based therapy (fractional bipolar radiofrequency) for vaginal laxity at no cost. Meanwhile, participants in the sham group will have the opportunity to receive the same therapy after the study concludes without cost, if the research demonstrates its efficacy in treating vaginal laxity.

- ***Scientific or social value***

  The value of this research is to provide valuable insights for medical professionals regarding the efficacy and safety of fractional bipolar radiofrequency therapy in treating vaginal laxity. The study seeks to introduce this new non-surgical modality as a potential treatment option for premenopausal women experiencing vaginal laxity. Additionally, it aims to provide evidence of histological changes or improvements resulting from fractional bipolar radiofrequency treatment, thereby enhancing the understanding of its therapeutic effects.

- ***Justification if enrolling potentially vulnerable subjects.***

  The study will not involve individuals from vulnerable populations.

- ***Travel compensation and compensation for injury***

Participants will receive a travel compensation of 400 baht for each treatment and follow-up visit, including the final visit for the sham group to receive treatment after three months of the study.

- **Plan of board consent**

  None

Study Timeline:

Activities	2024					2025										
	8	9	10	11	12	1	2	3	4	5	6	7	8	9	10	11	12
41.Literature review and proposal preparation																	
2. Proposal submission and approval																	
3. Data collection and analysis																	
4.Manuscript writing and submission																	

References:

1.Al-Mousa N, Al-Badr A, Al-Tannir (2022) Vaginal Laxity: Prevalence, Risk Factors, Diagnostic and Therapeutic Approaches. Gynecol Obstet Open Acc 6: 147. DOI: 10.29011/2577-2236.100147

2.Rogers RG, Pauls RN, Thakar R, et al. An International Urogynecological Association (IUGA)/International Continence Society (ICS) joint report on the terminology for the assessment of sexual health of women with pelvic floor dysfunction. Neurourol Urodyn. 2018;37(4):1220-1240. doi:10.1002/nau.23508

3.Krychman ML. Vaginal Laxity Issues, Answers and Implications for Female Sexual Function. J Sex Med. 2016;13(10):1445-1447. doi:10.1016/j.jsxm.2016.07.016

4.Dayan E. Noninvasive Vulvar and Intravaginal Treatments. Clin Plast Surg. 2022;49(4):505-508. doi:10.1016/j.cps.2022.07.004

5.Polland A, Duong V, Furuya R, et al. Description of Vaginal Laxity and Prolapse and Correlation With Sexual Function (DeVeLoPS). Sex Med. 2021;9(6):100443. doi:10.1016/j.esxm.2021.100443

6.The Basic Science of Radiofrequency-Based Devices dol:http://dx.doi.org/10.5772/intechopen.96652

7.Blusewicz TA, Coley KP, Moore RD, Miklos JR. The Novel Use of Bipolar Radiofrequency Microneedling in the Treatment of Lichen Sclerosus. Surg Technol Int. Published online December 1, 2023. doi:10.52198/23.STI.43.GY1743

8. Wattanakrai P, Limpjaroenviriyakul N, Thongtan D, Wattanayingcharoenchai R, Manonai J. The efficacy and safety of a combined multipolar radiofrequency with pulsed electromagnetic field technology for the treatment of vaginal laxity: a double-blinded, randomized, sham-controlled trial. Lasers Med Sci. 2022;37(3):1829-1842. doi:10.1007/s10103-021-03438-3

9.Millheiser LS, Pauls RN, Herbst SJ, Chen BH. Radiofrequency treatment of vaginal laxity after vaginal delivery: nonsurgical vaginal tightening. J Sex Med. 2010;7(9):3088-3095. doi:10.1111/j.1743-6109.2010.01910.x

10.Abdelaziz A, Blusewicz TA, Coley KP, Karram M. Safety, tolerability and short-term efficacy of transvaginal fractional bipolar radiofrequency therapy for symptoms of stress and or mixed incontinence in

conjunction with genitourinary syndrome of menopause. Neurourol Urodyn. 2023;42(4):807-813. doi:10.1002/nau.25170

11.Alcazar JL, Para E, Tomaizhe A, Laza MV, Guerriero S. Vaginal wall thickness as potential biomarker of vaginal health. A proposal for standardized ultrasound measurement using three-dimensional transvaginal ultrasound. J Clin Ultrasound. 2023;51(8):1366-1369. doi:10.1002/jcu.23547

12.QUICK REFERENCE GUIDE (QRG) Morpheus8V Date: November 2021

13. Dayan E, Chia C, Burns AJ, Theodorou S. Adjustable Depth Fractional Radiofrequency Combined With Bipolar Radiofrequency: A Minimally Invasive Combination Treatment for Skin Laxity. Aesthet Surg J. 2019 Apr 8;39(Suppl_3):S112-S119. doi: 10.1093/asj/sjz055. PMID: 30958550; PMCID: PMC6460431.