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Official Title: Assessment of Penile Vibratory Stimulation Using the Viberect in Men with Mild-Moderate ED

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**The protocol header contains a typo and incorrectly lists the approval number as IRB00130001 instead of the correct IRB00130002. There is no study with the approval number IRB00130001. The study has been closed out with the IRB and the study team is unable to submit a change in research to correct the typo. The study team is not permitted to make changes to an IRB-approved document so this title page serves to provide clarification and inform the reader that the correct IRB approval number is IRB00130002. The ClinicalTrials.gov record and the posted Informed Consent Form contain the correct IRB approval number of IRB00130002.*

Johns Hopkins Medicine - *e*IRB Protocol (eForm A)

- **Use the section headings to write the eForm A, inserting the appropriate material in each. If a section is not applicable, leave heading in and insert N/A.**
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1. Abstract

Erectile dysfunction (ED) is the inability to achieve and maintain an erection adequate for satisfactory sexual intercourse. ED is highly prevalent and associated with a significant reduction in both patient and partner quality of life. It is estimated that more than 30-65% of men in the general population aged 40 to 80 years suffer from ED. Current medical treatment options for ED have inconsistent safety and efficacy profiles, and the total financial expenditure for pro-erectile medications is over 5 billion dollars per year. A cheap, easy-to-use, and effective therapy for ED would offer a significant benefit and alleviate the burden in men suffering from this disease process.

Penile vibratory stimulation mimics rapid and repetitive manual stimulation of the penis. Vibratory stimulation of the genitalia is considered safe by the medical community and offers potential benefits, such as treatment of orgasmic dysfunction, and improvement in ejaculatory and erectile function. Penile erection is controlled by spinal autonomic centers, the activity of which is dependent on input from supraspinal centers and genitalia. Penile erection is a culmination of successful nerve reflexes that initiate a penile vascular event. By activating the pudendo-cavernosal reflex, vibratory stimulation of the penis at high frequency can lead to a reflexogenic increase in penile blood flow. In addition, penile stimulation initiates a rhythmic contraction of the perineal muscles via the bulbocavernosus reflex, which subsequently produces erection rigidity.

The purpose of this study is to assess the ease of use, safety, and patient satisfaction of on-demand use of the Viberect® device by men with mild to moderate erectile dysfunction. This research endeavor will be a phase I prospective trial exploring the use of a hand-held vibratory device for men with mild-to-moderate ED. The Viberet® device is Food and Drug Administration (FDA) approved for the use in men with ED, but limited studies have rigorously investigated the safety and patient effects of this device.

2. Study Procedures

This will be a single-center, prospective, phase I clinical trial. Subjects at JHMI will be recruited from the population of men who visit the urology outpatient clinics. Subjects who meet all study inclusions, and do not meet any study exclusions will be offered study participation. Patients will be referred to the study based on their initial clinic visit for ED consultation. We will not have any chart pre-screening and all the information gathered from a patient will be within the standard of care for their clinic consultation. Study eligibility will be determined from history and physical exam, response to validated erectile function questionnaires, and discussion on use of phosphodiesterase-5 (PDE-5) inhibitor and other medication use (dose, type, and need to obtain

successful penile erection). Should the patient wish to participate, the informed consent process will occur in a private clinic room and the patient will be given as much time as necessary to read and reflect upon the informed consent and all questions will be answered. No study procedures will be done prior to obtaining informed consent.

Those who wish to participate will sign an informed consent and will become familiar with the scope and protocol of the study. They will fill out the erectile function component of the international index of erectile function (IIEF-5), Erection Hardness Scale (EHS), Erectile Dysfunction Inventory of Treatment Satisfaction (EDITS), and Treatment Satisfactions Scale (TSS) questionnaires as a baseline. Patients will then be provided with a new Viberect stimulator and the manual, and will subsequently be instructed on the proper use of the device. Patients will demonstrate device use to ensure clarity with the explanation and instructions.

Prospective data will be collected from study subjects who will use the Viberect device. Men will be asked to perform vibratory stimulation of the penis while focused on sexual/erotic thoughts for approximately 7-10 minutes (depending on erectile response) for at least 3 times each week, at least 24 hours apart, throughout a four-week period. Men can perform the stimulation once daily, as long as each session is more than 24 hours apart. Men will record the frequency of device use, erectile response with stimulation, and whether they were able to achieve sexual satisfaction, which may include self-stimulation or penetrative intercourse.

Participants will fill out the IIEF-5, EHS, EDITS, and TSS questionnaires on week 4. The answers to these validated questionnaires will be compared to baseline to evaluate patient effect when using the device. The diaries will be evaluated to explore both the safety, as well as the patient effect when using the Viberect device.

If study subjects decide to use PDE-5 inhibitors during the 4-week study period (not provided by investigators), we ask that they record frequency of use, time, drug type, dosage, and commentary of sexual response as a result separately.

b. Study duration and number of study visits required of research participants.

The total duration of subject participation in this study is **4 weeks.** A total of 2 clinic visits will be included in this study. The first clinic visit will be the baseline evaluation and explanation of the study, and then a follow-up visit approximately 4 weeks after initiation of study period. This 4 week visit is standard of care visit, based on physician's discretion after starting a new therapeutic treatment of ED.

Initial visit: Perform the history and physical exam and to discuss the clinical study. Informed consent will be obtained at this visit if participant willing to proceed and meet inclusion criteria. Study subjects will fill out the IIEF-5, EHS, EDITS, and TSS for baseline documentation. Participants will receive their Viberect device, including the user manual (attached) and will receive instructions on the use of their device. Patients will do a brief demonstration of how to use the device in order to ensure patient understanding and proper utilization.

Follow up visit at four weeks: This is the standard follow-up appointment to discuss efficacy and

safety of the stimulator. The Viberect device is the patient's to keep, however if they are not interested in continuing use, then can bring the device back and it will be returned to Reflexonic by the team. The patient will fill out the IIEF-5, EHS, EDITS, and TSS forms again and will be collected from the patient by nursing staff or the investigators. Patients will have a penile examination to document any sores, lesions, or irritation.
Patients in this study will not be blinded, as we would not be able to blind patients to using a vibratory device or not, and there is only one treatment groupPatients in this study will not be compared to a non-treatment group. This is a phase I trial exploring safety of the device, and we therefore want all participants to use the device and provide their individual reports and feedback.

The standard of care for men presenting with mild-to-moderate ED and requesting treatment are PDE5-inhibitors (Viagra, Levitra, Cialis). While on study, patients will be able to use on-demand PDE5-inhibitors as per usual. Future studies may compare Viberect to PDE5-inhibitors, but the present study is exploring safety of the device.

Patients would be considered a treatment failure if they are unable to use the Viberect device as recommended for the trial due to either mechanical issues or inability to tolerate the penile sensation when using the device.

Once given the Viberect device, it will be the participants to keep. Should the patient not want to possess the device, the will be instructed to the device back at their follow-up appointment and it will be returned to the manufacturing company. Patients are able to continue using the Viberect device for personal use after the study is complete. Patients are still required to follow the instructions in regards to duration of use and technique of application.

3. Inclusion/Exclusion Criteria

i. Inclusion criteria:

- Men ages between 30-70 interested in treatment for erectile dysfunction
- IIEF-5 score equal to or greater than 13 but less than 25.

ii. Exclusion criteria:

- Men with neurological disease, including a history of spinal cord injury or trauma
- IIEF-5 score less than 13
- History of priapism
- Men with a history of radical prostatectomy within the past 2 years.
- Pre-existing penile skin lesions/ulcers
- Allergy to latex
- Inability to understand and demonstrate device use instructions.
- Patients with insulin-dependent diabetes who suffer peripheral neuropathy or other diabetes associated complications
- Patient unwilling to engage in sexual activity
- Patient is currently participating in another clinical investigation that would serve as a contraindication to applying a stimulatory device to augment erectile function

4. DRUGS/SUBSTANCES/DEVICES

The Viberect penile vibratory stimulation system is a medical device cleared by the

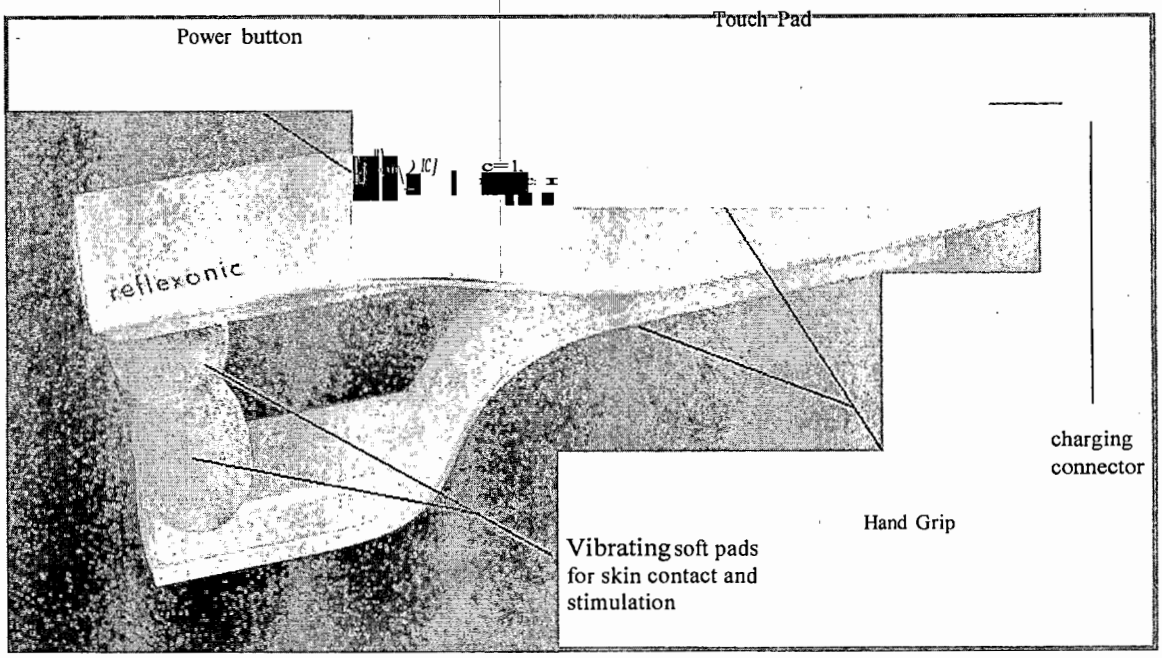
Food and Drug Administration (510k Clearance Letter attached). The FDA statement reads: "The Viberect is a medical device indicated to provoke erection in men who experience erectile dysfunction and to provoke ejaculation in spinal cord injured men." It is currently cleared for sale with, and without a doctor's prescription.

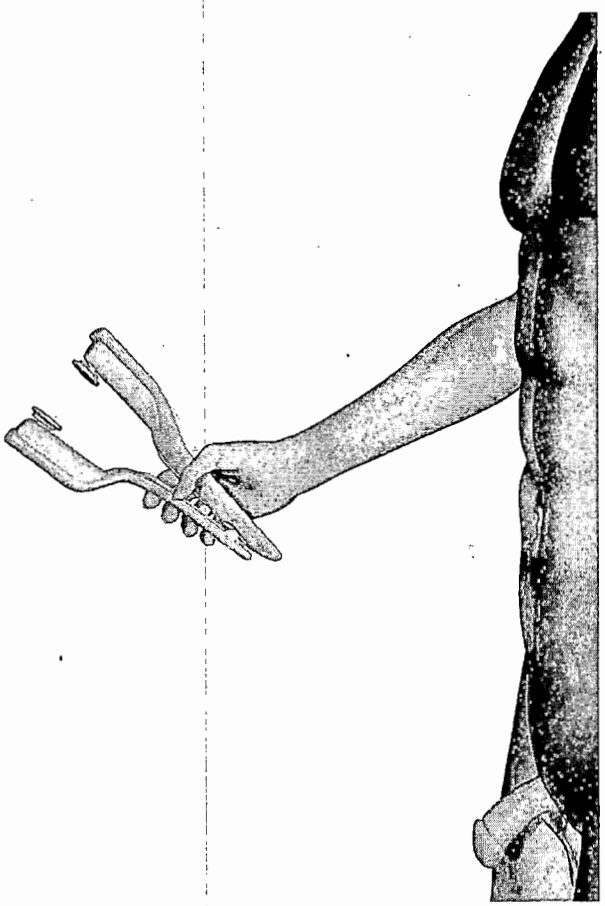
The Viberect is a class II medical device that is easy-to-use and when properly applied, stimulates the nerves of the penis, as a form of sexual aid. In addition, the vibratory mechanism stimulates the spinal nerve reflexes that are responsible for the initiation of penile erection and rigidity. The device is powered by a rechargeable battery. This device has two gentle vibrating motors that allows for simultaneous vibratory stimulation of both surfaces of the penis. The dorsal and ventral side of the male penis is supplied by the dorsal nerve and perineal nerve, respectively. Simultaneous stimulation of both nerves should increase the sexual response.

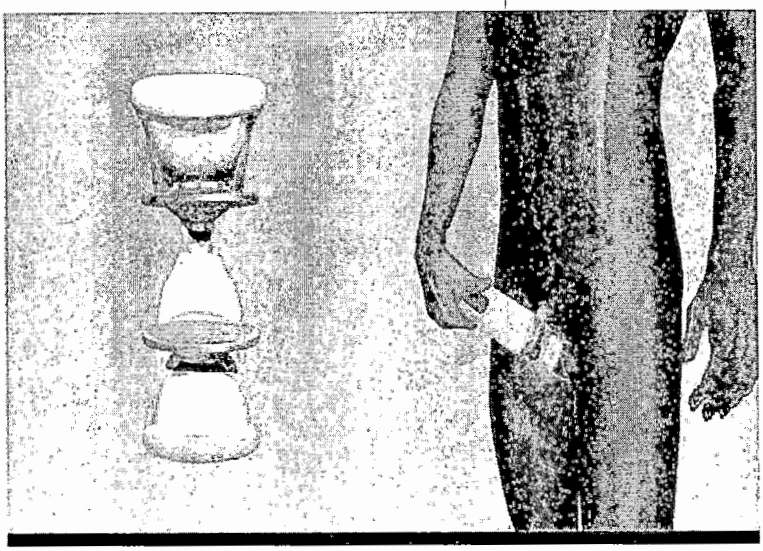
b. *Justification and safety information if FDA approved drugs will be administered for non-FDA approved indications or if doses or routes of administration or participant populations are changed.* **NA**

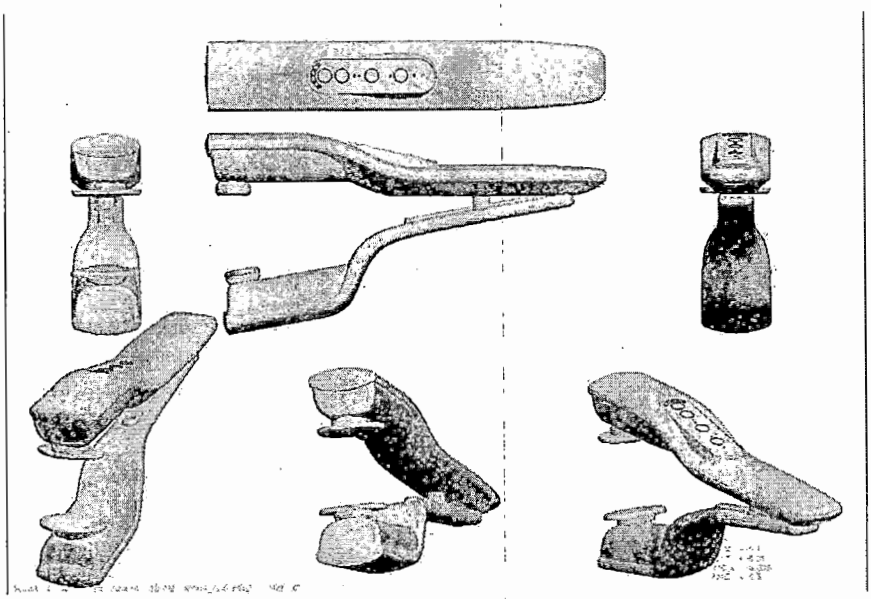
c. *Justification and safety information if non-FDA approved drugs without an IND# will be administered.* **NA**

d. For IND/IDE studies, a summary of preclinical and early human studies. **NA**

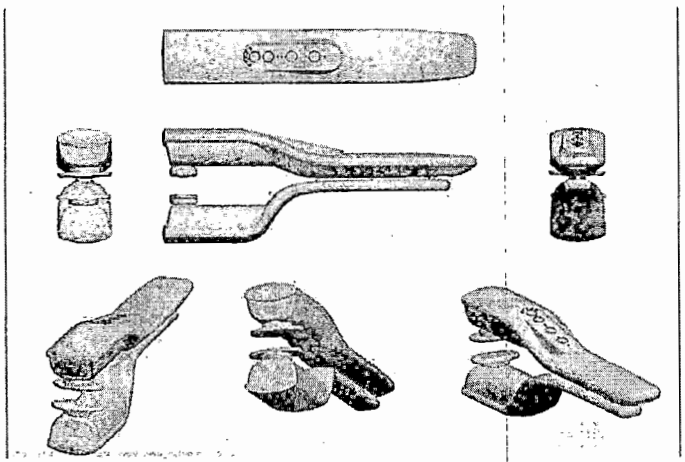

Power button
Touch Pad
reflexonic
charging connector
Hand Grip
Vibrating soft pads for skin contact and stimulation







device open



device closed

5. STUDY STATISTICS

a. Primary outcome variable.

The primary outcome parameter is safety, patient tolerability, and patient satisfaction with the hand-held penile vibratory system.

b. Secondary outcome variables.

The secondary outcome parameter is erectile response (erection, rigidity, orgasm) and subjective patient and/or partner sexual satisfaction, when applicable.

c. Statistical plan including sample size justification and interim data analysis.

This is a prospective study. Descriptive statistics will be performed based on pre-treatment and post-treatment responses to validated sexual function questionnaires. This data will be utilized to perform power analyses to generate future studies. We will recruit a total of **20 patients** for this study.

d. Early stopping rules.

Patients who stop the use of the Viberect early, will be recorded and their reasoning will be documented. Since this is a phase I trial, patient safety and satisfaction is the primary outcome and therefore it will be essential to understand why a patient stops use prematurely.

6. RISKS

a. Medical risks, listing all procedures, their major and minor risks and expected frequency.

Definition of adverse events: Adverse events related to the use of the Viberect device include any user discomfort during or after use of the device, including pain, fatigue, numbness, rash, or device malfunction.

Potential (anticipated) adverse events

-Pain, numbness of the penis or the hand holding the device

Adverse event reporting

i. Description of adverse events (see risk analysis)

ii. Serious adverse events

-potential serious adverse events include device malfunction, vibrating pad dislodgment and vibrating tip damaging the penis.

iii. Unanticipated adverse device effects

- Device overheats and burns. The device will not be used while connected to the electric outlet, therefore minimizing potential risk of burns or overheat

iv. Adverse event severity/strength: To be reported immediately to senior investigator and principal investigator.

v. Serious adverse event narratives: reports and narratives will be included

b. Time periods for adverse events reporting:

Weekly reporting to senior and principal investigator.

Risk	Occurrence Potential	Mitigation
Inability to correctly use the Viberect device according to User's Guide.	Mild	Detailed and Simplistic (with figures) instructions are included in the in the User's Guide. Also the manufacturer recommends in the User's Manual that the user perform the Viberect method for at least two occasions in a clinical setting before using at home.
Any user discomfort during or after use of the device, including pain, fatigue, numbness, rash, device malfunction or hand pain from holding the device.		Viberect Device must not be used more than 10 minutes per day with strict accordance to the User's manual. Also, manual includes A WARNING that states: "Vibratory stimulation may cause a superficial trauma to the skin resulting in bruising, bleeding or superficial ulceration. If any such condition occurs, refrain from vibrating and consult your physician. This device should not be used over swollen or inflamed areas or skin eruptions.
User does not respond to device.		User's Guide provides direction that the Viberect may have to be used multiple times before it is effective. Not all men will responds to this treatment.
Skin irritation, tear, or infection	Moderate	As specified in the User's Manual, the Viberect Device should not be used if visible penile skin irritation (e.g., swollen or inflamed areas or skin eruptions). Also, User's Guide warns that "Vibratory stimulation may cause a superficial trauma to the skin resulting in bruising, bleeding or superficial ulceration. If any such condition occurs, refrain from vibrating and consult your physician." The device should not be used for more than 10 minutes a day.
Serious Medical Conditions Such as Priapism.	Serious	If the user develops an erection that lasts for more than four hours, he may have developed priapism, which is a medical/surgical emergency. Contact your physician immediately or go to the emergency room for timely treatment.

Device malfunction, vibrating pad dislodgment and vibrating tip damaging the penis.	Device malfunction	As specified in the User's Manual the Viberect device should not be used over swollen or inflamed areas or skin eruptions. Also, the User's Guide will advise user to: □ check the surface of the pad over-mold for any signs of wear/degradation and replace if needed; and □ check the integrity of the pad-pad over-mold assembly.
Device overheats and burns.		The circuitry/power source is electrically isolated from the patient's skin by thick plastic cover; that is, no circuitry or electrical components are exposed to the skin. In addition, no conductible metallic components of the device are exposed to the outside.
Use of Device while Charging		User Manual specifies not to use the device while charging and connected to an electrical outlet.

Legal risks such as the risks that would be associated with breach of confidentiality.

All data collection and will be secured to assure confidentiality and the study database will be stored in encrypted database that is only available to senior and principal investigator or research coordinator who is responsible for data collection.

Financial risks to the participants.

There is no financial risk to the patient. The Viberect device will be provided for free to each participant. Clinic visits will be billed to the participant's insurance company as a consultation and a standard-of-care follow-up appointment. If the participant does not have insurance coverage for specialist appointments, they will be responsible for paying for their visits out-of-pocket. The study does not offer financial compensation, however the Viberect device will be provided for free to the participant.

Steps taken to minimize the risks.

A comprehensive user manual will be provided to each study subject, and detailed person

to person instructions will be given to them prior to enrolling in the study. A demonstration will be provided prior to the patient using the device independently to ensure they have a full understanding of how to use the device.

Plan for reporting adverse events unanticipated problems or study deviations.

The occurrence of any serious adverse effects will end the patient's participation in the study and halt enrollment in the study to determine the safety of continuing. Each and every possible adverse effect of Viberect will be investigated and treated individually to minimize the participant's discomfort. The safety of having the individual complete the study will also be assessed on an individual basis. At any time the participant can decide to terminate his participation in the study and no penalty or loss of benefits to which they are entitled.

7. Confidentiality

Paper consent forms, enrollment check sheets, and other source or study documentation will be kept in a study binder. This binder will be stored in a locked office available only to the study team. Electronic data will be housed in a secure password protected database maintained by the Data Informatics Services Core within the Johns Hopkins Biostatistics Center. Only the study team will have access to this secure database. To maintain the protected information of patients enrolled in this study, only the study Principal Investigator and primary coordinators will have the ability to export data containing identifying information from this master database. For the purposes of analysis, only de-identified data will be exported.

8. Benefits

i. Individual participant

The patient's erectile function and sexual satisfaction may improve as a result of participation in this study. However, there is no guarantee of this. The information from this research study may lead to a better treatment in the future for people with erectile dysfunction. The patients may not benefit from participation in this study. Their conditions may not get better or but it unlikely to become worse while they are in this study. The study does not offer financial compensation, however the Viberect device will be provided for free to the participant.

ii. Society

Erectile dysfunction is a highly prevalent medical and psychological condition that affects millions of men worldwide and is associated with a significant reduction in overall quality of life. The results of this study can lead to further investigations that can show the efficacy of this safe modality in the management of erectile dysfunction.

9. Payment and Remuneration

The study does not offer financial compensation, however the Viberect device will be provided for free to the participant.

10. Costs

The Viberect device will be provided to patients free of charge. There are no anticipated costs outside of the usual standard of care for patients with erectile dysfunction. Participants will be seen routinely in clinic as a standard part of their care plan. If patients decide to use PDE5 inhibitors (such as Viagra. Cialis, or Levitra) in addition to their use of Viberect, they will be responsible for the cost of this drug, as per usual.