EVALUATION OF PELVIC FLOOR MUSCLE WITH SURFACE ELECTRICAL STIMULATION

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Study Site: Women's Health Advantage, 2518 East Dupont Road, Fort Wayne, IN 46825

Supported by: Elidah, Inc.

Sponsor Contact: Gloria Kolb

Study Intervention Provided by: Elidah, Inc. 810 Main St. Ste C, Monroe CT 06468

Sponsor of IND (IDE): "Nonimplantable Electrical Incontinence Devices" are a Non-significant risk device, no IDE needed

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1. STUDY OBJECTIVES

Hypothesis: Surface Electrical Stimulation (SES) contracts pelvic floor muscles. It is not clear which muscles and how much contraction is produced.

1.1 Primary Objective

The primary objective is to assess pelvic floor muscle contraction with SES
Key Endpoints: *Displacement of bladder base during contraction.*

1.2 Secondary Objectives

The secondary objective is to understand which muscles are moving.

2. BACKGROUND AND RATIONALE

2.1 Background on Condition, Disease, or Other Primary Study Focus

Urinary incontinence (UI) is a widely prevalent condition affecting approximately 1 in 3 women over the age of 30, and 1 in 2 women over the age of 50, and is a major problem after prostatectomy.[1,2,3] Although a very private concern, it has far-reaching physical, psychological, social, and economic implications. For example: UI has been found to reduce health-related quality of life measures, with a strong correlation with depression,[4] UI is the number one reason for entry into nursing homes, and the annual cost to Medicare has been estimated at $10 billion, and at $20 billion for the entirety of the US healthcare system. 75% of these women are specifically affected with Stress Urinary Incontinence (SUI), which is the loss of continence due to weakened pelvic floor muscles, resulting from a variety of factors including child-bearing, athletic pursuits, trauma, and aging.[5,6,7] Their urine leakage occurs when physical exertion (e.g. sneezing, lifting, running) increases intra-abdominal pressure. There are no medications that

address SUI, and while surgery can provide relief, it is painful, expensive, and requires hospitalization and multiple weeks of recovery.

Non-surgical strengthening of the pelvic floor muscles has proven effective in treating most SUI, and this is typically achieved through Kegel exercises, biofeedback, weighted cones or intravaginal electrical muscle stimulation (EMS). However, subjects routinely struggle to perform Kegel exercises correctly or with sufficient frequency (3x/day for 3-6 months) which leads to low compliance. Introducing intravaginal devices or an intravaginal probe necessitates a private location and dedicated treatment time (often at a treatment center), further challenging the likelihood of adoption.[5,8,9,10]

To complicate matters, 4 out of 5 sufferers do not speak with their primary care physician until symptoms have intensified and persisted for numerous years (6.5 years on average), and others fail to consult a specialist (i.e. urologist) because they have no intent of having surgery.[9] This leads to two thirds of affected women suffering quietly without treatment while conditions worsen.[11] Thus, the need exists for a non-surgical means of strengthening the pelvic floor muscles that has a higher rate of subject adoption and compliance than current solutions.

2.2 Study Rationale

Use of intravaginal EMS for treatment of SUI is predicated on the assumption that proximity of the electrodes to the pelvic floor muscles is of primary importance. This is largely accurate. However, appreciating that subjects who seek help most often ultimately fail treatment due to adoption and compliance issues, it is equally important to consider whether the psychological or physiological barriers associated with intravaginal EMS offset any benefit from the treatment's intimate electrode placement.

Several recent clinical reports suggest that a pattern of surface electrodes placed in the suprapubic and ischial tuberosity regions are as effective as intravaginal electrodes at retraining the pelvic floor muscles.[12] In these studies, treatment was administered by a clinician who placed four separate electrodes on the defined tissue region and delivered prescribed pulse waves during regular training sessions. Unfortunately, the need to deliver this treatment in a clinical environment makes it burdensome to the subject and the health system.

Building on these findings, Elidah has developed a wearable, SUI specific EMS device configured for application by the subject and for use outside the clinic, allowing treatment at home and potentially accelerating the rate and efficacy of muscle retraining. This surface EMS device (SES) has been used clinically, with subject's confirmation of pelvic floor contractions. However, a more objective proof that the pelvic floor is actually contracting was requested, and subsequently an identification of which pelvic floor muscles would allow insight into the mechanism of SES.

3. SELECTION AND ENROLLMENT OF PARTICIPANTS

3.1 Inclusion Criteria

All subjects must meet all the inclusion criteria to participate in this study. Any waiver of these inclusion and exclusion criteria must be approved by the Investigator on a case-by-case basis prior to enrolling the subject, and must be documented by the Investigator and the Sponsor.

Initial Screening:

- Age:18-80y
- Gender: female

3.2 Exclusion Criteria

A subject meeting any of the exclusion criteria at baseline will be excluded if:

- Moderate-severe stress incontinence*: As determined by self-reported >3 accidents in 24-hr period
- Currently pregnant, may be pregnant (Unsure pre and peri-menopausal women should take a pregnancy test.)
- Active urinary tract infection (UTI)
- Pelvic pain, Painful bladder syndrome, underlying neurologic/neuromuscular disorder that may impact ability to partake in the trial
- implanted cardiac device or untreated cardiac arrhythmia
- Obesity as defined by BMI >= 30 (height, weight recorded)
- Anyone with impaired decision making, drug or alcohol dependence, or potentially suicidal.
- Anyone who lacks the capacity to consent for themselves or who requires a legal representative to give informed consent

* Stress urinary incontinence: as determined by an answer of “Yes” to a standard question (from King's Health Questionnaire): "Do you lose urine with physical activities such as coughing, sneezing, running?"

3.3 Number of Subjects

The goal is 8 subjects, up to 12, 5 minimum. The rationale for the small number is this is a single-arm pilot study with no comparator arm.

3.4 Subject Compensation

Subjects will be compensated $50 for their time in the form of gift cards or cash.

3.5 Study Enrollment Procedures

Subjects will be recruited through normal standard of care visits, office visits, and current subjects. A flyer will be posted in the waiting room.

1. The study director will go through the “Screening” checklist, which will include initial screening inclusion and exclusion criteria.
2. The Screening checklist will be kept in a Screening Log binder at the site and each screened potential subject will be recorded on the initial screening log chronologically.
3. If the subject is a candidate, the study administrator or physician will describe the study, walk the subject through the consent and obtain consent.
4. Day 1 of the study may be on the same day as initial screening if time allows, or up to 21 days later.
5. If subject is still a candidate, then the subject will be entered into the enrollment log and assigned the next subject/enrollment number. A copy of the initial screening will be put in the Case Report Sheet and the subject number recorded.

3.6 Early Termination

Not Applicable - as this is a single-sitting acute study.

3.7 Adherence Assessment

Not Applicable - as this is a single-sitting acute study.

3.8 Concomitant Medications

Not Applicable - as this is a single-sitting acute study.

3.9 Randomization/ Blinding

Not Applicable - as this is a single-arm acute study with no randomization.

4. PROTOCOL

4.1 Research Method

The research methods use standard and published methods of recording type and level of incontinence. Additionally, published methods of using transabdominal ultrasound for measuring base of bladder and pelvic floor contractions will be used. Measurements of distance moved will be used.

4.1 Initial Screening

Screening is based on above Screening Checklist/ Exclusion Criteria.

4.2 Informed Consent

If the subject meets the criteria and reviewed by the study director, then a single Informed Consent will be explained and obtained from the study director.

4.3 Pre-test

Subjects will be instructed to follow a standardized bladder-filling protocol, consisting of voiding, drinking 500 ml of water and waiting 45-60min (ideally 60 min before US pictures taken, but set up may start earlier)[13].

4.4 Ultrasound

Subjects will place the electrode on their perineal area based on instructions, and a test should be completed to see if the subject feels a contraction while slowly incrementing the generator. If the subject is not getting good skin contact, hair may need to be trimmed or shaved. If the subject feels there is not much of a contraction, the electrode can be repositioned (usually one inch posteriorly).

Subjects should be placed in a comfortable supine position with hips and knees flexed to 60°, with lumbar spine positioned in neutral position. (Subjects may have underwear/clothes on over electrode.) Subjects should not see the US image.

With transabdominal ultrasound imaging (ex. GE Voluson E6 ultrasound with a 5-9D curved linear array GE RIC probe), the probe should be placed supra-pubically, on the lower abdomen, in the mid-sagittal plane. The transducer should be angled to obtain a clear image of the inferior-posterior aspect of the bladder. A marker should be placed at the bladder base on the junction of the hyper- and hypo-echoic areas in the region at rest. A marker should be placed, marking the maximal displacement of the bladder base from resting position[14],[15]:

1) while doing a PFM Kegel contraction (Instructions should be the same to all: to draw in and lift the PFM.)
2) with the generator on, slowly incrementing, counting the clicks and making note of when they first feel a contraction, until a maximum comfortable intensity level.
3) at the maximum comfortable intensity level *while* doing a PFM Kegel contraction combined.

4) (Optional) with a second generator (Waveform B) on at maximum comfortable intensity level

After the three images and max displacement recorded, the test should be repeated and potentially the intensity increased to a new maximum level (the skin may get numb after which intensity increased.) There should be a minimum of 7 ultrasound images (1 baseline, 2 with Kegels, 2 with generator, 2 with Kegels and generator.)
Any evidence of prolapse visualized using ultrasound should be recorded on Case Report Form.

While the generator is on the ultrasound probe can be manipulated to see if there is any evidence or indication which muscles are being contracted. We want to understand which muscles in terms of depth (pelvic diaphragm with levantor ani, or perineal pouch with sphincter uretrhovaginalis, or more shallow perineal membrane) which may also help determine if localized around urethra or entire pelvic floor, and if there is a difference between Kegels and electrical stimulation.

5. ELIDAH ELECTRICAL STIMULATION

5.1 Description of Device

The Elidah Elitone is an incontinence specific device that helps deliver electrical stimulation to the pelvic floor muscles transcutaneous. The design allows for home-use and wearable, ideally increasing compliance and thereby accelerating the rate of efficacy of muscle training. The device is comprised of two components: a disposable electrode and a current generator.

5.2 Electrode

The electrode is configured as a single unit contoured to fit against the perineal tissues with a hole in the center through which bodily fluids can pass. The skin-contacting surfaces are conductive gel regions located at the four corners with a hole in the center of the pad. Snaps and a cable is used to connect to the generator which may be worn at the waist. Benchtop testing has been completed to ensure that the resulting current passing through the Elidah electrode is similar to currently marketed 2” square patch electrodes.

Packaging: Foil pouch
Reusability: The electrode is designed to be used for one hour or less. This is an acute study and it is not expected for electrodes to be reused. A new electrode should be used for each subject.
Storage: Unused electrodes should be stored in sealable storage bag so that the gels does not dry out.

5.2.1 Device Name and Identifier

Elidah Elitone (electrode)
Identifier: EE-1002

5.3 Current Generator

The current generator will be used to supply the current. The generator unit, or stimulator, comprises a circuit board, rechargeable battery, and user interface, all housed within a plastic housing approximately 2” x 1.5” x 0.5”. The device is programmed to deliver a variety of waveforms intended for electrical muscle stimulation. Output characteristics of the device into a 500Ω load are 0-100 volts (peak-to-peak) and 0-150mA (peak instantaneous), which is similar to numerous commercially available electrical muscle stimulation devices. The treatment intensity (i.e. voltage) is controlled by the user through a pair of increment and

decrement buttons. The device can deliver 4 twenty-minute treatments on a battery charge. Recharging of the 3.7V lithium polymer battery is achieved via conventional micro-USB to USB cable. The battery includes integrated overload protection circuitry. In addition to the increment/decrement buttons, which also serve to turn on and pause/stop the device, the user interface includes a series of colored LEDs that indicate power state, and treatment intensity. The generator includes a belt-clip to facilitate wearing the device on one's underwear or pants. The generator connects to the electrode through a custom 2-conductor cable. *The device has passed all the necessary IEC testing, including for home-use.*

5.3.1 Device Name and Identifier

Elidah Device (generator)
Identifier: EC-1003

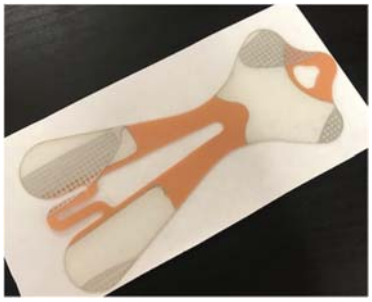
5.3.2 Generator Settings

- Freq: 2000Hz modulated at 50 Hz (sinewave), *Waveform B (same but square wave)*
- Timing: 6 sec on, 6s off
- Intensity: Current (mA) should be at max tolerable level, ideally to be increased, must record.

5b. Phase II:

In the event of successful implementation of the ultrasound protocol on women, a Phase II includes a pilot study on men. The protocol are identical with the exception of:

- Screening: Male instead of Female, pregnancy question removed
- Electrode: Is configured for male anatomy as seen in this prototype.



6. SAFETY ASSESSMENTS

Adverse events are the primary means for assessing safety of the device and the study subjects. All adverse events whether observed or volunteered will be recorded at every visit or during any contact such as emails or phone conversations with the subjects.

For all adverse events, sufficient information will be pursued and/or obtained so as to permit 1) an adequate determination of the outcome of the events (i.e., whether the effect should be classified as a serious adverse effect) and; 2) an assessment of the casual relationship between the adverse event and the investigational device or, if applicable, the other study treatment or diagnostic product(s).

Adverse event or abnormal test findings felt to be associated with the investigational device or, if applicable, other study treatment or diagnostic product(s) will be followed until the event or the abnormal finding resolves or stabilizes at a level acceptable to the investigator and sponsor.

6.1 Risks and Side Effects

The risks to those in the study will be similar to other transcutaneous electrical nerve stimulation (TENS) patches. Much of the known warnings and cautions of electrical stimulation with electrodes will be avoided due to the location-specific nature of the SUI device. However possible side effects may be:

- Electrical shock or pain
  - The generator is powered by a 3.7 Volt battery. Tampering with the generator or the electrode may cause damage to the circuitry and result in mild shock. There is no reason to tamper or open any component during this study.
  - The device is not meant to be used in water or during urinating. If exposed to liquids, the device may result in mild shock. If any component is exposed to a liquid please contact the research staff and investigator immediately.
- Pain on surface if the gel to skin contact is not secure.
  - If the device is not properly attached to the treatment site, the electrode may contact the skin directly. This may present as an uncomfortable burning or tingling sensation for the subject. In this event, a subject should turn off the device, remove the electrode and inspect the electrode for disconnections between the gel and electrode. If no issues are found, the subject should reapply the electrode and ensure that it securely contacting the skin at all points.
- Skin irritation (redness, sensitivity, etc.)
  - The electrodes used in this study are very similar to the electrodes currently on the market for TENS and other electrical devices. The gel which contacts directly with the skin may cause sensitivity or irritation to some subjects due to unique skin sensitivity.
  - With any adhesive that contacts the skin, redness or sensitivity may be present after removal of the electrode. This is a normal activity; such as redness experienced after removing a bandage. If recurring redness or sensitivity occurs, the subject should contact the study staff.

To minimize the risk, emphasis in the Instructions for Use will be placed on good skin contact/adherence. This risk is reasonable and similar to standard TENS electrode patches. The FDA considers similar device to have low risk: "*Nonimplantable Electrical Incontinence Devices are a Non-significant risk device, no IDE needed".* We do not foresee any psychological, financial, legal or other risk to subject associated with the study, except confidentiality which we address in other sections.

The intensity of the current/voltage of the device is modulated by the subject and not prescribed. The intensity will also start from 0 and incrementally increase with each level pressed by the subject. The above are known side effects with electrical stimulation devices and are not considered severe adverse events, nor unanticipated problems. It is possible that participants use this device improperly, or place it at an improper location. The electrode nor the generator may be applied while the subject urinates.

Loss of confidentiality represents an adverse event, however, we will take several steps to minimize the risk of breaching participant confidentiality/privacy, as described above.

Other Safety Considerations:
The device turns off automatically after 20 minutes however, it should not be left on for extended periods of time. The device cannot be used while charging. The device is not a life-sustaining device if it fails and stops working. The electrode cannot be used with standard generators due to a non-typical connector.

6.2 Adverse Events and Serious Adverse Events

An **adverse event (AE)** is generally defined as any unfavorable and unintended symptom or sign which either occurs during the study, having been absent at baseline, or if present at baseline, appears to worsen. Adverse events are to be recorded regardless of their relationship to the study intervention.

A **serious adverse event (SAE)** is generally defined as any untoward medical occurrence that results in death, is life threatening, requires insubject hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly. Solicited adverse events will be collected at the office visits.

6.3 Reporting Procedures

Adverse events will be reported from the clinical site to the sponsor within 24 hours.

The sponsor will use the following 0 to 4 scale to grade adverse events (AE): 0 = none or event is not clinically significant, 1 = mild AE that does not require treatment, 2 = moderate AE that does require treatment, but resolves completely and 3 = severe AE, e.g., results in temporary inability to conduct one or more everyday activities and requires ongoing medical attention, and 4 = life threatening or results in permanent inability to conduct one or more everyday activities.

In the event of an adverse event to a subject in the proposed study, the site investigator will discuss the available medical treatment options with the subject. If an AE occurs, the Sponsor will assist the subject in obtaining appropriate medical attention if unable to be performed by the Investigator. If treatment or hospitalization is required as a result of participation in this study, the subject and their insurance carrier are responsible for the cost of medical care. The subject will not lose any of their legal rights and they do not release the Sponsor, investigators, the study staff, or study site from liability for mistakes or intentional misconduct by participating in the study.

6.4 Followup for Adverse Events

The Investigator will follow up moderate and severe adverse events until it is resolved/stable. The study sponsor will be notified when the issue has been resolved.

7. INTERVENTION DISCONTINUATION

A participant in the trial has the right to discontinue treatment at any point within the trial for any reason. If the subject does choose to discontinue, a reason for discontinuation will be recorded and every effort will be made to collect end of study information. Every effort will be made by the Investigator to address any issues before discontinuing the subject such as answering questions on use.

Due to the exploratory nature of this intervention, a possible pause on enrollment and discontinuation of active subjects may occur if the sponsor discovers a serious issue with the use of the device. This could include events such as a subject hospitalization resulting from the direct use of the device. The study will not continue to enroll additional subjects until the root cause has been identified and corrected.

A study contract will be issued from the sponsor company to the investigator. Inability of the study investigator to meet expectations such as enrollment, documentation, or communication to the sponsor, may result in the study sponsor discontinuation of the study. The study sponsor has the ability to discontinue the entire study at any point and even between both phases for any reason necessary. The intervention is not a lifesaving device therefore it will not pose a risk to subjects.

8. STATISTICAL CONSIDERATIONS

8.1 General Design Issues

The primary objective of this study is to compare the comfort, tolerability of generator settings and demonstrate the effectiveness of the surface Elidah device.
In the first study of the Elidah device, the protocol was designed to remain as simple as possible for both the subject and the investigator while still obtaining the information necessary for the study sponsor to further development of the device. This study was broken into two distinct phases to first test comfort between generator settings. The second phase of the study will then evaluate efficacy.

8.2 Sample Size

The sample size was determined by the small pilot nature of this study and similar clinical studies. Study subjects are being recruited through advertisements, flyer or internal database. The number of recruited subjects will continue until the number of enrolled participants is satisfied. As this is an acute study, and enrollment is on day of study, we do not expect any dropouts prior to the study however an estimated 20% may not feel contractions.[16]

	Phase I
Subjects to be Enrolled	8 (12max)
Projected Withdraw Rate	20%
Total Number of Completers	5-6

Subjects will have a unique screen number, according to chronological screening entry, and a corresponding subject number after informed consent is received.

8.3 Interim Analyses and Stopping Rules

The study is small and acute, and so was purposely designed to avoid any interim analyses from occurring. In the event of a SAE with direct correlation to the device, the study will be temporarily halted until the safety issue can be addressed. Only 1 SAE will trigger this halting in enrollment. Due to the small enrollment size, the number of unanticipated problems or adverse events will not spur an interim analysis or early end to the study.

8.4 Outcomes

As discussed in Section 1, Study Outcomes, will be analyzed until the study has been closed to enrollment. Some outcome measures simply relate to the comfortability and usability of the device which is best described anecdotally and will contribute to future recommendations for better compliance. The objective data can be statistically analyzed to observe differences in treatment group and considerations including severity of UI, age, and demographic information.

8.4.1 Primary Outcome

- Movement of pelvic floor with electrical stimulation

8.4.2 Secondary Outcomes

- Comparison of movement with electrical stimulation, Kegels, and both
- Indication of which muscle groups are activating

9. DATA COLLECTION AND QUALITY ASSURANCE

Information and/or Specimen Management

Each device may be reused for different subject, with a wipe down with alcohol in between uses. Each subject will use a new electrode(s).

The label for the Elidah electrode will bear the following information:

- Name and address of the contact
- Investigational Trial Application statement
- Study number
- Storage instructions
- Contents
- Lot number

At the conclusion of the study, all unused Elidah electrodes and generators will be counted, reconciled with dispensing records, documented, and returned to Elidah or their designee. The Clinical Monitor will assure that a final report of electrode accountability is prepared and placed in both the Investigator's Study File and the Sponsor's Study File.

After completing the trial, all unused Elidah electrodes and returned generators will be shipped to Elidah at:

Elidah, Inc, 810 Main St., Monroe CT 06468

9.1 Data Collection Forms

The CRF data, with screening, will be recorded on paper forms or through spreadsheet, cloud folders.

Any electronic data shared between the study sponsor and the study site will only include subject numbers and will not include any identifying subject data. Any electronic forms will be stored on an external drive lockable or password-protected cloud system. At the conclusion of the study the study sponsor will retain all subject information and forms under lock and key for a minimum of seven years after last subject participation (based on HIPAA privacy). The study sponsor may decide to transfer all paper data to electronic data which will follow the same regulations.

9.2 Data Management

At the conclusion of the study and close-out monitoring visit the study site will transfer all data to the study sponsor. All management of the data entry will be the responsibility of the study sponsor in addition to auditing of the data. An individual at the study sponsor not directly in contact with study data will audit the transferring of data captured on paper to date entered into a digital database. A statistical analysis plan will be created which will also include procedures for auditing of the data.

9.3 Data and Safety Monitoring Plan

The Clinical director of Sponsor will oversee safety data collection as reported from subjects. Demonstration of use will be at the first visit, Instructions for Use will be sent home with the subjects, and a phone number for both the site and study sponsor will be provided to the subjects for any questions or reporting of adverse events. After the first week of use at home, a call will be made to each subject to ensure the subjects are using the device correctly and do not have any issues. Currently, electrical stimulation, such as TENS units, are sold over the counter and are used at home,

so we believe this level of monitoring is considered appropriate and the overall likelihood of harm is low.

To ensure that the rights and well-being of human subjects are protected; the reported trial data are accurate and complete, and verifiable from source documents; and the conduct of the trial is in compliance with the currently approved protocol, with GCP, and with the applicable regulatory requirements, an experienced Clinical Director will monitor the conduct of the study halfway through enrollment of both Phases of the study. In the plan, the clinical director will throughout the trial period:

- Act as the main line of communication between the Sponsor and the investigator
- Verify that facility, laboratories, equipment and staff are adequate to safely and properly conduct the trial
- Verify that the investigator
  - is adequately informed about the trial, as well as investigators' staff
  - has adequate qualifications and resources
  - follows the approved protocol and any amendments
  - receives all documents and supplies necessary
  - is enrolling only eligible subjects
  - provides all the required reports, notifications, applications and submissions
- Verify, for the investigational product:
  - That the storage times and conditions are acceptable, and that supplies are sufficient throughout the trial
  - That the SUI product is supplied only to subjects who are eligible to receive it and with the correct quantity
  - That the subjects are provided with necessary instruction on proper use, handling, storage, and return of the product
  - That the receipt, use, and return of the product are controlled, documented, and complies with regulations
- Verify that written informed consent was obtained before each subject's participation in the trial
- Report subject recruitment rate
- Verify that source documents and trial records are accurate, complete, and up to date
- Determine whether all adverse events are appropriately reported within time periods required
- Communicate deviations from the protocol and make appropriate actions.

In addition, a Data Safety and Monitoring Board will be established for this project and will review the study design, IRB protocol, adverse events and findings of the study.

9.4 Quality Assurance

9.4.1 Training

The sponsor will provide all study materials and review the protocol, procedures and all documentation. The site binder will include a Delegation of Authority Log which lists all study staff and the responsibilities in which they have been designated. The Investigator is responsible for ensuring that the staff can perform the responsibilities they have been assigned. The staff's signature represents that they have been trained, including understanding NIH Protection of Human Subjects Training and HIPPA before performing any function of the study.

9.4.2 Quality Control Committee

Due to the small nature of this study a Quality Control Committee will not exist. However, there will be auditing of all entered data.

9.4.3 Metrics

A statistical analysis plan will be created before any statistical analysis occurs. This plan will also include quality control measures for data entry prior to analysis.

9.4.4 Protocol Deviations

All protocol deviations should be reported to the sponsor within 48 hours. Included in the site Study Binder, a Protocol Deviation log will be included. This log will include the subject number, description of the deviation, and dates referring to occurrence of the deviation and date relayed to the study sponsor.

9.4.5 Monitoring

Staff will regularly monitor any possible concerns related to record keeping or protocol procedures.

10. PARTICIPANT RIGHTS AND CONFIDENTIALITY

10.1 Institutional Review Board (IRB) Review

This protocol and the informed consent document (see Appendix) and any subsequent modifications will be reviewed and approved by the IRB or ethics committee responsible for oversight of the study. The consent form should be separate from the protocol document.

10.2 Informed Consent Forms

An informed consent document that includes both information about the study and the consent form will be prepared and given to the subject. The document will be prepared in a language understandable to the subject and appropriately describes the responsibilities of the study staff and subject in partaking in the study and any potential risks. An individual from the Study site will review every page with the study subject. The subject is free to ask any questions and may take as much time to read through the document as possible.
If the subject agrees to the informed consent, they will sign two copies of the informed consent and the staff who gave informed consent will also sign both copies. One signed copy will remain in the subject folder, the second copy will be given to the study subject.
No minors will be enrolled in the trial, and those that are unable to consent for themselves will not be eligible to participate by a legal guardian. Individuals who do not speak English will be excluded from enrolling in this study in addition to those who cannot read. Due to the independent and at-home nature of the trial these populations would not be able to perform the daily activities required and no extra provisions will be made for them.

10.3 Participant Confidentiality

During the screening process, a potential participant will be assigned a screening number. The subject's name and identifying data such as contact information will be stored in the screening log. The screening log will remain within the screening binder in a locked cabinet at the site.
The enrollment log will be the only document which correlates subject number to subject name and contact information. The log will be stored in a locked cabinet within the study regulatory binder. All subject CRF's, Logs, and data will be referred to by subject number. All communication within study staff and study sponsor will ensure to use the subject number to reduce any confidentiality issues.

Personal or Identifying information will not be released without written permission of the

participant except as necessary by the IRB or FDA. In the event of written publication, the analysis will be performed as a group to reduce any possibility of identifying an individual subject.

10.4 Study Discontinuation

The study may be discontinued at any time by the IRB, the NCCIH, the OHRP, the FDA, the NSF Granting Agency, or other government agencies as part of their duties to ensure that research participants are protected.
The study may also be discontinued by the study sponsor at any time. A closure notification form will be formally distributed to the study site in the event of sponsor discontinuation.

11. APPENDICES

(As separate documents)

Screening Checklist
Informed Consent

REFERENCES

[1] Nitti, VW, "The prevalence of urinary incontinence", Rev Urol. 2001; 3(suppl1):S2-S6.
[2] Milsom I, "Lower urinary tract symptoms in women".Curr Opin Urol 2009, 19(4):337-41.
[3] Minassian V, Drutz H, Al-Badr A, "Urinary incontinence as a worldwide problem", Int J Obstet Gynecol 2002, 82:327-338.
[4] Sahin-Onat, Sule et al., "Relationship between urinary incontinence and quality of life/depression in elderly subjectsubjects," Journal of Clinical Gerontology and Geriatrics, Volume 5 , Issue 3 , pp 86 – 90.
[5] Bø K, Kvarstein B, Nygaard I: Lower urinary tract symptoms and pelvic floor muscle exercise adherence after 15 years. Obstet Gynecol 105:999-1005, 2005.
[6] "Decision Memo for Pelvic Floor Electrical Stimulation for Urinary Incontinence (CAG-0021N). Centers for Medicare & Medicaid Services (2000). https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?&NCAId=61&#1@bc=AAAAAAAAAAAQAA==@&from=https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=61@fromdb=true (accessed December 22, 2015).
[7] Hampel C., Weinhold D., Benken N., "Definition of overactive bladder and epidemiology of urinary incontinence". Urology 1997; 50: 4-14.
[8] Kondo A, Emoto A, Katoh K, et al: Long-term results of the pelvic floor muscle training for female urinary incontinence: an 8-year transition tree and predictive parameters. Neurourol Urodyn 26:495-501, 2007.
[9] Interviews by Gloria Kolb with more than a 20 urologists and gynecologists and 60 women and subjectsubjects. Unpublished, 2014-2015.
[10] Dumoulin, C, Hay-Smith EJC, Mac Habee-Seguin G, "Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women (Review)", Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD005654. DOI:10.1002/14651858.CD005654.pub3.
[11] "Women's Health: U.S. Markets for Female Urinary Incontinence Therapies." February 2014. MedTech Insight web site. http://www.medtechinsight.com/ReportA472.html. (Accessed March 12, 2014).
[12] Correia, CN; Pereira, VS; Hirakawa, HS; Driusso, P; "Effects of surface intravaginal electrical stimulation in the treatment of women with stress urinary incontinence: randomized controlled trial", Eur J Obstet Gynecol 2013.
[13] Thompson JA, O'Sullivan PB, Briffa K, Neumann P, Court S. Assessment of pelvic floor movement using transabdominal and transperineal ultrasound. Int UrogynecolJ (2005) 16:285–292
[14] Thompson JA, O'Sullivan PB, Briffa K, Neumann P. Comparison of transperineal and transabdominal ultrasound in the assessment of voluntary pelvic floor muscle contractions and functional manoeuvres in continent and incontinent women. Int Urogynecol J (2007) 18:779-786.
[15] Barton A, Serrao C, Thompson J, Briffa K, Transabdominal ultrasound to assess pelvic floor muscle performance during abdominal curl in exercising women. Int Urogynecol J (2015) 26:1789-1795.

[16] Dumoulin C, Hay-Smith EJC, Mac Habee-Seguin G, “Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence in women (Review)”, Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No.: CD005654. DOI:10.1002/14651858.CD005654.pub3.