The University of Miami, Miller School of Medicine
Desai Sethi Urology Institute
Clinical Research Protocol

Title:	**Modulating Intraoperative Vasectomy Pain Using the SmileyScope Virtual Reality Interface**
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1) **Protocol Title**

Modulating Intraoperative Vasectomy Pain and Anxiety Using SmileyScope VR Interface

2) **Objectives**

The primary objective of this study is to assess the feasibility of using virtual reality goggles to modulate pre-operative anxiety and intraoperative pain during vasectomy. Feasibility will be measured via the following parameters:

Pain will be quantified in the following manner:

- Pre-operative, intra-operative, and post-operative physiological parameters (heart rate, temperature, oxygen saturation) measured by FitBit Versa 3 device
- Numeric pain scale pre- and post-vasectomy

Anxiety will be measured in the following manner:

- Pre- and post-vasectomy State-Trait Anxiety Inventory (STAI) anxiety score

Feasibility will be further measured via subjective post-procedure satisfaction surveys. Further discussion of data analysis is detailed in the Research Procedures and Data and Specimen Banking sections of this protocol.

The secondary goal of this study will be to evaluate the effectiveness of interactive virtual reality versus static virtual reality in reducing pain during the procedure. Secondary objectives will be assessed using the same outcome measures as primary objectives. This study will attempt to expand the use of SmileyScope virtual reality goggles, which have already been proven to reduce procedural pain in the pediatric population.

3) **Background**

Vasectomy is a safe and effective procedure for permanent sterilization in males. More than 500,000 vasectomies are performed annually in the United States, and that number is expected to grow rapidly in the coming years. The procedure is safe and can be quickly performed in an outpatient setting. Complications of vasectomy are rare, and can include hematoma and infection, spermatic granulomas, and post-vasectomy pain syndrome in rare cases. Like all outpatient surgical procedures where the patient is not under general anesthesia, vasectomies involve intraoperative and immediate post-operative pain. While use of the no-scalpel technique and local anesthetic reduces intraoperative pain, expected operative pain is still one of the main reasons patients cite for not undergoing the procedure.

In our current study, we aim to further modulate intraoperative pain using virtual reality goggles. In clinical trials, the SmileyScope device has been shown to reduce procedural pain in the pediatric population during venipuncture or intravenous cannulation. Results from those studies showed a statistically significant reduction in pain during intravenous procedures in the emergency department. This VR headset is undergoing study for approval by the U.S. Food and Drug Administration (FDA) to reduce pain and anxiety in patients aged 4 years and older undergoing needle blood draw or injection procedures. Currently, this device has been granted entrance to the FDA Safer Technologies Program. In this study, the SmileyScope virtual reality interface is

considered an investigational device because it is not yet approved for use in adult males undergoing vasectomy. We aim to use this same virtual reality modality to reduce pain during vasectomies.

4) Inclusion and Exclusion Criteria

Inclusion criteria:

1. Adult males ≥ 18 years old undergoing elective vasectomy

Exclusion criteria:

1. Have a serious comorbid illness or condition that, in the opinion of the investigator, may compromise the safety or compliance of the subject or preclude successful completion of the study
2. History of chronic pain disorder or chronic narcotic use
3. Significant refractive error, unilateral blindness, epilepsy, or other conditions such as skin infections, cancers etc., which could compromise the physical function of the headset

5) Procedures Involved

Study Design

Patients will be randomized into one of three groups (interactive virtual reality, static virtual reality, and no virtual reality). Randomization sequence will be generated using a validated random number generator, and allocation concealment will be achieved via opaque envelope.

To ensure adequate power, the intended sample size has been calculated using the ANCOVA statistical test. Using G*Power 3.1.9.4 software, a medium effect size 0.25, alpha 0.05, power 0.8, 3 groups and 1 covariate, the required sample size is 162 patients (54 patients per group, 1:1:1 ratio). No loss to follow up is anticipated.

All patients will be asked to wear the FitBit Versa 3 in the waiting room before the procedure. Patients randomized into one of the two virtual reality groups will be asked to wear the virtual reality goggles in the procedure room before the vasectomy. Before and after the procedure, a survey will be used to assess anxiety. Before the procedure, patients will also be asked to complete a pain scale survey to quantify baseline pain. After the procedure, patients will complete a pain scale survey to quantify their post-procedure pain. Physiologic data will be extracted from the FitBit device before, during, and after the vasectomy.

Research Procedures

All patients will be provided a FitBit Versa 3* device which will be worn continuously during the pre-operative and intra-operative period. If randomized into one of two virtual reality groups, they will also be provided one pair of SmileyScope VR goggles* to wear. Physiologic data associated with subjective pain and peri-operative anxiety is of interest to the study team (i.e., heart rate, skin

temperature, oxygen saturation). Physiologic data during the pre-operative period will be used as a baseline to measure changes in intra-operative pain. Pre-operative anxiety will be assessed via a modified six-item State-Trait Anxiety Inventory (STAI-6) anxiety questionnaire scored from 0-24. The STAI-6 has been previously validated in the assessment of anxiety in surgical patients. Physiologic data will be correlated with subjective measures of average or maximal intra-operative pain (numeric pain scale; 0-10) and anxiety (STAI-6; 0-24). Effectiveness of the VR goggles in managing intraoperative pain will also be assessed by post-operative satisfaction surveys.

*Participants will not be held responsible for damaged or lost equipment provided by the study team. If any of the provided research hardware is damaged or deemed missing by the participant during the study period, replacements will be provided. Participants will be asked to return the FitBit Versa 3 and SmileyScope device after the procedure. The device will have a generic account associated with it, and data will be extracted from the device immediately after the procedure and deleted from the device.

Time Period of Data under Review

Data will be collected at enrollment, and during the procedure. Information will be kept for 3 years. De-identified data will be stored in a secure database for the duration of the study.

6) Data and Specimen Banking

The following datapoints will be collected at initial clinic visit:

- Medical Record Number
- Age
- Date of Birth
- Sex
- Race/Ethnicity
- Marital Status
- Medical History
- Medications

The following data will be collected pre-procedure:

- Numerical anxiety scale survey (Modified 6-term STAI-S anxiety scale)
- Baseline pain measure
    - "Please rate your current pain from 0 (no pain) to 10 (worst pain imaginable)."
- Physiologic data provided by FitBit Versa 3 – Data collected pre-procedure in waiting room. Data will be collected continuously during the time the patient is wearing the device. Data will be extracted from the FitBit after the procedure is finished and the patient has left.
    - Heart Rate
    - Oxygen saturation
    - Skin temperature

The following data will be collected post-procedure:

- Length of procedure (start and end time)

- Numerical anxiety scale survey (Modified 6-term STAI-S anxiety scale)
- Numerical pain scale survey:
    - Maximum pain felt during the procedure: "Please indicate the highest intensity of pain during the procedure on a scale of 0 (no pain) to 10 (worst pain imaginable)"
    - Average pain felt during the procedure: "Please indicate the average intensity of pain during the procedure on a scale of 0 (no pain) to 10 (worst pain imaginable)"
- Post-procedure satisfaction:
    - "How satisfied were you with today's procedure?"
    - "If your urologist was using VR, would you be more or less likely to have the procedure?"
    - "If your urologist was using VR, how likely would you be to recommend them to a friend undergoing the same procedure?"
    - "How helpful was VR in managing your vasectomy today"
    - "Do you have any comments on today's procedure?"
        - Free text form for patient comments
    - All questions will be answered via a 5-point Likert Scale as below:
        - 5 – Very Satisfied
        - 4 – Somewhat Satisfied
        - 3 – Neither Satisfied nor Dissatisfied
        - 2 – Somewhat Dissatisfied
        - 1 – Very Dissatisfied
        - 0 – Not applicable / Decline to Answer

- Physiologic data provided by FitBit Versa 3 - Data collected during the procedure and after the procedure in the waiting room
    - Heart Rate
    - Oxygen saturation
    - Skin temperature
- Adverse effects associated with goggles. Adverse effects are anticipated to be mild and not more than minimal risk. Patients can remove headsets at any time they wish, and adverse effects are anticipated to resolve with headset removal. Most common adverse effects include dizziness and nausea.

De-identified data will be stored in a secure database for 3 years.

- **Secure Storage**: Data will be housed in a HIPAA-compliant secure storage system, like REDCap or Box, within the University of Miami network with access restricted to approved members of the research team.
- **Limited Access:** Private identifiable information will be accessible only to IRB approved study team members with current IRB training.
- **Storage of Physical Records:** Physical records will be maintained for this study at a secure location where access is limited to approved personnel. The records will not be removed from University of Miami premises.
- **Storage of Specimens:** Specimens will be maintained for this study at a secure location where access is limited to approved personnel. The specimens will not be removed from University of Miami premises.

- **Retention/Destruction of Study Materials:** Study data/materials will be kept and/or destroyed according to applicable policy.

7) Data Management

De-identified data will be analyzed using IBM SPSS and GraphPad Prism statistical analysis software. Data will be reported as the correlation between pain scores and physiological data recorded from the FitBit V3.

8) Risks to Subjects

Adverse Events and Serious Adverse Events

An adverse event will be defined as any event that may harm the subject or require the subject to seek medical attention, and a serious adverse event will be defined as adverse events that require the subject to seek medical attention and may be life threatening.

Adverse events include dizziness, nausea, vomiting, or falls during or immediately after wearing the VR headset.

A serious fall during or immediately after wearing the VR headset constitutes a serious adverse event. Seizures constitute a serious adverse event. However, this is highly unlikely, as the VR scenarios developed do not present the flashing visual stimuli associated with seizures. In addition, patients with epilepsy and other seizure disorders will be excluded from the study.

9) Potential Benefits to Subjects

There may be reduction in vasectomy-associated pain for patients participating in this study, if they are randomized into one of the two VR headset groups. There may be no direct benefit if the patient is in the control group..

10) Setting

Single site study at the University of Miami.

11) Resources Available

Qualifications of staff:

The study PI is Ranjith Ramasamy, MD – Associate Professor, Director of Reproductive Urology. Research staff includes urology residents, medical students, and research fellows

at the University of Miami who will be trained in collecting and analyzing data from all pertinent research procedures. The study PI will oversee all staff involved in research.

In addition, the PI will delegate a study team member to conduct Quality Control/ Quality Assurance activities. The study will be evaluated for adherence with the protocol and for accuracy in relation to source documents.

12) Recruitment Methods

Potential subjects will be recruited from patients wanting to undergo vasectomy procedure with Dr. Ranjith Ramasamy (study PI). During their initial visit with Dr. Ramasamy, subjects will be asked if they would like to participate in the study. If so, they will be consented and be part of the study at their next appointment. If they do not wish to be part of the study, the clinic visit will proceed as normal and they will receive standard treatment. Recruitment methods may also include, but are not limited to, templates for flyers which can be utilized at approved clinic locations and as part of health fair materials; templates for print advertisements which can be utilized in newsprint and media campaigns; UMiamiHealthResearch.org, the secure registry linked with the University of Miami Health (UHealth) system Not all materials have been developed prior to trial initiation; however, each of these methods (the templates, final products, and services) will be reviewed and approved by the IRB prior to use.

13) Confidentiality

- **Secure Storage**: Data will be housed in a HIPAA-compliant secure storage system, like REDCap or Box, within the University of Miami network with access restricted to approved members of the research team.
- **Limited Access:** Private identifiable information will be accessible only to IRB approved study team members with current IRB training.
- **Unique ID Numbers and Coding:** Each patient will be assigned a unique ID number. The linking list will be kept secure. Direct identifiers listed in section 8 will be separated from the study materials (data and/or specimens) as soon as possible. During data abstraction, name and/or MRN are required for data verification purposes. After data abstraction is complete and data have been verified, the name will be removed (if collected). Only the MRN will be used to link the study ID/code to the individual after that point until the linking list is destroyed.
- **Destroying Identifiers:** The identifiers and the linking list will be destroyed as soon as scientifically possible and maintained only as long as necessary to abstract, analyze and verify data.
- **Storage of Physical Records:** Physical records will be maintained for this study at a secure location where access is limited to approved personnel. The records will not be removed from University of Miami premises.
- **Storage of Specimens:** Specimens will be maintained for this study at a secure location where access is limited to approved personnel. The specimens will not be removed from University of Miami premises.

- **Retention/Destruction of Study Materials:** Study data/materials will be kept and/or destroyed according to applicable policy.

The PHI to be accessed and reviewed is that which is minimally necessary to achieve the goals of this research. This includes:

- Medical Record Number
- Name
- Address (All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code)
- Telephone number
- Email address

Choose the statements below that are applicable to this research:

15(a). ☒ Data will be collected from the EMR or subjects at UHealth.
☒ Research Subjects will sign a HIPAA Authorization before the research will collect this data.
(Complete Section 17 below)

15(b). Data collected:
☒ Will include Protected Health information or Personally Identifiable Information

15(c). How will the research store the data?
☒ On a University of Miami electronic device (e.g. encrypted, password-protected computer)
☒ On a cloud-based storage system that is approved by the University of Miami

Select one of the following:

☒ The Principal investigator (and/or Study Team members) will record (e.g. write down, abstract) the data collected in a manner that does not include any direct identifiers (see list in the instructions for Section 15 of this protocol) of any subject. Instead, the Principal Investigator and/or Study Team members shall will assign a code (that is not derived in whole or in part from any direct or indirect identifiers of the individual) to each study subject and link the code to the study subject's identity. **The link to each subject's identity and/ or other identifiable information will be maintained on a document separate from the research data.**

Biospecimens

☒ Not applicable. No biospecimens will be collected

14) Provisions to Protect the Privacy Interests of Subjects

The study will be monitored by the PI to ensure appropriate study conduct, including obtaining proper access to data/specimens, compliance with the HIPAA Privacy Rule, compliance with University of Miami policy, and adhering to the plans outlined in the protocol for all study procedures, abstracting and recording data, data and/or specimen security and maintenance, and

data accuracy and integrity. Any adverse events, deviations, protocol exception requests, potential unanticipated problems involving risks to subjects or others, or other events will be submitted to the IRB in accordance with IRB reporting policy.

15) Waiver of Authorization for Use and Disclosure of Protected Health Information (HIPAA)

☒ This section is not applicable, we are not requesting a waiver of authorization.

Confirm that you will destroy the Protected Health Information (PHI) you and/or your Study Team acquire receive from UHealth at the earliest opportunity.

☒ ***I confirm***

Confirm that the Protected Health Inform (PHI) you acquire from UHealth will not be re-used or disclosed to any other person or entity, except as required by law or for authorized oversight of the research study or for other research for which the use or disclosure of PHI is permissible.

☒ ***I confirm***

16) Consent Process

All subjects must provide written consent to participate in this study. An informed consent form (ICF) will be given to each subject. The ICF will contain all United States federally required elements, all International Conference of Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) required elements, and Health Insurance Portability and Accountability Act Authorization (HIPAA) information in language that is understandable to the subject. The informed consent includes descriptions of all study related procedures, all possible risks to participant, and the time commitment involved with participating. All consent forms will have IRB approval. The ICF and review must be in a form understandable to the subject. Translation of ICFs will be done in accordance with local IRB procedures.

Potential participants will be approached by one of the study investigators or research coordinators. Information regarding study participation will be provided to the potential participant prior to consent. Subjects will be given ample time to review the ICF and ask questions before signing. The Investigator or designee and the subject must both sign and date the ICF after review, and before the any study procedures are performed. The subject will receive a copy of the signed and dated form, and the original will be retained in the site study files. The research staff member obtaining consent will document the informed process in the subject's chart for monitoring purposes. The Investigator or his/her designee must emphasize to the subject that study participation is entirely voluntary and that consent regarding study participation may be withdrawn at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Following informed consent process, participants will be provided with a FitBit Versa 3 and educated about operation of the devices.

Non-English Speaking Subjects
In addition to English-speaking subjects, Spanish-speakers will also be included in the trial. A certified translated version of the IRB approved English consent form will be made available to non-English speakers. Spanish version questionnaires and other patient facing materials will also be made available.

17) Process to Document Consent in Writing

Consent forms will be printed and signed by study participants at the initial visit. Copy of consent form attached to this application.