PART B
STUDY DESCRIPTION

TITLE OF PROTOCOL	**Self-Administered Nitrous Oxide (SANO) During Transrectal Prostate Biopsy to Reduce Patient Anxiety and Pain**
Principal Investigator	**Heidi Rayala, MD PhD**

B1. PURPOSE OF PROTOCOL

Nitrous oxide is a well-tolerated inhaled sedative that has been used for decades in pediatric and adult populations and is largely viewed as effective and safe. In addition to analgesic effect, nitrous oxide also produces a dissociative euphoria and amnesia that could potentially improve patients' anxiety and experience of cancer care. Over the past several decades nitrous oxide has become less common due to concerns of nitrous oxide environmental exposure to the care team. There are now FDA-approved systems that allow patient self-administered nitrous oxide (SANO), and importantly, include a scavenger system to eliminate exhaled environmental nitrous oxide. These systems are rapidly being adopted throughout the US in Urology practices, but to date, there have been no studies evaluating patient outcomes and possible risks with the adjunct use of SANO. We propose a prospective, randomized, controlled trial to assess patient perceived pain and anxiety related to prostate needle biopsy with or without SANO, and the frequency of complications associated with SANO. A secondary aim will be to demonstrate that the SANO at the time of prostate biopsy does not significantly increase burden on Urologist productivity, nor increase the difficulty of operator ease in performing the prostate needle biopsy.

Specific Aims:

Aim 1: To determine the effectiveness of Self-Administered Nitrous Oxide (SANO) in decreasing patient perceived anxiety and pain related to prostate needle biopsy.

Hypothesis 1.1: Patients receiving periprocedural SANO will have decreased anxiety during the procedure, as measured by STAI (State-Trait Anxiety Inventory) score, situational pain catastrophizing scale (SPCS) and patient vital signs.

Hypothesis 1.2: Patients receiving periprocedural SANO may have a decrease in pain as measure by VAS (visual analogue scale) score and patient vital signs.

Aim 2: To demonstrate that the SANO at the time of prostate biopsy does not significantly increase burden on Urologist productivity, nor increase the difficulty of performing the biopsy.

Hypothesis 1.1: Administration of periprocedural SANO will not significantly lengthen the time of the procedure relative to local anesthetic alone.

Hypothesis 1.2: Administration of periprocedural SANO will result in minimal side effects for the patients and will allow the patient to drive home independently.

Hypothesis 1.3: Administration of periprocedural SANO will allow the operating Urologist to perform the procedure with the same ease as on those patients who do not have SANO.

B2. SIGNIFICANCE AND BACKGROUND FOR THE STUDY

Burden of Transrectal Prostate Biopsies in the US

The number of prostate biopsies performed on US men annually is nearing 2 million (Wolinsky, 2021). Transrectal prostate needle biopsy is a very common procedure in the US that is associated with significant anxiety and discomfort for men. Historically, a prostate needle biopsy is performed via a transrectal ultrasound probe with a lidocaine local anesthetic block, without sedation or general anesthesia. In part, the prostate biopsy is performed without sedation or anesthesia due to added cost and time associated with an anesthesia team required for most anesthesia agents.

Until the early 2000s, prostate biopsy was frequently performed without the aid of local anesthetic. Current practice is to perform prostate biopsies with a periprostatic block using 10 ml of 1% lidocaine. Even with an anesthetic on board, studies have demonstrated the significant psychological impact of prostate needle biopsies, and this is further compounded in those patients requiring repeat biopsy.

Factors influencing the development of pain during a prostate biopsy can be divided into patient-associated factors (younger age, smaller prostate, and pre-biopsy anxiety) and procedure-associated factors (number of cores, use of local lidocaine block). With the advent of MRI fusion technology, we can now target suspicious areas with greater accuracy. However, this comes with the additional probe manipulation within the rectum and additional biopsies of suspicious areas, which has been associated with greater patient pain and anxiety (Chesnut, 2020).

Nitrous Oxide as an adjunct for Procedural Pain

Nitrous oxide has been used in dental offices for decades, accepted for both its analgesic and anxiolytic properties. The exact mechanism of action is not clear, but recent studies have hypothesized that the analgesic effect is from release of opioid peptides and stimulation of opioid receptors. The anxiolytic properties of nitrous oxide have been compared to benzodiazepine GABA-ergic pathway, resulting in moderate sedation, thereby reducing anxiety. Administration can be controlled by the patient and the effect of nitrous oxide is realized within 2-3 minutes with elimination within 2-3 minutes Nitrous oxide can be administered either independently or as an adjunct to locoregional blocks. These properties of nitrous oxide have led to becoming a standard of care in Obstetrics and Gynecology (AWHONN Practice Brief, 2018). In the United States, spinal analgesia is more commonly used than nitrous oxide during childbirth; however, nitrous oxide is routinely used elsewhere, with reported rates of 73% in Canada and 62% in the United Kingdoms. In Europe, Entonox, a 50% nitrous oxide: 50% oxygen mixture, is widely used in emergency medical care of patients in accident scenes and for mild sedation and analgesia.

Administration:

Inhaled nitrous oxide is typically administered at 30-70% concentration, mixed with oxygen. In dental practice, a nasal hood connected to a flometer is used to deliver the nitrous oxide. Typically, a separate tube associated with the nasal hood is connected to wall suction to scavenge the

exhaled waste gas. One of the key reasons nitrous has fallen out of favor in some settings is because the scavenging through a nasal hood is ineffective at containing and eliminating all exhaled nitrous.

The Nitrouseal® system has an adjustable-concentration digital flowmeter and includes an FDA-cleared exhaled waste gas scavenger, the Miniscav®. The Nitrouseal® system includes a proprietary disposable single-use full-face mask and breathing circuit that collects and contains the exhaled nitrous gas before it is scavenged into the Miniscav®.

It has been used in urology since 2017 in procedures such vasectomies, cystoscopies, UroLift® implants, bladder biopsies, prostate biopsies and Botox injections, with reported improvement in patient anxiety, relaxation and comfort. However, there have been no randomized controlled studies in the US that have studied the effects of nitrous oxide for prostate biopsies thus far.

B3. DESCRIPTION OF RESEARCH PROTOCOL

A. Study Design – Overview, Methods, Procedures

METHODS AND PROCEDURES:

Screening
After the Urologist has discussed and planned for prostate needle biopsy, the study team will examine the list of scheduled biopsies for the week, and a baseline examination by the clinical team for eligibility verification will be performed through a medical record review by a trained member of the research staff.

Recruitment and Obtainment of Informed Consent
A member of the research team will reach out by phone call and/or PatientSite email at least 1 week before their scheduled biopsy. When discussing prostate biopsy with the attending urologist, study will be introduced to patient and provide a flyer on laymen terms describing the protocol, risks and benefits and information about enrollment. When discussing prostate biopsy with the attending urologist, study will be introduced to patient and provide a flyer on laymen terms describing the protocol, risks and benefits and information about enrollment. The phone call (or PatientSite message) will give a brief description of the research study. If the patient expresses interest in in learning more about the study during the phone call (or by replying to the PatientSite message), a member of the study staff will then send a secure email to the patient with a copy of the informed consent form. Following this, a member of the study staff will call the patient to review the consent form and answer questions. Special care will be taken during the consent process to ensure subjects are fully competent and understand the nature of the questionnaires, as well as the nature of the randomization process (that they may receive Oxygen rather than SANO). If the patient desires to participate in the study, they will be asked to sign the electronic consent form on REDCap (Electronic Informed Consent (eIC)). Study staff will then send subjects an email containing a PDF version of the eConsent signed by both the subject and the staff member obtaining the consent.

Efforts will be made to attain a mix of study participants in terms of racial/ethnic representation, which is reflective of the population of the greater metropolitan Boston area: 63% white, 26% African American and 11% other.

Baseline Assessment:
After informed consent has been obtained, the patient will be directed to a REDCap questionnaire that will collect demographics, general medical history, and prior prostate biopsy information (See Pre-Procedure Evaluation Survey). This will be reviewed by research personnel to confirm eligibility to participate in the study based on pre-determined inclusion and exclusion criteria. If they do not qualify for the study, they will not be randomized to either arm, and will undergo a standard template biopsy with local anesthesia only.

In addition, patients will complete the Brief Pain Inventory, a well-validated measure that assesses intensity of current pain and interference of pain in the patient's life (Dworkin, 2005). If the patient

does not complete these two questionnaires electronically before the day of procedure, they will be offered the opportunity to complete on the day of their procedure prior to the biopsy.

Randomization
Subjects will be randomized 1:1 to either SANO (treatment) or oxygen (placebo control) after completion of baseline assessment. The results of the randomization will not be disclosed to patients as part of the study (patient-blinded). The randomization module in REDCap will be used to implement randomization of the subject to our two study groups.

Pre-procedure Evaluation
On the day of the biopsy, current standard procedure is to bring the patient to an exam room (separate from the biopsy room) where pre-procedure vitals are obtained. At this time, the pre-procedure STAI and VAS scores will be obtained. Information of inhaled gas administration and how to self-administer will be explained to the patient using templated verbal instructions. It will be emphasized that if at any point during the procedure, the patient feels uncomfortable with the inhaled gas, the team will help remove the mask.

Periprocedural Intervention
The patient will be moved to the biopsy room and standard procedure for lateral positioning and explaining prostate biopsy will be done in the routine manner preferred by the individual Urologist. Oxygen saturation monitor will be applied to the patient's finger and monitored throughout the procedure. The patient's heart rate will also be monitored accordingly.

The inhalation gas mask will be positioned on the patient's face, and the patient will then be instructed to begin breathing as previously instructed. Initially the patient will receive 100% oxygen at 10 Liters/minute. In the control group, this will be continued throughout the procedure.

After the Urologist describes the procedure, the SANO group will have nitrous oxide turned on to 30%, ensuring that the patient is relaxed but still conversant through the procedure. The nitrous will be adjust up or down based on the patient's response to the question "are you feeling the nitrous" and "are you happy at this level". The range will be between 25 - 45%. This may take 2-3 minutes. Both groups will be asked these questions. Both groups will be asked to take several deep breaths before inserting the rectal probe. The prostate biopsy for both study and control participants will include the normal routine administration of local peri-prostatic nerve block using preferred technique of the individual Urologist. During the procedure, the patient and patient's oxygen saturation will be monitored by a BLS-certified MA, RN, APP, or MD (separate from MD performing the procedure) and if at any point in time the patient is unhappy with gas inhalation, the observer will aid the patient in removing the mask. At the end of the procedure, the SANO group will be turned down to 0% nitrous oxide, and 100% oxygen will be administered through the mask for an additional 2-3 minutes as the patient is cleaned up and repositioned to the supine position. Assessment of the "time in" and "time out" of the procedure room will be recorded.

Measuring gas flow:
Maximum flow for this system is 19 L / min. The amount of gas flow is adjusted to match the patient's minute ventilation in order to maintain the black inspiration bag (inhalation reservoir) on the

Flowmeter about 3/4 full during the procedure. This varies from patient to patient depending upon respiratory rate, and volume of each breath. Excess gas flow simply flows through the circuit and into the scavenger and has no effect on the patient.

Periprocedural Data Collection

After the biopsy, the patient will be moved to the recovery room for routine post-procedure vitals as well as completion of post-procedure STAI score and Situational Pain Catastrophizing Score (S-PCS) on a tablet computer. The S-PCS was derived from the Pain Catastrophizing Scale (PCS), a validated questionnaire used to measure catastrophic thinking associated with pain. We will also question for side effects of the nitrous oxide including nausea, vomiting, dizziness, drowsiness, with an option to enter "other" as a manual entry. An additional question of whether the patient feels comfortable driving home independently will be assessed.

Patients who do not have an escort planned after their biopsy will be asked to perform two hand-eye coordination tests after completion of post-procedure surveys. First, the participants will be verbally instructed to extend one arm in front of them, and place one finger to the tip of their nose. After, the Trail-making test Part B will be administered. This test has been promulgated by the American Medical Association to screen for driving fitness. The Trails-making Part B test will ask participants to connect numbers (1-13) to letters (A-L) randomly written on a page. This test is scored according to accuracy and time required to make the connections (Joseph, 2013). If the participant is unable to accurately complete these tests, additional recovery time will be required. The participant's performance and disposition will be included in the documentation of study procedures performed during the visit.

The urologist who performed the biopsy procedure will be provided the Operator Survey to assess the ease of procedure.

Chart review will be performed to capture any unanticipated ED visits, admissions, or office visits for the 7 days following the procedure. We will also record any phone calls that are made by patients within 7 days of procedure that pertain to procedure concerns.

Lastly, participants who completed study procedures during their prostate biopsy will be asked to complete a survey 2-10 months following the study biopsy. This brief survey is designed to understand participant's recollection of pain and anxiety during the biopsy. The survey is estimated to take 2-3 minutes to complete.

Figure 1. Flowchart of Study Procedures

Management of Medical Gases Used in Study

As the research pharmacy does not procure nor dispense gaseous inhalants, medical gases used in the study will be managed per protocol and as per BIDMC's Compressed Gas Cylinder Storage and Handling Policy #: EC-62. Nitrous and oxygen cylinders will be procured through the OR materials management specialist. The tanks for study gases will be stored in an approved gas cylinder storage rack in (Room 385) of the Shapiro Clinic for immediate usage. There is also a gas tank

storage area in the Shapiro OR (close to the clinic) for additional storage. Both spaces are secured and locked off hours. Research staff will only access these supplies as necessary for the study.

B. Statistical Considerations

Sample Size Justification

Based on a previous study by Bringman *et al*, the mean (SD) of STAI anxiety score is 34(8). A clinically meaningful decrease, as determined by the Cochrane review group was 0.5 of SD.

Our sample size calculation to detect a 4-point change in pain score (p less than 0.05 significance level) was 64 patients per group (α=0.05, power=80%). We will inflate out sample size by 15% to account for any missing data or any withdrawal from the study; therefore, our estimated sample size will be 76 patients per group.

Data Analysis

All data will be collected and stored securely using the REDCap system. Data will be managed and analyzed by the PI and biostatistical support team at the BIDMC FIRST program. A Data Transfer Agreement will be created to allow for the study team's statistician, Kristin Schreiber MD/PhD at Brigham and Women's Hospital, to obtain and perform statistical analysis on de-identified data. At the conclusion of the study, de-identified study data will be exported out of REDCap and sent to Dr. Schreiber in a secure file via email message. Data will not be transferred until this agreement is approved and fully executed by both parties.

Primary outcome measure is patient anxiety and pain levels in the N2O group vs the oxygen only group as measured by the VAS and VAS A scores. We are specifically interested in the difference in scores between the two groups. Prostate biopsy mean VAS score with local anesthetic is around 3-4. We will also obtain a baseline pain index between the two groups. We will compare the perioperative VAS and VAS-A scores to the retrospective VAS and VAS-A scores collected during the survey administered 2-10 months after their biopsy.

We will also be obtaining 6 question Situational Pain Catastrophizing Scores for both groups and will compare the variation in response. Patients who have had a prior biopsy will also fill out a 13 question Pain catastrophizing score, which we will use as a baseline measure for biopsy related anxiety and hesitation.

Additional metric will include duration of biopsy, as measured by time in/time out of the procedure room for patients administered either nitrous or control oxygen when compared to patients who do not consent to the study (and will have no gas applied). Operator ease in performing the biopsy will be measured by 3 simple questions assessing patient positioning and ease of transrectal probe insertion. Prostate biopsies are generally performed as an outpatient procedure and patients can drive themselves home in most situations. Post biopsy side effects and ability of the patient to drive themselves home will be used as a surrogate to determine practicality of administering SANO in the outpatient setting.

C. Subject Selection

Subject Population

The study population will be all patients aged 21 to 85 years referred for prostate needle biopsy (both standard sextant and MRI-fusion guided) to BIDMC within 6 months' period. A total of 152 patients will be enrolled for the study.

Eligibility Criteria

Inclusion criteria:

(1) Biological male
(2) Aged 21 to 85 years
(3) Scheduled for prostate needle biopsy
(4) No learning disabilities
(5) Suitable for nitrous oxide/oxygen IHS with willingness to be randomized to inhaled SANO or inhaled oxygen during the procedure
(6) Access to an email and computer

Exclusion criteria:

(1) Perioral facial hair impeding good mask seal
(2) Learning disabilities and/or inability to cognitively complete survey questions
(3) Taken a pre-procedure benzodiazepine or narcotic.
(4) Has any of the following medical conditions:
    a. Inner ear, bariatric or eye surgery within the last 2 weeks,
    b. Current emphysematous blebs,
    c. Severe B-12 deficiency.
    d. Bleomycin chemotherapy within the past year.
    e. Class III or higher heart failure.
    f. Undergoing novel therapy for prostate cancer

B4. POSSIBLE BENEFITS

It is not possible to determine whether a subjects will directly benefit from participation. Patients receiving SANO may potentially experience decreased pain and anxiety when undergoing office prostate biopsy. Benefits would not be expected to occur for those patients in the placebo oxygen arm.

Taking part in the study will increase scientific knowledge regarding the ability of the inexpensive, commonly available agent to reduce procedural pain and anxiety. Moreover, as SANO is currently being used throughout the United States for prostate biopsies, this study may help us identify risks to SANO that are currently not known or described.

If there is a significant improvement in patient anxiety and pain with the nitrous oxide, this could lead to changes in the standard of care for patients undergoing prostate biopsy.

We also may be able to identify patient factors that in the future allow us to prospectively identify patients who would be expected to experience more benefits from nitrous oxide. At the same time, this may allow us to identify patients who would not have significant benefit and might minimize their risk of exposure to nitrous oxide.

There is potential to also extend knowledge obtained in this study to other commonly performed office procedures that are associated with pain and anxiety, such as LEEPs, vasectomies, cystoscopies, and others.

B5. POSSIBLE RISKS AND ANALYSIS OF RISK/BENEFIT RATIO

Risks related to the use of questionnaires

Minimal risks associated with the completion of questionnaires include subject fatigue and the possibility of increased anxiety in answering questions about baseline pain and pain related to the procedure. Subjects will be informed that they are free to discontinue their participation in the study at any time should they choose.

Risks related to Nitrous Oxide administration

Nitrous oxide is a well-known drug used in medicine for anesthetic and analgesic purposes since 1844. Its use during labor has been shown to be safe and effective, with no known long-term effects on the mother and no known effects on the infant. There are known long-term effects of environmental exposure to nitrous oxide, including infertility, when not using a scavenger system for the escaped environmental nitrous oxide. The Miniscav® nitrous waste gas evacuation pump has been FDA-approved for use in medical offices with the Nitrouseal® system. We will not be using the Nitrouseal® and Miniscav® nitrous waste gas evacuation pump in any capacity that is not already approved by the FDA.

Nitrous oxide does have a risk of nausea and vomiting. The reported rates have been reported as high as 13% in literature, however these are at higher concentration of nitrous oxide and with longer durations. The reported vomiting risk with the Nitrouseal® system is <0.5%. For the procedure, the patient is maintained in the lateral position, which should minimize any aspiration risk. Sweating, drowsiness, lightheadedness, tachycardia and facial flushing has also been reported. The patients are routinely monitored after the prostate biopsy procedure, and any ill effects of the procedure itself or of the nitrous oxide will be assessed and cared for by our study team and clinical staff. Some adults may feel a sense of panic at higher concentrations (60-70%) than we will be using in our study (40%).

Finally, as with any inhaled gas, there can be a concern of hypoxia or apnea with administration of nitrous oxide. This event has not been routinely reported in the literature as a risk or side effect of nitrous oxide. However, this will be one of the side effects that we will be most interested in following. During the procedure, patients will undergo continuous oxygen saturation and heart rate monitoring. These values will be documented in REDCap as part of the patient's study records.

If there are concerns of hypoxia, either objectively by the oxygen monitoring or subjectively by the patient, the protocol will be to immediately turn off the nitrous oxide and administer 100% oxygen until vitals return to baseline. All personnel in the room will have BLS training. The Shapiro Surgical Clinic has a code cart which is readily available. In addition, the clinic is in close physical proximity to the operating rooms, with anesthesiologists responding to Code Blues in the building.

Possible Unauthorized Use of Nitrous Oxide

Inhalation of nitrous oxide is used/abused in recreational settings with the purpose of causing euphoria and hallucinations. To prevent potential misuse, the nitrous oxide will be stored within the operating room storage area reserved for anesthetic gases during non-office hours.

Potential for Loss of Confidentiality

There is a potential for loss of confidentiality for participants in the study. Protections will be implemented to mitigate this risk. As detailed in our protocol, we will use REDCap to collect patient information and questionnaires. Though REDCap is generally considered secure for the purposes of PHI, it is a web-based application and the data is accessible to study team members on their own personal computers. Access to our REDCap will only be limited to study team members who are trained in protecting PHI. . Any electronic study files or information that is not stored on REDCap will be kept on a secure directory on the BIDMC server that is only accessible to research staff.

Only summaries of group data will be reported in any publications or presentations, with no identification of individuals. These precautions should serve to protect PHI in accordance with HIPPA regulations.

Reporting of Adverse Events

All adverse events will be reported to the BIDMC Human Research Committee promptly in accordance with guidelines.

Analysis of Risk/Benefit Ratio

Based on the above risks, the principal investigator views this study as moderate risk. With the precautions and procedures to minimize risk as described in this section, we anticipate minimal complications and discomfort. In light of the study's potential benefits, the principal investigator believes the risk:benefit ratio to be favorable.

B6. RECRUITMENT AND CONSENT PROCEDURES

Recruitment

The primary Urologist will introduce the SANO study to the patient and provide an informational handout at the time they discuss prostate biopsy with the patient. After the Urologist has discussed and planned for prostate needle biopsy, the study team will examine the list of scheduled biopsies for the week, and a baseline examination by the clinical team for eligibility verification will be performed through a medical record review by a trained member of the research staff.
. Those patients who meet criteria will be reviewed by their Urology Attending for appropriateness of study and will provide authorization to contact eligible subjects. Eligible patients will be sent a secure message via PatientSite (See Template Introductory Letter) to introduce the study. In addition, the patient will be called on their preferred clinical contact phone number by a study team member. The study team member will follow a templated introductory contact script (See Template Introductory Contact Script). In attempting to reach the patient, and in accordance with BIDMC Human Research procedure, no more than ten (10) phone attempts will be performed, and all calls will take place between 10am-9pm Monday thru Friday, and 10am – 5pm Saturday and Sunday. If there is no answer, study team member will leave a templated contact script (See Template No Answer Contact Script).

To assess interest in completing the post-biopsy survey, a letter will be sent to introduce the survey to participants who completed study procedures during their study biopsy (see Re-contact Letter script). We will wait for one week before further outreach to patient. For participants registered on PatientSite, a REDCap survey link will be sent via secure PatientSite message (see Re-contact PatientSite script). For participants who do not prefer PatientSite, we will call the patient directly (see Re-contact Telephone script). Patients will be asked to complete the survey via a REDCap link sent to the patient's email. If the patient prefers, we will offer the option to complete the survey questions over the phone . No more than three phone attempts will be performed, and all calls will take place between 10am – 9pm Monday-Friday, and 10am – 5pm Saturday and Sunday. If there is no answer, the study staff member will leave a templated voicemail (see Recontact Voicemail script).

In the event that individuals contacted are distressed in any way by the contact, we will contact the patient's Urology Attending, who will either personally reach out to the patient to alleviate

their concerns or have a designated team member reach out to the patient to alleviate their concerns.

Consent

Informed consent will be obtained for all participants who are potential study candidates. A qualified member of the research team will review the informed consent form with all patients who express interest in the study. The subject will be allowed to ask questions at any point. Study personnel will explain that the subject is free to refuse participation in this research study and that. All patients who agree to participate will be asked to sign the ICF electronically through REDCap. Consent will be obtained before any study-specific tests or procedures are performed. Study personnel will document the consent process. Subjects will be provided an electronic copy of the signed ICF.

Subject Protection

As subjects in the study may be patients of study investigators, measures will be taken to prevent coercion and undue influence. The study team will emphasize that participation is voluntary and will not impact their relationship with any individual at BIDMC. Investigators will be trained to conduct consent in a manner that does not lead to coercion and undue influence.

B7. STUDY LOCATION

Privacy

The study will be conducted on the premises of BIDMC Longwood Campus. We will obtain lists of patients intended for prostate biopsies in the following week, and study team members will review the OMR records for inclusion and exclusion criteria. The patient will be contacted by phone either from in-office phone call or through Doximity phone application (which provides the BIDMC Urology office as the caller ID). We will ask the patient whether they are in a location that affords privacy for discussion of medical information. If they are not, we will arrange an appropriate time when the patient will have privacy for study discussion. Phone interviews by study team members will be conducted in private space to avoid the interview being overheard.

Pre-procedure questionnaires will be emailed to private patient email via the REDCap server. Data collected will be kept within the REDCap server. Access to our REDCap will only be allowed for study team members who are trained in protecting PHI.

Operator Surveys will be on paper forms with patient identifying sticker on the form. At the end of the biopsy, the data will be input into the REDCap system by a study team member, and the paper version will be disposed of in a disposal unit intended for medical information waste.

Pre-procedure and post-procedure VAS, VAS-A score and Situational Pain Catastrophizing Score (S-PCS) and Trails-making Part B tests will be obtained in a private exam room where only the patient, study team members, and clinical staff measuring vitals will be present. Questionnaire answers will be input by the patient into a tablet computer. The tablet computer will be wiped with sanitizing wipe between uses given current COVID pandemic.

Physical Location

The biopsy procedure itself will take place in the Shapiro 3 Surgical Subspecialty clinic. Medical record reviews will occur at a secure workstation at BIDMC or through BIDMC's VPN server.

The nitrous tanks will be stored in an approved gas cylinder storage rack in (Room 385) of the Shapiro Clinic for immediate usage. There is also a gas tank storage area in the Shapiro OR (close to the clinic) for additional storage. Both spaces are secured and locked off hours.

B8. DATA SECURITY

All OMR access and assessment will be performed on the BIDMC server using the BIDMC firewall. As detailed in our protocol, we will use REDCap to collect patient information and questionnaires. Input of PHI data into the REDCap system by team members will only be through the BIDMC server using the BIDMC firewall. Access to our REDCap will only be allowed for study team members who are trained in protecting PHI. Only summaries of group data will be reported in any publications or presentations, with no identification of individuals.

Operator Surveys will be on paper forms with patient identifying sticker on the form. At the end of the biopsy, the data will be input into the REDCap system by a study team member, and the paper version will be disposed of in a disposal unit intended for medical information waste.

B9 Multi-Site Studies

Is the BIDMC the coordinating site? ☐ Yes ☐ No

Is the BIDMC PI the lead investigator of the multi-site study? ☐ Yes ☐ No

B10 Dissemination of Research Results

Participants will be thanked for their participation in the research study. Results of research conducted through this protocol will be published in peer-reviewed journals and presented in scientific conferences. No identifiable information will be published or presented

References

1. Wolinsky, H. (2021, April 21). *No more men need to die from transrectal prostate biopsies*. Medical News. https://www.medpagetoday.com/special-reports/apatientsjourney/92201.
2. Chesnut GT, Vertosick EA, Benfante N, Sjoberg DD, Fainberg J, Lee T, Eastham J, Laudone V, Scardino P, Touijer K, Vickers A, Ehdaie B. Role of Changes in Magnetic Resonance Imaging or Clinical Stage in Evaluation of Disease Progression for Men with Prostate Cancer on Active Surveillance. Eur Urol. 2020 Apr;77(4):501-507.
3. Collins, M OGNN - Use of Nitrous Oxide in Maternity Care: AWHONN Practice Brief Number 6. Journal of Obstetric, Gynecologic, and Neonatal Nursing Mar 2018 (239-242)

4. Bringman H, Giesecke K, Thorne A, Bringman S. Relaxing music as pre-medication before surgery: a randomised controlled trial. Acta anaesthesiologica Scandinavica. 2009;53(6):759-764.
5. Joseph, C. B. (2013). Physician's Guide to assessing and counseling older drivers. second edition. *Journal of the Medical Library Association : JMLA*, *101*(3), 230–231. https://doi.org/10.3163/1536-5050.101.3.017
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