UNIVERSITY OF PENNSYLVANIA RESEARCH SUBJECT INFORMED CONSENT AND HIPAA AUTHORITZATION FORM

PROTOCOL TITLE: **Imaging Predictors of Cryolysis Efficacy for Treatment of Obstructive Sleep Apnea (ICE-OSA)**

PROTOCOL VERSION: V1.2

SPONSOR: Cryosa Inc.

PRINCIPAL INVESTIGATOR: Raj C. Dedhia, MD, MSCR
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EMERGENCY CONTACT: (215) 662-2000 – Ask for E.N.T Resident on call

RESEARCH STUDY SUMMARY FOR POTENTIAL PARTICIPANTS

You are being invited to participate in the research study "Imaging Predictors of Cryolysis Efficacy for Treatment of Obstructive Sleep Apnea (ICE-OSA)". Your participation is voluntary, and you should only participate if you completely understand what the study requires and what the risks of participation are. You should ask the study team any questions you have related to participating before agreeing to join ICE-OSA. If you have any questions about your rights as a human research participant at any time before, during or after participation, please contact the Institutional Review Board (IRB) at (215) 898-2614 for assistance.

The purpose of the ICE-OSA study is to collect and evaluate data on patients participating in the ARCTIC-3 trial to determine if there are patient characteristics that predict improvement of obstructive sleep apnea (OSA) symptoms after treatment with the Cryosa Procedure and to investigate *how* the Cryosa Procedure affects OSA symptoms. The Cryosa Procedure, which is performed in ARCTIC-3, is a controlled cooling technique that reduces the volume of fat in the tongue and soft palate. ARCTIC-3 and ICE-OSA are similar in th+at they both aim to evaluate the efficacy and safety of the Cryosa Procedure, but the ICE-OSA study calls for additional procedures to visualize and image your airway and tissue, before and after the Cryosa Procedure.

It is important to note that the Cryosa Procedure is not part of ICE-OSA, but it is part of ARCTIC-3. Patients that are eligible for ICE-OSA must be enrolled in ARCTIC-3, must not have MRI contraindications (claustrophobia, ferromagnetic implants, etc.), and must not be pregnant or become pregnant during the time they are enrolled in the ICE-OSA study.

In addition to the ARCTIC-3 trial procedures, the key procedures for ICE-OSA include:

- Magnetic Resonance Imaging (MRI)
- Drug-Induced Sleep Endoscopy (DISE)
- Ultrasound (US)
- Tongue force measurements
- Digital morphometric photos

Key potential risks of ICE-OSA include discomfort of the tongue, mouth or nose during testing and nausea, headache or sleepiness after sedative medication. **Patients are not expected to benefit directly** from participating in ICE-OSA, but the knowledge gained from this study may lead to the development of more personalized plans to treat OSA and the improvement of our understanding of potential therapies for OSA.

If you choose to participate in ICE-OSA, your participation will last about 6 months.

This trial is not an alternate treatment of your OSA. Your participation is voluntary and will have no effect on your medical care or change your relationship with the Study Doctor or your eligibility and enrollment for the ARCTIC-3 trial. You are free to decline or stop participation at any time during or after the initial consenting process.

Please read this information carefully and ask as many questions as you would like before deciding whether you wish to participate or not. If you wish to participate, you will be asked to sign this form. You will be given a copy of the form to keep.

Please note that there are other factors to consider before agreeing to participate such as additional procedures, use of your personal information, costs, and other possible risks not discussed here. If you are interested in participating, a member of the study team will review the full information with you.

WHY IS ICE-OSA BEING DONE?

The purpose of ICE-OSA is to evaluate the effects of the Cryosa Procedure. We will investigate if and how certain measurements correlate with any changes in OSA symptoms after undergoing the Cryosa Procedure. If the Cryosa Procedure is found to be an effective treatment for OSA, understanding these factors may help us in identifying patients whose OSA may be treated by the Cryosa Procedure. Please ask study staff if you have any questions regarding the Cryosa Procedure you will be undergoing as part of the ARCTIC-3 trial, or refer to your Consent Form from the ARCTIC-3 trial for more information.

The ICE-OSA study will evaluate any changes in the amount of your tongue and soft palate fat and the position and movement of your tongue after the Cryosa Procedure. This will be done through imaging techniques, described in-detail in this form. These measurements may similarly aid us in understanding how the Cryosa Procedure affects OSA symptoms.

WHY AM I BEING ASKED TO TAKE PART?

You are being invited to participate in ICE-OSA because you are also enrolled in the ARCTIC-3 trial at the University of Pennsylvania. We are inviting ARCTIC-3 participants to partake in ICE-OSA because we want to identify patient characteristics that predict an improvement of OSA symptoms by undergoing the Cryosa Procedure.

Dr. Dedhia is the investigator in the ICE-OSA study. You do not have to participate in any research study offered by Dr. Dedhia. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. You may also decide to discuss the ICE-OSA study with your family, friends, or family doctor. Being in a research study is different from being a patient. As an investigator, your doctor is interested both in your clinical welfare and in the conduct of the ICE-OSA study.

If you decide to participate, you will be asked to sign this form. After signing this form, you will be considered enrolled in the ICE-OSA study.

HOW LONG WILL I BE IN THIS STUDY?

Your participation in ICE-OSA is expected to last about 6 months and will include three study visits, as described in the section below, "WHAT WILL I NEED TO DO IF I AGREE TO TAKE PART IN THIS STUDY"

HOW MANY PEOPLE WILL TAKE PART?

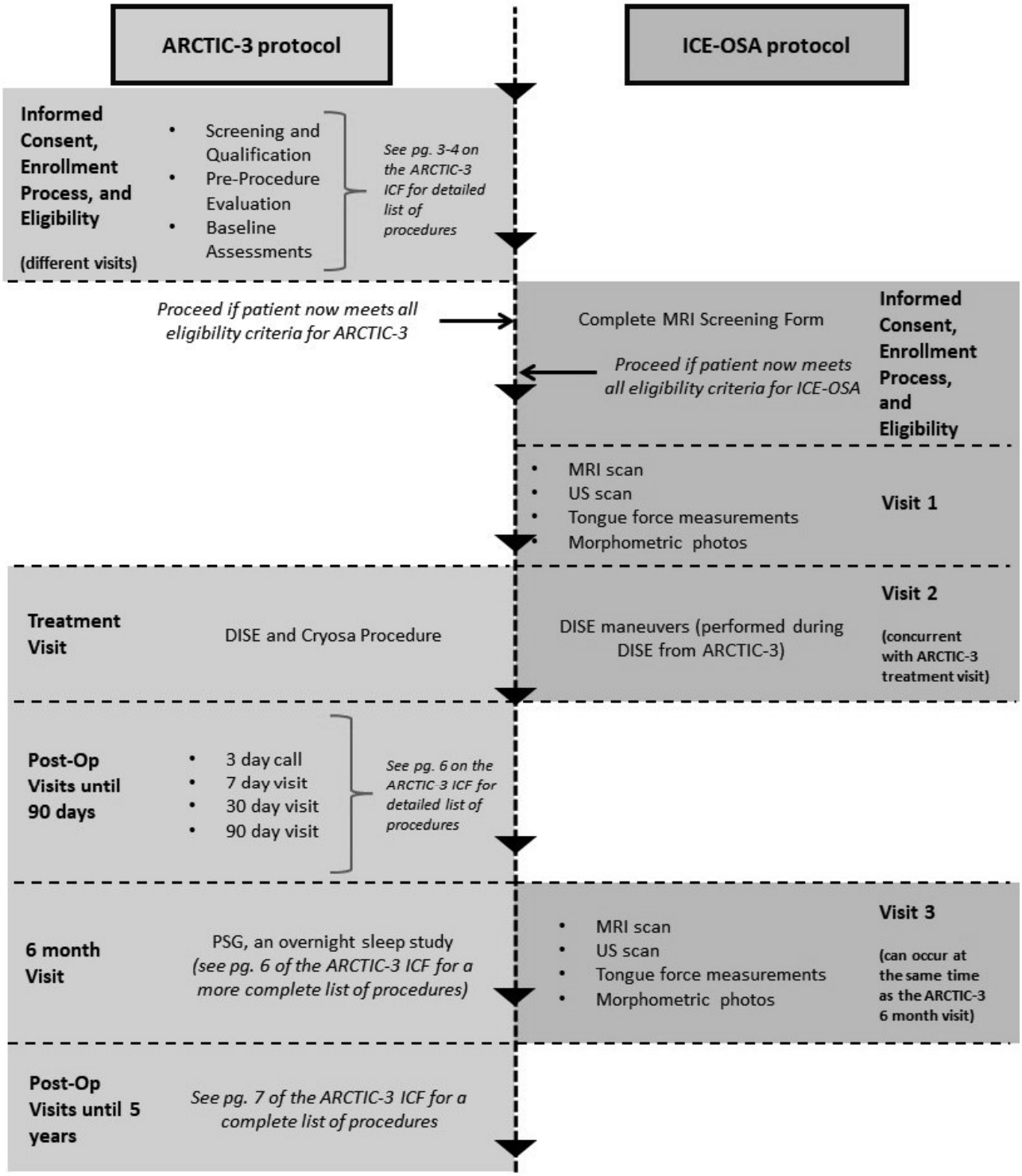
This is a single-site study at the University of Pennsylvania. We will enroll a maximum of 10 patients in ICE-OSA.

WHAT WILL I NEED TO DO IF I AGREE TO TAKE PART IN THIS STUDY?

You will be asked to sign and date this form before starting any ICE-OSA study activities.

It is important to remember that you are being invited to participate in ICE-OSA *in addition* to your enrollment and participation in the ARCTIC-3 trial. Therefore, many of these study procedures will occur during your visits for ARCTIC-3 to lessen any time and travel commitments as much as possible.

Please refer to the figure below which outlines the ICE-OSA visits in respect to the ARCTIC-3 visits.



Timing, Duration and Outline of Each Visit:

If you choose to participate in ICE-OSA, you will be asked to undergo the following procedures. All procedures listed in *italics* are further described in the following section.

Visit 1 occurs after you have consented and been enrolled in ICE-OSA. This visit will take about half a day, where you will complete the following procedures (see the next section, "Detailed description of all procedures" for further information):

- *MRI screening form*
- *MRI scan*
- *Ultrasound scan*
- *Digital morphometric photos*
- *Tongue force measurements*

Visit 2 will occur when the Cryosa Procedure is performed in ARCTIC-3. During this visit, you will be sedated with propofol and will undergo the *DISE procedure* and the Cryosa Procedure in the ARCTIC-3 study. This combined visit will take a full day to allow for your post-operative care, which is described in your ARCTIC-3 Consent Form. Participating in ICE-OSA includes the addition of two procedures to be completed immediately after your DISE and before beginning the Cryosa Procedure, while you are still sedated with propofol. These two additional maneuvers are described in the following section.

Visit 3 occurs around the time of the 6-month visit in ARCTIC-3. If you schedule Visit 3 at the same time as the 6-month visit in the ARCTIC-3 trial, this will be an overnight visit because the ARCTIC-3 6-month visit includes an overnight sleep study. However, you can schedule Visit 3 in this study at a different time than your ARCTIC-3 6-month visit. During Visit 3, you will be asked to undergo:

- *MRI scan*
- *Digital morphometric photos*
- *Tongue force measurements*
- *US scan*

If you complete Visit 3 at the same time as the ARCTIC-3 6-month visit, you will complete the MRI scan, US scan, photos, and tongue force measurements before the overnight sleep study.

Detailed description of all procedures:

MRI Screening Form – Answering this questionnaire will determine whether you are eligible for an MRI scan, namely ensuring that you do not have claustrophobia or have any implants or other foreign bodies that could cause an injury when undergoing MRI. This form takes about five minutes to complete.

In cases where there is insufficient information to evaluate the risks associated with an implant or foreign body, the MRI study will not be allowed to proceed, at which point you will be removed from the ICE-OSA study (not the ARCTIC-3 study). If it is determined that you do not have any MRI contraindications, you will be considered eligible to continue and participate in this study.

MRI Scans – You will undergo two MRI scans of your head and neck as part of this study. These scans enable us to visualize your airway and the surrounding tissue. One scan will occur before your Cryosa Procedure, and one will occur after your Cryosa Procedure. The scan takes about a half hour.

MRI is a type of scan that uses radio waves to take detailed pictures of the body. You will be asked to lie on an MRI table where the technologist will place a receiver on the part of your body to be studied. You will be provided a blanket for comfort and earplugs since the MRI makes noises while it is scanning. You will still be able to hear some sound to ensure you can communicate with the technologist and can follow any direction given throughout the MRI scan. The technologist will slowly slide you into the MRI magnet where radio waves will be transmitted into you. The MRI magnet looks like this:

There, radio waves (not radiation) will be transmitted into you. Your body will give off radio waves, which will be picked up by the receiver and made into detailed pictures. You will be awake for the MRI and not sedated and will not get any contrast dye injections.

Digital Morphometric Photography – Before and after your Cryosa Procedure, we will take several photographs of your face and inside your mouth with a digital camera. The digital camera has two parallel-oriented laser pointers to help with capturing accurate measurements. We will ensure the laser does not point into your eyes. You will be sitting in a chair, and we will ask you to sit with your head tilted back with your mouth closed, and then neutrally with your head tilted back and your mouth open. For one set of pictures, you will use a tongue depressor to hold down your tongue for pictures of the back of your mouth. This will take no more than 10 minutes.

Tongue Force Measurements – You will be asked to place a small bulb behind the front teeth and to press your tongue against the bulb as hard as possible for two seconds. This exercise will be repeated four times, with 30 seconds of rest in between each attempt. You will then be instructed to press and hold your tongue against the bulb as hard as possible for 35 seconds. This exercise will be repeated three times, with 2 minutes of rest in between each attempt.

Ultrasound Scans – As part of this study, you will be asked to undergo two ultrasound scans, one before your Cryosa Procedure, and one after your Cryosa Procedure. During this scan, you will be asked to lay back while a probe is placed on your neck. The probe will be moved up and down, examining the structures of your airway.

We will use an ultrasound machine to measure changes in your tongue's shape and position. This will take about 10 - 15 minutes.

Drug-Induced Sleep Endoscopy (DISE) – You will undergo a DISE procedure as part of the ARCTIC-3 study immediately before the Cryosa Procedure. Enrolling in the ICE-OSA study adds about 10 minutes to your DISE procedure with the addition of pharyngeal manometry and ultrasound.

The purpose of DISE is to further assess the location and extent of collapse of anatomical structures in the upper airway. DISE is performed in an operating room. Your doctor will monitor your heart and oxygen while you are given propofol intravenously, putting you to sleep. You will wear a sensor on your finger to monitor your oxygen levels throughout the procedure. We will put lidocaine jelly on your tongue and into each nostril to numb those areas. After you fall asleep, a flexible tube with a small camera at the tip is placed in your nose to take pictures of your nose and throat (the pictures may be saved on a video camera or computer). Because the effects of this medicine can take a little while to wear off completely, it may not be safe for you to drive home after this assessment visit. You will need to arrange for someone else to take you home afterwards. Please ask your doctor to further explain this procedure to you, and to answer any specific questions that you may have.

During your DISE, we will be completing these additional **DISE maneuvers**:

Pharyngeal Manometry – To measure the pressures in your throat and your breathing effort, 1-2 spaghetti-like tubes will be passed through one nostril and into your throat while you are still awake. Before inserting this tube into your nostril, a small amount of the numbing medicine will be squirted into your nostril to prevent sneezing. The numbing medication may leave a bitter taste in your throat and a burning feeling inside your nose for a short time. These tubes will be measuring the air pressure in your airway during the DISE procedure. This will add about 1 minute to your DISE procedure to pass the tubes through your nose and position them in your throat.

Ultrasound during DISE – We will perform an US scan of your upper airway after you are sedated and prior to inserting the endoscope in your nose. This will be done very similarly to the ultrasound scan from Visit 1, except you are already sedated. This will take about 5 – 10 minutes, and this allows us to observe and record tongue position and tongue motion while in a sleep-like state.

The addition of these two maneuvers during DISE extends the timing of the DISE procedure by about 10 minutes for a total of 40 minutes.

WHAT ARE THE POSSIBLE RISKS OR DISCOMFORTS?

There are separate possible risks with the study-related procedures.

Tongue Force Measurements

There are minimal risks associated with capturing these measurements. The measurements may be slightly uncomfortable, and you may experience mild tongue soreness after the tongue force assessment.

Ultrasound

Ultrasound uses sound waves to create pictures of the inside of your body. It is non-invasive and causes minimal discomfort.

Digital Morphometric Photography

There are minimal risks associated with digital morphometric photography. The measurements may be slightly uncomfortable, and the research team will ensure the laser pointers do not shine into your eyes while taking photographs of your face. The images and data collected about you will be stored on the department's institutionally-managed and access-restricted shared drive. Written information is stored in locked file cabinets or file rooms when not attended by study personnel. The digital images taken of you will be deleted one year after you have consented.

MRI

The known risks associated with MRI are minimal, but they require screening before you can undergo scanning.

Flying objects: The greatest risk of MRI is a magnetic object flying toward the magnet and hitting you. To reduce this risk, we require that all people involved with the study remove all magnetic metal from their clothing and all magnetic metal objects from their pockets. No magnetic metal objects are allowed to be brought into the magnet room at any time except by approved personnel. In addition, once you are in the magnet, the door to the room will be closed so that no one inadvertently walks into the room.

Medical implants and foreign bodies: There is also a potential risk of MRI for subjects with medical implants or other metallic objects in their bodies. All subjects undergoing MRI scanning must complete a risk evaluation in advance of the study for the presence of medical implants or other foreign bodies that could pose an injury, including wearable sensors, medicinal patches, certain types of tattoos, and hair weaves containing metallic threads. Every effort will be made to ensure that disclosed implants or foreign bodies do not pose a risk to subjects. In cases where there is insufficient information to evaluate the risks associated with an implant or foreign body, the MRI study will not be allowed to proceed.

Other possible MRI risks include anxiety/stress, claustrophobia, discomfort, nausea/vomiting, and tingling in arms.

Incidental findings

The MRI you will have in this study is not a clinical test. It is possible that during the research study, the research staff may notice unexpected finding(s). Should this occur, the information will be considered by the appropriate personnel and the Principal Investigator will inform you if needed. The information may or may not be significant and may lead to anxiety about your condition and to further work-up by your physician.

DISE

DISE may cause nose bleeds, and/or spasm of the vocal cords which can lead to difficulty breathing and speaking. Vocal cord spasm only occurs in about 0.1% patients during DISE and lasts for about 30 seconds, and difficulty breathing and speaking may occur in about 0.5% of patients and lasts for about 60 seconds during DISE. Enrolling in the ICE-OSA trial will add about 10 minutes to your DISE procedure, and in our experience, DISE procedures that are extended by 10 minutes have shown no increased risks. The risk associated with these additional 10 minutes is minimal.

Lidocaine jelly: The use of lidocaine jelly is part of the ARCTIC-3 DISE procedure. The risks of lidocaine are minimal but might include temporary numbness of your mouth and difficulty swallowing if too much lidocaine were applied. You may feel an initial burning sensation in your nostrils or tongue and an urge to swallow.

Sedation: Sedation is part of the ARCTIC-3 DISE procedure. Propofol will be given intravenously (through an IV tube in your arm) under the care of a skilled airway team (anesthesiologist and head and neck surgeon) and with equipment and personnel available to monitor and support your blood pressure, breathing rate, and heart rhythm. Because the effects of this medicine can take a little while to wear off completely, it may not be safe for you to drive home after the procedure. You will need to arrange for someone else to take you home afterwards.

Risks of Propofol (Dipirivan®): The use of propofol is part of the ARCTIC-3 DISE procedure.

- Common risks occurring in more than 20% of patients: fast or slow heart rate, low blood pressure, burning, stinging, or infection at the injection site, apnea (pauses or stops in breathing), rash, and itching.
- A serious, uncommon risk, occurring in less than 1% of patients, is seizure.

Pharyngeal manometry and videoendoscopy: These are minimally-invasive outpatient procedures and can be linked with mild discomfort. Passing the scope through the nostril may result in mild nasal irritation, nosebleed, and minor gagging.

Pregnancy Risks

Undergoing procedures with propofol can cause serious harm to an unborn child, and although there are no known risks related to MRI on pregnant women or a fetus, there is a possibility of yet undiscovered pregnancy related risks. Moreover, it is a requirement of the ARCTIC-3 baseline assessments that participants not be pregnant or plan on becoming pregnant within 3 months of their Cryosa Procedure. Therefore, we will not be enrolling pregnant women or women who plan on becoming pregnant in this protocol.

Women of childbearing potential will be asked to take a urine pregnancy test as part of their baseline assessments from the ARCTIC-3 protocol, and a separate urine pregnancy test is not required for ICE-OSA. If a patient becomes pregnant after enrolling in the ICE-OSA trial, they will be removed from ICE-OSA.

Privacy

There is also a risk that someone could get access to the information we collect about you. We will do everything we can to protect your privacy, but it is not possible to guarantee total privacy. Electronic medical records are kept in a secure, password-protected database, and written information is stored in locked file cabinets or file rooms when not attended by study personnel. Wherever possible, we will use code numbers instead of your name or other identifying information.

Unknown risks

There may be other risks or side effects from the study procedures that are not yet known. Discomforts and risks may also vary from person to person. There is always the possibility that unknown risks may happen. These may be mild or serious, and in some cases may be very serious, long-lasting, or may never go away. If any discomforts or risks happen, you should tell the study doctor.

WILL BEING ON ICE-OSA BENEFIT ME?

You are not expected to get any direct benefit from being in the ICE-OSA study. However, your participation in this research may help others in the future. The knowledge gained from this study may lead to the development of more personalized plans to treat patients with sleep apnea.

WILL I RECEIVE THE RESULTS OF RESEARCH TESTING THAT MAY BE RELEVANT TO MY HEALTH?

Results that may be relevant to your healthcare may be released to you, such as information from your MRI, DISE, and US procedures. Most tests done in research are only for research and have no clear meaning for health care. Additional research results will not be returned to you because they will not be relevant to your healthcare.

WHAT HAPPENS IF I AM INJURED FROM BEING IN THE STUDY?

If you believe you have sustained an injury or believe you have experienced a reaction to the study treatment, or if you have any questions, complains or concerns about the research, contact Dr. Dedhia at (215) 349-5009. In case of an emergency, and if you are unable to reach the study doctor first, call your local emergency number if not 911. If you call your local emergency number or 911, let Dr. Dedhia know about the emergency as soon as possible. Dr. Dedhia will review the matter with you, assist you in obtaining appropriate medical care and identify any resources that may be available to provide medical treatment.

Your insurance or health plan may be billed for this treatment. The sponsor, Cryosa Inc., will pay any charges that are not covered by insurance policy or the government, provided the adverse event was related to your participation in ICE-OSA, and not due to your underlying illnesses or conditions and was not caused by you or some other third party.

If you feel this injury was caused by medical error on the part of the study doctors or others involved in ICE-OSA, you have the legal right to seek payment, even though you are in the ICE-OSA study. You do not give up your legal rights by signing this form.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT PARTICIPATE?

If you choose not to participate in ICE-OSA, it will not affect your medical care outside of the study or your relationship with your health care providers. Choosing to not participate will also have no effect on your eligibility and enrollment in the ARCTIC-3 trial. You should still go to all your regular doctors' appointments as scheduled. You may wish to talk to your doctor about whether to participate. If you are a student or employee of the University of Pennsylvania, your decision will not affect your standing at the university in any way.

ARE THERE ANY COSTS TO ME FOR TAKING PART IN THIS STUDY?

There are no costs to you for any tests, doctor visits or procedures that are required for ICE-OSA.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

You will receive compensation to offset the cost of your travel and time in ICE-OSA, as shown in the table below, in addition to the compensation from the ARCTIC-3 study. Since research study sites are paid quarterly (every 3 months) you may not receive payment for a study visit until 3 months after you complete the study visit. Payments to you that total more than $600 will be reported to the IRS.

Study Visit	**Payment**		**Total Payment**
Visit 1	$150		$150
Visit 2	$25		$25
Visit 3	$150		$150
Total			**$325**

WHEN IS ICE-OSA OVER? CAN I LEAVE THE STUDY BEFORE IT ENDS?

The ICE-OSA study is expected to end after all participants have completed all visits, and all information has been collected. ICE-OSA may also be stopped at any time by your physician, the study Sponsor, or the Food and Drug Administration (FDA) without your consent because:

- The Primary Investigator feels it is necessary for your health or safety. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- The Sponsor, the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

Taking part in ICE-OSA is voluntary. The choice to participate or not to participate in ICE-OSA is yours. If you decide to participate, you will have the right to withdraw at any time. You may refuse to participate or discontinue participation in ICE-OSA at any time without penalty or loss of benefits to which you are otherwise entitled.

If you choose to discontinue participation in ICE-OSA, you will be asked to complete a final evaluation.

You will be notified of any significant new findings that arise throughout the course of the study, which may affect your willingness to continue in the study. You may be asked to sign a revised consent form if this occurs.

CAN I BE REMOVED FROM ICE-OSA WITHOUT MY APPROVAL?

The study doctor may stop your participation in ICE-OSA if:

- you have significant side effects from the study procedures,
- you do not follow the study instructions,
- new information becomes available that suggests you should not continue,

- it is in your best interest,
- you do not later consent to any future changes that may be made in the study plan,
- or for any other medical reason.

IS MY DOCTOR PAID TO BE IN THE STUDY?

The Sponsor, Cryosa Inc., in Arden Hills, Minnesota, will provide funding for ICE-OSA. Cryosa Inc. is paying your doctor or your doctor's health care organization to cover reasonable costs associated with being part of the ICE-OSA study. This includes complying with the FDA and the hospital's regulations for ICE-OSA, screening patients for ICE-OSA, completion of the data collection forms, reporting of adverse events, etc. This should in no way affect the quality of care given to you by your doctor.

Cryosa Inc. is providing money to the University of Pennsylvania to administer the ICE-OSA study. The study doctor may be paid to conduct the study. Neither the study doctor nor the university has additional interests in this research project or in the Sponsor. Please ask the study doctor or research staff if you have any questions about these arrangements.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

If you have questions, concerns or complaints regarding your participation in ICE-OSA, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the University of Pennsylvania IRB at the number listed on page one of this form.

HOW WILL MY PERSONAL INFORMATION BE PROTECTED DURING ICE-OSA?

If you agree to participate in the ICE-OSA study and sign this consent form, you are authorizing use and disclosure of your health information as described in the following sections.

We will do our best to make sure that the personal information obtained during the course of the ICE-OSA study will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if required by law. If information from ICE-OSA is published or presented at scientific meetings, your name and other personal information will not be used. The Institutional Review Board (IRB) at the University of Pennsylvania will have access to your records. If ICE-OSA is being overseen by the Food and Drug Administration (FDA), they may review your research records.

The confidentiality of your information will be protected in the following way during ICE-OSA: The information that will be stored or shared is *coded information*, meaning we will assign a study-specific code to your name upon enrollment so that when we record, reference or share your information from this trial, we do not have to use or list your personal identifiers (i.e. name, date of birth). We will indefinitely store the linking set (association your name to the study code), so future re-identification is possible but not intended nor planned.

WHAT INFORMATION ABOUT ME WILL BE COLLECTED, USED, OR SHARED WITH OTHERS?

The following information about you will be *collected* and stored indefinitely by the study team at Penn:

- Name, address, telephone number, date of birth
- Social Security number
- Personal and family medical history
- Results from a physical examinations, tests or procedures
- Video of upper airway and photos of facial structure

The following information about you will be *shared* with the sponsor:

- Date of birth, address
- Personal and family medical history
- Results from physical examinations, tests or procedures
- Video of upper airway and photos of facial structure

The images shared with Cryosa, Inc. will not include full-face photos, but your identity may be revealed in the photos and video images. Data shared to the study sponsor may be stored by the sponsor indefinitely. If you do not want your photos taken or your procedure videotaped for research purposes, you may not participate.

The photographs and video images will not be used for marketing purposes, unless you sign an additional form that gives your permission to do so. Cryosa, Inc. has no plans to pay you to use these videos.

WHY IS MY INFORMATION BEING USED?

Your information is used by the research team to contact you during ICE-OSA. Your information and results of tests and procedures are used to:

- do the research
- oversee the research
- to see if the research was done right
- to evaluate and manage research functions.

In addition, people from the Sponsor and its associates will be visiting the research site to evaluate if the study is being carried out correctly. They will review and may photocopy your records during that process, including records prior to your enrollment in ICE-OSA, if applicable.

The information may be given to the FDA. This is done so the Sponsor can report the results of the research and seek approvals. In addition, this information may be used to meet reporting requirements of government agencies.

WHO MAY USE AND SHARE INFORMATION ABOUT ME?

The following individuals may use or share your information for the ICE-OSA study:

- The investigator of the study and the study team
- Other authorized personnel at Penn Medicine and the University of Pennsylvania, including offices that support research operations

- Other research personnel with access to the databases for research and/or study coordination and as otherwise approved by the IRB

The doctor must get your authorization (permission) to use or give out any health information that might identify you.

WHO MIGHT GET THIS INFORMATION?

Information about you and your health, which may or may not identify you, may be given to the Sponsor (Cryosa Inc.) and their affiliates, the IRB at Penn, the FDA and other regulatory bodies. Your personal information may be given out if required by law. If information from ICE-OSA is published or presented at scientific meetings, your name and other personal information will not be used.

Once your personal health information is disclosed to others outside Penn Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to Penn Medicine procedures developed to protect your privacy.

WHERE MAY MY INFORMATION BE STORED?

Information related to your participation in clinical research will be contained in a clinical trial management system (CTMS). A CTMS is used to register your information as a participant in a study. This allows for your research data to be entered and stored for the purposes of study operational and financial applications and other activities required as part of the conduct of the research. Once placed in the CTMS, your information may be accessible to other authorized personnel at Penn Medicine that support research operations. Your information may be held in other research databases, such as at Cryosa, Inc.

HOW LONG MAY PENN MEDICINE USE OR DISCLOSE MY PERSONAL HEALTH INFORMATION?

Your authorization for use of your personal health information for the ICE-OSA study does not expire.

However, Penn Medicine may not re-use or re-disclose information collected in ICE-OSA for a purpose other than the ICE-OSA study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

FUTURE USE OF CODED INFORMATION FOR RESEARCH PURPOSES

Only your personal and family medical history and results from physical examinations, tests and procedures will be stored *for future research purposes*. The information that will be stored or shared is *coded information*, meaning we will assign a study-specific code to your name upon

enrollment so that when we record, reference or share your information from this trial, we do not have to use or list your personal identifiers (i.e. name, date of birth). We will indefinitely store the linking set (associating your name to your study code), so future re-identification is possible but not intended nor planned.

The future use of your information only applies to the information collected on ICE-OSA. This information may be stored indefinitely. Only Penn Medicine and Cryosa, Inc. would conduct future research with your information. Any future research studies will further investigate the safety and efficacy of the Cryosa procedure as treatment for OSA and help others by improving our understanding of health and disease. We will not follow up with you to tell you about the specific research that will be done. It is possible that you may have chosen not to participate in these future research studies, had you been approached for participation.

There is a risk of breach of confidentiality (unintentional release of your information). We will do our best to make sure that this doesn't happen. However, we cannot guarantee total privacy. We will protect your confidentiality during storage and sharing by controlling which individuals involved in ICE-OSA can have access to information from this trial. You will likely not directly benefit from future research with your information. If you have questions about the storage of your information or have changed your mind, you can contact Dr. Dedhia at (215) 349-5009.

ELECTRONIC MEDICAL RECORD AND RELEASE OF STUDY-RELATED INFORMATION

An Electronic Medical Record (EMR) is an electronic version of your medical chart within a health system. An EMR is simply a computerized version of a paper medical record.

If you have been a patient at Penn Medicine in the past, information from your research participation will be added to your existing medical record. If you have never received care within Penn Medicine and are participating in a University of Pennsylvania research study that uses Penn Medicine healthcare related services, an EMR will be created for you to maintain any information produced from your participation. If you do not already have an EMR, the creation of an EMR is required to participate in ICE-OSA. In order to create your EMR, the study team will need to obtain basic information about, similar to the information you would provide the first time you visit a hospital or medical facility (i.e. your name, the name of your primary doctor, the type of insurance you have).

WHAT MAY BE PLACED IN THE EMR?

Information related to your participation in the research (e.g., laboratory tests, notes from your physician, imaging studies, etc.) will be placed in your EMR.

Once placed in your EMR your information may be accessible to appropriate Penn Medicine workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by Penn Medicine to be appropriate to have access to your EMR (e.g. Health Insurance Company, disability provider, etc.).

Penn Medicine also participates in automated information sharing through Health Information Exchanges (HIEs). HIEs securely share parts of your electronic health record, including research information, with other healthcare organizations involved in your care. This information is shared to improve the quality, safety and efficiency of your healthcare. To request that your health information not be shared through HIEs, please call (215) 662-4484.

WILL I HAVE ACCESS TO RESEARCH RELATED INFORMATION WITHIN THE EMR?

As part of your participation in this research, you will have access to research related information within your EMR through Penn Medicine's patient portal – called MyPennMedicine (MPM).

Some information specific to the ICE-OSA study may be shared with you in a delayed manner, shared with you at the end of the study, or not shared with you. Not sharing or delaying certain research information within your EMR may be necessary to protect the integrity of the trial results or for other reasons.

CAN I CHANGE MY MIND ABOUT GIVING PERMISSION FOR USE OF MY INFORMATION?

Yes. You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the investigator for the ICE-OSA study. If you withdraw your permission, you will not be able to stay in ICE-OSA.

WHAT IF I TERMINATE MY PARTICIPATION IN THE STUDY?

This authorization does not expire. You have the right to revoke your permission whenever you want by writing to the principal investigator of ICE-OSA.

However, information that has already been gathered at the time you terminate your participation will continue to be used for the trial. The Sponsor, sponsor's representatives and government agencies will still have access to your records to audit and confirm the information gathered before your termination. If you withdraw your permission, you will not be able to stay in ICE-OSA and no more of your information will be collected. If you change your mind and withdraw from the trial, your trial-specific information that was stored at Penn will be destroyed.

WHAT IF I DECIDE NOT TO GIVE PERMISSION TO USE AND GIVE OUT MY HEALTH INFORMATION?

Then you will not be able to be in the ICE-OSA study.

You will be given a copy of this Research Subject Informed Consent and HIPAA Authorization Form describing your confidentiality and privacy rights for the ICE-OSA study.

By signing this document, you are permitting Penn Medicine to use and disclose personal health information collected about you for research purposes as described above.

MAY I REVIEW OR COPY MY INFORMATION?

Yes, but only after the research is over.

Do not sign this consent form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

If you agree to be in the ICE-OSA study, you will receive a signed and dated copy of this consent form for your records.

CONSENT

When you sign this form, you are agreeing to take part in the ICE-OSA study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your protected health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that protected health information to outside organizations or people involved with the operations of the ICE-OSA study.

A copy of this consent form will be given to you.

_____	_____	_____
Name of participant [print]	Signature of Participant	Date

_____	_____	_____
Name of Person Obtaining Consent [print]	Signature	Date

For use with Non-English-Speaking participants / LARs utilizing a short-form process:

_____	_____	_____
Name of Witness [Print]	Signature of Witness	Date

_____	_____	_____
Name of Interpreter [Print] *(When available)*	Signature of Interpreter	Date

For participants unable to give authorization, the authorization is given by the following authorized participant representative:

_____	_____	_____
Authorized participant representative [print]	Authorized participant representative signature	Date

_____

Provide a brief description of above person authority to serve as the participant's authorized representative.

Attestation Statement

I confirm that the research study was thoroughly explained to the subject. I reviewed the consent form with the subject and answered the subject's questions. The subject appeared to have understood the information and was able to answer the following questions correctly:

1. What is the purpose of this study?
2. If you decide to be in the study, what will you be asked to do?
3. What is the possible benefit of participating in this study?
4. What are the potential risks of participating in this study?
5. If you decide not to participate in this study, what options do you have?
6. What is the cost for participating in the study? If so, what will you have to pay for?
7. Do you have to be in this study?
8. If you decide to be in the study, can you leave the study when you want to?

_____	_____
Printed Name of Person Conducting the Informed Consent Discussion	Position
_____	_____
Signature of Person Conducting the Informed Consent Discussion	Date
_____	
Printed Name of Investigator's Name	
_____	_____
Signature of Investigator	Date