Protocol Title: CONE BEAM COMPUTED TOMOGRAPHY - GUIDED NAVIGATIONAL BRONCHOSCOPY FOR PERIPHERAL PULMONARY NODULES: A RANDOMIZED TRIAL

DF/HCC Principal Investigator(s) / Institution(s): Adnan Majid, MD/ Beth Israel Deaconess Medical Center

Main Consent

INTRODUCTION AND KEY INFORMATION

All research is voluntary. It is your choice whether you take part in this research or not. If you decide to participate, please sign and date at the end of this form. We will give you a copy and you can refer to this consent form at any time.

The following is a short summary of this research study to help you decide whether you would like to be a part of this study. More detailed information is provided later in this form.

For purposes of this research, you will be referred to as a "participant."

1. Why am I being invited to take part in a research study?

You are invited to take part in in this research study, because you have a lung nodule (a growth between one half to one inch) that is 1 to 3 cm in size.

2. Why is this research being done?

The purpose of this study is to determine if the cone beam computed tomography (CBCT)-guided electromagnetic navigation bronchoscopy (NB) is better in diagnosing lung nodules compared to NB alone.

3. Who is supporting this research?

Philips Medical Systems International BV is supporting this research study by providing funding for the research study.

4. What does this research study involve and how long will it last?

This research study involves a screening period, a procedure and follow up visits. You could be in the study for up to 6 months.

The names of the study interventions involved in this study are:

- CBCT-guided NB
- NB alone

The research study procedures include screening for eligibility and study treatment including evaluations and follow up visits.

You will receive the study procedure and will be followed for up to 6 months.

It is expected that about 136 people will take part in this research study.

Information about you and your health is personal and private. Generally it cannot be obtained without your written permission. By signing this form, you are providing that permission and your information may be obtained and used in accordance with this informed consent and as required or allowed by law. This means that researchers may obtain information regarding your past medical history, as well as specimens and samples from previous health care providers such as hospitals and labs.

5. What are the risks to participating in this study?

There are risks to taking part in any research study. We want to make sure you know about a few key risks right now. There may also be rare, serious and potentially life-threatening side effects. More detailed information is provided in the “What are the risks or discomforts of the research study?” section.

There is a risk that you could have side effects from the procedure. These side effects may be worse and may be different than you would get with other approaches for your cancer.

Some of the most common side effects that the study doctors know about are:

- Sore throat
- Fever
- Hoarseness

6. Will being in this study benefit me in any way?

We do not know if taking part in this study will benefit you. This study may help researchers learn information that could help people in the future.

7. What are my options?

Instead of being in this research study, you have other options which may include the following:

- Receive standard treatment including NB.
- Decide not to participate in this research study.
- Participate in another research study.
- Receive no therapy specific to your cancer.
- Comfort care, also called palliative care. This type of care may help to reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to treat the symptoms.

If you choose not to participate, are not eligible to participate, or withdraw from this research study, this will not affect your present or future care and will not cause any penalty or loss of benefits to which you are otherwise entitled.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions at any time.

A. WHY IS THIS RESEARCH STUDY BEING DONE?

This clinical trial examines the effectiveness of a treatment comparing it to another known treatment.

The U.S. Food and Drug Administration (FDA) has approved the electromagnetic navigation bronchoscopy as a treatment option for your disease.

The U.S. Food and Drug Administration (FDA) has approved the Cone-Beam CT scan as a treatment option for your disease.

In this research study, we are:

- Determining if cone beam computed tomography (CBCT)-guided electromagnetic navigation bronchoscopy (NB) is better in diagnosing lung nodules compared to NB alone

B. WHAT IS INVOLVED IN THE RESEARCH STUDY?

Because no one knows which of the study options is best, you will be "randomized" into one of the study groups: CBCT-guided NB or NB alone. Randomization means that you are put into a group by chance. It is like flipping a coin.

Neither you nor the research doctor will choose what group you will be in. You will have an equal chance of being placed in any of the following groups:

- Group A: CBCT-guided NB
- Group B: NB alone

Before the research starts (screening):
After signing this consent form, you will be asked to undergo some screening tests or procedures to find out if you can be in the research study. All of these tests and procedures are part of regular cancer care and may be done even if it turns out that you do not take part in the research study. This will be done up to 3 months prior to your procedure. If you have had some of these tests or procedures recently, they may or may not have to be repeated.

- **Demographics**
- **A medical history,** which includes questions about your health, current medications, and any allergies.
- **Clinical Exams*:*** During this visit you will have a physical exam including vital signs, height and weight. You will be asked questions about your general health and specific questions about any problems that you might be having and any medications you may be taking.
- **An assessment of your tumor** by one or more of the following standard assessment tools: X-ray, CT (Computerized Tomography) scan
- **Blood tests** (about 1-2 tablespoons of blood). This will be performed 1 week prior to the procedure if your doctor feels is necessary.
- **Pregnancy test (if applicable).** This will be either a urine or a blood test. If this is a blood test, about 1 teaspoon of blood will be used.
- **Electrocardiogram (EKG)** which measures the electric signals from your heart. This will be performed 1 week prior to the procedure if your doctor feels is necessary.

If these tests show that you are eligible to participate in the research study, you may begin the study treatment. If you do not meet the eligibility criteria, you will not be able to participate in this research study.

Study Visit: Procedure Visit

This visit will involve the following:

- **Clinical Exams*:*** During this visit you will have a physical exam, vital signs and you will be asked questions about your general health and

specific questions about any problems that you might be having and any medications you may be taking.
- **Scans (or Imaging tests):** We will assess your tumor by chest X-ray
- **Adverse Event Evaluation**. This will assess any side effects you are experiencing
- **Procedure**

Follow-up Study Visits: Follow-Up Visits may occur at Week 1, 4 and 24. This may vary depending on your final diagnosis, underline conditions and your doctor's preference.

This visit may be a clinic visit, a virtual visit or a phone call and may involve the following:

- **A medical history,** which includes questions about your health, current medications, and any allergies.
- **Clinical Exams***:* During this visit you will have a physical exam, vital signs and you will be asked questions about your general health and specific questions about any problems that you might be having and any medications you may be taking.
- **Scans (or Imaging tests):** We will assess your tumor by chest X-ray and chest CT-scan. This will be performed at week 1 and 24 visits only.
- **Adverse Event Evaluation**. This will assess any side effects you are experiencing

We would like to keep track of your medical condition. Keeping in touch with you and checking your condition helps us look at the long-term effects of the research study. During the time of your follow up on this study, you may also receive phone calls to check on your well-being and to remind you of your next appointment.

In addition, you can stop participating in the research study at any time, however, the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

C. WHAT ARE THE RISKS OR DISCOMFORTS OF THE RESEARCH STUDY?

There are risks to taking part in any research study.

All cancer treatments can have side effects, which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability among side effects of different cancer treatments and between

individuals. In a research study, all of the risks or side effects may not be known before you start the study. **You need to tell your doctor or a member of the study team immediately if you experience any side effects.**
During the research study, you will be notified of newly discovered side effects or significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

Risks Associated with Bronchoscopic Procedures:

- Sore throat
- Fever
- Apnea (breathing suddenly stops)
- Pneumothorax: Collection of air outside the lungs in the space surrounding the lungs. May require lung re-inflation with a chest tube.
- Bleeding
- Anesthesia related complications
- Tachycardia (fast heart beat)
- Bradycardia (slow heart beat) which can cause dizziness, fainting and tiredness.
- Myocardial infarction (heart attack): Decreased blood flow to part of the heart causing damage to the heart muscle. This may be serious or life threatening.
- Pulmonary edema: fluid in the lung (possible difficulty breathing)
- Bronchospasm (wheezing): Breathing distress caused by narrowing of the airways
- Laryngospasm (closing of the throat)
- Injury of your airway such as cracking or tearing which can result in difficulty breathing
- Dyspnea (shortness of breath)
- Prolonged hypoxemia: Low oxygen level, which may cause shortness of breath, confusion or drowsiness
- Pneumonia (infection of the lungs): The study procedure may cause an increased risk of infection. A low number of white blood cells may increase the risk of infection. It may become life-threatening. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.
- Hypercarbia (increased levels of carbon dioxide in your blood): This can result in difficulty breathing.
- Respiratory failure: Difficulty breathing with low levels of oxygen in the blood, which could be serious and life threatening and require you to

have a tube inserted into your windpipe that is hooked up to a machine to help you breathe.
- Hemoptysis: Vomiting or coughing up blood
- Epistaxis: Bloody Nose
- Seizure (Convulsion)

Cancer research often includes biopsies, scans, x-rays that are also provided as routine care. The following describes the side effects of procedures done only for the purposes of research.

Risks Associated with Biopsies:
Biopsies are normally performed under the guidance of an imaging technique. Each procedure requires a separate consent prior to the biopsy. The risks may include:
- Pain and discomfort. The amount of pain and discomfort will vary, depending on the location of the biopsy site. These risks can be discussed with the study doctor.
- Minor bleeding at the biopsy site.
- Tenderness at the biopsy site.
- Scarring at the biopsy site.
- Rarely, an infection at the biopsy site.

Uncommonly, complications from biopsies can be life threatening. As with any interventional procedure, other potentially serious complications from bleeding or organ damage may occur. These might require additional surgical intervention.

Radiation Risks Associated with Scans and X-Rays:
While you are in this research study, CT scans, and x-rays utilizing radioactivity may be used to evaluate your disease.

In the long term, over many years, there is a very low risk of developing a new cancer as a result of the radiological evaluation and treatment for your cancer.

Risks Associated with Contrast Agents Used During Scans:
There is a small risk with using a contrast agent that is injected into a vein during the CT scan. The contrast agent is a special dye that highlights organs, blood vessels or tissue to make them more visible. Depending on the type of contrast agent that is used, it may cause decreased kidney function or worsen kidney function in people who already have decreased kidney function. Therefore, we will monitor your kidney function closely while you participate in this study. If there is any change in your kidney function, we may have to remove you from the study.

Uncommonly, some people have allergic reactions (such as hives and itching) to the contrast agent. Serious reactions (for example, drop in blood pressure, difficulty breathing or severe allergic reaction and death) are rare.

Reproductive Risks:
The procedures used in this research study may affect a fetus.
While participating in this research study, you should not:

- Become pregnant
- Nurse a baby
- Father a baby

We can provide counseling about preventing pregnancy for either male or female study participants. Let your doctor know immediately if you become pregnant or find out that you are going to be the father of a child.

If your partner becomes pregnant while you are on the study, it may be critical to share information regarding your participation in this research study with that person. Your research doctor should also be told if this happens.

Non-Physical Risks:
Because of side effects or the time required for tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities.

D. WHAT WILL HAPPEN IF I AM REMOVED FROM THE STUDY OR DECIDE TO END MY PARTICIPATION IN THE RESEARCH?

You may be taken off the research study for any reason including:

- It is considered to be in your best interest
- The study treatment or procedures are found to be unsafe or ineffective
- There is any problem with following study treatments and procedures
- You are a female and become pregnant or plan to become pregnant
- Your condition worsens
- A decision is made to end the study
- Or for other unforeseen reasons that make it necessary to stop your participation in the research study

You can also choose to stop participating in the research study at any time. Tell the research doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop. Leaving the research study will not affect your medical care outside of the research study.

It is important to tell the research doctor if you are thinking about stopping so your research doctor can evaluate the risks from stopping the intervention.

It is important to note that although you may withdraw from study participation, the FDA requires that any information collected up to the point of your withdrawal cannot be removed from study records. Additionally, the research doctor may consult public records after you have withdrawn from the study.

E. WHAT ARE THE BENEFITS OF THIS RESEARCH STUDY?

Taking part in this research study may or may not benefit you. We hope the information learned from this research study will provide more information about CBCT-guided ENB and if it is more effective in diagnosing lung nodules compared to ENB alone.

F. WILL I BE PAID TO TAKE PART IN THIS RESEARCH STUDY?

You will not be paid for participating in this study.

G. WHAT ARE YOUR COSTS?

Taking part in this research study may lead to added costs to you or your insurance company. This may mean that you need to make more visits to the clinic or hospital than if you were getting the usual approach to treat your disease. You may:

- Have more travel costs
- Need to take more time off work
- Have other additional personal costs

You or your insurance company will be charged for portions of your care during this research study that are considered standard care including the procedure, blood tests and exams. Standard of care is the care that you would receive regardless of whether you were enrolled in the study or not. You may be responsible for co-payments, co-insurance, premiums and deductibles that are typical for your insurance coverage. This includes the cost of tests, procedures, or medicines to manage any side effects, unless you are told that certain tests, done for research only, are supplied at no charge.

If you have questions about your insurance coverage, or the items you might be required to pay for, please call financial services for information. The contact information for financial services are:

- Beth Israel Deaconess Medical Center: (617) 667-5661

The National Cancer Institute provides an online resource to help people participating in cancer clinical trials understand which services their insurance company is required by law to pay. This can be found at the website below or can be provided by the study team:

www.cancer.gov
or 1-800-4-CANCER (1-800-422-6237)

H. WHAT HAPPENS IF I AM INJURED OR BECOME SICK BECAUSE I TOOK PART IN THIS RESEARCH STUDY?

If you think you have been injured as a result of taking part in this research study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form.

The treating hospital will offer you the care needed to treat injuries directly resulting from taking part in this research. These treatments may be billed to you or your insurance company. You will be responsible for deductibles, co-payments and co-insurance. There are no plans to pay you or give you other compensation for the injury.

You do not give up your legal rights by signing this form.

We will need to collect certain personal information about you for insurance or payment reporting purposes, such as your name, date of birth, gender, social security number or Medicare identification number and information related to this research study. We may be required to report this information to the Centers for Medicare & Medicaid Services. We will not use this information for any other purpose.

If you go to the Emergency Room or to another hospital or doctor it is important that you tell them that you are in this research. If possible, you should give them a copy of this consent form.

I. WHOM DO I CONTACT IF I HAVE QUESTIONS ABOUT THE RESEARCH STUDY?

If you have questions about the study, please contact the research doctor or study staff as listed below:

Beth Israel Deaconess Medical Center

- Adnan Majid, MD: (617) 632-8252 or amajid@bidmc.harvard.edu

For questions about your rights as a research participant, please contact a representative of the Office for Human Research Studies at Dana-Farber Cancer Institute (617) 632-3029. This can include questions about your participation in the study, concerns about the study, a research related injury, or if you feel/felt under pressure to enroll in this research study or to continue to participate in this research study.

J. RETURN OF RESEARCH RESULTS

Tests done on samples in this research study are only for research and have no clear meaning for your health care. For this reason, your study doctor will not share the results with you.

K. CLINICALTRIALS.GOV (CT.GOV)

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This web site will not include information that can identify you. At most, the web site will include a summary of the results. You can search this web site at any time.

L. FUTURE USE OF DATA AND SPECIMENS

Your personal information and/or biospecimens collected during this study will not be used or distributed for future research studies even if the information is de-identified and cannot be linked back to you.

M. CONFIDENTIALITY

We will take measures to protect the privacy and security of all your personal information, but we cannot guarantee complete confidentiality of study data.

Medical information created by this research study may become part of your hospital medical record and may be forwarded to your primary doctor. Information that does not become part of your medical record will be stored in your study file. It may also become part of a research database.

Participation in this study involves providing a specimen of your tissue; please know that if the research doctor leaves the institution, the research and the tissue might remain at the research doctor's current institute or might be transferred to another institution.

The study team plans to publish the results of this research study and when we do, we may be asked to make the data we collect available to other researchers. We will not include information that identifies you in any publications or to the researchers who request the data to do additional research.

N. FINANCIAL DISCLOSURES

It is possible that certain researchers on this study may have earned money from, or own some publicly-traded stock in, the company that makes or is developing the study intervention. The amount of money that a researcher may earn and still take part in research is limited by the Harvard Medical School Faculty of Medicine Policy on Conflicts of Interest and Commitment. If you have further questions, please speak with a member of the study team or contact the Dana-Farber Cancer Institute Office of Research Integrity at 617-432-4557 or researchintegrity@dfci.harvard.edu.

O. GENETIC RESEARCH

This research will not involve genomic or germline testing.

P. PRIVACY OF PROTECTED HEALTH INFORMATION (HIPAA AUTHORIZATION)

The Health Insurance Portability and Accountability Act (HIPAA) is a federal law that requires Dana-Farber/Harvard Cancer Center (DF/HCC) and its affiliated research doctors, health care providers, and physician network to protect the privacy of information that identifies you and relates to your past, present, and

future physical and mental health conditions ("protected health information"). If you enroll in this research study, your "protected health information" will be used and shared with others as explained below.

1. What protected health information about me will be used or shared with others during this research?

- Existing medical records, including mental health records.
- New health information created from study-related tests, procedures, visits, and/or questionnaires

2. Why will protected information about me be used or shared with others?

The main reasons include the following:

- To conduct and oversee the research described earlier in this form;
- To ensure the research meets legal, institutional, and accreditation requirements;
- To conduct public health activities (including reporting of adverse events or situations where you or others may be at risk of harm); and
- To provide the study sponsor with information arising from an adverse event or other event that relates to the safety or toxicity of the drug(s) used in the study and for the purpose of this or other research relating the study drug(s) and their use in cancer;
- To better understand the diseases being studied and to improve the design of future studies; and,
- Other reasons may include for treatment, payment, or health care operations. For example, some medical information produced by this research study may become part of your hospital medical record because the information may be necessary for your medical care. (You will also be given a notice for use and sharing of protected health information.)

3. Who will use or share protected health information about me?

- DF/HCC and its affiliated research doctors and entities participating in the research will use and share your protected health information. In addition, other DF/HCC offices that deal with research oversight, billing or quality assurance will be able to use and share your protected health information.

4. With whom outside of DF/HCC may my protected health information be shared?

While all reasonable efforts will be made to protect the confidentiality of your protected health information, it may also be shared with the following entities:

- Outside individuals or entities that have a need to access this information to perform functions relating to the conduct of this research such as analysis by outside laboratories on behalf of DF/HCC and its affiliates (for example, data storage companies, insurers, or legal advisors).
- The sponsor(s) of the study, its subcontractors, representatives, business partners, and its agent(s): Philips
- Other research doctors and medical centers participating in this research, if applicable
- Federal and state agencies (for example, the Department of Health and Human Services, the Food and Drug Administration, the National Institutes of Health, and/or the Office for Human Research Protections), or other domestic or foreign government bodies if required by law and/or necessary for oversight purposes. A qualified representative of the FDA and the National Cancer Institute may review your medical records.
- Hospital accrediting agencies
- A data safety monitoring board organized to oversee this research, if applicable

Some who may receive your protected health information may not have to satisfy the privacy rules and requirements. They, in fact, may share your information with others without your permission.

5. For how long will protected health information about me be used or shared with others?

- There is no scheduled date at which your protected health information that is being used or shared for this research will be destroyed, because research is an ongoing process.

6. Statement of privacy rights:

- You have the right to withdraw your permission for the research doctors and participating DF/HCC entities to use or share your protected health information. We will not be able to withdraw all the information that already has been used or shared with others to carry out related activities such as oversight, or that is needed to ensure quality of the study. To

withdraw your permission, you must do so in writing by contacting the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"

- You have the right to request access to your protected health information that is used or shared during this research and that is related to your treatment or payment for your treatment, but you may access this information only after the study is completed. To request this information, please contact the researcher listed above in the section: "Whom do I contact if I have questions about the research study?"

Q. DOCUMENTATION OF CONSENT

My signature below indicates:

- I have had enough time to read the consent and think about participating in this study;
- I have had all of my questions answered to my satisfaction;
- I am willing to participate in this study;
- I have been told that my participation is voluntary and I can withdraw at any time

Signature of Participant or Legally Authorized Representative

Date

Relationship of Legally Authorized Representative to Participant

To be completed by person obtaining consent:

Adult Participant

The consent discussion was initiated on _____ (date).

Signature of individual obtaining consent: _____

Printed name of above: _____

Date: _____

☐ A copy of this signed consent form will be given to the participant or legally authorized representative.

☐ 1) The participant is an adult and provided consent to participate.

☐ 1a) Participant (or legally authorized representative) is a non-English speaker and signed the translated Short Form in lieu of English consent document:

☐ *As someone who understands both English and the language used by the participant, I interpreted and/or witnessed, in the participant's language, the researcher's presentation of the English consent form. The participant was given the opportunity to ask questions.*

Signature of Interpreter/Witness: _____

Printed Name of Interpreter/Witness: _____

Date: _____

☐ 1b) Participant is physically unable to sign the consent form because:

☐ The participant is illiterate.

☐ The participant has a physical disability.

☐ Other (please describe): _____

The consent form was presented to the participant who was given the opportunity to ask questions and who communicated agreement to participate in the research.

Signature of Witness: _____

Printed Name of Witness: _____

Date: _____

☐ 2) The participant is an adult who lacks capacity to provide consent and his/her legally authorized representative:

☐ 2a) gave permission for the adult participant to participate

☐ 2b) did not give permission for the adult participant to participate