The Cleveland Clinic Foundation
Consent to Participate in a Research Study

Study title: Comparison of use of indocyanine green (ICG) and 99mTc-labeled radiotracer for axillary lymphatic mapping in patients with breast cancer

Principal Investigator: Stephen R. Grobmyer, MD (phone 216-636-2843)

Study Coordinator: Courtney Yanda (phone 216-444-3159)

You are being invited to participate in a research study. A research study is designed to answer specific questions about new ways to prevent, detect, and treat disease. Being in a research study is different from being a patient. The purpose of this document is to provide a written summary of the discussion and exchange of research information you had with the research team. It is also for use as a reference during the study.

Please note:

- **You are being asked to participate in a research study**
- **Ask as many questions as needed so you can make an informed decision.**
- **Carefully consider the risks, benefits, and alternatives of the research**
- **Your decision to participate is completely voluntary and will have no effect on the quality of your medical care if you choose not to participate. You can also withdraw from the study at anytime.**

This research study has been approved by the Institutional Review Board (IRB). The IRB is a committee that reviews human research studies to ensure the safety and welfare of research volunteers are protected in accordance with federal human subject regulations and ethical principles.

1. INFORMATION ON THE RESEARCH

Why is the research study being done?

The purpose of this study is to evaluate the usefulness of indocyanine green (ICG) dye for lymph node mapping in patients with breast cancer. ICG will be compared to lymphatic mapping with 99mTc-labeled radiotracer, which is standard of care.

ICG is a dye which can be seen using a camera called a near infrared (or “PDE”). The use of ICG with this camera offers the ability to inject the dye while you are under anesthesia in the operating room and to see the dye move to the lymph nodes.

The use of ICG and the near infrared camera are cleared by the Food and Drug Administration (FDA) for use in humans for vascular tests, and ICG is cleared for use in liver function tests, but these have not yet been cleared for lymph node mapping in patients with breast cancer.

This research will take place only at the Cleveland Clinic and will include about 130 patients.

You are being asked to participate in this study because you are scheduled to undergo breast cancer surgery with lumpectomy or mastectomy and planned axillary sentinel node biopsy procedure.

What is involved if you decide to take part in this research study?
You will receive the same standard of care treatment whether or not you decide to participate in this study.

A member of the study staff will review the study with you and answer any questions you may have. If you agree to participate, we will ask you to sign this consent form before having any study-related tests performed. Your participation will include the standard of care pre-operative visit, and operating room time (which is not extended with this research procedure). The following will occur:

In accordance with routine clinical practice, you will undergo lymphatic mapping with 99mTc sulfur colloid. Injections of 99mTc sulfur colloid will take place the afternoon before your planned next morning surgery, or on the morning of surgery. This is within current standard of care and will be explained by your surgeon.

- There is more than one accepted method to map the lymph system for this procedure. This study will use only 99mTc sulfur colloid in order to standardize comparison. If you choose not to participate, your surgeon may use 99mTc sulfur colloid alone or in combination with blue dye or blue dye alone.

Immediately prior to operation, after you receive anesthesia in the operating room, a small amount of ICG solution will be injected under the skin close to the tumor after disinfection of the breast skin. Movement of the ICG dye under the skin (to your underarm region) will be seen and monitored by the PDE camera (fluorescence imaging). The ICG injection and PDE monitoring is the research-related part of your procedure.

In accordance with standard practice, an incision will be made to remove the fluorescent lymph nodes which uptake ICG and they will be sent for analysis. The lymph nodes that were removed will be tested for radioactivity. Finally, the region will be inspected to determine if there are any residual radioactive nodes, and if so, these nodes will be removed.

The study staff will collect the data from your surgical procedure, along with the following information from your medical record:

- The amount of time for ICG to move from the injection site to the lymph nodes
- size of tumor
- location of tumor
- tumor histology

- breast size
- age and BMI (height and weight)

Your information will be stored in a secure fashion for use as part of this study. This will be recorded in a secure Cleveland Clinic database. The database will not include your name but will include your medical record number and the information listed above. The data will be kept for approximately 2 years, and only the study staff will have access to this database.

The results of this research may be presented at meetings or in publications; however, all personal identifying information will be stripped so that your results cannot be associated with you.

2. ALTERNATIVES

What are the alternatives to participation in the research study?
You can choose not to participate in this research study. If you choose not to participate, this will not impact your current or future care at the Cleveland Clinic.

3. RISKS

What are the risks of participating in the research study?

Risk of indocyanine green (ICG)
Rare anaphylactic reactions (breathing problems) or urticarial (itching) reactions have been reported in patients with or without history of allergy to iodides. If such reactions occur, treatment with the appropriate agents (epinephrine, antihistamines, and corticosteroids) will be given in the operating room.

Confidentiality of Your Data
Your privacy is very important to us and we will use many safety measures to protect your privacy. There is a potential risk of loss of confidentiality of your data. Information from which you may be personally identified will be maintained in a confidential, locked file at the Cleveland Clinic, and will not be disclosed to third parties except with your permission or as may be required by law. There also may be other privacy risks that we have not foreseen.

4. BENEFITS

What are possible benefits of participating in the research?
Information gained from this research study may be used to help others in the future by providing a better diagnostic test for breast cancer.

5. COSTS

Are there any costs to you if you participate in this study?
There are no additional costs to you for participation in this research study. The study related procedures will be provided at no cost to you or your insurance company. The ICG materials will be provided by Mitaka, USA.

The cost for routine tests and services that would normally be performed even if you don't participate in the study will be billed to you or your insurance provider.

6. COMPENSATION

Are there any payments to you if you participate in this study?
You will not be paid for your participation in this research. There are no plans to provide financial compensation to you.

7. RESEARCH RELATED INJURY

What will happen if you are injured as a result of taking part in the research?
If you experience physical injury or illness as a result of participating in this research study, medical care is available at the Cleveland Clinic or elsewhere; however, the Cleveland Clinic has no plans to provide free care or compensation for lost wages. You are not waiving any legal rights by signing this form. Further information about research-related injuries is available from the Office of the Institutional Review Board (216-444-2924).

8. PRIVACY AND CONFIDENTIALITY

Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study
If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to Dr. Stephen R. Grobmyer and the research staff at Cleveland Clinic for the purposes of this research and to Case Western Reserve University for administration.

A note will be placed in your medical record to indicate your participation in this study. In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study such as the Cleveland Clinic Institutional Review Board, and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed (released) to the Food and Drug Administration; the Department of Health and Human Services; the National Cancer Institute (NCI); and Data Safety and Monitoring Boards

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to Stephen R. Grobmyer, MD, Department of General Surgery, Cleveland Clinic, 9500 Euclid Ave, A81, Cleveland,

OH, 44195**.** Your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, information already disclosed outside the Cleveland Clinic cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

The Cleveland Clinic will not use your information collected in this study for another research purpose without your written permission, unless the Cleveland Clinic Institutional Review Board (IRB) assures your privacy and confidentiality is protected. The IRB is a committee whose job it is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This Authorization does not have an expiration date.

9. QUESTIONS

Who do you call if you have any questions or problems?
If you have any questions about the research or develop a research related problem, you should contact Dr Stephen Grobmyer at 216-636-2843 during normal business hours. If you need assistance after 5pm, on holiday or weekend, call the Cleveland Clinic main hospital number at 216-444-2200 and ask for the General Surgery Resident on Call. If you have questions about your rights as a research subject, you should contact the Institutional Review Board at (216) 444-2924.

Where Can I Get More Information?
You may call the National Cancer Institute's Cancer Information Services at:
1-800-4-CANCER (1-800-422-6237) or TTY: 1-800-332-8615

You may also visit the NCI website at http://cancer.gov

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo

US National Institutes of Health (NIH) Clinical Trial Database
A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search the Website at any time.

10. VOLUNTARY PARTICIPATION

What are your rights as a research participant?
Taking part in this study is voluntary. You will be told of any new, relevant information from the research that may affect your health, welfare, or willingness to continue in this study. You may choose not to take part or may leave the study at any time. Withdrawing from the study will not result in any penalty or loss of benefits to which you are entitled.

11. SIGNATURES

Statement of Participant
I have read and have had verbally explained to me the above information and have had all my questions answered to my satisfaction. I understand that my participation is voluntary and that I may stop my participation in the study at any time. Signing this form does not waive any of my legal rights. I understand that a copy of this consent will be provided to me. By signing below, I agree to take part in this research study.

_____
Printed name of Participant

_____ _____
Participant Signature Date

Statement of Person Conducting Informed Consent Discussion
I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____
Printed name of person obtaining consent

_____ _____
Signature of person obtaining consent Date