Proprietary of MD Anderson Cancer Center Approval Date 06/06/2024

Informed Consent/Authorization for Participation in Research

Title of Research Study:	Lymphedema prevention through Immediate LYmphatic reconstruction (LILY) trial
Study Number:	2024-0255
Principal Investigators:	Mark Schaverien, MD, MB, ChB, MSc, MEd, FRCS Melissa Aldrich, MBA, PhD

_____ _____
Participant's Name Medical Record Number

Key Information

The following is a short summary of this study to help you decide whether or not to be a part of this study. More detailed information is listed later on in this form.

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

You are invited to take part in a research study because you will undergo possible immediate lymphatic reconstruction ILR, also termed prophylactic lymphovenous bypass (pLVB) at the time of your axillary lymphadenectomy for breast cancer.

What should I know about a research study?

- Someone will explain this research study to you.
- Whether or not you take part is up to you.
- You can choose not to take part.
- You can agree to take part and later change your mind.
- Your decision will not be held against you.
- You can ask all the questions you want before you decide.

Why is this research being done?

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The lymphatic system is a network of tubes that carry fluid and disease-fighting cells from tissues in the body to the bloodstream. When someone has lymphedema, there is a blockage that leads to swelling because of fluid retention (build-up) in the arm. Some cancer patients get lymphedema, and others do not. Immediate lymphatic reconstruction (ILR), also termed prophylactic lymphovenous bypass (pLVB), is a microsurgical procedure that is used to improve lymphatic fluid movement in patients that undergo axillary lymphadenectomy as part of their breast cancer treatment.

This goal of this research study is to learn if reconstruction of the lymphatic system at the time of axillary lymphadenectomy can improve the flow in patients' lymphatic system and reduce the risk of developing lymphedema.

This is an investigational study. The imaging scans in this study are performed using FDA-approved and commercially available methods. It is investigational to use them to check if the lymphatic system is affected by microsurgery.

How long will the research last and what will I need to do?

You are expected to be in this research study for about 24 months. You will have 5 study visits during this time.

More detailed information about the study procedures can be found under ***"What happens if I agree to be in this research?"***

Is there any way being in this study could be bad for me?

Before choosing to take part in this study, you should discuss with the study team any concerns you may have, including side effects, potential expenses, and time commitment.

More detailed information about the risks of this study can be found under ***"Is there any way being in this study could be bad for me? (Detailed Risks)"***

Will being in this study help me in any way?

It cannot be promised that there will be any benefits to you or others from your taking part in this research. However, it is possible that the imaging on this study could find areas of your body where the lymphatic system is not working properly. Future patients may benefit from what is learned. There may be no benefits for you in this study.

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What happens if I do not want to be in this research?

Participation in research is completely voluntary. You can decide to participate, not participate, or discontinue participation at any time without penalty or loss of your regular benefits.

You may choose to have ILR/ pLVB surgery without taking part in this study. You may choose not to have the procedure at all. These alternative treatments have risks and benefits that may be the same or different than those in this research study. The study doctor can discuss these alternative treatments, including their risks and benefits, with you.

Your alternative to participating in this research study is to not participate.

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Detailed Information

The following is more detailed information about this study in addition to the information listed above.

Who can I talk to if I have questions or concerns?

If you have questions, concerns, or complaints, or think the research has hurt you, talk Dr. Aldrich at 713-248-2642 or Dr. Schaverien at 713-794-1247.

This research has been reviewed and approved by an Institutional Review Board (IRB – an ethics committee that reviews research studies). You may talk to them at 713-792-6477 or IRB_Help@mdanderson.org if:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research participant.
- You want to get information or provide input about this research.

How many people will be in this study?

It is expected about 50 people at MD Anderson will be enrolled in this research study.

What happens if I agree to be in this research?

Screening Tests
Signing this consent form does not mean that you will be able to take part in this study. The following screening tests will help the doctor decide if you are eligible:

- You will be checked for skin conditions at the sites where the dye being used for the imaging scans will be injected.
- If you can become pregnant, you will have a urine pregnancy test. To take part in this study, you must not be pregnant.

The study doctor will discuss the screening test results with you. If the screening tests show that you are not eligible to take part in the study, you will not be enrolled. Other treatment options will be discussed with you.

Up to 50 participants will be enrolled in this study. All will take part at MD Anderson.

Study Procedures
If you agree to take part in this study, your clinic visit timing will be exactly the same time as would ordinarily be scheduled: before surgery, then 6, 12, 18, and 24 months after surgery.

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At each visit:

- Your arm volume will be measured using a non-invasive device called a perometer, and the amount of fluid in your arm will be measured using a non-invasive bioimpedance spectroscopy device.
- You will complete 2 questionnaires either on paper or on a secured iPad about any symptoms that may have in your arm that may be a sign of lymphedema, and any affects these have on your quality of life. It should take about 5-10 minutes to complete all of the questionnaires.
- A picture of your arms may also be taken.
- Blood (about 3 tablespoons) will be drawn for biomarker testing. Biomarkers are found in the blood/tissue and may be related to your reaction to the study drug.
- A member of the study staff will give you 12-20 injections of indocyanine green (ICG) dye into your arms. A red light (similar to a grocery store scanner) will then be pointed at the injected areas so the study staff can see how the dye spreads in your arm.
    - You will wear protective glasses during this.
    - The dye is removed from the body through the liver shortly after the injection.
    - A very small needle is used to help avoid discomfort. If needed, a numbing agent (such as ethyl chloride spray or lidocaine) may be applied to the skin before injection.
- Your vital signs (heart rate, temperature, and blood pressure) will be checked 15 minutes after the first injection and you will be monitored for side effects.

Each study visit should take about 2-3 hours.

Surgery
The surgery (ILR/ pLVB) will be performed exactly as normal as part of your standard care including the scheduling, and no additional procedures will be performed during the surgery that either increase the length of time your surgery takes or change your recovery from surgery. The study doctor will explain the surgery to you and answer all of your questions. You will also sign a separate consent form that explains the surgery in more detail, including its risks.

What are my responsibilities if I take part in this research?

If you take part in this research, there are no additional responsibilities for you outside of the usual standard of care.

What happens if I say yes, but I change my mind later?

You can leave the research at any time; it will not be held against you.

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If you withdraw from this study, you can still choose to be treated at MD Anderson. If you stop being in the research, already collected data may not be removed from the study database. You may be asked whether the study doctor can collect data from your routine medical care. If you agree, this data will be handled the same as research data.

Is there any way being in this study could be bad for me? (Detailed Risks)

While on this study, you are at risk for side effects. These side effects will vary from person to person. The more commonly occurring side effects are listed in this form, as are rare but serious side effects. You should discuss these with the study doctor. You may also want to ask about uncommon side effects that have been observed in small numbers of patients but are not listed in this form. Many side effects go away shortly after the procedure, but in some cases side effects may be serious, long-lasting or permanent, and may even result in hospitalization and/or death.

Tell the study staff about any side effects you may have, even if you do not think they are related to the procedure.

Indocyanine Green Dye Side Effects

It is not well known how often the following side effects of indocyanine green dye may occur.

• headache • itching	• sweating • hives • green stool color	• life-threatening allergic reaction (such as difficulty breathing, low blood pressure, and/or organ failure)

You may experience slight discomfort from the injections. If you choose to use a numbing agent to minimize the discomfort from injections, your skin may become numb, red, or itch for a short time where the cream or liquid is used.

Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or develop an infection with redness and irritation of the vein at the site where blood is drawn. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions.

Questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns about completing the questionnaire, you are encouraged to contact your doctor or the study chair.

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Although every effort will be made to keep study data safe, there is a chance that your personal health information could be lost or stolen, which may result in a **loss of confidentiality**. All study data will be stored in password-protected computers and/or locked file cabinets and will continue to be stored securely after the study.

In addition to these risks, this research may hurt you in ways that are unknown. These may be a minor inconvenience or may be so severe as to cause death.

You will be told about any new information that may affect your health, welfare, or choice to stay in the research.

Pregnancy Related Risks

Taking part in this study can result in risks to an unborn or breastfeeding baby, so you should not become pregnant or breastfeed a baby while on this study. You must use birth control during the study if you are sexually active. Examples of medically accepted birth control are pills, a condom or a diaphragm used with foam, or an intrauterine device (IUD), among others. Talk to the study doctor about what method may work best for you and your partner.

If you are pregnant, you will not be enrolled on this study. If you become pregnant or suspect that you are pregnant, you must tell your doctor right away.

Getting pregnant will result in your removal from this study.

Will it cost anything to be in this study? Will I be paid to be in this study?

There will be no additional cost to you to take part in this study. The ILR/ pLVB surgery itself is not part of the study, and you and/or your insurance provider will be responsible for the cost of this surgery as normal.

Certain tests, procedures, and/or drugs that you may receive as part of this study may be without cost to you because they are for research purposes only. However, your insurance provider and/or you may be financially responsible for the cost of care and treatment of any complications resulting from the research tests, procedures, and/or drugs. Standard medical care that you receive under this research study will be billed to your insurance provider and/or you in the ordinary manner. Before taking part in this study, you may ask about which parts of the research-related care may be provided without charge, which costs your insurance provider may pay for, and which costs may be your responsibility. You may ask that a financial counselor be made available to you to talk about the costs of this study.

Taking part in this study may result in added costs to you (such as transportation, parking, meals, or unpaid leave from work). You may have to pay for medication

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prescribed to treat or prevent side effects, and you may have to visit the clinic/hospital more often than if you were not participating in this study.

If you have insurance, talk to your insurance provider and make sure that you understand what your insurance pays for and what it does not pay for if you take part in this study. Also, find out if you need approval from your plan before you can take part in the study.

You may ask that a financial counselor be made available to you to talk about the costs of this study.

You will receive up to $250 ($50 for each study visit) in gift cards for your time and effort if you complete all 5 study visits.

What happens to the information collected for the research?

Efforts will be made to limit the use and disclosure of your personal information, including research study and medical records, to people who need to review this information. Complete secrecy cannot be promised. Organizations that may inspect and copy your information include the IRB and other representatives of this organization.

Any personal information that could identify you will be removed or changed before data are shared with other researchers or results are made public.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.

There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring United States federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the federal Food and Drug Administration (FDA). The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.

Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

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The sponsor, monitors, auditors, the IRB, and the Food and Drug Administration will be granted direct access to your medical records to conduct and oversee the research. By signing this document, you are authorizing this access. The results of this research may be published. However, your name and other identifying information will be kept confidential.

Federal law provides additional protections of your medical records and related health information. These are described below.

Will my data or samples be used for future research?

Your personal information and/or samples are being collected as part of this study. These data and/or samples may be used by researchers at MD Anderson or shared with other researchers and/or institutions for use in future research.

In some cases, all of your identifying information may not be removed before your data or research samples are used for future research. If future research is performed at MD Anderson, the researchers must get approval from the MD Anderson IRB before your data and/or research samples can be used. At that time, the IRB will decide whether or not further permission from you is required. If this research is not performed at MD Anderson, MD Anderson will not have oversight of any data and/or samples.

If identifiers are removed from your identifiable private information or identifiable samples that are collected during this research, that information or those samples could be used for future research studies or shared with another researcher for future research studies without your additional informed consent.

Some of your specimens and genetic and/or health information might also be placed into one or more external publicly-accessible scientific databases. Your name and other information that could directly identify you (such as your address or social security number) will never be placed into these external databases. A researcher who wants to study information from these databases must have an approved study and work with the group overseeing the database to obtain the information.

Can I be removed from the research study without my permission?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include if you enroll on the study but do not undergo any surgery, if you do not attend the study evaluations after surgery, or if you develop recurrence and require chemotherapy or develop serious illness.

What happens if I get hurt from being in this study?

If you get sick or hurt and it is related to your participation in this study, you will be given care at MD Anderson (if you are at the clinic when you are sick or hurt). If you get hurt or sick and you are not at the clinic (for example, you are at home or at another doctor's office):

- call your personal doctor right away (or in an emergency, call 911)
- tell your personal doctor or ER staff that you are in this study (try to give them a copy of this consent form or show them your participant card)
- call Dr. Aldrich at 713-248-2642 or Dr. Schaverien at 713-794-1247; or call 713-792-2121 (24 hours)

You will not be reimbursed for expenses or compensated financially by MD Anderson for this injury. Costs of treatment received because you were hurt or sick will be billed to you or your insurance company. No other form of payment is available.

You may also contact the MD Anderson IRB at 713-792-6477 with questions about study-related injuries. By signing this consent form, you are not giving up any of your legal rights.

What else do I need to know?

This research is being funded by National Institutes of Health (NIH)/ National Cancer Institute (NCI).

Dr. John C. Rasmussen (Study Collaborator) and Dr. Eva M. Sevick-Muraca are inventors of the imaging system that will be used in this study, and a patent has been issued for the imaging system. As such, Drs. Rasmussen and Sevick-Muraca could financially benefit from the outcome of this study in the future.

MD Anderson may benefit from your participation and/or what is learned in this study.

Your information and samples (both identifiable and de-identified) may be used to create products or to deliver services, including some that may be sold and/or make money for others. If this happens, there are no plans to tell you, or to pay you, or to give any compensation to you or your family.

Most tests done on samples in research studies are only for research and have no clear meaning for health care. If the research with your identifiable information or samples gives results that do have meaning for your health, the researchers will not contact you to let you know what they have found. If the researchers return genetic test results to you, it may be because they think you could have a health risk and want to recommend that the test should be re-done by a certified clinical laboratory to check the results. If this happens, then you may want to get a second test from a certified clinical laboratory,

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consult your own doctor, or get professional genetic counseling. You may have to pay for those additional services yourself.

This research study involves testing of small pieces of the RNA (ribonucleic acid) and the DNA (deoxyribonucleic acid) of your immune cells. We will not be performing whole genome sequencing and we will NOT look at RNA or DNA parts that can be used to identify you or family members.

Authorization for Use and Disclosure of Protected Health Information (PHI):

A. During the course of this study, MD Anderson will be collecting and using your PHI, including identifying information, information from your medical record, and study results. For legal, ethical, research, and safety-related reasons, your doctor and the research team may share your PHI with:
   - Federal agencies that require reporting of clinical study data (such as the FDA, National Cancer Institute [NCI], and OHRP)
   - The IRB and officials of MD Anderson
   - The NIH/NCI, who is a sponsor or supporter of this study, and/or any future sponsors/supporters of the study, and/or licensees of the study technology
   - Study monitors and auditors who verify the accuracy of the information
   - Individuals who put all the study information together in report form

   Study sponsors and/or supporters receive limited amounts of PHI. They may also view additional PHI in study records during the monitoring process. MD Anderson's contracts require sponsors/supporters to protect this information and limit how they may use it.

   The results of this research may be published in scientific journals or presented at medical meetings, but your identity will not be disclosed.

B. Signing this consent and authorization form is optional but you cannot take part in this study or receive study-related treatment if you do not agree and sign.

C. MD Anderson will do its best to protect the privacy of your records, but it is possible that once information is shared with people listed on this form, it may be released to others. If this happens, your information may no longer be protected by federal law.

D. The permission to use your PHI will continue indefinitely unless you withdraw your authorization in writing. Instructions on how to do this can be found in the MD Anderson Notice of Privacy Practices (NPP) or you may contact the Chief Privacy Officer at 713-745-6636. If you withdraw your authorization, you will be removed from the study and the data collected about you up to that point can be used and

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included in data analysis. However, no further information about you will be collected.

E. 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.

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CONSENT/AUTHORIZATION

I understand the information in this consent form. I have had a chance to read the consent form for this study, or have had it read to me. I have had a chance to think about it, ask questions, and talk about it with others as needed. I give the study chair permission to enroll me on this study. By signing this consent form, I am not giving up any of my legal rights. I will be given a signed copy of this consent document.

_____ _____
SIGNATURE OF PARTICIPANT DATE

_____
PRINTED NAME OF PARTICIPANT

WITNESS TO CONSENT

I was present during the explanation of the research to be performed under this protocol.

_____ _____
SIGNATURE OF WITNESS TO THE VERBAL CONSENT PRESENTATION (OTHER THAN PHYSICIAN OR STUDY CHAIR) DATE

A witness signature is only required for non-English speakers utilizing the short form consent process (VTPS) and patients who are illiterate.

_____
PRINTED NAME OF WITNESS TO THE VERBAL CONSENT

PERSON OBTAINING CONSENT

I have discussed this research study with the participant and/or his or her authorized representative, using language that is understandable and appropriate. I believe that I have fully informed this participant of the nature of this study and its possible benefits and risks and that the participant understood this explanation.

_____ _____
PERSON OBTAINING CONSENT DATE

_____
PRINTED NAME OF PERSON OBTAINING CONSENT

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TRANSLATOR

I have translated the above informed consent as written (without additions or subtractions) into_____and assisted the people
(Name of Language)
obtaining and providing consent by translating all questions and responses during the consent process for this participant.

_____	_____	_____
NAME OF TRANSLATOR	SIGNATURE OF TRANSLATOR	DATE

☐ Please check here if the translator was a member of the research team. (If checked, a witness, other than the translator, must sign the witness line.)