Dartmouth-Hitchcock

n to Take Part in a Human Research Study

Title of research study: A pilot study to evaluate single dose indocyanine green 24 hours prior to operative treatment of orthopaedic infection.

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Investigator: ***Ida Leah Gitajn, MD***

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.

We know that when bone has poor blood flow there is no way for antibiotics or immune cells to get to the bone to help clear the infection. Because of this, a critical part of treating your infection is surgically removing the bone and tissue that has poor blood flow (perfusion). However, there are no existing tools or methods that can help surgeons determine whether the blood flow to bone is adequate or not. This study investigates a specific imaging method to determine if it provides surgeons with information on bone blood flow that can help them to more accurately perform surgery for people with infections such as yours.

There is no direct benefit to you as a patient. Imaging data will be collected during your surgery and this imaging data will not be used to affect your treatment in any way. We want to compare the imaging during the surgery with information about the surgery and your health after the surgery. Generally, the risks and discomforts are minor, but rare instances of severe life-threatening allergy has occurred with the use of the contrast agent in this study.

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

We invite you to take part in a research study because you will be treated operatively (surgery to remove poorly perfused bone and tissue) for your orthopaedic infection as part of your care.

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.

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Why is this research being done?

The purpose of this study is to determine whether the use of indocyanine green (ICG) in combination with a fluorescence imaging system (Spy Elite or Zeiss Pentero 800) can provide surgeons with information about bone health or bone blood flow. This will help surgeons better understand the healing potential of bone and relative risk of complication. This is important to help surgeons select the most appropriate treatment for orthopaedic infections. Your surgery will not be affected by this research in any way. The imaging data will not be used to guide your surgery because we do not yet know if this information is helpful or accurate.

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

We expect that you will be in this research study for 6 months.

We will collect imaging data during your surgery. We expect to collect follow-up data about how you are doing over the course of 6 months following your surgery.

Approximately 24 hours prior to your surgery you will be administered the fluorescent agent (indocyanine green or ICG) thru an IV (intravenous) line. The IV is used to give dispense medicine into your blood stream and can also be used to draw blood if blood tests are needed. You will have an IV whether or not you participate in this study. On the day of your surgery, the surgeon will use a imaging device (SPY Elite® System or Zeiss Pentero 800) to assess the blood flow to, or health of, your bone and soft tissues. The assessment is not painful, and you will be under anesthesia while this takes place. The imaging device will take pictures that show where the ICG is in your bone and soft tissues.

There will be up to 10 minutes of additional anesthesia time needed for this study.

We will follow your recovery either at your normal clinic visits or over the phone for six months after your initial infection surgery.

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

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

The risks of this study are considered very small since ICG is FDA approved for human use in blood flow imaging for ophthalmology and cardiology applications and is given routinely to patients in these clinical settings, and the device is FDA cleared for imaging use. The research team will discuss possible problems and the chances that they will happen. Unknown problems may happen. You should report any problems to your doctor or the director of this study**: I. Leah Gitajn, MD at 603-650-5133**

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)"***

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Will being in this study help me in any way?

There are no benefits to you from your taking part in this research. We cannot promise any benefits to others from your taking part in this research. However, future patients may benefit from knowledge gained from the study and may save future patients from unnecessarily high risk from infection.

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

Participation in research is completely voluntary. You can decide to participate or not to participate.

Your alternative to participating in this research study is to not participate. Your treatment will be identical to what would happen if you decide not to participate.

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

Who can I talk to?

If you have questions, concerns, or complaints, or think the research has hurt you, talk to the research team at Dartmouth-Hitchcock Medical Center during normal business hours and they will be able to contact Dr. Gitajn for you. If Dr. Gitajn is not available, other members in the Orthopaedics Department at Dartmouth-Hitchcock will be available to answer your questions during normal business hours.

This research has been reviewed and approved by an Institutional Review Board ("IRB"). You may talk to them at (603) 650-1846 or irb@hitchcock.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 subject.
- You want to get information or provide input about this research.

How many people will be in this study?

We expect about 20 people here, at DHMC, will be in this research study. This study is not currently enrolling at any other study sites.

What happens if I say yes, I want to be in this research study?

The following activities will be done for research purposes only:

- Indocyanine Green (ICG) will be administered to you through either a central or peripheral intravenous (IV) line by a qualified member of your care team approximately 24 hours prior to your surgery. You may already have one or both of these types of IV lines in place as they are the IVs used to administer fluids and medications, such as sterile fluids. If you do not already have an IV, a qualified member of the care tem will insert one. Hospital staff will monitor your health and safety both during and after administering the ICG. If an IV is inserted to give you the ICG while you are an outpatient the IV will be removed before you leave the office.

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- Once you enter the operating room and after you are under anesthesia a trained member of the research team will image the blood flow of your infection using the SPY Elite ® Device or the Zeiss Pentero 800 a minimum of two times.
- Through-out the entire surgery and imaging process members of the operating room staff will conduct a focused examination to ensure your safety.

Indocyanine Green (ICG) is a dye, which the body quickly eliminates. It has a normal biological half-life of 2 ½ to 3 minutes. This means that within the first three minutes of injection into your IV, approximately half of the ICG administered will have been processed and eliminated by the body 3 minutes after it is given. You will be receiving as single, IV injection of ICG, 24 hours prior to your surgery.

Past studies have shown us that infected tissue can be hard to distinguish from healthy tissue when ICG is given immediately before optical imaging. Injection of ICG at an earlier time point should allow surgeons to better distinguish infected tissue from healthy tissue, as the ICG will have a better opportunity to permeate the infected tissue while it will have been expelled from the healthy tissue.

At all times during imaging and surgery, medical staff and your surgeon will monitor you closely to ensure your safety and wellbeing, and they will continue to monitor you for as long as necessary once imaging is completed, with focused examinations adding approximately 10 minutes to the length of your surgery.

We will follow your recovery for a total of 6 months after your injury. These follow-ups will occur either during your regularly scheduled clinic visits or over the phone.

Neither you nor your insurance company will be billed for the ICG given pre operatively, images taken on the SPY or Zeiss Pentero 800 imaging system, or any added anesthesia time that results from taking part in this study. There is no additional cost to you in association with participating in this study.

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

If you take part in this research, you will be responsible to

Your responsibilities as a person taking part in this study

(1) Be aware it is important for your safety that the research team knows about your medical history and current condition.
(2) Notify the research team in advance if you plan to undergo any other medical treatment during this study or are taking or plan to start taking any medications.
(3) Notify the research team immediately if you suffer any injury or unexpected reaction to the study medication or procedures.
(4) Seek treatment with the help of the research team if you suffer any injury or unexpected reaction to the study medication or procedures.
(5) Make reasonable efforts to follow the instructions of the research team.

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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.

If you stop being in the research, already collected data may not be removed from the study database.

You will be asked whether the investigator can collect data from your routine medical care. If you agree, this data will be handled the same as research data as explained in this form.

Is there a possibility being in this study could be bad for me or harm me? (Detailed Risks)

The risks of this study are considered very small since ICG is FDA approved for human use in blood flow imaging for ophthalmology and cardiology applications and is given routinely to patients in these clinical settings, and the device is FDA cleared for imaging use. The research team will discuss possible problems and the chances that they will happen. Unknown problems may happen. You should report any problems to your doctor or the director of this study**: Leah Gitajn, MD 603-650-5133**

Risks/Side Effects of ICG

- ICG does contain sodium iodide and patients with a history of allergy to iodides will be excluded from taking part in this study. The following reactions are rare but have been reported in patients both with and without a history of allergy to iodides:
    - Anaphylactic reaction- a severe allergic reaction that can be life-threatening, includes itching, constriction of the airway, and low blood pressure.
    - Urticarial reactions (hives and itching).
- Other side effects are very rare, but may include symptoms such as nausea, vomiting, hives, increased heart rate in subjects with particular sensitivity to the dye.
- Because this drug is given by IV, there may be some pain or mild bruising from the IV.
- Reported rates of mild reaction such as nausea are 1/670 individuals (or 0.15%); reported rates of moderate reaction such as urticarial reactions (hives and itching) are 1/500 individuals (or 0.2%) and risk of severe adverse reaction such as anaphylactic reaction is 1/2,000 individuals (or 0.05%)

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.

Because imaging will take place in the operating room, participating in this study may increase the amount of time spent under general anesthesia in the operating room. On average, this will take no more than 10 minutes. The risks associated with this minimal increase in anesthesia time is very low, as the major anesthesia risks occur during intubation (while you are being put to sleep) or extubation (while you are waking up) and not during sustained anesthesia. Furthermore, you are monitored at all time during the surgical procedure by the anesthesia team.

The risks of ICG to a pregnancy are unknown. Pregnant women or women who are breastfeeding may not take part in this research study. Women of childbearing potential who have not received a pregnancy test during their orthopaedic infection admission will receive a urine pregnancy test as part

of their standard of care pre-operative testing, prior to administration of the ICG. This pregnancy test will not be paid for by the study, but will be charged to your health care insurance company.

You and your insurance company will be charged for the health care services that you would ordinarily be responsible to pay, including any preoperative, standard of care tests. In some cases, insurance will not pay for services ordinarily covered because these services were performed in a research study. You should check with your insurance to see what services will be covered by your insurance and what you will be responsible to pay.

If you are injured or become ill as a result of research procedures or have an unforeseen reaction to the ICG injection, you will be provided with medical treatment but the following organizations do not plan to pay for this treatment.

- Mary Hitchcock Memorial Hospital
- Dartmouth-Hitchcock Clinic
- Dartmouth-Hitchcock Medical Center
- Trustees of Dartmouth College

If you have any questions or concerns about the legal responsibility of these organizations, please call the Mary Hitchcock Memorial Hospital Office of Risk Management at (603) 653-1250 during normal business hours.

If you agree to take part in this study and you sign this consent form, you are not giving up any of your legal rights.

What happens to the information collected for the research?

The information collected for this study includes:

- Demographic information including but not limited to; age, sex, gender, race, pre-existing conditions and health status
- Injury related information including but not limited to; how the injury occurred, previous treatment for the injury and infection (including medications), operative reports, culture information and injury / infection outcomes
- Blood flow video of your infected tissue during your surgery

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

Your information that is collected as part of this research will not be used or distributed for future research studies, even if all of your identifiers are removed.

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Federal law provides additional protections of your medical records and related health information. By signing this form, you allow the research team to use your health information and give it to others involved in the research. The research team includes the study director plus others working on this study at Dartmouth-Hitchcock Medical Center and elsewhere. You also permit any health care provider holding health information needed for this study to give copies of your information to the research team. Study 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. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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.

The information collected for this study may be used by researchers or officials of the following institutions.

- Dartmouth College
- Mary Hitchcock Memorial Hospital
- Dartmouth-Hitchcock Clinic
- Dartmouth-Hitchcock Medical Center
- The Dartmouth-Hitchcock Health Institutional Review Board (D-HH IRB)

In order to conduct this study, researchers need to use your health care information. This data is called Protected Health Information ("PHI"). PHI is protected by federal privacy laws (HIPAA). By signing this consent form, you give your permission to have your PHI collected, used and disclosed for purposes of this study. There is no intention to disclose your PHI to others outside of the study. There are protections in place to keep your PHI and research data confidential. However, HIPAA requires notification so you are aware that if your PHI is disclosed to others, it may no longer be protected by federal privacy laws.

If you do not allow (authorize) the collection, use, and disclosure of your protected health information (PHI) for this study, you cannot take part in this study. You may revoke your authorization; data that has already been collected will not be removed from the study database and will continue to be used. To revoke your authorization, please contact the researcher in writing. You may ask the research team to help you put your wishes in writing.

No publication or public presentation about the research described above will reveal your identity without another authorization from you.

Identifiable data collected for this study will be used for research purposes which are determined to be reasonable and in line with expectations by a review committee.

Once data collected for this research study is no longer identifiable, the data may be used or disclosed for other purposes.

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Your permission to use your health information for this study will not end until the study is completed. During this study, you and others who take part in the study may not have access to the study data. You may ask for study data once the study is over. You have a right to receive a copy of the information in your medical record at any time.

Can I be removed from the research without my OK?

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;

- Study imaging is not completed for any reason
- You withdraw consent
- You have an occurrence of a significant clinical event that precludes imaging

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

What else do I need to know?

Your information (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.

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Signature Block for Capable Adult

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

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Signature Block for Adult Unable to Consent

Your signature documents your permission for the named subject to take part in this research.

Printed name of subject	
Signature of legally authorized representative	Date
Printed name of legally authorized representative	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	