Informed Consent Cover Page for FDAAA consent posting:

Official Title:	Exploring Near Infrared Spectroscopy (NIRS) Technologies for Assessment of Muscle Physiology, Tissue Oxygenation, and Blood Flow in Patients With Sickle Cell Disease (SCD)
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PRINCIPAL INVESTIGATOR: Swee Lay Thein, M.D.

STUDY TITLE: Exploring Near Infrared Spectroscopy (NIRS) technologies for assessment of muscle physiology, tissue oxygenation, and blood flow in patients with Sickle Cell Disease (SCD)

STUDY SITE: National Heart, Lung and Blood Institute

Cohort: affected and healthy subjects

Consent Version: 06-25-2024

WHO DO YOU CONTACT ABOUT THIS STUDY?

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Study Coordinator, Dianna Lovins, RN, MSN; Building 10-CRC, Room 3NE-3-2472 Telephone: 240-552-0245; E-mail: dianna.lovins@nih.gov

KEY INFORMATION ABOUT THIS RESEARCH

This consent form describes a research study and is designed to help you decide if you would like to be a part of the research study.

You are being asked to take part in a research study at the National Institutes of Health (NIH). This section provides the information we believe is most helpful and important to you in making your decision about participating in this study. Additional information that may help you make a decision can be found in other sections of the document. Taking part in research at the NIH is your choice.

In this study we will look at the role of near infrared spectroscopy (NIRS) technologies as a monitoring tool in patients with sickle cell disease (SCD). This test measures oxygen levels, blood flow, and the make-up of skin and muscle. The study will be performed in the outpatient setting. Ethnically-matched healthy participants without sickle cell trait will be recruited to participate in baseline NIRS testing and serve as controls. If you choose to participate in this study, we will be assessing cardiovascular health, by including the six-minute walk test (6MWT), transthoracic echocardiography (TTE), and blood work.

You are invited to take part in this study because you have SCD or you are a Healthy Volunteer . You may also be followed on other NHLBI protocols. If you are eligible for the study, you will be placed in one of the two above mentioned groups (SCD or Healthy Volunteer).

Your participation in this study can last up to a maximum of 120 days. An initial visit will involve review of past medical history, a physical examination and blood samples which are used to determine eligibility. If eligible to proceed, you would return for an additional visit. This visit will include obtaining vital signs, blood samples, TTE, 6MWT, vital signs, oximetry, height, weight and NIRS measurement. You may be invited to return for a maximum of 4 additional visits to repeat this testing, which are optional.

The general risks associated with this study pertain to the following: blood draw, NIRS and 6MWT testing. The risks associated with the blood draws are minimal and involve pain at the site of blood withdrawal, mild bruising at the site and potential for local infection at the site. With NIRS you may experience temporary discomfort related to the cuff squeezing, where we place probes on the skin surface, and from holding your breath (for less than a minute). 6MWT is a low-risk medical evaluation. However in very rare instances, risks such as chest pain, shortness of breath, leg cramps, staggering, sweating, and/or pale or ashen appearance may occur.

You will be offered compensation for your time and inconvenience for participation and completion of the research study. In addition, reimbursement for travel will be provided under this protocol.

There is no immediate benefit to you by taking part in this study, but it could help others in the future.

The remaining document will now describe more about the research study. This information should be considered before you make your choice. Members of the study team will talk with you about the information described in this document. Some people have personal, religious, or ethical beliefs that may limit the kinds of medical or research treatments they would want to receive (such as blood transfusions). Take the time needed to ask any questions and discuss this study with NIH staff, and with your family, friends, and personal health care providers.

If the individual being asked to participate in this research study is not able to give consent for themselves, you, as the Legally Authorized Representative, will be their decision-maker and you are being asked to give permission for this person to be in this study. For the remainder of this document, the term "you" refers to you as the decision-maker and/or the individual being asked to participate in this research.

IT IS YOUR CHOICE TO TAKE PART IN THE STUDY

You may choose not to take part in this study for any reason. If you join this study, you may change your mind and stop participating in the study at any time and for any reason. In either case, you will not lose any benefits to which you are otherwise entitled. However, to be seen at the NIH, you must be taking part in a study or are being considered for a study. If you do choose to leave the study, please inform your study team to ensure a safe withdrawal from the research.

WHY IS THIS STUDY BEING DONE?

You are invited to take part in this study because you identify as belonging to one of the following categories: SCD or health volunteer. The purpose of this research is to study the role of near infrared spectroscopy (NIRS) technologies as a monitoring tool for measuring oxygen levels, blood flow, and the make-up of skin and muscle in patients with SCD. In this study, we will compare NIRS measurements and clinical measures of cardiovascular function in those with and out without SCD. **You will not receive experimental treatment under this protocol.**

WHAT WILL HAPPEN DURING THE STUDY?

A member of the study team will tell you about the study and ask you some questions to determine if you may be eligible for this study. If you decide to take part in this study, you will be asked to sign this consent form and participate in a screening visit in our outpatient clinic.

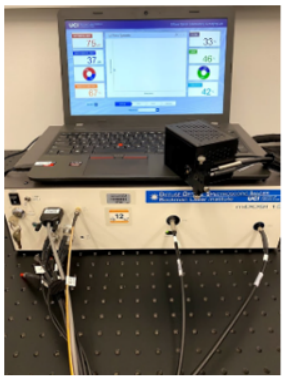
If you have had any of the required clinical tests done at the Clinical Center within 30 days of screening/enrollment ("Consent Visit"), we may use those results. This is done in an effort to minimize the amount of time spent and/or blood volume drawn to participate in this study.

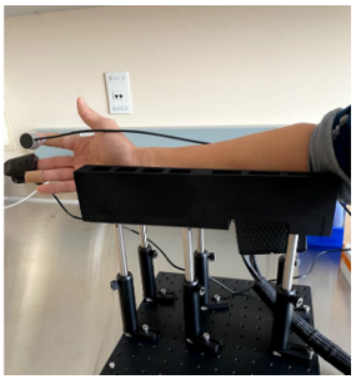
- **Visit #1: Consent (Screening) Visit**

  - Sign consent
  - Take down your medical history (will ask about your past health condition)
  - Perform a physical examination (like taking your vital signs and checking the general health of your body)
  - Review your medical records
  - Collect one teaspoon of blood)

Visit #2: Baseline Visit

- Vital signs
- Pulse Oximetry
- Obtain height and weight measurements
- TTE (Echocardiogram)
- 6MWT
- Collect 1 tablespoon of blood
- Do the NIRS testing as show in in the picture below:





With NIRS testing, probes will be placed on your skin to measure oxygen levels, blood flow, and the make-up of your skin and muscle. A blood pressure cuff will be placed on your arm. The cuff will be filled with air to briefly restrict the blood flow (for up to 5 minutes) in your arm and then released. You may also be asked to breathe at a certain rate or hold your breath for as long as you can during periodic measurements.

For each Follow Up Visit at the NIH:

- Vital signs
- Pulse oximetry
- Weight measurement
- Collect 1 tablespoon of blood
- Repeat NIRS testing, as described above.

HOW LONG WILL THE STUDY TAKE?

If you agree to take part in this study, your participation is expected to last for about 120 days. After your first initial visit, you will have one follow up visit. Each visit for the NIRS measurements will last no more than 1 hour, but generally about 45 minutes. You may however, be asked to return for a maximum of 4 additional visits for repeat testing, which is optional.

HOW MANY PEOPLE WILL PARTICIPATE IN THIS STUDY?

We plan to have approximately 40 people participate in this study at the NIH.
20 participants with SCD and 20 without SCD or trait (healthy participants).

WHAT ARE THE RISKS AND DISCOMFORTS OF BEING IN THE STUDY?

a) Blood collection: There may be some discomfort on your arm when we collect your blood with a needle. There is a small chance that you will get a bruise, feel lightheaded, faint, or have an infection at the place where you were pricked.

b) Near-infrared spectroscopy (NIRS): You may experience temporary discomfort related to the cuff squeezing, where we place probes, and from holding your breath.

c) 6 minute walk test (6MWT): 6MWT is a low-risk medical evaluation. However in very rare instances, risks such as chest pain, shortness of breath, leg cramps, staggering, sweating, and/or pale or ashen appearance may occur. You will be monitored during this test, which will be stopped immediately should there be any signs of adverse effects.

d) Transthoracic Echocardiography (TTE): There are no known risks related to echocardiogram.

e) Oximetry: There are no known risks related to oximetry.

f) Physical Examination: There are no known risks related to physical examination.

What are the risks related to pregnancy?

There are no risks related to pregnancy. However, because pregnancy changes the blood flow and may affect oxygen saturation in tissues, we cannot collect information for this study while you are pregnant. If you do become pregnant during the study period, you are requested to notify us. A pregnancy test will be done at screening, baseline, and any follow-up study visits.

WHAT ARE THE BENEFITS OF BEING IN THE STUDY?

You will not benefit from being in this study.

Are there any potential benefits to others that might result from the study?

There are no direct benefits for participating in this study. However, we believe that information obtained from this study will be important for better understanding the natural history of sickle cell disease.

WHAT OTHER OPTIONS ARE THERE FOR YOU?

You do not have to participate in this study if you do not want to. You may withdraw from this study at any time. If you decide to withdraw from the study, we would like to keep your test results to properly analyze this research study. If you have concerns about this, please speak with members of your research team.

DISCUSSION OF FINDINGS

New information about the study

If we find out any new information that may affect your choice to participate in this study, we will get in touch with you to explain what we have learned. This may be information we have learned while doing this study here at the NIH or information we have learned from other scientists doing similar research in other places.

Return of research results

You will be provided with the results of the standard clinical labs, but the results of our research studies will not be provided to you or your referring doctor.

EARLY WITHDRAWAL FROM THE STUDY

Discontinuing Participation:

- If you decide to stop participating in this study, you may request this by either informing the investigators or by writing to the research team to the address at the end of this consent (under Problems and Questions on last page of consent). You will not be asked for further

information or samples.
- If you are unwilling or unable to undergo the tests or procedures in this study.
- If we are unable to contact you or reach you.
- If you become pregnant.
- When the study has completed
- Death.

STORAGE, SHARING AND FUTURE RESEARCH USING YOUR SPECIMENS AND DATA

Will your specimens or data be saved for use in other research studies?

As part of this study, we are obtaining data from you. We will remove all the identifiers, such as your name, date of birth, address, or medical record number and label your data with a code so that you cannot easily be identified. However, the code will be linked through a key to information that can identify you. We plan to store and use these data for studies other than the ones described in this consent form that are going on right now, as well as studies that may be conducted in the future. These studies may provide additional information that will be helpful in understanding sickle cell disease, or other diseases or conditions. This could include studies to develop other research tests, treatments, drugs, or devices, that may lead to the development of a commercial product by the NIH and/or its research or commercial partners. There are no plans to provide financial compensation to you if this happens. Also, it is unlikely that we will learn anything from these studies that may directly benefit you.

I give permission for my identifiable data to be stored and used for future research as described above.

_____ Yes _____ No

Initials Initials

Will your specimens or data be shared for use in other research studies?

We may share your data with other researchers. The other researchers may be doing studies in similar areas to this study or in other unrelated areas. These researchers may be at NIH, other research centers and institutions, or at commercial entities. If we do share your specimens or data, we will know that the specimens and data came from you. However, the other researchers will not know that they came from you (i.e., they will be de-identified).

I give permission for my **de-identified** specimens and data to be shared with and used by other researchers for future studies.

_____ Yes _____ No

Initials Initials

If you change your mind and do not want us to store and use your data for future research, you should contact the research team member identified at the top of this document. We will do our best to comply with your request but cannot guarantee that we will always be able to destroy your data. For example, if some research with your data has already been completed, the information from that research may still be used. Also, for example, if the data have been shared already with other researchers, it might not be possible to withdraw them.

In addition to the planned use and sharing described above, we might remove all identifiers and codes from your data and use or share them with other researchers for future research at the NIH or other places. When we or the other researchers access your anonymized data, there will be no way to link the specimens or data back to you. We will not contact you to ask your permission or otherwise inform you before we do this. We might do this even if you answered "no" to the above questions. If we do this, we would not be able to remove your specimens or data to prevent their use in future research studies, even if you asked, because we will not be able to tell which are your specimens or data.

NIH policies require that your clinical and other study data be placed in an internal NIH database that is accessible to other NIH researchers for future research. Usually, these researchers will not have access to any of your identifiers, such as your name, date of birth, address, or medical record number; and your data will be labeled with only a code. We cannot offer you a choice of whether your data to be placed in this database or not. If you do not wish to have your data placed in this database, you should not enroll in this study.

How long will your specimens and data be stored by the NIH?

Your data may be stored by the NIH indefinitely.

Risks of storage and sharing of specimens and data

When we store your data, we take precautions to protect your information from others that should not have access to it. When we share your data, we will do everything we can to protect your identity, for example, when appropriate, we remove information that can identify you. Even with the safeguards we put in place, we cannot guarantee that your identity will never become known or someone may gain unauthorized access to your information. New methods may be created in the future that could make it possible to re-identify your data.

COMPENSATION, REIMBURSEMENT, AND PAYMENT

Will you receive compensation for participation in the study?

Some NIH Clinical Center studies offer compensation for participation in research. The amount of compensation, if any, is guided by NIH policies and guidelines.

You will be offered compensation for your time and inconvenience for participation and completion of the research study.

Upon completion of the research study, you may be compensated based on the table below.

Procedure(s)/Test(s)	IU	Amount	Frequency	Total amount
NIRS testing	4	$40	Up to 5	Up to $200

Medical History and Physical Exam	**2.5**	**$25**	**1**	**$25**
Blood Draw	**1**	**$10**	**Up to 5**	**Up to $50**
Six-minute walk test	**2**	**$20**	**1**	**$20**
Echocardiogram	**3**	**$30**	**1**	**$30**
OUTPATIENT- 1st HOUR	**NA**	**$20**	**Up to 5**	**Up to $100**
OUTPATIENT TIME- Not to Exceed More than 4 Hours	**3**	**$30**	**1**	**$30**
TOTAL				**Up to $455**

If you are unable to finish the study, you will receive compensation for the parts you completed. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

With few exceptions, study compensation is considered taxable income that is reportable to the Internal Revenue Service (IRS). A "Form 1099-Other Income" will be sent to you if your total payments for research participation are $600 or more in a calendar year. If you have unpaid debt to the federal government, please be aware that some or all of your compensation may be automatically reduced to repay that debt on your behalf.

Will you receive reimbursement or direct payment by NIH as part of your participation?

You may receive mile reimbursement for driving to the NIH Clinical Center for study visits or be provided a taxi. If you are traveling long distance (i.e., outside the DMV area) the study team may arrange alternative transportation at no cost to you.

Will taking part in this research study cost you anything?

NIH does not bill health insurance companies or participants for any research or related clinical care that you receive at the NIH Clinical Center.

- You will receive study care at no charge to you. This may include surgery, medicines, laboratory testing, x-rays or scans done at the Clinical Center, National Institutes of Health (NIH), or arranged for you by the research team to be done outside the Clinical Center, NIH if the study related treatment is not available at the NIH.
- There are limited funds available to cover the cost of some tests and procedures performed outside the Clinical Center, NIH. You may have to pay for these costs if they are not covered by your insurance company.
- Once you have completed taking part in the study, medical care will no longer be provided by the Clinical Center, NIH.

CLINICAL TRIAL REGISTRATION AND RESULTS REPORTING

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.

CONFIDENTIALITY PROTECTIONS PROVIDED IN THIS STUDY

You will be asked to supply your social security number in order to be compensated for participation, but your social security number is not retained by the protocol study team after it is entered in the NIH payment system. You can participate in research but cannot be compensated without supplying a social security number.

Will your medical information be kept private?

We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- The NIH and other government groups, (For example, the Food and Drug Administration (FDA) to help keep research safe.)
- National Institutes of Health Intramural Institutional Review Board

NIH and researchers doing this study follow special laws and policies to keep your information as private as possible. However, your identity and information about being in this study may accidentally be seen by others.

In most cases, NIH will not share any identifiable information about you unless you say it is okay in writing. More information about sharing your information is below.

Information gathered for this study is protected under a Certificate of Confidentiality and the Privacy Act.

Certificate of Confidentiality

To help us protect your privacy, NIH has a Certificate of Confidentiality (Certificate). With this Certificate, researchers may not release or use information about you except in certain cases.

NIH researchers must not share information that may identify you in any legal proceedings, such as if a court requests it with a subpoena.

The Certificate does not protect your information when it:

1. is shared with people connected with the research. For example, information may be used for internal reviews by NIH; or

2. is required by law to be disclosed. For example, information may be shared with the FDA or with public health agencies.

3. is for other research if allowed by other regulations;

4. is shared with your consent.

Researchers may provide your information when you say it is okay. The Certificate does not keep you from sharing your own information.

The Certificate will not prevent telling authorities about harm to yourself or others. Examples are child abuse and neglect.

Privacy Act

The Privacy Act helps keep your NIH medical information confidential. In some cases, it is different from the Certificate. Sometimes the Privacy Act allows sharing your information without your permission. An example is if Congress requests it.

Information may also be shared for some research. It can be given to some federal and state agencies. It can be used for HIV partner notification, or for infectious disease, abuse, or neglect reports. It may be shared with tumor registries, for quality and medical reviews. It may also be shared if NIH is involved in a lawsuit. However, NIH will only release medical record information if allowed by both the Certificate and the Privacy Act.

RESEARCH-RELATED INJURIES

The NIH Clinical Center will provide short-term medical care for any injury resulting from your participation in research here. In general, no long-term medical care or financial compensation for research-related injuries will be provided by the NIH, the NIH Clinical Center, or the Federal Government. However, you have the right to pursue legal remedy if you believe that your injury justifies such action.

PROBLEMS OR QUESTIONS

If you have any problems or questions about this study, or about your rights as a research participant, or about any research-related injury, contact the Principal Investigator, Swee Lay Thein, MD; sweelay.thein@nih.gov, 301-402-6699. Other researchers you may call are Dianna Lovins, RN at Telephone: 240-552-0245. You may also call the NIH Clinical Center Patient Representative at 301-496-2626, or the NIH Office of IRB Operations at 301-402-3713, if you have a research-related complaint or concern.

CONSENT DOCUMENT

Please keep a copy of this document in case you want to read it again.

Adult Research Participant: I have read the explanation about this study and have been given the opportunity to discuss it and to ask questions. I consent to participate in this study.

Signature of Research Participant	Print Name of Research Participant	Date

Investigator:

Signature of Investigator	Print Name of Investigator	Date