LAWSON
HEALTH RESEARCH INSTITUTE

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LETTER OF INFORMATION

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Place of Research: Medical-Surgical Intensive Care Unit
London Health Sciences Centre
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339 Windermere Rd
London, Ontario N6A 5A5

Development of an optical method for detecting cerebral ischemia during neurointensive care

In this Consent document, "you" always refers to the study participant. If you are a substitute decision maker (SDM) (i.e. someone who makes the decision of participation on behalf of a participant), please remember that "you" refers to the study patient. If an SDM is needed for this study, you will be asked to review and sign this consent form on behalf of the participant.

This Letter of Information describes a research study called Development of an Optical Method for Detecting Cerebral Ischemia During Neurointensive Care and what you may expect if you decide to participate. You are encouraged to read this letter carefully and to ask the person who presents it any further questions you may have before making your decision whether or not to participate. This study is being sponsored by Dr. St Lawrence through a grant from the Canadian Institutes of Health Research.

Purpose of the Study

You are being invited to participate in a study looking at the ability of a light-based technology called near-infrared spectroscopy (NIRS) to measure blood flow in the brain by probes placed on the scalp. This method has been tested on a swine model and healthy volunteers. It has also been used on infants in the neonatal intensive care unit. This study is part of a research program designed to develop a non-invasive method for monitoring brain blood flow in critical-care patients. As a patient who has had a subarachnoid haemorrhage (SAH), you are at risk of secondary brain injury caused mainly by the constriction of a brain blood vessel (a condition known as vasospasm). Our hope is that by monitoring brain blood flow, we will be able to detect reduced flow (i.e. ischemia) before brain damage occurs.

Participant's initials:

The purpose of this study is to determine if the brain blood flow measurements obtained by NIRS are correct. We will collect daily blood flow measurements over the first ten days following your brain bleed (hemorrhage). For comparison, images of brain blood flow and the arteries in your brain will be acquired by computed tomography (CT).

Procedure

If you agree to participate in this study, brain blood flow will be measured by our NIRS method at the bedside. The procedure requires placing four probes on the scalp over the brain region affected by the hemorrhage. Another probe, similar to one used by pulse oximetry, will be placed on a finger. Measuring brain blood flow requires injecting a contrast agent into your blood stream, followed by collecting NIRS data for approximately 1 minute. An established venous line will be used to inject the contrast agent. A 2-ml blood sample will be drawn to measure the concentration of red blood cells in your blood. The NIRS probes will remain on your head for six hours in order to monitor any possible changes in brain blood flow over that time period.

The entire NIRS procedure will be performed for 10 consecutive days. Each time will require placing the probes on the head, injecting the contrast agent, and collecting NIRS data for 6 hours. On the tenth day, or earlier based on clinical assessment by the neurologist, CT scanning will be performed to image brain blood flow for comparison to the NIRS measurements, and to measure the size of the arteries in your brain. The scanning procedure for each measurement requires injecting a CT contrast agent, following by approximately 1 min of CT imaging. It is very important to remain as still as possible during these measurements. The CT session will take less than 30 min to complete.

If you are feeling uncomfortable, or experience any side effects associated with the contrast agents (see *Risks and Discomforts* section), the procedure will be stopped immediately.

The study will involve 20 SAH patients between the age of 18 and 70 years. You may not participate in this study if you are pregnant, or if you have allergies to sulfonamide drugs or iodides.

Risks and Discomforts

The NIRS system uses a low-power class 3B laser that can damage the eye from direct or reflected light exposure. To avoid light exposure, the laser will only be turned on once the probes are in place on the scalp. Lasers can cause burning due to heating of the skin. To avoid this risk, the laser power will be within safety limits for skin exposure.

The NIRS procedure for measuring brain blood flow requires an intravenous injection of the contrast agent, indocyanine green (ICG). ICG is a very safe agent with few side effects. The frequency of any adverse reactions is less than 1%, and the most common are urticaria (hives), sensation of warmth, headache or nausea. The risk of death due to ICG administration is 1 in 333,333, which is believed to be a result of a serious allergic reaction (difficulty breathing, swollen lips and throat, and fast heartbeat). If it is necessary

to place an iv catheter for injecting ICG, it has a small risk of discomfort, bruising, clotting or infection.

There is risk associated with the low-level radiation exposure from the CT scan. The biological effect of radiation in humans is measured in terms of Severt equivalents, or "milliSevert (mSv)", which is a unit of body radiation exposure. You will be exposed to approximately 11 mSv for the two contrast-enhanced CT scans. The effects on your body of this radiation exposure will be added to your overall lifetime radiation risk. An average person receives 3.6 mSv per year from natural and man-made radiation. The radiation with the two scans is roughly equivalent to three times the average yearly background radiation. Your lifetime radiation risk also includes any radiation you may have received in the past for diagnosis or treatment, and any such radiation you may be exposed to in the future. The risk from radiation exposure of this amount is considered to be similar to other every day risks, such as driving a car. Please tell us if you have had any major radiation exposure in the past, particularly in the past two years, such as treatment with x-rays or radioactivity, or diagnostic x-rays, CT-scans or nuclear medicine scans.

The CT procedures for measuring brain blood flow and imaging the arteries in the brain each require an intravenous injection of a CT contrast agent, Omnipaque. Adverse reactions are usually of mild-to-moderate severity including dizziness, headaches and nausea. However, serious (less than 1%), life-threatening and fatal reactions have been associated with the administration of iodine-based contrast agents.

If you are harmed as a direct result of taking part in this study, all necessary medical treatment will be made available to you at no cost. You do not waive any legal rights by signing the consent form.

Benefits

There is no guarantee that you will personally benefit by participating in this research study. Your participation in this study will help the investigators learn more about the usefulness of NIRS for measuring brain blood flow in the intensive care unit.

Withdrawal

Participation in this study is completely voluntary. You may refuse to participate or withdraw from the study at any time. This will not affect your clinical care in any way. All data collected prior to voluntary withdrawal may be used as part of the study. An alternative to the procedures described above is not to participate in the study and continue on just as you do now.

Confidentiality

Confidentiality will be protected by storing a master file that contains personal identifiers in a locked filing cabinet in the Principal Investigator's office. Each participant will be assigned a study ID number that will be used to label all collected data. If the results of the study are published, your name will not be used and no information that discloses

your identity will be released or published. All data will be destroyed after fifteen years. Representatives of Western University Health Sciences Research Ethics Board and Lawson Quality Assurance and Education Program may contact you or require access to your study-related records to monitor the conduct of the research.

Contact Person

If you have any questions about the study procedure, contact Dr. Keith St. Lawrence at (519) 646-6100 x 65737.

If you have any questions about the conduct of this study or your rights as a research subject, you may contact The Office of Research Ethics (519) 661-3036; ethics@uwo.ca

Compensation

Procedures related to the study will be provided at any charge to you. You will not be paid for participating in this study. There are no additional expenses to you as a result of participating in this study.

Commercialization

The investigators of this study claim sole ownership of any research results consistent with this consent. By signing this consent, you agree that they can apply for patents and you will not receive any financial benefit that might come from the research.

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Consent to participate in the study entitled:

Development of an optical method for detecting cerebral ischemia during neurointensive care

I have read the Letter of Information, had the nature of the study explained to me and I agree to participate. All questions have been answered to my satisfaction. I will receive a copy of the Letter of Information and signed consent form.

Study Participant (print)	**Signature**	**Date**
Substitute Decision Maker	**Signature**	**Date**

Relationship to Study Participant

Your signature on this form indicates that you are acting as a substitute decision maker(s) for the participant and the study has been explained to you and all your questions have been answered to your satisfaction. You agree to allow the person you represent to take part in the study. You know that the person you represent can leave the study any time

Person Obtaining Consent	**Signature**	**Date**

Participant's initials: