UNITY HEALTH TORONTO

[Unity Health Toronto Site Logo]

Letter of Information and Consent to Participate in a Research Study

Study Title:		A prospective, multi-centered, assessor-blinded clinical performance study to evaluate the sensitivity and specificity of the proposed cell/tissue histopathology image processor cCeLL – Ex vivo (Confocal Fluorescence Endomicroscopy) for intraoperative brain tumor diagnosis.
Study Short Title:		**cCeLL – Ex vivo**
Study Team	**Principal Investigator:**	Dr. Sunit Das, MD, PhD, MA, BA Neurosurgery, St. Michael's Hospital Telephone number (hours of availability at that number)
	Co-Investigator(s):	Local Co-I Name, Credentials Department, Contact Information
	Research Staff:	Sorcha Kellett
	Name and Telephone Number	*Include the name and number of an after-hours contact for this study. This can be the name of a person or a group (e.g. cardiology residents, neurologist on-call).*
Study Sponsor:		VPIX Medical Inc.

CONFLICT OF INTEREST STATEMENT:
VPIX Medical Inc. is the sponsor of this study and is providing funding to Unity Health Toronto to cover the costs of conducting the study. The study investigators and research staff are not receiving any direct payments to do the study.

Introduction

You are being asked to consider participating in this research study because the physician thinks you may have a brain tumor and have been scheduled for neurosurgery at St. Michael's Hospital.

All research is voluntary – you do not have to participate and you can withdraw at any time.

Before agreeing to take part in this study, it is important that you read the information in this research consent form. It includes details we think you need to know in order to decide if you wish to take part in this study. If you have any questions, ask a study team member.

You should be aware that it is possible that the St. Michael's study investigator will also be your treating doctor.

If you choose to participate in this study, you will need to sign this Letter of Information and Consent form. You should not sign this form until you are sure you understand the information. You may also wish to discuss the study with others, such as your family doctor, a family member, and/or a close friend.

1. Background and Purpose of the Study

The usual practice for imaging brain tumor tissue during this type of operation, is to remove tissue from a suspicious lesion and send the tissue to the pathology department where they perform a test called "frozen section" The frozen section test cools the tissue to give a diagnosis of the tissue sample (e.g., cancerous or normal tissue). This process may take up to 40 minutes to perform and uses a lot of resources within the hospital. The operation can only be finished after this report is available to the surgeon. After the surgery, the tissue is assessed by pathology with a test called permanent section which can give more details about the tissue assessment. Permanent section results are not available until after the surgery is complete.

VPIX Medical Inc. has developed a system to image brain tumor tissue for the purpose of making a diagnosis (clinical decision) during the operation. This system uses Confocal Laser Endomicroscopy to image the removed tissue during the operation. This may be able to replace current standard 'frozen section analysis', which would decrease the resources needed to image the tissue, and provide faster results to the surgeon during the operation. We are performing this study to determine if this type of imaging is as accurate as frozen section and if can be performed faster.

The tissue samples that are being assessed by the study device will be removed as part of your normal surgery. This study will compare the results of the study device and the frozen section results. During your surgery, only the standard test results will be used to make decisions.

cCeLL is investigational in Canada, meaning that it has not been approved by Health Canada for use outside of a research study. Health Canada has reviewed and authorized its use in this study.

2. Study Design and Duration

STUDY DESIGN

This study is a prospective, ex-vivo, active-control, assessor-blinded study.

The following definitions are provided to help explain some of the words being used to describe this study:

Ex-vivo: This means that the testing will take place outside of the participant's body. The study device will image tissues that have already been removed from the brain tissue for analysis.

Active-control: This means that the results of the study device will be compared against the results from the usual method of testing.

Assessor-blinded: The pathologist that assesses the images for the study will be asked to make a diagnosis without any additional information besides the image.

PARTICIPANT POPULATION AND STUDY ENROLLMENT

This study will include 600 tissue samples from participants at 4 sites in Canada and Korea. St. Michael's Hospital is the only Canadian site participating in this study and there will be 50 participants included at this site. It is anticipated that each participant may have 1-4 tissue samples available for the study.

STUDY DURATION

Overall, this study will run for about 4 months. Your involvement in this study will last for 1 day and will be complete after your surgery.

3. Description of Research Activities

STUDY DEVICE AND CHANGES TO STANDARD CARE

The study device will be used to image a portion of the same brain tissue samples that will be removed as part of normal care for frozen section testing. The study device results will be assessed after the operation by an independent assessor and compared against the standard of care results.

The care that you receive for your condition will not be changed if you decide to participate in this study. All research interventions and activities will be in addition to usual care.

RESEARCH TESTS AND PROCEDURES

The following tests will be done as part of this study. Some of the tests will be done as part of your clinical care and the results will also be included in the study data, and some of the tests will be done only because you are in this study.

Frozen Section result

The frozen section is rapid tissue imaging performed by freezing the tissue sample. This is used to diagnose the lesion at the time of the operation to make clinical decisions. The results of this standard care test will be used for comparison in the study data.

Permanent Section result

A permanent section process treats the tissue samples with a series of chemical solutions to give a more accurate diagnosis of the tissue sample (cancerous or normal). This test takes up to a couple of weeks to complete and is used in follow up decision making after your operation. This is a standard of care test and considered the best accuracy available for tissue diagnosis. The results of this standard care test will be used for comparison in the study data.

BIOLOGIC SAMPLES FOR RESEARCH USE

A portion of the same tissue sample that is being removed for standard of care assessment during your operation will be imaged using the study device. This portion of tissue will be safely destroyed after the study imaging is completed.

COLLECTING HEALTH INFORMATION FROM MEDICAL RECORDS FOR RESEARCH USE

If you agree to participate in this study, the study team will collect the following health information from your Unity Health Toronto medical record:

- Date of birth
- Biological sex
- Diagnosis from frozen section analysis
- Final diagnosis after surgery from permanent section results

4. Description of Study Visits

You will be asked about your interest in this study at a visit prior to your operation. If you agree to participate and sign this consent form, your operation will take place as usual. The only difference to your standard care is that your tissue samples that are removed will be divided and imaged by the study device as well as frozen section.

You will not be required to do any additional testing or visits for the purpose of the study.

5. Participant Responsibilities

If you decide to take part in this study, it is important that you remember to:

- inform the study team if you have undergone a previous brain surgery

6. Potential Risks

POTENTIAL RISKS OF THE STUDY INTERVENTION

There are no additional risks to you from the study intervention. All testing will be performed on tissue that is already removed from your brain. The testing will be completed in addition to your standard care and will not be used to make clinical decisions.

POTENTIAL RISKS OF RESEARCH ACTIVITIES

Even with protections in place, there is a risk that your information could be released by accident.

7. Potential Benefits

There is no anticipated benefit to you for participation in this study.

There may be benefit to the healthcare system in the future if it is determined that this type of real-time imaging is just as accurate and faster than the current standard of care.

8. Alternatives to Participation

You do not need to participate in this study to receive treatment for your condition. There are other options available to you, including only receiving standard care treatment. In making your decision, you should keep in mind that being in a study is not a form of treatment and that participating in a study is not the same as being treated.

The other options that are available to you include:

- Not participating in this study or any study during your treatment
- Participating in other studies that may be available to you

A study investigator will discuss the other treatments for your condition with you before you decide whether you want to participate in this study. You can also discuss treatment alternatives with your treating doctor or health care practitioner.

9. Privacy and Confidentiality of Your Personally Identifying Information, Study Data and Samples

This section describes how your personally identifying information and study data and samples will be accessed, disclosed, and stored during this study. All persons involved in this study are committed to respecting your privacy. Other than the individuals or groups described in this section, no persons will have access to your personally identifying information without your consent, unless required by law.

Personally identifying information is any information that could be used to identify you; this includes name and address.

Study data is information that is generated by and/or collected for a study that has been stripped of personally identifying information.

Study samples are any biologic samples (e.g. brain tissue samples) that are taken from you for use in a research study.

PROTECTING YOUR PRIVACY

The study team will make every effort to keep your personally identifying information private and confidential in accordance with all applicable privacy legislation, including the Personal Health Information Protection Act (PHIPA) of Ontario.

In addition to the study team, other authorized employees of Unity Health Toronto may have access to your personally identifying information so that they can carry out regulatory or institutionally required duties. Unity Health Toronto may also store personally identifying information that is collected or used for these duties for a period of time, in accordance with regulations and institutional policies.

Representatives of the study sponsor will have restricted access to your medical records for the purpose of confirming the study data.

No personally identifying information will be allowed off site in any form, unless required by law or as described in this consent form.

All data and samples collected for research purposes will be labelled with a unique study identification number instead of any of your personally identifying information. The principal investigator at Unity Health site name is in control of the key that links your study identification number to you personally and will keep it stored separately from the study data.

MEDICAL RECORDS

Accessing and collecting information from your Unity Health Toronto medical record

By signing this form, you are authorizing access to your medical records by the study team. The study team will also collect information from your medical record. The information that will be collected is described in the Research Activities section. The study team will use this information to conduct this study.

You are also authorizing access to your medical records by representatives of the Unity Health Toronto Research Ethics Board, the study sponsor, and by applicable government regulatory authorities (e.g. Health Canada and/or regulatory agencies from other countries). Such access will only be used to verify the authenticity and accuracy of the information collected for this study, without violating your confidentiality, to the extent permitted by applicable laws and regulations.

Adding information into your Unity Health Toronto medical record

Your participation in this study will be recorded in your St. Michael's Hospital medical record. If you participate in this study, the following study related information will be added to your hospital file and stored in the hospital's electronic medical record system: signed consent form and documentation of consent discussion.

Unity Health Toronto shares the patient information stored on its electronic medical records system with other hospitals and health care providers in Ontario so that they can access the information if it is needed for your clinical care. Any of these people may see that you were in this study and the study data listed above when they access your medical record for clinical purposes.

10. Storage and Retention of Your Personally Identifying Information, Study Data and Samples

STUDY BIOLOGIC SAMPLE STORAGE AND RETENTION

Tissue samples will not be stored or retained outside of the hospital. After the imaging has been completed by the study device, those tissue samples will be destroyed by standard process.

Personally identifying information collected for research purposes will be kept by the Principal Investigator and Unity Health Toronto for as long as required by Health Canada regulation and Unity Health Toronto policy (currently 15 years after a study ends), at which point any documents with personally identifying information will be destroyed.

STUDY DATA STORAGE AND RETENTION

As a reminder, study data is information that is generated by or collected for a study that has been stripped of personally identifying information.

Study data will be securely stored at Unity Health Toronto. Study data may also be transferred outside of Unity Health Toronto and shared with others for purposes related to the conduct of this study.

Study data may be kept indefinitely and may be used for other research or analyses by the study investigators and the study sponsor.

Individual level study data may also be made available to scientific journals, their reviewers, other researchers inside or outside of Unity Health Toronto, or the public.

11. Study Results and Study Registration

RESULTS

The results of this study may be presented at a scientific conference or published in a scientific journal. If you are interested in obtaining the results of this study, you can contact the study team. We estimate that the results of this study will be available in 1 year.

You will never be personally identified in any publication, report, or presentation that may come from this study.

REGISTRATION

This study will be registered on http://www.ClinicalTrials.gov. The site will include information about the study but will not include any personally identifying information. You can search the site for this study; the registration number is NCTXXXXXXXX.

12. Potential Costs and Reimbursement

There are no costs to you for participation in this study. You will not be paid for your participation in this study.

If a discovery is made or a commercial product or method is derived from this study, it will be the property of the study sponsor and you will not be entitled to any financial benefits resulting from it.

13. Compensation for Injury

If you are injured due to your participation in this study, medical care will be provided to you in the same manner as you would ordinarily obtain any other medical treatment. In no way does signing this form waive your legal rights nor release the study investigator, study sponsor, or involved institution(s) from their legal and professional responsibilities.

14. Participation and Withdrawal

PARTICIPATION IN THIS STUDY

Your participation in this study is voluntary. If you choose not to participate, there will be no impact to the medical care received at, employment at, or other relationship with Unity Health Toronto now or in the future for you or your family.

WITHDRAWAL FROM THIS STUDY

If you choose to take part in this study, you can change your mind without giving a reason, and you may withdraw from this study at any time without any effect on the medical care, employment or other relationship you or your family have at or with Unity Health Toronto.

If at any time you choose to withdraw from this study, please contact a member of the study team.

This study may be terminated by the study investigators or by the study sponsor at any time for any reason.

Continued collection and use of your data after withdrawal
If you withdraw or are withdrawn from this study, no more data about you will be collected**.**
Any study data collected about you up to the time you withdraw will still be used for analysis unless you request for it to be removed.

We may be required to retain the personally identifying information and study data that we have already collected until after the end of this study (described in the Privacy and Confidentiality section).

Any data that has been added to your medical record cannot be deleted from the record.

Continued use of your samples after withdrawal
If you withdraw or are withdrawn from this study, data from samples that have already been analyzed will still be used unless you request for them not to be used. No further analysis will be done on your samples and any remaining samples will be destroyed.

15. New Information About this Study

We may make changes to this study as it progresses. We may also learn new things about this study that you may need to know. Some of the new information or changes might affect your decision to continue taking part in this study. You will be notified about any new or changed information in a timely manner and we will ask you if you consent to remain in this study. You may be asked to sign a new consent form at that time.

16. Research Ethics Board Contact

If you have any questions regarding your rights as a research participant, you may contact the Unity Health Toronto Research Ethics Board Office at 416-864-6060 ext. 42557 during business hours (9:00am to 5:00pm).

Unity Health Toronto is a health network that includes Providence Healthcare, St. Joseph's Health Centre, and St. Michael's Hospital.

17. Study Contacts

If at any time during this study you have questions about the study or the research activities, you should contact the Principal Investigator, Dr. Das, at (XXX) XXX-XXXX (hours of availability) or the research coordinator, Sorcha Kellett, at (XXX) XXX-XXXX (hours of availability).

18. Signature Page(s): Documentation of Informed Consent

STUDY TITLE: A prospective, multi-centered, assessor-blinded clinical performance study to evaluate the sensitivity and specificity of the proposed cell/tissue histopathology image processor cCeLL – Ex vivo (Confocal Fluorescence Endomicroscopy) for intraoperative brain tumor diagnosis.

Participant Statement of Consent

By signing this consent form, I acknowledge that:

- This research study has been explained to me, and my questions have been answered to my satisfaction.
- I have been informed of the alternatives to participation in this study.
- I know that I have the right not to participate and the right to withdraw from this study without affecting the medical care received at, employment at, or other relationship with Unity Health now or in the future for me or my family.
- The potential risks and benefits (if any) of participating in this study have been explained to me.
- I have been told that I have not waived my legal rights nor released the study investigator, study sponsor, or involved institutions from their legal and professional responsibilities.
- I know that I may ask, now or in the future, any questions I have about this study.
- I have been told that information about me and my participation in this study will be kept confidential and that no personally identifying information will be disclosed without my permission unless required by law.
- I have been given sufficient time to read the information in this consent form.
- I will be given a signed and dated copy of this consent form.

I consent to participate in this study.

Participant name (print)	Participant signature	Date	Time

I have explained to the above-named participant the nature and purpose, the potential benefits, and possible risks of participation in this study. All questions that have been raised about this study have been answered.

Name of person obtaining consent (print)	Position/Title of person obtaining consent (print)	Signature of person obtaining consent	Date	Time

STUDY TITLE: A prospective, multi-centered, assessor-blinded clinical performance study to evaluate the sensitivity and specificity of the proposed cell/tissue histopathology image processor cCeLL – Ex vivo (Confocal Fluorescence Endomicroscopy) for intraoperative brain tumor diagnosis.

Declaration of Assistance – Witness to Consent Process

Study Participant's Name (Print): _____

ASSISTANCE DECLARATION AND SIGNATURE:

I have provided assistance during the consent discussion between the potential participant and the person obtaining consent by (please check one):

- ☐ Acting as a witness to the consent discussion
- ☐ Acting as a witness to consent to participate in the study (signature or verbal agreement)
- ☐ Assisting in delivery of consent discussion (reading/oral), including communication of questions and responses
- ☐ Other: _____

I attest that the information was accurately explained to, and apparently understood by, the participant and the participant has freely given consent to participate in the research study.

Name of person assisting consent (print)	Signature of person assisting consent	Date	Time

Contact Information of Person Assisting Consent	Relationship To Study Participant

STUDY TITLE: A prospective, multi-centered, assessor-blinded clinical performance study to evaluate the sensitivity and specificity of the proposed cell/tissue histopathology image processor cCeLL – Ex vivo (Confocal Fluorescence Endomicroscopy) for intraoperative brain tumor diagnosis.

Declaration of Assistance – Interpreter

Study Participant's Name (Print): _____

INTERPRETER DECLARATION AND SIGNATURE:
I am competent in the English language and in the preferred language of the potential participant: _____ (name of language)

I am not involved in the research study or related to the participant. I agree to keep confidential all personally identifying information of the participant. I have faithfully interpreted the consent discussion, and provided a sight translation of the written informed consent form as directed by the study team member obtaining consent.

_____	_____	_____	_____
Name of interpreter (print)	Signature of interpreter	Date	Time

_____
Contact Information of Interpreter