Certification of Completion of the Informed Consent

IRB #

Title:

I have discussed the "Informed Consent for Participation in Research Activities" in its entirety for the above referenced research study, with the research participant listed below (or the research participant's legally authorized representative). During the review of the consent form, the possible benefits, risks and discomforts involved in his/her participation on the study, as well as potential alternatives were reviewed.

The research participant has been encouraged to ask questions, and all questions asked by the participant have been answered. The research participant affirmed that he/she has received all information that he/she desires at this time, and a copy of the signed consent form has been provided to the participant.

PRINTED NAME of Person Obtaining Informed (Consenter)	SIGNATURE	TITLE	DATE	TIME

ADULT INFORMED CONSENT

COH Protocol # 21466
TITLE: Assessment of the reproducibility and accuracy of a portable system for early detection of cardiac dysfunction in childhood cancer survivors
Version date:

PRINCIPAL INVESTIGATOR: Saro Armenian DO, MPH

DAY TIME TELEPHONE NUMBER FROM THE HOURS OF 8:00 AM TO 5:00 PM: 626-218-7320

EXPERIMENTAL PARTICIPANT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study, also known as an experiment or clinical trial. As a research participant, you have the following rights:

1. To be told what the research study is trying to find out.
2. To be told what will happen to you and whether any of the procedures to be used are different from what would be used in standard practice.
3. To be told about the discomforts, side effects and risks of the things that will happen to you as part of the research study.
4. To be told if you can expect any benefit from participating in the research study.
5. To be told of the other choices you have and how they may be better or worse than being in the research study.
6. To be told what medical treatment is available if any complications arise.
7. To be allowed to ask any questions concerning the research study, both before agreeing to be in the study and during the course of the study.
8. To refuse to participate in the research study or to change your mind about participation after the study is started. To be informed that this decision will not affect your right to receive the care you would receive if you were not in the study.
9. To receive a copy of the signed and dated research study consent form.
10. To be free of pressure when considering whether you wish to agree to be in the research study.

ADULT INFORMED CONSENT

COH Protocol # 21466
TITLE: Assessment of the reproducibility and accuracy of a portable system for early detection of cardiac dysfunction in childhood cancer survivors

PRINCIPAL INVESTIGATOR: Saro Armenian DO, MPH

KEY INFORMATION
You are invited to participate in a research study. This study is an evaluation of 200 childhood cancer survivors who previously underwent a one-time assessment of cardiac function by echocardiogram (echo), Cardiac Magnetic Resonance (CMR) Imaging, and iPhone®-based platform (Vivio) between November 2014 and May 2017. You were previously enrolled in this study which showed that Vivio, a handheld, portable system for early detection of heart dysfunction, can accurately show heart function similar to a CMR in a clinical setting. The current study will evaluate whether a standard blood pressure monitor is reliable, practical, and cost-effective for screening childhood cancer survivors in the clinic and home setting.

You will be asked to have a one-time clinical assessment of your heart through three screening measures: echo, CMR, and the SphygmoCor® Xcel and Oscar 2™ Ambulatory Blood Pressure Monitor (ABPM) systems. Afterwards, the study staff will teach you how to take self-measurements with the blood pressure (BP) cuff. When you are able to record three accurate measurements, you will be asked to bring the BP monitor and cuff home with you. That same day, you will perform three self-measurements in your home and then ship the device back to City of Hope with the prepaid label and box provided. The entire study will take no longer than 1 week, including the home measurements.

The main risk associated with this study include discomfort from the pressure associated with the echo. In addition, the CMR's narrow space may make some people uncomfortable, especially if they are claustrophobic (uneasy being in confined spaces).

You do not have to join this research study. If you are interested in learning more about this study, please continue to read below.

INTRODUCTION
You are invited to take part in this research study because you have previously enrolled in IRB# 14154, *Assessment of a novel iPhone®-based platform for early detection of cardiac dysfunction in childhood cancer survivors at risk for anthracycline-related heart failure.* We hope to learn that tonometry-based screening can be used accurately in both a clinical and non-clinical setting to monitor heart function. It is expected that about 200 people will take part in this research study.

We encourage you to take some time to think this over, to discuss it with other people and your primary doctor, and to ask questions now and at any time in the future. Please take as much time as you need to read the consent form. If you find any of the language difficult to understand, please ask questions. If you decide to participate, you will be asked to sign this form. We will give you a copy so that you can refer to it while you are involved in this research study. If you choose not to participate in this research study, the research doctors will discuss other treatment options with you and/or refer you back to your primary doctor.

A. WHY IS THIS RESEARCH STUDY BEING DONE?

Within the last 30 years, there have been significant improvements in childhood cancer treatments, leading to a growing number of childhood cancer survivors. However, some survivors may develop complications related to the cancer treatment that they received. Some patients have no complications while others may develop one or more problems related to their cancer treatment. Patients who received high doses of a type of chemotherapy called anthracyclines are at a higher risk for developing congestive heart failure (weakening of the heart muscle). Obvious symptoms of this complication may not appear until years after treatment is completed. Detecting a problem before symptoms start to show could help prevent more serious long-term damage to the heart.

Currently available screening tests for heart failure include echo and CMR. However, both tests require the patient to be seen in a clinic setting, with high costs and inconvenience due to time away from work/school. Recent advances in mobile technology have led to new diagnostic approaches that have the potential to combine the usefulness of an echo with the accuracy of CMR at a much lower cost in money and time. To better understand if such devices were useful in the survivorship population, our team tested the reliability of a Vivio device (neck) and found that the measurements from the Vivio device were as good as the CMR, which is currently the most accurate screening procedure.

The main goals of this research study are to test the accuracy and practicality of tonometry-based screening in the clinic setting and at home.

SphygmoCor® Xcel and Oscar 2™ ABPM systems have 510(k) U.S. FDA clearance as medical devices to perform non-invasive cardiovascular measurements as an adjunct to manage various cardiovascular conditions.

B. WHAT IS INVOLVED IN THE STUDY?

If you agree to participate, the following activities for this study will take place at clinic:

Clinic Visit Study Procedures:

- **Vital Signs:** Vital signs include the measurement of your heart rate, blood pressure, height, and weight. Your blood pressure will be measured using an automated BP cuff. A BP cuff will be placed over your upper arm about one inch above the bend of your elbow then the cuff will inflate and slowly deflate so that the machine can take your measurement.

- **Imaging tests:** We will look at your heart function using the three screening tests listed below:

    - **Echo:** This test is an ultrasound of the heart muscle. You will lie on a bed while a technician uses an ultrasound wand, pressed against your chest, to take images of your heart. Your echo will be sent for central review as part of quality control. The participant's identifiers and dates will be removed prior to the review. The echo is being done as part of the research study and is not considered standard of care. The results will not be shared with your personal doctor.
    - **CMR:** A Magnetic Resonance Imaging (MRI) is a procedure that uses a magnet linked to a computer to create pictures of an area inside the body. To have an MRI scan, you must not have any metal objects on or in your body, for example, brain aneurysm clips or a pacemaker. All jewelry must be removed before the scan. An MRI scan is performed like a CT scan except that the MRI uses radio frequency waves (like those in an AM/FM radio) instead of x-rays and has a powerful magnet. You will be asked to sign a separate consent form for this procedure. The CMR is being done as part of the research study and is not considered standard of care. The results will not be shared with your personal doctor.
    - **SphygmoCor® Xcel and Oscar 2™ ABPM:** You will be asked to have SphygmoCor® Xcel and Oscar 2™ ABPM readings the same day as your echo and CMR. The Xcel device consists of three parts: a blood pressure cuff, thigh cuff and the machine itself. A trained member of the study staff will gently place the BP cuff over your upper arm. The BP cuff will measure a routine blood pressure measurement. The sensors in the device will capture your BP and other relevant cardiac functions which will then be transmitted to the study laptop via a wire. Afterwards, the blood pressure cuff will be swapped out with a thigh cuff and with the aid of a carotid tonometer (a device that can measure pressure in your artery as blood flows through), your pulse wave velocity measurements (a measure of the stiffness and health of the main blood vessels) will be captured by placing the thigh cuff on your upper thigh while the tonometer is pressed against your carotid artery in your neck. Next, Oscar 2™ ABPM will be used to perform to perform normal blood pressure reading by placing a cuff over your upper arm. The SphygmoCor® Xcel and Oscar 2™ ABPM measurements are being done as part of the research study and is not considered standard of care. The result will not be shared with your personal doctor.

- **Oscar 2™ ABPM Measurements Training:** The study staff will conduct a brief training to teach you how to use Oscar 2™ ABPM device to take your own measurements. You will practice taking self-measurements with the study staff. They will answer any questions and confirm that you are able to do at least three accurate measurements by yourself before sending you home. Once you are ready to go home, the study staff will give you the Oscar 2™ ABPM device and a training brochure (on how to take self-measurements with the device) to take home.

- **Questionnaires:** You will be asked to complete questionnaires about yourself, your medical history and your family's medical history. The questionnaires are expected to take about 20 minutes to complete.

At Home Study Procedures:

- **Oscar 2™ ABPM Device Measurements:** Within 1-5 days of your clinic visit, you will be asked to take measurements using the device. The study staff will be available to help you with technical difficulties and will follow up with you to make sure you completed the measurements.
- **Return Shipment:** Once your self-measurements have been completed, you will be asked to use the prepaid shipping label and box provided to send the device and tablet back to City of Hope.

Information about what to expect during and between study visits are included in this study calendar below:

Research Study Calendar:

	Screening	**Clinic Visit**	**Home**
	Remote or City of Hope	At City of Hope	At Participant's Home
Screening	**X**		
Consent	**X**		
Vital Signs (Blood Pressure. Heart Rate, Height, Weight)		**X**	
Echo		**X**	
CMR		**X**	
Oscar 2™ ABPM Training		**X**	
Oscar 2™ ABPM Device Measurements		**X**	**X**
Return Oscar 2™ ABPM device			**X#**
Questionnaires@		**X**	

A prepaid shipping label and box will be given to you for shipment back to City of Hope.
@ Questionnaires will be completed electronically or at the in-person visit.

C. HOW LONG WILL I BE IN THIS RESEARCH STUDY?

The clinic portion of the study will take approximately 4 to 6 hours, while the home-based portion, including the self-measurements and return of the device and tablet, is expected to take no longer than 1 week.

D. WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

There are risks to taking part in any research study. Possible risks and discomforts you could experience during this study include:

Risks Associated with an Echo:

In this test, ultrasound (sound waves) is used to examine the heart. A colorless gel (sometimes cold) is first applied to the chest. An ultrasound wand is placed on the gel and is moved around to different parts of the chest. You may be asked to move slowly from side to side, to breathe slowly, or to hold your breath. This helps in obtaining higher quality pictures. The echo is non-invasive and is not associated with any health risks.

Risks Associated with CMR:

When having CMR imaging, you will lie still on a table that slides into a tunnel slightly wider than your body. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. If you feel uncomfortable in confined spaces, please tell your research doctor. Your doctor may give you a medication to make you feel more comfortable. As images are taken, a loud banging noise will be produced. Earplugs or headphones will be available if needed. The MRI can be stopped at any time at your request, but the scan may not be complete.

Risks Associated with the SphygmoCor® Xcel and Oscar 2™ ABPM device:

The SphygmoCor® Xcel and Oscar 2™ ABPM systems are non-invasive measurements and are not associated with any health risks. You may experience slight discomfort from the pressure of the blood pressure cuff pressing on the upper arm and thigh or from the pressure of the carotid tonometer pressing on your neck.

Risks Associated with Questionnaires:

Some of the questions in the questionnaires may make you feel uncomfortable or anxious. The questionnaires that are being used for this research study have been used in a previous study. To the best of our knowledge, they have not caused anyone serious problems. You do not have to answer any question that you don't want to. In addition to the risks described above, there may be unknown risks, or risks that we did not anticipate, associated with being in this study.

Risks associated with Breach of Confidentiality:

There is a small risk that people who are not connected with this study will learn your identity or your personal information.

Incidental Findings:

It is possible that the research procedures could find a medical problem unrelated to the purpose of this study that you did not know about before. If during the research procedures we learn information that may be important for you to know about, such as the possibility of a previously unknown medical condition, we will tell you. You may authorize the release and communication of the findings to your personal doctor. These findings may require additional testing or treatment. You will be responsible for the cost of any additional tests or related treatment.

E. WILL YOU RECEIVE NEW INFORMATION ABOUT THIS STUDY?

During the research study, you will be notified of newly discovered significant findings, which may affect your health or willingness to participate. You may be asked to sign a new consent form that shows that you have been informed of new information relating to this research study.

F. HOW WILL YOUR INFORMATION BE KEPT CONFIDENTIAL?

Any information learned from this study in which you might be identified will be confidential and disclosed only with your permission. Every effort will be made to keep any information collected about you confidential. However, it is impossible to guarantee that information about you will not be mistakenly released. If, despite our best efforts, identifying information about you is released, it could negatively impact you or your family members. This risk is small.

There are organizations that may inspect your records. These organizations are required to make sure your information is kept private, unless required by law to provide information. Some of these organizations are:

- The Institutional Review Board, IRB, is a group of people who review the research with the goal of protecting the people who take part in the study.
- Regulatory agencies such as the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), and the National Cancer Institute (NCI) in the U.S., and similar ones if other countries are involved in the study as required by law.

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.

Certificate of Confidentiality

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The Certificate protects against the release of information, documents or biospecimens that may identify you that was collected during the period the Certificate is in effect to individuals not connected with the research. For example, the researchers involved in the studies cannot be forced to disclose the identity or any information collected in the study in any legal proceedings at the federal, state, or local level, regardless of whether they are criminal, administrative, or legislative proceedings. However, federal agencies may review our records under limited circumstances, such as a DHHS request for information for an audit or program evaluation or an FDA request under the Food, Drug and Cosmetics Act.

The Certificate does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you choose to voluntarily disclose the protected information under certain circumstances (for example, if you request the release of information in writing), the Certificate does not protect against that voluntary disclosure. Additionally, the Certificate of Confidentiality will not protect against the required reporting by hospital staff of information on suspected child abuse, reportable communicable diseases, and/or possible threat of harm to self or others. The Certificate of

Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document, for other scientific research, as allowed by federal regulations protecting research subjects, or for your medical treatment.

G. WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART IN THIS RESEARCH STUDY?

We do not expect you to benefit directly from participation in this study. However, if we detect clinically meaningful abnormalities during the testing process, you and/or your physician will be notified of them. The knowledge gained from the current study may be used to develop improved screening strategies in populations at risk for congestive heart failure (CHF).

H. WHAT OTHER OPTIONS ARE THERE?

Your alternative is to not participate in this study. Choosing not to participate will not affect your ability to receive care at City of Hope.

I. ARE THERE ANY PAYMENTS TO YOU FOR TAKING PART IN THE STUDY?

You will receive modest compensation for your time and effort spent on the study. You will receive a $100 gift card at the following 2 time points (A total of $200 for both time points):

1. Completion of your clinic visit, and
2. Upon return of the Oscar 2™ ABPM device.

J. WHAT ARE THE COSTS?

Neither you nor your insurance carrier will be charged for participation in this study.

K. WHAT HAPPENS IF YOU GET INJURED AS A RESULT OF THIS STUDY?

If you think you have been hurt by taking part in this study, tell the person in charge of this research study as soon as possible. The research doctor's name and phone number are listed in this consent form. City of Hope will offer you the care needed to treat injuries directly resulting from taking part in this research. However, financial compensation will not be available.

You do not give up your legal rights by signing this form.

L. WHAT ARE YOUR RIGHTS IF YOU TAKE PART IN THIS STUDY AND WHAT WILL HAPPEN IF YOU DECIDE NOT TO PARTICIPATE?

Your participation in this research study is voluntary. You are free to withdraw your consent for participation in this study without any loss of benefits, penalty, or interference with any future treatment at City of Hope.

M. CAN YOU BE REMOVED FROM THE STUDY?

You may be removed from this study without your consent for any of the following reasons: you do not follow the study staff's instructions, at the discretion of the investigator, or the Oscar 2™ ABPM systems are no longer available for the study. If this happens, the study staff will discuss other options with you.

N. WHOM DO YOU CALL IF YOU HAVE QUESTIONS OR CONCERNS?

The principal investigator, Dr. Saro Armenian, or a member of their research staff has offered to and has answered any and all questions regarding your participation in this research study. If you have any further questions or in the event of a research related injury, you can contact Dr. Saro Armenian at (626) 218-7320.

This study has been reviewed and approved by the Institutional Review Board (IRB). If you have any questions regarding your rights as a research participant, you may contact a representative of that Board, from the Office of Human Research Subjects Protection, at (626) 256-HOPE (4673) ext. 62700.

O. SIGNATURE SECTION

SIGNATURE FOR CONSENT: By signing this consent form, you are making a decision to participate in this research study. Your signature on this informed consent form indicates that you:

1. Have read and understood the information in this form.
2. Have had the information in this form explained to you.
3. Have had a chance to ask questions and these questions were answered to your satisfaction.
4. Have been informed that you will receive a copy of this signed consent form, which includes the "Experimental Subject's Bill of Rights."

I hereby agree to be a research participant in this research study:

_____ _____ _____

Research Participant's Signature Date Time

(For paper consent only, date and time must be in research participant's handwriting)

_____

Print Research Participant's Name

INDIVIDUAL OBTAINING CONSENT SIGNATURE

_____ _____ _____

Signature of Individual Obtaining Consent Date Time

_____

Print Name of Individual Obtaining Consent

FOR USE WITH IRB APPROVED TRANSLATED SHORT/LONG CONSENT FORMS FOR NON ENGLISH SPEAKING PARTICIPANTS ONLY

NOTE: To determine who should sign below, review the guidance document, Consenting Non English Speaking Research Participants (Pediatric or Adult) – Who Signs What?

Interpreter: By signing here, I attest that I have acted as interpreter and facilitated this consent process.

_____ _____ _____

Interpreter's Signature Date Time

_____

Print Interpreter's Name

FOR USE WHEN A WITNESS IS REQUIRED:

Witness: By signing here, I attest that I witnessed the consent process and that the entire consent form was discussed.

_____ _____ _____

Witness' Signature Date Time

_____

Print Witness' Name

Assessment of the reproducibility and accuracy of a portable system for early detection of cardiac dysfunction in childhood cancer survivors

AUTHORIZATION TO USE AND DISCLOSURE OF YOUR PROTECTED HEALTH INFORMATION (PHI) FOR PURPOSES OF THIS STUDY:

I. **Purpose of this Authorization**: The information about your health is something that is protected by law and cannot, except for certain purposes, be disclosed (shared) without your permission. As part of this research, you are agreeing to allow City of Hope, its affiliated research doctors, healthcare providers, and physician network to use and share with others your protected health information ("PHI"), as needed for the research. If you agree to participate in the study named above (called the "Study"), you must sign this authorization in addition to the Study Consent Form.

II. **The Information About You that is Covered By this Authorization**: PHI refers to information that we maintain about you that identifies you and includes the information contained in your medical record. Your medical record consists of information related to your health and the treatment we provide to you, such as your medical history, the results of physical exams, blood tests, x-rays and other diagnostic and medical procedures. If you sign this authorization, you are allowing City of Hope and the individuals indicated below to use and share any PHI we maintain about you that is required for your participation in the Study.

III. **Purposes for Uses and Sharing of your PHI; Who Will Use, Share and Receive your PHI**: Your PHI will be used and shared with others for the purpose of doing this research as described in the Study Consent Form. Your PHI will also be used to keep the research sponsor informed about this Study, for reporting to those individuals and authorities responsible for overseeing our research activities to make sure that the activities are properly conducted, and to report to regulatory agencies as required by the Study.

The people authorized to use and share your PHI for purposes of the Study include the Principal Investigator and the research staff supporting the Study; your City of Hope physicians and the health care team; the Health Information Management Services Department (i.e., Medical Records Department), and affiliated research doctors and other medical centers participating in the research, if applicable. This

also includes any agents or contractors used by these individuals or groups for purposes of conducting or managing this Study. At the City of Hope, the Institutional Review Board ("IRB"), and other City of Hope research regulatory committees will have access to your PHI as necessary to monitor research.

You are also allowing your PHI to be shared with the Office for Human Research Protections ("OHRP") and with any person or agency as required by law. In addition, certain other regulatory agencies, including, the Food and Drug Administration ("FDA"); the National Cancer Institute ("NCI"), will have access to your PHI.]

This authorization will allow us to use and share your PHI for the Study. No other additional uses and disclosures other than for the purposes of the Study is included in this authorization. City of Hope's Notice of Privacy Practices will continue to protect your non-Study information. If necessary, another separate permission will be obtained from you for any non-Study uses or sharing of your PHI.

IV. **Expiration of this Authorization**: This authorization to use and share your PHI will expire twenty-five (25) years from the date that you sign this authorization.

V. **Further Sharing of Your PHI**: Your privacy is important and this is the reason for having rules which control who can use or see your PHI. City of Hope maintains control over your PHI at present, but once we share this information with a third party (for example, an individual or agency outside of the City of Hope), then it is no longer possible to maintain the same level of protection. The persons outside our control may not be governed by federal or state privacy laws and it is possible that they could share your PHI with others for whom you have not given permission.

The information from this Study may be published in scientific journals or presented at scientific meetings but your identity will be kept confidential.

VI. **Your Rights Under this Authorization**: You may cancel this permission to use and share your PHI at any time by contacting City of Hope's Privacy Officer at (626) 256-HOPE (4673) ext. 64025. You should ask for the form, Revocation (Cancellation) of Authorization for Use of Protected Health Information for Research. Fill this form out and return it as the form instructs. Your cancellation begins when the Health

Information Management Department of City of Hope receives this form. If you cancel this authorization to use and share your PHI, you will no longer be able to participate in the Study. This is because the research under this Study cannot be conducted without your PHI.

Once you cancel your permission to use and share your PHI, the researchers and others involved in conducting the Study will no longer be able to use or share your PHI for this research. PHI already used and shared up to this point as part of this Study will continue to be used for purposes of this research. This means that any uses of your PHI and any PHI shared about you by City of Hope prior to receiving your cancellation (revocation) form cannot be taken back. While no further PHI about you will be shared for the Study, your PHI already shared will continue to be used in the overall Study.

VII. **<u>Signing this Authorization is Your Choice</u>:** Your ability to obtain care at the City of Hope will not be affected by your decision to sign this authorization form. You will be able to continue to receive health care at City of Hope if you choose not to sign this authorization form or if you sign this form and later cancel your permission to use and share your PHI.

If you agree to the use and sharing of your PHI, please sign below. You will be given a copy of this authorization form.

_____ _____ _____

Research Participant's Signature Date Time

(For paper consent only, date and time must be in research participant's handwriting)

_____

Print Research Participant's Name

INDIVIDUAL OBTAINING CONSENT SIGNATURE

_____ _____ _____

Signature of Individual Obtaining Consent Date Time

_____

Print Name of Individual Obtaining Consent

FOR USE WITH IRB APPROVED TRANSLATED SHORT/LONG CONSENT FORMS FOR NON ENGLISH SPEAKING PARTICIPANTS ONLY

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Interpreter: By signing here, I attest that I have acted as interpreter and facilitated this consent process.

_____ _____ _____

Interpreter's Signature Date Time

_____

Print Interpreter's Name

FOR USE WHEN A WITNESS IS REQUIRED:

Witness: By signing here, I attest that I witnessed the consent process and that the entire consent form was discussed.

_____ _____ _____

Witness' Signature Date Time

_____

Print Witness' Name