Official Study Title: TELEHEALTH BASED INTERVENTION TO IMPROVE FITNESS IN SURVIVORS OF CHILDHOOD CANCER WITH SIGNIFICANTLY LIMITED EXERCISE TOLERANCE

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TELEHEALTH BASED INTERVENTION TO IMPROVE FITNESS IN SURVIVORS OF CHILDHOOD CANCER WITH SIGNIFICANTLY LIMITED EXERCISE TOLERANCE (CARTOXIII)

Key Information

To start we want to highlight the **risks and study requirements** that we think you should know before deciding if you want to take part in this research study. If you're still interested, we'll then get into more detail.

A. Why are you being asked to volunteer in this study?
You are being asked to take part in this clinical trial, a type of research study, because you are a SJLIFE study participant and may have a hard time exercising (exercise intolerance) due to side effects of cancer treatment you received as a child.

B. What is the usual approach to this condition?
To follow the Physical Activity Guidelines for Americans, exercising at least 150 minutes a week.

C. Why is this study being done?
This study is being done to determine if an individualized exercise plan will help childhood cancer survivors who have exercise intolerance become more active.

D. What will happen if you decide to take part in this study?
You will be chosen to either participate in an individualized exercise group or a more generalized exercise support group. The groups last 20 weeks and you will be asked to complete remote assessment sessions at that time and then again in 6 months.

E. What are the research risks and benefits of taking part in this study?
Risks of taking part of this study may include slight risk of injury when exercising, possible increased risk of cardiovascular events, and becoming uncomfortable physically or emotionally during the study assessments. Benefits include exercise recommendations and regular contact with a study staff to encourage regular exercise.

F. How many people will take part in this study?
160 SJLIFE participants.

G. What are your options?
a. Taking part in this research study is completely your choice.
b. If you decide to take part in this study, you can change your mind and stop at any time.
c. If you decide not to take part in this study, you may still be able to receive care at St. Jude.
d. You may choose no treatment or to seek treatment somewhere else.

If you are still interested in taking part in the CARTOXIII research study, more detail will be provided in the following pages.

St. Jude Children's Research Hospital
IRB NUMBER: 19-0253
IRB APPROVAL DATE: 10/28/2024

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1. Why are you being asked to volunteer for this research study?

You are being asked to take part in this clinical trial, a type of research study, because you are a survivor of childhood cancer who was treated at St. Jude Children's Research Hospital, you are participating in the SJLIFE Study, and you may have difficulty exercising due to the side effects of your cancer treatment. Please take your time in deciding and feel free to discuss it with your family, friends and St. Jude staff. Before agreeing, it is important that you read this consent form that describes the study. After you understand the study and if you agree to take part, you will be asked to sign this consent form. You will be given a copy to keep.

2. Who is sponsoring this study?

This study is being sponsored by St. Jude Children's Research Hospital and the National Institutes of Health.

The principal investigator (researcher) in charge of this study is Kirsten Ness, PhD, who can be reached by phone at 901-595-3300.

3. What is the purpose of this study?

The purpose of this study is to have SJLIFE childhood cancer survivors that have difficulty exercising due to side effects of their cancer treatment participate in either an individualized exercise program or a group that receives generalized exercise recommendations to promote increased regular physical activity. Difficulty exercising, or exercise intolerance, is a common condition among childhood cancer survivors at a relatively young age. However, it is possible that exercise intolerance can be improved, and past studies have shown that survivors respond well to exercise programs. Adopting an active lifestyle requires motivation and behavioral change and is one of the most important things people can do for their overall health. Individuals that exercise more frequently have better physical functioning and less fatigue. This study hopes to determine if an individualized approach, with professional coaching, is needed to promote increased physical activity in survivors or if general information and regular contact will be enough to help survivors to become more regularly active.

4. What will be done in this study?

All tests, procedures and activities in this study are done for research purposes only. If you agree to take part, any data collected as part of the SJLIFE study, including questionnaires, neurocognitive evaluation, medical history and physical, lab evaluations, height and weight measurements, blood pressure measurements, cardiopulmonary function evaluations and physical functioning assessment results may also be used as part of this study.

If you agree to take part in this study, you will complete all the study activities from home, and you will receive information about physical activity and its health benefits. You will complete 3 remote assessment sessions during this study: at the beginning of the study (baseline), at the end of the 20 week intervention period and 6-months after the end of the 20

week intervention period for follow-up. After the baseline assessment session, if you are medically cleared to participate, you will be randomly (by chance, like drawing straws) assigned to one of two groups: to an individually tailored exercise program with supervision or to a group that receives generalized exercise recommendations. The two groups will consist of an equal number of participants. You will participate in either the personalized exercise program or general program for 20 weeks.

Below are further explanations of the research tests and interventions done in this study:

Research Tests

These tests will be performed at the remote assessment sessions using an online meeting platform. The tests below will be performed at your first or baseline assessment session. All the tests, except for the first two listed, will be repeated at the follow-up assessment sessions. All the necessary equipment to complete these tests will be mailed to your home. You will receive instructions on how to create a user account in the online meting platform and how to sign into a video session with a study staff. You will participate in an orientation session to become familiarized with the equipment before completing the tests.

1. **Urine pregnancy testing:** If you are female, you will be sent a urine pregnancy test to complete at home before your baseline assessment session. You will report your results at your scheduled baseline assessment session.
2. **Health History and Physical Activity Readiness:** At your baseline assessment session, you will be asked physical activity related health history questions as well as questions from the Physical Activity Readiness Questionnaire to ensure exercise is safe. If your answers indicate that exercise will increase your risk for a heart problem or bone, joint or muscle injury, a study physician will contact you for additional information to determine whether or not it is safe for you to participate in the study.
3. **Vital signs:** You will be asked to wear a pulse oximeter on your finger. While at rest, your heart rate and blood oxygen levels will be read from the device. You will be asked to take your blood pressure using a wireless blood pressure monitor.
4. **Body Weight:** You will be asked to weigh yourself using an electronic scale.
5. **Fitness testing:** This test involves stepping in place for 2 minutes while wearing a heart monitor. The total number of steps you take will be recorded. Your heart rate will be taken after you complete the test and you will rate how hard you felt you were working during the test. You will be required to wear non-restrictive clothing and safe footwear for this test (no sandals or flipflops).
6. **Muscle strength:** Hand grip strength will be measured to assess upper body strength using a handheld device. You will squeeze the device as hard as possible for 2-3 seconds, twice for each hand. Leg strength will be measured to assess lower body strength while you attempt to stand and sit as quickly, as many times as possible, for 30 seconds.
7. **Physical Activity and Cardiovascular Health:** You will be asked to wear a heart rate monitor around the chest to collect heart rate and heart rate variability, as well as a physical activity monitor around your hips to collect physical activity over 3 days.

8. **Pulmonary function:** This is a test of how your lungs take in and release air. For this test you will be asked to breathe out into a tube that is attached to a machine that measures the air from your lungs. You will be instructed to take a deep breath and exhale into the mouthpiece as forcefully and quickly as possible, until you have fully emptied your lungs. You will do this test 3 times.
9. **Neurosensory integrity:** You will be asked questions about if you are experiencing any sensory problems (i.e. numbness or tingling) as well as if you have trouble with motor skills (i.e. using your hands or feet).
10. **Questionnaires:** Questionnaires include questions about general and emotional health. Other questionnaires ask about your current drug and alcohol use, ability to participate in social roles and activity, work productivity, activity impairment, quality of life questions, thinking and learning function, and your experience with the remote delivery of the study activities.
11. **Medical clearance and Randomization:** After the baseline assessment has been completed, a study physician will review your results along with your medical record to determine whether or not it is safe for you to participate in this study. A study staff member will discuss your results and inform you to which group you have been assigned and explain when the remaining study activities will occur. If you don't receive medical clearance, you will be contacted by a study staff member.
12. **Review of test results:** After each assessment session, you will receive a report that explains your test results. A study staff member will review the results with you and answer any questions you may have at that time.

Intervention

These are activities that will be completed during the intervention period, for the 20 weeks in between the baseline assessment and at the end of intervention follow up assessment sessions.

Group 1: Individually tailored exercise program

1. **Exercise testing results:** Participants will be provided with the results of their exercise testing.
2. **Program**: Individuals randomized to receive an individually tailored exercise program will virtually meet with an exercise specialist. After the baseline assessment session, the exercise specialist will review the results of their exercise testing and review the exercise program. Written instructions, videos of each strengthening exercise, a blue tooth enabled heart rate monitor, all necessary exercise equipment, and an iPad pre-loaded with heart rate monitor software, exercise videos and a shortcut to the web-based fitness platform (includes video conferencing) will be provided. The exercise specialist will demonstrate the exercises and the individual will practice. The exercise specialist will supervise and provide guidance to the individual via the web-based fitness platform during the first 2 weeks (3 sessions per week). Supervision will slowly decrease to twice a week in weeks 3-4, once a week in weeks 5-8, every other week in weeks 9-16, and to one time midway between weeks 17-20. A short questionnaire will be completed weekly during weeks 1-8 and every fourth week during weeks 9-20. The exercise program will be adjusted depending on the individual's progress.
3. **Adherence:** In order to assure the safety of the individually tailored exercise program and that you learn the exercises, supervision occurs more frequently at the beginning of the intervention. Additional support will be provided if you have difficulty completing the exercises as prescribed or if you repeatedly miss sessions.

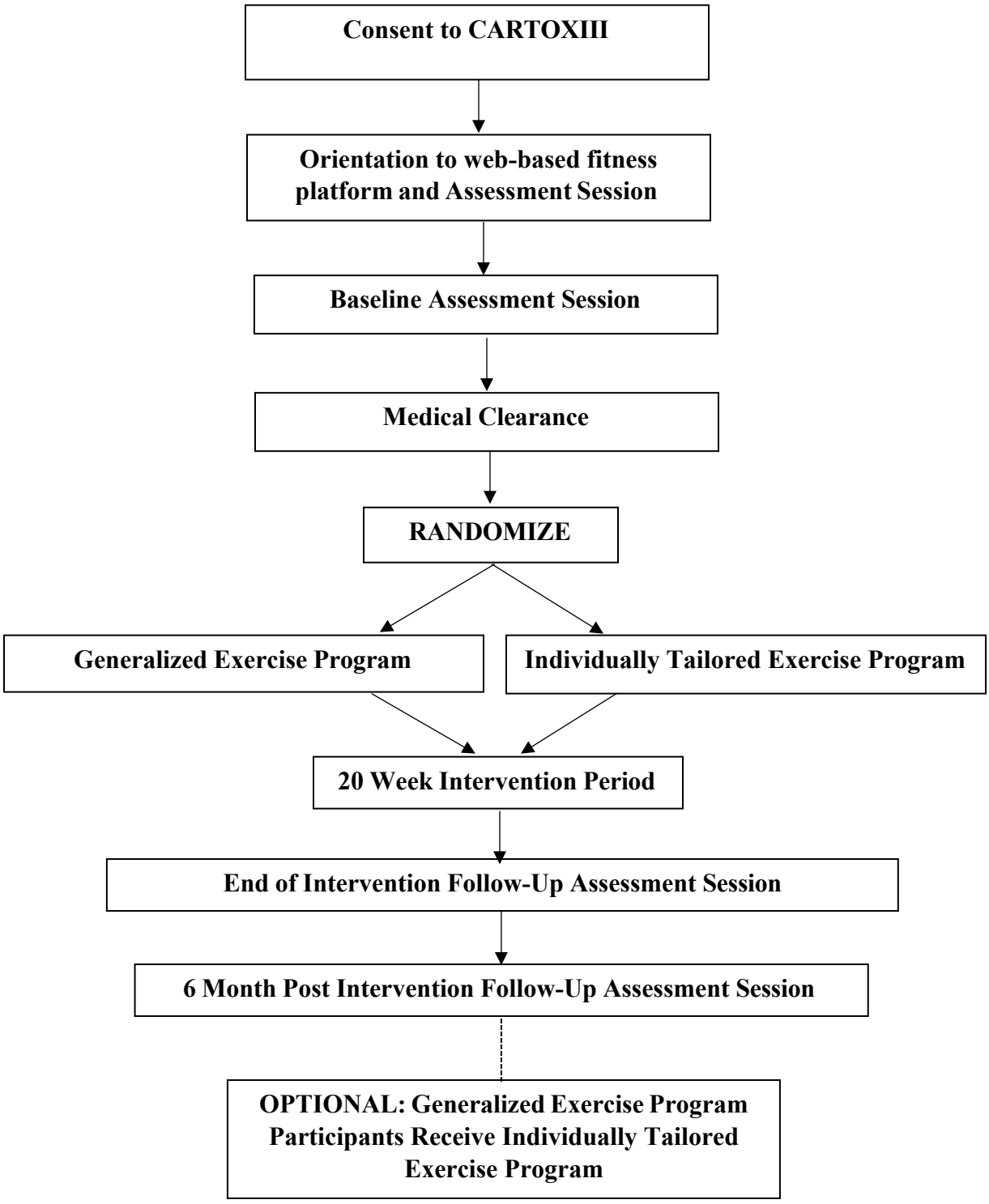
Group 2: Generalized exercise recommendations

1. **Exercise testing results:** Participants will be provided with the results of their exercise testing.
2. **Program:** Individuals randomized to receive the generalized exercise recommendations will receive a copy of the Physical Activity Guidelines for Americans. After the baseline assessment session, an exercise specialist will review these guidelines and answer questions about their exercise testing and encourage them to be physically active. A study staff member will contact them to complete a short questionnaire weekly during weeks 1-8 and monthly for weeks 9-20. At the completion of the assessment at week 44, the participants in Group 2 will be given the option to participate in the 20 week individually tailored exercise program. Participants will be provided an individually tailored exercise prescription, written by an exercise specialist, and approved by the study physician. Participants will be provided with written instructions, videos of each strengthening exercise, the Bluetooth enabled heart rate monitor (a Polar HR monitor – worn on the arm – www.polar.com), all necessary exercise equipment (e.g., bands, weights, hand/foot cycle; equipment will be shipped to the participant's home). These

participants will already have the study provided iPad with a shortcut to the web-based fitness platform.

Diagram of CARTOXIII Study

This chart shows the activities planned in the overall study, which will last about 10 months.



5. What are the risks and benefits of taking part in this study?

a. <u>Risks</u>

These are the main risk(s) of this study:

- **Physical Activity:** This study includes aerobic and strengthening exercises. Since all physical activity carries some risk of injury, there is the slight possibility that study participants may have a physical injury.
- **Cardiovascular Risks:** Engaging in exercise can temporarily increase the risk of cardiovascular events. Such as low blood pressure, causing you to feel dizzy or faint or abnormal heart beats called arrhythmias, which may occur immediately following exercise and should resolve shortly after you stop exercising. Although exceedingly rare, it is possible that exercise could provoke a heart attack.
- **Fitness testing:** The fitness test requires adults to exert physical effort and may result in physical discomfort associated with muscle tightness in the legs or arms, temporary shortness of breath, or light headedness. If you have existing ischemia (lack of blood flow to the heart) or underlying heart damage, you may also experience an abnormal heart rhythm, a drop in blood pressure, chest pain or, in very rare cases, a heart attack. Your heart rate is monitored throughout, and this test will end prior to excessive discomfort. You may choose to discontinue this test at any time by alerting the test administrator. This test requires subjects to exert physical effort that may result in momentary discomfort associated with muscle tightness in the legs or arms, and temporary shortness of breath.
- **Pulmonary function test:** The pulmonary function test requires some forced breathing and you may have some temporary shortness of breath or lightheadedness.
- **Muscle strength:** The study strength test requires you to exert physical effort that may result in momentary discomfort associated with muscle tightness in the hands and thighs and temporary shortness of breath. You may get tired.
- **Questionnaires:** Some of the questions included in the study questionnaires may make you uncomfortable, sad or frustrated. You may choose not to answer those questions.
- **Loss of privacy:** Another risk of this study is loss of privacy. Very rarely, personal information from your records could be given out by accident. This might make you upset, embarrass you or affect your ability to get insurance. To stop this from happening, we:
  - Store records apart from names or other personal information
  - Only allow members of the study team to see the records
  - Store electronic data only on computers protected with a password and encryption software
  - Report study results on the whole group and never identify one single person in any reports

  Protected health information you provide to researchers at St. Jude Children's Research Hospital for this study will not be given to anyone outside of St. Jude unless you agree. Your information will be kept in a locked file cabinet or secure computer database.

b. Benefits

We cannot guarantee that you will receive a direct benefit from taking part in this study. The information we collect may help us make recommendations for the treatment and follow-up of future adults treated for cancer during childhood.

Benefits of this study include receiving your results from exercise testing. Both groups receive exercise guidelines and regular follow up by study staff. You will also get to keep all the study provided equipment, except for the physical activity and heart rate monitors that measure your activity and cardiovascular health over a 3-day period at each assessment session.

6. Can you stop taking part in this study?

a. Can you change your mind about participating in this research study?
You may change your mind about taking part in this research study or stop at any time. The decision will not affect your care or your relationship with your doctor or St. Jude. If available, you may receive routine medical care at St. Jude Children's Research Hospital. You will be allowed to keep any study provided equipment upon completion of the study or if you withdraw early.

b. **Can you be taken out of this study without your consent?**

You may be taken out of the study without your consent for these reasons:

- The researcher decides that staying in the study would harm you.
- You miss so many appointments that we cannot use your data in the study.
- You do not follow the instructions given to you by the study team.
- If we learn, after your enrollment, that you do not meet study enrollment criteria.

7. What are your other options?

You may begin exercising on your own. It is recommended to have your physician medically clear you for exercise before beginning any physical activity program.

8. How much will it cost you?

If you have health care coverage, we will bill your health care insurer for all standard of care services, tests, and procedures. Billing your health care insurer impacts your annual deductible and life-time maximum, if any. This may affect your health care coverage to some extent if you go to another health care provider or institution in the future.

At St. Jude, you will not be responsible for or receive bills for co-pays, co-insurance, deductibles, or similar patient-liability amounts, or for the cost of medical care not covered by your health insurer. This includes research-only costs. Research-only tests and procedures

(such as optional biopsy or blood samples for biomarker testing) will not be billed to you or your health care insurer.

9. Will you be paid for your time or expenses?

You will be paid $25.00 to compensate for your time at each assessment timepoint, after you wear and return the physical activity and heart rate monitors (for a total of $75 if you complete all 3 assessment sessions).

10. What if there is a problem?

If you have any questions about this study or if you are injured because of this study, contact Dr. Kirsten Ness, at 901-595-3300 immediately. If you are injured from being in this research study, St. Jude will offer you reasonable and necessary medical treatment for that injury. If you need more care than St. Jude can provide or if you prefer to seek treatment elsewhere, we will help you find medical care somewhere else. St. Jude may bill your insurance company or other third parties, if appropriate. It is not the hospital's policy to provide payment for other types of costs, such as lost wages, disability, or discomfort if you are injured from being in this study. You are not giving up any of your rights by signing this consent form.

11. How will new findings related to your participation in this study be shared with you?

The researcher will tell you of any new information learned during your study participation which might cause you to change your mind about continuing the study.

12. How will you find out the results of this study?

The researcher will give you information about the overall results of this study. Whether you will know your personal test results will be discussed in another part of this document. St. Jude researchers share information with people in studies in many ways including:

- Articles on www.stjude.org
- In newsletters
- In medical or scientific journals
- In the media
- A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by the U.S. Law. This website will not include information that can identify you. At most the Website will include a summary of the results. You can search this Website at any time.

Published research results will only describe groups of people who took part in the study. Information that points out a single person will not be in research journals or other reports.

13. What about privacy and confidentiality?

Privacy

When you first registered at St. Jude, you received a copy of the St. Jude Notice of Privacy Practices. It tells how your PHI (protected health information) may be used or given to someone outside the hospital. You have the right to read the Notice of Privacy Practices before you sign this form. It may have changed since you first registered at St. Jude. You can find it at the bottom of every page on the St. Jude Internet website: www.stjude.org.

A decision to take part in this research means that you agree to let the research team use and share your PHI with other researchers for purposes of the study explained above. This information will be kept indefinitely. You have the right to see, copy, and ask for changes to your protected health information that will be used or given out. However, research information may not be seen until the end of the study.

Federal agencies such as the Food and Drug Administration (FDA), the Office of Human Research Protections (OHRP), the National Institutes of Health (NIH), and St. Jude Children's Research Institutional Review Board (IRB), your insurance company and other health benefits plan (if charges are billed to these plans), as well as other regulatory agencies, committees, or persons involved in overseeing research studies may review your research and medical record.

Dr. Kirsten Ness and her study team will have access to PHI. This data will be kept confidential by:

- Storing records apart from names and other personal information.
- Only allowing members of the study team to see the records.
- Storing electronic data only on computers protected with a password and encryption software.
- Reporting study results on the whole group and never identify one single person in any report.

Confidentiality

Researchers and study staff are required by law to report suspected child abuse, threat of harm to self or others, and certain diseases that spread from person to person.

To help us protect your privacy, the study has been granted a Certificate of Confidentiality from the federal government. With this Certificate, the researchers cannot be forced to give out your personal information, document or specimen, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other process. The researchers will use the Certificate to block any demands for information or specimens that would identify you, except in the cases listed below.

The Certificate cannot be used to resist a demand for information, documents or specimens from the United States Government, if that information is used to audit or check federally funded projects or to meet the needs of the U.S. Food and Drug Administration (FDA).

You should know that a Certificate of Confidentiality does not keep you or a member of your family from choosing to give out information, documents or specimens about you or your part

in this research. If an insurer, employer, or other person gets your written consent to receive research information, documents or specimens, then the researchers cannot use the Certificate to keep that information private.

The Certificate of Confidentiality will not keep researchers or hospital staff from making reports required of them. These include reports about suspected child abuse, about diseases that spread from person to person, or about possible threat of harm to yourself or others.

14. Permission to Use Your Data/Information: Authorization/HIPAA

If you sign this document, you give permission to Dr. Kirsten Ness and the study team at St. Jude Children's Research Hospital the University of Tennessee Health Sciences Center to use or disclose (release) your health information that identifies you for the research study described in this document.

The health information that we may use or disclose (release) for this research includes your patient reported data.

The health information listed above may be used by and/or disclosed (released) to all researchers and their staff at St. Jude Children's Research Hospital.

St. Jude Children's Research Hospital is required by law to protect your health information. By signing this document, you authorize St. Jude Children's Research Hospital to use and/or disclose (release) your health information for this research. Those persons who receive your health information may not be required by Federal privacy laws (such as the Privacy Rule) to protect it and may share your information with others without your permission, if permitted by laws governing them.

- You do not have to sign this Authorization, but if you do not, you may not receive research-related treatment.

Please note that you may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, St. Jude Children's Research Hospital may still use or disclose health information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to:

HIPAA Privacy Officer
St. Jude Children's Research Hospital
262 Danny Thomas Place, Mail Stop 280
Memphis, TN 38105

This Authorization does not have an expiration date.

15. Further Information and Contact Details for Questions about This Research Study

You are encouraged to ask any questions you wish, before, during or after your treatment. If you have any questions about the study, please speak to your study nurse or doctor, who will be able to provide you with up to date information about the procedure(s) involved. If you wish to read the research on which this study is based, please ask your study nurse or doctor.

If there is anything you do not understand, or have any other questions, please contact the researcher listed below.

IF AT ANY TIME DURING THE STUDY YOU EXPERIENCE ANY DISCOMFORT OR UNUSUAL SYMPTOMS, OR SIDE EFFECTS, PLEASE CONTACT ANY OF THE DOCTORS LISTED BELOW.

Principal Investigator, Researcher:
Dr. Kirsten Ness
St. Jude Children's Research Hospital
262 Danny Thomas Place
Memphis, TN 38105
Tel: (901) 595-3300

If you require any medical or surgical treatments outside of St. Jude such as with your local doctor or another hospital during this study, your researcher and their team would need to be informed.

You can get more details about your rights as a research participant by calling the St. Jude Institutional Review Board at 901-595-4357 or the Research Participant Advocate at 901-595-4644 or 901-595-1139. The Research Participant Advocate is an individual who is not part of the research study team and is available to you to discuss problems, concerns, and questions. The Advocate can help you obtain information and can relay any input you may have concerning the research to the research study team. If you are outside of the Memphis area, please call toll-free 1-866-583-3472 (1-866-JUDE-IRB).

If you decide you would like to take part, then please read and sign the consent form. You will be given a copy of this information and the consent form to keep. A copy of the consent form will be filed in your patient notes, one will be filed with the study records and one may be sent to the Research Sponsor.

You can have more time to think this over if you are at all unsure.

Thank you for taking the time to read this information sheet and to consider this study.

16. Optional Research Tests or Procedures (for newly enrolled participants ONLY that have consented to TBANK)

This section is about an optional research study you can choose to take part in if you participate in the main research study.

You will not get health benefits from any of these optional studies. There are no costs to you or your insurance or other payors. You will not be paid for taking part in these optional studies. If any of the research leads to new tests, drugs, or other commercial products, you will not share in any profits.

By signing this consent form, you are voluntarily and freely donating your samples such as blood, bone marrow, and tumor to St. Jude Children's Research Hospital.

The researchers leading the optional studies hope the results will help other people with cancer, HIV, sickle cell disease and other health problems in the future.

The results from these optional research study will not be added to your medical record nor will you or your doctor know the results.

You can still take part in the main study even if you say "no" to any or all of these optional studies. If you sign up for but cannot complete any of these optional studies for any reason, you can still take part in the main study. If you choose to take part in these studies later, you will be asked to sign a consent form.

What will happen in this Optional Study?
If you agree to take part in the optional study, here is what will happen next:
Optional Study #1

Test/Procedure	Time Point	Purpose
Pathologists will perform research studies on your saliva sample.	Collected during the assessment time points, baseline, end of intervention, and 6 months post intervention.	• To learn more about the aging process in childhood cancer survivors. • Aging biomarkers are a measure of biological age and are present in saliva. • Information gained from this study may help determine how interventions affect biological aging in childhood cancer survivors.
Please select and initial your choice: I agree to have my saliva sample used to study aging biomarkers.		☐ YES: _____ Initials ☐ N/A: _____ Initials ☐ NO: _____ Initials

Samples will be processed at the Hartwell Center and the Cancer Biomarkers Laboratory in the Department of Pathology at St. Jude Children's Research Hospital.

RESEARCH PARTICIPANT STATEMENT (Adult Participants 18 years and older):

I have read this document or it was read to me. I have been encouraged to ask questions and all my questions were answered. I agree to take part in this study.

_____	_____	_____AM/PM
Research Participant Signature	Date	Time (circle one)

RESEARCHER/DESIGNEE STATEMENT: I have explained the research to the participant and his/her parent(s) or legal guardian(s). The research participant and parent(s)/guardian(s) were encouraged to ask questions and all questions were answered to their satisfaction. A copy of this form has been given to the participant or his/her representative.

_____	_____	_____AM/PM
Research/Designee Signature	Date	Time (circle one)

_____

Print Name

_____	_____	_____AM/PM
Interpreter (if needed)	Date	Time (circle one)

PLEASE FAX CONSENT FORM TO CLINICAL TRIALS OPERATIONS
SCAN and EMAIL to: protocoleligibilityoffice@stjude.org or FAX to: (901) 595-6265