Official Study Title: ESTIMATING SETUP UNCERTAINTY IN PEDIATRIC PROTON THERAPY USING VOLUMETRIC IMAGING

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Estimating Setup Uncertainty in Pediatric Radiation Therapy Using Volumetric Imaging

NOTE: "You" refers to 'you' or 'your child' throughout this document. If you are the guardian of a minor or of a person under legal disability who is being asked to take part in this study, you may give consent on his/her behalf. When we talk about research, it can be called a clinical trial, research study or research protocol.

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 have cancer that needs radiation treatment.

B. What is the usual approach to this condition/cancer?
The standard treatment for your type of cancer is radiation therapy. No changes will be made to your standard of care radiation therapy during this study.

C. Why is this study being done?
The purpose of this study is to collect information about how a patient is setup and positioned for radiation therapy. This will help us to improve the setup and position of patients before and during treatment so that the prescribed dose of radiation is received.

D. What will happen if you decide to take part in this study?
You will receive standard of care radiation for up to 7 weeks, depending on your tumor type. During this study you will also receive research imaging scans, called cone-beam computed tomography (CBCT) that will help the doctors put you in the best setup or treatment position.

E. What are the research risks and benefits of taking part in this study?
One benefit to participating in the study is that we can position you more accurately during proton therapy so that the tumor receives the intended prescribed dose. A second possible benefit is that the treatment team will be more likely to detect your movement during treatment and take action to help you lie still if necessary. One study risk is that you will receive a small amount of additional radiation exposure by getting cone beam computed tomography (CBCT). Another risk could be related to possible side effects from anesthesia, which is sometimes required to help keep you still during radiation treatment or scan. Further benefits and risks will be discussed in this consent.

F. How many people will take part in this study?
1000 participants from St. Jude over 5 years.

G. What are your options?
1. Taking part in this research study is completely your choice.
2. If you decide to take part in this study, you can change your mind and stop at any time.

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3. If you decide not to take part in this study, you will still be able to receive care at St. Jude.
4. You may choose no treatment or to seek treatment somewhere else.

If you are still interested in taking part in the SJPROTON2 research study, more detail will be provided in the following pages.

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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 have cancer that requires treatment with radiation therapy. Radiation therapy delivers high radiation doses to the tumor while sparing the normal tissue surrounding the tumor. However, different factors influence how to setup and position a patient to get radiation therapy. We want to study these factors and their impact on radiation therapy delivery to improve the accuracy of radiation therapy in the future. 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.

The principal investigator (researcher) in charge of this study is Dr. Chia-ho Hua, who can be reached by phone at 901-595-3300, if you have any questions or concerns about this research.

3. What is the purpose of this study?

The purpose of this study is to collect information about how a patient is setup and positioned for radiation therapy. By having additional low dose cone-beam computed tomography (CBCT) imaging after selected treatment fractions in addition to standard-of-care pre-treatment CBCT, we will know if you are correctly setup before and during radiation treatment. This study will help us identify patients who are difficult to setup or likely to move or have moved during treatment.

4. What will be done in this study?

Standard of care

- Treatment planning - This will start after the initial consultation with the radiation doctor. During the treatment planning phase, called "simulation", customized devices to help setup and treat you will be created. During this visit, the radiation doctor will decide if you will lay on your stomach or back and if you would need a medicine to sleep during treatment. You will receive a CT scan designed to personalize your treatment plan. Skin marks or "tattoos" will be placed around the tumor area that will help "setup" your treatment target. The marks will be used by the radiation therapists as starting points to "position" you each day on the treatment table before radiation therapy.

- Image-guided positioning - After the radiation therapists align your skin marks with the treatment room lasers, you will receive a CBCT scan to fine-tune your position. CBCT is different from a regular CT scan in that the CBCT allows us to take pictures of a large part of your body with one rotation. We then compare that daily CBCT to the CT simulation

scan that your treatment plan is based on. This allows us to point the radiation to the right spot, by making sure your tumor is precisely in the intended treatment location before the beam is turned on. Here at St. Jude Children's Research Hospital, we have aspecial modified version of the CBCT that allows for better images at lower radiation exposure.

- Proton therapy delivery - After correcting your setup position based on your CBCT, you will receive your prescribed daily treatment and return each day excluding weekends until the end of your radiation therapy course.

Research

If you agree to take part in this study, you will receive between 2-9 additional scans, depending on the length of your radiation therapy course and tumor location.

- Post-correction CBCT – On the first treatment day, you will receive an additional CBCT scan. Normally, we deliver the radiation immediately after the patient's position is corrected based on the routine CBCT scan. This extra scan will be done right after the correction but before the beam is turned on to confirm that your position is indeed very accurate. If your position is not "perfect" (within 1 mm of the intended position), we will make necessary adjustments. You will only have this one post- correction CBCT in the entire treatment course of radiation therapy. If the post- correction CBCT cannot be performed on day 1 due to patient cooperation, time constraint or equipment issues, it will be done during the first week of radiation therapy.
- Weekly post-treatment CBCT – On a weekly basis during the radiation therapy course, you will receive a CBCT scan after your treatment. This scan will tell us if you move during the treatment on that day. Large (>3 mm) movement could cause your tumor to receive a lower radiation dose than prescribed and adjacent critical organs to receive higher doses than necessary. The treatment team will take necessary actions if large motion is discovered. Depending on how long your radiation therapy course is, you may receive a total of 1-6 scans, each scan lasting about 1 minute. This extra scan will require you to lie still on the treatment table for a little bit longer after treatment. If you require anesthesia during your treatment, this will add an additional two minutes of anesthesia time. If you receive craniospinal irradiation (radiation therapy to the entire brain and spinal cord), you will only receive the post-treatment CBCT, once during the entire treatment course.

During the Course of Radiation Therapy

Imaging Studies to be Performed	Day 0	Day 1	Day 2 to the End of Course
Pre-treatment CBCT (standard of care)	**Daily**		
Post-correction CBCT (research)		X	
Post-treatment CBCT (research)	**Weekly**		

5. How long will I be in this study?

The total length of your participation in this study will be between 1-7 weeks, depending on how long you are receiving radiation therapy. Once you have completed radiation therapy, your part in the study will be finished.

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

a. **Risks**

From the research scans, patients will receive a small amount of additional radiation exposure from the CBCT compared to patients who do not participate in this clinical trial. Theradiation dose you receive from these scans is very low, not much higher than the radiation you would normally receive from naturally occurring radiation present in the environment. We are constantly exposed to radiation from the earth, sun, air and food. To help you understand the amount of radiation you will be exposed to during these scans, we will compare it to the limits suggested by the government to be safe for doctors, nurses and scientists who work with radiation every day.

Another risk could be related to possible side effects from anesthesia. Participating in this study will increase your time on the treatment table by about 2-5 minutes (up to 20 minutes for craniospinal irradiation patients) on selected treatment days. If you require anesthesia for treatment, being on this study will make your time under anesthesia slightly longer. If sedation is required to help keep you still during radiation treatment or scan, a member of the sedation team will explain the possible side effects and you will be asked to sign a separate consent form.

The side effects from anesthesia/sedation include vomiting, sore throat, headache or backache, muscle pains, shivering, sleepiness, confusion and/or problems with urinating. With any anesthetic/sedation procedure, there may be serious risks or problems that cannot be prevented, and are not known about ahead of time. These may be allergic reaction, nerve damage, low blood pressure, spasms in the throat, voice box or breathing tubes, problems breathing, slow

breathing, heart attack, brain damage, numbness that does not go away, loss of movement, seizures, unusual reactions, or rarely, death.

Some anesthetics require medical devices around or in the mouth and nose. There may be soreness and bruising in the mouth, nose and throat. Sometimes, but not often, teeth my get knocked loose, chipped or damaged.

Anesthesia risks following the use of sedation and/or anesthetic drugs involve primarily the respiratory system e.g. brief halt in breathing, decreased oxygen saturation, airway obstruction, and possible use of airway devices. Other possible adverse effects include low blood pressure, slowed heart rate, fast heart rate, low body temperature, and possibly delayed awakening.

b. **Benefits**

By performing the CBCT scans, we can position you so that you are in the best possible setup each day for your radiation treatment. A possible benefit of this is that the tumor will receive the intended prescribed dose and normal tissues around the tumor will not be over-exposed to unplanned radiation. An accurate setup is important to maintain the treatment efficacy and help reduce the risk of complications with radiation therapy.

A second possible benefit is that the treatment team will be more likely to detect your movement during treatment if it occurs. Action will be taken to help you lie still if necessary.

7. What are the risks to pregnancy, to an unborn child and to the ability to have children when taking part in this study?

Female Risks:
Female participants must not be pregnant or breastfeeding a baby when entering the study and must not get pregnant during the study. The radiation in this study can be harmful to an unborn baby. You must use effective birth control while on this study. The researcher can tell you about the best methods to use during this study. Some methods might not be approved for use in this study. If you think you have become pregnant during the study, you must notify the researcher immediately. If you become pregnant, you will be taken out of the study. Birth control methods should be continued for 6 months after treatment to avoid pregnancy.

Male Risks:
Male participants who are able to father a child must use an effective form of birth control while on this study. Effective forms of birth control include oral contraceptives (for female partners), condoms and abstinence. Birth control methods should be continued for 6 months after treatment to avoid pregnancy.

8. Can you stop taking part in this study?

You can choose to stop the study at any time. Your taking part in the study is voluntary. Tell the study doctor if you are thinking about stopping or decide to stop. He will tell you how to stop safely. It is important to tell the study doctor if you are thinking about stopping so any risks from the radiation can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

You may refuse to be 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.

9. Can you be taken out of this study without your consent

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

- Your doctor decides that continuing in the study would be harmful for you
- You are unable to keep appointments or take therapy as instructed
- You need a treatment not allowed on this study
- Your condition gets worse
- New information is learned that a better treatment is available, or that the study is not in your best interest
- You become pregnant prior to or during radiation therapy

10. What are your other options?

You could choose not to participate in this trial.

11. 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.

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

You will not be paid for your time or expenses.

13. 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. Chia-ho Hua, 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.

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

We will tell you anything we learn during the study that might cause you to change your mind about staying in the study. If you are interested in learning more about when and how to get the results of this research study, please contact Dr. Chia-ho Hua at 901-595-3300.

15. 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.

16. What about privacy and confidentiality?

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.

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.

We will keep your medical records private to the degree allowed by law. We will not give information from your medical records to anyone outside the hospital unless we are required by law to do so. We will not identify you personally in any publication about this study. No information other than what is needed for the study is recorded.

If you consent to take part in this study, the records obtained while you are in this study as well as related health records will always remain strictly confidential. The information will be held securely on paper and electronically at your treating hospital and the main hospital site managing this research. Your name will not be passed to anyone else outside the research team. You will be allocated a trial number, which will be used as a code to identify you on all trial forms. Any research-related information about you which leaves the hospital will have your name and address removed so that you cannot be recognized. 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.

The study results will be kept in your research record for at least 6 years after the study is finished. At that time, the research data that has not been put in your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will also be kept for an unknown length of time.

Breach of confidentiality: Very rarely, data might be accidentally released from your records that could embarrass you or affect your ability to get insurance. We take several steps to prevent this from happening, including:

- Storing names or other personal information separately from research records
- Limiting access to members of the research team
- Storing electronic data only on password-protected computers
- Reporting study results on the whole group and never identifying individuals in any reports

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

If you sign this document, you give permission to Dr. Chia-ho Hua and his staff at St. Jude Children's Research Hospital 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 information from your medical record, results of physical examinations, medical history, lab tests, and medical tests and procedures.

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.

- The Office for Human Research Protections (OHRP)
- The National Institutes of Health (NIH)
- St. Jude Children's Research Hospital Institutional Review Board (IRB)

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.

18. 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 drug(s)/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. Chia-ho Hua
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.

PARENT/GUARDIAN STATEMENT (Required for participants younger than 18 years): I have read this document, or it was read to me. I have been encouraged to ask questions and all my questions have been answered. I give permission for my child to be in this research study.

_____	_____	_____ AM/PM
Parent/Legal Guardian Signature	Date	Time (circle one)

ASSENT DISCUSSION (Required for participants 7–13 years old)

☐ The research was explained to the minor participant in age-appropriate terms and the minor verbally agreed to take part in the study.

☐ Minor declined to take part in the study. The minor declined for the following reason(s):

_____

☐ An assent discussion was not initiated with the minor for the following reason(s):
- ☐ Minor is under 7 years of age.
- ☐ Minor is incapacitated.
- ☐ Minor refused to take part in the discussion.
- ☐ Other_____

RESEARCH PARTICIPANT STATEMENT (14–17 years old and 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 research 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
Researcher/Designee Signature	Date	Time (circle one)

_____
Print Name

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

*PLEASE FAX CONSENT FORM TO CLINICAL TRIAL OPERATIONS*SCAN and E-MAIL to:
protocoleligibilityoffice@stjude.org Or FAX to: (901) 595-6265

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