Prehabilitation of Frail Surgical Cancer Patients using Remote Ischemic Preconditioning

NCT03853473

Date of Document: December 6th, 2019

Purpose:
Remote ischemic preconditioning (RIPC) was first described three decades ago as an intervention to protect vital organs from ischemic injury. RIPC occurs when a tissue is made transiently ischemic (5 minutes) for repeated bouts (5 times) prior to the longer ischemic insult. Recently it has been shown exercise performance and motor function are improved in young, healthy individuals when RIPC is performed on the arm or leg using a simple blood pressure cuff to occlude blood flow to the limb. The application of RIPC to individuals with reduced functional capacity, however, is largely unexplored. Dr. Durand's group was the first to apply RIPC to chronic stroke survivors with reduced physical function, and two weeks of RIPC increases walking speed, paretic muscle strength and fatigue resistance. Advanced age and cancer are both dramatic accelerators of frailty and frail patients have poor surgical outcomes. Therefore, we propose to apply this non-invasive, simple intervention as a "prehabiliative" therapy to elderly patients with colon cancer during the perioperative period.

Previous Findings and Pilot Data:
RIPC is a safe, well-tolerated, cost-effective, and easy to administer stimulus that has been shown to improve motor function and muscle performance in healthy individuals. Dr. Durand's work in chronic stroke survivors with low physical function demonstrates that two weeks of RIPC improves muscle strength and increases self-selected walking speed. Exercise prehabilitation programs have shown positive effects on physical function in the preoperative period in patients scheduled for abdominal surgery; however elderly, frail colon cancer patients may not have the capacity to exercise at intensities required to derive physiological benefit, and adherence to exercise programs is generally low. The effects of RIPC to improve functional capacity in elderly frail cancer patients is unknown, as is the application of RIPC as a prehabilitative intervention prior to surgery in the elderly.

Hypothesis and Aims:
We hypothesize that daily RIPC for 2 weeks will decrease frailty in elderly colon cancer patients prior to surgery.

Specific Aim 1: Determine the efficacy of RIPC to decrease frailty in the preoperative period. RIPC will decrease frailty as evidenced by increased 6MWT distance in pre-surgical colon cancer patients compared to standard of care colon cancer patients.

Specific Aim 2: Investigate whether RIPC improves functional recovery postoperatively. Frail colon cancer patients who undergo RIPC in the preoperative period will exhibit decreased frailty assessed by the 6MWT 4-weeks postoperatively compared to standard of care patients.

Inclusion Criteria:
- be between ages of 55-85
- have a diagnosis of non-metastatic colon cancer
- be scheduled for curative resection of non-metastatic colon cancer

Exclusion Criteria:
- condition which prevents walking
- any condition in which compression of the arm or transient ischemia is contraindicated (e.g. wounds in the arm)
- neurodegenerative disorder
- unstable angina in previous month
- MI during previous month

Procedures:
1. A member of the study team will pre-screen patients who fit the study criteria by looking at the clinical schedules of Drs. Ludwig, Ridolfi and Peterson daily in Epic

2. When a potentially eligible patient is identified via Epic, the study team member will contact Drs. Ludwig, Ridolfi and Peterson via email prior to the clinic visit. If the patient is identified as a surgical candidate by the surgeon, the surgeon will introduce the study team member to the patient at the conclusion of their surgical consult visit.

3. The study team member will explain the study to the patient in an unoccupied consult room in the colorectal surgery clinical area and obtain written informed consent if the patient is interested.

4. After obtaining consent, the next contact the study team will have with the patient will be in-person at the patient's preadmission testing (PAT) visit (standard of care for colon cancer patients), which will be approximately 3 weeks prior to planned surgery. At the conclusion of the patients PAT clinical visit, a study team member will measure 1) 10 meter walk test, 2) 6 minute walk test, 3) handgrip strength, 4) timed up and go test. These measures will all either be collected in the hallway of the PAT clinic area, or in the case of handgrip and timed up and go, in an unoccupied consult room. The time to conduct all tests is approximately 15-20 minutes.

5. If the patient's 6-minute walk test distance is <80% of their age predicted distance [Predicted distance in 6 minutes (meters) = 868 – (age x 2.9) – (sex x 74.7) where age is in years and “1” is assigned for females and “0” is assigned for males.], they will continue in the study. If their 6-minute walk test distance is >80% of their age predicted norm, they will not be considered "frail" and will be excluded from the study.

6. After baseline measures of frailty are collected, the study participants will be randomized to receive either remote ischemic preconditioning (RIPC) or standard of care

7. Participants in the RIPC group will be given a handheld blood pressure cuff and instructions how to perform the RIPC procedure at home, daily, until their follow-up appointment prior to surgery

8. A member of the study team will call the study participants in the RIPC group 2-3 times to monitor compliance with the intervention.

9. Within 4 days of planned surgery, all participants will return to Froedtert Hospital and have their 6-minute walk test, 10 meter walk test, handgrip strength and timed up and go test re-evaluated at the 2nd floor Outpatient Rehabilitation Gym (Room 2112) by a member of the study team. This will be the conclusion of the intervention period for patients in the RIPC group.

10. Blood pressure variability data from the surgical procedure will be acquired from the anesthetic record

11. Participants will return to the 2nd floor Outpatient Rehabilitation Gym approximately 4 weeks after surgery to have the 10-meter walk test, 6-minute walk test, handgrip strength, and timed up and go test re-evaluated by a member of the study team. This will complete all study procedures.

Individual Procedures:

1. Remote Ischemic Preconditioning (RIPC): A handheld sphygmomanometer (Hokason DS400) and blood pressure cuff (Hokanson SC12) will be given to study participants in the RIPC group. To perform RIPC, the cuff will be inflated to 225 mmHg for 5 minutes on the non-dominant upper arm, then released for a 5-minute recovery period. Five cycles of inflation/recovery will be performed daily. Each participant must demonstrate competence completing a single cycle of inflation/deflation independently to continue with the study. To monitor compliance, participants must complete daily log sheets documenting the time and maximum pressure of each cuff inflation. The research coordinator will also place phone calls on days 3, 7 and 10 after baseline testing to ask if all sessions to date have been completed.

2. 6-Minute Walk Test (6MWT): The 6MWT is a submaximal test that evaluates the integrated responses required during exercise, has been validated in colorectal surgery patients, evaluates endurance during a moderate-intensity task, and predicts recovery after elective colon resection surgery. We will administer the 6MWT in accordance with guidelines set by the American Thoracic Society. For baseline evaluation, after a 10 minute rest, participants will walk down a 50 meter hallway marked in 3 meter increments in either the Preoperative Testing Clinic or 2nd floor Outpatient Rehab Gym at a pace they feel would be tiring after 6 minutes. The hallway will be marked with cones at the turnaround points, laps will be counted with a lap-counter, and the test administrator will ensure no one talks to the participant or crosses their path during the test. Participants will be told to pivot around the cones as quickly as possible and that they can slow down, rest, or stop as needed. Participants will rate their level of fatigue before and after the walk using the 10-point Borg scale of perceived fatigue. After baseline testing, the percent of age- and sex-specific predicted distance will be calculated using the following equation:

Predicted distance in 6 minutes (meters) = 868 – (age x 2.9) – (sex x 74.7) where age is in years and “1” is assigned for females and “0” is assigned for males.48

Since our goal is to examine the effects of RIPC on frail colon cancer patients, only participants who cover a distance ≤80% of the age- and sex-predicted norms will be included in the study. Others have shown that pre-surgical colon cancer patients walk 65 – 74% of age- and sex-specific norms during the 6MWT.

3. 10 Meter Walk Test (10MWT): The 10 MWT is a validated measure to assess self-selected walking speed, considered by some the “6th vital sign”. Slow walking speed has also been identified as one of five metrics which identify frailty, and is a strong predictor of adverse outcomes associated with frailty. In a hallway, participants will walk at their comfortable speed for 20 meters and be timed during meters 5-15 using a stopwatch to assess steady-state walking. 10MWT measures will be done in triplicate.

4. Handgrip Strength (HGS): Weak HGS has also been identified as a metric to identify frail patients. Patients with weak HGS are six times more likely to be frail, and HGS positively correlates with self-perceived fatigue, disability, morbidity, and mortality. Participants will squeeze a hydraulic hand dynamometer as hard as they can three times with their dominant hand and the maximal force generated will be recorded.

5. Timed up and Go (TUG): TUG is the time it takes a person to stand from an armed chair, walk three meters, turn around, walk back, and sit back down. Increased time during the TUG test has also been shown to be a sensitive and specific measure of frailty in elderly patients.

6. Intraoperative Blood Pressure Variability: We will query the Clinical Research Database Warehouse at the Medical College of Wisconsin and intraoperative blood pressure measurements will be extracted for each study participant. No other patient identifiers or clinical data will be revealed. BPV will be assessed as the product of magnitude x duration of SBP excursions outside the SBP range (>135 mmHg or <95 mmHg; area under the curve).

Statistical Analysis:

All statistical analysis will be overseen by Dr. Sergey Tarima, Ph.D. (Co-I). Randomization of frail, pre-surgical colon cancer patients to the two intervention groups will be performed by Dr. Tarima using randomized block designs (randomly chosen block sizes of 3, 6 and 9). Dr. Tarima will work directly with a member of the study team. When a study participant is enrolled, he or she will receive a sequential number which will have a randomization schedule assigned to it (i.e. no intervention or RIPC), and this will be communicated to the study team.

Statistical analysis for the primary study outcome, the change in 6-minute walk test distance in the pre-surgical period, will be based on the analysis of covariance model

(ANCOVA) with two predictors: group membership (RIPC vs. no intervention control) and the baseline value of 6MWT. To investigate power properties, we used a two-sample t-test (under the assumption that there will be no baseline effect of 6MWT). We plan to enroll 48 patients per group, but expect that 6 patients will be lost to follow-up based on an estimated attrition rate of 10-15% during the preoperative period. Thus, 42 patients will be available for comparing the intervention (RIPC) and control groups. Power calculations for a two sample t-test on 40 patients per group show that we will be able to detect a change in 6MWT distance of 30 meters from baseline to 48 hours pre-surgery between the groups with 82% power (SD=46 meters from literature review). A difference of ≥30 meters between the RIPC and standard of care groups is in agreement with previous work done by Gillis and colleagues which examined the effect of exercise prehabilitation on pre-surgical colon cancer patients and showed a difference in 6MWT distance of 41.6 meters between the exercise prehabilitation and standard of care groups. We will apply variance stabilizing transformations (natural logarithm or square root) to make ANCOVA residuals more normal if needed. If these transformations are not sufficient, we will proceed with a Mann-Whitney test. When we add 5% to 40 (asymptotic relative efficiency of Mann-Whitney to t-test is 96% under normality), then the Mann-Whitney test (a nonparametric alternative to the two-sample t-test) with 42 subjects per group will have similar statistical power when data comes from a normal distribution. We will use the same models for our pre-surgery secondary outcomes of self-selected walking speed during the 10-meter walk test, handgrip strength, and timed-up-and-go time.

The analysis of changes in 6MWT from pre-surgical values to 4-weeks post-surgery will be conducted relying on variance stabilizing transformations and ANCOVA; however, the power calculations change. We expect to lose approximately 5 subjects per group from the test conducted 48-hours prior to surgery to 4-weeks post-surgery and have planned for 37 subjects per group at 4 weeks after surgery. At 35 subjects per group for t-test and 37 per group for Mann-Whitney test, the detectable difference in 6MWT distance at 82% power between the groups is 0.7 standard deviations. Based on others work in post-surgical colon cancer patients showing a SD of 46 meters, we expect to detect a difference between the groups of ≥32 meters. We will use the same models for our post-surgery secondary outcomes of self-selected walking speed during the 10-meter walk test, handgrip strength, and timed-up-and-go time.

We will explore the distribution of intraoperative blood pressure variability as measured by area above or below 135 mmHg or 95 mmHg, respectively and apply variance stabilizing transformations. There is no baseline value to adjust for in this analysis. At 40 subjects per groups for t-test and 42 per group for the Mann-Whitney test, the detectable difference at 76% power between the groups is 0.6 standard deviations, and at 0.7 standard deviations difference the power will be 87%. If the number of subjects with all blood pressure data between the upper and lower boundaries (meaning blood pressure variability = 0) is higher than 5, we will rely on exact Mann-Whitney test.

Risks:

1. Remote Ischemic Preconditioning (RIPC): there is a risk that the repeated occlusions of blood flow to arm during the RIPC protocol may cause tingling and numbness in the arm or hand during the cuff inflation period which may be uncomfortable for the study participants.

2. Clinical test of frailty: Study participants may feel tired during the 6MWT and there is a risk that patients could fall during either the 6MWT, 10 meter walk test, or timed up and go test (TUG).

3. Adverse event during 6MWT: there is a small chance that study participants could have a cardiovascular event during the 6MWT.

4. Loss of confidentiality

Safeguarding Against Risks:

1. RIPC: any discomfort related to the occlusion of blood flow to the arm during the RIPC should be minor and transient based on our experience performing the protocol. Based on our experience performing the procedure, and a multitude of other studies which have performed RIPC, we do not anticipate any issues with study participants performing the procedures at home.

2. Clinical tests of frailty: There is a very minimal risk of falling during the walking tests or the timed up and go test. The test administrators will provide contact guard assistance as needed and a gait belt can be worn by participants if deemed necessary by study staff. Participants may feel fatigued during the 6- minute walk test. All participants will be instructed to proceed at their own pace, and there will be chairs at both ends and in the middle of the hallway where the test is being conducted so participants can sit and rest if needed.

3. Adverse event during 6-minute walk test: Although risk of a sudden cardiac event in response to moderate intensity exercise (50-60% target heart rate) in elderly colon cancer patients is relatively rare, we have taken several measures to safeguard the health of our participants. First, all participants will be carefully screened by the PIs or their physician (Drs. Ridolfi, Peterson or Ludwig) prior to exercise to determine the risk of an adverse response to exercise (e.g. uncontrolled hypertension or elevated resting vital signs). Blood pressure and resting heart rate will also be measured by Ms. Nguyen (clinical research assistant) immediately prior to beginning the 6MWT. Second, we will follow the guidelines for conducting the 6-minute walk test established by the American Thoracic Society. Specifically, we will ensure participants have not had unstable angina or a myocardial infarction in the previous month, that participants resting heart rate is below 120 beats per minute, systolic blood pressure is less than 180 mmHg, and diastolic blood pressure is less than 100 mmHg. The sites of 6MWT measurements [Peroperative Testing Clinic (baseline) and 2nd floor Outpatient Rehab Gym (48 hours pre-surgery and 4-weeks post-surgery)] are equipped with Automated External Defibrillators (AEDs), have physicians present at all times, and all members of the study team are certified in basic

life support. We will immediately terminate the 6-minute walk test if participants experience any of the following: chest pain, intolerable dyspnea, leg cramps, staggering, diaphoresis, or they develop a pale or ashen appearance.

4. Loss of Confidentiality: All personal information and protected health information will be collected and stored in a locked file cabinet in Dr. Durand's office. Only necessary research staff will have access to the personal information collected from the patients and access will be supervised by Dr. Durand. Each participant will be assigned a code and the data will be filed according to code.

Informed Consent:

The informed consent process will take place in the Colorectal Surgery Clinic at Froedtert Hospital. We will allow a minimum of 15 minutes to go through the consent and answer any questions. The minimum time between the informed consent process and the beginning of project related procedures will vary for each participant, and this will depend on the time and date of their scheduled surgery. The first project related procedure will occur 2-3 weeks prior to the participant's scheduled date of surgery.

Throughout the informed consent process, the study team member will continuously ask if the subject has any questions or concerns. The study team member will verbally stress the right of the individual to stop at any time, and that stopping will not negatively impact the medical care they are receiving.

Medical College of Wisconsin and Froedtert Hospital

INTRODUCTION TO THE INFORMED CONSENT

Name of Subject: _____

Prehabilitation of Frail Surgical Cancer Patients using Remote Ischemic Preconditioning

Matthew J. Durand, Ph.D.

Physical Medicine and Rehabilitation

414-955-5619

Medical College of Wisconsin

8701 Watertown Plank Road

Milwaukee WI 53226

You are invited to take part in this research. You can decide whether to take part in this project or not. You are free to say yes or no. If there is anything that you do not understand, please ask questions.

Definitions

- **Ischemia** – inadequate blood supply to an organ or part of the body
- **Ischemic preconditioning (IPC**) – a non-invasive treatment in which short bouts of ischemia provide protection to organs or parts of the body
- **Prehabilitation** – physical and/or lifestyle preparation designed to improve a patient's recovery after surgery

Purpose

This project is being done to determine the effects of a safe procedure called ischemic preconditioning (IPC) in patients who plan to undergo surgery for colon cancer aged 55-85.

Length

- You will be in this research project for about 7 weeks.

Procedures

There are two groups in this project, intervention group (who receives IPC) and a control group that receives standard of care (no IPC). You will be randomly assigned to one of these groups. Both groups will perform walking evaluations and strength tests.

List of visits:

- Baseline visit (3 weeks before surgery)
  - Total Number: 1
  - Total Time: 20 minutes
- Pre-surgery visit (1-4 days before surgery)
  - Total Number: 1
  - Total Time: 20 minutes
- Post-surgery visit (4 weeks after surgery)
  - Total Number: 1
  - Total Time: 20 minutes

Procedures that will occur at various visits:

Invasive Procedures
- None

Non-invasive Procedures
- 4 clinical tests measuring walking speed and distance, hand grip

Risks

This is a brief list of the most commonly seen risks The ***full consent form*** after this introduction contains a more complete list of potential research risks.

Intervention risks:

- Discomfort in arm due to ischemic preconditioning
- Tiredness and the possibility of falling during the tests
- Adverse response to exercise
- Loss of confidentiality

Benefits

This project may or may not help you, but we hope the information from this project will help us develop a better regimen for patients who are preparing for colon surgery.

My Other Options

You do not have to join this project. You are free to say yes or no.

- Whether or not you join this project, you are free to seek services from this or other agencies.

If you have more questions about this project at any time, you can call Dr. Durand at 414-955-5619.

If you have questions about your rights as a participant, want to report any problems or

CONSENT TO PARTICIPATE IN RESEARCH

A1. INTRODUCTION – WHY ARE WE ASKING YOU TO PARTICIPATE?

You are being invited to participate in this research because you have been diagnosed with colon cancer and are a candidate for surgery. Because of your condition, you may be eligible for a research study that will examine the effects of a non-invasive procedure, called ischemic preconditioning (IPC), on your physical fitness and mobility before and after surgery.

A total of about 96 people are expected to participate in this research at the Medical College of Wisconsin and Froedtert Hospital.

The Director of the project is Dr. Matthew Durand in the Department of Physical Medicine and Rehabilitation. A research team works with Dr. Durand. You can ask who these people are.

This project is supported by the National Institutes of Health.

A2. DO I HAVE TO PARTICIPATE?

You can decide whether to take part in this research or not. You are free to say yes or no. If you say no, your regular medical care will not change. Even if you join this project, you do not have to stay in it. You may stop at any time.

A3. WHY IS THIS PROJECT BEING DONE?

IPC is a procedure that reduces blood flow to a part of the body for a short time using a cuff, similar to when you have your blood pressure taken. In IPC, when the blood flow is restored, the cells in that part of the body are protected when blood supply is stopped in the future, leading to improvement in muscle performance. People who are being treated for cancer and are undergoing surgery can have decreased physical fitness and increased complications after surgery. In this study, we want to see if preparing for surgery ('prehabilitating') using IPC can improve physical fitness and reduce complications after surgery.

B1. WHAT WILL HAPPEN IF I PARTICIPATE?

You will be "randomized" into one of two study groups. One group will receive the intervention, and another group will not. Randomization means that you are put into a group by chance. It is like flipping a coin. You will have an equal chance of being placed in either group. Neither you nor the research doctor can choose what group you will be in.

All study procedures will be performed by trained research staff. If you feel any discomfort or have any questions during any of your testing procedures, please let a member of the research team know right away. You can stop being in the study at any time. With some of the testing procedures you will be able to rest if you get tired and continue to participate.

1. **Clinical assessments:** A research team member will have you perform various clinical assessments that measure your strength, walking distance, walking speed, and mobility.

    - There will be 3 total sessions involving these assessments: 3 weeks before surgery, within 4 days before surgery, and 4 weeks after surgery. Each session takes approximately 20 minutes to complete.

2. **Ischemic preconditioning (IPC):** We want to measure if preventing blood flow to your arm for short bouts will improve your physical fitness after you have surgery. If you are randomly assigned to this group, you will be given instructions on how to perform this protocol at home, daily, during the 2-3 weeks leading up to the surgery.

    - You will place a blood pressure cuff around your arm and inflate it to a pressure high enough to stop blood flow to your arm.

    - The cuff will be inflated for 5 minutes and then deflated for 5 minutes. This will be done 5 times for a total time of 45 minutes per session.

    - You can do this any time of the day. You will be given worksheets to document the times you do it.

B2. HOW LONG WILL I BE IN THE PROJECT?

You will be in this research project for about 7 weeks. You will be asked to participate in 3 testing sessions at Froedtert Hospital and up to 21 IPC sessions at home.

B3. CAN I STOP BEING IN THE PROJECT?

You are free to withdraw from the project at any time. If you leave, your regular medical care will not change. If you decide to leave the project, please let the research team know.

The research doctor may stop your participation in the project at any time for any reason without your consent. He will tell you if this happens.

C1. WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE PROJECT?

We watch everyone in the project for unexpected problems or side effects. **You need to tell the research doctor or a member of the research team immediately if you experience any problems, side effects, or changes in your health.**

1. **There may be temporary numbness and tingling sensations in the arm while the blood pressure cuff is inflated for 5 minutes.**
    - The discomfort with the inflated blood pressure cuff is generally minor and stops once the cuff is deflated.
    - If the pain persists, please tell the research team and we will stop the procedures.

2. **You may feel tired during the clinical tests, and there is a risk of falling while performing some of the clinical tests.**
    - The research team will provide assistance while you walk and use a walking belt if necessary.
    - You will be encouraged to proceed at your own pace, and there will be chairs where the test is located so you can sit and rest if needed.

3. **There is a risk that you could have heart problems during the walking tests.**
    - Risk of a sudden heart problem in response to mild exercise like walking is relatively rare in colon cancer patients. However, we have taken several measures to safeguard your health.
        - First, all you will be carefully screened by the study personnel to determine risk of a negative response to exercise (e.g., uncontrolled blood pressure, history of heart disease or elevated resting vital signs).
        - Second, all testing sessions will be performed in the hospital and in the presence of physicians and individuals who are certified in basic life support.
        - Third, we will follow guidelines for conducting the test set by the American Thoracic Society.
        - Finally, we will stop the testing if you begin to show signs such as pain, difficulty breathing, excessive sweating, and/or paleness at any time during the test.

Another risk may be loss of confidentiality. Every effort will be made to keep your research records confidential but we cannot guarantee it. Depending on the kind of information being collected, if your research information were accidentally seen, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the project director about whether this could apply to you.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The study team can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The study team will use the Certificate to resist any demands for information that would identify you.

C3. ARE THERE ANY BENEFITS TO TAKING PART IN THE PROJECT?

This project may or may not help you, but we hope the information from this project will help us develop a better routine to prepare patients before they have surgery.

D1. ARE THERE ANY COSTS TO BEING IN THE PROJECT?

There are no costs to you for any of the visits or services you receive in this project. Costs for the routine medical care to treat your condition are not part of this project and will be billed to you/your insurer. If you have questions regarding costs, please contact Dr. Durand.

D2. WILL I BE PAID FOR PARTICIPATING IN THE PROJECT?

You will receive $100 for each visit that involves testing. If all 3 sessions are completed, you will be compensated a total of $300. To pay you, we need your social security number. Any payment may be reportable as income on your taxes.

D3. WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this project. You are free to say yes or no. Whether or not you join this project, your usual medical services will not change.

D4. WILL I BE GIVEN NEW INFORMATION ABOUT THE PROJECT?

If we learn any important new information about the intervention that might change your mind about being in the project, we will tell you about it right away. You can then decide if you want to stay in the project.

D5. WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THE PROJECT?

Emergency medical treatment for injuries directly related to your participation in this research project will be provided to you. You or your health insurance will be billed for the costs of this emergency treatment. MCW will decide on a case by case basis if they will reimburse you or your insurer for emergency treatment costs. If your research-related injury requires medical care beyond this emergency treatment, you or your insurer will be responsible for the costs of this follow-up care.

At this time, there is no plan for any additional financial payments.

If you believe that you have been injured because of your participation in this project, contact the research doctors right away. Contact information: Dr. Durand, 414-955-5619.

Nothing in this consent form affects any legal rights you may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.

D6. WHO CAN ANSWER MY QUESTIONS ABOUT THE PROJECT?

- If you have more questions about this project at any time, you can call Dr. Durand at 414-955-5619.
- If you have questions about your rights as a research participant, want to report any problems or complaints, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

E. PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

E1. What health information will be collected and used for this project?

To be in this research project, the research team needs your permission to access, collect and use some of your health information. If you say no, you cannot be in the project. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the project.

The protected health information (PHI) originates from services you will or have received at one or more of the following locations: the Medical College of Wisconsin (MCW); BloodCenter of Wisconsin (BCW); Children's Hospital of Wisconsin (CHW); any Froedtert Health Affiliate-Froedtert Memorial Lutheran Hospital (FMLH), Inc.; Community Memorial Hospital (CMH) Menomonee Falls, Inc.; St. Joseph's Community Hospital (SJH) West Bend, Inc.; Froedtert & The Medical College of Wisconsin Community Physicians Clinics, Inc. (FMCWCP); the West Bend Surgery Center, LLC; and the Froedtert Surgery Center, LLC.

The health information we will collect and use for this project is:

We will collect your basic information, like your age, height, weight, and sex. We will also collect information regarding your past medical history, such as surgical procedures and any medical diagnosis relevant to our study. We will collect information specific to your cancer, such as the specifics of the cancer location and medications you are taking. We will also collect information related to your surgical procedure such as the type of procedure performed and details from the operating room like your blood pressure and medications given.

E2. Who will see the health information collected for this project?

The only people allowed to handle your health information are those on the research team at MCW/Froedtert Hospital, those on the Institutional Review Board (IRB) and those who check on the research activities to make sure the hospital's rules are followed.

If the costs of any necessary emergency medical treatment in the event of a research-related injury are billed to your health insurance, your health information may need to be disclosed to the insurer for billing purposes.

E3. What are the risks of sharing this health information?

One risk of taking part in a research project is that more people will handle your personal health information collected for this project. The research team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the research doctor about whether this could apply to you.

E4. How long will you keep the health information for this project?

If you sign this form, we plan to keep your information for 10 years after the research project ends in case we need to check it again for this project.

E5. Can I cancel my permission to share this health information?

If you change your mind later and do not want us to collect or share your health information, you need to send a letter to Dr. Matthew Durand at *8701 Watertown Plank Road, Milwaukee, WI 53226*. The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. At that time, we may decide that you cannot continue to be part of the project. We may still use the information we have already collected.

F1. FOR MORE INFORMATION ABOUT THE PROJECT

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.

You can look up this project by referring to the ClinicalTrials.gov number NCT03853473 or by asking the research team for a printed copy.

CONSENT TO PARTICIPATE

By signing my name below, I confirm the following:

- I have read (or had read to me) this entire consent document. All of my questions have been answered to my satisfaction.
- The project's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the research team use and share the health information and other information gathered for this project.
- I voluntarily agree to participate in this research project. I agree to follow the procedures as directed. I have been told that I can stop at any time.

IMPORTANT: You will receive a signed and dated copy of this consent form. Please keep it where you can find it easily. It will help you remember what we discussed today.

Subject's Name *please print*	**Subject's Signature**	**Date**