Mass General Brigham

Research Consent Form
General Consent Form Template
Version Date: November 2022

Subject Name:

MRN or DOB:

Subject Identification

Protocol Title: Treatment of Post Traumatic Knee Osteoarthritis with Extracorporeal Shockwave Therapy

Principal Investigator: Adam Tenforde

Site Principal Investigator: Kirstin Small

Description of Subject Population: Adults age 18-55 with post-traumatic knee osteoarthritis following ACL reconstruction

About this consent form

Please read this form carefully. It tells you important information about a research study. A member of our research team will also talk to you about taking part in this research study. People who agree to take part in research studies are called "subjects." This term will be used throughout this consent form.

If you decide to take part in this research study, you must sign this form to show that you want to take part. We will give you a signed copy of this form to keep.

Key Information

We are asking you to be in a research study. This form will tell you what you should expect if you agree to be in the study. You will find more information about each of the following points later in this form.

It is your decision whether or not to join the study. We are asking you to be in this study because you are a current or former athlete who had ACL reconstruction surgery over a year ago and have been diagnosed with knee osteoarthritis (OA) or have suspected OA based on pain. We are doing the research to investigate the effects of extracorporeal shockwave therapy (ESWT) on pain, function, biomechanics, knee range of motion and strength, inflammation, and joint structure and integrity of your knee. If you agree, you will complete questionnaires and physical measures of your knee and will be assigned to a true shockwave or sham shockwave group and will attend a total of seven to eleven in-person assessment and treatment visits over the course of four to eight months depending on your treatment group assignment. Each session will last approximately one to three hours. If you decide to participate for this part of the study, the study will take 8 months total.

The main risks of being in the study are tripping or falling, bruising, bleeding, skin irritation, muscle soreness, very low risk of infection from blood draw, and exposure to low amounts of radiation.

Benefits of participating in this study include ESWT treatment for osteoarthritis that may aid in your symptoms. Through participation in the study, you may help us understand how osteoarthritis develops after ACL reconstruction surgery and treatment options for this condition.

You will be paid $450 for taking part in this research study. You will find more information about the payment amount for each visit and a plan if you do not complete all study visits later in this form. Additionally, you will receive a report from your biomechanical analysis, valued at $350. You can call us with your questions or concerns. Our telephone numbers are listed below. Ask questions as often as you want.

Adam Tenforde, MD, is the person in charge of this research study. You can call him at (617) 952-6800 from Monday to Friday 9am-5pm. You can also call **Logan Gaudette and Michelle Bruneau at (617)-234-7724 from Monday to Friday 9am-5pm** with questions about this research study.

If you have questions about the scheduling of appointments or study visits, call **Logan Gaudette or Michelle Bruneau at (617)-234-7724.**

If you want to speak with someone **not** directly involved in this research study, please contact the Mass General Brigham IRB. You can call them at 857-282-1900.

You can talk to them about:

- Your rights as a research subject
- Your concerns about the research
- A complaint about the research
- Any pressure to take part in, or to continue in the research study

Detailed Information

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.

Why is this research study being done?

The purpose of this research study is to investigate the effects of extracorporeal shockwave therapy (ESWT) on pain, function, biomechanics, knee range of motion and strength, inflammation, and joint structure and integrity in individuals diagnosed with post traumatic osteoarthritis after ACL reconstruction. The results may help understand future treatment options for this condition and advance research on this topic.

The U.S. Food and Drug Administration (FDA) has approved extracorporeal shockwave therapy (the OrthoPlus Ultra 100/radial D-Actor and Duolith focused shockwave devices) to treat minor muscle aches and pain, temporary increase in local blood circulation, activation of connective tissue, and for treatment of plantar fasciitis, but the FDA has not approved extracorporeal shockwave therapy to treat knee osteoarthritis**.**

Who will take part in this research?

This study will involve current or former athletes who had ACL reconstruction surgery using an autograph (your own tissue) or allograft (donor tissue) over a year ago and have been diagnosed with osteoarthritis (OA). Up to 70 participants may be recruited for this study.

The President and Fellows of Harvard College and Department funds are paying for this research to be done. Storz Medical, the medical company that created the shockwave devices that will be used in this study, is also sponsoring the study.

What will happen in this research study?

If you decide to take part in the study you will be asked to come to the lab at the Spaulding Outpatient Center, Cambridge, as well as one of the MGB radiology sites for an MRI. You will be randomly assigned to one of two treatment groups: true ESWT or sham ESWT; however, regardless of the initial assigned treatment group, you will have an opportunity to receive ESWT treatment. The study is designed to be performed over seven in-person sessions, but you may elect to complete eleven in-person sessions if you wish to receive ESWT treatment based on your initial treatment group assignment. Below is a description of each visit.

If you choose to take part in this study, we will ask you to sign this consent form before we do any study procedures.

Baseline Visit 1
The first Baseline Visit will occur at Spaulding Rehabilitation Hospital in Cambridge, MA and will take about three hours. At this visit, we will review the online screening questionnaire that you completed to ensure that you still qualify to participate in the study. If you don't qualify, the study research personnel will tell you why.

At this visit, we will:

- Ask you to complete questionnaires on your medical history, health, pain, and functionality of your knee, limb dominance, emotional well-being, and health status
- Measure your height and leg length
- Assess bone health with a DEXA scan
- Perform X-rays of your knees
- Assess mobility and strength of your knees and thigh muscles
- Assess your walking and running mechanics
- Measure inflammation and electrical characteristics of your knee joint
- Assess pain sensitivity of your knee joint

Baseline Visit 2
The second Baseline Visit will occur at Brigham and Women's hospital and will take approximately one hour. At this visit, you will have an MRI on your knee that you had ACL reconstruction surgery and that has osteoarthritis.

Treatment Visit 1
The first Treatment Visit will occur at Spaulding Rehabilitation Hospital in Cambridge, MA and will take about one hour.
At this visit, we will:

- Randomize you to the true shockwave group or sham shockwave treatment group
- Review exercise program
- Ask you to complete questionnaires to help us understand any variables that may influence the frequency of biomarkers found in your blood
- Draw two blood samples (venous blood draw and finger stick)
- Administer shockwave or sham shockwave to your knee and surrounding muscles

Treatment Visit 2

The second Treatment Visit will occur at Spaulding Rehabilitation Hospital in Cambridge, MA and will take about one hour. This visit will occur approximately seven days following Treatment Visit 1.
At this visit, we will:

- Draw finger stick blood sample
- Ask you to complete questionnaires to help us understand any variables that may influence the frequency of biomarkers found in your blood
- Administer shockwave or sham shockwave to your knee and surrounding muscles

Treatment Visit 3
The third Treatment Visit will occur at Spaulding Rehabilitation Hospital in Cambridge, MA and will take about one hour. This visit will occur approximately seven days following Treatment Visit 2.
At this visit, we will:

- Draw finger stick blood sample
- Ask you to complete questionnaires to help us understand any variables that may influence the frequency of biomarkers found in your blood
- Administer shockwave or sham shockwave to your knee and surrounding muscles
- Complete questionnaires that you filled out during Baseline Visit 1

Follow Up Visit 1: 8 (NOT in person)
At eight weeks after Treatment Visit 3, you will be emailed a secure link to electronically complete questionnaires that you filled out during Baseline Visit 1.

Follow Up Visit 2 (In person)
Follow up Visit 2 will occur at Spaulding Rehabilitation Hospital in Cambridge, MA four months following Treatment Visit 3 and will take about 2.5 hours.

At this visit, we will:

- Ask you to complete questionnaires completed during Baseline Visit 1
- Assess mobility and strength of your knees and thigh muscles
- Assess your walking and running mechanics
- Measure inflammation and electrical characteristics of your knee joint
- Assess pain sensitivity of your knee joint
- Draw a blood sample
- Ask you to complete questionnaires to help us understand any variables that may influence the frequency of biomarkers found in your blood

Follow Up Visit 3 (In person)
Follow up Visit 3 will occur at Brigham and Women's hospital and will take approximately one hour. At this visit, you will have an MRI on your knee that you had ACL reconstruction surgery and that has osteoarthritis. This visit will occur within 2 weeks of Follow Up Visit 2.

If you were assigned to the sham shockwave treatment group, you will have the option to receive shockwave treatment. Treatment Visits 1 through 3 will be performed as listed above but this time you will receive true shockwave. You will complete a final follow up visit at 8 months. Each of the following measures will be repeated at the final follow up visit.

The following measures will be taken during the study:

Questionnaires
You will be asked to complete 10 short questionnaires on your basic demographic information (i.e. age, gender), pain, function, quality of life, limb dominance, diet and exercise on the day of each testing session, and menstrual history (females only) electronically.

Height & Leg Length
Your height will be measured with a wall-mounted stadiometer while your leg length will be measured with a tape measure.

Dual-energy X-ray Absorptiometry (DXA) scans
Bone mineral density scans will be completed at Spaulding Rehab Hospital Cambridge. Hip, lumbar spine, and total body scans will be performed. These scans will be performed using dual-energy x-ray absorptiometry (DXA). DXA is a whole-body scan that is used to measure body fat, muscle, and bone density. This assessment will take approximately 30 minutes to complete. These scans will use a dose figure of 0.026 mSv, which is equivalent to the does one gets in about 2 to 3 days through natural background radiation in the USA, which is 3 mSv per year on average. Scans will be performed by licensed and experienced technicians who follow standard quality control procedures. You will be asked if there is any possibility that you are pregnant. If you respond that there is a possibility that you may be pregnant, a urine pregnancy test will be provided.

Knee Radiographs (X-rays)

The X-ray imaging will take place at Spaulding Hospital Cambridge by trained technicians. X-rays use a form of electromagnetic radiation to take pictures of the human body. This assessment should take approximately 15 minutes to complete.

- Research personnel will bring you to the X-ray imaging department and check you in.
- A technologist will bring you into the imaging room and position you in a standing position. You will be asked to stand completely still and may hold onto a bar if you need to. Pictures of your knees will be taken

Knee Non-Contrast MRI

You will have an MRI (magnetic resonance imaging) of your knee obtained at enrollment and repeated at 4 months. If you participate in the elective cross-over portion of the study, you will complete a third MRI scan 8 months from time of enrollment. These visits will take place at Brigham and Women's hospital in Boston, Massachusetts. We will use Magnetic Resonance Imaging (MRI) to take images of your knee. The MRI scanner uses magnetic fields and radio waves to make a picture. This is a test that is routinely used in medical care. We will not inject you with any dyes.

We will ask you some standard questions to make sure that it is safe for you to have the MRI scan. A trained technician will also be able to answer any questions you may have.

- Because MR imaging uses a large magnet, you will be asked to remove all metal items before the scan. If you have certain metal implants you may not be able to have this scan.
- The scanner is shaped like a tunnel. You will be asked to lie on your back on the scanner table and stay still for the duration of the scan. You may have measuring devices placed on you such as ECG (electrocardiogram) sticky pads, which will be placed on your chest to record your heartbeat and a finger monitor which will measure the amount of oxygen in your blood.
- You will need to lie very still during the scan. You will be able to hear and speak to the research staff at all times during the scan. The MR scanner makes loud knocking or beeping sounds during imaging; earplugs will be provided to help reduce this noise.
- We will be taking detailed pictures of your knee which will last approximately 30 minutes.

You will be able to hear and speak to the research staff at all times during the scan. We can stop the scan at any time, if needed.

Thermal Imaging

Thermal patterns at your knee will be measured to learn about the inflammatory state of your joint. The measure will be taken before and after the biomechanical assessments and in between

the instrumented treadmill and overground assessment (3 times per session, 6 times total across the study). Thermal imaging will be taken using a thermal camera. Before the first thermal images are taken you will spend at least 10 minutes in the same room with your knee exposed and without touching your other knee to allow for knee thermal patterns to normalize. Images will then be taken of your knee joint bent at a 90-degree angle from the front and both sides of your knee while you are seated or lying on your back.

Tissue Electrical Characteristics

Tissue electrical characteristics of the knee joint will be measured using bioimpedance, a device that measures electrical currents. Sensors applied with gel will be placed on both sides of your knee joint to measure the electrical currents through your knee joint. You may feel a strong vibration. If it becomes uncomfortable, you can ask research personnel to turn off the device at any time. These measures will be taken before and after the biomechanical assessment.

Quantitative Sensory Testing

Pressure Pain Threshold (PPT) to assess pain sensitivity at the knee will be measured with a device called an algometer. This device will apply a pressure at the inside of your knee. Pressure will be gradually applied until it becomes painful, at which point you will tell the research personnel to stop. This will be repeated three times on each knee. You determine what feels like pressure compared to pain and can tell the research personnel to stop at any time.

Knee Range of Motion

Knee range of motion measurements will be taken by trained research personnel to determine how much motion you have in your knees. You will lie on your back on a treatment table and research personnel will measure how far you can straighten and bend your knees. Two measurements will be performed on each knee.

Dynamometry to Assess Knee Strength

You will sit on the end of a treatment table with straps around your hip and lower leg. A device called a dynamometer, which measures knee strength and power, will be secured to your lower leg. You will be asked to kick out as hard and fast as you can. We will record measurements of your knee strength and power. You will complete a warm-up that will consist of kicking your leg out and contracting your thigh muscle at 50, 75 and 100% of your self-perceived maximal effort with one minute of rest between each muscle contraction. After the warm-up, you will complete six maximal contractions, holding for approximately 3 seconds, with one minute of rest between each contraction. This will be performed on each leg.

Biomechanics:

The biomechanics assessment will involve recording your walking and running motion using digital video. Your confidentiality will be preserved by videotaping from the shoulders to your feet. Additionally, it will involve attaching reflective markers to your body and recording your movement using a system of high-speed cameras, recording your force through force plates inside the treadmill as well as attaching sensors to your trunk and leg muscles and joints (accelerometers and EMG) to see how quickly your legs move to produce force and to measure the activity of your muscles while walking and running.

Overground protocol

After we have attached the markers and/or sensors we will be using, you will be asked to walk along a walkway at your comfortable speed. You may be asked to repeat the walk until we can collect 10 trials with all the required data. This means you may have to walk across the walkway more than 10 times. You may also be asked to run at your comfortable speed. We may ask you to repeat the run until we have collected at least 10 trials with all the data that we need.

Treadmill protocol

Data collection will occur at the Instrumented Treadmill Laboratory. The treadmill assessment may involve participants first completing 3 vertical jumps on the treadmill while the treadmill belt is off so that no movement of the belt occurs. Participants may then walk on the treadmill at a self-selected and/or lab specified speed (approximately 3.0 mph). If you are comfortable with treadmill running, they may then run at a self-selected speed and standard lab speed (approximately 6.0 mph). You may also be asked to run at a variety of self-selected speeds representative of what they experience during training for their specific sport. Treadmill speed will be controlled by the investigator with participants providing feedback. The treadmill may be stopped at any time by the investigator or the participant via emergency stop buttons.

Blood Draw /Finger Stick

Throughout the study, there will be venous blood draws and point of care testing done using a fingerstick (or earlobe) capillary blood collection. The venous blood draws will occur during the first treatment visit and at the completion of the study (4 months). If you elect to participate in shockwave treatment if you were assigned to the other treatment group, another venous blood draw will occur at 8 months. The fingerstick blood collection will occur at each treatment visit for a total of three visits. If you elect to participate in shockwave treatment if you were assigned to the other treatment group, you will have a fingerstick blood collection at each of the three treatment visits, for a total of 6 fingerstick blood collections during the study. This is approximately 2 tablespoons.

Extracorporeal shockwave therapy (ESWT)
You will receive three treatments of either shockwave or sham shockwave. ESWT is a non-invasive, handheld therapeutic treatment device that is used to alleviate pain and promote healing of injured bones, tendons, ligaments, and muscles. When you receive shockwave therapy a gel will be applied to your skin. The study staff will then use a handheld device that will be placed in contact with your skin. The radial shockwave device will generate a pressure wave that results in a strike to the injured area from the device. The focused shockwave device will generate a sound wave that results in noise as energy is transmitted to the injured area from the device. You may feel some discomfort in the form of pressure, vibration, or pain. The machine providing the treatment will make a loud noise. If you elect to participate in shockwave treatment if you were assigned to the sham condition initially, you will have three additional shockwave treatments.

Study Information Included in Your Electronic Medical Record

A notation that you are taking part in this research study may be made in your electronic medical record. Information from the research that relates to your general medical care may be included in the record (for example, list of allergies, results of standard blood tests done at the hospital labs). Please ask your study doctor if you have any questions about what information will be included in your electronic medical record.

If you do not currently have an electronic medical record within MGB, you will be asked to register in the system as an MGB research participant and will be assigned a research medical record.

Mass General Brigham has an electronic system that lets your study doctors know if you are admitted to a Mass General Brigham Hospital, or if you visit a Mass General Brigham Hospital Emergency Department. We want to make sure the study doctors know about any possible problems or side effects you experience while you are taking part in the study.

How may we use and share your samples and health information for other research?

The information we collect in this study may help advance other research. If you join this study, we may remove all information that identifies you (for example, your name, medical record number, and date of birth) and use these de-identified samples and data in other research. It won't be possible to link the information or samples back to you. Information and/or samples

may be shared with investigators at our hospitals, at other academic institutions or at for-profit, commercial entities. You will not be asked to provide additional informed consent for these uses.

Will you get the results of this research study?

You will receive a biomechanical analysis containing a subset of the data collected during your data collection. This analysis may only be providable if all sections of the study are completed. We will also give you bone density (DXA) results and x-ray results along with MRI results at end of study.
You and your doctor should not expect to get information about the results of the research study or the results of your individual participation in the research study. We will study samples and information from many people. It could take many years before anyone knows whether the results have any meaning. There is a small chance that we could find out something from the study that might be important to your health. If this happens, we may contact you to find out if you would like to learn more. However, even if we find something important to your health, we cannot guarantee that you will be contacted.

What are the risks and possible discomforts from being in this research study?

Biomechanical Assessment
It is possible that you could slip, trip, or fall while on the treadmill or running through the laboratory. However, we will take precautions to reduce the chance of something like that happening. Treadmill speeds will be increased and decreased gradually. You will only be asked to run at speeds that you typically run and are comfortable with. The treadmill has a handrail that you can grab to steady yourself, and there is an emergency stop button on the handrail that you can push to stop the treadmill. The investigator will have the ability to stop the treadmill immediately in the case of an emergency. As with all physical activity, there is risk of musculoskeletal injury or cardiovascular events. However, we will not require you to stress yourself beyond your typical activity level. It is unlikely, but possible, that you may experience mild irritation from the tape adhesive on your skin. However, if you are being tested on the treadmill, you will be provided cues to keep you centered on the treadmill belt and the belt will be kept clear and free from debris. In the case of overground trials, the runway will be kept clear and free from debris.

Quantitative Sensory Testing

This test will temporarily elicit pain at the localized testing site on the knee to test this measure. You can ask the examiner to stop at any time. Soreness or bruising may occur at the localized site following testing.

Dynamometry to Assess Knee Strength

There may be a risk of bruising or skin irritation at placement site of the dynamometer and straps; however, we will minimize this by placing padding in between the limb and device and straps. Soreness may occur in the quadriceps muscle after multiple testing trials.

Tissue Electrical Characteristics

There may be slight discomfort with the removal of the electrodes as the adhesive may remove some hair or skin. You may experience skin irritation or burns from the sensors from the tissue electrical characteristics measures.

Blood Draw /Finger Stick

Possible risks of using a finger stick to draw drops of blood include discomfort from the fingerstick, bleeding, and bruising. Risks of drawing venous blood sampling include discomfort, bruising, and bleeding where the needle is placed. Rarely, an infection may occur at the place where the needle was inserted, but appropriate procedures will be taken to reduce this risk. Rarely, you may also feel faint or lightheaded during or shortly after blood drawing. To reduce the risk of injury, all blood draws will occur with you seated or laying down. You will also be educated on the importance of hydration before, during, and after venous blood draws.

ESWT

Treatment with ESWT may produce pain during treatment based on the proposed mechanisms for treatment and best clinical practice of targeting injured areas Reported discomforts of shockwave include bruising, swelling, increased pain. You can ask trained research personnel providing treatment to decrease the intensity or stop at any time during the treatment. You will be provided with a pre and post-treatment protocol of what to expect and we will monitor you for adverse events following ESWT.

Ionizing Radiation Risk Language: DEXA

As a result of your participation in this study, you will be exposed to radiation from DXA. Please ask your doctor if the study is necessary for your medical care or is for research purposes only. The total amount of radiation exposure you will receive from taking part in this study is equal to a whole-body exposure of fraction of a milliSieverts (mSv). A mSv is a unit of radiation dose. One gets about 3 mSv in a year from natural background sources from the earth and the sky.

Scientists disagree on whether radiation doses at these low levels are harmful. A possible effect that could occur at doses used in this study is a slight increase in the risk of developing cancer later in life. If you are pregnant or breast feeding, you may not be able to participate in this research study.

Bone mineral density scans will be completed at Spaulding Rehab Hospital Cambridge. Hip, lumbar spine, and total body scans may be performed. These scans will be performed using dual-energy x-ray absorptiometry (DEXA, GE Lunar, GE Healthcare, Chicago, IL). Scans will be performed by licensed and experienced technicians who follow standard quality control procedures.

Ionizing Radiation Risk Language: Radiographs (X-rays)

As a result of your participation in this study, you will be exposed to radiation from X-rays. Please ask your doctor if the study is necessary for your medical care or is for research purposes only. The total amount of radiation exposure you will receive from taking part in this study is equal to a whole-body exposure of fraction of a milliSieverts (mSv). A mSv is a unit of radiation dose. One gets about 3 mSv in a year from natural background sources from the earth and the sky.

Scientists disagree on whether radiation doses at these low levels are harmful. A possible effect that could occur at doses used in this study is a slight increase in the risk of developing cancer later in life. If you are pregnant or breast feeding, you may not be able to participate in this research study.

X-rays of both knees will be completed at Spaulding Rehab Hospital Cambridge. Scans will be performed by licensed and experienced technicians who follow standard quality control procedures.

Risks of the MRI Scans.

Scans MRIs use powerful magnets to make images. There are no known radiation risks associated with MRI. However, persons with metal implants, such as surgical clips, or pacemakers should not have an MRI. All credit cards and other items with magnetic strips should also be kept out of the MRI room. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow tube. The MRI makes loud banging noises as it takes images. Earplugs can be used to reduce the noises. The MRI can be stopped at any time at your request. If you are or suspect you are pregnant, you should not

participate in this study. The MRI has the potential, during normal routine use, to cause localized warming of your skin and the underlying tissues. You should immediately inform us if you experience discomfort due to warming and the procedure will be stopped.

Some people experience dizziness or rarely nausea when going into an MRI scanner and these sensations may be more common in scans with higher magnetic fields. In most cases, these symptoms only last a short time. However, some people may experience them throughout the scan and/or continue to experience them for a short period of time after; generally, less than half an hour. No case of permanent problems is known.

What are the possible benefits from being in this research study?

You will receive ESWT treatment for post traumatic OA, which may aid in your symptoms. Information on your biomechanics, imaging and laboratory test results that have standard values will be provided. Your participation in the study may help to influence how PTOA is treated in the future.

Can you still get medical care within Mass General Brigham if you don't take part in this research study, or if you stop taking part?

Yes. Your decision won't change the medical care you get within Mass General Brigham now or in the future. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could make you change your mind about taking part in this research study.

What should you do if you want to stop taking part in the study?

If you take part in this research study, and want to drop out, you should tell us. We will make sure that you stop the study safely. We will also talk to you about follow-up care, if needed.

Also, it is possible that we will have to ask you to drop out of the study before you finish it. If this happens, we will tell you why. We will also help arrange other care for you, if needed.

Will you be paid to take part in this research study?

You will also be given up to $450 for time required to participate in the study. Payment will be dispensed based on the amount of time and visits spent participating in the study. $100 will be given to you after baseline visits 1 and 2 are completed. $50 will be given out after the 3 treatment sessions have been completed. Another $50 will be given out after the follow up questionnaire's are completed (follow up visit 1). $100 will be given out after follow up visits 2 and 3 are completed. If you were originally placed in the sham shockwave arm and you elect to cross over, another $50 will be given out after the treatment sessions are completed. After all follow up sessions are completed, another $100 will be given out. You will also receive a report from your biomechanical analysis, valued at $350. Free parking is also available for participants at Spaulding Hospital Cambridge.

We may use your samples and information to develop a new product or medical test to be sold. The Sponsor, hospital, and researchers may benefit if this happens. There are no plans to pay you if your samples or information are used for this purpose.

What will you have to pay for if you take part in this research study?

You are not required to pay to take part in this research study.

Study funds will pay for certain study-related items and services. We may bill your health insurer for, among other things, routine items and services you would have received even if you did not take part in the research. You will be responsible for payment of any deductibles and co-payments required by your insurer for this routine care or other billed care. If you have any questions about costs to you that may result from taking part in the research, please speak with the study doctors and study staff. If necessary, we will arrange for you to speak with someone in Patient Financial Services about these costs.

What happens if you are injured as a result of taking part in this research study?

We will offer you the care needed to treat any injury that directly results from taking part in this research study. We reserve the right to bill your insurance company or other third parties, if appropriate, for the care you get for the injury. We will try to have these costs paid for, but you may be responsible for some of them. For example, if the care is billed to your insurer, you will be responsible for payment of any deductibles and co-payments required by your insurer.

Injuries sometimes happen in research even when no one is at fault. There are no plans to pay you or give you other compensation for an injury, should one occur. However, you are not giving up any of your legal rights by signing this form.

If you think you have been injured or have experienced a medical problem as a result of taking part in this research study, tell the person in charge of this study as soon as possible. The researcher's name and phone number are listed in the beginning of this consent form.

If you take part in this research study, how will we protect your privacy?

Federal law requires Mass General Brigham to protect the privacy of health information and related information that identifies you. We refer to this information as "identifiable information."

In this study, we may collect identifiable information about you from:

- Past, present, and future medical records
- Research procedures, including research office visits, tests, interviews, and questionnaires

Who may see, use, and share your identifiable information and why they may need to do so:

- Mass General Brigham researchers and staff involved in this study
- The sponsor(s) of the study, and people or groups it hires to help perform this research or to audit the research
- Other researchers and medical centers that are part of this study
- The Mass General Brigham ethics board or an ethics board outside Mass General Brigham that oversees the research
- A group that oversees the data (study information) and safety of this study
- Non-research staff within Mass General Brigham who need identifiable information to do their jobs, such as for treatment, payment (billing), or hospital operations (such as assessing the quality of care or research)
- People or groups that we hire to do certain work for us, such as data storage companies, accreditors, insurers, and lawyers
- Federal agencies (such as the U.S. Department of Health and Human Services (DHHS) and agencies within DHHS like the Food and Drug Administration, the National Institutes of Health, and the Office for Human Research Protections), state agencies, and

foreign government bodies that oversee, evaluate, and audit research, which may include inspection of your records

- Public health and safety authorities, if we learn information that could mean harm to you or others (such as to make required reports about communicable diseases or about child or elder abuse)
- Other:

Some people or groups who get your identifiable information might not have to follow the same privacy rules that we follow and might use or share your identifiable information without your permission in ways that are not described in this form. For example, we understand that the sponsor of this study may use your identifiable information to perform additional research on various products or conditions, to obtain regulatory approval of its products, to propose new products, and to oversee and improve its products' performance. We share your identifiable information only when we must, and we ask anyone who receives it from us to take measures to protect your privacy. The sponsor has agreed that it will not contact you without your permission and will not use or share your identifiable information for any mailing or marketing list. However, once your identifiable information is shared outside Mass General Brigham, we cannot control all the ways that others use or share it and cannot promise that it will remain private.

Because research is an ongoing process, we cannot give you an exact date when we will either destroy or stop using or sharing your identifiable information. Your permission to use and share your identifiable information does not expire.

The results of this research study may be published in a medical book or journal, or used to teach others. However, your name or other identifiable information **will not** be used for these purposes without your specific permission.

Your Privacy Rights

You have the right **not** to sign this form that allows us to use and share your identifiable information for research; however, if you don't sign it, you can't take part in this research study.

You have the right to withdraw your permission for us to use or share your identifiable information for this research study. If you want to withdraw your permission, you must notify the person in charge of this research study in writing. Once permission is withdrawn, you cannot continue to take part in the study.

If you withdraw your permission, we will not be able to take back information that has already been used or shared with others, and such information may continue to be used for certain purposes, such as to comply with the law or maintain the reliability of the study.

You have the right to see and get a copy of your identifiable information that is used or shared for treatment or for payment. To ask for this information, please contact the person in charge of this research study. You may only get such information after the research is finished.

Informed Consent and Authorization

Statement of Person Giving Informed Consent and Authorization

- I have read this consent form.
- This research study has been explained to me, including risks and possible benefits (if any), other possible treatments or procedures, and other important things about the study.
- I have had the opportunity to ask questions.
- I understand the information given to me.

Signature of Subject:

I give my consent to take part in this research study and agree to allow my health information to be used and shared as described above.

_____

Print Name

_____ _____ _____

Subject Signature Date Time (optional)

Signature of Study Doctor or Person Obtaining Consent:

Statement of Study Doctor or Person Obtaining Consent

- I have explained the research to the study subject.
- I have answered all questions about this research study to the best of my ability.

_____

Print Name

_____	_____	_____
Signature of Study Doctor or Person Obtaining Consent	Date	Time (optional)

Consent Form Version: 4

Consent Form Created on: 10/07/2025