Multicenter Phase II Study of Transanal Total Mesorectal Excision (taTME) With Laparoscopic Assistance for Rectal Cancer

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TITLE OF RESEARCH STUDY:

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WHAT IS A RESEARCH STUDY?

A research study is when scientists try to answer a question about something that we don't know enough about. Participating may not help you or others.

People volunteer to be in a research study. The decision about whether or not to take part is totally up to you. You can also agree to take part now and later change your mind. Whatever you decide is okay. It will not affect your ability to get medical care within the Mount Sinai Health System.

Someone will explain this research study to you. Feel free to ask all the questions you want before you decide. Any new information that develops during this research study that might make you change your mind about participating will be given to you promptly.

Basic information about this study will appear on the website http://www.ClinicalTrials.gov. There are a few reasons for this: the National Institutes of Health (NIH) encourages all researchers to post their research; some medical journals only accept articles if the research was posted on the website; and, for research studies the U.S. Food and Drug Administration (FDA) calls "applicable clinical trials" 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.

PURPOSE OF THIS RESEARCH STUDY:

Each year, 40,000 people are diagnosed with rectal cancer in the United States. Although, chemotherapy and radiation play an important role in the treatment of advanced rectal cancer, surgery is essential to the management of the disease.

The purpose of this research study is to discover whether this approach is effective compared to the standard laparoscopic or robotic technique.

taTME with Laparoscopic Assistance is a procedure that combines standard laparoscopy, or multiple small abdominal incisions, with surgery through the anus in order to remove rectal cancer. This procedure is an alternative to standard abdominal surgery to remove cancer of the rectum.

You may qualify to take part in this research study because you have been diagnosed with rectal cancer that has not spread to other organs and that may be treated with surgery alone, or with surgery combined with additional therapy including chemotherapy and radiation (CRT).

Funds for conducting this research are provided by the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)

LENGTH OF TIME AND NUMBER OF PEOPLE EXPECTED TO PARTICIPATE

Your participation in this research study is expected to last up to 5 years. It is expected that about 30 participants will be asked to take part in this research study at Mount Sinai Hospital Health System. A total of about 140 participants are expected to be asked to take part in this research study across all participating institutions.

DESCRIPTION OF WHAT'S INVOLVED:

If you agree to participate in this research study, the following information describes what may be involved.

All research visits will be conducted at the following locations:

Mount Sinai Hospital

Department of Surgery, Division of Colon and Rectal Surgery Faculty Practice,
5 East 98th Street, 14th Floor, Suite D.
New York, NY
or
The Susan and Leonard Feinstein IBD Clinical Center,
17 East 102nd Street, 5th Floor East,
New York, NY

Beth Israel

Department of Surgery, Division of Colon and Rectal Surgery
10 Union Square East, Suite 2N
New York, NY

Mount Sinai West
425 West 59th Street
New York, NY

You will receive surgery at

Mount Sinai Hospital
1468 Madison Ave
New York, NY

Or

Mount Sinai Beth Israel
First Ave and 16th street
New York, NY

Informed Consent Process (before screening):

At the time of your initial consultation for evaluation of rectal cancer, if you are identified as a potential study participant who meets study inclusion criteria and have no exclusionary criteria, one of the research team members, will describe to you the study and study procedure. A thorough description of the study procedure and alternatives including risks and benefits will be provided by the study surgeon based on the surgeon's standard practice; a paper copy of these descriptions is called an informed consent form. A copy of the informed consent will be provided for you to take home and review with your family and/or physician. Your choices of procedure will in no way affect your care at this institution and study participation is entirely voluntary.

Study Visit: You will be contacted by a member of the research team 48-72 hours following your initial visit to confirm your final eligibility and determine your interest in participating in the study. You will return to the office to review the protocol and study procedure with a research team member and consent for the research study will be obtained. If you already have completed preoperative chemoradiation or radiation, or if you do not require chemoradiation, the surgical consent for the study procedure may also be obtained at the same visit or at a later date based on your and your surgeon's preference.

If you are to undergo chemoradiation prior to your rectal cancer resection, informed consent will be obtained as described above, but the surgical consent for the study procedure will be deferred until after you complete chemoradiation, and after you have been re-evaluated by our surgeon.

You will be re-evaluated 4-6 weeks following completion chemoradiation at which time, if you still meet eligibility criteria and wish to continue participating in the study, the study procedure will be

reviewed again in detail by a member of the research team, and the surgical consent will be obtained by one of the study staff members.

Below is the study calendar that demonstrates the time commitment required for the study:

	Screening		Prior to Surgery		Postoperative						
					Week 1-2	Week 4-6	Year 1	Year 2	Year 3	Year 4	Year 5
Study Consent	X	REGISTATION		SURGERY							
Consent for surgical procedure			X								
Physical Exam	X		X[b]		X	X	Every 3-6 months		Every 6 months		
Rectal evaluation	X		X[a]				Every 3-6 months		Every 6 months		
Blood draws	X		X[b]		X		Every 3-6 months		Every 6 months		
Colonoscopy	X						X			X	
CT or PET CT Scans	X		X[a,c]				Every 6-12 months				
Pelvic MRI	X		X[a,c]						X		
Questionnaires	X		X[d]				X	X			
Follow up Visits					X	X	Every 3-6 months		Every 6 months		

a. Rectal evaluation, CT or PET CT scans and pelvic MRI may need to be repeated one more time after treatment with chemo/radiation to assess tumor response before surgery.
b. Blood draws and physical examination will need to be repeated preoperatively if older than 30 days prior to surgery.
c. Imaging, colonoscopy and rectal tumor biopsy performed up to 3 months prior to screening date (or prior to start of neoadjuvant treatment, if you are being enrolled in the study during or after your neoadjuvant treatment) can be used to determine eligibility.
d. For those receiving neoadjuvant treatment, questionnaires will be repeated between the end of treatment and day of surgery.

Before the research starts (screening):

The initial screening might last up to three weeks. At the initial screening visit, after signing the informed consent form to participate in the study, you will undergo standard rectal cancer evaluation. You will be interviewed and examined by the trial staff. At the interview, you will be asked some general questions about your personal data (date of birth, gender, ethnicity and race), your past and your actual medical history, your smoking habits, your medications (both current and previous medications), and allergies. The examination will consist of a physical examination, blood draws (approximately 3 tablespoons of blood), pregnancy test (if applicable), and rectal evaluation. Additional evaluation may include colonoscopy, CT or PET CT scans, pelvic MRI if not already performed around the time of your rectal cancer diagnosis.

The results of your screening tests will be reviewed at the multidisciplinary tumor board with the oncology team (surgeons, radiologists, oncologists) and your study eligibility will be confirmed. Once enrolled in the study, you will be assigned an enrollment number on the Enrollment log starting with "EN-" followed by a 4-digit number, where the first 2 numbers designate the study site, and the last 2 numbers designate the subject number (example, EN-01-05).

If you are found to have Stage I and subset of Stage II rectal cancer, you will be considered eligible to proceed directly to surgery of the cancer. Stage I rectal cancer is an early form or limited form of cancer. The cancer has broken through the inner lining of the rectum but has not made it past the muscular wall.

If you are found to have Stage II and III rectal Cancer, you will be offered to undergo either short-course preoperative radiation therapy followed by surgery 1-2 weeks later, or long-course preoperative chemoradiation therapy, followed by surgery 6-12 weeks later. Stage II rectal cancer is a little more advanced cancer. The tumor has penetrated all the way through the bowel wall. However, lymph nodes (small structures that are found throughout the body that produce and store cells that fight infection) are not involved at this stage. In Stage III rectal cancer, the cancer has spread to the lymph nodes.

After the screening procedures confirm that you are eligible to participate in the research study, and after being enrolled in the study, the following will take place:

- **Questionnaires**: As part of the research study, you will be asked to complete questionnaires to assess the functioning of your bowels, urination, and sexual function prior to receiving any treatment for your rectal cancer. These questionnaires require about 30-45 minutes to fill and can be completed in clinic during one of your scheduled visits, or via email based on your preference.

- **If you have stage I or early stage IIA rectal cancer** and have been considered eligible by the multidisciplinary tumor board to proceed directly to surgery, the surgical procedure will be reviewed in detail by a member of the research team including the associated risks, benefits and alternatives, and will be asked to sign the surgical informed consent form.

- **If you have stage II or III rectal cancer:**
  - **Preoperative chemoradiation**: You will be first treated with chemoradiation or radiation alone prior to surgery based on standards of care for rectal cancer. Based on the multidisciplinary tumor board recommendations, you will be offered to undergo either short-course radiation followed by surgery 1-2 weeks later, or long-course chemoradiation therapy followed by surgery 6-12 weeks later

- **Clinical evaluation during chemoradiation:** During chemoradiation, you will undergo standard physical exams and blood draws to monitor your health during treatment. Youu will be asked questions about your general health and specific questions about any problems that you might be having.
- **Post-chemoradiation clinical evaluation**: 4 to 6 weeks following completion of treatment, standard physical examination, rectal evaluation and blood draws (about 3 teaspoons) will be performed to assess your tumor response to chemoradiation. Additional imaging (CT or PET CT scans and pelvic MRI) may be obtained prior to surgery at the discretion of your surgeon to further assess tumor response.

  If there is no evidence of tumor progression, if there has been no change in eligibility criteria, and if you still wish to participate in the study, the study procedure will be reviewed again in detail by a member of the research team. The surgical procedure will also be explained in detail with all its risks and benefits, surgical consent will be obtained and the surgery date will be scheduled.
- **Post-chemo/radiation questionnaires**: As part of the research study, you will be asked to complete questionnaires to assess the functioning of your bowel, sexual, and urinary function following radiation or chemoradiation and prior to surgery.

Once you have signed the surgical consent form, you will be registered for the study and will be assigned a 4-digit Registration Identification Number starting with "R-". The first 2 digits of the Subject ID Number refer to the study site, and the last 2 digits refer to the subject number (example, R-02-04).

Preoperative preparation: Medical clearance will be obtained preoperatively as per standard practice. You will undergo routine blood draws, preoperative testing (electrocardiogram and chest X-ray). You will undergo oral mechanical bowel preparation. Bowel preparation is a cleansing of the intestines from stools and regular intestinal juices or secretions. You will be asked to take, as per routine presurgical care, oral antibiotics before the day of your surgery. Regardless of what type of surgery is performed, removal of the rectum for this type of rectal cancer may require a temporary diverting ileostomy also called a stoma (an ileostomy or stoma is a loop of small intestine which protrudes through an opening on the abdomen). A stoma is created in order to prevent breakdown of the bowel connection (connection between the colon and the anus). You will undergo standard preoperative teaching and stoma site marking in preparation for possible ileostomy. At this time, a mark will be made on your belly to show the area where the stoma will be made at the time of surgery. Once the bowel connection is healed, another surgery is required to close the ileostomy.

Surgery (transanal TME with laparoscopic assistance)

The research procedure consists in removing your rectal cancer using a technique that combines surgery through the anus and laparoscopic or robotic surgery through the abdomen. Laparoscopic

surgery is performed with the assistance of a video camera and several thin instruments which are introduced in the belly through small incisions of up to half an inch each.

Robotic surgery is laparoscopic surgery performed through a computer-assisted system where the surgeon who controls the arms of the robot using a console (similar to joysticks). The arms of the robot carry specialized instruments that are introduced through the belly through small holes of up to half an inch each.

At the end of the procedure, the rectum will be removed through the anus or through a small abdominal incision, your bowel will be re-connected to the anus and a temporary stoma will be created, which is standard of care following surgery for this type of rectal cancer. The procedure will take 4-6 hours. If at any time during your operation, your surgeon decides that your rectum cannot be safely removed using the research procedure, your rectum will be removed using standard laparoscopic or open surgery.

If at any point during surgery difficulties or complications are encountered that prevent the surgeon from completing the study procedure safely, the surgery will be completed either through multiple small incision on your belly (laparoscopically or robotically) or in an open fashion, through a large incision on your belly.

Other things to know:

- **Videotaping:** Your surgical procedure will be videotaped for teaching purposes, which is standard practice. There will be no record of your face or parts of your body that will in any way reveal your identity.
- **Photographs:** Photographs will be taken of your tumor to assess the results of the surgery which is standard practice. Care will be taken to ensure these do not reveal your identity.
- **Postoperative care:** You will receive standard postoperative care in the hospital including physical examinations, blood draws (2-3 tablespoons of blood), and additional tests as needed until you can safely be discharged.

  Your length of hospital stay is anticipated to be 4 to 7 days, which is standard following surgery for rectal cancer.

  - You will be allowed to drink and progress to food when you will tolerate swallowing down liquids and more solid foods. If you are left a drain in your belly, the drain will be taken out when very little or no fluid will be seen in the collection tube. If you receive an ileostomy, you will be educated on how to manage it before leaving the hospital. You will be discharged when stable, capable to walk, eat a low residue diet, and passing gas. You will be prescribed oral pain medications as needed.

- **Pathologic assessment of the surgical specimen:** The portion of colon and rectum that has been removed during surgery will be sent to Mount Sinai's Pathology Department to be analyzed as per standard protocol.

After you leave the hospital, the following will take place:

- **First Postoperative visit**: Routine physical examination will be performed within 2 weeks of your discharge from the hospital.
- ***Subsequent Postoperative* visit(s):** Standard postoperative evaluation(s) will be performed 1-2 months following surgery (and/or later, following completion of chemotherapy), at which time routine physical and rectal evaluation will be performed to assess healing of the bowel connection. If you don't require any other chemotherapy treatment, your coloanal anastomosis (the connection between your anus and the remaining portion of the colon) will be evaluated by gastrografin enema as per standard practice. If the bowel connection is healed, ileostomy reversal will be scheduled. If you need any other chemotherapy treatment after surgery, you will need to keep the ileostomy until the end of this needed treatment. Any additional visits will be provided as necessary.
- You will be asked to complete questionnaires regarding your postoperative bowel, sexual, and urinary function according to the schedule of the study calendar above.

- **Postoperative procedures:** All standard post-rectal cancer procedures will be performed:
  - **Postoperative chemotherapy:** You may need to receive standard postoperative chemotherapy. If you tumor was found to be more advanced than suspected before surgery, you may need to receive radiation as well, based on standard protocols.
  - **Gastrografin enema**: If you have an ileostomy, you will undergo standard gastrografin enema to assess the healing of the bowel connection. This test consists in injecting contrast as an enema and taking x-rays to determine whether the bowel connection is well healed. This test is routinely performed following rectal surgery prior to making the decision to close the ileostomy.
  - ***Stoma closure**: If the bowel connection is healed, you will be scheduled for ileostomy closure as per standard of care.*

Postoperative surveillance

- **Medical history, physical examination, blood draws and CT scans.** A medical history, physical examination and blood draws (about 3 teaspoons) will be obtained every 3 to 6 months for the first 2 years after surgery, every 6 months for the

subsequent 3 years, and yearly thereafter. CT scans will be obtained every 6-12 months for the 5 years after surgery.

- **Rectal evaluation** will be performed every 3 to 6 months for the first 2 years after rectal cancer surgery, and then every 6 months for the following 3 years.
- **Colonoscopy** will be performed 1 year after surgery and if normal, it will be repeated at 3 years after rectal cancer surgery, and every 5 years thereafter.
- **A pelvic MR** will be obtained 3 years after the rectal cancer surgery

You will be followed according to the standard guidelines for postoperative surveillance:

Year 1-2: (During the first two years after surgery):
- History and physical examination every 3-6 months
- CEA level every 3-6 months (about two teaspoons of blood will be drawn),
- CT scans of the chest, abdomen and pelvis every 6 -12 months

Year 3-5: (on the third, fourth and fifth year after your surgery)
- History and Physical examination every six months
- Blood draws every 6 months (about two teaspoons of blood will be drawn)
- CT scans of the chest, abdomen and pelvis every 6-12 months.
- MR of the pelvis on the third year after surgery

Year >5: Five and more years after your surgery
- Annual history and physical examination.

You will also be undergoing endoscopic surveillance according to standard postoperative and standard guidelines:

Year 1-2: Office rectal evaluation every 3-6 months.
- Colonoscopy will be performed 1 year after rectal cancer surgery, and if normal, 3 years later, and every 5 years thereafter

Year 3-5: Office rectal evaluation every 6 months

Year >5: Annual rectal evaluation

As part of the research study, you will be asked to complete following:

- **Questionnaires**: You will be asked to complete questionnaires regarding your postoperative bowel, sexual, and urinary function according to the schedule of the study calendar above. You can either fill out the questionnaires in paper form during one of your scheduled clinic visits, or electronically via email. If your preference is to complete the questionnaires electronically, the research team will need your permission to email you the questionnaires at the scheduled intervals using a secure online data collection server called RedCap. Instructions on how to fill out the questionnaires and submit them electronically will be provided in the email. You can change your preference on how to complete your questionnaires at any time.
- Do you given permission to the research team to send you the questionnaires electronically via a secure data collection server using your email address? (Please initial your choice)
- _____Yes, I give the research team permission to email me the questionnaires
- _____No, I DO NOT give the researchers permission to email me the questionnaires

For Women:

Since you are participating in a study that involves treatment with potential risks to a developing fetus, it is recommended, for your protection, that you not become pregnant for the duration of the study. Also, you should not participate if you are breastfeeding. Therefore, practicing effective contraception is important. No individual contraceptive is 100% effective.

Recommended methods of birth control are:

- The consistent use of an approved hormonal contraception (birth control pill/patches, rings),
- An intrauterine device (IUD),
- Contraceptive injection (Depo-Provera),
- Double barrier methods (Diaphragm with spermicidal gel or condoms with contraceptive foam),
- Sexual abstinence (no sexual intercourse) or
- Sterilization

Hormonal contraceptives, implants, and injections are only considered effective if used properly and started at least one month before you begin the study, continuing throughout the study and for one month after the end of the study. You should ask your study doctor if you should continue birth control for longer than 30 days after the end of the study. If you are unsure whether the method of birth control you use is acceptable to use while participating in this study, you should ask your study doctor before you begin the study. If you are less than one year post-menopausal, there is the potential that you could become pregnant. If you or your partner becomes pregnant or thinks either of you may be pregnant at any time during the trial, it is important that you tell your study doctor immediately. A

referral will be made to an obstetrician/gynecologist for follow-up. If you plan to become pregnant in the year following a clinical trial, speak with your study doctor.

If you have any questions about birth control, your study coordinator or study doctor will be able to answer your questions and give you advice.

Pregnant women are excluded from this study because chemotherapy and/or radiation, which may be required for rectal cancer treatment, have the potential to cause serious malformations to a developing fetus and can also cause abortion. Because there is an unknown but potential risk of adverse events in nursing infants secondary to treatment of the mother with chemotherapy and/or radiation, breastfeeding should be discontinued if the mother is treated with chemotherapy and/or radiation.

For Men:

Since you are participating in a study that involves treatment with potential risks to a developing fetus, it is recommended that you use a condom and not father a child or donate sperm while you are receiving treatment. Also, it is recommended that you use a condom and not father a child and/or donate sperm for 90 days after you stop treatment. This is because levels of chemotherapy drugs may be present in the sperm and/or seminal fluid even after you stop taking the chemotherapy. Continuing to use a condom and not donating sperm during this 90 day period may allow time for any drug that is still present in sperm and/or seminal fluid to be eliminated from your body before you attempt to father a child or donate sperm. You are encouraged to tell your female partner(s) and/or their doctor(s) that you are participating in a clinical trial.

YOUR RESPONSIBILITIES IF YOU TAKE PART IN THIS RESEARCH:

If you decide to take part in this research study you will be responsible for the following things:

- You must be willing to follow the study related procedures and have the relevant tests and procedures done as the study treatment requires including blood draws, urine samples, CT scans, and pelvic MRI.
- You must be willing to complete 3 to 4 sets of questionnaires regarding the functioning of your bowel, your urinary function, and your sexual function, from the time you enroll in the study until approximately 18 months following your surgery, or later in cases of delayed closure of your ileostomy.
- It is important that you tell the study staff about any other medication or dietary supplements you are taking before and during the study.
- Use the birth control method that is outline in the description of “What is Involved” section.

- While you are in the study you must tell the study doctor or study staff about any changes in your health or the way you feel, and tell the study doctor or study staff if you want to stop being in the study at any time.

COSTS OR PAYMENTS THAT MAY RESULT FROM PARTICIPATION:

You will not be paid for participating in this research study. You will not be reimbursed for your travel or time that may be required for study visits.

Participation in the study may lead to added costs to you or your insurance. The cost of the study procedure (transanal total mesorectal excision with laparoscopic assistance) will be charged to the insurance company. You may be responsible for co-payments and deductibles that are not covered by your insurance coverage.

POSSIBLE BENEFITS:

It is important to know that you may not get any benefit from taking part in this research. Others may not benefit either. However, possible benefits may be from potentially reduced incisional pain and long-term risk of abdominal wall hernia formation. By enabling transanal extraction of the surgical specimen, the study procedure may reduce the number and size of abdominal wall incisions otherwise required during standard open, laparoscopic or robotic rectal cancer surgery.

REASONABLY FORESEEABLE RISKS AND DISCOMFORTS:

There are risks to taking part in any research study. One risk is that the study procedure may result in complications (may have side effects).

All surgical procedures have potential risks (side effects), which can range from mild and reversible to severe, long lasting and possibly life-threatening. There is a great deal of variability in risks between individuals. For investigational surgeries, not all of the risks are known at this time. **You need to tell your doctor or a member of the study team immediately if you experience any complications.**

During the research study, you will be notified of newly discovered complications or significant findings, which may affect your health or willingness to participate.

Below are the potential risks associated with the study procedure:

Common (Chance of 10-50% that this will happen)

- Readmission to the hospital (for dehydration, infection, or intestinal blockage)

- Dehydration from frequent loose watery stools from the stoma. If severe it may require medication, intravenous fluids and possibly hospitalization
- Abnormally slow bowel contraction which can feel like constipation (sometimes severe) and may cause pain, nausea and vomiting
- Blockage of the intestine or bowel which can cause nausea, vomiting, and pain. It may be serious or life-threatening and may require hospitalization and surgery
- Difficulty emptying the bladder
- Wound infection
- Deep abdominal infection
- Inability to hold urine in the bladder
- Inability to have normal sexual function
- Poor bowel function
- Loss of bowel control

Occasional (Chance of 5-10% that this will happen)

- Urinary tract infection
- Infection of the lung
- Severe infection that is present in the blood and that can spread throughout the body
- Breakdown of the bowel connection which can cause fevers, pain, and a deep abdominal infection. It might require a procedure to drain the infection
- Blood clots that can lead to swelling in the arms and legs. These clots can travel to the lungs causing shortness of breath which may be serious or life threatening
- Kidney failure when your body holds fluid which can be serious or life threatening. Your blood pressure rises and harmful wastes build up in your body. You may experience fatigue, nausea, and loss of appetite. When this happens, you need treatment to replace the work of your failed kidneys (ex. dialysis).
- Heart attack
- Difficulty breathing with low levels of oxygen in the blood, which could be serious and life-threatening and require you to have a tube inserted into your windpipe that is hooked up to a machine to help you breathe.
- Hernia

- Abnormal narrowing of the bowel connection which may cause obstruction of bowel contents, nausea and vomiting, and which may require a procedure to correct
- Incomplete removal of the tumor, which may require another surgery
- Cancer recurrence

Rare (Chance of less than a 5% that this will happen)

- Difficulties with the procedure requiring having to convert to an open rectal surgery
- Bowel perforation (a hole in the intestines) that could result in a serious, life-threatening infection and may require surgery
- Damage to other organs during the operation that may require additional surgery
- An abnormal connection between two different organs (fistula) which may require another surgery
- Abnormal bleeding during or after the operation that may require blood transfusion and might require surgery.
- Blood clot in the lungs
- *Death*

Risks Associated with Radiological Scans and X-Rays:

You will have radiation-based examinations and/or procedures that are part of the regular care for your condition and you would have them whether or not you participate in this research. You will not be exposed to any additional radiation because you are participating in this research. In the long term, over many years, there is a very low risk of developing a new cancer as a result of the radiological evaluation and treatment for your cancer. There is a small risk with using the contrast agent that is injected into a vein during the scan. It may worsen kidney function in people who already have decreased kidney function. Therefore, we will monitor your kidney function closely while you participate in this study. If there is any change in your kidney function, we may have to remove you from the study.

Uncommonly, some people have allergic reactions (such as hives and itching) to the contrast agent. Serious reactions (for example, drop in blood pressure, difficulty breathing or severe allergic reaction and death) are rare.

Risks Associated with MRI Scans:

You will undergo MRI (Magnetic Resonance Imaging) examinations that are part of the regular care for your condition and you would have them whether or not you participate in this research.

When having an MRI scan, you will lie still on a table that slides into a tunnel slightly wider than your body. People who feel uncomfortable in confined spaces (claustrophobia) may feel uncomfortable in the narrow cylinder. If you feel uncomfortable in confined spaces, please tell your doctor. Your doctor may give you a medication to make you feel more comfortable. As images are taken, a loud banging noise will be produced.

Earplugs or headphones will be available if needed. The MRI can be stopped at any time at your request, but the scan may not be complete.

There is a small risk with using the contrast agent that is injected into a vein during the scan. It may worsen kidney function in people who already have decreased kidney function. Therefore, we will monitor your kidney function closely while you participate in this study. If there is any change in your kidney function, we may have to remove you from the study. Uncommonly, some people have allergic reactions (such as hives and itching) to the contrast agent. Serious reactions (for example, drop in blood pressure, difficulty breathing or severe allergic reaction and death) are rare.

Risks of Getting Blood Drawn:

The risks of a blood draw include pain, bruising, and the slight possibility of infection at the place where the needle goes in. Some people feel dizzy or may faint during or after a blood draw.

Reproductive Risks:

If you are or become pregnant, this research may hurt your baby or your pregnancy in ways that are unknown. The unknown risks might be minor or might be major (death). You should not become pregnant or father a baby while on this research study. Please read the acceptable method of birth control found under the description in the “What’s Involved” section.

Non-Physical Risks:

Because of side effects from surgery or the time required for treatments, tests and clinic visits while you are on this research study, you may be unable to keep up with your normal daily activities for approximately 4-6 weeks.

Risk of loss of private information; this risk always exists, but there are procedures in place to minimize the risk.

In addition to these risks, this research may hurt you in ways that are not known. The unknown risks might be minor or might be major (death).

OTHER POSSIBLE OPTIONS TO CONSIDER:

You may decide not to take part in this research study without any penalty. The choice is totally up to you.

Instead of being in this research study, your choices may include:

- Open abdominal or laparoscopic surgery (surgery to remove your rectal cancer through a large abdominal incision or through several small abdominal incisions)
- Transanal surgery (surgery to remove your rectal cancer through the anus)
- Transanal total mesorectal excision with laparoscopic assistance (taTME) without being part of this study (multiple small abdominal incisions with surgery through the anus in order to remove rectal cancer.)
- No surgical therapy for your cancer
- Comfort care, also called palliative care. This type of care may help to reduce pain, tiredness, appetite problems and other problems caused by the cancer. It does not treat the cancer directly, but instead tries to treat the symptoms

Please talk to the research doctor about your options before you decide whether you will take part in this research study.

IN CASE OF INJURY DURING THIS RESEARCH STUDY:

If you are injured or made sick from taking part in this research study, medical care will be provided. Generally, this care will be billed to you or your insurance in the ordinary manner and you will be responsible for all treatment costs not covered by your insurance, including deductibles, co-payments and coinsurance. This does not prevent you from seeking payment for injury related to malpractice or negligence. Contact the investigator for more information.

ENDING PARTICIPATION IN THE RESEARCH STUDY:

You may stop taking part in this research study at any time without any penalty. This will not affect your ability to receive medical care at any of the Mount Sinai Health System hospitals or to receive any benefits to which you are otherwise entitled.

You have the right to choose not to sign this form. If you decide not to sign this form, you cannot participate in this research study.

If you decide to stop being in the research study, please contact the Principal Investigator or the research staff.

If you stop being in the research study, already collected information may not be removed from the research study database and will continue to be used to complete the research analysis. You may be

asked whether the investigator can collect information from your routine medical care. If you agree, this data will be handled the same as research data

You may also withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use the information that was already collected if that information is necessary to complete the research study. Your health information may still be used or shared after you withdraw your authorization if you have an adverse event (a bad effect) from participating in the research study.

Withdrawal without your consent: The study doctor, the sponsor or the institution may stop your involvement in this research study at any time without your consent. This may be because the research study is being stopped, the instructions of the study team have not been followed, the investigator believes it is in your best interest, or for any other reason.

CONTACT PERSON(S):

If you have any questions, concerns, or complaints at any time about this research, or you think the research has hurt you, please contact the Principal Investigator at 212-241-7943 or 212-241-7626.

If it is a true medical emergency, please call 911 or go to the emergency room.

This research has been reviewed and approved by an Institutional Review Board. You may reach a representative of the Program for Protection of Human Subjects at the Icahn School of Medicine at Mount Sinai at telephone number (212) 824-8200 during standard work hours for any of the reasons listed below. This office will direct your call to the right person within the Mount Sinai Health System:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You are not comfortable talking to the research team.
- You have questions about your rights as a research subject.

You want to get information or provide input about this research.

DISCLOSURE OF FINANCIAL INTERESTS:

Sometimes, physicians/researchers receive payments for consulting or similar work performed for industry. Effective September 2014 Mount Sinai reviews only payments to an individual totaling more than $5,000 a year per entity when determining potential conflicts of interest. If you have questions regarding industry relationships, we encourage you to talk your physician/researcher or visit our website at http://icahn.mssm.edu/ where Mount Sinai publicly discloses the industry relationships of our faculty.

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Dr. Patricia Sylla (the Principal Investigator) of this study receives financial compensation as a consultant for Johnson & Johnson, a company that manufactures medical devices and provides grant support toward this study.
Dr. Sylla also receives financial compensation as a consultant for Olympus, Karl Storz and Medtronic, companies that manufacture medical devices and had provided grant support for this study in the past.

If you have questions regarding paid relationships that your physician/researcher may have with industry, we encourage you to talk with him or her, or check for industry relationships posted on individual faculty pages on our website at http://icahn.mssm.edu/.

MAINTAINING CONFIDENTIALITY – HIPAA AUTHORIZATION:

As you take part in this research project it will be necessary for the research team and others to use and share some of your private protected health information. Consistent with the federal Health Insurance Portability and Accountability Act (HIPAA), we are asking your permission to receive, use and share that information.

What protected health information is collected and used in this study, and might also be disclosed (shared) with others?

As part of this research project, the research team at the hospital(s) involved in the research will collect your name, address, telephone/fax numbers, dates directly related to the individual (birth, admission, discharge, date of death, etc..), email/internet protocol addresses or we universal resource locators (URL's), social security number, medical record number, health plan numbers, account numbers, and/or certificate/license numbers.

The researchers will also get information from your medical record from your private doctors and any visits and admission to Mount Sinai Hospital.

During the study the researchers will gather information by:

- taking a medical history (includes current and past medications or therapies, illnesses, conditions or symptoms, family medical history, allergies, etc.)
- doing a physical examination that generally also includes blood pressure reading, heart rate, breathing rate and temperature
- completing the tests, procedures, questionnaires and interviews explained in the description section of this consent.

Why is your protected health information being used?

Your personal contact information is important to be able to contact you during the study. Your health information and the results of any tests and procedures being collected as part of this research study will be used for the purpose of this study as explained earlier in this consent form. The results of this

study could be published or presented at scientific meetings, lectures, or other events, but would not include any information that would let others know who you are, unless you give separate permission to do so.

The Principal Investigator may also use and share the results of these tests and procedures to treat you in collaboration with others in the Mount Sinai Health System.

The research team and other authorized members of The Mount Sinai Health System ("Mount Sinai") workforce may use and share your information to ensure that the research meets legal, institutional or accreditation requirements. For example, the School's Program for the Protection of Human Subjects is responsible for overseeing research on human subjects, and may need to see your information. If you receive any payments for taking part in this study, the Mount Sinai Finance Department may need your name, address, social security number, payment amount, and related information for tax reporting purposes. If the research team uncovers abuse, neglect, or reportable diseases, this information may be disclosed to appropriate authorities.

Who, outside Mount Sinai, might receive your protected health information?

As part of the study, the Principal Investigator, study team and others in the Mount Sinai workforce may disclose your protected health information, including the results of the research study tests and procedures, to the following people or organizations: (It is possible that there may be changes to the list during this research study; you may request an up-to-date list at any time by contacting the Principal Investigator.)

- Other collaborating research center(s) and their associated research/clinical staff who are working with the investigators on this project.
- Research data coordinating office and/or their representative(s) who will be responsible for collecting results and findings from all the centers: Mount Sinai Hospital.
- Outside pathology department who will be independently review all photodocumentation of the completeness of TME resections for all specimens fr all the research centers involved in this project: Cleveland Clinic Florida, Weston, Florida.
- Contract Research Organization (whose job is to help organizations fulfill their responsibilities in the research and development process): Biomedical Research Alliance of NY (BRANY)
- A Data Safety Monitoring Board that will monitor the study on an ongoing basis for safety: Tisch Cancer Center at Mount Sinai Hospital.
- The United States Department of Health and Human Services and the Office of Human Research Protection.

In all disclosures outside of Mount Sinai, you will not be identified by name, social security number, address, telephone number, or any other direct personal identifier unless disclosure of the direct identifier is required by law. Some records and information disclosed may be identified with a unique code number. The Principal Investigator will ensure that the key to the code will be kept in a locked

file, or will be securely stored electronically. The code will not be used to link the information back to you without your permission, unless the law requires it, or rarely if the Institutional Review Board allows it after determining that there would be minimal risk to your privacy. It is possible that a sponsor or their representatives, a data coordinating office, a contract research organization, may come to inspect your records. Even if those records are identifiable when inspected, the information leaving the institution will be stripped of direct identifiers. Additionally, when applicable, the monitors, auditors, the IRB, the Office of Human Subjects Protection (OHRP) of the Department of Health and Human Services as well as the Food and Drug Administration (FDA) will be granted direct access to your medical records for verification of the research procedures and data. OHRP and FDA are authorized to remove information with identifiers if necessary to complete their task. By signing this document you are authorizing this access. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

For how long will Mount Sinai be able to use or disclose your protected health information?

Your authorization for use of your protected health information for this specific study does not expire.

Will you be able to access your records?

During your participation in this study, you will have access to your medical record and any study information that is part of that record. The investigator is not required to release to you research information that is not part of your medical record.

Do you need to give us permission to obtain, use or share your health information?

NO! If you decide not to let us obtain, use or share your health information you should not sign this form, and you will not be allowed to volunteer in the research study. If you do not sign, it will not affect your treatment, payment or enrollment in any health plans or affect your eligibility for benefits.

Can you change your mind?

You may withdraw your permission for the use and disclosure of any of your protected information for research, but you must do so in writing to the Principal Investigator at the address on the first page. Even if you withdraw your permission, the Principal Investigator for the research study may still use your protected information that was already collected if that information is necessary to complete the study. Your health information may still be used or shared after you withdraw your authorization if you should have an adverse event (a bad effect) from being in the study. If you withdraw your permission to use your protected health information for research that means you will also be withdrawn from the research study, but standard medical care and any other benefits to which you are entitled will not be affected. You can also tell us you want to withdraw from the research study at any time without canceling the Authorization to use your data.

If you have not already received it, you will also be given The Hospital's Notice of Privacy Practices that contains more information about how The Hospital uses and discloses your protected health information.

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It is important for you to understand that once information is disclosed to others outside Mount Sinai, the information may be re-disclosed and will no longer be covered by the federal privacy protection regulations. However, even if your information will no longer be protected by federal regulations, where possible, Mount Sinai has entered into agreements with those who will receive your information to continue to protect your confidentiality.

If as part of this research project your medical records are being reviewed, or a medical history is being taken, it is possible that HIV-related information may be revealed to the researchers. If that is the case, the following information concerns you. If this research does not involve any review of medical records or questions about your medical history or conditions, then the following section may be ignored.

Notice Concerning HIV-Related Information

If you are authorizing the release of HIV-related information, you should be aware that the recipient(s) is (are) prohibited from re-disclosing any HIV-related information without your authorization unless permitted to do so under federal or state law. You also have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the New York State Division of Human Rights at (888) 392-3644 or the New York City Commission on Human Rights at (212) 306-5070. These agencies are responsible for protecting your rights.

Signature Block for Capable Adult

Your signature below documents your permission to take part in this research and to the use and disclosure of your protected health information. A signed and dated copy will be given to you.

DO NOT SIGN THIS FORM AFTER THIS DATE →

Signature of subject	Date
Printed name of subject	Time

Person Explaining Study and Obtaining Consent

Signature of person obtaining consent	Date
Printed name of person obtaining consent	Time

Witness Section: For use when a witness is required to observe the consent process,, document below (for example, subject is illiterate or visually impaired, or this accompanies a short form consent):

My signature below documents that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the subject, and that consent was freely given by the subject.

Signature of witness to consent process	*Date*
Printed name of person witnessing consent process	Time

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