CONSENT FORM TO PARTICIPATE IN A RESEARCH STUDY

Study Title: Micro-ultrasound-Guided Focal Laser Ablation (MicroUSgFLA) Treatment for Management of Intermediate-Risk Prostate Cancer: Evaluation of Safety and Effectiveness

Investigator/Study Doctor: Dr. Sangeet Ghai

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Introduction:
You are being asked to take part in a research study. Please read the information about the study presented in this form. The form includes details on study's risks and benefits that you should know before you decide if you would like to take part. You should take as much time as you need to make your decision. You should ask the study doctor or study staff to explain anything that you do not understand and make sure that all of your questions have been answered before signing this consent form. Before you make your decision, feel free to talk about this study with anyone you wish including your friends, family, and family doctor. Participation in this study is voluntary.

Background/Purpose:
Focal Laser Ablation is a treatment for localized prostate cancer in which high power laser light is used to "ablate" the tumour by raising it to a very high temperature for a short period of time. This is achieved by inserting small laser fibre optic probes into the tumour and surrounding areas inside the prostate, only for the duration of the treatment, and delivering the laser light through these fibres. While Focal Laser Ablation is considered experimental many hospitals are offering this treatment to certain groups of patients; here at Princess Margaret Cancer Centre we have 15 years and approximately 100 patients experience performing this treatment.

The standard of care treatment for your disease at Princess Margaret Cancer Centre is Radical Prostatectomy or Radiation Therapy.

The fibre optic probes are inserted into the prostate either under magnetic resonance imaging (MRI) guidance or traditional transrectal ultrasound (TRUS) guidance, but the issue is that while the tumour can be seen on MRI, so making MRI a useful guiding tool to insert the fibre optic probes and monitor the treatment, treatment under MRI guidance

takes many hours to complete and only major hospital centres have access to MRI and the people trained to use it for this purpose.

On the other hand Focal Laser Ablation under TRUS guidance only takes 2 or 3 hours to complete, but while the fibre optic probes can be seen clearly with standard TRUS making it easy to insert them, the tumour itself is not normally visible, rather the doctor must know from a prior MRI where precisely within the prostate the tumour is and direct the probes to that location.

A new type of ultrasound known as “micro-ultrasound” is showing promise to see the tumour within the prostate because it empowers the physician with 3 times the image resolution compared to conventional TRUS. At this resolution features of the tumour become visible where they would not normally be on standard TRUS. Apart from this the micro-ultrasound system is no different from any TRUS system.

Micro-ultrasound was demonstrated in a clinical study with 25 participants at Johns Hopkins Medical Center to have improved the ability to visualize cancerous areas compared to standard low-resolution TRUS, and more recently in another study of nearly 1,800 patients performed at 5 Centres including Princess Margaret Cancer Centre, the new technology demonstrated increased detection of prostate cancer compared to conventional TRUS.

Therefore, what is being tested in this study is the usefulness of micro-ultrasound to guide a Focal Laser Ablation treatment. It is believed that micro-ultrasound may help to better guide the fibre optic probes to the precise location within the prostate because the tumour will now be seen on ultrasound, and to monitor treatment as it’s being delivered. If it shows promise there may be patients in future who might benefit from micro-ultrasound guided Focal Laser Ablation rather than having the more complex treatment of MRI-guided Focal Laser Ablation.

You are being asked to take part in this study because you have been diagnosed with intermediate-risk localized prostate cancer which is of the type that is considered treatable through this sort of minimally invasive technique, and because you may not wish to pursue the standard of care treatment of surgical removal of the prostate or radiation therapy of the prostate at this time.

Seven patients are expected to take part in this study.

Study Visits and Procedures:

The study inclusion MRI and biopsy are standard of care procedures. The questionnaires described under Visits 1, 4 and 5, the Micro-ultrasound-Guided Focal Laser Ablation procedure described under Visit 2 and follow-up catheter removal under Visit 3, the MRI under Visits 3 and 5 and biopsy under visit 5 are all related to the study. Likewise blood tests described under Visits 1, 4 and 5 are study related. These procedures and known risks associated with them are detailed below.

Visit 1
If you decide to participate you will be given quality of life and performance questionnaires to assess urinary and erectile function. These are known as IPSS (asking questions about your urinary performance when you go to the washroom), ICIQ-UI-SF (asking about whether there may be any urine leaking at other times) and IIEF-15 (asking about your potency). You will also provide a medical history, blood and urine samples and undergo a physical examination, including a digital rectal examination, and you will have a micro-ultrasound prostate imaging session to be sure the tumour can be seen on micro-ultrasound. The blood sample, which would be approximately a teaspoon full, the urine sample, questionnaires and micro-ultrasound scan will take approximately 1.5 hours to complete.

Visit 2
The Micro-ultrasound-Guided Focal Laser Ablation treatment will be performed at a later date under appropriate anesthesia (regional or general, or conscious sedation, as determined by the anesthesiologist) in the Toronto General Hospital Interventional Radiology Suite or similar facility.

The treatment is expected to last 2 to 3 hours.

In addition to 2 or 3 of a special type of miniature thermometer that will be placed nearby in the prostate to monitor temperature during treatment, the doctor may decide to place one or more of these thermometers temporarily through the skin into the space between the prostate and rectum as an additional way to ensure that the rectum remains at a low temperature, and, the doctor may perform an ultrasound contrast agent-enhanced micro-ultrasound scan during and/or immediately after the procedure as an additional way to track treatment success right at the time, compared to MRI which will be done later. Ultrasound contrast agents are small, harmless bubbles that pass through the blood vessels. They are used because ultrasound is sensitive to them, and this may help to distinguish the region that was treated from the rest of the prostate that was left untouched. If so, the contrast agent will be administered using the existing intravenous access catheter that was placed by the anesthesiologist and it is completely cleared from the body, mostly by the liver and lungs simply by breathing within 90 minutes.

Please note that an application specialist from the Micro-ultrasound device company may be in the room to ensure proper functioning of the device during the treatment.

After the treatment you will be transferred to an appropriate recovery area and you will be able to return home the same day after a period of observation. The Foley catheter that was placed during treatment will remain in place for three days.

Visit 3
Three days after treatment you will have the Foley catheter removed by a nurse who will then ask you to go to the washroom to be sure you are able to void your bladder nor-

mally and, as MRI is known to help in determining how successful this type of treatment is, you will have an MRI scan similar to the one you had before entering the study to further check that the ablation zone covered the tumour target. A Gadolinium MRI contrast agent injection will be included. The voiding trial and MRI will take about 1.5 hours to complete.

Visit 4
Three months after treatment you will be given the same questionnaires as Visit 1 to assess urinary and erectile function and you will give a blood sample in order to assess prostate specific antigen (PSA). This will take about 1 hour to complete.

Visit 5
Six months after treatment the steps at Visit 4 will be repeated and you will undergo a final MRI scan similar to Visit 3, and have a transrectal biopsy of the treated region of your prostate. This will be the last visit required under this study. All steps of Visit 5 will take about 3 hours to complete.

Calendar of Visits:

Procedure	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
Physical Exam	X		X	X	X
Medical History	X				
Digital Rectal Examination (DRE)	X				X
Micro-ultrasound scan	X				
MRI			X		X
Transrectal targeted biopsy					X
Focal Laser Ablation Procedure		X			
Foley catheter removal, trial void			X		
Urinalysis	X			X	X
Blood Tests	X			X	X
Adverse Events	X	X	X	X	X
Vital Signs	X	X	X	X	X
Questionnaires	X			X	X
Check Other Medications	X	X	X	X	X
Meeting with Study Anesthetist	X				

Risks:
Taking part in this study has risks. Some of these risks we know about. There is also a possibility of risks that we do not know about and have not been seen in humans to date. Please call the study doctor if you have any side effects even if you do not think it has anything to do with this study.

Risks Related to the Focal Laser Ablation Procedure

Risks related to the treatment may include:

Common

- Perineal discomfort: The tissue around the area where the needles were inserted through the skin may be sore for a few days following the treatment.
- Hematuria: Blood in the urine which should clear within a few days following the treatment.
- Hematospermia: Blood in the ejaculate which should clear within a few days following the treatment.
- Fatique.
- Urination problems: Tissue around the prostate may be weakened for several weeks. It may cause problems in urination including burning sensation, frequency, urgency and retention (the inability to pass urine spontaneously), all of which should clear within a few weeks following the treatment.

Rare

- Incontinence and Impotence: Other possible risks are incontinence (lack of ability to control your bladder or bowels), stress incontinence (inability to control your bladder when you feel an urge to urinate), and impotence. Bowel incontinence has never occurred in the approximately 100 patients we have treated with Focal Laser Ablation. In terms of urinary continence, none of the previously treated laser patients have had to use pads for urinary leakage though a few had temporary stress incontinence which resolved with time. The IPSS questionnaires did not show any significant change between baseline to 6 months follow-up. There was also no significant change in IIEF-15 questionnaire scores between baseline and 6 months after treatment in the previously treated patients though about 24% of patients had at least mild erectile dysfunction following treatment. 92% of men had erections sufficient for penetration following treatment.

- Bleeding: Bleeding either from the bladder or the prostate may result in blood in the skin and tissue around the prostate. You should not take any medications, including non-prescription medications such as aspirin without informing your study doctor. In the approximately 100 patients we have treated with Focal Laser Ablation blood in the tissue around the prostate, known as a hematoma has occurred once and this resolved with time.

Rare but Serious

- Rectal Injury: The rectum may be injured during the procedure, although it is monitored during the procedure with micro-ultrasound. If the rectum is injured, an opening between the rectum and the urethra could develop. An opening between the urinary tract and skin could also develop if the urethra is injured. If these injuries occur, you might need to be operated on. In the approximately 100 patients we have treated with Focal Laser Ablation this has never occurred.

Please notify your study doctor immediately should any side effects or complications occur.

Risks of MRI with Gadolinium Contrast

It is painless but noisy. If you have any metal in your body, for your safety, please tell the staff. There is no radiation. Some people may feel a little 'closed-in' in the MR machine, but you will be able to speak with someone at all times and can stop the test at any time.

Gadolinium is a contrast agent used in MR imaging that helps to see better any abnormal tissues and see blood vessels. It has been in routine use for over 20 years. Gadolinium contrast is not safe to use in people who have kidney problems. If you have had a problem with your kidneys, please inform the study team of this problem before the procedure. There is a small risk, in about 1 out of every 10,000 to 100,000 people of allergic reaction with gadolinium that can include symptoms of itchiness or rash. Rarely, a serious reaction may develop involving your kidneys leading to hardened skin lesions all over your body and stiffening of your joints. You must seek medical attention immediately if you develop any symptoms of allergic reaction.

Risks of Transrectal Targeted Prostate Biopsy

This procedure can cause:

- Mild pain in the biopsy area: Ultrasound probe insertion and rotation to obtain complete images of the prostate can be uncomfortable.
- Hematuria (blood in the urine): In up to 63% for minor cases and less than 1% significant cases with blood clot retention.
- Hematosperima (blood in the ejaculate): Is frequently seen following prostate biopsy (in about 90%) and resolves on its own.
- Hematochezia (blood in the feces): In at least 20% of patients. It resolves on its own and/or is controlled with direct pressure with the ultrasound probe.
- Urinary retention: Occurs in less than 1% of men undergoing biopsy, but men with enlarged prostate and significant bothersome lower urinary tract symptoms on standardized questionnaires (IPSS) are at increased risk. If urinary retention occurs, men typically need a urethral catheter for several days and then symptoms resolve.
- Urinary tract infection: Febrile urinary tract infection requiring hospitalization and intravenous antibiotics occurs in approximately 2% of men undergoing prostate biopsy.
- Bacterial infection: Whether prostatitis (infection of the prostate) or sepsis (severe whole-body infection), these infection rates are rare, in the range of 4% – 5% despite the patient being on a broad range of antibiotics.

Risk Related to Drawing Blood

There is a possibility of pain, bruising, swelling, or infection related to giving blood.

Benefits:
You may not receive direct benefit from being in this study. Information learned from this study may help to offer micro-ultrasound guided Focal Laser Ablation to more patients in the future.

Alternatives to Being in the Study:
You do not have to participate in this study to receive treatment for prostate cancer. Other treatments available to you are Radical Prostatectomy or Radiation Therapy.

Confidentiality:
Personal Health Information
If you agree to join this study, the study doctor and his/her study team will look at your personal health information and collect only the information they need for the study.

Personal health information is any information that could be used to identify you and includes your:

- Name.
- Address.
- Date of birth.
- New or existing medical records, that includes types, dates, and results of medical tests or procedures.

The study doctor will keep any personal health information about you in a secure and confidential location for 10 years.

Your participation in this study will also be recorded in your medical record at this hospital. This is for clinical safety purposes.

Research Information in Shared Clinical Records
If you participate in this study, information about you from this research project may be stored in your hospital file and in the UHN computer system. The UHN shares the patient information stored on its computers with other hospitals and health care providers in Ontario so they can access the information if it is needed for your clinical care. The study team can tell you what information about you will be stored electronically and may be shared outside of the UHN. If you have any concerns about this, or have any questions, please contact the UHN Privacy Office at 416-340-4800, x6937 (or by email at privacy@uhn.ca).

Representatives of the University Health Network including the Research Ethics Board may look at the study records and at your personal health information to check that the information collected for the study is correct and to make sure the study followed proper laws and guidelines.

Study Information that Does Not Identify You

All information collected during this study, including your personal health information, will be kept confidential and will not be shared with anyone outside the study unless required by law.

You will not be named in any reports, publications, or presentations that may come from this study.

Withdrawal from the Study
If you decide to leave the study, the information about you that was collected before you left the study will still be used. No new information will be collected without your permission.

Voluntary Participation:
Your participation in this study is voluntary. You may decide not to be in this study, or to be in the study now and then change your mind later. You may leave the study at any time without affecting your care. We will give you new information that is learned during the study that might affect your decision to stay in the study.

Costs and Reimbursement:
You will not have to pay for any of the procedures involved with this study. You will not be reimbursed for transportation, meals, time, inconvenience, etc.

Rights as a Participant:
If you are harmed as a direct result of taking part in this study, all necessary medical treatment will be made available to you at no cost.
By signing this form, you do not give up any of your legal rights against the investigators or involved institutions for compensation, nor does this form relieve the investigators or involved institutions of their legal and professional responsibilities.

Conflict of Interest:
The hospital and researchers have an interest in completing this study. Their interests should not influence your decision to participate in this study. You should not feel pressured to join this study.

Commercialization:
It is possible that new ideas, techniques, technologies or future standardized methods for treating localized prostate cancer, including technologies or processes that may receive patent protection will arise from this study. If so, you will not share in those potential intellectual or financial benefits.

Questions about the Study:
If you have any questions, concerns or would like to speak to the study team for any reason, please call: Dr. Sangeet Ghai at 416-340-4656.

If you have any questions about your rights as a research participant or have concerns about this study, call The Chair of the University Health Network Research Ethics Board

(REB) or the Research Ethics office number at 416-581-7849. The REB is a group of people who oversee the ethical conduct of research studies. These people are not part of the study team. Everything that you discuss will be kept confidential.

You will be given a signed copy of this consent form.

Consent:

This study has been explained to me and any questions I had have been answered. I know that I may leave the study at any time. I agree to the use of my information as described in this form. I agree to take part in this study.

Print Study Participant's Name	Signature	Date

My signature means that I have explained the study to the participant named above. I have answered all questions.

Print Name of Person Obtaining Consent	Signature	Date

(continue if applicable)

Was the participant assisted during the consent process? ☐ **YES** ☐ **NO**
If **YES**, please check the relevant box and complete the signature space below:

☐ The person signing below acted as an interpreter, and attests that the study as set out in the consent form was accurately sight translated and/or interpreted, and that interpretation was provided on questions, responses and additional discussion arising from this process.

Print Name of Interpreter	Signature	Date

Relationship to Participant	Language

☐ The consent form was read to the participant. The person signing below attests that the study as set out in this form was accurately explained to, and has had any questions answered.

Print Name of Witness	Signature	Date

Relationship to Participant