Informed Consent Form for Participation in a Research Study

Study Title: Evaluating the Feasibility, Safety and Efficacy of Radiofrequency Ablation (RFA) for Curative Treatment of Small Low-Risk Thyroid Papillary Cancer: A Pilot Single Arm Clinical

Study Doctor: Dr. Sangeet Ghai - Joint Department of Medical Imaging
(416) 340-4656

Funder: MSH-UHN AMO Innovation Fund

Emergency Contact Number (24 hours / 7 days a week):
(416) 340-3155 ask for interventional radiology on-call

INTRODUCTION

You are being invited to participate in a clinical trial (a type of study that involves research). You are invited to participate in a research study because you have Small Low-Risk Thyroid Papillary Cancer. This consent form provides you with information to help you make an informed choice. Please read this document carefully and ask any questions you may have. All your questions should be answered to your satisfaction before you decide whether to participate in this research study. You may find it helpful to discuss it with your friends and family.

Please take the time you need to make your decision.

Taking part in this study is voluntary. You have the option to not participate at all or you may choose to leave the study at any time. Whatever you choose, it will not affect the usual medical care that you receive outside the study.

IS THERE A CONFLICT OF INTEREST?

Researchers have an interest in completing this study. Their interests should not influence your decision to participate in this study.

WHAT IS THE BACKGROUND INFORMATION FOR THIS STUDY?

Papillary thyroid carcinoma (PTC) is the most common type of thyroid cancer. The current standard of care includes surgery (removal of part or all of the thyroid gland) or active surveillance. Surgery may lead to lifelong hormone replacement along with surgical risks. These small cancers often grow very slowly (<2 cm), and in some cases, they may not grow at all.

Radiofrequency ablation (RFA) is a minimally invasive treatment that uses heat generated by high-frequency electrical currents to destroy abnormal tissue.

RFA has been used safely and effectively for many years to treat benign (non-cancerous) thyroid nodules, with well-documented clinical benefits. These procedures have resulted in "good outcomes" refer to the following measurable results observed in clinical studies:

- Significant reduction in nodule volume, typically 50-80% shrinkage within 6-12 months for benign nodules.
- Improvement or resolution of nodule-related symptoms, such as pressure, discomfort, or cosmetic concerns.
- Low complication rates, with only minor, transient side effects reported (e.g., temporary pain, mild swelling, temporary voice changes), and major complications occurring rarely <1%).
- Preservation of normal thyroid function, with most patients maintaining stable thyroid hormone levels and not requiring lifelong thyroid medication.
- Rapid recovery, including same-day discharge, return to routine activities within 24-72 hours, and no need for general anesthesia or surgical incisions. However, the use of RFA for treating small thyroid cancers is still being studied. Early research suggests that RFA may be a safe and effective treatment option for carefully selected patients with low-risk PTC, but more evidence is needed.

If RFA is shown to be successful, it could offer patients a non-surgical option with fewer side effects, no need for general anesthesia, preservation of thyroid tissue, and a quicker return to daily activities.

The radiofrequency ablation (RFA) system used in this study is approved by Health Canada for the treatment of benign thyroid nodules. However, Health Canada has not approved the sale or use of this device for treating papillary thyroid carcinoma (thyroid cancer). Health Canada, the regulatory body that oversees the use of medical devices in Canada, has allowed the RFA system to be used in this study for research purposes.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is evaluate the safety and feasibility of Radiofrequency Ablation (RFA) in treating localized papillary thyroid cancers (PTCs) measuring < 2cm cm within a follow-up time frame of 12 months post-procedure. Feasibility will be assessed across recruitment (≥2/month), procedure delivery and follow up data completeness.

Procedure technical success rate will be measured as proportion of planned RFA procedures completed per protocol. Follow up data completion will be measured as proportion of patients completing predefined follow up visits, ultrasound, and biopsy. The results may be used as a guide for larger studies, although there is no guarantee that they will be conducted. Participation in a pilot study does not mean that you will be eligible to participate in a future larger study.

WHAT OTHER CHOICES ARE THERE?

You do not have to take part in this study to receive treatment for thyroid cancer. Other treatments available to you are surgery or Active Surveillance.

Please talk to your usual doctor or the study doctor about the known benefits and risks of these other options before you decide to take part in this study. Your usual doctor or the study doctor can also discuss with you what will happen if you decide not to undertake any treatment at this time.

HOW MANY PEOPLE WILL TAKE PART IN THIS STUDY?
It is anticipated that about 30 participants will take part in this study at UHN.

This study should take 2 years to complete, and the results should be known in about 3 years.

WHAT IS THE STUDY INTERVENTION?

If you agree to take part in this study, you will have a procedure called **Radiofrequency Ablation (RFA)**. This is the experimental intervention being tested in this research study. This procedure uses a thin, needle-like probe that is gently inserted through the skin of your neck and guided into the thyroid nodule using ultrasound imaging. Once the probe is in place, a small amount of electrical energy is used to heat and destroy the targeted tissue, while protecting that surrounding healthy thyroid. The procedure will be performed by an interventional radiologist at Toronto General Hospital

The procedure will be done under local anesthesia, which means you will be awake, but the area in your neck will be numbed so that you do not feel pain. The procedure will take about 45 minutes to 1 hour, followed by a short observation period (approximately 1 hour) to ensure you are recovering well. You will be able to return home the same day.

Because this is a single-arm pilot study**,** all participants will receive this RFA treatment once during the study. You will then be followed for one year with scheduled clinic visits and imaging to assess safety, feasibility, and treatment response.

WHAT ELSE DO I NEED TO KNOW ABOUT THE STUDY INTERVENTION?

If you experience any side effects or unexpected symptoms after the Radiofrequency Ablation (RFA) procedure, the study doctor may delay, modify, or stop your participation in the study to ensure your safety. Your follow-up visits or additional tests may also be adjusted as needed. Normally, patients with small, low-risk papillary thyroid cancer are offered standard treatments such as surgery (removal of part or all of the thyroid gland) or active surveillance **(**regular monitoring with ultrasound and bloodwork). By taking part in this study, you will receive RFA instead of these usual treatment options**.**

Participating in this study does not prevent you from receiving other standard treatments in the future. If you or your study doctor decide that you should stop participating, you can still choose to undergo surgery or active surveillance at any time.

An application specialist from the RFA device company may be present during your procedure to ensure that the equipment is working correctly. This individual will not take part in your medical care and will not have access to any of your personal information.

WHAT ARE THE STUDY PROCEDURES?
The study involves six visits over a period of one year. Some of the procedures listed below are part of your standard medical care for thyroid cancer (for example, ultrasound or biopsy), while others are being done only for research purposes, such as questionnaires to measure quality of life and satisfaction.

The Radiofrequency Ablation (RFA) treatment is the experimental procedure being studied.
If any of the results from your tests show that it is unsafe or not appropriate for you to continue,

the study doctor will discuss this with you.

All visits will take place at Toronto General Hospital, part of the University Health Network (UHN) in Toronto, Canada.
No hospitalizations are expected, and you will return home the same day after each visit.
The study team will review parts of your UHN electronic medical record, such as your medical history, imaging, lab results, and medication list, to ensure safe monitoring of your care.

Visit 1 – Screening/Baseline (Before RFA Procedure)

If you decide to participate, you will:

- Provide your medical history and undergo a physical examination.
- Provide a blood sample (approximately 10–15 mL, or about 1 tablespoon) to assess your thyroid function and general health.
- Undergo a laryngoscopy, performed by your Head & Neck surgeon, to examine your vocal cords before treatment.

  A laryngoscopy is a simple procedure that allows the doctor to look at your voice box (larynx) and the back of your throat. The doctor uses a small, thin tube with a light and camera on the end, which is gently passed through your nose or mouth. This helps the doctor see how your vocal cords are working and check for any problems such as swelling, irritation, or growths. The procedure is usually quick and may feel a little uncomfortable, but it should not be painful. You may feel pressure, a tickling sensation, or the urge to cough. A numbing spray may be used to make it more comfortable. After the procedure, you can return to your normal activities.

- Complete several questionnaires to assess your quality of life, satisfaction, and emotional well-being. These include:
  - SAPS – Questions assessing satisfaction with care and treatment
  - Voice Handicap Index-10 (VHI-10) – To assess any voice changes and their impact on daily life
  - EORTC QLQ-THY34 and EORTC QLQ-C30 – To assess overall health-related quality of life for thyroid cancer
  - ASC – To measure fear and worry experienced by cancer survivors about recurrence and health

The visit will take approximately 2 hours to complete.

Visit 2 - Radiofrequency Ablation (RFA) Procedure

You will undergo RFA treatment at the Toronto General Hospital Biopsy Centre Suite (or a similar UHN facility).

- Local anesthesia will be used to numb the area.
- A thin probe will be inserted into the thyroid nodule using ultrasound guidance.
- Heat will be delivered to destroy the cancerous tissue while sparing surrounding structures.
- The procedure will last approximately 45 minutes to 1 hour, followed by about 1 hour of observation.

After observation, you will be discharged home the same day.

The visit will take approximately 2 hours to complete.

Visit 3 – 1-2 weeks After Treatment

You will return for a clinic appointment to evaluate recovery and monitor for any treatment-related side effects such as:

- Pain, swelling, or bruising around the neck
- Skin changes
- Voice changes or hoarseness
- Undergo a follow-up laryngoscopy to evaluate your vocal cords.

The visit is part of standard post-procedure and will take approximately 30 minutes to complete.

Visit 4 – 3 months after Treatment

You will:

- Have a physical examination of your neck and thyroid area.
- Undergo a neck ultrasound to assess the treated area.

  A neck ultrasound is a simple, painless test that uses sound waves to create pictures of the inside of your neck. During the test, a technician or doctor moves a small handheld device called a "probe" over the skin of your neck. A warm gel is applied to help the probe glide smoothly and create clear images. This test helps the doctor see the thyroid gland, lymph nodes, and other structures in your neck. It does **not** use radiation, and there are no known risks. The procedure usually takes about 10–20 minutes, and you can return to your normal activities right afterward.

- Provide a blood sample (about 10–15 mL) to check thyroid function.
- Laryngoscopy will be done only if required by the physician per standard of care.
- Complete the same quality-of-life questionnaires from Visit 1 and one additional questionnaire:
  - Decision Regret Scale – Assesses your feelings about your treatment choice.

The visit will take about 3 hours to complete.

Visit 5 – 6 months After Treatment

You will:

- Have a physical exam and neck ultrasound to evaluate healing.
- Provide a blood sample (about 10–15 mL) to check thyroid function.
- Complete the quality-of-life questionnaires again.
- A thyroid biopsy may be performed at this visit or at the 12-month visit, depending on how the treated area appears on ultrasound. The biopsy uses a fine needle to remove a small tissue sample (about 2–3 mm, or the size of a sesame seed).
- Laryngoscopy will be done only if required by the physician per standard of care.

All procedures are standard of care except questionnaires, which are part of research. The visit will take approximately 2 hours to complete.

Visit 6 – 12 months After Treatment

You will:

- Have a final physical exam, neck ultrasound, and blood test (10–15 mL) to check thyroid function.
- Complete the quality-of-life questionnaires again.
- A thyroid biopsy may be performed if needed to confirm no remaining disease.
- Laryngoscopy will be done only if required by the physician per standard of care.

The visit will take about 2 hours to complete.

Summary of Tests and Procedures

Tests	**Visit 1**	**Visit 2**	**Visit 3/ Week 1-2**	**Visit 4/ Month 3**	**Visit 5/ Month 6**	**Visit 6/ Month 12**
Informed Consent	X					
Medical History	X					
Physical Exam	X		X	X	X	X
Blood tests	X			X	X	X
Laryngoscope	X		X	**	**	**
Questionnaires	X			X	X	X
Thyroid RFA Procedure		X				
Adverse Events		X		X	X	X
Vital Signs	X	X		X	X	X
Check Other Medications	X	X		X	X	X
Neck Ultrasound				X	X	X
Thyroid Biopsy						X

** - Laryngoscopy will be done only if required by the physician per standard of care at Visit 4, 5 and Visit 6.

WHAT ARE THE RESPONSIBILITIES OF STUDY PARTICIPANTS?

If you choose to participate in this study, you will be expected to:

- Tell the study doctor about your current medical conditions.
- Tell the study doctor about all prescription and non-prescription medications and supplements, including vitamins and herbals, and check with the study doctor before starting, stopping or changing any of these.
- Return any questionnaires that you take home to complete.
- Tell the study doctor if you become pregnant before your Thyroid RFA procedure.

HOW LONG WILL PARTICIPANTS BE IN THE STUDY?

The study intervention will take place over one day, and you will be followed for a period of one year. You will be asked to return to the hospital 1–2 weeks after your procedure, and again at 3, 6, and 12 months.

You may be seen more often if the study doctor determines that this is necessary.

CAN PARTICIPANTS CHOOSE TO LEAVE THE STUDY?

You can choose to end your participation in this research (called withdrawal) at any time without having to provide a reason. If you choose to withdraw from the study, you are encouraged to contact the study doctor or study staff.

If you decide to leave the study, you can ask that the information that was collected about you not be used for the study. Let the study doctor know if you choose this. Otherwise, information that was recorded before you withdrew will still be used by the researchers for the purposes of the study, but no information will be collected after you withdraw from the study.

CAN PARTICIPATION IN THIS STUDY END EARLY?

The study doctor may stop your participation in the study early, and without your consent, for reasons such as:

- The study doctor no longer feels this is the best option for you
- The Principal Investigator decides to stop the study
- The Regulatory Authority/ies (for example, Health Canada) or Research Ethics Board withdraw permission for this study to continue
- If you plan to or become pregnant before your Thyroid RFA procedure

If this happens, it may mean that you would not receive the study intervention described in this consent form.

If you are removed from this study, the study doctor will discuss the reasons with you and plans will be made for your continued care outside of the study.

WHAT ARE THE RISKS OR HARMS OF PARTICIPATING IN THIS STUDY?

You may experience side effects from participating in this study. Some side effects are known and are listed below, but there may be other side effects that are not expected. You should discuss these with the study doctor.

The study doctor will watch you closely to see if you have side effects. When possible, other medicine will be given to you to make side effects less serious and more tolerable. Many side effects go away shortly after the study intervention is stopped, but in some cases side effects can be serious, long-lasting, permanent, or may even cause death.

If you experience a side effect that requires treatment between regular clinic or hospital visits, it is important that you make every effort to return to the hospital where the Radiofrequency Ablation (RFA) procedure was done. Because RFA is considered an experimental procedure for thyroid cancer and is only performed in specialized research settings, any side effects may be best treated by these clinics.

If you experience a serious side effect and need immediate treatment and are unable to return

to the hospital, please call 911 or go to the nearest emergency room. Then the study doctor should be contacted as soon as possible.

Risks related to the treatment may include:
Very likely (21–100%)
In 100 people receiving RFA, between 21 and 100 may have:

Risk	Description
Pain or discomfort	Most common during or after the procedure; typically, mild.
Vasovagal reaction	Most common during or after the procedure: typically, mild.
Swelling or bruising	Most common during or after the procedure; typically, mild.
Localized hematoma or neck fullness	Often resolves without intervention
Post-procedural fever or fatigue	Low-grade fever and fatigue may occur due to tissue necrosis; usually self-limited.

Less likely (5–20%)
In 100 people receiving RFA, between 5 and 20 may have:

Risk	Description
Voice changes (hoarseness)	May occur due to thermal injury or irritation of the recurrent laryngeal nerve; usually temporary but may be permanent in rare cases.
Skin burns or thermal injury	Rare if proper hydro-dissection and technique are used.
Infection or abscess	Rare; may require antibiotics or drainage.

Rarely (1–4%)
In 100 people receiving RFA, between 1 and 4 may have:

Risk	Description
Voice changes (hoarseness)	May occur due to thermal injury or irritation of the recurrent laryngeal nerve; usually temporary but may be permanent in rare cases.
Skin burns or thermal injury	Rare if proper hydro-dissection and technique are used.
Infection or abscess	Rare; may require antibiotics or drainage.

Risks of study related procedures:

Risks of Thyroid FNA/Biopsy

- Mild pain or discomfort in the biopsy area: There is small possibility of pain, bruising, swelling or infection related to the biopsy procedure at 6 or 12 months.

Risks of Blood Draw/Catheter Blood Draw – There is a possibility of pain, bruising, swelling, or infection related to giving blood.

WHAT ARE THE REPRODUCTIVE RISKS?

The effects that Thyroid RFA may have on an unborn baby (fetus), eggs, or sperm are unknown. The study doctor will discuss family planning with you to ensure that you do not become pregnant prior to your RFA treatment, indicating an awareness of potential risk during pregnancy, although minimal. The study excludes pregnant or breastfeeding individuals.

WHAT ARE THE BENEFITS OF PARTICIPATING IN THIS STUDY?

If you agree to take part in this study, the experimental intervention may or may not be of direct benefit to you.
Information learned from this study may help doctors decide whether to offer RFA to other patients with papillary thyroid cancer in the future.

HOW WILL PARTICIPANT INFORMATION BE KEPT CONFIDENTIAL?

If you decide to participate in this study, the study doctors and study staff will only collect the information they need for this study.

Your data will be shared as described in this consent form and/or as required by law and/or applicable research regulations. Records identifying you at this centre will be kept confidential and, to the extent permitted by applicable laws, will not be disclosed or made publicly available.

Authorized representatives of the following organizations may come to the hospital or be given remote access to an electronic portal (via Internet) to look at your original (identifiable) medical/clinical study records at the site where these records are held, to check that the information collected for the study is correct and follows proper laws and guidelines. When using the electronic portal, we will share your medical record number using a secure method, so that your records are included as part of their review.

- Representatives of the University Health Network including the UHN Research Ethics Board, who oversees the ethical conduct of this study at UHN and Health Canada, because they oversee the use of medical devices in Canada.

These individuals have completed privacy training and signed confidentiality agreements and/or are required by law to keep your information confidential.

Whether on-site or remotely, UHN makes all efforts to ensure that your information is shared in a way that is secure and private (encrypted). However, any electronic communication carries some risk of third parties gaining unauthorized access to information.

Information that is collected about you for the study (called study data) may also be sent to the organizations listed above. Any information about you that is sent out of the hospital will have a number and will not show any information that directly identifies you. e.g. participant code.

If the results of this study are published, your identity will remain confidential. It is expected that the information collected during this study will be used in analyses and will be published/ presented to the scientific community at meetings and in journals.

Even though the likelihood that someone may identify you from the study data is very small, it can never be completely eliminated.

The study doctor will keep any personal health information about you in a secure and confidential location for 15 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).

WILL FAMILY DOCTORS/HEALTH CARE PROVIDERS KNOW WHO IS PARTICIPATING IN THIS STUDY?

Your family doctor/health care provider will not be informed by the study team that you are taking part in the study. You can choose to let your family doctor/health care provider know if you like.

WILL INFORMATION ABOUT THIS STUDY BE AVAILABLE?

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.

Study results will be shared with you if/when they become available after the entire study is completed. It is expected that this may take a number of years. The results will be shared with you based on your preferred communication method indicated in UHN's medical record system. Please talk to your study doctor if you have any questions about the results.

WHAT IS THE COST TO PARTICIPANTS?

You will not have to pay for any of the procedures involved with this study.

Taking part in this study may result in added costs to you. For example:

- There may be costs associated with hospital visits. For example, parking or transportation, or snacks/meals during your stay.
- You may miss work as a result of participation in this study.

ARE STUDY PARTICIPANTS PAID TO BE IN THIS STUDY?

You will not be paid for taking part in this study.

WHAT WILL HAPPEN IF PARTICIPANT IS INJURED DURING THE STUDY?

In the case of research-related side effects or injury, medical care will be provided by your doctor or you will be referred to appropriate medical care.

COMMERCIALISATION

It is possible that the research conducted using your study data may eventually lead to the development of new diagnostic tests, new drugs or devices, or other commercial products. There are no plans to provide payment to you if this happens.

WHAT ARE THE RIGHTS OF PARTICIPANTS IN A RESEARCH STUDY?
You will be told, in a timely manner, about new information that may be relevant to your willingness to stay in this study.

Your rights to privacy are legally protected by federal and provincial laws that require safeguards to ensure that your privacy is respected.

By signing this form you do not give up any of your legal rights against the study doctor, sponsor or involved institutions for compensation, nor does this form relieve the study doctor, sponsor or their agents of their legal and professional responsibilities.

WHAT IF RESEARCHERS DISCOVER SOMETHING ABOUT A RESEARCH PARTICIPANT?
During the study, the researchers may learn something about you that they didn't expect. These are called incidental findings. For example, follow-up imaging or the 1-year biopsy may show unrelated thyroid changes (such as new benign nodules, thyroiditis, or other suspicious areas) or findings in the neck, such as enlarged lymph nodes, parathyroid lesions, or blood vessel changes.

If any new clinically important information about your health is found, it will be revied by the study radiologist and shared with your treating physician or primary care provider. They will discuss the results with you and arrange any necessary follow-up, following hospital policy.

WHOM DO PARTICIPANTS CONTACT FOR QUESTIONS?
If you have questions about taking part in this study, or if you suffer a research-related injury, you can talk to your study doctor, or the doctor who is in charge of the study at this institution. That person is:

Dr. Sangeet Ghai	416-340-4656
Name	Telephone

If you have questions about your rights as a participant or about ethical issues related to this study, call the Chair of the University Health Network Research Ethics Board (UHN 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. The UHN REB is not involved in the study at all. Everything that you discuss will be kept confidential.

You will be given a copy of this signed and dated consent form prior to participating in this study.

TITLE: Evaluating the Feasibility, Safety and Efficacy of Radiofrequency Ablation (RFA) for Curative Treatment of Small Low-Risk Thyroid Papillary Cancer: A Pilot Single Arm Clinical

- All of my questions have been answered
- I allow access to medical records and related personal health information as explained in this consent form
- I do not give up any legal rights by signing this consent form,
- My family doctor/health care provider may be informed of study participation
- I agree to take part in this study.

Signature of Participant	PRINTED NAME	Date

I have explained to the above-named participant the nature and purpose, the potential benefits, and possible risks of participation in this study. All questions that have been raised about this study have been answered.

Signature of Person Conducting the Consent Discussion	PRINTED NAME & ROLE	Date

The following attestation must be provided if the participant is unable to read or requires an oral translation:

If the participant is assisted during the consent process, 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

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 the participant, and any questions have been answered.

PRINT NAME of witness	Signature	Date

Relationship to Participant