CONSENT FOR CANCER RESEARCH

Project Title: CASE 4318: A Feasibility Study of Temporally Feathered Radiation Therapy (TFRT) for Head and Neck Squamous Cell Carcinoma: Means of Toxicity Reduction

Sponsor: Research Program Committees, Cleveland Clinic

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Cancer research studies are coordinated by physicians and scientists from Cleveland Clinic, University Hospitals and Case Western Reserve University (CWRU) through the NIH National Cancer Institute (NCI) designated Case Comprehensive Cancer Center (Case CCC). The goal of this collaboration is to enhance cancer treatment and research in Northeast Ohio. This study is being offered at Cleveland Clinic (CC).

What is the usual approach to treating my squamous cell carcinoma of the head and neck?
Cancers of the head and neck region are typically squamous cell carcinoma. Squamous cells are the type of cells that line the inner surface of the mouth and throat region. The parts of the head and neck that are included on this study are the oropharynx, nasopharynx, larynx, and hypopharynx. The current treatment options for head and neck cancers include using either surgery, radiation, or chemotherapy combined with radiation as the primary treatment.

The current standard of care radiation treatment uses a technique called intensity modulated radiation therapy (IMRT). The goal of IMRT is to treat the head and neck tumor and spare the normal healthy tissues nearby. IMRT uses special equipment to position the patient and shape radiation beams around the normal tissues. Research has shown that using IMRT has decreased the side effects from radiation both in the short-term and the long-term.

What are my other choices if I do not take part in this study?
If you decide not to take part in this study, you have other choices. For example:

- you may choose to have the usual approach described above
- you may choose to take part in a different study, if one is available
- or you may choose not to be treated for cancer. For example: comfort/palliative care

Why is this study being done?
The purpose of this study is to evaluate if it feasible to use a more advanced radiation technique in the clinic. This new technique of radiation therapy is called Temporally Feathered Radiation Therapy (TFRT). TFRT is meant to decrease the side effects of radiation. Though advances in

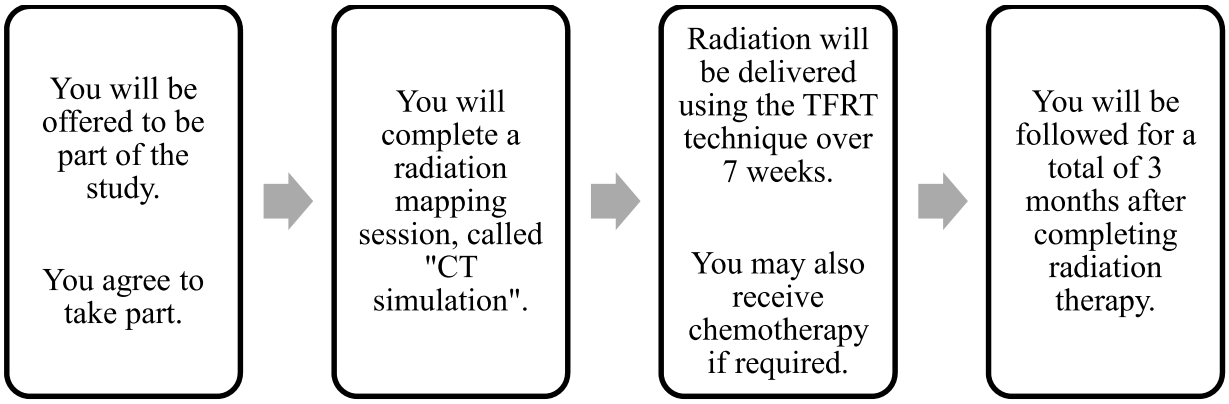
modern medicine has allowed us to decrease the side effects from radiation therapy using IMRT as described above, we find that most of our patients still develop short-term and long-term side effects. Prior research has shown that TFRT may lessen these side effects.

When using IMRT, a single radiation plan is created and delivered on a daily basis Monday-Friday for a total of 7 weeks. In contrast, when using TFRT, up to 5 different plans are created and delivered each specific day of the week. Treatments will still occur on a daily basis Monday-Friday for 7 weeks. In each of these radiation plans used for TFRT, the radiation dose that will be delivered to the nearby healthy tissues will vary, allowing for increased time for normal tissue to recover from radiation-induced damage. Please take note that the radiation dose that will be delivered the areas of cancer will not be changed. In this study, only the radiation dose delivered to the normal healthy tissues will be changed.

What are the study groups?

All study participants will get the same study intervention. It will include the radiation therapy using the TFRT technique described above. Patients may also receive chemotherapy if the physician decides it is required.

To find out what will happen to you during this study read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



How long will I be in this study?
You will receive Temporally Feathered Radiation Therapy for a total of 7 weeks. You will be assessed for side effects during your regularly scheduled doctors' visits during that time. In addition, after you finish radiation therapy, your doctor will continue to watch you for side effects and follow your condition for 3 months while on the study.

What extra tests and procedures will I have if I take part in this study?
All doctors' visits will be according to the standard of care. The only additional test will be a questionnaire that you will complete on paper so that you can accurately describe how you are feeling during treatment.

Before you begin the study:

No extra tests are necessary before, during, or after the study aside from the questionnaires as described above. Before enrolling on the study your diagnosis will be made according to the standard of care with appropriate imaging and biopsy.

What possible risks can I expect from taking part in this study?
If you choose to take part in this study, there is a risk that:

- You may lose time at work or home and spend more time in the hospital or doctor's office than usual

There is also a risk that you could have side effects from the study approach.

Here are important points about side effects:

- The study doctors do not know who will or will not have side effects.
- Some side effects may go away soon, some may last a long time, or some may never go away.
- Some side effects may be serious and may even result in death.

Here are important points about how you and the study doctor can make side effects less of a problem:

- Tell the study doctor if you notice or feel anything different so they can see if you are having a side effect.
- The study doctor may be able to treat some side effects.

The tables below show the most common and the most serious side effects that researchers know about. There might be other side effects that researchers do not yet know about. If important new side effects are found, the study doctor will discuss these with you.

Possible side effects of Temporal Feathering Radiation Therapy are the same as potential side effects from conventional radiation therapy using IMRT techniques, which is the usual approach to treatment for this type of cancer. The side effects may include, but are not limited to, the following below:

COMMON, SOME MAY BE SERIOUS In 100 people receiving Temporally Feathered Radiation Therapy, more than 20 and up to 100 may have:
▪ Skin redness, irritation, peeling and tanning ▪ Sores in the mouth and swallowing tube (esophagus) which can cause pain and difficulty swallowing ▪ Dry mouth ▪ Thick oral secretions ▪ Dehydration ▪ Weight loss ▪ Appetite changes ▪ Taste changes ▪ Mild pain

OCCASIONAL, SOME MAY BE SERIOUS In 100 people receiving Temporally Feathered Radiation Therapy, from 4 to 20 may have:
▪ Permanent hair loss ▪ Trouble swallowing ▪ Temporary need for feeding tube ▪ Neck stiffness ▪ Nausea

RARE, AND SERIOUS In 100 people receiving Temporally Feathered Radiation Therapy, 3 or fewer may have:
▪ Need for feeding tube more than one year ▪ Need for tracheostomy, which is a surgical opening through the neck for breathing tube ▪ Osteonecrosis of the mandible, which is damage to jaw bone ▪ Narrowing of the esophagus ▪ Pneumonia requiring hospitalization ▪ Secondary radiation-induced cancer development

What possible benefits can I expect from taking part in this study?
You will receive medical care during the study. You may not receive direct benefit from being in this study. However, taking part may help patients with head and neck cancers get better care in the future.

Can I stop taking part in this study?
Yes. You can decide to stop at any time. If you decide to stop for any reason, it is important to let the study doctor know as soon as possible so you can stop safely. If you stop, you can decide whether or not to let the study doctor continue to provide your medical information to the organization running the study.

The study doctor will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

The study doctor may take you out of the study:
- If your health changes and the study is no longer in your best interest
- If new information becomes available
- If you do not follow the study requirements
- If the study is stopped by the sponsor, Institutional Review Board (IRB), or FDA.

What are my rights in this study?
Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

What are the costs of taking part in this study?
Your involvement in this research study is voluntary and you will not be paid for your participation.

You and/or your health plan/insurance company will need to pay for some or all of the costs of treating your cancer in this study (i.e. medical history, review of medications, physical exams, performance status, pregnancy test, and radiation therapy). Some health plans will not pay these costs for people taking part in studies. Check with your health plan or insurance company to find out what they will pay for. Taking part in this study may or may not cost your insurance company more than the cost of getting regular cancer treatment.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at http://www.cancer.gov/clinicaltrials/learningabout.

What happens if I am injured or hurt because I took part in this study?
If you believe that you are injured as a result of the research procedures being performed, please immediately contact the study doctor.

If injury occurs as a result of your involvement in this research, medical treatment is available from the Cleveland Clinic or another medical facility but you/your medical insurance will be responsible for the cost of this treatment. A research injury is an injury that happens as a result of taking part in this research study. If you are injured by a medical treatment or procedure that you would have received even if you weren't in the study, that is not considered a "research injury". There are no plans for payment of medical expenses or other payments, including lost wages, for any research related injury. To help avoid injury, it is very important to follow all study directions.

Further information about research-related injuries is available by contacting the Cleveland Clinic Institutional Review Board at (216) 444-2924.

HIPAA AUTHORIZATION
Authorization to Use or Disclose (Release) Health Information that Identifies You for a Research Study

If you volunteer to participate in this research, your protected health information (PHI) that identifies you will be used or disclosed to **Nikhil Joshi, MD,** and the research study staff at Cleveland Clinic for the purposes of this research and to Case Western Reserve University for administration.

The PHI that we may use or disclose (release) for this research may include your name, address, phone number, date of birth, Social Security number, information from your medical record, lab tests, or certain information relating to your health or condition.

Some of the tests done solely for this research study may also be placed in your medical record so other doctors know you are in this study. Upon completion of the study, you may have access to the research information that is contained in your medical record.

In addition to the investigators and research staff listed above, your PHI may be looked at by other groups involved with the study such as the Cleveland Clinic Institutional Review Board,

and the Case Comprehensive Cancer Center Protocol Review and Monitoring Committee. Your PHI may also be used by and/or disclosed (released) to:

- Case Comprehensive Cancer Center members and collaborators;
- The Food and Drug Administration;
- The Department of Health and Human Services;
- The National Cancer Institute (NCI);
- Other Institutional Review Boards;
- Data Safety and Monitoring Boards;

Once your personal health information is released it may be re-disclosed and no longer protected by privacy laws.

Your research information may be used and disclosed indefinitely, but you may stop these uses and disclosures at any time by writing to:

Nikhil Joshi, MD
Case Comprehensive Cancer Center
Cleveland Clinic-CA50
9500 Euclid Ave.
Cleveland, OH 44195

Your participation in the research will stop, but any information previously recorded about you cannot be removed from the records and will continue to be used as part of this research. Also, information already disclosed outside the Cleveland Clinic cannot be retrieved. This will not affect your rights to treatment or benefits outside the research study.

The Cleveland Clinic will not use your information collected in this study for another research purpose without your written permission; unless the Cleveland Clinic Institutional Review Board (IRB) assures your privacy and confidentiality is protected. The IRB is a committee whose job is to protect the safety and welfare of research subjects.

By signing this informed consent form, you are authorizing such access to your research and medical record information. If you choose not to sign this consent form, you will not be able to participate in this research study. This Authorization does not have an expiration date.

Voluntary Participation
Your participation in this research study is voluntary. Choosing not to participate will not alter your usual health care or involve any penalty or loss of benefits to which you are otherwise entitled. If you decide to join the study, you may withdraw at any time and for any reason without penalty or loss of benefits. If information generated from this study is published or presented, your identity will not be revealed.

In the event new information becomes available that may affect the risks or benefits associated with this study or your willingness to participate in it, you will be notified so that you can decide whether or not to continue participating.

Questions about the Research
If you have any questions, you can ask the Principal Investigator and/or research staff at 216-444-6630.

Emergency or after-hours contact information
You should contact the page operator at (216) 444-2200 or toll free at (800) 223-2273, and ask for the radiation oncologist (cancer doctor) that is on call.

Where Can I Get More Information?
If the researchers cannot be reached, or if you would like to talk to someone other than the researcher(s) about: concerns regarding the study; research participant's rights; research-related injury; or other human subjects issues, you may contact the Institutional Review Board (IRB) at Cleveland Clinic IRB 216-444-2924.

You may call the National Cancer Institute's Cancer Information Service at:
1-800-4-CANCER (1-800-422-6237)

You may also visit the NCI Web site at http://cancer.gov/

- For NCI's clinical trials information, go to: http://cancer.gov/clinicaltrials/
- For NCI's general information about cancer, go to http://cancer.gov/cancerinfo/

You will get a copy of this form. If you want more information about this study, ask your study doctor.

US National Institutes of Health (NIH) Clinical Trial Database:
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.

Signature

Signing below indicates that you have been informed about the research study in which you voluntarily agree to participate; that you have asked any questions about the study that you may have; and that the information given to you has permitted you to make a fully informed and free decision about your participation in the study. By signing this consent form, you do not waive any legal rights, and the investigator(s) or sponsor(s) are not relieved of any liability they may have. A copy of this consent form will be provided to you.

_____	_____	_____
Signature of Participant	Date	Printed Name of Participant

I have discussed the information contained in this document with the participant and it is my opinion that the participant understands the risks, benefits, alternatives and procedures involved with this research study.

_____	_____
Signature of Person Obtaining Consent	Date

_____
Printed Name of Person Obtaining Consent