Protocol Title: A Pilot Single Arm Study of Intensity Modulated Radiation Therapy Elective Nodal Dose De-Escalation for HPV-Assoiciated Squamous Cell Carcinoma of the Oropharynx

NCT#: NCT01891695

Version date: June 3, 2013

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Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____ **Medical Record #** _____

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Sponsor: UVA Health System, Department of Radiation Oncology

What is the purpose of this form?

This form will help you decide if you want to be in the research study. You need to be informed about the study, before you can decide if you want to be in it. You do not have to be in the study if you do not want to. You should have all your questions answered before you give your permission or consent to be in the study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will get a copy of this form.

Who is funding this study?

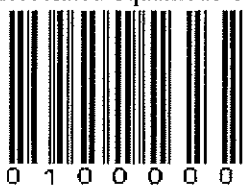
This study is being sponsored by the Department of Radiation Oncology at the University of Virginia Health System.

Why is this research being done?

The dose of radiation most commonly used to treat oropharyngeal cancer results in side effects including sores in the mouth and throat, dry mouth and thick saliva, loss or altered taste, swallowing problems including pain or inability to swallow requiring feeding tubes to be placed in the stomach, hoarseness or breathing problems from swelling requiring tracheostomy or a hole surgically placed in your windpipe to allow you to breathe, nausea and vomiting, fatigue and loss of energy, decreased hearing from fluid behind the ear drums in the middle ear, skin redness tenderness and blistering.

The purpose of this study is to determine if we can reduce the dose of radiation to the lymph nodes in the neck in order to reduce the side effects from your treatment, and still adequately kill any cancer cells that may be

IRB-HSR
APPROVAL DATE 06/06/13
EXPIRATION DATE 05/27/14



contained in those lymph nodes. Lymph nodes in your neck may have small numbers of cancer cells in them which are difficult to detect using the national standard of care methods. **This is done using Intensity Modulated Radiation Therapy (IMRT)**

Patients with certain types of cancers of the oropharynx (base of tongue or tonsil) that are related to the human papilloma virus (HPV) have tumors that are more sensitive to radiation compared to tumors that are not related to the HPV virus. We will determine if your tumor is related to the HPV virus by testing your tumor biopsy for the presence of HPV DNA or protein (called p16). This study will only include patients with oropharyngeal cancer that have the p16 protein in them.

You are being asked to be in this study, because you have a tumor that arose in your oropharynx (base of tongue or tonsil) that contains the p16 protein and you will be treated with radiation as a part of your cancer treatment. These treatments will be targeted to any cancer in your oropharynx and to any lymph nodes in your neck that contain cancer cells as determined by standard radiology studies such as contrast enhanced CT scans or MRI scans and PET CT scans.

We will also target lymph nodes in your neck that might contain microscopic amounts of cancer cells with radiation, and in this study we will treat these lymph nodes with about 20% less radiation compared to our current treatments, 39.6 Gray in 22 treatments (a Gray is a measure of radiation dose) will be given compared to 50.4 Gray in 28 treatments. We hope to learn if this reduced dose of radiation is as effective at killing any microscopic amounts of cancer cells in these lymph nodes as higher doses of radiation and if this results in less radiation-related toxicity. If any of the lymph nodes in your neck are determined to contain greater than microscopic amounts of cancer cells then you will be treated with the national standard full radiation dose.

The radiation treatments will be administered to you using standard clinical guidelines. The only difference in your treatment that is experimental and being done for research purposes is that the number of treatments and the radiation dose that we give to certain lymph nodes will be approximately 20% less than if you were not on this study.

Up to **45** people will be in this study at UVA.

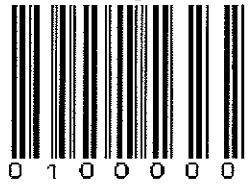
How long will this study take?

Your participation in this study will require daily radiation treatment for 7 weeks and 12 study visits over 3 years. Study visits will last about 2 hours, except for the Screening Visit which will take approximately 4 hours to complete.

What will happen if you are in the study?

SCREENING (will take approximately 4 hours to complete):

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening period. You will have tests and procedures during



this time to make sure you are eligible and it is safe for you to participate. You will need to have some or all of the following exams, tests or procedures to find out if you can be in the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study doctor.

The following exams, tests or procedures are **part of regular cancer care** and will be done even if you do not join the study:

- Review of your medical history
- Physical exam and vital signs (blood pressure, heart rate, etc.)
- A pregnancy test if you are capable of becoming pregnant (this will be done within 14 days prior to receiving study treatment)
- Neck imaging (contrast enhanced CT or MRI scan of the neck and/or PET CT scan)
- Test of your tumor biopsy for HPV DNA and/or the p16 protein

The following exams, tests or procedures are not part of regular cancer care and will be done for research purposes:

- You will be asked to complete three (3) questionnaires before and after treatment. These questionnaires ask about:
  - how you are feeling
  - your lifestyle habits
  - daily activities

These questionnaires will take about 30 minutes to complete.

If these tests show you are eligible, you will return within 30 days to begin your radiation treatment.

STUDY TREATMENT (each radiation treatment visit will last about ***20 minutes***):

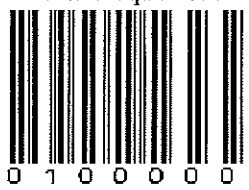
Prior to radiation your doctors will examine you and obtain several images (a CT scan or MRI scan of your neck and a PET CT scan) to determine the full extent of cancer in your body.

You will undergo a special CT scan in the department of Radiation Oncology that will be used for planning your radiation treatments.

Any tissues that contain cancer will be targeted for radiation treatment with 70 Gy given over 35 daily treatments. This will require you to come for radiation treatment 5 days per week (Monday through Friday) for 7 weeks.

Lymph nodes in your neck at risk to contain very small amounts of cancer will be targeted with 39.6 Gy given over the first 22 treatments (for research purposes)

For the purpose of this study, you will be treated with an advanced radiation treatment technique called ntensity Modulated Radiation Therapy (IMRT) which allows your radiation oncology treatment team to target your radiation treatment to tissues that are known to have cancer with the highest doses of radiation, tissues that



may have very small amounts of cancer with lower doses of radiation, and to minimize radiation dose to adjacent normal tissues that are not at risk to contain cancer cells.

We will obtain x-ray or CT images each day prior to each radiation treatment to make sure that your body is set up accurately for your radiation treatment. These are all done as part of your clinical care, however, the results will be recorded for research purposes.

At each radiation treatment visit, you will be asked about any side effects you may be feeling. At one visit per week of your radiation treatment, you will have the following exams, tests or procedures.

These procedures are part of regular cancer care and the results from these procedures will be recorded for research purposes.

- Review of your medical history
- Physical exam and vital signs (blood pressure, heart rate)

You may also receive chemotherapy during the radiation treatment or have surgery to remove lymph nodes that contained cancer after the radiation treatments are complete, however, this is not a part of the research treatment in this study.

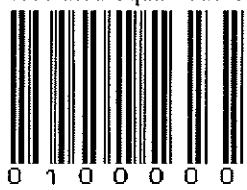
FOLLOW UP:

Follow-up visits will be conducted per standard clinical care, at **about 1, 3, 6, 9, 12, 15, 18, 21, 24, 30, and 36 months** after you complete your radiation treatment. To check your well-being and the status of your cancer, you will undergo these tests and procedures that are part of regular cancer care:

- Review of your medical history
- Physical exam and vital signs (blood pressure, heart rate, etc.)
- Your doctor will examine your nose, voice box and throat using a small, flexible, scope (about half the width of a pencil) inserted into one of your nostrils
- You will be asked about any side effects which may have occurred after your treatment

You will also be asked to complete three (3) questionnaires. **These questionnaires are being done for research purposes only.**

During follow-up visits at **1, 12, 24 and 36 months** after your radiation treatment, your doctor will perform either a CT or PET scan of your neck to check the status of your cancer. This procedure is part of regular cancer care and will be done even if you do not join the study. Additional CT or PET CT scans will be obtained at other times if there is any clinical concern that you may have recurrence of cancer. Results of these scans may be recorded for research purposes.



Study Schedule

	Screening (Visit 1)	Radiation treatment (weeks 1-7)	Follow-up
Informed Consent	x		
Medical History	x	x	x
Physical Exam	x	x	x
Blood pressure and heart rate	x	x	x
Neck CT or PET scan	x		x (at 1, 12, 24 and 36 months only)
Questionnaires	x		x
Review side effects		x	x

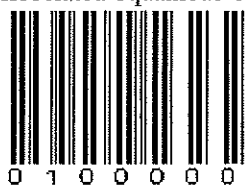
If you want to know about the results before the study is done:

During the study your study leader will let you know of any test results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

The major risk of this study is that the lower radiation dose used to treat the lymph nodes at risk for microscopic amounts of cancer in your neck is not enough to kill these cancer cells and cancer regrows or recurs in these lymph nodes after radiation treatment is completed. We will follow you carefully to try to detect any recurrence or regrowth of cancer. If your cancer recurs or comes back in the lymph nodes in your neck we will recommend surgery to remove these lymph nodes (called a neck dissection), and possibly more radiation and or chemotherapy. There is a chance that you could die if your cancer recurs in these lymph nodes and we cannot remove them or kill the recurrent cancer with additional radiation and or chemotherapy.

Side effects of radiation for the treatment of oropharyngeal cancer include side effects that occur during and last up to 90 days after the radiation (acute radiation side effects) and those that occur or develop more than 90 days after completion of radiation (late radiation side effects). Serious side effects can occur from radiation treatments used to treat patients with oropharyngeal cancer and 'Serious' is defined as side effects that may require hospitalization or may be irreversible, long-term, life threatening or fatal



Because chewing and/or swallowing are likely to be difficult, the study doctor may recommend placing a feeding tube before or during treatment so you can receive the nutrition you need. You might need a long term or permanent feeding tube. You should talk to your study doctor about this.

You will have up to 35 days of radiation exposure using Intensity-Modulated Radiation Therapy (IMRT). Your neck will receive 2 Gy of radiation therapy dose each day for a total dose of 70 Gy over the entire treatment period. Your neck will receive the highest doses of radiation because IMRT has the ability to target very specific areas of the tumor. The surrounding tissues or organs may receive much smaller doses of radiation IMRT is used routinely to treat cancers of this type, however has the following side effects:

Likely side effects are:
- Loss of appetite
- Temporary fatigue and weakness
- Fewer platelets, causing increased bruising and bleeding, particularly nosebleeds or bleeding of the gums

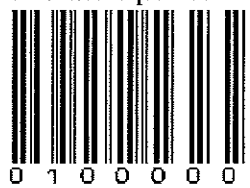
Less likely side effects are:
- Fewer red blood cells, causing fatigue and weakness
- Fewer white blood cells, causing increased risk of infections
- General body pain

Rare but serious side effects are:
- Changes in heart rate

The side effects related to radiation would not be less if you were not on this study and include:

Very Likely

- Redness and irritation of skin within the treatment area
- Difficulty, pain or burning sensation when swallowing, difficulty opening your jaw
- Sores in the mouth and or throat that can be painful and make it difficult to chew or swallow food
- Mouth dryness and changes in your ability to taste food that may be permanent
- Thick saliva
- Pain around your neck and lymph nodes
- Ear pain or pressure, difficulty hearing, or ringing in the ears
- Hoarseness
- Hair loss at the treatment area
- Nausea and/or vomiting, dehydration and weight loss
- Loss of appetite and/or taste
- Skin in treatment area may remain permanently dry
- Decrease in blood counts while undergoing treatment
- Fatigue, insomnia, anxiety or depression
- Loss of teeth or cavities in the teeth if strict dental care is not followed



- Swelling in your face

Less Likely

- Voice hoarseness may remain after treatment
- Decrease in the function of the thyroid gland, which may require pills for thyroid replacement
- Serious ear infections or hearing loss
- Breathing problems
- Difficulty with swallowing food that may require placement of a long term or permanent feeding tube and the possibility of inhaling food or liquids into the lungs, which may result in pneumonia
- Temporary pain or scarring around nerves in the shoulder that can cause numbness or weakness
- A different cancer

Less Likely, But Serious

- Injury to the jaw, voice box, or tissue of the neck
- Thyroid gland dysfunction requiring thyroid hormone pills in the future
- Irritation of the spinal cord
- Fainting
- Stroke

Other unexpected risks: You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?

We cannot promise that you will be helped by being in this study. You may benefit from being in this study. Possible benefits from this study include less side effects from the radiation treatment for your cancer. In addition, the information researchers get from this study may help others in the future.

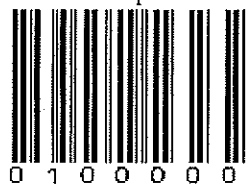
What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include treating the lymph nodes in your neck at risk for containing microscopic amounts of cancer with 50.4 Gy of radiation in 28 treatments.

If you are an employee of UVa your job will not be affected if you decide not to participate in this study.
If you are a student at UVa, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will not get any money for being in this study.



Will being in this study cost you any money?

The following procedures/tests, which are being done for research purposes, will be provided at no cost to you or your health insurance: 1) completion of questionnaires.

You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask for an estimate of your financial costs. You may also wish to check with your insurance company before the study starts. Ask what they will cover and if they require you to get their permission before you decide to be in the study.

What if you are hurt in this study?

If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover. You do not give up any legal rights, such as seeking compensation for injury, by signing this form.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

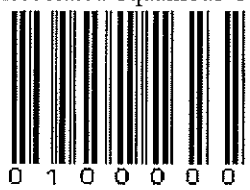
Even if you do not change your mind, the study leader can take you out of the study. Some of the reasons for doing so may include

a) Your study doctor is concerned about your health
b) Your disease gets worse
c) The side effects of the treatment are too dangerous for you
d) New information shows the treatment will not work or is not safe for you
e) You do not follow your doctor's instructions
f) The study sponsor closes the study for safety, administrative or other reasons

If you decide to stop being in the study, we will ask you to continue to complete the questionnaires. The questionnaires will be mailed to you for you to complete at return by mail at your convenience.

How will your personal information be shared?

The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVa.



If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address, date of birth,
- Your health information. If required for this study, this may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers (if required for this study, this may include mental health care records, substance abuse records, and/or HIV/AIDS records
- Your medical records and test results from before or during the study from any of your doctors or health care providers. Only information related to your throat or oropharyngeal cancer will be collected.
- Information needed to bill others for your care

Who will see your private information?

- The researchers to make sure they can conduct the study appropriately, observe the effects of the study and understand its results
- People or committees that oversee the study to make sure it is conducted correctly
- People who pay for the study (UVA Health System, Department of Radiation Oncology), including insurance companies
- Tax reporting offices (if you are paid for being in the study)
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA)

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

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.

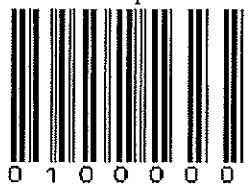
What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation. UVa researchers will do everything possible to protect your privacy.

A copy of this consent form will be put in your medical record. (This is not the same as the record of this research study.) This means that everyone who is allowed to see your records will be able to find out that you are in this study.

Please contact the researchers listed below to:

- Obtain more information about the study



- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator:
Paul W. Read, MD PhD
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Phone: 434-924-5191
Fax: 434-982-3262 pwr3u@ hscmail.mcc.virginia.edu

What if you have a concern about a study?

You may also report a concern about a study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483 Charlottesville, Virginia 22908 Telephone: 434-924-2620

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study. You will receive a copy of this document.

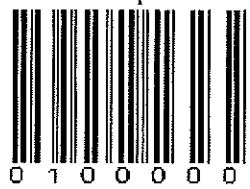
Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Consent From Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.



I agree the information in this informed consent form was presented orally in my presence to the subject and the subject had the opportunity to ask any questions he/she had about the study. I also agree that the subject freely gave their informed consent to participate in this trial.

_____
NAME OF IMPARTIAL WITNESS

_____ _____
SIGNATURE OF IMPARTIAL WITNESS DATE

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE