

NRG ONCOLOGY
Radiation Therapy Oncology Group

RTOG 0815

(ClinicalTrials.gov NCT #: 00936390)

**A PHASE III PROSPECTIVE RANDOMIZED TRIAL OF DOSE-
ESCALATED RADIOTHERAPY WITH OR WITHOUT SHORT-TERM
ANDROGEN DEPRIVATION THERAPY FOR PATIENTS WITH
INTERMEDIATE-RISK PROSTATE CANCER**

Amendment 4: April 21, 2015

RTOG 0815

Informed Consent Template for Cancer Treatment Trials **(English Language)**

A Phase III Prospective Randomized Trial of Dose-Escalated Radiotherapy With or Without Short-Term Androgen Deprivation Therapy for Patients With Intermediate-Risk Prostate Cancer

This is a clinical trial, a type of research study. Your study doctor will explain the clinical trial to you. Clinical trials include only people who choose to take part. Please take your time to make your decision about taking part. You may discuss your decision with your friends and family. You can also discuss it with your health care team. If you have any questions, you can ask your study doctor for more explanation.

You are being asked to take part in this study because you have prostate cancer.

Why is this study being done? (12/10/10)

The purpose of this study is to compare the effects of dose-escalated radiation therapy with or without hormone therapy on your prostate cancer. Prior studies have suggested possible advantages to the administration of hormonal therapy with radiation. However, those studies were performed with radiation techniques that do not match those commonly used in clinical practice today (that is, dose-escalated radiotherapy). Therefore, we will be testing to see if similar benefits for hormonal therapy are seen when used with current radiation therapy techniques.

In current clinical practice, either radiation therapy alone (called Arm 1 or Group 1 in this study) or radiation therapy combined with hormone therapy (called Arm 2 or Group 2 in this study) would be considered an acceptable standard treatment for patients with a newly diagnosed intermediate risk prostate cancer. The researchers conducting this study are testing the hypothesis that the side effects of hormonal therapy are outweighed by an advantage in prostate cancer cure rates for patients receiving that treatment.

There are 2 treatment groups in this study:

- 1) Patients who receive radiation therapy only
- 2) Patients who receive radiation therapy plus hormone therapy

If you agree to participate in this study, you will receive one of these 2 treatments.

How many people will take part in the study?

About 1520 people will take part in this study.

What will happen if I take part in this research study?

Before you begin the study ...

You will need to have the following exams, tests or procedures to find out if you can be in the study. These exams, tests, or procedures are part of regular cancer care and may be done even if you do not join 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.

- History and physical exam, including a digital rectal exam (DRE), an assessment of your ability to carry out activities of daily living (which will include questions such as whether you are able to feed, bathe, and dress yourself), and an assessment of other health conditions you may have (comorbidity).

- Blood tests to determine your PSA (prostate-specific antigen) and for blood count. The PSA value is a number that helps determine the aggressiveness of your prostate cancer.
- A CT (Computed Tomography) scan or MRI (Magnetic Resonance Imaging) of your pelvis and abdomen to determine if there is any evidence of cancer spread to the pelvic lymph nodes. A CT scan is a study using x-rays to look at one part of your body. An MRI is imaging using a strong magnetic field to look at one part of your body.
- A bone scan (for some patients, if applicable) to determine if the cancer has spread to the bones

During the study ... (5/23/12)

If the exams, tests and procedures show that you can be in the study, and you choose to take part, then you will need the following tests and procedures. They are part of regular cancer care.

- Transrectal ultrasound assessment of the prostate (brachytherapy patients only)
- Blood tests to measure testosterone and liver function
- An assessment of urinary symptoms and function (brachytherapy patients only)
- You will be asked to provide information regarding any cholesterol-lowering drugs you may be taking or have taken in the past

You will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the study groups. Neither you nor your study doctor can choose the group you will be in. You will have an equal chance of being placed in either group.

If you are in group 1 (often called "Arm 1"): You will receive radiation treatments to the prostate gland and seminal vesicles once daily, 5 days a week, Monday through Friday, for a total of 44 treatments. Each radiation treatment will take approximately 20 minutes but may be specific to the center in which you are being treated. If you choose to receive brachytherapy (permanent or temporary radiation seed implant), the total number of daily treatment sessions will be 25. The logistics of the brachytherapy implant procedure (if you have chosen to undergo this type of treatment) should be thoroughly reviewed by your treating physician.

If you are in group 2 (often called "Arm 2"): You will receive radiation treatments to the prostate gland and seminal vesicles as specified under group 1 above.

You also will receive hormone therapy for 6 months. The hormone therapy will begin 2 months before the start of the radiation treatments. There are two parts to the hormone therapy. You will take injections of a luteinizing hormone releasing hormone (LHRH) agonist, either under the skin or in the muscle (typically every 1 to 3 months), and you will take a pill, either flutamide three times per day or bicalutamide once per day. The injected LHRH agonist will reduce the amount of circulating testosterone and the pill will interfere with the action of any remaining testosterone.

During Radiation Therapy or Radiation Plus Hormone Therapy:

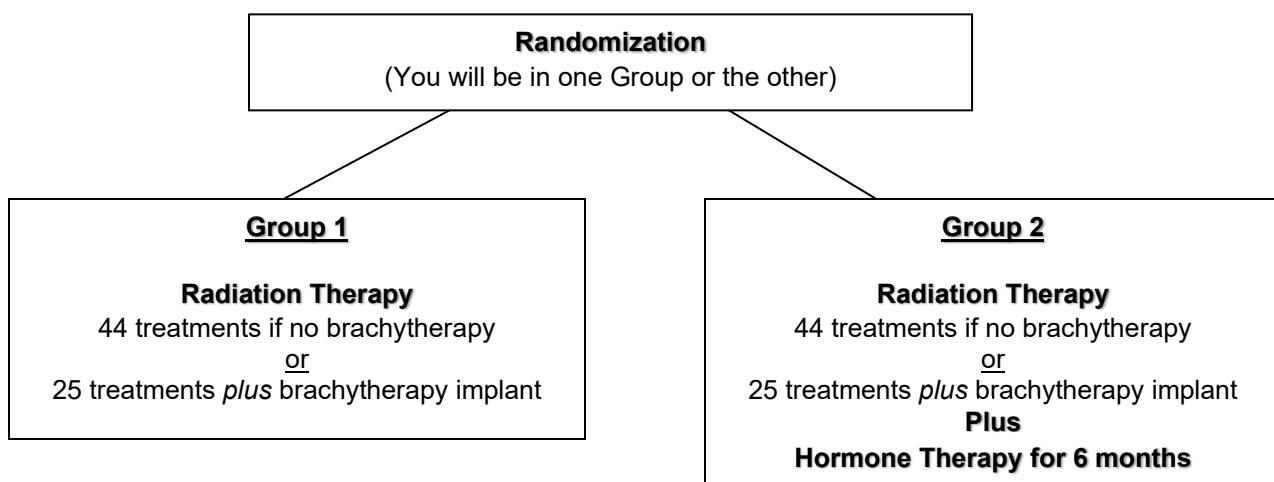
- You will be seen weekly during radiation treatment to check for any side effects you may be experiencing as a result of the treatment.
- During the third week and the last week of radiation treatment, your ability to carry out activities of daily living (which will include questions such as whether you are able to feed, bathe, and dress yourself) will be assessed.
- If you are receiving brachytherapy: Blood test for blood count during the first and fifth weeks of treatment
- If you are receiving hormone therapy: Blood test to measure testosterone; monthly blood tests for liver function

When you are finished receiving radiation therapy or radiation plus hormone therapy, you will need these tests and procedures:

- PSA measurement will be obtained at 6-8 weeks after finishing radiation treatment and prior to each follow-up visit.
- A physical assessment, including a digital rectal exam (DRE) and an assessment of your ability to carry out activities of daily living (which will include questions such as whether you are able to feed, bathe, and dress yourself) at 3 (group 1 only), 6, 9, and 12 months after finishing radiation treatment, every 6 months for 4 years, and yearly thereafter.
- If you receive hormone therapy: Testosterone levels will be checked every six months for three years or until they return to normal levels.
- Additional testing may be ordered as deemed clinically appropriate by your treating physician.

Study Plan

Another way to find out what will happen to you during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



How long will I be in the study? (5/23/12)

You will receive 44 radiation treatments over approximately 2 months. If you choose to receive the brachytherapy implant, you will receive 25 daily treatments plus the implant procedure over a timeframe of approximately 6 weeks. Hormone therapy, if given, will last 6 months. After you are finished receiving therapy, the study doctor will ask you to visit the office for follow-up exams at 3, 6, 9, and 12 months after finishing radiation treatment, every 6 months for 4 years, and yearly thereafter. The study doctors would like to keep track of your medical condition by seeing you every year for your lifetime.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the radiation and hormone therapy (if given) can be evaluated by him/her. Another reason to tell your study doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

The study doctor may stop you from taking part in this study at any time if he/she believes it is in your best interest; if you do not follow the study rules; or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, researchers don't know all the side effects that may happen. Side effects may be mild or very serious. These side effects may be related either to the radiotherapy, hormonal therapy (if randomized to receive it), or both. There are several radiotherapy options allowed on this study in the form of external beam radiation, low dose rate brachytherapy, and high dose rate brachytherapy. Each of these may be associated with subtle differences in their side effect profiles. ***The type of radiotherapy you receive on this study is a choice to be made between you and your physician.***

Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop radiation or hormone therapy (if given). In some cases, side effects can be serious, long lasting, or may never go away.

You should talk to your study doctor about any side effects that you have while taking part in the study.

Risks and side effects related to the *radiation therapy* include those which are:

Likely

- Increased urinary frequency or urgency
- Burning or discomfort/straining with urination
- Increased frequency of bowel movements or change in stool consistency
- Increased straining/discomfort with bowel movements
- Mild fatigue

Less Likely

- Rectal bleeding (usually mild)
- Chronic bowel/bladder symptoms as described above
- Temporary blockage of urination requiring use of a catheter
- Erectile dysfunction

For patients undergoing brachytherapy, risks associated with aspects of an invasive procedure such as those associated with anesthesia, infection, and bleeding must be considered and discussed with your treating physician. If permanent seed brachytherapy is used, there is a possibility of loss or migration of seeds leading to areas of under- or overdosage in certain parts of the prostate or elsewhere. Rectal or bladder complications may occur if these organs are affected because of seed misplacement.

Rare, But Serious

- Permanent rectal or bladder injury requiring surgery for treatment

Risks and side effects related to the *hormone therapy* include those which are: (5/23/12)

Likely

- Hot flashes
- Erectile dysfunction
- Loss of libido
- Mild fatigue
- Breast tenderness or mild enlargement
- Diarrhea

Less Likely

- Headaches
- Bone/joint pain
- Liver toxicity (detected on a blood test) requiring reduced dose or stopping treatment
- Severe fatigue
- Skin rash/hives
- Swelling

- Decrease in bone mineral density
- There may be increased risk of rectal or bladder side effects as a result of the interaction between the hormone therapy and the external beam radiation therapy.

Rare, But Serious

- Severe allergic reaction
- Increased long-term risk of cardiovascular disease
- Increased long-term risk of developing diabetes
- Death due to heart disease

Patients receiving treatment with LHRH agonists should undergo periodic monitoring of blood glucose and/or glycosylated hemoglobin (HbA1c) for signs of developing diabetes or worsening of blood glucose control in patients with diabetes, and also for the signs and symptoms suggestive of the development of cardiovascular disease.

Reproductive risks: You should not father a baby nor donate sperm while on this study or during the first 3 months after the completion of therapy because the radiation and drugs in this study can affect an unborn baby. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study. Some of the drugs and radiation used in this study may make you unable to have children in the future.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your health better. It is not known how much of a benefit combining hormone therapy with radiation therapy will have for your type of prostate cancer compared to the usual treatment. We do know that the information from this study will help researchers learn more about the combination of hormone therapy plus radiation therapy as a treatment for prostate cancer. This information could help future cancer patients.

What other choices do I have if I do not take part in this study?

Your other choices may include:

- Getting treatment or care for your cancer without being in a study; this could include the following options, either alone or in combination with each other:
 - Radiation therapy (external beam radiation therapy and/or brachytherapy)
 - Radiation therapy plus hormone therapy
 - Hormone therapy
 - Surgery
- Taking part in another study
- Getting no treatment

Talk to your study doctor about your choices before you decide if you will take part in this study.

Will my medical information be kept private? (4/21/15)

Data are housed at NRG Oncology Statistics and Data Management Center in a password-protected database. We will do our best to make sure that the personal information in your medical record will be kept private. However, we cannot guarantee total privacy. Your personal information may be given out if

required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used.

Organizations that may look at and/or copy your medical records for research, quality assurance, and data analysis include:

- NRG Oncology
- The National Cancer Institute (NCI) and other government agencies involved in keeping research safe for people, like the Central Institutional Review Board (CIRB) and the Food and Drug Administration (FDA)
- The Cancer Trials Support Unit (CTSU), an organization sponsored by the NCI to provide greater access to cancer trials

A description of this clinical trial will be available on <http://www.ClinicalTrials.gov>, as required by U.S. Law. This web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

[Note to Informed Consent Authors: the above paragraph complies with the new FDA regulation found at 21 CFR 50.25(c) and must be included verbatim in all informed consent documents. The text in this paragraph cannot be revised.]

What are the costs of taking part in this study?

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. 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.

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

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at <http://cancer.gov/clinicaltrials/understanding/insurance-coverage>. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, _____ [investigator's name(s)], if you feel that you have been injured because of taking part in this study. You can tell the study doctor in person or call him/her at _____ [telephone number].

You will get medical treatment if you are injured as a result of taking part in this study. You and/or your health plan will be charged for this treatment. The study will not pay for medical treatment.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

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

A Data Monitoring Committee (DMC) will be regularly meeting to monitor safety and other data related to this study. The Committee members may receive confidential patient information, but they will not receive your name or other information that would allow them to identify you by name.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor _____ [name(s)] at _____ [telephone number].

For questions about your rights while taking part in this study, call the _____ [name of center] Institutional Review Board (a group of people who review the research to protect your rights) at _____ (telephone number). *[Note to Local Investigator: Contact information for patient representatives or other individuals in a local institution who are not on the IRB or research team but take calls regarding clinical trial questions can be listed here.]*

*You may also call the Operations Office of the NCI Central Institutional Review Board (CIRB) at 888-657-3711 (from the continental US only). *[*Only applies to sites using the CIRB.]*

Please note: This section of the informed consent form is about additional research that is being done with people who are taking part in the main study. You may take part in this additional research if you want to. You can still be a part of the main study even if you say 'no' to participating in this additional research.

(5/23/12)

Note to Institutions: On March 22, 2012, the Quality of Life (QOL) Substudy of RTOG 0815 closed to patient enrollment, as the substudy met its patient enrollment goal. After closure to enrollment of the QOL substudy, new patients will not be offered the opportunity to participate in the following part of the RTOG 0815 study. Institutions should follow their local IRB policy regarding removal of the QOL study text from the sample consent.

Quality of Life Study

We want to know your view of how your life has been affected by cancer and its treatment. This "quality of life" study looks at how you are feeling physically and emotionally during your cancer treatment. It also looks at how you are able to carry out your day-to-day activities.

This information will help doctors better understand how patients feel during treatments and what effects the medicines are having. In the future, this information may help patients and doctors as they decide which medicines to use to treat cancer.

You will be asked to complete 4 questionnaires at the following times: before treatment begins, during the last week of radiation therapy (with or without hormone therapy), and at 6 months, 1 year, and 5 years after the end of radiation therapy. It takes about 15 minutes to fill out each questionnaire. If any questions make you feel uncomfortable, you may skip those questions and not give an answer.

In addition, if you agree to participate in this part of the study, you will have blood drawn before you start radiation therapy treatment (with or without hormone therapy) and during the last week of radiation therapy treatment. We would like to keep about 2 tablespoons of blood at each of these times for future

research. If you agree, this blood will be kept to be used in research to learn more about cancer and other diseases.

If you decide to take part in this study, you will be asked to fill out the questionnaires and have blood drawn. You may change your mind about completing the questionnaires and having blood drawn at any time.

Just like in the main study, we will do our best to make sure that your personal information will be kept private.

Please circle your answer.

I choose to take part in the Quality of Life Study. I agree to fill out the Quality of Life Questionnaires and have blood drawn.

YES

NO

(4/21/15) You can say “yes” or “no” to the following study. Please mark your choice below.

Use of Tissue and Blood for Research

About Using Tissue and Blood for Research

You are going to have a biopsy (or surgery) to see if you have cancer. Your doctor will remove some body tissue to do some tests. The results of these tests will be given to you by your doctor and will be used to plan your care.

We would like to keep some of the tissue that is left over from your surgery for future research. If you agree, this tissue will be kept and may be used in research to learn more about cancer and other diseases.

In addition, if you agree, you will have blood drawn before you start radiation therapy treatment (with or without hormone therapy) and during the last week of radiation therapy treatment. We would like to keep about 2 tablespoons of blood at each of these times for future research. This blood will be kept to be used in research to learn more about cancer and other diseases.

Your tissue and/or blood may be helpful for research. The research that may be done is not designed specifically to help you. It might help people who have cancer and other diseases in the future. Reports about research done with your tissue and/or blood will not be given to you or your doctor. These reports will not be put in your health record. The research will not have an effect on your care.

Things to Think About

The choice to let us keep the left over tissue and/or blood for future research is up to you. No matter what you decide to do, it will not affect your care or your participation in the main part of the study.

If you decide now that your tissue and/or blood can be kept for research, you can change your mind at any time. Just contact us and let us know that you do not want us to use your tissue and/or blood. Then any tissue and/or blood that remain will no longer be used for research and will be returned to the institution that submitted it.

In the future, people who do research may need to know more about your health. While the study doctor/institution may give them reports about your health, it will not give them your name, address, phone number, or any other information that will let the researchers know who you are.

Sometimes tissue and/or blood are used for genetic research (about diseases that are passed on in families). Even if your tissue and/or blood are used for this kind of research, the results will not be put in your health records.

Your tissue and/or blood will be used only for research and will not be sold. The research done with your tissue and/or blood may help to develop new treatments for cancer in the future.

Benefits

The benefits of research using tissue and blood include learning more about what causes cancer and other diseases, how to prevent them, and how to treat them.

Risks

The greatest risk to you is the release of information from your health records. We will do our best to make sure that your personal information will be kept private. The chance that this information will be given to someone else is very small.

Making Your Choice

Please read each sentence below and think about your choice. After reading each sentence, circle "Yes" or "No". If you have any questions, please talk to your doctor or nurse, or call our research review board at _____ [IRB's phone number].

No matter what you decide to do, it will not affect your care.

1. My specimens may be kept for use in research to learn about, prevent, or treat cancer, as follows:
 - Tissue Yes No
 - Blood Yes No

2. My specimens may be kept for use in research to learn about, prevent, or treat other health problems (for example: diabetes, Alzheimer's disease, or heart disease), as follows:
 - Tissue Yes No
 - Blood Yes No

3. Someone may contact me in the future to ask me to take part in more research.
 Yes No

Where can I get more information? (5/23/12)

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.

Signature

I have been given a copy of all _____ [insert total of number of pages] pages of this form. I have read it or it has been read to me. I understand the information and have had my questions answered. I agree to take part in this study.

Participant _____

Date _____