INDEX

RADIATION THERAPY ONCOLOGY GROUP

RTOG

Institution # _____
RTOG 0415
Case #

ELIGIBILITY CHECKLIST (4/18/06)(7/9/09)

localization allowed for very tight CTV-PTV margins, and the use of IMRT resulted in decreased volumes of normal tissue receiving high doses.

1.4 Randomized Trials of Hypofractionated Regimens

To date the preliminary results from two randomized trials examining fractionation schedules for

and increased patient convenience. Secondly, a mo

limited, a final selection of the most promising markers will be made upon the completion of the ongoing studies involving the completed protocols 86-10, 92-02, and 94-13. Approximately 10 years will be required for the protocol to mature

previously demonstrated to be involved in RT-induced tissue damage and repair pathways. Genomic DNA for SNP analysis can be most effectively isolated from buffy coat leukocytes using standard procedures. Banking of buffy coat leukocytes can be performed at any time in the patient's trajectory, whether before, during or after treatment.

1.10 Health-Related Quality of Life (HRQOL) (9/50/07)

In a noninferiority study where traditional prostate cancer outcomes of disease-free survival, progression, and overall survival are hypothesized to be similar, the outcomes of toxicity, health related quality of life (HRQOL) and resources gain an importance.

These later outcomes will play a significant role in patient, clinician and possibly even policy interpretations of the results of this study. As ju

The EQ-5D instrument is intended to complement other forms of QOL measures, and it has been
_____ cardinal index of health, thus giving it considerable potential for

[49] The EQ-5D has been used
to assess QALYs and the svinemic value of prostate cancer screening, [50] as well as treatment of 1198 T661.6

use in svinemic evaluation. The EQ-5D has been used across numerous dise
cancer. For example, the EQ-5D mean score for 95 patients with non-small cell lung cancer

developed to generate a *generic*

(93% male, mean age 62 years) was 0.58 (SD 0.32) as measured by the questionnaire and 0.58
ual analogue scale (VAS) version.

obtained in the 1 year prior to treatment to a

(RPC) web site. Visit

SKIN

(AdEERS) application AND to the Radiation Therapy Oncology Group (RTOG) as directed

This study will utilize the Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 for grading of all adverse events. A copy of the CTCAE v3.0 can be downloaded from the Cancer Therapy Evaluation Program (CTEP) home page (http://ctep.info.nih.gov) or the RTOG web site (http://www.rtog.org/members/toxicity/main.html).

Adverse Events (AEs) and Serious Adverse Events (SAEs) that meet the criteria defined above experienced by patients accrued to this protocol must be reported via AdEERS. SAEs must be reported within 24 hours of discovery of the event. Contact the CTEP Help

(chemotherapy, other new agents). Patients with biochemical relapse or other nonlocal failures may be observed or treated with salvage hormone therapy or other systemic treatments.

10.0 TISSUE/SPECIMEN SUBMISSION (See Section 10.3.4 for a summary table) (9/20d07)(7/9/09)

Patients must be offered the opportunity to participate in the correlative components of the study, such as tissue/specimen submission. If the patient consents to parti

unstained slides (please use charged or “Plus” slides) from the block should submitted.

11.0 PATIENT ASSESSMENTS

11.1 Study Parameters (7/9/09)

Assessments	Pre-Entry	Weekly During RT	Follow-Up (months)							
			3	6	9	12	15	18	21	24
History, physical exam	X	X	X	X	X	X	X	X	X	X [c]

abnormality after complete disappearance of previous abnormalities. Needle biopsy is recommended. The presence of palpable disease must be recorded on the data collection

Drug therapy for moderate hypertension	32,600
Mammography screening for breast cancer in patients aged 80-75 yrs	20,000-50,000

13.0 STATISTICAL CONSIDERATIONS

We want to show that the hazard rate of Arm 2 (ς_{L2}

instruments (EPIC, HSCL-25, the Utilization of Sexual Medications/Devices, and EQ-5D) will be collected on all cases participating in the trial.

The EPIC, HSCL-25, the Utilization of Se xual Medications/Devices, and EQ-5D will be collected at pretreatment (baseline) and at 6, 12, 24 months, and 5 years after therapy starts. Patient self-assessment of symptoms will be performed using three primary EPIC scales:

by an explicit model for the missing data mechanism[79] and then an imputation method such as multiple imputation will be applied. All results from the imputed analysis using the multiple imputation will be compared to the complete case analysis results to assess any potential biases.

We will describe the distributions of QOL data collection patterns over all collection points in each treatment arm. Longitudinal data analysis, specifically the general linear mixed-effect model,[80] will be performed to describe the change trend of the EPIC, HSCL-25 and EQ-5D scores over time across the two treatments. The primary objective in the HRQOL analysis is to determine the QOL differences. The response will be the change of measurement from baseline for each measurement. z- test statistics will be used to test the null hypothesis that responses are the same across the two treatment arms versus the alternative hypothesis that

the nominal significance level. Lan-DeMets's alpha-spending function[70] was chosen for the efficacy test because, in practice, the information accumulated at each time point may not be equally spaced. We chose the alpha spending function that behaves like the O'Brien-Fleming boundary.[71] The null hypothesis (H_0) of the primary endpoint is that the hazard rate of Arm 2 (ς_2) will be worse than that of Arm 1 (ς_1

evidence to support a difference in treatment outcome and race in either study. Thus, we do not expect to see any evidence of a treatment difference between the two arms in the African American pop

all regressions including the Cox models.

Planned Gender and Minority Inclusion

19. Green H et al. Variation in the manganese superoxide dismutase gene (SOD2) is not a major cause of radiotherapy complications in breast cancer patients. Radiother Oncol 63, 213-216, 2002.
20. Severin DM et al. Novel DNA sequence variants in the hHR21 DNA repair gene in radiosensitive cancer patients. Int. J. Radiat. Oncol. Biol. Phys. 50, 1323-1331, 2001.

21. Brookes AJ. The essence of

55. Hough R, Landsverk J, Stone J, et al. Comparison of psychiatric screening questionnaires for primary care patients. Final report for NIMH Contract No. 278-81-0036 (DB). 15 June 1995; 22 (12): 913-921.

56. Hesbacher P, Rickels K, Downing RW, Stepansky P. Assessment of psychiatric illness severity by family physicians. Social Science & Medicine 1978; 12(1-A):45-47.

57. Hesbacher PT, Rickels K, Morris RJ, Newman H, Rosenfeld H. Psychiatric illness in family practice. J Clin Psychiat 1980; 41:6-10.

58. Derogatis LR, Melisaratos N. The brief symptom inventory: an introductory report. Psychol Med 1983; 13:595-605.

59. Bolton P. Cross-cultural validity and reliability testing of a standard psychiatric assessment instrument

76. Mantel N. Evaluation of survival data and two new rank order statistics arising in its consideration. Cancer Chemother Rep 1966; 50:166-170.

77. Kim K, Tsiatis AA. Study duration for clinical trials with survival response and early stopping rule. Biometrics 1990; 46:81-92.

78. Schoenfeld D. The asymptotic properties of nonparametric test for comparing

APPENDIX I (4/18/06)(9/20/07)(12/3/07)

Informed Consent Template for Cancer Treatment Trials (English Language)

RTOG 0415

A PHASE III RANDOMIZED STUDY OF HYPOFRACTIONATED 3D-CRT/IMRT VERSUS

How long will I be in the study?

You will receive radiation treatments for either 5 and a half or 8 weeks. After you are finished receiving radiation, the study doctor will ask you to visit the offine for follow-up exams every 3 months for the first 2 years following the start of radiation, then every 6 months for the next 3 years. After that, the study doctors would like to keep track of your medical condition indefinitely by seeing you for follow-up exams every year.

Can I stop being in the study? (12/3/07)

Less Likely

- Urinary obstruction requiring the placement of a temporary urinary catheter

Rare but Serious (7/9/09)

- Injury to the bladder, urethra, bowel, or other tissues in the pelvis or abdomen
- Intestinal obstruction
- Inability to achieve an erection (inability of the penis to become hard)
- Rectal bleeding that requires medication or surgery to stop

Reproductive Risks

You should not father a baby while on this st

Will my medicat information be kept private?

We will do our best to make sure that the personat information in your medicat record will be kept private. However, we cannot guarantee total privacy. Your personat 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 personat information will not be used.

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

- The Radiation Therapy Oncology Group
- The Nationat Cancer Institute (NCI) and other government agencies involved in keeping research safe for people, like the Centrat Institutionat Review Board (CIRB) and the Food and Drug Administration (FDA)
-

Consent Form for Use of Tissue and Blood for Research

About Using Tissue and Blood for Research (9/20/07)

You have had a biopsy (or surgery) to see if you have cancer. You have signed a consent form to allow the use of your 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 biopsy 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. Please read the information sheet called "How is Tissue Used for Research" to learn more about tissue research. This information sheet is available to all at the following web site: http://www.rtog.org/tissue%20for%20research_patient.pdf

Your tissue and blood will be used only for research and will not be sold. The research done with your tissue and blood may help to develop new products in the future. You will not be paid for taking part in this study.

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 (9/20/07)
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 tissue/blood may be kept for use in resear

APPENDIX II (7/9/09)

APPENDIX III

AJCC STAGING SYSTEM
PROSTATE, 6th Edition

DEFINITION OF TNM

Primary Tumor, Clinical (T)

APPENDIX V (9/20/07) (7/9/09)

BLOOD COLLECTION KIT INSTRUCTIONS

Instructions for use of serum, plasma, or buffy coat collection kit (collected as required by protocol):

This kit includes:

- Ten (10) 1 ml cryovials
- Biohazard bags
- Absorbent shipping material
- Styrofoam container (inner)
- Cardboard shipping (outer) box
- Pre-paid shipping label(s)

Serum (if requested):

Çx

Process:

1. Centrifuge EDTA (purple top) tube within one hour of

DATA SUBMISSION AND RECONCILIATION

-	1	9

3. Do not send adverse event reports to the CTSU.

4. Secondary AML/MDS/ALL reporting: Report occurrence of secondary AML, MDS, or ALL via the NCI/CTEP AML-MDS Report Form in lieu of AdEERS. Submit the completed form and supporting documentation as outlined in the protocol.

DRUG PROCUREMENT
Not applicable to this study.

REGULATORY AND MONITORING
Study Audit

To assure compliance with Federal regulatory requirements [CFR 21 parts 50, 54, 56, 312, 314 and HHS 45 CFR 46] and National Cancer Institute (NCI)/ Cancer Therapy Evaluation Program (CTEP) Clinical Trials Monitoring Branch (CTMB) guidelines for the conduct of clinical trials and study data