SUMMARY OF CHANGES
Amendment #2, Version Date: April 25, 2006

RTOG 0321, "Phase II Trial of Combined High Dose Rate Brachytherapy and External Beam Radiotherapy for Adenocarcinoma of the Prostate"

Study Chair: I-Chow Hsu, M.D, (415)353-7175, hsu@radonc17.ucsf.edu

RTOG 0321 has been amended as follows:

Title Page: Contact information for James Purdy, PhD, was updated.

Eligibility Checklist, question 13: This question was modified for consistency with the change made to Section 3.2.8.

Section 3.2.8: This criterion was modified to be consistent with RTOG's current standard wording for this criterion.

Section 6.2.1: The following sentence was deleted in order to leave the sequence of treatment to the discretion of the investigator: "However, each institution must be consistent with the timing of their implant, so all the patients enrolled from each institution are treated similarly."

Sections 6.4.1 and 6.4.2: These sections were updated to reflect RTOG's current standard wording for AE reporting in trials without a drug component.

Sections 6.4.3 and 6.4.4: These sections were deleted to reflect RTOG's current standard wording for AE reporting in trials without a drug component. All relevant information from these sections are now included in the modified Sections 6.4.1 and 6.4.2.

Section 12.1: Instructions were added for a copy of the T1 to be sent to RTOG Headquarters and the Image-Guided Therapy Center (ITC).

Section 12.2.1: The zip code for ITC was updated.

Consent:

- Under "What Is Involved In The Study," under "Standard procedures being done because you are in this study," the Schedule for Hormonal Therapy was changed to "May be given prior to radiotherapy starting ≤ 120 days prior to registration…" for consistency with the text of the protocol.
- Under "What Is Involved In The Study," under "Extra procedures being done because you are in this study," "depending on your institutions" was deleted from
the Schedule for High Dose Rate Brachytherapy for consistency with the change made to Section 6.2.1.
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RTOG 0321 has been updated as follows:

Section 11.1: First row, fourth column “At 3 months from start of treatment, then at 6, 9 and 12 months…” has been changed from, “… 7, 9 and 12 months…” to maintain consistency with the follow-up schedule in Section 11.2.2.

Section 12.2: Digital Protocol Treatment Form code has changed to DDSI from T2 per ITC. Also, “Color” was added to DVH per ITC; and “Post Implant Data Form (See ATC web site)” was removed as this does not apply per ITC.

NOTE: This is an editorial/administrative change to the protocol. NCI now requires that these changes be documented on the protocol title page with the date of the update noted as “Update Date”, not as a revision.

An updated protocol is available on the RTOG website: http://www.rtog.org/
RTOG 0321, “Phase II Trial of Combined High Dose Rate Brachytherapy and External Beam Radiotherapy for Adenocarcinoma of the Prostate”

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RTOG 0321 has been updated as follows:

Appendix I - Informed Consent: Under “What Is Involved in This Study?,” Second Table:

- Procedure Section: “Bone scan” was deleted for consistency with deletion in Amendment 1, Sections 3.1.3 and 11.

NOTE: These are editorial/administrative changes to the protocol. NCI now requires that these changes be documented on the protocol title page with the date of the update noted as “Update Date,” not as a revision.

An updated protocol is available (no password required) on the RTOG website: http://www.rtog.org/
SUMMARY OF CHANGES
Amendment #1, Version Date: March 23, 2005

RTOG 0321, “Phase II Trial of Combined High Dose Rate Brachytherapy and External Beam Radiotherapy for Adenocarcinoma of the Prostate”

Study Chair: I-Chow Hsu, M.D., 415-353-7175, hsu@radonc17.ucsf.edu

RTOG 0321 has been amended as follows:

Schema Page, Patient Population:

- “Prostate biopsy tumor grading by the Gleason Score classification” was deleted to correspond with the change in Section 3.1.7 (see below).
- “Or pathologically” was deleted from lymph node involvement because lymph node involvement in this protocol is assessed by clinical evaluation.

Eligibility Checklist, Page 1:

- Question 4 was changed to “Are nodes clinically negative by imaging (pelvic CT, MRI)?” to correspond with the change in Section 3.1.2 (see below).
- Question 5 was deleted due to redundancy with question 4. All subsequent questions were renumbered.
- Former question 6 (current question 5; renumbered due to deletion above) was changed to “Is the patient clinically M0” to correspond with the change in Section 3.1.3 (see below).
- Question 7 was deleted due to redundancy with current question 5. All subsequent questions were renumbered.
- Former question 9 (current question 7; renumbered due to deletions above) was changed to “What is the PSA level (prior to hormone therapy, if applicable)” to correspond with the deletion of Section 3.1.6 (see below).
- Former question 12 (current question 10, renumbered due to deletions above), “90 days” was changed to “120 days” to correspond with the change in Section 3.1.5 (see below).

Eligibility Checklist, Page 2:

- Question 15, “Treatment” was changed to “Radiotherapy” for increased clarity.
- Question 17, “90 days” was changed to “120 days” to correspond with the change in Section 3.1.5 (see below).

Section 3.1.2: The timing stipulation that imaging must be done within 90 days prior to registration was deleted as an eligibility criterion and instead added as the new Section 4.2. All subsequent portions of Section 4.0 were renumbered. A corresponding change was made to the Eligibility Checklist, question 4.
Section 3.1.3: The need for a bone scan within 90 days prior to registration was deleted as an eligibility criterion because the risk of having a positive bone scan is very low in the study population (PSA < 20). A corresponding change was made to the Eligibility Checklist, current question 5/former question 6 and Appendix I.

Section 3.1.5: The acceptable time frame for induction hormonal therapy was changed from “≤ 90 days” to “≤ 120 days” prior to registration. Corresponding changes were made to Section 3.2.5, Section 9.1, and the Eligibility Checklist, current question 10/former question 12 and question 17.

Section 3.1.6: This section was deleted because (1) the time frames were deemed unnecessary and (2) PSA collection without a time frame is redundant due to other eligibility criteria. All subsequent portions of Section 3.0 were renumbered. A baseline PSA prior to treatment was instead added as Section 4.4. Corresponding time frame deletions were made to Section 9.1; Section 11.1, footnote a; and the Eligibility Checklist, current question 7/former question 9.

Section 3.1.7: This section was deleted because it was deemed redundant due to the inclusion of necessary clinical, Gleason, and PSA combinations in the subsequent eligibility criterion. All subsequent portions of Section 3.0 were renumbered. A corresponding deletion was made on the Schema Page, Patient Population.

Section 3.2.5: Revised for consistency with Section 3.1.5 (see above).

Section 4.0: The word “recommended” was deleted because the evaluations listed in this section are not optional.

Section 4.2: Added. See Section 3.1.2 above.

Section 4.3: Renumbered from former Section 4.2 due to addition above.

Section 4.4: Added. See Section 3.1.6 above.

Section 6.1.2.1: The border of the whole pelvis field was changed from “SI joint” to “L5.” The upper border of the field was changed, because a recent study (RTOG 9413) suggests that patients may benefit from a larger pelvic field.

Section 6.1.2.2: The border of the whole pelvis field was changed from “SI joint” to “L5.” The upper border of the field was changed, because a recent study (RTOG 9413) suggests that patients may benefit from a larger pelvic field.

Section 6.1.2.3: The margin around the posterior border of the prostate was changed from “1.5 cm” to “1-1.5 cm,” because it is more consistent with clinical practice.

Section 6.1.3.1: The PTV margin was changed from “1.5 cm” to “1-1.5 cm,” because it
is more consistent with clinical practice.

**Section 6.2.2.2:** The section was revised from “No fewer than 15 catheters should be used to cover the clinical target volume” to “No fewer than 14 catheters must be in the clinical target volume for adequate coverage without excessive hot spots.” The change was made for purposes of increased clarity and accuracy and because some sites reported that 1 less catheter should be allowed for patients with a smaller prostate.

**Section 9.1:** Revised for consistency with **Section 3.1.5** and **Section 3.1.6** (see above).

**Section 11.1:**

- Table, Bone Scan, Pre-Study Entry: “X^b^” was deleted for consistency with **Section 3.1.3** (see above).
- Footnote a: Revised for consistency with **Section 3.1.6** (see above).

**Section 11.2.2:** The 7 month follow-up time was changed to 6 months, because it was specified in error.

**Section 12.1:** The 7 month follow-up time was changed to 6 months on the F1 form, because it was specified in error.

**Appendix I:** Under “What Is Involved in This Study?,” First Table:

- Work Up Section: “Bone scan” was deleted for consistency with deletion in **Section 3.1.3**.
- Follow Up Section: The 7 month follow-up time was changed to 6 months, because it was specified in error.

**An updated protocol is available (no password required) on the RTOG website:**

SUMMARY OF CHANGES
Update Date: July 30, 2004

RTOG 0321, “Phase II Trial of Combined High Dose Rate Brachytherapy and External Beam Radiotherapy for Adenocarcinoma of the Prostate”

Study Chair: I-Chow Hsu, M.D., 415-353-7175, hsu@radonc17.ucsf.edu

RTOG 0321 has been updated as follows:

All hyperlinks were made active.

All references were removed to appendices deleted prior to NCI approval.

Section 3.1 — Subsection numbers were reformatted to appear in numerical order.

Section 3.2 — Subsection numbers were reformatted to appear in numerical order.

Section 6.2 — Subsection numbers were reformatted to appear in numerical order.

Section 11.2 — Subsections were reformatted for consistent alignment.

Section 12.0 — The mailing address for the American College of Radiology was changed to reflect a new address.

Section 12.1 — Under “Adverse Event Form,” “Due” column, the wording was changed to: “Post RT follow-up every 3 months from start of treatment x 1 year; then, if applicable” for increased clarity.

Section 12.2 — Under “Brachytherapy Dosimetry”:

- “Digital Data Submission Form” was changed to “Digital Protocol Treatment Form” for increased clarity.
- “Digital Data (DD)” was added as a heading for “HDR Treatment Plan,” “Contours and Isodose Distribution,” and “DVH and Post Implant Data Form” and the formatting was changed to bullets for increased clarity.

NOTE: These are editorial/administrative changes to the protocol. NCI now requires that these changes be documented on the protocol title page with the date of the update noted as “Update Date,” not as a revision.

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