For Protocol Amendment #4 of: RTOG 0526, A Prospective Phase II Trial of Transperineal Ultrasound-Guided Brachytherapy For Locally Recurrent Prostate Adenocarcinoma Following External Beam Radiotherapy

NCI/Local Protocol #: RTOG-0526/RTOG 0526

NCI Protocol Version Date: April 16, 2014 (Broadcast Date: April 28, 2014)

<table>
<thead>
<tr>
<th>Section</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title page</td>
<td>Due to the transition to the NCI National Clinical Trials Network (NCTN), “Radiation Therapy Oncology Group” and “RTOG Headquarters” were replaced with “NRG Oncology”.</td>
</tr>
<tr>
<td>Title page</td>
<td>Dr. Dignam has replaced Dr. Hunt as Senior Statistician for the trial. The Document History table was updated for the amendment.</td>
</tr>
<tr>
<td>6.10</td>
<td>As required by CTEP, references to the “Adverse Event Reporting System (AdEERS)” have been changed to “CTEP Adverse Event Reporting System (CTEP-AERS)” throughout this section.</td>
</tr>
</tbody>
</table>
RTOG 0526, “A Prospective Phase II Trial Of Transperineal Ultrasound-Guided Brachytherapy For Locally Recurrent Prostate Adenocarcinoma Following External Beam Radiotherapy”

Study Chair: Juanita Crook, MD, 250-979-6623; jcrook@bccancer.bc.ca

RTOG 0526 has been updated as follows:

Section 5.2.1: Updated per RTOG regulatory requirements.

Section 10.7: RTOG Biospecimen Resource street address was updated.

Appendix I (Sample Consent): Under “Where can I get more information”, the NCI’s TTY number is no longer in service and was deleted.
RTOG 0526, “A Prospective Phase II Trial Of Transperineal Ultrasound-Guided Brachytherapy For Locally Recurrent Prostate Adenocarcinoma Following External Beam Radiotherapy”

Study Chair: Juanita Crook, MD, 250-979-6623; jcrook@bccancer.bc.ca

RTOG 0526 has been updated as follows:

Global: All web links and related descriptions to sub-pages of the RTOG web site were updated.

Title Page: Dr. Hunt’s e-mail address was updated; a protocol document history table was added per current RTOG standard.

Section 5.2.1.1: This subsection regarding translation of regulatory documents was added, per current RTOG standard.

Section 10.5: The RTOG reimbursement text was updated. The updated text includes a web address for the Reimbursement and Case Credit Schedule located on the RTOG web site.

Section 11.1: In the “post-implant prostate CT” row of the study parameters table, the superscript h was deleted from the “parameters” column and placed in the “follow-up” column, for clarity. Also, underneath the table, the text denoted by the superscript e was revised for clarity.

Appendix I (Sample Consent): Under, “About Using Tissue for Research”, in the last two sentences of the second paragraph, the NCI web site address was updated to the current web link.
SUMMARY OF CHANGES
Amendment 3: March 15, 2011
(Broadcast: March 29, 2011)

RTOG 0526, “A Prospective Phase II Trial Of Transperineal Ultrasound-Guided Brachytherapy For Locally Recurrent Prostate Adenocarcinoma Following External Beam Radiotherapy”

Study Chair: Juanita Crook, MD, 250-979-6623; jcrook@bccancer.bc.ca

RTOG 0526 has been amended as follows:

As mandated by NCI-CTEP, Section 6.10.1 (second paragraph under AdEERS Reporting Requirements and first paragraph under RTOG Reporting Requirements) has been amended to require the use of CTCAE, version 4 for grading of all adverse events reported via AdEERS as of April 1, 2011.

Note: References to CTCAE, version 3.0 may remain in the protocol. These are appropriate, as treatment decisions for patients enrolled on this study were based on that version.

Other Changes

Section 6.10.1: In the next to last paragraph of the section (above Section 6.10.2), first sentence, “to RTOG via the AE/SAE telephone line” was replaced with “via AdEERS”. The last paragraph regarding 24-hour telephone notification to CTEP was added.

Section 6.10.2: Amended as required per current NCI-CTEP reporting requirements for acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS) via AdEERS.
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Study Chair: Juanita Crook, MD, 250-979-6623; jcrook@bccancer.bc.ca

RTOG 0526 has been amended as follows:

Title Page: Dr. Trabulsi has been added as the Urology Co-Chair.

Section 3.0 (Eligibility)

- **3.1.2**: The oncologic criteria concerning initial presentation of disease have been relaxed; Gleason scores of 7 are now allowed for patients that have PSA 20 ng/mL. Corresponding changes were also made to the Schema, to the bulleted items under "Patient Population" on the Schema page, and to question 2 on page 1 of the Eligibility Checklist.

- **3.1.5**: A note regarding the use of alpha blockers was added. A corresponding change was made to question 7 on page 1 of the Eligibility Checklist, along with the addition of a follow-up question, and to the table in Section 11.1.

- **3.1.8**: Prostate size is no longer limited to 45 cc, provided that it will not pose technical difficulties at the time of implantation. To ensure this requirement is met, men with a prostate size > 45 cc will have to have had a pubic arch evaluation demonstrating adequate clearance. Accordingly, the phrase, "or pubic arch interference ruled out" was added to this eligibility criterion. This change was also included in question 10 on page 1 of the Eligibility Checklist.

- **3.2.2**: The phrase, "such that the minimum dose to the prostate", was added for clarity here and in question 13 on page 1 of the Eligibility Checklist.

- **3.2.6**: The duration of prior hormonal therapy at the time of initial diagnosis and treatment has been revised from a maximum of 8 months to no specified limit provided that men have a normal serum testosterone at the time of consideration for this salvage treatment. "Note 2" at the end of the section was revised to include, "If > 8 months, evidence of a normal serum testosterone must be
documented". This change was also included in question 19 on page 2 of the Eligibility Checklist.

**Section 4.1.2**: Serum testosterone was added to the list of additional highly recommended pretreatment evaluations (documentation of normal serum testosterone may be needed, per Section 3.2.6). Corresponding changes were included in the table in **Section 11.1** and under, "What will happen if I take part in this research study/Before you begin the study", in **Appendix I (Informed Consent)**.

**Section 6.1.1**: A note regarding definition of the CTV and PTV was added.

**Section 6.4.1.2**: The last sentence was added.

**Section 6.7.1**: The evaluation criteria for the implant have been relaxed to allow implantation and dose coverage of a reduced volume (60% of the gland).

**Section 12.2.1**: A typo in the ITC web address was corrected and the ITC e-mail address was updated.
SUMMARY OF CHANGES
Amendment 1, Version Date: June 10, 2009
(Broadcast Date: July 30, 2009)

RTOG 0526, "A Prospective Phase II Trial Of Transperineal Ultrasound-Guided Brachytherapy For Locally Recurrent Prostate Adenocarcinoma Following External Beam Radiotherapy"

Study Chair: Juanita Crook, MD, 250-979-6623; jcrook@bccancer.bc.ca

RTOG 0526 has been amended as follows:

Section 3.2.2 (Conditions for Patient Ineligibility): Prior to Amendment 1, patients that had received prior external beam radiotherapy (EBRT) to the prostate that exceeded 72 Gy (2 Gy fractions) or 75.6 Gy (1.8 Gy fractions) were not eligible for participation in the study.

In Amendment 1, the allowed EBRT dose was increased. Section 3.2.2 now states that patients that have received EBRT dose to the prostate that exceeded 78 Gy (2 Gy fractions) or 79.8 Gy (1.9 Gy fractions) or 81 Gy (1.8 Gy fractions) are not eligible for participation in the study.

Question 13 on page 1 of the Eligibility Checklist was revised as a result of this change.

OTHER CHANGES TO THE PROTOCOL INCLUDE:

Title Page: The contact information for Dr. Crook, the Principal Investigator, was updated. Also, contact information for the RTOG Senior Statistician for this trial, Dr. Hunt, was added.

Eligibility Checklist (page 4): Questions 18-20 were revised for compliance with NCI Common Data Element requirements.

Section 5.2: Regulatory pre-registration requirements were added in accordance with current RTOG procedures. The subsequent sections were renumbered, and the section referred to in Section 5.3 (Step 1 of the registration procedures) was revised from Section 5.3 to Section 5.4.

Sections 6.6 and 12.2: "Copy to RTOG Headquarters" was added next to the post-implant dosimetry report that is to be submitted to the Image-Guided Therapy Center (ITC).

Section 6.10: Was updated as a result of revision of the standard RTOG Protocol Template since the activation of the protocol.
Section 10.0: Was updated to include the contact information for the RTOG Biospecimen Resource at the University of California San Francisco. Also, REFERENCES to "2-mm diameter core of tissue punched from the tissue block containing the tumor with a skin punch" were replaced with "unstained slides". This change is being implemented by the Biospecimen Resource because there is a very low success rate of obtaining adequate tumor tissue from prostate needle core tissue blocks when using the RTOG standard 2-mm skin punch. Appendix VI was deleted from the protocol as a result of this change.

Section 12.2.1: "FTP" was revised to "SFTP" to indicate the secured nature of the network submission account assigned to the submitting institution by the ITC.

Appendix I (Sample Consent): In the Consent Form for Use of Tissue Research, under "About using tissue for research", the web site address for the tissue information sheet was updated.

Appendix II: (Performance Scale): REFERENCES to the Karnofsky scale were deleted per current RTOG standard for studies using the Zubrod scale.

Appendix VI: Was deleted; see Section 10.0 above.
SUMMARY OF CHANGES
Update Date: May 11, 2007

RTOG 0526, "A Prospective Phase II Trial Of Transperineal Ultrasound-Guided Brachytherapy For Locally Recurrent Prostate Adenocarcinoma Following External Beam Radiotherapy"

Study Chair: Juanita Crook, MD, 416-946-2919, juanita.crook@rmp.uhn.on.ca

RTOG 0526 has been updated as follows:

The International Prostate Symptom Index (IPSS) was replaced with the American Urological Association Symptom Index for Benign Prostatic Hyperplasia (AUA BPH) in the following sections: Index, Eligibility Checklist, Sections 3.1.5, 6.9.4, 11.1, and 12.1.

The timing of AUA BPH collection was changed in the following sections:

- **Section 6.9.4; Section 11.1; Section 12.1**
- **Consent:** Under "During the study/After the prostate seed implantation is complete..." text was added to reflect collection of AUA BPH data through year 3.

Eligibility Checklist: On page 2, question 17, the typo in the fourth bullet was corrected: "focussed" was changed to "focused".

Section 3.2.6: The typo in the fourth bullet was corrected: "focussed" was changed to "focused".

Section 10.2: For clarity, text was added regarding central review and confirmation of eligibility status.

Section 10.4.1.1: The last sentence was added for clarity.

Section 10.8: Submission of immunohistochemistry specimens, if available, was added to the Specimen Collection Summary to be consistent with Sections 10.2 and 10.4.1.1.

NOTE: This update is an editorial/administrative change to the protocol. NCI requires that this change be documented on the protocol title page with the date of the update noted as "Update Date," not as an amendment.

An updated protocol is available (no password required) on the RTOG Web site, [www.rtog.org](http://www.rtog.org).