For Protocol Amendment 6 of: RTOG 0534, A Phase III Trial of Short Term Androgen Deprivation with Pelvic Lymph Node or Prostate Bed Only Radiotherapy (SPPORT) in Prostate Cancer Patients with a Rising PSA After Radical Prostatectomy

NCI/Local Protocol #: RTOG-0534/RTOG 0534

NCI Protocol Version Date: November 16, 2015 (Broadcast: December 21, 2015)

<table>
<thead>
<tr>
<th>Section</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Document Footer</td>
<td>The protocol version date was updated.</td>
</tr>
<tr>
<td>Document History table</td>
<td>This amendment was added.</td>
</tr>
<tr>
<td>1.4</td>
<td>Urine collection timepoints were updated: Paragraph 2, sentence 5: “at 3, 6, and 12 months in year 1, and then yearly for 6 years” was removed and “per Section 10 and Appendix IV” was added.</td>
</tr>
</tbody>
</table>
| 10.3.1, Specimen Collection table | Based on updates to urine collection schedule and shipping instructions:  
- Revisions were made in rows 3, 4, and 6.  
- A footnote was added: “Effective with amendment 6, urine will be collected only at year 5 after completion of RT. If sites collected urine at other timepoints (3, 6, and 12 months after RT, and yearly between 12 months and 5 years) prior to this change they should still submit them to the tissue bank.”  
**Note:** Only submit the timepoints listed in this protocol. If the site has already collected the other timepoints prior to this protocol version, the site should ship those samples to the Biospecimen Bank. |
| 10.3.3 Appendix IV | NRG Oncology Biospecimen Bank is replaced with NRG Oncology Biospecimen Bank – San Francisco  
RTOG@ucsf.edu is replaced with NRGBB@ucsf.edu |
| 11.3.5 | To correspond to the amended urine collection schedule, the existing paragraph was replaced with:  
“If the patient has consented to participate in the tissue/blood/urine component of the study, specimens are collected after completion of RT per Section 10 and Appendix IV.” |
| Appendix I, Study Parameter:: Assessments in Follow up | To correspond with the amended urine collection schedule:  
- New row 12 added  
| Appendix IV | BLOOD COLLECTION KIT AND INSTRUCTIONS  
Revisions were made to account for the updating of logistics according to collection standards. |
For Protocol Consent Amendment 6 of: RTOG 0534, A Phase III Trial of Short Term Androgen Deprivation with Pelvic Lymph Node or Prostate Bed Only Radiotherapy (SPPORT) in Prostate Cancer Patients with a Rising PSA After Radical Prostatectomy

NCI/Local Protocol #: RTOG-0534/RTOG 0534

NCI Protocol Version Date: November 16, 2015 (Broadcast: December 21, 2015)

<table>
<thead>
<tr>
<th>Section</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Header</td>
<td>The version date was updated for this amendment.</td>
</tr>
<tr>
<td>About Using Tissue, Blood, and Urine for Research</td>
<td>Changes were made to reflect update in urine collection schedule. In paragraph 3:</td>
</tr>
<tr>
<td></td>
<td>Sentence 1:</td>
</tr>
<tr>
<td></td>
<td>• “, and” was removed and immediately after a new sentence was added: “Urine will also be collected at year 5 post treatment.”</td>
</tr>
<tr>
<td></td>
<td>• “Blood will also be drawn” was added before “during the 6th week”</td>
</tr>
<tr>
<td></td>
<td>Sentence 4”</td>
</tr>
<tr>
<td></td>
<td>• Added “(all time points)” after “two tablespoons of blood”</td>
</tr>
<tr>
<td></td>
<td>• Added “(all time points prior to treatment completion, and at 5 years after completion of treatment)” after “5 tablespoons of urine”</td>
</tr>
</tbody>
</table>
For Protocol Amendment #5 to: RTOG 0534, A Phase III Trial of Short Term Androgen Deprivation with Pelvic Lymph Node or Prostate Bed Only Radiotherapy (SPPORT) in Prostate Cancer Patients with a Rising PSA After Radical Prostatectomy

NCI/Local Protocol #: RTOG-0534/RTOG 0534

NCI Protocol Version Date: December 31, 2014 (broadcast March 2, 2015)

<table>
<thead>
<tr>
<th>Section</th>
<th>Change</th>
</tr>
</thead>
</table>
| Global  | • Due to the transition to the National Clinical Trials Network (NCTN), “Radiation Therapy Oncology Group”, “RTOG Headquarters”, and “RTOG” were replaced with “NRG Oncology”, or deleted, as appropriate, throughout the protocol.  
  • References to the “Radiological Physics Center (RPC)” were replaced with “IROC Houston”.  
  • To comply with CTEP’s new formatting/document requirements, the protocol was reformatted (protocol section numbers were updated to reflect formatting revisions) and the sample consent (formerly Appendix I, now a separate document) was removed from the appendices. The remaining appendices were renumbered. |
| Title pages | • On the 1st title page, the text beginning “This trial is part of the National Clinical Trials Network…” was inserted per current NRG Oncology standard format, and the group name, email address, and suite number for the Senior Statistician were updated.  
  • On the 2nd title page, the document history table was updated for the amendment, and the “protocol agent” and “participating sites” details were added.  
  • On the 3rd title page, the CTSU address and contact information table was updated. |
<p>| Eligibility Checklist | At the top of the fourth page, the typographical error, “page 3 of 4” was corrected to “page 4 of 4”. |
| 3.1 | The instruction to contact the study data manager with questions about patient eligibility was added. |
| 5.1 5.2 | These sections were updated to correspond with current pre-registration procedures. |
| 5.4 5.5 | These sections were updated per current CTSU and NRG Oncology text. |
| 6.4 | The “note” regarding structure labeling for digital data submission was inserted at the beginning of the section. |
| 6.4.3 | The first and fifth sentences under “PLNRT Planning for 3D-CRT” were placed in bold font. Also, the structure names were updated in the table at the end of the section. |
| 6.6.1 | Imaging terminology updated: “port film” replaced with “portal image”; “planning program” replaced with “planning software”. |
| 6.8.1 | The RT QA review text was revised per the current process for this study. |
| 7.1.1 | Fourth sentence: “Last day of treatment” was revised to “last day of radiation treatment”, for clarity. |
| 7.8 | In the title of the AE expedited reporting table, “CTP-AERS” was corrected to “CTEP-AERS”. |</p>
<table>
<thead>
<tr>
<th>Section</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 Appendix IV (Biospecimen Collection)</td>
<td>Information regarding the RTOG Biospecimen Resource was updated with the new NRG Oncology Biospecimen Bank information.</td>
</tr>
<tr>
<td>10.4</td>
<td>The reimbursement information was revised per the new NCI National Clinical Trials Network (NCTN) Program.</td>
</tr>
<tr>
<td>12</td>
<td>The suite number for the NRG Oncology office was updated.</td>
</tr>
<tr>
<td>12.1</td>
<td>“Copy to HQ and ITC” was deleted from next to the “Radiotherapy Form (T1)”.</td>
</tr>
<tr>
<td>12.2</td>
<td>Digital data submission details were updated in the table.</td>
</tr>
<tr>
<td>Appendix I (Study Parameter Tables)</td>
<td>The Appendix was reformatted into separate tables for pre-treatment, during treatment, and follow-up assessments.</td>
</tr>
</tbody>
</table>

For **Protocol Consent** Amendment #5 to: RTOG 0534, A Phase III Trial of Short Term Androgen Deprivation with Pelvic Lymph Node or Prostate Bed Only Radiotherapy (SPPORT) in Prostate Cancer Patients with a Rising PSA After Radical Prostatectomy

NCI/Local Protocol #: RTOG-0534/RTOG 0534

NCI Protocol Version Date: December 31, 2013 (broadcast March 2, 2015)

<table>
<thead>
<tr>
<th>Section</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Global</td>
<td>To comply with CTEP’s new formatting/document requirements the sample consent (formerly Appendix I) was removed from the protocol appendices and is now a separate document.</td>
</tr>
<tr>
<td>Will my medical information be kept private?</td>
<td>Due to the transition to the National Clinical Trials Network (NCTN), “RTOG Headquarters” and “Radiation Therapy Oncology Group” were replaced with “NRG Oncology Statistics and Data Management Center” and “NRG Oncology,” respectively.</td>
</tr>
<tr>
<td>About Using Tissue and Blood for Research</td>
<td>The web link for the tissue research information sheet was updated.</td>
</tr>
</tbody>
</table>
For **Protocol** Administrative Update of RTOG 0534, A Phase III Trial of Short Term Androgen Deprivation with Pelvic Lymph Node or Prostate Bed Only Radiotherapy (SPPORT) in Prostate Cancer Patients with a Rising PSA After Radical Prostatectomy

NCI/Local Protocol #: RTOG-0534/RTOG 0534

NCI Protocol Version Date: November 23, 2011    *Update Broadcast Date: April 29, 2014*

<table>
<thead>
<tr>
<th>Section</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>7.7</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 these sections.</td>
</tr>
<tr>
<td>7.8</td>
<td>This update was added to the Document History table.</td>
</tr>
</tbody>
</table>

2nd Title page
For **Protocol** Administrative Update of RTOG 0534, A Phase III Trial of Short Term Androgen Deprivation with Pelvic Lymph Node or Prostate Bed Only Radiotherapy (SPPORT) in Prostate Cancer Patients with a Rising PSA After Radical Prostatectomy

**NCI/Local Protocol #: RTOG 0534**

**NCI Protocol Version Date: November 23, 2011  Update Broadcast Date: December 10, 2013**

<table>
<thead>
<tr>
<th>Section</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Title Page</td>
<td>Dr. Zhang has replaced Dr. Hunt as senior statistician; his contact information was added. Dr. Balogh’s e-mail address was updated. The city, state, and zip code were added to Dr. Bruner’s address. This administrative update was added to the Document History table.</td>
</tr>
</tbody>
</table>
| Title Page | The Oncology Patient Enrollment Network (OPEN) will be used to register patients to this study. The following sections of the protocol were updated accordingly:  
* The CTSU information text box (before the Index page) was updated.  
* Eligibility Checklist: Pages 2-4, questions 1-5, 10, 12-15, and 17-25.  
* 1st paragraph of Section 5.0  
* Section 5.5  
* Appendix V (CTSU Logistics) was removed; the subsequent appendices were renumbered, throughout the protocol and in the Index. |
| Eligibility Checklist | RTOG is using TRIAD to collect RT digital data. TRIAD provides sites participating in RTOG clinical trials with a secure method to transmit DICOM RT and other digital data. TRIAD anonymizes and validates the images and information objects as they are transferred via the internet. The following sections of the protocol were updated to include logistics for TRIAD use for RT digital data submission:  
* Section 5.0, 1st paragraph was added  
* Sections 5.1.1 and 5.1.2  
* Section 5.2.2  
* A new Section 5.3 was added; subsequent sections were renumbered  
* Beginning of Section 6.0  
* Section 6.5.7, replaced ITC web site address with RTOG web site address  
* Sections 6.6.2 and 6.6.3 “ITC” replaced with “RTOG”  
* Section 12.1  
* Section 12.2  
* Section 12.2.1 was deleted |
| 5.0 | 
| 6.0 | 
| 12.0 | 
| Eligibility Checklist | The quality of life component of this study (which includes the neurocognitive test battery) closed to patient accrual. The following sections of the protocol were updated accordingly:  
* Eligibility Checklist: pages 3-4, questions 25-27 were deleted  
* Sections 11.8 and 11.9: The “note” regarding QOL substudy closure was added at the beginning of each section.  
* Appendix I (Sample Consent): The QOL section of the sample consent was placed in shaded box format with a note to institutions to follow local IRB policy regarding removal of the section from the sample consent. |
<p>| 11.8 |
| 11.9 |
| Appendix I (Sample Consent) | Other updates to the protocol include: |
| 5.2.1 | The last sentence of the section was updated from “…RTOG Headquarters will notify the institution that the site can enroll patients on the study” to “…RTOG Headquarters will notify the institution that the IMRT credentialing requirement has been met”. |</p>
<table>
<thead>
<tr>
<th>Section</th>
<th>Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.4</td>
<td>The regulatory pre-registration requirements were updated to current RTOG standard text.</td>
</tr>
<tr>
<td>6.4</td>
<td>Target structure names throughout each section were updated to standard DICOM names; the target and critical structures naming table was inserted at the end of Section 6.4.3.2.</td>
</tr>
<tr>
<td>6.6.1</td>
<td>Deleted; the subsequent sections were renumbered.</td>
</tr>
<tr>
<td>6.8.1</td>
<td>The first sentence, beginning “RTQA will facilitate the review”, was updated; the second sentence, beginning “After an institution has demonstrated”, was deleted.</td>
</tr>
</tbody>
</table>
SUMMARY OF CHANGES
Update: January 17, 2012
(Broadcast: January 17, 2012)

RTOG 0534, “A Phase III Trial Of Short Term Androgen Deprivation With Pelvic Lymph Node Or Prostate Bed Only Radiotherapy (SPPORT) In Prostate Cancer Patients With A Rising PSA After Radical Prostatectomy”

Study Chair: Alan Pollack, MD, PhD, (305) 243-4916, APollack@med.miami.edu

RTOG 0534 has been updated as follows:

Dr. Wefel is the new Neuropsychology Co-Chair; his name and contact information has been inserted in place of Dr. Meyers’ information in the following sections of the protocol:

• Title Page
• Section 11.9
• Appendix VII (Neurocognitive Battery)

Section 11.8.1: Dr. Bruner’s e-mail address updated.
SUMMARY OF CHANGES
Amendment 4: November 23, 2011
(Broadcast: January 17, 2012)

RTOG 0534, “A Phase III Trial Of Short Term Androgen Deprivation With Pelvic Lymph Node Or Prostate Bed Only Radiotherapy (SPPORT) In Prostate Cancer Patients With A Rising PSA After Radical Prostatectomy”

Study Chair: Alan Pollack, MD, PhD, (305) 243-4916, APollack@med.miami.edu

RTOG 0534 has been amended as follows:

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

Title Page: Dr. Balogh added as a study co-chair; Dr. Hunt added as Senior Statistician; contact information for Drs. Low and Bruner was updated; protocol document history table added per RTOG format.

Eligibility Checklist:
- Time “in days” inserted for questions 2, 7, 8, 17 on pages 1-2. These changes also have been included in Sections 3.1 and 3.2.
- Page 1, question 9, first bulleted item, “of the pelvis” inserted after “CT scan” and “MRI of the abdomen and pelvis” replaced with “MRI of the pelvis” for consistency with Section 3.1.7.2.
- Page 2, questions 17 and 18, clarifications regarding finasteride or dutasteride use were inserted, for consistency with Sections 3.2.3 and 3.2.4.
- Page 2, question 19, “prior to prostatectomy” replaced with “before or after prostatectomy”.
- Page 2, question 23, addition of “superficial bladder cancer” within the last 5 years to the exclusion criteria, consistent with Section 3.2.9.
- Page 3, question 25 regarding RT dose was deleted. The subsequent questions were renumbered.

Section 1.4: Details regarding blood and urine collection were added to the end of the second paragraph.

Section 2.2.10: “Buffy coat cells” replaced with “whole blood”, per RTOG Biospecimen Resource collection procedures.

Section 3.1.7.2: For clarity, “of the pelvis” inserted after “CT scan” and “a noncontrast CT is permitted if the patient is not a candidate for contrast” added.

Sections 3.2.3 and 3.2.4: Clarifications regarding finasteride or dutasteride use added.

Section 3.2.5: “Prior to prostatectomy” replaced with “before or after prostatectomy”.

Section 3.2.9: Exclusion of patients with “superficial bladder cancer” within the last 5 years added.

Section 4.2.2: In the first sentence, “simulation” added after “non-contrast CT”; in the second sentence, “simulation or CT scan and MRI” was replaced with “simulation or MRI”.

Section 5.2.2: In the first sentence, “and/or” was replaced with “and”.

Section 5.3: Regulatory pre-registration text added, per RTOG standard.

Section 5.4: The web support e-mail address was updated in the next to last paragraph.
**Section 6.0:** Timing clarifications (“+/- 1 week” replaced with “+/- 14 days”; “weeks and months” throughout replaced with “days”) inserted for radiotherapy start at the beginning of the section (bold text) and at the beginning of Section 6.1.

**Sections 6.1, 6.3, 6.4.1-6.4.3, 6.5.4, 6.7, and 6.8:** Revised throughout for clarity regarding radiation therapy. In particular, the DVH criteria for the bladder and rectum were changed, replacing deviations with secondary variations because these have been very difficult to achieve, especially for Arm 3. It should be noted that prior studies never incorporated DVH criteria for the bladder, rectum and bowel. This study represents a significant advance in terms of acquiring data on these parameters that will be used to more clearly define such parameters in the future. It was premature to define deviations in this trial.

**Sections 6.4.3.1 and 6.4.3.2:** Revised the RTOG web site address for the Prostate Pelvic Lymph Node Contouring Atlas.

**Sections 6.6.1 and 6.8.1:** “RTQA” inserted in place of “The ITC” in the first sentence of each subsection.

**Section 6.6.3:** Deleted “for the axial and coronal planes (or multiple axial planes as outlined in QA Guidelines)” from the sentence.

**Section 7.0:** Timing clarification (+/- 2 weeks) inserted for short term androgen deprivation start at the beginning of the section (bold text).

**Sections 7.1.1 and 7.1.2:** Clarification added regarding the duration of antiandrogen and LHRH agonist treatment.

**Section 7.2.2:** “Trelstar” inserted after “Lupron”.

**Sections 7.3.2 and 7.4.2:** In each section, the font of the next to last sentence (regarding termination of flutamide/bicalutamide) was bolded for clarity regarding drug administration timing.

**Section 7.7.1:** At the end of the first paragraph following “CTEP NCI Guidelines: Expedited Adverse Event Reporting Requirements”, the date “January 2005” was replaced with “July 26, 2011”.

**Section 10.3.1.2 and 10.3.1.3:** “Buffy coat” replaced with “whole blood”, per RTOG Biospecimen Resource collection procedures; -20° C replaced with -80° C. Also, “buffy coat” was replaced with “whole blood” in Sections 1.4, 2.2.10, 11.2.2.4, 11.3.5, and 13.1.2.15.

**Section 10.3.1.3:** The DNA collection times in the collection summary table were reduced; timing clarifications (e.g., +/- 1 month; +/- 2 months) inserted for specimen collection in the summary table; specimen collection details updated per RTOG Biospecimen Resource procedures.

**Section 10.3.3:** The street address for the RTOG Biospecimen Resource was updated.

**Section 10.4:** 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.

**Sections 11.2 and 11.3:** Timing clarifications inserted throughout for radiotherapy treatment start (+/- 2 weeks) and for assessments during follow-up (e.g., +/- 2 weeks; +/- 1 month).

**Section 11.2.2.4:** “Buffy coat” replaced with “whole blood”, per RTOG Biospecimen Resource collection procedures.

**Section 11.3.5:** “Buffy coat cells” deleted.

**Section 12.2:** Under Preliminary Dosimetry Information, “C1, C3” removed from the digital data submission list.
Section 13.1.2.15: “Buffy coat cells” replaced with “whole blood”, per RTOG Biospecimen Resource collection procedures.

Section 13.3: Second paragraph, third sentence, deleted “double-secret”.

Appendix I (Sample Consent):
What side effects or risks can I expect from being in the study?
- “Increased long-term risk of developing diabetes” and “increased long-term risk of cardiovascular disease” were inserted in the list of “Rare and Possibly Serious” hormone therapy risks; a sentence regarding LHRH agonists was added.
- In the paragraph about reproductive risks, “nor donate sperm…or during the first 3 months after cessation of therapy” was inserted for consistency with the protocol (Section 7.4.3).

Will my medical information be kept private?
- Per NCI, the paragraph beginning “A description of this clinical trial will be available…” [new FDA language per 21 CFR 50.25(c)] and the “Note to Informed Consent Authors” were inserted to provide additional details to participants and the local institution.

About Using Tissue, Blood, and Urine for Research
- In the second paragraph under “About Using Tissue, Blood, and Urine for Research”, the web link for the tissue information sheet was updated.

Things to Think About
- Fourth paragraph, second sentence, “is” replaced with “are”.

Where can I get more information?
- The NCI’s TTY number is no longer in service and was deleted.

Appendix VI (Biospecimen Collection Appendices): Updated per current RTOG Biospecimen Resource procedures.
SUMMARY OF CHANGES
Amendment 3: Version Date: December 23, 2010
(Broadcast: January 11, 2011)

RTOG 0534, "A Phase III Trial Of Short Term Androgen Deprivation With Pelvic Lymph Node Or Prostate Bed Only Radiotherapy (SPPORT) In Prostate Cancer Patients With A Rising PSA After Radical Prostatectomy"

Study Chair: Alan Pollack, MD, PhD, (305) 243-4916, APollack@med.miami.edu

RTOG 0534 has been amended as follows:

As mandated by CTEP, CTCAE version 3.0 reporting requirements in Section 7.7 of the protocol will be converted to CTCAE version 4 for grading of all adverse events reported via AdEERS beginning January 1, 2011. All case report forms will continue to use CTCAE version 3.0.

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

Other Changes
Section 7.7.3: This section was amended as required by CTEP to instruct sites to report AML or MDS via AdEERS.
RTOG 0534, "A Phase III Trial Of Short Term Androgen Deprivation With Pelvic Lymph Node Or Prostate Bed Only Radiotherapy (SPPORT) In Prostate Cancer Patients With A Rising PSA After Radical Prostatectomy"

Study Chair: Alan Pollack, MD, PhD, (305) 243-4916, APollack@med.miami.edu

RTOG 0534 has been amended as follows:

Section 3.1.4: Prostatectomy Gleason score revised from "8 or less" to "9 or less". Corresponding changes were made to the following sections of the protocol:

- Schema (stratification)
- "Patient Population" text on the Schema page
- Eligibility Checklist: Question 4 on page 1 and question 22 on page 3
- Section 13.2.1

Section 3.1.7.2: The CT scan or MRI of the abdomen was deleted; it is no longer a requirement for study entry. This assessment also was removed from the following sections of the protocol:

- Appendix I (Sample Consent), under "What will happen if I take part in this research study/Before you begin the study"
- Appendix II (Study Parameter Table)

Sections 3.2.5, 3.2.6, and 3.2.7: Eligibility criteria added; the subsequent items were renumbered.

Section 5.2: For clarity, the sentence "Institutions that previously have been credentialed for one IMRT delivery technique…must repeat the credentialing process when they change to a different technology…." was added under the pre-registration requirements for the IMRT treatment approach.

Section 6.0: Revised in several subsections (6.4.1, 6.4.2, 6.4.3, 6.7.1, and 6.7.2) to clarify treatment planning and to update the compliance criteria scoring terminology to reflect the standard RTOG language.

Section 12.2: The reference to QA guidelines next to the T6 form and the ATC website address above the "note" at the bottom of the section were deleted.

Appendix V (CTSU Logistics): The ITC e-mail address was updated under
"Requirements for RTOG-0534 site registration" (second bullet).
SUMMARY OF CHANGES
Update: October 22, 2009
(Broadcast October 22, 2009)

**RTOG 0534**, "A Phase III Trial Of Short Term Androgen Deprivation With Pelvic Lymph Node Or Prostate Bed Only Radiotherapy (SPPORT) In Prostate Cancer Patients With A Rising PSA After Radical Prostatectomy"

**Study Chair:** Alan Pollack, MD, PhD, (305) 243-4916, APollack@med.miami.edu

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**RTOG 0534** has been updated as follows:

**Eligibility Checklist:** Question 25, the prescribed RT dose must be recorded in gray (Gy) rather than centigray (cGy) units.

**Section 3.1.3.1:** For clarity, "with or without a positive prostatectomy surgical margin" was added.

**Section 3.1.10:** The parenthetical notation regarding the requested serum testosterone value was added for clarity.

**Section 5.3.1:** The RTOG web support address in the next to the last paragraph was updated.

**Section 6.0:** For clarity, "+/- 1 week" was added following the treatment times specified. Also, "1.8 Gy per fraction" was added next to each treatment arm immediately above Section 6.1 and at the end of the "Dose Specifications" paragraph.

**Section 7.0:** In the paragraph immediately above Section 7.1, "+/- 1 week" was added following the treatment time specified for clarity.

**Section 10.3.2:** This section was added to the protocol to provide additional information to participating sites regarding the storage of biospecimens.

**Section 10.3.3:** "U.S. Postal Service" added to the mailing address for non-frozen specimens; "UPS" inserted in place of "DHL" in the Courier address for frozen specimens.

**Section 11.9:** The reference to "Section 11.9.4" corrected to "Section 11.9.5" immediately above the table.

**Section 12.1:** For patients in Arms 2 and 3, the "PQ" form is due to RTOG Headquarters 2 weeks prior to the start of radiation therapy. This data submission due date is included in Sections 11.2.1.1 and Appendix II of the protocol and was added to this section for consistency.
Section 12.2: The ATC web site address for the "Digital Data Submission Information" form was updated; the address is case-sensitive. The ITC e-mail address was updated.

Appendix II: The separate column, "Beta Amyloid Testing" was merged with the "Blood, urine for banking" column. Blood for beta amyloid testing is included in the blood collection for banking, if the patient consents to blood collection.

Appendix III: REFERENCES to the Karnofsky scale were deleted per RTOG standard for studies using the Zubrod scale.

Appendix VI: Updated per RTOG Biospecimen Resource standards for specimen collection and shipping.

Appendix VII: Revised to include additional information regarding neurocognitive certification. Corresponding changes were made to Section 11.9.5.
SUMMARY OF CHANGES
Update: March 31, 2009
(Broadcast: March 31, 2009)

RTOG 0534, "A Phase III Trial Of Short Term Androgen Deprivation With Pelvic Lymph Node Or Prostate Only Radiotherapy (SPPORT) In Prostate Cancer Patients With A Rising PSA After Radical Prostatectomy"

Study Chair: Alan Pollack, MD, PhD, (305) 243-4916, APollack@med.miami.edu

RTOG 0534 has been updated as follows:

Neurocognitive testing optional for institutions: Participation in the neurocognitive test battery is no longer mandatory for institutions. As a result, the following sections of the protocol were updated:

- Eligibility Checklist, page 4
- Sections 10.1, 11.2.1.3, 11.2.2.3, 11.3.6, 11.9.5, and 11.10

Institutions participating in the neurocognitive test battery must follow the certification process specified in the protocol.

Other changes to the protocol include:

Eligibility Checklist: Page 3, Item 24 regarding specification of pathology stage (stratification variable) was added. Specification of LHRH agonist planned duration is now Item 29.

Section 4.2: The text for pre-treatment tissue/blood/urine banking and the quality of life and neurocognitive assessments was removed from this section; these assessments are specified in Sections 10.0 and 11.0 of the protocol.

Sections 10.3 and 10.4: In accordance with RTOG Biospecimen Resource procedures, prostate tissue needle cores will not be collected; REFERENCES to the tissue cores were removed. As a result, Appendix VII (Specimen Plug Kit and Instructions) was deleted from the protocol and the remaining Appendices were renumbered. Also, the schedule for specimen collection was added to the table in 10.3.1.3.

Appendix I (sample consent): Under "About Using Tissue, Blood, and Urine for Research", the web address for the information sheet on tissue research was updated.

Appendix VII (Neurocognitive Battery): Question 4 was revised for clarity; RTOG will not provide translation of the assessments.
RTOG 0534, "A Phase III Trial Of Short Term Androgen Deprivation With Pelvic Lymph Node Or Prostate Only Radiotherapy (SPPORT) In Prostate Cancer Patients With A Rising PSA After Radical Prostatectomy"

Study Chair: Alan Pollack, MD, PhD, (305) 243-4916, APollack@med.miami.edu

RTOG 0534 has been amended as follows:

- PSA doubling time (PSADT) as an eligibility criterion and stratification variable was removed from the protocol. (PSA values will still be collected so that PSADT may be calculated later.) The following sections of the protocol were revised as a result:
  - Schema
  - Eligibility Checklist, pages 1 and 3
  - Section 1.1
  - Sections 3.1 and 3.2
  - Sections 13.2.1, 13.5.1, 13.5.2, 13.5.3, 13.5.4, 13.5.5, 13.5.6, and 13.7
  - REFERENCES: Revised throughout the protocol

- The required protocol entry PSA is now $\geq 0.1$ and $< 2.0$ ng/mL. The following sections of the protocol were revised as a result:
  - Schema
  - Eligibility Checklist, pages 1 and 3
  - Section 3.1.2
  - Section 13.2.1

- Pathology stage (pT2 and margin negative vs. all others) was added as a stratification variable. The following sections of the protocol were revised as a result:
  - Schema
  - Sections 13.2.1, 13.5.1, 13.5.2, 13.5.3, 13.5.4, 13.5.5, 13.5.6, and 13.7

Other revisions to the protocol include:

Title Page: The contact information for Drs. Pollack and Bruner was updated.
ECOG has endorsed this study; the contact information for Dr. Whittington, the ECOG Co-Chair, was added.

- **Eligibility Checklist:**
  - Page 1, "pN0" and "pNx" were added to the text.
  - Page 1, Questions 2, 3, 7, 9, 10, and 12 were revised for consistency with changes made in Section 3.0.
  - Page 3, Question 18 (medical oncologist) was deleted; it is not a requirement for the study.
  - Pages 3-4, the following questions were added to the Checklist:
    24. Specify prescribed RT dose (_____ cGY)
    27. Specify LHRH agonist planned duration (4, 5, or 6 months)

- Page 3, the following was added to Question #25:
  If no, please specify the reason from the following:
  1. Patient refused due to illness
  2. Patient refused for other reason: specify ______
  3. Not approved by institutional IRB
  4. Tool not available in patient's language
  5. Other reason: specify________

- Page 4, the question regarding health care data was deleted, as the RTOG Health Services Research and Outcomes (HSRO) Committee has decided not to routinely collect social security numbers for Medicare patients for the EQ-5D. Cost utility analysis will be done by means of modeling costs.

**Section 1.1:** Paragraphs 5 and 6 were added to include the rationale for the removal of PSA doubling time as a criterion for eligibility and stratification and the decrease in study entry PSA from ≥0.2 ng/mL to ≥0.1 ng/mL.

**Section 1.4:** The timing for specimen collection in the last paragraph was revised for consistency with other areas of the protocol.

**Section 2.2.4:** The phrase, "...and genomic (single nucleotide polymorphisms) patterns..." was added to this section for clarity of objective.

**Section 3.1.1.1:** Was revised to clarify that there is no time limit for the date of radical prostatectomy prior to protocol entry.

**Section 3.1.3.2:** Was revised to include margin negative patients.

**Section 3.1.7.1:** The time point for the digital rectal exam was changed to within 8 weeks prior to registration.
Sections 3.1.7.2 and 3.1.7.3: The timing for CT scan/MRI/bone scan was changed from 90 days prior to registration to 120 days prior to registration.

Section 3.1.8: The protocol entry hemoglobin value was changed to ≥ 10.0 g/dl.

Section 3.1.10: A required value (≥ 40% of the lower limit of normal) was added for serum total testosterone.

Section 3.2.7.7: The number for the protocol section referenced in parentheses was revised to 3.1.9, to be consistent with the numbering changes made to this section of the protocol.

Section 4.1.2: Was deleted from this section ("Required Pretreatment Evaluations") and moved to "Highly Recommended Pretreatment Evaluations" (Section 4.2.4).

Section 4.2.1: Buffy coat was included to be consistent with other sections of the protocol, e.g., Section 10.3.

Section 6.3.1: The requirement for a retrograde urethrogram or MRI was deleted because the inferior bladder beak or penile bulb are excellent anatomic landmarks for XRT planning which are now part of the consensus guidelines included in Section 6.4.

Section 6.4.1.1: Consensus definitions for the clinical target volume (CTV) were added to this section.

Section 6.4.1.2: For clarity, "for 3D-CRT technique" was added to the fourth sentence.

Sections 6.4.3.1 and 6.4.3.2: Atlases for the prostate bed CTV and lymph node CTV are now available on the RTOG website and are referenced in the protocol.

Section 6.4.3.2: The sentence, "Rotational IMRT treatments are permitted, as long as the constraints are met" was added to the paragraph for clarity.

Sections 6.5.5, 6.5.6, and 6.7.2.2: Minor changes were made to the text for clarity.

Section 6.11: The referenced section numbers were updated.

Section 7.5: Was deleted from the protocol, as the text is not applicable to this study.

Sections 7.7.1 and 7.7.2: The referenced section numbers were updated; the citation was updated in the first paragraph of Section 7.7.1, and "any adverse drug experience" was updated to "any adverse experience" in 7.7.2.

Section 10.5: The RTOG Patient Tissue Consent Frequently Asked Questions website address was updated.
Sections 11.2 and 11.3: Were revised to clarify the timing of patient assessments and to be consistent with Appendix I (sample consent) and Appendix II of the protocol.

Section 11.9.5: Was updated.

Section 12.1: The due dates for the follow-up form and the AUA SI were corrected for consistency with other areas of the protocol; the Neurocognitive form name and form abbreviation were updated.

Section 12.2: "DD" was added in parentheses next to "Preliminary Dosimetry Information".

Section 13.4.2: The Arm 3 hazard rate was corrected to 0.0051.

Section 13.4.3: The full definition of Schoenfeld's formula, which was typed incompletely, was included.

Section 13.5.7: All occurrences of the efficacy p-value of 0.002 were corrected to 0.001 for consistency with Section 13.2.2.

REFERENCES: Three new REFERENCES were added to the list; the reference numbers were revised in this section and throughout the protocol.

Appendix I (sample consent):

- Under "Before you begin the study", a minor change was made to the final bulleted item for clarity.
- Under "After entering the study and prior to radiotherapy", a minor change was made to the text to clarify that the tests and procedures in that section are for patients on Arms 2 and 3 only.
- Under "During radiation therapy", a minor change was made to the final bulleted item for clarity.
- Under "When you are finished receiving radiation" and "How long will I be in the study?", the timing of patient assessments was revised for consistency with other areas of the protocol.
- Under "What side effects or risks can I expect from being in the study?", the following was added at the end of the paragraph for clarity: "The risks of side effects related to the radiation may be higher in group 3, which includes the treatment of the pelvic lymph nodes".
- Under "Risks and side effects related to the radiation therapy"
  - Likely: The risks were revised slightly.
  - Rare but serious: The phrase "such as a colostomy (bag for stool)" was added to the first bulleted item as an example of a procedure that might be required.
- Under "Risks and side effects related to the hormone therapy", potential risks were added under Likely, Less Likely, and Rare but serious.
• Under "Quality of Life study", the neurocognitive component of the study was separated to clarify that patients can participate in the QOL component of the study without taking part in the neurocognitive portion.
• Under "Quality of Life study", the paragraph describing the need for the social security number of patients for whom health care is covered at least in part by Medicare was deleted, as the RTOG Health Services Research and Outcomes (HSRO) Committee has decided not to routinely collect social security numbers for Medicare patients for the EQ-5D. Cost utility analysis will be done by means of modeling costs.
• Under "About using tissue, blood, and urine for research", the timing of patient assessments was revised for consistency with other areas of the protocol.

Appendix II (Study Parameter Table): Was revised for consistency with Sections 3.0, 4.0, 11.0, and Appendix I of the protocol.

Appendix IV: Updated to include pathologic nodal staging.

Appendix VIII (Neurocognitive Battery): The instructions to institutions were updated and Question 4 was added to allow for patient participation in the QOL component of the study even if they decline to participate in the neurocognitive portion of the study.
**SUMMARY OF CHANGES**

*Update: February 13, 2008 (Broadcast 2/13/08)*

**RTOG 0534**, "A Phase III Trial Of Short Term Androgen Deprivation With Pelvic Lymph Node Or Prostate Only Radiotherapy (SPPORT) In Prostate Cancer Patients With A Rising PSA After Radical Prostatectomy"

**Study Chair**: Alan Pollack, MD, PhD, (215) 728-2940, alan.pollack@fccc.edu

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**RTOG 0534** has been updated as follows:

**Title page**: The acronym in the title was changed from "SPORT" to "SPPORT"; this change also was made in the title on the Schema page and on the first page of Appendix I, the sample consent.

**Index**: Appendix VIII, the PSA Doubling Time Worksheet, was deleted, and the subsequent appendix was renumbered appropriately.

**Section 3.1.5**: Since Appendix VIII, the PSA Doubling Time Worksheet, was deleted, instructions for calculating PSA Doubling Time were added to this section. No change to eligibility was made.

**Section 7.8**: The Adverse Event reporting guidelines were updated to current RTOG standard.

**Section 10.0**: The RTOG Tissue Bank has been relocated. The phrase, "RTOG Tissue Bank" was updated with the name of the new facility, "RTOG Biospecimen Resource" throughout this section. In addition, **Section 10.1** was updated with the location of the new facility, the University of California San Francisco, and contact information was provided for the RTOG Biospecimen Resource in **Section 10.3.2** and **Appendices VI and VII**.

**Section 10.3**:

- Consistent with the renumbering of the appendices on the Index page, in **Section 10.3.1.1**, Appendix V was changed to Appendix VI, and in **Section 10.3.1.2**, Appendix VI was changed to Appendix VII.
- **Section 11.9.5**: Consistent with the renumbering of appendices on the Index page, the reference to Appendix IX was changed to Appendix VIII.

**Section 12.2** was updated per current ITC digital data submission guidelines.

**Section 13.5.6**: The reference to Appendix II was deleted, as it was seen as unnecessary.
Appendix II, Study Parameter Table:

- In the pretreatment column, the word, "Recommended" was replaced by "If patient consents" for clarity for the following assessments: Alk phos, tissue for banking, blood, urine for banking, and beta amyloid.
- Under "Follow up After RT", in the "Annually thereafter" column, the phrase, "For 5 yrs post-RT" was added for clarity for the following assessments: blood, urine for banking and beta amyloid.
- Under "Long-term Follow up", an instruction, "As indicated in Sections 11.2 and 11.3", was added for clarity.

Appendix V, CTSU Logistics: At the request of the CTSU, hours of operation were changed from 8:00 am-8:00 pm to 9:00 am-5:30 pm Eastern Time in the following pages:

- Page 1, under "Address And Contact Information For RTOG-0415, CTSU Patient Registration";
- Page 2, under "CTSU Procedures for Patient Enrollment, #3".

Appendix VIII, Neurocognitive Battery: Consistent with the renumbering of appendices on the Index page, all REFERENCES to Appendix IX were changed to Appendix VIII. In addition, "NCI #" was added after "Institution Number/Name", and under "For Dr. Meyer's Use Only", the fax number was corrected.