SUMMARY OF CHANGES
Amendment 18, Version Date: March 21, 2008

(Broadcast date: April 15, 2008)

RTOG 9406, A Phase I/II Dose Escalation Study Using Three Dimensional
Conformal Radiation Therapy for Adenocarcinoma of the Prostate

Study Chair: James D. Cox, MD, 713-563-2317, jcox@notes.mdacc.tmc.edu

RTOG 9406 has been amended to add follow-up buffy coat cell collection and banking
for Single Nucleotide Polymorphisms (SNPs) analysis to the protocol, as follows:

Title page: Contact information for study co-chairs was corrected (in one case, a co-chair
had been replaced); a new co-chair was added to handle specimen collection; and all
information was corrected and completed to RTOG standard.

Index: An entry for a new appendix containing specimen collection instructions was
added to the table of contents.

Section 1.6-1.6.1: Background information regarding SNPs was added.

Section 2.5: Specimen collection was added as an objective.

Section 10.0: A pathology section was added to include information about specimen
collection.

REFERENCES: An existing reference was corrected. **REFERENCES cited in new
Section 1.0 text were added.

Appendix I: Blood collection consent text was added.

Appendix X: Specimen collection instructions were added.
The following changes are in effect:

**Cover Page** E-mail addresses were added; the participants’ list was updated and moved to Appendix IX (new).

**Dose Level Escalation**

This dose escalation study was originally designed with three total dose levels: Level I 68.4 Gy, Level II 73.8 Gy and Level III 79.2 Gy; all given at 1.8 Gy per day. After dose level II (disease groups 1 and 2) was shown to be safe and the patient accrual to dose level III (79.2 Gy) had been completed a fourth dose level was added. It was the consensus of the participating investigators to increase the daily fraction size from 1.8 Gy to 2.0 Gy for dose level IV and for any additional dose levels in order to keep the total treatment time at a reasonable level for the patient. Therefore the minimum PTV dose for dose level IV was 74.0 Gy given at 2.0 Gy per day. The preliminary analysis of dose level III shows it to be safe. Dose level IV (for disease groups 1 and 2) has finished accruing and the participating investigators have decided to escalate to one final dose. The minimum PTV dose for dose level V will be 78.0 Gy given at 2.0 Gy per day.

The three disease groups defined by disease extent will be receiving the following dose levels:

<table>
<thead>
<tr>
<th>Disease Group</th>
<th>Dose Level V: 78.0 Gy/ 2.0 Gy per fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease Group 1</td>
<td></td>
</tr>
<tr>
<td>Disease Group 2</td>
<td></td>
</tr>
<tr>
<td>Disease Group 3</td>
<td>Closed to accrual.</td>
</tr>
</tbody>
</table>

Disease group 3 has recently reached its accrual for dose level II and will not be escalated due to slow accrual.

This amendment affects the Schema, Eligibility Checklist (Q7), and Sections 6.1.5-7 (new) and 13.1.4 (new).
SUMMARY OF CHANGES

RTOG 94-06 Prostate October 5, 1998

The following changes are in effect:

**Cover Page** Dr. Landry replaces Dr. Benton as PI (Emory)

**Dose Escalation**

Patient accrual to Dose Level III (79.2 Gy) has been completed; however the acceptability of Dose Level III has not yet been determined. It is the consensus of the participating investigators to increase the daily fraction size from 1.8 Gy to 2.0 Gy, total dose 74.0 Gy. This new fraction size is only for patient groups 1 and 2. Patient group 3 will continue to accrue at the 73.8 Gy Dose Level.

The following sections have been amended to reflect this change:

Schema

Section 6.1.4 (new, subsequent sections were renumbered)

Section 13.1.3 (new)

REFERENCES 81 and 82 (new)

All patients registered by 3D-approved participating institutions will therefore be treated as follows:

GROUP 1: 74.0 Gy
GROUP 2: 74.0 Gy
GROUP 3: 73.8 Gy

**Note:** The T2 form has been updated; please visit the RTOG 3D Quality Assurance Center web site (www.rtog.org) for the current version.
SUMMARY OF CHANGES

RTOG 94-06 Prostate June 17, 1998

The following changes are in effect:

Cover Page

Dr. Kenneth Russell is the new PI at the University of Washington (9856)

New participants were added:

Upstate Carolina CCOP (J. Bearden, M.D.) (2132)

Toledo CCOP (P. Schaefer, M.D.) (8803)

Ohio State University (R. Gahbauer, M.D.) (4101)
SUMMARY OF CHANGES

RTOG 94-06 Prostate March 10, 1998

The following changes are in effect:

Cover Page – additional participants were approved:

Medical College of WI (R. Byhardt, M.D.) (7001)

Ann Arbor Regional CCOP (M. Pilepich, M.D.) (7717)

Correction to #13 (2/2/98) – Dr. Schmidt-Ullrich (1701) is at the Medical College of Virginia, not UVA.

Section 5.1, line 4-change to Appendix VIII; line 6-the Dry Run QA test is described on page 32, section 7a.
The following changes are in effect:

**Cover Page** additional participants were approved for study entries

Allegheny-Hahnemann (*B. Micaily, M.D.*) *(1301)*

University of VA (*R. Schmidt-Ullrich, M.D.*) *(1701)*

Albert Einstein Medical Center (*S. Asbell, M.D.*) *(5101)*

Montefiore Medical Center (*B. Vikram, M.D.*) *(1514)*

Western PA Hospital (*J. Figura, M.D.*) *(7008)*

**Eligibility Checklist, p.2 - Add**

Is any component of the patient’s care at a military or VA facility?
SUMMARY OF CHANGES

3D/OG 94-06 Prostate November 17, 1997

The following changes are in effect:

**Cover Page**

Dr. Benton is the new PI for Emory University.

**Sections 4.3 and 11.1**

Serum testosterone will be done pretreatment and at first followup

**Dose Level III for Group 2**

(79.2 Gy) has completed accrual
SUMMARY OF CHANGES

3D/OG 94-06 Prostate June 9, 1997

The following changes are in effect:

Dr. Roach replaces Dr. Phillips as 3D PI for UCSF.

Effective immediately, patients will be registered using only your regular RTOG institution number. You will receive $400. reimbursement for each case as of 6/9/97; however, an additional case credit will no longer be offered. The University of Washington will continue to use #9856.
SUMMARY OF CHANGES

3D/OG 94-06 Prostate May 12, 1997

The following change is in effect:

Cover Page

The Mayo Clinic has been approved for this study.
SUMMARY OF CHANGES

3D/OG 94-06 Prostate

April 1, 1997

The following clarifications have been made:

Cover Page

Thomas Jefferson University has joined this study.

Section 5.1 The Full Member limitation was dropped.

Section 6/1/3 (p. 8) Group 1: Treatment group was corrected to PTV=CTV1 + 0.5 to 1.0 cm.
SUMMARY OF CHANGES

3D/OG 94-06 Prostate

January 24, 1997

The following clarifications have been made:

Cover Page

Dr. Carlos Perez will represent Washington University, replacing Dr. Emami.

Section 5.0 was expanded to include the pre-approval process

Section 6.1 was divided into two sections: one for Dose Levels I and II, and one for Dose Level III

CURRENT DOSE LEVEL STATUS

<table>
<thead>
<tr>
<th>9851 (UCSF), 9853 (Miami), 9854 (Michigan), 9857 (WI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 = Option 7</td>
</tr>
<tr>
<td>Group 2 = Option 8</td>
</tr>
<tr>
<td>Group 3 = Option 6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>9850 (Fox Chase), 9852 (Chicago), 9855 (UNC), 9856 (Seattle), 9858 (St. Louis), 2423 (Davis), 5901 (MDA) and 7501 (Alberta)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1 = Option 4 (closed 8/5/96)</td>
</tr>
<tr>
<td>Group 2 = Option 5 (closed 12/24/96)</td>
</tr>
<tr>
<td>Group 3 = Option 6</td>
</tr>
<tr>
<td>(this is the only option open for this dose level)</td>
</tr>
</tbody>
</table>

All groups: 73.8 Gy

Institution #1523 (Emory)

Group 1 = Option 1
Group 2 = Option 2
Group 3 = Option 3
All groups: 68.4 Gy

_Institutions at Dose Levels I and II are encouraged to complete their accrual and dry runs toward their respective next dose levels._
SUMMARY OF CHANGES

3D/OG 94-06 Prostate

August 5, 1996

The following changes are in effect:

Cover Page

Dr. Cox's new numbers are:

(713) 792-3411 (phone)

(713) 792-3660 (fax)

The University of Alberta has joined the study

The new PI at Emory University is Dr. William Thoms

Accrual of Group 1 to Level II (73.8 Gy) is complete.

Institutions treating to that dose may enter only Group 2 and 3 patients.

Institutions accruing at the 68.4 Gy level may still enter all three groups.

Note: Data and dosimetry must be submitted exactly as specified in Section 12.0. Both RTOG HQ and WU are getting the other's materials.

A replacement cover is attached.