Brachytherapy in Cooperative Group Clinical Trials

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and staff of the Radiological Physics Center
Acknowledgements

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Issues

• Why is it important to understand requirements of clinical trials?
• Protocol requirements
• Credentialing
• Analysis
Why is it important?

- Most US radiation therapy facilities participate in clinical trials (~1,400/2,250)
- Patients often put on trials by surgeons and medical oncologists - radiation therapy staff may not be aware
- Clinical trials often raise the standards
Protocol Requirements

• Specification of volumes
  – Many protocols today require ICRU-50/62 terminology

• Specification of procedure
  – PBI specifies HDR Mammosite® or multicatheter
  – Prostate trials require seeds listed on registry
  – GYN trials specify dose distribution
    • Proposals to specify volumes on MRI
Definition of Volumes

Planning target volume for evaluation (PTV_EVAL)
- equals - planning target volume (PTV)
- equals - clinical target volume (CTV)

1.5 cm
5 mm inside skin
Excision Cavity
Excludes pectoralis muscles and chest wall

SLICE: -151.32 CM
ZOOM: 1
Brachy Seed Registry

Welcome This month we’re highlighting several recent and upcoming events. First, we’d like to call your attention to the Quality Assurance of Radiation Therapy Symposium, scheduled for February 20-22, 2007, at the Omni Mandalay Hotel at Las Colinas in Dallas. This three-day program focuses on quality assurance concepts and procedures used in modern-day radiation therapy, including both established and emerging image-based and adaptive radiation therapy modalities. For more information, visit this link. This program is co-sponsored by ASTRO and the AAPM, and sponsorship from NCI is pending.

The RPC has presented at several scientific meetings recently, including AAPM, ESTRO and ASTRO, and our presentations and posters are available on our web page under the RPC Presentations link in the Publications section. Our presentations at the recent CIRMS meeting are available at their web site. We will be attending and presenting at the DANTRM conference on Quality Assurance and New Techniques in Radiation Medicine to be held at the IAEA this month; our presentations will appear in this space soon afterwards. And we have several presentations at RSNA which will likewise be available here the week after the meeting.

New NCI Guidelines for IMRT The 2006 NCI IMRT letter and guidelines.

Publication on Physics of Clinical Trials We recommend AAPM Report 86 for physicists who want to know more about the conduct of clinical trials and their physics and QA requirements.

CIRMS The Council on Ionizing Radiation Measurements and Standards will hold its next meeting in October 23-25, 2006 on "Implications of Uncertainty in Radiation Measurements and Applications". Sessions on medical applications will be included.

Radiation Dosimetry Services offers mailed dosimeters and anthropomorphic phantoms for dosimetry QA.

The ADCL at M. D. Anderson Cancer Center is fully accredited for external beam and brachytherapy calibrations. FAQ about ADCL.

Third party checks of iodine and palladium seeds: Click here to display the AAPM’s recommendations for 3rd party brachytherapy seed calibration and physicist responsibilities.
Brachy Seed Registry (Cont.)

The AAPM, through its Brachytherapy Subcommittee, has determined that the following brachytherapy source models comply with the AAPM’s dosimetric prerequisites as set forth in “Dosimetric prerequisites for routine clinical use of new low energy photon interstitial brachytherapy sources: Recommendations of the American Association of Physicists in Medicine Radiation Therapy Committee” Med. Phys. 25, 2269-2270 (1998).
Brachy Seed Registry (Cont.)

Joint AAPM/RPC Registry of Brachytherapy Sources Meeting the AAPM Dosimetric Prerequisites

<table>
<thead>
<tr>
<th>Source Registry</th>
<th>Prerequisites</th>
<th>Dosimetry Datasets</th>
<th>Application for Registry</th>
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<td>Disclaimer</td>
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### 125I Sources

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<thead>
<tr>
<th>Manufacturer</th>
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<tr>
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<td>OncoSeed</td>
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<tr>
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<td>Implant Sciences Corp.</td>
<td>I-Plant</td>
<td>900</td>
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<td>IBT</td>
<td>Intersource 125</td>
<td>1251L</td>
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<tr>
<td>IsoAid, LLC</td>
<td>Advantage 1-125</td>
<td></td>
</tr>
<tr>
<td>Mills Biopharmaceuticals, Inc. (subsidiary of Mentor Corp.)</td>
<td>ProstaSeed @</td>
<td>125SL 125SH</td>
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### 103Pd Sources

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<tr>
<td>Best Medical International Inc</td>
<td>Best Palladium - 103</td>
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<tr>
<td>IBT</td>
<td>OptiSeed - 103</td>
<td>1032P</td>
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<tr>
<td>North American Scientific</td>
<td>Prospera Pd - 103</td>
<td>Med 3633</td>
</tr>
<tr>
<td>Theragenics Corporation®</td>
<td>TheraSeed @</td>
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</table>
Brachy Seed Registry (Cont.)

I-Plant Model 3500

Implant Sciences Corporation, 107 Audobon Road, #5
Wakefield, MA 01880 (781) 246-9700

http://www.brachyseeds.com/products/implantseeds/default.html

Distributed by: Implant Sciences Corporation
Customer service: (877) 732-7333
http://www.brachyseeds.com


- Wallace R., Model 3500 $^{125}$I brachytherapy source dosimetric characterization. Applied Radiation and Isotopes, 56 (4) 581-587, April 2002


added to Registry, February 7, 2002
Protocol Requirements (cont’d.)

• Specification of planning system abilities
  – Digital submission to ITC
  – DVHs
  – Dose matrix (e.g., 2 mm x 2 mm x slice thickness)

• Dosimetry (example from RTOG 0232)
  – Variation acceptable: $D_{90}$ for the ETV is greater than 80% of the prescription dose, but less than 90% of the prescription dose, or greater than 130% of the prescription dose.
  – Deviation unacceptable: $D_{90}$ for the ETV is less than 80% of the prescription dose.
Credentialing LDR and HDR Brachytherapy

- Evaluate
  - Implant technique
  - Dosimetry
  - Documentation
  - Protocol compliance
Brachytherapy Studies Requiring Credentialing

- Cervix
  - GOG 165, 191
  - RTOG 0116, 0128
- Breast
  - RTOG 95-17
  - RTOG 0413 / NSABP B-39
- Prostate
  - NCCTG N-0052
  - RTOG 98-05, 0019, 0232, 0321
  - ACOSOG, CALGB, NCIC
General Credentialing Process

- Previous patients treated with technique
- Facility Questionnaire
- Knowledge Assessment Questionnaire
- Benchmark case
- Electronic data submission
- RPC QA & dosimetry review
- Clinical review by radiation oncologist

Feedback to Institution
Knowledge Assessment Form

Prostate Brachytherapy QA

ATC CREDENTIALING PROCEDURES FOR PROSTATE IMPLANT PROTOCOLS
KNOWLEDGE ASSESSMENT FORM

Institution ___________________________ RTF# ___________________________
Physicist ___________________________ Radiation Oncologist ___________________________

Protocol Specifications:
Planning:
The CTV is determined from pre □ or post □ implant ____________ images and defined to be
______________________________________________________.
The PTV is the CTV expanded by the following margins.
  lateral ________________
  anterior ________________
  posterior ________________
  cephalad ________________
  caudal ________________
The monotherapy dose prescription is ________ Gy for $^{125}$I and ________ Gy for $^{103}$Pd.
The boost dose prescription is ________ Gy for $^{125}$I and ________ Gy for $^{103}$Pd.
Evaluation:
The ETV is determined from pre □ or post □ implant ____________ images and defined to be:
______________________________________________________.
The urethra will be drawn as:
Facility Questionnaire

II. Experience of personnel:
A. For the Radiation Oncologist named above
   How many ultrasound guided prostate implants have been performed? ________
   Has this person been credentialed previously? by RTOG? ☐ by ACOSOG? ☐ date: ______
B. For the Physicist named above
   How many ultrasound guided prostate implants have been planned using ultrasound? ___
   How many ultrasound guided prostate implants have been evaluated with post implant CT?
   Has this person been credentialed previously? by RTOG? ☐ by ACOSOG? ☐ date: ______

III. Equipment:
A. Ultrasound unit (vendor and model): ____________________________
B. CT scanner (vendor and model): ____________________________
C. Treatment planning system

Preplan or Realtime plan:
Vendor and version: ____________________________
How are ultrasound images entered for planning? videotape ☐ digitized ☐
   Other (explain): ____________________________
__________________________________________
How are prostate and normal tissue contours entered?
   Defined on planning system ☐ defined on ultrasound unit and input as above ☐
   Other (explain): ____________________________
__________________________________________
Is a point source approximation used? Yes ☐ No ☐
   If yes, do you use an: anisotropy constant ☐ anisotropy factors ☐
   If not, explain your procedures for determining and accounting for seed orientation.
Facility Questionnaire (cont’d.)

IV. Quality Assurance Procedures: (attach additional sheets if necessary)

A. Source strength verification:
   1. Dosimetry system used for in-house verification of seed activity:
      Vendor: ___________________________  Model: ___________________________

   2. How is the calibration of this system directly traceable to NIST? (Attach copies of ADCL certificates)

   3. What are the QA procedures to verify that the calibration of this system has not changed?

   4. For each seed model, what is the NIST calibration date to which your chamber calibration is traceable?

   7. Number of seeds assayed per patient: ____% or ____ seeds

   8. What is your criterion for agreement with the vendor?  +/-5% □,  +/-7% □,  +/-10% □,
      Other (explain) ________________________________________________________________

   9. What seed strength is used for treatment planning?  your own measurements □  vendor □
QA Requirements

• For prostate brachy, include verification of source strength
• Requires ADCL-calibrated well chamber
• 3rd party radiopharmacy may be used, but must meet same requirements (only 2 have been approved)
• AAPM guidance recommends the physicist perform the verification
Benchmark Plan (Geometric Case)

- Institution submits calculations for single source, and geometric arrangement
- RPC recalculates doses and DVHs
- Agreement within 5% or 0.5 mm
Benchmark Treatment Plan
Errors, Inconsistencies, and Misunderstandings Discovered Through Credentialing

- TPS used incorrect grid size, displayed isodoses in error
- TPS truncated dose value; isodose incorrect
- Errors applying NIST 1999 correction
- Misunderstandings about TG-43
- Misunderstandings of protocol, volumes
- Poor brachytherapy technique
Evaluation of Submitted Plans
• Evaluation of Submitted Plans (DVH)

$V_{90} = 88\%$

30.6 Gy (90%)
Poor Brachytherapy Technique

• Seeds implanted in base of penis
• Rad. Onc. advised to seek training
## Credentials Awarded (based on benchmarks)

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Credentials</th>
<th>Institutions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate LDR (0232)</td>
<td>70</td>
<td>63</td>
</tr>
<tr>
<td>Prostate HDR (0321)</td>
<td>11</td>
<td>7</td>
</tr>
<tr>
<td>Breast 3D CRT (0413)</td>
<td>792</td>
<td>364</td>
</tr>
<tr>
<td>Breast Mammosite®</td>
<td>497</td>
<td>245</td>
</tr>
<tr>
<td>Breast Multicatheter</td>
<td>115</td>
<td>41</td>
</tr>
<tr>
<td>Other 3D CRT (NCCTG)</td>
<td>52</td>
<td>52</td>
</tr>
<tr>
<td>Cervix (GOG)</td>
<td>55</td>
<td>46</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td><strong>1,592</strong></td>
<td><strong>611</strong></td>
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## Results of Credentialing (closed studies)

<table>
<thead>
<tr>
<th>Study</th>
<th>Major Deviations</th>
<th>Minor Deviations</th>
<th>Number of Patients</th>
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</thead>
<tbody>
<tr>
<td>GOG 165 HDR Cervix Credentialed inst</td>
<td>0</td>
<td>15</td>
<td>70</td>
</tr>
<tr>
<td>RTOG 95-17 HDR &amp; LDR Breast (all)</td>
<td>0</td>
<td>4</td>
<td>100</td>
</tr>
<tr>
<td>RTOG 0019 LDR Prostate (values for dose only)</td>
<td>0</td>
<td>6</td>
<td>117 reviewed (total 129 eligible)</td>
</tr>
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</tr>
<tr>
<td>Credentialed inst</td>
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</tr>
<tr>
<td>Non-credentialed</td>
<td>57</td>
<td>87</td>
<td>275</td>
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<tr>
<td>RTOG 95-17 HDR &amp; LDR Breast (all)</td>
<td>0</td>
<td>4</td>
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<tr>
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</table>
Total Percent Deviations for Credentialed and Non-Credentialed Institutions

- Credentialed (62 patients):
  - Per Protocol: 13.4%
  - Minor: 4.7%
  - Major: 0.0%
  - Off Study: 0.3%

- Non-Credentialed (275 patients):
  - Per Protocol: 37.1%
  - Minor: 25.2%
  - Major: 16.6%
  - Off Study: 3.0%
Total Percent Deviations for two cervix protocols

- **Per Protocol**: 63%
- **Variation Acceptable**: 17%
- **Deviation**: 7%
- **Other**: 10%

84 patients reviewed
25 patients reviewed

ACMP 2007
Total Percent Deviation for a Breast Protocol (94 patients)

- Per Protocol: 95%
- Variation Acceptable: 4%
- Deviation: 1%
- Other: 0%
Total Percent Deviations (753 patients evaluated out of 1019)

- Per Protocol: 82.3%
- Minor: 15.7%
- Major: 0.4%
- Resubmit: 1.6%
Percent Deviation for 2 Prostate Protocols

- 85% Per Protocol
- 83% Variation Acceptable
- 13% Deviation
- 1% Other
- 3% Other (138 patients on protocol)
- 2% Other (101 patients on protocol)
Summary

- Many brachytherapy patients treated on trials
- Physicists need to be familiar with trials
- Credentialing improves quality of trials
- Credentialing does not limit participation but delays while institution corrects problems
- Feedback even when institutions pass
- Clinical trials contribute to improved radiation therapy