Brachytherapy in Cooperative Group Clinical Trials

Geoffrey S. Ibbott, Ph.D.
and staff of the Radiological Physics Center
Acknowledgements

• RPC Staff, especially Irene Harris, Franklin Hall, Jessica Lowenstein, Joye Roll and David Followill

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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 (~1,400/2,200)
• 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)

5mm inside skin

1.5 cm

Excision Cavity

Excludes pectorals muscles and chest wall
Brachy Seed Registry

I-Plant Model 3500

Implant Sciences Corporation, 107 Audobon Road, #5
Wakefield, MA 01880 (781) 246-0700

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.
Credentialeding
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

Page 1 of 2

ATC CREDENTIALING PROCEDURES FOR PROSTATE IMPLANT PROTOCOLS
KNOWLEDGE ASSESSMENT FORM

Institution ___________________________ RTF# ___________________________
Physician ___________________________ 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 __________________________
  caudad __________________________

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

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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
- Misunderstanding of protocol, volumes
- Poor brachytherapy technique
Evaluation of Submitted Plans
Evaluation of Submitted Plans
• Evaluation of Submitted Plans (DVH)

$V_{90} = 88\%$

$30.6\ \text{Gy (90\%)}$
Poor Brachytherapy Technique

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

<table>
<thead>
<tr>
<th></th>
<th>Credentials</th>
<th>Institutions</th>
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</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>
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<tr>
<td>Breast Mammosite®</td>
<td>497</td>
<td>245</td>
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<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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<tbody>
<tr>
<td>GOG 165</td>
<td>0</td>
<td>15</td>
<td>70</td>
</tr>
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<td>HDR Cervix Credentialed Inst</td>
<td></td>
<td></td>
<td></td>
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<tr>
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<td>0</td>
<td>4</td>
<td>100</td>
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<tr>
<td>HDR &amp; LDR Breast (all)</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>RTOG 0019</td>
<td>0</td>
<td>6</td>
<td>117 reviewed</td>
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<td>LDR Prostate (values for dose only)</td>
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<tr>
<td>Credentialed inst</td>
<td></td>
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</tr>
<tr>
<td>Non-credentialed</td>
<td>57</td>
<td>87</td>
<td>275</td>
</tr>
<tr>
<td>RTOG 95-17 HDR &amp; LDR Breast (all)</td>
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<td>4</td>
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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