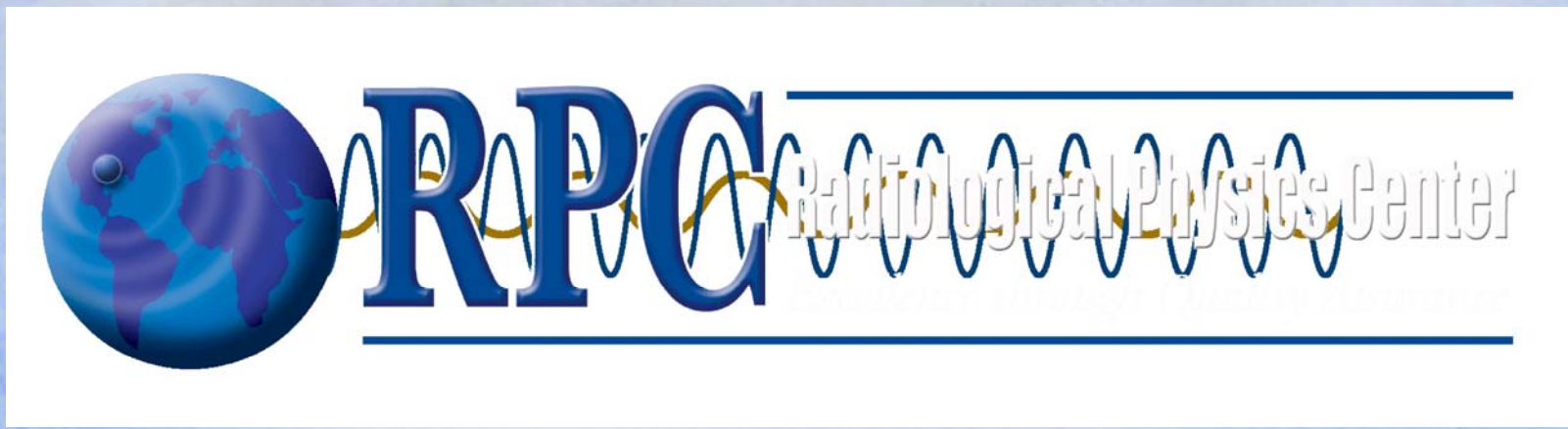
Brachytherapy in Cooperative Group Clinical Trials

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

- Research funds from IsoRay Corp.
- Supported in part by PHS grants CA10953 and CA81647 awarded by the NCI, DHHS. Educational grant from Varian

Issues

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

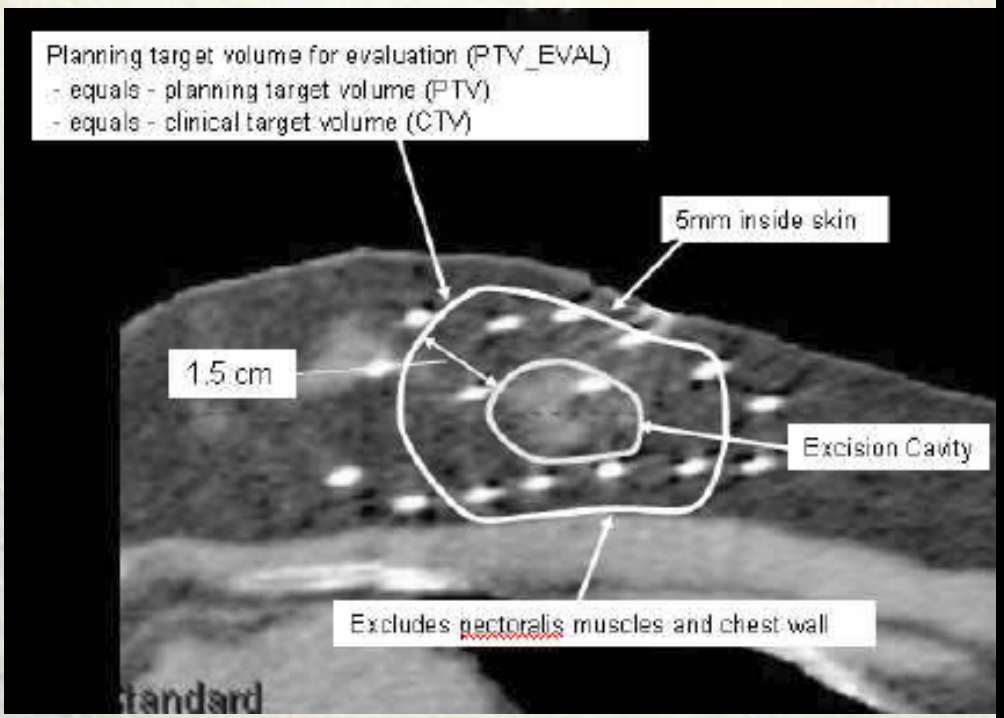
Why is it important?

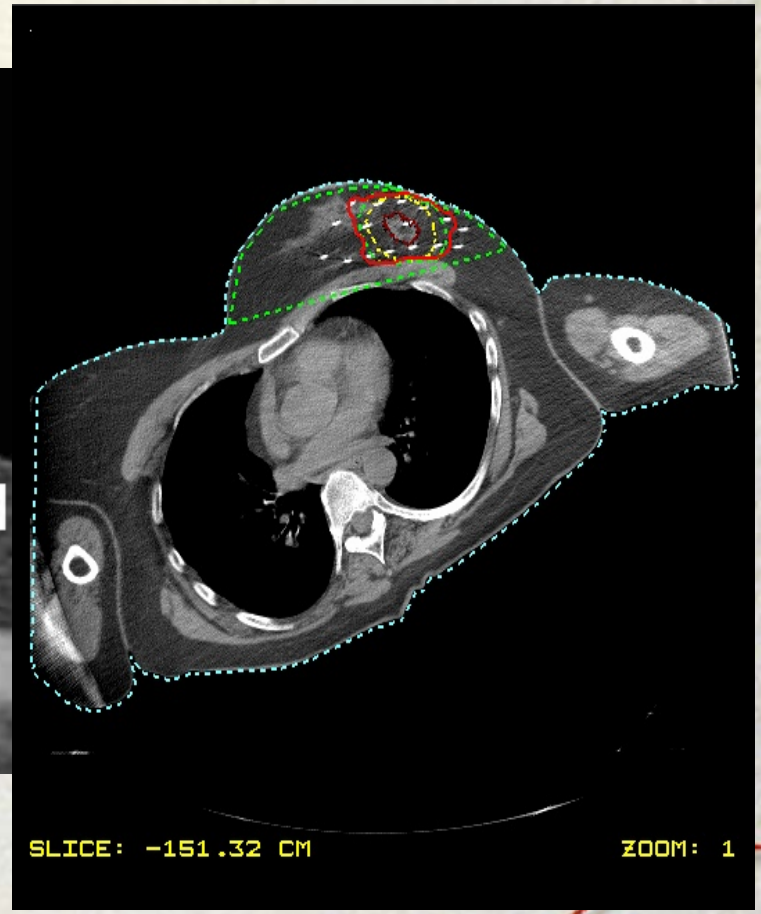
- Most US radiation therapy facilities participate in clinical trials (~1,400/2,250)
- Patients often put on trials by surgeons and medical oncologists - radiation therapy staff may not be aware
- Clinical trials often raise the standards

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





Brachy Seed Registry

RPC Radiological Physics Center
Excellence through Quality Assurance

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Tel: 713-745-8989

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Office Hours: 8 A.M. to 5 P.M. M-F Central time.

- Services
- Forms
- Publications
- Brachy Sources
- Research/TG-51
- Upcoming Meetings

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 QANTRM 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.

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

ADCL 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 calibrations and physicist responsibilities.

Contact us rpc@mdanderson.org

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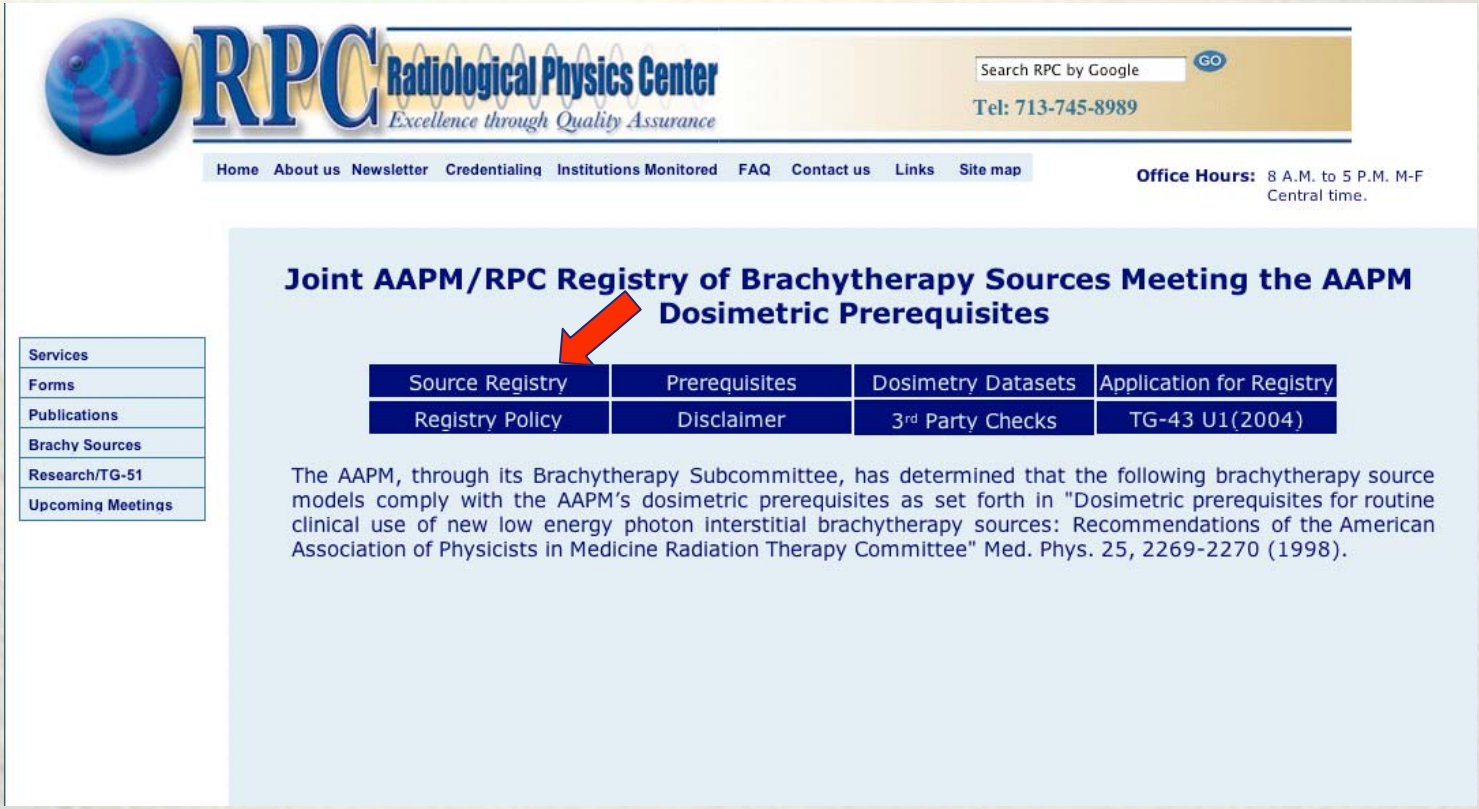
NATIONAL CANCER INSTITUTE

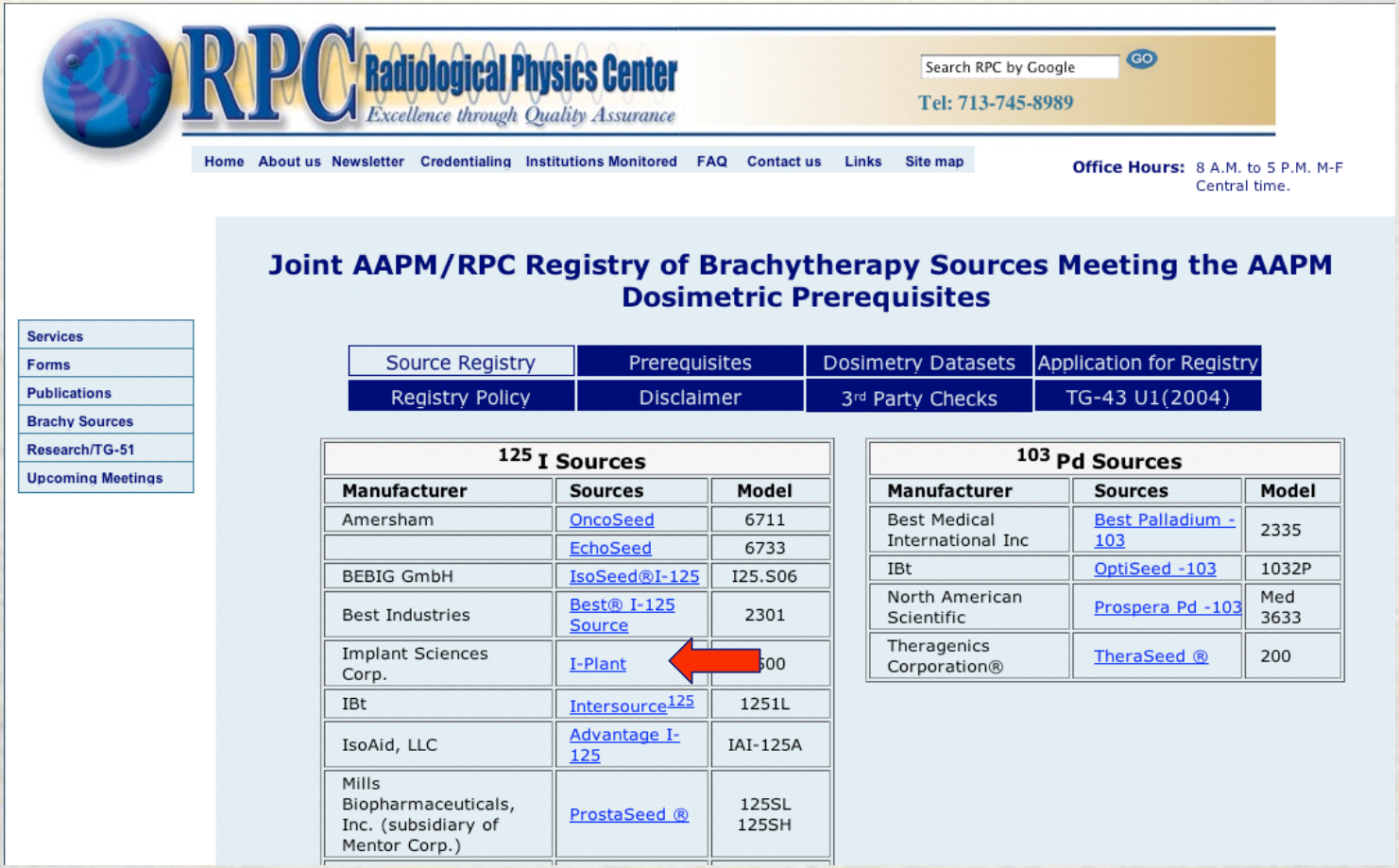
aapm online

Updated on: 11/15/2006
You are visitor #11594.

Brachy Seed Registry (Cont.)



Brachy Seed Registry (Cont.)



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

Source Registry | Prerequisites | Dosimetry Datasets | Application for Registry
Registry Policy | Disclaimer | 3rd Party Checks | TG-43 U1(2004)

^{125}I Sources

Manufacturer	Sources	Model
Amersham	OncoSeed	6711
	EchoSeed	6733
BEBIG GmbH	IsoSeed®I-125	I25.S06
Best Industries	Best® I-125 Source	2301
Implant Sciences Corp.	I-Plant	600
IBt	Intersource^{125}	1251L
IsoAid, LLC	Advantage I-125	IAI-125A
Mills Biopharmaceuticals, Inc. (subsidiary of Mentor Corp.)	ProstaSeed ®	125SL 125SH

^{103}Pd Sources

Manufacturer	Sources	Model
Best Medical International Inc	Best Palladium -103	2335
IBt	OptiSeed -103	1032P
North American Scientific	Prospera Pd -103	Med 3633
Theragenics Corporation®	TheraSeed ®	200

Brachy Seed Registry (Cont.)

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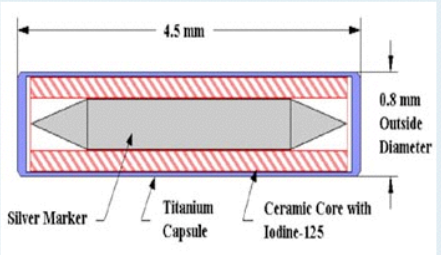
I-Plant Model 3500

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

- Duggan D. M., Johnson B. L., "Dosimetry of the I-Plant Model 3500 iodine-125 brachytherapy source," **Med. Phys. 28(4) 661-670, April 2001**.
- Wallace R., Model 3500 ^{125}I brachytherapy source dosimetric characterization. **Applied Radiation and Isotopes, 56 (4) 581-587, April 2002**
- Rivard, M.J., Comprehensive Monte Carlo calculations of AAPM Task Group Report No. 43 dosimetry parameters for the Model 3500 I-Plant ^{125}I brachytherapy source. **Applied Radiation and Isotopes. 57 (2002) 381-389**

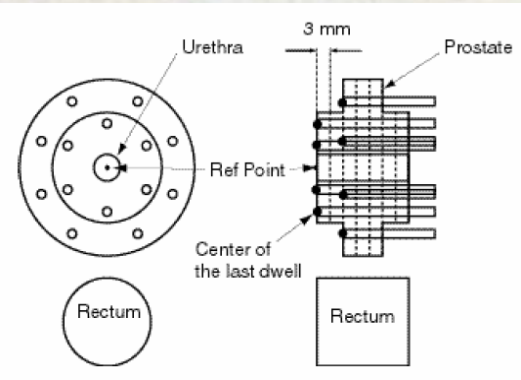
added to Registry, February 7, 2002

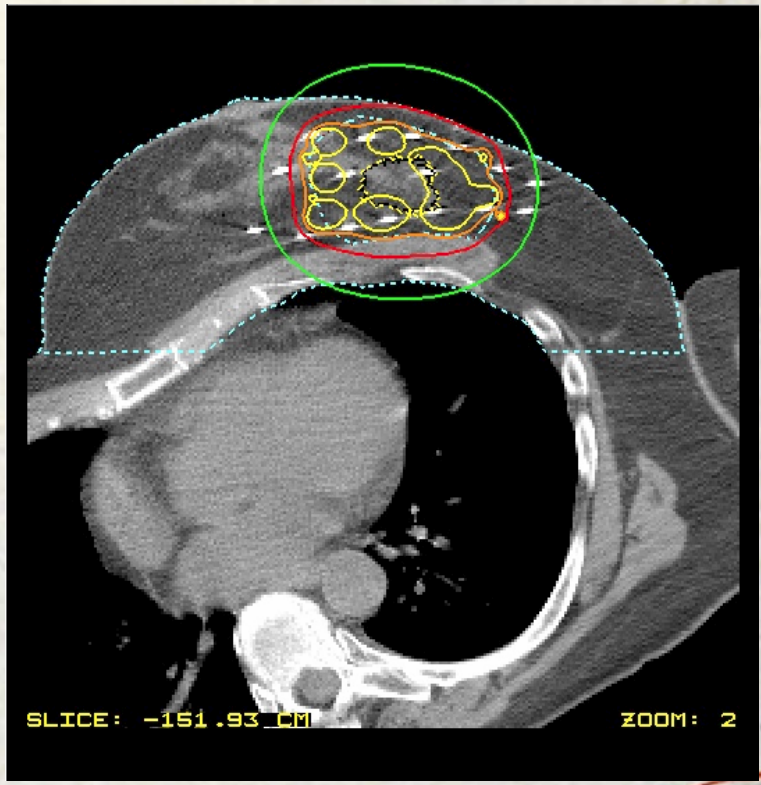
Protocol Requirements (cont'd.)

- 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

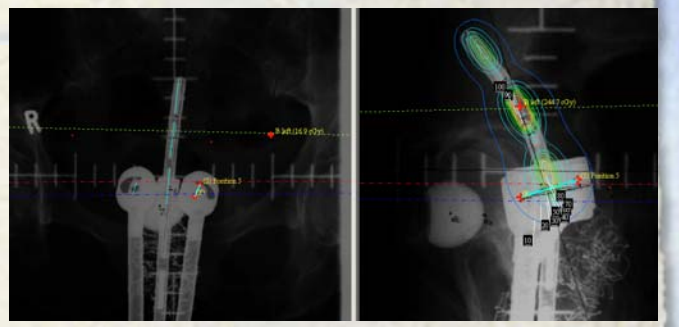
- Evaluate
  - Implant technique
  - Dosimetry
  - Documentation
  - Protocol compliance

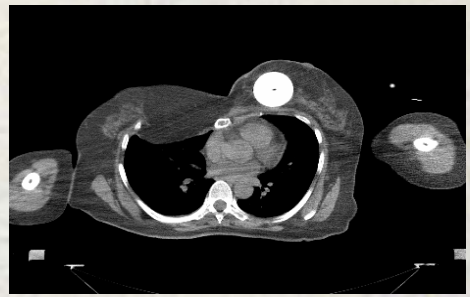




Brachytherapy Studies Requiring Credentialing

- 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

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 _____

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) _____

   _____

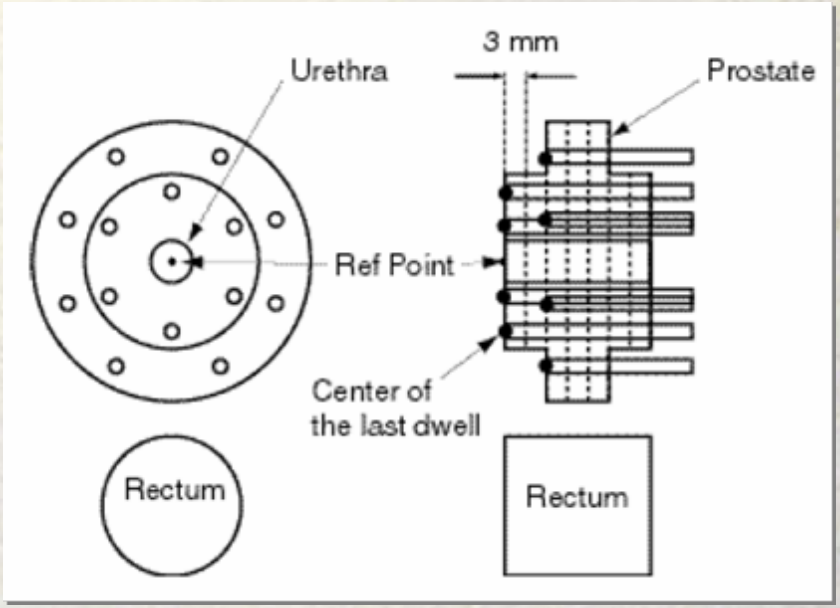
9. What seed strength is used for treatment planning? your own measurements ☐ vendor ☐

QA Requirements

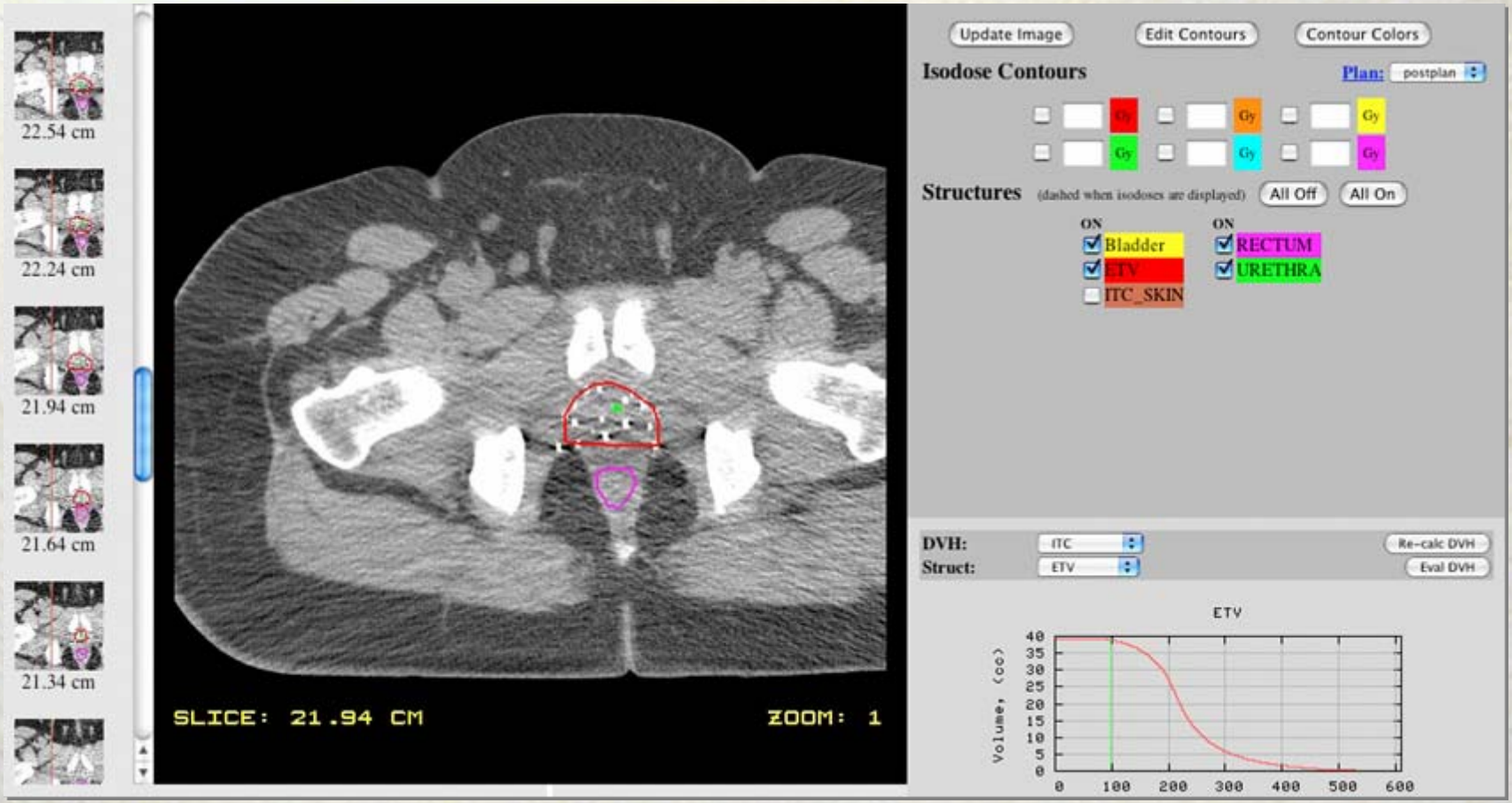
- For prostate brachy, include verification of source strength
- Requires ADCL-calibrated well chamber
- 3rd party radiopharmacy may be used, but must meet same requirements (only 2 have been approved)
- AAPM guidance recommends the physicist perform the verification

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



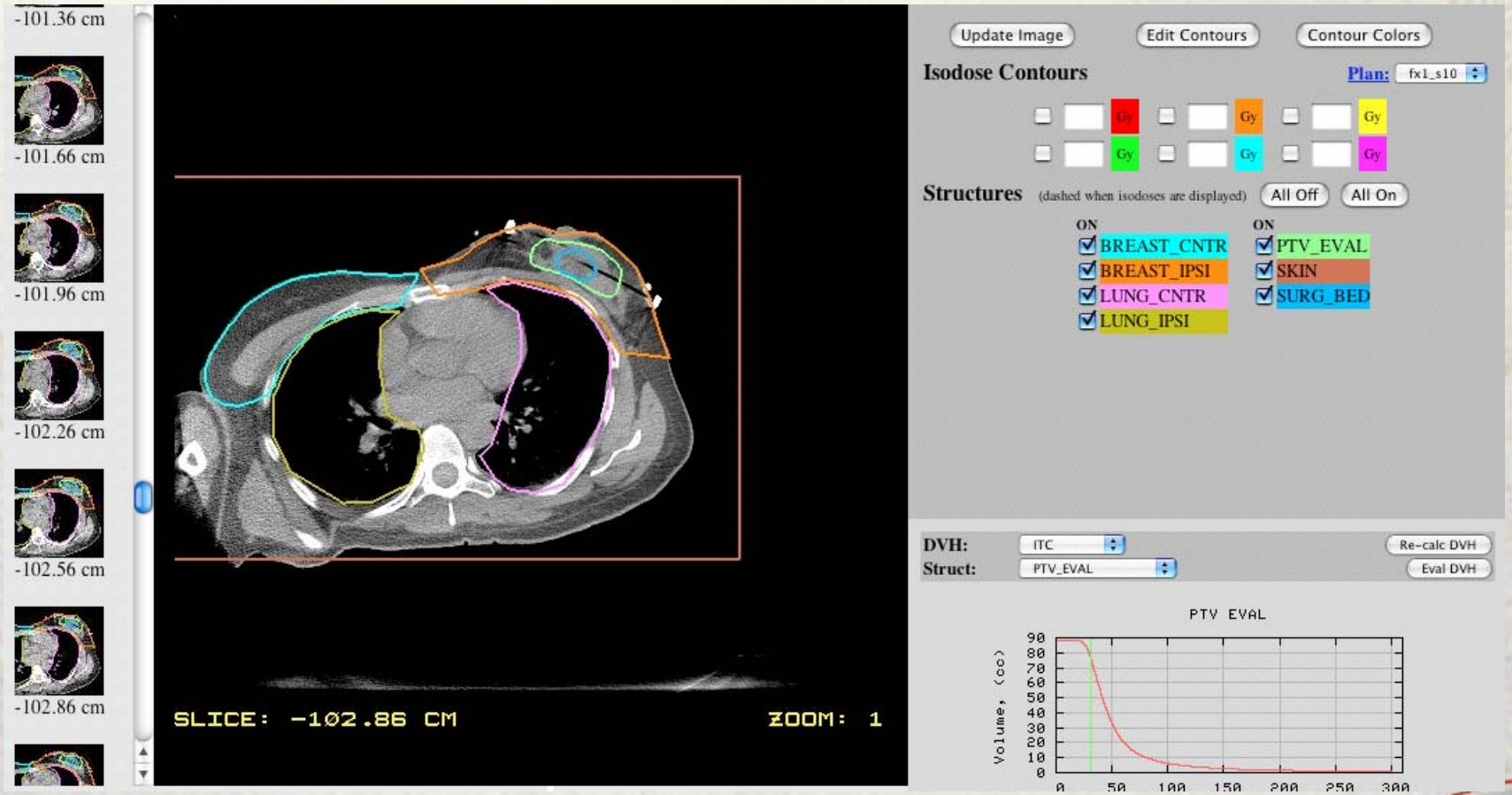
Benchmark Treatment Plan



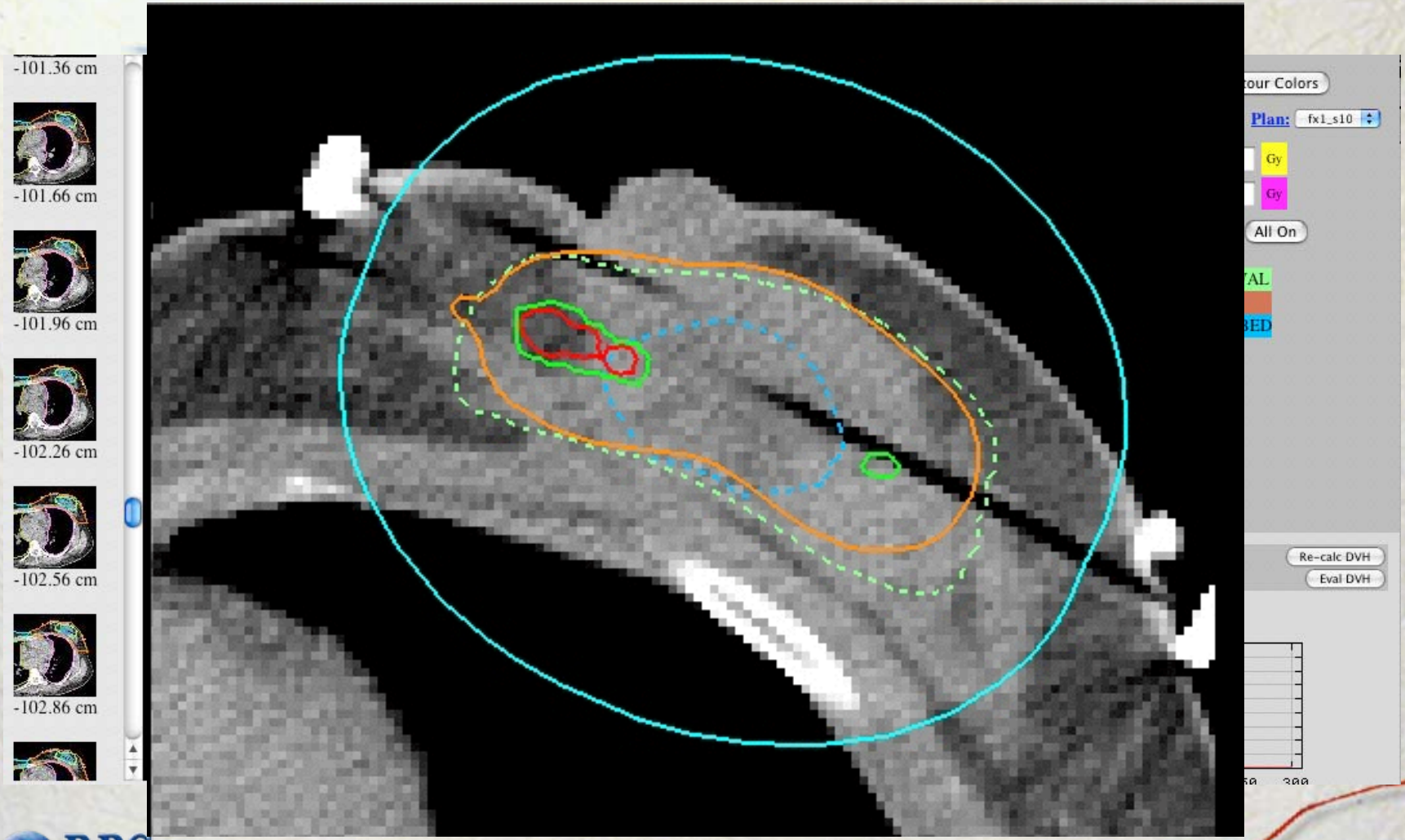
Errors, Inconsistencies, and Misunderstandings Discovered Through Credentialing

- 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

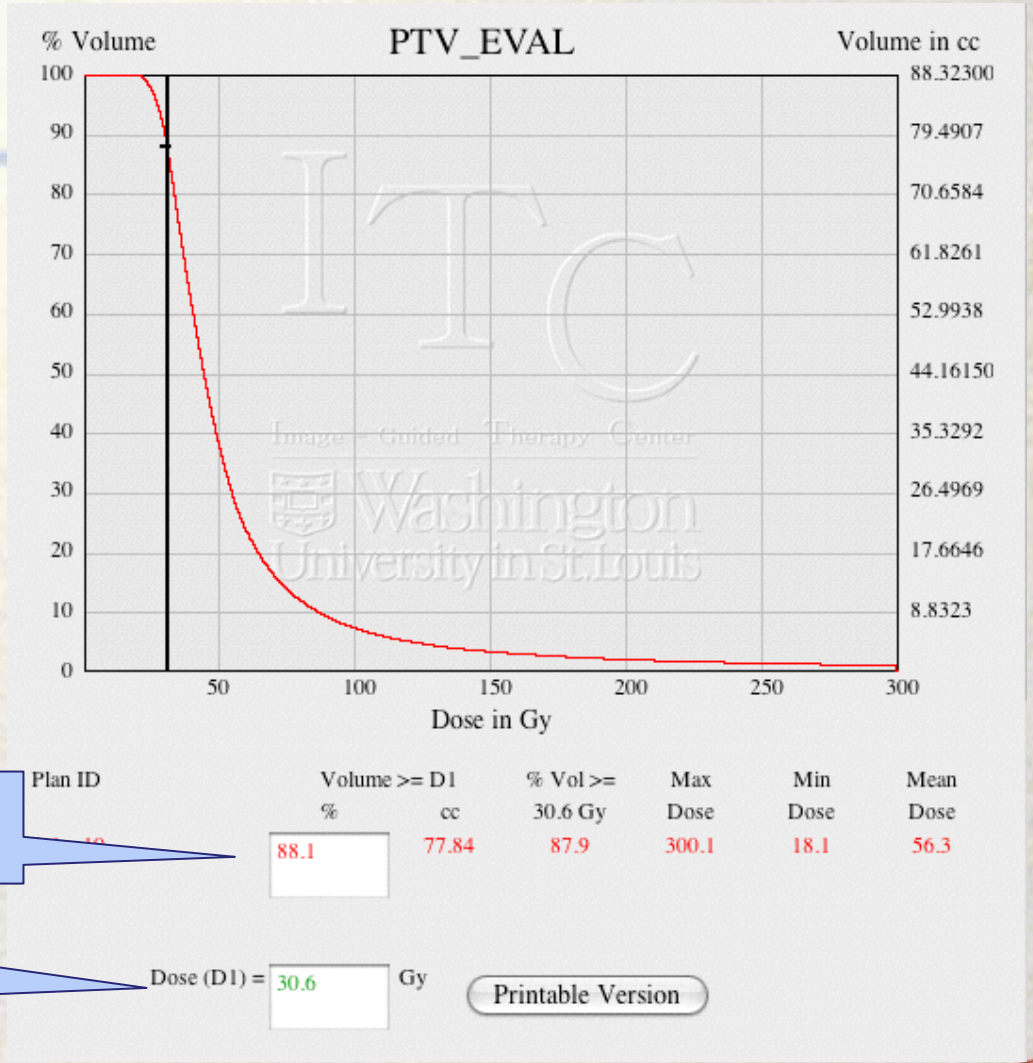
Evaluation of Submitted Plans



Evaluation of Submitted Plans



- Evaluation of Submitted Plans (DVH)



V_{90} = 88%

30.6 Gy (90%)

Poor Brachytherapy Technique

- Seeds implanted in base of penis
- Rad. Onc. advised to seek training

Credentials Awarded (based on benchmarks)

	Credentials	Institutions
Prostate LDR (0232)	70	63
Prostate HDR (0321)	11	7
Breast 3D CRT (0413)	792	364
Breast Mammosite®	497	245
Breast Multicatheter	115	41
Other 3D CRT (NCCTG)	52	52
Cervix (GOG)	55	46
TOTAL	**1,592**	**611**

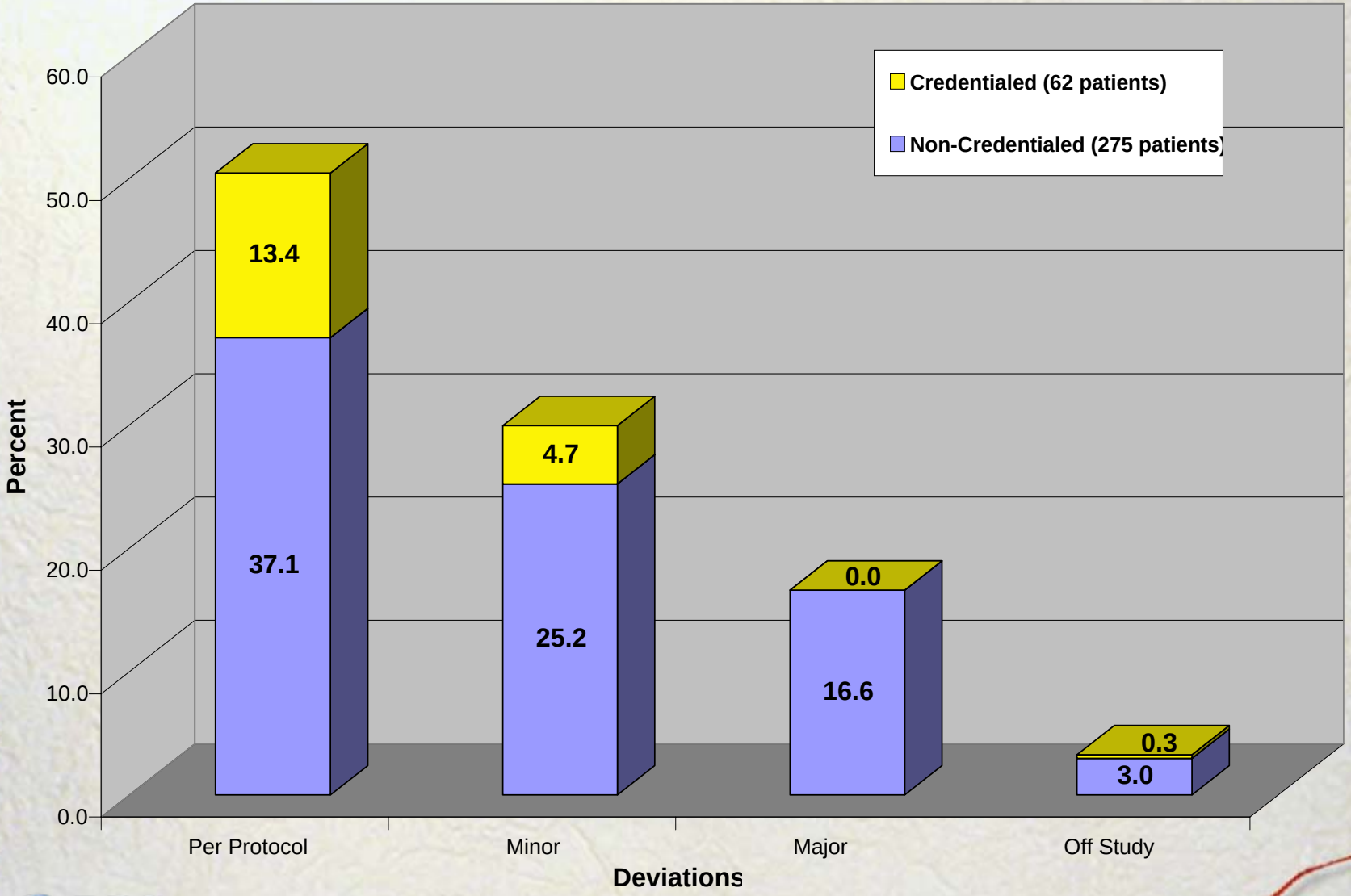
Results of Credentialing
(closed studies)

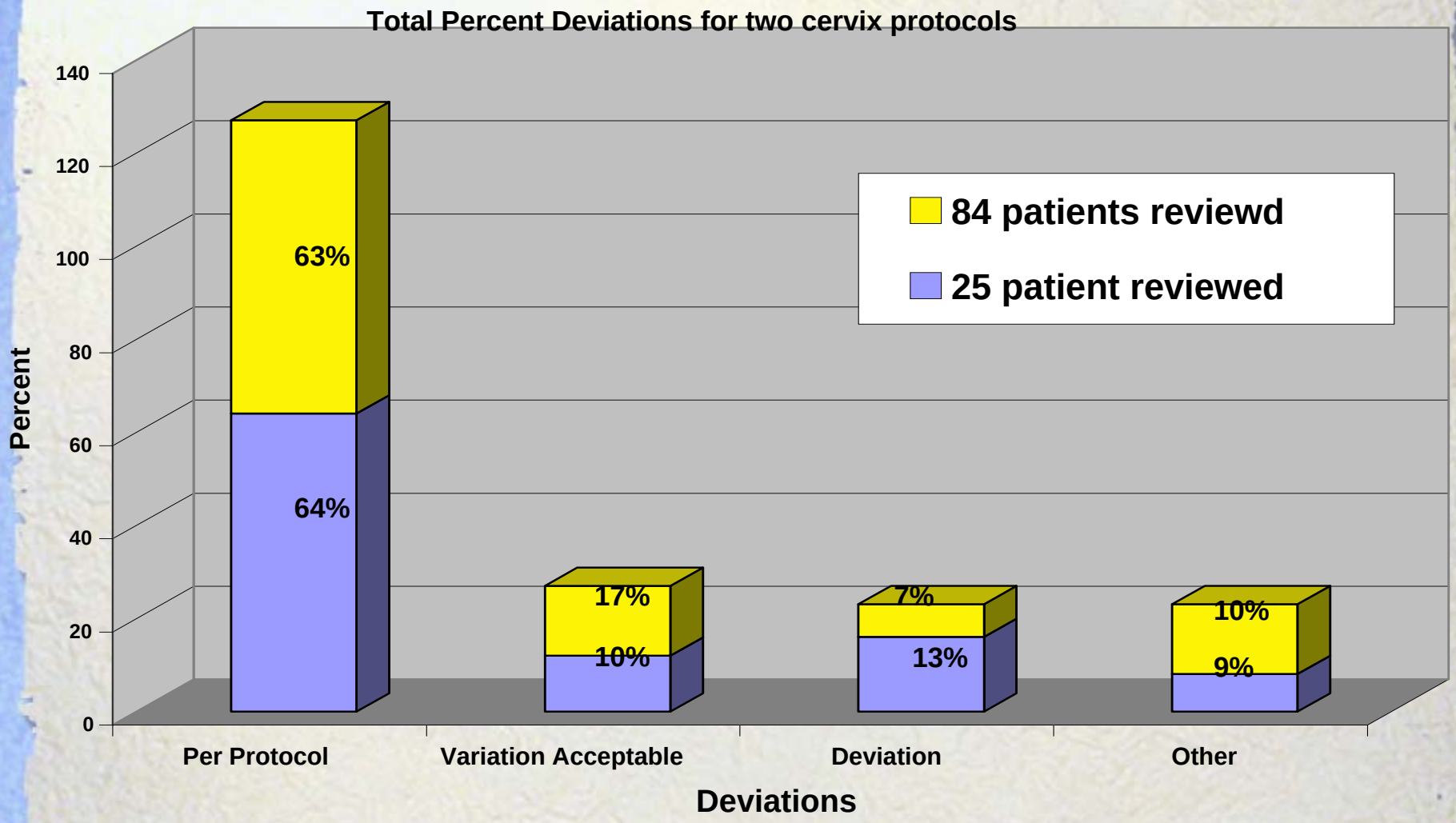
Study	Major Deviations	Minor Deviations	Number of Patients
GOG 165 HDR Cervix Credentialed inst	0	15	70
RTOG 95-17 HDR & LDR Breast (all)	0	4	100
RTOG 0019 LDR Prostate (values for dose only)	0	6	117 reviewed (total 129 eligible)

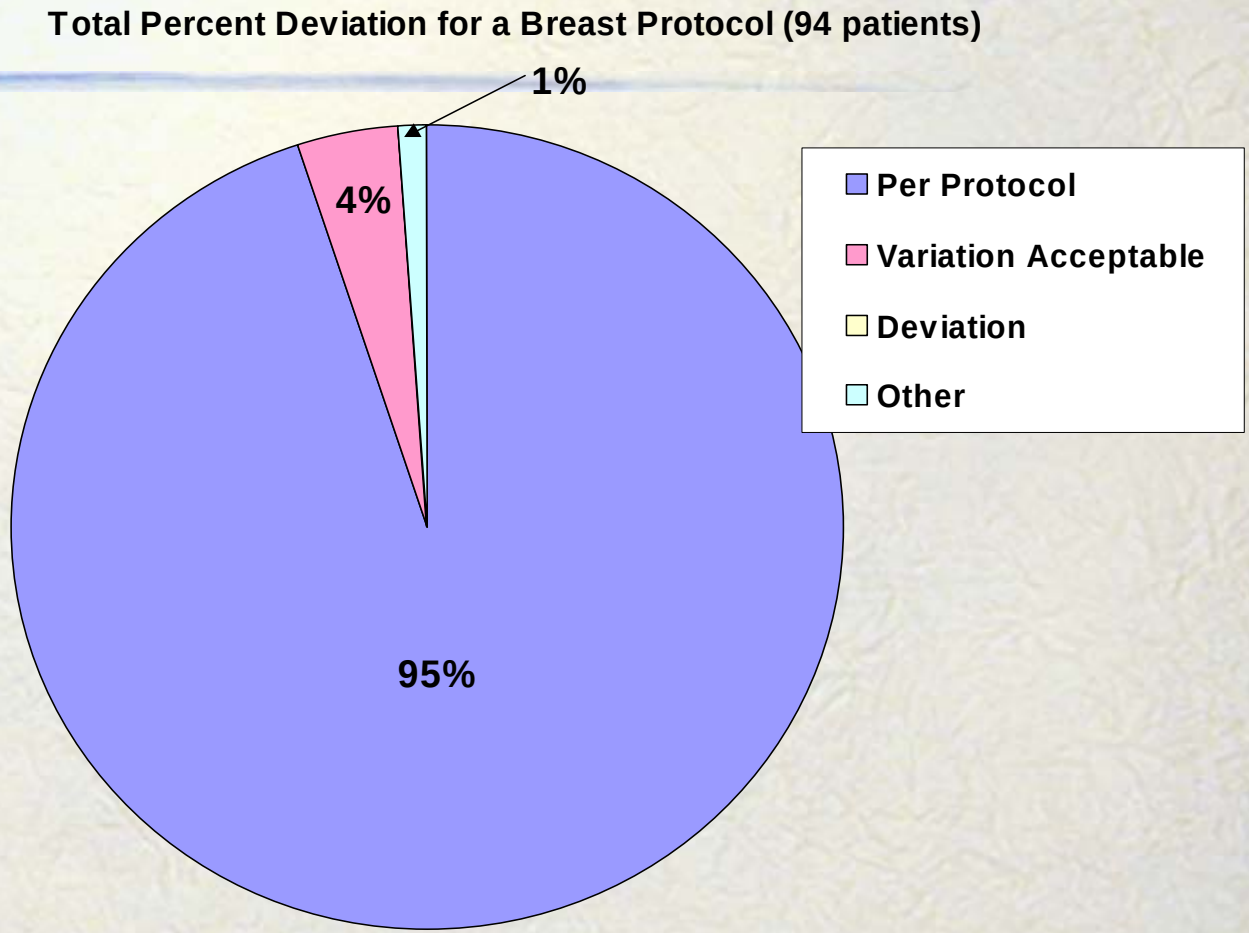
Results of Credentialing
(closed studies)

Study	Major Deviations	Minor Deviations	Number of Patients
GOG 165 HDR Cervix Credentialed inst	0	15	70
Non-credentialed	57	87	275
RTOG 95-17 HDR & LDR Breast (all)	0	4	100
RTOG 0019 LDR Prostate (values for dose only)	0	6	117 reviewed (total 129 eligible)

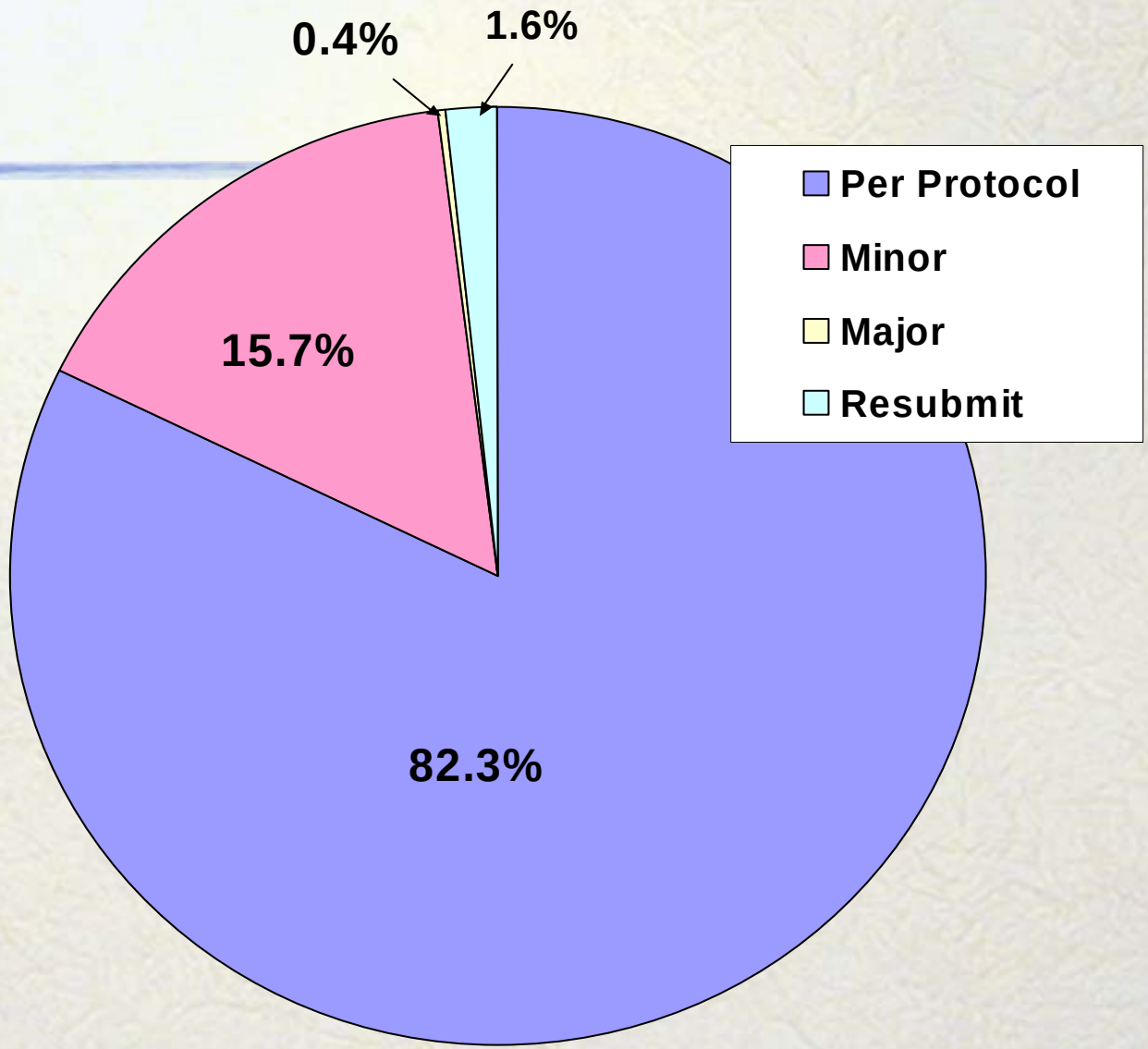
Total Percent Deviations for Credentialed and Non-Credentia Institutions

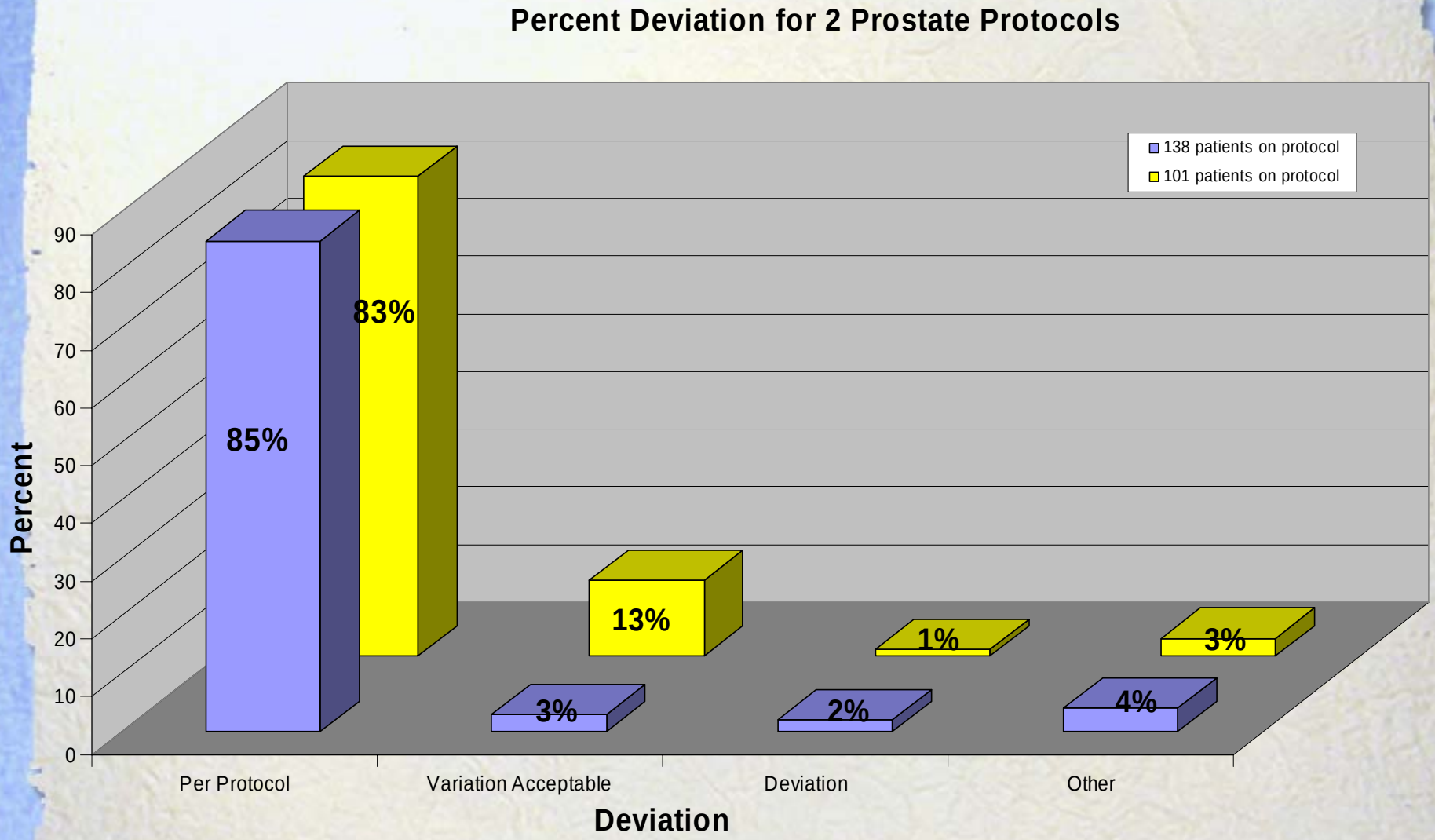



Total Percent Deviations for two cervix protocols
140
120
100
80
60
40
20
0
Percent
63%
64%
17%
10%
7%
13%
10%
9%
84 patients reviewd
25 patient reviewed
Per Protocol
Variation Acceptable
Deviation
Other
Deviations


Total Percent Deviation for a Breast Protocol (94 patients)
1%
4%
95%
Per Protocol
Variation Acceptable
Deviation
Other

Total Percent Deviations (753 patients evaluated out of 1019)




Percent Deviation for 2 Prostate Protocols
138 patients on protocol
101 patients on protocol
Percent
0
10
20
30
40
50
60
70
80
90
85%
83%
3%
13%
2%
1%
4%
3%
Per Protocol
Variation Acceptable
Deviation
Other
Deviation

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