

Brachytherapy for the Treatment of Prostate Cancer

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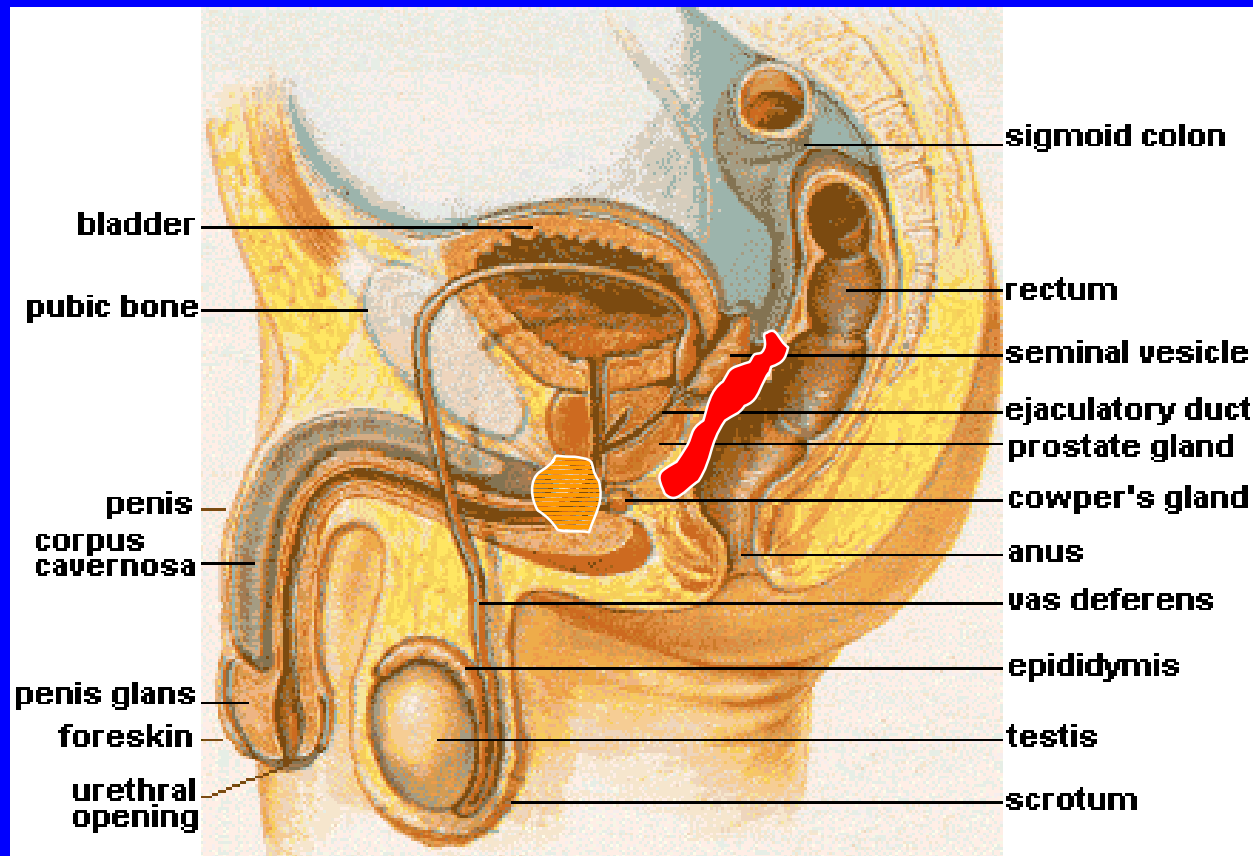
- # Clinical Considerations
- **Prostate Cancer grows slowly**
 - **Early detection is more common**
 - **Larger Doses are required to control Prostate tumors**
 - **Life expectancy is longer**
 - **Quality of life is affected by side effects and complications**

The most common treatments for

- **surgery**
- **prostate cancer include:**
- **external beam radiotherapy (EBRT)**
- **hormone therapy**
- **radioactive seed implants (TPPI)**
- **watchful waiting.**

- **External Beam Radiation Therapy**
 - Classical 2-D planning
 - 3D-Conformal RT (3D-CRT)
 - IMRT
- **Permanent Implants**
 - Nomogram and rule based
 - Preplanned and preloaded
 - Intraoperative Interactive dose planned
- **HDR Brachytherapy**

It is what lays around the prostate that affects the limits of RT



Dose Response in Prostate Ca

3DCRT DOSE – RESPONSE FUNCTIONS: ACTUARIAL FIVE – YEAR bNED CONTROL

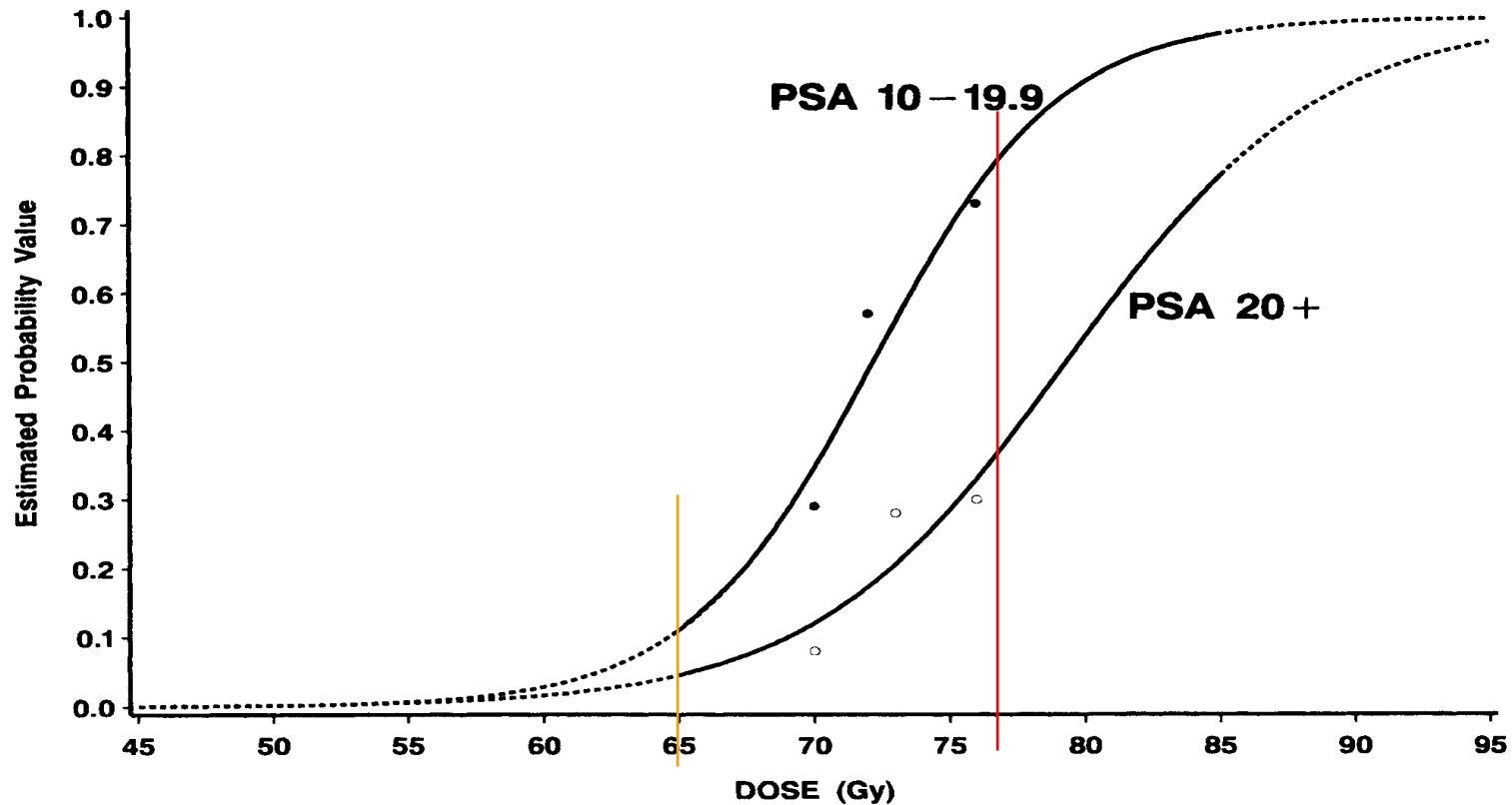


Fig. 2. Logistic response models for bNED for two pretreatment PSA groups.

3DCRT DOSE – RESPONSE FUNCTIONS: ACTUARIAL FIVE – YEAR LATE MORBIDITY

Morbidity Vs. Dose

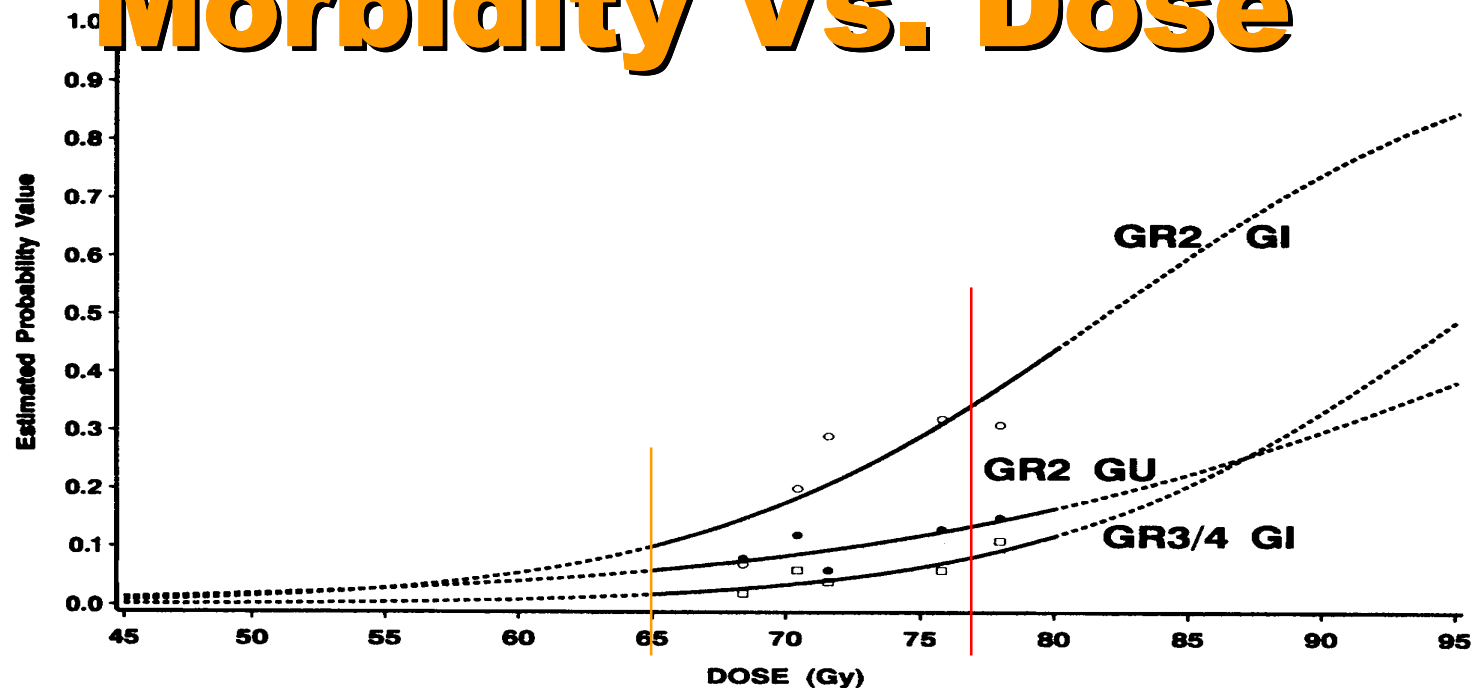
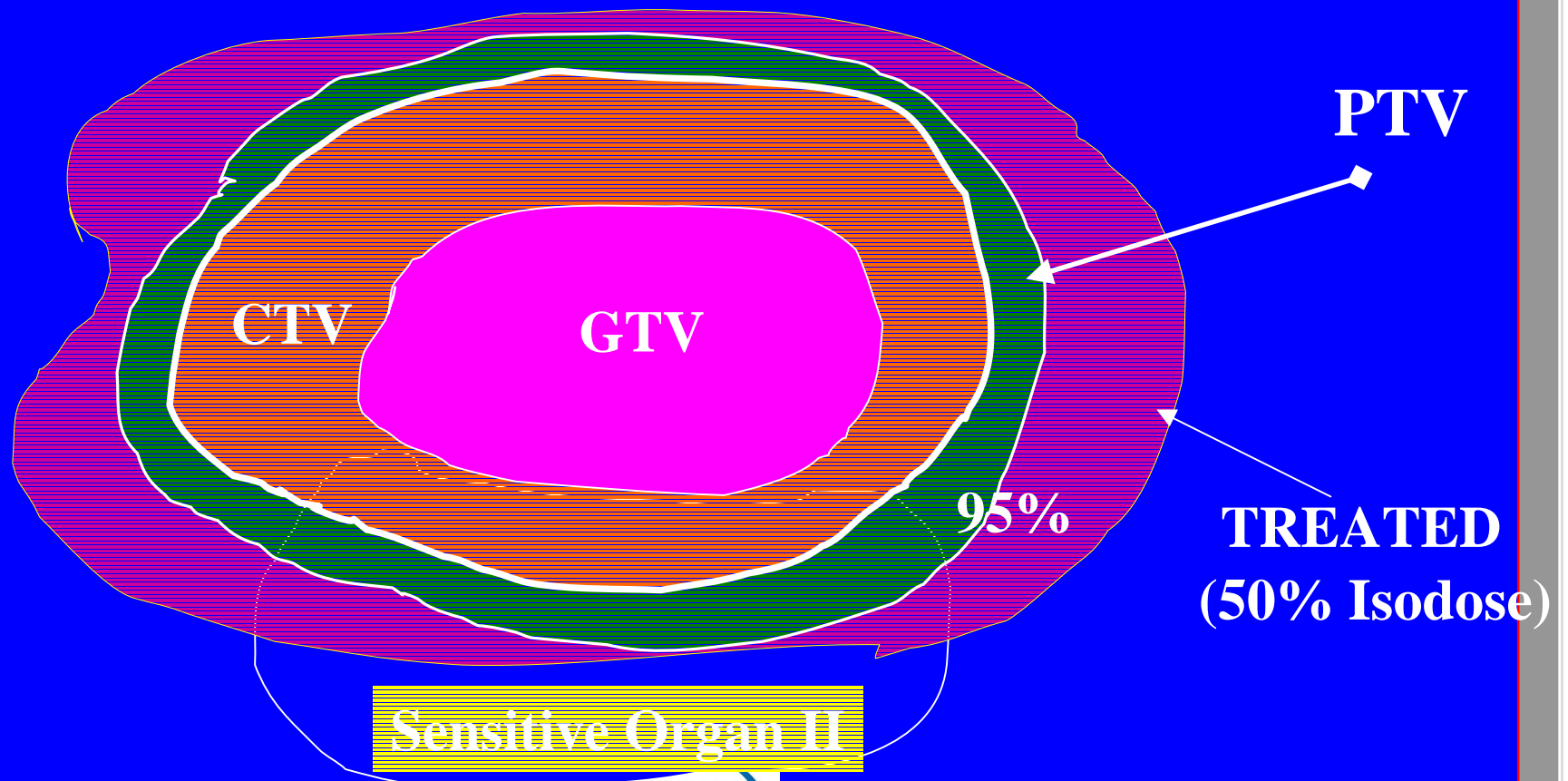


Fig. 5. Logistic response models for gastrointestinal and genitourinary radiation sequelae.

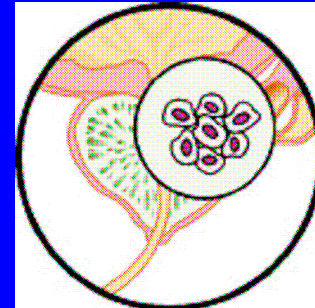
From: G.E. Hanks et. al., IJROBP, June 1998

Spatial Relations between Volumes typical of EBRT

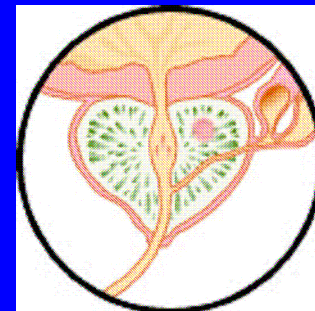
Sensitive Organ I



Stages amenable to Brachytherapy



- **T1 - The tumor is located within the prostate gland and is too small to be detected by DRE. It may be discovered through other diagnostic procedures (PSA test, biopsy) Generally produces no Physical symptoms.**



- **T2 Stage - The tumor is still located within the prostate gland but it can be felt during a DRE exam or**

Sources of uncertainty in EBRT that can be avoided in Brachytherapy

- **Physiological movements and variations in size, shape and position of the Prostate gland in relation to anatomic landmarks or an internal reference point. The CTV is expanded by the Internal Margins (IM) to create the Internal Target Volume (ITV).**
- **Typically Internal Margins are:**
 - A: 5 mm posterior
 - B: 10 mm anterior and lateral, and
 - C: Two slices each, superior and inferior, “copied” from the last delineated slice. Slices are 3 mm apart so the IM=6 mm.

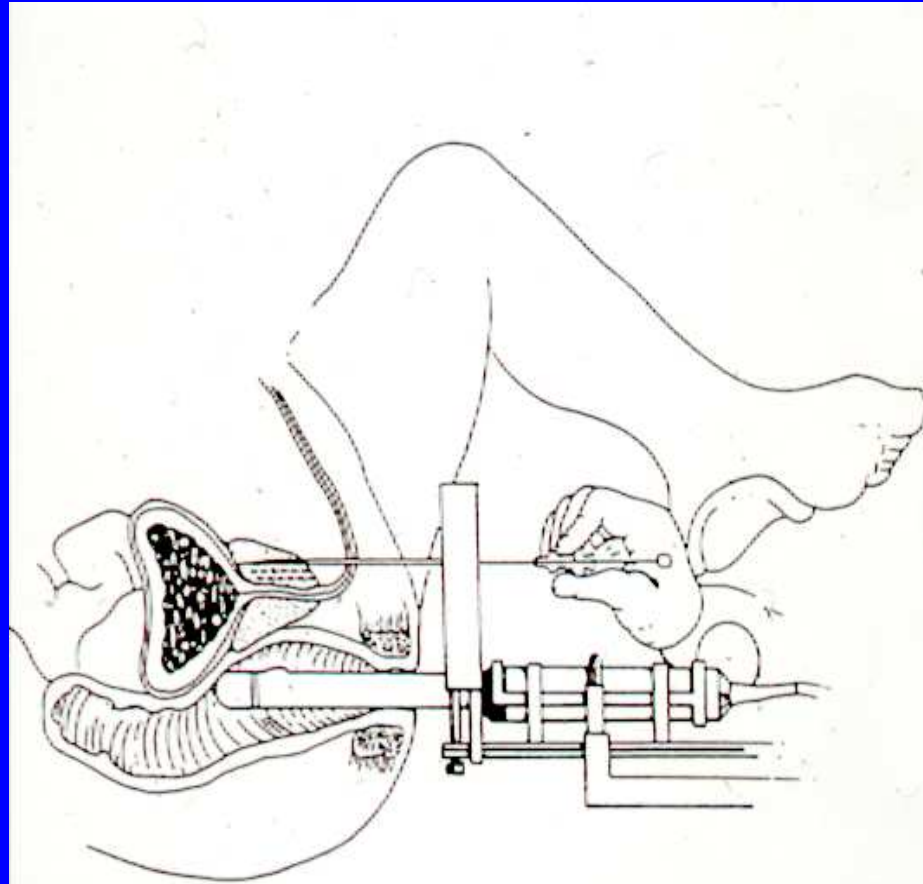


Prostate seed implants

- Prostate implants were developed in the 1960's at Memorial Sloan Kettering Cancer Center and on the West coast. The initial technique involved open access to the prostate.
- On the last fifteen years, Transperineal prostate implants became predominant in the USA, pioneered by SPI - Washington State, Mt Sinai and MSKCC in NY.
- More than 800 papers published on this subject since 1990.



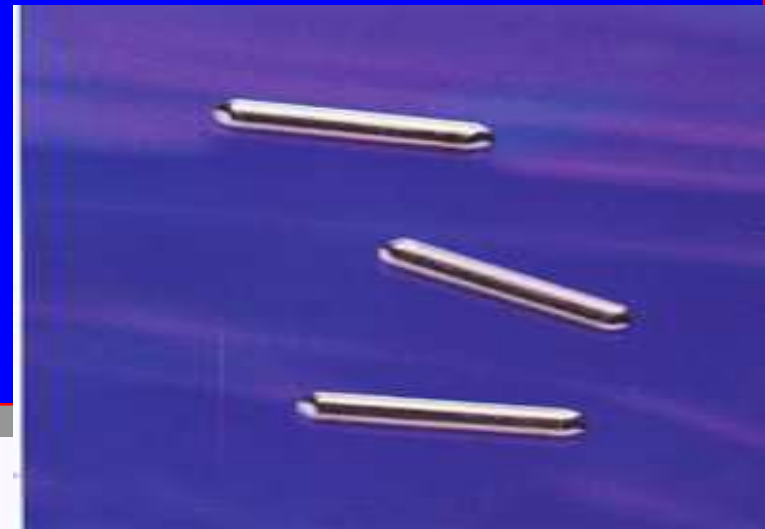
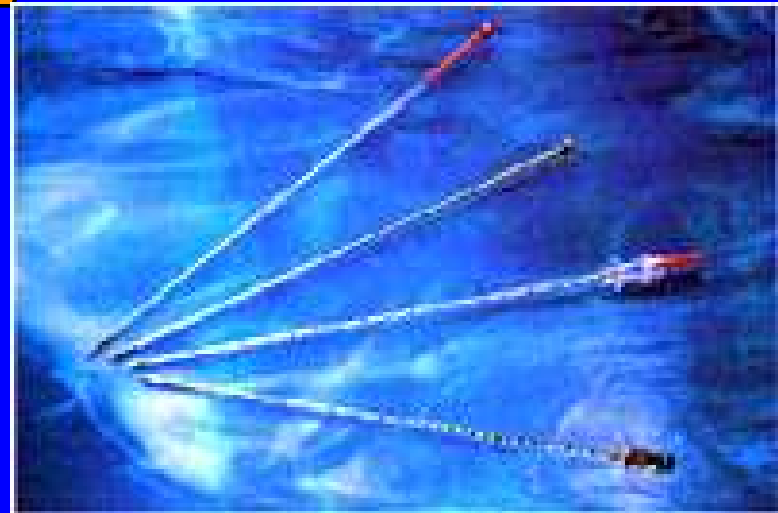
Transrectal Ultrasound Guided Brachytherapy





- **High Lithotomy**
- **Patient to edge of table**
- **Symmetry of legs**
- **Tilt US forward to remove air from the**

Different implant techniques



- **The American Brachytherapy Society (ABS) recommends an RX of 145 Gy and 125 Gy for ^{125}I and ^{103}Pd , in monotherapy brachytherapy, and 110 Gy of ^{125}I and 100 Gy ^{103}Pd if used as a boost following pelvic EBRT of 40 to 50 Gy.**
- **Typically the doses are prescribed to the minimum peripheral dose (MPD) which is the maximum dose that cover 100% of the target volume. Usu. 90% of the target volume will receive the prescription dose.**

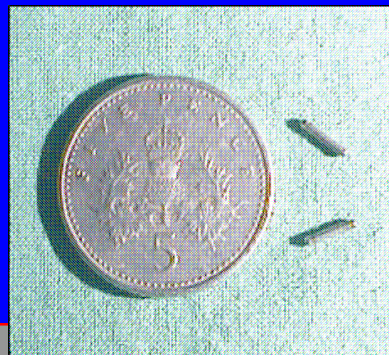
- **The Mean Peripheral dose is the average of the dose at the surface of the target volume, and varies less than the MPD with seed position.**

- **Iodine 125 (^{125}I) and Palladium 103 (^{103}Pd) are the most commonly used isotopes.**

LDR Seed selection

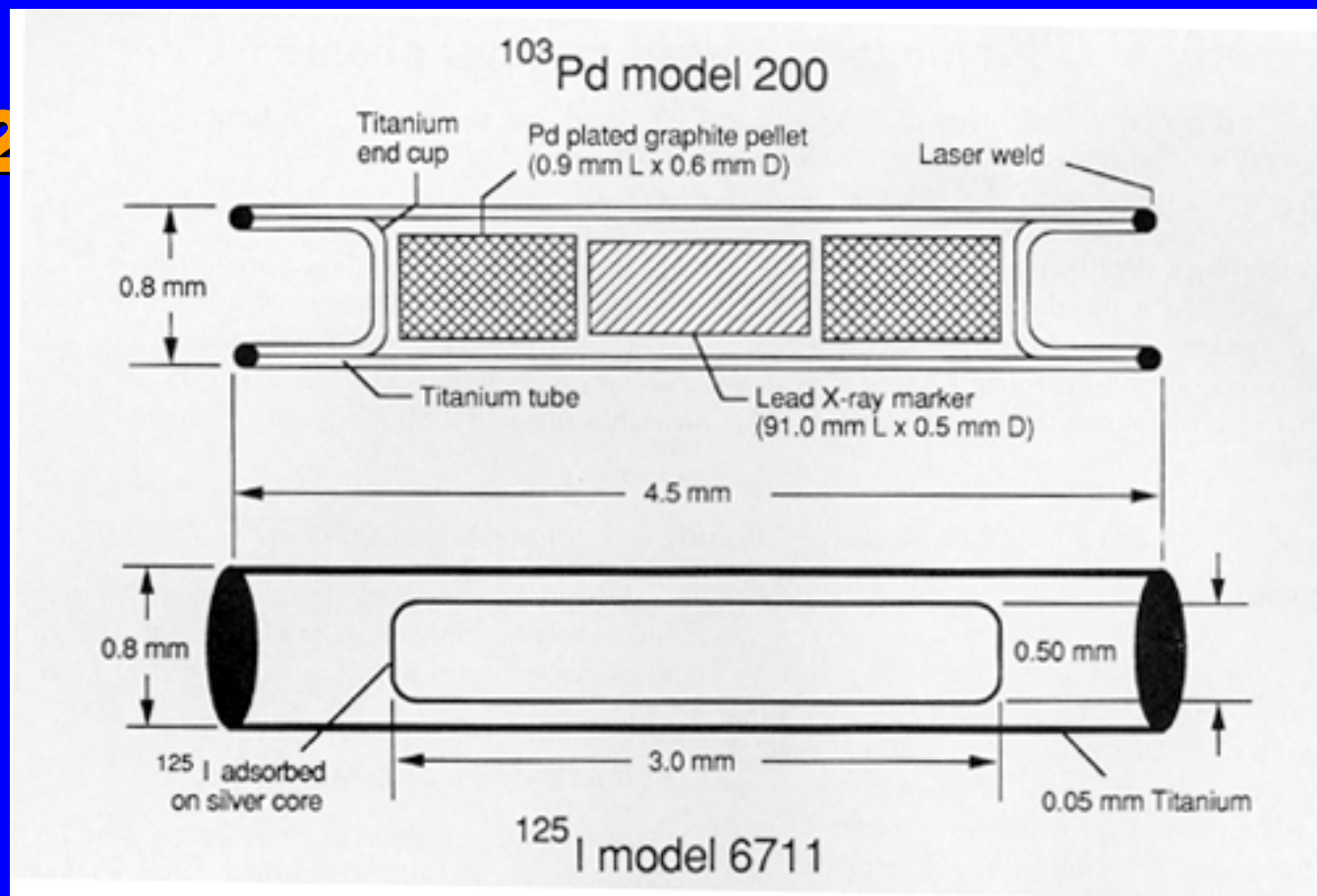
Properties:

	^{125}I	^{103}Pd
• Half life (d)	59.4	17
• Energy (kV)	28	21
• Radiobiologic Equiv.	1.4	1.9

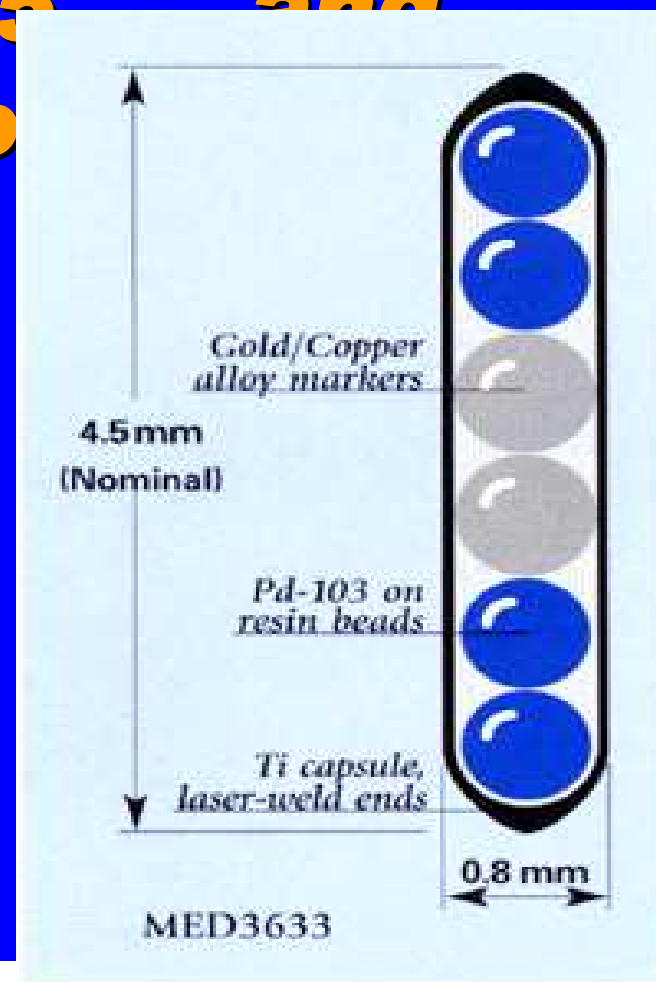
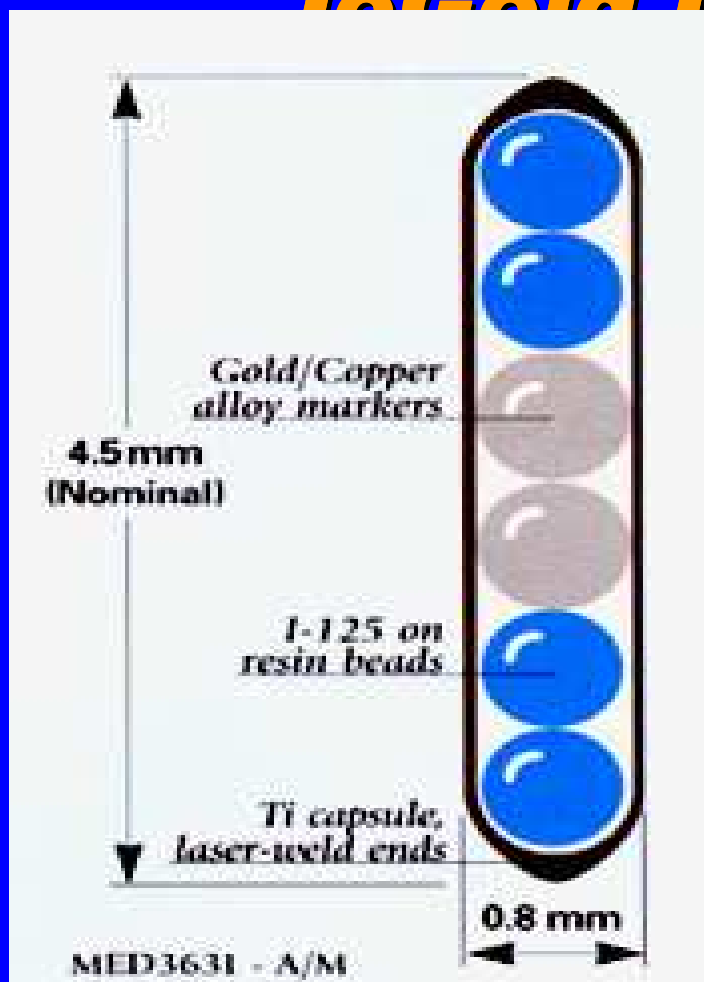


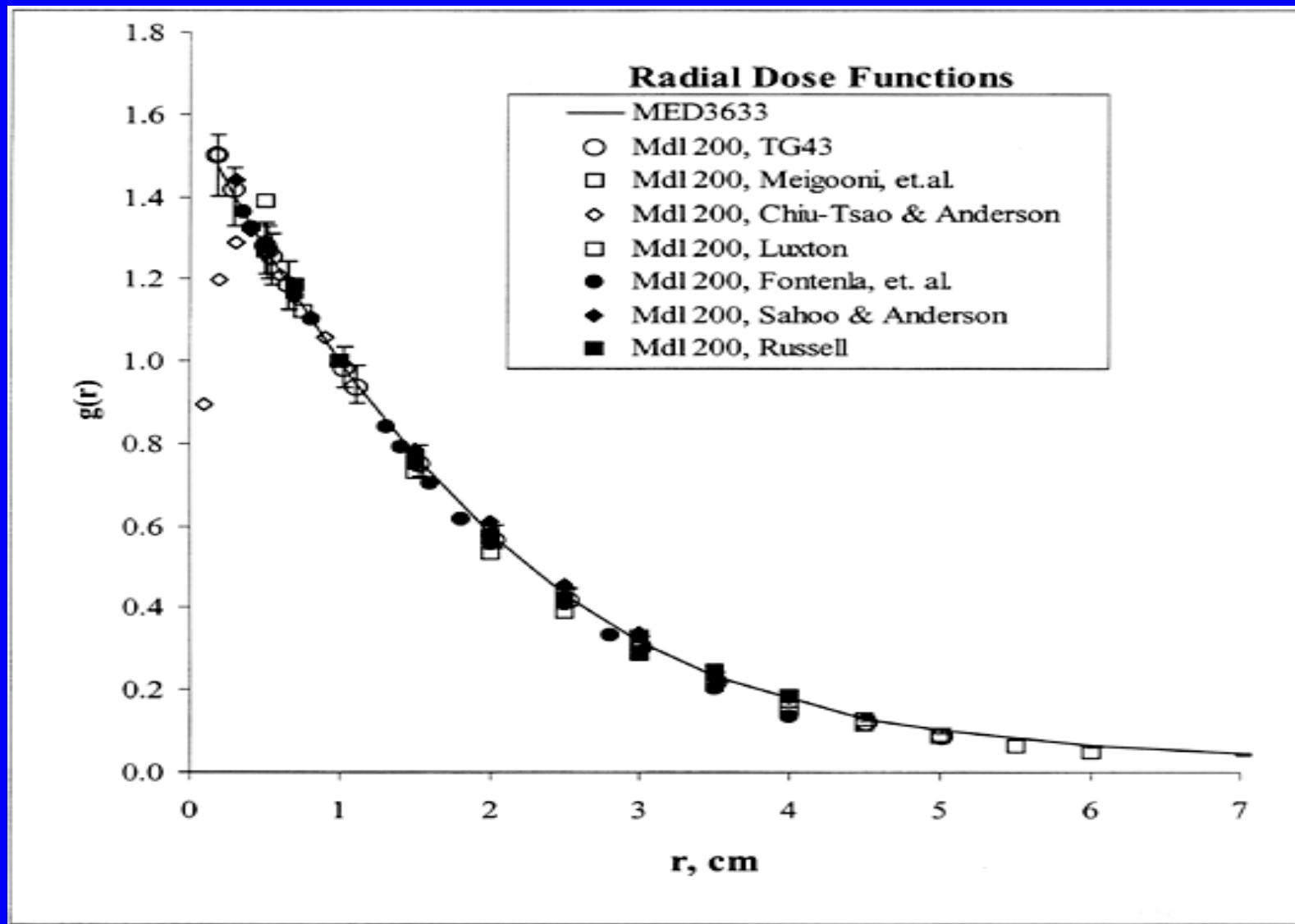
I-125

0



I-125 and Pd-103



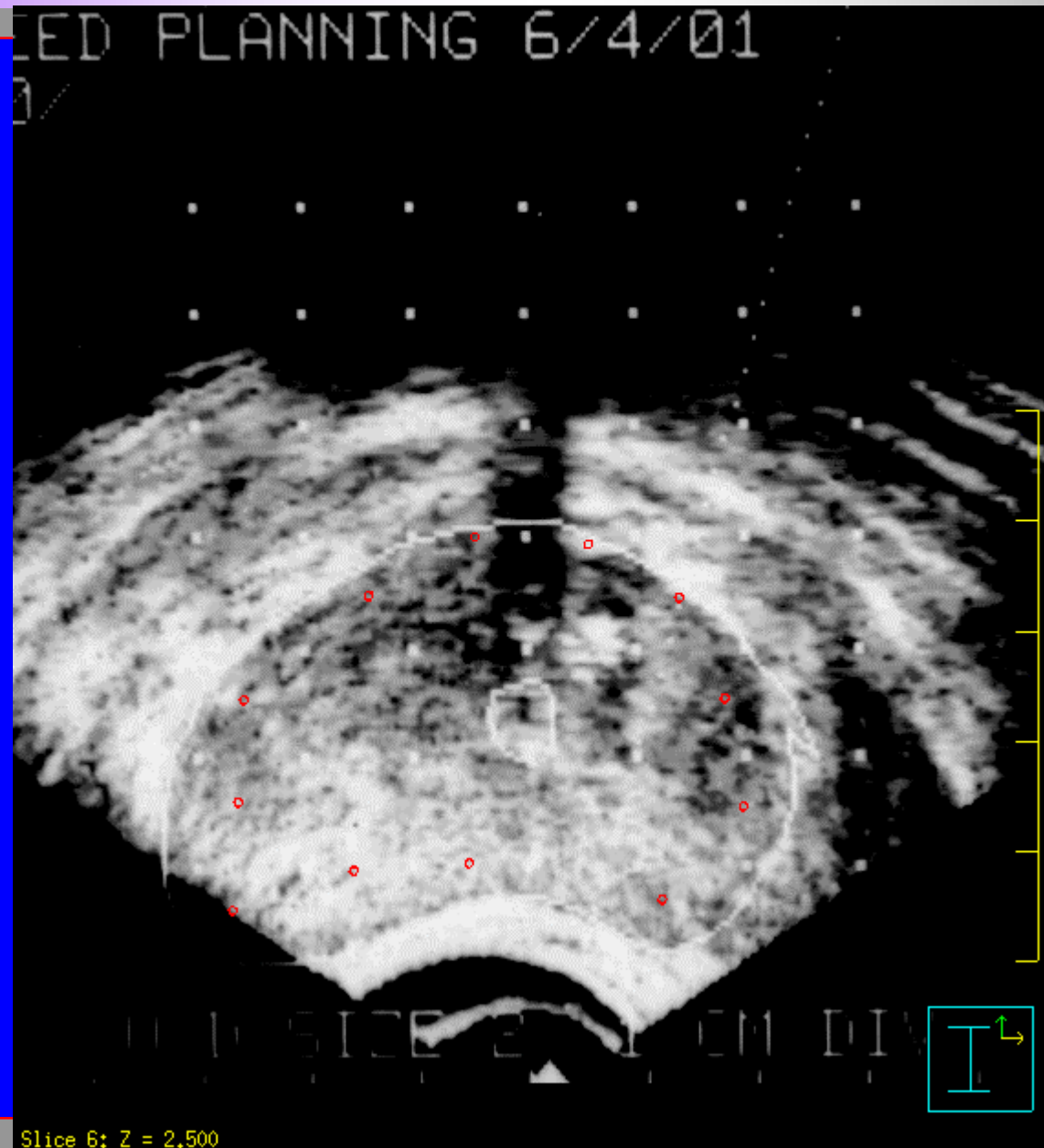


Advantages of seed implants:

- **Recent clinical data shows a high percentage of implant patients remaining disease free than with either radical prostatectomy or external beam therapy.**
- **Seed implantation normally takes about one or two hours. The patient usually leaves the hospital the same day. Many patients resume normal activities within a few days.**
- **Seeds can deliver two to three times more dose than EBRT.**
- **Incontinence occurs in less than 5% of patients under the age of 60. More often for patients over the age of 60.**
- **This procedure is better tolerated than surgery or external radiation.**

Disadvantages of seed implants:

- **The long term results are fully established yet. The current clinical data show good results up to seven years.**
- **It is common to experience problems with urination for several months after seed implantation. These symptoms will, however, gradually ease and eventually disappear.**
- **Although the seeds remain radioactive for several months, the energy and activity of the seeds is so low that there is negligible risk of exposure to others and only simple precautions are necessary for the first 2-3 months.**



1. RTOG 98-05:

“Phase II Trial of TRUS Permanent Radioactive Implantation of the Prostate for the Definitive Management of Localized Adenocarcinoma of the Prostate.”

**2. American Brachytherapy Society: *”The ABS Recommendations for Permanent Prostate Brachytherapy Post implant Dosimetric Analysis”*
*Int.J.Radiat Oncol Biol Phys, 2000;46,N 1:221-230”***



RTOG Objectives

- **Evaluate effectiveness of TRUS permanent implantation of the prostate for organ confined adenocarcinoma as compared with historical data of prostatectomy or external beam.**
- **Establish & Test QA standards for future protocols.**
- **Test dosimetric evaluation of implants.**

RTOG Parameters:

- ***Criteria for Patient Selection.***
- ***Definition of Planning Target Volume:
(PTV = Pre-implant TRUS+margins)***
- ***Evaluation Target Volume
(ETV = Post-Op CT).***
- ***Seed Calibration and Handling.***
- ***Post-Op evaluation.***
- ***Dose Volume Histogram.***



• Evaluation criteria

- Per Protocol : $\geq 80\%$ of ETV receives at least 90% of PD.
- Variation, Acceptable: $\geq 50\%$ of the ETV receives at least 90% of PD
- Deviation, Unacceptable: $\geq 50\%$ of the ETV receives $< 90\%$ of PD.



GENERAL LISTING OF I-125 SEED IMPLANT INFORMATION

Iodine-125 Properties

I-125 sealed in metal *seed*

Average energy = 28 keV,

Patient Dose:

**(Assuming 145 Gy isodose at the surface of
the prostate of diameter = 5cm)**

**Average Dose Rate=7cGy/hour =168 cGy/day
(Similar to external beam therapy).**



Total dose (calculated for Half Life x 1.44)

Total Dose = 7 cGy x 24 hour x 60 days x 1.44

hour day
=14,500 cGy = 145 Gy

Shielding

Half Value Layer = 0.025 mm lead = 20 mm tissue. So, 10 cm of tissue attenuates 97% of x-rays.

External Exposure

Pelvic surface = 2 - 20 mrem/hour

Three foot distance = 0.1 -> 1 mrem/hour

Background = 2 mrem/week

- **Pre-planning (PP)**: Creation of a plan a few days or weeks before implant procedure.
- **Intra-operative Planning (IOP)**: Tx Planning in the OR: Pt and TRUS probe are not moved between the volume study and the seed insertion.
- **Interactive Planning (IP)**: Stepwise refinement of the Tx plan using computerized dose calculations derived from image-base needle position feedback.
- **Dynamic Dose Calculation (DDC)**: Constant updating of dose distribution calculations using continuous

- **Used for most RTPS.**
- **It eliminates the need to determine the orientation of the source longitudinal axis from imaging studies.**

1-D isotropic point source calculation

$$\dot{D}(r) = S_K \cdot \Lambda \cdot \frac{G_X(r, \theta_0)}{G_X(r_0, \theta_0)} \cdot g_X(r) \cdot \phi_{an}(r)$$

1D anisotropy function

$$\phi_{an}(r) = \frac{\int_0^\pi \dot{D}(r, \theta) \sin(\theta) d\theta}{2 \dot{D}(r, \theta_0)}$$



- **Source ^{125}I [STM 1251] [NIST 99]**
- **Radial Dose Function, source description and anisotropy factor**

TG-43 Source

Source Name
I-125 (STM 1251) [NIST 99]

Conversion Factor (U/mCi)
1.270

Dose Rate Constant (cGy/(h U))
0.980

Half Life (Days)
59.400

Radial Dose Function

r(cm)	Radial Dose
0.00	0.8790
0.10	0.9410
0.20	1.0030
0.30	1.0240
0.50	1.0330
0.75	1.0220
1.00	1.0000
1.50	0.9370
2.00	0.8560
2.50	0.7720
3.00	0.6910
3.50	0.6120
4.00	0.5400
4.50	0.4750
5.00	0.4150
6.00	0.3140
7.00	0.2360
8.00	0.1760
9.00	0.1310
10.00	0.0969
11.00	0.0703
12.00	0.0510
13.00	0.0375
14.00	0.0258

Aniso Factors
Aniso Functions
Strands

Source Model
Aniso Constant

Active Length (cm)
0.380

Physical Diameter (cm)
0.080

Physical Length (cm)
0.450

Aniso Factors
Aniso Functions
Strands

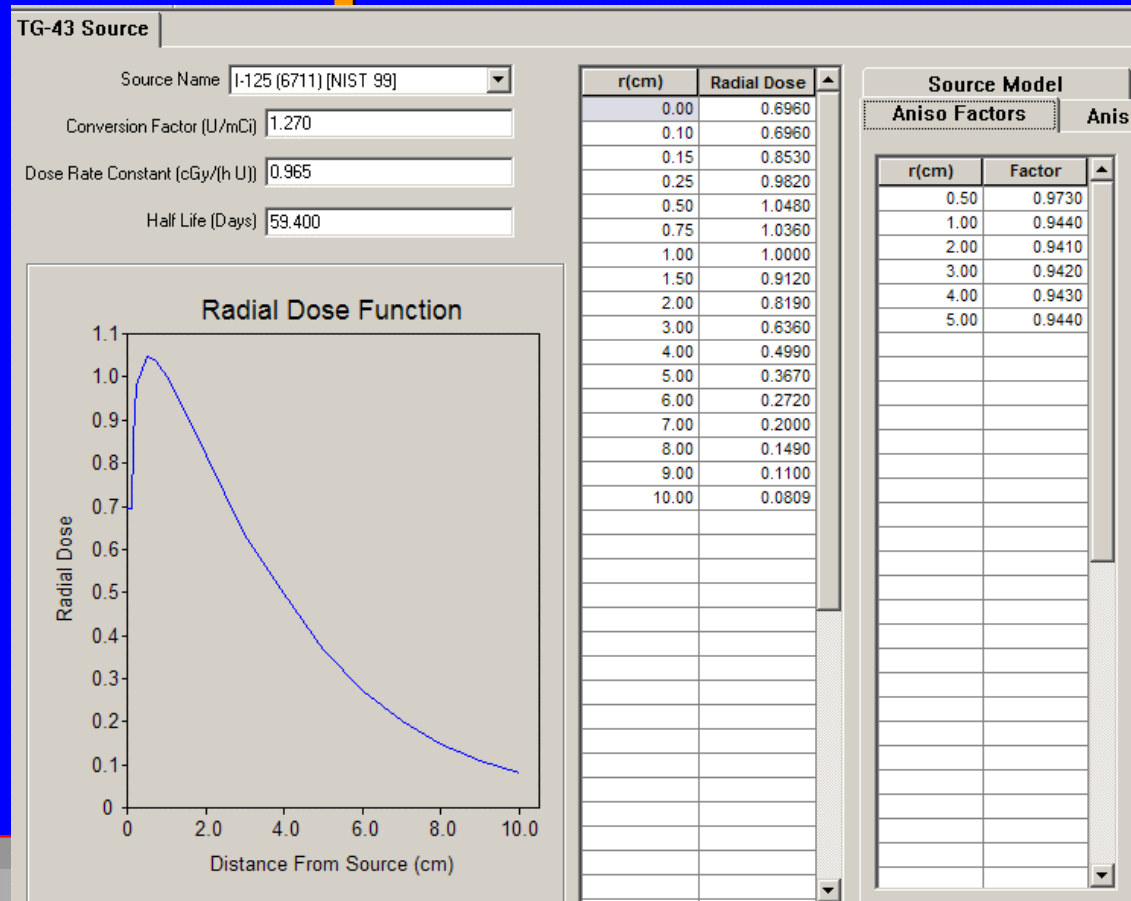
Source Model
Aniso Constant

Active Length (cm)
0.380

Physical Diameter (cm)
0.080

Physical Length (cm)
0.450

- **Source ^{125}I [6711] [NIST 99]**
- **Radial Dose Function and anisotropy factor?**



- **“Each institution planning to provide brachytherapy should have the ability to independently verify the source strength provided by the manufacturer”. (TG-40).**
- **The Medical Physicist (MP) should independently measure 10% of the sources to be implanted in the patient (TG-56).**
- **The MP is responsible for the dose given to the patient.**

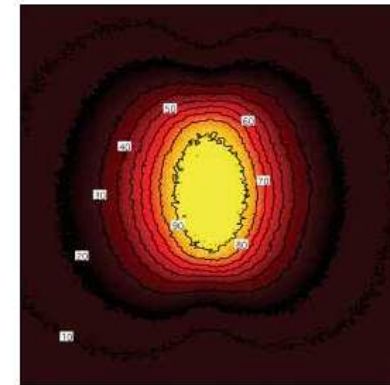


Figure 1a. Surface contour plot of an Amersham model 6711 LDR ^{125}I source made with an autoradiograph.

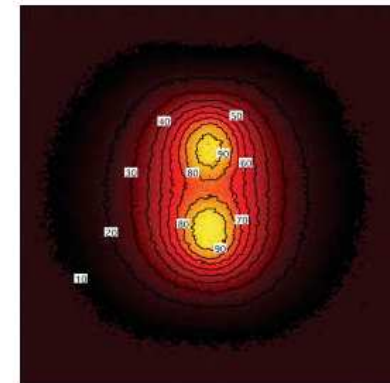
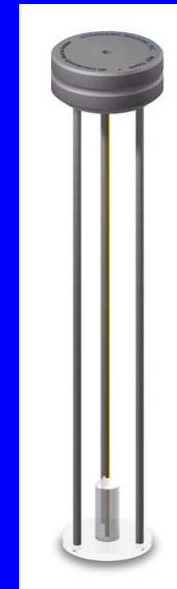
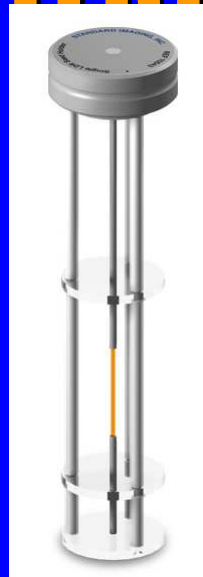


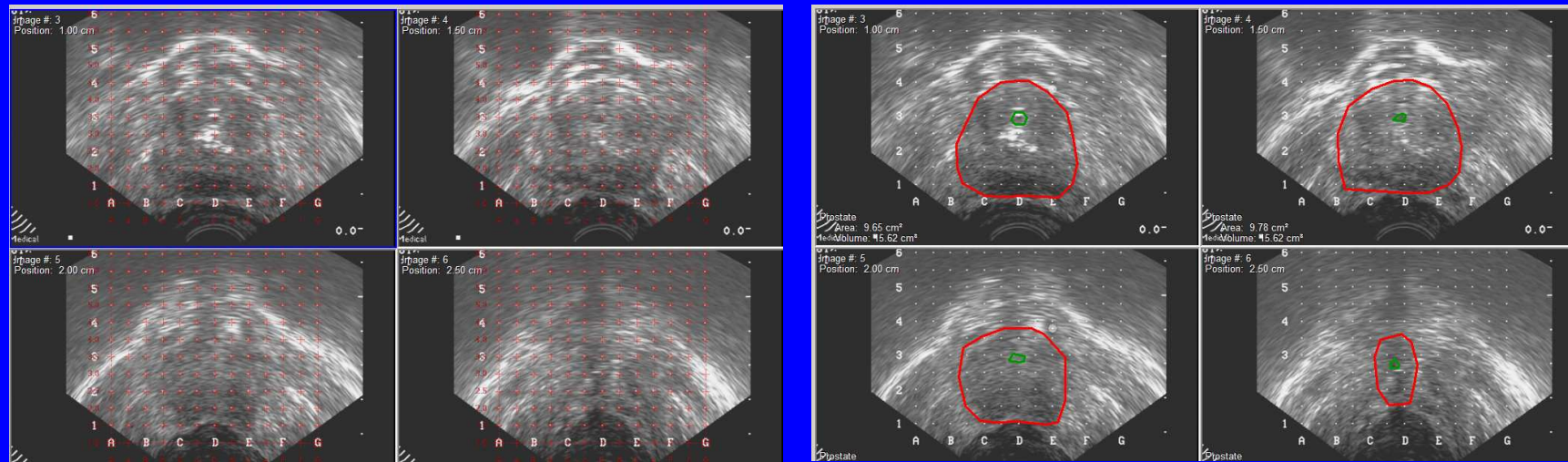
Figure 1b. Surface contour plot of a North American Scientific model MED3631-A/M LDR ^{125}I source made with an autoradiograph.

From: De Werd, L. "Calibration of Brachytherapy sources", Med. Phys. Monograph 31:153-171.

Ionization Chamber and inserts for single seed and cartridge

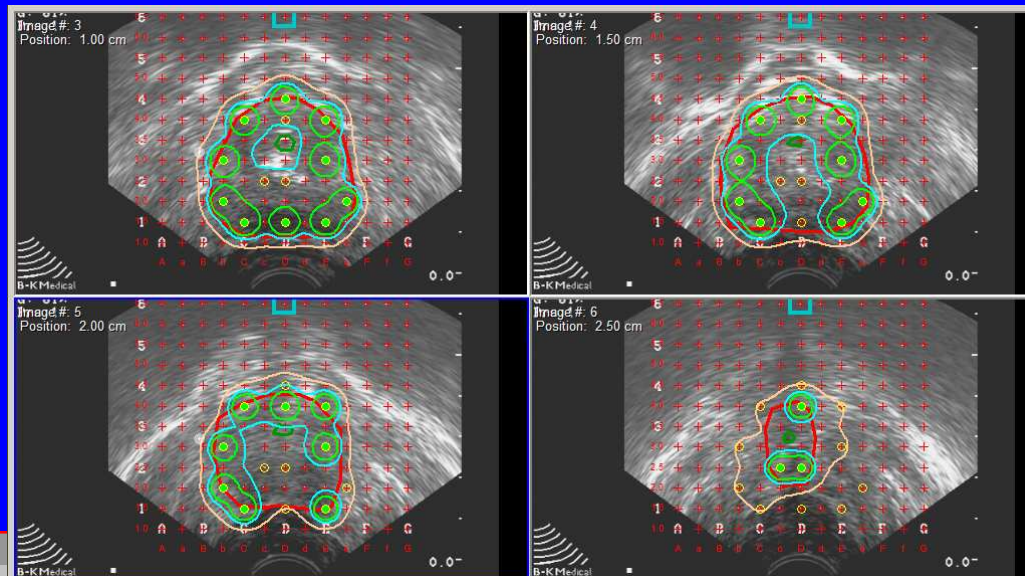
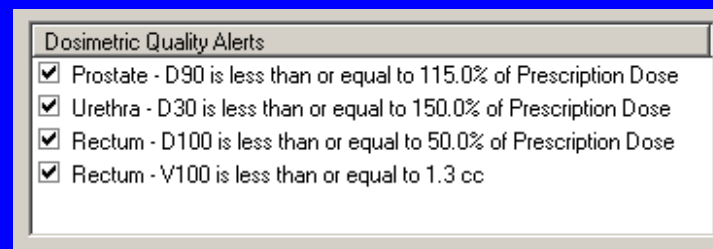


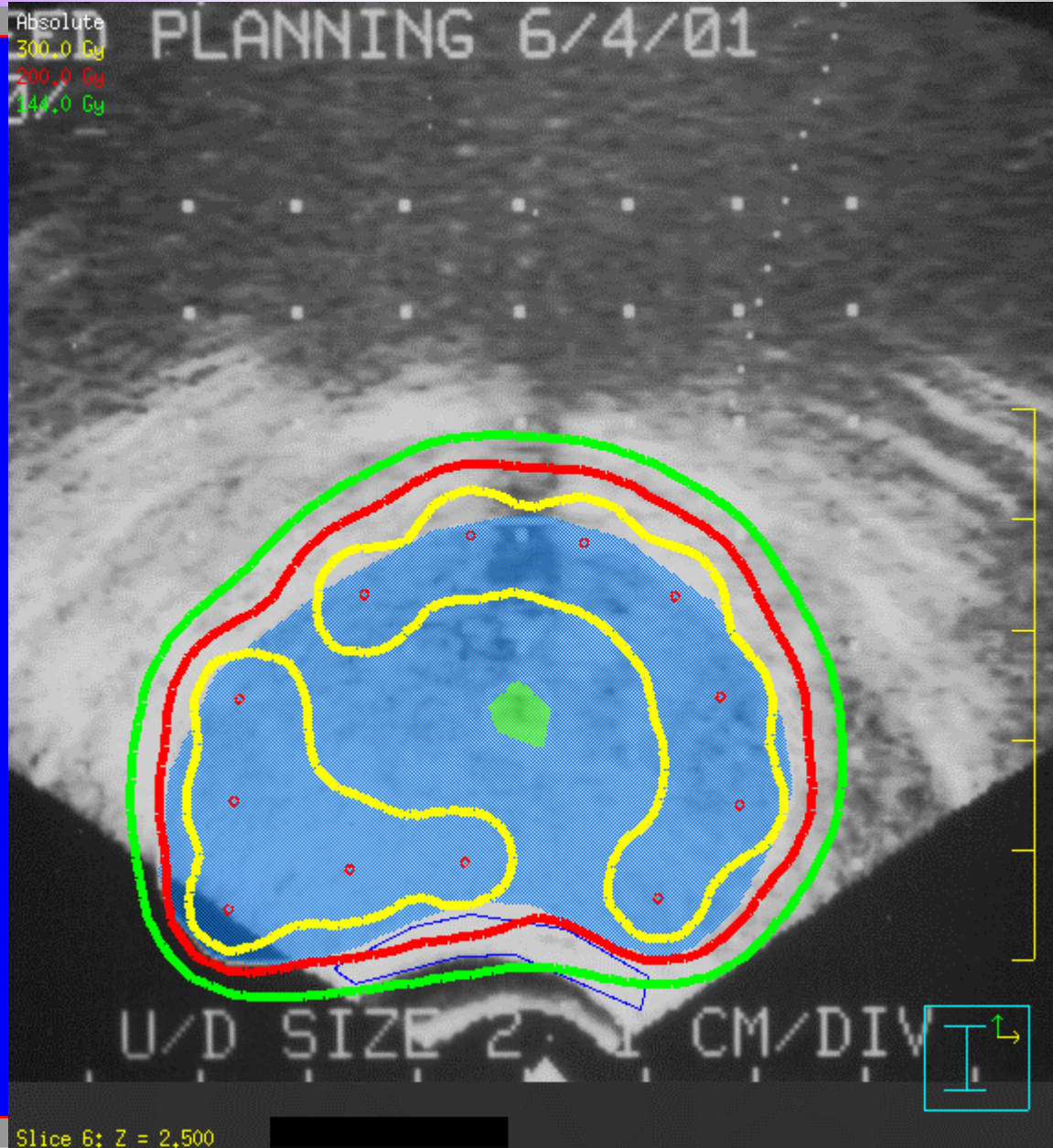
- **Acquisition and contouring of US images**
In OR Planning



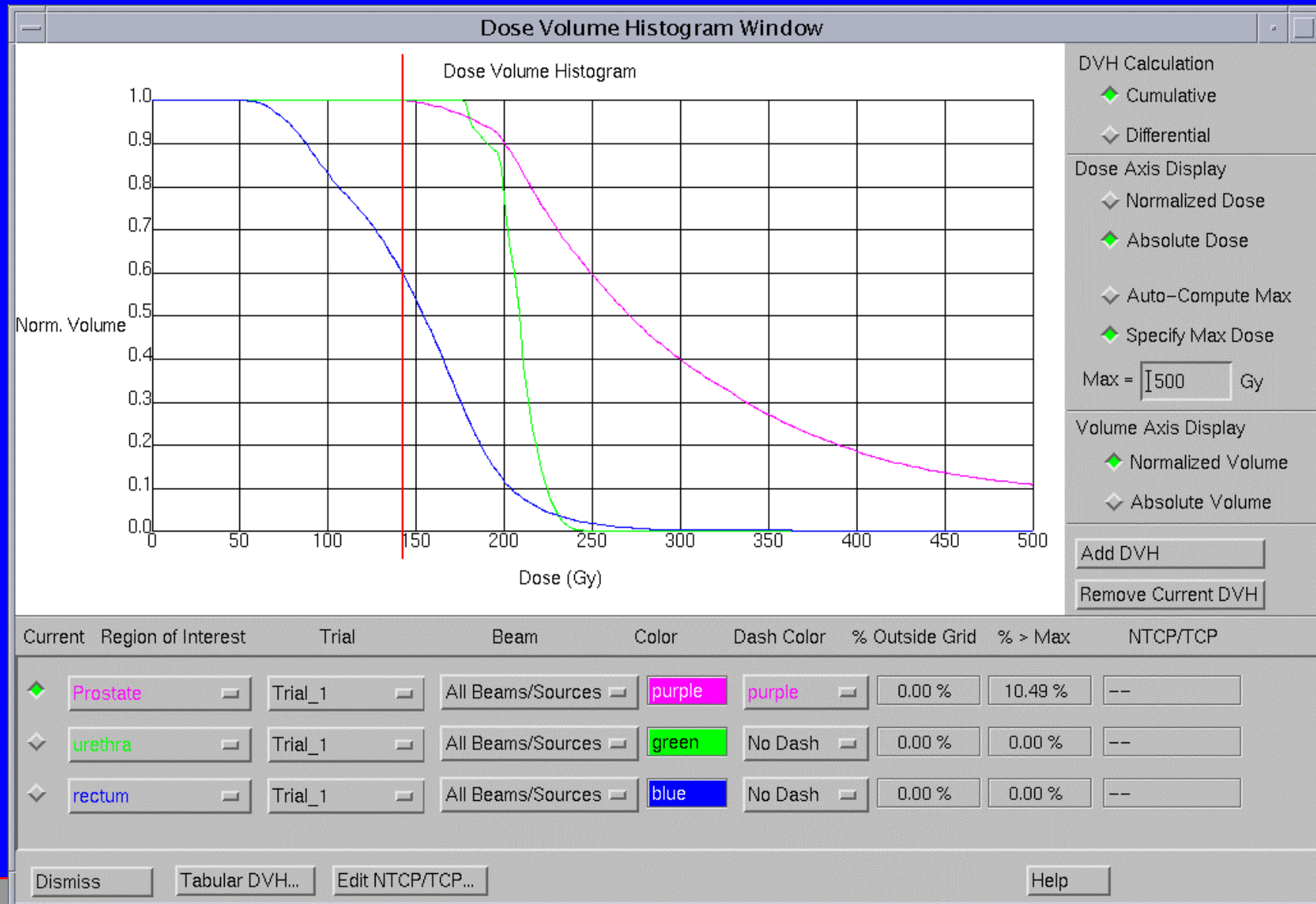
..In OR Planning

- **Seed placement and plan evaluation (100%, 150% and 200% isodoses displayed)**

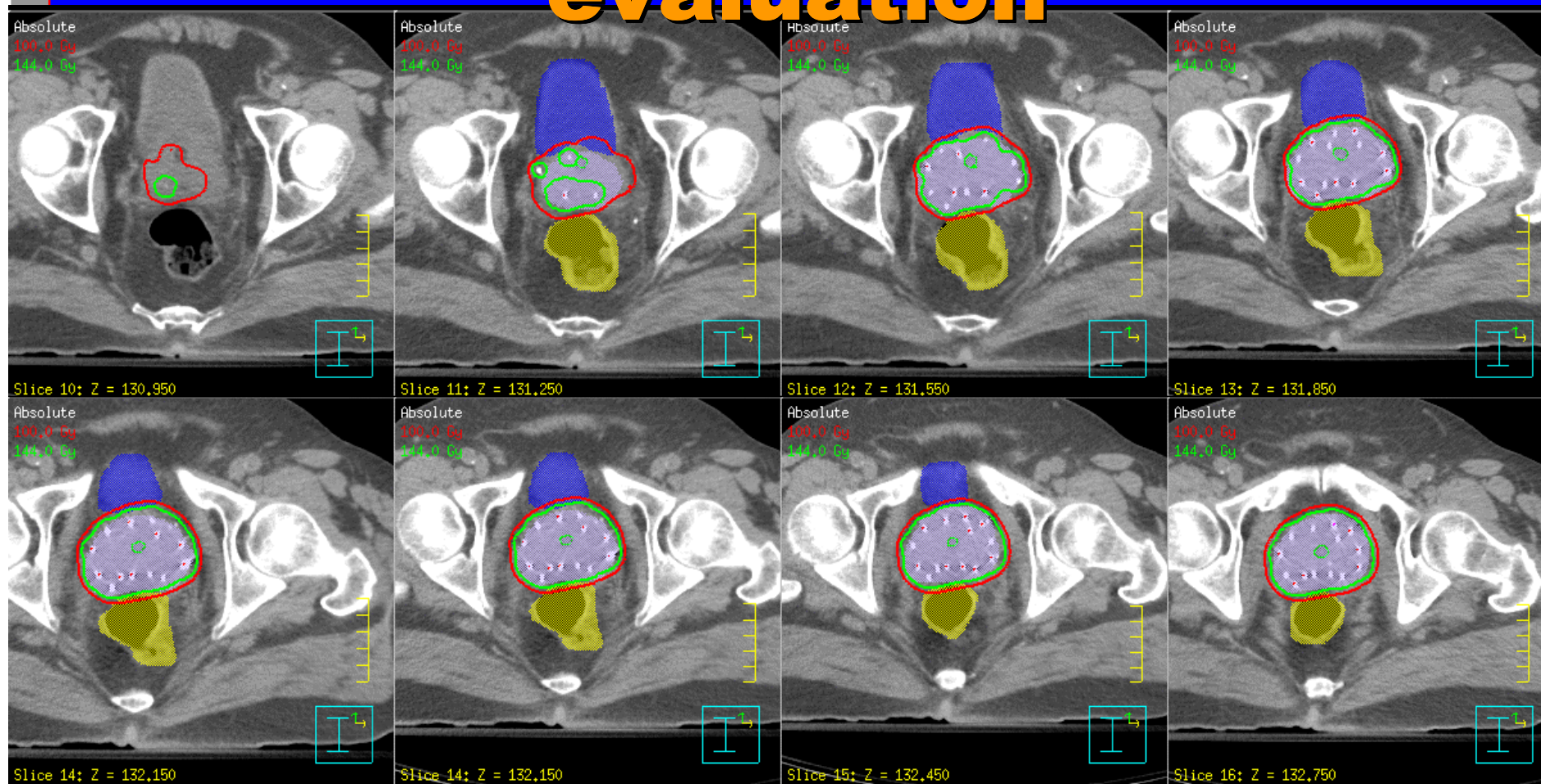




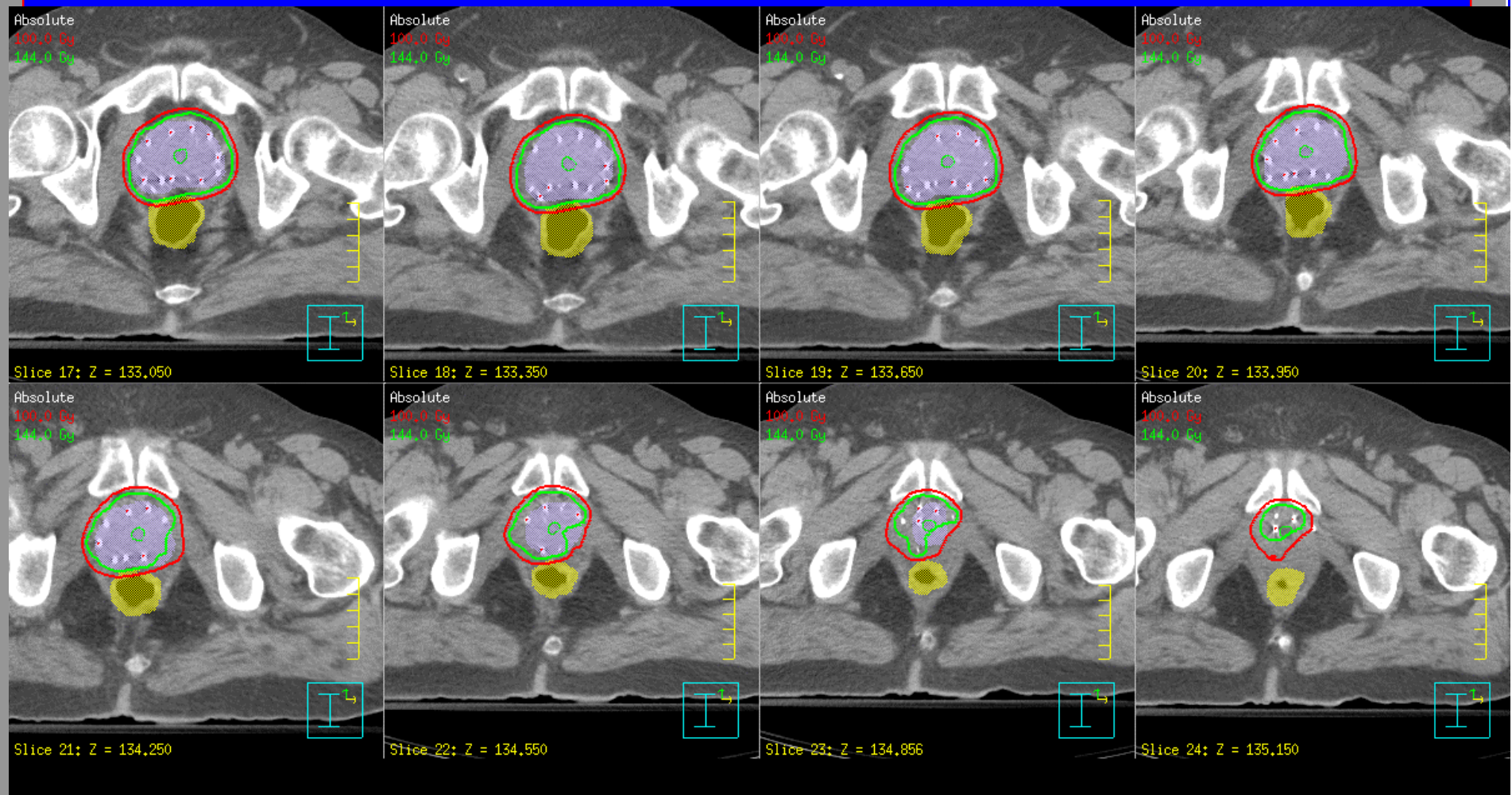
LIJ Pre-implant, TRUS-based, Planned DVH



Post-Implant CT-based evaluation

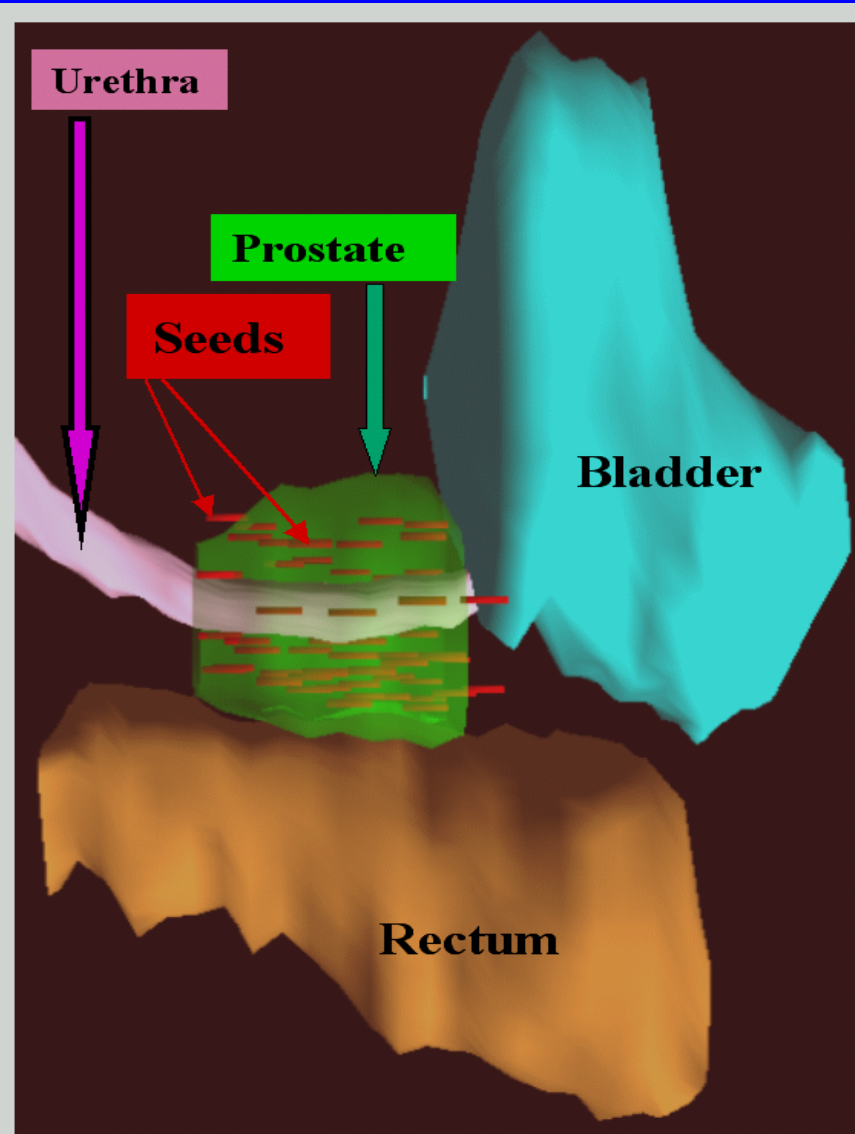


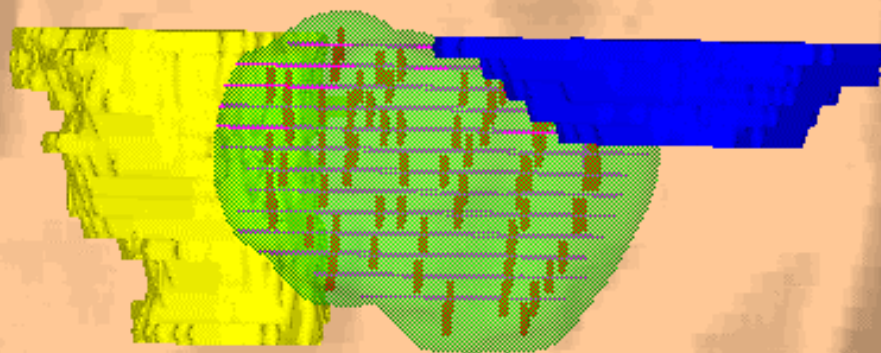
Post-Implant CT-based evaluation

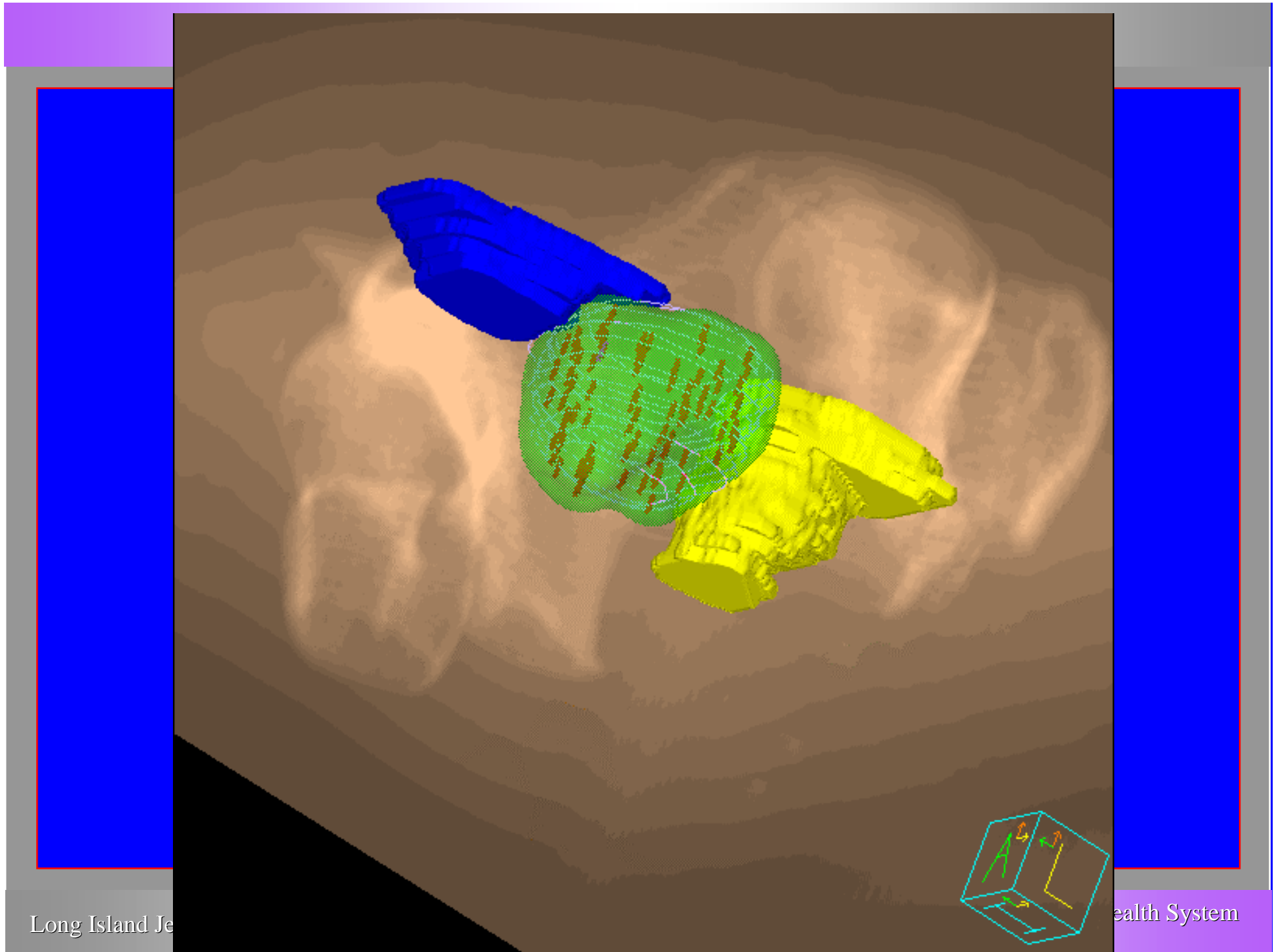


**3-D gr
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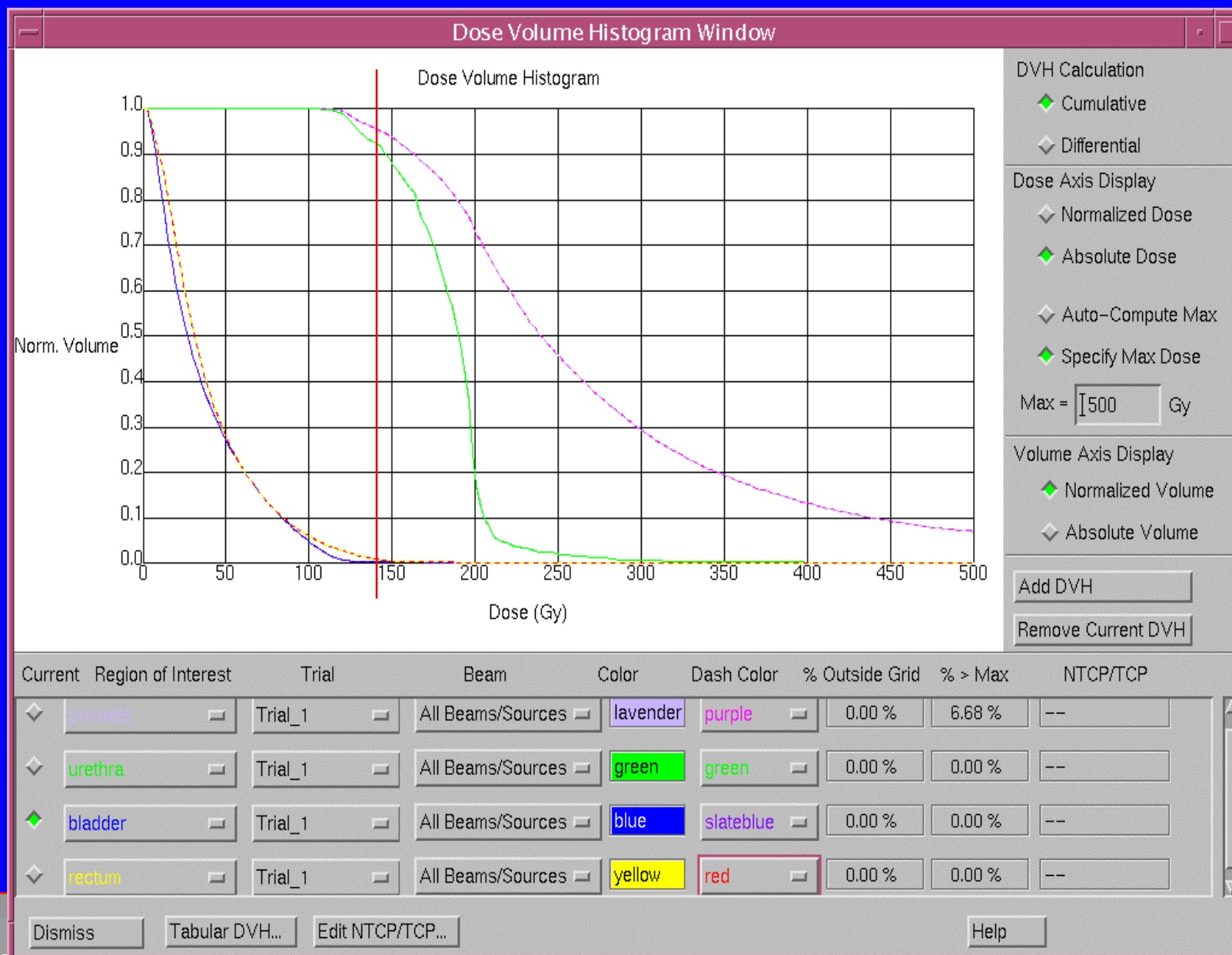




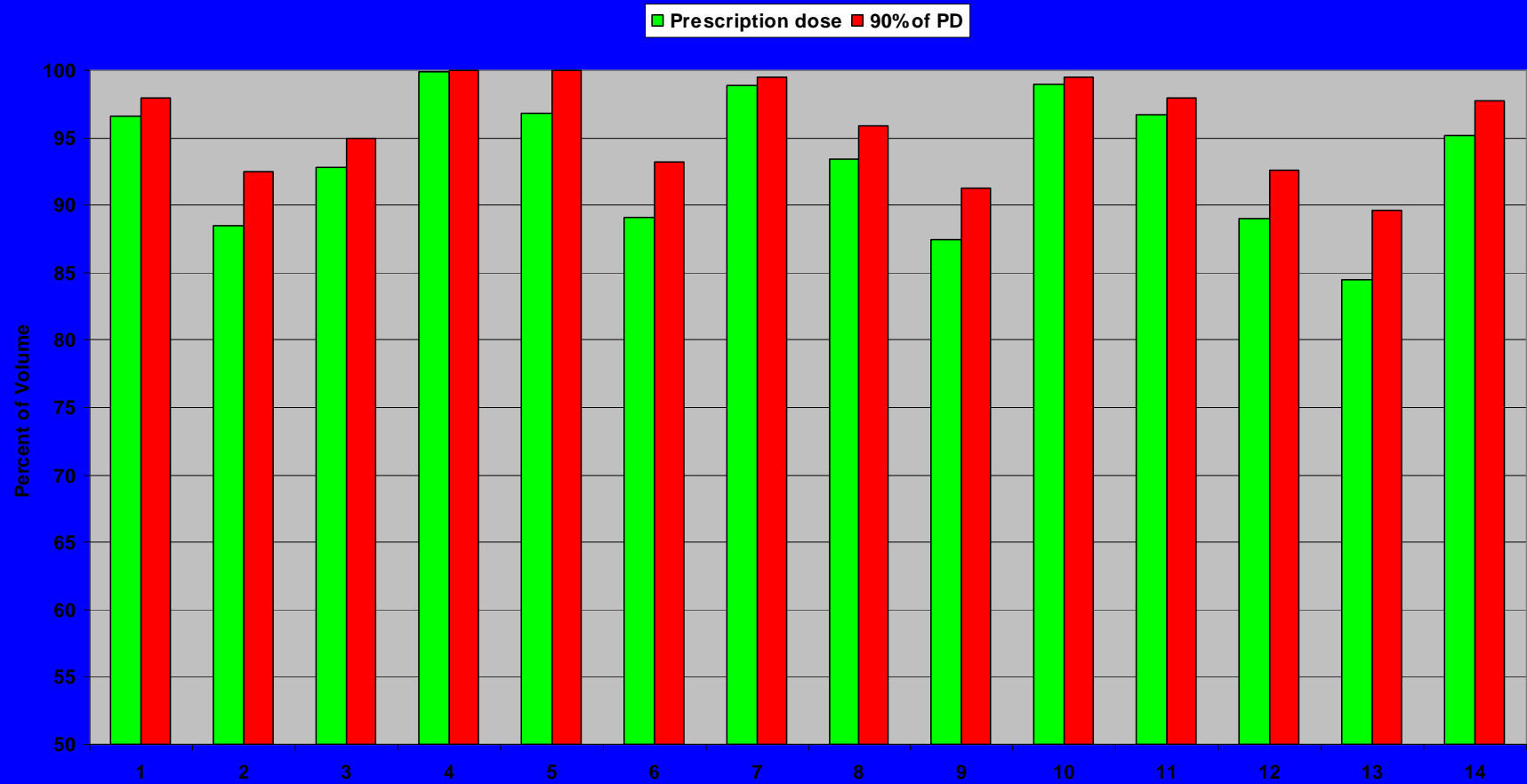
Long Island Je

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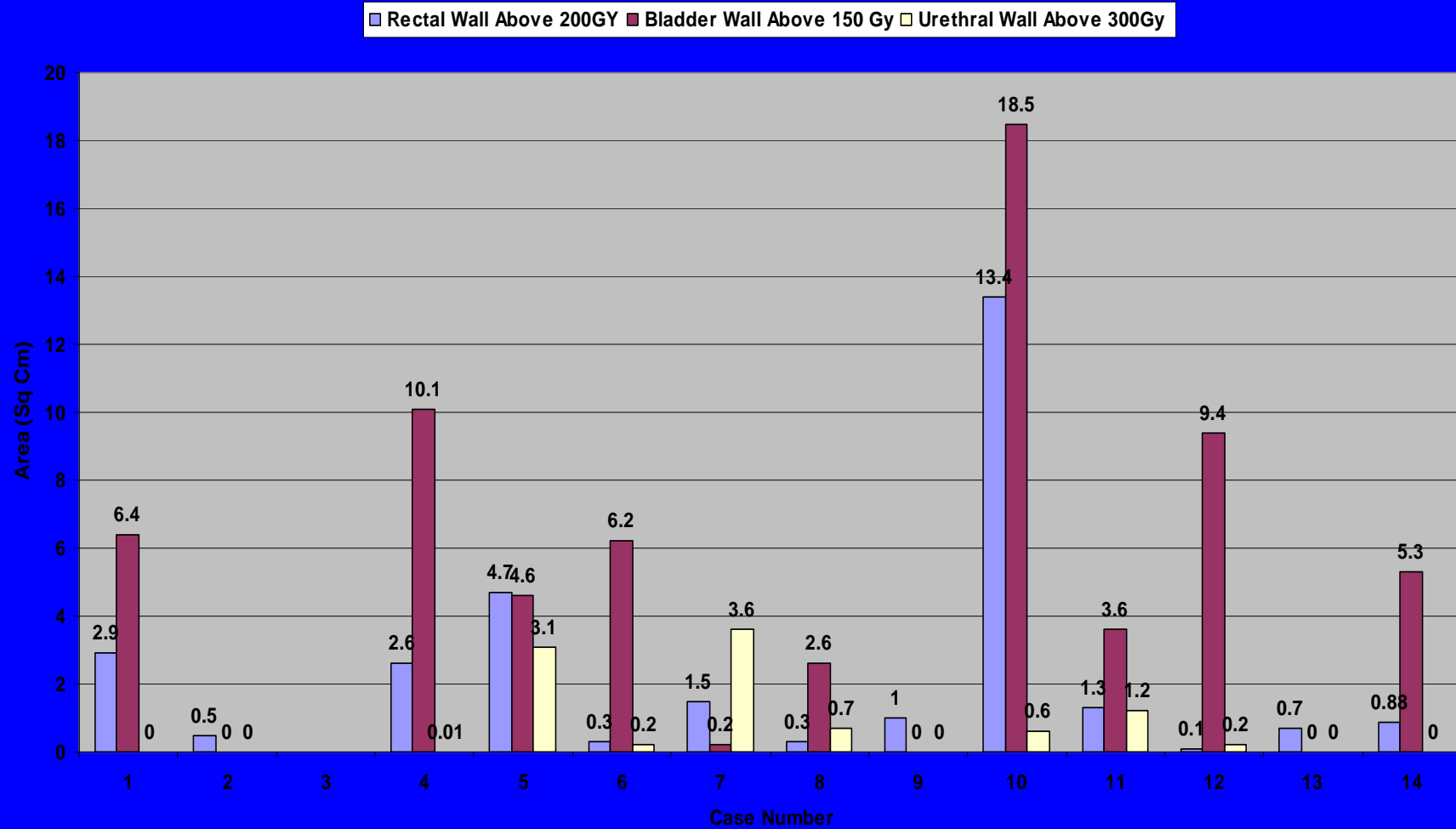
LIJ Post-Implant, Ct-based, DVH Evaluation



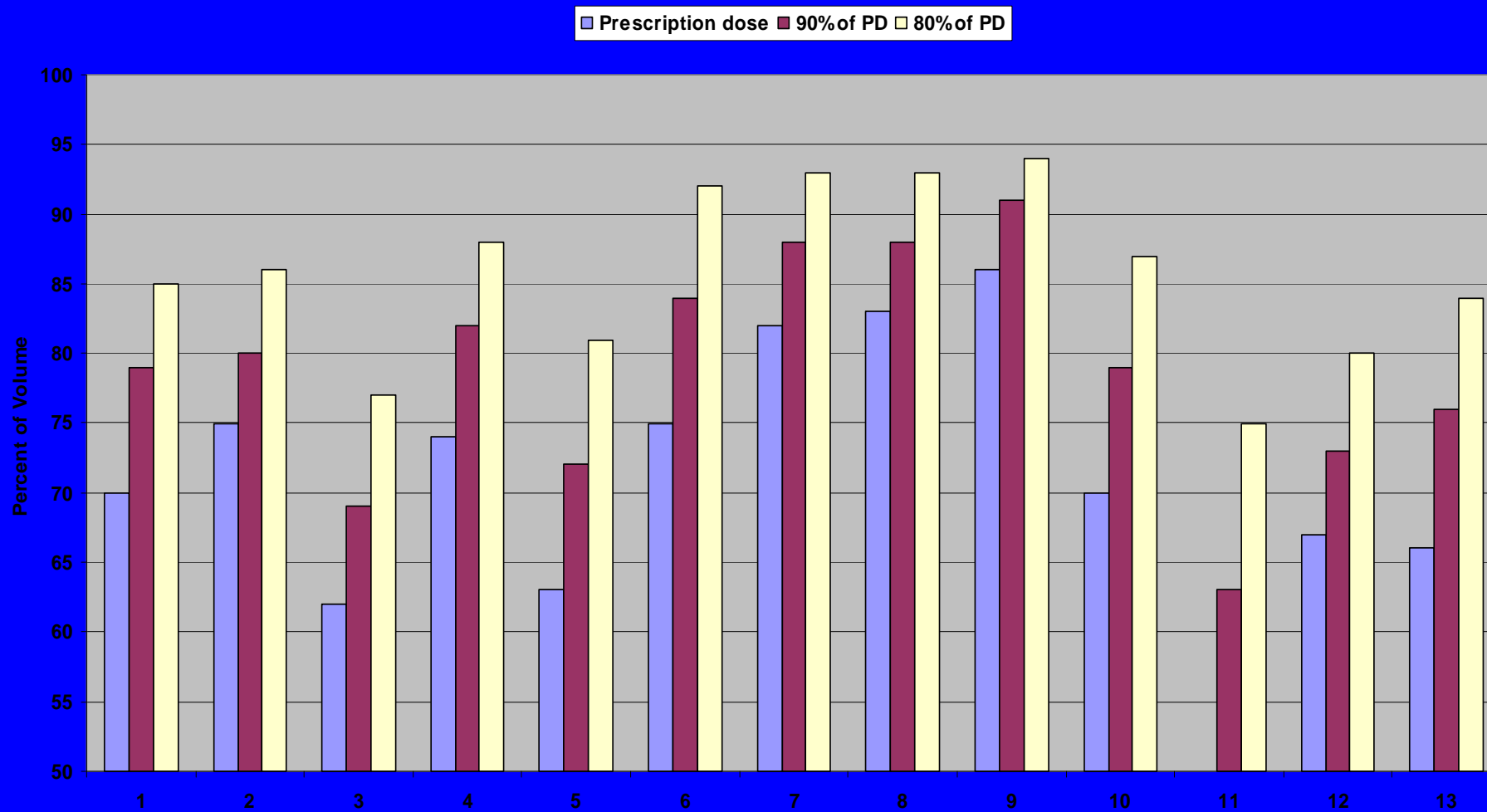
Prostate Tissue Coverage- Preplanned and Preloaded Needle Technique



Areas of Sensitive Organ Surfaces Receiving High Doses-LIJ



Prostate Tissue Coverage- Nomogram and Loose Seed Technique



Dosimetric Comparison of techniques

	Preplan + Preload		Nomogram + Loose Seeds	
	AVERAGE	St.Dev.	AVERAGE	St.Dev.
% Prostate Volume Covered by the Prescription Dose	93.4	4.9	71.0	9.8
% Prostate Volume Covered by 90% of the Prescription	95.9	3.5	78.8	8.1
% Prostate Volume Covered by 80% of the Prescription	97.5	2.4	85.8	6.3

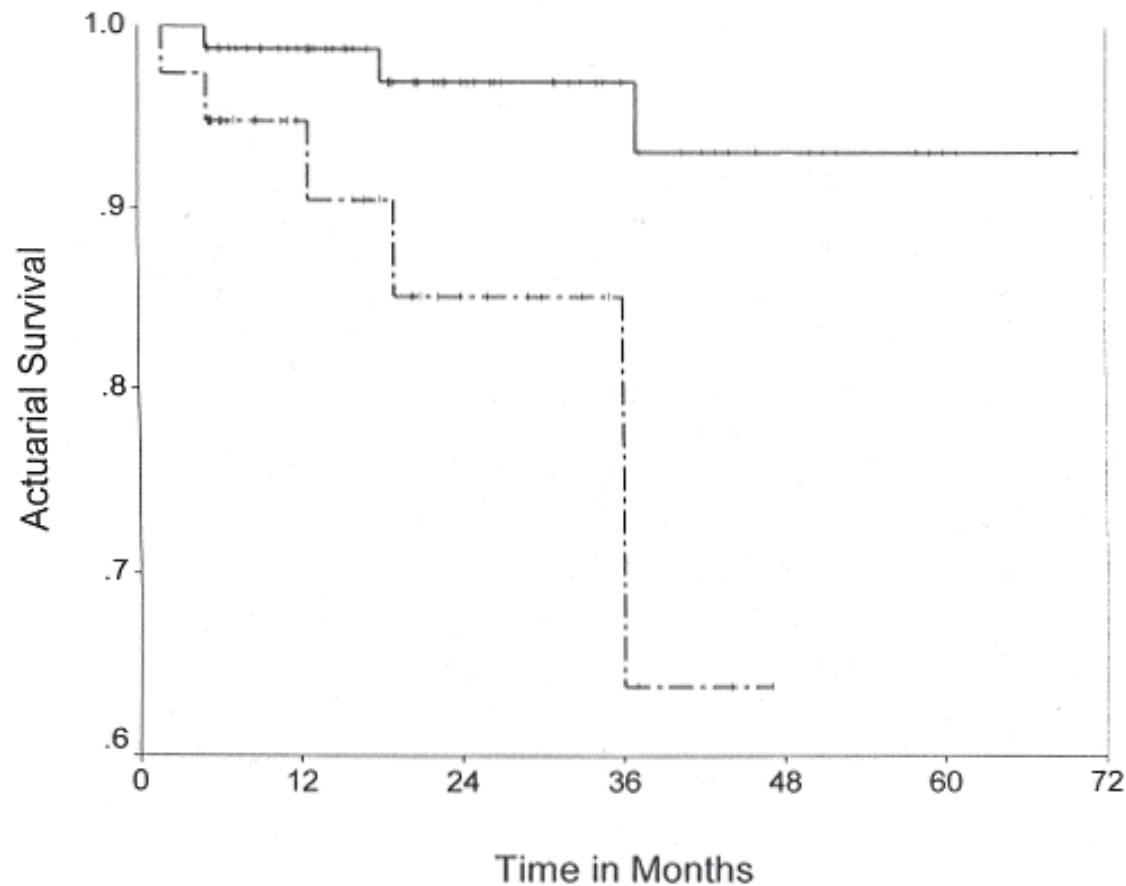


Fig. 3. Actuarial PSA relapse-free survival for patients treated with iodine divided by the dose cutoff value of the D90 dose <90%, ≥90% of the prescribed dose ($p = 0.04$) (Solid line, D90 ≥90% of the prescribed dose; dashed line, D90 <90% of the prescribed dose).

From: L.Potters et. al.: *HPROBP* 50(3), 605-614, July 2001



Table 6. Actuarial 48-month PSA-RFS comparing the D90 dose <90% or ≥90% of the prescribed dose for Pd-103, I-125, TIPPB as monotherapy, and TIPPB combined with EBT

Factor	D90 dose	4-yr. PSA-RFS	n	p value
Palladium	<90	83.4	178	.01
	≥90	93.3	423	
Iodine	<90	63.8	38	.04
	≥90	93.0	80	
No hormones	<90	81.0	134	.001
	≥90	93.4	335	
Hormones	<90	79.3	82	.001
	≥90	92.5	168	
EBT + TIPPB	<90	87.9	77	.13
	≥90	88.23	122	
TIPPB alone	<90	74.3	136	.001
	≥90	94.6	384	

From: L.Potters et. al.: *IJROBP* 50(3), 605-614, July 2001



***Permanent Prostate Brachytherapy
Real-Time Dosimetry Algorithm***

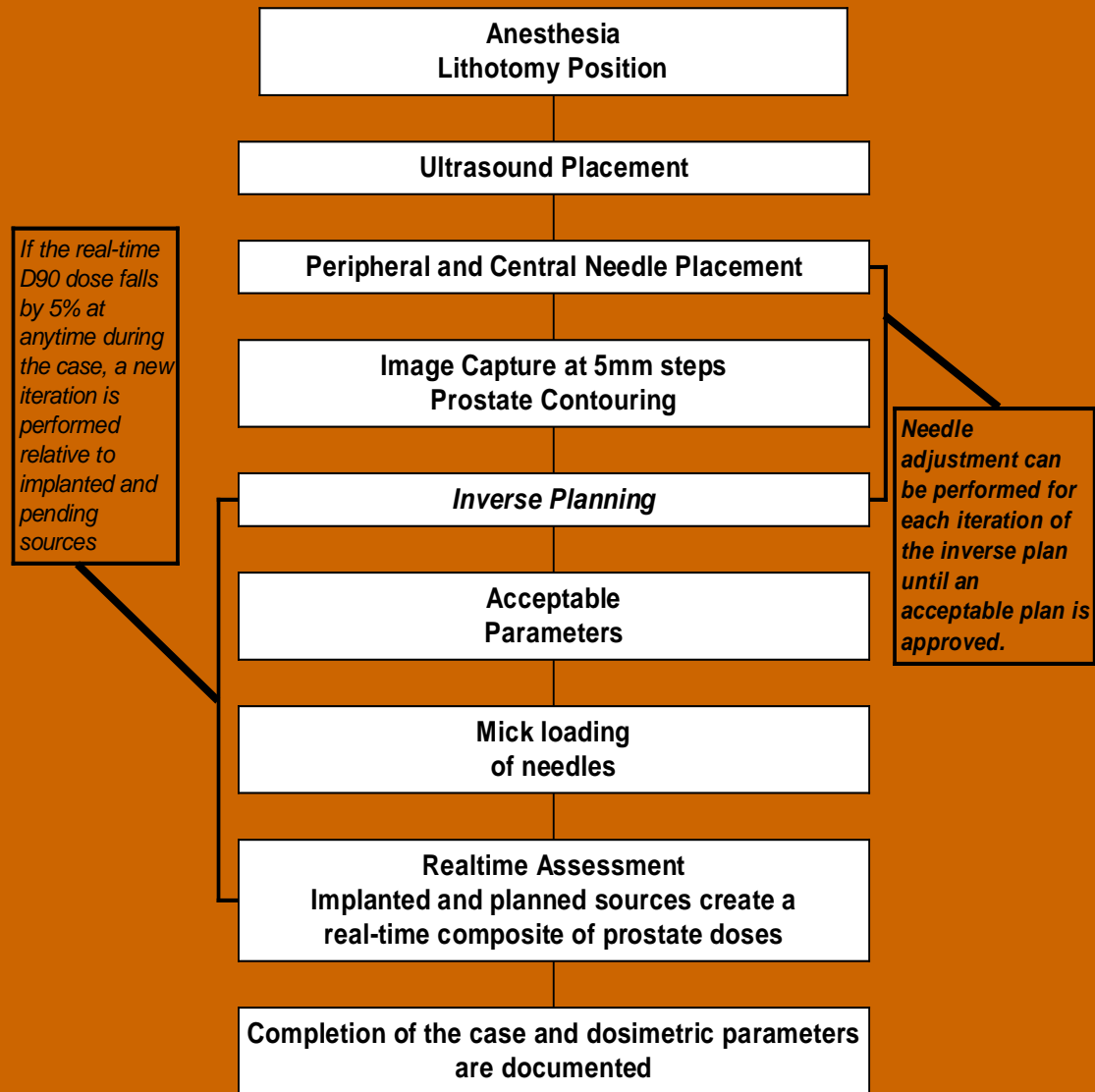
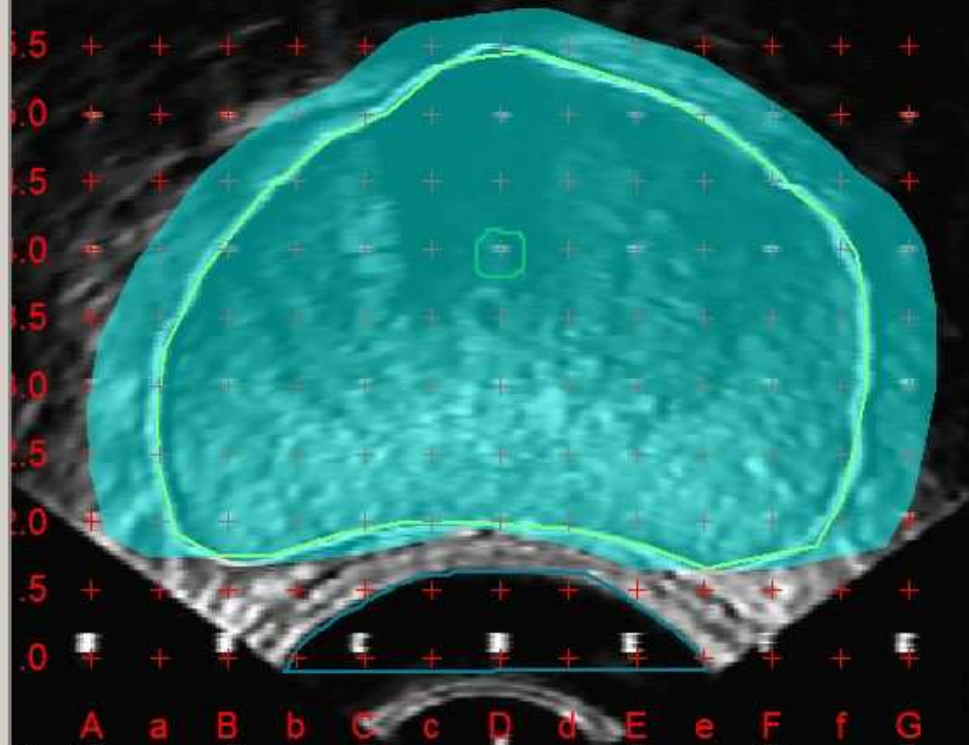


Image #: 5
Position: 2.00 cm



Prostate
Area: 15.06 cm²
Volume: 48.52 cm³

Contour Margining

Dimensions (cm)

☐ Uniform:

Extent: 0.0

☒ Independent:

In Plane

Left: 0.5

Right: 0.5

Anterior: 0.3

Posterior: 0.0

Out of Plane

Superior: 0.5

Inferior: 0.5

Structure Selection:

Originating Structure: Prostate

Resulting Structure: PTV

Progress

Preview

OK

Cancel

Prescription Dose/Isodose Levels

145.0 Gy

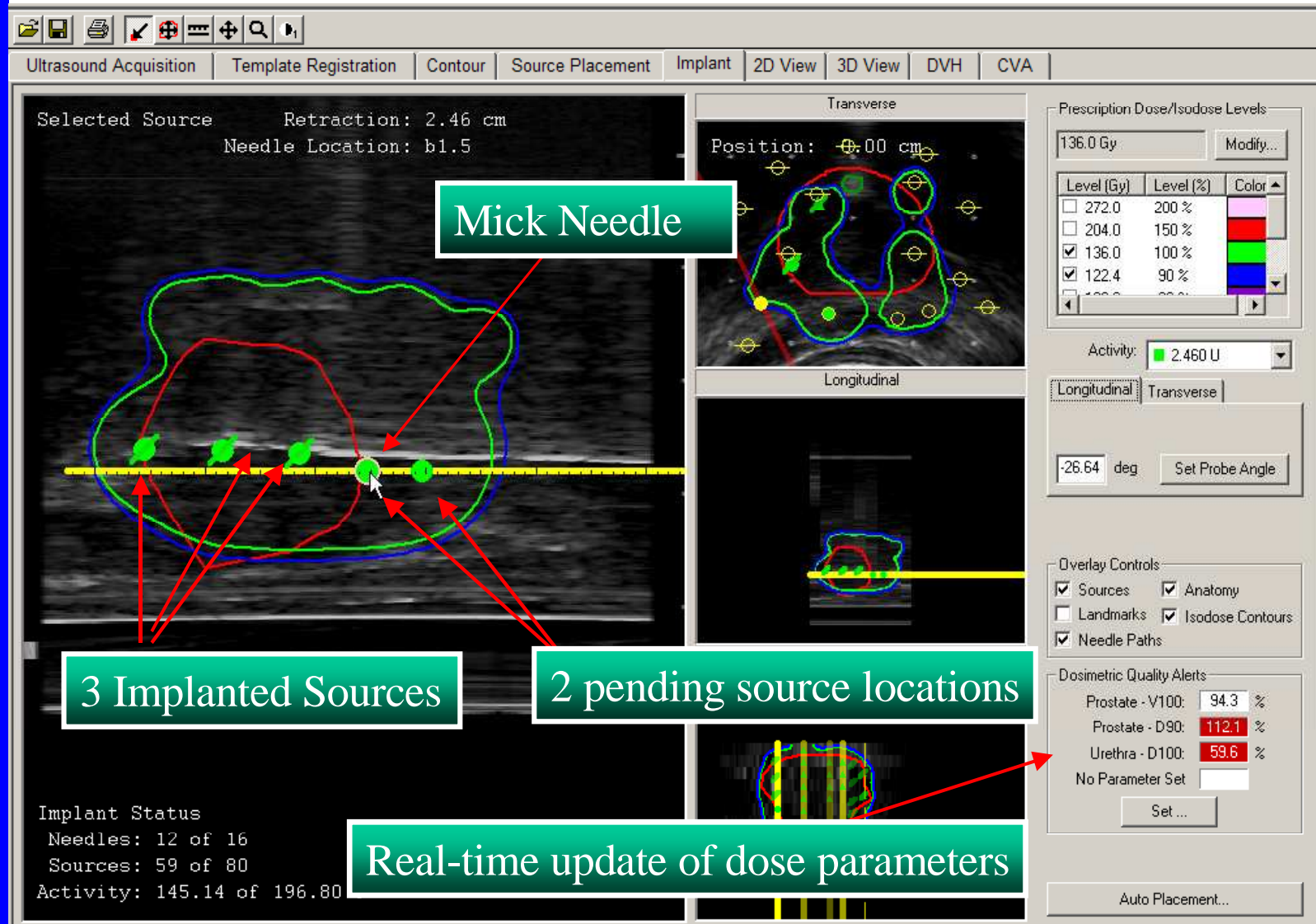
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Structure

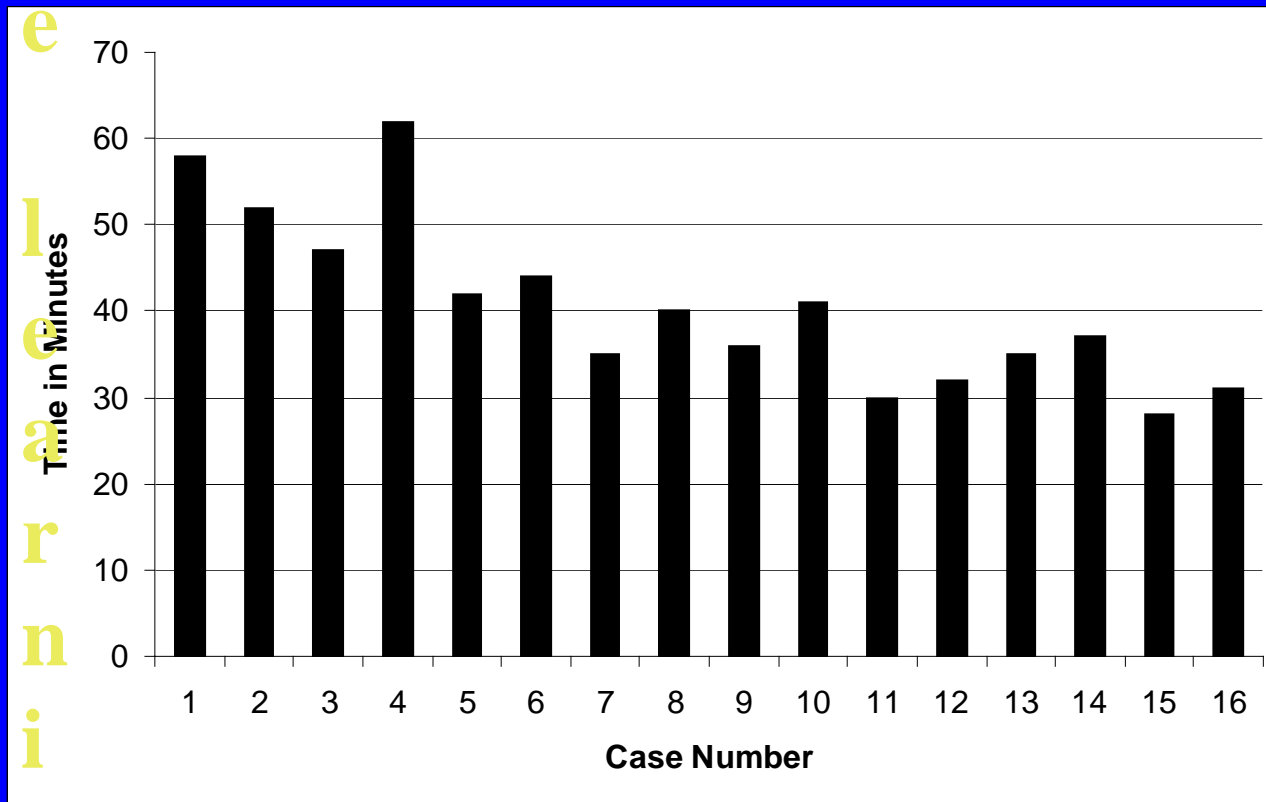
Arch

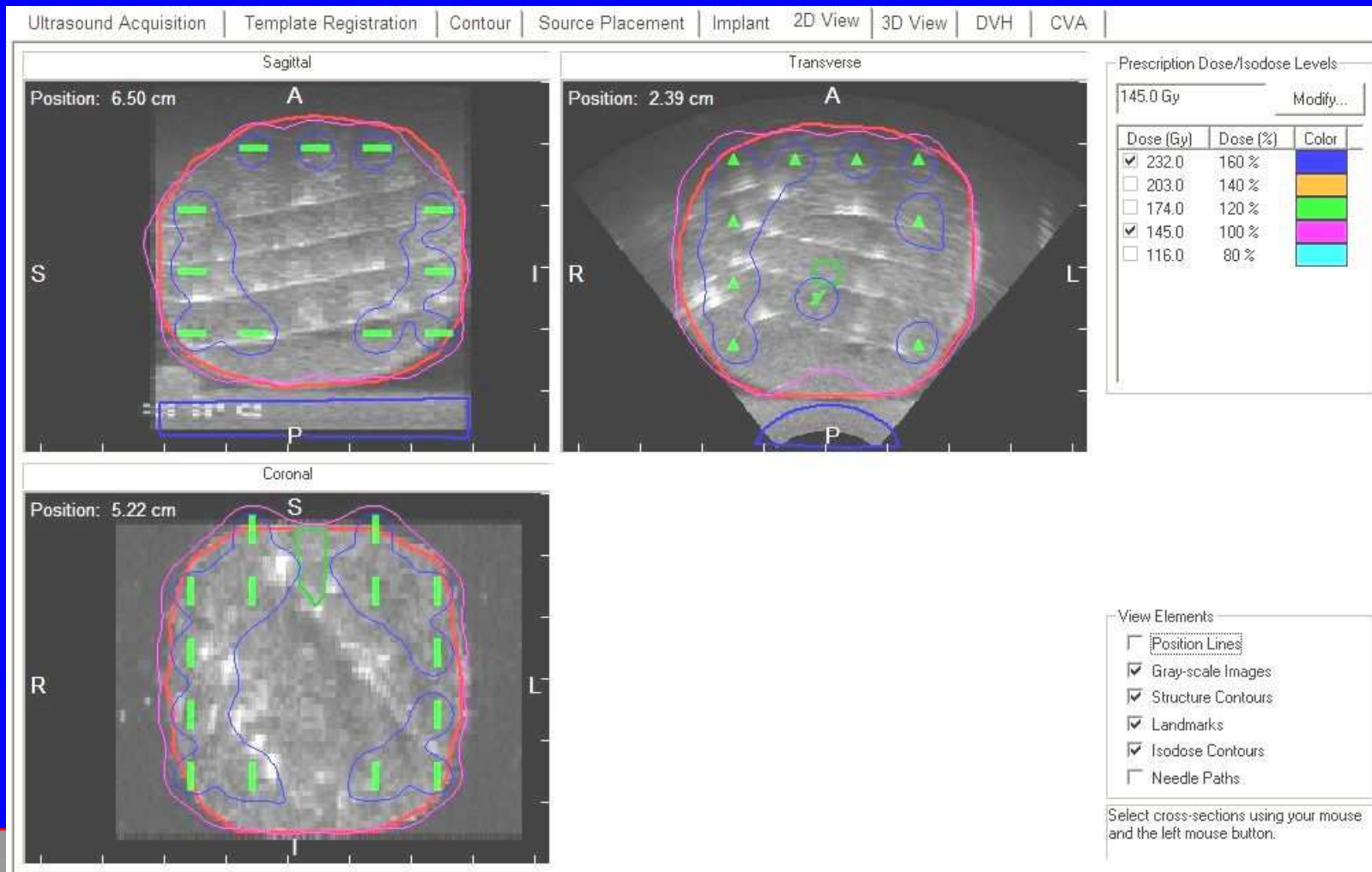
Landmark

Margin Structure...



The learning curve...

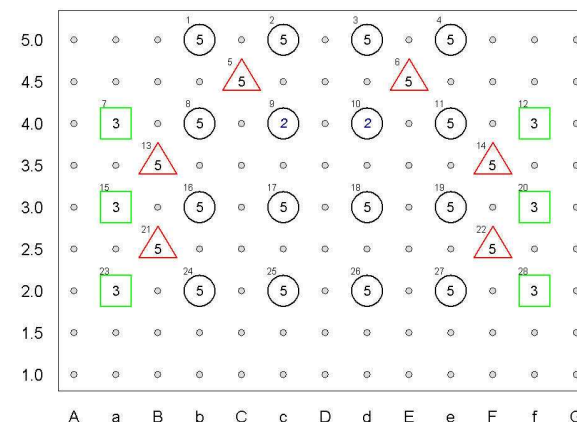










VariSeed: Needle Loading Report [Page 1]

5/29/2003 1:44:39 PM

Name: Demo Studies PID: Demo Dept. ID:	Study: Pre/I-125/Primary/US Video 1 Variation: Default Images: 10 Template: B & K Standard Shift: X = 0.00cm Y = 1.00cm	Source: I-125 (6711) [NIST 99] Comment: Sources: 122 Anisotropy: Constant (Point Model) [0.930] Source Activity: 0.432 U [0.340 mCi]
Procedure Date: N/A	Prescription Dose: 145.0 Gy	Total Activity: 52.704 U [41.499 mCi]

[illegible]

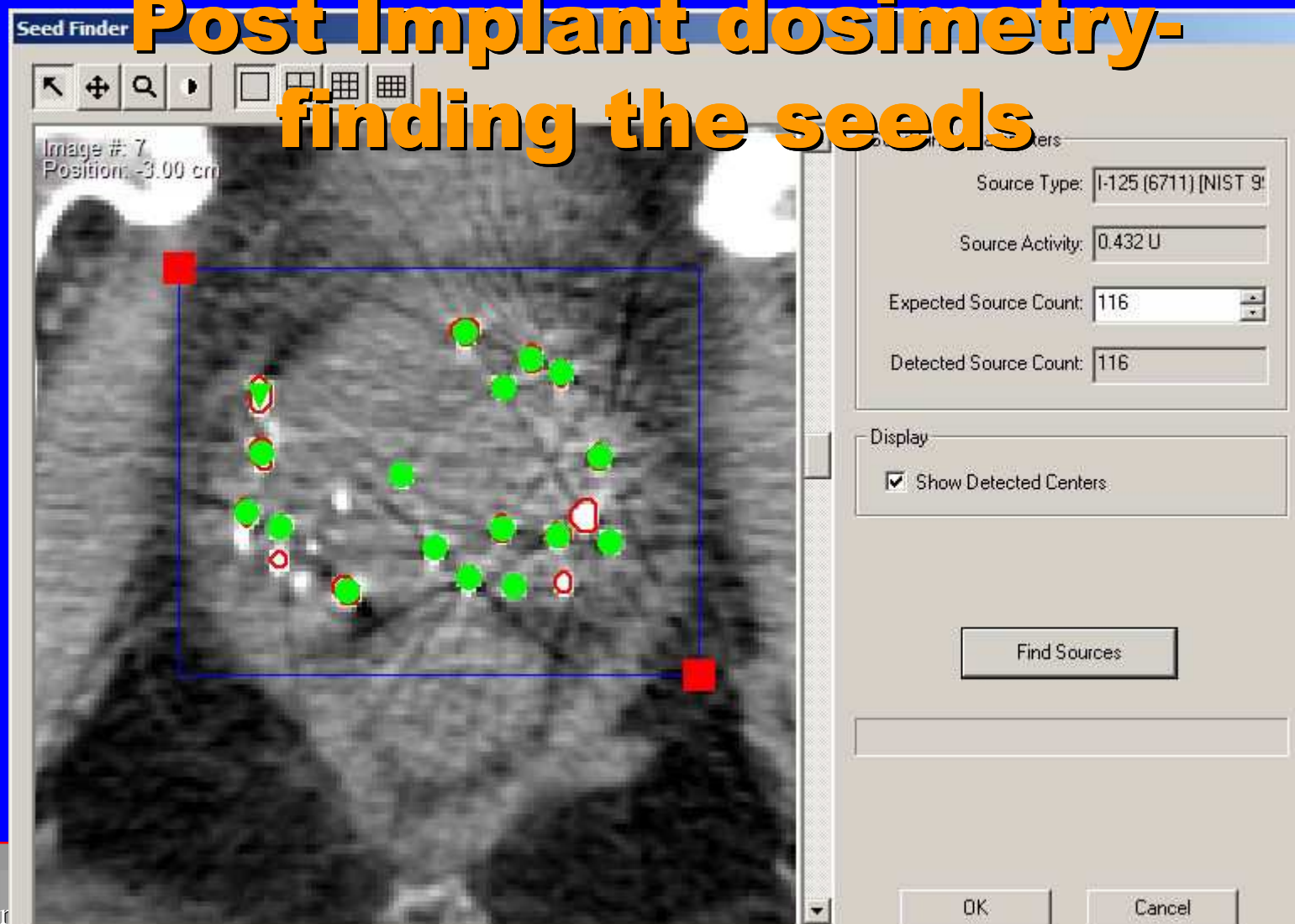
Retraction Legend					
Plane 0	Plane 1	Plane 2	Plane 3	Plane 4	Special
0.00 cm	0.50 cm	1.00 cm	1.50 cm	2.00 cm	Other
					

Number of Needles	Seeds per needle	Plan Summary	
2	2	Total Activity [U]	52.70
6	3	Total Activity [mCi]	41.50
20	5	Total Needles	28
		Total Seeds	122
		Extra Seeds	
		Total Seeds to Order	

Study Created by _____

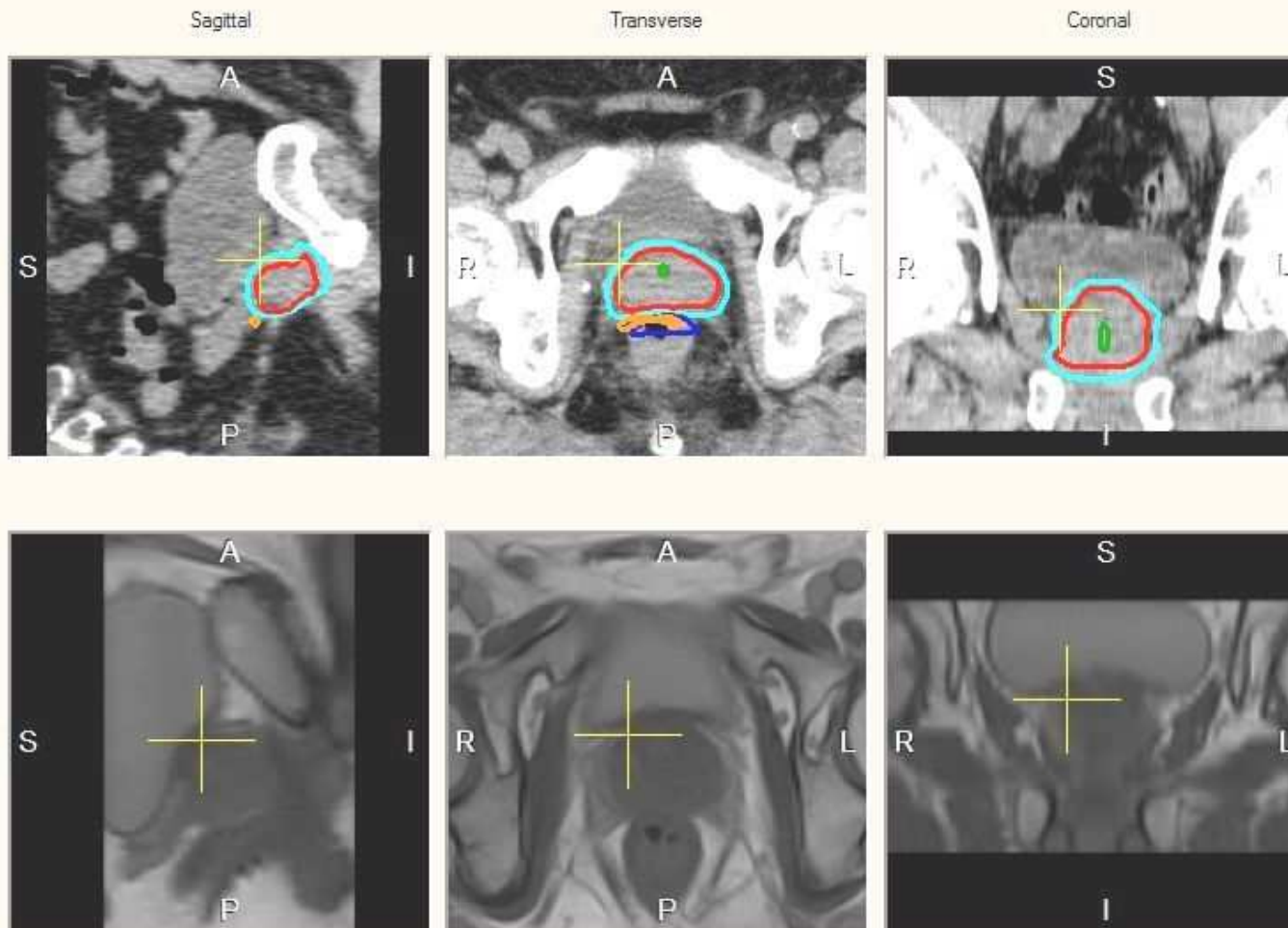
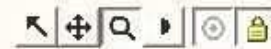
Study Approved by _____

Post Implant dosimetry- finding the seeds



Registration

Least Squares | Manual



Matched Pairs

Use	Name	Color
<input checked="" type="checkbox"/>	1	■
<input checked="" type="checkbox"/>	2	■
<input checked="" type="checkbox"/>	3	■

Add Delete Delete All

Transformation

RMS Error (mm): 3.69

Matched Pairs

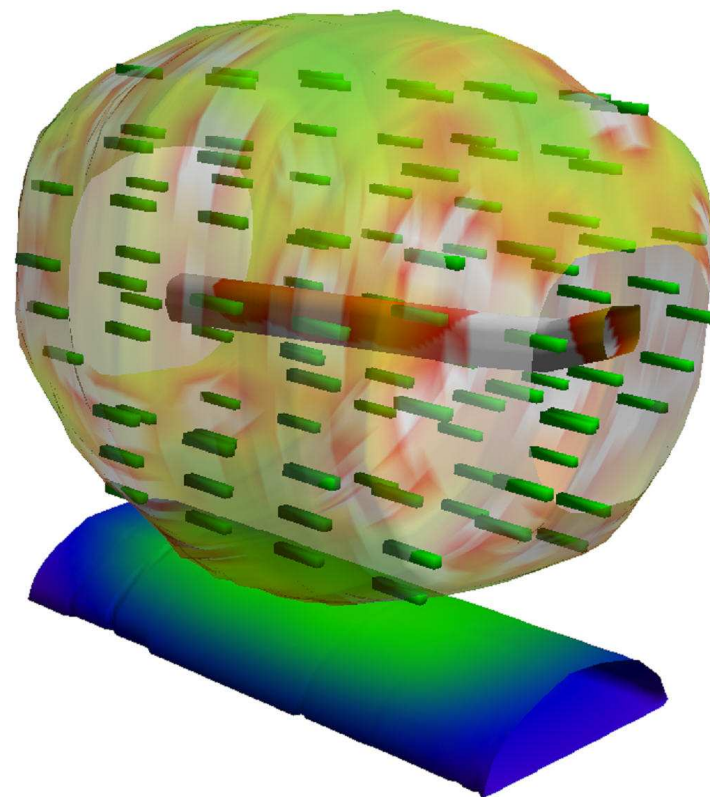
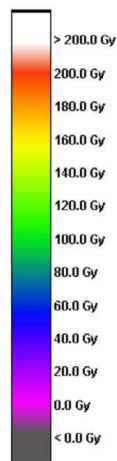
Reset to Matched Pairs Transform

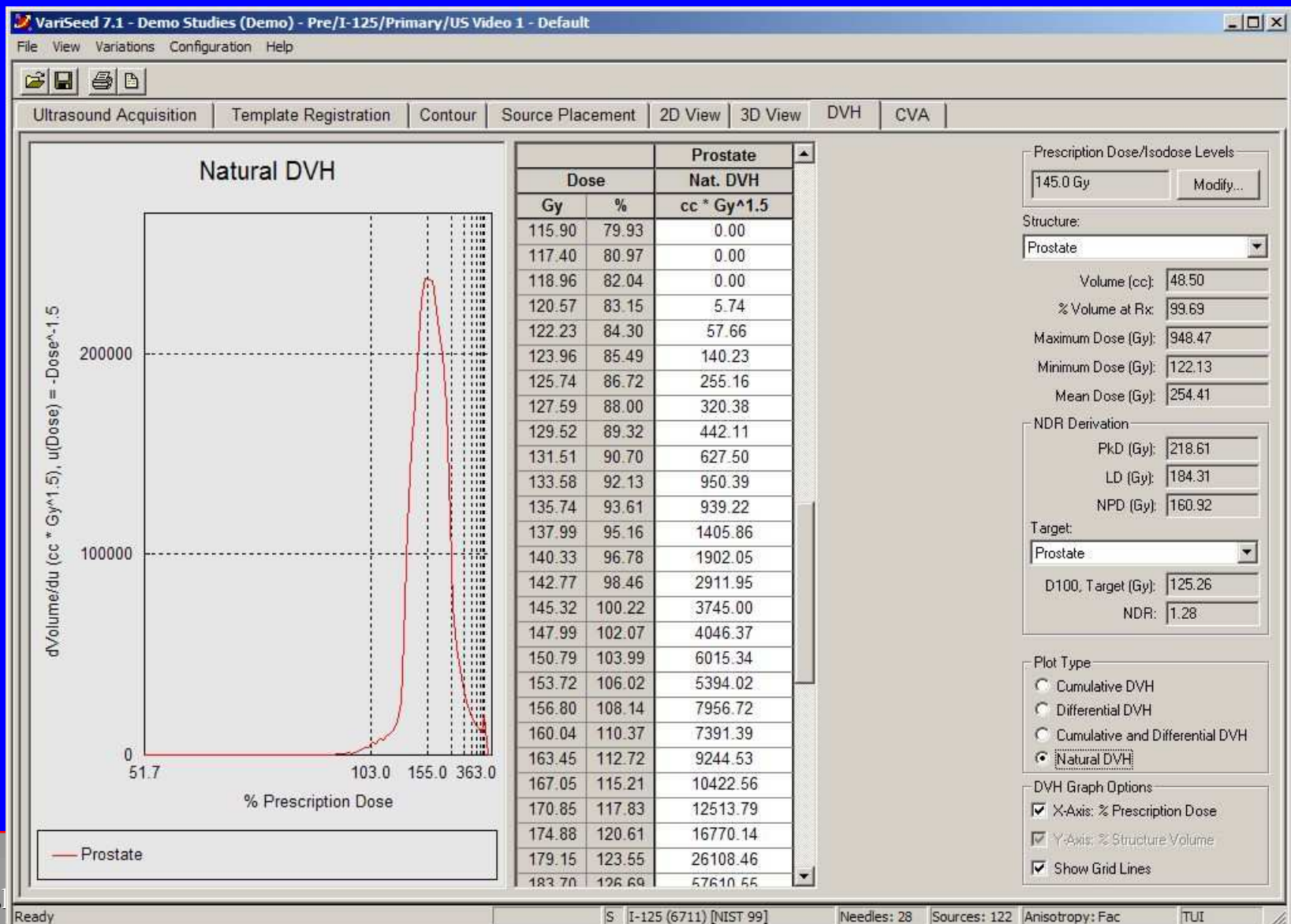
Dose display for evaluation and reporting

VariSeed: 3D View Report [Page 1]

5/29/2003 1:50:56 PM

Name: Demo Studies PID: Demo Dept. ID:	Study: Intra-Op Variation: Default Images: 56 Template: B & K Standard	Source: I-125 (6733) [NIST 00] Comment: Sources: 100 Anisotropy: Factors (Point Model) Source Activity: 0.432 U [0.340 mCi]
Procedure Date: 5/29/2003	Prescription Dose: 145.0 Gy	Total Activity: 43.200 U [34.016 mCi]





HDR Brachytherapy for Prostate

- **Used as boost to 45 Gy EBRT**
- **HDR dose given in 2 fractions of 8 Gy each**
- **EBRT given after HDR**
- **Gold markers placed at base and at**



Dose equivalence for complete RT course

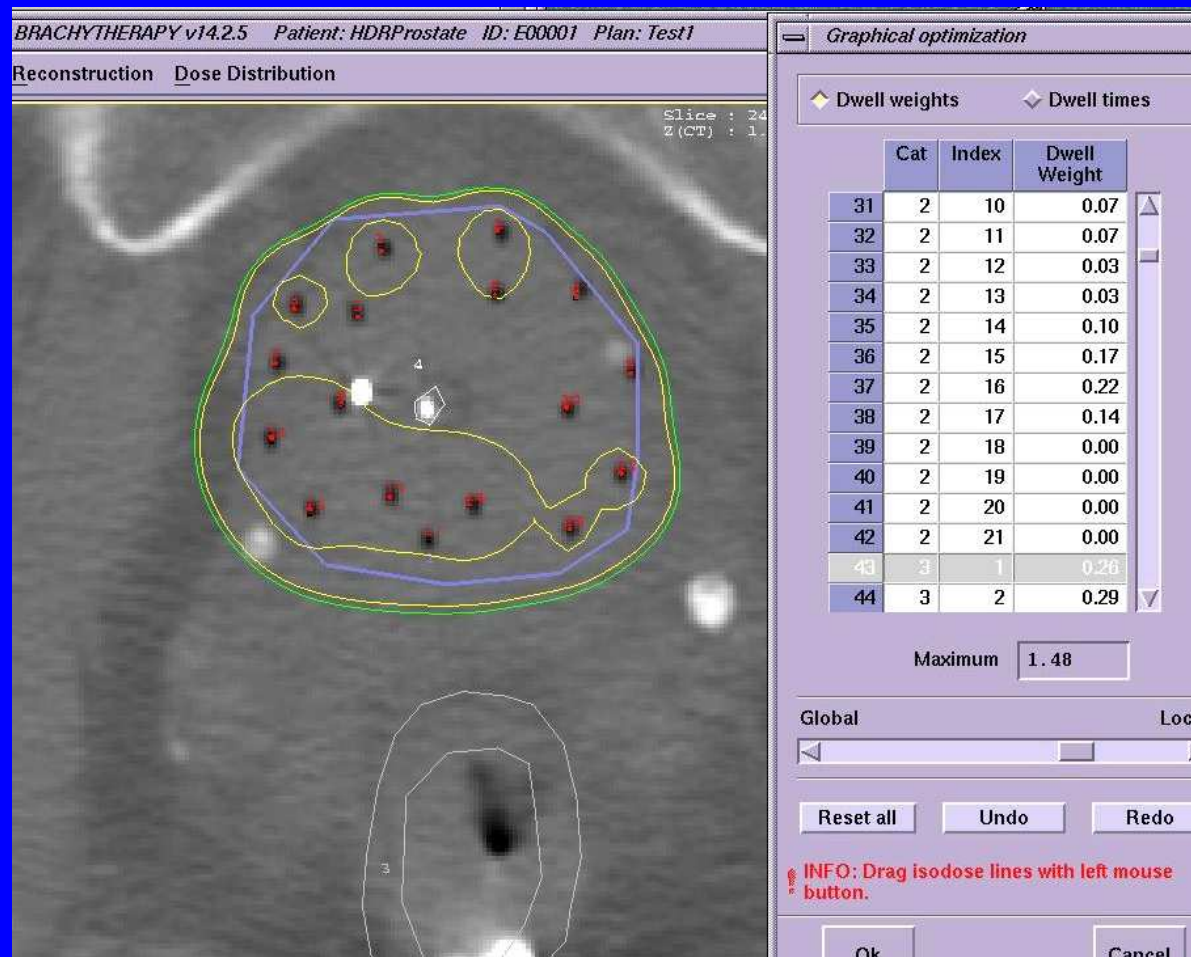
- **$ERD = d\{1 + d/(\alpha/\beta)\}$**
- **for $(\alpha/\beta) = 1.5$**
- **$ERD(HDR) = 8\{1 + 8/1.5\} = 50 \text{ Gy}$**
- **Total dose = $2 \times 50 + 45 = 145 \text{ Gy}$**

(similar to seed implant with I-125)

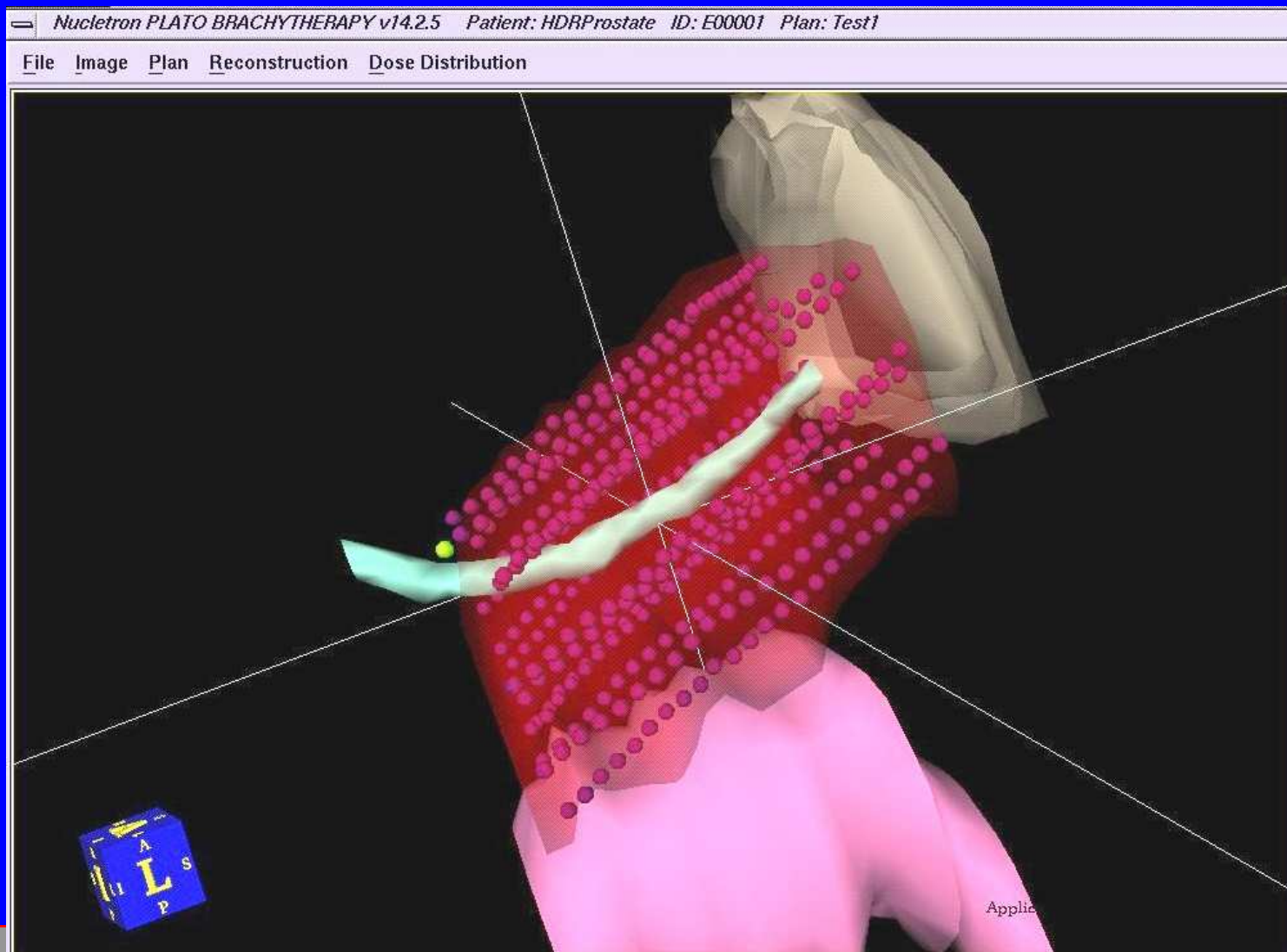
Planning Procedure

- **CT based anatomy delineation**
- **Catheter tracking**
- **Inverse planning**
- **Review and adjustment of
Isodose distribution**

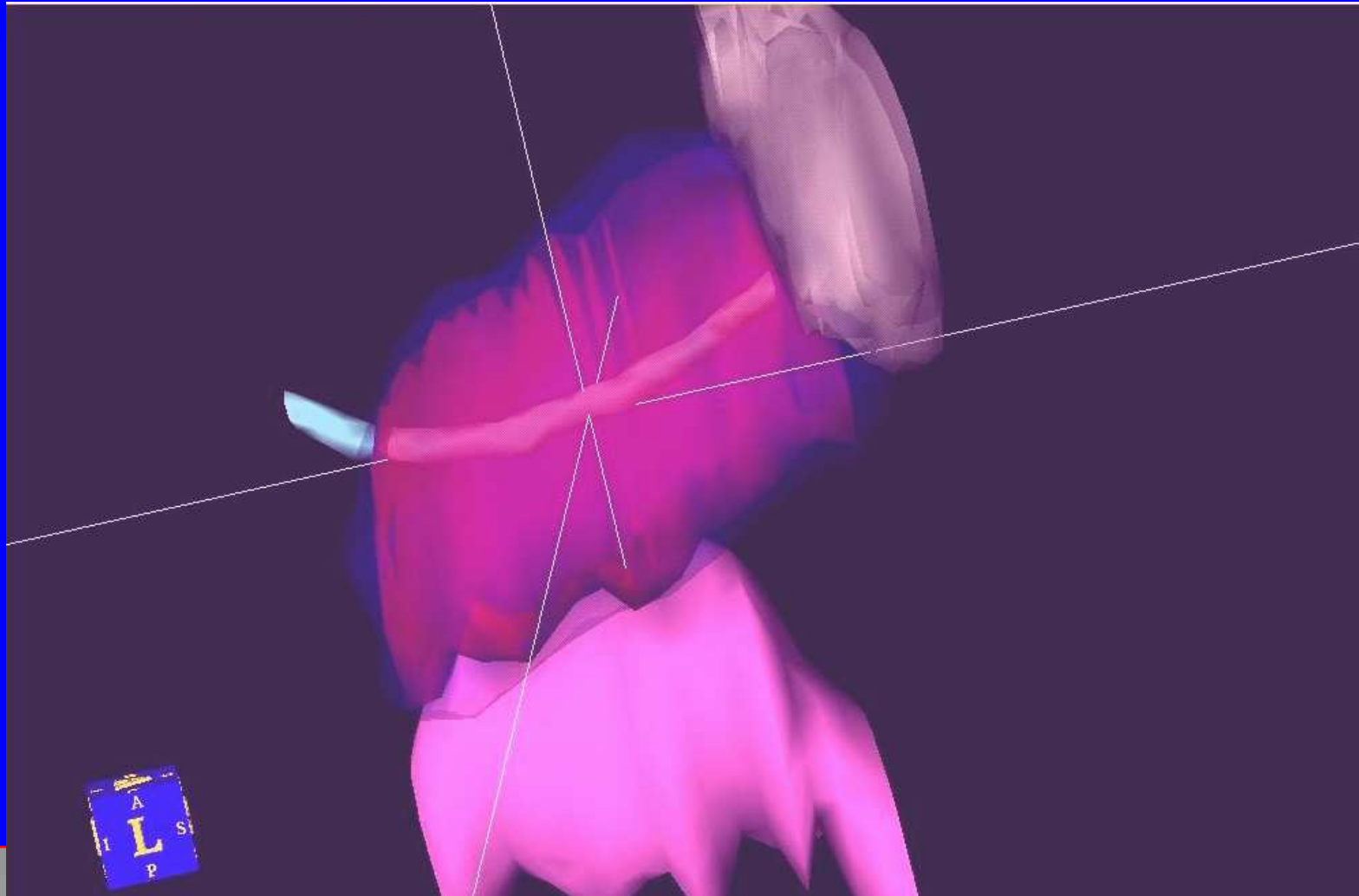




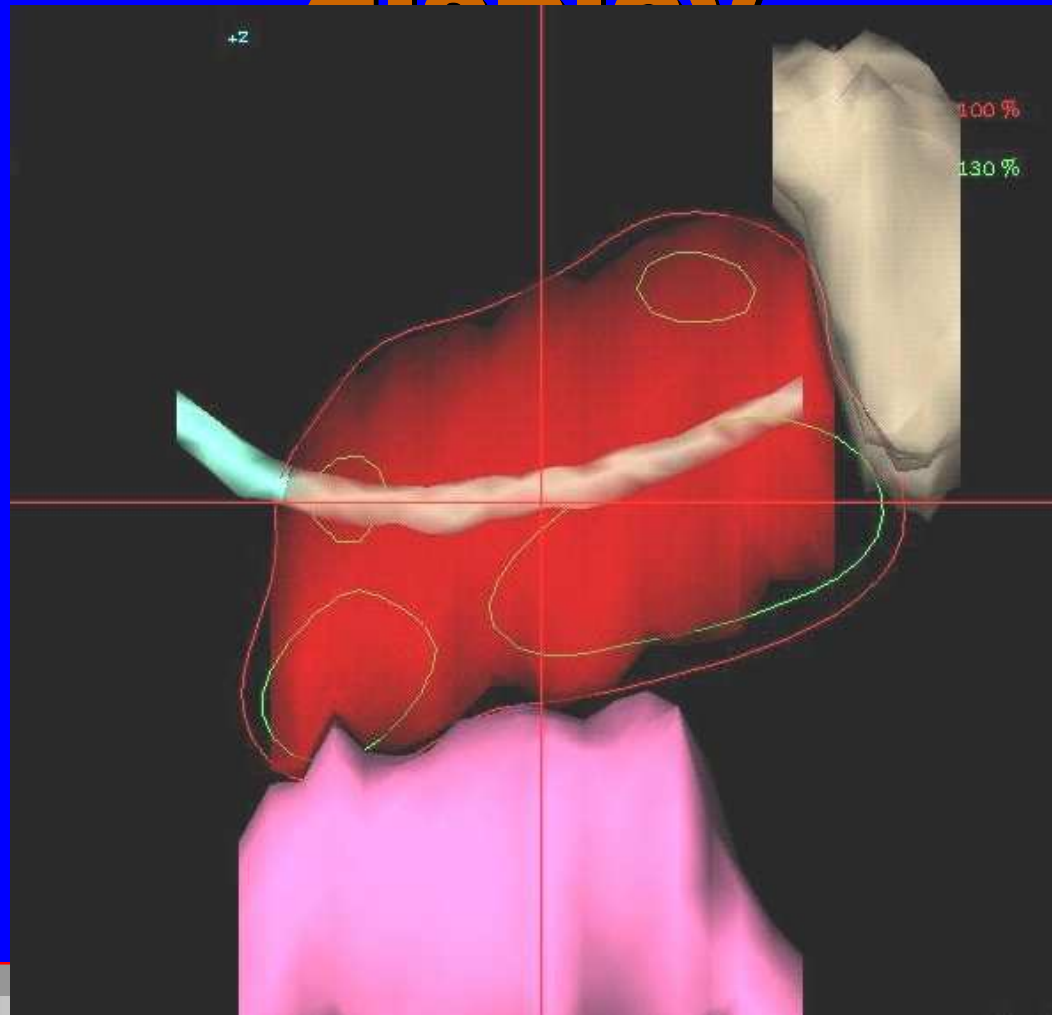
Catheter tracks with prospective dwell positions

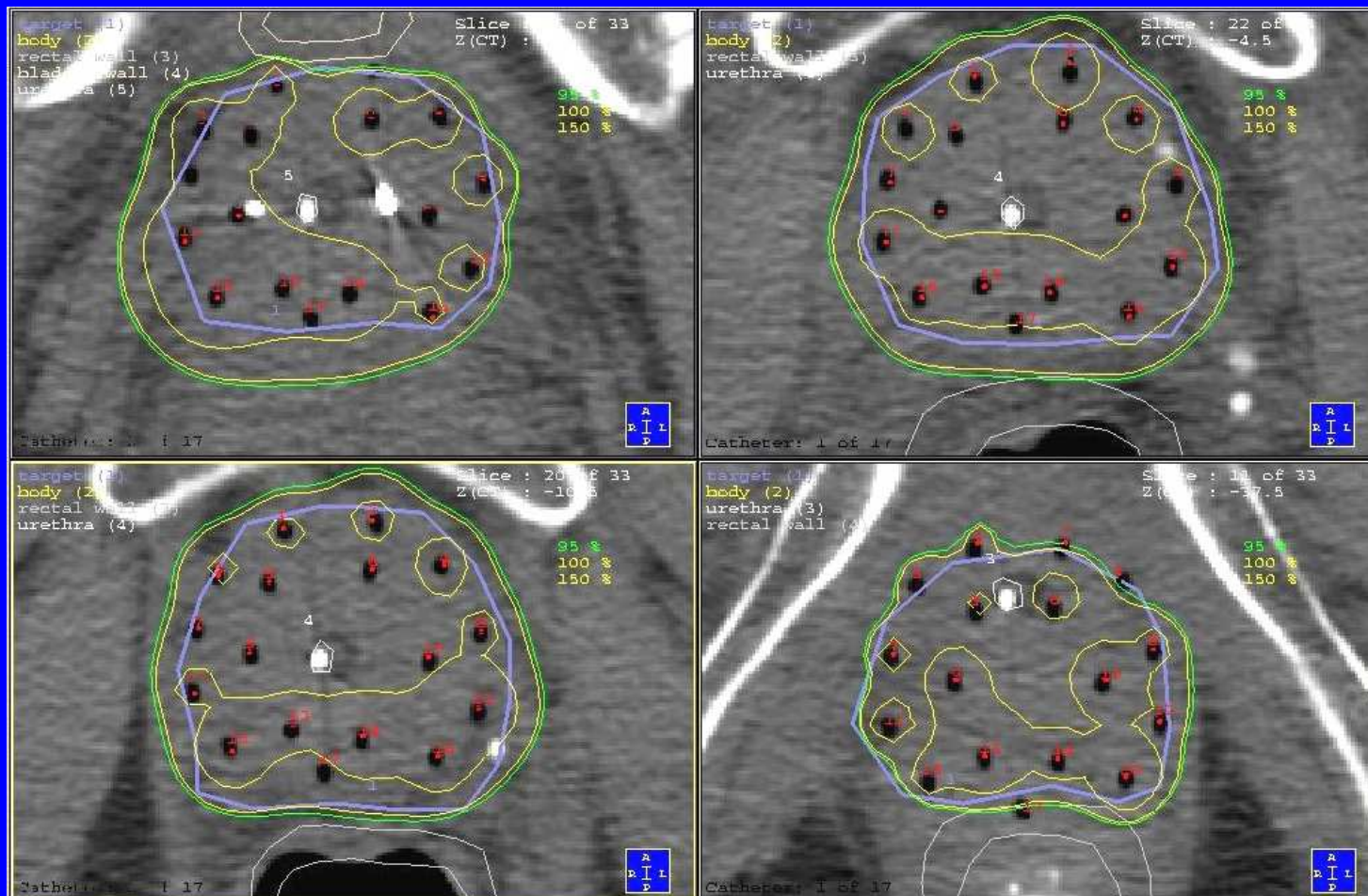


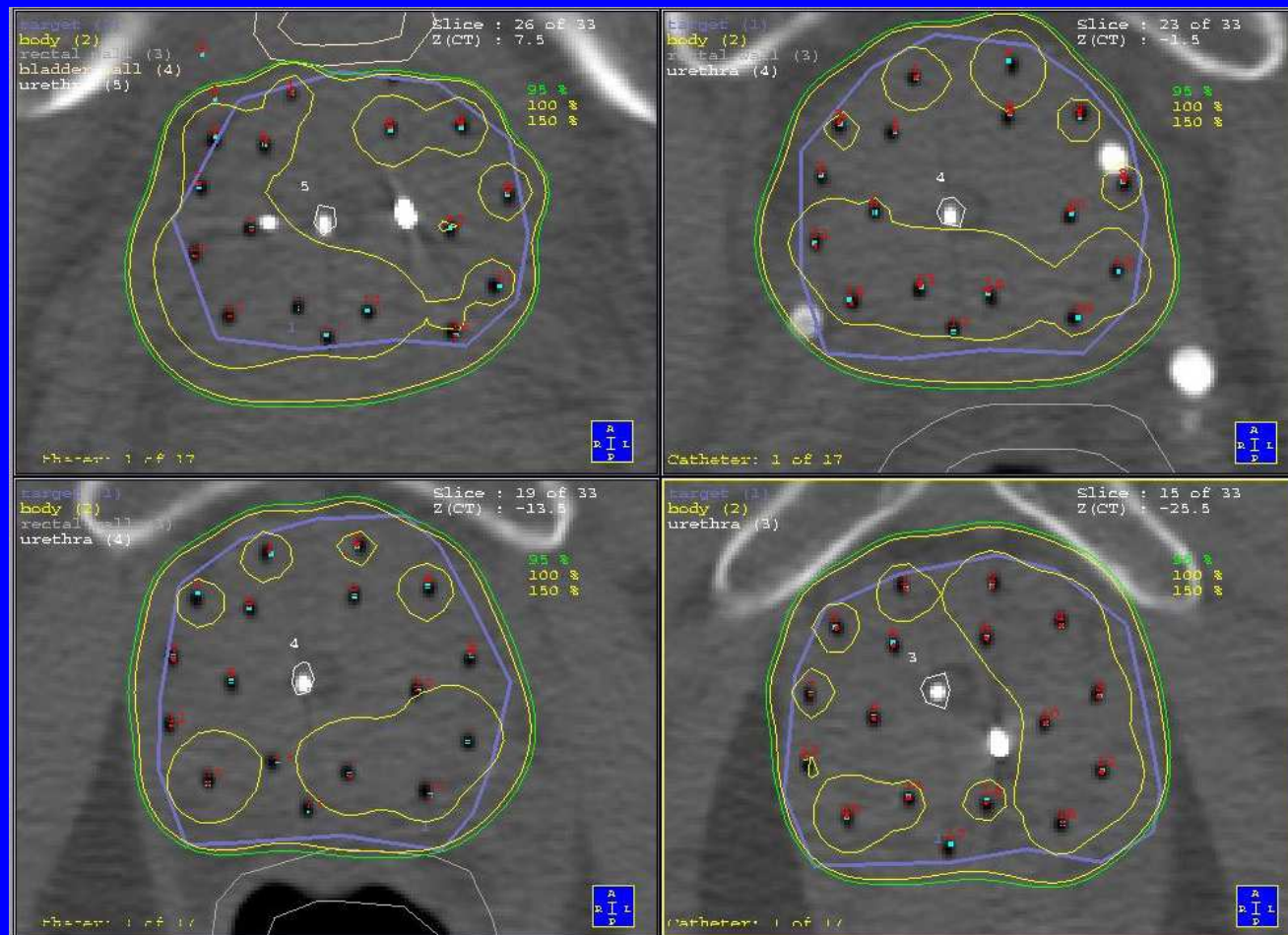
**Dose cloud at 8 Gy covers
the Prostate tightly
The Rectum and Bladder are**



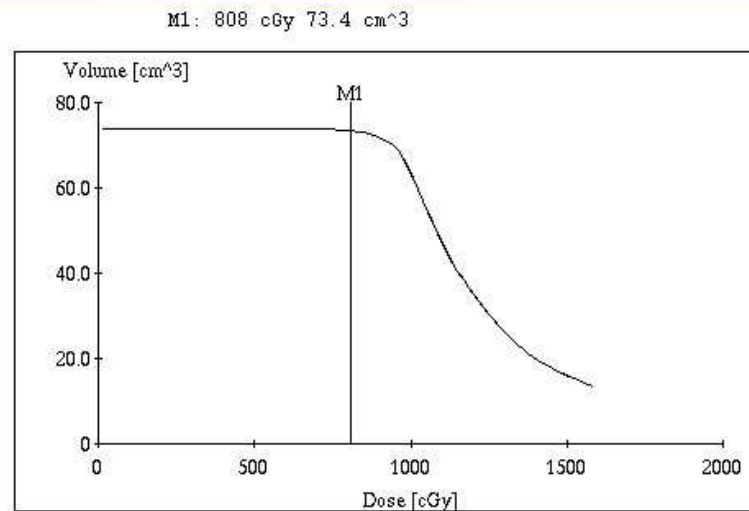
2-D dose distribution display



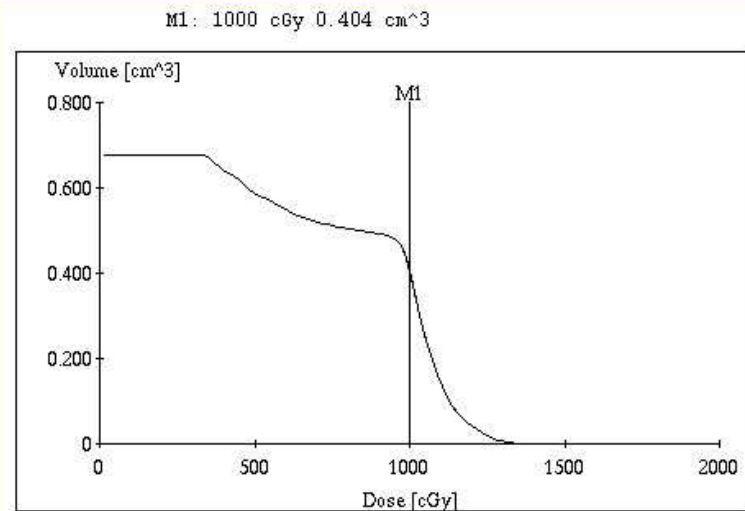




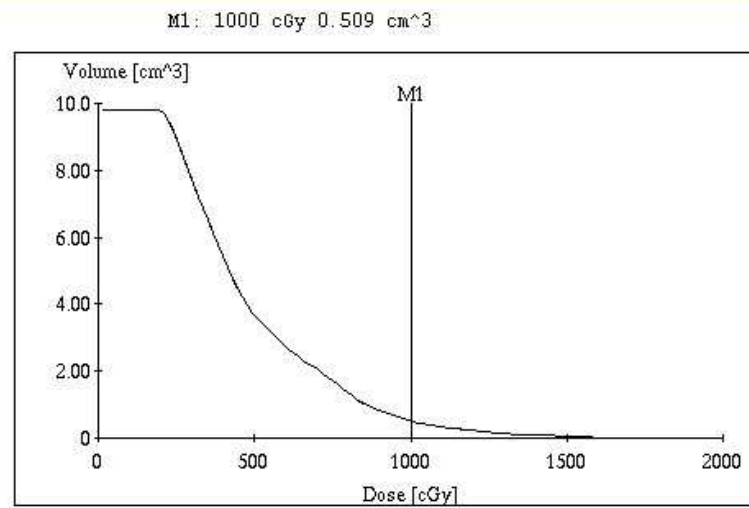
Pre-implant plan DVH evaluations



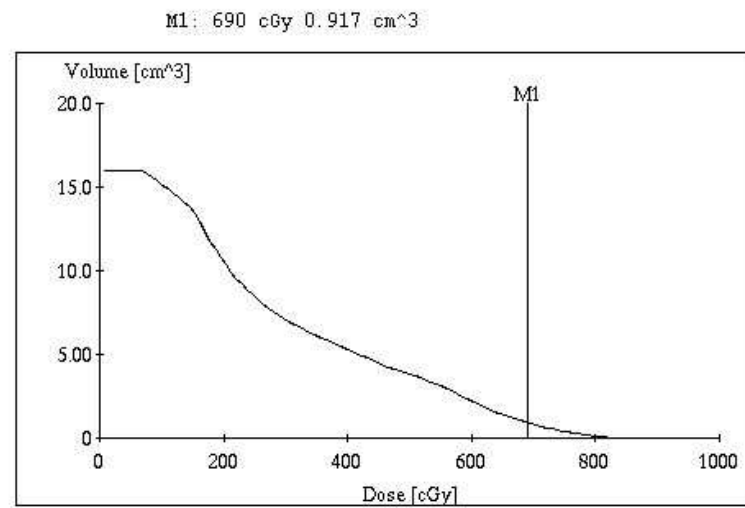
DVH_0 : Cumulative DVH on target. State : Consistent.



DVH_5 : Cumulative DVH on urethra. State : Consistent.



DVH_1 : Cumulative DVH on bladder wall. State : Consistent.



DVH_3 : Cumulative DVH on rectal wall. State : Consistent.

Choices

Optimization

Optimization method

☒ Geometry
 ☒ On specified points
 ☒ Manual dwell times

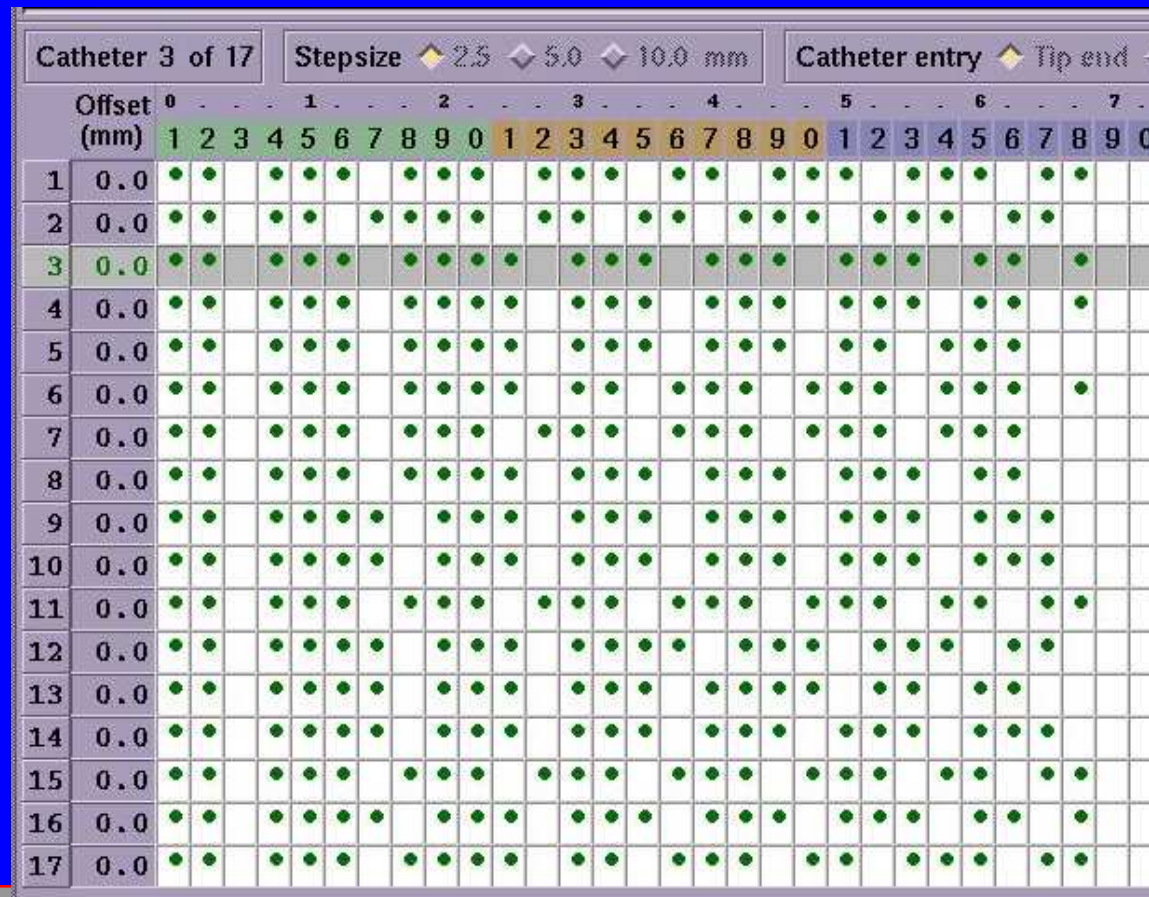
☒ Dose points
 ☒ Manual dwell weights
 ☒ Inverse optimization

Dwell time gradient

VOI	Margin (mm)	Organ type	Dose limit (%)	Dose range (%) (min - max)	Cat	Index	Dwell Weight
bladder wall	0.00	Ignored	100	-	1	1	1.00
body	0.00	Ignored	100	-	1	2	1.00
rectal wall	0.00	Ignored	100	-	1	3	1.00
target	0.00	Target	100	-	1	4	1.00
urethra	0.00	Organ at risk	140	-	1	5	1.00
					1	6	1.00
					1	7	1.00
					1	8	1.00
					1	9	1.00
					1	10	1.00
					1	11	1.00
					1	12	1.00
					1	13	1.00
					1	14	1.00
					1	15	1.00
					1	16	1.00
					1	17	1.00
					1	18	1.00
					1	19	1.00
					1	20	1.00
					1	21	1.00
					2	1	1.00
					2	2	1.00
					2	3	1.00
					2	4	1.00
					2	5	1.00
					2	6	1.00

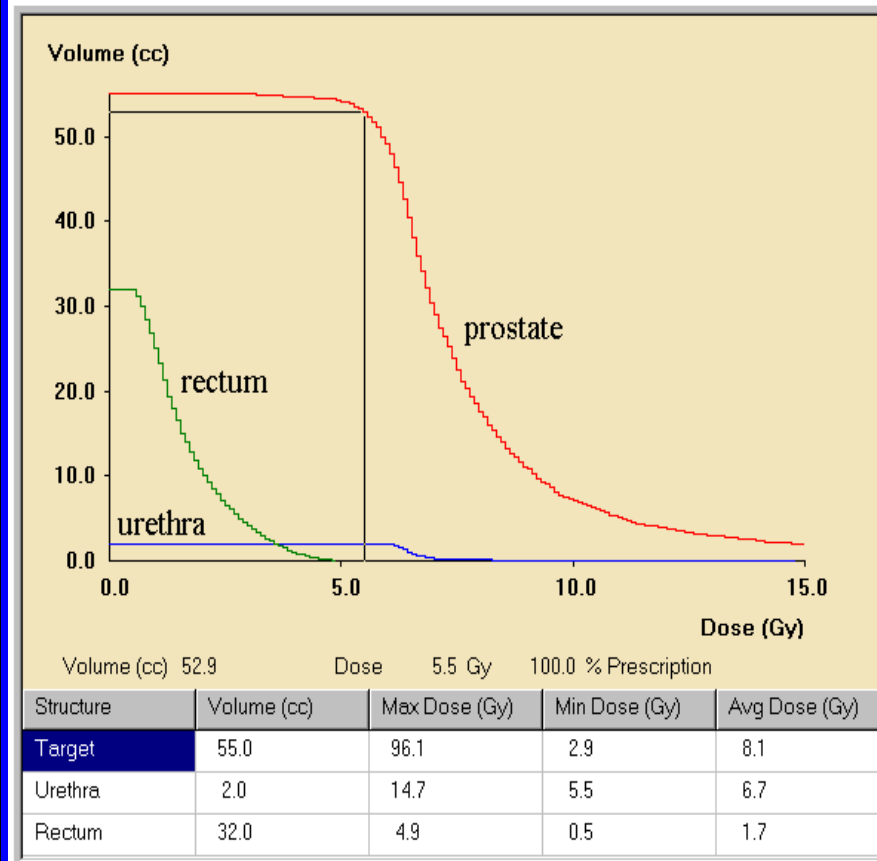
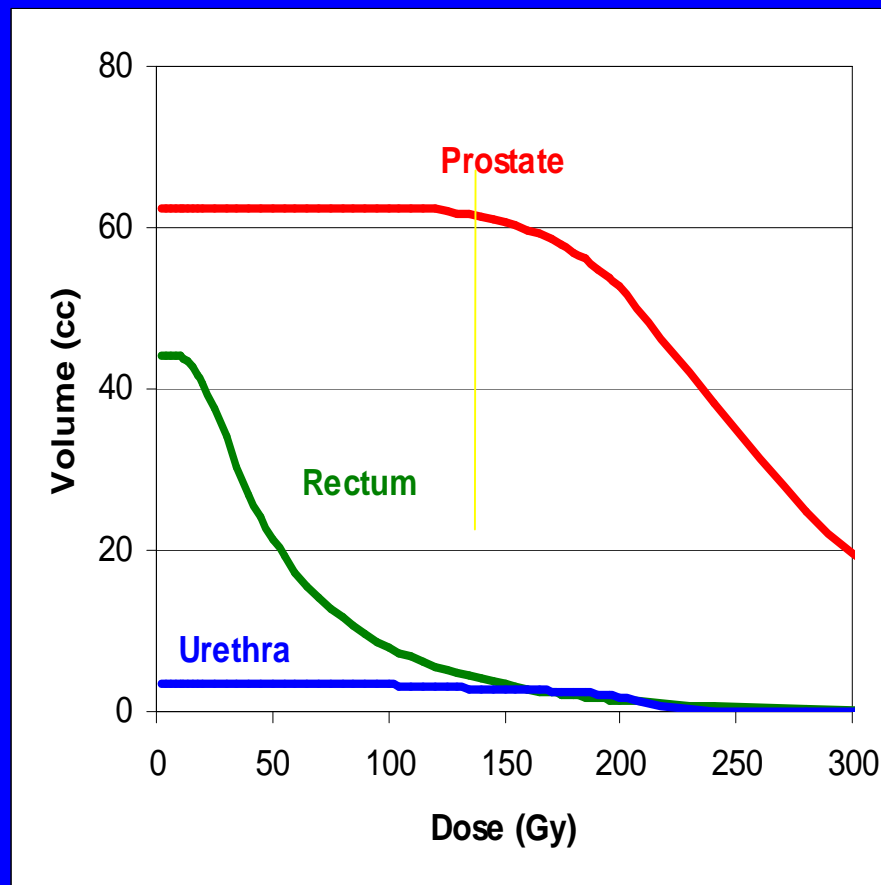
Minimize

Dwell positions offers great flexibility for Optimizing the Dose



Prostate Brachytherapy

DVH evaluation



Permanent seed implant

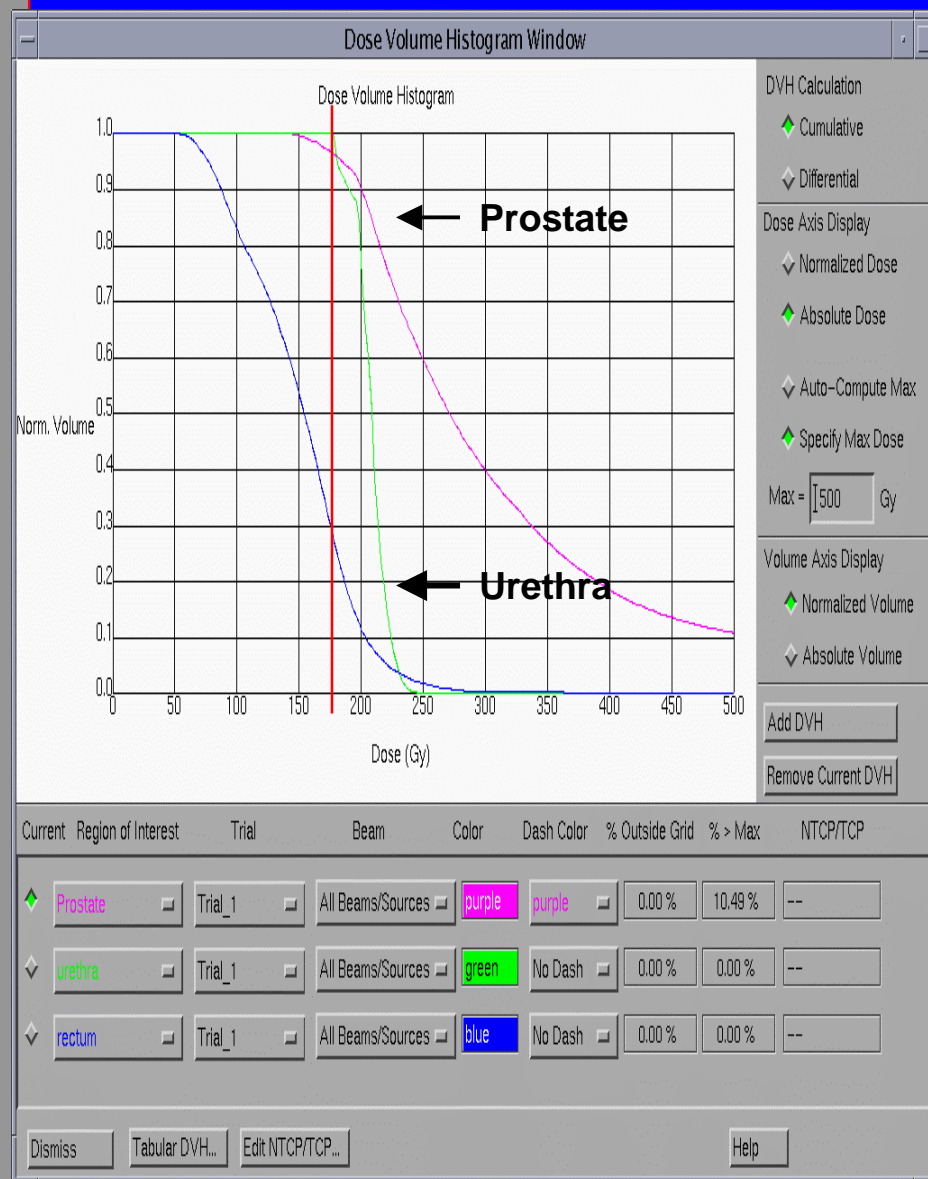
Long Island Jewish Medical Center
LDR



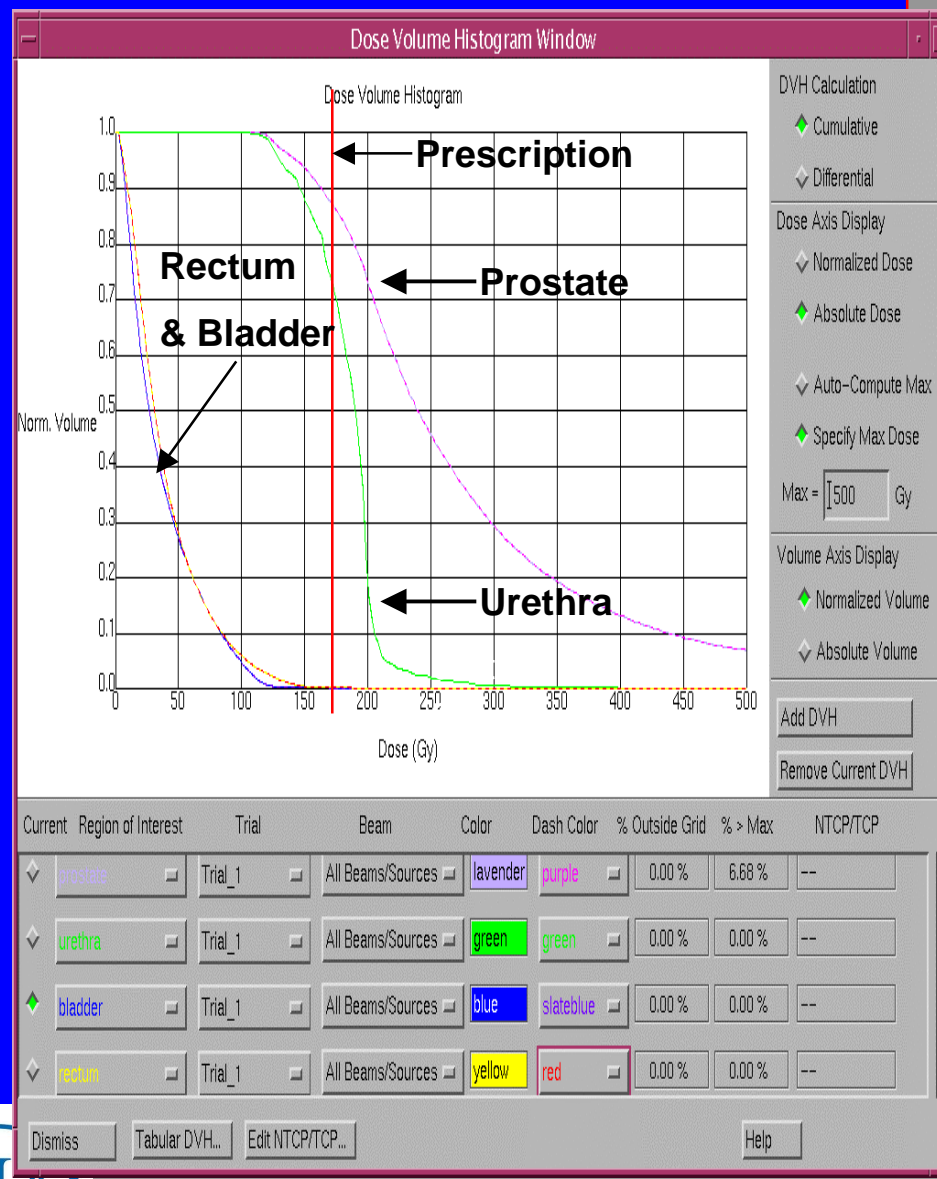
HDR with remote afterloader

North Shore-LIJ Health System

Pre-implant , TRUS-based, Planned DVH



Post-Implant, Ct-based, DVH Evaluation



Comparison of Biological Effectiveness for all Four Modalities

Modality	Fractionation	Total Dose (Gy)	BED (Gy)
I-125	1 x 144	144.0	123
EBRT	44 x 1.8	79.2	170
EBRT	25 x 1.8	45.0	99
I-125	1 x 115	115.0	98
EBRT + I-125			197
EBRT	25 x 1.8	45.0	99
HDR	2 x 8	16.0	101
EBRT + HDR			200

