PROSTATE AND NORMAL TISSUE CONSTRAINTS TO OPTIMIZE PROSTATE HDR BRACHYTHERAPY

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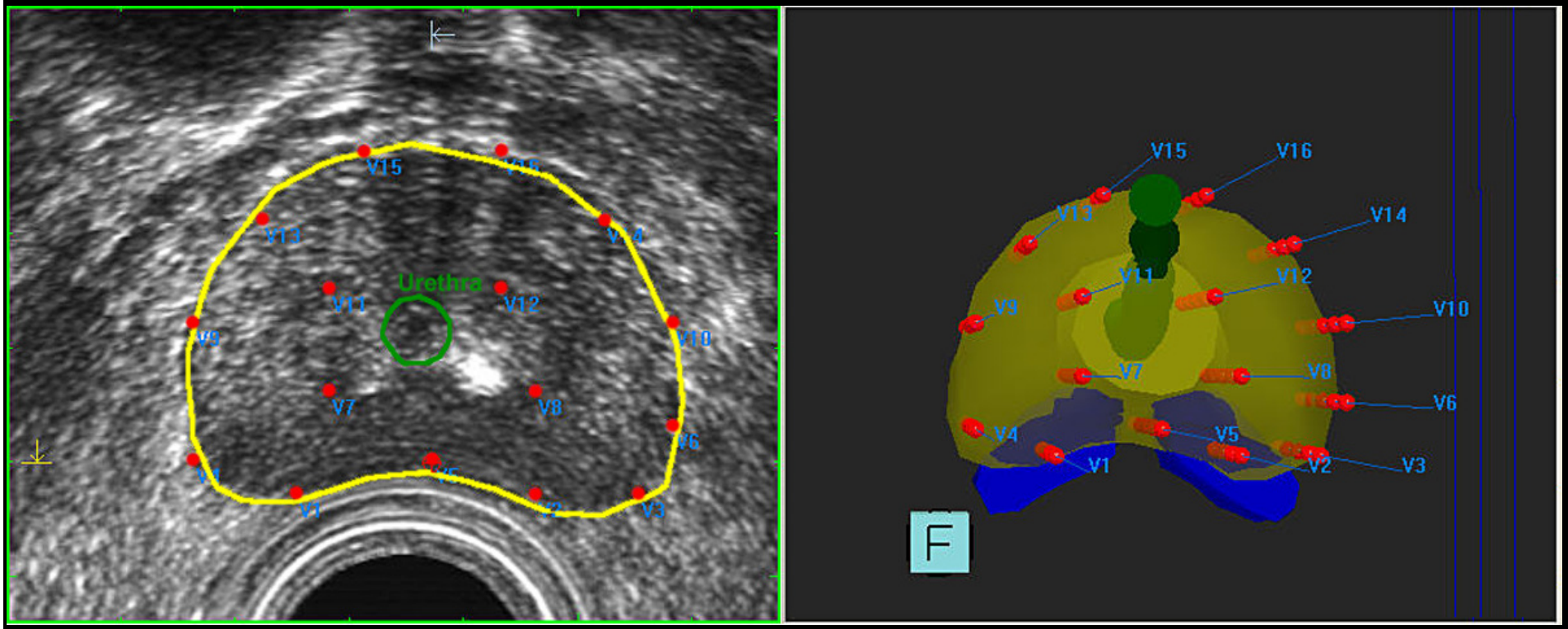
HDR, LDR, CYBERK, VMAT

A FOOL WITH
A GREAT TOOL
IS STILL A FOOL!!!!

BACKGROUND - INNOVATION

- IT WAS A TEMPLATE BASE TECHNIQUE
- IT WAS A TECHNIQUE OF IMAGE GUIDANCE, "TRUS" BASED FROM NEEDLE INSERTION, GUIDANCE WITH ON-LINE 3D INVERSE PLANNING AT BEAUMONT
- AT OTHER CENTERS, TRUS GUIDANCE WITH CT-PLANNING.
- TRUS WITH REAL-TIME 3D PLANNING SAVES TIME AND IMPROVES HDR DELIVERY PRECISION.

REAL TIME Needle guidance and dosimetry



2D

3D

Developed in-house 1991

BACKGROUND - INNOVATION

- IN 1991 WE BEGAN THE DOSE ESCALATED BOOST TRIAL FOR HIGH RISK WITH TRUS GUIDANCE AND REAL-TIME 3D PLANNING.
- IN 1995, WE BEGAN THE HDR PROSTATE MONOTHERAPY PROGRAM AT BEAUMONT FOR PATIENTS WITH LOW / INTERMEDIATE RISK
- BOTH WERE HIC APPROVED PROTOCOLS FROM MULTIFRACION TO A SINGLE ONE

IS THE LQM APPROPRIATE FOR PREDICTING EQUIVALENCE AT ALL DOSE LEVELS??

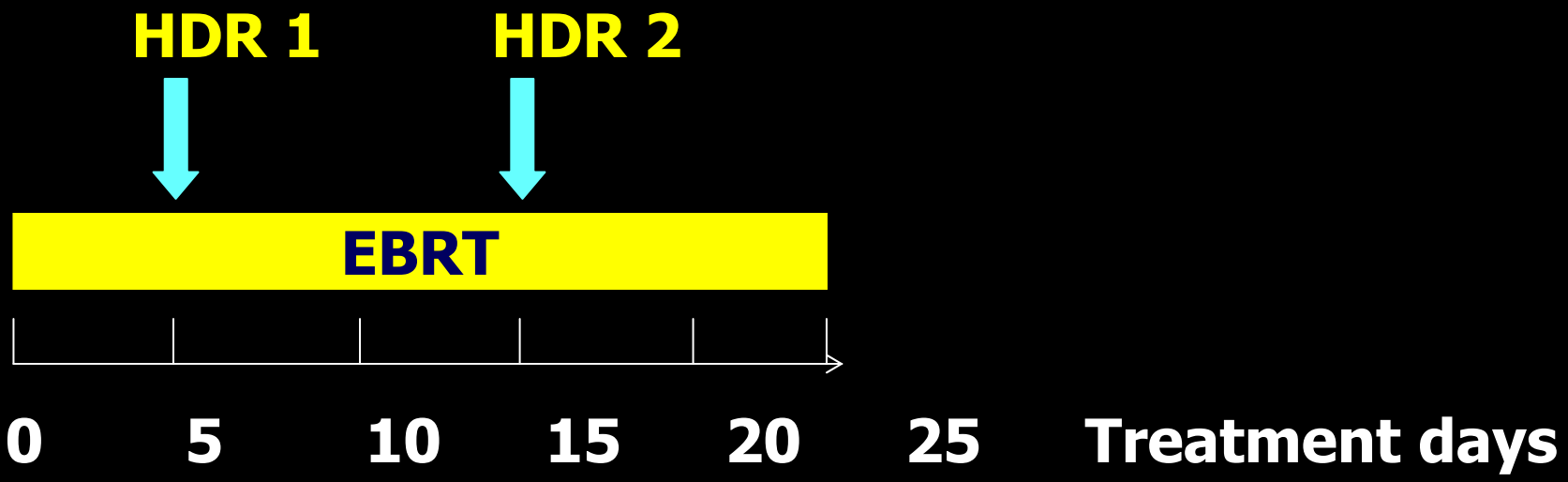
- IN THE RADIOBIOLOGY WORLD, THERE IS CONTROVERSY IF THE LQM IS A GOOD EQUIVALENCE PREDICTOR WHEN VERY LARGE SINGLE DOSES ARE DELIVERED.
- MOST PEOPLE BELIEVES IT DECREASES THE EFFICACY AS THE DOSE INCREASES.
- I WILL USE MY LARGE EXPERIENCE TO DEMONSTRATE CLINICALLY THAT IT IS GOOD ENOUGH AND THE BEST WE HAVE

Interdigitated Pelvic EBRT + HDR boost protocol @ WBH

EBRT total dose 46 Gy in 23 fractions of 2 Gy/fraction

Technique – pelvis 4 field 3D CRT, including pelvic nodes

HDR boost 11.5 Gy on day 5 and day 15 of EBRT w/o interruption



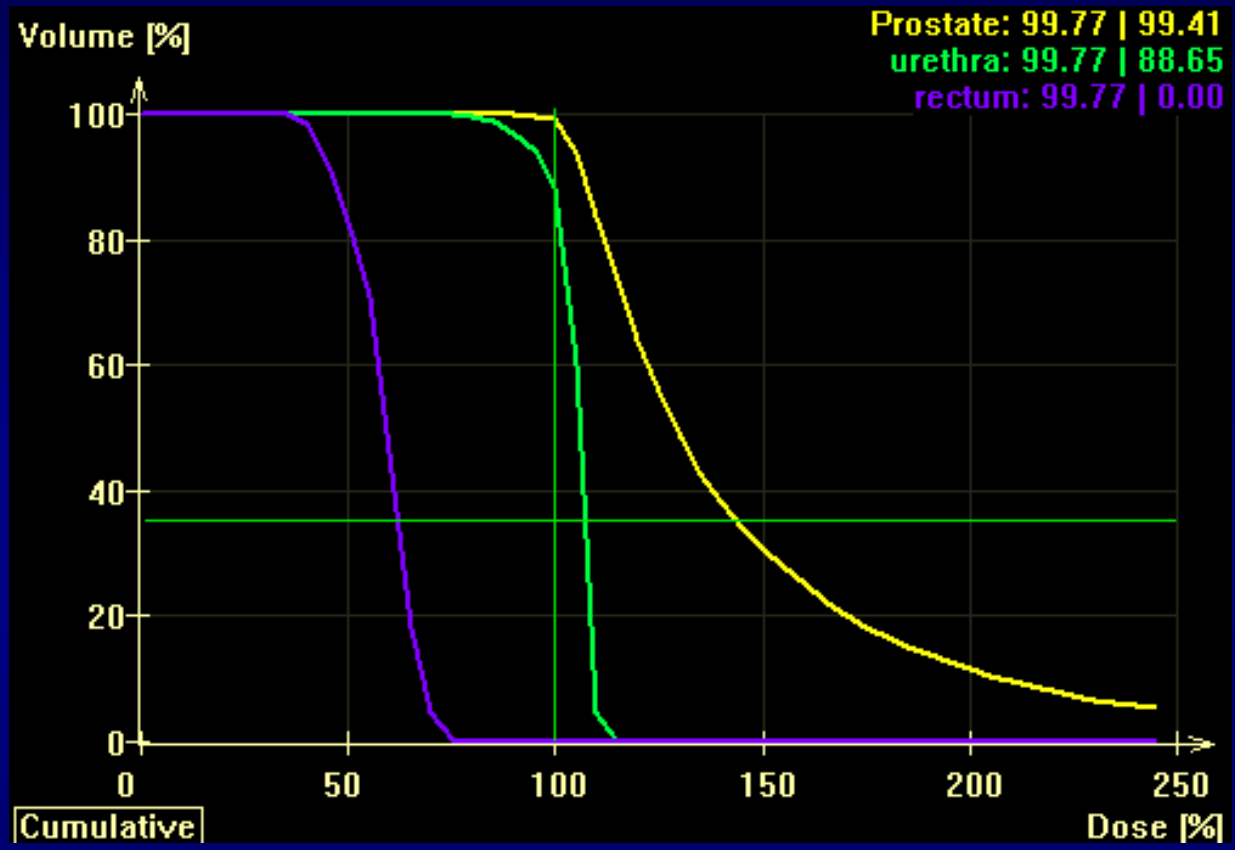
BED OF EBRT+ HDR BOOST

	DOSE LEVEL	# PTS	MEAN FU YEARS	BED* - Gy $\alpha/\beta = 10$	BED* - Gy $\alpha/\beta = 1.2$
low	5.50 Gy x 3	26	10.8	67.1	215
	6.00 Gy x 3	21	9.9	70.0	231
	6.50 Gy x 3	32	10.2	72.6	248
	8.25 Gy x 2	44	8.7	72.0	253
high	8.75 Gy x 2	44	8.4	74.2	268
	9.50 Gy x 2	111	8.1	78.0	292
	10.50 Gy x 2	124	6.3	82.9	327
	11.50 Gy x 2	69	6.0	87.0	366

* BIOLOGICAL EQUIVALENT DOSE TO EXTERNAL BEAM

Dosimetry Constraints for HDR Boost

- **Prostate**
  - V_{100} > 97%
  - V_{125} < 65%
  - V_{150} < 30%
- **Urethra**
  - V_{100} < 90%
  - V_{115} < 10%
- **Rectum**
  - V_{75} < 1%



Software evolution: geometric, point-dose → inverse, DVH

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5 WEEK EBRT + HDR BOOST

DOSE ESCALATION IMPROVES CANCER-RELATED EVENTS AT 10 YEARS FOR INTERMEDIATE- AND HIGH-RISK PROSTATE CANCER PATIENTS TREATED WITH HYPOFRACTIONATED HIGH-DOSE-RATE BOOST AND EXTERNAL BEAM RADIOTHERAPY

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Martinez et al. *Int J Radiat Oncol Biol Phys* 2011;79:363-370

OUTCOMES FOR 472 PATIENTS

Dose group	No. of cases (n = 472)	BF (nadir +2)	BF(nadir +5 in 24 month, then nadir +2)	Locoregional failure	Distant metastasis failure	Clinical failure	Clinical DFS	Prostate cancer-related events
Low dose	167	43.1%	41.2%	14.3%	12.4%	23.4%	55.2%	39.4%
High dose	305	18.9%	15.5%	2.8%	5.7%	7.7%	71.9%	18.9%
p value		<0.001	<0.001	0.001	0.028	<0.001	0.014	0.001
All cases	472	29.4%	26.6%	7.8%	8.3%	14.3%	64.8%	27.5%

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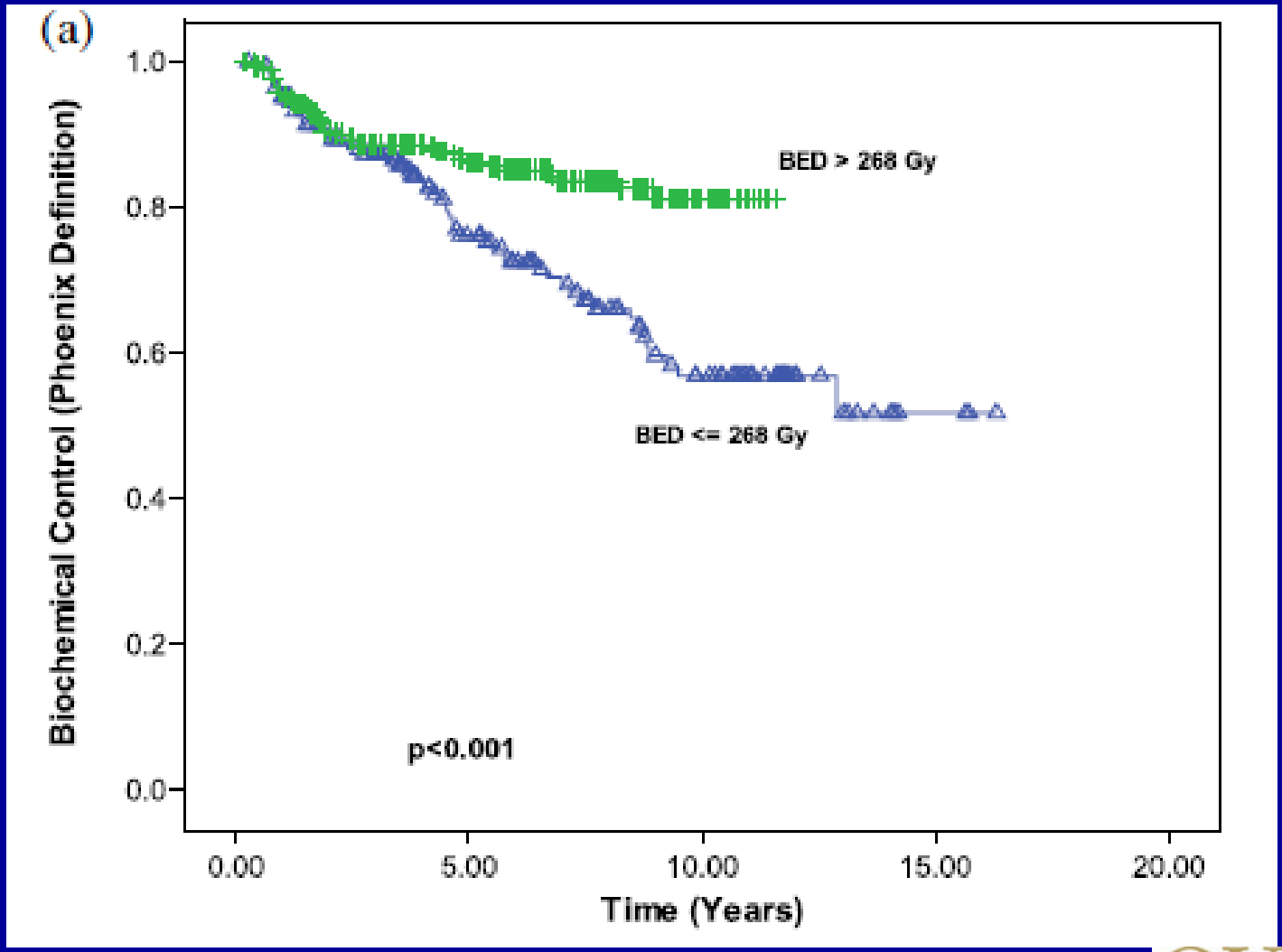
BIOCHEMICAL CONTROL 472 Pts



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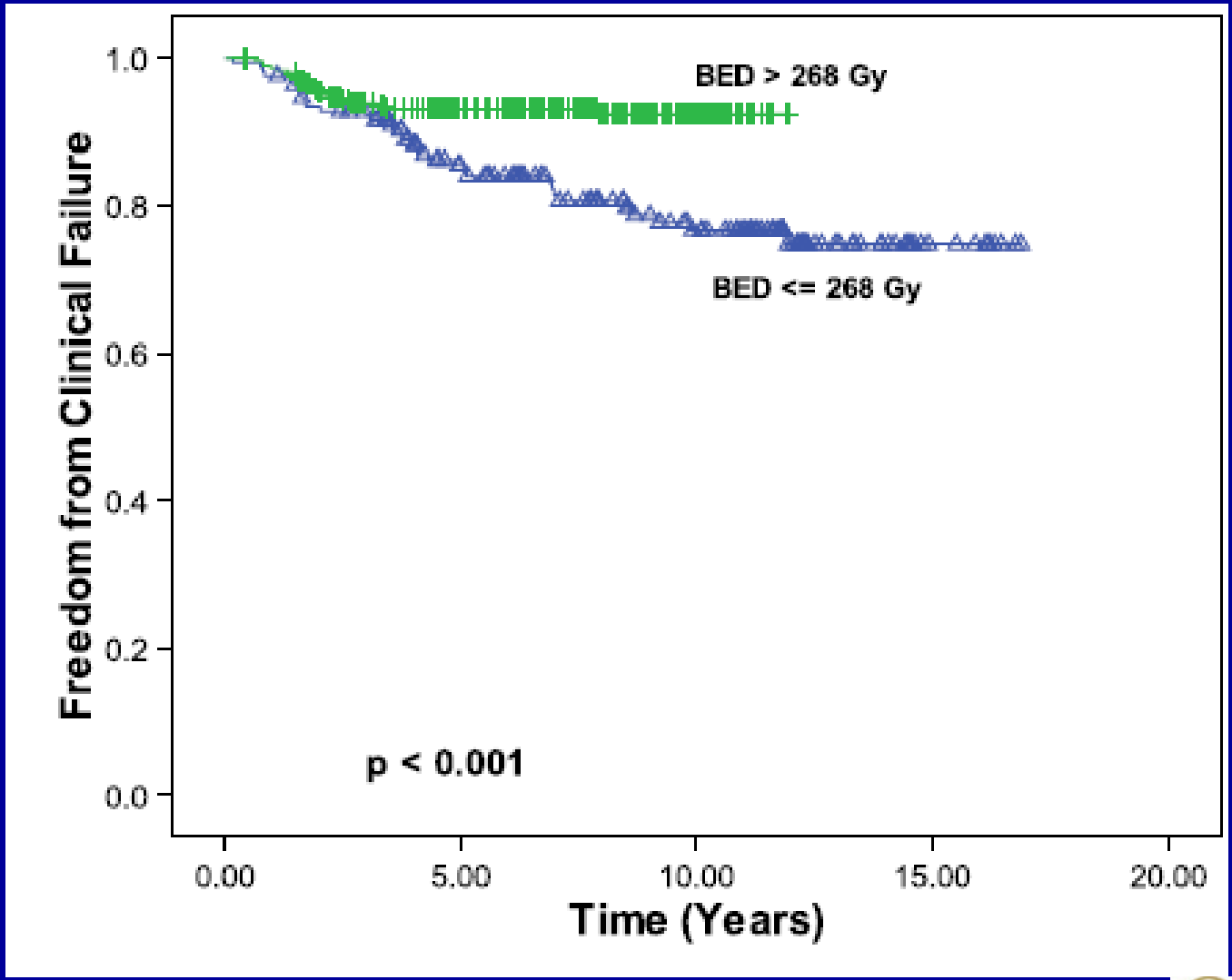
CLINICAL FAILURE 472 Pts



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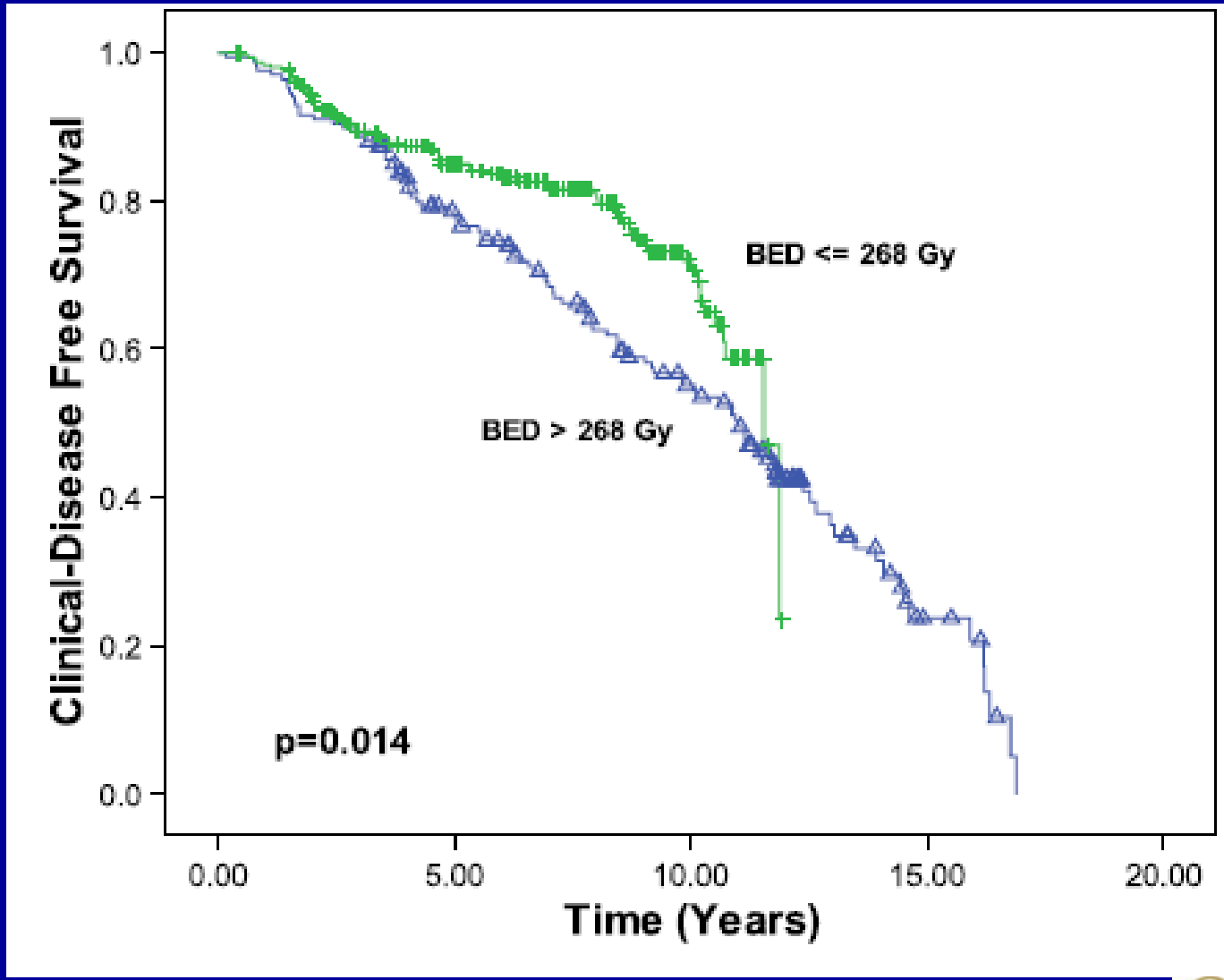
DISEASE FREE SURVIVAL 472 Pts



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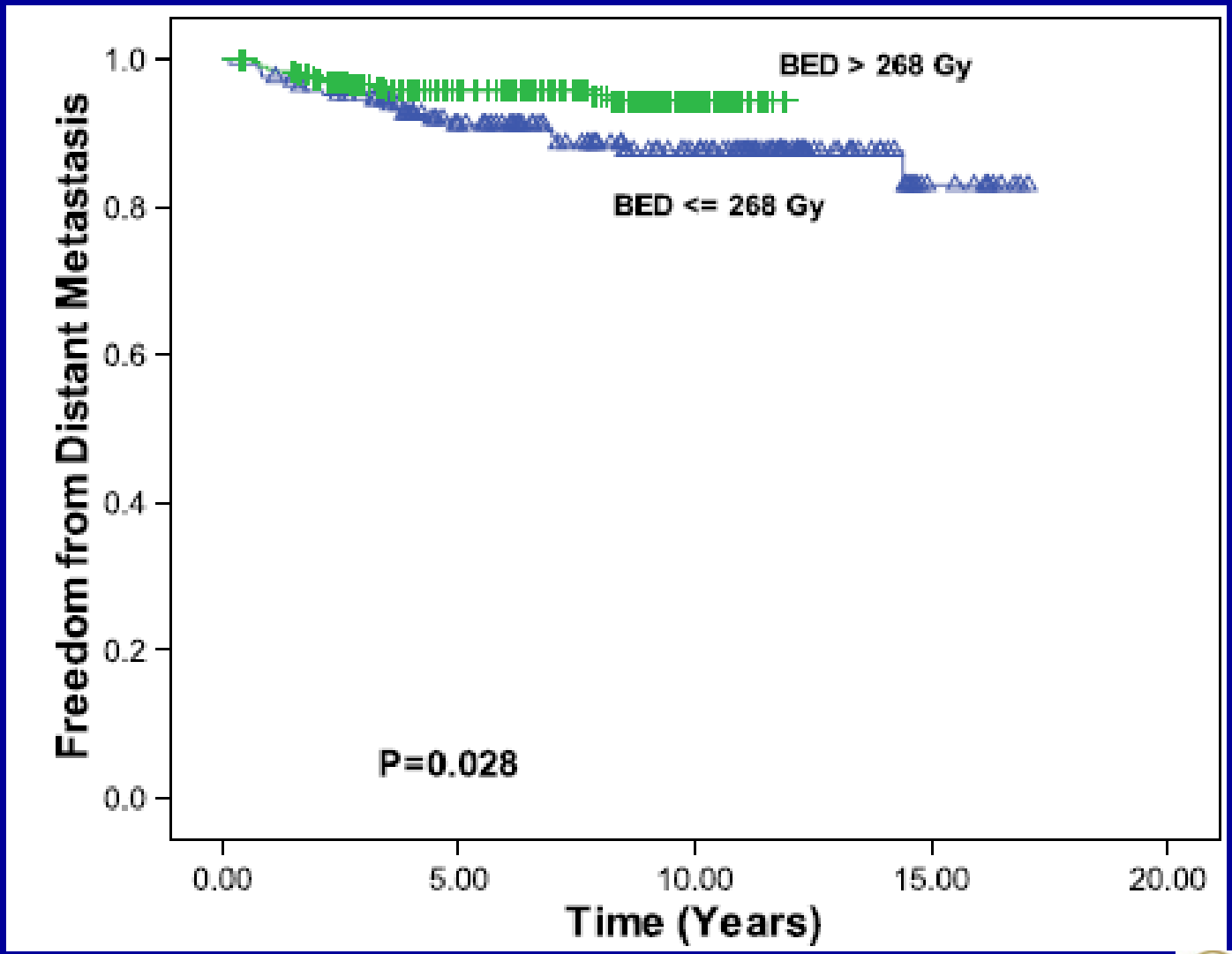
METASTASIS FREE SURVIVAL 472 Pts



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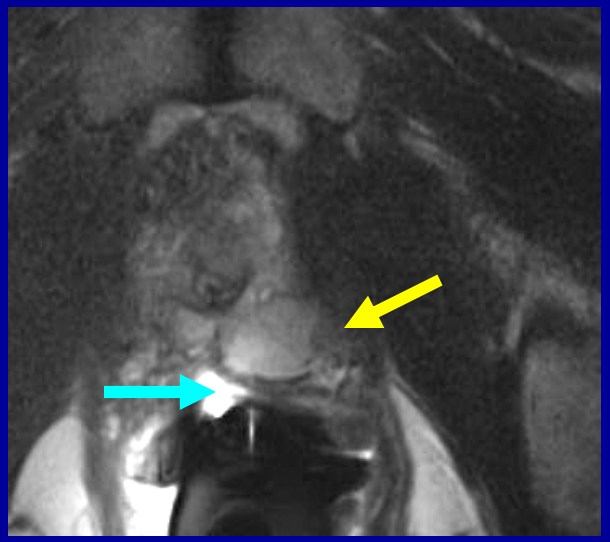
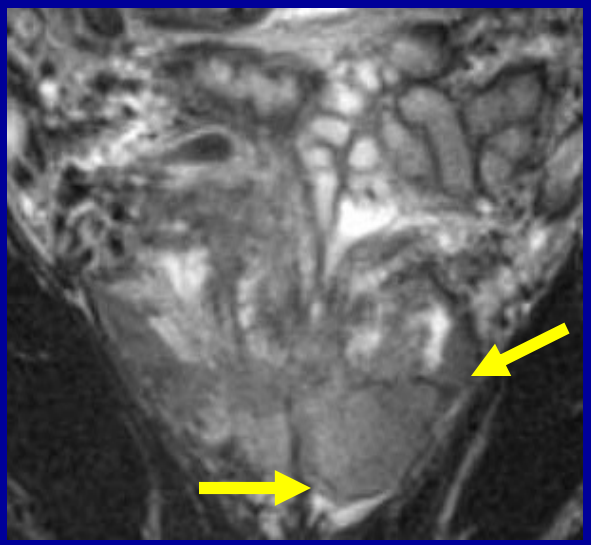
64 Yr male with an increasing PSA from 5.2 TO 14.1 ng/ml in one year.
Digital Exam palpable nodule on the lt, TRUS hypoechoic nodule on the lt. Volume of 72cc. MR confirms nodule, +ECE
Biopsy: Gleason 9 (4+5) in 12/18 cores with up to 80% core involvement and + PNI. AUA Score of 15
PMH: in good general healh.

Treatment HDR BOOST+2 yr ADT

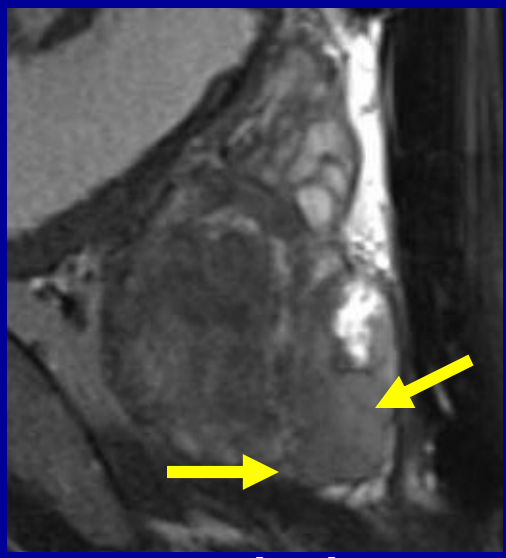
T3a prostate adenoca Gleason 9
High-resolution 3T-MRI



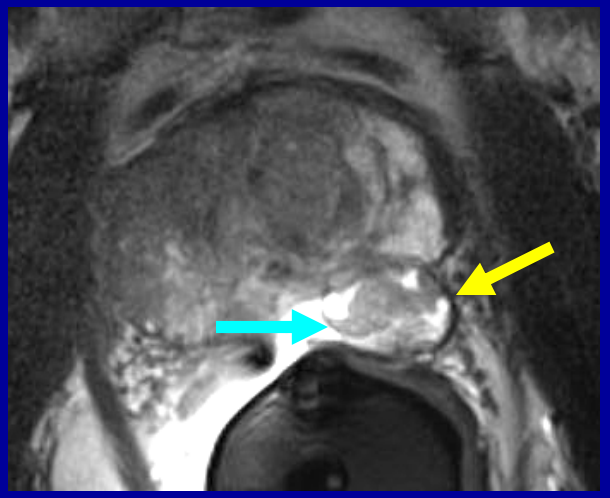
axial

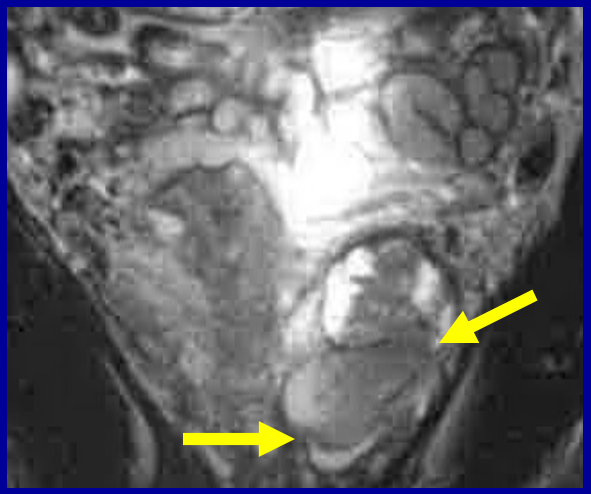


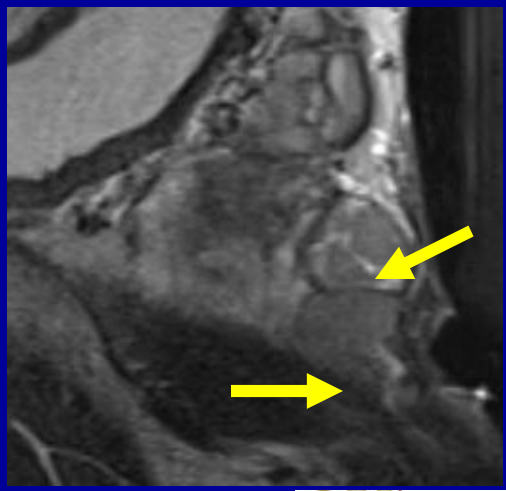
coronal



sagittal







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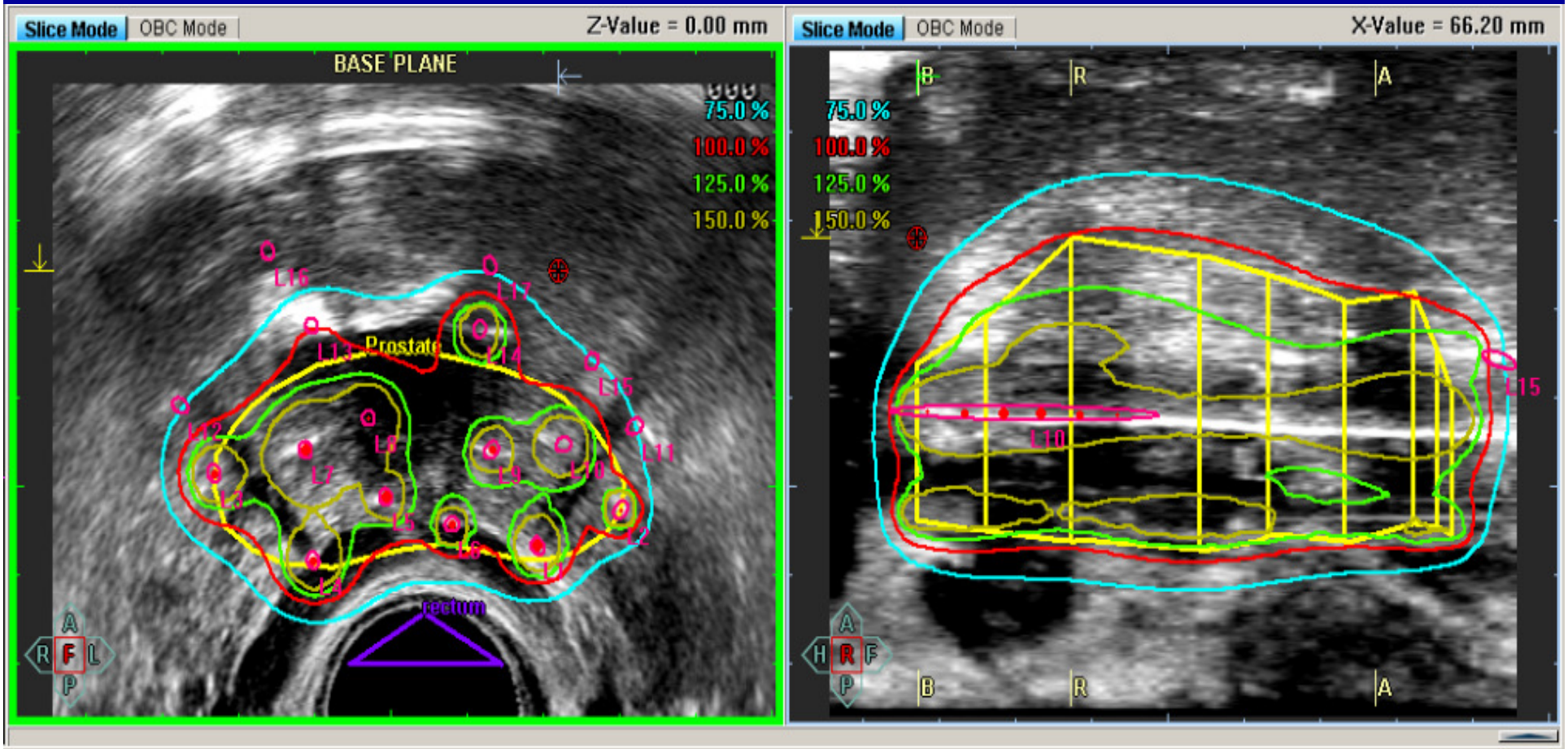
PROSTATE BASE 1



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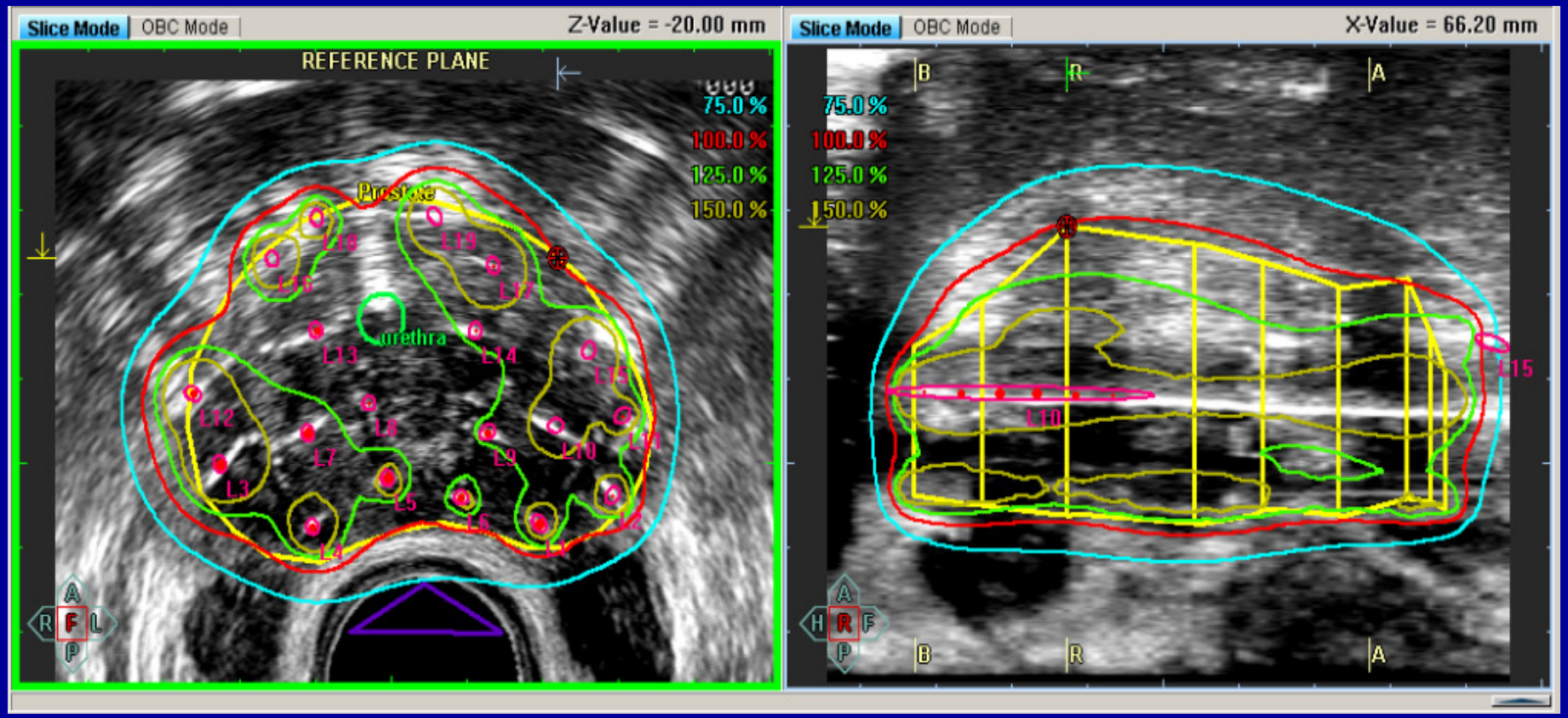
REFERENCE PLANE



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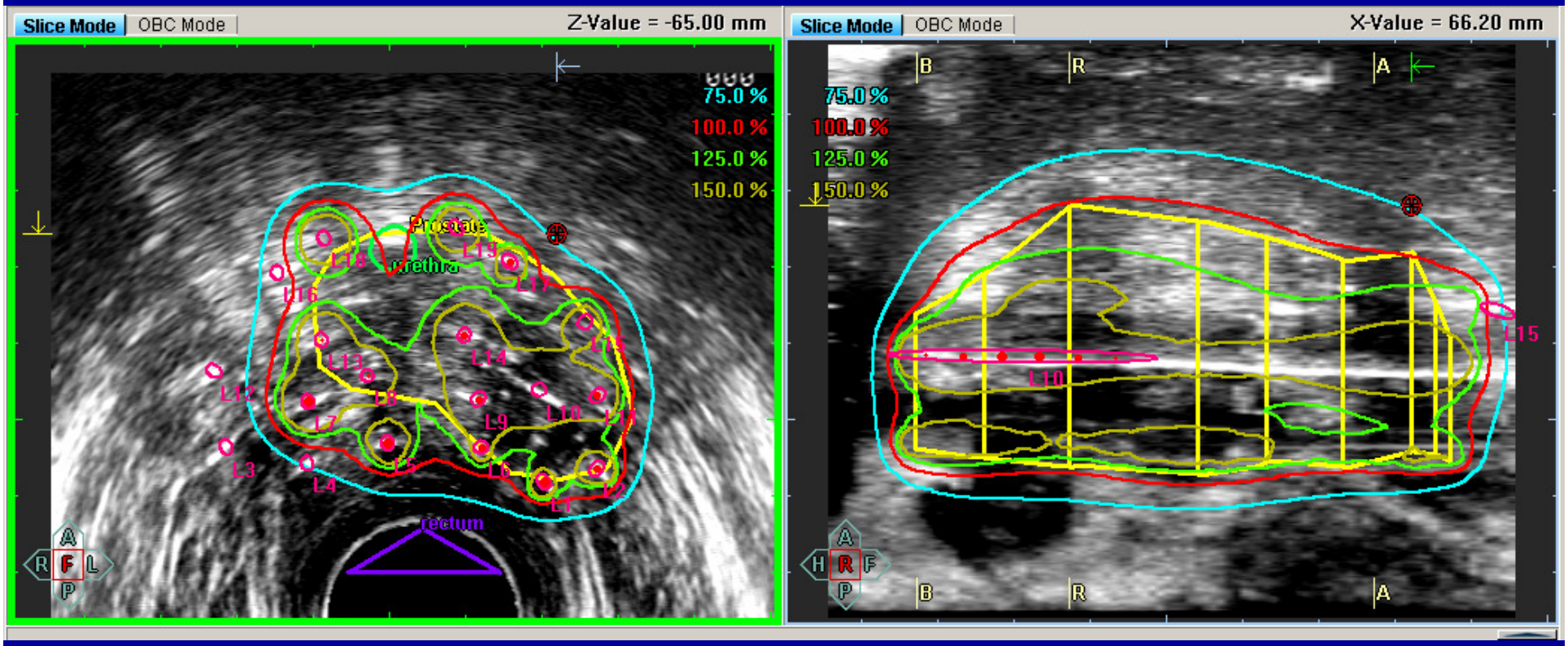
Apex Nodule 2



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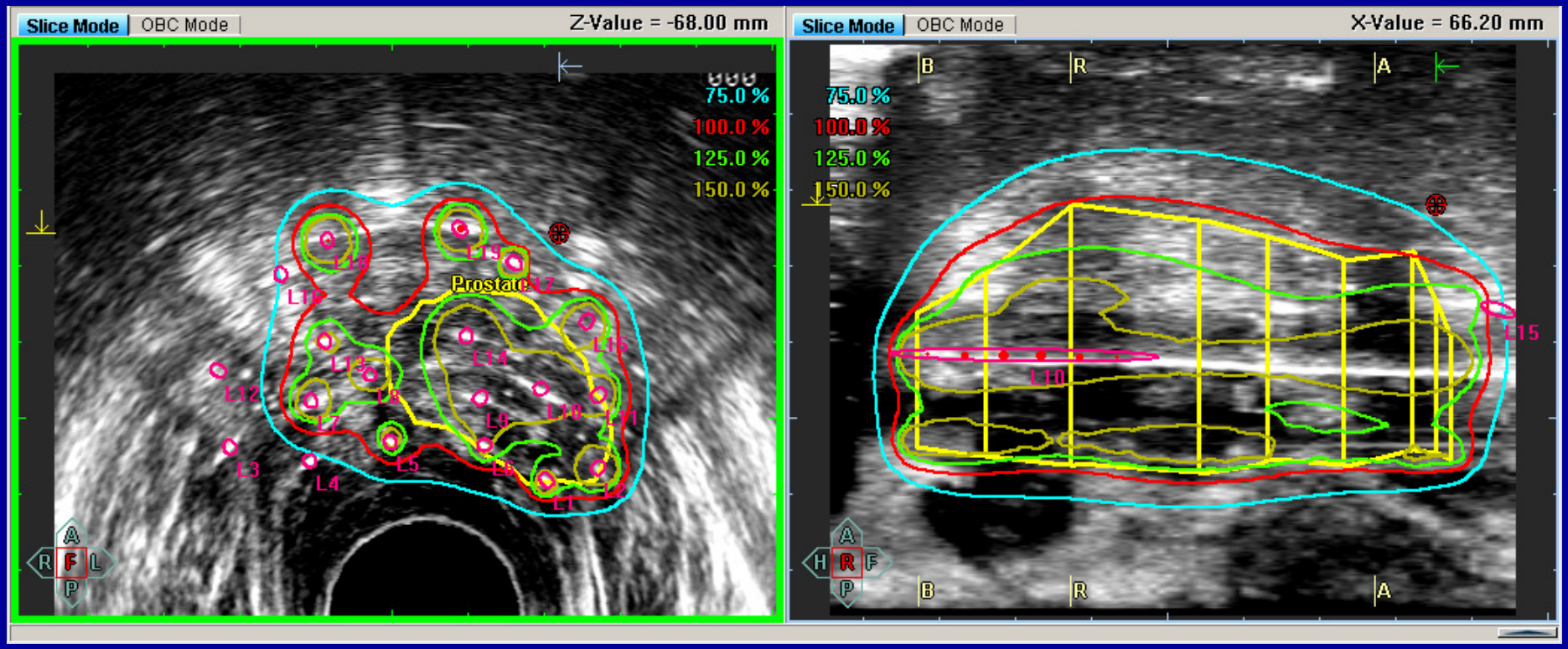
Apex Nodule 3



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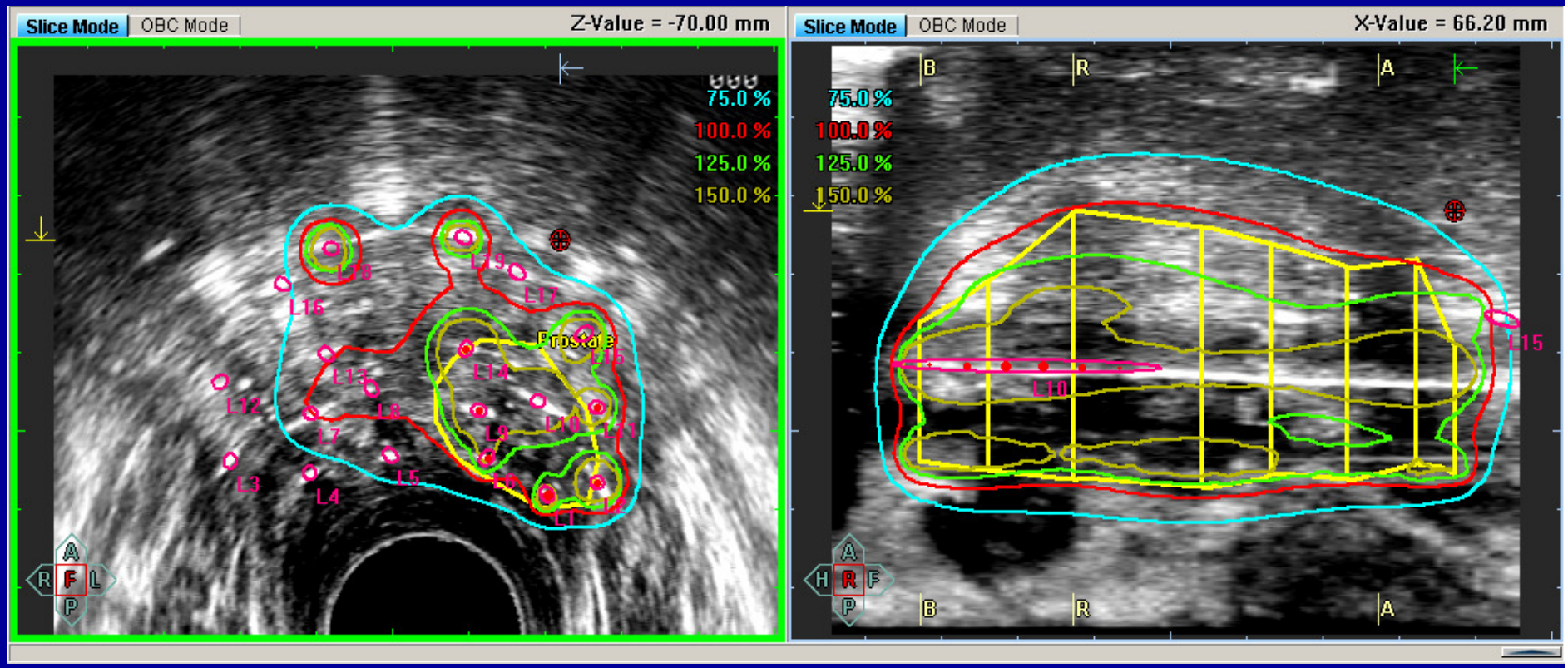
Apex Nodule 4



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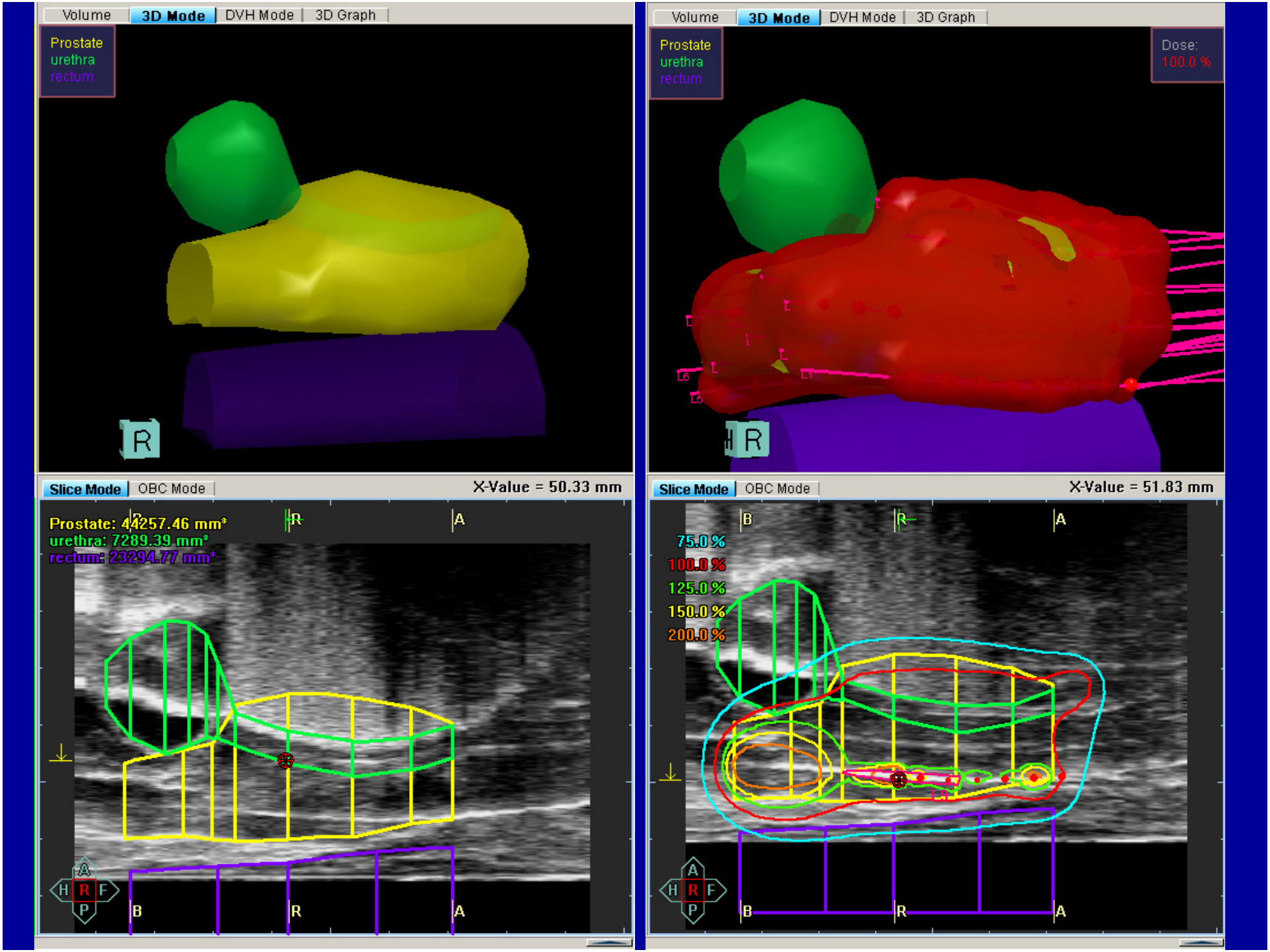
Digital Exam palpable nodule on the lt, TRUS hypoechoic nodule on the lt. Volume of 72cc. MR confirms nodule, +ECE
Biopsy: Gleason 9 (4+5) in 12/18 cores with up to 80% core involvement and + PNI. AUA Score of 15
PMH: in good general healh.

Treatment HDR BOOST+ 2 yr ADT

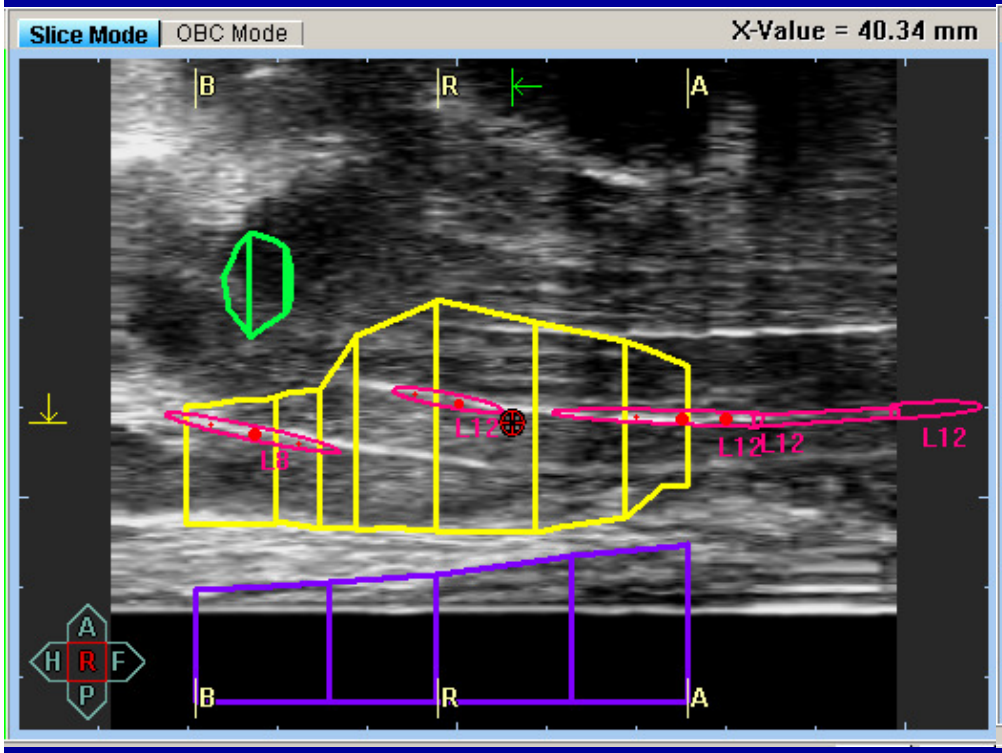
At 6.4 yr, undetectable PSA, (-)DRE

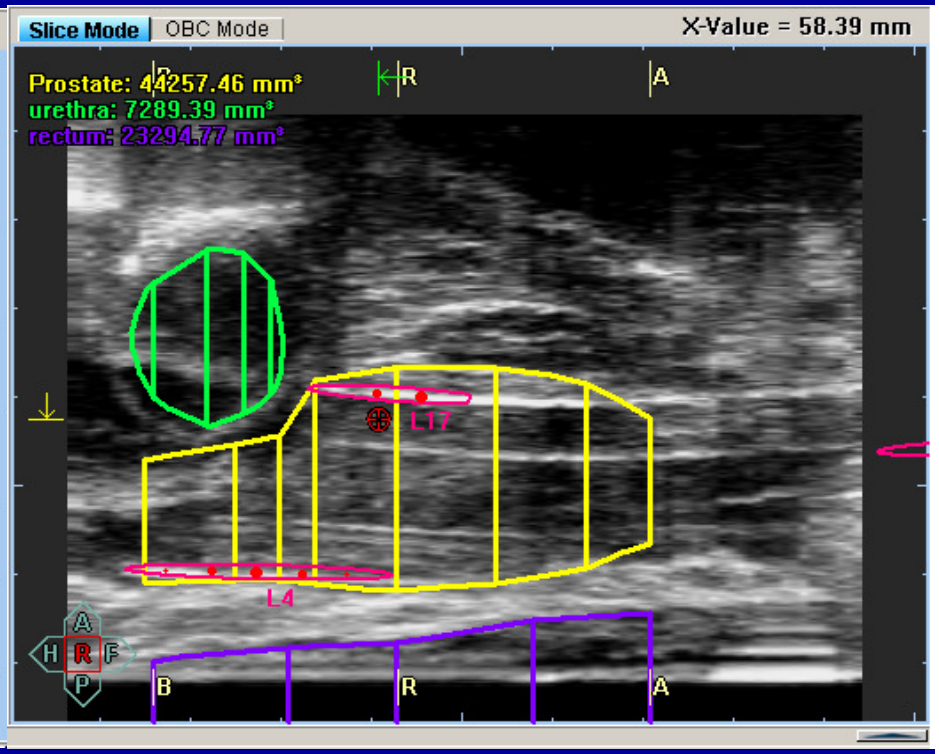
77 Yr male with an increasing PSA from 6.2 TO 9.4 ng/ml in one year. Antibiotics given and minimal PSA change.
Digital Exam palpable nodule on the Rt into SV, TRUS hypoechoic nodule on the Rt. Into SV, volume of 66cc. Biopsy: Gleason 7 (4+3) in 6/18 cores with up to 80% core involvement bilateral and + PNI. p+ SV's. AUA score of 18
PMH: in good general healh.

Treatment HDR BOOST


Volume
3D Mode
DVH Mode
3D Graph
Prostate
urethra
rectum
R
Volume
3D Mode
DVH Mode
3D Graph
Prostate
urethra
rectum
Dose:
100.0 %
R
Slice Mode
OBC Mode
X-Value = 50.33 mm
Prostate: 44257.46 mm³
urethra: 7289.39 mm³
rectum: 23294.77 mm³
R
A
A
H
R
F
P
B
R
A
Slice Mode
OBC Mode
X-Value = 51.83 mm
B
R
A
75.0 %
100.0 %
125.0 %
150.0 %
200.0 %
A
H
R
F
P
B
R
A

MULTIPLANAR SEMINAL VESICAL HDR PROSTATE IMPLANT





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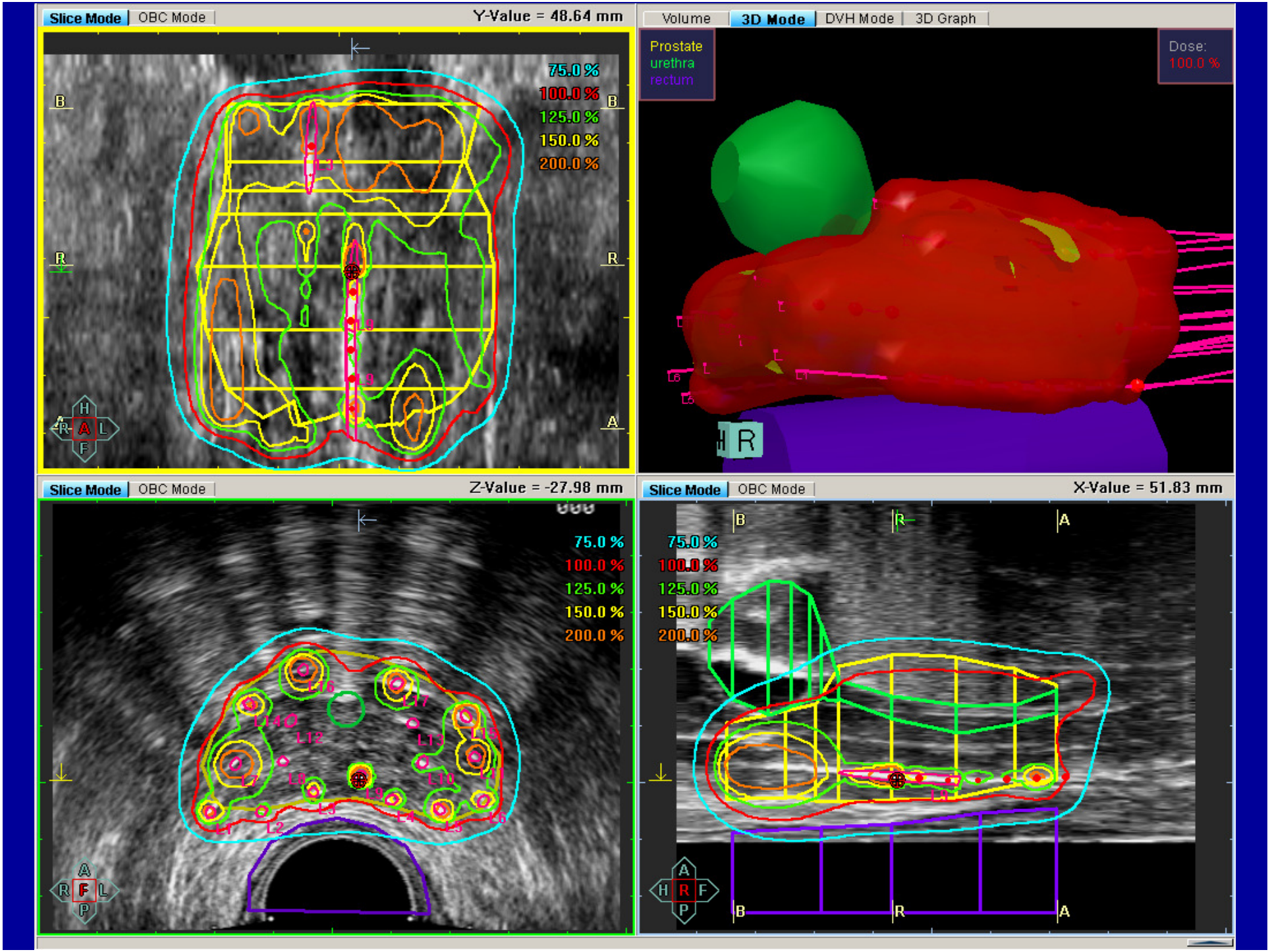
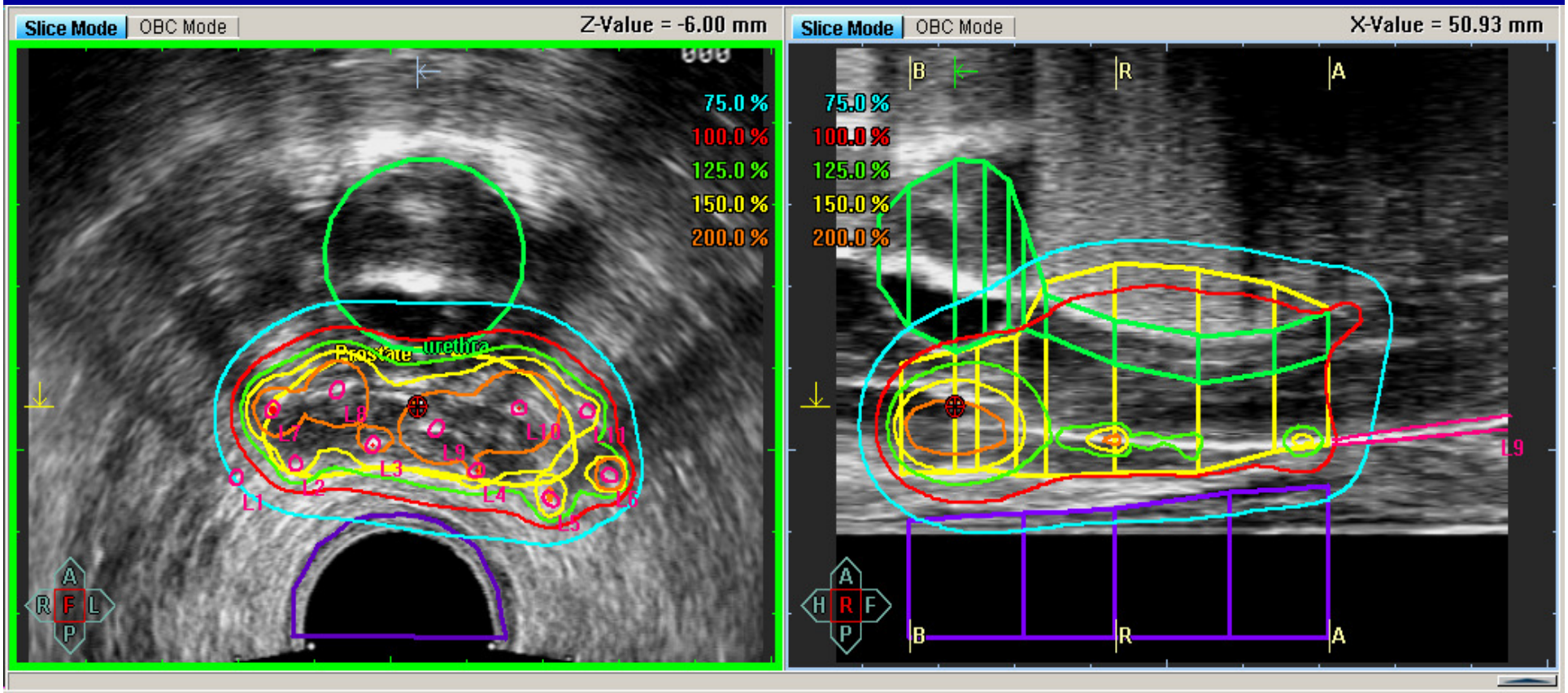

Slice Mode
OBC Mode
Y-Value = 48.64 mm
75.0 %
100.0 %
125.0 %
150.0 %
200.0 %
Volume
3D Mode
DVH Mode
3D Graph
Prostate
urethra
rectum
Dose:
100.0 %
Slice Mode
OBC Mode
Z-Value = -27.98 mm
75.0 %
100.0 %
125.0 %
150.0 %
200.0 %
Slice Mode
OBC Mode
X-Value = 51.83 mm
75.0 %
100.0 %
125.0 %
150.0 %
200.0 %

DOSIMETRY AT THE LEVEL OF THE SEMINAL VESICLES



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BED BASED ON α/β RATIOS

	1.5	3.0	5.0
4 X 9.5 Gy= 38	267	133	110
2 x 12 Gy= 24	208	103	82
2 x 13.5 Gy= 27	264	130	101
1 x 19 Gy	260	139	91
45 x 1.8 Gy =81 Gy MPD-IMRT	174	122	96

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MONOTHERAPY HDR CONSTRAINTS

PROSTATE

V100 ≥ 95%

V125 < 55%

V150 < 25%

URETHRA

V115 < 1%

V110 < 3%

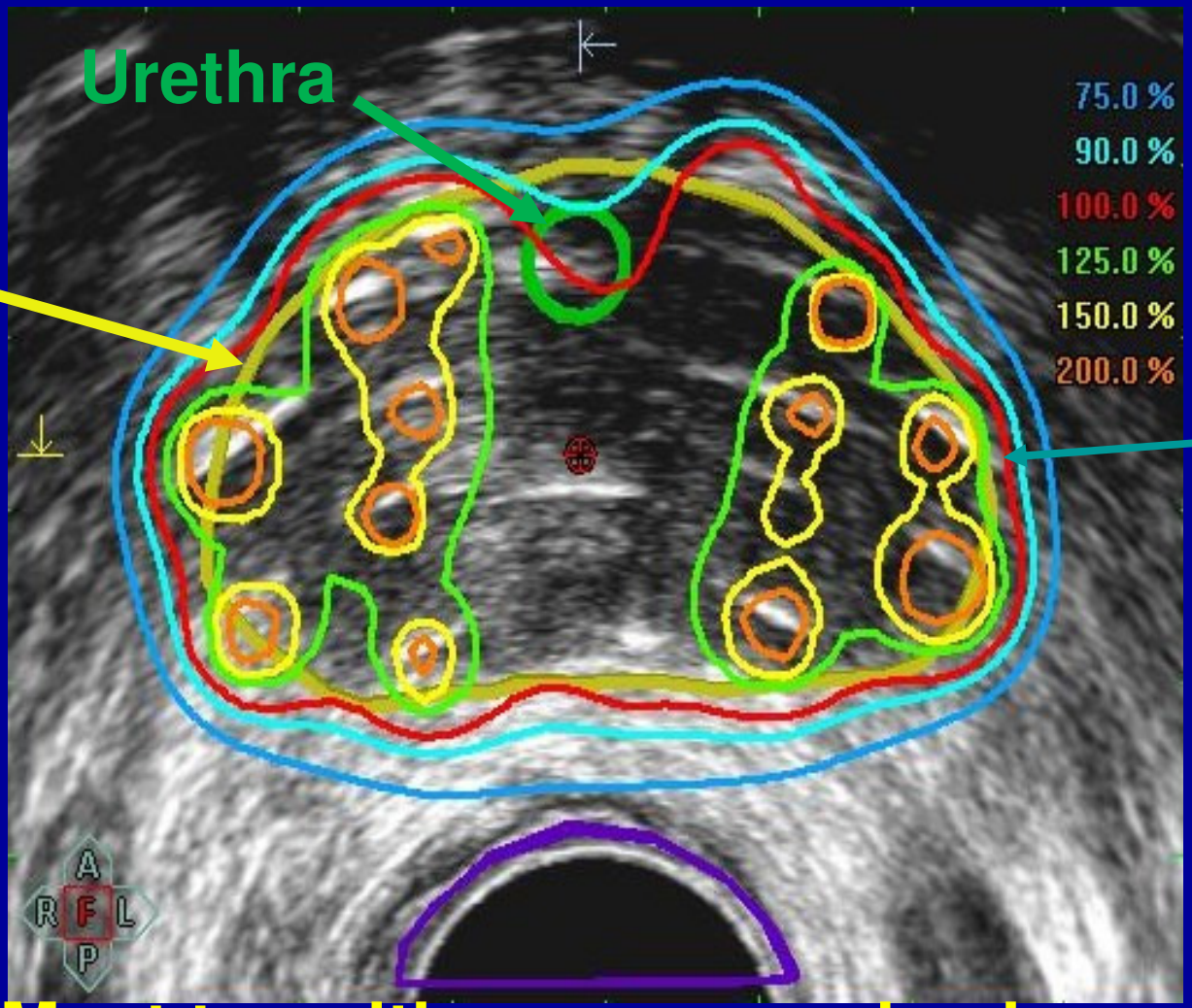
V90 ≤ 90%

RECTUM

<75% TO 1cc

WBH - Real-time TRUS Final Dosimetry

T2a Gleason 6 Lt, 7 Rt, PSA 9.2



Most transition zone received 125% green, wider margin on Rt

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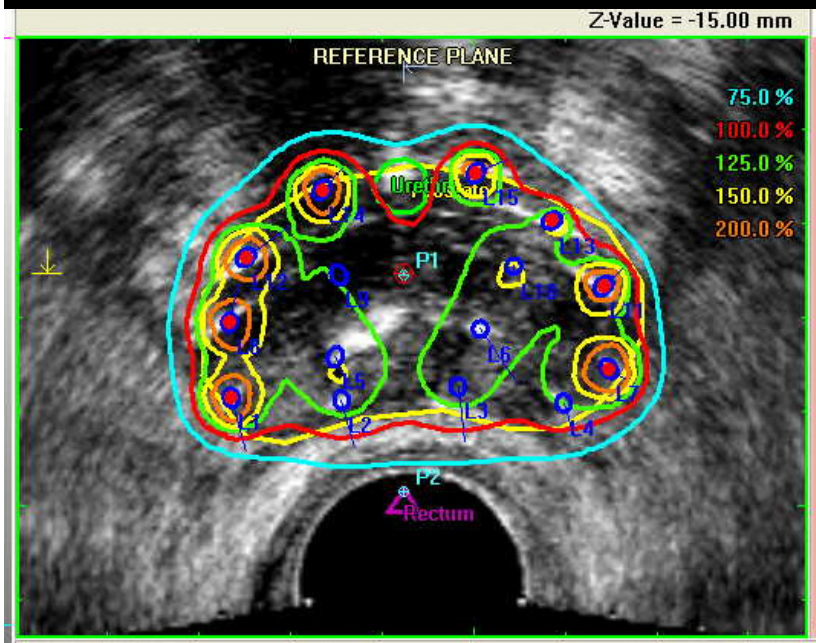
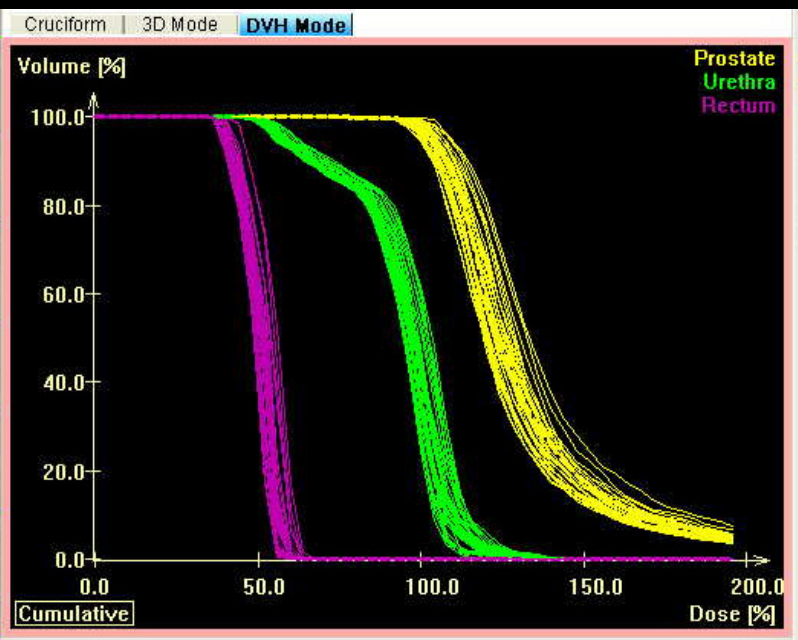




Optimization

Multi Inverse Planning

Geometrical

Inverse Optimization

Inverse Optimization

Manual | Graphical

Inverse Plan

Dose Sampling Settings

Optimization Settings

Decision Settings

Optimize

History

Activate

Undo

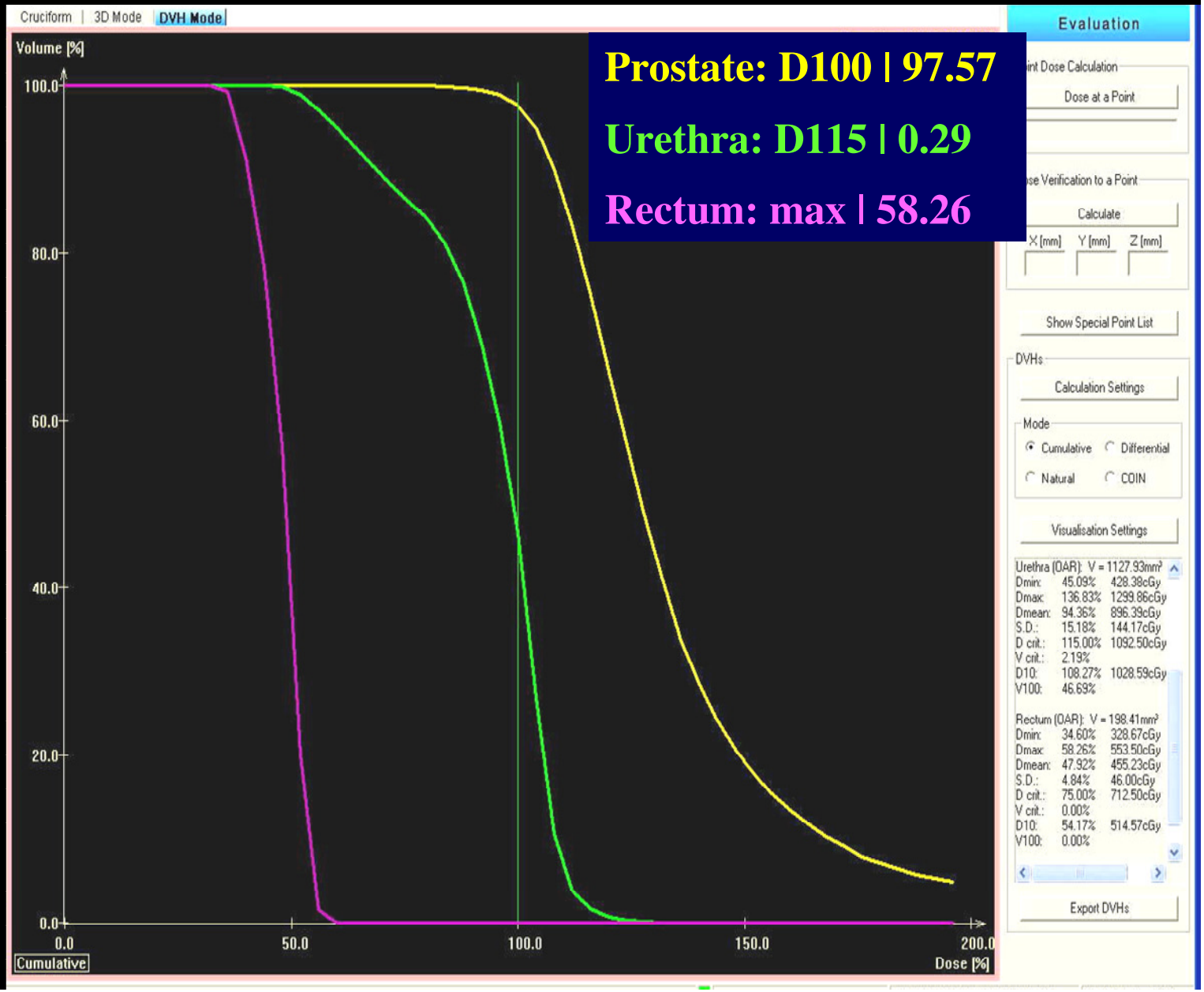
No.	PTV-V100[%]	PTV-V125[%]	Urethra-Vcrit.[%]	Rectum-Dmax[%]
22	99.600	69.550	9.500	64.225
6	99.400	63.400	8.575	65.750
25	99.400	63.400	8.575	65.750
30	99.400	63.400	8.575	65.750
31	99.400	61.350	9.300	62.362
24	99.200	67.675	5.100	65.132
29	99.100	52.575	5.975	61.020
14	99.000	59.450	6.100	61.147
10	98.900	56.225	6.600	60.754
5	98.600	53.125	9.800	62.566
13	98.500	49.475	4.625	61.337
20	98.400	51.150	9.100	59.747
3	98.200	56.425	7.300	64.520
21	98.200	53.025	3.325	61.213
9	98.100	53.500	1.775	60.793
23	98.100	53.500	1.775	60.793
8	98.000	46.450	7.850	58.919
35	97.900	50.850	6.525	60.062
16	97.500	47.725	5.450	59.637
11	97.200	45.975	6.175	58.577
32	97.200	47.925	1.525	61.206
26	97.000	45.100	4.325	57.708
33	97.000	47.825	5.175	59.894
34	96.900	43.625	3.900	59.157
15	96.700	43.300	1.675	58.352
27	96.500	43.525	3.050	58.740

PROSTATE IG-HDR BRACHYTHERAPY

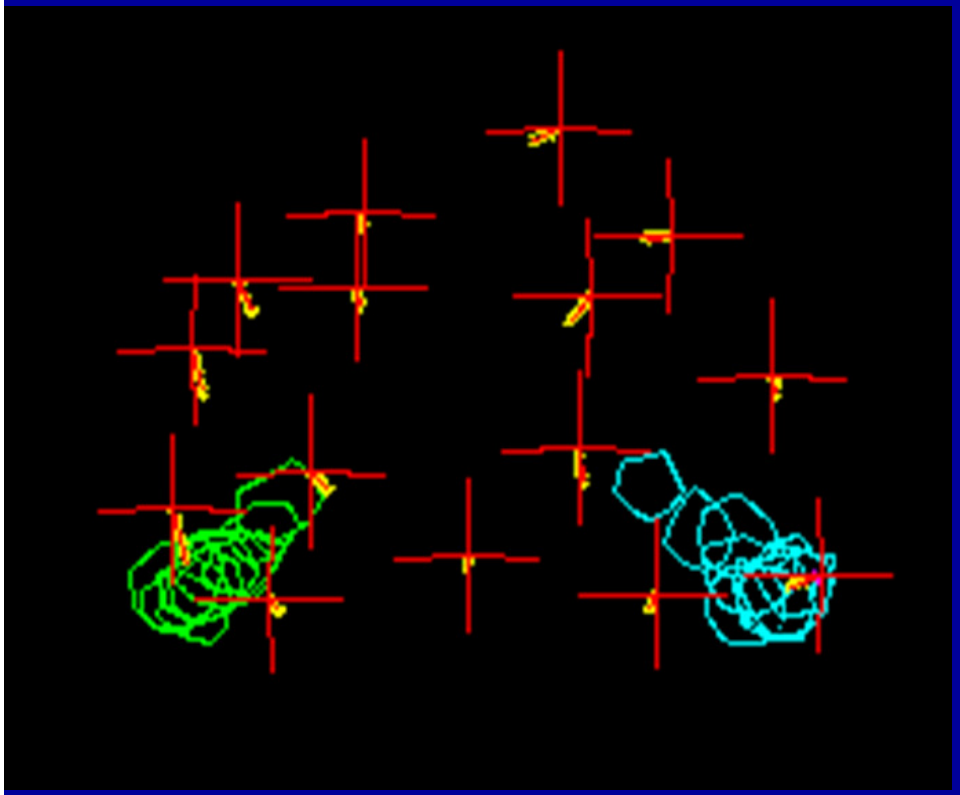
Intra-op

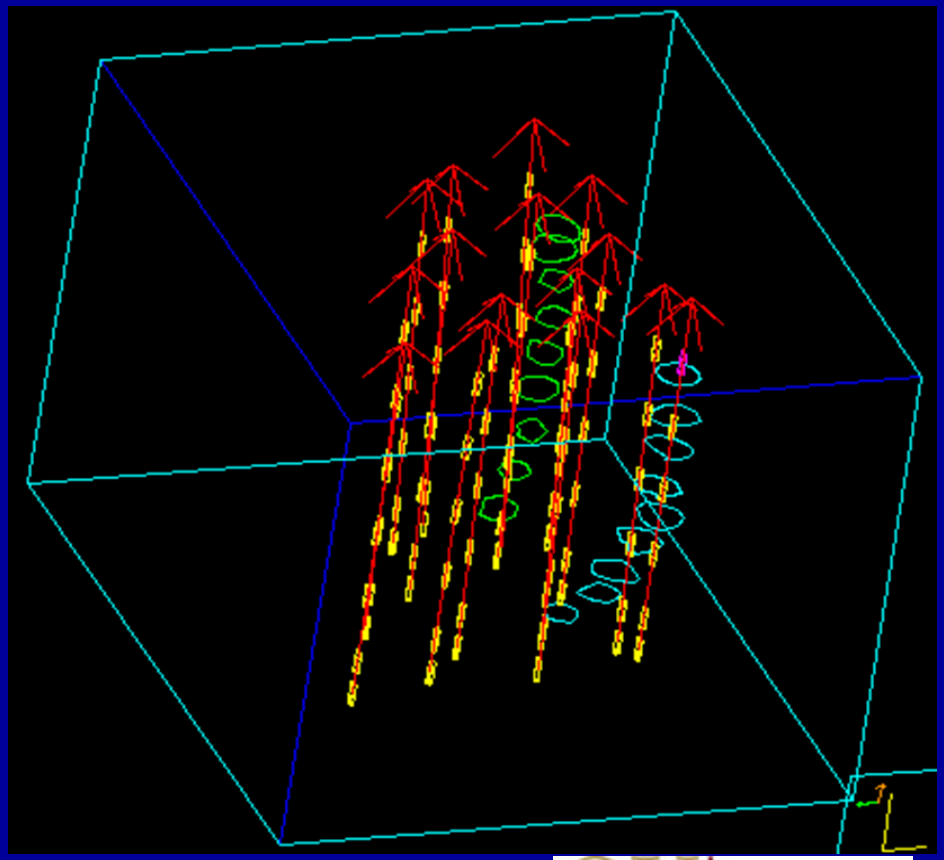
DVHs for

Prostate
Urethra
Rectum



SPATIAL RELATIONSHIP OF THE NVB AND HDR NEEDLES





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PURPOSE

- USING THE CTCAE v 3.0, TO PRESENT THE COMPARISON OF
  - ACUTE GU & GI TOXICITIES OF THE 3 BRACHYTHERAPY DOSE SCHEDULES
  - CHRONIC GU & GI TOXICITIES OF 38 Gy (9.5 Gy X 4) & 24 Gy (12 Gy X 2)
  - PSA CONTROL AND OS FOR THESE 2 BRACHYTHERAPY DOSES SCHEDULES

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FOLLOW UP BY HDR SCHEDULE
Stage ≤T2b, Gleason ≤7, PSA ≤15

	All Patients	9.5 Gy x 4	12 Gy x 2	13.5 Gy x 2
# of patients	484	320	72	92
F/U mean range	5.1 0.6-11.3	6.9 0.9-11	4.6 0.8-6.4	2.4 0.6-3.9

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CTCAE v 3.0
Chronic Gastro-Intestinal Toxicity

	9.5 Gy x 4		12 Gy x 2	
	Grade 1	Grade 2	Grade 1	Grade 2
Diarrhea	4 (1.3%)	0	1 (1.4%)	0
Rectal Bleeding	1 (0.3%)	1 (0.3%)	0	0
Proctitis	1 (0.3%)	1 (0.3%)	0	0
Rectal Pain / Tenesmus	1 (0.3%)	0	0	0
Rectal Fistula	0	0	0	0
Anal Fissure	0	0	0	0

No grade 3 or 4 was found.

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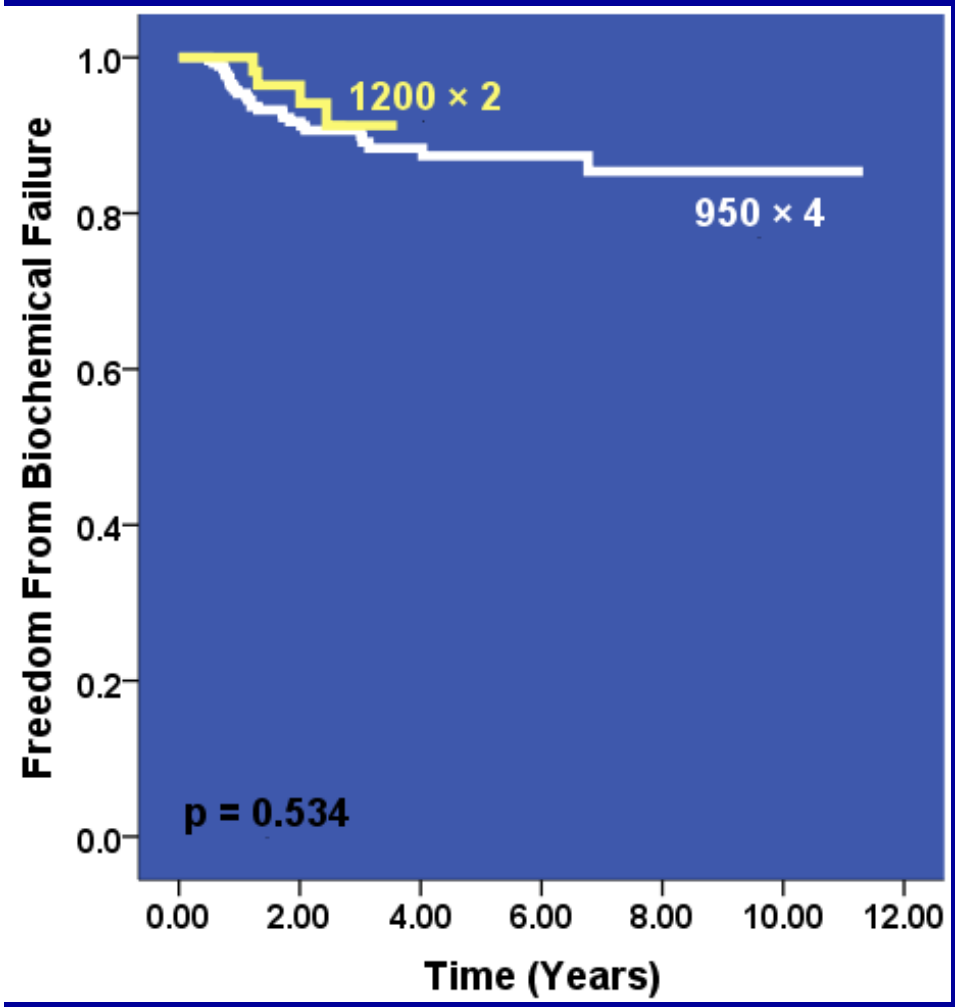
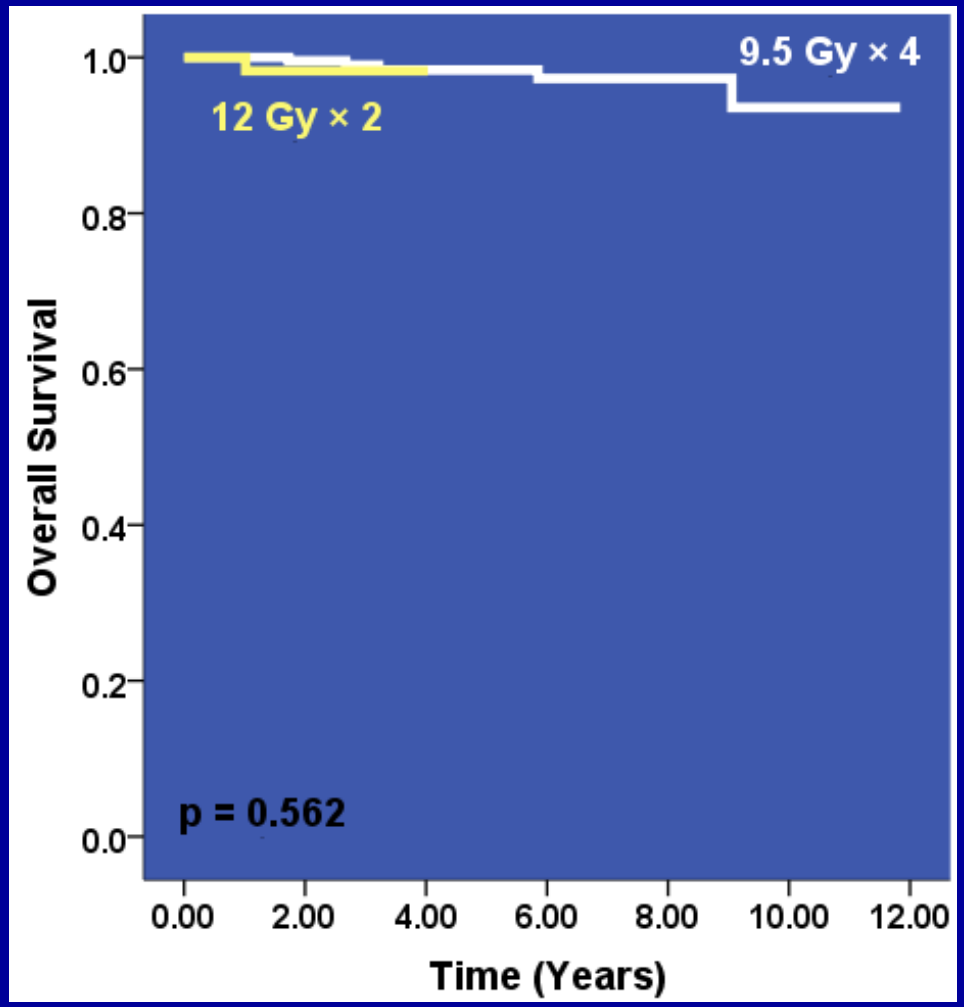
CTCAE v 3.0
Chronic Genito-Urinary Toxicity

	9.5 Gy x 4			12 Gy x 2		
	Grade 1	Grade 2	Grade 3	Grade 1	Grade 2	Grade 3
Dysuria	13 (4.2%)	9 (2.9%)	1 (0.3%)	4 (5.7%)	1 (1.4%)	0
Frequency/Urgency	42 (13.5%)	10 (3.2%)	0	14 (20%)	3 (4.3%)	0
Retention	13 (4.2%)	1 (0.3%)	2 (0.6%)	6 (8.6%)	0	0
Incontinence	8 (2.6%)	1 (0.3%)	1 (0.3%)	1 (1.4%)	0	0
Hematuria	3 (1.0%)	1 (0.3%)	0	2 (2.9%)	0	0
Urethral Stricture	2 (0.6%)	0	4 (1.3%)	0	0	0

No grade 4 was found.

OUTCOMES





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CONCLUSIONS CHRONIC TOXICITIES 9.5Gy X 4 & 12 Gy X 2, n=392

- NO SD IN CHRONIC GU OR GI TOXICITIES AMONG THE ABOVE 2 HDR SCHEDULES
- GI ,DIARRHEA WAS THE MOST COMMON WITH 1.3% AND 1.4% G1. NO G3-G4 WERE SEEN
- GU WITH FREQ/URG THE MOST COMMONLY SEEN WITH 13.5% G1, 3.2% G2 AND 20% G1, 4.3% G2 RESPECTIVELY. UP TO 1% G3 FOR BOTH AND NO G4 SEEN.
- THE ABOVE 2 HDR SCHEDULES WERE VERY WELL TOLERATED

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CONCLUSIONS : BC AND OS
9.5Gy X 4 & 12 Gy X 2, n=392

- NO SD IN BC OR OS AMONG THE ABOVE 2 HDR SCHEDULES
- FOR PATIENTES WITH LOW AND INTERMEDIATE RISK DISEASE, BC OF 90% AND OVERAL SURVIVAL OF 97% AT 5 YEARS ARE VERY GOOD

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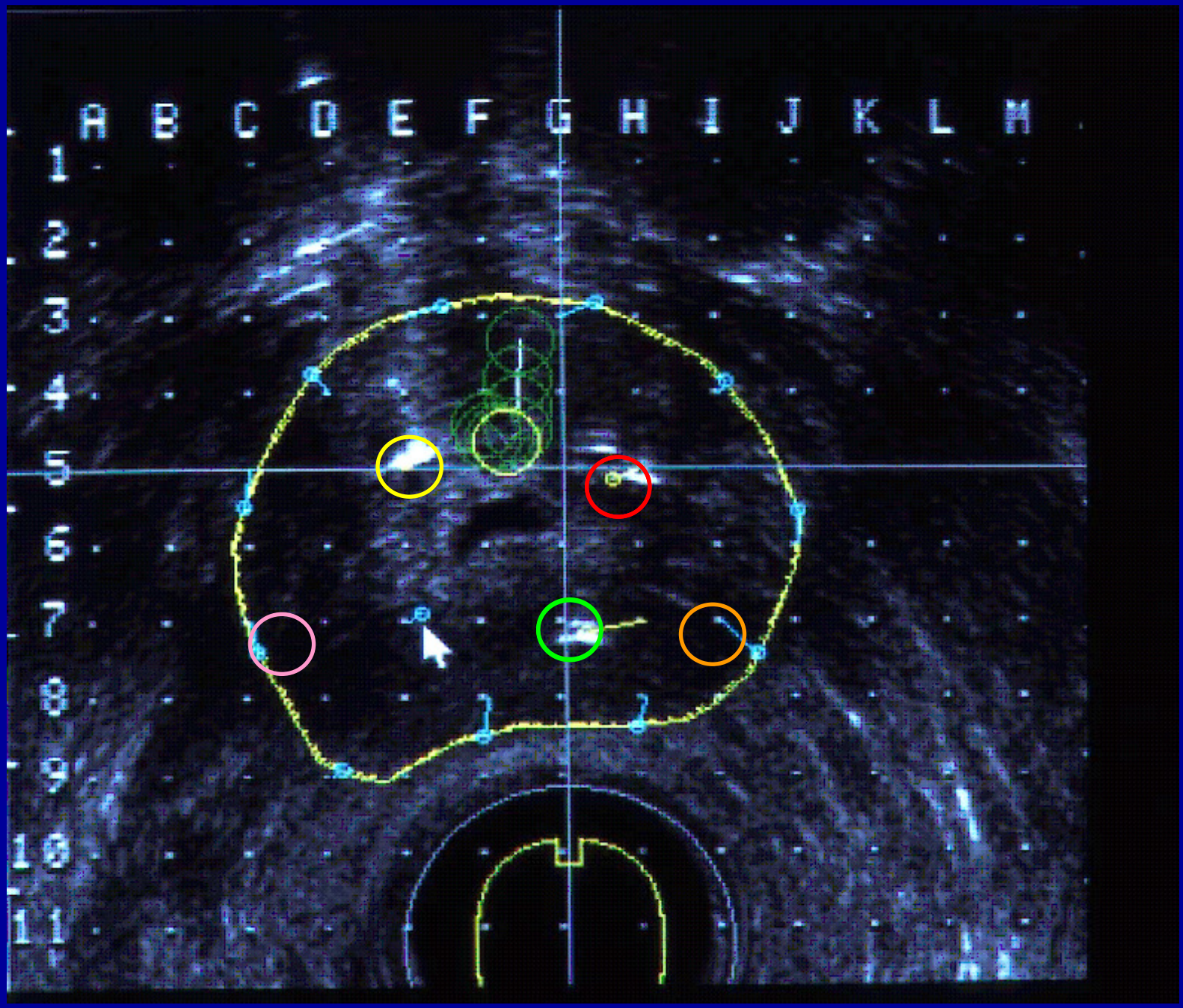
A B C D E F G H I J K L M
1
2
3
4
5
6
7
8
9
10
11

MONO & BOOST HDR CONSTRAINTS

PROSTATE

V100 ≥ 95%	V 100 ≥ 97%
V125 < 55%	V 125 <65%
V150 < 25%	V150 <30%

URETHRA

V115 < 1%	V115 < 10%
V110 < 3%	V100 < 90%
V90 ≤ 90%	

RECTUM

<75% TO 1cc	<75% TO 1%

Establishments Attitude (RO)

Whenever a new discovery is reported to the scientific world, they say first, "Its probably not true."

Thereafter when the truth of the proposition has been demonstrated beyond question, they say, "Yes, it may be true, but it is not important."

Finally, when sufficient time has elapsed to fully evidence its importance, they say, "Yes, surely it is important, but it is no longer new."

- Michel de Montaigne (1533-1592)

"ANY SIDE EFFECTS FROM YOUR PROSTATE RADIATION TREATMENTS?"

HDR 2463 Patients

THE LQM IS CLINICALLY AS GOOD AS IT GETS

THANKS TO OUR UROLOGIST & PATIENTS