HDR Brachytherapy: Results and Future Studies in Monotherapy

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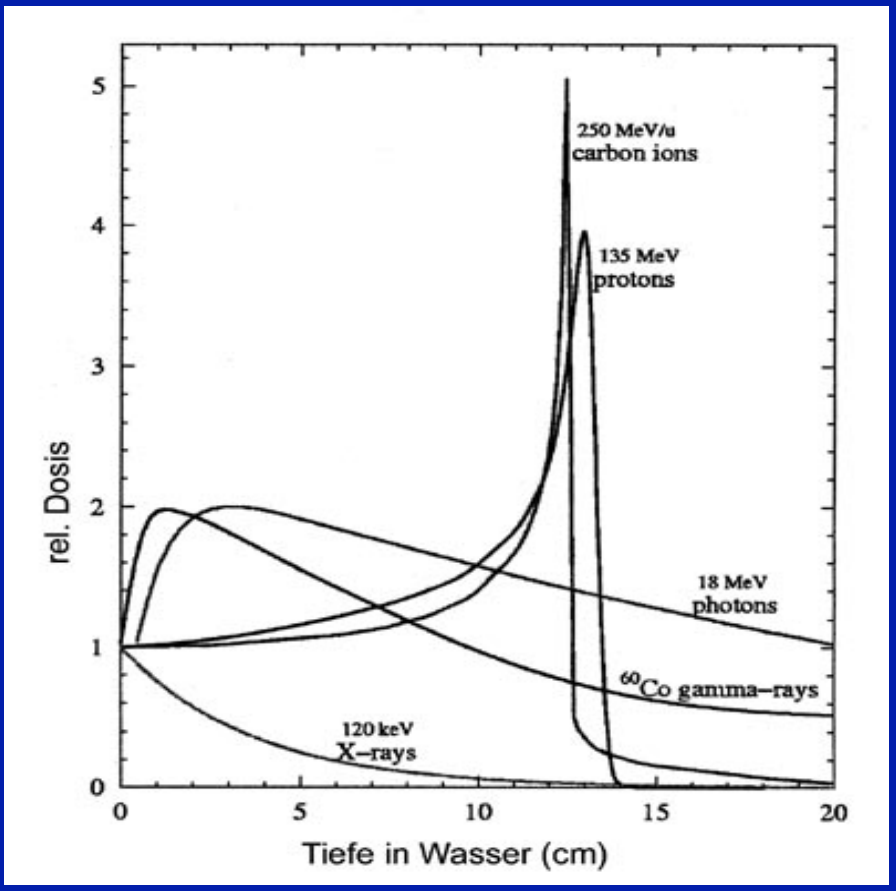
Prostate Brachytherapy
UK & Ireland Conference 2013

Comparison of Physics:

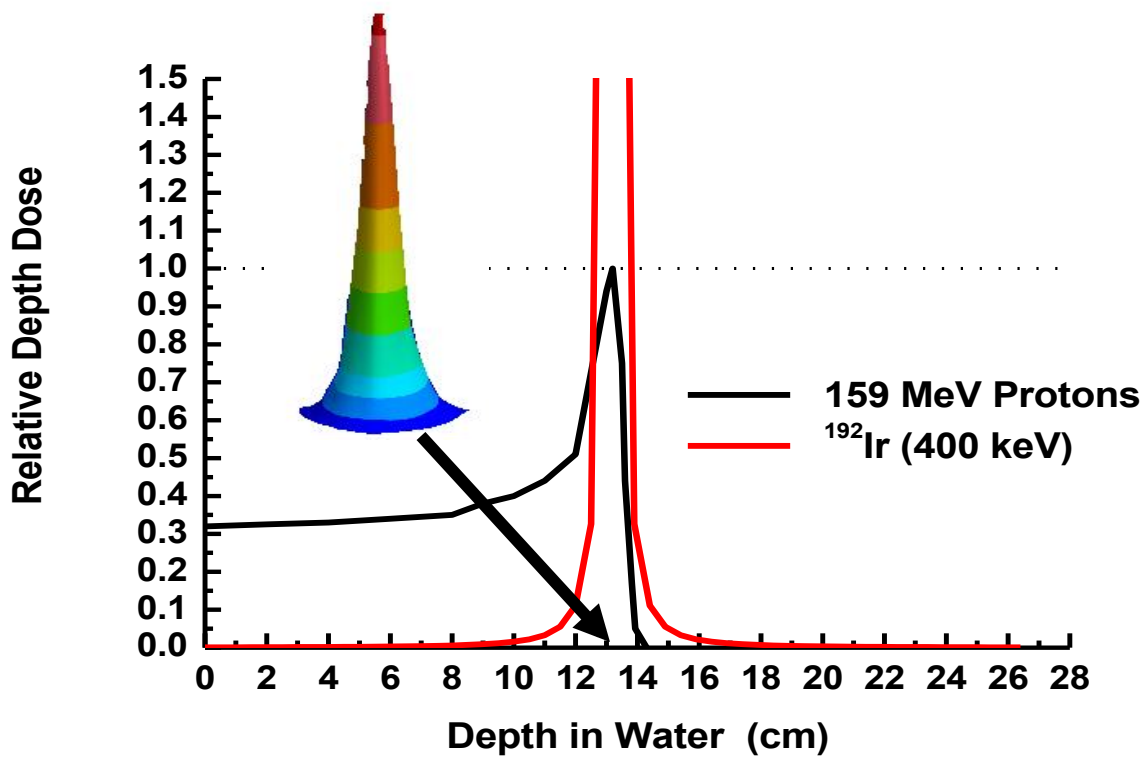
External Radiotherapy vs HDR Brachytherapy

3D Conformal Brachytherapy (3D CFBRT)

Dosimetric Kernel: Depth ➔ The Spot



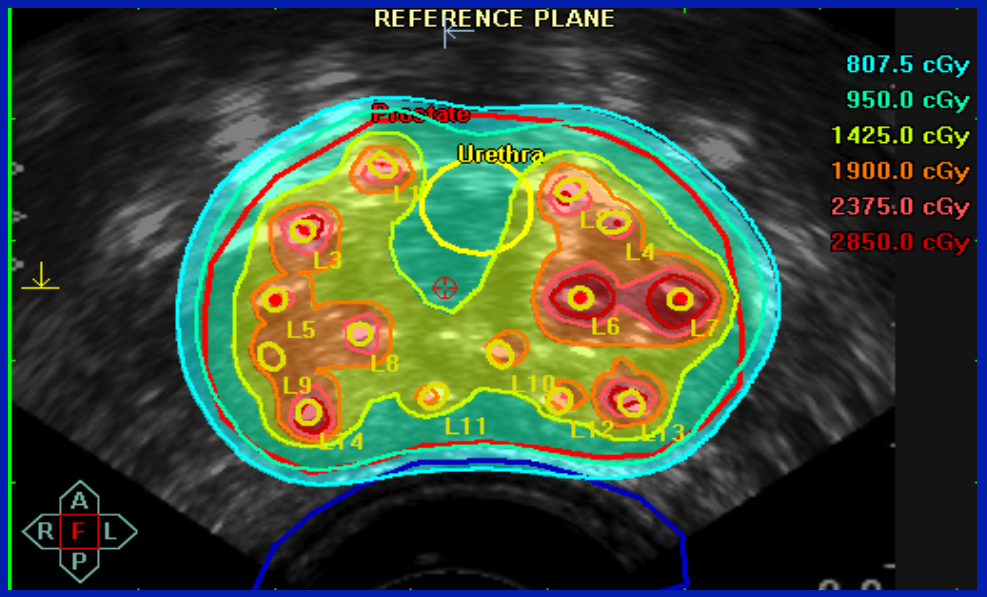
Protons vs. BRT

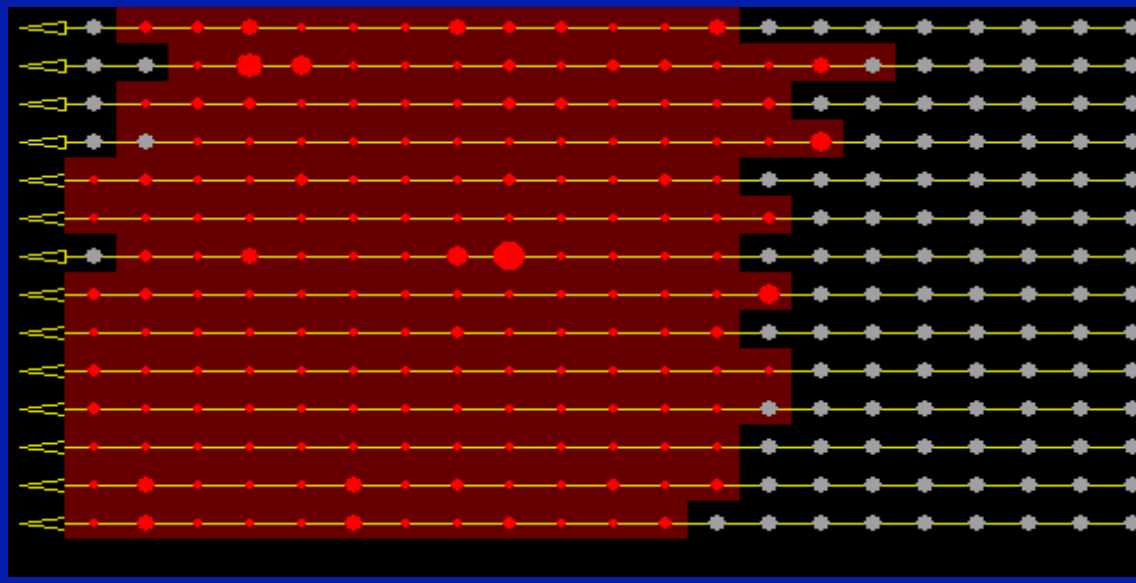


Stepping source:
Possibility of dose optimization

Conformal Radiotherapy (3D CFRT)

IMBRT



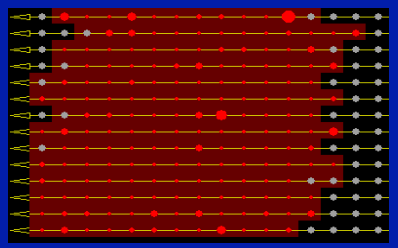


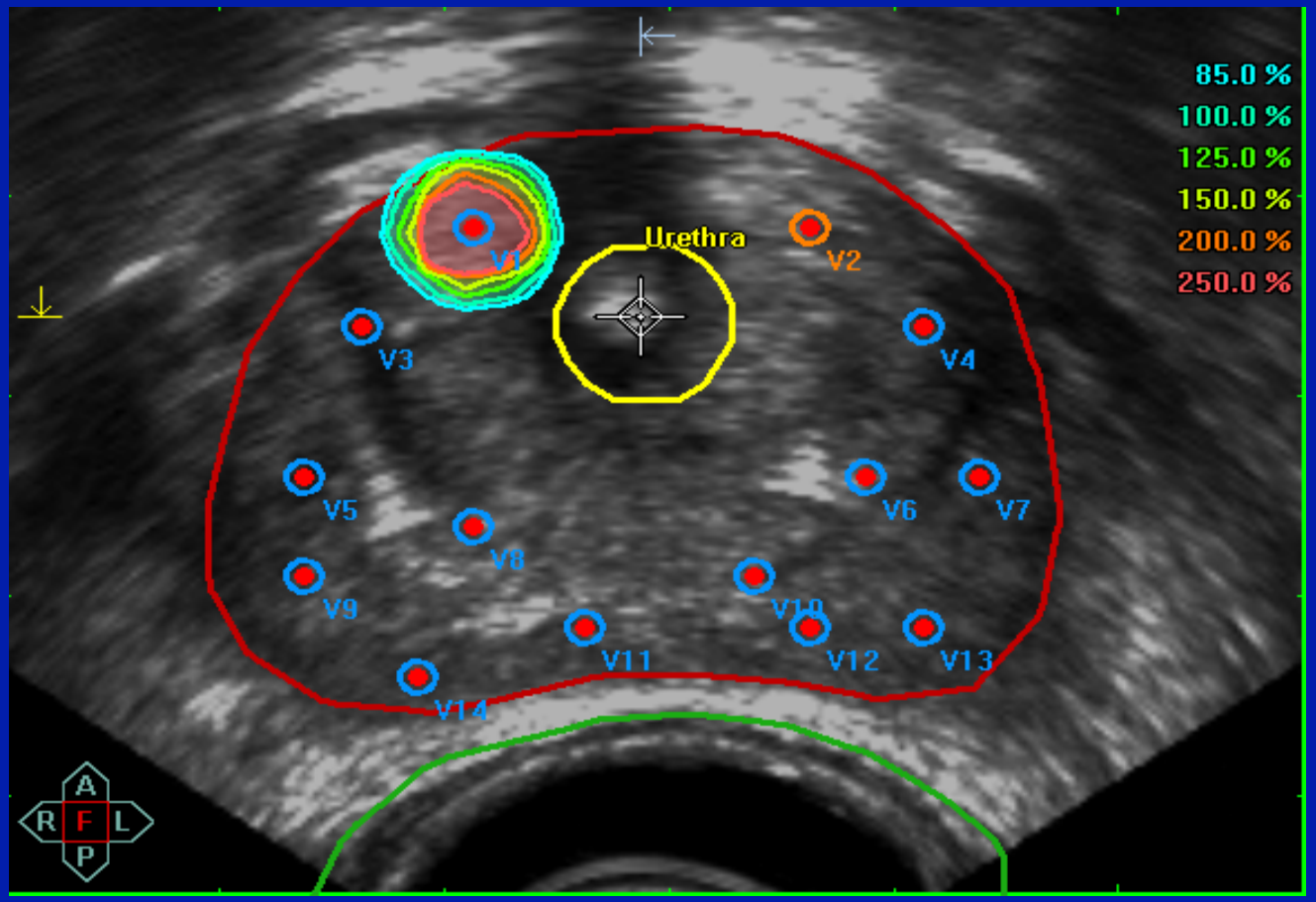
Highly inhomogeneous dwell times and positions

Dose Guided Radiotherapy

(DGRT)

DGRT (Dose Guided ...)





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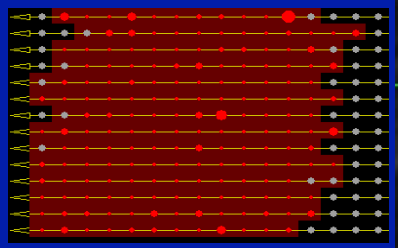

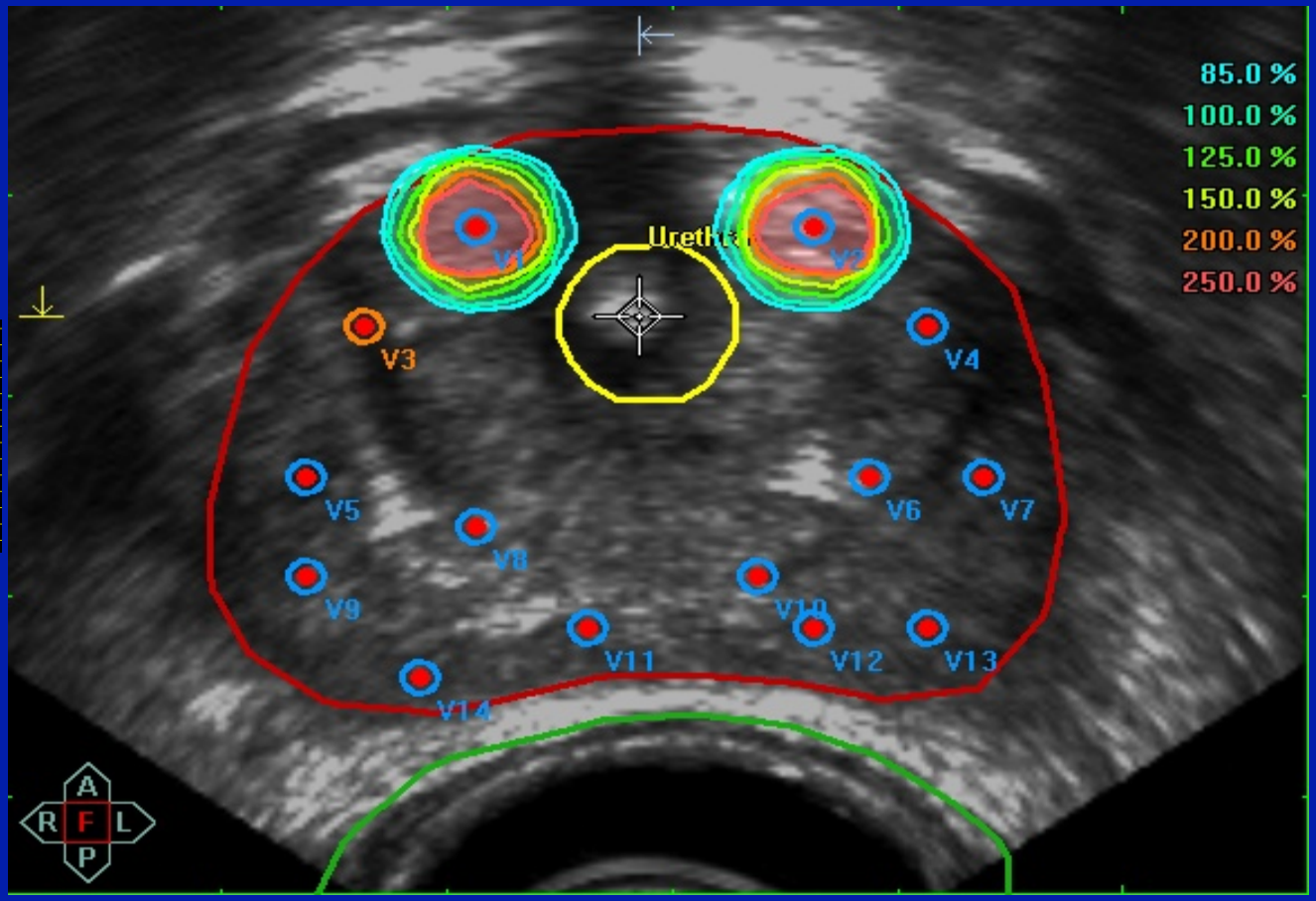

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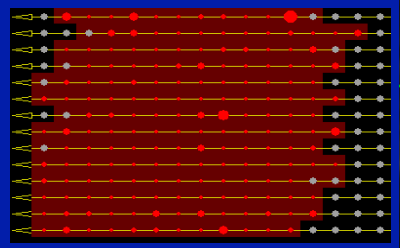

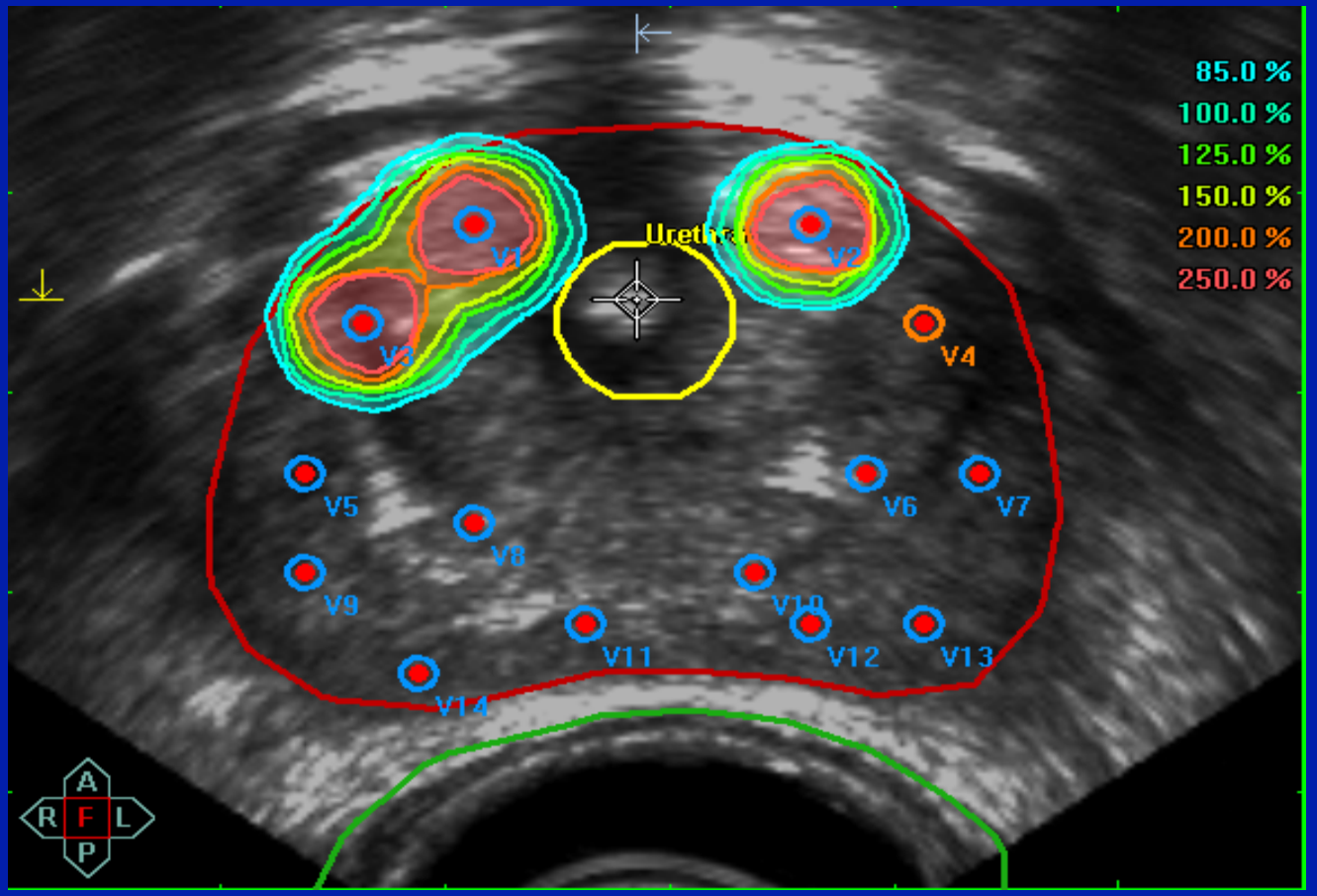

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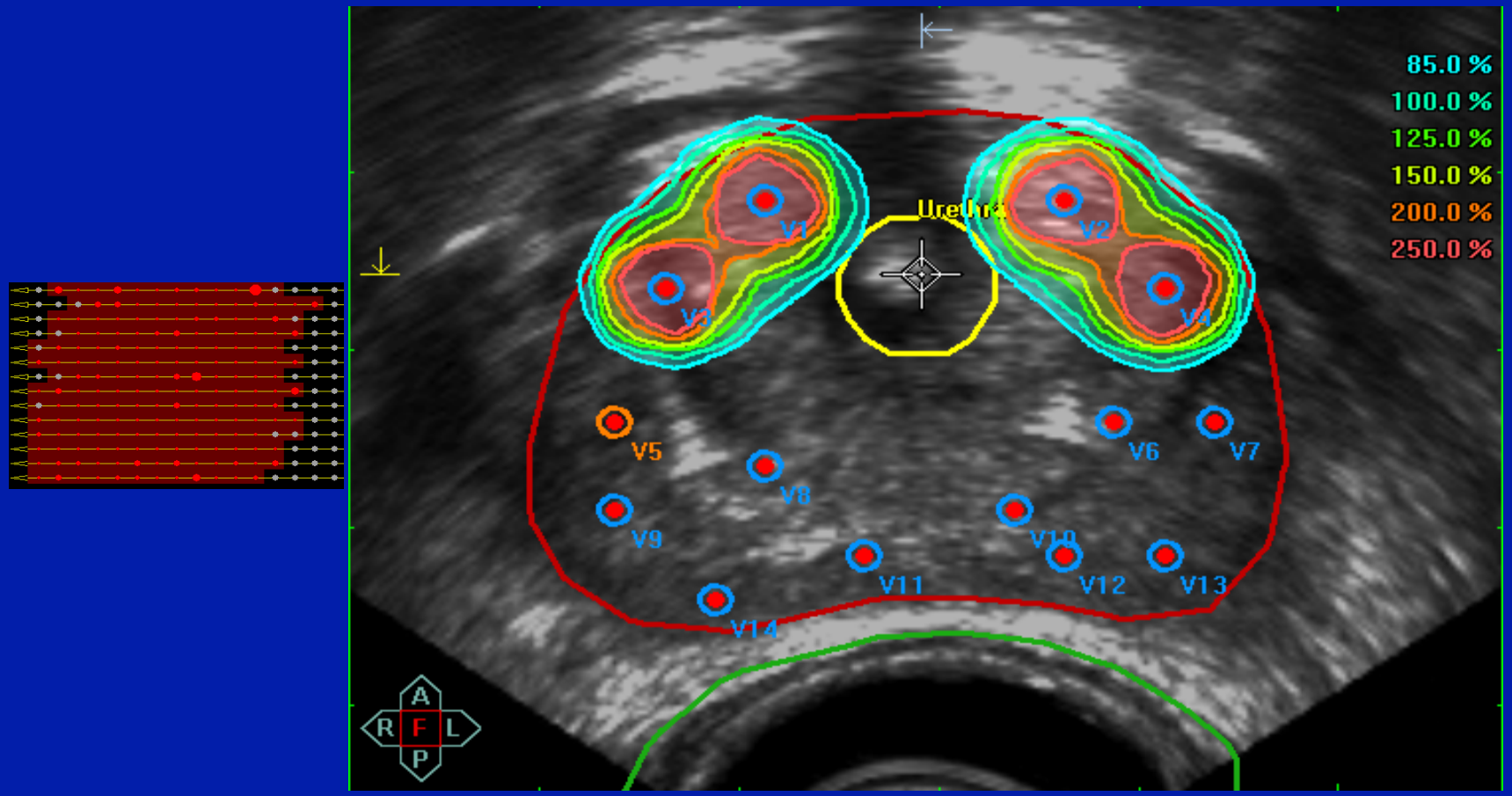

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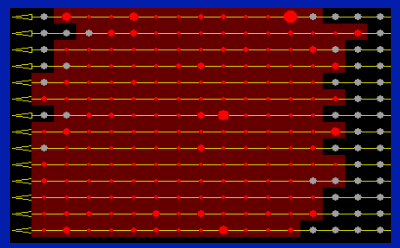

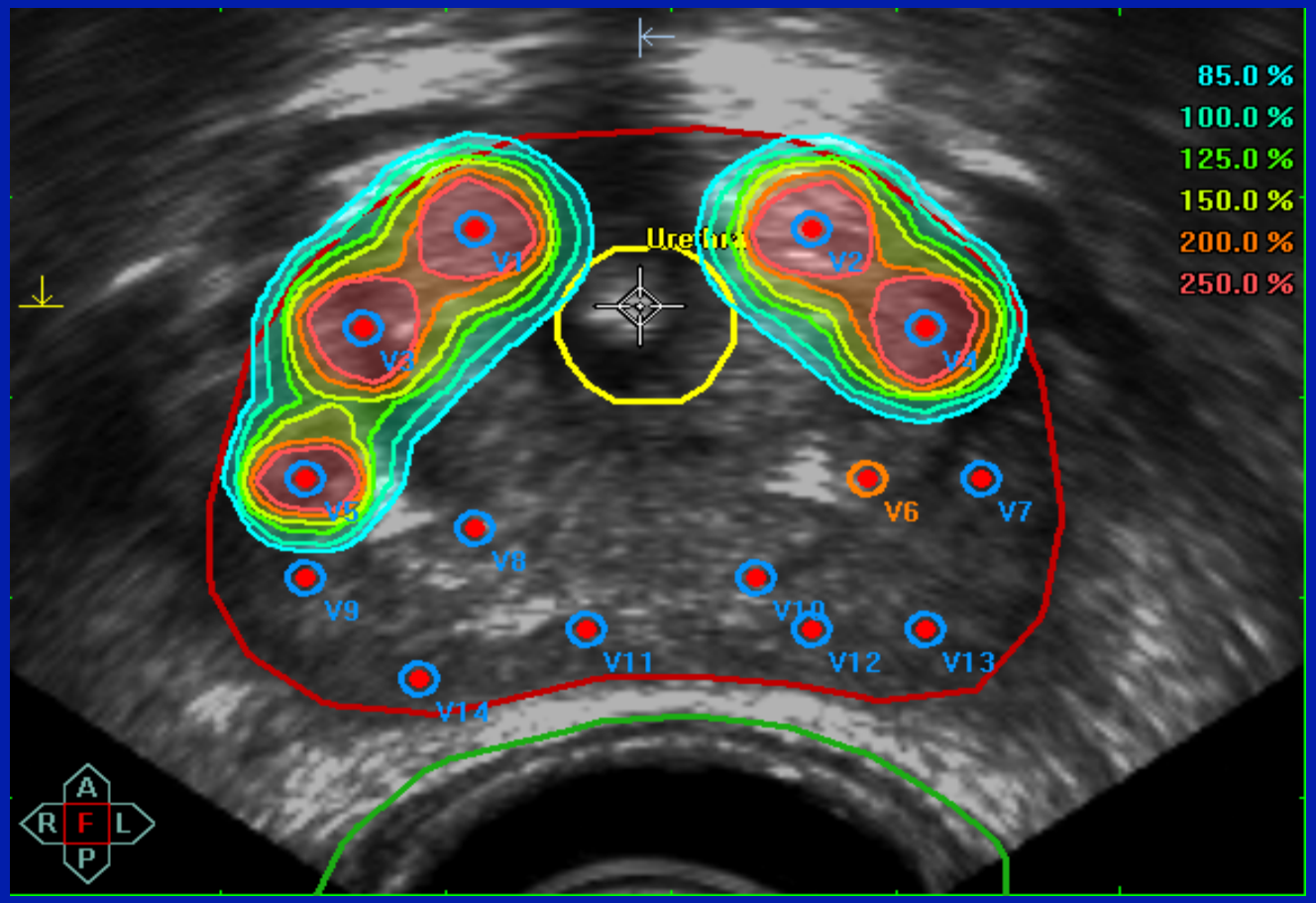

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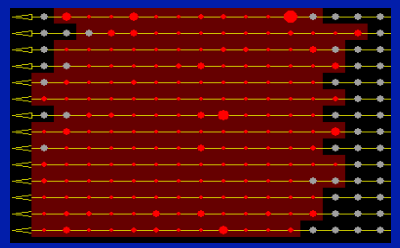

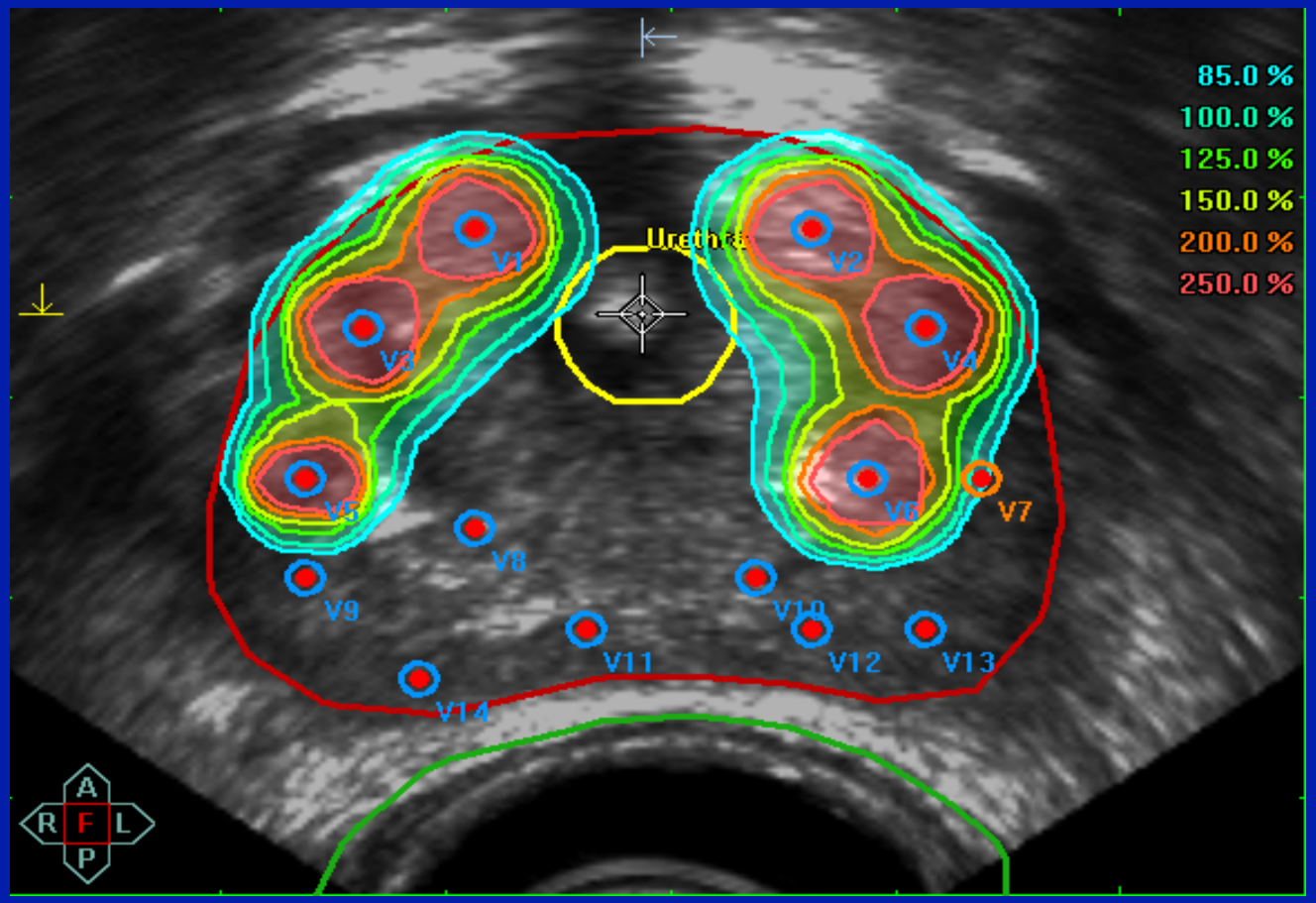

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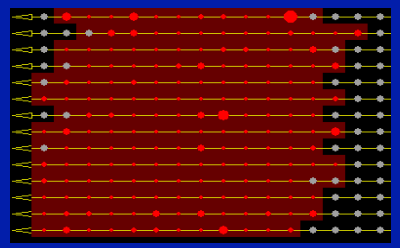

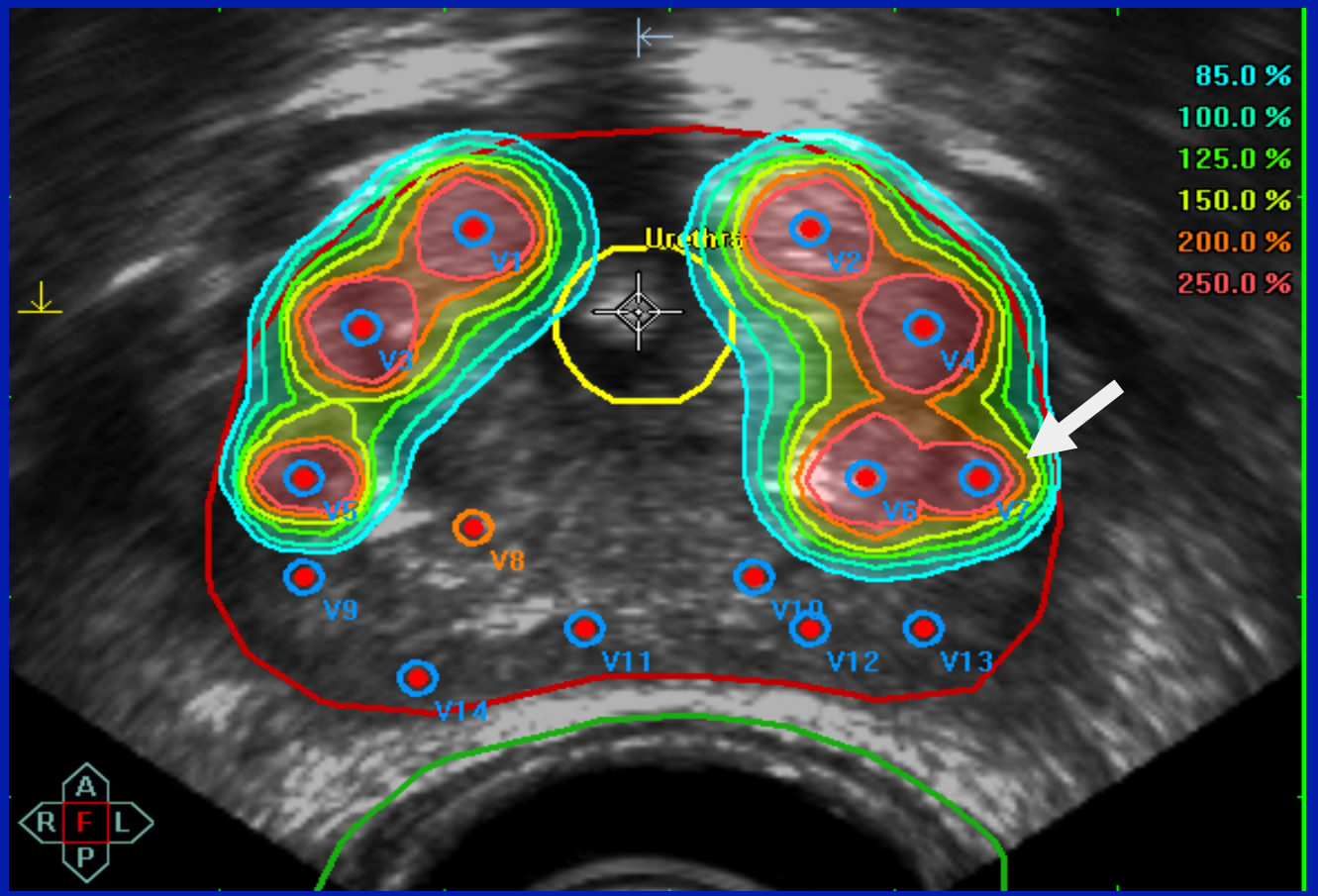

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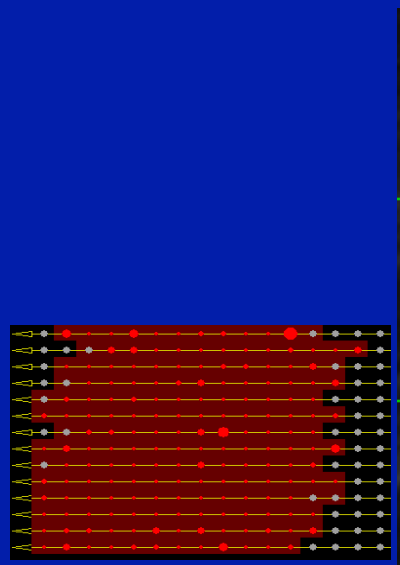

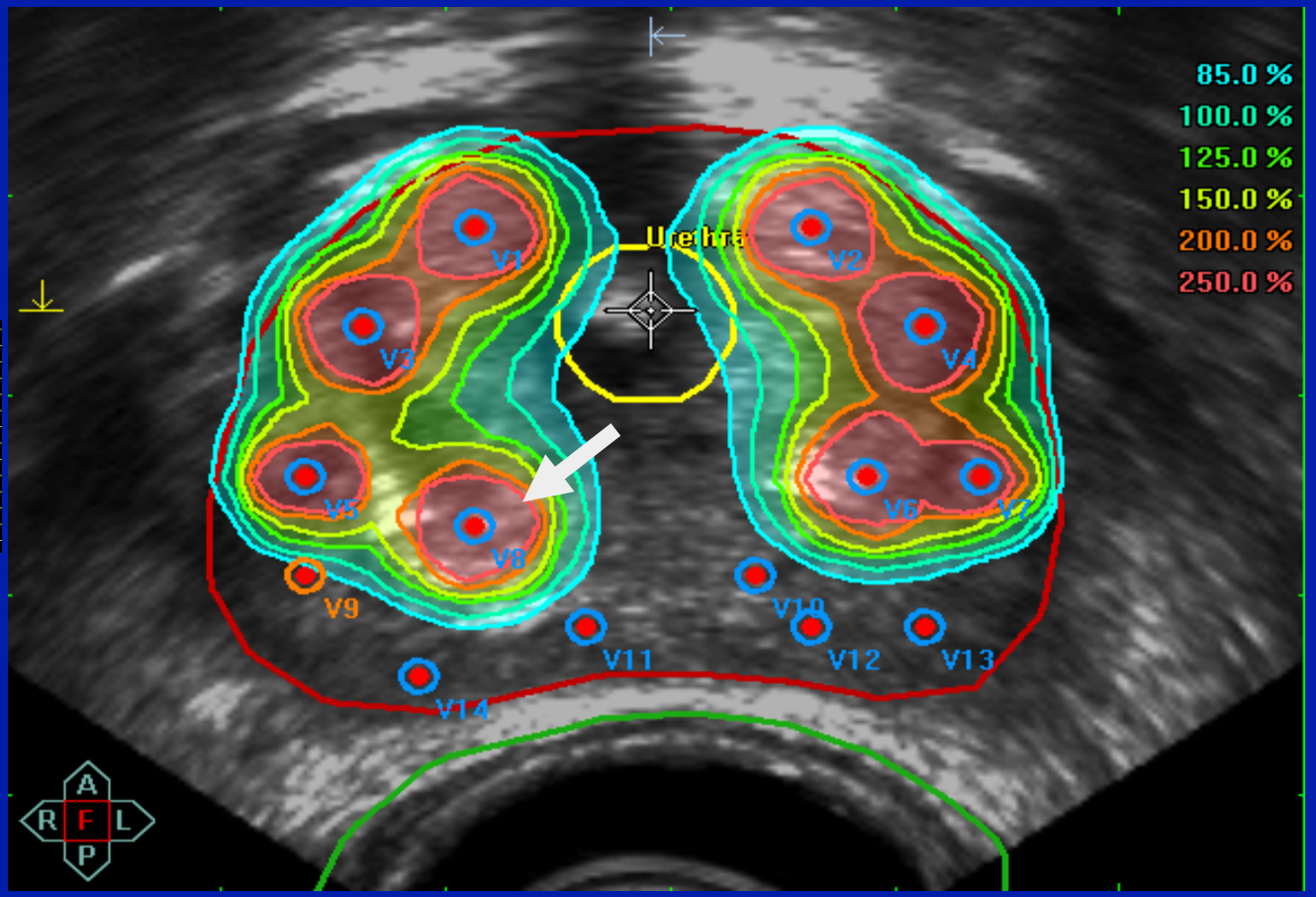

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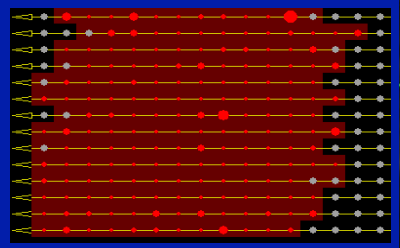

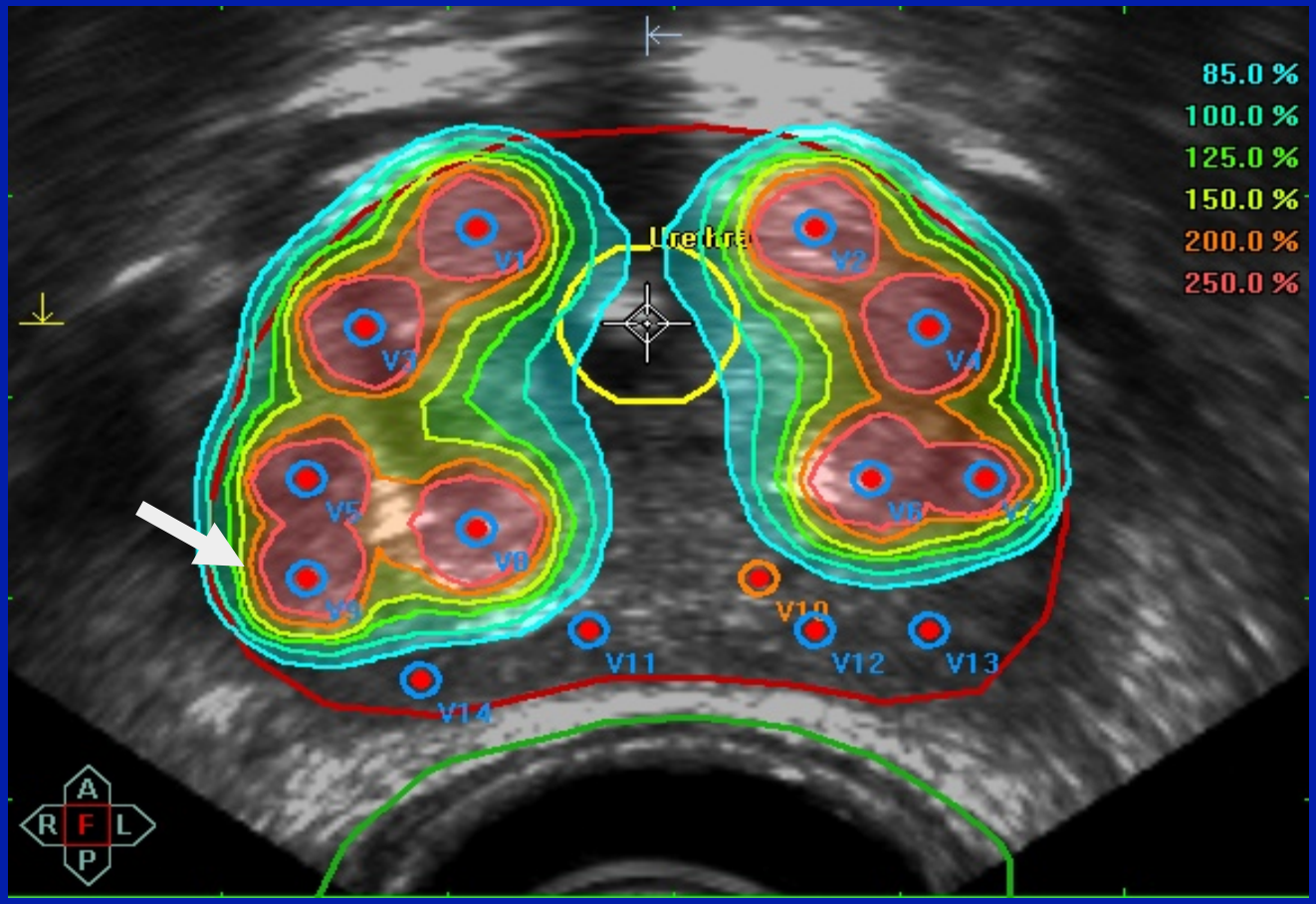

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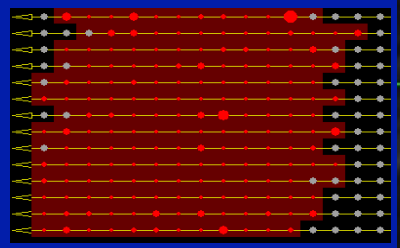

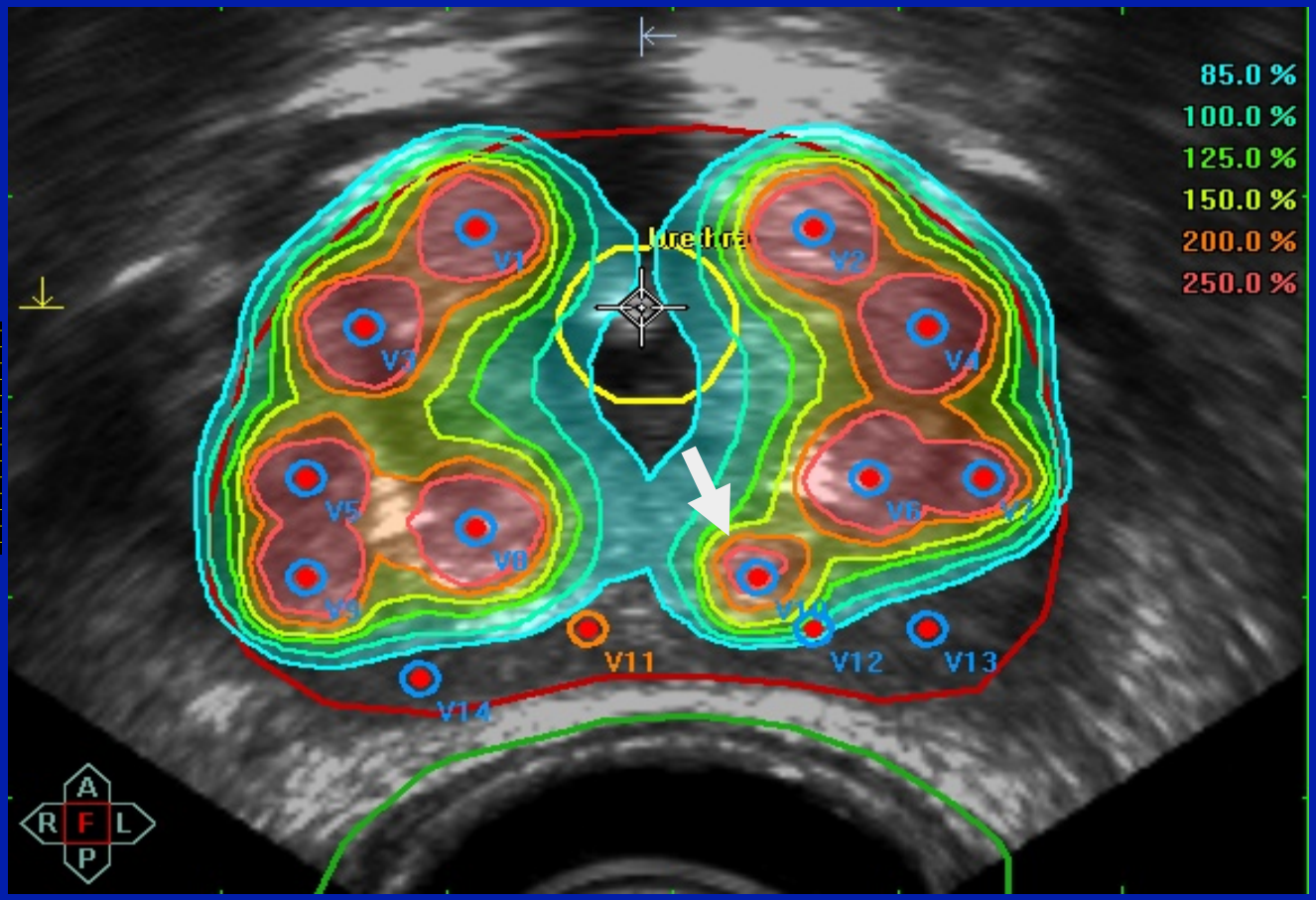

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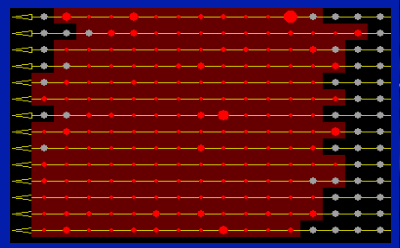

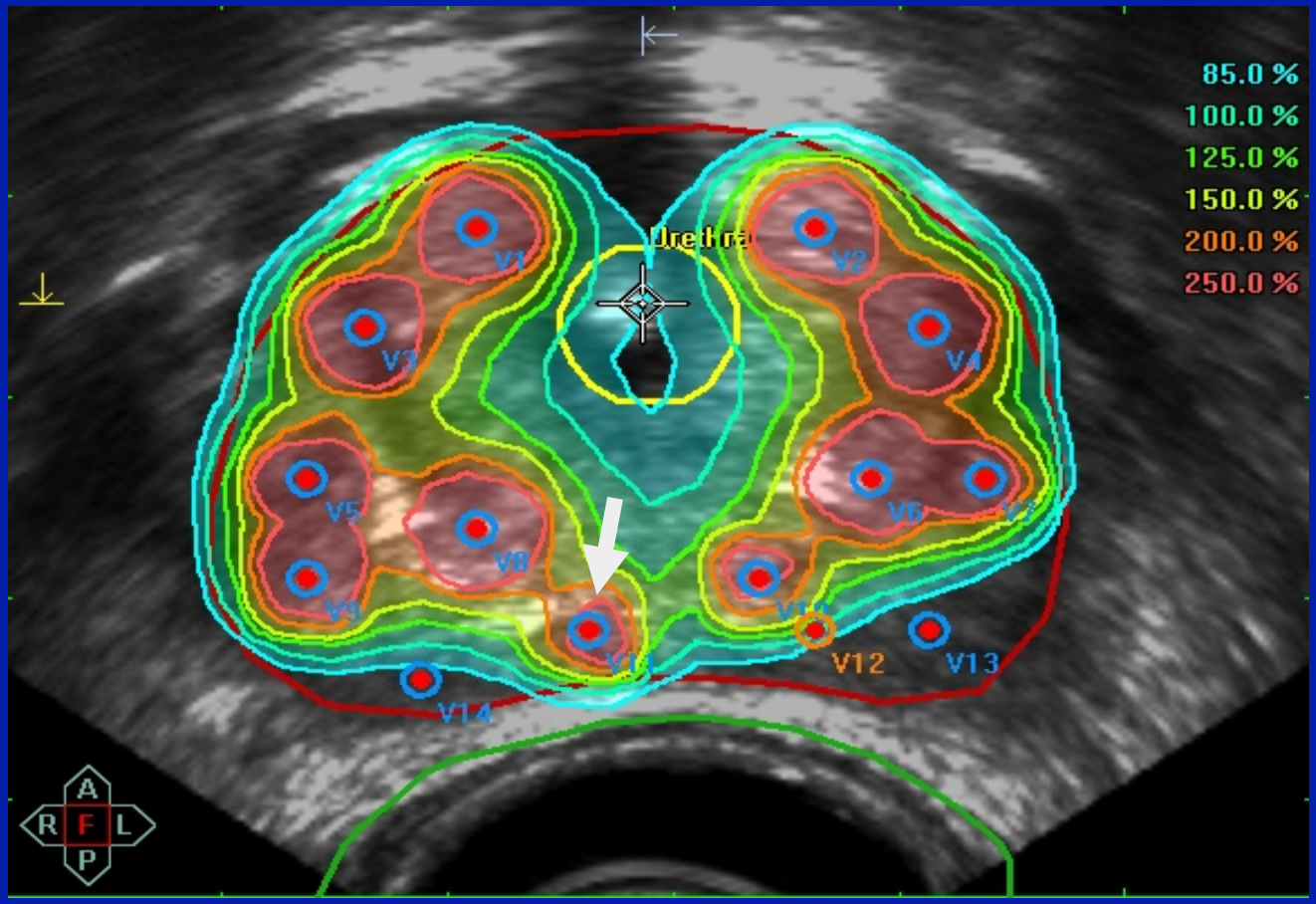

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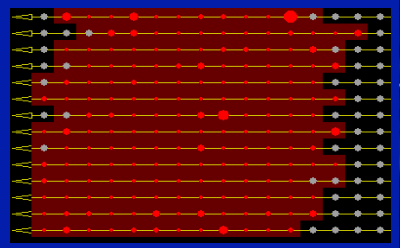

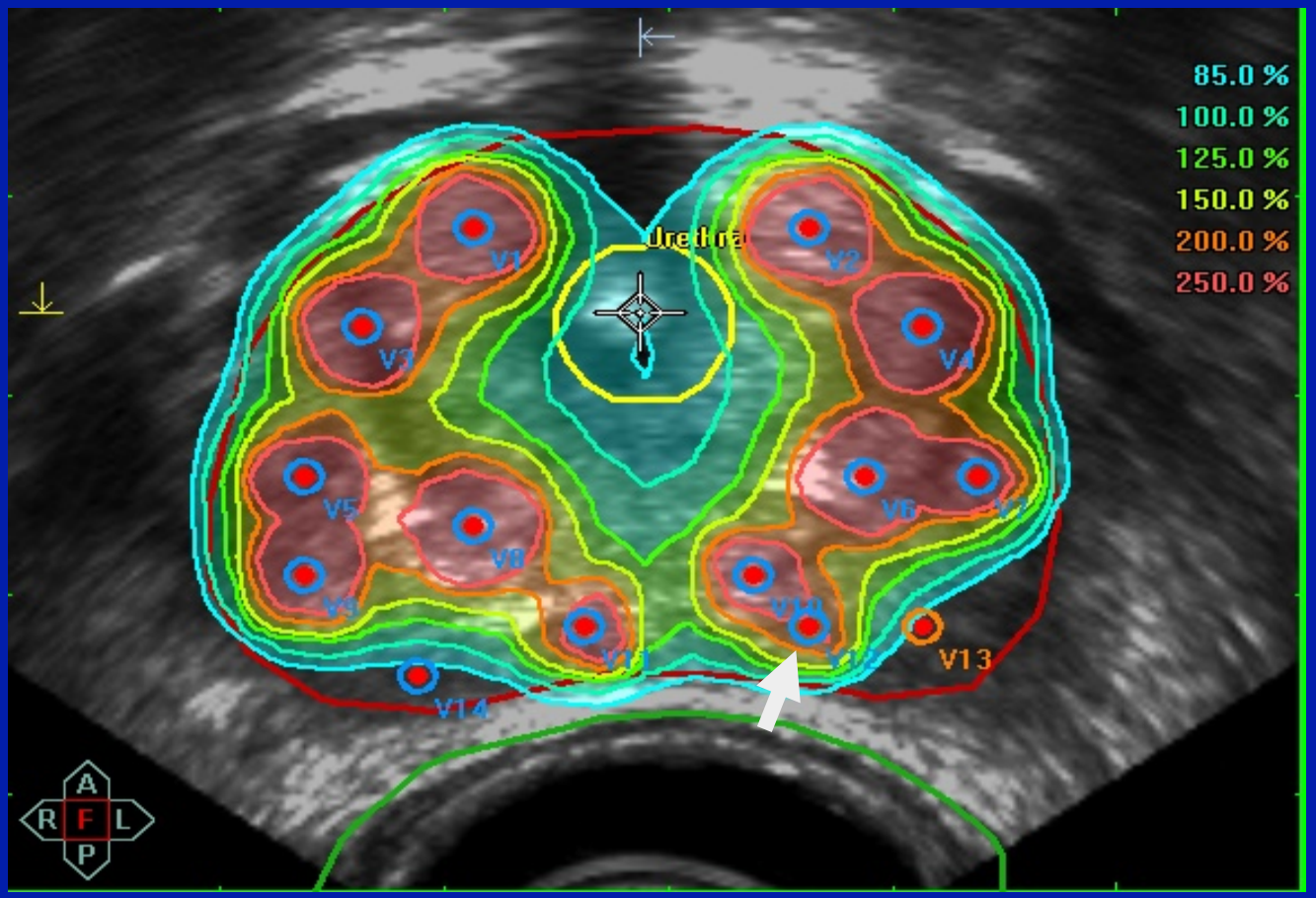

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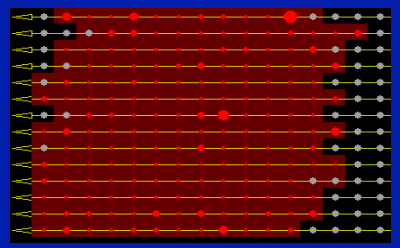

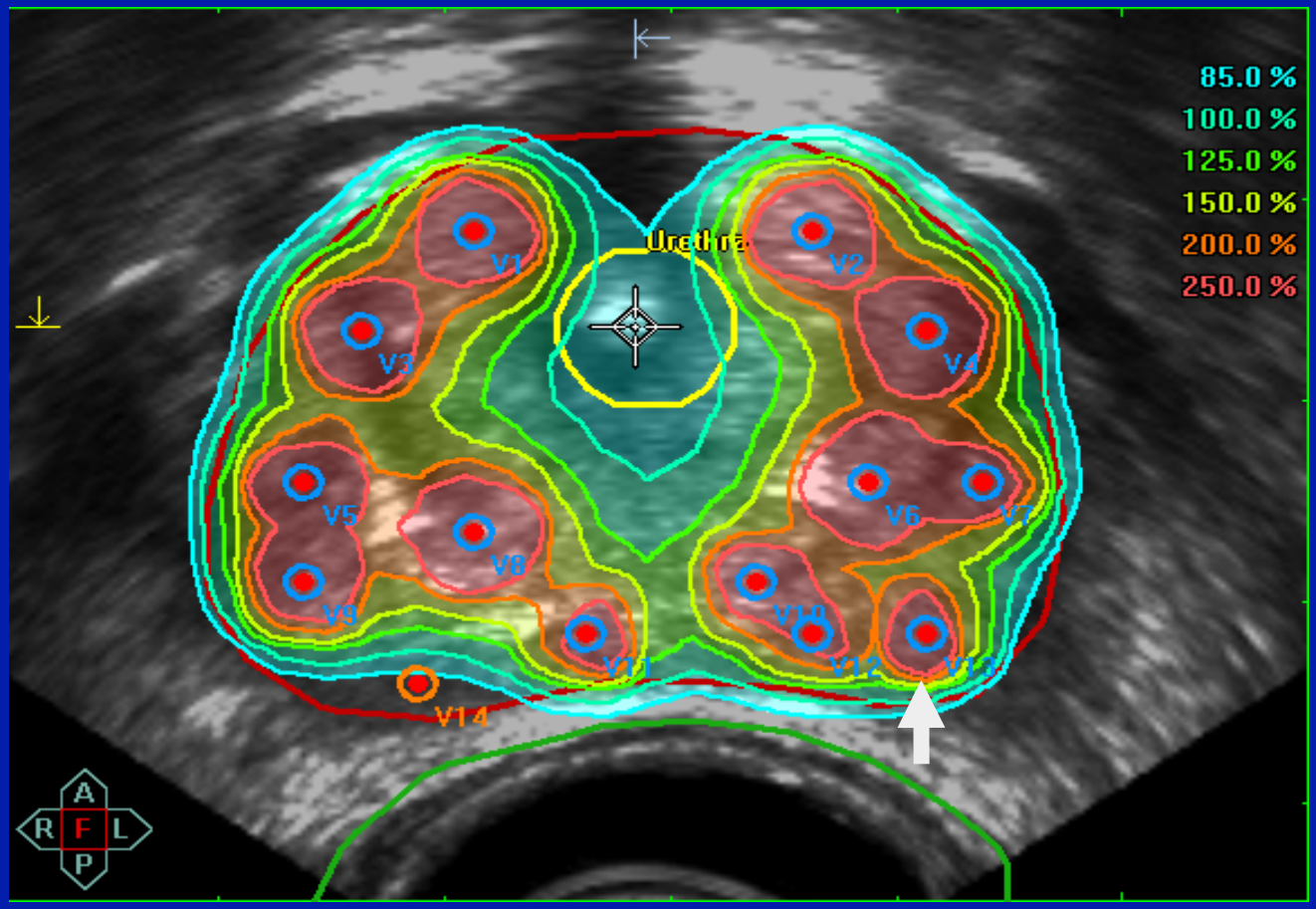

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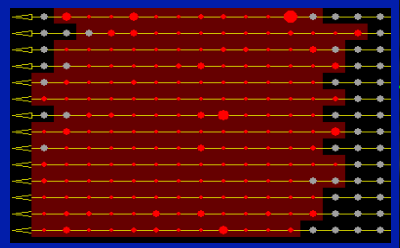
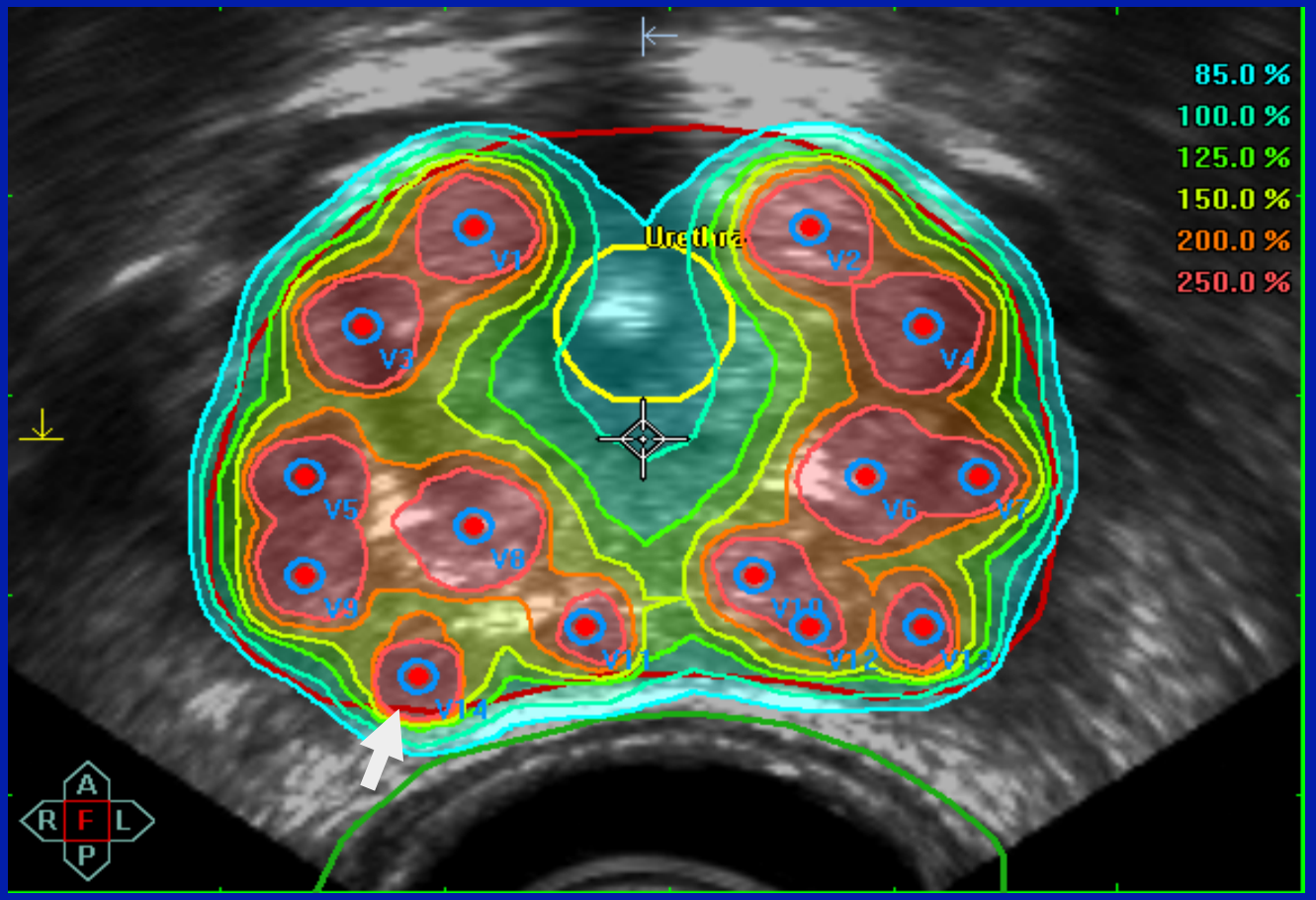




HDR Brachytherapy:

Most conformal RT- Method for Prostate Cancer

Radiobiology

HDR-Brachytherapy

Radiobiological Advantage

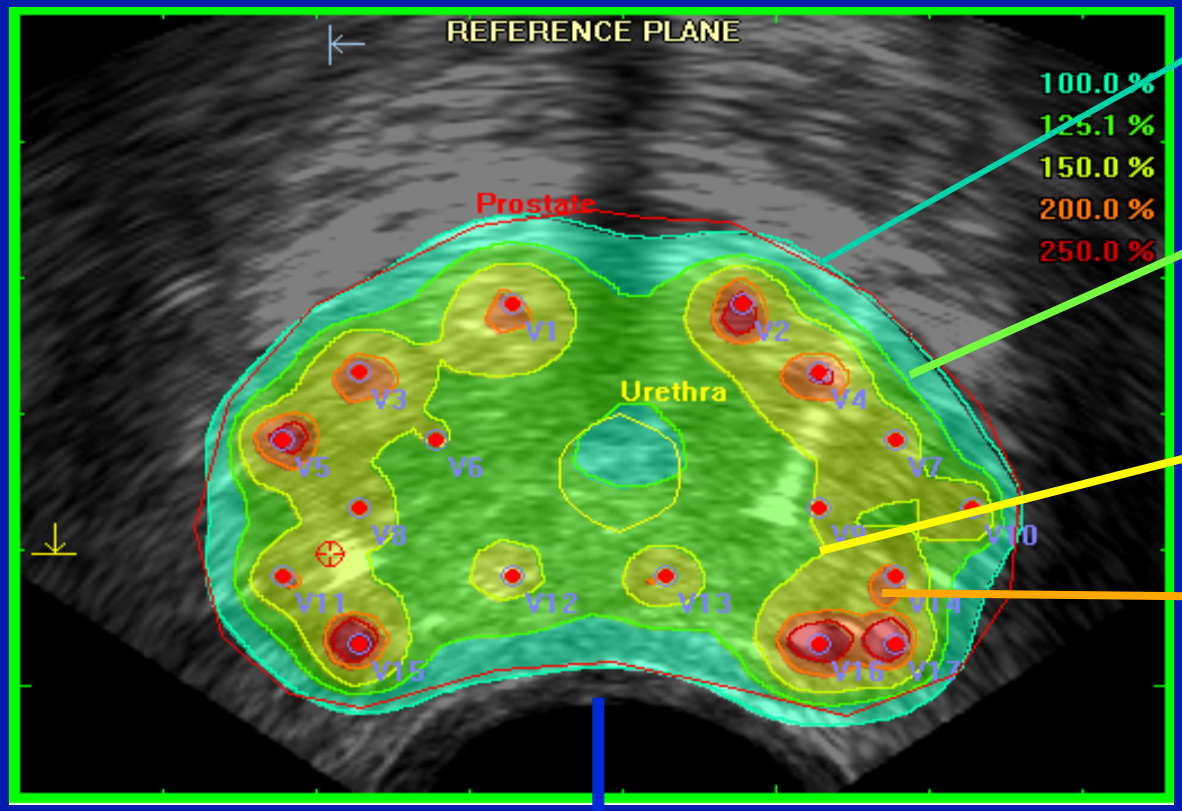
Low α/β-value

Brenner et Hall, 1999: [EBRT vs I-125] α/β = 1.5

Fowler et al, 2001: [EBRT vs I-125/Pd-103] α/β = 1.49

Dose escalation through Hypofractionation

1 Implant with 4 x 9.5 Gy



BED 279 $Gy_{1.5}$

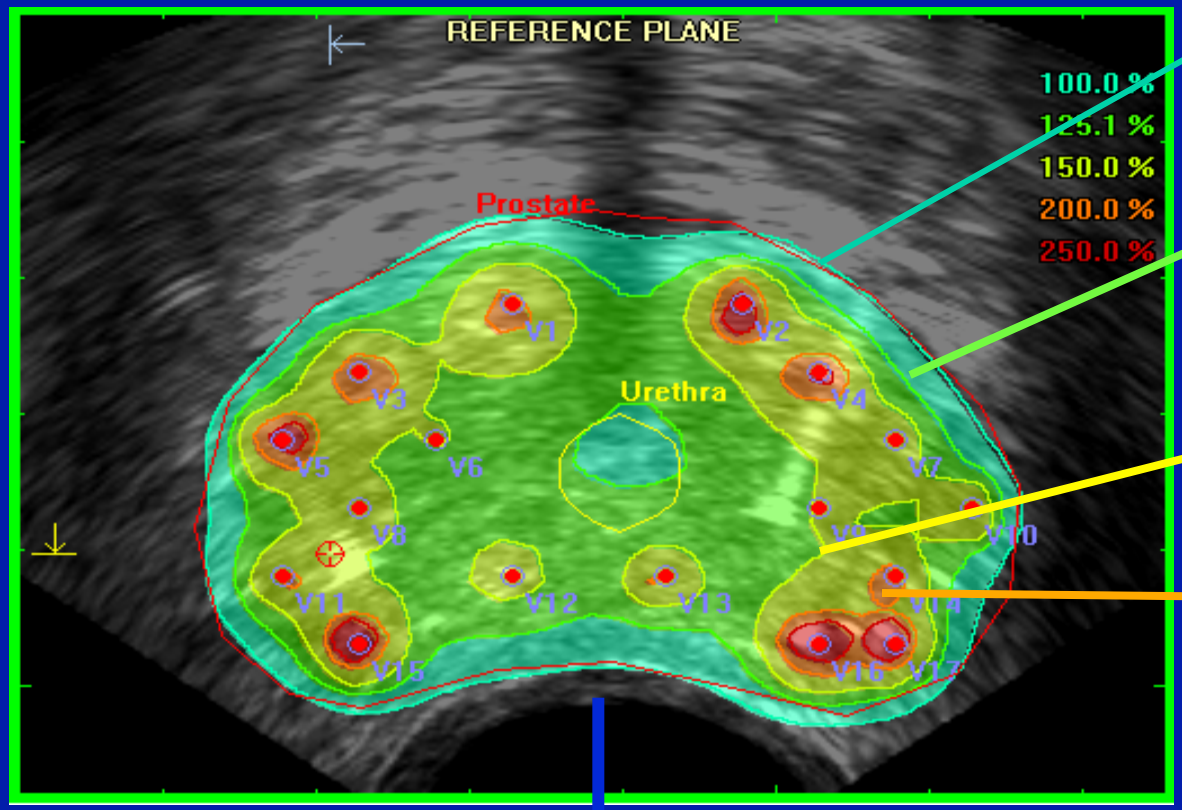
BED 346 $Gy_{1.5}$

BED 415 $Gy_{1.5}$

BED 554 $Gy_{1.5}$

D_{10} Rectum < 75 % : BED 74 Gy_{10}

3 Implants of 11,5 Gy



BED 294 Gy $_{1.5}$

BED 370 Gy$_{1.5}$

BED 445 Gy$_{1.5}$

BED 594 Gy$_{1.5}$

D $_{10}$ Rectum < 75% : BED 74 Gy $_{10}$

HDR Brachytherapy:

Most conformal RT-Technique for Prostate Cancer

Most extreme Biological Dose Escalation

HDR – MONOTHERAPY

Offenbach experience

2002-2009: 718 consecutive patients with localized prostate cancer

Transperineal Implantation under TRUS-guidance

2002-2004 (A): 1 Implant (4 x 9.5 Gy)	**CT- Plan (n=141)**
2004-2008 (B): 2 Implants (2 x 9.5 Gy/Implant)	**TRUS-Plan (n=351)**
2008-2009 (C): 3 Implants of 11,5 Gy	**TRUS-Plan (n=226)**

Group A : 1 Implant

2002-2004 (A): 1 Implant (4 x 9.5 Gy) **CT- Plan (n=141)**

9.5 Gy —6h→ **9.5 Gy** —6h→ **9.5 Gy** —6h→ **9.5 Gy**

Group B : 2 Implants

2004-2008 : 2 Implants (2 x 9.5 Gy/Implant) TRUS-Plan (n=351)

9.5 Gy —6h→ **9.5 Gy**

after 14 days 2nd Implant

9.5 Gy —6h→ **9.5 Gy**

Group C : 3 Implants

2008-2009 (C): 3 Implants of 11,5 Gy **TRUS-Plan (n=226)**

1x 11.5 Gy

after 21 days 2nd Implant

1x 11.5 Gy

after 21 days 2nd Implant

1x 11.5 Gy

1. Question

How consistent is the distribution of the isodoses within the prostate implants?

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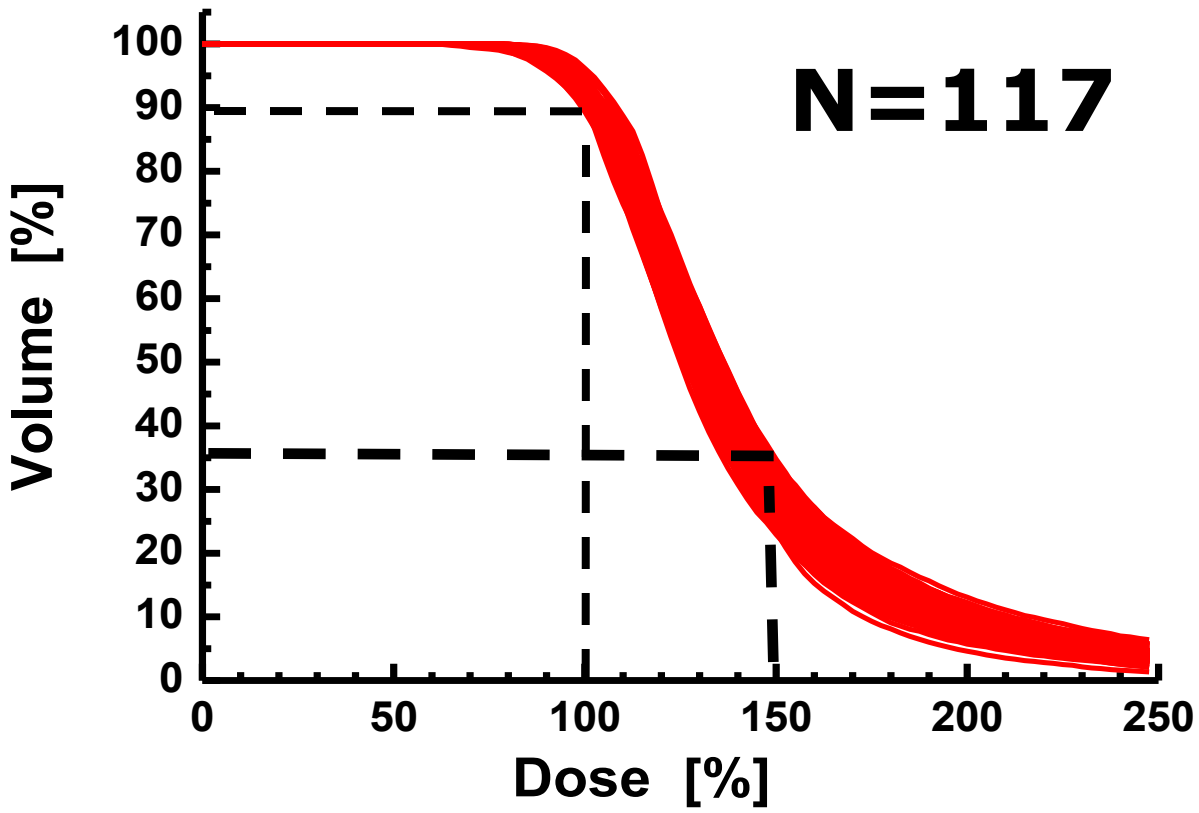
Answer : Evaluation of reproducibility through cumulative DVH´s

Reproducibility of Treatment Delivery

PTV (38.9 ± 16) cm³



Constrains
Prostate (PTV = CTV 1):

D_{90}	≥	100%
V_{100}	≥	90%
V_{150}	≤	35%

Results:

D_{90} = (102.5 ± 2.0)%

V_{100} = (92.0 ± 1.6)%

V_{150} = (29.1 ± 3.2)%

2. Question

How accurate can the planned dose be delivered?

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How accurate can the planned dose be delivered?

Answer (a): 4D Verification

4D analysis of influence of patient movement and anatomy alteration on the quality of 3D U/S-based prostate HDR brachytherapy treatment delivery[a)]

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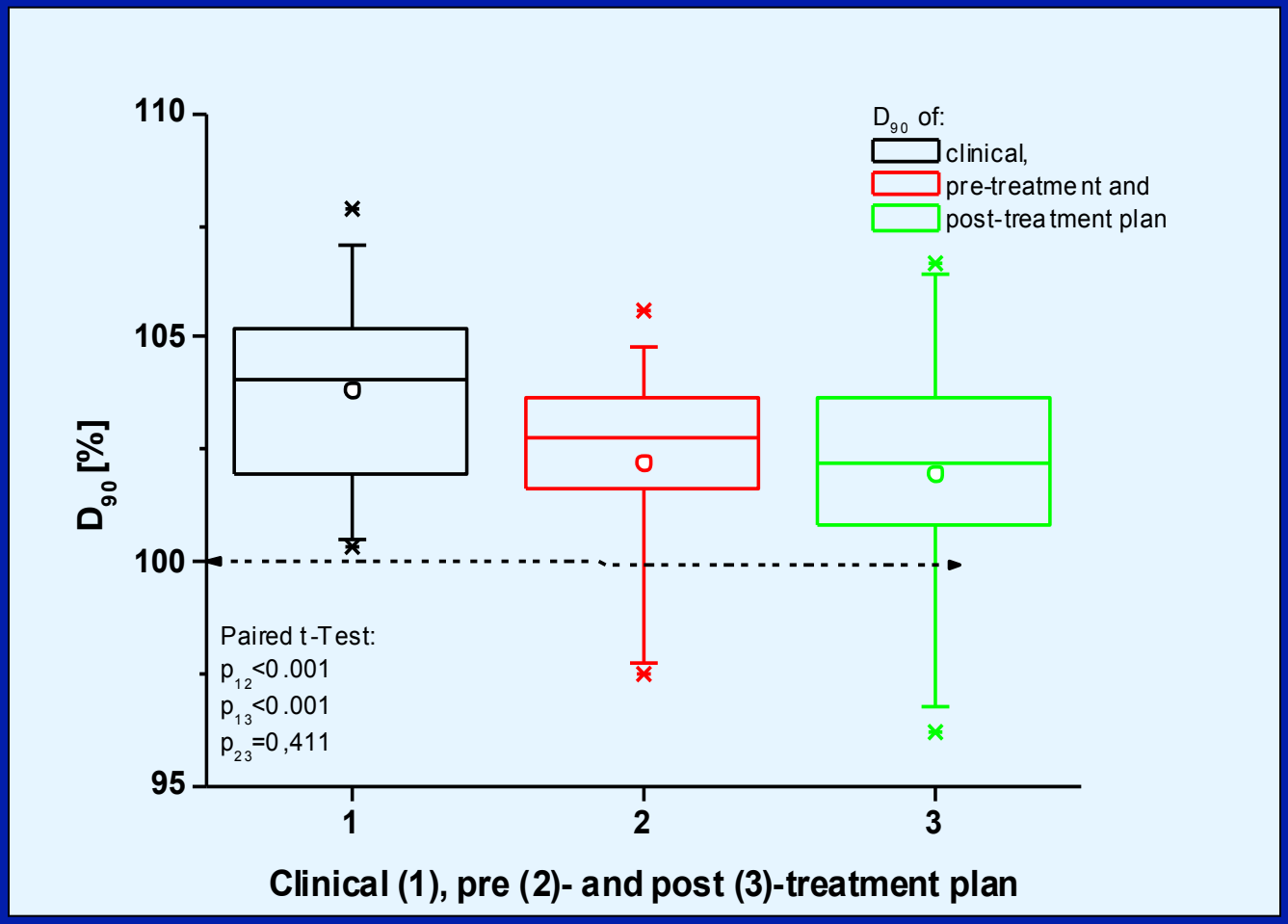
We compared in 25 patients three HDR prostate treatment plans:

1. After implantation

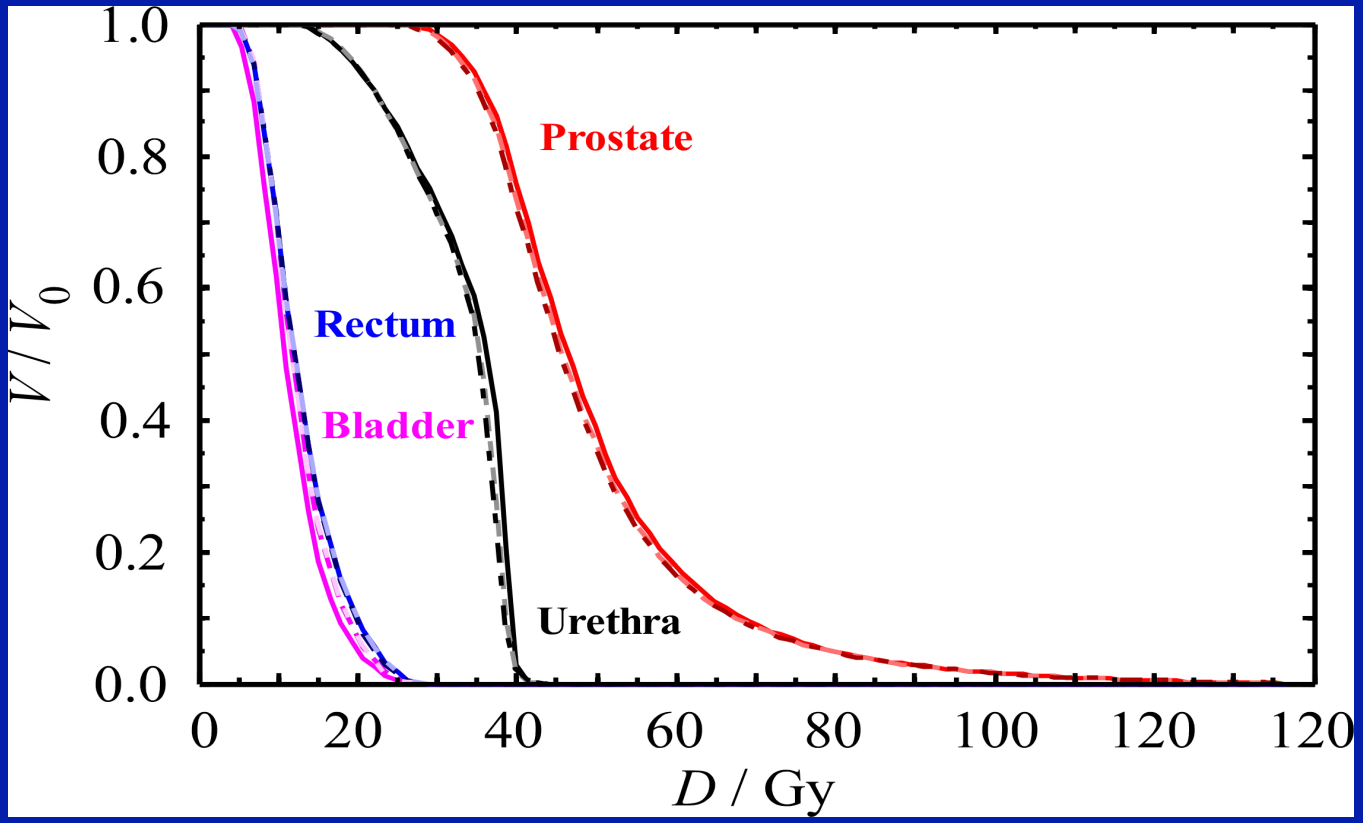
2. Just before starting the treatment execution (pre-irradiation acquisition)

3. Just after finishing the treatment delivery (post-irradiation acquisition)

Comparison of the DVH Parameters



Results: Dosimetric Impact ➔ δDose



The average DVHs of the prostate gland (red), urethra (black), bladder (pink) and rectum (blue) are presented for the three HDR treatment plans, namely 1. after implantation (clinical acquisition) (solid), 2. just before starting the treatment execution (pre-irradiation acquisition) (dashed) and 3. just after finishing the treatment delivery (post-irradiation acquisition) (dotted-dashed). The total dose of 34.5 Gy delivered by three fractions of 11.5 Gy is considered to be the total prescription dose (100%).

3. Question

How accurate can the planned dose be delivered?

Answer (a): 4D Verification

(b): Dosimetric Verification

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PHYSICS CONTRIBUTION

IN VIVO THERMOLUMINESCENCE DOSIMETRY DOSE VERIFICATION OF TRANSPERINEAL ^{192}Ir HIGH-DOSE-RATE BRACHYTHERAPY USING CT-BASED PLANNING FOR THE TREATMENT OF PROSTATE CANCER

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Purpose: To evaluate the potential of *in vivo* thermoluminescence dosimetry to estimate the accuracy of dose delivery in conformal high-dose-rate brachytherapy of prostate cancer.

Methods and Materials: A total of 50 LiF, TLD-100 cylindrical rods were calibrated in the dose range of interest and used as a batch for all fractions. Fourteen dosimeters for every treatment fraction were loaded in a plastic 4F catheter that was fixed in either one of the 6F needles implanted for treatment purposes or in an extra needle implanted after consulting with the patient. The 6F needles were placed either close to the urethra or in the vicinity of the median posterior wall of the prostate. Initial results are presented for 18 treatment fractions in 5 patients and compared to corresponding data calculated using the commercial treatment planning system used for the planning of the treatments based on CT images acquired postimplantation.

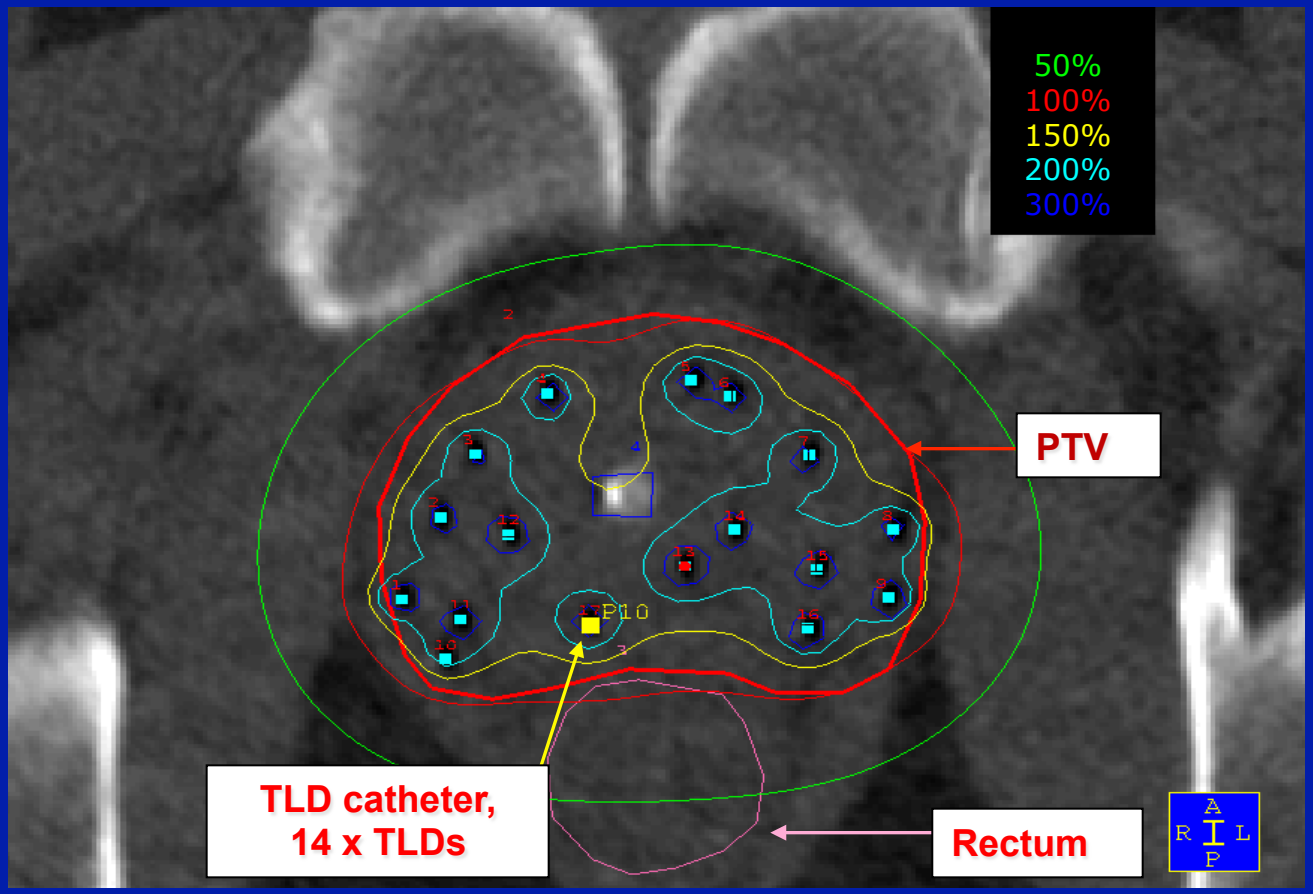
Results: The maximum observed mean difference between planned and delivered dose within a single treatment fraction was 8.57% ± 2.61% (root mean square [RMS] errors from 4.03% to 9.73%). Corresponding values obtained after averaging results over all fractions of a patient were 6.88% ± 4.93% (RMS errors from 4.82% to 7.32%). Experimental results of each fraction corresponding to the same patient point were found to agree within experimental uncertainties.

Conclusions: Experimental results indicate that the proposed method is feasible for dose verification purposes and suggest that dose delivery in transperineal high-dose-rate brachytherapy after CT-based planning can be of acceptable accuracy. © 2003 Elsevier Inc.

Brachytherapy, Prostate, *In vivo*, TLD.

Treatment Delivery Verification

5 x cases , 18 x Fractions, 14 x TLDs



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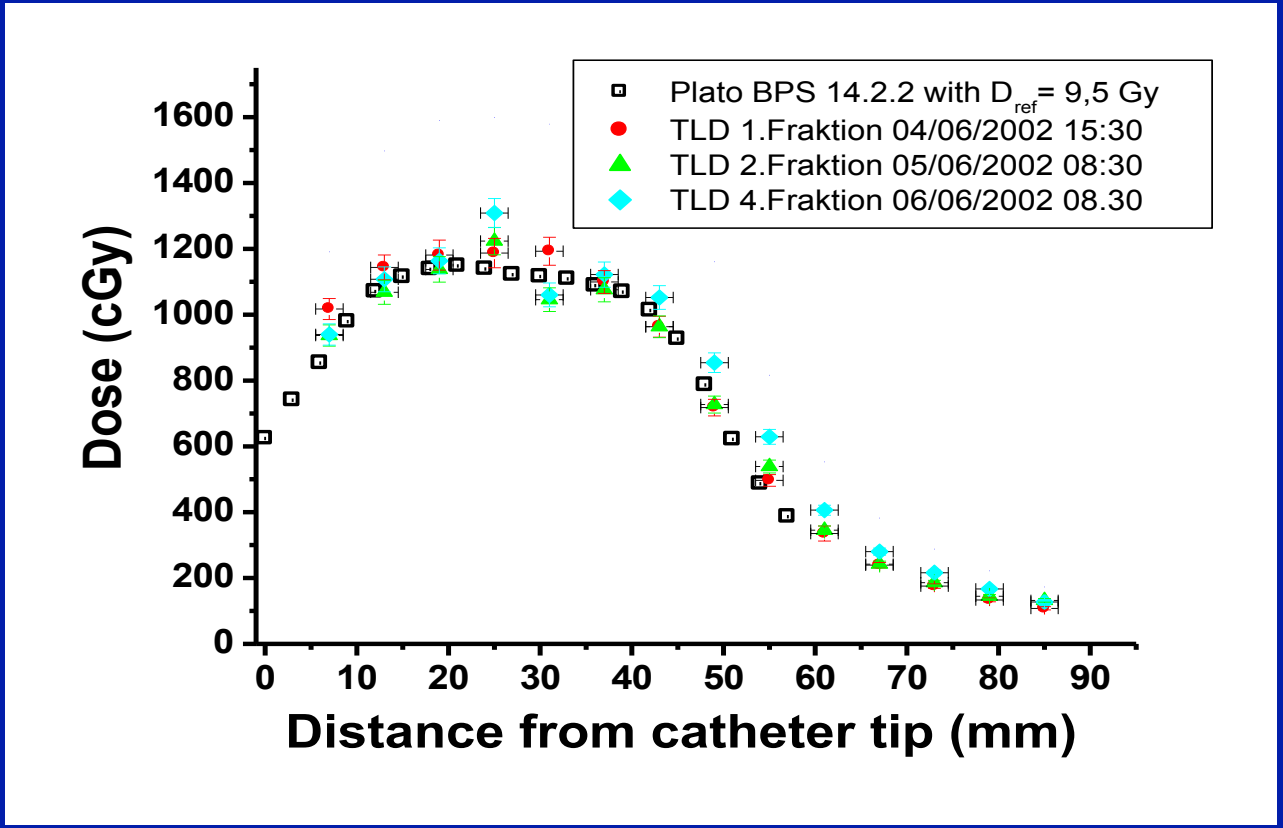

Clinical Results

Offenbach experience

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Clinical Investigation: Genitourinary Cancer

High-Dose-Rate Interstitial Brachytherapy as Monotherapy for Clinically Localized Prostate Cancer: Treatment Evolution and Mature Results

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Patient characteristics

	Group A (n = 141)	Group B (n = 351)	Group C (n = 226)
Median follow-up (months)	Median overall follow-up 52.8 months		
Median Gland volume (cc)	40 (20-90)	39 (16-107)	36 (11-90)
Risk group (MSKCC) Low Intermediate High	Low risk: n= 395 (55 %) Intermediate: n= 177 (25 %) High risk: n= 146 (20 %)		

Protocol characteristics

Treatment group	*PTV*	*BED* $_{1.5/3.0}$
Group A (9.5 Gy x 4)	38.0 Gy	279/158 Gy
Group B (9.5 Gy x 4)	38.0 Gy	279/158 Gy
Group C (11.5 Gy x 3)	34.5 Gy	294/162 Gy

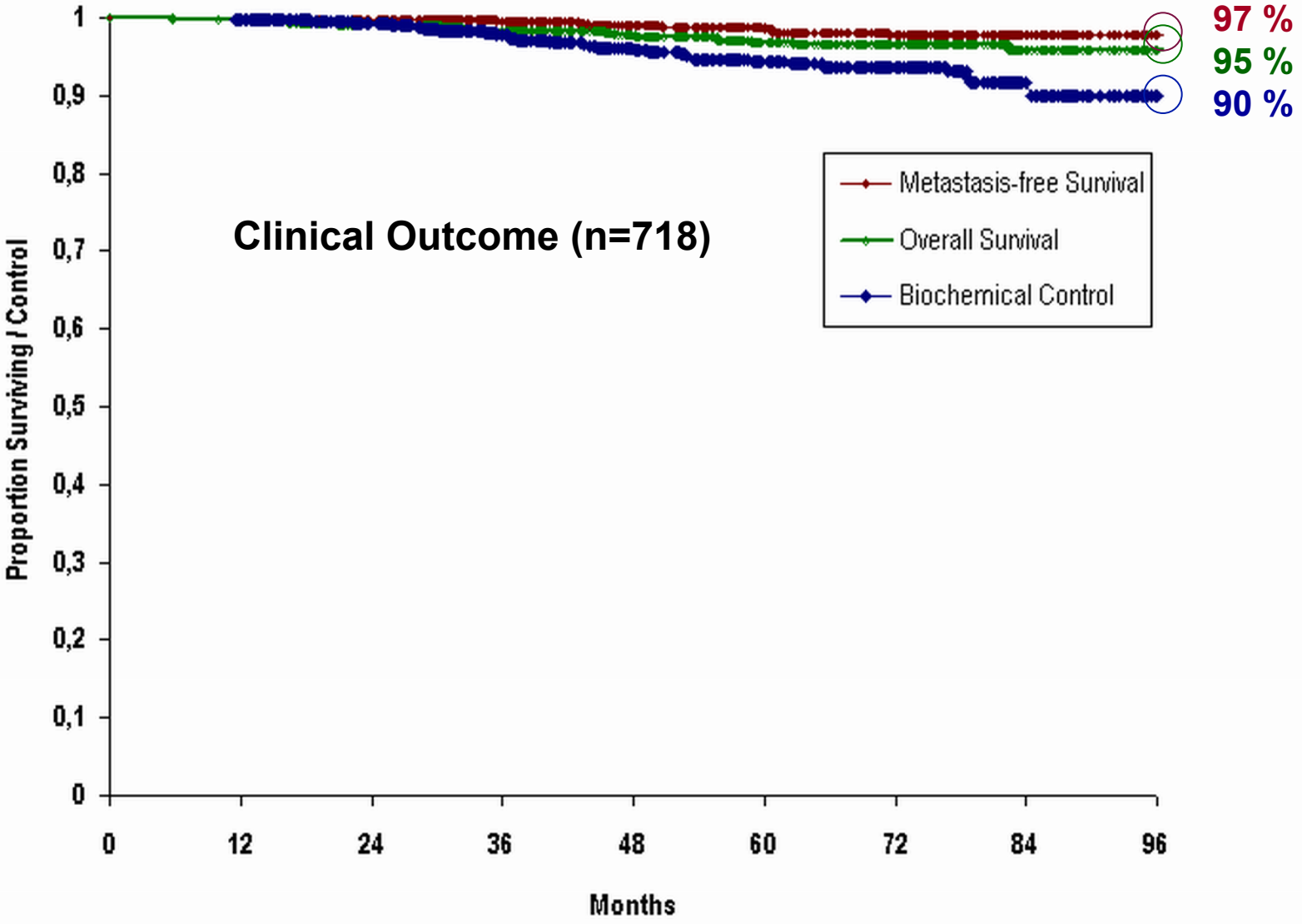
Potential doubling time of T_{pot}= 42 days (Treatment completion within 42 days)

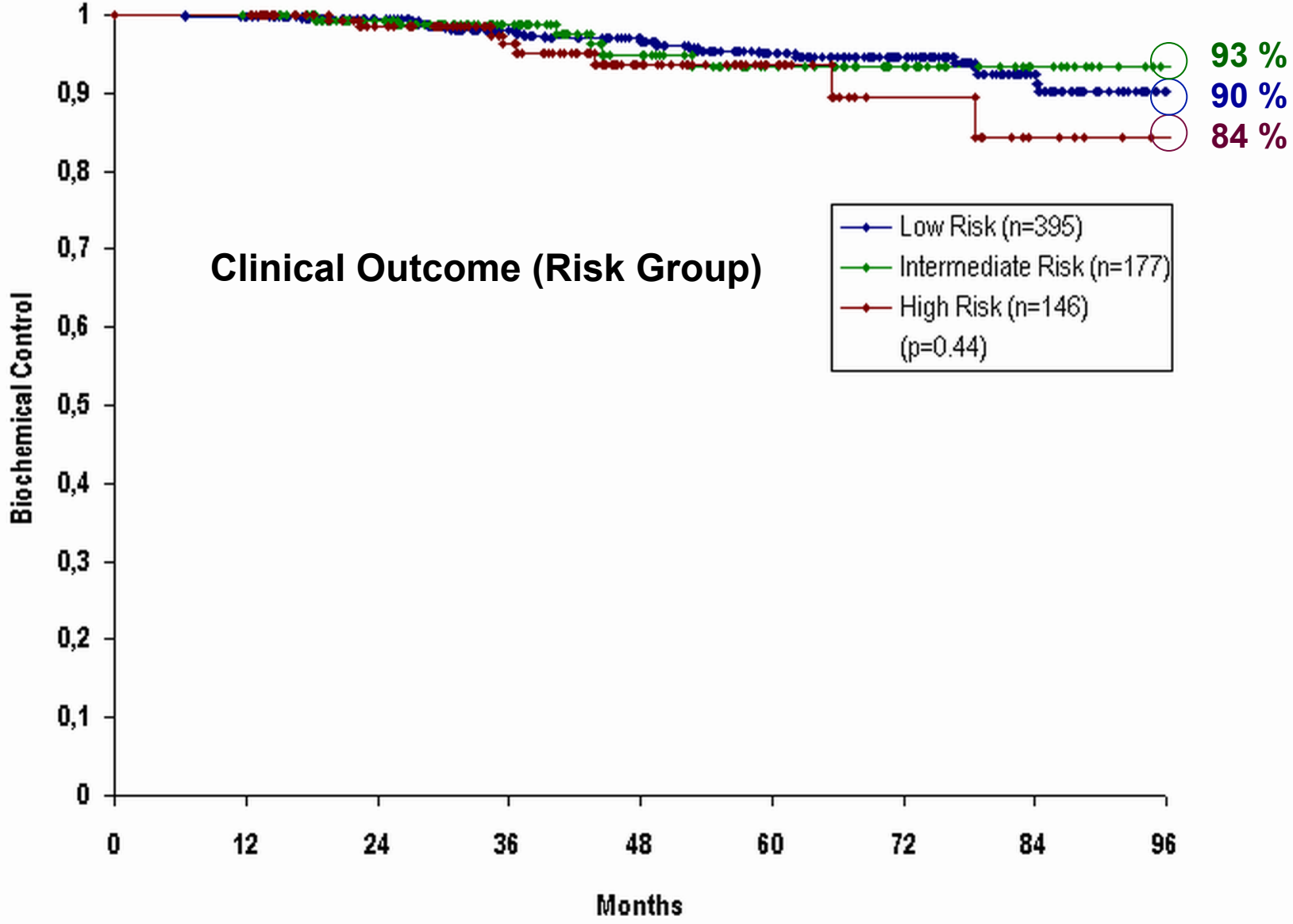
Evaluation

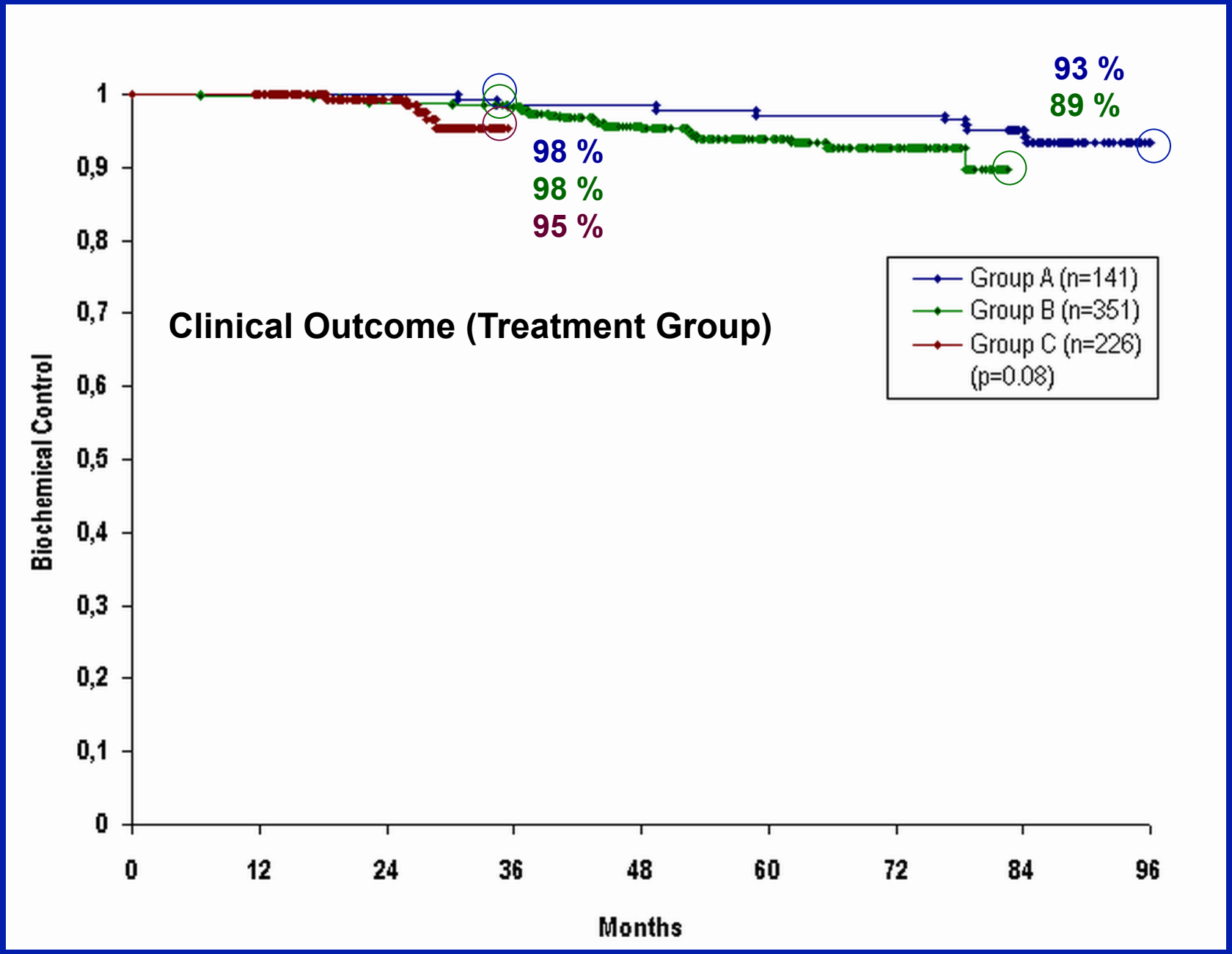
Survival estimates according to Kaplan-Maier method

Biochemical Control based on Nadir +2 *(Phoenix Criteria)*

Toxicity according CTC Version 3


Clinical Outcome (n=718)
Proportion Surviving / Control
1
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0
0
12
24
36
48
60
72
84
96
Months
Metastasis-free Survival
Overall Survival
Biochemical Control
97 %
95 %
90 %


Clinical Outcome (Risk Group)
Biochemical Control
1
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0
0
12
24
36
48
60
72
84
96
Months
Low Risk (n=395)
Intermediate Risk (n=177)
High Risk (n=146)
(p=0.44)
93 %
90 %
84 %


Clinical Outcome (Treatment Group)
Biochemical Control
1
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0
0
12
24
36
48
60
72
84
96
Months
93 %
89 %
98 %
98 %
95 %
Group A (n=141)
Group B (n=351)
Group C (n=226)
(p=0.08)

Late Toxicity (n=717)

2 patients with incontinence indicating permanent urostomy

	Group A (n = 141)			Group B (n = 351)			Group C (n = 225)		
	2	3	4	2	3	4	2	3	4
Genitourinary									
Frequency/Urge	9.2%	2.1%	-	4.8%	0.5%	-	7.5%	-	-
Incontinence	7.8%	0.7%	0.7%	5.1%	0.3%	-	7.5%	0.4%	0.4%
Retention	6.3%	2.8%	-	5.4%	2.0%	-	4.4%	0.8%	-
Errect. dysfunction	21.2%	12.0%	-	15.7%	16.5%	-	18.2%	19.1%	-
Gastrointestinal									
Pain	0.7%	0.7%	-	0.3%	0.3%	-	-	-	-
Mucositis	0.7%	3.5%	-	0.8%	1.2%	-	0.4%	0.4%	-

2 patients with endoscopically Grade 3 rectal necrosis: colostomy
3 patients with endoscopically grade 3 rectal mucositis: laser coagulation procedures

Results of HDR Monotherapy

Author, y (ref.)	No. of patients	Gy/fraction	Fractions (no. of implants)	Total	Median follow up (y)	Biochemical control (risk group)
Yoshioka et al, 2011 (14)	111	6	9 (1 implant)	54 Gy	5.4	85% low risk at 5 y 93% intermediate risk at 5 y 79% high risk at 5 y
Hoskin et al, 2012 (15)	197	8.5 9	4 (1 implant)	34 36 Gy	4.5 5	95% intermediate risk at 4 y
		10.5	3 (1 implant)	31.5 Gy	3	
		13	2 (1 implant)	26 Gy	0.5	87% high risk at 4 y
Rogers et al, 2012 (19)	284	6	6 (2 implants)	36 Gy	3	94% intermediate risk at 5 y
Mark et al, 2010 (13)	301	7.5	6 (2 implants)	45 Gy	8	88% all
Prada et al, 2012 (20)	40	19	1 (1 implant)	19 Gy	1.6	100% low risk at 32 mo 88% intermediate risk at 32 mo
Martinez et al, 2010 (12)	248	7	6 (2 implants)	42 Gy	4.8	91% low and intermediate risk at 5 y (WBH series)
		9.5	4 (1 implant)	38 Gy		87% low and intermediate risk at 5 y (CET series)
Demanes et al, 2011 (17)	298	7	6 (2 implants)	42 Gy	5.2	97% low and intermediate risk at 5 y
		9.5	4 (1 implant)	38 Gy		
Present study	718	9.5	4 (1 implant)	38 Gy	4.4	95% low risk at 5 y
		9.5	4 (2 implants)	38 Gy		
		11.5	3 (3 implants)	34.5 Gy		93% intermediate risk at 5 y 93% high risk at 5 y

Comparison of different fractionation schemes

(Baltas D … Zamboglou N. sub. for Pub)

Table 7. Comparison of the complication-free tumor control probability (P_+), tumor control probability (P_B) and normal tissue complication probability (P_I) for the different fractionation schemes.

	P_+ (%)	P_B (%)	P_I (%)
Standard fractionation schemes			
1 x 20 Gy	88.8 ± 4.6	98.5 ± 0.7	9.7 ± 4.9
2 x 14 Gy	83.9 ± 6.8	98.6 ± 0.9	14.6 ± 7.1
3 x 11 Gy	86.0 ± 5.0	97.5 ± 1.4	11.5 ± 5.5
4 x 9.5 Gy	82.3 ± 6.7	97.8 ± 1.4	15.6 ± 7.2

How do we proceed?

On-going Study :

1 Implant of 1 fraction of 20 Gy