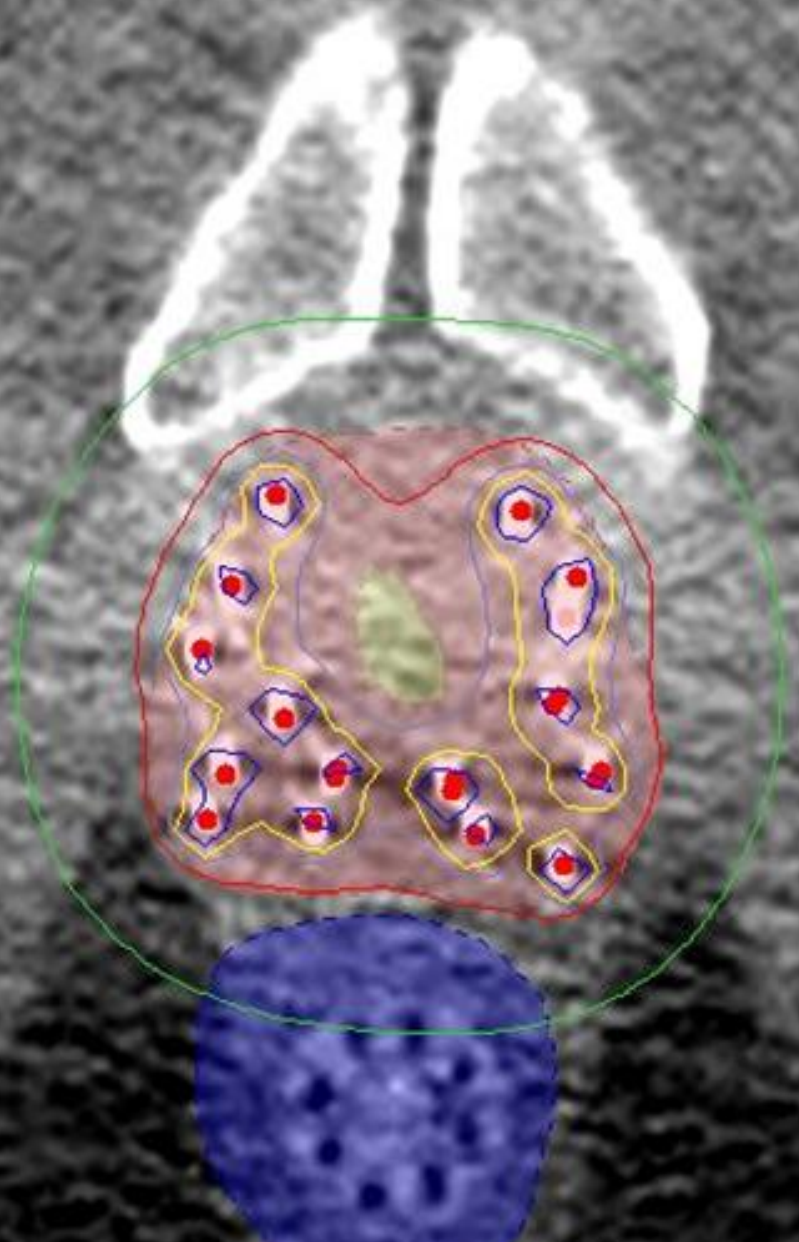
Radioablacyjna wartość wysokich dawek frakcyjnych w teleradioterapii i brachyterapii raka stercza. Kiedy mniej znaczy więcej?

Dr n. med. Piotr Wojcieszek

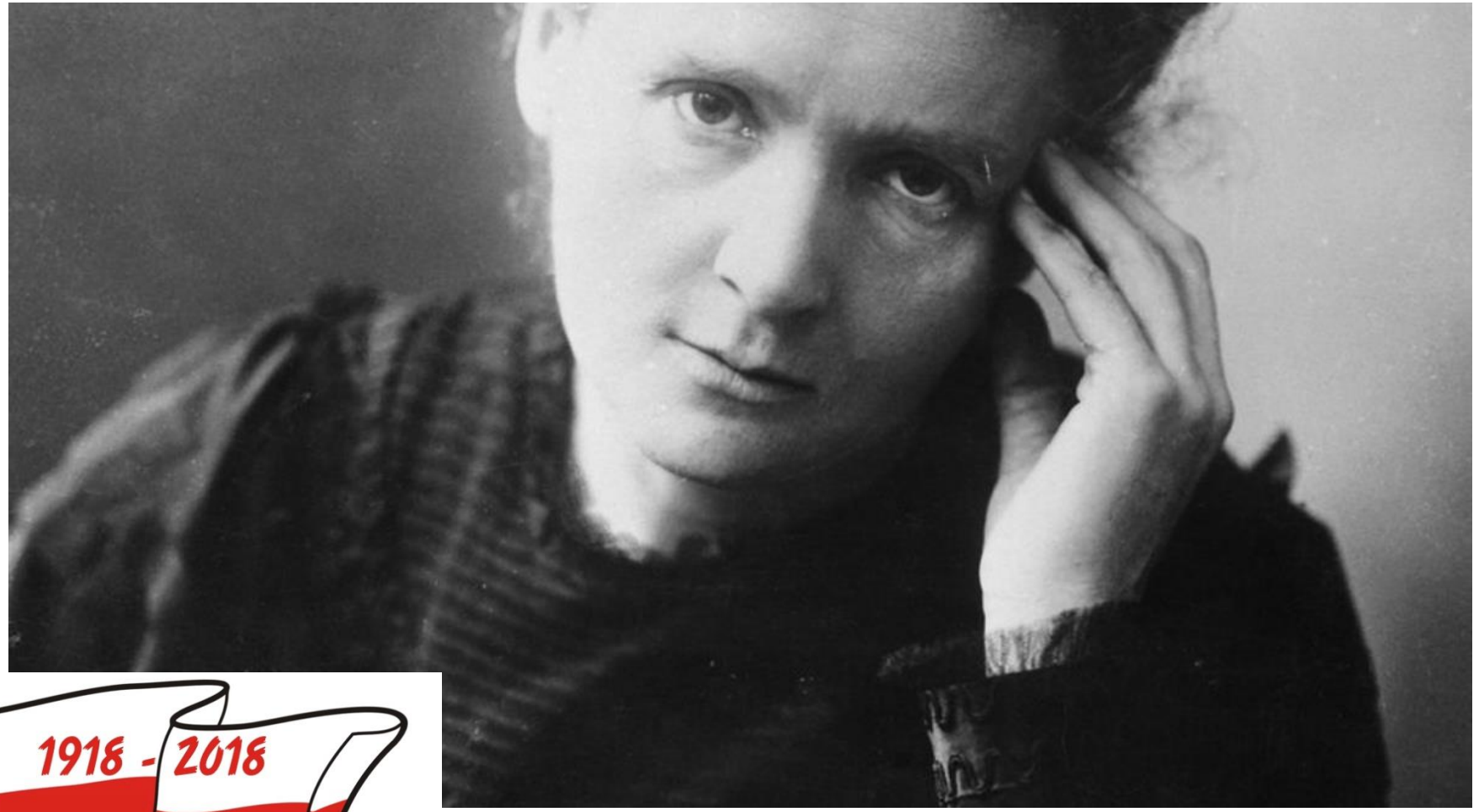
Zakład Brachyterapii CO-I Gliwice



…my mother was a tailor…

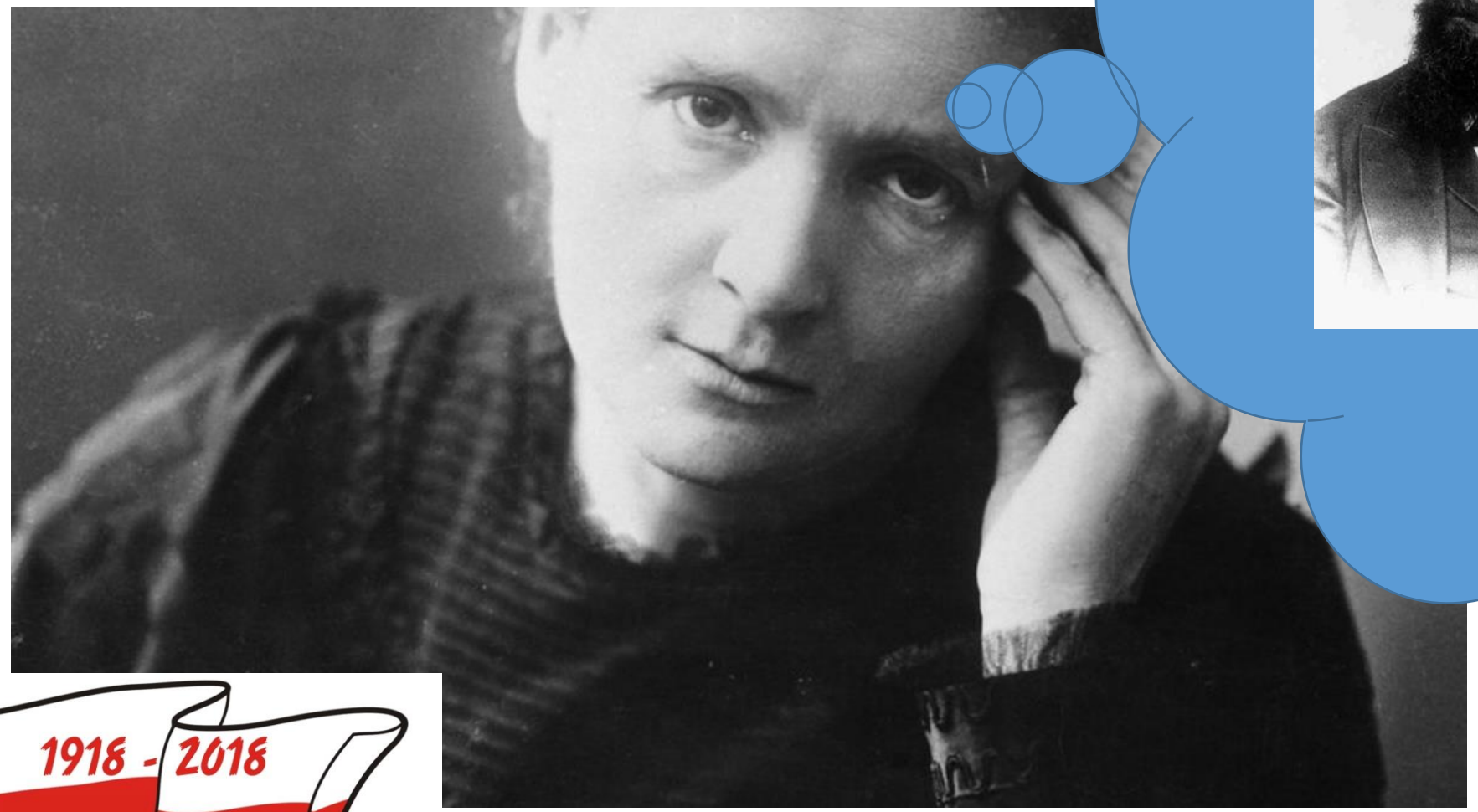
…my father was a gambling man…

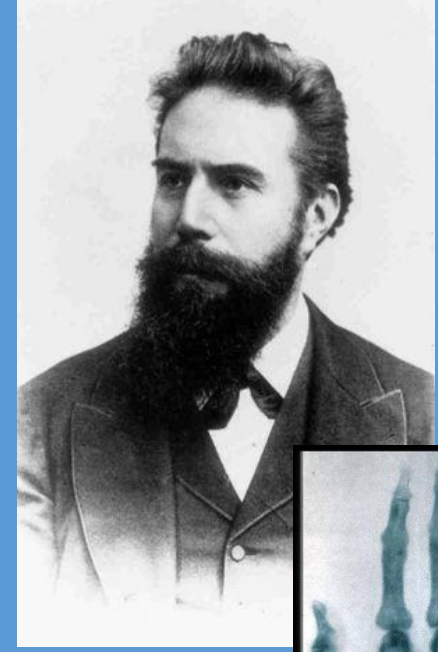
The House Of The Rising Sun – The Animals

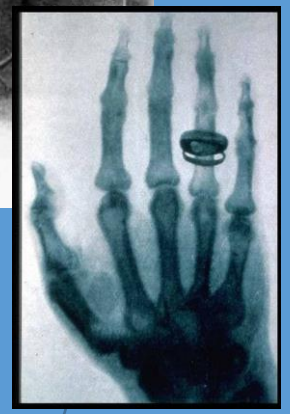


1918 - 2018

100 ROCZNICA
ODZYSKANIA NIEPODLEGŁOŚCI

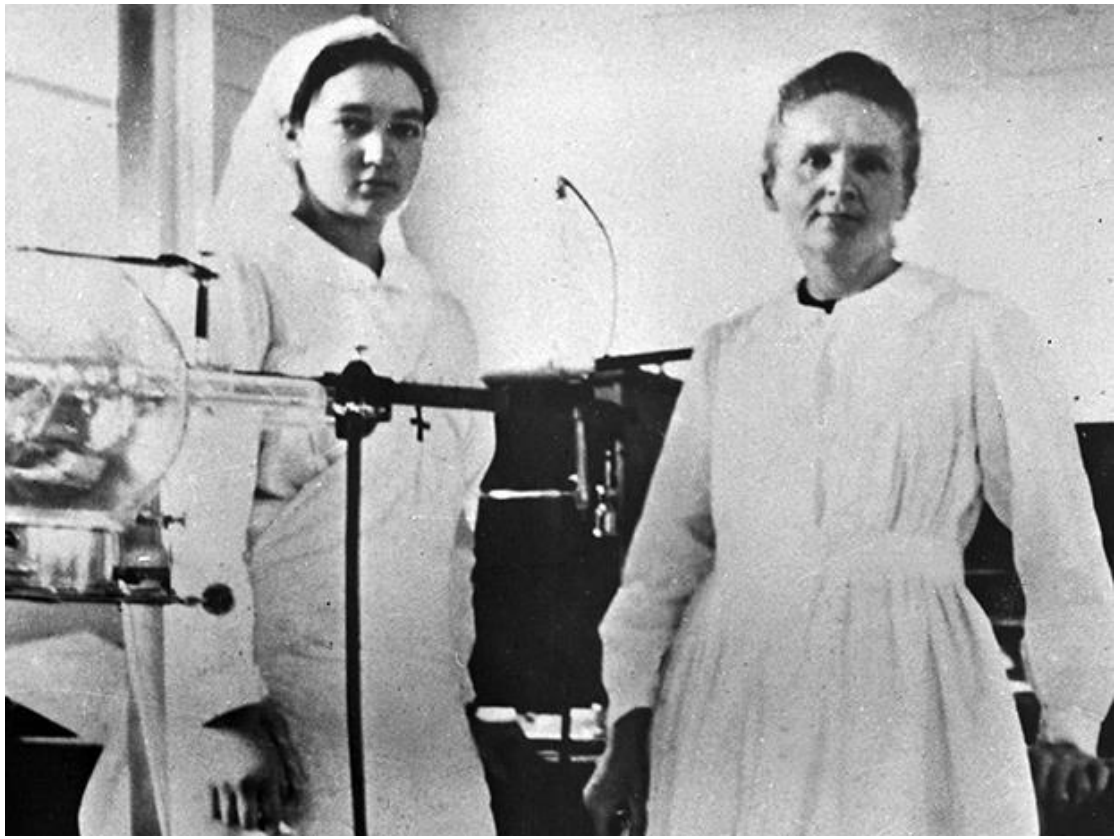






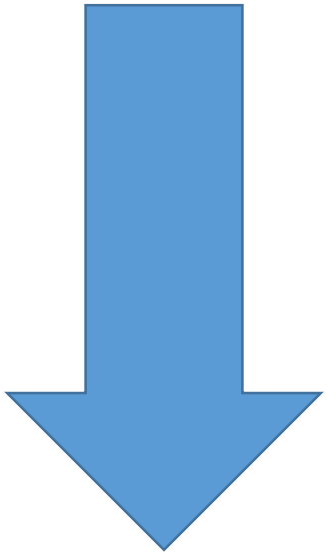
1918 - 2018

100 ROCZNICA
ODZYSKANIA NIEPODLEGŁOŚCI



Innowacje technologiczne

Porzucenie dogmatu



Badania kliniczne

Praktyka kliniczna

Zysk terapeutyczny


Flexitron


CyberKnife

Radiobiologia niepowodzenia radioterapii: czy powinniśmy gonić oporny ogon?

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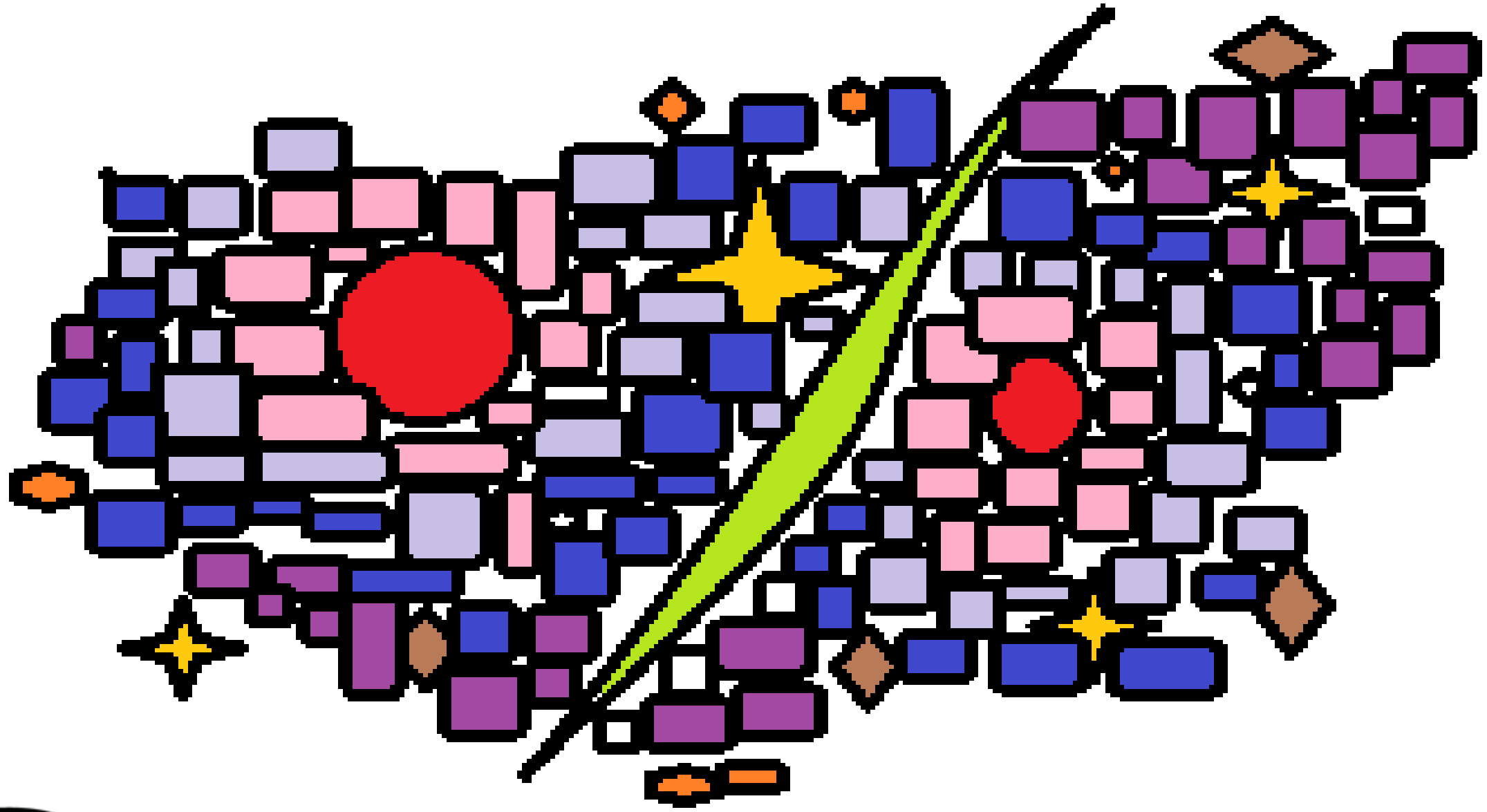
Radiobiologia

Repopulacja	**R**epopulation
Reoksygenacja	**R**eoxygenation
Nap**R**awa	**R**epair
Redystrybucja	**R**edistribution
Opo**R**ność tkankowa	**R**esistance (intrinsic)



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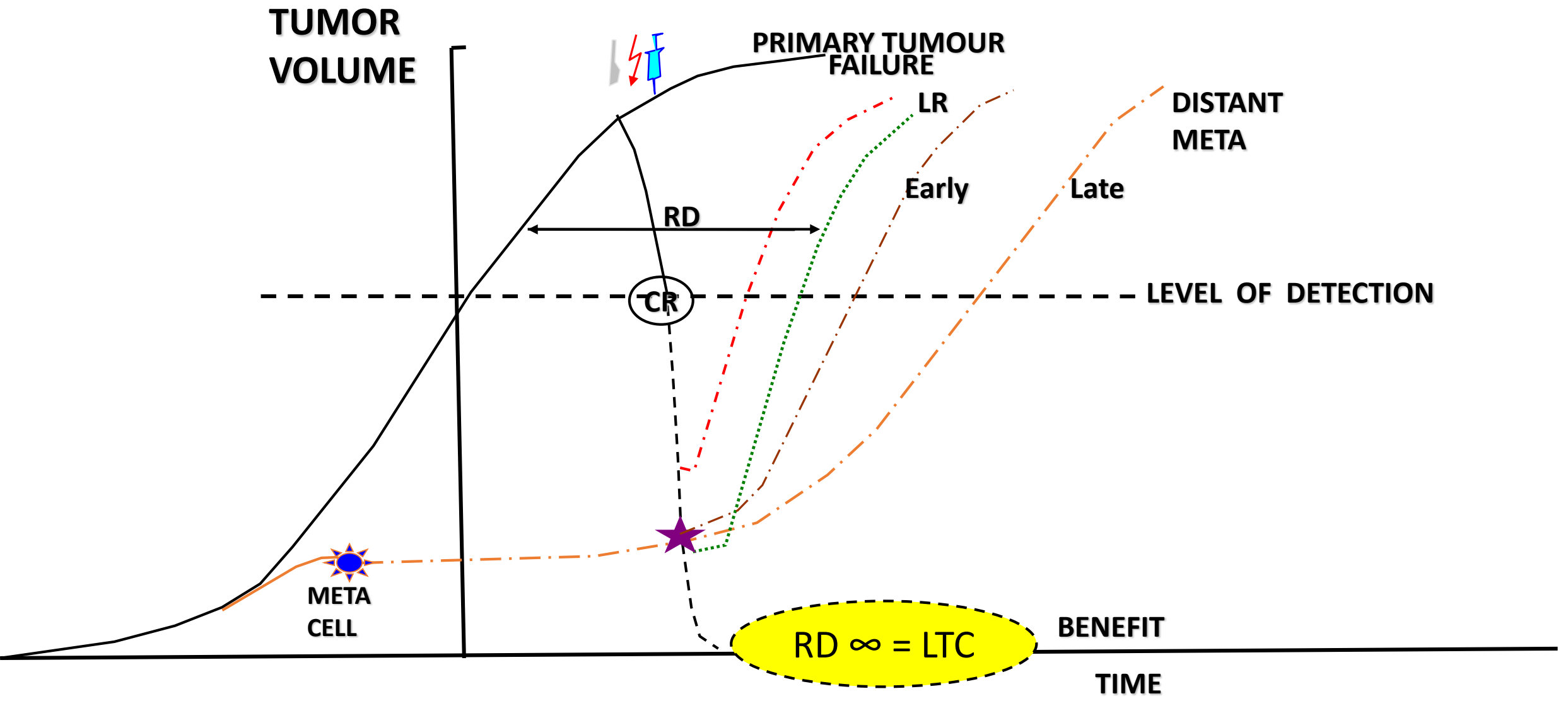

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Za Prof. B. Maciejewski

Radiobiologia

Repopulacja	**R**epopulation
Reoksygenacja	**R**eoxygenation
Nap**R**awa	**R**epair
Redystrybucja	**R**edistribution
Radiowrażliwość	**R**adiosensitivity (intrinsic)

Ekstremalne hipofrakcjonowanie– problemy

- Oporne frakcje komórkowe:
  - Hipoksja
  - Oporność wewnętrzna
  - Cykl komórkowy?
  - Naprawa DNA?
  - Repopulacja!?
- Tolerancja tkanek typu F (odczyn późny)

Ekstremalne hipofrakcjonowanie– problemy

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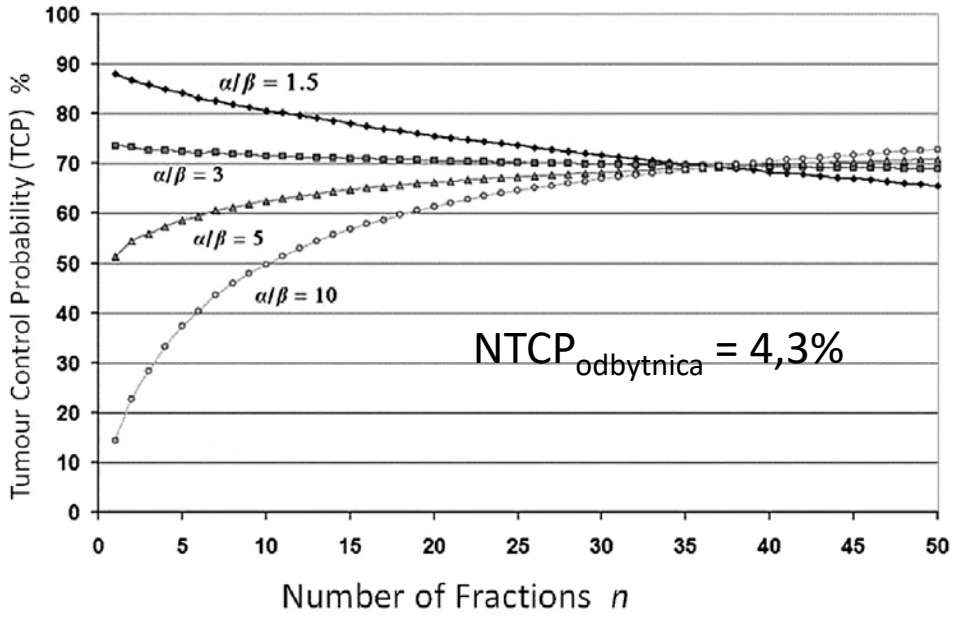
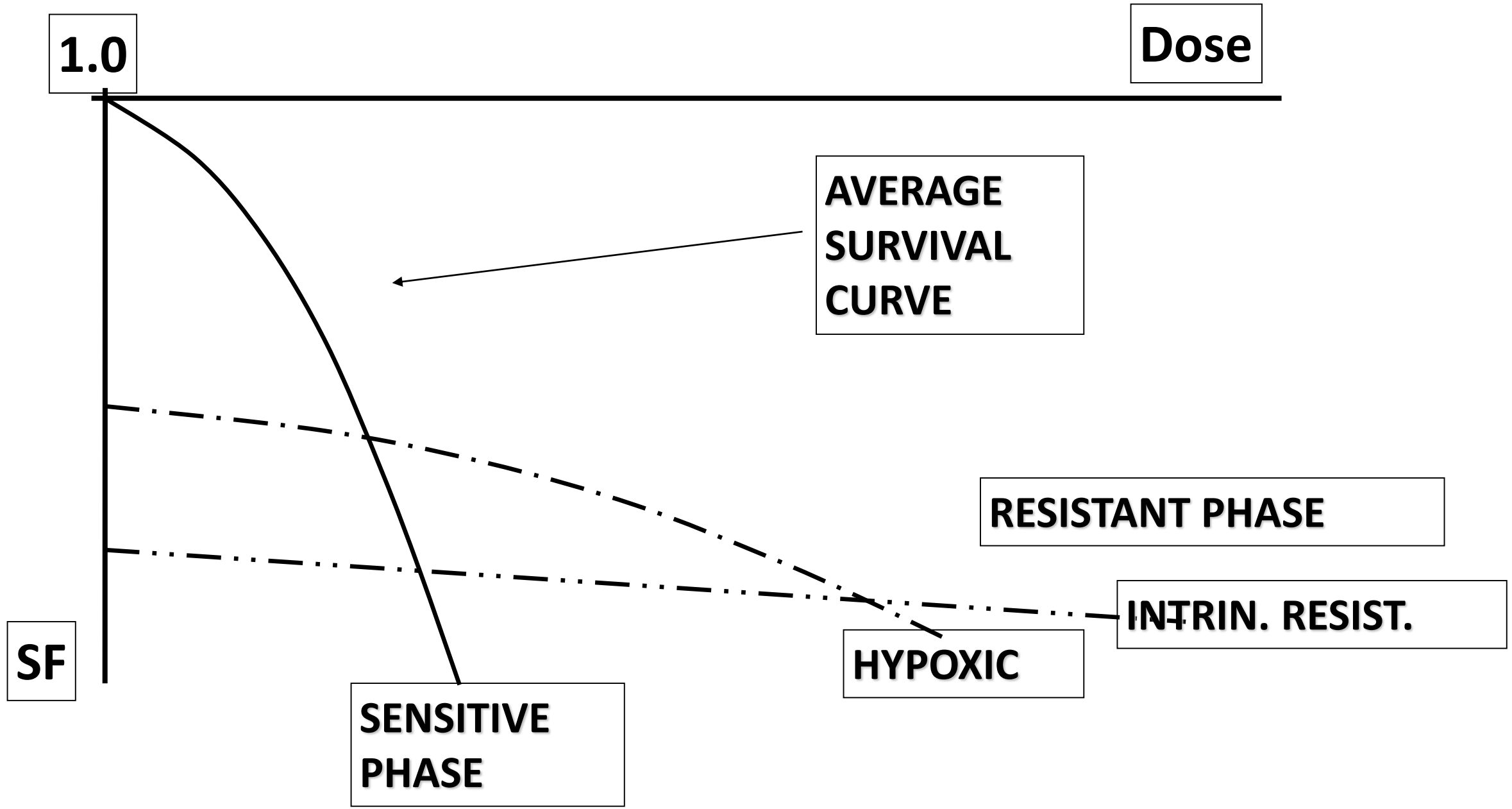
  - Hipoksja
  - Oporność wewnętrzna
  - Cykl komórkowy?
  - Naprawa DNA?
  - Repopulacja!?
- Tolerancja tkanek typu F (odczyn późny)



Dawka radioablacyjna powinna być wystarczająca do uzyskania efektu terapeutycznego z uniknięciem niepotrzebnych powikłań, jednocześnie.



Za Prof. B. Maciejewski

Radiooporność

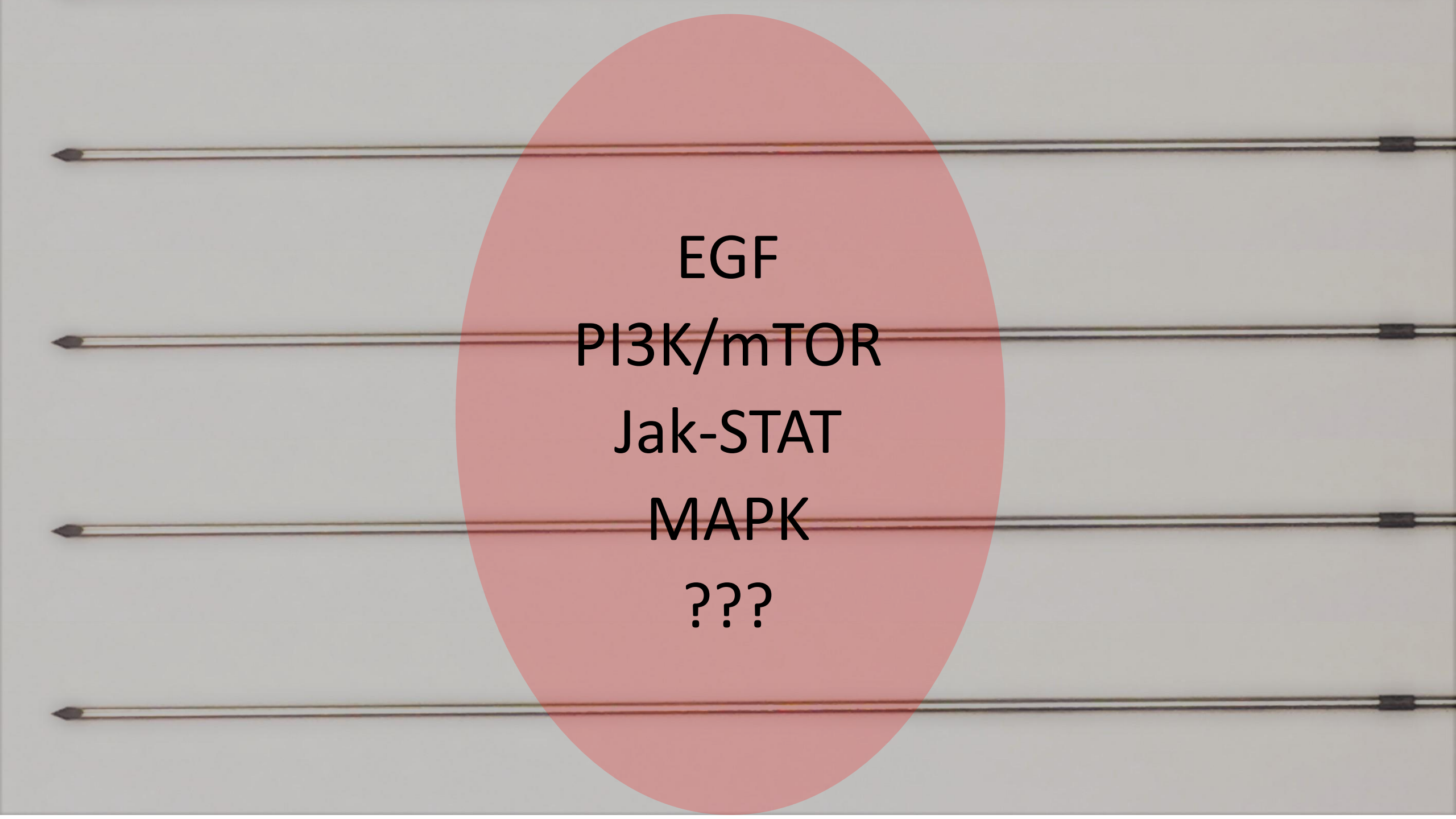
EGF

PI3K/mTOR

Jak-STAT

MAPK

???


EGF
PI3K/mTOR
Jak-STAT
MAPK
???

Między słowami:
jak zrozumieć śródtkankowe napromienianie?

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Brachyterapia
brachy- gr. krótki

- śródtkankowa
- kontaktowa
  - powierzchniowa
  - dojamowa

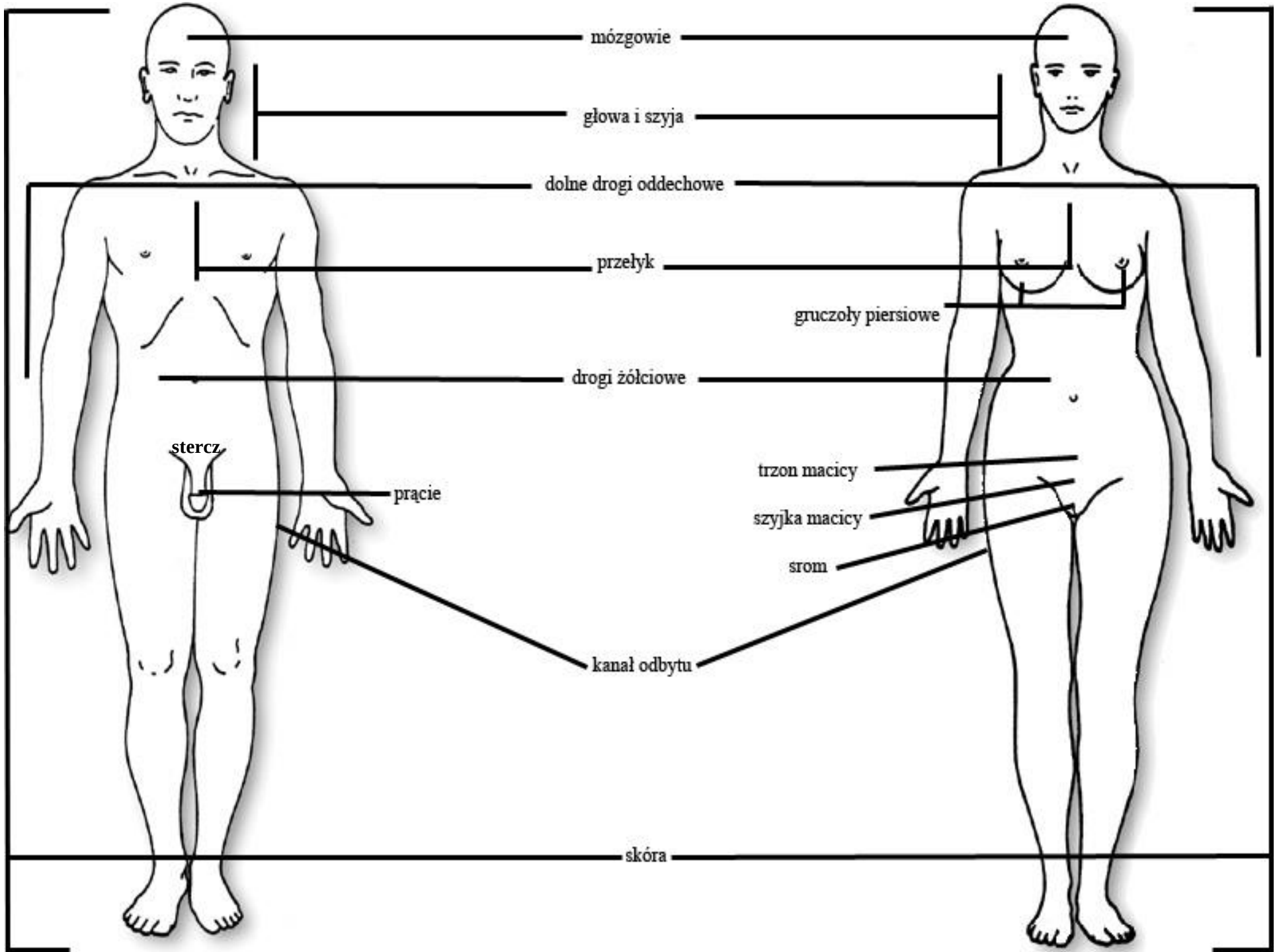
Brachyterapia
Moc dawki

LDR	MDR	HDR	PDR
0,4-2 Gy/h	2-12 Gy/h	>12 Gy/h	0,5-1 Gy/h

Brachyterapia
Czas aplikacji

Implanty stałe
LDR

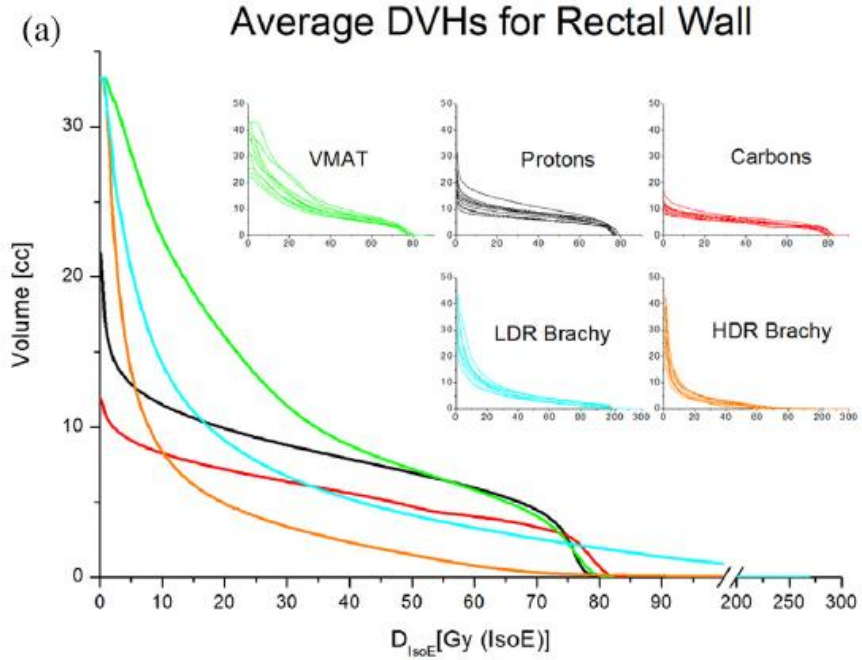
Implanty czasowe
HDR

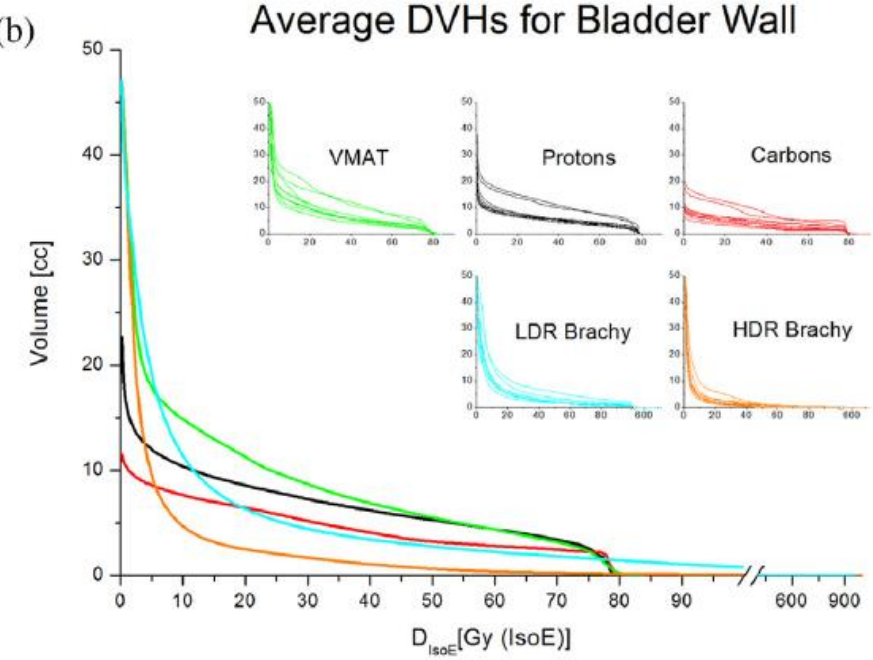

mózgowie
głowa i szyja
dolne drogi oddechowe
przełyk
gruczoły piersiowe
drogi żółciowe
stercz
prącie
trzon macicy
szyjka macicy
srom
kanał odbytu
skóra

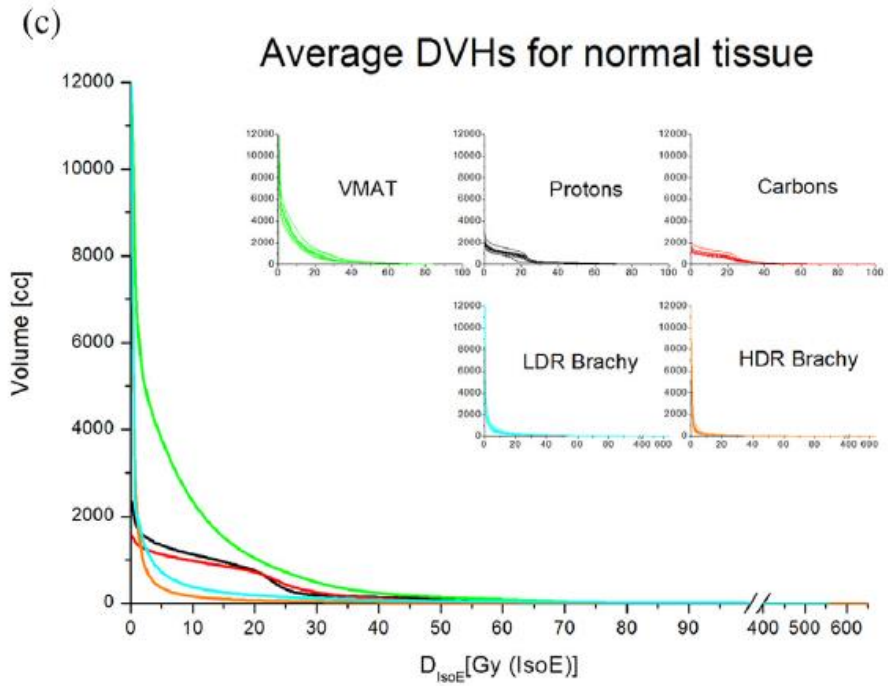
Brachyterapia

Zalety
- Mała objętość leczona
- Wysoka dawka
- Krótki czas leczenia

Wady
- Mała objętość leczona
- Wysoka dawka
- Leczenie inwazyjne
- Ryzyko aplikacji suboptymalnej

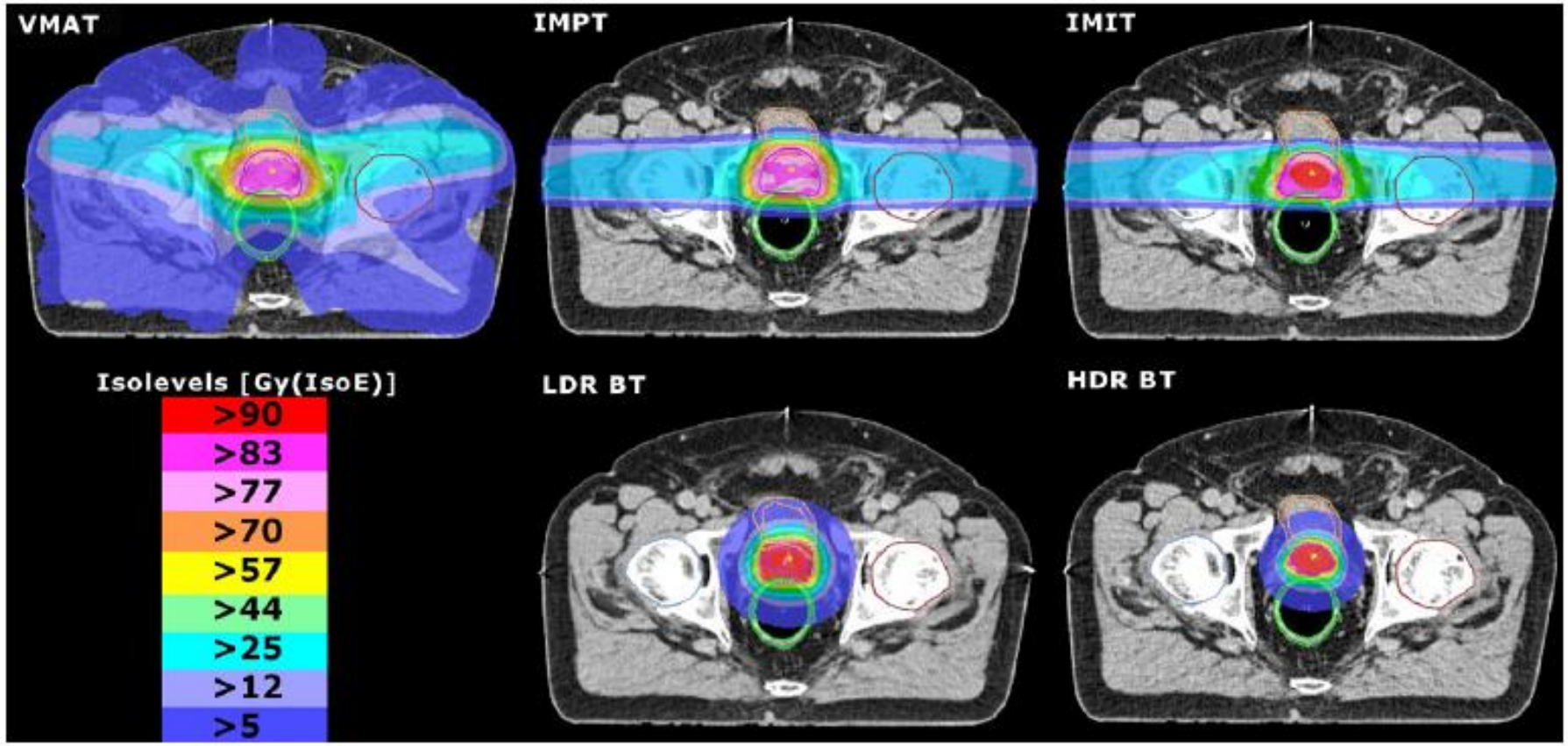






Dosimetric Considerations to Determine the Optimal Technique for Localized Prostate Cancer Among External Photon, Proton, or Carbon-Ion Therapy and High-Dose-Rate or Low-Dose-Rate Brachytherapy

Georg et al. (2013)



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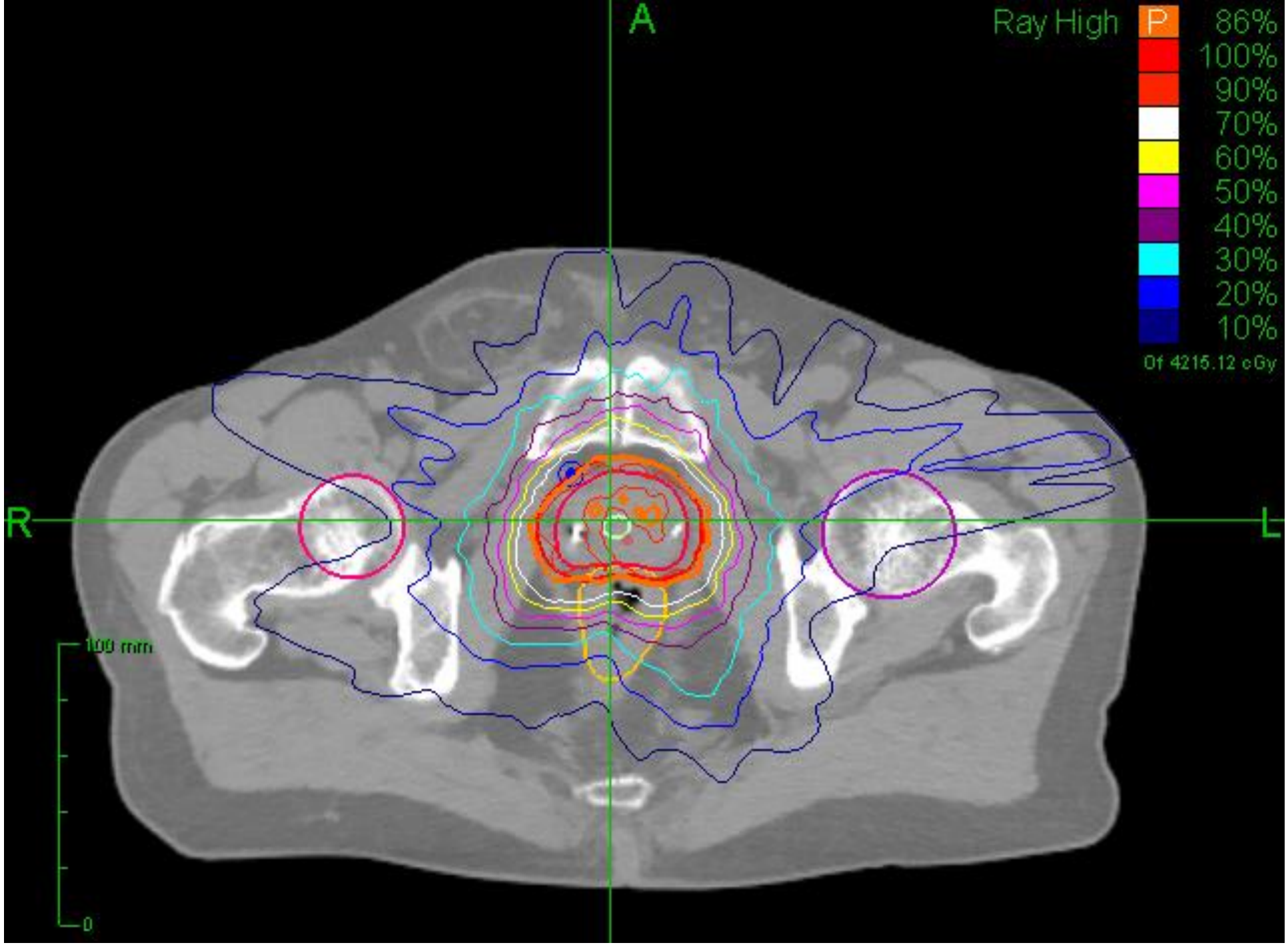
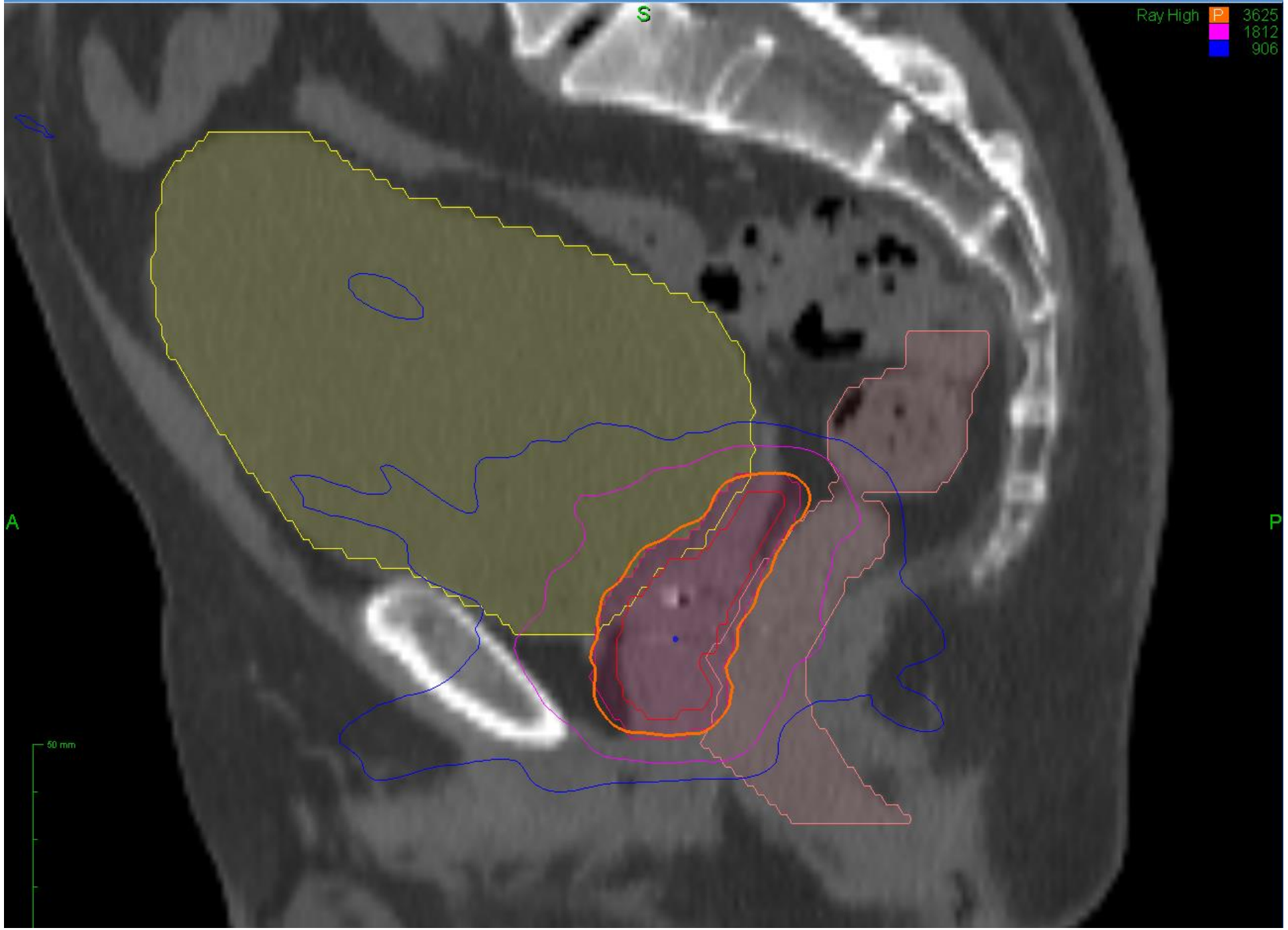
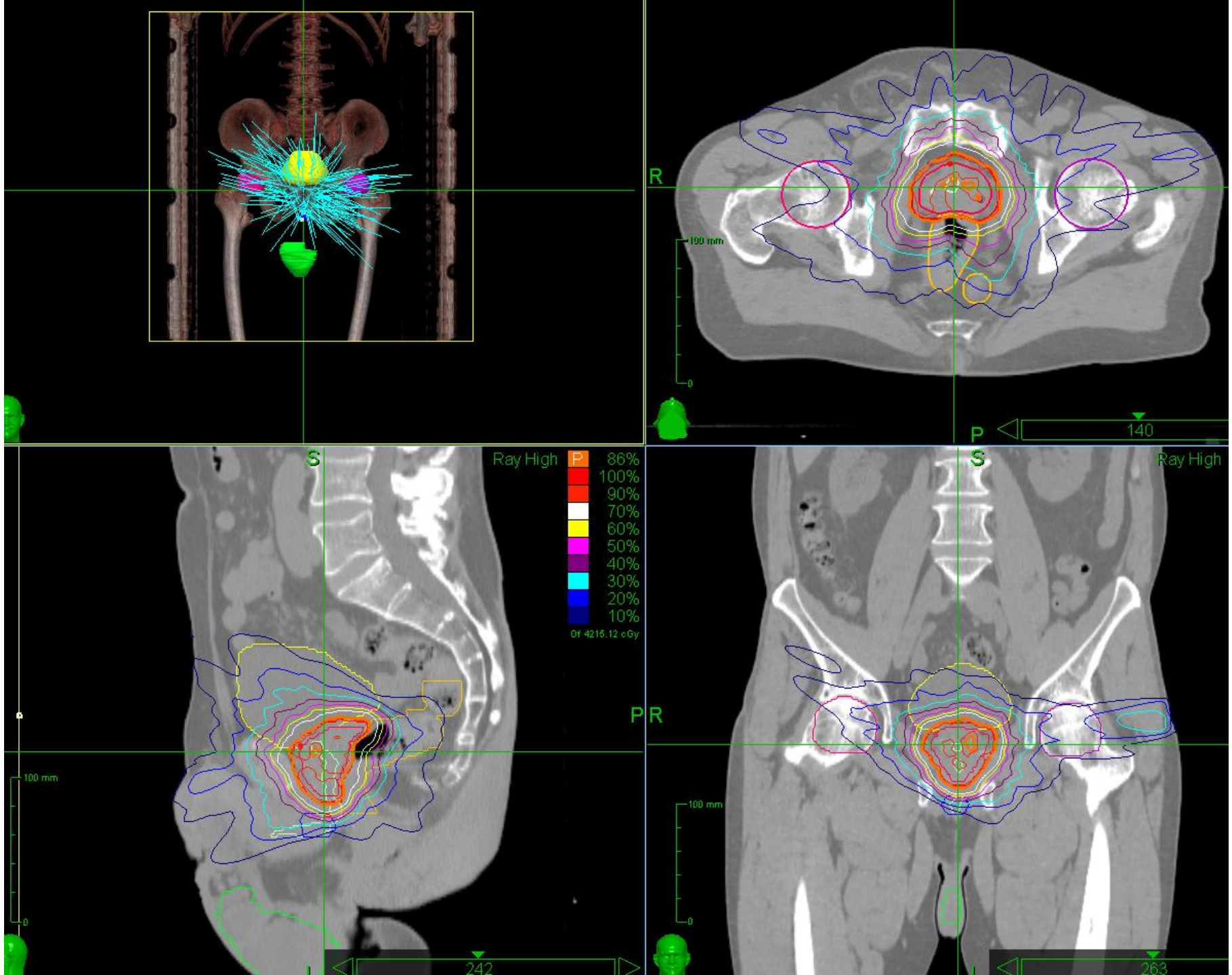
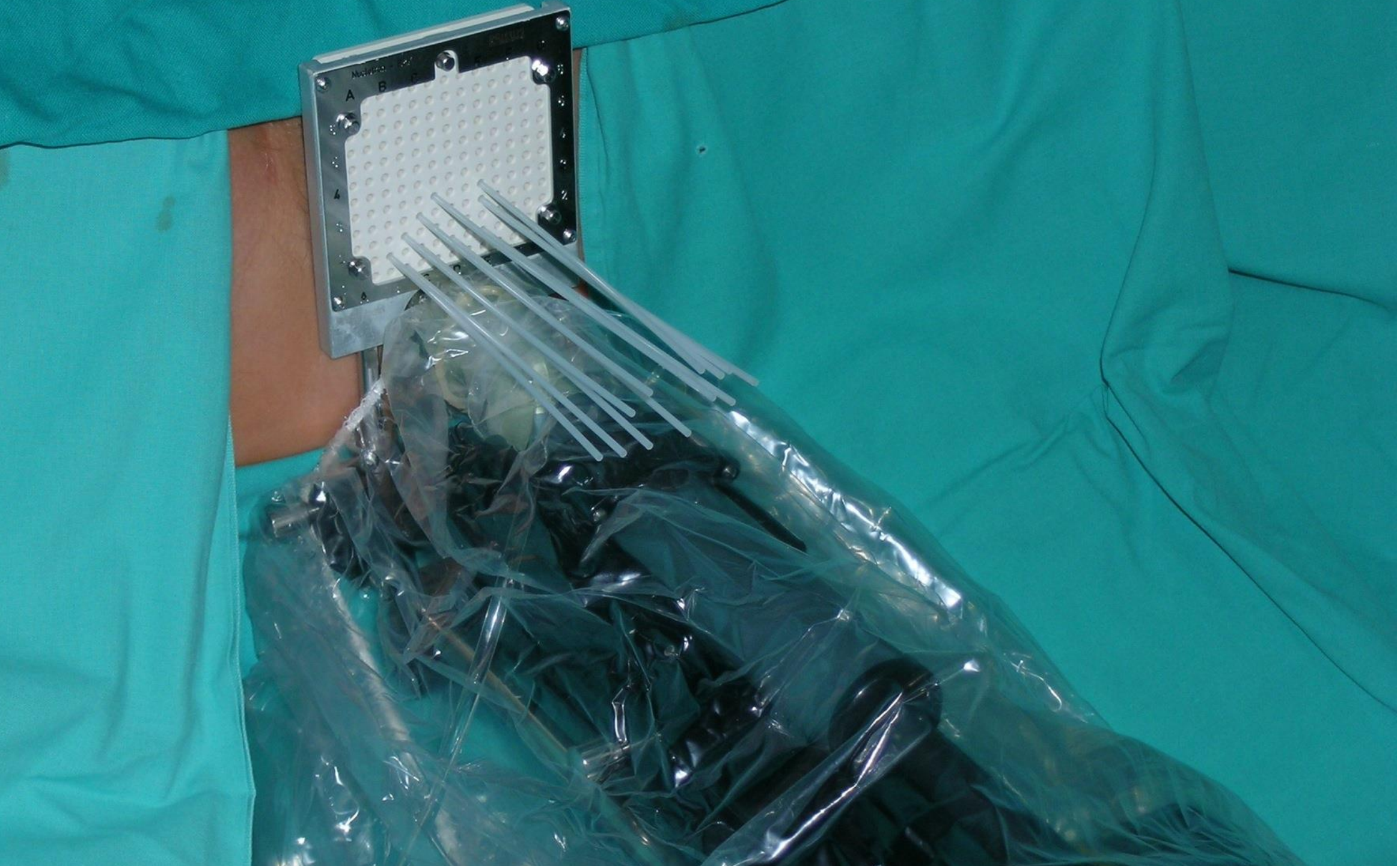
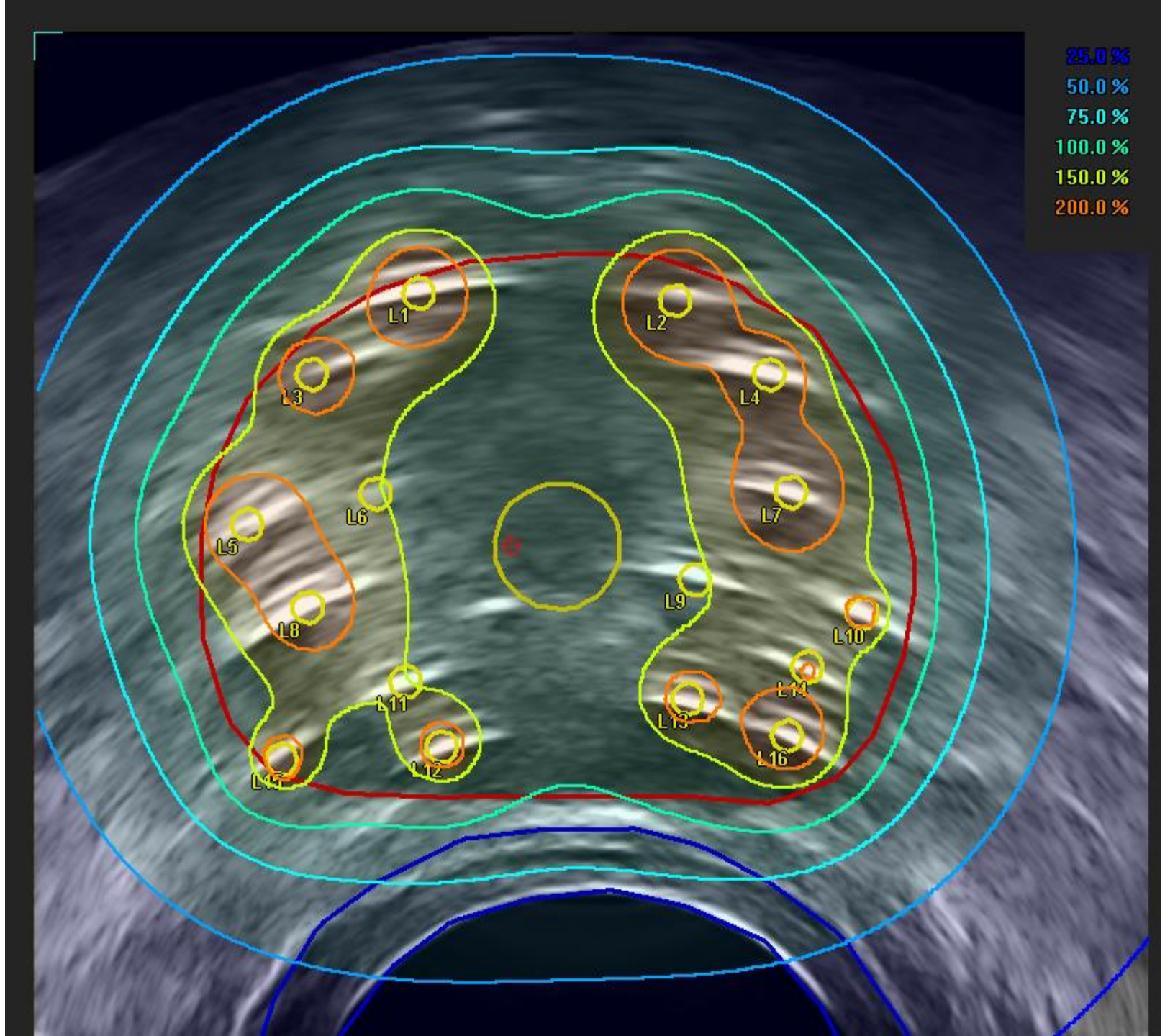
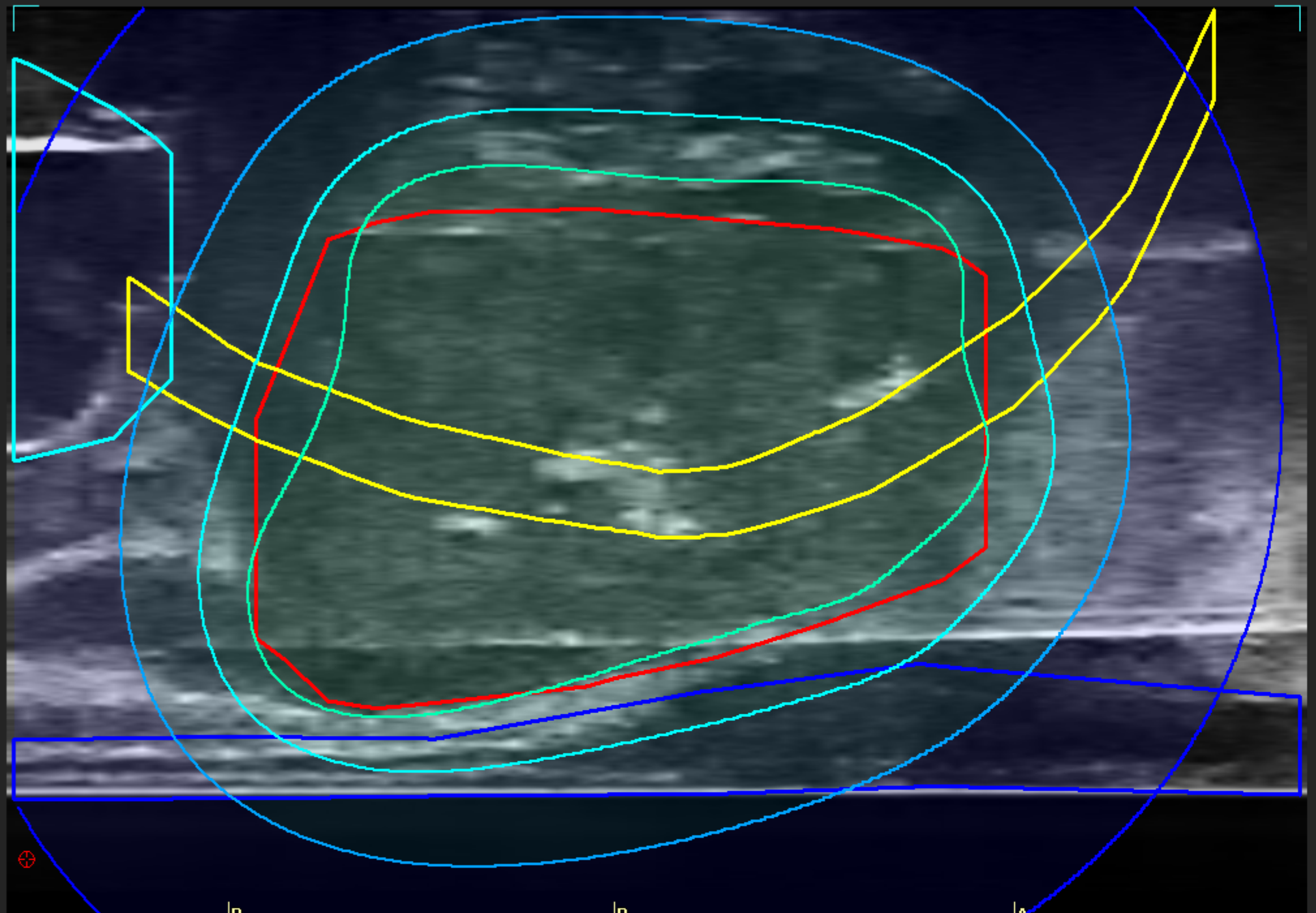

A
Ray High
P
86%
100%
90%
70%
60%
50%
40%
30%
20%
10%
Of 4215.12 cGy
R
L
100 mm
0

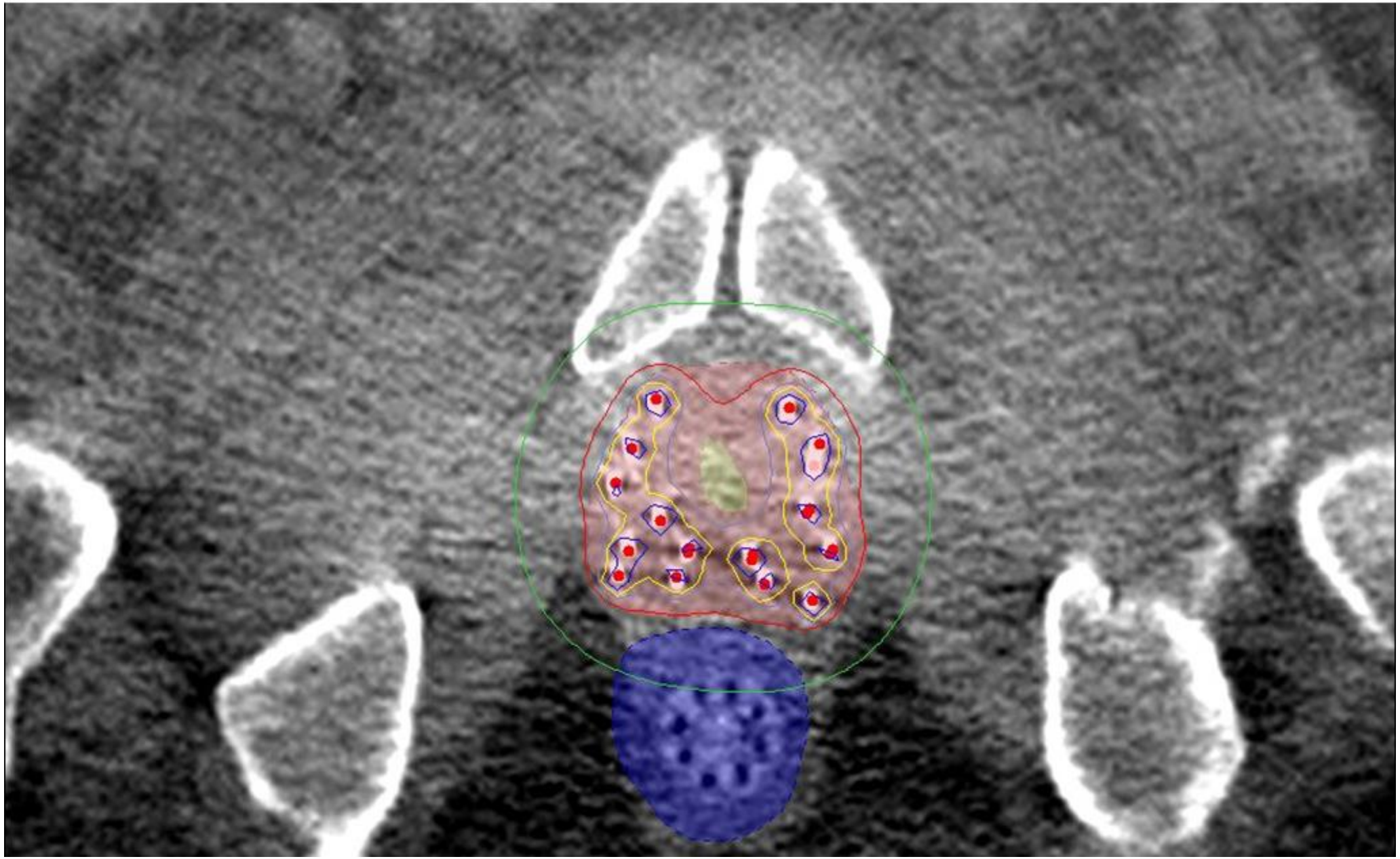

S
Ray High
P
3625
1812
906
A
P
50 mm


R
100 mm
0
P
140
S
Ray High
P
86%
100%
90%
70%
60%
50%
40%
30%
20%
10%
Of 4215.12 cGy
P R
100 mm
0
242
S
Ray High
R
100 mm
0
263

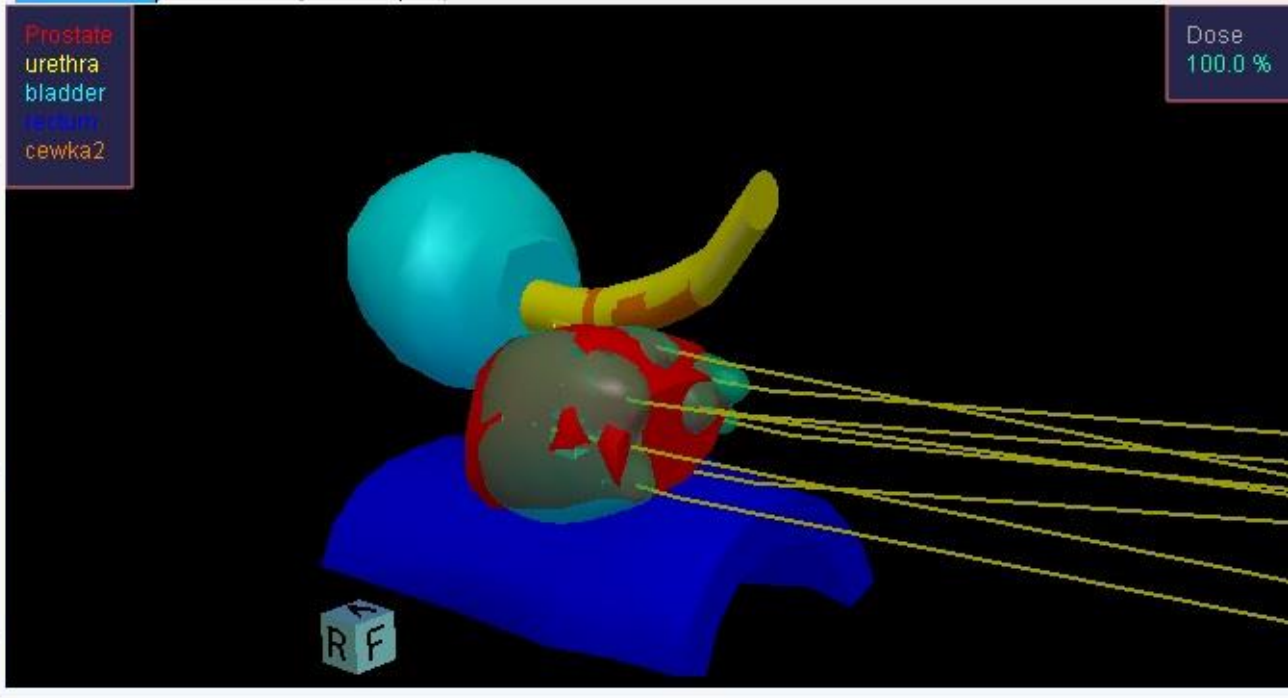


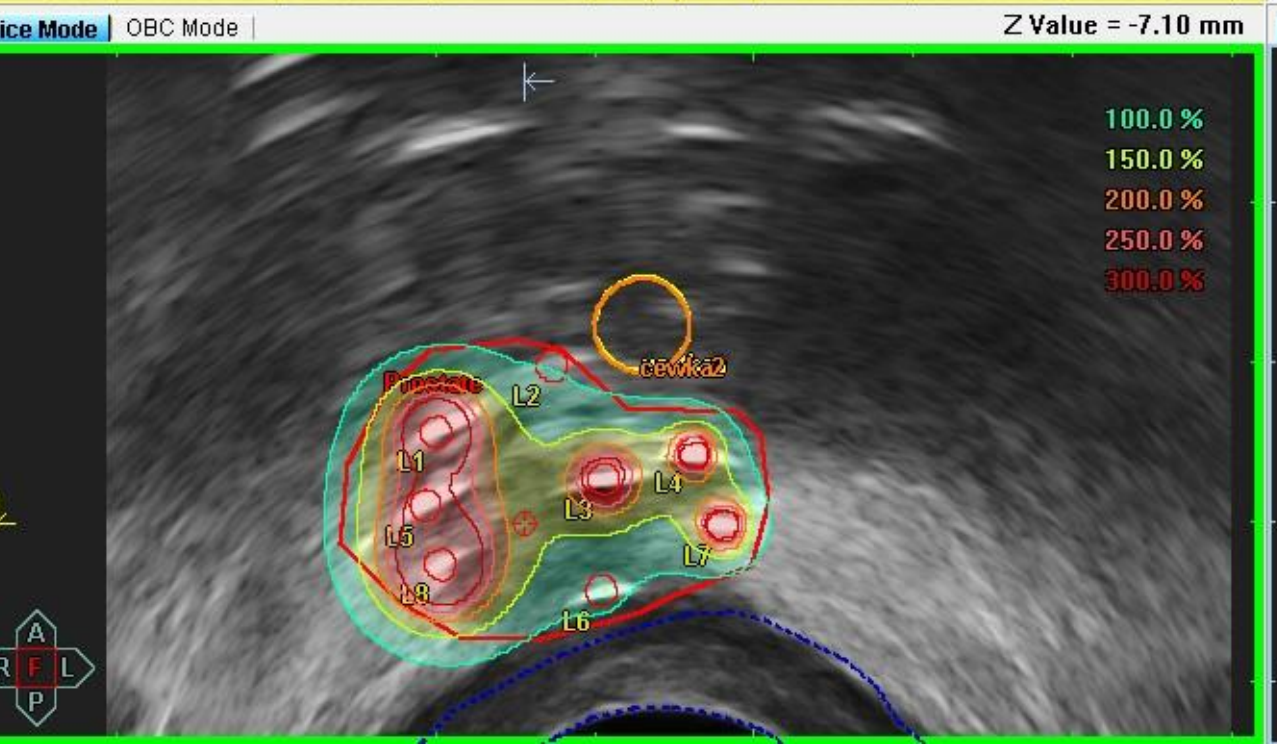

25.0 %
50.0 %
75.0 %
100.0 %
150.0 %
200.0 %
L1
L2
L3
L4
L5
L6
L7
L8
L9
L10
L11
L12
L13
L14
L16

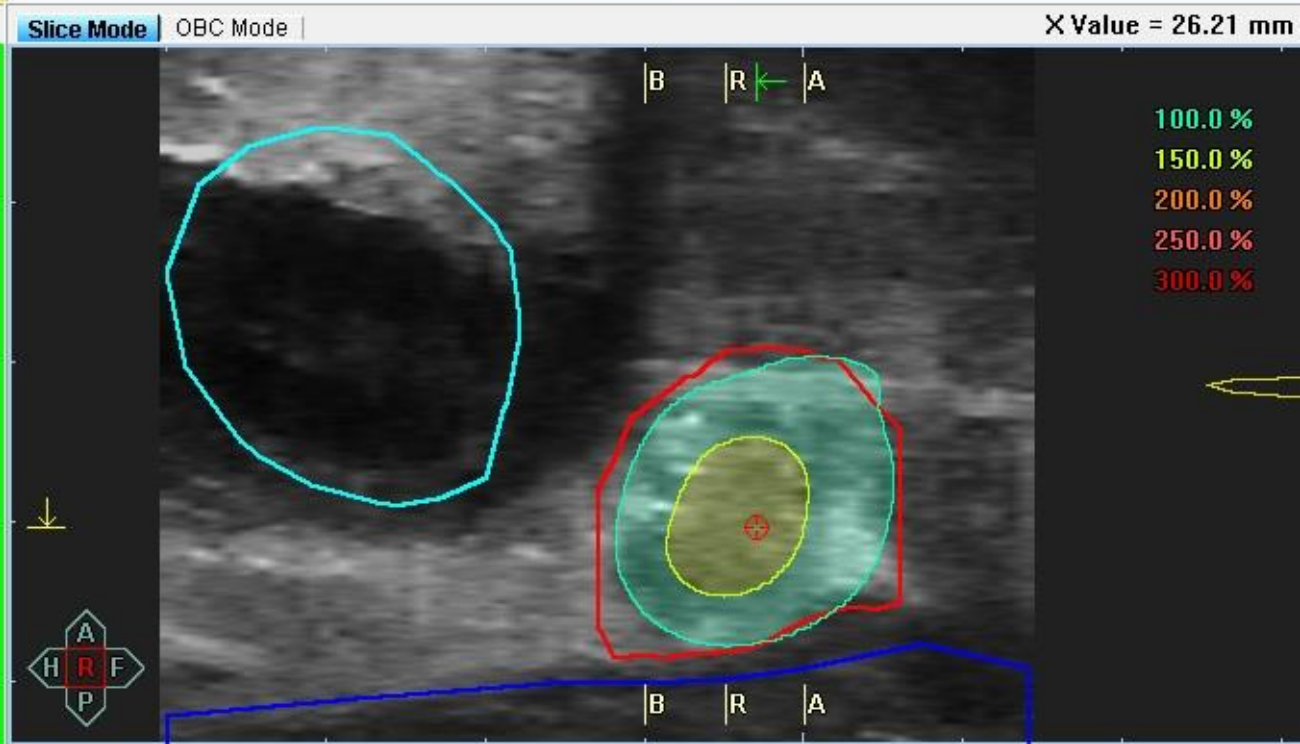

100.0 %
150.0 %
200.0 %

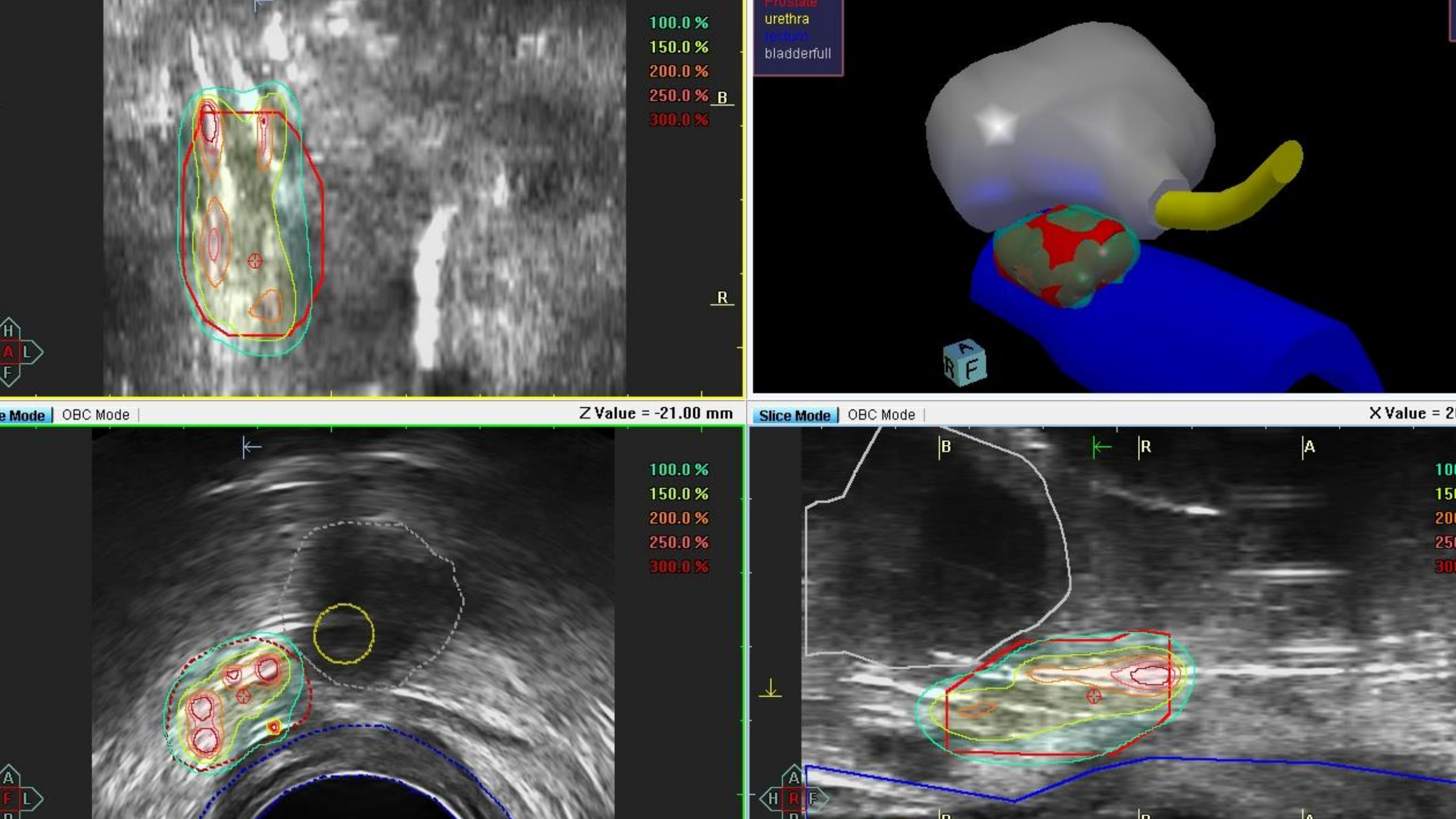


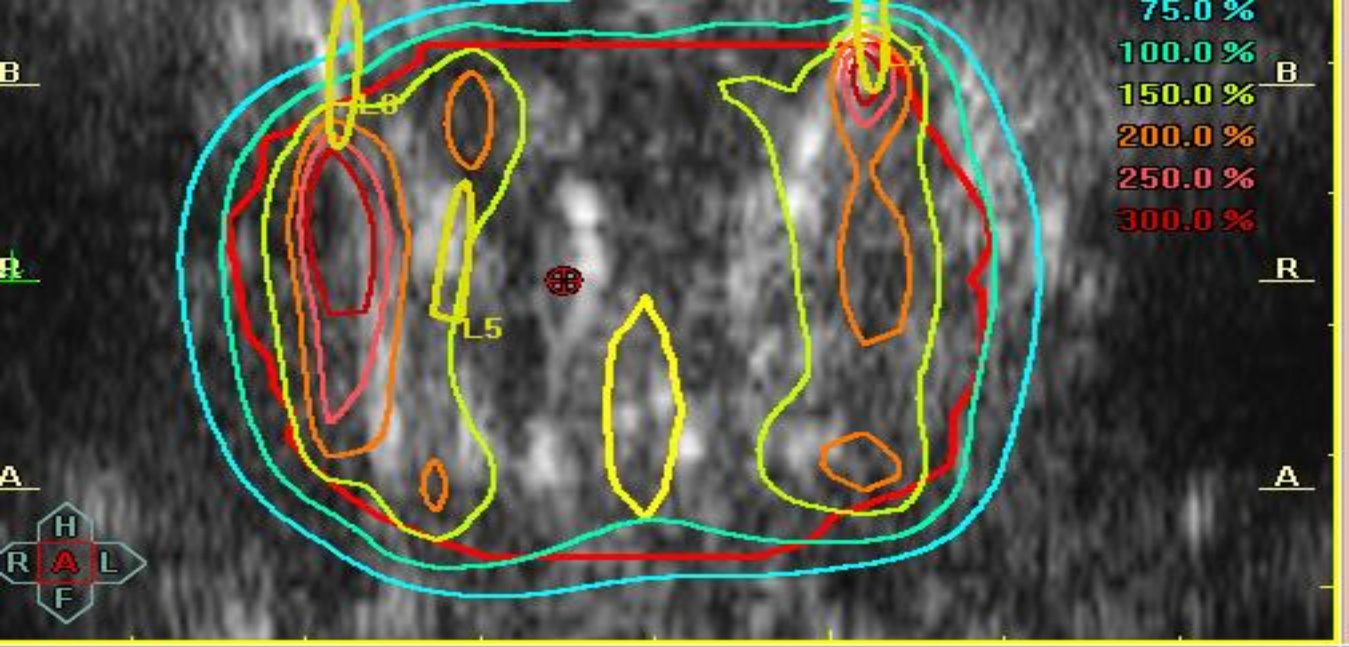

100.0 %
150.0 %
200.0 %
250.0 %
300.0 %
L7
B
R
A

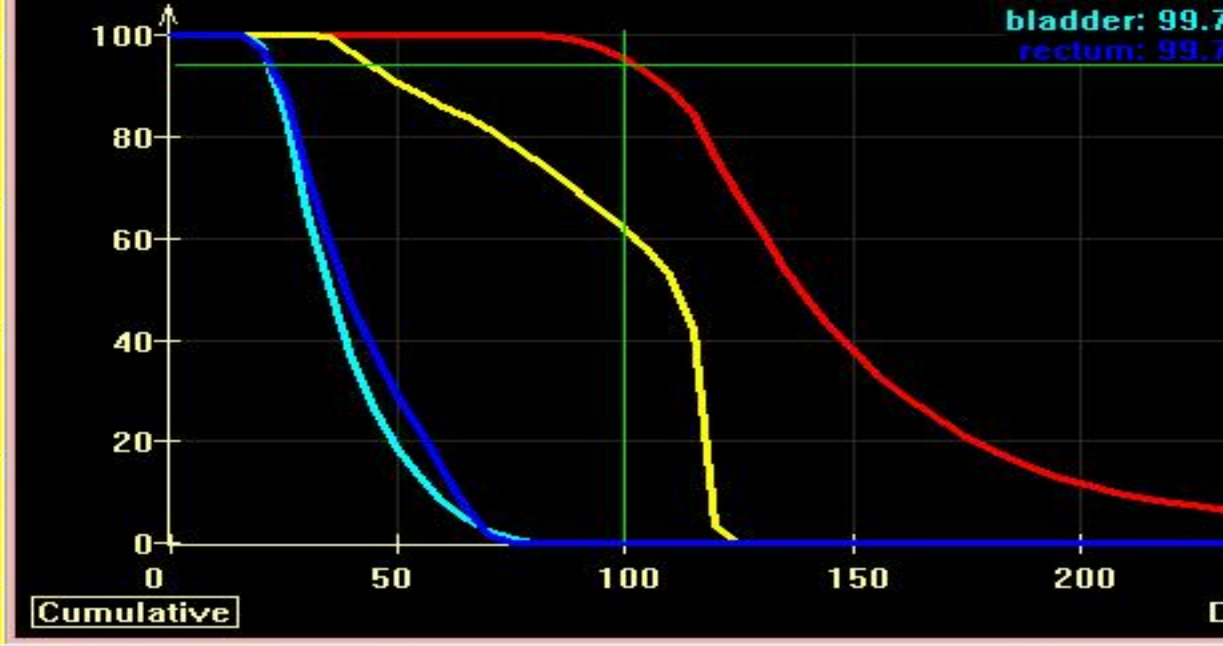

Prostate
urethra
bladder
rectum
cewka2
Dose
100.0 %

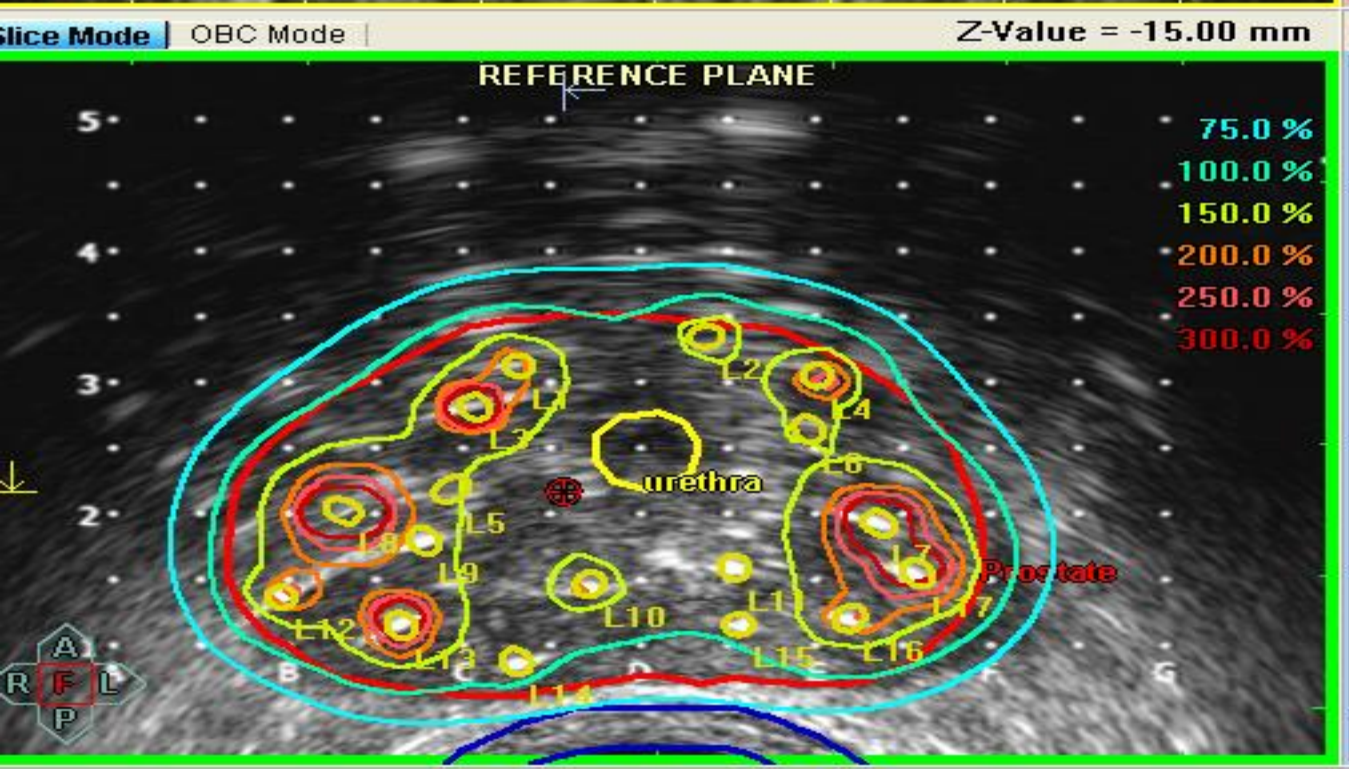

ice Mode | OBC Mode
Z Value = -7.10 mm
100.0 %
150.0 %
200.0 %
250.0 %
300.0 %
cewka2
L1
L2
L3
L4
L5
L6
L7
L8

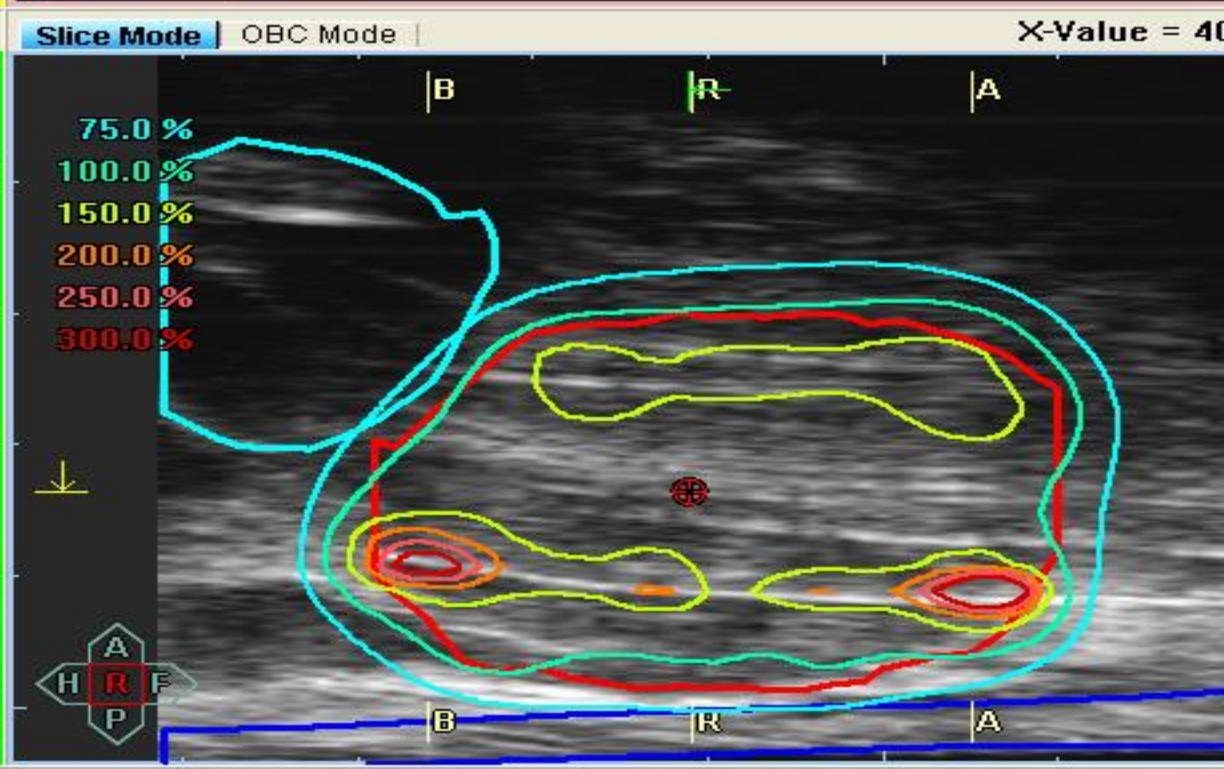

Slice Mode | OBC Mode
X Value = 26.21 mm
B
R
A
100.0 %
150.0 %
200.0 %
250.0 %
300.0 %

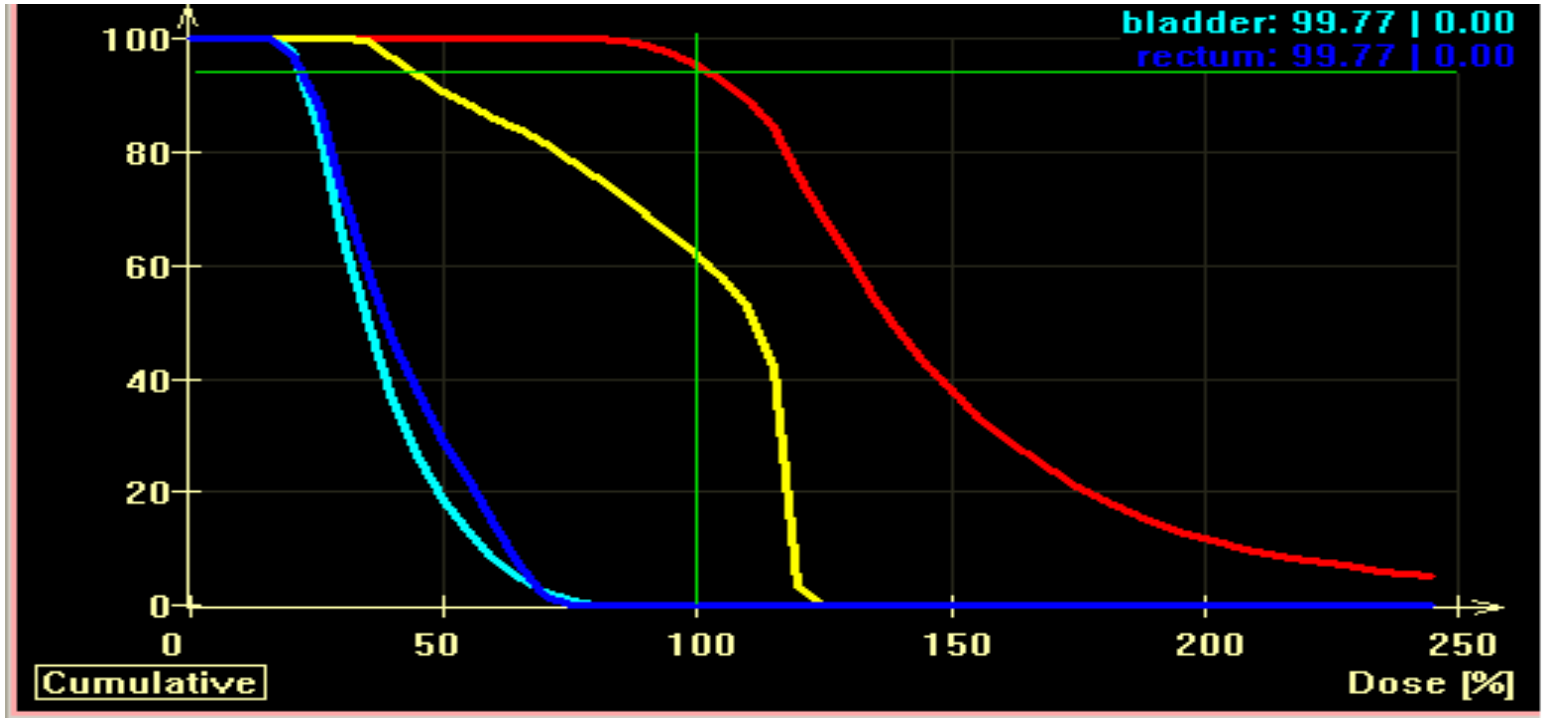

100.0 %
150.0 %
200.0 %
250.0 %
300.0 %
B
R
urethra
bladderfull
Mode | OBC Mode |
Z Value = -21.00 mm
Slice Mode | OBC Mode |
X Value = 2
A
R

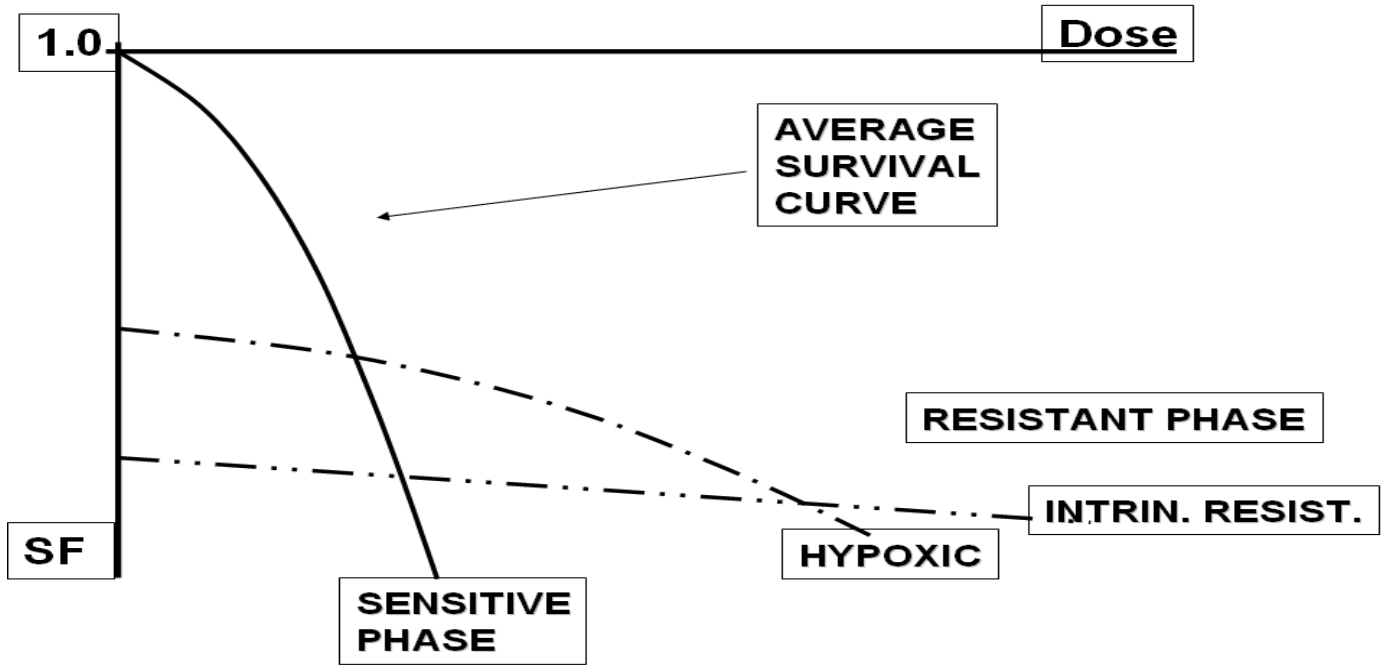

75.0 %
100.0 %
150.0 %
200.0 %
250.0 %
300.0 %
B
R
A
L5
H
R
A
L
F


bladder: 99.7
rectum: 99.7
100
80
60
40
20
0
0
50
100
150
200
Cumulative


Slice Mode
OBC Mode
Z-Value = -15.00 mm
REFERENCE PLANE
75.0 %
100.0 %
150.0 %
200.0 %
250.0 %
300.0 %
5
4
3
2
urethra
Prostate
L2
L4
L6
L5
L9
L10
L11
L12
L13
L14
L15
L16
A
R
F
L
P


Slice Mode
OBC Mode
X-Value = 40
75.0 %
100.0 %
150.0 %
200.0 %
250.0 %
300.0 %
B
R
A
H
R
F
P


bladder: 99.77 | 0.00
rectum: 99.77 | 0.00
100
80
60
40
20
0
0
50
100
150
200
250
Cumulative
Dose [%]


1.0
Dose
AVERAGE SURVIVAL CURVE
RESISTANT PHASE
INTRIN. RESIST.
HYPOXIC
SF
SENSITIVE PHASE

Nóż, igła czy skalpel:
porównanie brachyterapii, prostatektomii i SBRT.

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Uzupełniająca RT po prostatektomii

Badanie	Liczba pacjentów	kryteria	schemat	10-letni bDFS	10-letni OS
SWOG 8794	431	pT3	60-64Gy vs obs.	53% vs 30%	74% vs 66%
EORTC 22911	1005	pT3 lub pT2R1	60Gy vs obs.	61% vs 41%	81% vs 77% NS
ARO 96-02	388	pT3	60Gy vs obs.	72% vs 54% 5-letnie	-

Adjuvant Radiation Therapy, Androgen Deprivation, and Docetaxel for High-Risk Prostate Cancer Postprostatectomy: Results of NRG Oncology/RTOG Study 0621

Mark D. Hurwitz, MD[1]; Jonathan Harris, MS[2]; Oliver Sartor, MD[3]; Ying Xiao, PhD[1]; Bobby Shayegan, MD[4]; Paul W. Sperduto, MD[5,6]; Kasra R. Badiozamani, MD[7]; Colleen A. F. Lawton, MD[8]; Eric M. Horwitz, MD[9]; Jeff M. Michalski, MD[10]; Kevin Roof, MD[11]; David C. Beyer, MD[12]; Qiang Zhang, PhD[2]; and Howard M. Sandler, MD[13]

Cancer

- 74 chorych
- 95% ≥T3
- ADT + prostatektomia + EBRT + docetaxel
- Mediana obserwacji 4,4 lata
- Ostre powikłania ≥3 st. – 77%
- Nietrzymanie moczu ≥2 st. – 24%
- 3-letnie FFP – 73%

Autor	Dawka frakcyjna (Gy)	Liczba frakcji	Dawka całkowita (Gy)	BED [α/β=1.5 Gy] (Gy)	5-letnie bDFS średnie /wysokie ryzyko
Agoston et al.	2/10	30+1	60+10	217 (140+77)	84%/82%
Cury et al..	2.5/10	20+1	50+10	210 (133+77)	91%/n.a
Galalae et al.	2/9	25+2	50+18	223 (117+126)	71%/72% (64%/67%)
Kapraelian et al.	1.8/6	25+3	45+18	189 (99+90)	84%/80%
Khor et al.	2/6.5	23+3	46+19,5	211 (107+104)	84%/74%
Kotecha et al.	1.8/5.5-7.5	28+3	50.4+16.5-22.5	188-246 (111+77-135)	90%/57%
Marina et al.	2/9.5-11.5	23+2	46+19-23	246 – 306 (107+139-199)	91%/n.a.
Morton et al.[36]	1.8/10	25+2	45+20	252 (99+153)	98%/n.a.
Prada et al.[37]	2/11.5	23+2	46+23	306 (107+199)	89%/72-80%
Savdie et al.[38]	1.8/5.5	25+3	45+16.5	176 (99+77)	n.a./80% n.a./53%
Zwahlen et al.[39]	2/6-5	23+3-4	46+18-20	194-197 (107+87-90)	80%/n.a.

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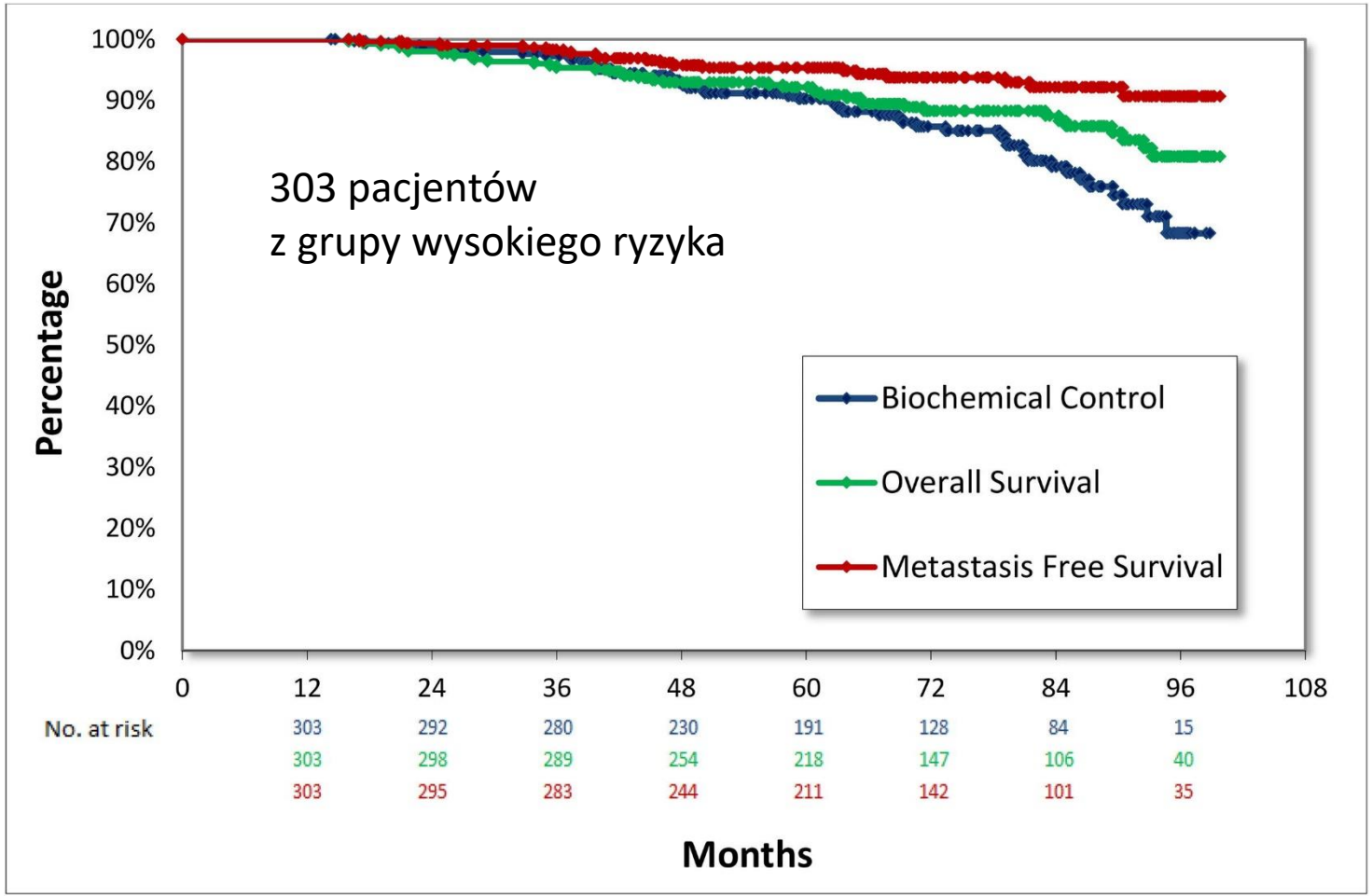
Original article

Combined high dose rate brachytherapy and external beam radiotherapy for clinically localised prostate cancer

Iosif Strouthos [a,*], Georgios Chatzikonstantinou [b], Nikolaos Zamboglou [b,c], Natasa Milickovic [d], Sokratis Papaioannou [d], Dimitra Bon [e], Constantinos Zamboglou [a,g], Claus Rödel [b], Dimos Baltas [f,g], Nikolaos Tselis [b]



Cyberknife®

Autor	Dawka frakcyjna (Gy)	Liczba frakcji	Dawka całkowita (Gy)	BED [α/β=1.5 Gy] (Gy)	5-letnie bDFS średnie /wysokie ryzyko
King et al.	7.25	4-5	36.25	211	84%/81%
Katz et al.	7.25	5	35-36.25	198-211	89.3%/68.5%

frontiers in ONCOLOGY

ORIGINAL RESEARCH ARTICLE
published: 24 November 2014
doi: 10.3389/fonc.2014.00321

Virtual HDR CyberKnife SBRT for localized prostatic carcinoma: 5-year disease-free survival and toxicity observations

Donald Blake Fuller[1]*, John Naitoh[2] and George Mardirossian[1]

[1] *Division of Genesis Healthcare Partners Inc., CyberKnife Centers of San Diego Inc., San Diego, CA, USA*
[2] *Division of Genesis Healthcare Partners Inc., Coast Urology Medical Group Inc., La Jolla, CA, USA*

9,5Gy x 4 = 38 Gy

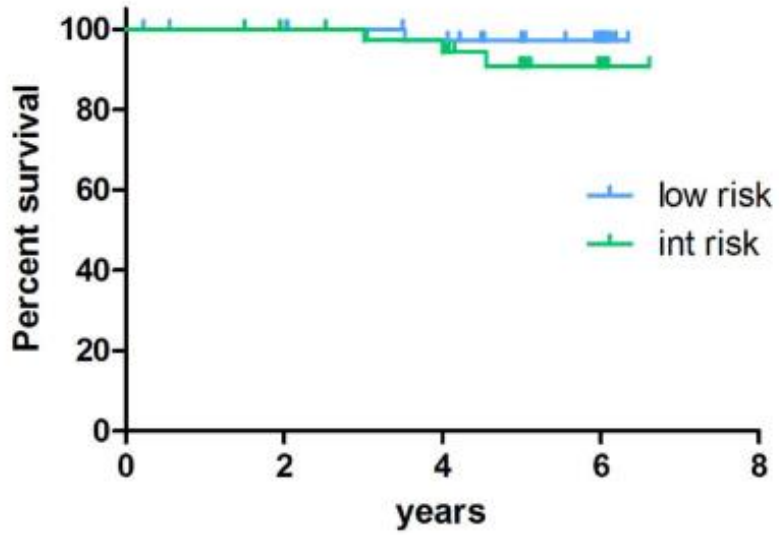


FIGURE 4 | Biochemical-relapse-free survival post-SBRT stratified by risk-group: Phoenix definition.

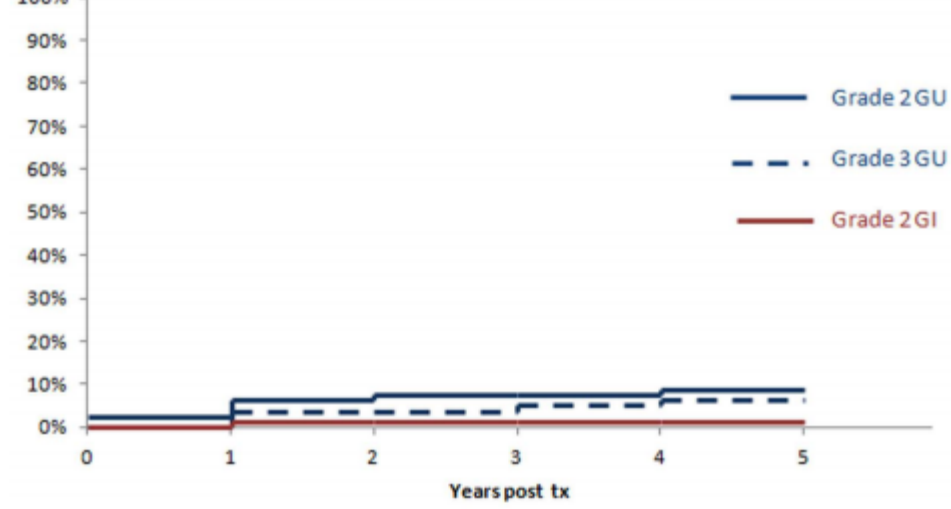


FIGURE 6 | Cumulative incidence of long-term grade 2 or higher GU or GI morbidity, annualized to 5 years. There were no further events beyond 5 years in this study.

Samodzielna HDR BT

Autor	Dawka frakcyjna (Gy)	Liczba frakcji	Dawka całkowita (Gy)	BED [α/β=1.5 Gy] (Gy)	5-letnie bDFS średnie /wysokie ryzyko
Yoshioka et al.	6	9	54	270	93%/79%
Zamboglou et al.	9.5-11.5	3-4	34.5-38	279-299	93%/93%
Hoskin et al.	9	4	36	252	95%/87%

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Original article

High dose rate brachytherapy as monotherapy for localised prostate cancer ☆

Iosif Strouthos [a,*,1], Nikolaos Tselis [b,1], Georgios Chatzikonstantinou [b], Saeed Butt [c], Dimos Baltas [d,e], Dimitra Bon [f], Natasa Milickovic [c], Nikolaos Zamboglou [b]

Characteristics	(n = 450)
Median follow-up (months)	56.3 (4.4–91.7)
Age at treatment (years)	
Mean	69.1
Median	70.3
Pre-treatment PSA (ng/ml)	
Mean	7.5
Median	6.6
	n (%)
Stage	
T1b-c	151 (33.6%)
T2a	153 (34.0%)
T2b	80 (17.8%)
T2c	64 (14.2%)
T3a	2 (0.4%)
Gleason Score	
≤6	303 (67.3%)
7	102 (22.7%)
>7	45 (10.0%)
Pre-treatment PSA (ng/ml)	
≤10	403 (89.6%)
11–20	42 (9.3%)
>20	5 (1.1%)
Age at treatment (years)	
<60	54 (12.0%)
60–69	160 (35.6%)
≥70	236 (52.4%)
Androgen deprivation therapy	58 (12.8%)
Risk group	
Low	198 (44.0%)
Intermediate	135 (30.0%)
High	117 (26.0%)

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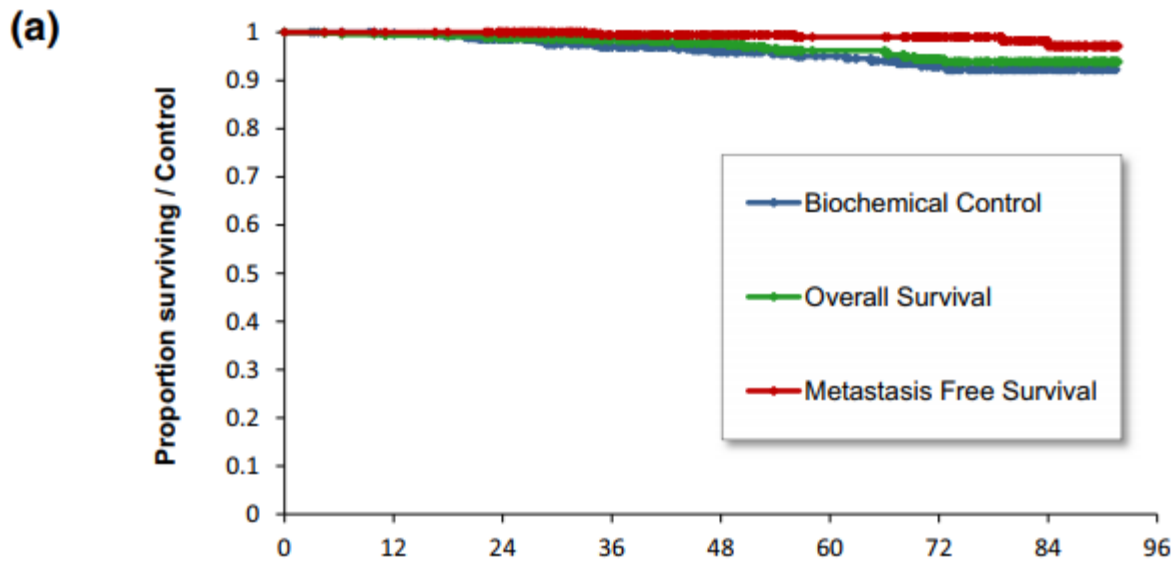

Patients at risk								
biochemical control	450	443	409	325	256	200	145	57
overall survival	450	447	434	350	278	218	168	89
metastasis-free survival	450	447	434	347	278	218	168	89

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High dose rate brachytherapy as monotherapy for localised prostate cancer ☆

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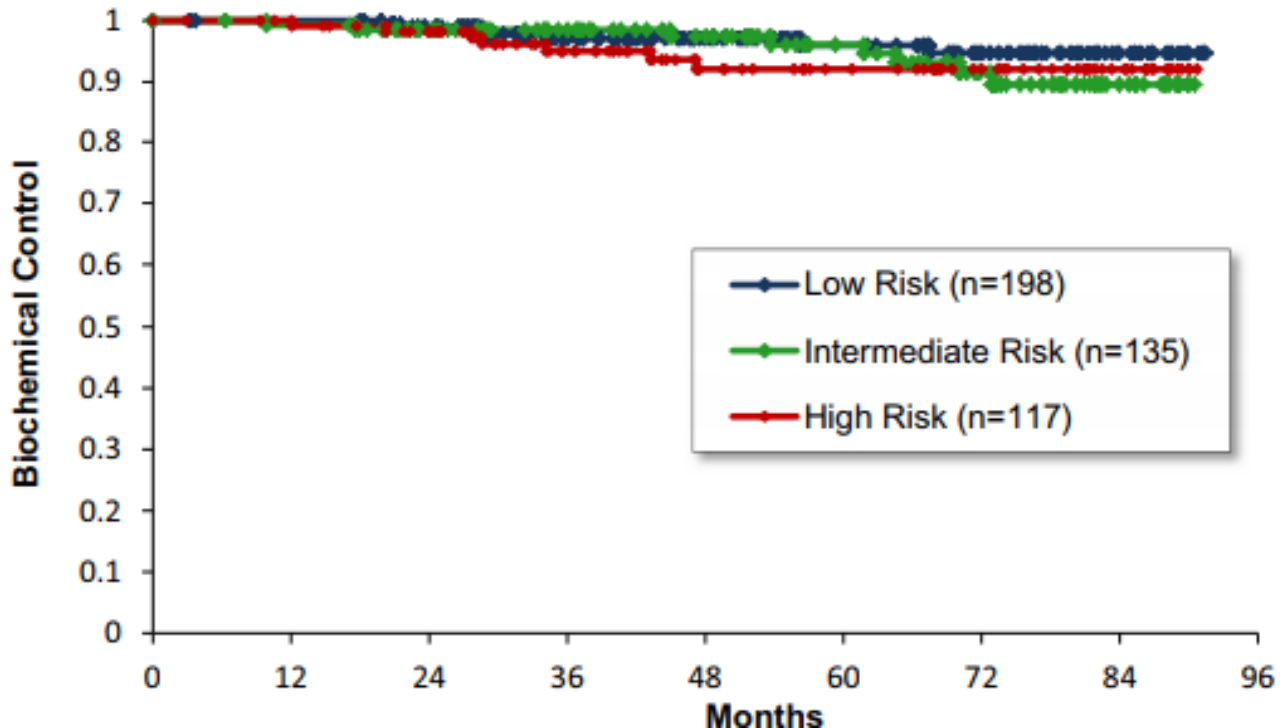

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Prostate brachytherapy

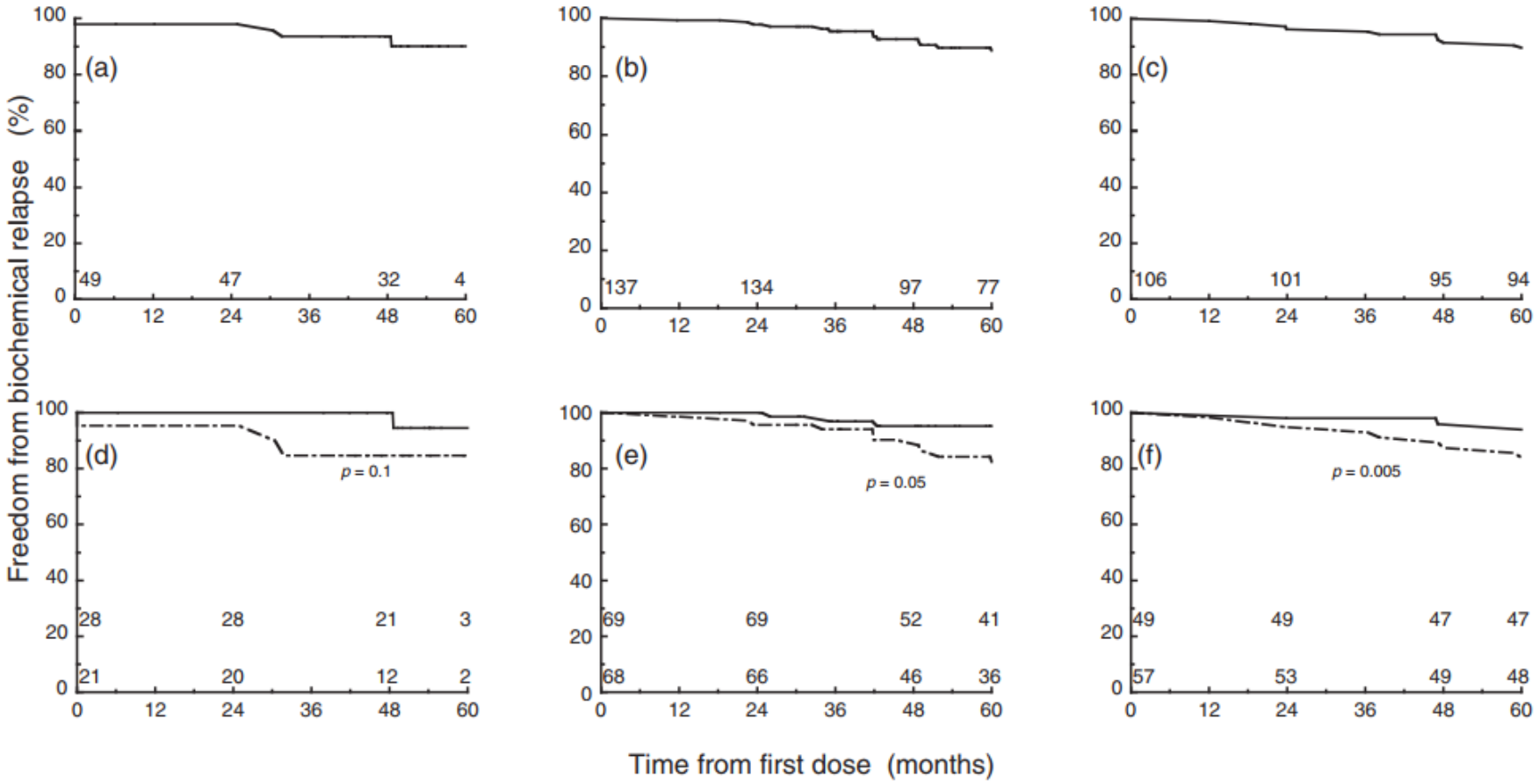
Single-dose high-dose-rate brachytherapy compared to two and three fractions for locally advanced prostate cancer

Peter Hoskin, Ana Rojas *, Peter Ostler, Robert Hughes, Roberto Alonzi, Gerry Lowe

Mount Vernon Hospital, Cancer Centre, Northwood, UK

- 293 pacjentów w trzech podgrupach
- 1 × 19 Gy lub 1 × 20 Gy (A = 49)
- 2 × 13 Gy (B = 138)
- 3 × 10.5 Gy (C = 106)

A B C


Freedom from biochemical relapse (%)
(a)
(b)
(c)
(d)
(e)
(f)
p = 0.1
p = 0.05
p = 0.005
49 47 32 4
137 134 97 77
106 101 95 94
28 28 21 3
21 20 12 2
69 69 52 41
68 66 46 36
49 49 47 47
57 53 49 48
0 12 24 36 48 60
Time from first dose (months)

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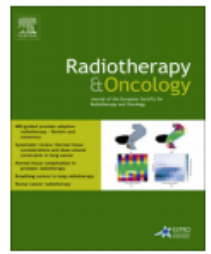

Prostate cancer brachytherapy

High-dose-rate interstitial brachytherapy as monotherapy in one fraction for the treatment of favorable stage prostate cancer: Toxicity and long-term biochemical results

Pedro J. Prada [a,*], Juan Cardenal [a], Ana García Blanco [a], Javier Anchuelo [a], María Ferri [a], Gema Fernández [c], Elisabeth Arrojo [c], Andrés Vázquez [b], Maite Pacheco [b], José Fernández [d]

[a] *Department of Radiation Oncology;* [b] *Department of Radiation Physics, Hospital Universitario Marqués de Valdecilla, Santander;* [c] *Department of Radiation Oncology; and* [d] *Department of Radiation Physics, Hospital Universitario Central de Asturias, Oviedo, Spain*

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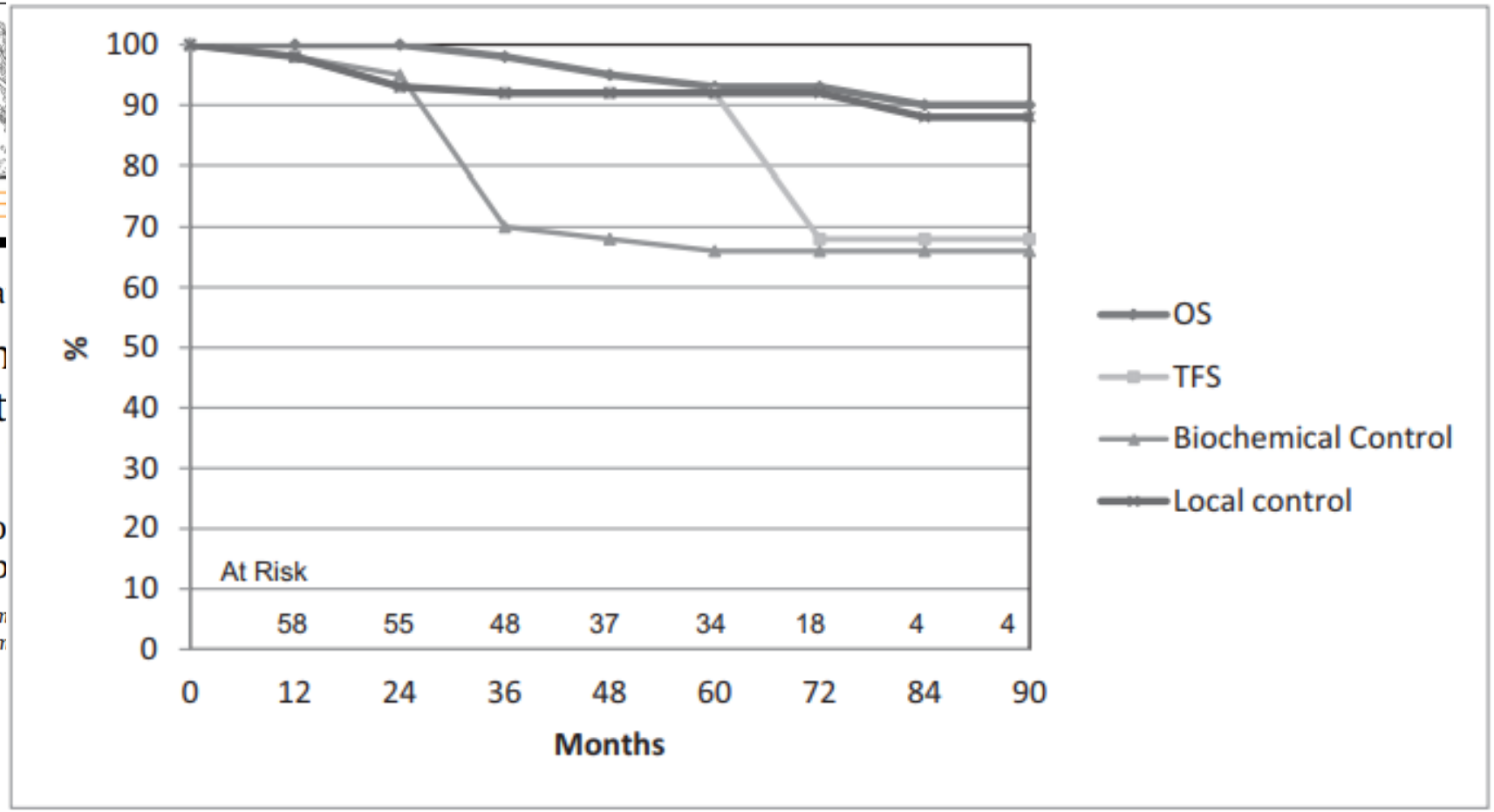
[a] Departm
[d] Departm



65th ASTRO 2018, San Antonio, TX

- 195 prac #brachytherapy
- Trial RTOG 0232 wyróżniony nagrodą BEST of ASTRO

Whole-Pelvic Versus Prostate-Only Radiation Therapy in Unfavorable Intermediate-Risk and High-Risk Prostate Cancer Treated with Androgen Deprivation Therapy and Brachytherapy Boost

D.D. Yang et al.

- 7292 pacjentów z NCDB
- Mediana FU 6,3 lata
- WPRT vs PORT
- HR 1.02, 95% CI (0.91-1.14, P =0.702) – cała grupa
- HR 1.12, 95% CI (0.93-1.35, P =0.246) – średnie ryzyko
- HR 0.98, 95% CI (0.85-1.12, P =0.726) – wysokie ryzyko
- HR 1.00, 95% CI (0.89-1.13, P =0.985) –>15 % rozsiewu do ww. chł.

Brachytherapy Improves 10-year Overall Survival Compared to Prostatectomy Alone in Young Men (≤60) with Low- and Intermediate-Risk Prostate Cancer: An NCDB Analysis

J. Kodiyan et al.

- 128 399 pacjentów z bazy NCDB
- 18 – 60 lat
- Oceniano 10 letnie przeżycie całkowite w zależności od metody leczenia
- RT vs Prostektomia (81.5% vs. 87.91, $p<0.0001$) – wszyscy
- BT vs Prostektomia (93.0% vs. 91.7%, $p< 0.001$) – niskie ryzyko
- EBRT+BT vs Prostektomia (91.43% vs. 85.76%, $p<.0001$) – średnie ryzyko
- BT vs Prostektomia(84.34% vs. 86.33%, $p=0.1158$) – wysokie ryzyko

Patient Reported Outcomes of NRG Oncology/RTOG 0232: A Phase III Study Comparing Combined External Beam Radiation and Transperineal Interstitial Permanent Brachytherapy with Brachytherapy Alone in Intermediate Risk Prostate Cancer

J. Moughan et al.

- 530 pacjentów - 255 EBRT + BT vs 275 BT

Domain/ Subscale	24 mos Δ mean ± SD		p-value ($\lvert\mu_B - \mu_{EBT+B}\rvert > 0$)	Effect Size
	EBT+B	B		
Urinary	-11.2 ± 15.7	-5.6 ± 13.6	0.0002	0.38
Urinary-irritative	-11.9 ± 17.4	-4.8 ± 14.3	<0.0001	0.44
Bowel	-7.1 ± 12.6	-2.4 ± 9.9	<0.0001	0.42
Sexual	-16.7 ± 23.4	-10.6 ± 21.0	0.0072	0.27

Acute and Subacute Complications of Brachytherapy for Prostate Cancer: A Single Institution Claims-Based Analysis

D. Lee et al.

- 582 pacjentów:
- 97 pacjentów leczonych HDR (^{192}Ir)
- 485 pacjentów leczonych LDR (^{125}I lub ^{103}Pd)

Complications	N	%
None	477	82.0
LUTS	49	8.4
Bladder Injury	23	4.0
Urinary Retention	22	3.8
Urinary Stricture	10	1.7
Rectal	3	0.5
Cardiopulmonary	11	1.9

Prostatektomia ratująca

Author	No of pts	MedianFU (years)	treatment	BFS	DMFS	OS
Bianco et al. (2005)	100 (1984-2003)	5	N/A	PFS 55%	b.d.	63% (10-years)
Ward et al. (2005)	199 (1967-2000)	7	Cystoprostatectomy /retropubic	PFS 8,7 vs 4,4 years	b.d.	b.d. (65%) (10-years)
Paparel et al. (2009)	146 (1984-2006)	3,8	Prostatectomy (2 surgeons)	65/146	54% (RFS)	b.d. (96%)
Chade et al. (2011)	404 (1985-2009)	4,4	Prostatectomy	48%	83%	b.d. (92%)

Ratujące SBRT

Author	No of pts	Median FU (months)	Dose	BFS	DMFS	OS
Fuller et al. (2015)	29 (2009-2014)	24	34Gy/5fx (HDR-like)	82% (2-year)	n.a.	n.a.
Zerini et al. (2015)	22/32 (2008-2013)	21.3	[SBRT/CK] 25-30Gy/df 3-6Gy	40.6% (whole group)	78.2% (whole group)	87.5% (whole group)
Leroy et al. (2017)	23 (2011-2014)	22.6	[CK] 36Gy/6fx (isodose 80%; 95% PTV)	54% (2-year)	n.a.	100% (2-year)
Mbeutcha et al. (2017)	18/28 (2011-2015)	14.5	[CK] 35Gy/5fx (isodose 80%)	10/18 (55.6%)	1/18	n.a.

Brachyterapia HDR ratująca

Author	No of pts	Median FU (months)	Dose	BFS	DMFS	OS
Chen et al. (2013)	52 (1998-2009)	59,6	36Gy/6fx 2 implantations	51%	b.d.	92%
Yamada et al. (2013)	42 (2007-2011)	36	32Gy/4fx 1 implantation	68,5%	81,5%	79% (90,3%)
Jo et al. (2011)	11 (2006-2009)	29 (average)	22Gy/2fx 1 implantation	7/11	10/11	b.d.
Kukiełka et al. (2014)	34 (2007-2013)	13	30Gy/3fx+HT(25) 3 implantations	74% (2-year)	32/34	34/34
Wojcieszek et al. (2016)	83 (2008-2012)	41	30Gy/3fx 3 implantations	67%	78%	86%

MRI-guided focal salvage high-dose-rate brachytherapy for recurrent prostate cancer

UMC Utrecht

Marieke van Son, MD
Jochem van der Voort van Zijp, MD, PhD
Max Peters, MD, PhD
Marinus Moerland, Ir, PhD

Jan Lagendijk, Ir, PhD
Wietse Eppinga, MD
Raquel Dávila Fajardo, MD
Juus Noteboom, MD, PhD

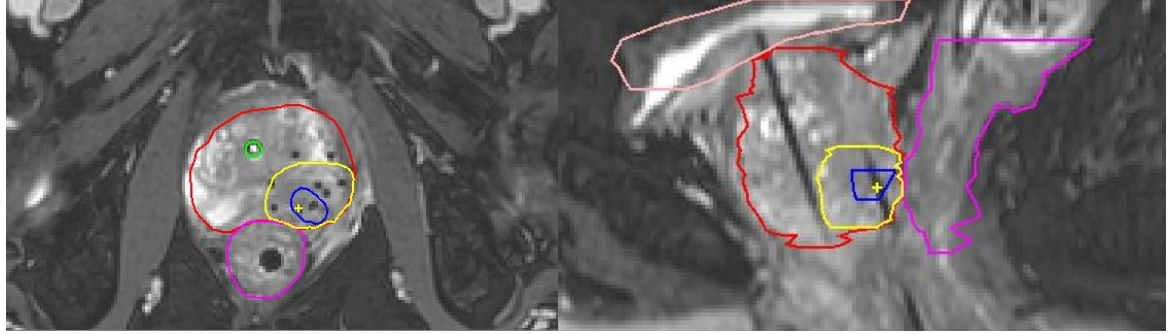
Intra-operative planning

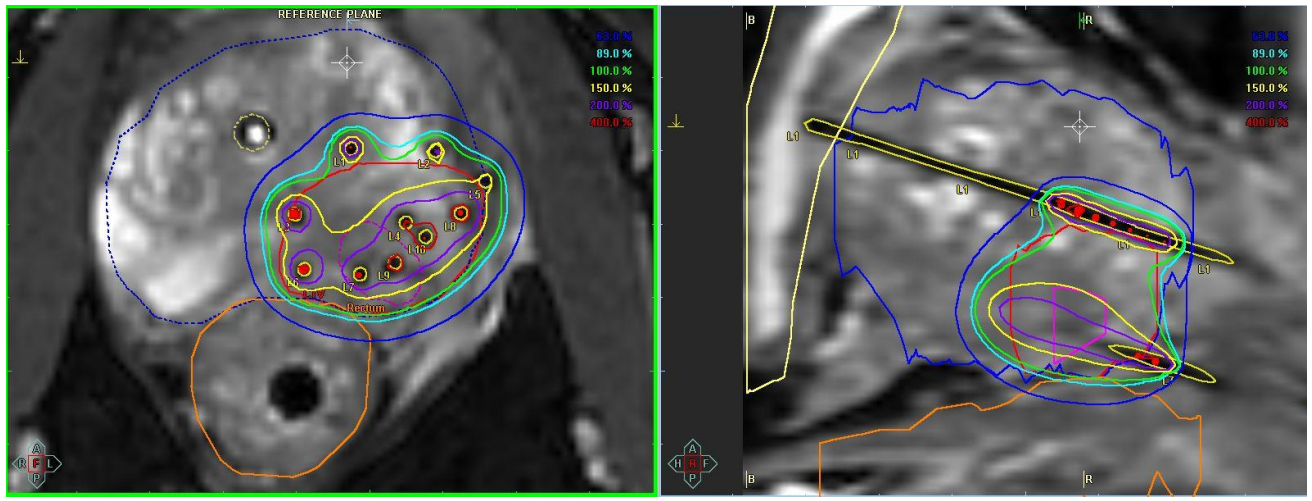
1. MRI:

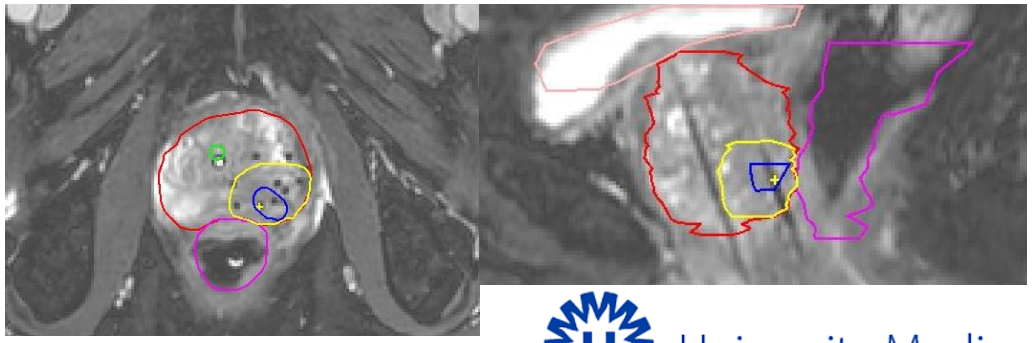
- Catheter reconstruction
- Contour adjustments

2. Dose planning

3. Position verification MRI



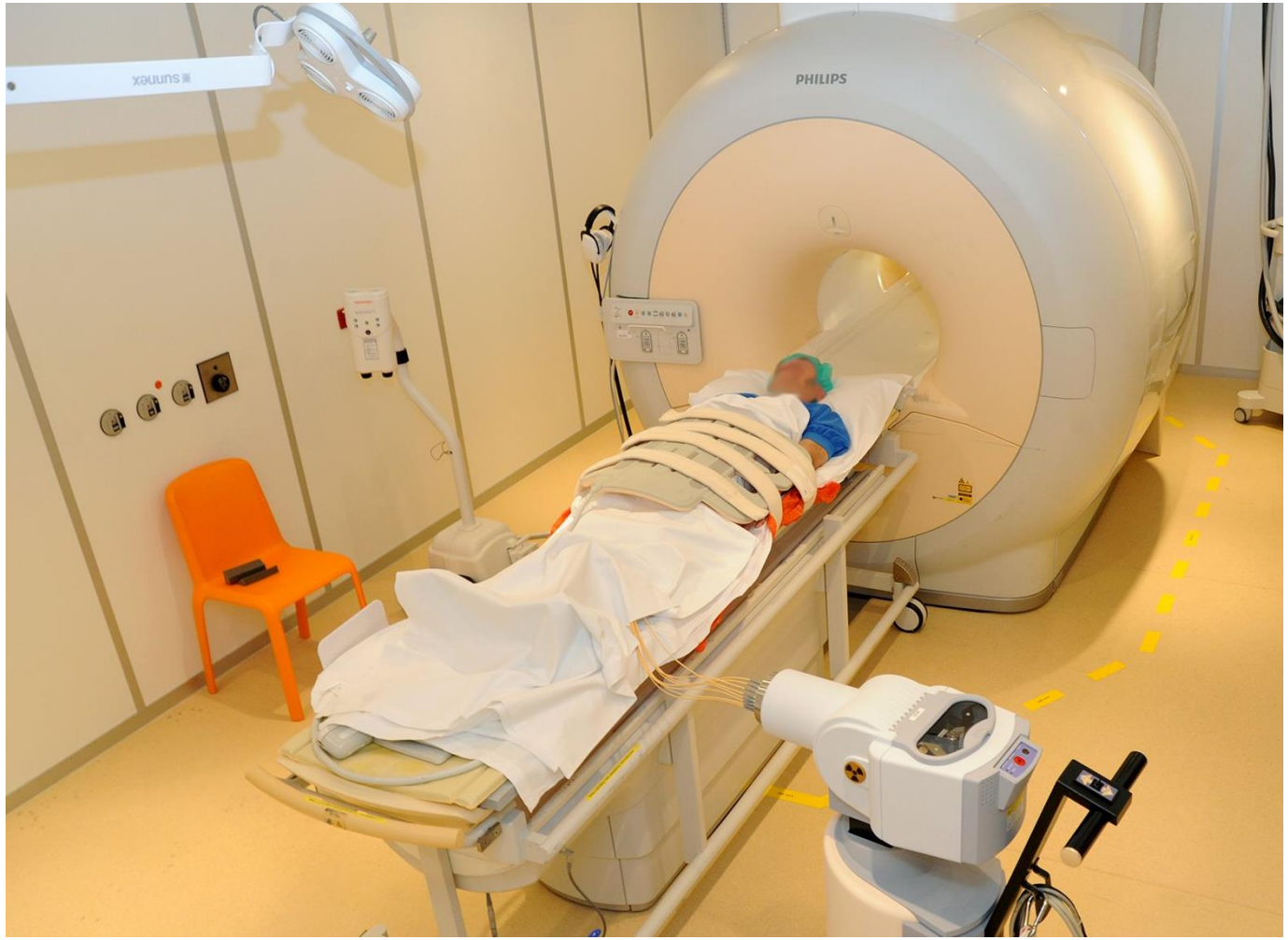




University Medical Center Utrecht

Irradiation

Iridium-192 source



University Medical Center Utrecht

Results

- No acute grade 3 GU or GI toxicity
- 2 patients with late grade 3 GU toxicity (urethral stricture)

≈ 2.5%

	GU/GI	ED
ADT:	≈100%	
Whole-gland salvage:	≈20-30%	≈100%
Focal salvage HIFU/cryo:	≈5-10%	

Toxicity – CTCAE 4.0

Table – Toxicity focal salvage HDR-brachytherapy

		Pre-op At risk=80	1 mo At risk=80	3 mo At risk=61	6 mo At risk=63	9 mo At risk=39	12 mo At risk=44	18 mo At risk=26	24 mo At risk=16	Grade >2 GU/GI toxicity n=80
GU	2	5 (6%)	14 (18%)	6 (10%)	14 (22%)	6 (15%)	10 (23%)	5 (19%)	-	
grade	3	-	-	-	1 (2%)	-	-	-	1 (6%)	2 new cases
GI	2	1 (1%)	1 (1%)	1 (2%)	1 (2%)	1 (3%)	2 (5%)	1 (4%)	-	
grade	3	-	-	-	-	-	-	-	-	0 new cases
ED	2	28 (35%)	37 (46%)	29 (48%)	33 (52%)	19 (49%)	18 (41%)	13 (50%)	2 (13%)	
grade	3	15 (19%)	17 (21%)	16 (26%)	15 (24%)	10 (26%)	12 (27%)	7 (27%)	9 (56%)	

University Medical Center Utrecht

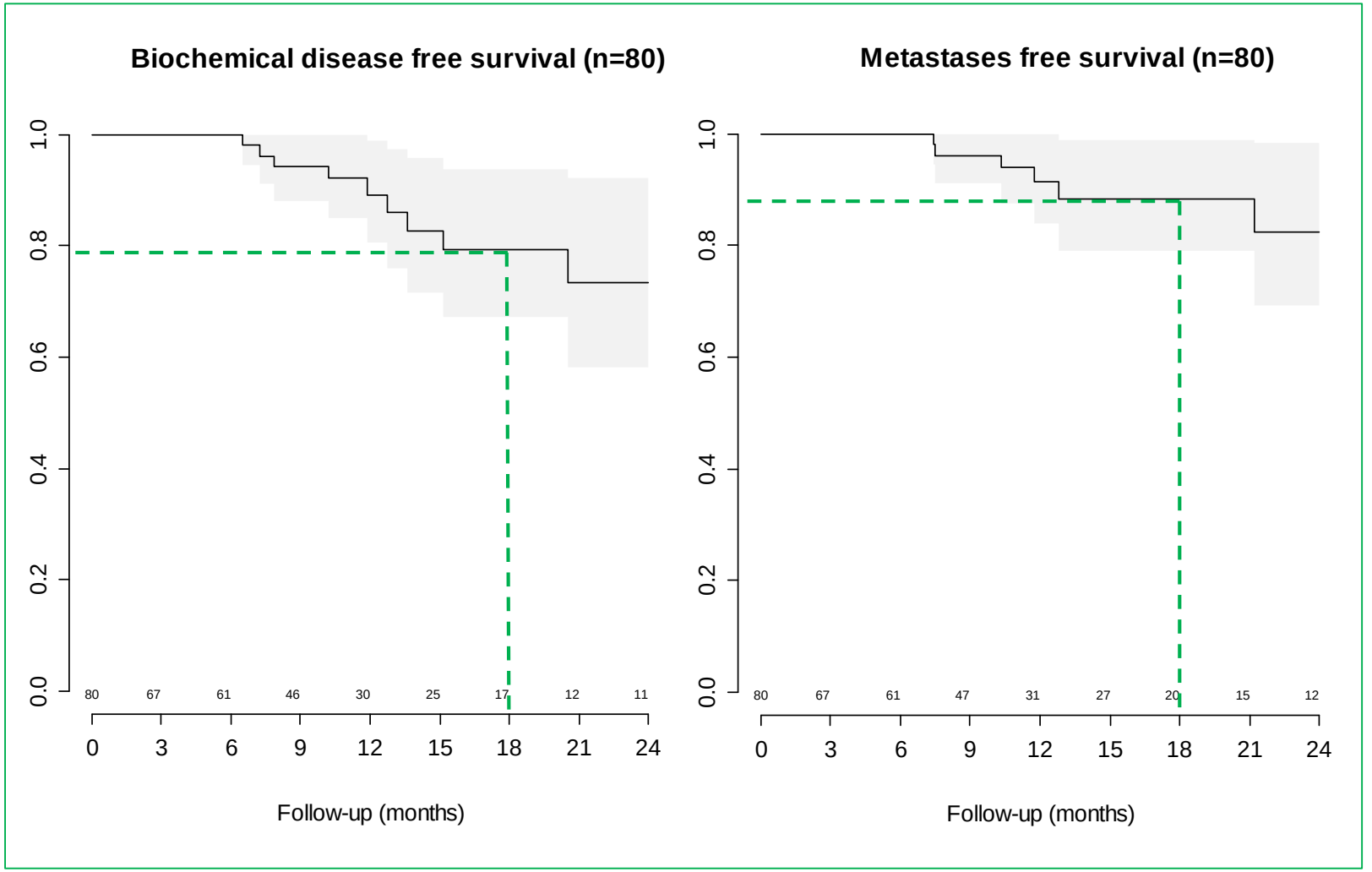
Results

At 18 months:

BDFS **79%** (95%CI 67-94%)

MFS **88%** (95% CI 79-100%)

Total group: PSA >20 (n=4), PSADT <9 months (n=9), T3/T4 (n=28)



University Medical Center Utrecht

Przekraczając znaną dawkę:
wyniki leczenia schematami radioablacyjnymi.

doi:10.4149/neo_2015_081

Acute toxicity of robotic ultrahypofractionated radiotherapy CyberKnife™ in prostate cancer patients

G. GLOWACKI*, W. MAJEWSKI, P. WOJCIESZEK, K. GRABINSKA, E. CHAWINSKA, D. BODUSZ, G. WOZNIAK, H. URBANCZYK, A. KALETKA, L. MISZCZYK

Radiotherapy Department – Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice, Poland

**Correspondence: geno@poczta.onet.pl*

Received February 8, 2015 / Accepted May 13, 2015

Toxicity	GU	GI
Grade 0	86 (83%)	92 (88%)
Grade 1	17 (16%)	8 (8%)
Grade 2	1 (<1%)	3 (3%)
Grade 3	0	1 (<1%)
Grade 4	0	0

Cyberknife Radioablation of Prostate Cancer – Preliminary Results for 400 Patients

Leszek Miszczyk[1]*, Agnieszka Namysł Kaletka[1], Aleksandra Napieralska[1], Grzegorz Woźniak[1], Małgorzata Stąpór Fudzińska[2], Grzegorz Głowacki[1], Andrzej Tukiendorf[3]

	RT end	1 month	4 months	8 months	14 months	20 months	26 months	32 months	38 months
N of observed patients	400	250	343	303	242	143	87	40	14
No ADT [%]	41.8	61.5	56.3	75.7	82.2	86.1	97.7	95	100
GI 0 [%]	90.7	89.6	94.4	95	97.5	93.7	96.5	100	92.9
GI 1 [%]	8.8	8.4	4.7	4.3	2.1	5.6	2.3	-	7.1
GI 2 [%]	0.5	1.6	0.6	0.7	0.4	0.7	1.2	-	-
GI 3 [%]	-	0.4	0.3	-	-	-	-	-	-
GU 0 [%]	77.5	70.1	90.1	95.7	91.3	96.5	95.3	92.5	100
GU 1 [%]	16	25.5	7	3.6	7.1	2.1	2.3	5	-
GU 2 [%]	6	4	2.9	0.7	1.6	1.4	2.4	2.5	-
GU 3 [%]	0.5	0.4	-	-	-	-	-	-	-
PSA mean	3.8	1.8	0.9	0.7	0.7	0.5	0.5	0.4	0.2
PSA median	2.3	0.8	0.2	0.2	0.2	0.2	0.2	0.1	0.1

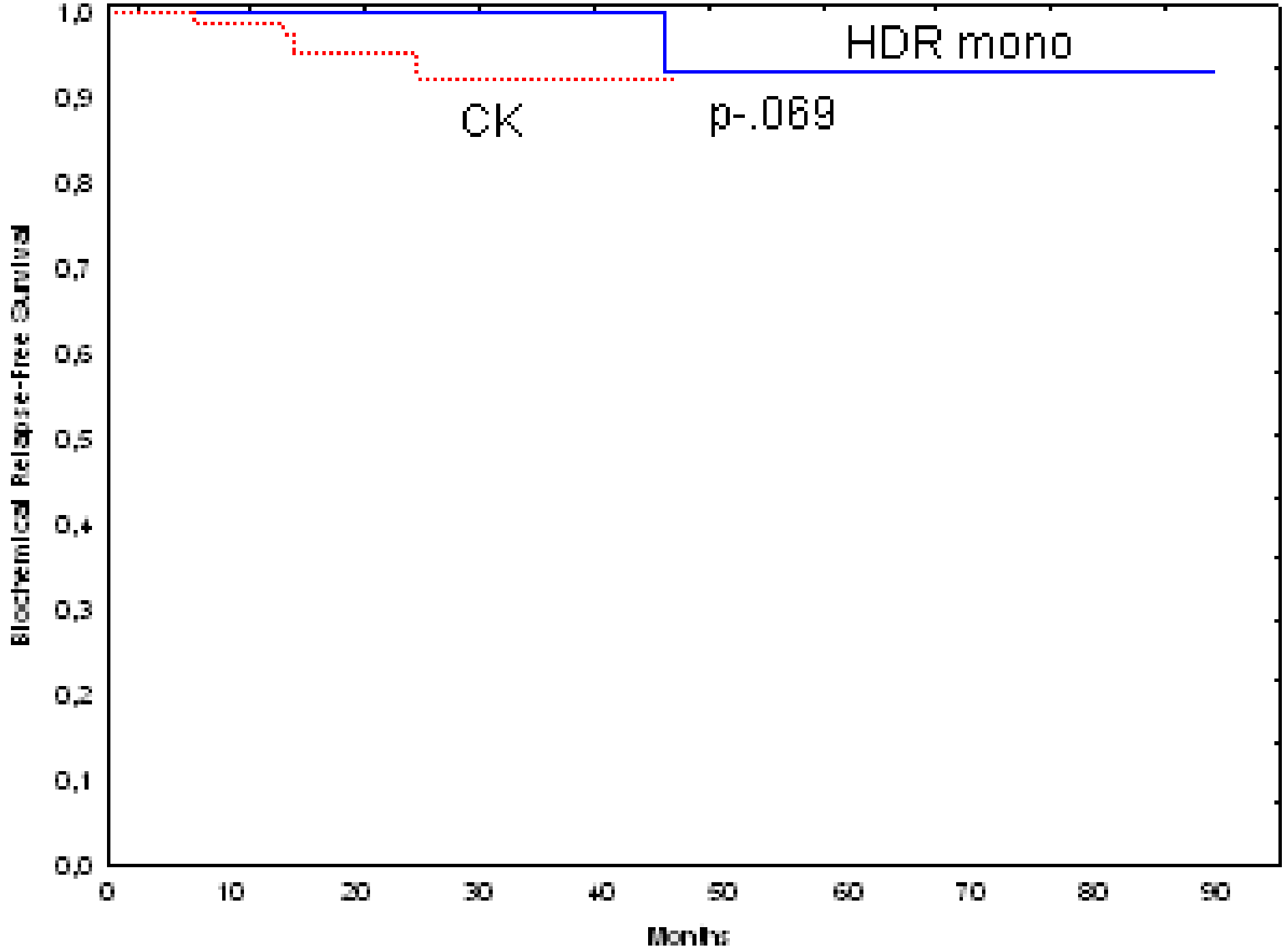
ADT , Androgen Deprivation Therapy; GI , Gastro-Intestinal; GU , Genito-Urinary; PSA , Prostate Specific Antigen; FU , Follow-Up

Doświadczenia własne
Zakładu Brachyterapii CO-I Gliwice

HDR mono vs CK

N=190	HDR mono	CK	
Wiek (lata)	63 (39-79)	68 (53-82)	p-.0000
Gleason ≤6	80	88	p-.13
7	15	7	
T1c	61	64	p-.62
T2a	30	20	
T2b	3	8	
T2c	1	3	
Ryzyko niskie	63	66	p-.66
średnie	32	29	
PSA max (ng/ml)	7,53 (1,87-13,47)	7,63 (2,6-15,4)	p-.39

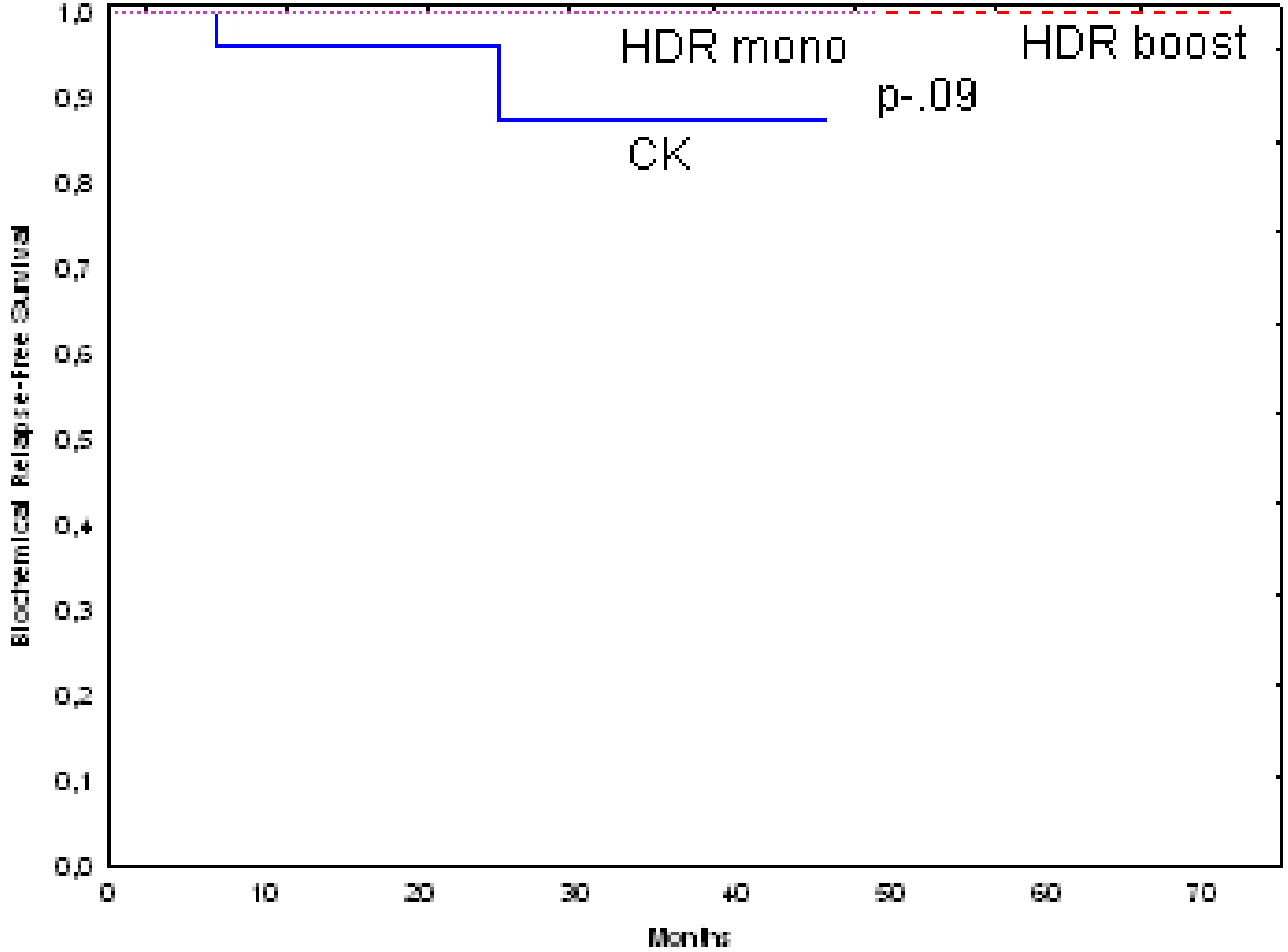
	HDR mono	CK	
2-letni bDFS	93%	92%	p-.069
Ostry odczyn GU			
0	42	66	
1	47	19	p-.03
2	2	7	
3	4	3	
Ostry odczyn GI			
0	95	90	
1	-	5	p-.002
2	-	-	
3	-	-	
Czas obserwacji (miesiące)	20 (6-90)	18 (6-46)	p-.04
PSA ost (ng/ml)	0,339 (0,002-5,997)	0,231 (0,002-5,237)	p-.03


HDR mono
CK
p-.069
Biochemical Relapse-Free Survival
1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
0
10
20
30
40
50
60
70
80
90
Months

HDR mono vs HDR boost vs CK

N=87	HDR mono	HDR boost	CK	
Wiek (lata)	66 (39-79)	67 (44-76)	69 (56-80)	p-.11
Gleason ≤6	14	12	22	p-.009
7	15	17	7	
T1c	17	9	11	p-.62
T2a	8	9	7	
T2b	3	7	8	
T2c	1	4	3	
Ryzyko średnie	29	29	29	
PSA max (ng/ml)	8,98 (1,87-13,47)	7,59 (1,49-17,84)	10,67 (3,75-15,4)	p-.03

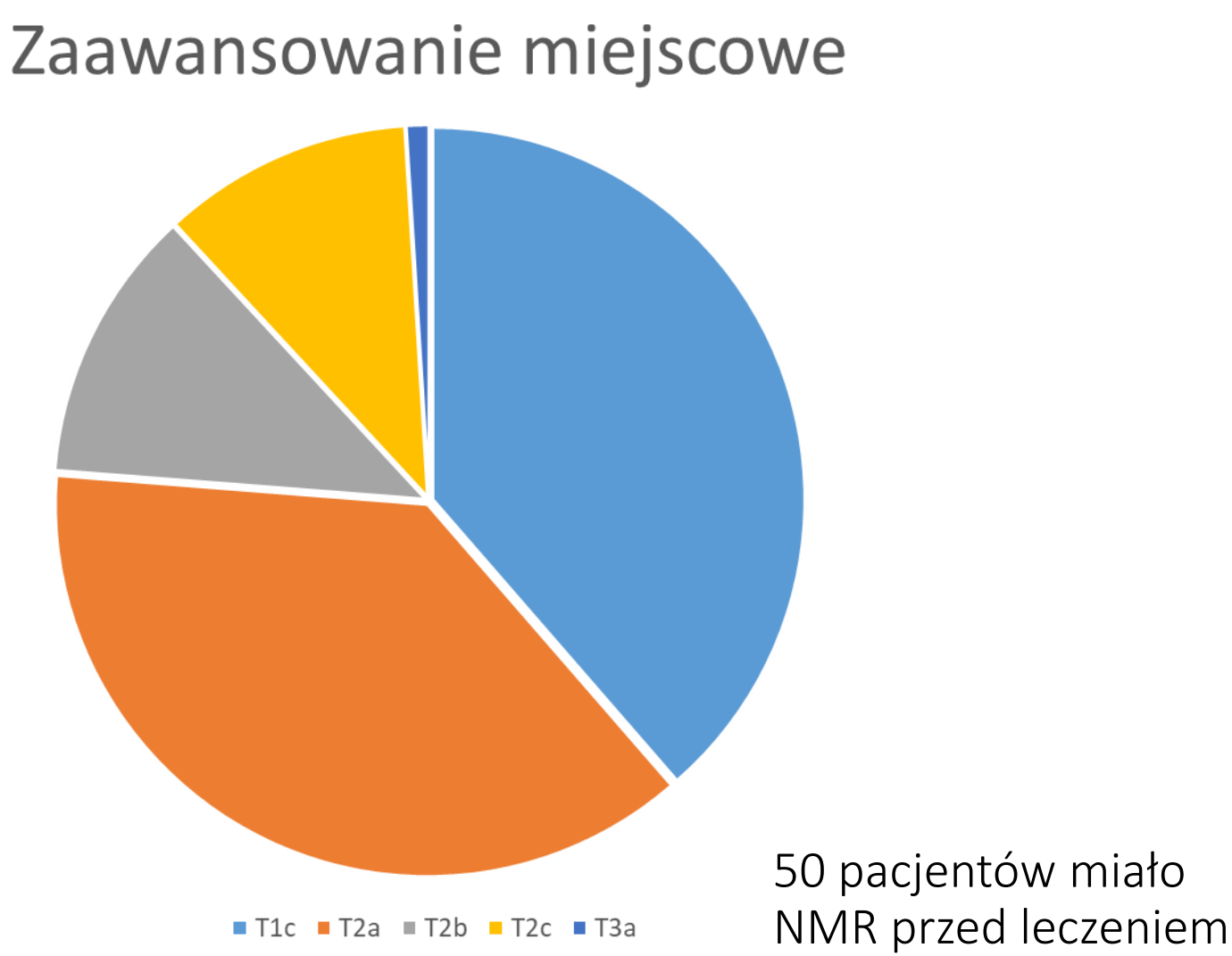
	HDR mono	HDR boost	CK	
2-letni bDFS	100%	100%	96%	p-.09
Ostry odczyn GU				
0	14	9	16	
1	14	16	11	p-.34
2	1	4	1	
3	-	-	1	
Ostry odczyn GI				
0	29	24	22	
1	-	5	6	p-.02
2	-	-	1	
3	-	-	-	
Czas obserwacji (miesiące)	16 (6-49)	36 (10-72)	19 (6-46)	p-.002
PSA ost (ng/ml)	0,202 (0,002-5,997)	0,089 (0,005-0,917)	0,148 (0,002-4,6)	p-.0000


HDR mono
HDR boost
p-.09
CK
Biochemical Relapse-Free Survival
1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
0
10
20
30
40
50
60
70
Months

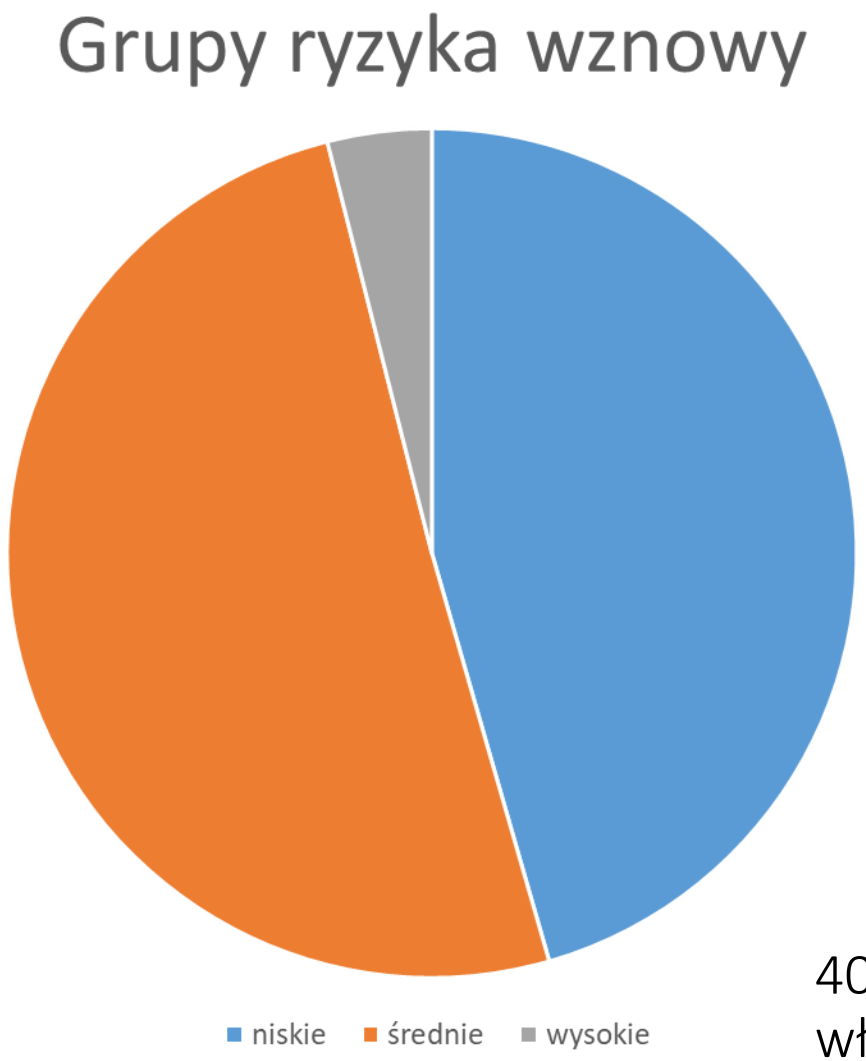
HDR mono 2x13Gy

Od 17/03/2016 – 133 pacjentów

- Analizie poddano 101 mężczyzn (2016-2017)
- Mediana wieku – 65 (50-84) lat
- Mediana obserwacji – 12 (4-25) miesięcy
- Mediana PSA $_{\text{pierwotne}}$ – 7,7 (0,655-21,25) ng/ml
- Mediana PSA $_{\text{ostatnie}}$ – 0,558 (0,002-10,069) ng/ml



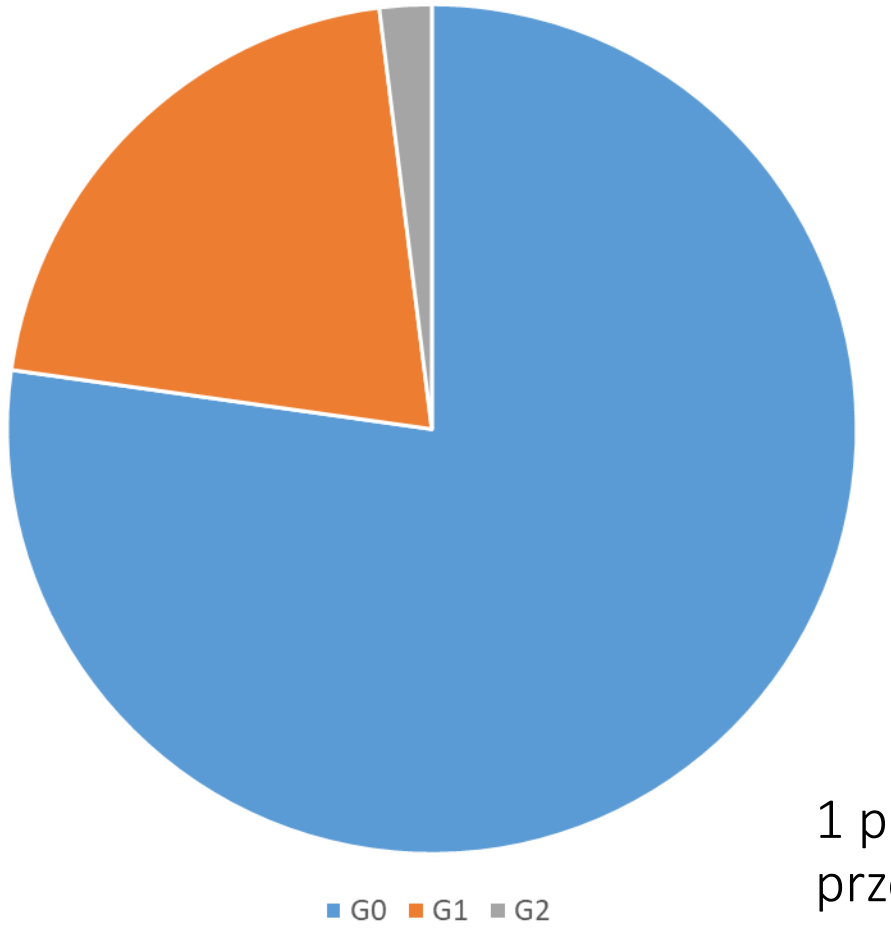
50 pacjentów miało NMR przed leczeniem



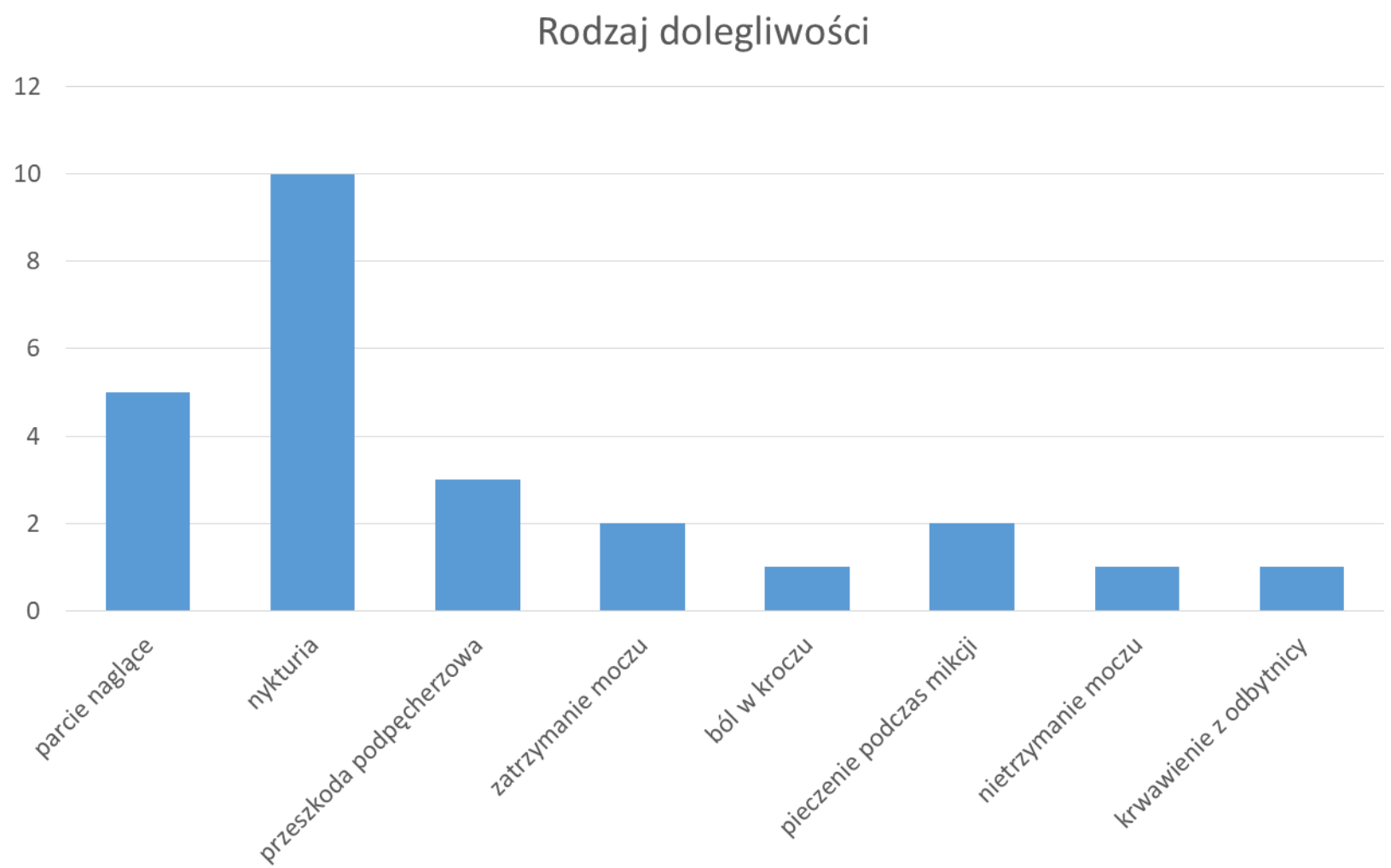
40 pacjentów miało włączone ADT

	V stercz [cm3]	Igły	V100 [%]	Cewka D10 [%]
I frakcja	42 (13,6-92)	18 (12-26)	95,25 (84,5-99,6)	115,7 (110,3-121,5)
II frakcja	44,7 (20,4-92,3)	18 (13-26)	95,3 (74-99,3)	114 (107-119)

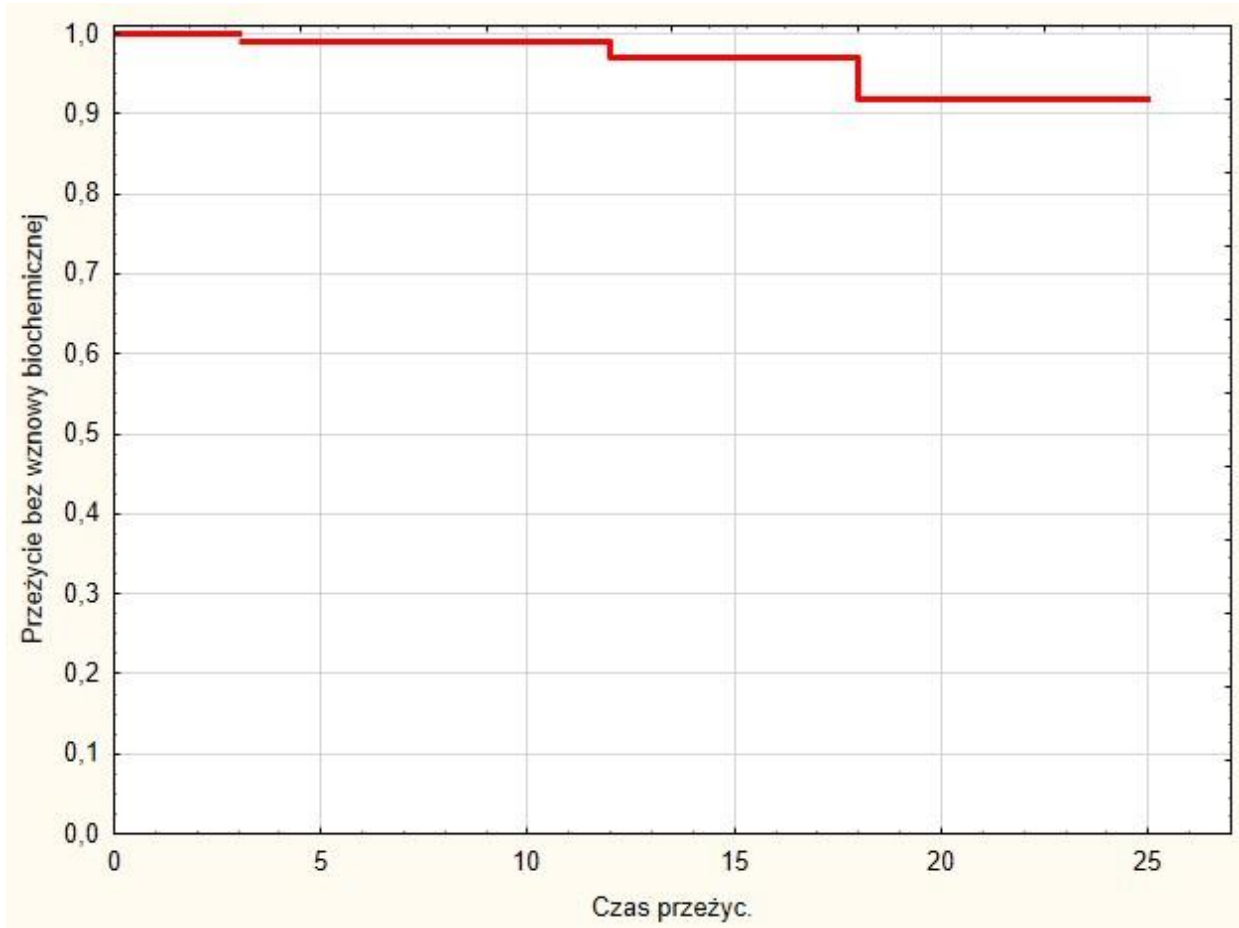
Odczyn ze strony układu moczowego



1 pacjent miał przejściowo odczyn ze strony odbytnicy-G1


Rodzaj dolegliwości
12
10
8
6
4
2
0
parcie naglące
nykturia
przeszkoda podpęcherzowa
zatrzymanie moczu
ból w kroczu
pieczenie podczas mikcji
nietrzymanie moczu
krwawienie z odbytnicy

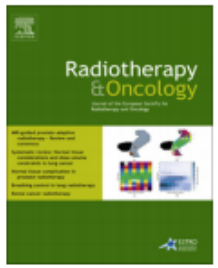
- Mediana PSA $_{ostatnie}$ – 0,558 (0,002-10,069) ng/ml
- 6 PSA bounce
- 3 wznowy/2 (1?) biochemiczne
- 1-roczny bDFS 97%


Przeżycie bez wznowy biochemicznej
1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
0
5
10
15
20
25
Czas przeżyc.

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com



Prostate cancer brachytherapy

Salvage high-dose-rate brachytherapy for locally recurrent prostate cancer after primary radiotherapy failure

Piotr Wojcieszek [a,*], Marta Szlag [b], Grzegorz Głowacki [c], Agnieszka Cholewka [b], Marzena Gawkowska-Suwińska [d], Sylwia Kellas-Ślęczka [a], Brygida Białas [a], Marek Fijałkowski [a]

[a] *Brachytherapy Department;* [b] *Radiotherapy and Brachytherapy Treatment Planning Department;* [c] *Radiotherapy Department; and* [d] *III Department of Radiotherapy and Chemotherapy, MSC Memorial Cancer Centre and Institute of Oncology, Gliwice, Ul. Wybrzeze Armii Krajowej 15, 44-100 Gliwice, Poland*

CENTRUM ONKOLOGII – INSTYTUT
IM. MARII SKŁODOWSKIEJ-CURIE
ODDZIAŁ W GLIWICACH

10 lat doświadczenia

08/04/2008-08/04/2018

164 chorych

3x10 Gy

3 implanty

28 dni

>6 m. FU

150 chorych

Mediana wieku - 70 years

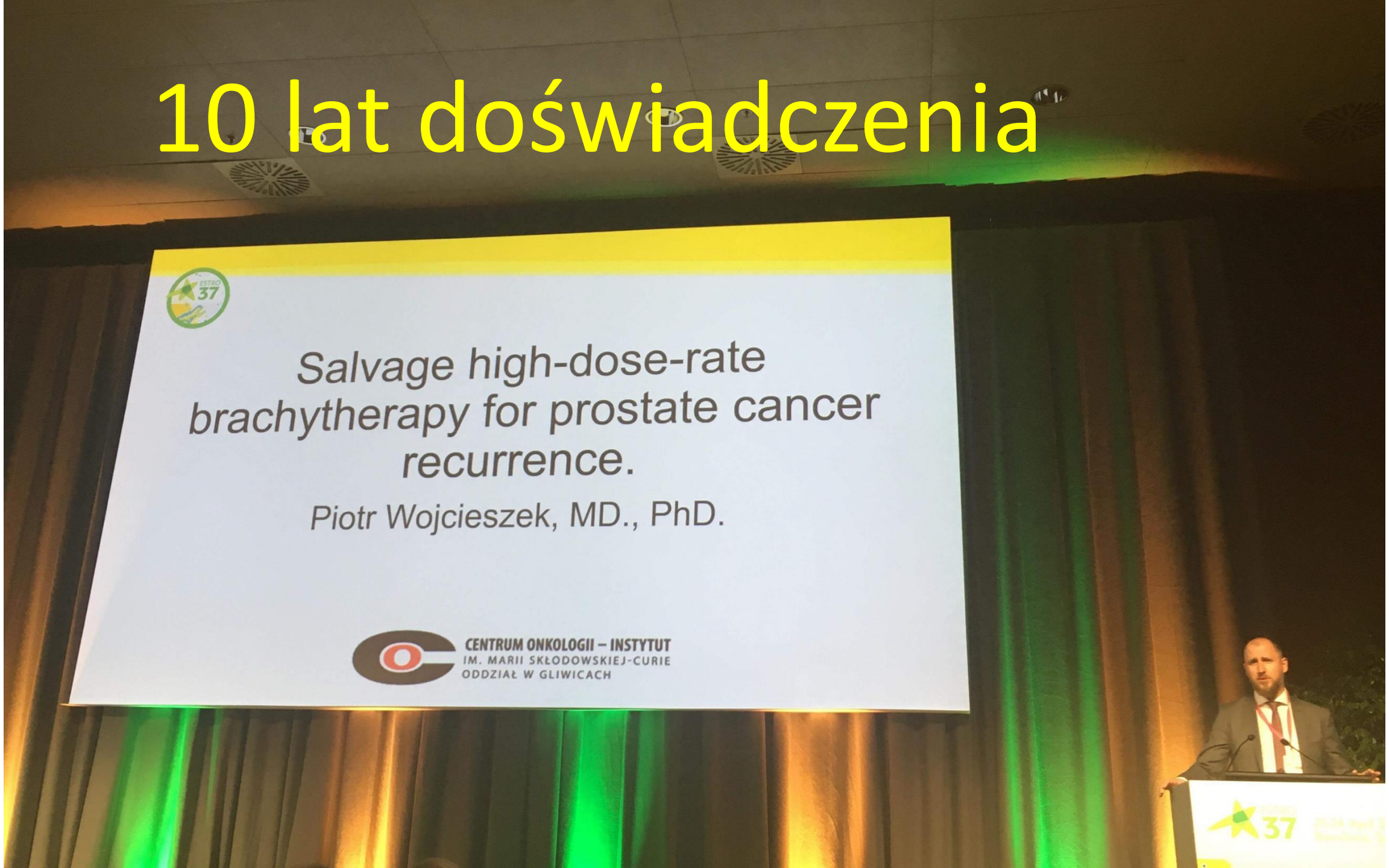
Mediana FU - 45 mo

Mediana max. PSA:

Pierw. =13,5 ng/ml

RAT = 2,8 ng/ml

10 lat doświadczenia



Strahlenther Onkol (2017) 193:683–691
DOI 10.1007/s00066-017-1157-2

REVIEW ARTICLE

High-dose-rate brachytherapy as salvage modality for locally recurrent prostate cancer after definitive radiotherapy

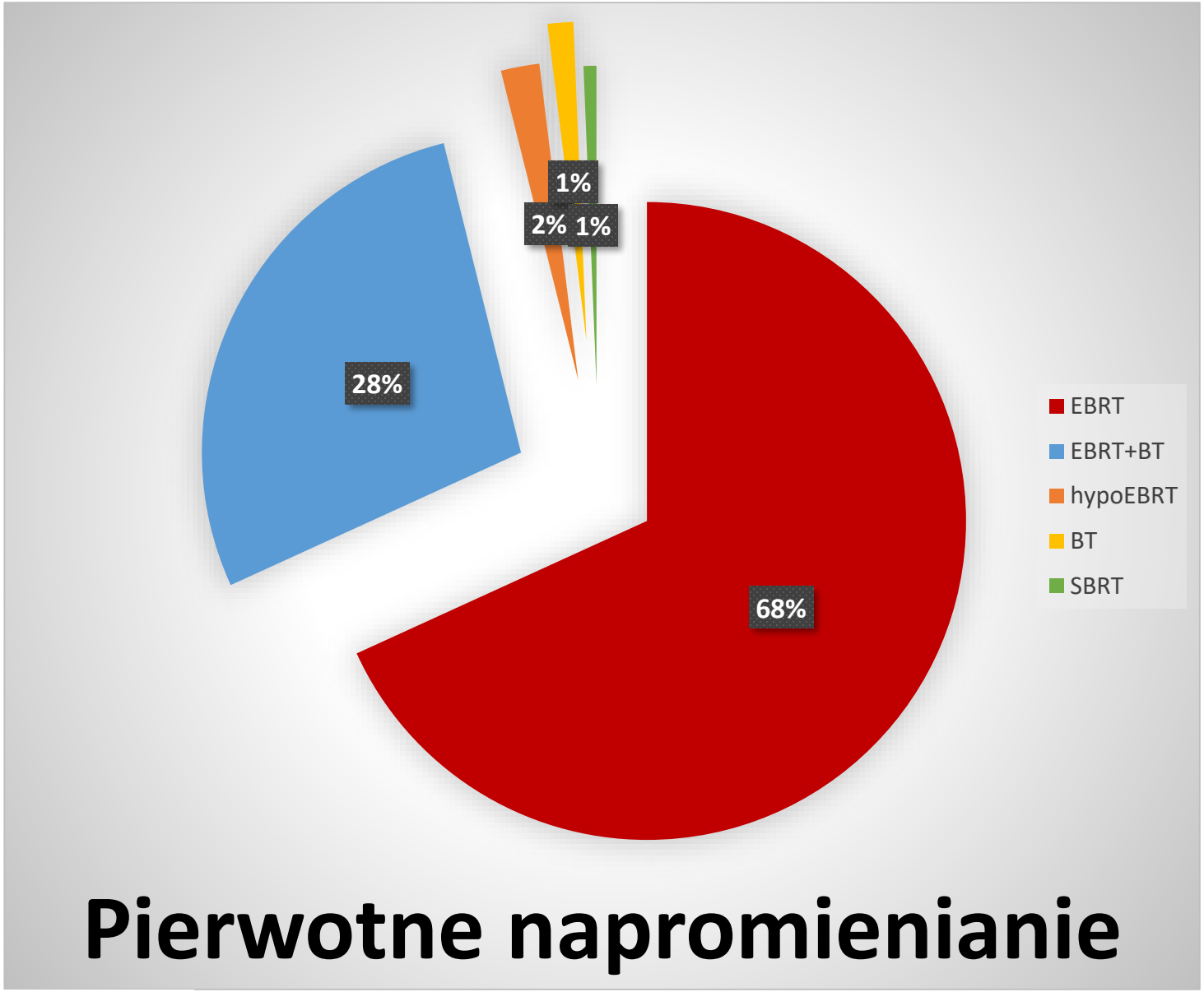
A systematic review

Georgios Chatzikonstantinou[1] · Nikolaos Zamboglou[1] · Claus Rödel[1] · Eleni Zoga[2] · Iosif Strouthos[3] · Saeed Ahmed Butt[4] · Nikolaos Tselis[1]

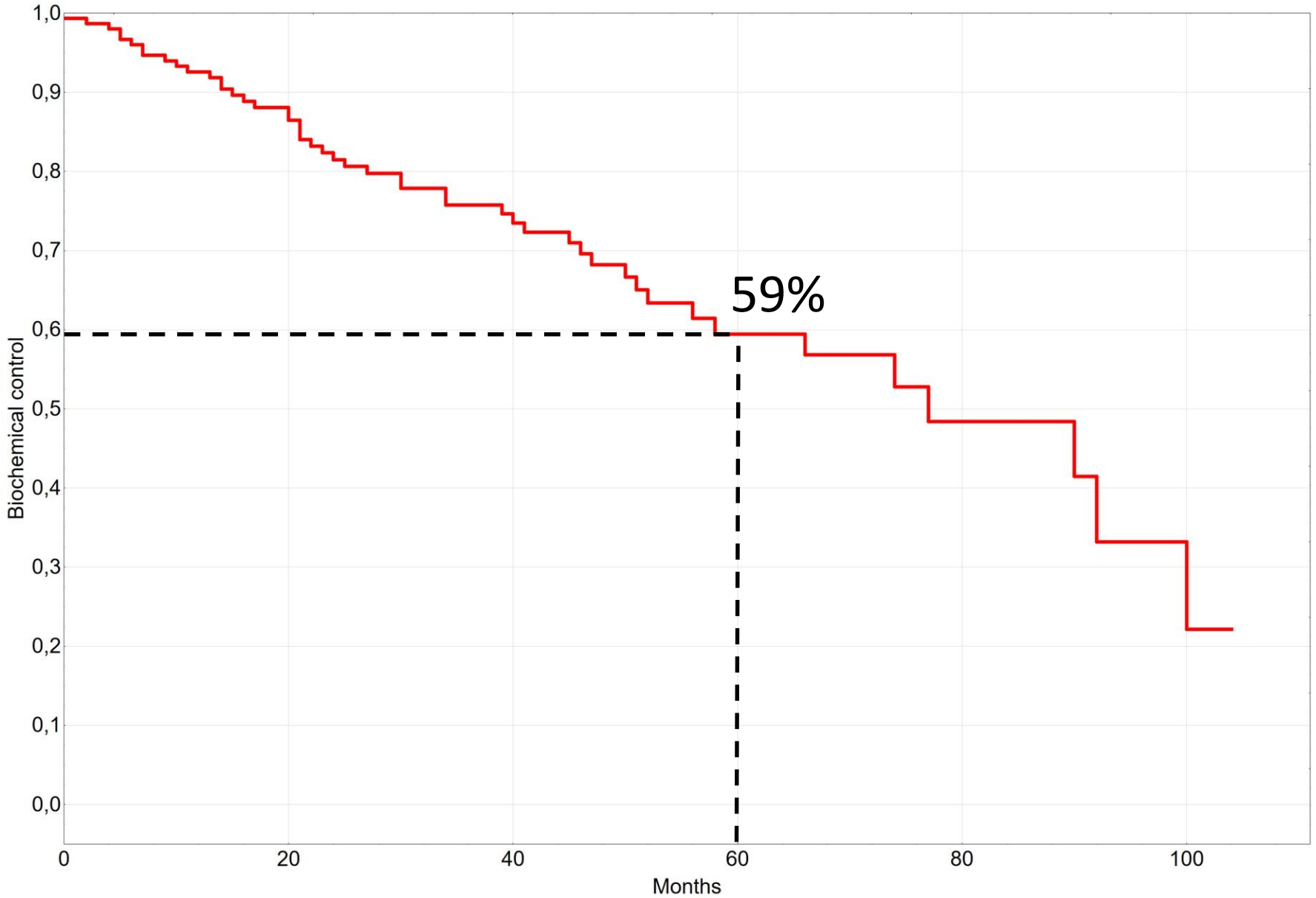
Table 1 Overview of patient characteristics in salvage HDR studies for locally recurrent prostate cancer

Study	*n*	Pretreatment (%)/ median dose	iT stage	iGS (%)	iPSA (%)	pADT (%)	pGS (%)	pPSA (%)
Lyszek et al., [6]	115	RP (9.5) EBRT (62)/52 Gy HDR (22.5)/30 Gy EBRT+HDR (6)	cT1 (6) cT2 (52) cT3 (33) cTx (7)	≤6 (44) 7 (18) ≥8 (12) GSx (16)	≤10 (35) 10.1–19.9 (24) ≥20 (29) PSAx (12)	N. R.	N. R.	N. R.
Jo et al., [7]	11	EBRT (9)/72 Gy EBRT+HDR (55)/36.8 + 24 Gy HDR (36)/37.5 Gy	cT1 (27) cT2 (27) cT3 (46)	≤6 (36) 7 (46) ≥8 (18)	≤10 (55) 10.1–19.9 (9) ≥20 (36)	No	≤6 (27) 7 (46) ≥8 (27)	≤10 (73) 10.1–19.9 (27)
Tharp et al., [8]	7	EBRT (43)/68.4 Gy LDR (43) EBRT+LDR (14)	N. R.	≤6 (86) GSx (14)	≤10 (43) 10.1–19.9 (43) PSAx (14)	7 (100)	≤6 (28) 7 (44) ≥8 (28)	≤10 (86) 10.1–19.9 (14)
Yamada et al., [9]	45	EBRT (100)/81 Gy	N. R.	N.R	N.R.	18 (43)	≤6 (7) 7 (60) ≥8 (33)	<4 (55) 4.0–10 (33) >10 (12)
Chen et al., [10]	52	EBRT (77) EBRT+LDR (4) LDR (15) EBRT+protons (4)	cT1c (33) cT2 (47) cT3 (20)	≤6 (54) 7 (33) ≥8 (13)	<4 (6) 4–10.0 (50) 10.1–20.0 (36) >20 (8)	24 (52)	≤6 (4) 7 (44) ≥8 (52)	<4 (38) 4–10.0 (52) 10.1–20.0 (8) >20 (2)
Kukieka et al., [11]	25	EBRT (100)/73.9 Gy	cT1 (36) cT2 (44) cT3 (20)	≤6 (60) 7 (28) ≥8 (4) GSx (8)	Median 16.3	9 (36)	≤6 (20) 7 (40) ≥8 (20) GSx (20)	Median 2.8
Wojcieszek et al., [12]	83	EBRT (62)/74 Gy EBRT+HDR (38)/54 + 10 Gy	cT1 (40) cT2 (53) cT3 (6) cTx (1)	≤6 (60) 7 (20) ≥8 (4) GSx (16)	<10 (29) 10.0–20 (39) >20 (25) PSAx (7)	44 (53)	≤6 (19) 7 (27) ≥8 (7) GSx (47)	Median peak 3.1
Henriquez et al., [16]	56	EBRT (82)/72 Gy LDR (18)	cT1c (41) cT2 (46) cT3 (13)	≤6 (66) 7 (29) ≥8 (5)	<10 (46) 10.0–20 (32) >20 (22)	9 (60)	≤6 (16) 7 (25) ≥8 (14) GSx (45)	<10 (91) 10.0–20 (7) >20 (2)

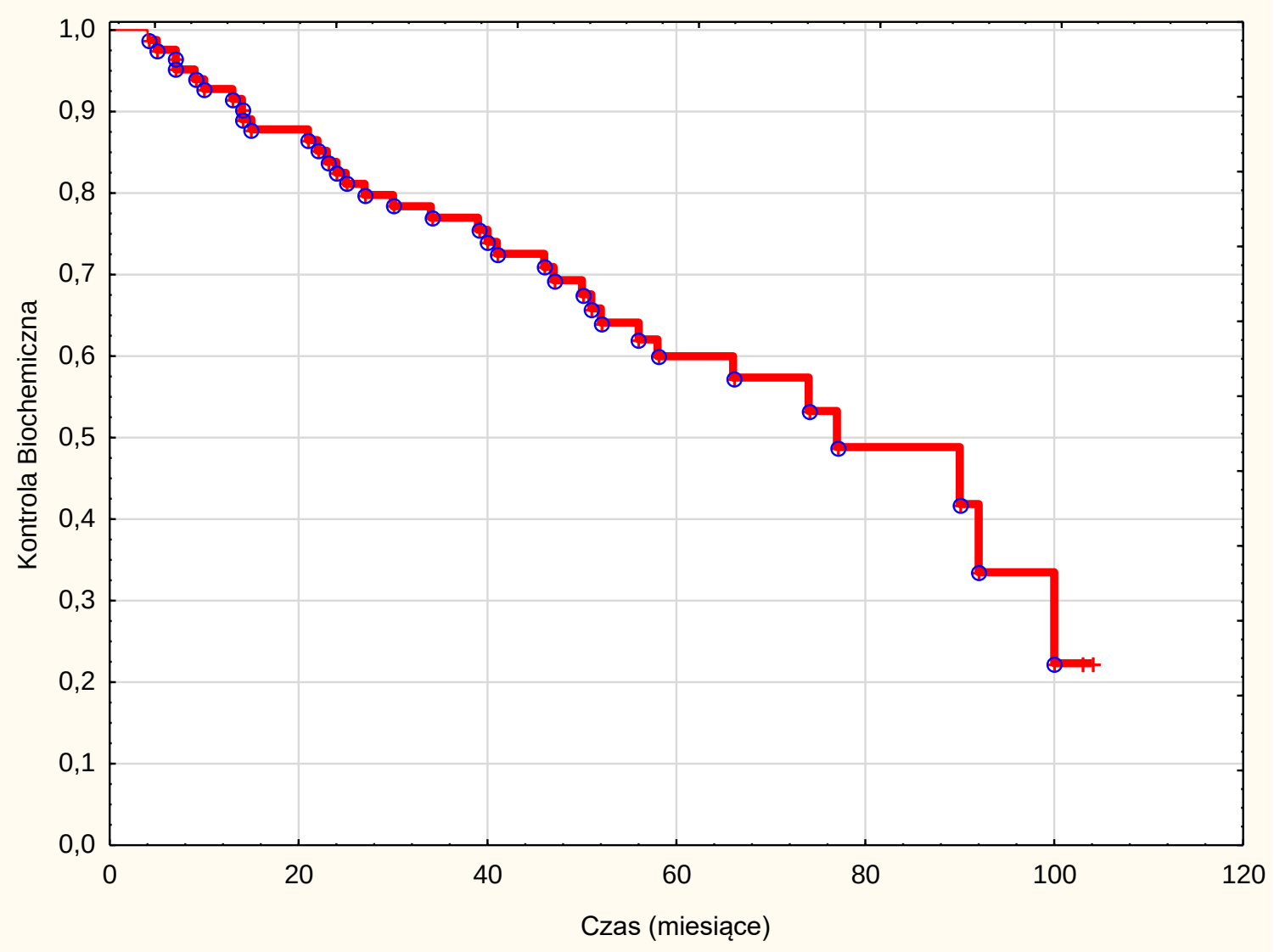
Wojcieszek et al. [12] reported on 83 patients receiving sHDR BRT after previous definitive RT either by exclusive EBRT (median 74 Gy) or EBRT combined with HDR BRT boost (EBRT median 54 Gy plus 10 Gy single-fraction HDR BRT). Local recurrence was confirmed by 12 core biopsy with a median peak presalvage PSA of 3.1 ng/ml and 7% of cases with GS ≥ 8. The sBRT schedule consisted of 3 HDR fractions of 10 Gy delivered by single-fraction implants separated by 21 days to a total physical dose of 30 Gy. Median follow-up was 41 months with an actuarial 3- and 5-year biochemical disease-free survival of 76% and 67%, respectively. The corresponding 5-year rates for cause specific and overall survival (OS) were 87% and 86%. The only factor associated with BC was time to salvage PSA nadir. The 5-year BC for patients with time to nadir >238 days was 77% compared to 56% for patients with time to nadir ≤238 days ($p = 0.004$). The reported rates of acute overall adverse events were 52% grade 1 and 35% grade 2 toxicities. In 5 cases, sHDR BRT had to be stopped after the second fraction as a result of acute urinary retention. Grade 2 late GU toxicity was recorded in 32 patients (39%). All patients presenting grade 3 late GU toxicity (13%) underwent either transurethral resection of the prostate or urethrotomy for urinary obstruction. Grade 1 late GI adverse events were documented in 6% of cases with no higher grade late GI toxicities.



Pierwotne napromienianie


1,0
0,9
0,8
0,7
0,6
0,5
0,4
0,3
0,2
0,1
0,0
Biochemical control
59%
0
20
40
60
80
100
Months

Mediana obserwacji >60 miesięcy



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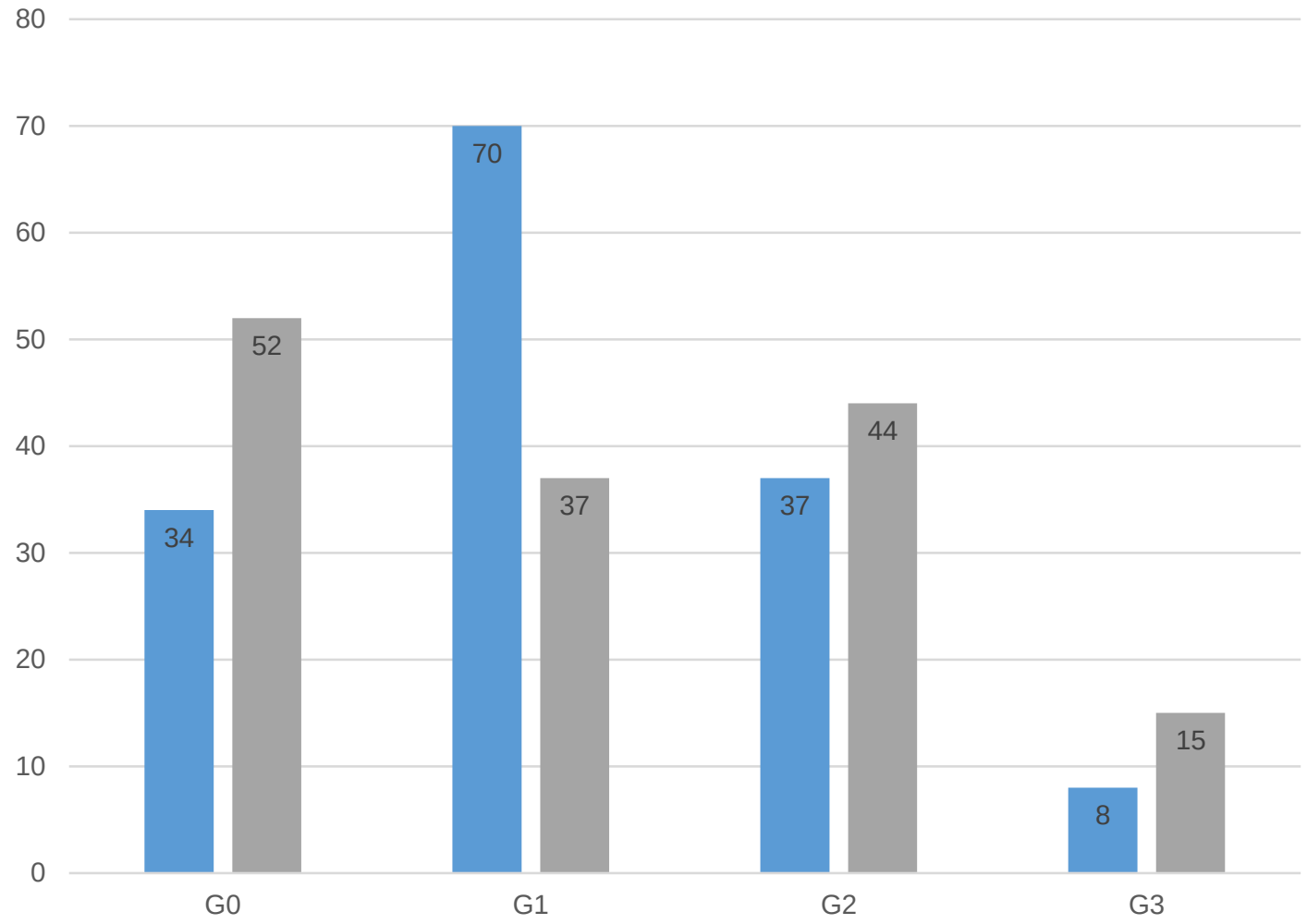
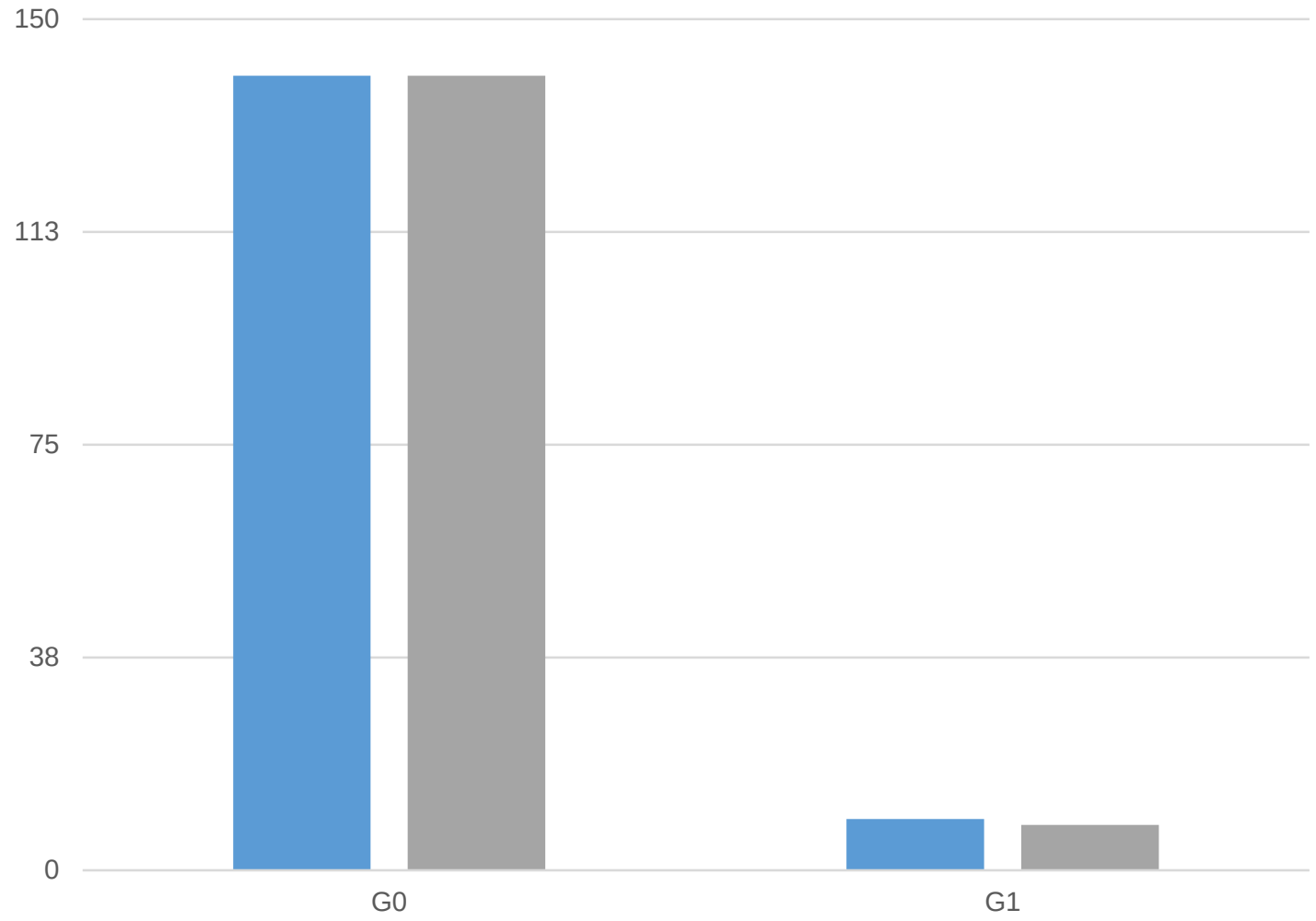


Odczyn ze strony układu pokarmowego wczesny/późny



PRINCIPLES OF RADIATION THERAPY

Definitive Radiation Therapy General Principles

- Highly conformal RT techniques should be used to treat localized prostate cancer.
- Photon or proton beam radiation are both effective at achieving highly conformal radiotherapy with acceptable and similar biochemical control and long-term side effect profiles (See Discussion).
- Brachytherapy boost, when added to EBRT plus ADT in men with NCCN intermediate and high/very high risk prostate cancer, has demonstrated improved biochemical control over EBRT plus ADT alone in randomized trials, but with higher toxicity.
- Ideally, the accuracy of treatment should be verified by daily prostate localization, with any of the following: techniques of IGRT using CT, ultrasound, implanted fiducials, or electromagnetic targeting/tracking. Endorectal balloons may be used to improve prostate immobilization. Perirectal spacer materials may be employed when the previously mentioned techniques are insufficient to improve oncologic cure rates and/or reduce side effects due to anatomic geometry or other patient related factors, such as medication usage and/or comorbid conditions. Patients with obvious rectal invasion or visible T3 and posterior extension should not undergo perirectal spacer implantation.
- Various fractionation and dose regimens can be considered depending on the clinical scenario (See Table 1). Dose escalation has been proven to achieve the best biochemical control in men with intermediate and high risk disease.
- SBRT is acceptable in practices with appropriate technology, physics and clinical expertise.
- Biologically effective dose (BED) modeling with the linear-quadratic equation may not be accurate for extremely hypofractionated (SBRT/SABR) radiation.
- For brachytherapy:
  - Patients with a very large prostate or very small prostate, symptoms of bladder outlet obstruction (high IPSS), or a previous TURP are more difficult to implant and may suffer increased risk of side effects. Neoadjuvant ADT may be used to shrink the prostate to an acceptable size; however, increased toxicity would be expected from ADT and prostate size may not decline in some men despite neoadjuvant ADT. Potential toxicity of ADT must be balanced against the potential benefit of target reduction.
  - Post-implant dosimetry must be performed to document the quality of the low dose-rate implant.

Definitive Radiation Therapy by Risk Group

- Very low risk
  - Men with NCCN very low risk prostate cancer are encouraged to pursue active surveillance.
- Low Risk
  - Prophylactic lymph node radiation should NOT be performed routinely. ADT or antiandrogen therapy should NOT be used routinely
- Favorable Intermediate Risk
  - Prophylactic lymph node radiation is not performed routinely, and ADT or antiandrogen therapy is not used routinely. Prophylactic lymph node radiation and/or ADT use is reasonable if additional risk assessments suggest aggressive tumor behavior.
- Unfavorable Intermediate Risk
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Continued

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Continued

National Comprehensive Cancer Network®

NCCN Guidelines Version 4.2018
Prostate Cancer

NCCN Guidelines Index
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Discussion

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Mniej znaczy więcej; nie mniej więcej

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Continued

1. Dawka radioablacyjna jest kluczem do bezpiecznego leczenia w nowoczesnej onkologii
2. SBRT i HDR mogą być bezpiecznie stosowane u różnych grup chorych
3. Brachyterapia HDR jest jedną z najskuteczniejszych i bezpiecznych metod w leczeniu wznowy.
4. Kierunki rozwoju:
   - Kwalifikacja do leczenia na podstawie najnowocześniejszego obrazowania
   - Mniej implantacji z krótszym OTT
   - Randomizowane badania kliniczne

BrachyTeam Gliwice

Dziękuję za uwagę

The Song Remains
The Same.

Led Zeppelin