Nowe technologie
w
Radioterapii

Piotr Milecki

Oddział Radioterapii I i Zakład Radioterapii I

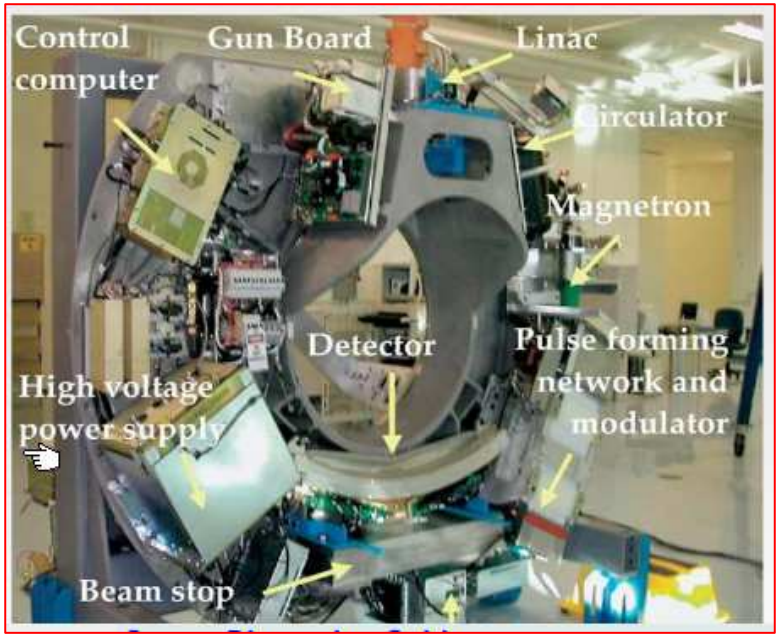
Wielkopolskie Centrum Onkologii
Poznań

Radioterapia

- 3DCRT
- IMRT
- SBRT, CyberKnife
- Protonoterapia

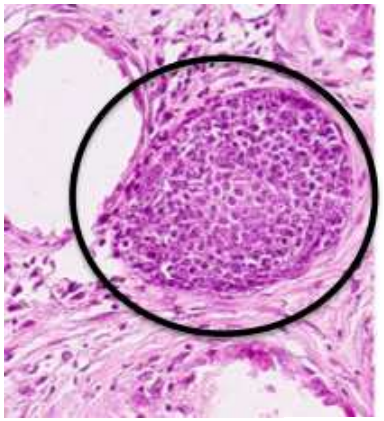
- Brachyterapia (HDR, LDR)

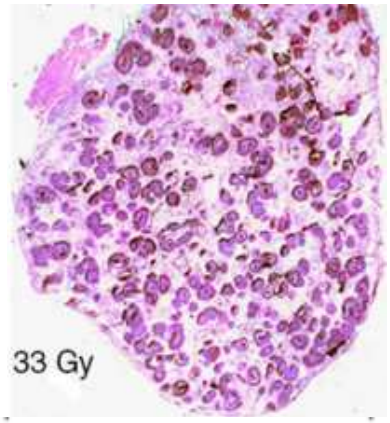
- IMRT +/- HDR, IMRT +/- LDR
- IMRT +/- SBRT-CyberKnife

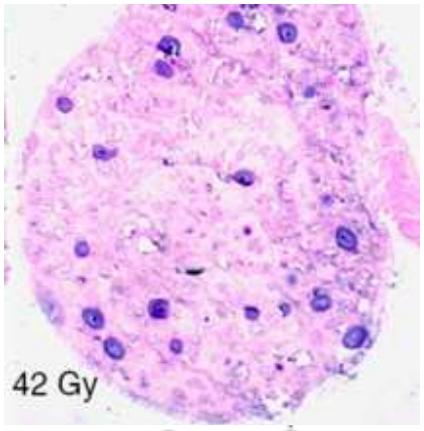

Control computer
Gun Board
Linac
Circulator
Magnetron
Detector
Pulse forming network and modulator
High voltage power supply
Beam stop

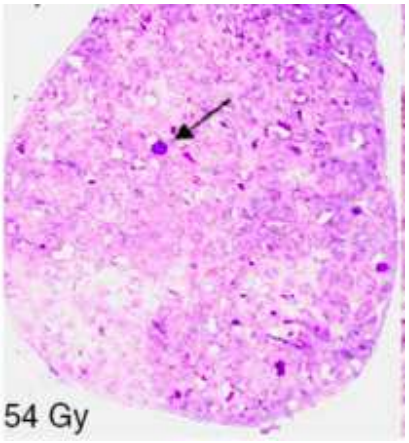
Radioterapia PCa
wyzwania

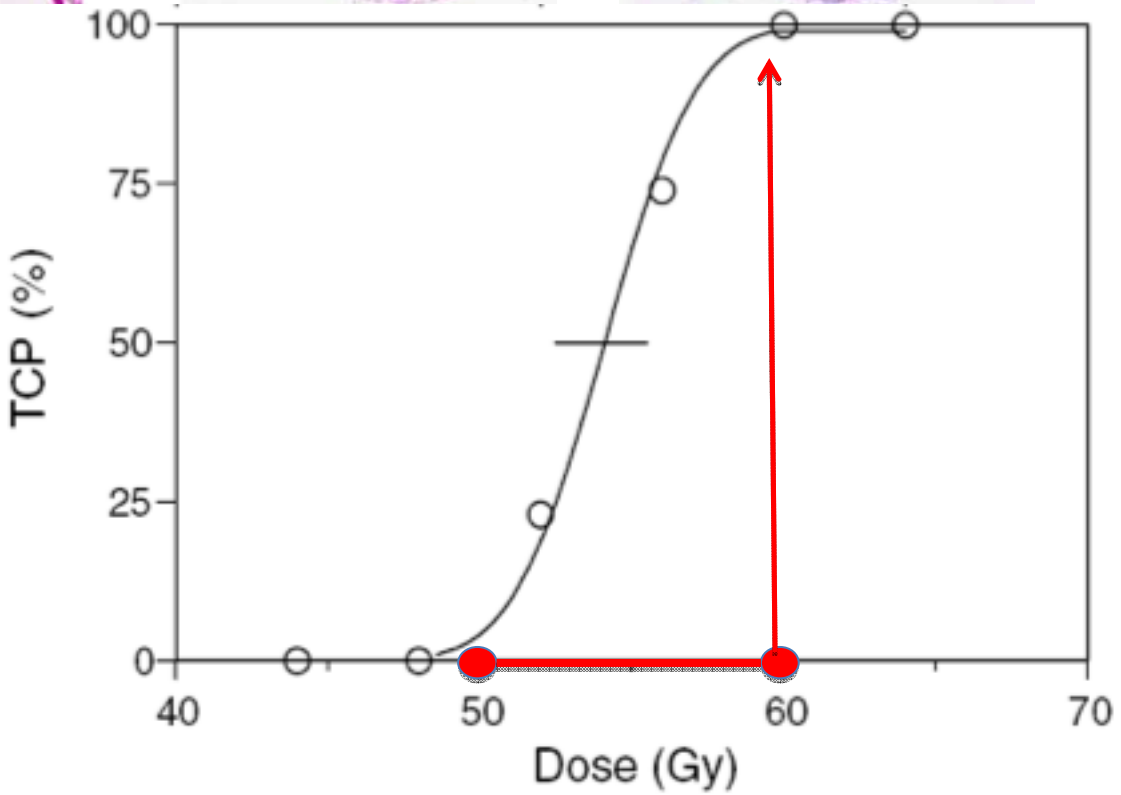
- Eskalacja dawki
- Obniżenie intensywności powikłań
- zmniejszenie obecności mikroprzerzutów





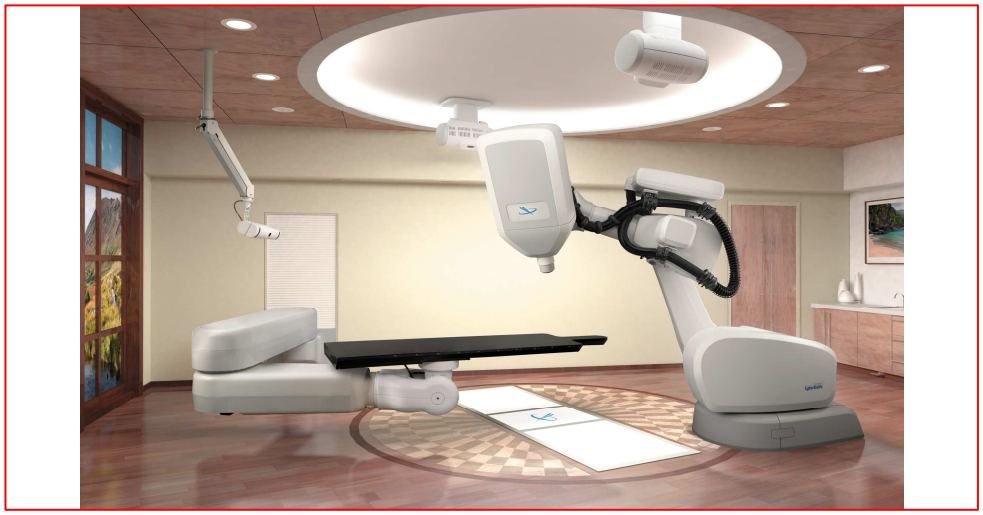






Trott. Stem Cells 1997;363–399;
Krause M, et al. Radiother Oncol 2006;80:112–122

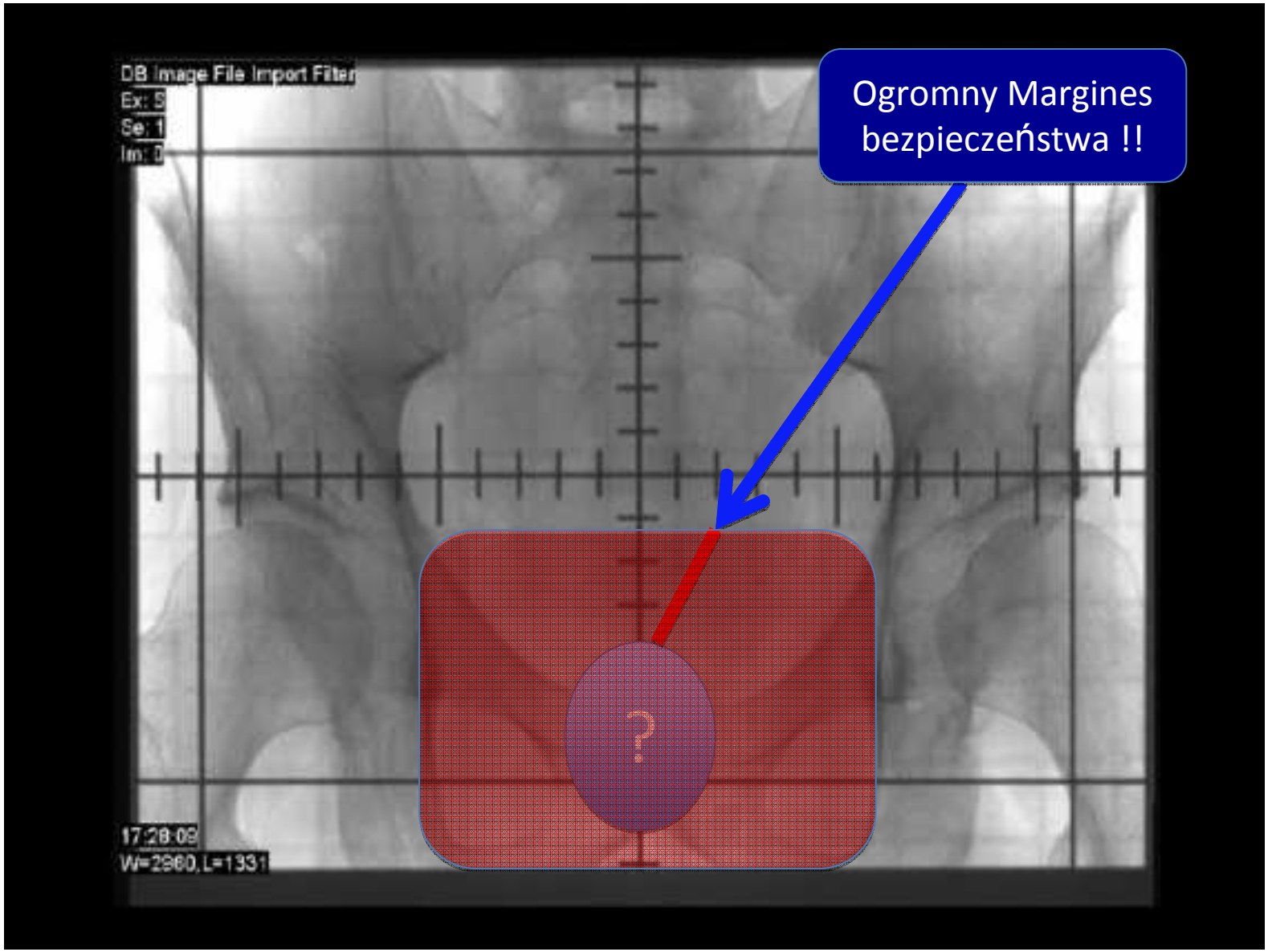
Tylko 10 Gy a efekt biologiczny?
5% vs. 95%



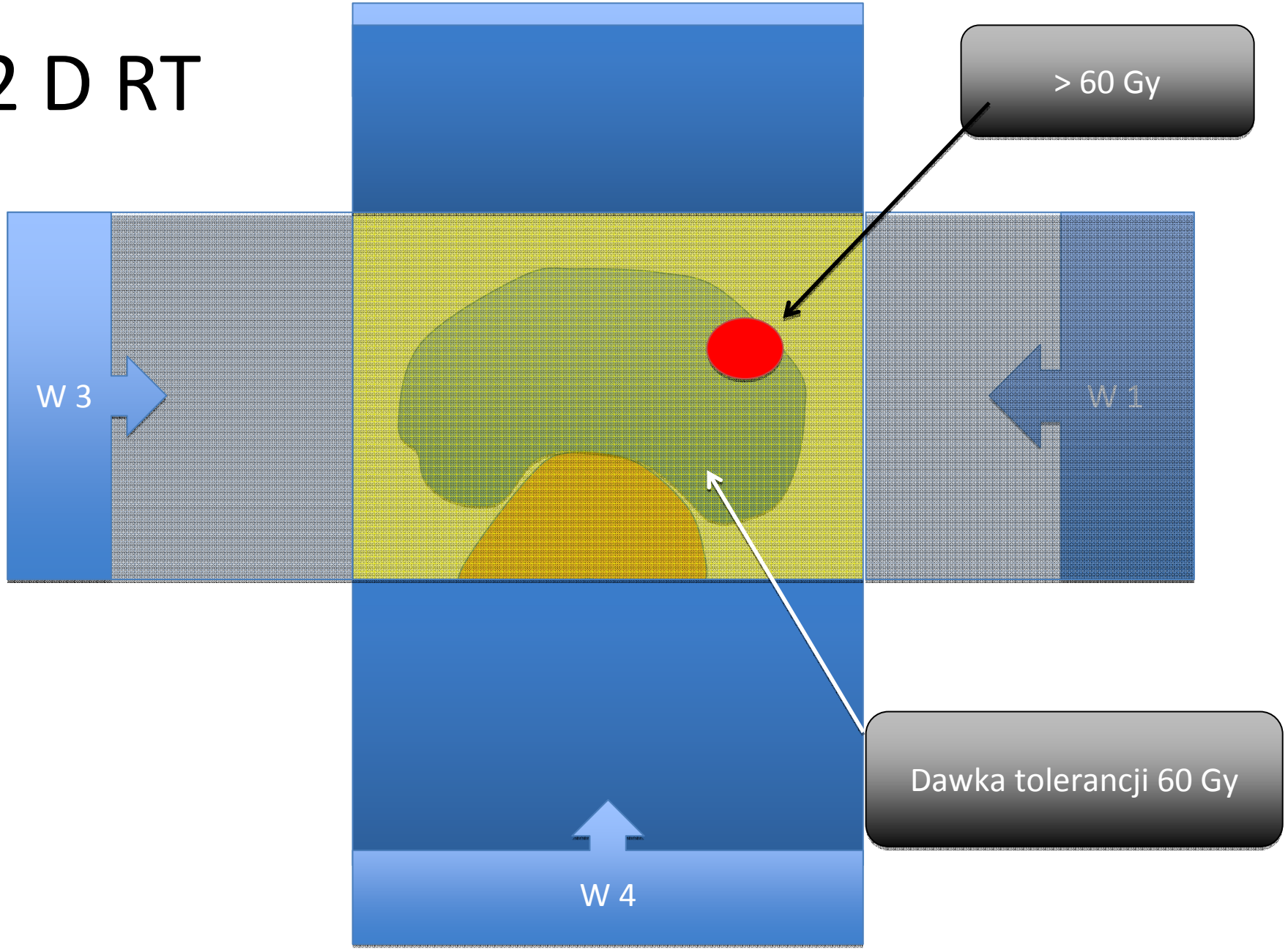
(R)Ewolucja technik

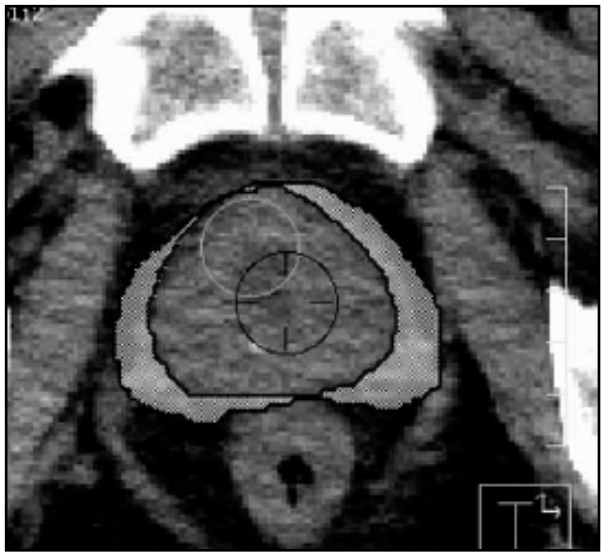
1D – 2D – 3D – IMRT – 4D - IGRT– SBRT

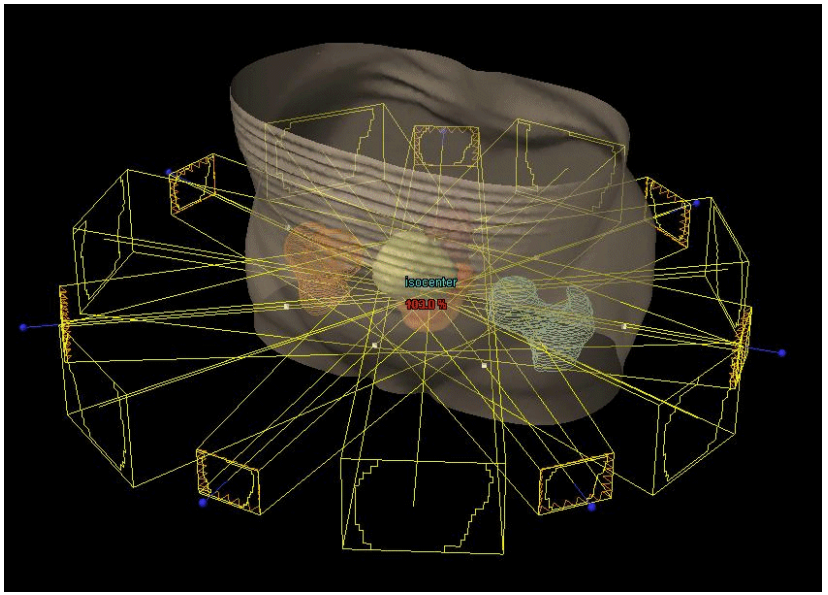
2D RT

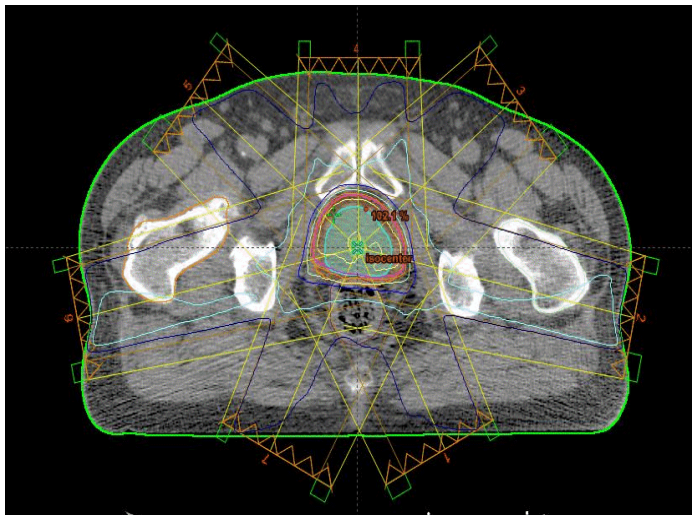

DB Image File Import Filter
Ex: 5
Se: 1
Im: 0
Ogromny Margines bezpieczeństwa !!
17:28:09
W=2960, L=1331

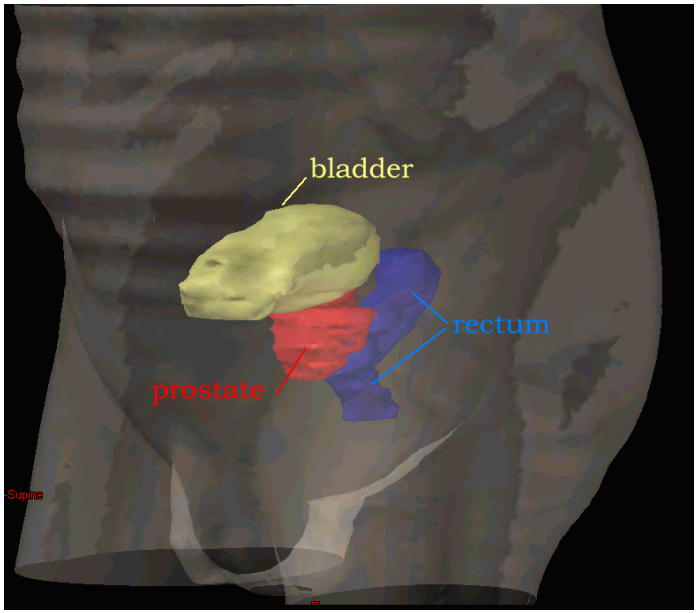
2 D RT



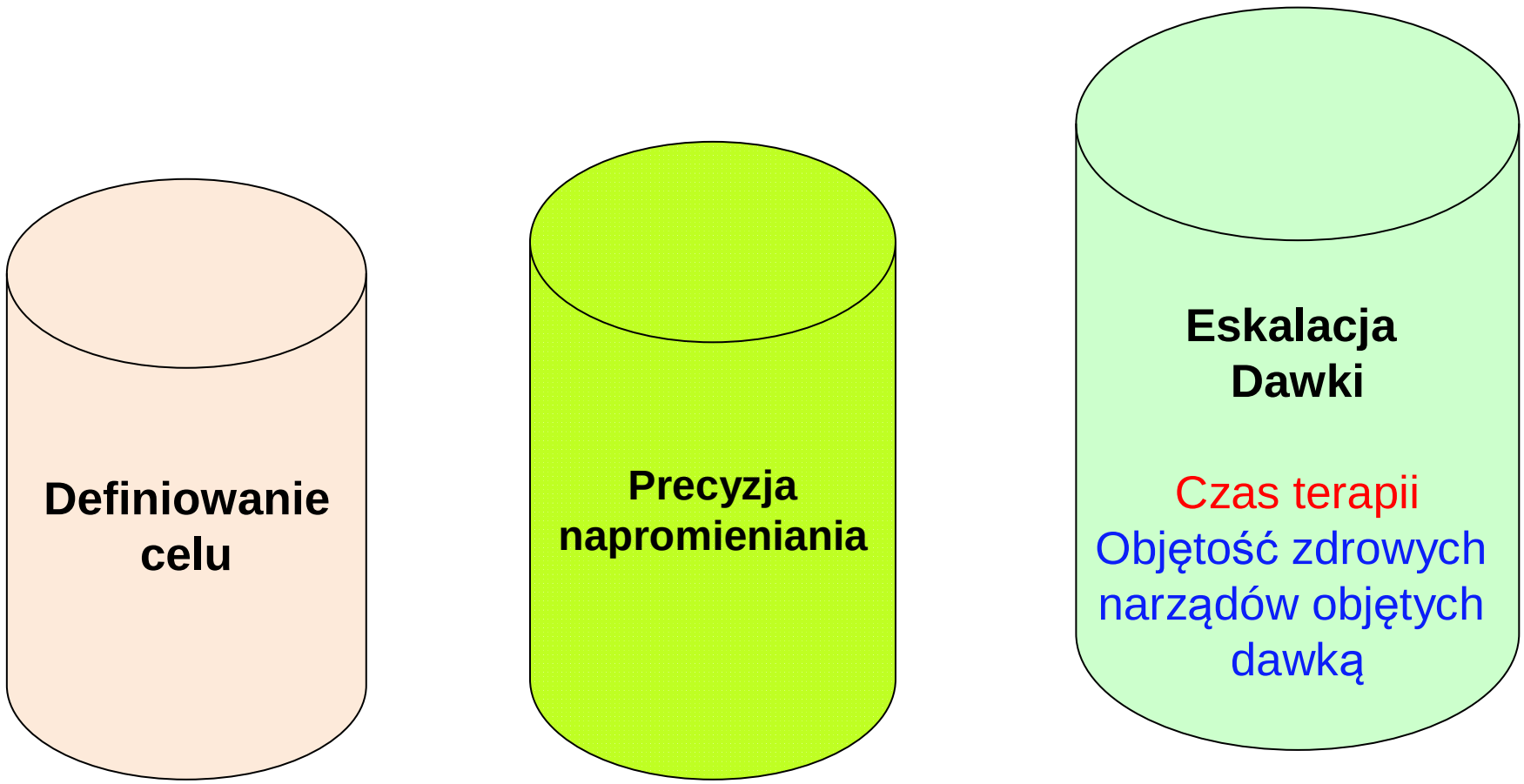


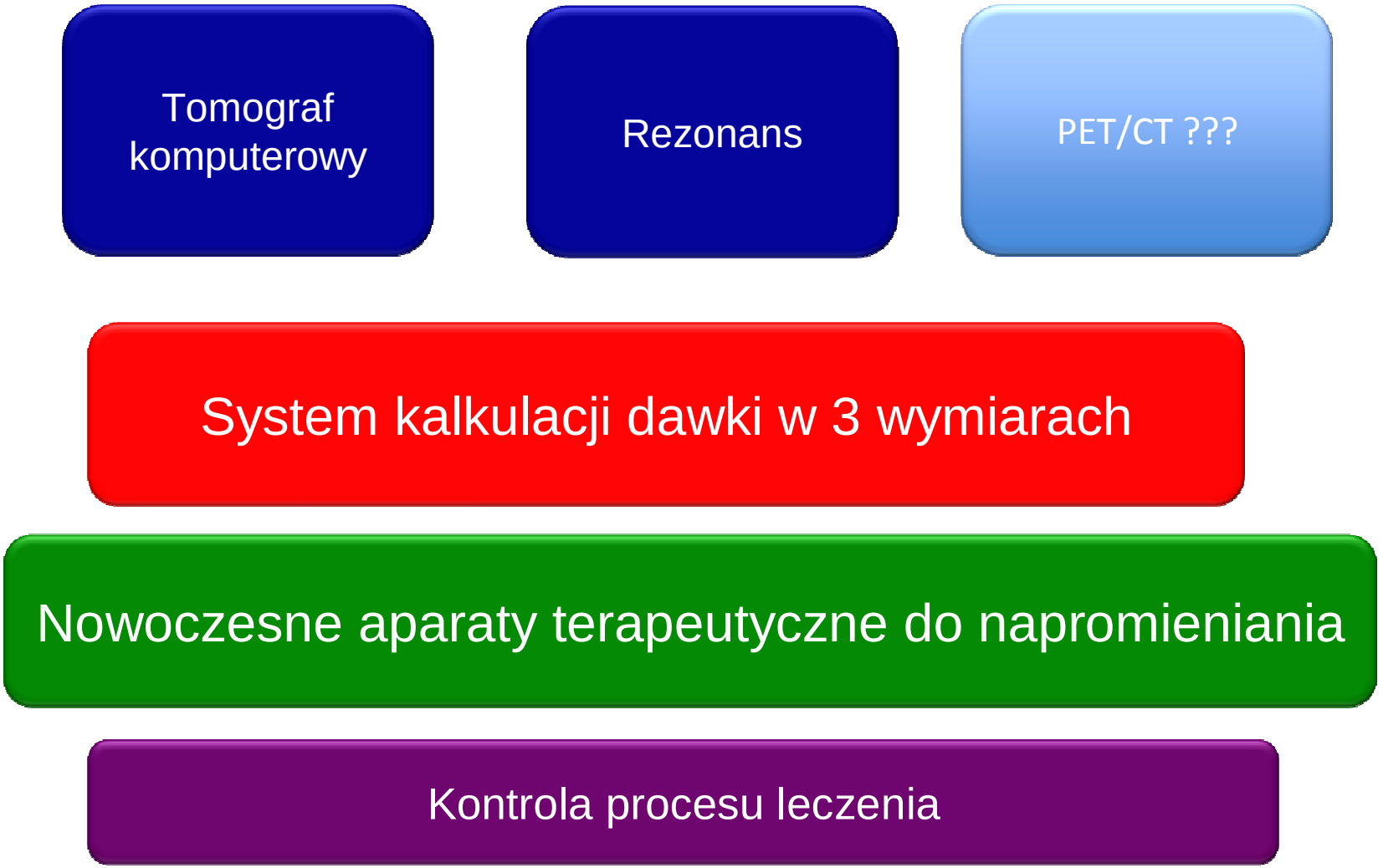

isocenter
105.0 %


isocenter


bladder
rectum
prostate
Supine

Efektywność radioterapii




Tomograf komputerowy
Rezonans
PET/CT ???
System kalkulacji dawki w 3 wymiarach
Nowoczesne aparaty terapeutyczne do napromieniania
Kontrola procesu leczenia

Dlaczego nie 2D
Rak płuca

Błędy geograficzne

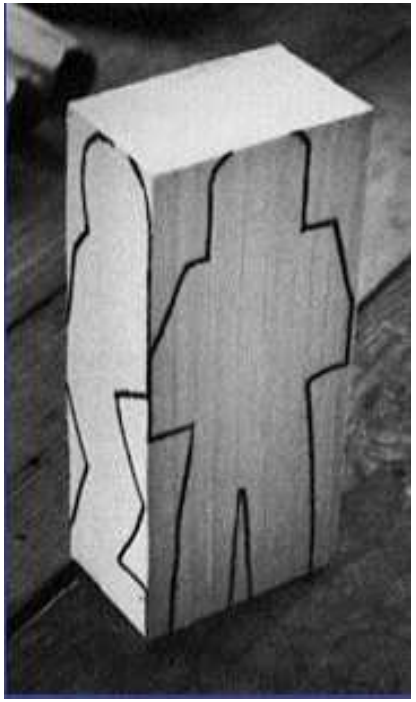
Study	Year	Patients	major errors
RTOG 7301	'82	316	12%
SWOG 7628	'82	140	31%
RTOG 8311	'93	832	6 %
CALGB 8433	'90	155	23 %
EORTC 8844	'91	332	15 %
INT 0139	'03	194	19 %

Mała efektywność, dużo powikłań

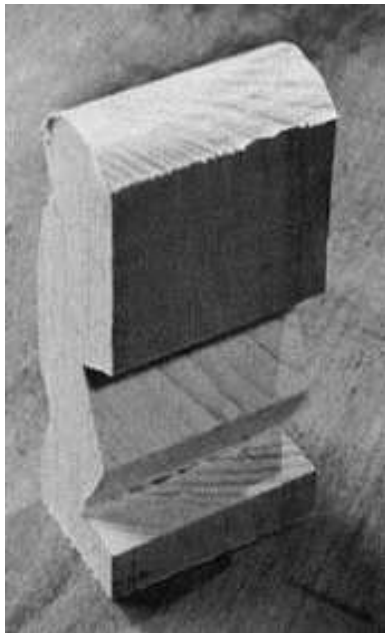
Ewolucja technik napromieniania WCO

- 3 DCRT: 1996 r
- Intensity Modulated RT (IMRT): 2000 r
- Brachyterapia HDR, LDR
- Image Guided RT (IGRT): 2012 r
- Sterotactic Body RT (SBRT): 2013 r
- Protonoterapia – w planach ?
- Personalizacja leczenia ?

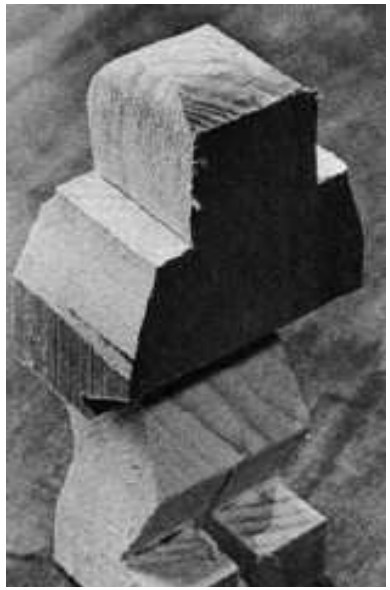
guz



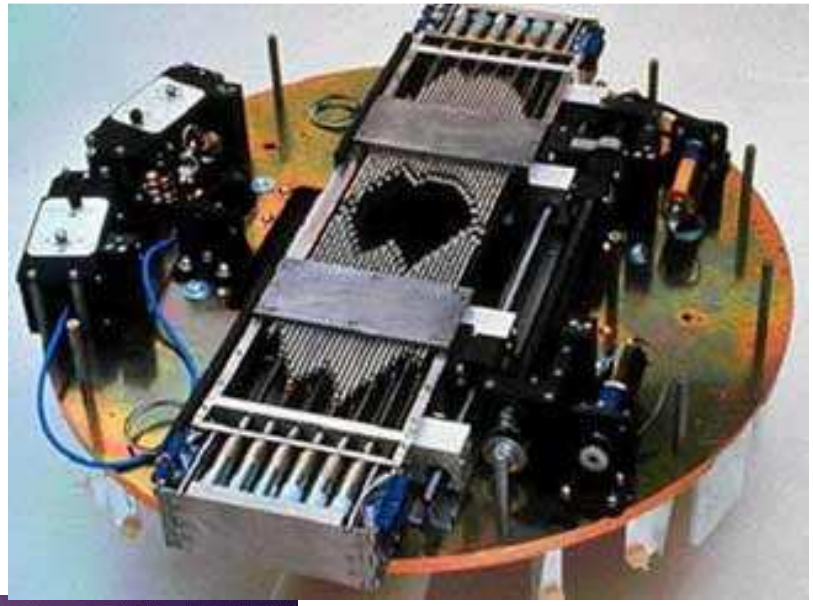
2DRT



3DCRT

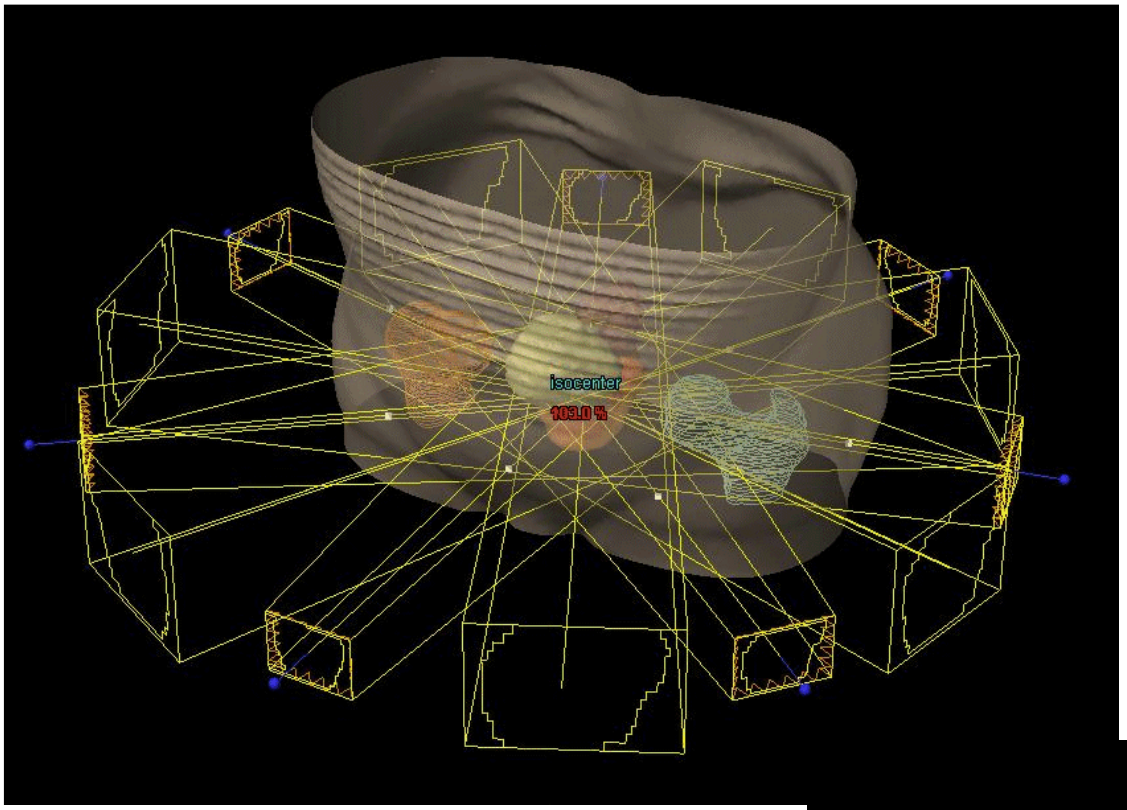


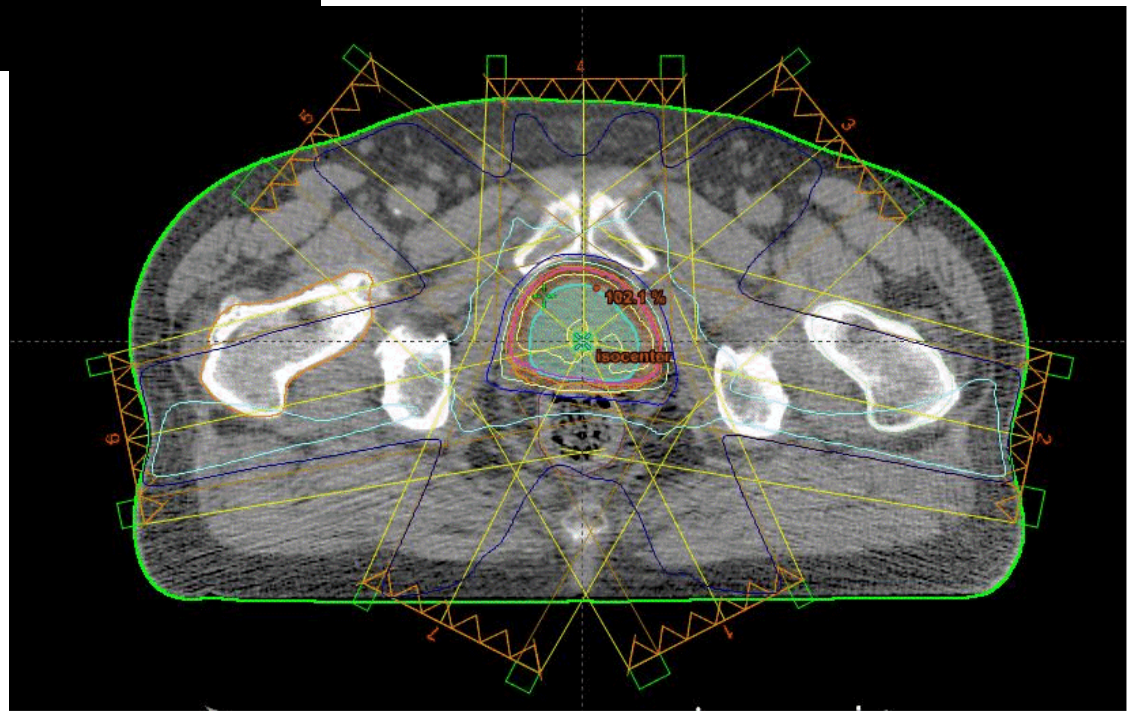
IMRT




VARIAN
CLINAC 23EX

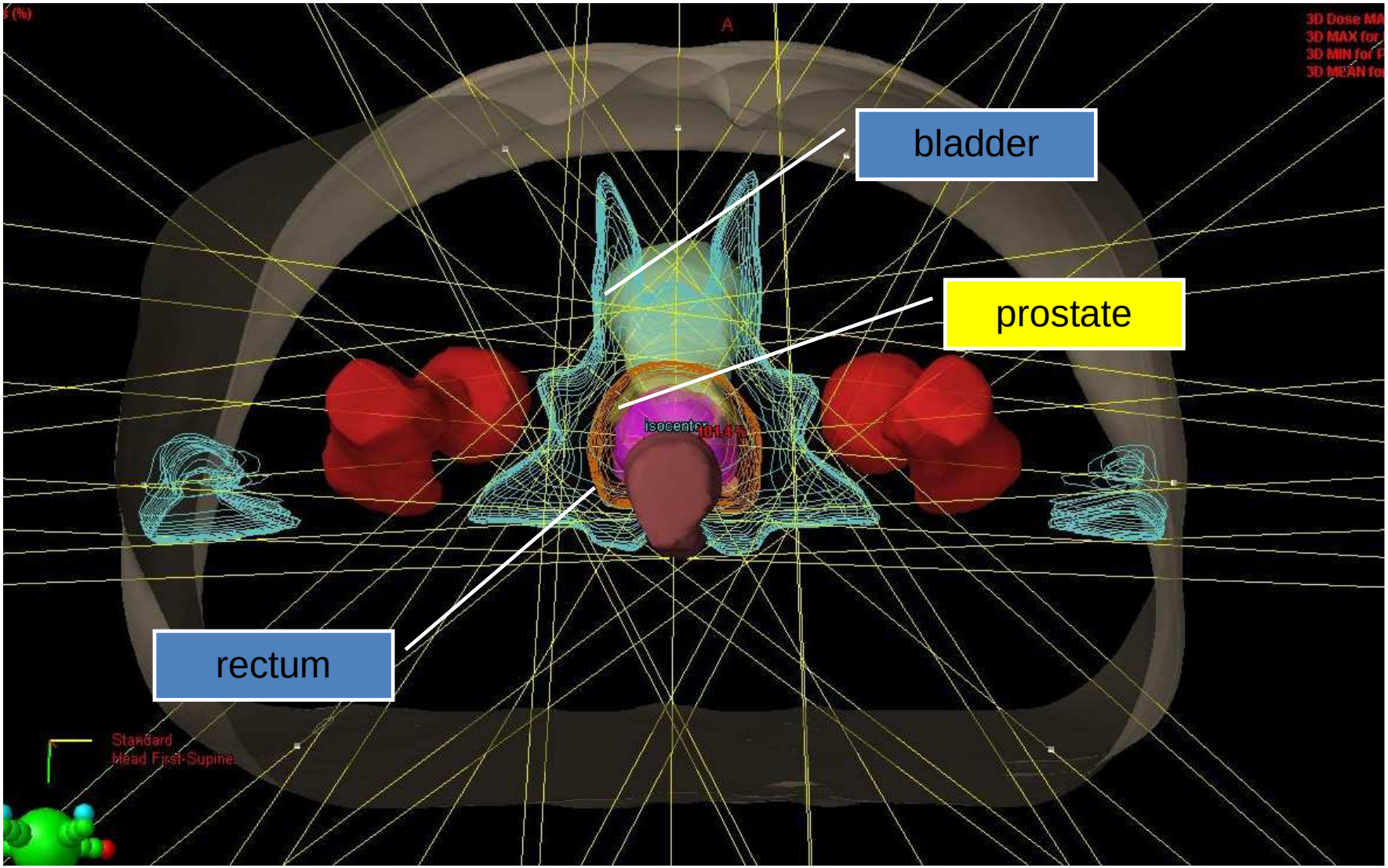

© Varian Medical Systems 1999


isocenter
103.0 %


102.1 %
isocenter

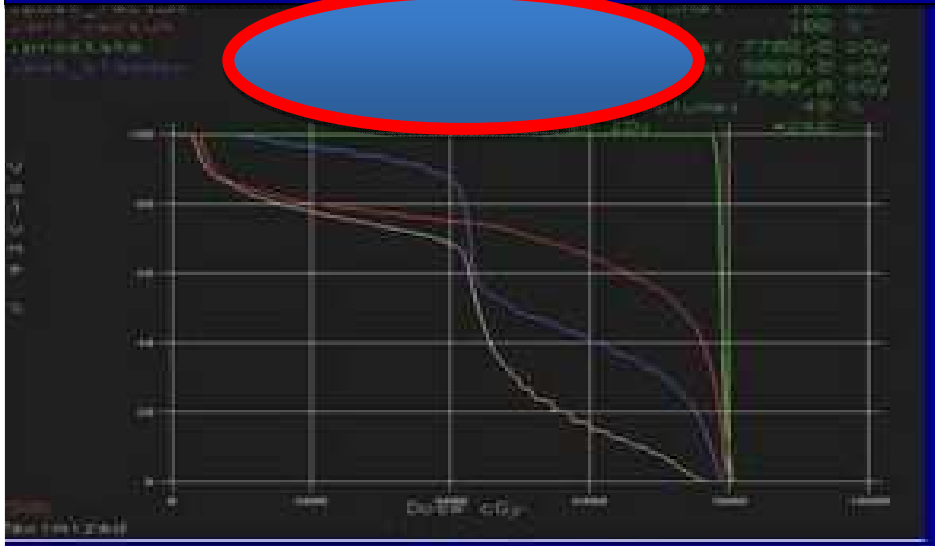
IMRT

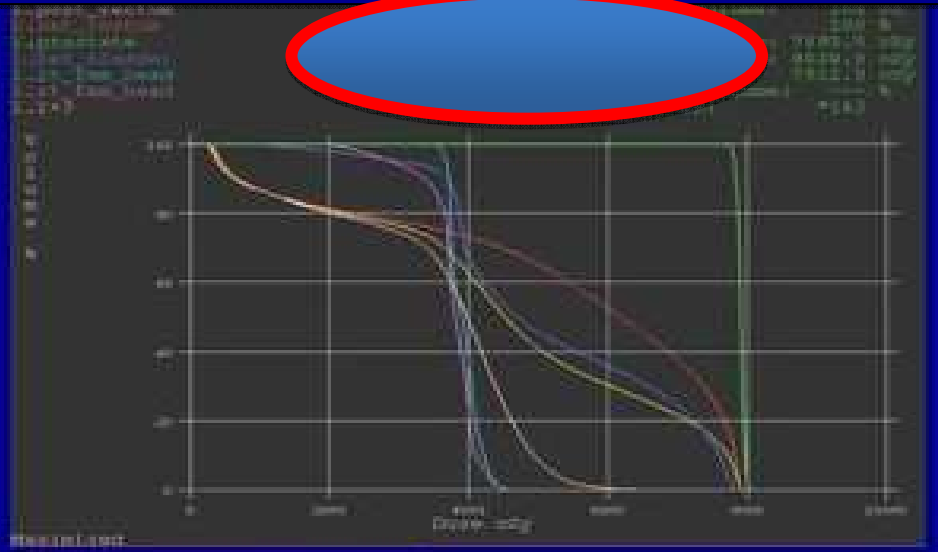
The radiation dose clouds that surround the target

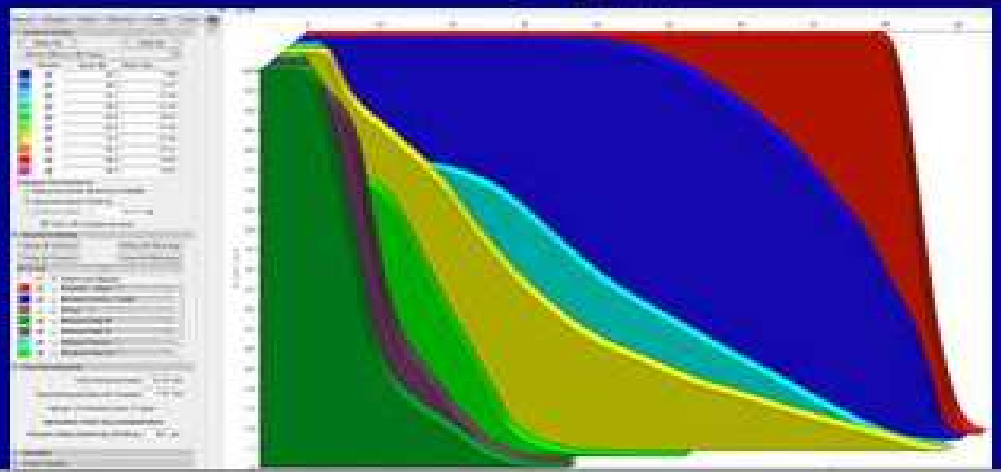


Eskalacja dawki

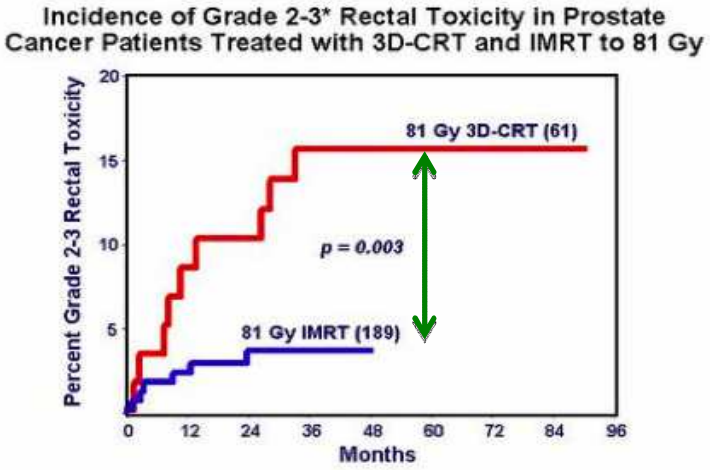
Jaka objętość odbytnicy (%) otrzymuje dawkę zaplanowaną w sterczu ?

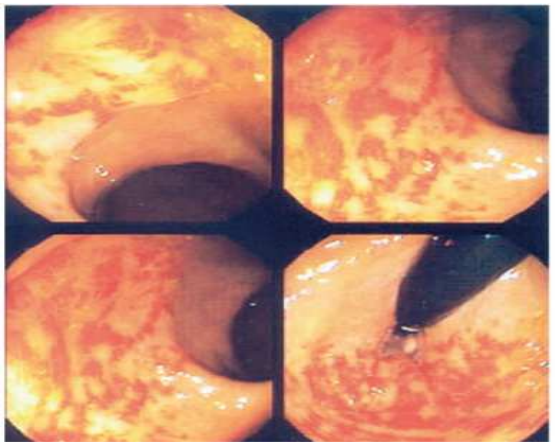






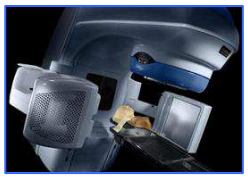
		GU Toxicity by RTOG Grade				GI Toxicity by RTOG Grade			
Technique	**Patients**	0	1	2	**3**	0	1	2	**3**
	30	7%	40%			13%	23%		
6-Field Conformal	30	7%	57%	30%	7%	17%	13%	67%	3%
IMRT	50	52%	18%	30%	0%	74%	12%	14%	0%





MGRT
BGRT
IGRT
SBRT
?

IGRT
SBRT



IGRT

IMRT

3DCRT

2DRT

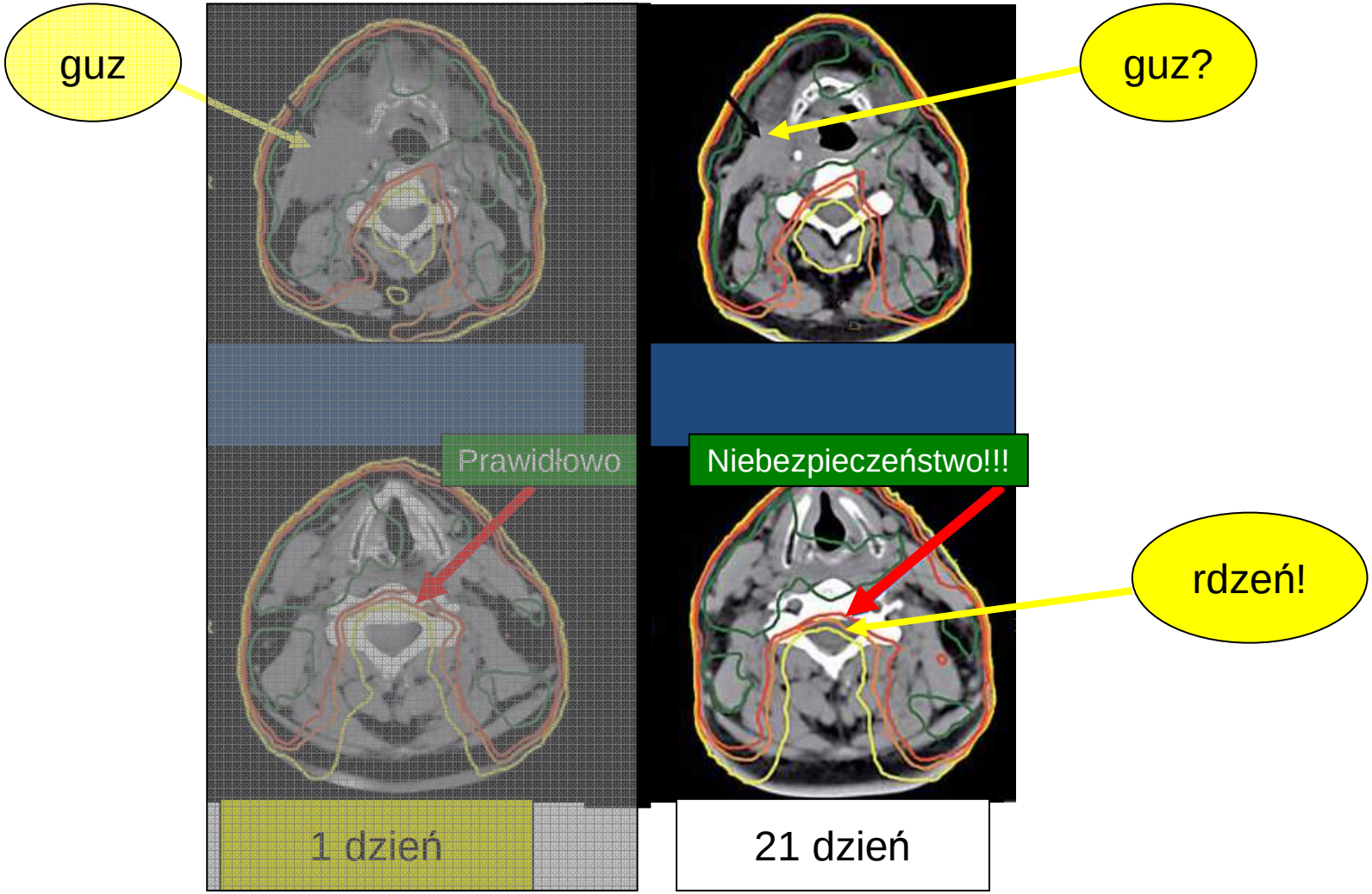
Ostatnie 25 lat ……

Target

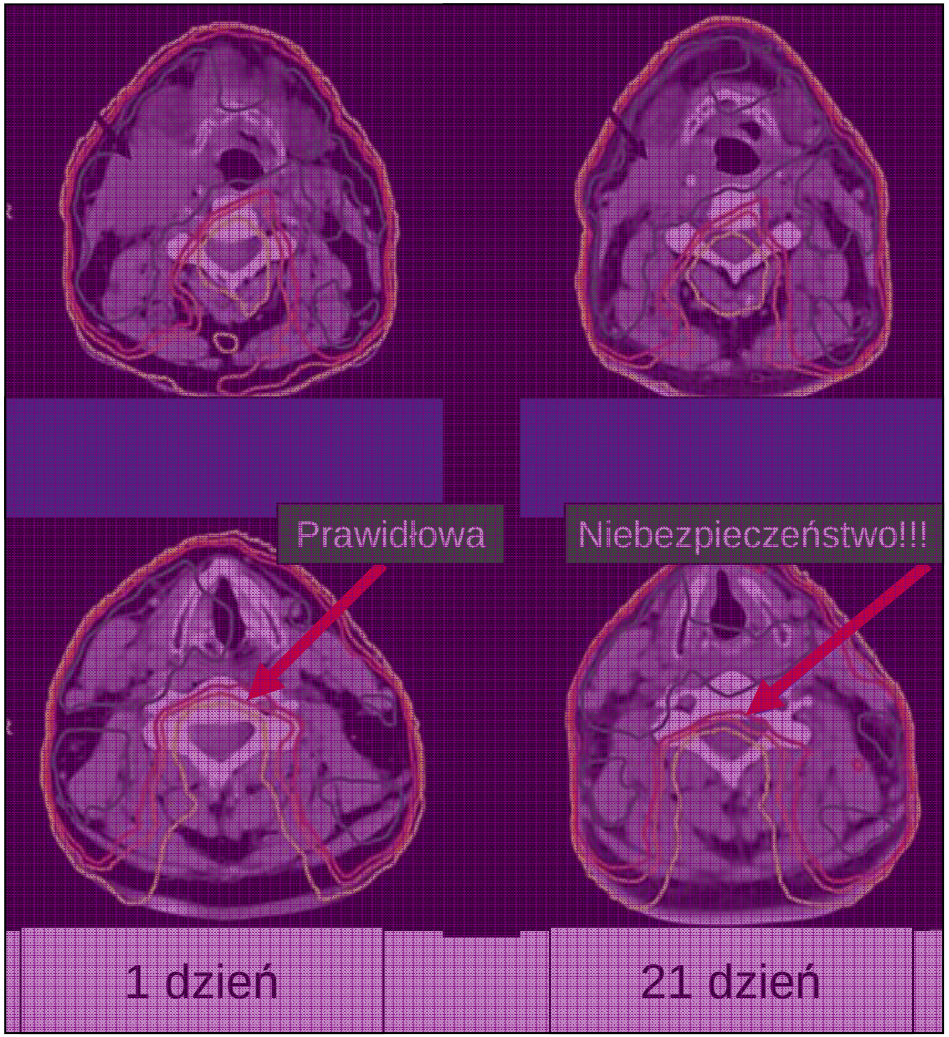
GUZ NOWOTWOROWY

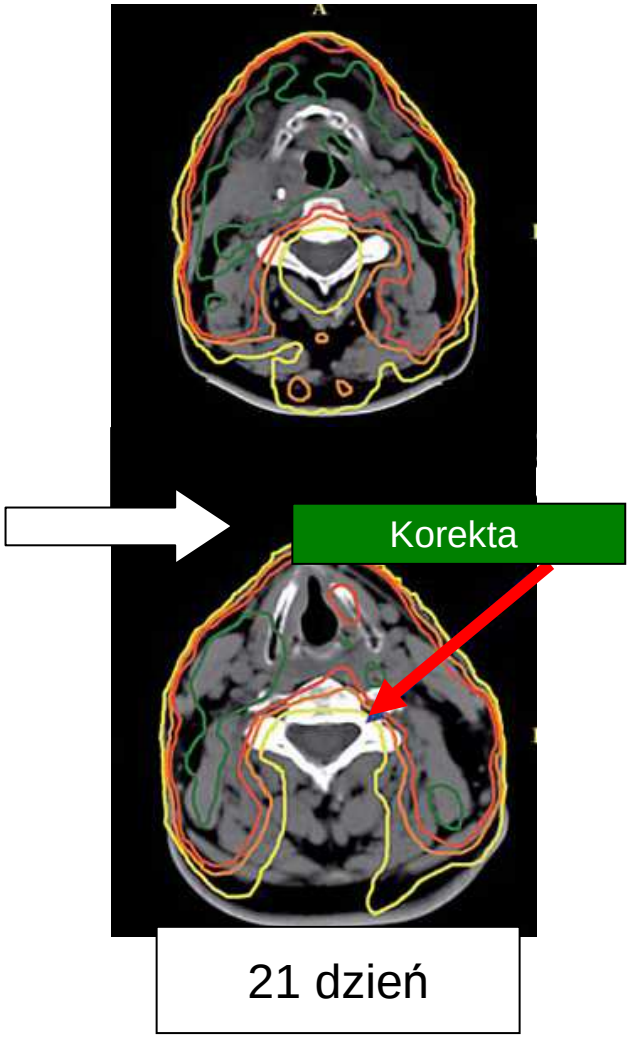
zmiana położenia

ruchomość



Spadek masy ciała 5%
Zmniejszenie objętości guza nowotworowego



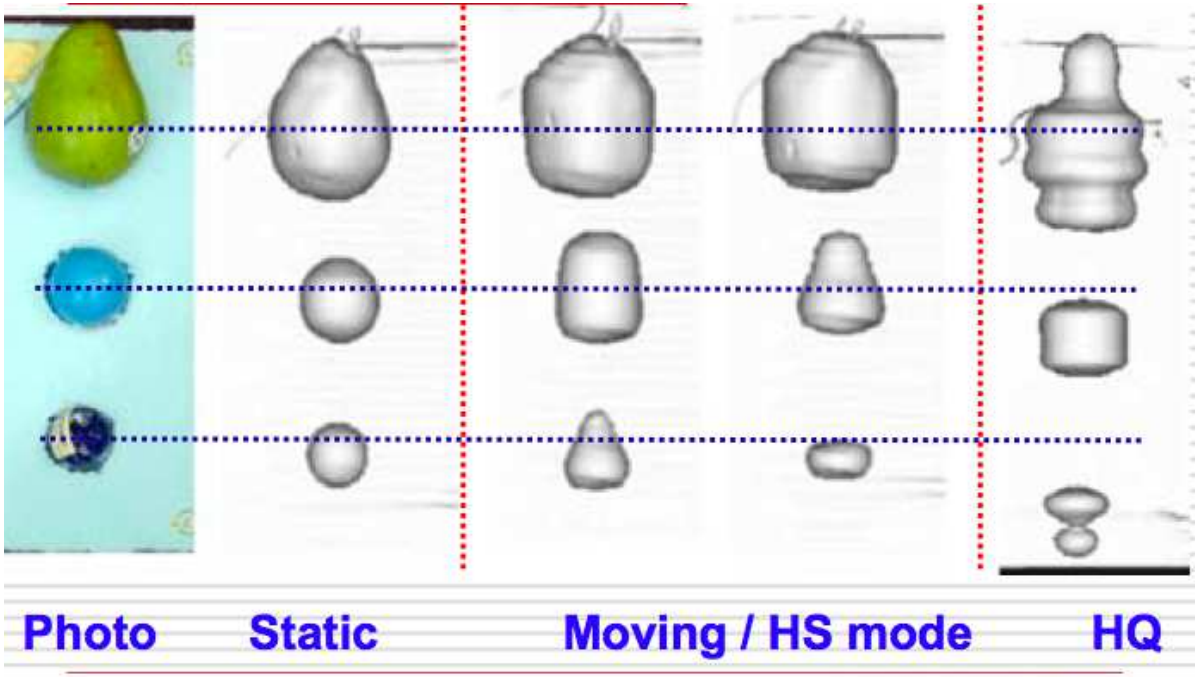


Spadek masy ciała 5%
Zmniejszenie objętości guza nowotworowego

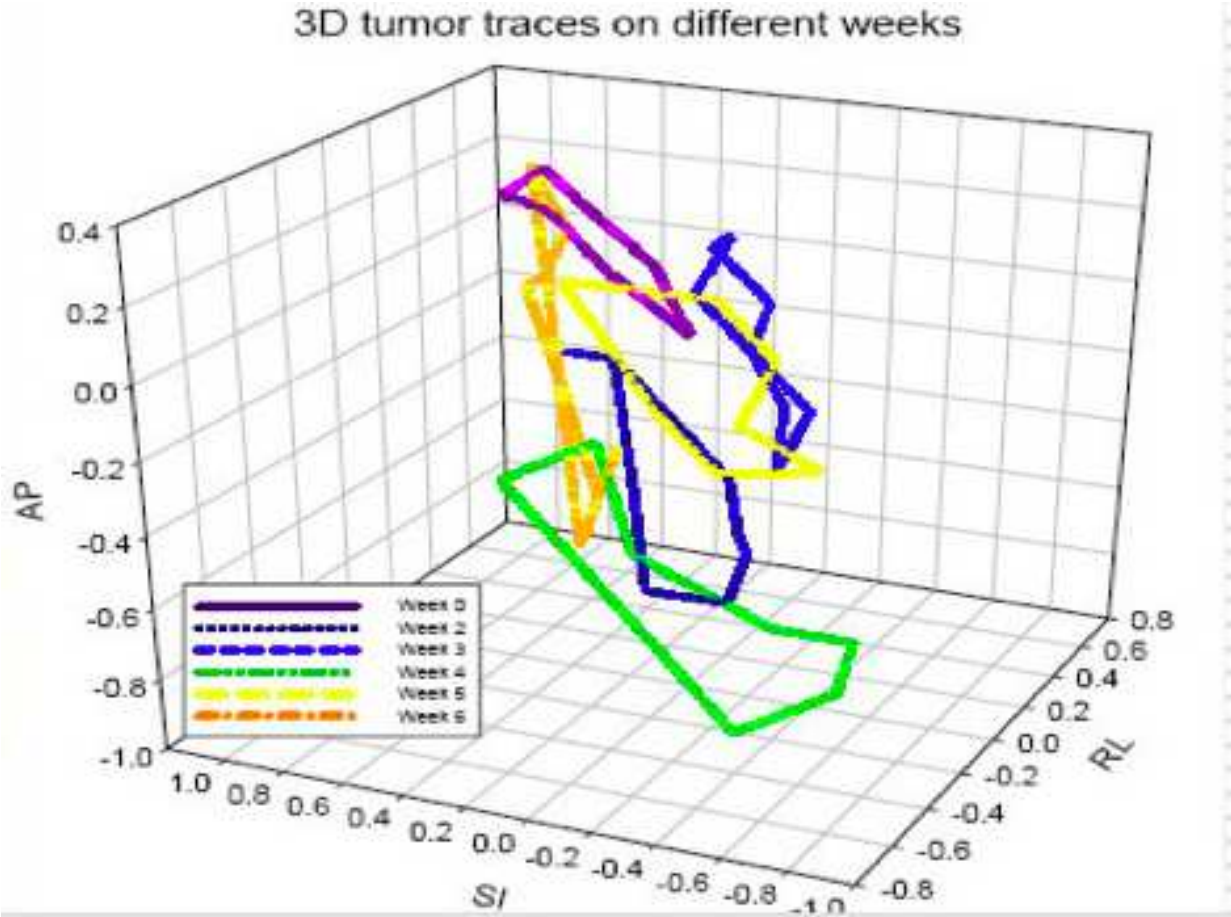
Ruchomość na etapie zbierania danych do planowania

Video courtesy of George T.Y. Chen

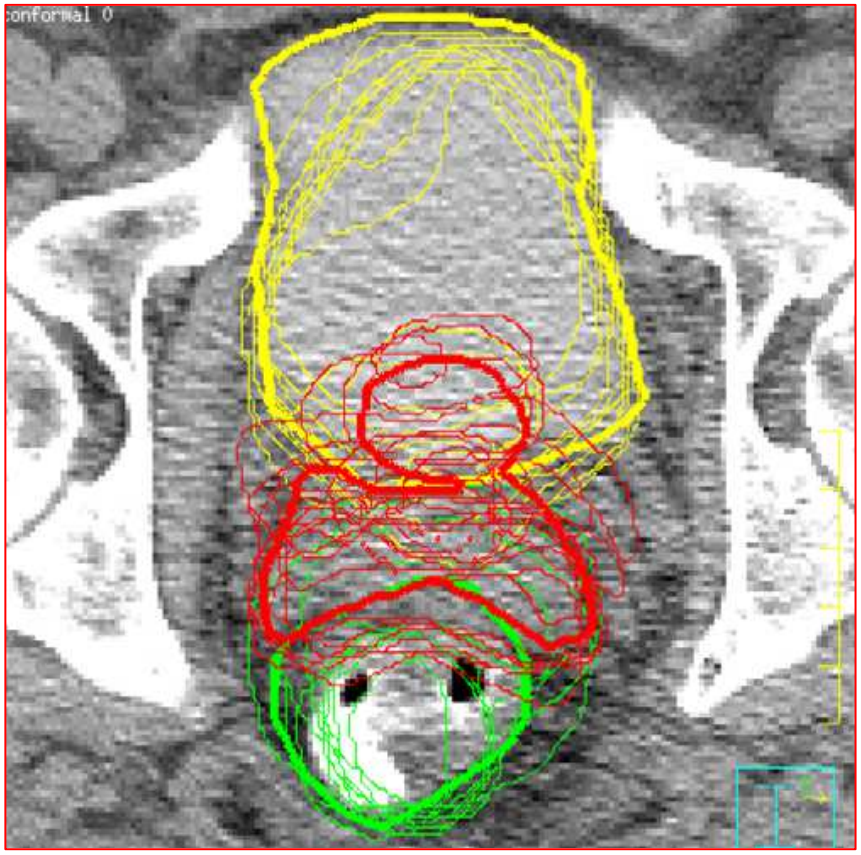
Chen, Kung, and Beaudette, *Semin Radiat Oncol.* 14(1):19-26, 2004.



Ruchomość na etapie realizacji leczenia

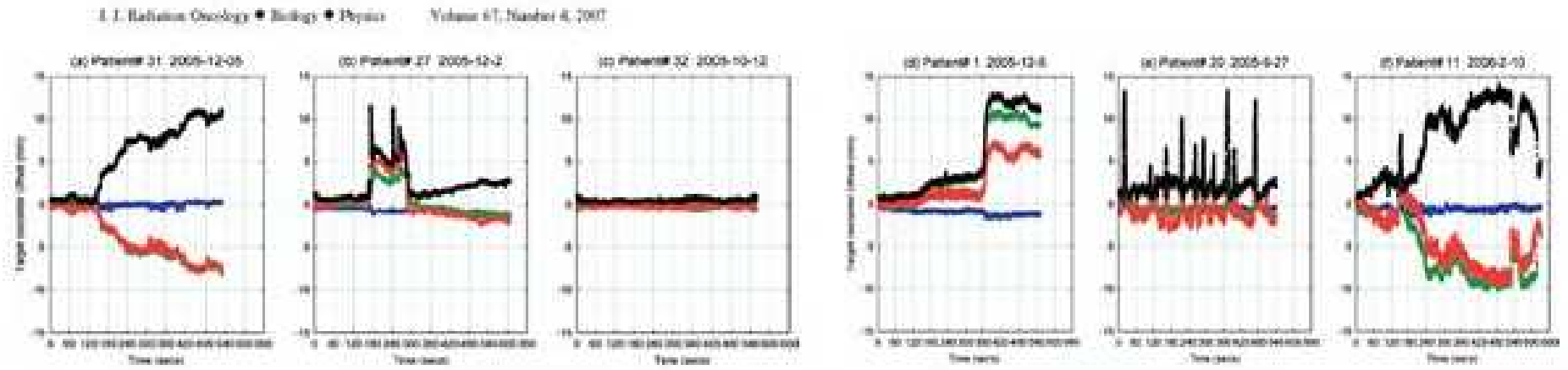


Target w trakcie RT raka stercza



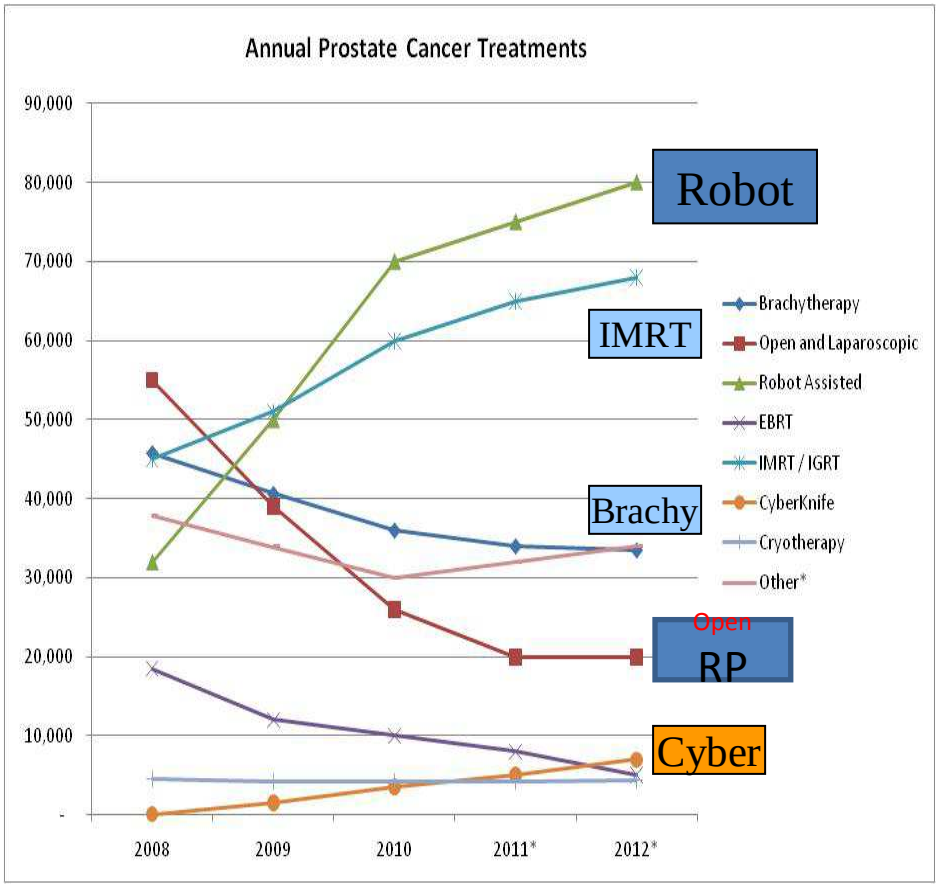
Zmiana położenia prostaty

Changing anatomy - Prostate



Patient	No. fractions analyzed	Fractions with >3-mm excursion for >30 s cumulative		Fractions with >5-mm excursion for >30 s cumulative	
		#	%	#	%
All (n = 35)	1157	473	41	179	15

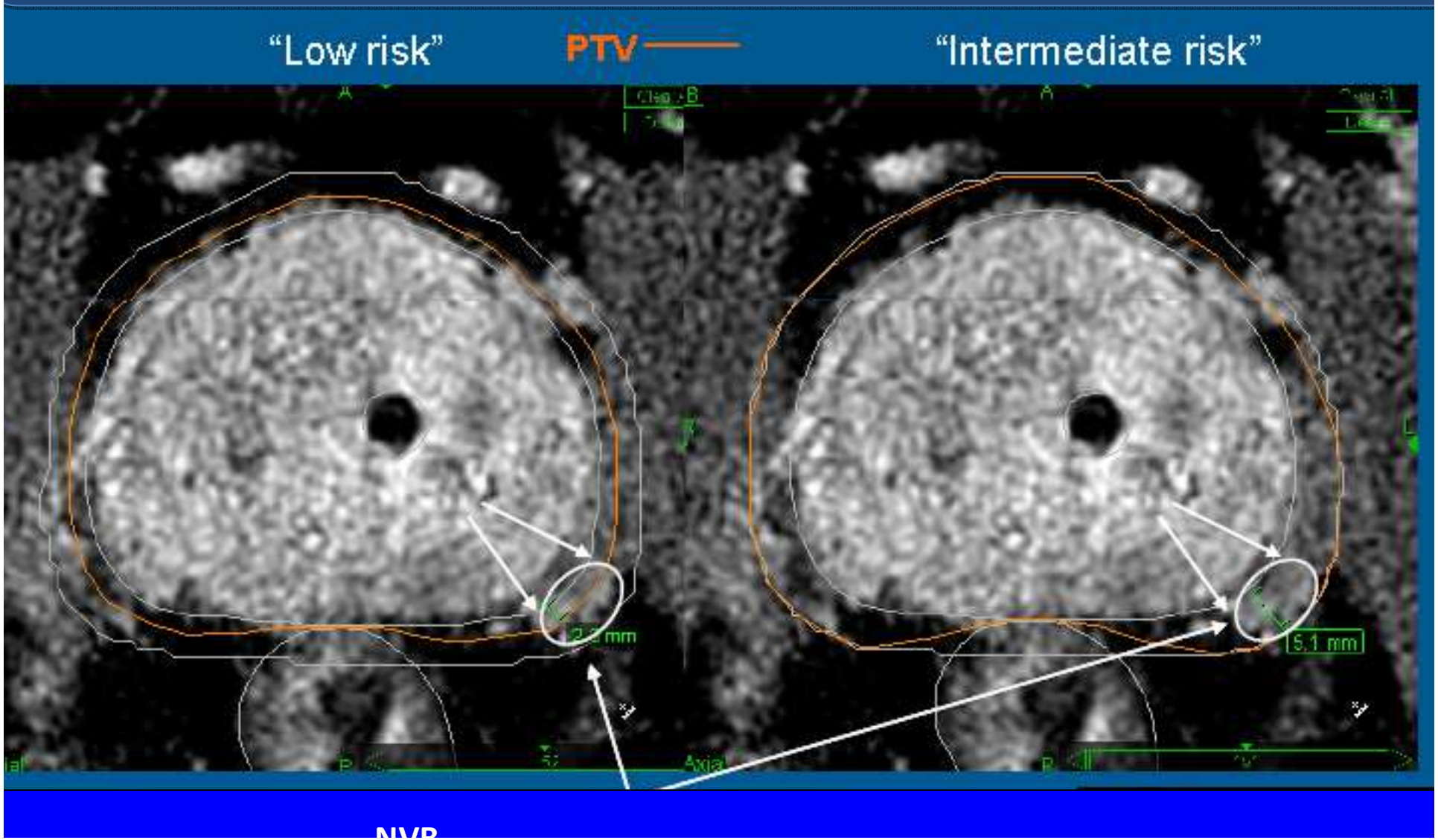
Czy możemy skorygować napromienianie tak aby uwzględnić ruchomość targetu?



Tak

cyberknife

Rozkład dawki dla CK

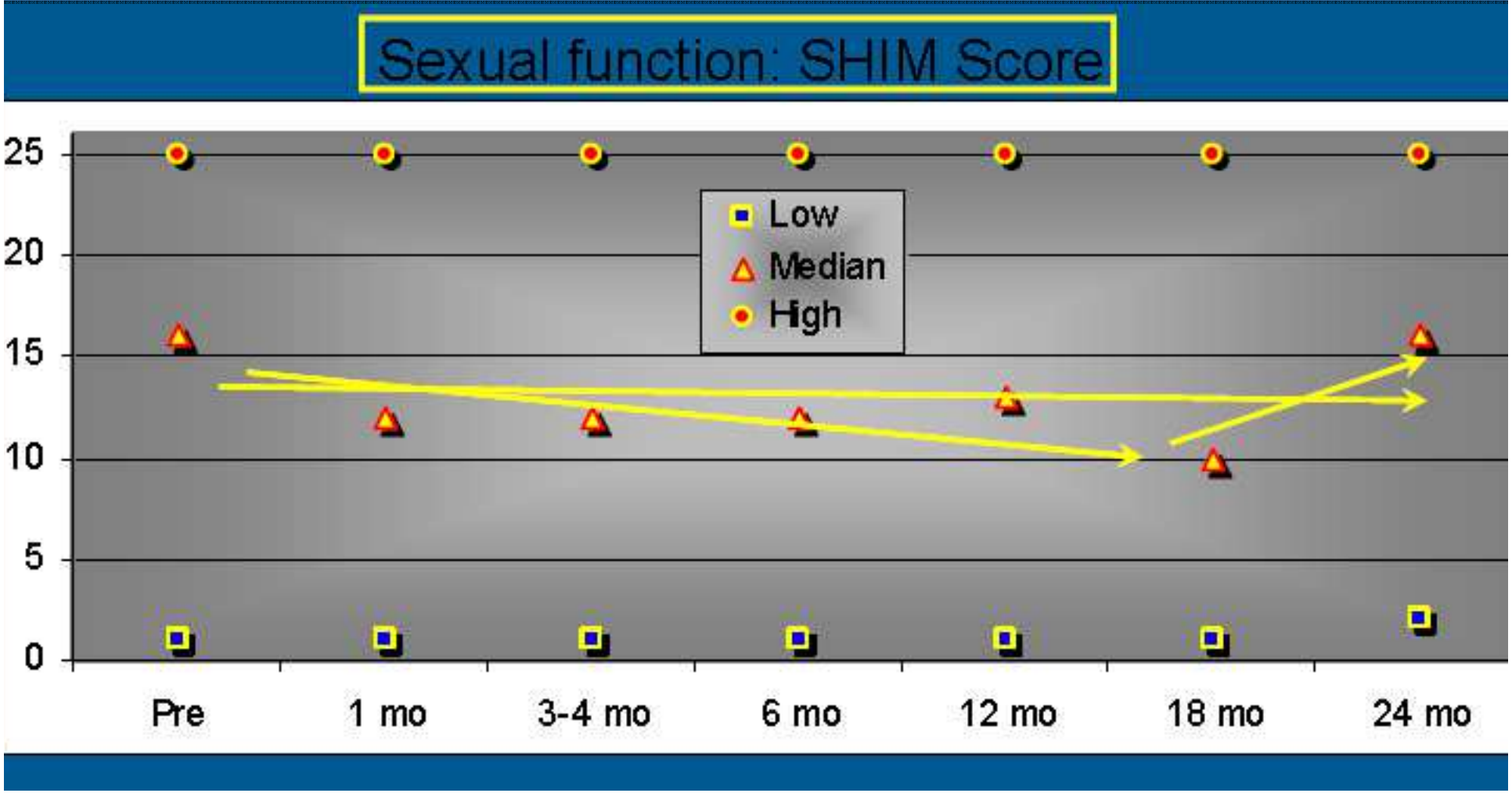


Cyberknife

Thomas Bennett, MD, 65 lat
DG: zlokalizowany rak stercza,

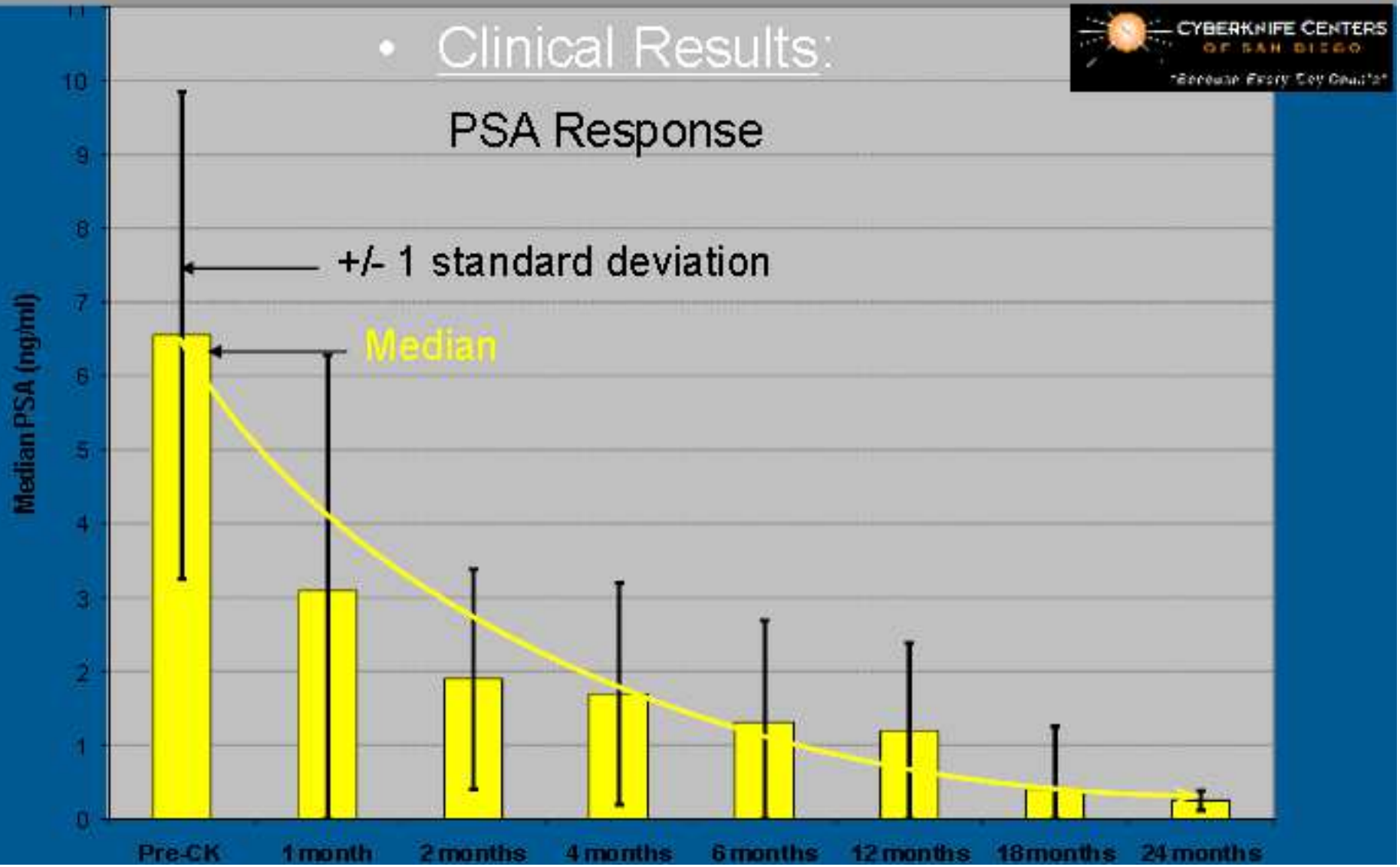
Wybrał napromienianie 5x zamiast BT

CYBERKNIFE
JAKOŚĆ ŻYCIA



Virtual HDR® Prostate CyberKnife Radiosurgery: PSA-response, Toxicity and Quality of Life Evaluation

- Clinical Results:



RAK PŁUCA

Konwencjonalna RT

60 – 66 Gy (1,8 – 2,0 Gy):

- **5-yr LC:** **30%** - 40%
- 5-yr OS: 10% - 30%

KRT vs SBRT

- D.frakcyjna 2 Gy vs 20 Gy
- D.całkowita 60-66 Gy vs 60 Gy

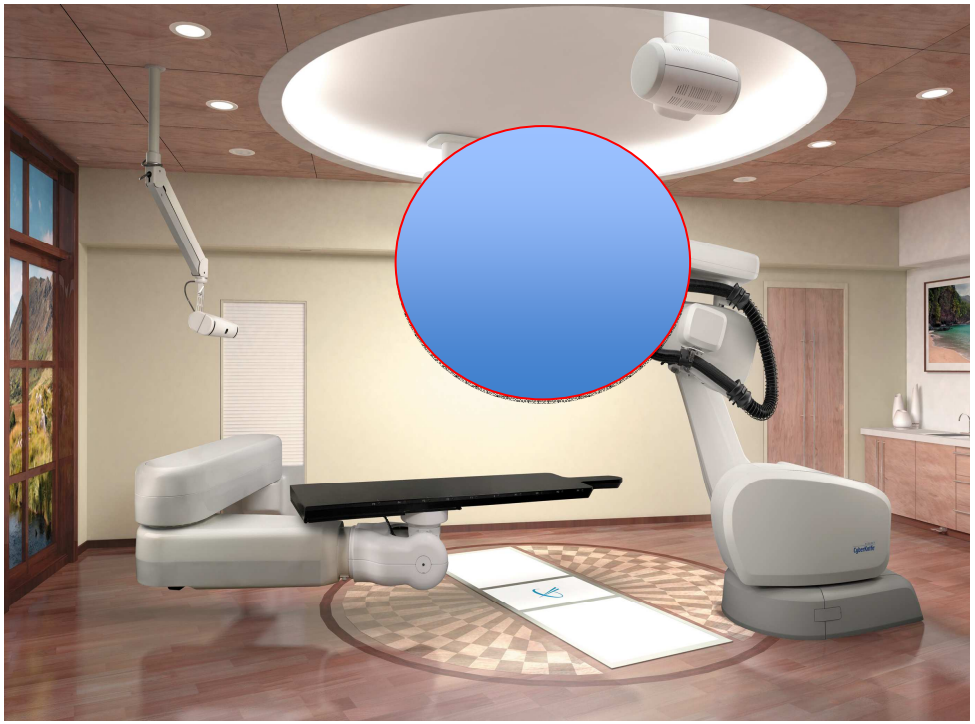
RT schedule	BED_{10}	Reference
60-66 Gy/30-33fr	72-79 Gy	Standard RT
48Gy/4 fr	105 Gy	Japanese SBRT dose
30 Gy/1 fr	120 Gy	SRS - Germany
60 Gy/ 3 fr	180 Gy	RTOG SBRT dose

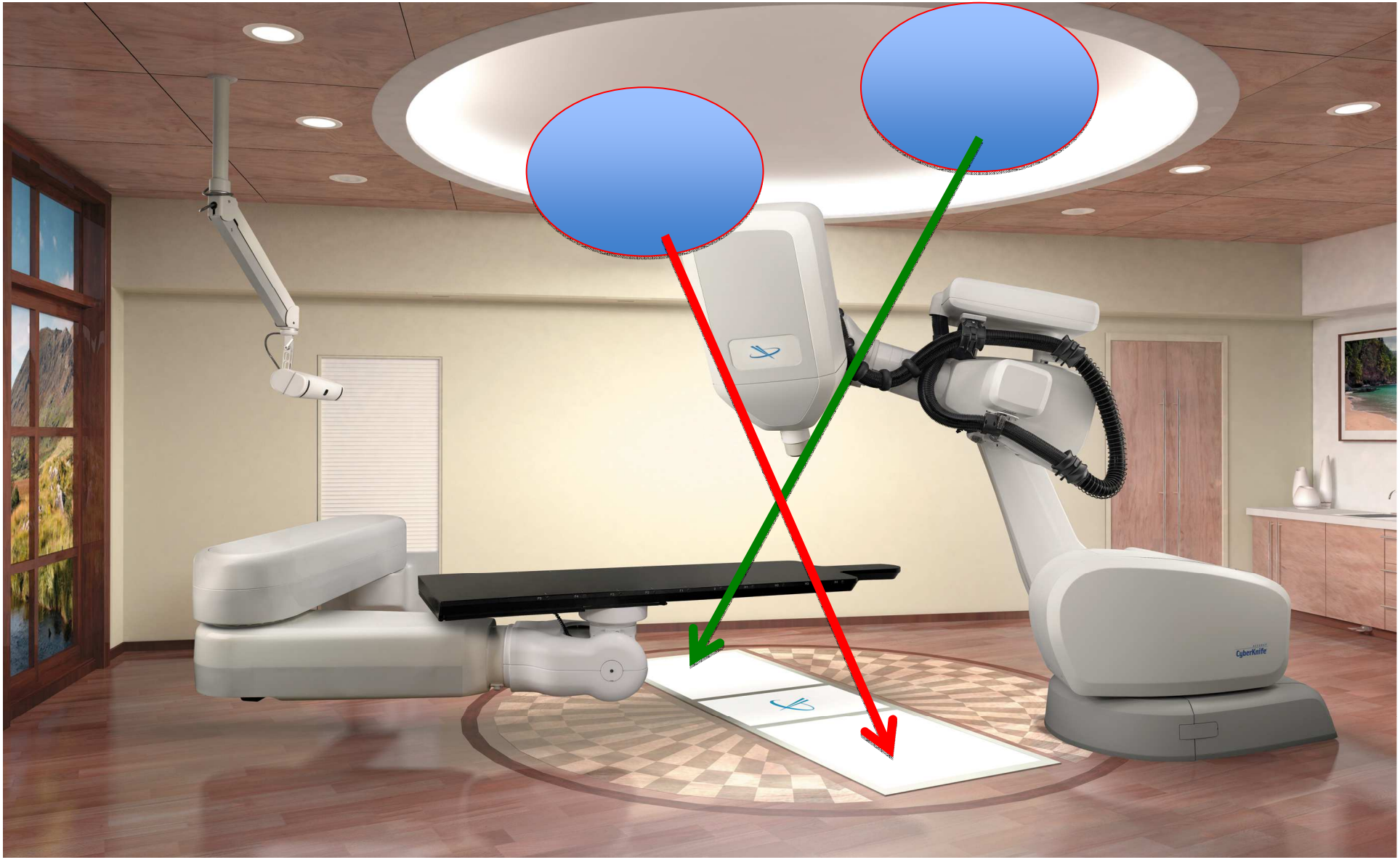
SBRT: RAK PŁUCA

EFEKTYWNOŚĆ MIEJSCOWA

Institution	# Patients	Local Control
Yamanishi, Japan	257	86%* (92%)
Japan	131	96%
Aarhus (Denmark)	89	89%
Wash U	70	83%
Indiana U (protocol)	70	88%
Cleveland Clinic	94	97%
Amsterdam	206	97%

Widoczne różnice
CYBERKNIFE

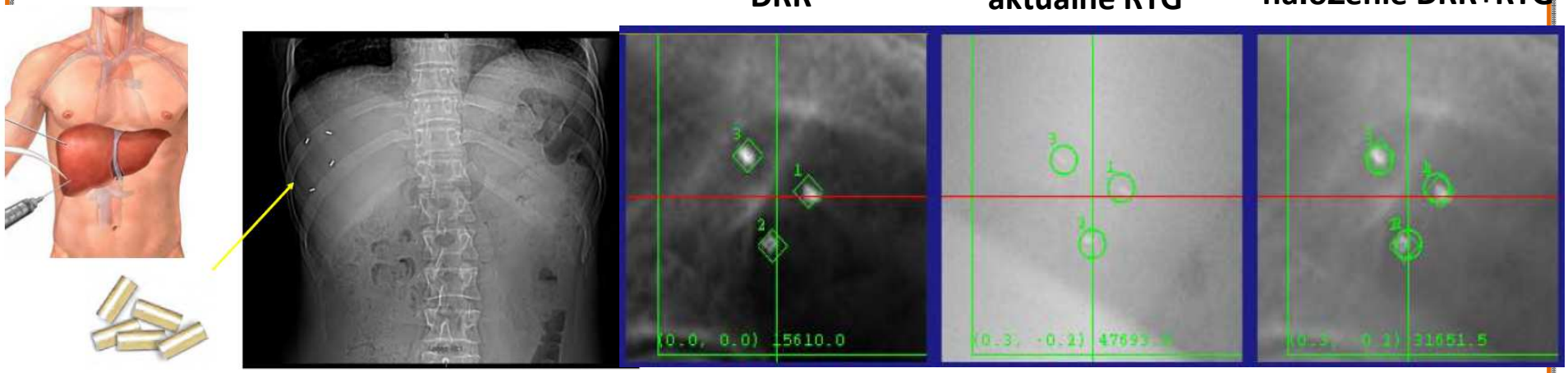




wielkopolskie centrum onkologii

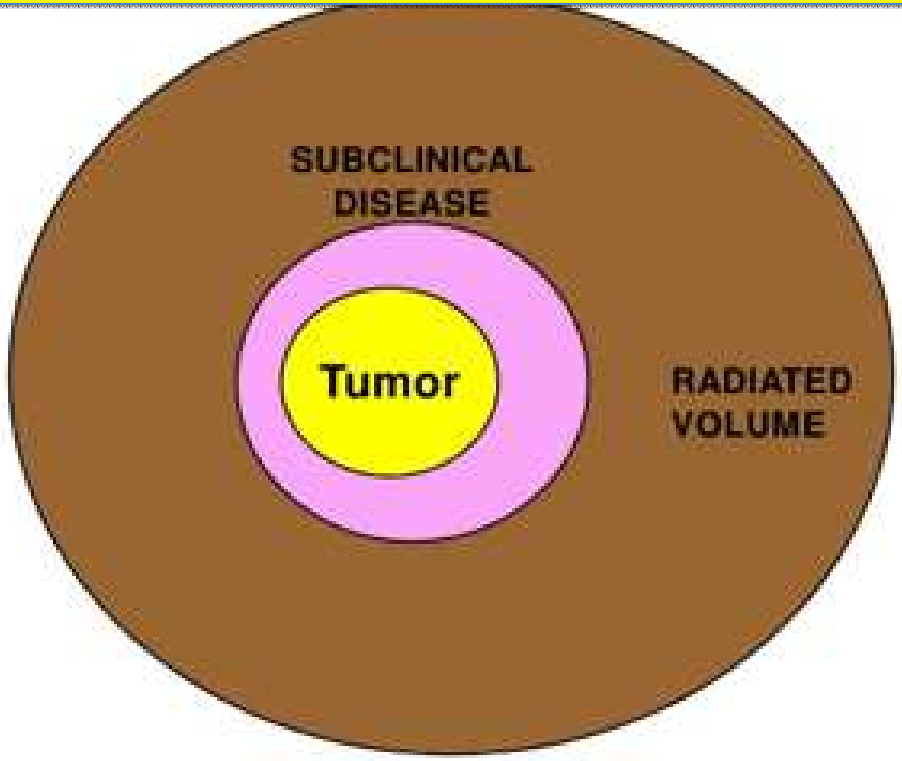
System „śledzenia” – Znaczniki

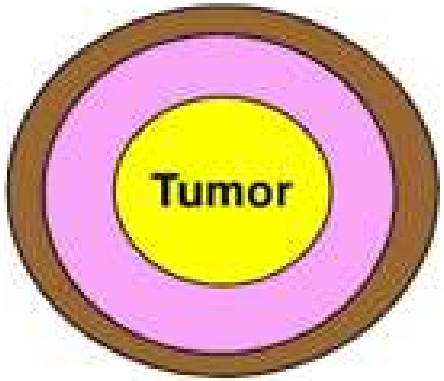
1. Znaczniki złote umieszczone w tkankach miękkich (wątroba, prostata, płuco, itp.)
2. Automatyczne detektowanie, śledzenie i korygowanie ich przesunięć w trakcie napromieniania



Konwencjonalna RT

Cyberknife





Różnica w marginesie napromienianych tkanek zdrowych jest proporcjonalna do 3 potęgi

Czas terapii

- Konwencjonalna (6 – 7 – 8 tygodni)

Hypofrakcjonowana SBRT (1 – 5 – 10 dni)

minimalna zmiana geometrii guza !!!! Pacjenta !!!

- **Paliatywna RT:**

przerzuty do OUN, kości, wątroby, tkanek miękkich

- **Radykalna RT:**
- Prostata
- Płuco
- wątroba, trzustka
- nowotwory łagodne

Total Dose	Reference	BED Gy10	NTD, Gy 2-Gy Fractions)	Estimated Progression-free Survival at 30 Mo. (Assuming No Hypoxia)
Conventional fractionation	—	(Fig. 1.1)	—	—
60 Gy, 30 fractions	—	72	60	15%
70 Gy, 35 fractions	—	84	70	24%
SBRT	—	(Fig. 1.2)	—	—
48 Gy, 4 fractions	(6)	106	63	34%
45 Gy, 3 fractions	(2)	113	94	95%
48 Gy, 3 fractions	(2)	125	104	99%
60 Gy, 5 fractions	(12)	132	110	>99%
60 Gy, 3 fractions	(3)	180	150	>99%
69 Gy, 3 fractions	(33)	228	190	>99%

BED, biologically equivalent dose; NTD, normalized total dose in 2-Gy fractions; SBRT, stereotactic body radiation therapy; NSCLC, non–small cell lung cancer; Tk, ; Td, ; LQ, linear–quadratic.

Fowler JF, Tome WA, Welsh JS. Estimation of the Required Doses in Stereotactic Body Radiation Therapy. In *Stereotactic Body Radiation Therapy*, Kavanagh BD and Timmerman RD, eds. Lippincott Williams & Wilkins, 2005.

Leczenie operacyjne a SBRT ?

Outcomes After Stereotactic Lung Radiotherapy or Wedge Resection for Stage I Non–Small-Cell Lung Cancer

Inga S. Grills, Victor S. Mangona, Robert Welsh, Gary Chmielewski, Erika McInerney, Shannon Martin, Jennifer Wloch, Hong Ye, and Larry L. Kestin

See accompanying editorials on pages 905 and 907

A B S T R A C T

Purpose
To compare outcomes between lung stereotactic radiotherapy (SBRT) and wedge resection for stage I non–small-cell lung cancer (NSCLC).

Patients and Methods
One hundred twenty-four patients with T1-2N0 NSCLC underwent wedge resection (n = 69) or image-guided lung SBRT (n = 58) from February 2003 through August 2008. All were ineligible for anatomic lobectomy; of those receiving SBRT, 95% were medically inoperable, with 5% refusing surgery. Mean forced expiratory volume in 1 second and diffusing capacity of lung for carbon monoxide were 1.39 L and 12.0 mL/min/mmHg for wedge versus 1.31 L and 10.14 mL/min/mmHg for SBRT (P = not significant). Mean Charlson comorbidity index and median age were 3 and 74 years for wedge versus 4 and 78 years for SBRT ($P < .01$, $P = .04$). SBRT was volumetrically prescribed as 48 (T1) or 60 (T2) Gy in four to five fractions.

Results
Median potential follow-up is 2.5 years. At 30 months, no significant differences were identified in regional recurrence (RR), locoregional recurrence (LRR), distant metastasis (DM), or freedom from any failure (FFF) between the two groups ($P > .16$). SBRT reduced the risk of local recurrence (LR), 4% versus 20% for wedge ($P = .07$). Overall survival (OS) was higher with wedge but cause-specific survival (CSS) was identical. Results excluding synchronous primaries, nonbiopsied tumors, or pathologic T4 disease (wedge satellite lesion) showed reduced LR (5% *v* 24%, $P = .05$), RR (0% *v* 18%, $P = .07$), and LRR (5% *v* 29%, $P = .03$) with SBRT. There were no differences in DM, FFF, or CSS, but OS was higher with wedge.

Conclusion
Both lung SBRT and wedge resection are reasonable treatment options for stage I NSCLC patients ineligible for anatomic lobectomy. SBRT reduced LR, RR, and LRR. In this nonrandomized population of patients selected for surgery versus SBRT (medically inoperable) at physician discretion, OS was higher in surgical patients. SBRT and surgery, however, had identical CSS.

J Clin Oncol 28:928-935. © 2010 by American Society of Clinical Oncology

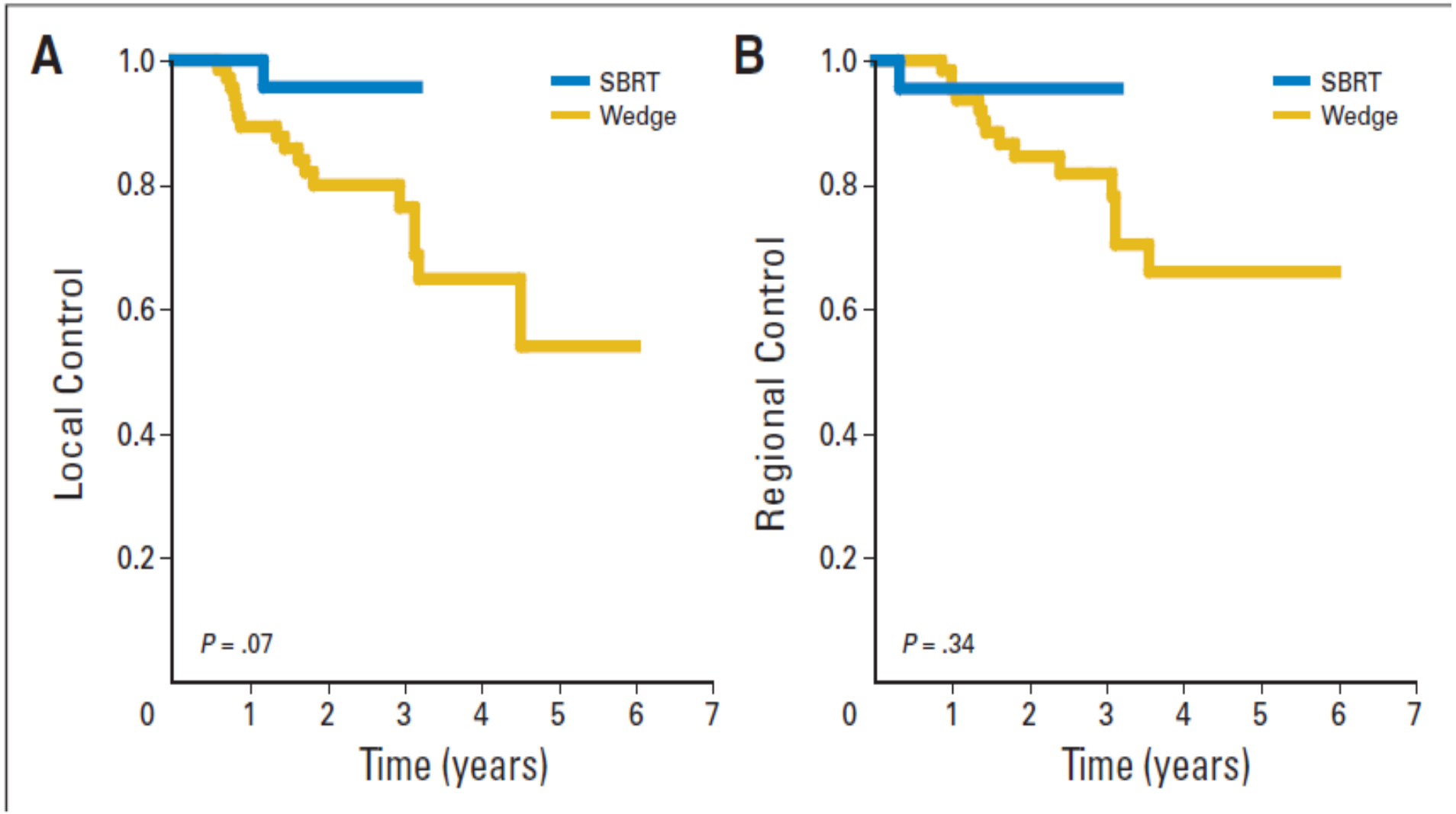
Network

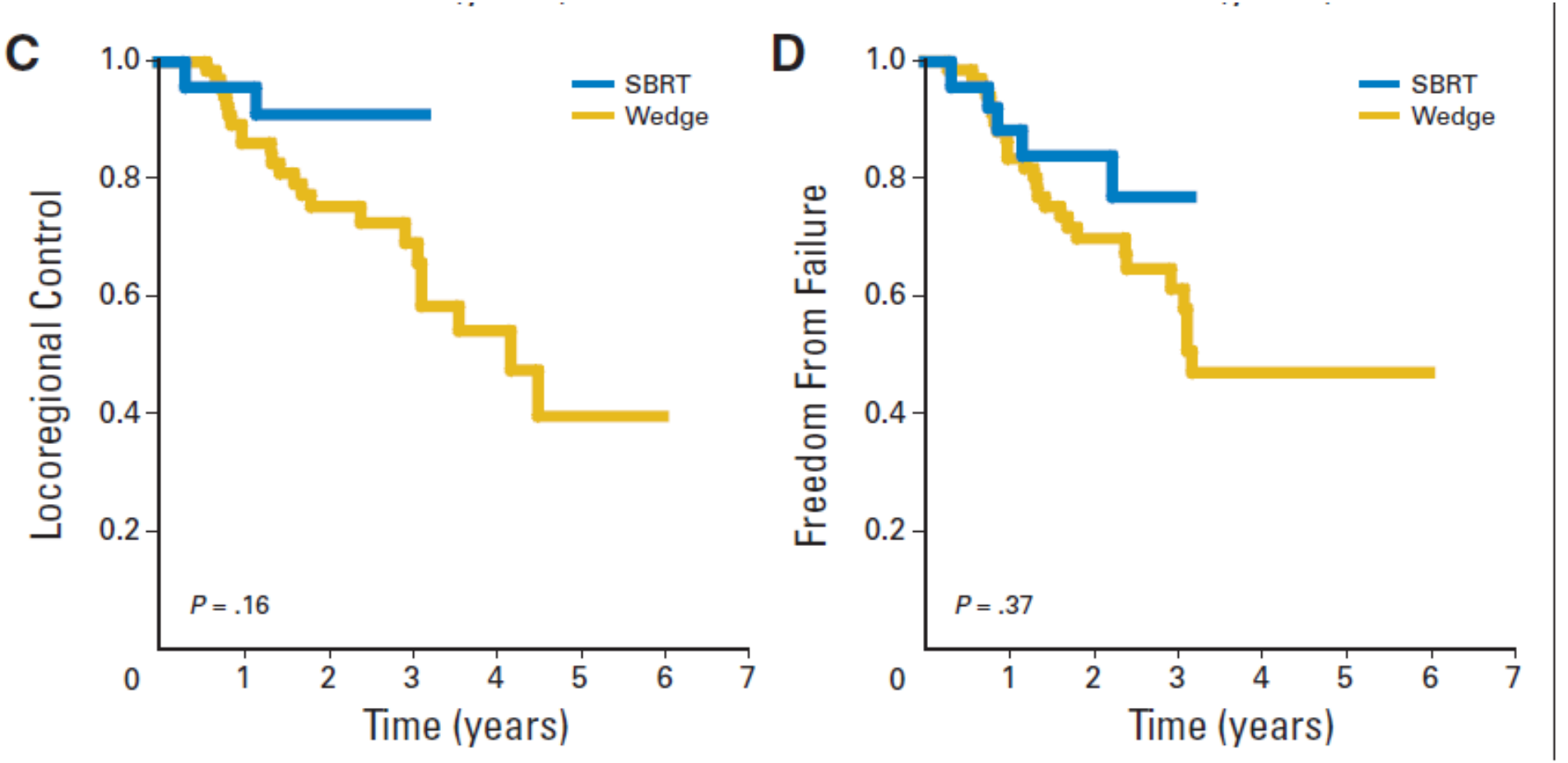
Table 2. Wedge Resection Versus Lung SBRT: 30-Month Outcomes Comparison

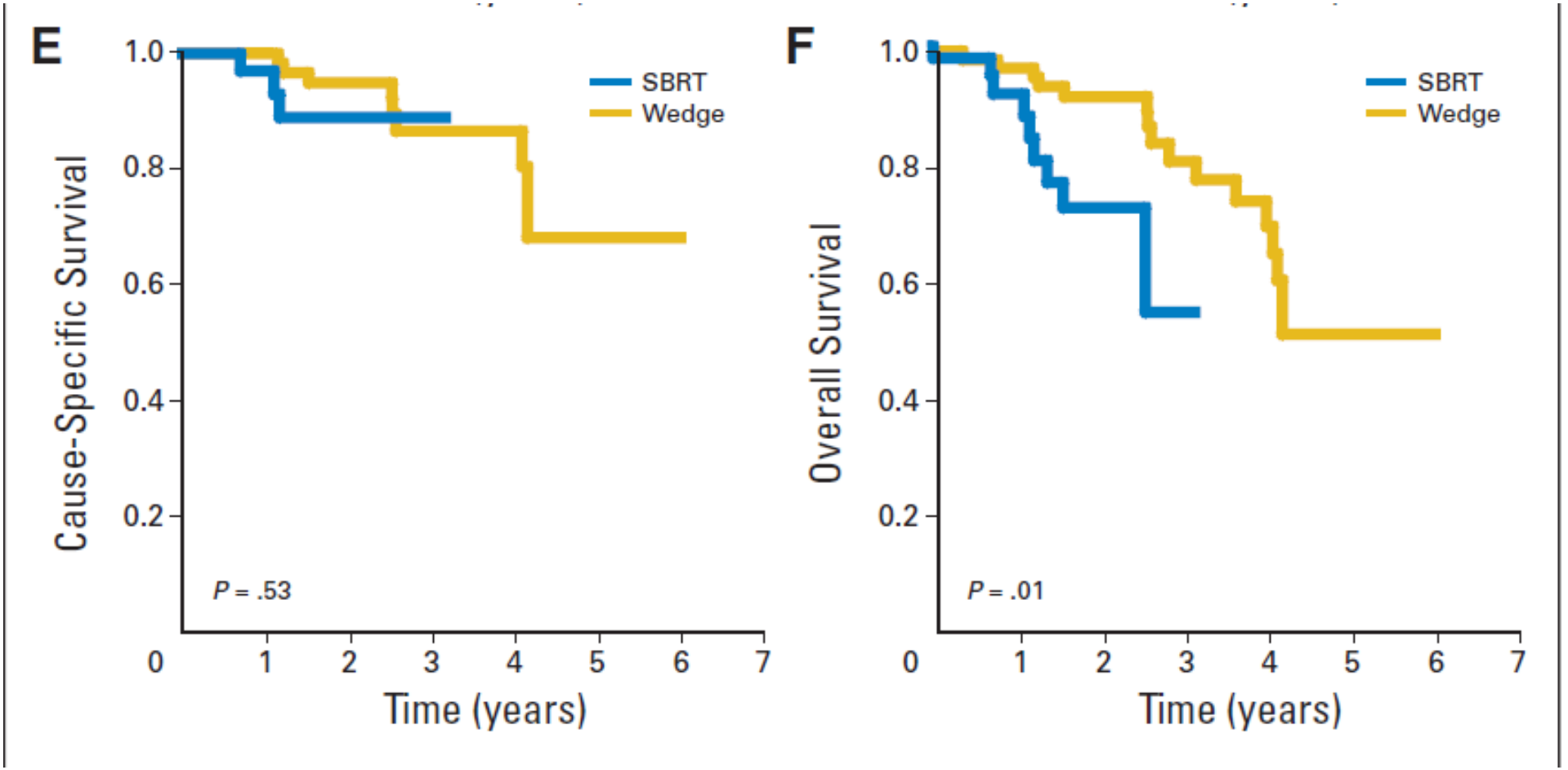
Patient Group	% of Patients						
	LR	RR	LRR	DM	FFF	OS	CSS
All patients, n = 124							
SBRT, n = 55	4	4	9	19	77		93
Wedge resection, n = 69	20	18	27	21	65		94
P	.07*	.34	.16	.96	.37	.01	.53
Exclude pT4, synchronous primary, no biopsy, n = 110							
SBRT, n = 52	5	0	5	15	80	70	92
Wedge resection, n = 58	24	18	29	22	61	85	93
P	.05	.07*	.03	.51	.12	.02	.62

Abbreviations: SBRT, stereotactic radiotherapy; LR, local recurrence; RR, regional recurrence; LRR, locoregional recurrence; DM, distant metastasis; FFF, freedom from any failure; OS, overall survival; CSS, cause-specific survival.

*Statistical trend only.


A
1.0
0.8
0.6
0.4
0.2
Local Control
SBRT
Wedge
P = .07
0
1
2
3
4
5
6
7
Time (years)
B
1.0
0.8
0.6
0.4
0.2
Regional Control
SBRT
Wedge
P = .34
0
1
2
3
4
5
6
7
Time (years)


C
1.0
0.8
0.6
0.4
0.2
0
Locoregional Control
SBRT
Wedge
P = .16
1
2
3
4
5
6
7
Time (years)
D
1.0
0.8
0.6
0.4
0.2
0
Freedom From Failure
SBRT
Wedge
P = .37
1
2
3
4
5
6
7
Time (years)


E
1.0
0.8
0.6
0.4
0.2
0
Cause-Specific Survival
SBRT
Wedge
P = .53
1
2
3
4
5
6
7
Time (years)
F
1.0
0.8
0.6
0.4
0.2
0
Overall Survival
SBRT
Wedge
P = .01
1
2
3
4
5
6
7
Time (years)

JCO Feb 2010 – two editorials

Stereotactic Body Radiation Therapy Versus Wedge Resection for Medically Inoperable Stage I Lung Cancer: Tailored Therapy or One Size Fits All?

Nasser K. Altorki, *Division of Thoracic Surgery, New York-Presbyterian Hospital/Weill Cornell Medical Center, New York, NY*

See accompanying editorial on page 907 and article on page 928

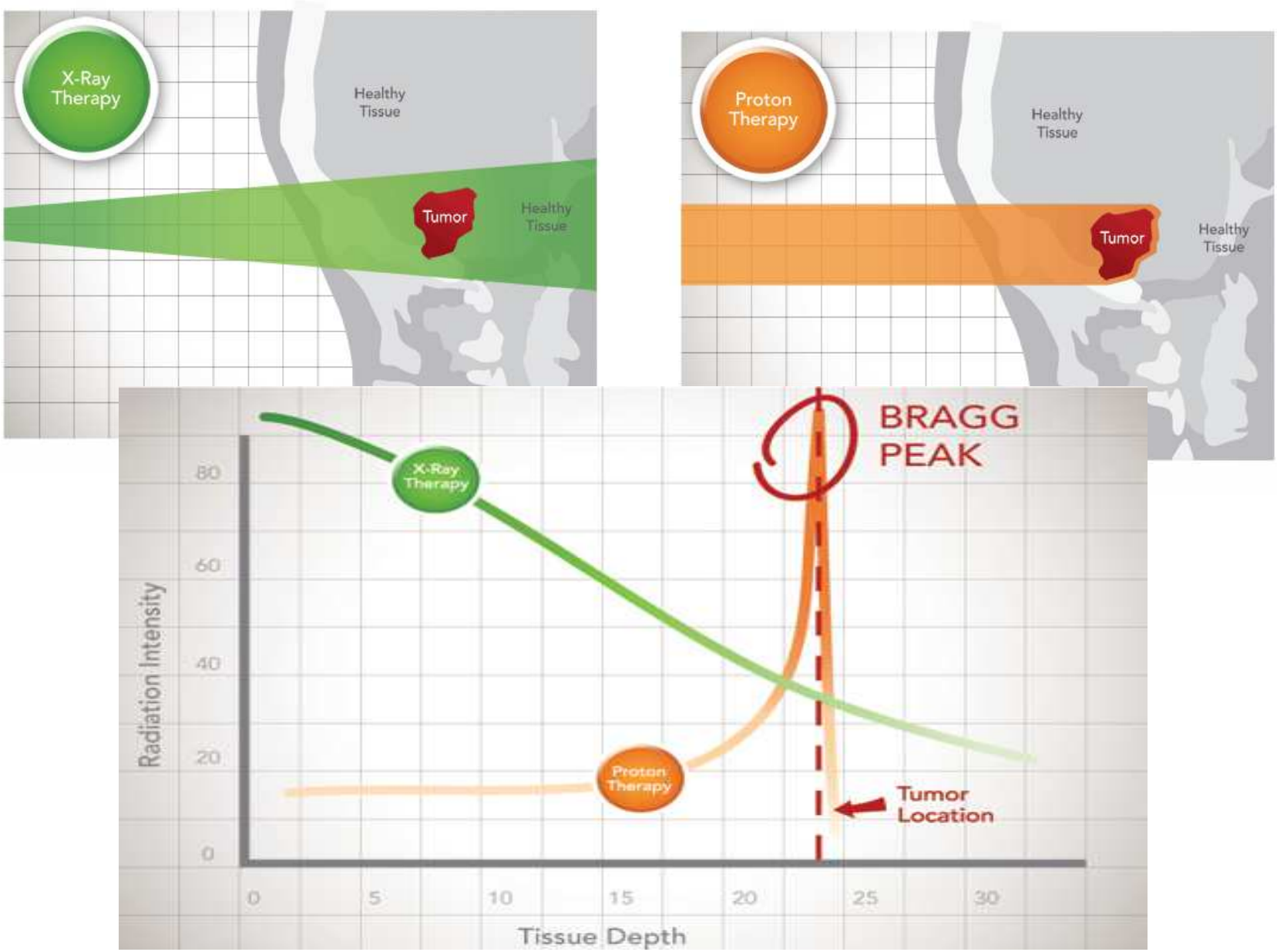
Surgery Versus Stereotactic Body Radiation Therapy for Early-Stage Lung Cancer: Who's Down for the Count?

Robert D. Timmerman, *Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX*

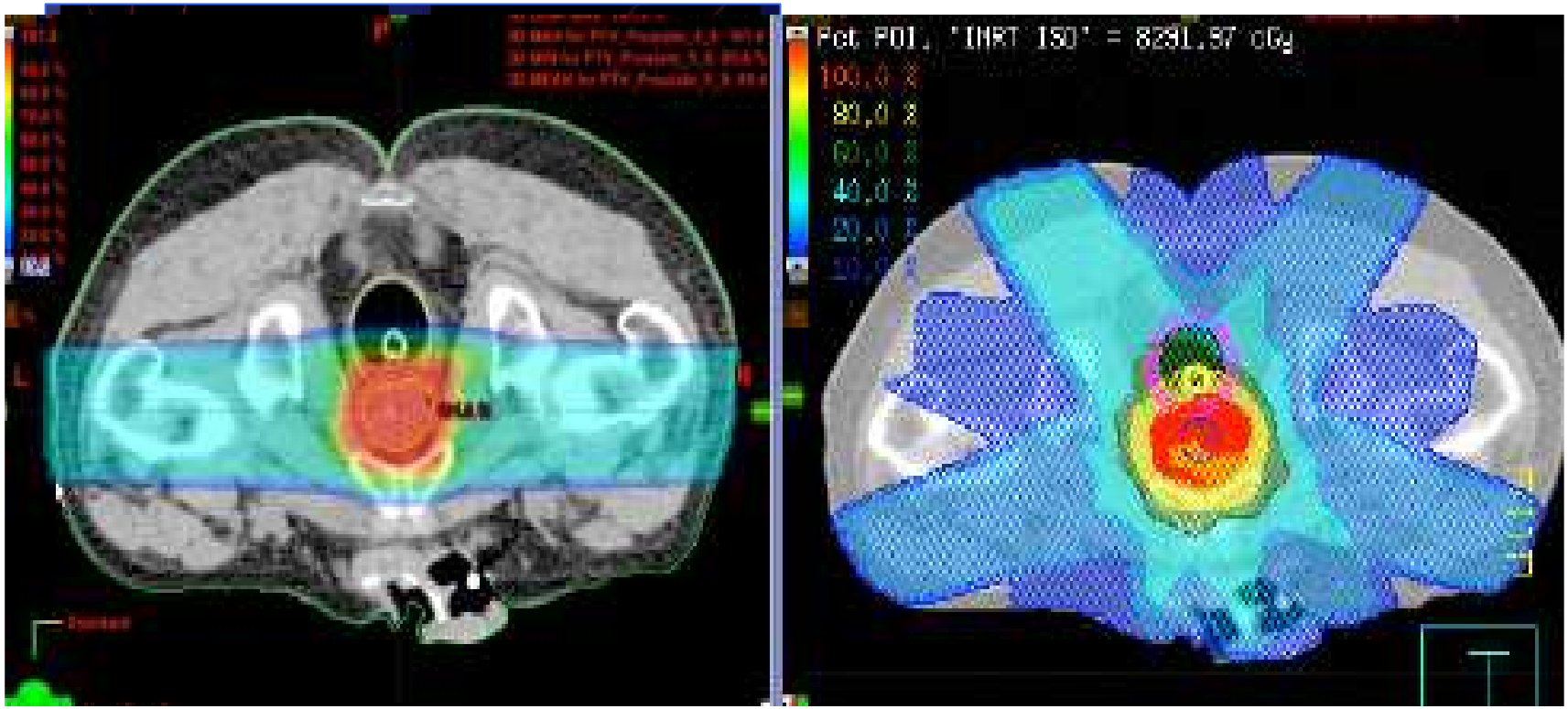
See accompanying editorial on page 905 and article on page 928

PROTONOTERAPIA

PROTONOTERAPIA

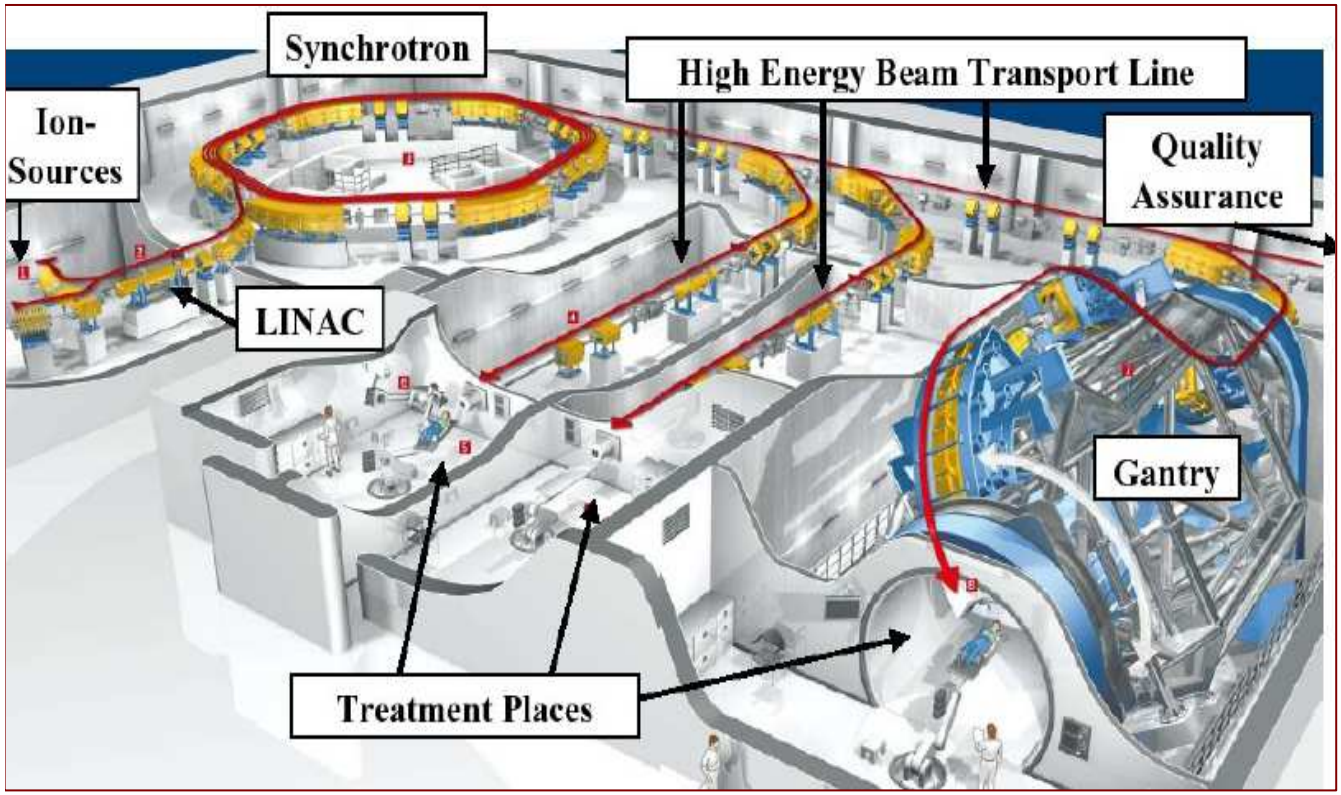


protony vs. fotony



Coraz bardziej popularna!!

Koszt centrum; 120 – 300 mln $



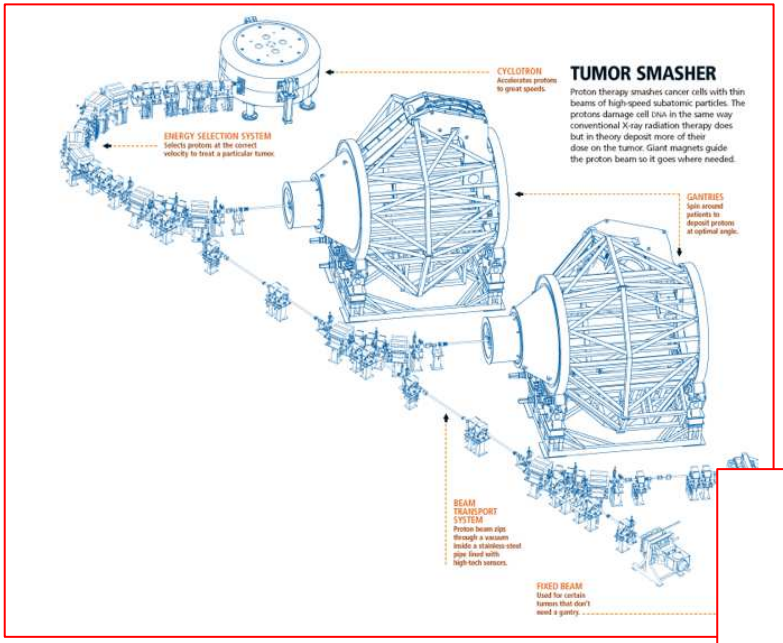
- 4 pokoje terapeutyczne = około 1800 betoniarek betonu
- Serwis; 24 godz ekipa serwisowa inżynierów

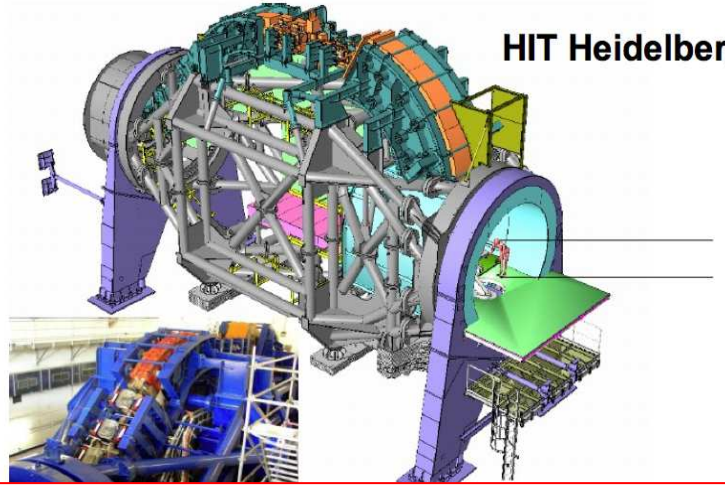
The status of Proton Treatment centers in the United States is:

- LLUMC: James M. Slater, M.D. Proton Treatment and Research Center at Loma Linda University and Medical Center, California (Over 20 years).
- MGH: Francis H. Burr Proton Center at Massachusetts General Hospital.
- MPRI: Midwest Proton Radiotherapy Institute at Indiana, University.
- UFPTI: The University of Florida Proton Therapy Institute.
- MD Anderson: Anderson Cancer Center's Proton Center Houston, TX.
- PPTCOK: ProCure Proton Therapy Center Oklahoma City, OK.
- UPENN: The Roberts Proton Therapy Center at University of Pennsylvania Health System.
- HUPTI: Hampton University Proton Therapy Institute. VA.

Others in process:

- NIPTRC: Northern University Proton Therapy and Research Center West Chicago (On Hold)
- CDH: CDH Proton Therapy Center, Warrenville, Illinois (Due to open 19 October at 11AM).
- PPTCNJ: ProCure Proton Therapy Center, New Jersey (Groundbreaking Ceremony took place on 7 April 2010). 40 miles from downtown Manhattan.
- PTCTN: ProCure Proton Therapy Center University of Tennessee Medical Center. (Scheduled to open in 2012/13,)
- SFPC: South Florida Proton Center scheduled to open in 2012.

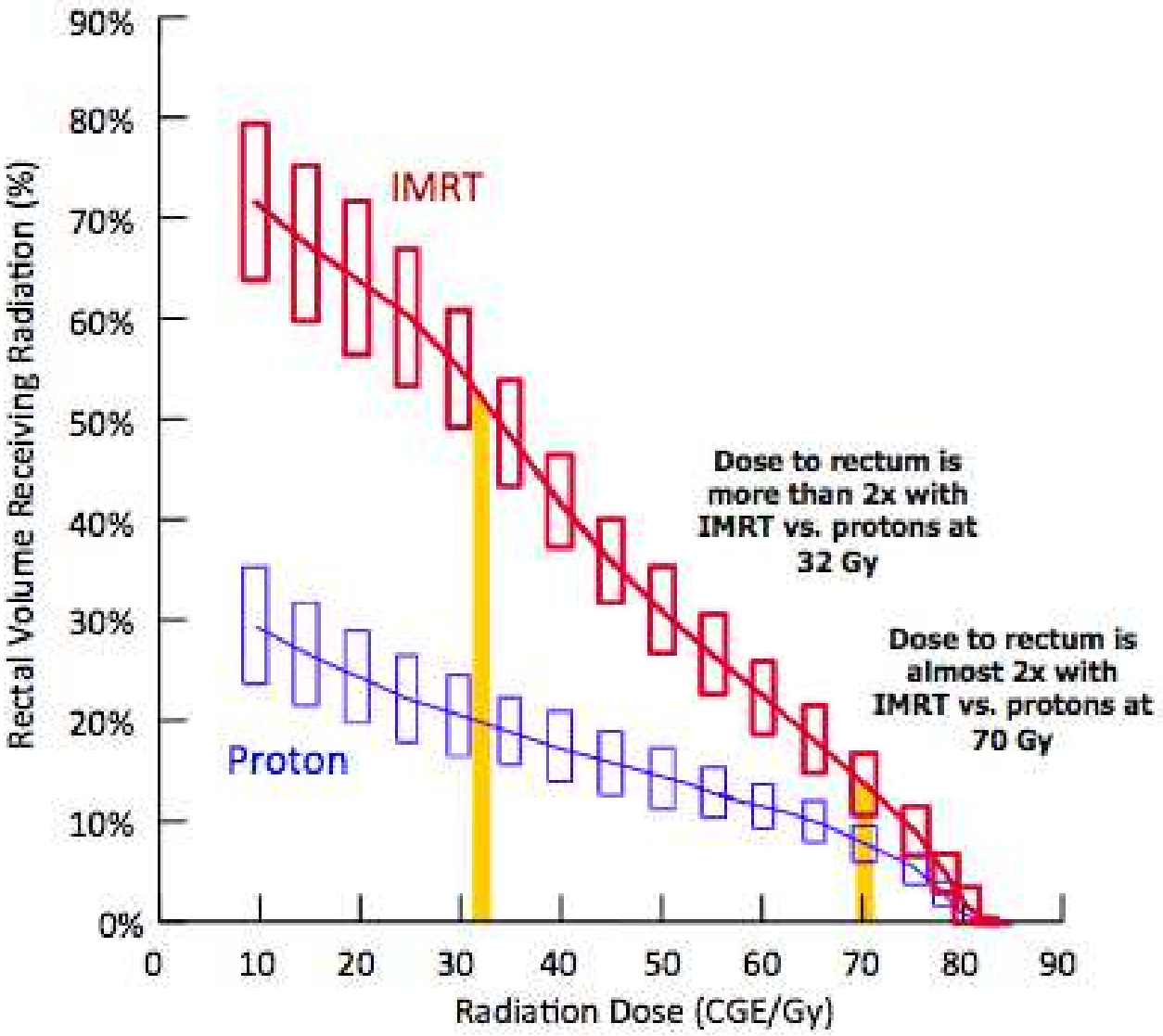




1 ośrodek terapii protonowej / 10^7 mieszkańców

1 ośrodek terapii węglowej / 4 10^7 mieszkańców

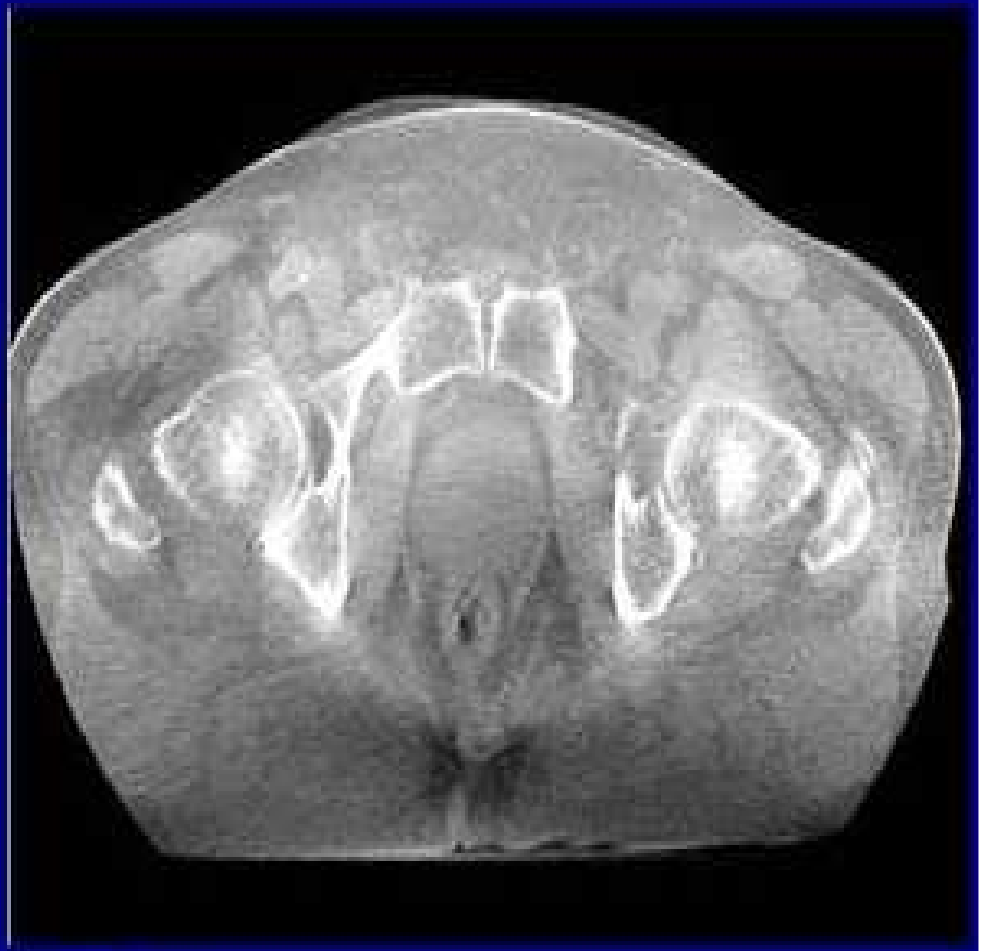
Raport TERA, 2006


90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
Rectal Volume Receiving Radiation (%)
IMRT
Proton
Dose to rectum is more than 2x with IMRT vs. protons at 32 Gy
Dose to rectum is almost 2x with IMRT vs. protons at 70 Gy
0
10
20
30
40
50
60
70
80
90
Radiation Dose (CGE/Gy)

IMRT + IGRT

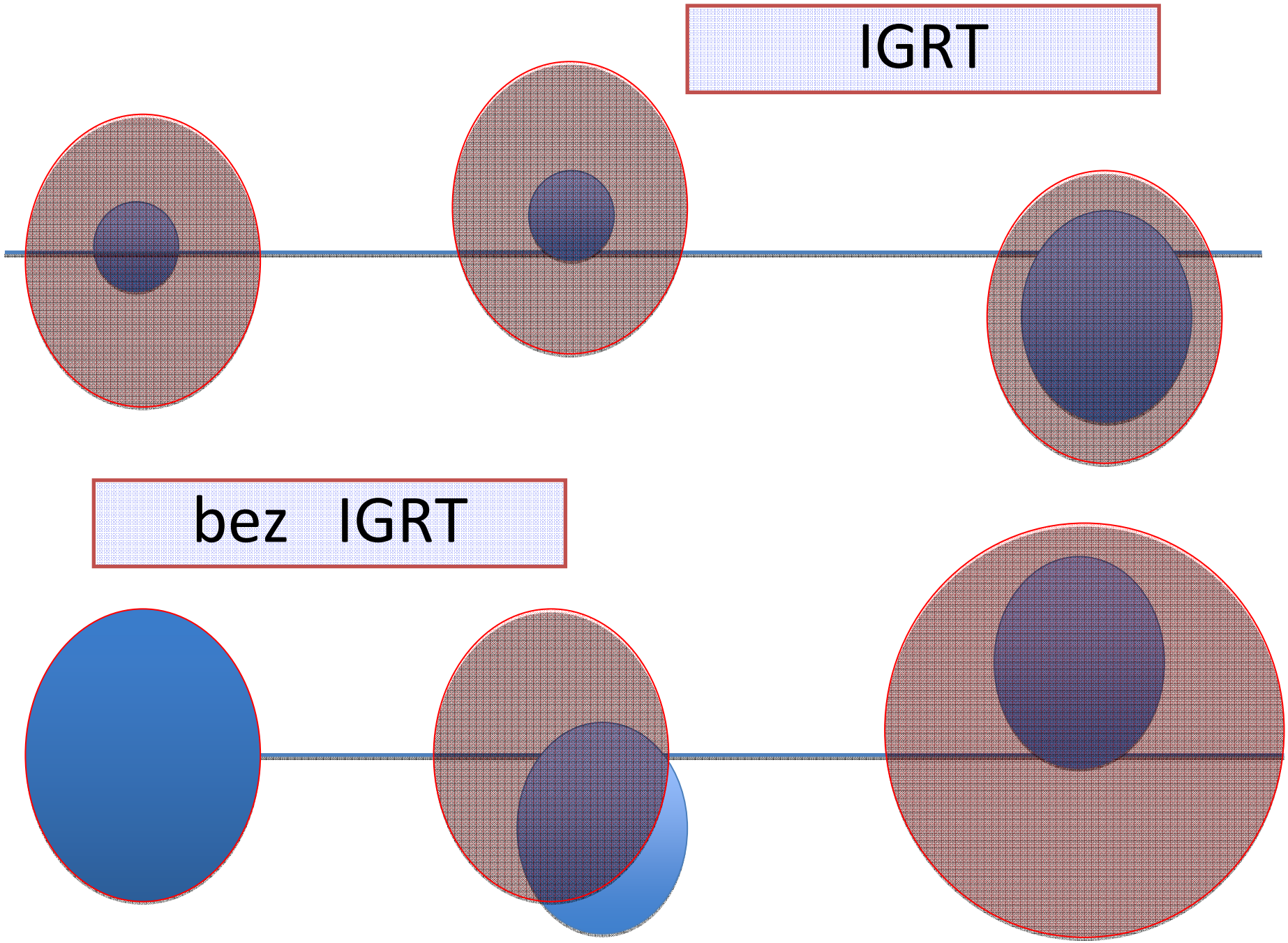
IGRT

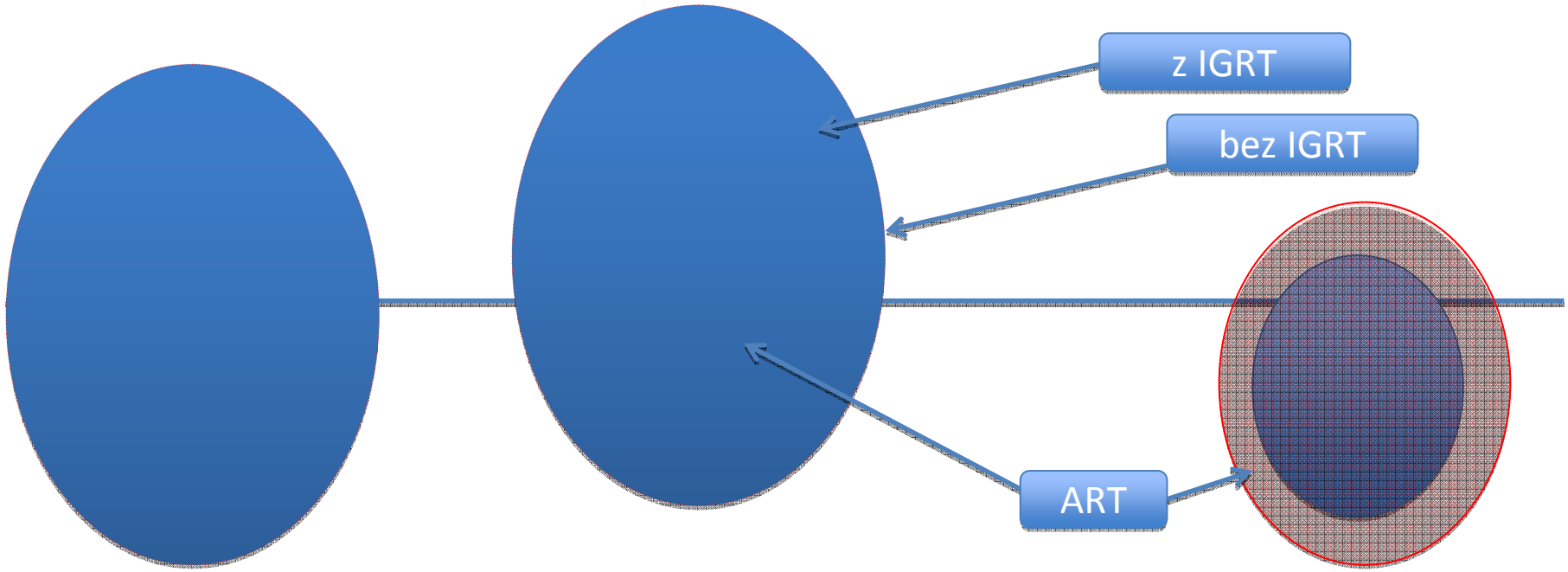
IGRT



IGRT
markery

FDA 2002 r

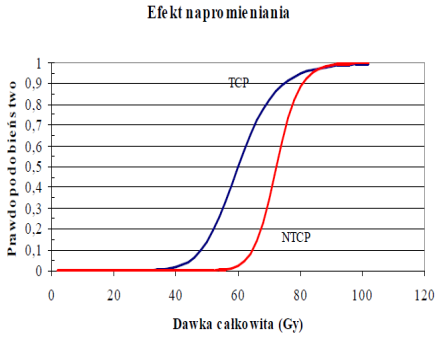

IGRT
bez IGRT



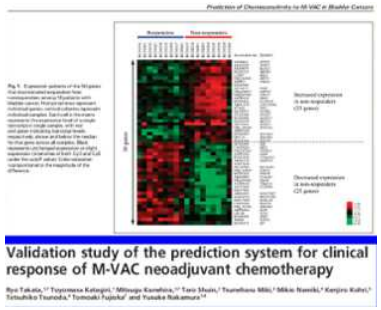
Radioterapia Adaptacyjna

Co w przyszłości ?

- Eskalacja dawki



- Nowe markery



wysoka dawka RT + HT ?

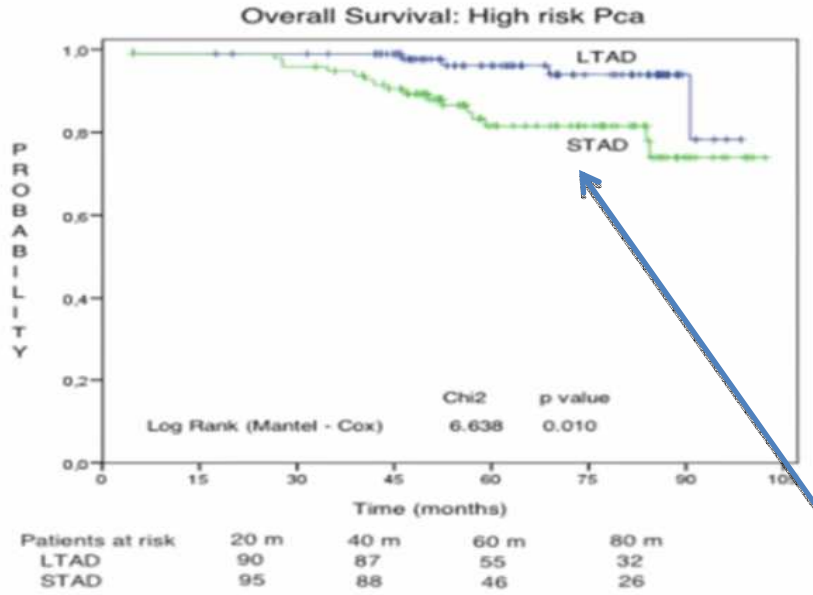
Tak !!

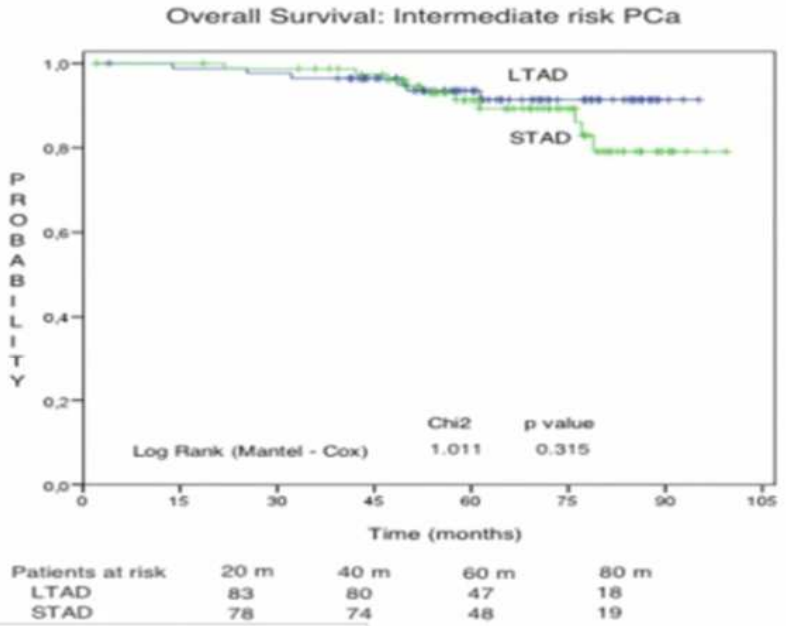
THE LANCET Oncology

High-dose radiotherapy with short-term or long-term androgen deprivation in localised prostate cancer (DART01/05 GICOR): a randomised, controlled, phase 3 trial

Dr Almudena Zapatero, PhD, Araceli Guerrero, MD, Xavier Maldonado, MD, Ana Alvarez, MD, Carmen Gonzalez

Results: Overall Survival

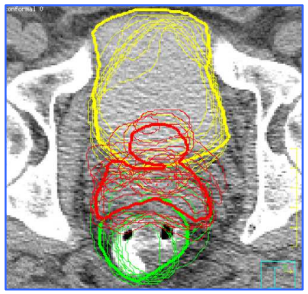




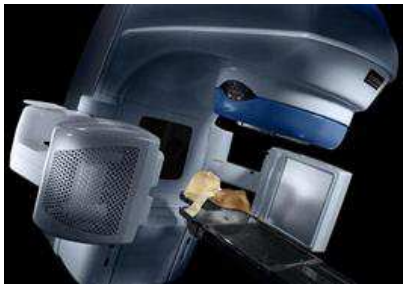
		95%CI
HIGH - RISK		
LTAD		(93.9 – 98.3)
STAD		(77.1 – 85.9)
INTERMEDIATE - RISK		
LTAD	93.5%	(90.7 – 96.3)
STAD	91.3%	(87.9 – 94.7)

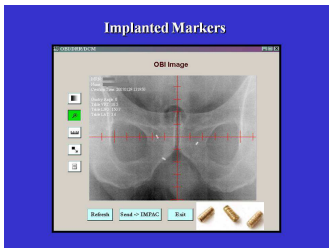
Eskalacja dawki

Ruchomy target !!!



IGRT (Image Guided RT)



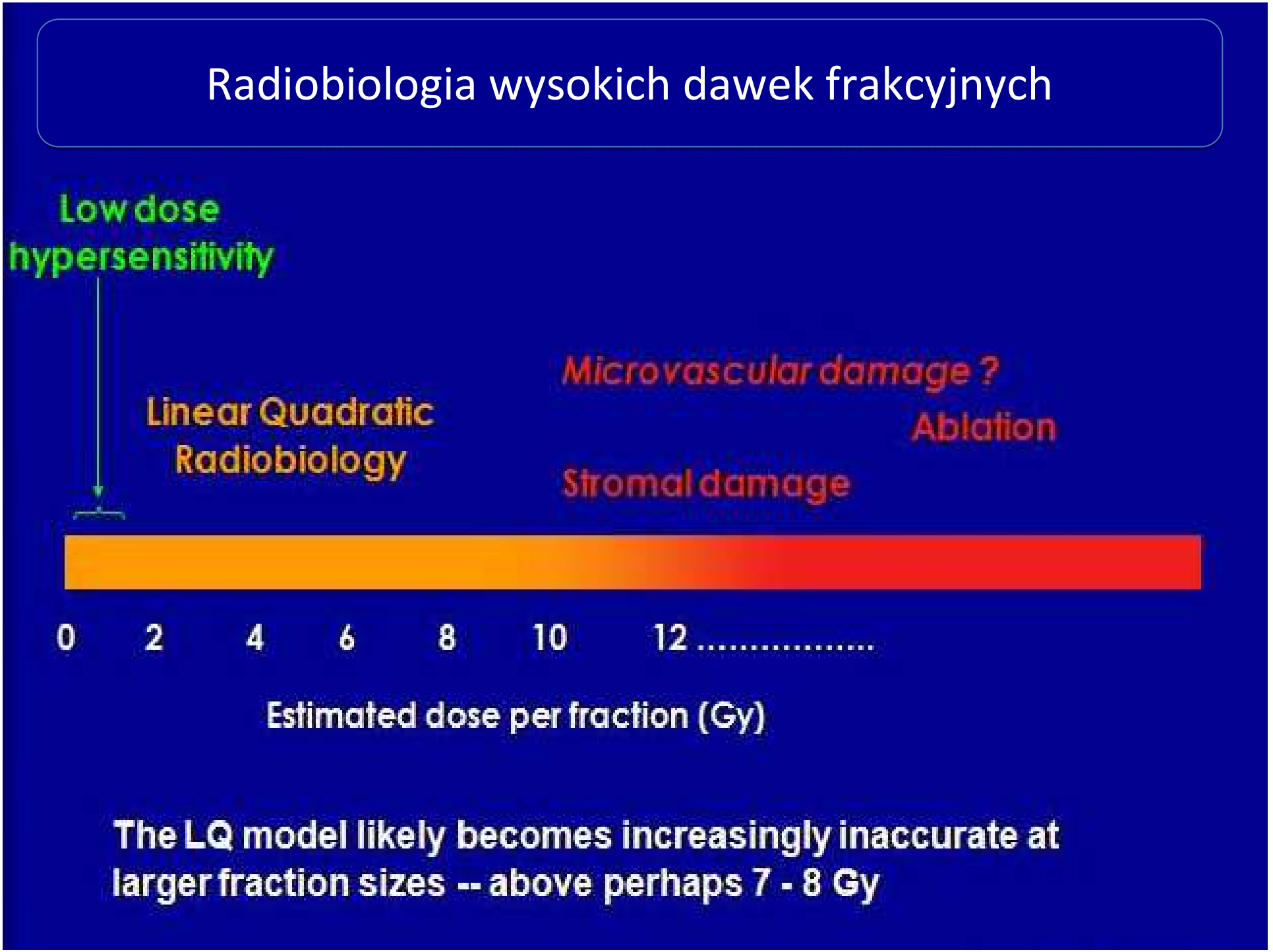


Hypo-frakcjonowanie

komórki raka stercza bardzo wrażliwe na wysokie dawki frakcyjne

- zysk terapeutyczny,
- obniżenie kosztów terapii,
- bardziej wygodne dla pacjenta

Radiobiologia wysokich dawek frakcyjnych



The LQ model likely becomes increasingly inaccurate at larger fraction sizes -- above perhaps 7 - 8 Gy

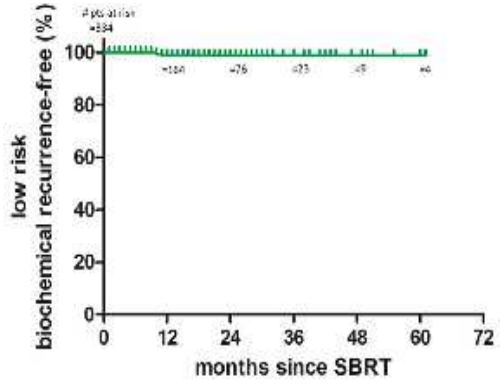
SBRT

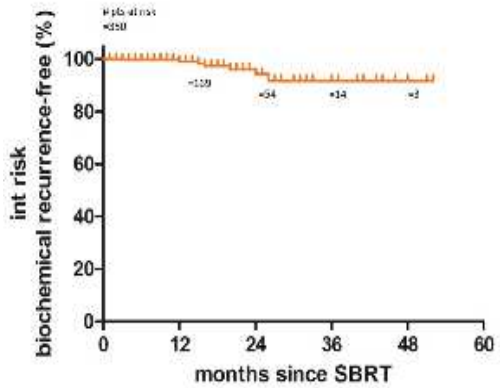
Stereotactic Body RT

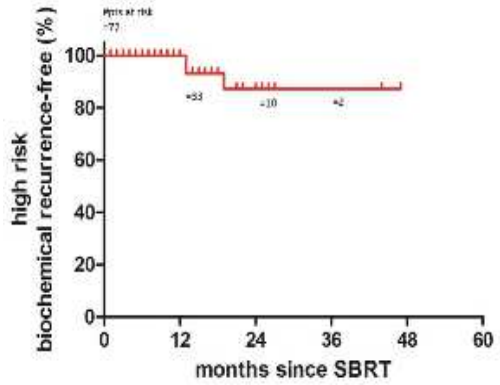
Multi-institutional registry for prostate cancer radiosurgery: a prospective observational clinical trial

Debra Freeman[1]*, Gregg Dickerson[2] and Mark Perman[3]

[1] *Naples Radiation Oncology, Naples, FL, USA*
[2] *Anova Cancer Center, Denver, CO, USA*
[3] *South Florida Radiation Oncology, Stuart, FL, USA*







SBRT: Efektywność onkologiczna

Multi-institutional pooled data; 8 institutions

1100 patients, ~ 3 yr median FU (6-72 mos)

335 cases with a >4 years follow-up (median 53 mos)

35-40 Gy in 4-5 fractions, ADT in14%

Risk groups:

Low:	639	59%
Intermediate:	326	30%
High:	124	11%

Subset with longer follow-up:

335 cases with >4 years follow-up (median: 53 months)

King et al, Radiother Oncol. 109:217-21, 2013

Chorzy leczeni CK

ONCOLOGY

RESEARCH Open Access

Hypofractionated SBRT versus conventionally fractionated EBRT for prostate cancer: comparison of PSA slope and nadir

CK: N=43
EBRT: N=75

Nadir PSA

Time to nadir

Rate of PSA drop

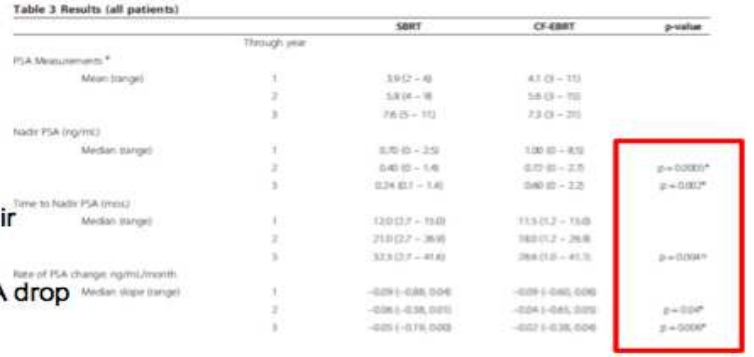
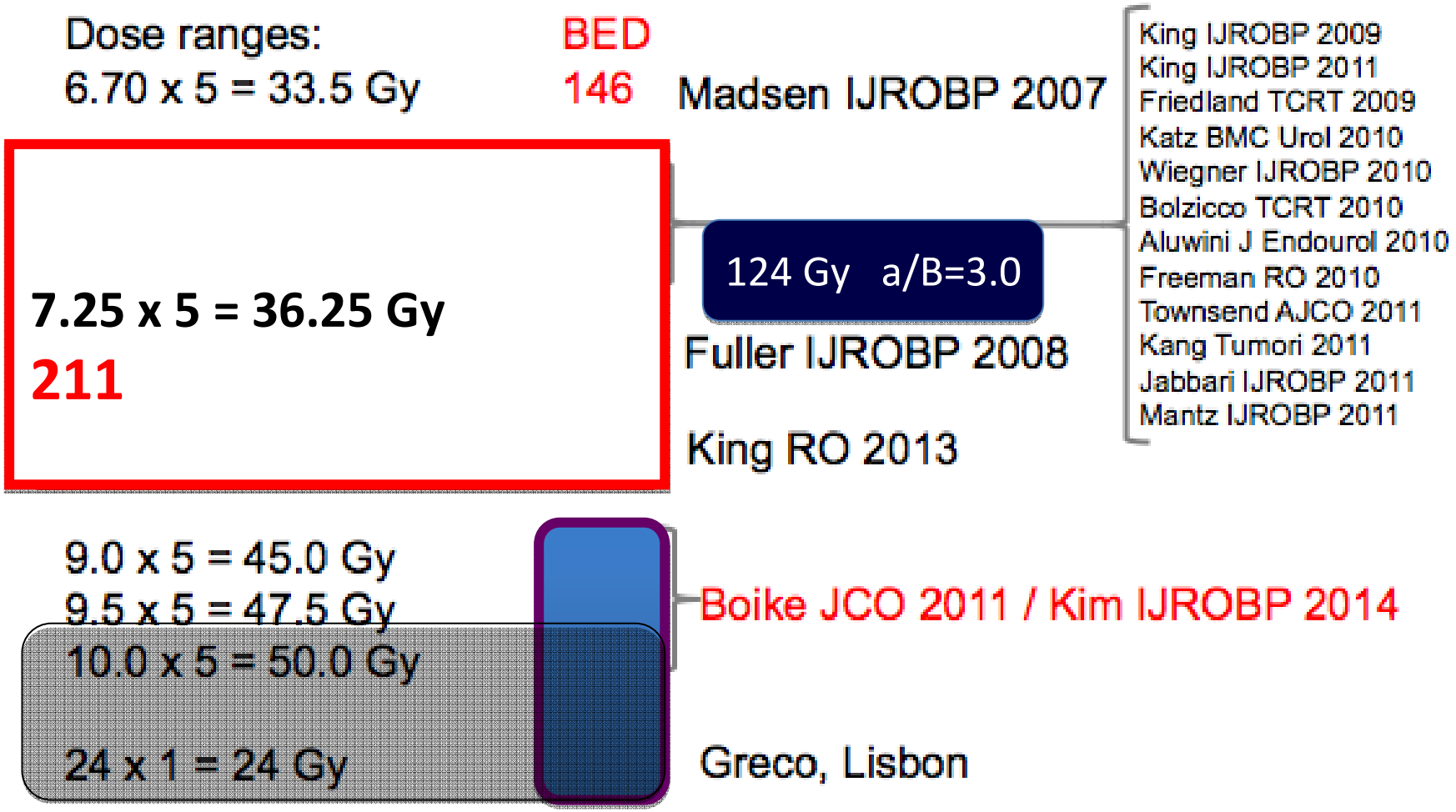


Table 3 Results (all patients)

		SBRT	CF-EBRT	p-value
	Through year			
PSA Measurements *				
Mean (range)	1	3.9 (2 – 6)	4.1 (3 – 11)	
	2	5.8 (4 – 9)	5.6 (3 – 11)	
	3	7.6 (5 – 11)	7.3 (3 – 21)	
Nadir PSA (ng/mL)				
Median (range)	1	0.70 (0 – 3.5)	1.00 (0 – 8.5)	
	2	0.40 (0 – 1.4)	0.72 (0 – 2.5)	p = 0.0003*
	3	0.24 (0.1 – 1.4)	0.60 (0 – 2.2)	p = 0.002*
Time to Nadir PSA (mos)				
Median (range)	1	12.0 (2.7 – 15.0)	11.5 (1.2 – 15.0)	
	2	21.0 (2.7 – 26.9)	16.0 (1.2 – 26.9)	
	3	32.3 (2.7 – 41.6)	28.6 (1.0 – 41.7)	p = 0.004*
Rate of PSA change: ng/mL/month				
Median slope (range)	1	-0.09 (-0.66, 0.04)	-0.09 (-0.60, 0.06)	
	2	-0.06 (-0.38, 0.01)	-0.04 (-0.65, 0.03)	p = 0.04*
	3	-0.05 (-0.19, 0.00)	-0.02 (-0.38, 0.04)	p = 0.006*

SBRT dawki

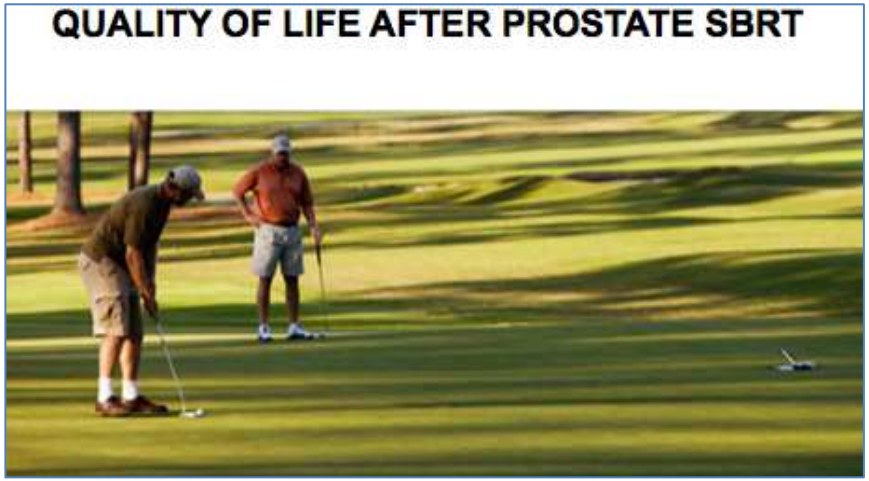

Dose ranges:
6.70 x 5 = 33.5 Gy
BED
146
Madsen IJROBP 2007
King IJROBP 2009
King IJROBP 2011
Friedland TCRT 2009
Katz BMC Urol 2010
Wiegner IJROBP 2010
Bolzicco TCRT 2010
Aluwini J Endourol 2010
Freeman RO 2010
Townsend AJCO 2011
Kang Tumori 2011
Jabbari IJROBP 2011
Mantz IJROBP 2011
7.25 x 5 = 36.25 Gy
211
124 Gy a/B=3.0
Fuller IJROBP 2008
King RO 2013
9.0 x 5 = 45.0 Gy
9.5 x 5 = 47.5 Gy
10.0 x 5 = 50.0 Gy
24 x 1 = 24 Gy
Boike JCO 2011 / Kim IJROBP 2014
Greco, Lisbon

SBRT RCT ?

NCI: dominują badania oceniające SBRT

- Widmark: 42.7 at 6.1 Gy vs 78 at 2Gy
  7 fractions 39 fractions

Podsumowanie
Sesja QOL w raku stercza
ASTRO 2014, San Francisco



SBRT

Wiele publikacji, dobre wyniki, bardzo dobre, różne techniki realizacji

1 publikacja wskazuje na nieakceptowalny poziom powikłań

- Madsen IJROBP 2007
- Fuller IJROBP 2008
- King IJROBP 2009
- King IJROBP 2011
- Friedland TCRT 2009
- Katz BMC Urol 2010
- Wiegner IJROBP 2010
- Bolzicco TCRT 2010
- Aluwini J Endourol 2010
- Freeman RO 2010
- Townsend AJCO 2011
- Kang Tumori 2011
- Jabbari IJROBP 2011
- Mantz IJROBP 2011
- Kim IJROBP 2014

SBRT

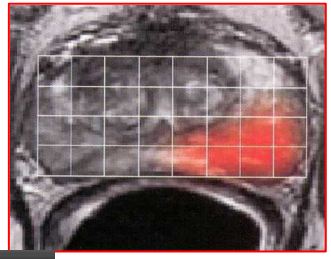
ważna jest jakość leczenia !!

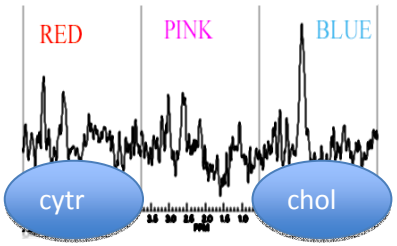
Strahlenther Onkol. 2015 Mar 8. [Epub ahead of print]

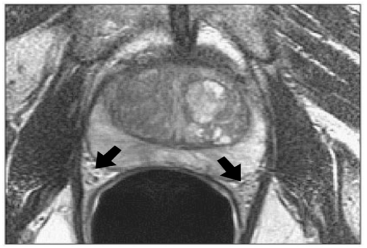
A feasibility dosimetric study on prostate cancer : Are we ready for a multicenter clinical trial on SBRT?

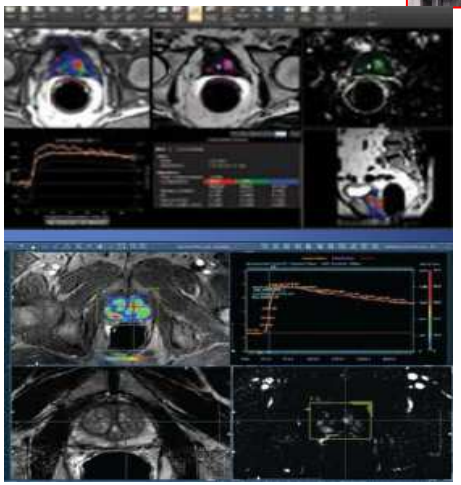
CONCLUSION: Important dosimetric differences with possible clinical implications, in particular related to OARs, were found. Replanning allowed a reduction in the OAR dose and decreased standard deviations. Multicenter clinical trials on SBRT should require a preplanning study to standardize the optimization procedure.

Obrazowanie (GPS) + SBRT



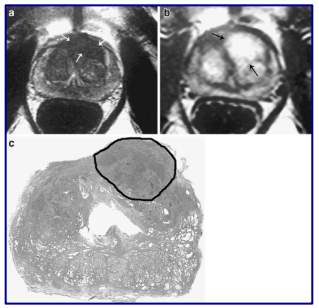


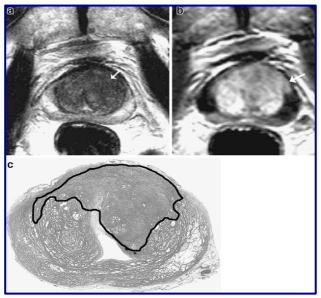




MRI-S
Dynamic Contrast Enhanced (DCE)MRI
Diffusion Weighted Imaging (DWI) MRI

Multiparametric MRI





Eskalacja dawki

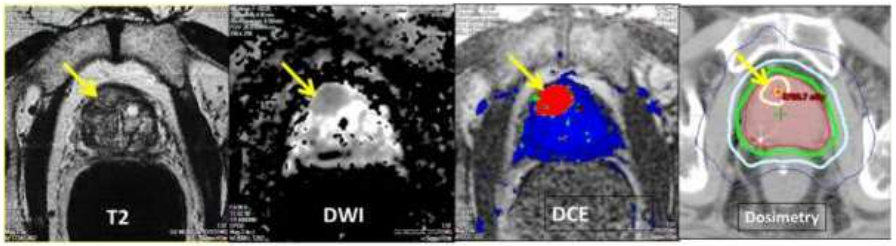
intra prostatic lesion

- IMRT
- BT
- SBRT - CyberKnife

OMICS J Radiol. Author manuscript; available in PMC 2015 Feb 23.
PMCID: PMC4337
Published in final edited form as:
NIHMSID: NIHMS657
OMICS J Radiol. 2014 Dec; 3(4): 170.
Published online 2014 Dec. doi: 10.4172/2167-7964.1000170

Early Outcome of Prostate Intensity Modulated Radiation Therapy (IMRT) Incorporating a Simultaneous Intra-Prostatic MRI Directed Boost

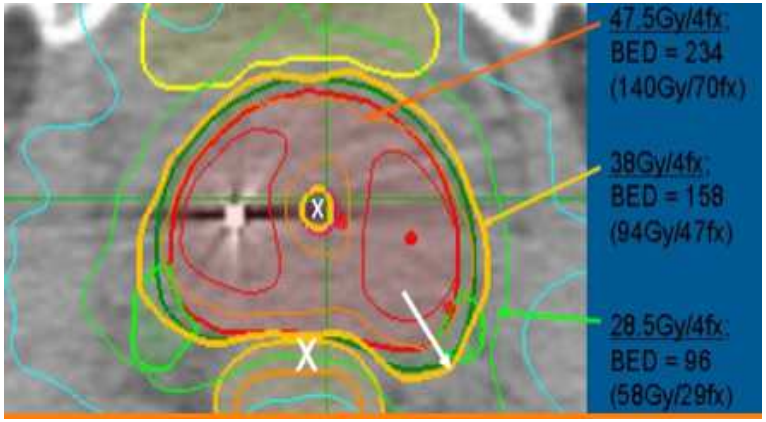
Michael H Schild, Steven E Schild,* William W Wong, Sujay A Vora, Alvin C Silva, Annelise M Silva, Thomas B Daniels, and Sameer R Keole

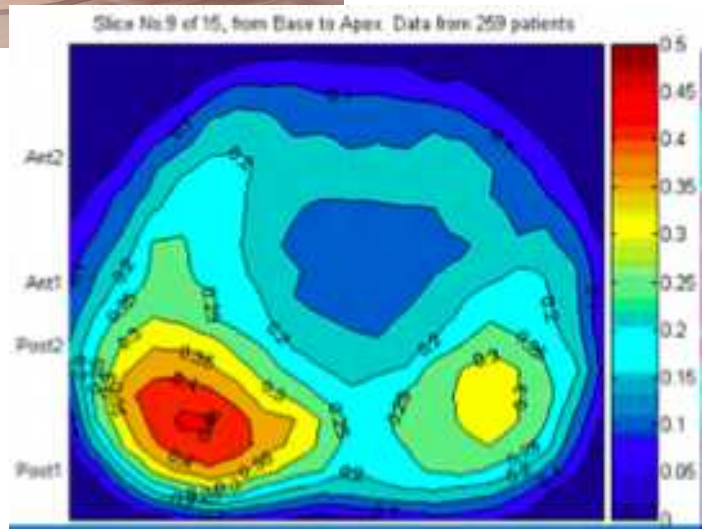


First 3 images are multi parametric axial MRI aquisitions (T2-weighted, diffusion-weighted (DWI), and dynamic contrast-enhanced (DCE) images). The malignancy is shown with an arrow. The forth image is the dosimetry from this example radiotherapy plan with various isodose lines shown including a boost of 83 Gy (yellow) around the tumor, 77Gy (lime green) around the prostate, 60 Gy (light blue) and 40 Gy (dark blue).

CyberKnife

Heterogenny rozkład dawki





SBRT

- 4 frakcje x 9,5 Gy (38 Gy)
- 4 frakcje x 11 Gy (44 Gy)

Cost Effectiveness Analysis of Stereotactic Body Radiation Therapy (SBRT) versus Intensity Modulated Radiation Therapy (IMRT) for Low or Intermediate Risk Prostate Cancer: A Markov Model Decision Analysis

J. C. Hodges[1], T. Boike[1], Y. Lotan[2], R. Benton[1], D. A. Pistenmaa[1], H. Choy[1], R. Timmerman[1], *[1]Department of Radiation Oncology, University of Texas Southwestern Medical Center, Dallas, TX, [2]Department of Urology, University of Texas Southwestern Medical Center, Dallas, TX*

Dokonano porównania cost-effectiveness SBRT do IMRT
dla chorych low-risk Pca

Wykorzystano „drzewo decyzyjne Markov" dla 70 letniego pacjenta
SBRT (non-robotic) 35 Gy / 5 frx vs. IMRT 79,2 Gy/ 44 frx
FU – 10 lat

QALYs SBRT vs IMRT: 19,155 $ vs. 32,468 $

Conclusions: Compared to IMRT, SBRT for low or intermediate prostate cancer has great potential cost savings for our healthcare system and may improve access to radiation, increase patient convenience, and boost quality of life for patients. Our model also suggests that the incremental cost effectiveness ratio of SBRT over IMRT is highly sensitive to quality of life outcomes which should be adequately and comparably measured in current and future prostate SBRT studies.

Radioterapia paliatywna
oligometastases

- Przerzuty do kości
- SBRT > 16 Gy, efekt p-bólowy CR > 80%
- RTOG 0631 16 Gy v. 8 Gy

Radioterapia raka stercza

- Eskalacja dawki
- IMRT, VMAT, CyberKnife
- IGRT
- Hipofrakcjonowanie, SBRT, BT
- Eskalacja dawki w ogniskach o najwyższej agresywności (hipoksja)
- Kojarzenie z leczeniem systemowym

Radioterapia po 2015 roku

- Diagnostyka przed leczeniem – MRI/PET (PET/MRI) = definicja ogniska o większej agresywności
- Diagnostyka przed leczeniem – MRI/PET = definicja ognisk przerzutowych: czy będziemy leczyć chorych miejscowo/systemowo w zaawansowanej chorobie (oligometastases) ?
- Eskalacja dawki +/- terapia systemowa ?
- Nowe czynniki prognostyczne i predykcyjne = Personalizacja leczenia

Przyszłość

Dawka homogenna

Dawka heterogenna

Intra-prostatic lesion; 5 x 10 Gy (SBRT)
Kim DW, IJROBP 2014

Personalizacja leczenia

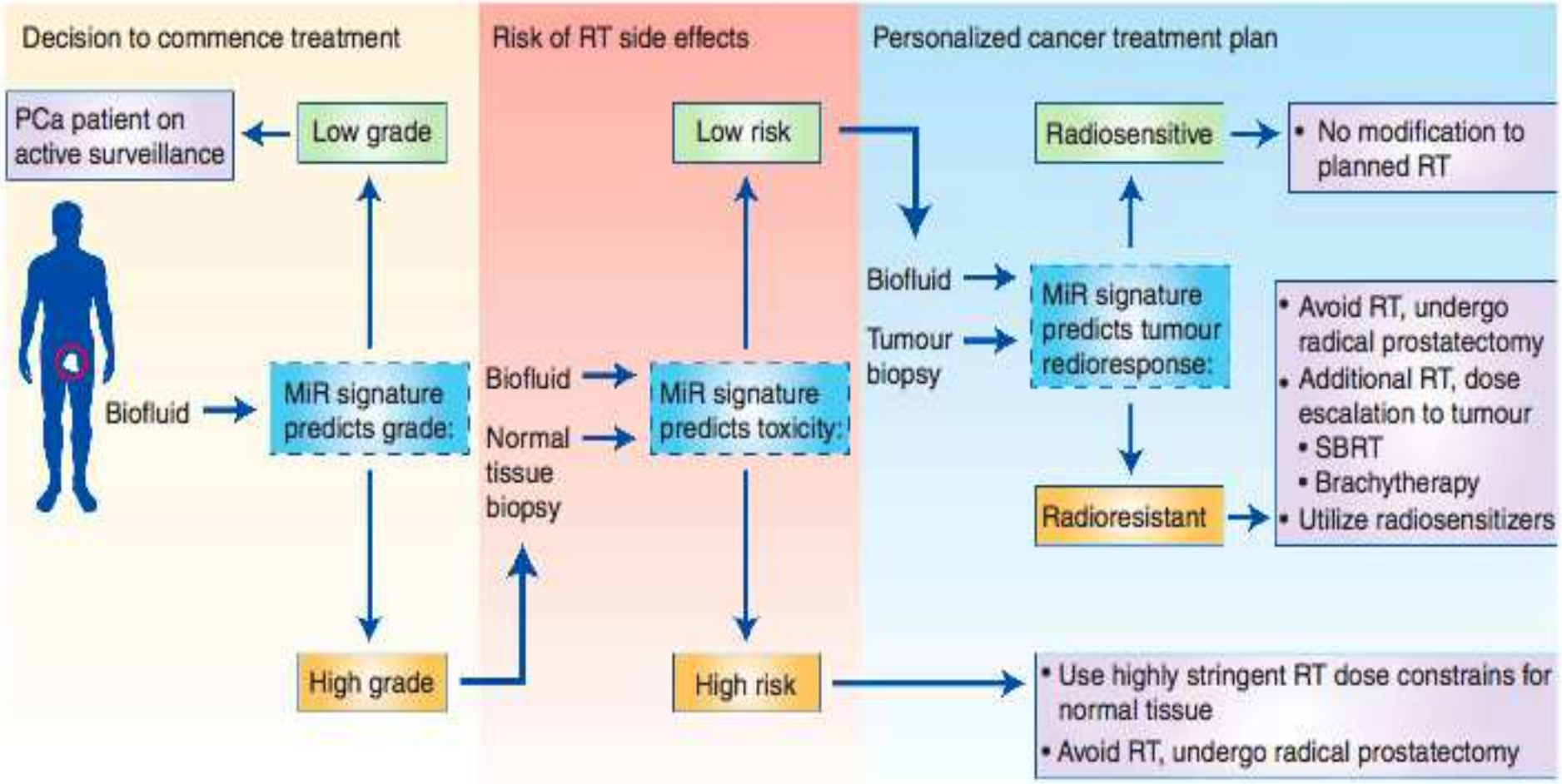
BJC

British Journal of Cancer (2015) 112, 777–782 | doi: 10.1038/bjc.2015.6

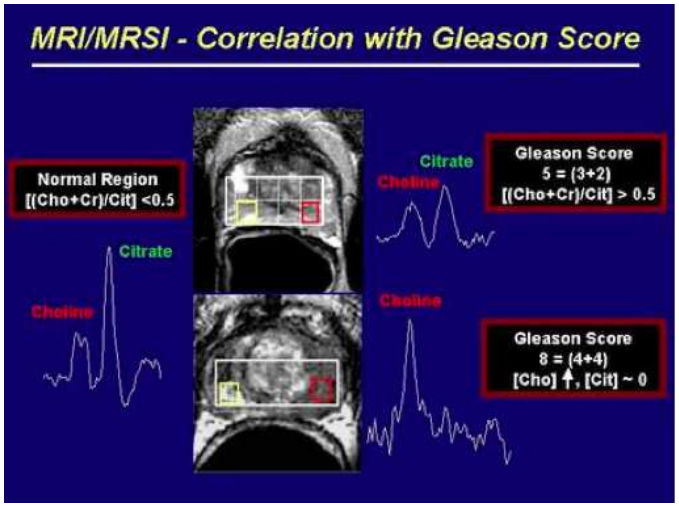
Keywords: microRNA; miR; radiation; radiotherapy; cancer; radioresistance; biomarkers; therapeutics

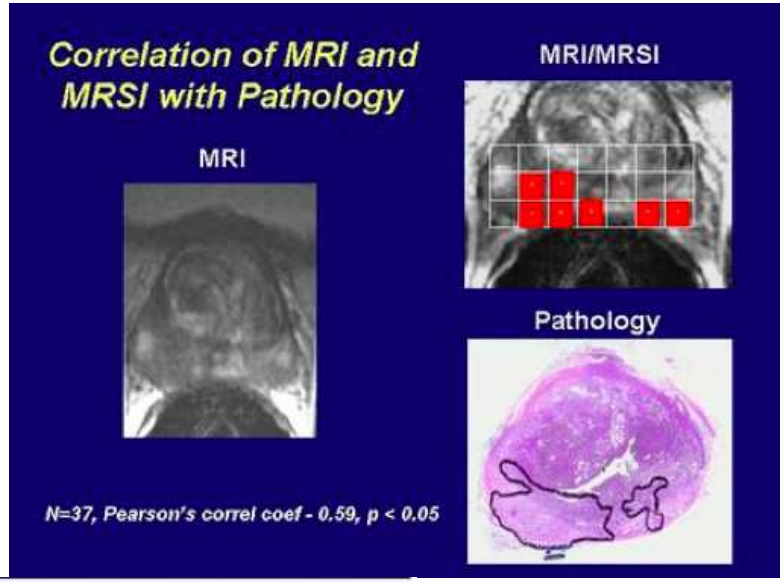
MicroRNA in radiotherapy: miRage or miRador?

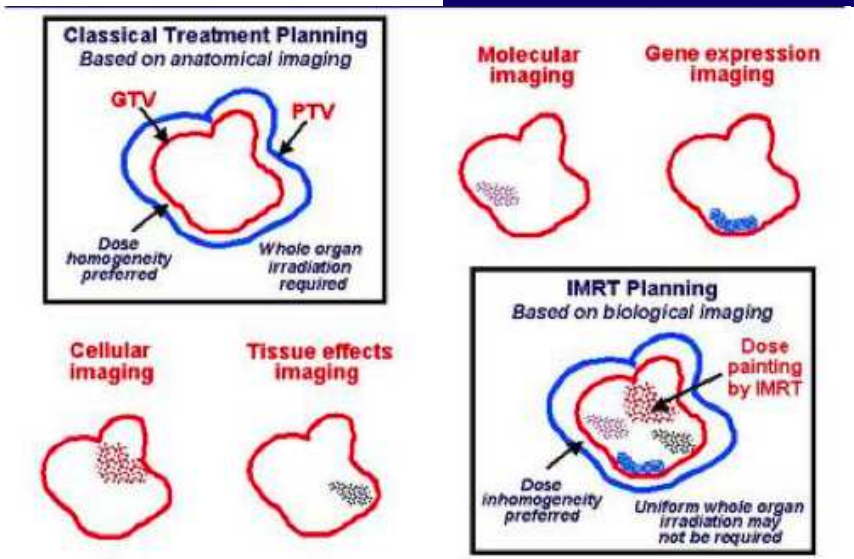
E Korpela[1,2], D Vesprini[1,3,4] and SK Liu*[,1,2,3,4]



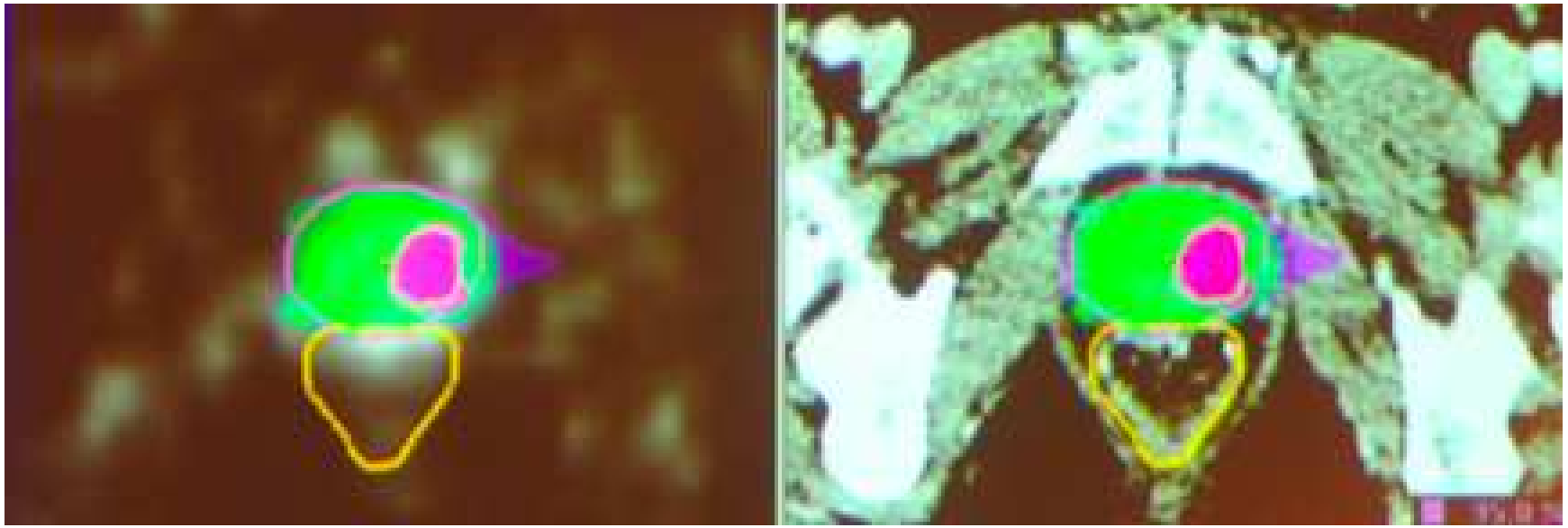
Tomorrow
Metabolic guided radiotherapy



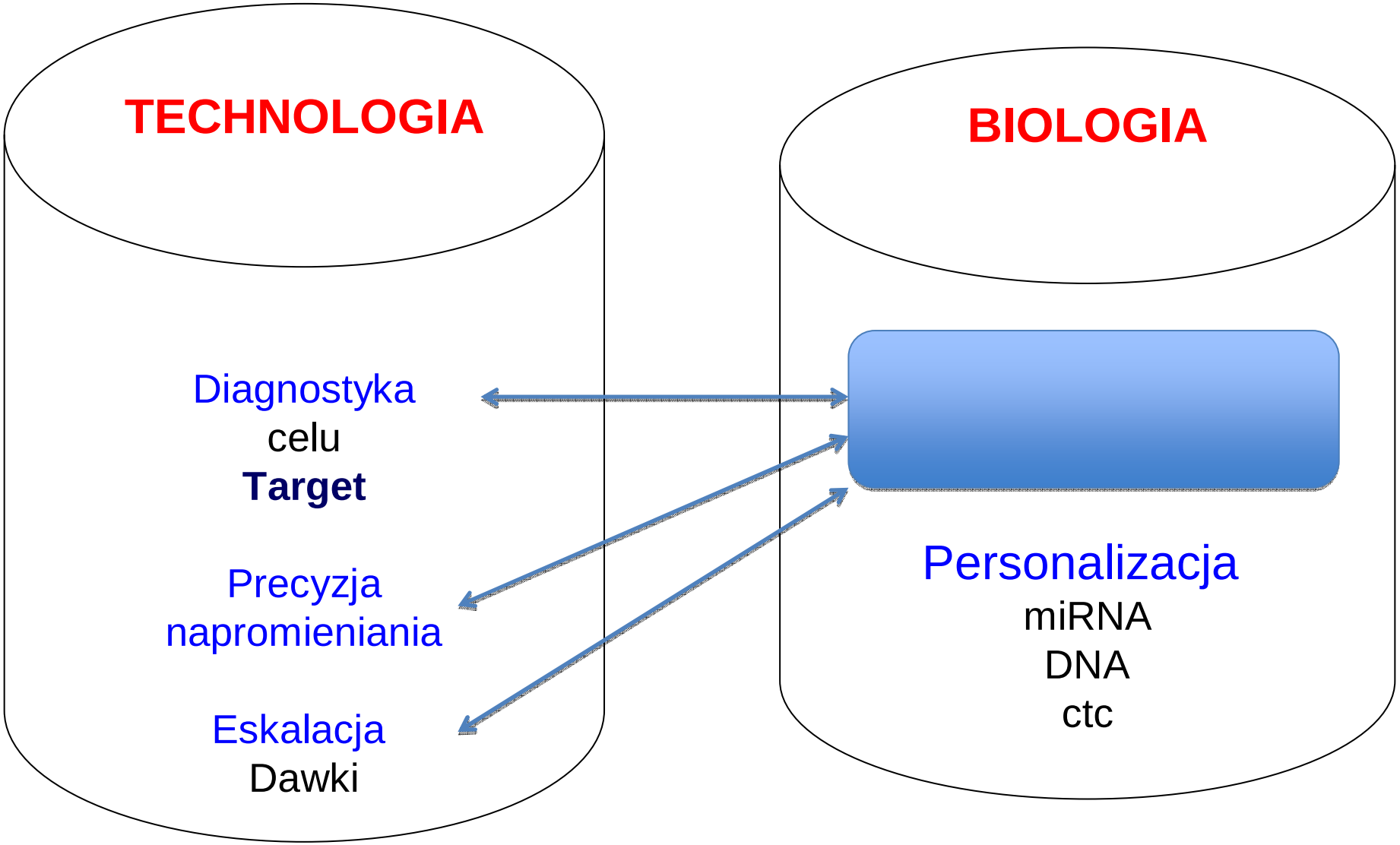


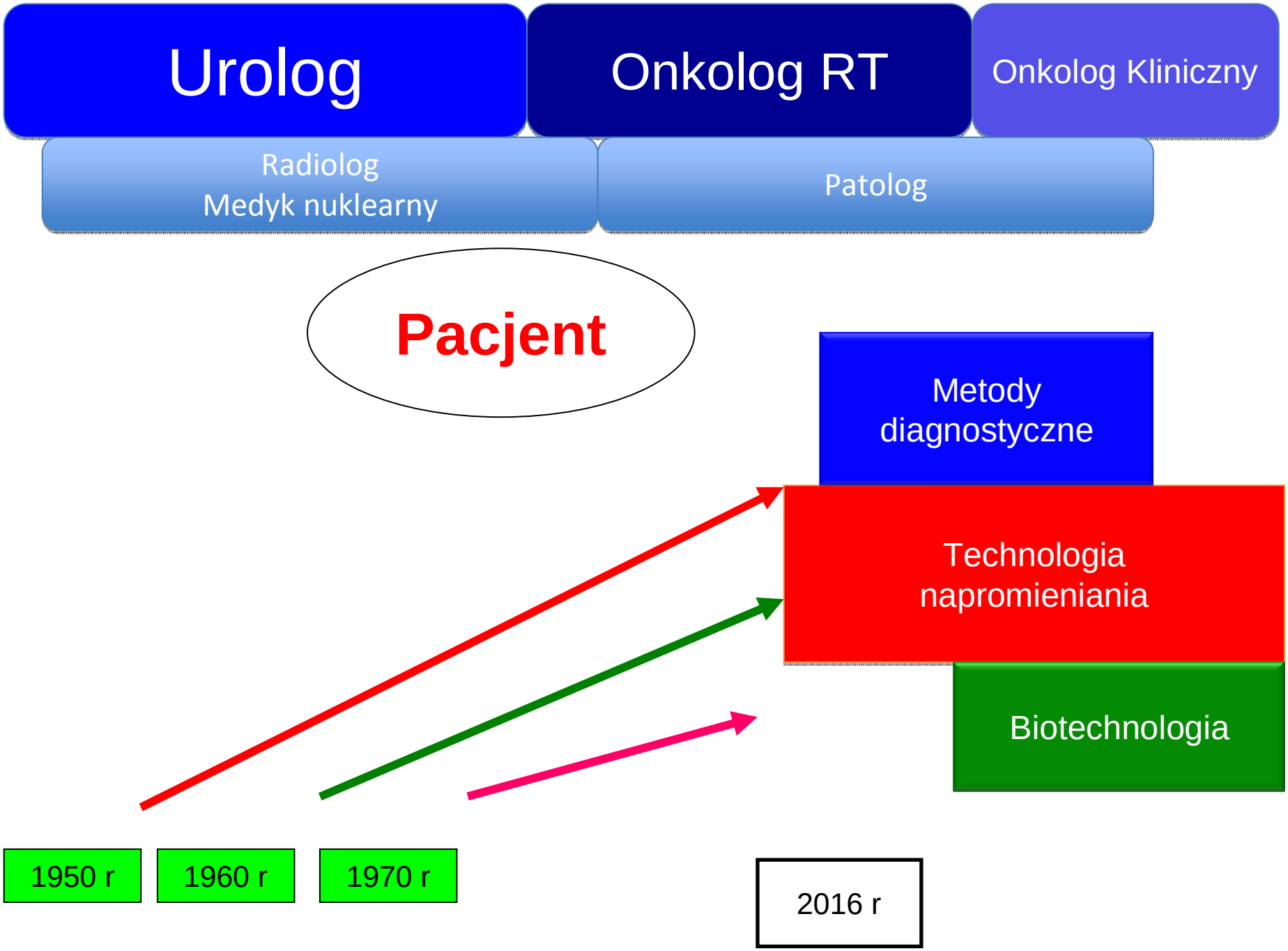


PET – Cholina
boost XRT



Efektywność radioterapii




Urolog
Onkolog RT
Onkolog Kliniczny
Radiolog
Medyk nuklearny
Patolog
Pacjent
Metody diagnostyczne
Technologia napromieniania
Biotechnologia
1950 r
1960 r
1970 r
2016 r

HDR-LIKE SBRT FOR POST-RADIOTHERAPY LOCALLY RECURRENT PROSTATIC CARCINOMA:
PSA response, DFS and toxicity assessment

DONALD B. FULLER, MD[1], JAMES WURZER, MD[2], PHD, GEORGE MARDIROSSIAN, PHD[1]
1. Genesis Healthcare Partners, San Diego, CA 2. AtlantiCare Cancer Care Institute, Egg Harbor Township, NJ

Purpose / Objectives

- There is no uniformly accepted local salvage option for patients who locally relapse post-radiotherapy
- Many receive "observation" or "palliative" hormone suppressive treatment
- **Many are not even diagnosed!** (i.e. - rising PSA post-RT ⟶ straight to systemic therapy without work-up; due to a community perception of no good local retreatment option?)
- ALL local retreatment options have potentially significant risk, however, there have been promising salvage results with high dose rate (HDR) interstitial brachytherapy
- This is a Prospective study of non-invasive "HDR-like" stereotactic body radiation therapy (SBRT) – SBRT Treatment regimen designed to noninvasively emulate HDR brachytherapy
- Assess PSA response, Disease-free survival, and Toxicity

ELIGIBILITY

- ☑ History of prior pelvic radiation therapy for prostate cancer
- ☑ No complication higher than grade I from their prior course of radiotherapy
- ☑ Histologically confirmed, locally recurrent adenocarcinoma of the prostate
- ☑ Clinical stages T1 - T3 (AJCC 6th Edition, see Appendix III)
- ☑ Greater than 2 years since the original radiotherapy course
- ☑ No distant metastases, no clinically or pathologically involved lymph nodes
- ☑ No major medical or psychiatric illness
- ☑ Hormonal therapy is not encouraged, but will not represent a study exclusion either
- ☑ No history of inflammatory bowel disease
- ☑ Signed study-specific informed consent form prior to study entry

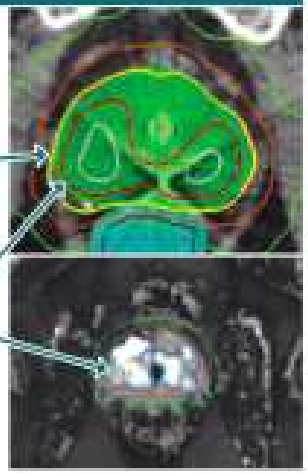
ZERO ADDED CTV → PTV MARGIN

"err" on the side of minimizing collateral dose

DOMINANT LESION(S)-BASED DOSIMETRY

Required: 34 Gy/5 fx to PTV (GTV + 0mm)

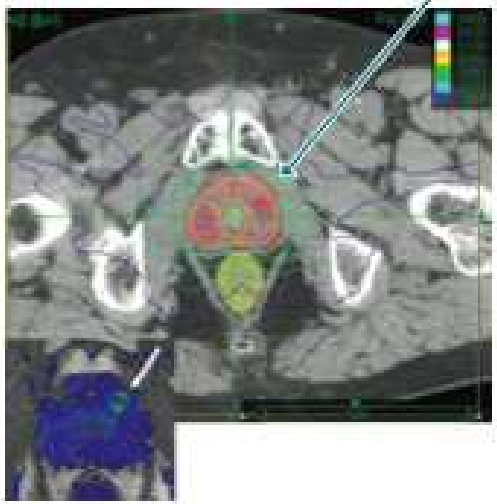
Goal: 50 Gy/5 fx to Dominant Intraprostatic Lesion (DIL)(s)* (mean)



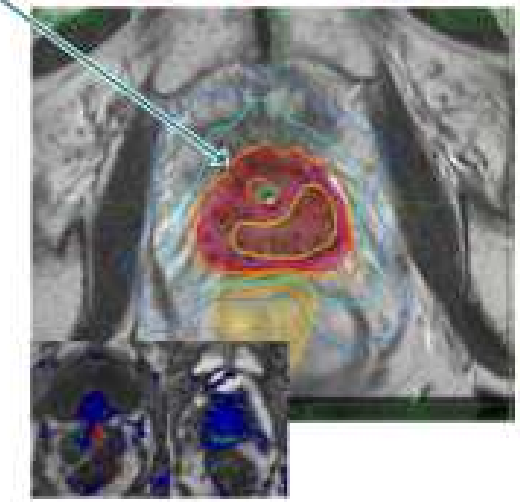
HDR-like Boost to Areas of "hyper-enhancement" on Dynamic Contrast Enhanced (DCE) MRI

Example "HDR-Like" SBRT Salvage Dose Maps

CASE 1 *Post-EBRT salvage*



CASE 2 *Post-Brachytherapy Salvage*



19 PATIENTS

with clinically localized, biopsy-proven local recurrent prostate cancer > 2 years after initial Radiotherapy (RT)

MEDIAN PRIOR RT DOSE

MEDIAN INTERVAL TO SBRT SALVAGE

(RANGE: 32-200)

RECURRENCE TOTAL

GLEASON SCORE

9 → 2 PATIENTS
8 → 4 PATIENTS
7 → 9 PATIENTS
6 → 4 PATIENTS

INITIAL RADIOTHERAPY METHOD PRE-SALVAGE

"Conventional" EBRT (2D, 3DCRT or IMRT)	16 CASES
^{125}I Brachytherapy	1 CASE
Proton Beam radiotherapy	1 CASE
SBRT (35Gy/5 fx)	1 CASE

SBRT SALVAGE REGIMEN: 34 GY/5 FRACTIONS

- Heterogeneous intraprostatic HDR-like dose escalation
- EUD$_{2}$ = 42Gy/5 fx
- Dmax urethra, bladder, rectal wall (to 120%, 100%, 100%
- GTV (Prostate + any contiguous disease extension) = CTV = PTV –
- No margin expansion
- Toxicities assessed using CTCAE v 3.0 criteria

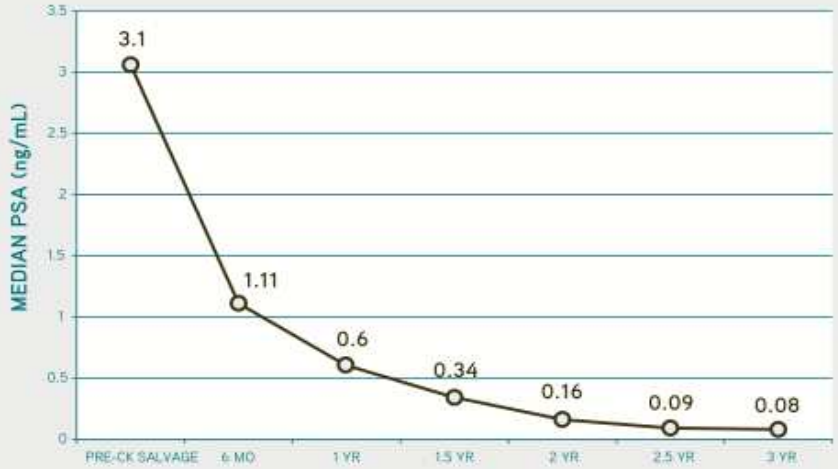
Results

19 PATIENTS W MEDIAN 18 MO. FOLLOW-UP (RANGE, 6-42)

1 patient declined f/u after 6 months – Incl. for acute tox. analysis only

GU TOXICITY	Acute:	Grade 2 – 0/19; Grade 3 – 1/19
	Chronic:	Grade 2 – 1/18; Grade 3 – 1/18; Grade 4 – 1/18
	NOTE: 2/3 pts. with > Grade 2 GU toxicity had residual Grade 1 toxicity from their initial RT course	
GI TOXICITY	Acute:	Grade 2 – 0/19; Grade 3 – 0/19
	Chronic:	Grade 2 – 0/18; Grade 3 – 0/18
DISEASE-FREE SURVIVAL	Crude Biochemical RFS:	83% (15/18 pts. w stable or decreased PSA at last f/u)
	Crude Clinical RFS:	100%

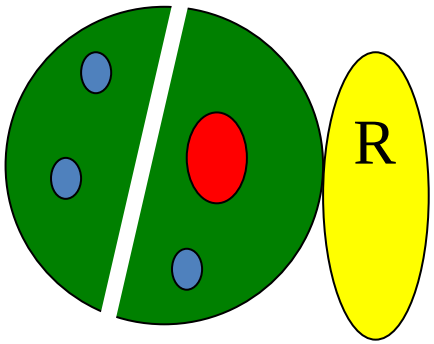
PSA-RESPONSE POST CK SBRT SALVAGE



Focal External Beam Radiation Therapy in Management of Low-Risk Prostate Cancer: A Radiobiological Analysis

J. F. Williamson[1], J. C. Ford[1], M. C. Carlone[2], M. S. Anscher[1], [1]*Virginia Commonwealth University, Richmond, VA,* [2]*Princess Margaret Hospital, Toronto, ON, Canada*

- Duża TD ognisko
- Mała TD pozostała P
- Mniejsza toks
- Większa skuteczność



MRI
wykrywa wewnątrz-stercza
ognisko index lesion

Inne niewykryte – mała dawka

De-escalation: 67 Gy

NTCP: 1% vs. 15%,
QUANTEC data

Boost – ognisko: 78 Gy

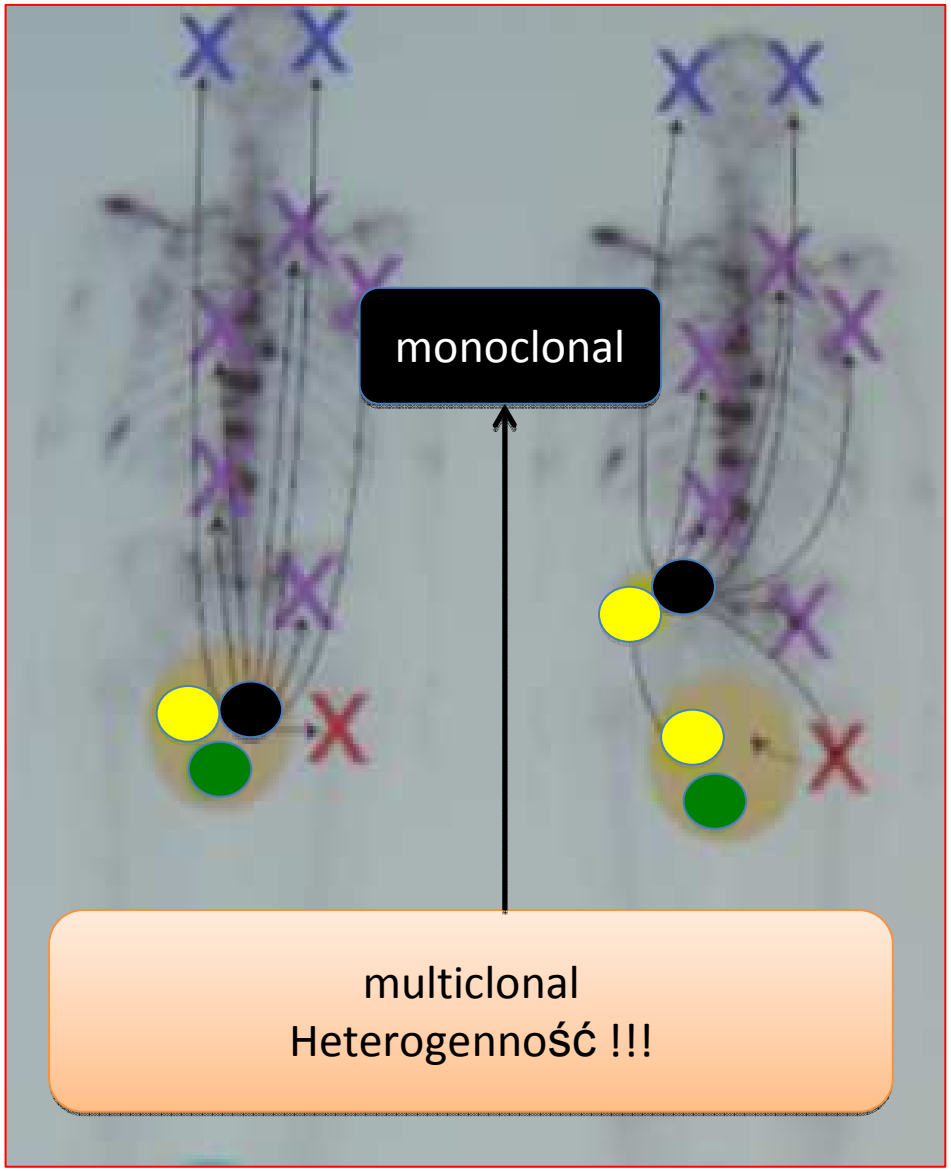
Conclusions: Prostate dose de-escalation with dominant intraprostatic lesion boost is a novel alternative to all-or-none surgical focal therapies with potential to significantly lower normal tissue toxicity while addressing small-volume multifocal disease that may not be accurately detected by dynamic MR imaging. Poisson TCP models must assume a minimum of 40,000 active clonogens/tumor in order to duplicate clinically observed dose responses curves.

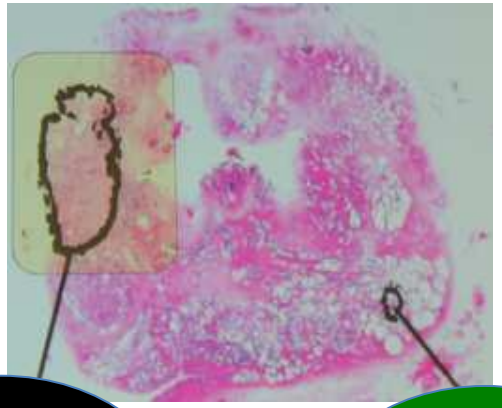
Index lesion – index cancer

- Ognisko o największej złośliwości, które powinno być wyeliminowane, tak aby pozostałe w długiej perspektywie lub już nigdy nie zagrażały pacjentowi.

- Wydaje się, że jego usunięcie jest kluczem do uzyskania sukcesu terapeutycznego, ponieważ pozostałe nie mają istotnego klinicznego znaczenia.

Ahmed HU. The index lesion and the origin of prostate cancer. N Engl J Med 2009;361:1704-6.





Metastatic lethal

Non metastatic

Metastatic Non-lethal

Leczenie oszczędzające
minimalnie inwazyjne

Targeted”

- „Focal”
- „Conformal”
- „Zonal”
- „Hemi-treatment”
- „Lumpectomy”

Focal therapy
jaka metoda ?

- Cryotherapy (Cryoablation, Criosurgery)
- HIFU (High-Intensity Focused Ultrasound)
- RFA (Radio Frequency Ablation)

„focal therapy”

- PDT (Photodynamic Therapy)
- FLA (Laser Ablation)

- CyberKnife (radioterapia, SBRT)
- BT (brachyterapia

„whole-gland therapy”

RCT :

- **FLAME** (3 fazy): Utrecht (van Pulpen)
  77 Gy v. 95 Gy

- **HEIGHT** (2 fazy): Maiami (Pollack)
  80 Gy + boost do 90 Gy

- **TARGET** (2 fazy): Princess Margaret (Menard)
  76 Gy + boost do 95 Gy