WSPÓŁCZESNA RADIOTERAPIA

TNM vs. TUMOR VOLUME CHALLENGE

D_{100} CZY D_{95} ?

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2018

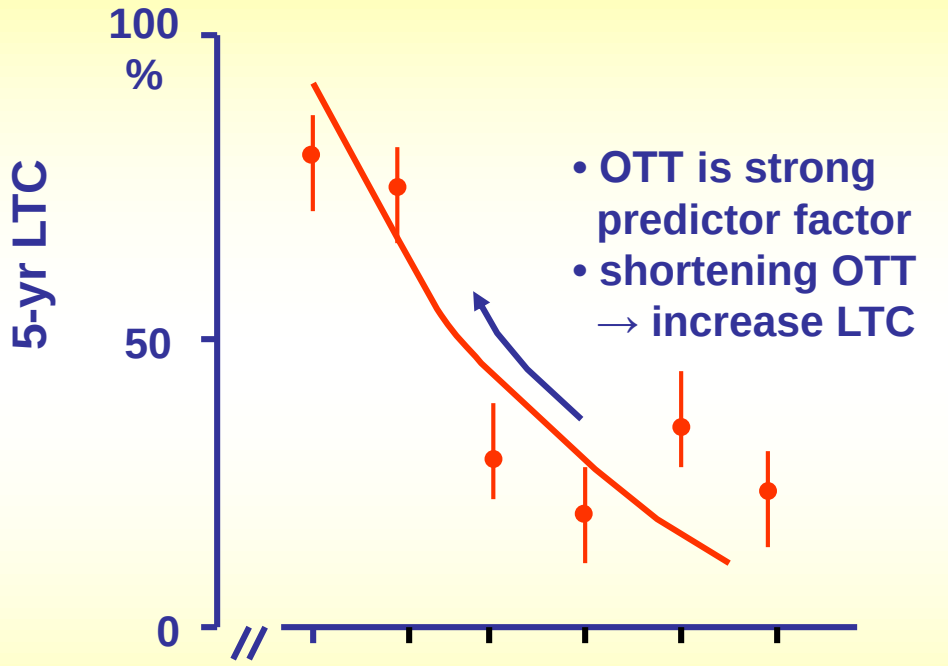
TNM → FOR SURGERY **YES**

IF TUMOR IS RESECTABLE
ITS SIZE DOES NOT PLAY
A ROLE

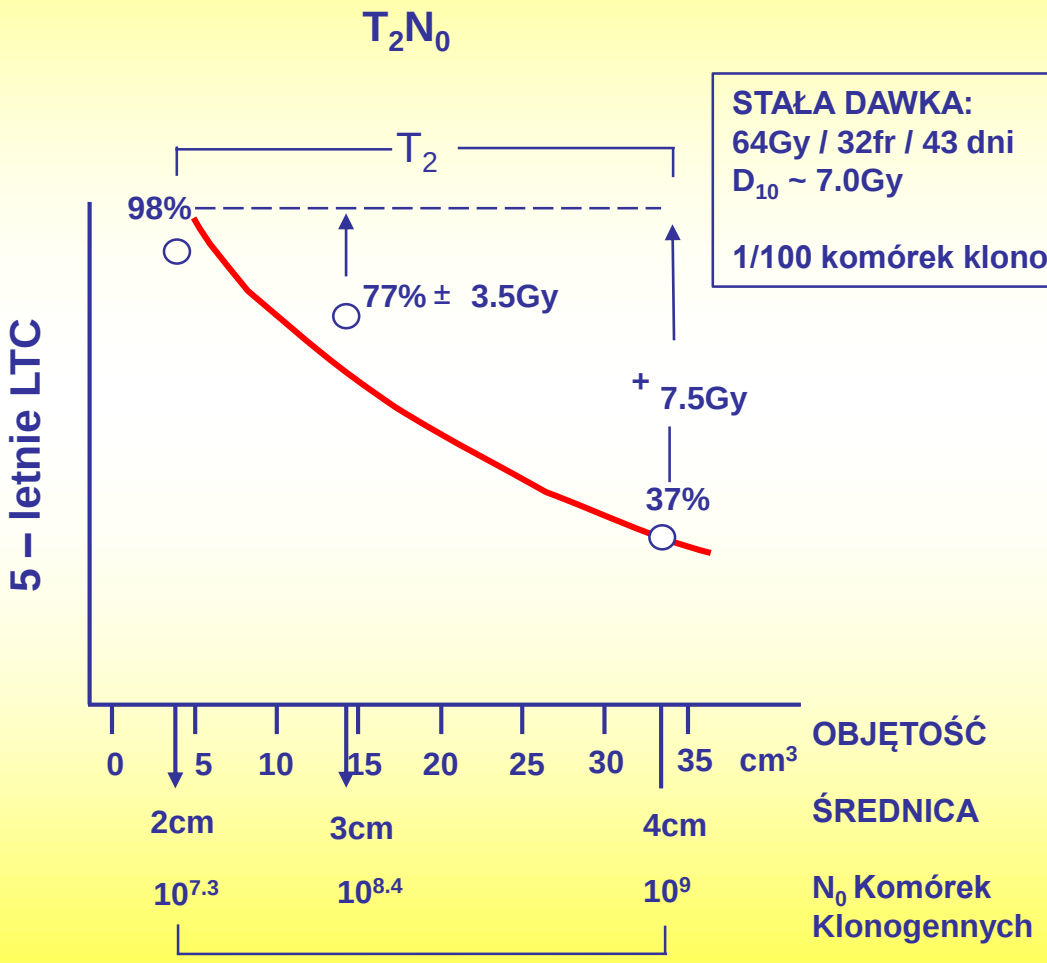
FOR CYTOTOXIC KILLING **NO**

TUMOR VOLUME (INITIAL CELL NUMBER)
DICTATES RADICAL DOSAGE
NOT RANK - STAGE

FOR TCD_{50} ≈ equiv. 1616 ret (± 5%)

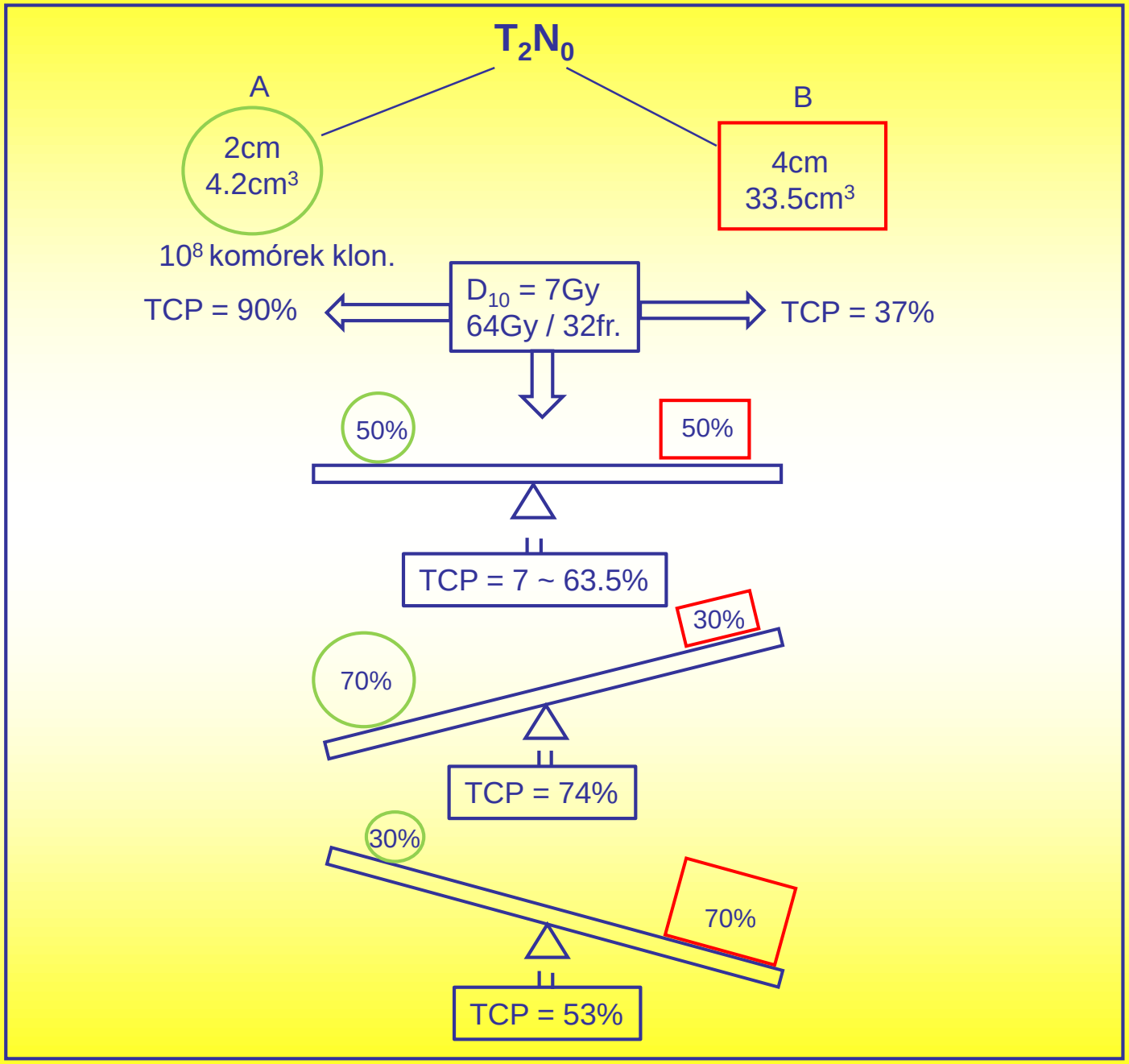


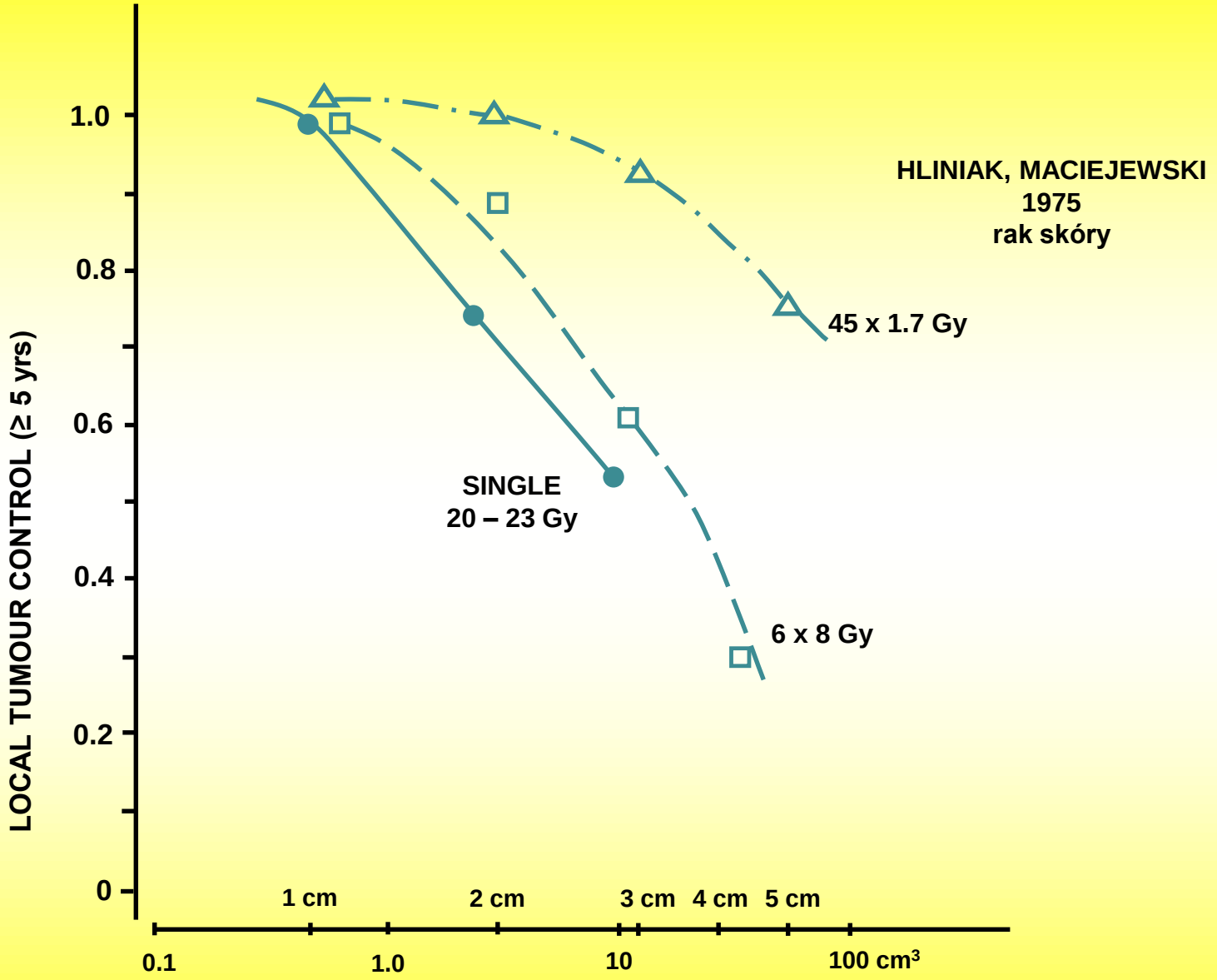
TEN SAM STOPIEŃ T
ale
RÓŻNE OBJĘTOŚCI GUZA (N_0 Kom. Klon.)

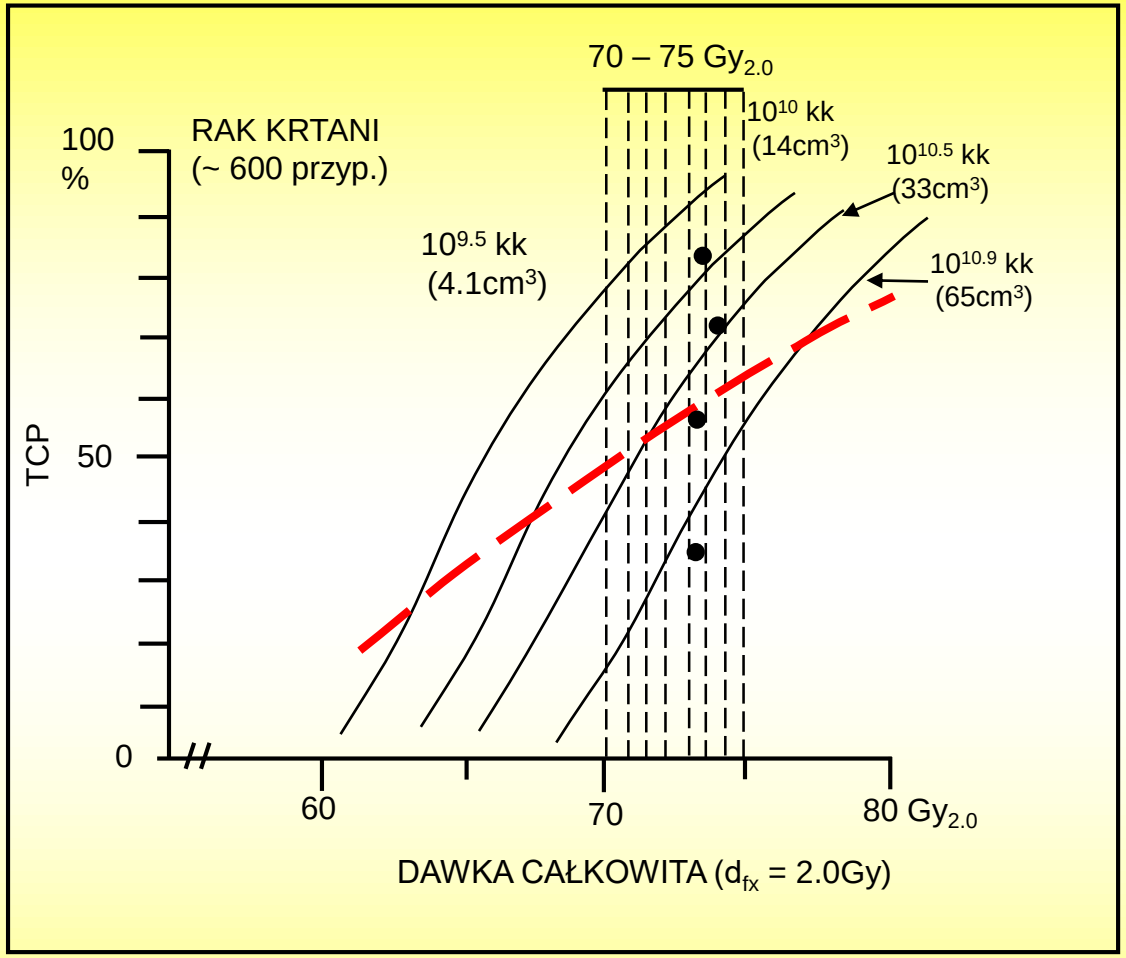


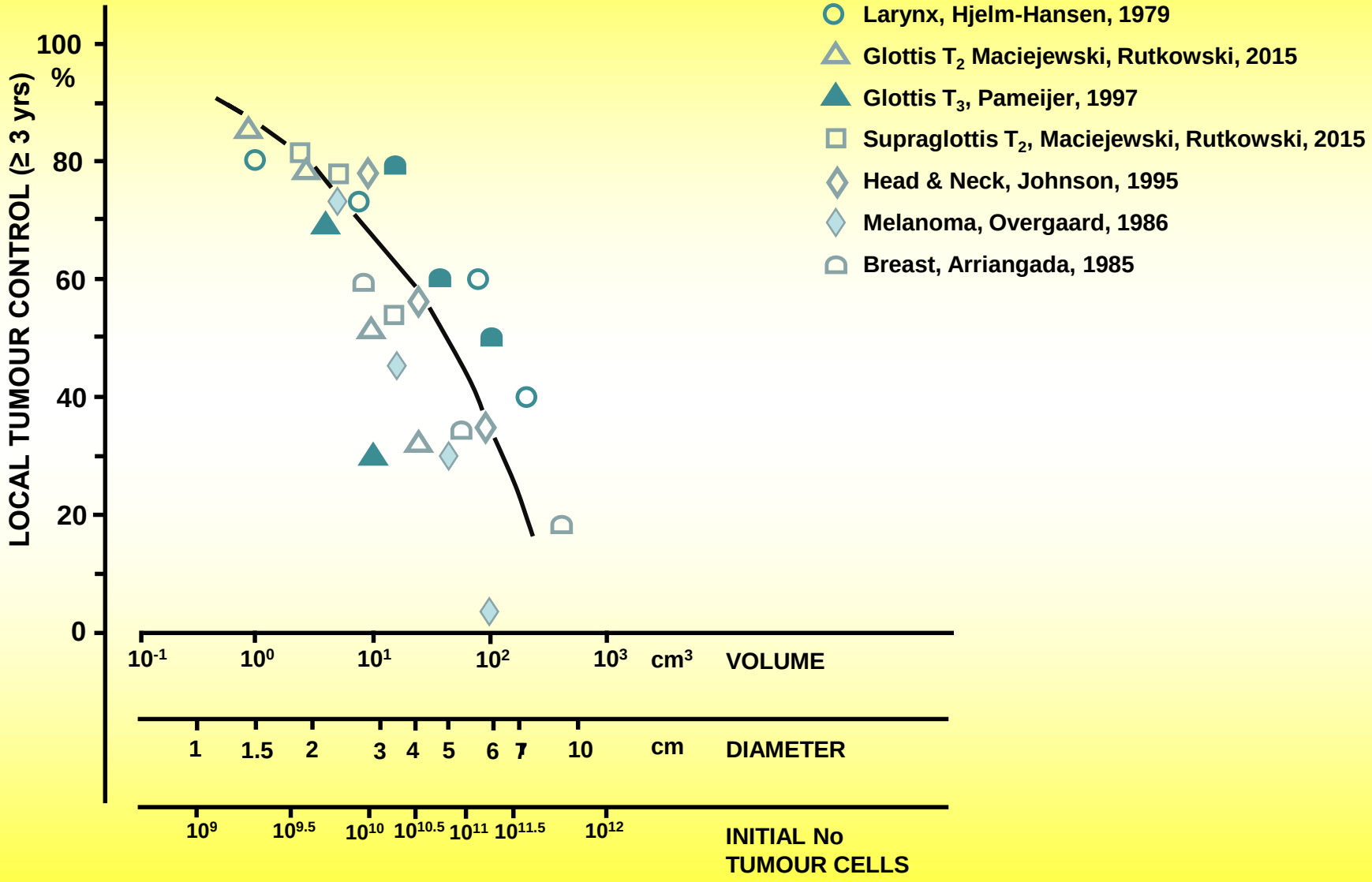
STAŁA DAWKA:
64Gy / 32fr / 43 dni
D_{10} ~ 7.0Gy

1/100 komórek klonogennych


T2N0
A
2cm
4.2cm3
B
4cm
33.5cm3
108 komórek klon.
TCP = 90%
D10 = 7Gy
64Gy / 32fr.
TCP = 37%
50%
50%
TCP = 7 ~ 63.5%
30%
70%
TCP = 74%
30%
70%
TCP = 53%

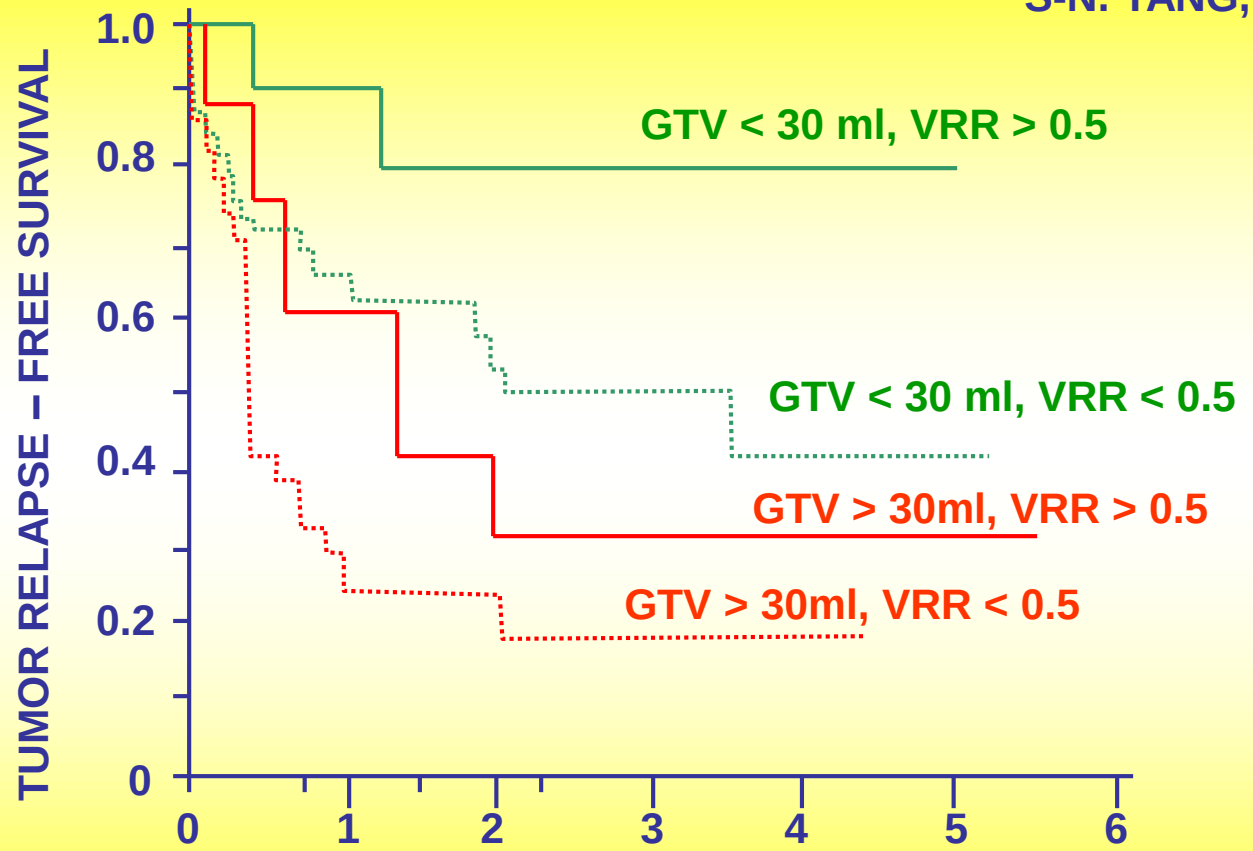

LOCAL TUMOUR CONTROL (≥ 5 yrs)
1.0
0.8
0.6
0.4
0.2
0
HLINIAK, MACIEJEWSKI
1975
rak skóry
45 x 1.7 Gy
SINGLE
20 – 23 Gy
6 x 8 Gy
1 cm
2 cm
3 cm
4 cm
5 cm
0.1
1.0
10
100 cm³

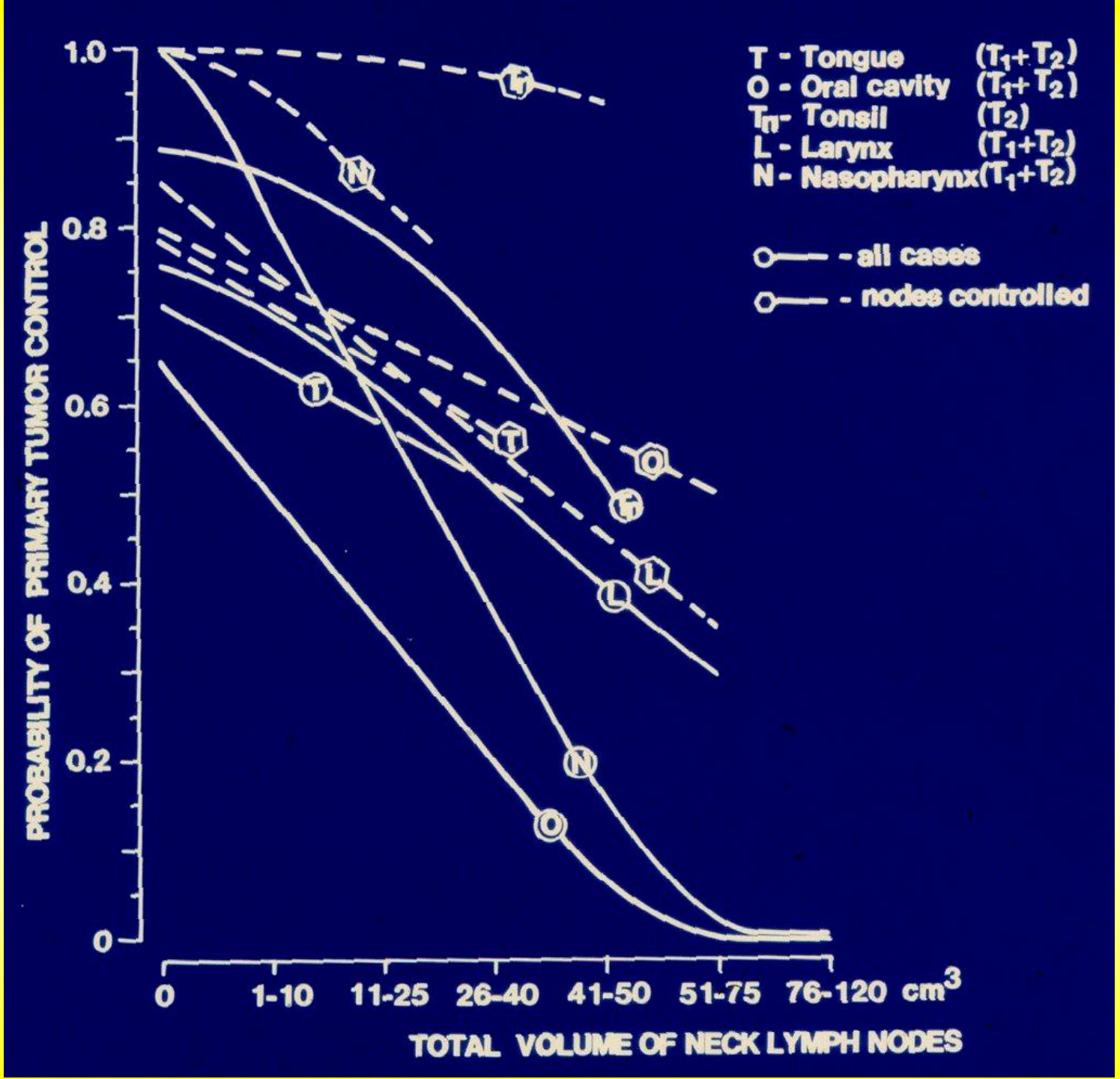

70 – 75 Gy2.0
RAK KRTANI
(~ 600 przyp.)
100
%
50
0
TCP
10^10 kk
(14cm^3)
10^10.5 kk
(33cm^3)
10^9.5 kk
(4.1cm^3)
10^10.9 kk
(65cm^3)
60
70
80 Gy2.0
DAWKA CAŁKOWITA (dfx = 2.0Gy)


LOCAL TUMOUR CONTROL (≥ 3 yrs)
100 %
80
60
40
20
0
Larynx, Hjelm-Hansen, 1979
Glottis T2 Maciejewski, Rutkowski, 2015
Glottis T3, Pameijer, 1997
Supraglottis T2, Maciejewski, Rutkowski, 2015
Head & Neck, Johnson, 1995
Melanoma, Overgaard, 1986
Breast, Arriangada, 1985
10-1 10^0 10^1 10^2 10^3 cm3 VOLUME
1 1.5 2 3 4 5 6 7 10 cm DIAMETER
10^9 10^9.5 10^10 10^10.5 10^11 10^11.5 10^12
INITIAL No TUMOUR CELLS

OROPHARYNGEAL S.C.C.
IMRT

S-N. YANG, 2011



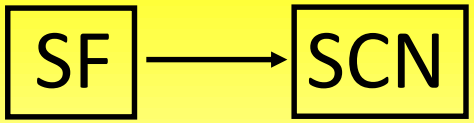

T - Tongue (T_1+T_2)
O - Oral cavity (T_1+T_2)
T_n - Tonsil (T_2)
L - Larynx (T_1+T_2)
N - Nasopharynx (T_1+T_2)
- all cases
- nodes controlled
PROBABILITY OF PRIMARY TUMOR CONTROL
1.0
0.8
0.6
0.4
0.2
0
0
1-10
11-25
26-40
41-50
51-75
76-120 cm3
TOTAL VOLUME OF NECK LYMPH NODES

FOWLER → 3D – (IMRT, IGRT)
SHRS

A LOT TO A SMALL IS BETTER
THAN
A LESS TO A LARGE !

AND

D_{100} IN STEAD OF D_{95}
AT LEAST IN GTV

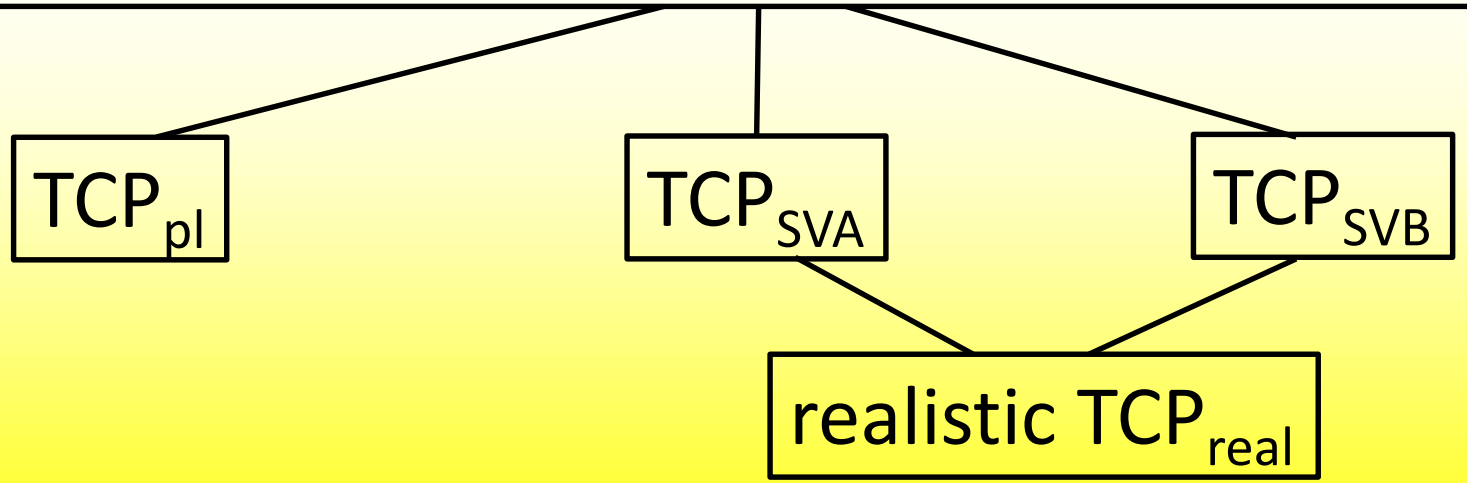


Survived Clonogen Number

for e $D_{10} \cong 7Gy$ **(5)**

$$SCN_i = 10^{-(TD_{i/e} D_{10})} \quad \textbf{(6)}$$

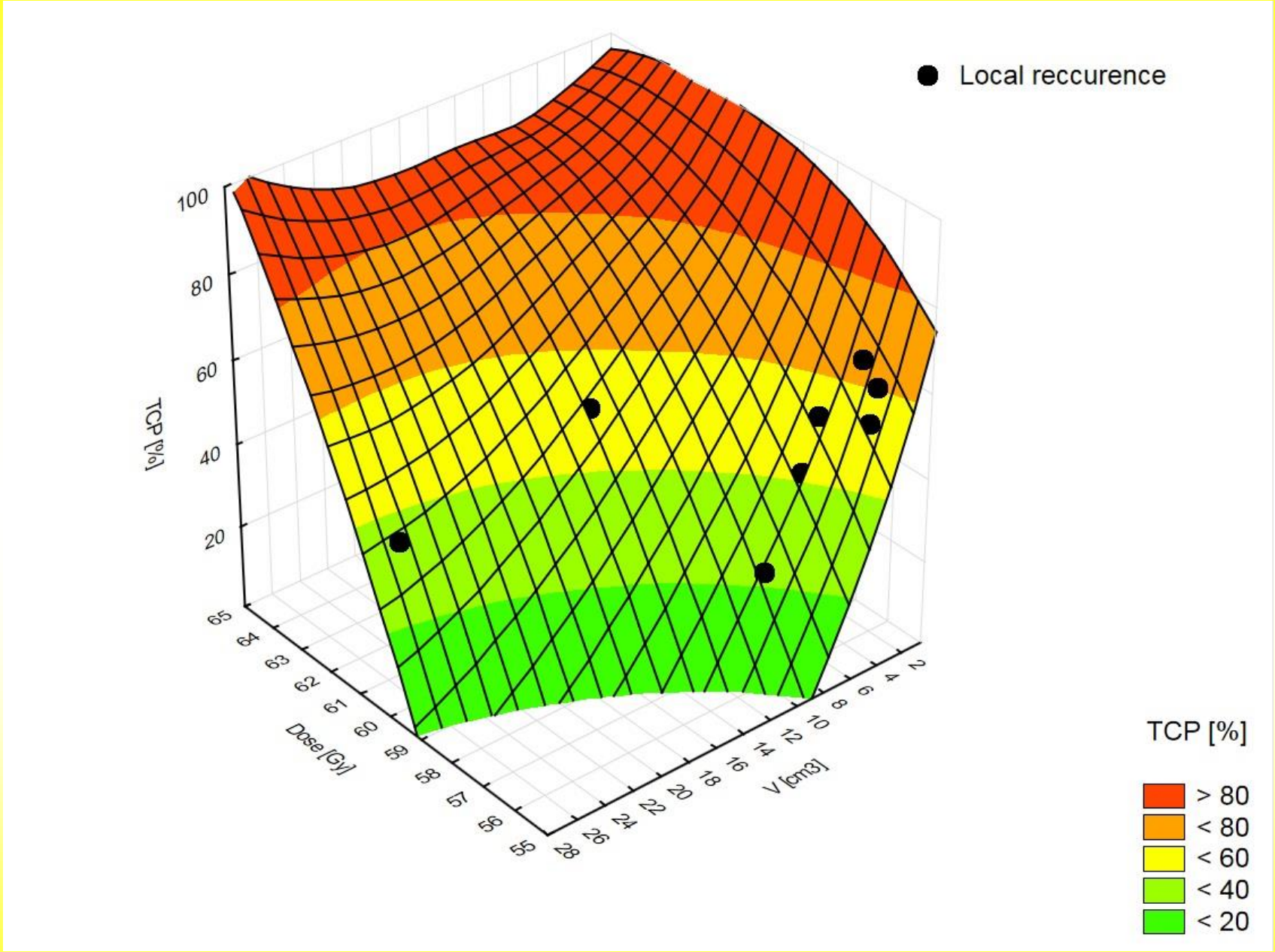
$$TCP_i = \exp\left[-(10^7 \bullet \text{Log}\,(Vi\,/0.52) \bullet (10^{-TD_{i/e}\,D_{10}})\right]$$

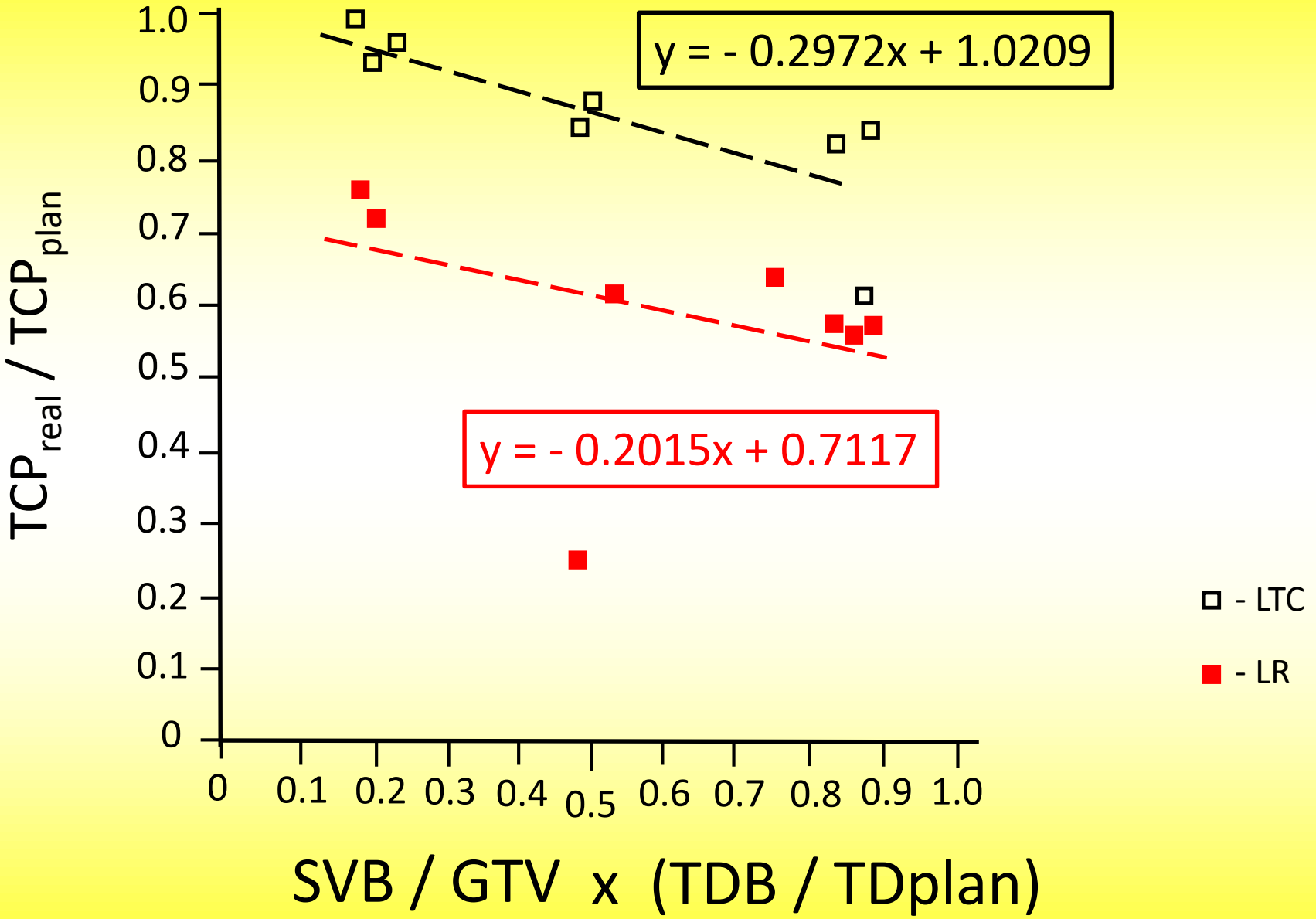


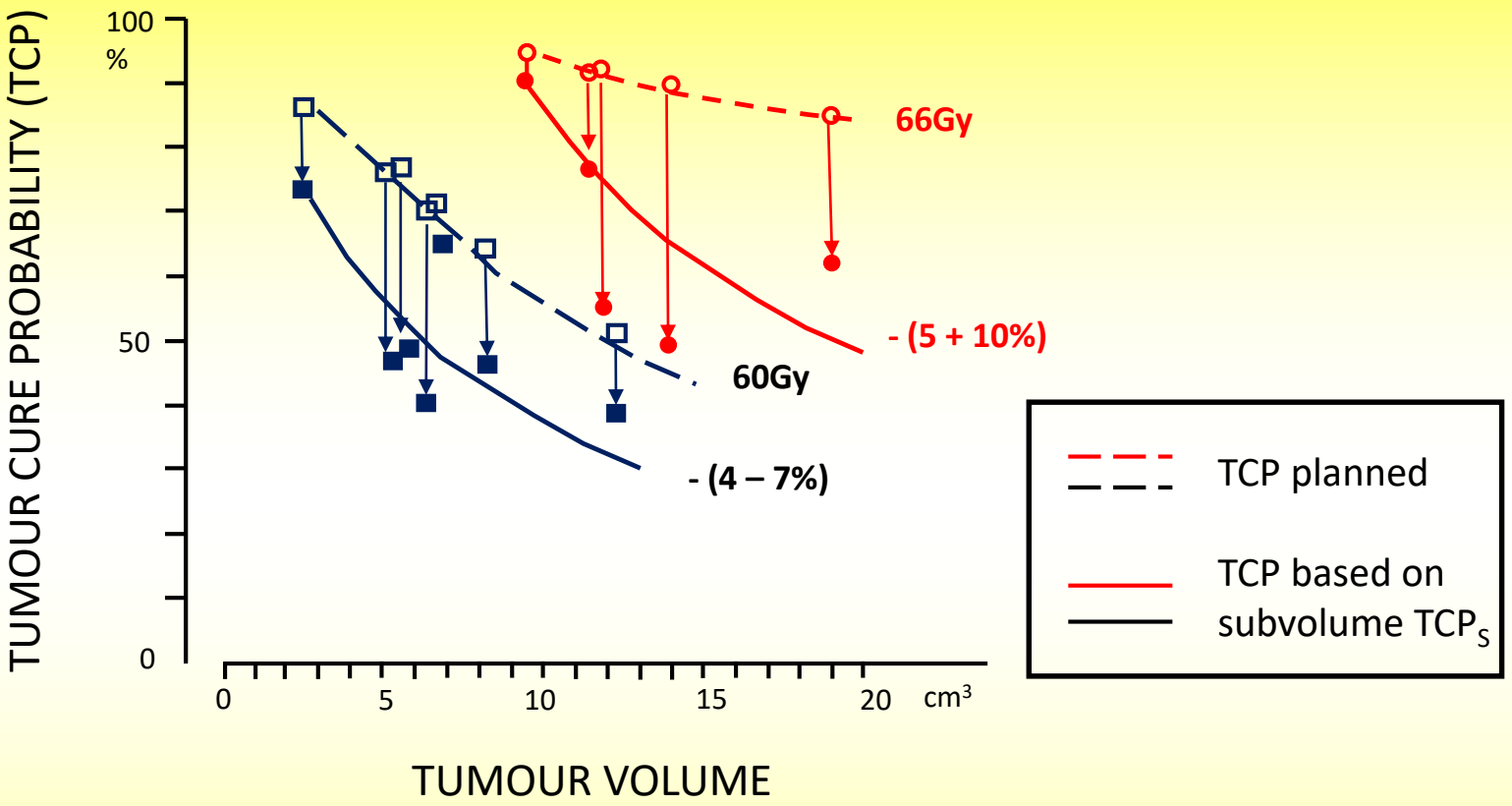
Pts N_0	T Stage	VOL. (GTV) cm^3	Log_{10} K p	NTD p izobio Gy_2	Planned TCP p
1	T1			60	
2	T1			70	
3	T1			60	
4	T1			60	
5	T2			60	
6	T2			60	
7	T2			60	
8	T2			66	
9	T2			66	
10	T2			66	
11	T2			60	
12	T2			66	
13	T2			70	
14	T2			66	
15	T2			70	
16	T2			63	

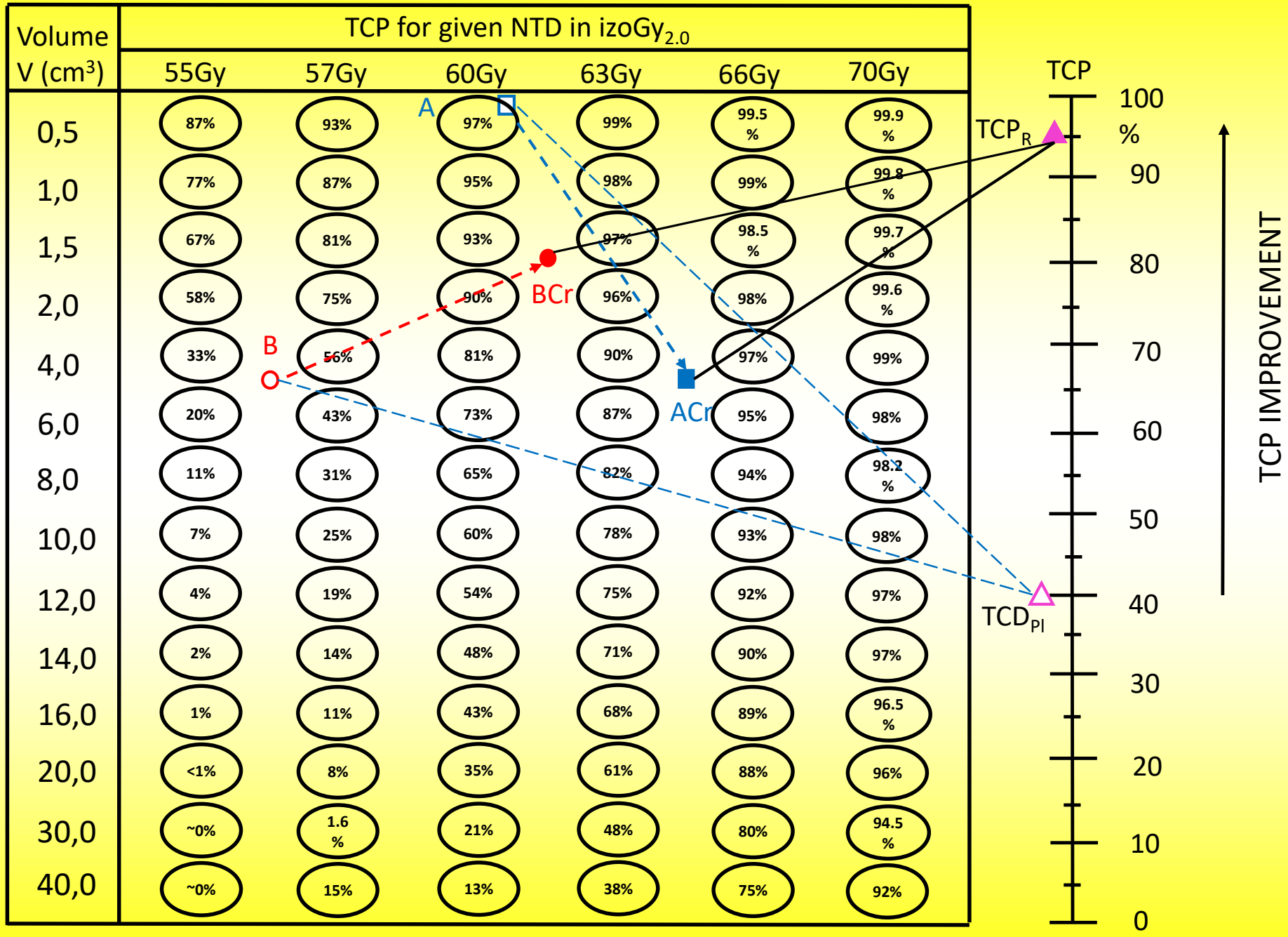
Pts N_0	SUBVOLUME A			SUBVOLUME B (V_{90-95})			TCP_{ESTIM} (TCP_A x TCP_B)	TCP_P - TCP_E	3yrs follow-up
	$\%VOL_{GTV}$	NTD_A $izoGy_{2.0}$	TCP_A	$\%VOL_{GTV}$	NTD_B $izoGy_{2.0}$	TCP_B			
1	V_{48}	60Gy	94%	V_{52}	56.8Gy	78%	73%	-15%	DFS
2	V_{73}	70Gy	99.5%	V_{27}	61.1Gy	95%	94%	-5%	DFS
3	V_{43}	60Gy	88%	V_{57}	55.8Gy	53%	47%	-41%	LR
4	V_{21}	60Gy	94%	V_{79}	56.8Gy	52%	49%	-28%	LR
5	V_{6}	60Gy	98%	V_{94}	56.7Gy	41%	40%	-31%	LR
6	V_{79}	60Gy	78%	V_{21}	57.4Gy	86%	67%	-4%	DFS
7	V_{71}	60Gy	76%	V_{29}	55.9Gy	62%	47%	-18%	LR
8	V_{82}	66Gy	95%	V_{18}	63.2Gy	97%	92%	-3%	DFS
9	V_{5}	66Gy	99%	V_{95}	62.4Gy	78%	77%	-15%	DFS
10	V_{5}	66Gy	99%	V_{95}	60Gy	56%	55%	-37%	DFS
11	V_{80}	60Gy	59%	V_{20}	56.3Gy	65%	38%	-13%	LR
12	V_{4}	66Gy	99.5%	V_{96}	60.1Gy	51%	50%	-40%	LR
13	V_{40}	70Gy	99%	V_{60}	56.5Gy	23%	23%	-74%	LR
14	V_{13}	66Gy	98%	V_{87}	63.1Gy	73%	71%	-16%	DFS
15	V_{45}	70Gy	98%	V_{55}	64.2Gy	85%	83%	-13%	DFS
16	V_{12}	63Gy	94%	V_{88}	60.7Gy	35%	33%	-25%	LR

Pts N_0	SUBVOLUME A			SUBVOLUME B (V_{90-95})			TCP_{ESTIM} (TCP_A x TCP_B)	TCP_P - TCP_E	3yrs follow-up
	$\%VOL_{GTV}$	NTD_A $izoGy_{2.0}$	TCP_A	$\%VOL_{GTV}$	NTD_B $izoGy_{2.0}$	TCP_B			
1	V_{48}	60Gy	94%	V_{52}	56.8Gy	78%	73%	-15%	DFS
2	V_{73}	70Gy	99.5%	V_{27}	61.1Gy	95%	94%	-5%	DFS
3	V_{43}	60Gy	88%	V_{57}	55.8Gy	53%	47%	-41%	LR ●
4	V_{21}	60Gy	94%	V_{79}	56.8Gy	52%	49%	-28%	LR ●
5	V_{6}	60Gy	98%	V_{94}	56.7Gy	41%	40%	-31%	LR ●
6	V_{79}	60Gy	78%	V_{21}	57.4Gy	86%	67%	-4%	DFS
7	V_{71}	60Gy	76%	V_{29}	55.9Gy	62%	47%	-18%	LR ●
8	V_{82}	66Gy	95%	V_{18}	63.2Gy	97%	92%	-3%	DFS
9	V_{5}	66Gy	99%	V_{95}	62.4Gy	78%	77%	-15%	DFS
10	V_{5}	66Gy	99%	V_{95}	60Gy	56%	55%	-37%	DFS
11	V_{80}	60Gy	59%	V_{20}	56.3Gy	65%	38%	-13%	LR ●
12	V_{4}	66Gy	99.5%	V_{96}	60.1Gy	51%	50%	-40%	LR ●
13	V_{40}	70Gy	99%	V_{60}	56.5Gy	23%	23%	-74%	LR ●
14	V_{13}	66Gy	98%	V_{87}	63.1Gy	73%	71%	-16%	DFS
15	V_{45}	70Gy	98%	V_{55}	64.2Gy	85%	83%	-13%	DFS
16	V_{12}	63Gy	94%	V_{88}	60.7Gy	35%	33%	-25%	LR


Local reccurence
TCP [%]
100
80
60
40
20
Dose [Gy]
65
64
63
62
61
60
59
58
57
56
55
V [cm3]
28
26
24
22
20
18
16
14
12
10
8
6
4
2
TCP [%]
> 80
< 80
< 60
< 40
< 20


y = - 0.2972x + 1.0209
y = - 0.2015x + 0.7117
TCP real / TCP plan
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
SVB / GTV x (TDB / TDplan)
- LTC
- LR


TUMOUR CURE PROBABILITY (TCP)
100
%
50
0
0
5
10
15
20
cm³
TUMOUR VOLUME
66Gy
- (5 + 10%)
60Gy
- (4 – 7%)
TCP planned
TCP based on
subvolume TCP$_S$


Volume V (cm3)
TCP for given NTD in izoGy2.0
55Gy
57Gy
60Gy
63Gy
66Gy
70Gy
0,5
1,0
1,5
2,0
4,0
6,0
8,0
10,0
12,0
14,0
16,0
20,0
30,0
40,0
87%
93%
97%
99%
99.5 %
99.9 %
77%
87%
95%
98%
99%
99.8 %
67%
81%
93%
97%
98.5 %
99.7 %
58%
75%
90%
96%
98%
99.6 %
33%
56%
81%
90%
97%
99%
20%
43%
73%
87%
95%
98%
11%
31%
65%
82%
94%
98.2 %
7%
25%
60%
78%
93%
98%
4%
19%
54%
75%
92%
97%
2%
14%
48%
71%
90%
97%
1%
11%
43%
68%
89%
96.5 %
<1%
8%
35%
61%
88%
96%
~0%
1.6 %
21%
48%
80%
94.5 %
~0%
15%
13%
38%
75%
92%
A
B
O
BCr
ACr
TCP
TCP_R
TCD_PI
100 %
90
80
70
60
50
40
30
20
10
0
TCP IMPROVEMENT

Pts N_0	SUBVOLUME A → ACr			SUBVOLUME B → BCr			TCP_{real} (TCP_{ACr} x TCP_{BCr})
	$V_A \rightarrow V_{AR}$	$NTD_A \rightarrow NTD_{AR}$ (izo $Gy_{2.0}$)	TCP_{ACr}	$V_B \rightarrow V_{BR}$	$NTD_B \rightarrow NTD_{BR}$ (izo $Gy_{2.0}$)	TCP_{BCr}	
1	48% → 70%	60Gy → 62Gy	95%	52% → 30%	56.8Gy → 59Gy	95%	90%
2	change not needed			change not needed			94%
3	42% → 70%	60Gy → 65Gy	96%	56% → 30%	55.8Gy → 61Gy	95%	91%
4	21% → 70%	60Gy → 65Gy	96%	79% → 30%	56.8Gy → 61Gy	94%	90%
5	6% → 70%	60Gy → 65Gy	95%	94% → 30%	56.7Gy → 61Gy	95%	90%
6	79%	60Gy → 65Gy	95%	21%	57.4Gy → 61Gy	95%	90%
7	63% → 70%	60Gy → 66Gy	95%	37% → 30%	55.9Gy → 62Gy	95%	90%
8	change not needed			change not needed			92%
9	5% → 70%	66Gy	95%	95% → 30%	62.4Gy → 63Gy	94%	89%
10	5% → 70%	66Gy	96%	95% → 30%	60Gy → 63Gy	94%	90%
11	80%	60Gy → 67Gy	95%	20%	56.3Gy → 63Gy	95%	90%
12	4% → 70%	70Gy	97%	96% → 30%	60.1Gy → 64Gy	94%	90%
13	40% → 70%	70Gy	97%	60% → 30%	56.5Gy → 63Gy	97%	94%
14	13% → 70%	66Gy → 68Gy	95%	87% → 30%	63.1Gy → 65Gy	94%	89%
15	45% → 80%	70Gy	97%	55% → 20%	64.2Gy → 66Gy	99%	96%
16	12% → 70%	63Gy → 70Gy	96%	88% → 30%	60.7Gy → 66Gy	97%	93%

WNIOSKI

- ZAAWANSOWANE WOLUMETRYCZNE W ODRÓŻNIENIU OD TNM UMOŻLIWIA :

  - OZNACZENIE WYJŚCIOWEJ LICZBY KOMÓREK NOWOTWOROWYCH → KOMÓREK KLONOGENNYCH (1/100)

  - WYZNACZENIE FRAKCJONOWANEJ DAWKI CAŁKOWITEJ (DC = x • D_{10}) KONIECZNEJ DO WYJAŁOWIENIA KOMÓREK KLONOGENNYCH, ABY FRAKCJA PRZEŻYWAJĄCA (SF = $10^{-(x+1)}$) STWORZYŁA SZANSĘ TCP ≈ 90%

  - W PLANOWANIU RT 3D-CRT (IMRT, IGRT, SHRS) NALEŻY POSŁUŻYĆ SIĘ ROZKŁADEM D_{100} W GTV A NIE D_{95} –
    5 – 10% NIEDODAWKOWANIA W PODOBJĘTOŚCI GTV (COLD SPOT) SKUTKUJE ZNAMIENNYM OBNIŻENIEM REALNEGO TCP W PORÓWNANIU DO PLANOWANEGO

  - „ZIMNA” PODOBJĘTOŚĆ >50% GTV Z NIEDODAWKOWANIEM (DC – 5%) WYMAGA REPLANOWANIA ROZKŁADU DAWKI W OBJĘTOŚCI, W CELU ZMNIEJSZENIA, A NAJLEPIEJ ELIMINACJI „ZIMNEJ” PODOBJĘTOŚCI GTV I ZWIĘKSZENIA DAWKI W TYM OBSZARZE