Radiobiologia clinica e contributo delle cellule staminali nel trattamento radioterapico del carcinoma prostatico.

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INTRODUZIONE

Estimation of a Self-Consistent Set of Radiobiological Parameters From Hypofractionated Versus Standard Radiation Therapy of Prostate Cancer

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Table 1 Clinical data of the external beam treatment of prostatic cancer (biochemical relapse-free survival) used to estimate the radiobiological parameters and to verify the results

Author (reference)	Study size (n)	Dose/fraction (Gy)	No. fractions	Total dose (Gy)	OTT	ADT	Low-risk	Interm-risk	High-risk	All risks
Data used to estimate the parameters										
Kupelian (7)	189	2.0	39	78	53	No	0.95	0.83	1.00	-
	310	2.5	28	70	38		0.95	0.84	0.64	-
Lukka (8)	470	2.0	33	66	45	No	0.66	0.38	0.28	-
	466	2.62	20	52.4	26		0.59	0.47	0.29	-
Yeoh (9)	109	2.0	32	64	44	No	0.76	0.57	0.42	-
	108	2.75	20	55	26		0.73	0.67	0.64	-
Zelefsky (10)	116	1.8	38	68.4	52	No	-	0.54	-	-
	94	1.8	44	79.2	60		-	0.79	-	-
Arcangeli (11)	85	2.0	40	80	54	Yes	-	-	0.79	-
	83	3.1	20	62	28		-	-	0.85	-
Pollack 1 (12)	150	2.0	35	70	49	No	-	-	-	0.64
	151	2.0	37	78	53		-	-	-	0.74
Pollack 2 (13)	152	2.0	38	76	52	Yes	-	-	-	0.85
	151	2.7	26	70.2	36		-	-	-	0.86

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$$\frac{d_b D_b - d_a D_a}{\frac{1}{\alpha}\left[C + \frac{\ln 2}{T_d}(T_b - T_a)\right] - (D_b - D_a)} = \frac{\alpha}{\beta}$$

d = dose frazione

a, b = frazionamento 1 e 2

T = tempo di trattamento

D = dose totale

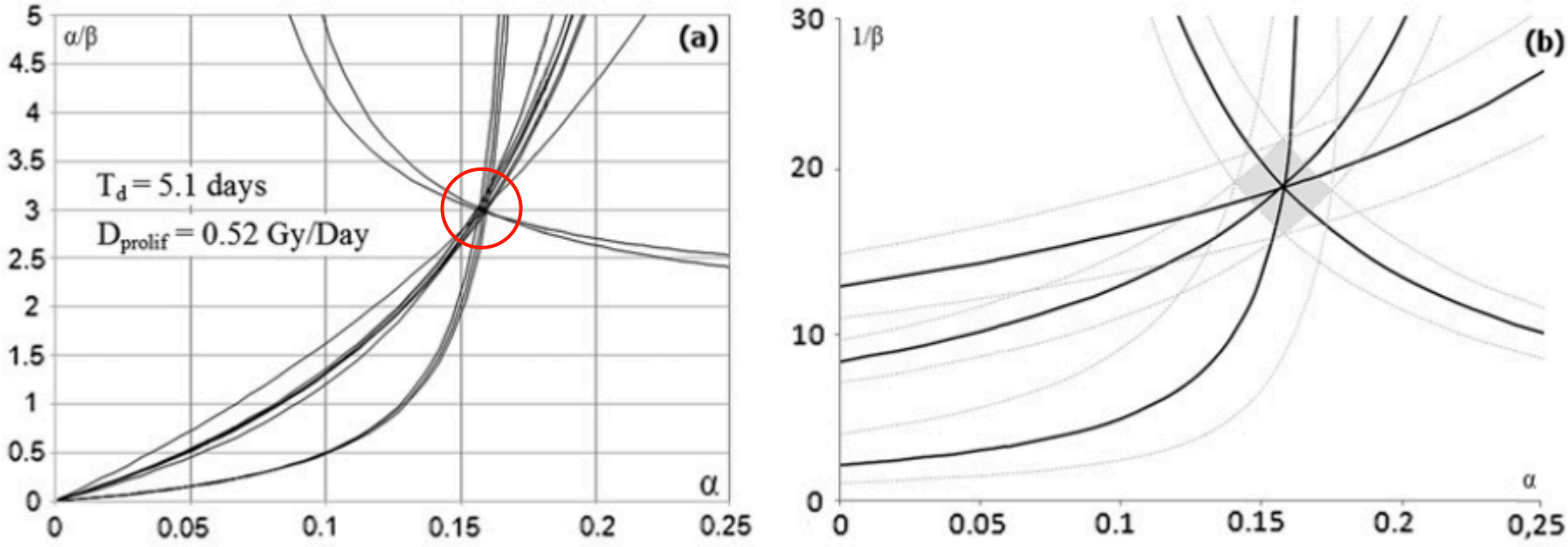

Fig. 1. The relation of α and α/β of prostate tumor: to graph the curves, T_d is used as a free-variable parameter by varying its value until the coincidence for all curves is obtained. Crossing the curves gives the best estimate of α, α/β, and T_d (a). The relationship of α and *1*/β: black curves represent the best estimate for different schedules of fractionation (only 4 curves shown), and gray curves represent the corresponding 95% confidence interval (b) and the intervals by forced variation of T_d (c). The shaded areas indicate the range of α and *1*/β that satisfy all the conditions.

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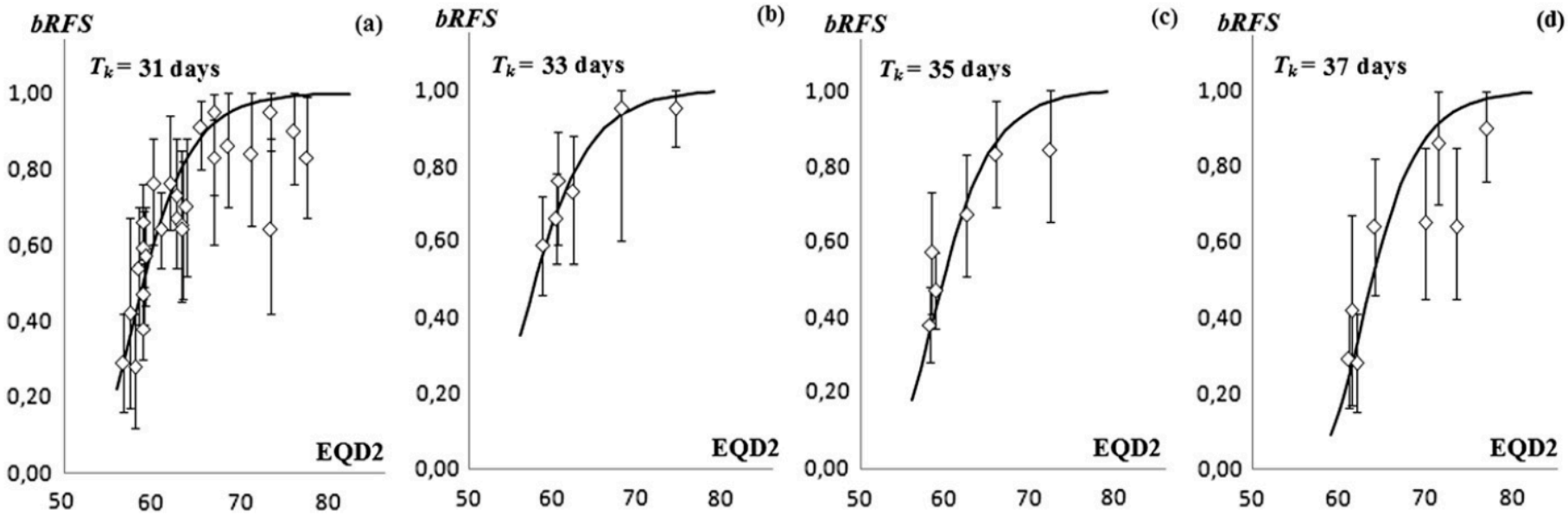

Fig 4. Outcomes for all the data (a) and the low- (b), intermediate- (c), and high-risk (d) patient groups along with fitted values of α, β, and T_d. Solid lines are obtained from Eq. 3 by varying N. Open symbols represent clinical data normalized to 2-Gy fractions and corrected for temporal factors by varying T_k. Error bars represent the 95% confidence interval of clinical data (data from Miralbell and Valdagni included) (1, 14).

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Table 2 Best estimated parameters and their confidence intervals (CI) for overall data and for the low-, intermediate-, and high-risk subgroups

Parameters	Best estimate	95% CI	Forced variation	Propagation
All				
α (Gy^{-1})	0.16	0.14-0.18	0.10-0.23	0.09-0.25
β (Gy^{-2})	0.054	0.051-0.058	0.047-0.055	0.045-0.059
α/β (Gy)	2.96	2.41-3.53	2.12-4.22	1.54-5.55
T_d (d)	5.1	4.2-7.2	2.6-10.2	2.2-11.6
D_{prolif} (Gy)	0.52	0.32-0.68	0.20-1.37	0.16-1.75
T_k (d)	31	22-41	-	-
N (clonogens)	6.5×10^6	1.5×10^6-2.1×10^7	-	-
γ_{50} (slope)	5.55	5.04-5.96	-	-
Low risk				
α (Gy^{-1})	0.14	0.10-0.18	0.06-0.26	0.04-0.28
β (Gy^{-2})	0.044	0.028-0.068	0.023-0.072	0.021-0.073
α/β (Gy)	3.18	2.62-4.10	2.51-3.60	0.98-8.71
T_d (d)	5.8	3.8-10.5	2.9-11.6	2.5-13.4
D_{prolif} (Gy)	0.52	0.21-1.17	0.15-2.25	0.12-3.38
T_k (d)	33	26-43	-	-
N (clonogens)	4.5×10^5	2.5×10^5-1.1×10^6	-	-
γ_{50} (slope)	4.63	4.43-4.94	-	-
Intermediate risk				
α (Gy^{-1})	0.15	0.13-0.17	0.07-0.24	0.06-0.22
β (Gy^{-2})	0.048	0.043-0.054	0.030-0.066	0.028-0.069
α/β (Gy)	3.12	2.72-3.60	2.32-3.63	1.10-6.26
T_d (d)	5.3	4.0-9.8	2.7-10.6	2.0-11.2
D_{prolif} (Gy)	0.53	0.25-0.80	0.17-1.92	0.16-2.66
T_k (d)	35	26-42	-	-
N (clonogens)	3.0×10^6	8.4×10^5-8.5×10^6	-	-
γ_{50} (slope)	5.29	4.85-5.65	-	-
High risk				
α (Gy^{-1})	0.15	0.13-0.17	0.08-0.23	0.06-0.25
β (Gy^{-2})	0.058	0.051-0.067	0.044-0.062	0.042-0.069
α/β (Gy)	2.59	1.94-3.33	1.86-4.56	0.87-5.95
T_d (d)	5.1	4.0-9.3	2.6-10.2	2.1-12.4
D_{prolif} (Gy)	0.51	0.24-0.75	0.19-1.59	0.14-2.19
T_k (d)	37	29-46	-	-
N (clonogens)	2.0×10^7	9.1×10^6-5.2×10^7	-	-
γ_{50} (slope)	5.94	5.67-6.27	-	-

Abbreviations: N = number of clonogens; T_d = repopulation doubling time; T_k = kick-off time for accelerated repopulation.

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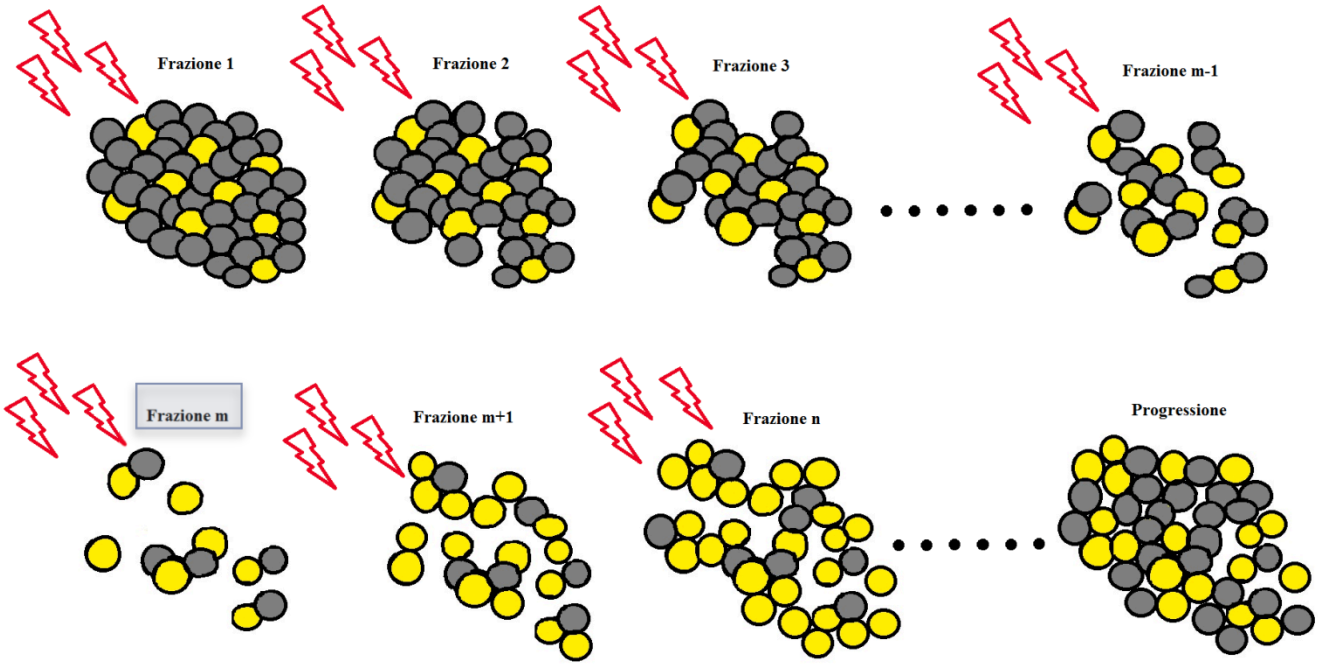
LETTER TO THE EDITOR

Kickoff Time for Accelerated Cell Repopulation During Radiation Therapy: The Hypothesis of Stem Cells

http://dx.doi.org/10.1016/j.ijrobp.2013.08.016

$$N_A = N_0 \cdot e^{-md(\alpha+\beta d)}$$



Tk = m (7/5)

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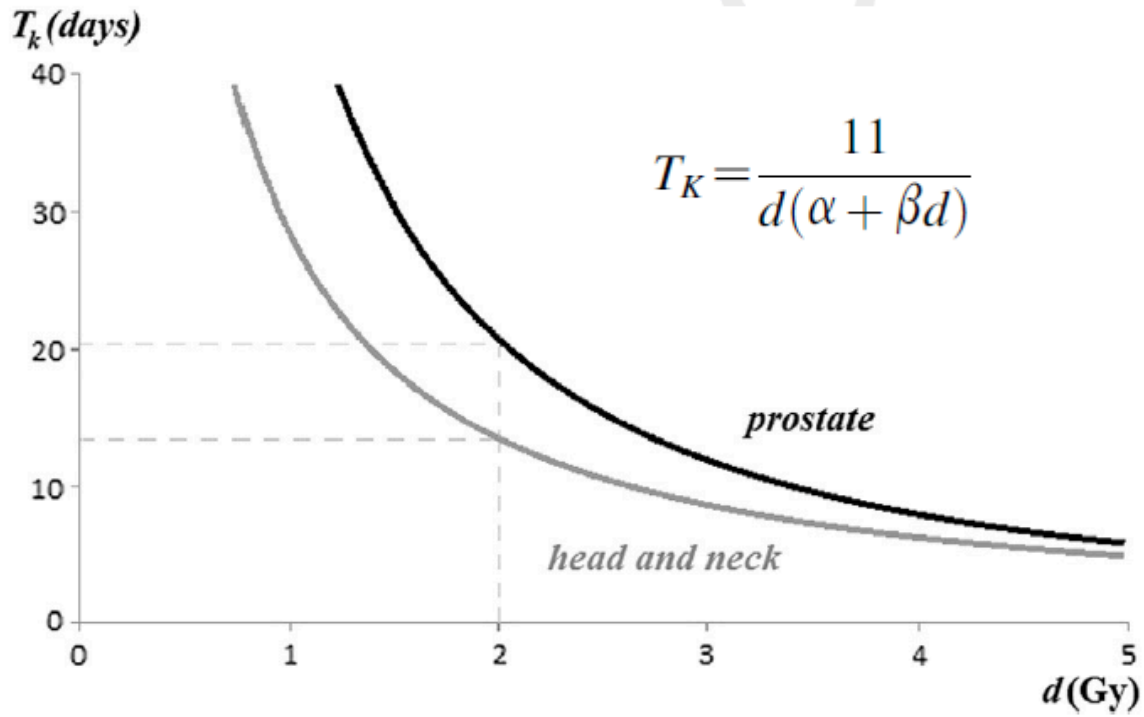
Kickoff Time for Accelerated Cell Repopulation During Radiation Therapy: The Hypothesis of Stem Cells

$$N_A = N_0 \cdot e^{-md(\alpha+\beta d)}$$

Tk = m (7/5)

$$T_K = \frac{7\ln(N_0/N_A)}{5d(\alpha+\beta d)}$$



CONCLUSIONI

- L'attivazione delle cellule staminali varia in base alla radiosensibilità.
  - Il Tk non è unico, varia in base alla patologia e al frazionamento.

- Importanti conseguenze per riformulare modalità di erogazione della dose di radiazione

Thanks for your attention