Simposio AIRO-AIRB

Radiobiologia clinica: impostazione meccanicistica bio-molecolare o modellistica?

Roma 19 Novembre 2012

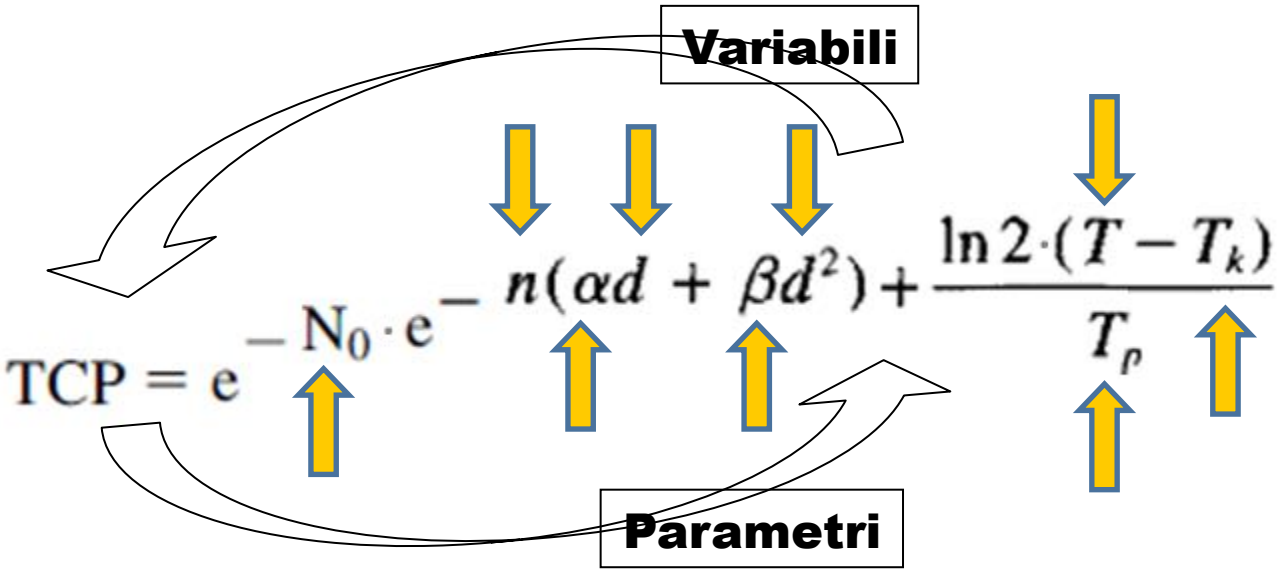
Modelling matematico per la stima dei parametri radiobiologici e dei fattori predittivi della risposta alla radioterapia

Piernicola Pedicini

IRCCS CROB

Istituto di Ricovero e Cura a Carattere Scientifico

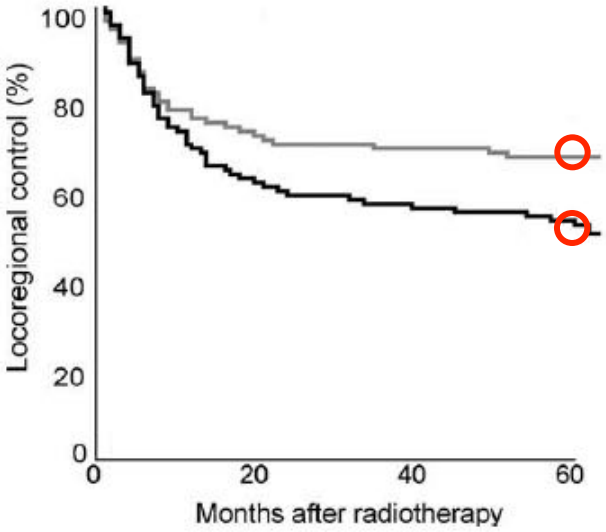
Tumor Control Probability



Clinica ⇒ **Parametri** ⇒ **Variabili** ⇒ **Risultato**

Radiobiologia ⇒ **Risultato** ⇒ **Variabili** ⇒ **Parametri**

Clinical Efficacy Factor



$$LCR_a = e^{-N_0 e^{-\alpha(BED(d)_a - BED(T)_a)}}$$

$$LCR_b = e^{-N_0 e^{-\alpha(BED(d)_b - BED(T)_b)}}$$

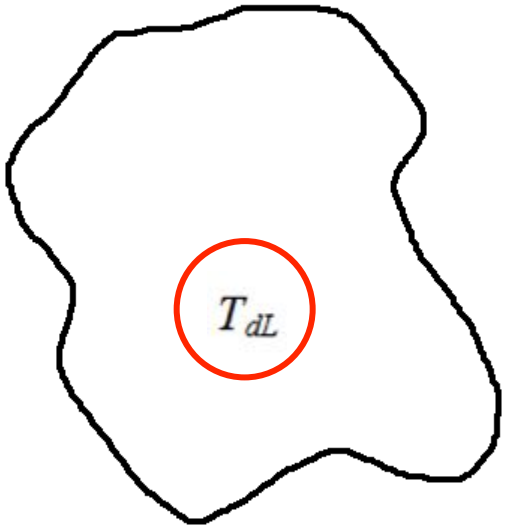
$$\ln\left(\frac{lnLCR_a}{lnLCR_b}\right) = -\alpha\left(BED(d)_a - BED(d)_b\right) + \left(BED(T)_a - BED(T)_b\right)$$

α β T_p N_0 T_k

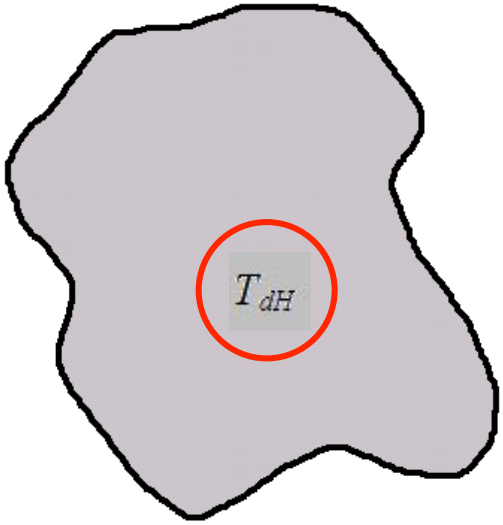
α β T_p

Epidermal Growth Factor Receptor

Low EGFr expression



High EGFr expression



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Radiotherapy and Oncology 74 (2005) 93–100

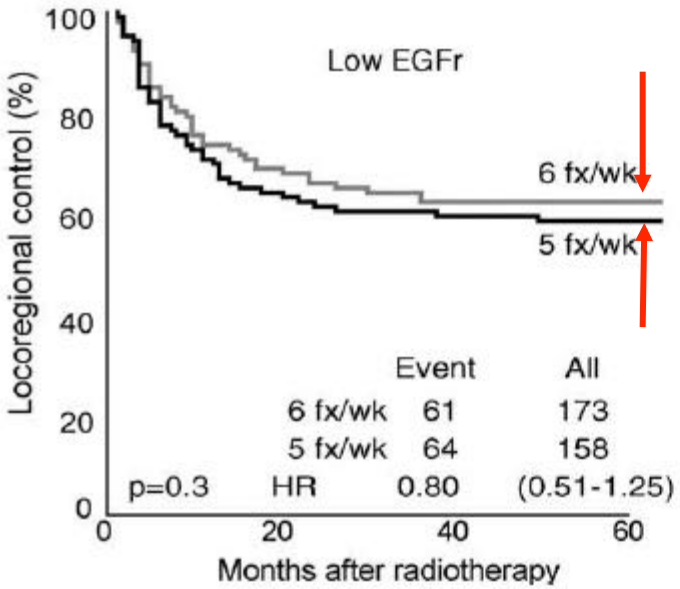
ELSEVIER

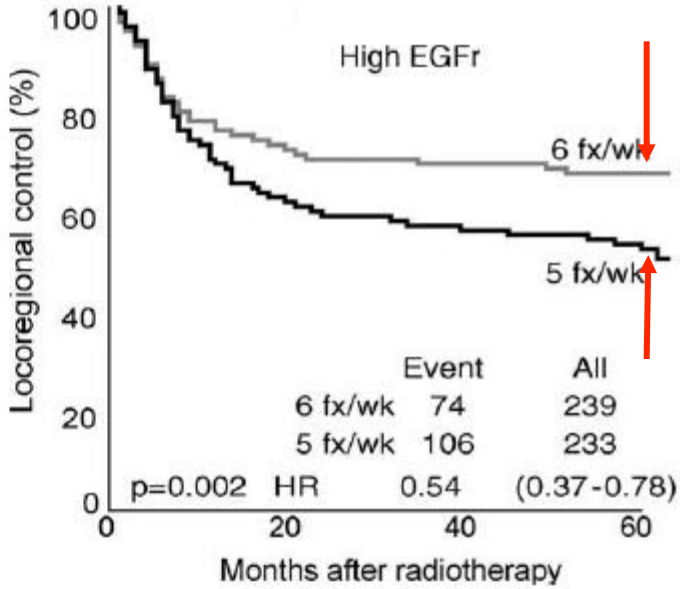
RADIOTHERAPY & ONCOLOGY

www.elsevier.com/locate/radonline

The influence of epidermal growth factor receptor and tumor differentiation on the response to accelerated radiotherapy of squamous cell carcinomas of the head and neck in the randomized DAHANCA 6 and 7 study☆

Jesper G. Eriksen[a,*], Torben Steiniche[b], Jens Overgaard[a],
On behalf of the Danish Head and Neck Cancer study group (DAHANCA)





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Pedicini et al. Radiation Oncology 2012, 7:143
http://www.ro-journal.com/content/7/1/143

RADIATION ONCOLOGY

RESEARCH Open Access

Correlation between egfr expression and accelerated proliferation during radiotherapy of head and neck squamous cell carcinoma

Piernicola Pedicini[1*], Antonio Nappi[1], Lidia Strigari[2], Barbara Alicia Jereczek-Fossa[3,4], Daniela Alterio[3], Marta Cremonesi[3], Francesca Botta[3], Barbara Vischioni[7], Rocchina Caivano[1], Alba Fiorentino[1], Giuseppina Improta[1], Giovanni Storto[1], Marcello Benassi[5], Roberto Orecchia[3,4] and Marco Salvatore[6]

Author	Fractionation	OTT(days)	SI_H %	SI_L %	TCP_H	TCP_L	HR	S
Eriksen AO a [6]	33x2Gy	66	SI≥50	SI<50	0.15	0.44	Y	N
Eriksen AO b [6]	33x2Gy	45	SI≥50	SI<50	0.64	0.55	Y	N
Eriksen AO c [6]	33x2Gy	38	SI≥50	SI<50	0.77	0.57	Y	N
Eriksen RO a [7]	33x2Gy	45	SI≥50	SI<50	0.57	0.63	Y	N
Eriksen RO b [7]	33x2Gy	38	SI≥50	SI<50	0.70	0.62	Y	N
Bentzen JCO a [8]	33x2Gy	45	SI≥40	SI<40	0.30	0.45	N	N
Bentzen JCO b [8]	36x1.5Gy	12	SI≥40	SI<40	0.54	0.49	N	N
Suwinski IJROBP a [9]	35x1.8Gy	47	SI≥33	SI<33	0.33	0.70	N	Y
Suwinski IJROBP b [9]	35x1.8Gy	35	SI≥33	SI<33	0.58	0.73	N	Y
Smid IJROBP a [10]	25x2Gy+5x2.5Gy	~ 46	A/m	M/I	0.69	0.65	N	Y
Smid IJROBP b [10]	25x2Gy+5x2.5Gy	~ 34	A/m	M/I	0.91	0.68	N	Y
Chung IJROBP a [11]	35x2Gy	47	SI≥80	SI<80	0.36	0.61	N	N
Chung IJROBP b [11]	30x1.8Gy+12x1.5Gy	38	SI≥80	SI<80	0.54	0.68	N	N

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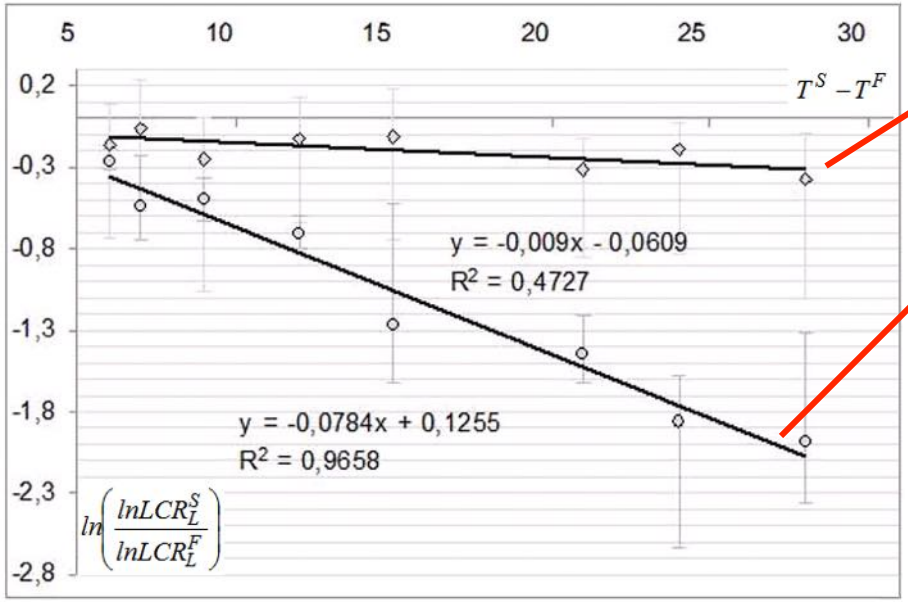
$$T_d = \frac{T_{pot}}{1-\varphi}$$

$$\ln\left(\frac{lnLCR_a}{lnLCR_b}\right) = \alpha\,(BED(T)_a - BED(T)_b) \Rightarrow \ln\left(\frac{\ln LCR_a}{\ln LCR_b}\right) = \frac{\ln 2}{T_d}\cdot(T_a - T_b)$$



***Td* (low) = 77 days** → ***Dprolif* = ~ 0.05 Gy/day**

***Td* (high) = 8.8 days** → ***Dprolif* = ~ 0.44 Gy/day**

***Td* (high) Oral-cavity = 5.9 days**

***Td* (high) Oro-pharinx= 5.9 days**

***Td* (high) Hypo-pharinx = 4.6 days**

***Td* (high) Larinx = 14.3 days**

XXII CONGRESSO AIRO

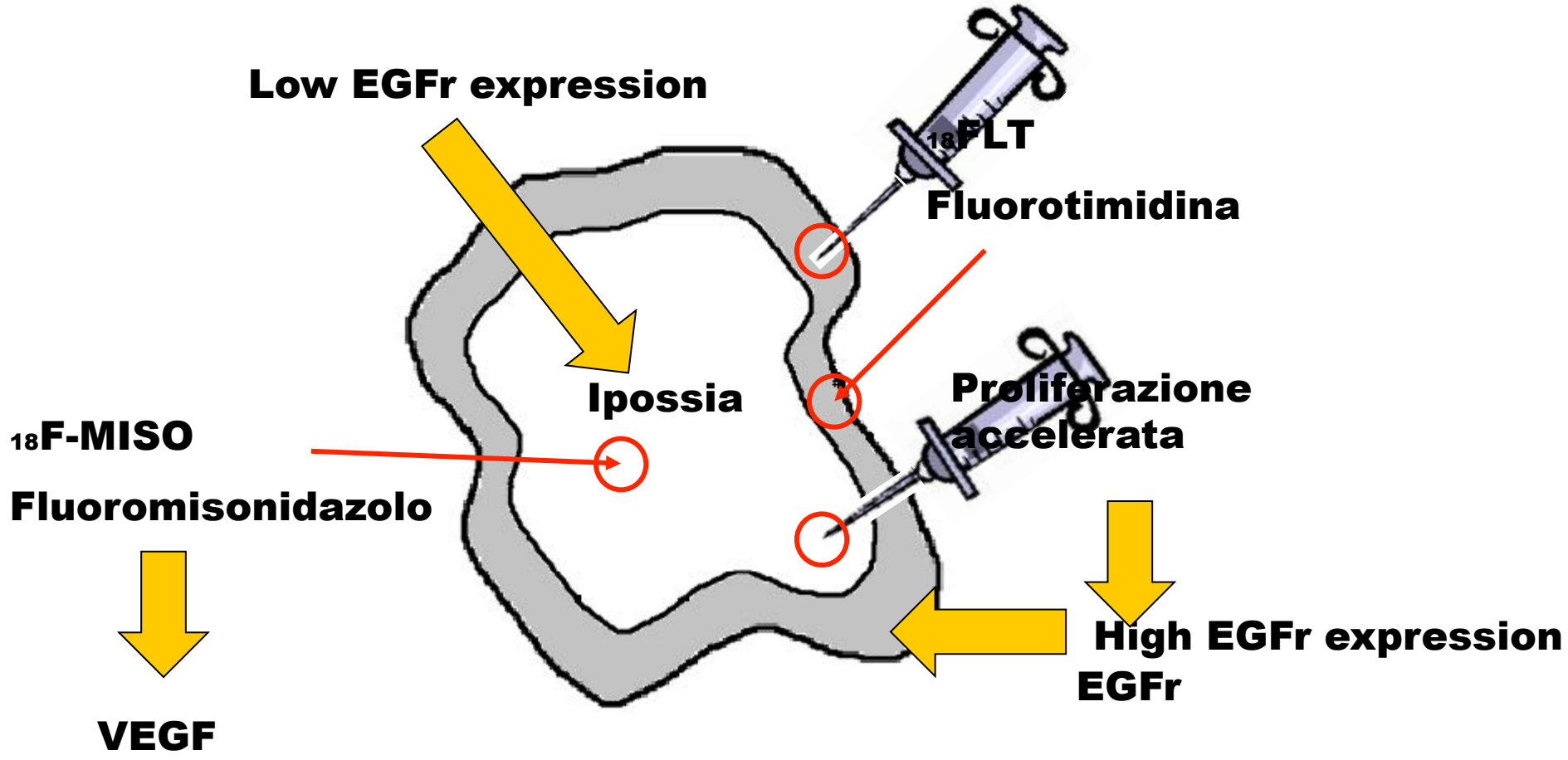
Pedicini et al. Theoretical Biology and Medical Modelling 2012, 9:23
http://www.tbiomed.com/content/9/1/23

THEORETICAL BIOLOGY AND MEDICAL MODELLING

RESEARCH Open Access

Modelling the correlation between EGFr expression and tumour cell radiosensitivity, and combined treatments of radiation and monoclonal antibody EGFr inhibitors

Piernicola Pedicini[1,2,8], Rocchina Caivano[1], Barbara Alicia Jereczek-Fossa[2,3], Lidia Strigari[4], Barbara Vischioni[5], Daniela Alterio[2,3], Marta Cremonesi[6], Francesca Botta[6], Antonio Nappi[1], Giuseppina Improta[1], Giovanni Storto[1], Marcello Benassi[7], Roberto Orecchia[2,3] and Vincenzo Fusco[1]



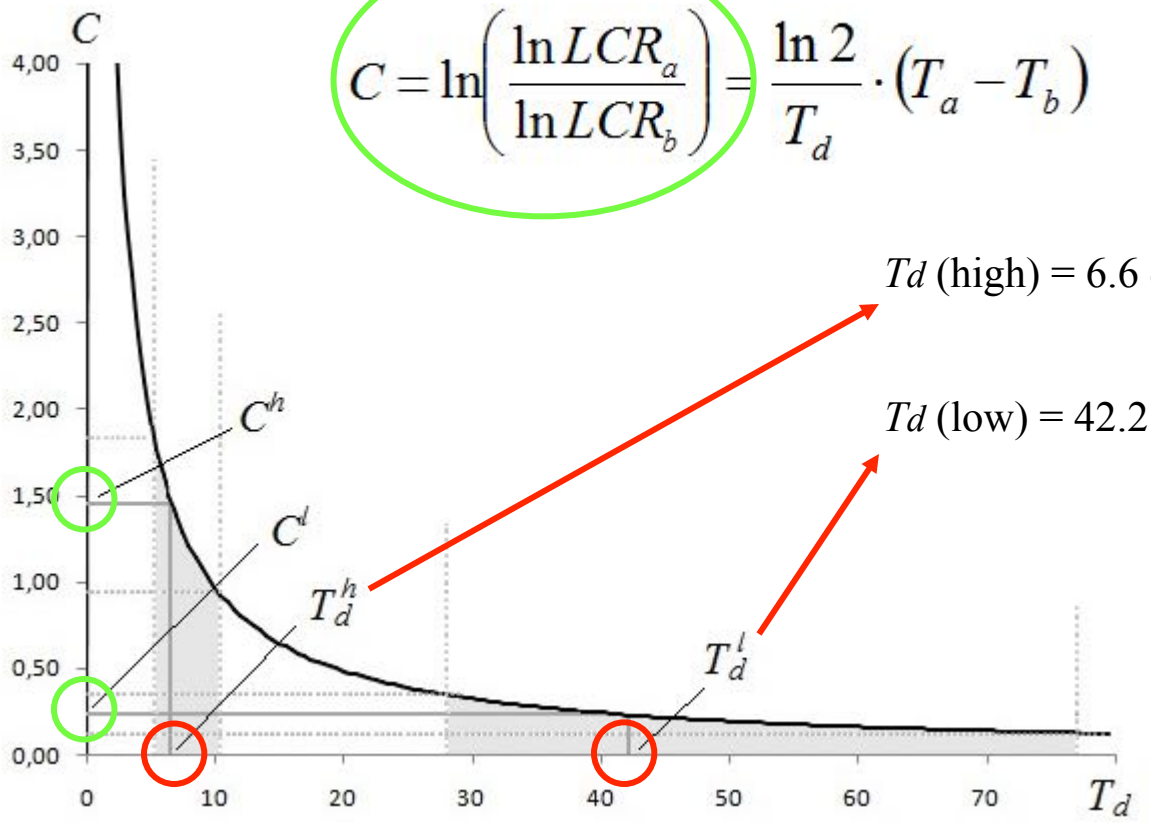
XXII CONGRESSO AIRO

Estimate of the accelerated proliferation by PTEN over expression in postoperative radiotherapy of head and neck squamous cell carcinoma

P Pedicini et al

I.R.C.C.S. C.R.O.B Regional Cancer Hospital, Rionero in Vulture, Italy

$$C = \ln\left(\frac{\ln LCR_a}{\ln LCR_b}\right) = \frac{\ln 2}{T_d} \cdot (T_a - T_b)$$



XXII CONGRESSO AIRO

Estimate of the accelerated proliferation by PTEN over expression in postoperative radiotherapy of head and neck squamous cell carcinoma

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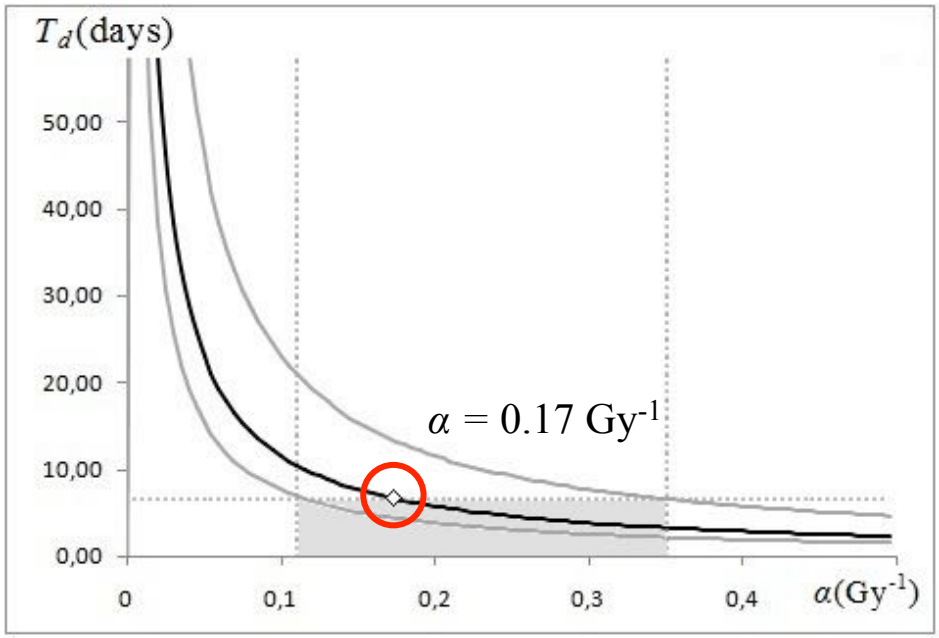
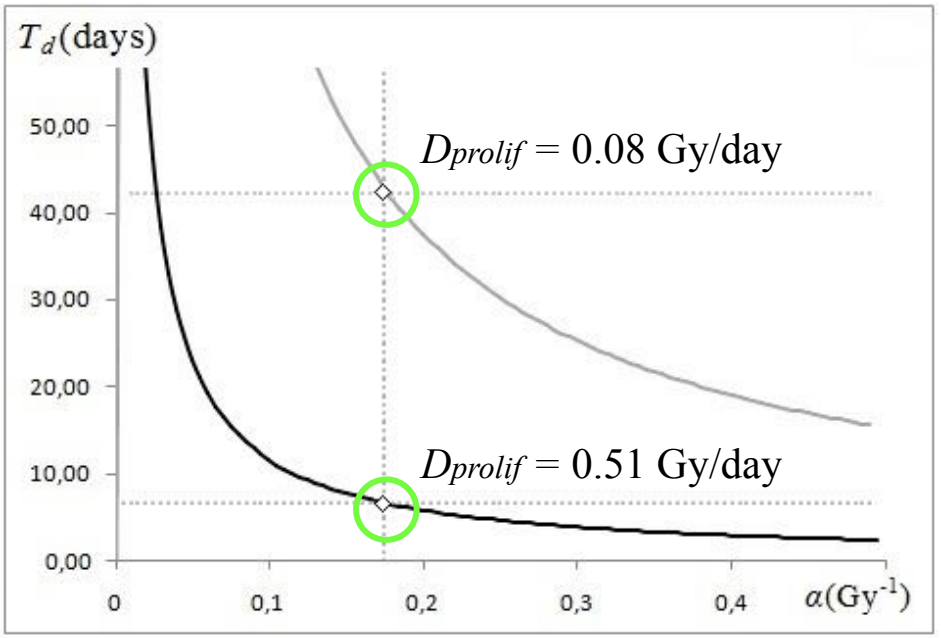
I.R.C.C.S. C.R.O.B Regional Cancer Hospital, Rionero in Vulture, Italy

$$T_d = \frac{T_{pot}}{1-\varphi} = 6.6 \text{ days}$$



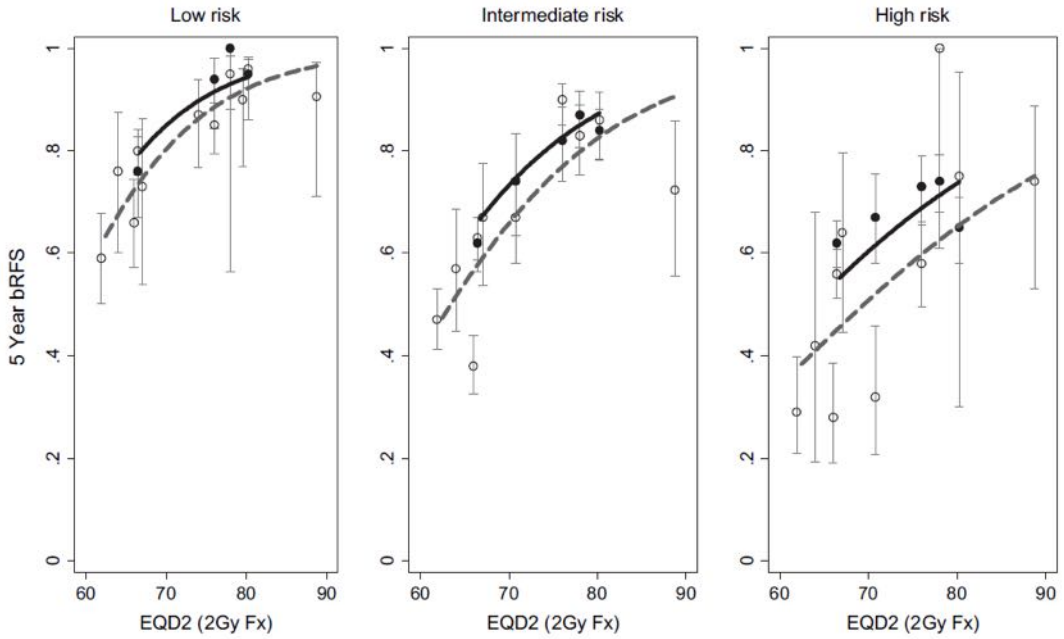


XXII CONGRESSO AIRO

DOSE-FRACTIONATION SENSITIVITY OF PROSTATE CANCER DEDUCED FROM RADIOTHERAPY OUTCOMES OF 5,969 PATIENTS IN SEVEN INTERNATIONAL INSTITUTIONAL DATASETS: α/β = 1.4 (0.9–2.2) GY

RAYMOND MIRALBELL, M.D.,*† STEPHEN A. ROBERTS, PH.D.,‡ EDUARDO ZUBIZARRETA, M.D.,§ AND JOLYON H. HENDRY, PH.D.‖

Int. J. Radiation Oncology Biol. Phys., Vol. 82, No. 1, pp. e17–e24, 2012



20 90 221

k		
Low	3.0	(1.1–5.0)
Intermediate	4.5	(2.6–6.5)
High	5.4	(2.9–7.9)
α (Gy^{-1})		
Low	0.010	(0.000–0.024)
Intermediate	0.036	(0.022–0.050)
High	0.044	(0.023–0.066)
α/β (Gy)		
Low	0.6	(0–1.5)
Intermediate	1.7	(0.9–3.6)
High	1.6	(0.8–2.7)

ARTICLE IN PRESS

Letter to the Editor

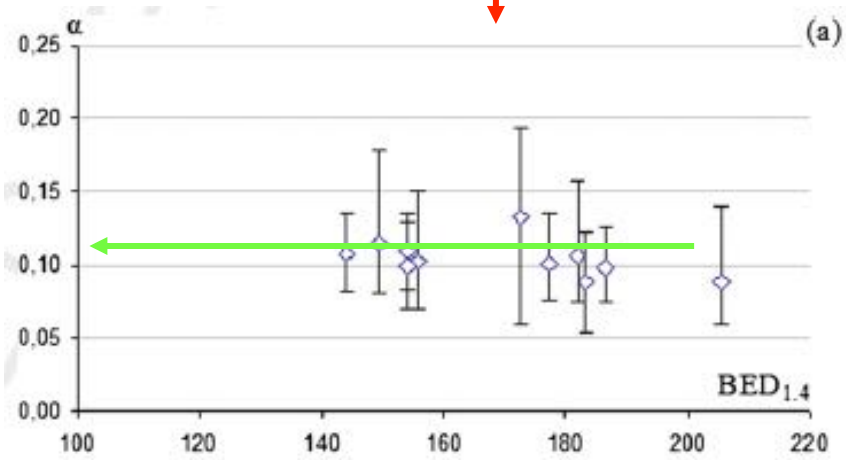
Is a Very Low α/β Ratio Compatible With an Extremely Low Intrinsic Radiosensitivity (α) in Prostate Cancer?

International Journal of Radiation Oncology biology • physics

www.redjournal.org

P. Pedicini R. Caivano L. Strigari M. Benassi A. Fiorentino V. Fusco

$$\alpha = \frac{\frac{\ln 2}{T_d}(T - T_k) - \ln\left(\frac{1}{N}\ln\left(\frac{1}{bRFS}\right)\right)}{BED_{\alpha/\beta}}$$



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ACCEPTED

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Estimation of a Self Consistent Set of Radiobiological Parameters from Hypofractionated versus Standard Radiotherapy of Prostate Cancer

P. Pedicini L. Strigari M. Benassi

International Journal of Radiation Oncology biology • physics

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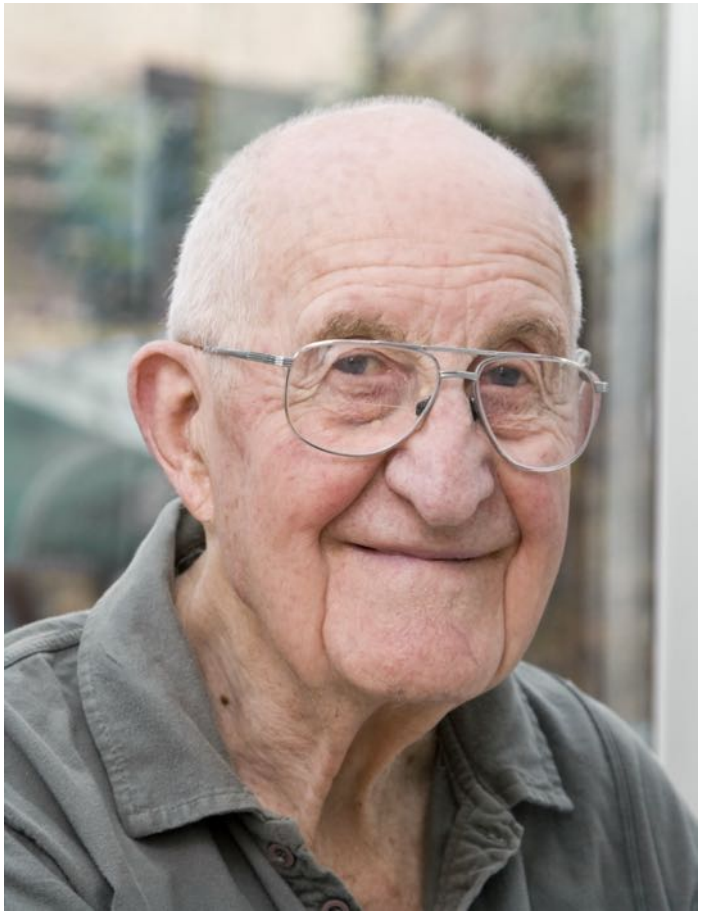
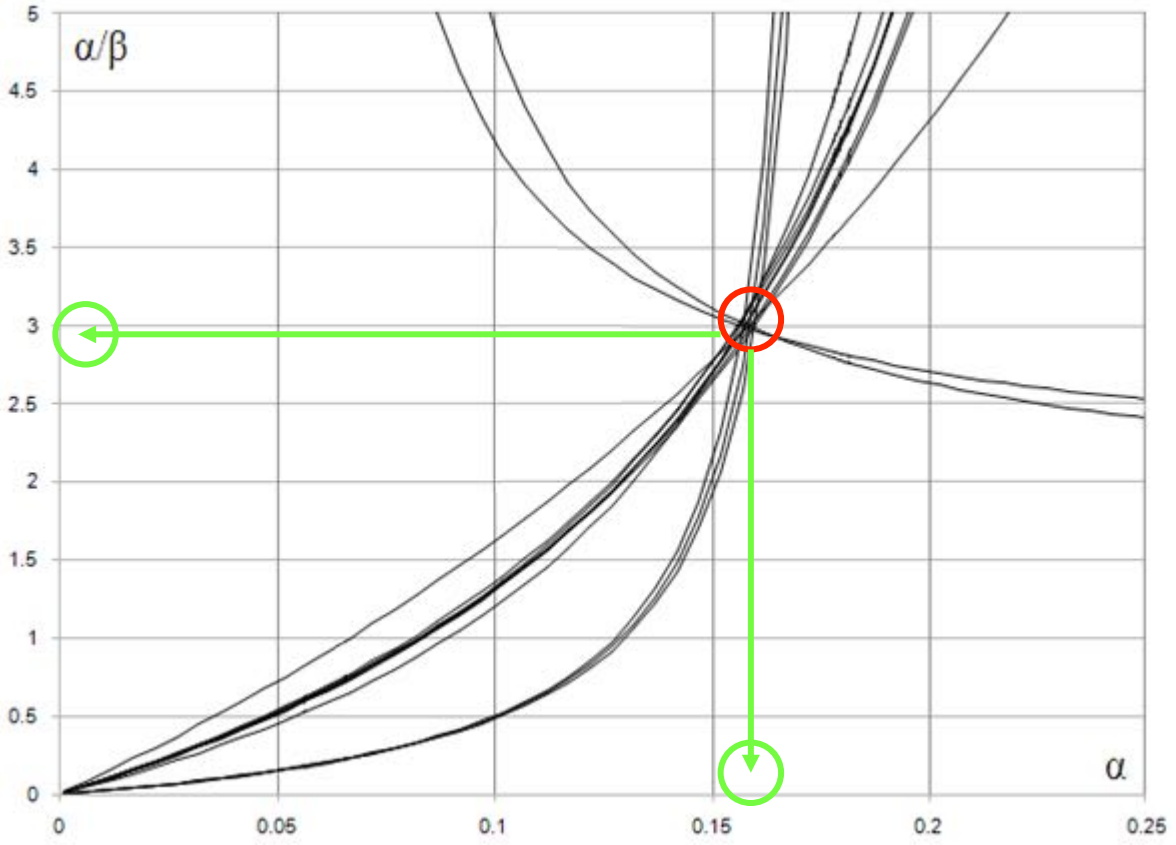
$$\ln\left(\frac{lnLCR_a}{lnLCR_b}\right) = -\alpha\left(BED(d)_a - BED(d)_b\right) + \left(BED(T)_a - BED(T)_b\right)$$





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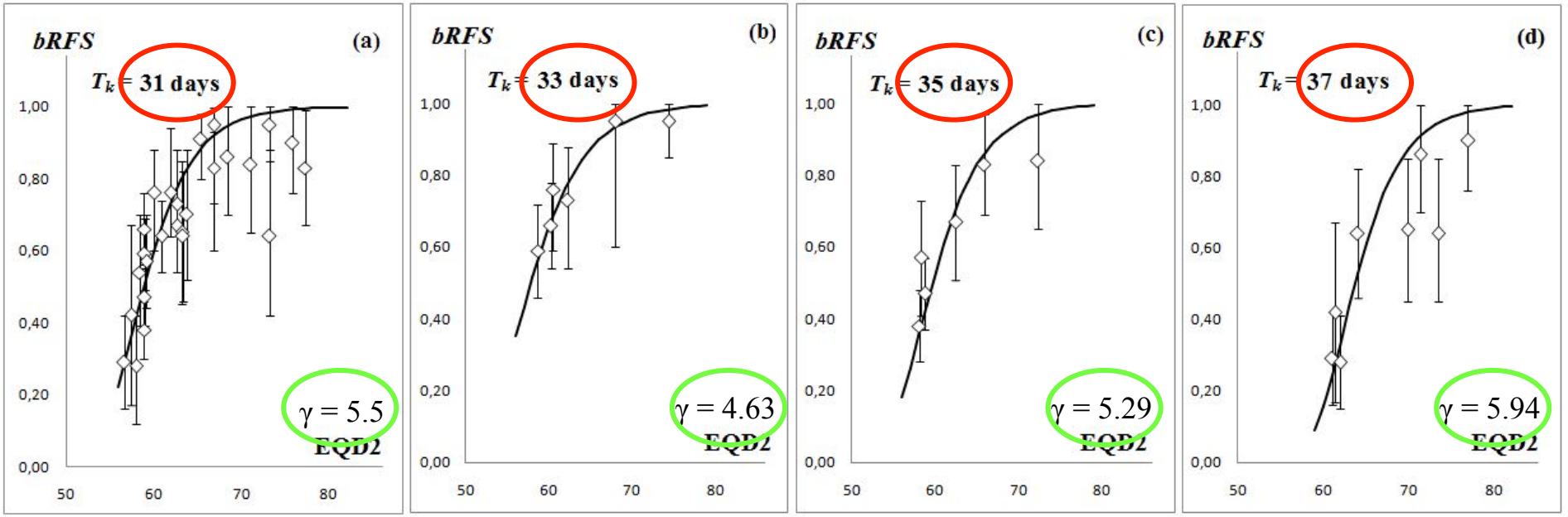

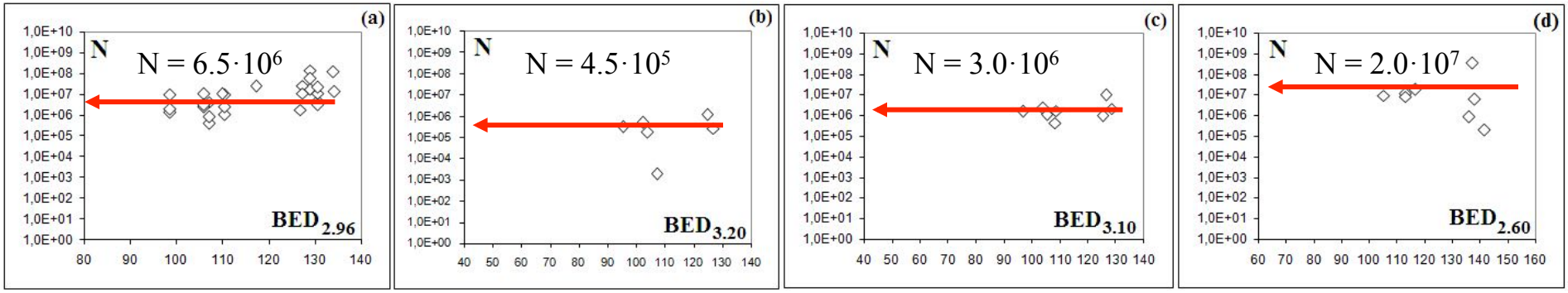

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Estimation of a Self Consistent Set of Radiobiological Parameters from Hypofractionated versus Standard Radiotherapy of Prostate Cancer

P. Pedicini L. Strigari M. Benassi

$$T_d = \frac{T_{pot}}{1-\varphi} = 5.1 \text{ days}$$

$D_{prolif} = 0.52$ Gy/day

Stem cells?

Grazie dell'attenzione

Piernicola Pedicini

IRCCS CROB
Istituto di Ricovero e Cura
a Carattere Scientifico