Curso de Radiobiología
UDELAR
Facultad de Ciencias
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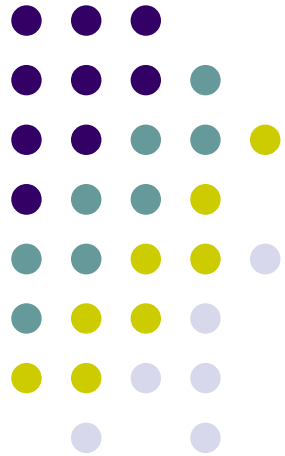


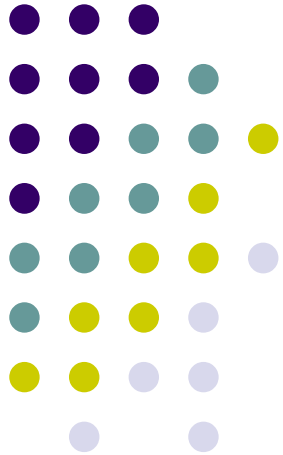
Radiobiología.

Aplicaciones en Radioterapia

Proliferación

Créditos:

Dr. Hatim Fakir



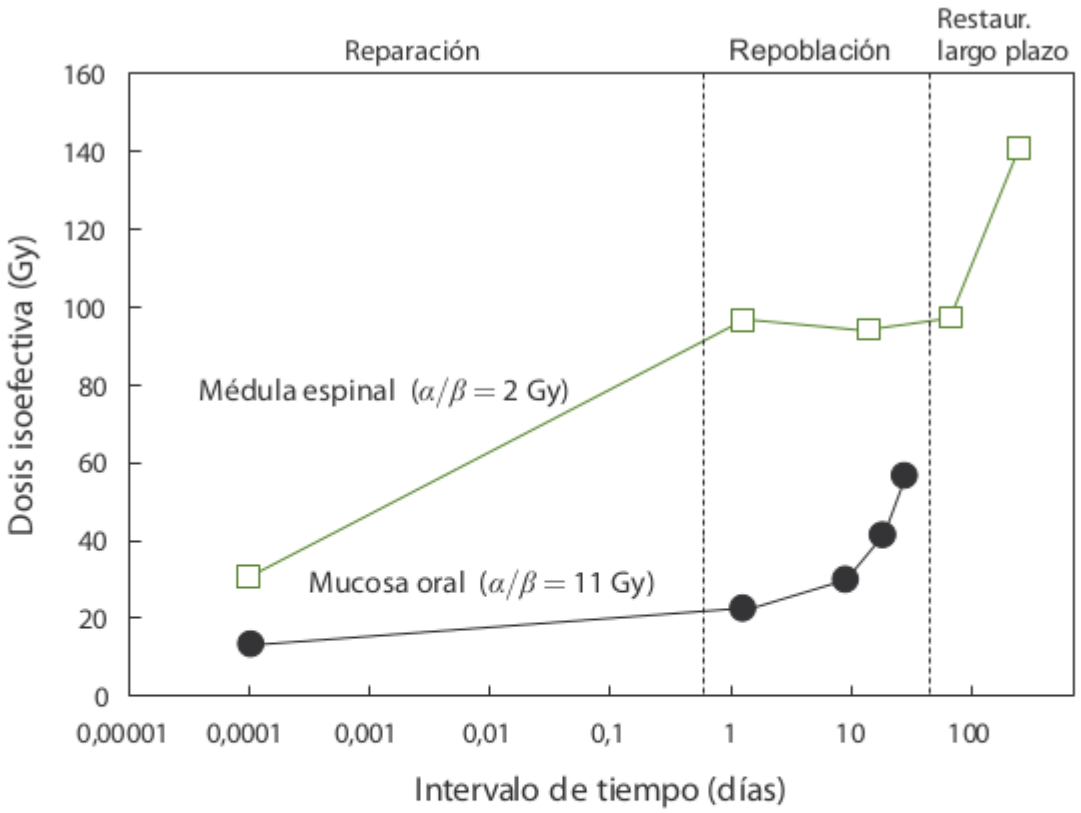


Figura 1. Cambios en la tolerancia de los tejidos normales con el tiempo, expresados como la dosis absorbida total equivalente a la administrada en fracciones de 3 Gy. Para tiempos menores de un día el proceso dominante es la reparación del daño subletal y afecta, fundamentalmente, al tejido de respuesta lenta (α/β bajo). Entre un día y varias semanas (esto es, la duración del programa de Radioterapia) la tolerancia aumenta debido a la proliferación para los tejidos de respuesta rápida (α/β alto). Finalmente, para tiempos largos tras la Radioterapia, algunos tejidos de respuesta lenta, como la médula espinal, se recuperan de parte del daño que les produjo la radiación. Tomada de Dörr (Dörr 2009).

Time-Delayed Repopulation

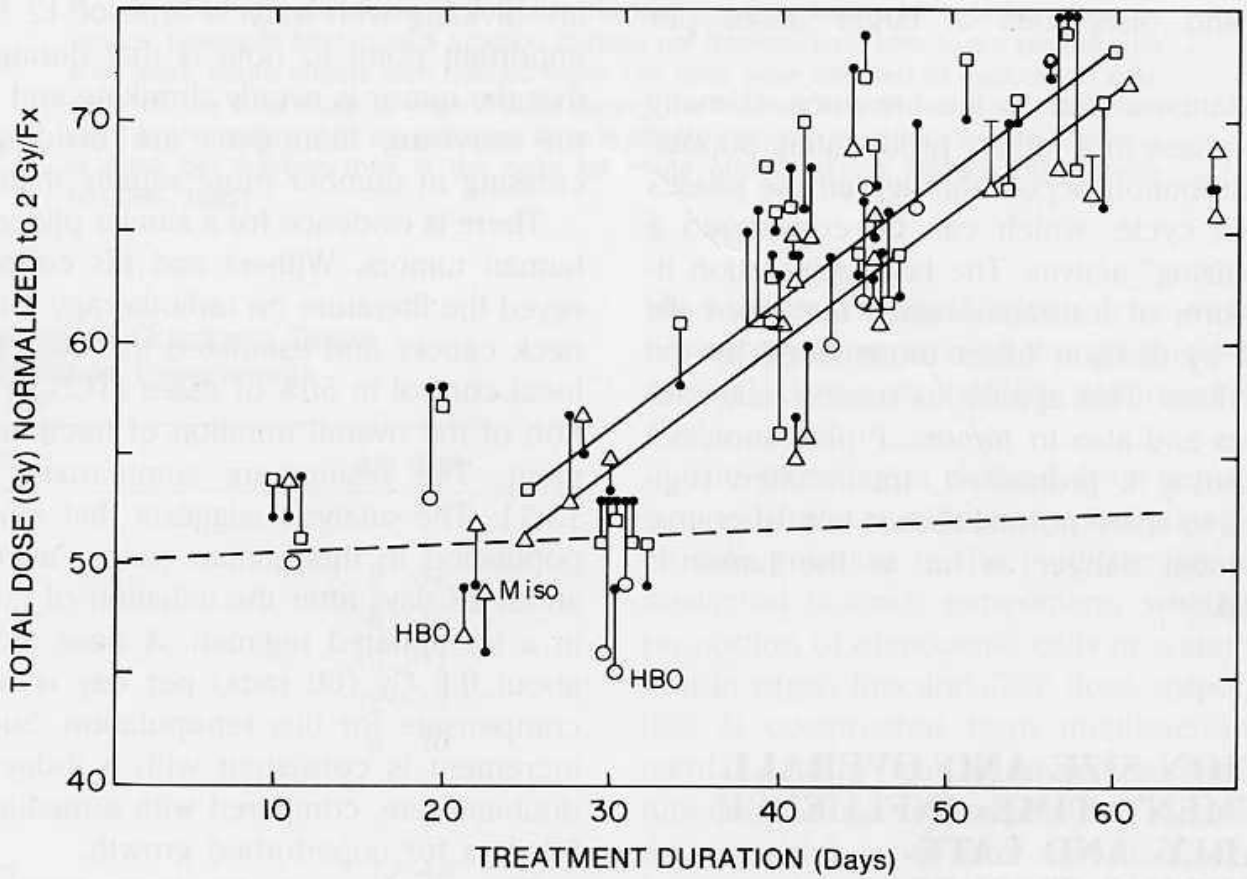


Figure 13-11. Doses to achieve local control in 50% of cases (TCD_{50}), as a function of overall treatment time, for squamous cell tumors of the head and neck. The data points include many published results from the literature, including high-pressure oxygen trials (HBO), and the trial of misonidazole (Miso). The dashed line shows the rate of increase in TCD_{50} predicted from a 2-month clonogen doubling rate. (From Withers HR, Taylor JMG, Maciejewski B: Acta Oncol 27:131–146, 1988)

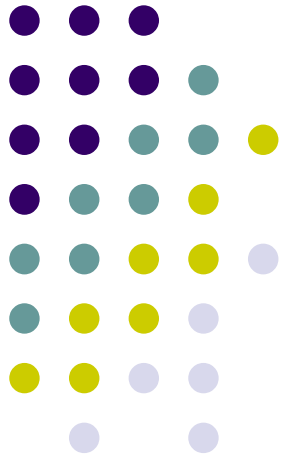
DBE considerando el factor tiempo, k, relacionado con la repoblación celular

$$DBE = \frac{E}{\alpha} = n\,d\left(1 + \frac{d}{\alpha/\beta}\right) - \kappa\,T$$

$$\kappa = \ln 2/(\alpha\,T_D).$$

DBE considerando el factor tiempo, k, relacionado con la repoblación celular acelerada

$$DBE = n\,d\left(1 + \frac{d}{\alpha/\beta}\right) - \kappa\,\mathrm{MAX}(T - T_0, 0)$$



BED including tumour proliferation

$$E = nd(\alpha + \beta d) - \gamma(T - T_k)$$

$$\gamma = \frac{\ln(2)}{T_{pot}}$$

- *T* is overall treatment time
- T_k *: time at which cells start active proliferation (time for kickoff)*
- T_{pot} ~14-21 days

$$BED = \frac{E}{\alpha} = nd\left(1 + \frac{d}{\alpha / \beta}\right) - \frac{\ln 2(T - T_k)}{\alpha T_{pot}}$$

Table 7.4 Cell kinetic parameters of human tumours derived from *in vivo* labelling with iododeoxyuridine (IdUrd) or bromodeoxyuridine (BrdUrd) and measured by flow cytometry

Site	Number of patients	LI (%)	T_S (hours)	T_{pot} (days)
Head and neck	712	9.6 (6.8–20.0)	11.9 (8.8–16.1)	4.5 (1.8–5.9)
Central nervous system	193	2.6 (2.1–3.0)	10.1 (4.5–16.7)	34.3 (5.4–63.2)
Upper intestinal	183	10.5 (4.9–19.0)	13.5 (9.8–17.2)	5.8 (4.3–9.8)
Colorectal	345	13.1 (9.0–21.0)	15.3 (13.1–20.0)	4.0 (3.3–4.5)
Breast	159	3.7 (3.2–4.2)	10.4 (8.7–12.0)	10.4 (8.2–12.5)
Ovarian	55	6.7	14.7	12.5
Cervix	159	9.8	12.8	4.8 (4.0–5.5)
Melanoma	24	4.2	10.7	7.2
Haematological	106	13.3 (6.1–27.7)	14.6 (12.1–16.2)	9.6 (2.3–18.1)
Bladder	19	2.5	6.2	17.1
Renal cell carcinoma	2	4.3	9.5	11.3
Prostate	5	1.4	11.7	28.0

Fraction of cells in S phase (LI), duration of S phase (T_S) and potential doubling time (T_{pot}) were taken from Haustermans *et al.* (1997) and Rew and Wilson (2000). Ranges (in parenthesis) represent variations in median values between studies; ranges for individual tumours are considerably larger.

Basic Clinical Radiobiology. Chapter 7 Table 7.4

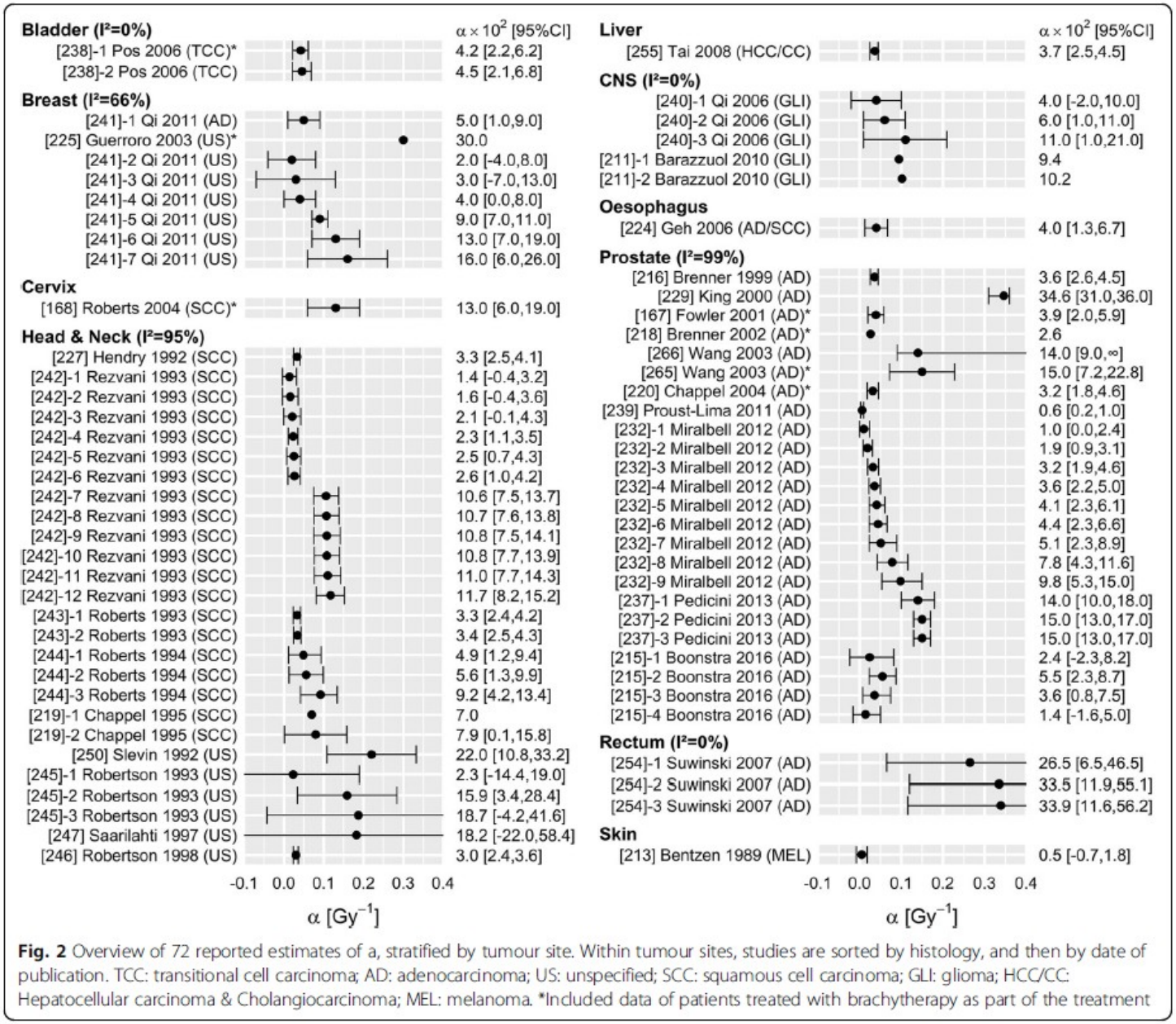


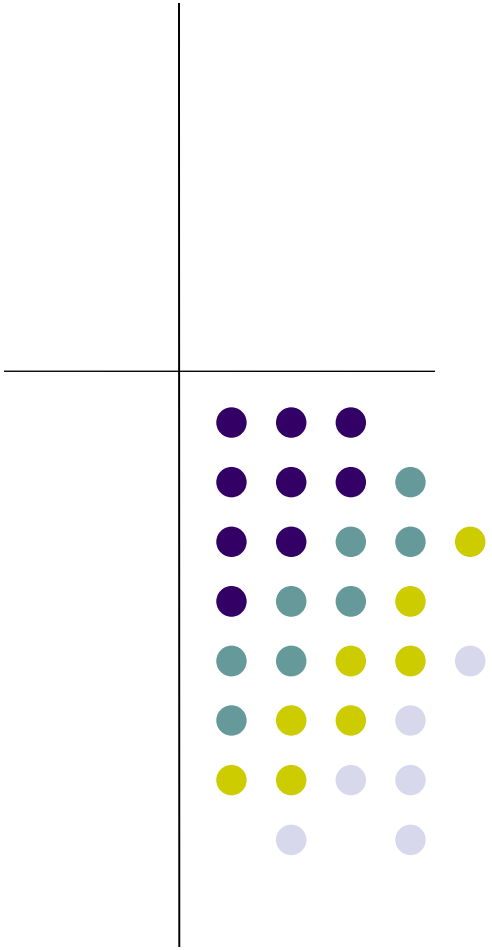
Fig. 2 Overview of 72 reported estimates of a, stratified by tumour site. Within tumour sites, studies are sorted by histology, and then by date of publication. TCC: transitional cell carcinoma; AD: adenocarcinoma; US: unspecified; SCC: squamous cell carcinoma; GLI: glioma; HCC/CC: Hepatocellular carcinoma & Cholangiocarcinoma; MEL: melanoma. *Included data of patients treated with brachytherapy as part of the treatment

The alfa and beta of tumours: a review of parameters of the linear-quadratic model, derived from clinical radiotherapy studies. van Leeuwen et al. Radiation Oncology (2018) 13:96

Tumor	Efecto del tiempo total de tratamiento	Factor tiempo (Gy/día)	Referencias
Cabeza y cuello	Significativo	0,6	Withers y cols. 1988; Maciejewski y cols. 1989
	Significativo	1,09	Suwinski y cols. 2003
Glotis	No significativo	0,48 [−0,88; 1,83][a]	Saarilahti y cols. 1998
Laringe	Significativo	0,64-0,73	Barton y cols. 1992
	Significativo	0,5 (T2), 0,6 (T3)	Slevin y cols. 1992
	Significativo	0,8 [0,5; 1,1][a]	Roberts y cols. 1994
	Significativo	0,6-0,8	Hendry y cols. 1994
	Significativo	0,89 [0,35; 1,43][a]	Robertson y cols. 1998
	Significativo	0,76 [0,51; 1,26][a]	Chappell y cols. 1995
Faringe/laringe	No significativo	0,3 [−9,2; 1,3][a]	Chappell y cols. 1995
Nasofaringe	No significativo	—	Lee y cols. 1995
Orofaringe	Significativo	0,68 [0,05; 1,3][a]	Bentzen y cols. 1991
Esófago	No significativo (T1)	−3,75	
	Significativo (T2)	0,24 [0,1; 1,96][a]	Kajanti y cols. 1995
Pulmón	Significativo	—	Cox y cols. 1993
(non-small cell)	Significativo	0,45	Koukourakis y cols 1996; Chen y cols. 2000
Mama	No significativo		Thames y cols. 1990
	Significativo		Bese y cols. 2005
Cuello uterino	Significativo (est. III)	—	Lanciano y cols. 1993
	Significativo	—	Fyles y cols. 1992; Girinsky y cols. 1993; Pérez y cols. 1995; Petereit y cols. 1995
	No significativo	—	Erridge y cols. 2002
Vejiga	Significativo	0,36	Maciejewski y Majewski 1991
	No significativo	—	De Neve y cols. 1995; Moonen y cols. 1998
	Significativo	0,20	Majewski y cols. 2004
Próstata	No significativo	—	Kajanti y cols. 1993
	Significativo (si $D > 72$ Gy)	—	Pérez y cols. 2004
	Significativo	—	D'Ambrosio y cols. 2008
	Significativo	0,24 [0,03; 0,45][a]	Thames y cols. 2010
	Significativo	0,34 [0,21; 0,47][a]	Miralbell y cols. 2012

[a] Intervalo de confianza del 95%

Tabla 1. Resultados de varios estudios clínicos sobre la influencia del tiempo total de tratamiento en el control local y factor tiempo estimado en ellos para varios tipos de cáncer. El factor tiempo para la ecuación de isoefecto, κ, se calcula multiplicando el factor tiempo de esta tabla, que corresponde a un esquema de 2 Gy por fracción, por $[1 + 2/(\alpha/\beta)]$, donde α/β se toma de acuerdo con el tipo de tumor considerado (Hendry y cols. 1996).



Example 3

- A patient is scheduled for preoperative radiotherapy with a prescription of 5 fractions of 5Gy each (Mon.-Fri). Due to machine breakdown, Wednesday's treatment was missed. What dose is required for Thurs. and Fri. treatment to yield the same tumour isoeffective dose?
- What effect does this have on the normal tissue in the area?