Practical radiobiologic concepts all physicists should know well

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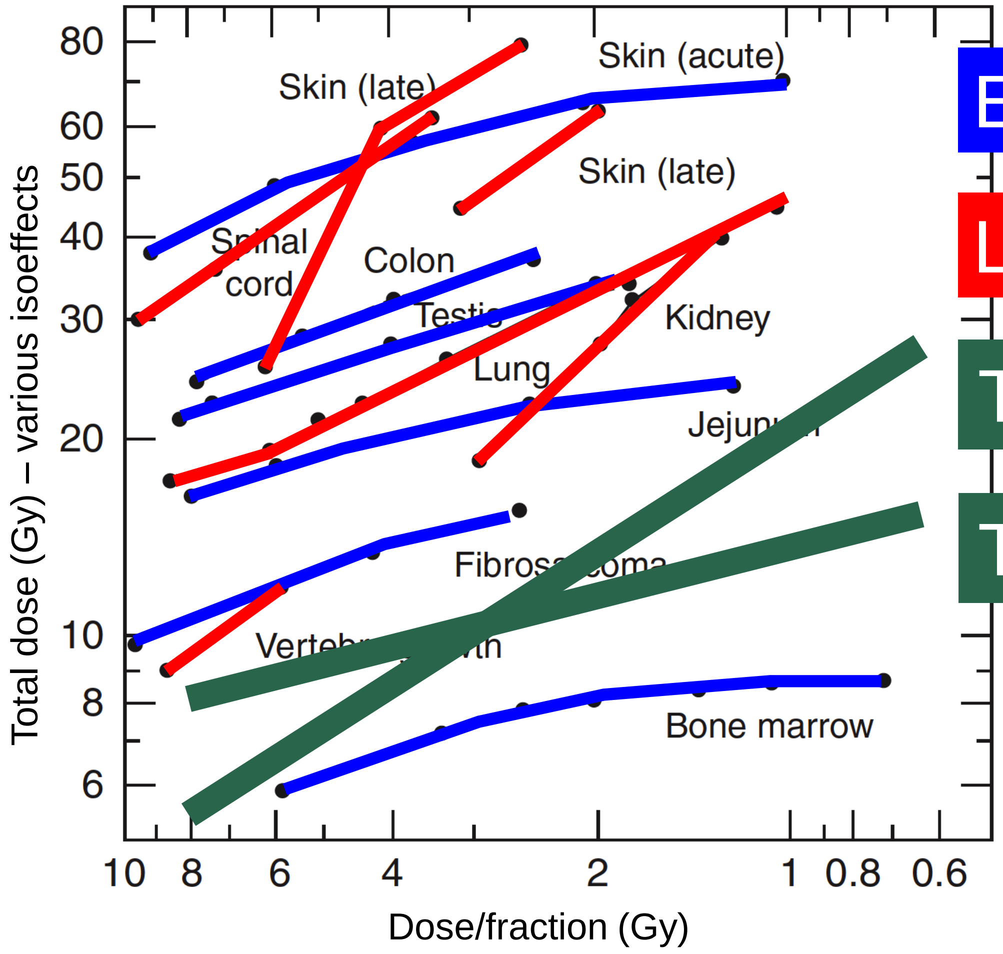
What we will cover

- Total dose versus dose per fraction:
  α/β, BED, EQD2
- Incomplete repair
- Account for time between fractions <24 h
- Account for extended delivery times for each fraction
- Changes in overall time
- Gamma values
- Retreatment – review chapter 23 in BCR 5



Early

Late

Tumor: give Hypo

Tumor: give Hyper

Thames et al.
Int J Radiat Oncol Biol Phys
1982;8:219

EQD2

EQuivalent **D**ose in **2**-Gy fractions

$$\boxed{\mathrm{EQD2} = D\left(\frac{d + a/b}{2 + a/b}\right)}$$

$$\mathrm{BED} = \mathrm{EQD0} = D\left(1 + \frac{d}{a/b}\right) = \mathrm{EQD2}\left(1 + \frac{2}{a/b}\right)$$

EQD2 is recommended by ICRU (Bentzen et al 2012)

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EQD2 simple example

Patient has metastatic bone pain localized to the 5th thoracic vertebra. Propose palliative treatment of 4 × 5 Gy which includes spinal cord. Is this safe?

Take α/β = 2 Gy for radiation myelopathy

$$\mathrm{EQD2} = 20\left(\frac{5+2}{2+2}\right) = 35$$

Currently accepted limit on spinal cord dose from QUANTEC:
50 Gy in **2-Gy** fractions

Incomplete repair

2 fractions per day

$$\mathrm{EQD2} = D\left(\frac{d\left(1+H_m\right)+a/b}{2+a/b}\right)$$

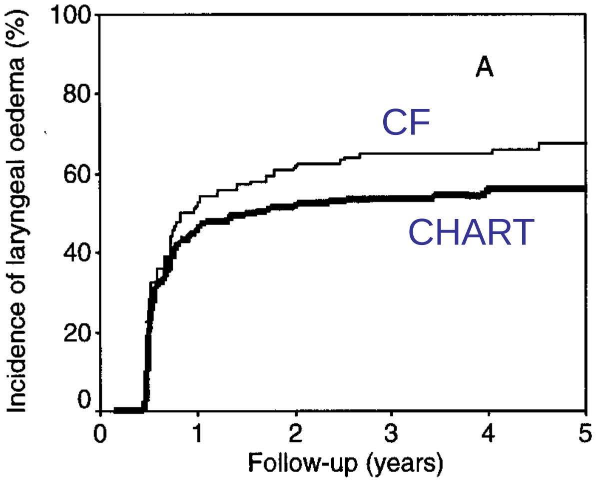
$$H_m = \exp\left(\frac{-\,\mathrm{D}T\ln 2}{T_{1/2}}\right)$$

e.g. if $\Delta T = T_{1/2}$ $\quad H_{\mathrm{m}} = 0.5$

if $\Delta T = 24$ h $\quad H_{\mathrm{m}} < 0.04$

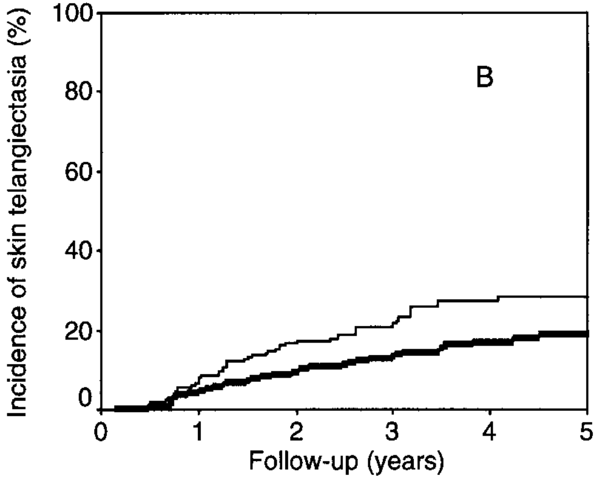
Repair $T_{1/2}$: CHART head and neck

Laryngeal Edema



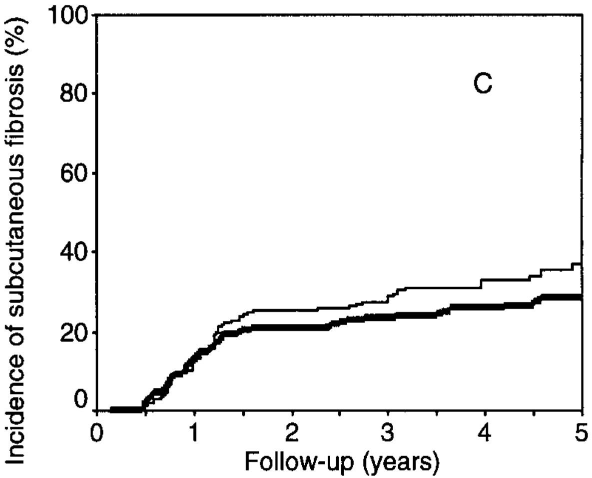
4.9 h (3.2–6.4)

Telangiectasia



3.8 h (2.5–4.6)

s.c. Fibrosis



4.4 h (3.8–4.9)

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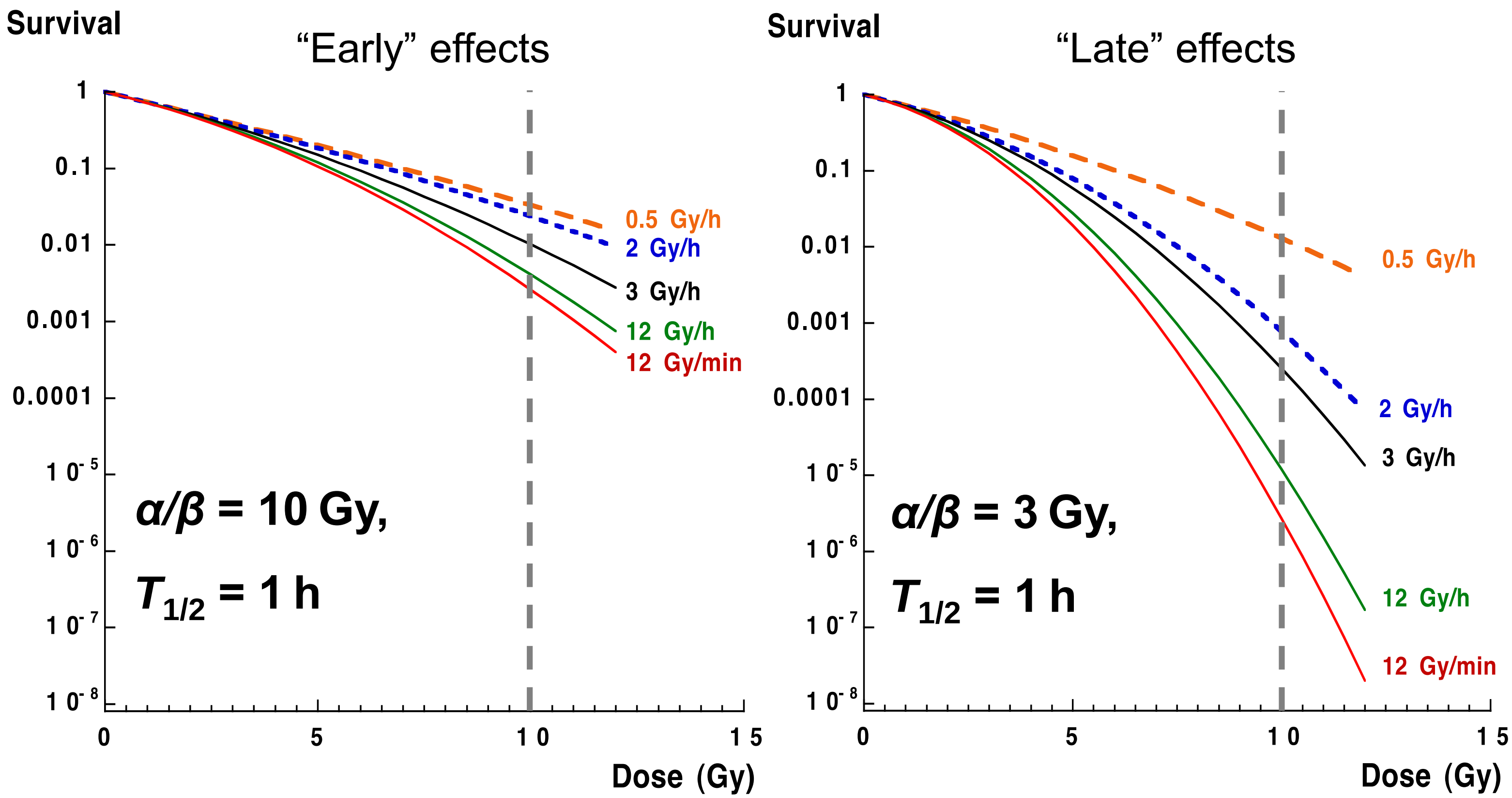
Bentzen et al. *Radiother Oncol* 53:219-26, 1999

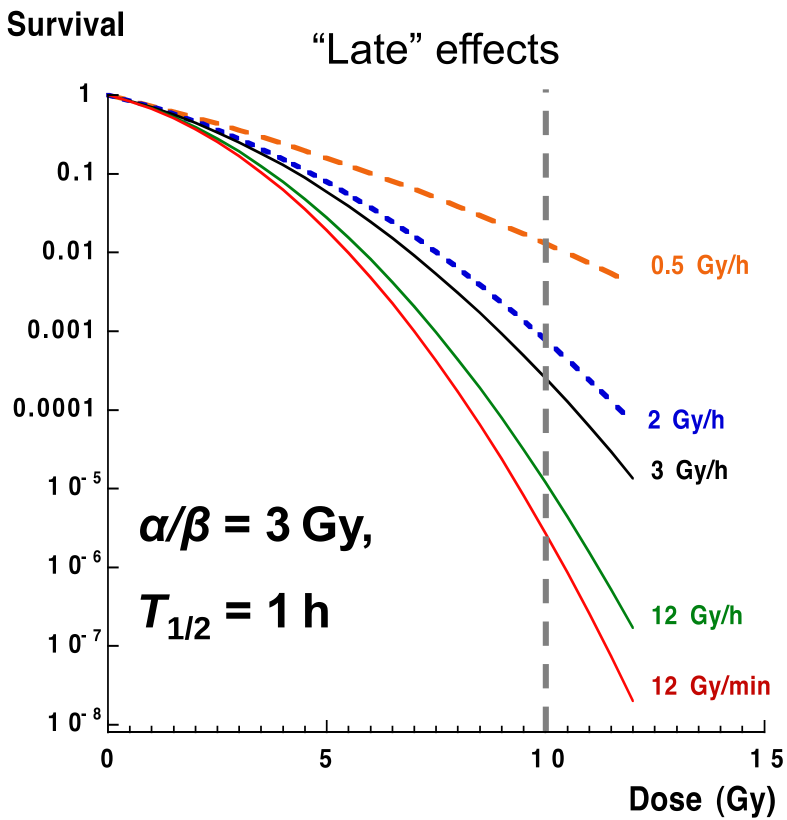
Slow repair in late reacting tissues

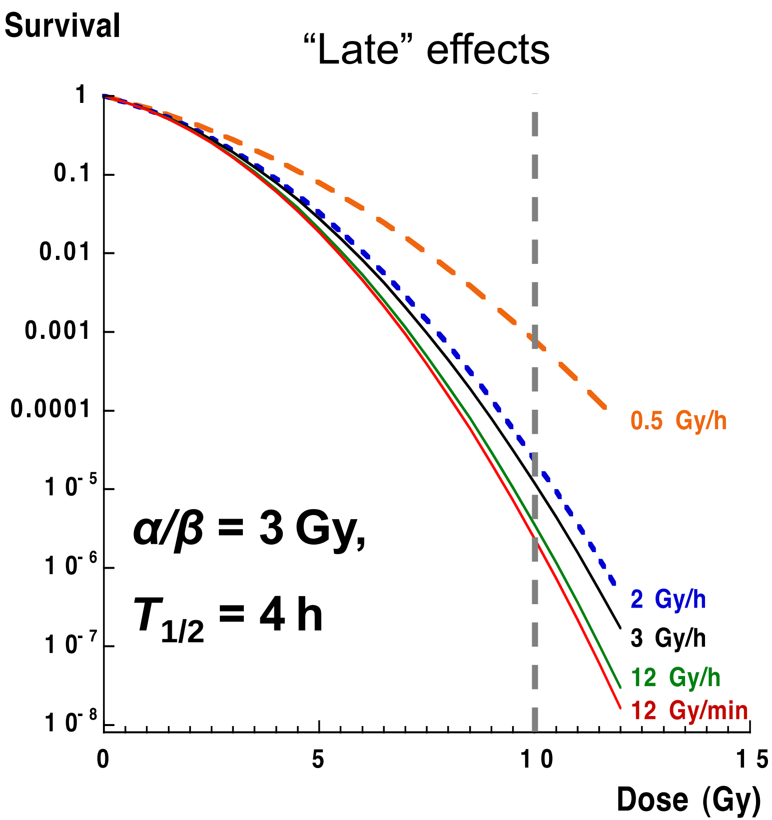
- Do **NOT** do 3 fractions per day, even avoid 2
- If 2 per day, space as far apart as possible (max 12 h)
- Avoid 2 per day more than once per week
  - do it on Friday
  - safer to give the extra fraction on the Saturday
- Leave longer times between larger dose fractions
  - safer to do SBRT no quicker than 3 × per week

Dose rate effect: variation in α/β



Low α/β: variation in $T_{1/2}$

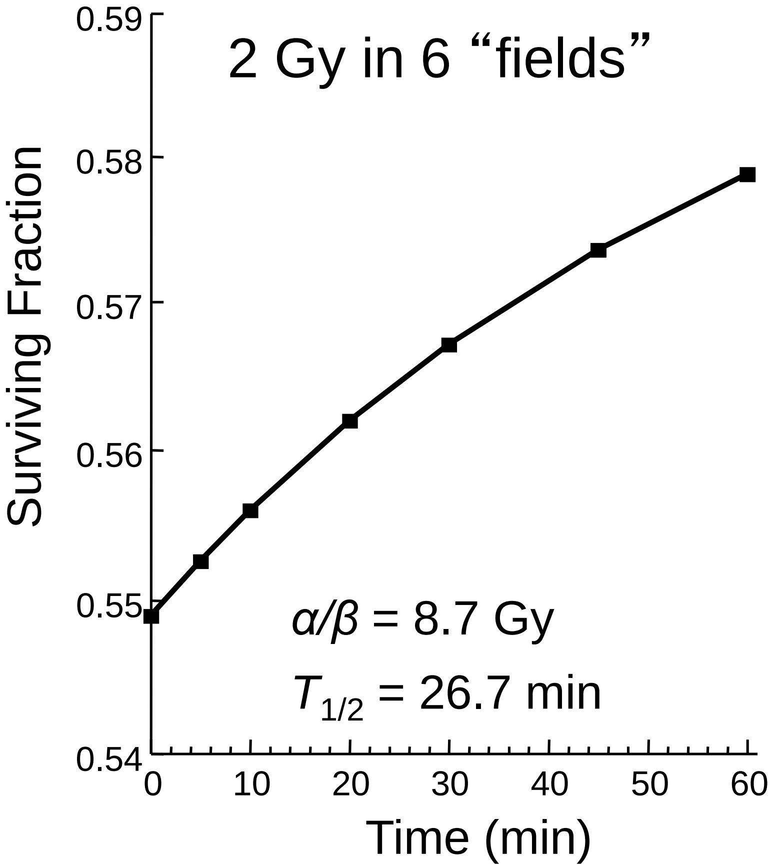




Dose rate effect

- For **short** repair half-times (<1.5 h), α/β is more important
- For **longer** repair halftimes (>1.5 h), α/β is less important and effectiveness is dominated by $T_{1/2}$

Prostate PC3



Loss in effective dose:

Acute to 60 min: **8**%

5 min to 45 min: **6**%

5 min to 30 min: **4**%

Joiner et al. *Med Phys* 2010;37:2457-65

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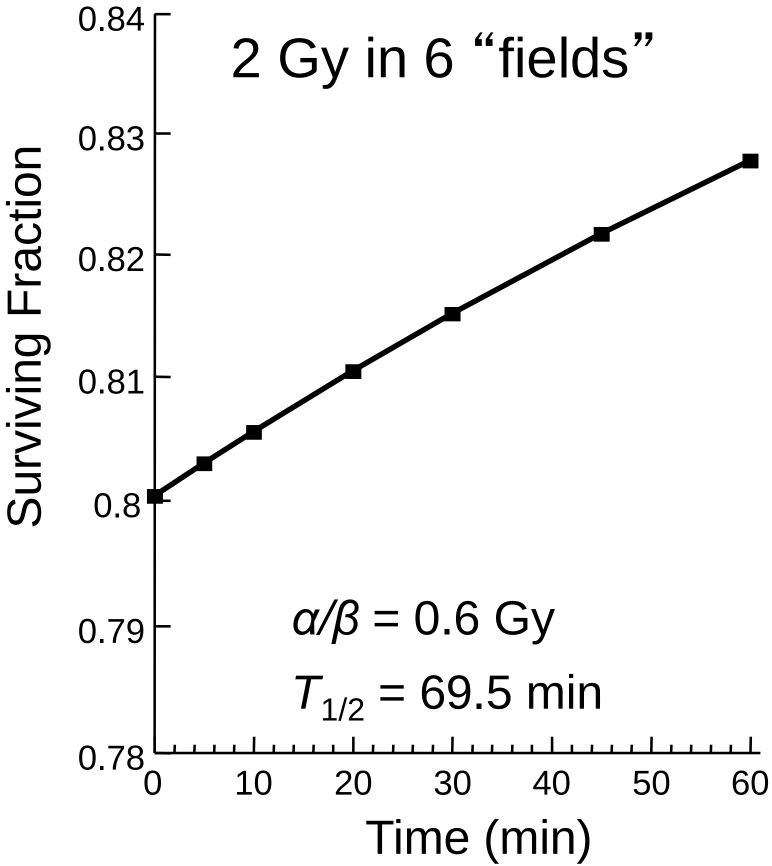
Glioblastoma HGL21



Loss in effective dose:

Acute to 60 min: **18**%

5 min to 45 min: **12**%

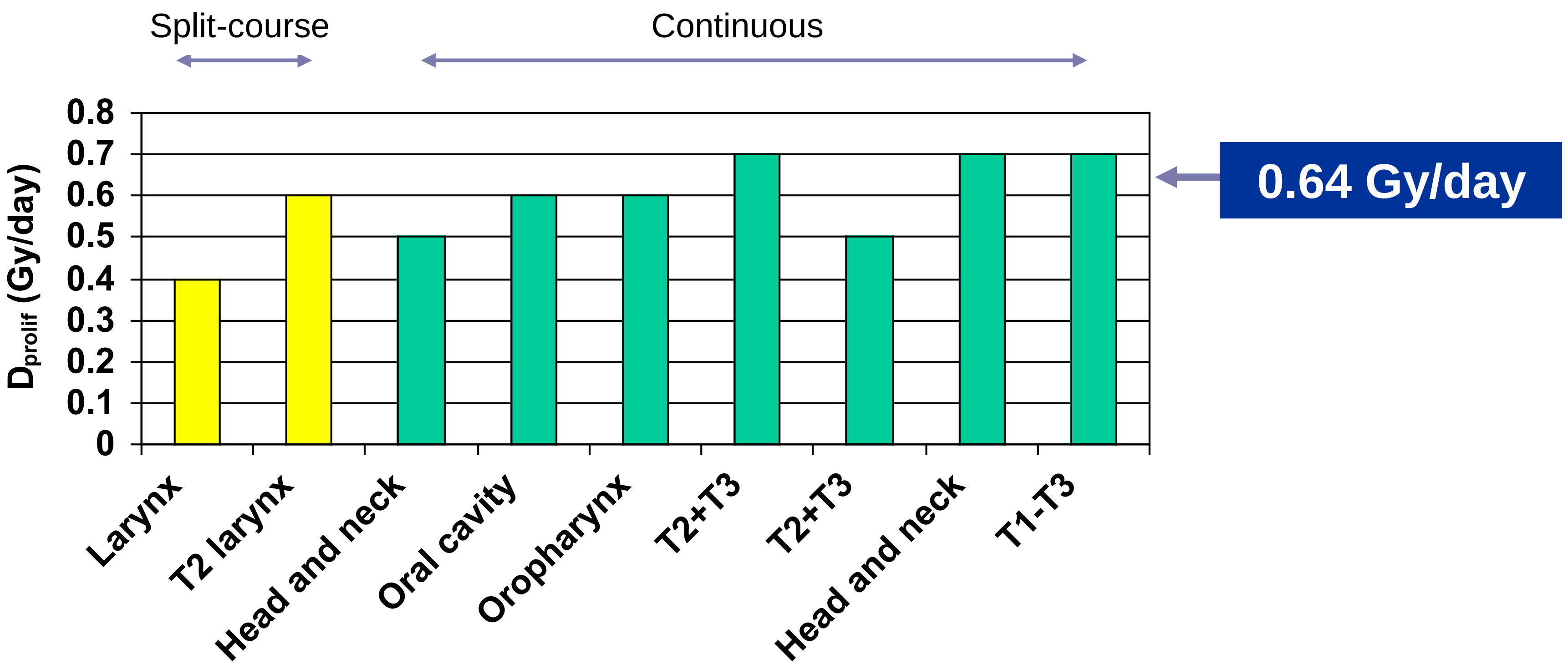
5 min to 30 min: **7**%

Joiner et al. *Med Phys* 2010;37:2457-65

Avoid long dose delivery times

- Patient inconvenience
- Can be significant loss in effective dose
- Tumor loses more effective dose (short $T_{1/2}$)
- Late effects lose less effective dose (long $T_{1/2}$)
- More variability in treatment outcome

Overall treatment time: SCC head and neck



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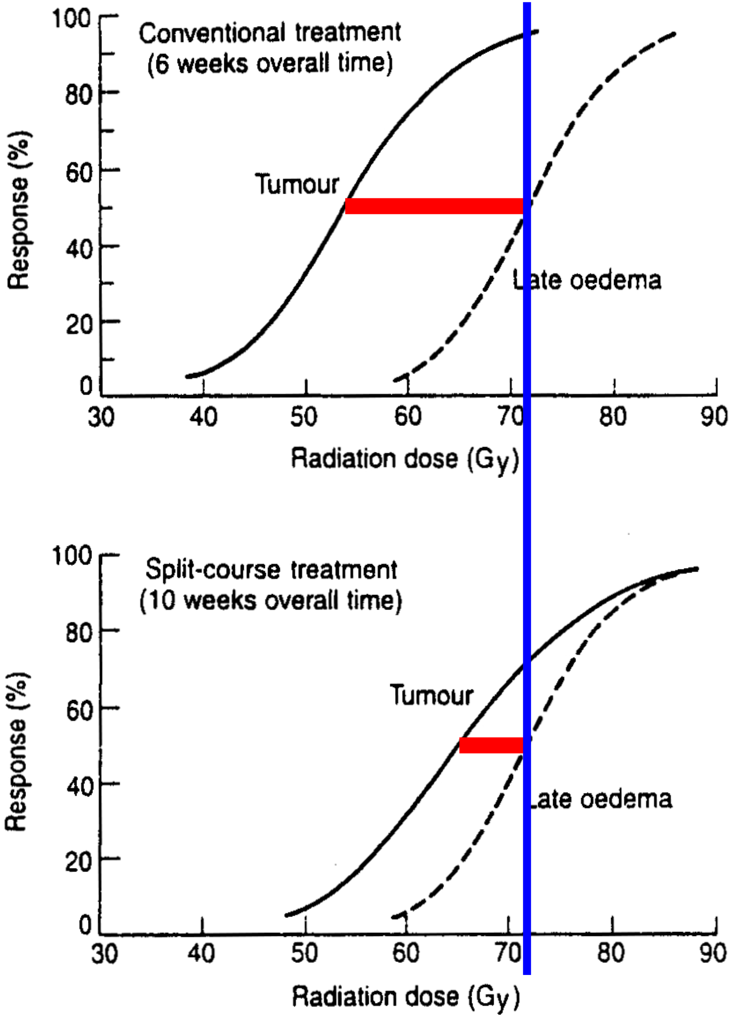
Hendry et al. *Clin Oncol* 1996;8:297

Split course treatment

Protraction of
overall treatment time
is detrimental



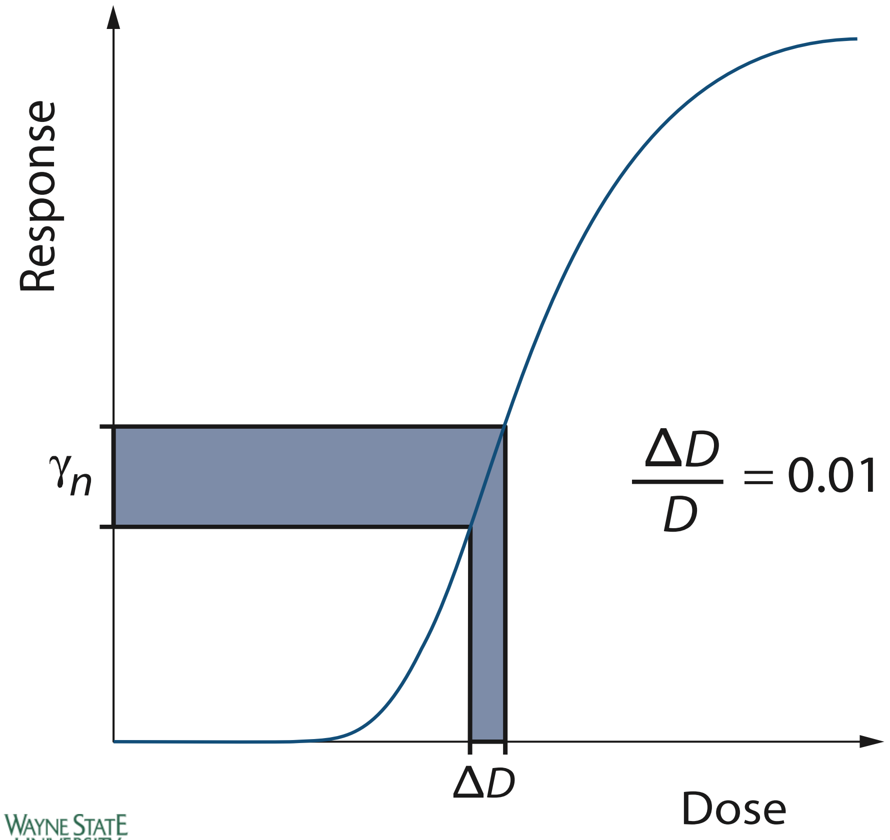
Bentzen and Overgaard (1996)

Lost dose from overall treatment time extension

	D_{prolif} Gy day^{-1}	T_k days	Source
Head & Neck	0.64	30	Hendry et al
NSCLC	0.60	30?	Bentzen et al
Oesphagus	0.59		Geh et al
Prostate	0.24	52	Thames et al
Breast	0.60		Haviland et al
Medulloblastoma	0.52	21	Hinata et al
GBM	0.30	37	Pedicini et al

Note: D_{prolif} is shown here in EQD2

Conversion of dose to effect: Gamma



Normalized
dose response gradient, γ :

$$DP \approx g \frac{DD}{D}$$

$\boxed{\text{1\% change in dose gives increase in response} = \gamma\ \%}$

Usually defined at
the steepest part of curve:
With Poisson model,
at Response = 37% (0.3679…, e^{-1})

Bentzen SM. *Radiother Oncol* 1994;32:1-11

Very important principles

- Never extend overall time
- Avoid unscheduled gaps during treatment
- If gaps occur, compensate without extending overall time
- Automatic treatment acceleration (gaining effective dose) usually occurs with hypofractionation/SBRT
- Retreatment – ask an expert!

What we have covered

- Total dose versus dose per fraction – Know α/β, use EQD2
- Incomplete repair – Avoid it if possible
- Account for it if time between fractions <24 h
- Avoid long delivery times for each fraction
- Never extend overall time
- Using Gamma can shock you!