Workshop 1
Part 2

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Learning objectives

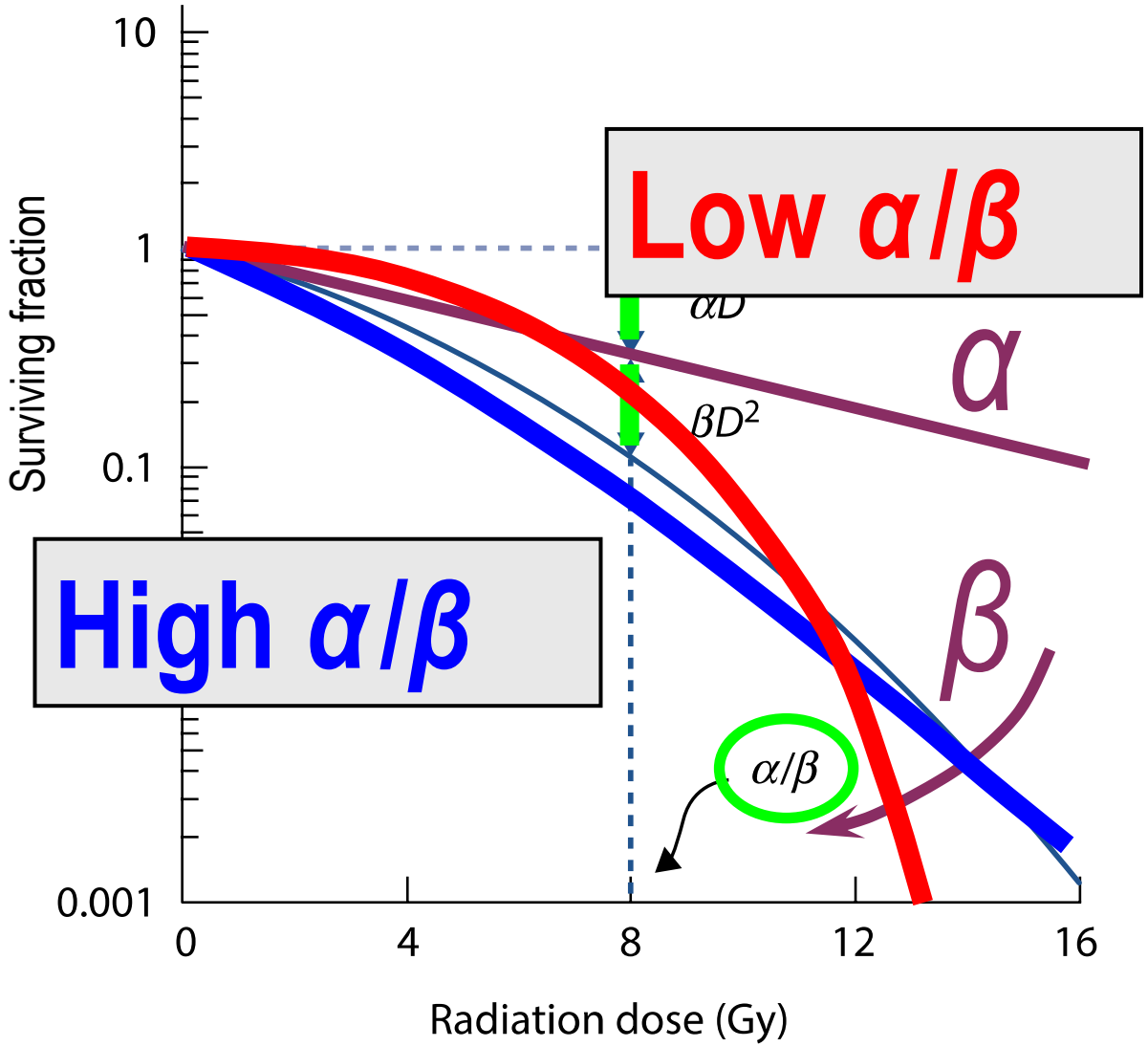
- Recap some key concepts re: *α/β, fractionation and BED/EQD2*
- Practice calculations

α/β and fractionation

$$S = e^{-aD - bD^2}$$

$$-\log_e S = aD + bD^2$$

Interpretation of alpha and beta?



Interpretation of alpha and beta separately?

For sure:
A quadratic term means that radiation is more and more efficient as we give higher dose

Speculation:
Due to interaction between radiation tracks
Due to multiple “hits” turning non-lethal damage into lethal damage
Saturation of repair machinery

Not:
Reflecting SSBs and DSBs – cell kill is always about DSBs!

Low α/β

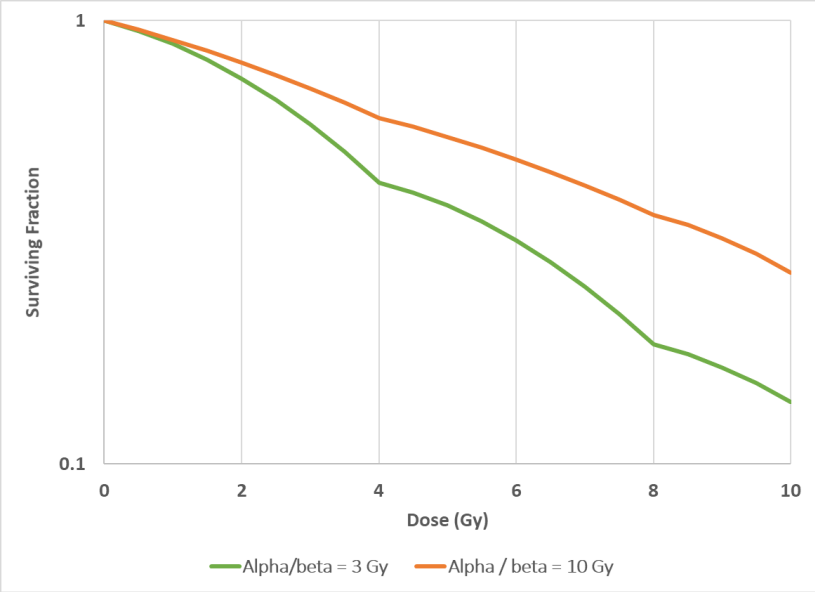
- Bendier
- High capacity for repair/recovery
- More effect of fractionation
- Smaller dose per fraction – a lot of sparing
- Typical of late responding tissues
- 2-3

High α/β

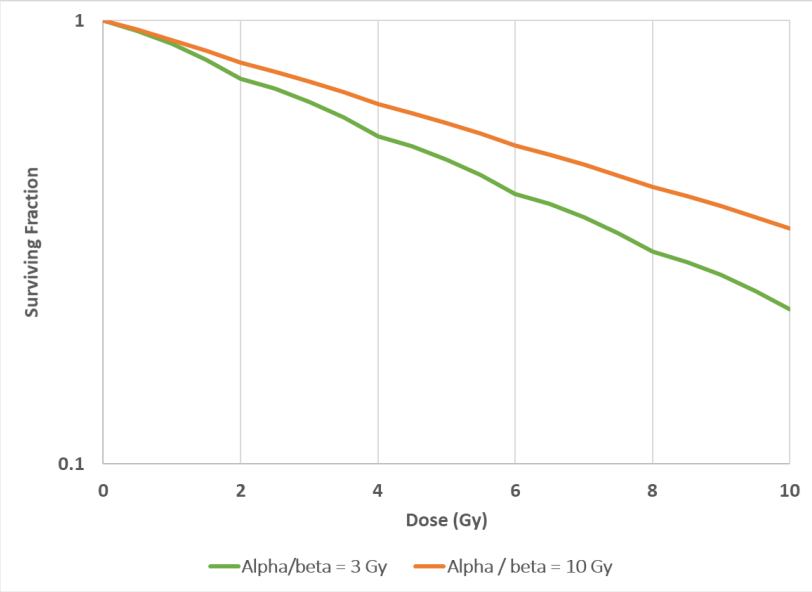
- Straighter
- Low capacity for repair/recovery
- Less effect of fractionation
- Smaller dose per fraction – a little sparing
- Typical of tumors (head-and neck, lung) and acute responding tissues
- 8-10

Understand α/β ratio as describing "bendiness of cell survival curve and "sensitivity to fractionation"

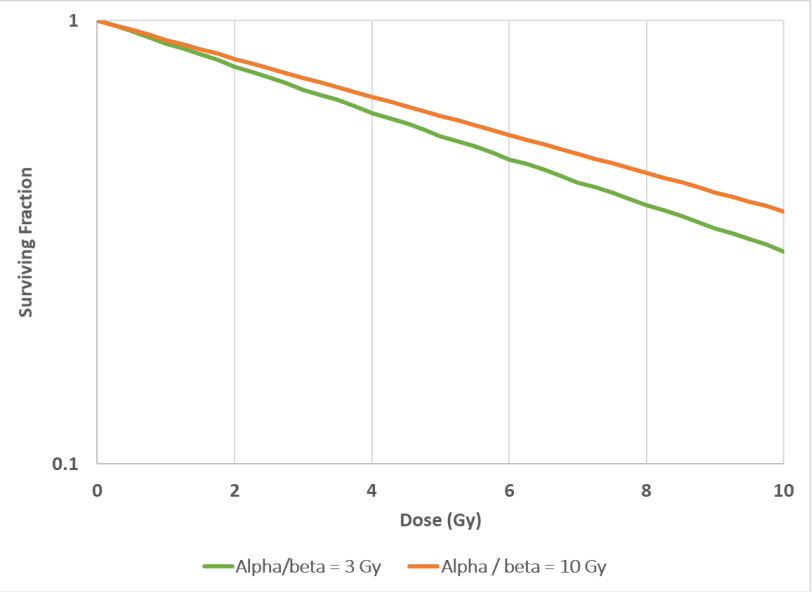
4Gy per fraction



2Gy per fraction



1Gy per fraction



- All tissues are spared when we fractionate more (smaller dose per fraction)
- Tissues with low α/β are spared more than tissues with high α/β
- To achieve equal effect we therefore have to increase the total dose

α/β and fractionation

High α/β

Spared less by smaller fractions

Low α/β

Spared more by smaller fractions

1. What determines whether smaller or larger fractions is beneficial for therapeutic ratio?
2. How do we maintain tumor control when we hyper-fractionate?
3. How do we restrain normal tissue damage when we hypo-fractionate?

Why EQD2 or BED?

70 NOK

12 MYR

$8.8 CAD

$3.41 CAD

BED: Biologically equivalent dose

EQD2: The total dose that would give the same effect if I had given it in 2Gy fractions

Why EQD2 or BED?

$$BED = D\left(1 + \frac{d}{\alpha/\beta}\right)$$

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

BED = EQD0

BED is an attractive mathematical concept, no physical interpretation.

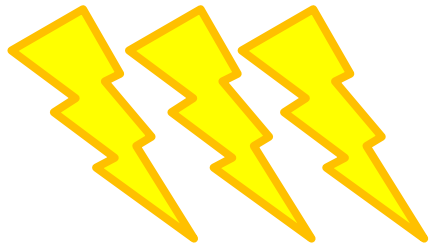
Tolerance doses and proliferation factors are often given in EQD2

Why EQD2 and BED?

1 x 12 Gy = 12 Gy

3 x 8 Gy = 24 Gy

20 x 1.8 Gy = 36 Gy



n x 2Gy =

n x 2Gy =

n x 2Gy =

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

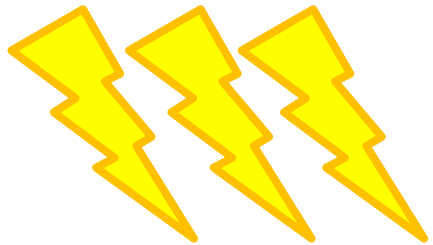
Why EQD2 and BED?

α/β = 10

1 x 12 Gy = 12 Gy

3 x 8 Gy = 24 Gy

20 x 1.8 Gy = 36 Gy



11 x 2Gy = 22 Gy

18 x 2Gy = 36 Gy

17.7 x 2Gy = 35.4 Gy

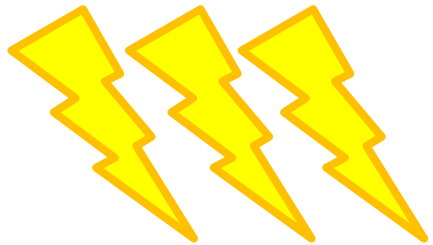
$$EQD2 = D\left(\frac{d + a/b}{2 + a/b}\right)$$

Why EQD2 and BED?

$\alpha/\beta = 3$

1 x 12 Gy = 12 Gy

18 x 2Gy = 36 Gy



3 x 8 Gy = 24 Gy

26.4 x 2Gy = 52.8 Gy

20 x 1.8 Gy = 36 Gy

17.28 x 2Gy = 34.56 Gy

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

What if two schedules are combined?
(Treatment time kept constant)

20 x 1.8 Gy = 36 Gy followed by 1 x 12 Gy = 12 Gy

α/β = 3

EQD2 = 34.56Gy + EQD2 = 36Gy EQD2 = 70.56Gy

α/β = 10

EQD2 = 35.5Gy + EQD2 = 22Gy EQD2 = 57.5Gy

What if two schedules are combined with time in between?

(Most relevant for re-treatment)

Normal tissues: Have to know how much recovery.

Example: 50%. Assuming $\alpha/\beta = 3$

EQD2 = 34.56Gy. Tissue “forgot” 50%, still remembers EQD2 = 17.28Gy

Is 17.28Gy + 36Gy above tolerance dose?

What if two schedules are combined with time in between?

Tumors: Have to know and correct for D_{prolif} if treatment time is extended.
If extended by 10 days for HN tumor (D_{prolif} = 0.6), assuming ***α/β = 10***

EQD2 = 35.5Gy + 22Gy – 0.6*10 = 51.5Gy

$$EQD2 = D\left(\frac{d + a/b}{2 + a/b}\right) - D_{prolif}\left(T - T_k\right)$$

How would that extension affect TCP?

Wanted EQD2 = 57.5 Gy, but achieved 51.5 Gy
Lost EQD2 = 6Gy

Need to use the gamma factor! Assume g = 2.

2*(6Gy/57.5Gy) = 0.21 21% reduction in TCP

How do we compensate for a treatment gap in practice?

First principle: Never exceed prescribed overall treatment time!

Compensate by:

- Adding a fraction on Saturday
- Two fractions per day (at least separated by 8 hours, preferably more)

How could we tailor fraction dose (d)?

Prescription is 35 x 2 Gy = 70 Gy

You want to deliver an equitoxic dose in 20 fractions. How?

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

EQD2 = 70 Gy $\alpha/\beta = 3$

D = n*d n=20

Solve for d! (Quadratic equation)