Basic Clinical Radiobiology

The LQ-model workshop

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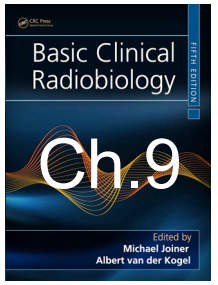

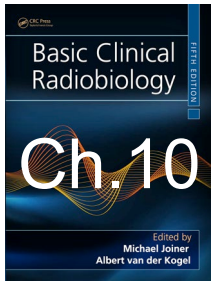

Basic Linear-Quadratic (LQ) equation

$$-\log_e SF_n = E = n\left(\alpha d + \beta d^2\right) = D\left(\alpha + \beta d\right)$$

$$E = \alpha D + \beta d D$$

EQD2 illumination

What is EQD2 ?

Its **EQ**uivalent **D**ose in **2**-Gy fractions.

Like BED (**B**iologically **E**ffective **D**ose) but using a different scale.
US $ and Canadian $ both measure money, using different scales.
EQD2 is currently recommended by ICRU (Bentzen et al 2012).

What do you need to calculate EQD2 ?

The value of α/β for the tissue or tumor under consideration.
Just as you do for BED.

How do you work out EQD2 ?

D: Total Dose

d: Dose per Fraction

E: a constant level of effect:

In LQ, $E = -\ln(\text{Surviving Fraction of this effect})$, $\therefore E = \alpha D + \beta d D$

$$\text{BED} = \frac{E}{\alpha} = D\left(1 + \frac{d}{\alpha/\beta}\right) = \text{EQD2}\left(1 + \frac{2}{\alpha/\beta}\right) \qquad (1)$$

$$\therefore \quad \text{EQD2} = \text{BED} \Big/ \left(1 + \frac{2}{\alpha/\beta}\right) \qquad (2)$$

or,

$$\boxed{\text{EQD2} = D\left(\frac{d + \alpha/\beta}{2 + \alpha/\beta}\right)} \qquad (3) \qquad \text{QED}$$

EQD2 vs BED

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

$$BED = EQD0 = D\left(\frac{d+\alpha/\beta}{0+\alpha/\beta}\right) = D\left(1+\frac{d}{\alpha/\beta}\right)$$

Including change in overall time: D_{prolif}

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

T_k	Day (from start) at which proliferation begins
T	Days, overall treatment time
D_{prolif}	EQD2 per day lost to proliferation.
	Only if $T \geq T_k$, otherwise zero

Using D_{prolif} with BED

$$D_{\text{prolif BED}} = D_{\text{prolif EQD2}}\left(1+\frac{2}{\alpha/\beta}\right)$$

$$\text{BED} = D\left(1+\frac{d}{\alpha/\beta}\right) - D_{\text{prolif BED}}\left(T - T_k\right)$$

So why use EQD2? What are advantages over BED?

Example 1 The simplest demonstration…

Metastatic bone pain is localized to the 5th thoracic vertebra.
Propose to give palliative treatment of which includes spinal cord.
Dose is 4 × 5 Gy. Is this safe?

Take α/β = 2 Gy for myelopathy.
Note: in this case choosing a lower α/β is more conservative, giving a higher EQD2.

Put numbers into Equation 3:

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

What is the now accepted limit on spinal cord dose from QUANTEC?

Its **50 Gy**.
In **2-Gy** fractions!

Therefore the proposed treatment of 4 × 5 Gy is considered safe

What if	5 × 5 Gy?	EQD2 =	**43.75**
	6 × 5 Gy?	EQD2 =	**52.5**
	5 × 6 Gy?	EQD2 =	**60**

Example 2

Your standard treatment for early-stage organ-confined prostate cancer has been 39 × 2 Gy = 78 Gy, 5 fractions per week. This takes **53** days.

Under pressure to shorten treatment time, you wish to deliver treatment in 3.5 Gy fractions. **How many fractions and to what total dose, $D_{3.5}$?**

You want to treat to nominally the same tolerance as 39 × 2 Gy.
So first, you identify the limiting normal tissues and select their α/β.

Brenner (2004) and Liao et al (2010) give α/β for human rectum as high as 5 Gy. Stewart et al (1984) give α/β for mouse bladder even higher.

As in Example 1, using lower α/β estimates $D_{3.5}$ more conservatively so we will choose α/β = 3 Gy for these critical late-responding organs.

We know what is EQD2: 78 Gy. So set up Equation 3 for EQD2 as:

$$\text{EQD2} = 78 = D_{3.5}\left(\frac{3.5+3}{2+3}\right) \qquad \therefore \qquad D_{3.5} = 78 \times \frac{5}{6.5} = 60$$

Note: If we used $\alpha/\beta = 5$ Gy, this would give $D_{3.5} = 64$ Gy.

60 is not integrally divisible by 3.5. Nearest conservative number of fractions is 17. Therefore planned protocol is **17 × 3.5 Gy = 59.5 Gy**.

With 5 F/week this could be delivered in as short as 23 days. But to guard against the bigger negative effects of slower repair in normal tissues at higher doses per fraction, it would be safer to give only 3 F/week (Mon-Wed-Fri) which would be an overall delivery time of 38 days, still saving the patient 2 weeks over conventional treatment.

The low α/β for the prostate cancer constitutes a further advantage of this hypofractionation. A weighted average from three human studies (Proust-Lima et al 2011, Leborgne et al 2012, Miralbell et al 2012) gives this ***α/β* = 1.5 Gy**.

Now use Equation 3 to calculate the tumor EQD2 expected from 17 × 3.5 Gy = 59.5 Gy:

$$\mathrm{EQD2} = 59.5\left(\frac{3.5+1.5}{2+1.5}\right) = 85$$

Thus hypofractionating with 17 × 3.5 Gy in prostate cancer could:

1. Increase effective dose to the malignancy from 78 Gy to 85 Gy (9%)
2. Slightly reduce effective dose on bladder and rectum by at least 1%
3. Reduce overall treatment time by at least 2 weeks

Summary of useful formulæ

For interfraction intervals of 1 day or greater:

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

And…

$$\mathrm{EQD2} = \mathrm{BED}\Big/\left(1+\frac{2}{\alpha/\beta}\right) \qquad \mathrm{BED} = \mathrm{EQD2}\left(1+\frac{2}{\alpha/\beta}\right)$$

Summary of useful formulæ: Incomplete Repair

For two or more fractions per day:

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

For H_m, see *Basic Clinical Radiobiology*

For continuous low dose rate exposures:

$$\mathrm{EQD2} = D\left(\frac{dg+\alpha/\beta}{2+\alpha/\beta}\right)$$

For g, see *Basic Clinical Radiobiology*

References

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