QUANTIFYING CELL DEATH AND SURVIVAL

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Disclosures: None







Colony assay: in vitro survival









 Plating efficiency (PE)

 40/100 = 0.4
 16/200 = 0.08

 Surviving fraction (SF) = 0.08/0.4 = 0.2

 Temerty Medicine
 Clinical a



Jejunal crypt assay















Cell sensitivity to radiation



Cell kill by radiation has a stochastic component

Whether a cell lives or dies after a dose of radiation depends on:

- initial damage
- repair capacity
- (- propensity to activate cell death processes)









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Cell kill: stochastic

$$P(a,n) = \underline{a^n e^{-a}}{n!}$$

a: average # events n: actual # events

"event" = lethal hit by radiation

Probability of
Survival =
$$P(a,0) = \underline{a^0 e^{-a}} = e^{-a}$$

0!





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Dose 0: 256





$$S = e^{-\alpha L}$$

The linear-quadratic equation. The LQ model.

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Why are survival curves bendy?

Higher radiation doses are more efficient at killing cells than low radiation doses *per unit dose*

- Lesion interaction
- Repair saturation

We do not assign α and β biological interpretation. Only the α/β ratio is known for tissues/tumors.





How do we describe and compare responses?



 $DMF_{0.1} = 5.9/4 = 1.475$



Limitations of the LQ model





The Linear Quadratic model overestimates cell kill at high doses







The Linear Quadratic model underestimates cell kill at very low doses

$$\alpha = \alpha_r \left(1 + \left(\alpha_s / \alpha_r - 1 \right) e^{-D/D_c} \right)$$

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Medicine

Radiation Oncology



Dose/Gy

There are many other models!

- Many were developed to illuminate the underlying molecular biology
 - Now obsolete
- Problematic, either:
 - Do not give good data fits
 - Have too many parameters to be useful

The LQ model gives adequate data fits with few (2) parameters and is clinically applicable!

- We use models to:
 - Make quantitative descriptions and comparisons
 - help make clinical predictions from experimental and data
 - predict the change in outcome when we alter treatment
- This is possible because radiation biology is a quantitative discipline



Thank you!

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