Clinical and Experimental Radiobiology Course

Tutorial 4

Wi-Fi

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Piazza

https://piazza.com/utoronto.ca/winter2025/**mbp1301h**

Tutorial 4

- **Lecture 11: Pathogenesis of Normal Tissue Side Effects**
  - ***Dr. Jennifer Kwan***
- **Lecture 12: The Volume Effect for Normal Tissues**
  - ***Dr. Jennifer Kwan***
- **Lecture 13: Modified fractionation schedules (and limits)**
  - ***Dr. Scott Bratman***

Lecture 11: Pathogenesis of Normal Tissue Side Effects

A breast cancer patient is being considered for either 30 Gy or 40 Gy. Which statement (one only) is true regarding acute reactions after the two schedules?

A. **Acute skin reactions are worse with the 40 Gy schedule compared to the 30 Gy schedule after 1 week of treatment.**

B. **Reactions will occur sooner with 40Gy.**

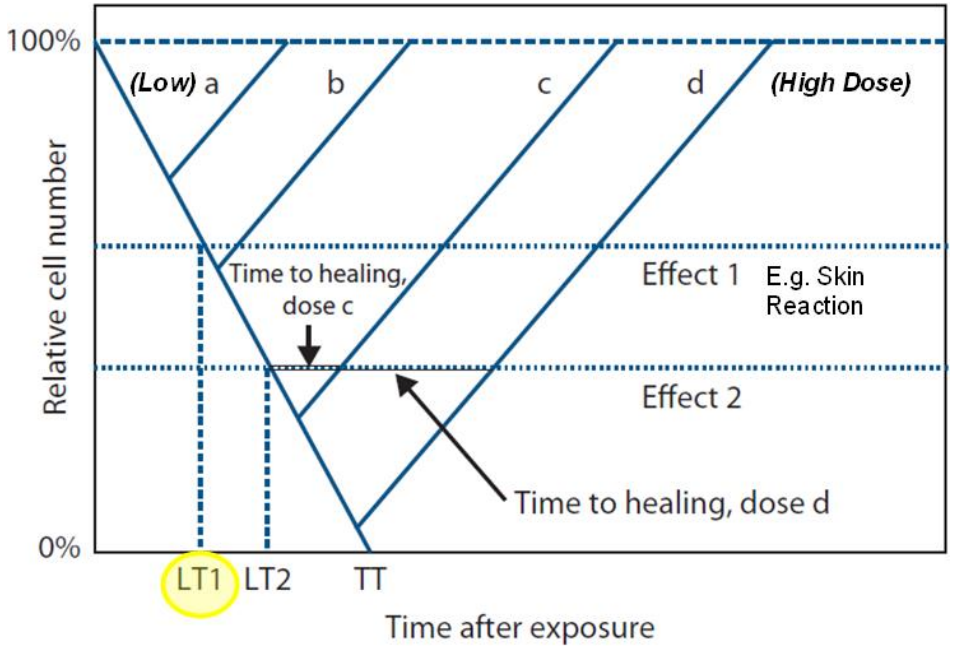
C. **Senescence of epidermal stem cells contributes to acute skin reactions.**

D. **There is increased residual skin reactions with the 40 Gy schedule by week 7.**

Lecture 11: Pathogenesis of Normal Tissue Side Effects

Early Reactions

Clinical Manifestations



Tissue Dependent

1. Turnover Time (Rate of Cell Loss)
2. **Latent Time of Clinical Manifestation**

Option A: **Acute skin reactions are NOT worse with the 40 Gy schedule compared to the 30 Gy schedule after 1 week of treatment.**

Option B: **Reactions will NOT occur sooner with 40Gy.**

Dose Dependent

1. Healing Time

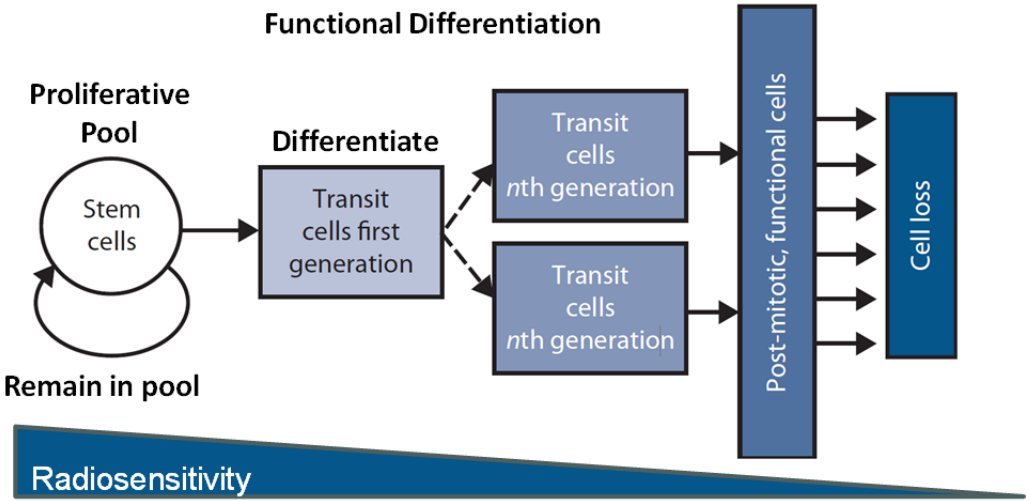
Lecture 11: Pathogenesis of Normal Tissue Side Effects

Early Reactions

Hierarchical Proliferative Tissue Organization

Stem Cell Concept/ Target Cell Hypothesis

- **Radiation tolerance depends on number and intrinsic radiosensitivity of stem cells**

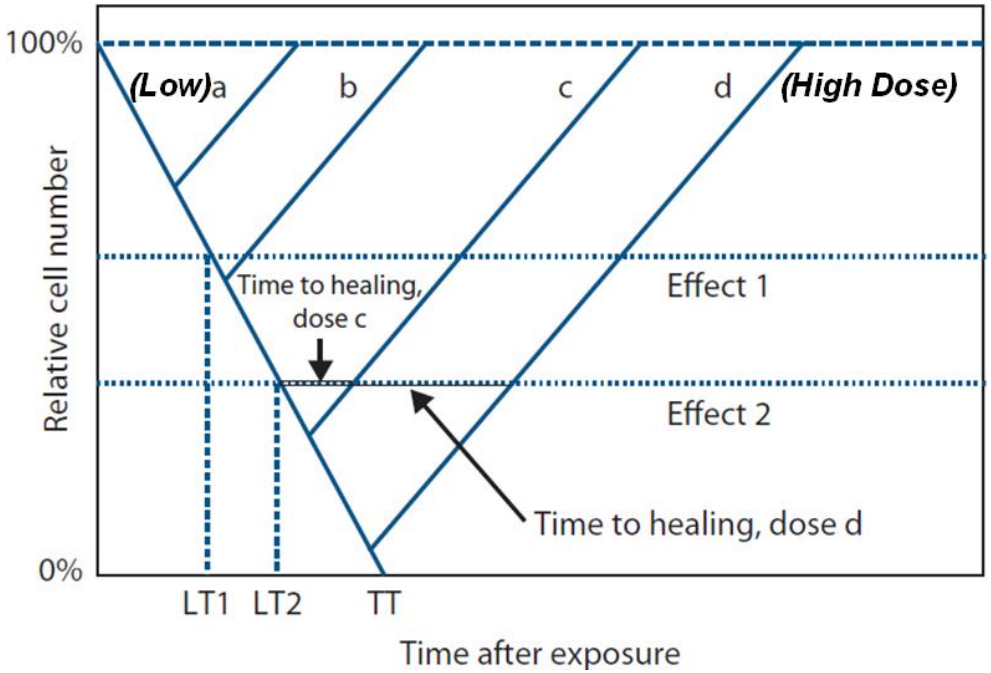


Option C: ~~Senescence~~ DIFFERENTIATION of epidermal stem cells contributes to acute skin reactions.

Lecture 11: Pathogenesis of Normal Tissue Side Effects

Early Reactions

Clinical Manifestations



Tissue Dependent

1. Turnover Time (Rate of Cell Loss)
2. Latent Time of Clinical Manifestation

Dose Dependent

1. **Healing Time**
   i.e. *Higher doses will require increased healing time*

Option D: There is increased residual skin reactions with the 40 Gy schedule by week 7.

Lecture 11: Pathogenesis of Normal Tissue Side Effects

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   A. **Acute skin reactions are worse with the 40 Gy schedule compared to the 30 Gy schedule after 1 week of treatment.**

   B. **Reactions will occur sooner with 40Gy.**

   C. **Senescence of epidermal stem cells contributes to acute skin reactions.**

   D. **There is increased residual skin reactions with the 40 Gy schedule by week 7.**

Reference: L11 slide 13

Lecture 11: Pathogenesis of Normal Tissue Side Effects

2. A breast cancer patient is being considered for either 40 Gy or 50 Gy to the chest wall. Which statement (one only) is true regarding the two schedules?

A. **The 40 Gy will result in worse late cosmetic outcome.**

B. **Cosmetic effects will appear at the same time.**

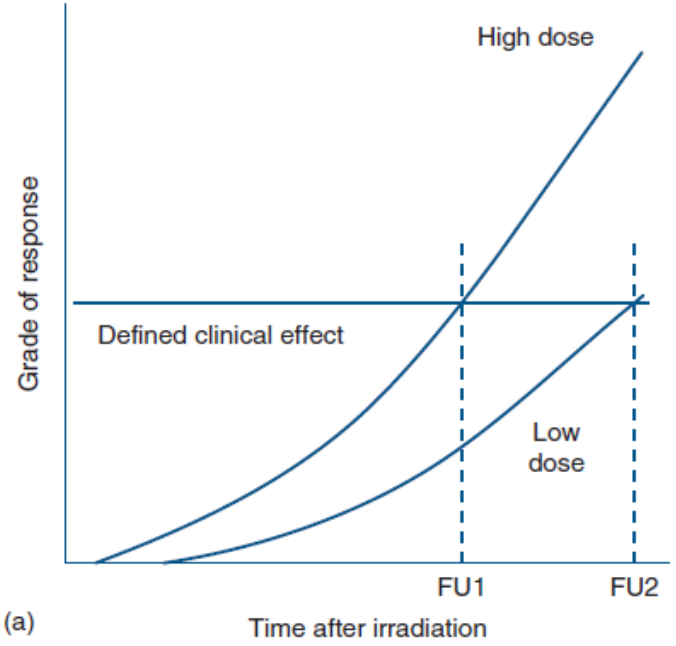
C. **Late fibrosis is characteristically associated with vascular changes in the chest wall.**

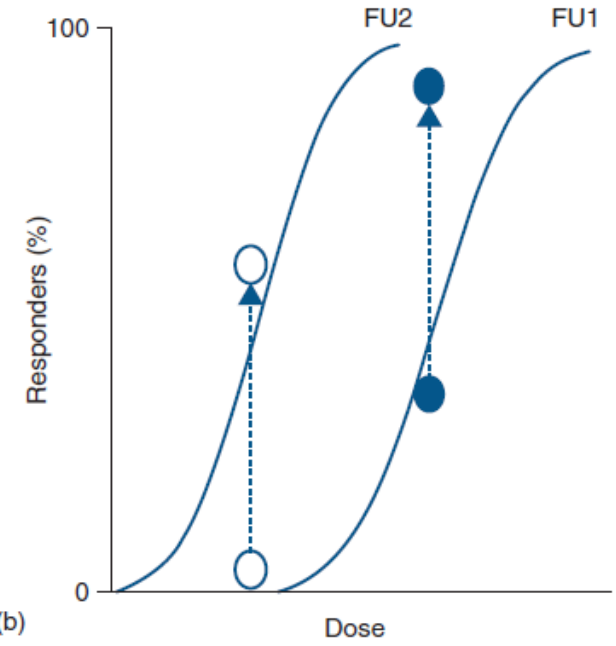
D. **Cosmetic outcome worsens with time after radiation but will recover slowly and completely after 5 to 10 years.**

Lecture 11: Pathogenesis of Normal Tissue Side Effects

Late Reactions

Clinical Manifestations





Dose Dependent

1. Latent Time
2. Progression Rate

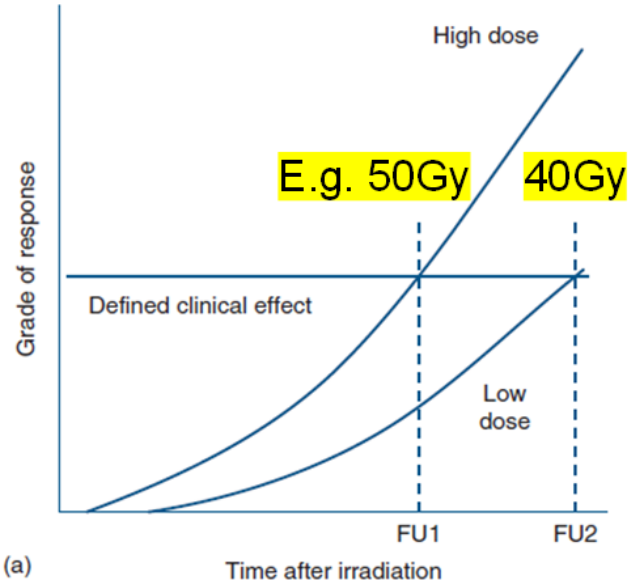
Option A: The ~~40Gy~~ 50Gy will result in worse late cosmetic outcome.

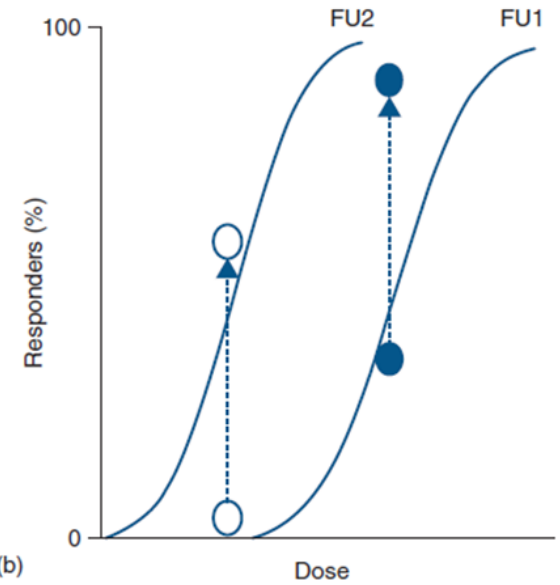
Lecture 11: Pathogenesis of Normal Tissue Side Effects

Late Reactions

Clinical Manifestations

Option B: Cosmetic effects will **NOT** appear at the same time.





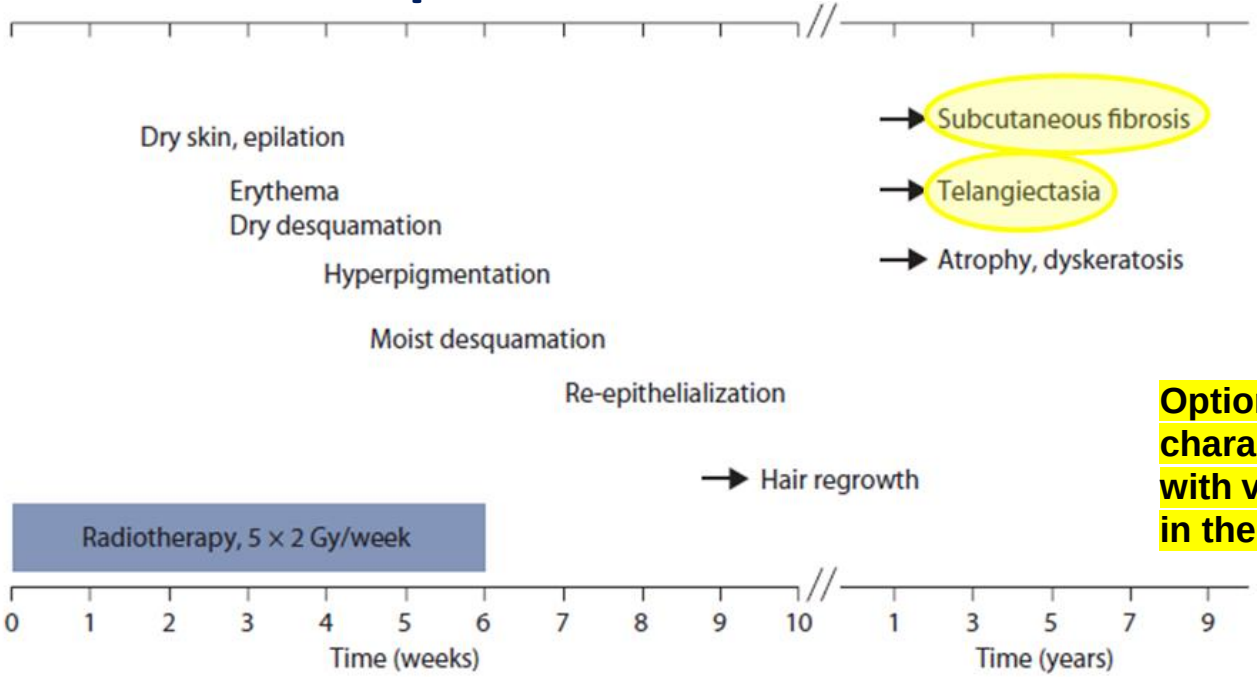
Dose Dependent

1. Latent Time
2. Progression Rate

Lecture 11: Pathogenesis of Normal Tissue Side Effects

Example: Skin

Sequence of Radiation Effects

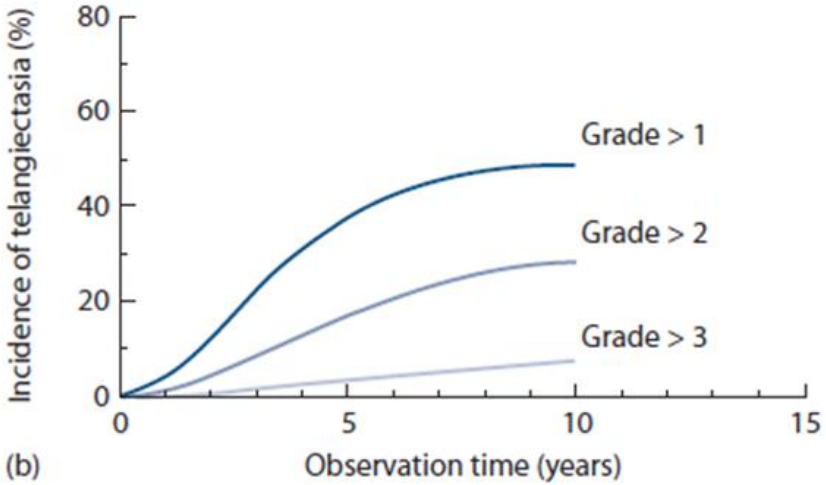


Option C: Late fibrosis is characteristically associated with vascular changes in the chest wall.

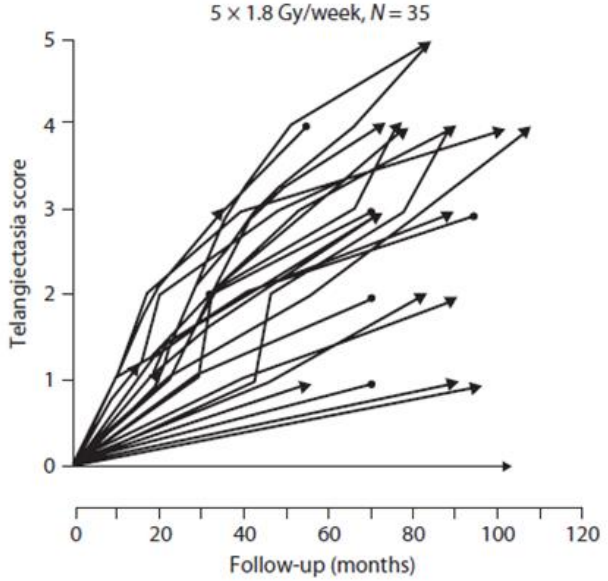
Lecture 11: Pathogenesis of Normal Tissue Side Effects

Example: Skin

↑ Incidence Over Time



↑ Severity Over Time



Option D: Cosmetic outcome worsens with time after radiation but will **NOT** recover slowly and completely after 5 to 10 years.

Lecture 11: Pathogenesis of Normal Tissue Side Effects

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Reference: L slide 26

Lecture 12: The Volume Effect in Radiotherapy

1. **Volume effects in normal tissues:**

   A. **NTCP models adequately describe volume effects in all normal tissues.**

   B. **The architecture of normal tissues is either parallel or serial.**

   C. **The dose distribution within tissues (e.g. lung) is irrelevant.**

   D. **The clinical consequences of partial volume irradiation of organs depend on the functional status of the non-irradiated tissue volume.**

Lecture 12: The Volume Effect in Radiotherapy

NTCP Models

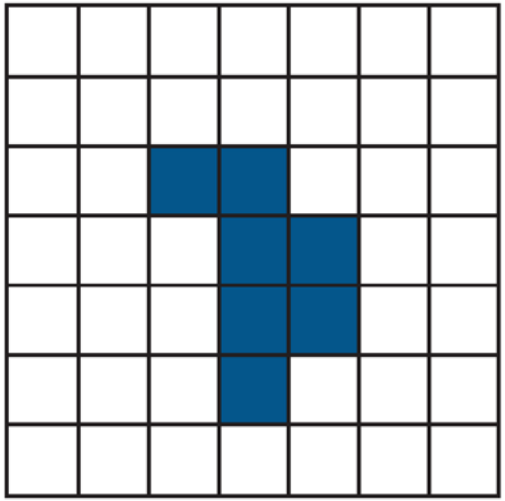
- NTCP = Normal Tissue Complication Probability
- Theoretical mathematical models to estimate NTCP for:
  - Partial-volume irradiation
  - Inhomogeneous dose distributions
- Models have limitations/uncertainties and need to be validated against clinical data emerging from new treatment methods

Option A: NTCP models **DO NOT** adequately describe volume effects in all normal tissues.

Lecture 12: The Volume Effect in Radiotherapy

FSU Organization

Parallel
(lung, kidney, liver)



Requires "threshold damage"

Serial
(spinal cord, esophagus, intestine)

Failure of one FSU can lead to organ failure

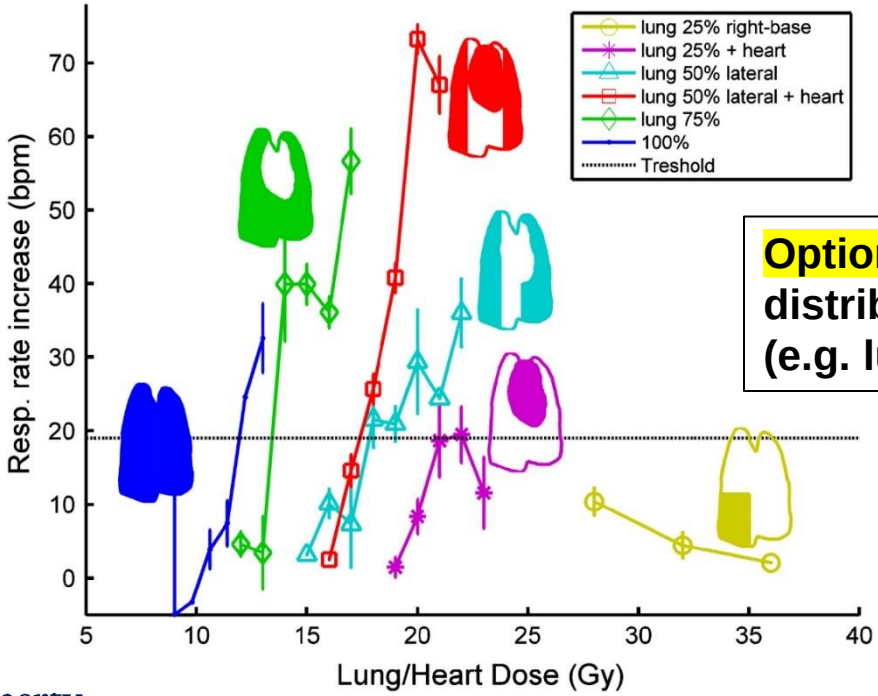
Most organs or tissues show both serial and parallel components

Option B: The architecture of normal tissues **can be ~~is either~~** parallel **and** serial.

Lecture 12: The Volume Effect in Radiotherapy

Volume Effects in Lung Tolerance

Effect of Location/ Relationship to Heart



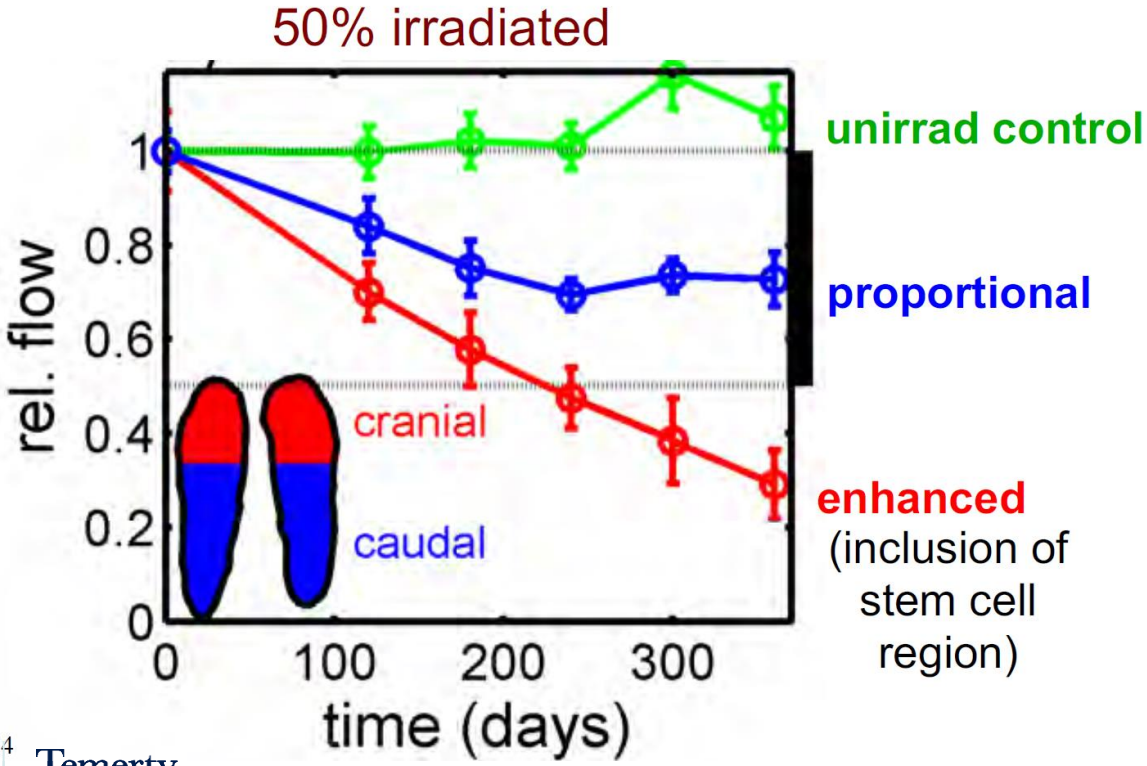
Option C: The dose distribution within tissues (e.g. lung) is ~~ir~~relevant.

Courtesy of Dr. Albert van der Kogel
P. Van Luijk et al IJROBP 2007 (Rat Lung)

Lecture 12: The Volume Effect in Radiotherapy

Irradiating Sub-Volumes

Option D: The clinical consequences of partial volume irradiation of organs depend on the functional status of the non-irradiated tissue volume.



Courtesy of Dr. Albert van der Kogel
van Luijk, Coppes, et al. 2012 (Rat Parotid)

Lecture 12: The Volume Effect in Radiotherapy

1. **Volume effects in normal tissues:**

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   B. **The architecture of normal tissues is either parallel or serial.**

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   D. **The clinical consequences of partial volume irradiation of organs depend on the functional status of the non-irradiated tissue volume.**

Reference: L12 slide 19

Lecture 12: The Volume Effect in Radiotherapy

2. Because of the "Volume Effect", as the length of irradiated spinal cord decreases below 1cm, the total dose needed to cause myelopathy:

A. **Increases**

B. **Decreases**

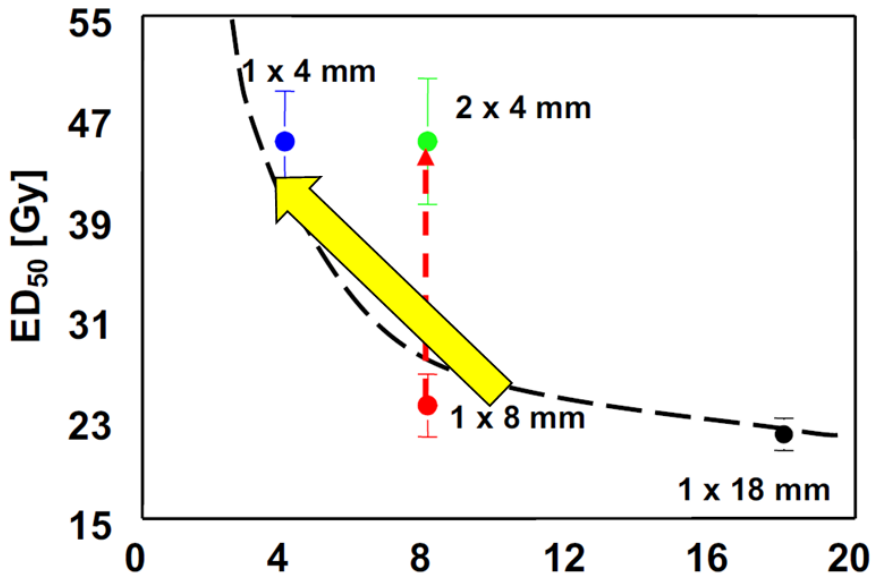
C. **Depends less on LET**

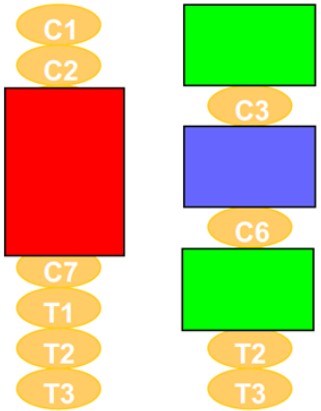
D. **Becomes independent of dose per fraction**

Lecture 12: The Volume Effect in Radiotherapy

Volume Effects in Spinal Cord Tolerance

Rat spinal cord tolerance rises steeply for lengths < 1 cm





2 X 4 ≠ 8

Option A: Increases

Lecture 12: The Volume Effect in Radiotherapy

2. Because of the "Volume Effect", as the length of irradiated spinal cord decreases below 1cm, the total dose needed to cause myelopathy:

A. Increases

B. Decreases

C. Depends less on LET

D. Becomes independent of dose per fraction

Lecture 13: Modified Fractionation

Accelerated fractionation is used to characterize schedules that:

A. **Deliver the total dose in less than 5 weeks**

B. **Deliver more than 2 fractions per day**

C. **Deliver more than 10 Gy per week**

Reference: L13 slide 15

Lecture 13: Modified Fractionation

Compared with a conventional fractionation regimen of 78Gy/2Gy/7.8wks, 60Gy/3Gy/4wks is an example of:

A. **Hyperfractionation**

B. **Accelerated fractionation**

C. **Hypofractionation**

D. **Accelerated and hypofractionation**

Reference: L13 slides 26, 30

Lecture 13: Modified Fractionation

Hyperfractionation should be considered if:

A. **The tumor is rapidly proliferating**

B. **The tumor α/β ratio is lower than the critical normal tissue α/β**

C. **The critical normal tissue α/β is lower than the tumor α/β**

Reference: L13 slide 9, 35

Lecture 13: Modified Fractionation

Hypofractionation is increasingly used for whole breast irradiation because:

A. **α/β for subclinical breast cancer is similar to α/β for late responding tissue**

B. **α/β for subclinical breast cancer is higher than α/β for late responding tissue**

C. **Subclinical breast cancer is a rapidly proliferating malignancy in most cases**