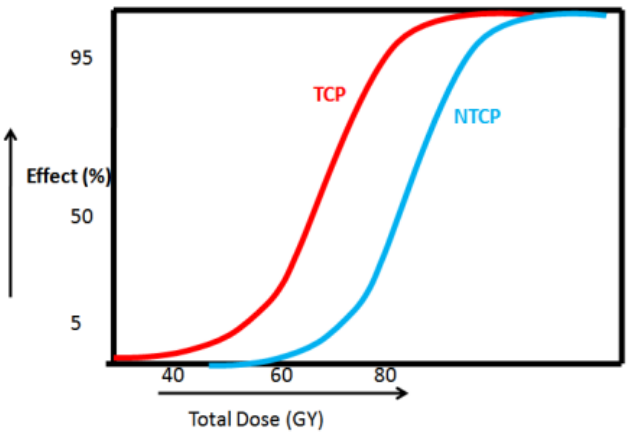
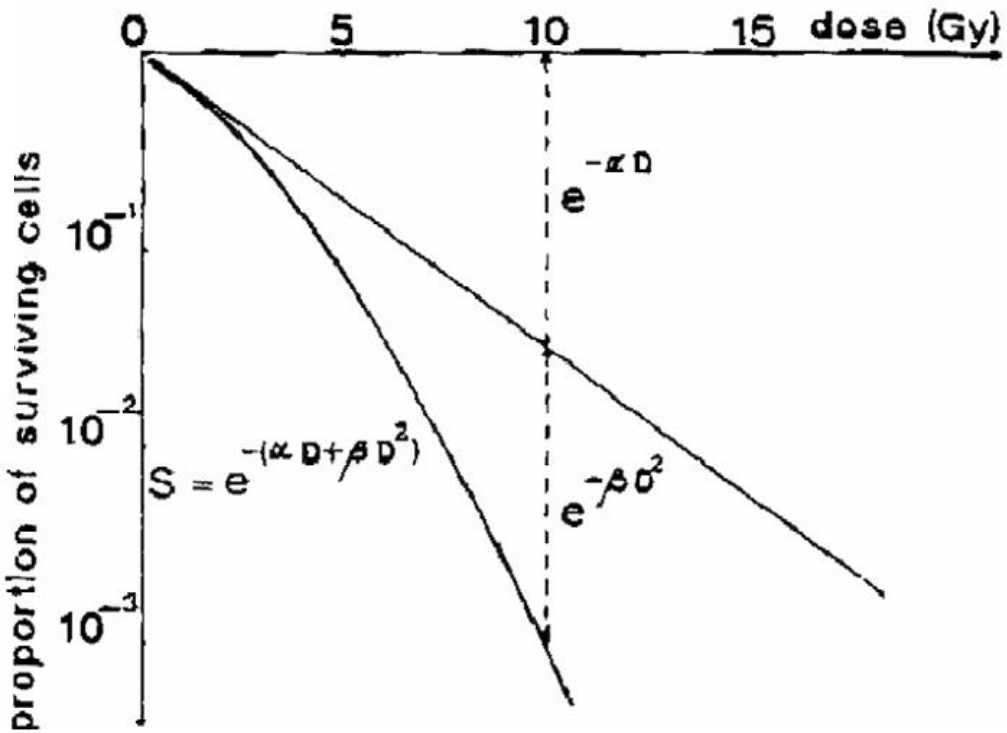
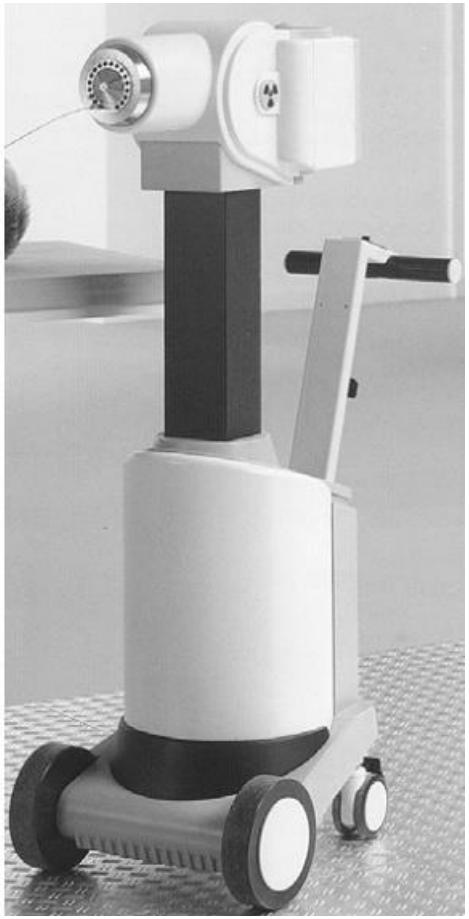
Radiobiology of Cervical Brachytherapy: Transition from LDR to HDR



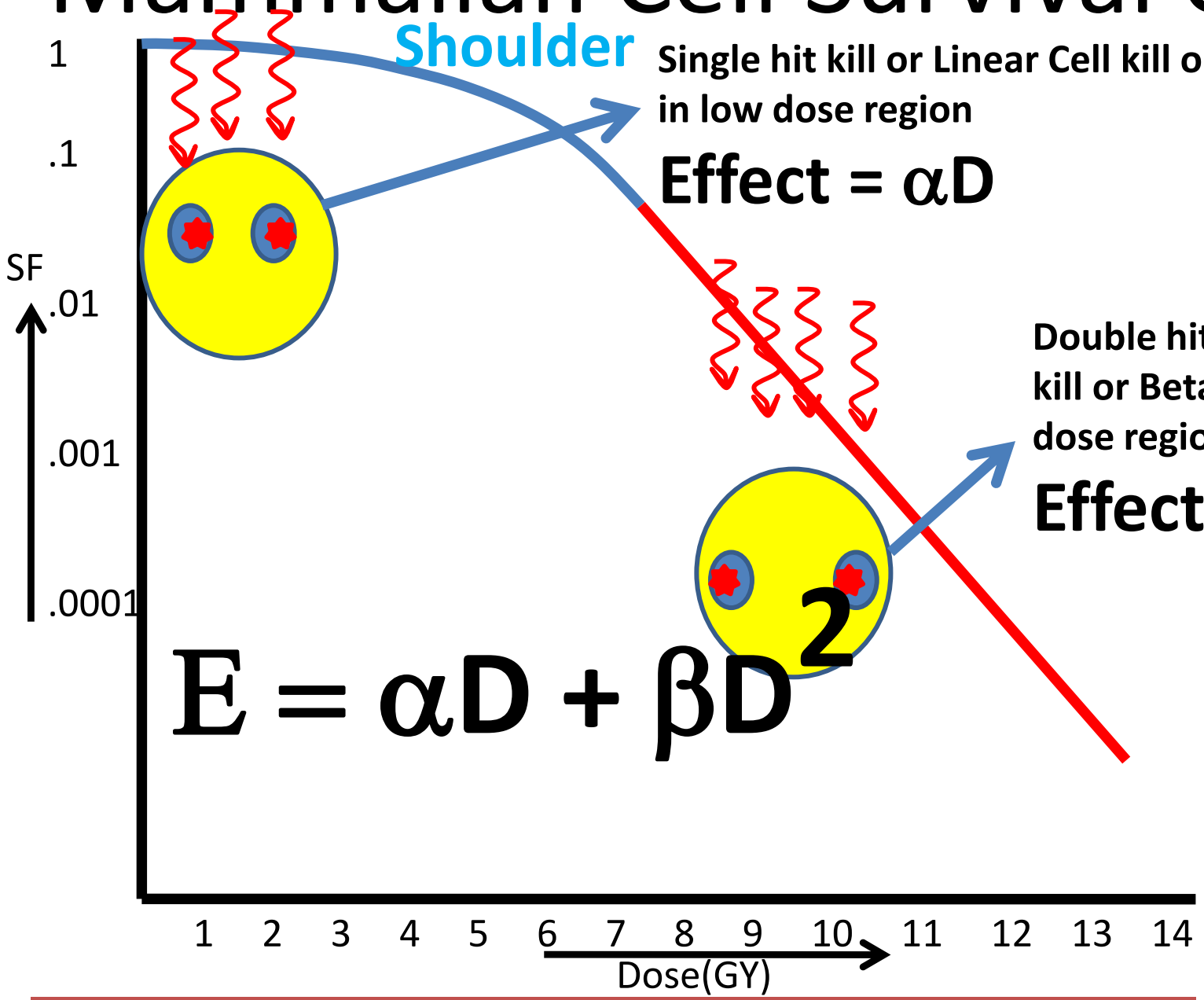




ICRO PG Teaching, Varansi
6th May 2023

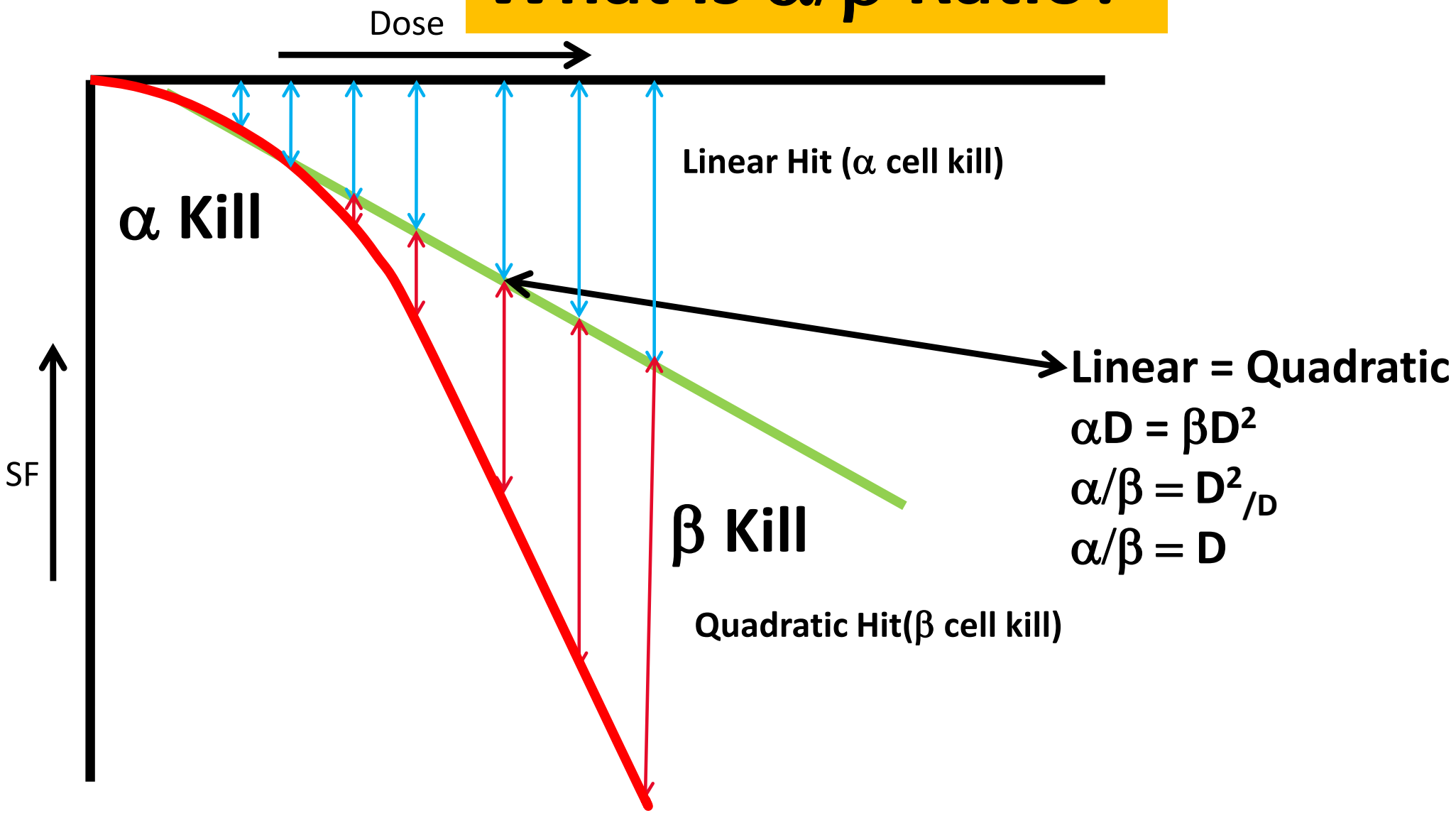
Prof Manoj Gupta
AIIMS, Rishikesh

Mammalian Cell Survival Curve



Linear-Quadratic Model

What is α/β Ratio?

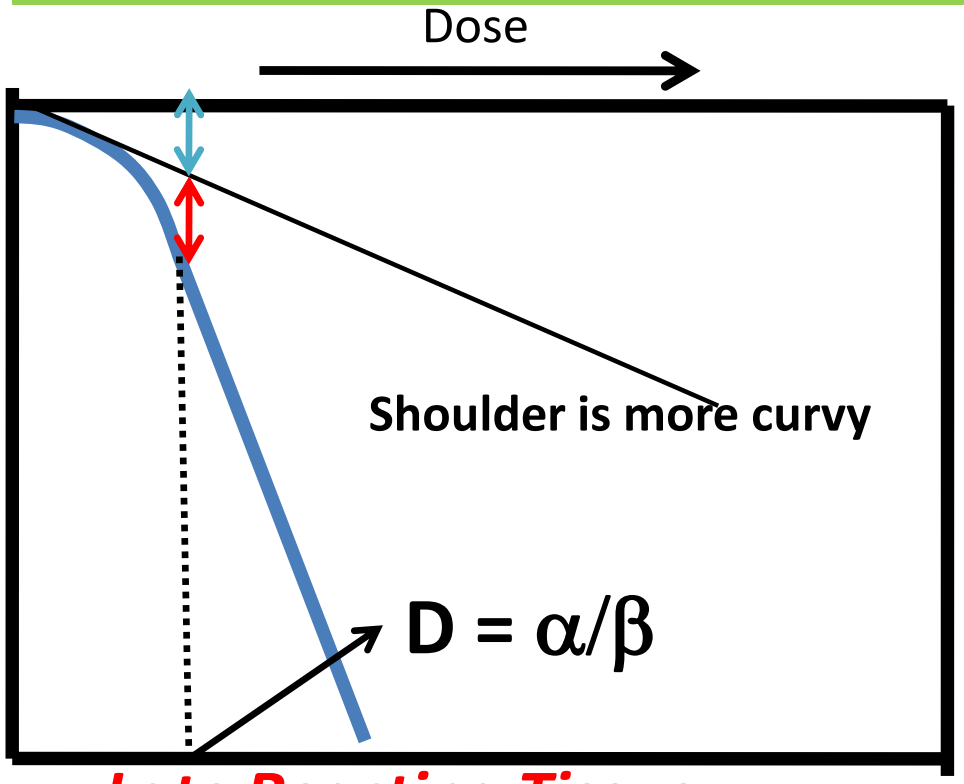


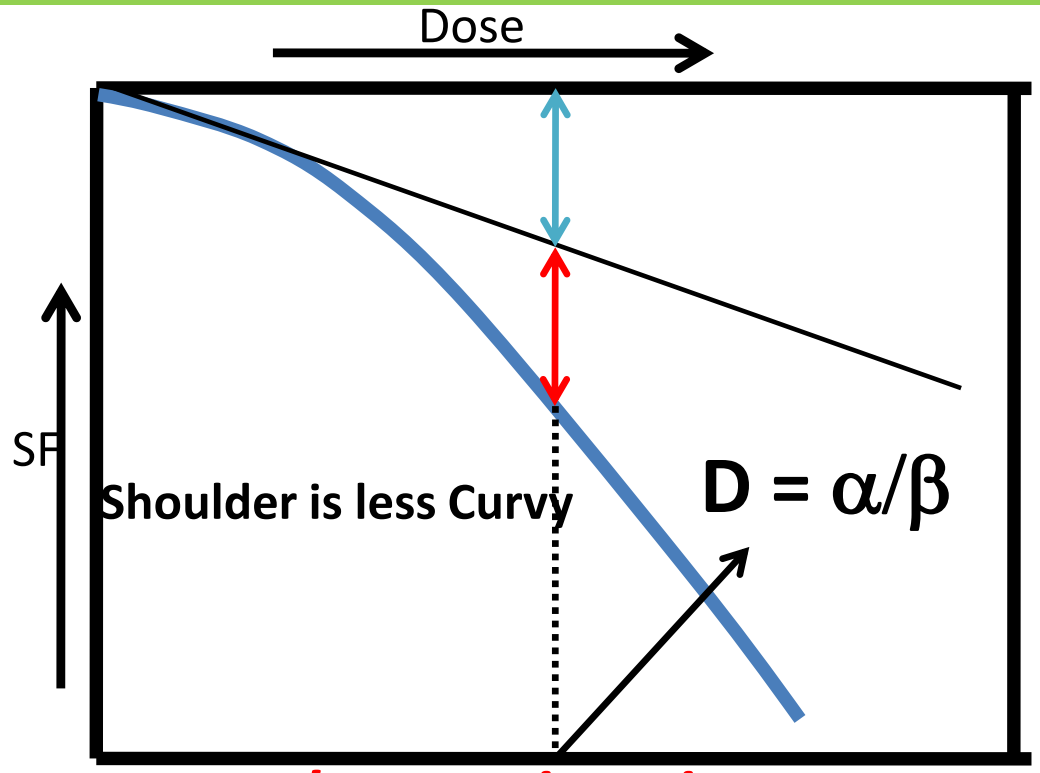
➢So α/β can be defined as the dose at which contribution by single hit (Linear) kill becomes equal to double hit (Quadratic) kill.

α/β Ratio defines "curviness" of survival curve

Based on α/β ratio, the body tissues have been divided into two category.

Malignant Tumors behave like early reacting tissue
α/β = 10





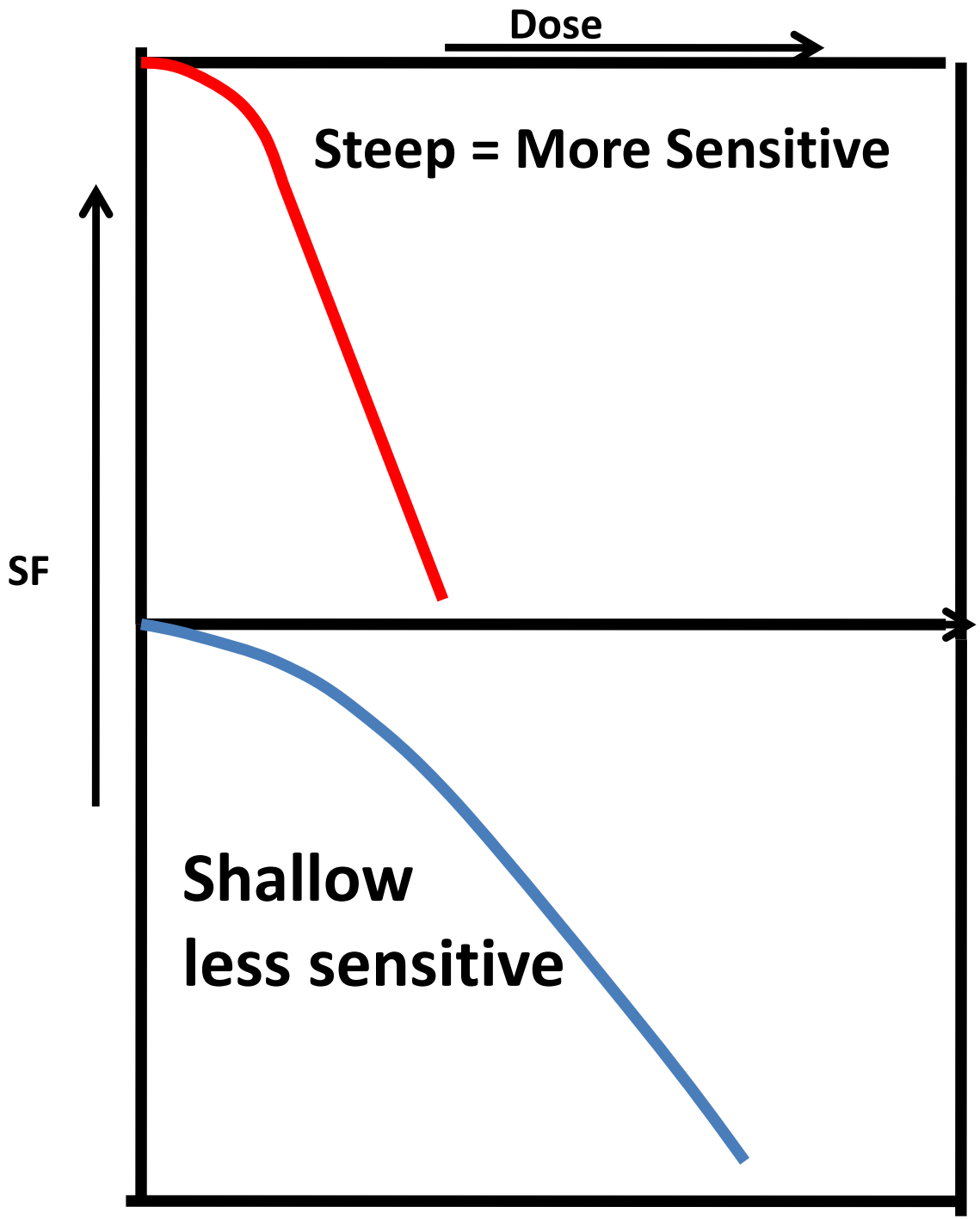
Late Reacting Tissue

α/β = 1Gy to 7 Gy (3Gy)
Responsible for late effect of radiation
Eg. Spinal cord, urinary bladder, kidney, liver etc.

Early Reacting Tissue

α/β = 6Gy to 15 Gy (10Gy)
Responsible for acute effect of radiation
Eg, skin, mucosa, lining of intestine, bone marrow etc.

Slope of the curve represent sensitivity

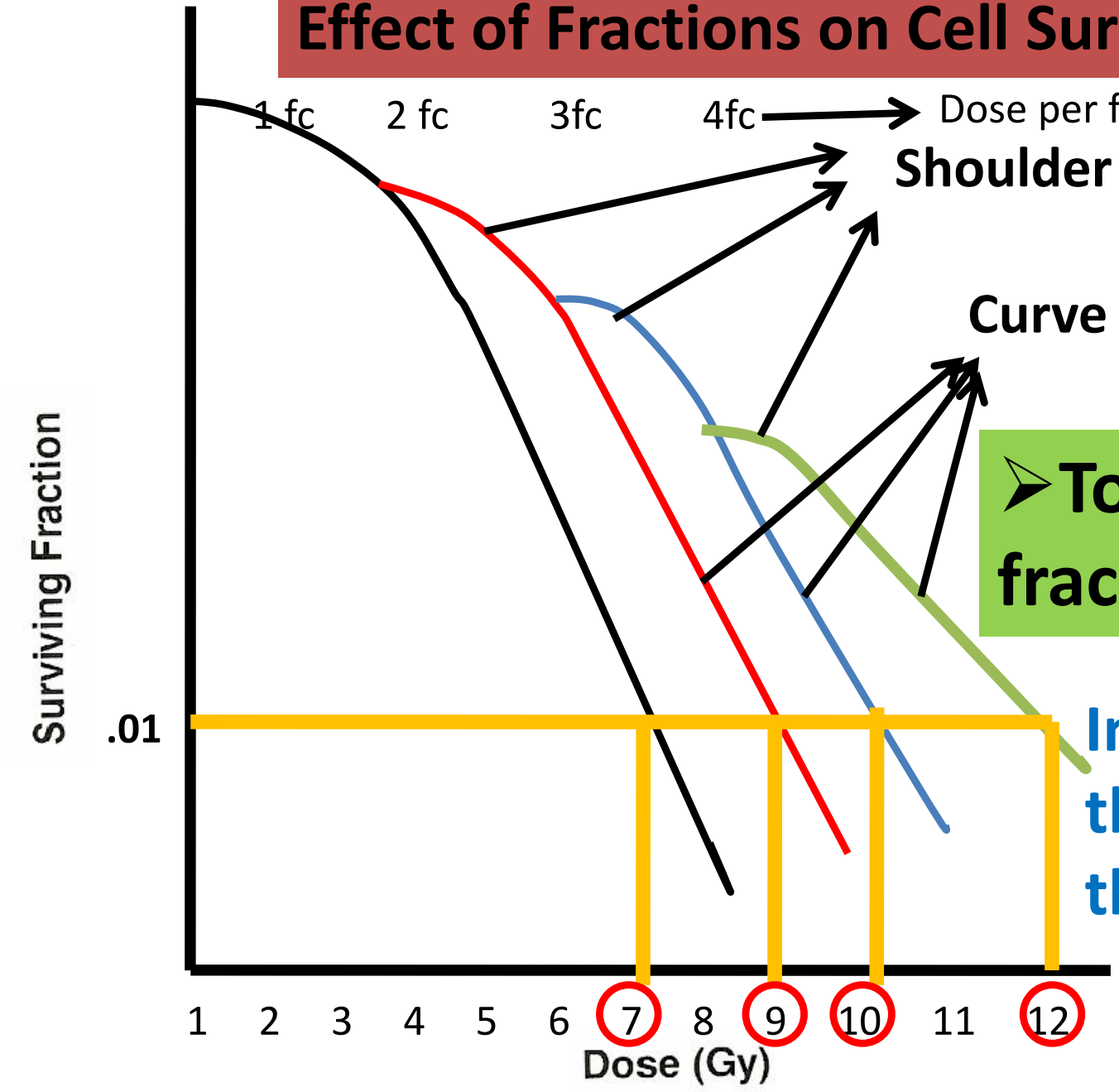


How radiation effects change in shifting from LDR to HDR

Dose rate in brachytherapy is similar to dose per fraction in EBRT

- **High Dose Rate = high dose per Fc (SRS, SBRT)**
- **Low Dose Rate = low dose per Fc (Conv Fc RT)**

Effect of Fractions on Cell Survival Curve

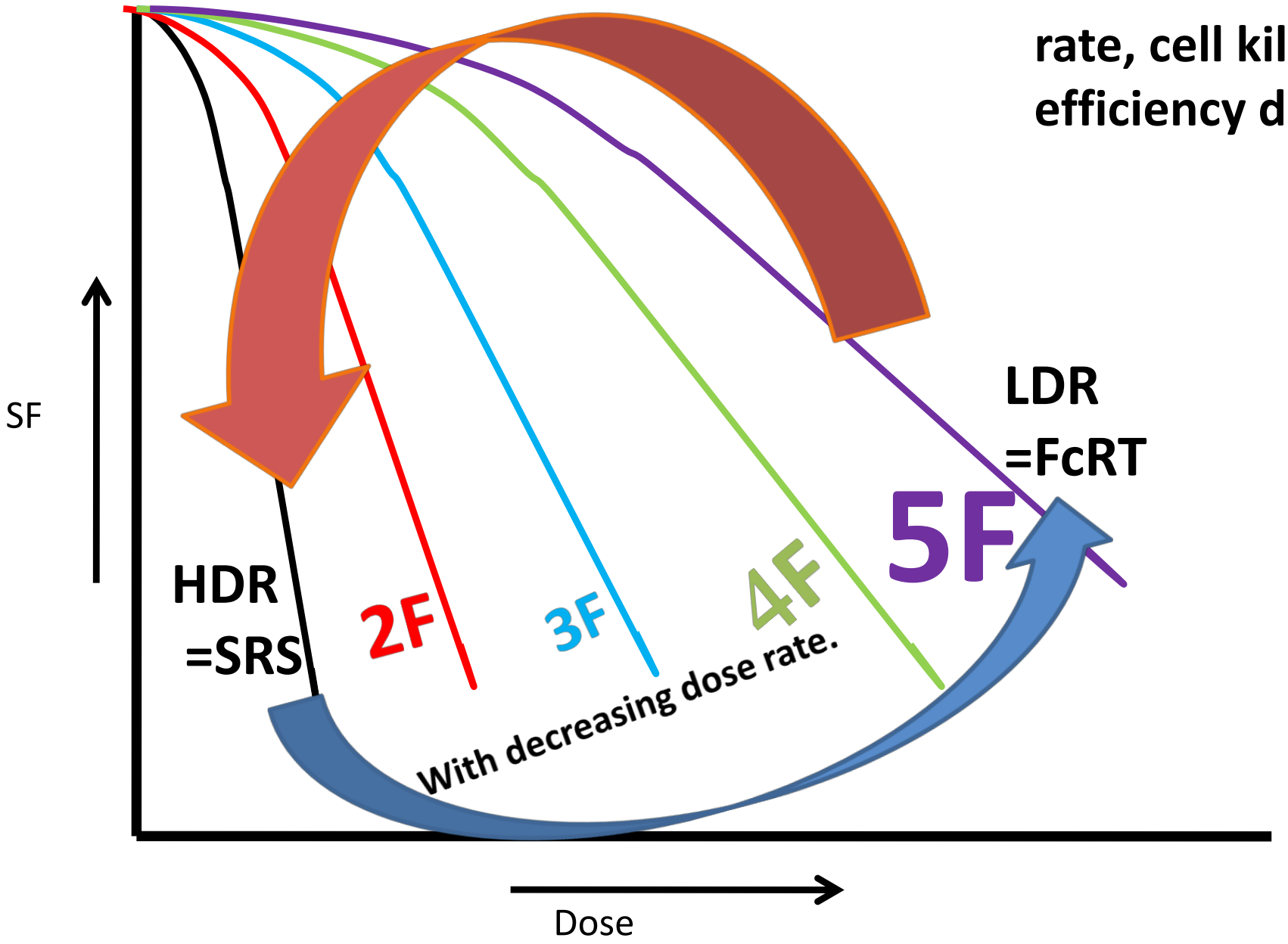


➢ **Total dose α no of fractions**

In fractionated RT the efficiency to kill the cell decreases.

Similarly in brachy, as the dose rate decreases the curve gets shallower and Cell killing efficiency decreases.

Dose Rate Effect



➢With decreasing dose rate, cell killing efficiency decreases

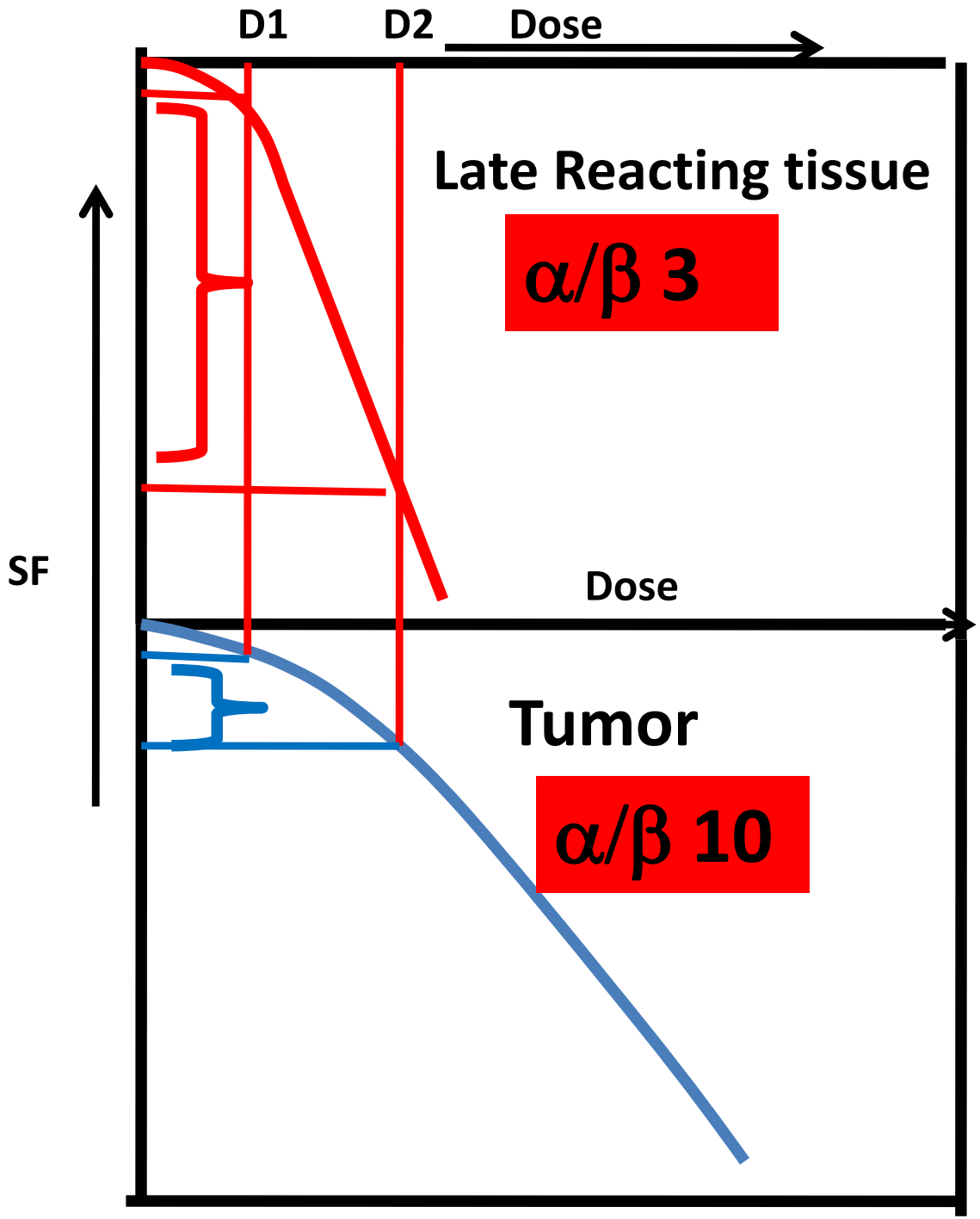
Important Points

1. Shifting from LDR to HDR will result into more cell kill.

A. Tumor Cells
B. Normal Cells (Late Reacting Tissues)

Is there differential cell killing between Tumor and normal cell?

Fraction size (Dose per fraction)



- Increase in dose per fraction will damage late reacting tissue more than tumor
- Increasing dose rate will Kill late reacting tissue more than tumor

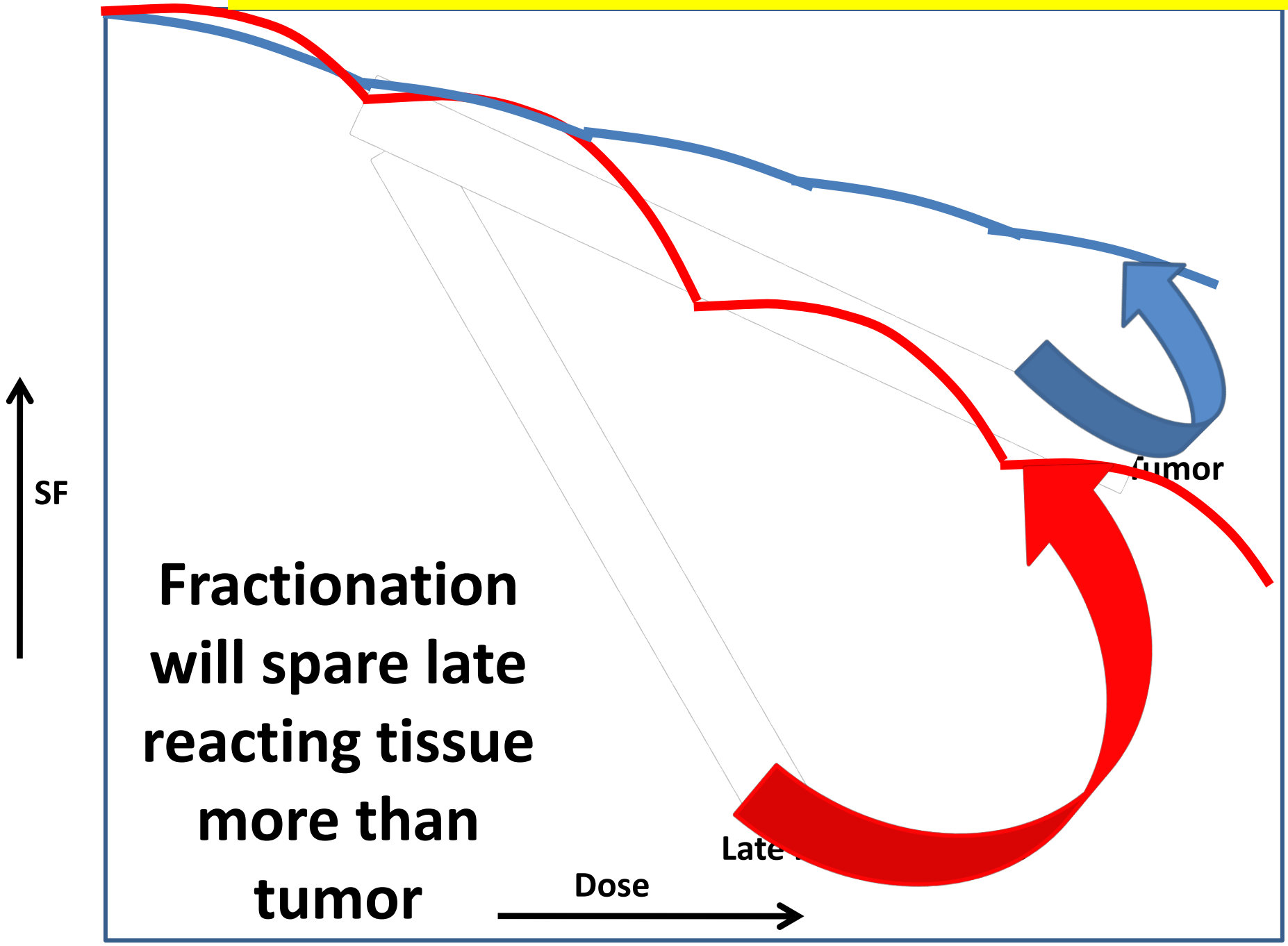
Important Points

1. Shifting from LDR to HDR will result into more cell kill.

2. Shifting from LDR to HDR will cause more damage to late reacting tissues.

How to overcome this and get a therapeutic Advantage?

Effect of Fractionation on Tumor and Late Reacting Tissues



Important Points

1. Shifting from LDR to HDR will result into more cell kill.

2. Shifting from LDR to HDR will cause more damage to late reacting tissues.

3. Fractionation spare late tissue more than tumor. HDR always fractionated.

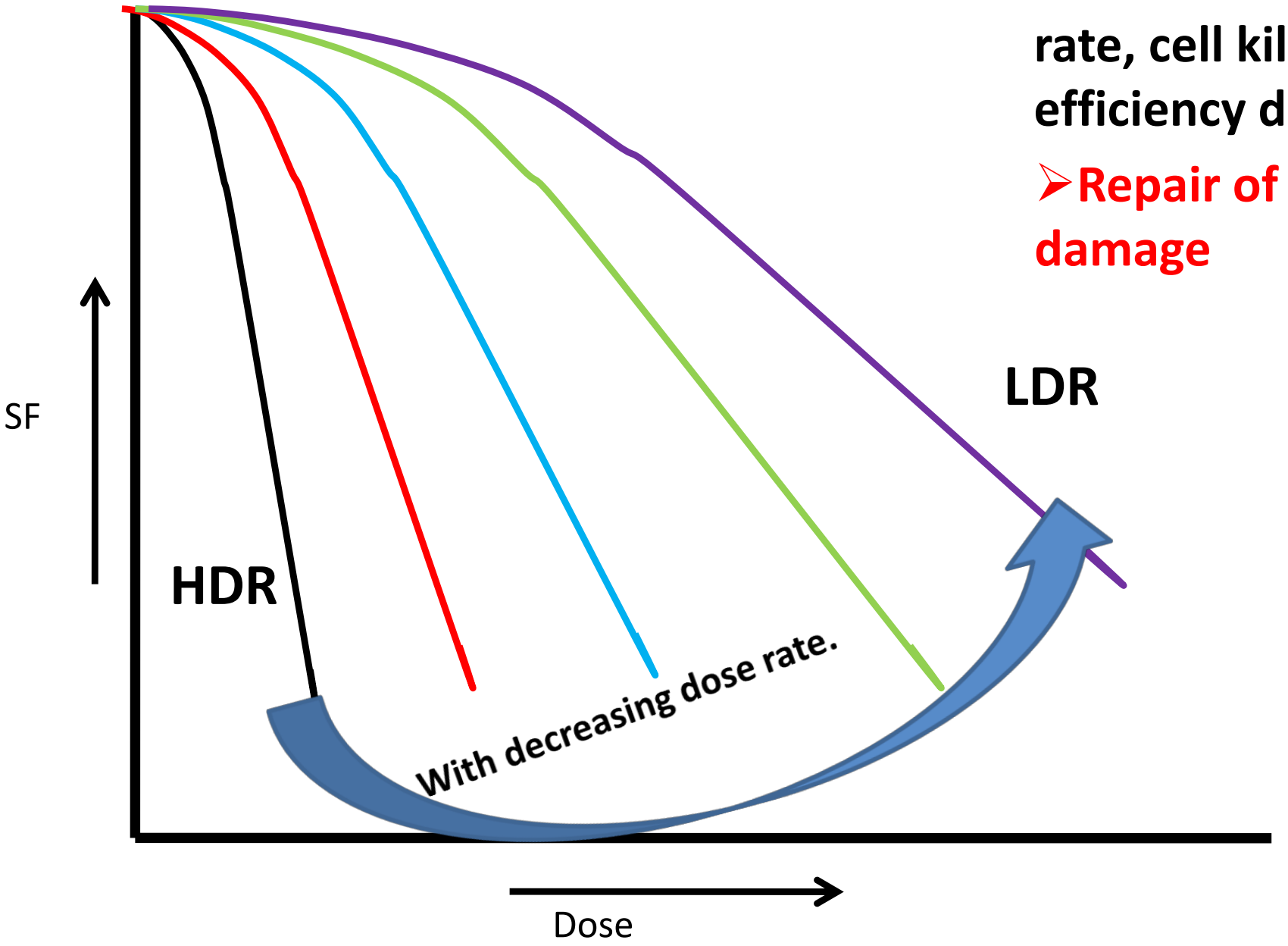
4 Rs of Radiobiology

Forms the basis of fractionated radiotherapy

1. Repair of Sub-lethal damage
2. Re-oxygenation
3. Redistribution or Re-assortment
4. Repopulation Or Regeneration

Dose Rate Effect

Dose Rate Effect



- With decreasing dose rate, cell killing efficiency decreases
- Repair of sub-lethal damage

Repair of Sub Lethal Damage

- Since repair starts within 15 to 30 minutes of irradiation, during LDR treatment itself the process of SLDR sets .
- Repair of sub-lethal damage will negate the overall effect of radiation.

$$E = \alpha D + \beta D^2$$

- So a time factor is to be incorporated in equation for LDR

$$E = \alpha D + \beta g D^2$$

Dose Rate Effect

$$E = \alpha D + \beta g D^2$$

- g depends upon half time for repair(T1/2)
- and total duration of treatment(t)

- As the treatment duration increases (dose rate decreases) the value of g decreases from 1 and for very long duration of treatment as in LDR the value becomes Zero

$$E = \alpha D$$

- All the cell killing is by linear Hits (α cell kill)

Dose Rate Effect

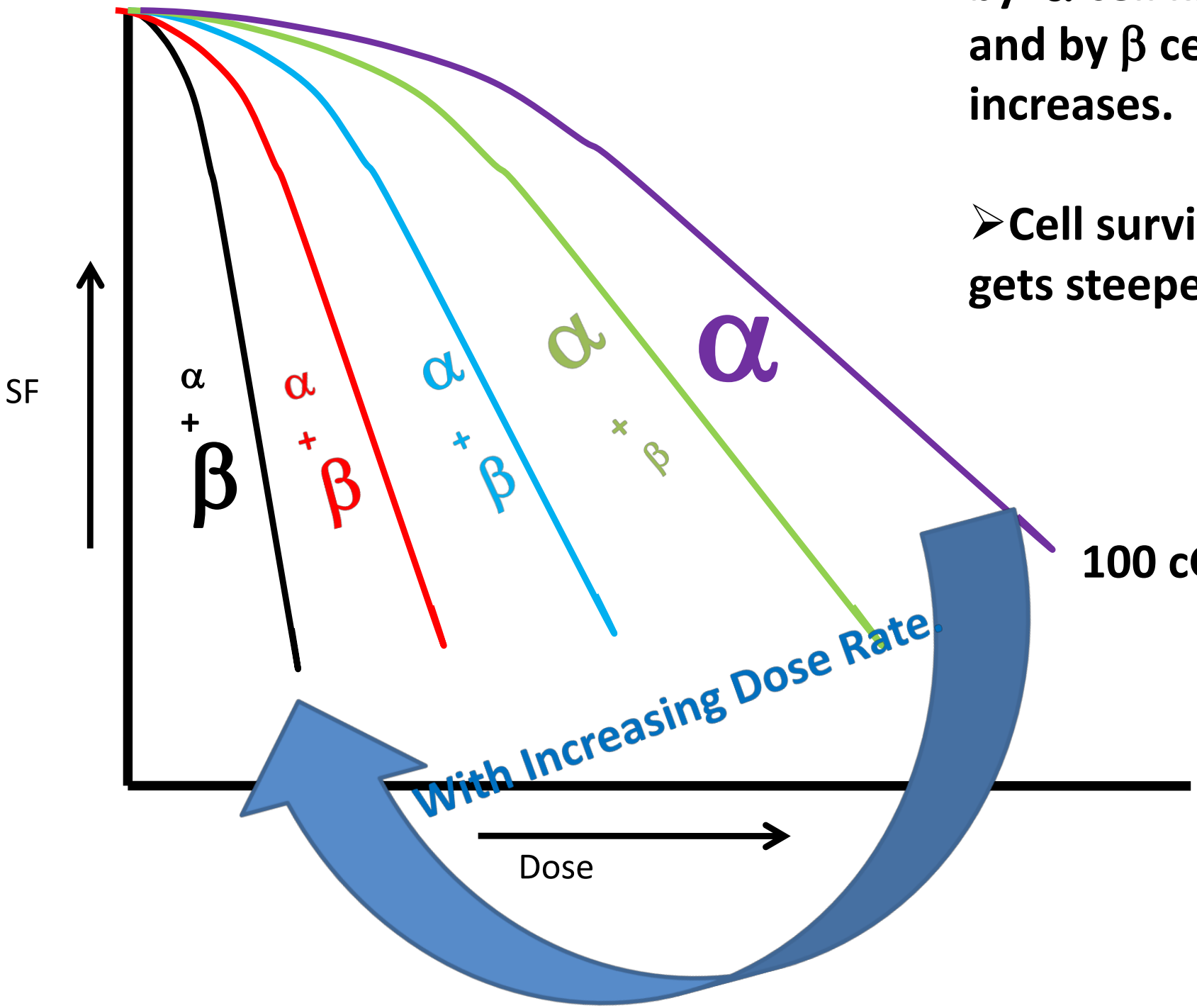
$$E = \alpha D + \beta g D^2$$

- If treatment duration is very less as in EBRT or HDR Brchytherapy then g = 1

$$E = \alpha D + \beta D^2$$

- Cell killing is by both process
  - Linear (α kill)
  - Quadratic (β kill)

Dose Rate Effect



- Relative contribution by α cell kill decreases and by β cell kill increases.
- Cell survival curve gets steeper.

100 cGy per hour

Dose Rate Effect Clinical Application

Carcinoma Cervix

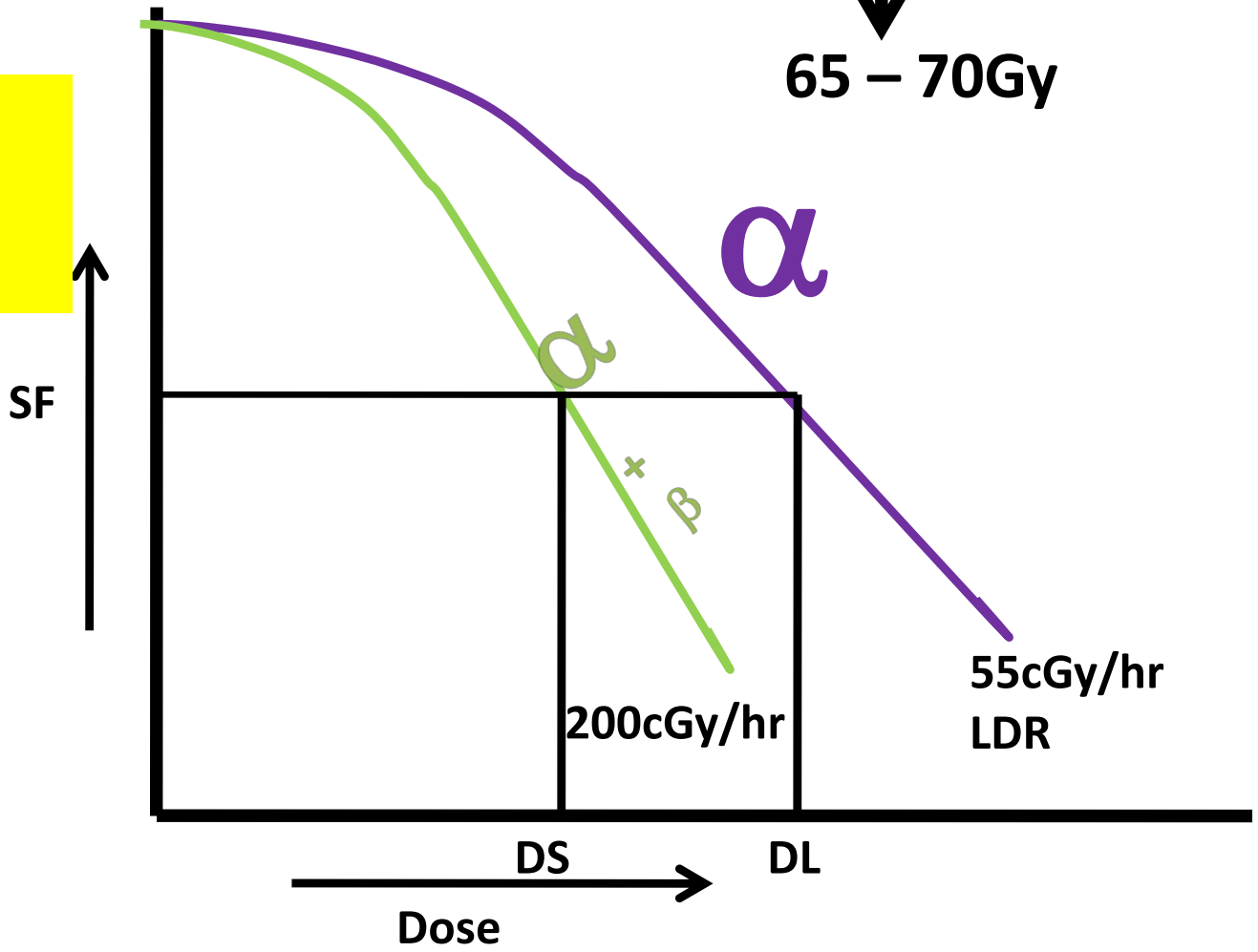
- LDR 53cGy/hr and total dose delivered was 75Gy at point A
- At this dose rate all the cell kill is by α kill (<100cGy/hr).
- Selectron Brachytherapy 140-200cGy/hr,

10 – 20%

65 – 70Gy

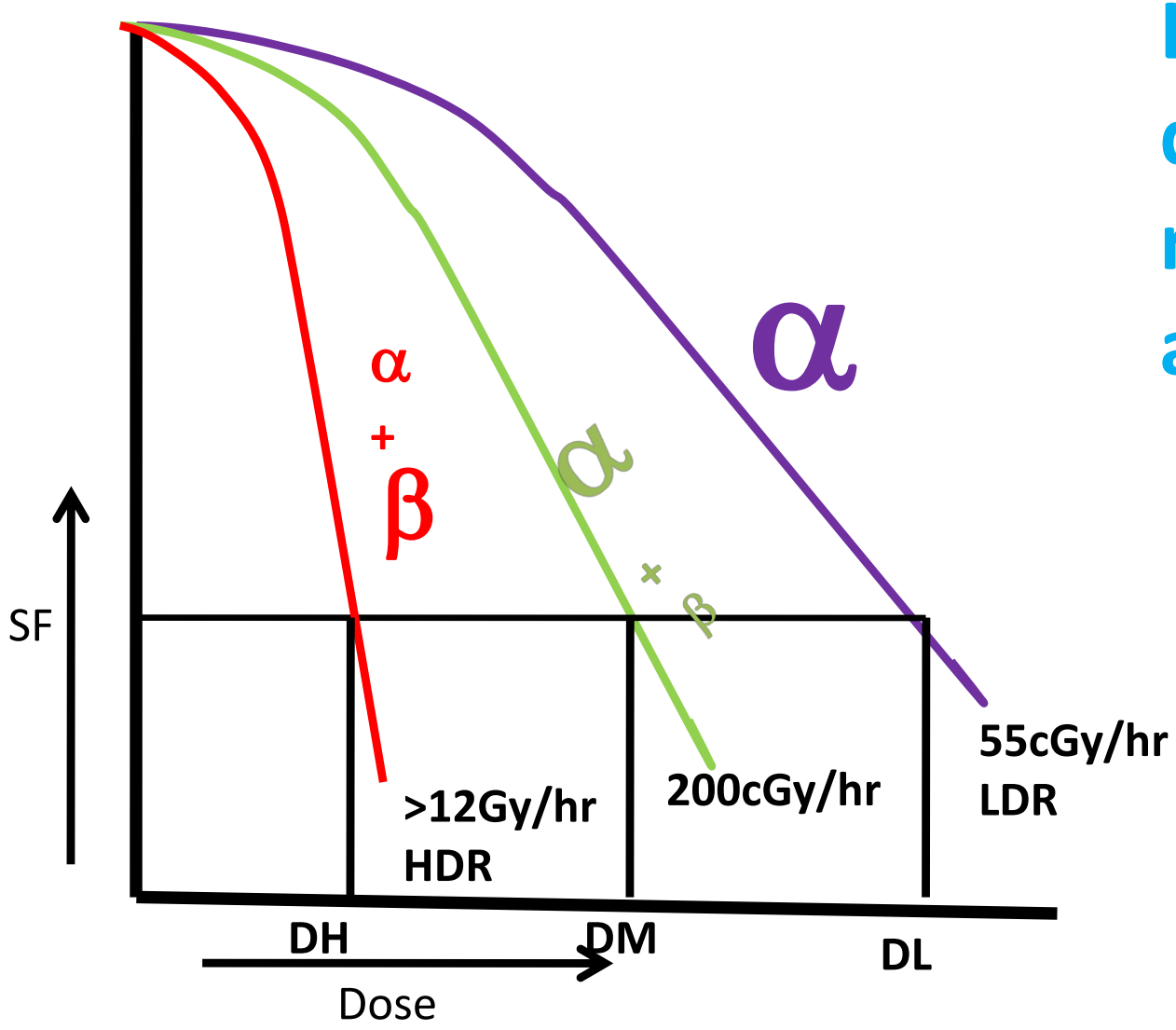
LDR to Selectron

DS < DL



Dose Rate Effect Clinical Application

LDR to HDR



When we shift form LDR to HDR, total dose is to be reduced roughly by a factor of 30 – 40%

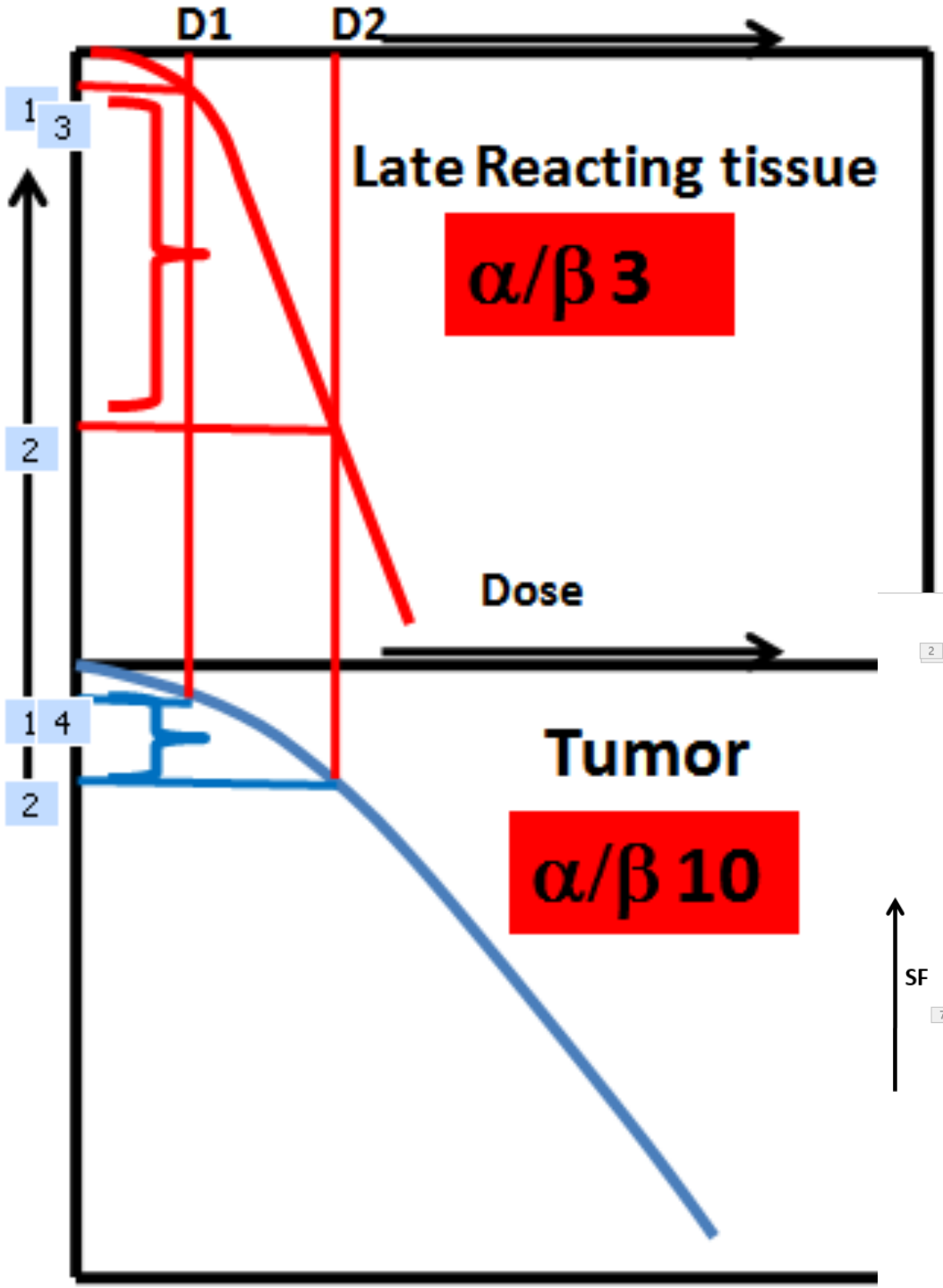
Total Dose for ca cervix after EBRT is 21 to 24 Gy which is equivalent to 35 Gy by LDR

Take Home

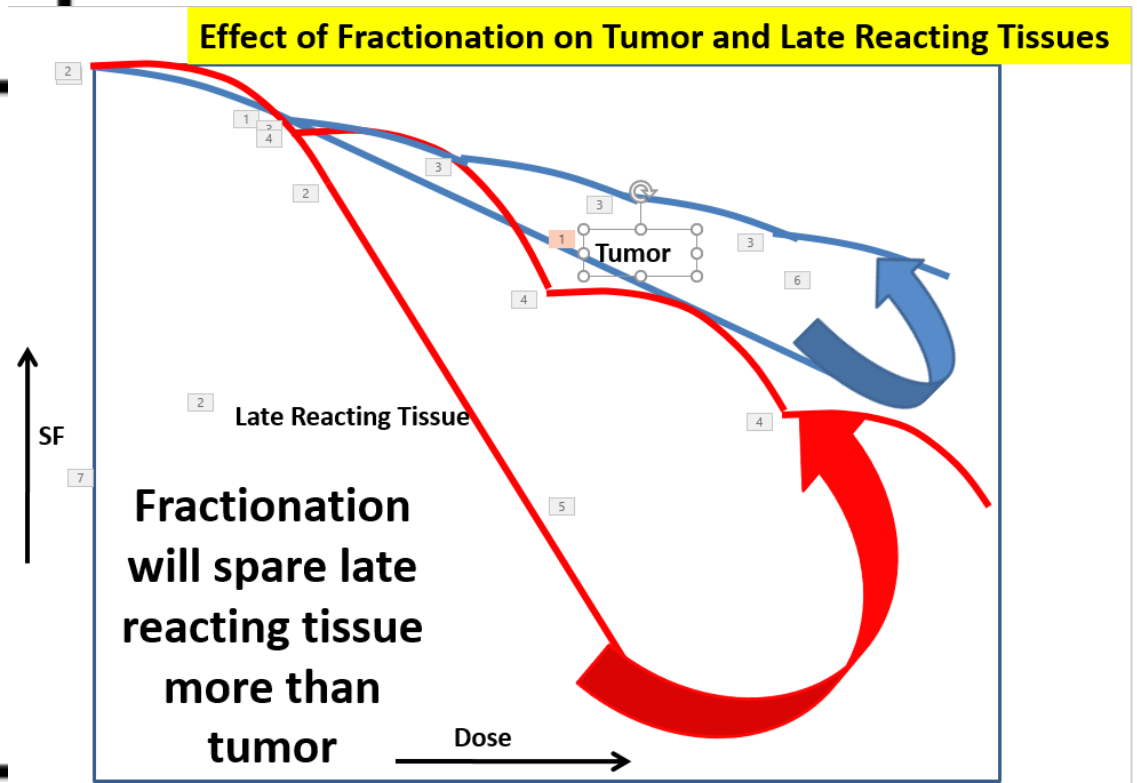
- **When you shift from LDR to HDR, total dose needs to be reduced.**

Should we give total dose in single fraction?

HDR Brachytherapy



Increasing Dose rate will damage late reacting tissue more than tumor

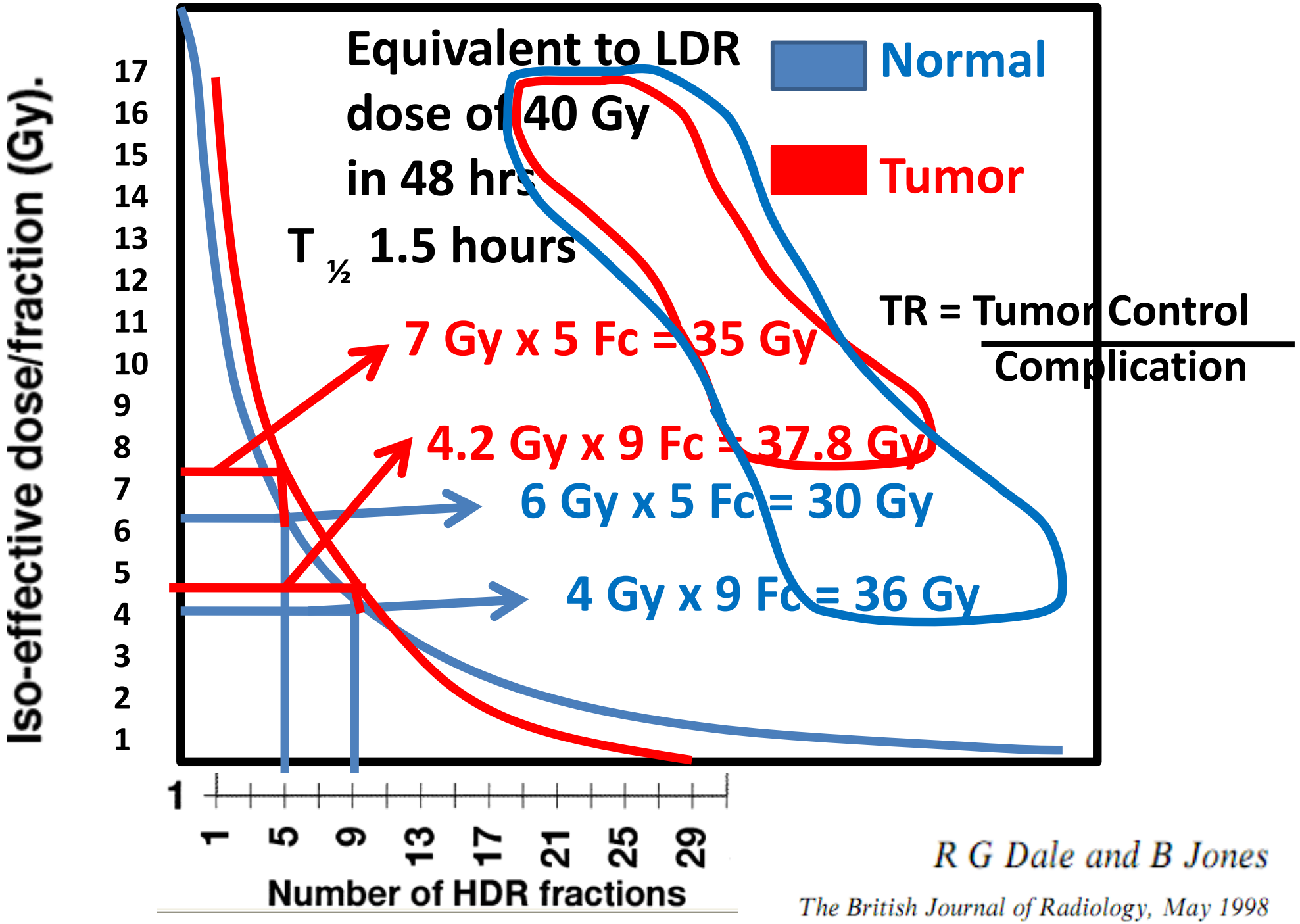


Take Home

- **When you shift from LDR to HDR, total dose needs to be reduced.**
- **With HDR, total dose is to be delivered in fractions.**

What must be the optimum no of fraction to get the same Therapeutic Ratio (TR) as with LDR ?

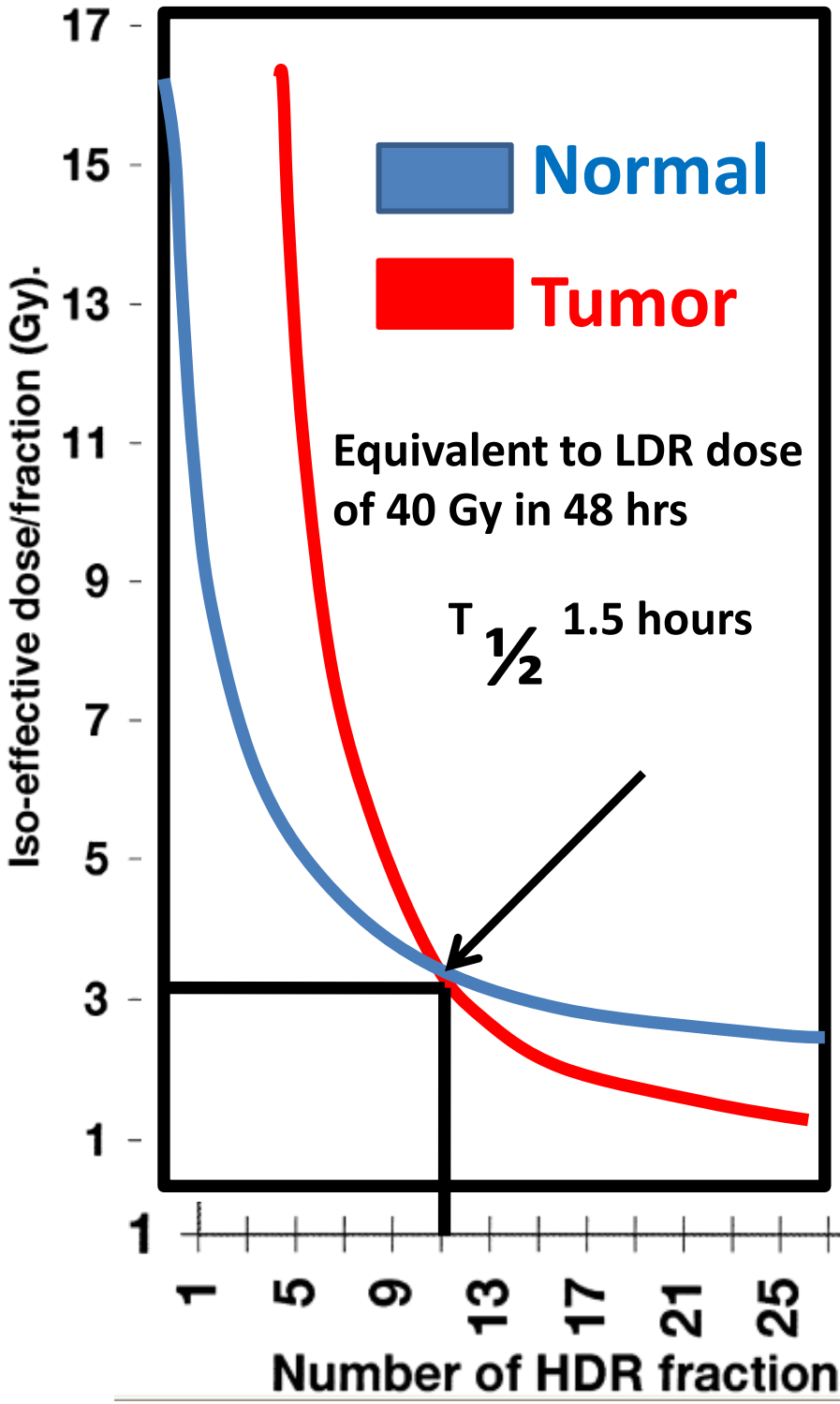
Fractionations in HDR Brachytherapy



R G Dale and B Jones

The British Journal of Radiology, May 1998

Fractionations in HDR Brachytherapy



What should be the ideal no. of fractions?
TR(HDR) = TR(LDR)

3 Gy x 11 Fc = 40 Gy in 48 hours

Can we further reduce the number of fractions?

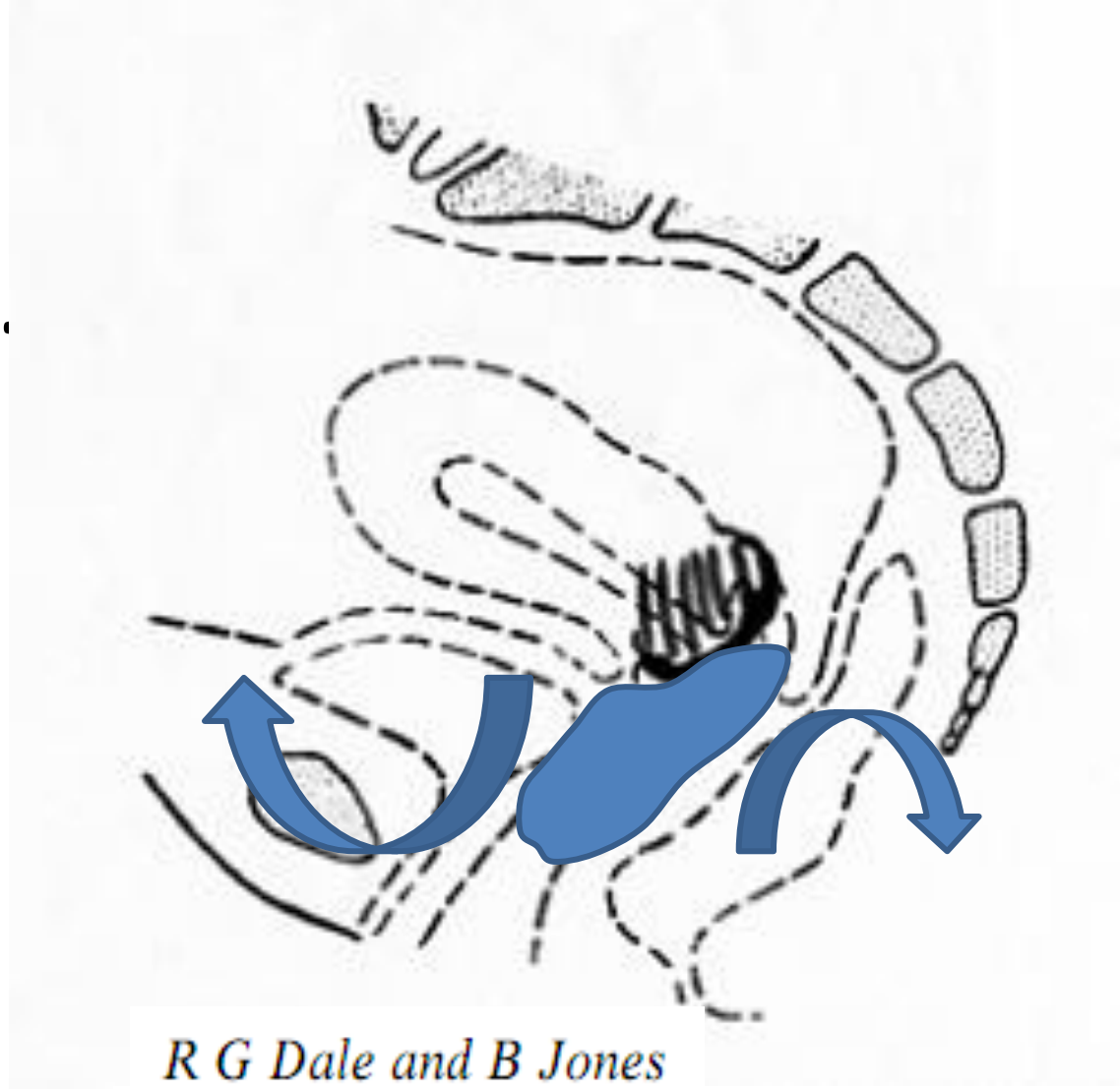
By Geometrical Sparing of Normal Tissues

R G Dale and B Jones
The British Journal of Radiology, May 1998

Geometrical Sparing of Normal Tissues (Ca Cervix)

By Packing the distance of rectum & Bladder from radiation sources increases.

- **Dose rate falls of rapidly.**
- **BED falls of rapidly**



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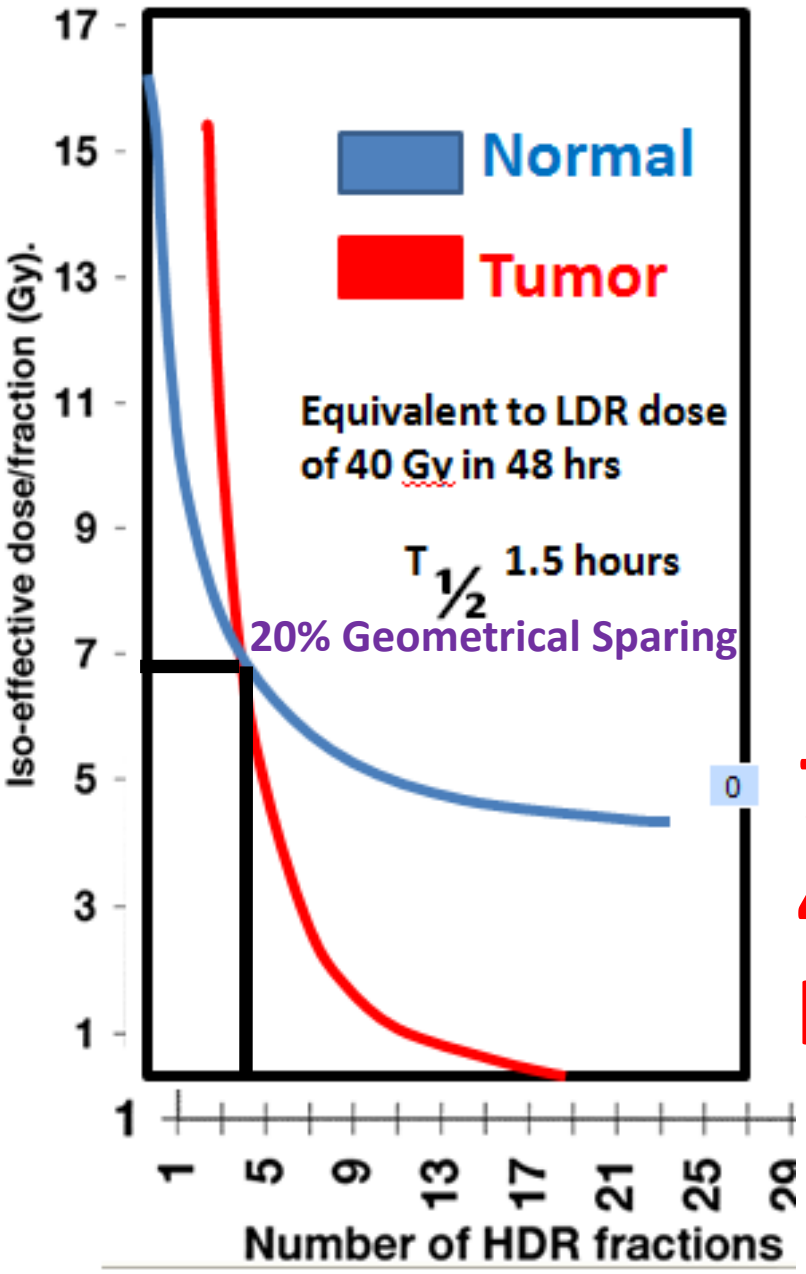
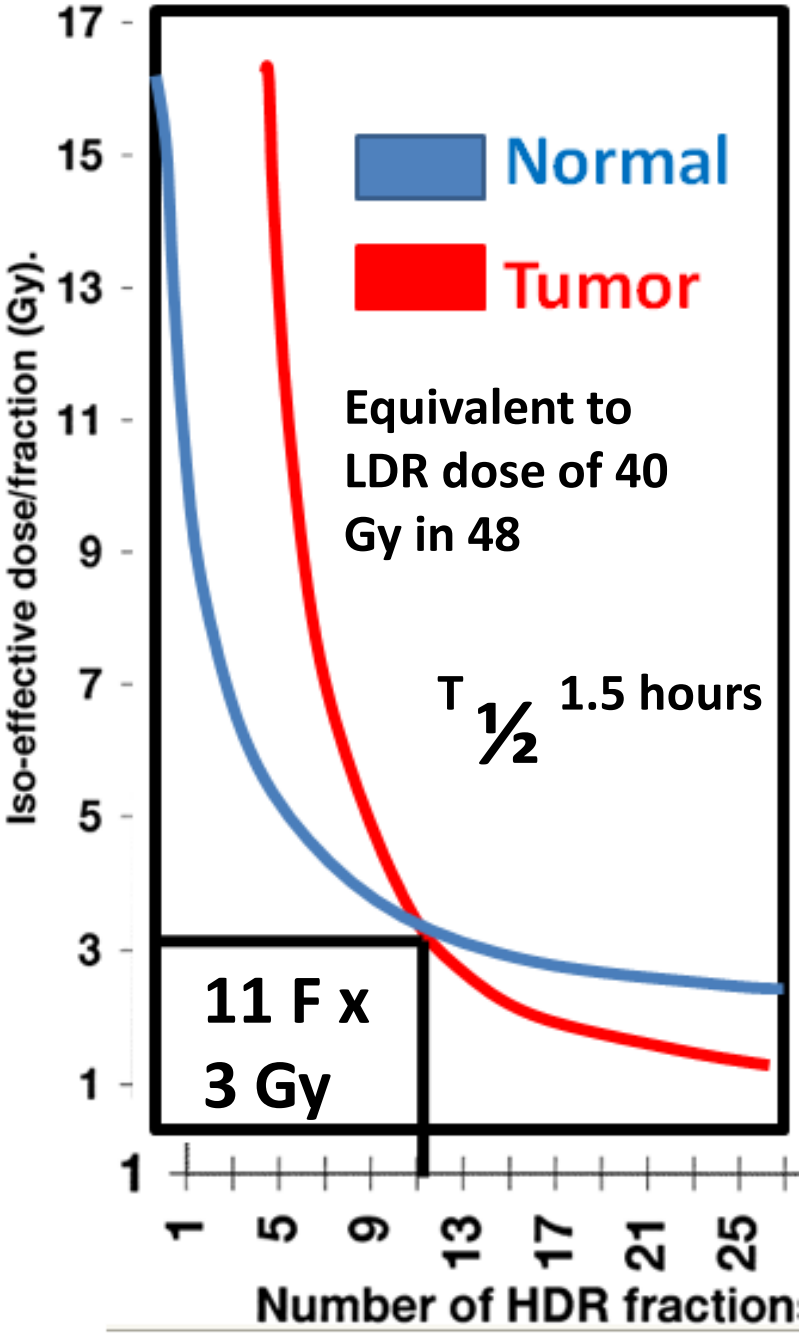
Fractionations in HDR Brachytherapy



TR(HDR) = TR(LDR) at 4 fractions

7 Gy x 4 Fc = 40 Gy in 48 hours



Take Home

- When you shift from LDR to HDR, total dose needs to be reduced.
- With HDR, total dose is to be delivered in fractions.
- With HDR, always try to achieve geometrical sparing of the critical organ i.e. rectum and bladder.
- Do not underestimate the importance of good packing in cervix brachytherapy

Repopulation

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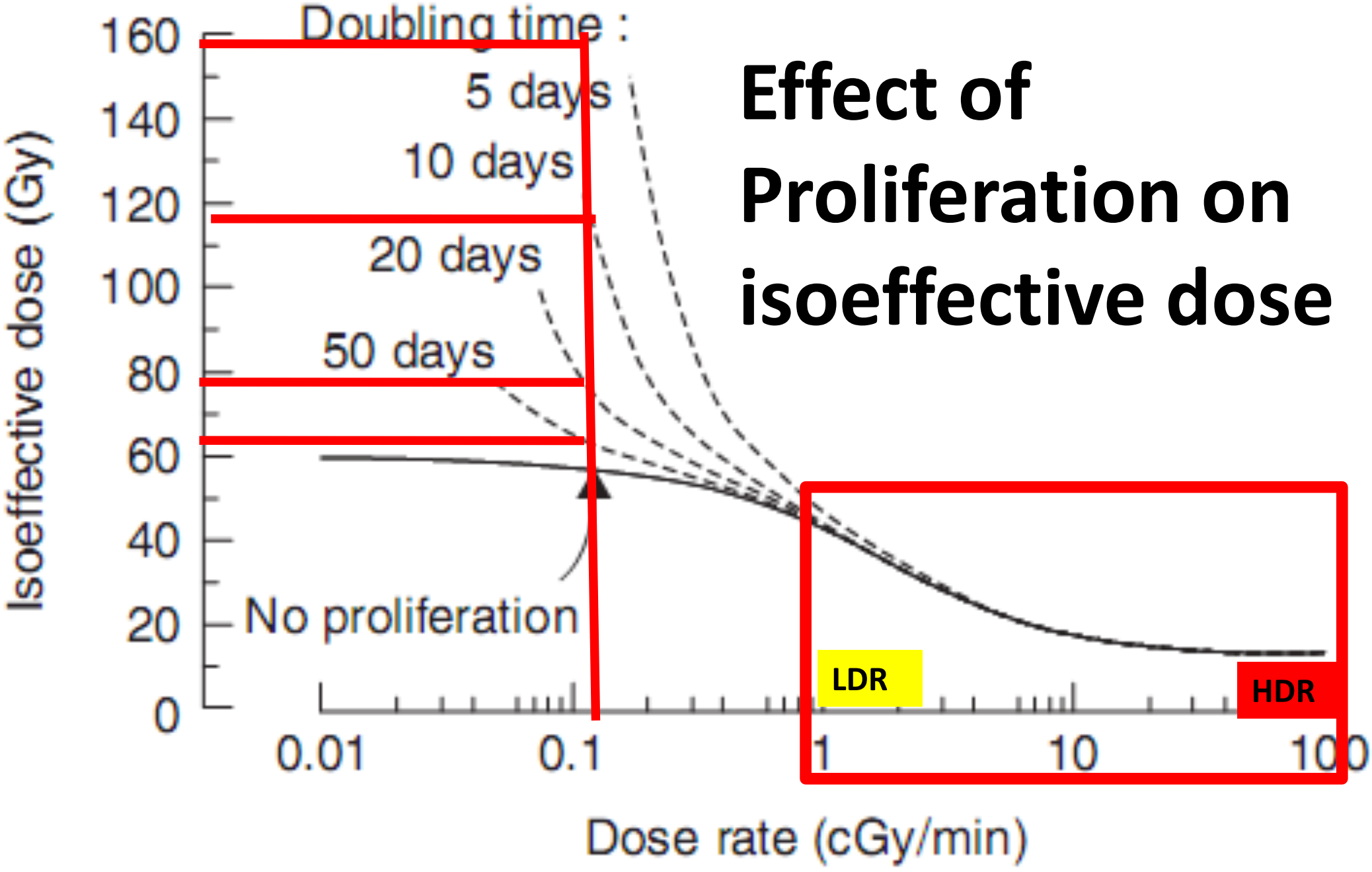
The British Journal of Radiology, May 1998



Effect of Proliferation on isoeffective dose

Reoxygenation

- **Slow Process.**
- **The radiation delivery completes very fast in few days.**
- **Disadvantage in LDR Brachy therapy.**
- **Other process of reoxygenation may triggered like recirculation in closed vessel leading to temporary increase in blood flow.**
- **OER is 1.6 to 1.7 with low dose radiation**

Equieffective Dose (EQD2)

- 60 Gy/ 15 Fraction = Dose/fraction 4 Gy

- What will be isoeffective total dose delivered in 2Gy/Fc.
- Biological Effective Dose (BED)

Biologically Effective Dose (BED) $= (nd) \times \left(1 + \frac{d}{\alpha/\beta}\right)$ (4)

60 Gy/ 15 Fraction = Dose/fraction 4 Gy

EQD2 in 2 Gy/Fc

(BED)2 = (BED)1 **EQD2 = BED/1.2**

EQD2 = BED/1.2

EBRT 46Gy/23F + 7Gy X 3F ICRT

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

Summary

- **Repair of the sub-lethal damage is the most important radiobiological process defining the dose rate effect.**
- **In HDR brachytherapy, the TR can be improved with fractions and geometrical sparing.**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Thanks


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