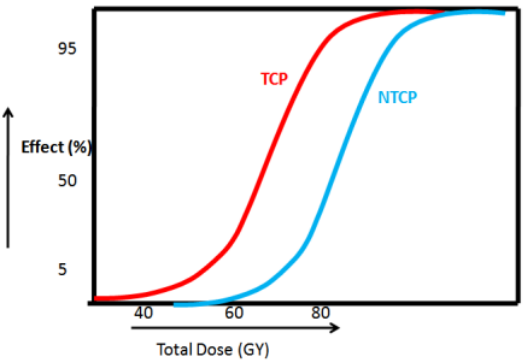
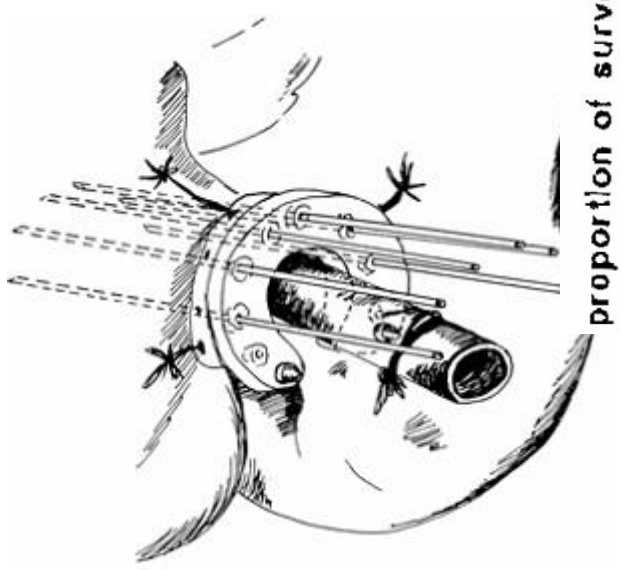
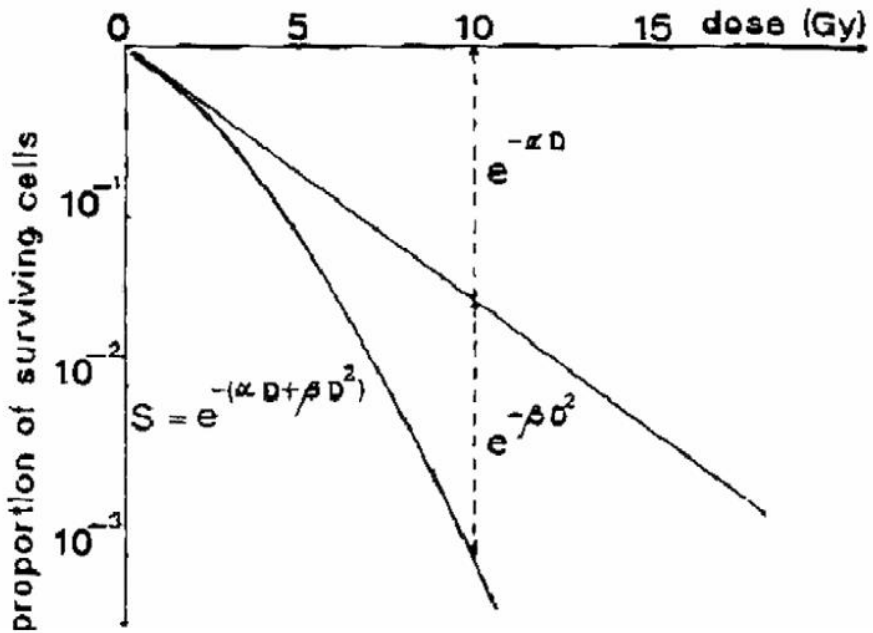
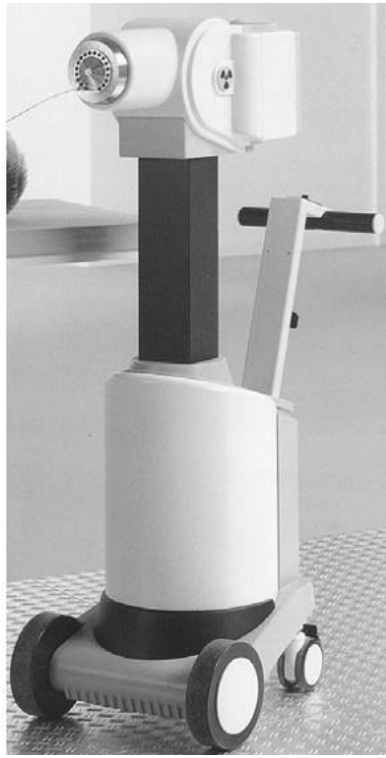
Radiobiology of Brachytherapy





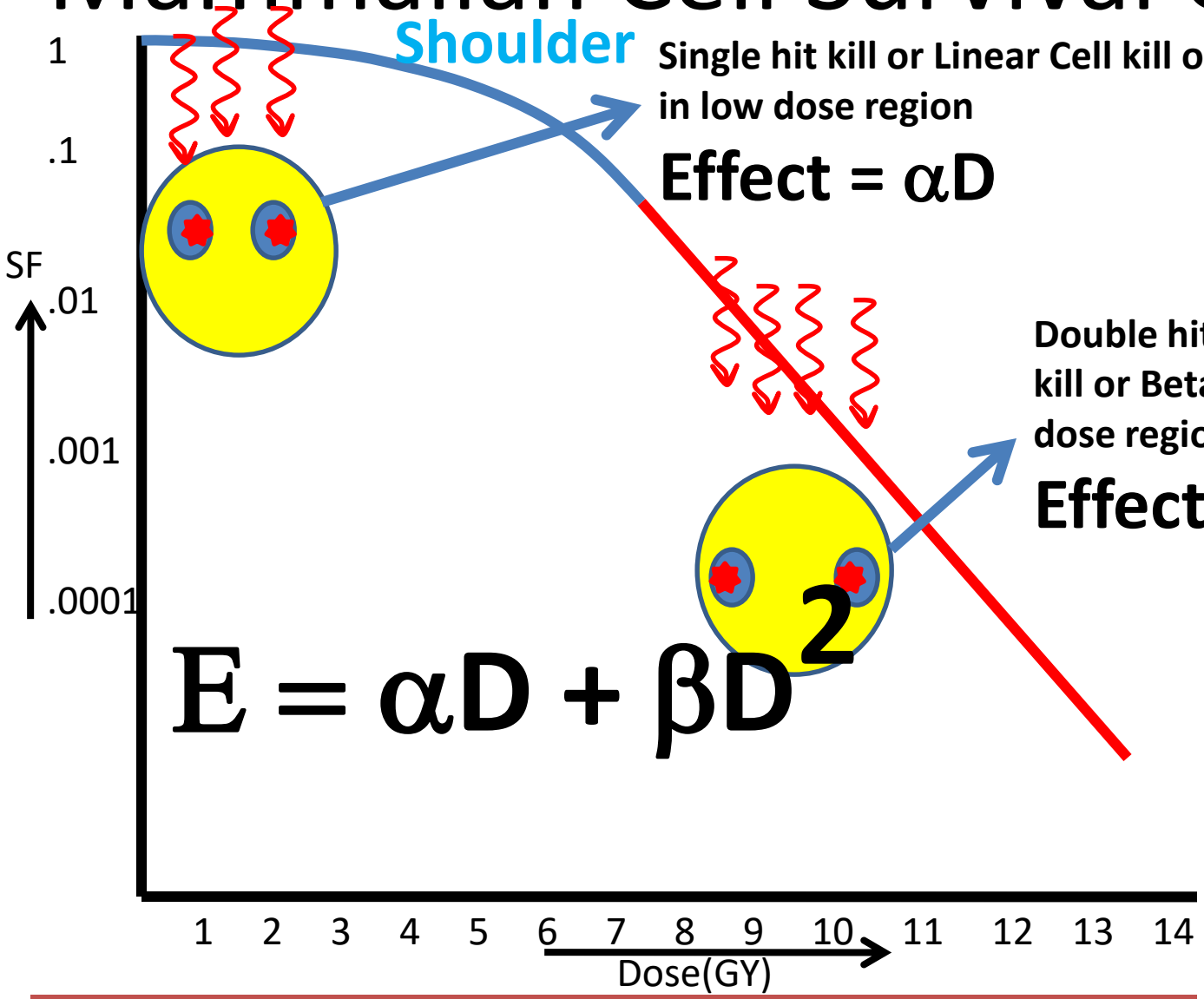




4 June, 2022

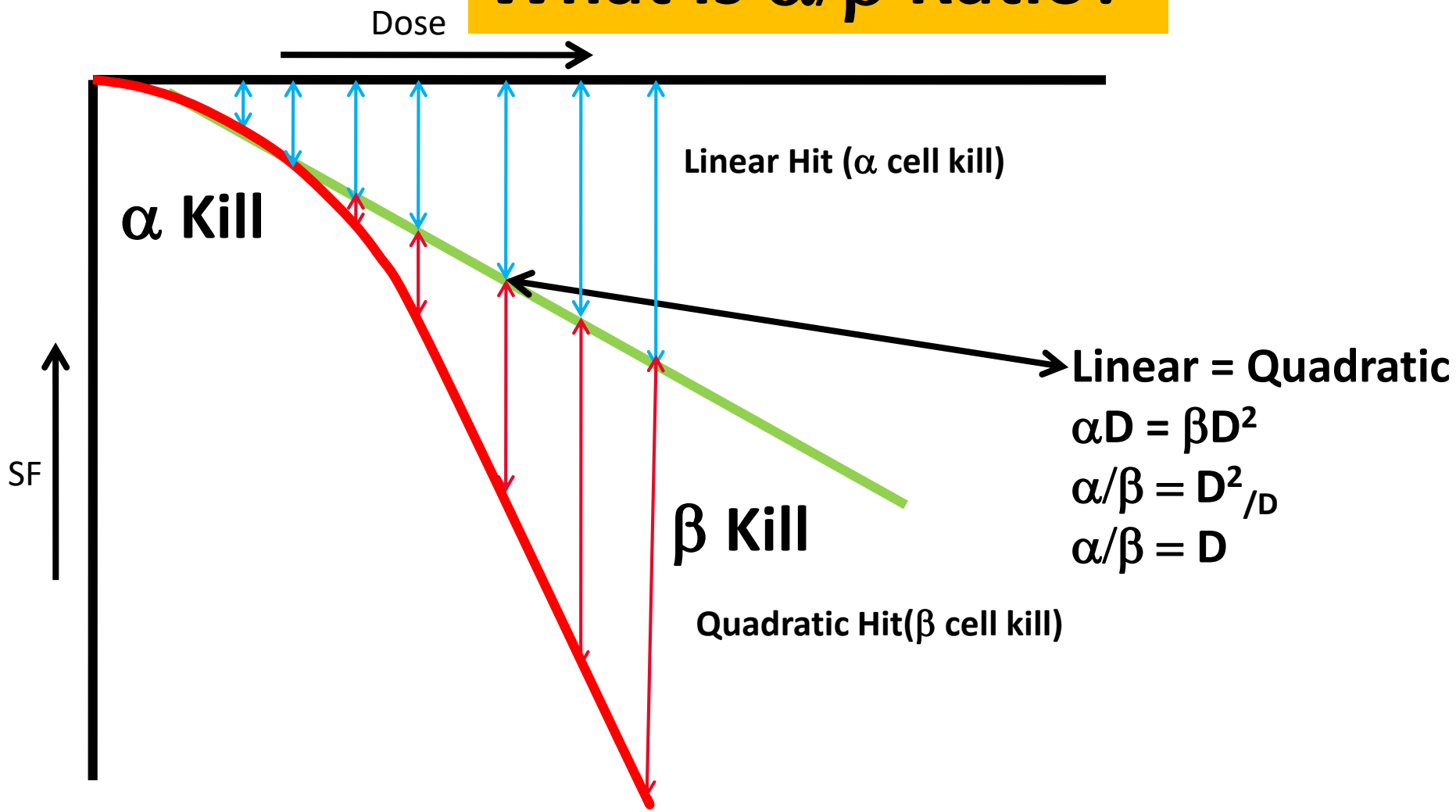
Prof Manoj Gupta
AIIMS, Rishikesh

Mammalian Cell Survival Curve



Linear-Quadratic Model

What is α/β Ratio?



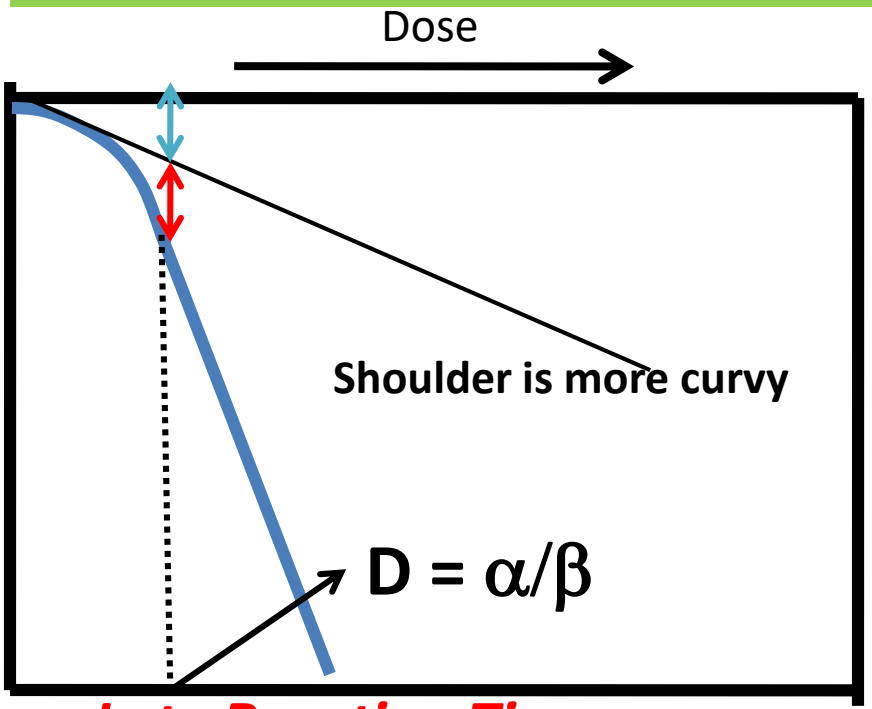
➢So α/β can be defined as the dose at which contribution by single hit (Linear) kill becomes equal to double hit (Quadratic) kill.

α/β Ratio defines "curviness" of survival curve

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

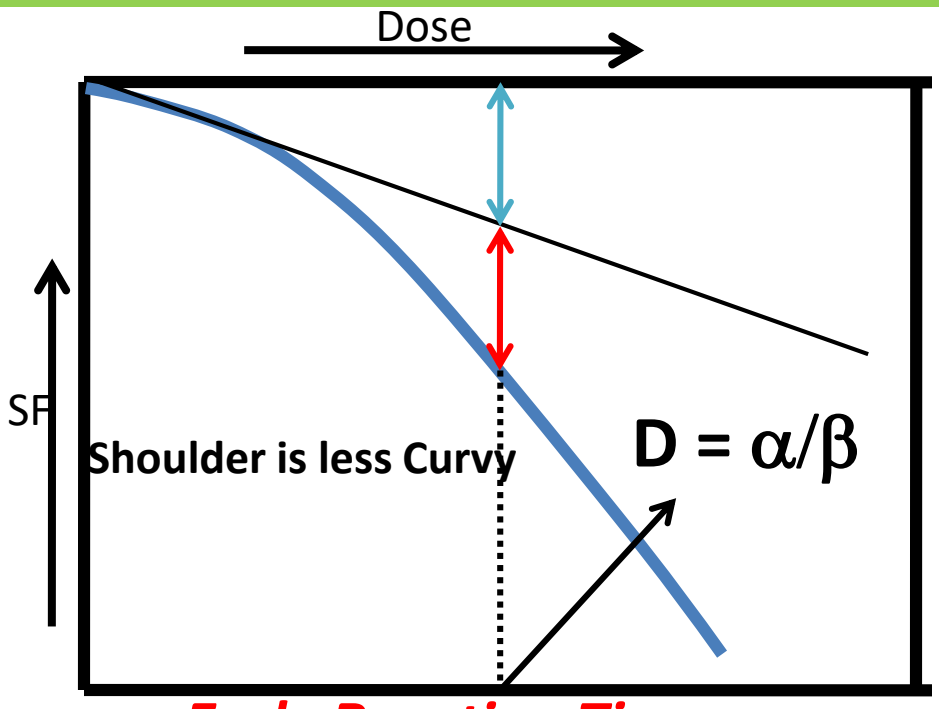
Malignant Tumors behave like early reacting tissue

α/β = 10



Late Reacting Tissue

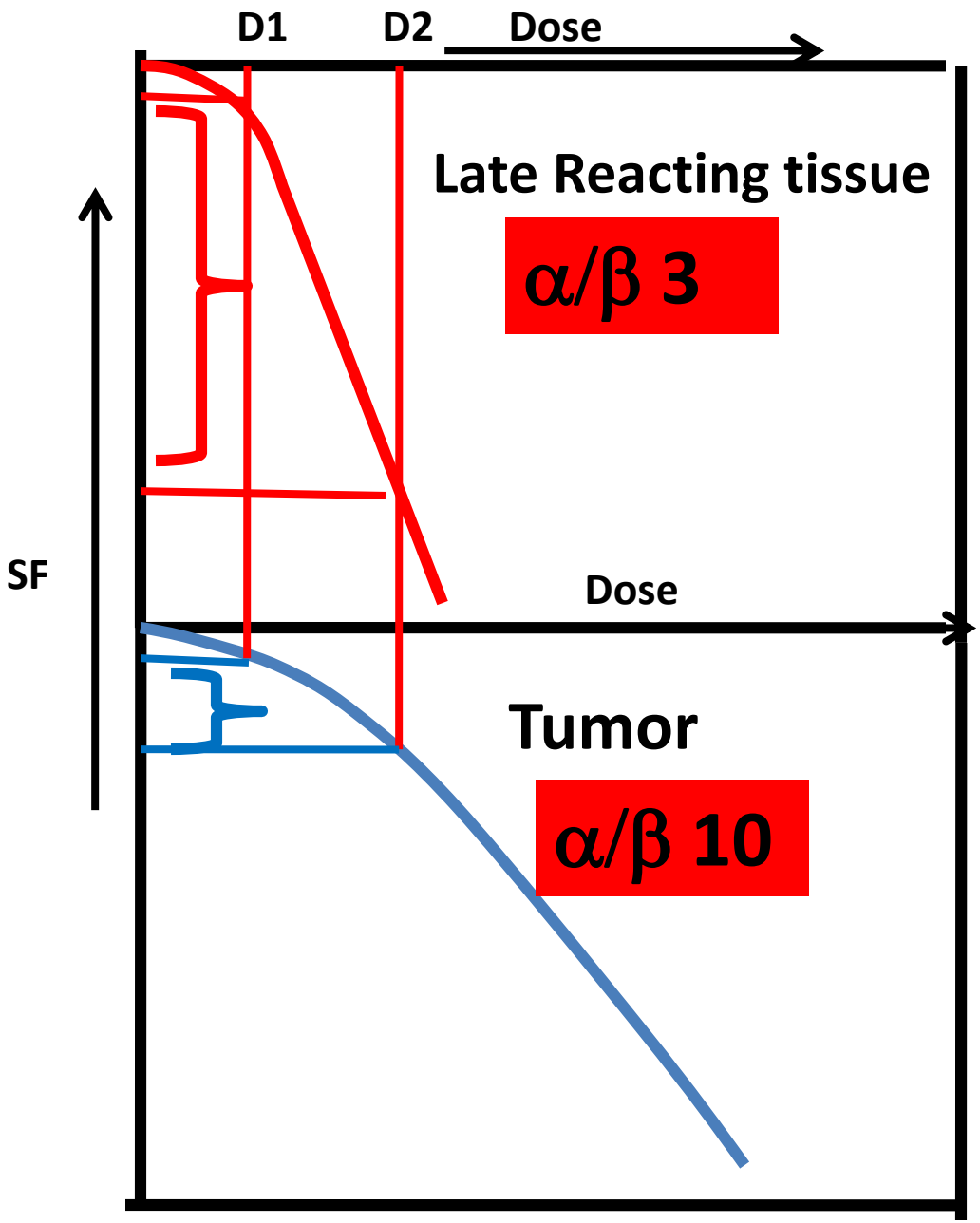
α/β = 1Gy to 7 Gy (3Gy)
Responsible for late effect of radiation
Eg. Spinal cord, urinary bladder, kidney, liver etc.



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.

Fraction size (Dose per fraction)

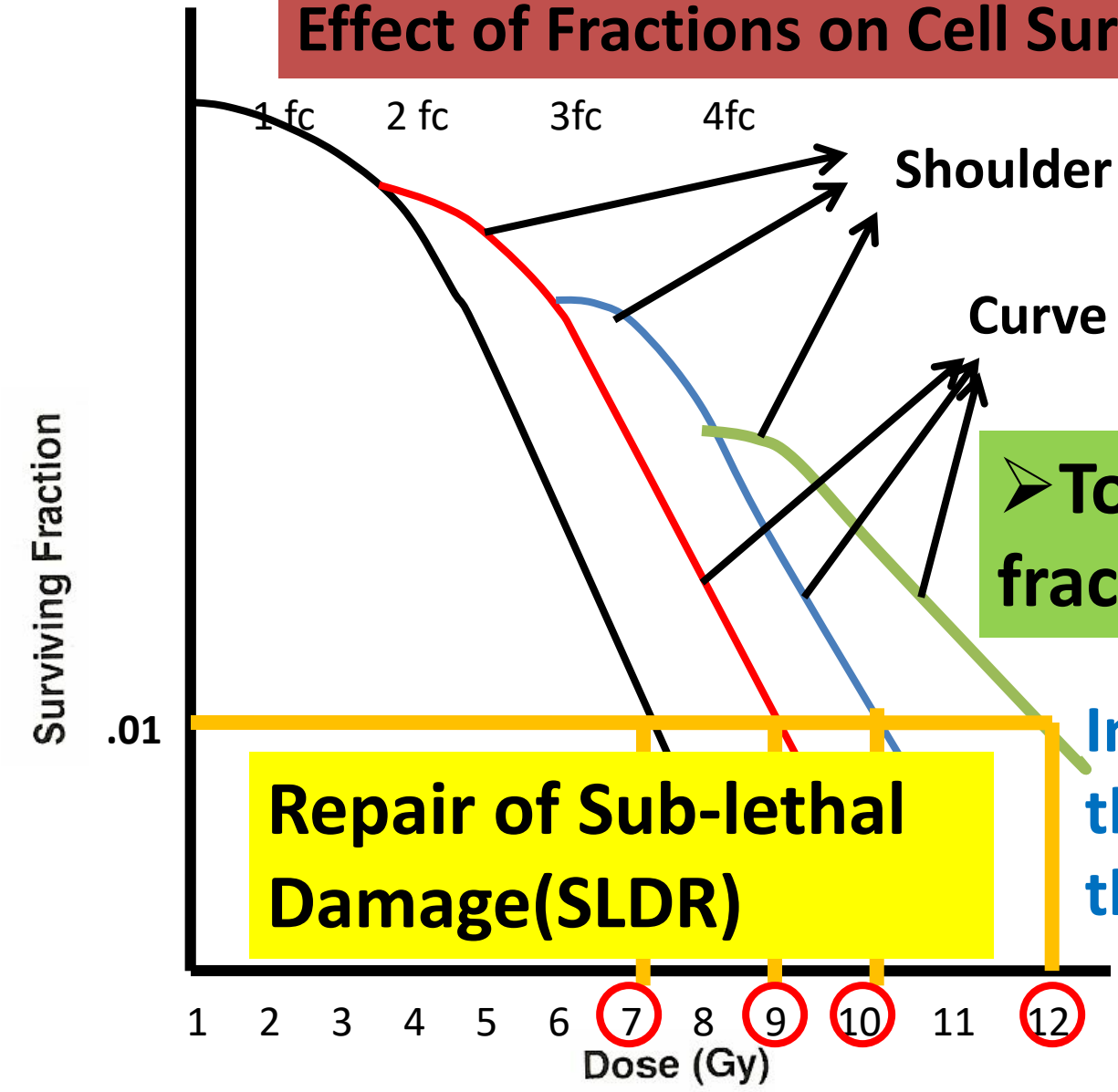


- Increase in dose per fraction will damage late reacting tissue more than tumor
- Decrease in dose per fraction will spare late reacting tissue more than tumor
- Dose per Fc is similar to dose rate
  - High Dose Rate = high dose per Fc (SRS, SBRT)
  - Low Dose Rate = low dose per Fc (Conv Fc RT)

Important Points

1. Shifting from LDR to HDR will affect the late reacting tissues more than tumor.

Effect of Fractions on Cell Survival Curve

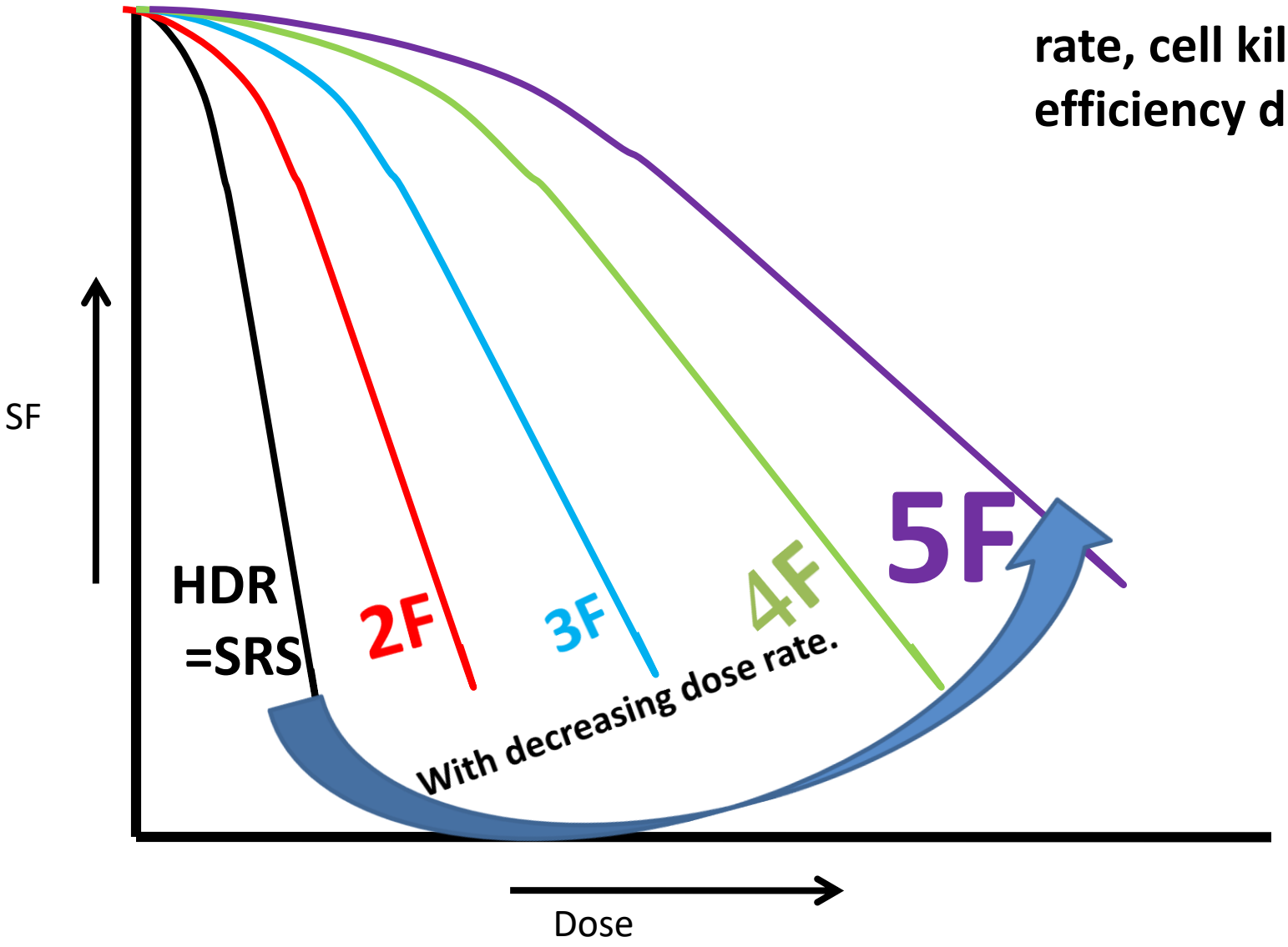


➢ Total dose α no of fractions

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

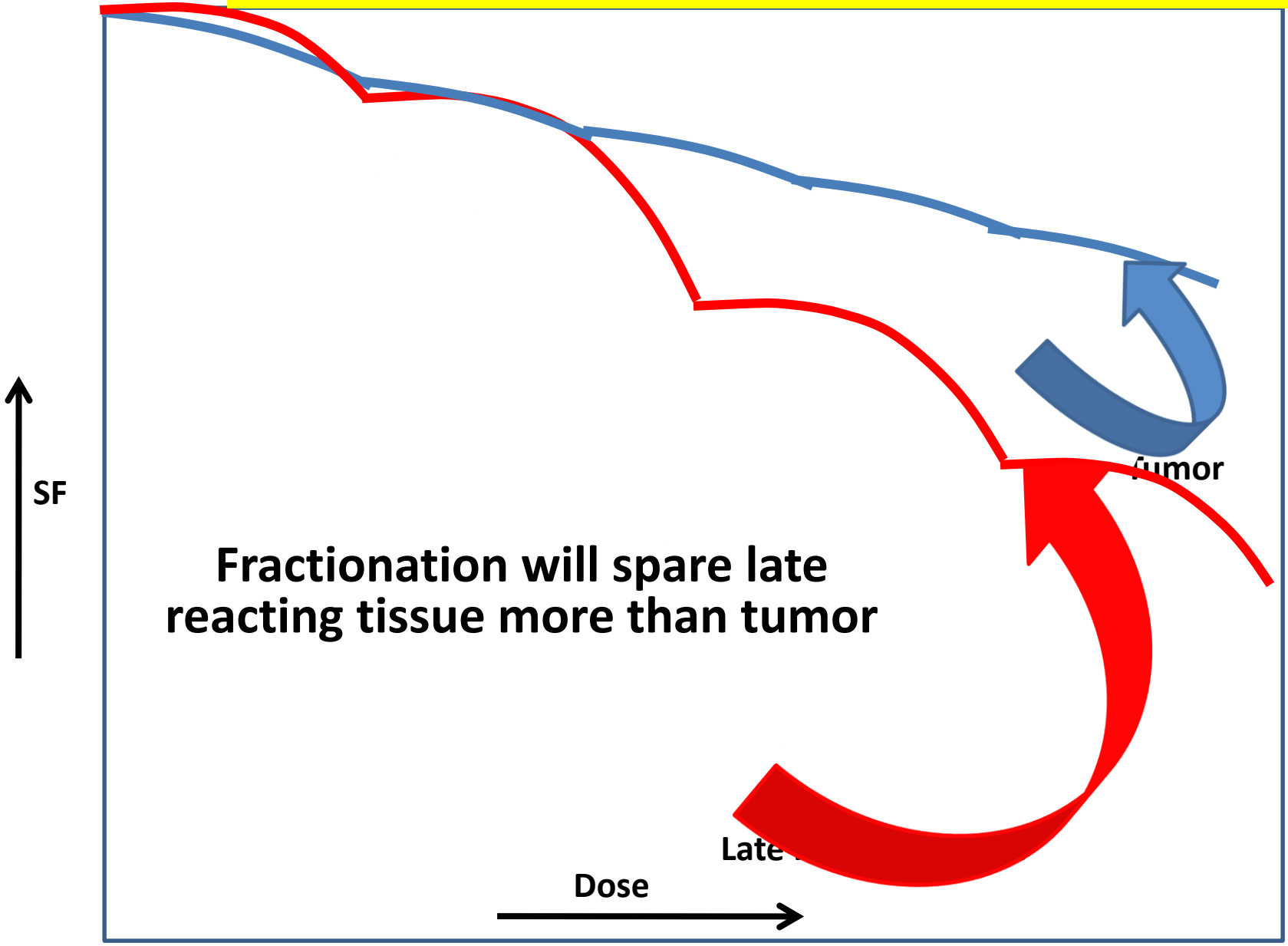


➢**With decreasing dose rate, cell killing efficiency decreases**

Important Points

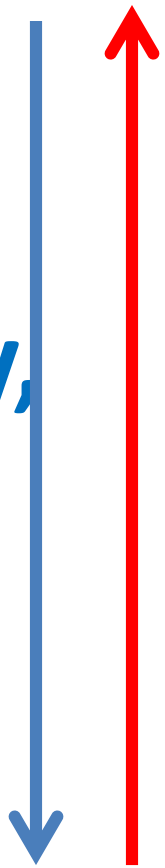
1. Shifting from LDR to HDR will affect the late reacting tissues more than tumor.
2. As the dose rate decreases curve become shallower reflecting decreasing cell killing efficiency.

Effect of Fractionation on Tumor and Late Reacting Tissues



Important Points

1. Shifting from LDR to HDR will affect the late reacting tissues more than tumor.
2. As no of Fc increases or in Brachy, dose rate decreases curve become shallower reflecting decreasing cell killing efficiency.
3. Fractionation spare late tissue more than tumor. HDR always fractionated.



Dose Rate

- **LDR** **0.4- 2 Gy per hour**
- **HDR** **> 12 Gy per hour**

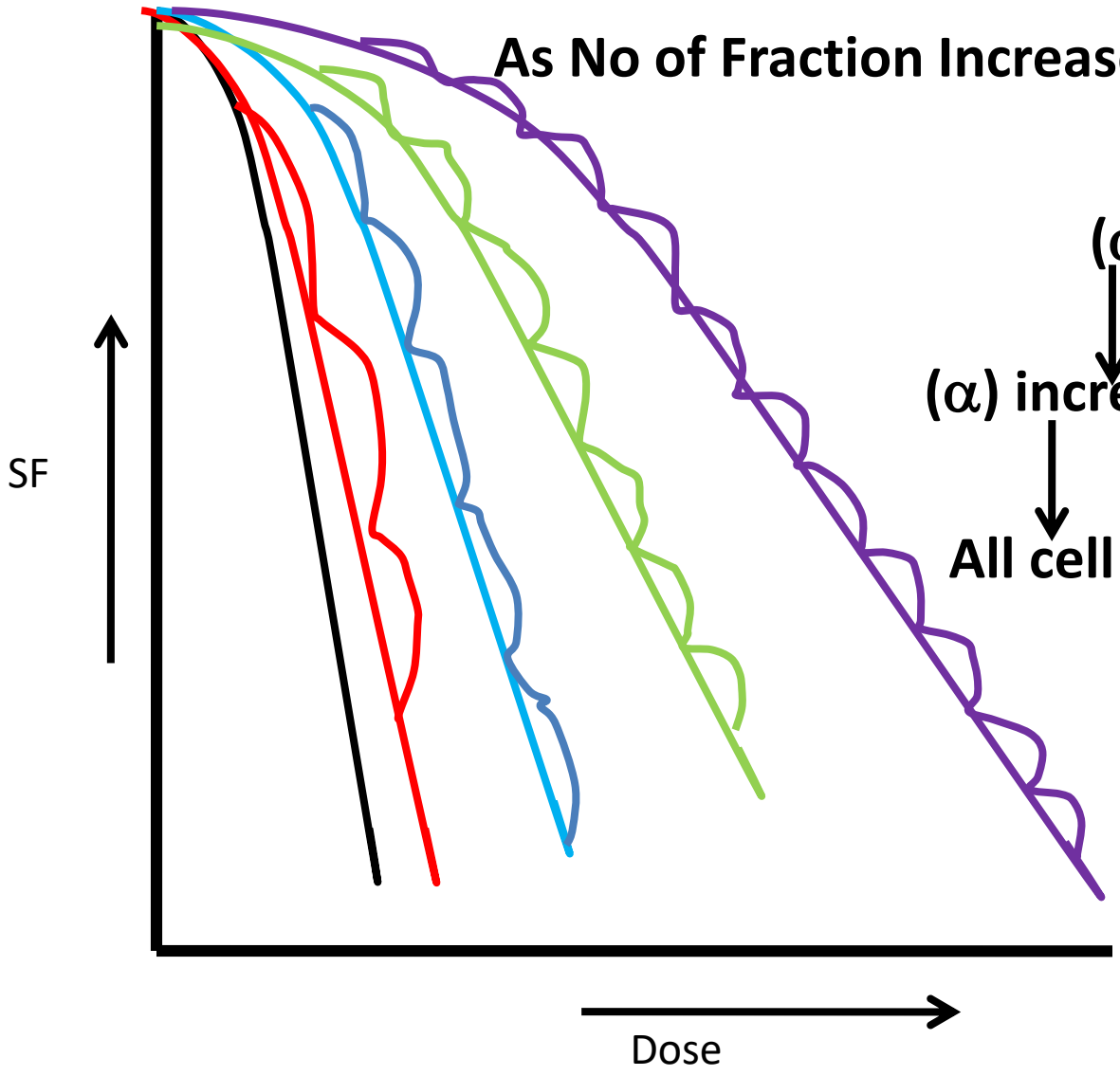
4 Rs of Radiobiology

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

Effect of fraction on cell survival curve



As No of Fraction Increases, Dose per Fc decreases

(α)

(β)

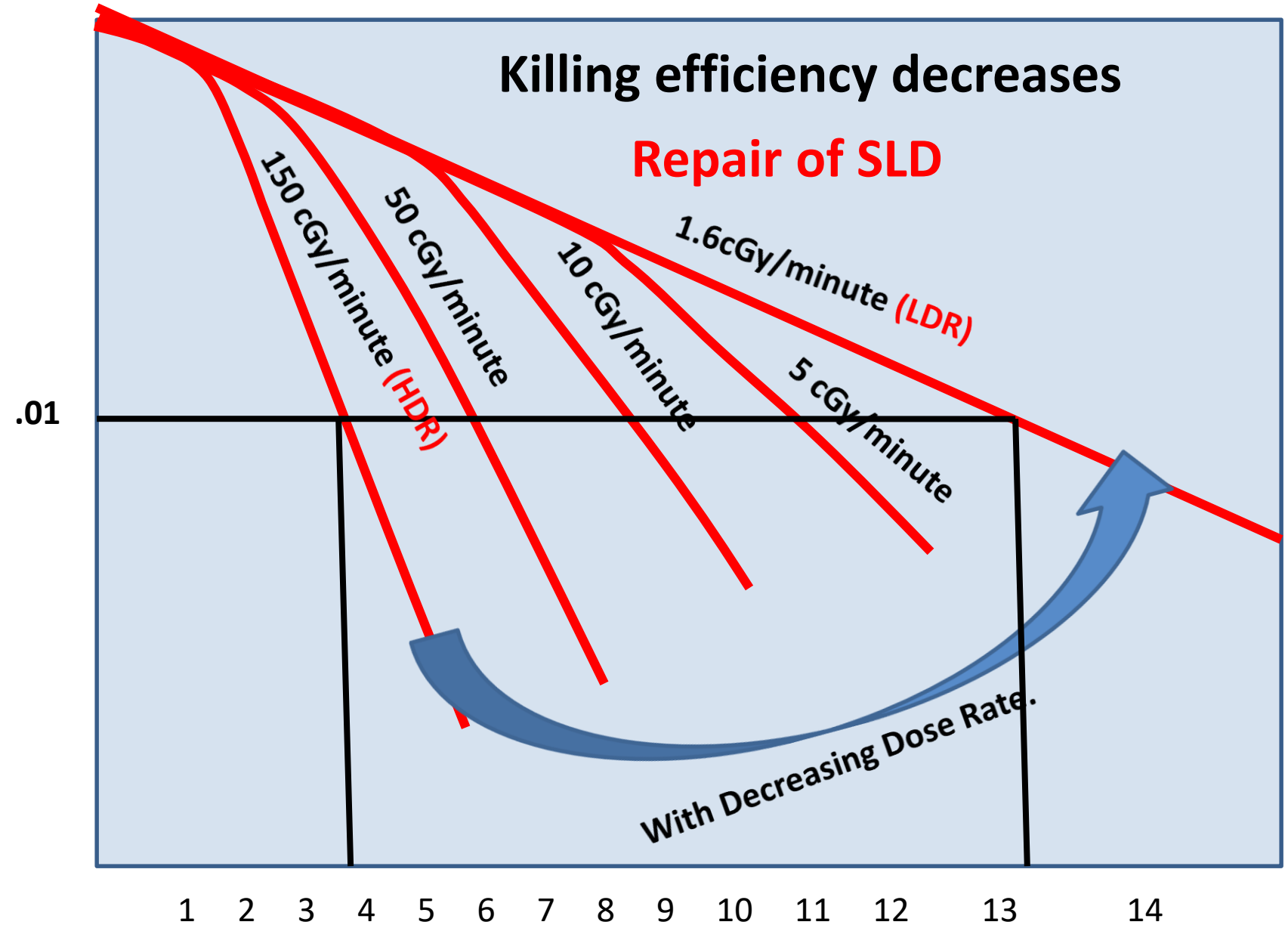
(α) increases

(β) decreases

All cell Kill by (α)

No contribution by (β)

Effect of Dose Rate on Cell Survival Curve

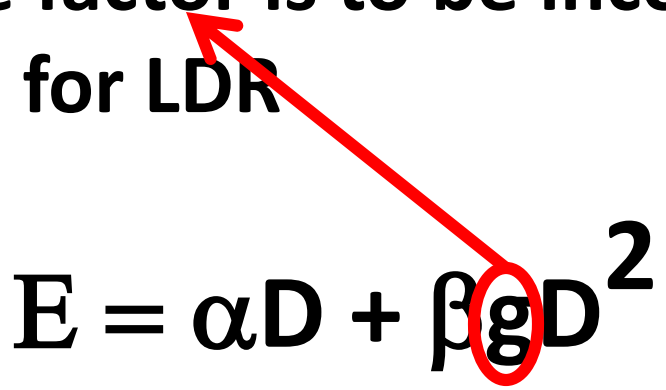


Repair of Sub Lethal Damage

- 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)

- 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 of Linear and Quadratic Hits

Dose Rate Effect

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

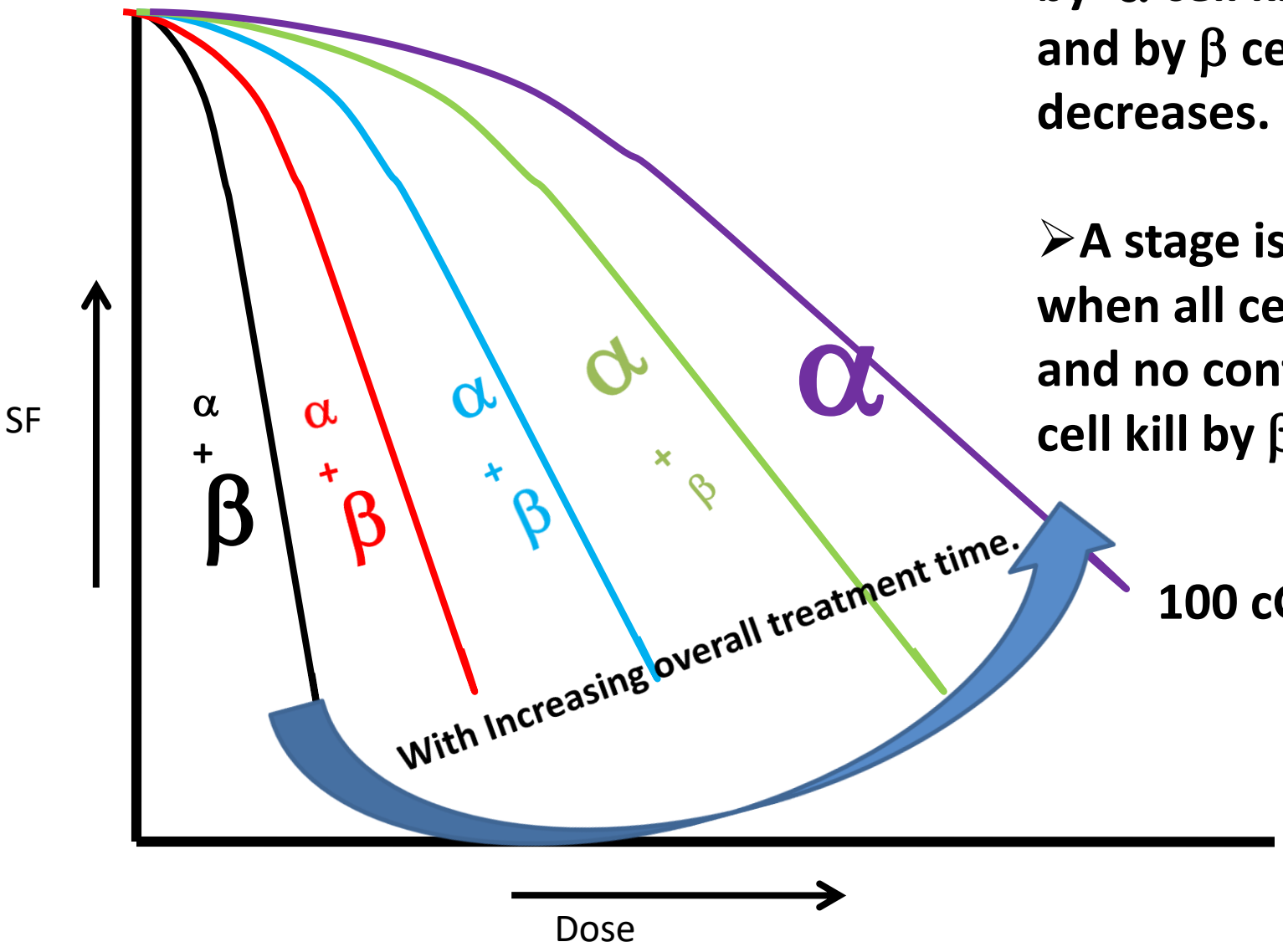
- As the treatment duration increases the value of g decreases from 1 and for very long duration of treatment as in LDR the value becomes Zero

$$E = \alpha D$$

- All the cell killing is by linear Hits

- As treatment duration increases the relative contribution by quadratic kill (β) keeps decreasing and by linear kill (α) keeps increasing till all the cell kill is by linear kill(α) and gradually cell survival curve become shallower.

Dose Rate Effect



- Relative contribution by α cell kill increases and by β cell kill decreases.
- A stage is reached when all cell kill is by α and no contribution in cell kill by β

100 cGy per hour

Dose Rate Effect Clinical Application

Carcinoma Cervix

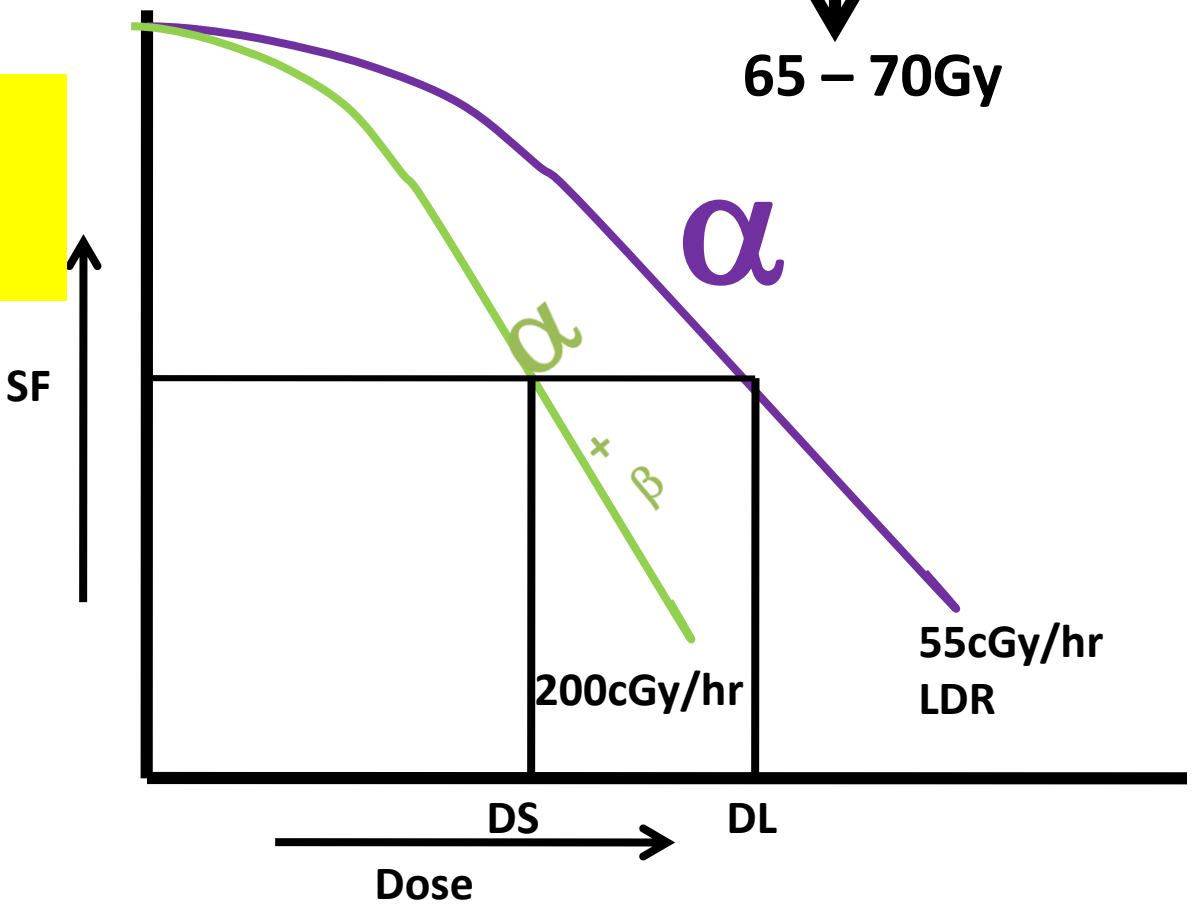
- LDR 53cGy/hr and total dose delivered was 75Gy at point A
- At this dose rate all the cell kill is by α kill (<100cGy/hr).
- Selectron Brachytherapy 140-200cGy/hr,

10 – 20%

65 – 70Gy

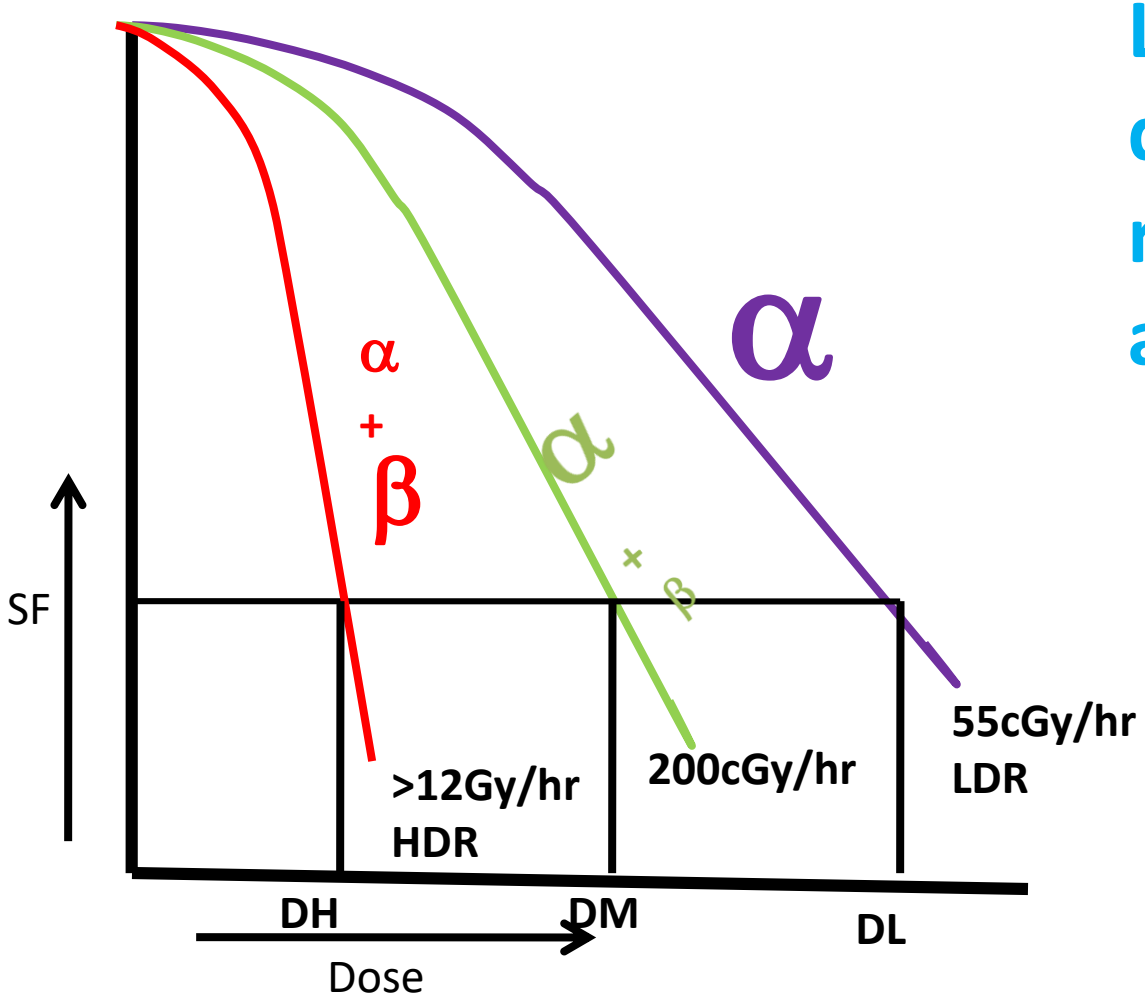
LDR to Selectron

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%

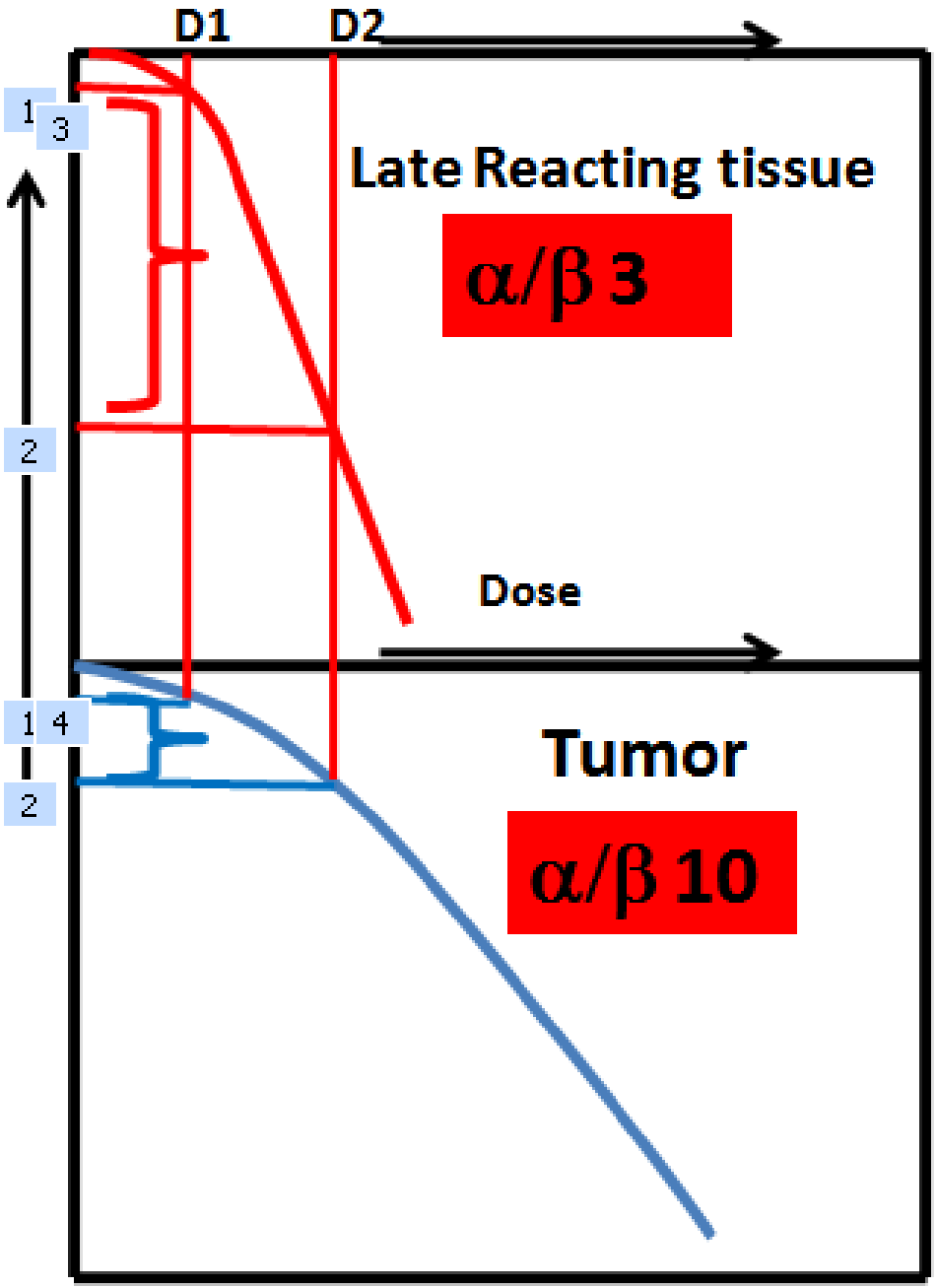
Total Dose for ca cervix after EBRT is 21 to 24 Gy which is equivalent to 35 Gy by LDR

Take Home

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

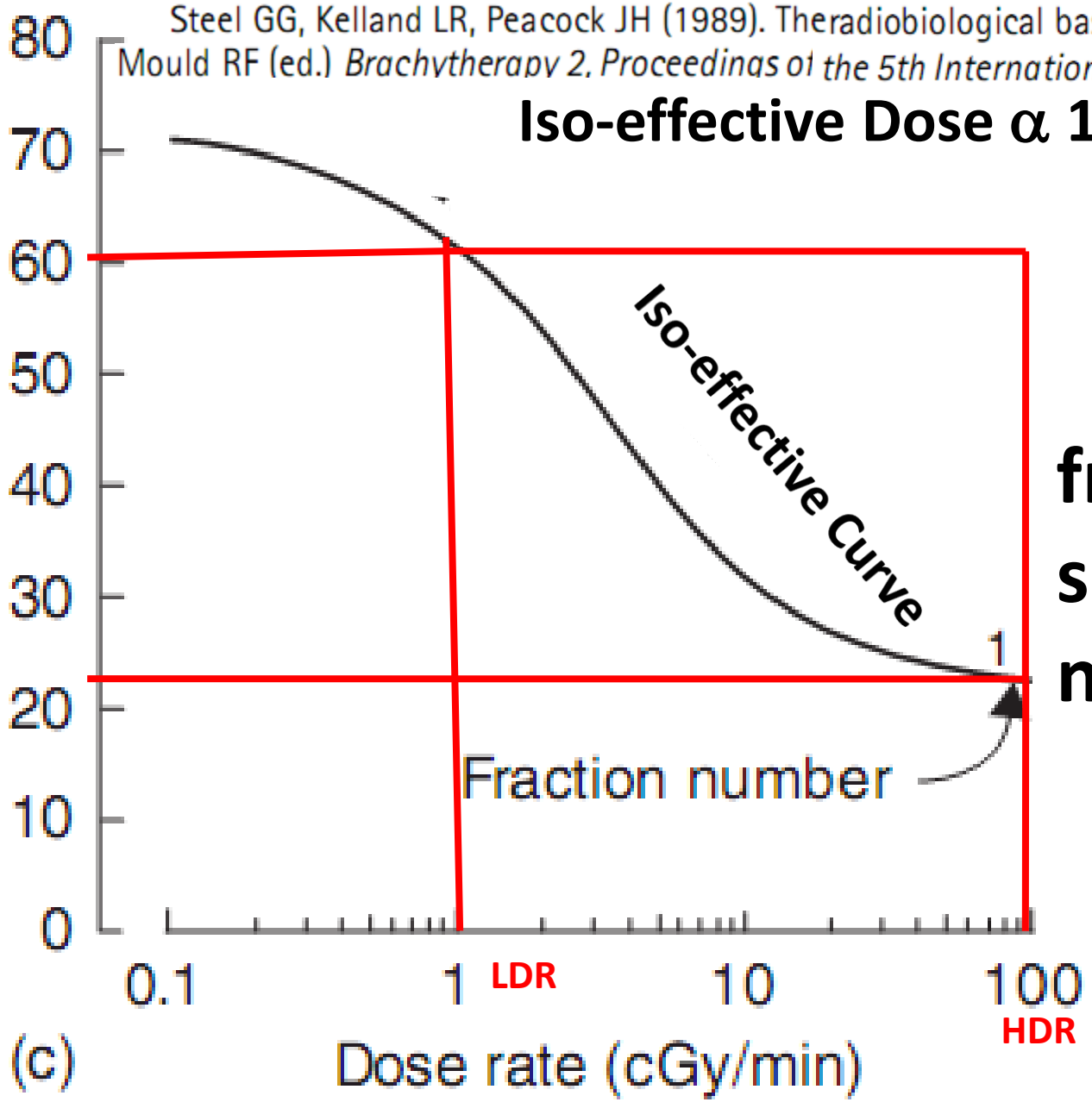
Should we give total dose in single fraction?

HDR Brachytherapy



Increasing Dose rate will damage late reacting tissue more than tumor

HDR Brachytherapy



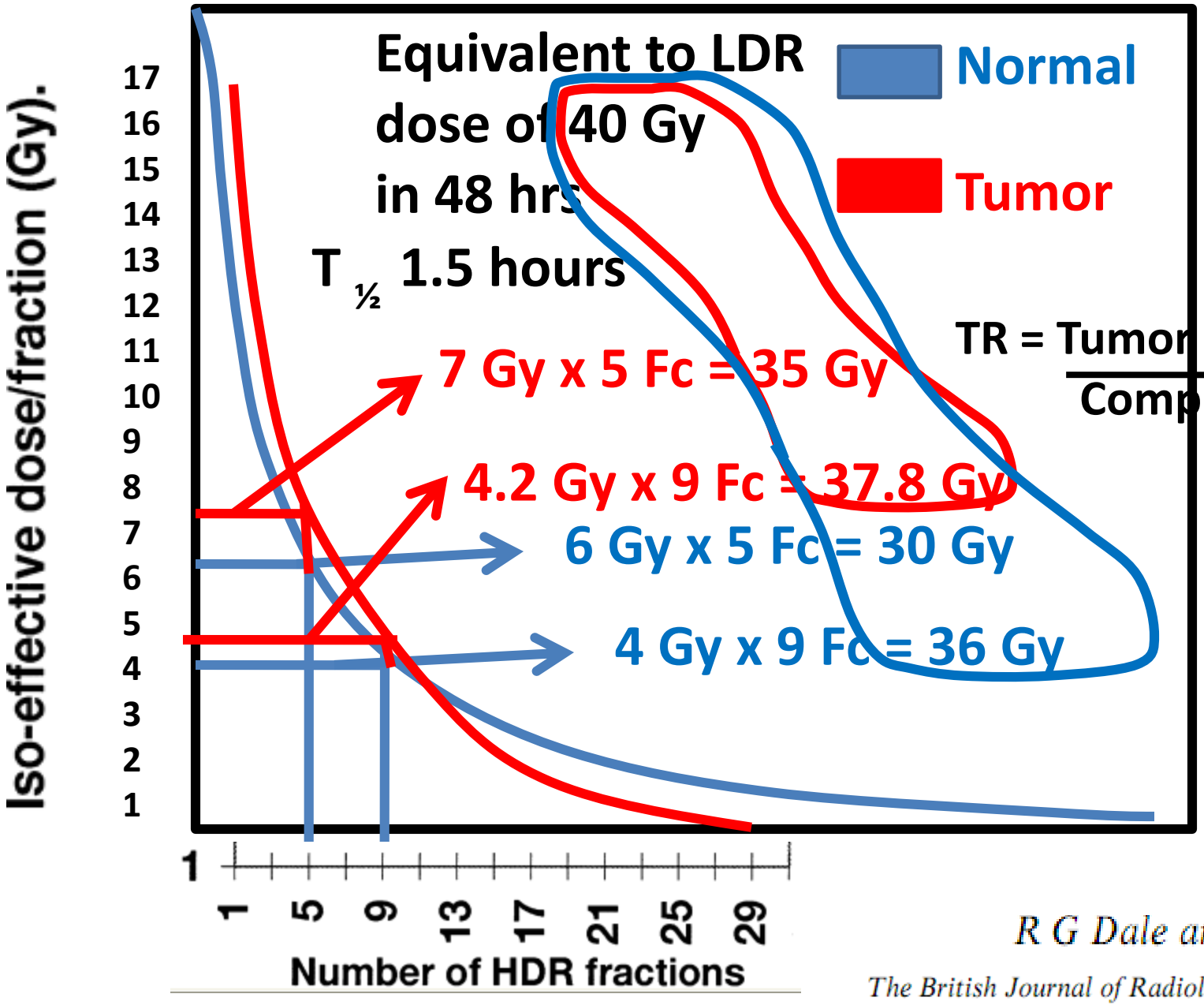
fractionation spares the normal tissues

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 ?

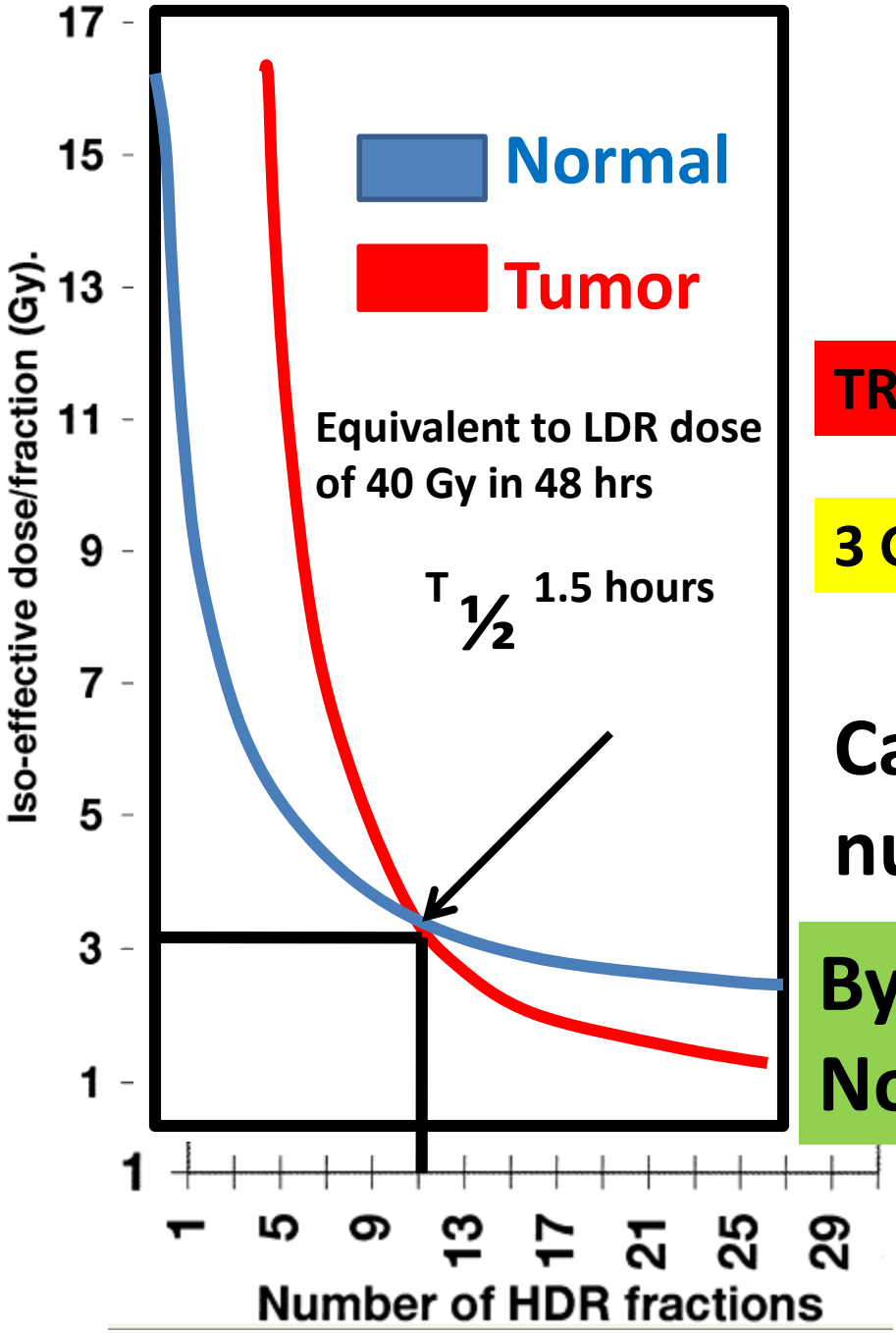
Fractionations in HDR Brachytherapy



R G Dale and B Jones

The British Journal of Radiology, May 1998

Fractionations in HDR Brachytherapy



TR(HDR) = TR(LDR)

3 Gy x 11 Fc = 40 Gy in 48 hours

Can we further reduce the number of fractions?

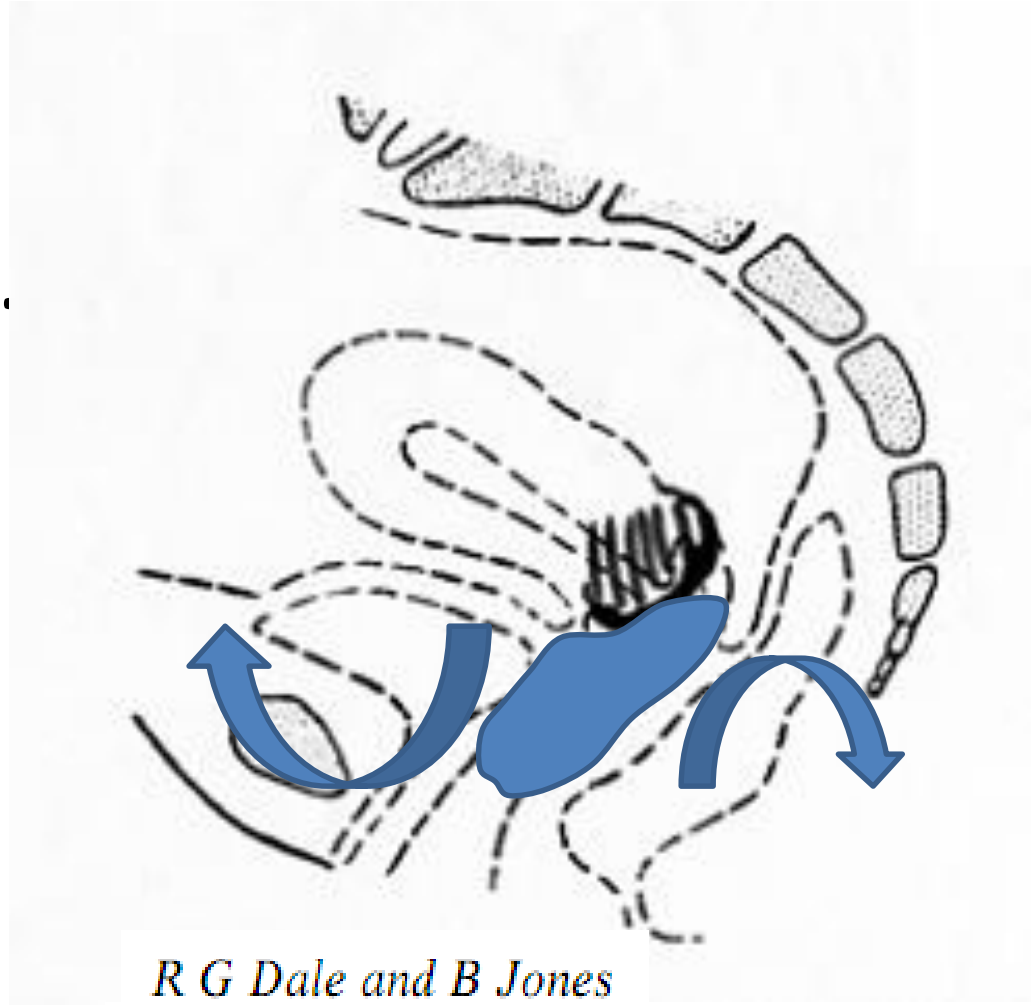
By Geometrical Sparing of Normal Tissues

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**

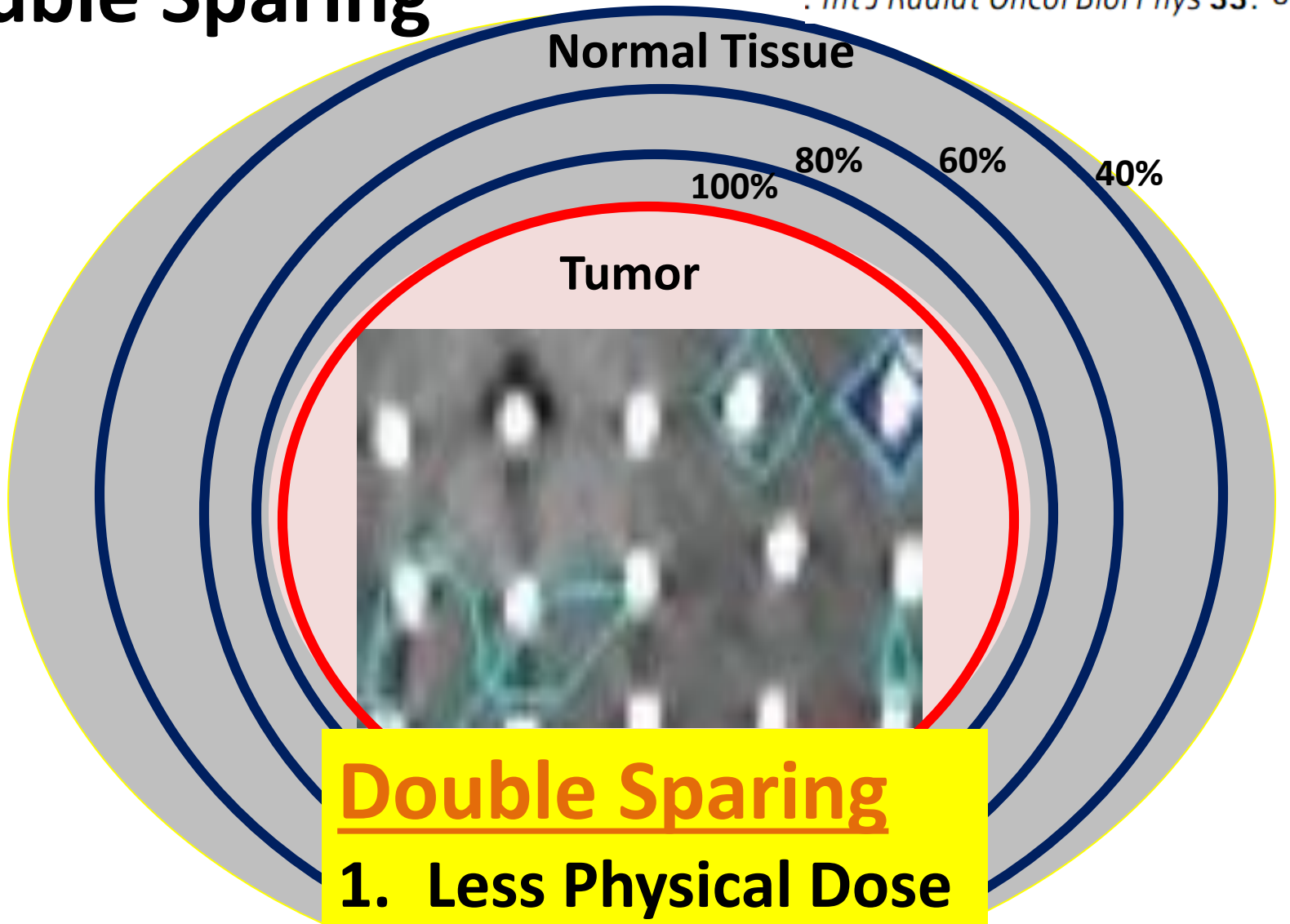


R G Dale and B Jones

The British Journal of Radiology, May 1998

Double Sparing

Lee SP, Leu MY, Smathers JB, McBride WH, Parker RG,
. *Int J Radiat Oncol Biol Phys* **33**: 375–89.



Double Sparing

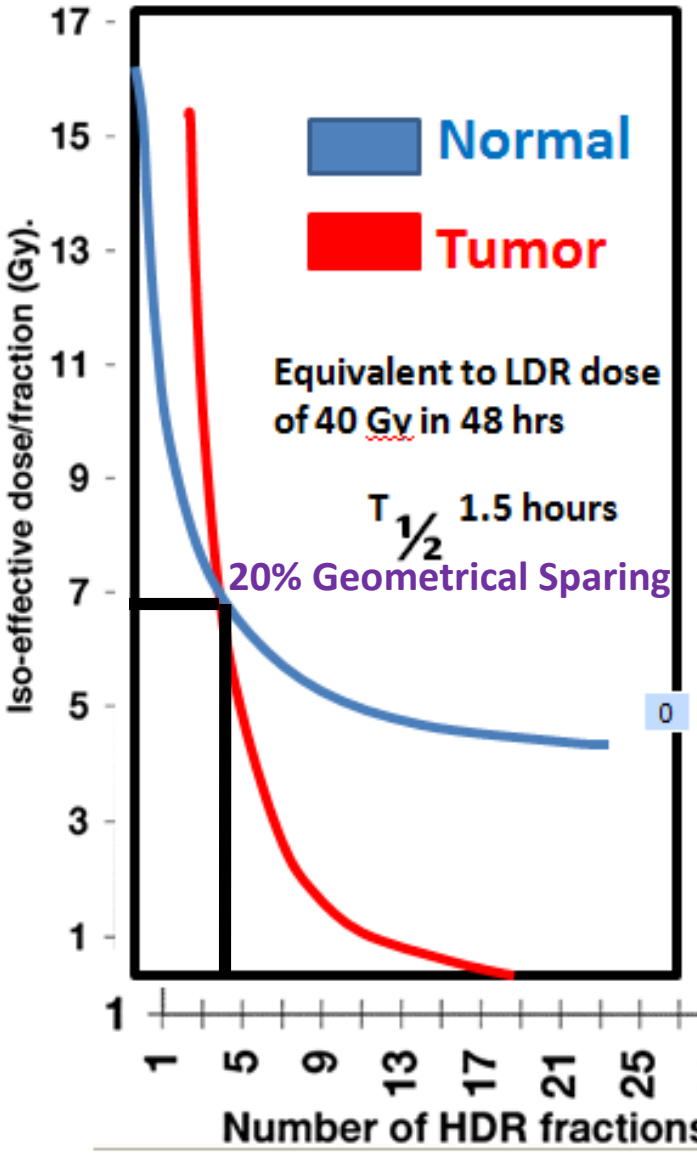
1. **Less Physical Dose**
2. **Less BED**

Dose Rate Decreases **Inverse Square Law**

R G Dale and B Jones

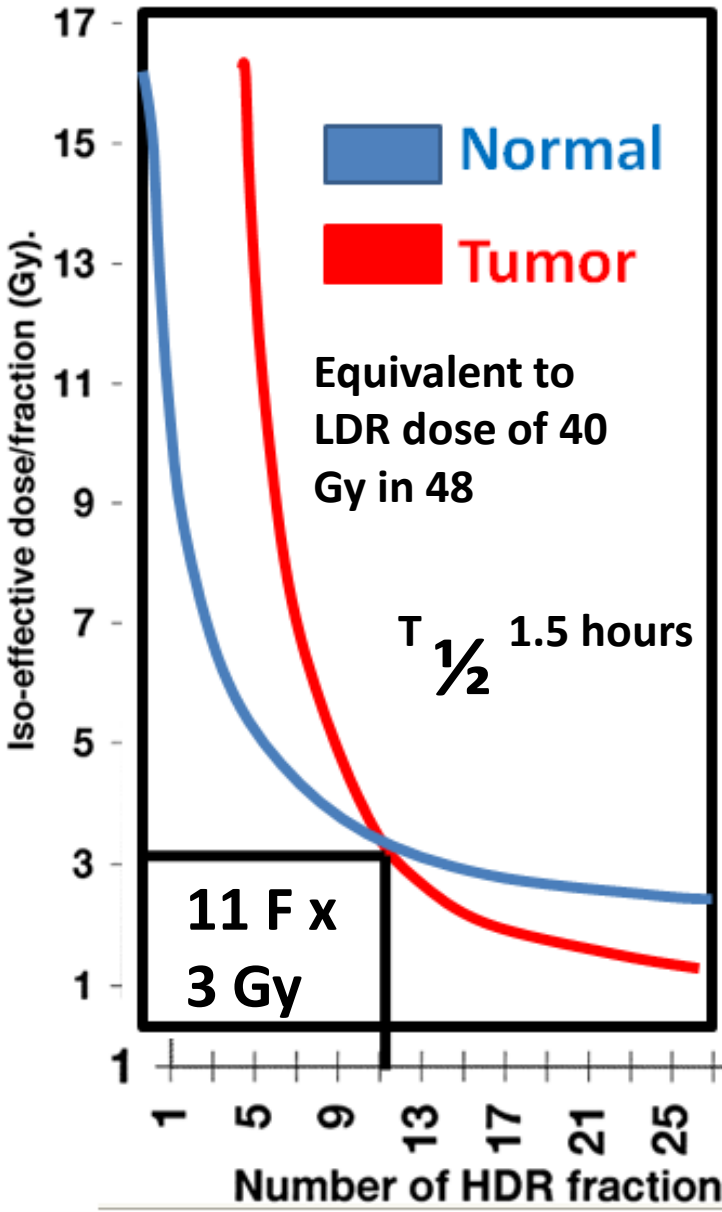
The British Journal of Radiology, May 1998

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 geographical sparing of the critical organ wherever possible specially in ca cervix.**
- **Do not underestimate the importance of good packing in cervix brachytherapy**

Repopulation

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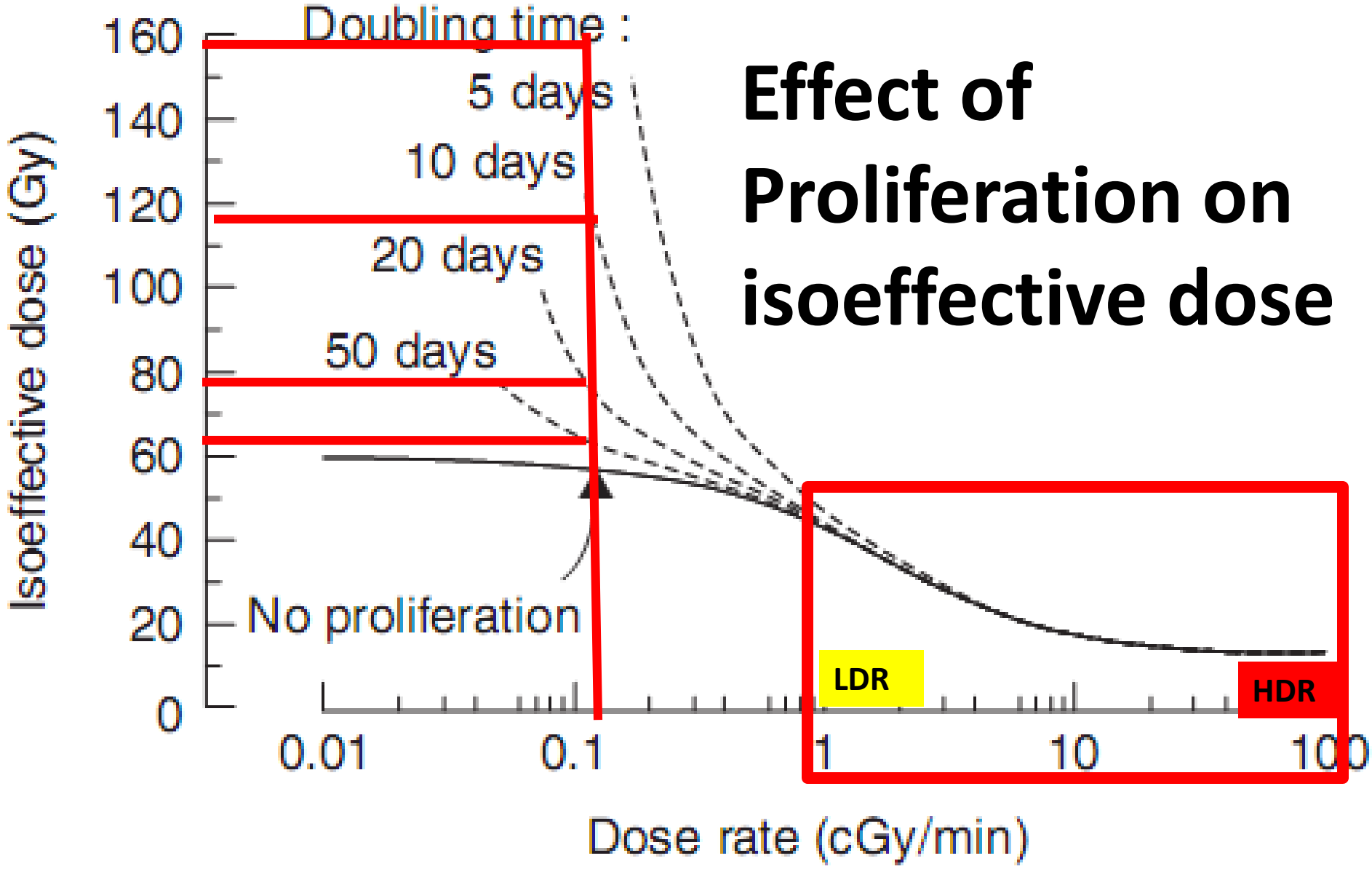

Effect of Proliferation on isoeffective dose

Repopulation

- **Slowest process.**
- **It does not start as overall treatment time is less than the time repopulation start.**
- **Advantageous in brachytherapy.**
- **Significant when total treatment time is more than few weeks as in permanent implant like prostate implants.**

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

(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 geographical sparing.**


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Thanks


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All India Institute of Medical Sciences, Rishikesh