Radiobiology of Brachytherapy

29 October, 2020
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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.
  - Low Dose Rate = low dose per Fc.
Important Points

1. Shifting from LDR to HDR will affect the late reacting tissues more than tumor.
Effect of Fractions on Cell Survival Curve

- Shoulder Reappear
- Curve getting Shallower
- Total dose $\alpha$ 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.
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

Fractionation will spare late reacting tissue more than tumor.
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) increases

(β) decreases

All cell Kill by (α)

No contribution by (β)
Effect of Dose Rate on Cell Survival Curve

Killing efficiency decreases

Repair of SLD

- 150 cGy/minute (HDR)
- 50 cGy/minute
- 10 cGy/minute
- 1.6 cGy/minute (LDR)
- 5 cGy/minute

With Decreasing Dose Rate...
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

\[ E = \alpha D + \beta gD^2 \]

- \( g \) 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

\[ E = \alpha D + \beta gD^2 \]

- 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 (\( \beta \)) keeps decreasing and by linear kill (\( \alpha \)) keeps increasing till all the cell kill is by linear kill (\( \alpha \)) and gradually cell survival curve become shallower.
Dose Rate Effect

- Relative contribution by $\alpha$ cell kill increases and by $\beta$ cell kill decreases.

- A stage is reached when all cell kill is by $\alpha$ and no contribution in cell kill by $\beta$.

With increasing overall treatment time.

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 $\alpha$ kill (<100cGy/hr).
- Selectron Brachytherapy 140-200cGy/hr,

LDR to Selectron

DS < DL

55cGy/hr LDR

200cGy/hr

SF

10 – 20%

65 – 70Gy
Dose Rate Effect Clinical Application

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


Iso-effective Dose $\propto 1/$Dose Rate

fractionation spares the normal tissues

Iso-effective Curve

LDR

HDR

(c)
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

Equivalent to LDR dose of 40 Gy in 48 hrs.

\[ T_{\frac{1}{2}} = 1.5 \text{ hours} \]

- \( 7 \text{ Gy} \times 5 \text{ Fc} = 35 \text{ Gy} \)
- \( 4.2 \text{ Gy} \times 9 \text{ Fc} = 37.8 \text{ Gy} \)
- \( 6 \text{ Gy} \times 5 \text{ Fc} = 30 \text{ Gy} \)
- \( 4 \text{ Gy} \times 9 \text{ Fc} = 36 \text{ Gy} \)

TR = Tumor Control Complication

R G Dale and B Jones

The British Journal of Radiology, May 1998
Fractionations in HDR Brachytherapy

Equivalent to LDR dose of 40 Gy in 48 hrs

\[ TR(\text{HDR}) = TR(\text{LDR}) \]

\[ 3 \text{ Gy} \times 11 \text{ Fc} = 40 \text{ Gy in 48 hours} \]

Can we further reduce the number of fractions?

By Geometrical Sparing of Normal Tissues

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**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 off rapidly.
- BED falls off rapidly.

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

1. Less Physical Dose
2. Less BED

Dose Rate Decreases

Inverse Square Law
Geometrical Sparing of Normal Tissues (Ca Cervix)

More effective with HDR as compare to with LDR Brachytherapy

Out side 2 cm³ volume the sparing of normal tissue more with HDR

R G Dale and B Jones
The British Journal of Radiology, May 1998
Equivalent to LDR dose of 40 Gy in 48 hours

\[ \text{TR(HDR)} = \text{TR(LDR)} \text{ at } 4 \text{ fractions} \]

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

\( (BED)_2 = (BED)_1 \)  

EQD\(_2\) = \( \frac{BED}{1.2} \)
EQD2 = BED/1.2

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

(BED) = (nd) × \left(1 + \frac{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.
Thanks