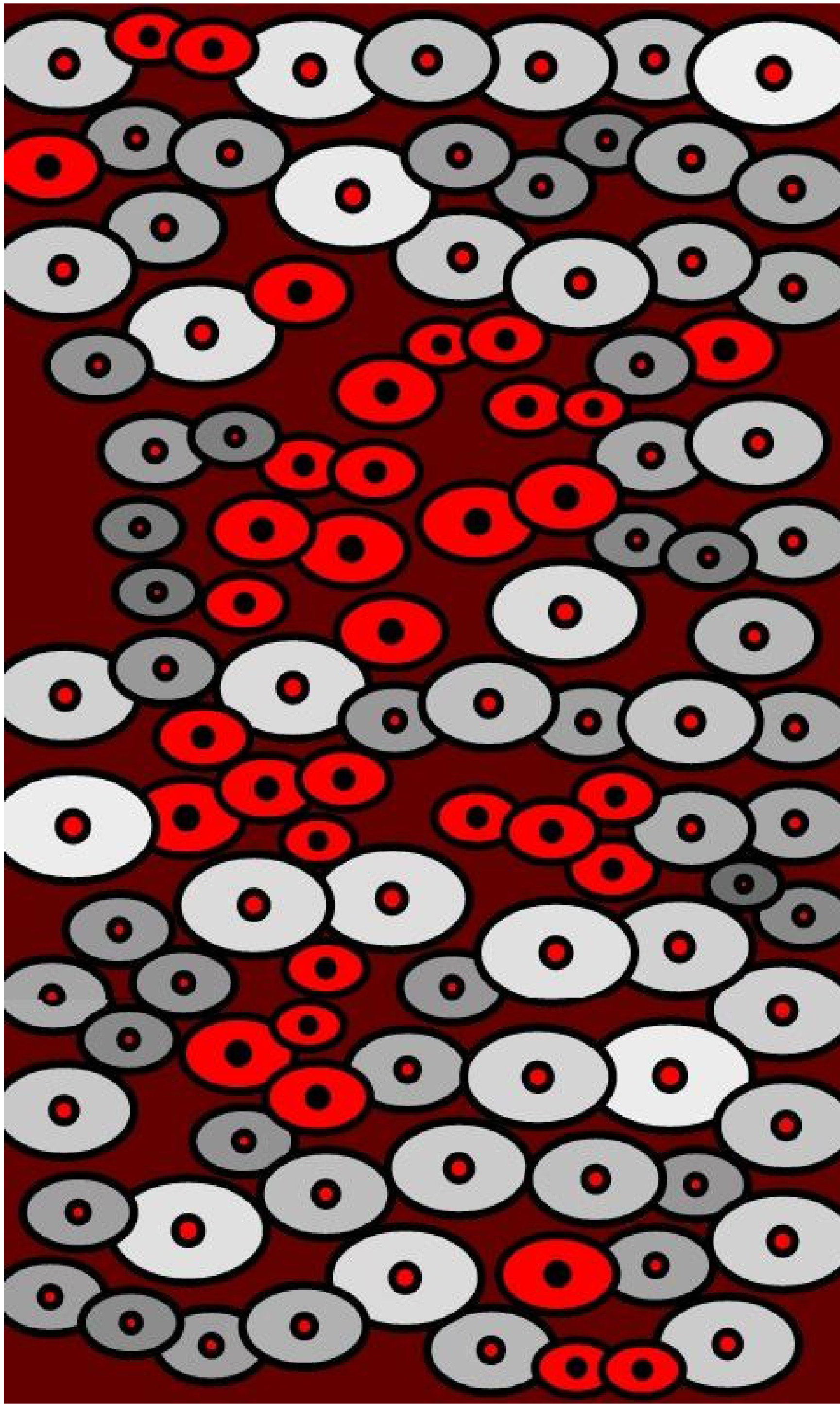

Radiobiology in Brachytherapy

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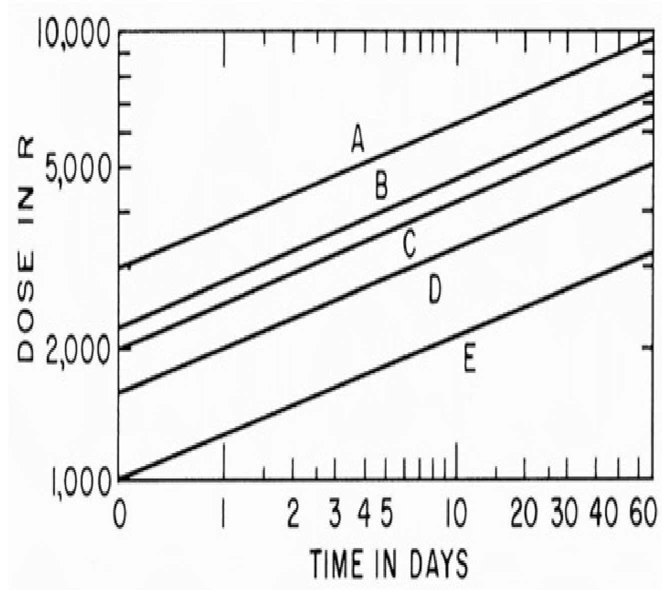
Radiobiology

- For changing the fractionation schedules
- Change of dose rate systems (LDR/HDR)
- Gap correction
- Combining EBRT with Brachytherapy
- Choosing the right isotope
- Comparison of data between centres



- Experimental- Ram testis
- Stranquist Curves 1944
- NSD –Ellis 1969
- Orton TDF Brachytherapy 1974
- Elkind kind of repair
  - Inter Fr time, Dose/Fr, Dose Rate
- Cummulative Response Dose(CRE)
  - Kirk et al
- Tumor Significant Dose (TSD)

- It does not take all complex biological process
- Doubts on validity of NSD relation with tissue type
- Doubts on validity of NSD relation with different effect in same tissue type
- Range of number of fractions. The formula is provided
- Concern on the time factor taken.

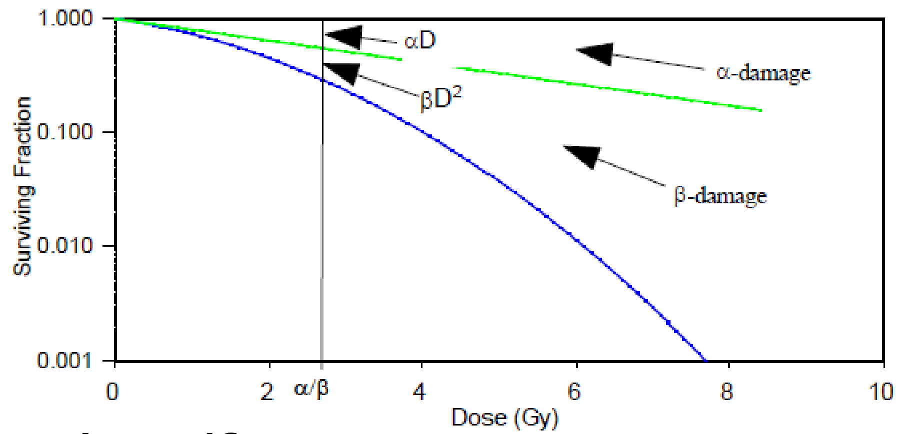
Radiobiology(RB)

- Dose Rate
- Fractionation
- Overall treatment time
- Biology Of Tumor (Radiosensitivity)
- Biology of Normal Tissue (sensitivity and repair mechanisms)

Biological Models

- Linear Quadratic Model
  - Lea & Catcheside
- Various modifications of LQ model
- BED : Biological Equivalent dose
- EUD : Equivalent Uniform Dose

L Q model



- It quantitatively predicts the dose/fraction dependence.The principal determinents are α & β
- α – Linear portion in Cell Survival Curve.
  - Occurs along a single ionizing tract
  - Tumor cells (rapid proliferation rates & short duration for repair)
- β - Quadratic portion in Cell Survival Curve
  - Occurs along a two different ionising tracts
  - Normal cells (co ordinated repair & hence requiring double hit)
- α/β ratio
  - Dose where there is proportionate of cell death due to linear & quadratic portions

Interpretation of α/β

- High α/β ratio

For a particular dose of radiation either the

- α DNA injury is higher

or

- β DNA injury is lower

- Low α/β ratio

For a particular dose of radiation either the

- α DNA injury is lower

or

- β DNA injury is Higher

Pros & Cons

Low α/β means

↓ in dose/fraction

less injury to normal tissue

High α/β means

↑ in dose/fraction

More injury to normal tissue

- Limitations

Fractionated Rx delivered @ regular interval period (once in 24hrs) & 5Fr/Wk.

Gap in Rx in pt NOT considered

Biological Effective Dose (BED)

- Concept used to compare the effectiveness of cell killing by different fractionation regimen by using LQ Model
- Use
  - Intercomparison of various RT schedules
  - Intercomparison of different types of radiotherapy
- Formula

  = Total Physical dose [D] x Relative effectiveness [RE]

Factors considered in BED

- Physical
  - Dose
  - Dose/fr
  - Inter fraction interval .
- Radiobiology
  - α/β
  - Repair rate
  - T pot
  - Repopulation & Redistribution .
  - Overall treatment time

- BED differs for different normal tissue & also for different tumor biology
- BED is represented as numerical value of dose with suffix indicating the α/β value.
- Eg: 100 BED_3 , 65 BED_{10}
- Relative Effective factor

  = Phy Factor + RB Factor

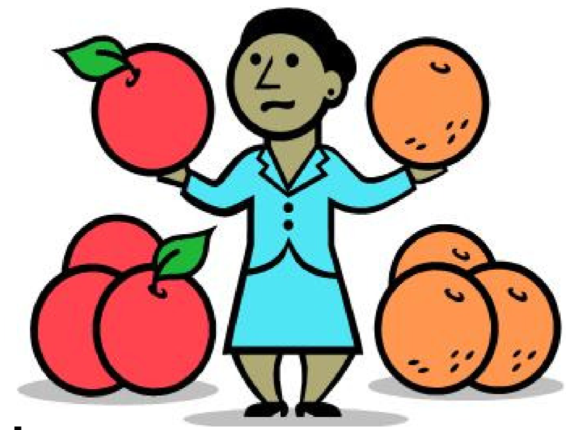
Repopulation

- RE for repopulation when taken into consideration uses subtractive repopulation correction factor w.r.t repopulation rate and Rx time.
- BED = D X RE – RCF (repopulation correction factor)
- RCF = K (T-T_{delay})

  T_{delay} is delay time after beginning of treatment before the repopulation rate becomes significant.

Eg: 28 days for HNSCC

Differences



EBRT

- Large Volume
- Homogeneous
- -5% to +7% acceptable
- Small dose, protracted time (weeks)
- Full repair

Brachytherapy

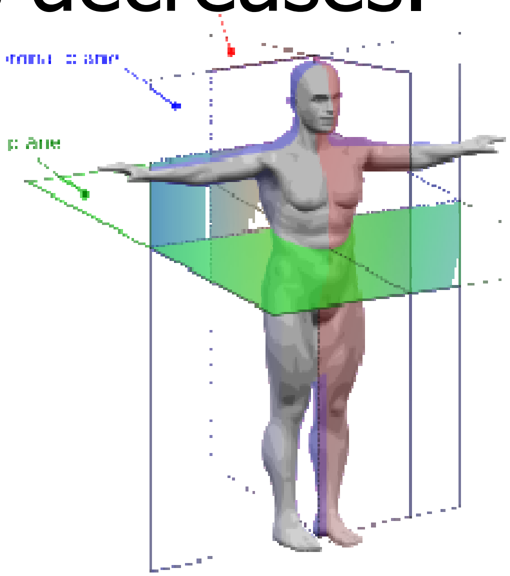
- Isodose encircling a small target volume
- Very heterogenous
- High dose, short treatment (hours to days)
- Short interval (HDR), Continuosly (LDR)

LDR vs HDR

- Several Trials comparing LDR Vs HDR
  - Historical data
- Most cases similar results
- HDR beneficial with equivalent normal tissue tolerance & the tumoricidal doses
- Severe Complications
  - 3.44% (>7 Gy)& 1.28% (<7 Gy)

Volume, Anatomical site

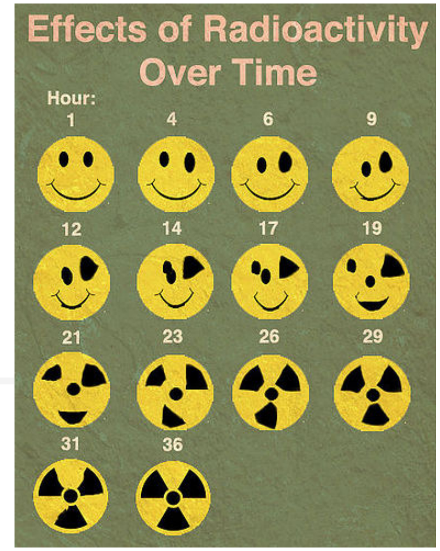
- The Dose reqd increases with size of tumor
- As Dose increases tolerance of late responding normal tissues decreases.



Tumor shrinkage

- Combining HDR with EBRT
  - Eg: Ca Cervix
- Important in permanent implants. Outcome depends on shrinkage which is difficult to predict.

Reirradiation



- High doses can be delivered to previously irradiated area
- Can be tolerated if delivered to a limited volume. recovery seems to be less in some like CNS

- No clarity regarding minimal interval between two irradiations.

Combined with EBRT

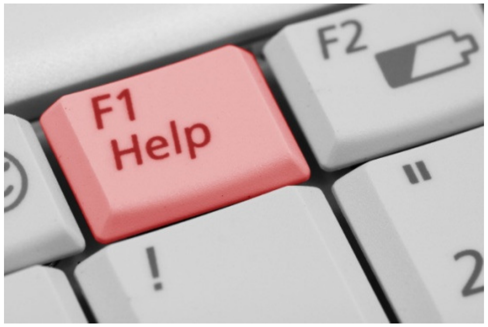
- Because BEDs are additive the determination of biological effects associated with combined modality treatments is straightforward.
- Total BED

  $= BED_{(EBRT)} + BED_{(Brachy)} - RCF$

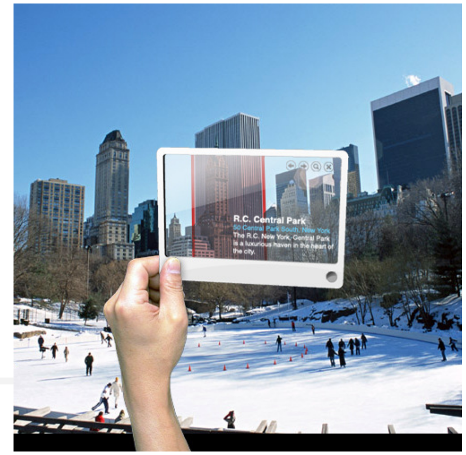
  RCF (repopulation correction factor) is reqd only for tumor calculations and should be calculated using the overall treatment time of the combined treatments.
- In Brachytherapy calculation allowance for dose gradient effect. Should also be considered.

The radiobiological models helps in

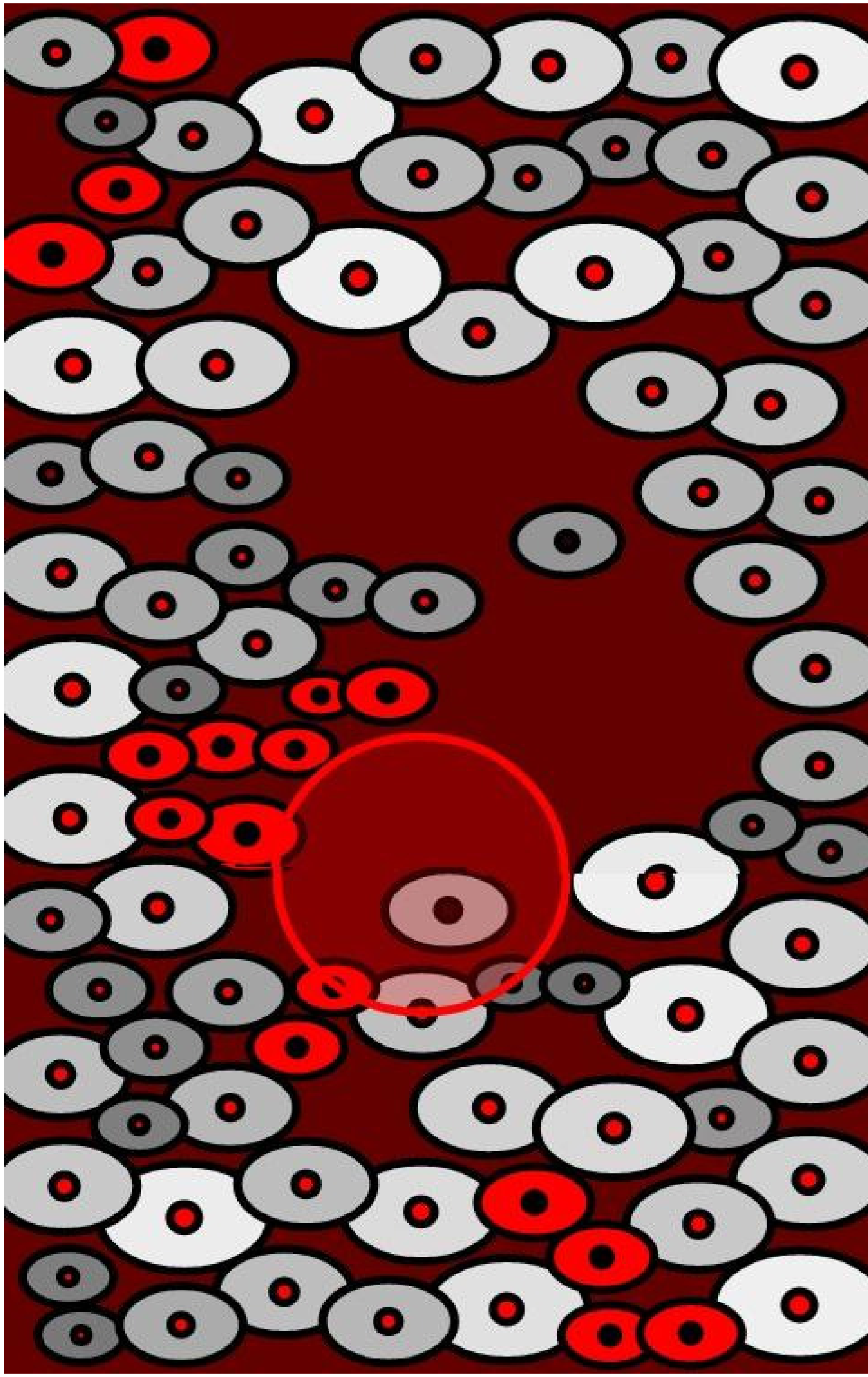
- Quantification of CLDR & FHDR
- Quantification of dose rate effect
- Quantification Permanent implants
- Quantification of PDR Brachytherapy
- Treatment intercomparison
- Designing new Fr & Rx schedules
- Calculating dose equivalence used with different isodose



Future



- Commercially TPS incorporating biological models
  - Bioplan
  - Orbit
  - LQ Survivor



Dose correction

- Recommended when dose rate >1Gyhr
  -
- At 1.5-2Gyhr little differential effect is expected but fractionation (2-3Fr) compensates to some extent
- RB interpretation of clinical data should therefore combine dose rate & dose fractionation parameters.

Dose conversion CLDR to FHDR

- BED = Total Dose x [1+ 2R /μ (α/β ratio)]
- R = dose rate, μ = Constant .5
- Eg 40 Gy in 48Hrs, BED10 (Tumor) 3 (Late normal tissue) HDR
- $CLDR_{tumor}$ = 40x[1+2(40Gy/48hr)/ .5x10] = $53.3Gy_{10}$
- $CLDR_{normal}$ = 40x[1+2(40Gy/48hr)/ .5x3]
  - $84.4Gy_{3}$

- BED_{10}= 6 FHDR= 53.3Gy

  6d x [1+d/10] = 53.3 Gy, d=5.67Gy
- HDR_{normal} = 34.02x[1+2(5.67/10)]

  = 98.3Gy_{HDR}

Compared to 84.4Gy_{LDR}

in order to achieve 10% less dose to normal tissue, equivalent to LDR then

- HDR_{normal} = 34.02x[1+2({5.67-10%}/10)]

  = 82.7 Gy

- In other words in order to achieve the same tumor control the dose as per HDR should be 5.67Fr.
- Dose to be reduced from 40 Gy > 34.02 Gy

- Also in order to achieve the same normal tissue toxicity the dose as per HDR should be 5.1Gy/Fr instead of 5.67Fr without compromising on the tumor control