ISOEFFECT CALCULATION IN HDR BRACHYTHERAPY (BASIC CLINICAL RADIOBIOLOGY)

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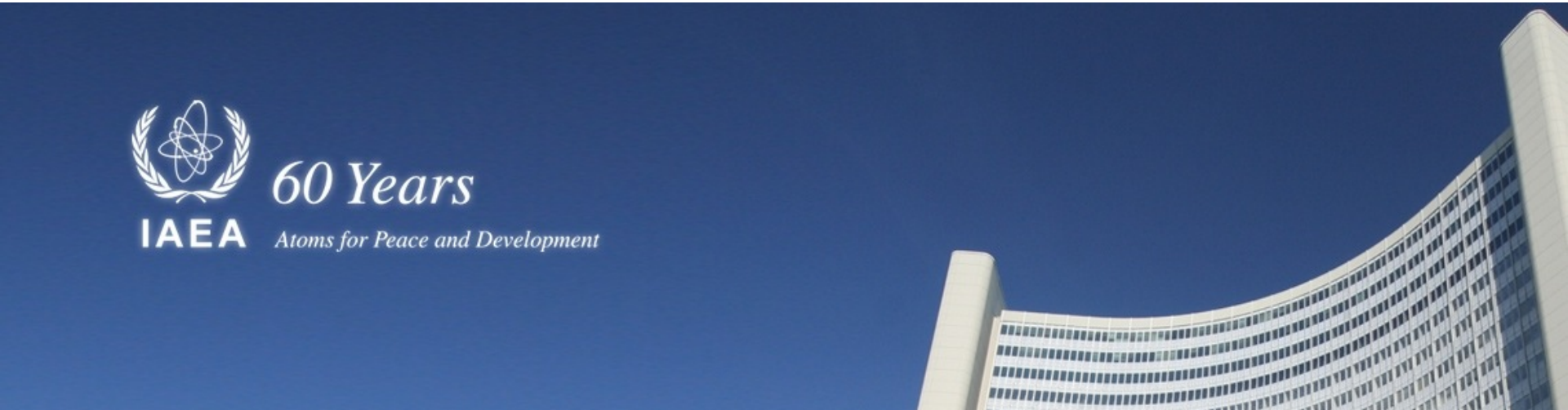
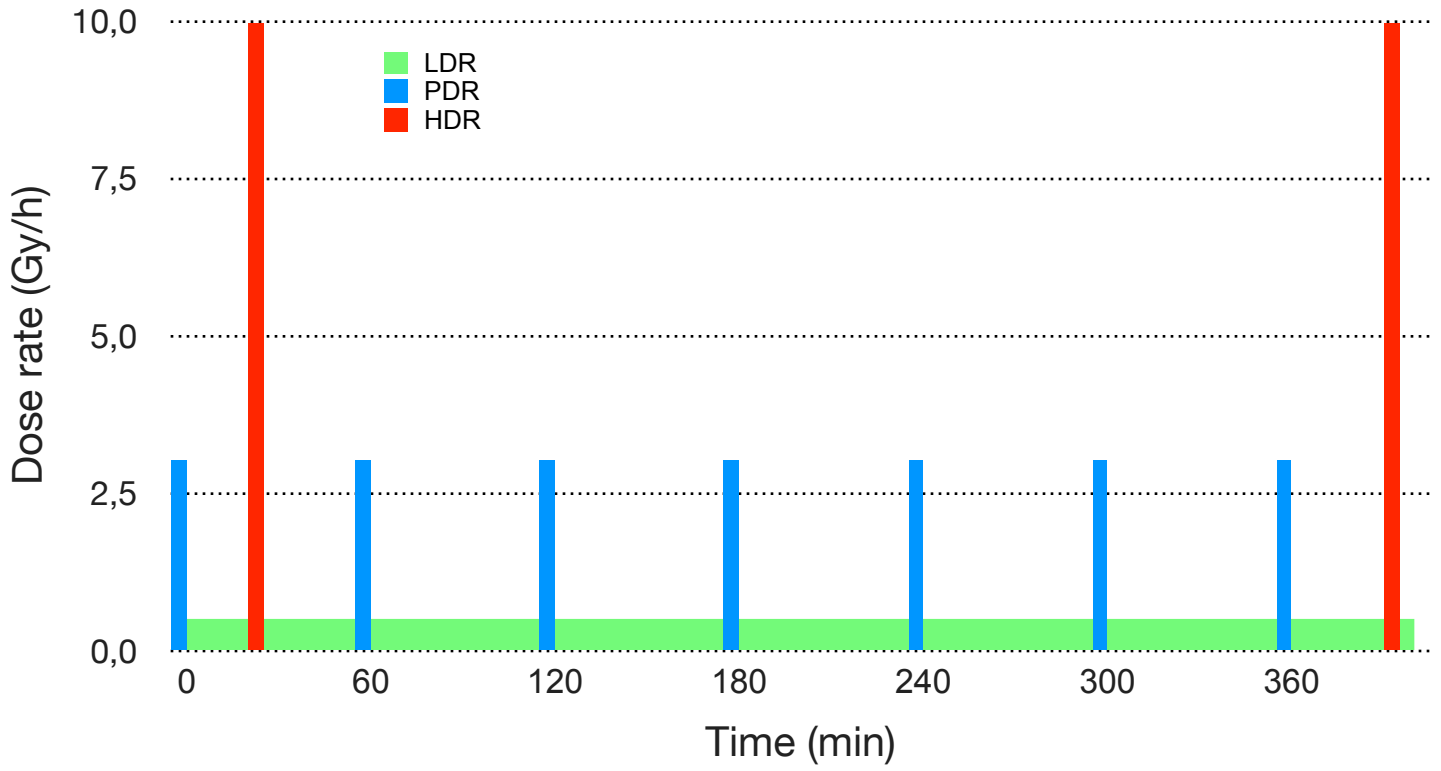
Division of Human Health

International Atomic Energy Agency



TYPES OF BRACHYTHERAPY PROCEDURES (ICRU REPORT 38)

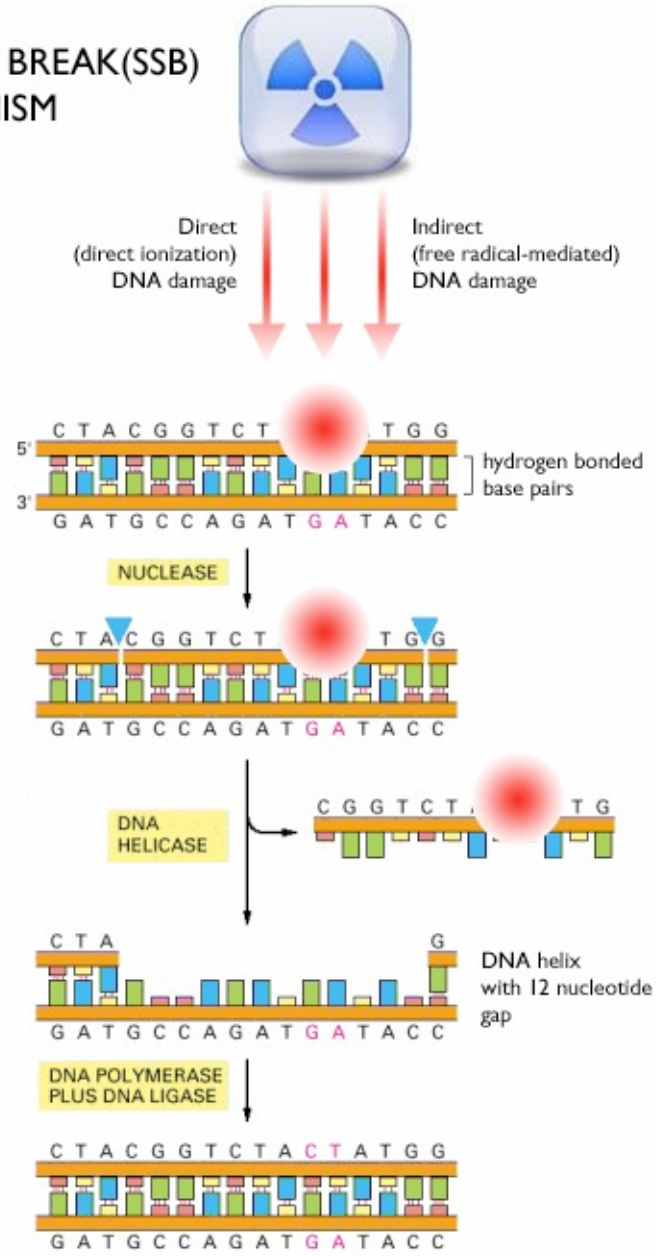


Clinical work of Brachytherapy since 1950 was to optimise the therapeutic ratio by exploiting the differential response of healthly and malignant tissue to the delivery of the maximal tumoricidal dose in as short time as possible.

B. Pierquin 1992

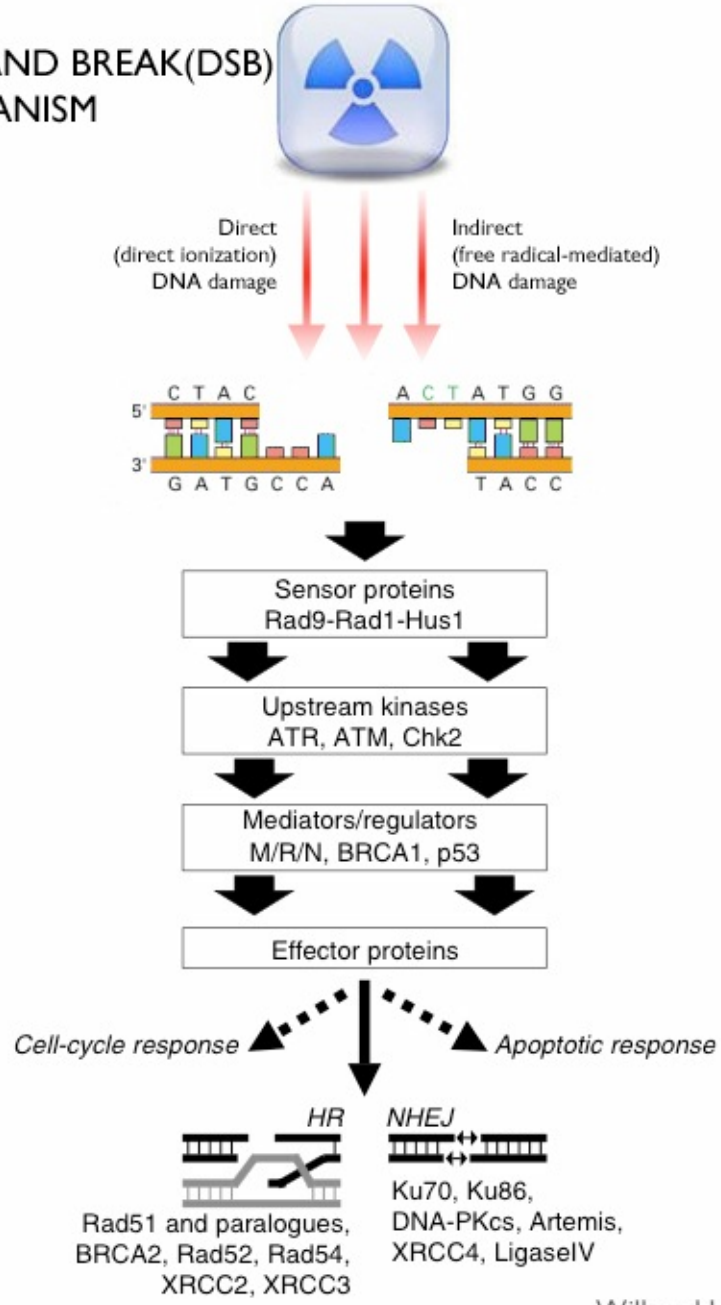
BASIC RADIATION DAMAGE

SINGLE STRAND BREAK(SSB) REPAIR MECHANISM



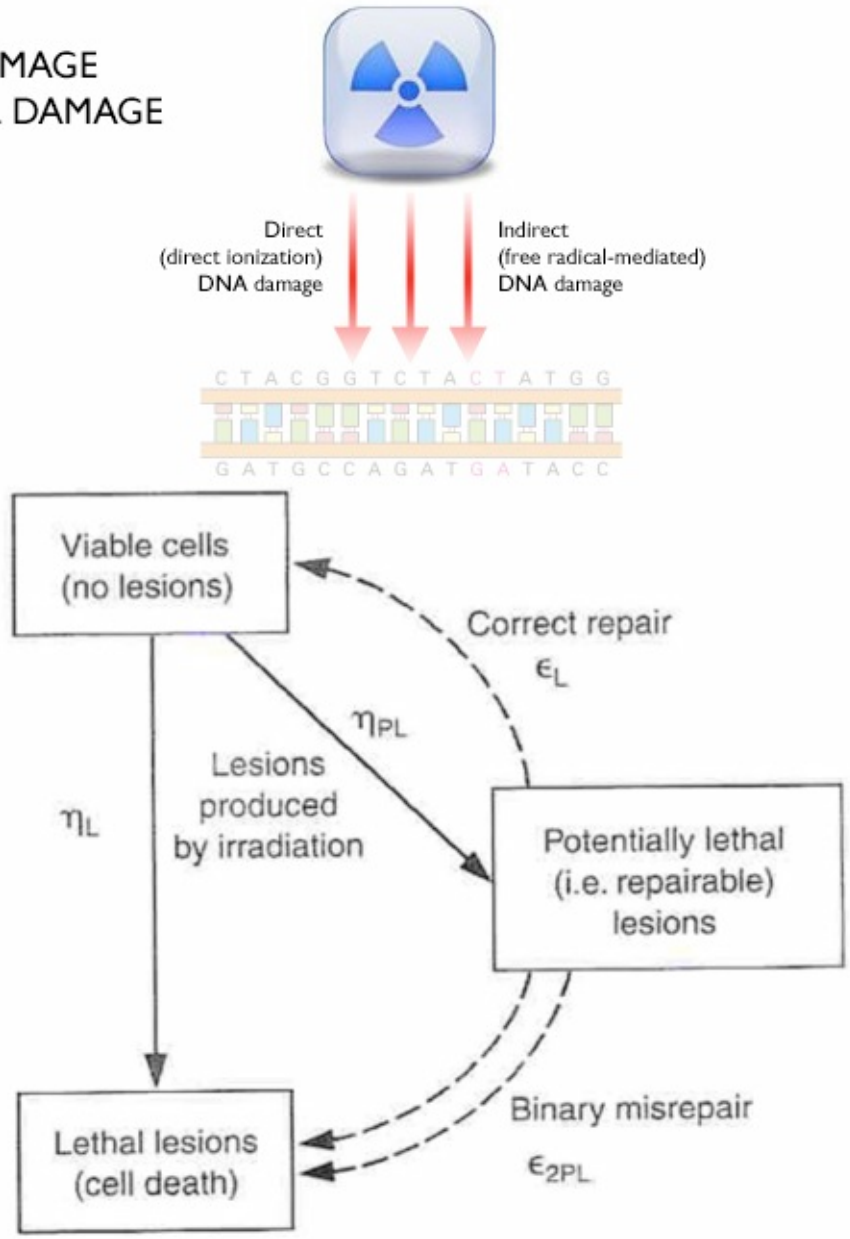
Alberts B. Molecular biology of the cell. 1994

DOUBLE STRAND BREAK(DSB) REPAIR MECHANISM

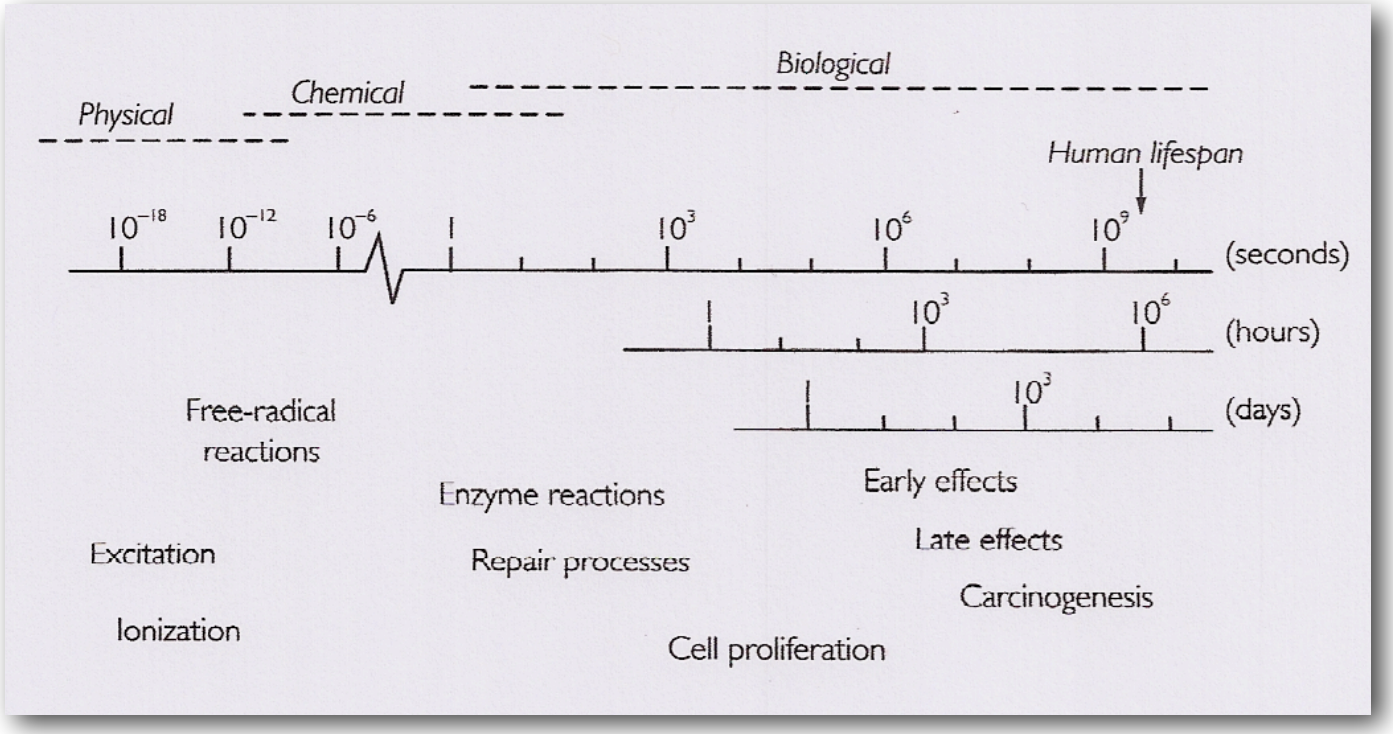


Willers H, et al. BJCancer 2004

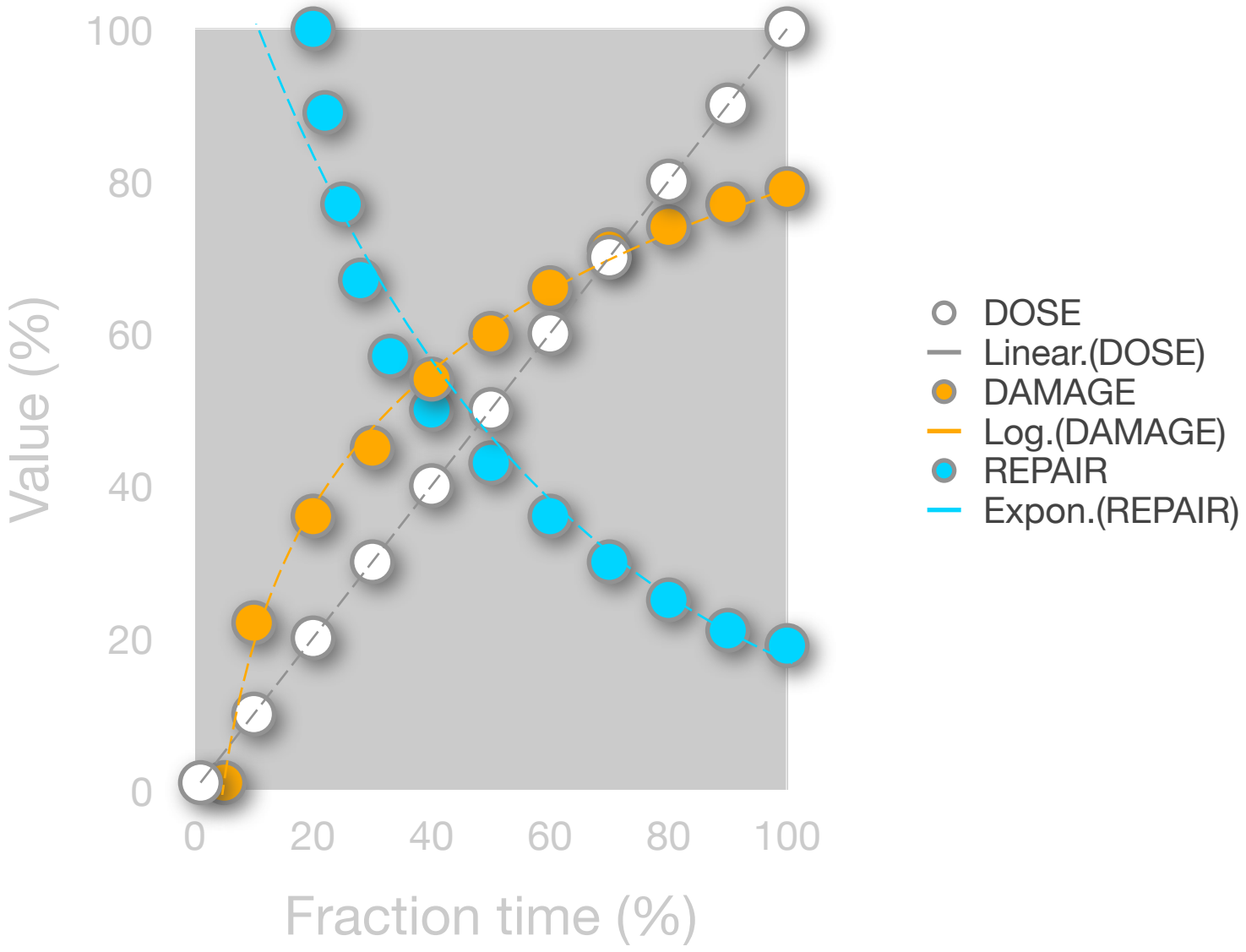
LETHAL DAMAGE
SUBLETHAL DAMAGE



Steel G. Basic clinical radiobiology. 2002


Physical
Chemical
Biological
Human lifespan
10^{-18}
10^{-12}
10^{-6}
1
10^{3}
10^{6}
10^{9}
(seconds)
10^{3}
10^{6}
(hours)
10^{3}
(days)
Free-radical reactions
Enzyme reactions
Early effects
Excitation
Repair processes
Late effects
Carcinogenesis
Ionization
Cell proliferation

INSIDE A FRACTION



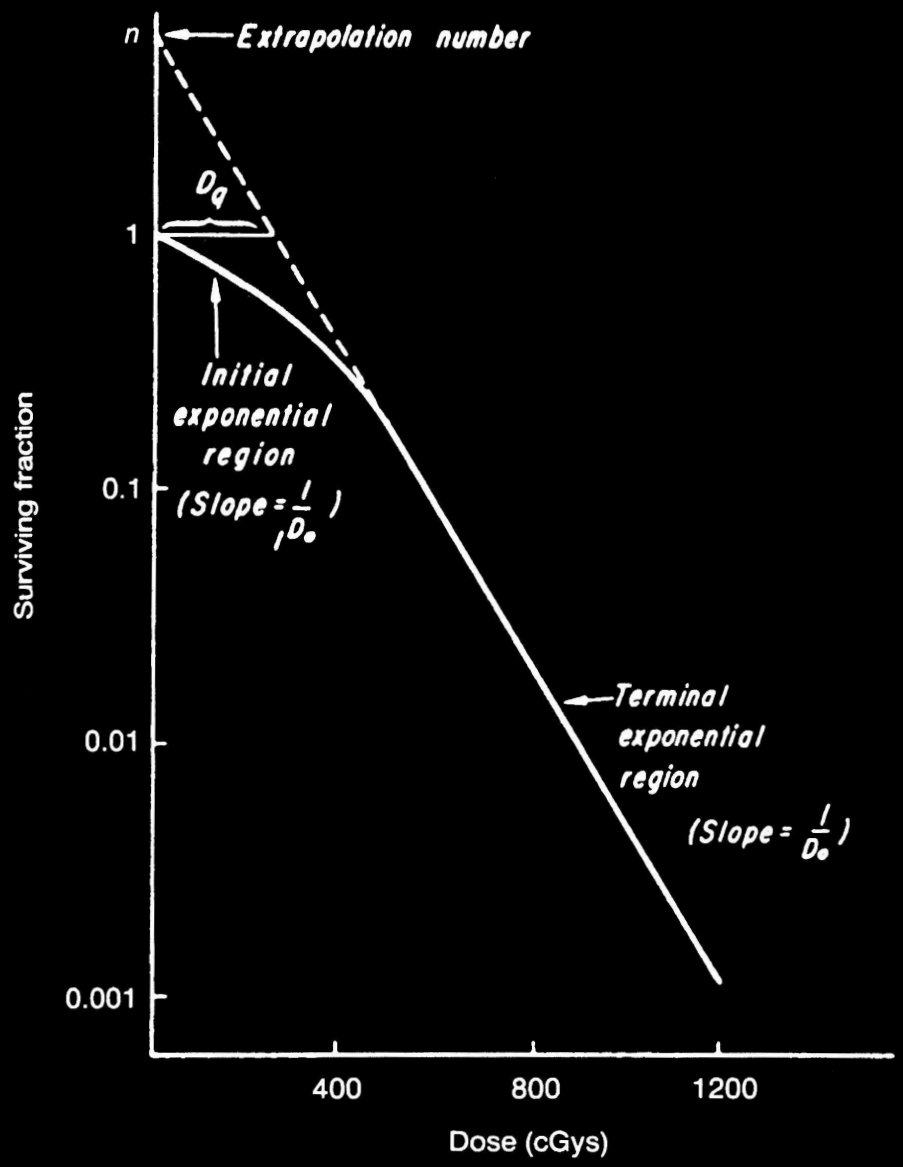
LINEAR QUADRATIC MODEL

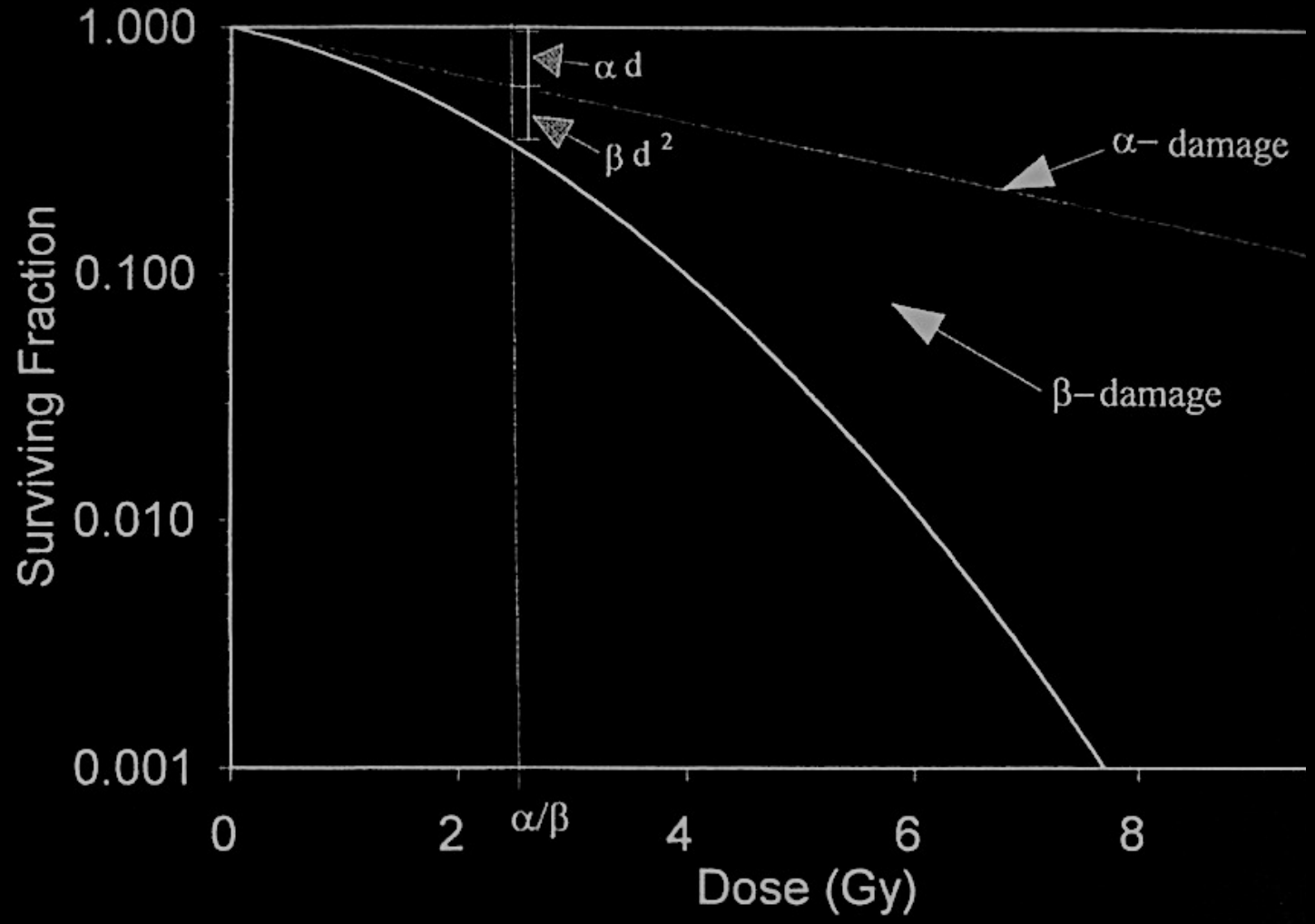
NSD: Nominal standard dose (Ellis, 1969)

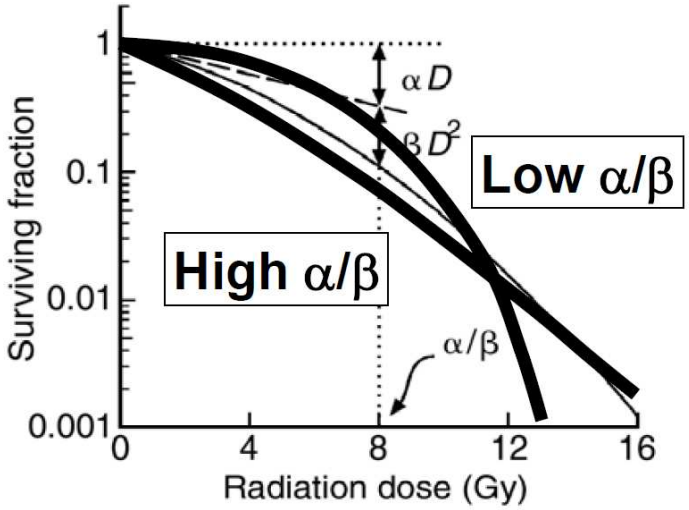
TDF: time-dose-fractionation (Orton & Ellis, 1973)

ERD: extrapolated response dose (Barendsen, 1982)

LQ: linear-quadratic (Orton & Cohen, 1988)

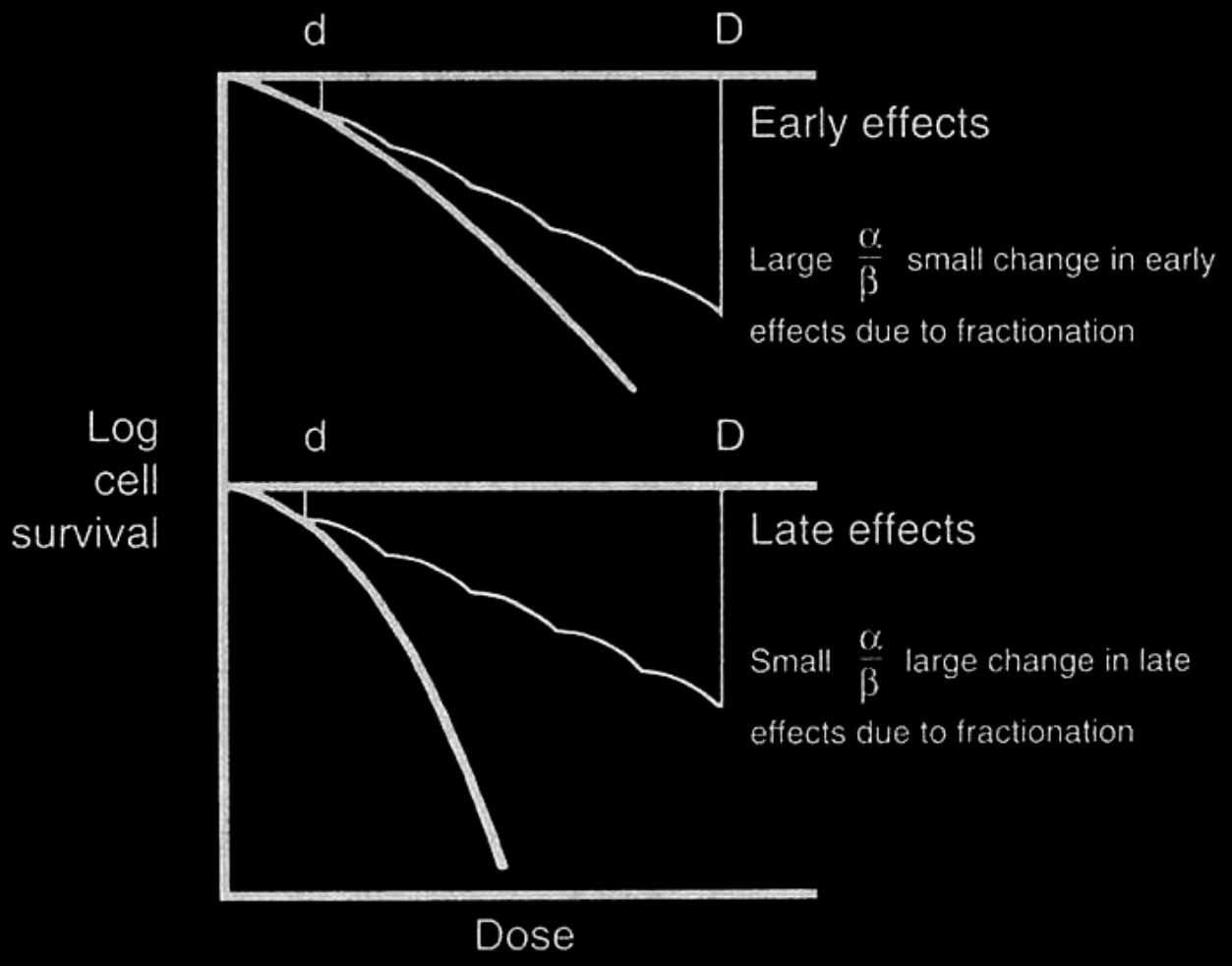

n
Extrapolation number
D_q
1
Initial exponential region
(Slope = $\frac{1}{D_o}$)
0.1
0.01
Terminal exponential region
(Slope = $\frac{1}{D_o}$)
0.001
Surviving fraction
400
800
1200
Dose (cGys)


1.000
0.100
0.010
0.001
Surviving Fraction
α d
β d 2
α– damage
β– damage
0
2
α/β
4
6
8
Dose (Gy)



- **α:** Parámetro que expresa la muerte celular por impacto único/daño letal (parte lineal). Valor en Gy^{-1}
- **β:** Parámetro que expresa la muerte celular por impacto doble/daño subletal (parte cuadrática). Valor en Gy^{-2}
- **α/β:** proporción entre el daño letal respecto al subletal de un tejido. Valor en Gy.

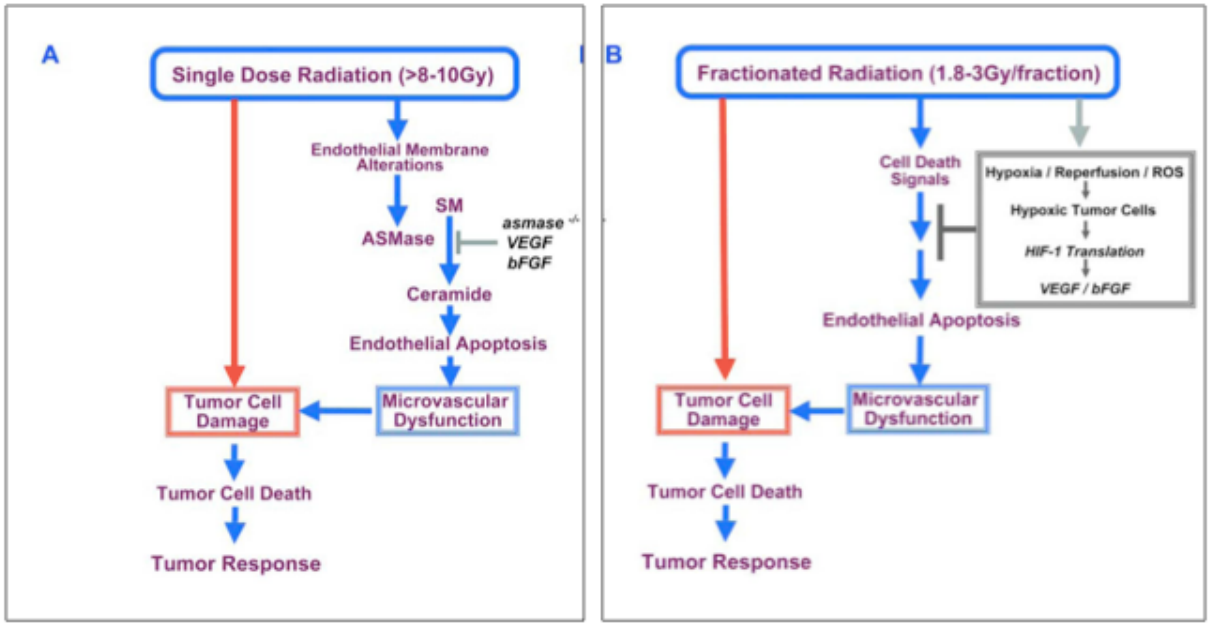
Conventional hypofractionation * Grey zone * Extreme hypofractionation



Rapid proliferative tissues are less sensitive to changes in fractionation (large doses per fraction or higher dose rate)

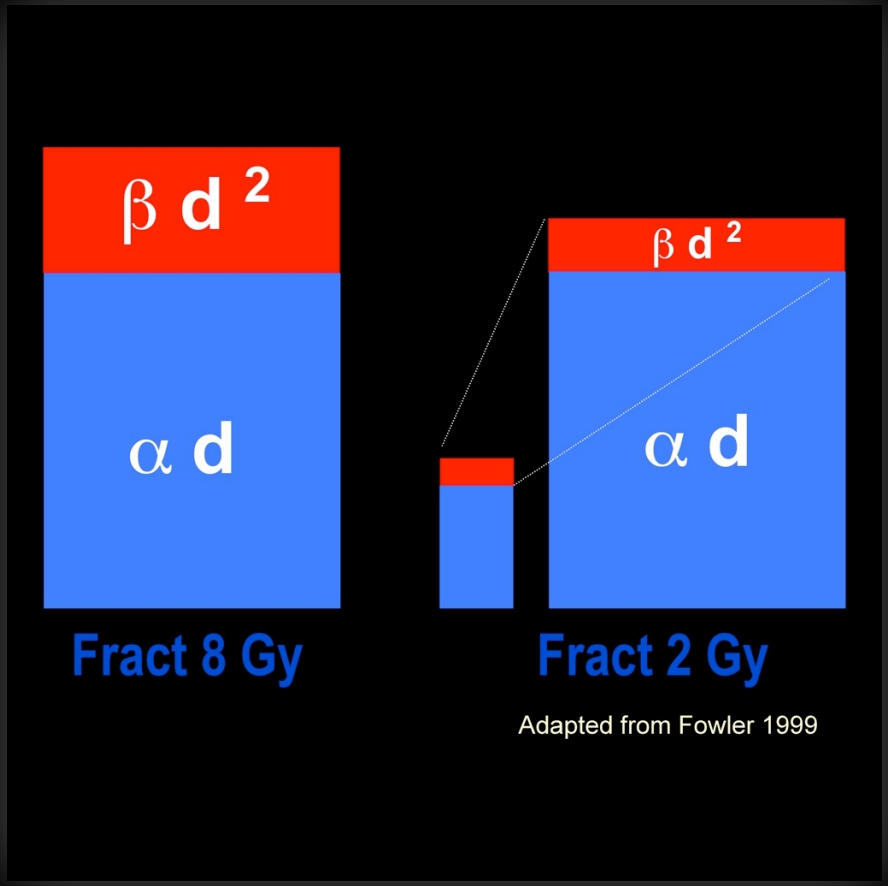
Slow proliferative tissues are more sensitive to changes in fractionation (large doses per fraction or lower dose rate)

ENDOTELIAL MEDIATED CELL DAMAGE



Fuks Z, Kolesnick R. Engaging the vascular component of the tumor response. Cancer Cell. 2005;8:89-91.

INSIDE A FRACTION

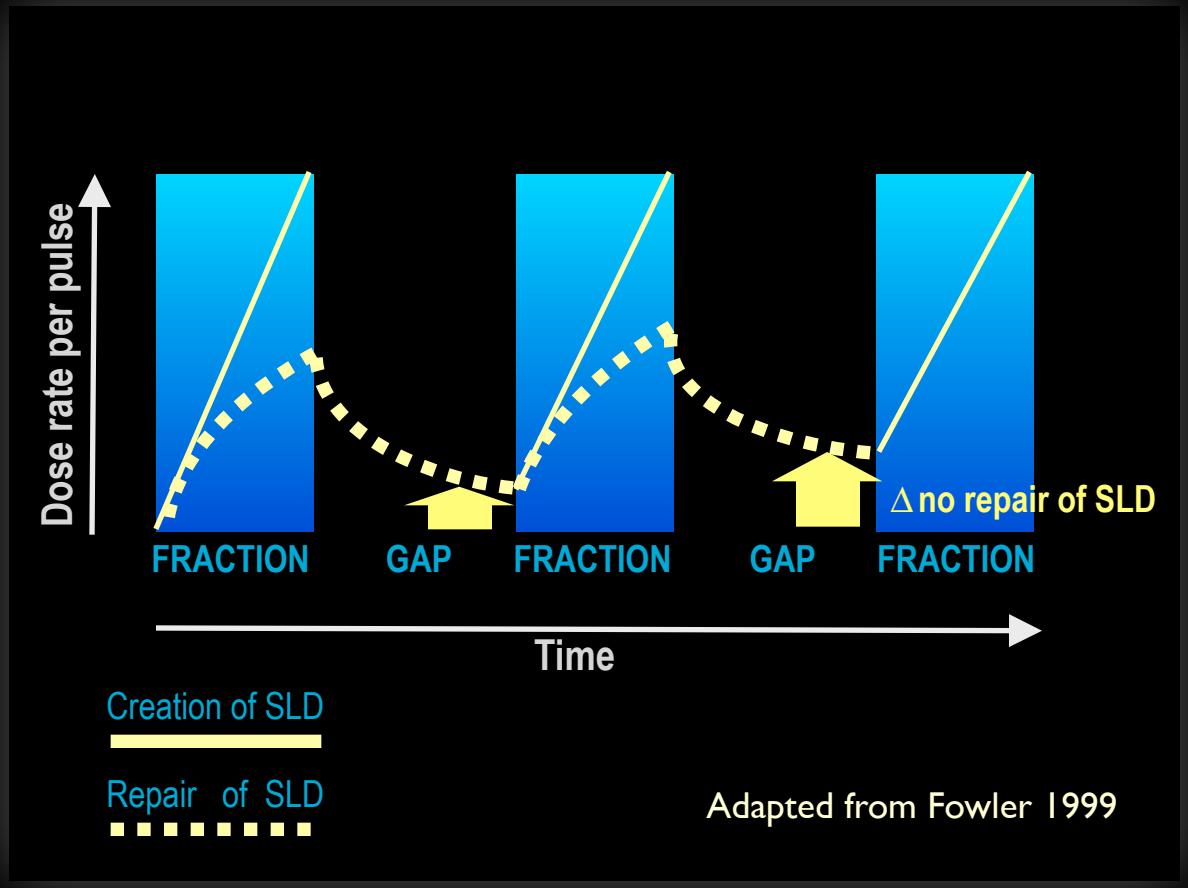


The much smaller proportion at 2 Gy than 8 Gy per pulse is showed

Only the red proportion is altered by α/β, $T_{1/2}$ and dose per pulse

Keeping low the dose per pulse guarantees minimal risk of excess damage in late tissues

BETWEEN FRACTIONS



SUBLETHAL DAMAGE REPAIR: incomplete repair

Thames HD et al. Incomplete repair model for survival after fractionated and continuous irradiation. IJRO 1985; 47: 319

Dale RG et al. The application of the LQ formula dose-effect equation to fractionated and protracted radiotherapy. B J Radiol 1985; 58: 515

1. Conventional EBRT/HDR daily fractions (>24h) permit enought time between fractions for full repair to occur.
2. If interfraction time is reduced to less than aprox 8h, repair between fraction may be incomplete and cell survival decreased.
3. A potential for therapeutic gain exists when the fractionation sensitivity α/β for the host dose limiting late reacting normal tissues is greater than a tumor lying within such tissue.

BASIC MODEL FOR ISOEFFECT CALCULATION

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Int. J. Radiation Oncology Biol. Phys., Vol. 46, No. 2, pp. 507–513, 2000

0360-3016/00/$–see front matter

PII S0360-3016(99)00330-2

PHYSICS CONTRIBUTION

A SIMPLE METHOD OF OBTAINING EQUIVALENT DOSES FOR USE IN HDR BRACHYTHERAPY

SUBIR NAG, M.D., AND NILENDU GUPTA, PH.D.

Division of Radiation Oncology, Arthur G. James Cancer Hospital and Research Institute, Ohio State University, Columbus, OH

$$\mathrm{BED} = nd\left[1 + \frac{\mathrm{d}}{(\alpha/\beta}\right] \qquad (1)$$

$$\mathrm{D_{Eq}} = \frac{\mathrm{BED}}{\left(1 + \frac{\mathrm{d_{REF}}}{(\alpha/\beta)}\right)} \qquad (2)$$

ELSEVIER

Seminars in
RADIATION
ONCOLOGY

The Linear-Quadratic Model Is an Appropriate Methodology for Determining Isoeffective Doses at Large Doses Per Fraction

David J. Brenner, PhD, DSc

The tool most commonly used for quantitative predictions of dose/fractionation dependencies in radiotherapy is the mechanistically based linear-quadratic (LQ) model. The LQ formalism is now almost universally used for calculating radiotherapeutic isoeffect doses for different fractionation/protraction schemes. In summary, the LQ model has the following useful properties for predicting isoeffect doses: (1) it is a mechanistic, biologically based model; (2) it has sufficiently few parameters to be practical; (3) most other mechanistic models of cell killing predict the same fractionation dependencies as does the LQ model; (4) it has well-documented predictive properties for fractionation/dose-rate effects in the laboratory; and (5) it is reasonably well validated, experimentally and theoretically, up to about 10 Gy/fraction and would be reasonable for use up to about 18 Gy per fraction. To date, there is no evidence of problems when the LQ model has been applied in the clinic.
Semin Radiat Oncol 18:234-239

AAPM REPORT NO. 166

The Use and QA of Biologically Related Models for Treatment Planning

Report of AAPM Task Group 166
of the Therapy Physics Committee

March 2012

CONCLUSIONS