TRAINING COURSE ON RADIATION DOSIMETRY:

Radiobiology Basics – RBE, OER, LET

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Thu. 22/11/2012, 18:30 – 19:30 pm

Culturing Mammalian Cells

tissue → trypsin → single cell suspension → seeding →(medium+incubation) →crisis →established

THREE POPULAR ESTABLISHED CELL-LINES

HeLa Cells (human cancer cells)

CHO Cells (Chinese hamster ovary cells)

V79 Cells (Chinese hamster lung fibroblast cells)

CELL DEATH

For proliferating cells of an established cell-line, death is defined as *reproductive death* when cells no longer have the capacity for sustained proliferation and colony formation (*clonogenic*)

Cells may lose reproductive capacity through

- Apoptosis
- Giant cell formation
- Death attempting cell division (***mitotic death***)

For most cultured cells mitotic death is the dominant mode

The fate of cells exposed to radiation

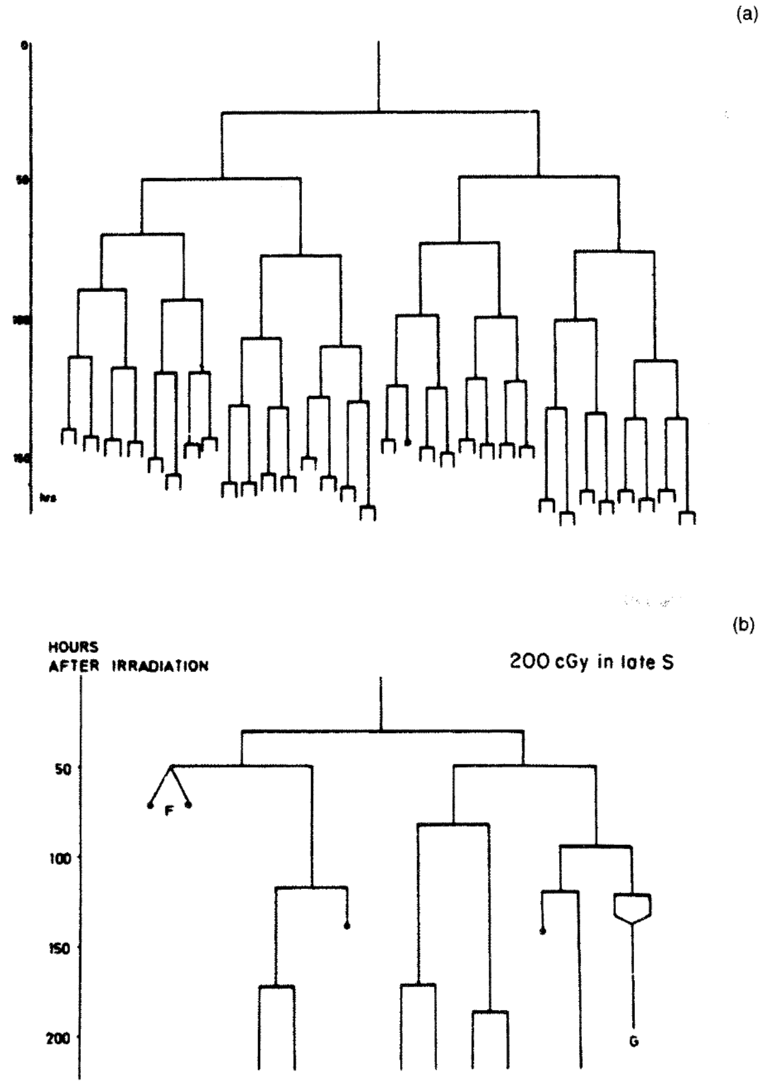


Figure 6.8. Pedigrees of L cells: (a) control cell; (b) cell treated with 200 cGy. F=fragmentation; G=giant cell; and dots indicate cell death. (Reproduced from Trott, 1969, by permission of WILEY-VCH Verlag GmbH, Postfach 10 11 61, DH 69451, Weinheim.)

Nias Chapter 6

The first mammalian cell survival curve

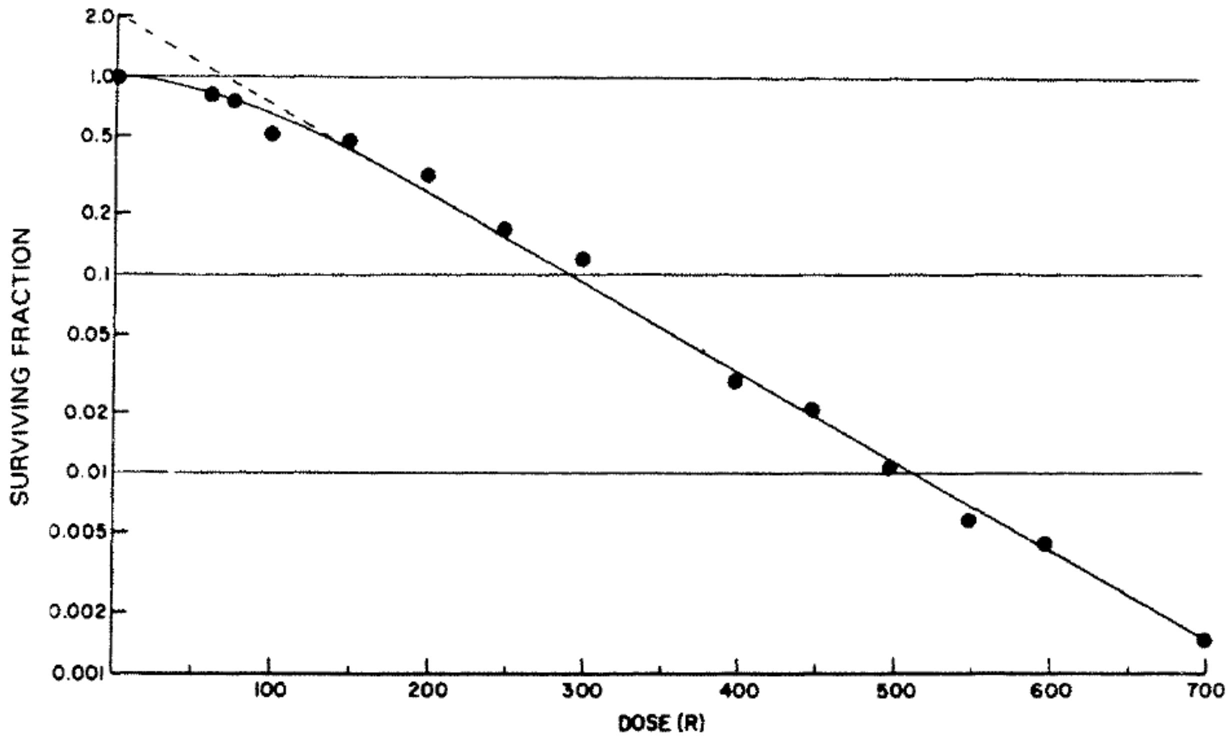
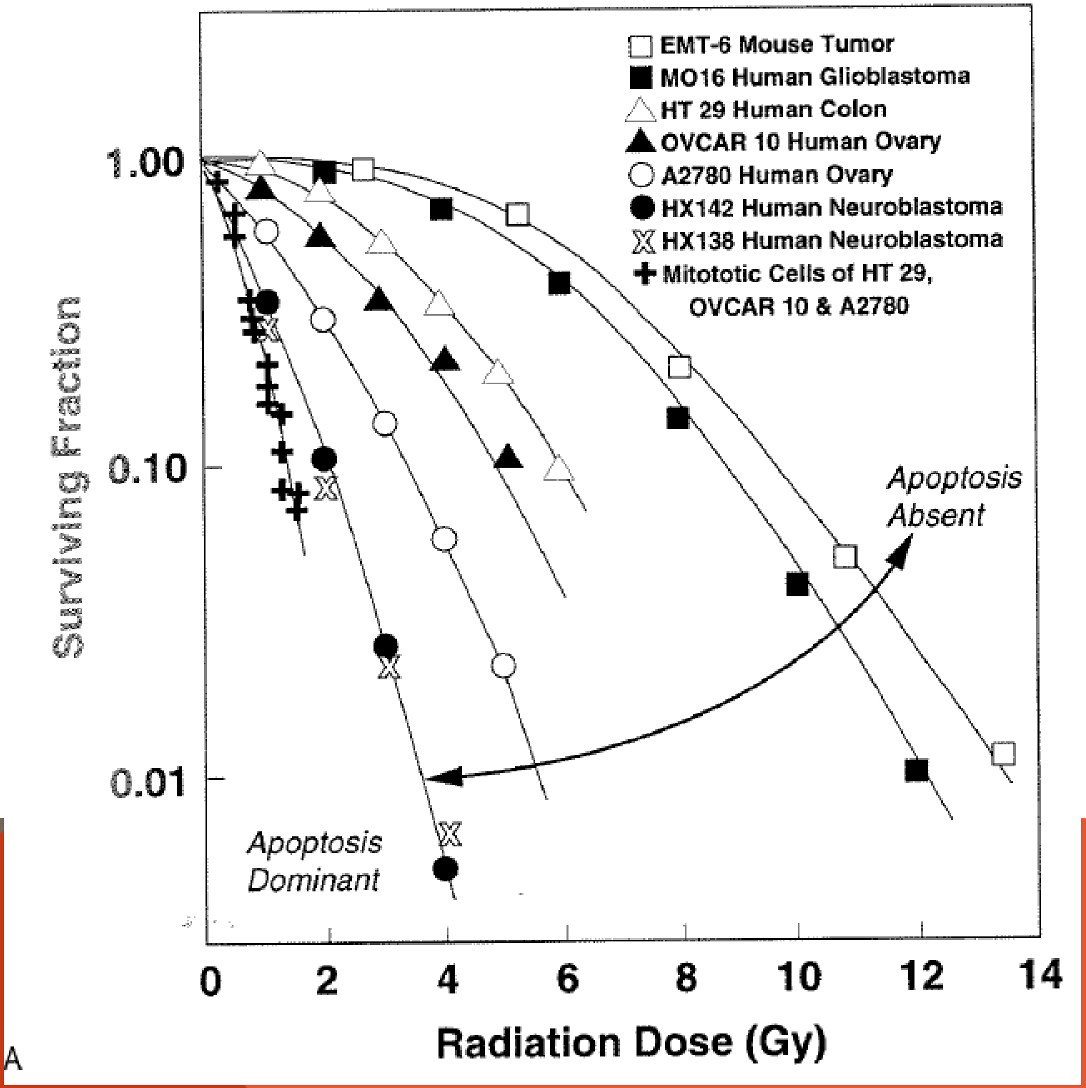


Figure 8.1. Radiation dose–response of human cancer cells *in vitro*. (Reproduced from Puck and Marcus, 1956, by copyright permission of The Rockefeller University Press.)

Over the past 50 years many cell lines have been investigated and, apart from their practical value for improving the therapeutic use of radiation, the shape of the survival curve itself helps our understanding of the mechanisms underlying radiation damage



Hall Chapter 3

RELATIVE BIOLOGICAL EFFECTIVENESS (RBE) FOR CELL SURVIVAL

RBE is the ratio of the absorbed dose for a reference radiation, usually 250 kVp X-rays or Co-60 gamma rays to the absorbed dose from a test radiation to give the same level of effect, usually cell survival

RELATIVE BIOLOGICAL EFFECTIVENESS (RBE) FOR CELL SURVIVAL

RBE is an experimentally measured quantity

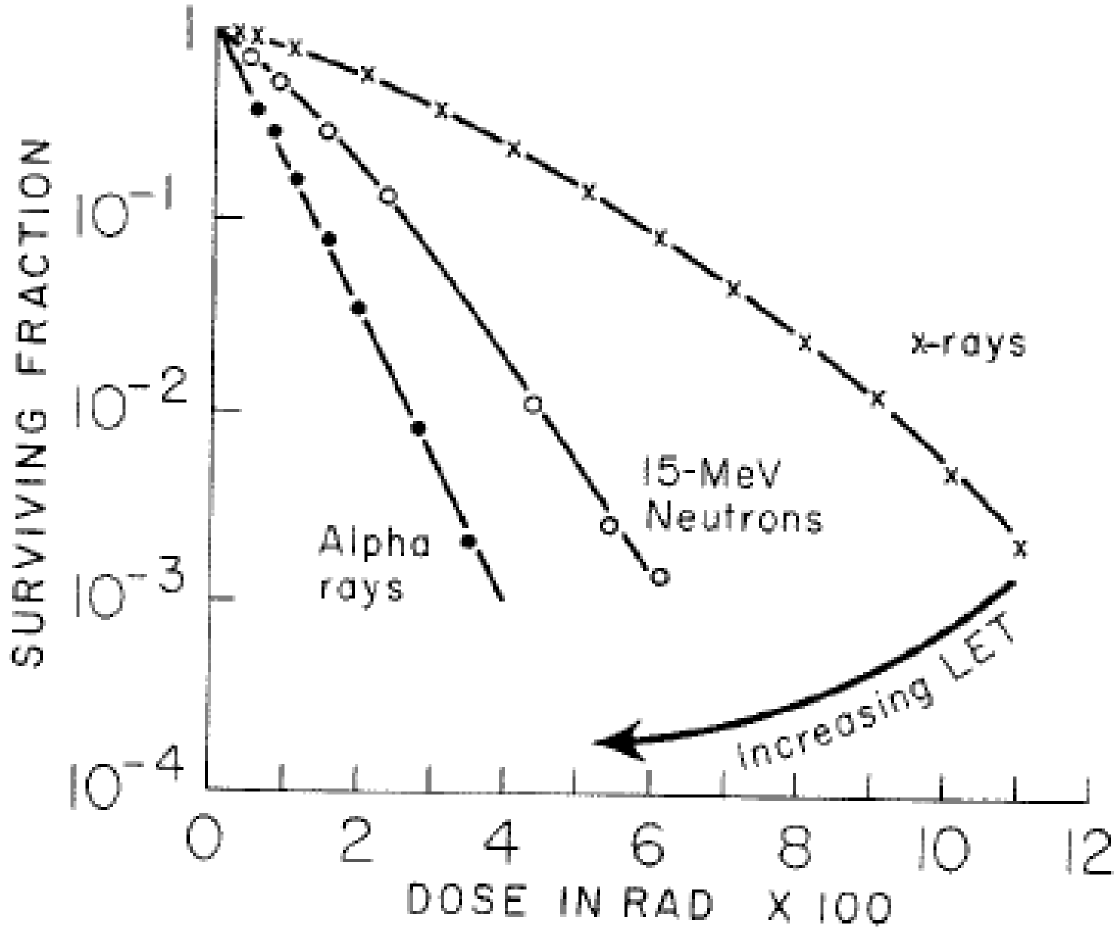
For shouldered survival curves RBE increases with deceasing dose to a maximum value that depends on the initial slope of the reference radiation survival curve

RBE depends on the biological system used (e.g cell line)

RBE depends on the end-point investigated (e.g. survival)

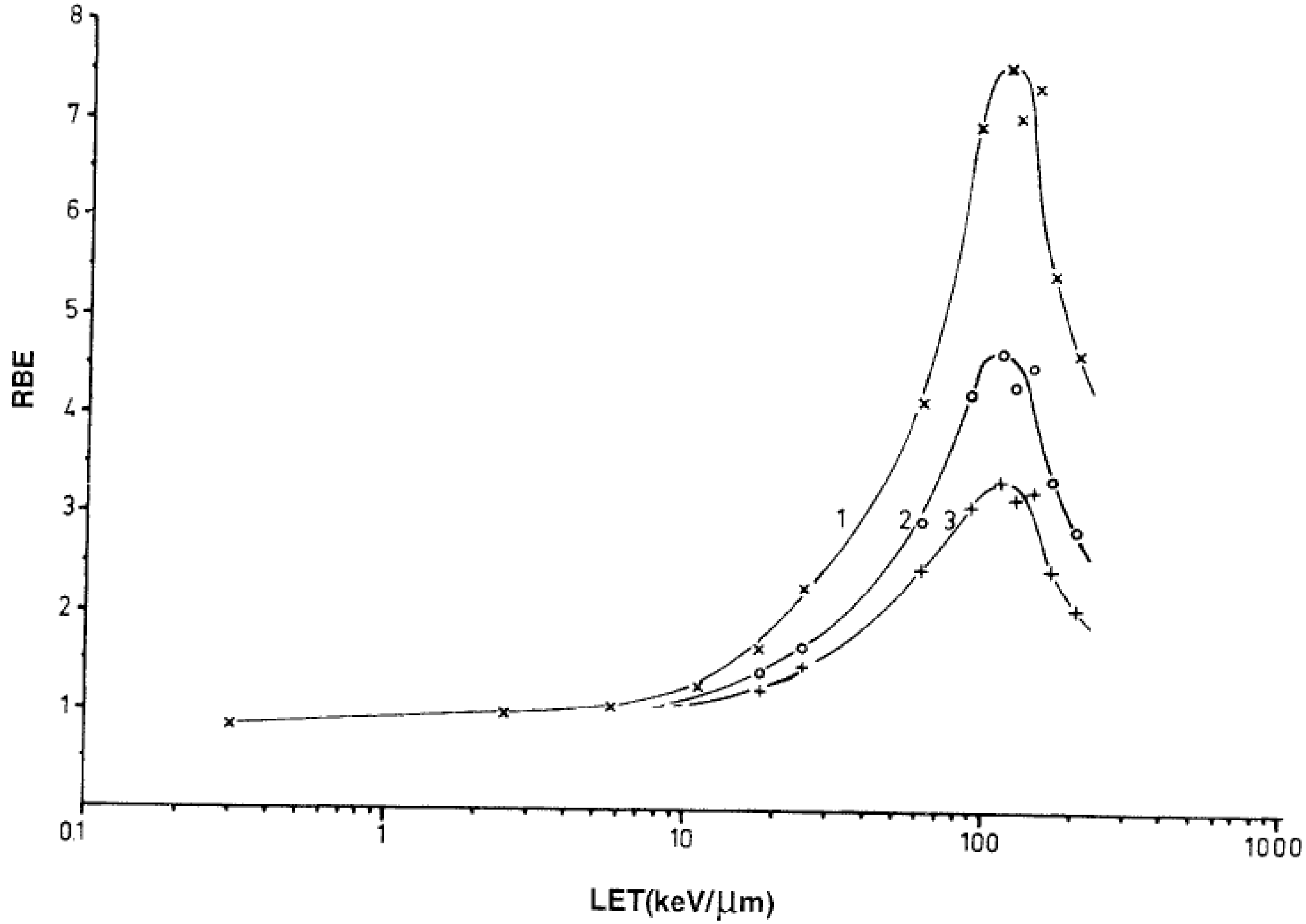
CELL SURVIVAL AND LINEAR ENERGY TRANSFER

For the same end-point RBE for mammalian cells (and other complex biological systems) is generally seen to increase with increasing ionization density (LET)



Hall Fig. 7.5

CELL SURVIVAL AND LINEAR ENERGY TRANSFER



Curves labeled 1,2,&3 refer to different levels of survival (0.8,0.1 0.01). For mammalian cells RBE is seen to increase and reach a maximum around 100 keV/μm and then subsequently decrease

Hall Fig. 7.6

CELL SURVIVAL AND LINEAR ENERGY TRANSFER

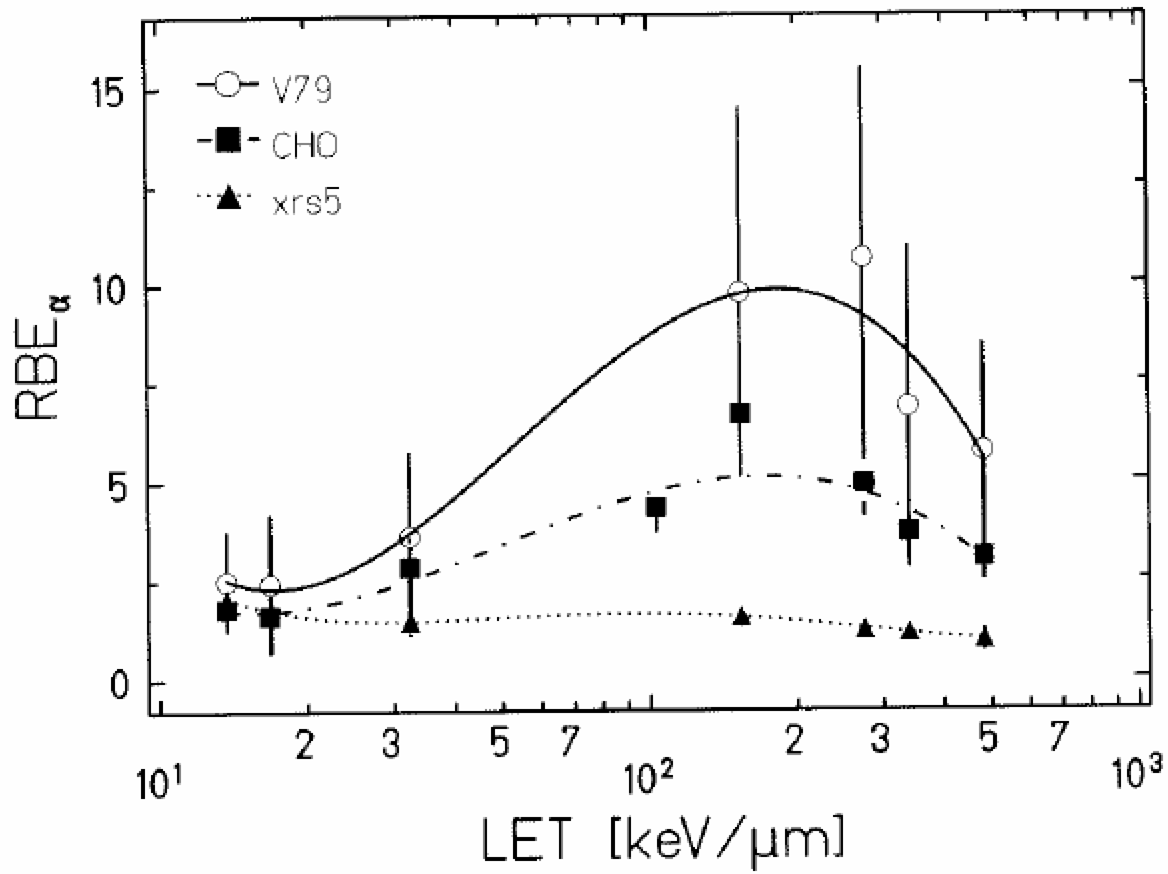
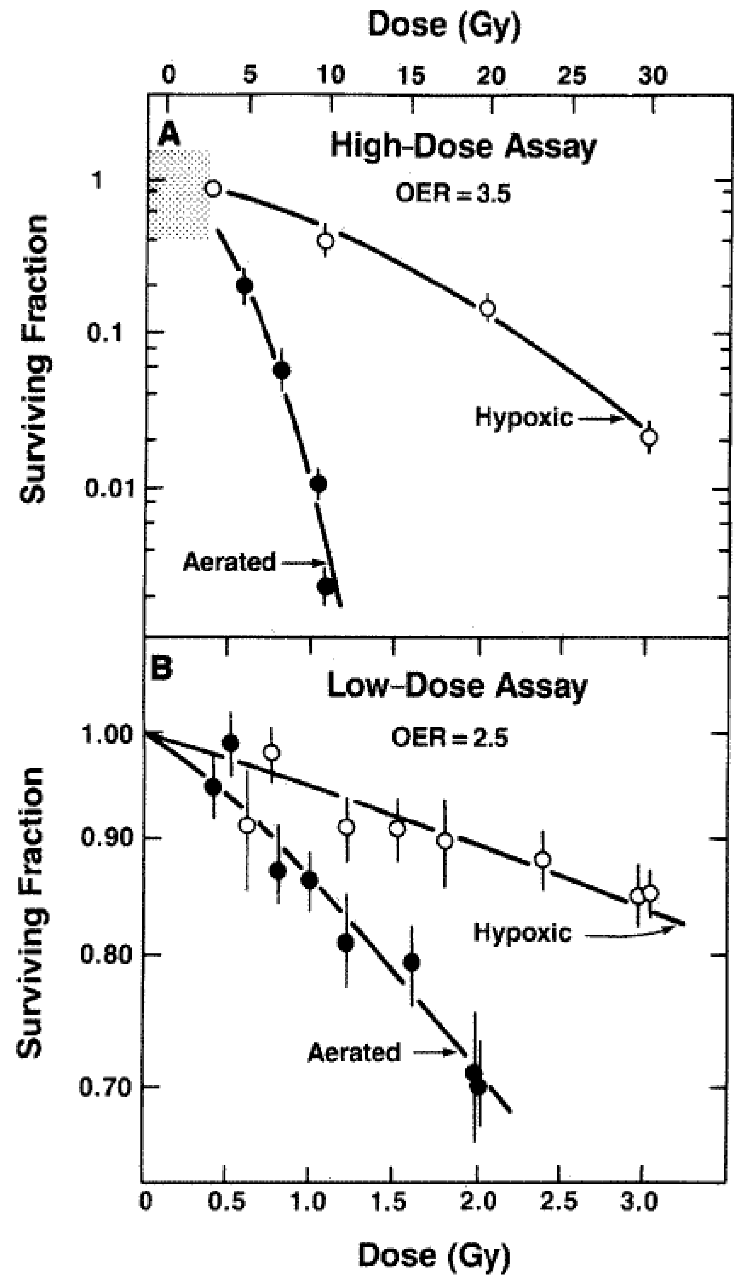


Fig. 28. Dependence of RBE on the biological system. V79, CHO cells: repair-proficient normal cells; XRS cells: repair-deficient, sensitive cells. (Redrawn from Weyrather et al., 1999.)

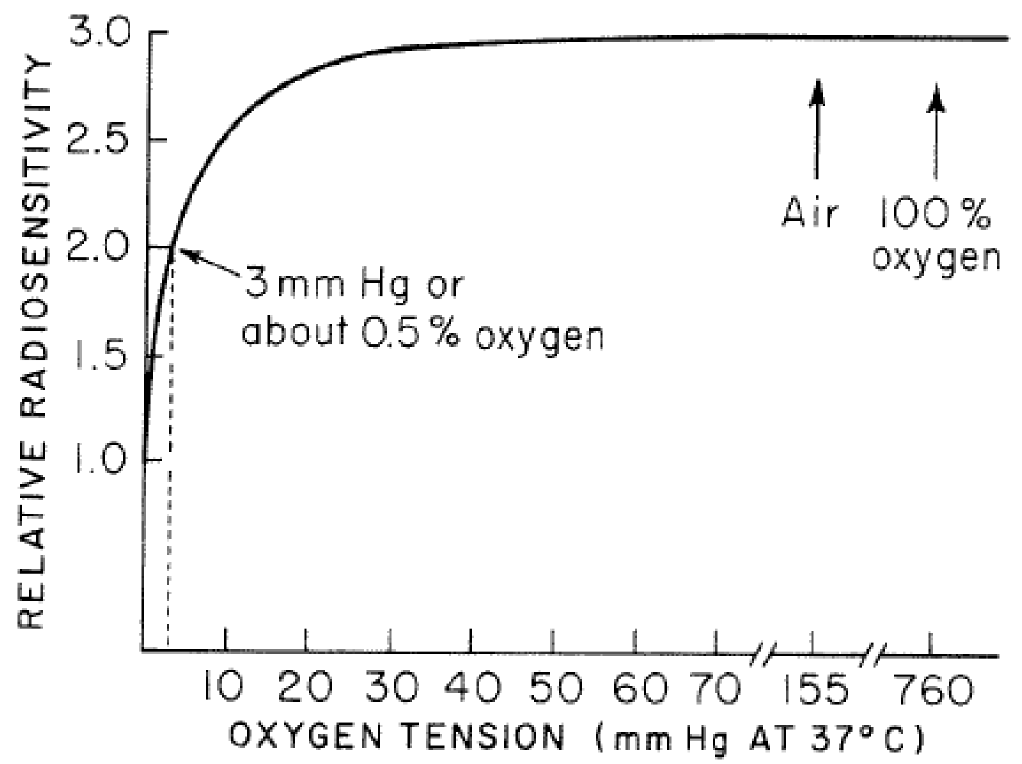
RBE also depends on cell-type and the ability of the cell to repair DNA double strand breaks

THE OXYGEN EFFECT



Hall Fig. 6.1

THE OXYGEN EFFECT – HOW MUCH OXYGEN IS NEEDED

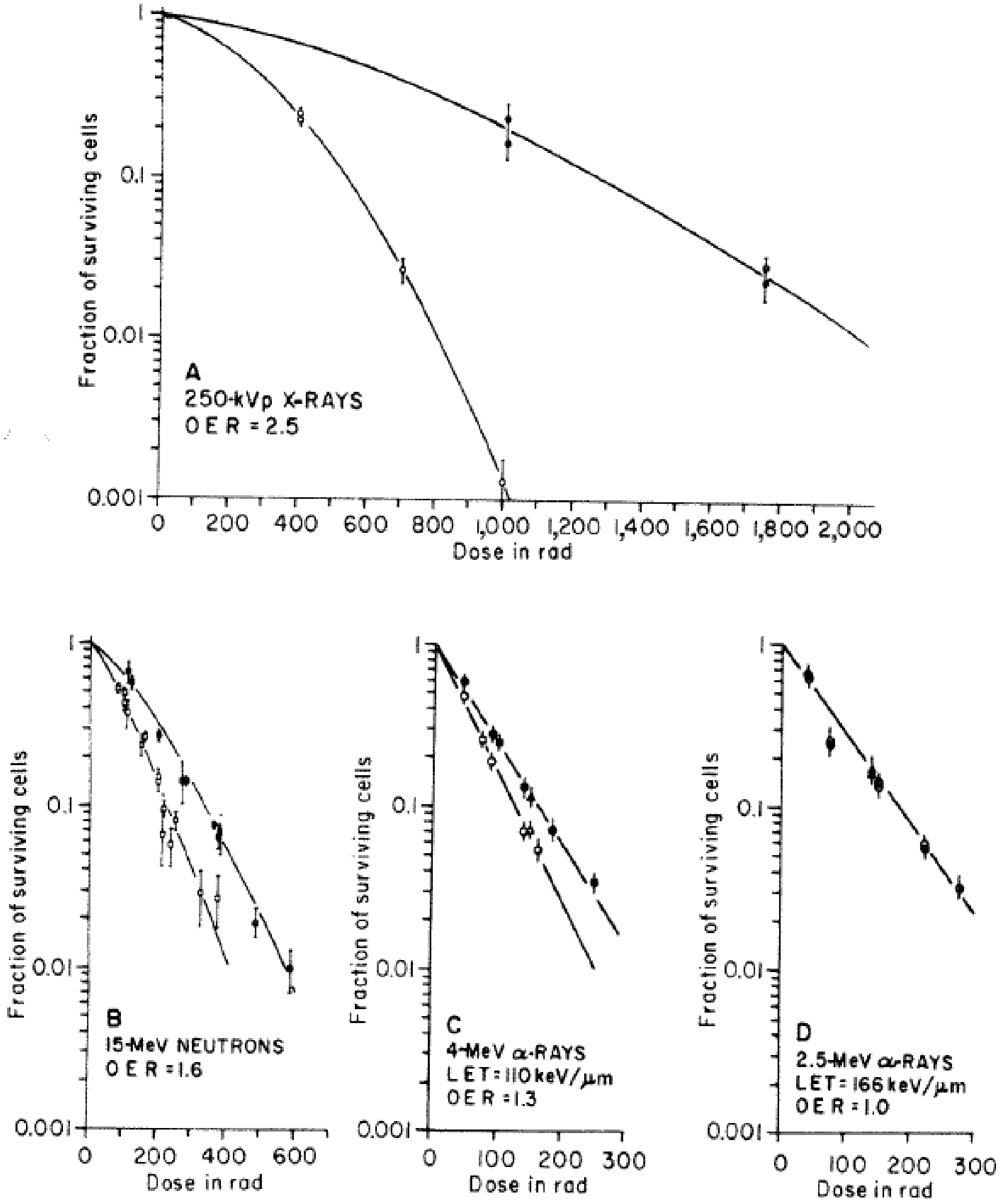


Hall Fig. 6.5

OER AND LET

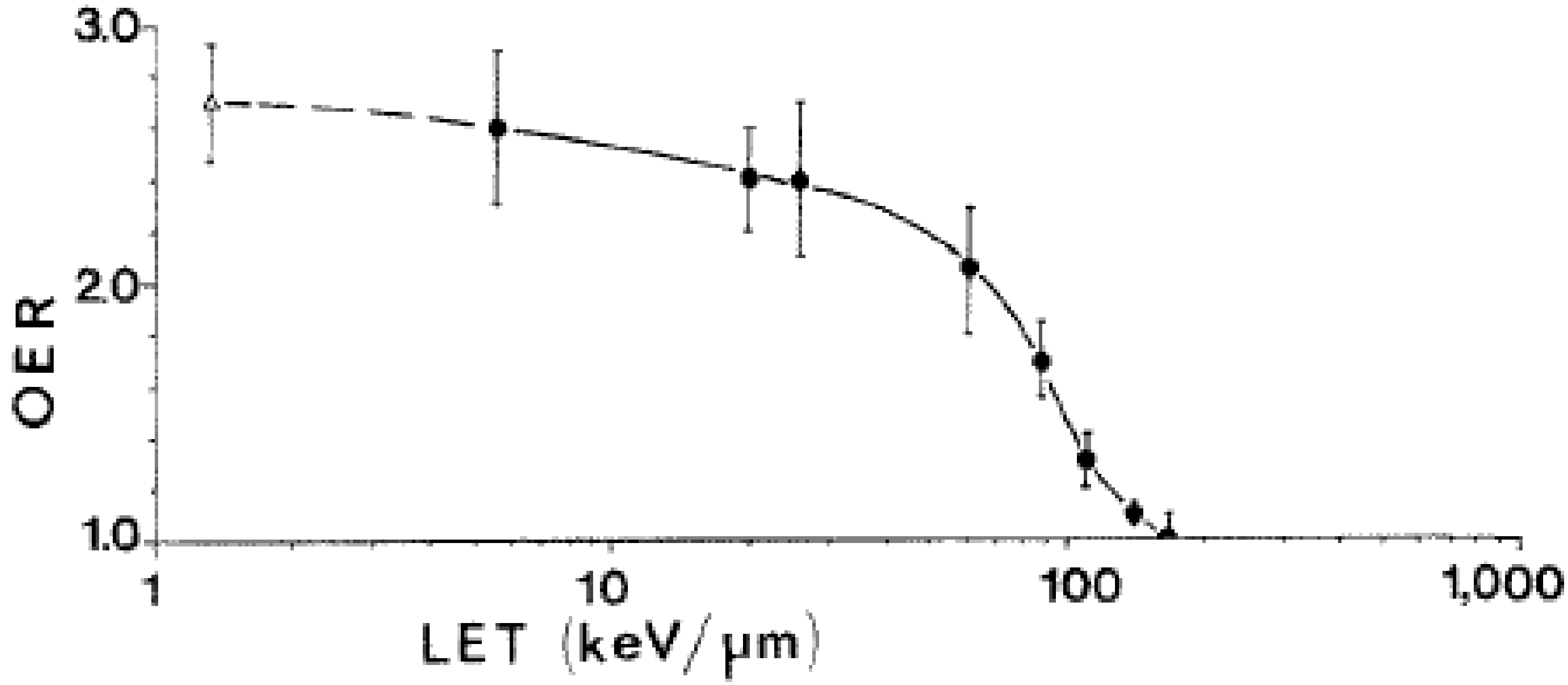
The OER decreases with increasing LET and at high LET (alpha particles) is 1.0 i.e no oxygen effect.

Why?



Hall Fig. 7.8

OER AND LET



Hall Fig. 7.9

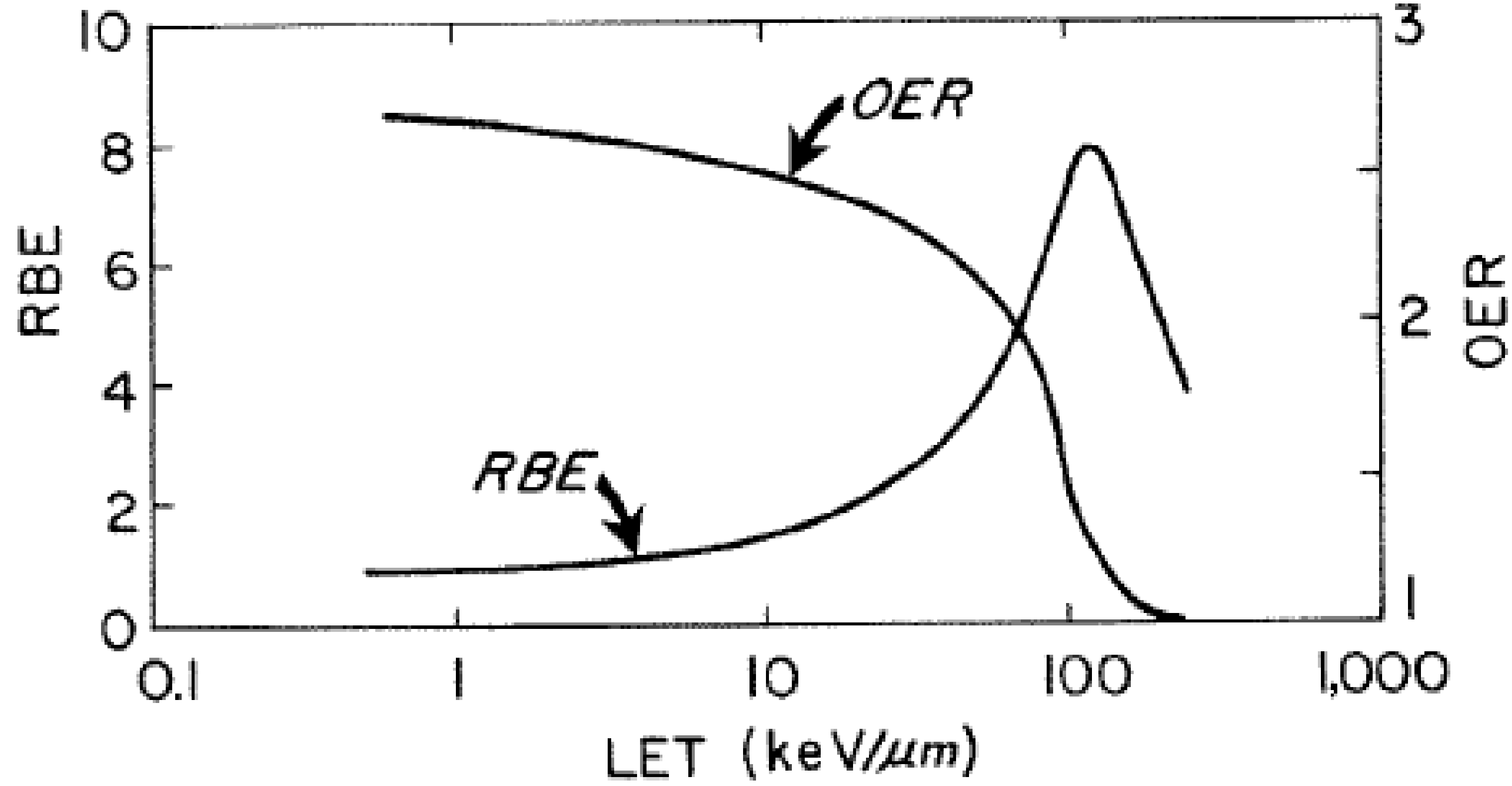
RBE, LET AND OER SUMMARY

RBE varies according to the tissue or end-point studied. In general RBEs are higher for cells or tissues that can accumulate and repair sublethal damage (X-ray dose-response curve has a broad shoulder)

For organisms with double-stranded DNA the RBE will reach a maximum for radiation of LET around 100 keV/μm, thereafter decreasing with higher LET due to energy 'wastage' or overkill

The oxygen enhancement ratio has a value around 3 for low LET radiation, which falls when the LET is around 30 keV/μm and reaches unity (1.0) at an LET of around 200 keV/μm

OER, RBE AND LET



Two good reasons to think about using high LET radiation for cancer therapy

Hall Fig. 7.10

HIGH-LET THERAPY

Rationale for high-LET therapy

- Increased RBE for cell killing
- Lower OER for dealing with hypoxic tumour cells
- Improved dose distribution for critical tissues

High LET Modalities

- Fast Neutrons
- Negative pi-mesons
- Boron Neutron Capture Therapy
- Protons
- Carbon ions