Curso de Radiobiología UDELAR

Facultad de Ciencias

Unidad de Física Médica

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Partículas cargadas

LET y RBE

Créditos:

Dr. Jerry Battista

Radiobiology Lecture # 2
Charged Particles on the Move
LET and RBE Concepts

Read Chapters 1, 6, 7, 15, 24

Dr. J. Battista
January 18, 2011

http://autos-cars-new-2011.blogspot.com/2010/05/super-fast-cars-picture.html

Lecture # 2

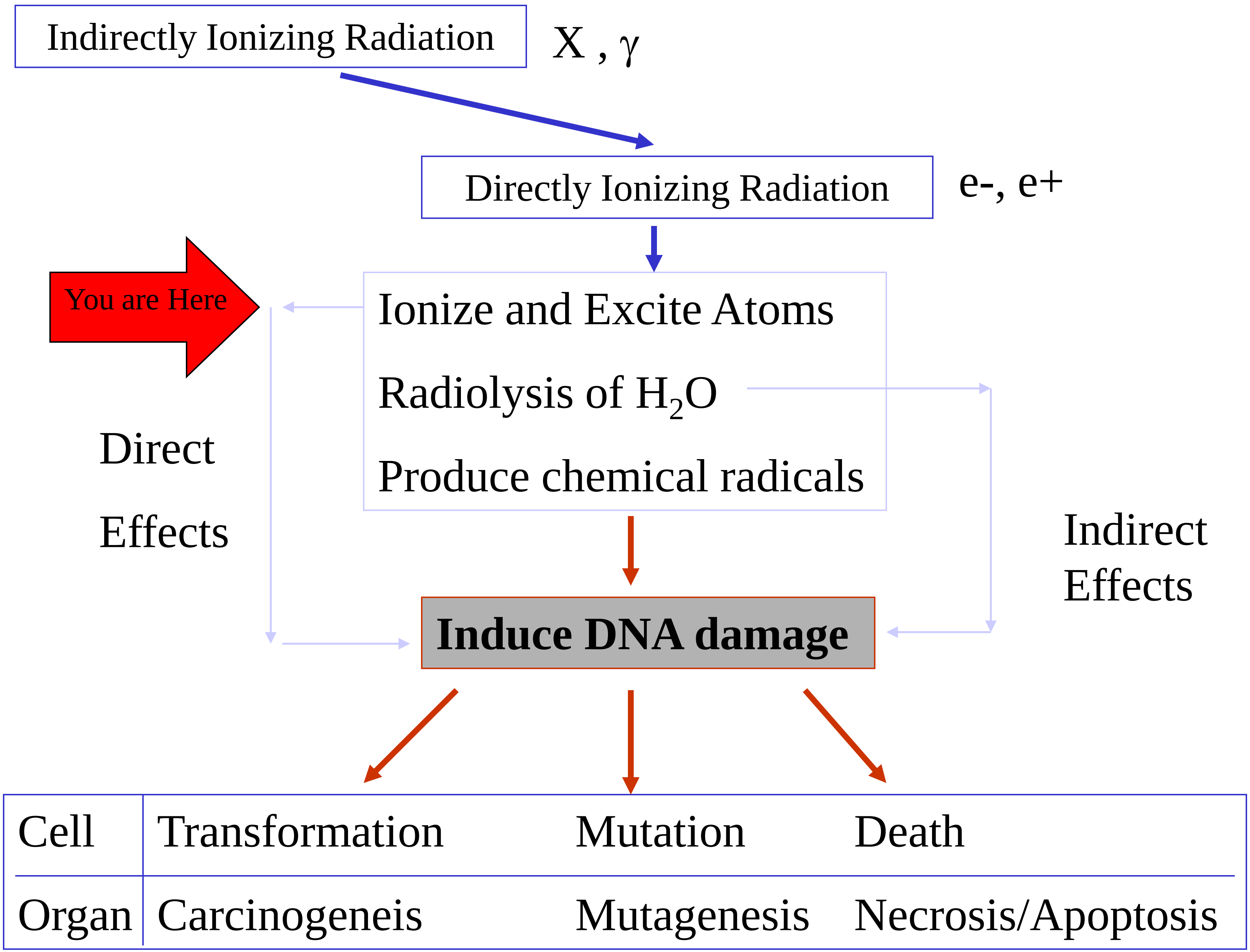
Basic Idea

Radiation damage not only depends on the amount of energy deposited (dose) but also on <u>how this energy is spatially laid down (LET)</u>

What is this lecture all about ?

Type or "quality" of ionizing radiation
Linear Energy Transfer (LET)
Relative Biological Effect (RBE)
Absorbed Dose (physical)
Equivalent Dose (biological)

http://www.scienceclarified.com/images/uesc_04_img0203.jpg


Indirectly Ionizing Radiation
X , γ
Directly Ionizing Radiation
e-, e+
You are Here
Ionize and Excite Atoms
Radiolysis of H2O
Produce chemical radicals
Direct
Effects
Indirect
Effects
Induce DNA damage
Cell
Transformation
Mutation
Death
Organ
Carcinogeneis
Mutagenesis
Necrosis/Apoptosis

Ionizing Radiation – Temporal

- Physics (10^{-18} sec)
  - photoelectric, Compton effects, Pairs
  - electrons and positrons in motion
  - They slow down in the absorber
- Radiation Chemistry (10^{-6} sec)
  - Ionization of H_2O
  - DNA damage
- Radiation Biology (> 10^5 sec)
  - cell survival
  - Pathology
  - Carcinogenesis
  - Inherited genetic damage

Time

And Here !

RECAP
x-γ rays liberate
charged particles with kinetic energy (K)

Photoelectric Effect –

Photoelectrons

Auger electrons

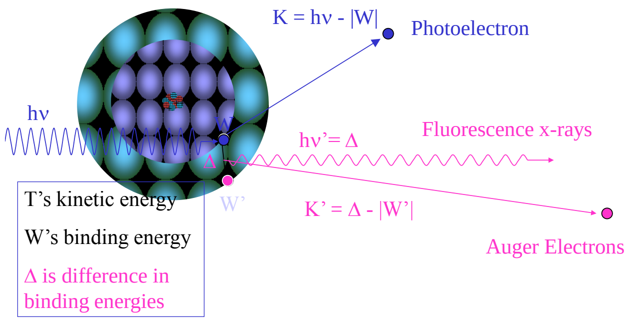
Compton Effect –

Compton recoil electrons

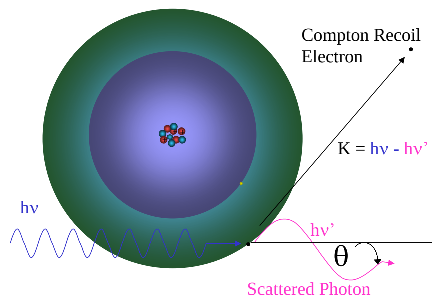
Pair Production –

Electrons and Positrons

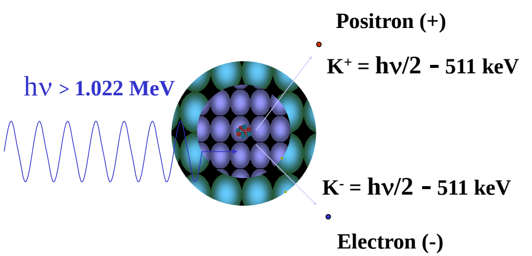
Photoelectric Effect



Compton Scattering

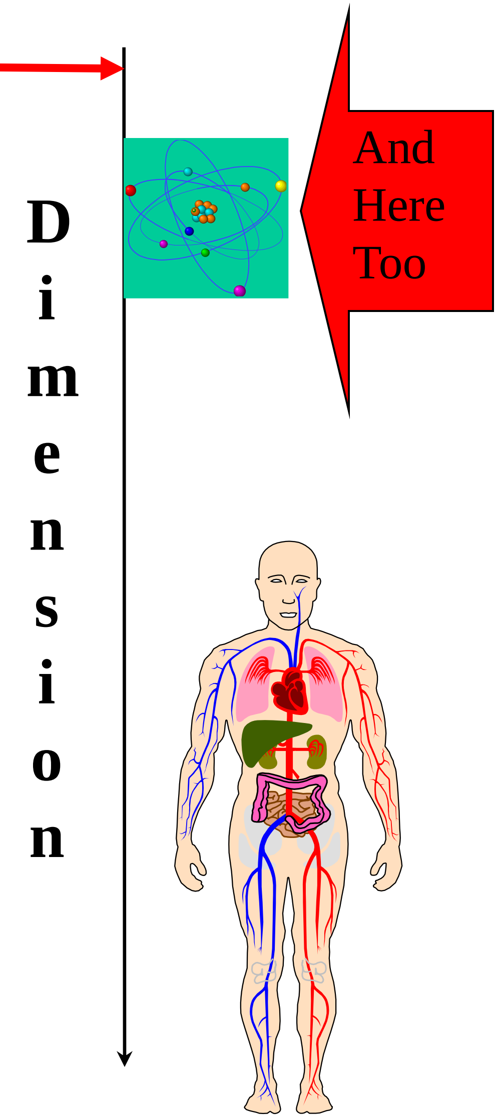


Pair Production



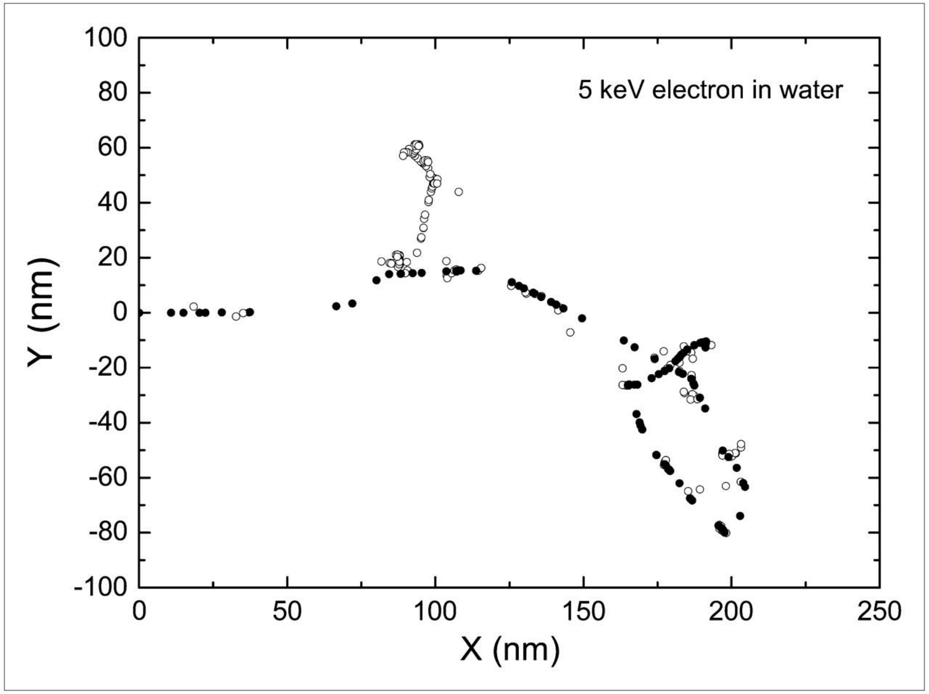
Ionizing Radiation - Spatial

- Physics (fm)
  - photoelectric, Compton effects, Pairs
  - electrons and positrons in motion
  - They slow down in the absorber
- Radiation Chemistry (nm)
  - Ionization of H_2O
  - DNA damage
- Radiation Biology(>μ m)
  - cell survival
  - “4 R’s” of radiobiology
- Pathology and Physiology (cm to m)
  - organ, whole body, progeny

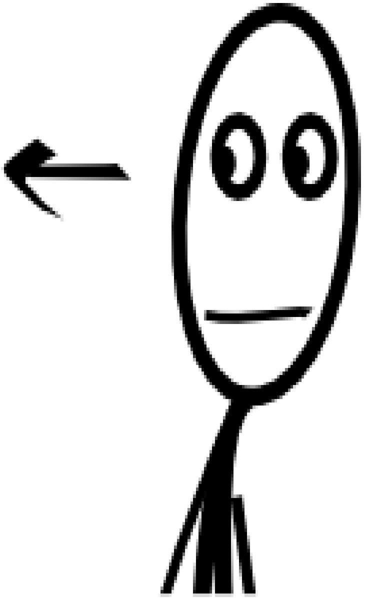


Saying # 3

“Keep a close eye on those darn charged particles”

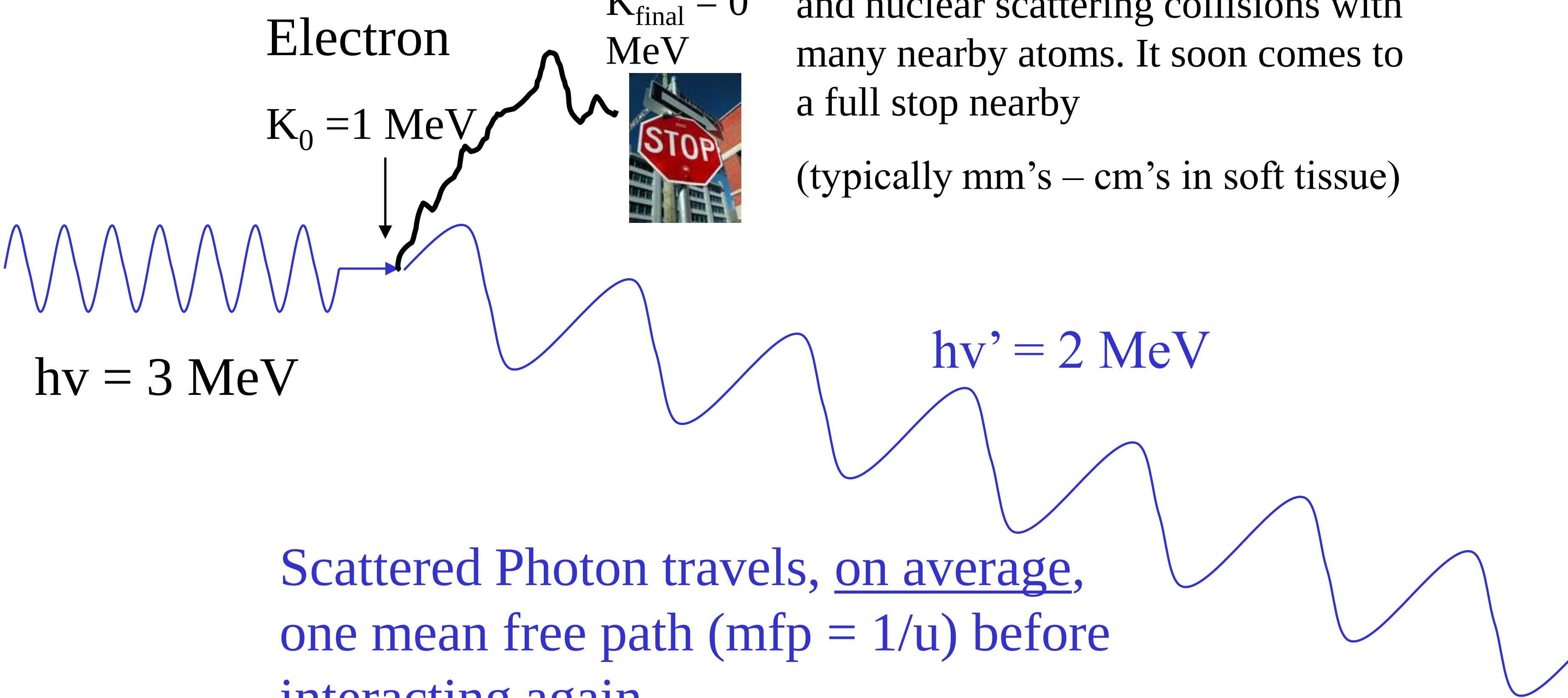


http://jnm.snmjournals.org/cgi/content-nw/full/49/1/151/FIG2



http://www.clker.com/clipart-10938.html

What is the fate of these charged particles ?



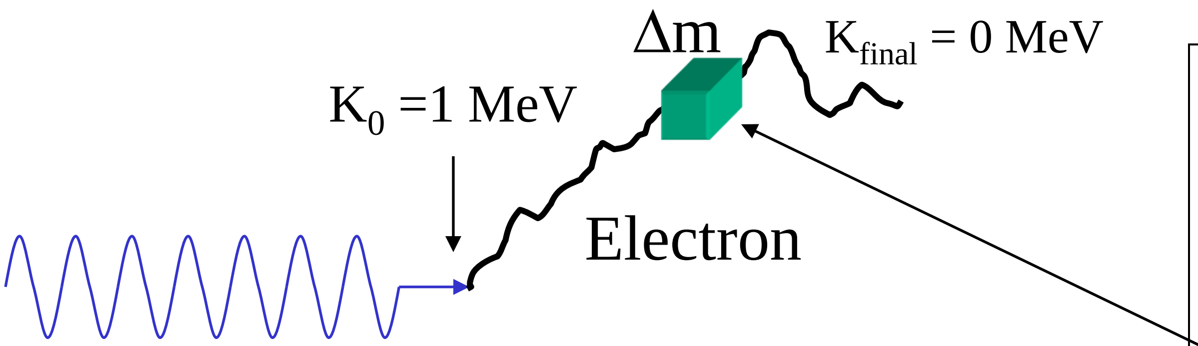
Electron undergoes continuous Coulomb energy-deposition events and nuclear scattering collisions with many nearby atoms. It soon comes to a full stop nearby

(typically mm's – cm's in soft tissue)

Scattered Photon travels, <u>on average</u>, one mean free path (mfp = 1/u) before interacting again

(typically 10's of cm in soft tissue)

Absorbed Dose Concept



Exposure (Roentgens)
$X = \Delta Q/\Delta m$
Released electric <u>charge</u>
ΔQ in Air (only)

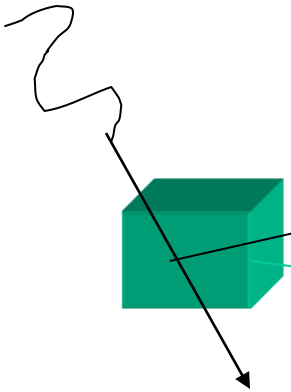
Energy absorbed per unit mass of the absorbing "voxel"

(any absorber)

$D = \Delta E/\Delta m$

Average all the energy left behind in the green voxel by a multitude of all types of particles

UNITS - Absorbed Dose



$$D = \frac{\Delta E}{\Delta m} \qquad \left[\frac{J}{kg} = 1 Gray \right]$$

– Unit is Gray [Gy]

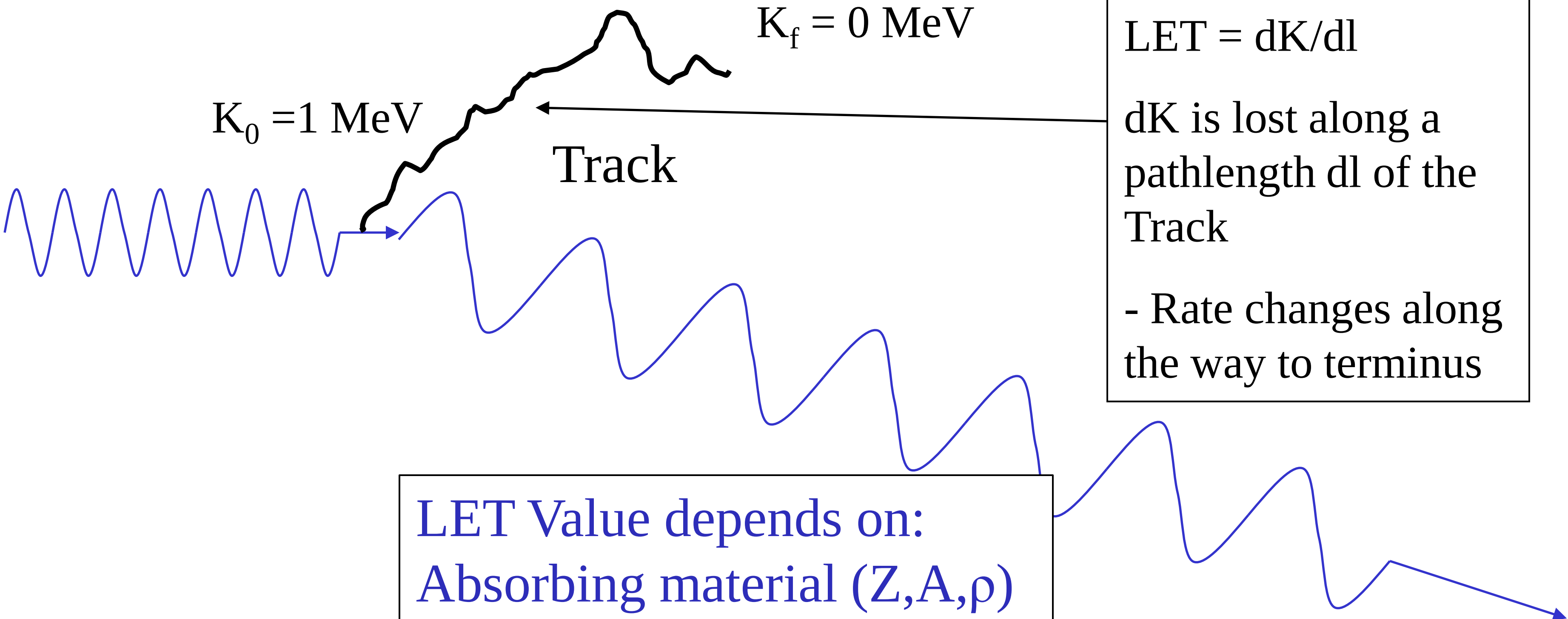
– Older Unit is the “rad” (100 ergs/g)

– 1 Gy = 100 cGy = 100 rads

– 1 cGy = 1 rad

See Chapter 15

Linear Energy Transfer (LET)



Spatial rate of energy loss along the path

LET = dK/dl

dK is lost along a pathlength dl of the Track

- Rate changes along the way to terminus

LET Value depends on:
Absorbing material (Z,A,ρ)
Particle Charge (Z)
Particle Energy - Speed (v)

Typical LET Values in Water

(depends on particle charge, energy (speed), absorber type, and its density)

TABLE 7.1. *Typical Linear Energy Transfer Values*

Radiation	Linear Energy Transfer, KeV/μm	
Cobalt-60 γ-rays	0.2	
250-kV x-rays	2.0	
10-MeV protons	4.7	
150-MeV protons	0.5	
	Track Avg.	Energy Avg.
14-MeV neutrons	12	100
2.5-MeV α-particles	166	
2-GeV Fe ions	1,000	

Other Charged Particles

Particle	Symbol	Relative Mass	Rest Mass Energy (MeV)	Mean Life-Time (sec)	Charge
Electron	e^-	1	0.51	∞	1^-
Positron	e^+	1	0.51	∞	1^+
Positive pion	π^+	273	140	2.5×10^{-8}	1^+
Negative pion	π^-	273	140	2.5×10^{-8}	1^-
Proton	p	1836	939	∞	1^+
Neutron	n	1850	944	720	0
Deuteron	$_1H^1$	3690	1880	∞	1^+
Alpha particle	$_2He^4$	7380	3760	∞	2^+

LET Tracks seen in the context of a cell

LET

Fast Proton → Moderate

Slow Proton → High

Fast Electron → Low

Slow Electron → Moderate

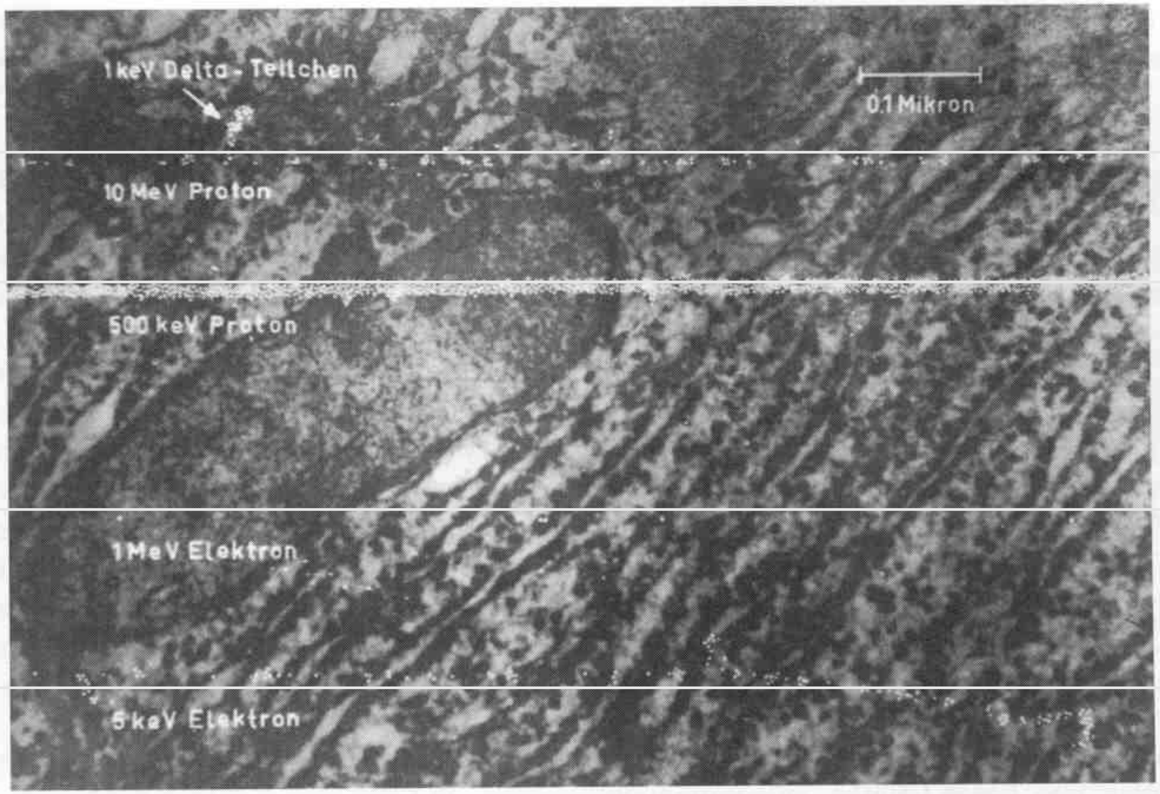
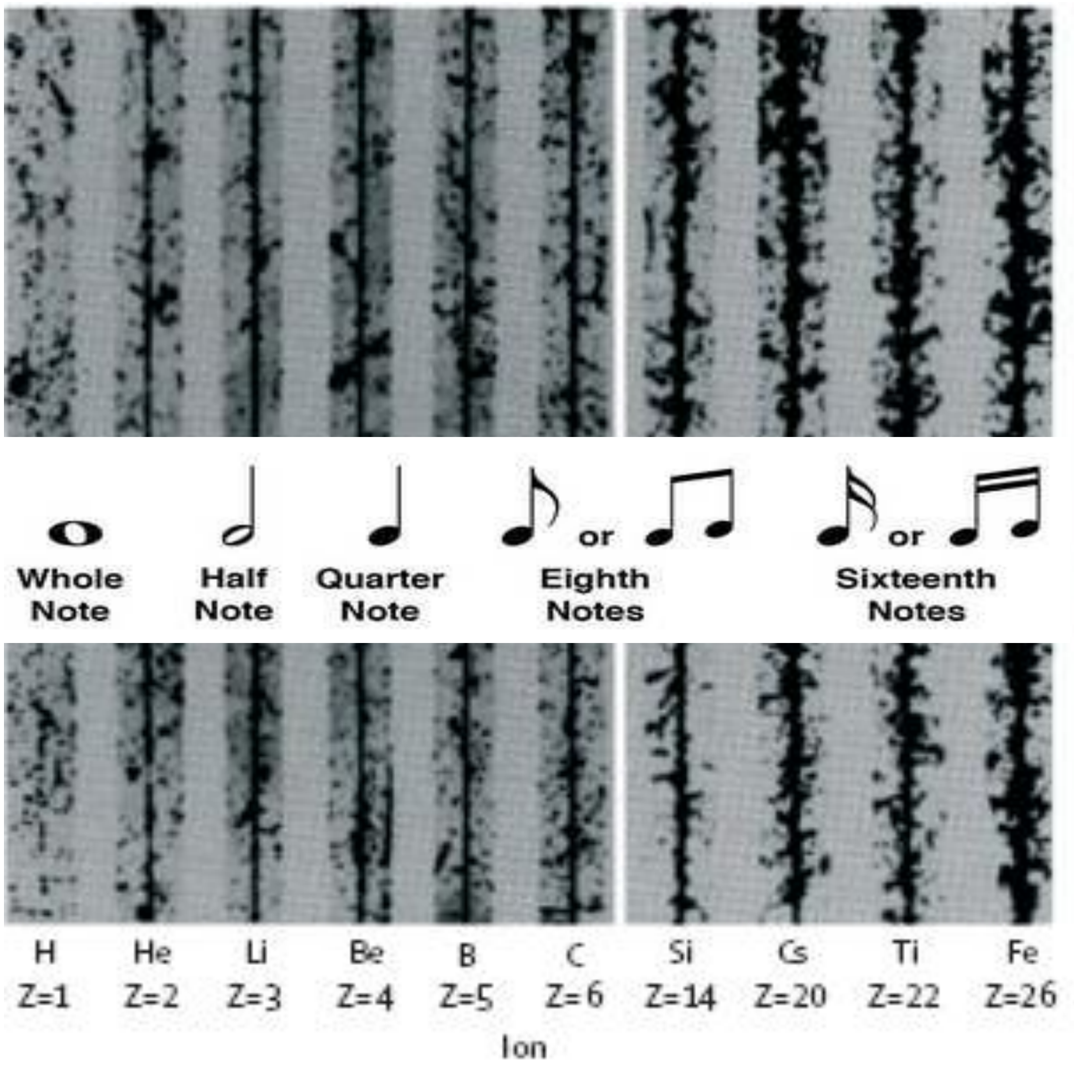
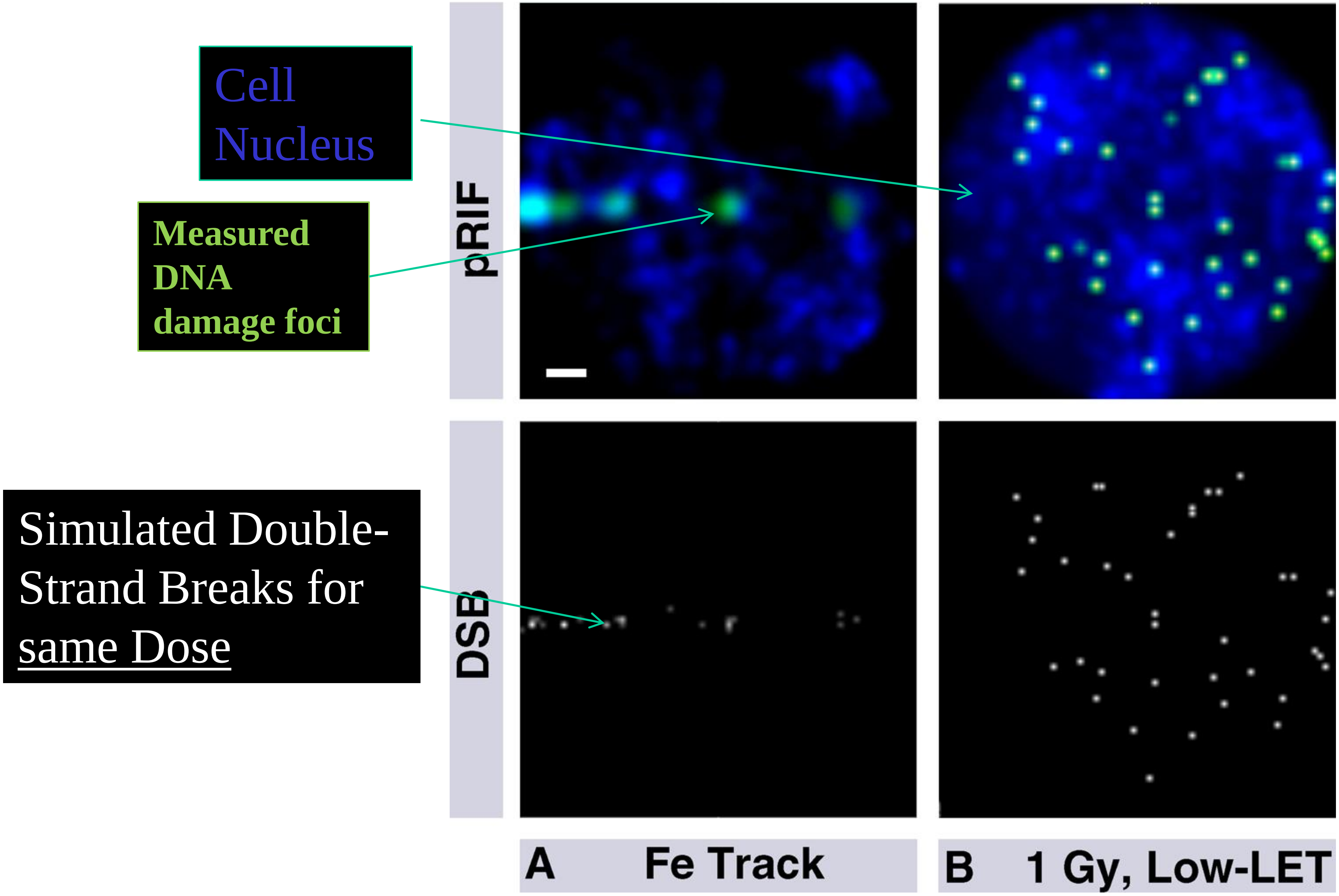


Figure 7.1. Variation of ionization density associated with different types of radiation. The background is an electron micrograph of a human cell. The white dots represent ionizations. **Top to bottom:** A 10-MeV proton, typical of the recoil protons produced by high-energy neutrons used for radiotherapy. The track is intermediate in ionization density. Also shown is a secondary 1-keV γ-ray, an electron set in motion by the proton. A 500-keV proton, produced by lower-energy neutrons (*e.g.*, from fission spectrum) or by higher-energy neutrons after multiple collisions. The ionizations form a dense column along the track of the particle. A 1-MeV electron, produced, for example, by photons of cobalt-60 γ-rays. This particle is very sparsely ionizing. A 5-keV electron, typical of secondary electrons produced by x-rays of diagnostic quality. This particle is also sparsely ionizing but a little denser than the higher-energy electron. (Courtesy of Dr. Albrecht Kellerer.)

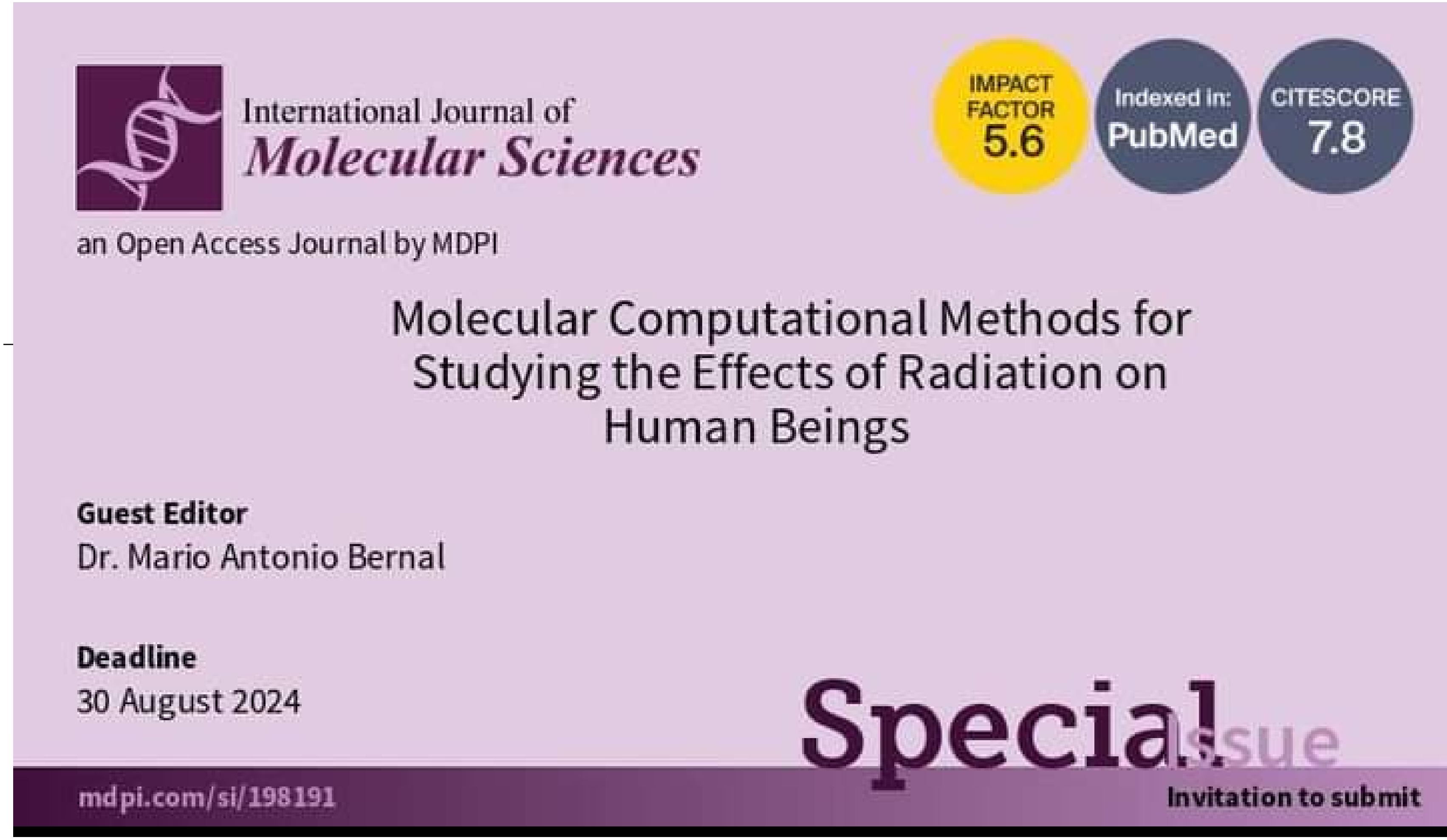
LET and Ionization Density vs Charge (Z): A Musical Analogy



Cucinotta et al. Lancet 2006



S. Costes et al. PLoS Computational Biology | www.ploscompbiol.org 0001 August 2007 | Volume 3 | Issue 8 | e155


International Journal of
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CITESCORE 7.8
Molecular Computational Methods for Studying the Effects of Radiation on Human Beings
Guest Editor
Dr. Mario Antonio Bernal
Deadline
30 August 2024
Special Issue
mdpi.com/si/198191
Invitation to submit

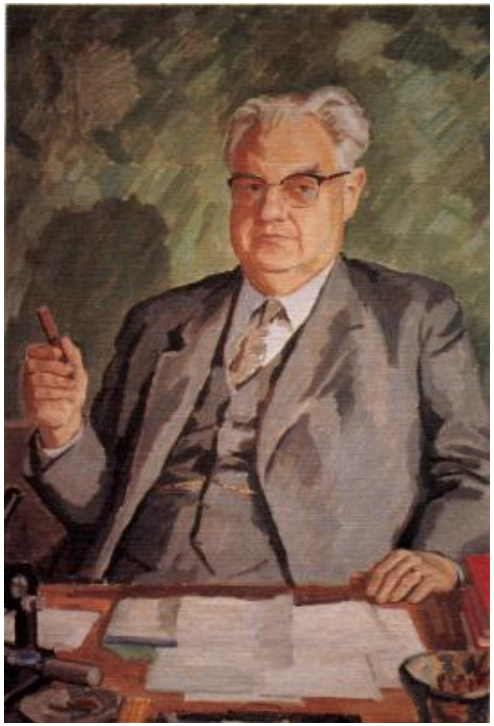
Equivalent Dose combines Dose and LET

- Formerly called 'dose equivalent'
- Takes account of physical dose and LET bio-effects
- Product of physical absorbed dose and radiation weighting factor W_R
- W_R (function of LET) relates to tissue sensitivity and importance to survival

$$D_{eq} = D \times W_R(LET)$$

  - Unit is Sievert = Sv
  - Older Unit is "rem" (if D is in rads, then ED is in rems)
  - 1 Sv = 100 rems, 1 cSv = 1 rem

Rolf



Radiation Weighting Factors

TABLE 15.1. *Radiation Weighting Factors*

Type and Energy Range	Radiation Weighting Factor
Photons, all energies	1
Electrons and muons, all energies	1
Neutrons, energy <10 keV	5
10 keV to 100 keV	10
>100 keV to 2 MeV	20
>2 MeV to 20 MeV	10
>20 MeV	5
Protons, other than recoil protons, energy >2 MeV α-Particles, fission fragments, heavy nuclei	20

Data from International Commission on Radiation Units and Measurements: Recommendations. Report. No. 60. New York, Pergamon Press, 1991.

ICRP Publication 103

Table 2. Recommended radiation weighting factors.

Radiation type	Radiation weighting factor, w_R
Photons	1
Electrons[a] and muons	1
Protons and charged pions	2
Alpha particles, fission fragments, heavy ions	20
Neutrons	A continuous function of neutron energy (see Fig. 1 and Eq. 4.3)

All values relate to the radiation incident on the body or, for internal radiation sources, emitted from the incorporated radionuclide(s).

[a] Note the special issue of Auger electrons discussed in paragraph 116 and in Section B.3.3 of Annex B.

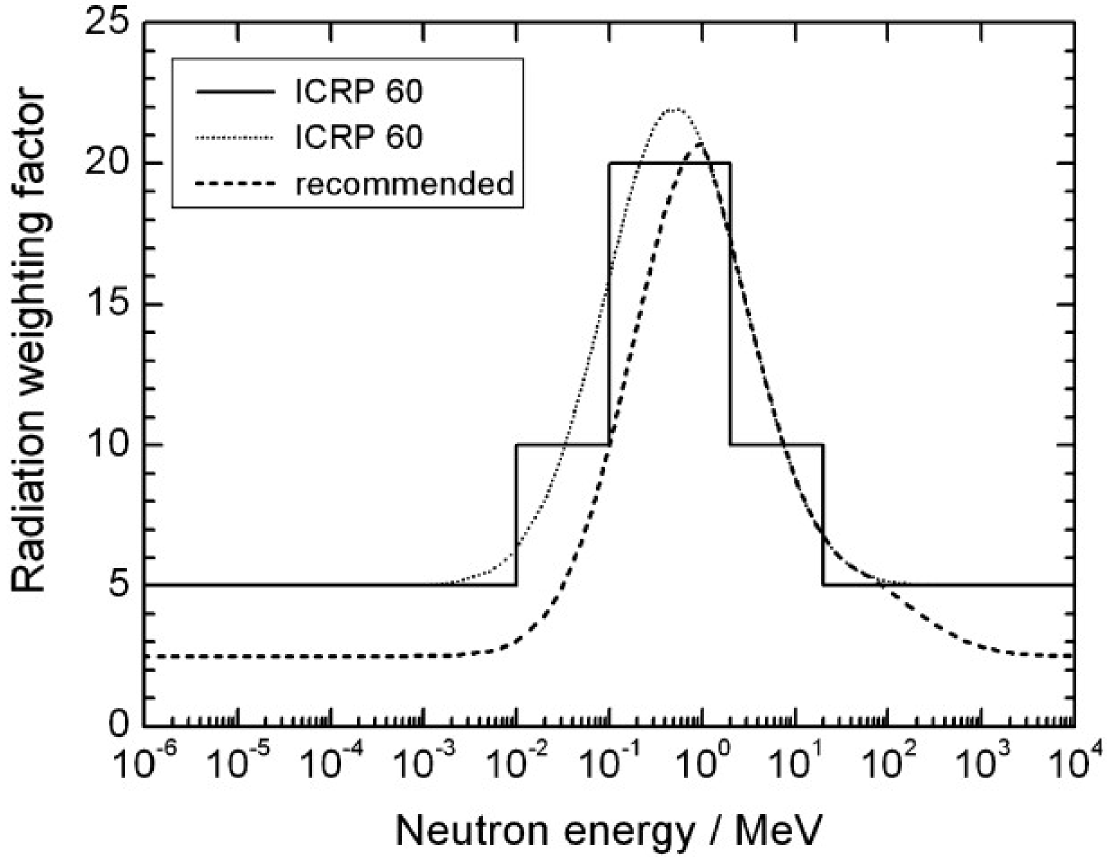


Fig. B.4. Radiation weighting factor, w_R, for neutrons versus neutron energy. Step function and continuous function given in *Publication 60* (ICRP 1991b) and function adopted in the 2007 Recommendations.

$$w_R = \begin{cases} 2.5 + 18.2\, e^{-[\ln(E_n)]^2/6}, & E_n < 1 \text{ MeV} \\ 5.0 + 17.0\, e^{-[\ln(2E_n)]^2/6}, & 1 \text{ MeV} \leqslant E_n \leqslant 50 \text{ MeV} \\ 2.5 + 3.25\, e^{-[\ln(0.04E_n)]^2/6}, & E_n > 50 \text{ MeV} \end{cases}$$

Saying # 4

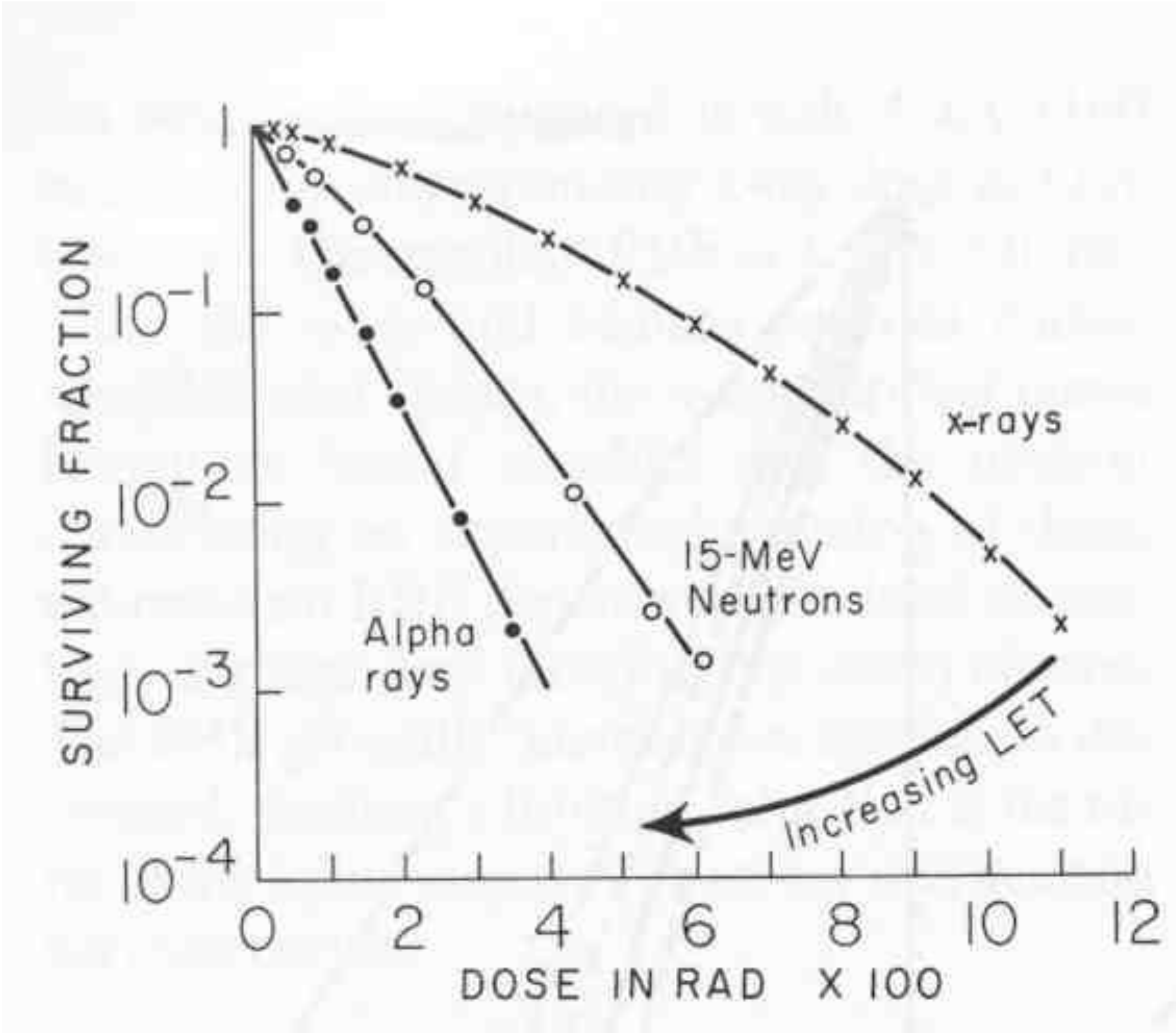
"All Ionizing Radiation Damage is

Deposited by Charged Particles."

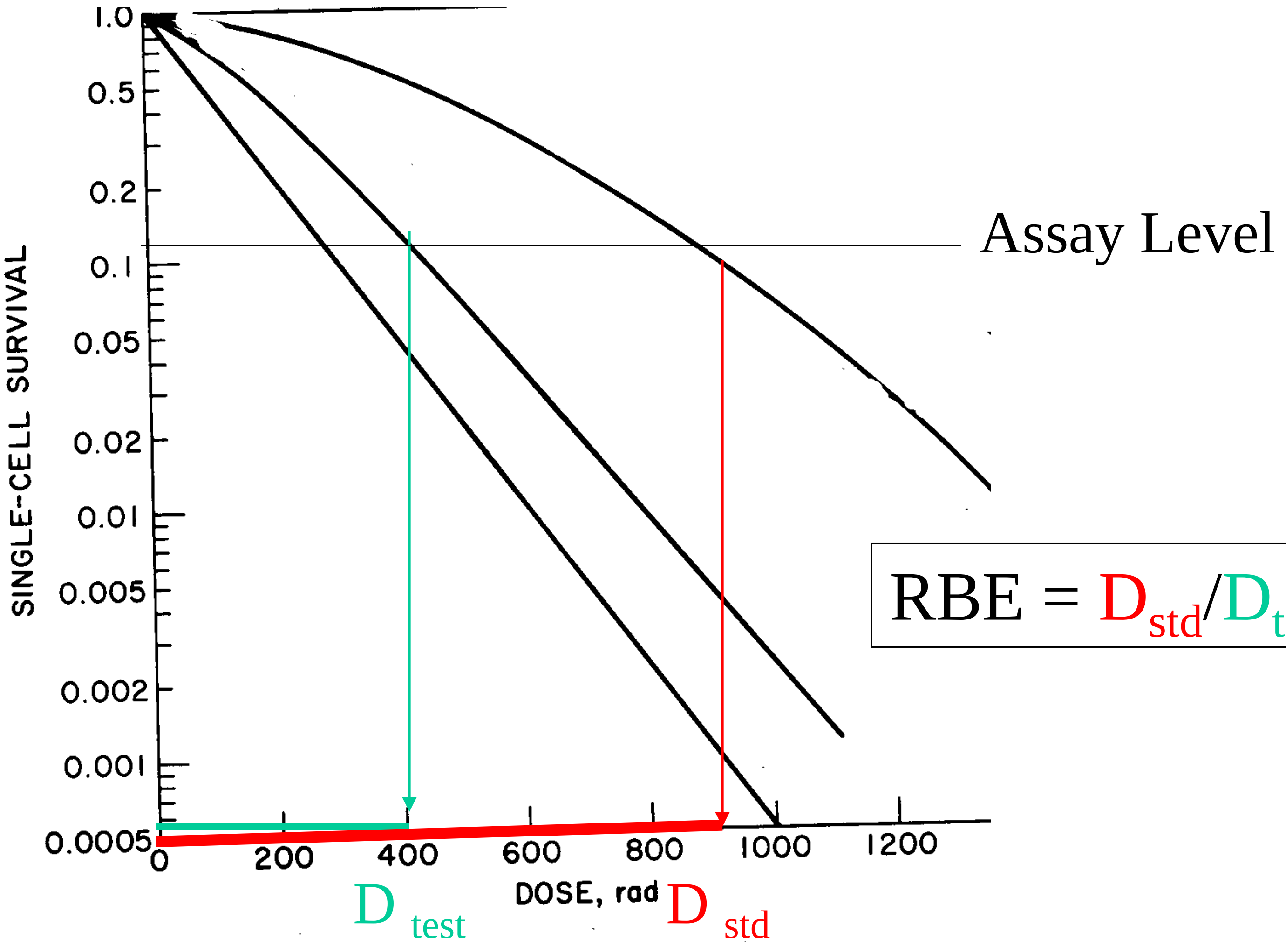
Impact of LET on Biological Response:

Cell Survival, RBE, and OER

LET affects Cell Killing

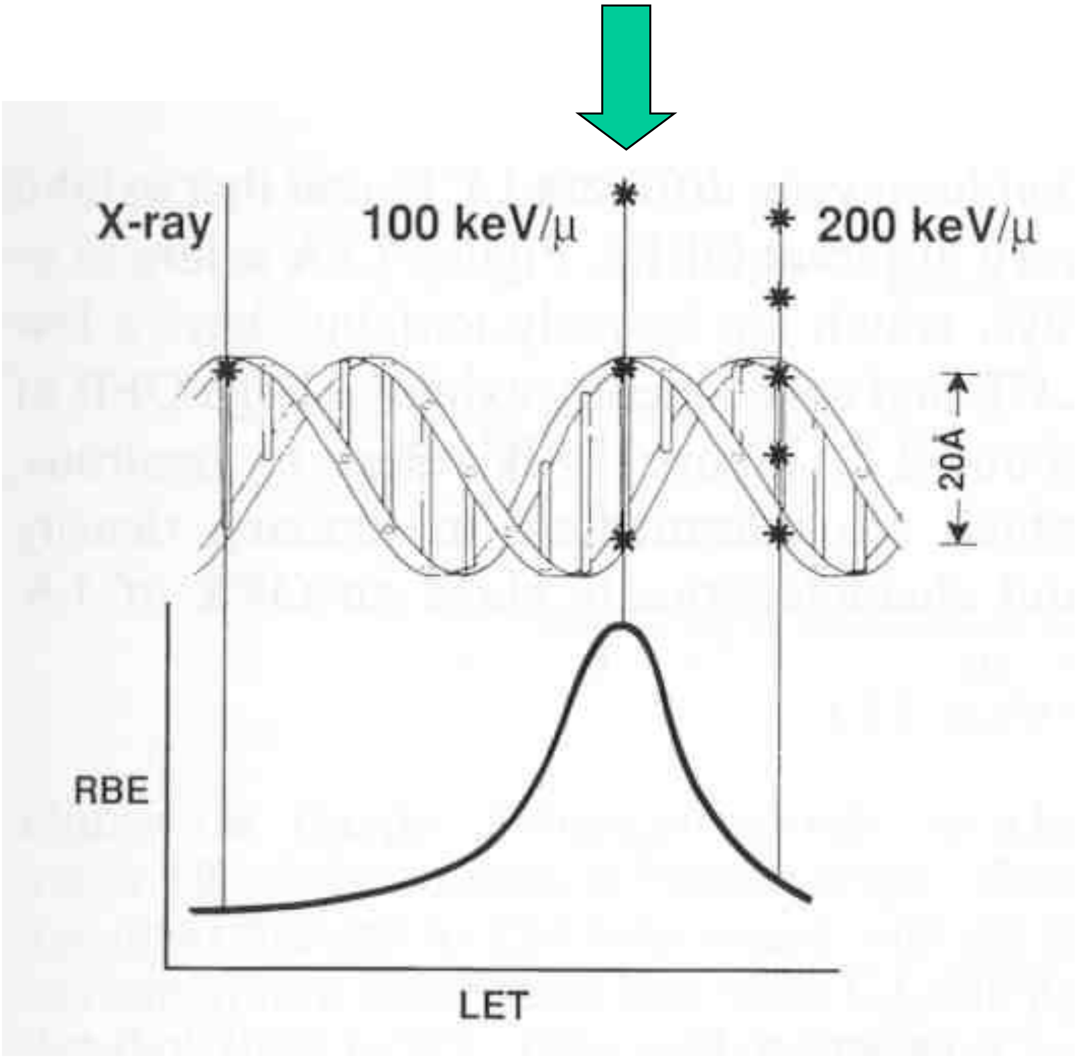


Definition of RBE (Relative Biological Effect)



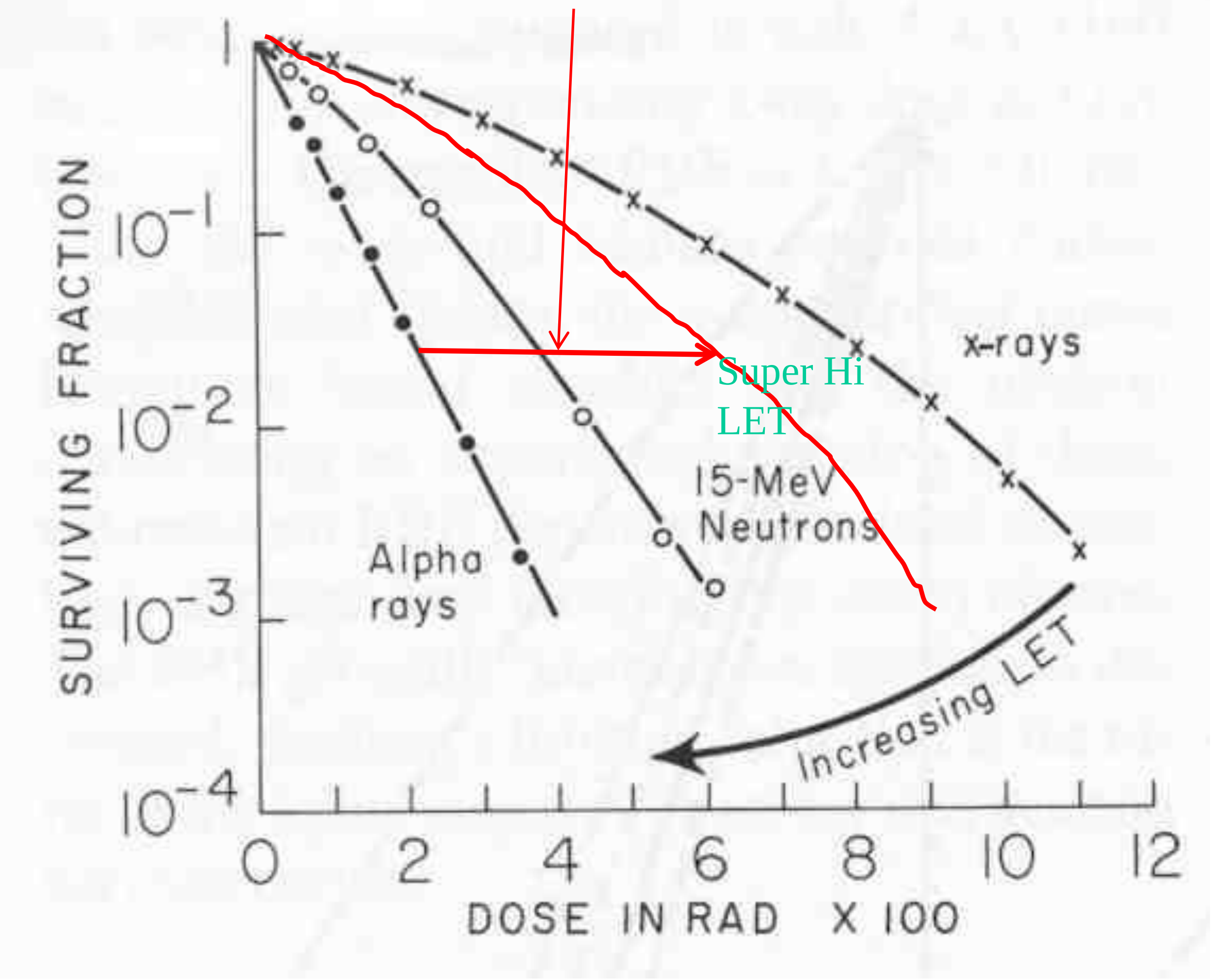
RBE = D_{std}/D_{test}

Is there an Optimal LET ? Why ?

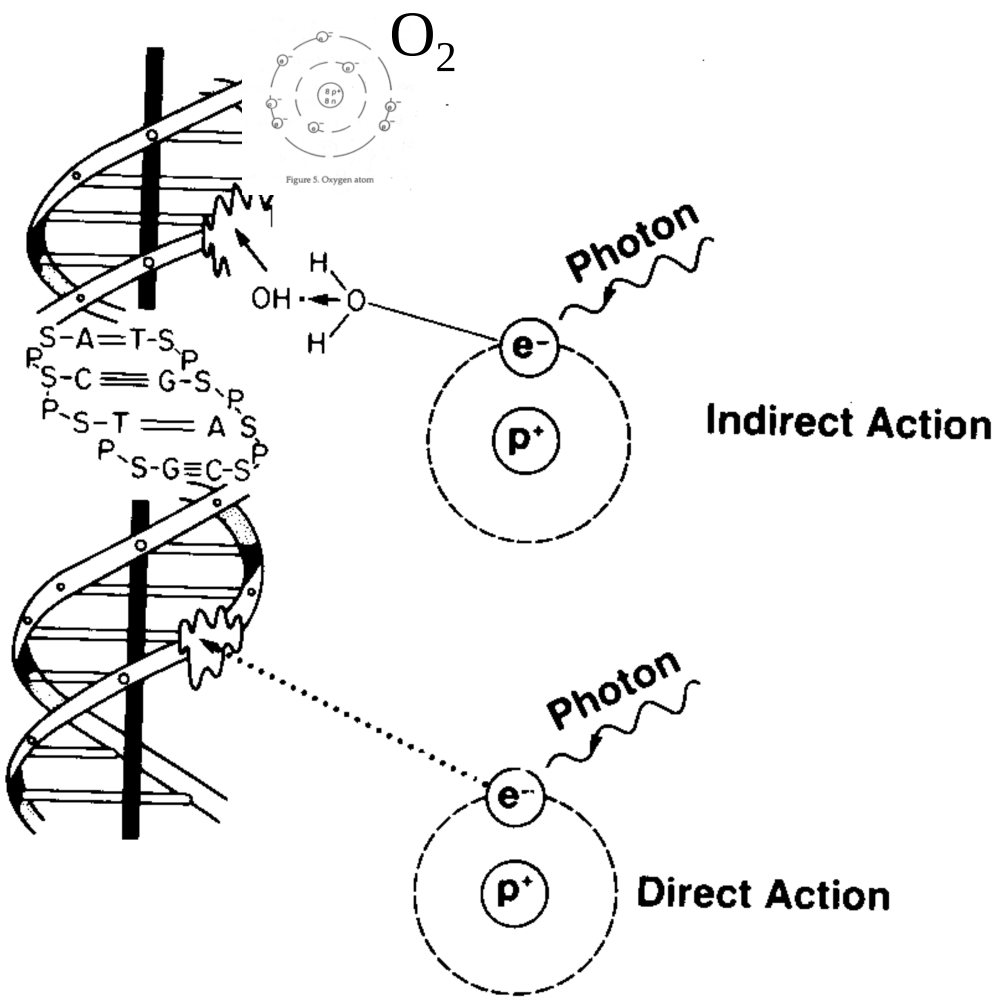


Caution: (Exception not shown in book)

Super-Hi LET (> Optimal) causes apparent reversal in LET trend due to Wasted Dose



LET affects the balance between Direct and Indirect Action



Reduced with higher LET

Enhanced with higher LET

LET affects the importance of the Presence of Oxygen (radiosensitizer)

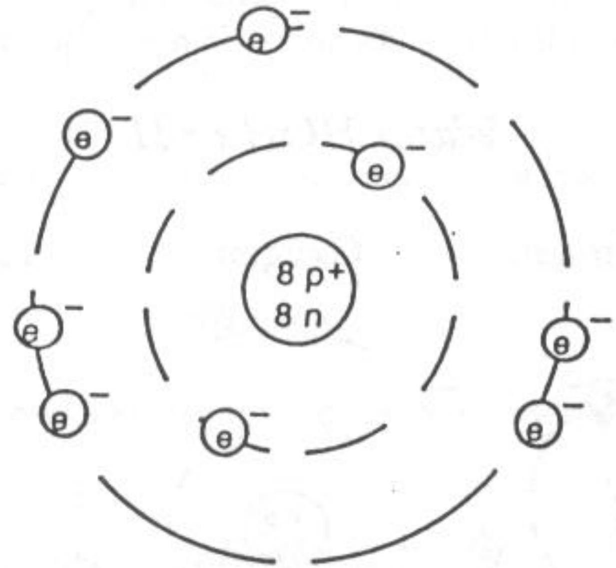
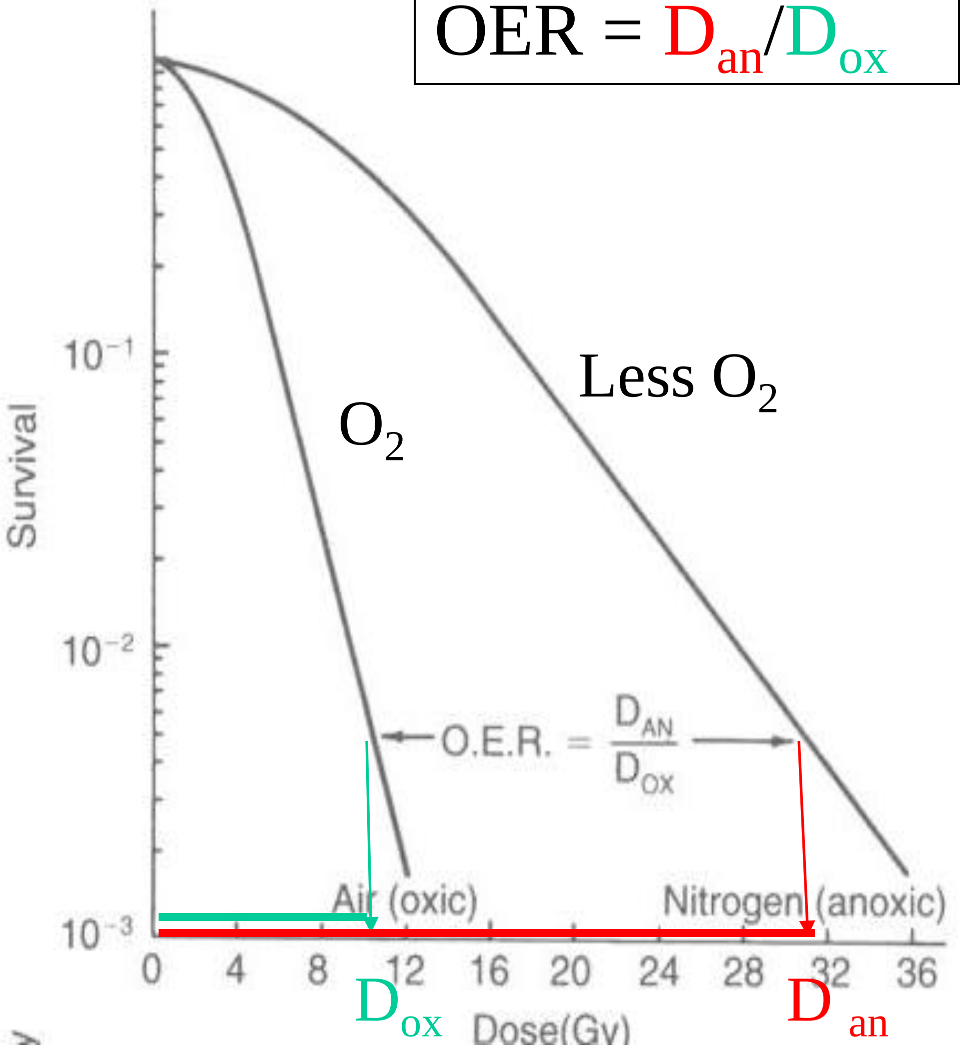


Figure 5. Oxygen atom

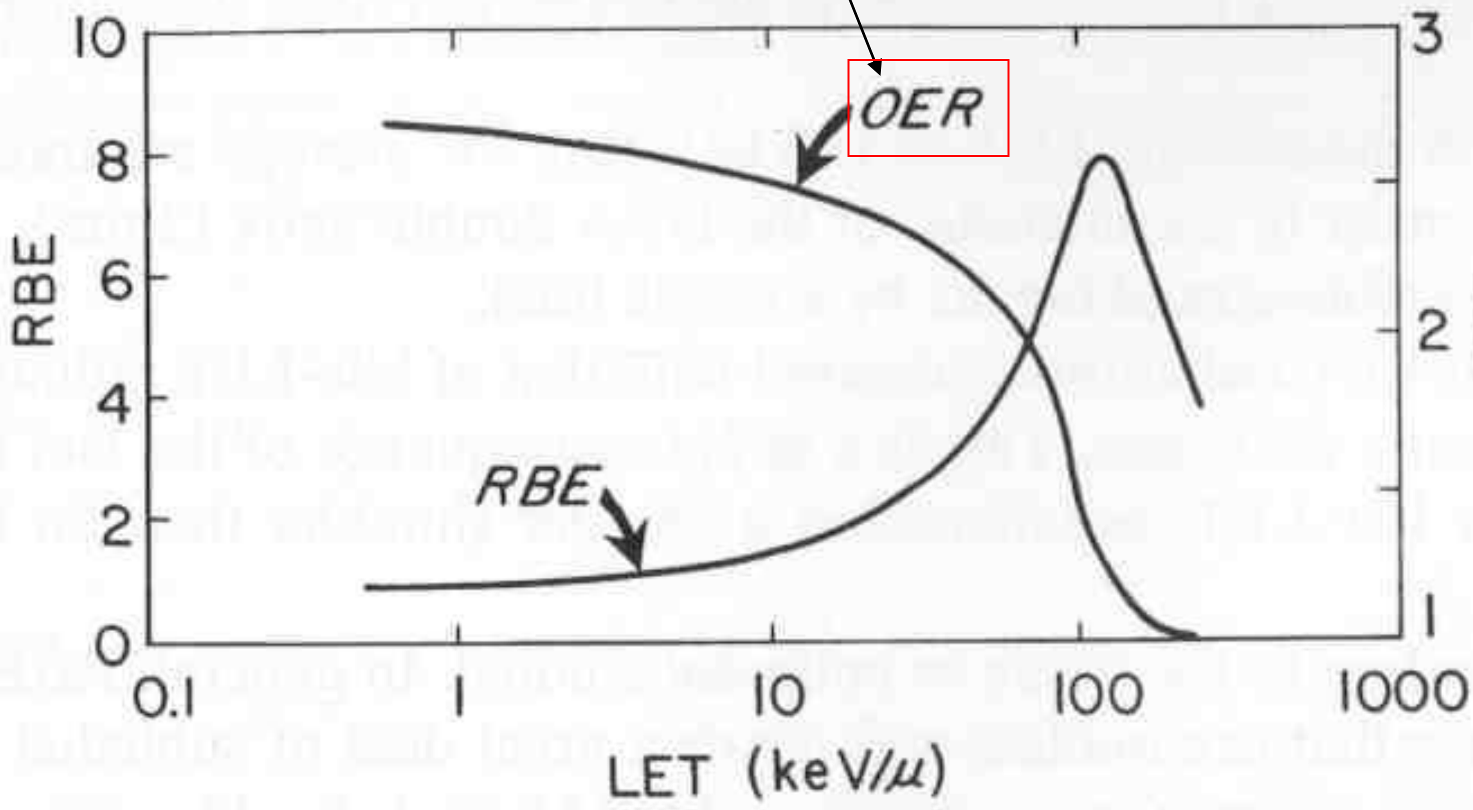
Oxygen Enhancement Ratio (OER)

Figure 6.2

$OER = D_{an}/D_{ox}$

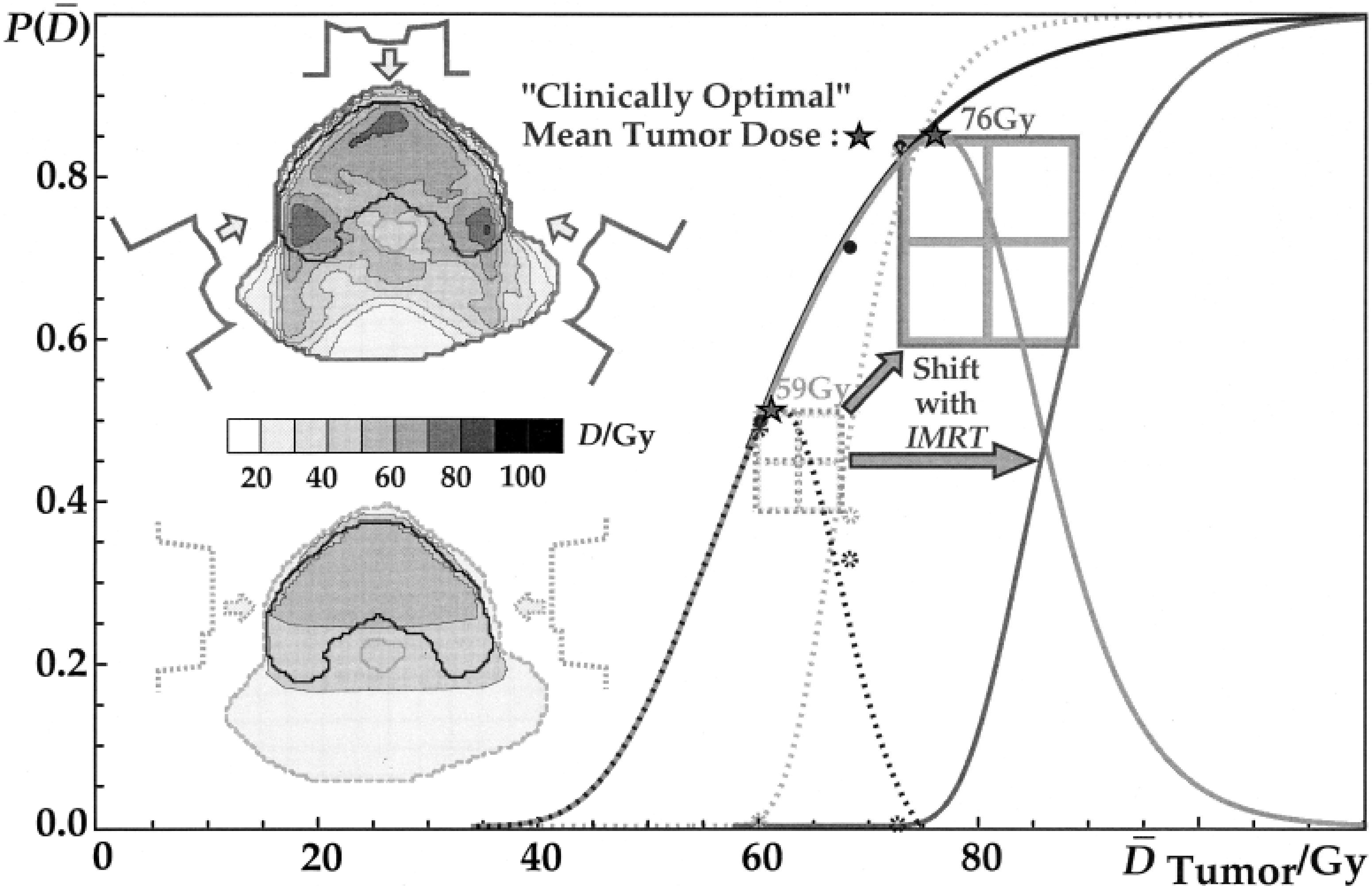


Higher LET lessens the dependence of DNA damage on the presence of oxygen (OER reduction)



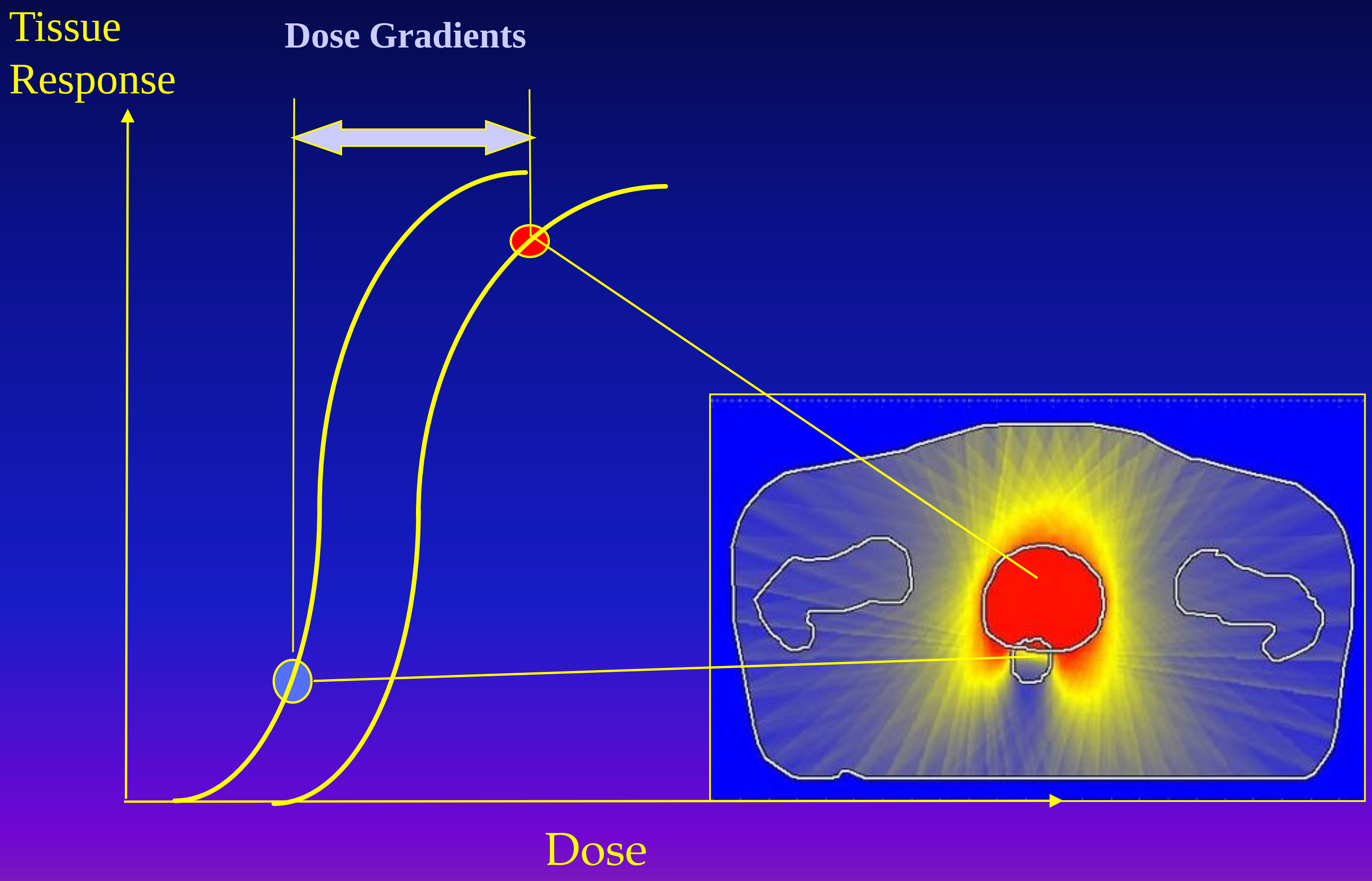
Radiation Beams:
Is there a magic bullet ?

Chapter 24



P(D̄)
"Clinically Optimal"
Mean Tumor Dose :
76Gy
59Gy
Shift
with
IMRT
D/Gy
20 40 60 80 100
0.8
0.6
0.4
0.2
0.0
0 20 40 60 80
D̄ Tumor/Gy

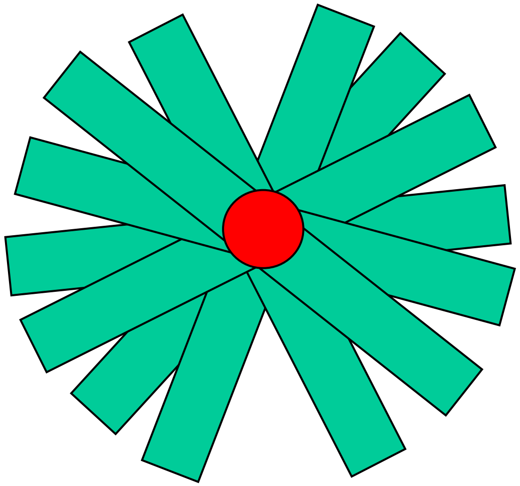
Physics Strategy: Dose Gradients



J2B

Cone, Fan, and Pencil Beam Geometries

Radiation Beam Optimization Criteria



Depth Dose Curve

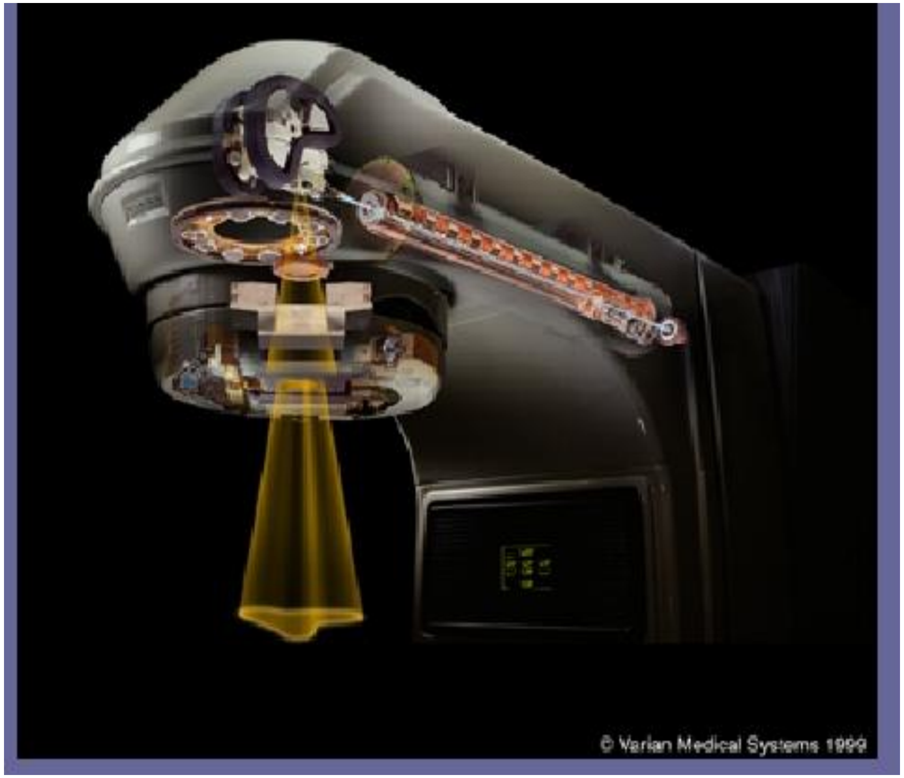
- single beam
- multiple cross-fired beams

Differential LET along beam path

- Differential Biological Effects along path
- Different RBE and OER

External Beam Radiotherapy

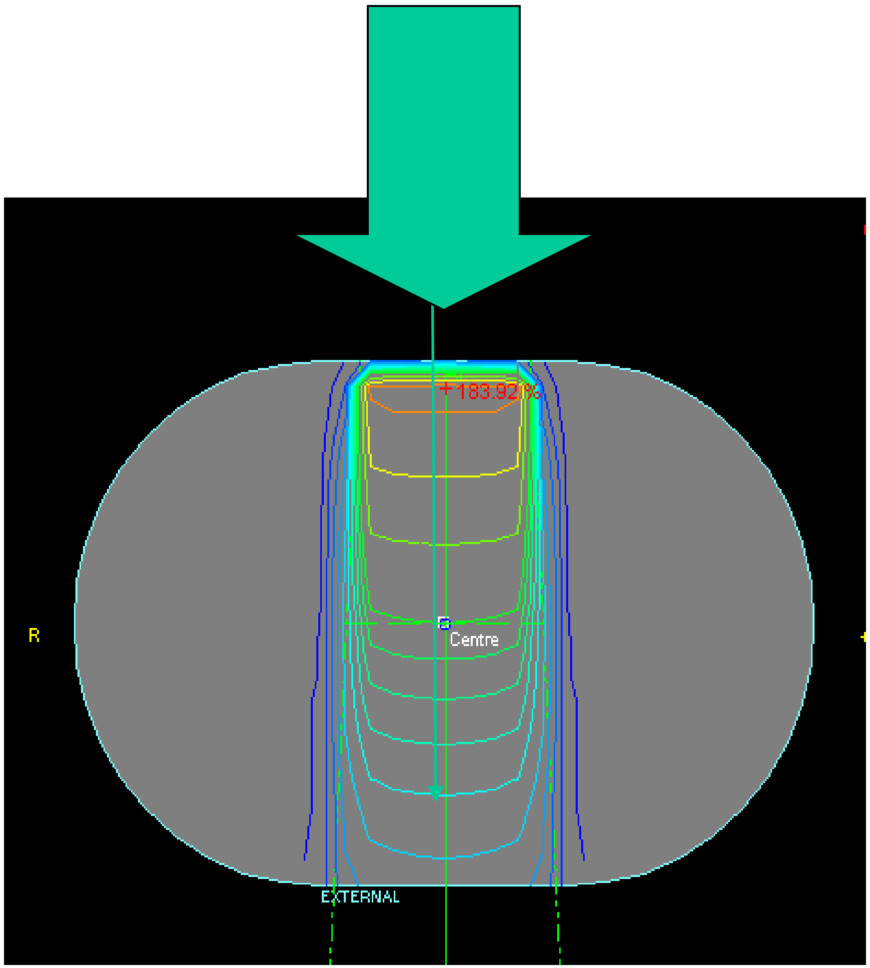
with High Energy X-rays or Electron Beams

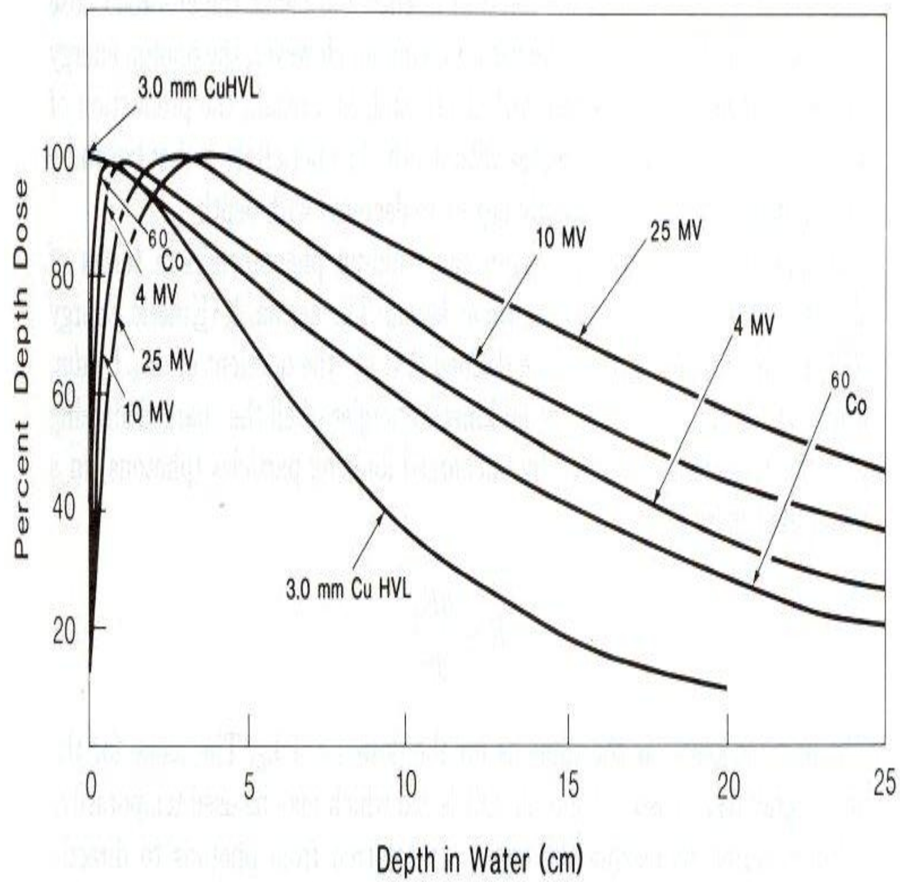


Courtesy of Varian

Single Photon Field (X-rays)

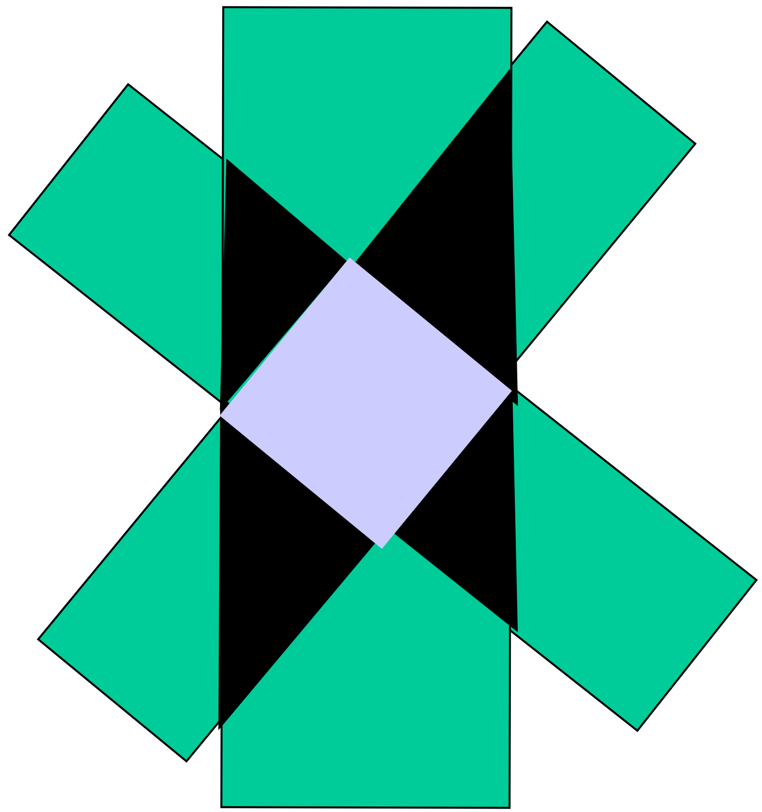
Depth-Dose Curves



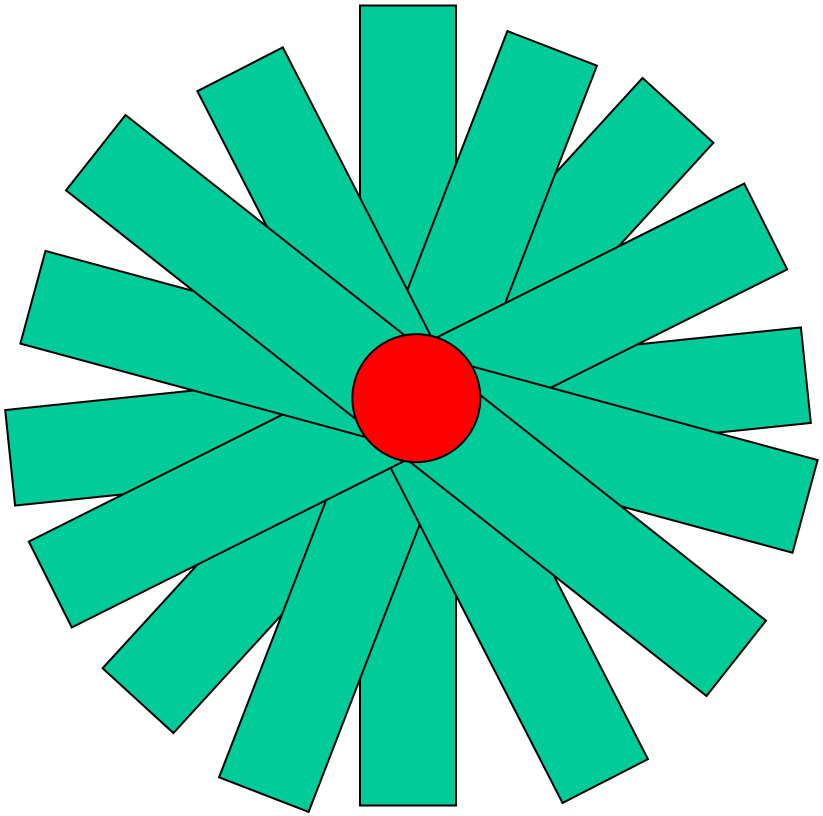


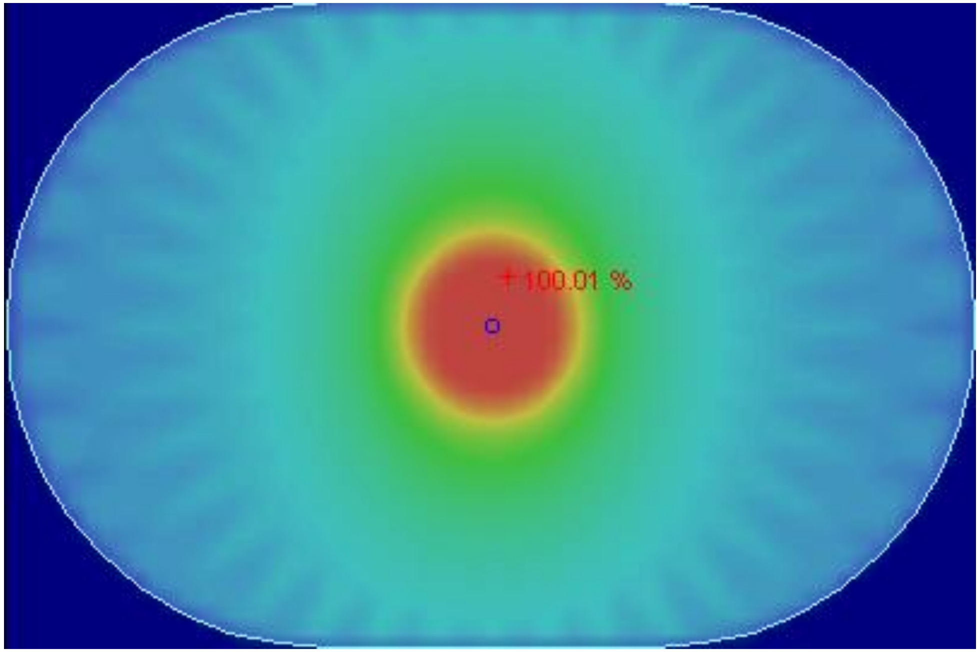
F. Khan

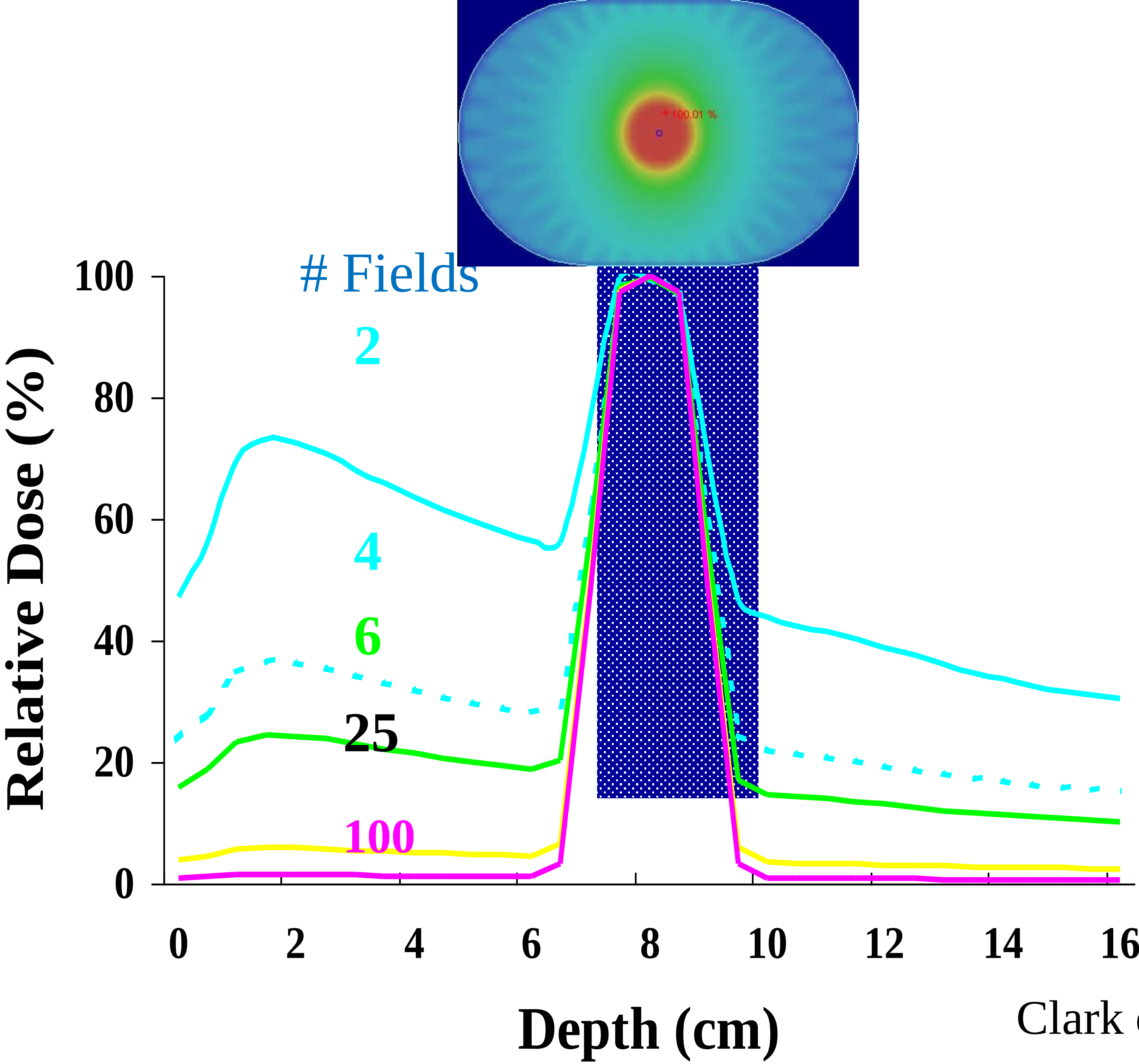
Superposition Principle



“Arc Therapy”





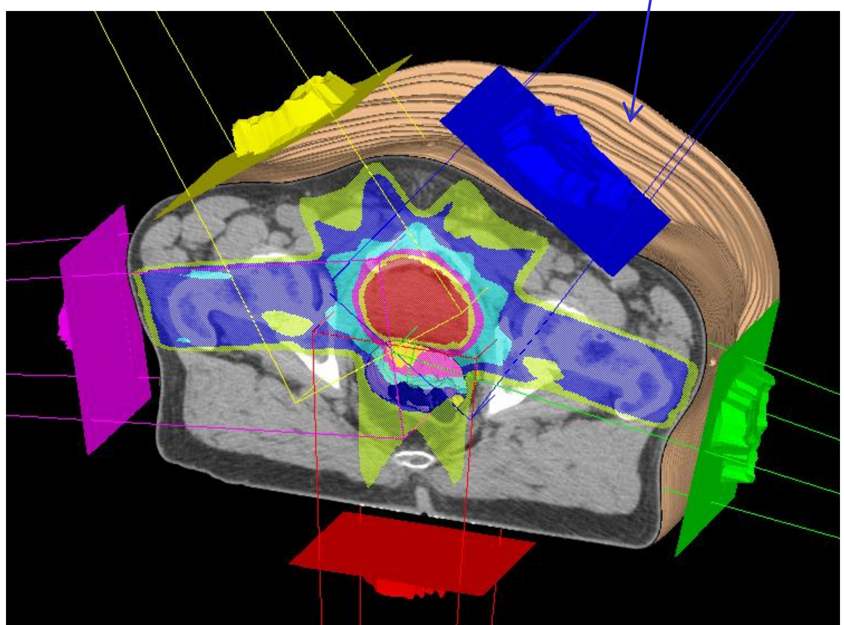


Fields
2
4
6
25
100
100
80
60
40
20
0
Relative Dose (%)
0
2
4
6
8
10
12
14
16
Depth (cm)

Clark et al

Intensity-Modulated Radiotherapy (IMRT)

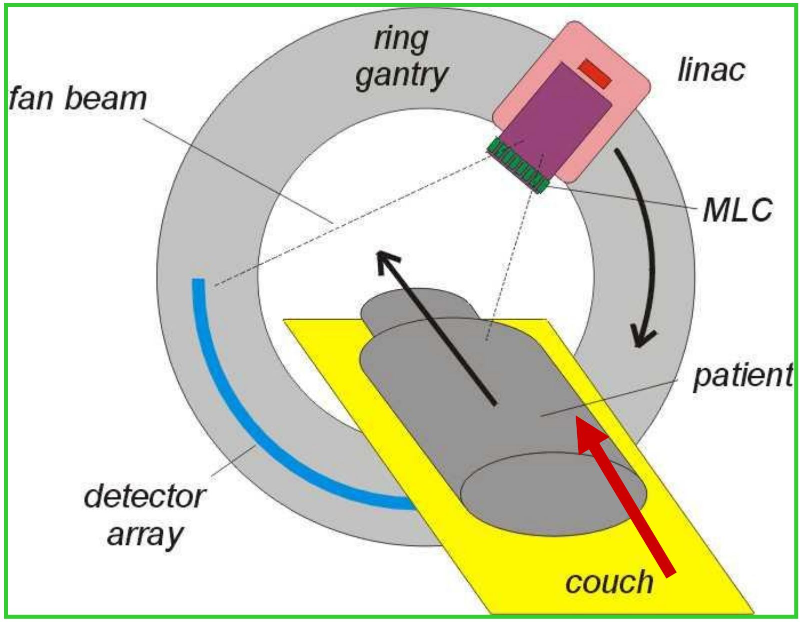
- The intensity pattern is non-uniform within each radiation field
- Produces more concentrated shaped dose distribution in body



http://www.aoctr.com/Services.html

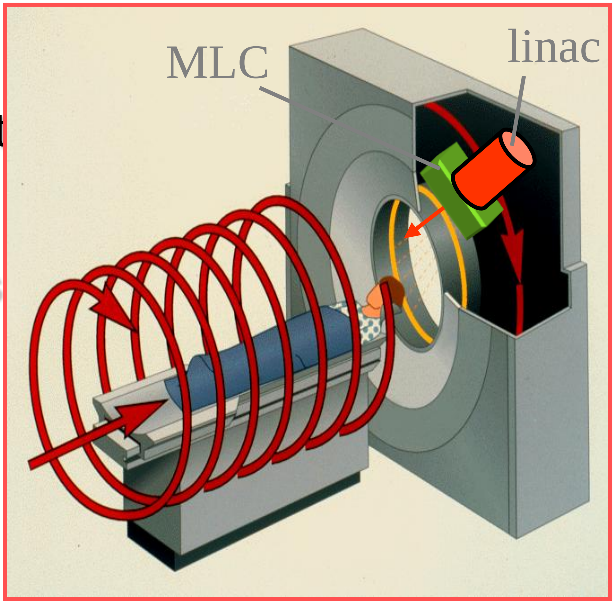

TomoTherapy
HI·ART
CAUTION

Helical Tomotherapy



Helical Delivery using continuous couch movement and gantry rotation.

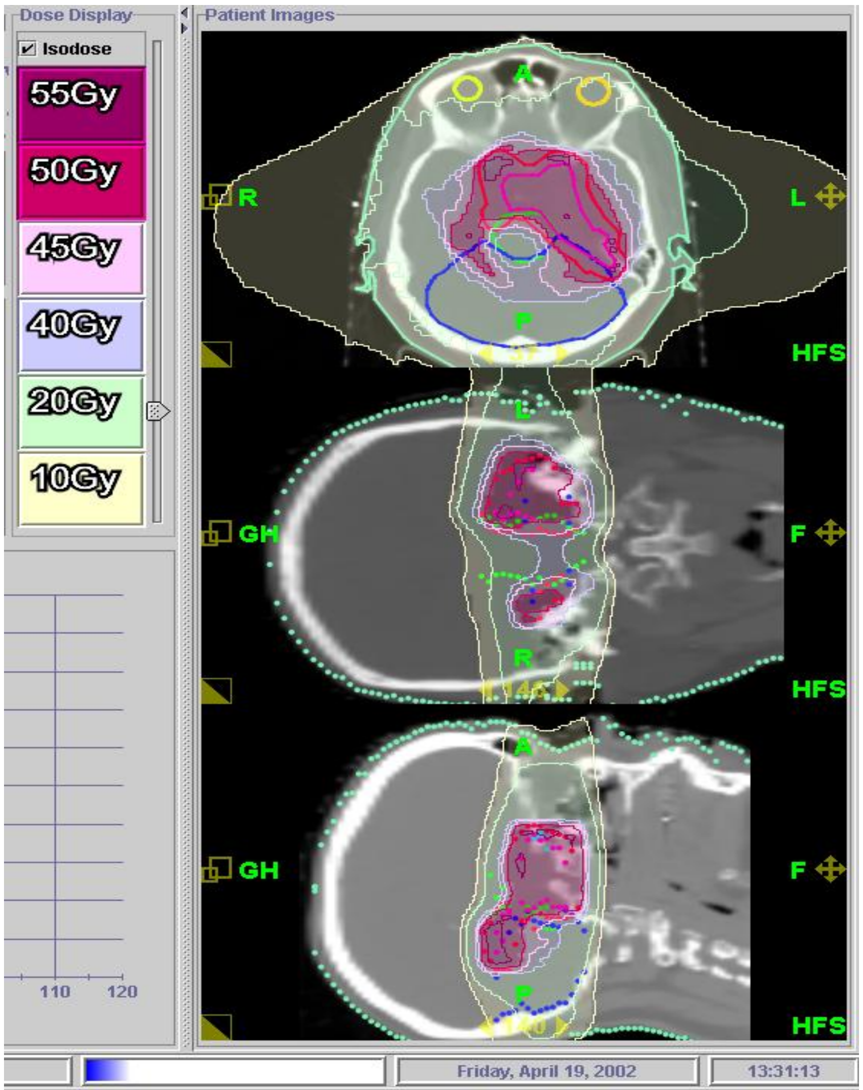
51 angular beam projections per rotation, each with 64 beamlets of different intensity



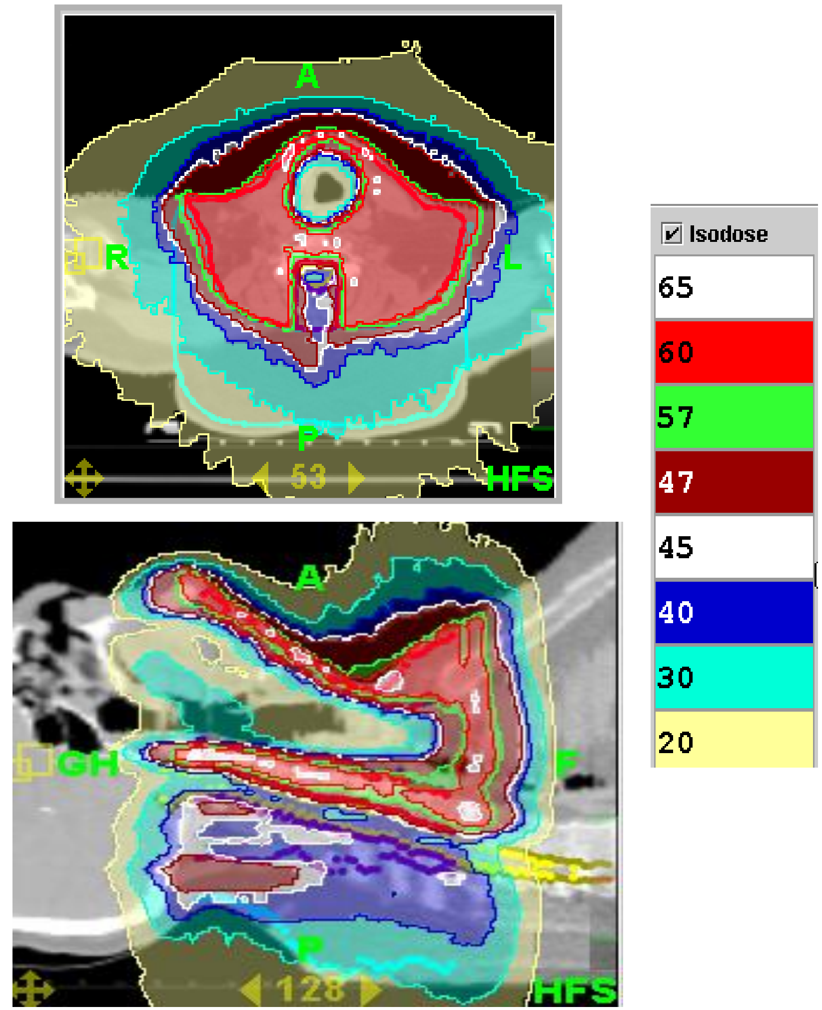
London Regional Cancer Program
LONDON HEALTH SCIENCES CENTRE

Photon Dose Sculptures

Head & Neck Case

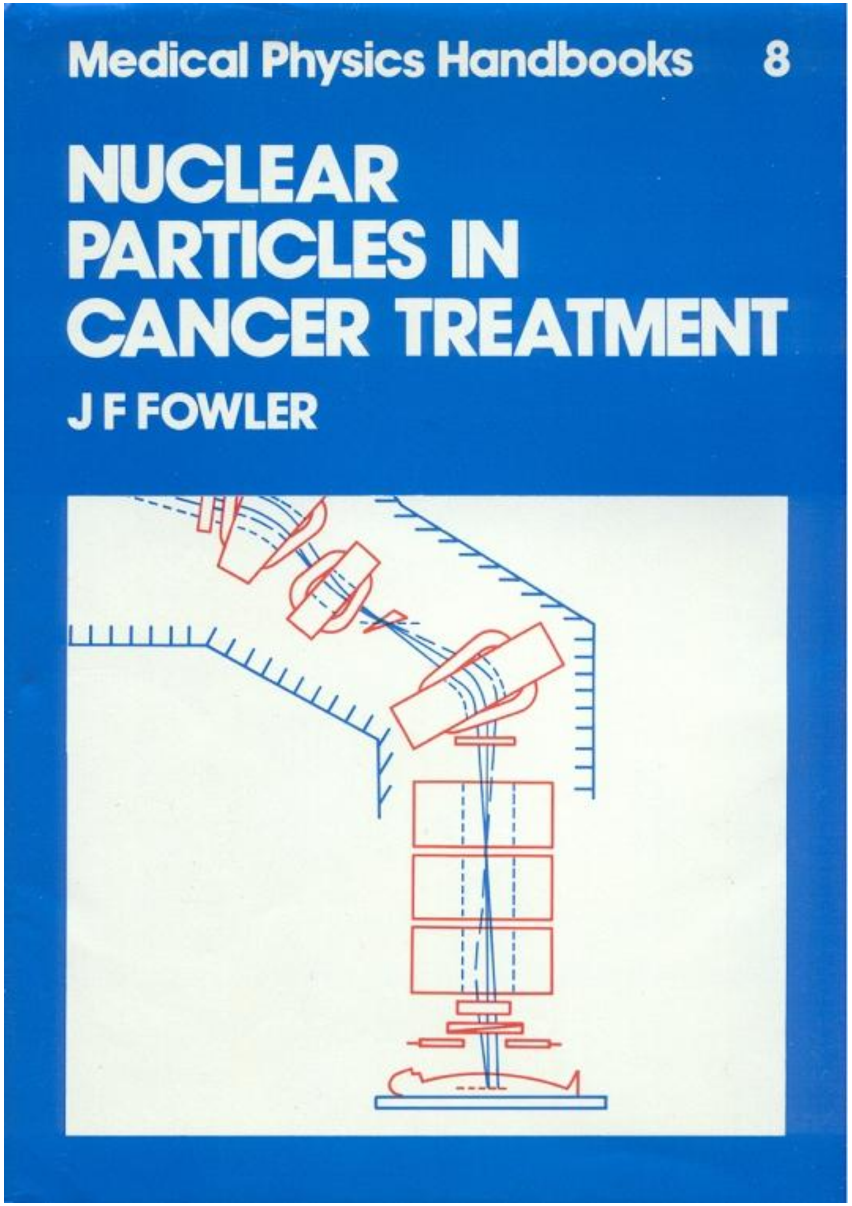


Thyroid Case

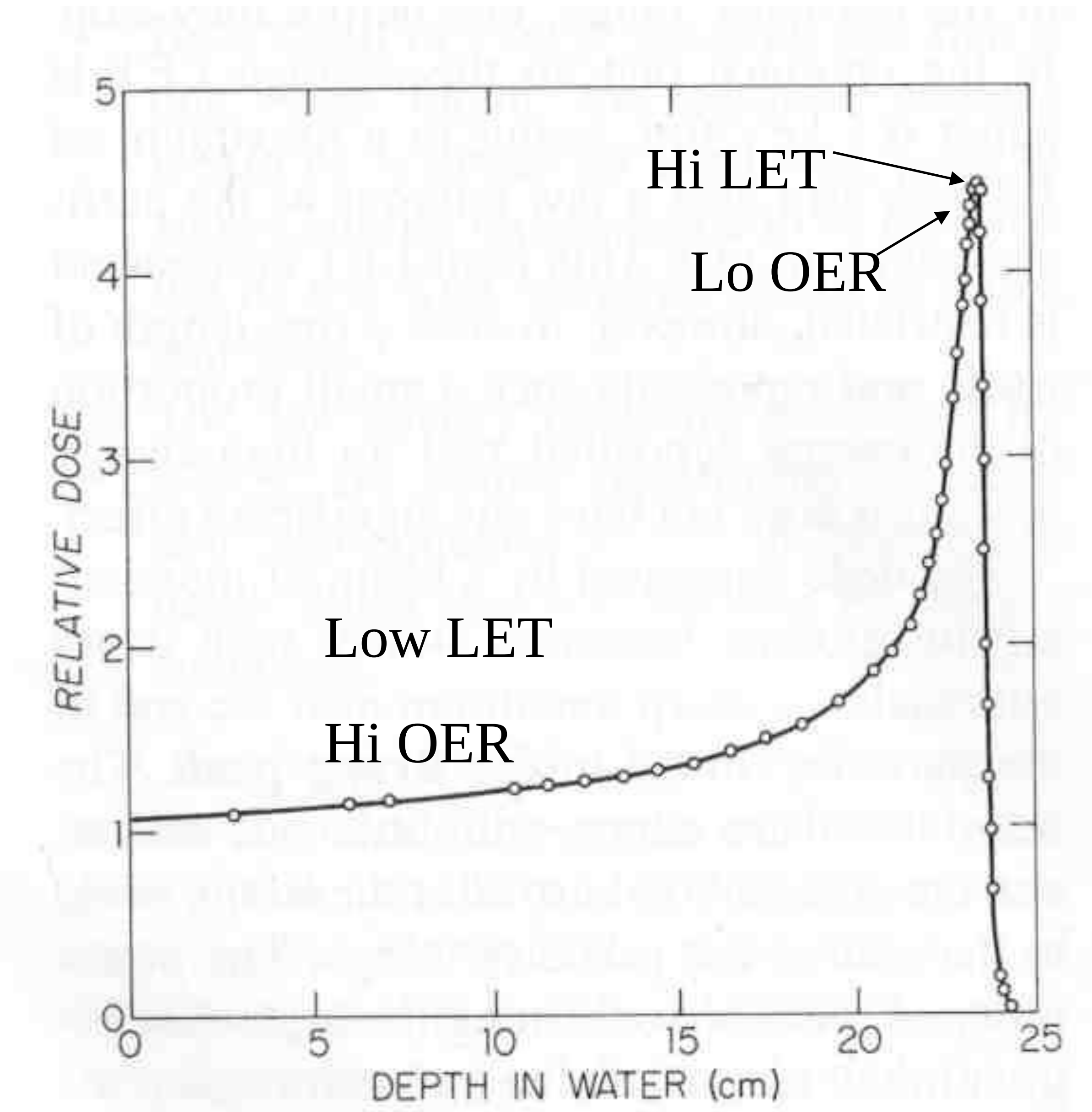


Tomotherapy - Kron, Yartsev et al.

Are there Better Radiation Bullets ?

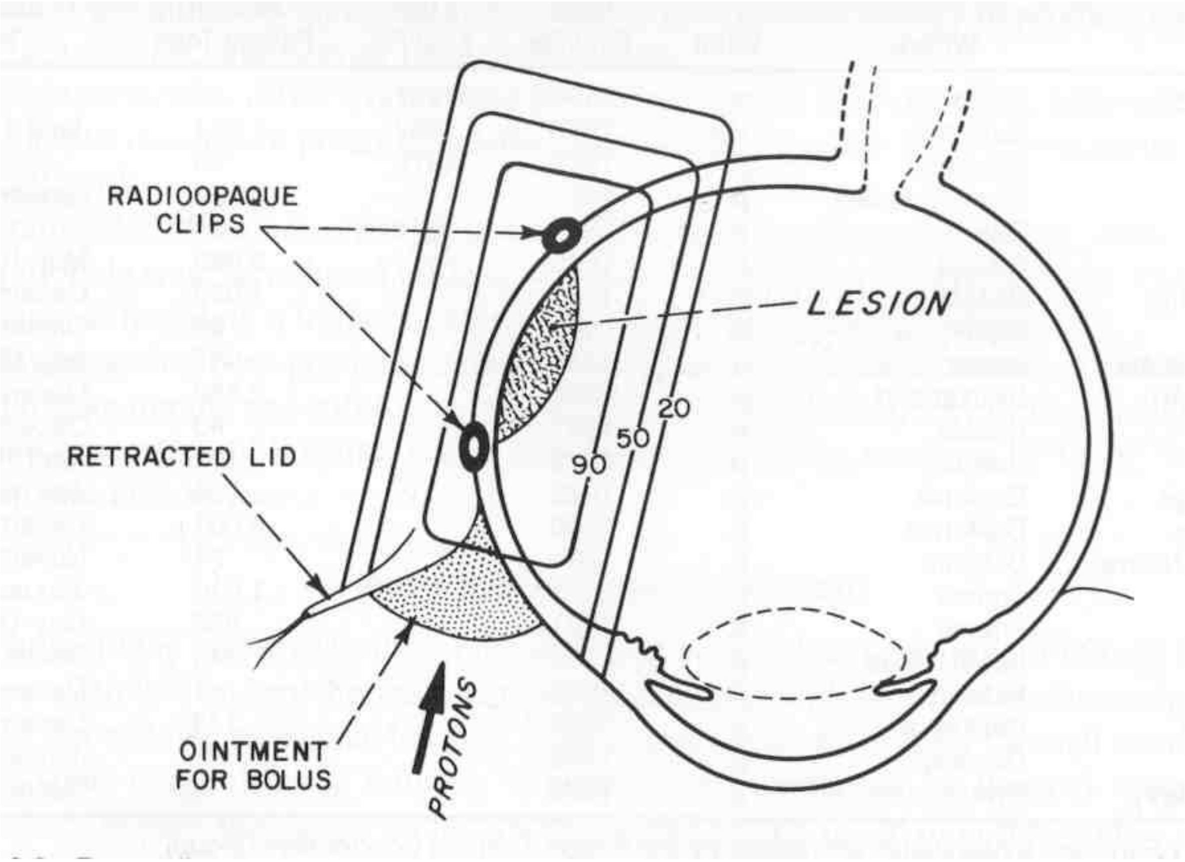


Ideal Single Beam



Protons –

Treating small tumours at the back of the eye



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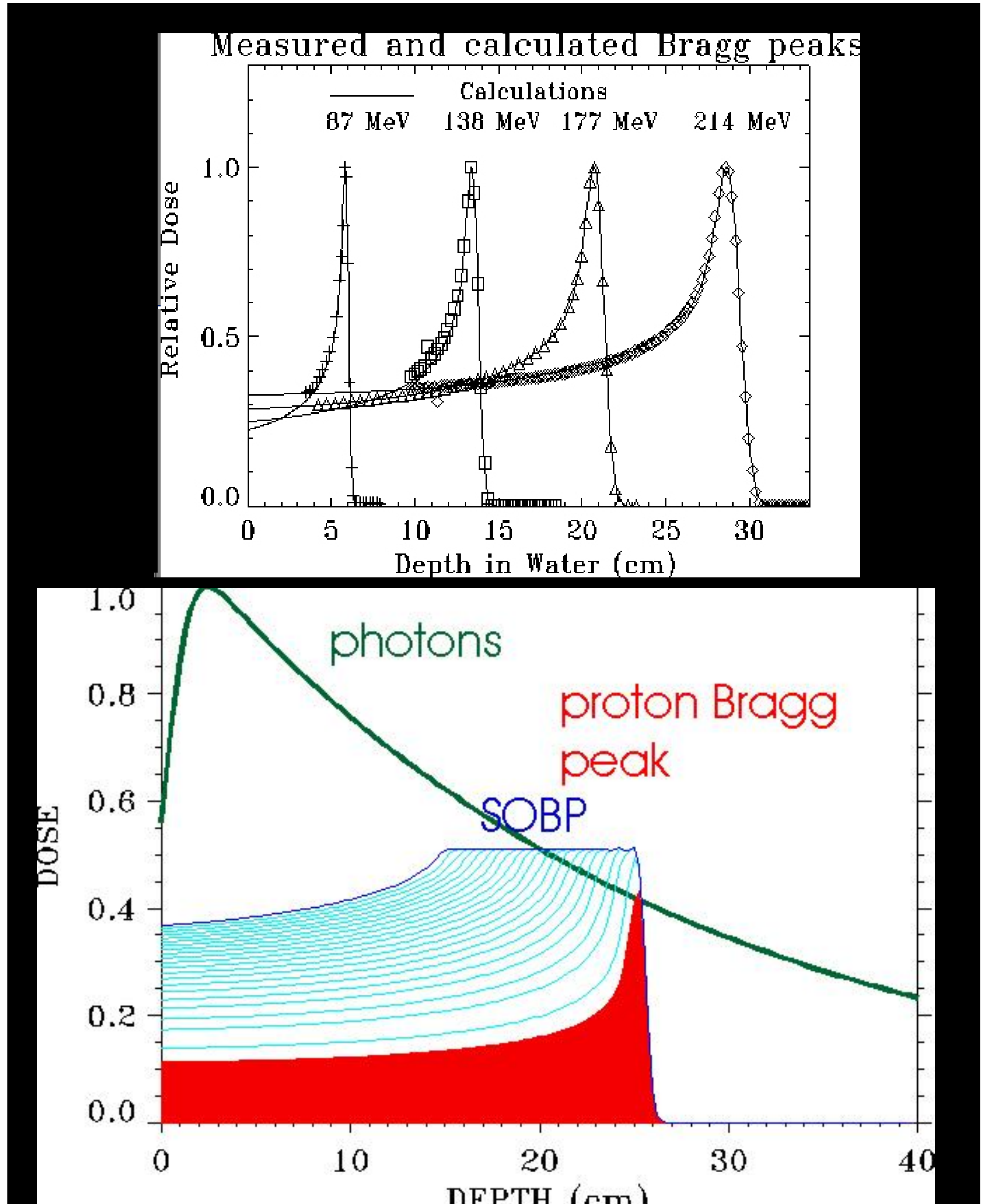
PSI

Protons

Spread Out Bragg Peak (SOBP) is obtained through the weighted superposition of proton beams of different energies



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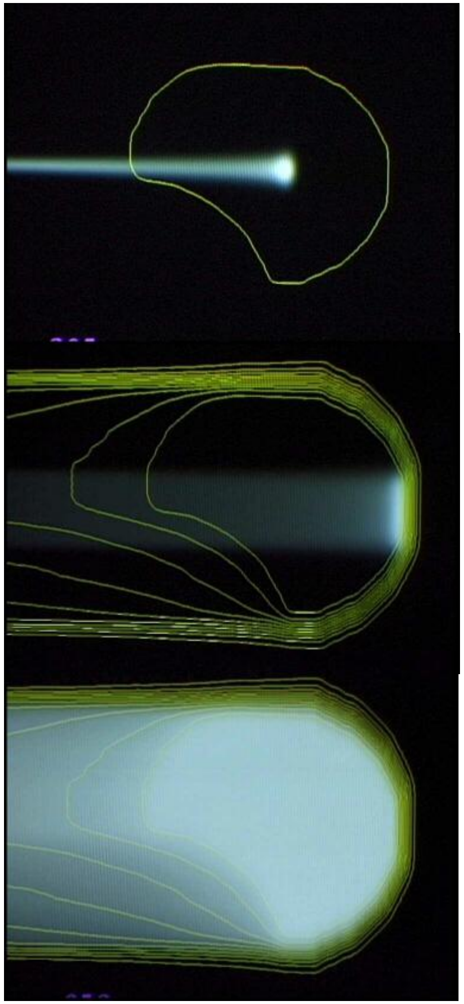
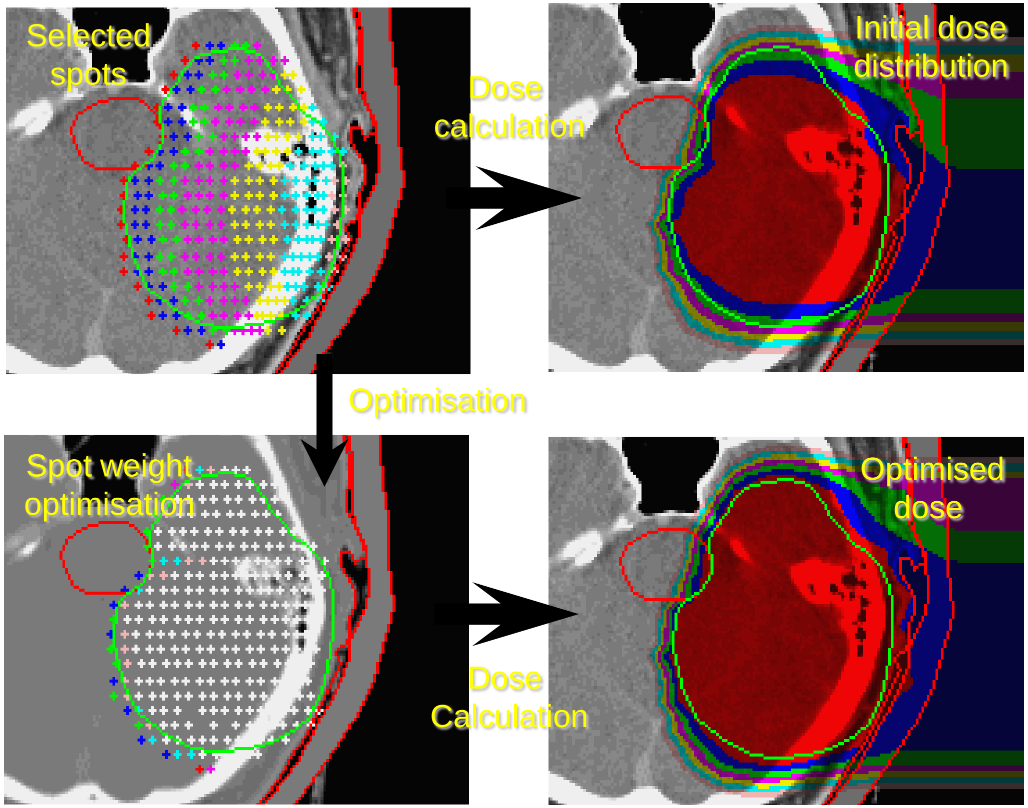
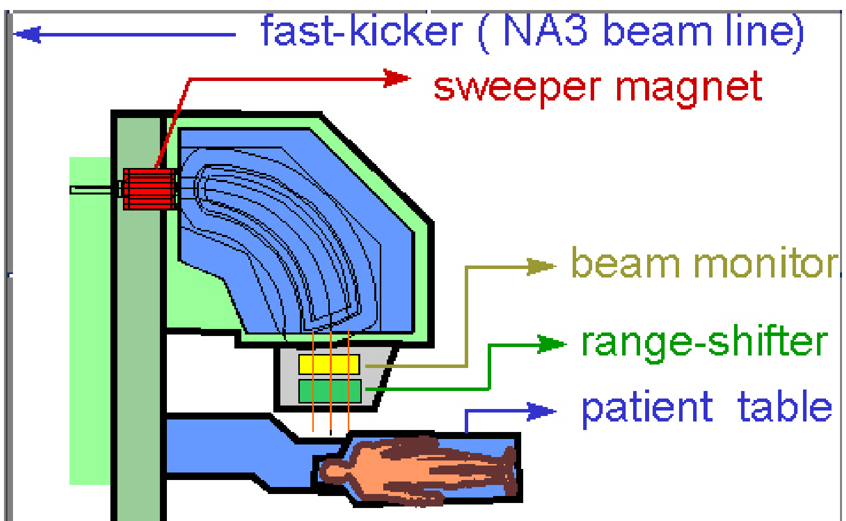
Spot scanning proton (SSP) technique

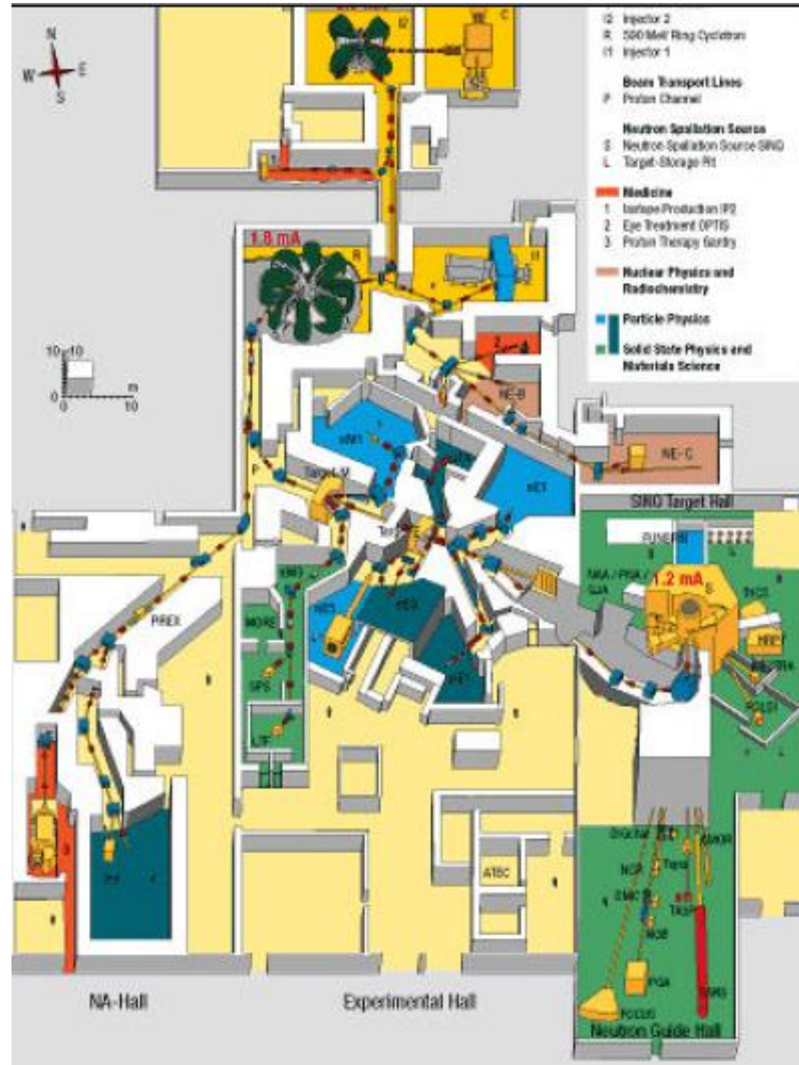




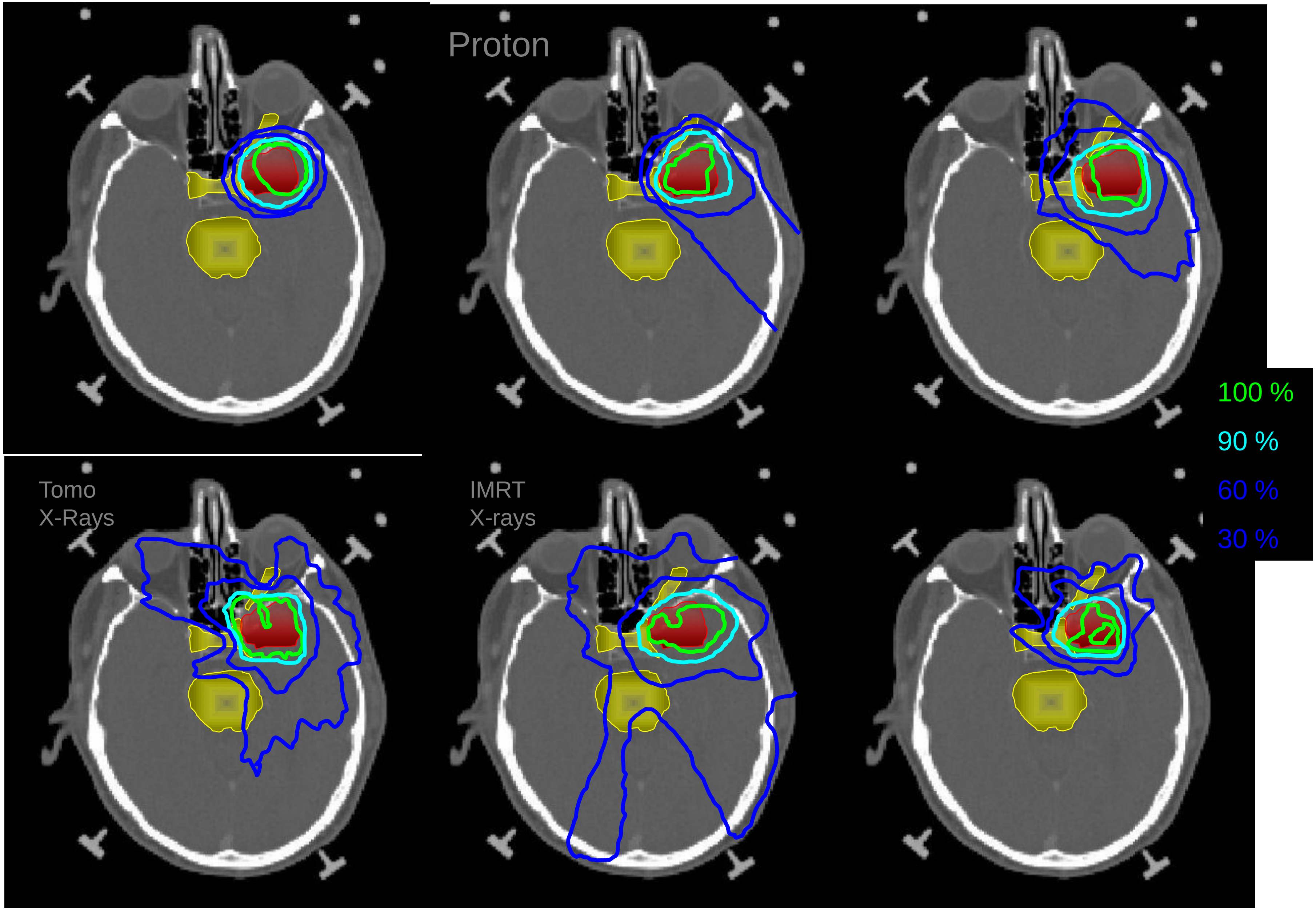
©L. Cozzi,

PAUL SCHERRER INSTITUT



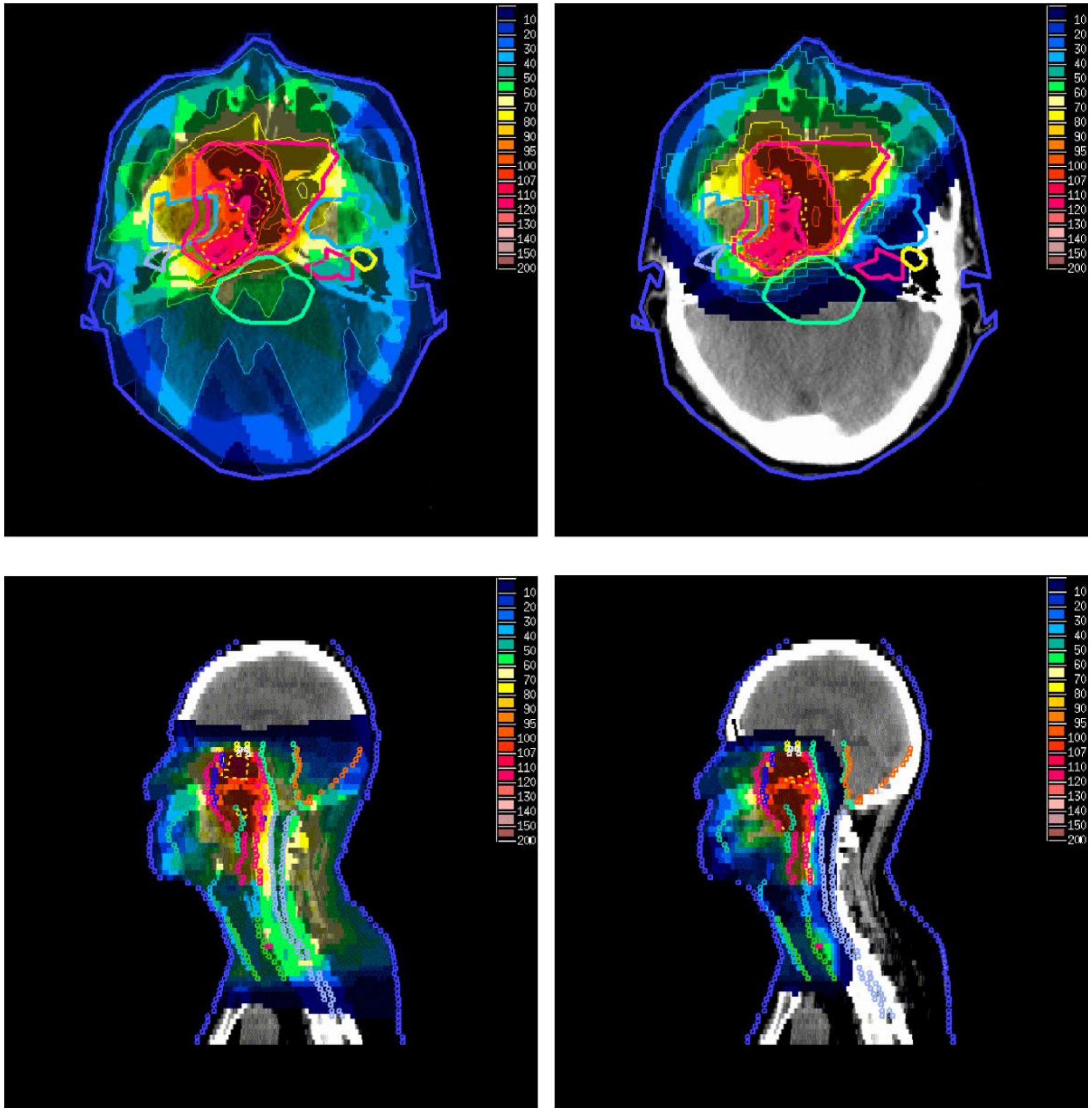


Photons or Protons ?



L. Cozzi et al.

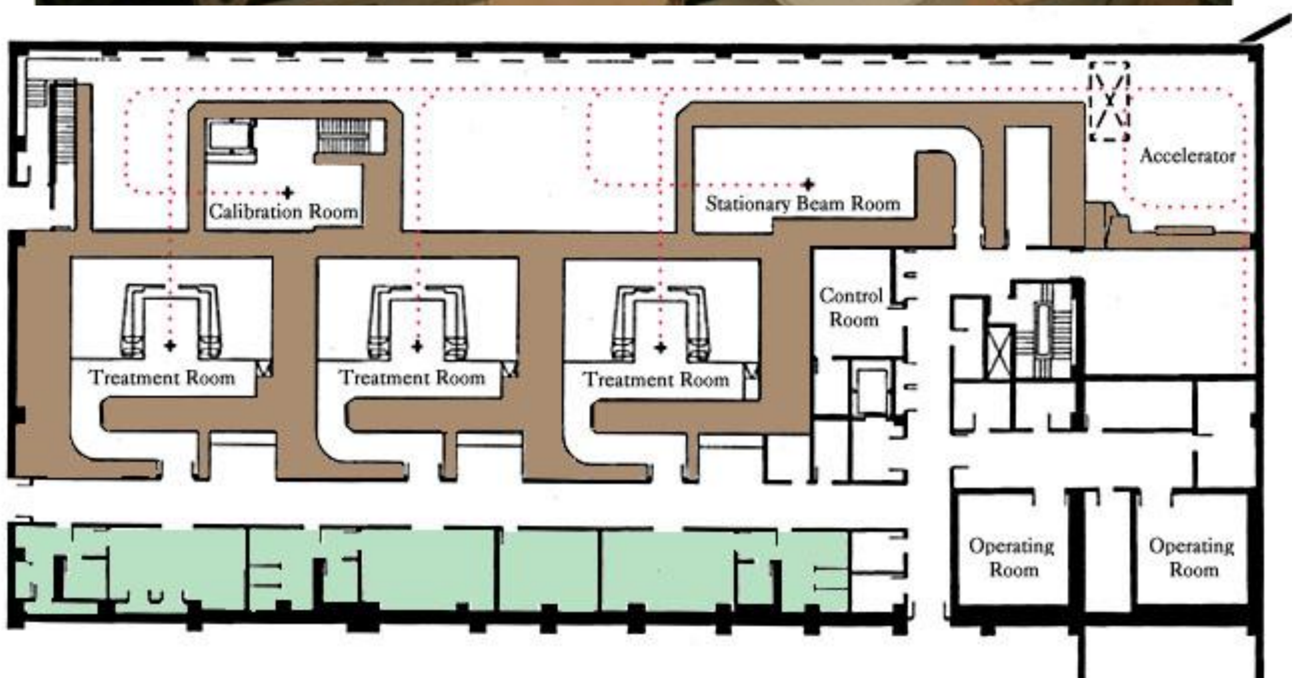
x-rays Protons



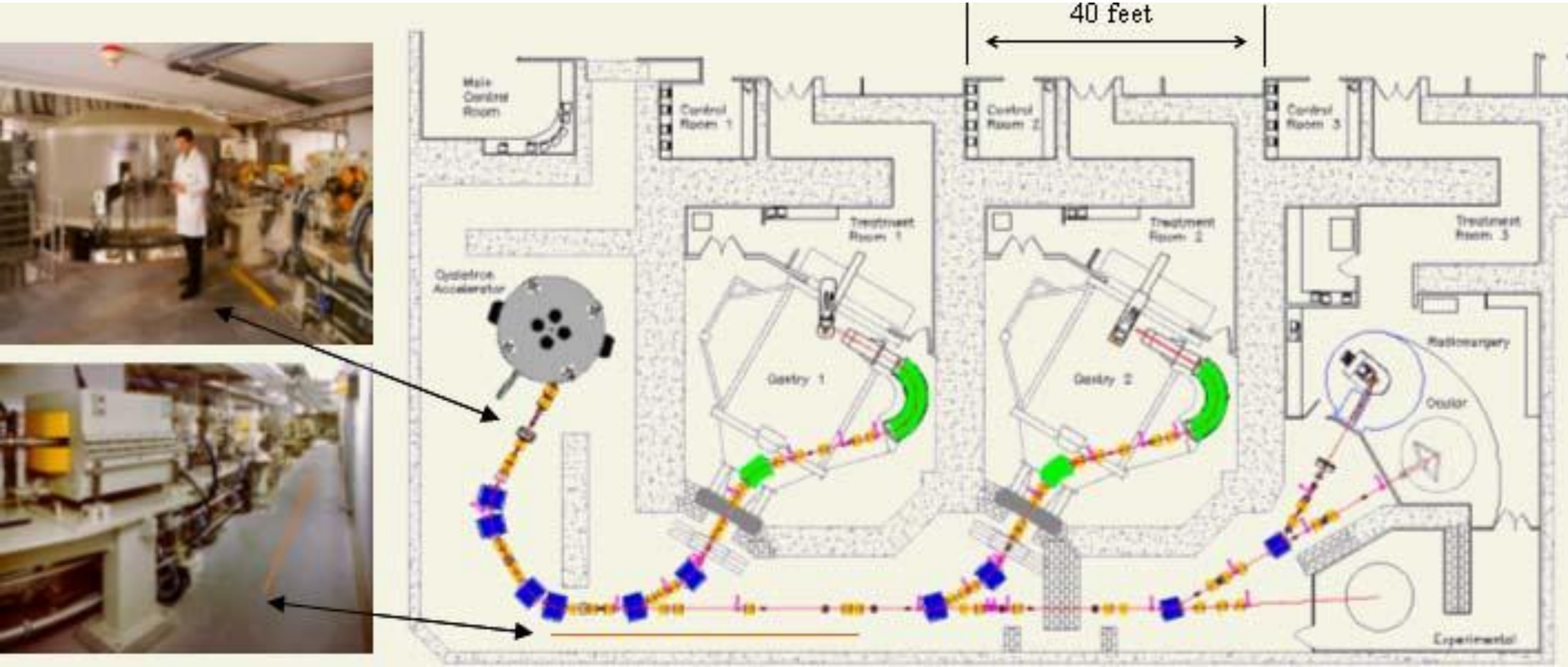
Less “bath” of unwanted radiation may reduce incidence of radiation-induced secondary tumours

http://en.wikipedia.org/wiki/File:Comparison_of_dose_distributions_between_IMPT_(right)_and_IMRT_(left).jpg

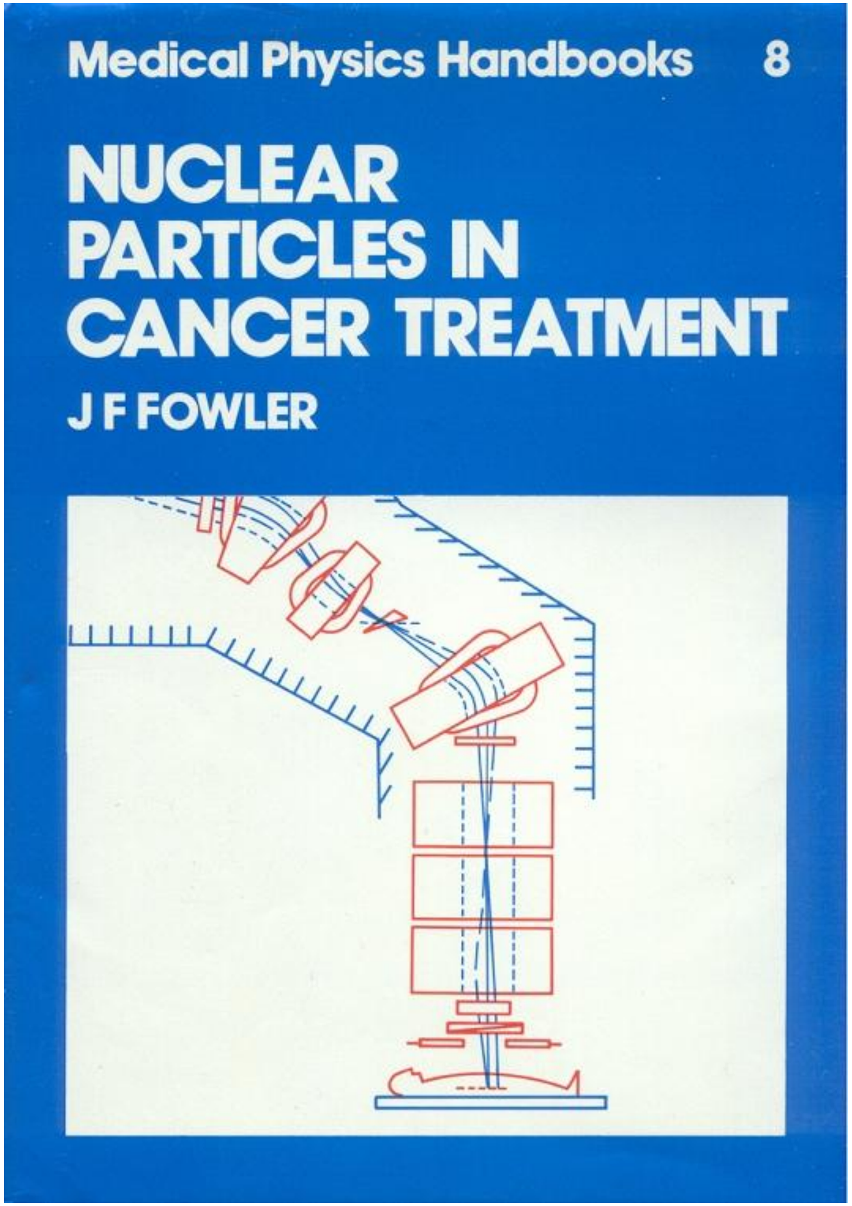
Loma Linda Proton Facility



MASSACHUSETTS GENERAL HOSPITAL
CANCER CENTER™



Layout of the Francis H. Burr Proton Therapy Center treatment level showing the FDA approved radiation delivery system, which includes a cyclotron (upper left insert) and an array of over 50 magnets, each weighing between 1,000 and 5,000 pounds (highlighted in orange, blue and green). Protons can be delivered sequentially to any of the 3 treatment rooms by bending the beam using the magnets.
Radiation is isolated to individual treatment rooms with 6 feet thick concrete walls.



Consumer's Report

A - Depth Dose Curve

B - LET increasing with depth

C - OER decreasing with depth

Particle Menu

PARTICLES FOR RADIOTHERAPY

A. Physical Aspects

PARTICLE	RELATIVE MASS	RELATIVE CHARGE	SOURCE	DOSE RATE (rad/min.)	ENERGY (MeV)	RANGE IN WATER (cm)
X-γ ray (x-γ)	0	0	isotopes, linacs	200	25MV	22(50%)
electron (β)	1	-1	linac, betatron	200	25	13
π- meson (pion)	273	-1	LAMPF	12	85	18
neutron (n)	1839	0	TAMVEC	80	(50 ($^2_1$H))	14(50%)
proton (p)	1836	+1	Harvard cyclotron	100	160	16
helium ion (α)	7350	+2	Berkeley cyclotron	100	230/nucleon	27
carbon ion (C)	22050	+6	Bevatron	300	400/nucleon	25
neon ion (Ne)	36750	+10	Bevalac	200	500/nucleon	15
argon ion (A)	66150	+18	Bevalac	100	500/nucleon	13

PARTICLES FOR RADIOTHERAPY

B. Biological Aspects

PARTICLE	RELATIVE BIOLOGICAL EFFECT			OXYGEN ENHANCEMENT RATIO	
	Plateau	Peak	Gain Ratio	no sensitizer	with sensitizer
X (220 KV)	1.0	1.0	1.0	2.8	1.3
γ (1.3 MeV)	0.8	0.8	1.0		
e	0.7	0.7	1.0		
π-	0.9	1.1	1.2	2.2	?
n	1.9	1.9	1.0	2.0	?
p	1.0	1.0	1.0	2.9	?
α	1.0	1.2	1.2	2.4	1.3
C	1.0	1.5	1.5	1.7	1.2
Ne	1.9	2.3	1.2	1.6	1.1
A	2.0	2.0	1.0	1.4	1.3

PARTICLES FOR RADIOTHERAPY

C. Over Appraisal

PARTICLE	DOSE LOCALIZATION	RBE GAIN	OER REDUCTION+	OVERALL++
X-γ	●	●	(●●●)	●● (●●●)
e	●●	●	(●●●)	●●● (●●●)
π-	●●	●●	●● (?)	●●● ●●● (?)
h	●	●	●● (?)	●●●● (?)
p	●●●	●	● (?)	●●●●● (?)
α	●●●	●●	● (●●)	●●●●●● (●●)
C	●●●	●●●	●●◐ (◐)	●●●●●●●●◐ (◐)
Ne	●●◐	●●	●●◐ (◐)	●●●●●●● (◐)
A	●●◐	●	●●◐ (◐)	●●●●●● (◐)

● Poor

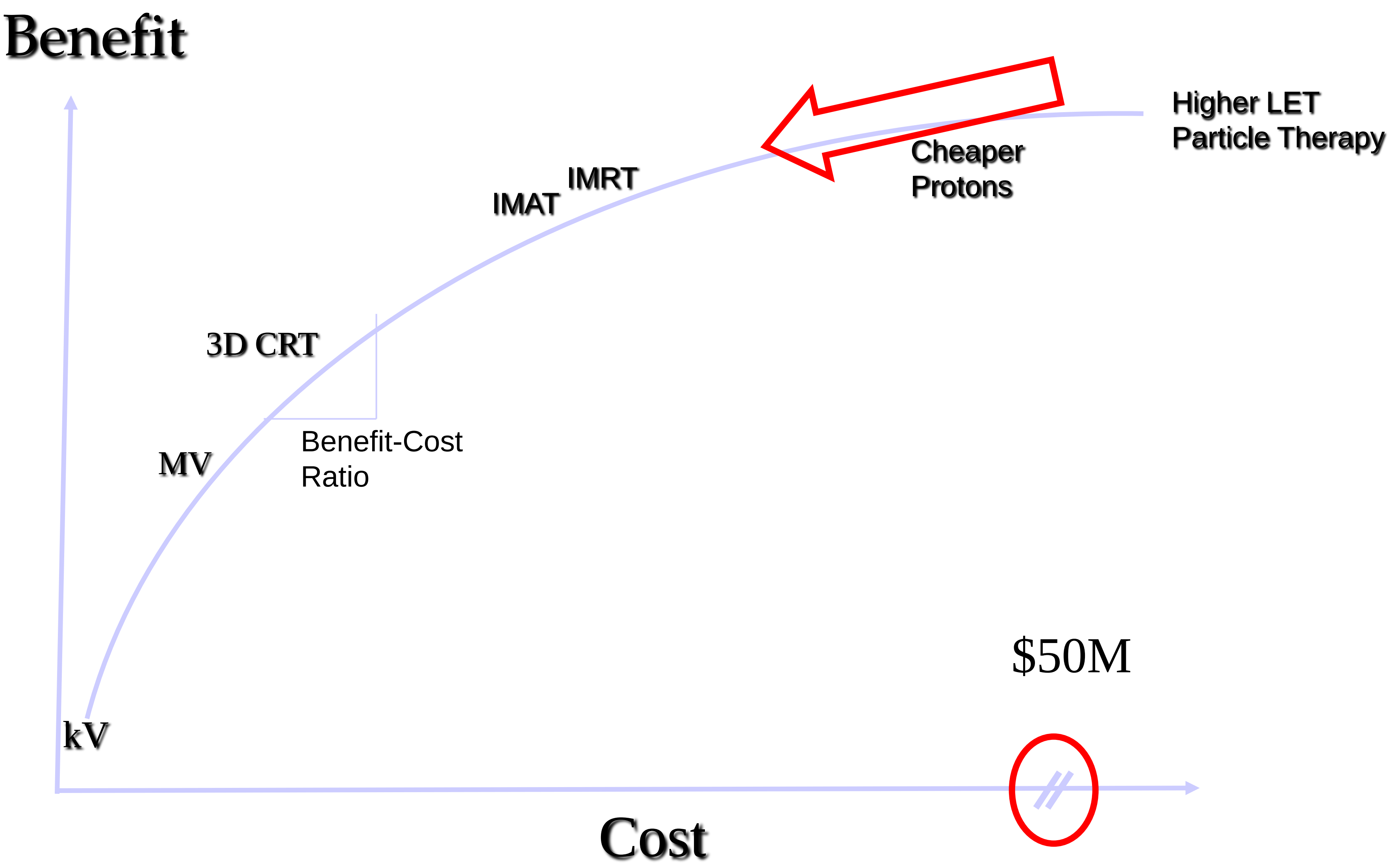
●● Good

●●● Excellent

+( ) With hypoxic cell sensitizer

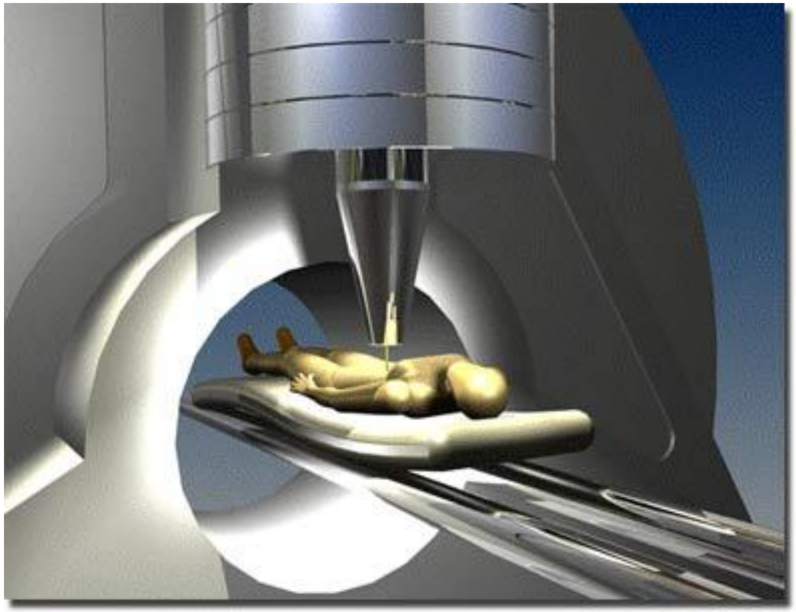
++ Assuming equal importance to each factor

Cost-Benefit Perspective



E. Wong, LRCP

TomoTherapy Inc.



Varian Proton Therapy
A milestone in cancer treatment

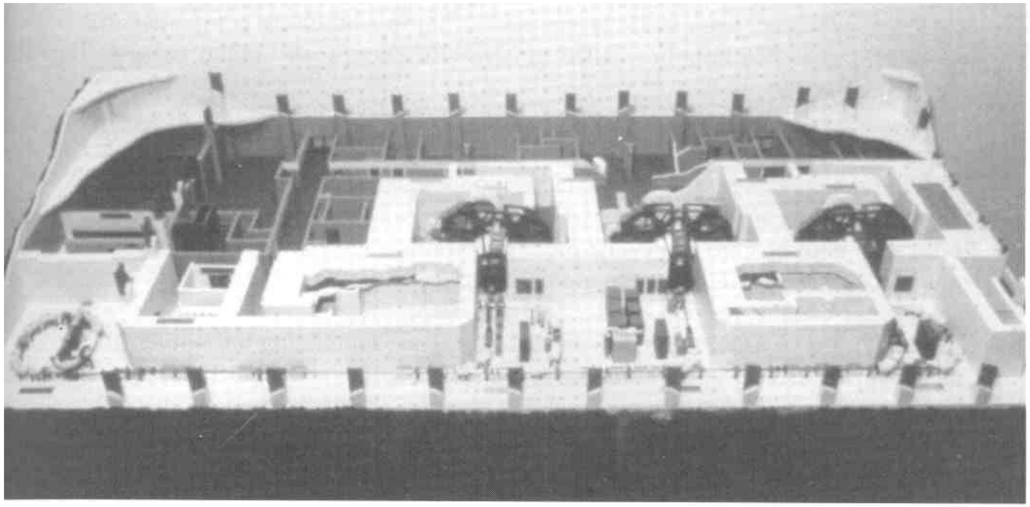
The first and only fully Varian-compatible system to deliver
a collaborative solution in Proton therapy.

Sep 9, 2008

MIT, ProTom team up on proton therapy

Researchers at MIT's Bates Linear Accelerator Center (Middleton, MA) are collaborating with ProTom International (Fort Worth, TX) to develop an advanced proton-therapy system for cancer treatment. ProTom holds the exclusive US rights for a next-generation synchrotron technology originating at the Lebedev Physics Institute in Russia.

http://medicalphysicweb.org/cws/article/industry/35751



Hi-LET Beams

Fewer Beams ? yes

Tiny Tumours ? yes

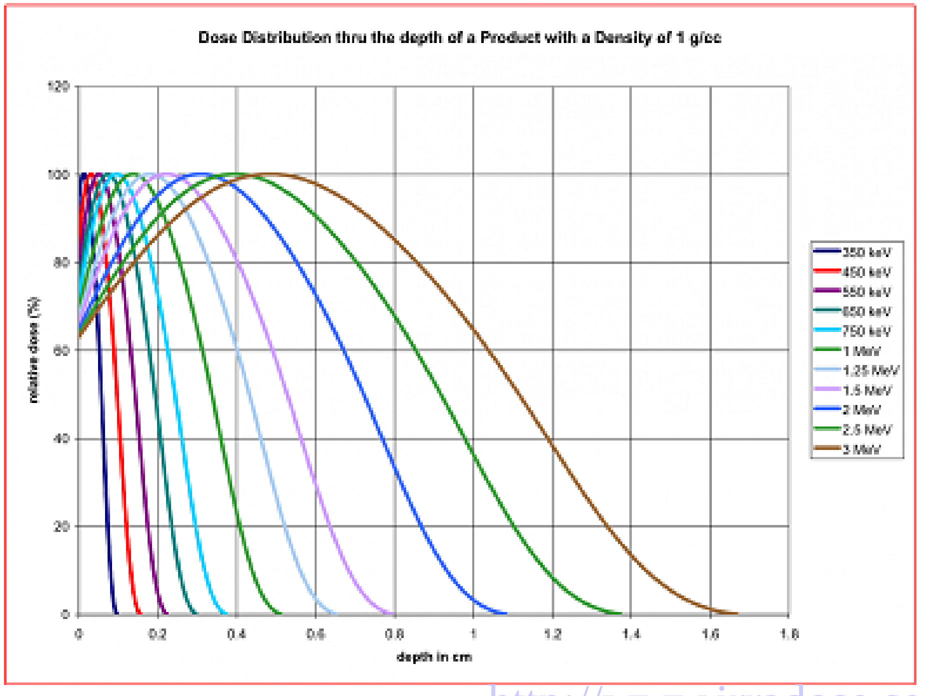
Treat Hypoxic Tumours ? maybe

Less Dose Spillage and 2^{nd} tumours ? maybe

Low Cost ? NOT YET

Recap of Lecture 2

- x-γ rays liberate fast <u>charged particles</u>
- these charged particles eventually slow down within a few mm's (imaging sources) or cm's (therapy sources) within tissue



http://www.irradose.se/index1_2_technical.htm

Recap of Lecture 2

- The radiobiological effect depends upon:
  - Absorbed Dose (energy deposited)
  - LET (pattern of energy deposition)
  - LET determines W_R (type of radiation)
  - Exposure environmental conditions

    e.g. Oxygen (OER)

Recap of Lecture 2

- x-γ ray beams offer more ‘range’ in tissue but with an exponential drop-off
  - overlapping beams are used to offset this limitation
  - intensity-modulated beams (IMRT) also help

- Hi-LET particle beams have less range and sharper drop off, often boosted with an accented “peak” at depth
  - great for eye lesions
  - fewer beams can be used compared with x-γ rays
  - BUT they are (still) very expensive (> 10 times)
  - Role for hypoxic tumours (drug-free)
  - Less probability of inducing a secondary tumour ?
  - **Are they proven clinically ?**