HEAVY PARTICLE RADIOTHERAPY

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jectives Of This Presentation

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Define particle therapy and its role in radiation therapy

To recapitulate the basic physics and radiobiology related to particle therapy

To understand the differences between conventional therapy and particle thera

Brief online of particle therapy delivery systems

mportance of understanding the uncertainties in particle therapy

To discuss the advances and benefits that particle therapy provides compared v
conventional photon radiation therapy

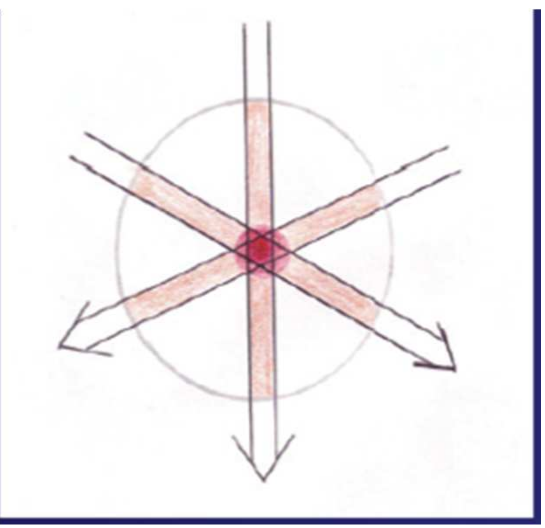
To compare protons vs carbon ion therapy

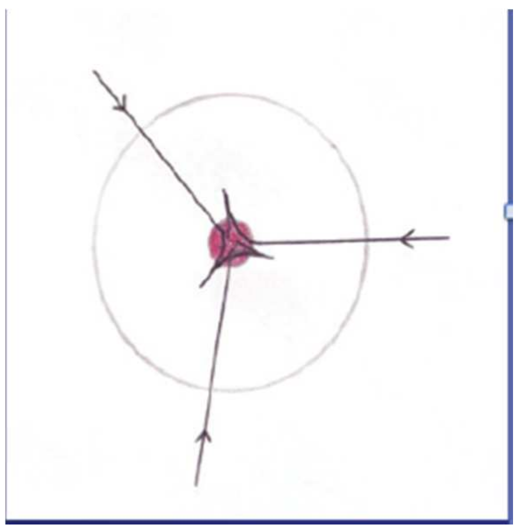
roduction

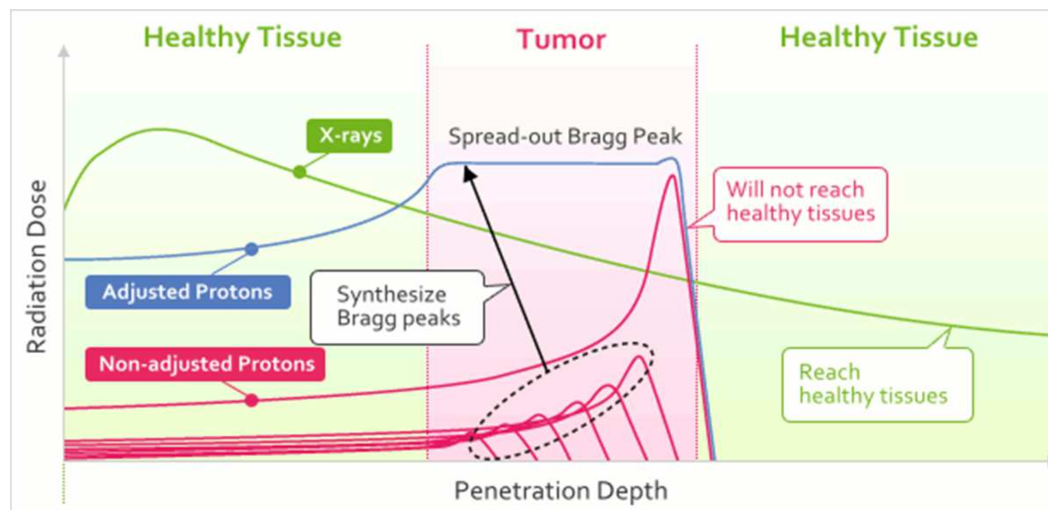
The goal of radiation therapy is to deliver as large a dose possible to cancer cel
while avoiding radiation to nearby normal cells

To achieve this, photon therapy requires multiple beams exposing normal tissu
high volumes of low doses of radiation: limitation of radiation dose escalation

Particle therapy has the ability to reduce the exposure of normal tissues beyond
targeted cells







roduction

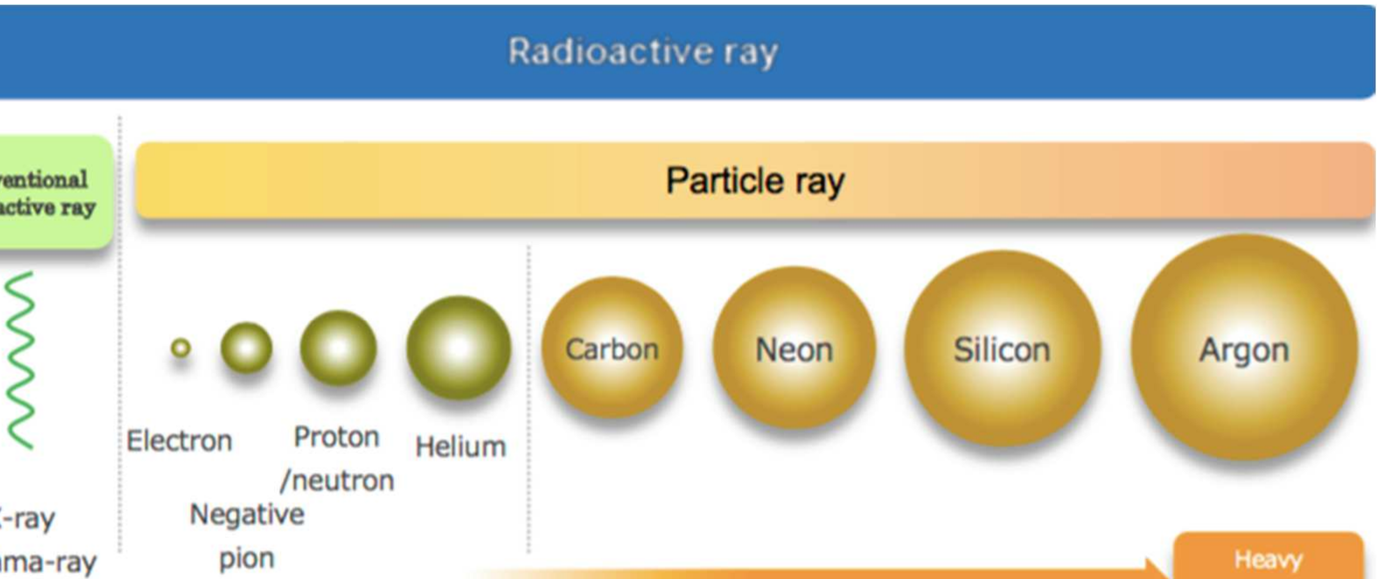
leavy ion therapy is a novel technique of high precision external radiotherapy.
t yields a better perspective for tumor cure of radio-resistant tumors

advantages of using heavy ion therapy are:

ligher tumor dose and improved sparing of normal tissue in the entrance chann
Лore precise concentration of the dose in the target volume with steeper gradie
o the normal tissue
ligher radiobiological effectiveness for tumors which are radio-resistant during
onventional therapy
hese properties make it possible to treat radio-resistant tumors with great succ
including those in close vicinity to critical organs

The term "heavy ions" is used here for ions heavier than helium ions. The prin
ationale for radiotherapy with heavy charged particles is the sharp increase of c
n a well-defined depth (Bragg peak) and the rapid dose fall-off beyond that
naximum

eavy Particle Radiotherapy



avy ion beams are defined as radiation that is obtained by accelerating charged nuclei heavier than protons.

ong various types of ion beams, carbon ion beams in particular are used for cancer therapy

maximum energy can be spread out, making it possible for a single beam to cover the target three dimensio

y are considered to have the most balanced, ideal properties due to their potential ability of selective irradiatio nsive killing effects on cancers

...ONS matter constituents
spin = 1/2, 3/2, 5/2, ...

...n =1/2

...2	Electric charge
...$^{-9}$	0
...1	−1
...10^{-9}	0
	−1
...0^{-9}	0
	−1

Quarks spin =1/2

Flavor	Approx. Mass GeV/c^2	Electric charge
u up	0.002	2/3
d down	0.005	−1/3
c charm	1.3	2/3
s strange	0.1	−1/3
t top	173	2/3
b bottom	4.2	−1/3

...graph below.

...ntum of particles. Spin is given in units of ħ, which is the quantum ... = h/2π = 6.58×10^{-25} GeV s =1.05×10^{-34} J s.

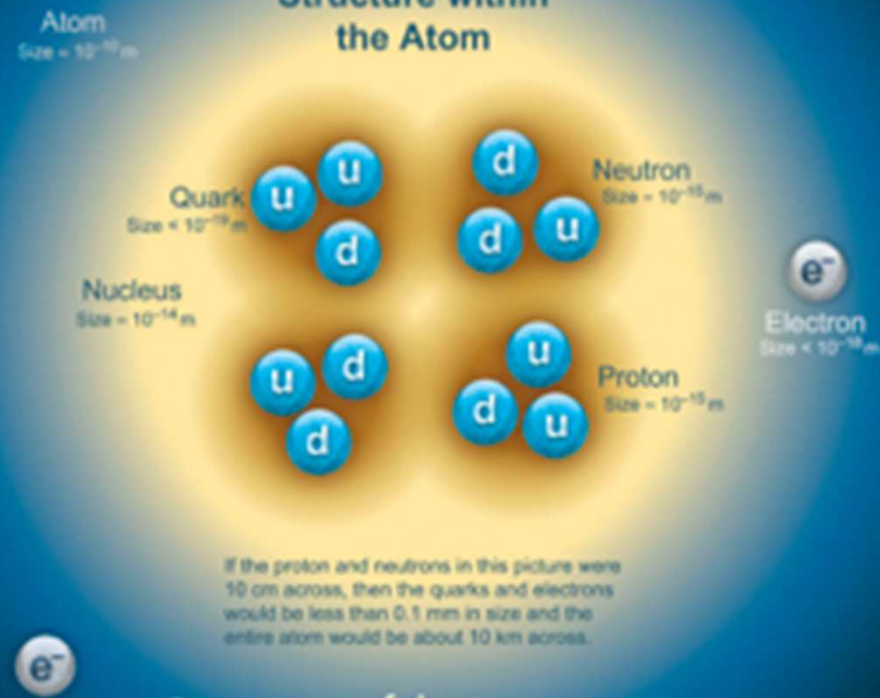
... of the proton's charge. In SI units the electric charge of the proton

...s is the electronvolt (eV), the energy gained by one electron in ...e volt. **Masses** are given in GeV/c^2 (remember $E = mc^2$) ...^{0} joule. The mass of the proton is 0.938

...supernovae, reactors, accelerator ...s. Any produced neutrino can be ...flavor states ν_e, ν_μ, or ν_τ, labelled by the ...with its production. Each is a defined ...e-mass neutrinos ν_L, ν_M, and ν_H for ...s are shown in the table. Further ...rinos may yield powerful clues to puzzles ... evolution of stars and galaxy structures.

...rresponding antiparticle type, denoted by ...ss + or − charge is shown). Particle and ... spin but opposite charges. Some ... γ, and $\eta_c = c\bar{c}$ but not $K^0 = d\bar{s}$) are their

Structure within the Atom



If the proton and neutrons in this picture were 10 cm across, then the quarks and electrons would be less than 0.1 mm in size and the entire atom would be about 10 km across.

BOSONS

force ca... spin = 0, ...

Unified Electroweak spin = 1

Name	Mass GeV/c^2	Electric charge
γ photon	0	0
W⁻	80.39	−1
W⁺ W bosons	80.39	+1
Z^0 Z boson	91.188	0

Strong...

Name...
g gluon

Higgs...

Name...
H Higgs

Higgs Boson

The Higgs boson is a critical component of the Standard Mod... mechanism by which fundamental particles get mass.

Color Charge

Only quarks and gluons carry "strong charge" (also called "co... interactions. Each quark carries three types of color charge. T... with the colors of visible light. Just as electrically-charged par... in strong interactions, color-charged particles interact by exch...

Quarks Confined in Mesons and Baryons

Quarks and gluons cannot be isolated ... particles called **hadrons**. This confine... exchanges of gluons among the color-... color-charged particles (quarks and gl... color-force field between them increas... converted into additional quark-antiqu... then combine into hadrons; these are t...

Two types of hadrons have been obse... **baryons** qqq. Among the many types ... (uud), antiproton ($\bar{u}\bar{u}\bar{d}$), and neutron (u... way as to make the proton have charg... the many types of mesons are the pio...

Learn more at ParticleAd...

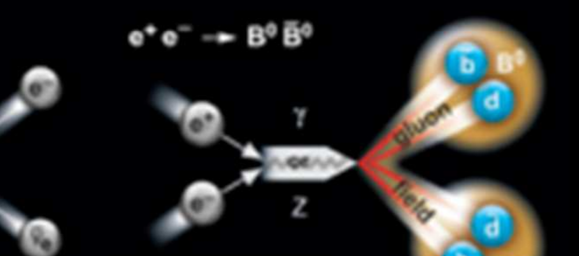
Properties of the Interactions

The strengths of the interactions (forces) are shown relative to the strength of the electromagnetic force for two u quarks separated by the specified distances.

Property	Gravitational Interaction	Weak Interaction (Electroweak)	Electromagnetic Interaction	Strong Interaction
Acts on:	Mass – Energy	Flavor	Electric Charge	Color Charge
Particles experiencing:	All	Quarks, Leptons	Electrically Charged	Quarks, Gluons
Particles mediating:	Graviton (not yet observed)	W⁺ W⁻ Z^0	γ	Gluons
Strength at 10^{-18} m	10^{-41}	0.8	1	25
Strength at 3×10^{-17} m	10^{-41}	10^{-4}	1	60

...Particle Processes

...nception. Orange shaded areas represent the cloud of gluons.



...s proton

An electron and positron (antielectron) colliding at high...

Unsolved Mysteries

Driven by new puzzles in our understanding of the physical world, particle physicists are following paths to new wonders and st... discoveries. Experiments may even find extra dimensions of space, microscopic black holes, and/or evidence of string th...

Why is the Universe Accelerating?

The expansion of the universe appears to be accelerating. Is this due to Einstein's Cosmo...

Why No Antimatter?

Matter and antimatter were created in the Big Bang. Why do we now see only matter except

What is Dark Matter?

Invisible forms of matter make up much of the mass observed in galaxies and clusters of

Are the...

An indicat... extreme w...

e interaction of radiation with matter

The type and strength of the interaction of radiation with matter depends on the kind of radiation

Directly Ionising radiation: High-energy charged particles that directly cause ionisation in the medium

ndirectly Ionising Radiation: Neutral particles (Photons or Neutrons) that set charged particles the medium into motion which then go on to cause ionisation he medium

ygen Effect: Basic concepts

onising radiation creates ion pairs in water
Indirect action; direct action creates ion pairs in DNA)

on pairs in water reacts with molecules to form free radical R (nanoseconds)

Free radicals are eliminated by sulfhydryl containing free radical scavengers, su
as Glutathione GSH (microseconds)

Oxygen reacts with free radicals in DNA to form peroxides ROO which cannot be
easily repaired (Oxygen Fixation)

Oxygen increases the indirect effect of ionising radiation if it is present during o
within microseconds after irradiation

t does not matter what the oxygen concentration is seconds pre- or post-
rradiation

ygen Fixation Hypothesis

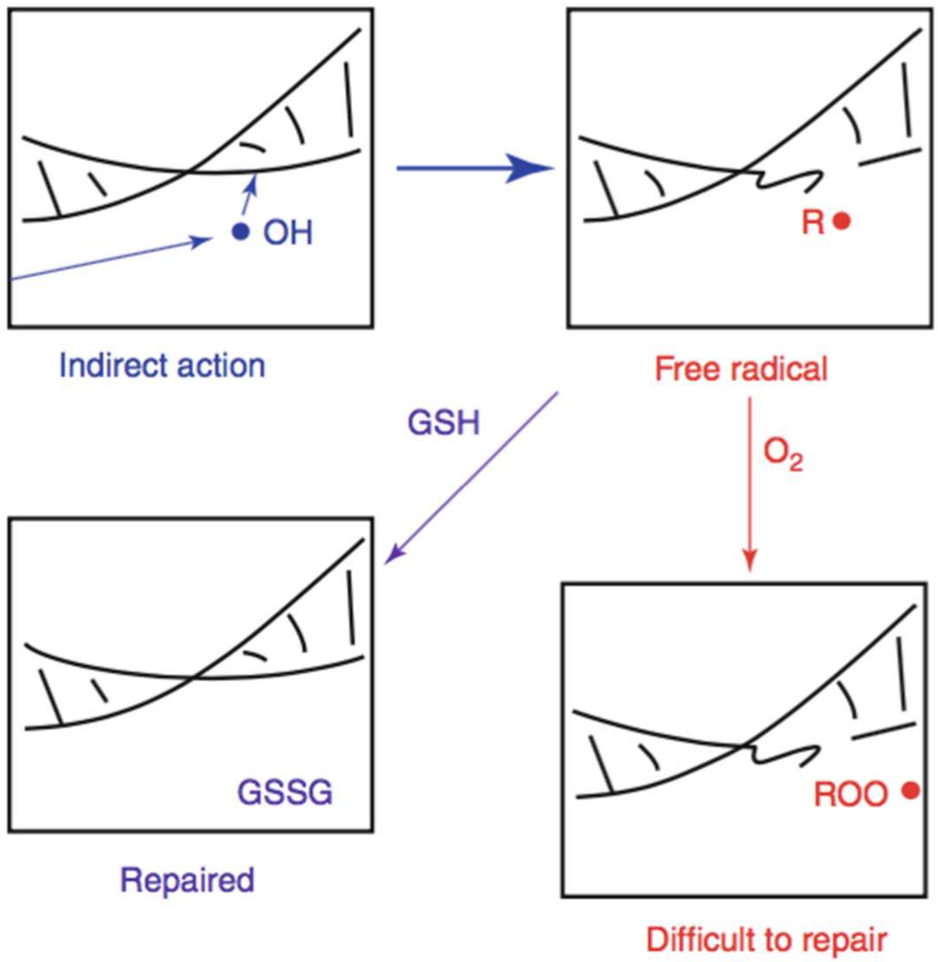


Fig. 22.1 The oxygen fixation hypothesis. Free radicals are easily repaired by antioxidants, but molecular oxygen can convert them into peroxides that are more difficult to repair.

w much oxygen is needed for oxygen effect

The Oxygen Effect operates at very low concentrations of O2

.001 % O2 (0.008 mm Hg): Fully anoxic, no oxygen effect

.05 % O2 (4 mm Hg): Half oxygen effect

% O2 (16 mm Hg): Full oxygen effect, no significant difference with further increase of O2

Oxygen level for comparison

.13 % O2 (1 mm Hg): Fully hypoxic tissue

- 5 % O2 (20-40 mm Hg): Venous blood

- 13 % O2 (60- 100 mm Hg): Arterial blood

0 % O2 (150 mm Hg): Room air

ygen Enhancement Ratio (OER)

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atio of doses that achieve the same biological endpoint (such as cell survival)

$$OER = \frac{\text{Dose (Hypoxic) to cause an effect}}{\text{Dose (Normoxic) for same effect}}$$

linically relevant OER (for megavoltage photons) is around 3 (2.5- 3.5). In order ill as many cells as 2 Gy of Co-60 under normoxic conditions, you would need 6 Gy under ypoxic conditions

ER is greater at high fraction size (-3.5) compared to low fraction size (-2.5)

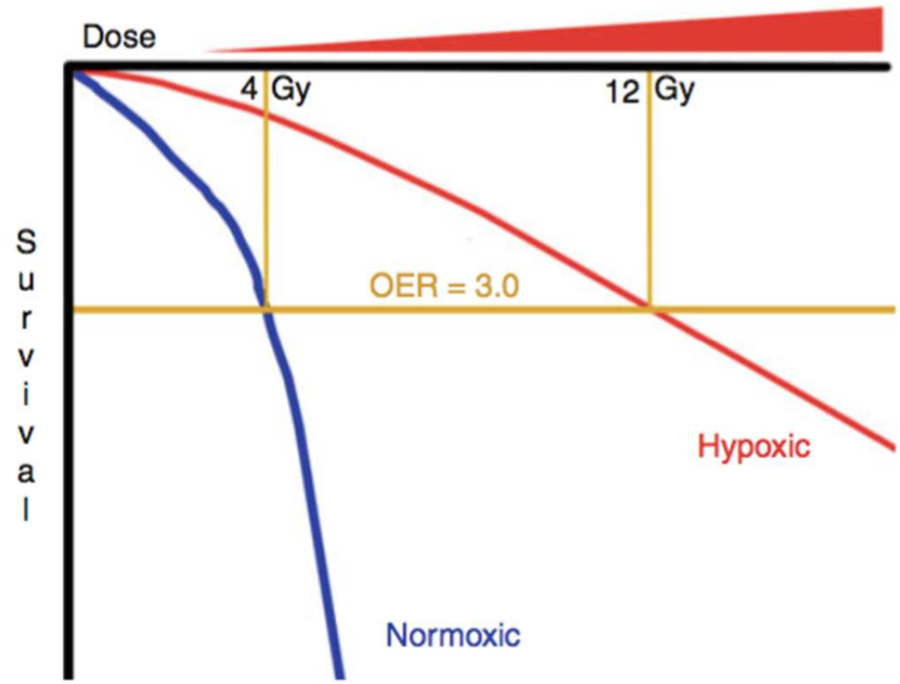
nall fractions: survival curve is dominated by most sensitive cells (G2/M) which have (Lowest OER)

rge fractions: survival curve is dominated by most resistant cells (S) (highest OER)

is behaviour is the opposite of RBE

ygen Enhancement Ratio (OER)

Fig. 22.2 Oxygen enhancement ratio: OER is defined as a ratio of doses that achieve the same effect, as shown by the horizontal orange line.



)ER varies depending on the type of radiation:

)amage from low LET radiation is mostly mediated by indirect action and has a large OER (-3)

ligh LET radiation causes more damage through direct action, which is NOT oxygen dependent)ER -1)

lative Biological Effectiveness (RBE)

Ratio of doses that achieve the same biological endpoint

$$RBE = \frac{\text{Dose of standard radiation to cause an effect}}{\text{Dose of test radiation for same effect}}$$

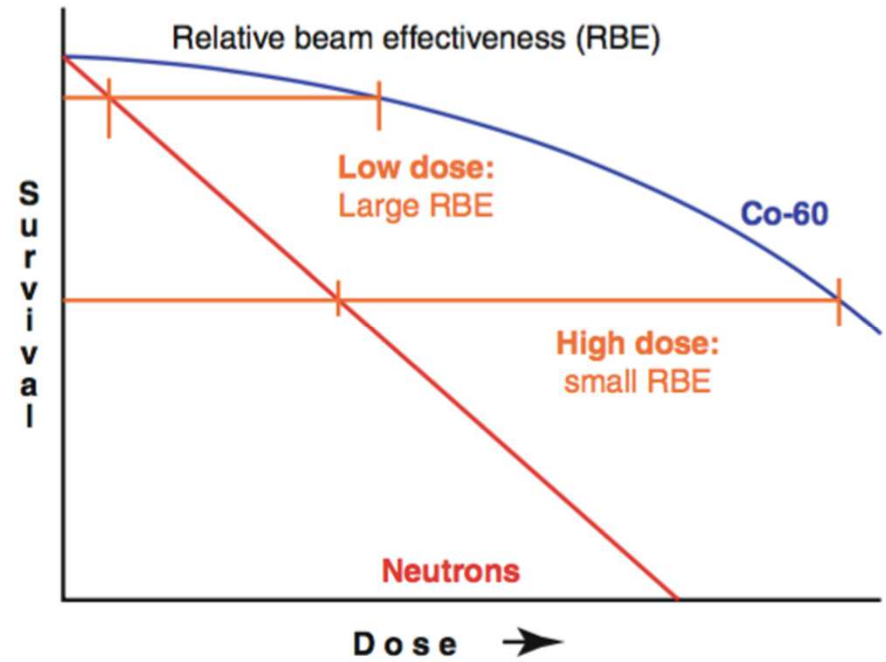
Standard radiation may be defined as 250 kVp X-rays (Hall & Giaccia) or Co-60 (as in Cobalt Gray Equivalent). At an RBE of 3, you need 3 Gy of standa radiation to achieve the same cell kill as 1 Gy of test radiation

RBE is usually measured by acute effects, does not predict late effects (big prob for neutron irradiation)

RBE varies by cell type: radioresitant cells are resistant to standard radiation, so the RBE of high LET radiation increases

lative Biological Effectiveness (RBE)

Fig. 22.3 RBE and Dose: RBE is defined as a ratio of doses that achieve the same effect, as shown by the horizontal line. RBE is greater at small fraction size than at large fraction size.



RBE is greatest at a small fraction size:

mall fractions: Repair predominates for standard radiation, but is ineffective for high-LET radiat

arge fraction: Repair is overwhelmed even with standard radiation

his behaviour is the opposite of OER (OER is greatest with large fraction sizes)

near Energy Transfer (LET)

Measure of interaction between a particle and a medium

Amount of energy that the article deposits in local ionisations per unit path leng

LET increases with the particle's charge (Q2)

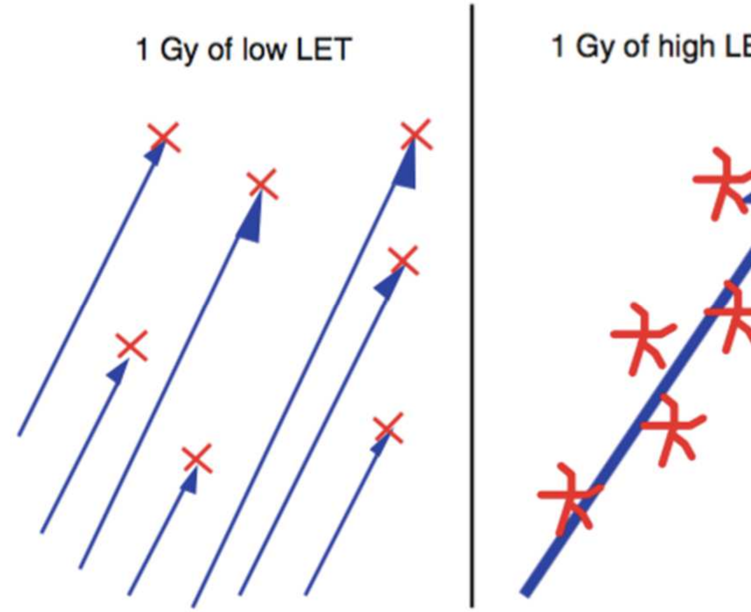
LET decrease with particle's velocity (1/Q2)

LET increases with medium's density

LET decreases with the medium's atomic number (Z)

near Energy Transfer (LET)

Fig. 22.4 A diagram of low LET radiation versus high LET radiation. Both deposit the same radiation dose (ionizations, *red stars*). However, the low LET ionization events are widely scattered while the high LET ionization events occur in a dense track.



pical LET for different forms of radiation

gavoltage X, Gamma, e: 0.2- 0.5 keV/µm

st protons: 0.5 keV/µm

ovoltage X, Gamma: 2- 4 keV/µm

w protons: -5 keV/µm

st neutrons and alphas: -100 keV/µm

avy ions (carbon etc): 200- 1000 keV/µm

lationship between LET, RBE and OER

LET is a measure of how densely ionising a radiation beam is

As LET increases, RBE increases until it reaches a peak at 100 keV/μm

Decreased repair due to high density of ionisations

ncreased direct action, less oxygen dependent

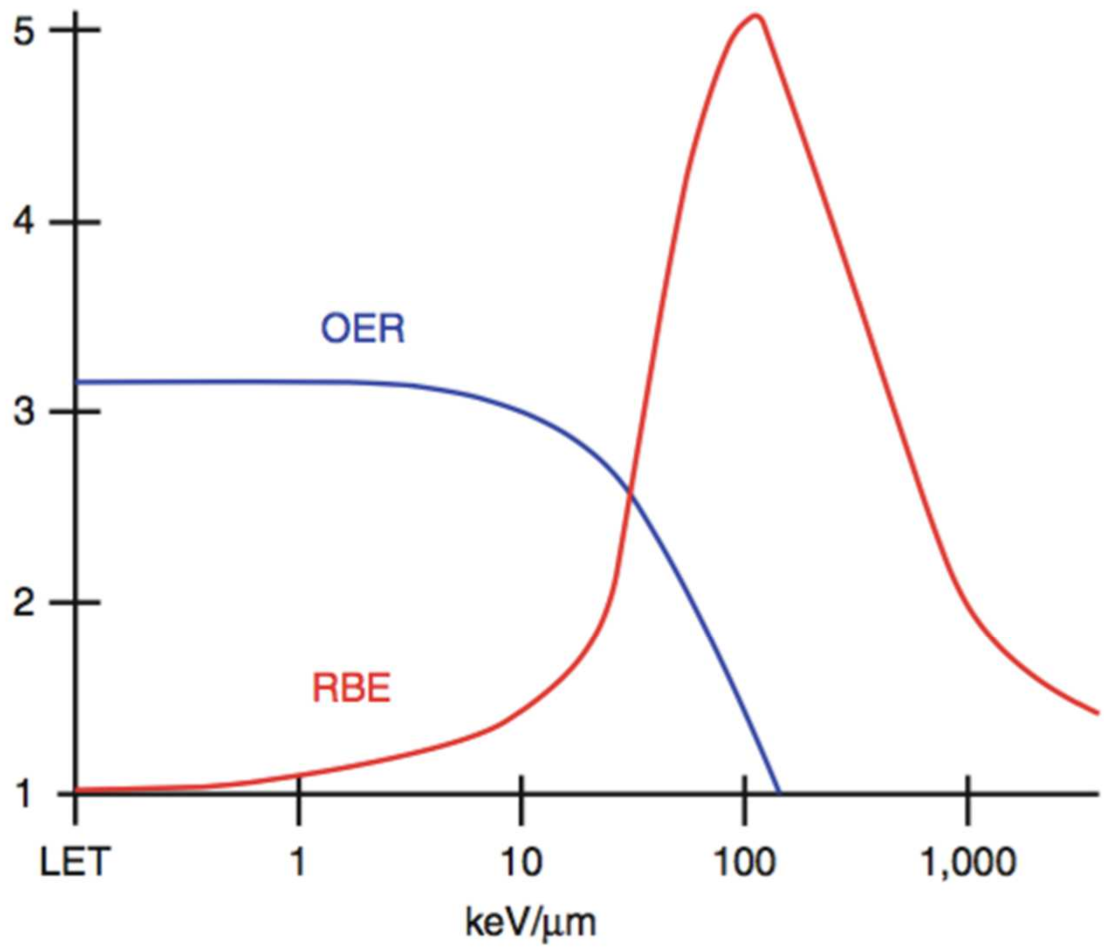
100 keV/μm corresponds to one ionisation per 2 nm, which is the diameter of a DNA strand (optimal LET for cell killing)

After 100 keV/μm, RBE decreases with LET: A single particle deposits much more ene han is required to kill a cell. Therefore, it kills less cells per absorbed dose (Overkill eff

OER strictly decreases as LET increases

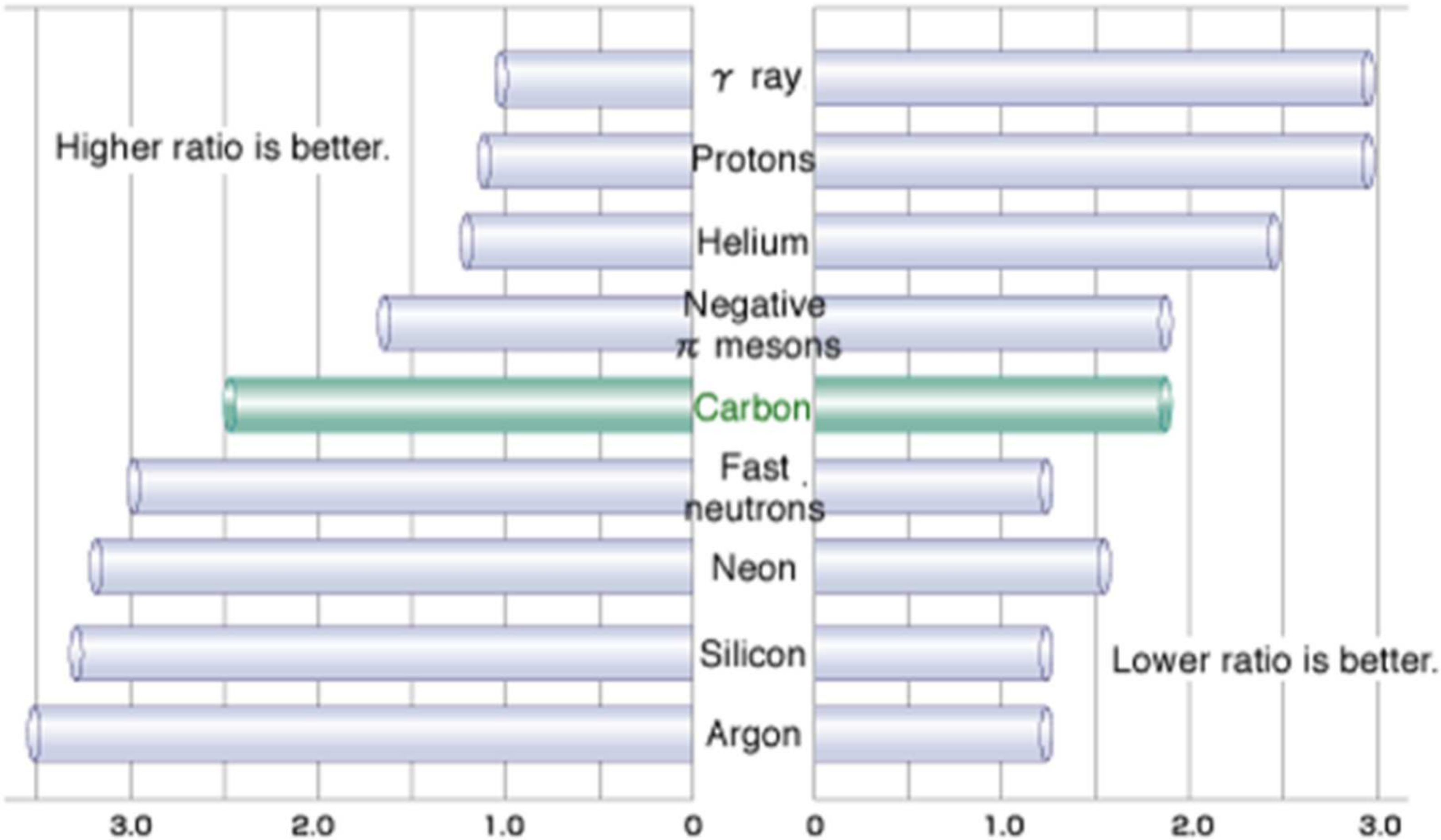
Relationship between LET, RBE and OER

Fig. 22.5 OER and RBE versus LET: As LET increases, RBE peaks around ~100 keV/μm before it trends back down. OER strictly decreases with LET until it reaches 1 at ~100 keV/μm.



BE And OER Of Various Radiation Types

Relative biological effectiveness (RBE) and
oxygen enhancement ratio (OER) of various radiation types



RBE represents the biological effectiveness of radiation in the living body.
The larger the RBE, the greater the therapeutic effect on the cancer lesion.

OER represents the degree of sensitivity of hypoxic cancer cells to radiation.
The smaller the OER, the more effective the therapy for intractablecancer cells with low oxygen concentration.

eraction Of radiation With matter

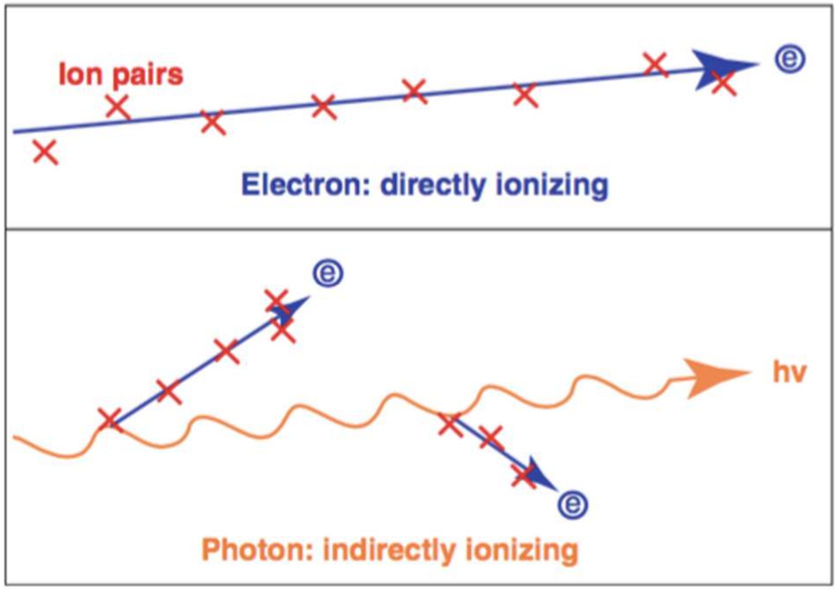
Overview

nteraction of electromagnetic radiation with matter: outline

nteraction of particulate radiation with matter: a little detail

- **Absorption**: Loss of photons from a beam due to photon energy being absorbed by matter.
- **Scatter**: Loss of photons from a beam due to photons changing direction.
- **Attenuation**: Loss of photons from **Absorption** AND **Scatter**.

Fig. 4.1 Directly vs indirectly ionizing radiation. Charged particles directly ionize other atoms in the medium by exerting coulombic forces to budge electrons directly off of atoms (see Chapt. 5). Indirectly ionizing radiation is not charged and largely relies on secondary electrons to cause the actual ionizations.



eraction Of Electromagnetic Radiation With Matter

Electromagnetic Radiation: Photons. They have both electrical and magnetic properties and are not deflected by either electric or magnetic fields

- Coherent Scatter
- Photoelectric Effect
- Compton Scatter
- Pair Production
- riplet production
- Photonucleear Disintegration

eractions Of Particulate Radiation With Matter

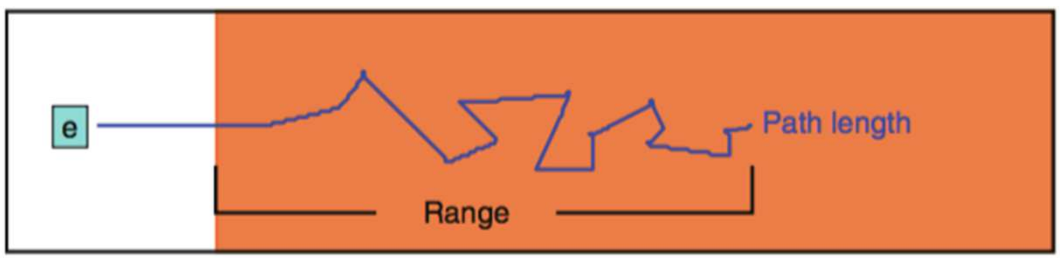
Particulate radiation has a definite RANGE which is approximately how far they travel in a medium before stopping

arged and Uncharged Particles

Charged particles can directly interact with electrons and nuclei, through coulomb nteractions. Therefore they are directly ionising and are generally less penetrating thar uncharged particles

Uncharged particles cannot interact through coulombic forces so they are indirectly onising. Heavy uncharged particles are more likely to interact with nuclei than with electrons, and they are relatively more penetratin nt and Heavy Particles

- Light particles are particles with a mass similar to electrons (basically just elect and positrons)
- Due to their mass, they change directions (scatter) very easily: Path length is m longer than range!



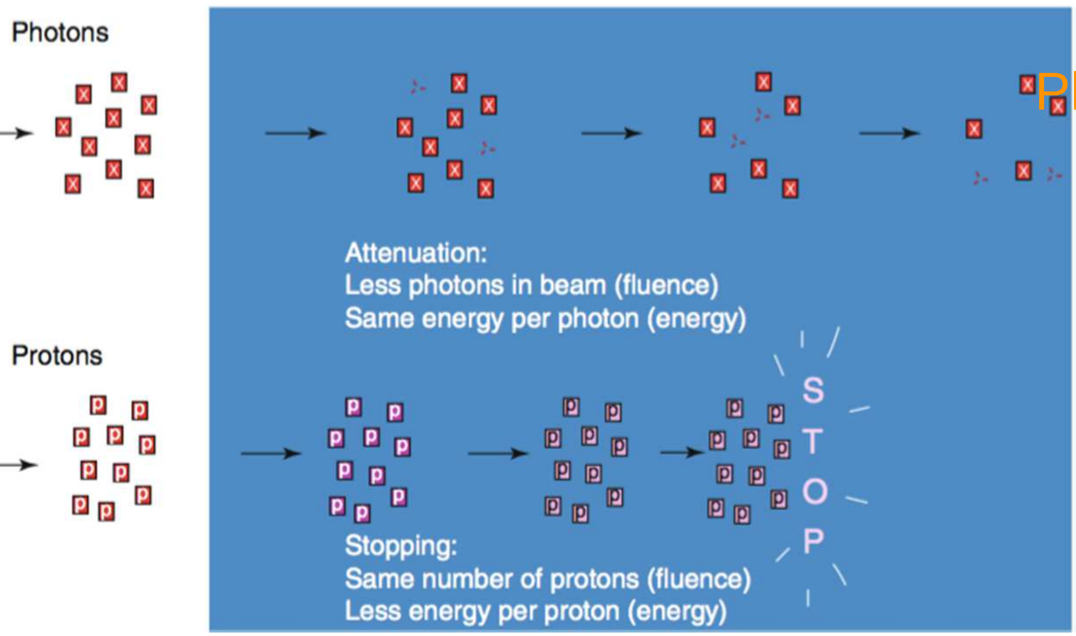
- Heavy particles are significantly heavier than electrons
- Due to their mass, they travel in a nearly straight line!

ow Do Charged Particles Interact?

Unlike photons, charged particle are directly ionising

Charged particles have a variable velocity (Photons always move at the speed of light):
/elocity and energy are directly related to each other

PARTICLES GRADUALLY LOSE ENERGY as they interact with the medium (This is in con
o Attenuation, decreasing the number of photons in the beam, without changing the
energy of individual photons)



Photons will undergo multiple scatterings and in a random fashion that will decrease the r

Protons and other particles will have paths that decrease in energy as the interact with more atoms through coulo forces but gradually they will slow dov and eventually come to a stop

pes Of Collision

stic Collision

Kinetic energy and momentum are both conserved

Energy is transferred between the particle and the medium

All the energy is kept in the form of motion

astic Collision

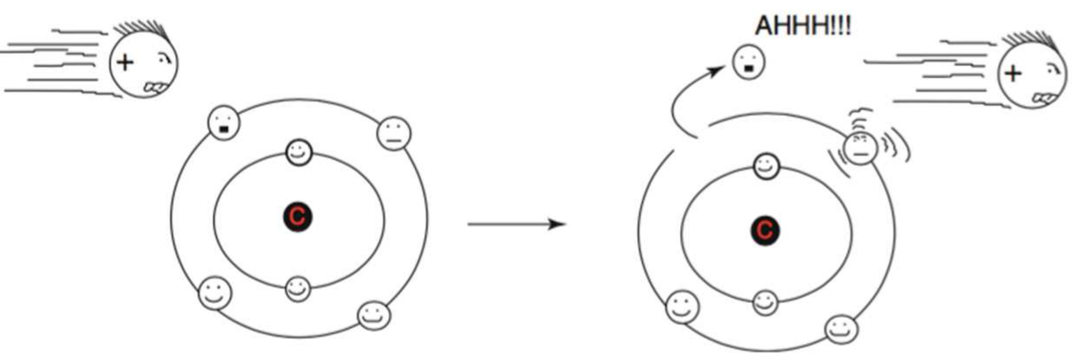
Kinetic energy and momentum are not conserved

Particle transfers energy to the medium and slows down

This energy may be released as a photon, or it may be transferred to an electron (caus
onisation)

eavy Charged Particle Interactions

- These principles are the same for protons and heavy ions
- astic Collision with Electrons
- As a heavy charged particle speeds through a medium, its positive charge attracts housands of orbiting electrons
- Some electrons are merely excited, others are ionised
- Each interaction slows the charged particle a little. As it slows, it is more likely to intera with both electrons and nucleus
- The charged particle is very heavy, so it does not change direction appreciably



Proton is speeding by an electron orbital and sucks an electron right off it orbital causing ionisation.
Every time it does this, it slows down a little and ultimately creates havoc

agg's Peak

As a charged particle is slowed down by the interactions in the medium, it intera
more and more (higher LET) until it finally stops

The burst of energy released around the stop point is known as Bragg's Peak

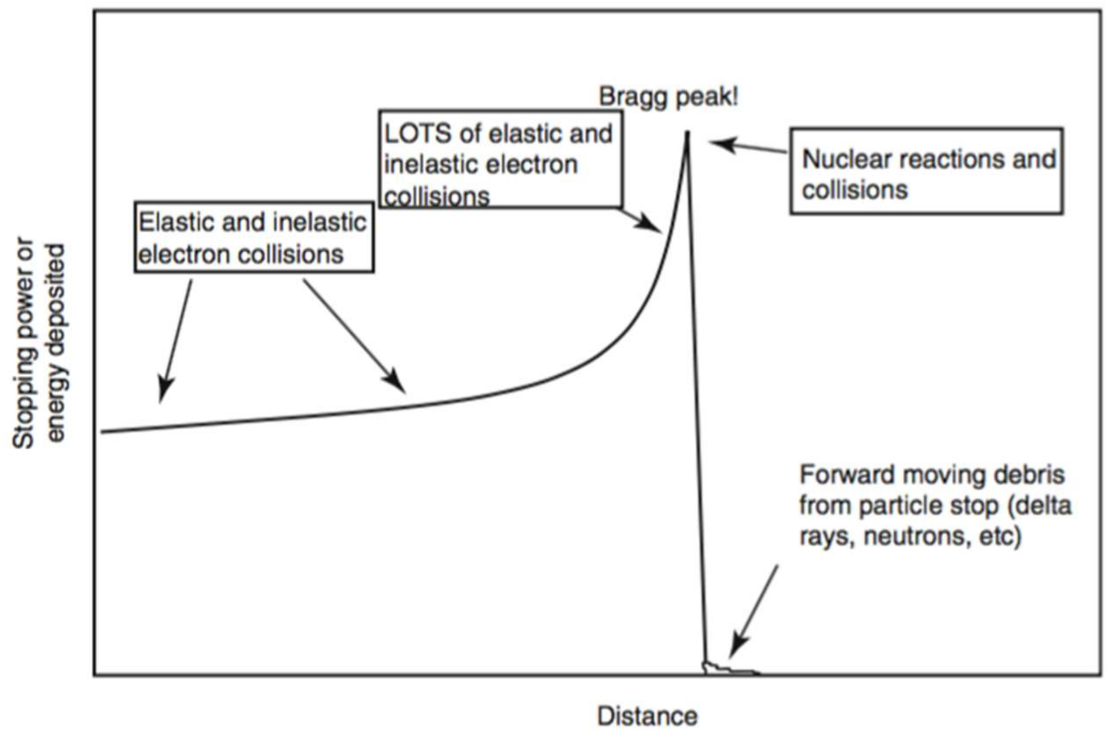


Fig. 5.7 Energy deposition of a charged particle: As a charged particle moves through the medium, it slows down more and has time to do more damage until it comes to a stop and does mega-damage. Even after the final peak of rage, there is a small amount of secondary damage from the debris that was caused at the bragg peak.

read Out Bragg Peak (SOBP)

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Vhen a beam of monoenergetic heavy charged particles enters the patient body he depth-dose distribution is characterized by a relatively low dose in the entra egion (plateau) near the skin and a sharply elevated dose at the end of the ran Bragg peak)

o treat an extended target, the Bragg peak is spread out to cover the required olume by modulating the energy of the particles to form a spread-out Bragg pea SOBP)

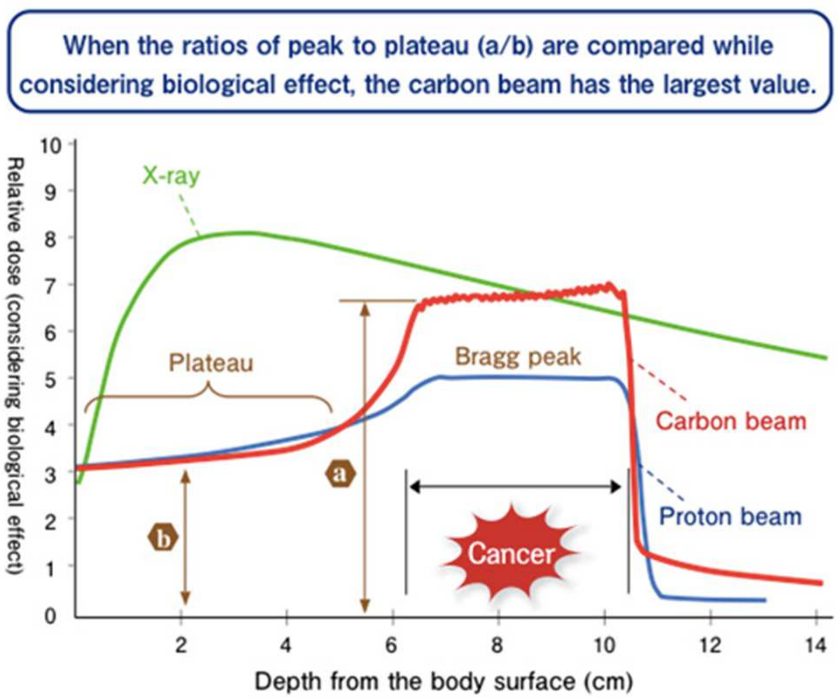
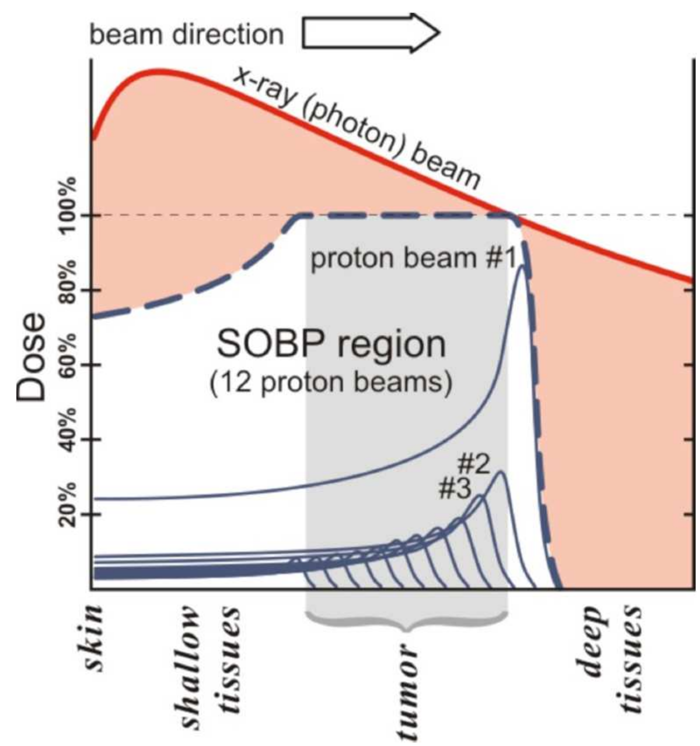


Illustration courtesy of National Institute of Radiological Sciences (NIRS)



chnical Aspects of Charged Particle Therapy

- Beam production with Cyclotrons and Synchrotron
- Beam-Delivery System (Gantries)
- Beam Application System
    - Passive Beam Shaping
    - Active Beam Shaping
- Patient Positioning
- Treatment planning
- Biological Modeling

Cyclotron or Synchrotron?

Cyclotrons create a higher dose rate with a uniform intensity

Synchrotrons achieve a continuously variable energy

Although cyclotrons are reliable, compact, and easy to operate; synchrotrons ha
he ability to generate the energies needed to treat the patient

Extraction of required energy eliminates the need of energy degraders downstre

Energy degraders ▸ ▪ extra interaction with the pencil beam ▸ ▪ increased creation of secondary neutrons ▸ ▪ increase in the amount of shielding needed near the beam exit

Disadvantage of synchrotron is complex system needed to extract the precise energy

n addition, the current is less than a cyclotron, producing longer treatment time

am Production

. proton beam of 150 MeV can penetrate 16 cm in water, the same radiologica
epth is achieved with carbon ions of 3000 MeV or 250 MeV/u (energy per nuc

o accelerate particles to such high energies, synchrotrons are better suited tha
yclotrons

o inject the ions into a synchrotron ring, they have to be accelerated first in a li
ccelerator (Linac) injector to several MeV/u

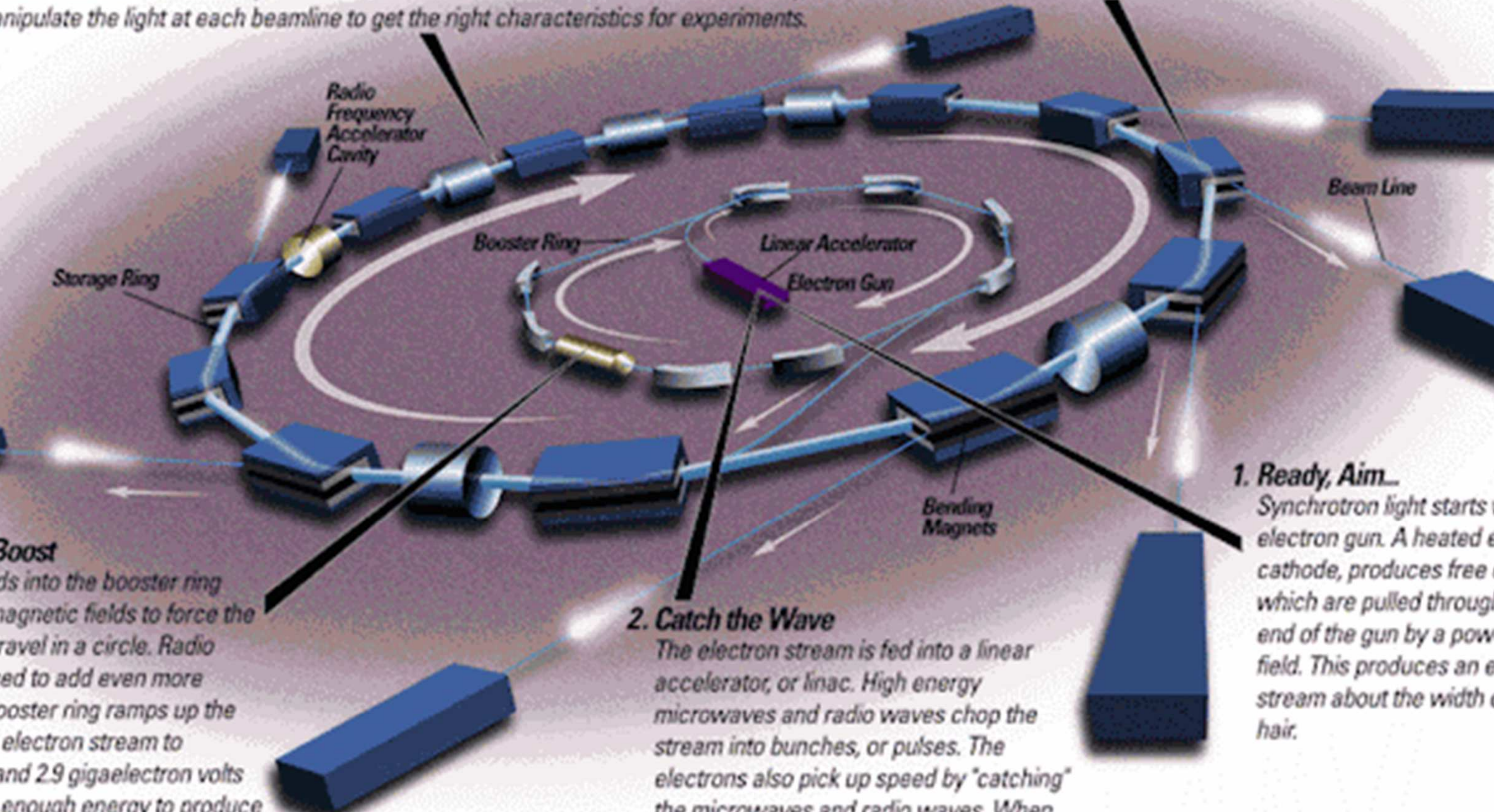
uch a Linac consists of a radiofrequency cavity and a drift tube and has severa
neters length

g
ing feeds electrons into the storage ring, a many-sided donut-shaped tube. The tube is
nder vacuum, as free as possible of air or other stray atoms that could deflect the
n. Computer-controlled magnets keep the beam absolutely true.

light is produced when the bending magnets deflect the electron beam; each set of
nets is connected to an experimental station or beamline. Machines filter, intensify, or
nipulate the light at each beamline to get the right characteristics for experiments.

5. Focusing the Beam

Keeping the electron beam absolutely true is vital
the material you're studying is measured in billion
a metre. This precise control is accomplished wit
computer-controlled quadrupole (four pole) and
sextupole (six pole) magnets. Small adjustments v
these magnets act to focus the electron beam.



1. Ready, Aim...

Synchrotron light starts
electron gun. A heated e
cathode, produces free
which are pulled throug
end of the gun by a pow
field. This produces an e
stream about the width
hair.

2. Catch the Wave

The electron stream is fed into a linear
accelerator, or linac. High energy
microwaves and radio waves chop the
stream into bunches, or pulses. The
electrons also pick up speed by "catching"
the microwaves and radio waves. When
they exit the linac, the electrons are
travelling at 99.99986 per cent of the speed of

Boost

ds into the booster ring
nagnetic fields to force the
ravel in a circle. Radio
ed to add even more
ooster ring ramps up the
electron stream to
and 2.9 gigaelectron volts
enough energy to produce
ight in the infrared to hard

Source: University of S

am Delivery Systems (Gantries)

Experience with charged particle therapy has been acquired in the past mainly research laboratories using horizontal beam lines

n RT, the success of treatment is strongly related to the possibility of applying t beam to the target volume using multiple fields

The freedom to apply the beam on a gantry that rotates around a patient offers significant advantages

To validate the outcome of charged particle as compared with conventional radiation, it is necessary to apply both modalities at the same level of complexit

tient Positioning

)ue to the high spatial accuracy that is achievable with ion beams, patient fixat
ind positioning requires special attention

Patient fixation is usually achieved with individually prepared mask systems or
vhole-body moulds

Highest accuracy during the initial positioning can be achieved by the use of
tereotactic methods

Prior to every fraction, the position is verified using X-ray imaging in treatment
position

The X-ray images are compared against digitally reconstructed radiographs
btained from the treatment planning CT

am Delivery Systems (Gantries)

The major drawback of gantries for charged particle is the enormous size and weight of the rotating structure supporting the beam

AN ISOCENTRIC GANTRY FOR CARBON ION IS EXPECTED TO HAVE A WEIGHT OF ABOUT 600 TONS AND A DIAMETER OF 13 METERS

The enormous size and weight of such gantry together with high spatial accura required for the beam position at the isocenter is probably the reason why no gantry has been built up to now

nstead of flexible beam delivery systems: Fixed inclined beam lines (Japan)

Another possibility is to move the patient rather than the beam: treatment chair and holds that can be rotated around the patient's longitudinal axis are availab

am Application Systems

Two principle methods to shape the beam and thus to tailor the dose to the targ
volume

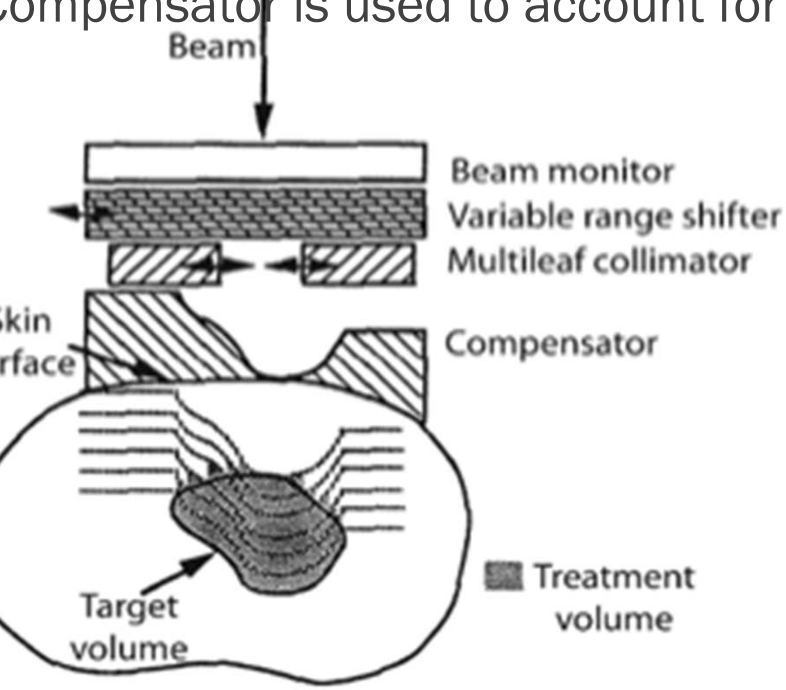
Passive beam shaping (Passively scattered particles)

Active beam shaping (Pencil beam scanning particles)

ssive beam shaping

t method to develop, most commonly used

- Depth dose of monoenergetic beam is modulated by variable degrader. Modulator is designed t d a predefined dose profile
- To move the modulated Bragg peak (SOBP) to the desired radiologic depth, an additional range fter is needed (homogenous plastic plates)
- Small size beam has to be spread out laterally to cover the whole target homogeneously. achiev ner by a double scattering system or by a magnetic wobbling system that moves the beam over ined area
- Lateral extent of each treatment field is adapted by using a collimator
- Compensator is used to account for tissue inhomogeneities



Smearing is a process that modifies the compensa design to take into account the internal motion of th tumour and setup uncertainties

Disadvantages:
Depth dose can only be tailored to the distal end of target but not to the proximal end because compensator shift the SOBP towards entrance reg
A considerable amount of high dose region (and hi LET region) is therefore located in the normal tissu

tive Beam Shaping (PBS)

System takes advantage of electrical charge of particles to produce tightly focused pencil beam

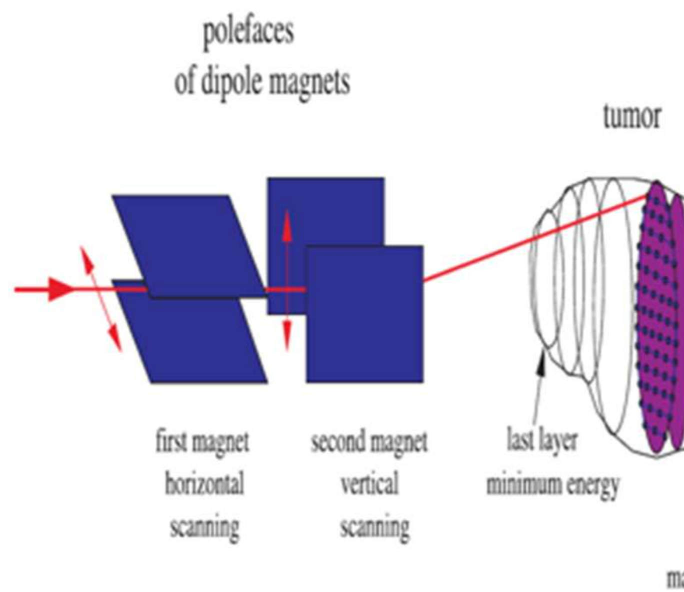
This beam is deflected laterally by 2 magnetic dipoles to allow a scanning of the beam over the reatment field

When the beam is produced by synchrotrons, the energy can be switched from pulse to pulse to adapt the range of particle in the tissue. Hence, target volume can be scanned in 3 dimensions he dose distribution can be tailored to any irregular shape without any passive absorbers or pa specific devices, like compensators or collimators

High dose region can also be conformed to proximal end

o types of PBS

- Uniform Scanning: Uniform dose distribution throughout the tumour with each beam, each beam could treat the tumour to the full dose if treated independently
- Nonuniform Scanning: Nonuniform dose per beam to make the composite dose uniform. Similar modulation technique to IMRT



eatment Planning: TPS for Active Beam Shaping

Research TPS developed at GSI (Gesselschaft fur Schwerionenforschung) in Darmstadt, Germany

Combination of a versatile graphical user interface for RT planning, called VIRTU and a program called TRiP (Treatment planning for particles)

Dose calculation for active beam shaping systems is very similar to the pencil b models used for conventional photon therapy

eatment Planning: TPS for Passive Beam Shaping

For the passive depth-dose shaping system, the depth dose profile is fixed by th modulator hardware throughout the irradiation field and no further optimisation necessary

Algorithm is very similar to that used in conventional photon therapy

Beam transport models are relatively simple:
Lateral scattering of carbon ions is very small
Lateral penumbra of the primary beam is preserved almost completely in depth

The radiologic depth of a proton or ion beam in tissue is calculated by using an empirical relation between radiograph CT numbers and measured particle rang which is valid for all tissues but not for material with high Z values, such as met mplants

eatment Planning Uncertainties

Range uncertainties

Relative biologic effectiveness

Setup errors

External edge effects

nternal edge effects

Anatomic change

mparing Protons and carbon Ions: Physical Characteristics

Both provide superior dose distribution compared with most advanced photon technology

Advantage of particle is based on finite range in tissue

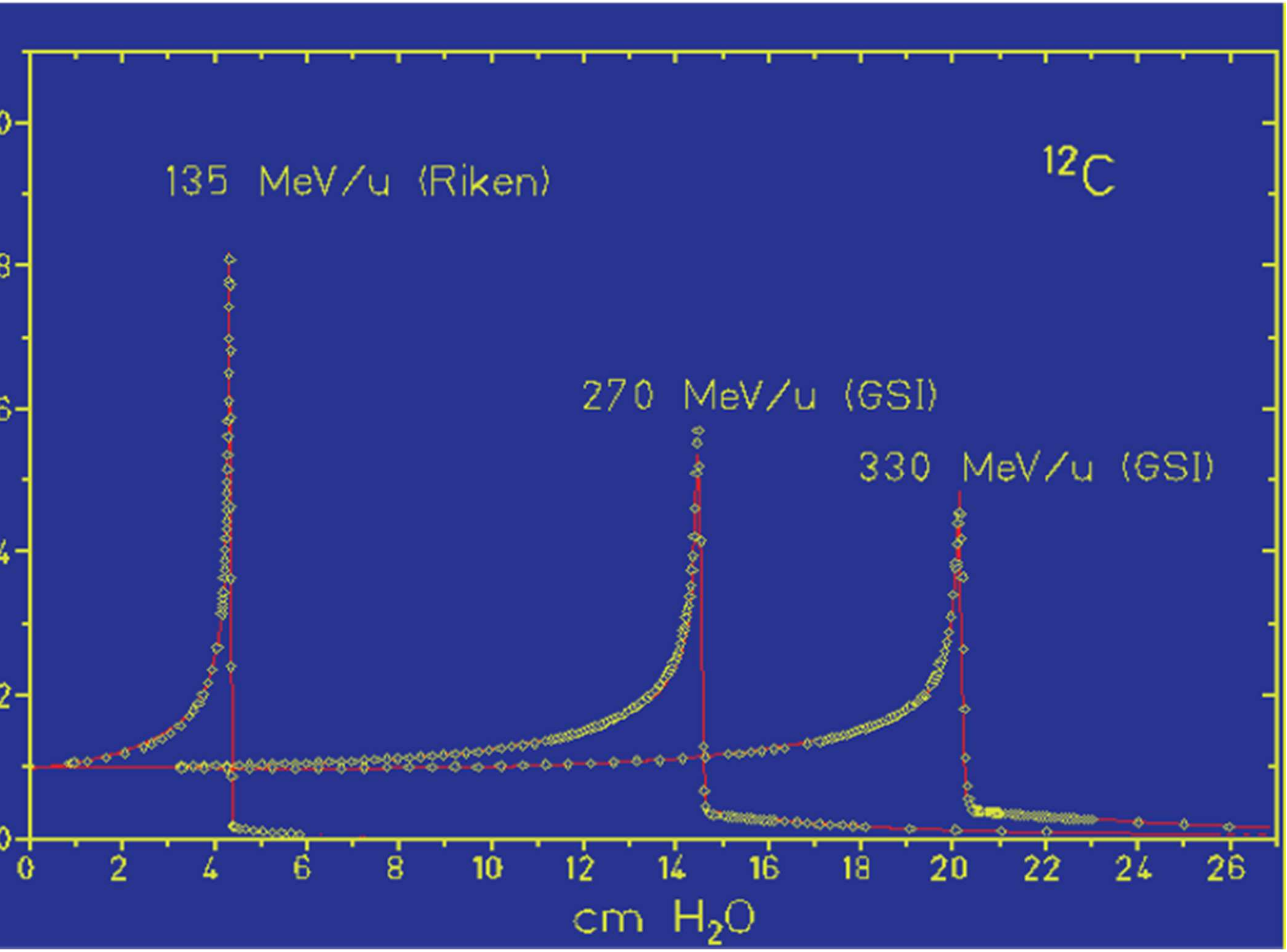
Depth of penetration depend on initial energy of the beam and composite of the tissue

Bragg's peak

Because of nuclear interactions of carbon ions with atoms of the irradiated tiss fragmentations of carbon ion occurs. Most of these fragments are low energy ic of boron, beryllium, lithium, and helium

Some of these deposit their energy beyond the range of range of C12 in the so called fragmentation tail

netration Depth Can Be Varied According To Ion Energy



sential,
choice of the heavier ion beam becomes important

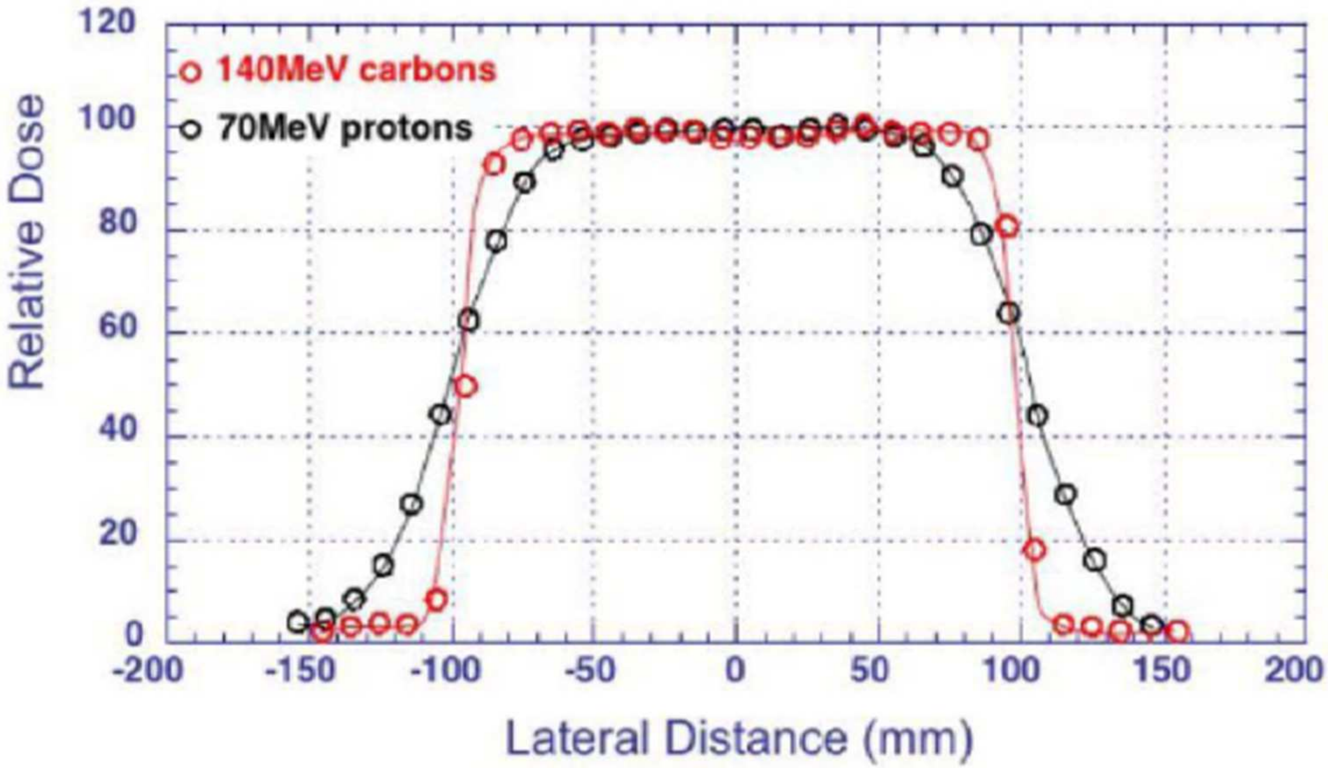
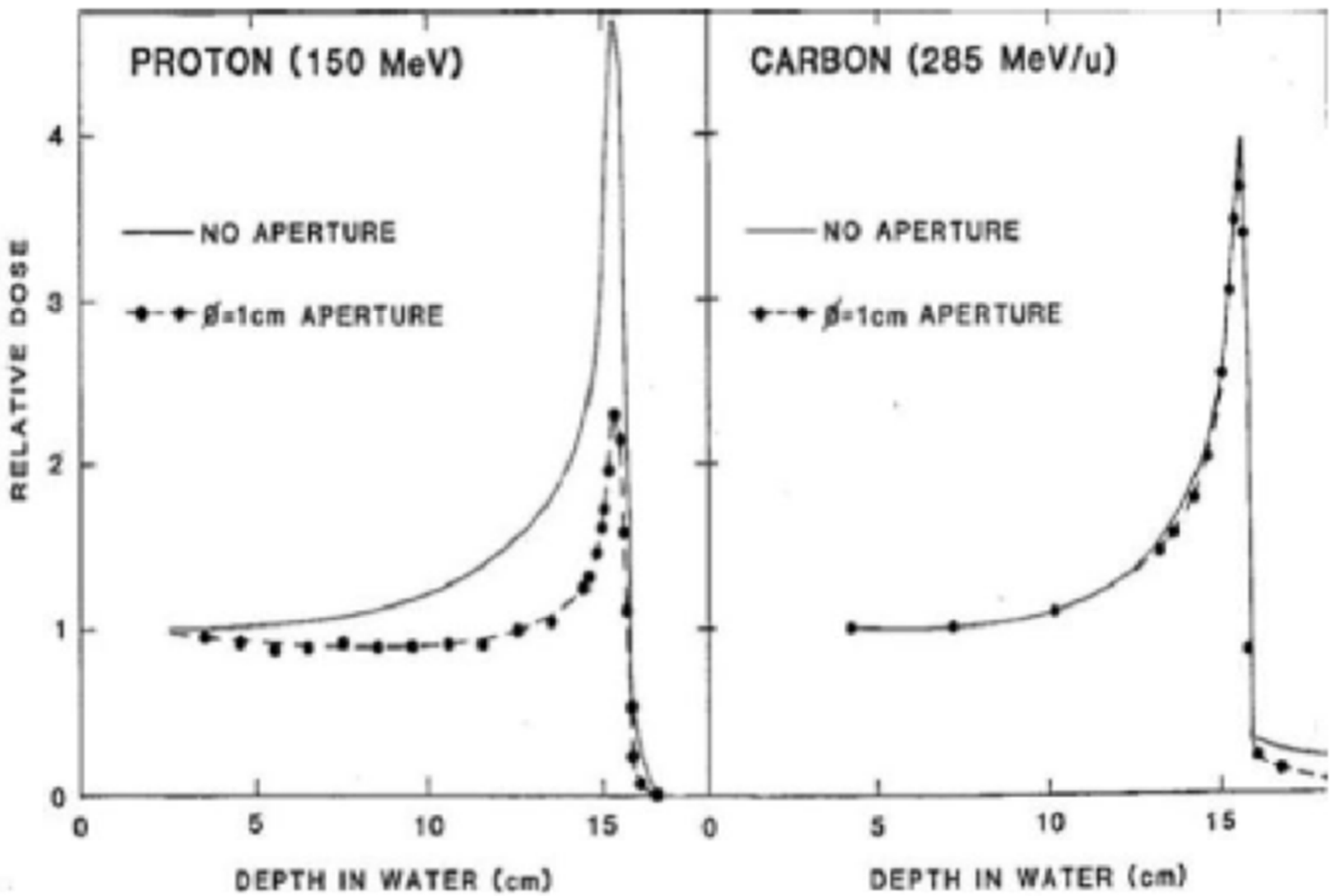


FIG. 4. The penumbra of a carbon beam is much sharper (dose distribution with a steeper edge slope) than that of a proton beam (less steep edge slope) of comparable range. (Based on the paper presented by H. Tsujii, at the 39th meeting of PTCOG (Particle Therapy Co-operative Group), San Francisco, October 2002).

limated and other uncollimated ; whereas, the Bragg peak is much suppressed the collimated proton beam



mparing Protons and carbon Ions: Biological Characteristics

Generally, higher the mass of charged particle, the higher the rate of energy los while penetrating tissue

Thus the LET is higher for carbon ions compared with protons

Clinical proton beams are low LET with comparable RBE to photons

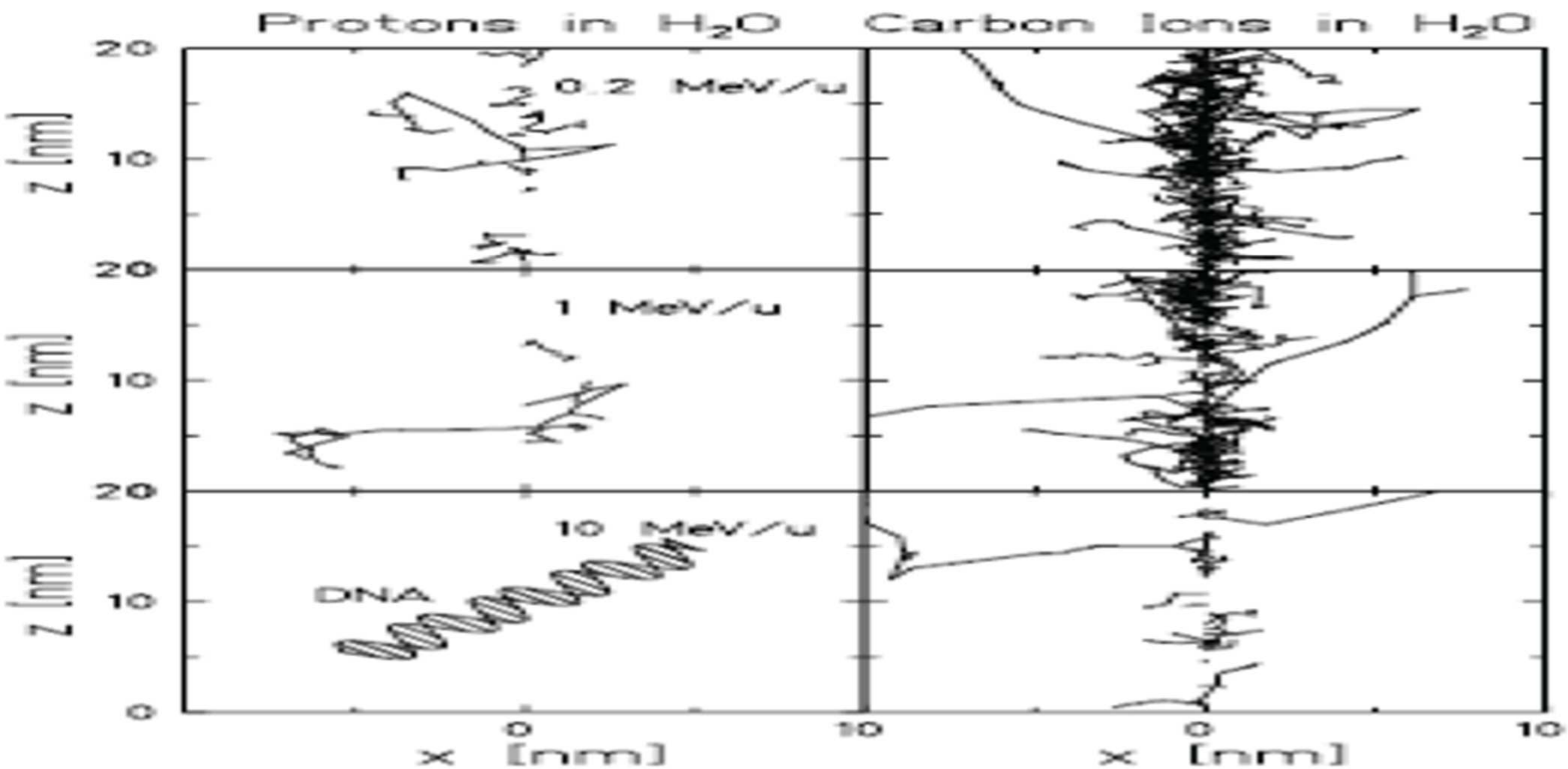
Recommended RBE for proton therapy of ICRU is 1.10

RBE of carbon ion ranges between 3- 5

ncreasing the dose per fraction leads to lower RBE of the tumour and the norm tissue. Nevertheless, the RBE of tumour decreases more slowly than the RBE o normal tissue

Hence, hypofractionated carbon ion treatment is often used to spare the organ risk while escalating the dose to the tumour

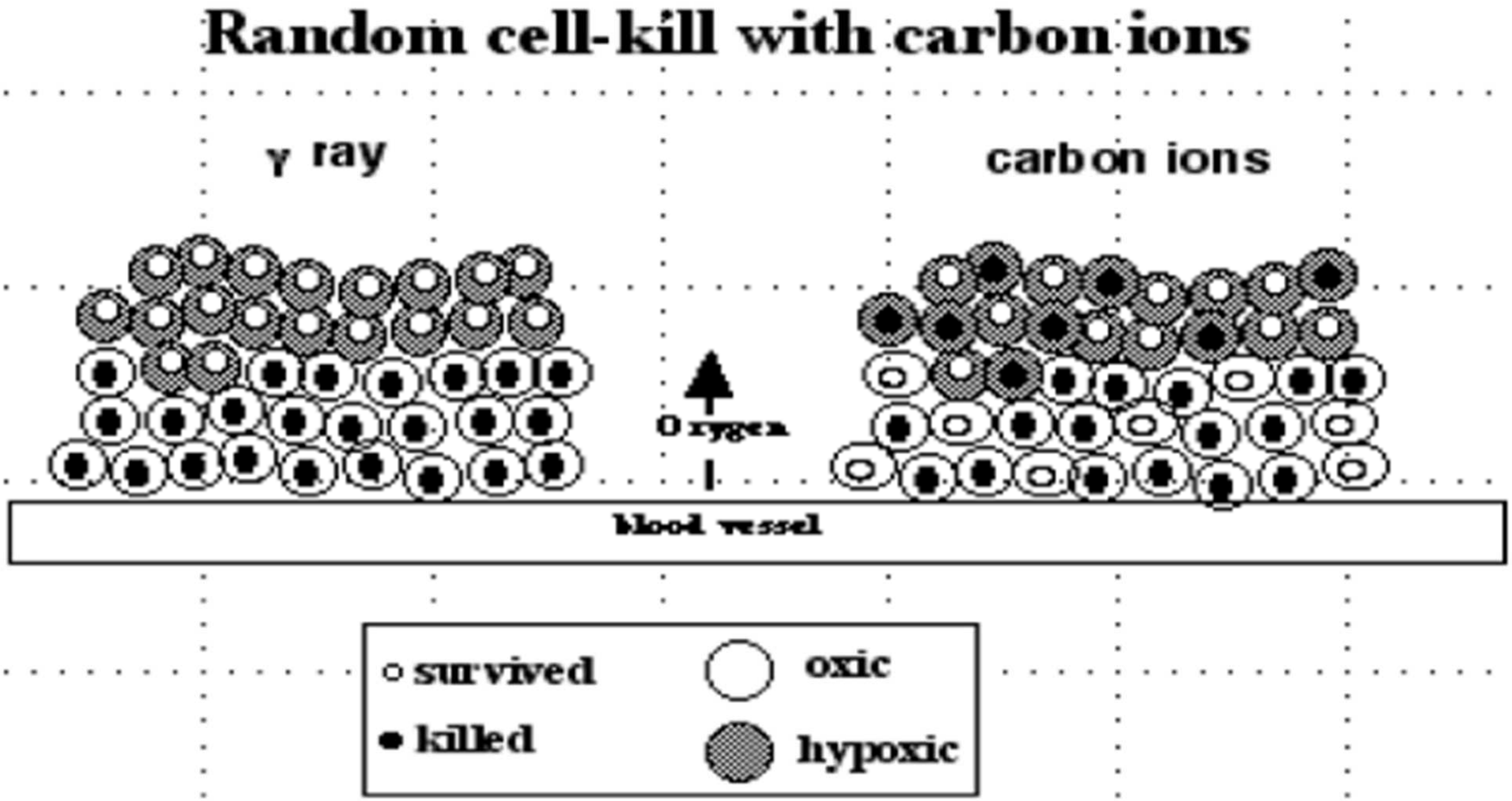
oton vs Carbon Ion DNA Damage



Locally correlated DNA damage can only be produced by increasing the macroscopic dose

Many electron tracks are produced that cause locally multiply damage tracks within the DNA

n Beams Kill Hypoxic Cells More



mparing Protons and carbon Ions: Technical Characteristics

Currently, most of the centers are using passive techniques with modulators, collimators, and compensators to spread out protons and carbon ions

Passive beam delivery is relatively easy for planning and quite robust in treatme of moving target

However, dose to normal tissues in entrance path is higher than with active techniques: higher risk of secondary malignancies

Active beam

nical Aspects

Carbon ions have similar physical properties as protons but additionally offer a higher biological effectiveness in specific tumour types

Since RBE is different for different biologic endpoints and for different tissues, radiobiological aspects are of high relevance

Carbon ion RT offers the highest ratio of RBE values between the Bragg peak ar the plateau for tumours with a ow intrinsic radio sensitivity against conventiona photon RT (low α/β ratio in the cell survival curve and a pronounced shoulder of curves indicating a high repair capacity)

RBE values of carbon ion might also be high for normal tissue structures in clos vicinity to the irradiated tumours that fulfil the same biological criteria and have be included in the target volume for oncological regions

nical Aspects

ow RBE values for carbon ion RT is assumed in tumour cells showing good response to photor ndicated by high α/β ratios of the cell survival curves

aking into account radiobiological aspects, the highest benefit of carbon ion RT in the form of ncreased biological effect and minimum toxicity can be expected for tumours relatively adioresistant to photon RT, which are located within sensitive normal tissues

on the other hand, it may be disadvantageous in the treatment of radio responsive tumours loc n relatively radioresistant tissue

otential indications for carbon ion RT may be therefore:

- ordomas
- ondrosarcomas
- alignant salivary tumours with high RBE values
- ostate Cancer
- ng cancer
- one and soft tissue sarcoma

nical Aspects

- Because of higher conformal beam delivery with particles, a dose escalation to tumour can potentially be performed without exposing the adjacent organs at ri to higher doses
- Thus, a prospective randomised trial comparing photons and particles with the same delivered dose is not realizable
- Compared with photon therapy, a lower integral dose to the normal tissue and a lower neutron exposure to the whole body by using particles are assumed

mmary

The physical selectivity of ion beams is comparable to, or better than, the best LET therapy techniques. The penumbra is narrow and the dose ratio between t SOBP and entrance plateau is better than with the best low LET radiation (protons). Nuclear fragmentation of the ion beams is a potential disadvantage because some energy is deposited beyond the Bragg peak. However, this aspe probably not clinically significant because the dose is low and the fragments ar lower LET particles

The LET in the ion beam, and consequently the RBE, increases with depth, and this increases the ratio of the biologically weighted doses between the SOBP a the entrance plateau. The RBE is comparable to neutrons, but the physical dos selectivity is vastly improved for ions

mmary

At the level of the SOBP, where the PTV is located, high LET makes heavy ion beams specifically effective for the treatment of some tumour types that are resistant to low LET radiation

After fractionated irradiation, there is reduced possibility for repair for cells in t PTV located in the SOBP, because the LET is highest there. In contrast, the nor tissues located outside the SOBP, in the entrance plateau region, are exposed lower LET radiation and thus may benefit from an increased repair opportunity Therefore, from a radiobiological point of view, fractionation in ion therapy sho bring a significant advantage and should be exploited. It is recognized, howeve that this radiobiological advantage may be balanced by the advantage of reduc treatment times to reduce the effect of tumour cell repopulation and also by sc economic consideration

rticle Therapy statistics

Total of all facilities (in and out of operation):		
He	2054	1957-1992
Pions	1100	1974-1994
C-ions	15736	1994-present
Other ions	433	1975-1992
Protons	118195	1954-present
Grand Total	137179	

NATIONAL JOURNAL f PARTICLE THERAPY

Particle Therapy Statistics in 2014

Martin Jermann, MSc

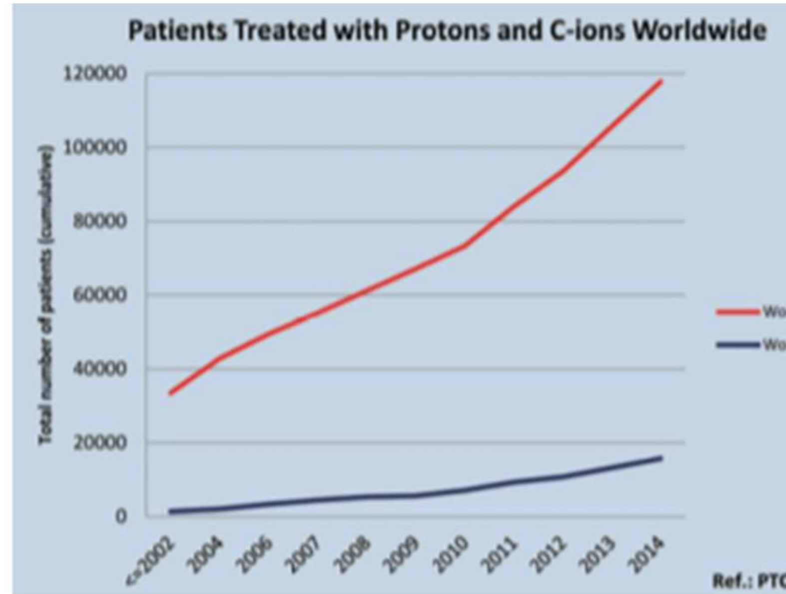
Secretary of the Particle Therapy Cooperative Group
Paul Scherrer Institute, Villigen, Switzerland

More than 137 000 patients were treated with particle therapy worldwide from 1954 to 2014, including 15 000 in 2014, 86% of which were treated with protons and 14% with carbon ions and with other particles (**Table 1**). In 2014, about 10% of patients were pediatric and another 10% were treated for ocular melanomas. Forty-eight particle therapy facilities were in clinical operation at the end of 2014 (**Figure 1**). Two facilities in Asia (one in Lanzhou and the other in Wanjie) were temporarily shut down for technical upgrades and extensions in 2014. One facility in the United States (Indiana University Health Particle Therapy Center, Bloomington, IN) was closed down at the end of 2014 after 10 years of clinical operation. Five new particle therapy centers started patient treatments in 2014. These include two facilities in Asia (Shanghai Proton and Heavy Ion Center in Shanghai, China, and Aizawa Hospital Proton Therapy Center in Nagano, Japan) and three facilities in the United States (the Provision Center for Proton Therapy in Knoxville, TN, the Scripps Proton Therapy Center in San Diego, CA, and the Willis Knighton Proton Therapy Center in Shreveport, LA). **Figure 2**, **Figure 3**, and **Figure 4** depict the number of patients treated with proton and carbon ions and their location.

At the beginning of 2015, more than 30 particle therapy centers, with a total of about 80 treatment rooms, were under construction worldwide. Half of these centers are in the United States and one-third in Asia. About 15 centers expect to start technical and/or clinical commissioning in 2015 and about half of them should be ready for patient treatment before the end of 2015.

article Therapy Co-Operative Group

n-profit organisation for those interested in proton, light ion and heavy charged particle radiotherapy



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Thank You!