SUMMARY OF THE COURSE
in master's programme Biomedical Engineering
Course 141.B07 Introduction to medical physics aspects of ion beam therapy

Summary of the lecture

Executed by: Daniela L.
Student ID number: -

Supervisor: Assistant Prof. Dipl.-Ing. Dr.techn. Albert Hirtl,
Univ.Lektor Mag. Peter Kueß,
Univ.Prof. Univ.Lektor Dipl.-Ing. Dr.techn. Dietmar Georg

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1 Introduction to Radiation Oncology, Ion beam therapy and medical (radiation) physics

1.1 View on Radiation Oncology

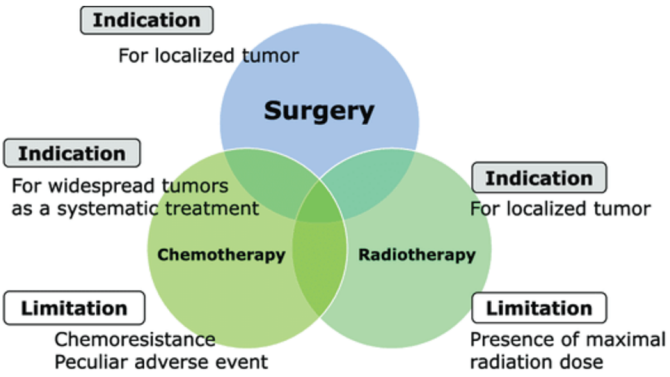


Figure 1: Cancer management.

External Beam Therapy The radiation source is located outside and can be an X-ray tube, for example. By means of various "filters" (collimators), the beam is precisely adapted to the size of the tumour. The patient must be placed precisely to ensure ideal radiation.

Brachytherapy The tumour is punctured with a hollow needle. A tube is attached to this needle. The radioactive source enters the needle directly into the tissue affected by the tumour via this tube. The radiation is therefore administered inside the patient.

Both therapy options require high geometric and dosimetric precision. In order to avoid incorrect irradiation. $\longrightarrow$ Non-linear dose response relation

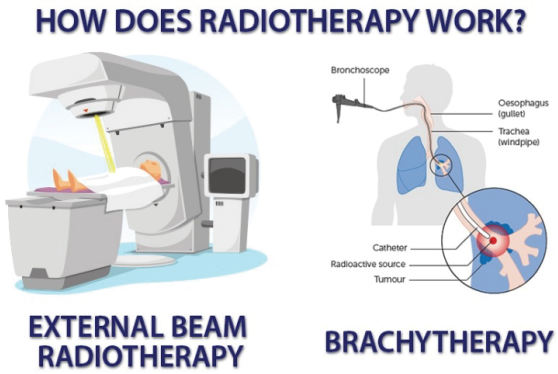


Figure 2: Two types of therapy, external beam and brachytherapy.

Radiation therapy is always image guided.

3D Shape, size of tumour

4D "Observation" of the tumour; Pictures before each irradiation to check what the tumour is doing and how it is developing. "Next level" Radiation needed for imaging also affects the tumour and healthy tissue

5D Observation of changes in tumour biology over time

Adaptive radiotherapy (ART) is the incorporation of repeated imaging and image driven decision into workflow. The automation needs standardization.

Motivation for particle therapy (= Ion beam therapy):

- Treatment of tumours close to radiation resistant organs (Organs at Risk (OAR)) possible
- Treatment of radiation resistant tumour possible
- Improved protection of normal tissue & Reduction of side effects
- Pediatrics (*Kinderheilkunde*)

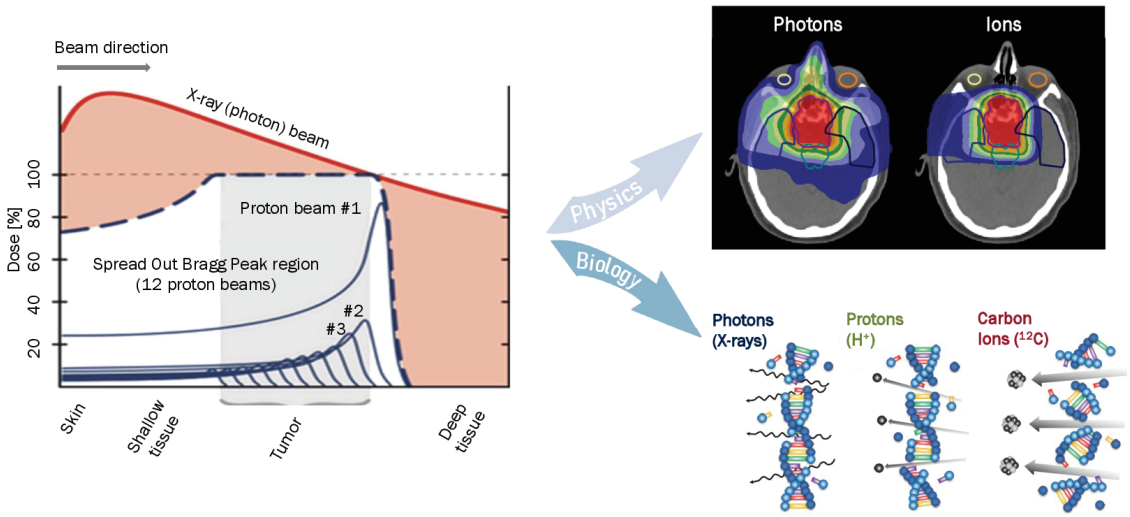


Figure 3: Ion beams therapy for superior cancer therapy.

1.2 View on Ion Beam therapy

General concepts of radiation oncology, patient workflow and task for professionals does not differ between photon therapy and particle therapy!

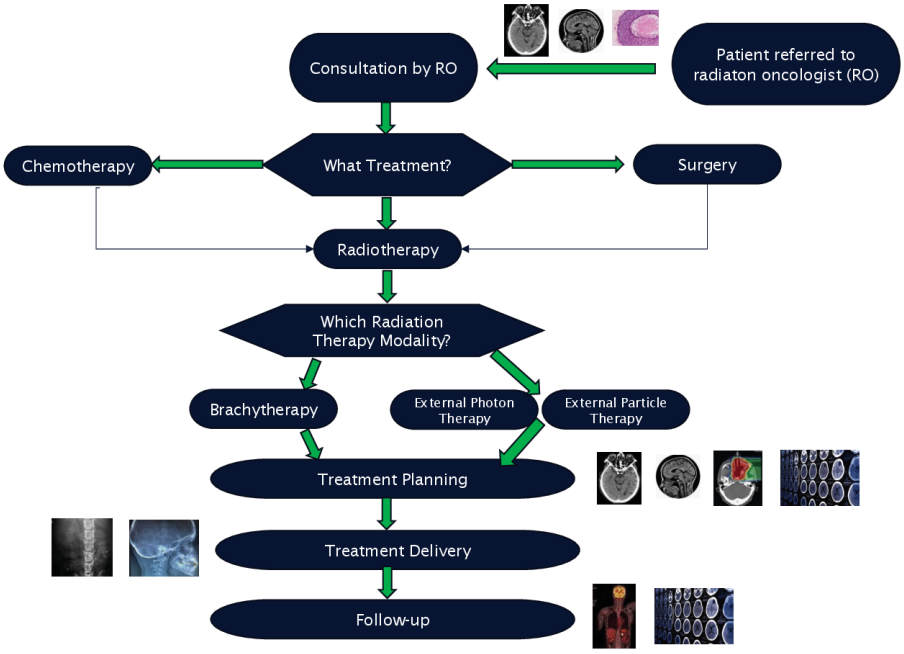


Figure 4: The workflow for a patient treatment.

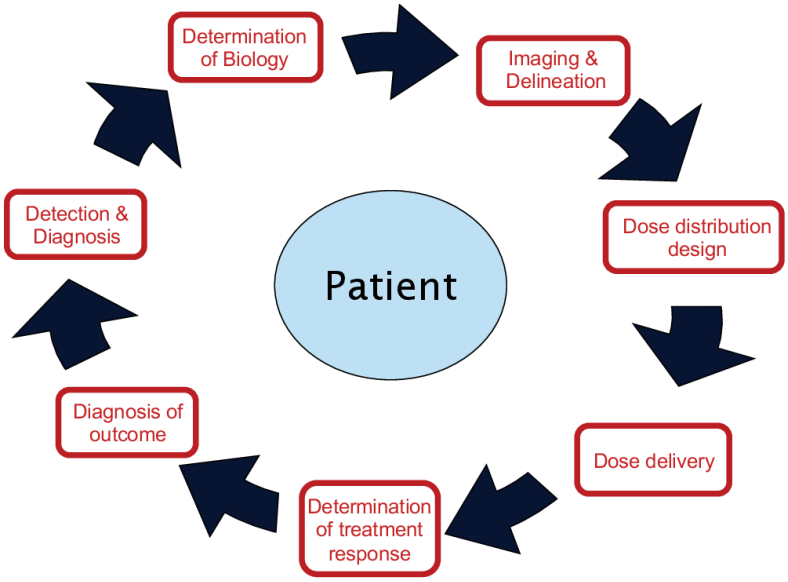


Figure 5: Treatment-cycle.

Indications for particle therapy:

- Reduce serious complications
  - especially relevant for tumours near the Central nervous system (CNS)
  - reduce secondary cancer risk, especially in children and adolescents

- Dose escalation and increased tumour control

1.3 View on Medical Physics

Medical Physics Expert (MPE) as an expert in radiation physics or radiation technology applied to exposure,...
...whose training and competence to act is recognized by the competent authorities.
...and who, as appropriate, acts or gives advice on patient dosimetry, on the development and use of complex techniques and equipment, on optimization, on quality assurance, including quality control, and on other matters relating to radiation protection, concerning exposure within the scope of this Directive".

Of the Medical Exposure Directive (MED) the following articles requires:

6.3 MPE be closely involved in radiotherapeutic practices.

7.1 MPEs have adequate theoretical and practical training.

2 Physics & Technology & Dosimetry - Basics

2.1 Motivation

Ion beam therapy has many advantages, one of which is that the depth of penetration is precisely defined and there is a very sharp pick that disappears quickly. Furthermore, tumours that are resistant to other treatments can be treated with this therapy. The exact depth also allows treatments close to OAR. The Relatvie biological effectiveness (RBE) is increased while the integral dose is reduced. The treatment can also be used for children, especially since one of the advantages is that the risk of secondary tumours is low.

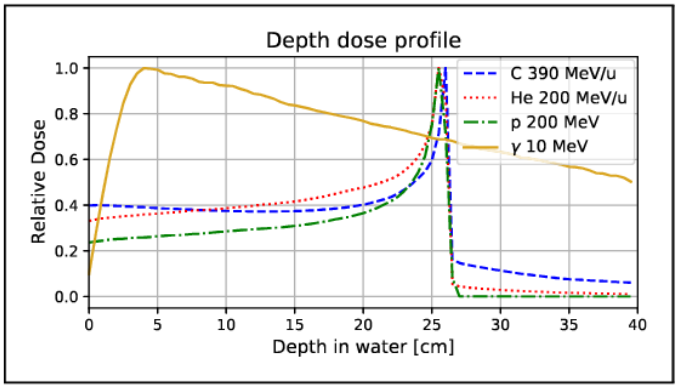


Figure 6: Depth dose of ion beam therapy.

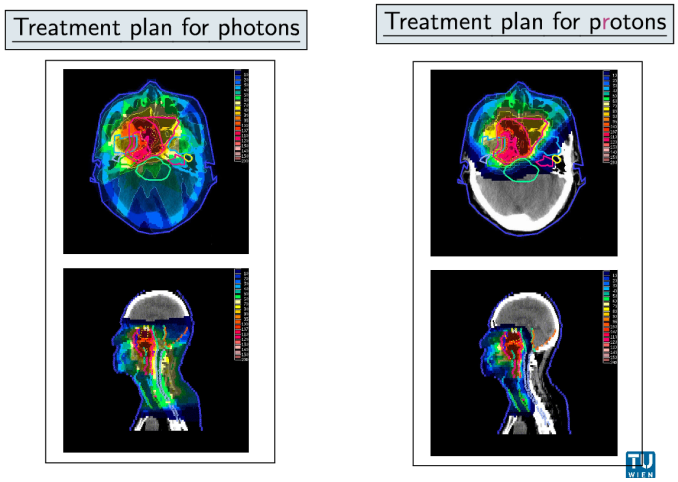


Figure 7: Difference between the treatment plans.

2.2 Nuclear reactions

2.2.1 Some general terminology

Table 1: Three important cases of nuclear reactions.

Energy ratio	Scattering	Description	Examples
E_Q=0	elastic	Kinetic energy of al particles is not change. incoming channel = outgoing channel	
E_Q>0	inelastic	more energy gets out than activation energy was supplied or in other words Kinetic energy increases at the expense of rest energy	fire, nuclear fusion, nuclear fission
E_Q<0	inelastic	endothermal reaction; Energy must be supplied from outside or in other words rest energy increases at the expense of kinetic energ	photosynthesis, nuclear reaction

inelastic scattering $\longrightarrow$ incoming and outgoing particle are identical!

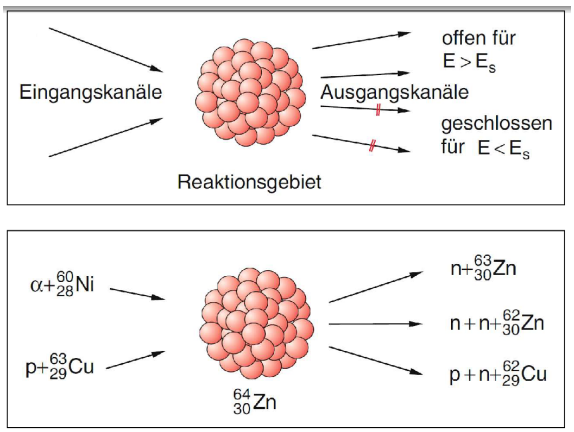


Figure 8: Projectile a (Ni, Cu) hits on target X (Zn), production ejectile b (Zn, Cu) and nucleus Y.

2.2.2 The cross section σ

———— Additional information NOT exam relevant ————

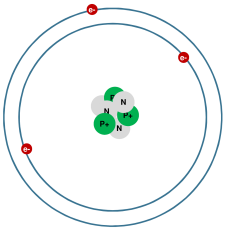


Figure 9: Aufbau eines Atoms. In der Mitte ist der Atomkern um den Kern sind die Schallen angeordnet.

Atomkern: Protonen und Neutronen
Hülle: Elektronen

Anzahl Elektronen = Anzahl Protonen $\rightarrow$ ungeladenes Atom
Anzahl Elektronen $\neq$ Anzahl Protonen $\rightarrow$ Ion

The cross section σ is the probability that a reaction between projectile a and target X take place due to an interaction. It depends on the reaction energy of the particle. σ is a "area" where projectil a and target X have to meet that a reaction can happen.

Important σ is NOT the geometric area defined by the nuclear radii!!!
It is the area in which the gravity of the cell nucleus acts and thus bremsstrahlung can occur.

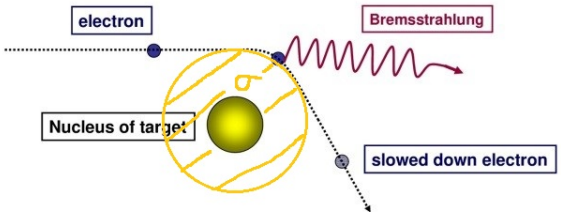


Figure 10: What is the cross section.

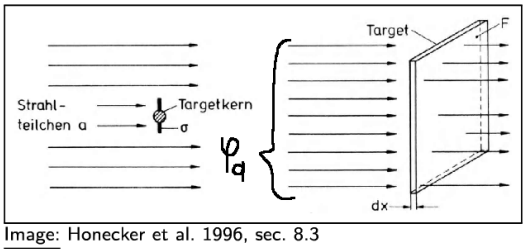


Image: Honecker et al. 1996, sec. 8.3

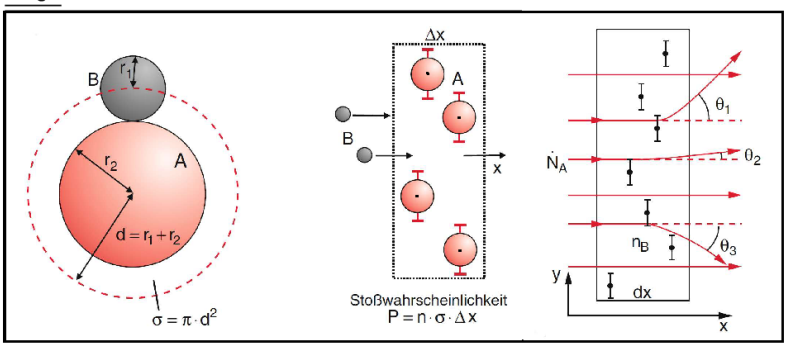


Figure 11: Cross section calculation. Top: projectils a hits target X. Bottom: The target X consists of several individual atoms which all have a certain diameter. If a particle is fired at the target from outside, an atom can be hit with a certain probability. Energy is lost as a result. Alternatively, the particle can be deflected if it is found near the nucleus.

The sum of all particles per area and time is called flux density φ_a. The particle flux decreases after traversing the target.

$$\sigma = \frac{dn_a}{\varphi_a \cdot n_X} \tag{1}$$

σ	cross section	[m^2 = b] 1b=1*10^{-28} m^2
dn_a	particle per second interact	[1/s]
φ_a	flux density	[1/m^2 s]
n_X	nuclei in the target	[ ]

When we integrate this over the layer thickness we get.

$$\varphi_a(x) = \varphi_a(0) \cdot \exp^{-\sigma N_X x} \tag{2}$$

$\varphi_a(x)$	flux density after target	[1/m^2 s]
$\varphi_a(0)$	flux prior to entering the target	[1/m^2 s]
σ	cross section	[m^2 = b] 1b=1*10^{-28} m^2
N_X	nuclei per m^3	[1/m^3]
x	Thickness of the target	[m]

The macroscopic cross section ($\Sigma = \sigma N_x$) is equivalent to the linear attenuation coefficient μ!

2.3 Interaction of charged particles with matter

2.3.1 Interaction of heavy charged particles with matter

———— Additional information NOT exam relevant ————

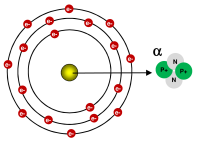
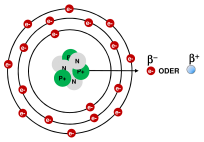
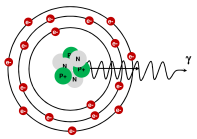
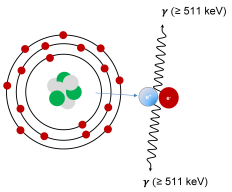
Strahlungsart	Bild	Aufbau des emittierten Partikels	Berechnung
α		2 Protonen + 2 Neutronen	$Z \longrightarrow Z-2$ $N \longrightarrow N-2$ $A \longrightarrow A-2$
β		1 Elektron/ 1 Positron	$\beta^+ : p \longrightarrow n + e^+ + v$ $\beta^- : n \longrightarrow p + e^- + v$ $EE : p + e^- \longrightarrow n + v$
γ		Photon	$Z \longrightarrow Z$ $N \longrightarrow N$ $A \longrightarrow A$
Annihilationsstrahlung (Paarvernichtung)		2 Photonen	$e^+ + e^- \longrightarrow 2\gamma(\geq 511\,keV)$

Table 2: Verschiedene Strahlungsarten.

An element is characterised by the number of protons which is called the atomic number Z. A neutral atom has the same number of electrons as protons.

Figure 12: A. . . mass number / number of protons and neutrons Z. . . atomic number / number of protons N. . . number of neutrons (A-Z) X. . . Symbol of element.

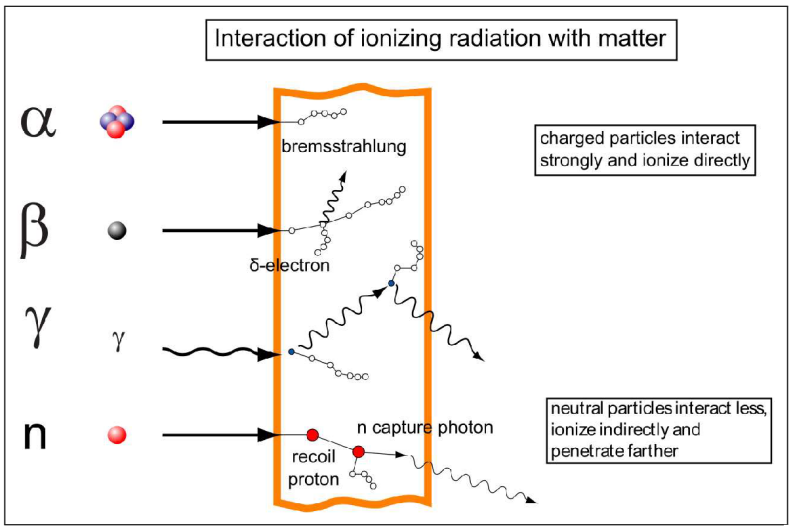


Figure 13: Interactions of ionizing radiation with matter.

Ionising radiation interacts with matter in various processes. The energy emitted by the radiation is converted into heat or leads to a change in the physical, chemical and biological properties of matter.

Incident particles exerts electrical force on orbital electrons. Three possibilities:

1. force strong enough to remove electrons from hull $\longrightarrow$ ionisation
2. force not strong enough for ionisation $\longrightarrow$ excitation
3. particle penetrates hull and interacts with nucleus $\longrightarrow$ bremsstrahlung

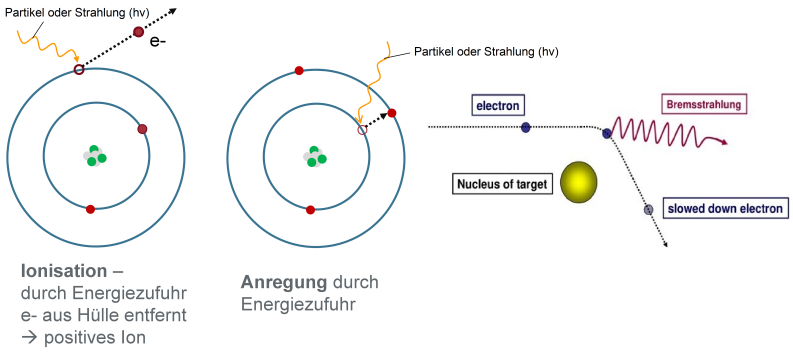


Figure 14: Types of interactions with electrons that are in the shells.

The mechanism of the mentioned process for the total energy loss is completely different for light (electrons and positrons) and for heavy charged particles (protons, α-particles, light nuclei) and depends strongly on the energy!

Two principle features to characterise passage:

1. loss of energy by the particle

2. deflection of particle from incident direction

Primarily result of two processes:

1. inelastic collision with atomic electrons and nuclei

2. elastic scattering from nuclei

Their cumulative result accounts for the effects observed!

Inelastic collisions are almost always responsible for the loss of energy. Since the particles transfer their energy during the collision. This either excites the shell electrons or knocks them out of the shell (=ionisation). In thin layers a high energy loss possible.

Average energy loss per unit path length $\longrightarrow$ stopping power = Bethe-Bloch equation ($-\frac{dE}{dx}$).

$$-\frac{dE}{dx} = 2\pi N_a r_e^2 m_e c^2 \rho \frac{Z}{A}\frac{z^2}{\beta^2}\left[\ln\left(\frac{2m_e\gamma^2 v^2 W_{max}}{I^2}\right) - 2\beta^2 - \delta - 2\frac{C}{Z}\right] \tag{3}$$

$\frac{dE}{dx}$	stopping power	[eV m^2/kg]
N_a	Avogadro number	[1/mol]
r_e	classical electron radius	[m]
m_e	electron mass	[kg]
c	speed of light	[m/s]
ρ	density of absorber	[kg/m^3]
Z	atomic number of absorber	[ ]
A	mass number of absorber	[ ]
z	charge of projectile	[eV]
β	$\frac{v}{c}$	[ ]
γ	$\frac{1}{\sqrt{1-\beta^2}}$	[ ]
v	instantaneous velocity of the particle	[m/s]
W_{max}	max. E transfer in single collision	[kg m^2/s^2]
I	mean excitation potential	[kg m^2/A s^3]
δ	density correction	[ ]
C	shell correction	[ ]

$$W_{max} \approx 2m_e c^2(\beta\gamma)^2 \tag{4}$$

Important for high energies $\longrightarrow \sigma$
Leading to a shielding from that electric field for electrons far from the path of the particle. Collisions with these electrons will contribute less than predicted by the Bethe-Bloch equation.

Important for low energies $\longrightarrow$ C
Accounts for situations where the velocity of the particle is comparable to or smaller than the velocity of the atomic electrons. At low energies the assumption that the electrons are stationary with respect to the incoming particle no longer holds and the Bethe-Bloch equation collapses.

Bragg curve depends when the Beth-Bloch equation is plotted as function of penetration depth, the amount of ionisation at end of the track will increase.

The rang number-distance curve shows the continuos energy loss of the particles. It depends on the type of material, particle type and the energy. The curve goes down over a certain spread of thickness.

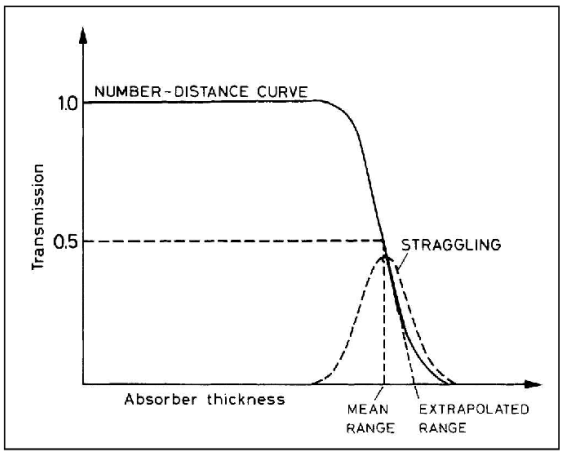


Figure 15: Distribution is Gaussian; mean value = mean range; mean range = midpoint in descending slope, half of the particles is absorbed; absorption of all particle s= drop to background level.

2.4 Interaction of photons with matter

2.4.1 Interaction mechanisms

Energy transfer from gamma-ray energy from the photon to an electron has three major types:

1. photoelectric effect, photon gives all of his energy to an electron and stimulates it to go in a energetically higher level. Predominant mode of interaction for gamma-rays of low energy.

2. Compton scattering, the wavelength from a photon get lower after the scattering. The electron is ejected from the atom. Klein-Nishina formula is used to calculate the cross section for Compton scattering.

3. pair product, In Coulomb field of a nucleus a x-ray or gamma photon can create matter-antimatter pair, electron and positron. Only in matter. Positron as anti-particle cannot exist long in “particle-world” and annihilates fast with electron; release of the rest-mass energy of both particles as two photons of both 511 keV at an angle of 180° this is used in a PET.

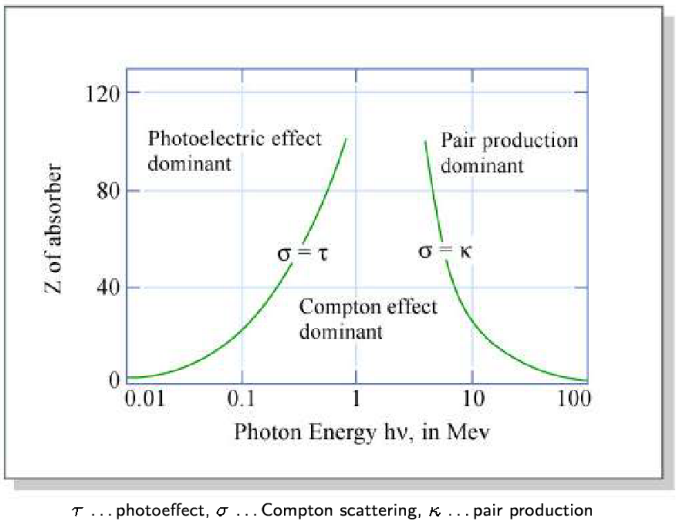


Figure 16: Interaction of the different effects.

2.4.2 Attenuation of photon beams

Weakening of the photon beam depends on the material and thickness of the absorber and the energy. After the passing though the absorber the photon intensity is exponential decreasing. Each interaction process remove photons from the initial photon beam either by absorption or by scattering them away from the detector.

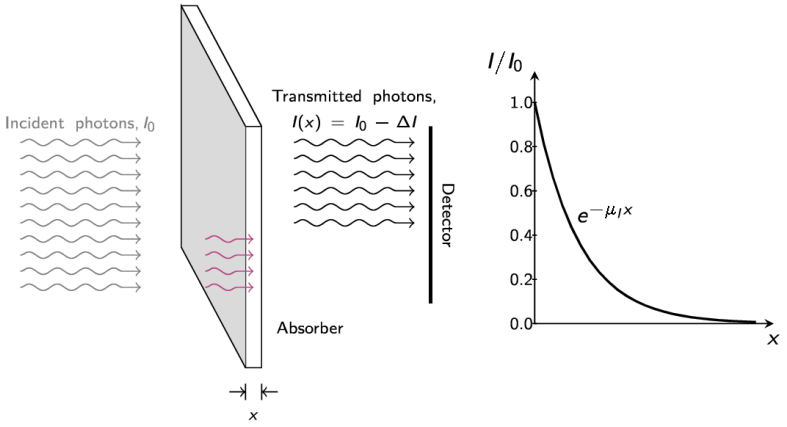


Figure 17: Weakening of photon beams.

$$I(x) = I_0 \exp^{-\mu x} \tag{5}$$

$I(x)$	transmitted photons	[ ]
I_0	photons at beginn	[ ]
μ_I	linear attenuation coefficient	[1/m]
x	thickness of absorber	[m]

Linear attenuation coefficient is limited since it varies with the density of the absorber to avoid this problem μ_I is divided by the density (ρ).

Table 3: Some Attenuation factors.

Material	I(x)
Adip. tiss	41
Water	39
Lead	0
Air	90

2.5 Radiation detectors

2.5.1 General properties of detectors

The radiation must interact with (be stopped in) the detector material. In most detectors this results in the appearance of an amount of charge Q.

The energy distribution of the incident radiation is the radiation spectroscopy. Important parameters are:

- energy resolution, response of detector to a mono energetic source of radiation. If the same number of counts are recorded is the area under the curve the same, only the widths differs. If we have a large width the amount of fluctuation from pulse to pulse is also large. Fine details can be resolved if the width is small.
- detection efficiency, radiation detectors give output pules for each quantum of radiation interacting in it. Charged particles interact immediately upen entry into the detector. Interaction probability of uncharged radiation is low. See below formula for absolute counting efficiency (ϵ_{abs}) and intrinsic counting efficiency (ϵ_{int}).
- dead time, Minimum amount of time that must separate two events in order that they can be recorded as separate events (Resolution). Problems by higher counting rates.

$$\epsilon_{abs} = \frac{number\ of\ pulses\ recorded}{number\ of\ radiation\ quanta\ emitted\ by\ source}$$

$$\epsilon_{int} = \frac{nubmer\ of\ pulses\ recorded}{number\ of\ radiation\ quanta\ incident\ on\ detector}$$

2.5.2 Gas-filled detectors

Ionisation radiation creates electron-ion pairs. This pairs drift to the electrodes and create an electrical current. Number of electron-ion pairs is proportional to the height of the signal. Small number of charge carriers results in a small signal. This detector is inefficient for γ-rays. The ionisation chamber works only in the saturation region, below this there is the recombination region where no signal is producing.

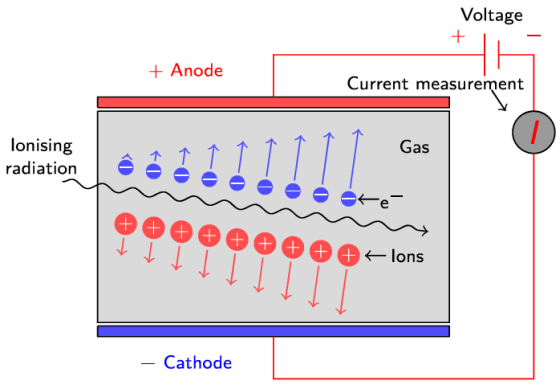


Figure 18: Functional principle of a ionisation chamber.

Proportional counters are special optimised ionisation chambers which operates with higher voltage. The radiation creates electron-ion pairs. This happens when a charge avalanche (*Lawine*) is triggered. In this process additional gas atoms are ionised and drift slowly to the cathode and gets collected. The electrons between the electrodes makes it possible that a current flow. For this type of ionisation chamber the signal is almost crated by ions. This detector is inefficiency for high energetic γ-rays.

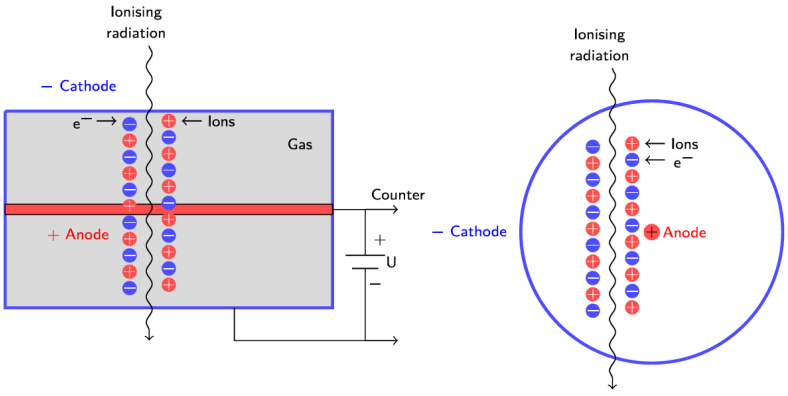


Figure 19: Functional principle of a Proportional counter.

Electrons released by the interaction with UV-photons drift to the anode and cause a charge avalanche in its vicinity. Electrons are quickly collected at the anode and cause a constant signal which is independent of the photon energy so the proportionality is lost. This detector is only for counting of events.

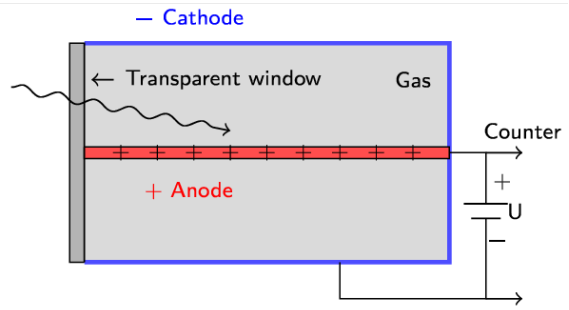


Figure 20: Functional principle of a Geiger-Müller detector.

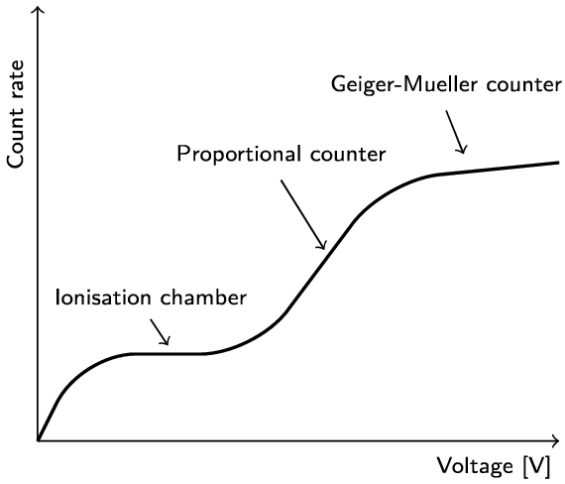


Figure 21: Operating range of gas-filled detectors.

2.5.3 Scintillation detector principles

To convert the ionisation radiation in a measurable quantity we need scintillator detectors. This detectors has to components, the scintillator which converts the ionisation radiation into visible light and the photomultiplier which converts this light into a electrical impulse.

Scintillators It gives inorganic and organic scintillators the choice of the material is important to get a high light output. The ionisation radiation excitant hull electrons (e gets in higher state). This energetically higher electrons are stored in the scintillator material. When the material is heating up the electrons get triggered to emit luminescence photons. The sum of this luminescence photons is proportional to the absorbed energy. It is also possible that the energetically higher electrons go back to her ground state and they emits luminescence radiation (= de-excitation).

2.5.4 Photomultiplier tubes - PMTs

The scintillator convert gamma photons in many light photons. This luminescenc radiation hits a single electron out of the photo-cathode. The Photomultiplier is a system of many dynodes.

When the single e^- hits the dynode 2 e^- appears. The dynode rise ever electron um 2 more in the Photodetector. At the end the Electronic system processes the signal and produce the image by the incoming data.

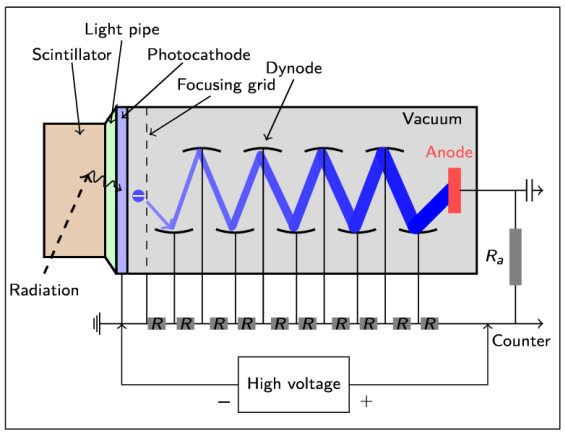


Figure 22: Functional principle of a Gamma-camera.

2.6 Components and design of ion beam therapy centres

2.6.1 Medical accelerators

Cyclotrons Proton in the middle. The magnetic field produce the Lorenz force = Centre pedal force. The proton starts to turn in a helix direction. The proton get a speed till he flies out from the cyclotron.

Synchrotrons Ring is filled whit ions of few MeV. The ions get accelerated to a desired energy. When the desired energy is reached, the particles are removed from the beam line.

2.6.2 Beam line design

Monoenergetic ions produce a single Bragg-paek. This peak has a very high dose in only a very small area. Otherwise, the dose is very low. Since tumours do not consist of individual points, it is usually necessary to irradiate a larger region. To achieve this, several individual Bragg peaks are superimposed. For this, the beam must be modulated. This can be done in two ways:

- passive beam modulation; changing of beam energy and material in the beam, use passive elements (= Collimator) to fit a 3D target volume
- active beam modulation; Target volume is split in voxels and is scanned, use of two dipole magnets which deflect the beam, the small beam spot scan the target area

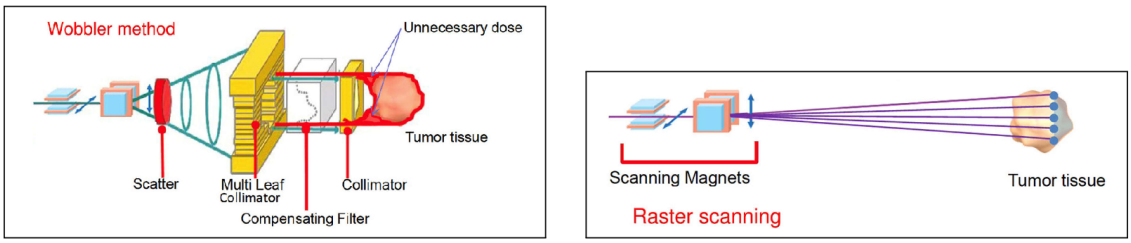


Figure 23: Left: passive beam modulation; Right: active.

2.7 The MedAustron facility

The MedAustron use proton and carbon ion beams for cancer therapy and non-clinical research. The carbon ions have a 27 cm depth dose in water.

3 identical electron cyclotron resonance (ECR) sources are used for $H_3{}^+$ and C^{4+}, one source is empty.

The radio-frequency quadrupole (RFQ) has a extraction energy of the particles from 400 keV. The interdigital H-mode-structure has a extraction energy of the particles from 7 MeV. A Stripping foil, at the end of the injection chain, removes remaining electrons from the ions.

2.8 Measurement of energy dose

2.8.1 Radiation fields

A radiation source emits ionising radiation and thus creates a radiation field. If there are substances in it then energy is transferred via various interaction processes. The task of dosimetry is to determine the energy transferred to the material. The basic quantities are the energy dose and the energy dose rate

Radiation fields in the vicinity of sources are describe by:

- number of each location
- direction
- energy

Characterisation of radiation field, scalar radiometric quantities:

Number of particles N Number of particles that are emitted, transferred or received.

Particle flux $\dot{N}$ Particle per time interval transported in the radiation field.

Particle fluence Φ Particles that traverse an area.

Particle flux density φ Number of particles form all directions and within the time frame that orthogonally traverse the area.

Particle fluence Φ Integral of particle flux density over time.

Particle radiation $\dot{\Phi}_\Omega$ Fluence rate of particles propagating within a solid angle around a certain direction.

Energy R Energy of particles that are emitted, transferred or received.

Energy flux $\dot{R}$ See Particle flux.

Energy fluence Ψ See Particle fluence.

Energy flux density ψ Sum of energies without rest mass within the time frame that orthogonally traverse the area.

Energy fluence Ψ Integral of the energy flux density over time.

Energy radiance $\dot{\Psi}_\Omega$ Energy fluence rate of particles propagating within a solid angle around a certain direction.

Characterisation of radiation field, vector radiometric quantities:

Vector energy flux density $\overrightarrow{g}$ Sum of vectors for all particles that orthogonally traverse the area of the elementary sphere around a radius in the time t.

Vector energy fluence $\overrightarrow{G}$ Integral of the vector energy flux density. It describes the energy that is transported through the directed area element.

Dosimetric quantities are products of radiometric quantities and interaction coefficients.

2.8.2 Energy dose

Lineal energy transfer (y) for micro-dosimetry (nm scale) $\longrightarrow$ stochastic
linear energy transfer (LET) for macro-dosimetry (mm or cm scale) $\longrightarrow$ non-stochastic

Absorbed dose or Energy dose D (J/kg = Gy) The absorbed dose is defined as the amount of energy stored in a substance by ionising radiation.

Absorbed dose rate or energy dose rate $\dot{D}$ **(J/kg s = Gy/s)** The absorbed dose rate is the rate at which an absorbed dose is absorbed and a dimension for the intensity of the radiation dose.

Kinetic enrgy released in matter Kerma = K (Gy) Describes how much kinetic energy is transferred to matter in a mass element.

Bremsstrahlungs loss B (Gy) The energy dissipated by bremsstrahlung is called bremsstrahlung losses and represents a type of radiation loss.

$$D = K - B - \frac{1}{\rho}\overrightarrow{\nabla} \cdot \vec{G}_{ch} \tag{6}$$

D	Absorbed dose	[Gy = J/kg]
K	Kerma	[Gy]
B	Bremsstrahlungs loss	[Gy]
ρ	Density	[kg/m^3]
$\vec{G}_{ch}$	vector energy fluence of charged particles	[J/m^3]

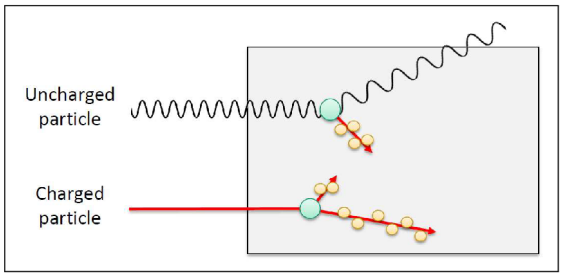


Figure 24: Blue blobs: Conversion of energy, Yellow blobs: Deposition of energy.

2.8.3 Measurement of dose

Since the dose in tissues cannot be measured directly, two alternative methods are used. Detectors are brought into the vicinity of the target site through body orifices and measure the radiation there. The energy dose is calculated from the ion dose using certain conversion factors.

Dosimetric probe is a radiation detector with a sensitive volume filled with a substance yielding a dose or dose rate dependent measurement value. The probe is placed at a location in the material. The measurement value (M) gives information about the energy dose (D_P) or dose rate. Under certain conditions the energy dose (D_M) in the material at the location without probe can be determined $\longrightarrow$ correction factors. M $\longrightarrow$ D_P $\longrightarrow$ D_M

If there is equilibrium of any electrons transported in or out, then the dose in the probe is generated solely by the photons. Photons are secondary ionising particles. $\longrightarrow$ secondary particle equilibrium

For photon radiation fields and with secondary particle (electrons) equilibrium, the energy dose can be calculated from the energy fluence of photons. The probe should not have any influence on the energy fluence.

$$D = \frac{\mu_{ab}}{\rho}\Psi \quad \dot{D} = \frac{\mu_{ab}}{\rho}\psi \tag{7}$$

D	Absorbed dose	[Gy = J/kg]
μ_{ab}	mass absorption coefficient	[1/m]
ρ	Density	[kg/m^3]
Ψ	Energy fluence	[J/m^2]
$\dot{D}$	Absorbed dose rate	[Gy/s = J/kg s]
ψ	Energy flux density	[J/m^2 s]

Energy dose measured in probe should be the same as energy dose in material. For high energetic ionising radiation the secondary charged particles equilibrium is not fulfilled. For this type we us the Bragg-Gray-principle.

Dose measurement is reduced to a measurement of charge. Chambers using charged particles equilibrium are mainly used for photon radiation below 3 MeV. Chambers are surrounded by a wall made of the same gas with width equal to the maximal range of the secondary

charged particles. Bragg-Gray chambers psses very thin walls and are for energy ranges 0.1 MeV to 100 MeV.

3 Dosimetry

Dosimetry is needed to verify that the patient is receiving the required dose. It is also used to protect staff from radioactive contamination.

Ionisation and excitation: Biological effect $\longrightarrow$ number of ionisations
Photons and electrons: Biological effect $\longrightarrow$ energy absorbed

It can be measured:

- Absorbed dose, delivered dose for the patient
- Relative dose, e.g. depth dose, homogenity of the field

Table 4: Types of Dosimetry.

Name	Description	Short
Absolute Dosimetry	Measurement of a quantity whit a instrument of the highest metrological quality.	direct determination of dose; performed in primary laboratories (= calibration laboratory)
Reference Dosimetry	Measurement of the absorbed dose in water. Using a ionization chamber and a beam in the user's institution. Correction factors k is needed.	performed at user's institution; apply initial calibration factor; correction factors required
Relative Dosimetry	Measurement under non-reference conditions like depth dose normalized to maximum value. No calibration coefficient. Use of different detectors possible.	Non-reference conditions; No calibration required; Relative to a known parameter

Absorbed Dose D [Gy] In relation to the mean energy added (mean value of all rays supplied), the absorbed dose is the energy absorbed by the medium. Water is similar to human tissue, hence it is measured in water.

Bragg-Gray Theory Cavity theory is the basis of operation for ionization chambers used in reference dosimetry. Cavity theory relates measured dose in a cavity, such as an ion chamber, to dose at the same point in the medium in absence of the cavity. Bragg-Gray theory relates dose to the medium, to dose to the cavity fill gas, via the ratio of mass collision stopping powers (which is the ratio of stopping power to the material density.) between the medium and gas. Assumptions:

1. Charged particle equilibrium exists

2. All electrons causing ionization in the cavity (= Ionization chamber) arise from the phantom material (= water)

3. Secondary electron spectrum is unchanged by presence of cavity (= ionisation chamber)

4. Energy of secondary electrons created inside the cavity (=ionization chamber) are deposited locally

2) and 3) imply a small cavity volume
4) requires large volume to collect all electrons
Spencer-Attix Cavity Theory resolves Bragg-Gray issues, so it applies for small cavities and Uses cutoff energy.

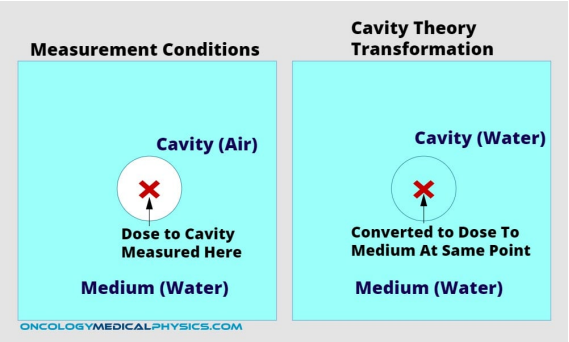


Figure 25: Bragg-Gray Cavity Theory. The cavity is the ionization chamber filled whit air. The phantom material is the medium water.

Interactions:

- Indirectly ionising particles
  - photons
  - neutrons
- Directly ionising particles
  - electrons, positrons
  - protons, antiprotons, ions

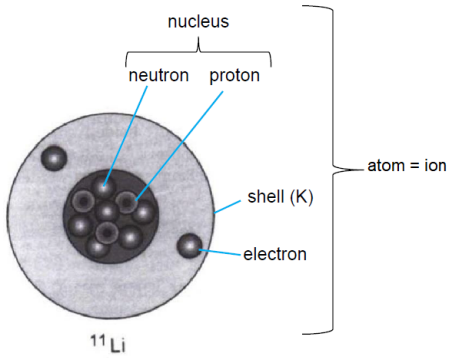


Figure 26: Picture of an atom.

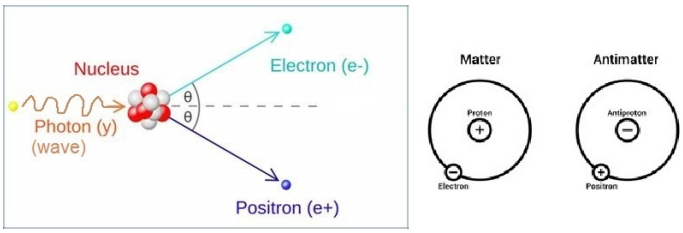


Figure 27: Left: Photon Radiation of an atom. Right: In the Syncrotron the matter gets to antimatter.

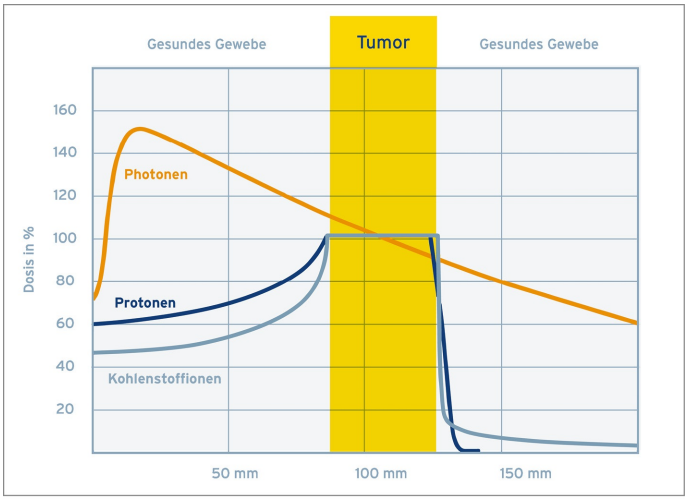


Figure 28: Differences Photon vs. Particle Dosimetry. RBE for protons = 1.1.

Carbon Ions has a less coloumb scattering the spot size is very small and the Linear energy transfer (LET) is high. Variable RBE.

3.1 Uncertainties

Guide to the expression of uncertainty in measurement (GUM) is a framework for evaluating and expressing uncertainties of measurement, a international standard (=ISO). GUM ensure that measurements are accurate, reliable and traceable to international standards.

Two typs of unvertainities:

Type A is calculated from a series of observations where the data was measured directly by oneself; standard-, random/statistical uncertainty; calculation of arithmetic mean, standard deviation and degrees of freedom

Type B is evaluated using available information; systematic error / non-statistical error; Calibration reports, manuals, industry guidelines

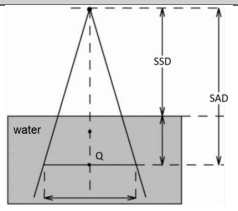
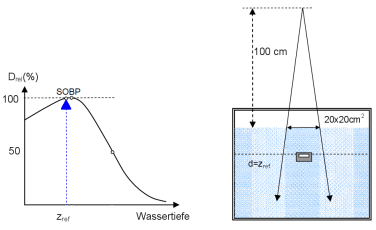
3.2 Detector Calibration

Various standards are available for the calibration of detectors. It is important that the calibration is carried out by a major laboratory. Furthermore, the laboratory must provide information on the standard and method used for the calibration. All this information, including the correction factor, can be found on the calibration certificate.

$$D_w = M \cdot N_{D,w} \tag{8}$$

D_w	Dose	[Gy]
M	Detector reading	[C]
$N_{D,w}$	Calibration factor	[Gy/C]

Table 5: Geometry of dose measurement.

Radiation	Picture	Method
Photons		source-surface-distance (SSD) or source-axis-distance (SAD)
Protons and carbon-ions		Measurement in reference depth in the Spread-out Bragg-peak (SOBP) in water

For any measurement of dose the reference conditions are necessary. This conditions includes distance and depth, field size, material and dimension of the used phantom, temperature, pressure and relative air humidity. The calibration factor applies to a specific set of reference conditions values. If these are not exceeded or fallen short of, no further corrections

are necessary. Furthermore, the parameters, except for air pressure, air humidity and dose rate in 60-Co, can be influenced manually. If the values vary too much, correction factors must be taken into account when calculating the dose (D_w).

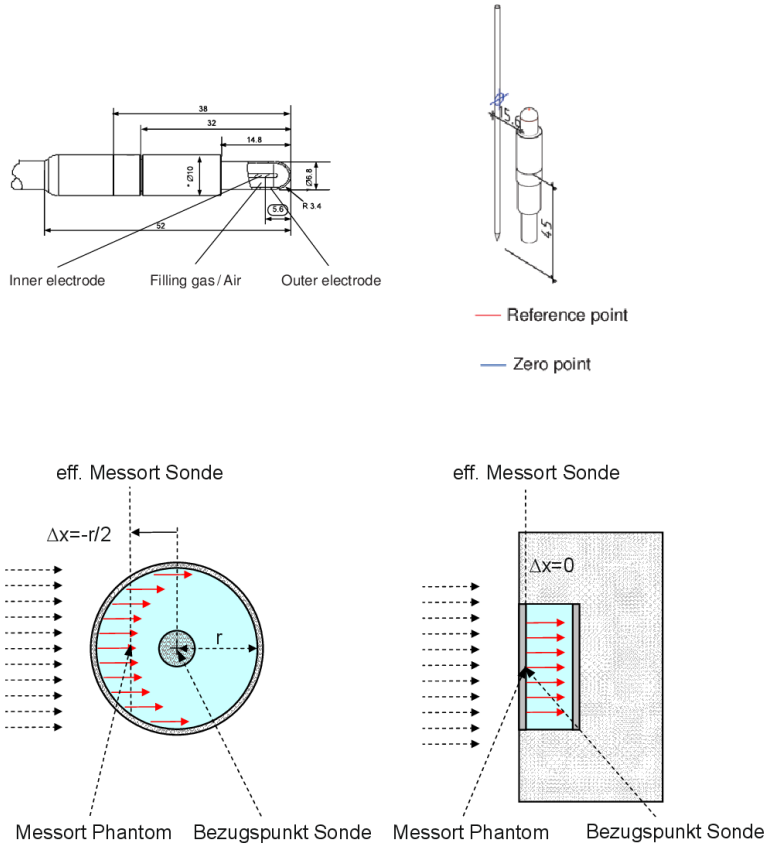


Figure 29: Point of Interest $\neq$ Position of detector. Top: Structure and 3D image of an ionisation chamber. Bottom Left: Cylindrical ionization chamber Right: Plane-parallel ionization chamber.

Point of interest ($\triangle x$) Position where dose shall be determined

Reference point of probe Middle of central electrode. Center of backside of entrance window.

$$k_{p,T} = \frac{p_0}{p} \cdot \frac{T}{T_0} \tag{9}$$

$k_{p,T}$	Correction factor for air pressure and temperature	[ ]
p_0	Air pressure during calibration	[Pa]
p	Air pressure during measurement	[Pa]
T_0	Temperature during calibration	[K]
T	Temperature during measurement	[K]

If the pressure is high or the Temperature low more atoms in probe this means more ionization occurs. The change of the gas volume changes the dosimetric characteristics.

The beam quality correction factor (k_{Q,Q_0}) is defined as the ratio, at the qualities Q (can be proton or carbon-ion beams, photon, electrons) and Q_0 (is the 60-Co reference beam quality). To get k_{Q,Q_0} you can do reference measurments in the beam quality Q and Q_0 or Use N_{D,w,Q_0} and theoretically derive k_{Q,Q_0}. Because of the lack of experimental data for carbon ions, it gives no carbon-ions standard lab, beam quality correction factor (k_{Q,Q_0}) must be calculated. For this it gives Tables whit beam quality correction factors.

$$D_{w,Q} = M_Q N_{D,w,Q_0} k_{Q,Q_0} \tag{10}$$

$D_{w,Q}$	Absorbed dose to water in beam quality Q	[Gy]
M_Q	Detector reading in beam quality Q	[C]
N_{D,w,Q_0}	Calibration coefficient	[Gy/C]
k_{Q,Q_0}	Beam quality correction factor	[ ]

Because not all detectors are calibrated in a standard laboratory for this a cross-calibration can be performed. You must do 4 steps:

1. Irradiate reference detector; Warm-up of detector and zeroing of electrometer, 3-7 measurements of identical irradiation plan
2. Irradiate Detector of interest; Warm-up of detector and zeroing of electrometer, 3-7 measurements of identical irradiation plan irradiation plan
3. Irradiation of reference detector; 3-7 measurements of identical irradiation plan
4. $N_{D,w}[Gy/C] = \frac{Values\ \ reference\ \ detector}{Values\ \ interested\ \ detector}$

3.3 Beam monitor calibration

Calibration of particle beams are mostly based on broad fields, fore scanned beams it is more practical to calibrate in terms of Does area product (DAP).

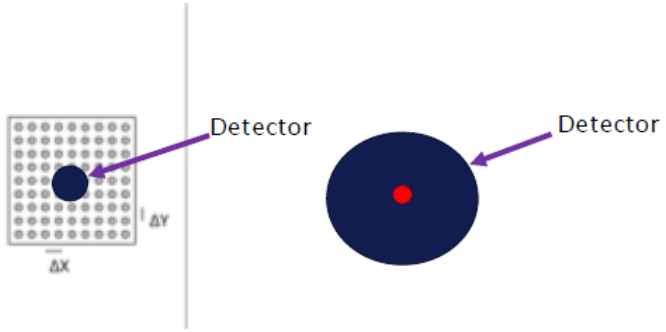


Figure 30: Scanned beams. Left: single layer method Right: single spot method

DAP by Single Layer method Same number of particles per beamlet. Constant shape of pencil beam at different positions. Detector close to ideal point detector.

DAP by Single spot method Using of a large area ionisation chamber (LAIC) to measure the absorbed dose.

3.4 Relative Dosimetry

Is used for:

- Routine daily clinical physics activity
- Beam line commissioning
- Collecting data for Treatment Planning System (TPS)
- Periodic QA

Table 6: Beispiel für die Beschriftung einer Tabelle.

Dimension	Resolution	Examples
1D	one signal at specific location	Ionisation chamber, solid stat detector
2D	spatial resolution in 2D	Films, detector array line
3D	spatial resolution in 3D	Gels, detector array block

Films Film changes color when exposure to radiation. It is used for relative and absolute dosimetry and have a high spatial resolution. It must be stored dry and dark. Orientation should be maintained at all times as there is some percentage difference in scanning portrait/landscape.

Range Measurements Using one stationary detector and using of objects (shielding) in front of the detector. Or one moving detector which moves in beam direction. Energy = Range. Water equivalent thickness (WET) is a way to determine how thick a material needs to be to have the same properties as water.WET can be calculated and measured by range shift.

3.5 QA

QA is subject to certain guidelines, laws and standards. Furthermore, it is not only regulated how, what and how often a QA must be carried out, but also what must be documented in order to enable complete traceability. The QA should be designed as easy as possible to enable a fast working method, but still be as precise as possible.

Must included in the report:

1. Time schedule
2. Measurement
3. Evaluation & analysis
4. Report & Alert

4 Imaging

4.1 Motivation

Imaging is for:

- To create a treatment planing and delineate structures
- Plan Adaptions
- Beam Verification

If you can't see it, you can't hit it, and if you can't hit it, you can't cure it.

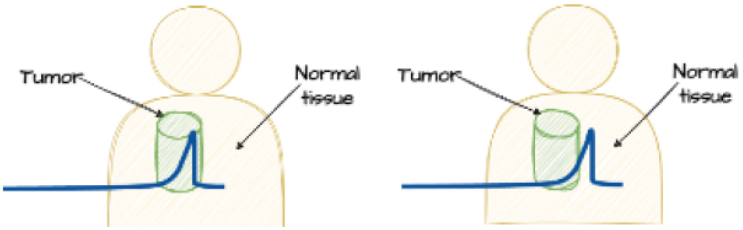


Figure 31: For ion beam therapy a high precision in the monitoring is needed. If you hit very precise you can also miss very precise!

4.2 Physical Background

X-ray Using Photo electrical effect, Compton scattering, Pair production to create the radiation. X-ray diagnostics is based on the different absorption of X-rays by the various human tissues. Bones have a high attenuation, Soft tissue is low.

CT Many single X-ray imaging in different angels. Algorithms needed for 2D reconstruction. Attenuation coefficient = Haunsfield unit. The Hounsfield scale describes the attenuation of X-rays in different tissue types in CT, in relation to water and air as reference values.

Portal Imaging For penitent positioning before irradiation whit photons. Image is compared to the planing image (CT).

Magnetic resonance imaging (MRI) Photon has spin and charge and behaves like a small rotating magnet. When applying the photon in a external magnetic field all photons align themselves identically to the magnetic field. The alignment of the nuclear spins alone would not produce an image representation. Therefore, a short high-frequency pulse is irradiated perpendicular to the direction of the magnetic field. The pulse has the following consequences: The nuclear spins aligned along the outer magnetic field are briefly made to "wobble" or "flip". The gyroscopic motion of all atomic nuclei is briefly synchronised. This creates a transverse magnetisation perpendicular to the field lines of the external magnetic field. This movement then emits a measurable signal in the form of an alternating voltage until the movement has subsided.

Diffusion weighted MRI (DWI) The DWI sequence is a combination of spin-echo sequence and echo planar imaging. It measures Brownian molecular motion (non-directional thermal motion of particles in liquids or gases) or diffusion of water molecules. The respective contribution of each factor depends on the tissue and the pathology. The further a water molecule diffuses during the sequence, the more it is exposed to different gradient strengths and the more it is dephased, which reduces the MRI signal. The lower the diffusion, the brighter the DWI signal and the darker the Apparent diffusion coefficient (ADC). $DWI = T2 \cdot \exp^{-bADC}$

Dynamic Contrast Enhanced MRI (DCE) Tracer or contrast agent is administrated into blood stream before or during acquisition series of images. MRI signal changes with changed contrast agent concentration. Gives information about physiological tissue characteristics such transport from blood to tissue and blood volume.

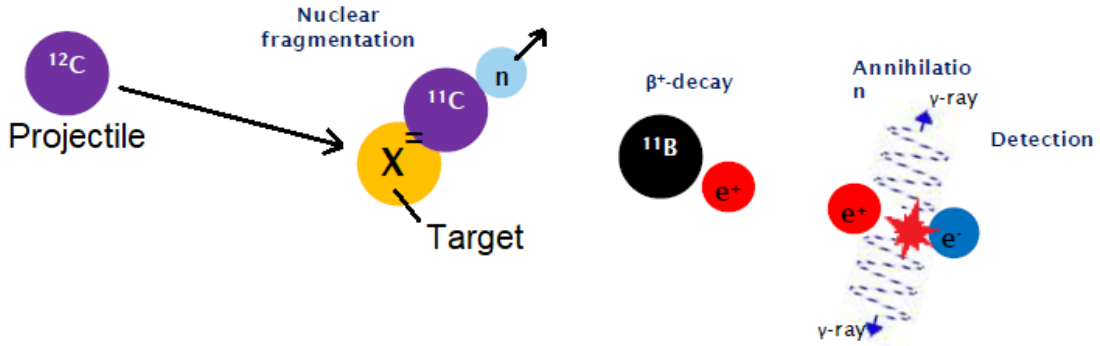
PET For a PET examination, the patient is given a radiopharmaceutical is administered to the patient. During the decay of a proton in the nucleus, positrons are released which quickly hit an electron in the environment. This releases so-called gamma radiation photons (annihilation radiation), which are collected by a PET scanner and processed into an image by means of a computer. The photons radiate at an angle of 180° and are therefore only used as a signal if two opposing cameras receive a signal at the same time.

4.3 Particle Therapy PET

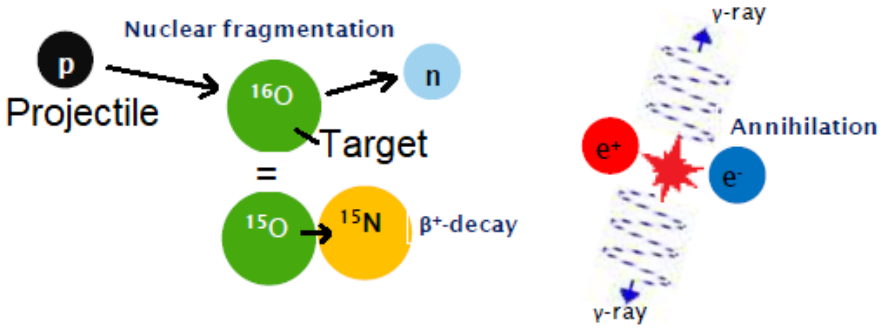
No contrast agent is administrated to the patient, the recorded activity results from nuclear interactions between particle beam and tissue.

Principle of Particle therapy PET (PT-PET):

1. Nuclear fragmentation
    - Projectile fragmentation: Projectile loses on neutron when interacting whit target.



    - Target Fragmentation: Projectile knocks out one neutron form target.



2. β^+-decay, Production of one positron (e^+)
3. e^- e^+ annihilation, γ-ray of 511 keV
4. Detection whit PET

Activity $\neq$ Dose

In order to compare the planned dose with the measured activity, it is necessary to take an intermediate step. A Monte Carlo simulation of the beta decay is used to calculate how large the activity should be. This calculated activity can be compared with the measured activity.

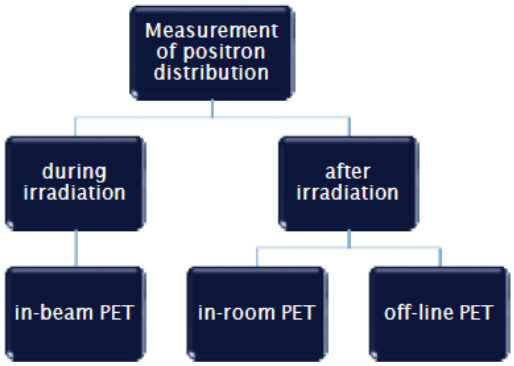


Figure 32: Different methods of PT-PET.

In-beam PET Integration on PET cameras into beam line. PT-PET measurements only possible during beam spills.

Off-line PET Standard PET-CT for verification. High influence of metabolic processes.

In-room PET Better counting statistic an less washout.

4.4 Synthetic CTs

Air and bone is better visible on CT, soft contrast information on MRI is better. The CT is used for dose calculation. To reduce the image radiation for the patient and no uncertainties appears you can calculate out of a MRI image a synthetic CT image. For this today deep

learning is used. An Artificial Intelligence trains itself using a given data set.

The transfer of photon or proton experience with MRI only to carbon-ion therapy is not possible because of:

- complex patient positioning
- unique anatomical situations
- limited training data

5 Radiation Biology - Part 1

5.1 Introduction & (molecular) background

Physical and chemical reactions in response to radiation run their course within the first minutes. Biological response to radiation starts within the first second and lasts an entire human life span. Biological response includes sensing of Deoxyribonucleic acid (DNA) damage, DNA damage repair and all cellular reactions involved in tumor control, early or late NT reactions and carcinogenesis.

Direct radiation effects Radiation hits DNA directly and disrupt molecular structures. Critical damaged DNA will lead to cell death. Mainly caused by high dose.

Indirect radiation effects The radiation hits an intracellular water molecule and produces a free radical. The free radical has a unpaired electron in the structure which interact whit the DNA and cause a structural damage. Main mechanism of photons, electrons and protons.

Waters Experiment shows that the Target structure for any radiation-based medical intervention with the goal of killing cells must be the DNA.

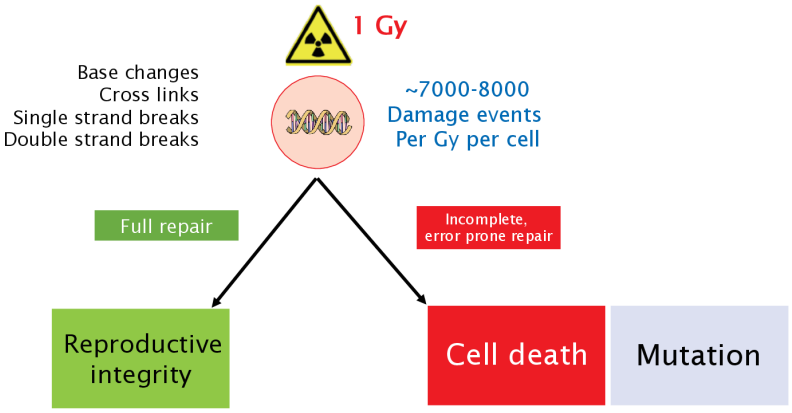


Figure 33: Radiation induced DNA damage.

Helium ions are good because they have a reduced beam broadening and sharp beam penumbra. The LET range is relatively low.

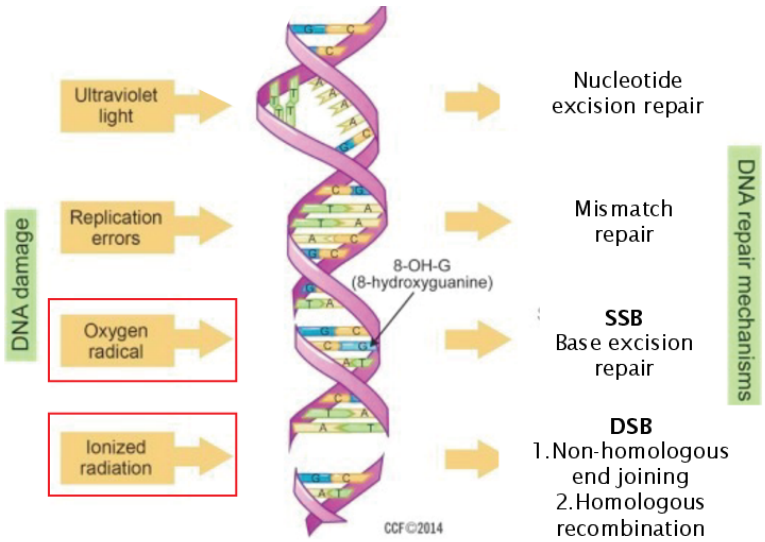


Figure 34: DNA repair mechanisms. SSB= Single strand breaks; DSB= double strand breaks.

Programmed cell death (= apoptosis) is a controlled an regulated response to injury, disease and part of normal development. This effect should occur in tumours after radiation treatment. Necroses is the death of a cell after a trauma and is not wanted after treatment.

Apoptosis Eliminates damaged, infected or redundant cells

Autophagy Natural, conserved degradation of cells.

Necrosis Form of cell injury which results in the death of the cell.

Non-apoptotic proframmed cell deaths Other causes of cell death.

5.2 "Biological" optimization in ion beam therapy

Louis Harold Gray discovered the RBE. This compares how effectively a radiation source kills cells compared to X-rays. The LET model is used to calculate how many cells survive. α is dominant for low doses. β is dominant for high doses. For ion-beam therapy the RBE models all based on existing in-vitro and in-vivo data.

The amount of radiation induced damaged generated depend on:

- Radiation type
- Dose and fractionation
- LET

Local effect model (LEM) The nucleus in a cell is divide into smaller sub-volumes. Sub-volume assigned with a threshold value and calculation of a cell survival curve from linear quadratic model. One calculation whit Photon track the other whit Carbon ion

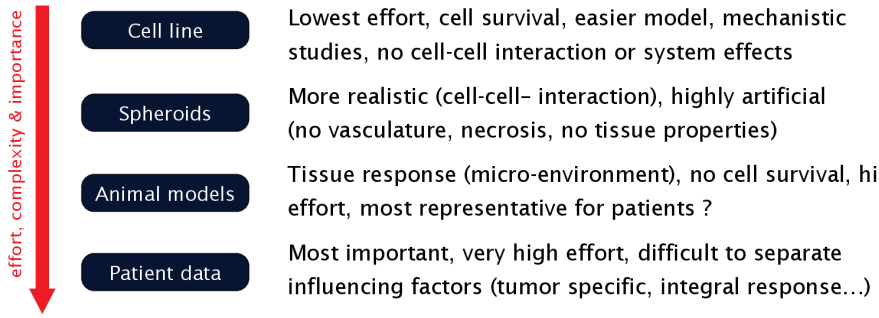


Figure 35: Ion beam research RBE-model system.

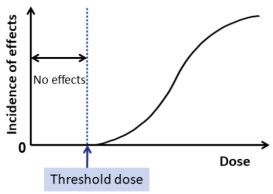
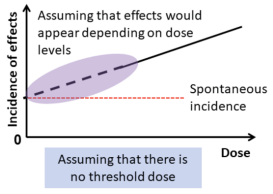
track. Uses the concept of „local dose“. Equal local doses lead to equal local effect, independent of the radiation quality.

Microdosimetric kinetic model (MKM) Based on calculations and measurements. Cell is divided to domains. Probability of a particle to interact in a domain. 2 types ot radiation damage, (1) cell can survive and be repaired, (2) domain is inactivated. Follows microdosimetric principles. Number of lethal events in a small volume of cell nucleus is postulated to be proportional to the square of the specific energy.

6 Radiation Biology - Part 2

6.1 Radiobiology & clinical aspects

Table 7: Deterministic vs. stochastic effects.

Effects	Picture	Description
Deterministic		Occur after a threshold dose is exceeded
Stochastic		Do not have a threshold dose the dose-effect relationship is linear

Severity Depends on dose; e.g. how many stem cells survive.

Latency Depends on tissue and directly on the turnover time.

Different tissues have different radiosensitivity. The same organ at different stages of development can have different radiation sensitivity.

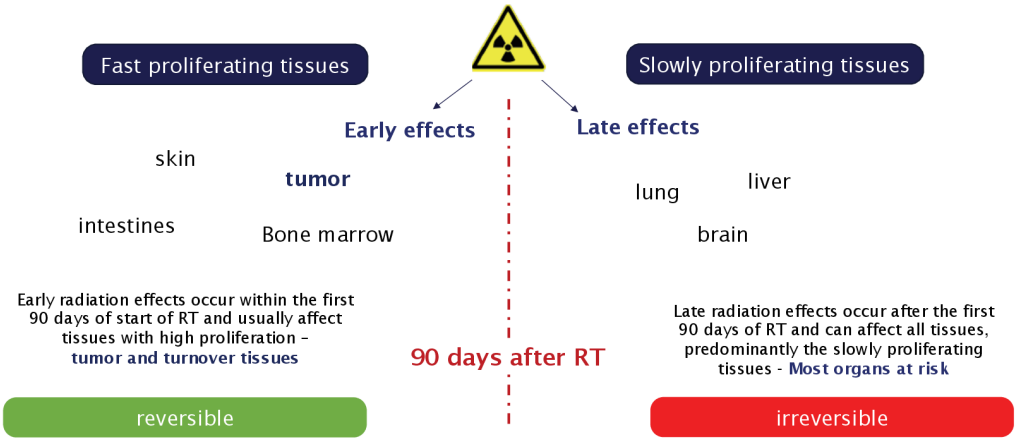


Figure 36: Time line of tissue effects. Key challenge in radiation oncology: maximize radiation dose to cancer cells while minimizing damage to surrounding healthy tissue.

The R's:

1. intRinsic radiation sensitivity, different patients have different radiation sensitivity
2. Recovery, Treatments with breaks are more effective
3. Repopulation, Interfraction periods should be long enough to allow normal tissue cell repopulation BUT not too long to encourage faster tumour cell repopulation
4. Redistribution, Different amounts of radiation are absorbed in the respective cell phase
5. Reoxygenation, Tumour needs more oxygen
6. irRadiated volume, OAR functionally either in Serial, Parallel and Seriel-parallel structurs
7. Restauration, retreatment tolerance of previously irradiated tissues
8. molecular Radiopathology, radiation response of tissues is an orchestrated event with many key (molecular) players

Presentation page 19 up 28 Advantages and disadvantages of in-vivo, in-vitro and patient experiments. Not described again in detail here.

6.2 Ion Beam Therapy and its perceptions

Precise modelling of radiobiological effectiveness has always been a clinical interest for Treatment plan optimization, Dose prescription and Outcome analysis.

6.3 Body of evidence

Not many young patients are treated with protons because there is a lack of information on the long-term effects. Furthermore, there are many studies in progress that lack a certain international standardisation.

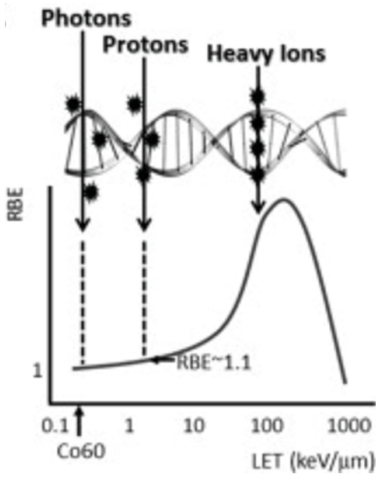


Figure 37: RBE modelling in clinical treatment planning.

7 Monte Carlo Simulation - Basics

7.1 Simulation of experiments

7.1.1 The Monte Carlo method

Measurement quantities are governed by different probability distributions. Experimental data can be modelled following these distributions using a set of random numbers.
Monte Carlo (MC) simulation is a method from stochastics or probability theory in which random samples of a distribution are repeatedly drawn with the help of random experiments. The aim is to numerically solve problems that cannot be solved analytically or can only be solved at great expense with the help of the drawn samples. The law of large numbers is the main basis for this. The random experiments can either be carried out in real life - for example by rolling dice - or in computer calculations using MC algorithms. In MC algorithms, random numbers or pseudo-random numbers are used to simulate random events.

—————— Additional information NOT exam relevant ——————
Stepps of MC:

1. Establish the mathematical model
2. Determine the input values
3. Create a sample dataset
4. Set up the Monte Carlo simulation software
5. Analyze the results

Stages in a MC producer:

1. Series of random variables is generated according to a uniform distribution in the interval $0 < r < 1$.

2. The random variables are used to determine another sequence (x values). It is distributed to a probability density function (Gauss).

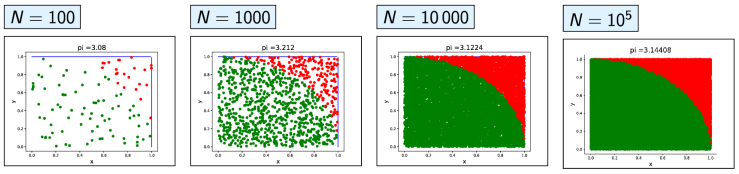


Figure 38: Determine π with simulation. Higher number of simulated points gives a better resolution for π.

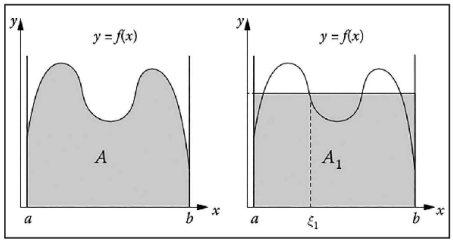


Figure 39: If N$\longrightarrow \infty$ then $A_N \longrightarrow$ A.

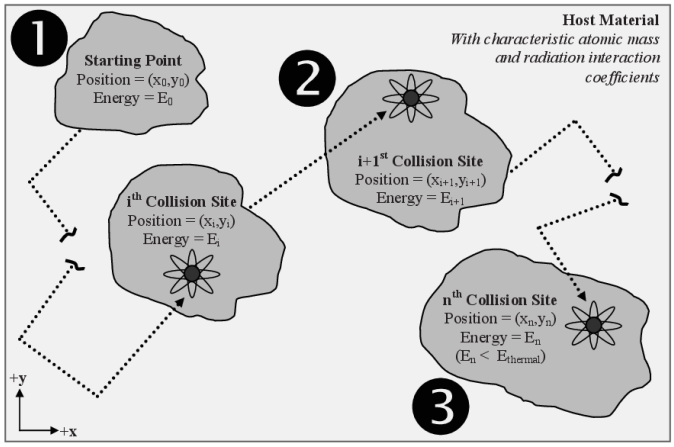


Figure 40: Basic Steps of a MC Radiation Transport Simulation.
(1) Provide each radioactive particle with initial values (such as initial position, initial energy, etc).
(2) Calculate the properties of the radioactive particle (such as position and energy) at each collision site using the approximations made to solve thetransport equation for the radiation type whose transport is simulated. At particular spatial locations within the domain of interest, one can calculate (i.e. tally), amongst others: (1) Particle flux (2) Dose delivered by particle flux
(3) To perform a realistic simulation, the radioactive particle will eventually attain an energy below some threshold energy. This indicates that the particle has reached the end of its life and at this point will no longer be tracked.

In Summary the photon interaction simulated with MC passage of each particle is discretized into small steps. At each step:

- the interaction probabilities are calculated
- effects of interaction (energy transfer, particle generation etc...) are simulated
- length of next step is determined (depending on energy etc.)

This is, of course, very computationally expensive, so people are looking for methods to speed it up.

7.1.2 GATE/Geant4

Particle transport through medium can be modelled with GATE. This use a parallelisation to calculate the transport.

Step by step for each particle:

1. Produce particle with a particle gun; momentum direction, particle type,...
2. "world" in steps
    - step size by cross sections
    - steps end at volume borders
    - apply processes; destroy particle, change,...
3. continue until no particle is left

8 Treatment Planning

Any radiation that hits non-tumorous tissue is over-irradiation and should be avoided. The irradiation with protons allows precise and targeted punctual irradiations. In this way, treatments that would not be possible with conventional methods can also be carried out in the vicinity of OAR.
For carbon ions, the RBE increases with depth.

Treatment planning includes:

- Beam modelling
- Imaging
- Structure delineation and point creation
- Plan design and machine parameters
- Dose optimisation and calculation
- Evaluation
- QA modules and documentation

8.1 Beam modelling

For the planning of the beam, it is necessary to plan the lateral dose profile and integral depth dose in addition to the absolute dose. For surface tumours, a range shifter is used. This is mounted at the exit of the unit and is not patient specific, it serves to increase the spot size. A bolus is individually designed for the patient and has no air gap. Absorbers are placed on the patient and are designed to protect critical areas of the body.

8.2 Imaging

CT Images are used to determine the density of tissues. This is necessary because different densities attenuate the beam differently. For the delineation of structures, PET or MRI images.

Distribution of CT numbers:

1. Determine CT number of voxel; Voxel refers to a data point in a three-dimensional grid and thus corresponds to a pixel in a 2D image.

2. Derive density from look-up table

3. Assign material composition based on density; The respective densities are assigned to the voxels

The stopping power relative to water can be calculated by

$$\rho_s = \rho_e \frac{\ln\left(\frac{2m_e c^2 \beta^2}{I_m\,(1-\beta^2)}\right) - \beta^2}{\ln\left(\frac{2m_e c^2 \beta^2}{I_w\,(1-\beta^2)}\right) - \beta^2} \tag{11}$$

ρ_s	Stopping power relative to water	[ ]
ρ_e	relative electron density	[ ]
m_e	electron mass	[kg]
c	speed of light	[m/s]
β	particle velocity/c	[m/s]
I_m	mean ionization potential solid	[eV]
I_w	mean ionization potential water	[eV]

Images only provide information about a temporary physiological and anatomical condition as an example. A bladder fills during the course of the day and thus shows different physiological and anatomical behaviour. It is advisable to superimpose the images of different imaging procedures for optimal planning, as different structures are highlighted depending on the procedure. With CT and X-rays, artefacts caused by metal parts can occur.

Intramodal Registation CT-CT, MRI-MRI

Intermodal Registration CT-MRI, PET-MRI

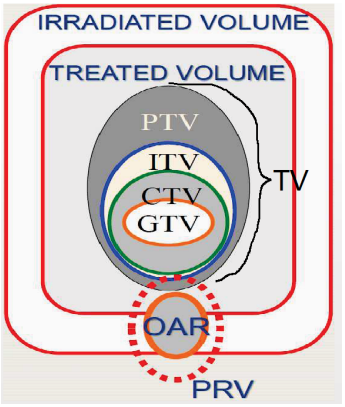


Figure 41: Radiation area.

8.3 Structure Delineation

Irradiated Volume receives dose, tolerance based on dose

Treated Volume representing minimal target dose

Target Volume (TV) takes into account expected movements, expected variation in size & shape and inaccuracies or variations in setup

Have Anatomical or physiological basis	Planning target volume (PTV)	CTV + geometric uncertainties; depends on the irradiation technique as well on centre specific position accuracy
	Internal target volume (ITV)	-
	Plaining organ-at-risk volume (PRV)	-
introduced to match the prescription & constraints	Clinical target volume (CTV)	GTV + microscopic spread
	Gross tumour volume (GTV)	visible tumour
	Organs at Risk (OAR)	Normal tissues and organs within the treatment field receive radiation; OAR must not overlap with the PTV; PRVs to ensure OAR protection

Point of interest (POI) Virtrual isocentre correspondening to the external CT markers; Beam isocentre is usually centre of PTV

Margins depend of the motion of the organs and patient setup. Choose margins so that the

target is in the treated field at least 95% of the time!

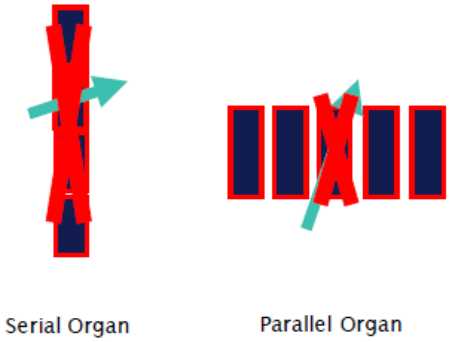


Figure 42: Serial organ: is damaged if one of its sup-volume is damaged. Parallel organ: will lose functionality only if all sub-volume are damaged.

8.4 Plan Design & Machine Parameters

Beam can be created and change by using/change

- Horizontal (90°) and vertical (0°) beam lines, ration of the Patient table
- Gantry angles, full or half gantry angles possible depends on design
- Beam isocenter, Centre of Target volume

To reduce the penumbra (*Halbschatten*) you must decrease the distance between beam exit window an patient surface. So it is important that the room geometry is included in the TPS.

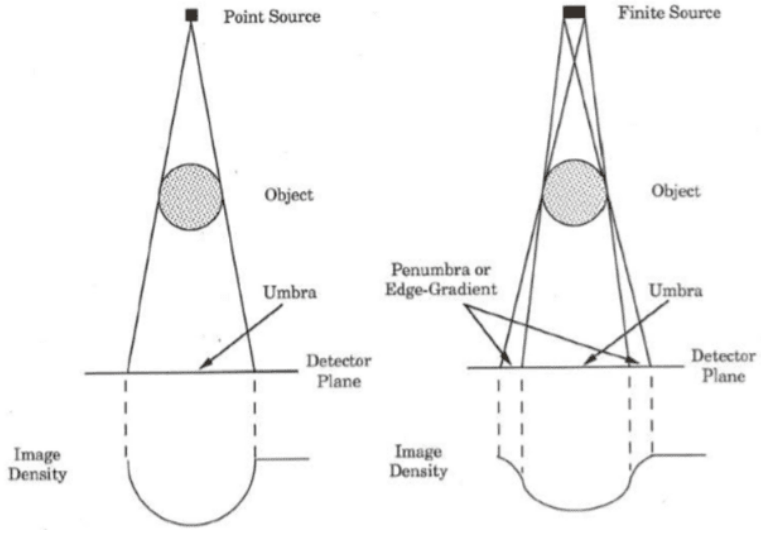


Figure 43: Penumbra (*Halbschatten*) creation.

8.5 Dose Optimization & Calculation

Today standard for proton therapy dose calculation is MC algorithms. Each particle trajectory through tissue.
Grid resolution should be reduce. CT resolution vs. dose grid resolution, Large dose uncertainties can be introduced when choosing wrong dose grid resolution.

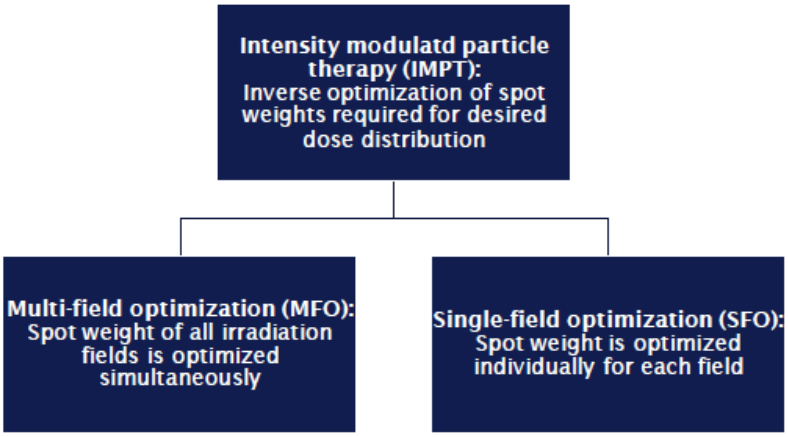


Figure 44: Optimization Strategy.

Single field optimization (SFO) possible with active and passive scanning, homogeneous target dose, protection of OARs

Multi-field optimization (MFO) only possible with active scanning, Dose distribution of an individual field is heterogeneous, Improved protection of OARs

Boosting concepts Delivering a high dose to a sub-volume of the target, sequential boost use two treatment plans, simultaneous integrated boost one use one treatment plan

Differences Photon vs. Particles TP:

- density change rang of particles more
- particle therapy sensitive on tissue heterogeneities
- manageable range of particles

8.6 Evaluation

“Isodose curves are lines that join points of equal dose. They offer a planar representation of the dose distribution and easily show the behavior of one beam or a combination of beams with different shielding, wedges, bolus, etc.

A 3-D treatment plan consists of dose distribution information over a 3-D matrix of points over the patient’s anatomy. Dose volume histogram (DVH)s summarize the information contained in the 3-D dose distribution and are extremely powerful tools for quantitative evaluation of treatment plans

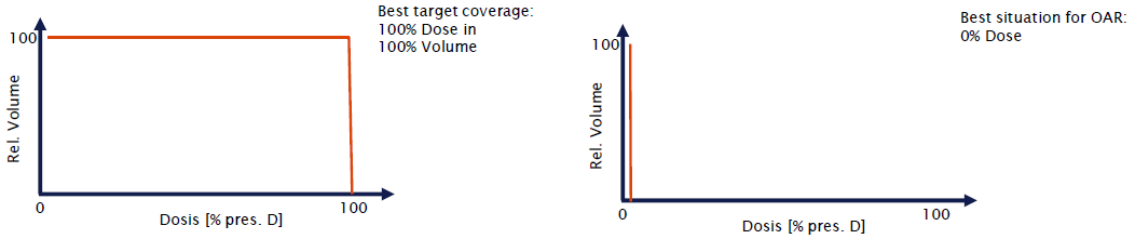


Figure 45: DVH for Left: Tumour Right: OAR.

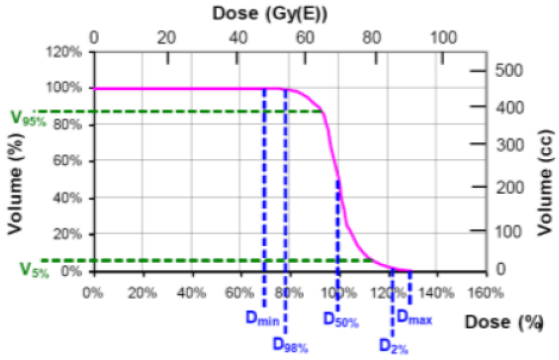


Figure 46: DVH parameter.

8.7 QA modules & Documentation

Includes:

- Patient specific QA methods
  - Measurements
  - dose calculation
- Plan report
  - patient and beam set data
  - Treatment plan data
  - general data
  - beam
  - patient setup

8.8 Moving Tumours

To solve the problem of irradiation moving tumours it gives tree possibilities:

1. Patient hold on the breath, control with different monitoring methods
2. Gating, Irradiation only takes place during certain breathing movements so that the same spot is always irradiated.

3. Tracking, Beam follows the tumour movement

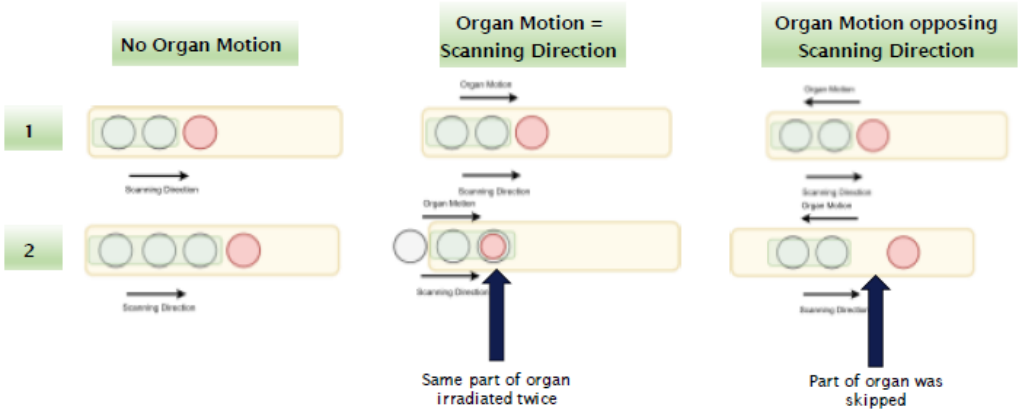


Figure 47: Interplay effect. The interplay effect in radiotherapy refers to the dose variation due to the interplay between the speed of scanning and the movement of the organ. In order to solve this problem, the particles per spot are delivered in multiple phases (re-scans).

List of Figures

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List of Abbreviations

ADC Apparent diffusion coefficient

ART Adaptive radiotherapy

CNS Central nervous system

CT Computed tomography

DAP Does area product

DCE Dynamic Contrast Enhanced MRI

DNA Deoxyribonucleic acid

DVH Dose volume histogram

DWI Diffusion weighted MRI

EBM Evidence based Medicine

ECR electron cyclotron resonance

GUM Guide to the expression of uncertainty in measurement

LAIC large area ionisation chamber

LEM Local effect model

LET Linear energy transfer

MC Monte Carlo

MED Medical Exposure Directive

MKM Microdosimetric kinetic model

MPE Medical Physics Expert

MRI Magnetic resonance imaging

NT normal tissue

OAR Organs at Risk

PET Positron emission tomography

PT-PET Particle therapy PET

QA Quality Assurancee

RBE Relatvie biological effectiveness

RFQ radio-frequency quadrupole

SAD source-axis-distance

SOBP Spread-out Bragg-peak

SSD source-surface-distance

TPS Treatment Planning System

WET Water equivalent thickness