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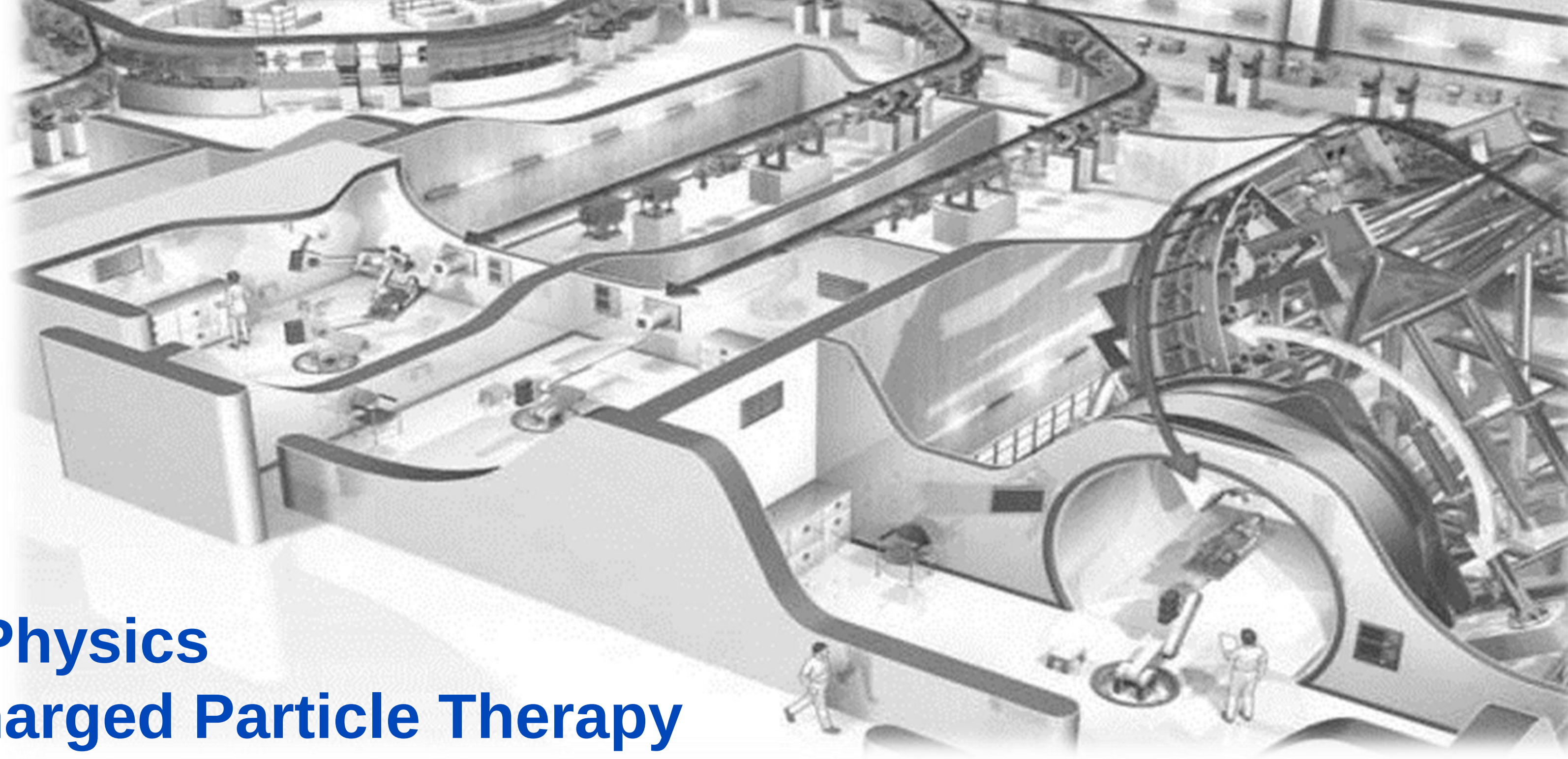

# The Physics of Charged Particle Therapy

## Introduction to Particle Therapy

## Part I/II – Fundamental Concepts and Physics

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# !! Disclaimer !!

Most (all) slides courtesy of

**Dr. Paulo Martins**

DKFZ - Division of Biomedical Physics
in Radiation Oncology / E041

# Literature

- **Radiation Oncology: A Physicist's-Eye View**, Michael Goitein, Springer, Ch. 10, pp. 211-245
- Proton Therapy Physics, Harald Paganetti, Taylor & Francis, Ch. 2-6, pp. 19-190
- The physics of proton therapy, W. D. Newhauser and R. Zhang, *Phys. Med. Biol.* **60** (2015) R155-R209
- Nuclear physics in particle therapy: a review, M. Durante and H. Paganetti, *Rep. Prog. Phys.* **79** (2016) 096702 (59pp)

# Additional Literature

- Schardt, Dieter, Thilo Elsässer, and Daniela Schulz-Ertner. "*Heavy-ion tumor therapy: Physical and radiobiological benefits.*" Reviews of modern physics 82.1 (2010): 383.
- Wilson, Robert R. "*Radiological use of fast protons.*" Radiology 47.5 (1946): 487-491.

# Overview

- **Introduction to Radiotherapy**
- Physics:
  - Energy Loss
  - Lateral Beam shape
- Beam Delivery Techniques

# The Ideal Irradiation Type

In cancer, the ideal radiation delivers:

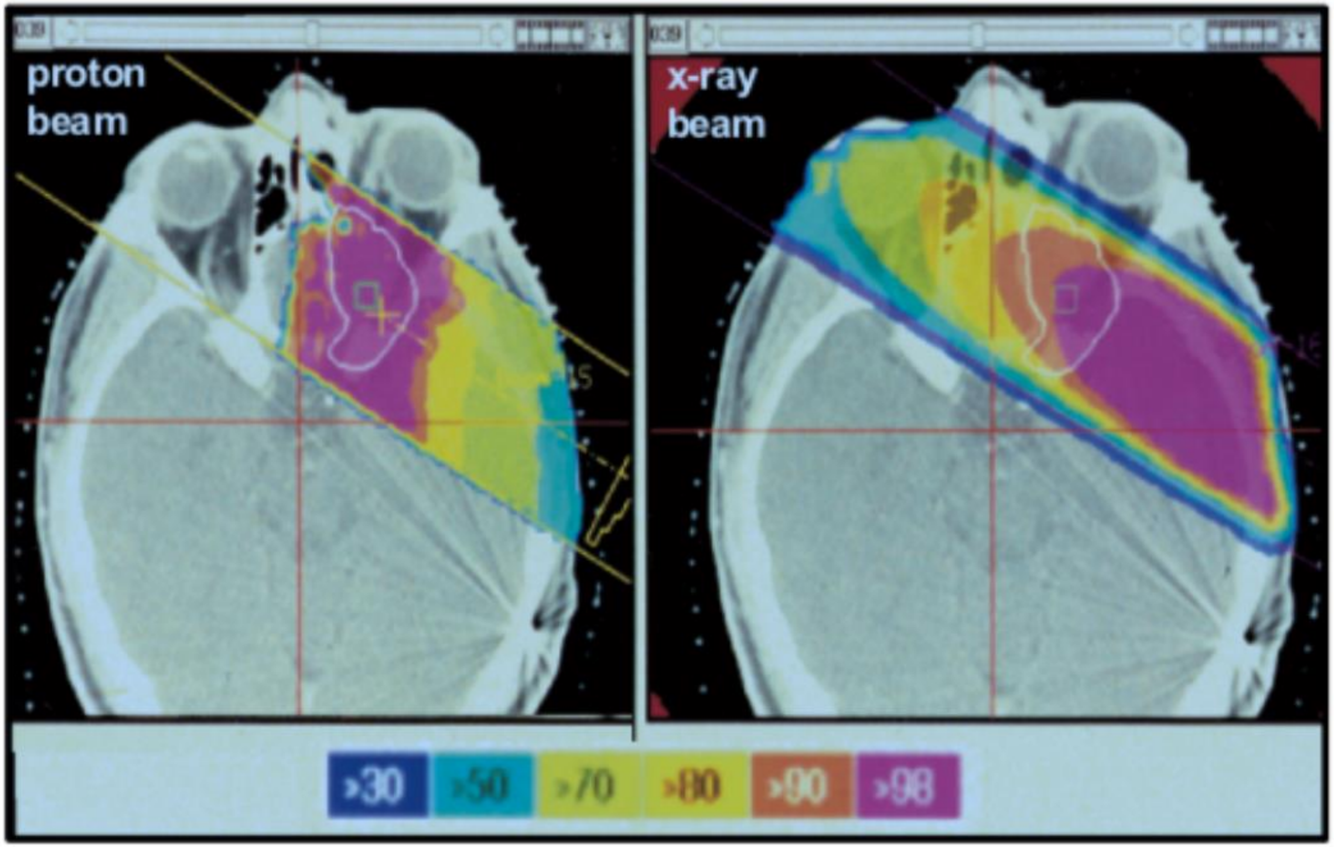
**In theory:**

- defined dose distribution within the target volume (generally a uniform);
- None outside it.

**In practice:**

- most of the dose within the target volume
- relatively little outside it

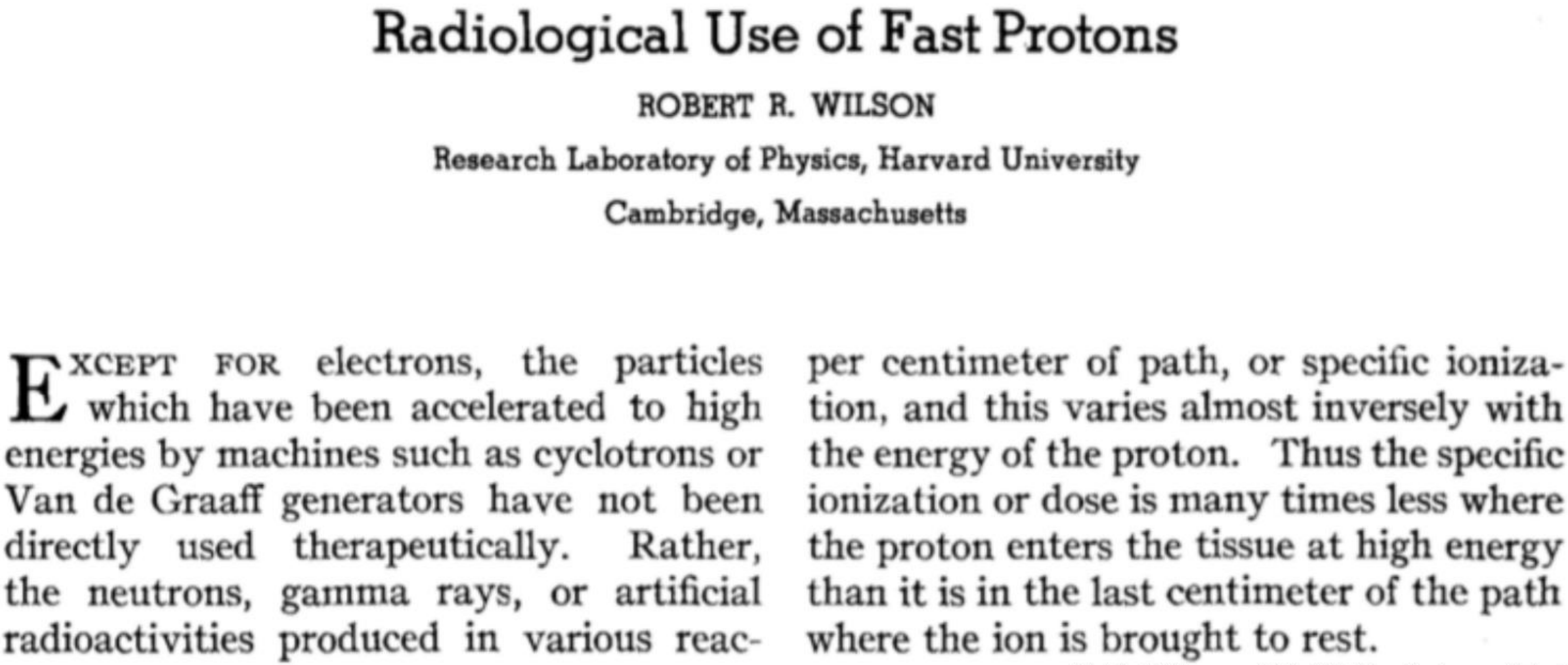
# A Quick Comparison



Proton and a photon posterior-oblique beam

*M. Goitein 2008*

# An Old but Good Idea



## Radiological Use of Fast Protons

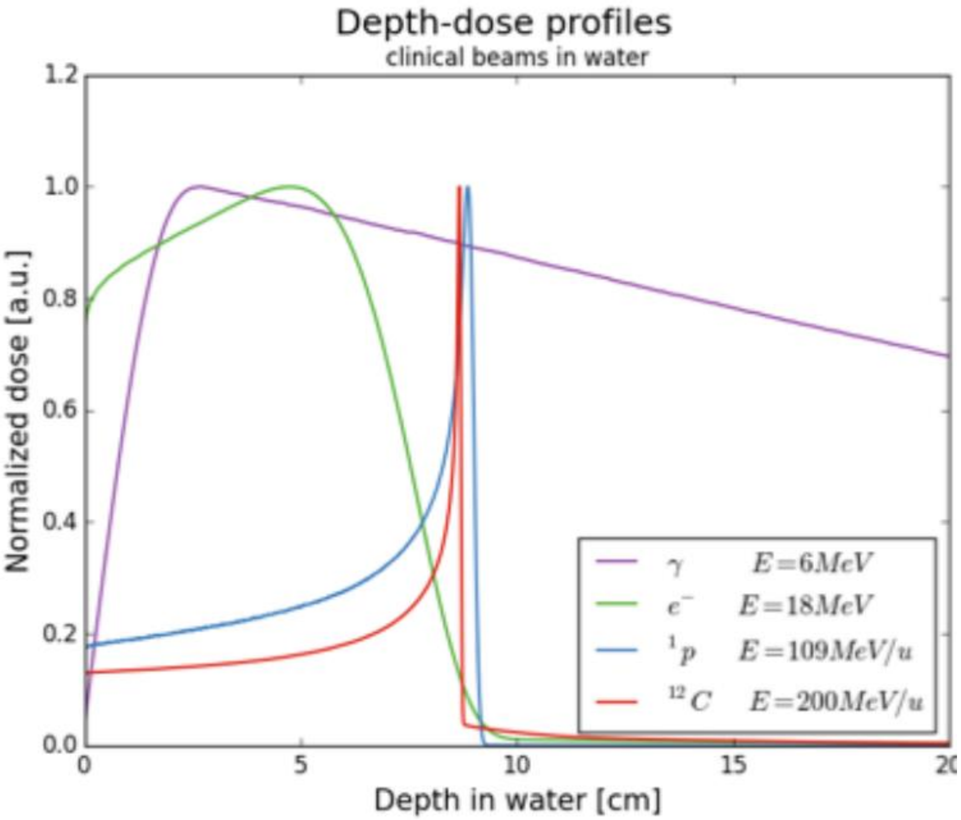
ROBERT R. WILSON

Research Laboratory of Physics, Harvard University
Cambridge, Massachusetts

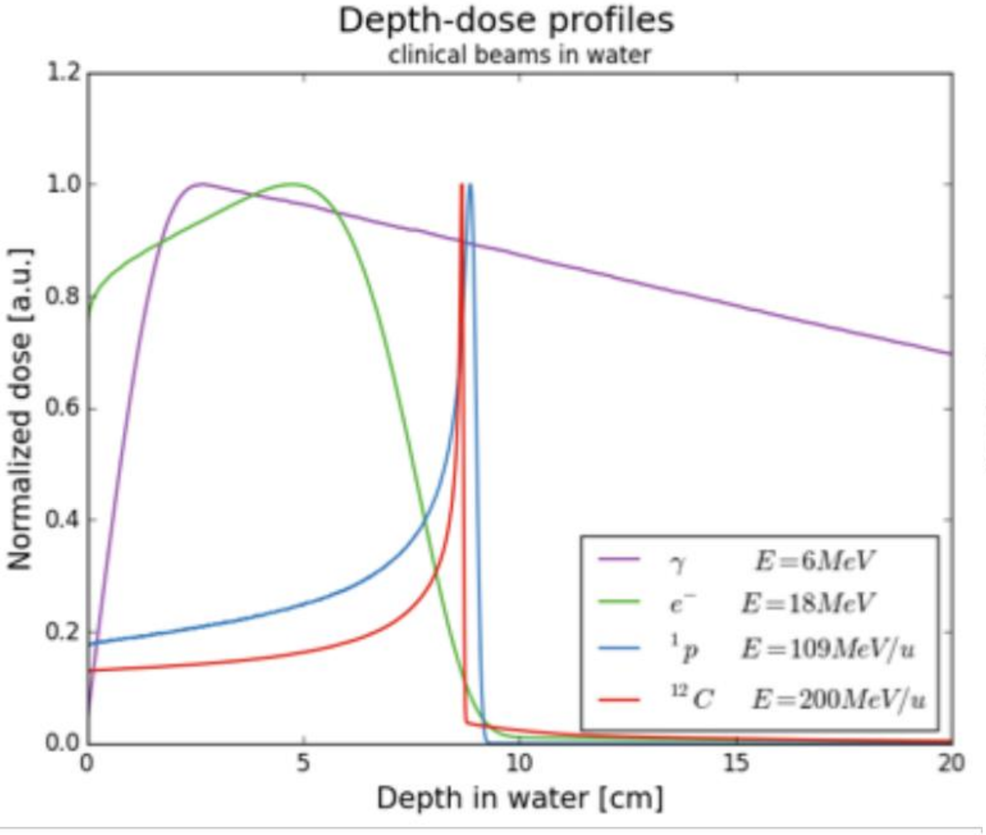
EXCEPT FOR electrons, the particles which have been accelerated to high energies by machines such as cyclotrons or Van de Graaff generators have not been directly used therapeutically. Rather, the neutrons, gamma rays, or artificial radioactivities produced in various reac- … per centimeter of path, or specific ionization, and this varies almost inversely with the energy of the proton. Thus the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the ion is brought to rest.

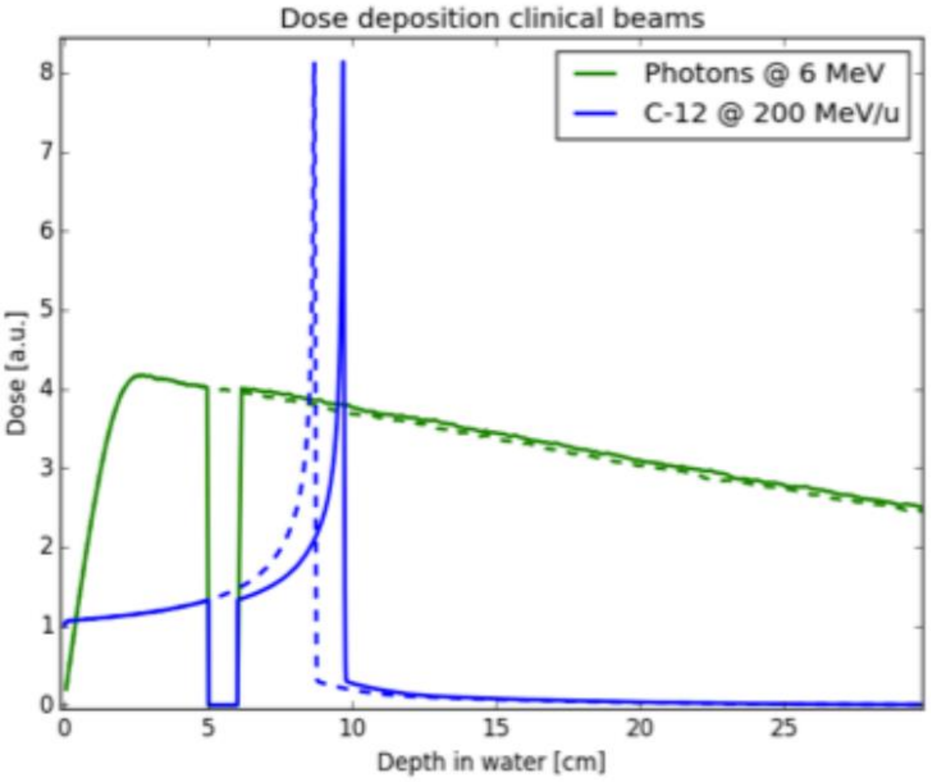
*R.R. Wilson, (1946) Radiology 47, 5*

# Dose Deposition



# Dose Deposition





# Overview

- Introduction to Radiotherapy
- **Physics:**
  - **Interaction Types of Particles with Matter**
  - Energy Loss in Material
  - Lateral Beam Shape
- Beam Delivery Techniques

# Physics of Particles

Three main phenomena:

- Coulomb interactions with atomic electrons
- Coulomb interactions with atomic nuclei
- Nuclear interactions with atomic nuclei

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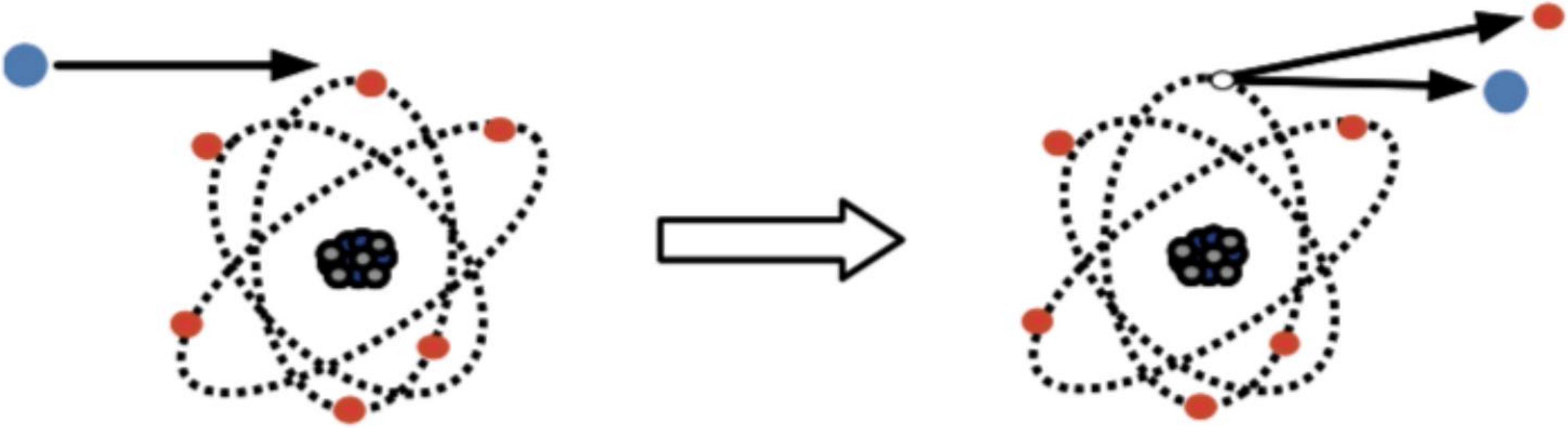
# Coulomb Interaction with Electrons



Coulomb interaction of a proton with an atomic electron

*M. Goitein 2008*

# Coulomb Interaction with Electrons

**Protons** lose energy as they penetrate matter,
mainly due to **Coulomb interactions** of the protons with the **orbiting electrons of atoms**
**->** protons and electrons are attracted and the protons “take electrons with them” (ionization)
**->** the escaping electrons further ionize other atoms

**Protons experience 100,000s of interactions per cm before coming to rest (low energy per ionization and low deflection)**

# !! Important !!

**The penetration depth is determined by the beam energy**

# !! Important !!

**The penetration depth is determined by the beam energy**

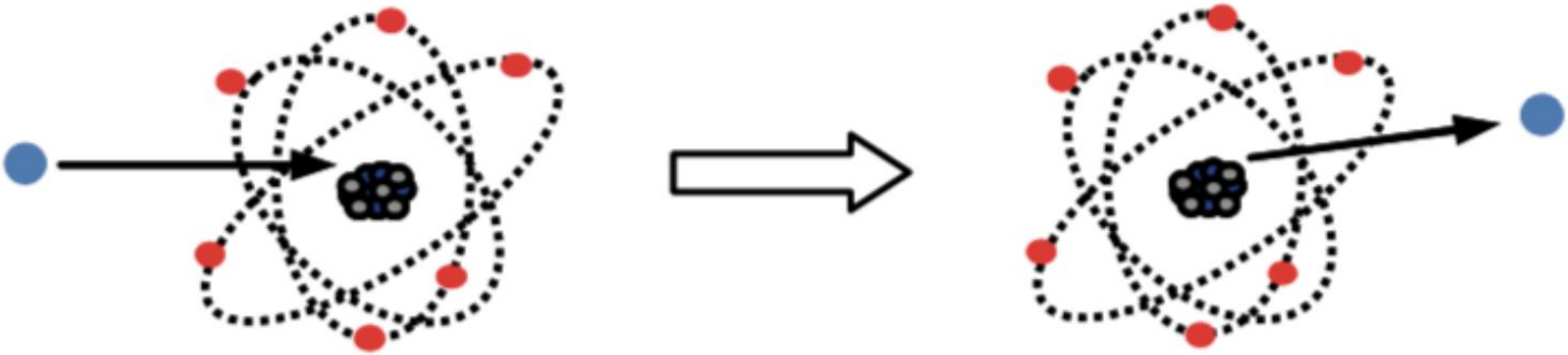
**(and material)**

# Physics of Particles

Three main phenomena:

- Coulomb interactions with atomic electrons
- Coulomb interactions with atomic nuclei
- Nuclear interactions with atomic nuclei

# Coulomb Interaction with Nuclei



Coulomb scattering of a proton by an atomic nucleus

*M. Goitein 2008*

# Coulomb Interaction with Nuclei

Conversely to the interactions with electrons, protons experience a **strong repulsive force** when they approach closely the **charged nucleus** of an atom

Deflection through larger angles (although still small)

These deflections add up and result in a net **angular** and **radial** deviation -> “multiple Coulomb scattering”

# Coulomb Interaction with Nuclei

Highland Formula describes the lateral scattering in a first approximation as a Gaussian with $\alpha_\theta$

$$\sigma_\theta[\mathrm{rad}] = \frac{14.1\ \mathrm{MeV}}{\beta p c} Z_p \sqrt{\frac{d}{L_{\mathrm{rad}}}} \left[1 + \frac{1}{9} \log_{10}\left(\frac{d}{L_{\mathrm{rad}}}\right)\right].$$

| | |
|---|---|
| $L_{rad}$ | *Radiation Length of Material* |
| $d$ | *Thickness of absorber* |
| $Z_p$ | *Charge of particle* |
| $p$ | *Momentum of particle* |

Highland, V. L., 1975, "Some practical remarks on multiple scattering," Nucl. Instrum. Methods Phys. Res. **129**, 497–499.
Highland, V. L., 1979, "Erratum," Nucl. Instrum. Methods Phys. Res. **161**, 171.

# Coulomb Interaction with Nuclei

The **lateral acceleration** impinged to protons in the atomic nucleus field results in the emission of a **spectrum of photons** – *Bremsstrahlung*

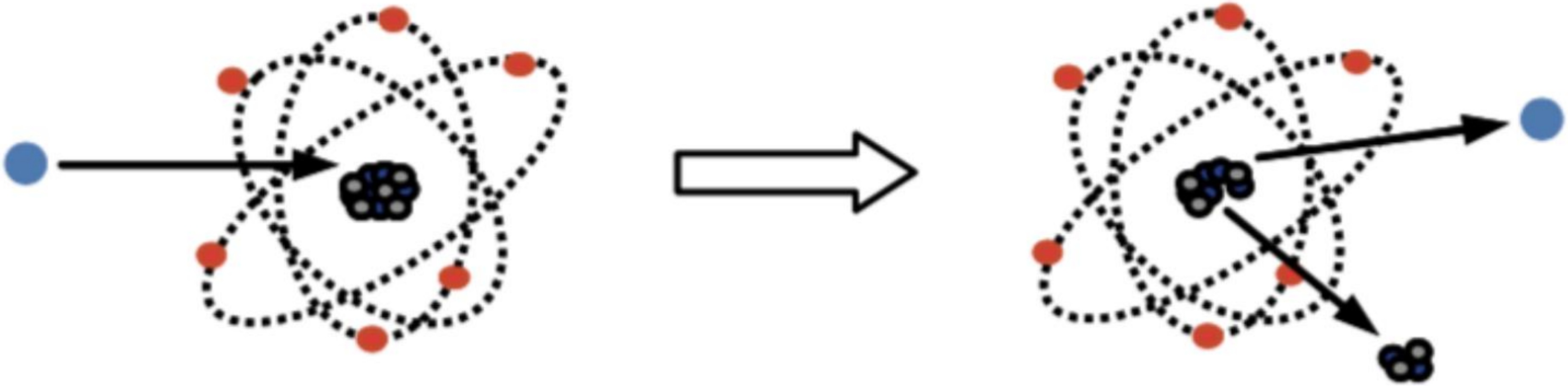
Proportional to $1/m^2$ -> much less intense in proton therapy ($\sim 10^6$)

# Physics of Particles

Three main phenomena:

- Coulomb interactions with atomic electrons
- Coulomb interactions with atomic nuclei
- Nuclear interactions with atomic nuclei

# Nuclear Interactions



Non-elastic nuclear collision of a proton with an atomic nuclei

*M. Goitein 2008*

# Nuclear Interactions

Nuclear interactions via “strong nucleon-nucleon force”

**Elastic collisions**:

$p + {}^{16}O \rightarrow p + {}^{16}O$

(the nucleus remains intact and the proton is deflected by several degrees – strong energy reduction)

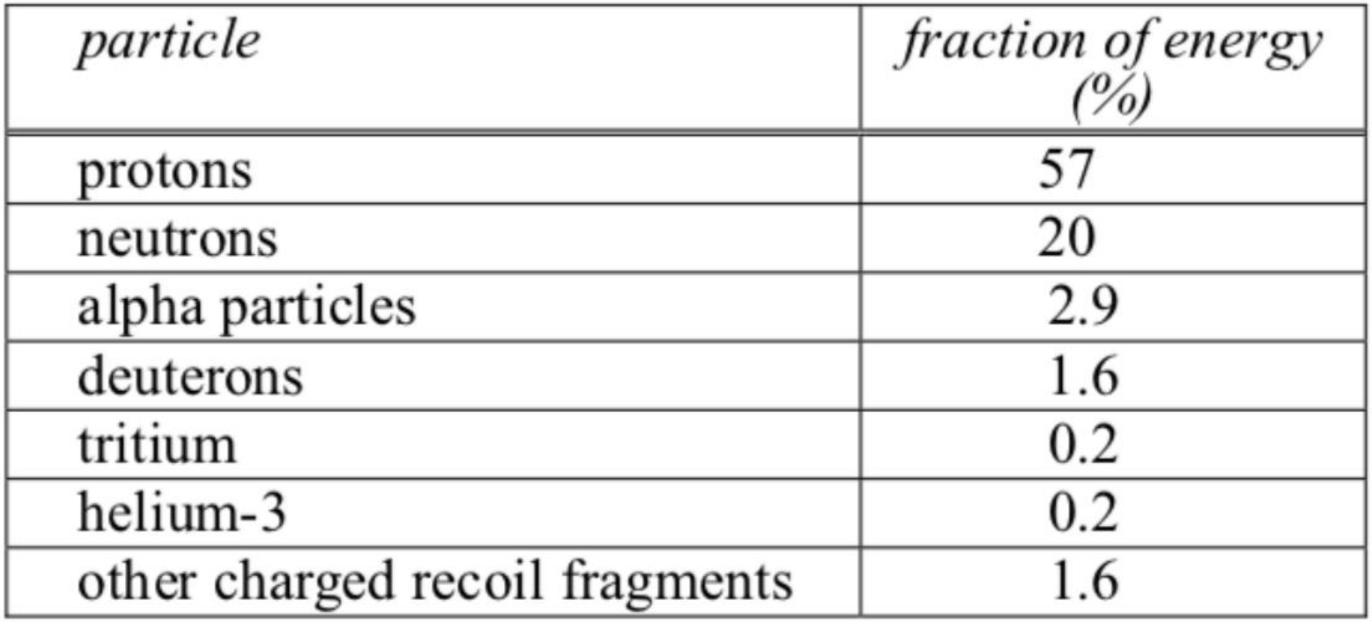
**Non-elastic collisions**:

$p + {}^{16}O \rightarrow p + {}^{15}N + p$

(break-up of the nucleus and also large deflection and proton energy loss)

# Nuclear Interactions

Protons
(150 MeV)
-> $^{16}$O nucleus



| *particle* | *fraction of energy (%)* |
|---|---|
| protons | 57 |
| neutrons | 20 |
| alpha particles | 2.9 |
| deuterons | 1.6 |
| tritium | 0.2 |
| helium-3 | 0.2 |
| other charged recoil fragments | 1.6 |

Light fragment are knocked out with high speed and heavy fragment remains close to the initial position

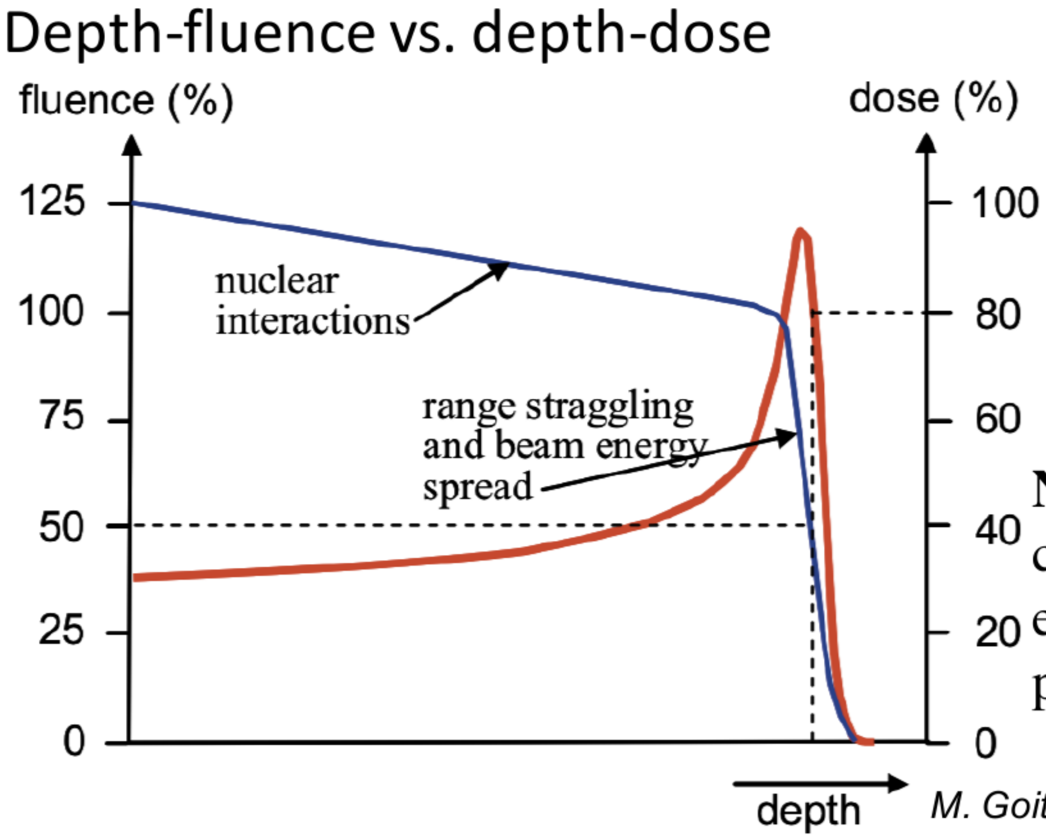
*M. Goitein 2008*

# Nuclear Interactions

## Nuclear interactions

- ~ 1% per $g \cdot cm^{-2}$
- Threshold ~ 20 MeV
- Occur until last few mm of the range

# Nuclear Interactions



*M. Goitein 2008*

80 % dose BP falling edge
same depth
50 % fluence FD falling edge

**Near-flat plateau** – fortuitous cancellation between increasing energy deposition and decreasing primary protons (nucl. interactions)

# Nuclear Interactions

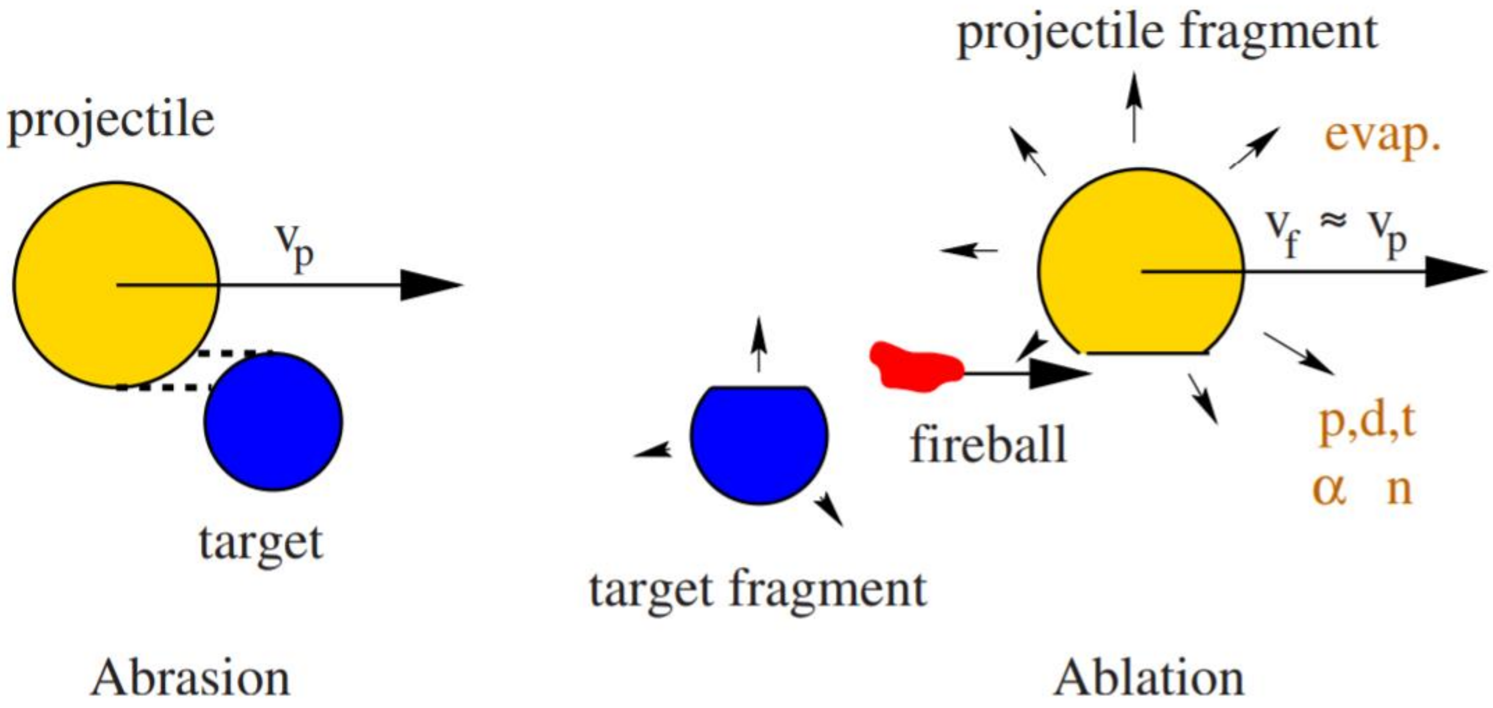
## Nuclear interactions

- Proton beam (160 MeV) loses 20% of its protons by the range end
- Halo of scattered primary protons and knocked-out secondary $^1$p
- ”tail” to the lateral dose profile
- Heavily ionizing fragments with very high stopping power

  -> deposit dose close to the interaction point (high RBE)
- Halo of neutrons escape the patient w/o further interaction

# Nuclear Interactions of Heavy Projectiles

Heavy particles (e.g. Carbon, Oxygen, Neon ions) also undergo fragmentation

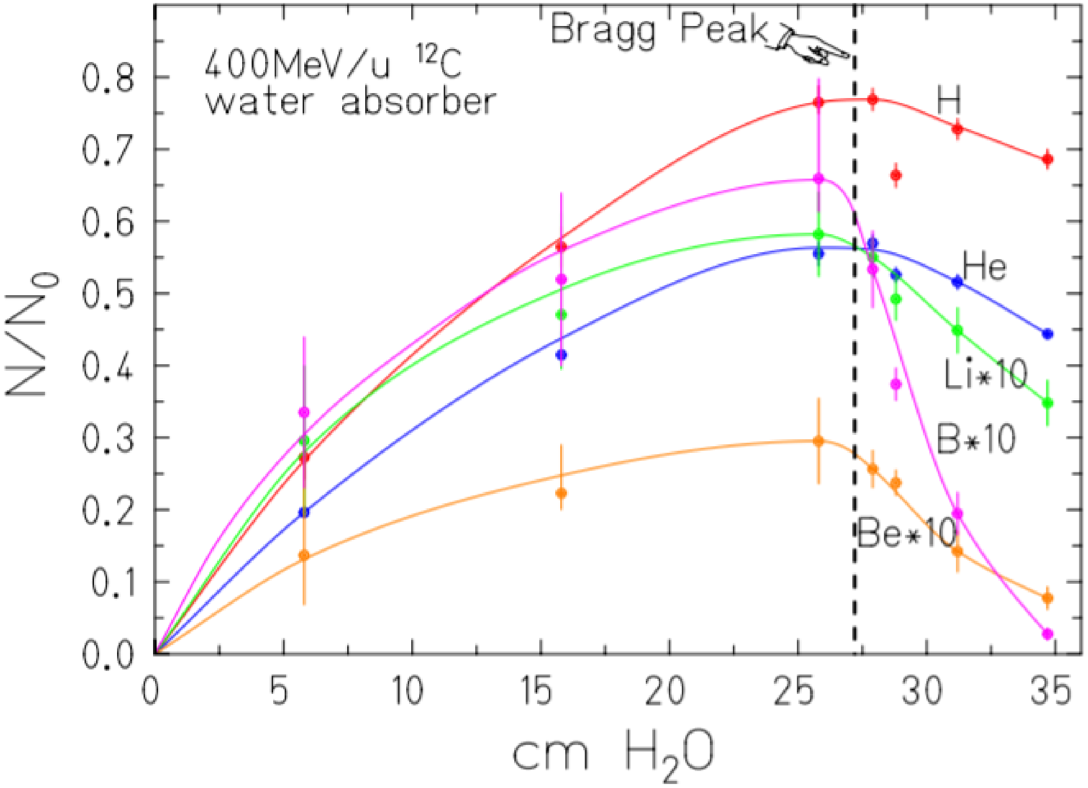


*Taken from Schardt 2010 et al.*

# Nuclear Interactions of Heavy Projectiles

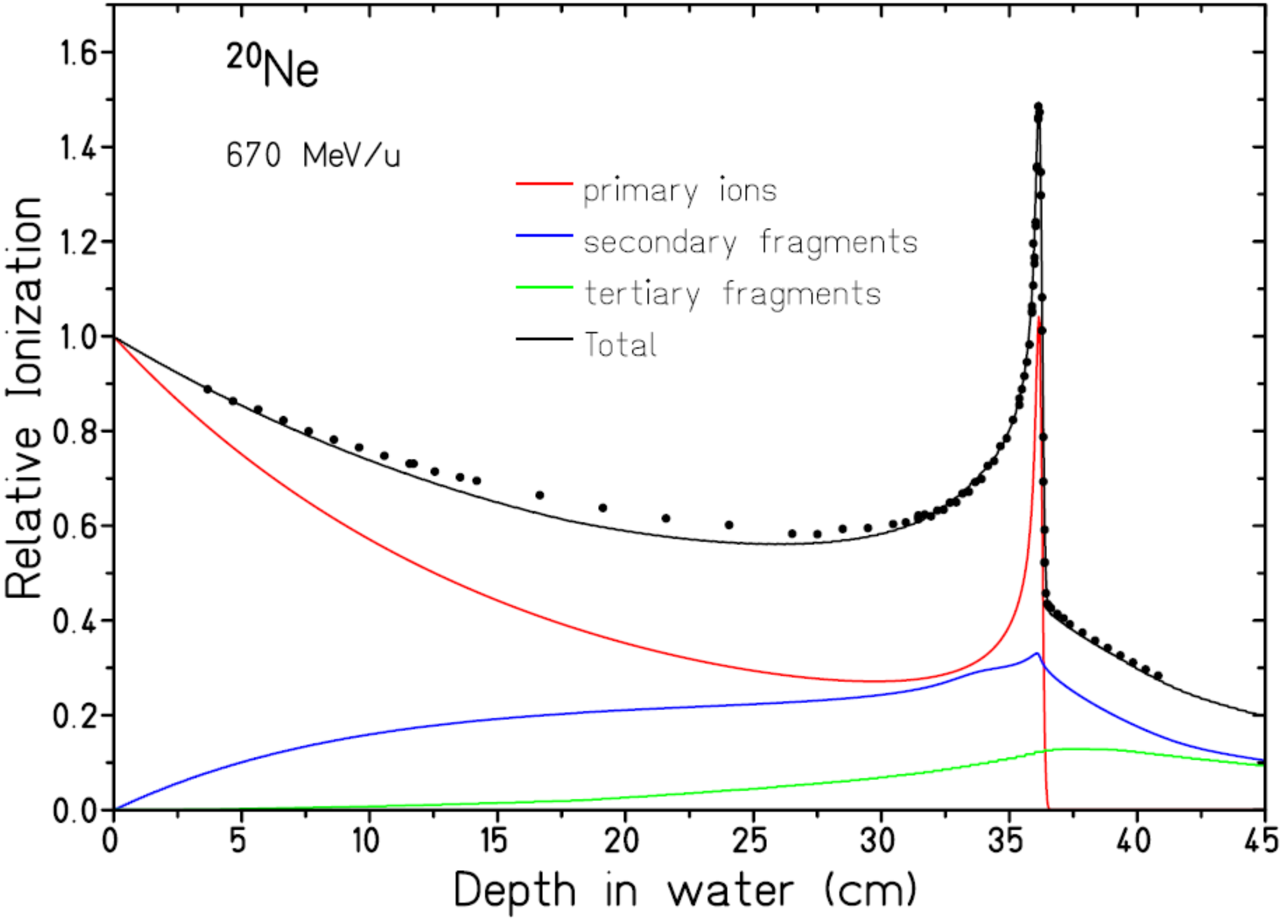
400 MeV/u $^{12}$C Beam in water

Seconardy fragments buildup with depth in water



*Taken from Haettner et al. 2006*

# Nuclear Interactions of Heavy Projectiles



*Taken from Schardt 2010 et al.*

**Secondary fragments contribute significantly to the dose for heavy ions!**

# Nuclear Interactions of Heavy Projectiles

Abrasion ablasion model can be used to describe nuclear reactions in heavy particles ($^{4}$He, $^{12}$C, $^{16}$O)

Nuclear interactions of heavy ions

- produce secondary particles
- have a higher relative secondary particle count with depth in water
- produced fragments have increased range

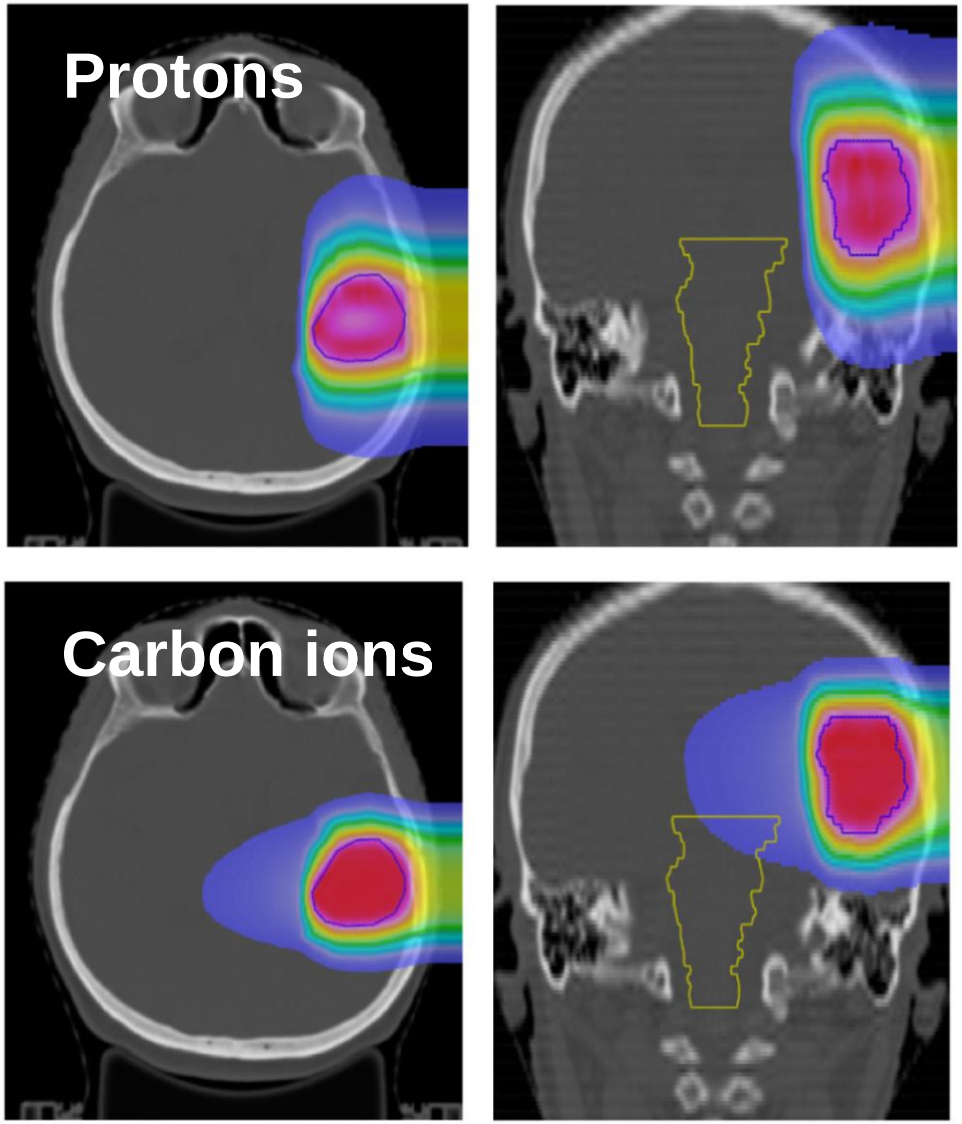
→ Creates tail after the Bragg Peak

# Nuclear Interactions of Heavy Projectiles

Protos scatter more laterally

Heavy ions have a tail

In this example, the tail dose reaches the brain stem (yellow) of the patient.



*Adapted from Kopp et al. 2020*

# Overview

- Introduction to Radiotherapy
- **Physics:**
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  - Lateral Beam Shape
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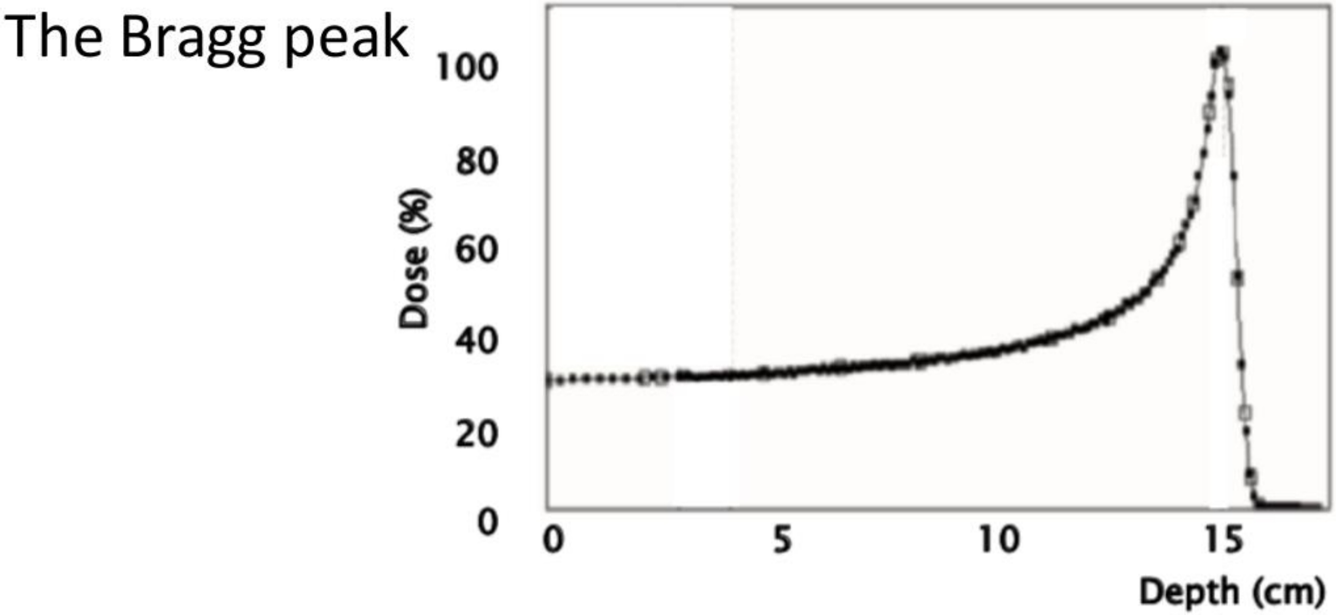
# !! Important !!

**The dose deposited by protons rises sharply near the end of their range, originating the so-called Bragg peak**

# The Bragg-Peak



Depth dose distribution of a mono-energetic proton beam (150 MeV)

*(B. Gottschalk) M. Goitein 2008*

# The Bragg-Peak

**Energy loss due to Coulomb interaction with atomic electrons**

Slow energy loss, mainly transferred to atomic electrons, give rise to the Bragg peak

In a stopping medium, the proton's linear rate of energy loss (linear energy transfer – LET or stopping power) is given by the Bethe-Block formula:

$$\frac{dE}{dx} \propto \frac{1}{v^2}\left(\frac{Z}{A}\right)z^2$$

**Local energy deposition increases as protons slow down**

# The Bethe-Bloch Formula

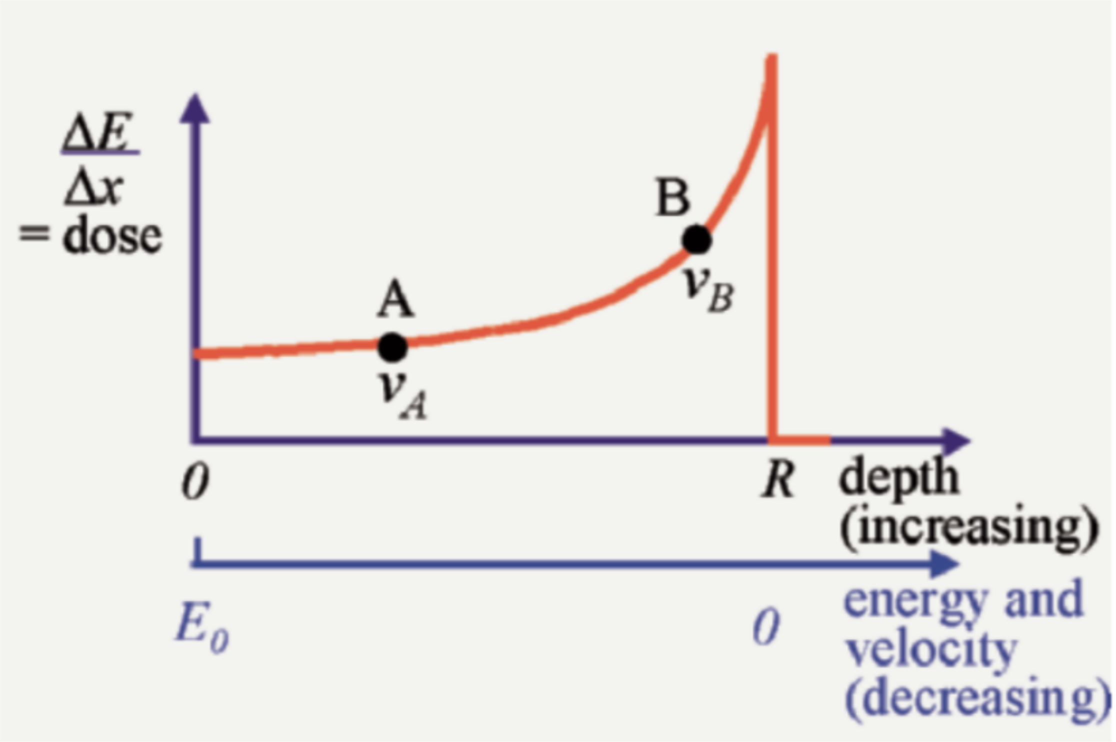
The energy loss of a particle can be described by the Bethe-Bloch formula (including correction terms):

$$-\frac{\mathrm{d}E}{\mathrm{d}x} = 2\pi r_e^2 m_e N_e \frac{Z_p^2}{\boldsymbol{v}^2}\left[ ln\left(\frac{2m_e c^2\beta^2\left(1/\sqrt{1-\beta^2}\right)^2 T_{max}}{\langle I\rangle^2}\right) - 2\beta^2 - 2\frac{C}{Z_t} - \delta\right]$$

At energies at about 10 MeV/u projectiles recombine with free electron and the effective charge must be used.

$$Z_{\mathrm{eff}} = Z_p[1 - \exp(-125\beta Z_p^{-2/3})]$$

# The Bethe-Bloch Formula



- $v_A > v_B$
- $D_A < D_B$

End of range:
v -> 0
Dose drops to zero
Highly asymmetric peak

*M. Goitein 2008*

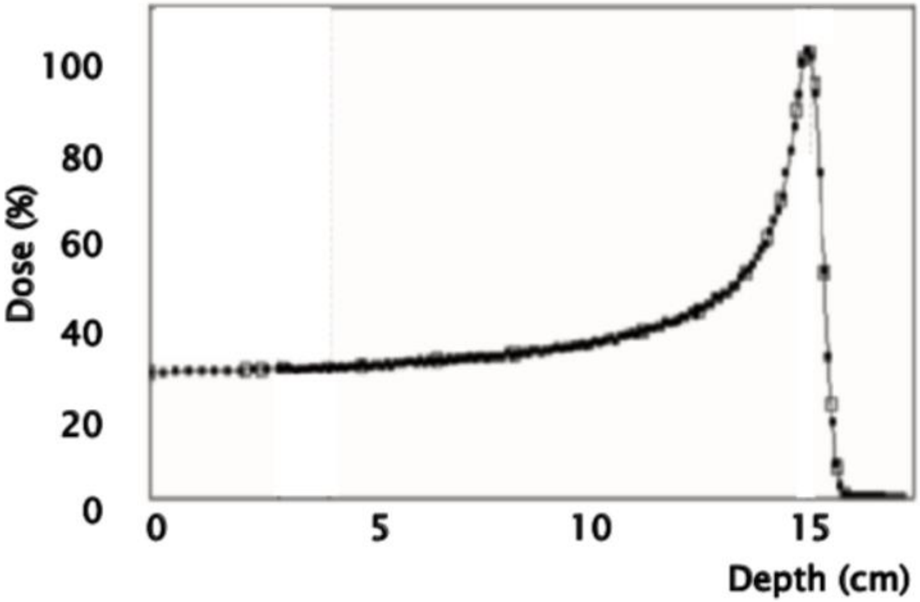
# The Bragg-Peak

## Range straggling and energy spread blurs out the ionization peak

- Range straggling results from statistical fluctuations in the ionization process
  -> the depth of penetration is smeared out (1% range)

- Beams are never monoenergetic due to energy spread in the protons' production (also 1%)

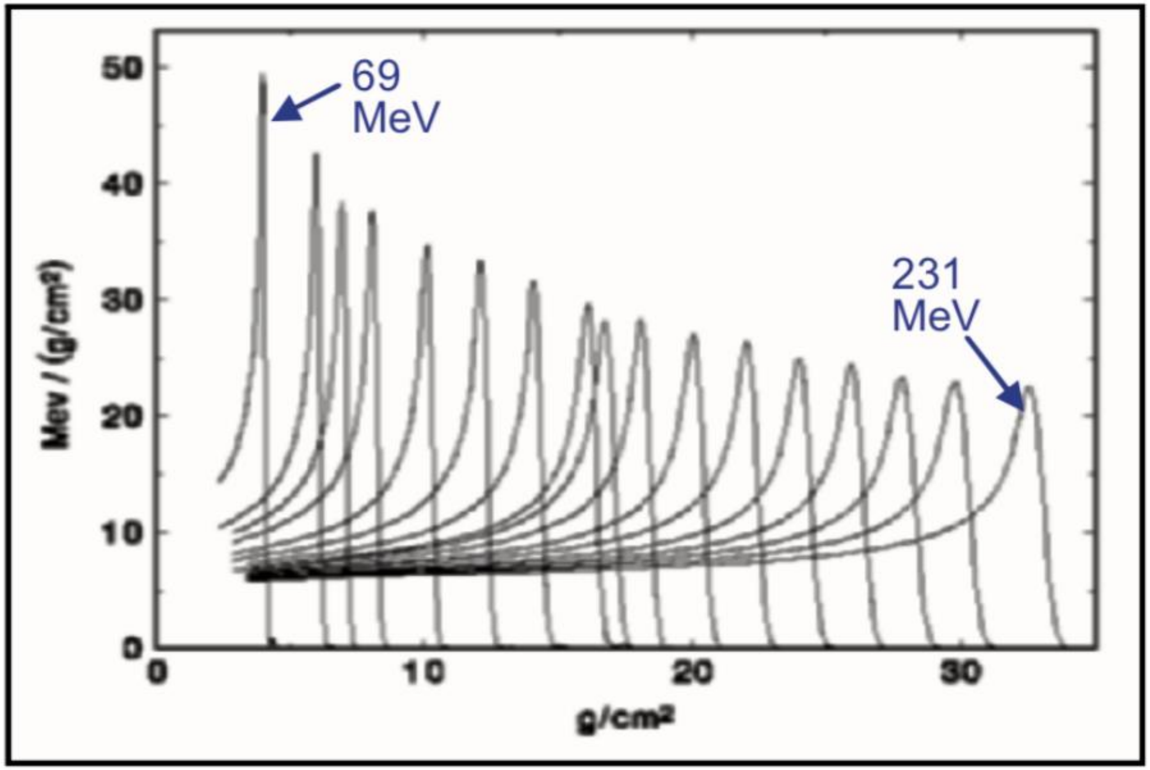
# The Bragg-Peak



Near-Gaussian spread function (broader, more round and more symmetric)

*(B. Gottschalk) M. Goitein 2008*

# Range Straggling



Lower energies
-> narrower BPs
-> higher peak-to-plateau ratio

Range straggling and energy spread spread out the BP (1.5% range)

*B. Gottschalk 2004*

# Proton Range and Path length

Total path length of a particle is defined by:

$$R(E) = \int_0^E \left( \frac{dE'}{dx} \right)^{-1} dE' ,$$

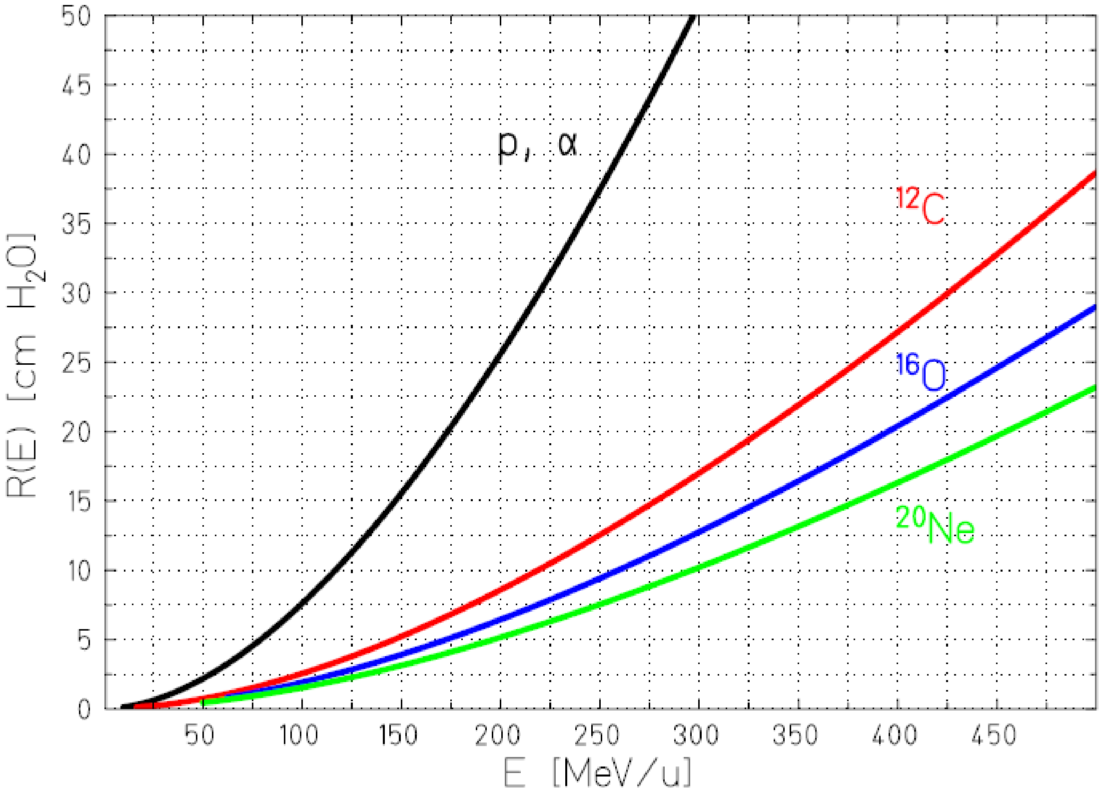
For heavy ions, the path length is very close to the range of the beam.

**The range of a particle with specific energy (MeV/u) scales with A/Z².**

*Taken from Schardt et al. 2010*

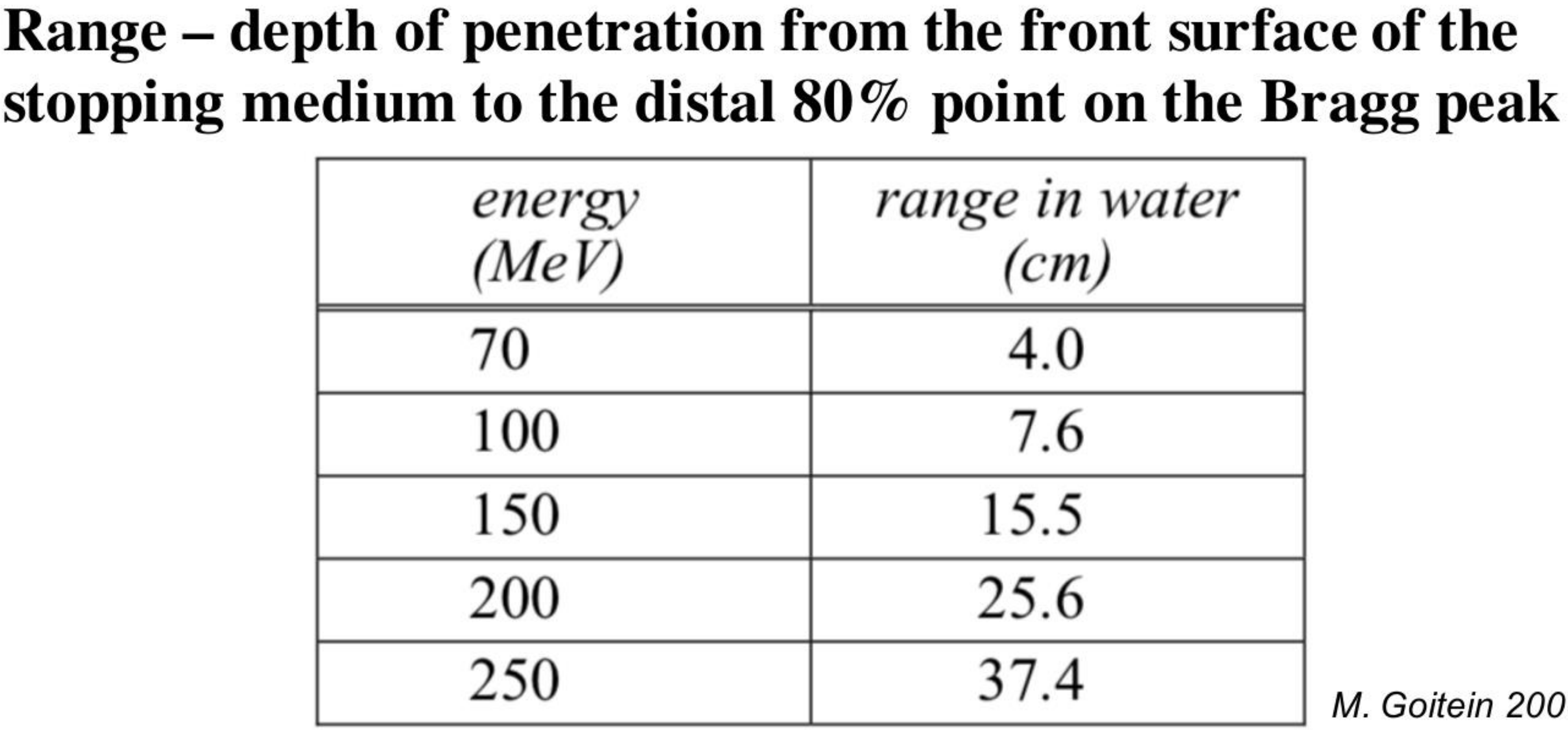
# Mean range of ions in water

$^4$He ions have the same range as protons for the same specific energy!



*Taken from Schardt et al. 2010*

# Proton Range



**Range – depth of penetration from the front surface of the stopping medium to the distal 80% point on the Bragg peak**

| *energy (MeV)* | *range in water (cm)* |
|---|---|
| 70 | 4.0 |
| 100 | 7.6 |
| 150 | 15.5 |
| 200 | 25.6 |
| 250 | 37.4 |

*M. Goitein 2008*

# !! Important !!

**No matter what the incident proton energy, the same amount of energy is deposited in the last couple of $g{\cdot}cm^{-2}$ of a proton's path in the medium**

# Facts of Proton Beams

**Penumbra – distal falloff of dose from 80% to 20%**

**Protons (150 MeV):**

- Range: 15.5 cm
- Peak-to-plateau ratio - 3:1
- Peak width – 6 mm
- Penumbra - 4 mm

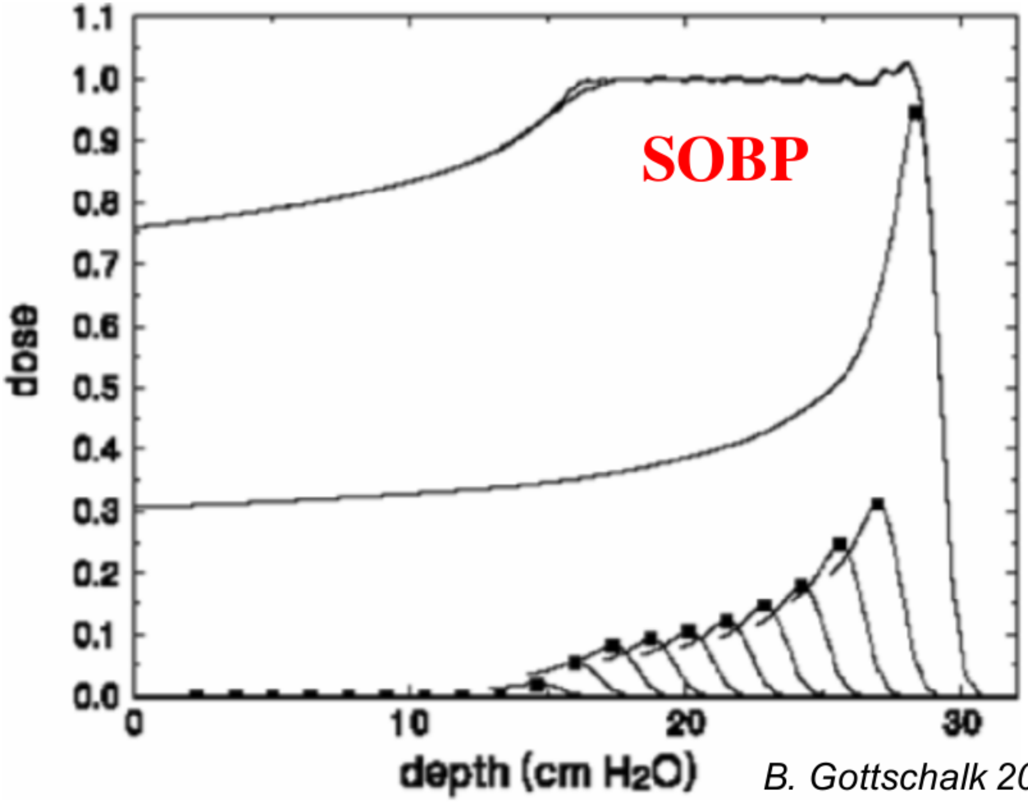
**Protons (200 MeV):**

- Range: 25.6 cm
- Penumbra - 7 mm

**Protons (70 MeV):**

- Range: 4 cm
- Penumbra - 1 mm

# The Spread-Out Bragg Peak (SOBP)



*B. Gottschalk 2004*

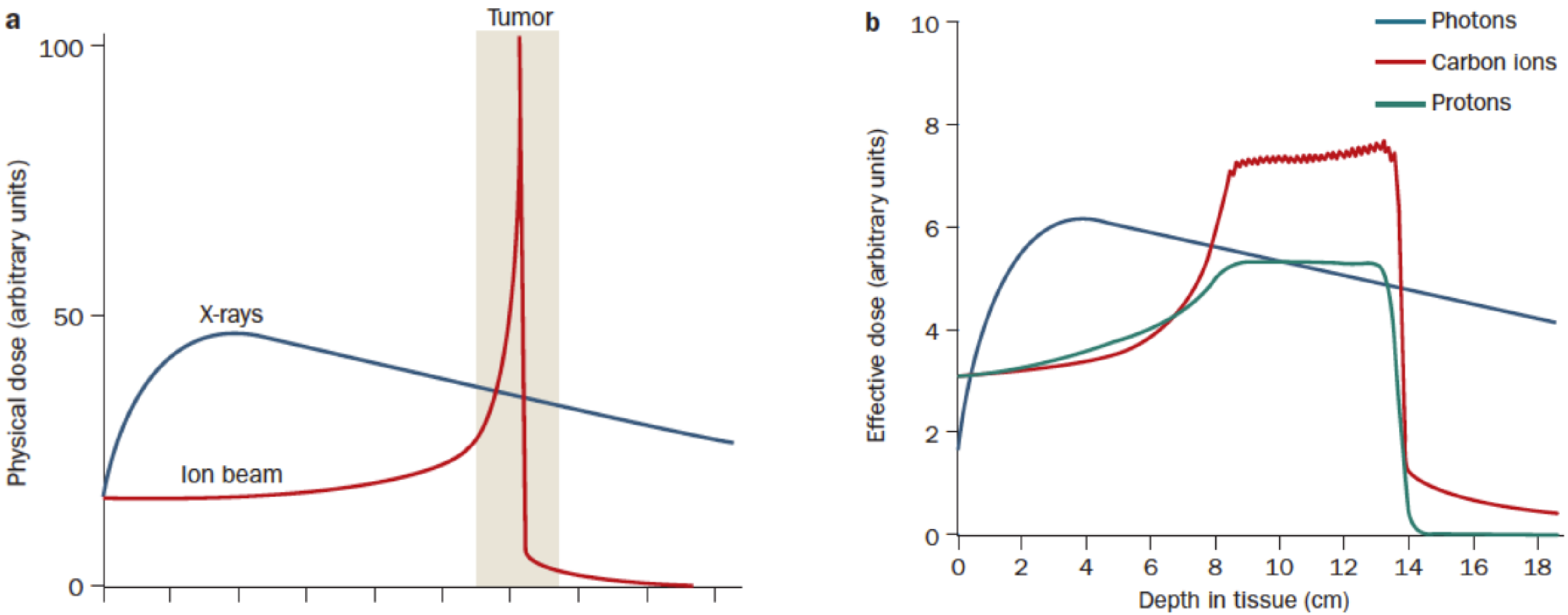
**Tumors may extend more than 10 cm**

This extension is achieved by delivering many BPs with different ranges/energies and weights

More proximal –> less weight

Near-constant high dose at distal region -> **spread-out Bragg peak (SOBP)**

# The Spread-Out Bragg Peak (SOBP)

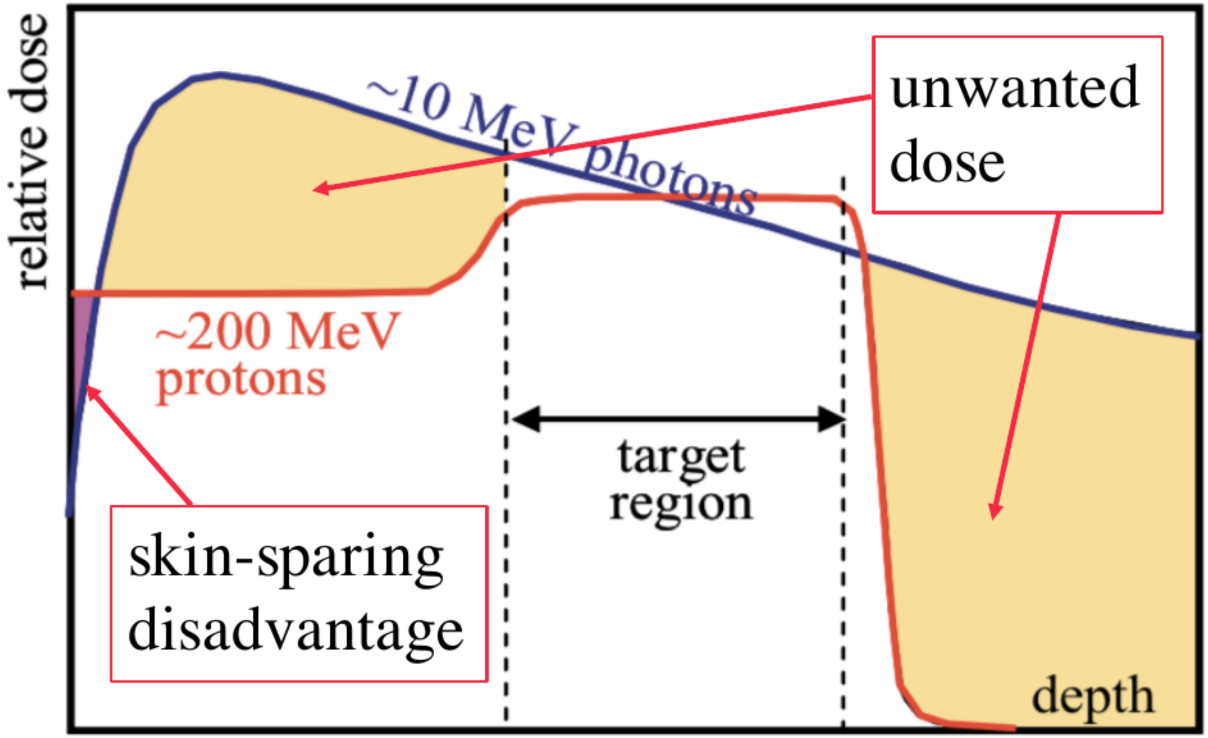


Single BP within the tumor

Beams of different energies superimposed to produce a spread-out Bragg peak (SOBP) that covers the whole tumor

*M. Durante & J. Loeffler., (2010) J. S. Nat. Rev. Clin. Oncol. 7, 37*

# The Spread-Out Bragg Peak (SOBP)



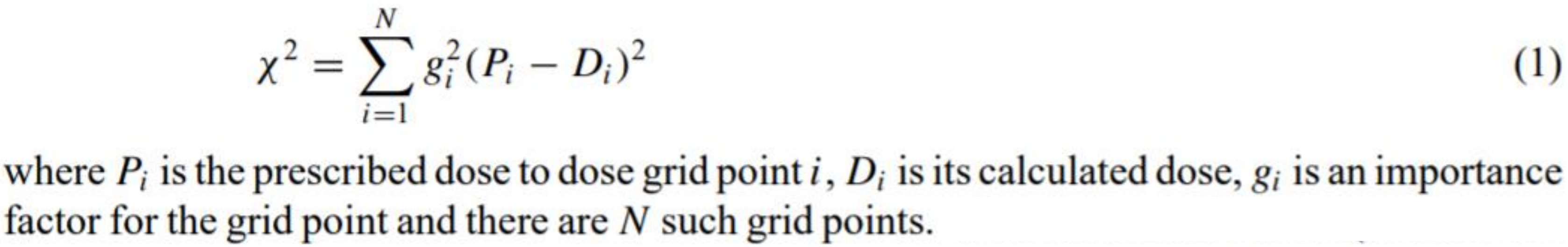
M. Goitein 2008

Proton SOBP dose distribution much superior to the one from a photon beam (LINAC)

Entrance dose depends SOBP extent -> up to 80%

# Optimizing a SOBP

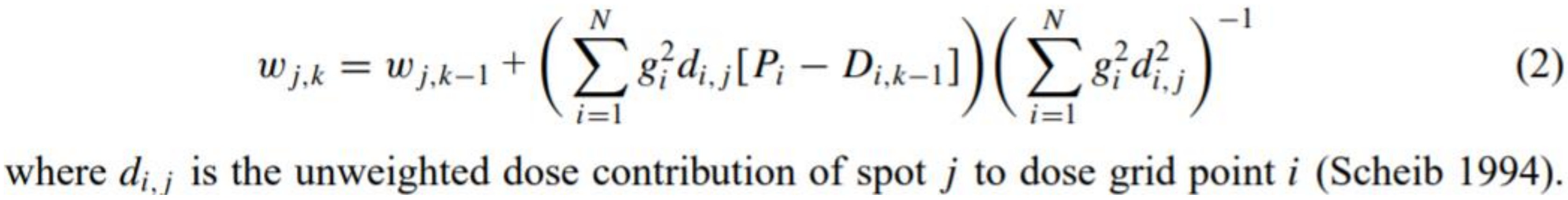
How to create a SOBP
→ Algorithms and Optimization



$$\chi^2 = \sum_{i=1}^{N} g_i^2 (P_i - D_i)^2 \tag{1}$$

where $P_i$ is the prescribed dose to dose grid point $i$, $D_i$ is its calculated dose, $g_i$ is an importance factor for the grid point and there are $N$ such grid points.

With the solution:

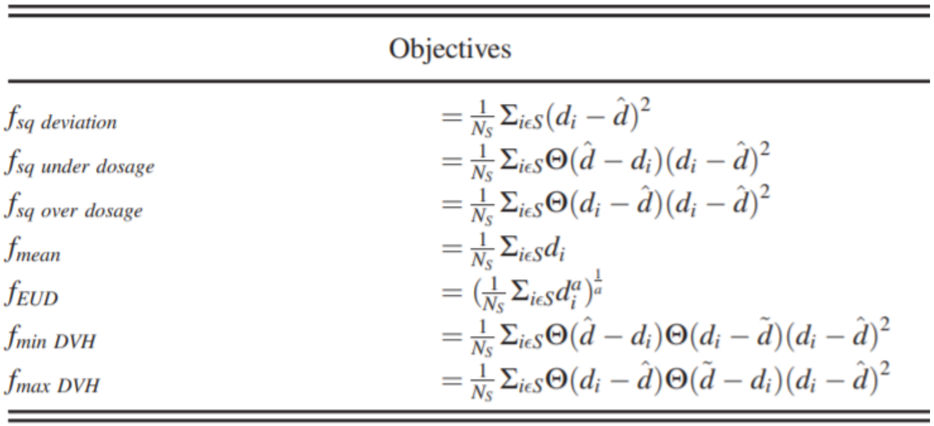


$$w_{j,k} = w_{j,k-1} + \left( \sum_{i=1}^{N} g_i^2 d_{i,j} [P_i - D_{i,k-1}] \right) \left( \sum_{i=1}^{N} g_i^2 d_{i,j}^2 \right)^{-1} \tag{2}$$

where $d_{i,j}$ is the unweighted dose contribution of spot $j$ to dose grid point $i$ (Scheib 1994).

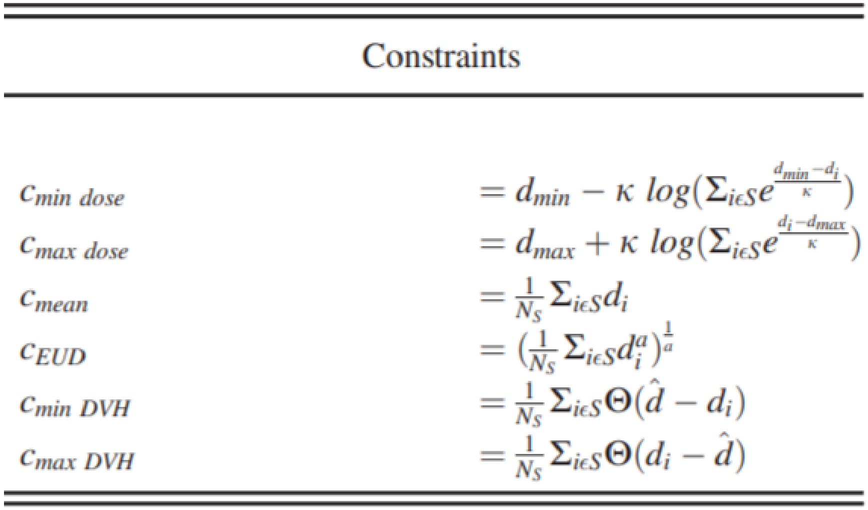
*Lomax 1999*

# Optimizing a SOBP in modern times



| Objectives | |
|---|---|
| $f_{sq\ deviation}$ | $= \frac{1}{N_S}\Sigma_{i\epsilon S}(d_i - \hat{d})^2$ |
| $f_{sq\ under\ dosage}$ | $= \frac{1}{N_S}\Sigma_{i\epsilon S}\Theta(\hat{d} - d_i)(d_i - \hat{d})^2$ |
| $f_{sq\ over\ dosage}$ | $= \frac{1}{N_S}\Sigma_{i\epsilon S}\Theta(d_i - \hat{d})(d_i - \hat{d})^2$ |
| $f_{mean}$ | $= \frac{1}{N_S}\Sigma_{i\epsilon S}d_i$ |
| $f_{EUD}$ | $= (\frac{1}{N_S}\Sigma_{i\epsilon S}d_i^a)^{\frac{1}{a}}$ |
| $f_{min\ DVH}$ | $= \frac{1}{N_S}\Sigma_{i\epsilon S}\Theta(\hat{d} - d_i)\Theta(d_i - \tilde{d})(d_i - \hat{d})^2$ |
| $f_{max\ DVH}$ | $= \frac{1}{N_S}\Sigma_{i\epsilon S}\Theta(d_i - \hat{d})\Theta(\tilde{d} - d_i)(d_i - \hat{d})^2$ |

Objectives are goals the optimziation is trying to reach (dose in tumor)



| Constraints | |
|---|---|
| $c_{min\ dose}$ | $= d_{min} - \kappa\ log(\Sigma_{i\epsilon S}e^{\frac{d_{min}-d_i}{\kappa}})$ |
| $c_{max\ dose}$ | $= d_{max} + \kappa\ log(\Sigma_{i\epsilon S}e^{\frac{d_i-d_{max}}{\kappa}})$ |
| $c_{mean}$ | $= \frac{1}{N_S}\Sigma_{i\epsilon S}d_i$ |
| $c_{EUD}$ | $= (\frac{1}{N_S}\Sigma_{i\epsilon S}d_i^a)^{\frac{1}{a}}$ |
| $c_{min\ DVH}$ | $= \frac{1}{N_S}\Sigma_{i\epsilon S}\Theta(\hat{d} - d_i)$ |
| $c_{max\ DVH}$ | $= \frac{1}{N_S}\Sigma_{i\epsilon S}\Theta(d_i - \hat{d})$ |

Constraints ensure that a *sensible* solution is reached

*Wieser et al. 2017*

# Overview

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    - **Lateral Beam Shape**
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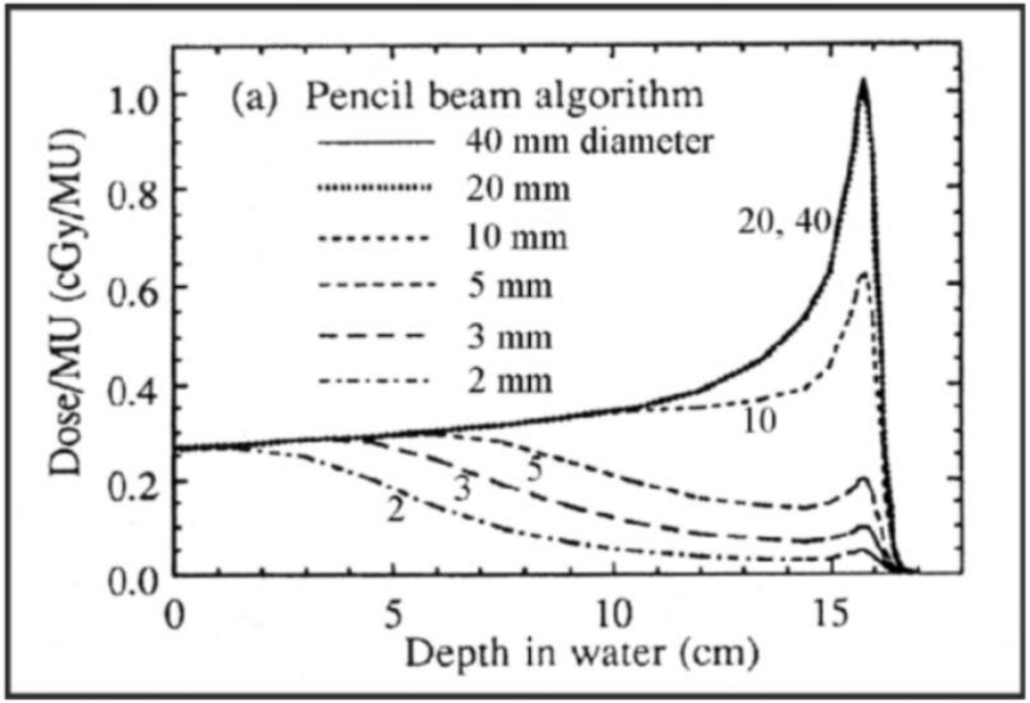
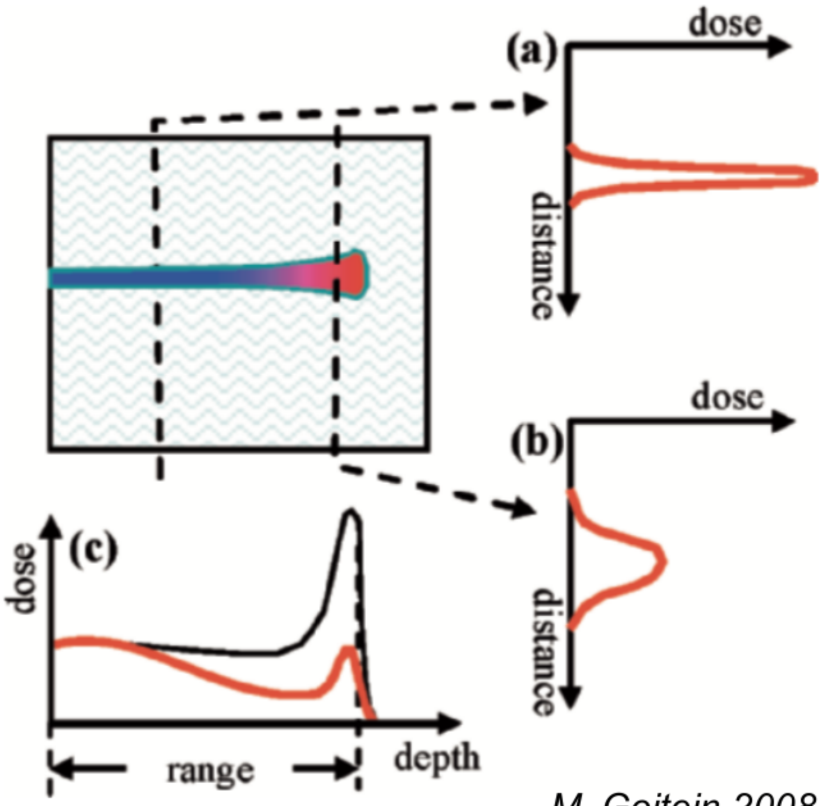
# Lateral Beam Shape



A small-diameter proton beam is substantially degraded due to multiple Coulomb scattering of the protons

*L. Hong et al, (1996) Phys. Med. Biol. 41*

# Lateral Beam Shape



*M. Goitein 2008*

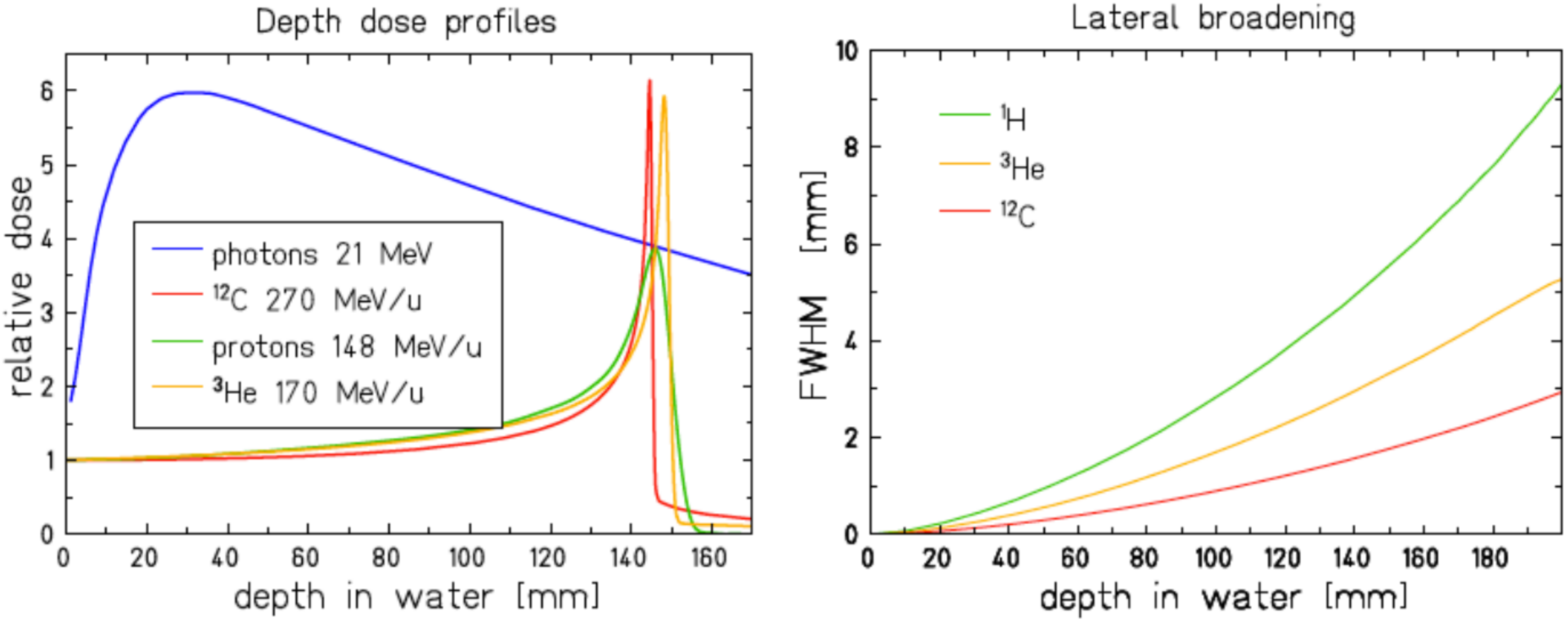
Lateral dose distribution are broader but shallower at larger depths (lower amplitude but great lateral extent)

Protons going deeper are more scattered and spread out and the energy at the BP is smeared out laterally

-> not well suited for very small (mm) deep seated tumors (many cm)

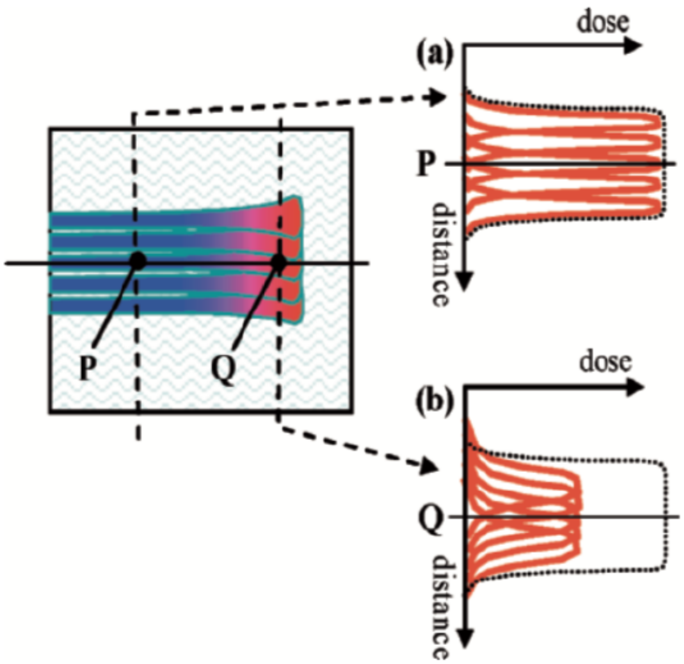
# Lateral Beam Shape

## Lateral dose distribution of charged particles



*Krämer et al., (2016) Med. Phys. 43 (4), 1995*

# Lateral Beam Shape



**A broad beam can be considered to be made up of a superposition of pencil beams, side by side**

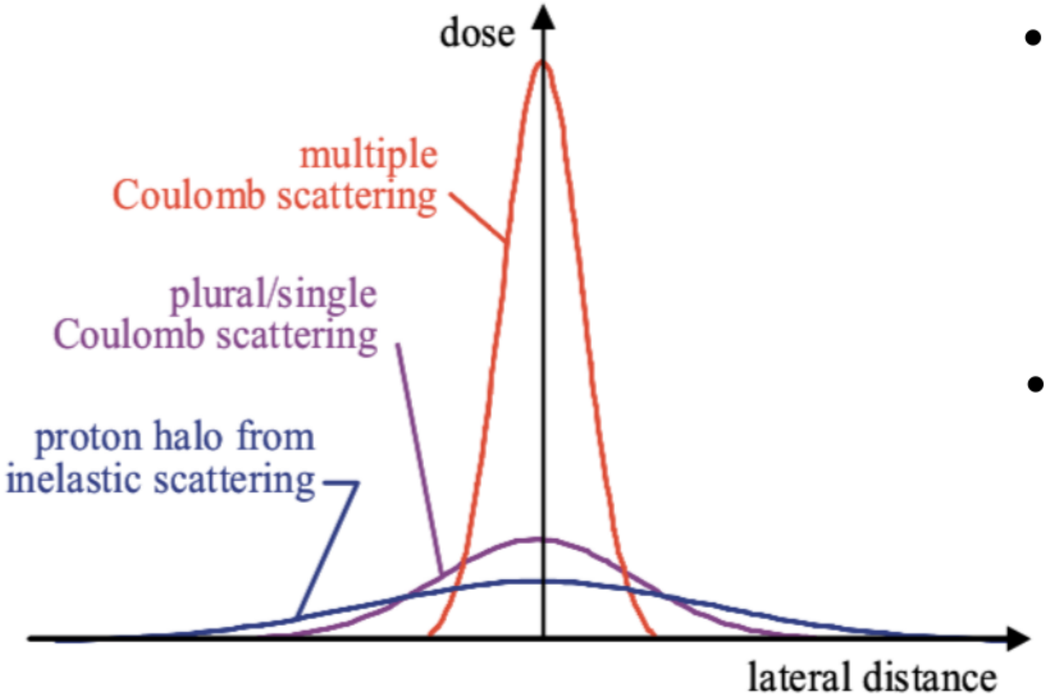
(essential to compute the dose delivered by a scattered broad beam within the patient)

P – dose from one pencil beam

Q – dose from several adjacent pencil beams

*M. Goitein 2008*

# Lateral Beam Shape

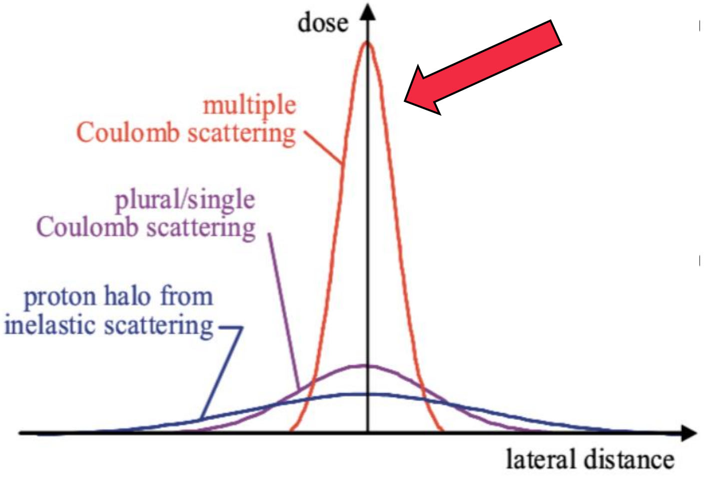


- Multiple Coulomb scattering:
  - near-Gaussian core
  - long tail
- Nuclear interactions:
  - protons
  - neutrons

*M. Goitein 2008*

Three charged particle components of the lateral profile of a pencil beam

# Lateral Beam Shape



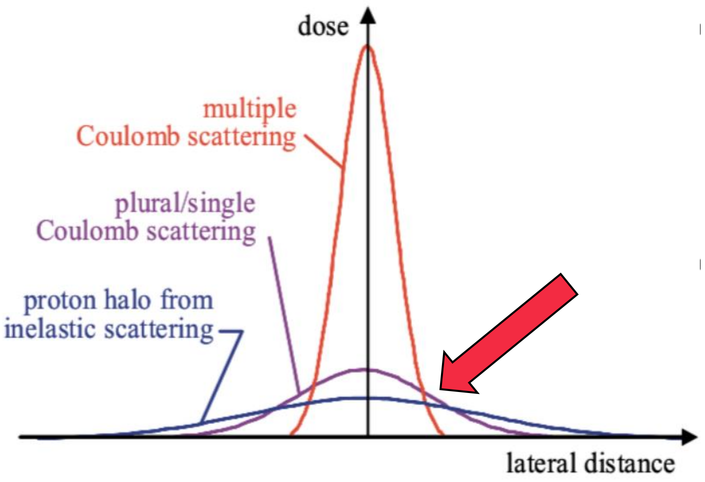
*M. Goitein 2008*

Multiple Coulomb scattering (near-Gaussian core)

- Nearly Gaussian distribution in the angle of deviation and in the lateral spread of a pencil beam ($\sigma_{\text{lateral distribution}}$= 2% range)

Protons (150 MeV) –> R = 15 g·cm$^{-2;}$ $\sigma$ = 3 mm; FWHM = 7 mm

# Lateral Beam Shape

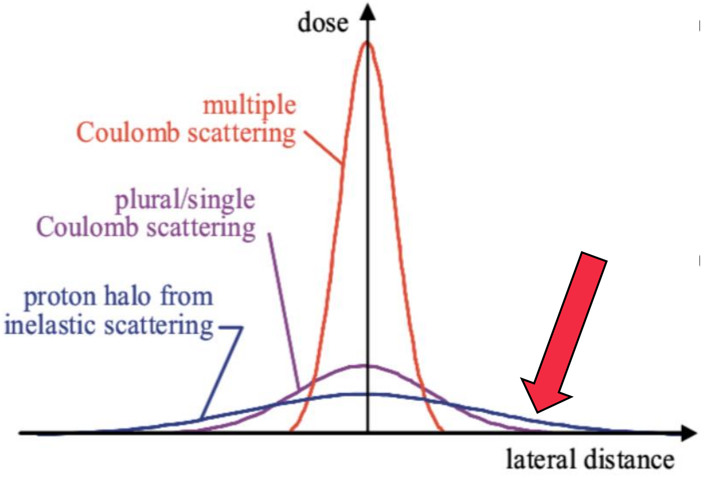


*M. Goitein 2008*

Multiple Coulomb scattering (long tail)

- The profile of the pencil beam is not precisely Gaussian in shape
- Long tail due to large angle scattering in one or few collisions
- Low amplitude and approximated by a second broader Gaussian

# Lateral Beam Shape

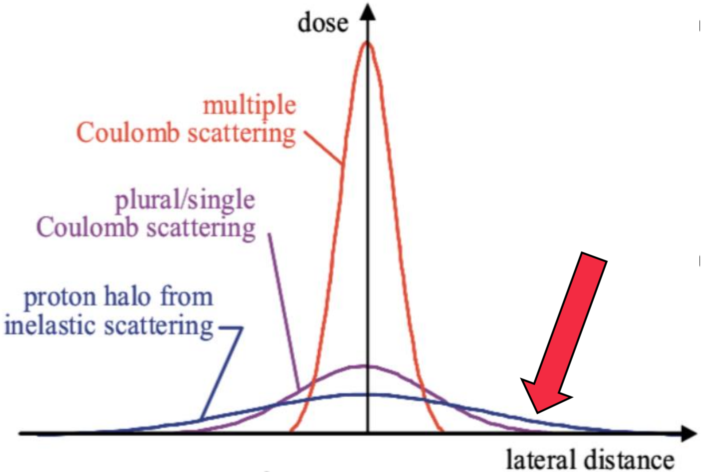


*M. Goitein 2008*

Nuclear interactions (protons)

- The scattered or knocked-out protons with high energy contribute to the tails of pencil beam’s lateral dose distribution
- Create a halo of dose around the beam that grows as the depth increases and is also approximated by a Gaussian

# Lateral Beam Shape

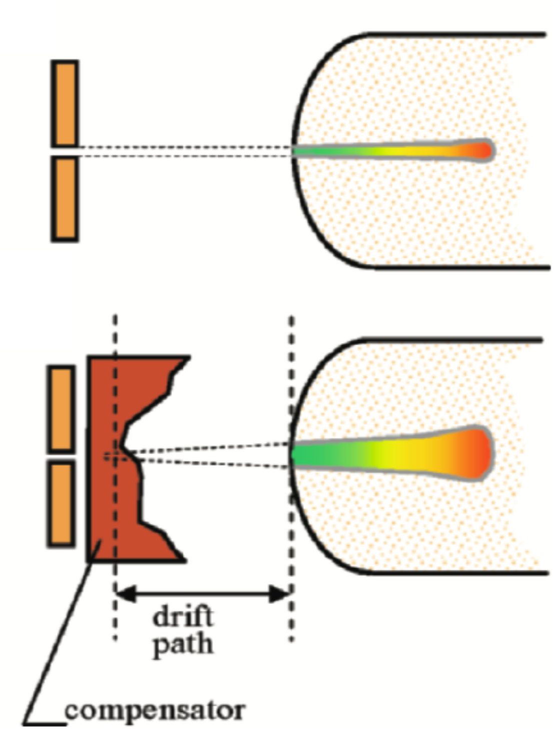


*M. Goitein 2008*

Nuclear interactions (neutrons)

- Nuclear interactions create a halo of neutrons that escape the patient without further interaction, but are responsible for a low dose in and outside the beam (cause secondary malignancies)

# Lateral Beam Shape



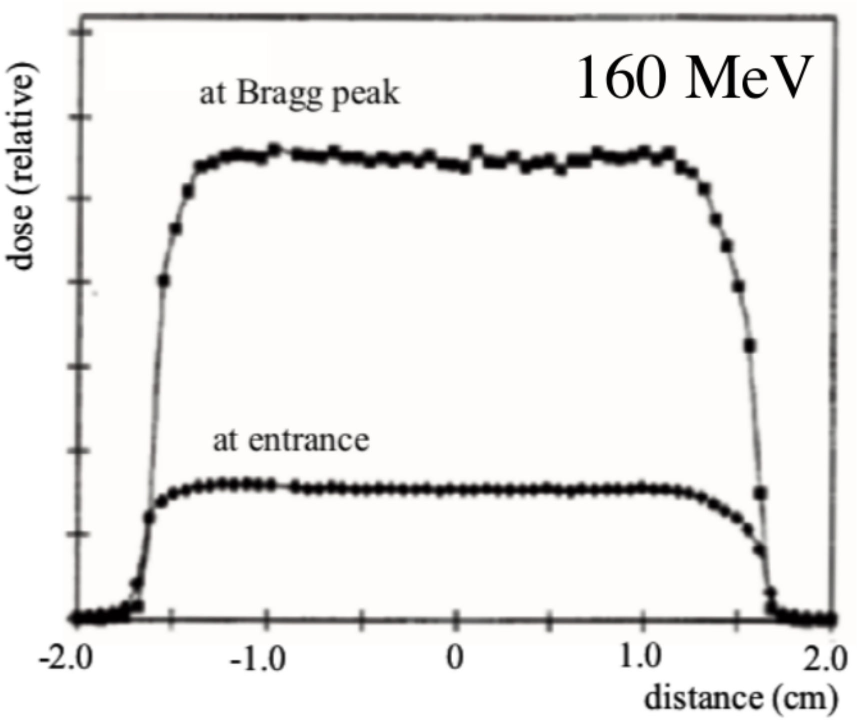
Scattering in upstream material is exacerbated by any drift path (gap) between the material and the patient

<u>Causes</u>:

- Irradiation technique (passive or active)
- Energy control
- Double scatterers
- Location of aperture
- Path in air after the last upstream material

*M. Goitein 2008*

# Lateral Beam Shape

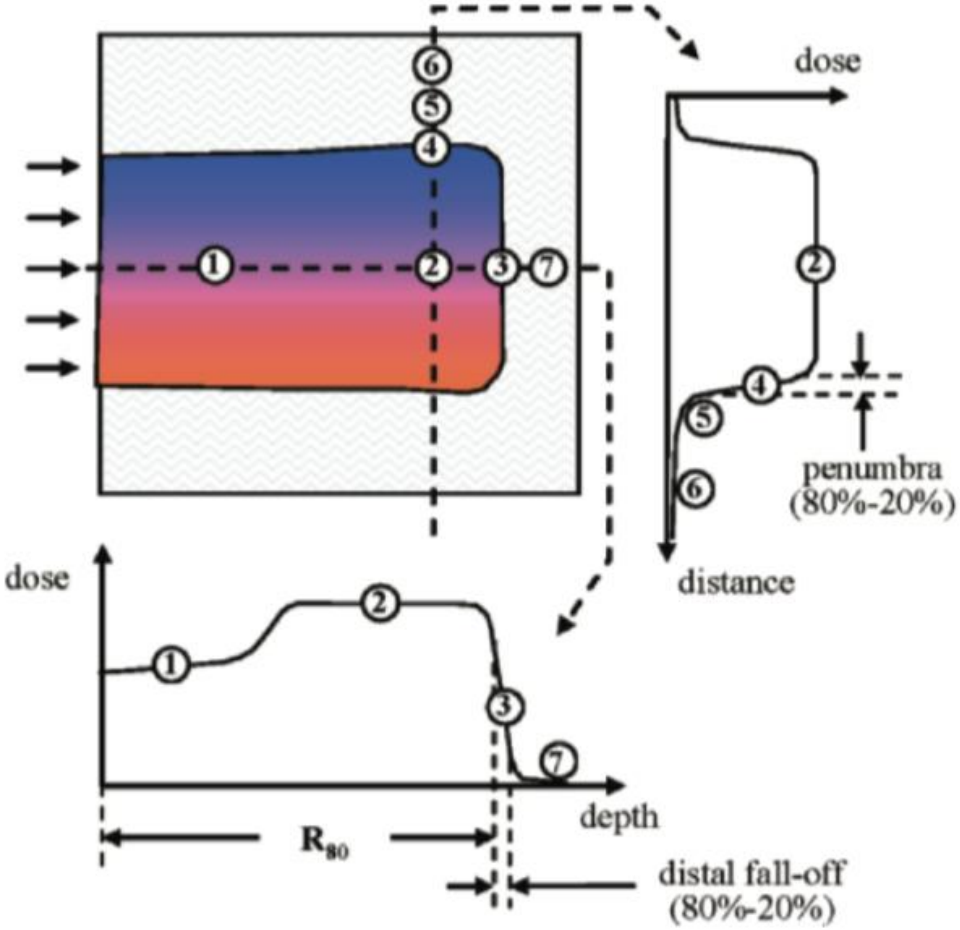


Lat. Pen. (R=15 cm) = 5 mm (~3.5%)
Photons = 6-9 mm

- For large energies, the lateral penumbra is dominated by the scattering in the target material
- For small energies, the lateral penumbra is dominated by blurring effects upstream of the patient (scattering in material)
- Both effects are comparable

*(B. Gottschalk) M. Goitein 2008*

# Schema of principal contributions



1 plateau protons – excitation/ionization; & nuclear interactions

2 excitation/ionization (Bragg peaks); & nuclear interactions

3 range straggling and energy spread

4 multiple Coulomb scattering off nuclei

5 wide angle Coulomb scattering off nuclei

6 protons and neutrons from nuclear interactions

7 neutrons from nuclear interactions

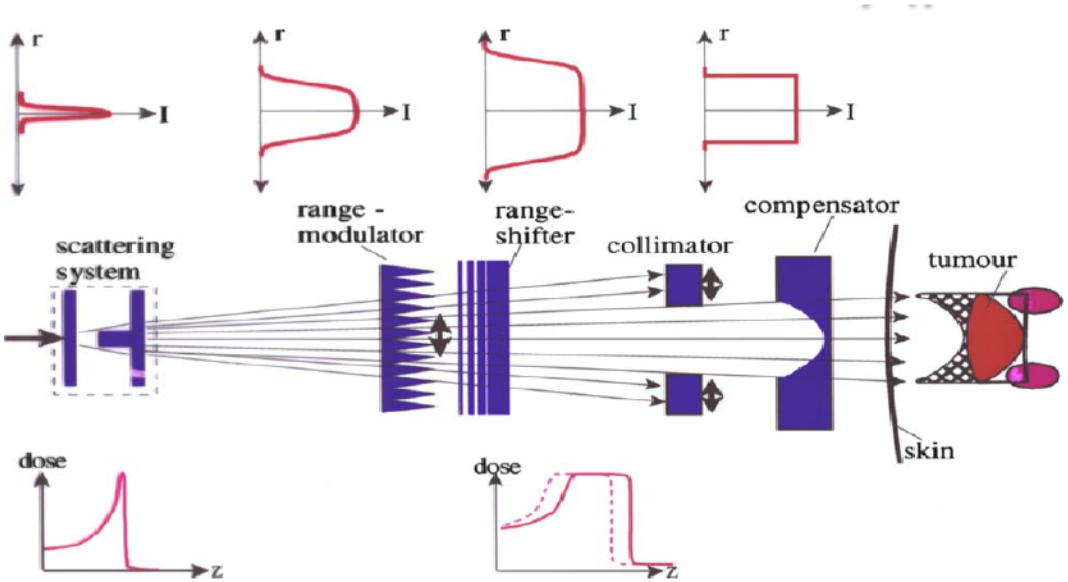
Schema of the principal contributions to the dose at several points within and outside the broad beam

*M. Goitein 2008*

# Overview

- Introduction to Radiotherapy
- Physics:
  - Interaction Types of Particles with Matter
  - Energy Loss in Material
  - Lateral Beam Shape
- **Beam Delivery Techniques**

# Passive Beam Delivery



**Single-scatter:**

Excellent penumbral quality

Not too large fields

**Double-scatter:**

Larger penumbra

Must be very well centered

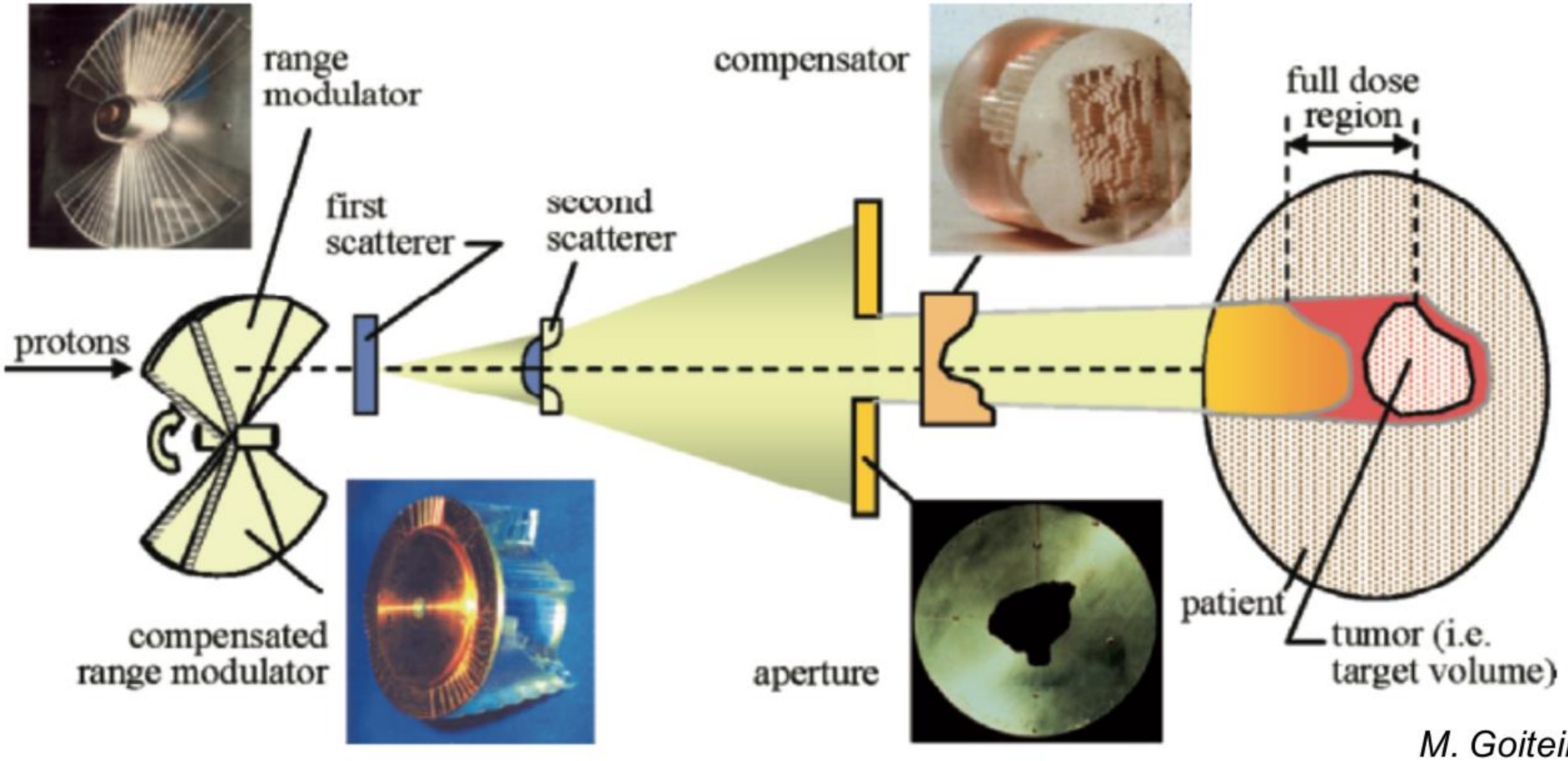
More efficient (transmits up to 45% of the beam)

Reduction of secondary dose

- Double-scattering system generates a flat transversal profile (spreading laterally)
- Mono-energetic Bragg peak is spread out by a range modulator (spreading in depth)
- SOBP can be shifted in depth by absorber plates (“range shifter”)
- The collimator cuts out the field area defined by the largest target contour
- The range compensator adjusts the distal depth pattern

*Schardt & Elsässer, (2010) Rev. Mod. Phys. 82, 383*

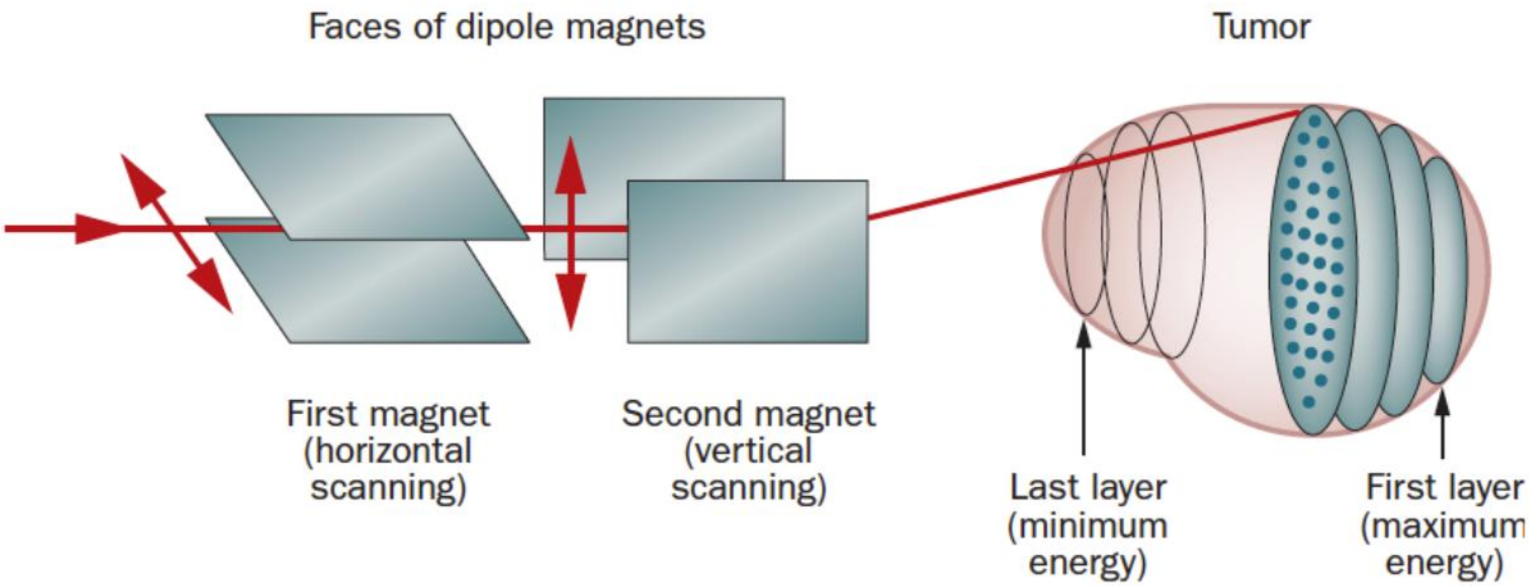
# Passive Beam Delivery



*M. Goitein 2008*

# Active
Beam Delivery

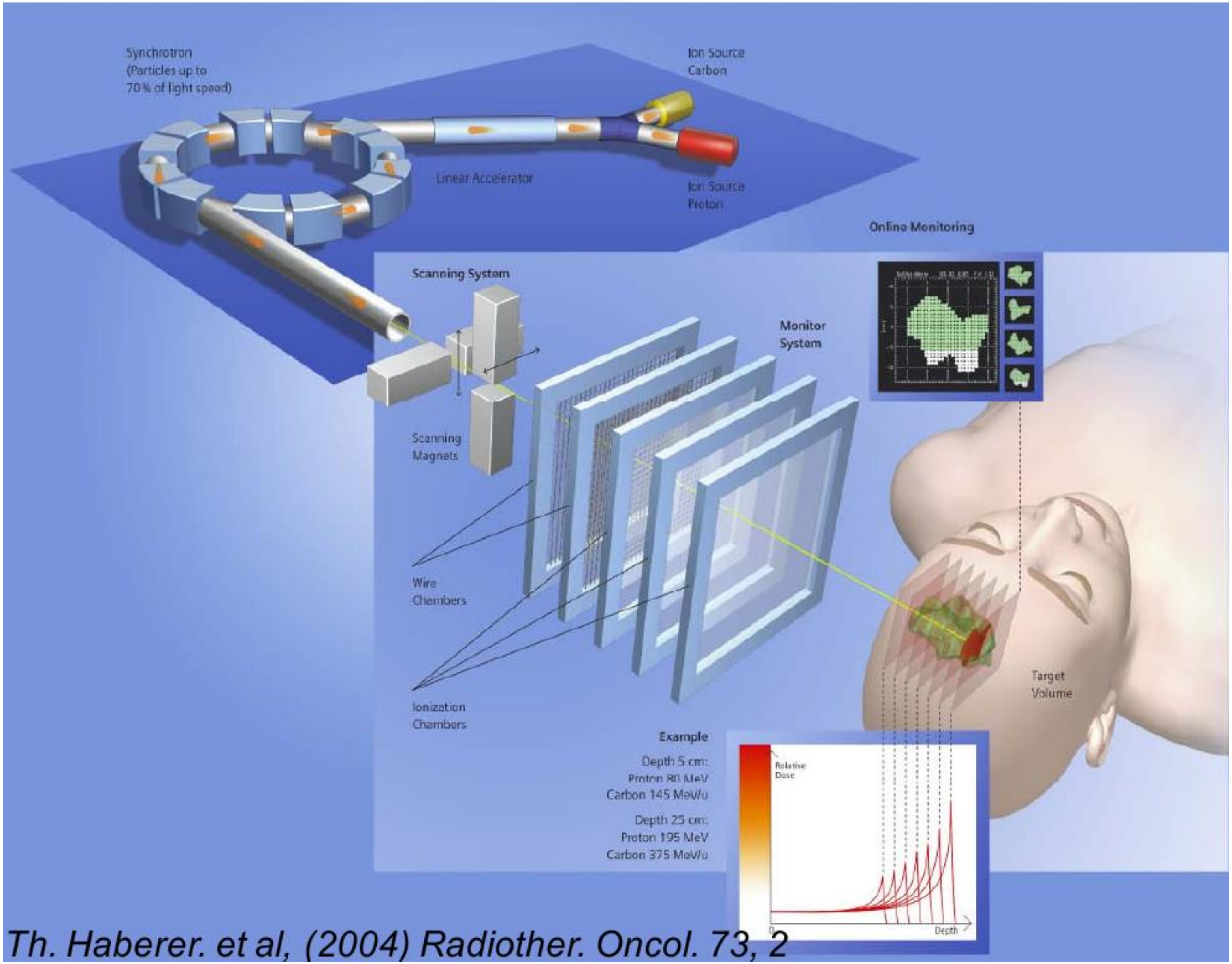
## Intensity-controlled magnetic raster scanning



**Pencil-like ion beam whose position is precisely controlled by rapid dipole magnets**

*M. Durante & J. Loeffler., (2010) J. S. Nat. Rev. Clin. Oncol. 7, 37*

# Active Beam Delivery



*Th. Haberer. et al, (2004) Radiother. Oncol. 73, 2*

# Active Beam Delivery

Intensity-controlled magnetic raster scanning

- It can “paint” any physically possible dose distribution
- It uses protons very efficiently as compared to passive scattering techniques (more than 50% of protons have to be “thrown away”)
- It generally requires no patient-specific hardware
- The neutron background is substantially reduced
- Scanned beam delivery allows the implementation of IMRT with protons – termed intensity-modulated proton therapy (IMPT).

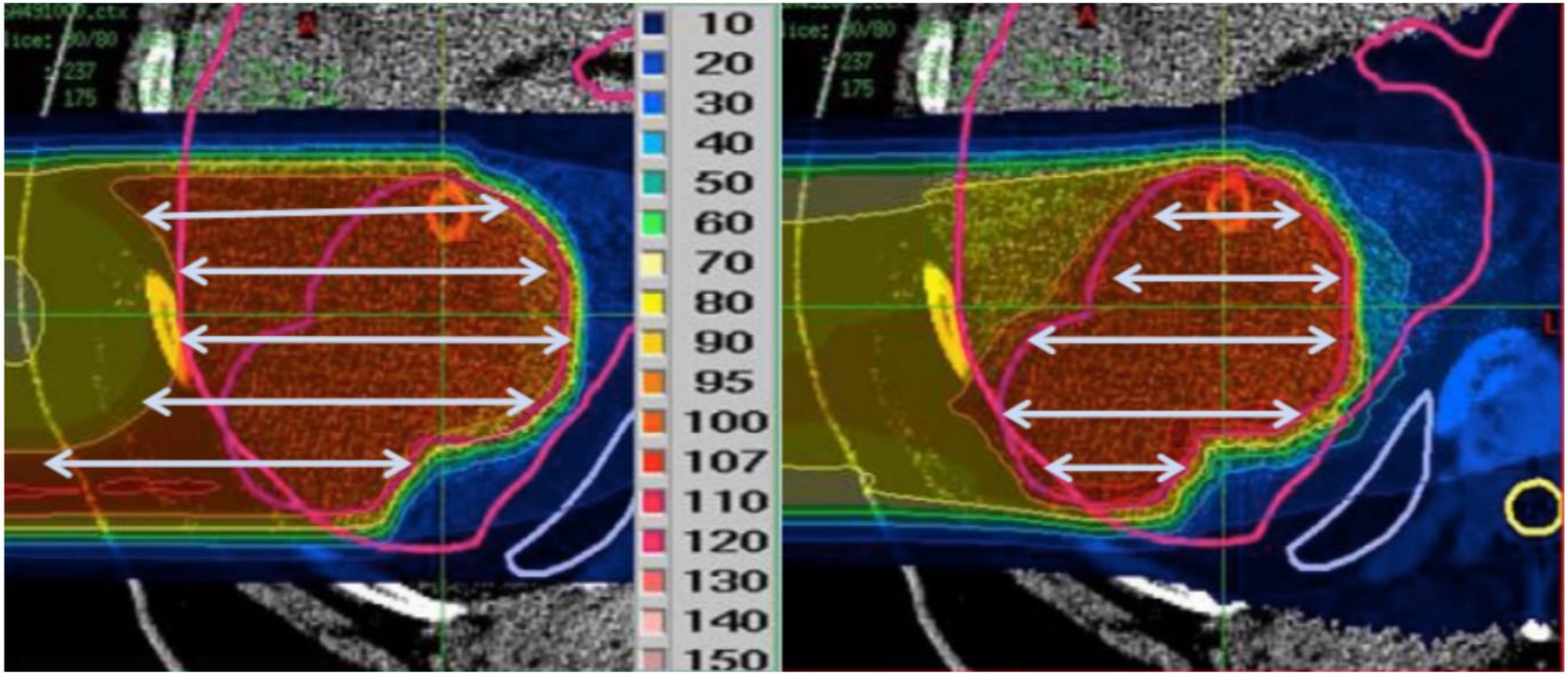
# Active
Beam Delivery

Intensity-controlled magnetic raster scanning

- The need for heightened safety measures due to the dire consequences of instrumental or control system failure (e.g., high intensity pencil beam lingering on the patient, rather than moving on to the next position)
- The need to overcome interplay effects induced by organ motion.

# Active vs Passive Beam Delivery

## Liver treatment with scanning



*(C. Gillmann 2014) O. Jäkel 2018*

# End of Part I/II

Any Questions?

Send me an E-mail: **B.Kopp@dkfz-heidelberg.de**