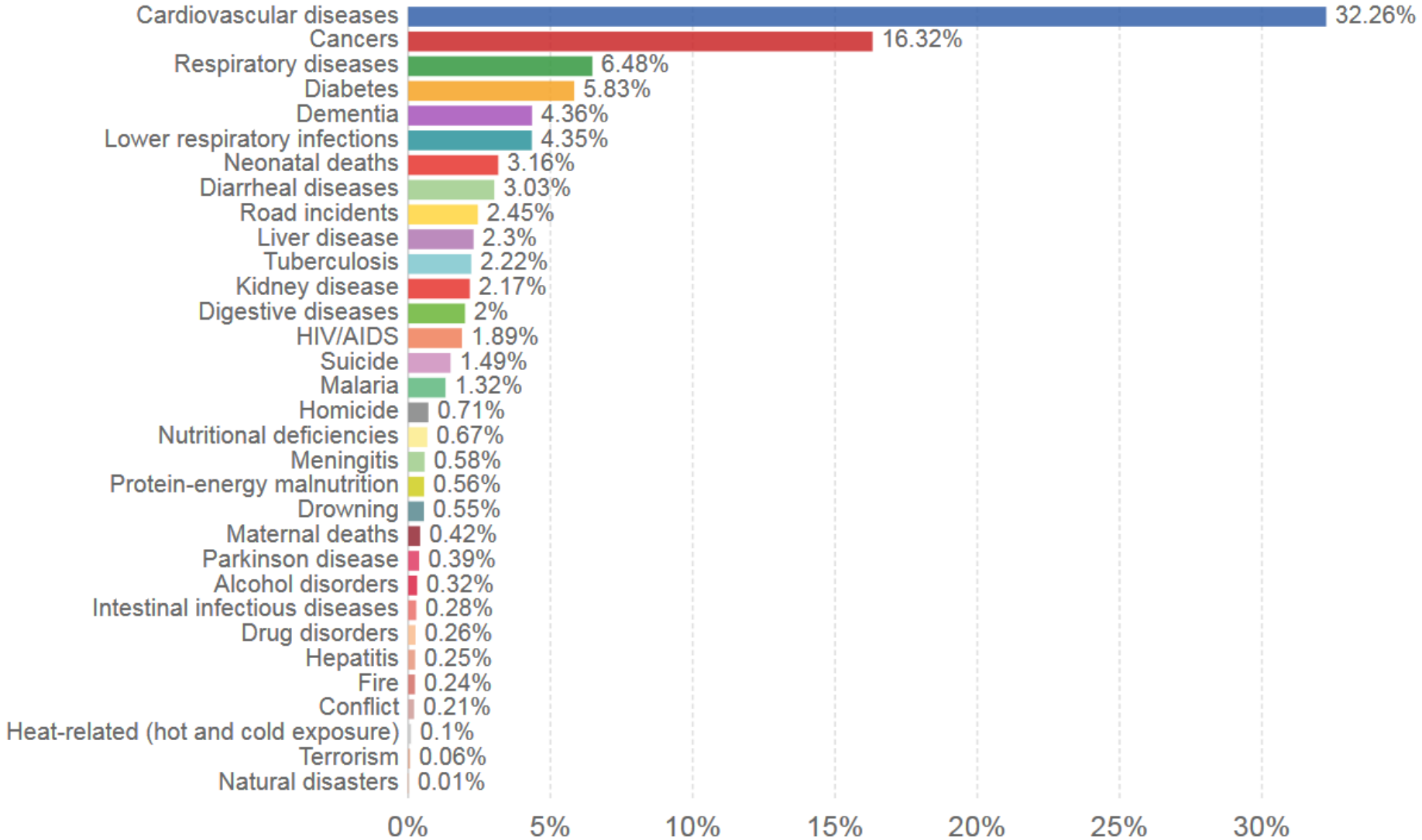
Share of deaths by cause, World, 2016

Data refers to the specific cause of death, which is distinguished from risk factors for death, such as air pollution, diet and other lifestyle factors. This is shown by cause of death as the percentage of total deaths.



Source: IHME, Global Burden of Disease

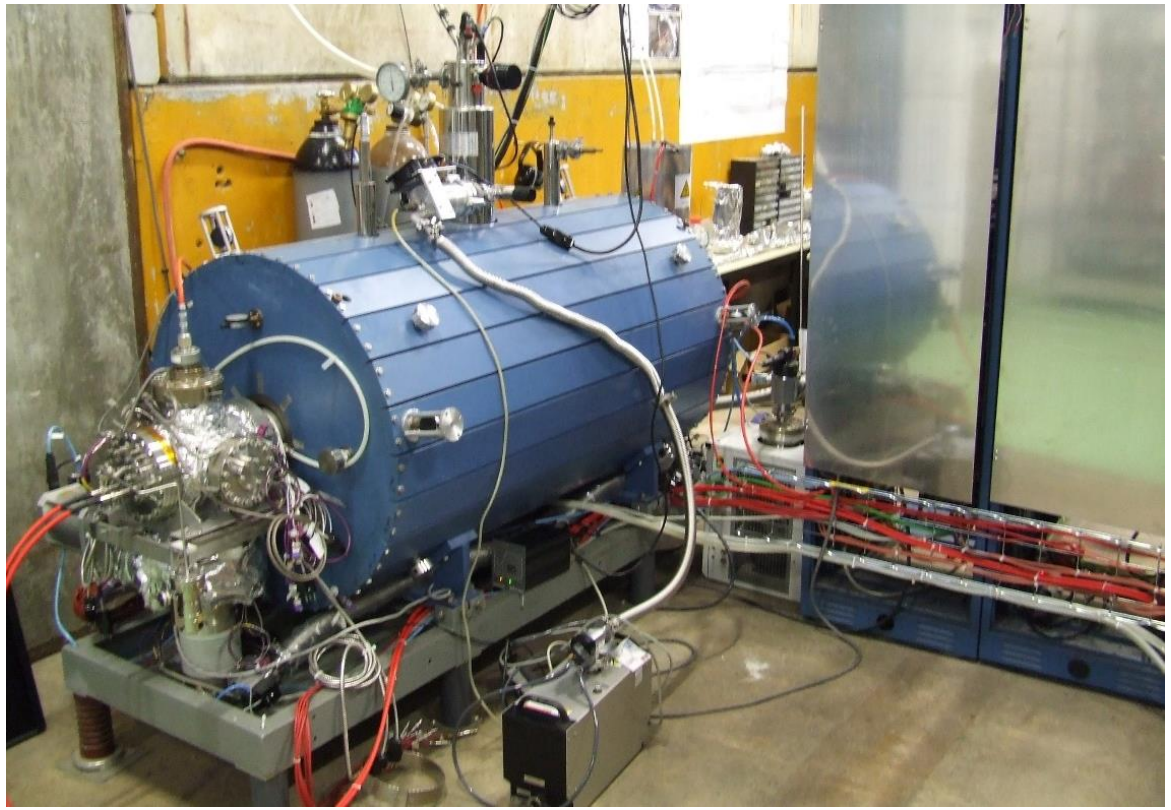
Statistic

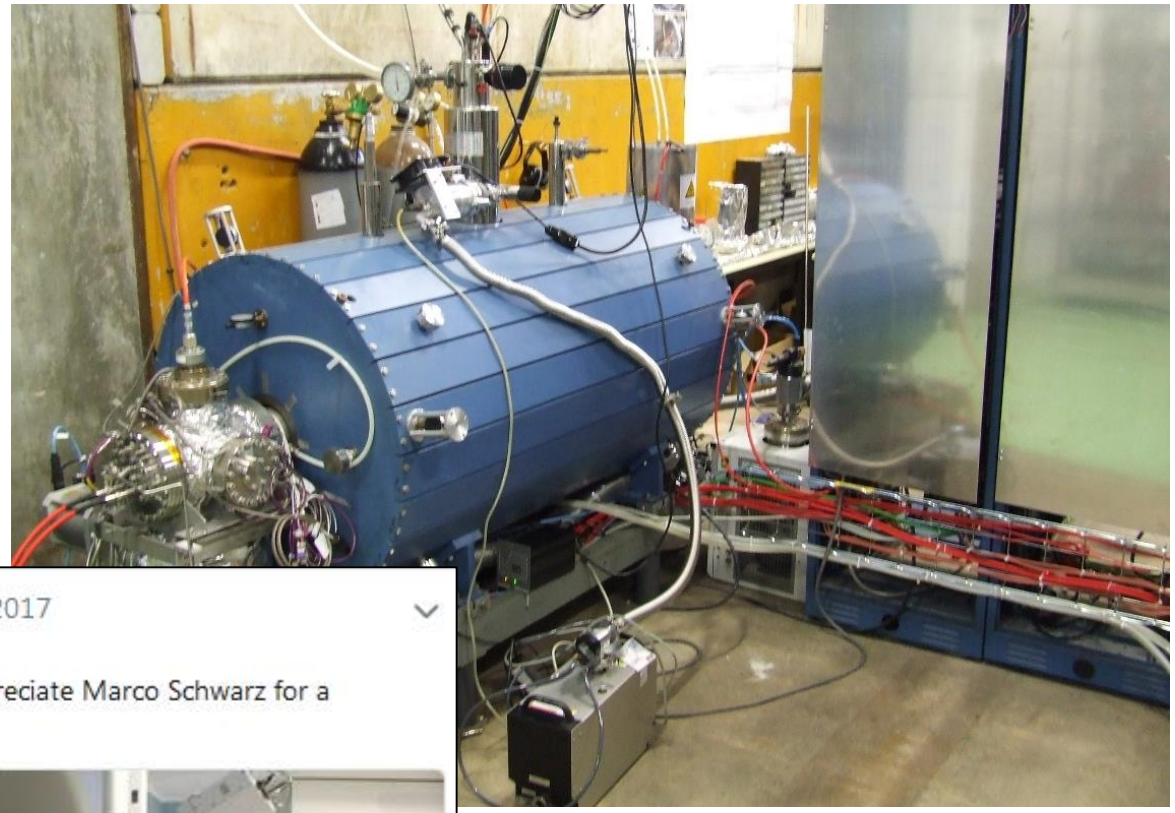
Beams for Cancer Treatment

Johanna Pitters

31/07/2018

Summer Camp Lecture

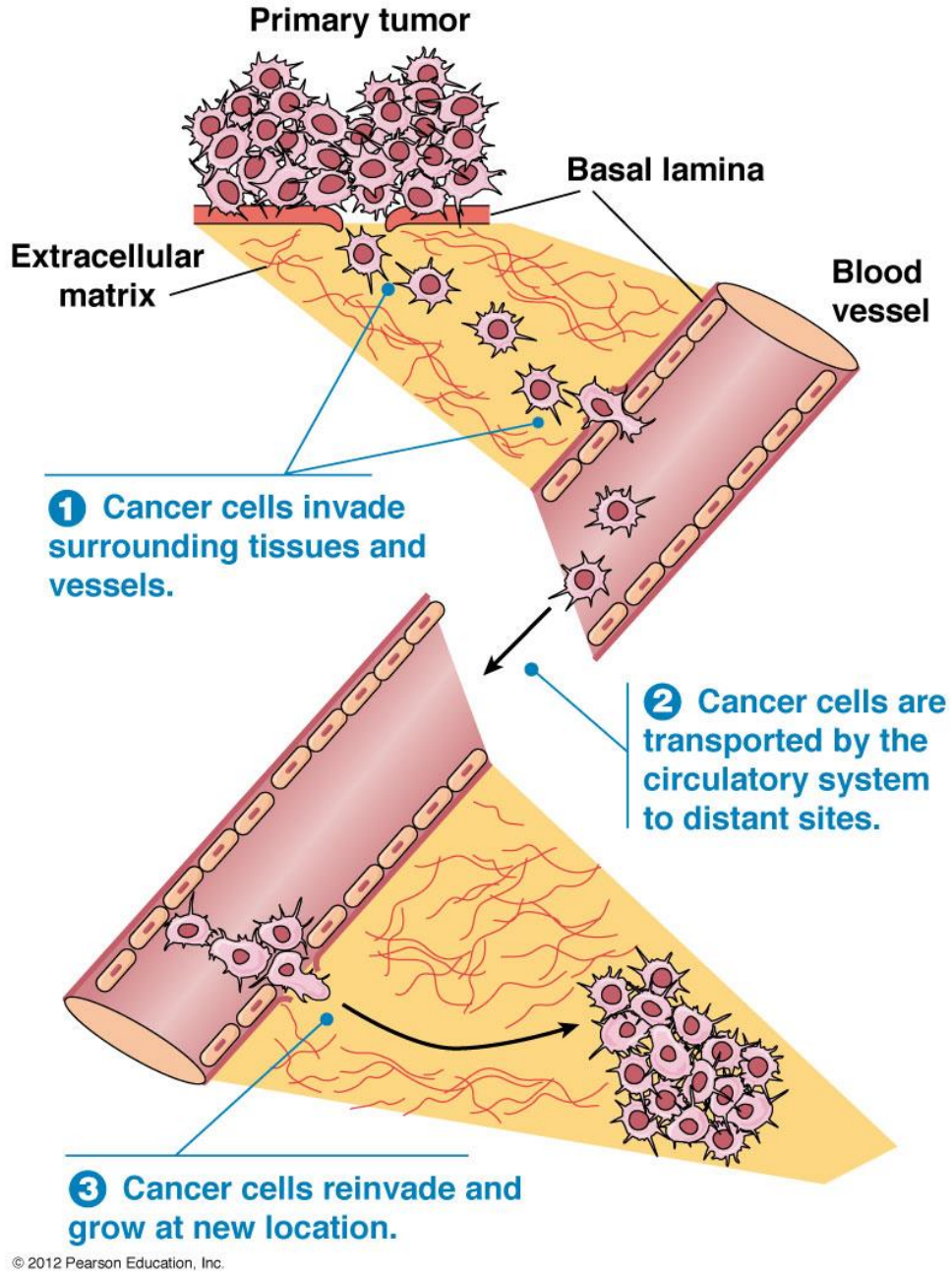




Medicis-Promed @MedicisPromed · 10 Jun 2017

Guess, where we were today?
Trento, Proton Therapy Center. We highly appreciate Marco Schwarz for a wonderful excursion into the facility.

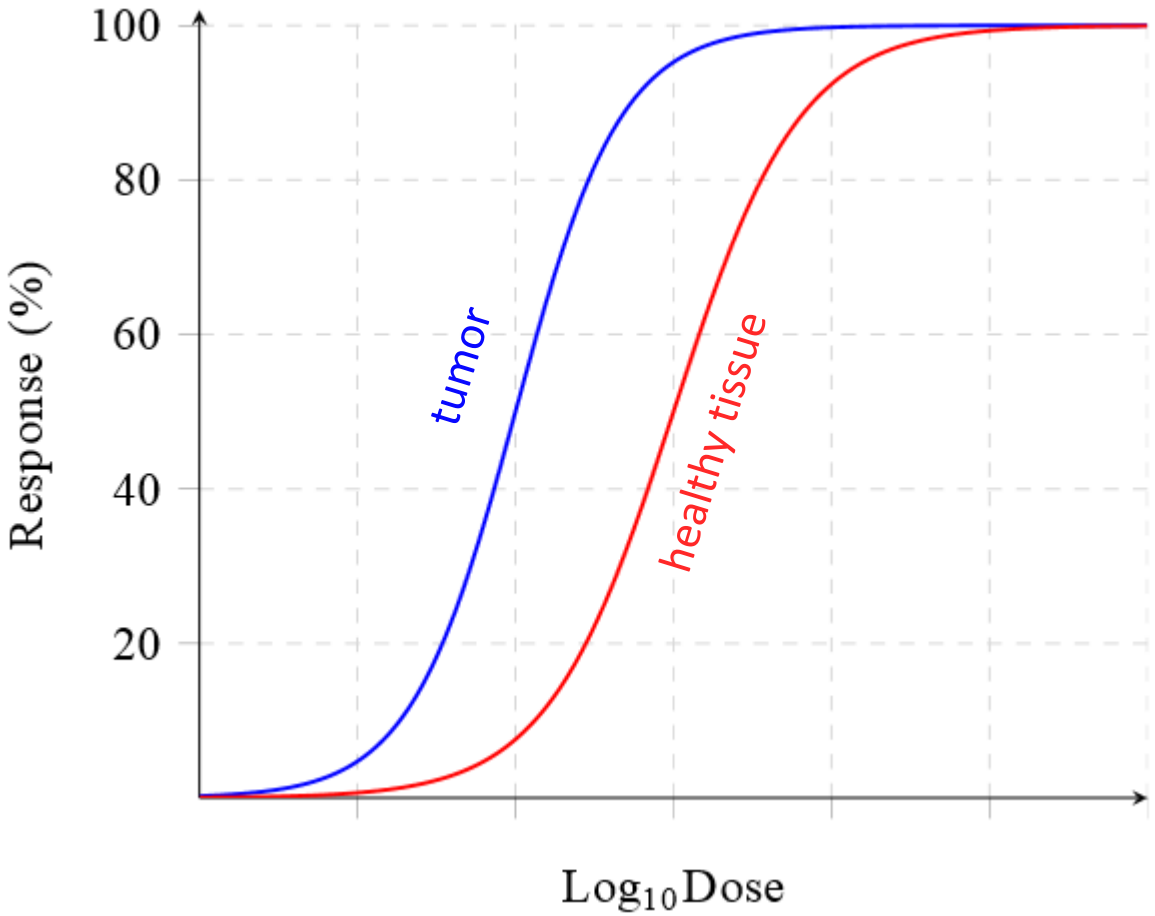
What is cancer?



https://www.mun.ca/biology/desmid/brian/BIOL2060/BIOL2060-24/CB24.html

Dose-Response-Curve

- Treatment: higher response from cancer cells than normal, healthy tissue
- Harm to healthy tissue may induce unwanted side effects



Treatment methods

Chemotherapy (Systemic therapy)

Treatment methods

Chemotherapy (Systemic therapy)

Surgery

Treatment methods

Chemotherapy
(Systemic
therapy)

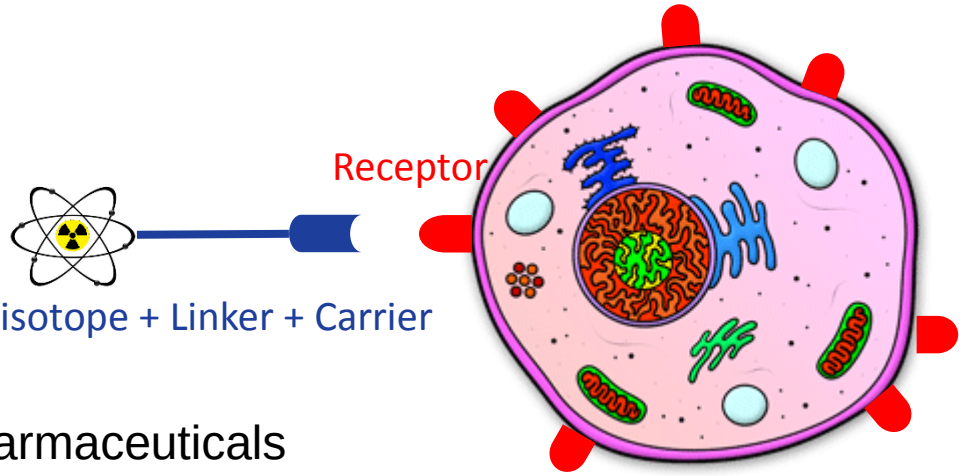
Radiopharmaceuticals
(Targeted therapy)

Surgery

Production of radioisotopes
at CERN Medicis facility

Treatment methods

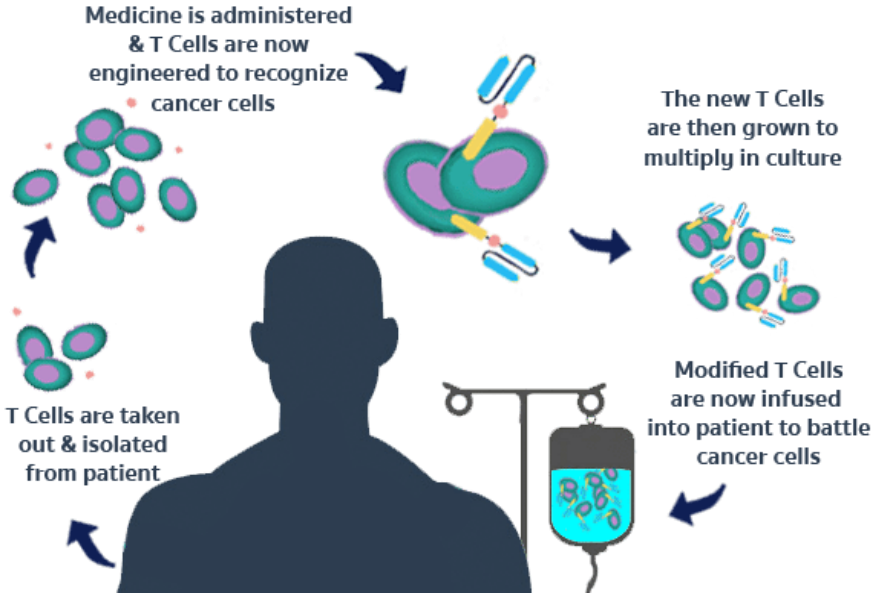
Chemotherapy (Systemic therapy)



Radiopharmaceuticals (Targeted therapy)

Surgery

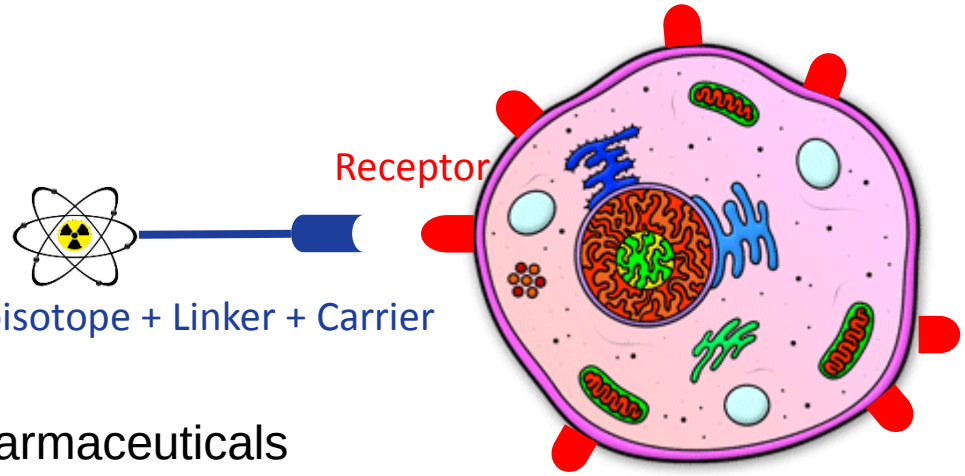
Immunotherapy



https://www.treatmesothelioma.org/treatment/complementary/immunotherapy/

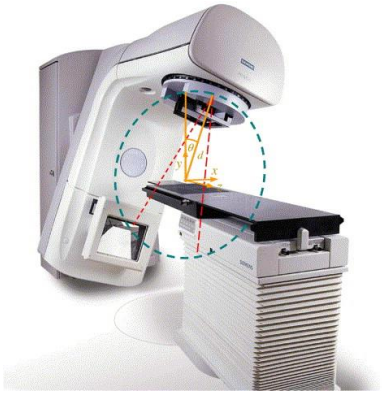
Treatment methods

Chemotherapy (Systemic therapy)



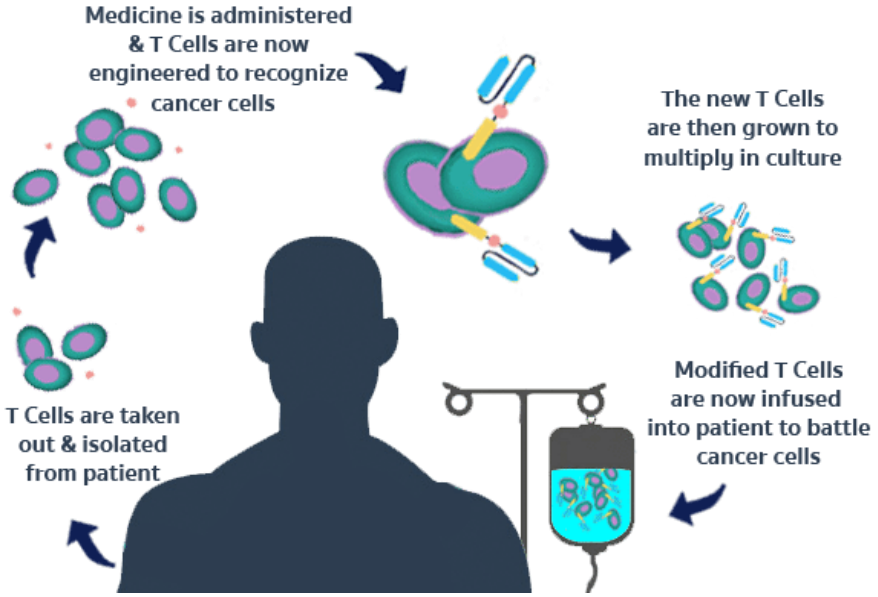
Radiopharmaceuticals (Targeted therapy)

External beam irradiation



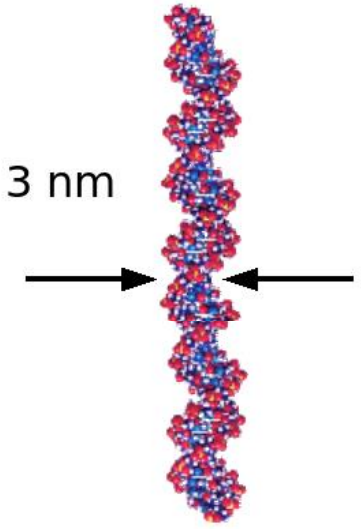
Surgery

Immunotherapy

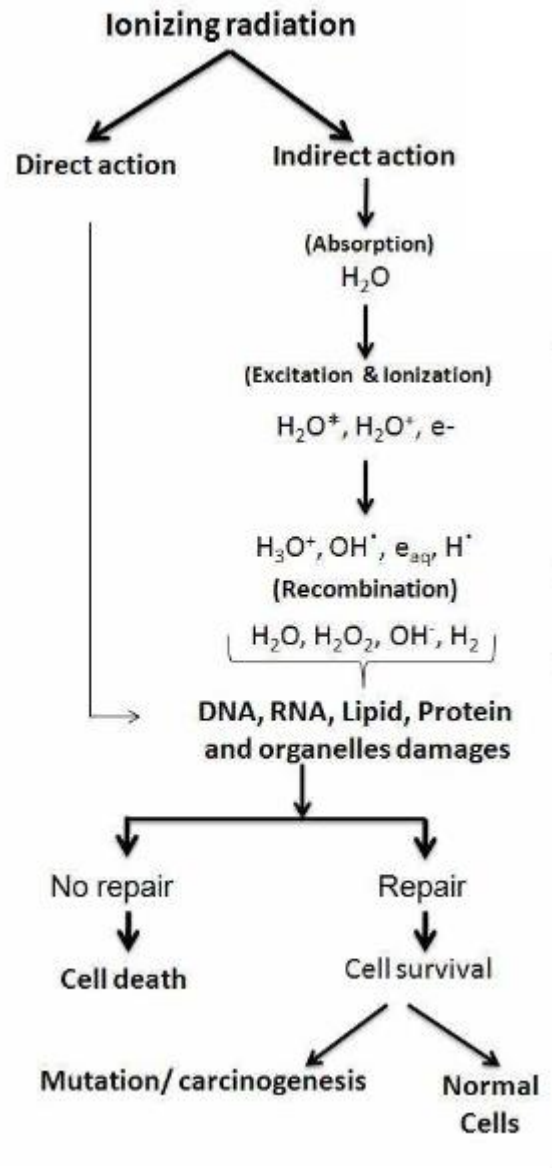


https://www.treatmesothelioma.org/treatment/complementary/immunotherapy/

Cell damage through ionizing radiation



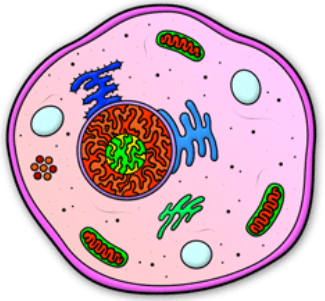
DNA Segment



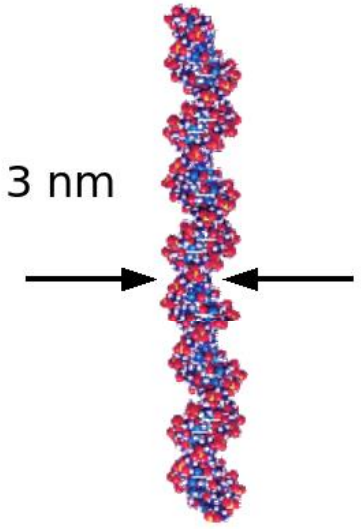
Physical stage:
Excitation and Ionization

Chemical stage:
-> chemical bonds break
-> formation of free radicals

Biological stage:
cell cycle stops while cell attempts to repair

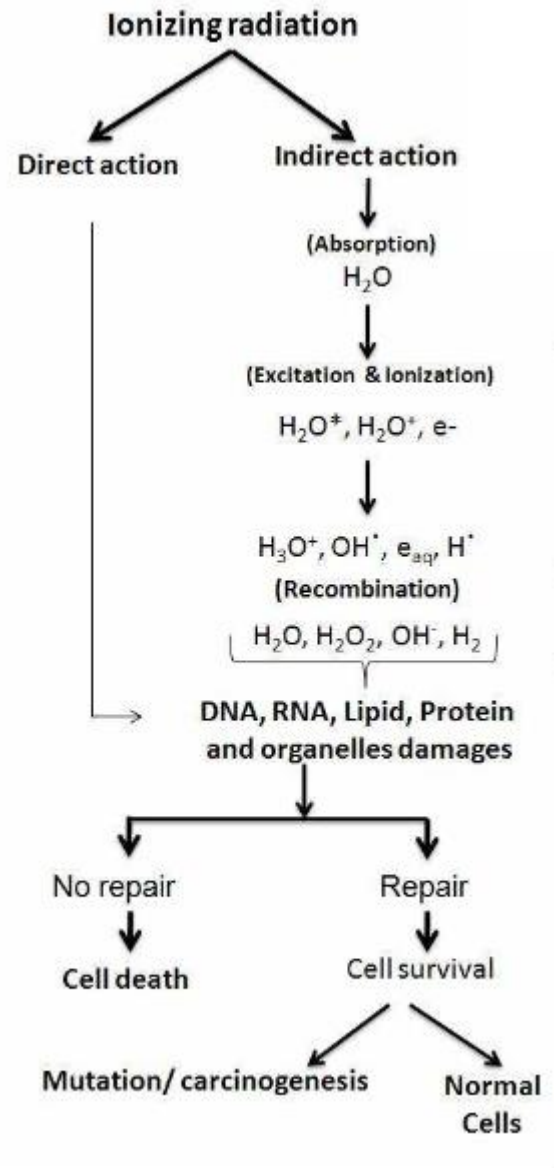


Cell damage through ionizing radiation



DNA Segment

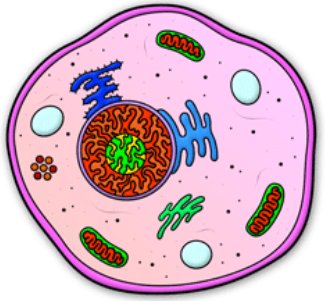
Irreversible DNA damage
-> Apoptosis



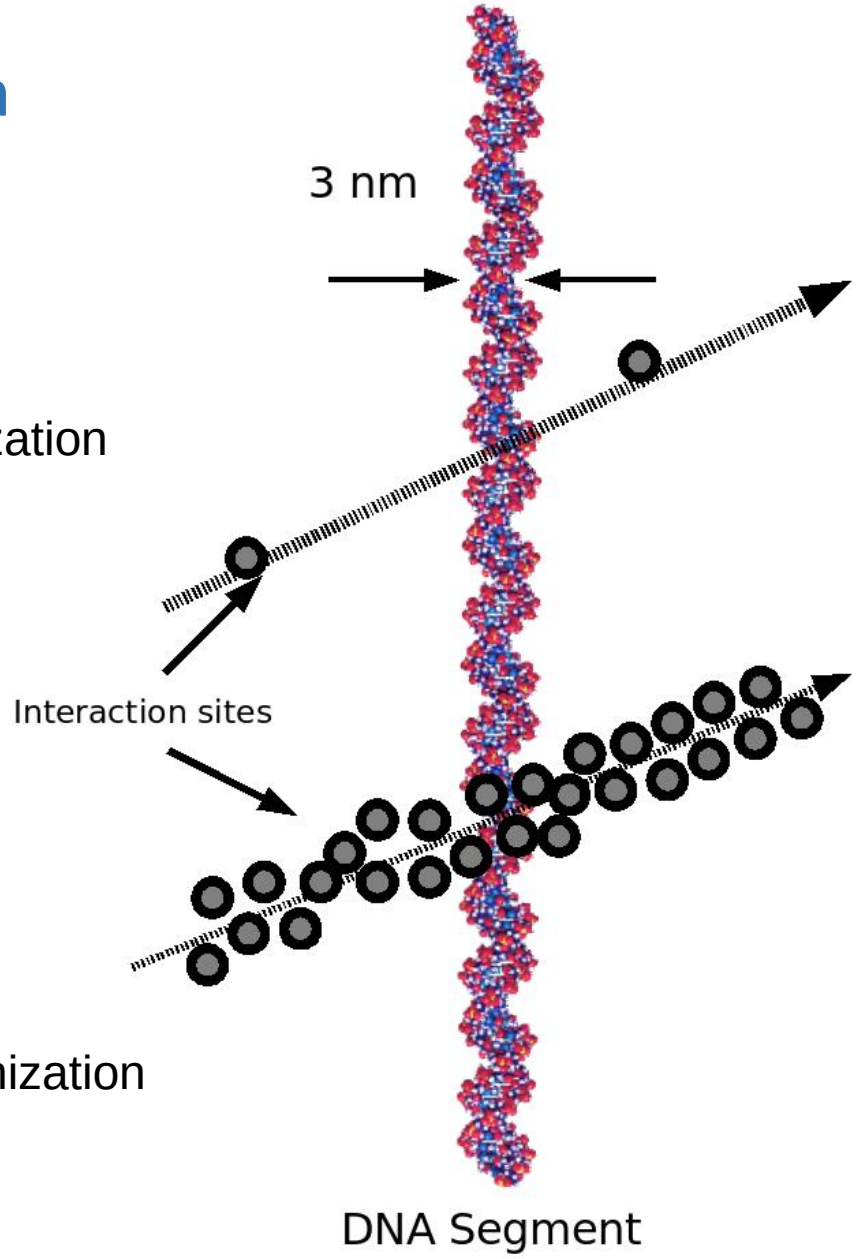
Physical stage:
Excitation and Ionization

Chemical stage:
-> chemical bonds break
-> formation of free radicals

Biological stage:
cell cycle stops while cell attempts to repair



Cell damage through ionizing radiation



More likely to cause severe DNA damage e.g. through double-strand breaks

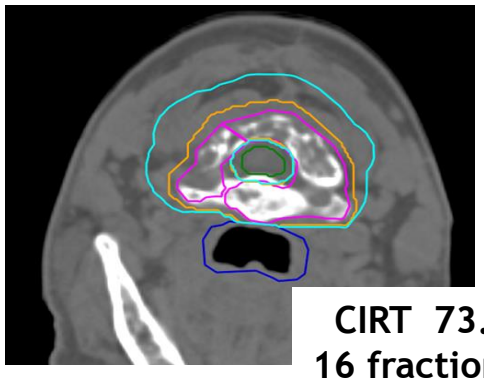
http://radioactivityci2010.pbworks.com/w/page/30525316/Fast%20Neutron%20Therapy

Dose

Dose

Gy [J/kg]

Energy deposited in tissue



CIRT 73.6 GyE
16 fractions IMPT

Equivalent dose

Sv [J/kg]

Damage to tissue weighted: radiation

Photons (1)
Electrons (1)
Protons (2)
Heavy ions (20)
Neutrons
...

Effective dose

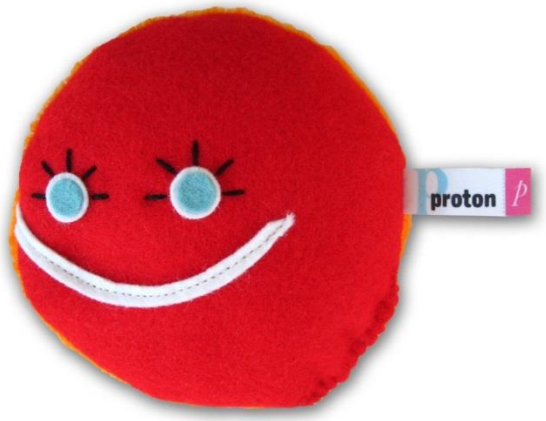
Sv [J/kg]

Damage to organ weighted: tissue

Organ/tissue	ICRP (2007)
Breast	0.12
Bone marrow	0.12
Colon[a]	0.12
Lung	0.12
Remainder	0.12[b]
Stomach	0.12
Gonads[d]	0.08
Bladder	0.04
Liver	0.04
Oesophagus	0.04
Thyroid	0.04
Bone surfaces	0.01
Brain	0.01
Salivary glands	0.01
Skin	0.01

External Beam Irradiation

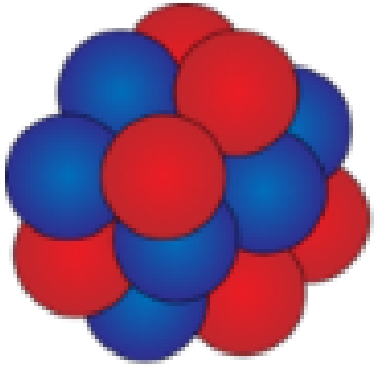
electron



proton

photon

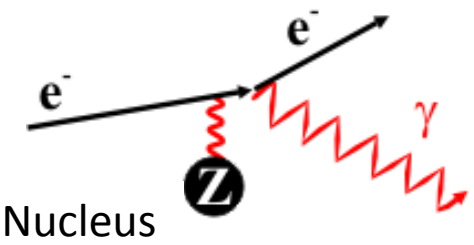
carbon ion



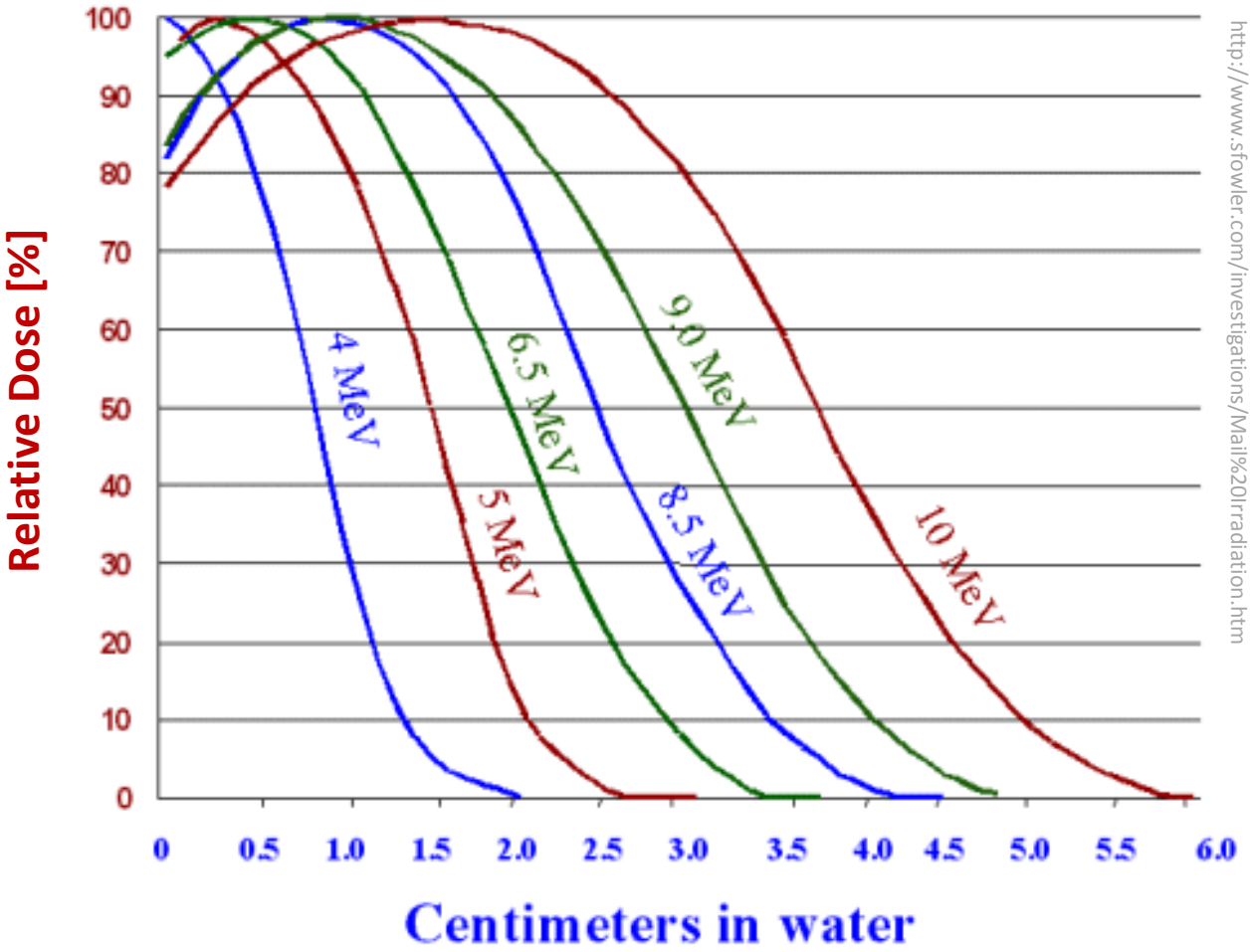
How do they deposit energy in the tissue?
Where do they deposit energy in the tissue?

Electrons

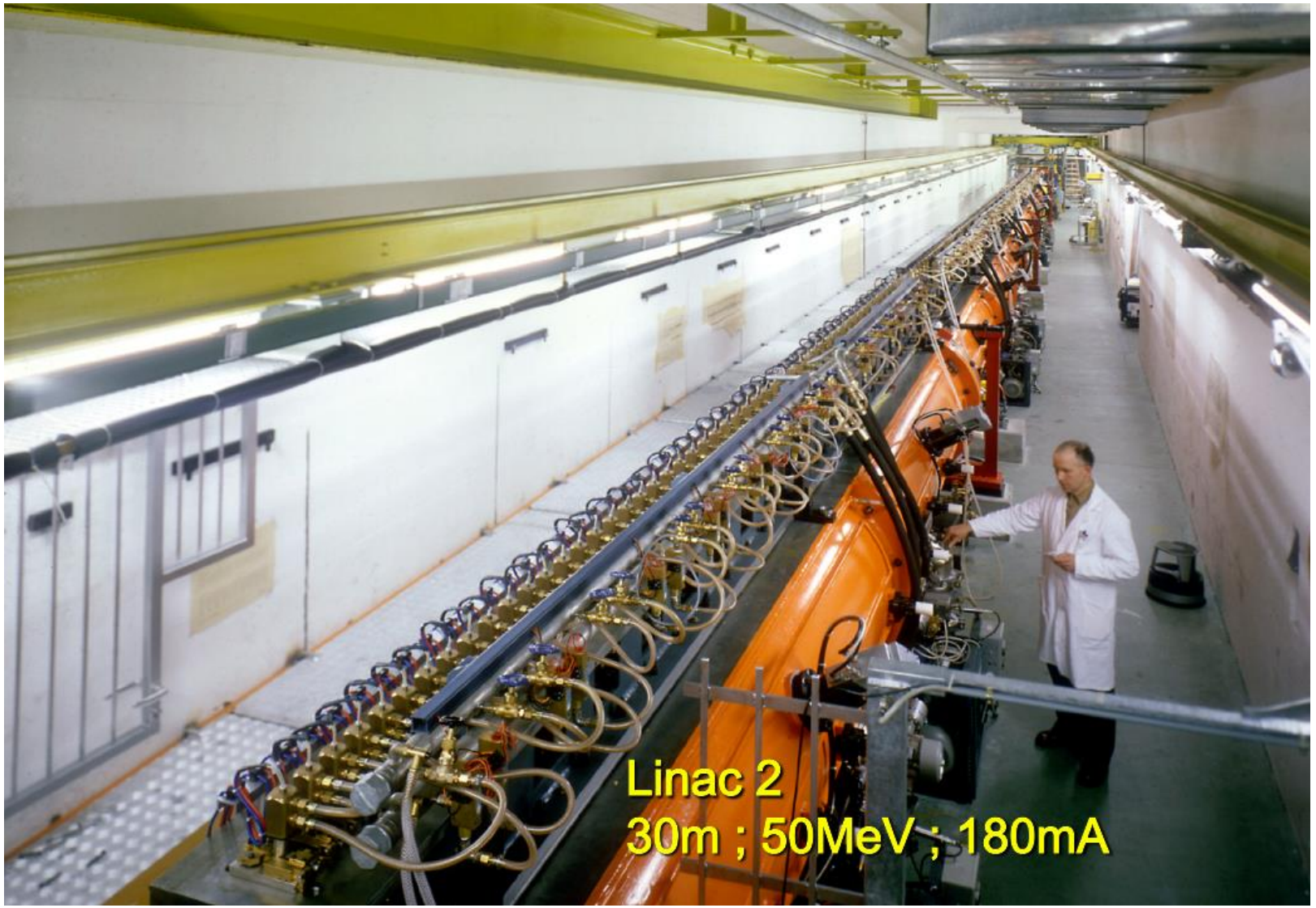
Energy loss:
- Inelastic scattering -> excitation, ionization
- Radiative stopping → 'bremsstrahlung'
(goes up with electron energy and Z)



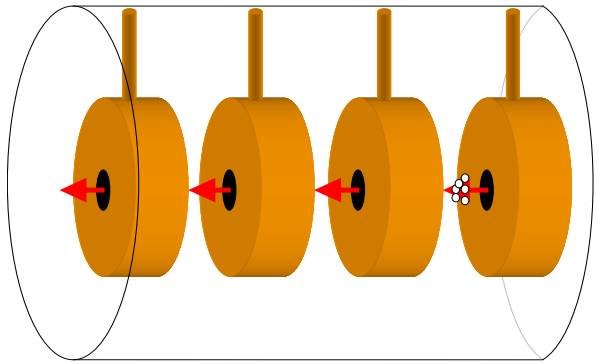
Scattering through collisions
-> broadening of the beam

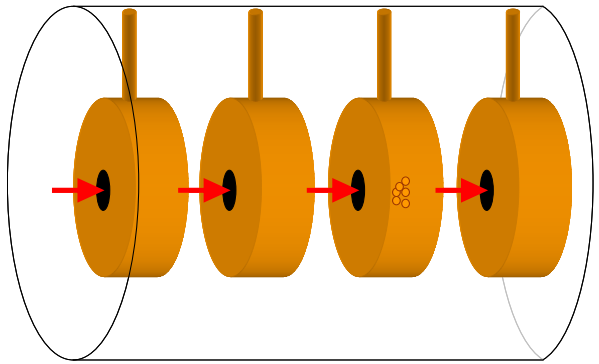


Electrons

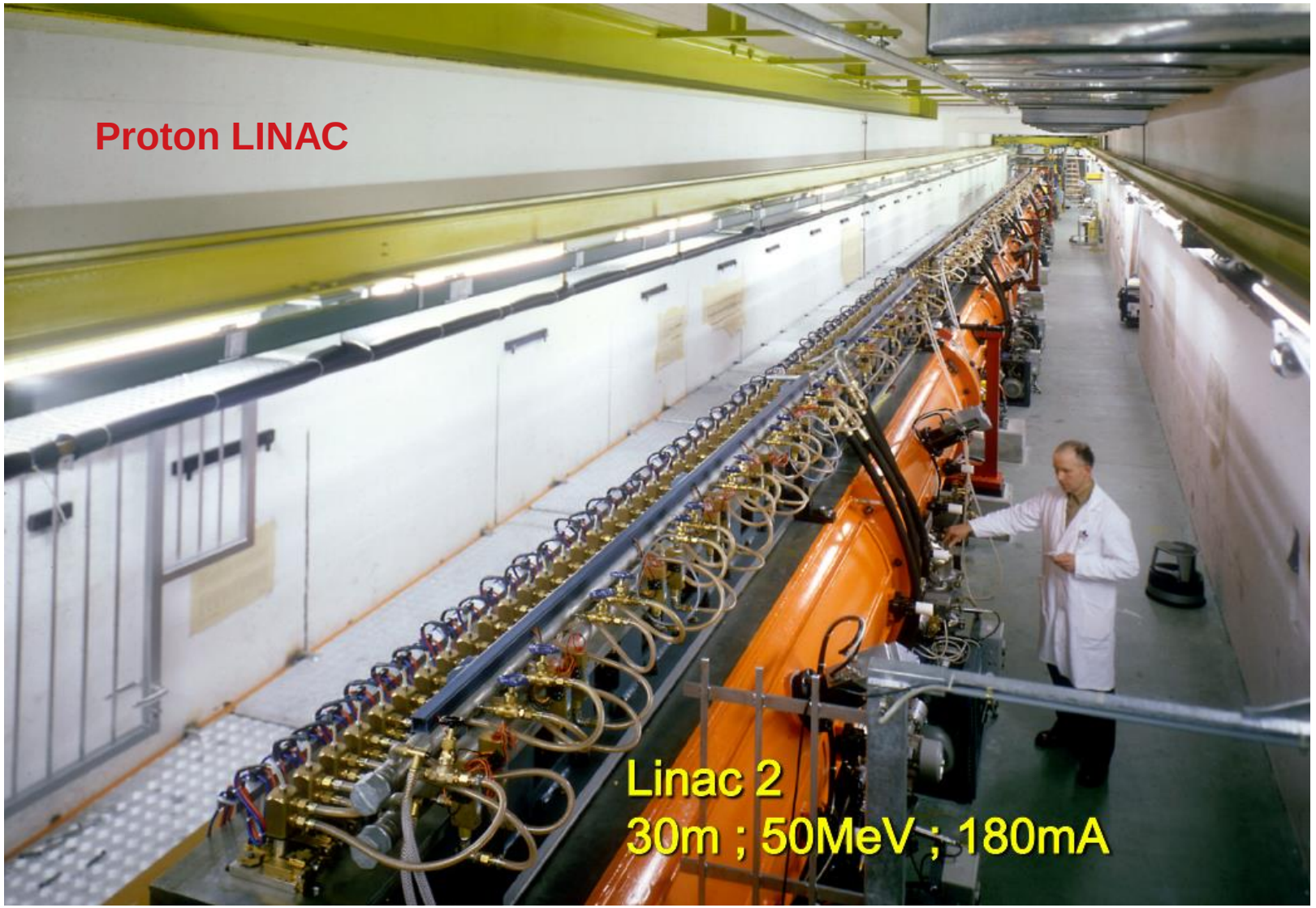


LINAC – linear accelerator

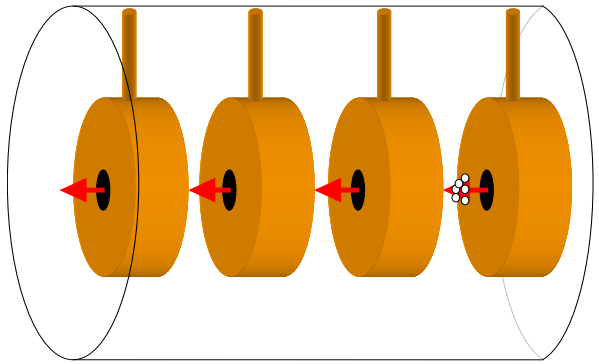


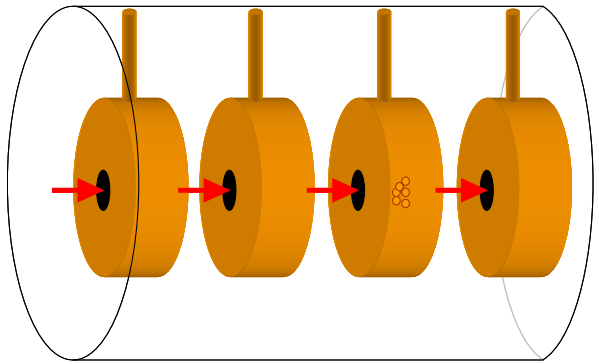


Electrons

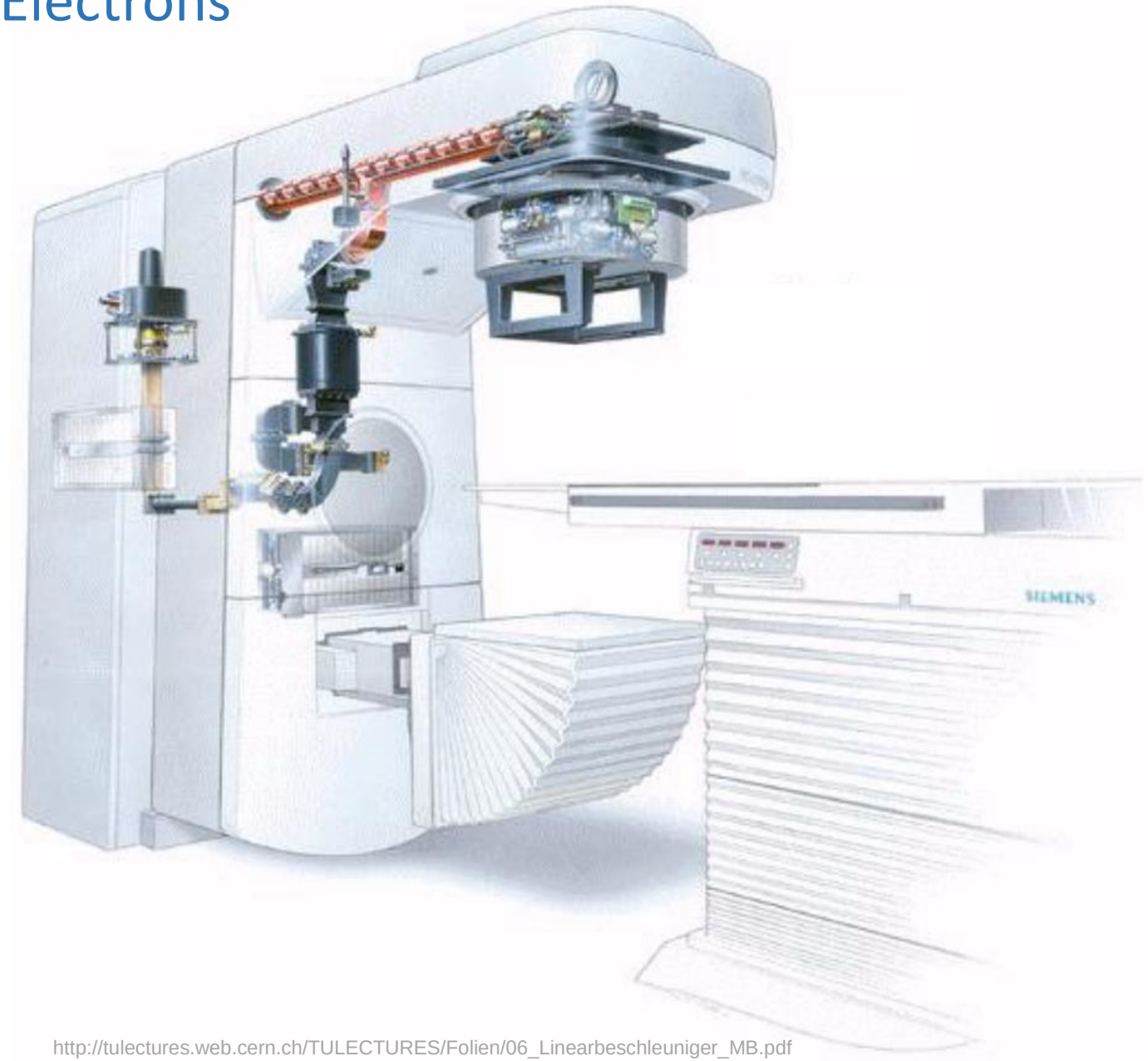


LINAC – linear accelerator





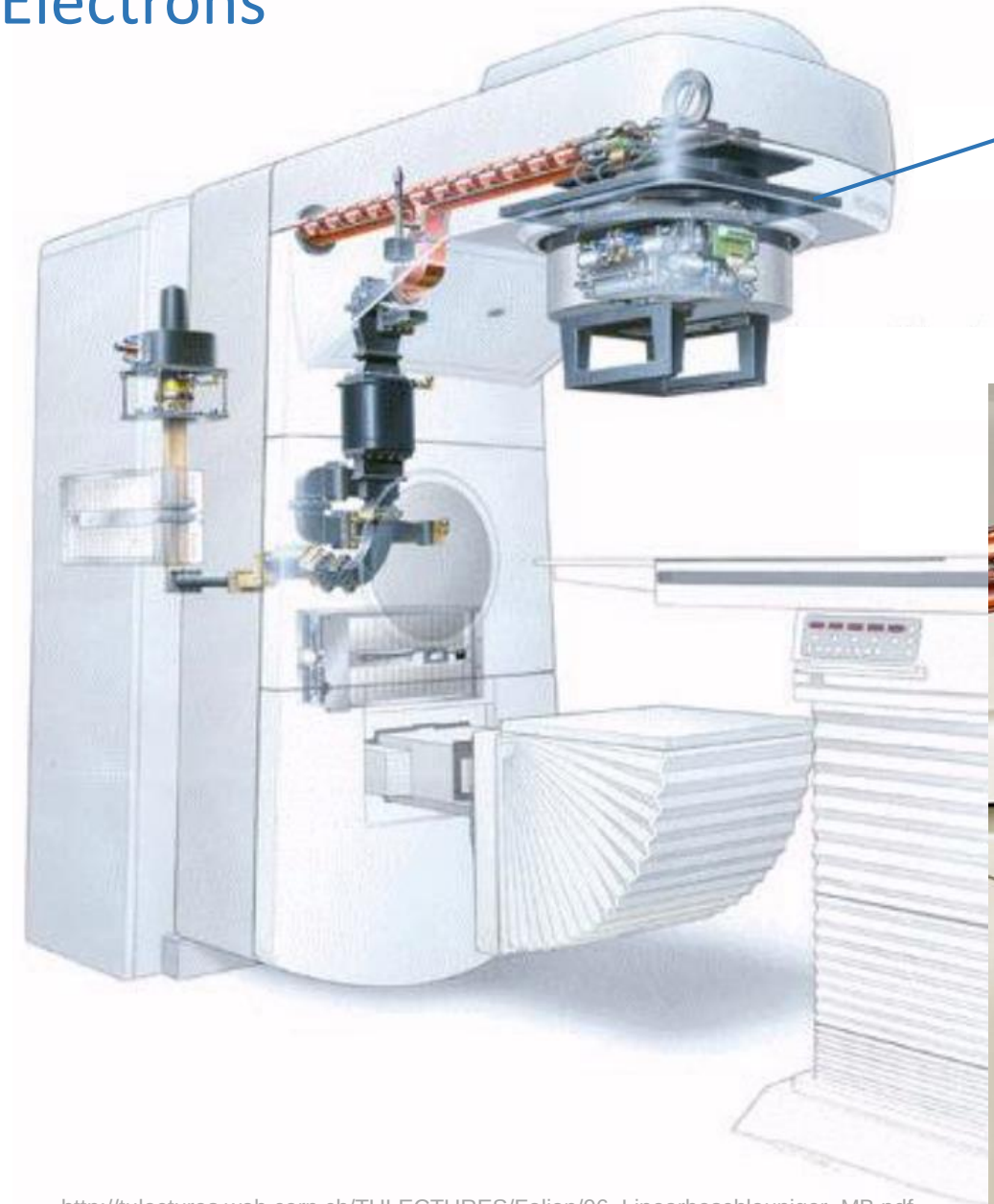
Electrons



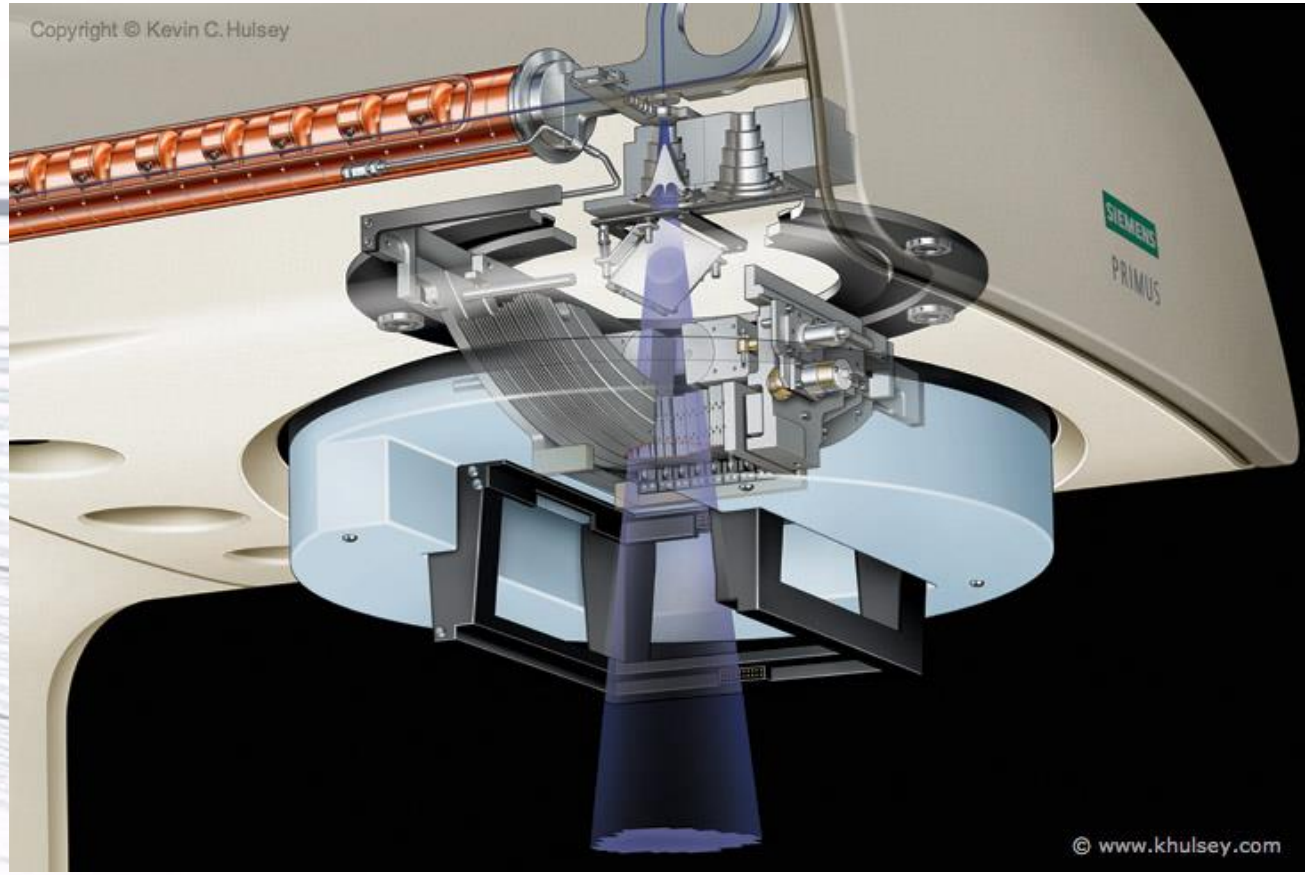
Electron LINAC
4 – 25 MeV electrons

http://tulectures.web.cern.ch/TULECTURES/Folien/06_Linearbeschleuniger_MB.pdf

Electrons

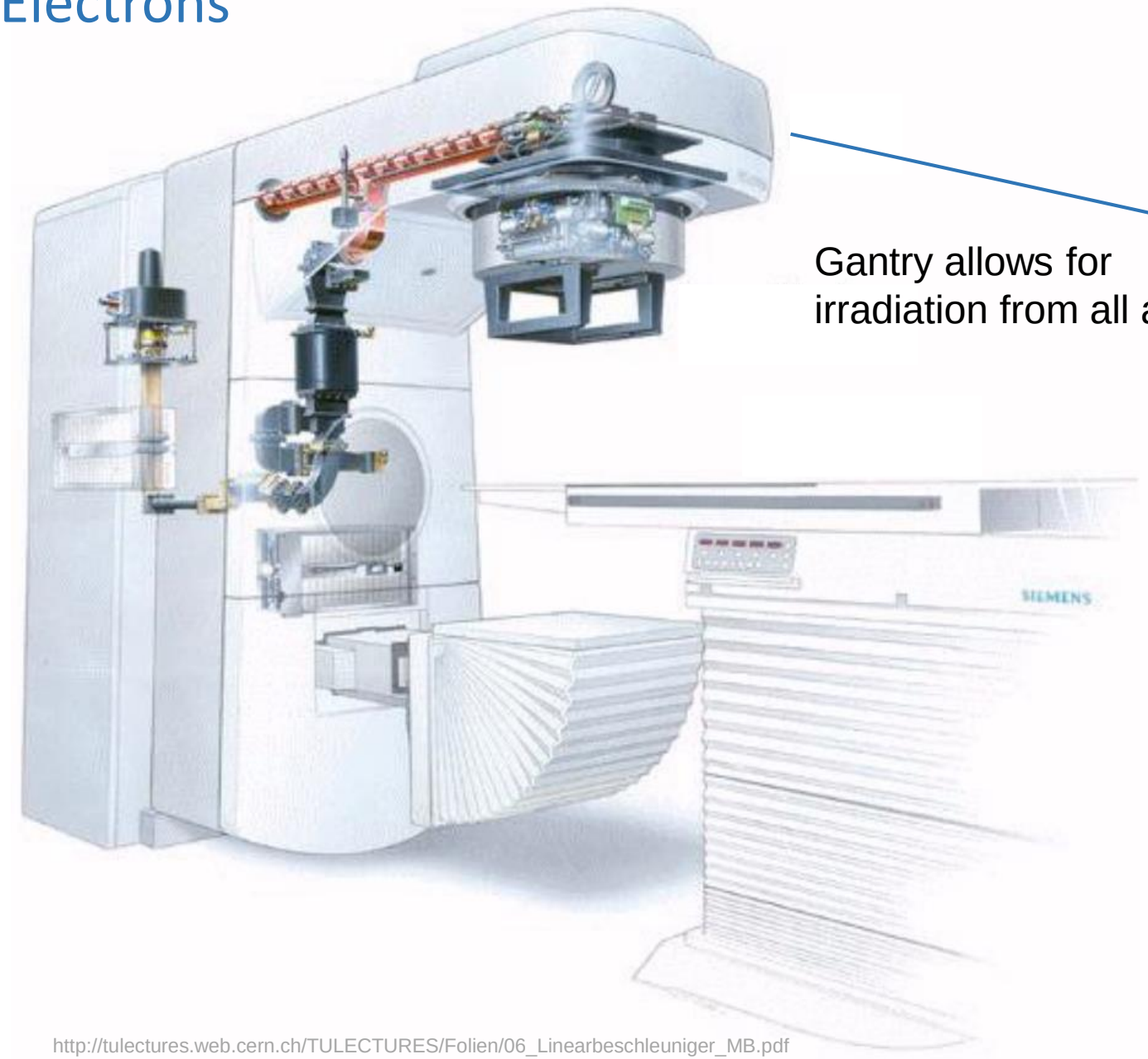


Collimator
for transverse beam shaping

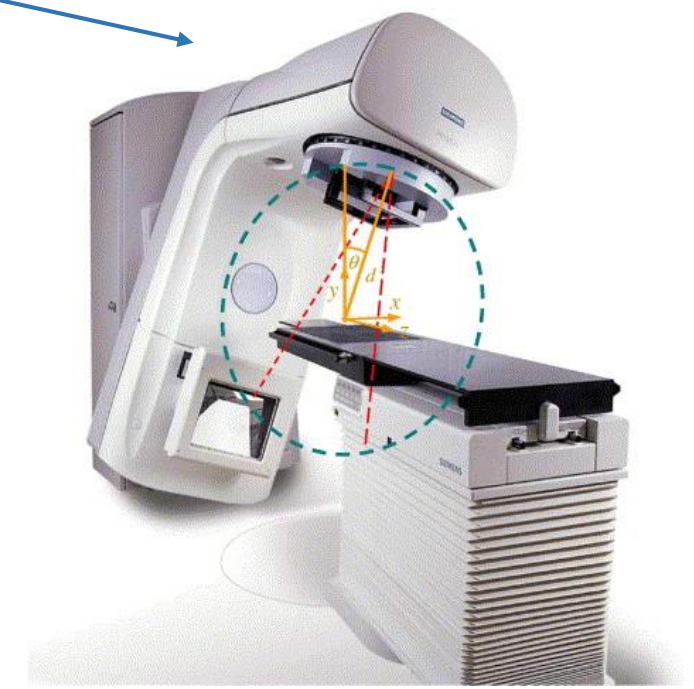


http://tulectures.web.cern.ch/TULECTURES/Folien/06_Linearbeschleuniger_MB.pdf

Electrons



Gantry allows for
irradiation from all angles



http://tulectures.web.cern.ch/TULECTURES/Folien/06_Linearbeschleuniger_MB.pdf

Photons

Intensity of photons decreases exponentially with penetration depth

$$I = I_0 \cdot exp^{-\mu x}$$

Interaction with matter through:

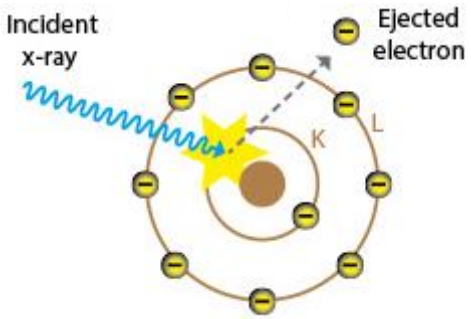
Photons

Intensity of photons decreases exponentially with penetration depth

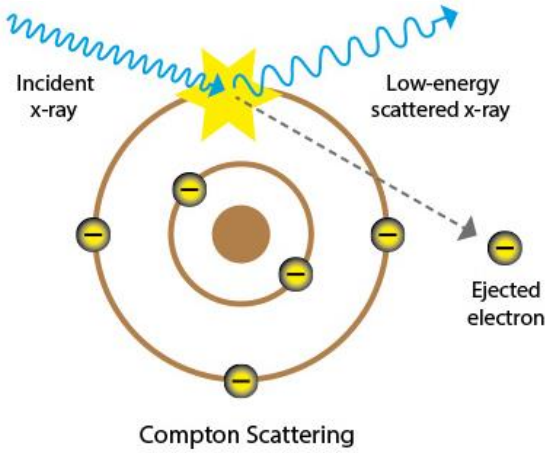
$$I = I_0 \cdot exp^{-\mu x}$$

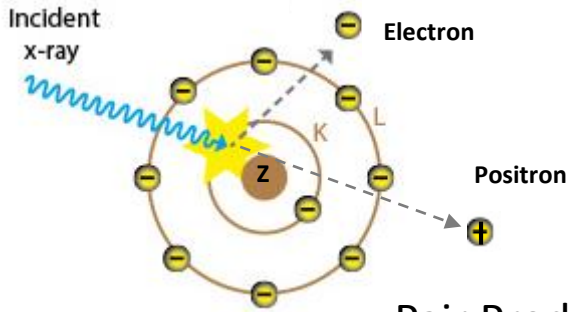
Interaction with matter through:

Photoeletric Effect



Compton Scattering





Pair Production

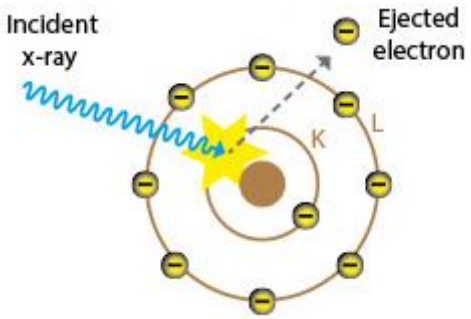
Photons

Intensity of photons decreases exponentially with penetration depth

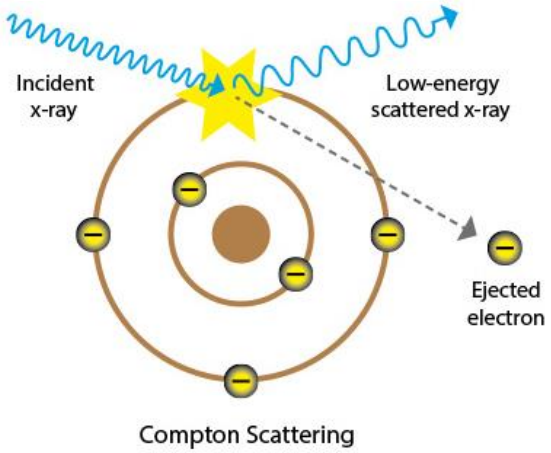
$$I = I_0 \cdot exp^{-\mu x}$$

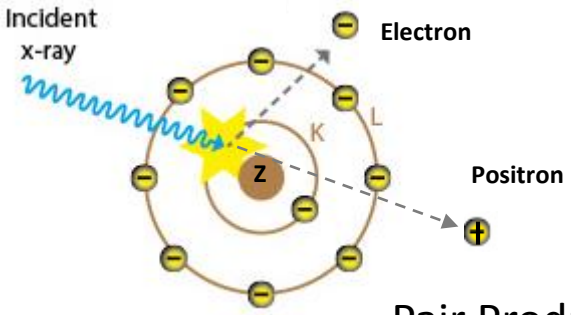
Interaction with matter through:

Photoeletric Effect

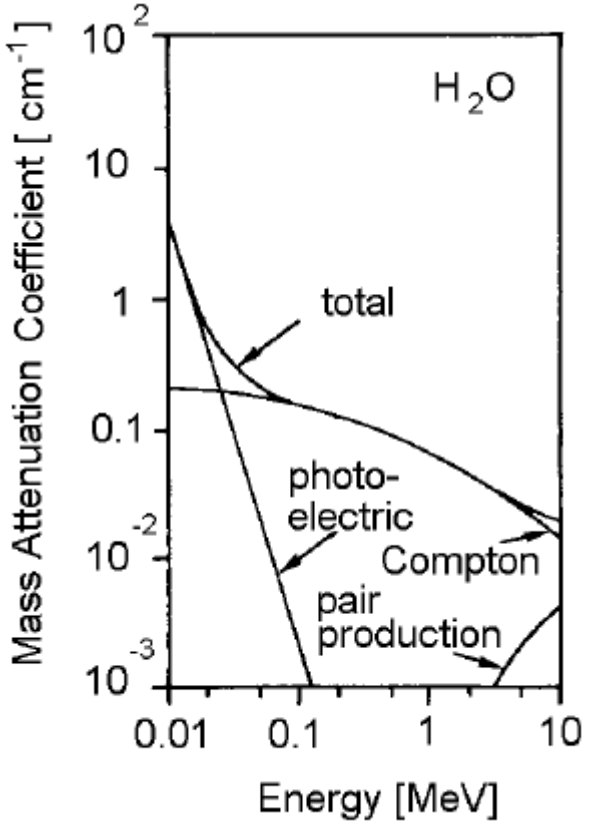


Compton Scattering





Pair Production



Photons

Intensity of photons decreases exponentially with penetration depth

$$I = I_0 \cdot exp^{-\mu x}$$

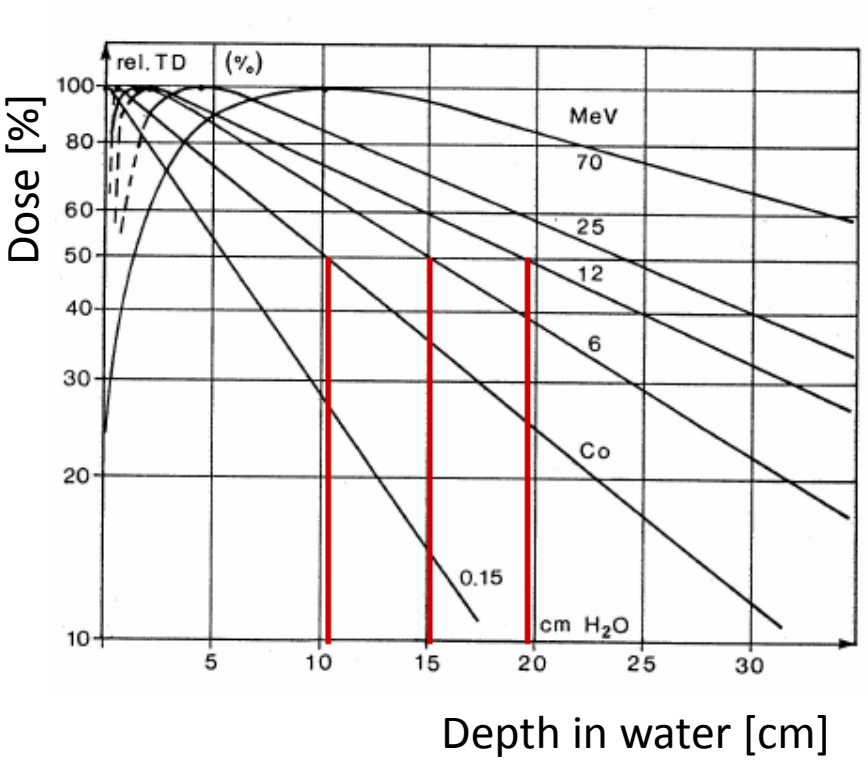
Interaction with matter through:

- Photoelectric effect
- Compton scattering
- Pair production

Most of the biological effect comes from secondary electrons

Dose buid-up as electrons tend to move in forward direction

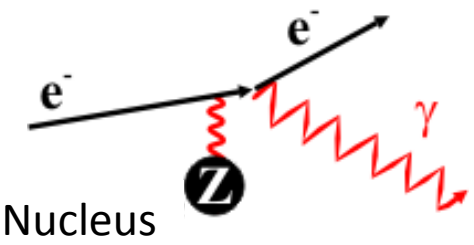
Dose build-up



Photons

Electrons

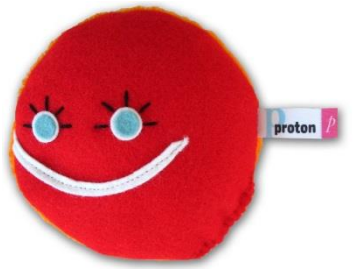
Energy loss:
- Inelastic scattering -> excitation, ionization
- Radiative stopping → ‘bremsstrahlung’ (goes up with electron energy and Z)



Scattering through collisions
-> broadening of the beam

Production of photons from bremsstrahlung of electrons on target

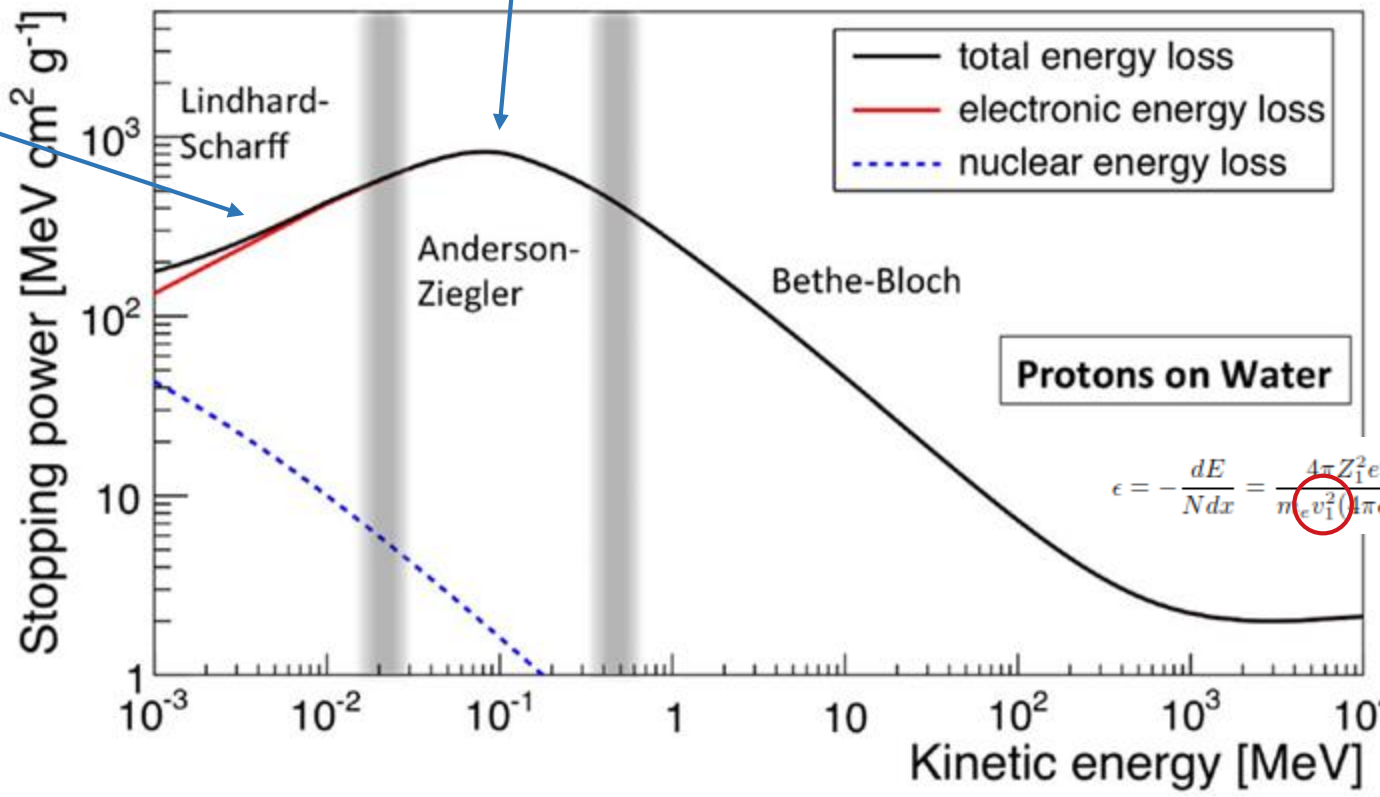
Protons



Ion approaches Bohr-velocity

Viscous drag ~v

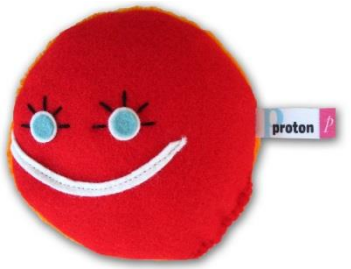
DOI=10.3389/fonc.2015.00150



Excitation and ionization of target electrons

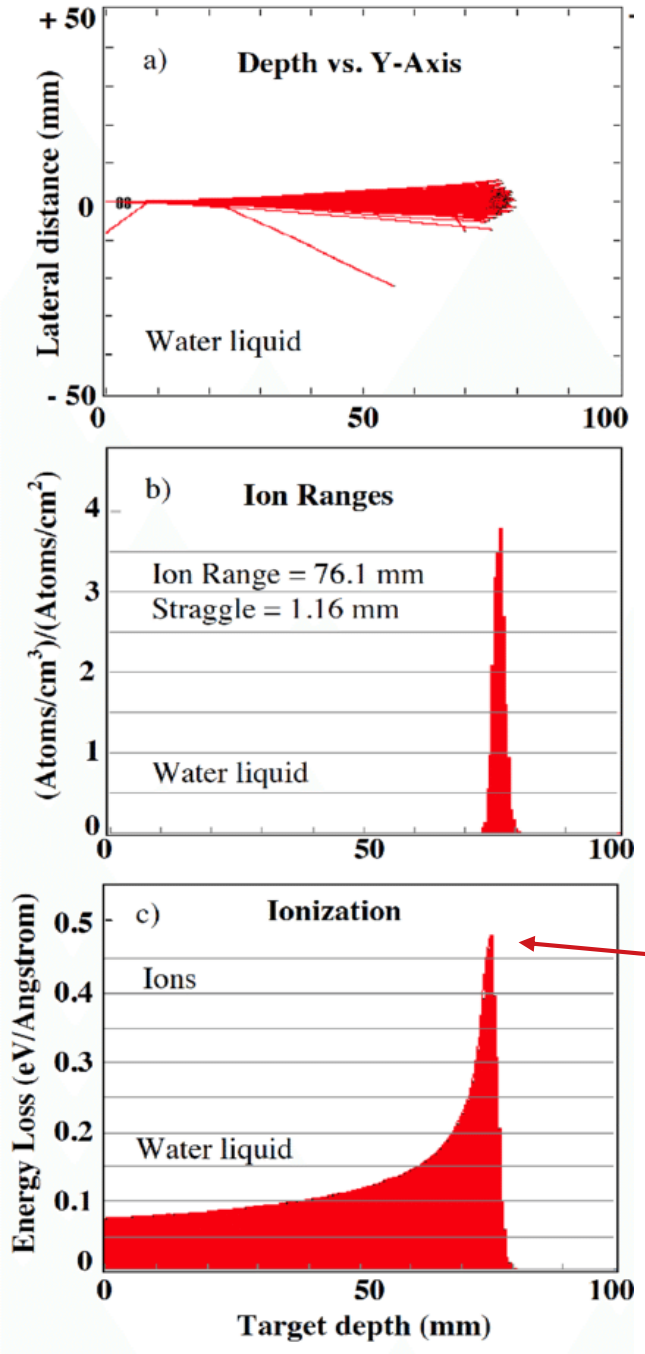
$$\epsilon = -\frac{dE}{Ndx} = \frac{4\pi Z_1^2 e^4}{m_e v_1^2 (4\pi\epsilon_0)^2} Z_2 \left[\ln \frac{2m_e v_1^2}{I} + \ln \frac{1}{1-\beta^2} - \beta^2 - \frac{C}{Z_2} - \frac{\delta}{2} \right]$$

Protons



Protons stop!

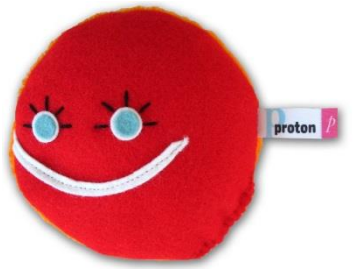
Protons lose most of their energy towards the end of their track!



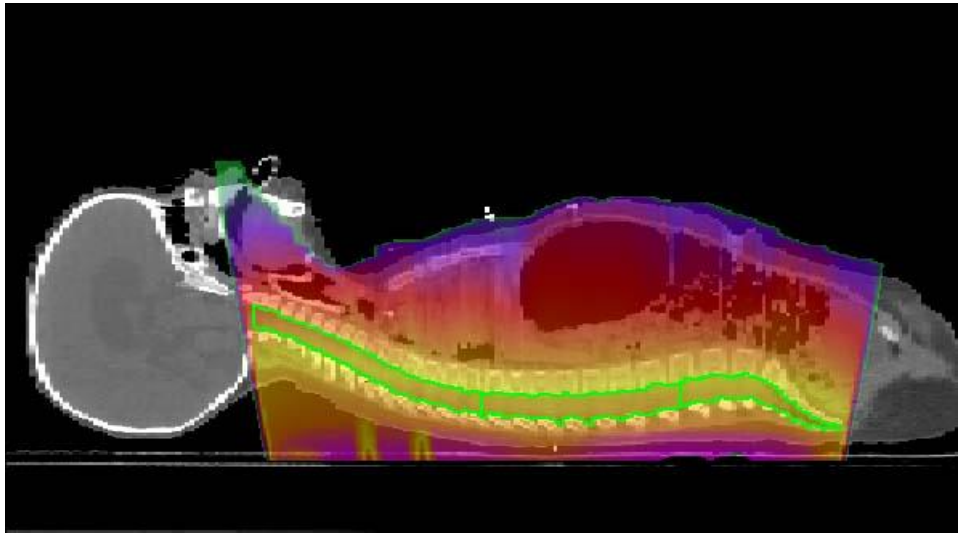
Bragg peak

DOI: 10.2174/1872210509999141222224121

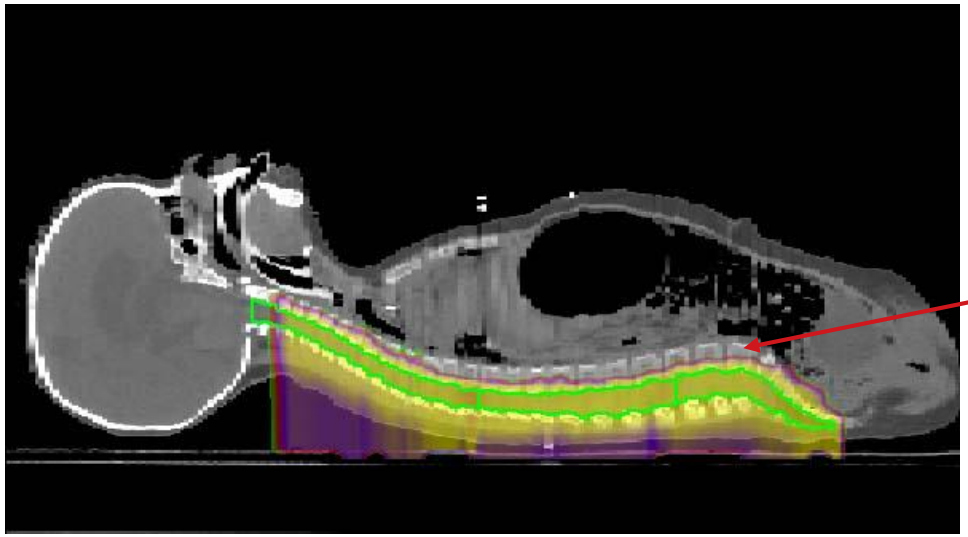
Protons



Photons



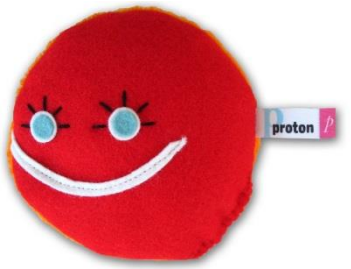
Protons



Bragg peak

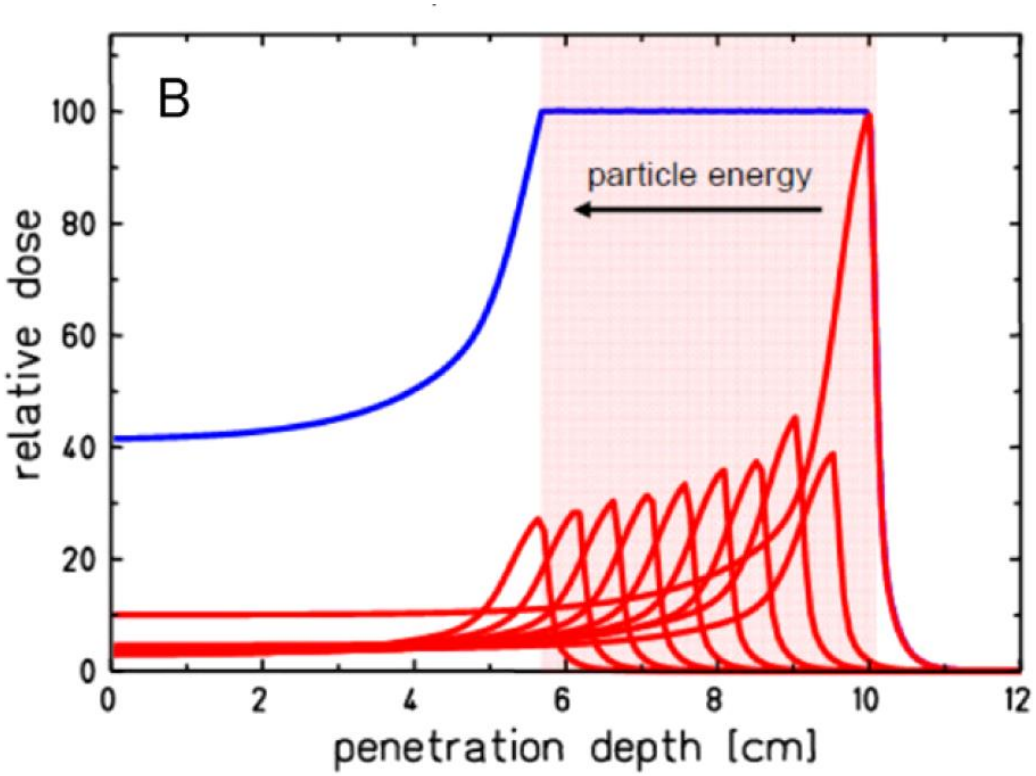
+ healthy tissue can be spared
+ very precise dose deposition

Protons

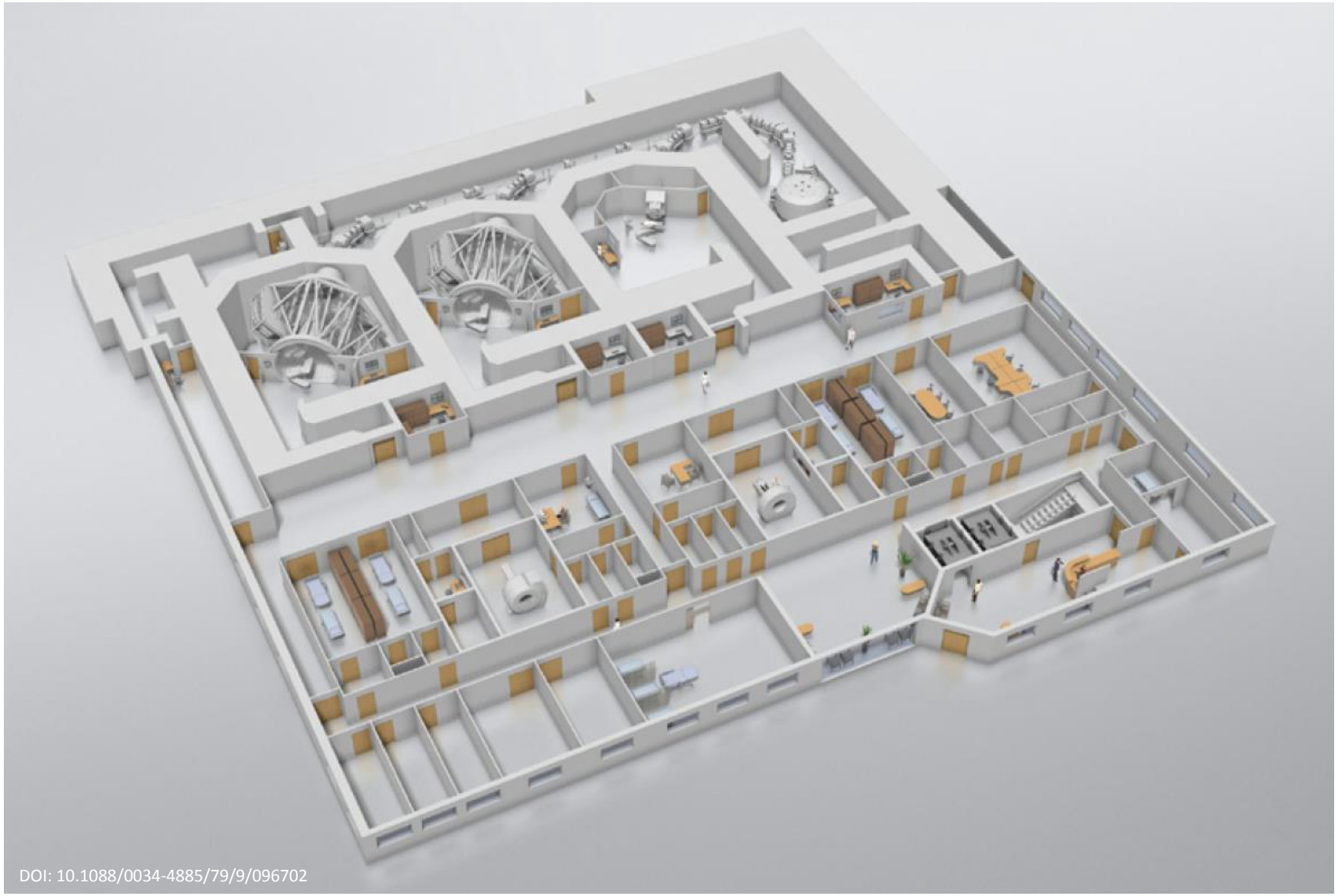


Beam delivery:
SOB – Spread-out Bragg peak

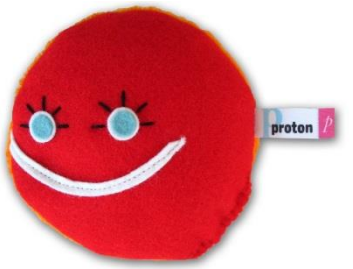
Tumor divided in slices, each slice at a certain depth irradiated with corresponding energy

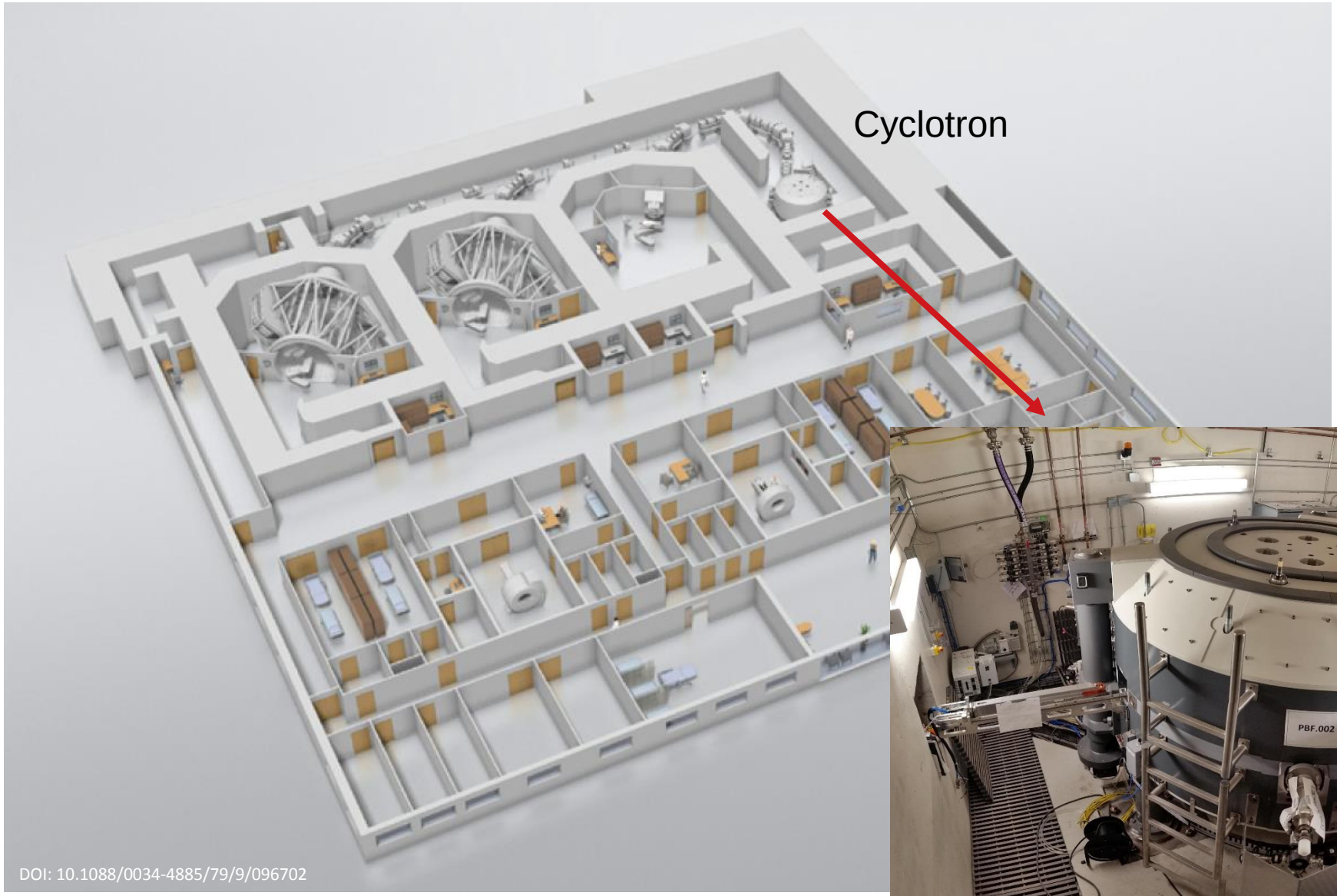


Protons

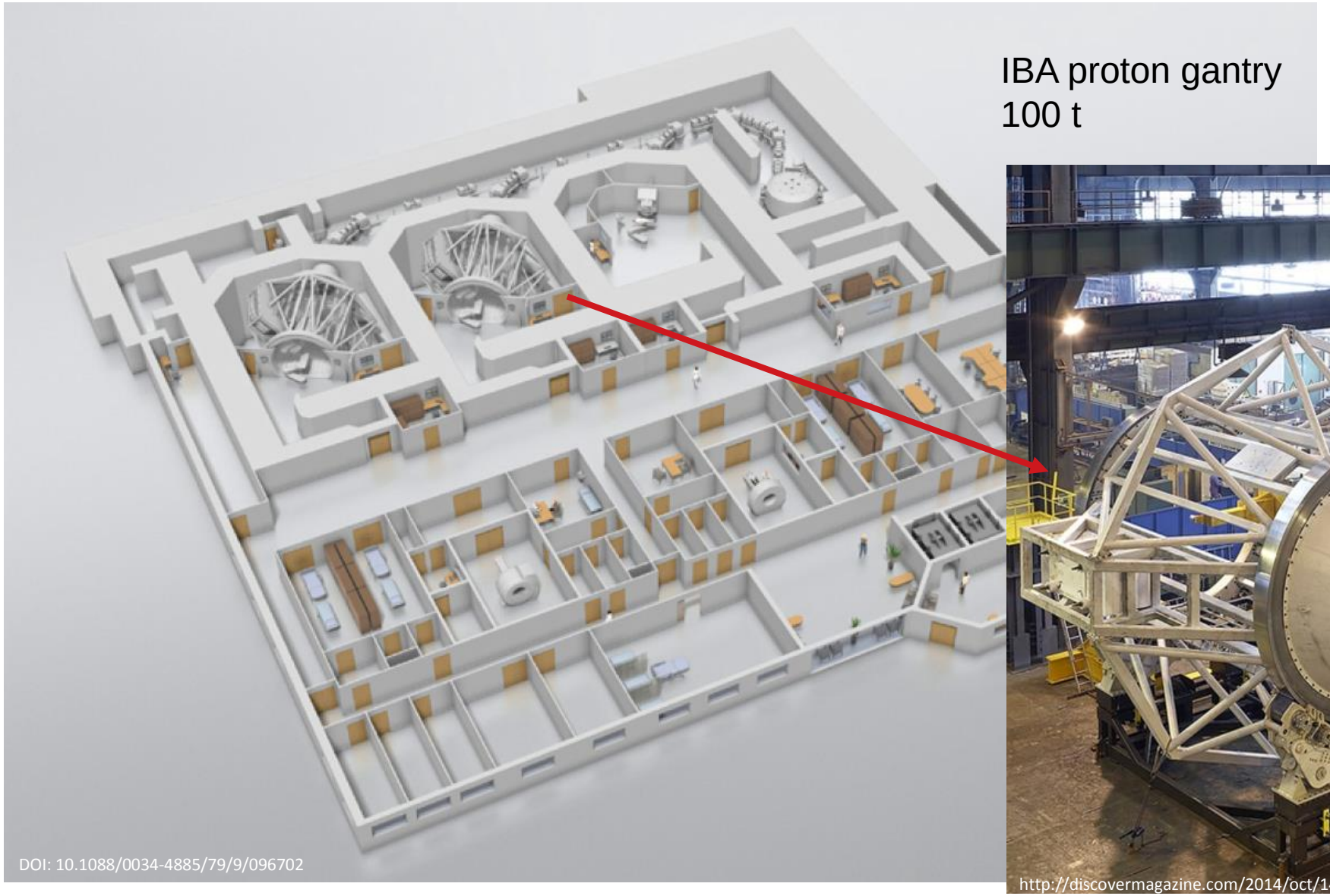


Protons





Protons

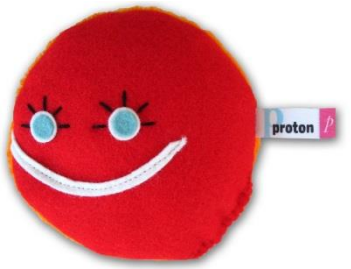


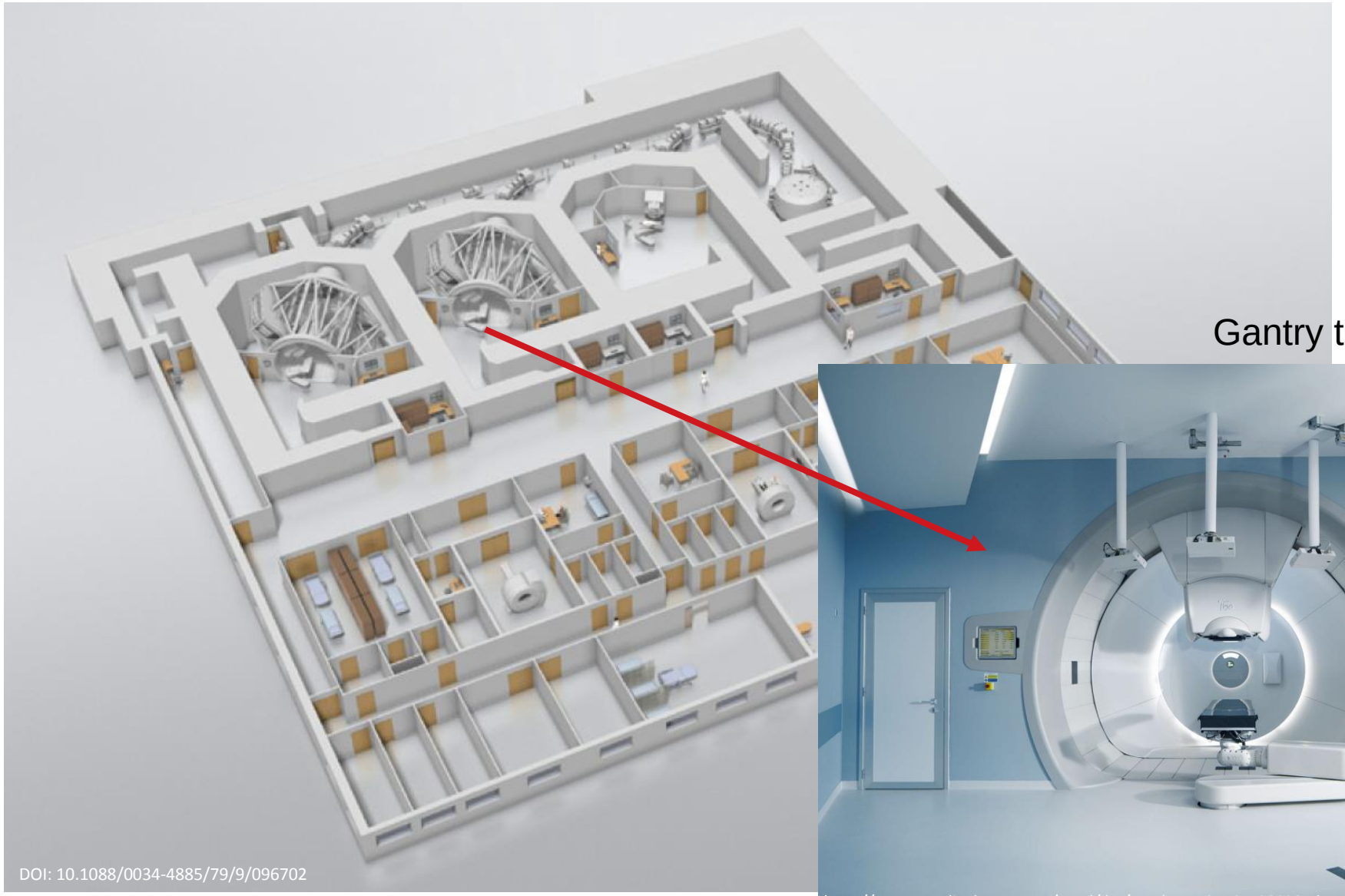
DOI: 10.1088/0034-4885/79/9/096702

IBA proton gantry
100 t

http://discovermagazine.com/2014/oct/14-precision-vs-profits

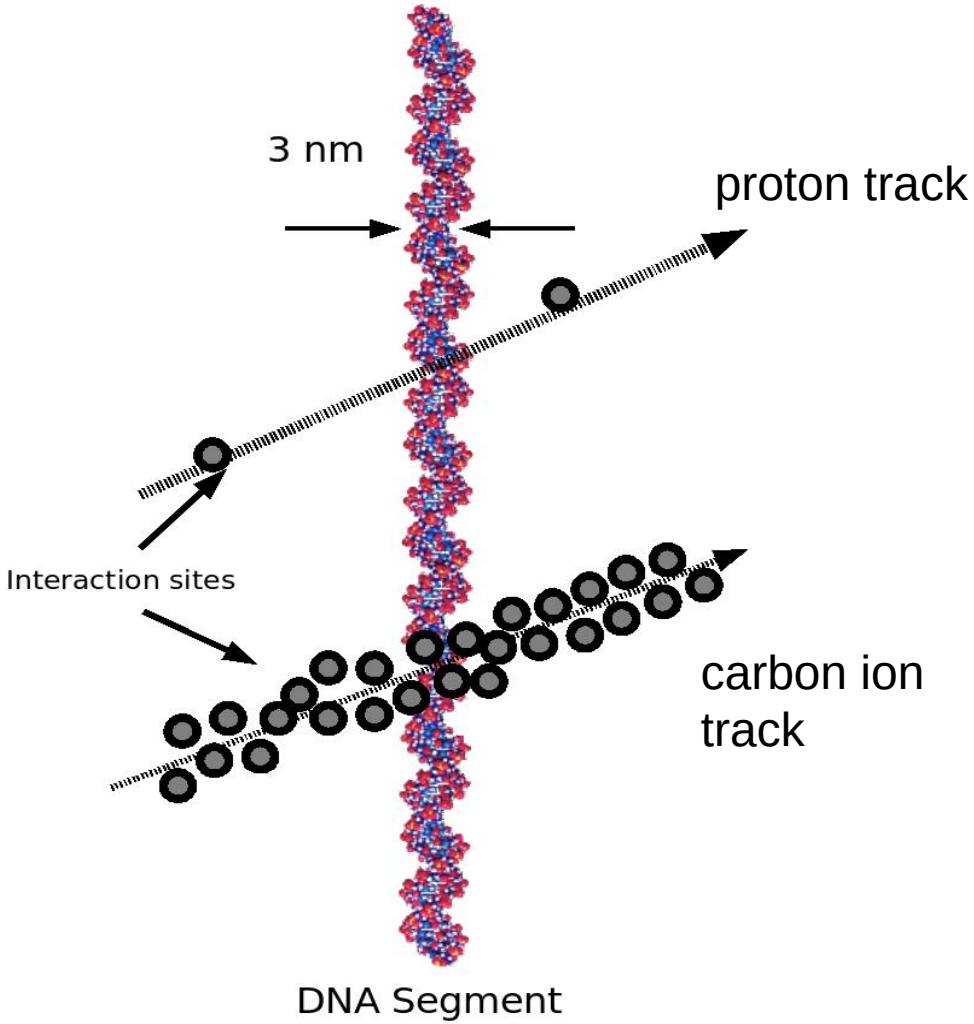
Protons

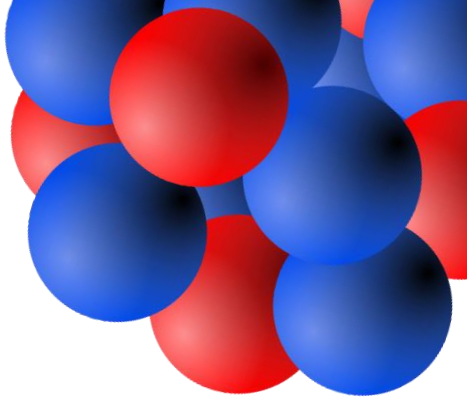




Gantry treatment room

Carbon Ions

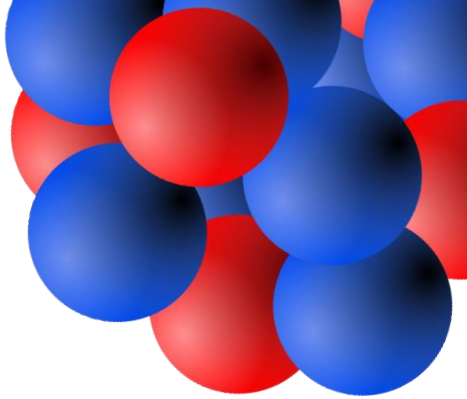


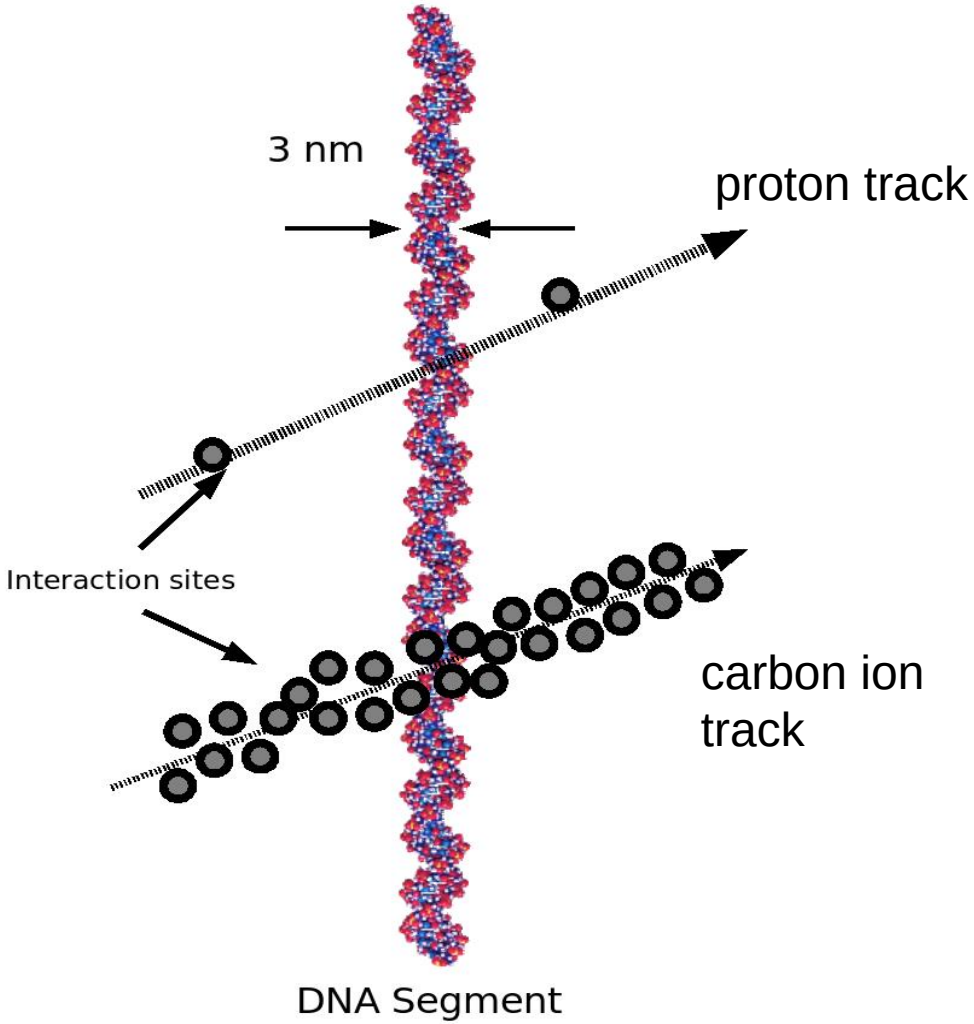


High density ionization:
→ High biological effectiveness
→ DNA double-strand breaks
→ Radioresistant tumors

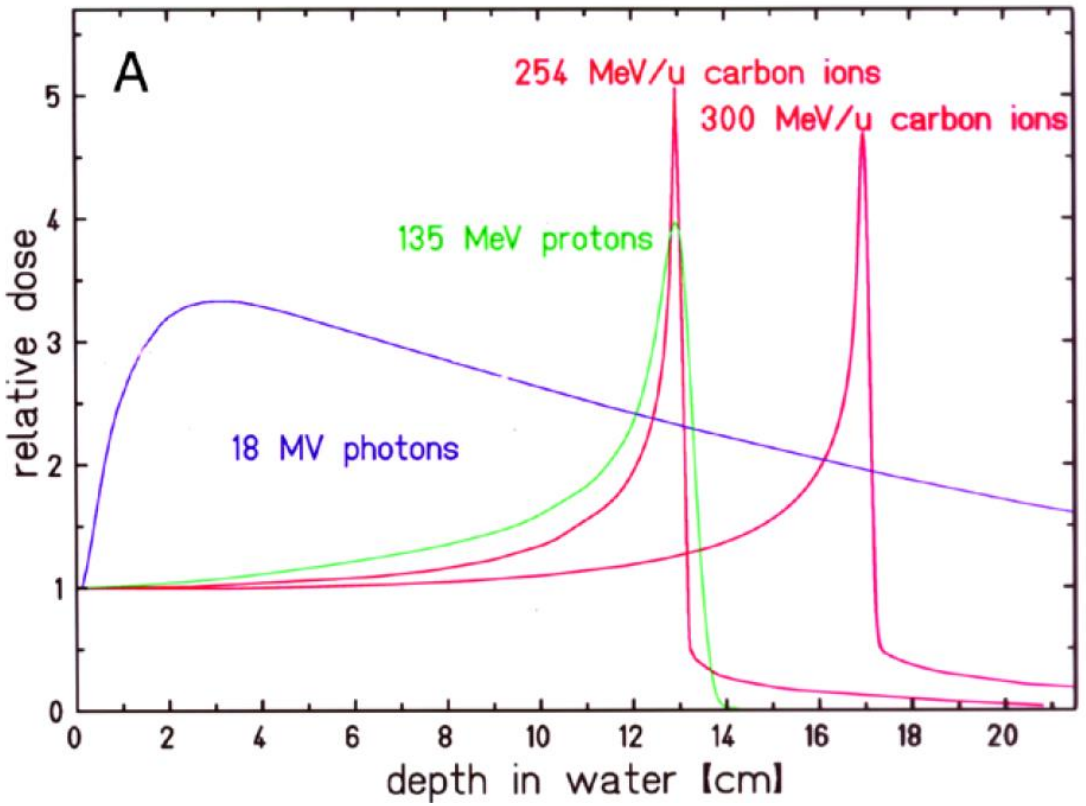
http://radioactivityci2010.pbworks.com/w/page/30525316/Fast%20Neutron%20Therapy

Carbon Ions

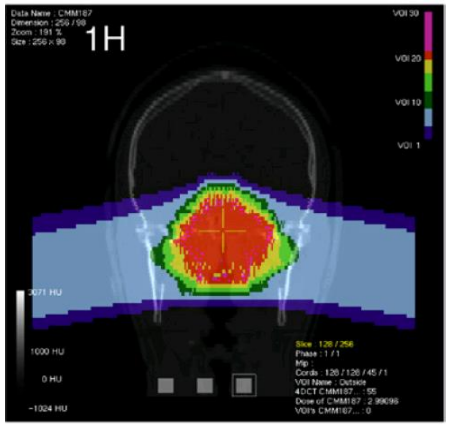


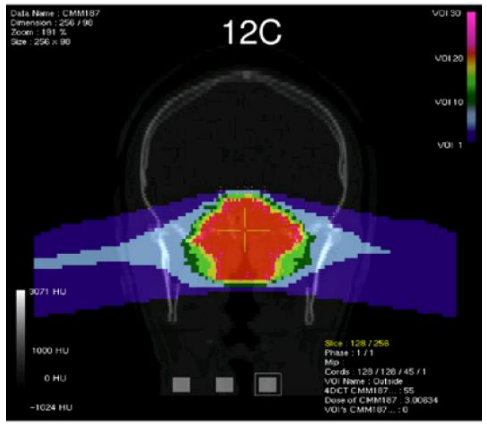


High density ionization:
→ High biological effectiveness
→ DNA double-strand breaks
→ Radioresistant tumors

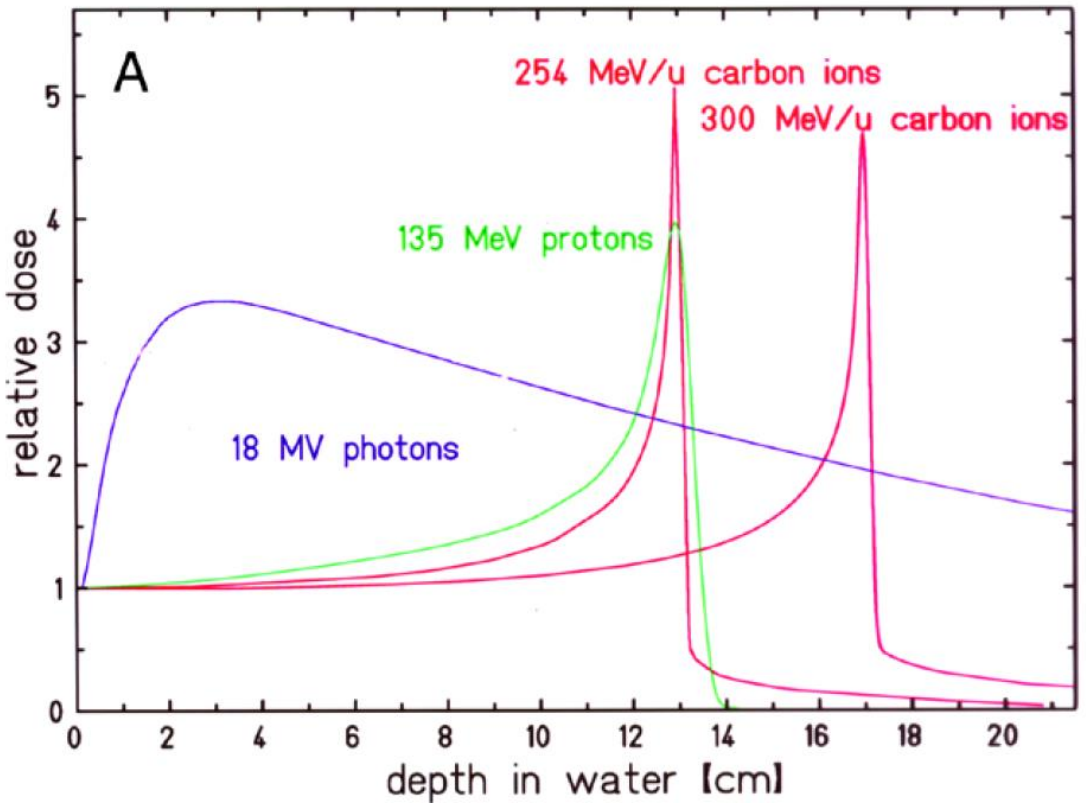


Carbon Ions

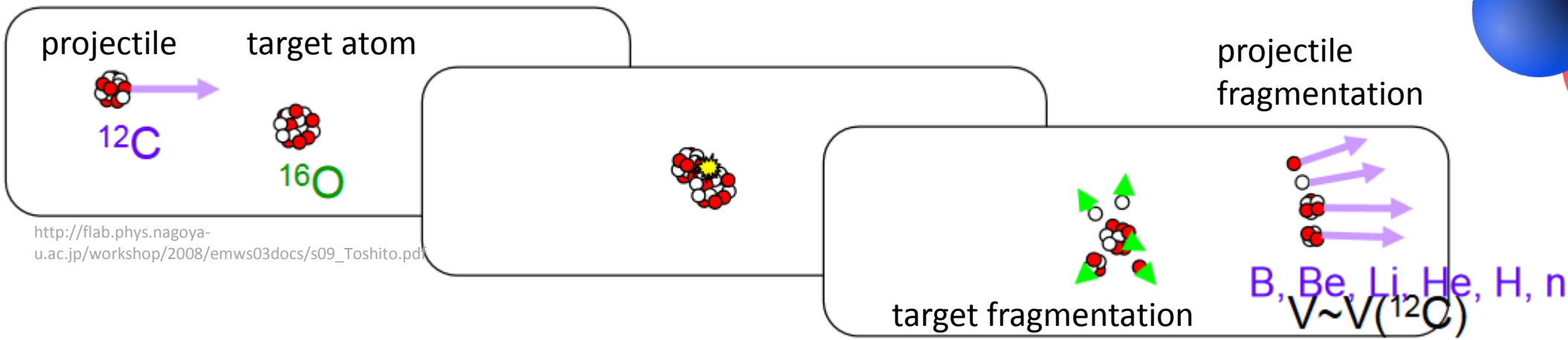




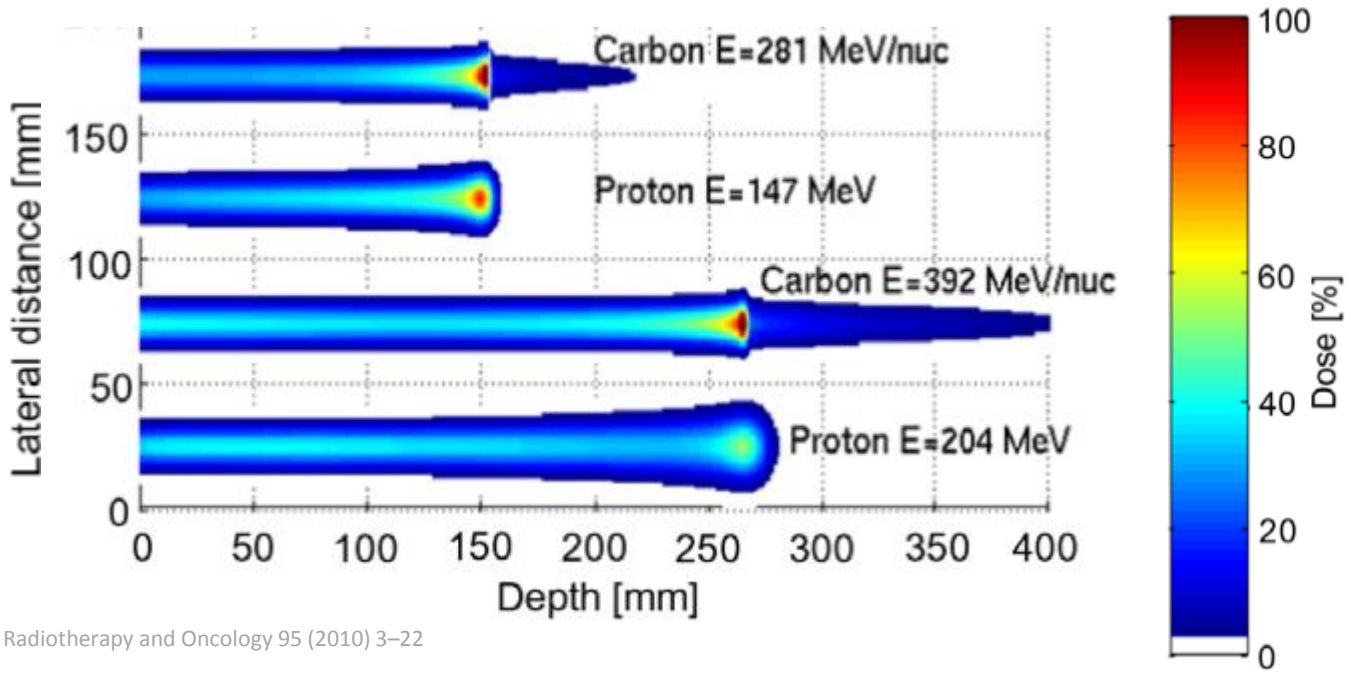
High density ionization:
→ High biological effectiveness
→ DNA double-strand breaks
→ Radioresistant tumors



Carbon Ions



http://flab.phys.nagoya-u.ac.jp/workshop/2008/emws03docs/s09_Toshito.pdf

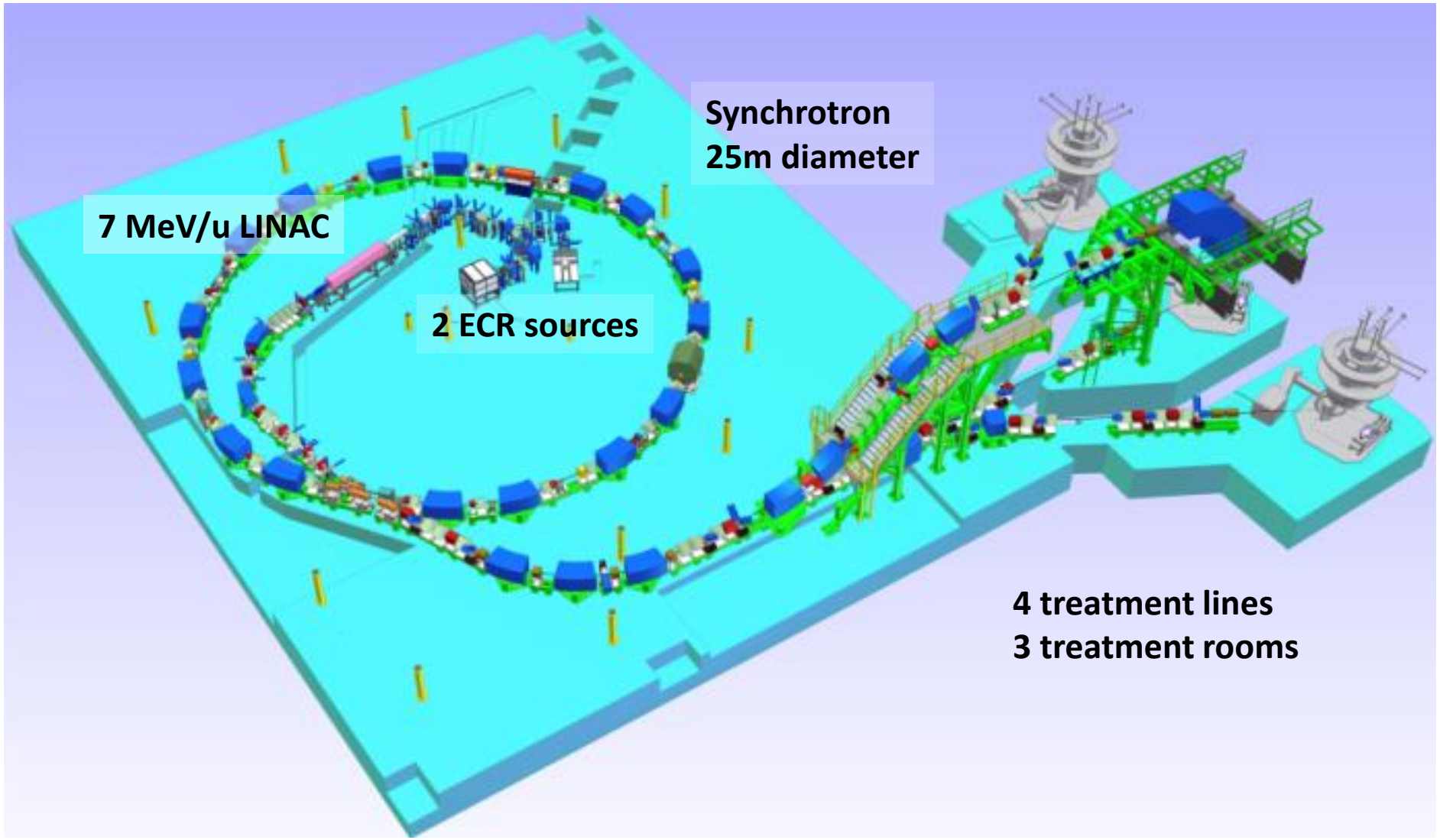


Radiotherapy and Oncology 95 (2010) 3–22

Projectile fragments can travel beyond the Bragg peak

→ fragmentation tail

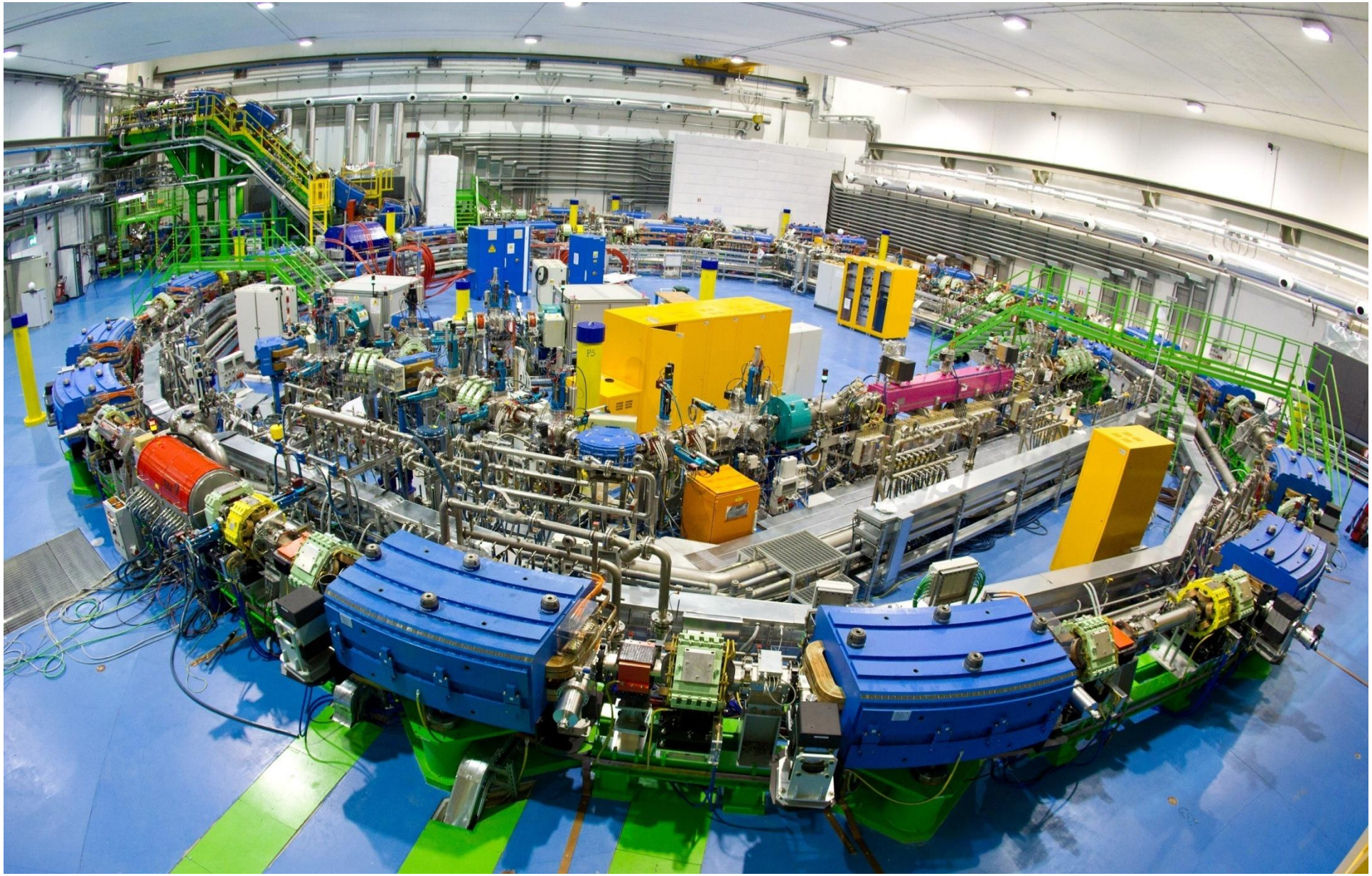
Carbon Ions

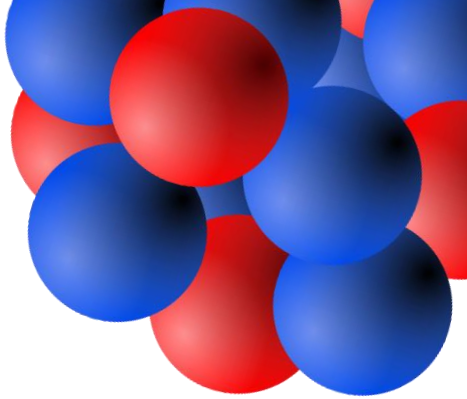


Synchrotron for
protons and carbon ions

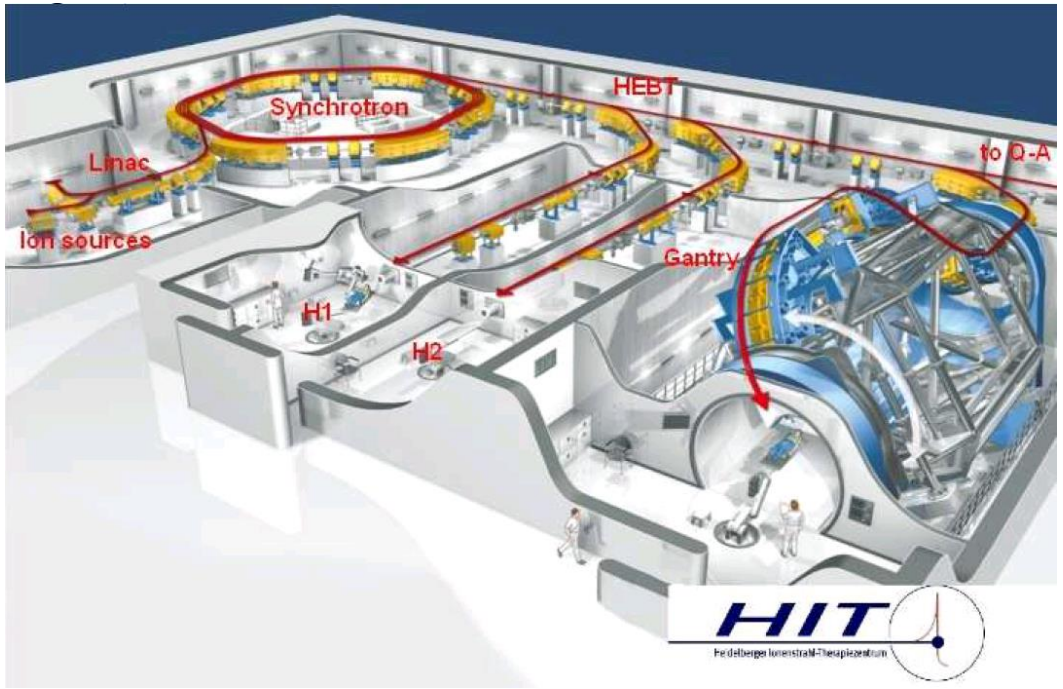
World-wide
only 10 centers

Carbon Ions





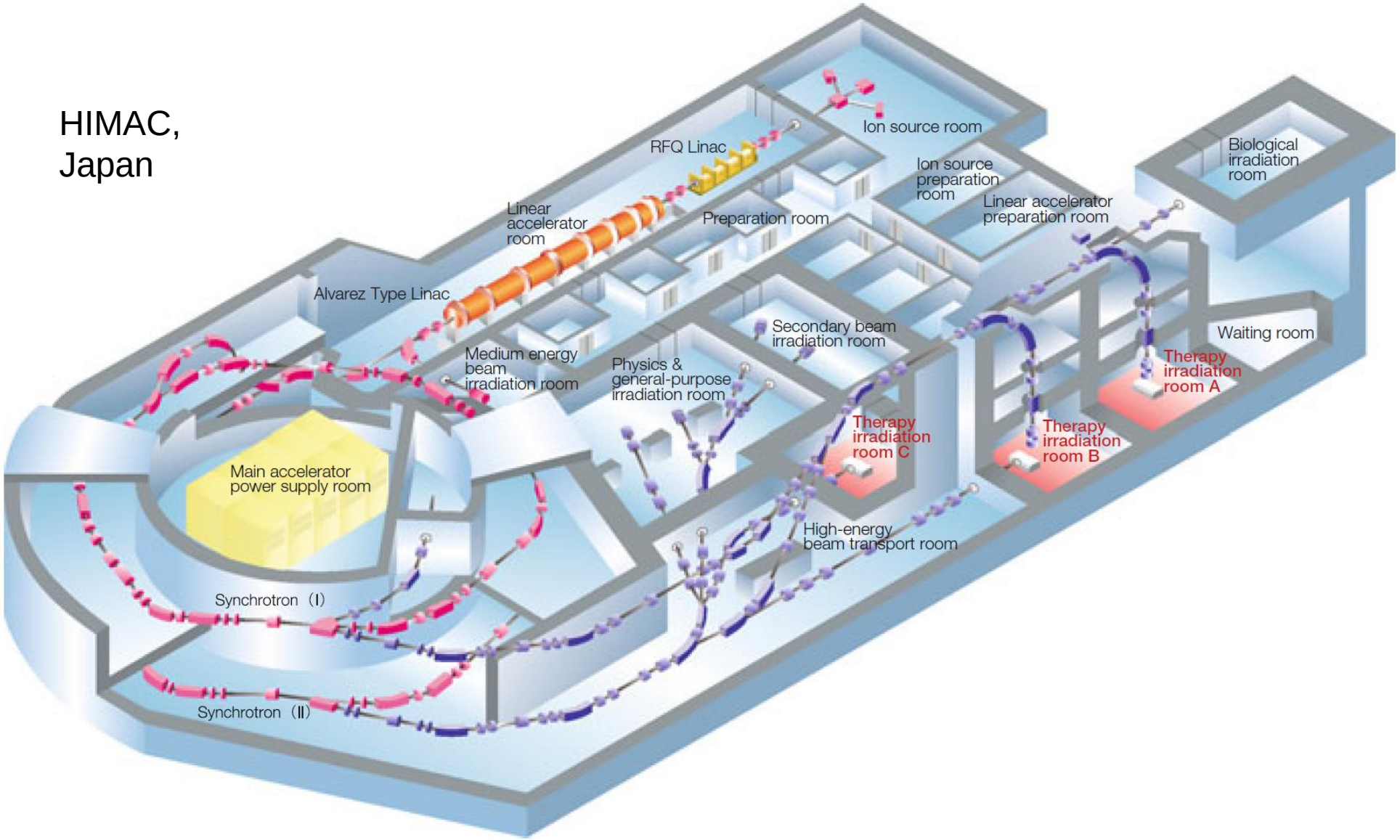
Carbon Ions



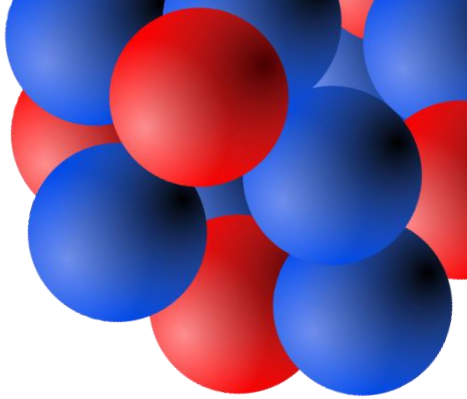
HIT carbon ion gantry
450 t of rotating parts

Carbon Ions

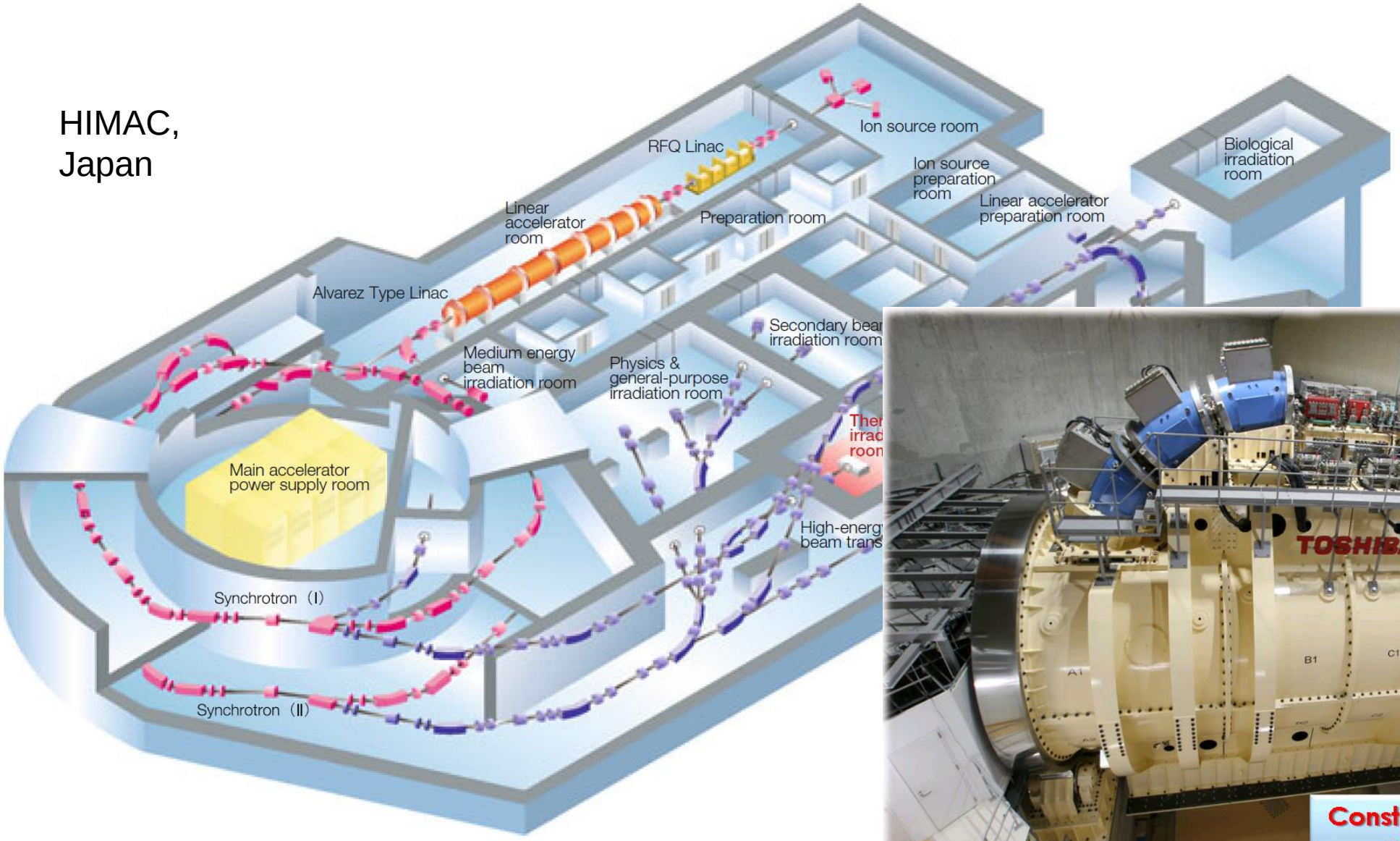
HIMAC,
Japan



Carbon Ions



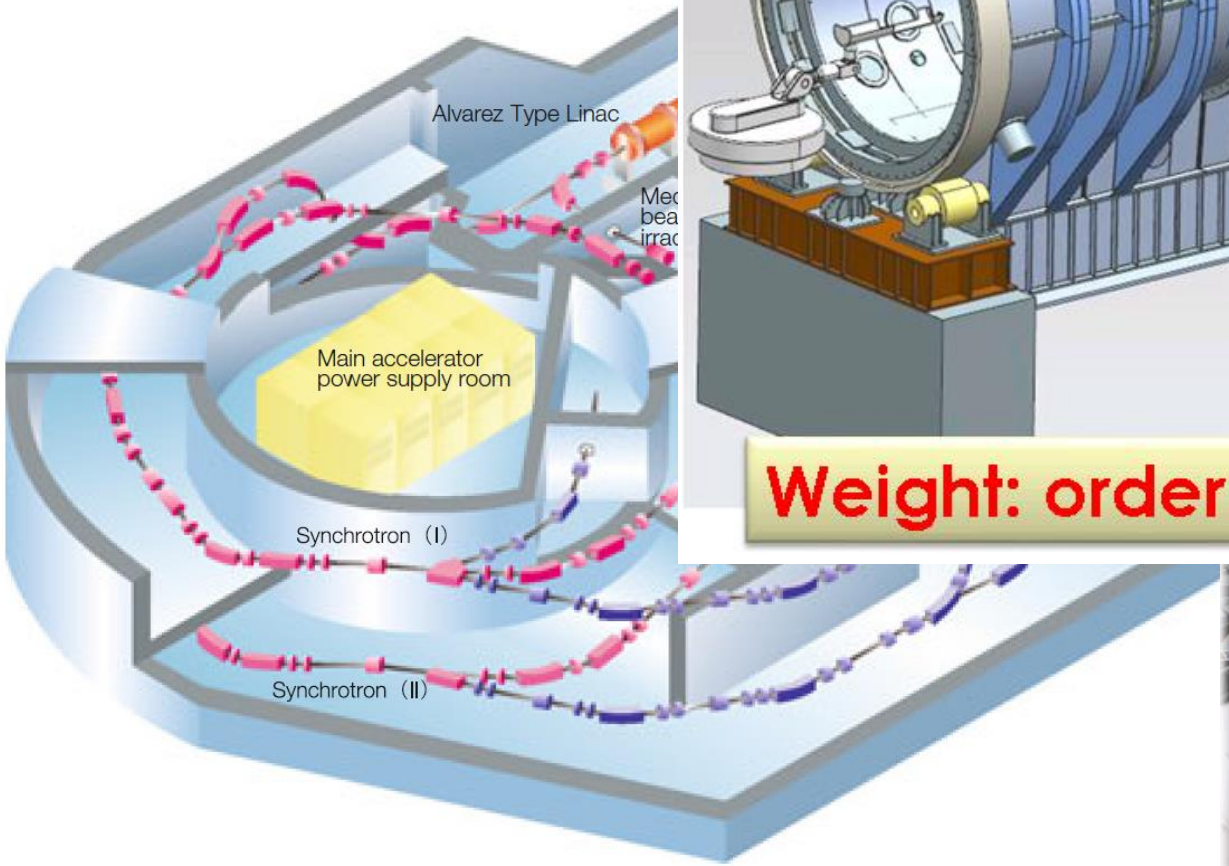
HIMAC,
Japan

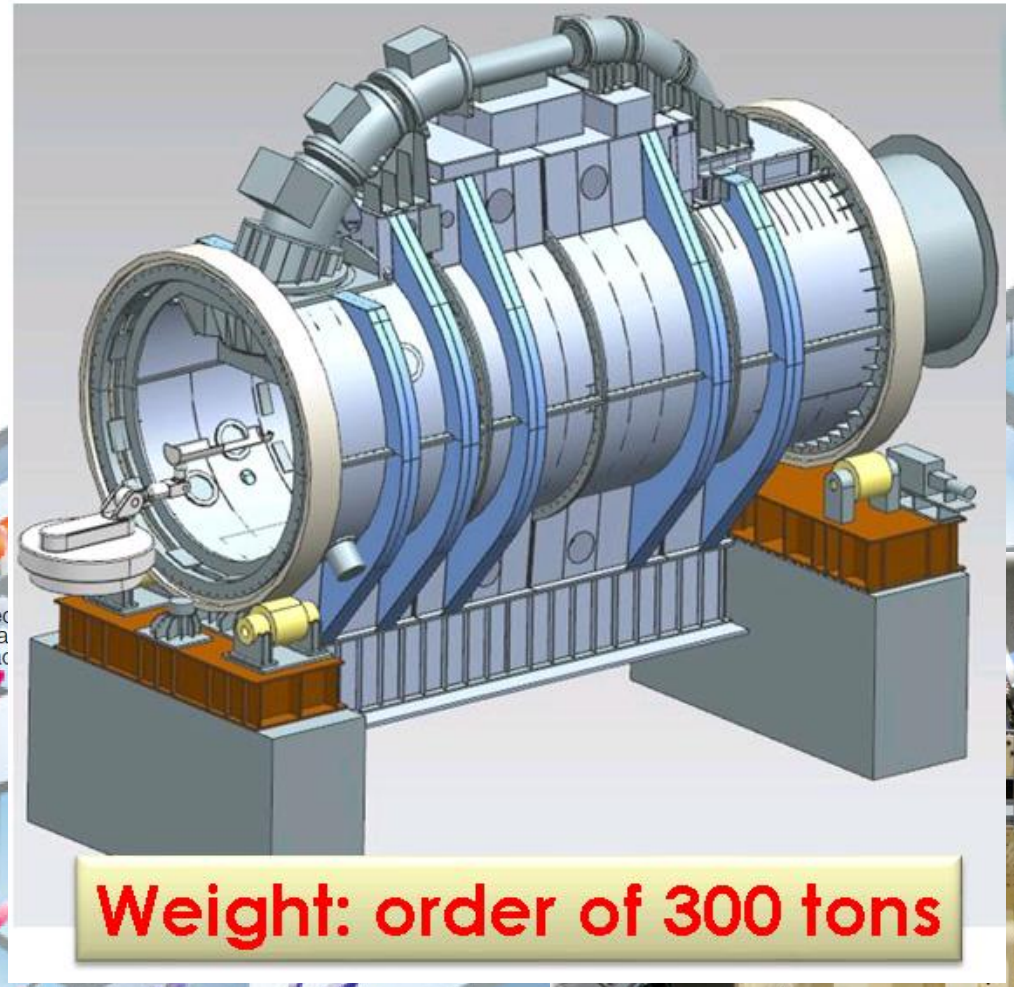


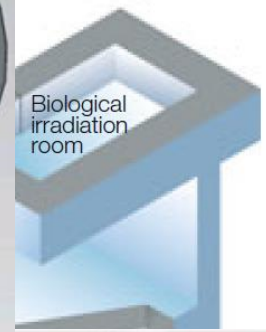
'compact' superconducting gantry

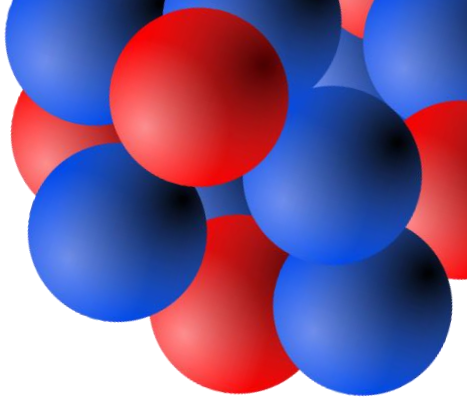
Carbon Ions

HIMAC,
Japan

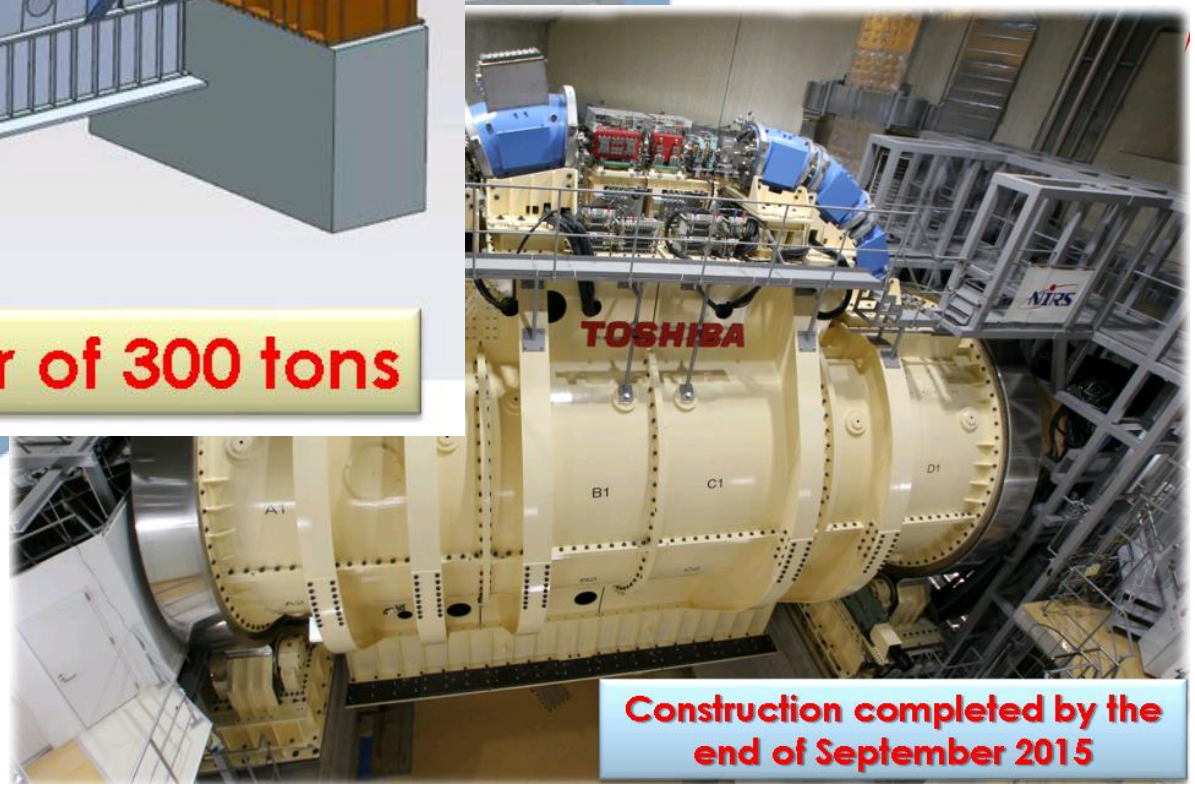








'compact'
superconducting
gantry



Proton and Carbon Centers world-wide

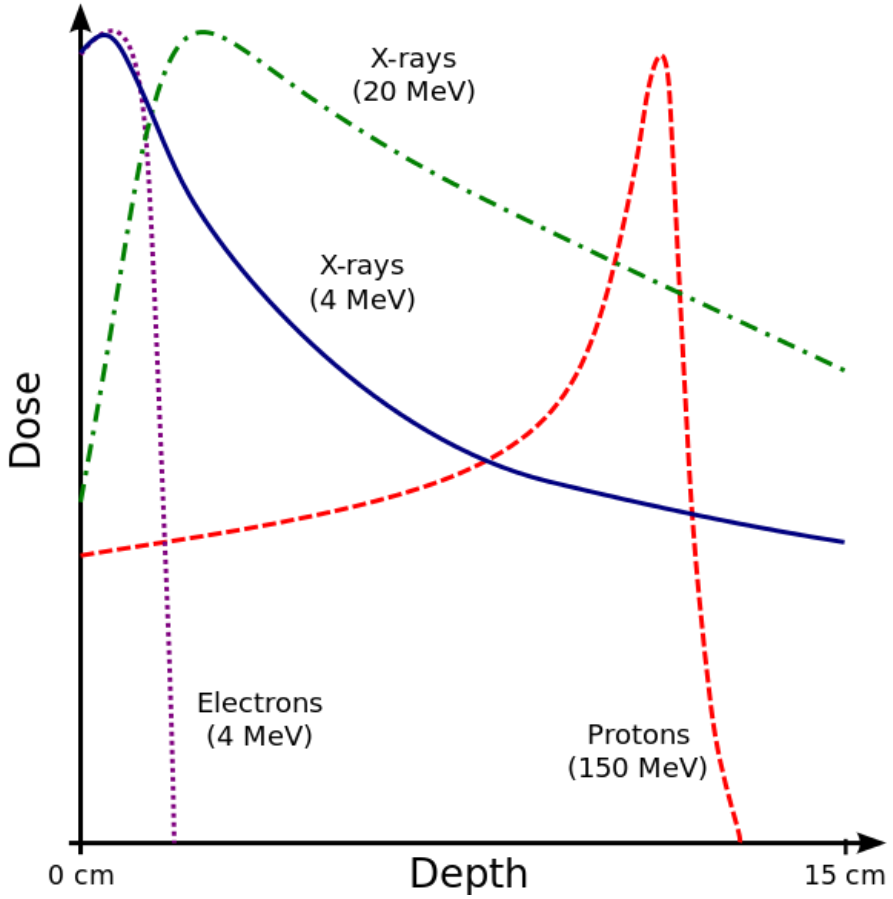
60 Proton Centers
10 Carbon Ion Centers

More than
120 Centres
expected for 2022

Durante M, Orecchia R, Loeffler JS, 2017

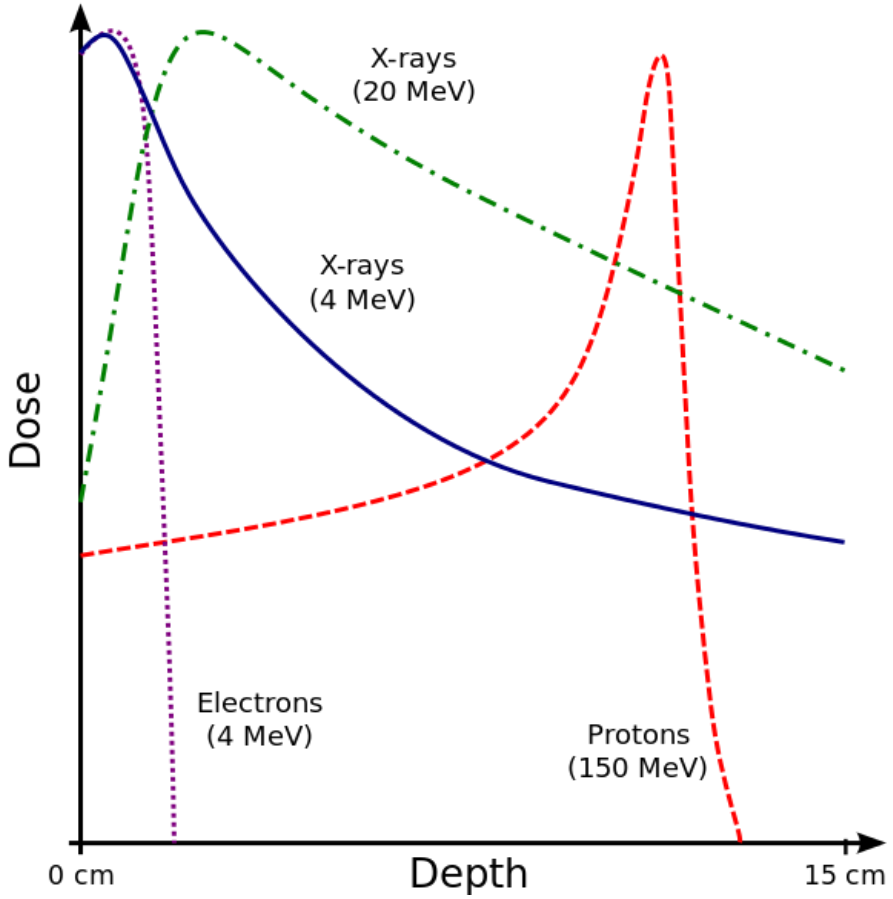
Nature Reviews | Clinical Oncology

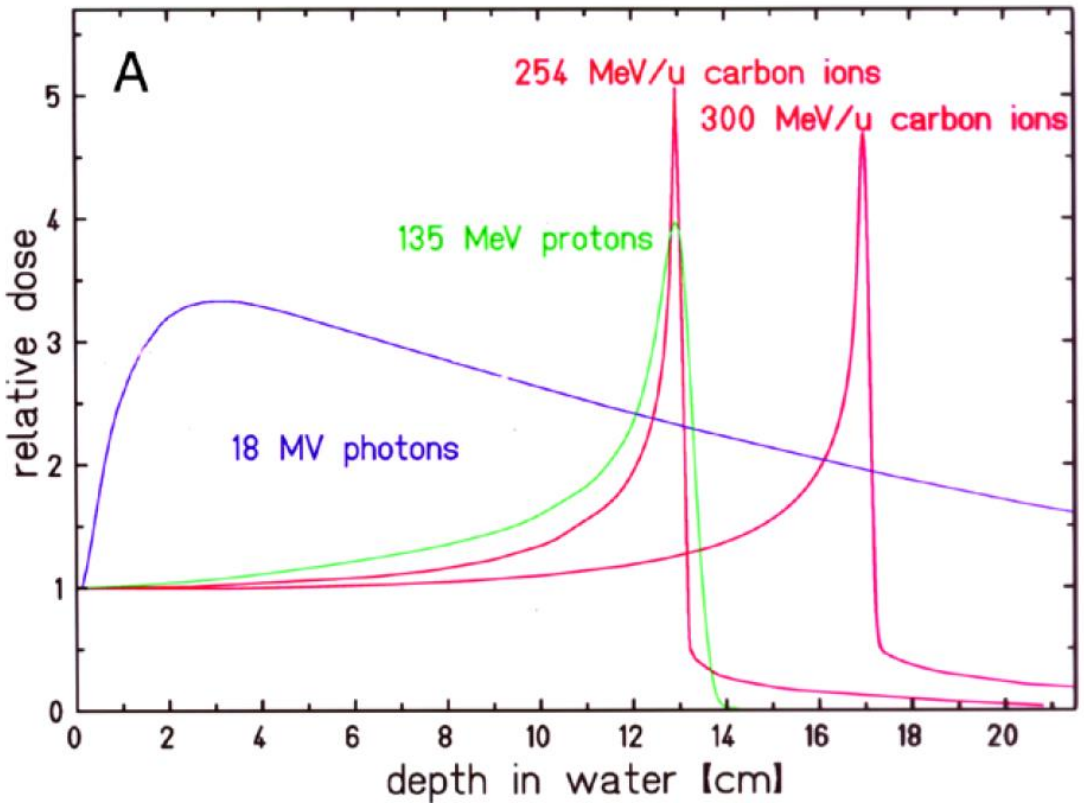
Summary: Dose-depth profile



http://www.wikiwand.com/en/Electron_therapy

Summary: Dose-depth profile





http://www.wikiwand.com/en/Electron_therapy

Your turn!

Which treatment would you suggest for these patients?

#	Patient	
1	well localized brain tumor close to brain stem at 10 cm depth	
2	widespread bronchial carcinoma (lung cancer) at 10 cm depth, heart should be spared	
3	tumor on chest wall, healthy heart muscle starts at 2.5 cm depth	
4	Aderhautmelanom (tumor of the eye), healthy eye tissue and optic nerve must not be irradiated!	
5	Chondrosarcoma, tumor on scull base, radioresistant	
6	inoperable liver tumor, skin should be spared as far as possible	
7	skin cancer, reaching 3 cm deep, critical organ at 5 cm depth	

#	Treatment
A	5 MeV electrons
B	9 MeV electrons
C	Photons
D	Photons
E	60 MeV protons
F	115 MeV protons
G	Carbon ions

Your turn!

Which treatment would you suggest for these patients?

#	Patient	
1	well localized brain tumor close to brain stem at 10 cm depth	F
2	widespread bronchial carcinoma (lung cancer) at 10 cm depth, heart should be spared	
3	tumor on chest wall, healthy heart muscle starts at 2.5 cm depth	
4	Aderhautmelanom (tumor of the eye), healthy eye tissue and optic nerve must not be irradiated!	
5	Chondrosarcoma, tumor on scull base, radioresistant	
6	inoperable liver tumor, skin should be spared as far as possible	
7	skin cancer, reaching 3 cm deep, critical organ at 5 cm depth	

#	Treatment
A	5 MeV electrons
B	9 MeV electrons
C	Photons
D	Photons
E	60 MeV protons
F	115 MeV protons
G	Carbon ions

Your turn!

Which treatment would you suggest for these patients?

#	Patient	
1	well localized brain tumor close to brain stem at 10 cm depth	F
2	widespread bronchial carcinoma (lung cancer) at 10 cm depth, heart should be spared	C
3	tumor on chest wall, healthy heart muscle starts at 2.5 cm depth	
4	Aderhautmelanom (tumor of the eye), healthy eye tissue and optic nerve must not be irradiated!	
5	Chondrosarcoma, tumor on scull base, radioresistant	
6	inoperable liver tumor, skin should be spared as far as possible	
7	skin cancer, reaching 3 cm deep, critical organ at 5 cm depth	

#	Treatment
A	5 MeV electrons
B	9 MeV electrons
C	Photons
D	Photons
E	60 MeV protons
F	115 MeV protons
G	Carbon ions

Your turn!

Which treatment would you suggest for these patients?

#	Patient	
1	well localized brain tumor close to brain stem at 10 cm depth	F
2	widespread bronchial carcinoma (lung cancer) at 10 cm depth, heart should be spared	C
3	tumor on chest wall, healthy heart muscle starts at 2.5 cm depth	A
4	Aderhautmelanom (tumor of the eye), healthy eye tissue and optic nerve must not be irradiated!	
5	Chondrosarcoma, tumor on scull base, radioresistant	
6	inoperable liver tumor, skin should be spared as far as possible	
7	skin cancer, reaching 3 cm deep, critical organ at 5 cm depth	

#	Treatment
A	5 MeV electrons
B	9 MeV electrons
C	Photons
D	Photons
E	60 MeV protons
F	115 MeV protons
G	Carbon ions

Your turn!

Which treatment would you suggest for these patients?

#	Patient	
1	well localized brain tumor close to brain stem at 10 cm depth	F
2	widespread bronchial carcinoma (lung cancer) at 10 cm depth, heart should be spared	C
3	tumor on chest wall, healthy heart muscle starts at 2.5 cm depth	A
4	Aderhautmelanom (tumor of the eye), healthy eye tissue and optic nerve must not be irradiated!	E
5	Chondrosarcoma, tumor on scull base, radioresistant	
6	inoperable liver tumor, skin should be spared as far as possible	
7	skin cancer, reaching 3 cm deep, critical organ at 5 cm depth	

#	Treatment
A	5 MeV electrons
B	9 MeV electrons
C	Photons
D	Photons
E	60 MeV protons
F	115 MeV protons
G	Carbon ions

Your turn!

Which treatment would you suggest for these patients?

#	Patient	
1	well localized brain tumor close to brain stem at 10 cm depth	F
2	widespread bronchial carcinoma (lung cancer) at 10 cm depth, heart should be spared	C
3	tumor on chest wall, healthy heart muscle starts at 2.5 cm depth	A
4	Aderhautmelanom (tumor of the eye), healthy eye tissue and optic nerve must not be irradiated!	E
5	Chondrosarcoma, tumor on scull base, radioresistant	G
6	inoperable liver tumor, skin should be spared as far as possible	
7	skin cancer, reaching 3 cm deep, critical organ at 5 cm depth	

#	Treatment
A	5 MeV electrons
B	9 MeV electrons
C	Photons
D	Photons
E	60 MeV protons
F	115 MeV protons
G	Carbon ions

Your turn!

Which treatment would you suggest for these patients?

#	Patient	
1	well localized brain tumor close to brain stem at 10 cm depth	F
2	widespread bronchial carcinoma (lung cancer) at 10 cm depth, heart should be spared	C
3	tumor on chest wall, healthy heart muscle starts at 2.5 cm depth	A
4	Aderhautmelanom (tumor of the eye), healthy eye tissue and optic nerve must not be irradiated!	E
5	Chondrosarcoma, tumor on scull base, radioresistant	G
6	inoperable liver tumor, skin should be spared as far as possible	D
7	skin cancer, reaching 3 cm deep, critical organ at 5 cm depth	

#	Treatment
A	5 MeV electrons
B	9 MeV electrons
C	Photons
D	Photons
E	60 MeV protons
F	115 MeV protons
G	Carbon ions

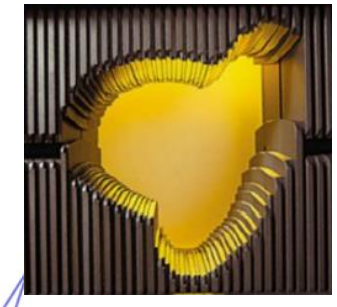
Your turn!

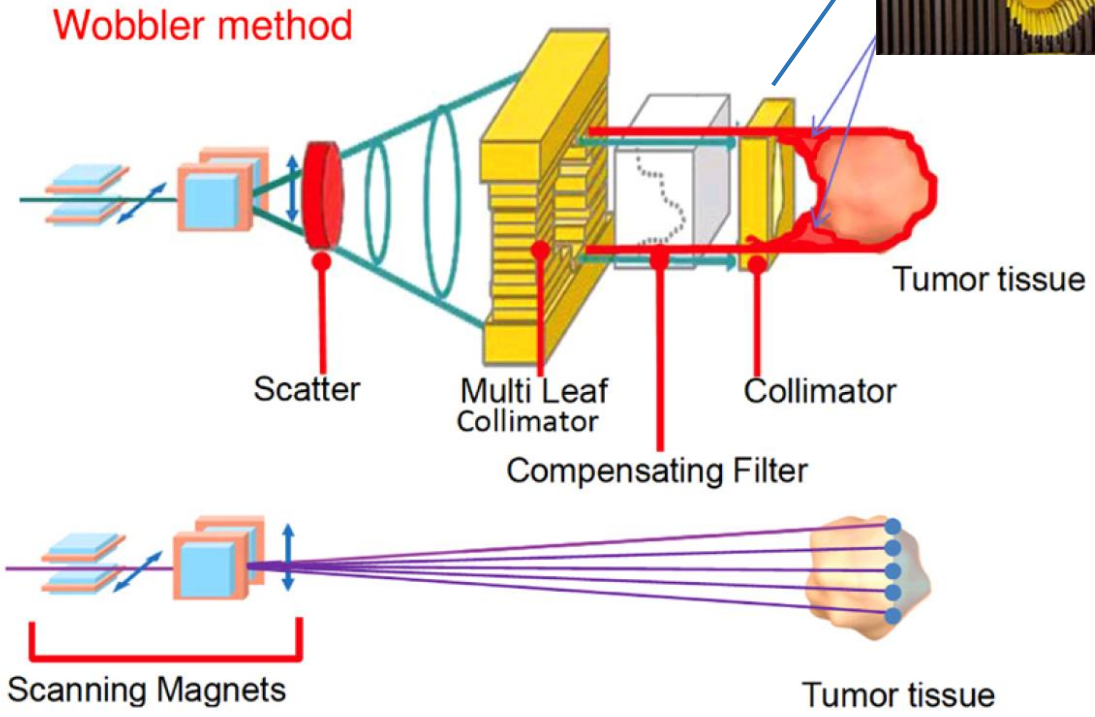
Which treatment would you suggest for these patients?

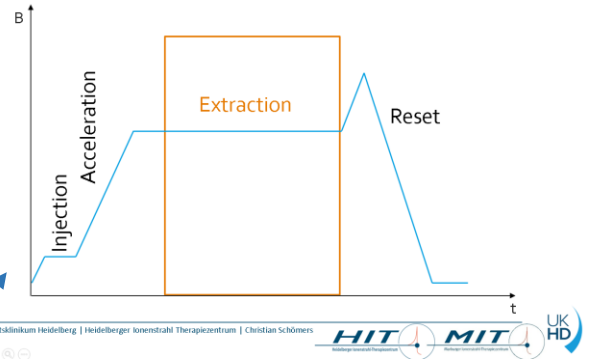
#	Patient	
1	well localized brain tumor close to brain stem at 10 cm depth	F
2	widespread bronchial carcinoma (lung cancer) at 10 cm depth, heart should be spared	C
3	tumor on chest wall, healthy heart muscle starts at 2.5 cm depth	A
4	Aderhautmelanom (tumor of the eye), healthy eye tissue and optic nerve must not be irradiated!	E
5	Chondrosarcoma, tumor on scull base, radioresistant	G
6	inoperable liver tumor, skin should be spared as far as possible	D
7	skin cancer, reaching 3 cm deep, critical organ at 5 cm depth	B

#	Treatment
A	5 MeV electrons
B	9 MeV electrons
C	Photons
D	Photons
E	60 MeV protons
F	115 MeV protons
G	Carbon ions

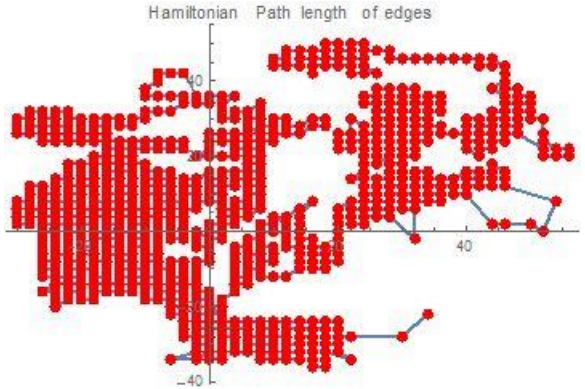
Beam delivery







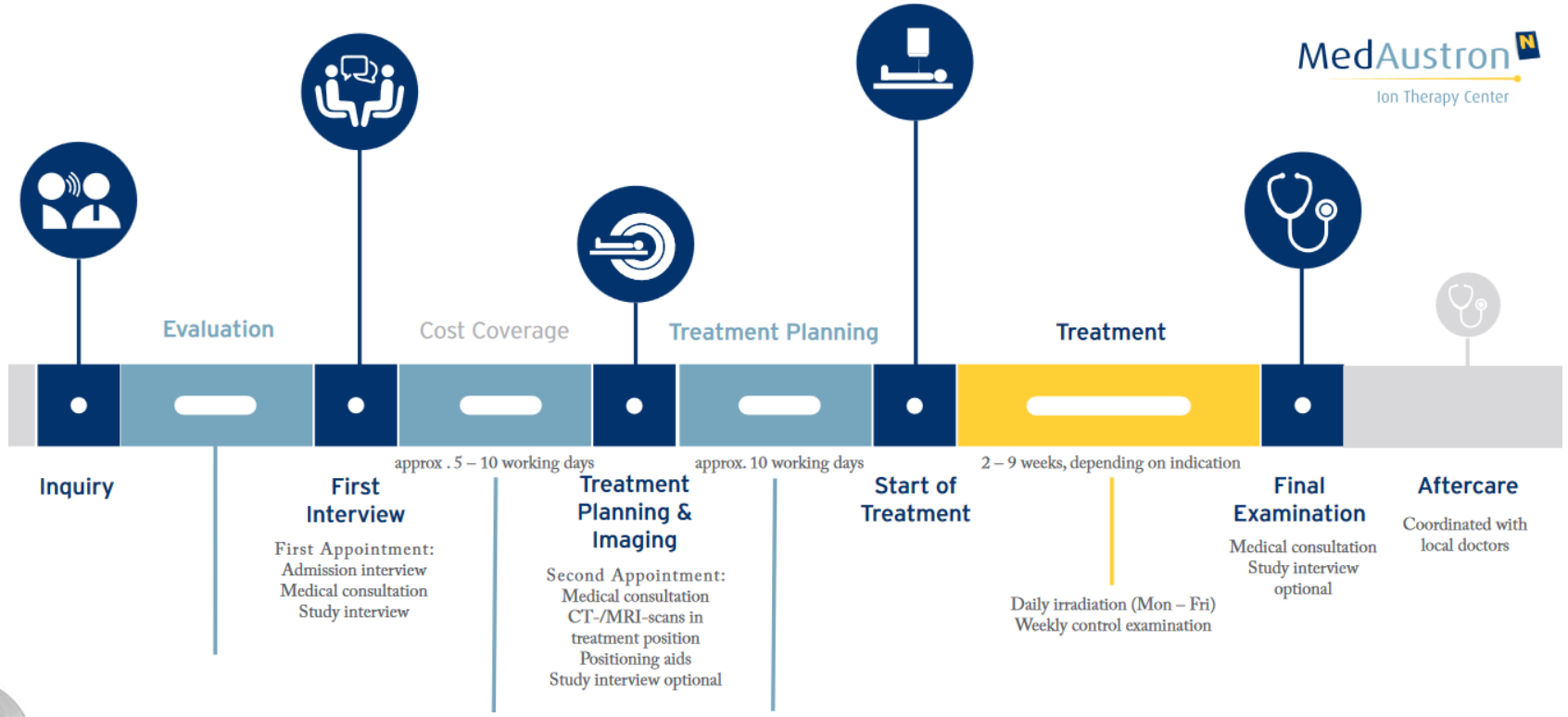
3D scanning:
Tumor divided in voxels
→ Z: energy slice
→ XY: raster scanning

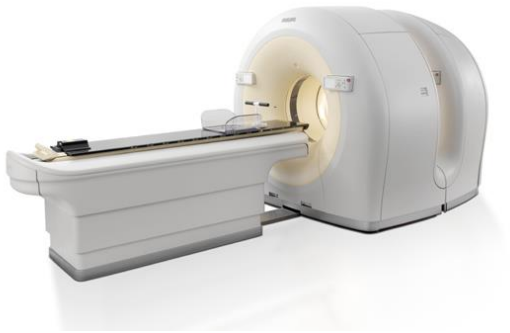


Additional challenge:
patient movements
→ beam gating
→ on-line imaging?

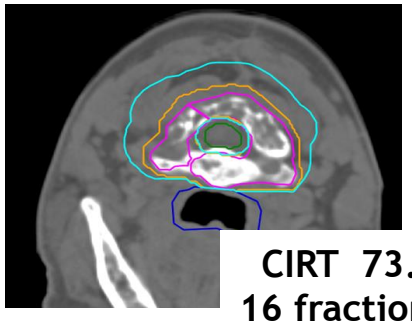
M. Pullia 2018 – Ions for cancer therapy, Workshop Archamps

Procedure



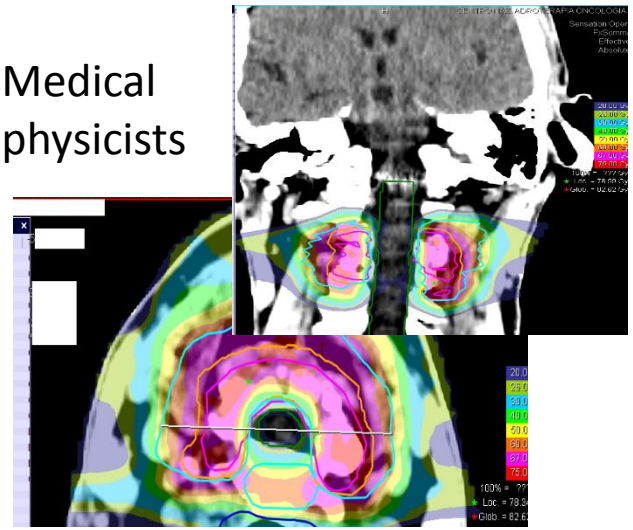


Medical doctor
-> marks boundaries
-> dose



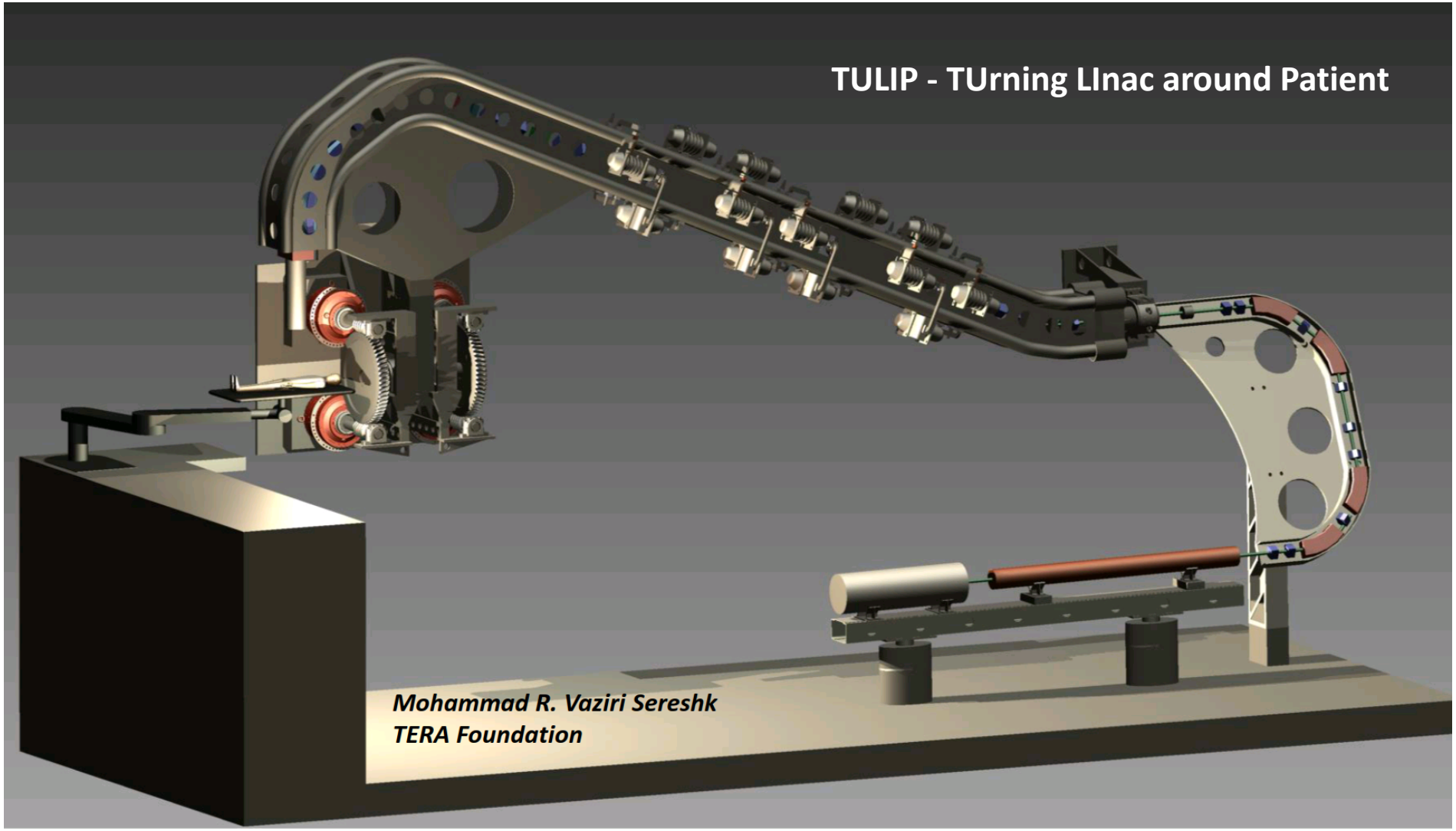
CIRT 73.6 GyE
16 fractions IMPT

Medical physicists



Video

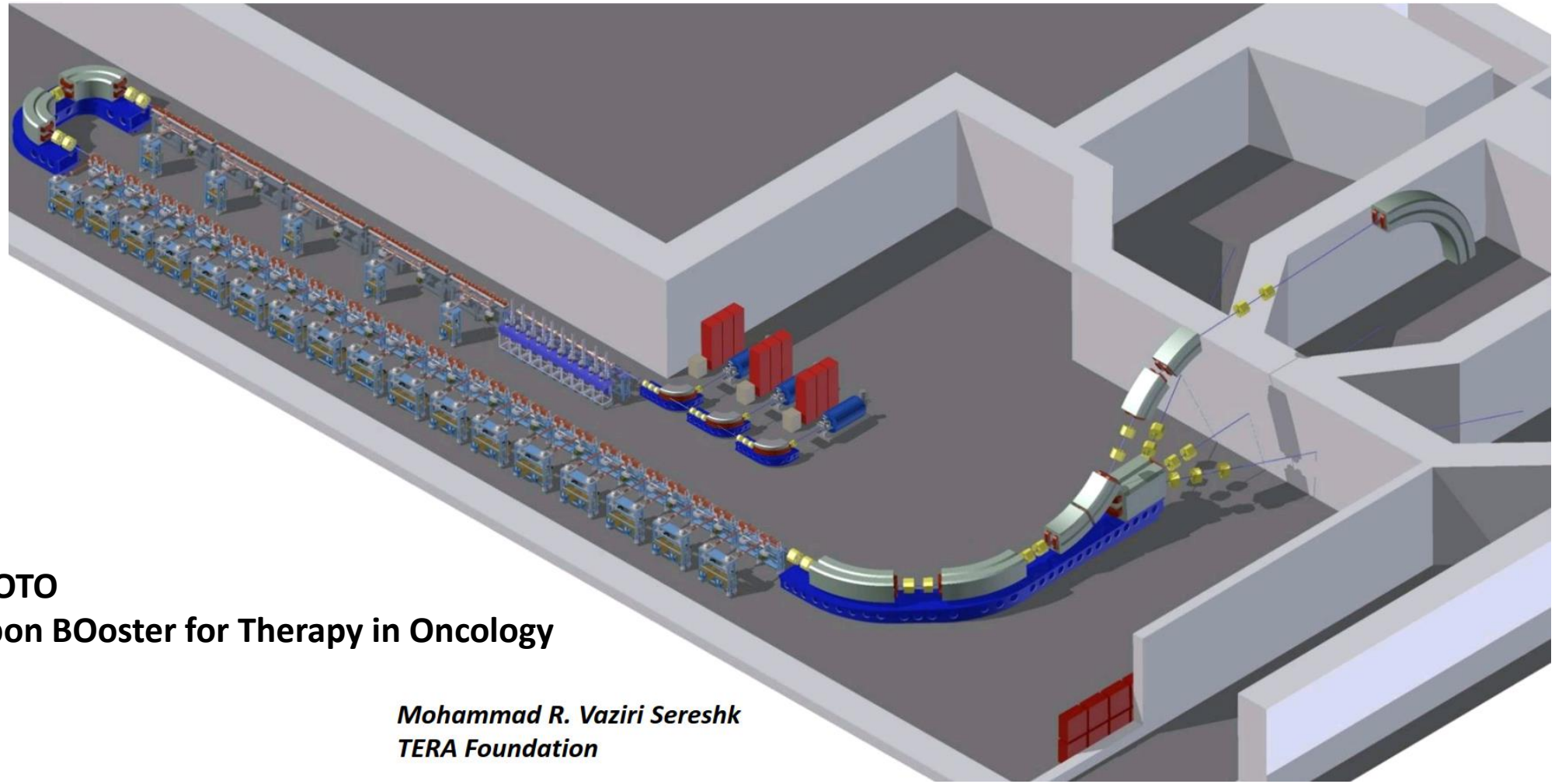
Ideas for the future – smaller, cheaper, faster



LINAC-based:

+ compact
+ fast energy change
+ shorter treatment time

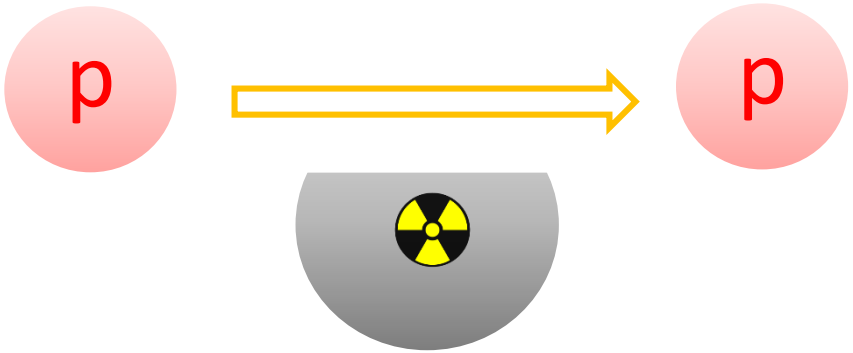
Ideas for the future



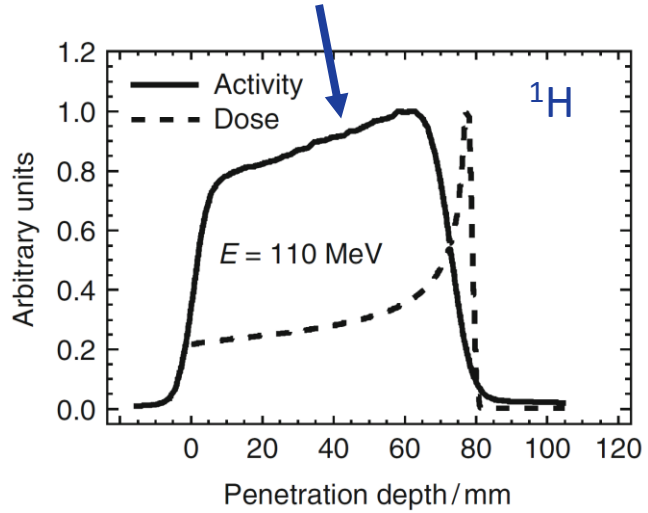
CABOTO
CArbon BOoster for Therapy in Oncology

Mohammad R. Vaziri Sereshk
TERA Foundation

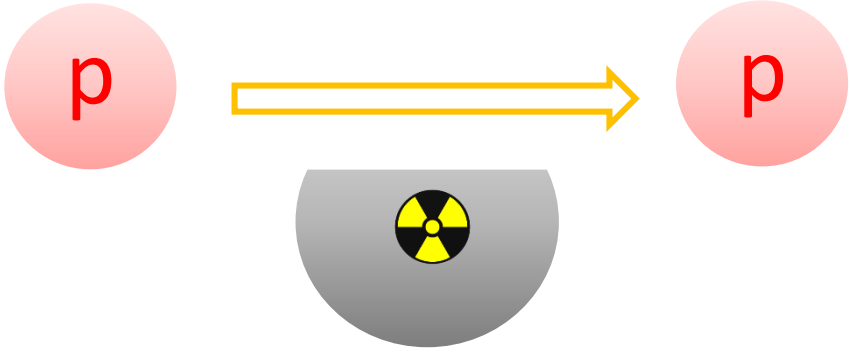
Spare slides on PET imaging in hadron therapy

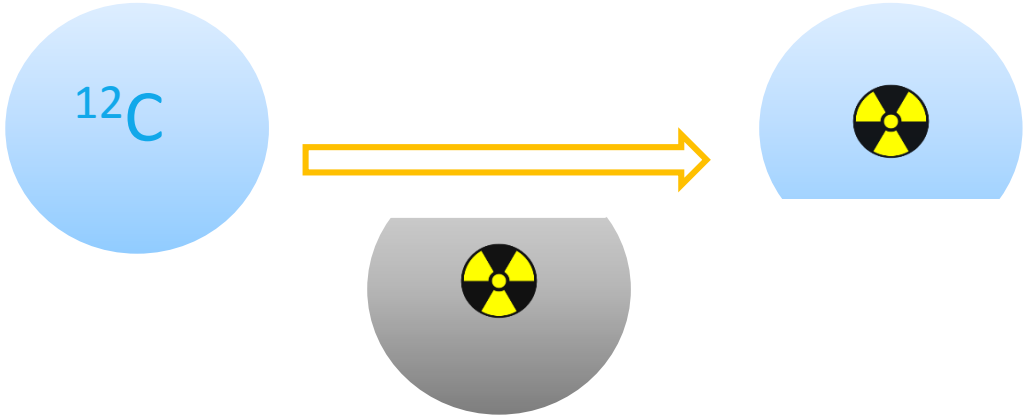


target fragmentation

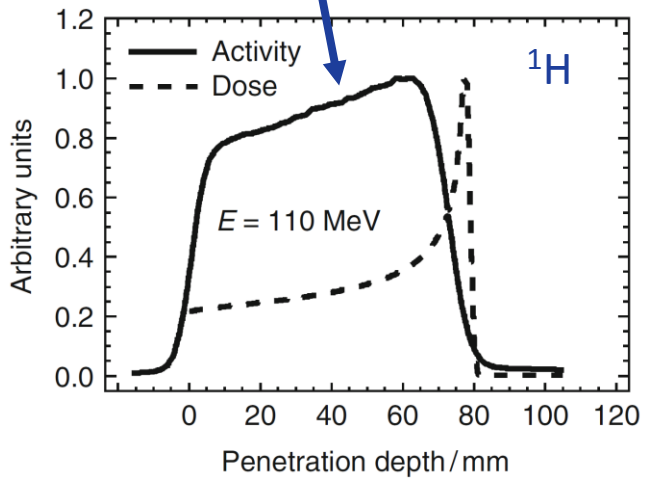


Fiedler et al., in *Ion Beam Therapy*, Springer-Verlag Berlin Heidelberg 2012

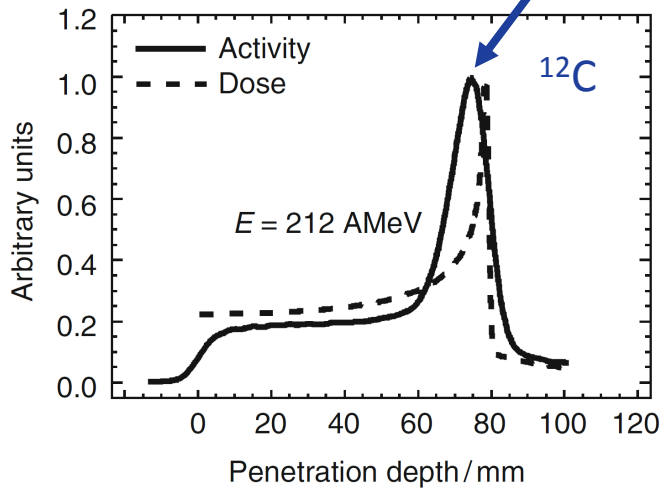




target fragmentation



projectile fragmentation

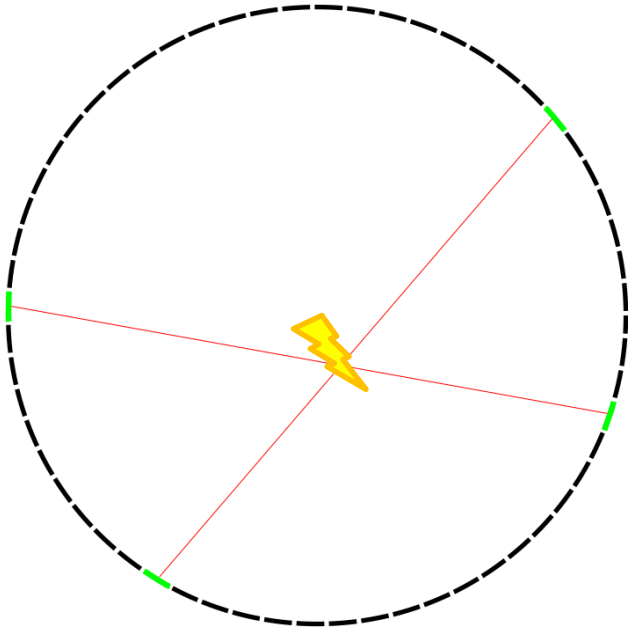


Fiedler et al., in *Ion Beam Therapy*, Springer-Verlag Berlin Heidelberg 2012

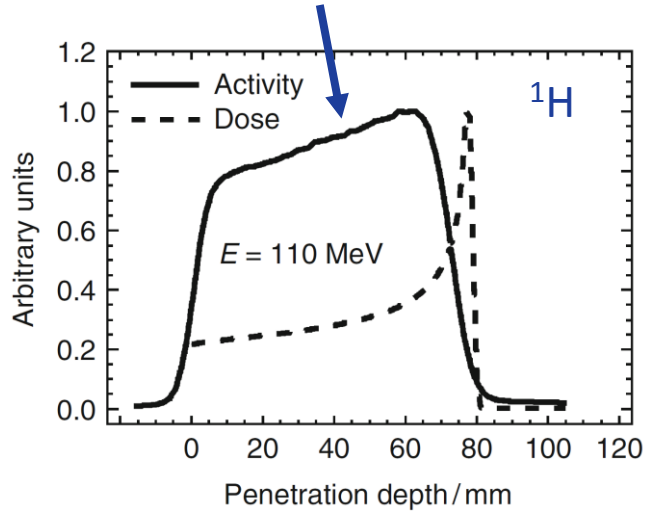
PET scanning in hadron therapy

Positron
Emission
Tomography

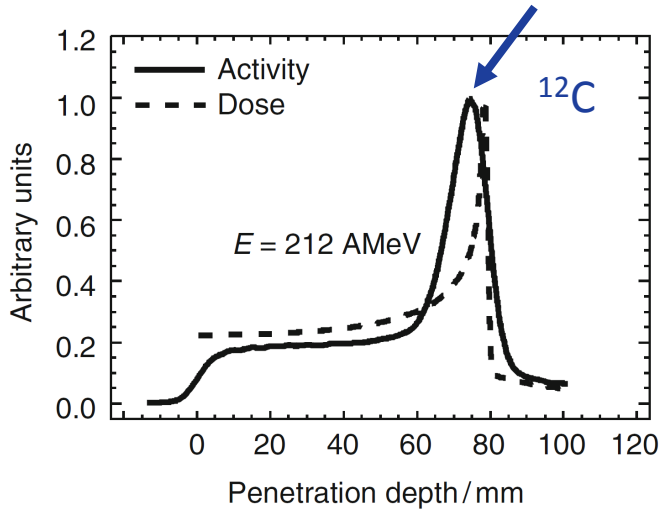
+ therapy control
+ dose verification
- biological washout
- low intensities



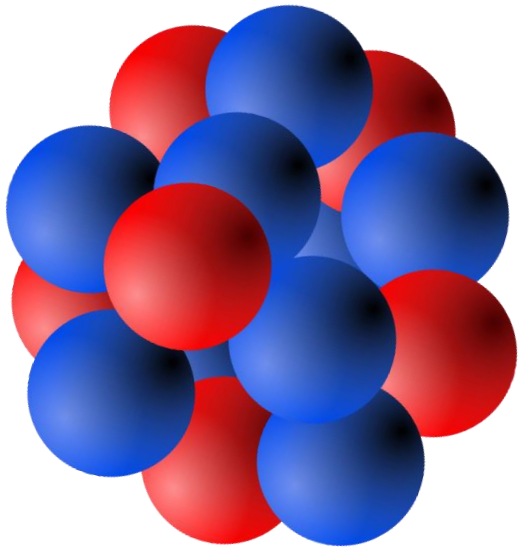
target fragmentation

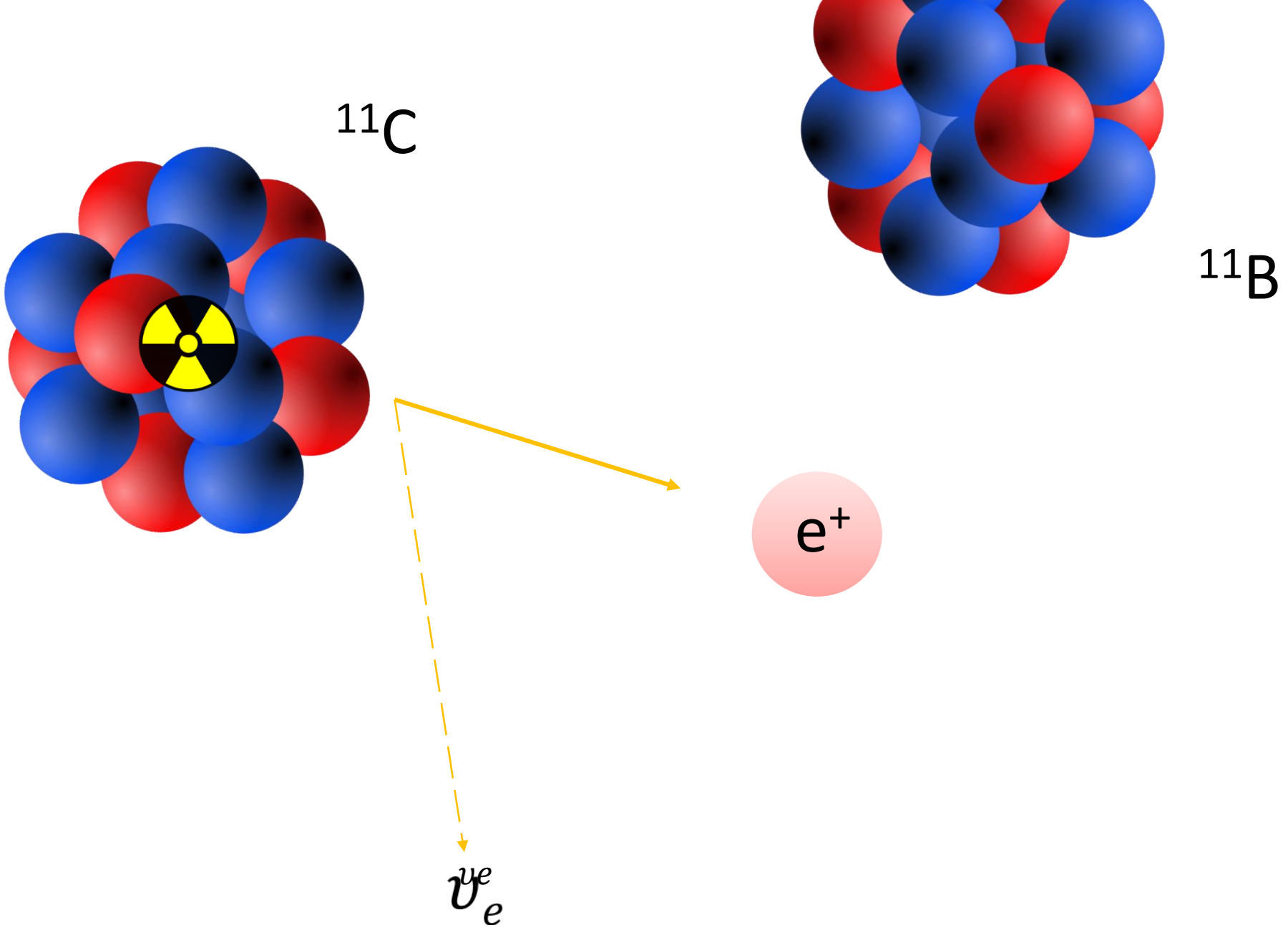


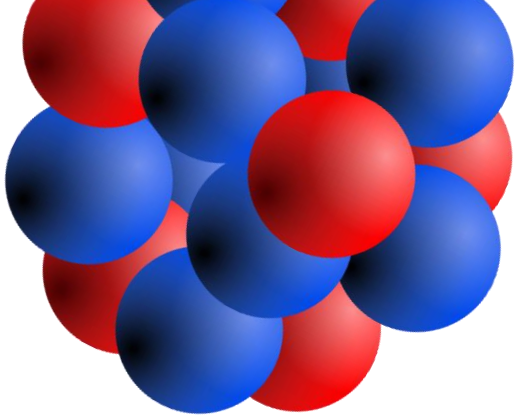
projectile fragmentation

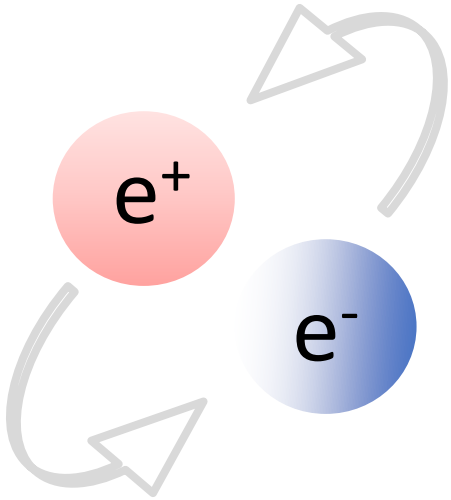


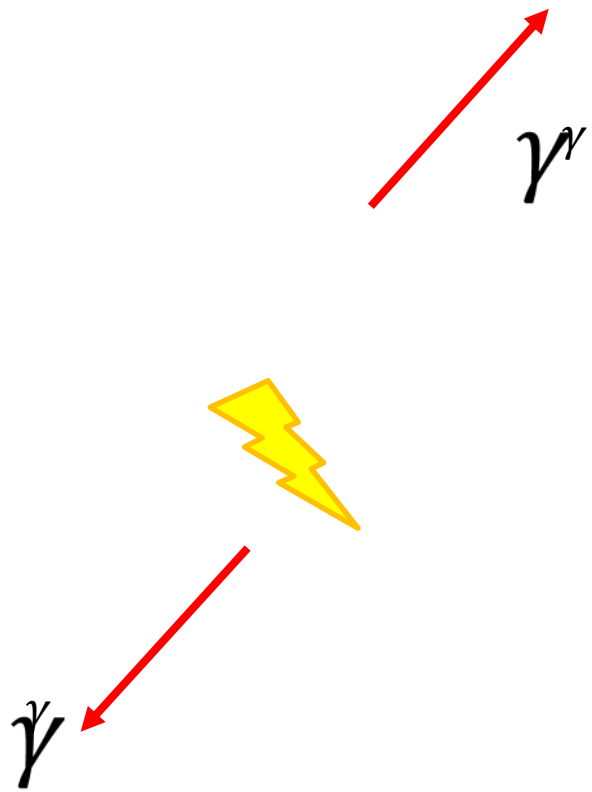
Fiedler et al., in *Ion Beam Therapy*, Springer-Verlag Berlin Heidelberg 2012

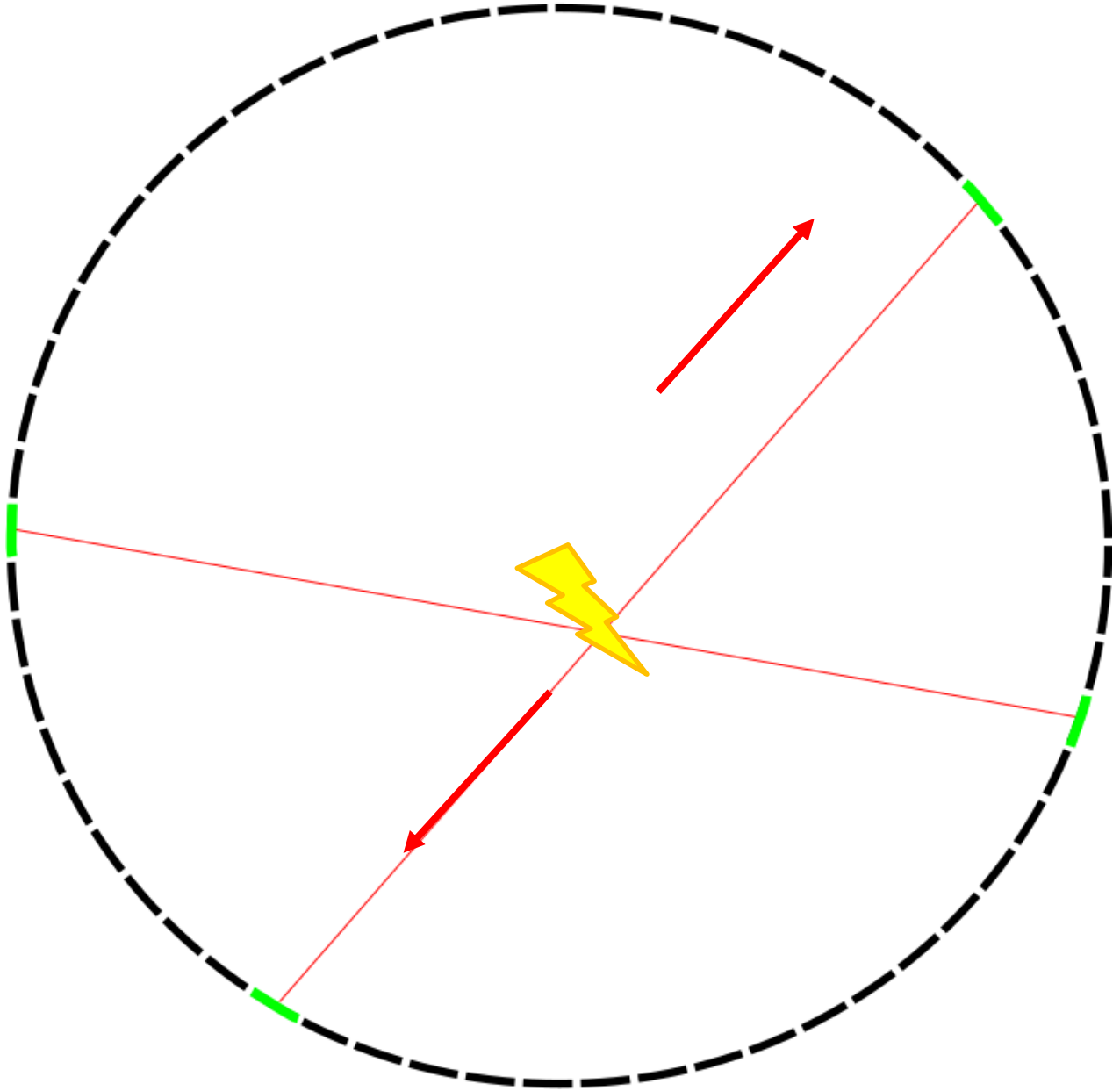


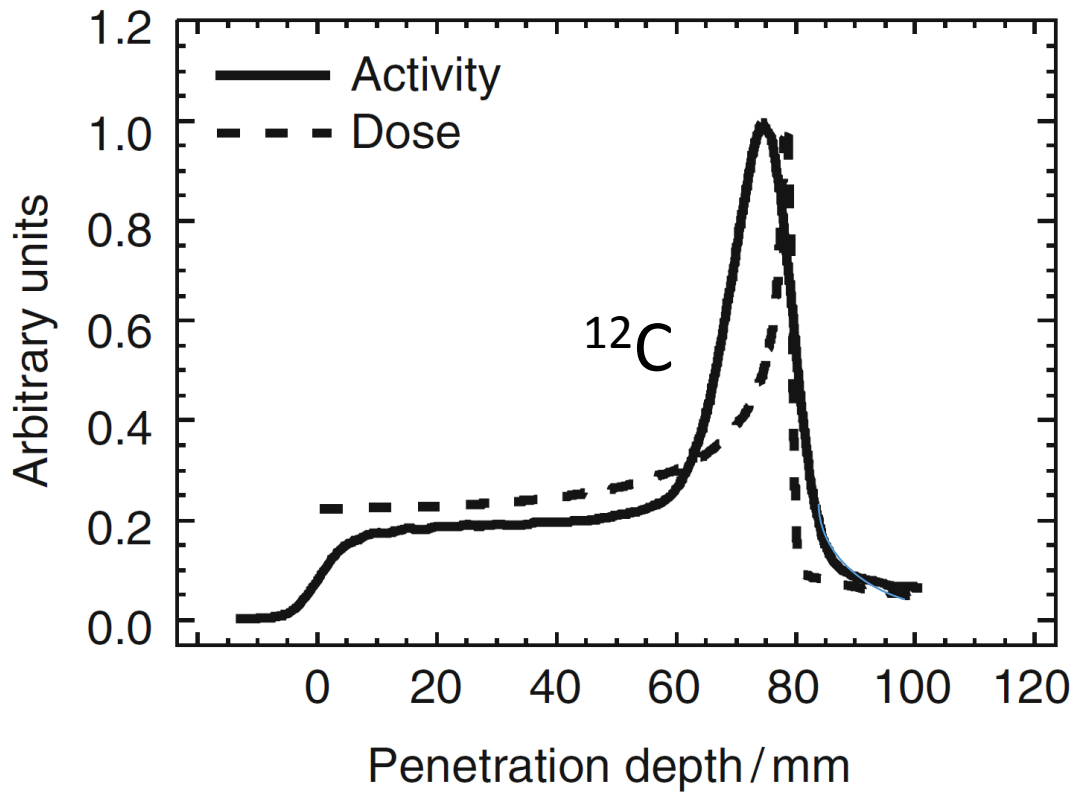

^{11}C
^{11}B
e^+
ν_e

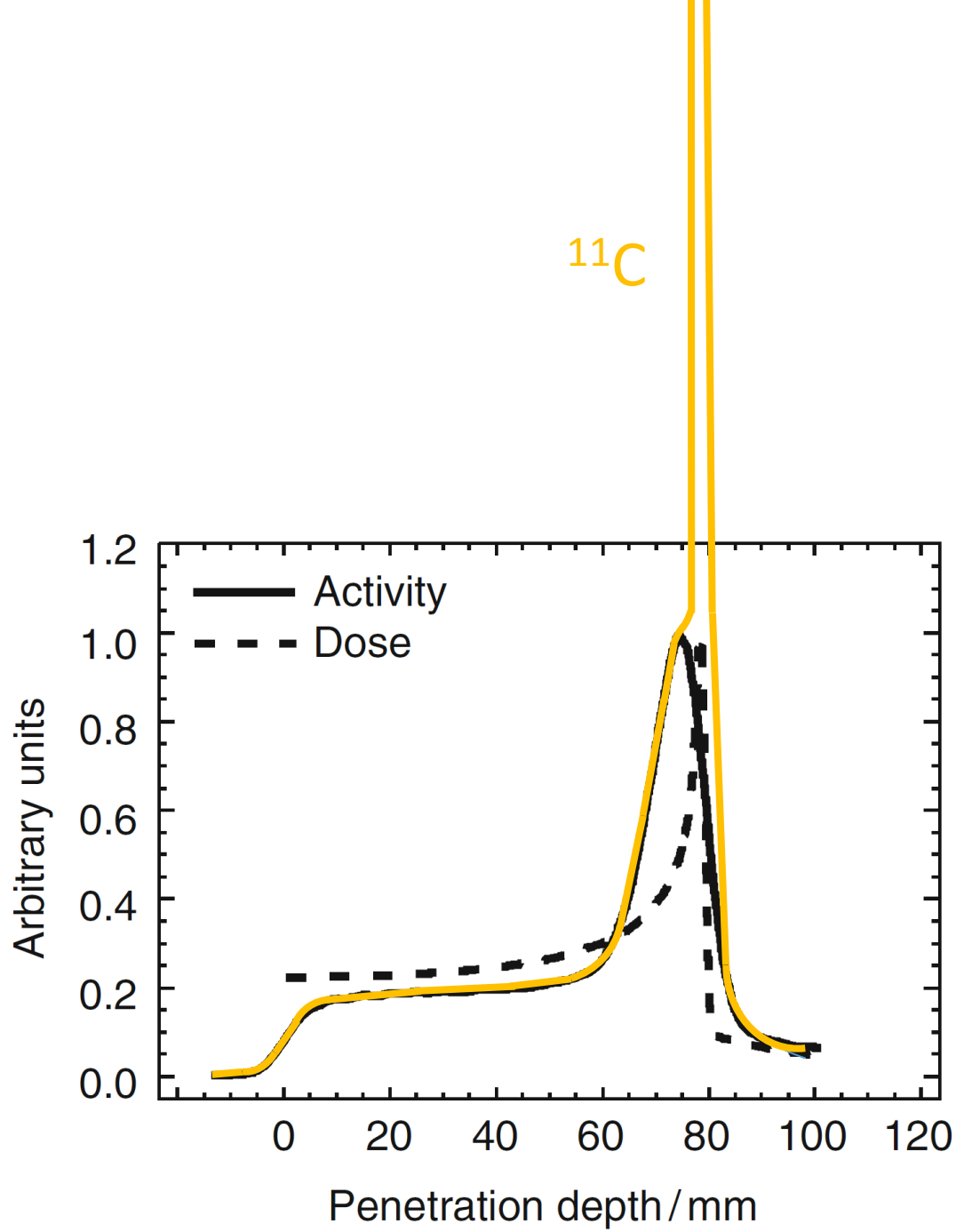



e+
e-


γ^{ν}
γ

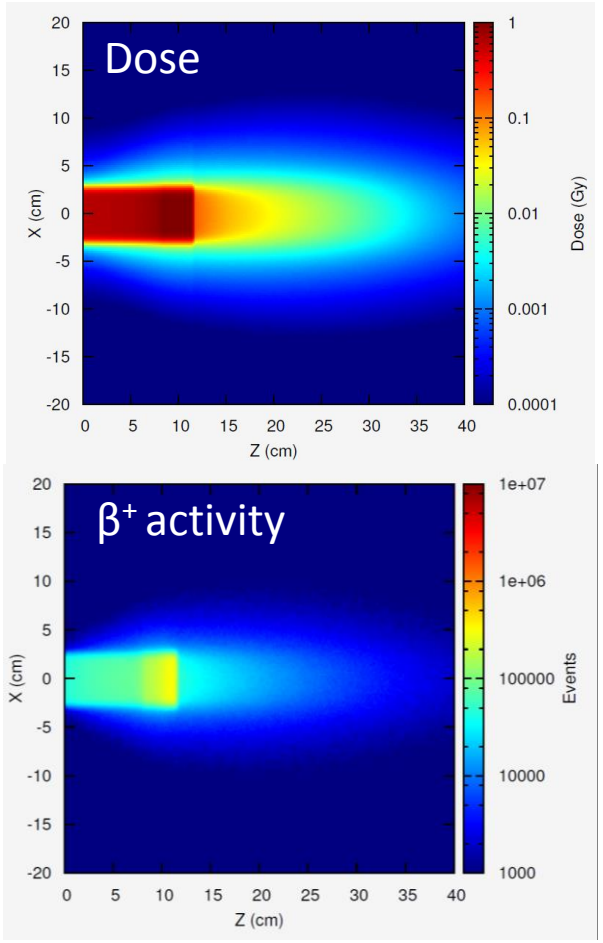



Activity
Dose
^{12}C
Arbitrary units
Penetration depth / mm
0.0
0.2
0.4
0.6
0.8
1.0
1.2
0
20
40
60
80
100
120

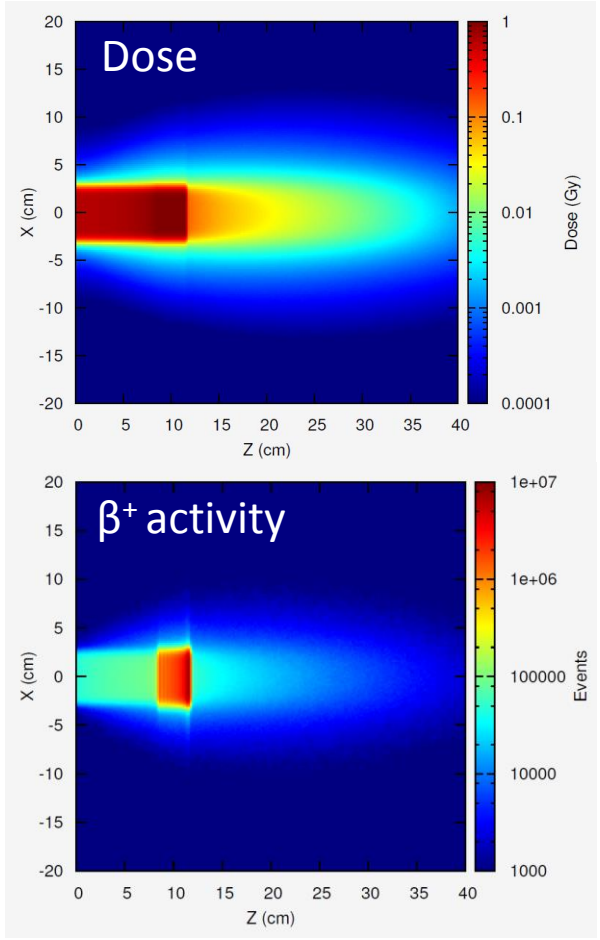

^{11}C
Activity
Dose
Arbitrary units
1.2
1.0
0.8
0.6
0.4
0.2
0.0
0
20
40
60
80
100
120
Penetration depth / mm

11C aided hadron therapy

12C



11C

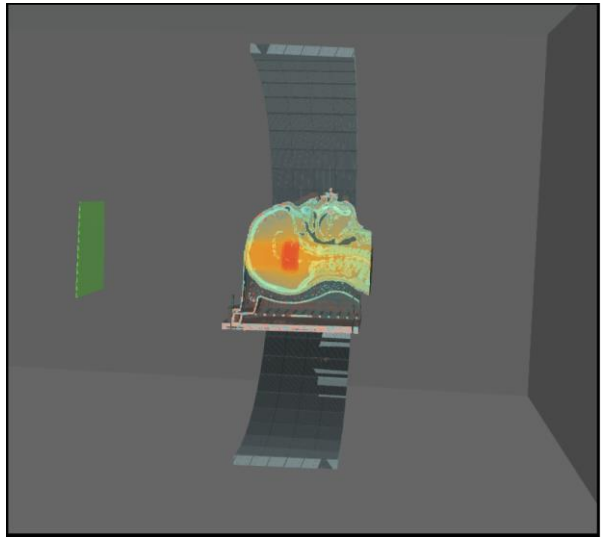


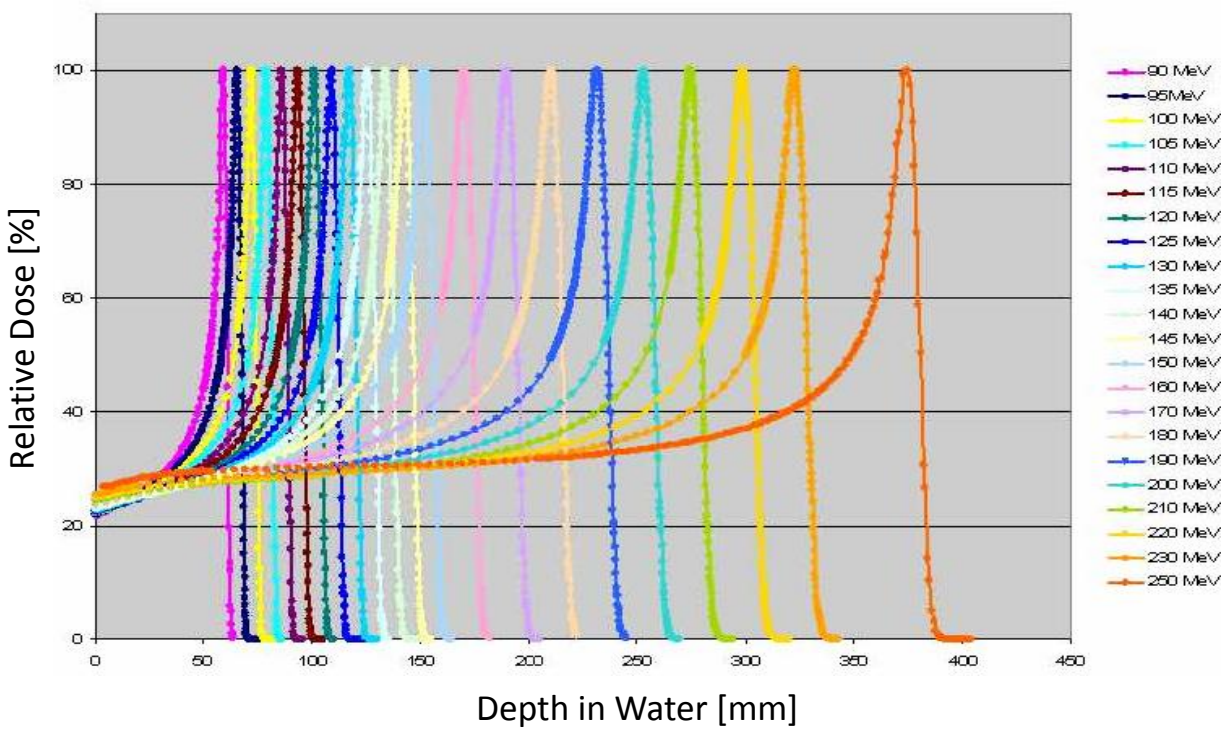
R. S. Augusto et al., NIM B376 (2016) 374-378

^{11}C primary beam

- increased β^+ activity
- maximum at Bragg peak

  -> **PET imaging** for dose verification




Relative Dose [%]
Depth in Water [mm]
0
20
40
60
80
100
0
50
100
150
200
250
300
350
400
450
90 MeV
95MeV
100 MeV
105 MeV
110 MeV
115 MeV
120 MeV
125 MeV
130 MeV
135 MeV
140 MeV
145 MeV
150 MeV
160 MeV
170 MeV
180 MeV
190 MeV
200 MeV
210 MeV
220 MeV
230 MeV
250 MeV