Hadrontherapy against cancer: an overview

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Outline

What is ion beam therapy?

- In Ion Beam Therapy (IBT, or *hadrontherapy*) ion beams for treatment of deep seated tumours are used
- Profile characterized by a low dose in the entrance channel and by a sharp peak near the end of the path (*Bragg peak*)
- Very good control in all three spatial dimensions

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Short history of IBT

- **1946: Robert Wilson publishes "Radiological Use of Fast Protons". The *Bragg peak* of heavy charged particles can be used against cancers**
- First treatments: 1954 Berkeley, 1957 Sweden, 1983 Japan
- Facilities in Italy: 2002 CATANA, 2011 CNAO, 2014 Proton Therapy Center

A tough journey

Electrons
Mass $0.5\,\mathrm{MeV}/c^2$
Requested energy $10\,\mathrm{MeV}$

Protons
Mass $1\,\mathrm{GeV}/c^2$
Requested energy $> 200\,\mathrm{MeV}$

IBT costs are 2 - 3 times higher respect to conventional RT!

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Protons

Mass 1 GeV$/c^2$

Requested energy $>$ 200 MeV

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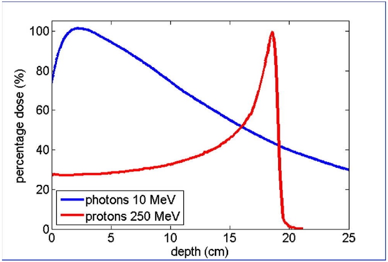
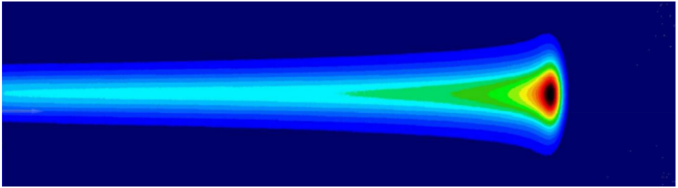
Photons

The attenuation of a photon beam in a medium is a decreasing exponential in depth and can be written as:

$$I(x) = I_0 e^{-\mu x}$$



Heavy charged particles



- inelastic collisions with electrons of the material → energy loss
- elastic scattering with nuclei → deflection from incident direction

Bethe-Bloch formula

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

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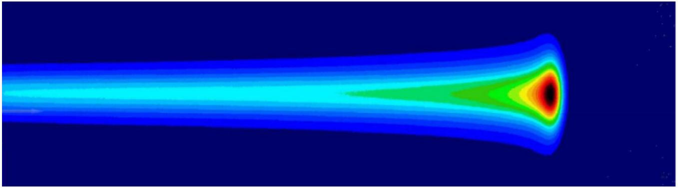

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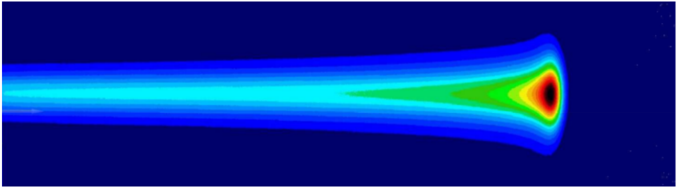

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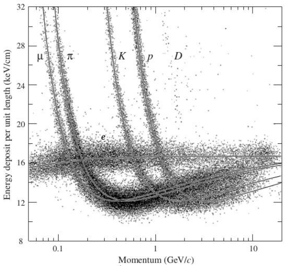
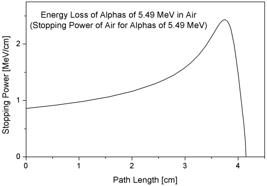
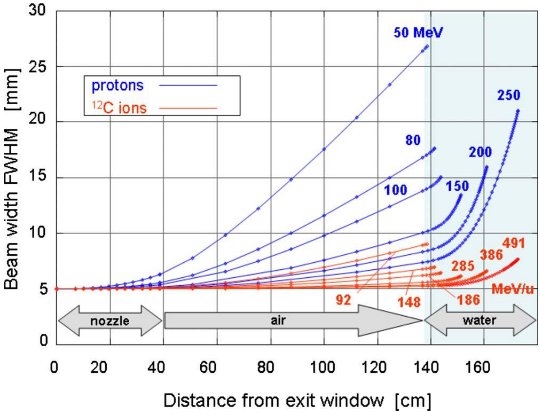
Stopping power





Multiple Coulomb Scattering



MCS formula

$$\sigma_\theta = \frac{14.1\,\text{MeV}}{\beta p c} \cdot Z_p \sqrt{\frac{d}{L_{\text{rad}}}} \left[1 + 1/9 \ln\left(\frac{d}{L_{\text{rad}}}\right)\right]$$

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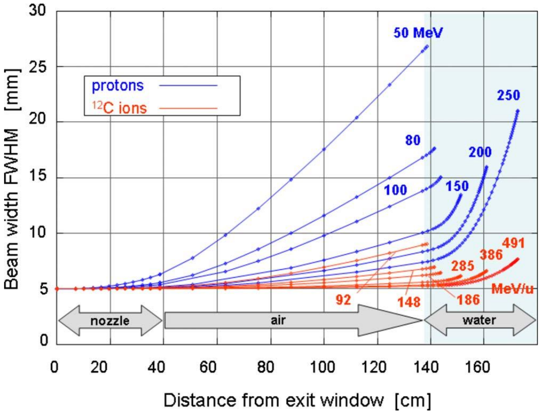

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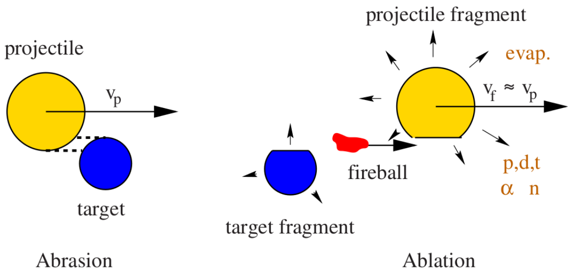
Nuclear fragmentation with heavy ions



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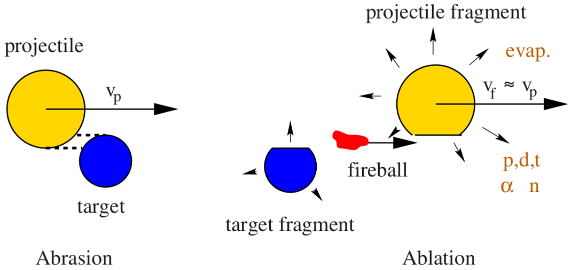
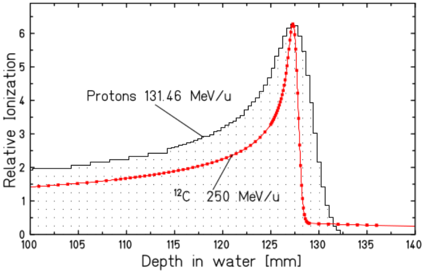
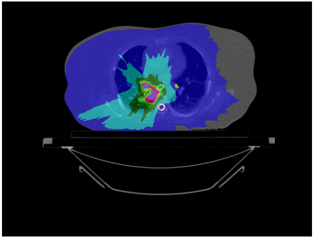
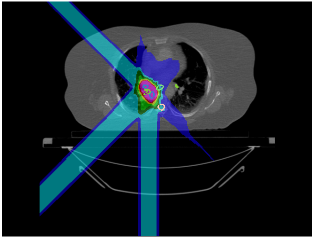


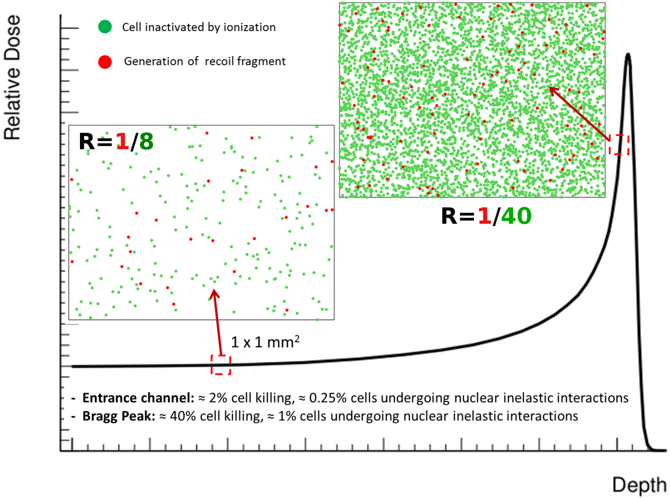


RT vs IBT





Nuclear fragmentation with protons



- **Entrance channel:** ≈ 2% cell killing, ≈ 0.25% cells undergoing nuclear inelastic interactions
- **Bragg Peak:** ≈ 40% cell killing, ≈ 1% cells undergoing nuclear inelastic interactions

What can we do?

We need a target fragmentation experiment...

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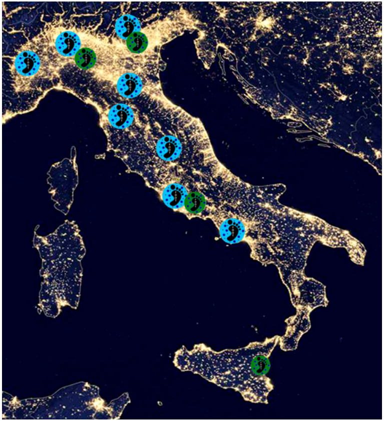

The FOOT experiment

- What about shooting a proton with $\beta = 0.6$ on a patient (98% H, C and O nuclei) at rest? **NO!** too much difficult to detect
- So, let's shoot a $\beta = 0.6$ patient on a proton at rest and measure how it fragments! **YES!** inverse kinematics

How to measure:

- use patient ion beams (mainly ^{16}O, ^{12}C) with the right energy;
- use twin targets made of C and polyethylene $(C_2H_4)_n$ and obtain the H target result by subtraction;
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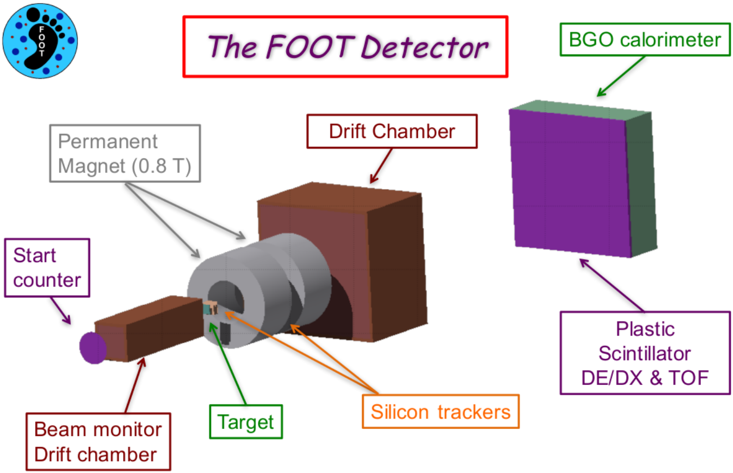
To-do-list

- Target fragmentation of p on O,C @$100 - 200\,\mathrm{MeV}/u$;
- Projectile fragmentation of O on C @$200 - 400\,\mathrm{MeV}/u$;
- Projectile fragmentation of C on C @$200 - 350\,\mathrm{MeV}/u$;
- Evaluation of the β^+ emitters production from C, O on C @$200 - 400\,\mathrm{MeV}/u$;
- Fragmentation measurements of several beams on $(C_2H_4)_n$ of interest for radioprotection in space.

The detector



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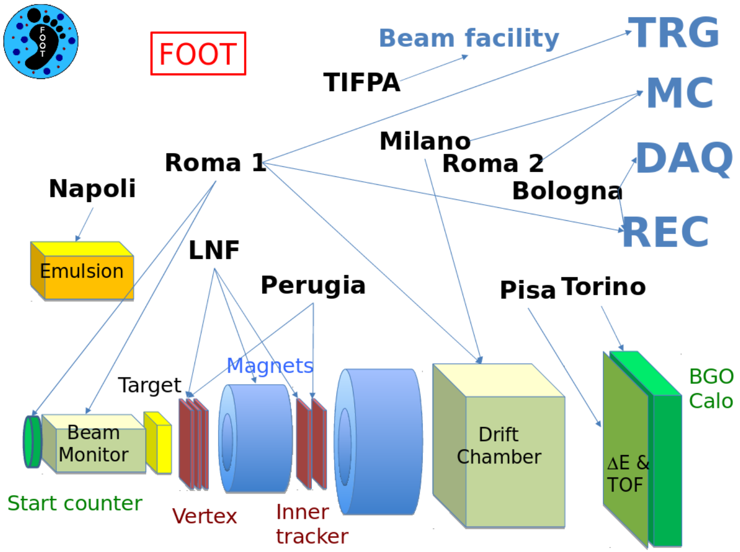
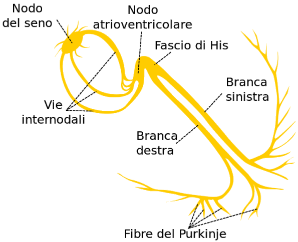
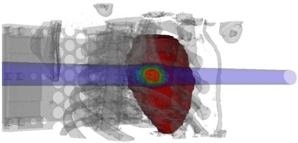


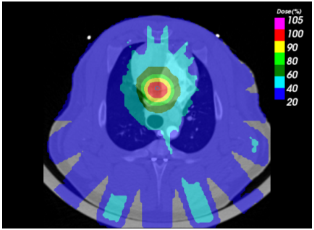
Results

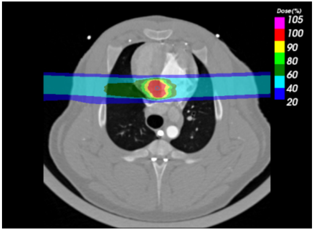
- *Uveal melanoma* $\rightarrow$ 5-yr survival$=80.8\%$, 5-yr TCP$=96.4\%$
- *Lung cancer* $\rightarrow$ 5-yr survival$=84.7\%-96.3\%$ (RT only 30%), 5-yr TCP$=91.5\%$
- *Liver cancer (HCC)* $\rightarrow$ 5-yr survival$=71\%$, 3-yr TCP$=73\%$
- *Chordoma and chondrosarcoma* $\rightarrow$ 5-yr survival$=80\%-95\%$ (RT only 40%)

Candidate pathologies





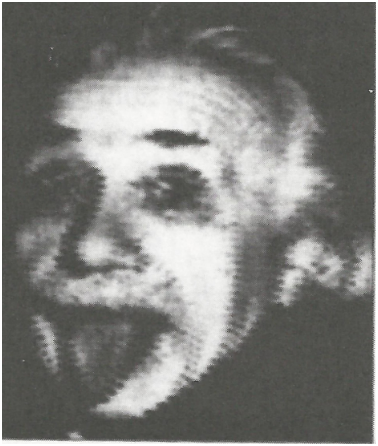




Conclusions

- OAR sparing
- drastic reduction of side effects (pediatric tumours)
- space and cost
- nearly sixty protontherapy centres, ten with carbon ions
- nowadays patients number grows of 8% every year
- a lot of work needs to be done!

Thank for your attention!



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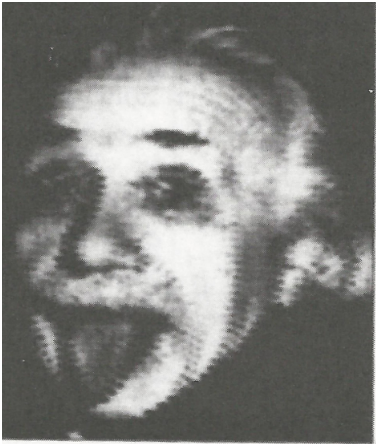
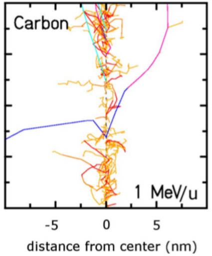
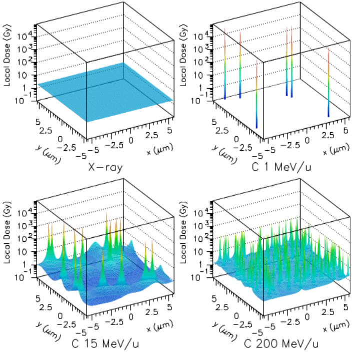
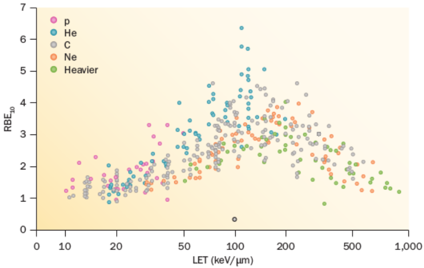
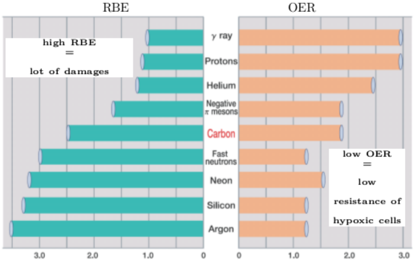



Carbon
1 MeV/u
-5
0
5
distance from center (nm)

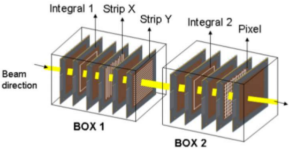

Local Dose (Gy)
X−ray
C 1 MeV/u
C 15 MeV/u
C 200 MeV/u
y (µm)
x (µm)


p
He
C
Ne
Heavier
RBE$_{10}$
LET (keV/µm)
0
10
20
50
100
200
500
1,000


RBE
OER
high RBE
=
lot of damages
γ ray
Protons
Helium
Negative π mesons
Carbon
Fast neutrons
Neon
Silicon
Argon
low OER
=
low
resistance of
hypoxic cells

$$K = \frac{1}{2} m v^2 = \frac{q^2 B^2 R^2}{2m}.$$

$$m = \frac{m_0}{\sqrt{1-\beta^2}} = \gamma m_0 \qquad \nu = \frac{\nu_0}{\gamma} = \nu_0 \sqrt{1-\beta^2}$$



$$Q(E) = e \cdot \left(\frac{I_{\text{fascio}} \cdot \Delta t \cdot \rho \cdot \Delta x}{W} \cdot \frac{dE}{dx} \right)$$

Gantries

- allow beam to enter from several angles
- magnetic rigidity issue of protons and mostly of carbon ions

$$\frac{mv^2}{\rho} = qvB \qquad B\rho = \frac{A m_{\mathrm{av}} v}{ne}$$

$$B[T]\,\rho[m] = \frac{1}{0.299792458} \cdot \left(\frac{A}{n}\right) \cdot p_{\mathrm{av}}\,[\mathrm{GeV}/c]$$

Radiobiology

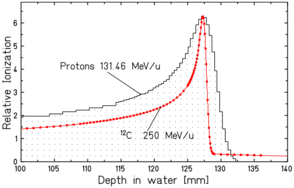
What is radiobiology?

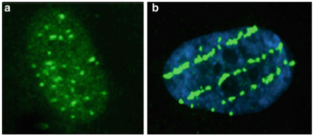
In oncological RT field radiobiology studies the interactions between ionizing radiations and living organisms and their effects.

Four fundamental quantities

- Absorbed dose
- LET, *Linear Energy Transfer*
- RBE, *Relative Biological Effectiveness*
- OER, *Oxygen Enhancement Ratio*

Protons vs ^{12}C





OER value for carbon ions ($\simeq 1$) allows treatment of hypoxic tumours (the only solution so far)!

Real-time PET, *Positron Emission Tomography*

- PET is a nuclear medicine technique used in order to obtain functional images of patients' body
- a short half-life isotope is bound in a molecule requested by tumour in its life cycle: when this isotope begins to decay through β^+ positron annihilates with an electron of the tissue, thus creating the well-known photon pair
- in IBT autoactivation is used for monitoring the dose delivery

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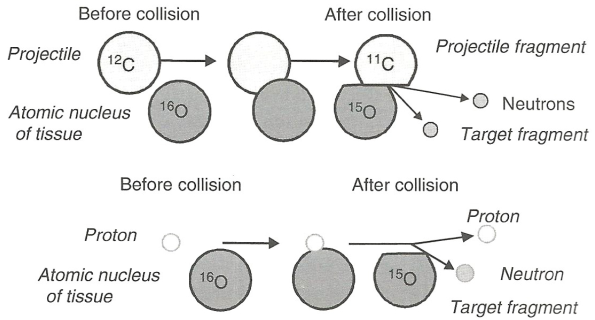
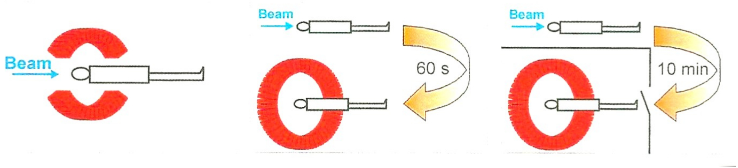
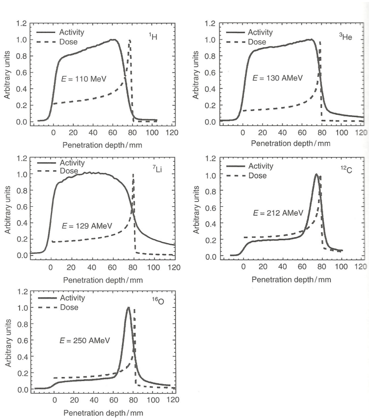



Beam
Beam
60 s
Beam
10 min

β^+ emettitor	$T_{1/2}$
^{11}C	20.4 min
^{10}C	19.2 s
^{15}O	122 s
^{13}N	9.96 min


Activity
Dose
^{1}H
E = 110 MeV
Arbitrary units
Penetration depth / mm
^{3}He
E = 130 AMeV
^{7}Li
E = 129 AMeV
^{12}C
E = 212 AMeV
^{16}O
E = 250 AMeV

Passive scattering vs active scanning