NUCLEAR PHYSICS FOR MEDICINE - HADRON THERAPY

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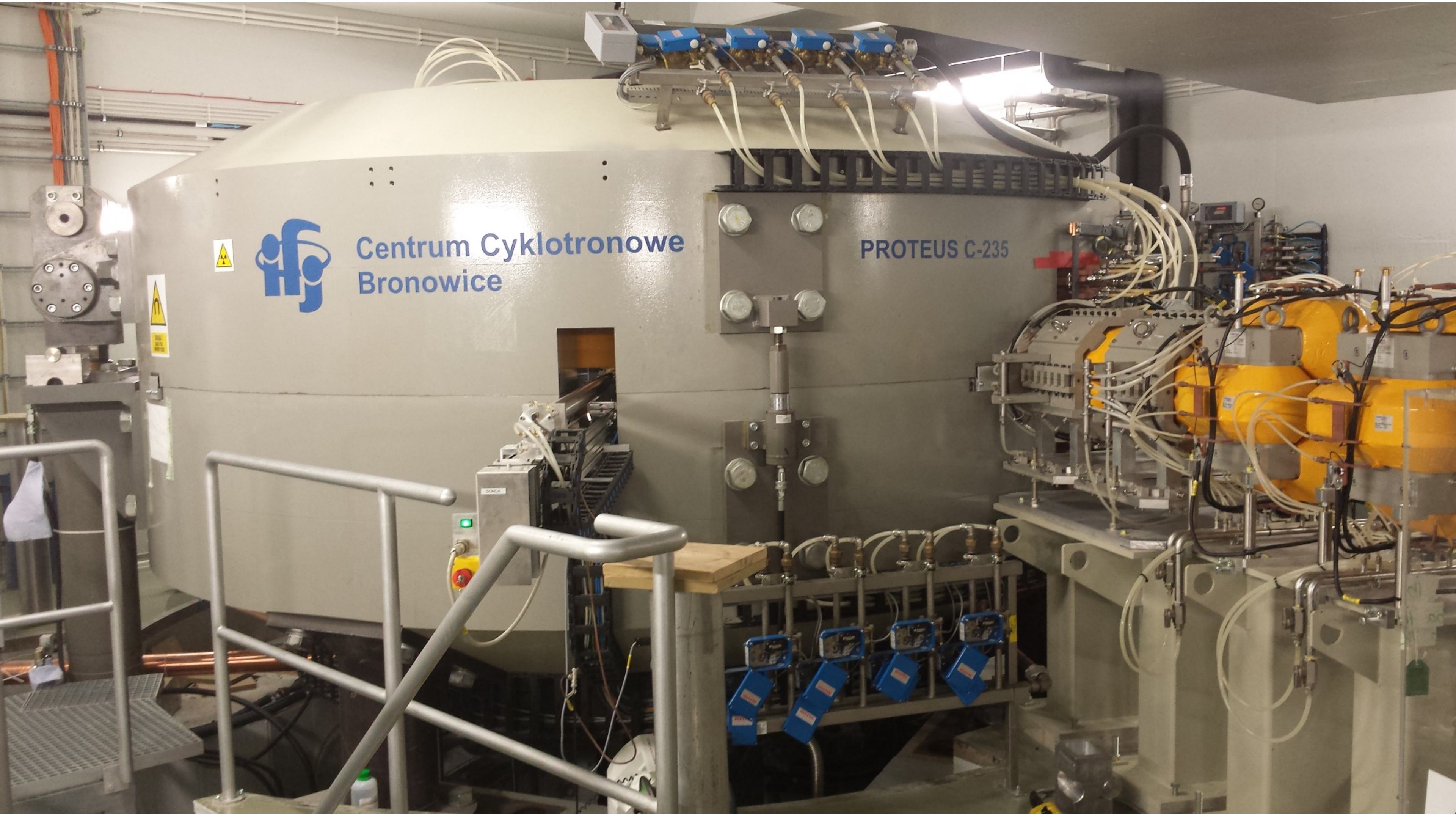
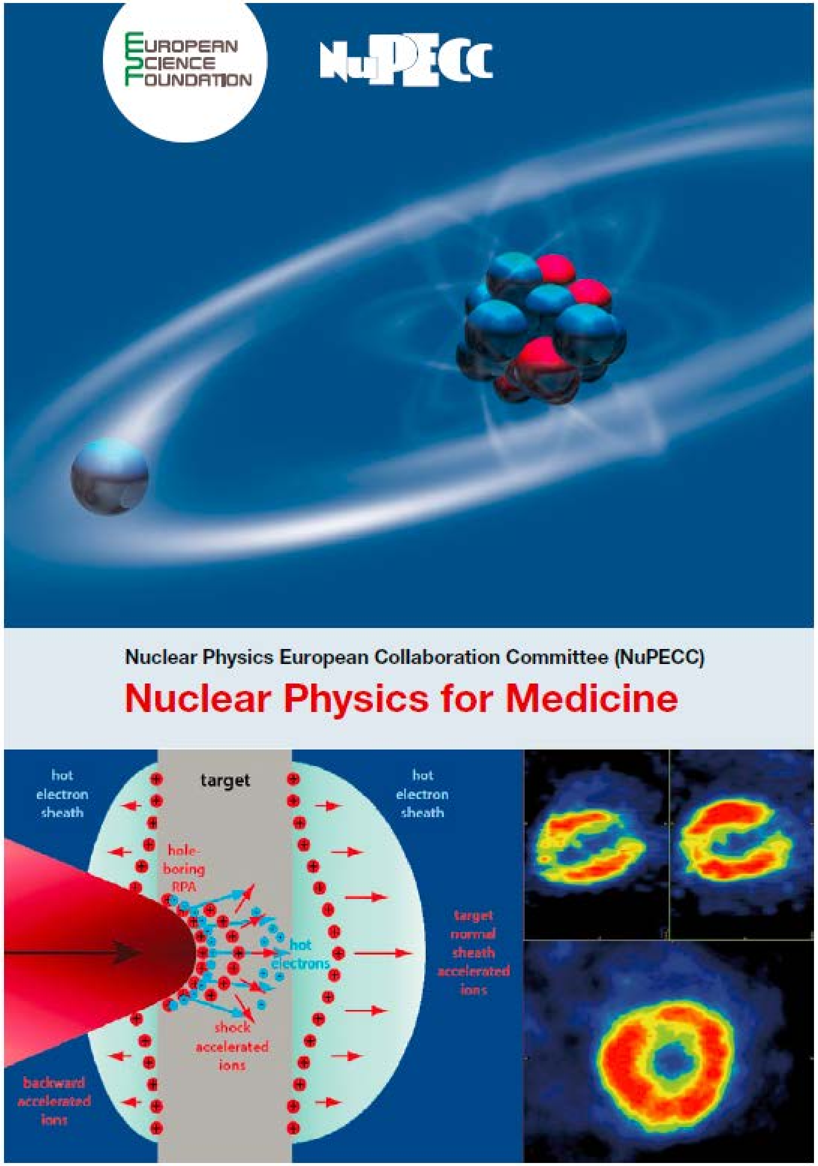


The NuPECC report: Nuclear Physics in Medicine



http://www.nupecc.org/pub/npmed2014.pdf

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- **Nick van der Meulen** (Belgium)
- **Piet Van Duppen** (Belgium)
- **Claas Wessels** (France)

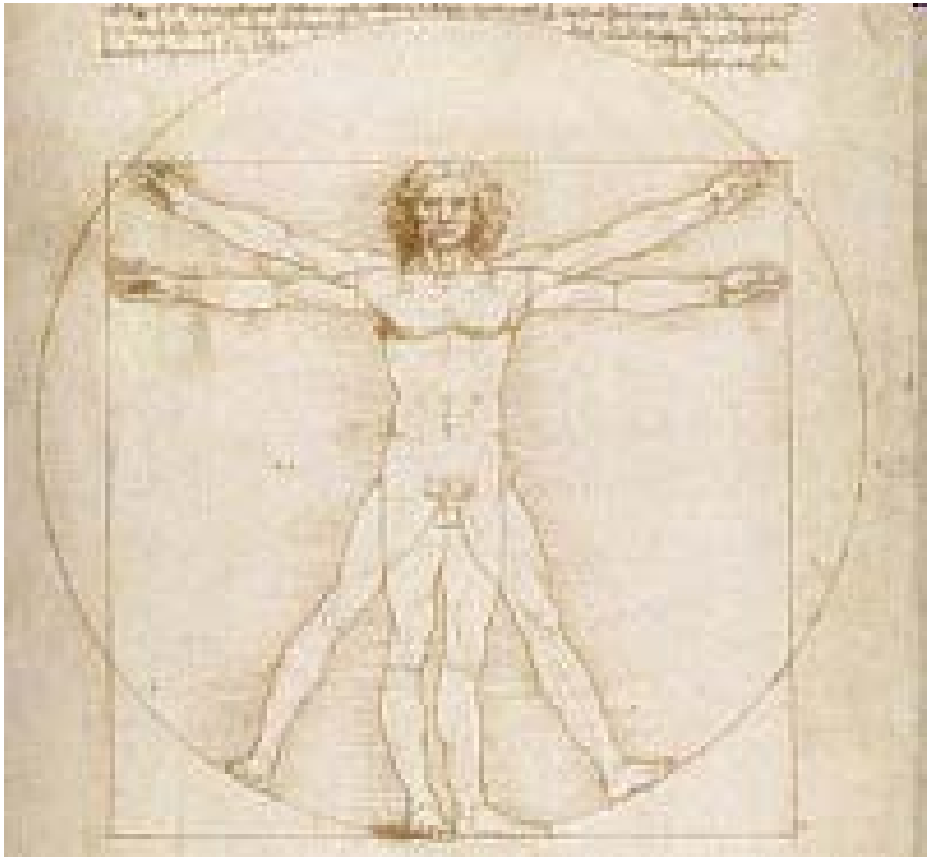
Outline

1. **Why hadrons for cancer therapy?**

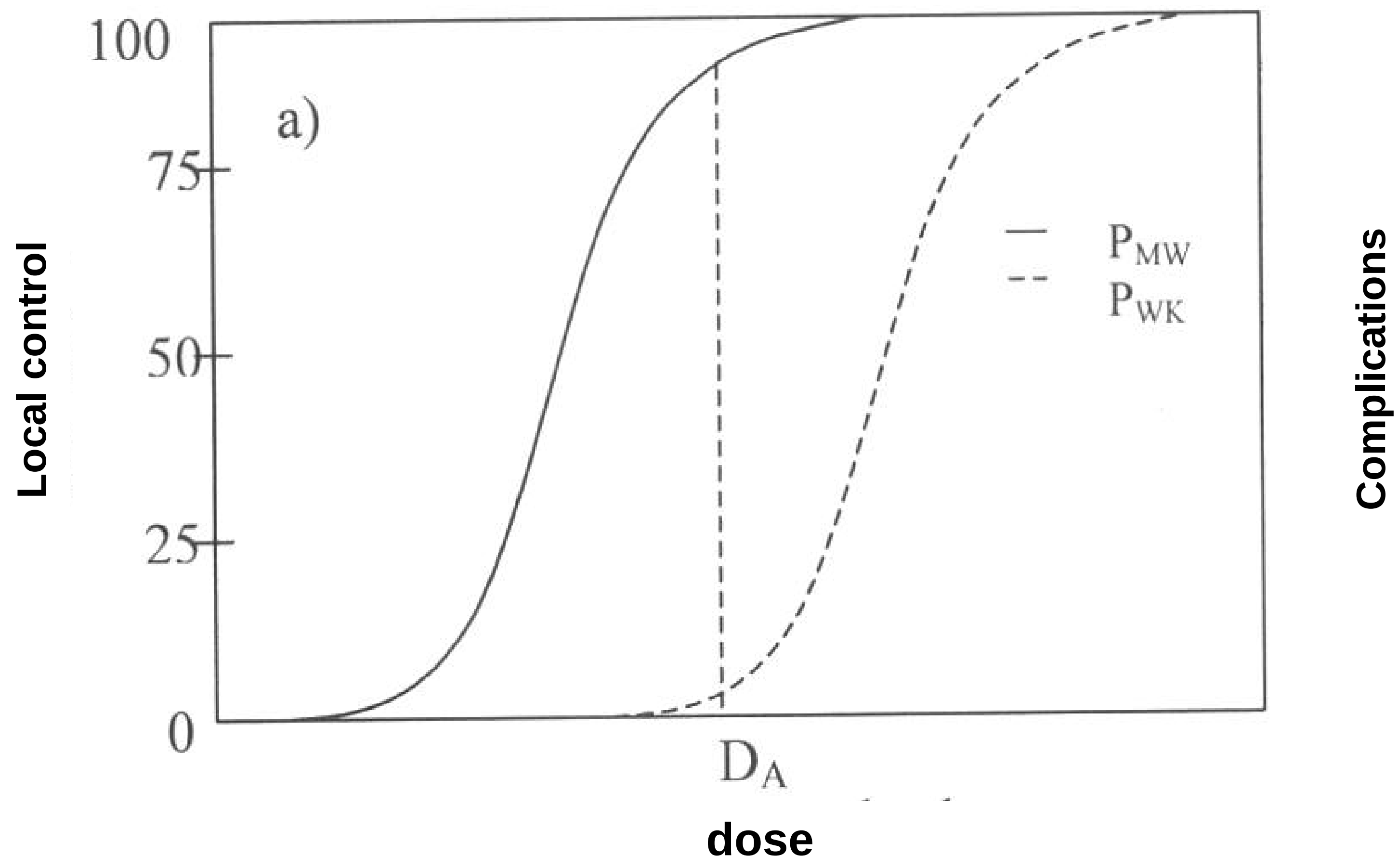
2. **Physics for hadron therapy**

    a) Accelerators
    b) Tools for Quality Assurance

3. **Proton therapy at IFJ PAN**



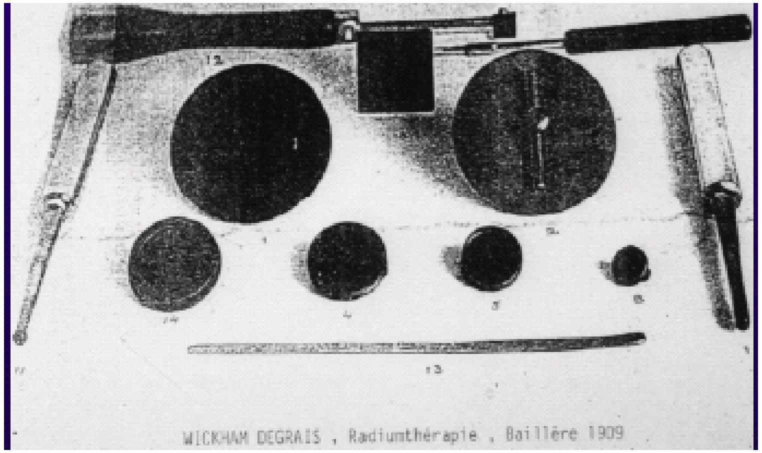
Principles of proton radiotherapy



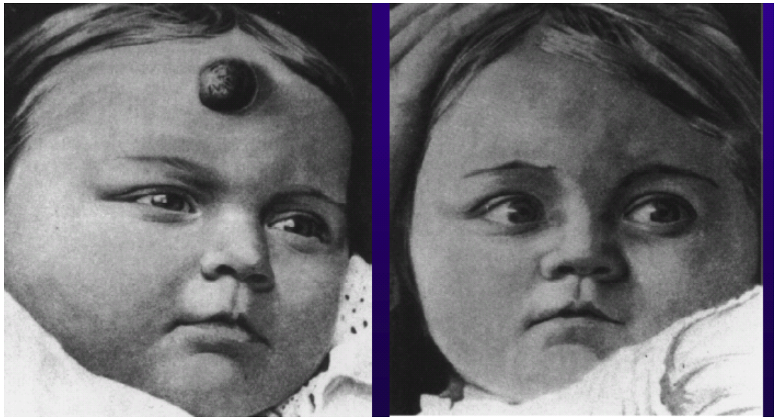
Required dose in the treated volume – minimal dose to healthy tissue

Progress in radiotherapy was always related to the improved dose distribution

Maria Skłodowska Curie

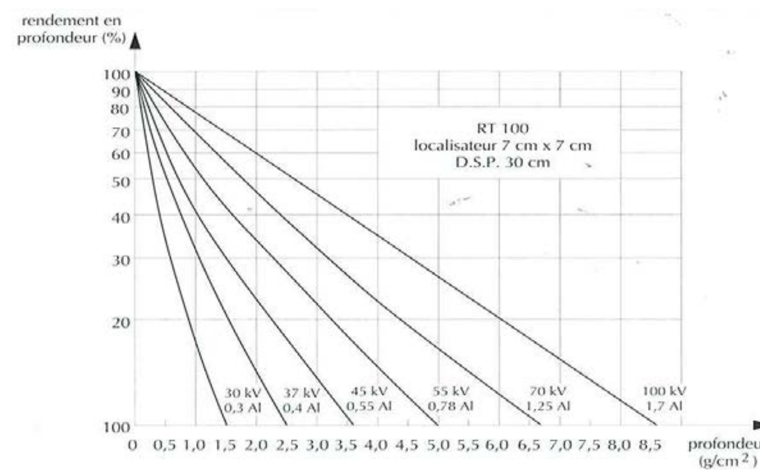


Surface radium applicator Ra-226 (1909)



Progress in radiotherapy was always related to the improved dose distribution

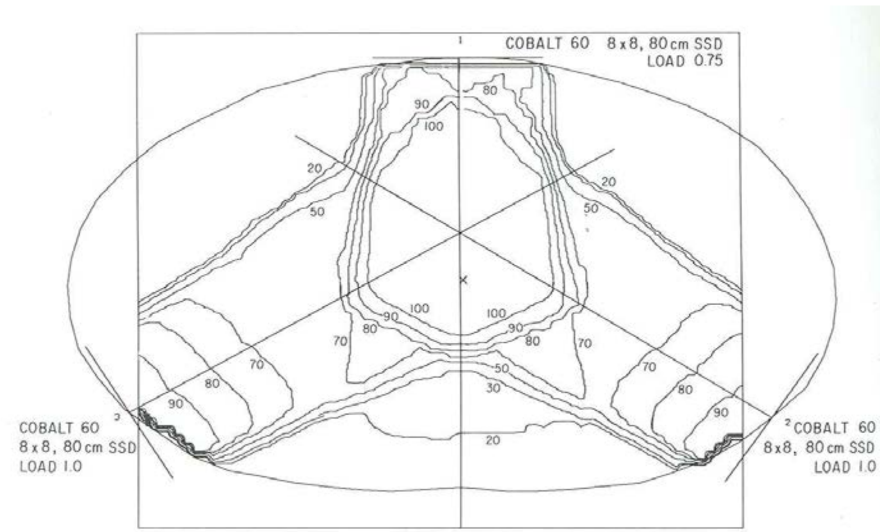
kV X-ray radiotherapy unit, 1930s, Pensylvania Univ.



Poor depth dose distribution
at kV X-rays

Progress in radiotherapy was always related to the improved dose distribution

1960s



Gamma radiation from Co-60 - the „cobalt bomb”

Hadron therapy

Neutron therapy

Ion therapy

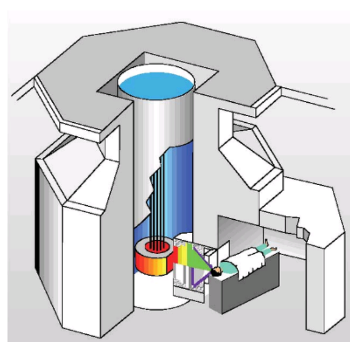
Fast neutrons

6-50 MeV

The advantage: radiobiology

Boron Neutron Capture Therapy BNCT

0.025- 1 eV

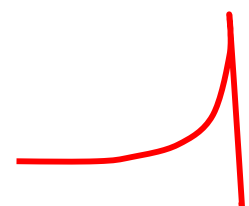


$^{10}B + n \rightarrow {}^{4}He + {}^{7}Li$

Local cell irradiation

Proton therapy

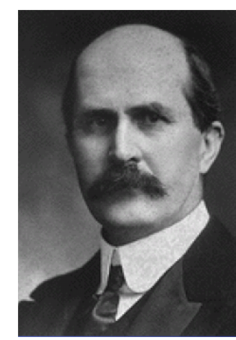
60-250 MeV



The advantage: dose distribution

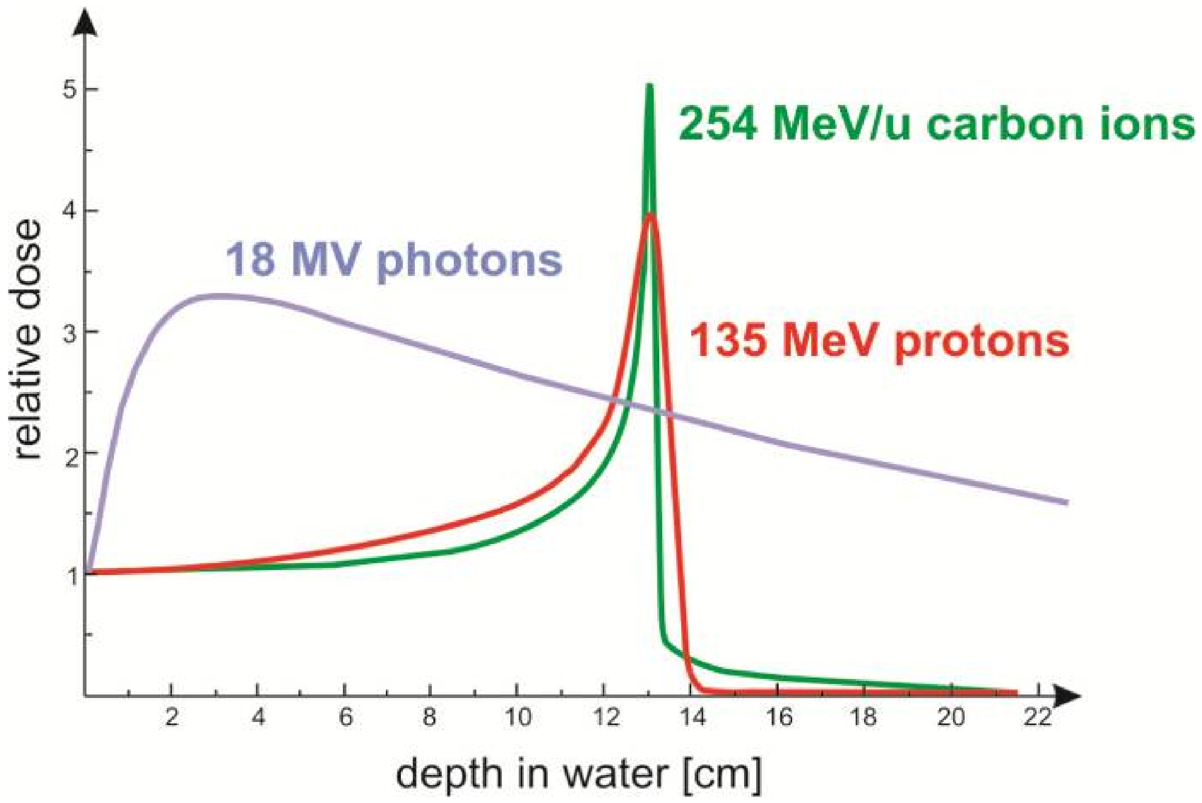
Carbon (He, O) ion therapy

250 - 400 MeV/amu



(William Henry) Bragg (1862 – 1942)

Progress in radiotherapy was always related to the improved dose distribution



Rober R. Wilson, 1946

Proton and ion beams therapy offer very good dose distrubtion

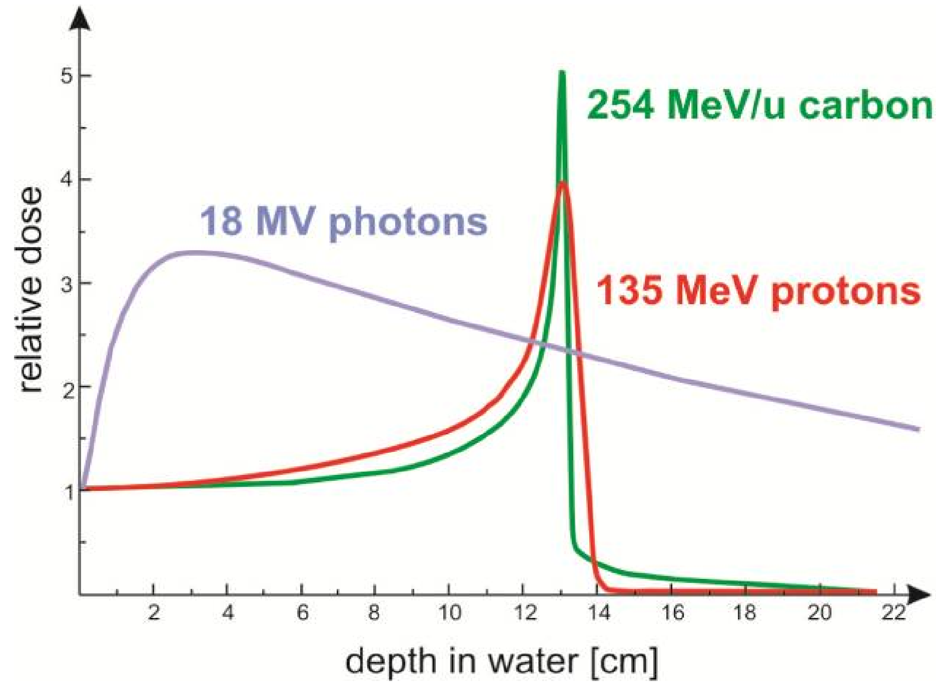
The rationale of hadron therapy

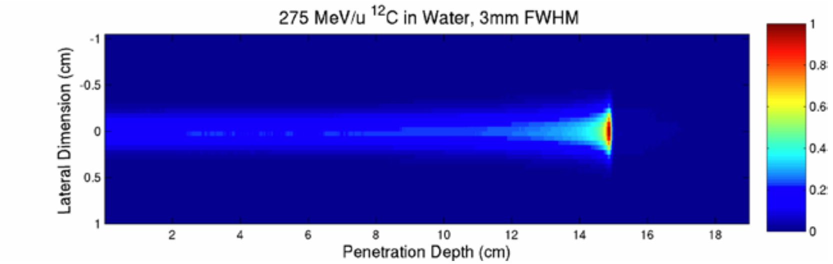
Conformal dose distribution results in saving healthy tissue

- **Dose distribution**

- Verification

- Radiobiology





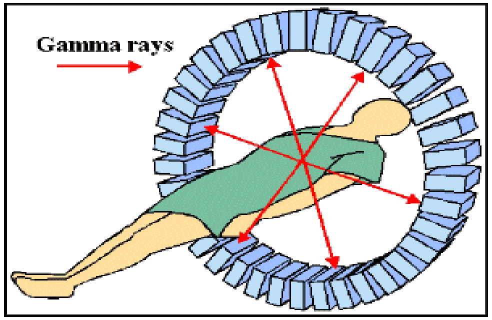
The rationale of hadron therapy

- Dose distribution

- **Verification**

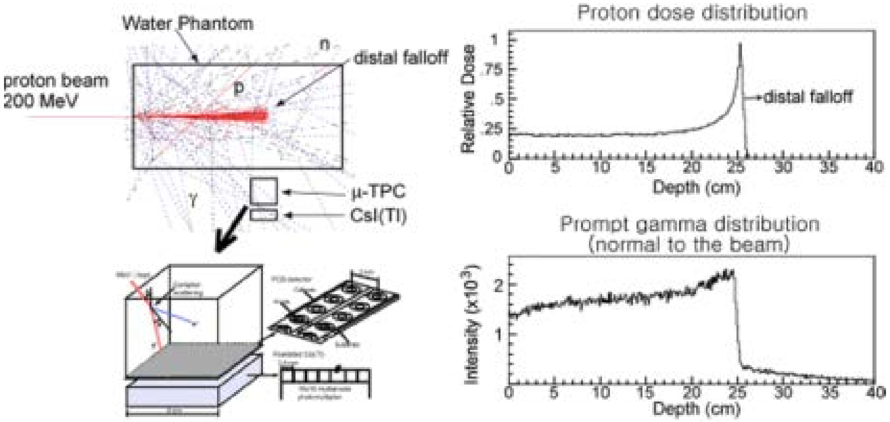
- Radiobiology

PET verification of dose distribution



Ion induced $\beta+$ isotopes allow for verification of dose distribution (K. Parodi, this conference)

Prompt gamma for Bragg peak verification



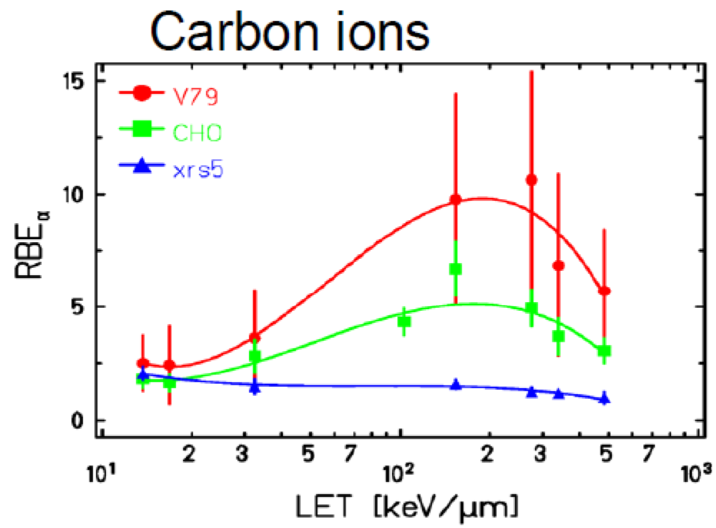
B. Kang, J. Kim, IEEE Nucl. Sci. 2009

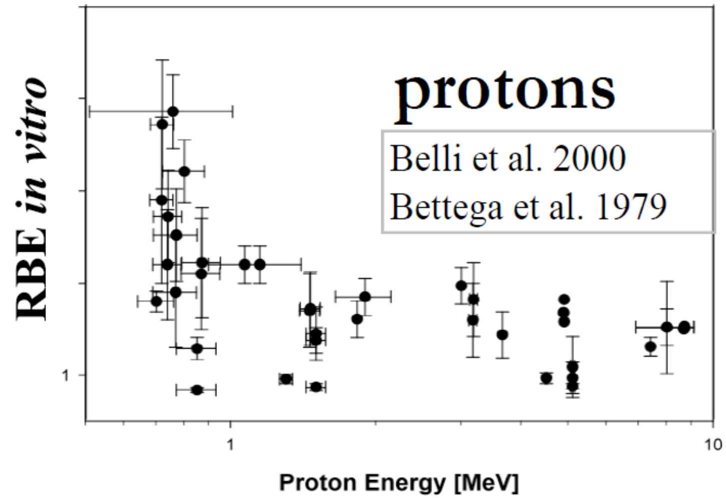
The rationale of hadron therapy

- Dose distribution

- Verification

- **Radiobiology**



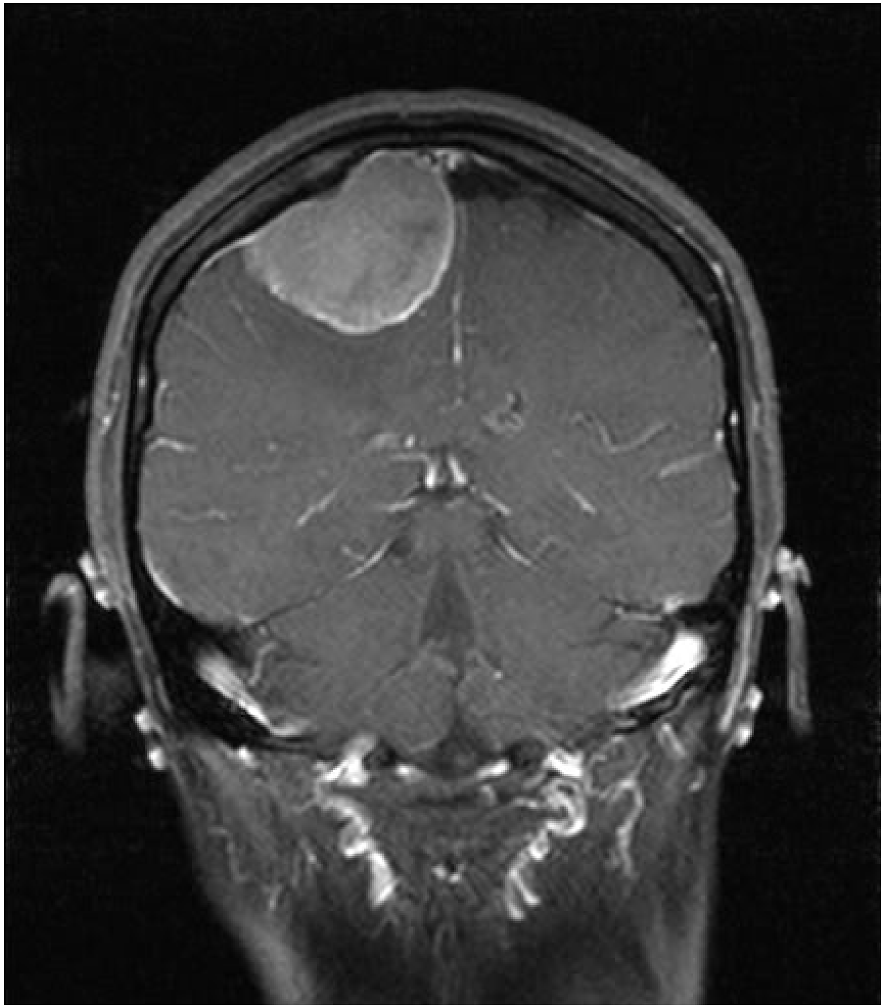


Clinical advantages of proton radiotherapy

- **Higher dose in the target volume**
- **-> higher probability of local control**

- **Limiting dose at Organ At Risk**
- **-> less complications**

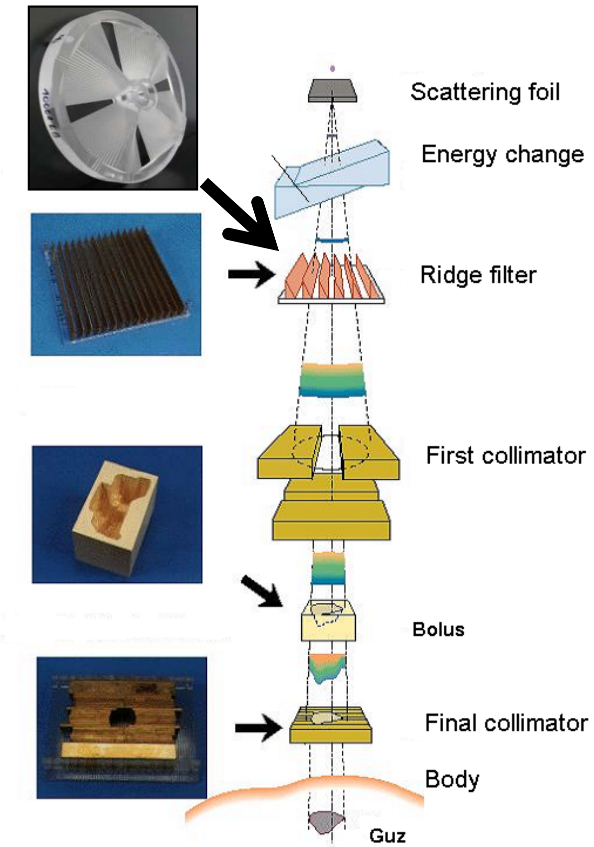
- **Less scattered radiation**
  -> lower probability of secondary cancers



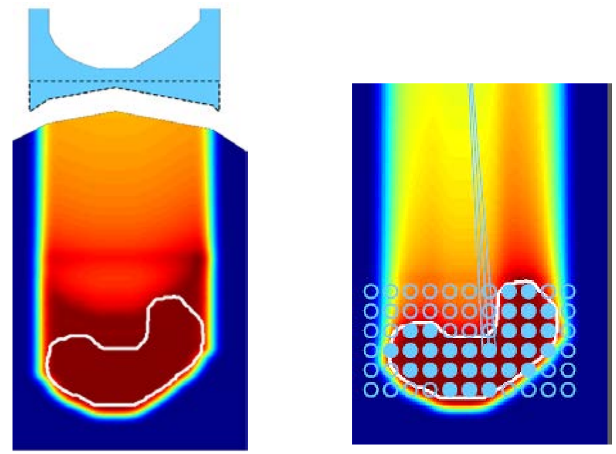
Progress in accelarators

Double Scattering versus Pencil Beam Scanning, PBS

Scattered beam



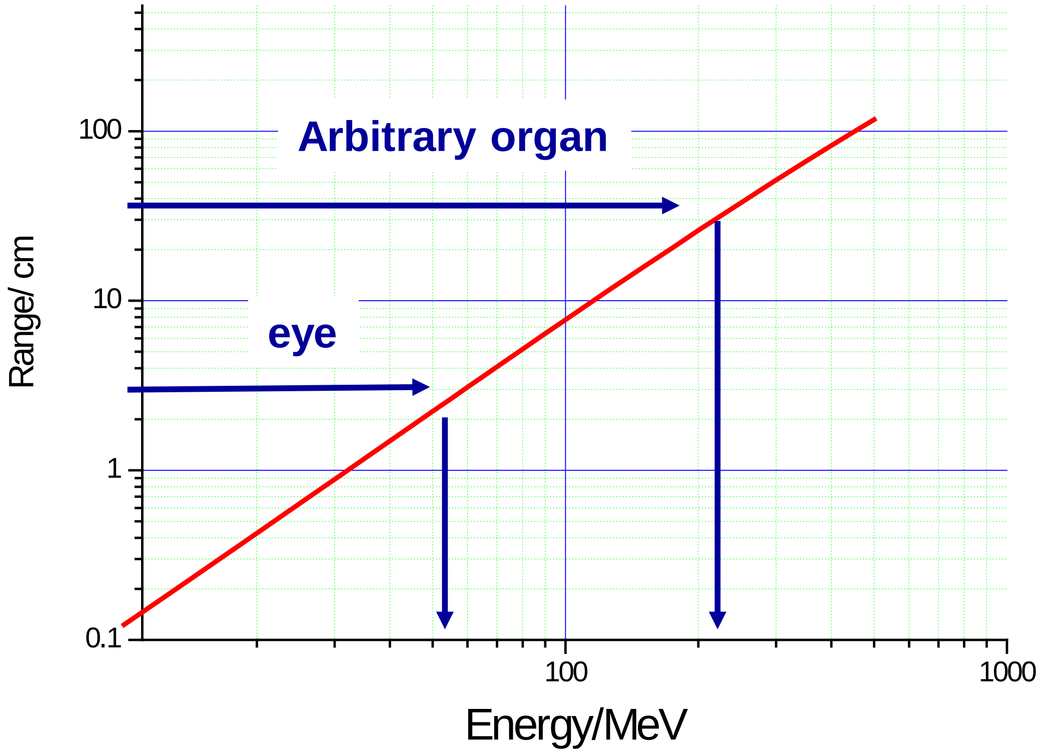
Scanning beam



Advantages of PBS

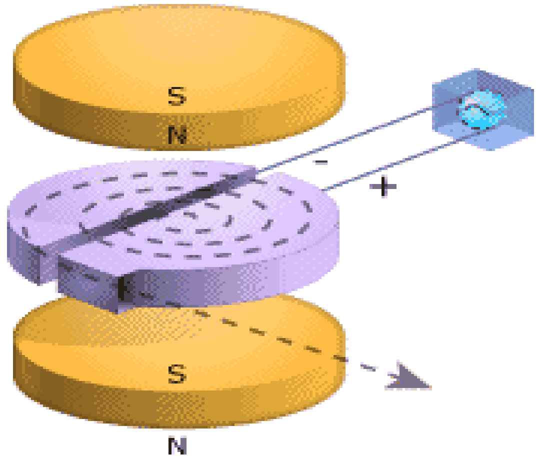
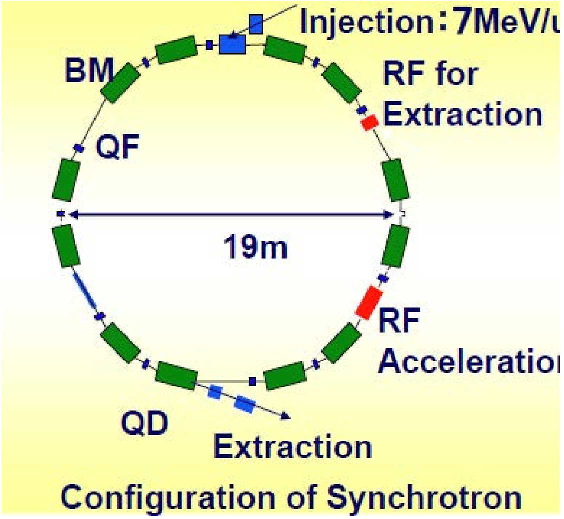
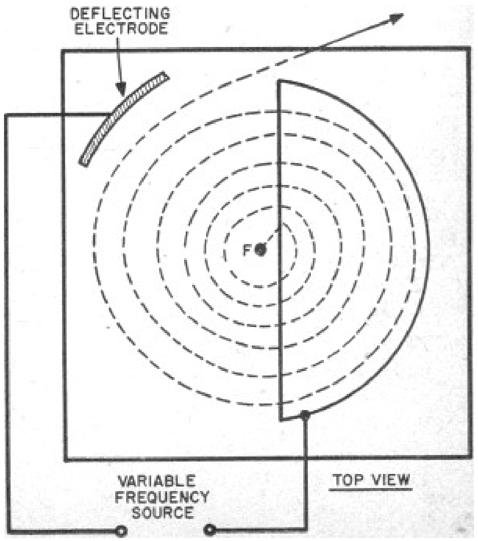
- **Proximal dose shaping**
- **Intensity Modulated Proton Therapy possible (patching)**
- **No collimator or compensator needed**
- **Reduced neutron dose**

Beam parameters required in proton radiotherapy



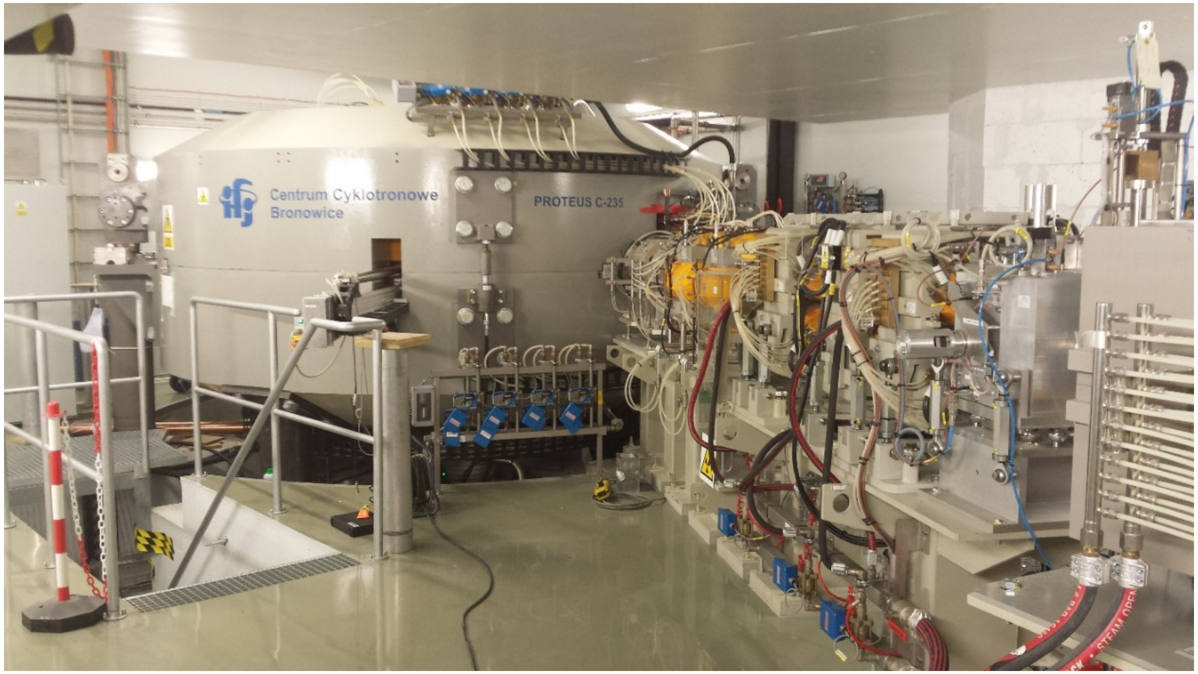
Energy: 70 MeV < E < 250 MeV -> RANGE….
Current: 1 nA < I < 1000 nA -> DOSE RATE….
Change of energy within about 1 s -> SCANNING ….
Fast (100 μs) switch on - switch off -> SCANNING…..

Types of accelerators applied in proton therapy

cyclotrons	synchrotrons	synchrocylotrons
		
B= const f = const d ~ 4-5 m P = 300- 500 kW	B= var f = var d ~ 20 m P = 150 - 200 kW	B= const f = var d ~ 1.5 - 2 m P = 50 kW

Dedicated medical accelarators

C-235 Proteus cyclotron



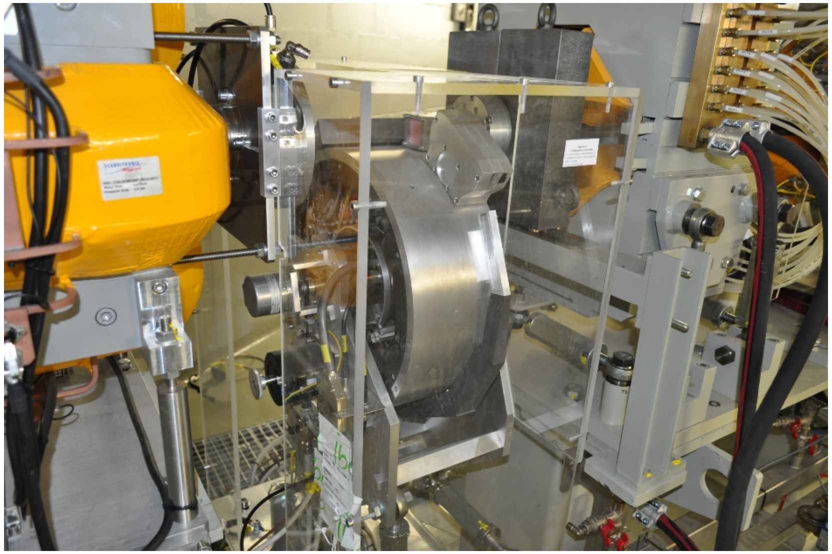
cyclotron:	**isochronic, 4-sectors, CW**
particles	**protons**
ion source:	**P.I.G with hot cathod**
proton energy:	**230 MeV (β = 0.596, γ = 1.245),**
energy dispersion:	**$\Delta E/E$ < 0.7%**
beam intensity:	**600 nA (4 x 10^{12} p/s) – 0.1 nA (6 x 10^{8} p/s)**

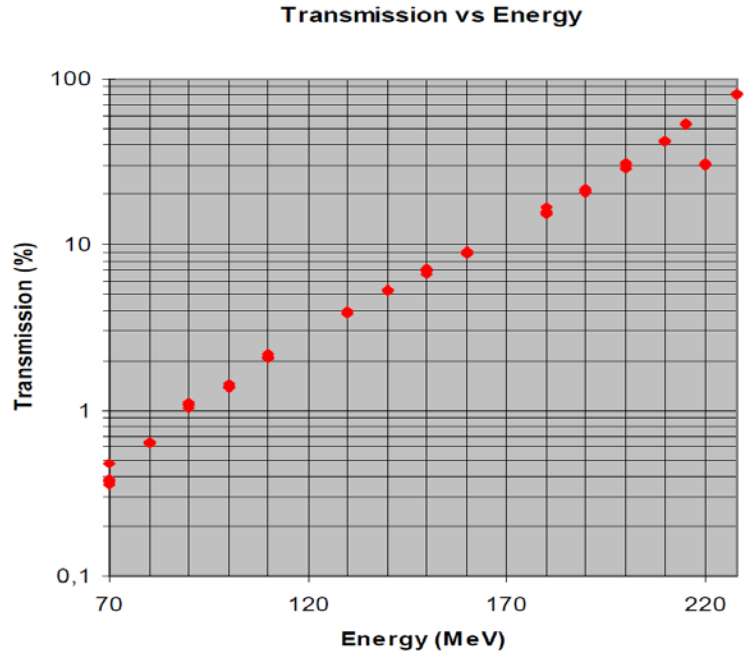
diameter	**434 cm**
height:	**210 cm**
Weight:	**240 T**

Ion Beam Applications S.A. (IBA), Louvain-la-Neuve, Belgium

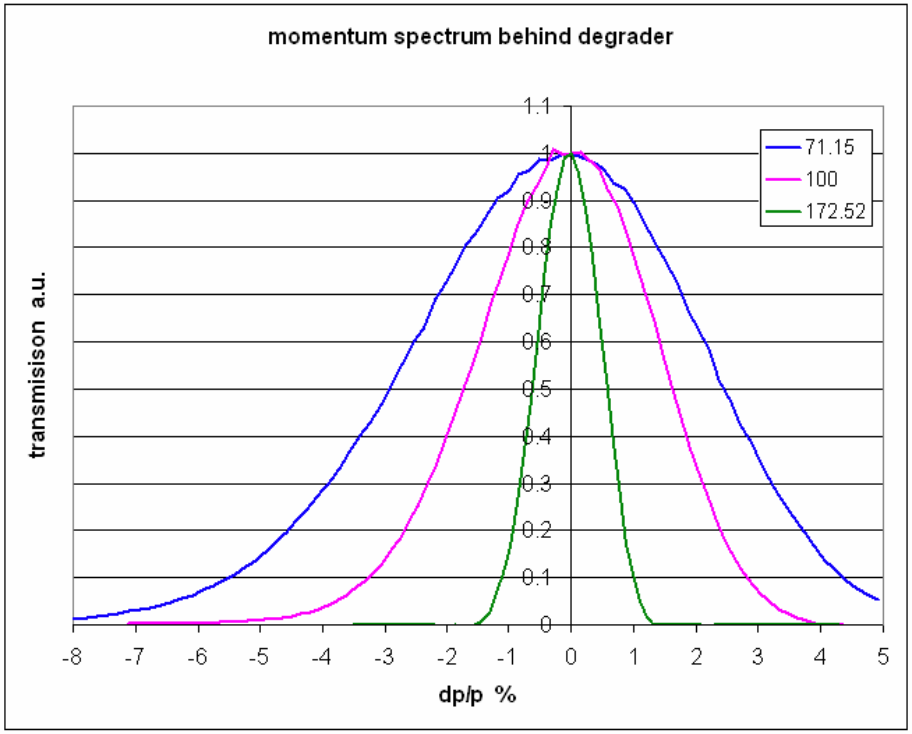
For cyclotrons beam energy degradation needed ☹

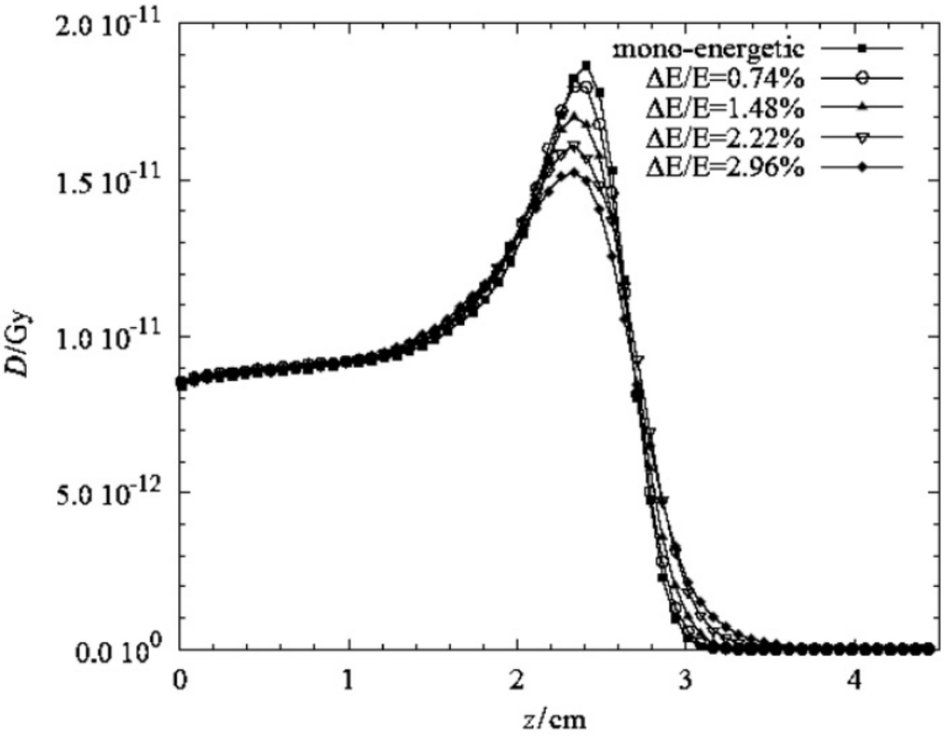
- **Proton current 230 MeV minimum 500 nA**
- **Transmission from 230 MeV do 70MeV only 0,4% (for Be)**
- **We need 70 MeV, 2 nA, distal fall-off < 2 mm**





Scattering of initial proton beam



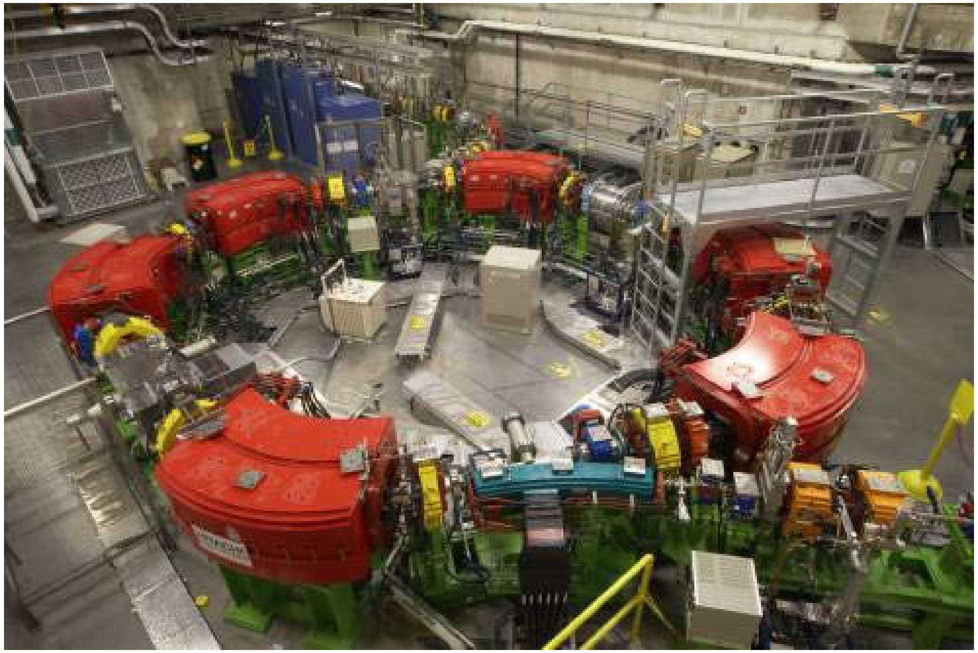


source: PSI Villigen

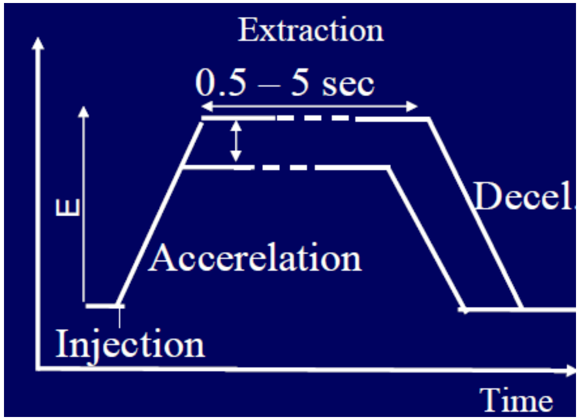
broader energy distribution –> larger distall fall off

Dedicated medical accelarators

Hitachi Synchrotron – MD Anderson

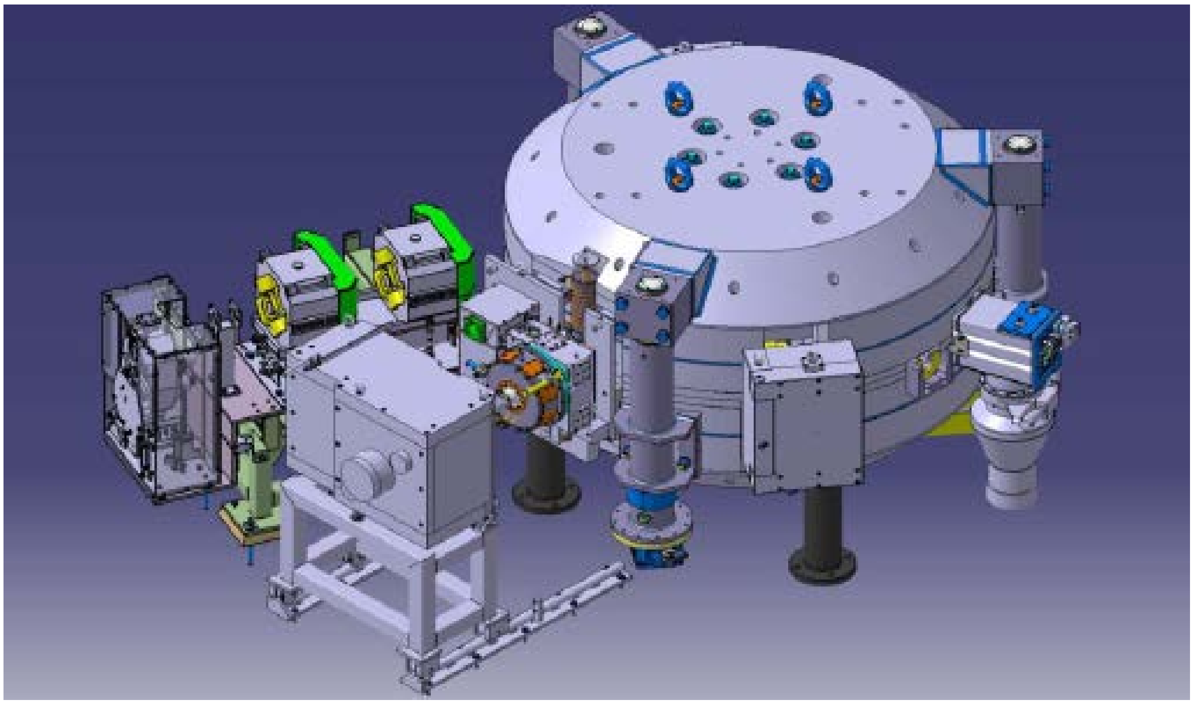


Energy: 70 -250 MeV
Pulse time: 0.5 – 5 s
No energy degradation needed!
No activation of elements
Larger vault needed



Dedicated medical accelarators

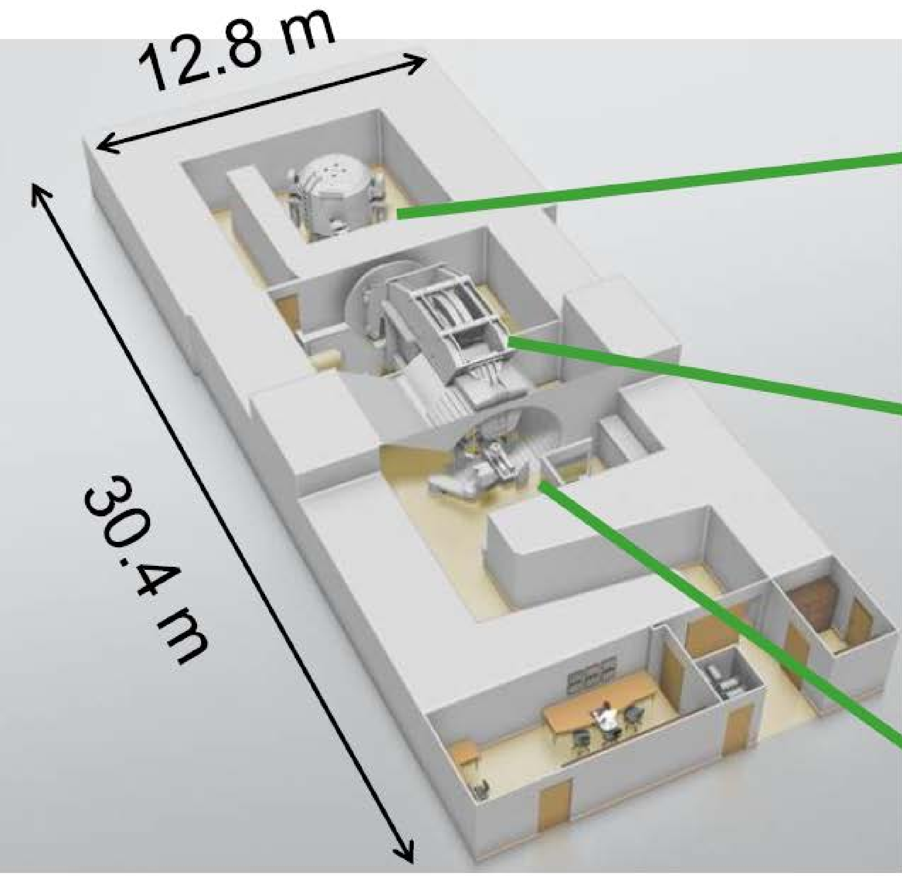
S2C2 synchrocyclotron (IBA)

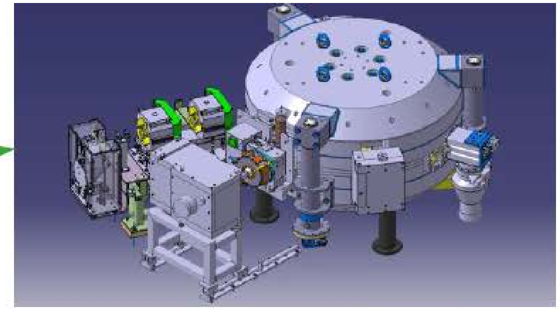


Maximum Energy	230/250 MeV
Size	
yoke/pole radius	1.25 m/0.50 m
weight	50 tons
Coil	NbTi - wire in channel
ramp up rate / time	2-3A/min / 4 hours
windings/coil	3145
stored energy	12 MJ
Magnetic field	
central/extraction	5.7 T/5.0 T
Cryo cooling	conductive
	4 cryocoolers 1.5 W
initial cooldown	12 days
recovery after quench	less than 1 day
Beam pulse	
rate/length	1000 Hz/7 μsec
RF system	self-oscillating
frequency	93-63 MHz
voltage	10 kV

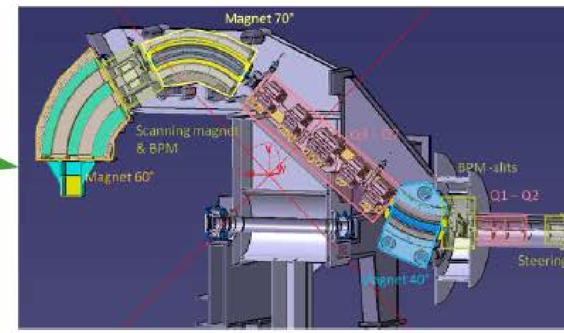
IBA S2C2 synchrocylotron for compact proton therapy

Proteus-One





Synchrocyclotron with superconducting coil: S2C2



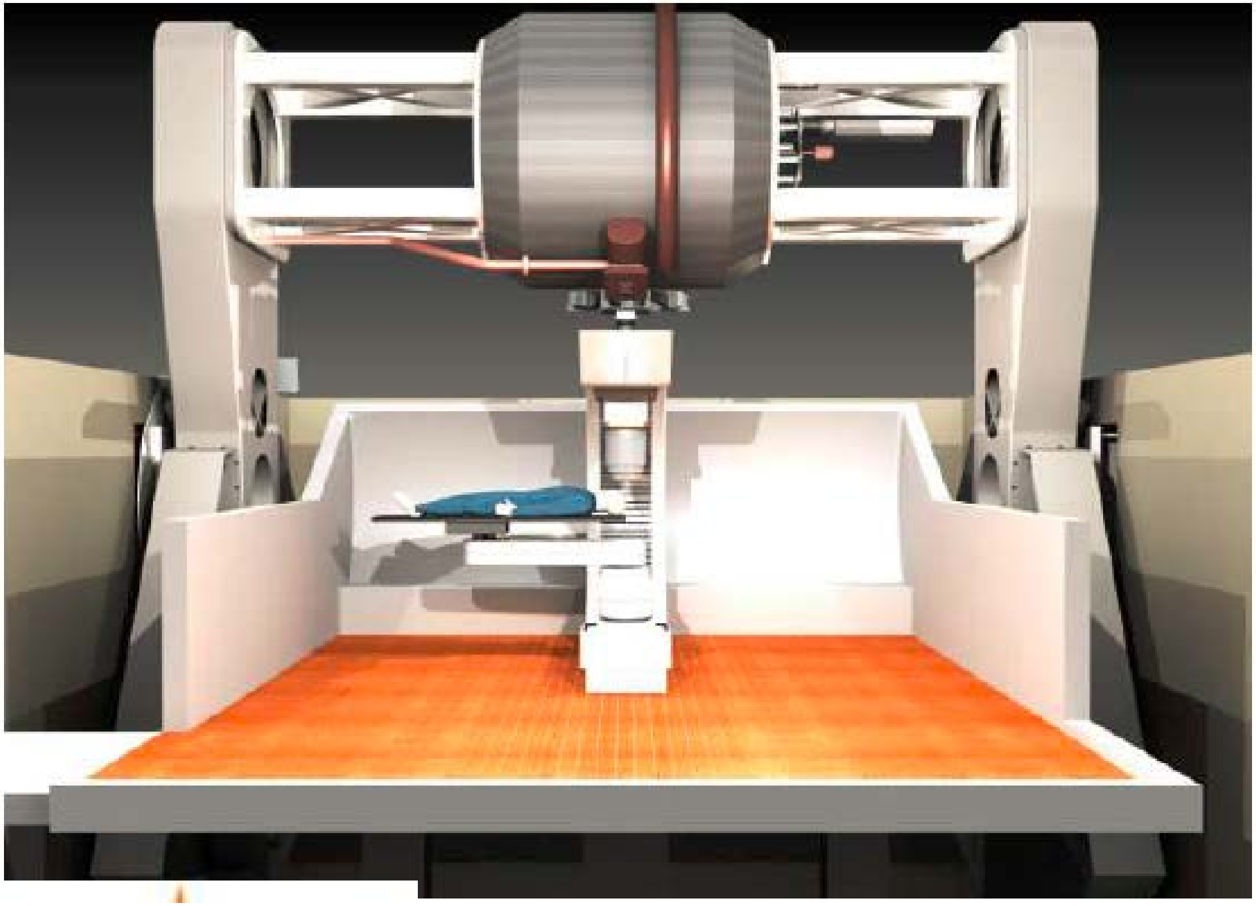
New Compact Gantry for pencil beam scanning

Patient treatment room

iba

Protect, Enhance and Save Lives - 3 -

MEVION the smallest synchrocylotron for proton therapy



http://www.asgsuperconductors.com

Cyclotron rotates around tha patient!

First center: S. Lee Kling Proton Therapy Center at the Siteman Cancer Center, Missouri, USA

High magnetic field based on superconducting alloy
9.4 T!!!

MEVION medical systems

Example 3: Still River/ Mevion
Dedicated foundation by former MGH people; basic cyclotron design by MIT, Boston

Harvard (700 tons)
Synchrocyclotron

IBA/Sumitomo (220 tons)
Isochronous Cyclotron

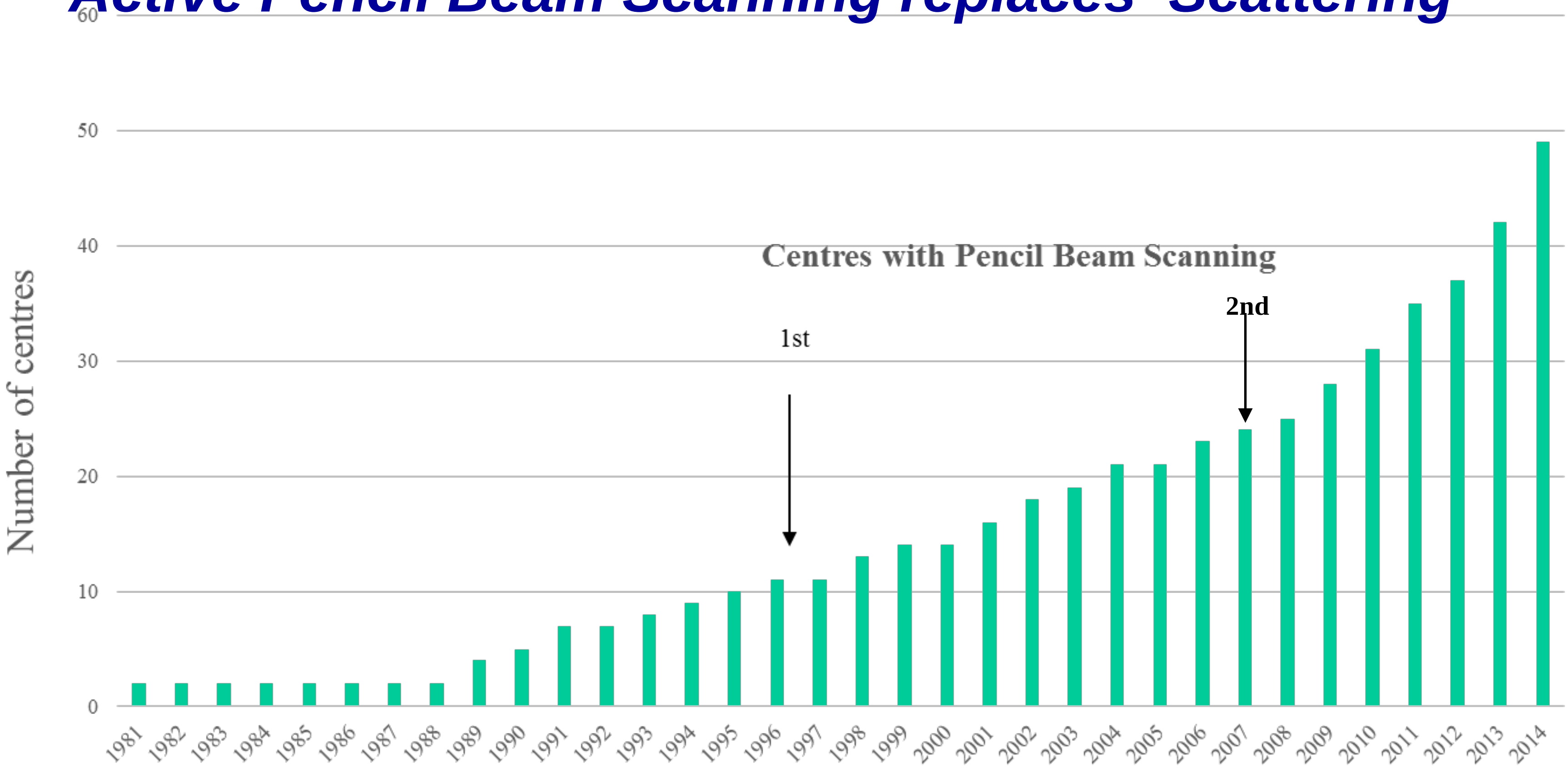
Varian/Accel (90 tons)
Isochronous Cyclotron

IBA (50 tons)
Synchrocyclotron

Mevion Medical Systems (<20 tons)
Synchrocyclotron mounted on Gantry

From presentation of Dr. Detlef Krischel; ICABU, DAEJEON, Nov 11, 2013

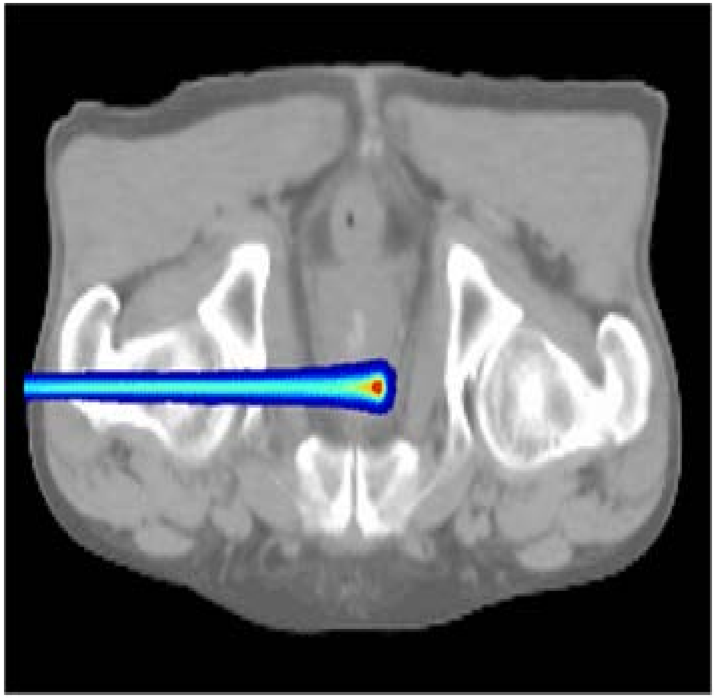
Active Pencil Beam Scanning replaces Scattering

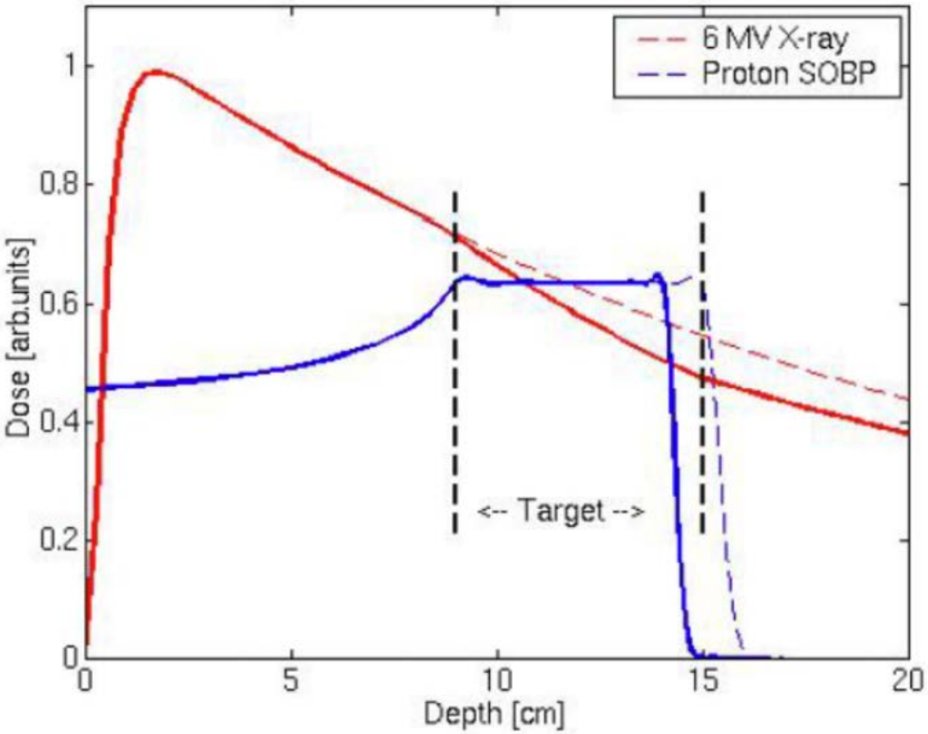


- **In 2008 only two proton centers in the world treated with PBS**
- **No Treatment Planning Systems, TPS, available**
- **No specialized QA and dosimetry available**
- **Intensity Modulated Proton Radiotherapy (IMPT) known only in theory**

Tools and Methods for Quality Assurance

Disadvantages of proton therapy -
the range uncertainties



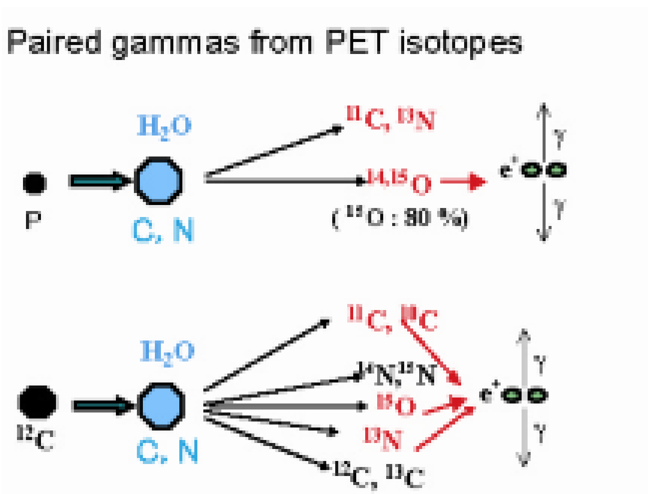


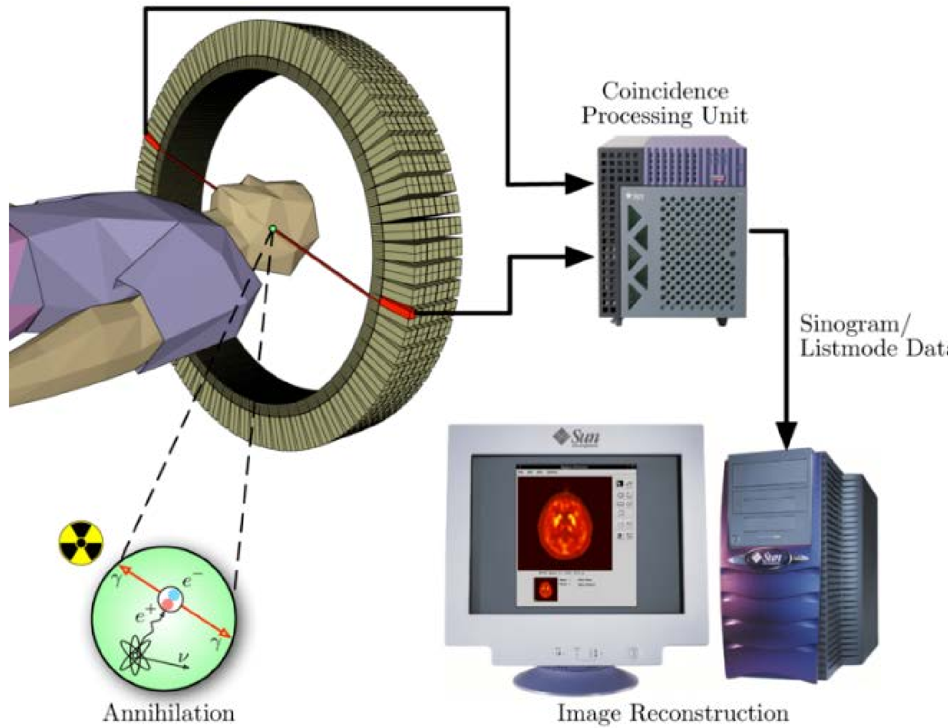
Non- homogenous tissue leads to uncertainty of range.

Stopping power in tissue dependent on proton energy.

Uncertainties of range

verification using induced β^+ radioactivity



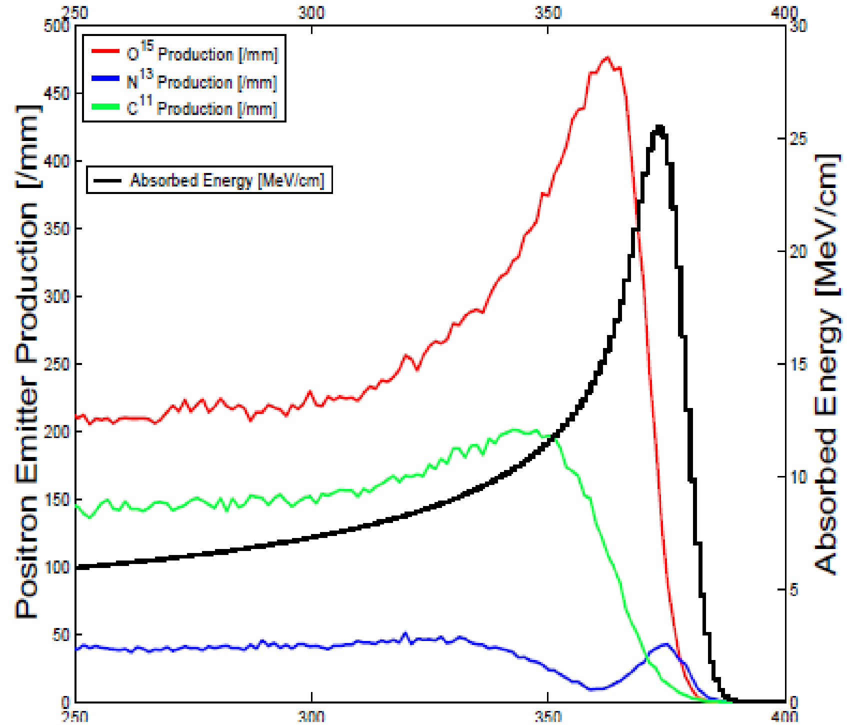


PET tomograph is used to measure proton induced activity in tissue

Uncertainties of range

verification using proton induced β^+ radioactivity

Cross sections for induction of β+ isotopes by protons in tissue do not overlap with the energy deposition (Bragg peak)



Therefore depth distribution of induced activity does not mimic the Bragg peak. The distal edge of the Bragg peak can be assessed.

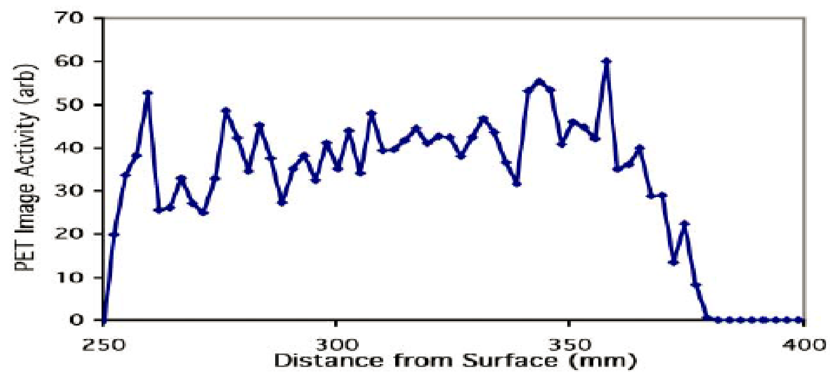
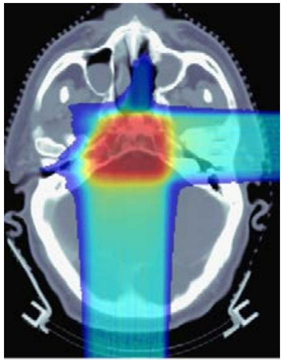


Fig.6 Depth distribution of induced activity as determined from PET image.

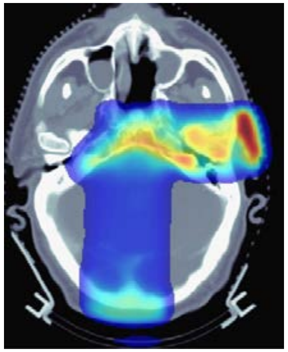
J.J.Beebe-Wang, 2002

Uncertainties of range

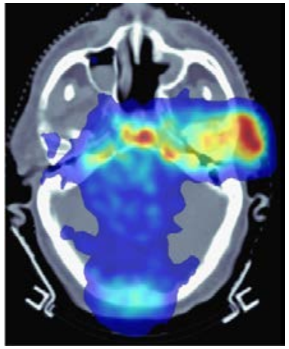
First installation in GSI Darmstadt for C-12



-Calculated dose distribution

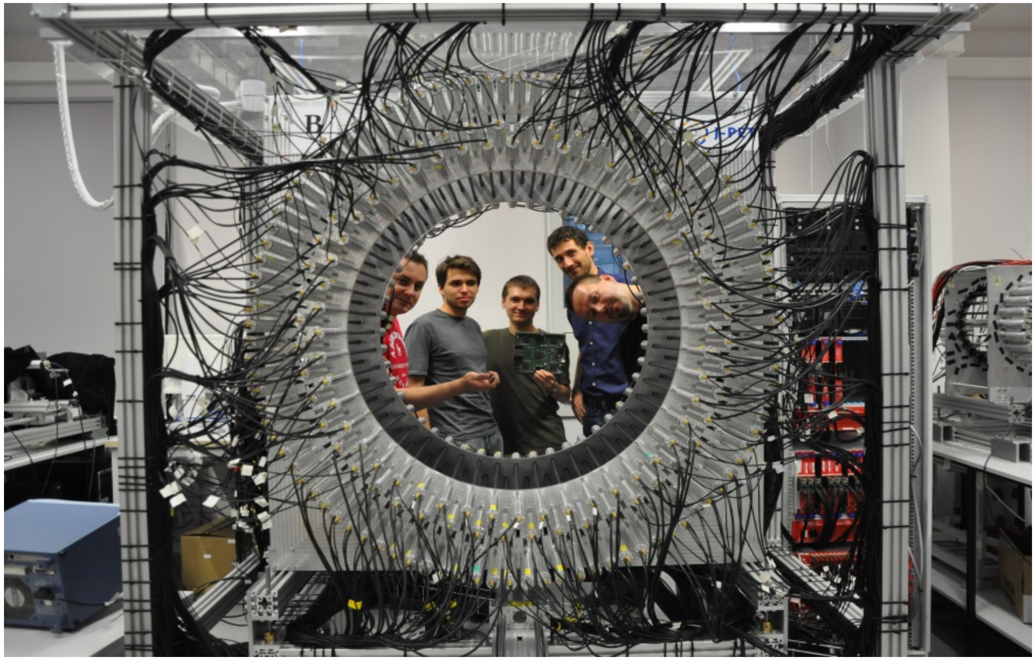


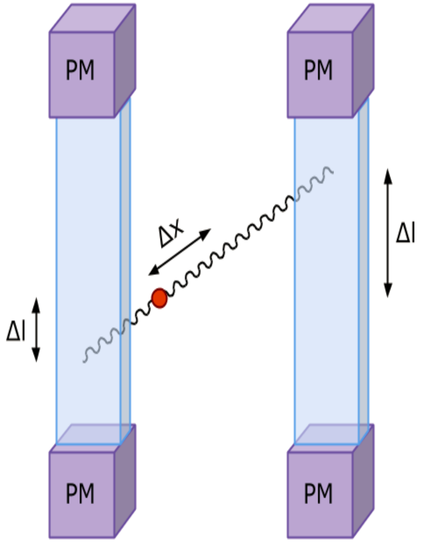
-Calculated activity distribution



-Measured activity distribution

Jagiellonian PET – based on TOF



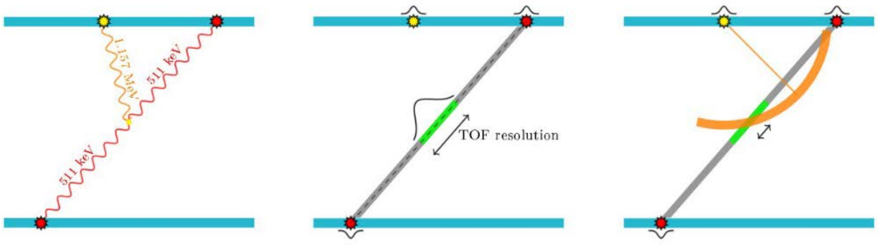


crystals → plastics

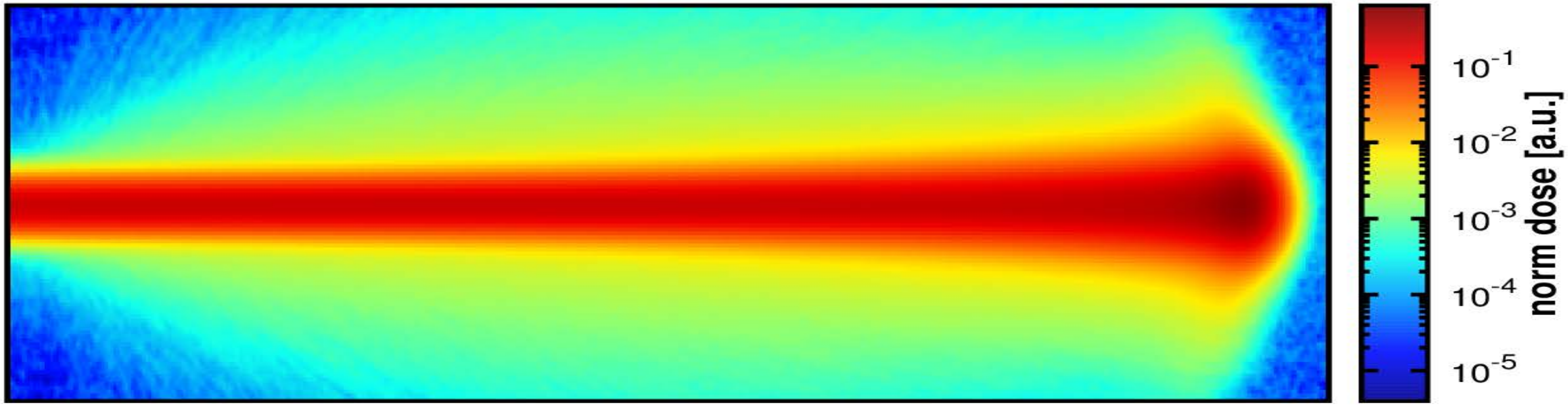
AFOV: 17 cm → 50 cm
TOF: 520 ps → 260 ps

P. Moskal et al., NIM A 764 (2014) 317.
P. Moskal et al., NIM A 775 (2015) 54.
L. Raczynski et al., NIM A 764 (2014) 186.
L. Raczynski et al., NIMA 786 (2015) 105.
16 International Patent Applications

3γ multi-tracer tomography

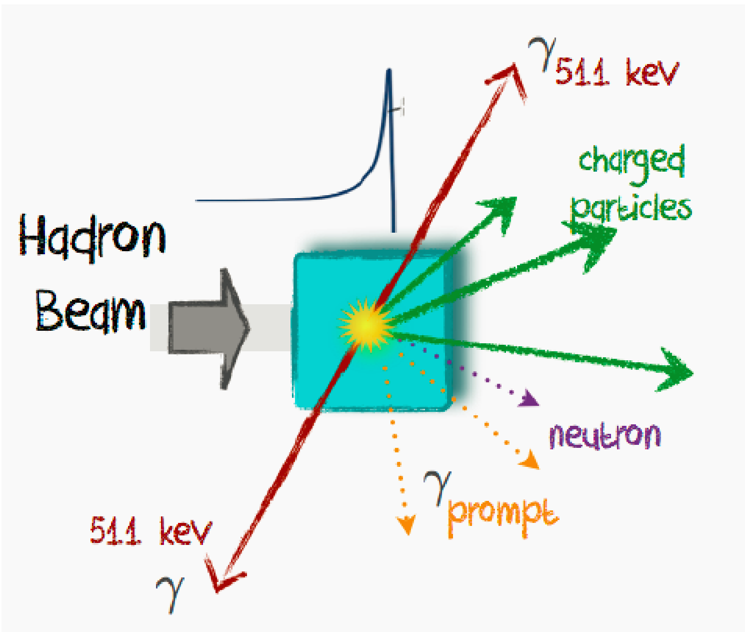


Scattering of proton beam

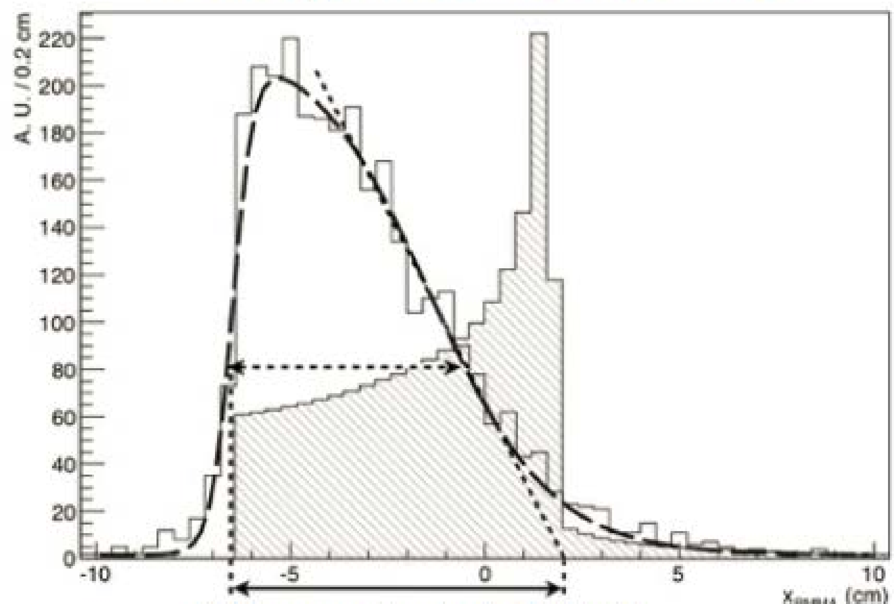


M. Kłodowska, PTFM 2015

Charged Secondary Tracker



charged secondaries

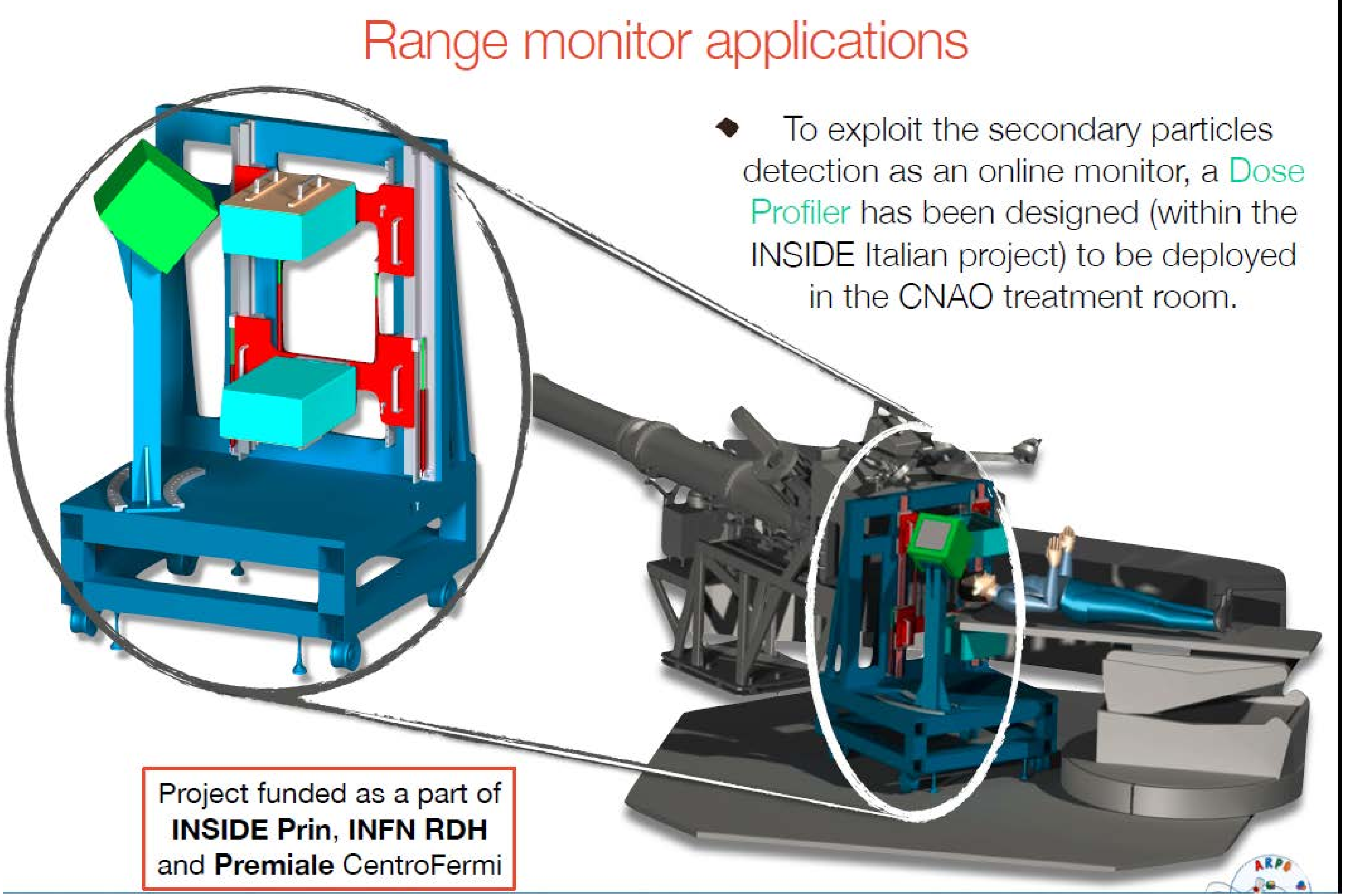


[Piersanti et al. 2014]

INSIDE collaboration

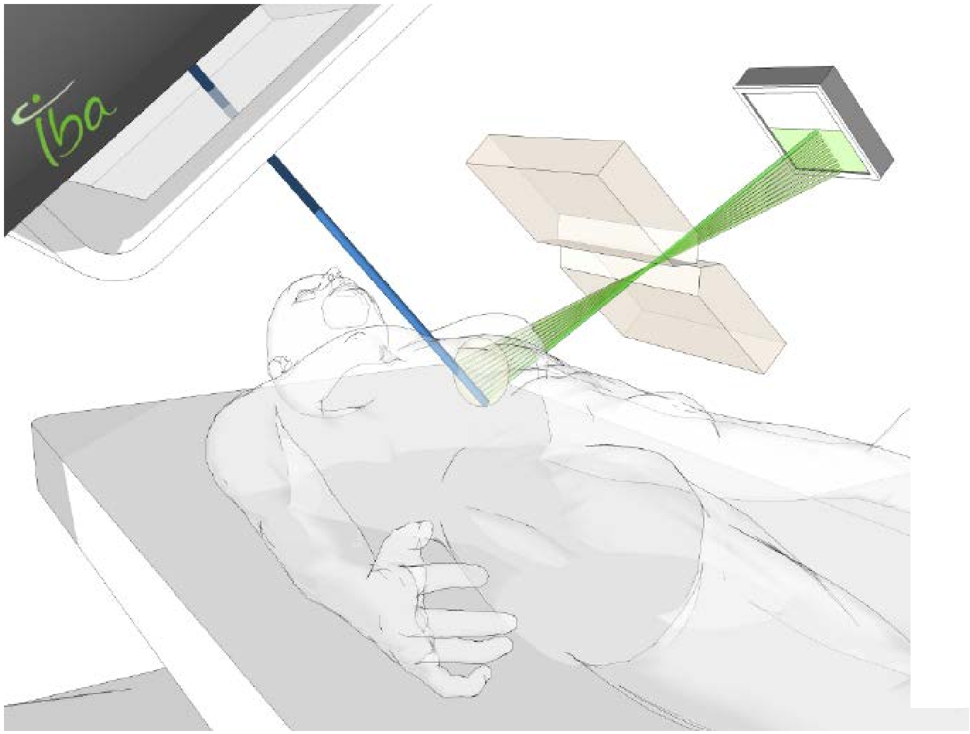
G.Battistoni[i], F. Bellini[a,b], F. Collamati[a,b], E. De Lucia[c], R. Faccini[a,b], F. Ferroni[a,b], M. Marafini[a,e], I. Mattei[i], S. Morganti[b], S. Muraro[i], R. Paramatti[b], V. Patera[b,d,e], D. Pinci[b], L. Piersanti[c,d], *A. Rucinski[b,d], A. Russomando[a,b,f], A. Sarti[c,d], A. Sciubba[b,d], E. Solfaroli Camillocci[f], M. Toppi[c], G. Traini[a,b], C. Voena[a,b]

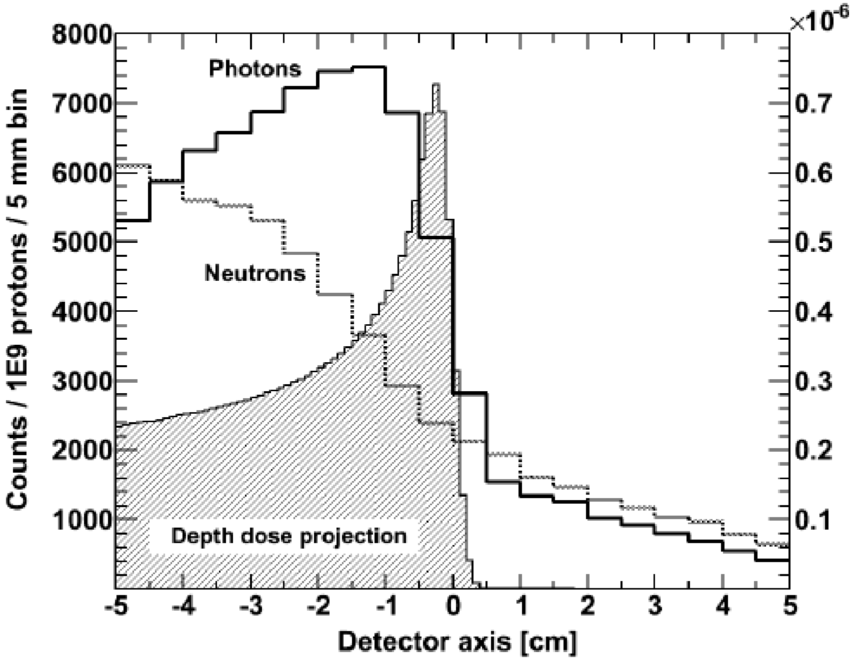
Charged Secondary Tracker



Court. A. Rucinski

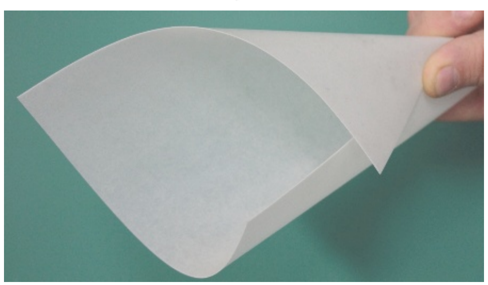
Slit camera to determine position of the Bragg peak





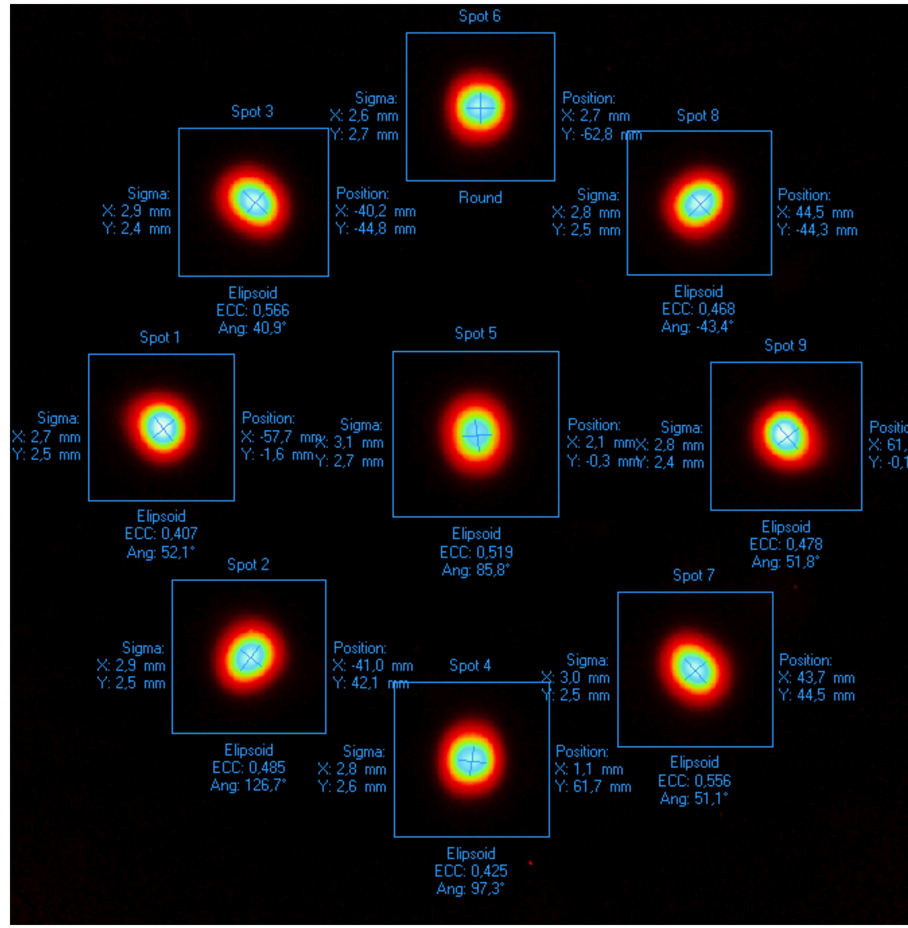
J. Smeets, 2012, thesis

Two dimensional thermoluminescence dosimetry (2D TLD)



TLD reader and foil developed at IFJ PAN J. Gajewski, L. Czopyk, M. Kłosowski

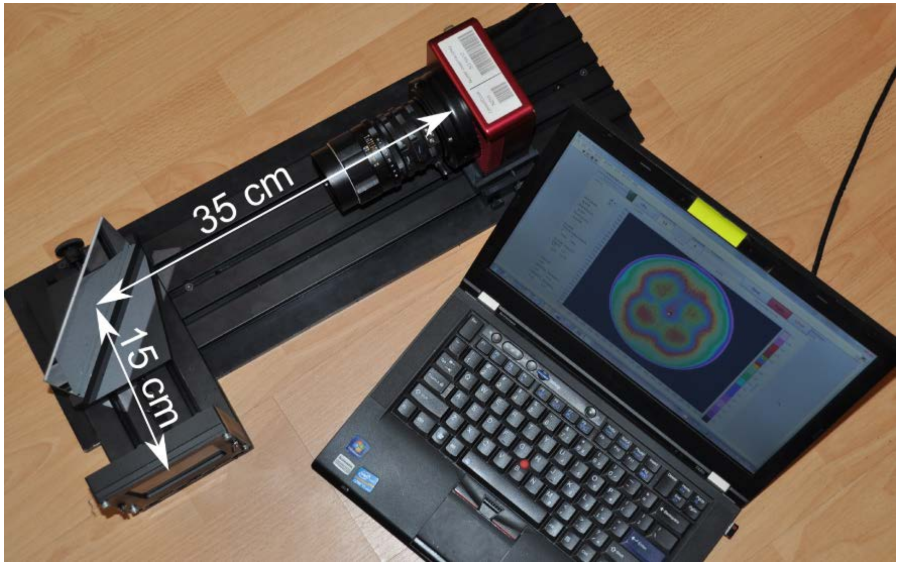
Jan Gajewski, IFJ PAN



Variation of spot shape with regard to gantry position

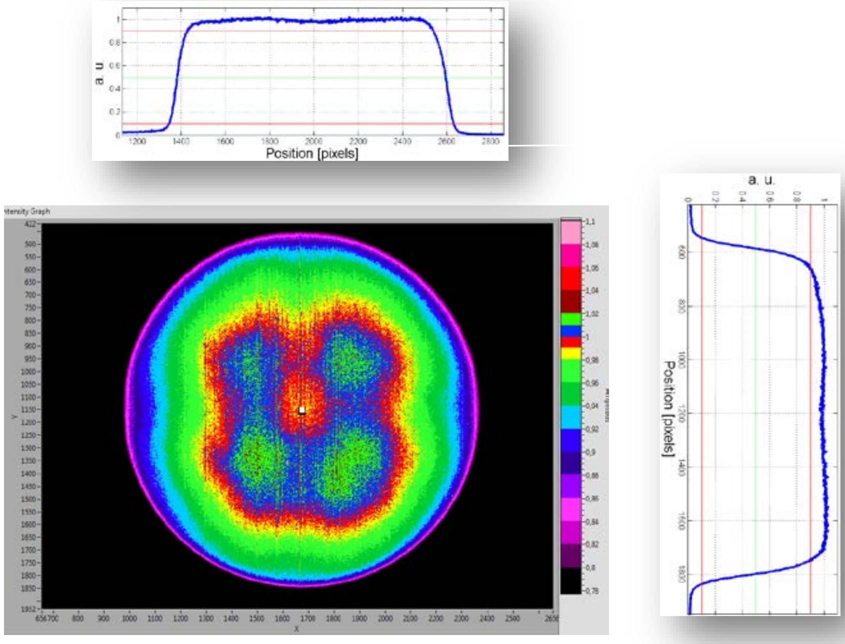
ProBImS for QA of beam profiles at the eye PT

Scintillator + CCD camera + software



Effective resolution 0.04 mm

Developed at IFJ PAN by: M. Rydygier J. Swakon



Profile of the 60 MeV proton beam from AIC-144 cyclotron

Proton therapy in Kraków

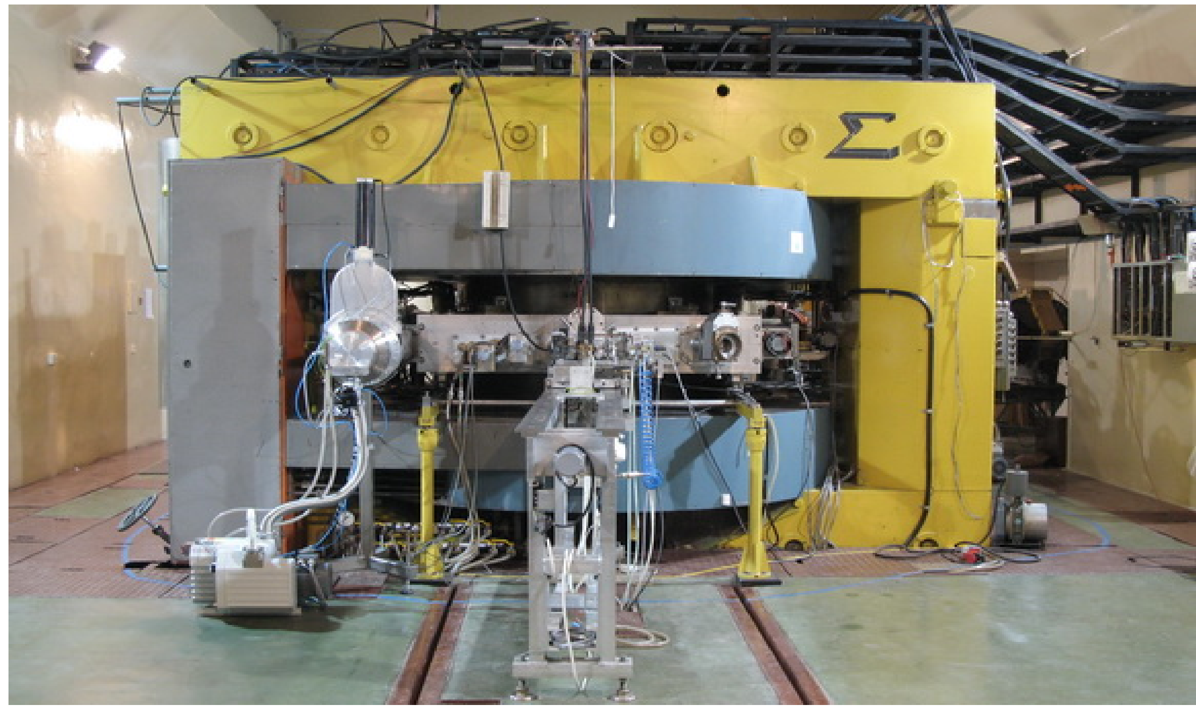
Cyclotrons at IFJ PAN Krakow

- first cyclotron in Poland developed by IFJ , 48 cm (1955)

- classical cyclotron U-120 (opened 22.11.1958, stopped 1994)

-**cyclotron isochronic AIC-144 (from 80's) 60 MeV protons**

- **Proteus C-230 (Ion Beam Applications, IBA)**



AIC-144 60 MeV proton cyclotron developed at IFJ PAN in 1995

60 MeV protons for eye therapy

IFJ PAN eye treatment room at AIC-144

Therapy room developed at IFJ 2006-2009 in collaboration with Helmholtz Centre, Berlin

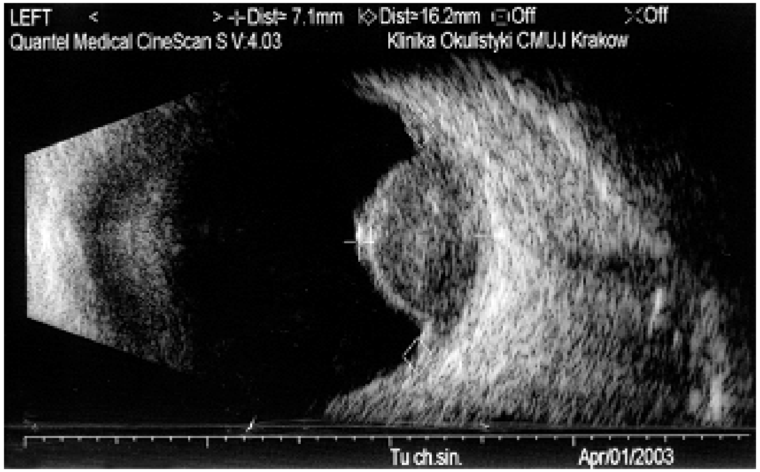
Eye melanoma

Eye melanoma:
-malignous cancer,
-growing inside the eye-ball
-mainly in white population,
-250 cases/year in Poland

Proton radiotherapy of eye - the most successful cancer treatment – survival > 90%

In Europe 7 centers
- **Berlin, HMI, D**
- **Catania, INFN, I**
- **Orsay, Inst. Curie, F**
- **Nice, F**
- **Claterbridge, UK**
- **PSI Villigen, CH**
- **IFJ PAN Kraków, PL**

Eye melanoma cancer



USG of eye cancer

Regular patient treatment

- **The first patient treated at IFJ PAN in February 2011**
- **From April 2013 the eye proton therapy financed by the National Health System**
- **110 patients till now**

Proton therapy is booming in Europe

● **Operational: 9 centres**

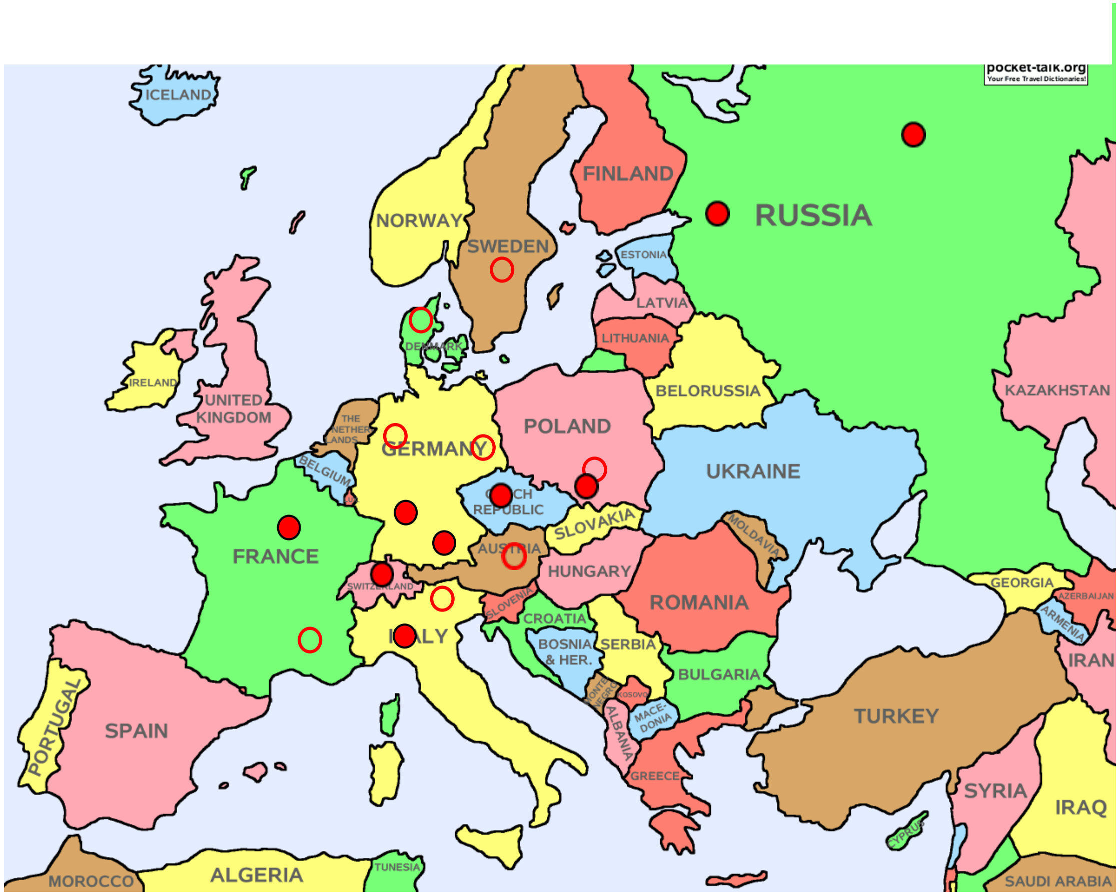
1. **DKFZ Heidelberg**
2. **Dresden (2014)**
3. **Essen (2014)**
4. **Munchen**
5. **Orsay**
6. **Pavia (2013)**
7. **PSI Villigen**
8. **PTC Prague (2013)**
9. **Trento (2014)**

○ **In tests: 4 centers**

1. **Krakow (2015)**
2. **Nice (2016)**
3. **Uppsala (2015)**
4. **Wiener Neustadt (2017)**

Contracts signed:

- **Aarhus (DK), 2018**
- **Archade, Caen (F), 2018**
- **Delft (2017)**
- **Groningen (NL)**



● **In operation** ○ **In construction**

Tenders & Planned:

- **UK (London, Manchester, Oxford)**
- **Maastricht (NL) – 2019**
- **Amsterdam (2019)**
- **Belgium – 2 centers**
- **Poznań, Warsaw**

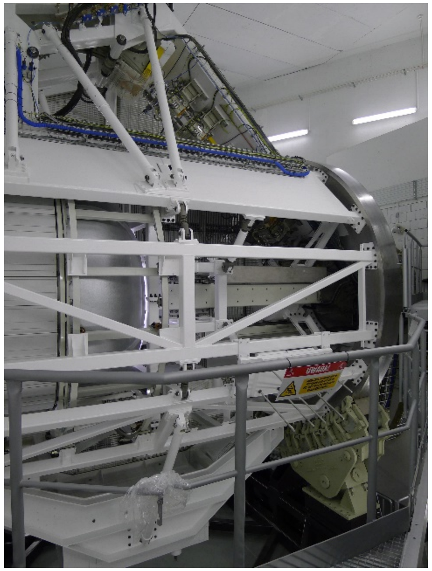
Time schedule of the NCRH-CCB and CCB- Gantry projects

The CCB project

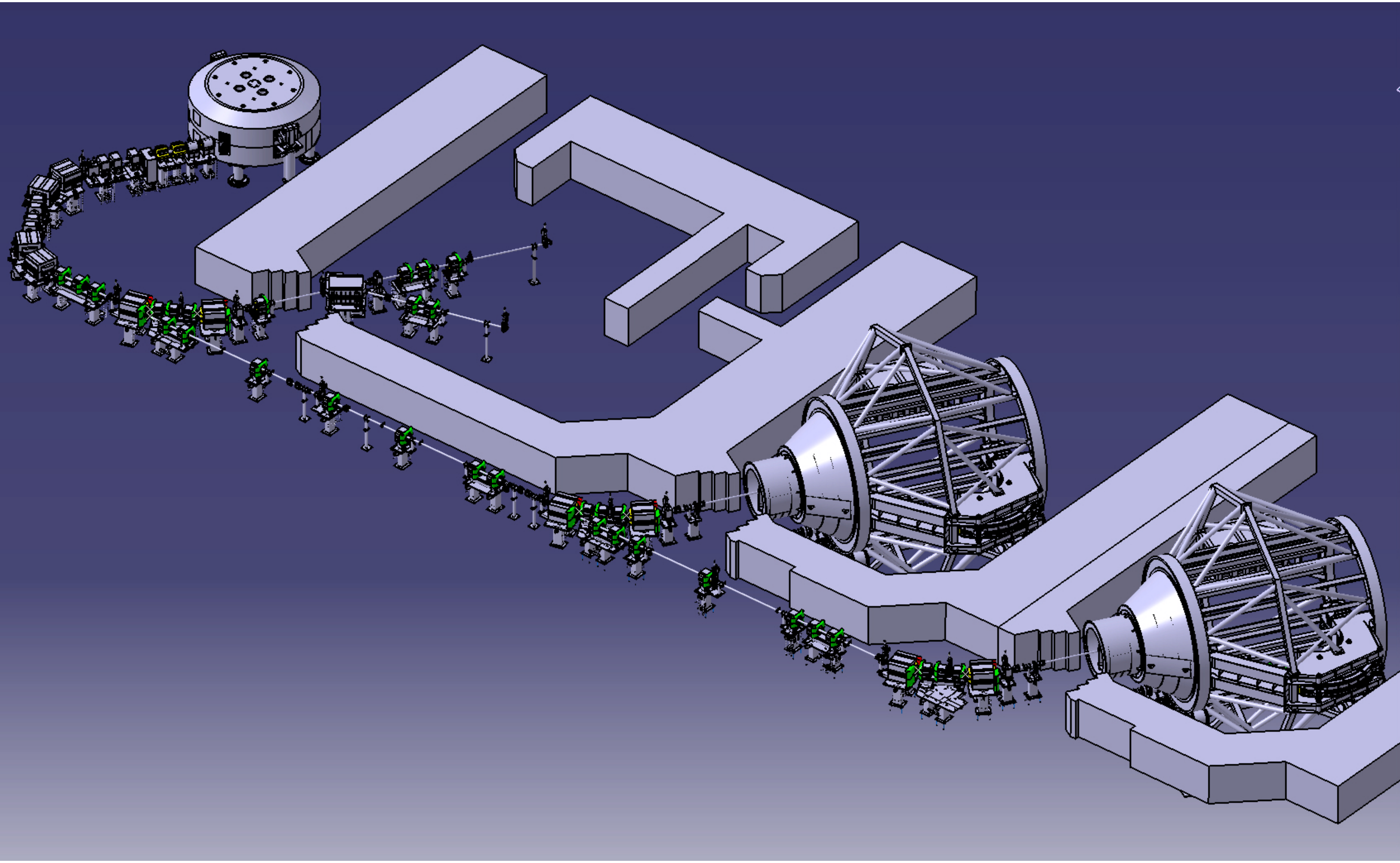
-signing the contract	08.2010
- start of the construction	03.2011
- cyclotron installation	05.2012
- start of experiments	01.2013

The gantry project:

- gantry 1 operational	06.2014
- gantry 2 operational	06.2015
- end of the contract	09.2015

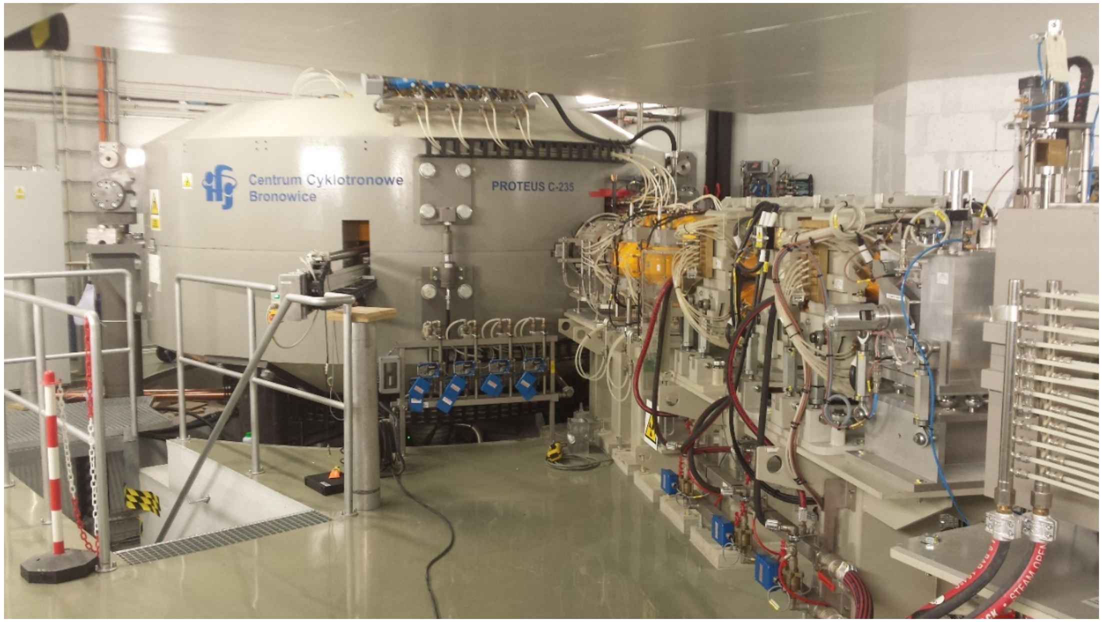


Beam lines at NCRH-CCB



Facility and equipment at NCRH-CCB

- **230 MeV cyclotron**
- 2 gantries with PBS
- TPS/OIS
- Computer Tomography
- Dosimetry and QA
- Eye treatment room
- Experimental hall



C-235 Proteus produced by Ion Beam Applications S.A. (IBA), Louvain-la-Neuve, Belgium

energy selector : 70 MeV – 230 MeV

time to change energy by 10 MeV: < 1 s

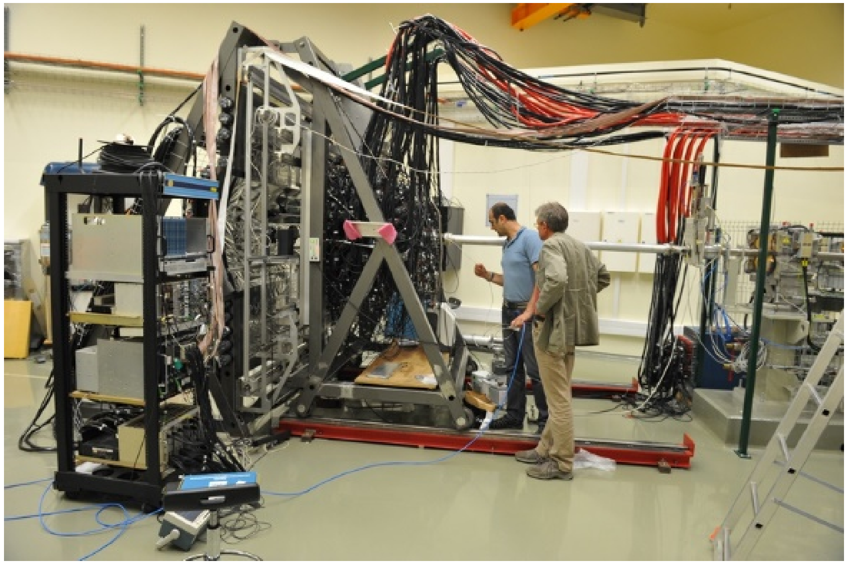
Facility and equipment at NCRH-CCB

- 230 MeV cyclotron
- **2 gantries with PBS**
- TPS/OIS
- Computer Tomography
- Dosimetry and QA
- Eye treatment room
- Experimental hall

- **dedicated IBA gantry (Pencil Beam Scanning)**
- **360 degrees**
- **2 spot sizes 1 σ = 2.7 mm and 4 mm (at 230 MeV)**
- **irradiat. 1 liter volume to 2Gy in less than 90 s**
- **max. field 30 cm x 40 cm**
- **robotic treatment table, 6 degrees of freedom**
- **orthogonal kV X-rays positioning**
- **Vision RT optical positioning**
- **gating**
- **anesthetic arm**

Facility and equipment at NCRH-CCB

- 230 MeV cyclotron
- 2 gantries with PBS
- TPS/OIS
- Computer Tomography
- Dosimetry and QA
- Eye treatment room
- **Experimental hall**



- **nuclear physics (Prof. A. Maj)**
- **radiobiology: RBE of protons**
- **tests of electronics for space flights**
- **detector testing**

Bogdan Fornal (IFJ PAN Kraków) –
NLC: two-center (Krakow-Warsaw) facility in Poland (25')

International Advisory Committee evaluates proposals for experiments

Our main clinical partners

Adults

Center of Oncology
Prof. B. Sas-Korczyńska
5.5 km from IFJ PAN

Eyes

University Hospital
Prof. B. Romanowska-Dixon
7 km from IFJ PAN

Children

Children University Hospital
Dr. K. Małecki
30 km by highway

Proton therapy facility

IFJ PAN – NCRH CCB

Operation of CCB-NCRH

- 230 MeV cyclotron is used for research since January 2013
- The medical part of the center will be fully operational in October 2015
- The first patient on the gantry is planned for January 2016
- After the initial learning period (1-2 years) it will be possible to treat in CCB up to <u>600-800 patients</u> per year (250-350 patients per one gantry plus 100 patients in the eye treatment room)
- The procedure is still not reimbursed by the National Health Fund (NFZ).

Summary and Conclusions

- Proton therapy, due to perfect dose distribution, offers for clinicians higher probability of local control, lower complications and chance or secondary cancer

- Quick progress of accelarator technology leads to decrease the price and increasing availability of the proton radiotherapy

- At IFJ PAN , patients with eye tumor are irradiated since 2011. The Bronowice Cyclotron Center at IFJ PAN with new eye-line and two dedicated gantries with active Pencil Beam Scanning will be fully operational in mid of October 2015.