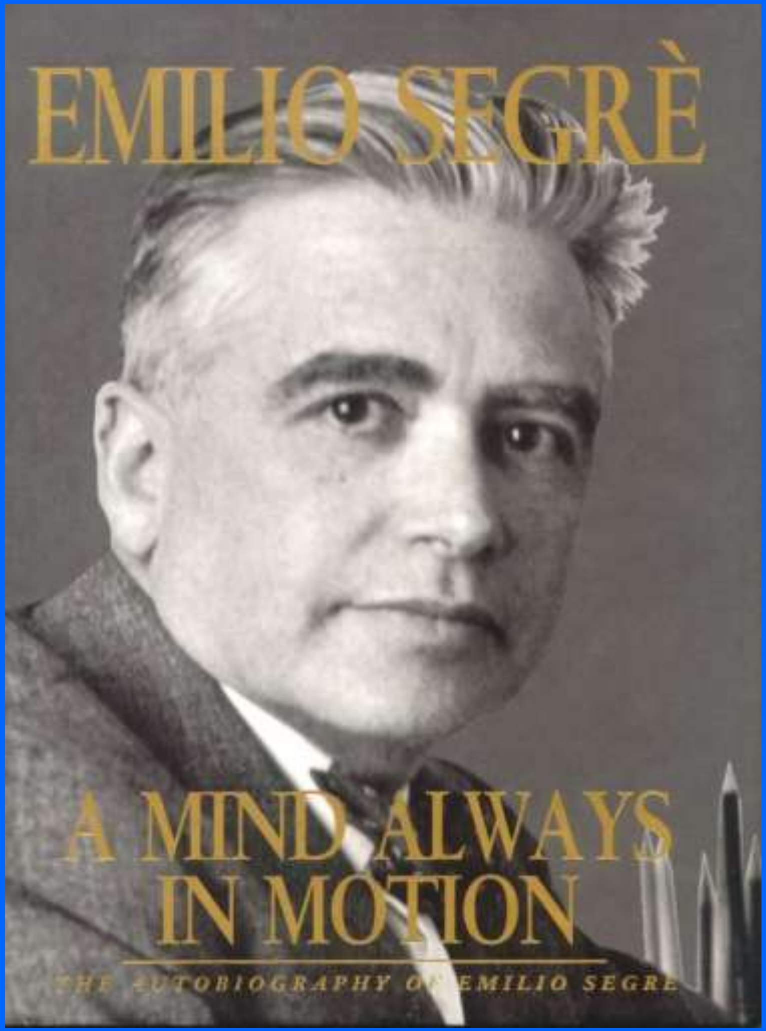
PARTICLE ACCELERATORS IN DIAGNOSTICS AND CANCER THERAPY

Ugo Amaldi

University Milano Bicocca and TERA Foundation

Nuclear medicine

Radioactivity in diagnostics: SPECT = Single Photon Emission Computer Tomography

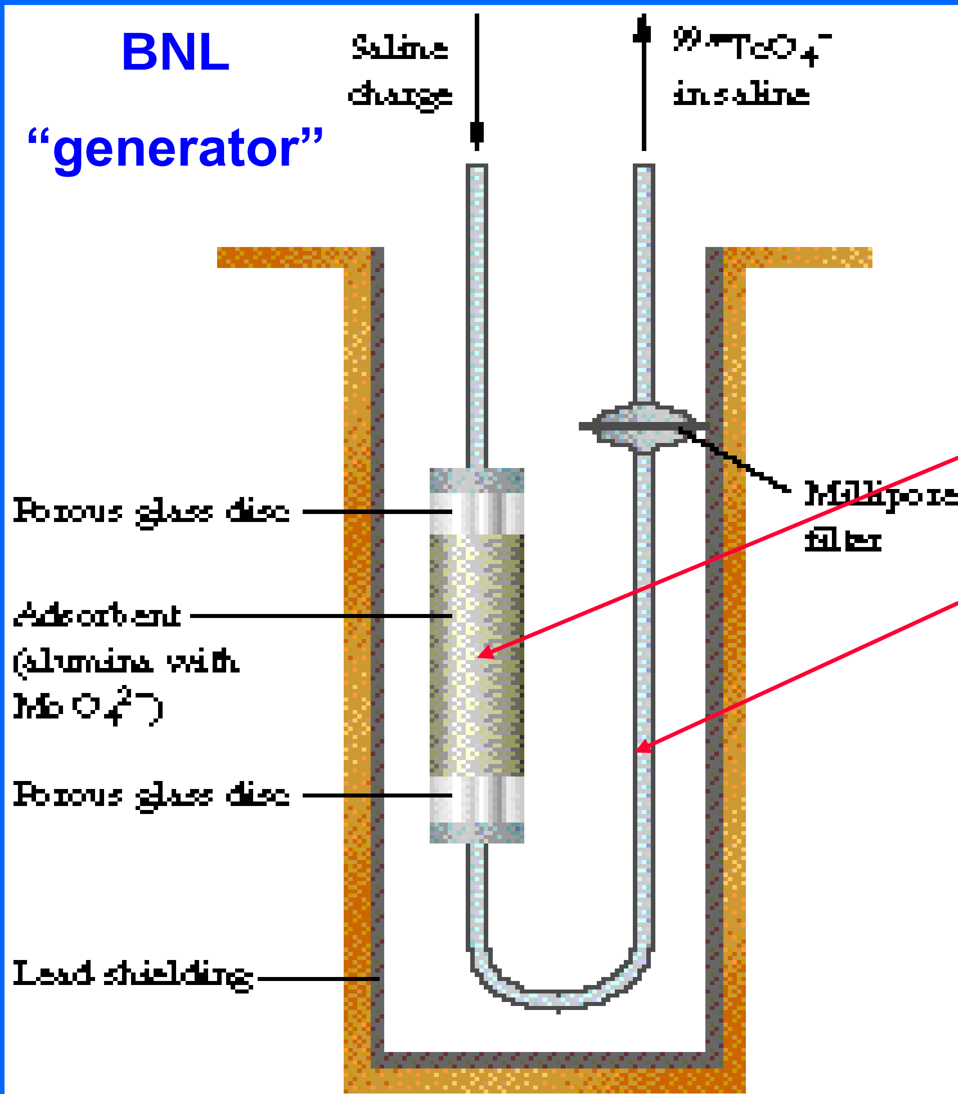


Emilio Segrè

1936: Discovery of technetium with Perrier

1938: discovery of ^{99m}Tc with Ed McMillan

In the 50s at BNL the « cow » was made productive



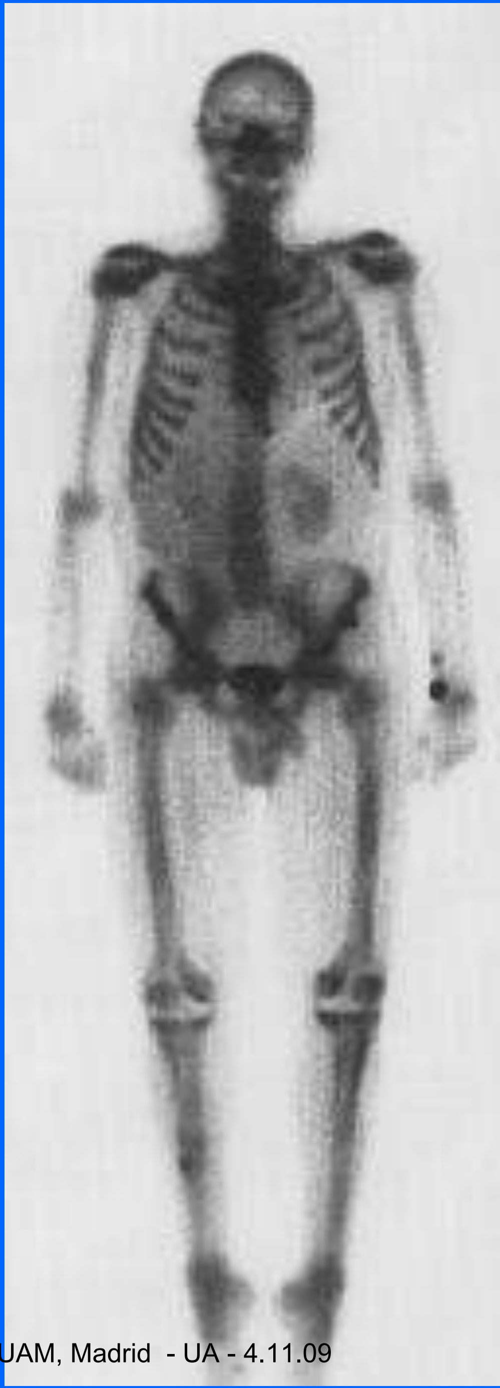
In reactors <u>slow neutrons</u>

produce ^{99}Mo through fission

^{99}Mo (66 h) = ^{99m}Tc (6 h) + e^- + v

Walter Tucker and Powell Richards

SPECT scanner

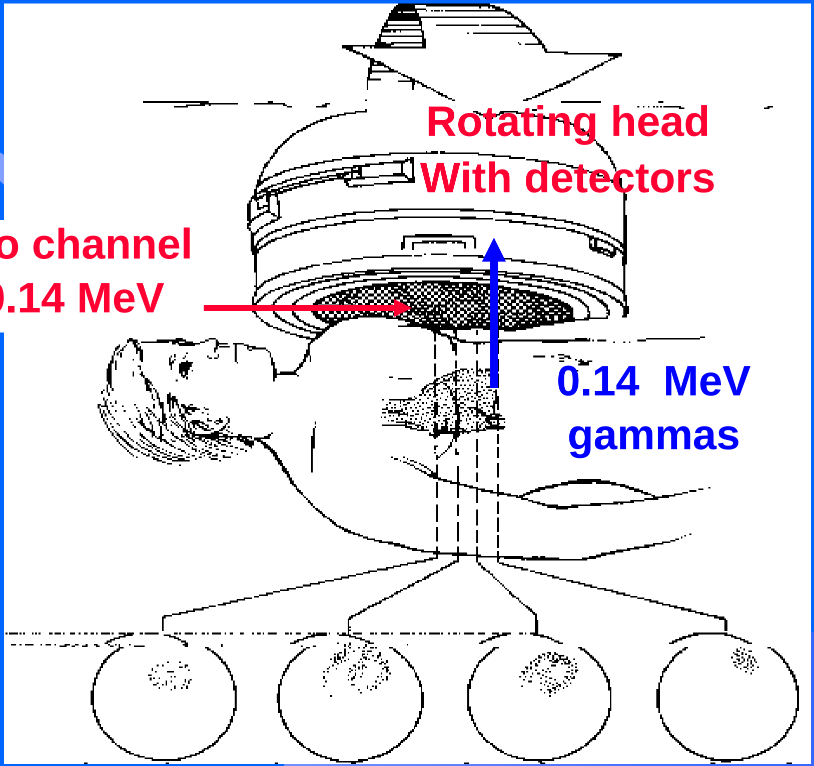


85% of all nuclear medicine examinations use molibdenum/technetium generators for diagnostics of

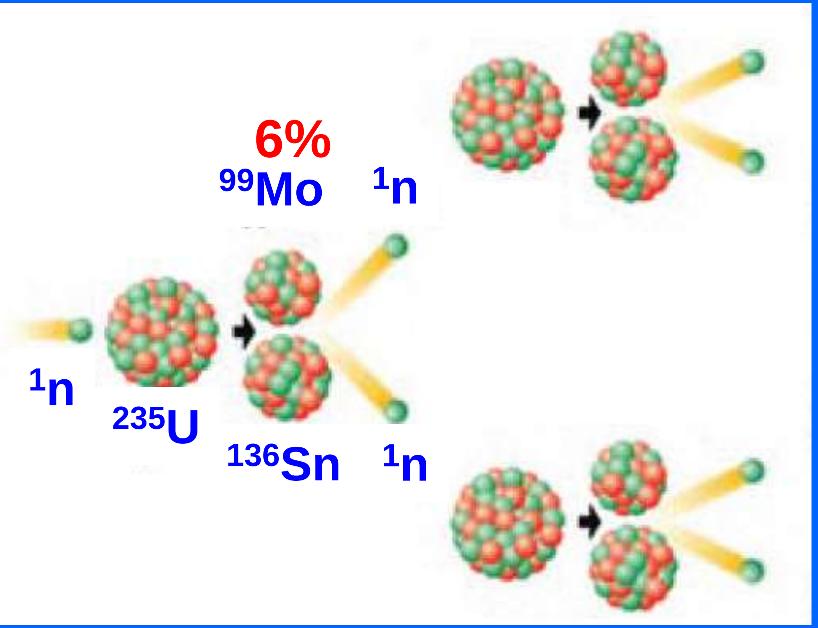
… liver

lungs

bones ……



Production of ^{99}Mo: present



A. Fission chain in nuclear reactors

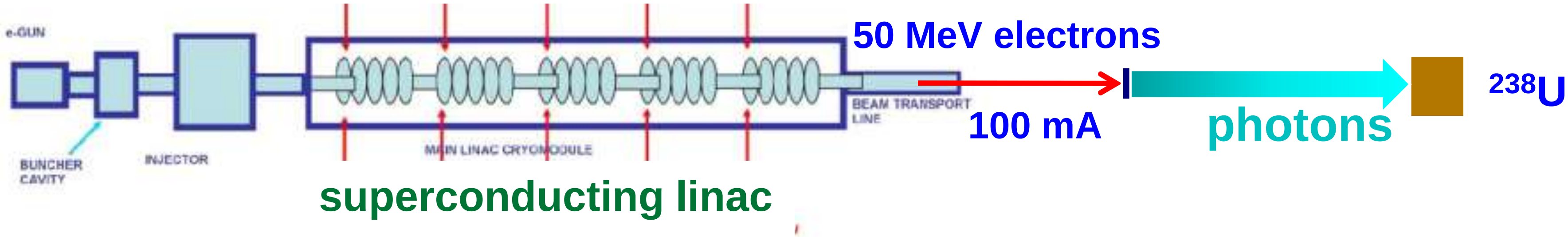
B. Reprocessing of the special fuel bars

Worldwide production of 100 000 curies per year at aging nuclear reactors for 30 million examinations/year:

BR2 Belgium	
NRU Canada	(50%)
OSIRIS France	
HFR Netherlands	(40%)
SAFARI-1 South Africa	

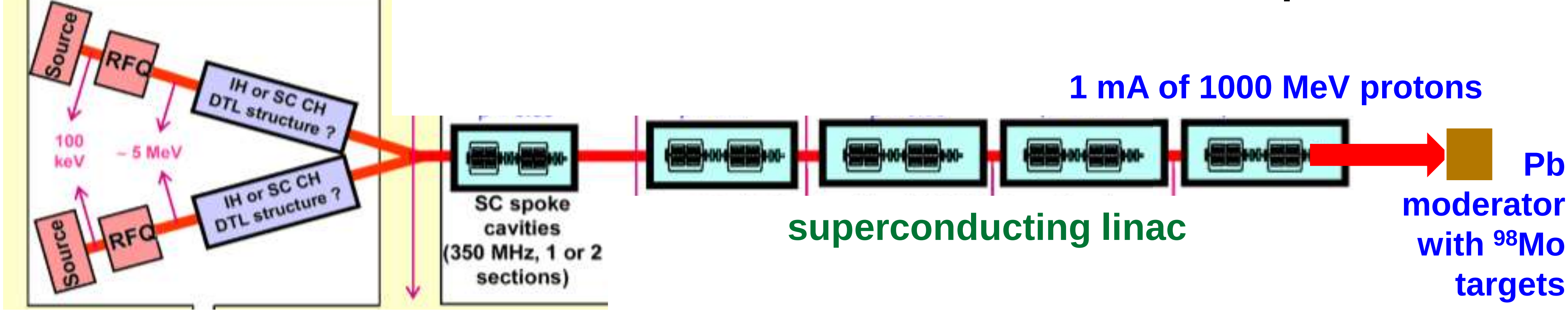
Production of ^{99}Mo: possible solutions of a serious problem

Photofission of Uranium



Triumph and NDS Nordion (Canada): could cover 10% of the market

Neutron capture on ^{98}Mo



Advanced Accelerator Applications (CERN spin-off): could cover 100% of the market

High-current cyclotrons used in medicine

Baby Cyclotrons (below 18 MeV)

In-house facility

Mainly used for production of short-lived positron emitters like ^{18}F, ^{11}C, ^{13}N, ^{15}O.

Medium Energy Cyclotrons (below 40 MeV)

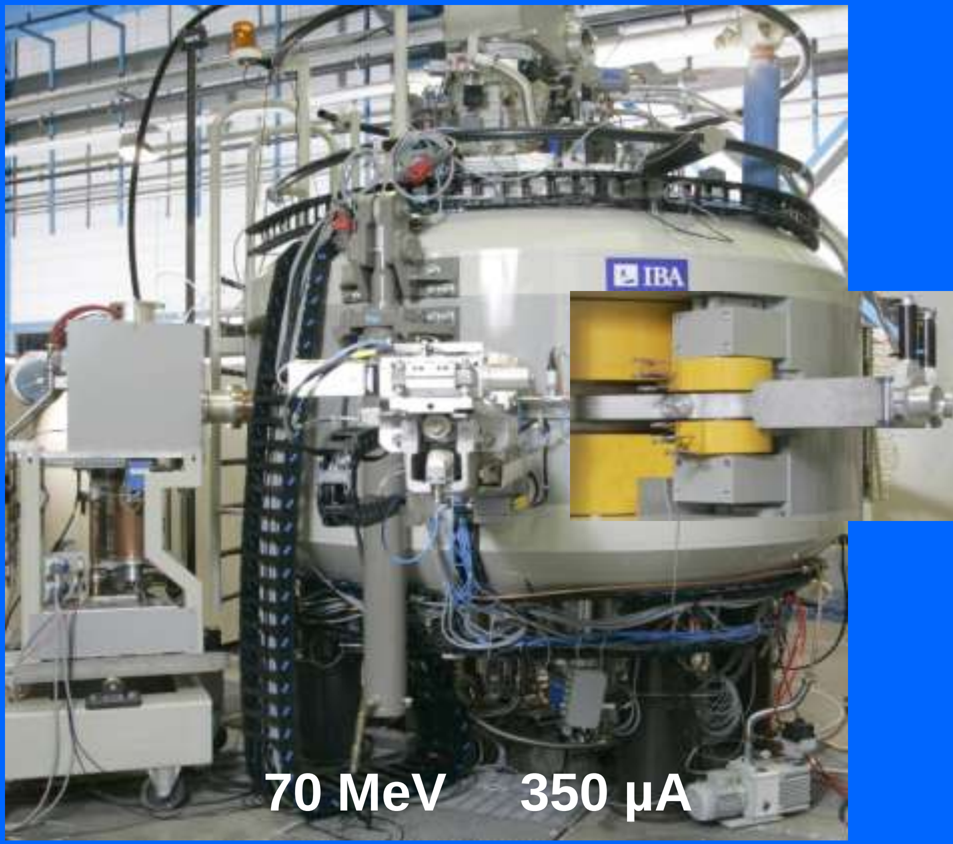
Centralised facility

Majority of the cyclotron produced isotopes are produced using such machine viz, ^{123}I, ^{201}Tl, ^{67}Ga, ^{68}Ga, ^{103}Pd etc.

High Energy Cyclotrons (above 40 MeV)

Centralised facilities and research institutions

Used for production of few radioisotope requiring high energy for production viz, ^{67}Cu, ^{82}Sr, ^{211}At…..



IBA's ARRONAX in Nantes

4 Particles: H^- / D^- / He^{2+}/ HH^+

Variable energy: 15 MeV → 70 MeV

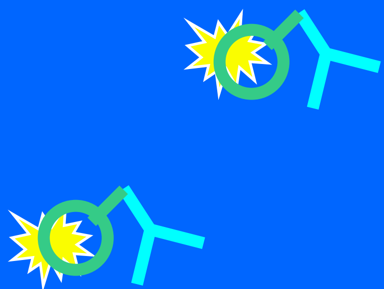
Performances:

- 750 µA H^-
- 35 µA He^{2+}

Examples of endotherapy with radioisotopes

^{213}Bi

^{211}At



Alfa-decay:

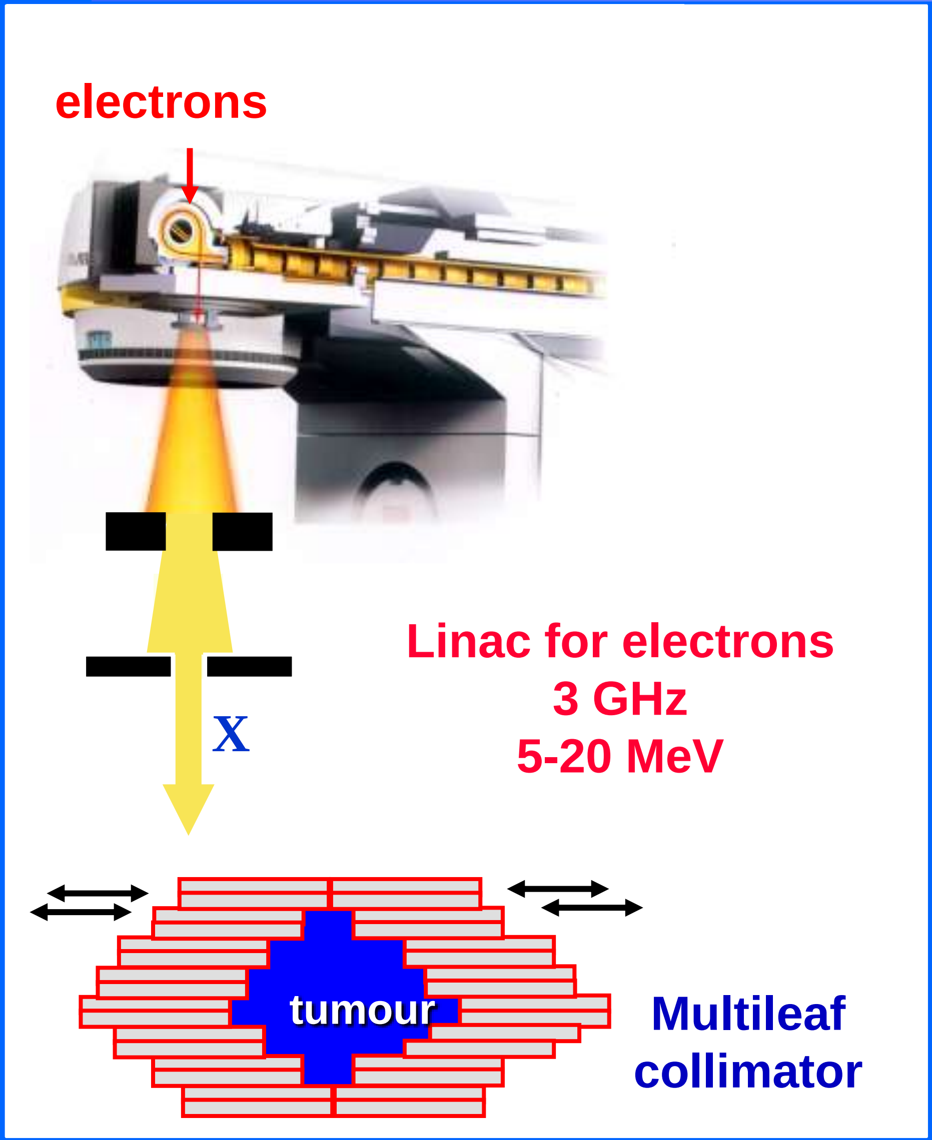
Helium nucleus

It can be called:
"Systemic hadrontherapy"

Ourtesy of ARRONAX – Nantes - France

Cancer therapy with X ray and hadron beams

‘Conventional’ radiotherapy: linear accelerators dominate

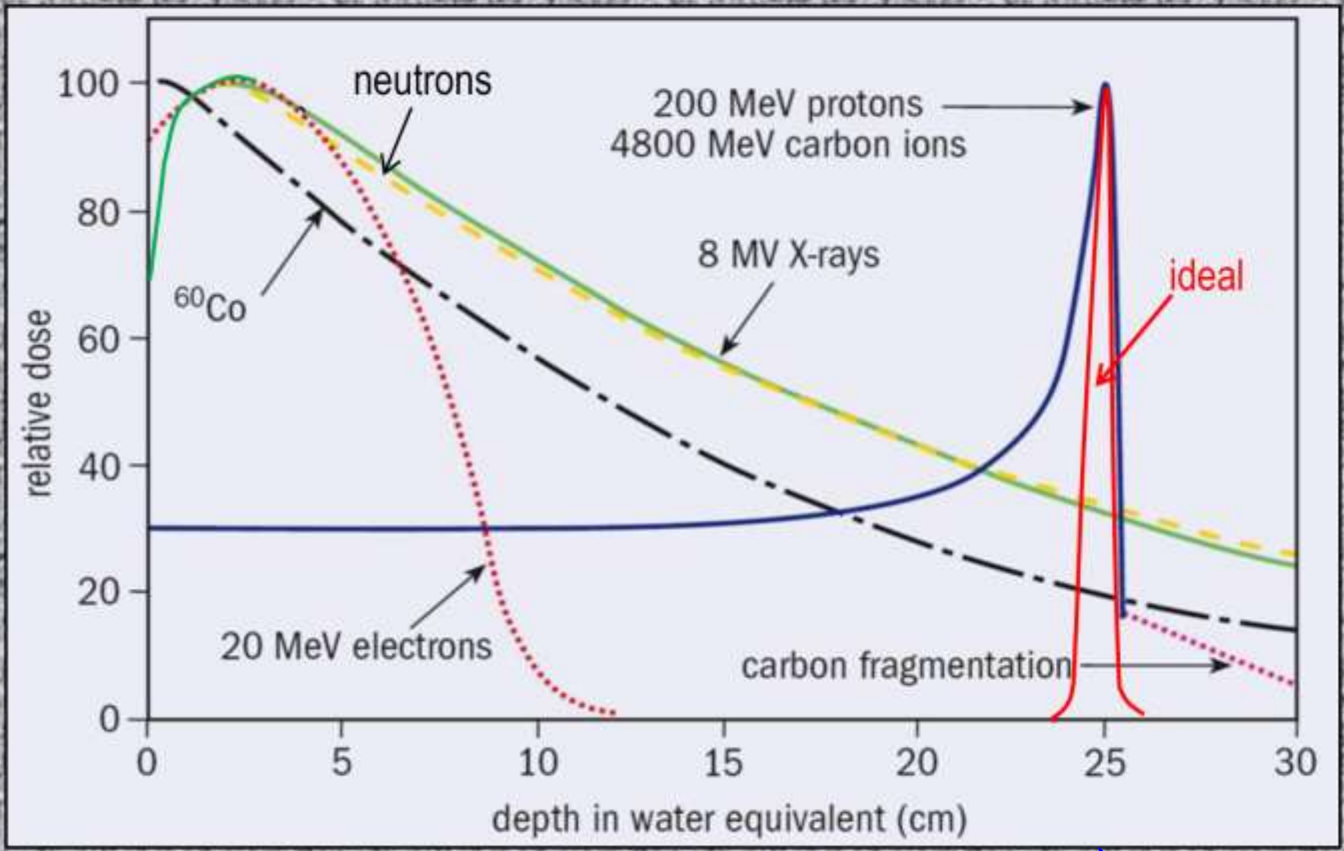


In the world radiation oncologists

use 15 000 electron linacs

40% of all the existing accelerators

The icon of radiation therapy with charged hadrons



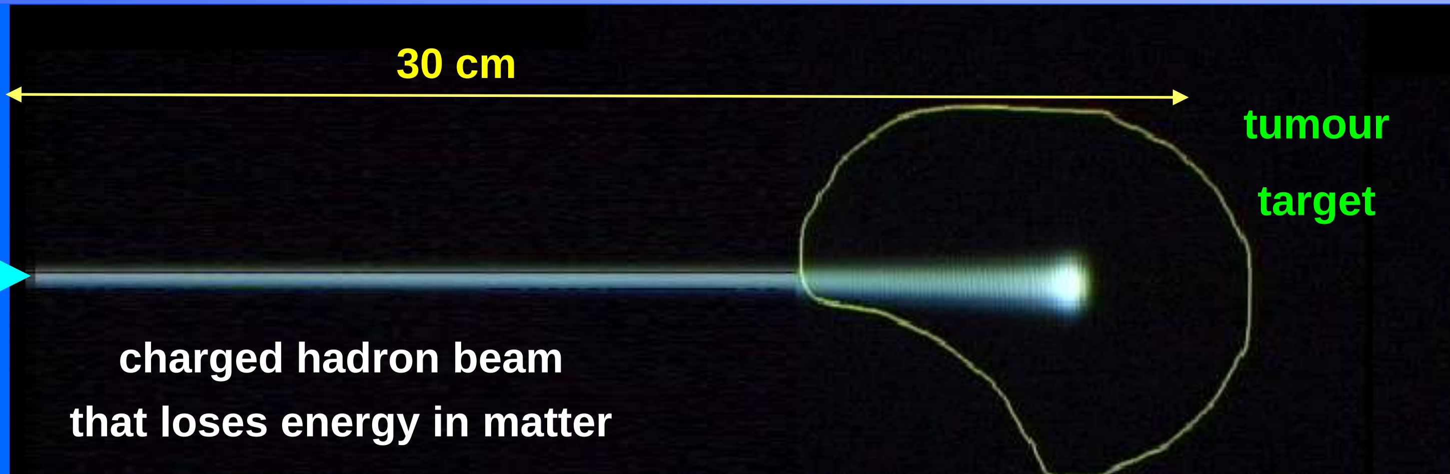
Radiation beam in matter

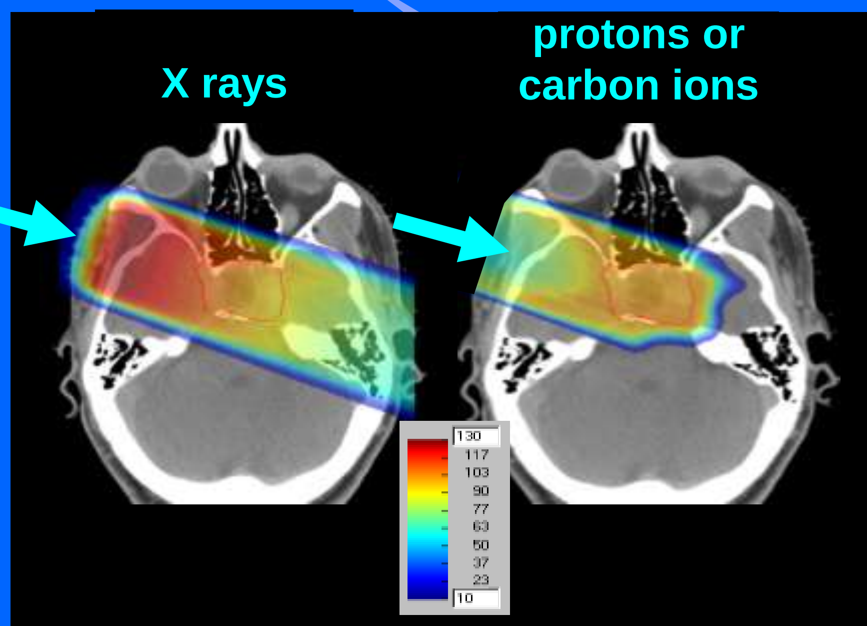
Protons and ions spare healthy tissues

200 MeV - 1 nA protons

4800 MeV – 0.1 nA carbon ions

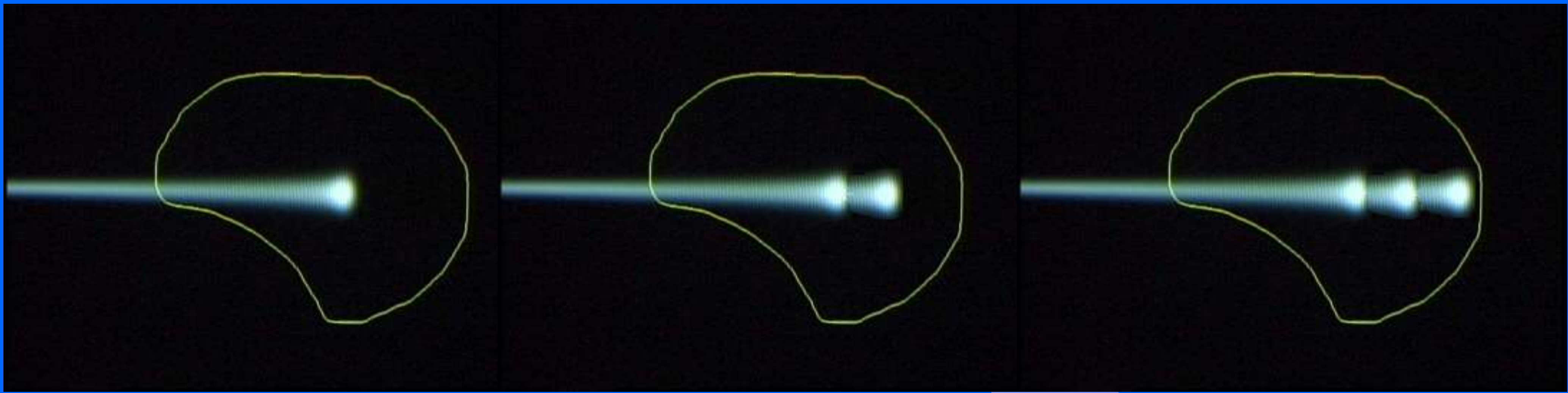
which can control radioresistant tumours





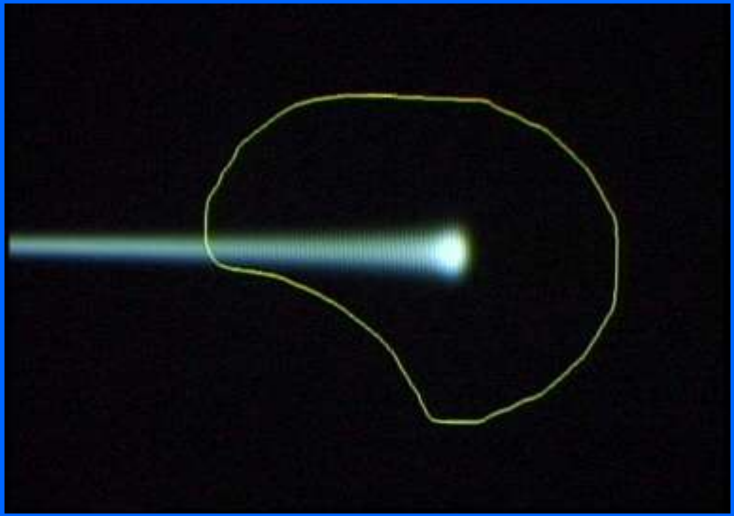
Charged hadrons can deliver the dose in three dimensions

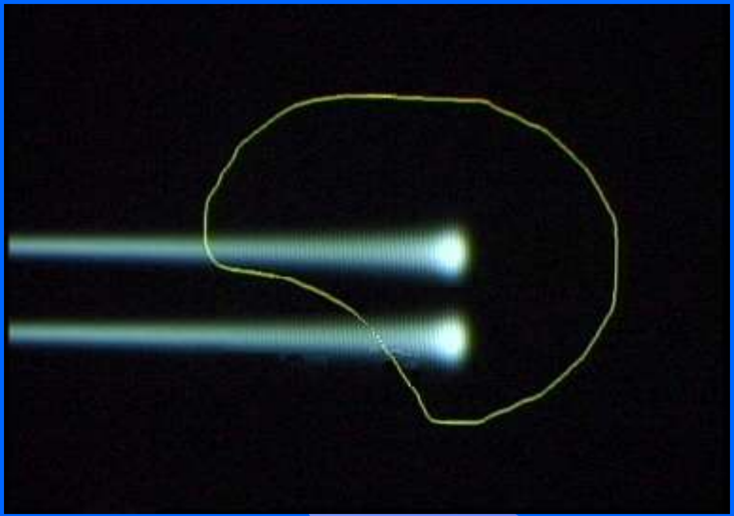
Longitudinal mouvement by varying the energy of the beam



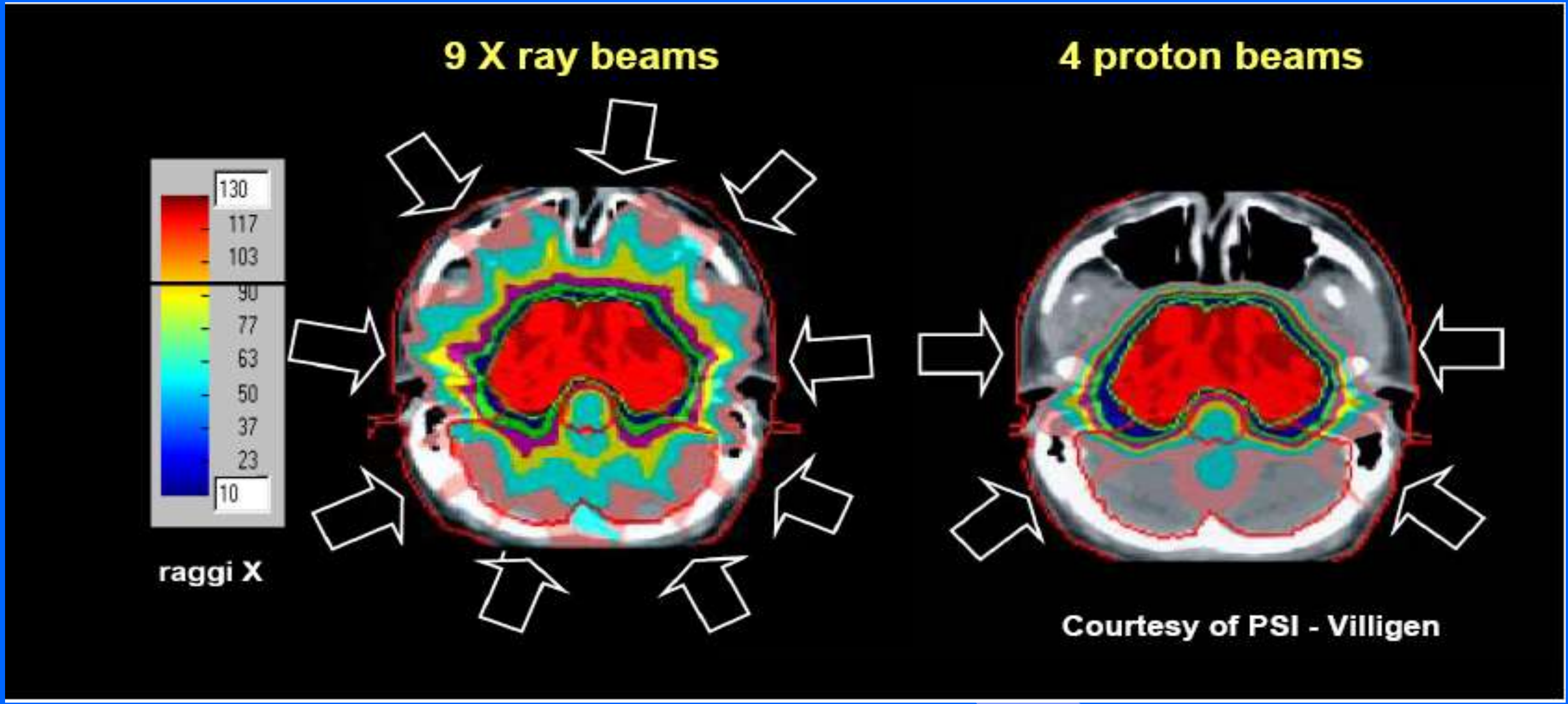
Charged hadrons can deliver the dose in three dimensions

Lateral movement with a transverse magnetic field

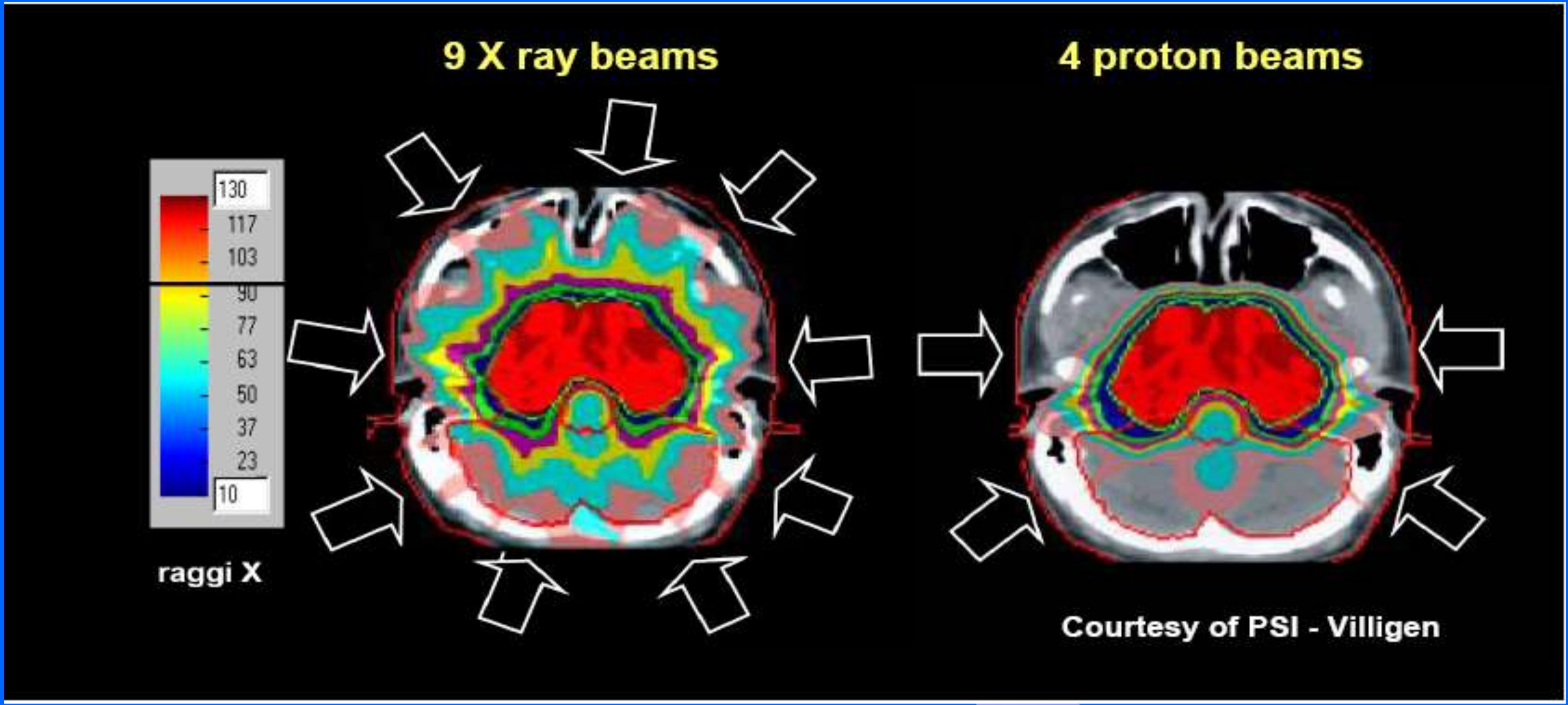




Protons are quantitatively different from X-rays



Carbon ions are *qualitatively* different from X-rays



Carbon ions deposit in a cell 24 times more energy than a proton

producing not reparable multiple close-by double strand breaks

Carbon ions can control radio-resistant tumours

Accelerators for hadrontherapy (*)

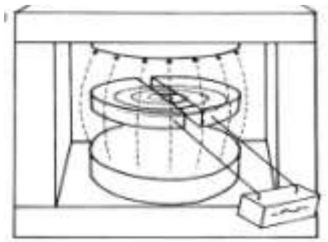
(*) Also hadron therapy, particle therapy

The accelerator is only a 'small' part of a therapy centre

The accelerators used today in hadrotherapy are "circular"

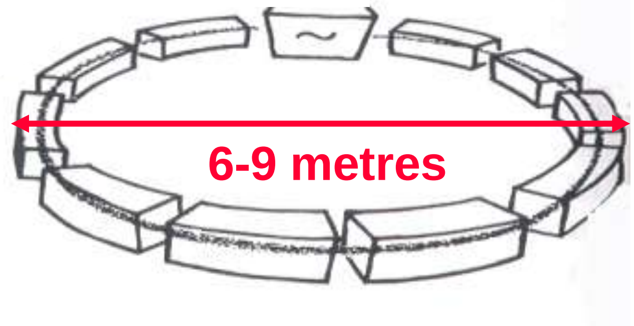
Teletherapy with protons (200-250 MeV)

CYCLOTRONS (*) (Normal or SC)



4-5 metres

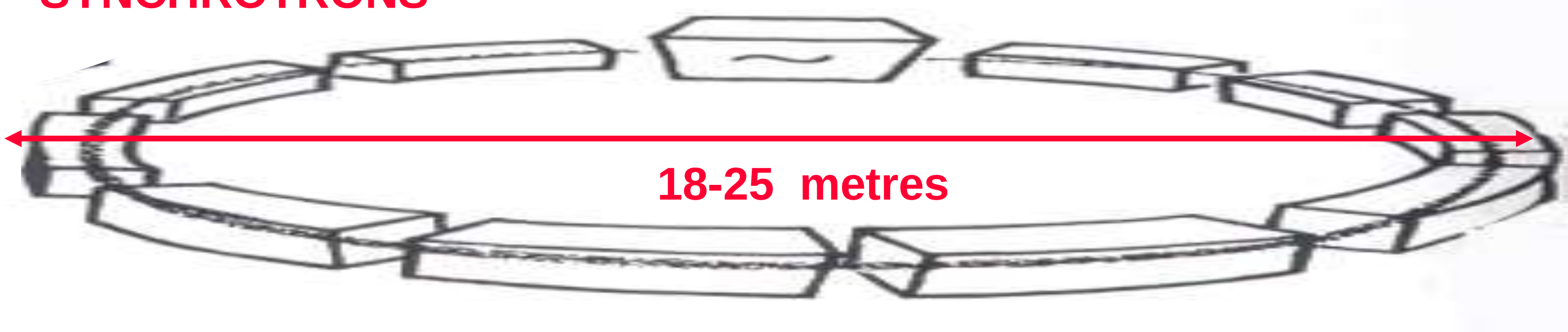
SYNCHROTRONS



(*) also synchrocyclotrons

Teletherapy with carbon ions (4800 MeV = 400 MeV/u)

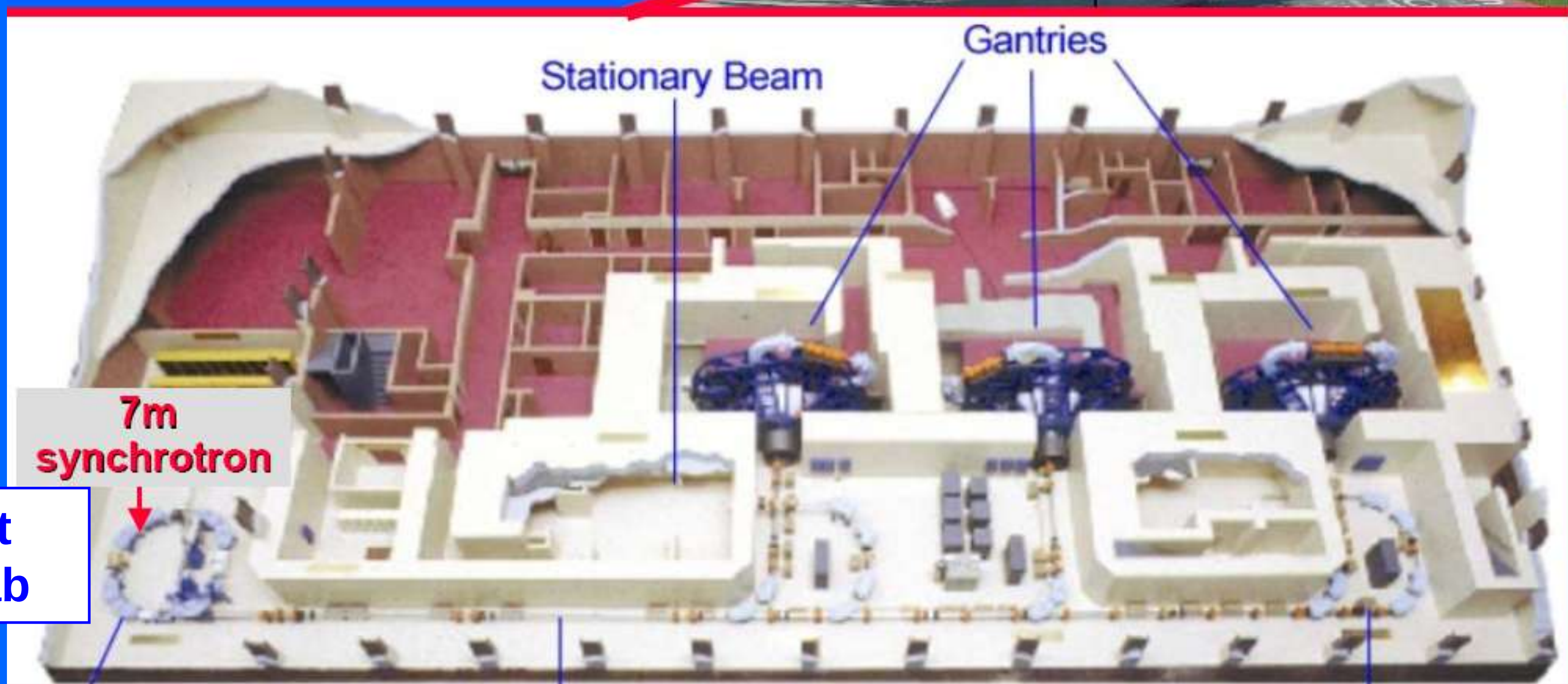
SYNCHROTRONS



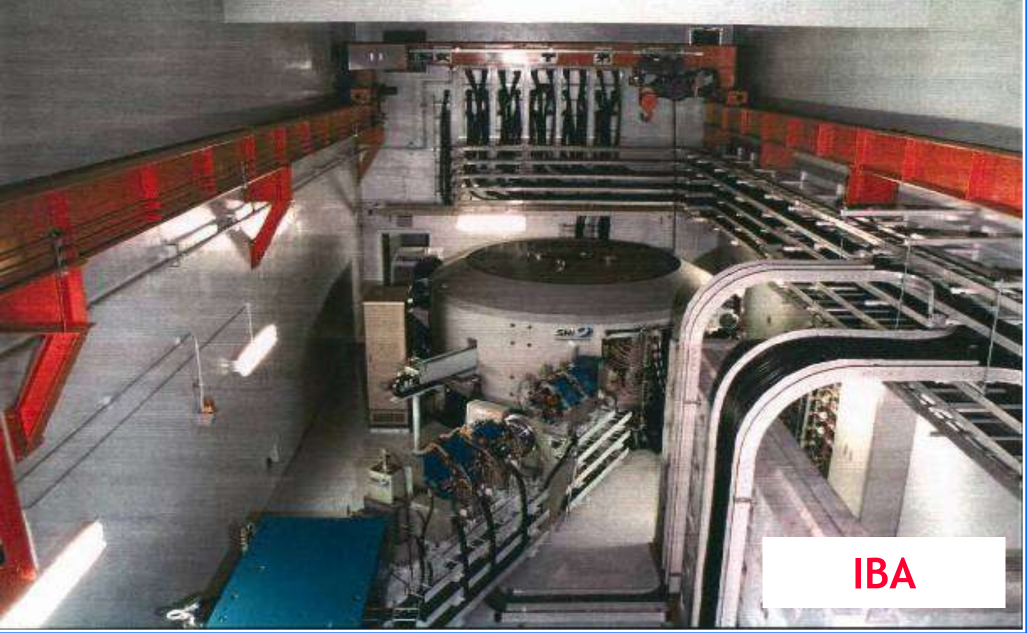
Loma Linda Medical University Centre: first patient 1992

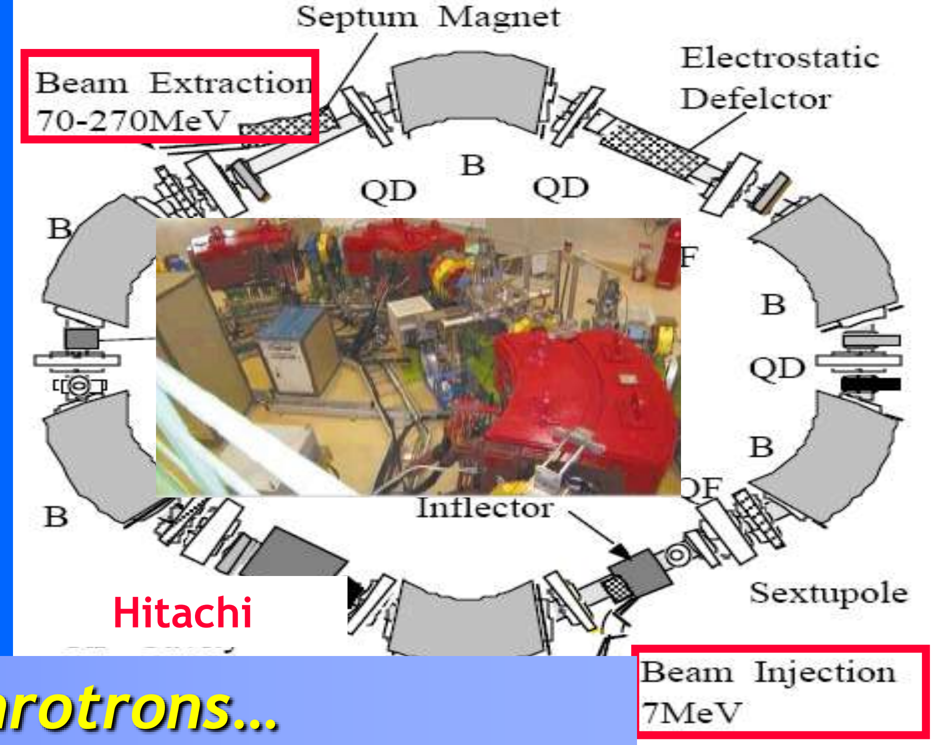
- First hospital-based proton-therapy centre

1500 patients/year



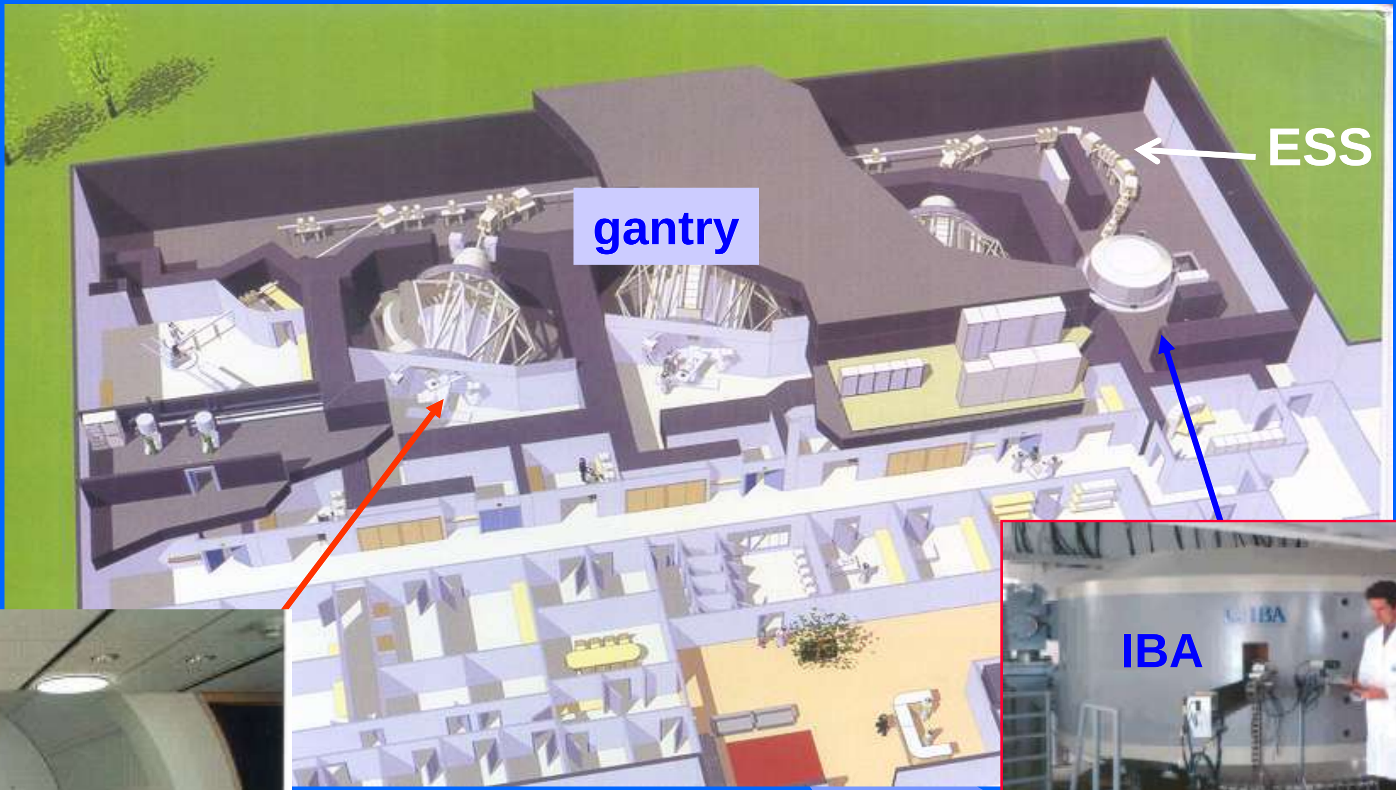
Built at Fermilab





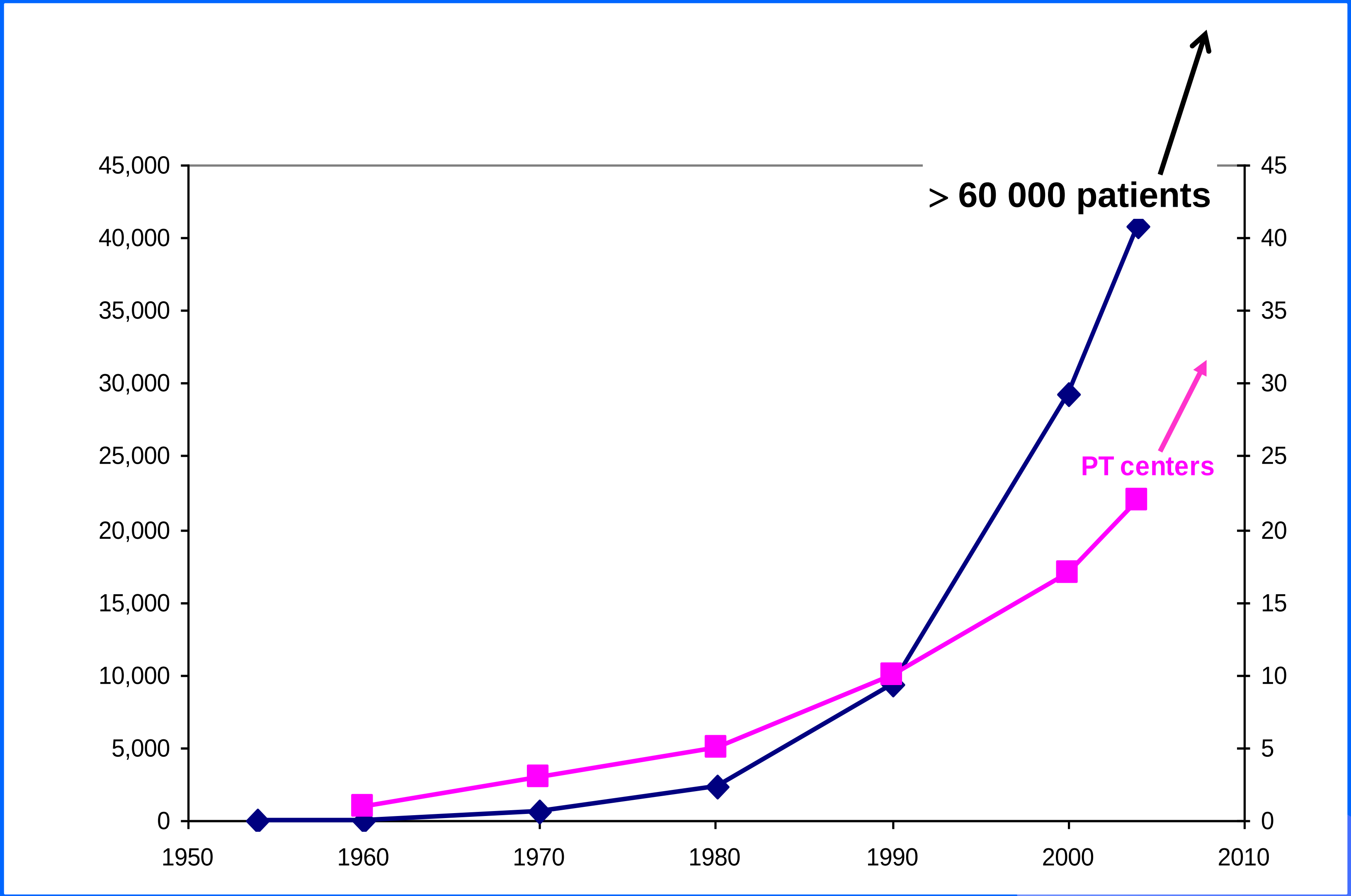
Protontherapy: cyclotrons and synchrotrons...

Cyclotron for protons by Ion Beams Applications - Belgium



Five companies offer turn-key centres for 120 Meuro.
If proton accelerators were 'small' and 'cheap',
no radiotherapist would use X rays.

Protontherapy is booming

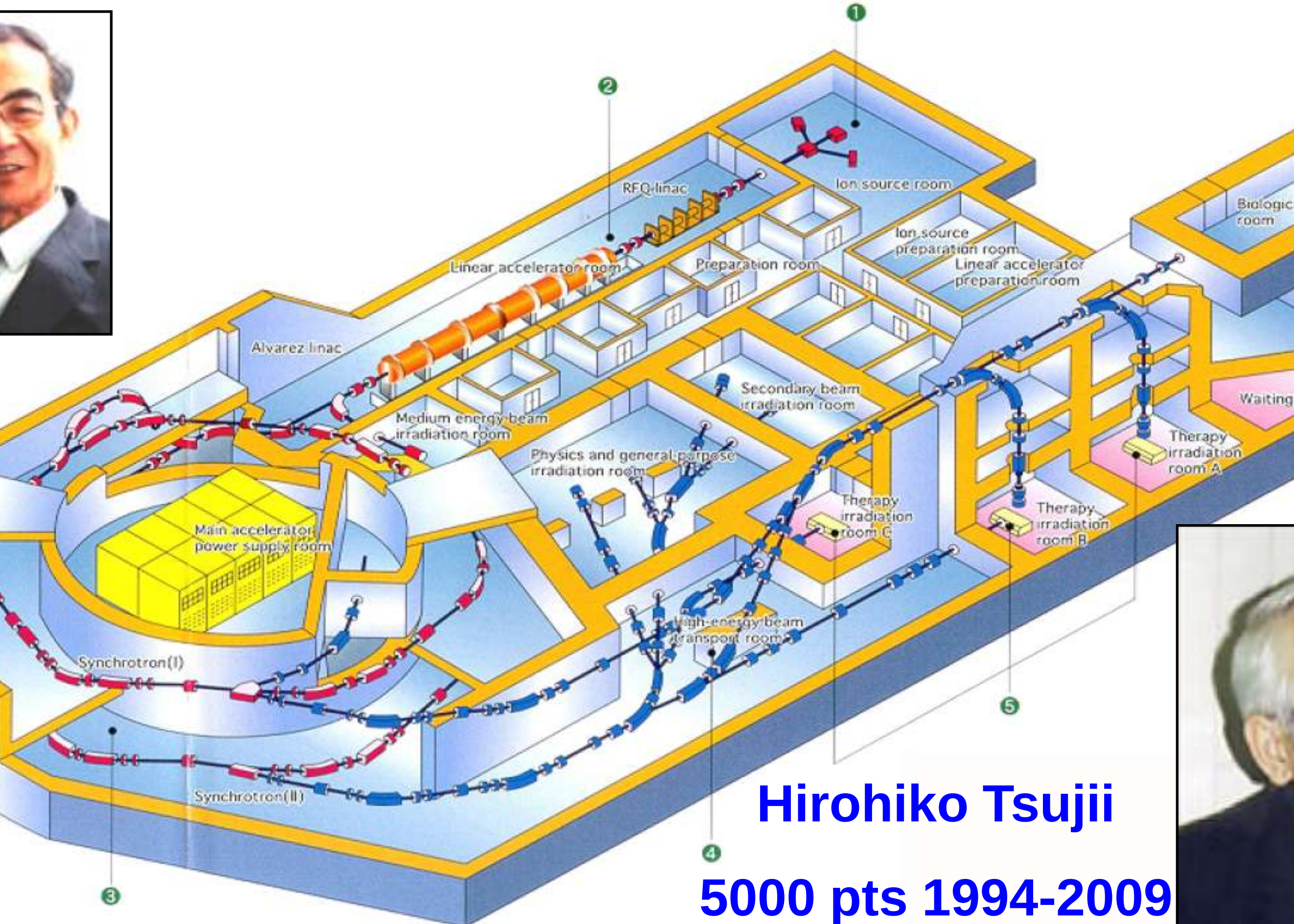


Therapy with carbon ions

HIMAC in Chiba is the pioner of carbon therapy (Prof H. Tsujii)

Yasuo Hirao

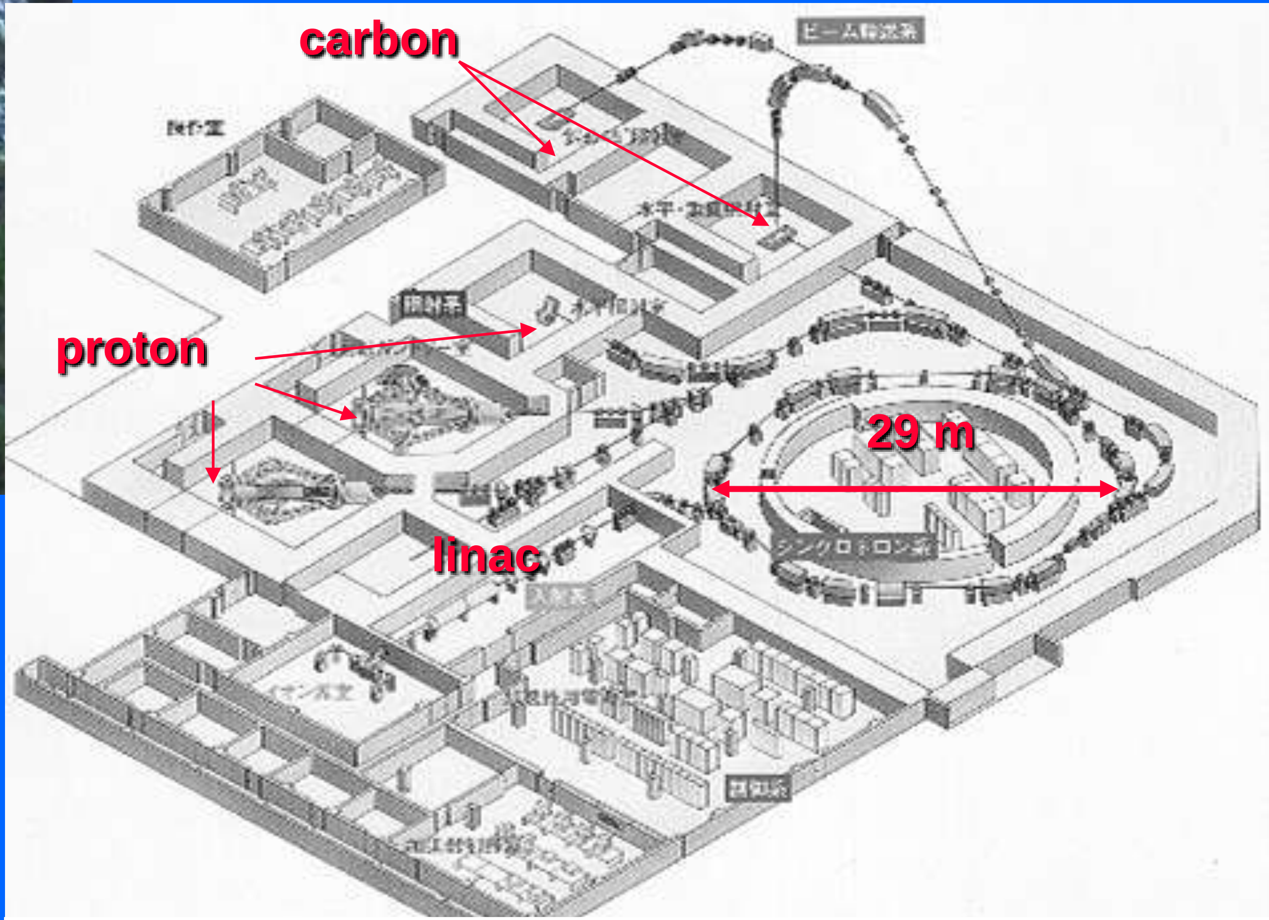
[15] Hirao, Y. et al, "Heavy Ion Synchrotron for Medical Use: HIMAC Project at NIRS Japan" Nucl. Phys. A538, 541c (1992)



Hirohiko Tsujii

5000 pts 1994-2009

The Hyogo 'dual' Centre



Mitsubishi: turn-key system

End 2008

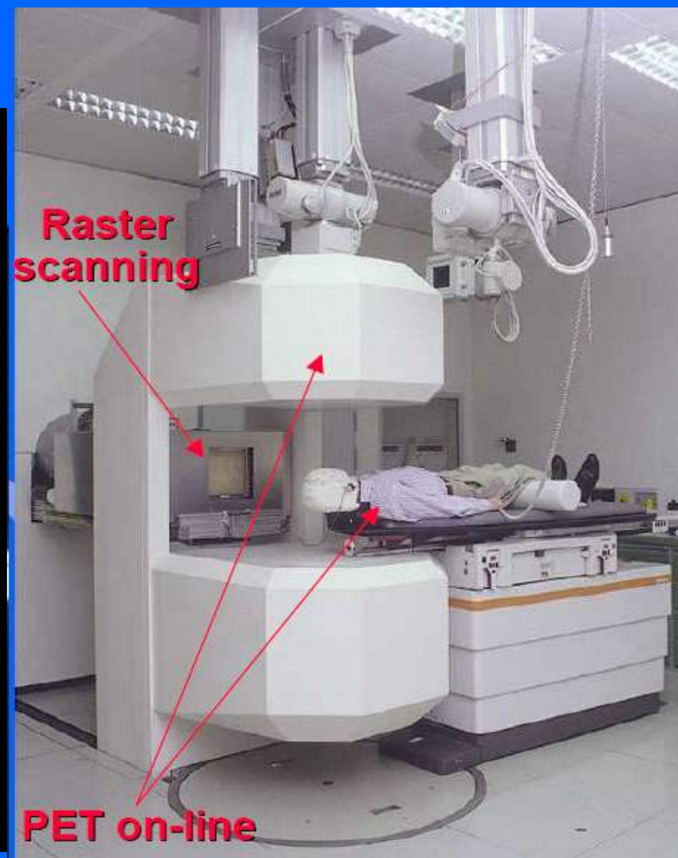
protons: 2000 patients

carbon ions: 500 patients

Germany: the GSI pilot project

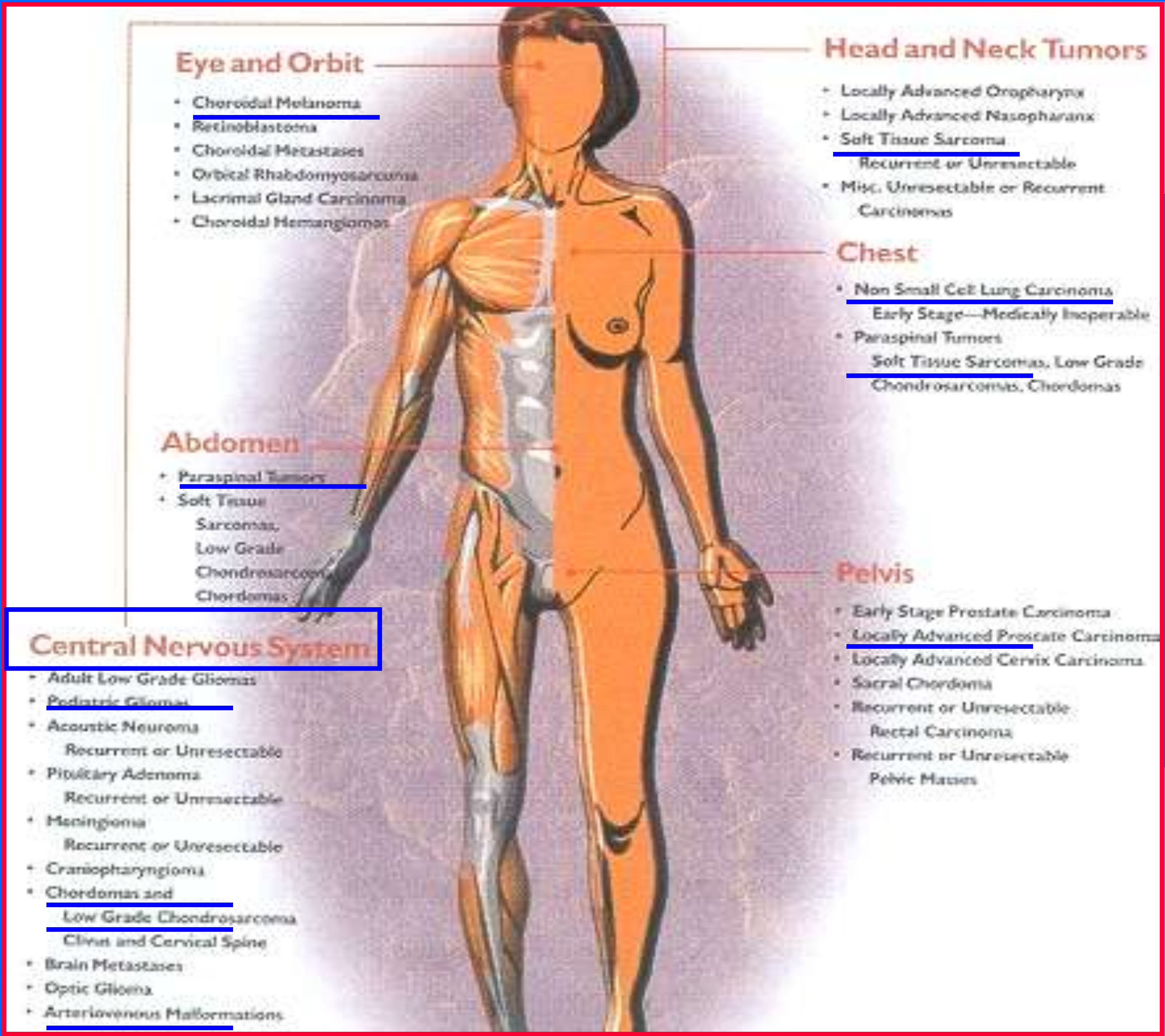
J. Debus

1998-2009
500 patients treated
with carbon ions



Patients of hadrontherapy

The site treated with hadrons



In the world

protontherapy:

60'000 patients

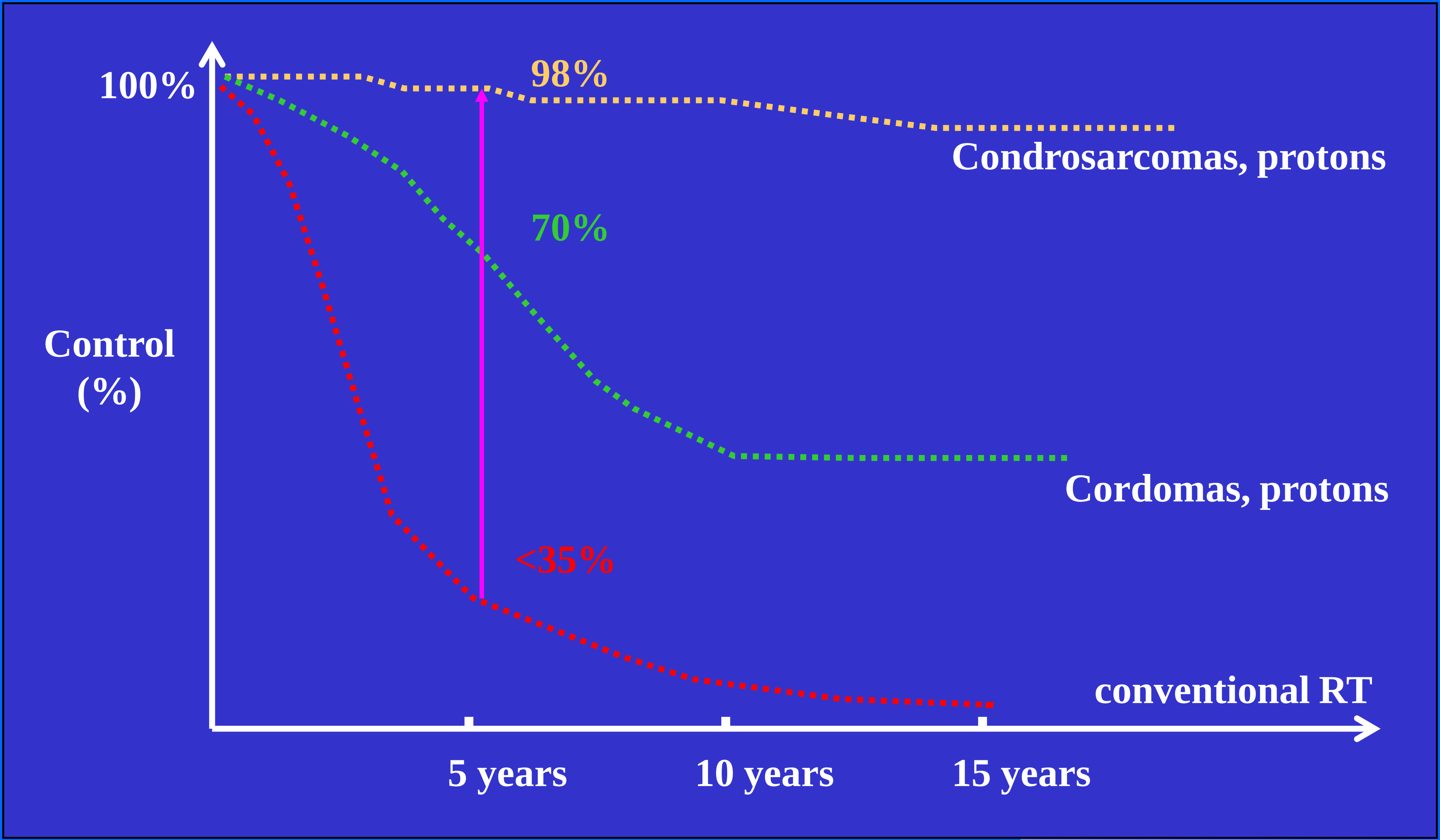
carbon ion

therapy

5 000 patients

mainly at HIMAC

First important results obtained with protontherapy



Indication	End point	Results photons	Results carbon HIMAC-NIRS	Results carbon GSI
Chordoma	local control rate	30 – 50 %	65 %	70 %
Chondrosarcoma	local control rate	33 %	88 %	89 %
Nasopharynx carcinoma	5 year survival	40 -50 %	63 %	
Glioblastoma	av. survival time	12 months	16 months	
Choroid melanoma	local control rate	95 %	96 % (*)	
Paranasal sinuses tumours	local control rate	21 %	63 %	
Pancreatic carcinoma	av. survival time	6.5 months	7.8 months	
Liver tumours	5 year survival	23 %	100 %	
Salivary gland tumours	local control rate	24-28 %	61 %	77 %
Soft-tissue carcinoma	5 year survival	31 – 75 %	52 -83 %	

Table by G. Kraft 2007
Results of C ions

Numbers of potential patients (*)

X-ray therapy

every 10 million inhabitants: 20'000 pts/year

Protontherapy

12% of X-ray patients 2'400 pts/year

Therapy with Carbon ions for radio-resistant tumour

3% of X-ray patients 600 pts/year

TOTAL every 10 M **about 3'000 pts/year**

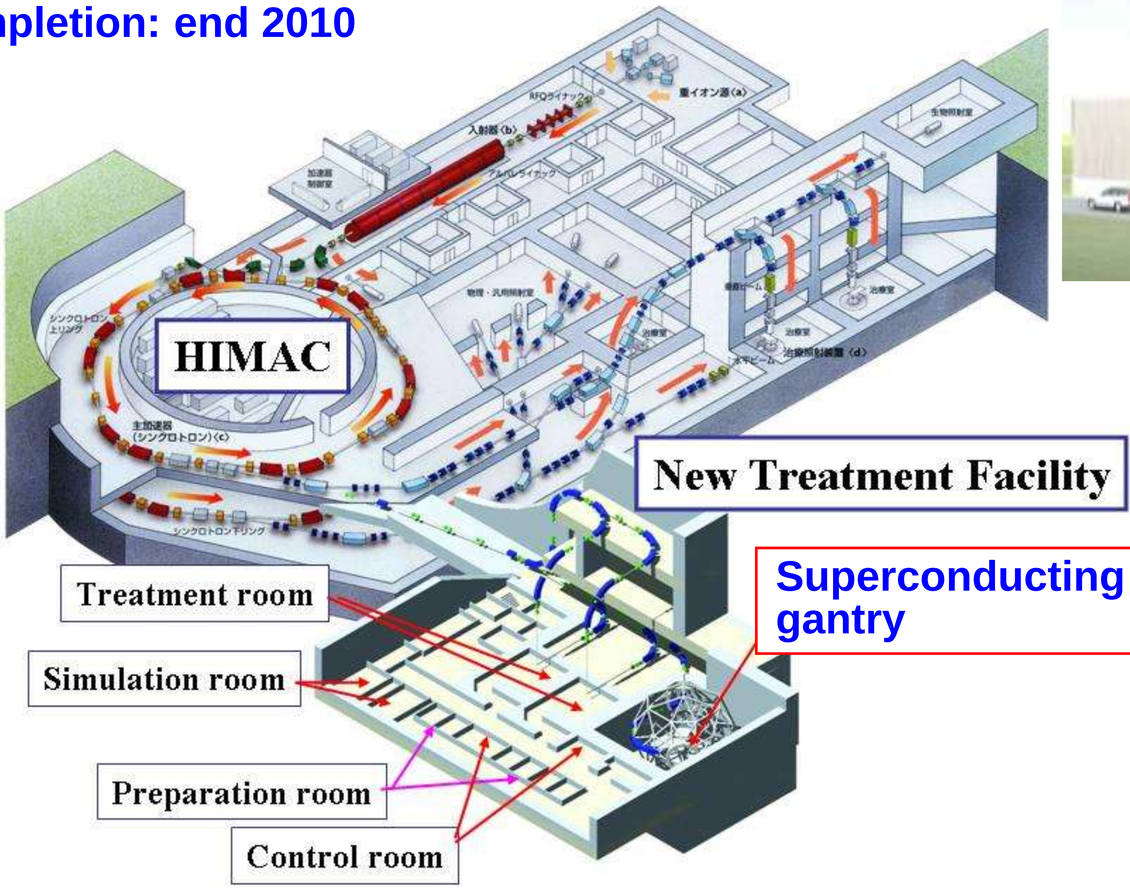
(*) Combining studies made in Austria, Germany, France, Italy and Sweden - ENLIGHT

New centres for carbon ion therapy

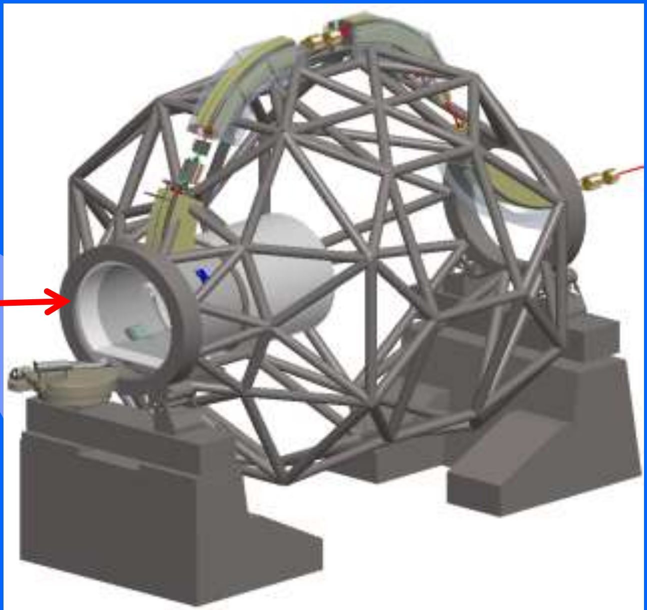
Courtesy H. Tsujii

HIMAC new facility

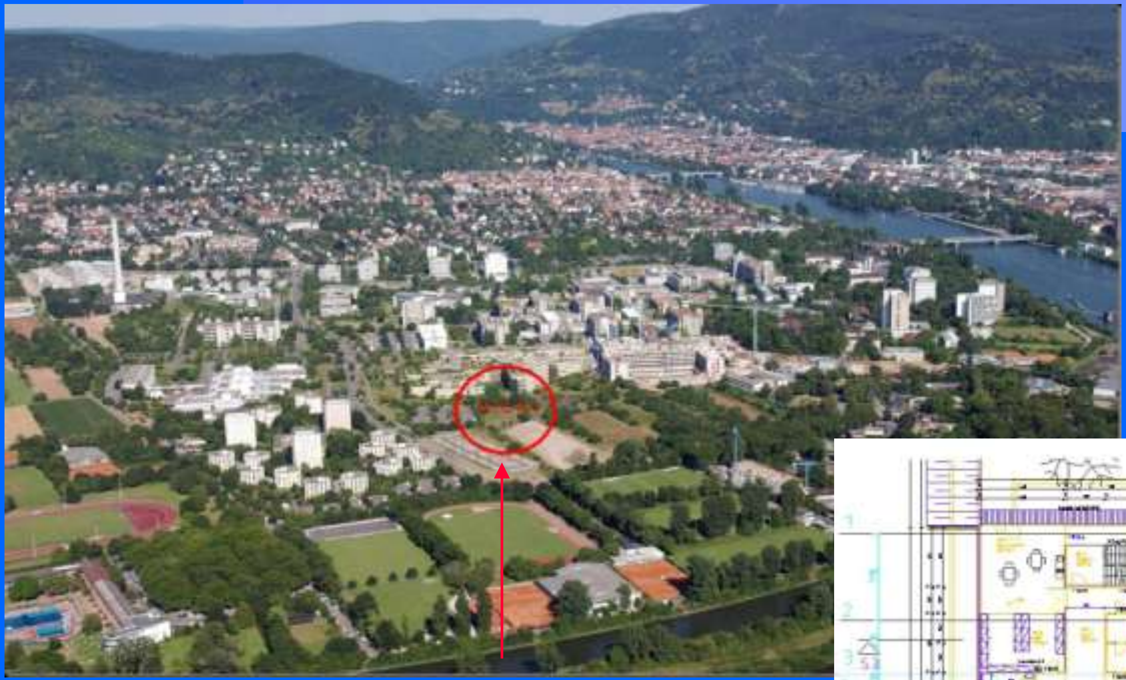
Completion: end 2010



Superconducting gantry



The site of HIT
the Heidelberg Ion Therapy



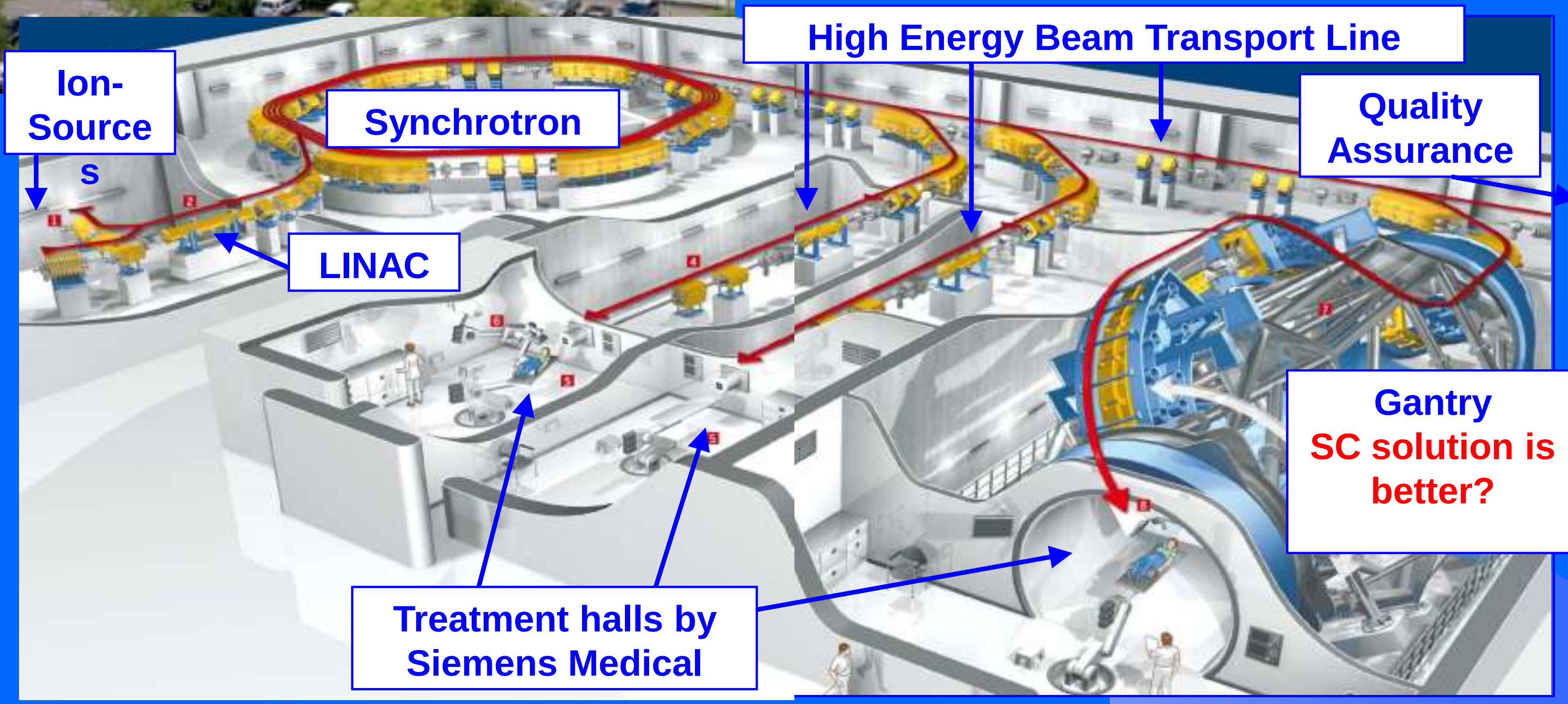
Medical Director: J. Debus

Technical Director: T. Haberer

HIT at Heidelberg

First beam extracted in 2007

First patient: End of 2009



TERA programmes since 1992

TERA has proposed and designed the ‘dual’ National Centre for carbon ions and protons

1. CNAO is being built in Pavia

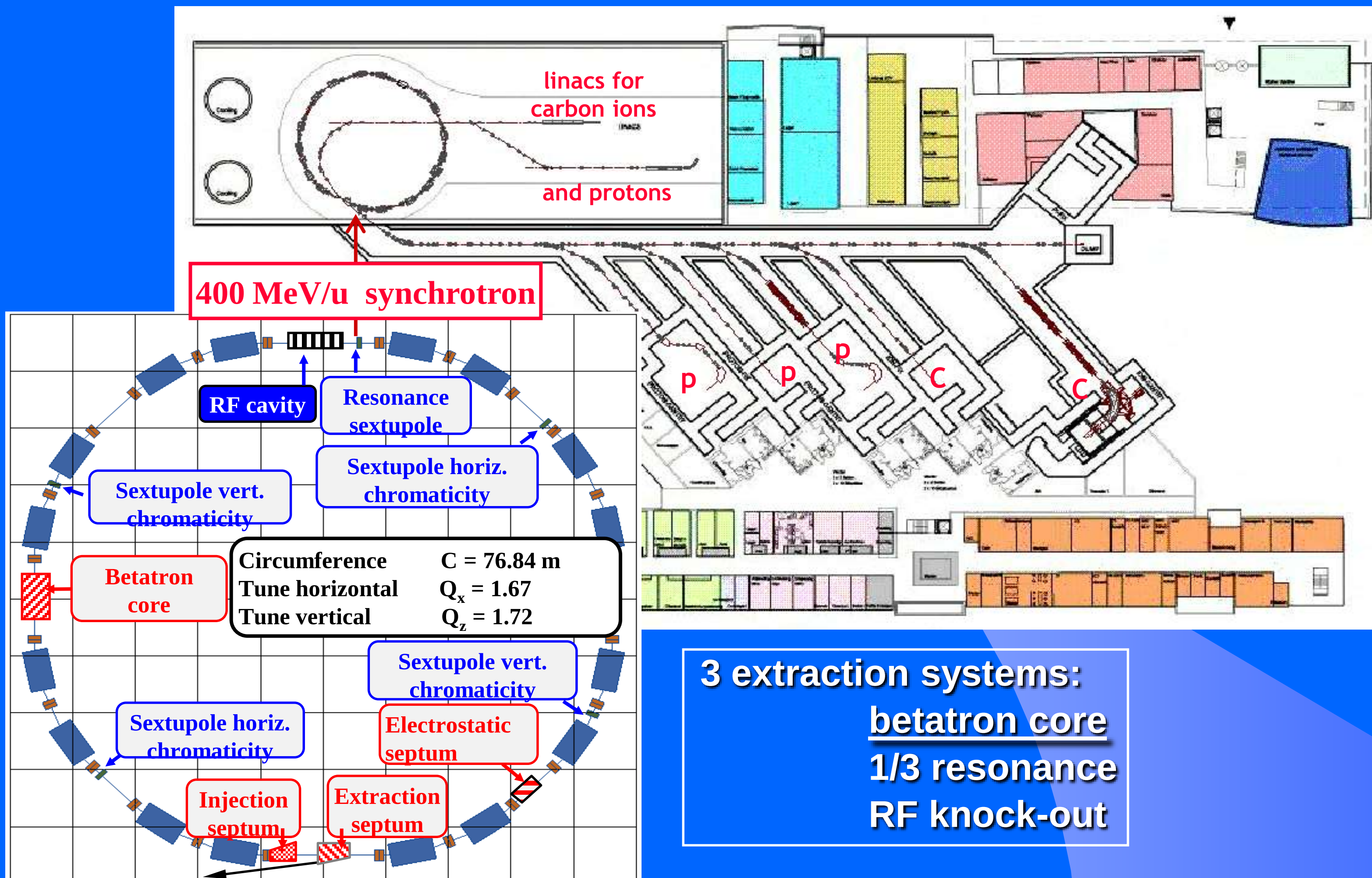
TERA has introduced and developed a novel type of accelerator:

the “cyclinac”

2. “cyclinacs for protons and carbon ions

CERN–TERA–MedAustron Collaboration for optimized medical synchrotron

Project leader: P. Bryant **Chairman of the PAC: G. Brianti**

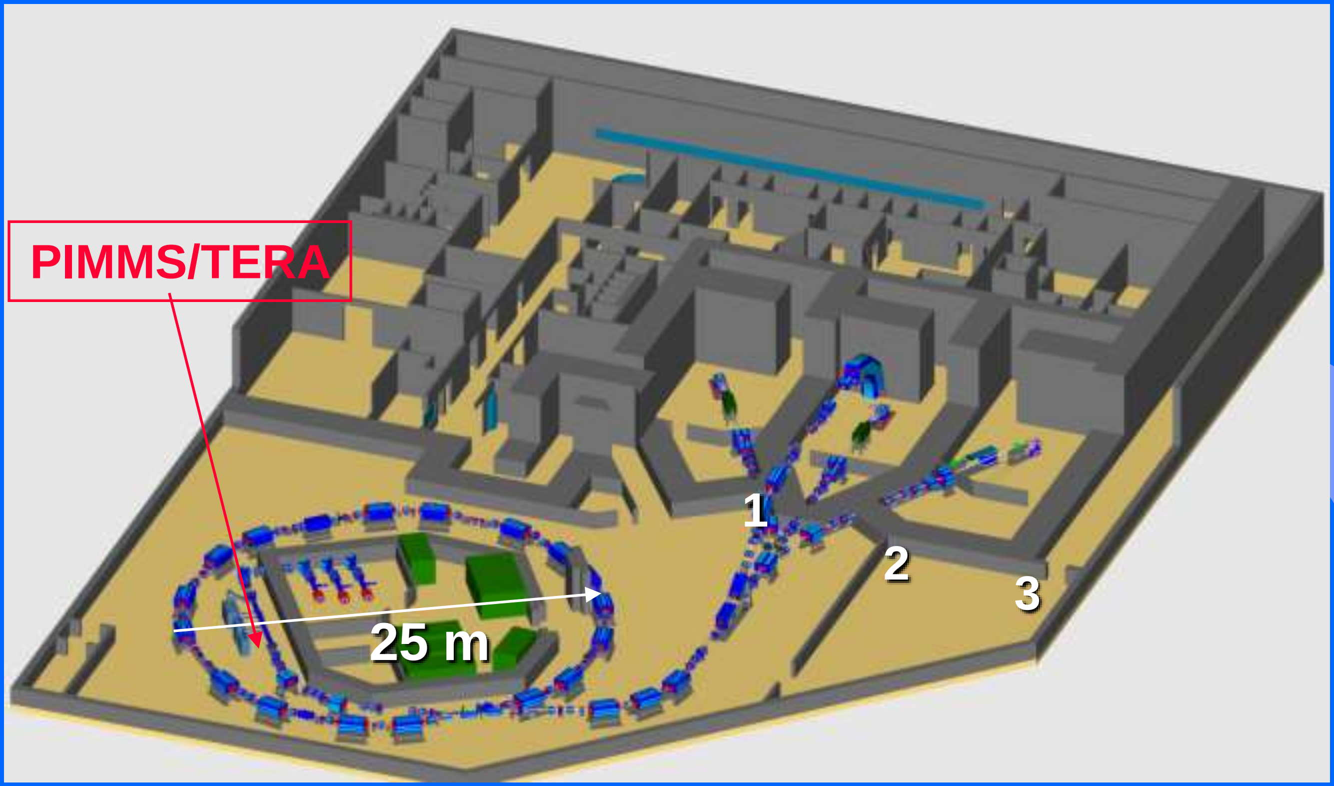


3 extraction systems:
- <u>betatron core</u>
- 1/3 resonance
- RF knock-out

CNAO = Centro Nazionale di Adroterapia

CNAO Foundation created by the Italian Government in 2002:
4 Hospitals in Milan, 1 Hospital in Pavia and TERA

In October 2003 TERA passed to CNAO
the design of CNAO (3000 pages) and 25 people



Since 2004 INFN is "Istitutional Participant" with people and important construction responsabilities

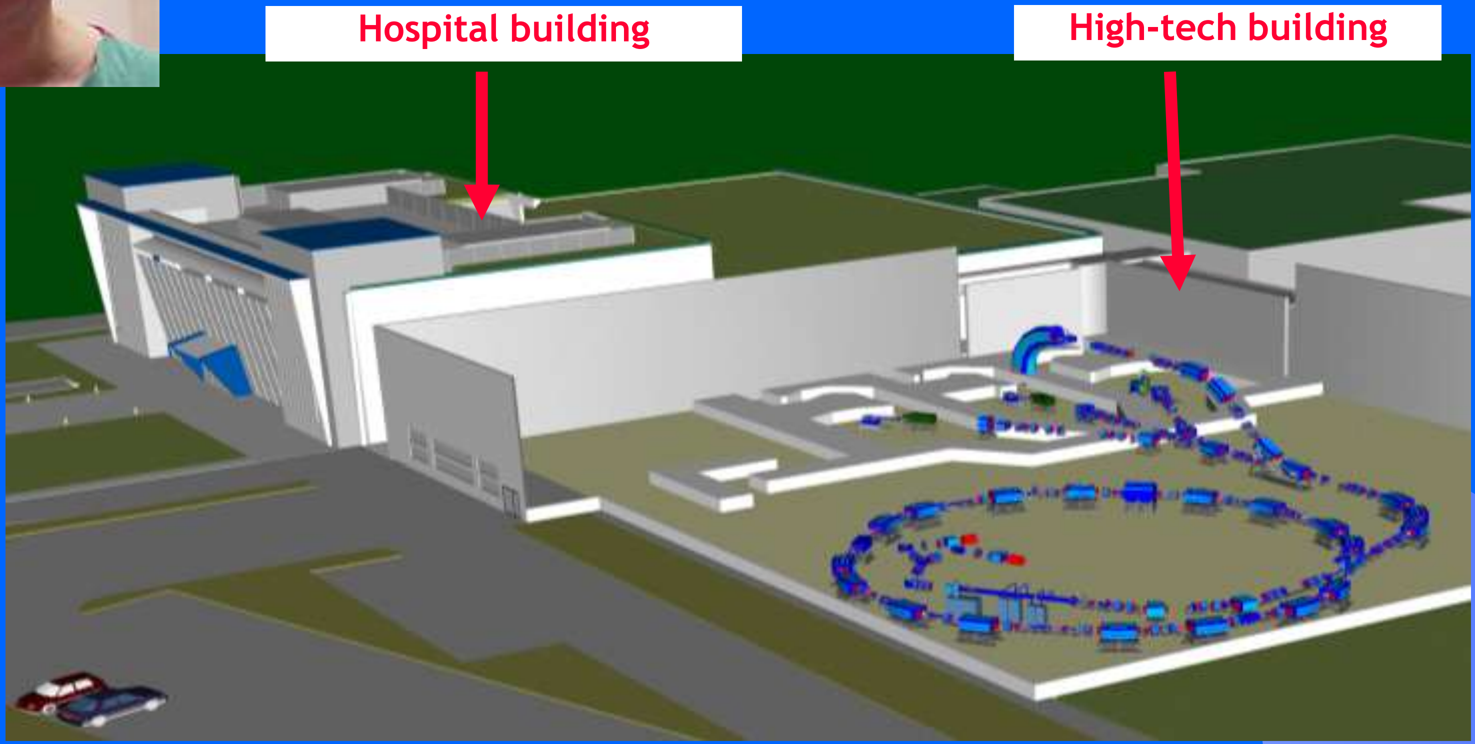
(Caudio Sanelli)

INFN runs CATANA for eye protontherapy in Catania

CNAO = Centro Nazionale di Adroterapia at Pavia

President: Erminio Borloni

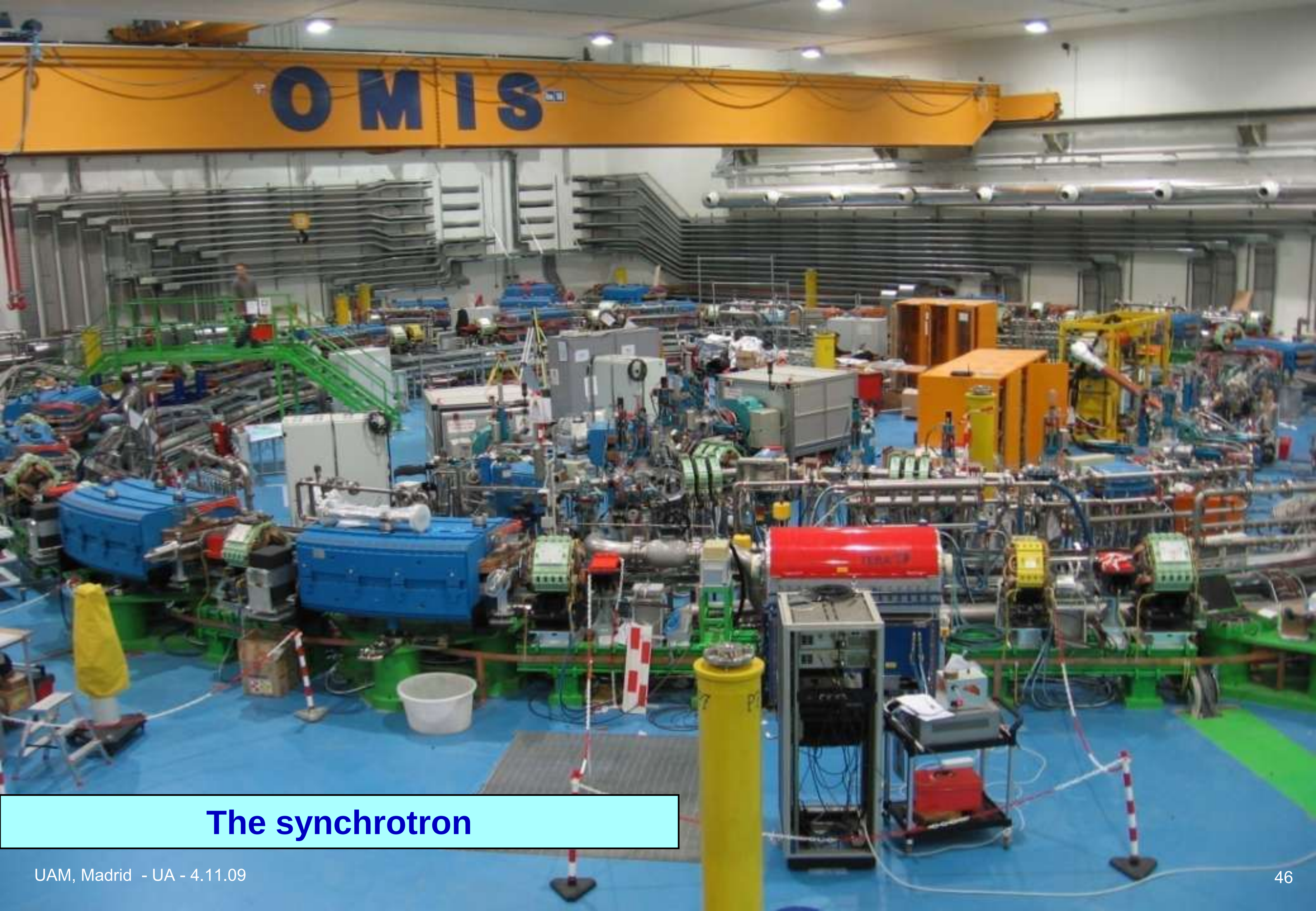
Medical Director: Roberto Orecchia **Technical Director: Sandro Rossi**



CNAO = Centro Nazionale di Adroterapia at Pavia

CNAO = Centro Nazionale di Adroterapia at Pavia

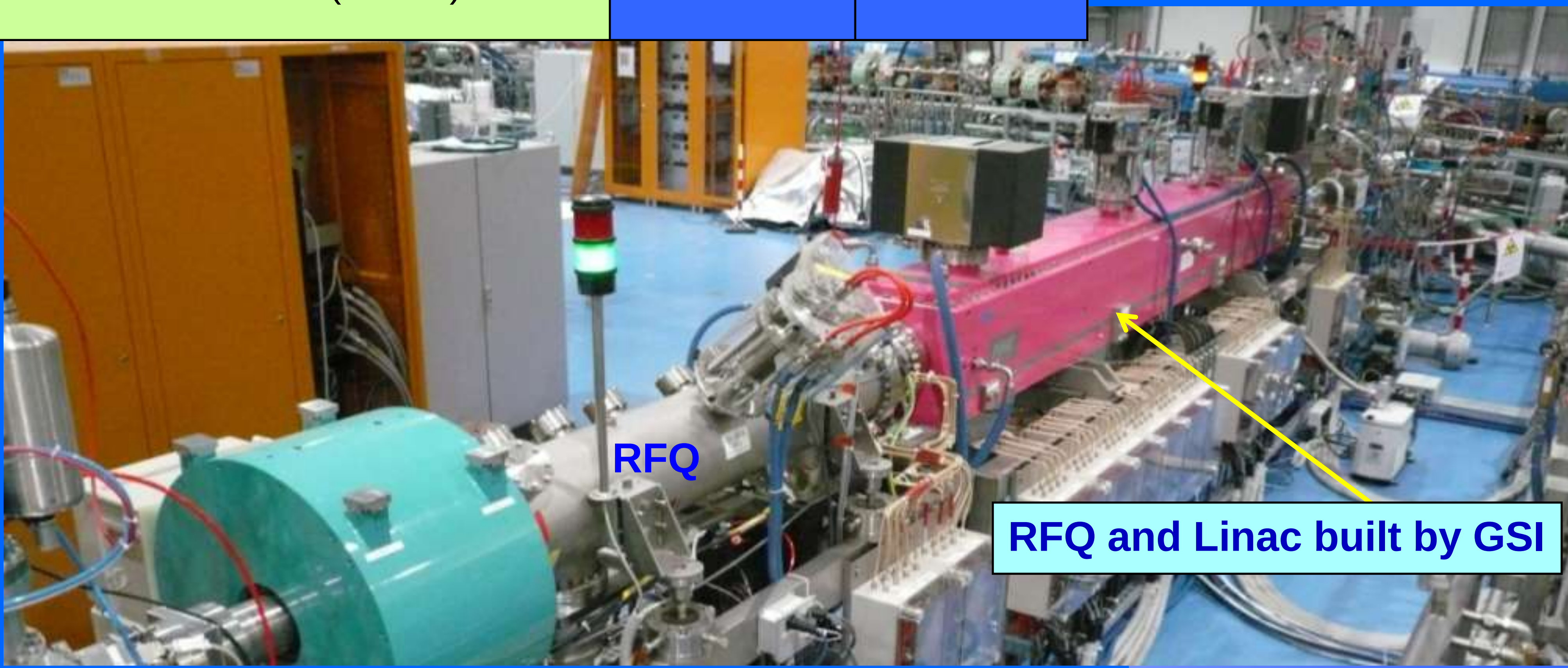
Patient reception



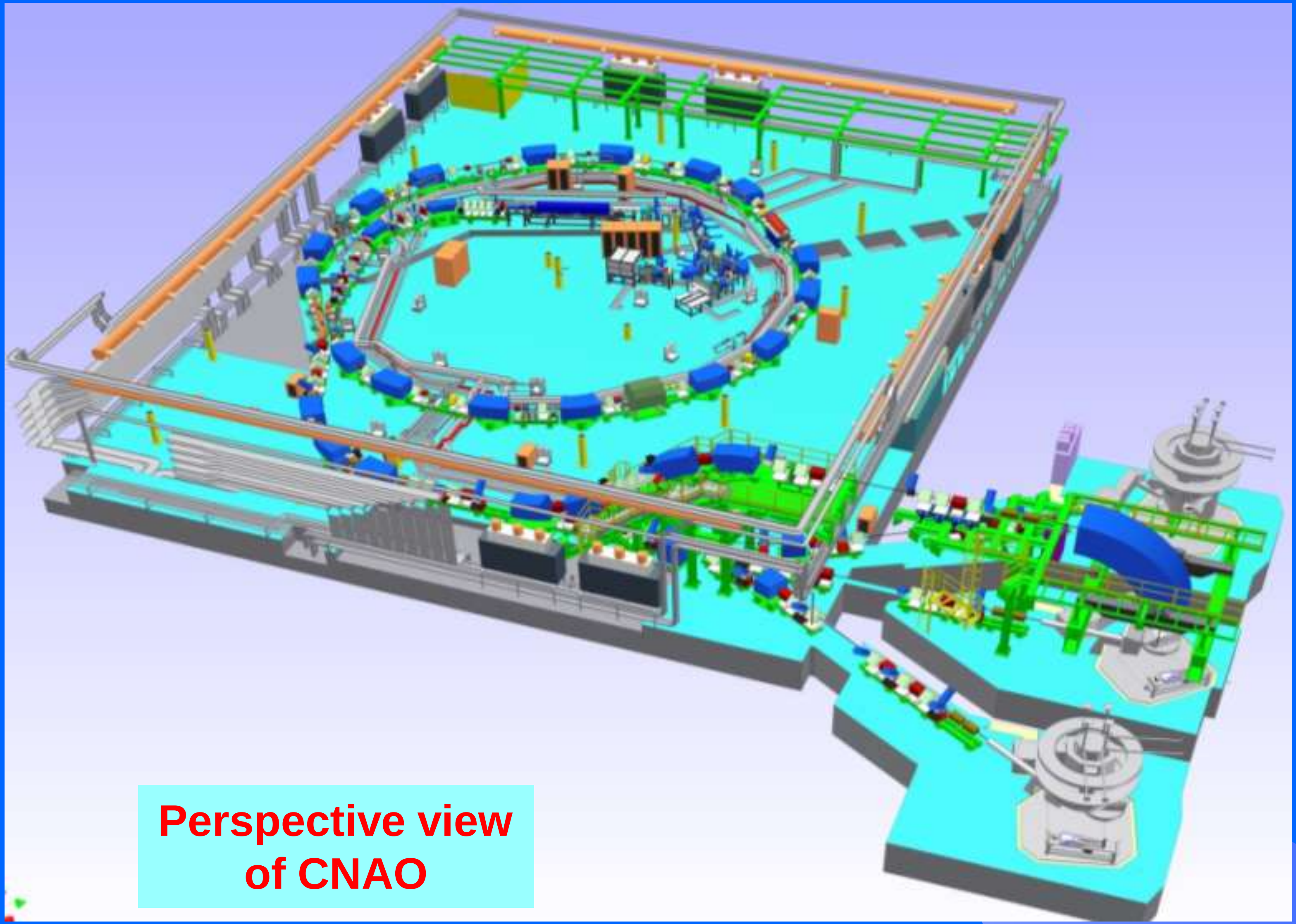
The synchrotron

Linac tests: July 2009

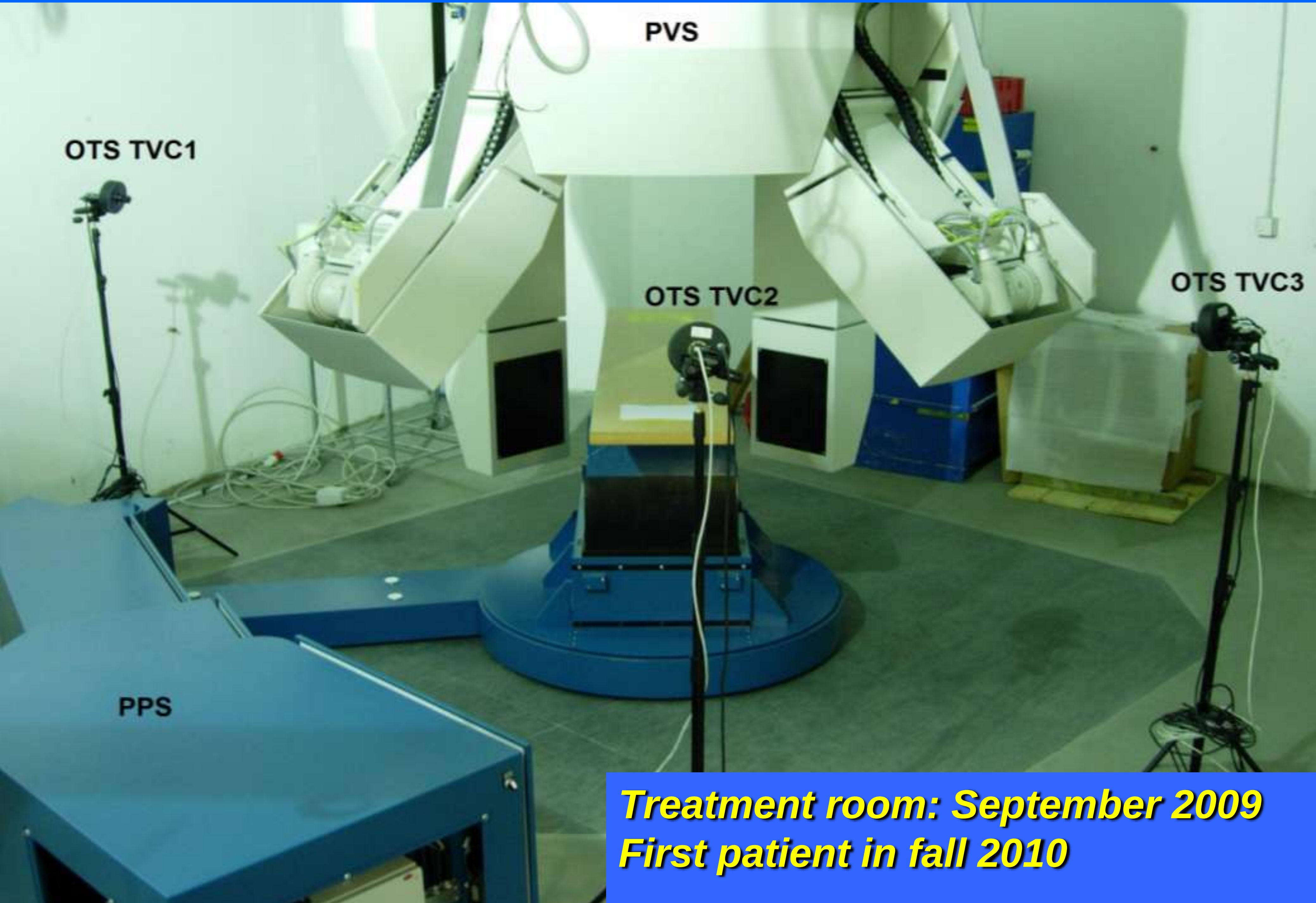
At the LINAC output	Measured	Project vaue
C6+ current (7 MeV/u)	135 microA	120 microA
H+ current (7 MeV)	1200 microA	750 microA



CNAO at Pavia



Perspective view of CNAO

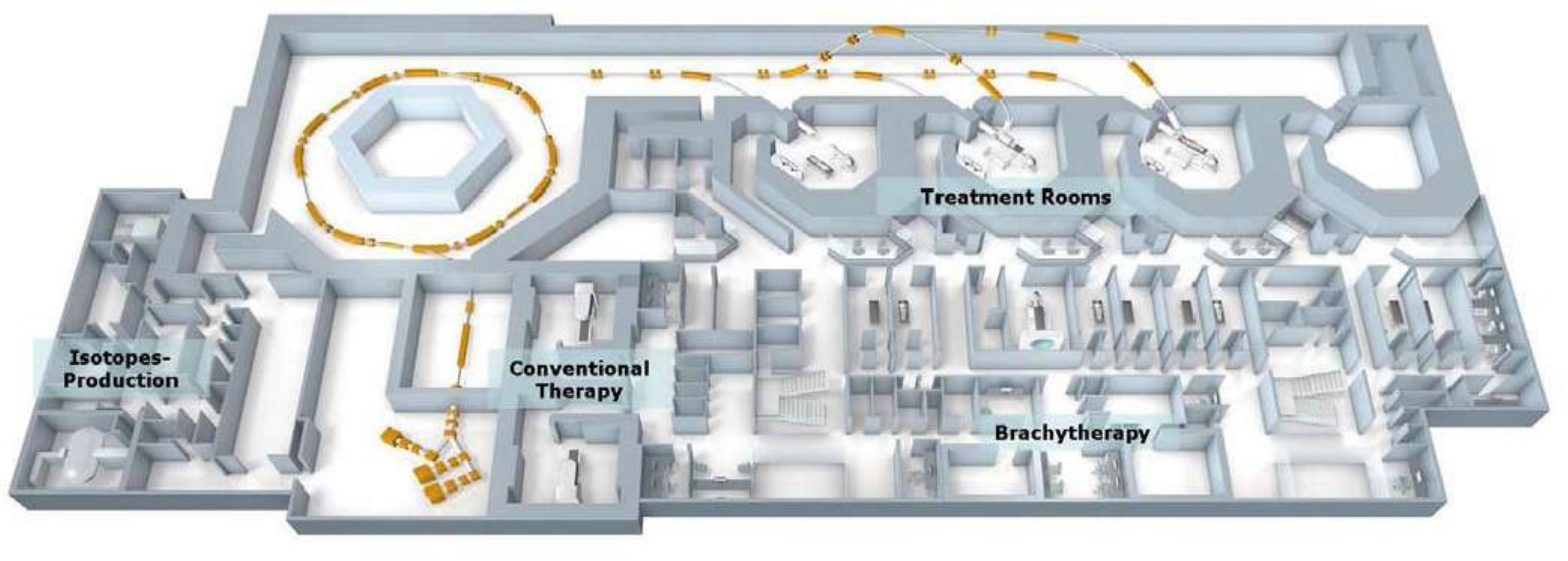


Treatment room: September 2009
First patient in fall 2010

Siemens Medical is building for 2012 a 'dual' centre in Kiel (*)

NRoCK

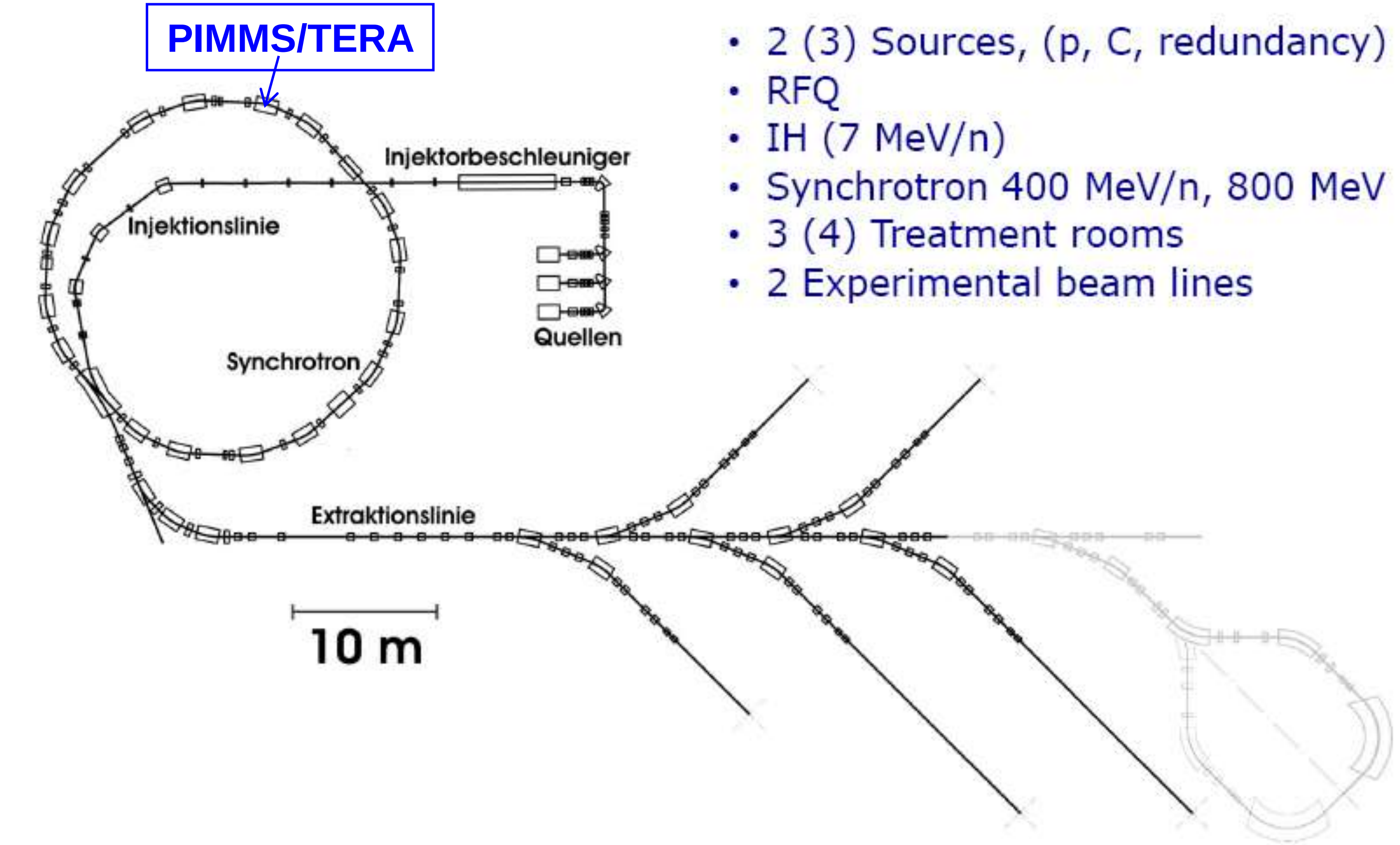
North European Radiooncological Center Kiel



(*) And another one in Marburg

Courtesy M. Benedikt

In 2007 MedAustron has been approved for Wiener Neustadt



- 2 (3) Sources, (p, C, redundancy)
- RFQ
- IH (7 MeV/n)
- Synchrotron 400 MeV/n, 800 MeV
- 3 (4) Treatment rooms
- 2 Experimental beam lines

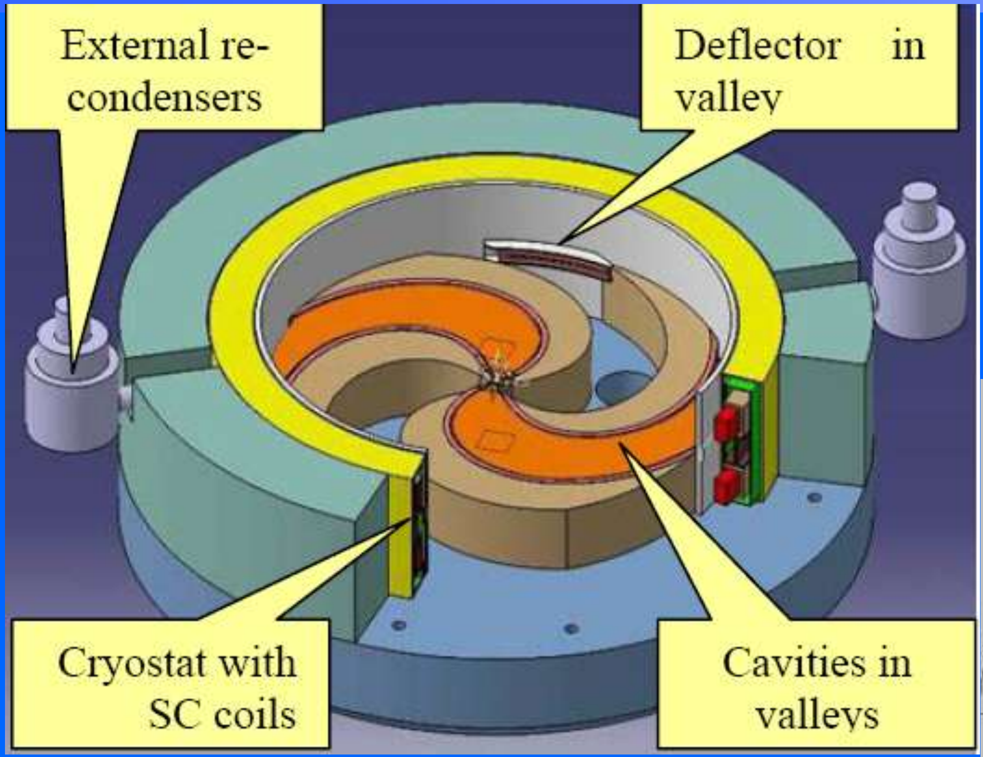
MedAustron will build a centre based on the CNAO construction drawings (by agreement with CERN-CNAO-INFN)

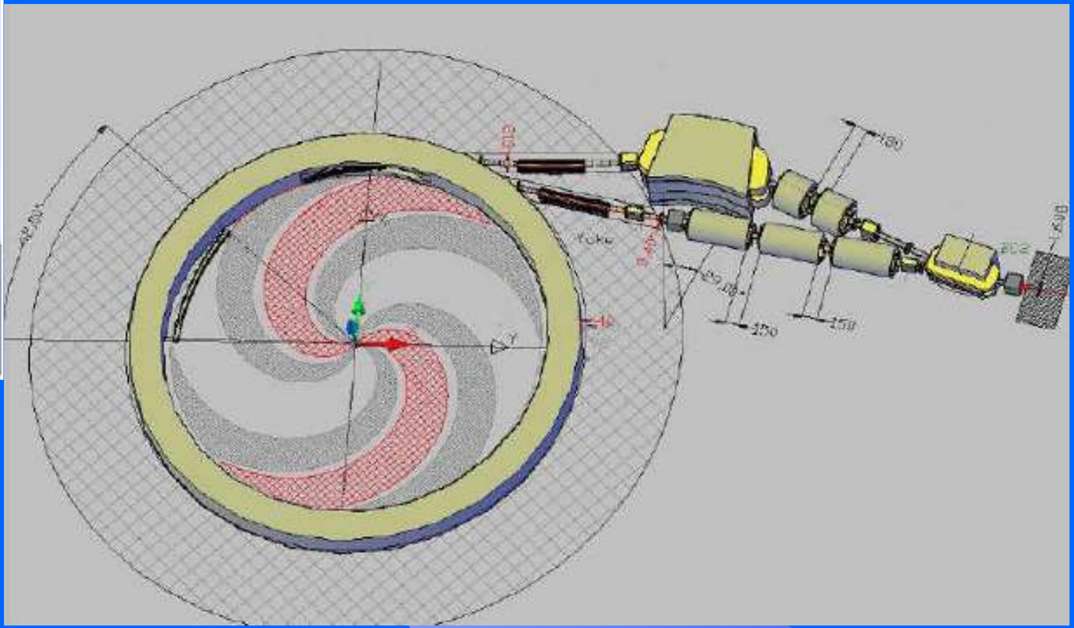
Projet ETOILE

End of 2009: Choice of the constructor

Courtesy Y. Jongen

"Archade" (At Ganil in Caen, Fr) is based on the new IBA400 MeV/u superconducting cyclotron





- As soon as the agreement with Archade is finalized, IBA will start the construction of the prototype

ENLIGHT and the European projects

European Network for LIGht-ion Hadron Therapy – 2002 - 2005

- GSI project for the University of Heidelberg Clinics (ready to treat)
- TERA project for CNAO in Pavia (completing construction)
- Marburg and Kiel centres (in construction by Siemens Medical)
- Med-Austron for Wiener Neustadt (approved)
- ETOILE in Lyon (approved)
  Competitive tendering

SINCE 2002 THESE GROUPS + CERN + GSI AND MANY OTHERS ARE PART OF THE

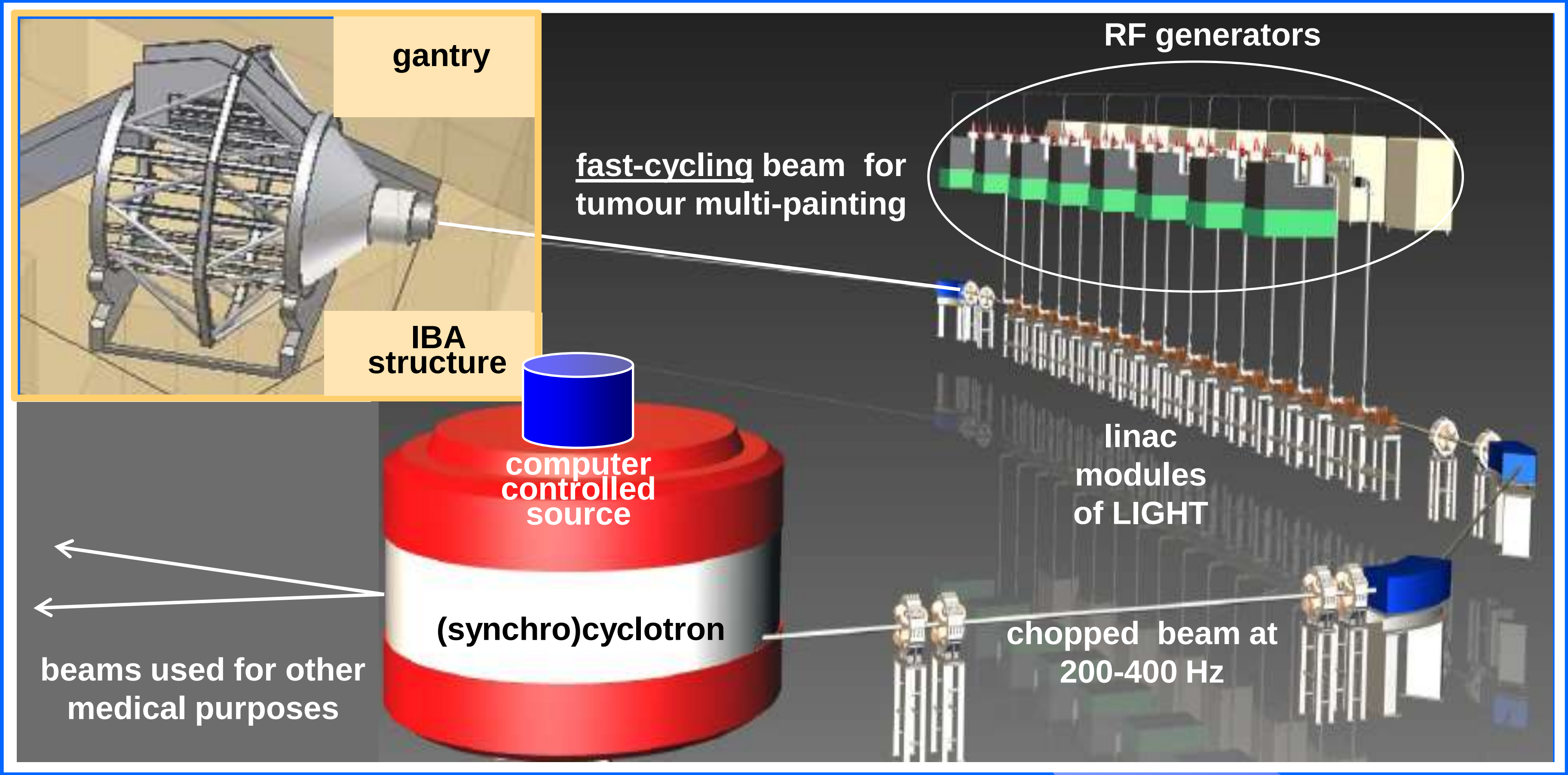
ENLIGHT PLATFORM co-ordinated by Dr. Manjit Dosanjh

Programs approved in FP7 : PARTNER , ULICE , ENVISION

for a total of 20 MEuro

The next fast cycling accelerators for carbon ion therapy

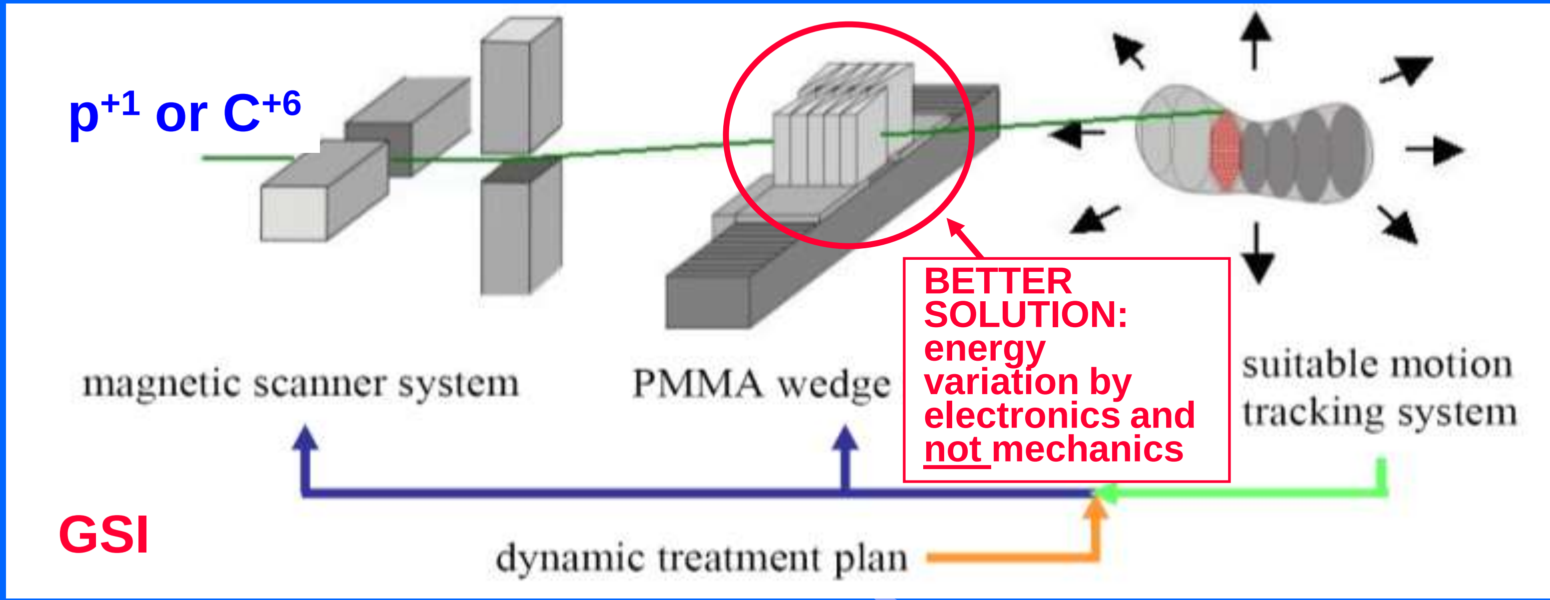
TERA Cyclinac = Cyclotron+Linac for Image Guided HadronTherapy



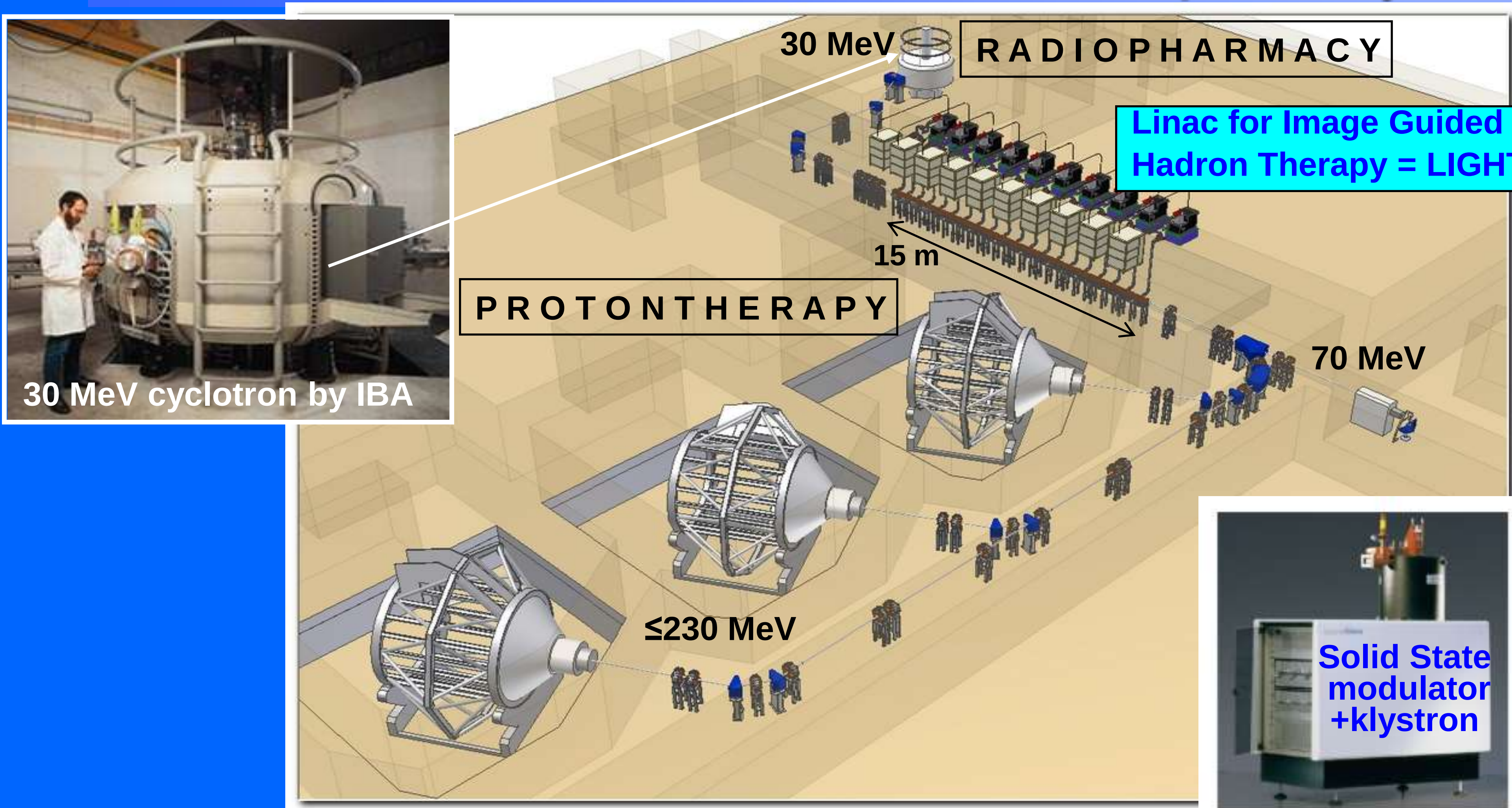
The energy is adjusted in 2 ms in the full range by changing the power pulses sent to the 16-22 accelerating modules

The charge in the next spot is adjusted every 2 ms with the computer controlled source

GSI approach to treat moving organs: depth with fast absorbers



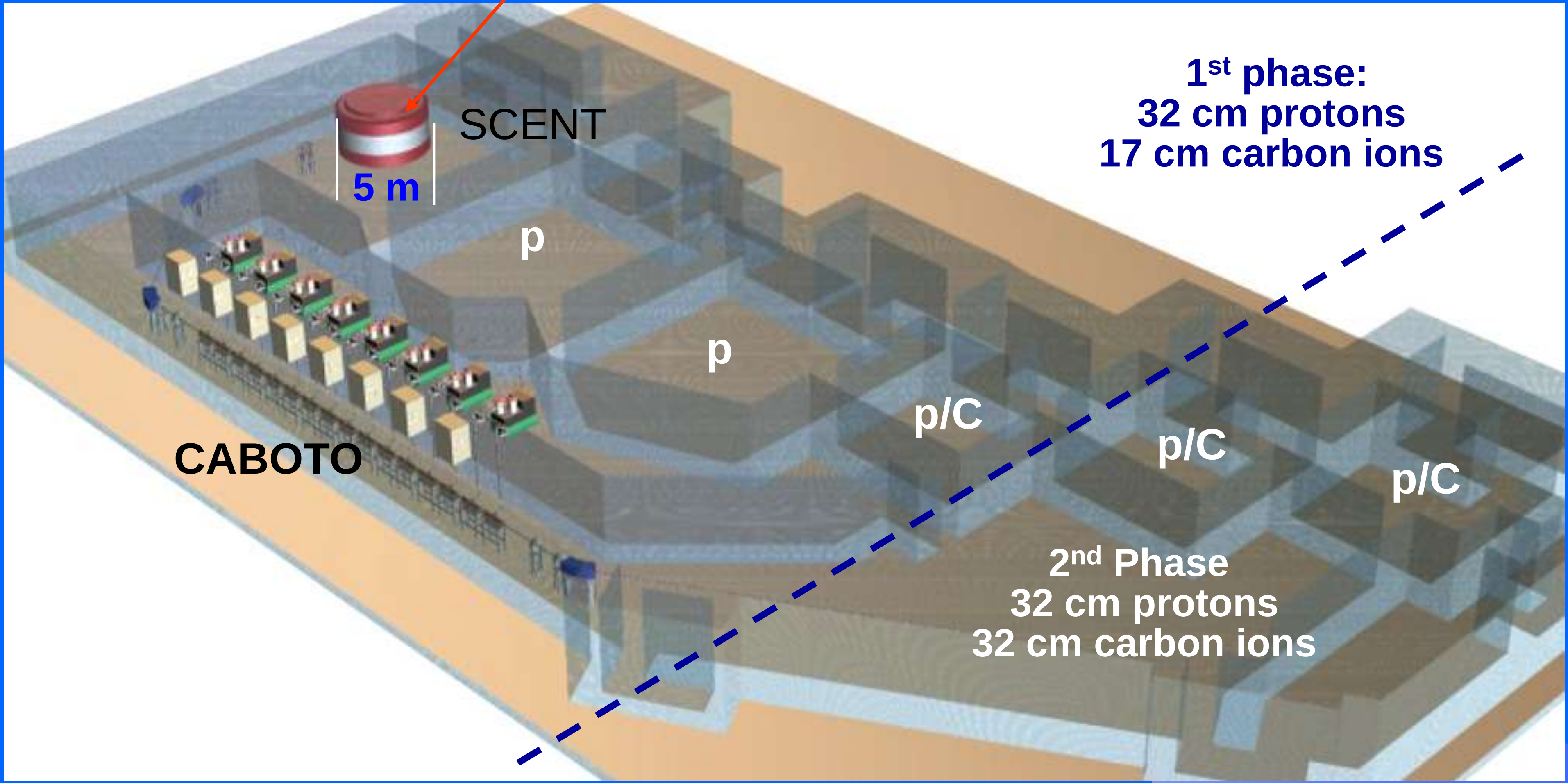
IDRA = Institute for Diagnostics and Radiotherapy : a proton cyclinac



A.D.A.M. SA, Application of Detectors and Accelerators to Medicine, a CERN spin-off company will build LIGHT, and has an agreement with IBA for the delivery of the rest and the overall control

The two phases of the dual centre for Catania

Superconducting cyclotron by LNS/IBA (250 MeV protons and 3600 MeV carbon ions) is commercialized by IBA



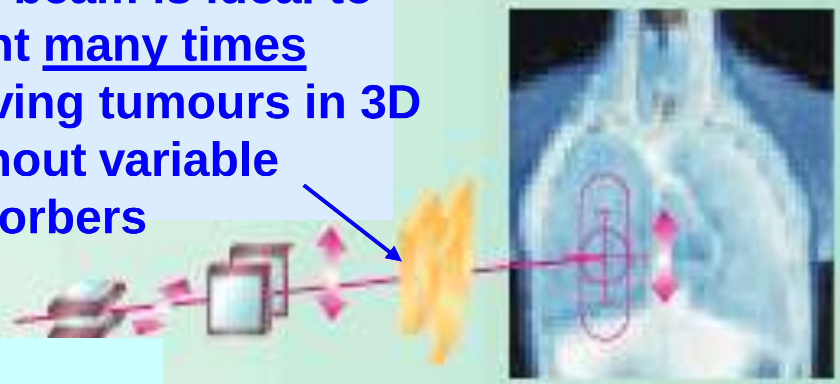
Properties of fast-cycling accelerators

Accelerator	Beam always present during treatments	Energy variation by electronic means	Time needed for varying the energy
Cyclotron	<u>Yes</u>	No	80é100 ms (*)
Synchrotron	No	<u>Yes</u>	1 second
FCA	<u>Yes</u>	<u>Yes</u>	1 millisecond

The energy is changed by adjusting the RF pulses to the modules

(*) With movable absorbers

The beam is ideal to paint <u>many times</u> moving tumours in 3D without variable absorbers



Summary

Many 15-70 MeV high-current cyclotrons are commercially available for isotope production. Systemic hadrontherapy could cure metastases. High current accelerators may help solving the technetium crysis.

For protontherapy, which is booming, five companies offer cyclotron/synchrotron based turn-key centres

For carbon ion therapy, Europe is well advanced (5 centres in construction) and four companies offer synchrotron based centres, but the difficulty still is in the dimensions of the ion gantry (1st challenge: new superconducting gantries).

For the 2nd challange, i.e the following of moving tumour targets, a fast cycling accelerator with variable energy would allow electronically driven multipainting : cyclinacs are the closest solution.


THE END
CNAO in Pavia