ACCELERATORS AND CANCER THERAPY

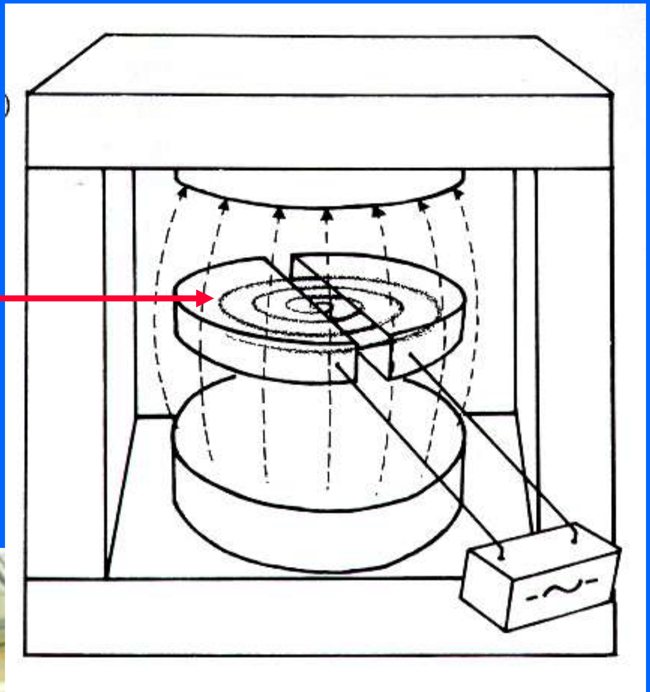
Ugo Amaldi

University Milano Bicocca and TERA Foundation

Accelerators

1930: invention of the cyclotron

Spiral tajectory of an accelerated nucleus



Ernest Lawrence

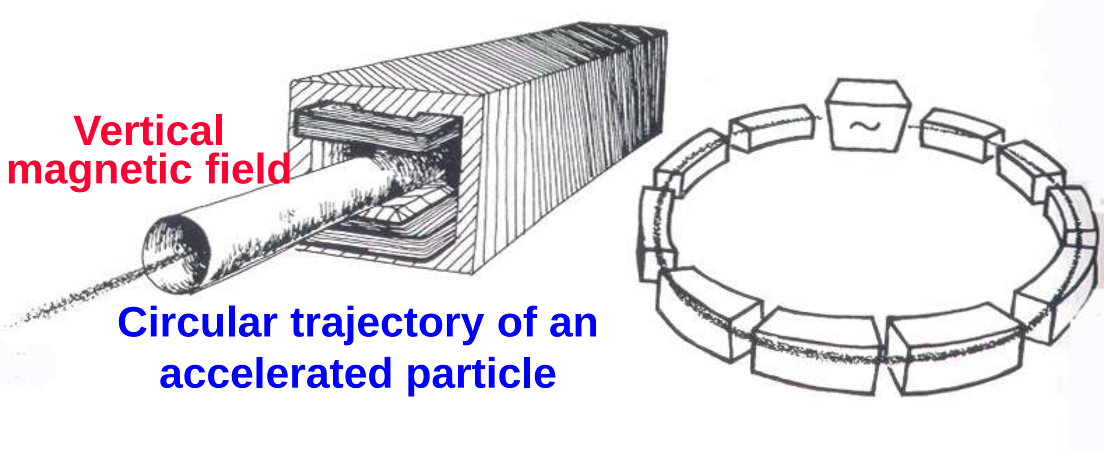
(1901 – 1958)

Modern cyclotron

1944: E. McMillan and V.J.Veksler

The «synchrotron»

"Phase stability principle"



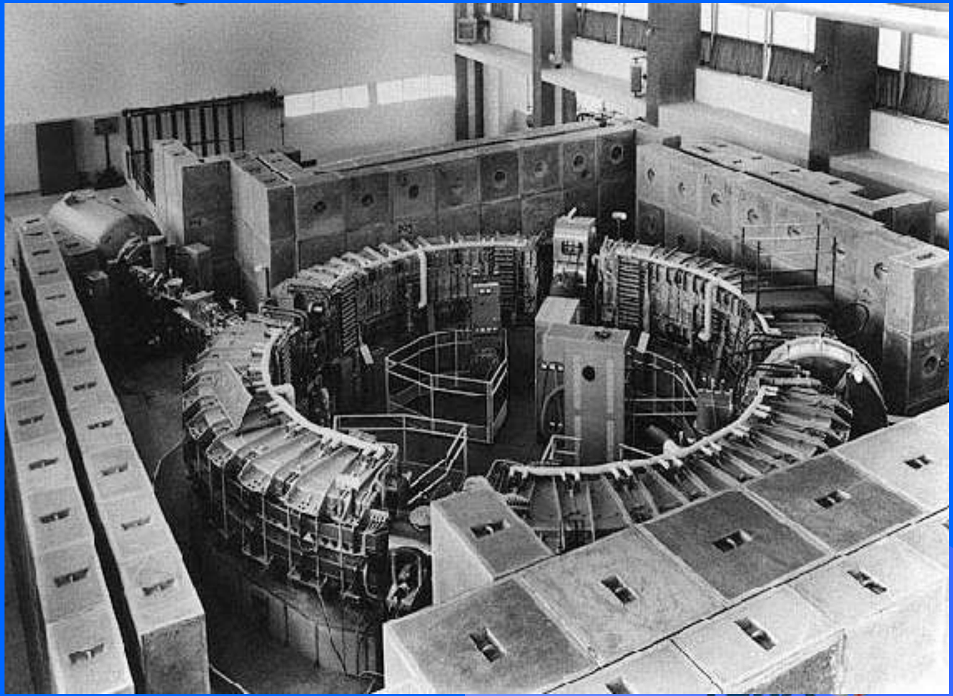
1 GeV

electron synchrotron

Frascati - INFN - 1959

1959: Veksler visits McMilan

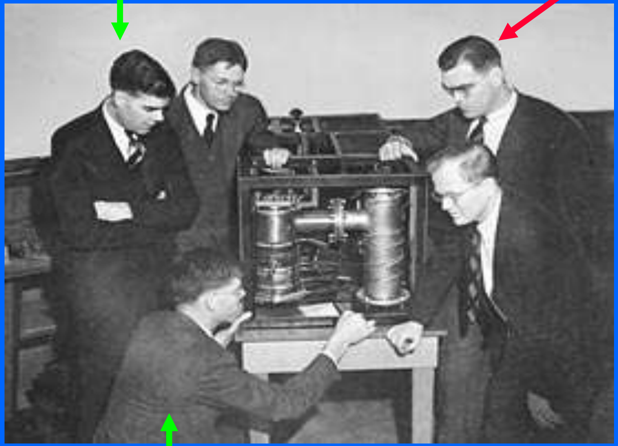
at Berkeley



The first electron linac

Sigmur Varian

William W. Hansen



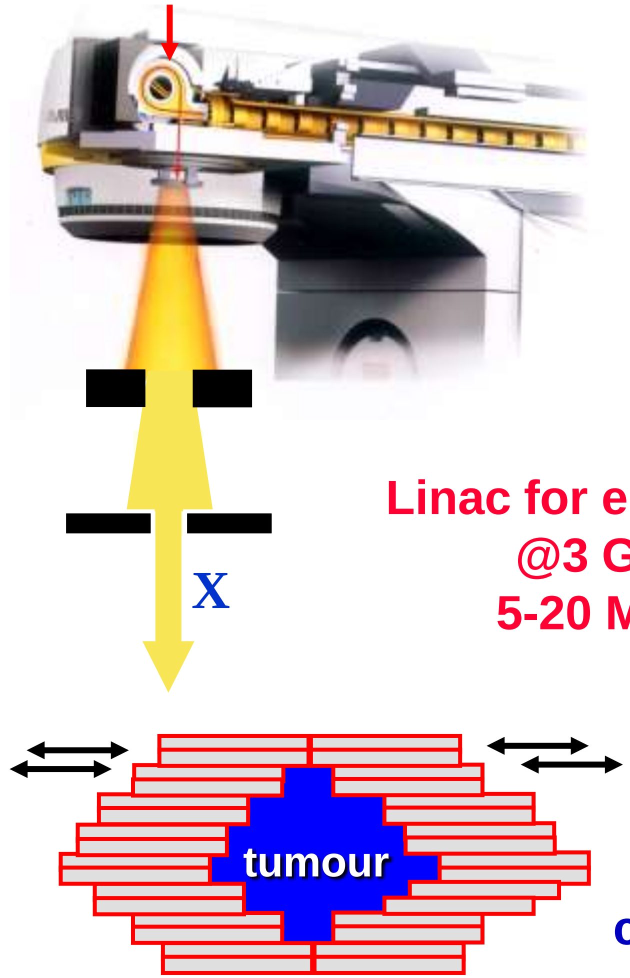
Russell Varian

1939

Invention of the klystron

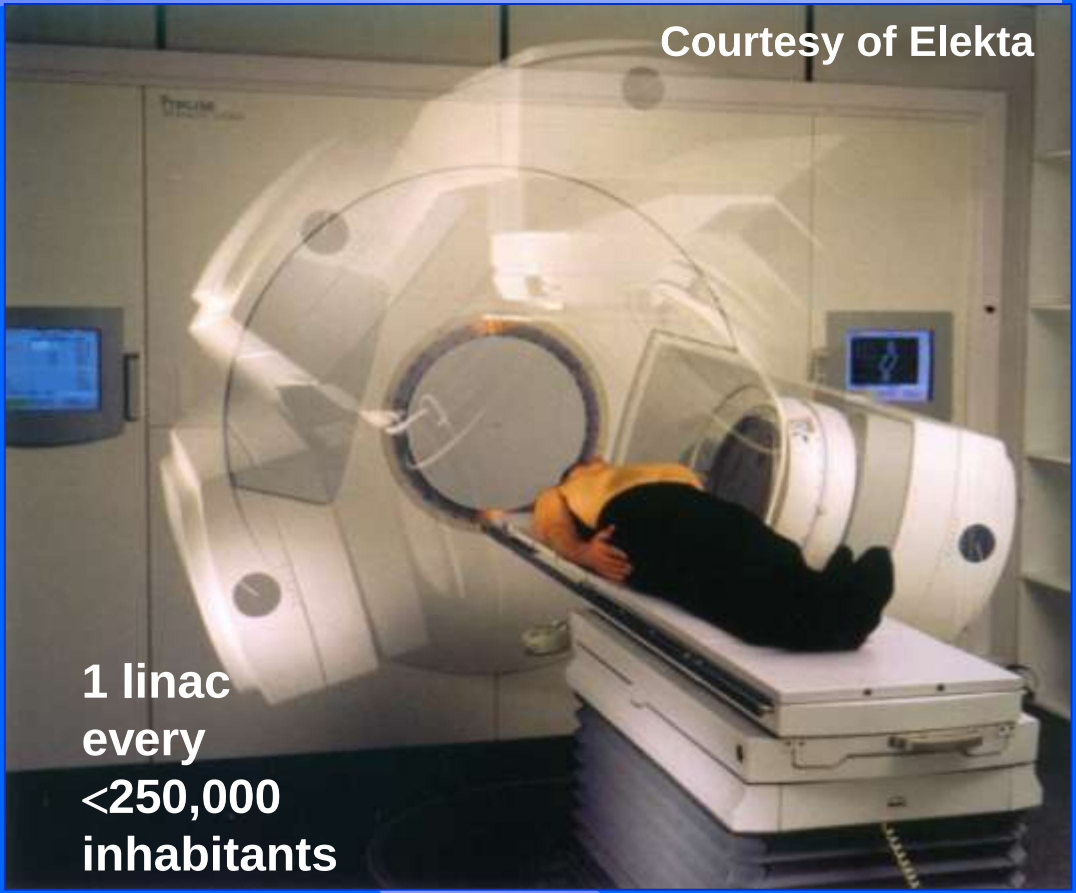
1947
linac for electrons
1.5 MeV at 3 GHz

'Conventional' radiotherapy: linear accelerators dominate



Linac for electrons
@3 GHz
5-20 MeV

Multileaf collimator



20 000 patients per year every 10 million inhabitants

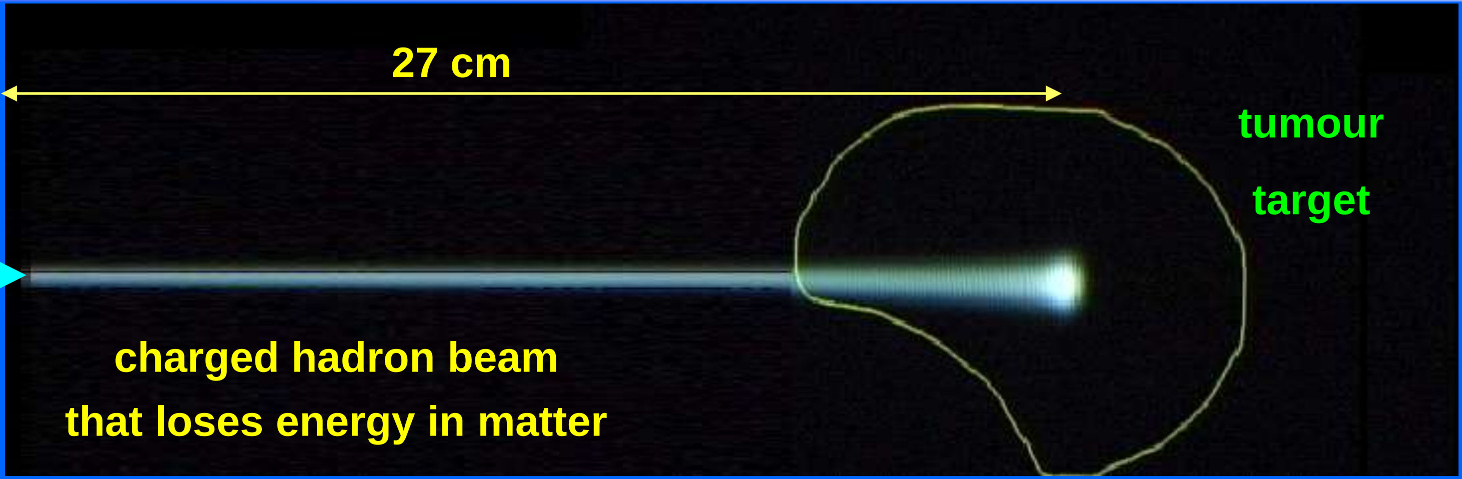
Macroscopic distribution of the dose

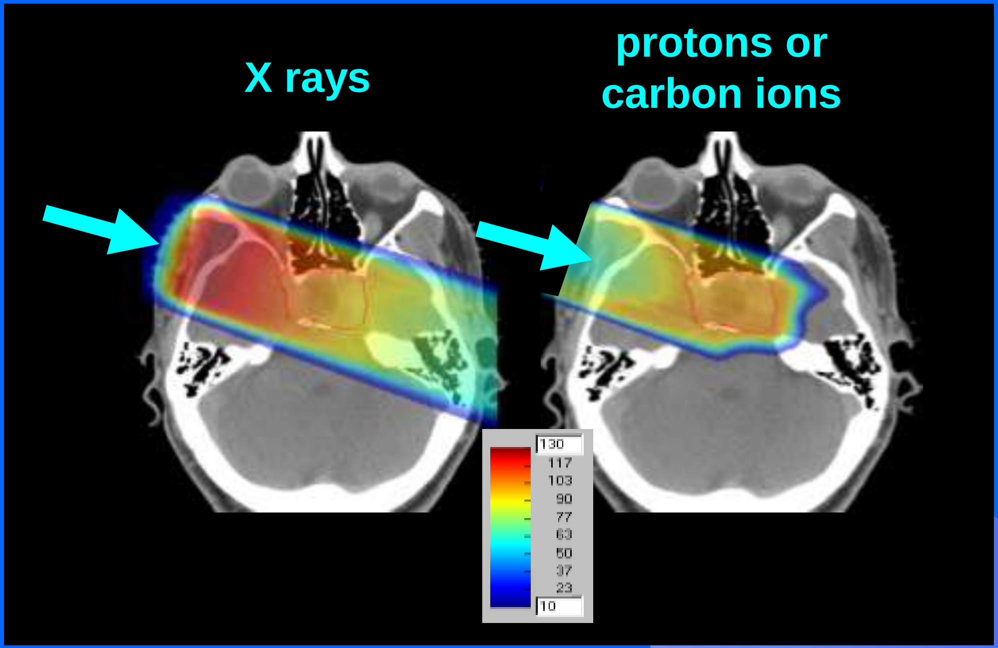
Protons and ions spare healthy tissues

200 MeV - 1 nA protons

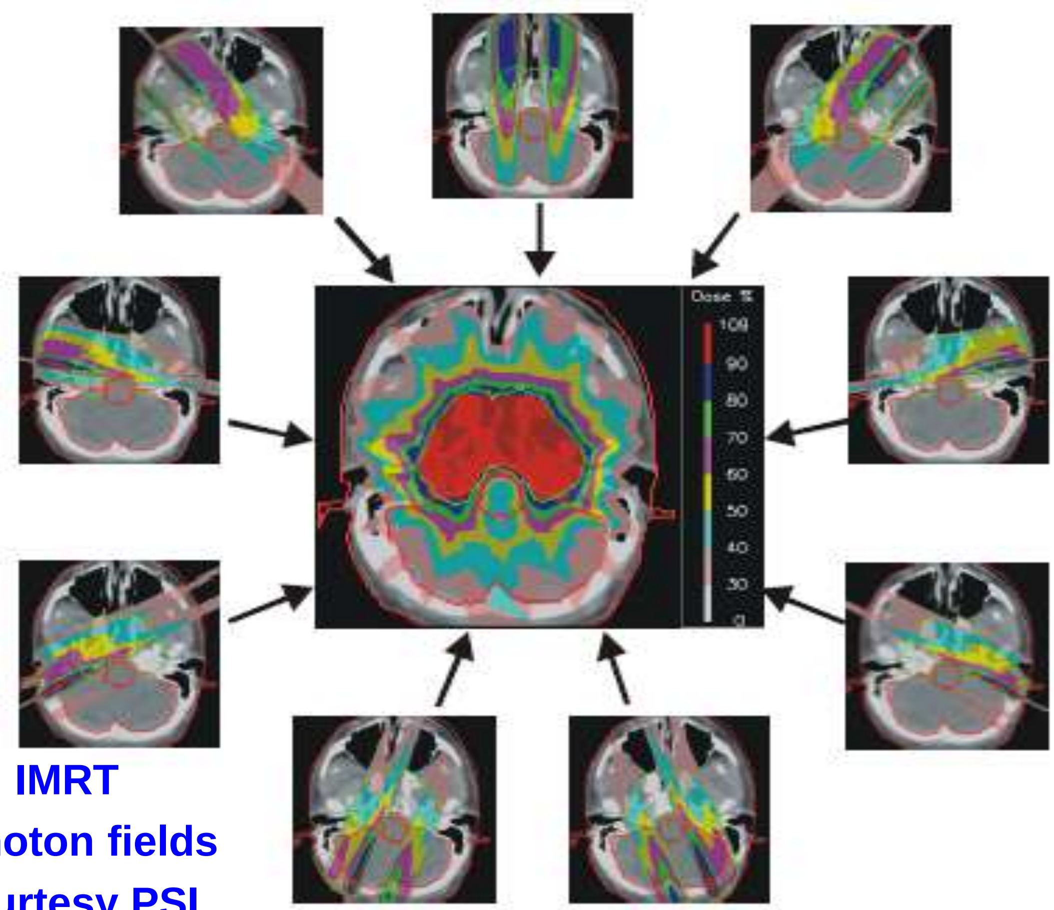
4800 MeV – 0.1 nA carbon ions

which can control radioresistant tumours





Macroscopic distribution of the X ray dose

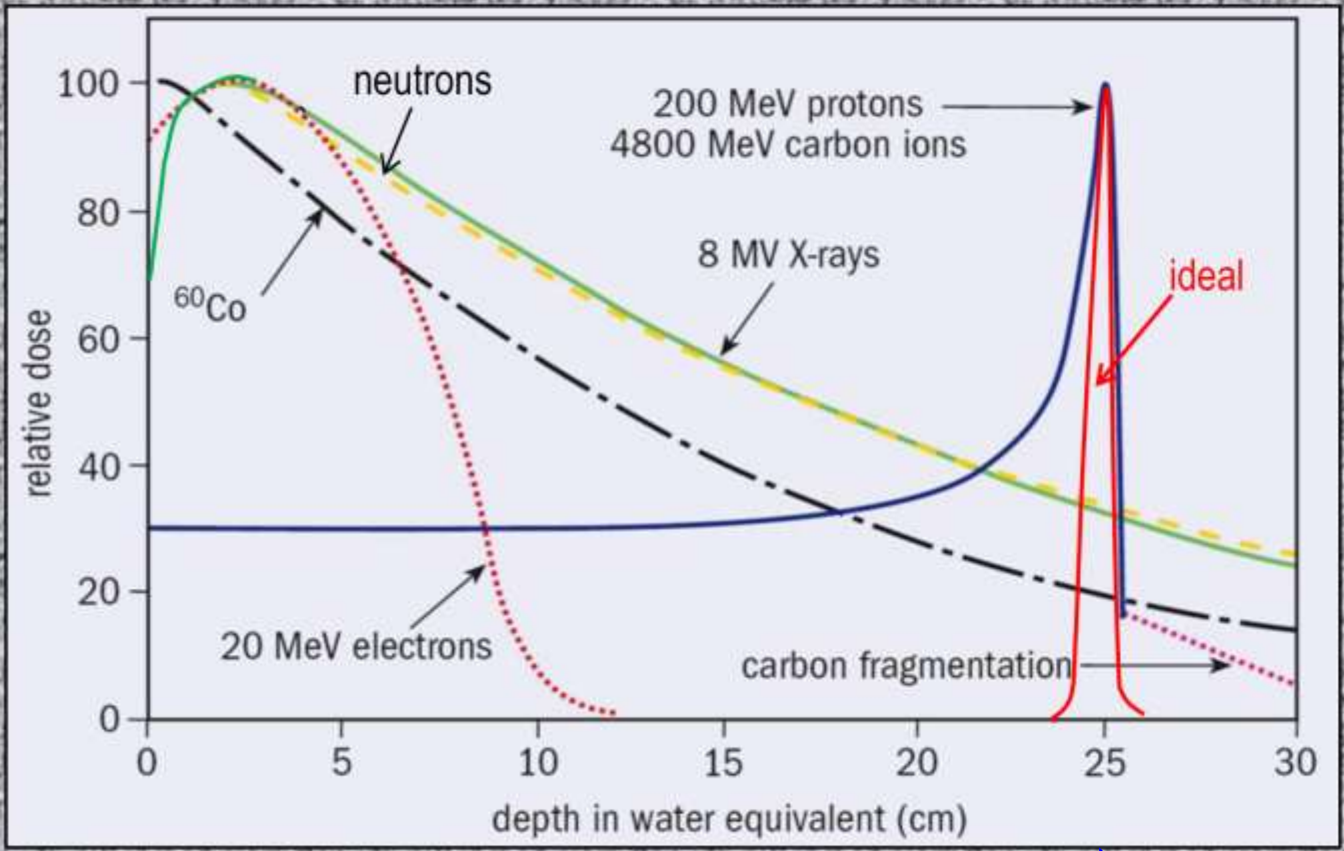


IMRT
9 photon fields
Courtesy PSI

At present the best is " Intensity Modulated Radiation Therapy" = IMRT
In future "Image Guided Radio Therapy" to follow moving organs

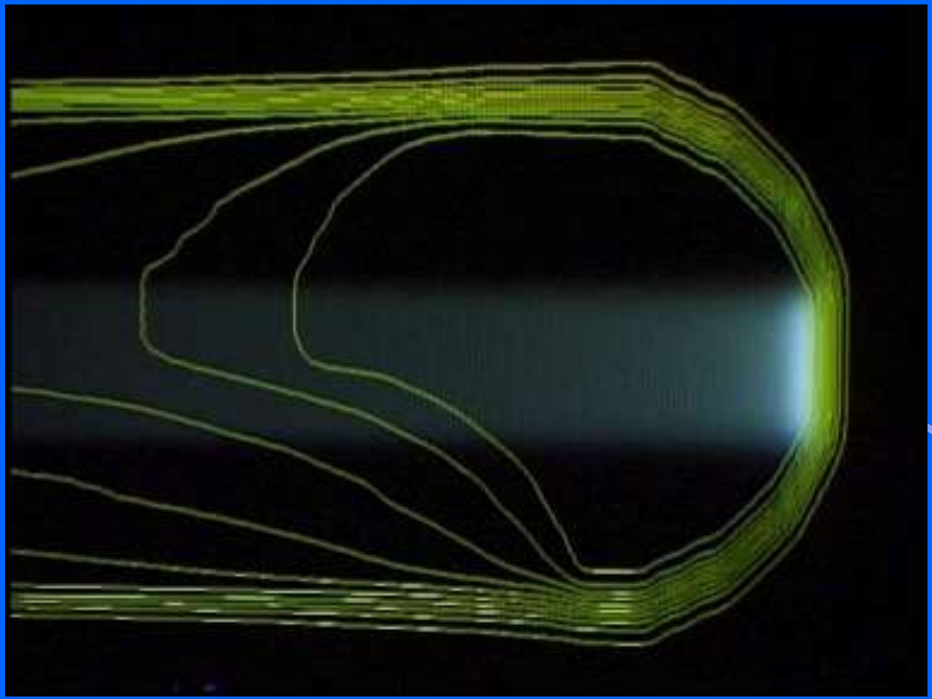
Dose delivery to a tumour target

The icon of radiation therapy with charged hadrons



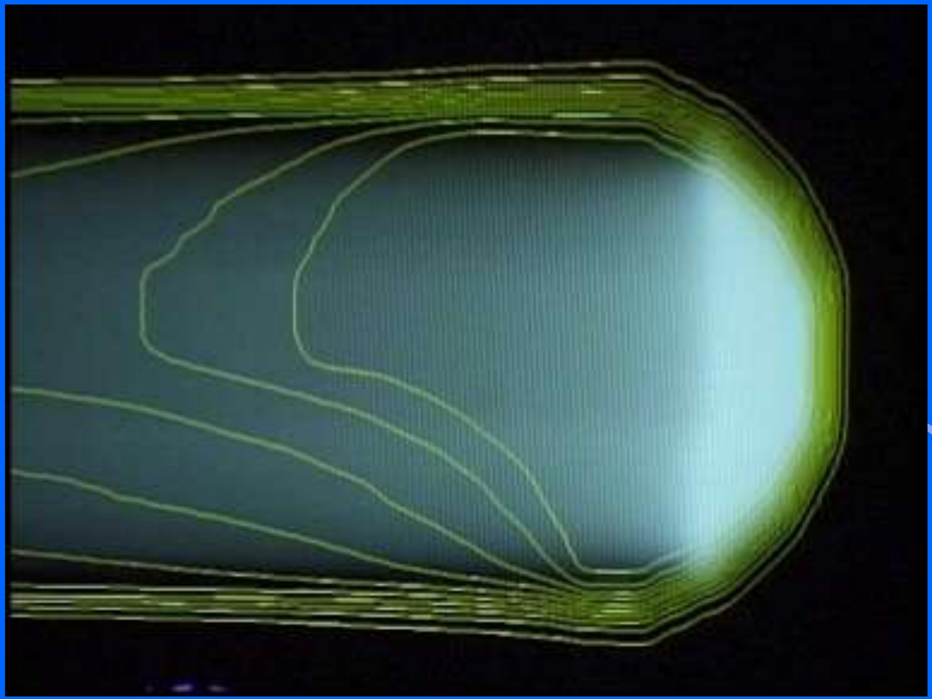
Radiation beam in matter

Optimal dose distribution: active ‘spot scanning’ á la PSI



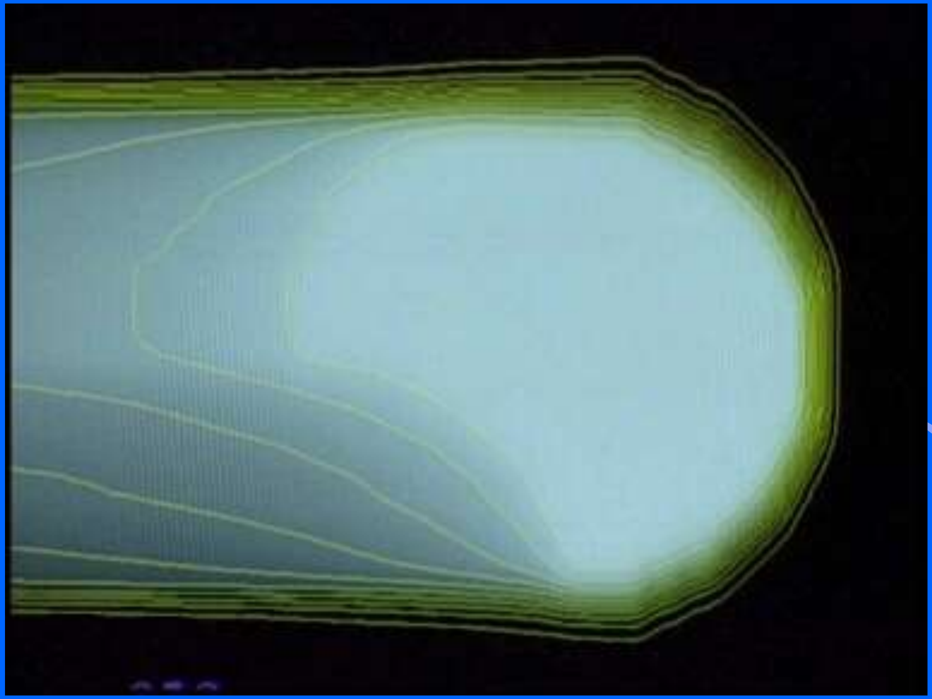
- PROTONS

Optimal dose distribution: active 'spot scanning' á la PSI



❖ PROTONS

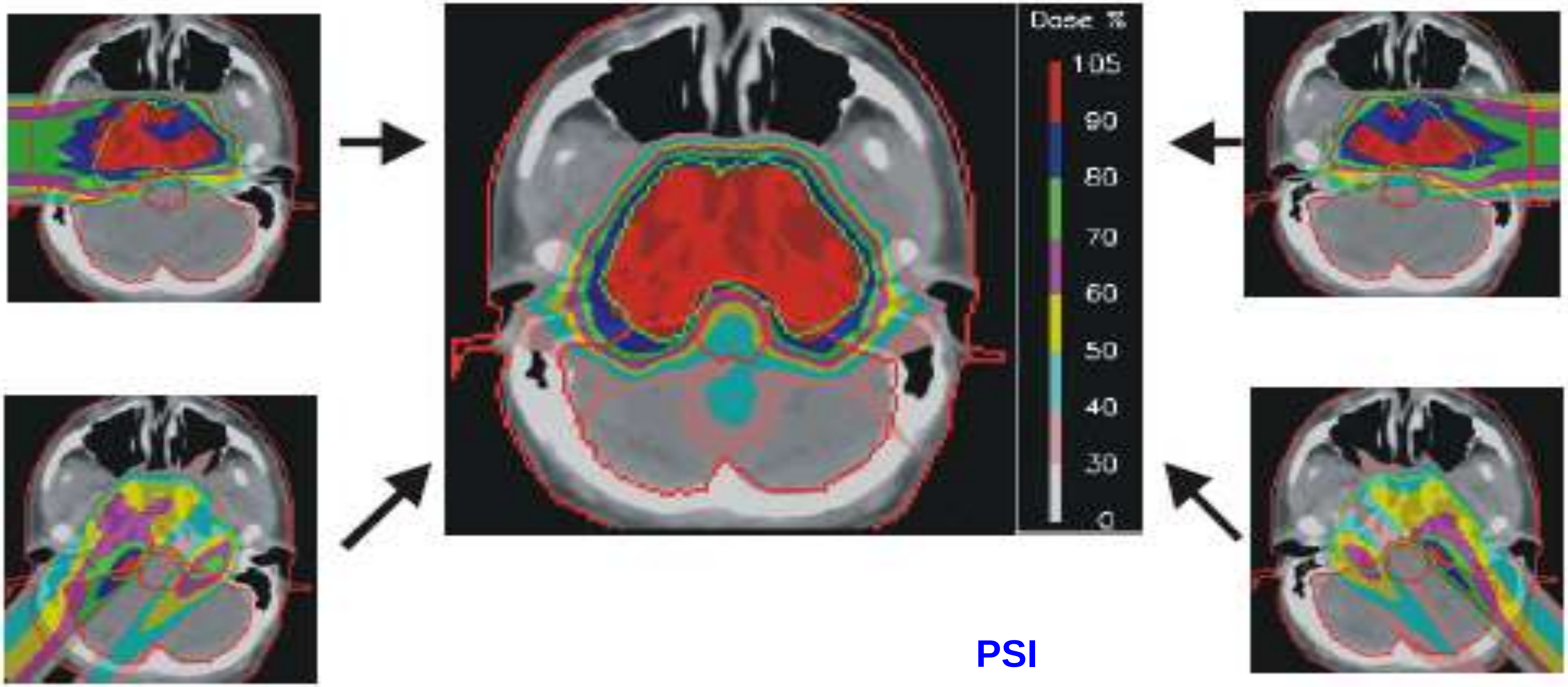
Next: Spot scanning compensated by correcting the spot position



❖ **PROTONS**

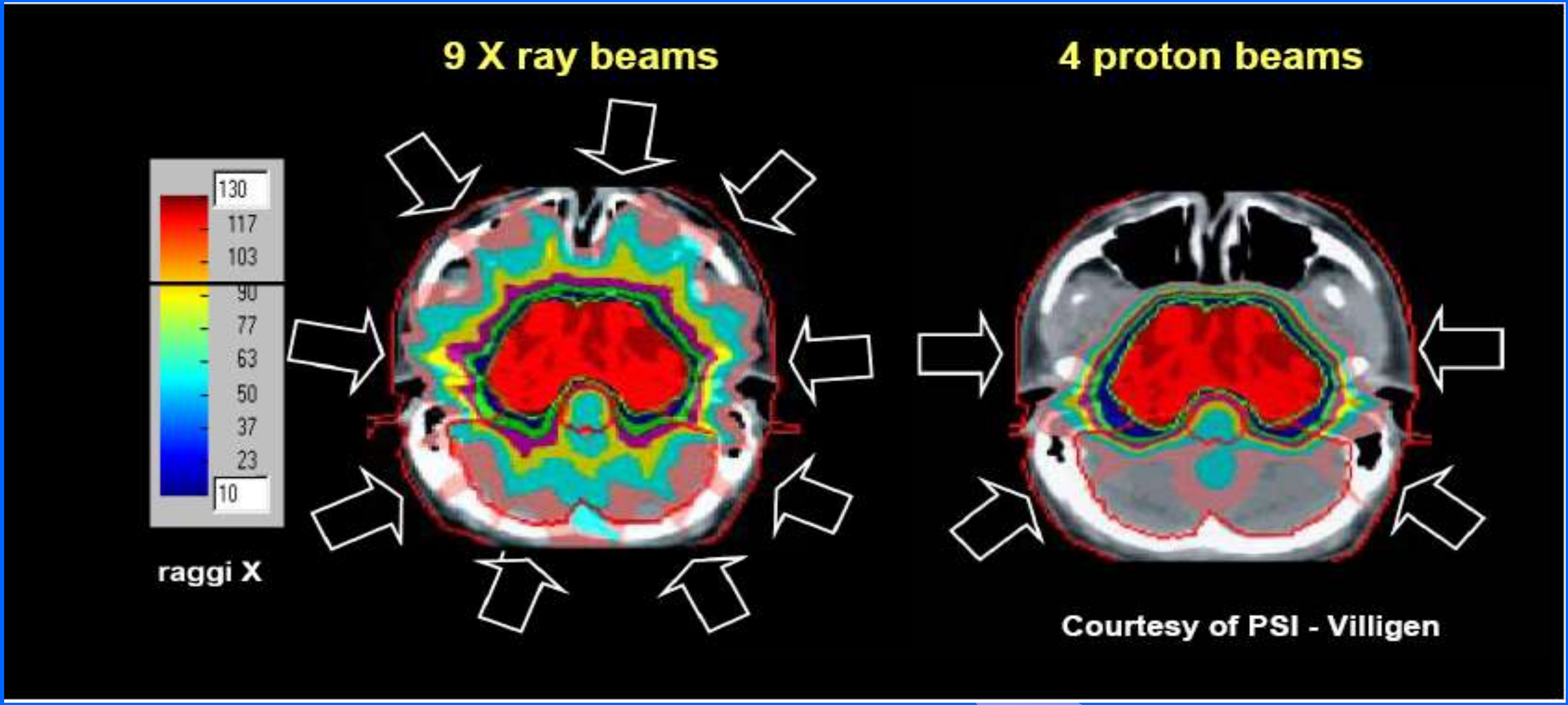
IMPT = Intensity Modulated Particle Therapy with protons

4 NON-UNIFORM FIELDS

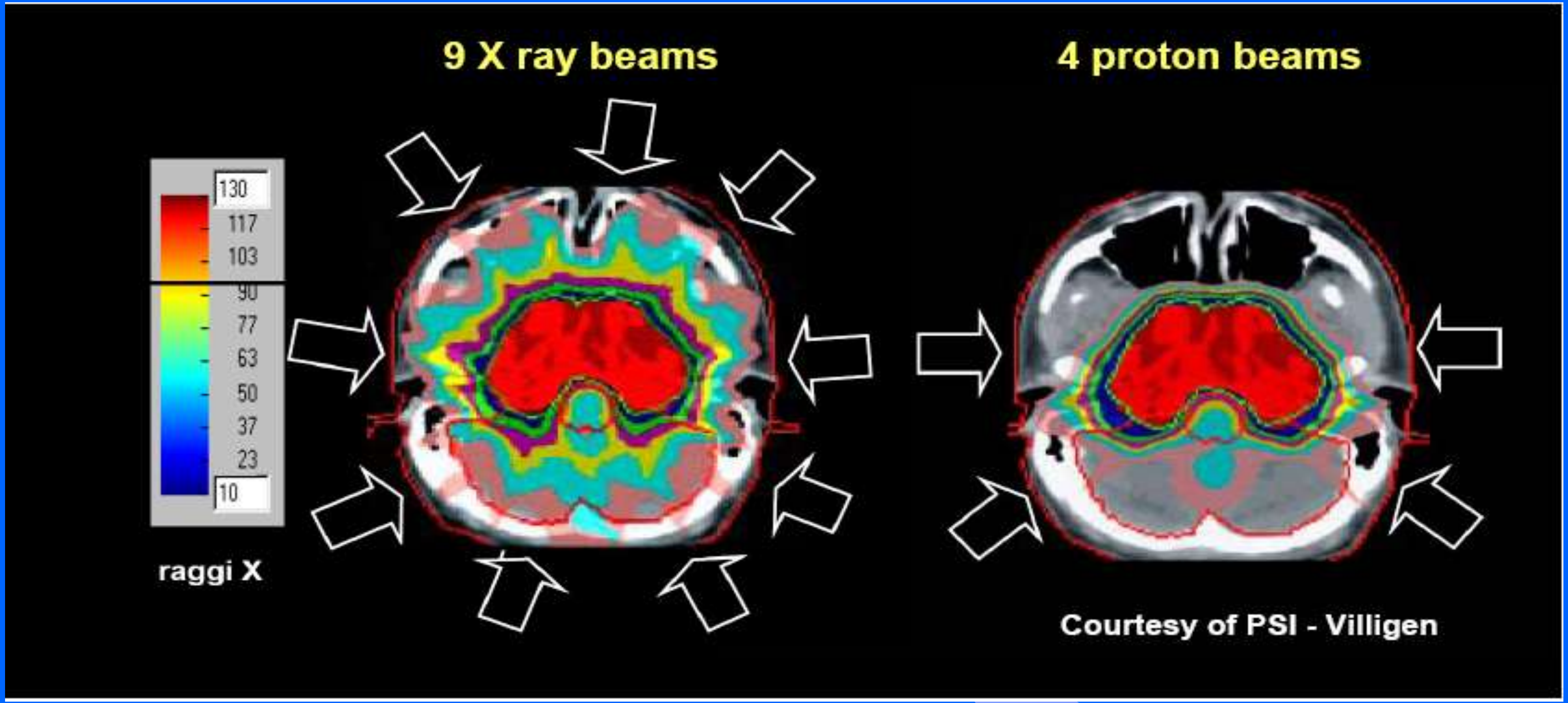


PSI

Protons are quantitatively different from X-rays



Carbon ions are *qualitatively* different from X-rays

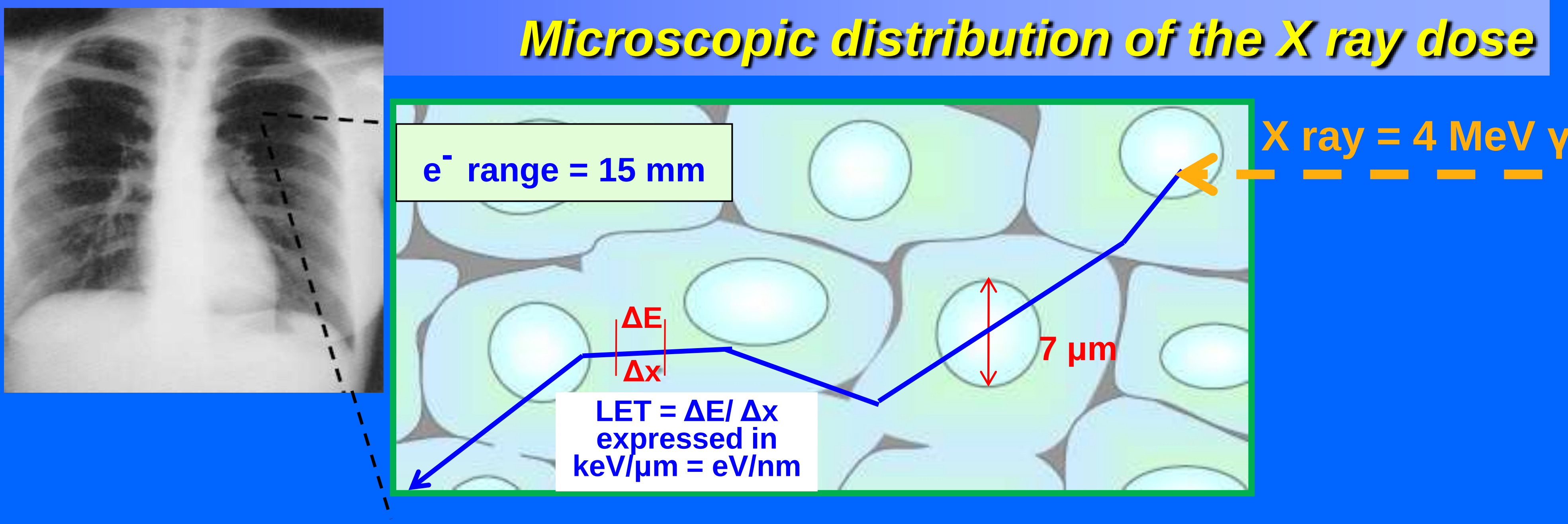


Carbon ions deposit in a cell 24 times more energy than a proton producing not reparable multiple close-by double strand breaks

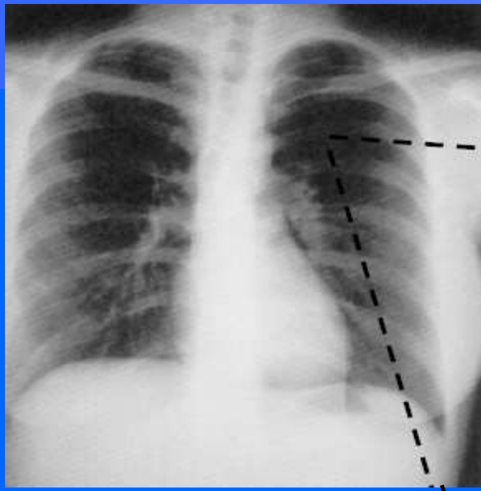
Carbon ions can control radio-resistant tumours

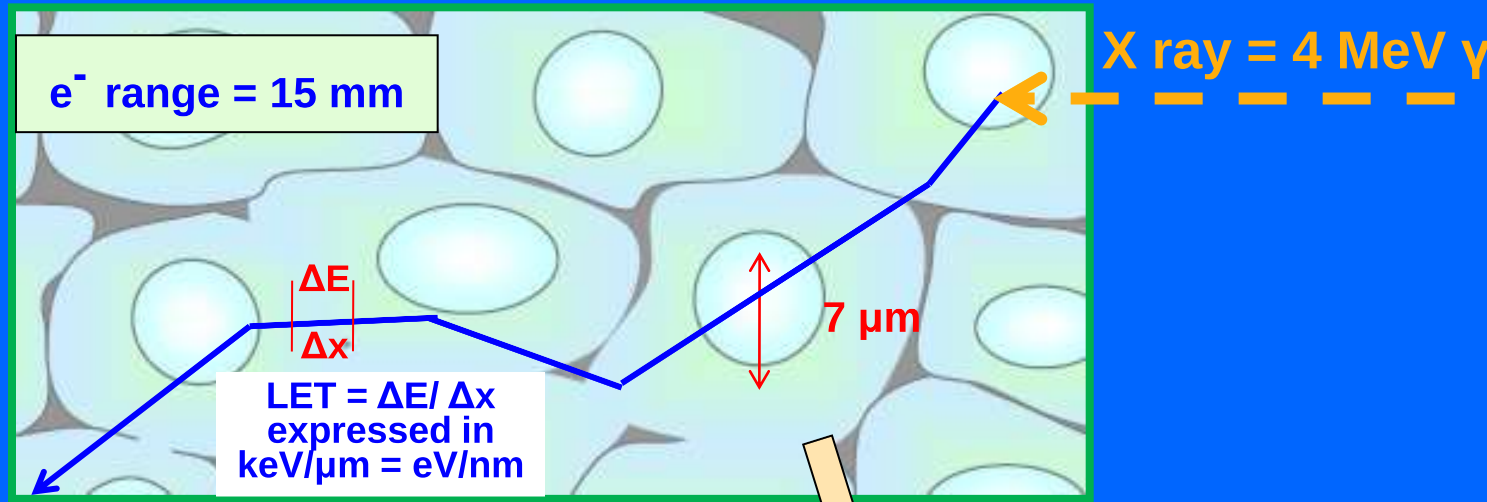
WHY?
Microscopic distribution of the dose

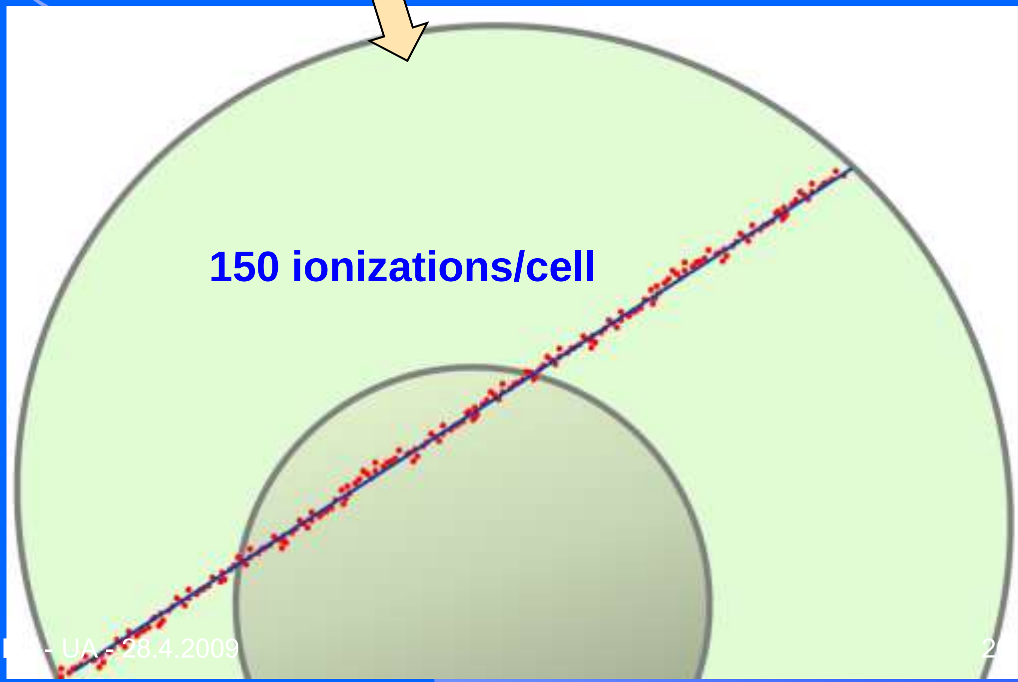
Microscopic distribution of the X ray dose



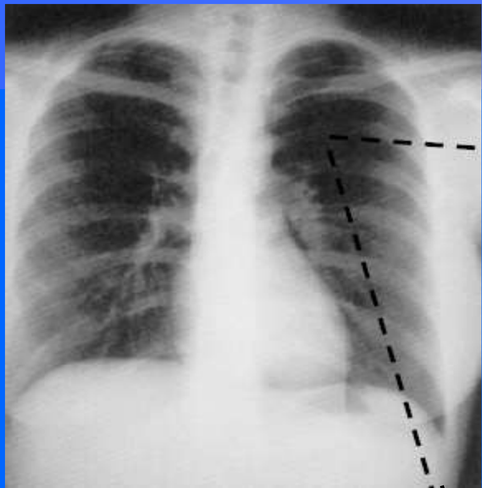
Microscopic distribution of the X ray dose

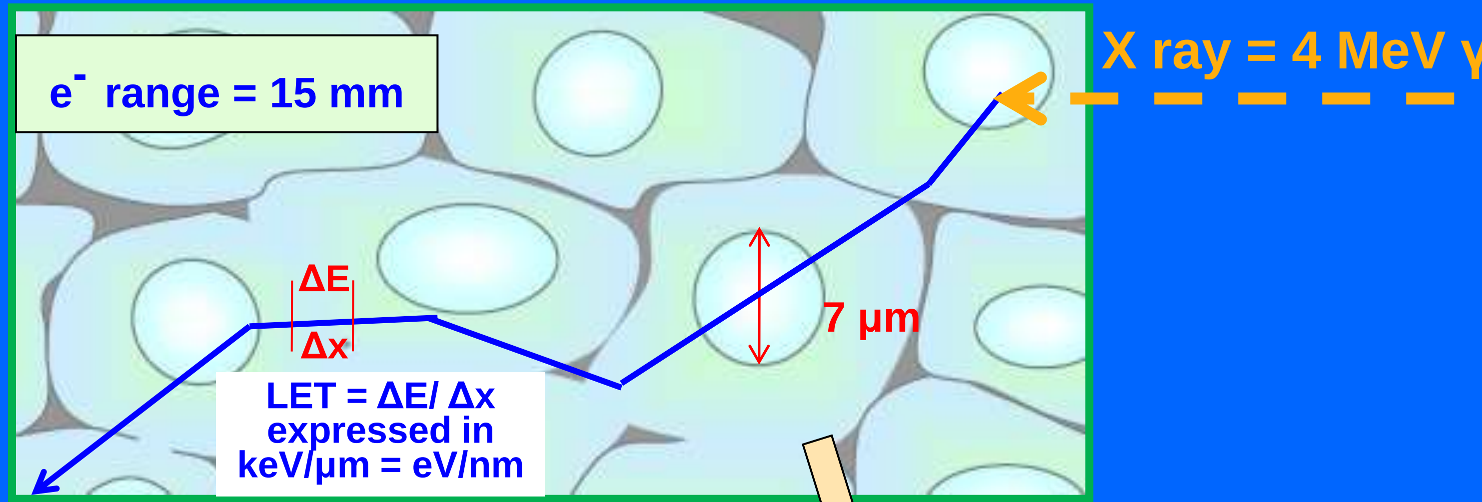


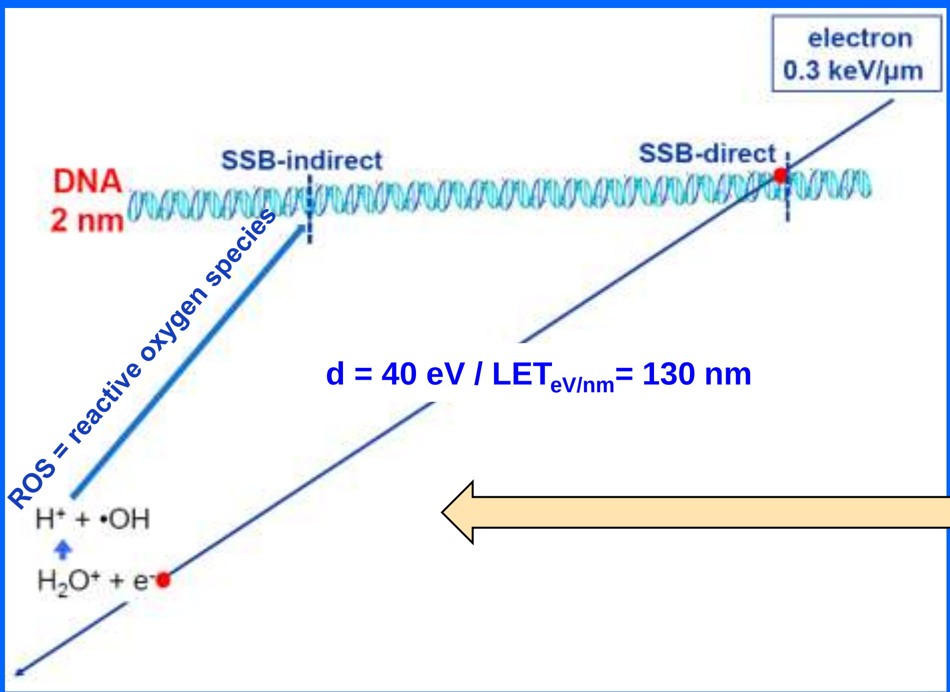


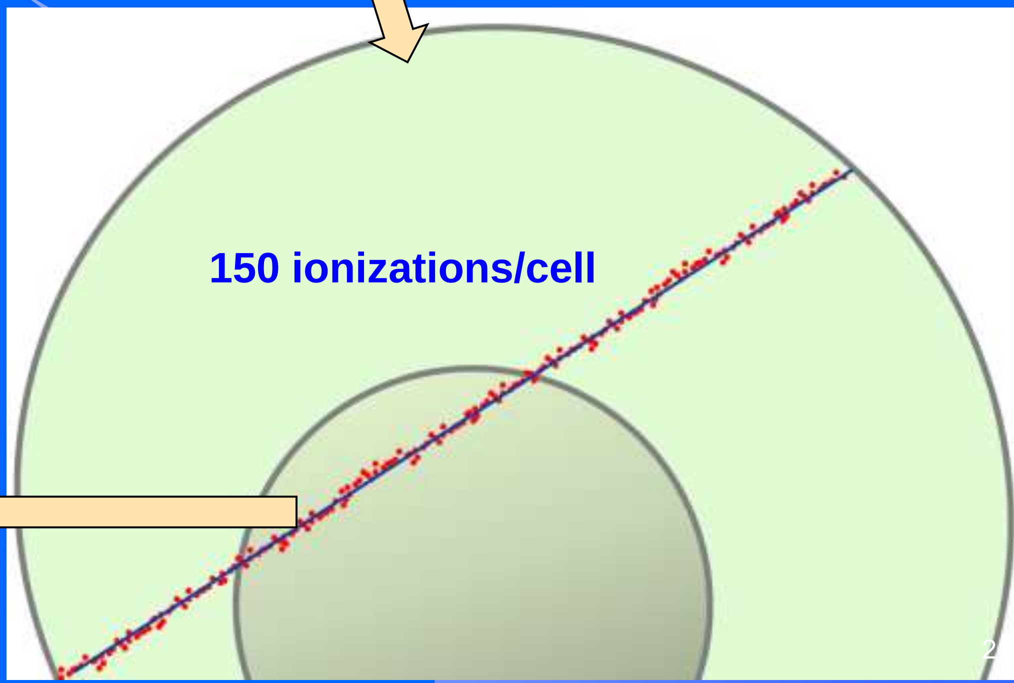


Microscopic distribution of the X ray dose

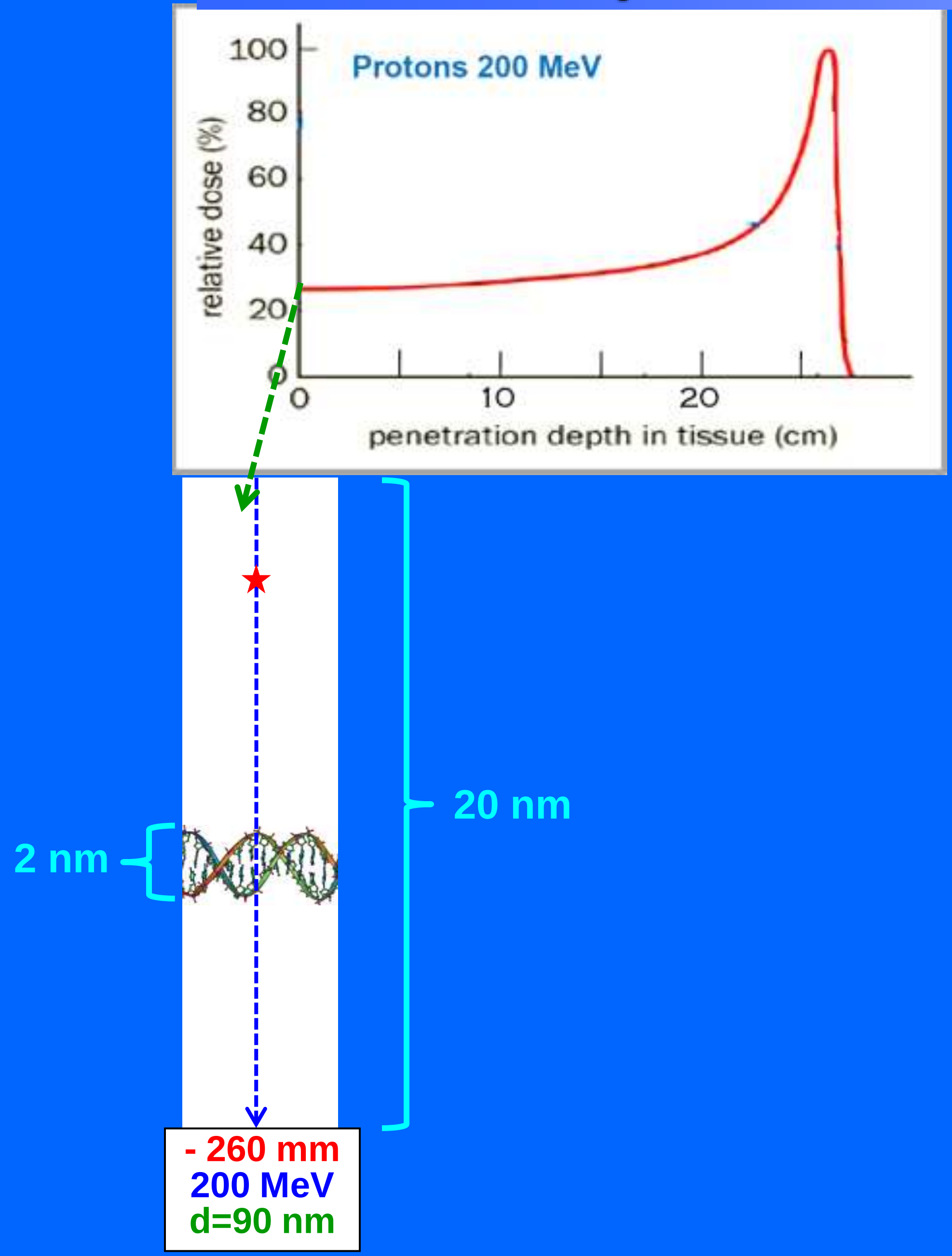




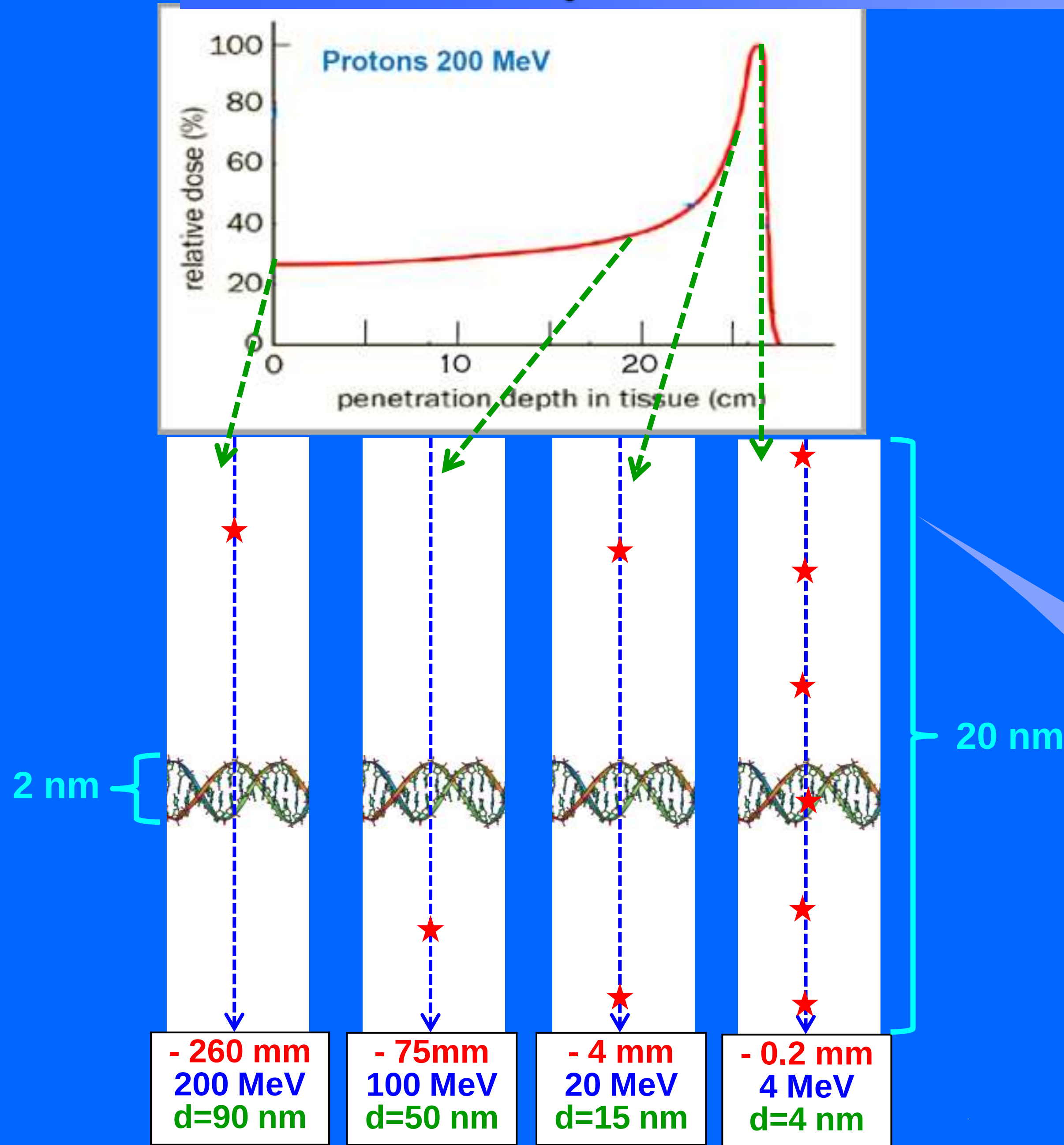




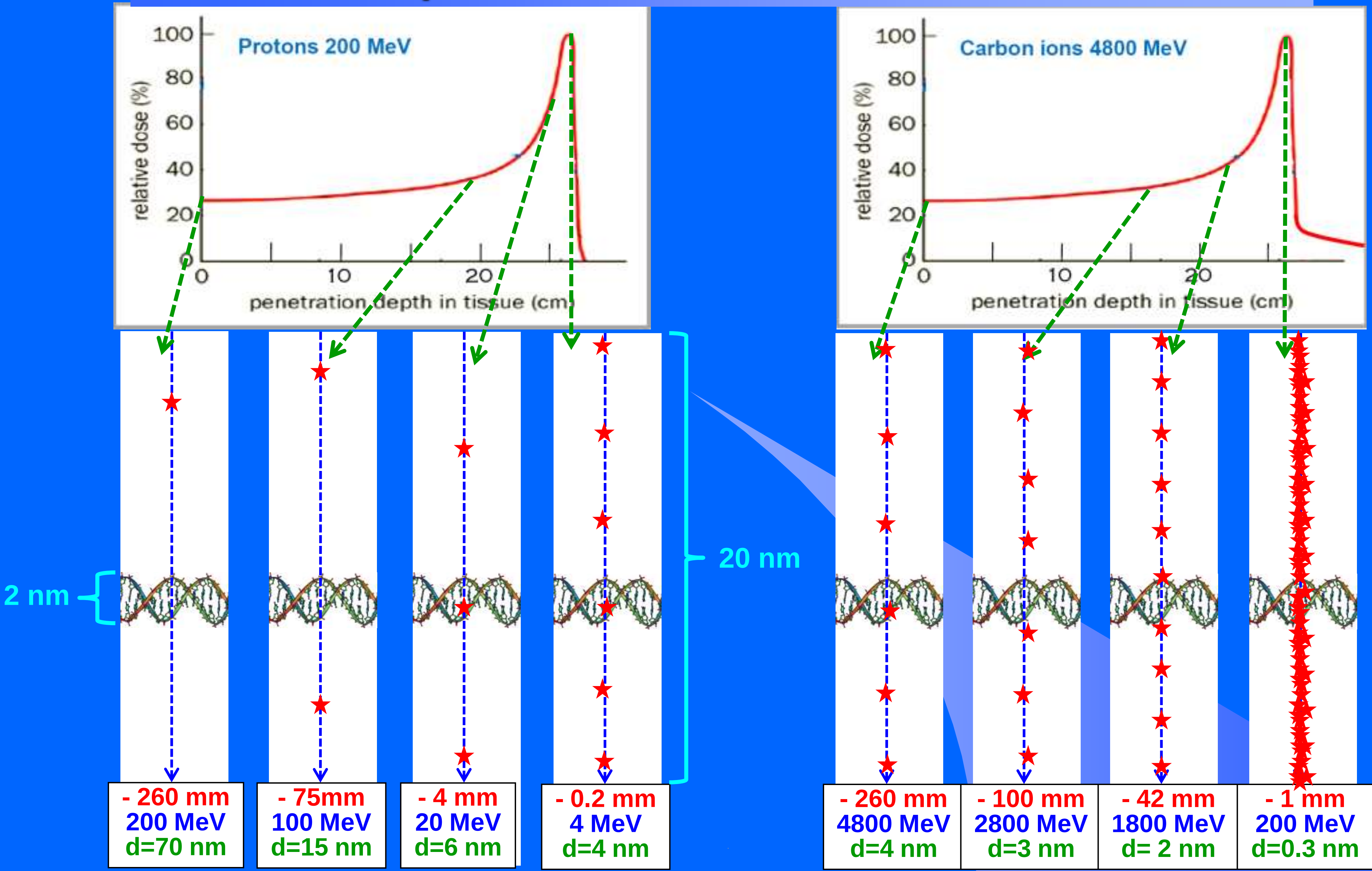
Microscopic distribution of the hadronic ionizations:



Microscopic distribution of the hadronic ionizations: ★



Microscopic distribution of the hadronic ionizations: ★

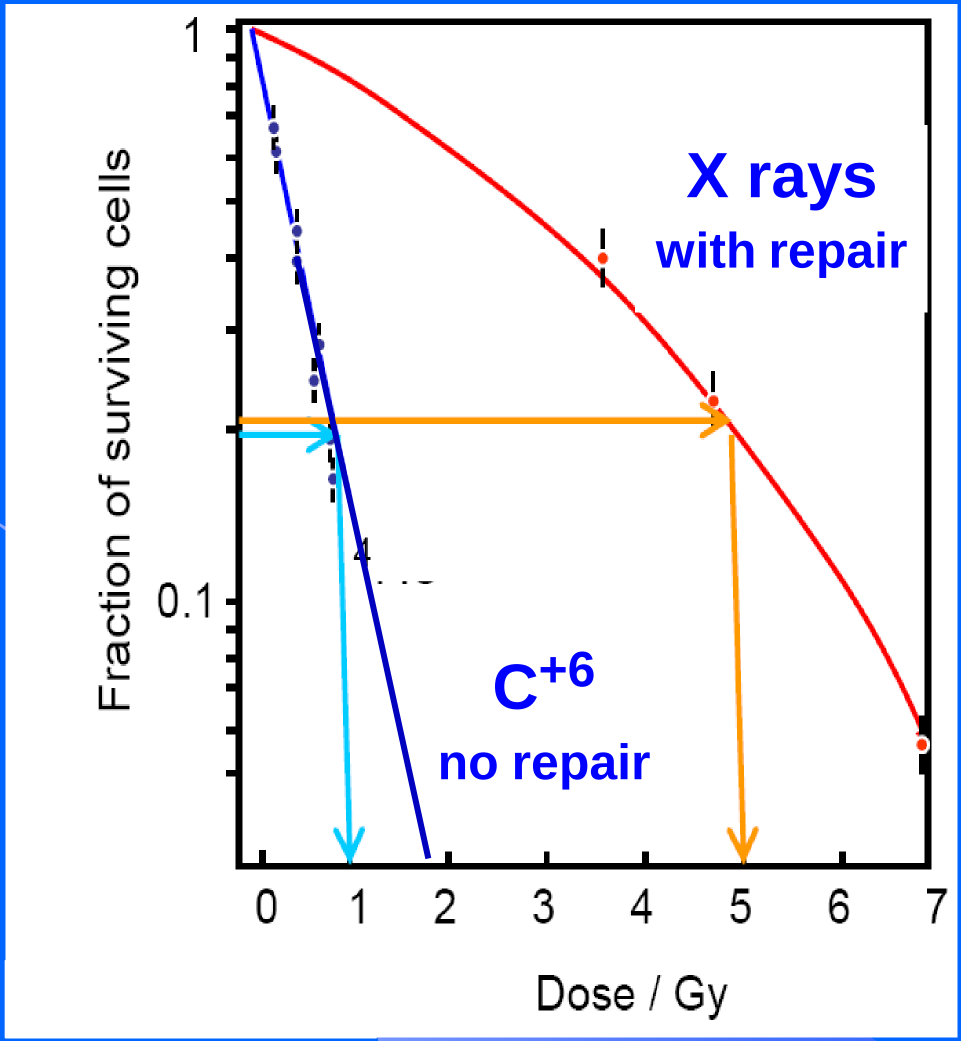


Definition of Radio-Biological Effectiveness

RBE is defined with respect to standard X rays:

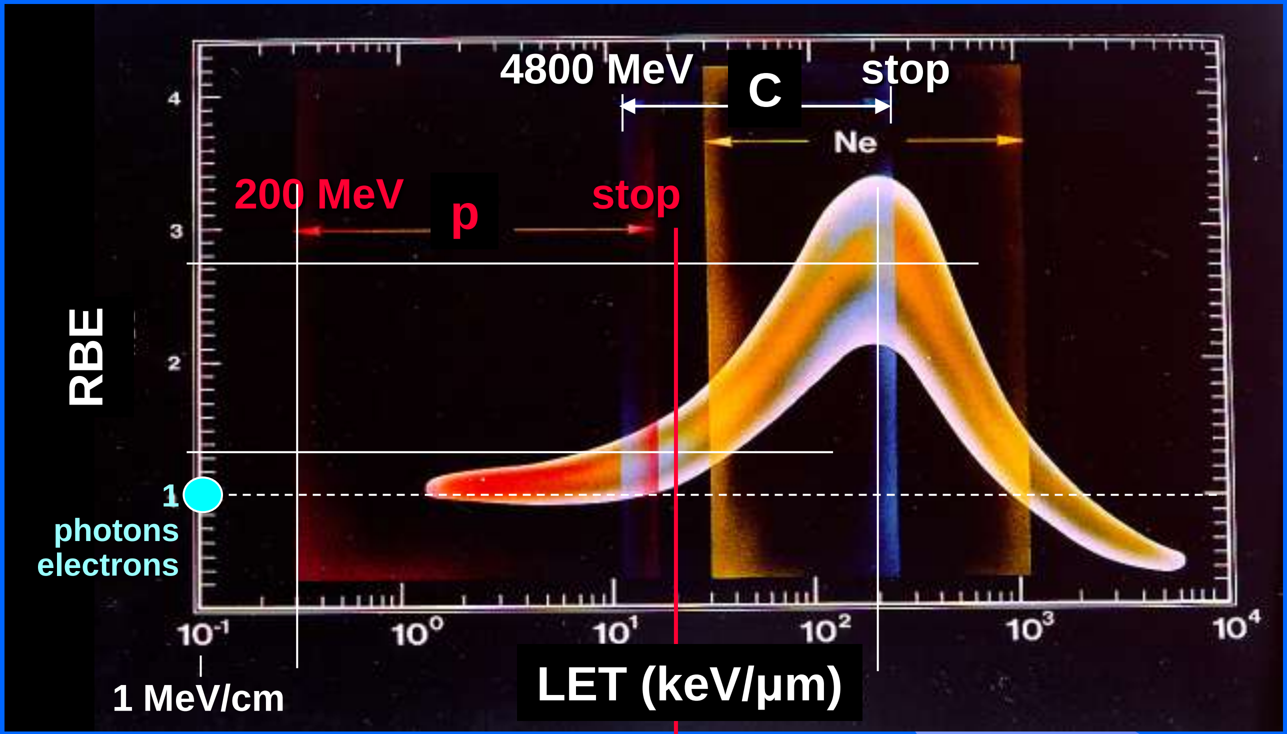
$$RBE = \frac{D\gamma}{D} = \frac{5}{1} = 5$$

For a given effect on a given cell the RBE value is a function of LET



Effect of ΔE/Δx = LET on RBEs of many cells for many 'end-points

'Radio Biological Effectiveness'

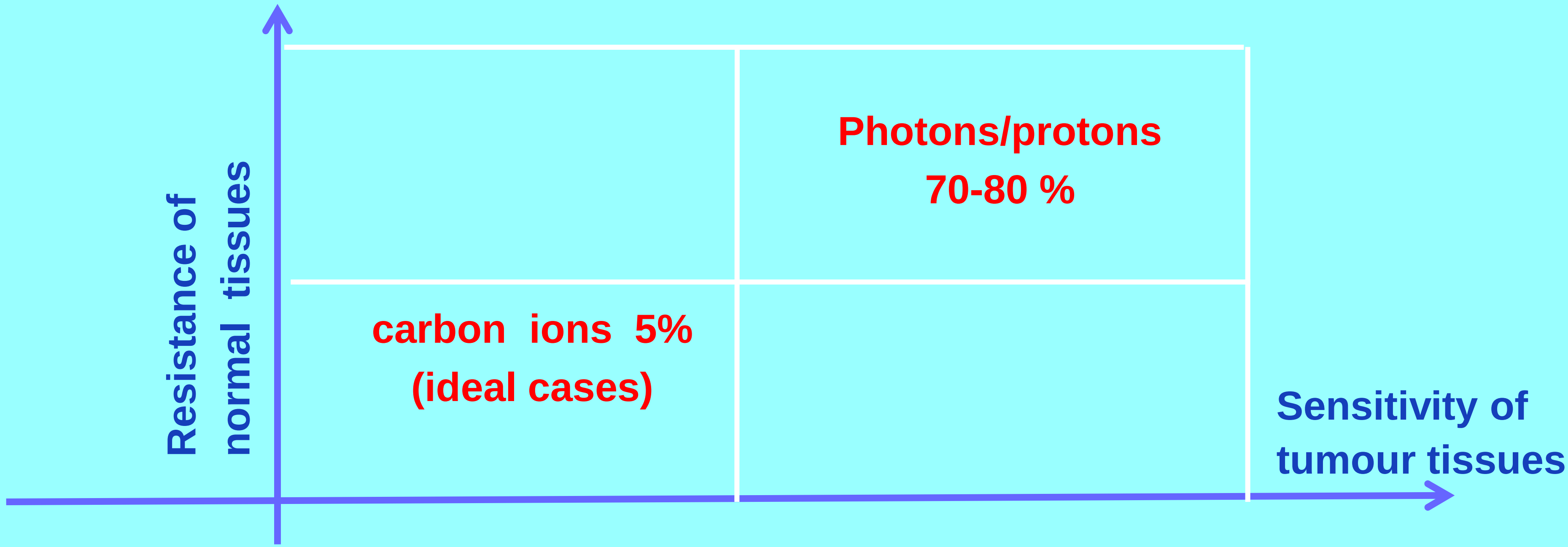


LET > 20 keV/μm = 200 MeV/cm

d < 2 nm

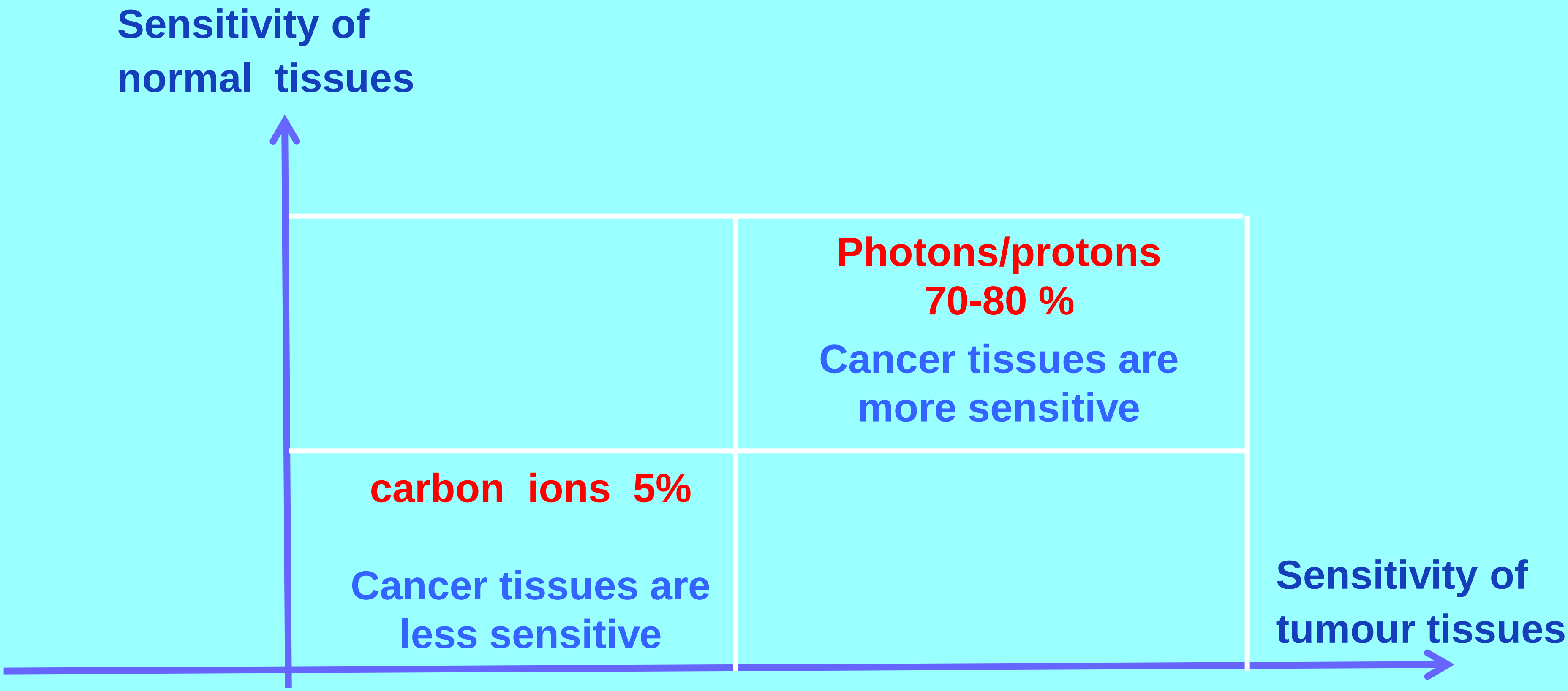
Production of many unreparable localized double strand breaksd and clustered damages

When should protons and carbon ions be used?



[M. Scholz, GSI]

When should protons and carbon ions be used?



[M. Scholz, GSI]

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**

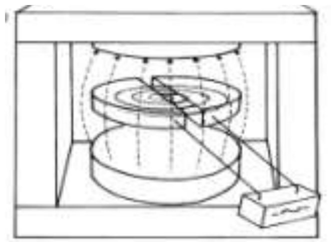
(*) Combining studies made in Austria, Germany, France and Italy in the framework of ENLIGHT - Coordinator: Manjit Dosanjh – Projects in FP7: ULICE, PARTNER, ENVISION

Protontherapy

The accelerators used today in hadrotherapy are "circular"

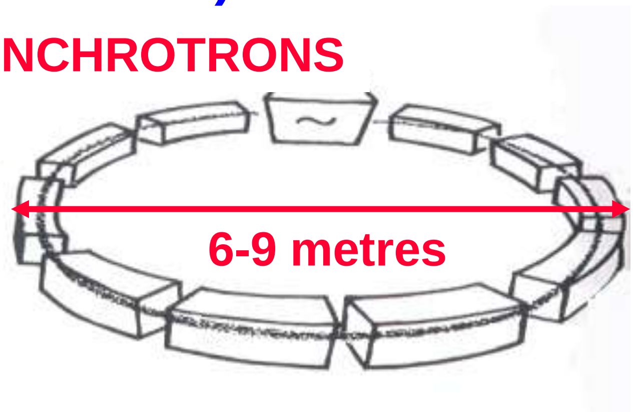
Teletherapy with protons (200-250 MeV)

CYCLOTRONS (*) (Normal or SC)



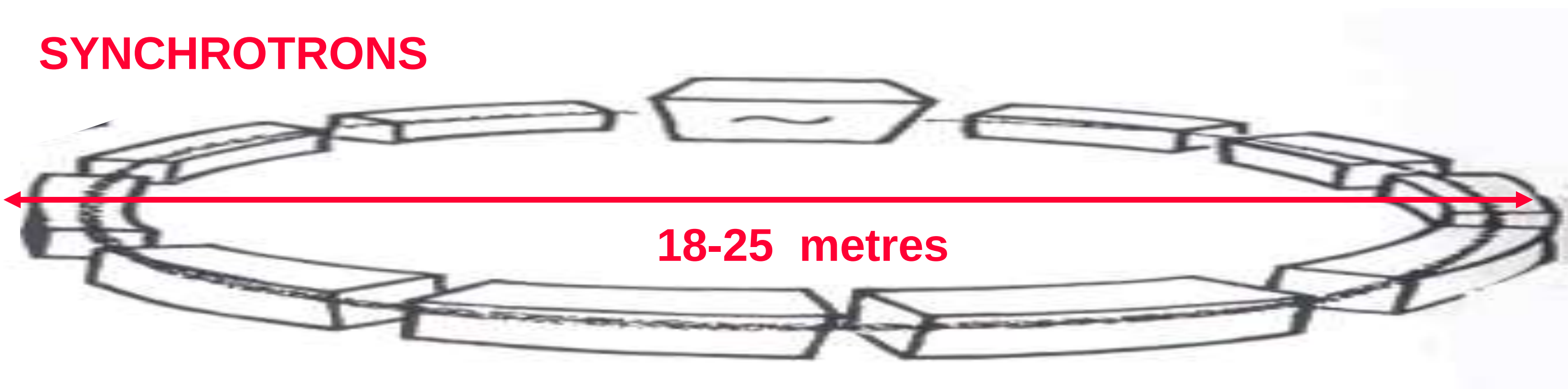
(*) also synchrocyclotrons

SYNCHROTRONS

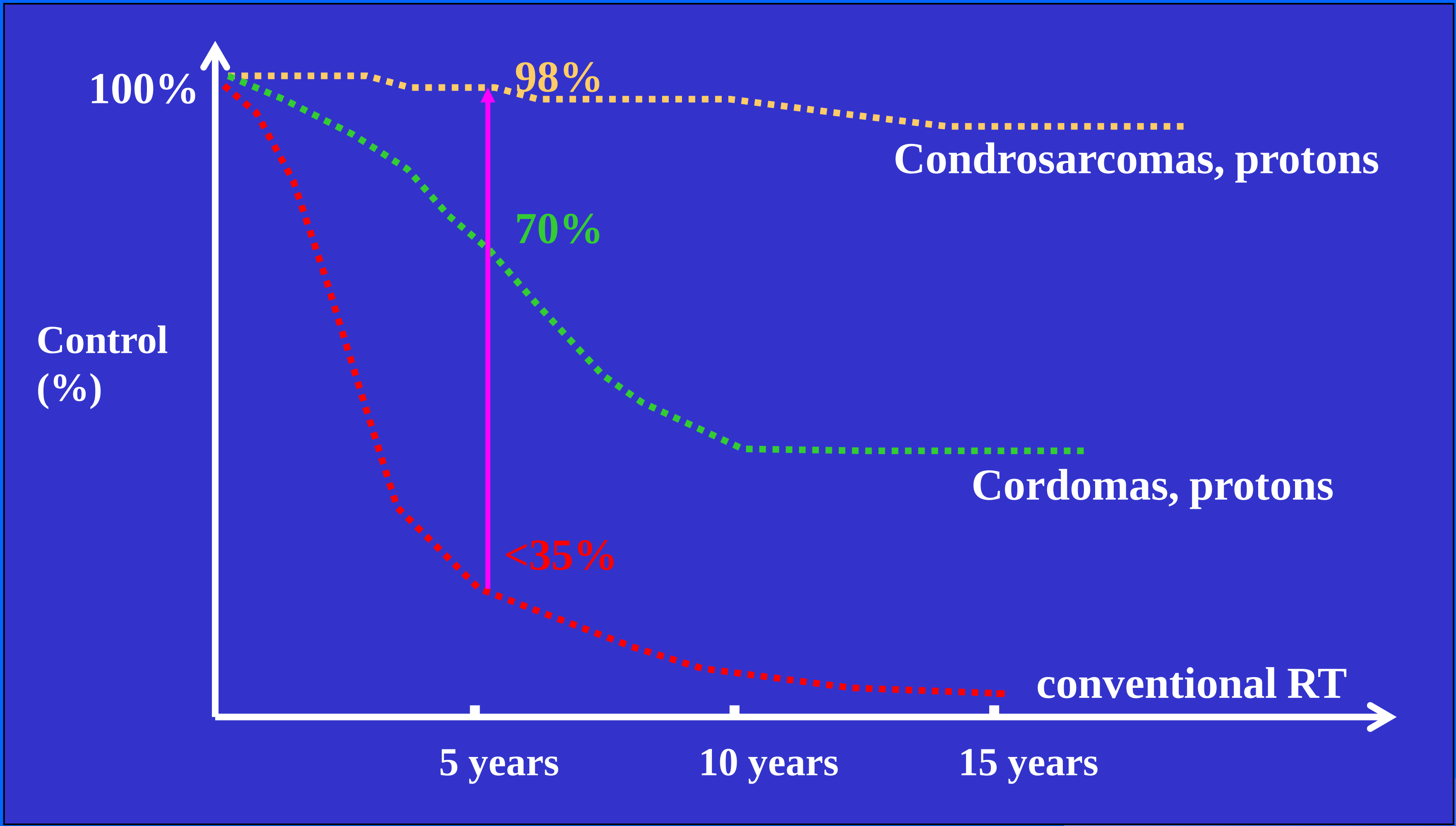


Teletherapy with carbon ions (4800 MeV = 400 MeV/u)

SYNCHROTRONS

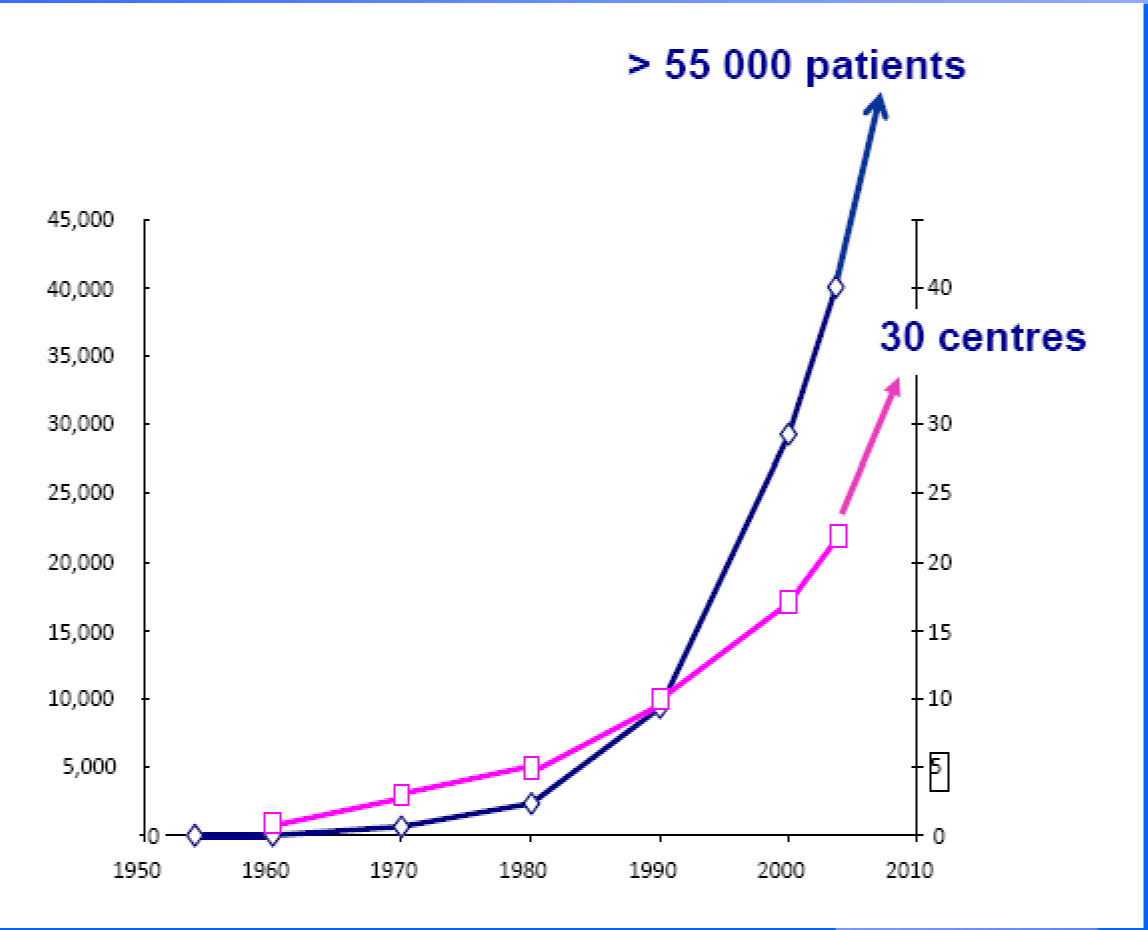


Mas General Hospital results obtained at the Harvard proton cyclotron in the 80s



TERA

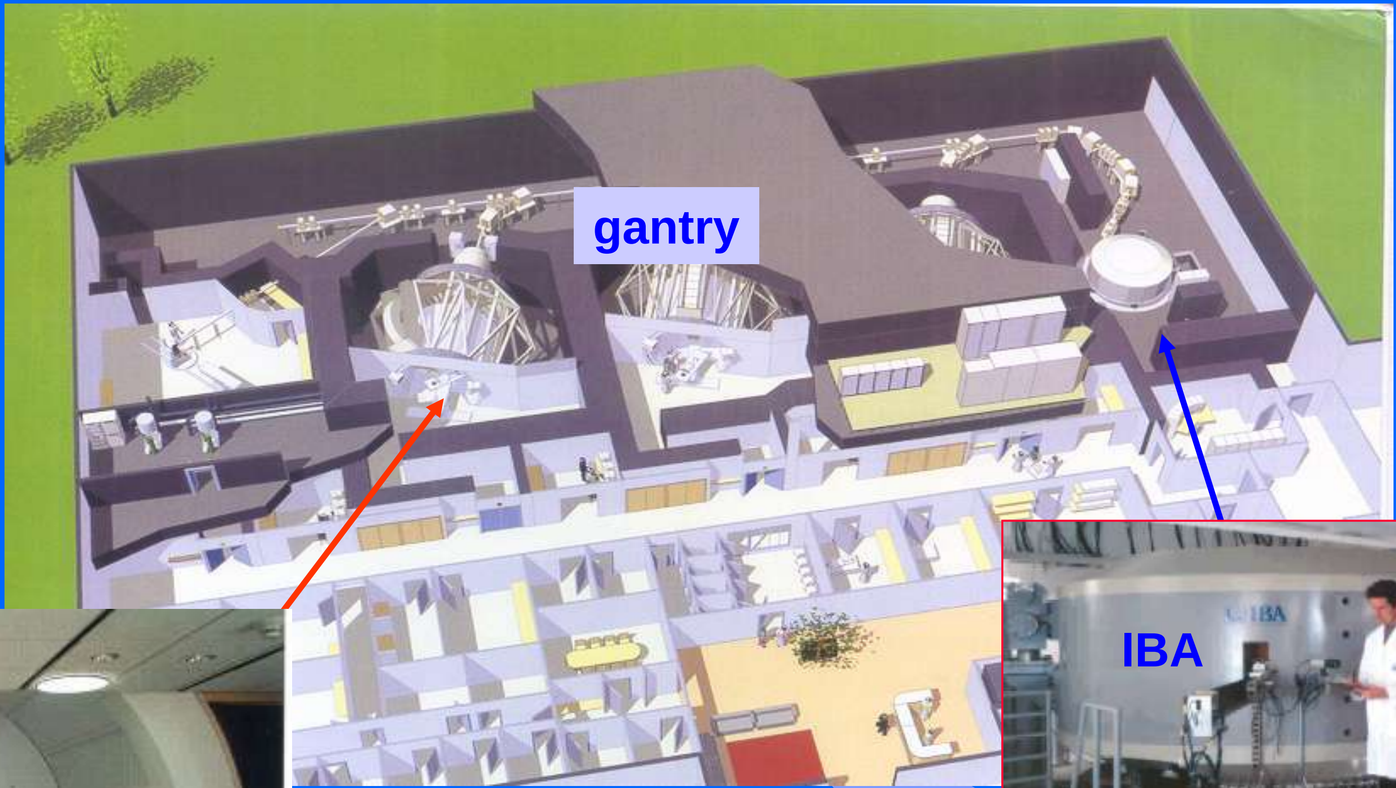
For these reasons protontherapy is booming



20-25 sessions per patient

European cost of a full treatment:
IMRT: 7-8 k€
Protontherapy: 20-25 k€

Cyclotron for protons by Ion Beams Applications - Belgium



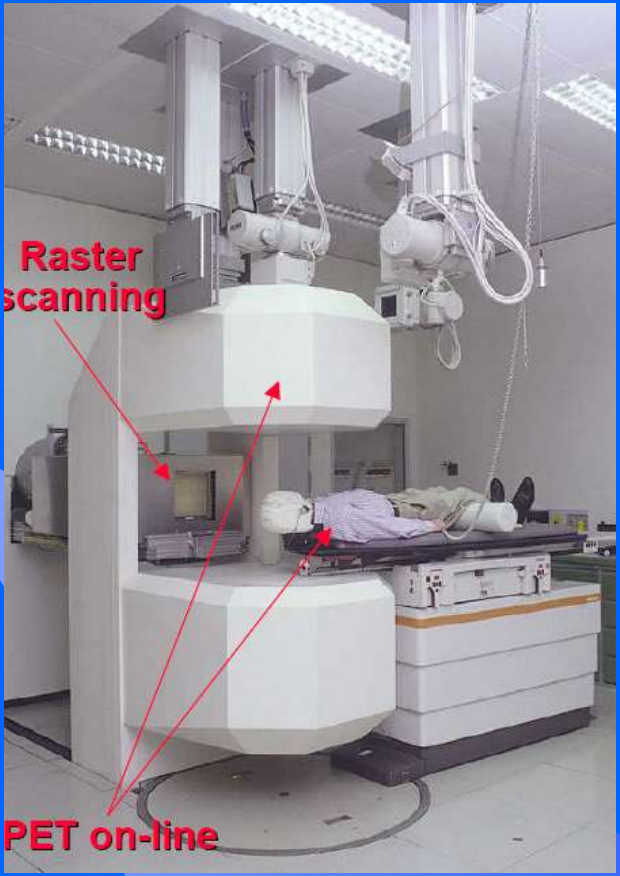
Five companies offer turn-key centres for 120-150 M€.
If proton accelerators were 'small' and 'cheap',
no radiation oncologist would use X rays.

Carbon ion therapy

The GSI pilot project : 1997-2008

J. Debus

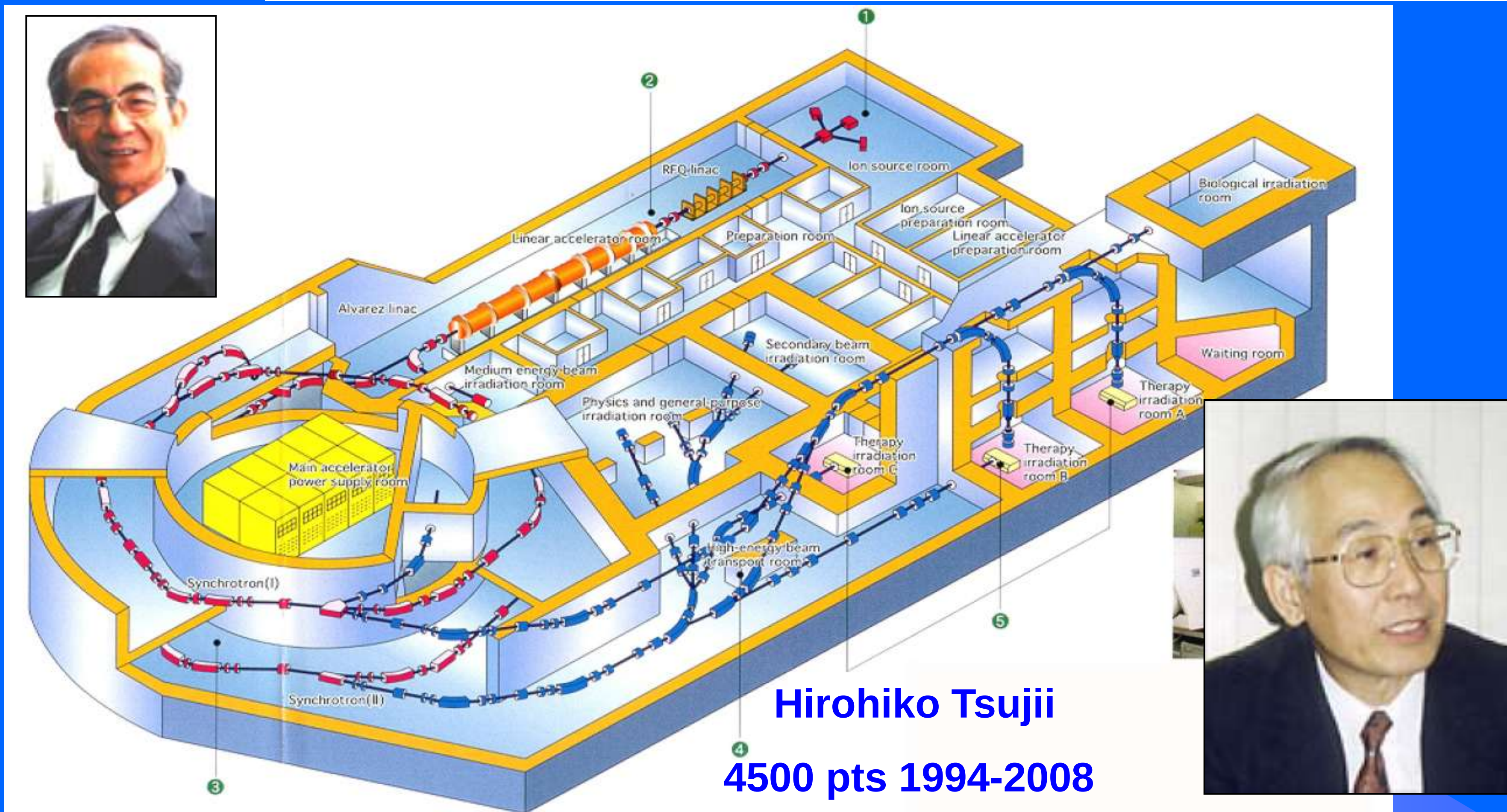
450 patients treated
with carbon ions



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)



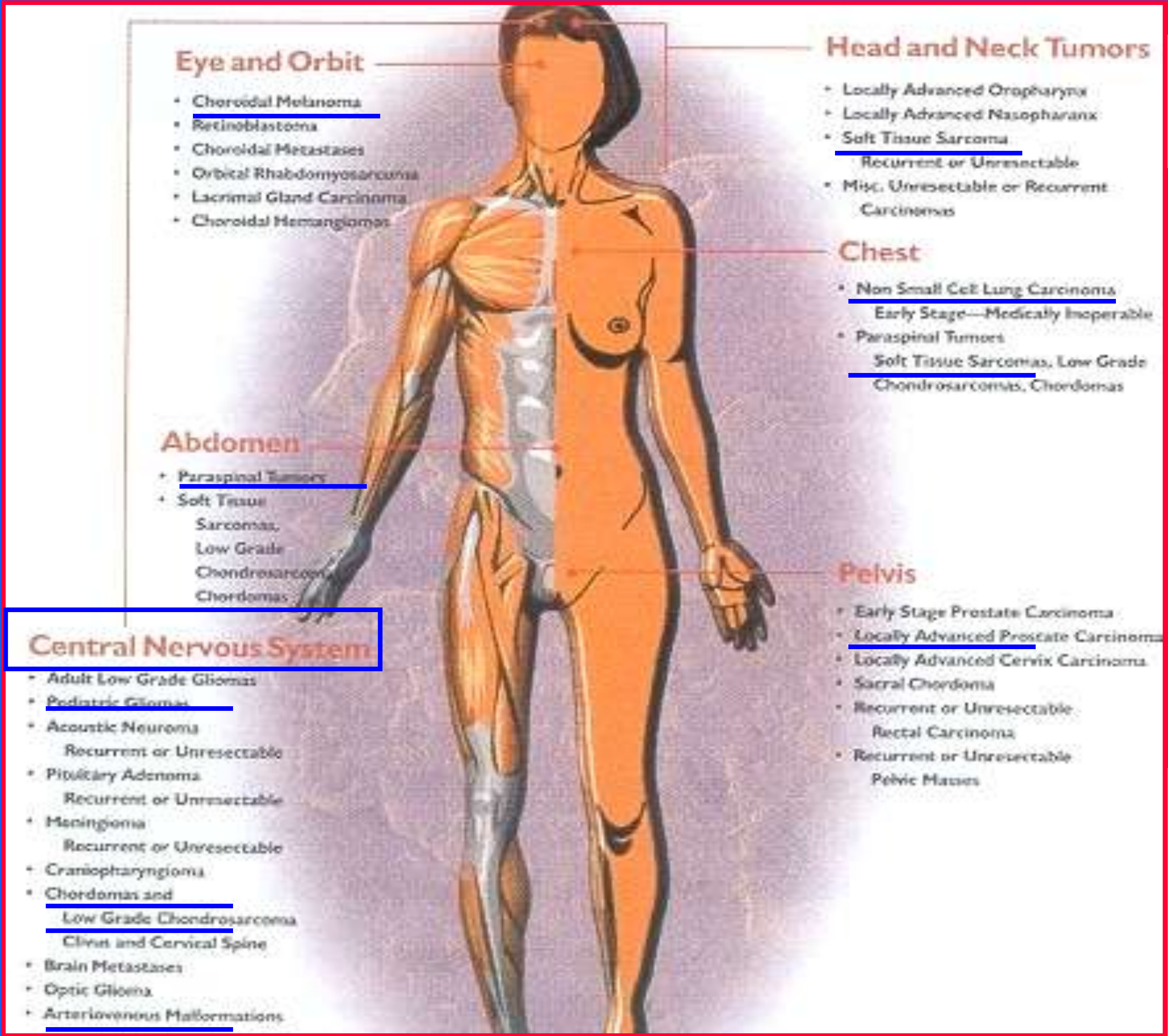
Hirohiko Tsujii

4500 pts 1994-2008

Since the cells do not repair. less fractions are possible

HIMAC: 4-9 fractions!

Results and number of patients



The site treated with hadrons

In the world

protontherapy:

55'000 patients

carbon ion

therapy

4500 patients

BUT

less than 1% with 'active' dose distribution systems

at PSI and GSI

with spot/raster scanning

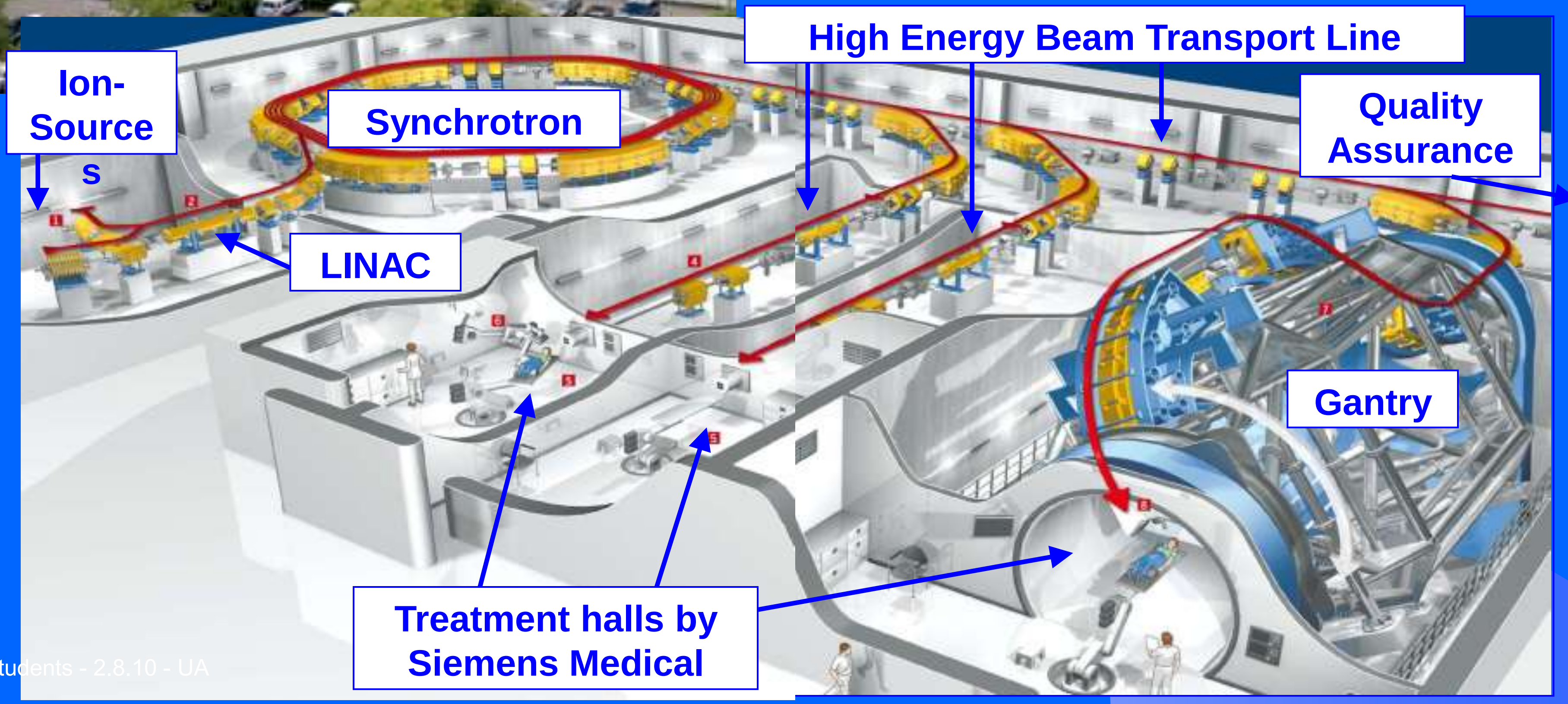
TERA

European projects for carbon ion (and proton) therapy

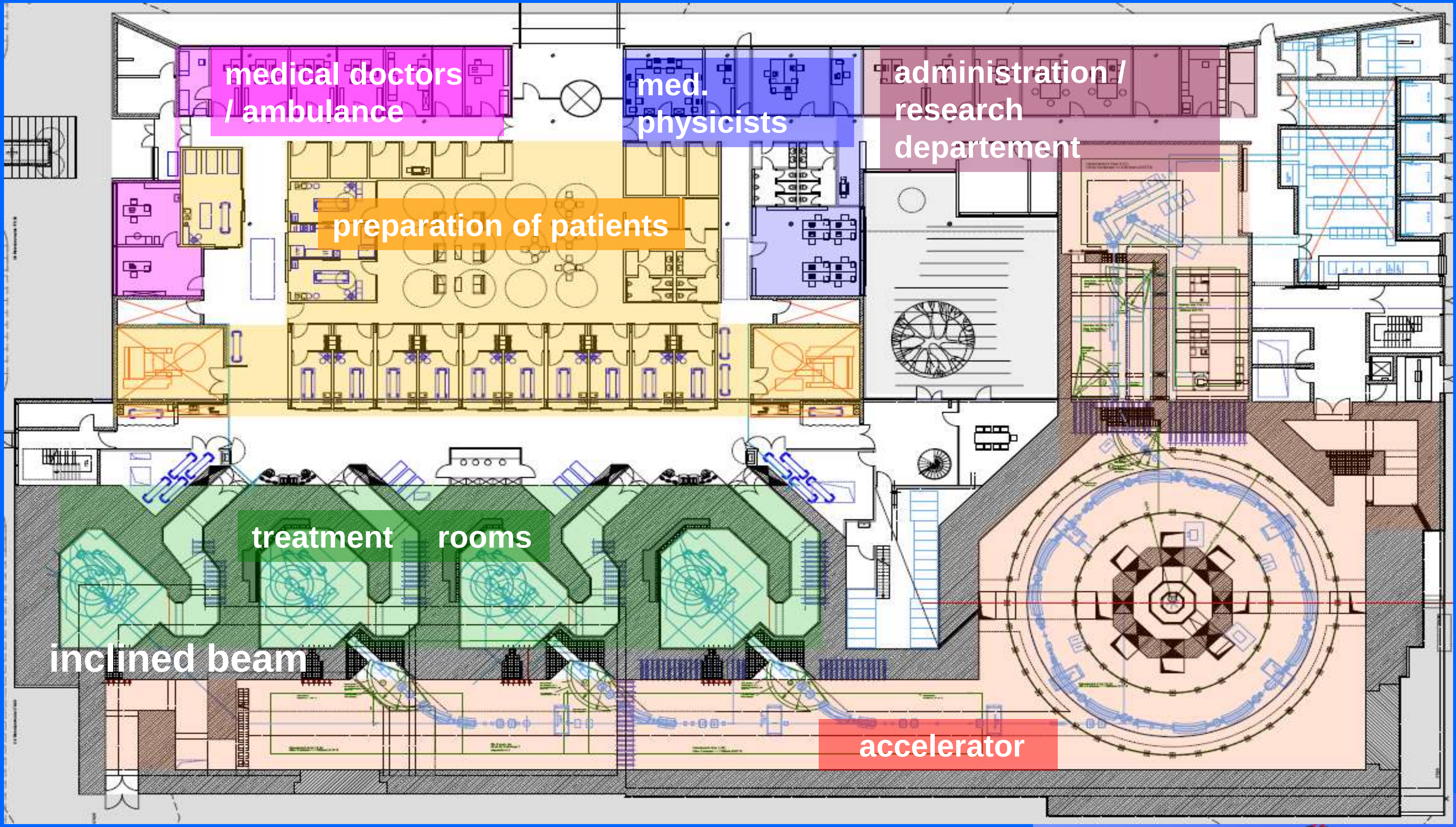
HIT at Heidelberg

First beam extracted in 2007

First patient: spring 2009



Siemens Medical is building for 2010 a 'dual' centre in Marburg



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"

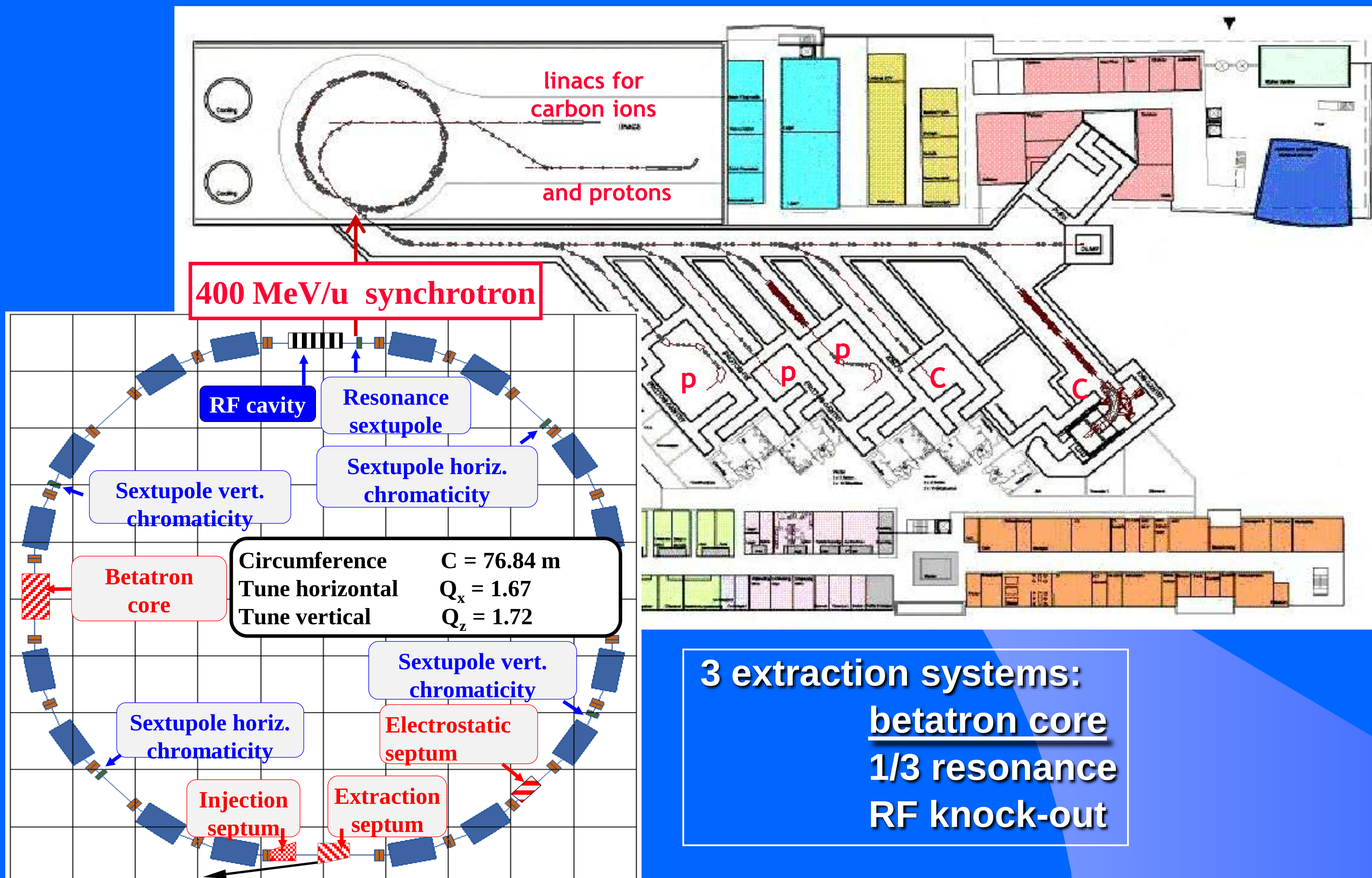
↓

2. "cyclinacs" for protons and carbon ions

PIMMS at CERN from 1996 to 2000

CERN–TERA–MedAustron Collaboration for optimized medical synchrotron

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



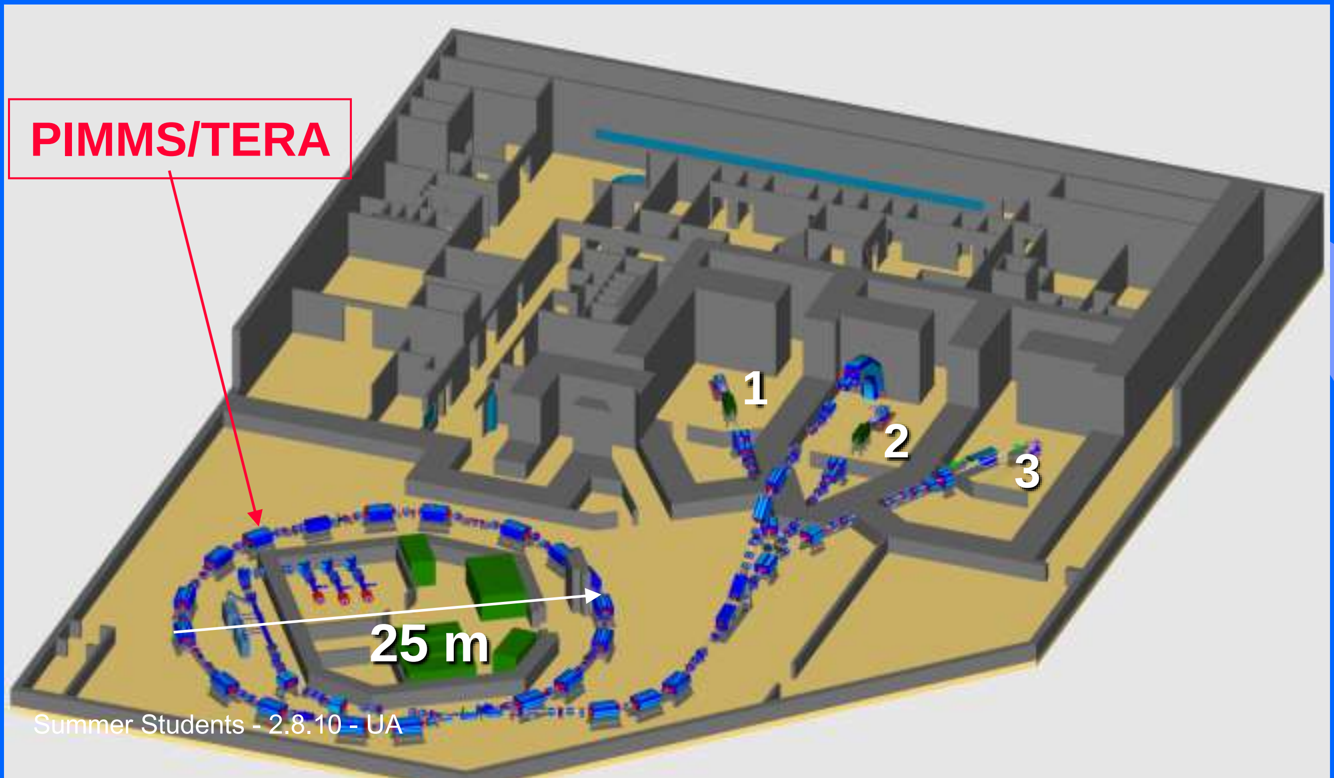
3 extraction systems:
- betatron core
- 1/3 resonance
- RF knock-out

TERA

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

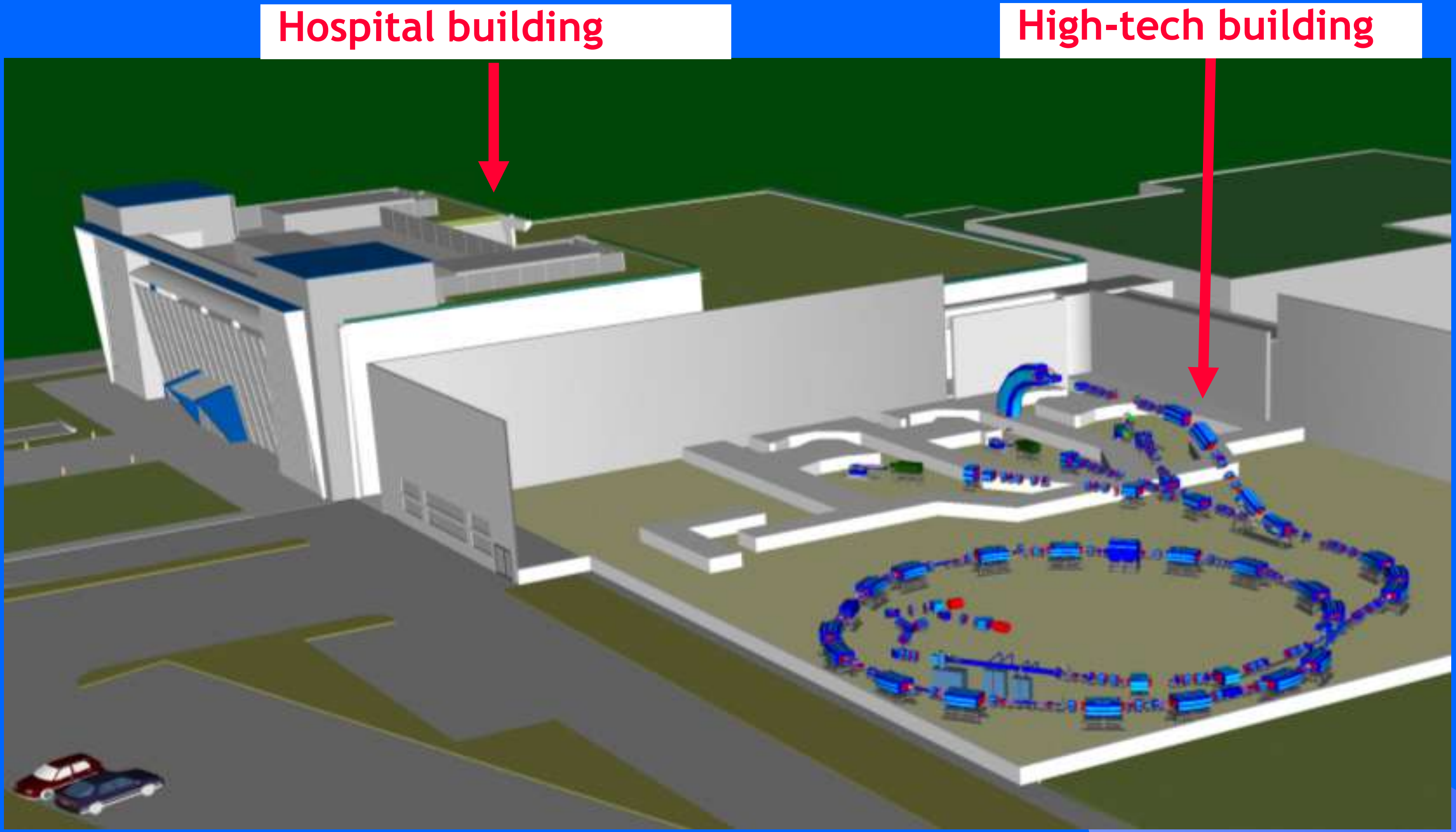
(Caudio Sanelli)

INFN runs CATANA for eye protontherapy in Catania

CNAO = Centro Nazionale di Adroterapia

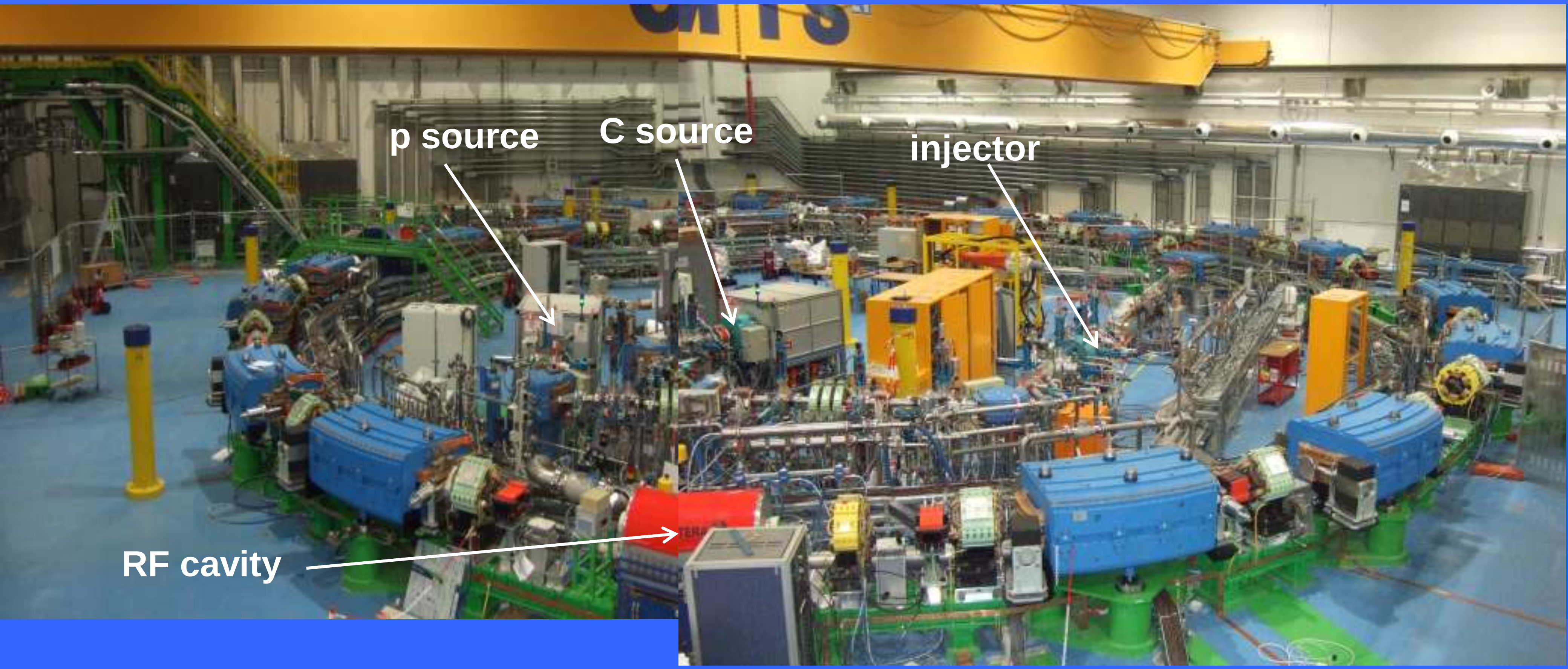
President: Erminio Borloni

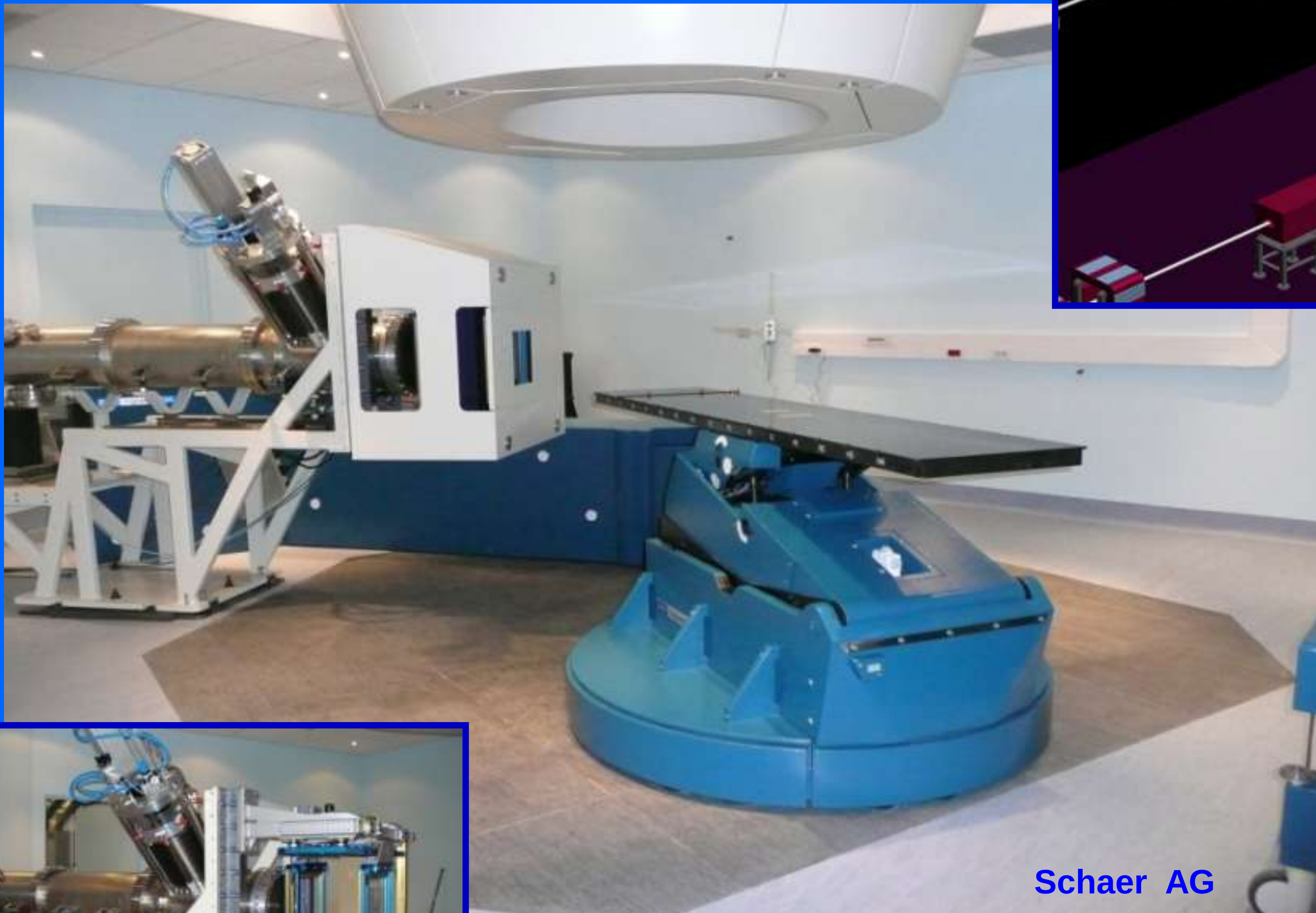
Medical Director: Roberto Orecchia   Technical Director: Sandro Rossi

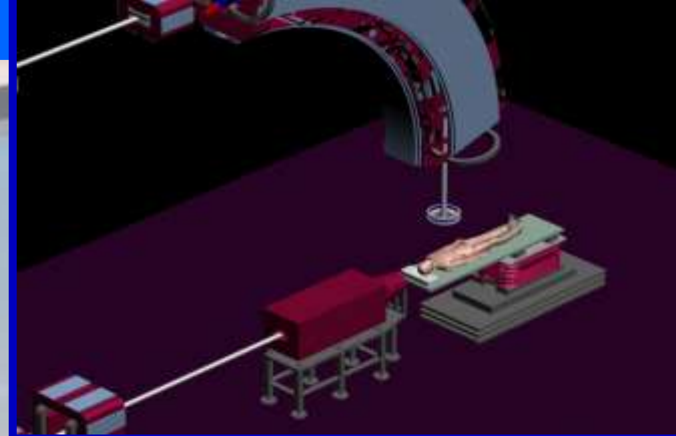


TERA

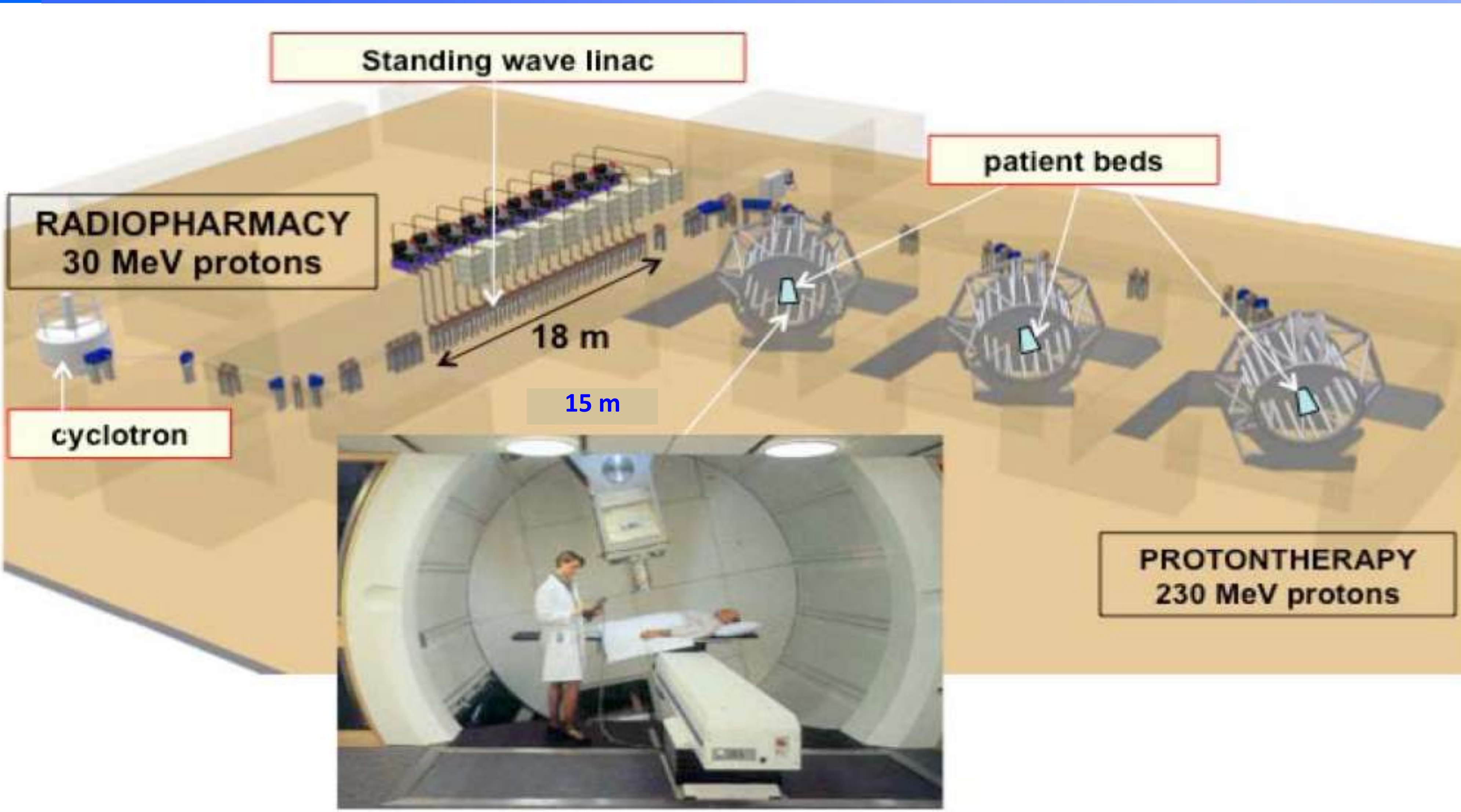
The synchrotron area in October 2008




Schaer AG



IDRA design passed to A.D.A.M. (Geneva) in 2008

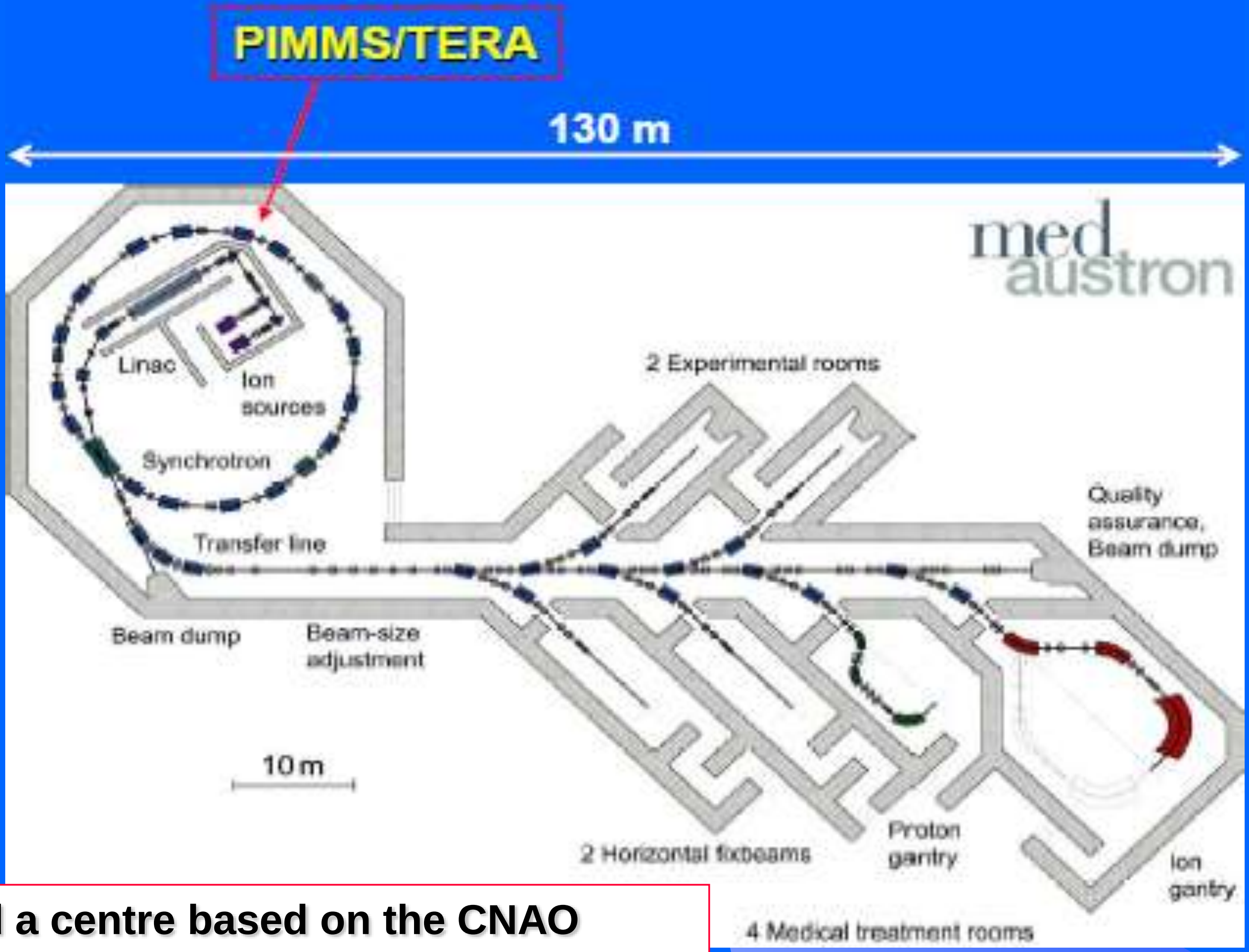


IDRA = Institute for Diagnosics and Advanced Radiotherapy
A.D.A.M. = Applications of Detectors and Accelerators to Medicine

The FIRST UNIT of IDRA has been built by A.D.A.M.

In 2007 MedAustron has been approuved for Wiener Neustadt

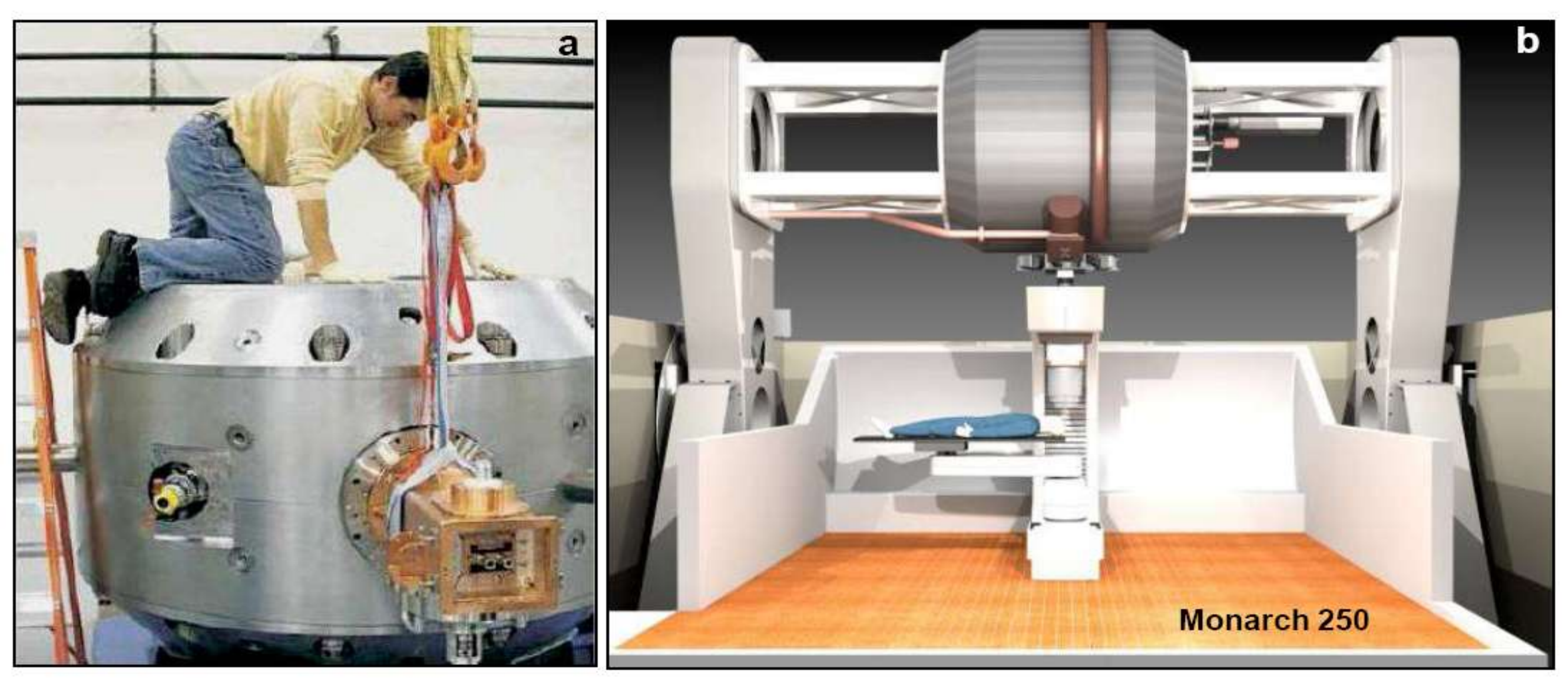
Approved in 2007
by the Government of
Lower Austria



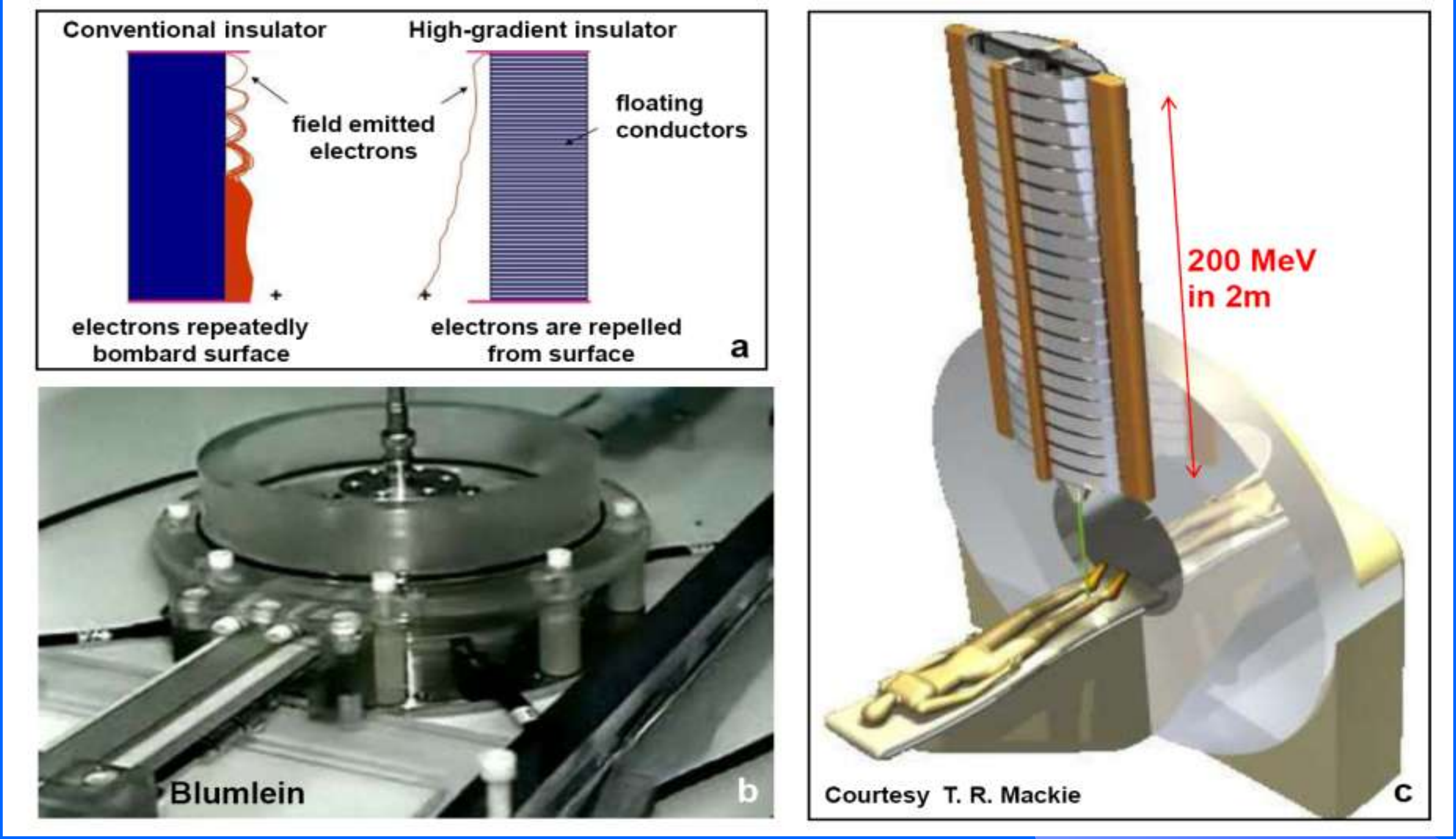
MedAustron will build a centre based on the CNAO construction drawings (CERN-CNAO-INFN Agreement)

Single room facilities

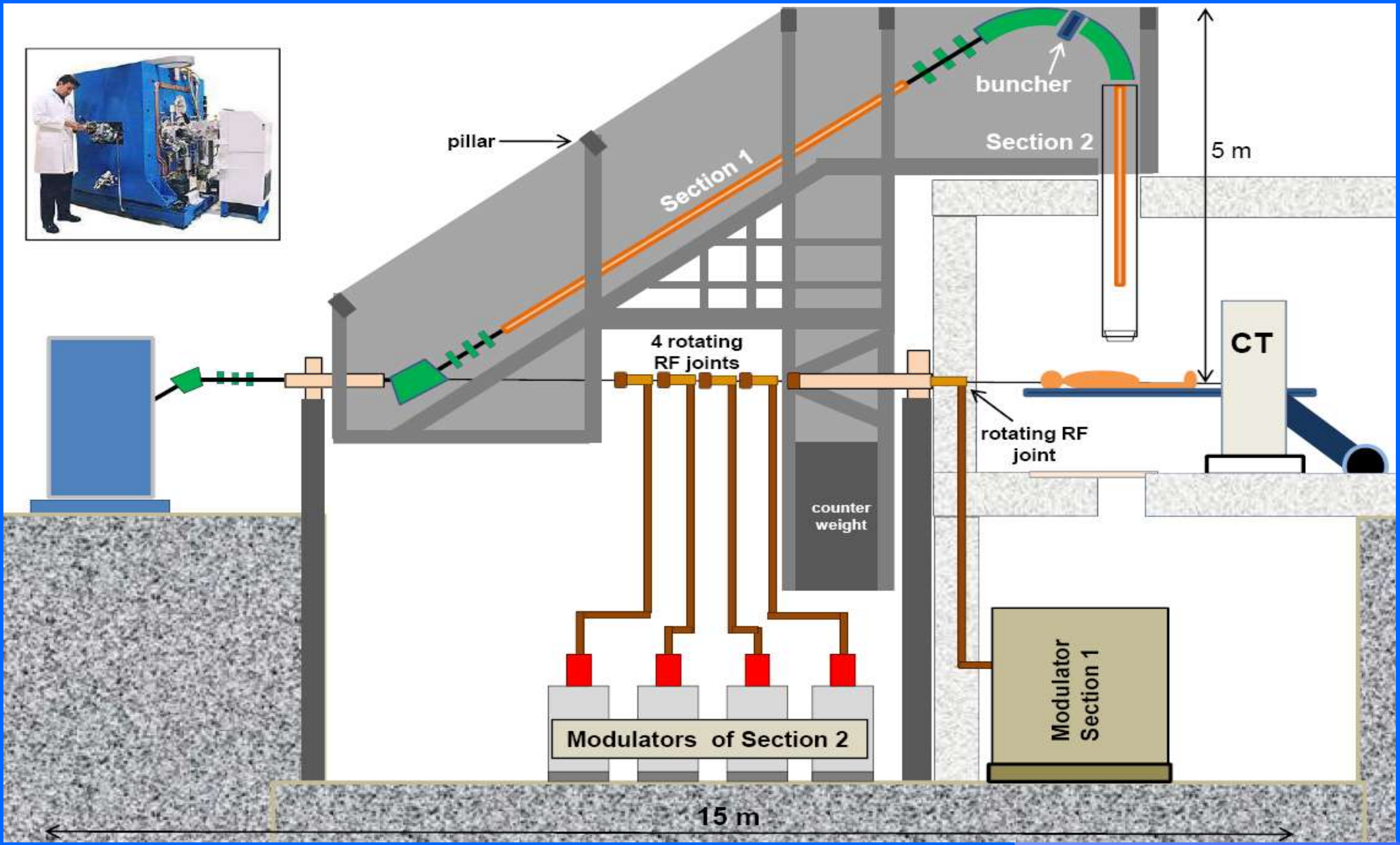
First single room facility: Still River synchrocyclotron



Dielectric Wall Accelerator: in future

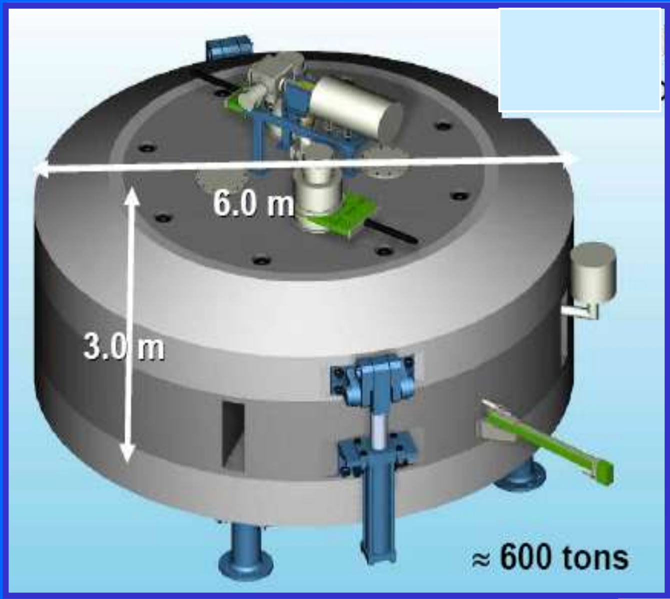


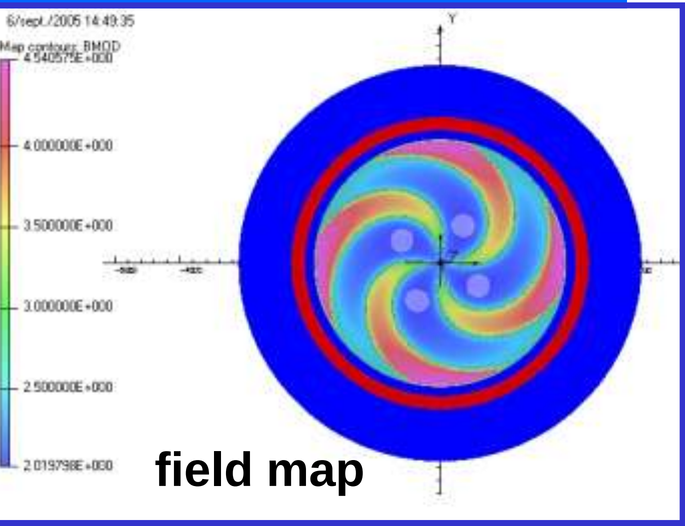
General layout of TULIP by TERA

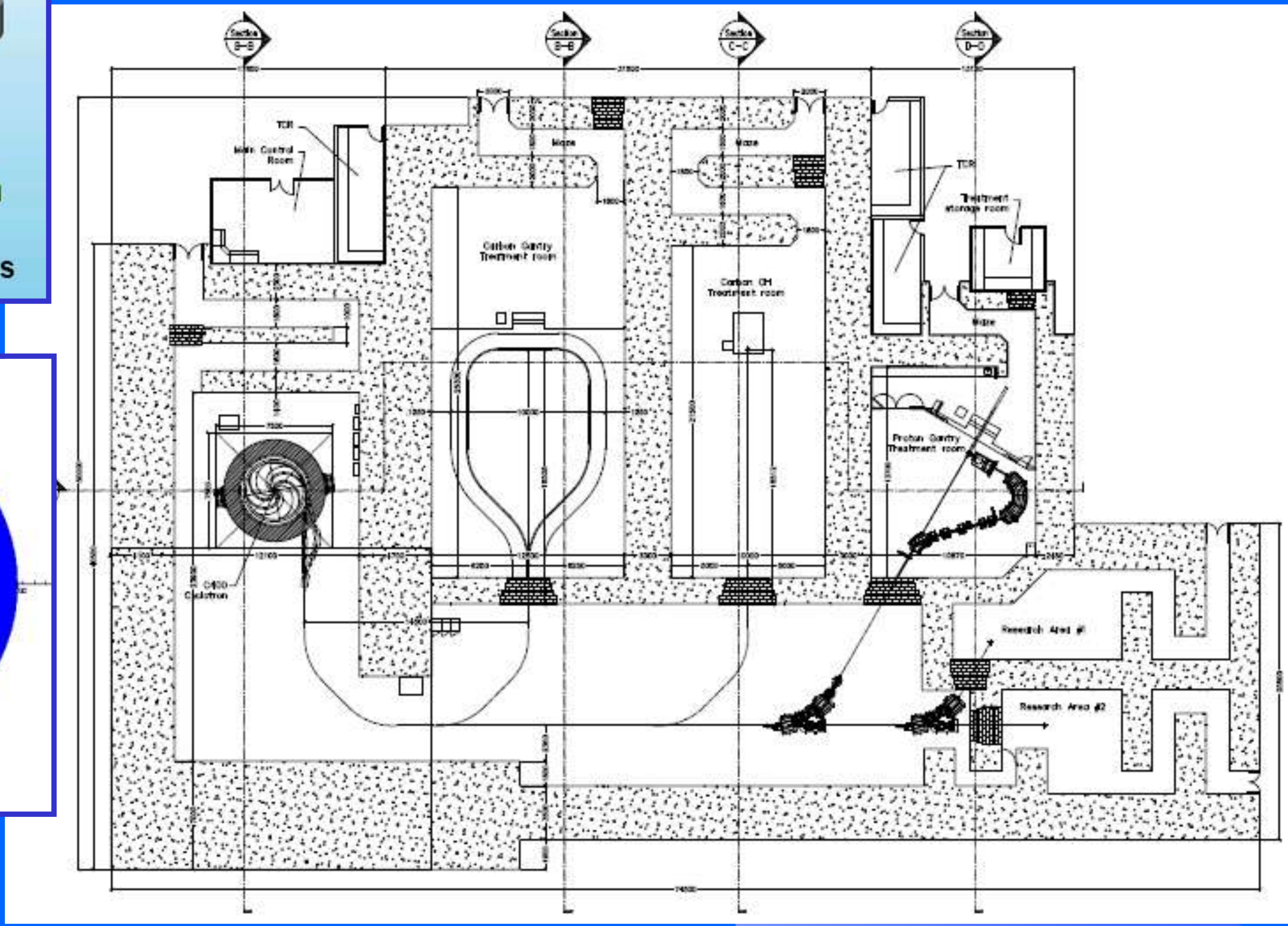


New centers for carbon ions

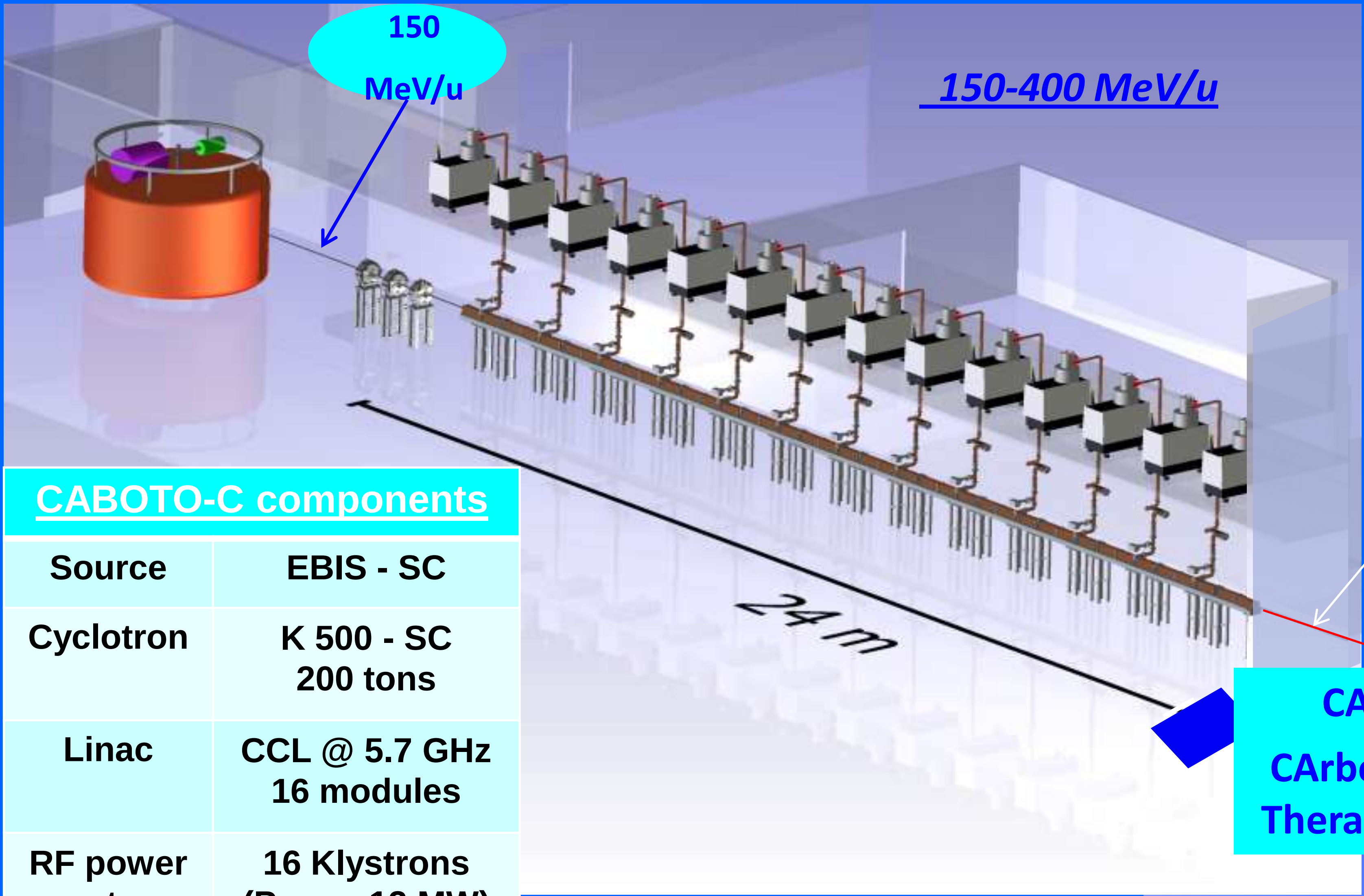
"Archade" (Caen) is based on the new IBA 400 MeV/u superconducting cyclotron







The CYCLINAC solution for carbon ions

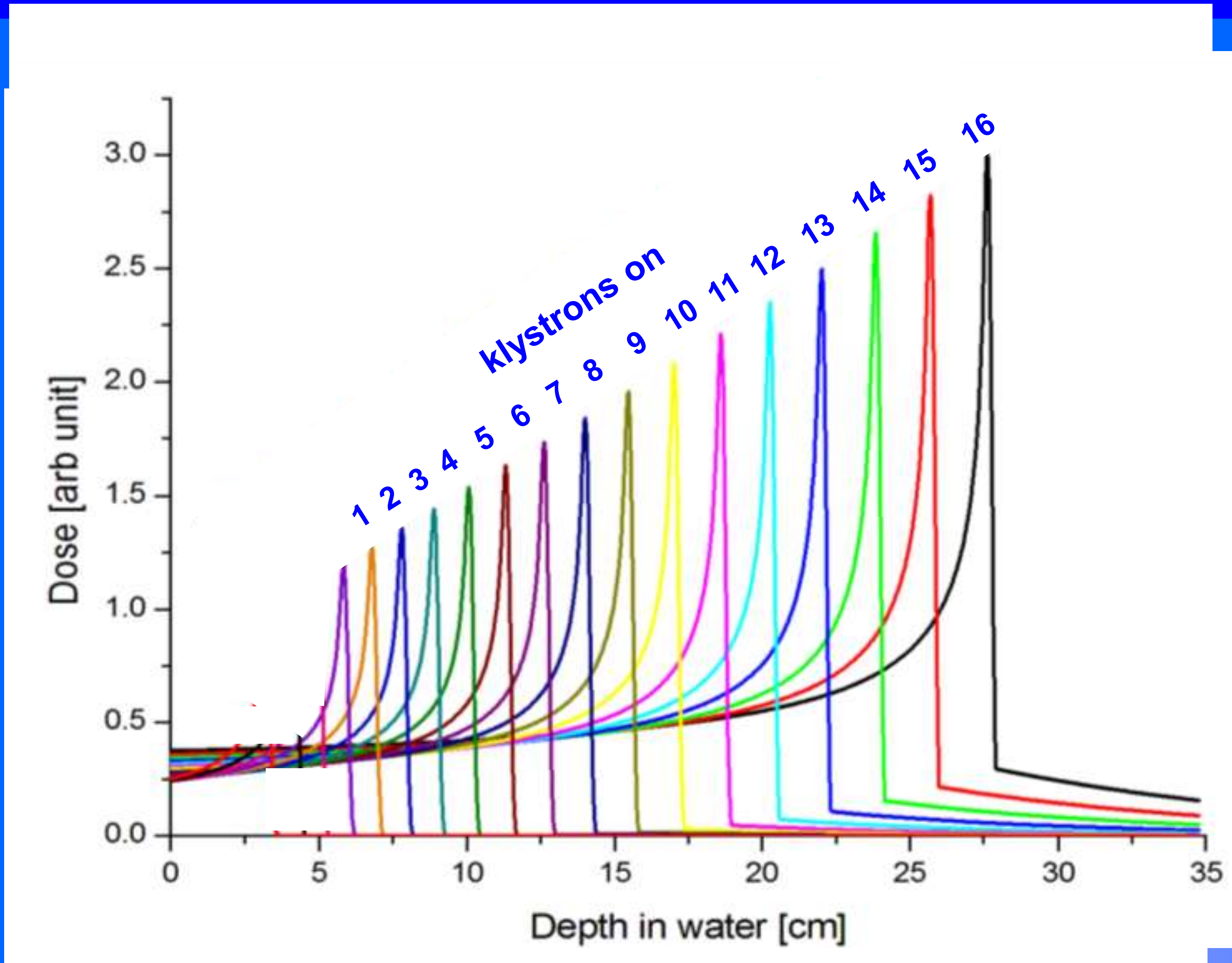


CABOTO-C components	
Source	EBIS - SC
Cyclotron	K 500 - SC 200 tons
Linac	CCL @ 5.7 GHz 16 modules
RF power system	16 Klystrons (P_{peak} = 12 MW)

CABOTO – C =

CArbon BOoster for Therapy in Oncology

Fast active energy modulation

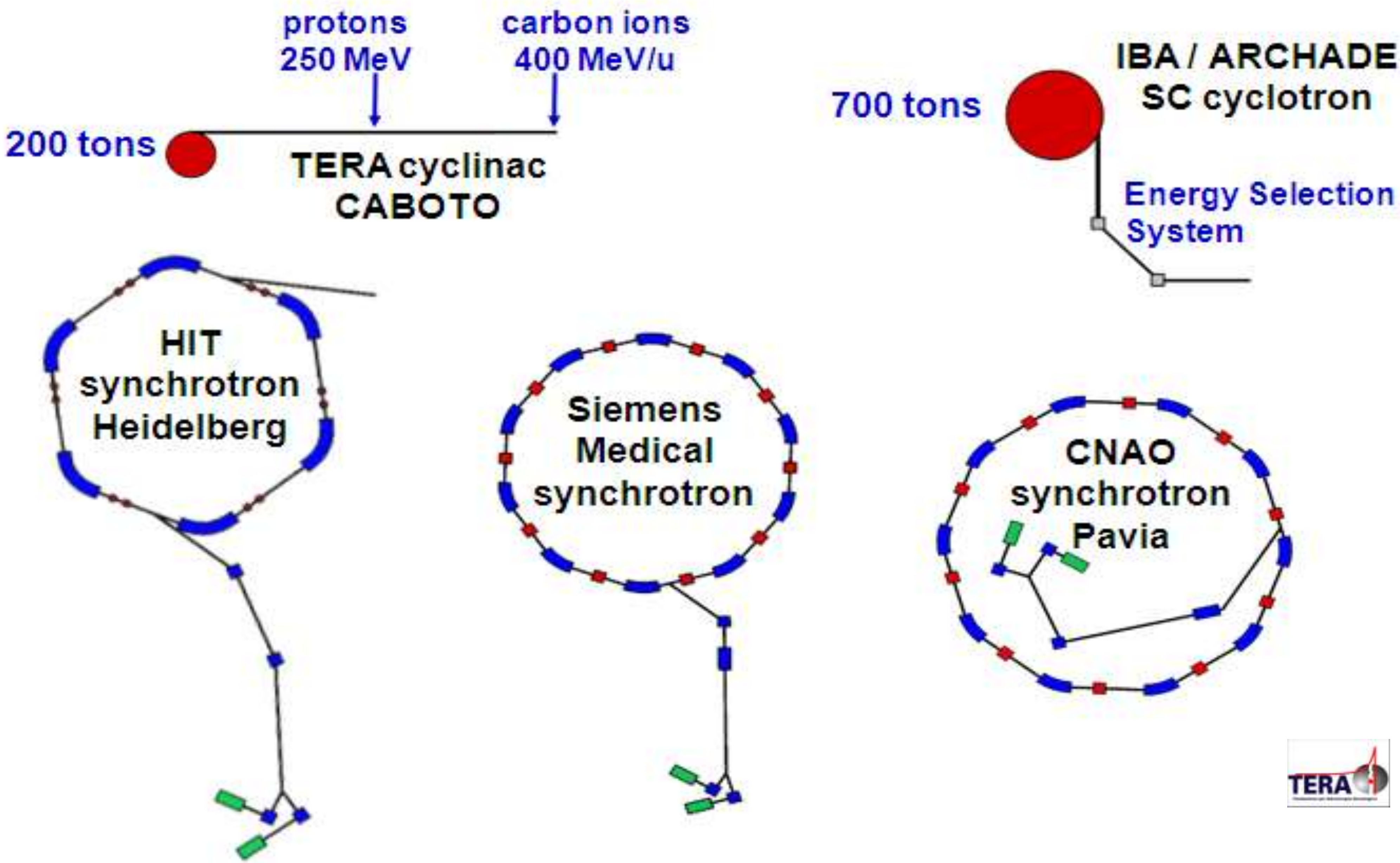


Active Energy Modulation
+
3D feedback system

Treatment of MOVING ORGANS

TERA

Dimensional comparison among carbon ion accelerators



Conclusions

Protontherapy is on the market and the number of centres and patients increases exponentially

Carbon ion therapy is delivering the promised results for radioresistant tumours but many clinical studies are still needed

As far as dual centres are concerned Europe is doing very well: Heidelberg, Pavia are almost finished, Margburg will start in 2010, Wiener Neustadt, Lyon and Kiel will come next

At present the focus of accelerator development is on single room facilities for protons and novel carbon ion accelerators

THE END

Accelerators and cancer therapy

Ugo Amaldi
University Milano Bicocca and TERA Foundation

‘Hadrontherapy’, or ‘particle therapy’, is a collective word which covers all cancer therapy modalities which irradiate patients with beams of hadrons.

The most used hadrons are protons and carbon ions. Protontherapy is developing very rapidly: more than 65'000 patients have been treated and five companies offer turn-key centres. Carbon ions, used for about 6000 patients, have a larger radiobiological effectiveness and, being a qualitatively different radiation, require still radiobiological and, in particular, clinical studies to define the best tumour targets.

After a review of the European effort in carbon ion therapy, the two challenges facing the physicists developing the accelerators for hadrontherapy will be described: the construction of ‘single-room’ facilities for protons and of multi-room facilities, not based on synchrotrons, for carbon ions.