PARTICLE ACCELERATORS IN CANCER THERAPY

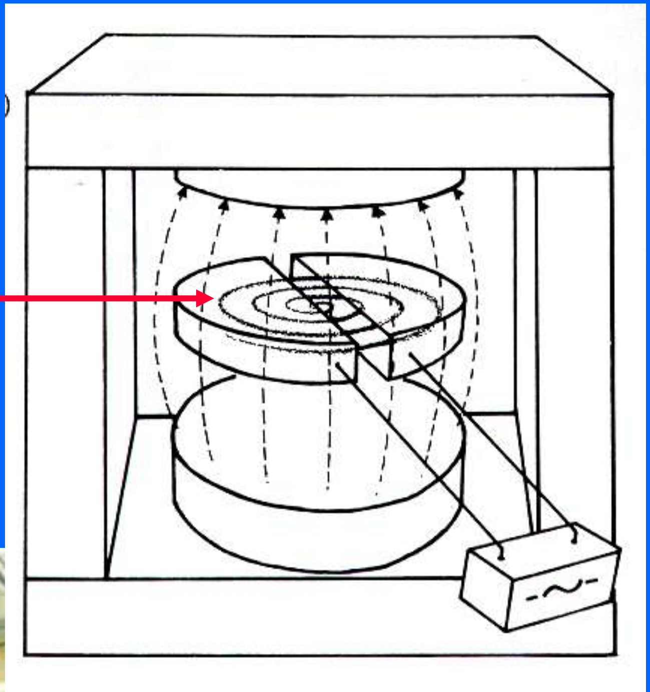
Ugo Amaldi

University Milano Bicocca and TERA Foundation

Accelerators

1930: invention of the cyclotron

Spiral tajectory of an accelerated nucleus



Modern cyclotron

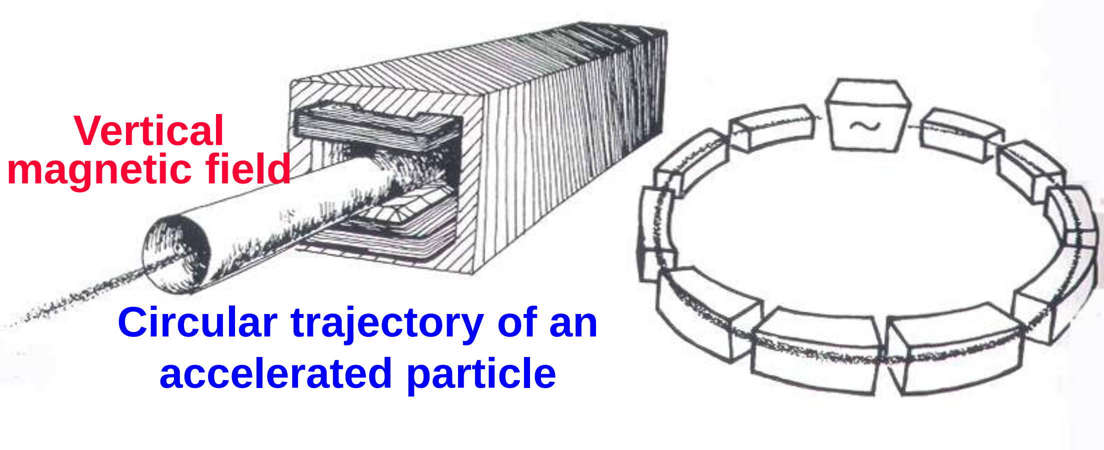
Ernest Lawrence

(1901 – 1958)

1944: E. McMillan and V.J.Veksler

The «synchrotron»

"Phase stability principle"



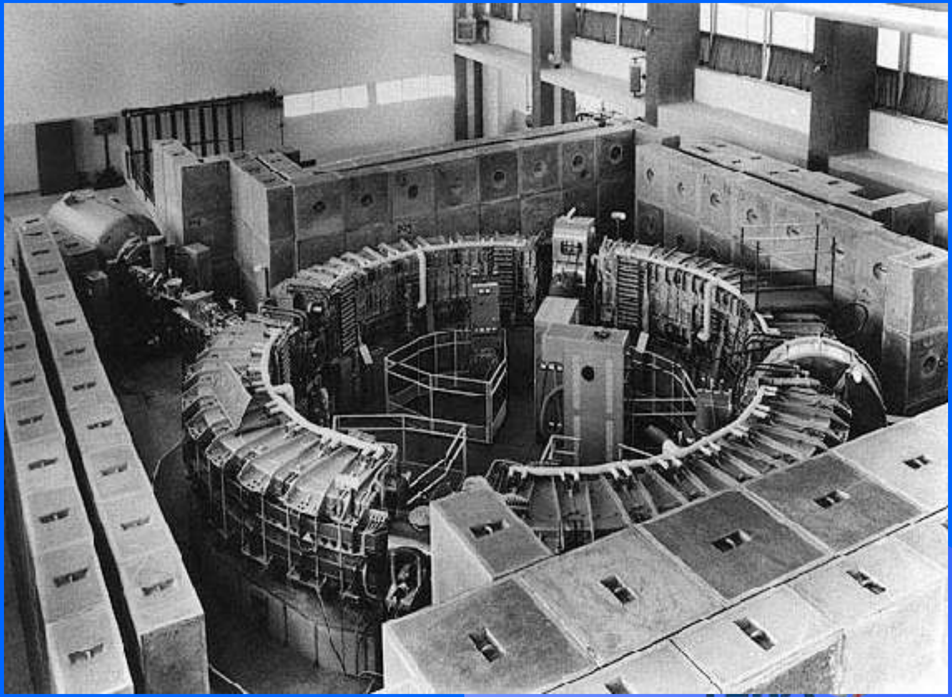
1 GeV

electron synchrotron

Frascati - INFN - 1959

1959: Veksler visits McMilan

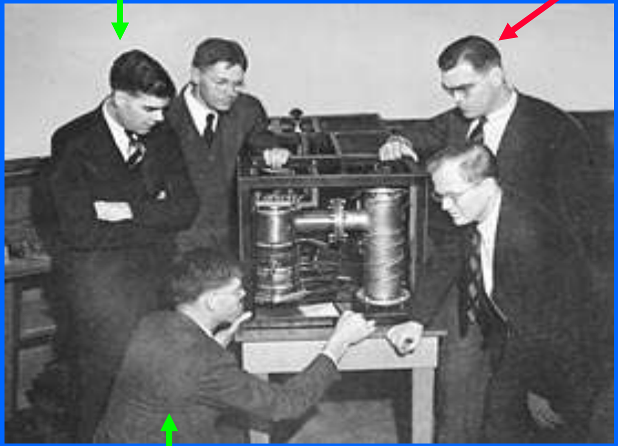
at Berkeley



The first electron linac

Sigmur Varian

William W. Hansen



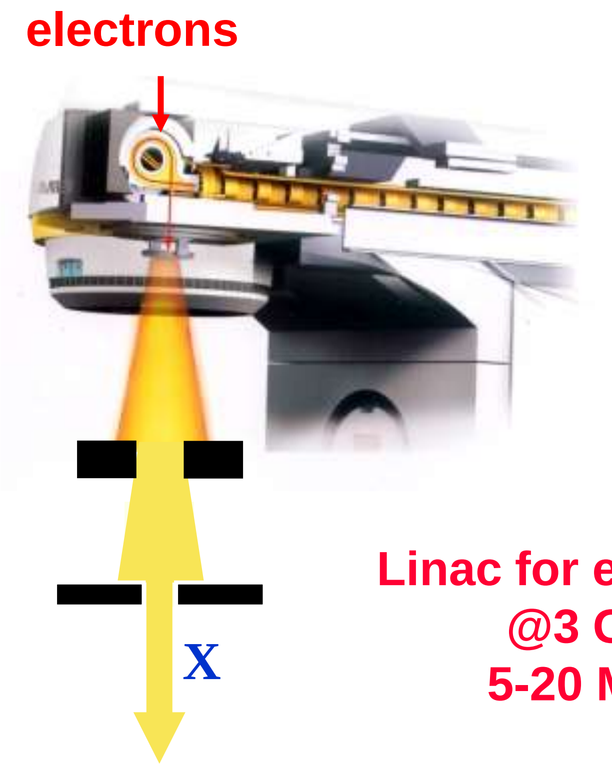
Russell Varian

1939

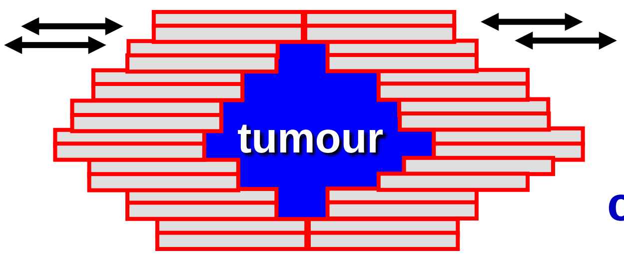
Invention of the klystron

1947
linac for electrons
1.5 MeV at 3 GHz

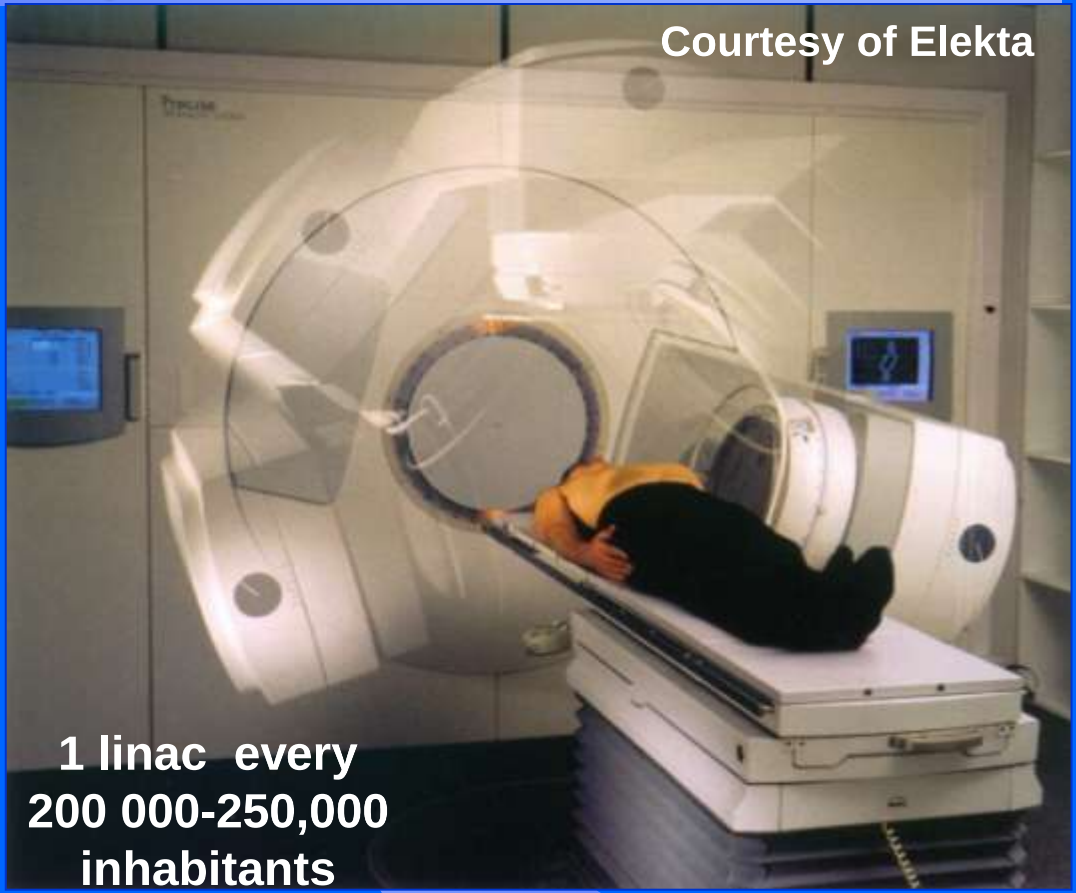
‘Conventional’ radiotherapy: linear accelerators dominate



Linac for electrons
@3 GHz
5-20 MeV



Multileaf collimator



20 000 patients per year every
10 million inhabitants
have a 30 session treatment of
about 2 J/kg = 2 grays (Gy)

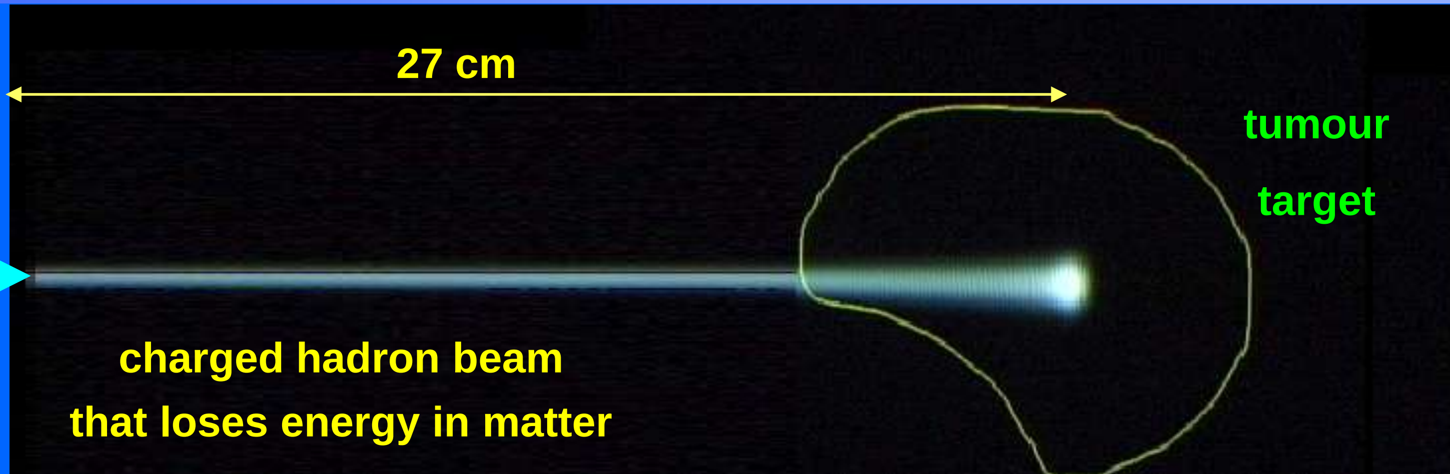
Macroscopic distribution of the dose

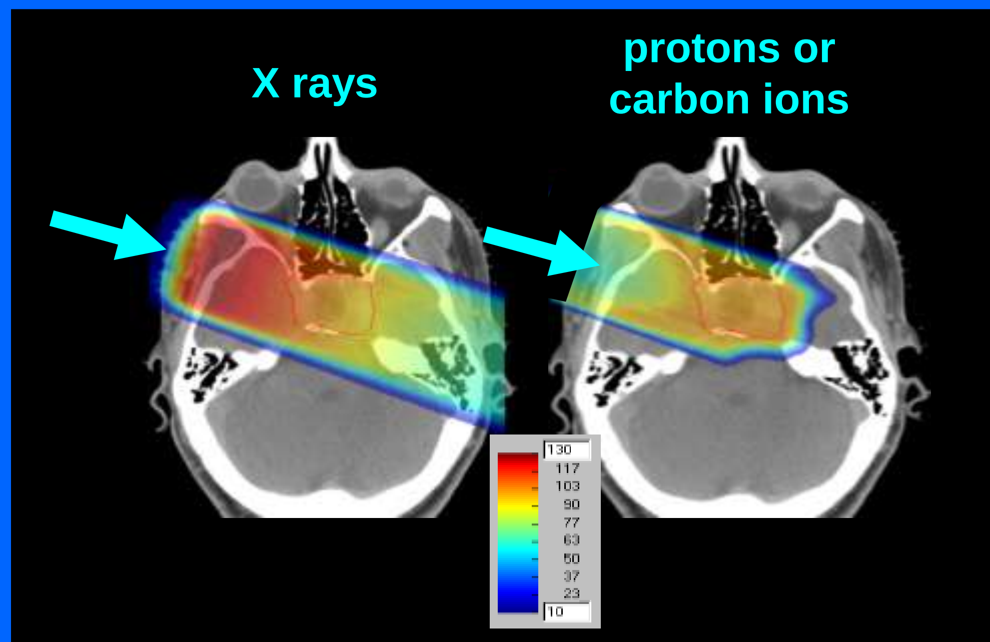
In “hadrontherapy” (*) protons and ions spare healthy tissues

200 MeV - 1 nA protons

4800 MeV – 0.1 nA carbon ions

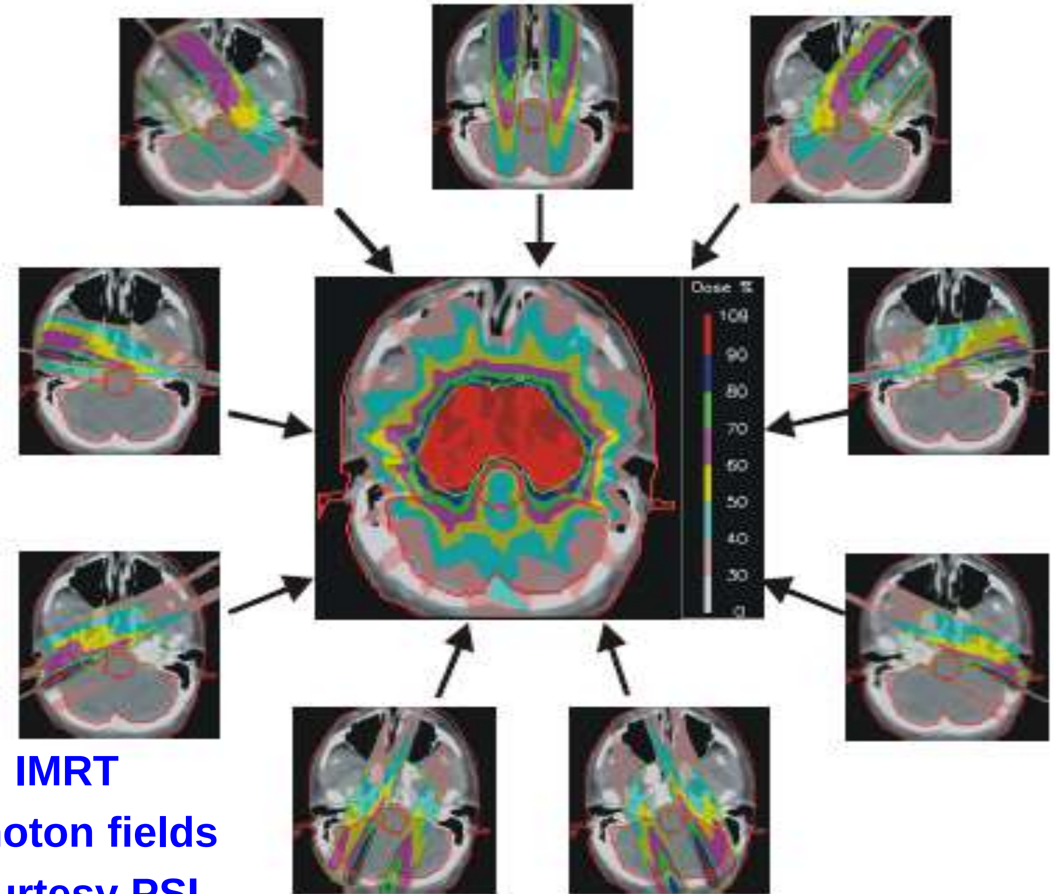
which can control radioresistant tumours





(*) Also “hadron therapy” and “particle therapy”

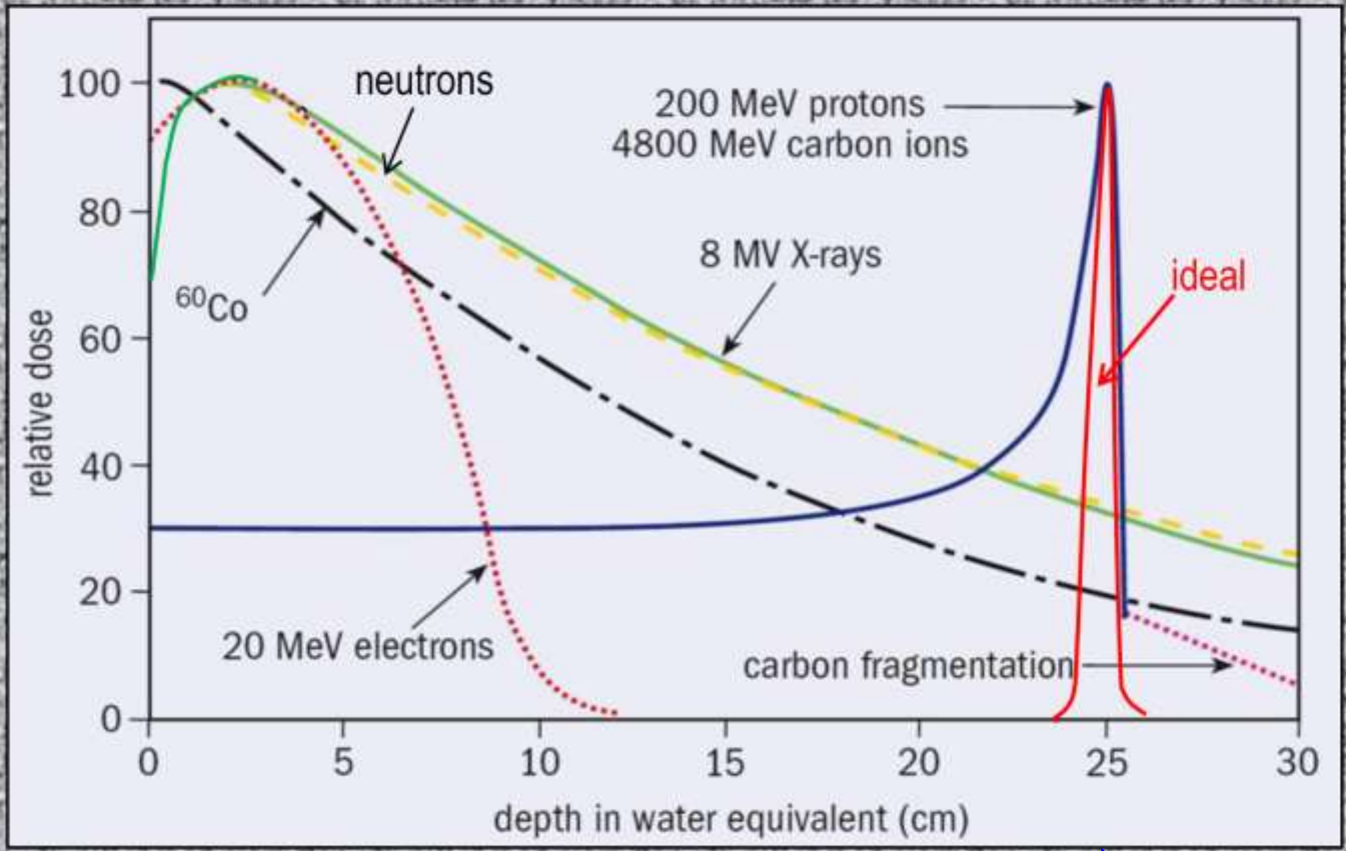
Macroscopic distribution of the X ray dose



IMRT
9 photon fields
Courtesy PSI

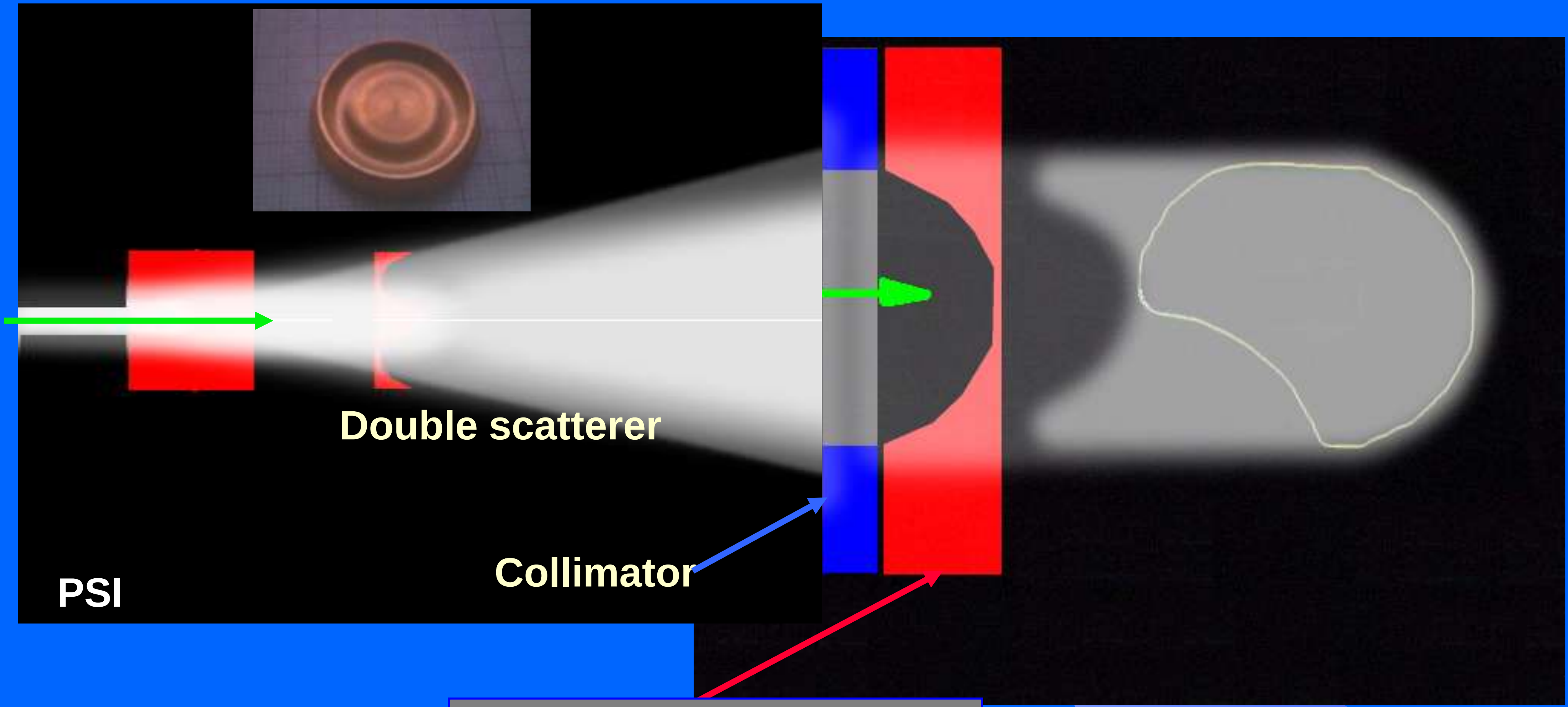
At present the best is " Intensity Modulated Radiation Therapy" = IMRT
In future "Image Guided Radio Therapy" to follow moving organs

The icon of radiation therapy with charged hadrons



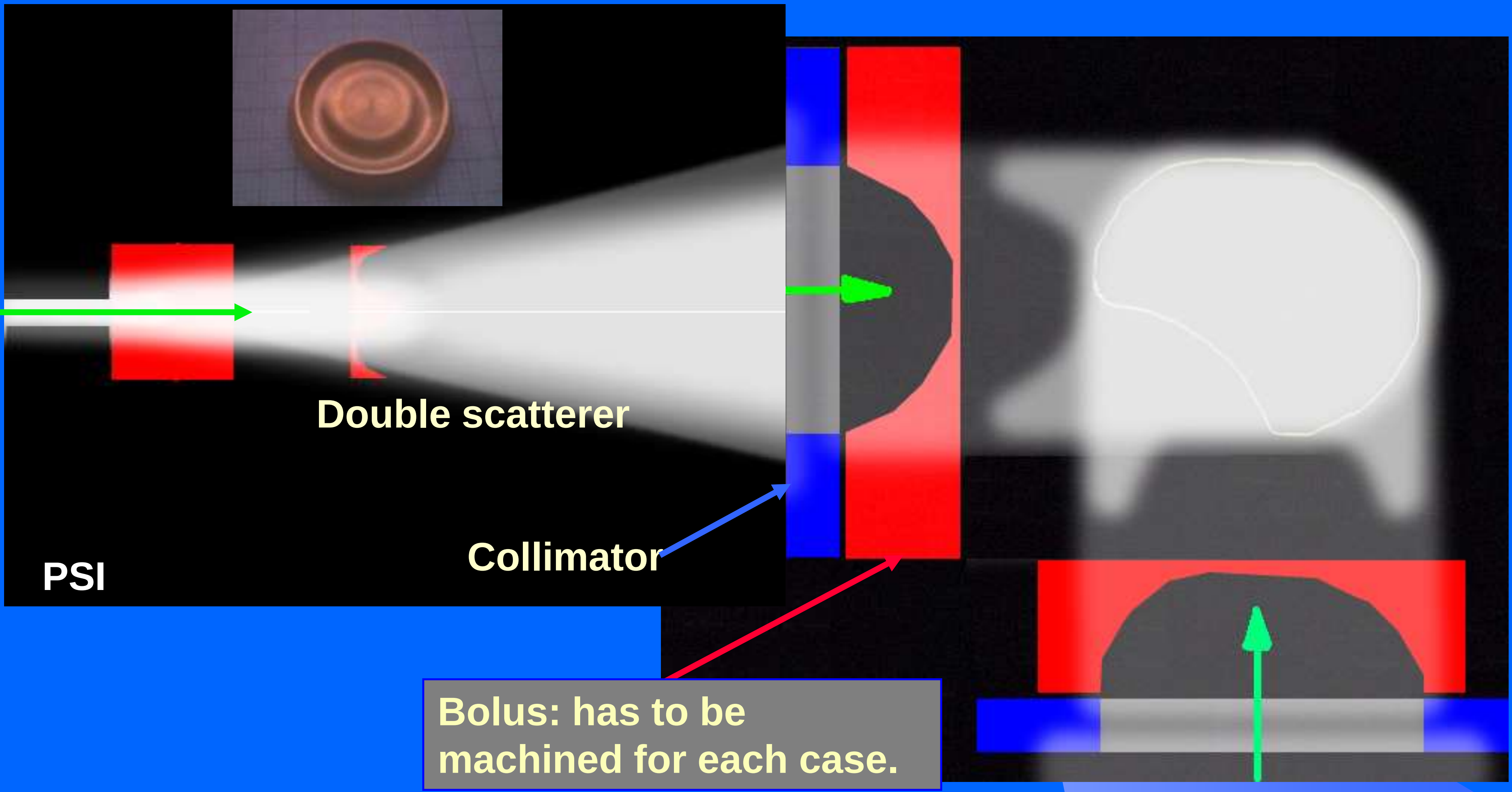
Radiation beam in matter

1A. Standard procedure: Passive beam spreading with respiratory gating

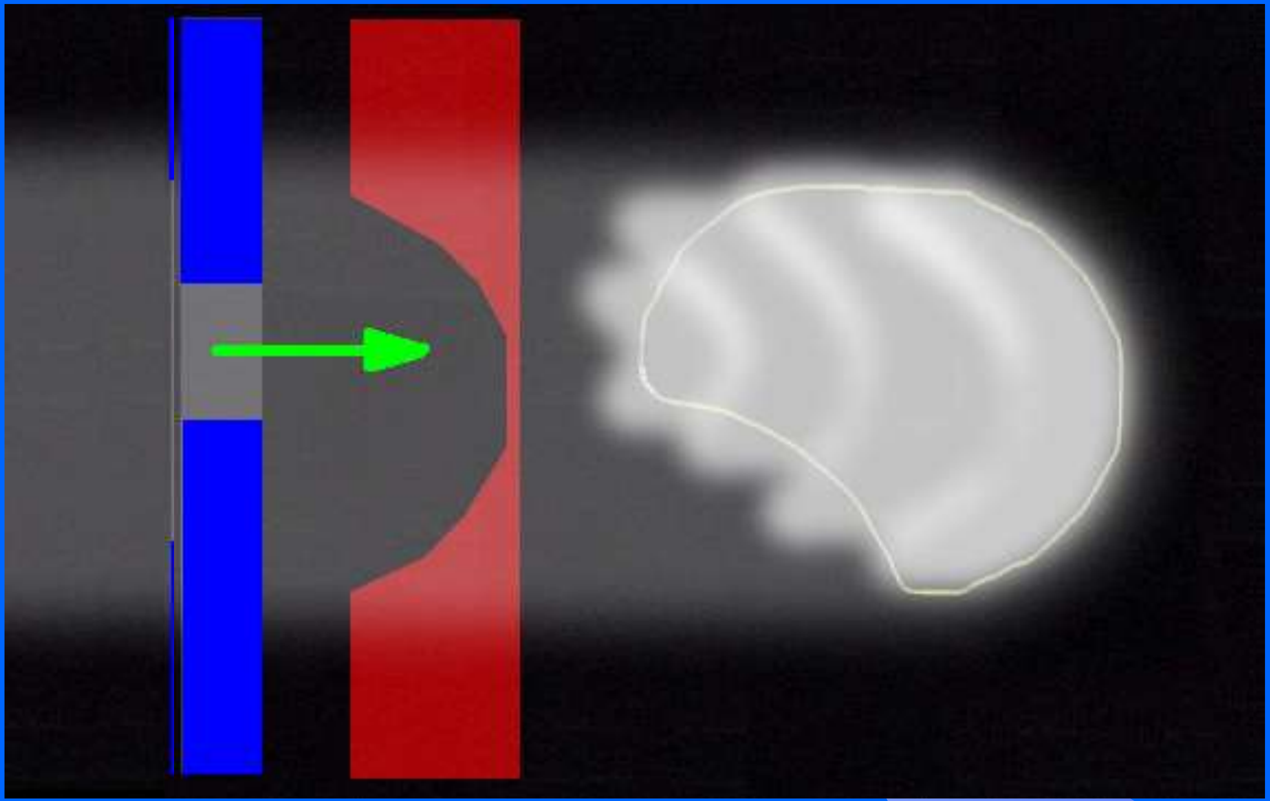


Bolus: has to be machined for each case.

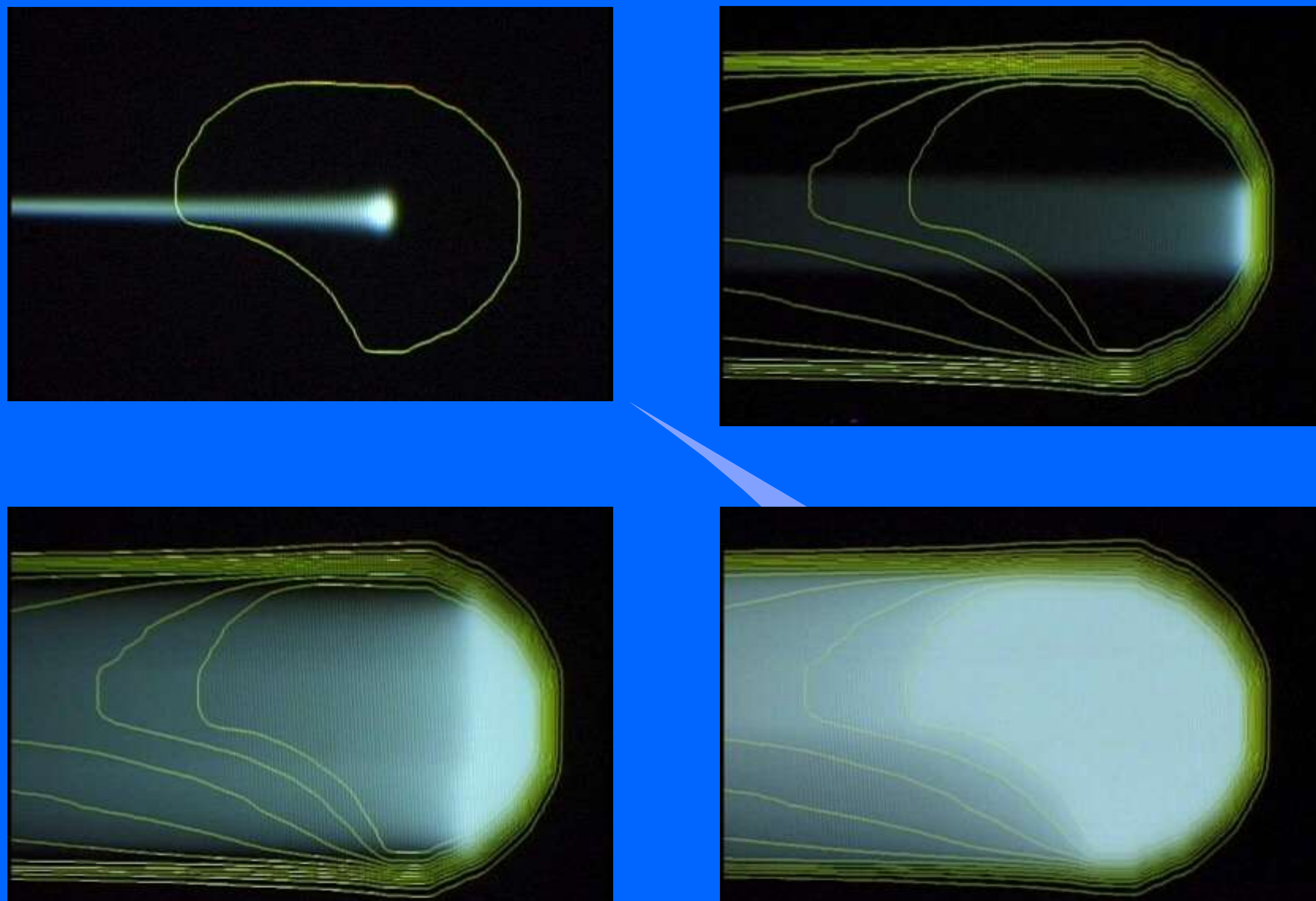
1A. Standard procedure: Passive beam spreading with respiratory gating



1B. Advanced procedure: layer stacking with respiratory gating



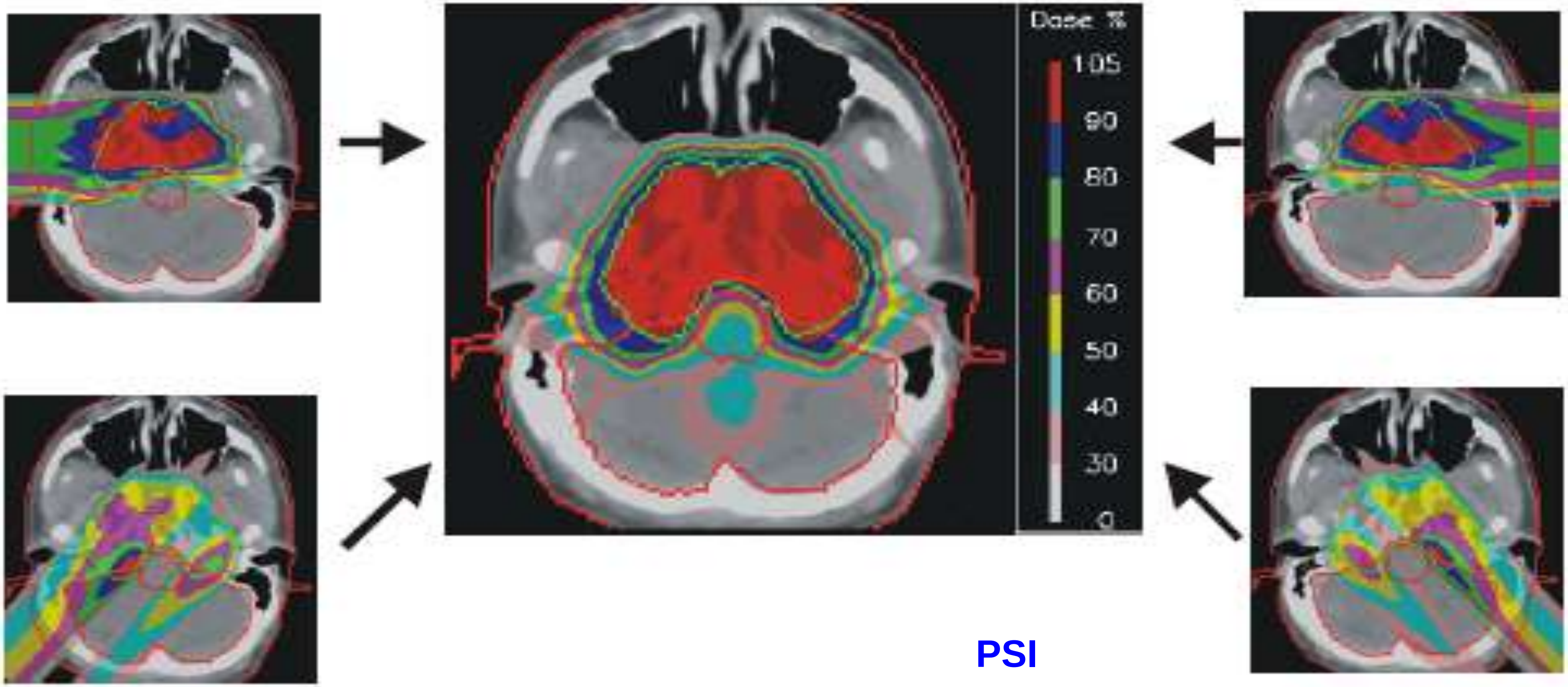
2A. Active “spot scanning” technique by PSI with respiratory gating (Villigen)



- **PROTONS**
  - Courtesy PSI

IMPT = Intensity Modulated Particle Therapy with protons

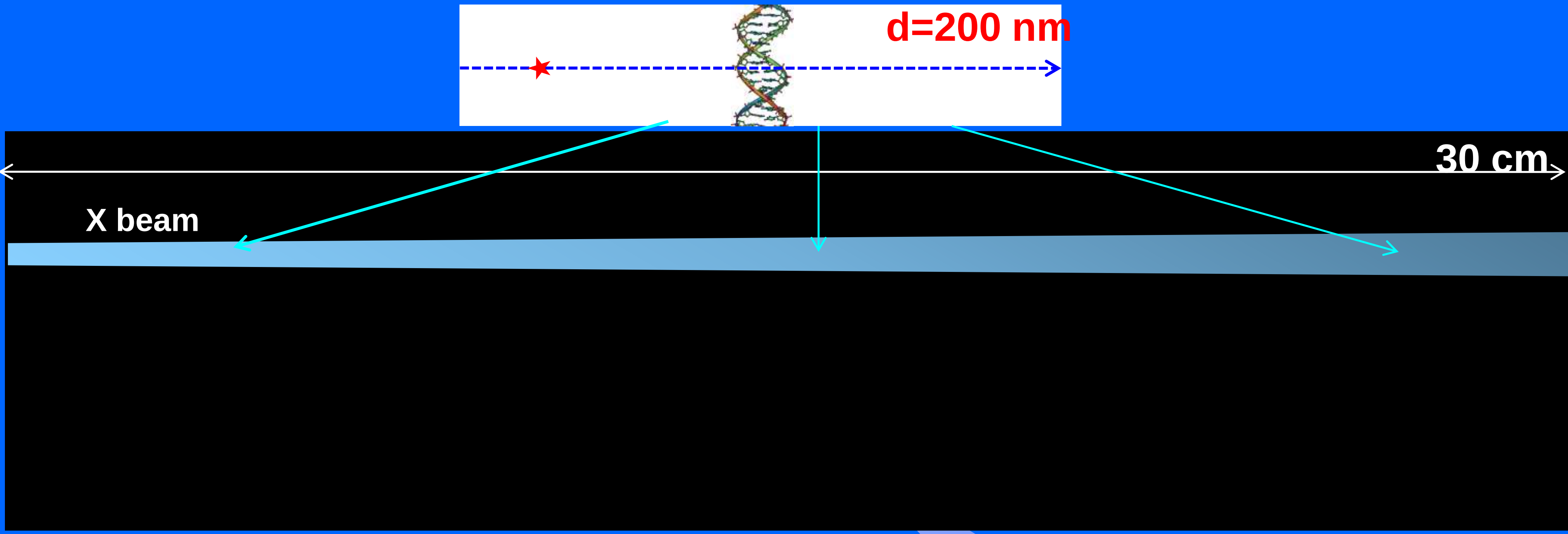
4 NON-UNIFORM FIELDS



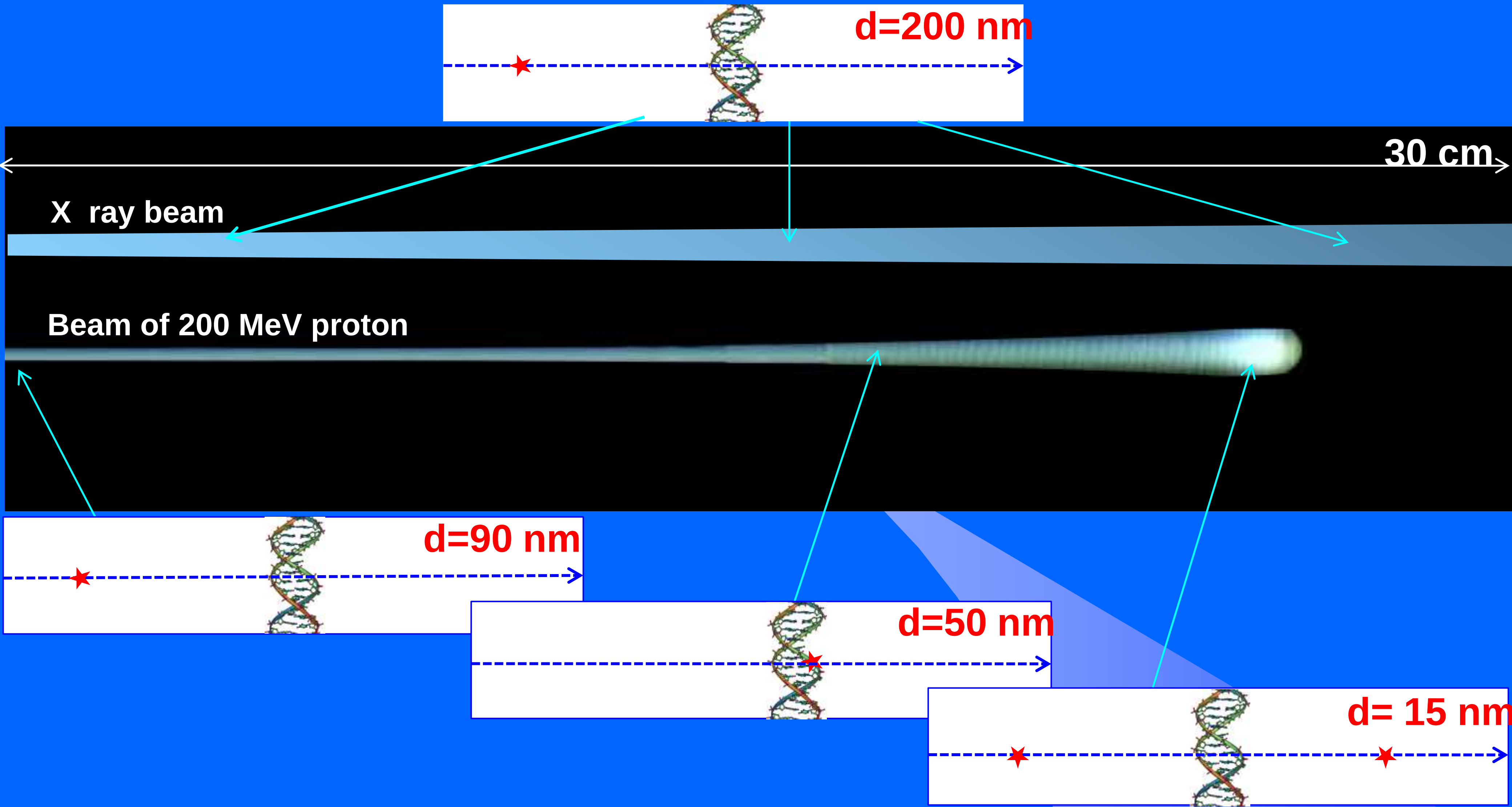
PSI

Microscopic distribution of the dose

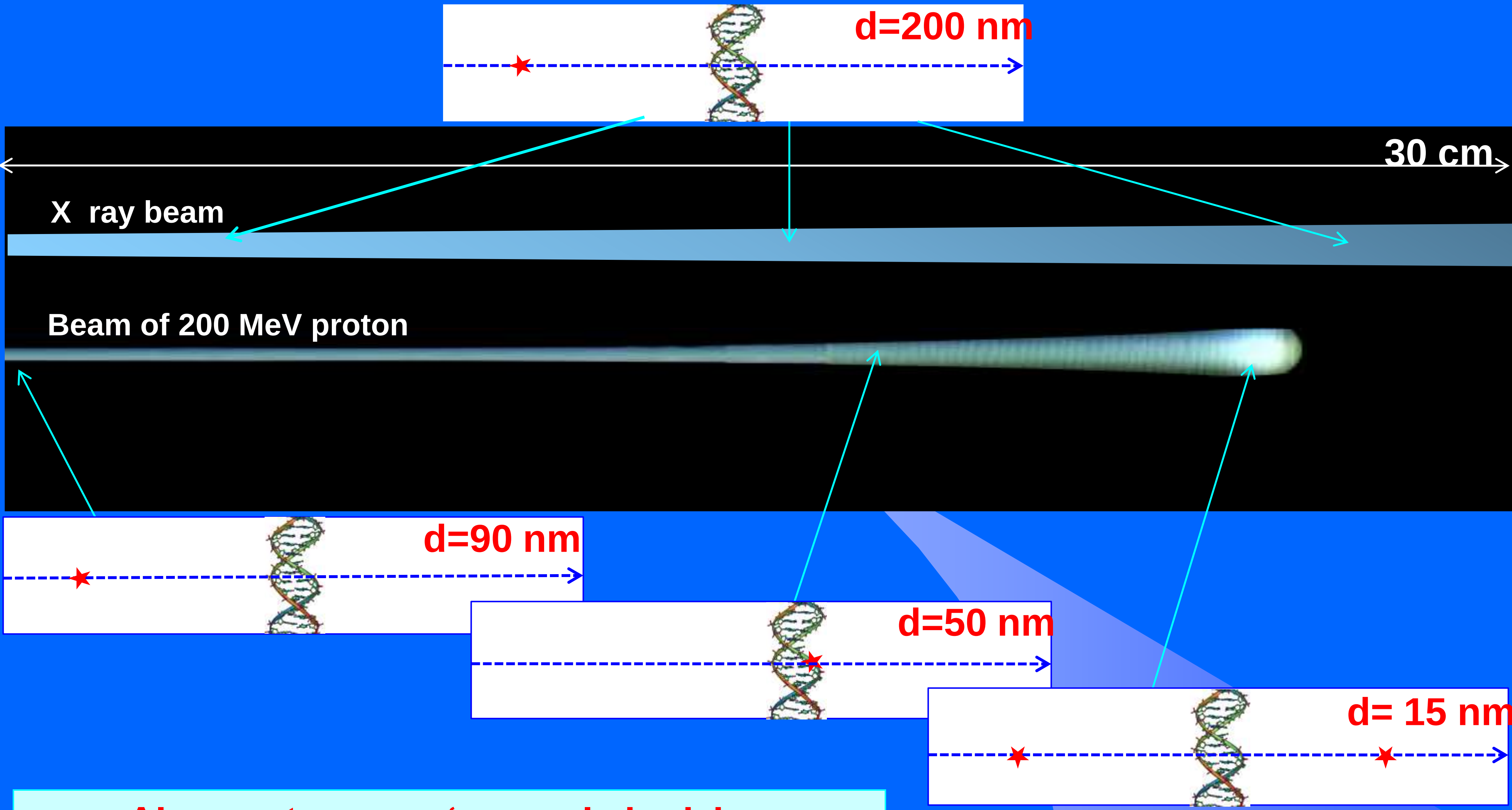
Electrons put in motion by X rays: "sparsely ionizing"



Protons1: more favorable dose- 2. same ‘indirect effects’

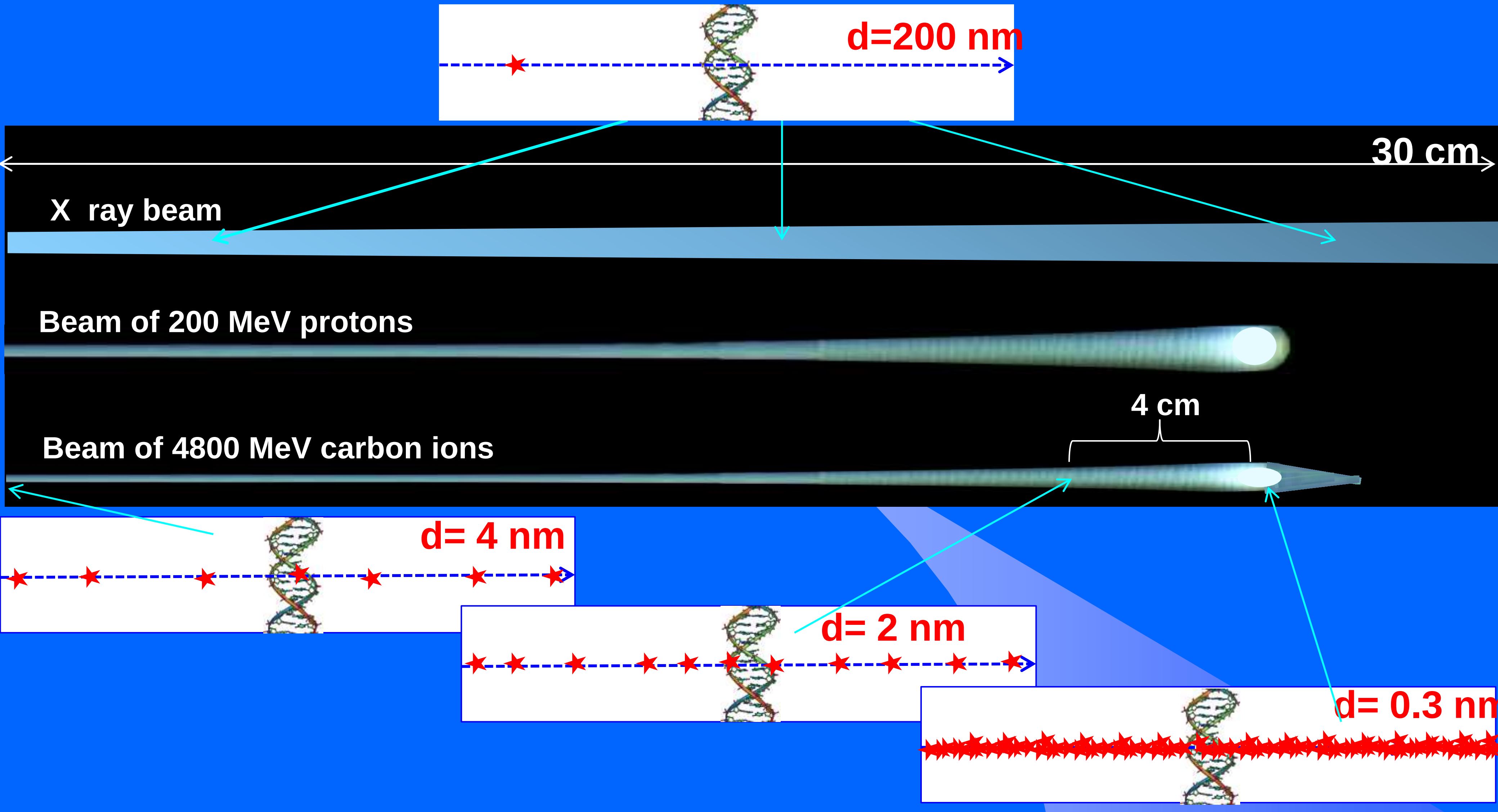


Protons1: more favorable dose- 2. same 'indirect effects'

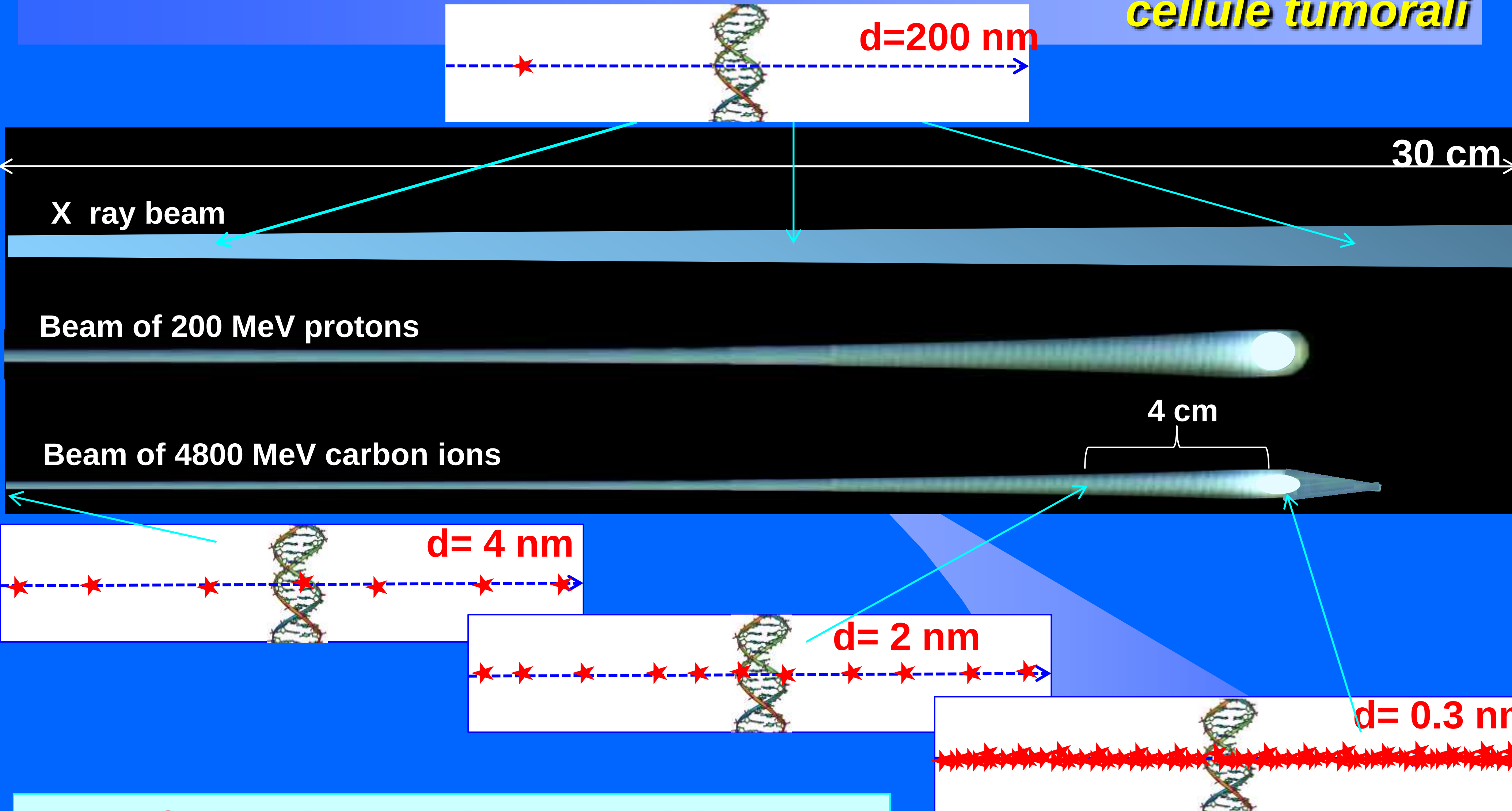


Also protons are 'sparsely ionizing

Carbon ions: 1. more favorable dose- 2. 'direct effects"

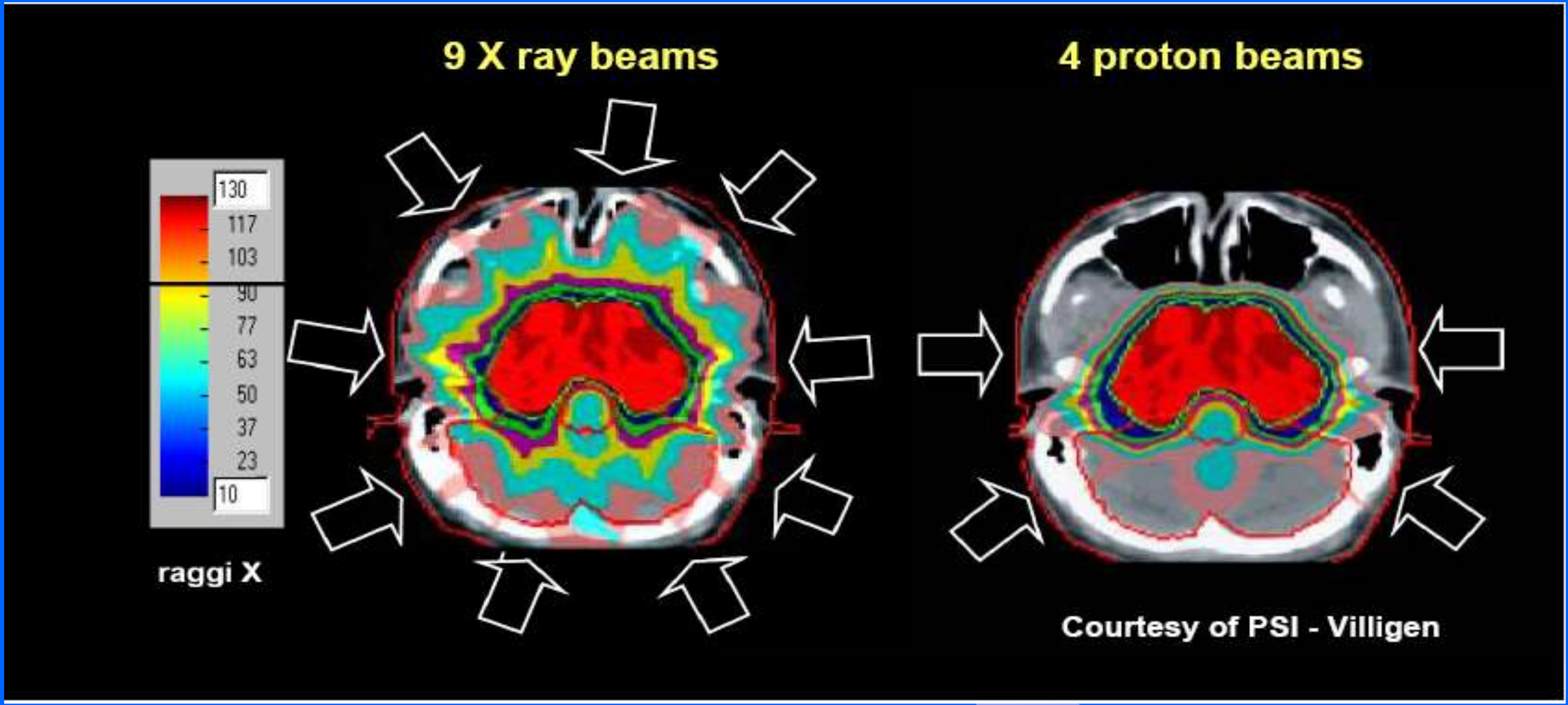


Ioni carbonio: 1. dose più favorevole - 2. effetti 'diretti' sulle cellule tumorali

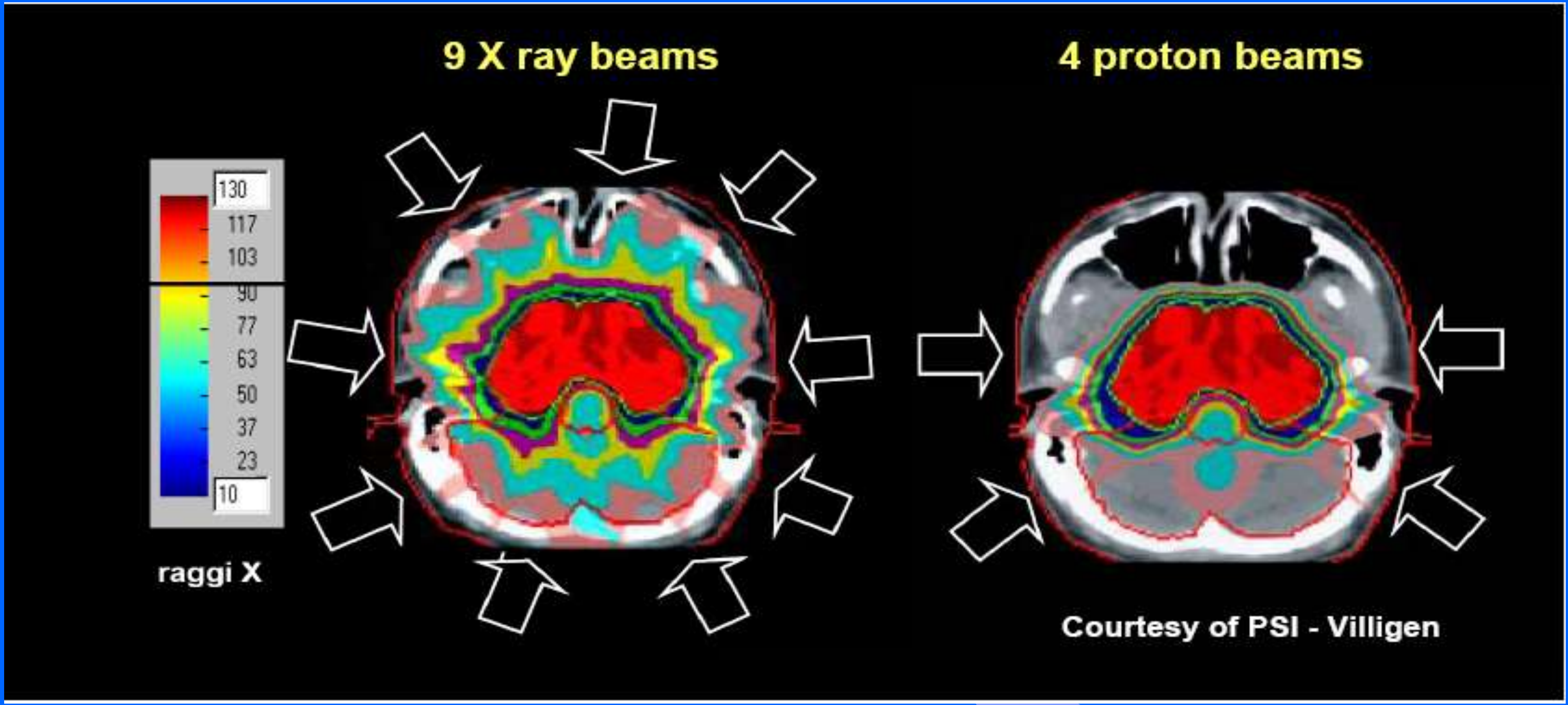


Carbon ins are 'densely ionizing

Protons are quantitatively different from X-rays



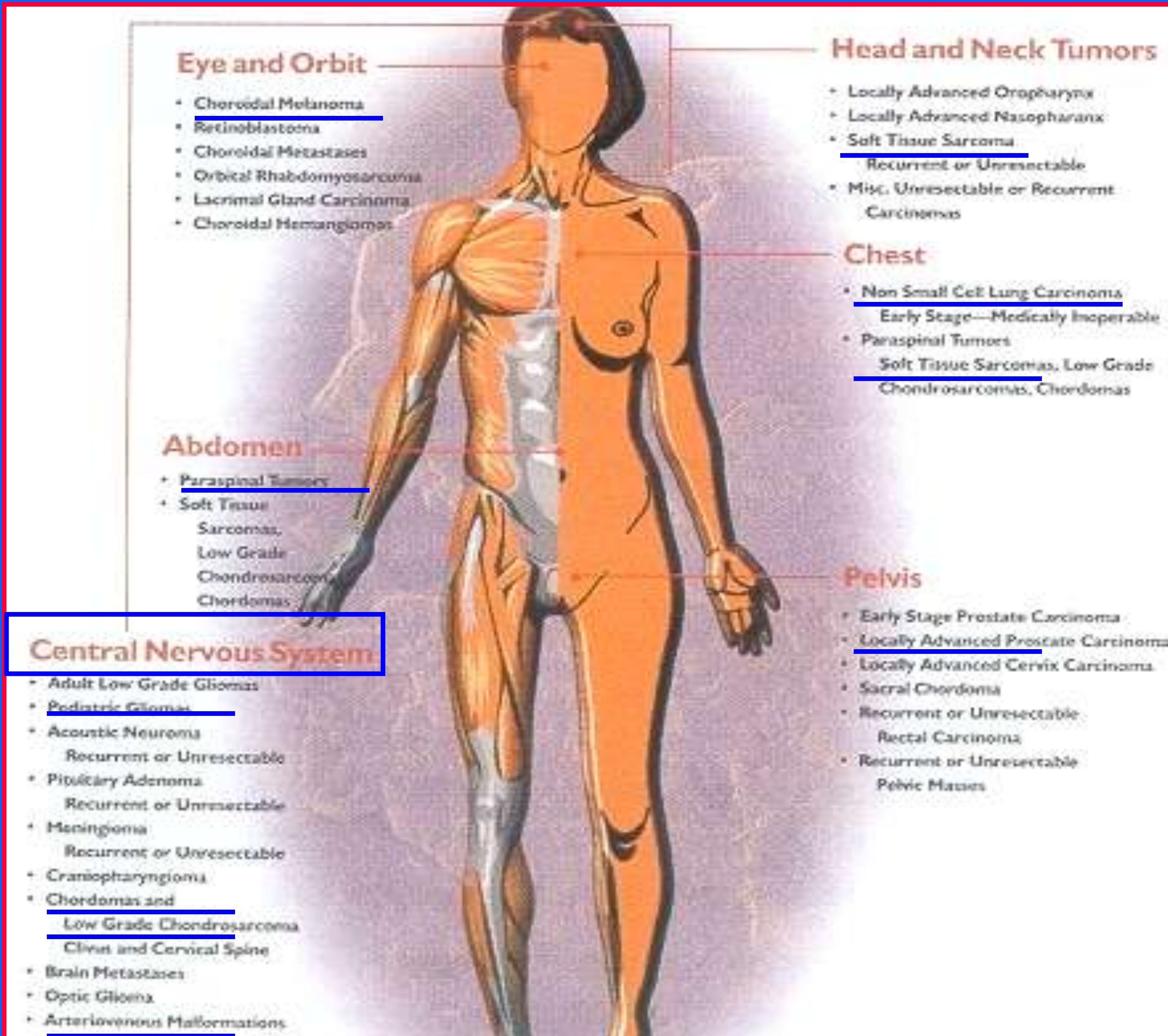
Carbon ions are qualitatively different from X-rays



Carbon ions deposit in a cell about 25 times more energy than a proton producing not reparable multiple close-by double strand breaks

Carbon ions can control radio-resistant tumours

Number of patients



The site treated with hadrons

In the world

protontherapy:

90'000 patients

carbon ion therapy

8500 patients

BUT

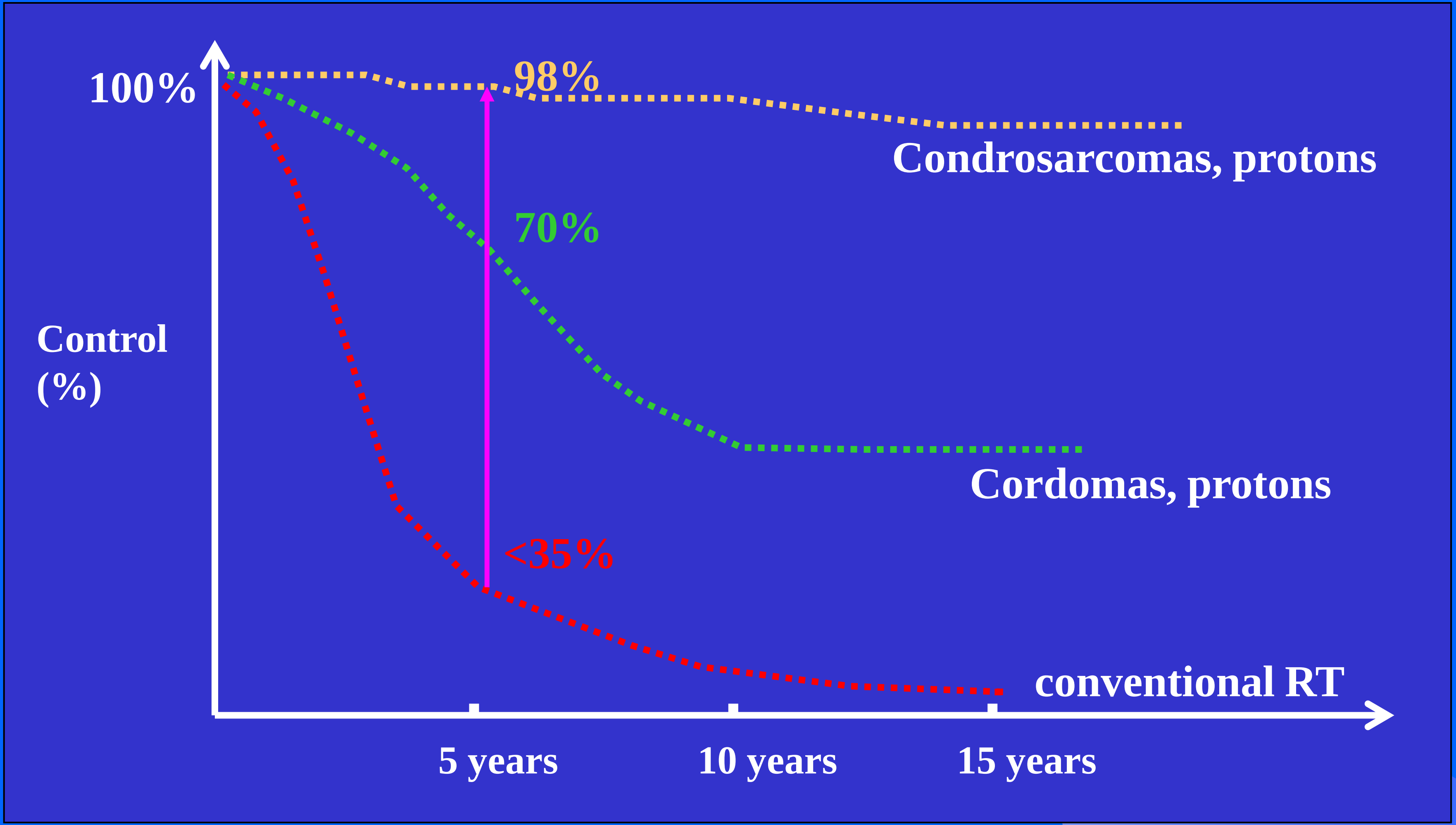
only 1% with 'active' dose distribution systems

PSI and GSI

with spot/raster scanning

TERA

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



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: Prof. Manjit Dosanjh –

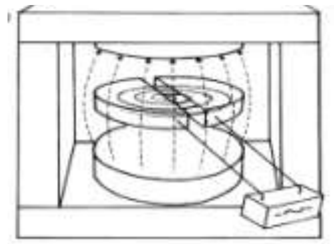
Projects in FP7: ULICE, PARTNER, ENVISION

Protontherapy

The accelerators used today in hadrotherapy are "circular"

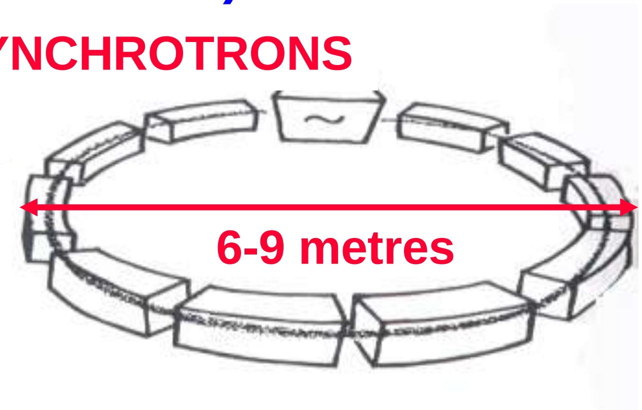
Teletherapy with protons (200-250 MeV)

CYCLOTRONS (*) (Normal or SC)



4-5 metres

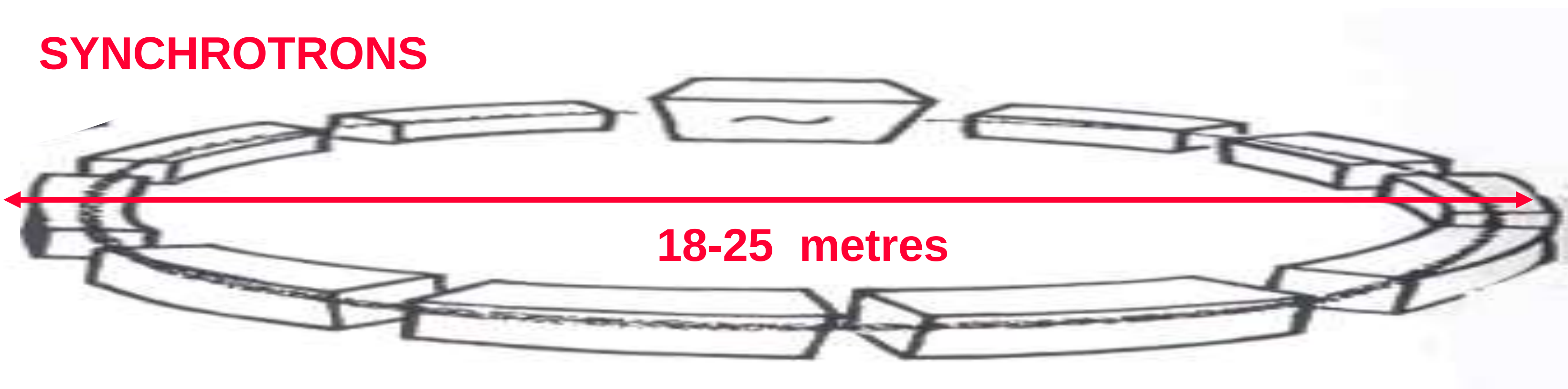
SYNCHROTRONS



(*) also synchrocyclotrons

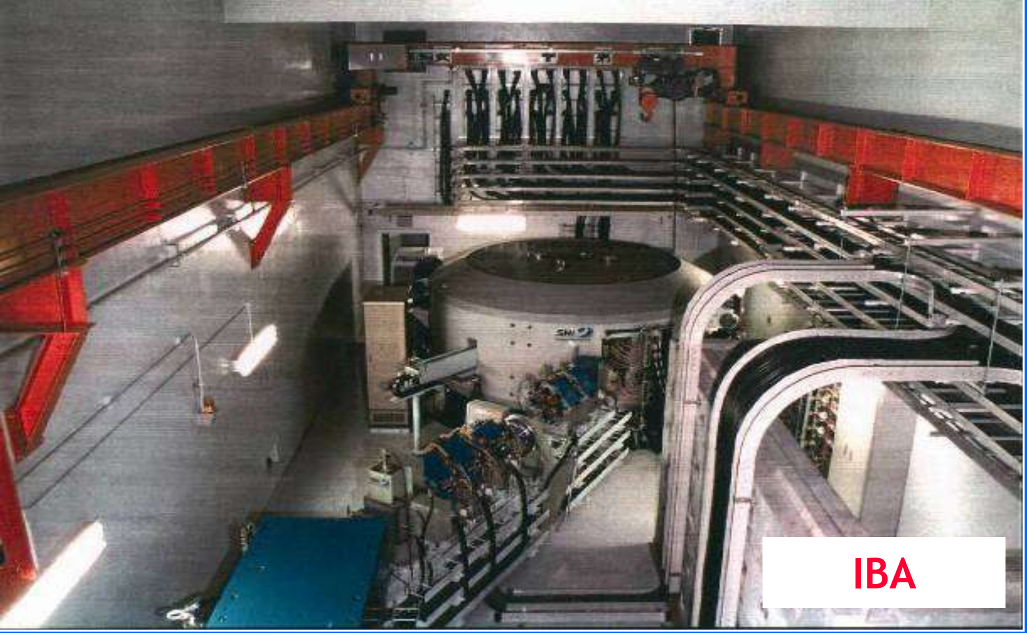
Teletherapy with carbon ions (4800 MeV = 400 MeV/u)

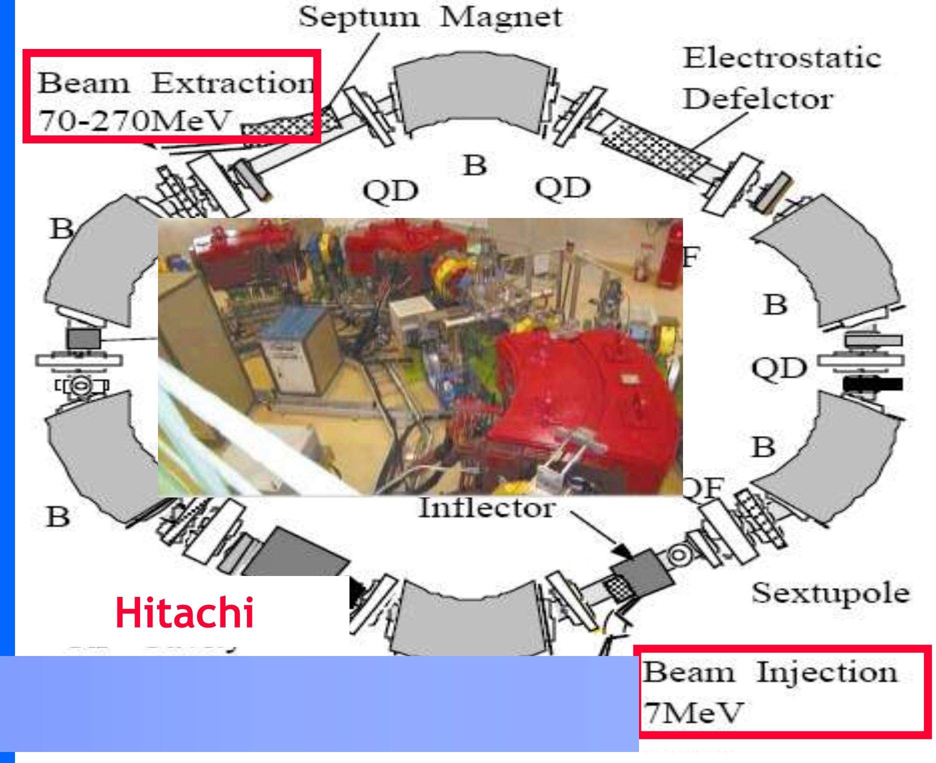
SYNCHROTRONS



Cyclotron for protons by Ion Beams Applications - Belgium

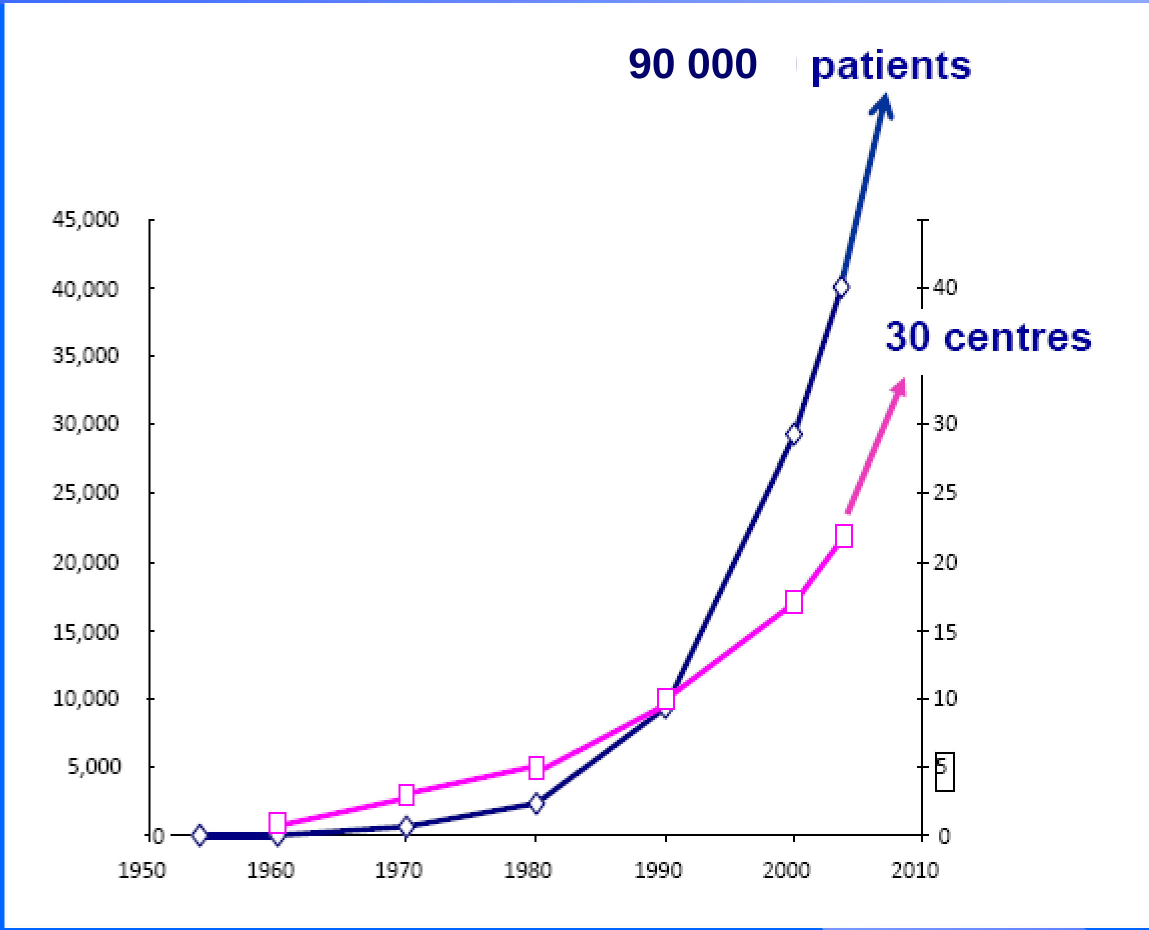
**Five companies offer turn-key centres for 120-150 M€.
If proton accelerators were 'small' and 'cheap',
no radiation oncologist would use X rays.**





Protontherapy: a mature market…

For these reasons protontherapy is booming



20-25 sessions per patient

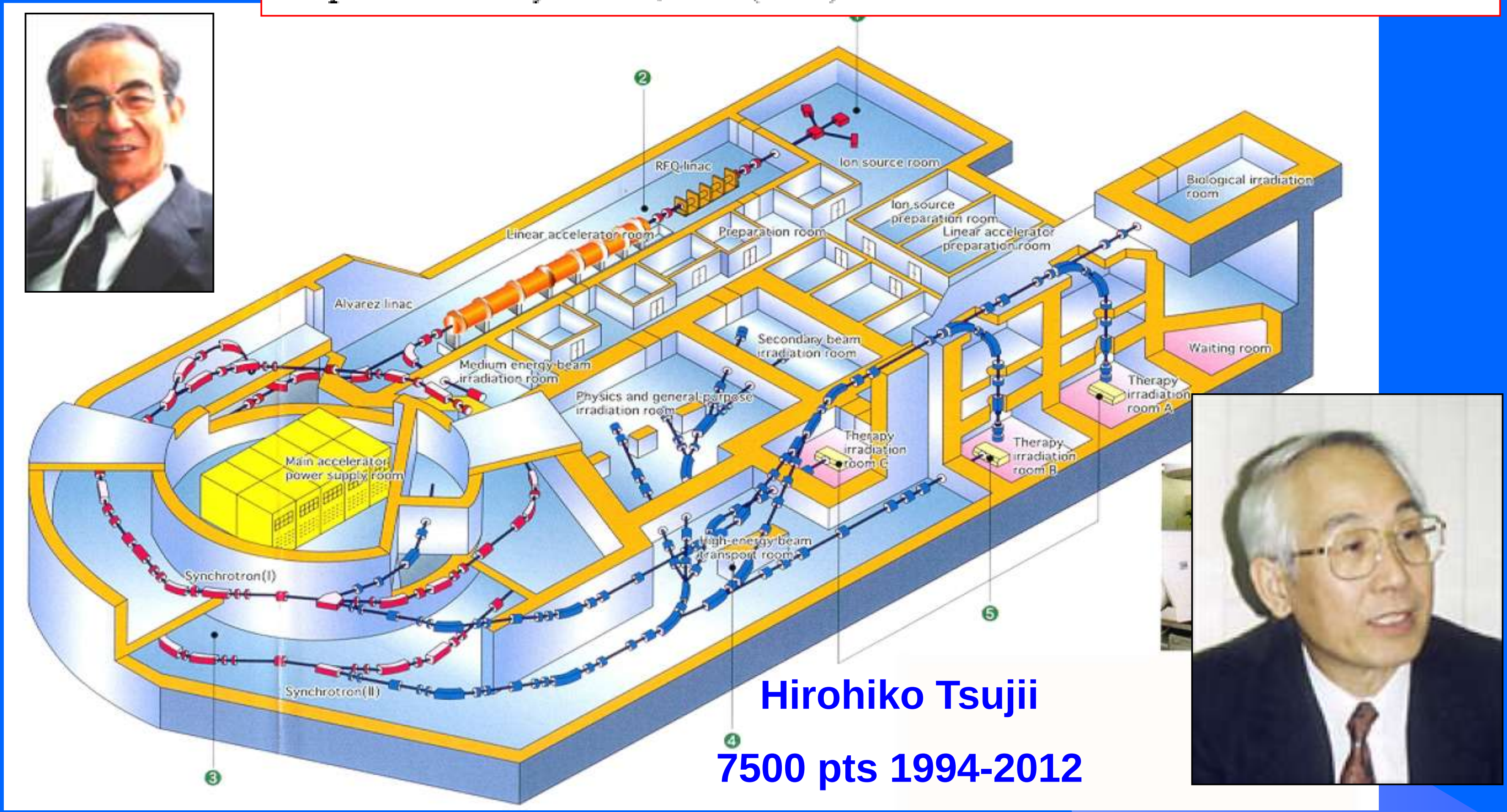
European cost of a full treatment:
IMRT: 7-8 k€
Protontherapy: 20-25 k€

The origins of carbon ion therapy after the radiobiology of the 70-80s in Berkeley

HIMAC in Chiba : Prof H. Tsujii was the pioneer of carbon ion therapy

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

7500 pts 1994-2012

Since the cells do not repair. less fractions are possible

HIMAC: 4-9 fractions!

Centers for carbon ion (and proton) therapy in Europe

TERA programmes since 1992

TERA has proposed and designed the 'dual' National Centre for carbon ions and protons based on the Proton Ion Medical Machine Study (PIMMS) made by CERN, TERA, MedAustron in 1996-2000

1. CNAO is ready in Pavia

TERA has introduced and developed a novel type of accelerator:

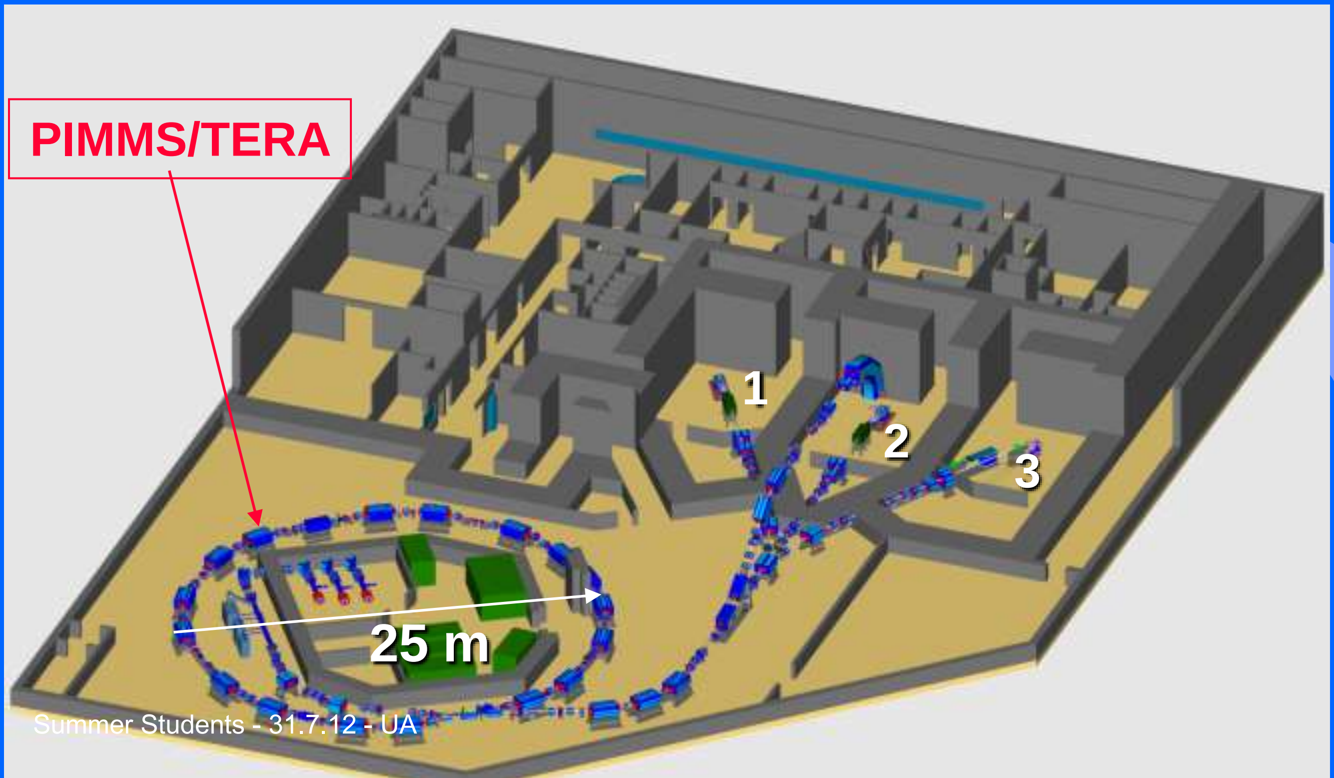
the "cyclinac"

2. "cyclinacs" for protons and carbon ions

CNAO = Centro Nazionale di Adroterapia Oncologica

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

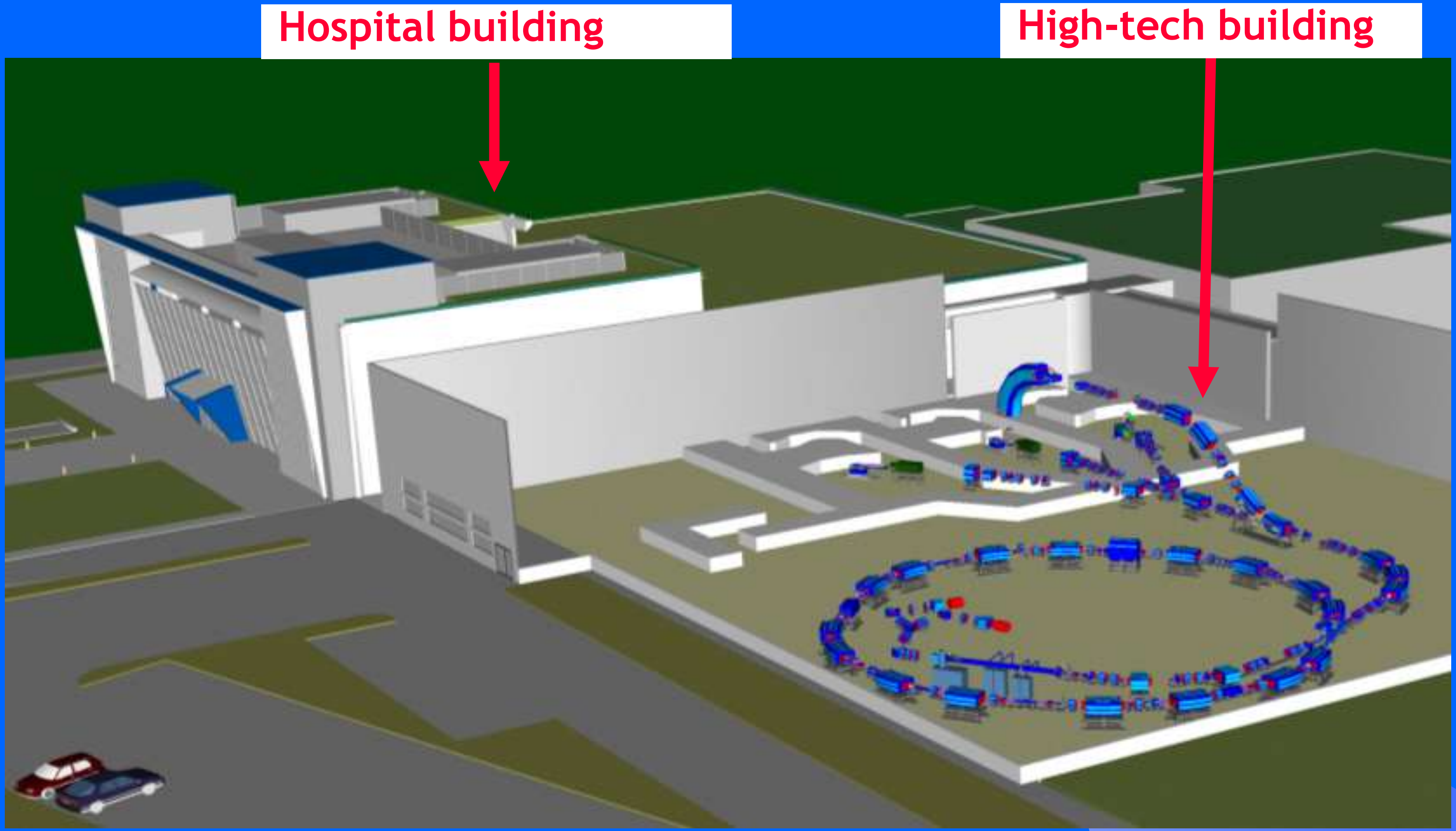


Since 2004 INFN is "Istitutional Participant" with people and important construction responsabilities

CNAO = Centro Nazionale di Adroterapia

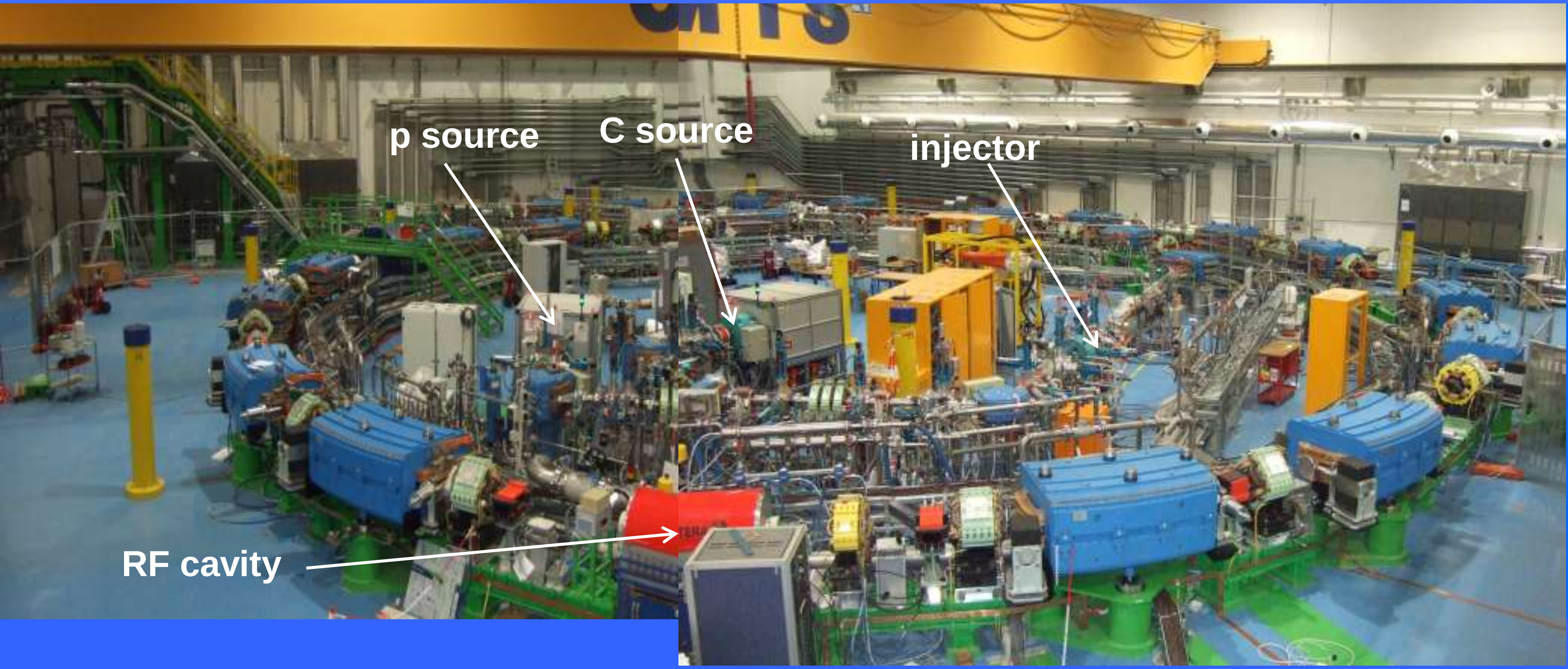
President: Erminio Borloni

Medical Director: Roberto Orecchia   Technical Director: Sandro Rossi

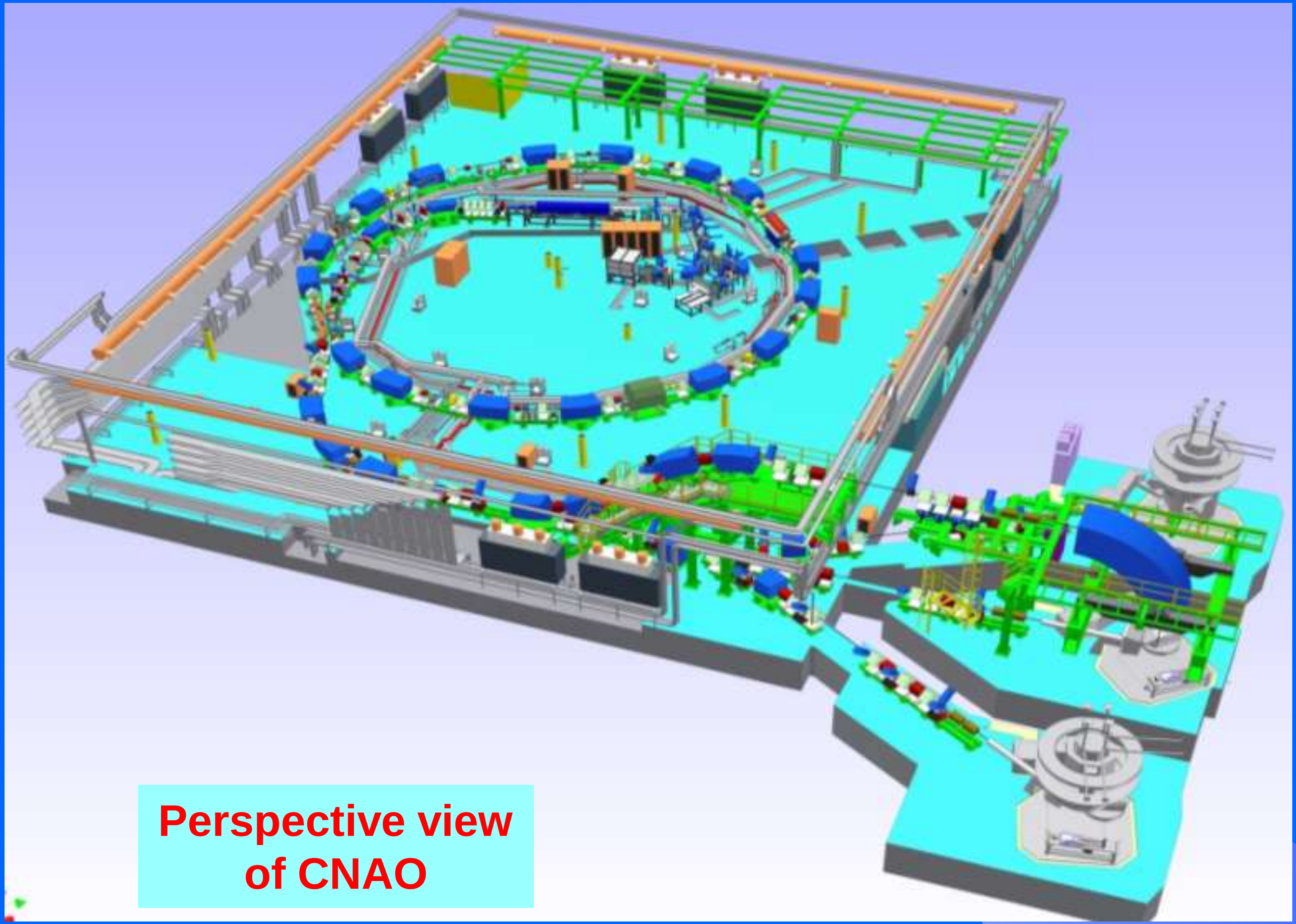


CNAO = Centro Nazionale di Adroterapia

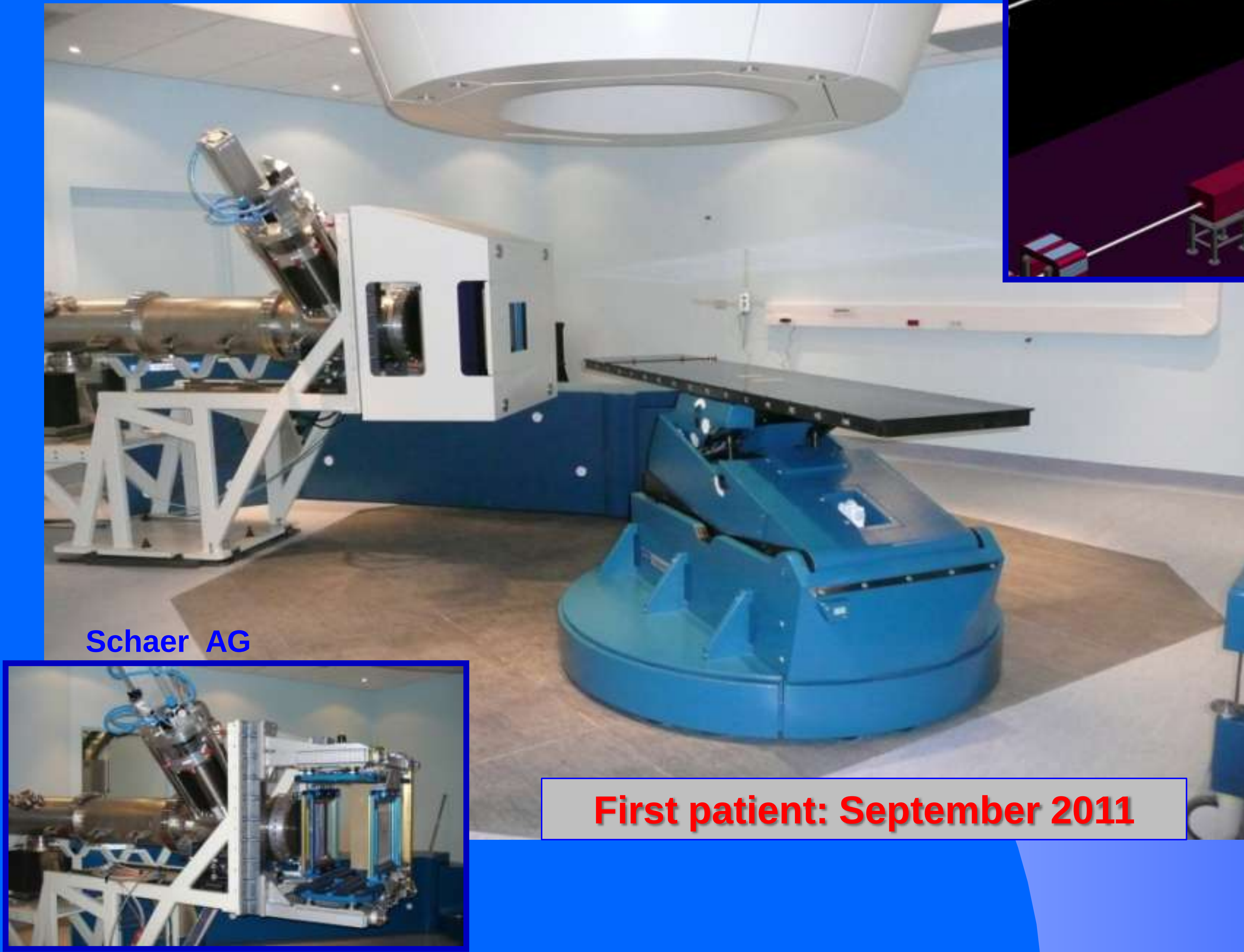
The synchrotron area in October 2008

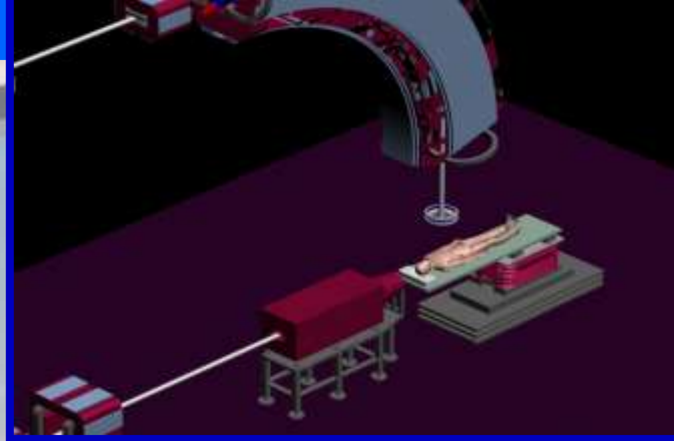


CNAO at Pavia



Perspective view of CNAO





Schaer AG

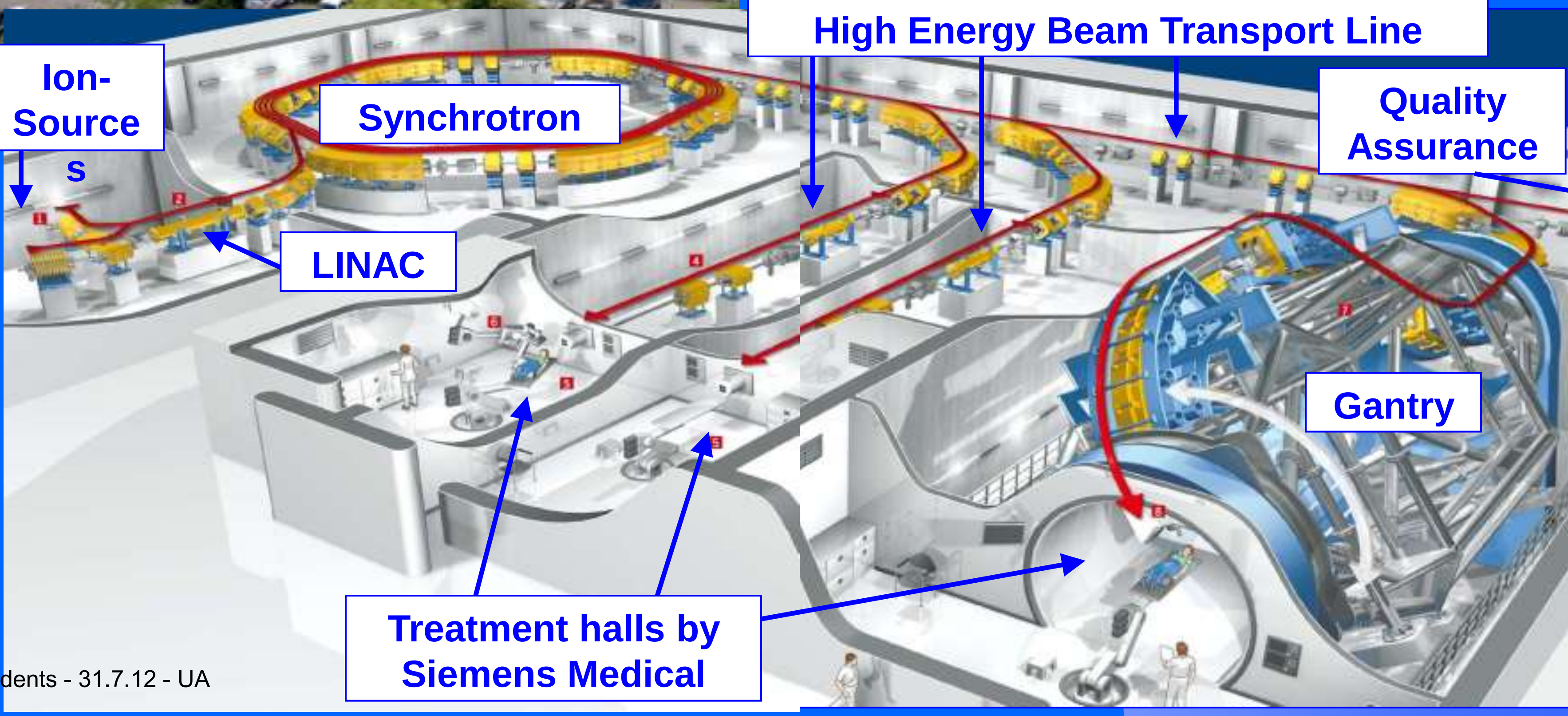
First patient: September 2011

HIT at Heidelberg

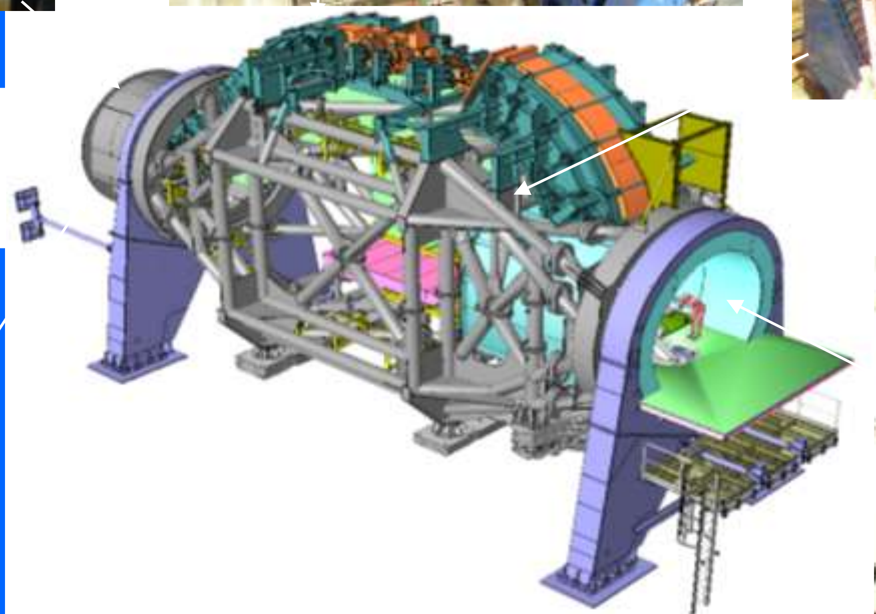
First beam extracted in 2007

First patient: September 2009

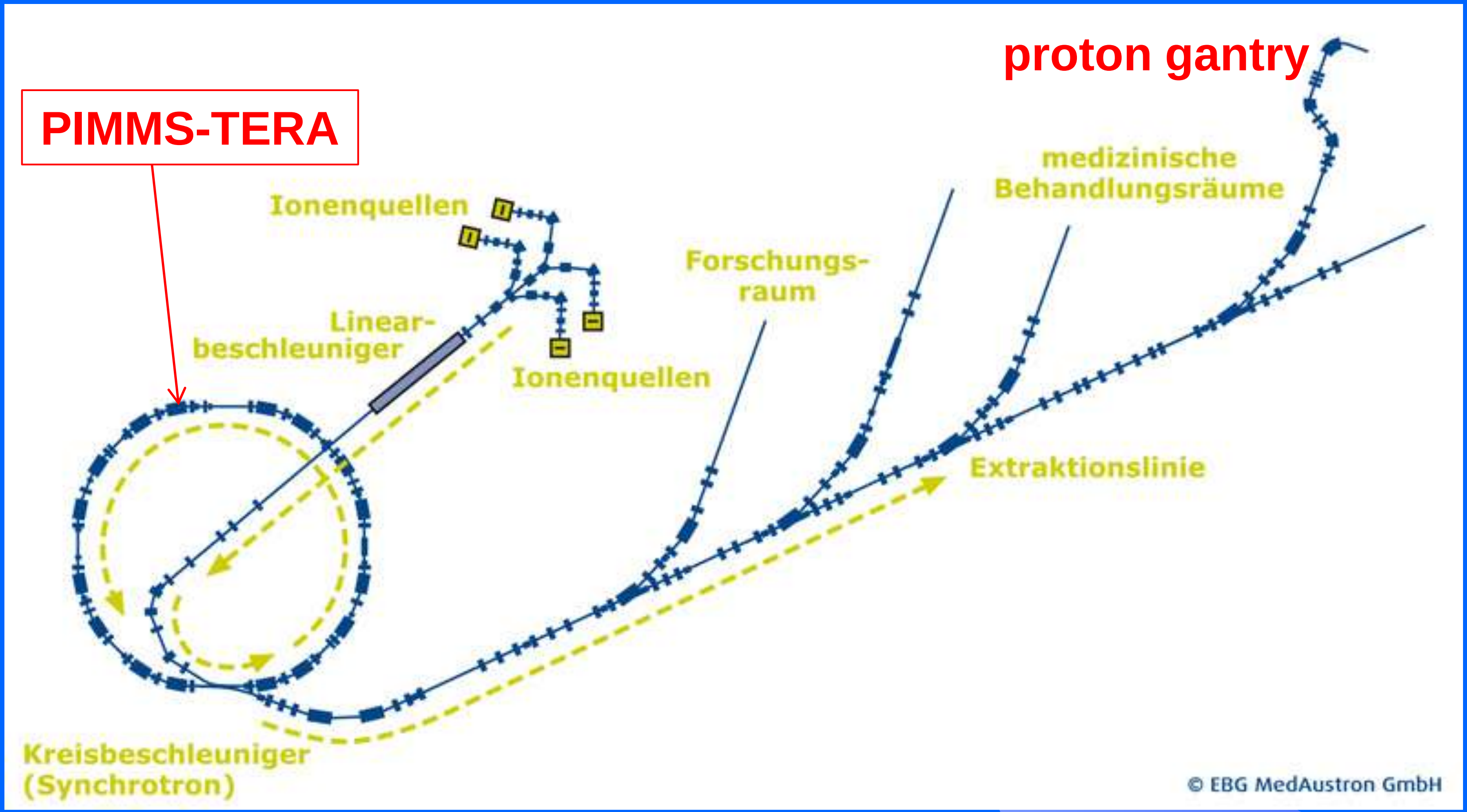
By now about 750 patients



The ion gantry of HIT: 700 tons – 400 kW



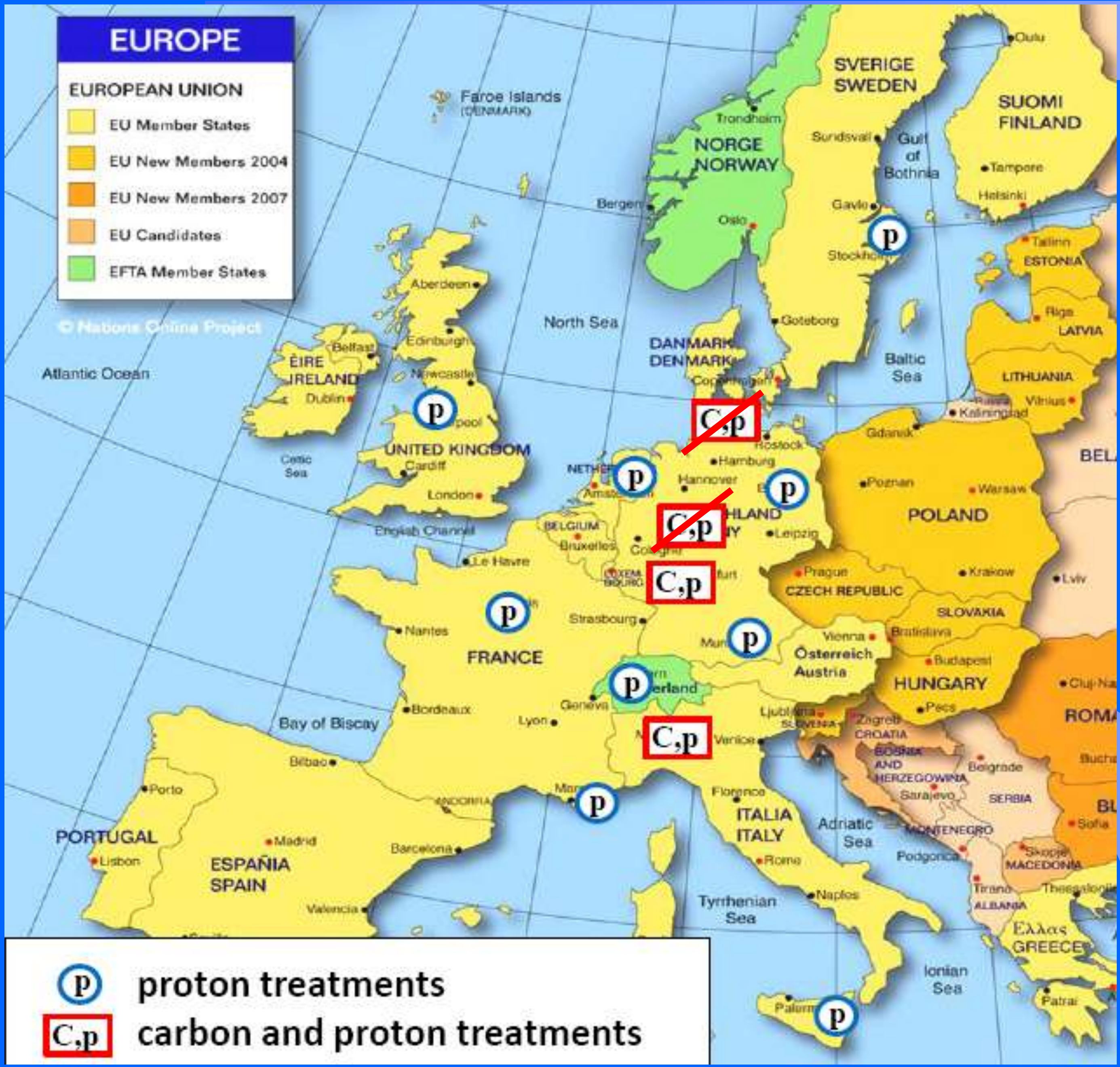
In 2007 MedAustron has been approuved for Wiener Neustadt



MedAustron has bought the CNAO construction drawings for 3.2 MEuro

MedAustron will be ready in 2015

European Centres

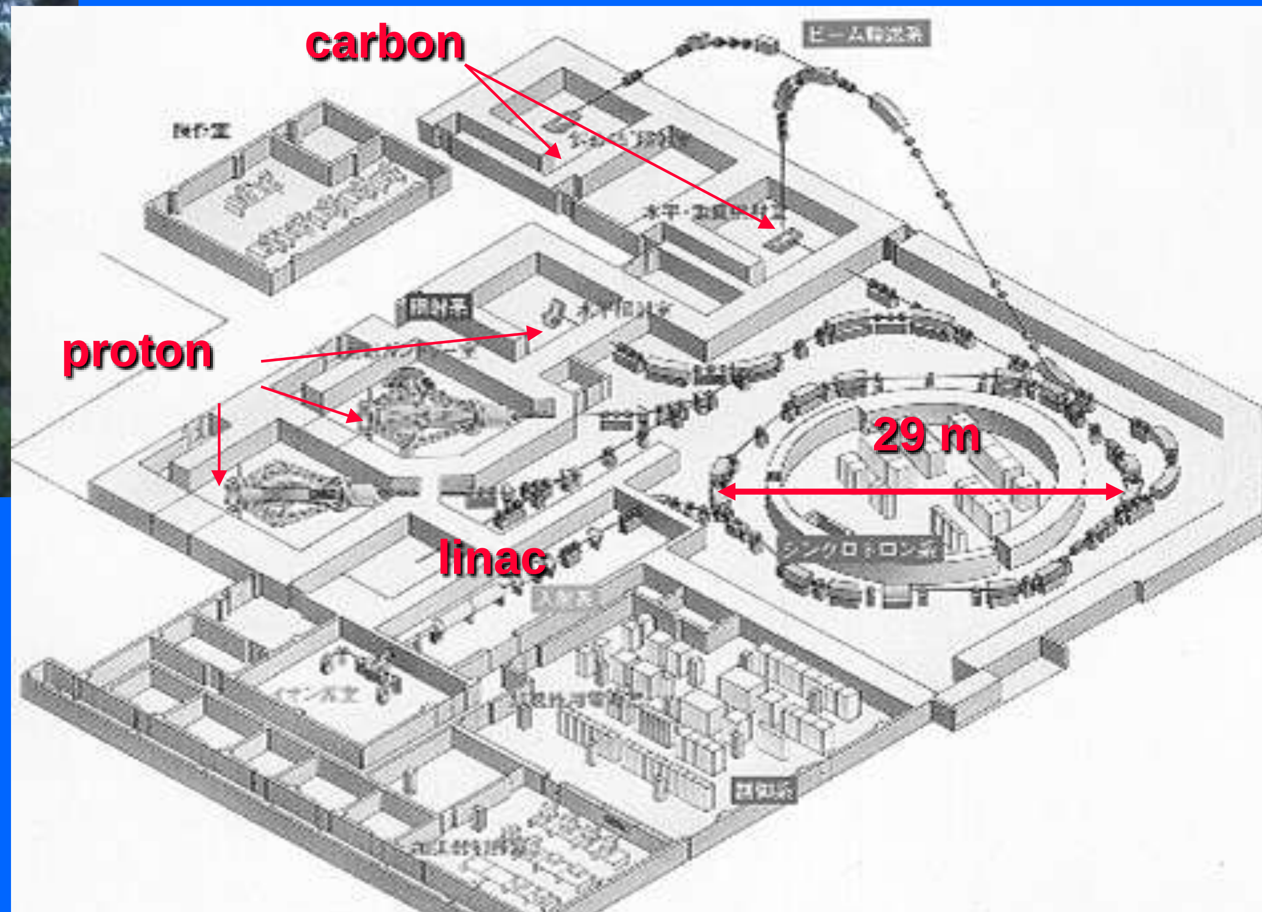


In 2011 Siemens stopped the realization of the C,p centres in Marburg and Kjel

TERA

Centers for carbon ion (and proton) therapy in Japan

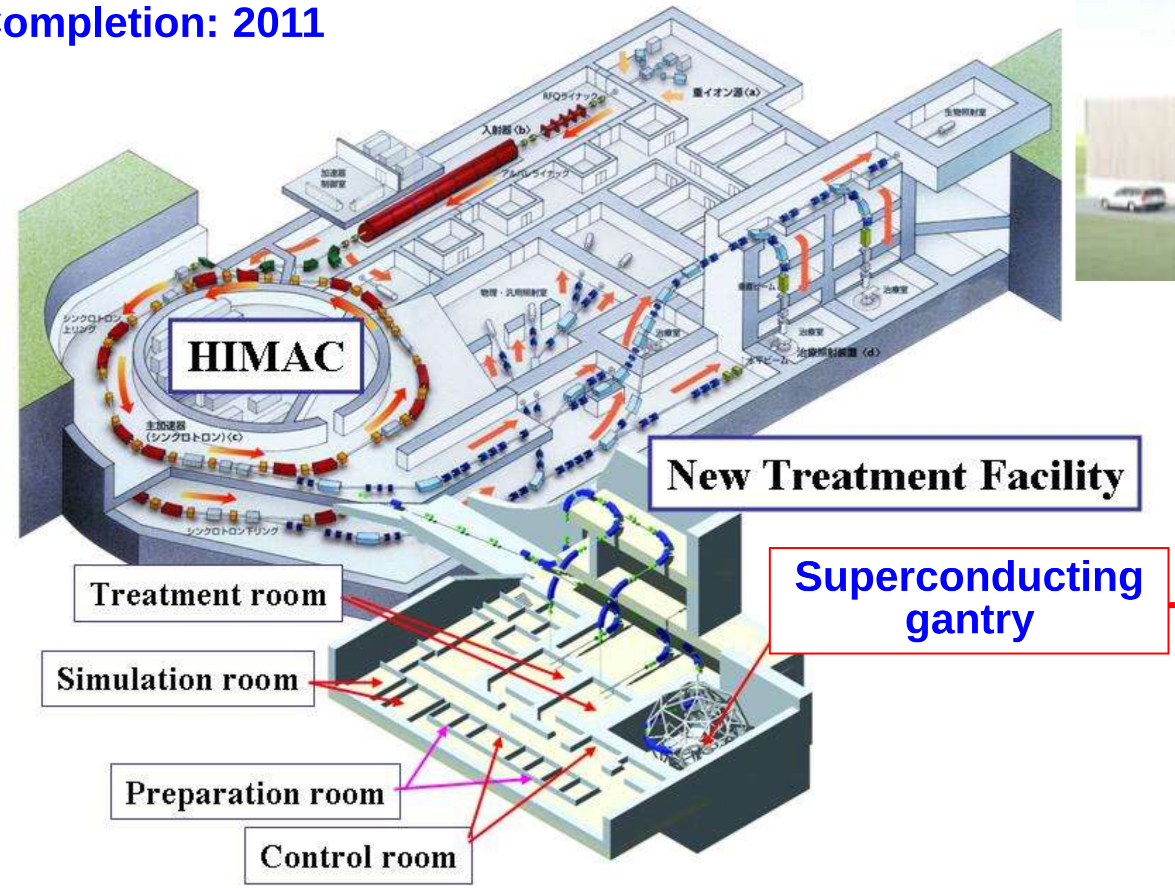
The Hyogo 'dual' Centre has treated 700 patients with carbon ions

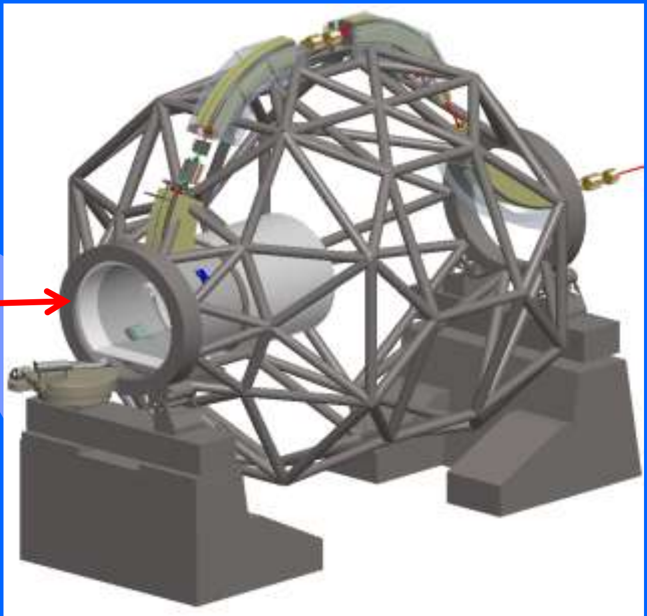


Mitsubishi: turn-key system

HIMAC new facility

Completion: 2011



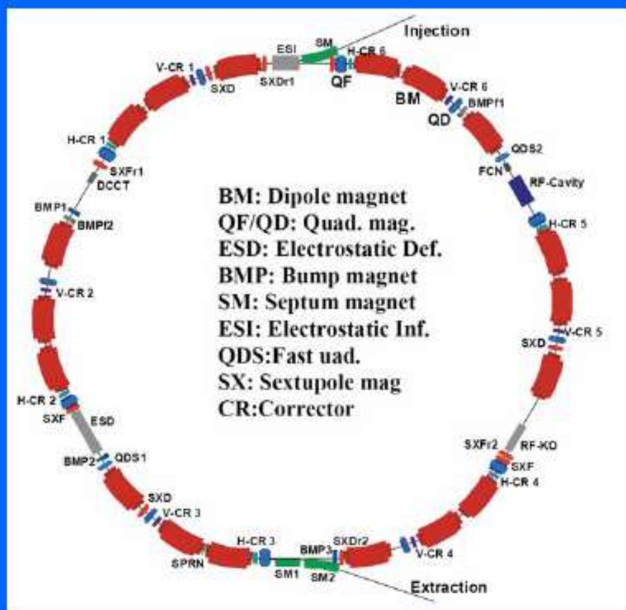


Gunma University: completed

Proceedings of APAC 2004, Gyeongju, Korea

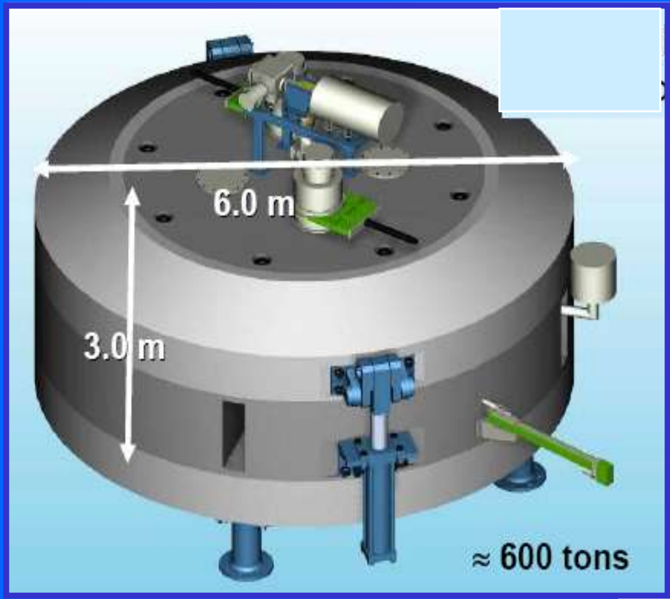
HIMAC AND NEW FACIILITY DESIGN FOR WIDE SPREAD USE OF CARBON CANCER THERAPY

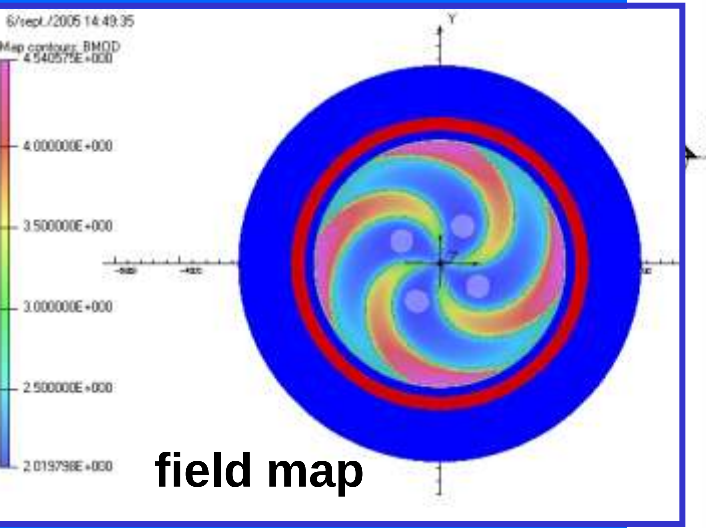
K. Noda, T. Fujisawa, T. Furukawa, Y. Iwata, T. Kanai, M. Kanazawa, N. Kanematsu, A. Kitagawa, Y. Kobayashi, M. Komori, S. Minohara, T. Murakami, M. Muramstsu, S. Sato, Y. Sato, S. Shibuya, F. Soga, E. Takada, O. Takahashi, M. Torikoshi, T. H. Uesugi, E. Urakabe, K. Yoshida, S. Yamada,
National Institute of Radiological Sciences,

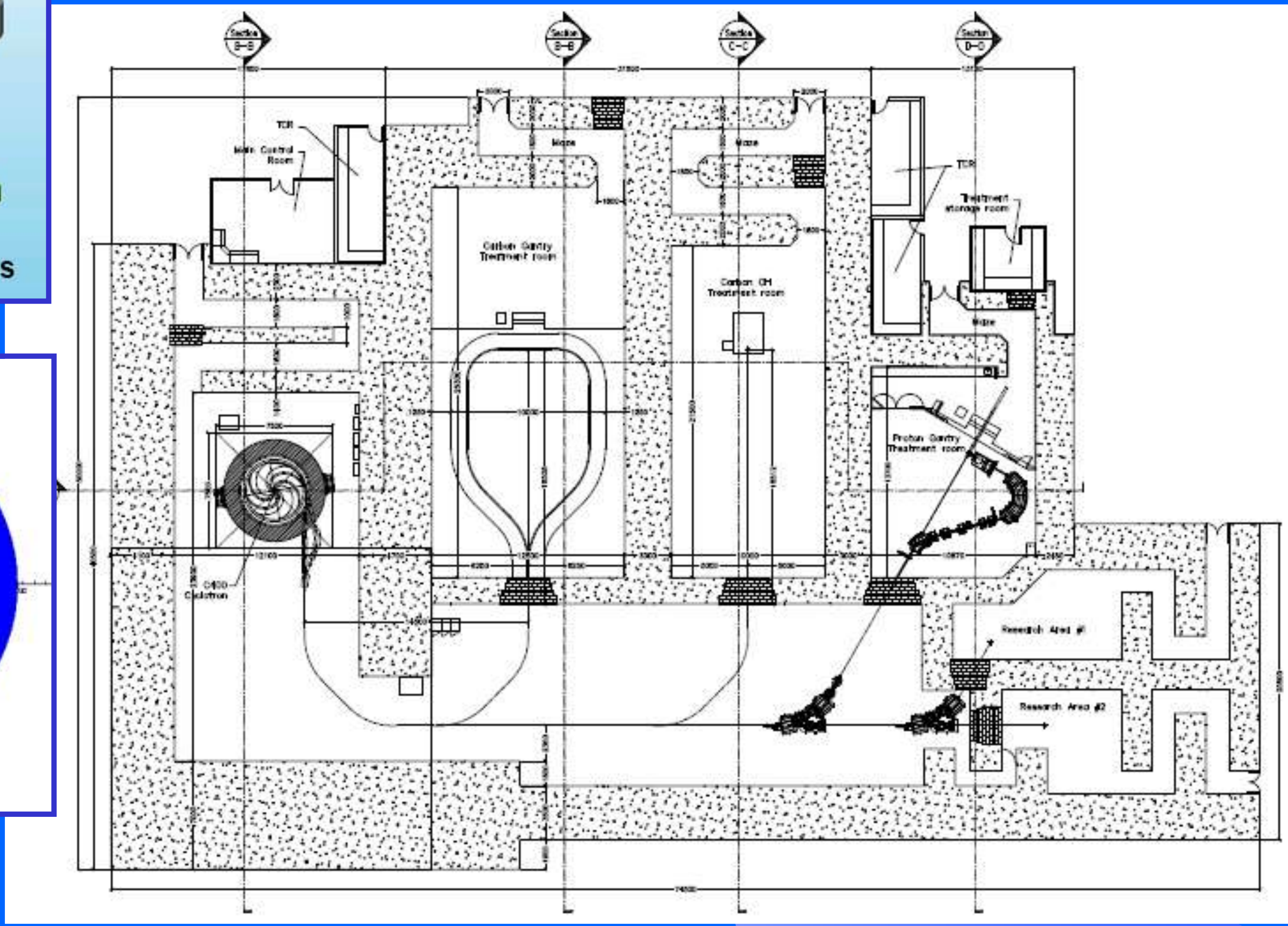


Next generation of accelerators for carbon ion therapy

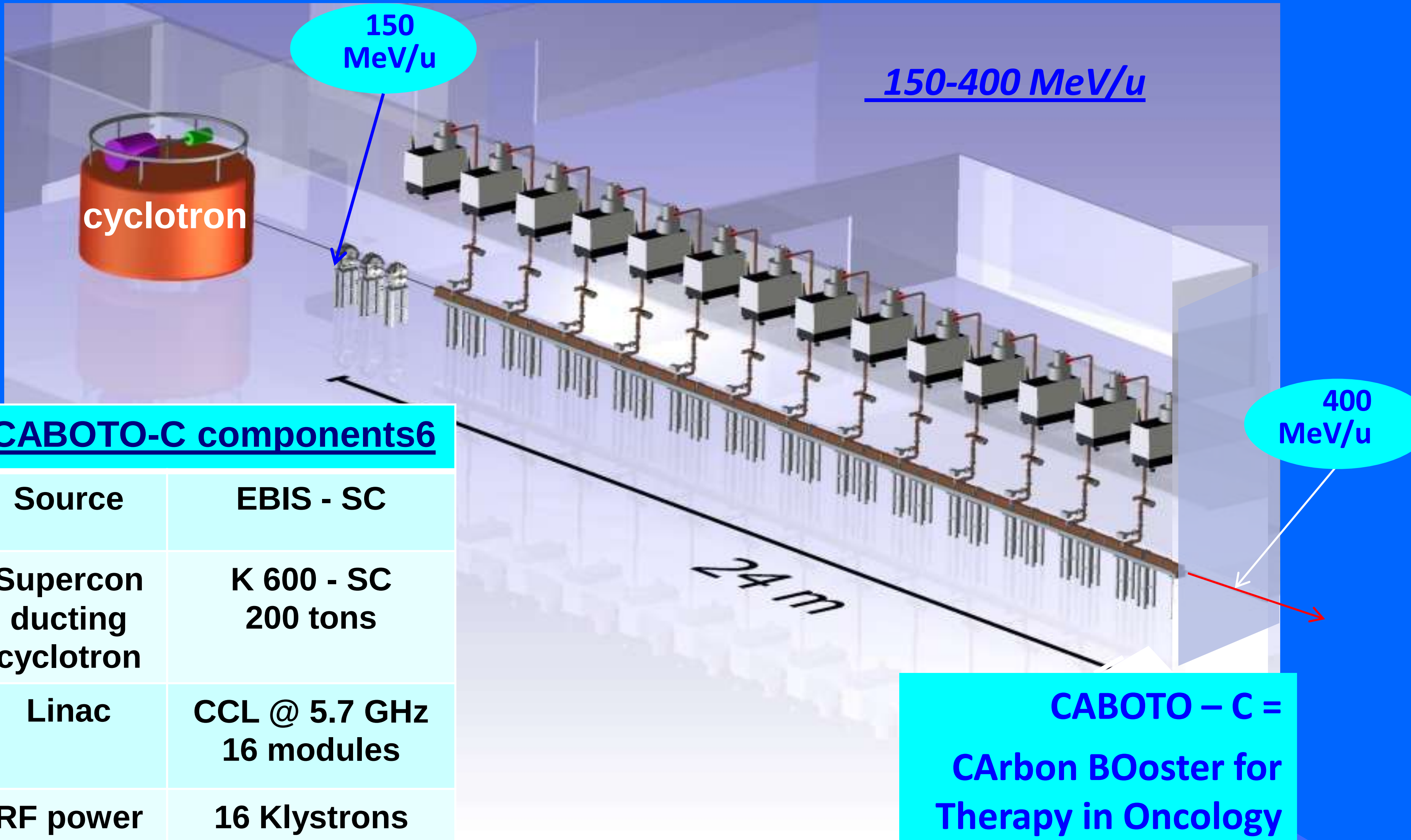
"Archade" (Caen) is based on the new IBA 400 MeV/u superconducting cyclotron







The CYCLINAC solution for carbon ions by TERA

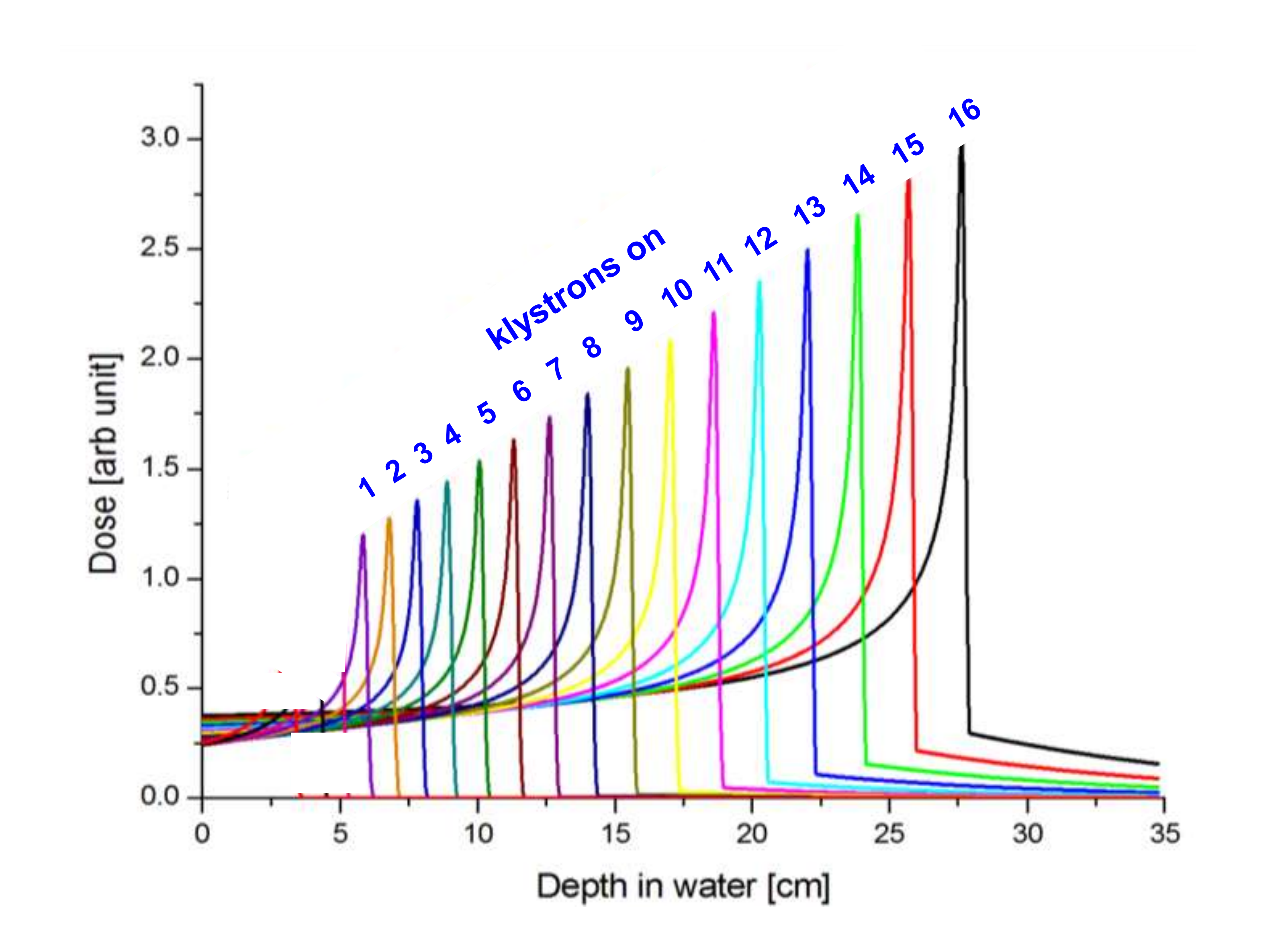


CABOTO-C components6	
Source	EBIS - SC
Superconducting cyclotron	K 600 - SC 200 tons
Linac	CCL @ 5.7 GHz 16 modules
RF power system	16 Klystrons (P_{peak} = 12 MW)

CABOTO – C =

CArbon BOoster for Therapy in Oncology

CABOTO unique properties: energy variation in milliseconds

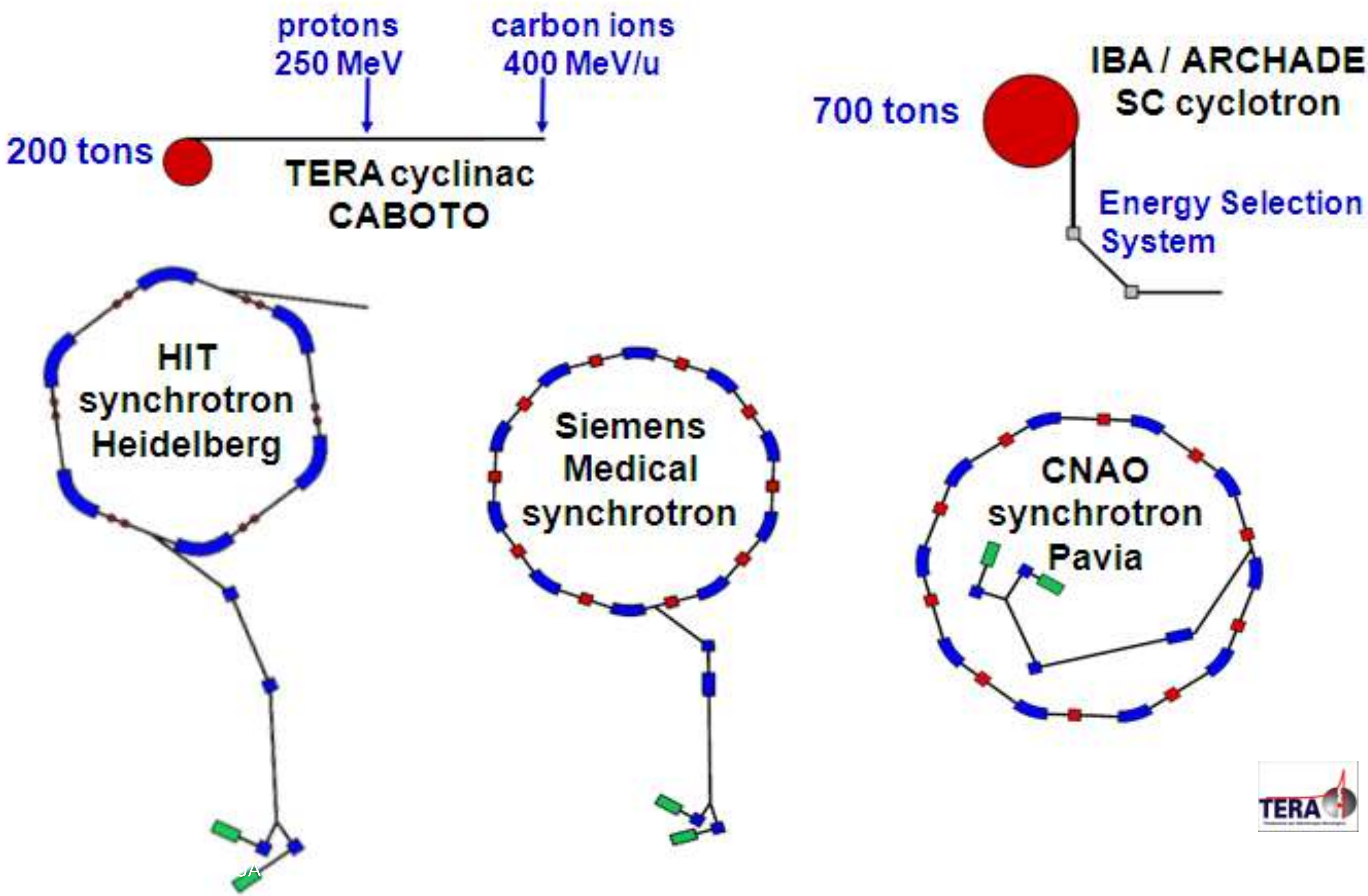


Active Energy Modulation
+
3D feedback system

Treatment of MOVING ORGANS

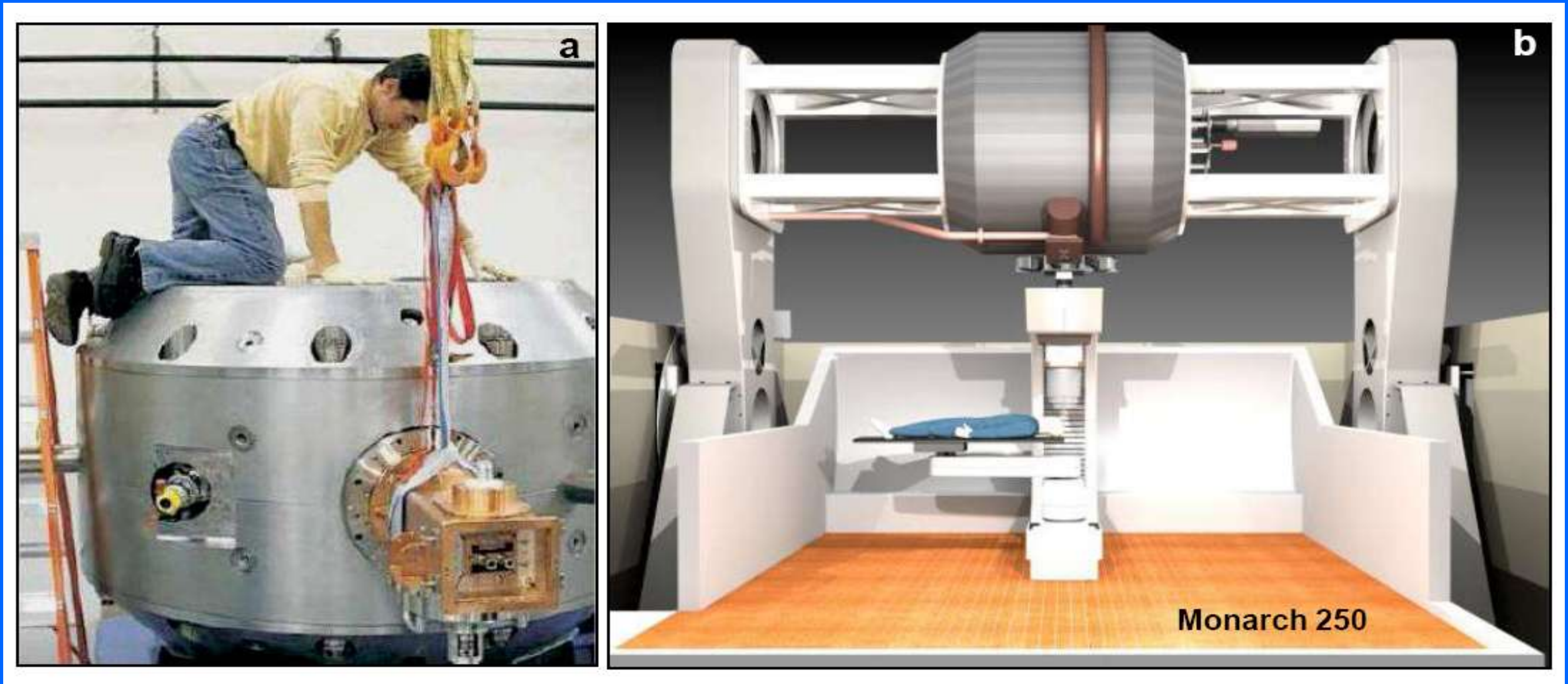
The FIRST UNIT for protons has been built by A.D.A.M.

Dimensional comparison among carbon ion accelerators



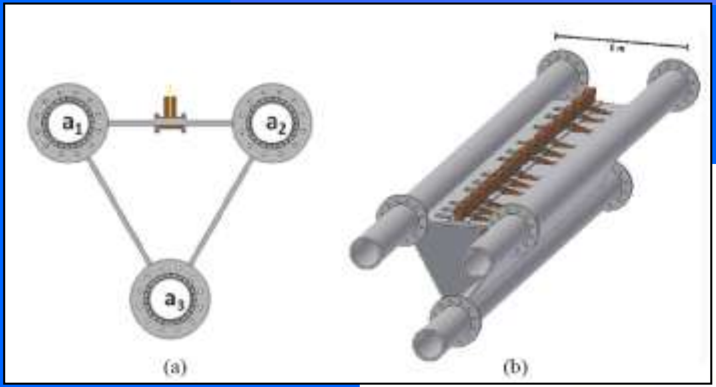
Proton “single room facilities”: one can serve 1.2 million people

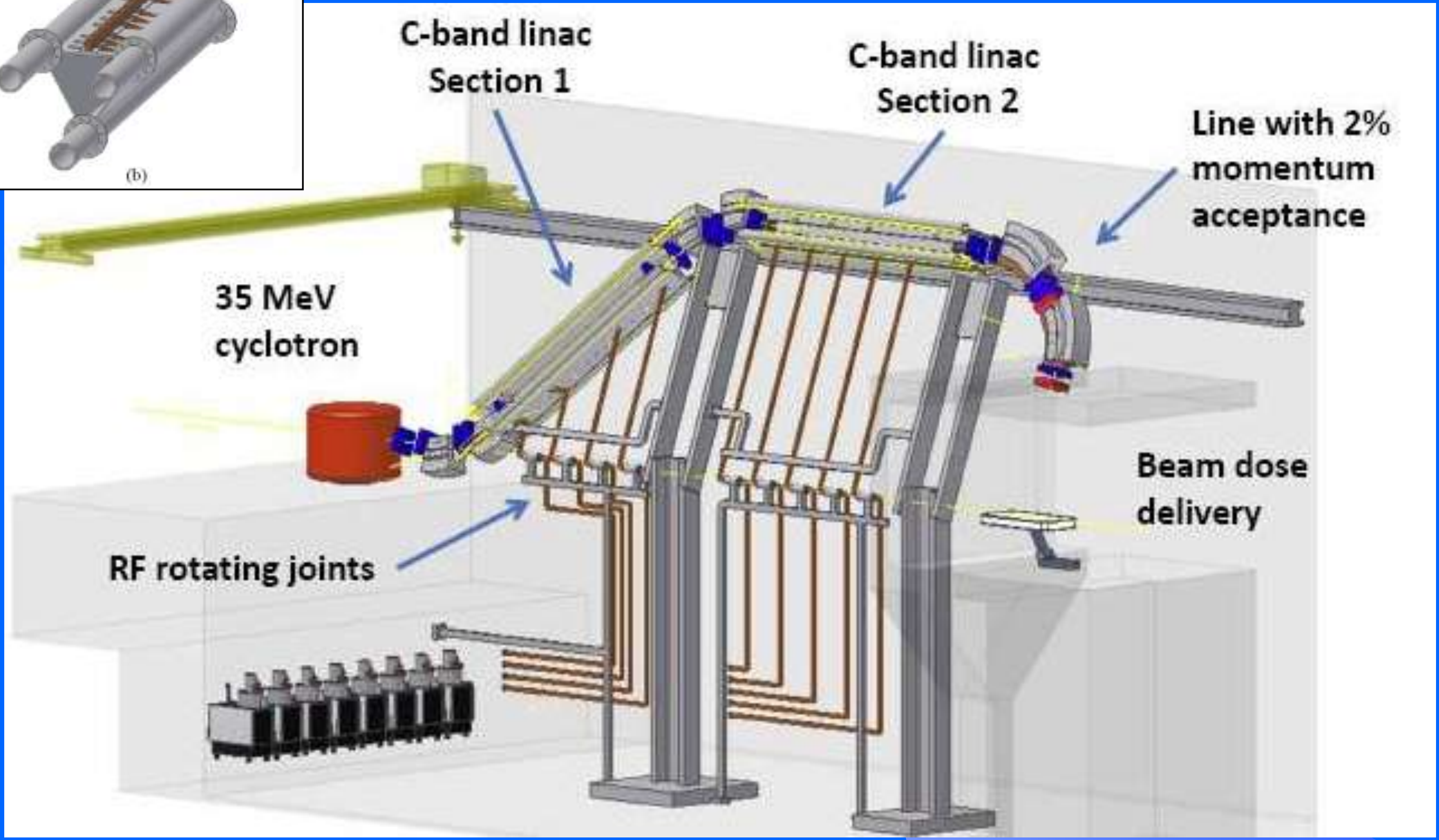
First single room facility: Still River synchrocyclotron rotating around the patient



Under test, waiting for FDA approuval

TERA: TUrning Linac for Protontherapy = TULIP





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 is treating patients, Pavia is starting in two months,
Wiener Neustadt will come next.
Coordination by ENLIGHT (Dr. Manjit Dosanjh, CERN)

At present the focus of accelerator development is on (a) novel carbon ion accelerators, (b) "single room facilities" for protons and (c) ion gantries