ADVANCED ACCELERATOR TECHNOLOGY ASPECTS FOR HADRONTHERAPY

Luciano Falbo, CNAO, Italy
HIAT 2012, Chicago

Overview

- Radiotherapy and Hadrontherapy
- Hadrontherapy facility design criteria
- Layout of a typical carbon synchrotron for hadrontherapy
- Hadrontherapy in the world and future perspectives

Radiotherapy and hadrontherapy

Cancer is one of the major world health problems: more than 7 million deaths per year

Radiotherapy is an important technique in the cancer cure : about 40% of cancer patients are cured by radiotherapy, either alone (25%) or in combination with other techniques.

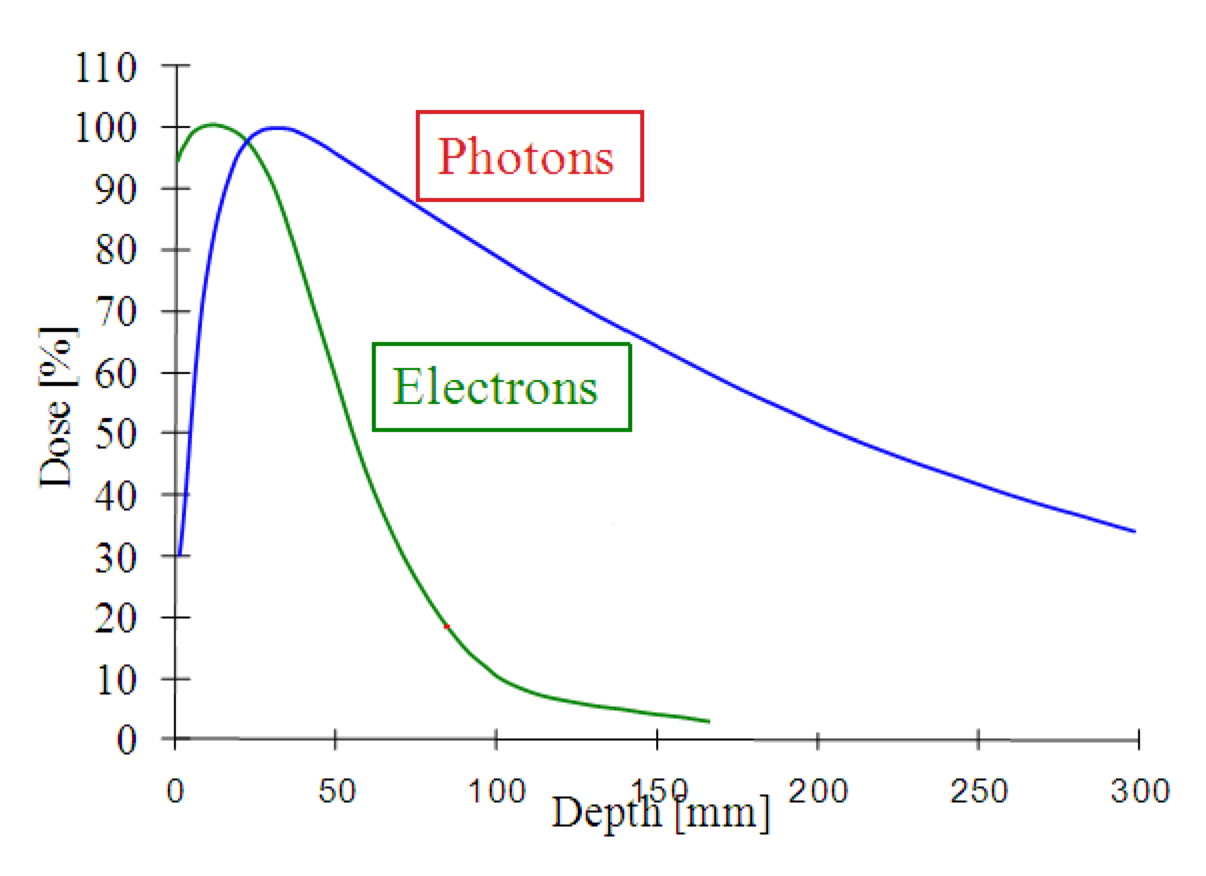
Accelerators running in the world

CATEGORY OF ACCELERATORS	NUMBER IN USE (*)	
High Energy acc. (E >1GeV)	~120	
Synchrotron radiation sources	>100	
Medical radioisotope production	~200	
Radiotherapy accelerators	> 7500	9000
Research acc. included biomedical research	~1000	
Acc. for industrial processing and research	~1500	
Ion implanters, surface modification	>7000	
TOTAL	> 17500	

(*) W. Maciszewski and W. Scharf: Int. J. of Radiation Oncology, 2004

Radiotherapy and hadrontherapy

Radiotherapy uses electrons and photons to kill cancer cells damaging the DNA.
These particles loose energy at beam entrance and then exponentially.
The depth-dose deposition characteristics cause great damage to the healthy tissues too.

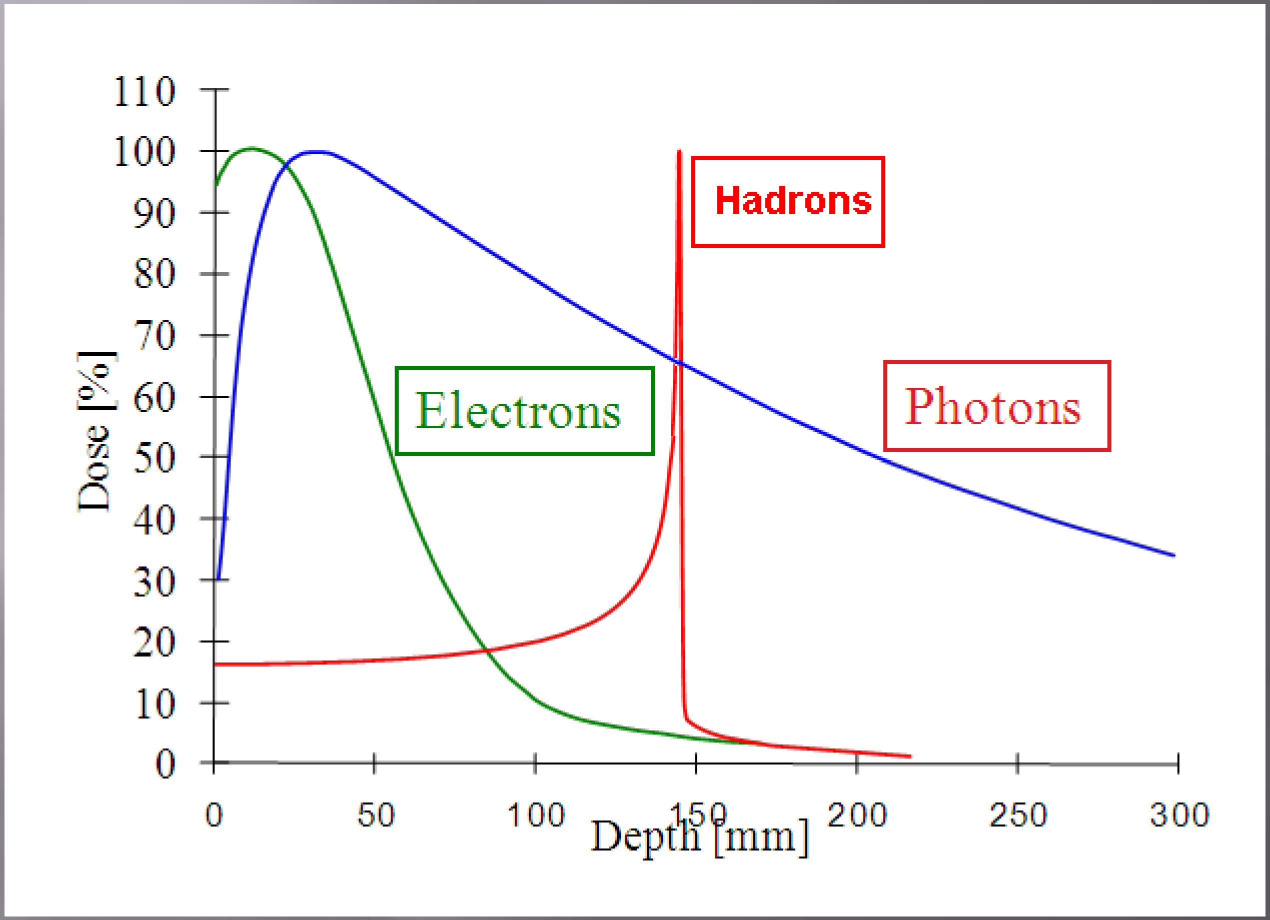


Computer-aided treatment plans (IMRT) allows to reduce this counterpart but the problem remains.

Radiotherapy and hadrontherapy

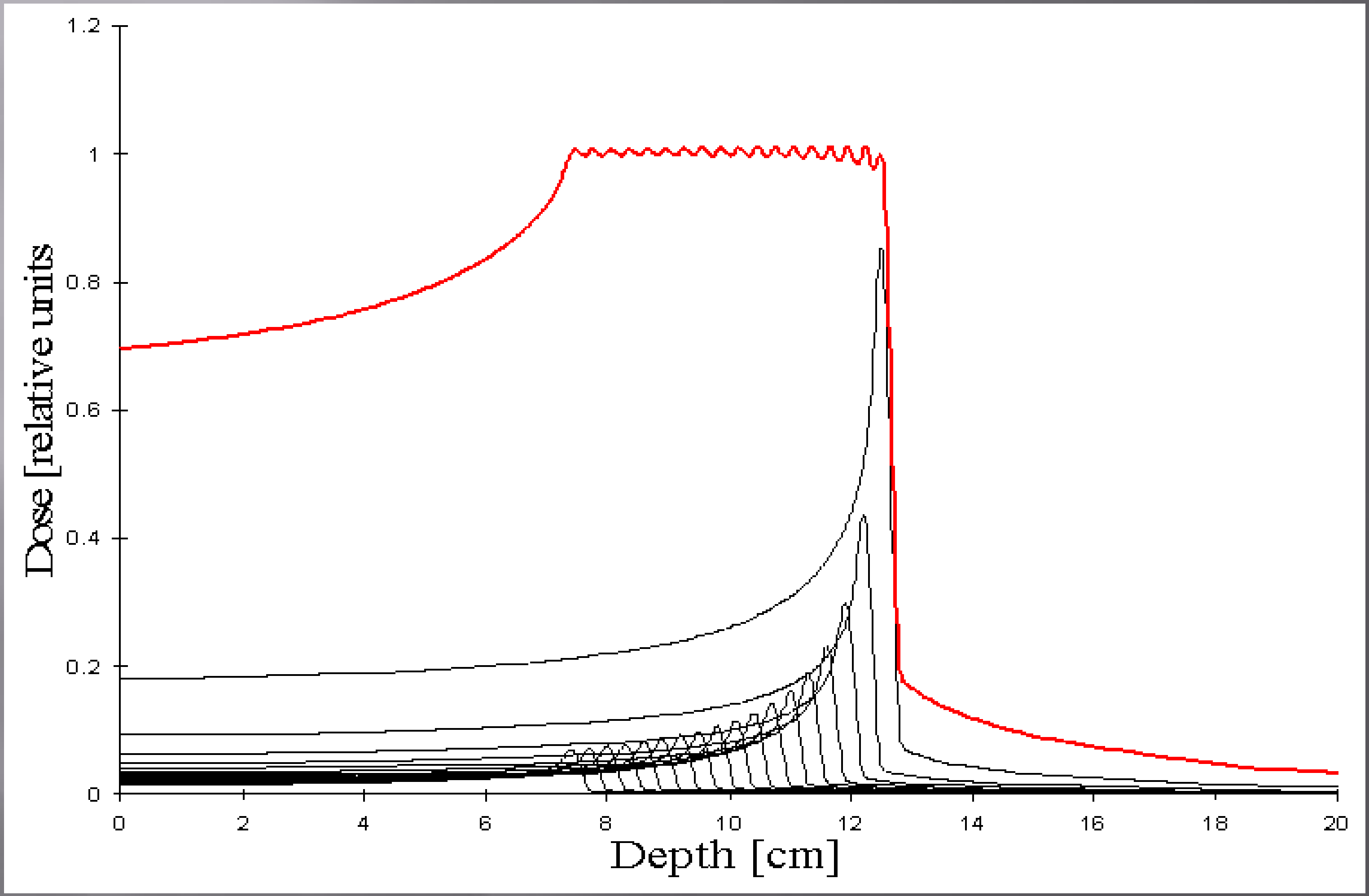
Hadrontherapy is the solution!!!!!

It uses hadrons (protons and heavy ions) that have a very localized depth-dose depositior



Radiotherapy and hadrontherapy

It is possible to localize longitudinally the irradiation only on the tumour target: hadrontherapy is a high precision kind of radiotherapy.



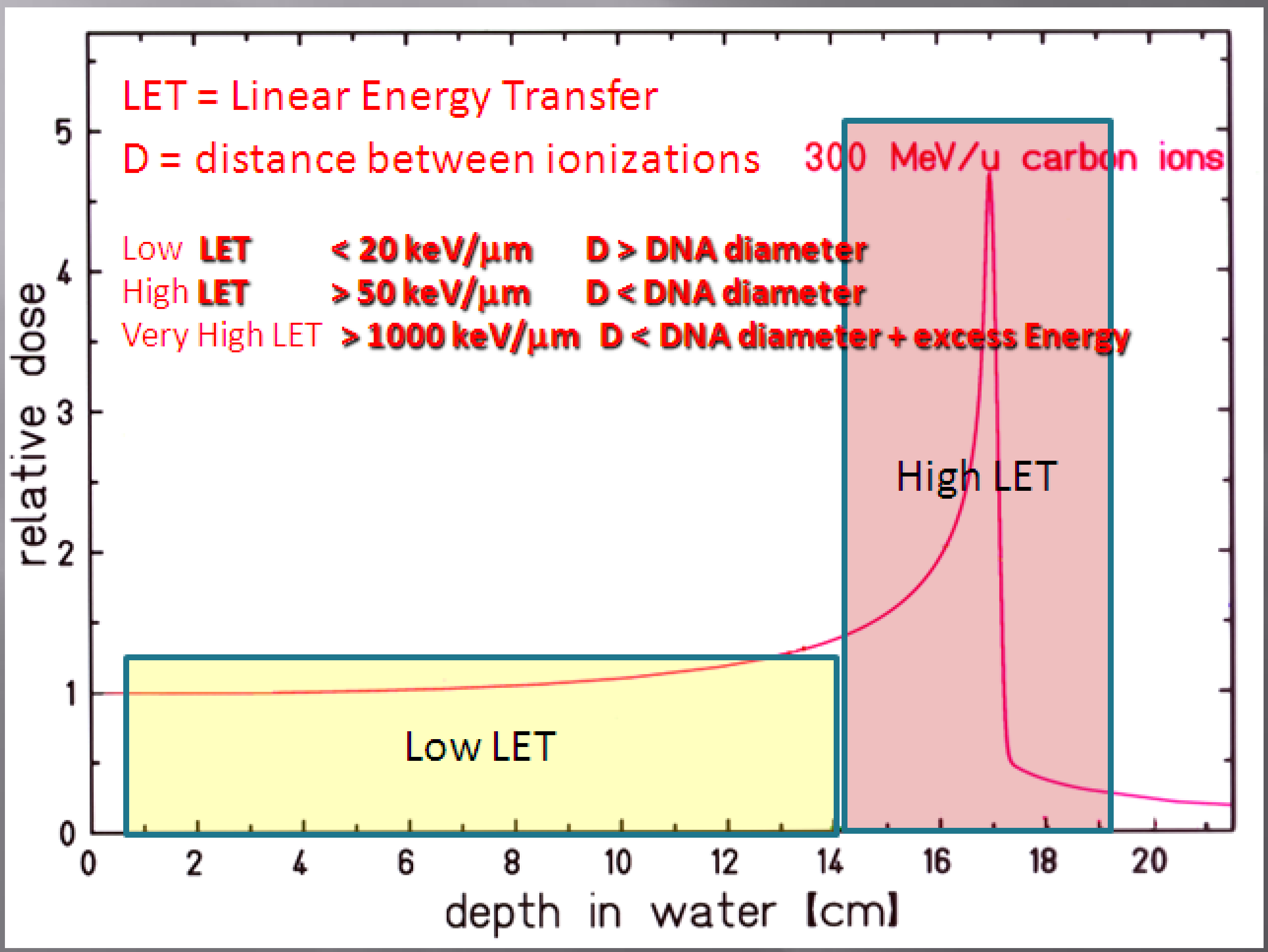
Radiotherapy and hadrontherapy

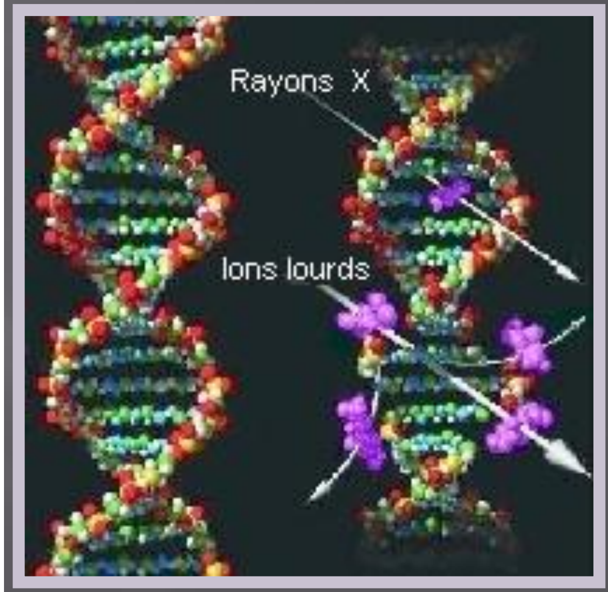
Other figures of Biological merit:

- LET: Linear Energy Transverse
- RBE: Relative Biological Effectiveness
- OER: Oxygen Enhancement Ratio
- Multiple transverse scattering

LET

Particle	Cobalt gamma rays	protons	Heavy ions
Maximum LET	10 keV/µm	100 keV/µm	1000 keV/µm





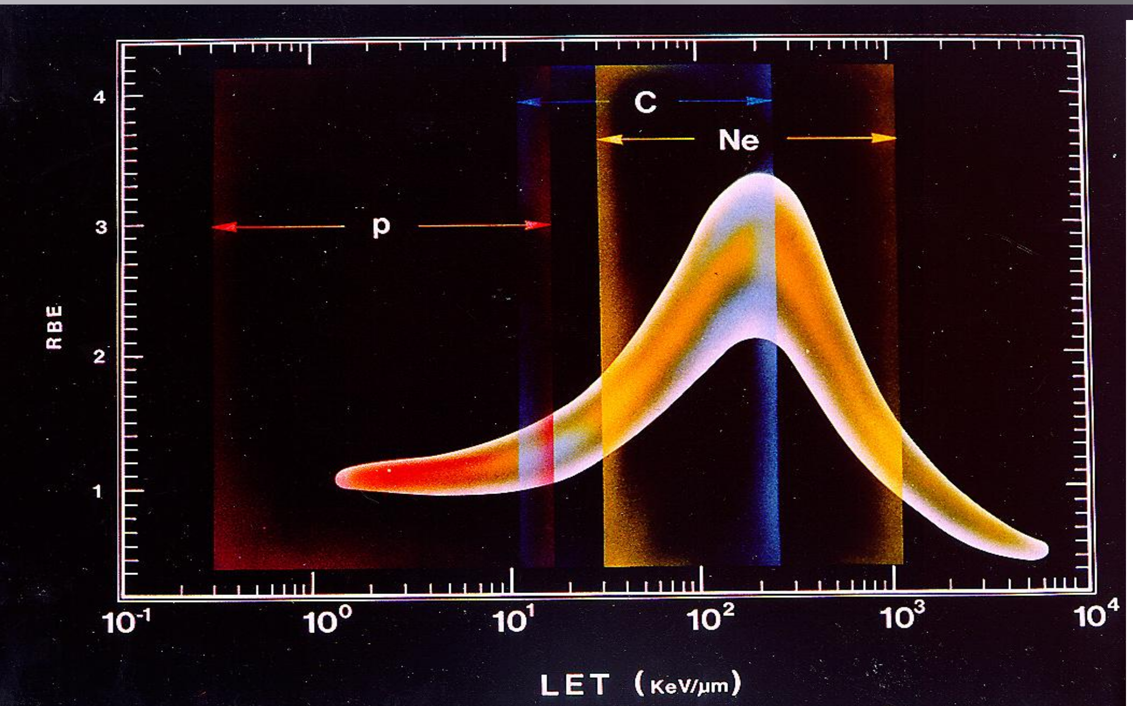
RBE

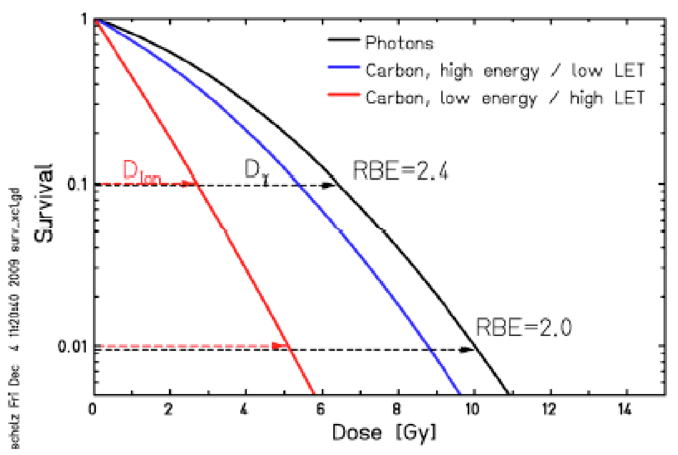
RBE= the ratio between the photon and the ion doses which are necessary for producing the same biological effect. It gives the efficiency in killing the cells.

Proton RBE = 1.1

Carbon RBE > 3 in the Bragg peak region

>= 1 in the entry channel.





The survival curve for the target cells for late injury is "curvier" than that for acute effects

OER and Multiple scattering

OER=Oxygen Enhancement Ratio: the dose to produce a biological effect in the absence of oxygen to the dose to produce the same effect in oxygen presence.
Photon OER 2.5-3
OER decreases with increasing LET; OER about 1 at LET = 300 keV/µm.

When increasing mass the multiple scattering decreases increasing the quality of lateral and longitudinal treatment.
However when increasing mass nuclear fragmentation is greater, tailing Bragg peak.

All the biological consideration indicate that heavy ions have more advantages than protons.
$Z>6$ heavy ions are not clinically interesting.
Carbon ions have indicated in ‘80s as the best medical choice.

$1<Z<=6$ heavy ions could be interesting
but experimentation is needed and recommended

Design criteria

The kind of the accelerator depends mainly on:

1. The species to be accelerated

particle	Penetration range	Energy range	Brho range
Proton	30-300 mm	60-250 MeV/u	1.16-2.31 Tm
Carbon	30-300 mm	120-400 MeV/u	3.18-6.34 Tm

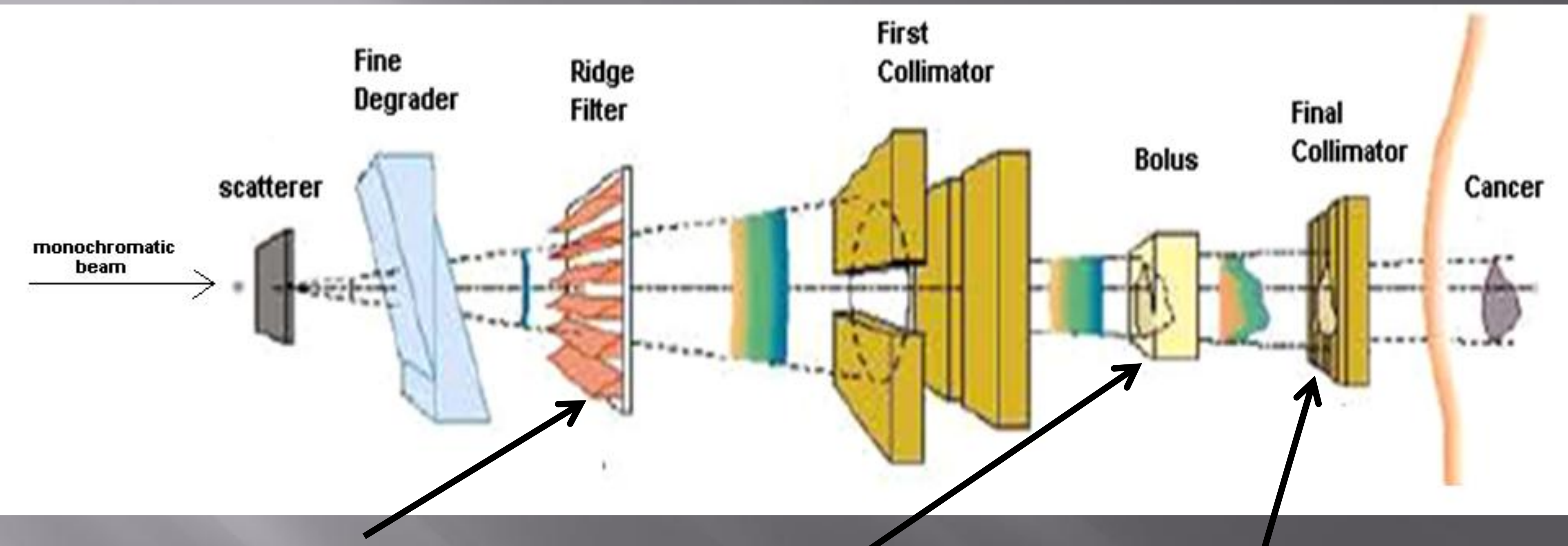
2. The radiation shaping and delivery method

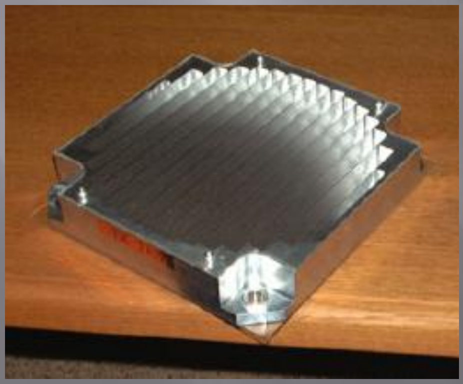
Passive Scanning

Active Scanning

Passive Scanning

Passive scanning is based on putting several absorbers before the patient to change longitudinal and transverse characteristics





Ridge filter

Bolus

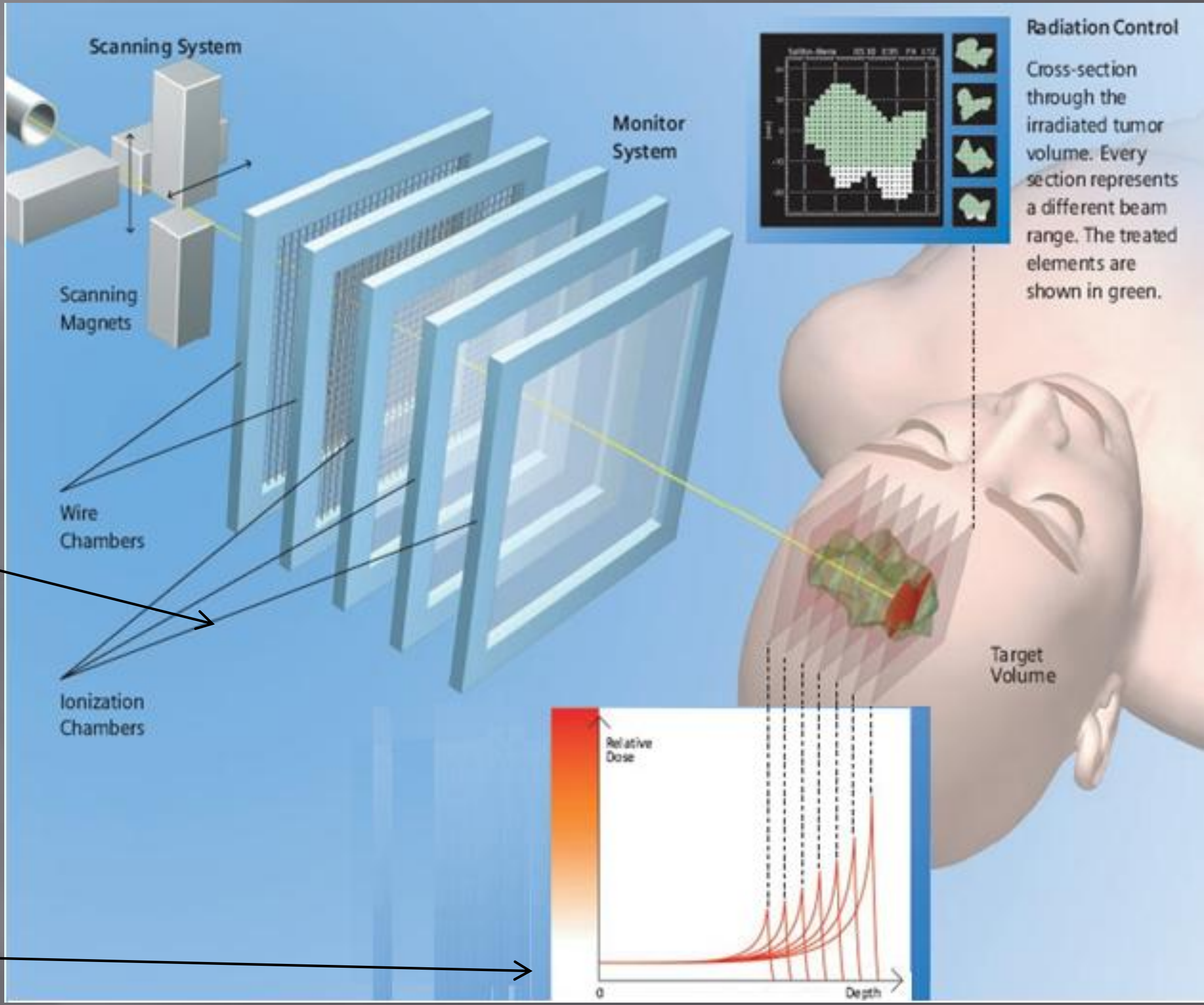
Multi-leaf final collimator

Active Scanning

Fast magnets paint the tumour transversally

A nozzle system controls the dose delivered

Several Bragg peaks from the accelerator paint the tumour longitudinally



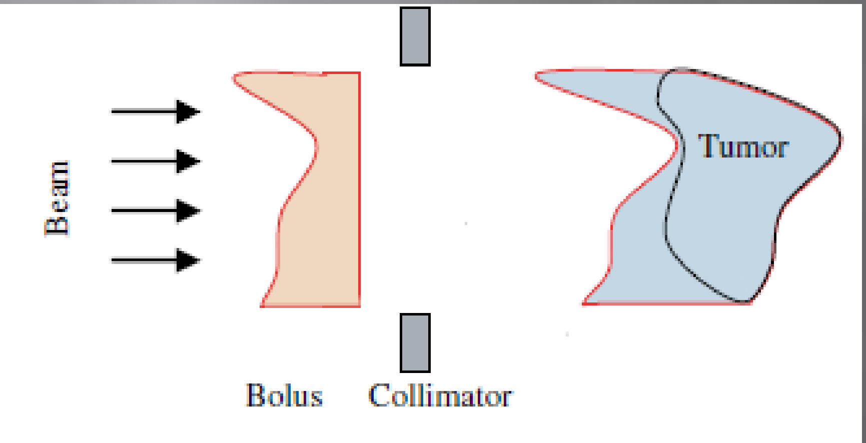
First use in Japan (1980) and then regularly used at GSI, PSI, HIT, CNAO

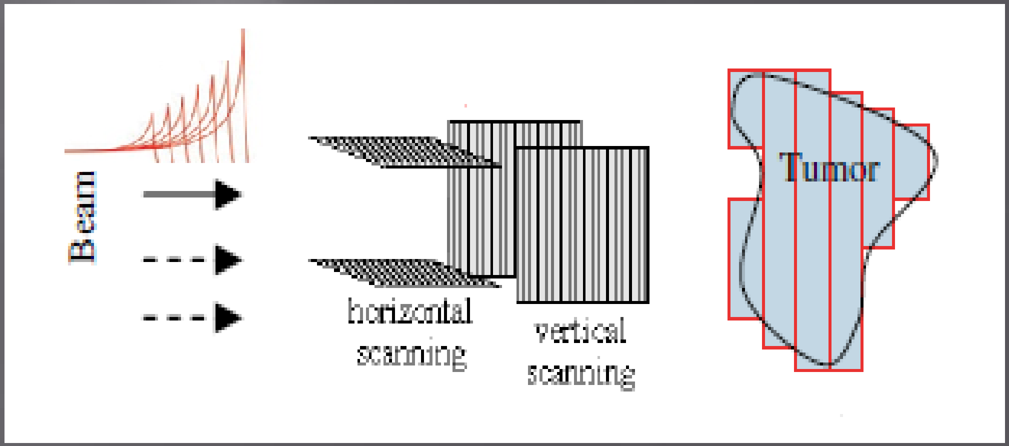
Active vs Passive

Passive system needs patient-specific hardware: Bolus, Multileaf collimator

There are errors on dose irradiation:
• Bolus conforms the most distal surface
•Absorbers → Nuclear Fragmentation → Tailing of Bragg Peak
•Heavy ions need thicker absorbers → greater energy and currents from the accelerator.

Active system needs a more challenging control of beam characterisations and of the scanning magnets but **allows a more precise dose irradiation of the tumor target**



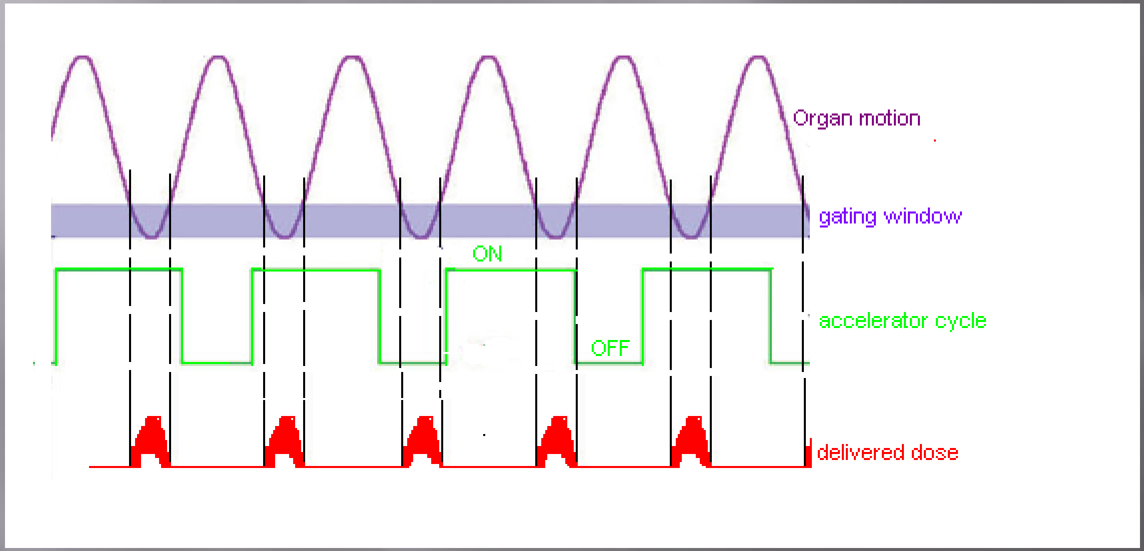


Moving organs

Active system is critical in the case of moving organs. R&D is in progress worldwide about several techniques: Gating, repainting, beam tracking

Repainting consists in underdosing the tumour and increasing the treatment sessions

Gaiting consists in irradiating only at a specific position of the organ



Beam Tracking is an adjustment in real-time of treatment plan considering the 4D organ motion signal.

Types of accelerators

Three accelerators can provide clinical beam: LINAC, Cyclotrons, Synchrotrons.

The energy and the species of hadrontherapy make LINAC not very practical and feasible

Nowadays Hadrontherapy centers are Cyclotrons and Synchrotrons

Cyclotrons	Synchrotrons
Compact (4 m diameter)	More complicated
cheaper	More expensive
DC beam	Pulsed beam
High current (hundreds nA)	Smaller current(tens nA)

BUT…

Types of accelerators

... BUT

Cyclotrons are easy for protons; only a CHALLENGING PROPOSAL exists for carbon
Cyclotron compactness is partially offset by the place required by the medical structure
Passive scanning is needed with cyclotrons because the energy from accelerator is fixed

On the contrary

Synchrotrons can accelerate protons and carbons.
A synchrotron designed for 300mm C6+ can accelerate 1<=Z<=6 and O up to 19 cm.
Synchrotron can perform active scanning.

Nowadays the best technological layout for a hadrontherapy center is a **Carbon Synchrotron equipped with active scanning**.

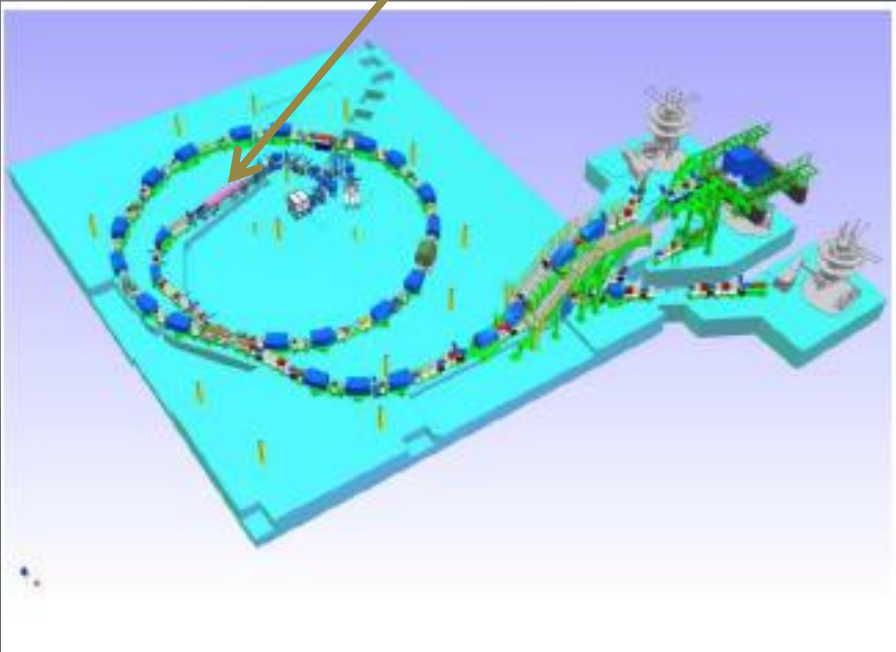
A carbon synchrotron facility is made up of:

1. A low energy injector
2. A ring
3. The extraction lines

Synchrotron facility layout: Injector

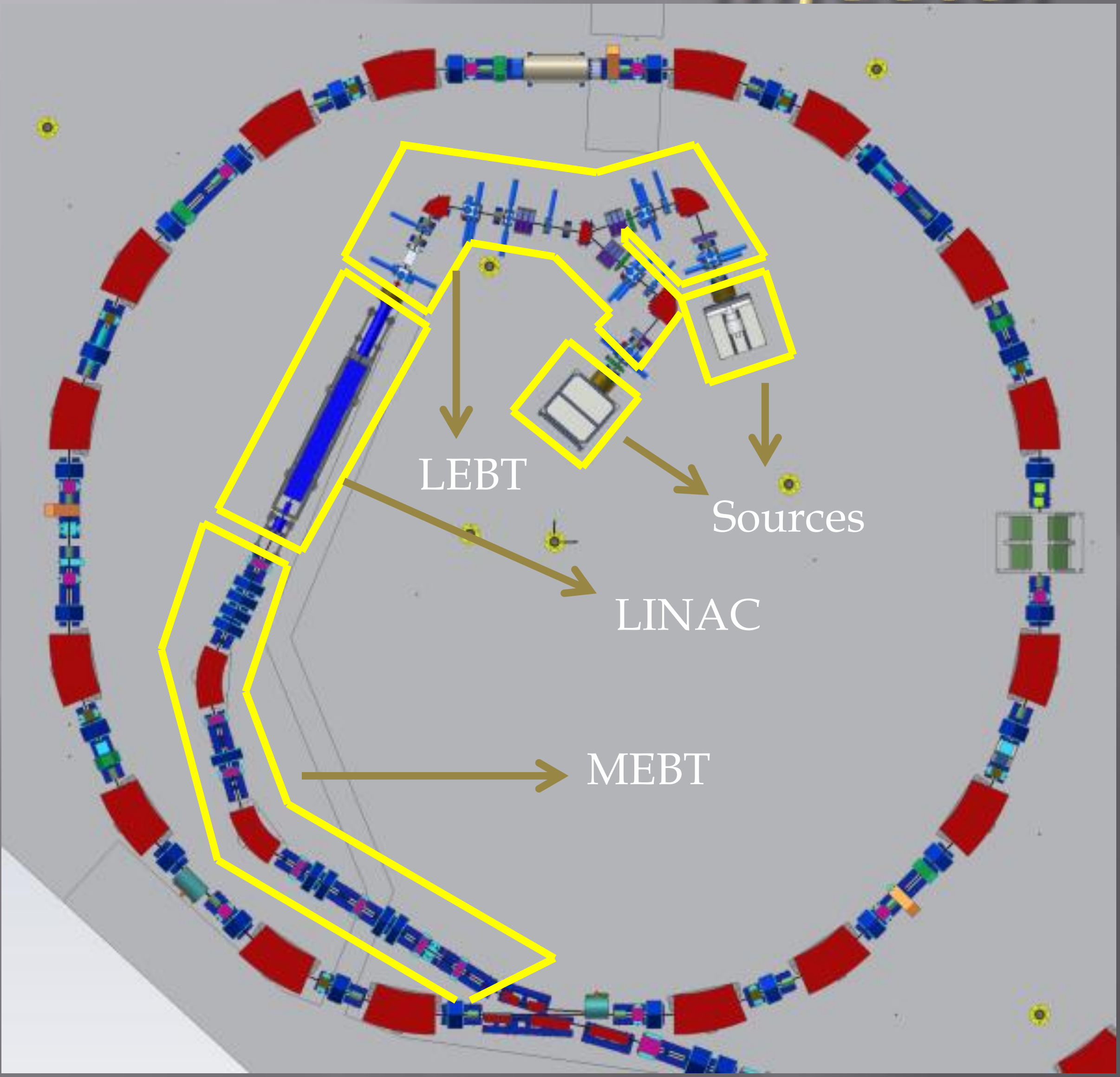
The injector is placed outside the ring for easier maintenance or inside to save space

HIT (Heidelberg, Germany)



CNAO (Pavia, Italy)

Synchrotron facility layout: Injector



An injector is made up of:

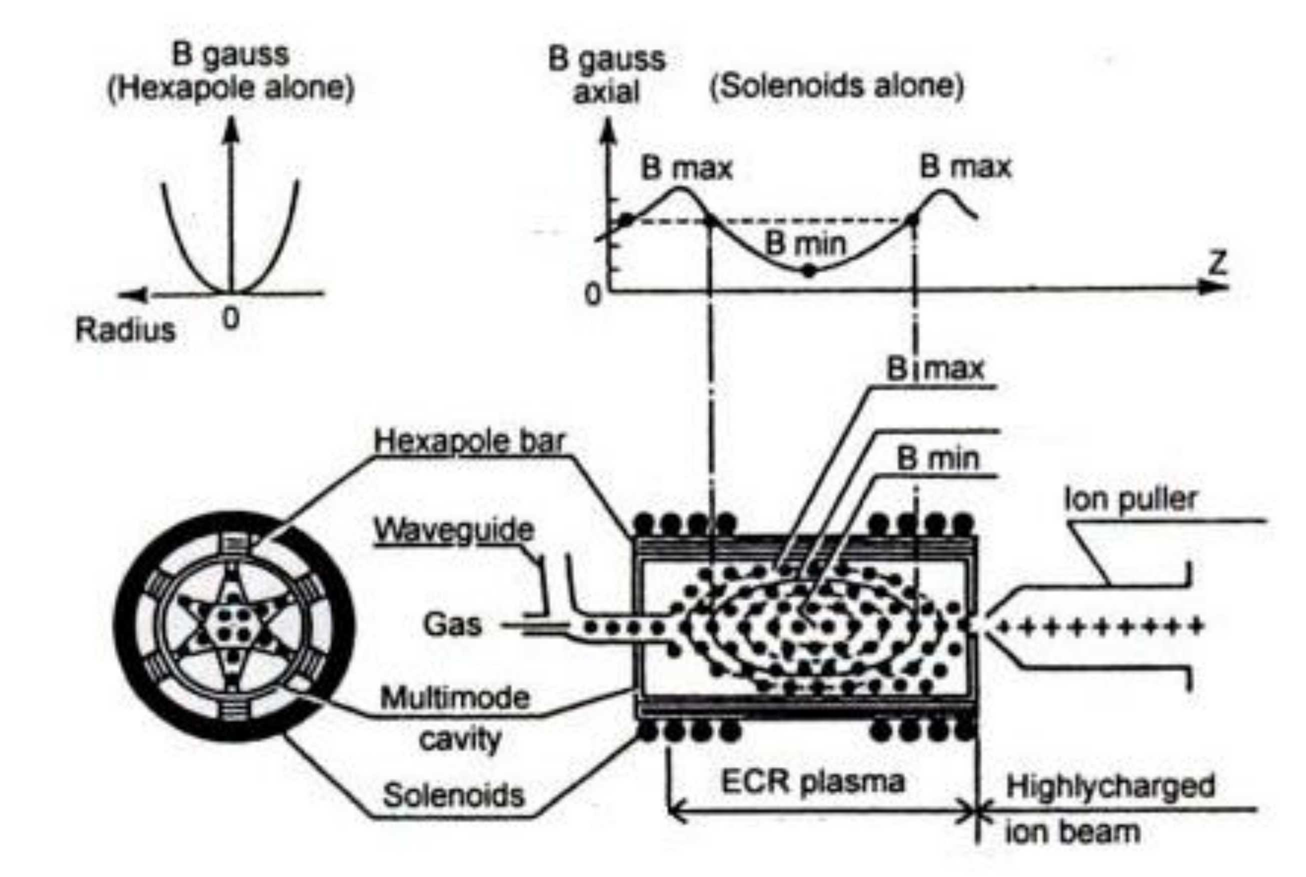
1. Two or three sources
2. A LEBT (Low Energy Beam Transfer line)
3. A low energy Linac
4. A MEBT (Medium Energy Beam Transfer line)

Injector: Sources

The type of heavy ions sources are PIG, EBIS but, above all,

ECR (Electron Cyclotron Resonance)

Gas are ionized by RF power at electron cyclotron resonance frequency (10-18 GHz)
The magnetic trap fro the electrons is obtained by a solenoid and an exapolar magnet

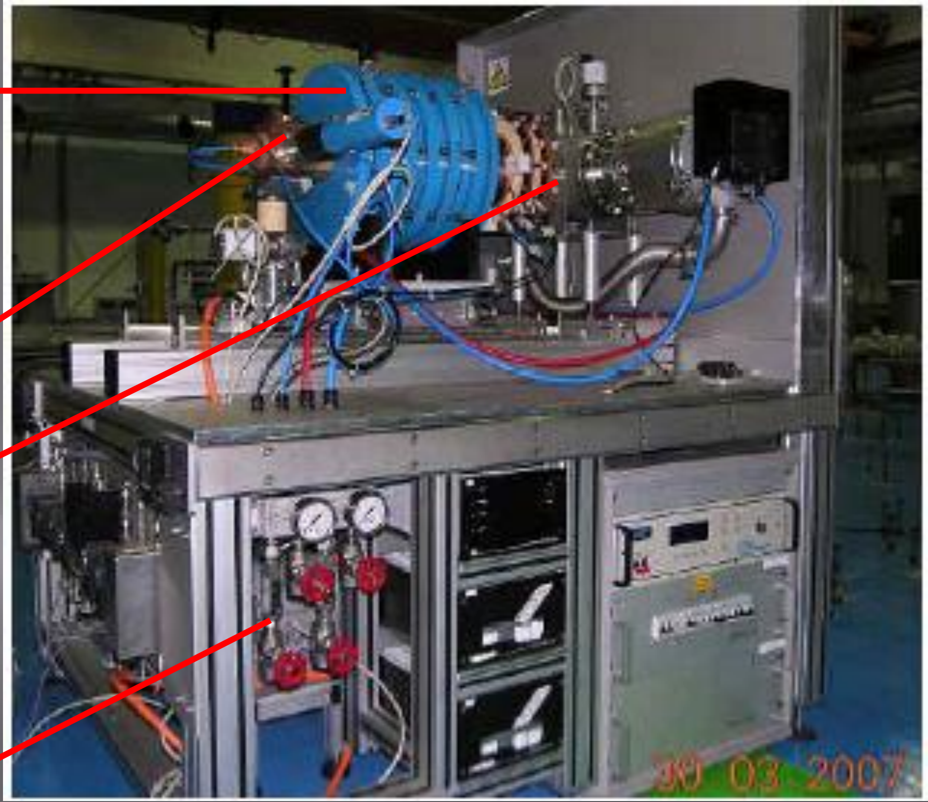


SUPERNANOGAN: CNAO ECR source

Permanent magnet (Max 1.2 T)
Double wall, water cooled plasma chamber,
7 mm diameter aperture for beam extraction.

Flexible frequency variable travelling wave tubes amplifiers (TWTA); An RF generator of about 400 W at 14.5 GHz
(the effective power used is 8 W for H3+ and 180W for C4+).

A DC bias system to add electrons to the plasma and decrease the plasma potential.



He, CO2, H2 gas

0.008 MeV/u, ~ 1 mA , 0.67 Pi mm mrad H^{3+}
0.008 MeV/u, ~ 0.25 mA, 0.56 Pi mm mrad C^{4+}

Continuous beam → **A electrostatic chopper at the end of the LEBT makes a pulsed beam**

A switching magnet in the LEBT allows to select the source and then the species

Synchrotron facility layout: Linac

RFQ+IH

RFQ

217 MHz

IH

3	Integrated magnetic triplet lenses	
56	Accelerating gaps	
Energy range		0.4 – 7 MeV/u
Tank length		3.77 m
Inner tank height		0.34 m
Inner tank width		0.26 m
Drift tube aperture diam.		12 – 16 mm
RF power loss (pulse)		≈ 1 MW
Averaged eff. volt. gain		5.3 MV/m

Four-rod like type

Energy range = 8 – 400 keV/u

Electrode length = 1.35 m,

Electrode voltage = 70 kV

RF power loss (pulse): about 100 kW

Low duty cycle: around 0.1%

RFQ

0.008-0.4 MeV/u H^{3+}

0.008-0.4 MeV/u C^{4+}

IH

0.4-7 MeV/u H^{3+}

0.4-7 MeV/u C^{4+}

Injector: MEBT

Stripping foils

Positions:	10
Foil material:	Carbon
Foil thickness:	100-200 µg/cm²
Foil diameter:	15 mm
Beam diameter:	5 mm
Position accuracy:	±0,5 mm

$$H_3^+ \rightarrow H^+$$

$$C^{4+} \rightarrow C^{6+}$$

CNAO debuncher cavity

Multiturn injection: a 70 microsec beam injected in a ring with 3 microsec revolution frequency using a variable magnetic bump on the electrostatic septum

Ring: Slow Extraction

Dose homogeneity must be ± 2.5% → a single turn extraction (<1 μsec) not possible

↓

It consists of making unstable beam betatron oscillations: the motion amplitude grows until an electrostatic septum allows the extraction of the particle.

↓

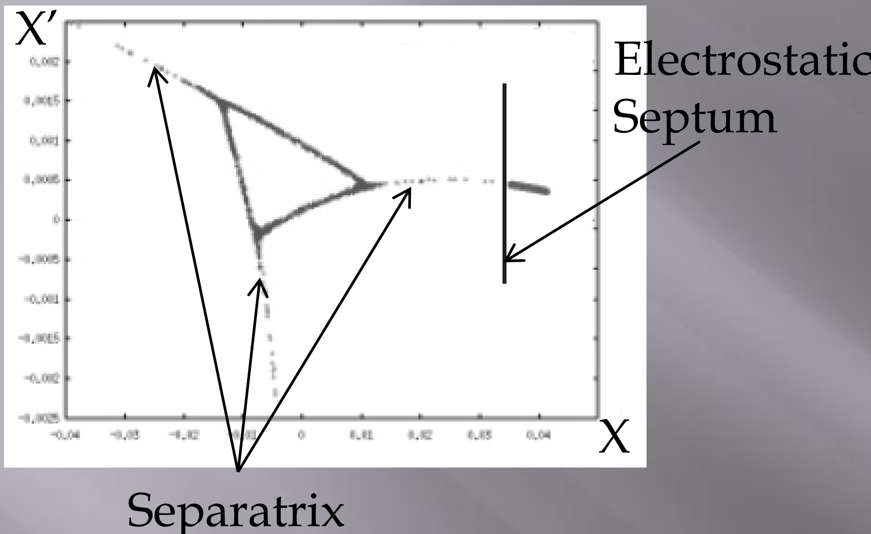
Extraction mechanism strongly influences the ring design

Optical layout must guarantee a machine tune near to an unstable value during the extraction. When extracting beam must acquire the resonance tune.

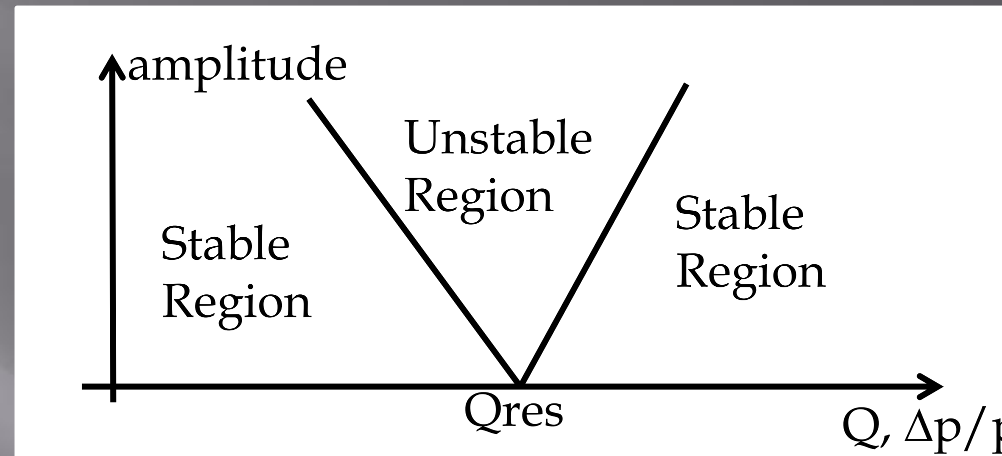
In the present facilities the unstable tune is chosen N/3. A sextupolar field feeds the resonance:
THIRD ORDER RESONANCE SLOW EXTRACTION MECHANISM

Ring: Slow Extraction

Horizontal Phase Space at the resonant tune



Steinbach diagram

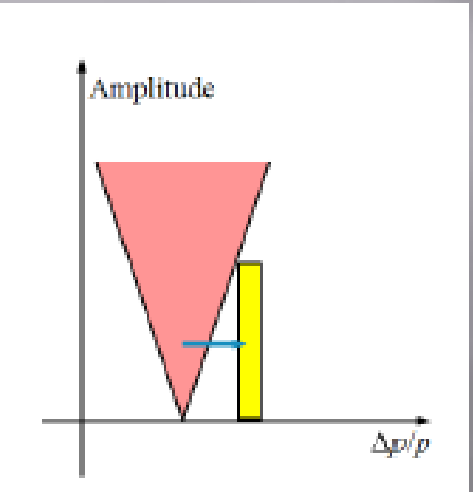


Beam is driven to the resonance condition by three methods:

- amplitude selection
- amplitude-momentum selection
- RFKO

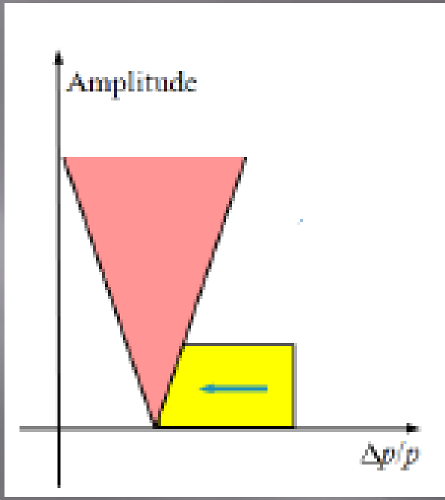
Ring: Slow Extraction

amplitude selection.



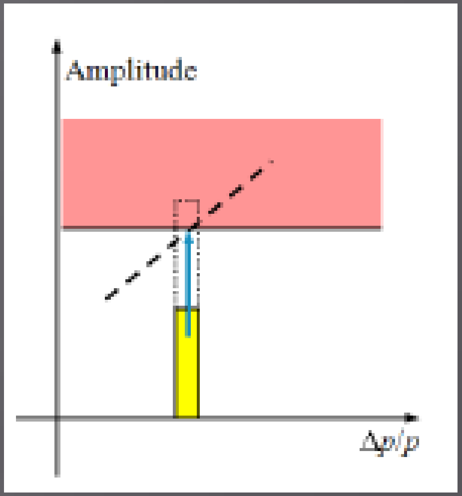
•Not constant optics
•Narrow dp/p
•Not constant position, size, energy of extracted beam
•No more used

amplitude-momentum selection



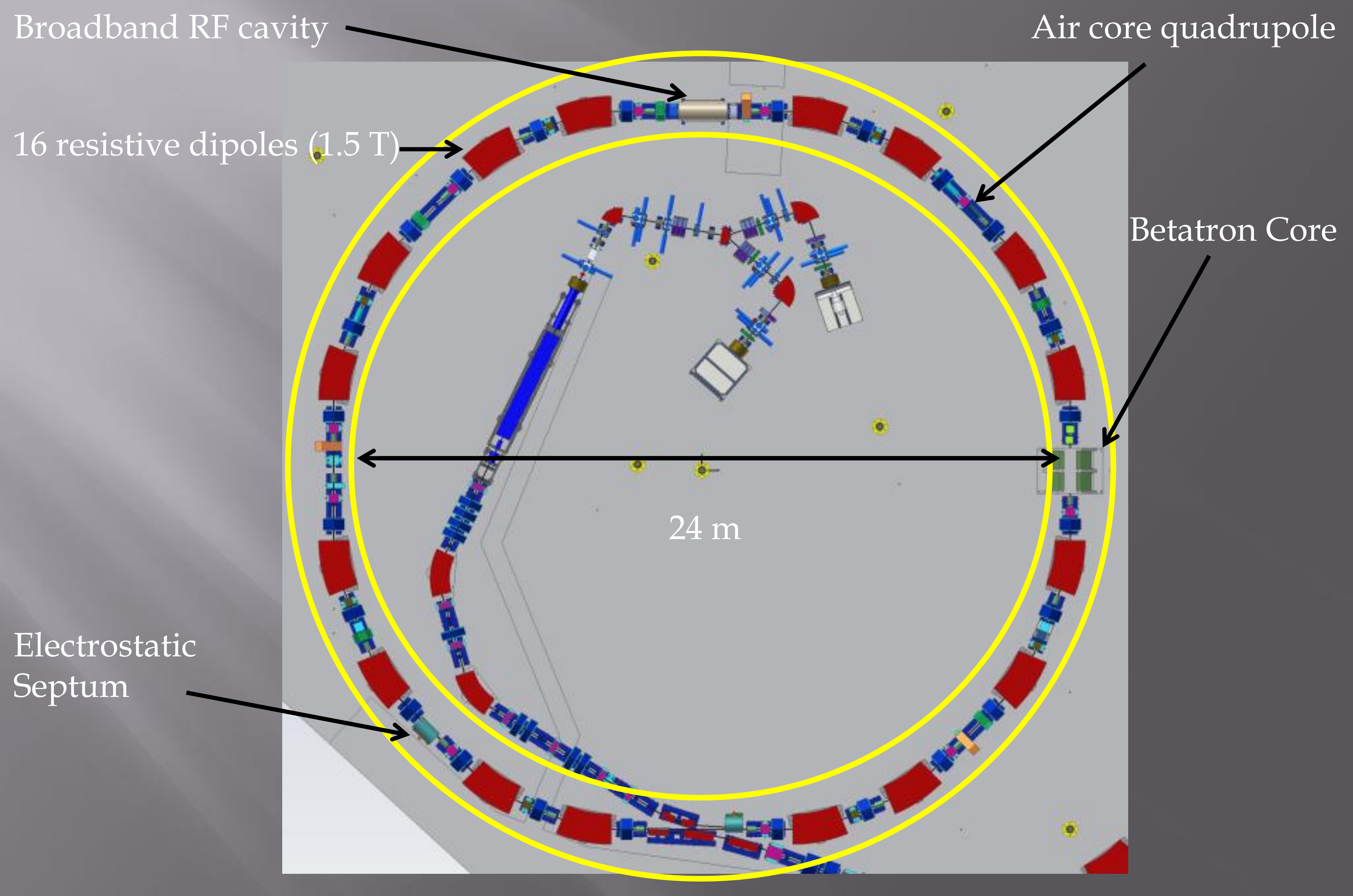
•Constant optics
•Large beam dp/p
•Constant position, size, energy of extracted beam
•Use of a betatron core

RFKO



•Constant optics
•Constant position, size, energy of extracted beam
•Use of a transverse RF exciter

Synchrotron facility layout: Ring



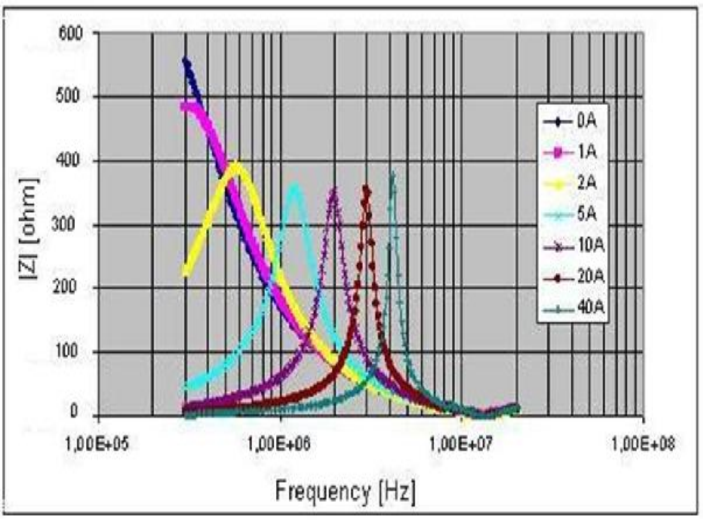
Ring : RF cavity

Acceleration is performed with a single RF cavity at harmonic 1 or 2 based on the principle of ferrite-loaded cavities and with tetrode or solid state technology for the amplifier.

Nowadays ferrite often is replaced by amorphous alloy to reduce cavity length

CNAO RF Cavity

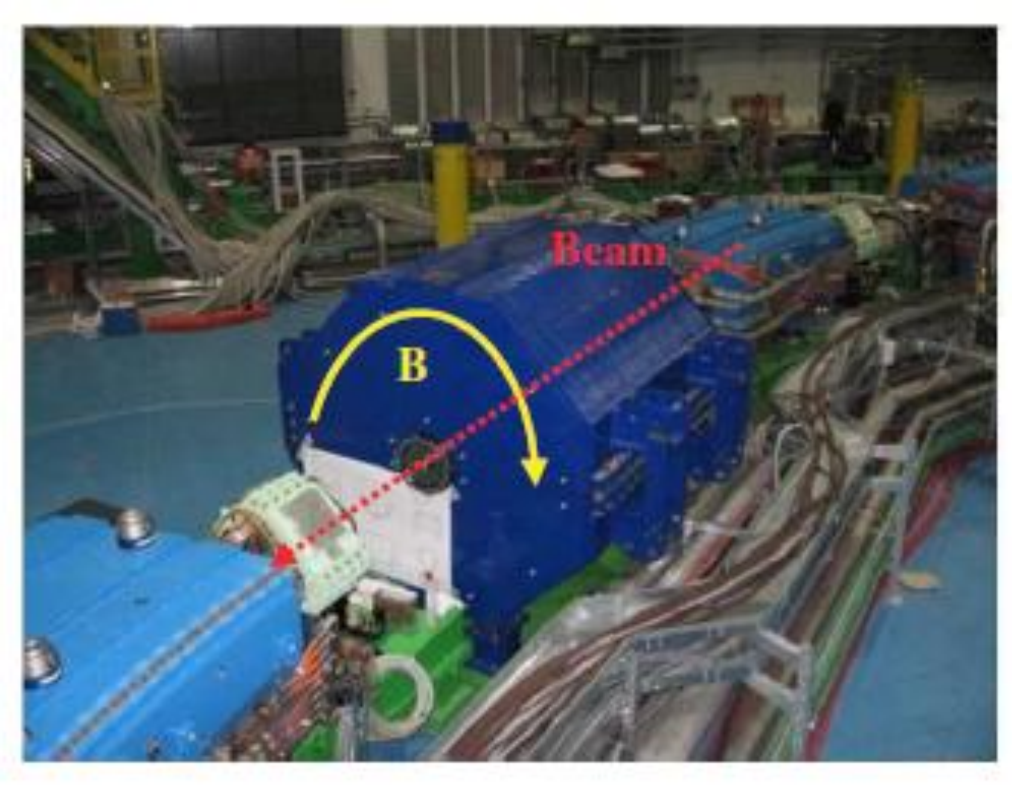
Vitrovac amorphous alloy Fe-Co

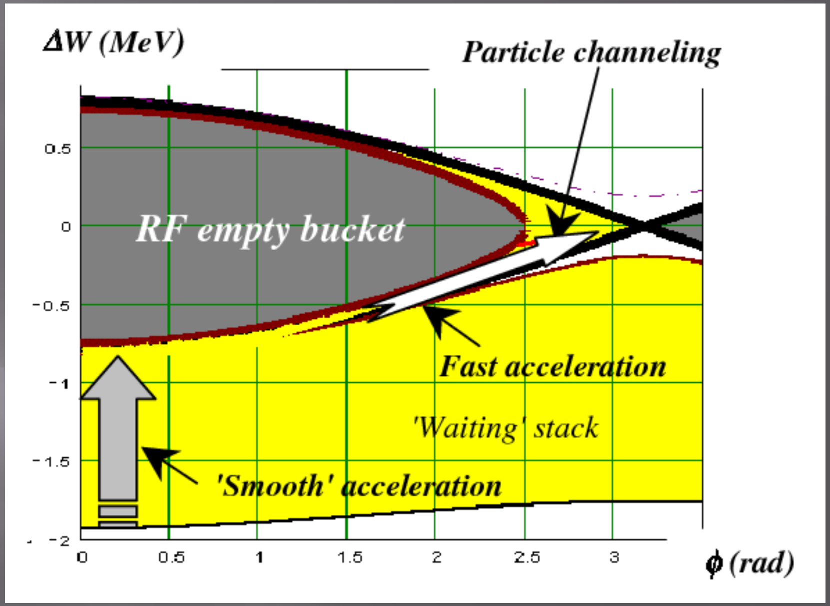


Frequency Range	0.4 MHz-3 MHz
Voltage Range	50 V-10000 V
Vitrovac current	0-10 A
Cavity length	1.3 m
Q	1-5
Rshunt	900-500 ohm

Ring: Betatron Core

High inductance device: intrinsically smooth in its operation





The time to cure a voxel is about 5 msec considering the dose homogeneity beam must be controlled in the scale of 10 kHz.

To reduce ripple spill in this range RF cavity is used with the technique of empty bucket channelling

Extraction lines

•The beam quality at all the energies (stable position, possibility to have round beams with more dimensions, RT control of the dose) → constraints on magnetic lattices, power supplies, magnets, control system, Nozzle.

•Irradiation from different directions is mandatory. It can be realized:

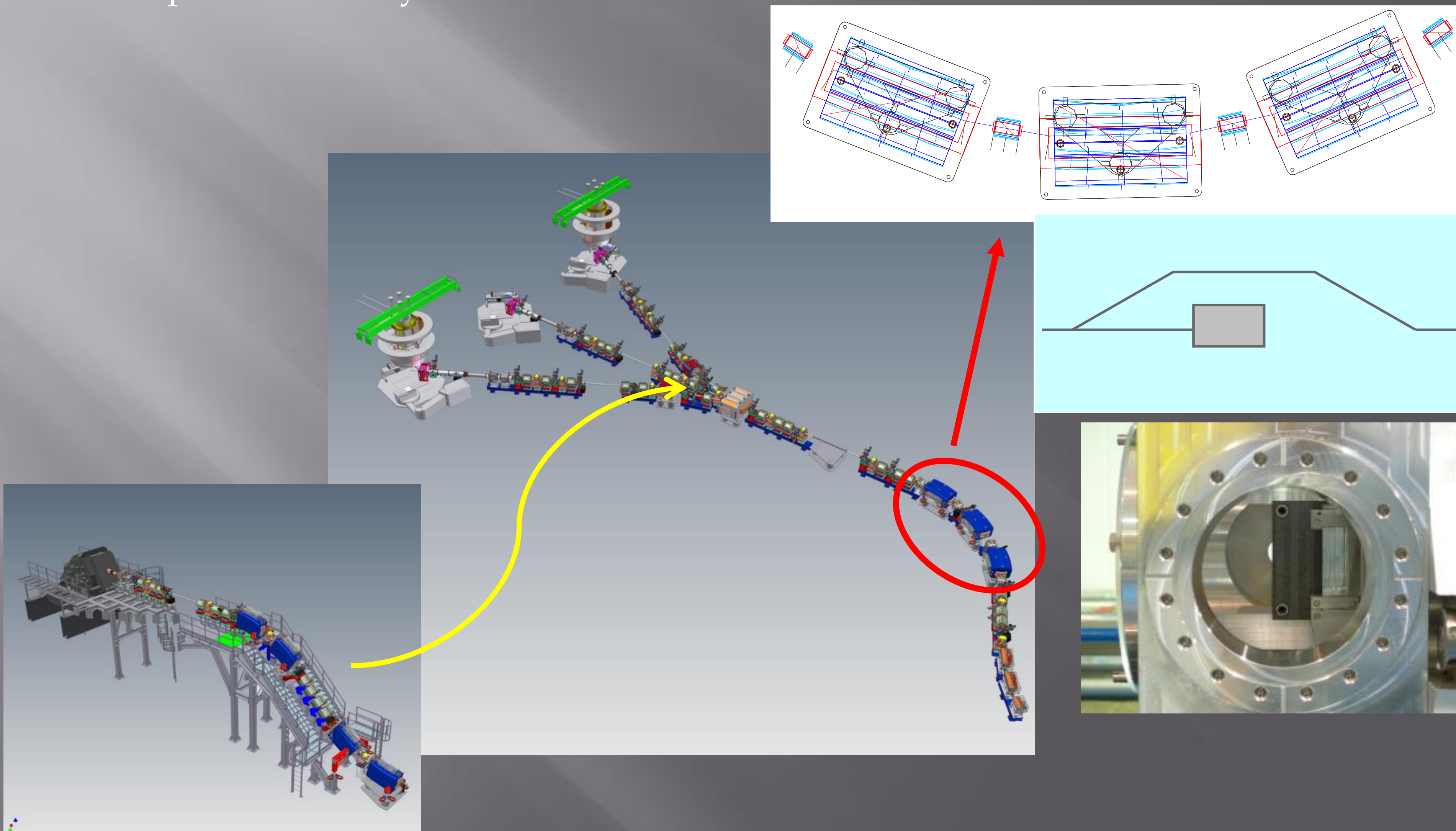
1. Displacing the patient
2. Several lines in the same room
3. Gantry

Nowadays gantries for protons are present in most facilities.
A gantry for carbon is more challenging!
To date only HIT is equipped with a carbon ions gantry
(600 tons at 13 m against the standard 100 tons at 10 m)

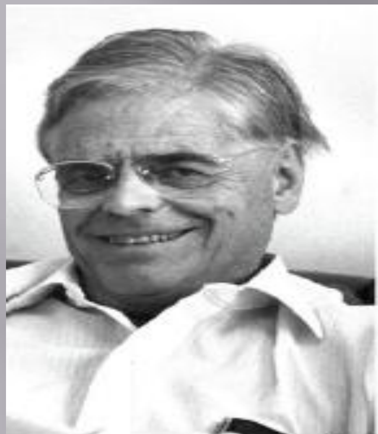
First heavy ions gantry at Heidelberg

CNAO Extraction lines

CNAO lines: 3 treatment rooms: 2 with horizontal line and 1 with horizontal and vertical one. The beginning of the line has 4 fast magnets (100 microsec) to dump the beam for patient security.



Hadrontherapy first proposed by R. Wilson in 1946



R.R. Wilson, "Foreword to the Second International Symposium on Hadrontherapy," in Advances in Hadrontherapy, (U. Amaldi, B. Larsson, Y. Lemoigne, Y., Eds.), Excerpta Medica, Elsevier, International Congress Series 1144: ix-xiii (1997).

Radiological Use of Fast Protons

ROBERT R. WILSON
Research Laboratory of Physics, Harvard University
Cambridge, Massachusetts

EXCEPT FOR electrons, the particles which have been accelerated to high energies by machines such as cyclotrons or Van de Graaff generators have not been directly used therapeutically. Rather, the neutrons, gamma rays, or artificial radioactivities produced in various reactions of the primary particles have been applied to medical problems. This has, in [...]e part, been due to the very short [...]ation in tissue of protons, deut[...] particles from prese[...] [...]r-energy mach[...] [...] how[...]

per centimeter of path, or specific ionization, and this varies almost inversely with the energy of the proton. Thus the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the ion is brought to rest.

These properties make it possible to irradiate inter[...]ly a strictly localized region [...]

Radiology 47: 487-491, 1946

In 1954: 30 patients treated with protons at LBL (Lawrence Berkeley Laboratory)

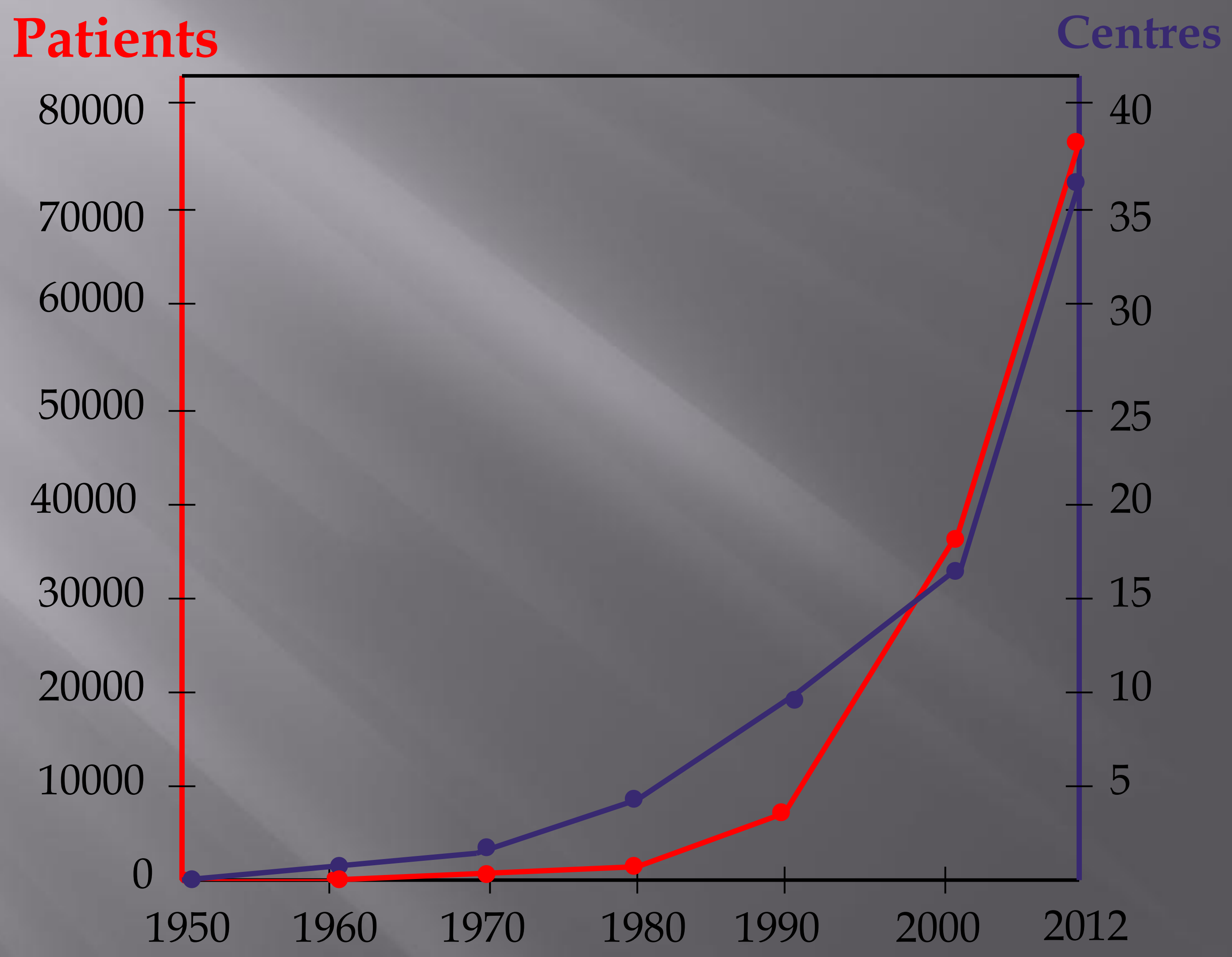
In the next years other treatments in other research centers have been performed (Uppsala, Harvard, Dubna, St.Petersburg, Moscow, PSI, Chiba, Tsukuba)

In 1990 the first dedicated hospital facility has started treatments at Loma Linda (LLUMC

First dedicated hospital center for proton therapy: LLUMC (Lomalinda), USA

Proton synchrotron (70-250 MeV) equipped with a fixed beam room with two beam lines, three rotating gantries and a research room with three beam lines.
To date over 15000 patients have been treated.

Hadrontherapy history: Rapid Growth



Hadrontherapy in the world

TRIUMF(Vancouver),Canada

UCSF(California), USA
LLUMC(Lomalinda),USA
IUHealthPTC,(Bloomington),USA
NPTC(Boston),USA
MDACC(Houston),USA
UFPTI(Jacksonville),USA
Upenn(Philadelfia),USA
CDH(Warrenville),USA
HUPTI(Hampton),USA
Procure PTC(New Jersey),USA
Procure PTC(Oklahoma),USA

Uppsala , Sweden
Clatterbridge, England
Nice , France
Orsay, France
HZB(Berlin), Germany
RPTC(Munich),Germany
HIT(Heidelberg),Germany
PSI(Villigen),Switzerland
IFJ-PAN, Poland
LNS(Catania), Italy
CNAO (Pavia), Italy

ITEP(Moscow), Russia
St. Petersburg, Russia
Dubna, Russia
WPTC(Zibo),China
IMP(Langzhou), China
NCC, South Korea

NCC (Kashiwa), Japan
PMRC (Tsukuba), Japan
WERC (Shizuoka), Japan
PATRO (Hyogo),Japan
HIMAC (Chiba),Japan
GHMC (Gunma),Japan
STPTC(Koriyama),Japan
Medipolis Medical Research Institute (Ibusuki), Japan

iThemba LABS, South Africa

Dec 2011: 38 centers
75571 patients of which 7881 with carbon ions

Hadrontherapy in the world:Cyclotrons

Uppsala , Sweden
Clatterbridge, England
Nice , France
Orsay, France
HZB(Berlin), Germany
RPTC(Munich),Germany
PSI(Villigen),Switzerland
IFJ-PAN, Poland
LNS(Catania), Italy

Dubna, Russia
WPTC(Zibo),China
NCC, South Korea

TRIUMF(Vancouver),Canada

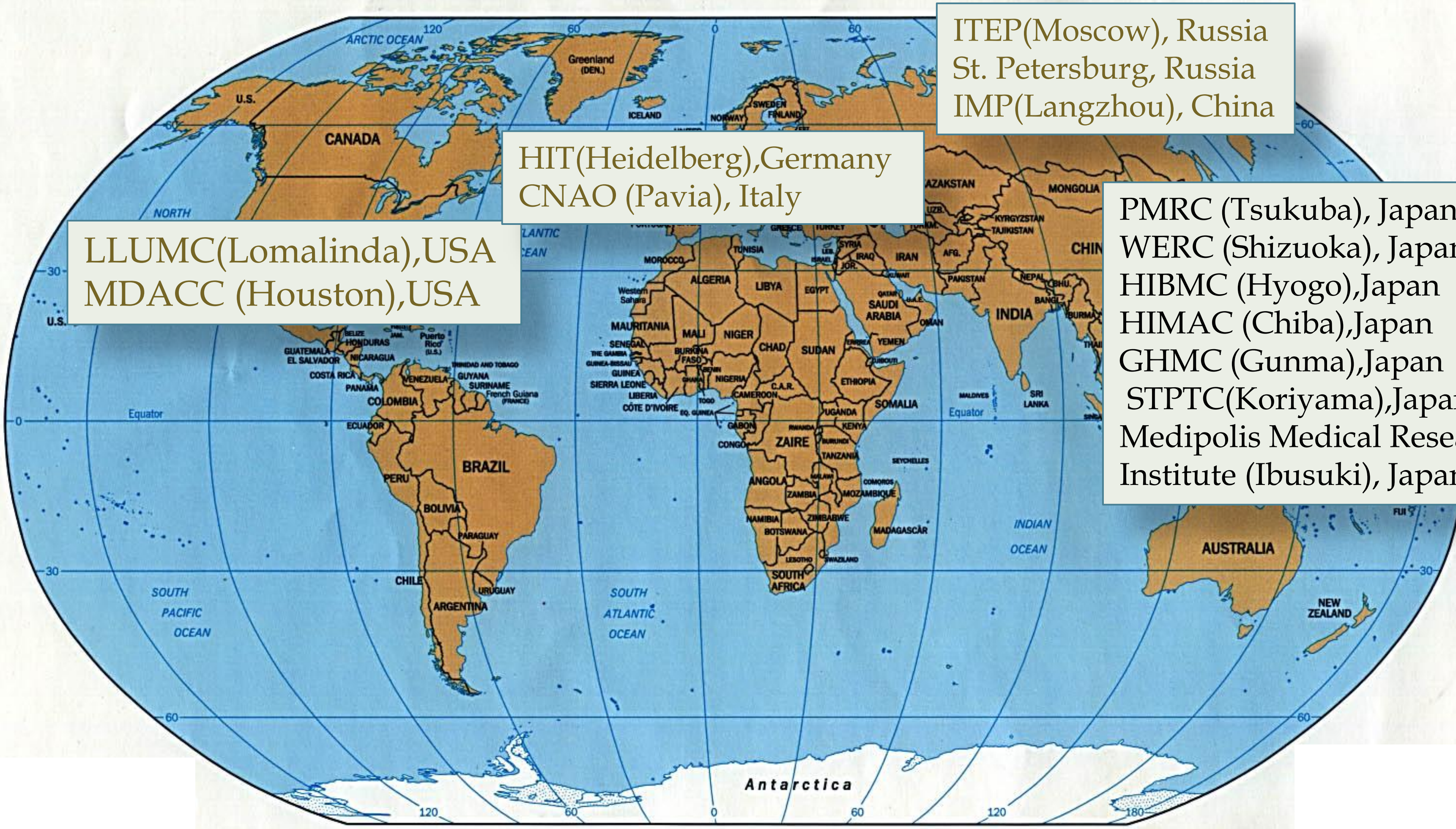
UCSF(California), USA
IUHealthPTC,(Bloomington),USA
NPTC(Boston),USA
UFPTI(Jacksonville),USA
Upenn(Philadelfia),USA
CDH(Warrenville),USA
HUPTI(Hampton),USA
Procure PTC(New Jersey),USA
Procure PTC(Oklahoma),USA

NCC (Kashiwa), Japan

iThemba LABS, South Africa

24 cyclotron facilites

Hadrontherapy in the world: Synchrotrons



ITEP(Moscow), Russia
St. Petersburg, Russia
IMP(Langzhou), China

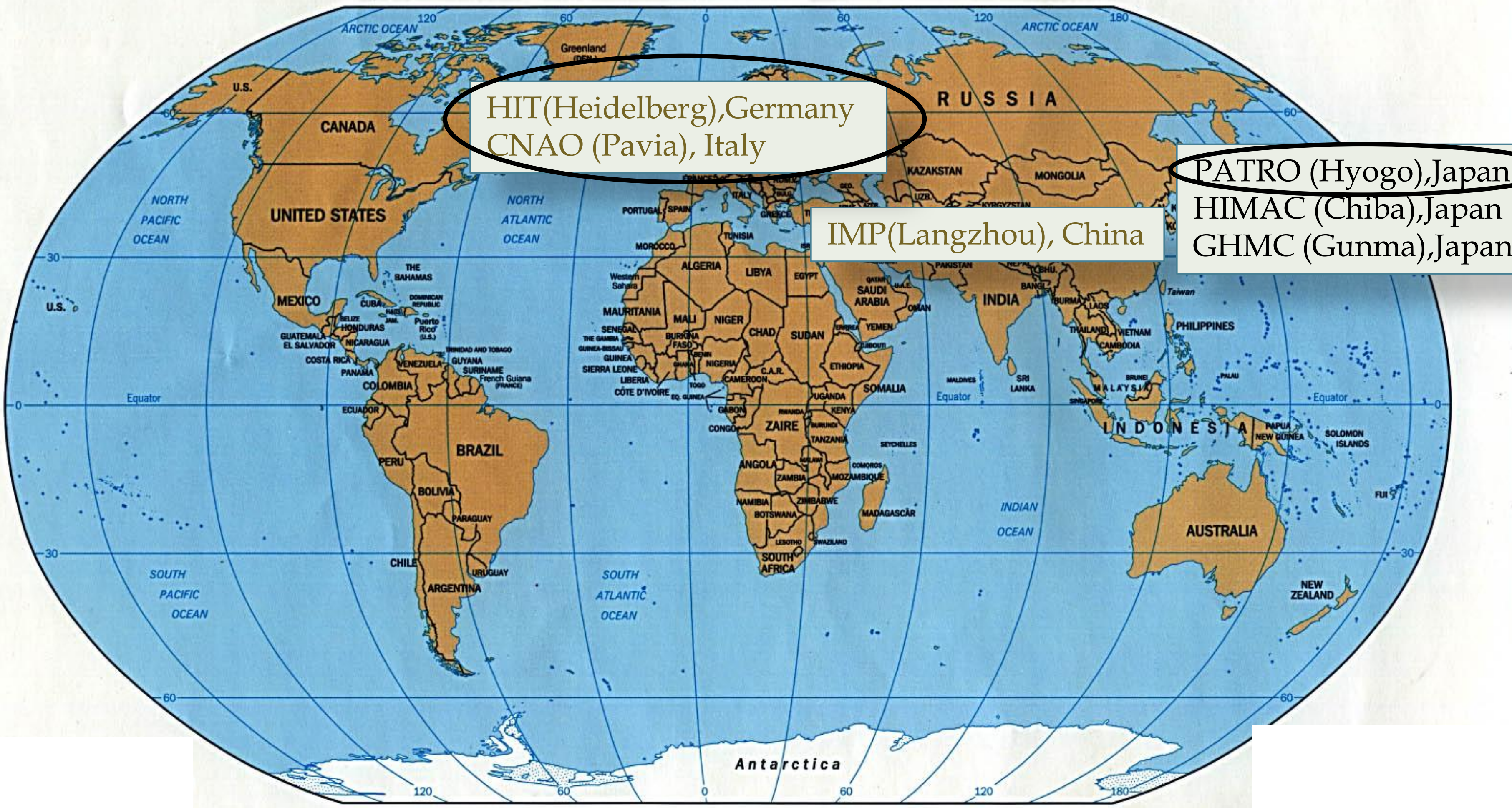
HIT(Heidelberg),Germany
CNAO (Pavia), Italy

LLUMC(Lomalinda),USA
MDACC (Houston),USA

PMRC (Tsukuba), Japan
WERC (Shizuoka), Japan
HIBMC (Hyogo),Japan
HIMAC (Chiba),Japan
GHMC (Gunma),Japan
STPTC(Koriyama),Japan
Medipolis Medical Research Institute (Ibusuki), Japan

14 synchrotron facilities

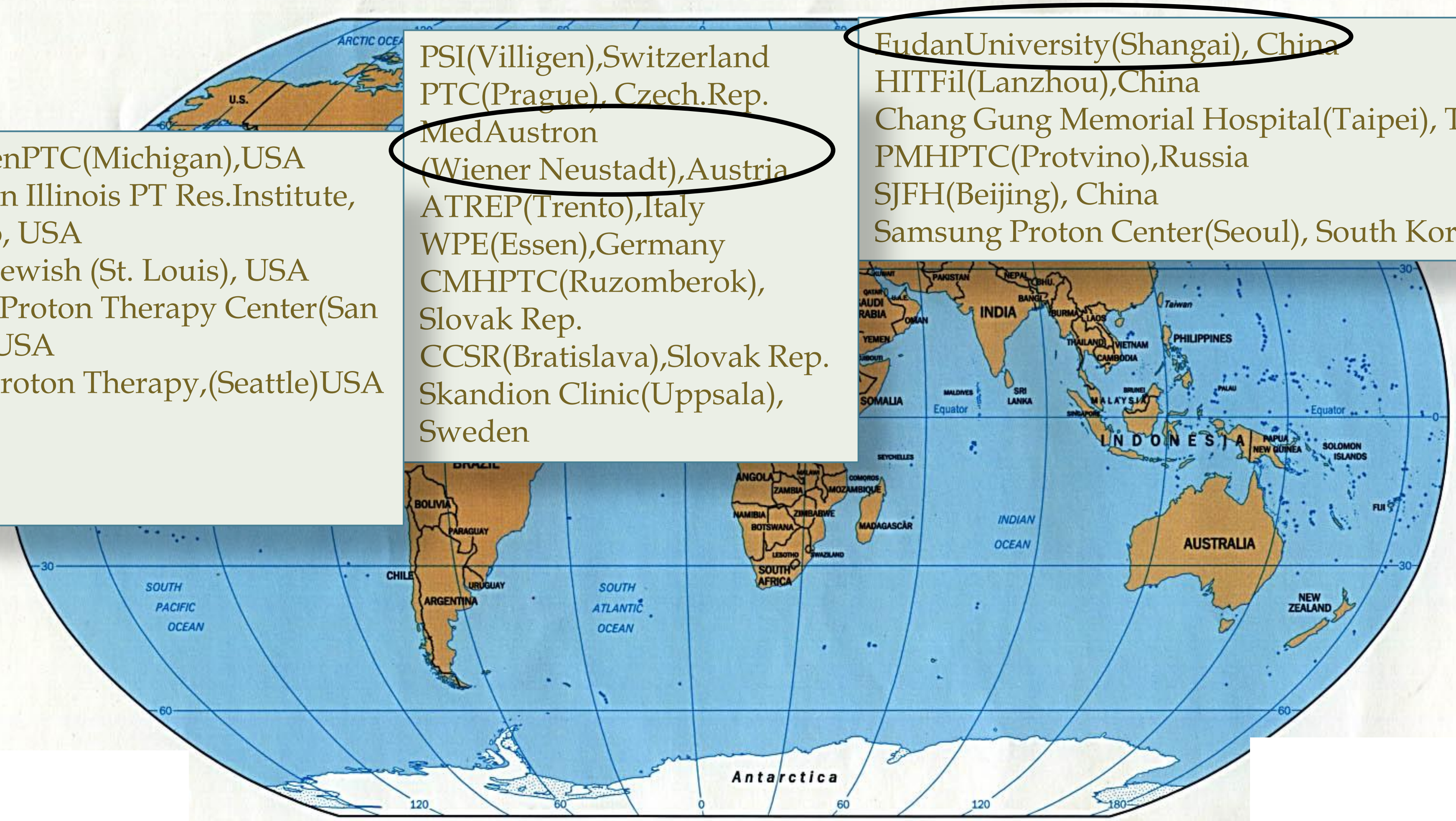
Hadrontherapy in the world: Carbon Synchrotrons



6 carbon synchrotron facilities:

only HIT, CNAO and PATRO produce both clinical protons and carbon ions

Hadrontherapy in the world: New facilities (under construction or ready to start)



cLarenPTC(Michigan),USA
orthern Illinois PT Res.Institute,
nicago, USA
arnes Jewish (St. Louis), USA
ripps Proton Therapy Center(San
iego),USA
CCA Proton Therapy,(Seattle)USA

PSI(Villigen),Switzerland
PTC(Prague), Czech.Rep.
MedAustron
(Wiener Neustadt),Austria
ATREP(Trento),Italy
WPE(Essen),Germany
CMHPTC(Ruzomberok),
Slovak Rep.
CCSR(Bratislava),Slovak Rep.
Skandion Clinic(Uppsala),
Sweden

FudanUniversity(Shangai), China
HITFil(Lanzhou),China
Chang Gung Memorial Hospital(Taipei), Taiwa
PMHPTC(Protvino),Russia
SJFH(Beijing), China
Samsung Proton Center(Seoul), South Korea

USA, Europe, Asia: 12 proton cyclotrons; 2 proton-carbon synchrotrons;

2 proton synchrotrons; 1 carbon synchrotron; 1 proton synchro-cyclotron

Hadrontherapy business

The idea of hadrontherapy facilities has passed from the research field to the businees field with lots of commercial firms:
IBA, Hitachi, Mitsubishi, Sumitomo, Varian, Still River, Optivus, Siemens

•IBA: the greatest number of sold centres: 14 proton resistive cyclotrons. Unique proposal of carbon cyclotron
•Varian (bought ACCEL in 2007): proton superconducting cyclotrons
• Optivus: proton synchrotron similar to LLUMC
•Hitachi: proton synchrotrons similar to LLUMC (4 sold centres)
•Mitsubishi: proton synchrotron (4 sold centres); carbon and proton synchrotron (PATRO)
•Sumitomo: proton cyclotron; carbon synchrotron: injectors installed but not yet full centre
•Siemens: proton-carbon synchrotrons. In July 2011 it communicated its lost of interest: Kiel and Marburg will be dismantled.
•Still River:compact proton superconducting synchrocyclotron(1^{st} under construction,USA

The field is not only for firms;
Hadrontherapy field is still technologically challenging then research centres still contribute to the design and the construction of facilities: e.g. CNAO was born from the PIMMS and built by the help of a strong net of research international collaborations : INFN-CERN-GSI-LPSC-NIRS-italian universities (Milan,Pavia,Turin)

Hadrontherapy future

Worldwide R&D for more compact and/or advanced accelerators:

•FFAG: Fixed Field alternating Gradient: in the middle between a cyclotron and a synchrotron. DC beam with fast energy change! The radius change slightly because B changes with the radius. A fast energy change could be a good solution in treating moving organs
• LIBO: Linac Booster Linac @ 3 GHz, 27MV/m for protons from 30 MeV to 250 MeV exploiting the standard 30 MeV cyclotrons for radioisotopes as injector.
•Laser: heavy ions acceleration by high power lasers
•DWA: dielectric wall induction linac: new dielectrics 100 MV/m (instead of 10)

↓

250 MeV proton linac 3 m long

Conclusions

The present clinical results have shown the importance of hadrontherapy and in particular the advantages of the carbon beams over the proton.

The choice of the beam shaping technique is very important. Active scanning appears to be the future but research is mandatory in the case of moving organs.

Synchrotrons designed for carbon beams can easily be adapted also for proton beams.

The more complete centre nowadays is a proton-carbon synchrotron with active scanning

In the last decades hadrontherapy had a rapid growth with lots of facilities under the form of cyclotrons and synchrotrons for protons and carbon ions.

New centres are under design all around the world.

R&D is mandatory on the clinical characteristics of other species and in the design of more compact and improved layout