A SHORT HISTORY
OF HADRON THERAPY: 1935-2015

Ugo Amaldi

TERA Foundation (Novara), CNAO Foundation (Pavia), Tera-Care Foundation (Geneva)

About nomenclature

I prefer ‘hadrontherapy’ or ‘hadron therapy’ to ‘particle therapy’ because:

- The photons of X rays, used in all Radiotherapy Departments, are also ‘particles’
- The electrons , used in many Radiotherapy Departments and in modern ‘FLASH therapy’ are also ‘particles’

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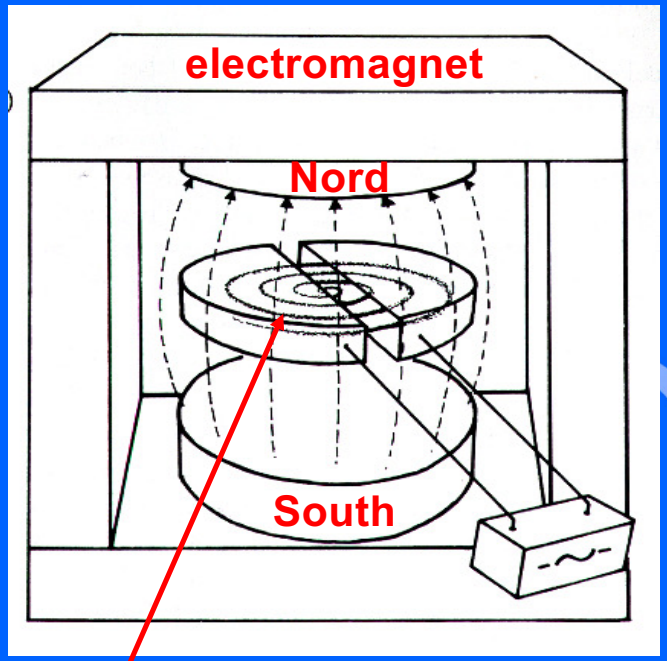
I prefer ‘light ions’ to ‘heavy ions’ because:

- Following the International Commission on Radiation Units - ICRU
  “all ions with a charge number Z<10 (NEON) will be referred to as ‘light ions’ ”

‘HEAVY PARTICLE THERAPY’ IS SCIENTIFICALLY CORRECT

The beginnings: neutron beams

1930 – Invention of the cyclotron



Spiral tajectory of an accelerated particle

Ernest Lawrence

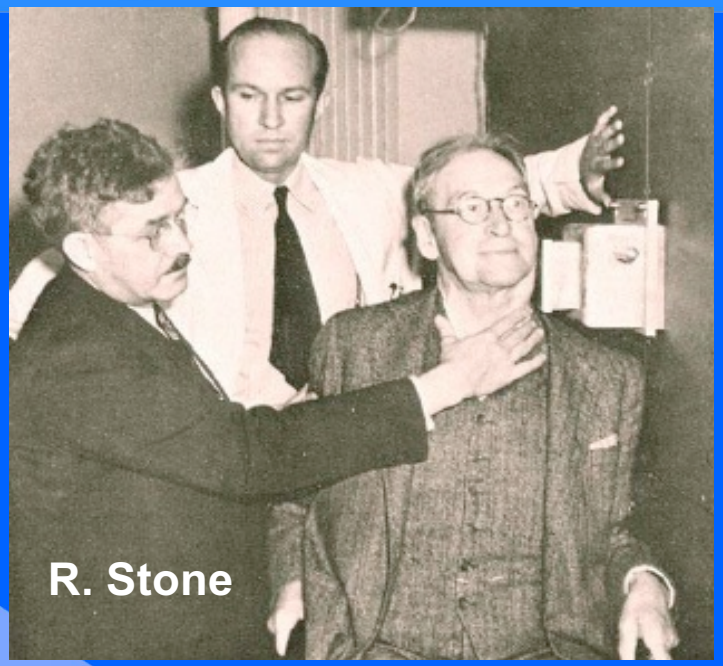
proton energy
= 0.001 GeV

John Lawrence was a MD at Yale

1935: Ernest Lawrence persuaded his brother, John Lawrence, to come to Berkeley and use his cyclotron to treat cancer and produce medical radioisotopes

Control of 37-inch cyclotron

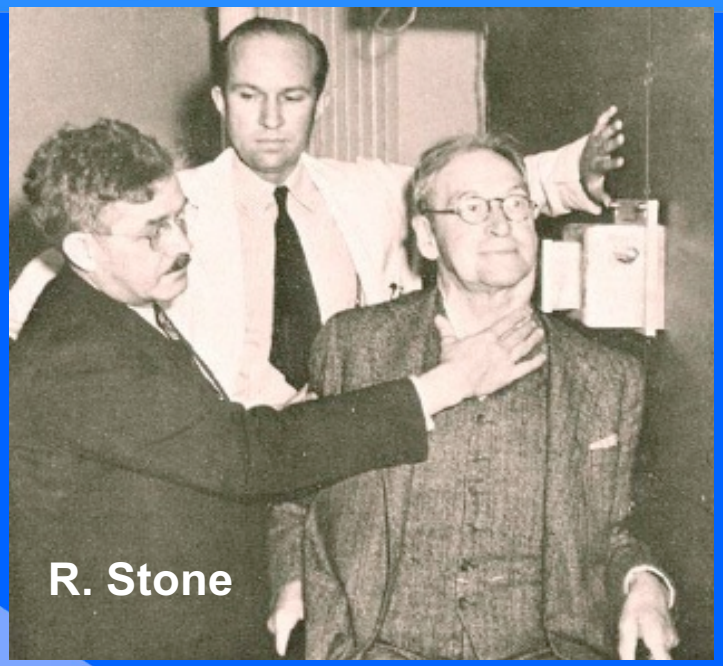
60-inch Crocker medical cyclotron



Robert Stone and John Lawrence treat a patient with neutrons from the 60- inch cyclotron:

deuterium + beryllium → fast neutrons

60-inch Crocker medical cyclotron



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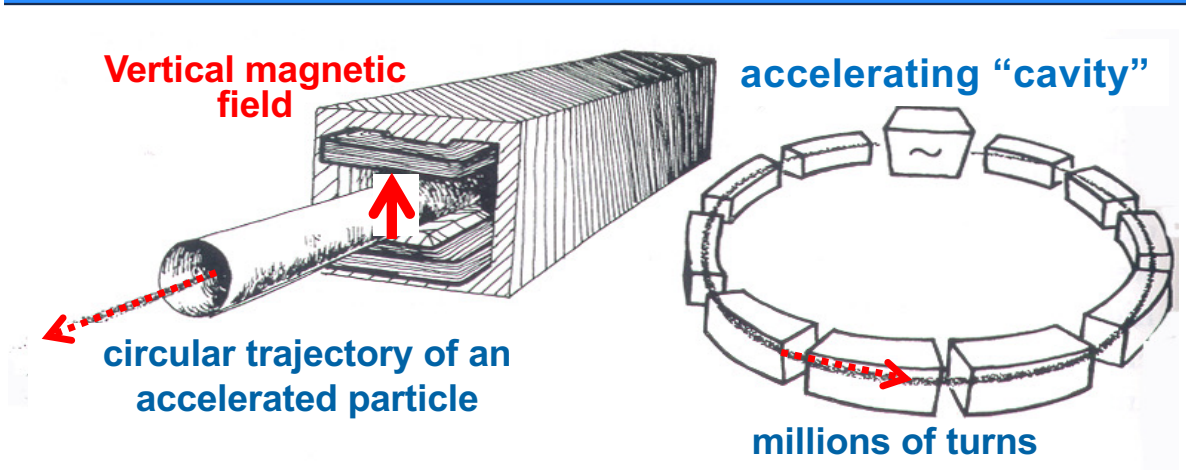
1948: R. Stone wrote

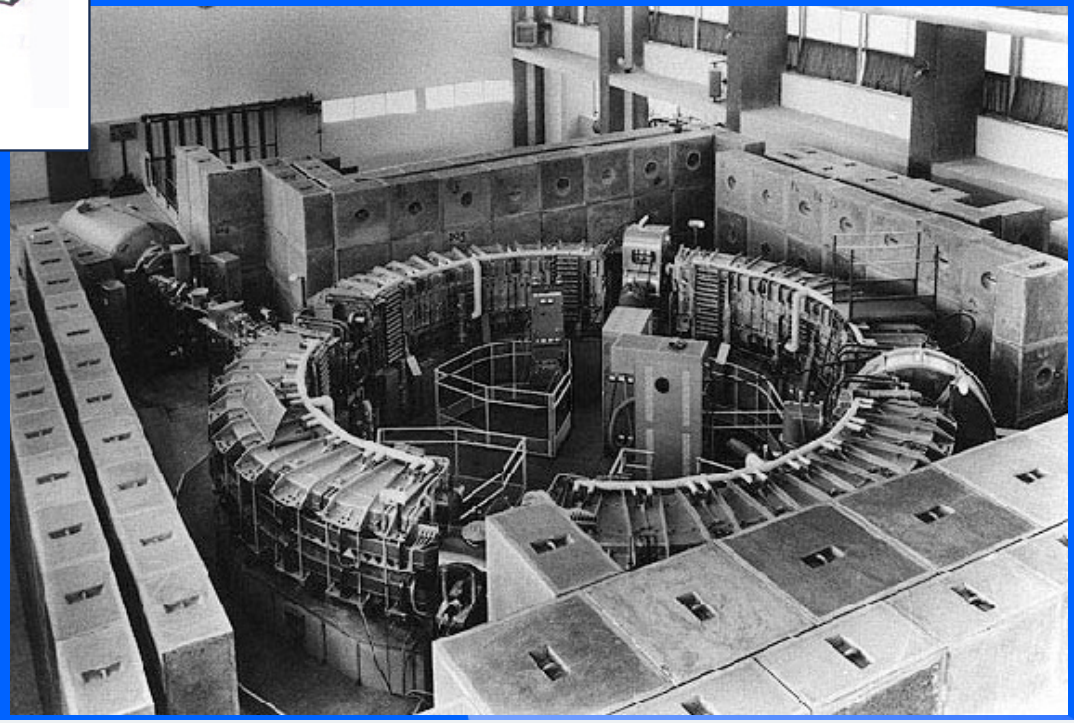
"Neutron therapy as administered by us has resulted in such bad late sequelae in proportion to the few good results that it should not be continued"

1945 – Invention of the synchrotron



1959
Synchrotron that accelerates electrons

Frascati Laboratories - INFN



Wilson's proposal: protons and carbon ions in therapy

Lawrence student
Founder and first director of Fermilab

The first steps at the Berkeley Laboratory

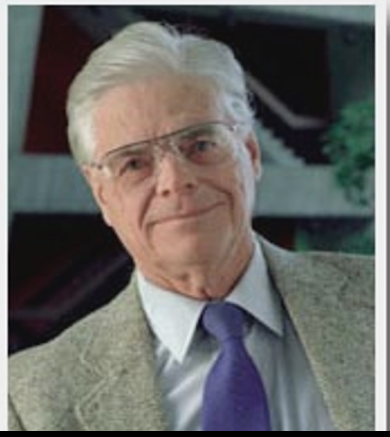
In 1946 Robert (Bob) Rathbun Wilson (*):

Protons can be used clinically

Carbon ions can also be effectively used

(*) Wilson, R.R. (1946), "Radiological use of fast proton". Radiology 47, 487.

The first steps at the Berkeley Laboratory



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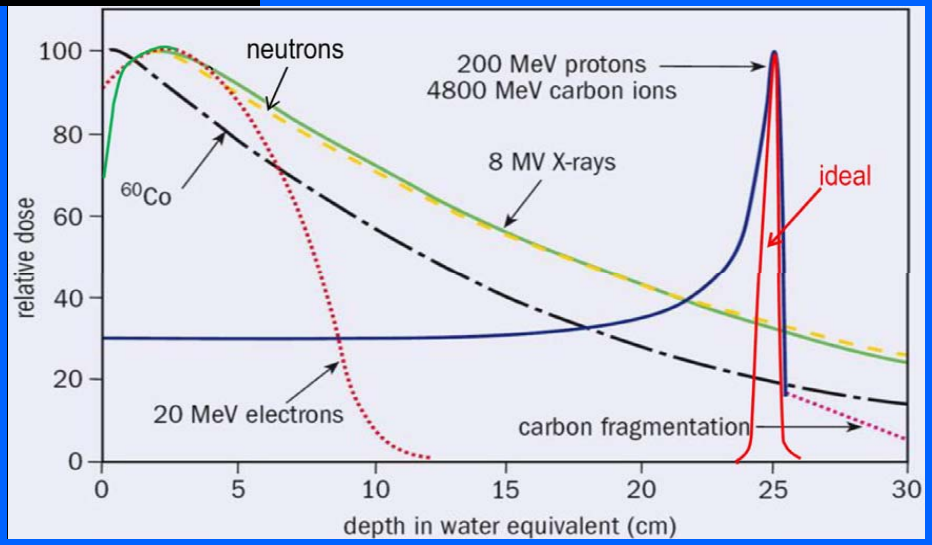
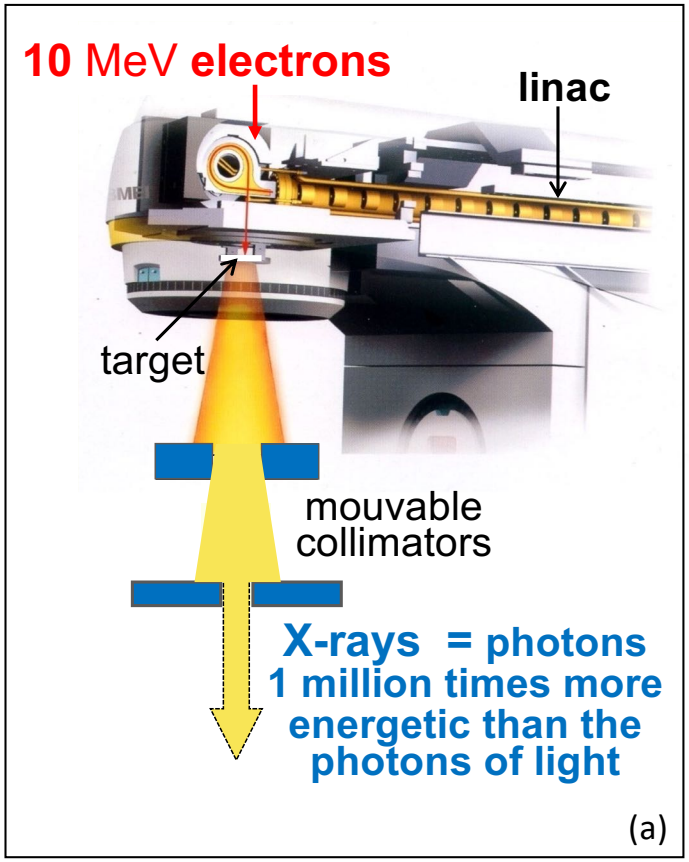


THE 'ICON OF HADRON THERAPY'

particles made of quarks

Therapy with X-ray beam and charged hadron beams

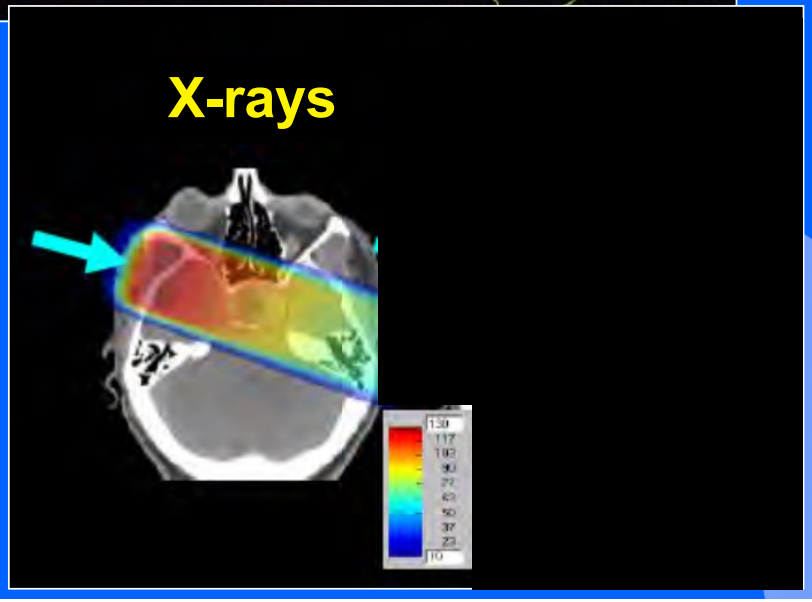
Electrons produce the high X-rays of usual radiotherapy.



Conventional X-ray therapy : 3000 patients / 1 million people
in High-Income Countries

Energy deposition by X-ray beams

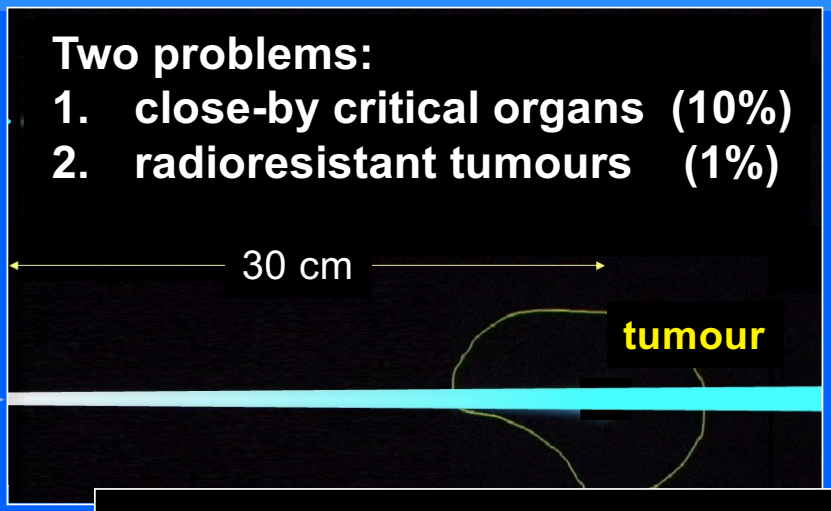
X-rays by
10 MeV electrons



Energy deposition by X-ray beams

Two problems:

1. **close-by critical organs (10%)** — **300 pts / 1 million**
2. **radioresistant tumours (1%)** — **30 pts / 1 million**



X-rays by
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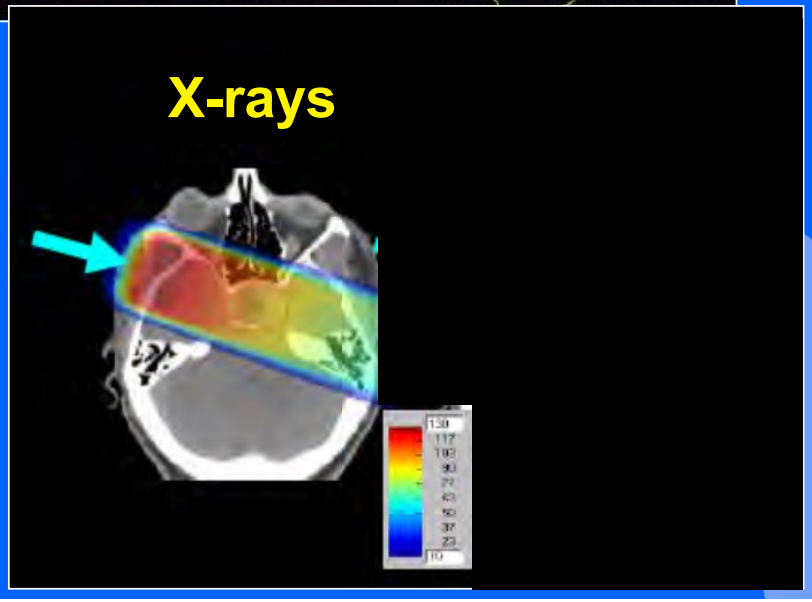
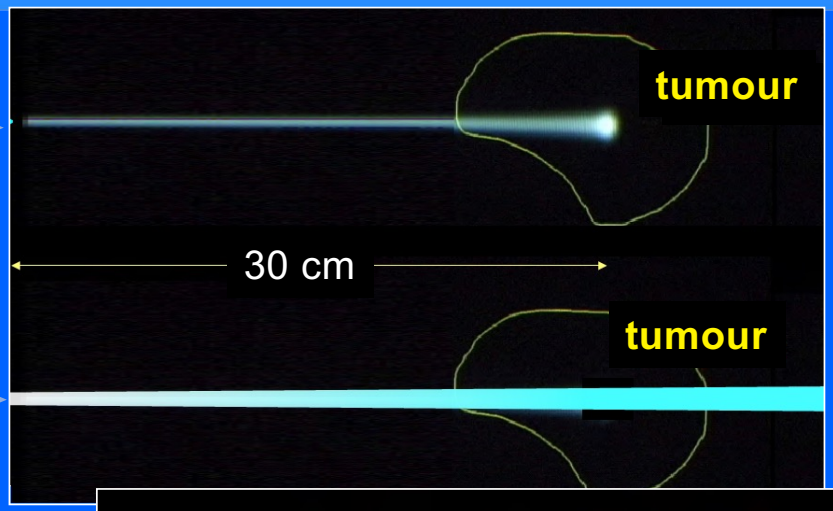


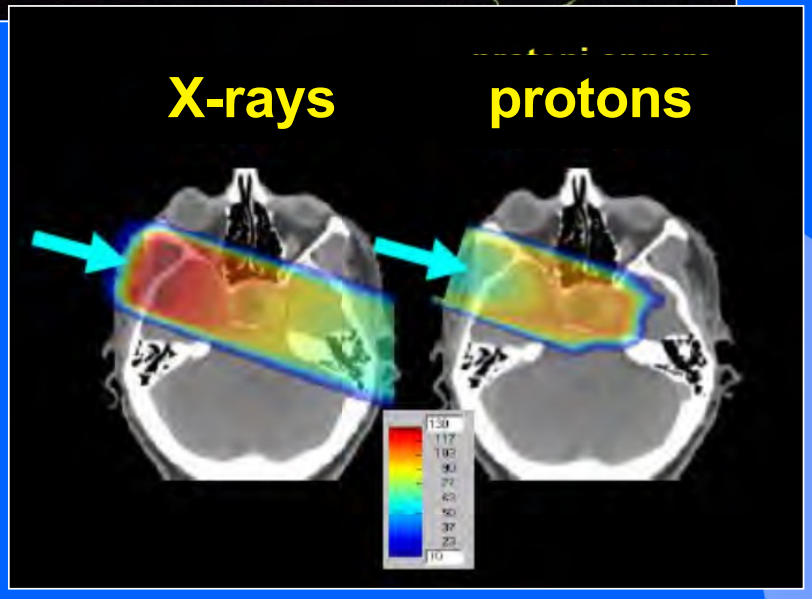
1. Protons can cure tumours close to a critical organ

protons 250 MeV

X-rays by
10 MeV electrons



300 pts / 1 million

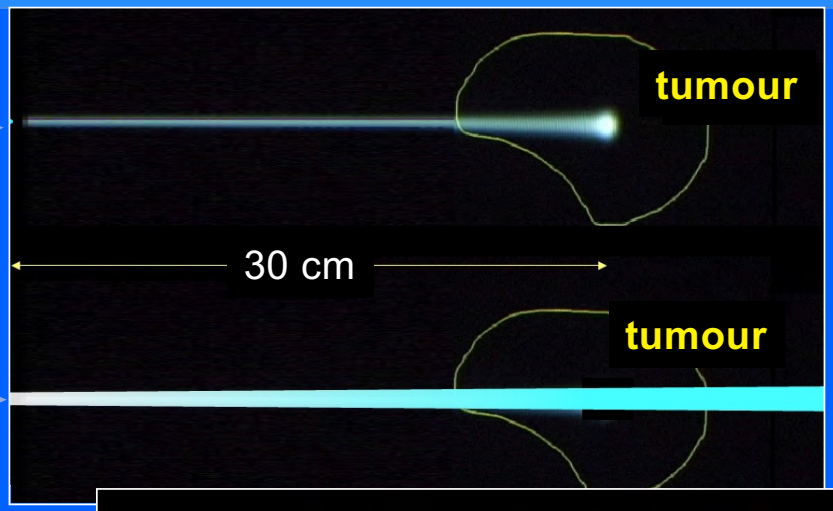


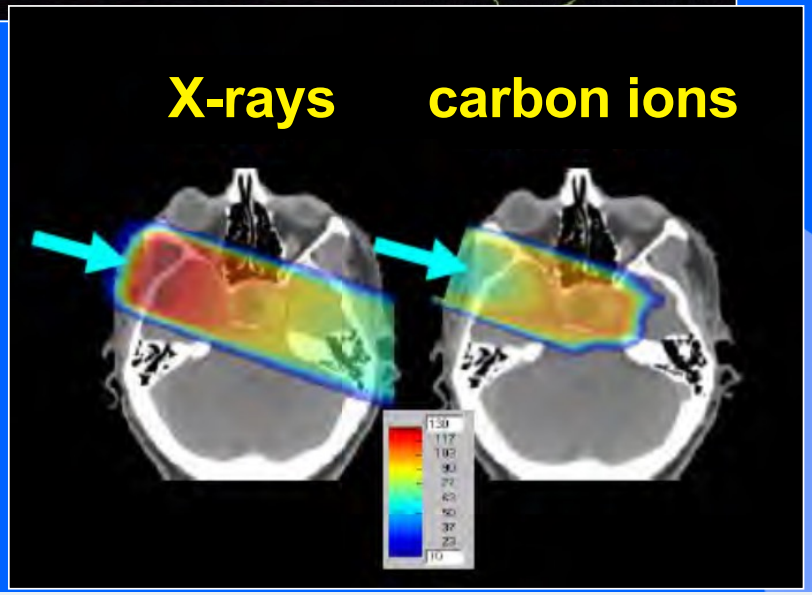
TERA

2. Carbon ions can cure also radioresistant tumours

carbon ions 5000 MeV

X-rays by
10 MeV electrons





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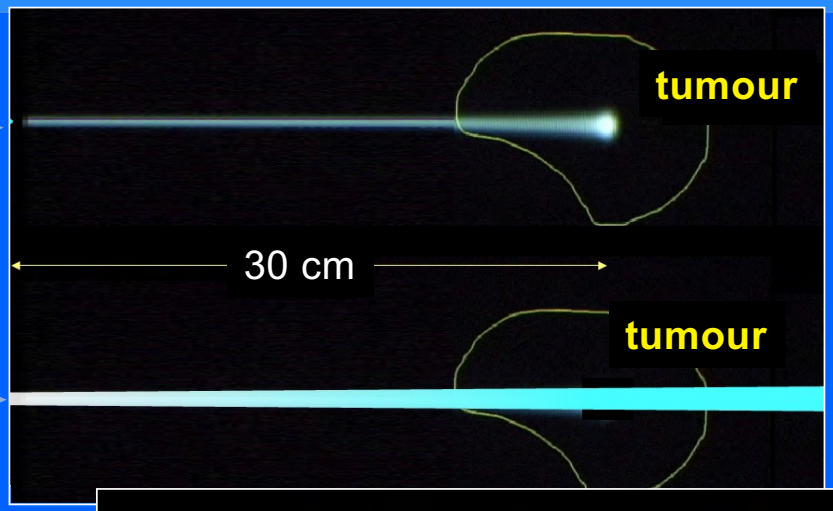

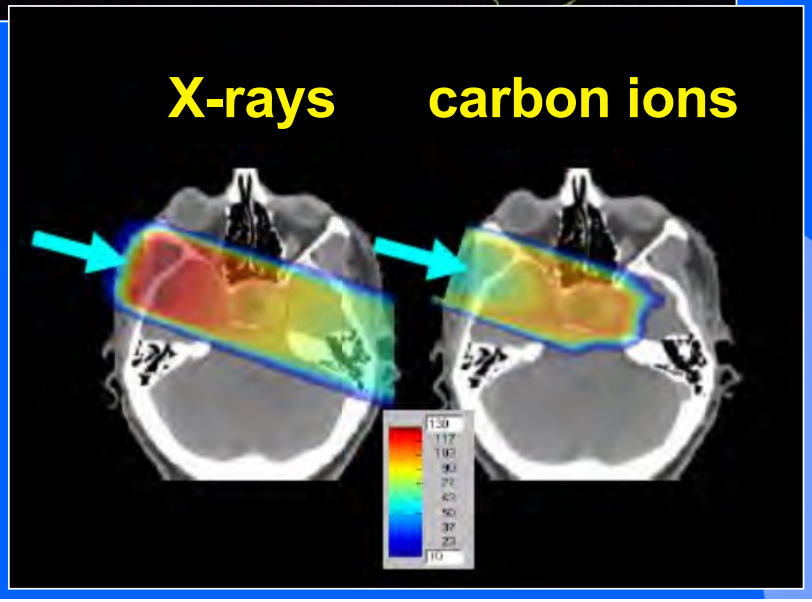

In each traversed cell a C-ion leaves 5000/250 = 25 more energy and strips 25 times more electrons from the molecules it passes through producing in the DNA **multiple double-strand-breaks that are not repaired**

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X-rays by
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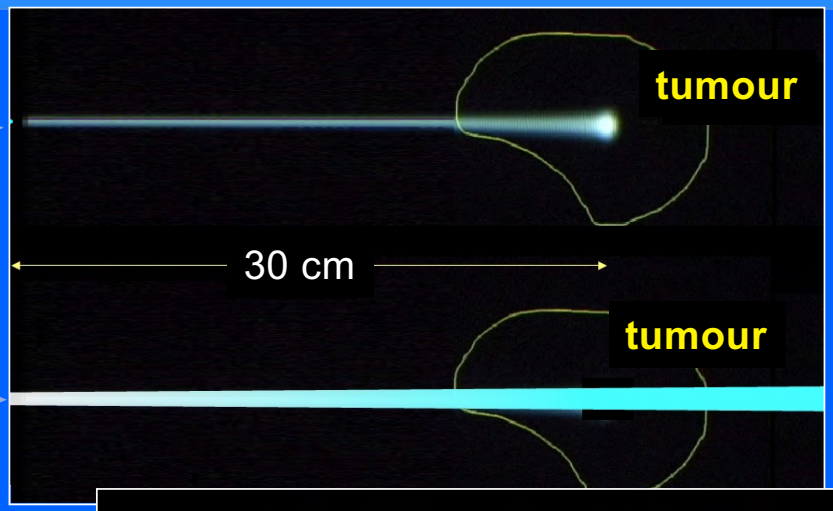
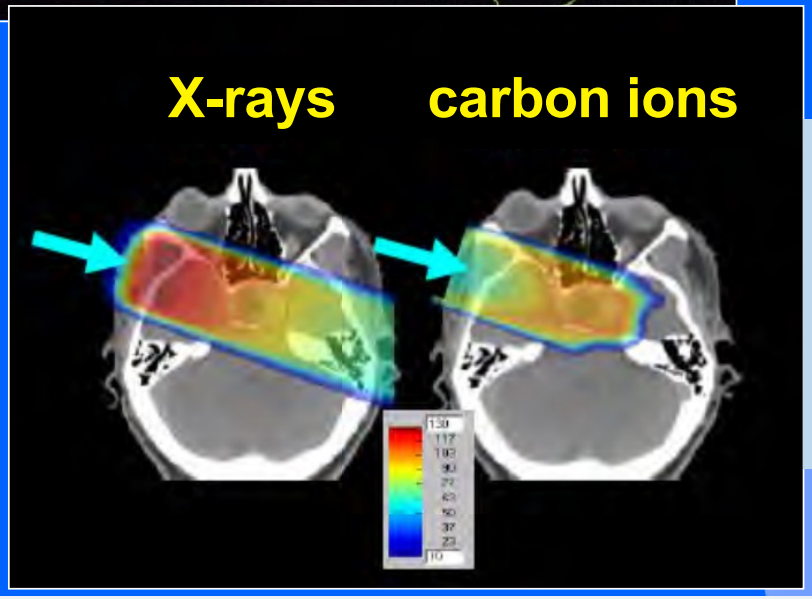


30 pts / 1 million



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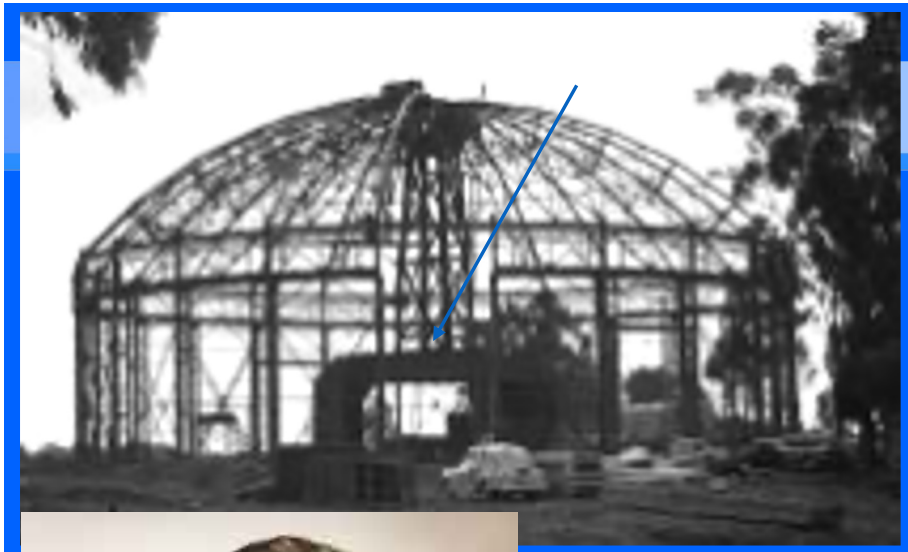
Thus
Carbon ions are a DIFFERENT type of radiation with respect to X-rays and protons

Major steps forward in proton therapy

The 184-inch cyclotron - 1946



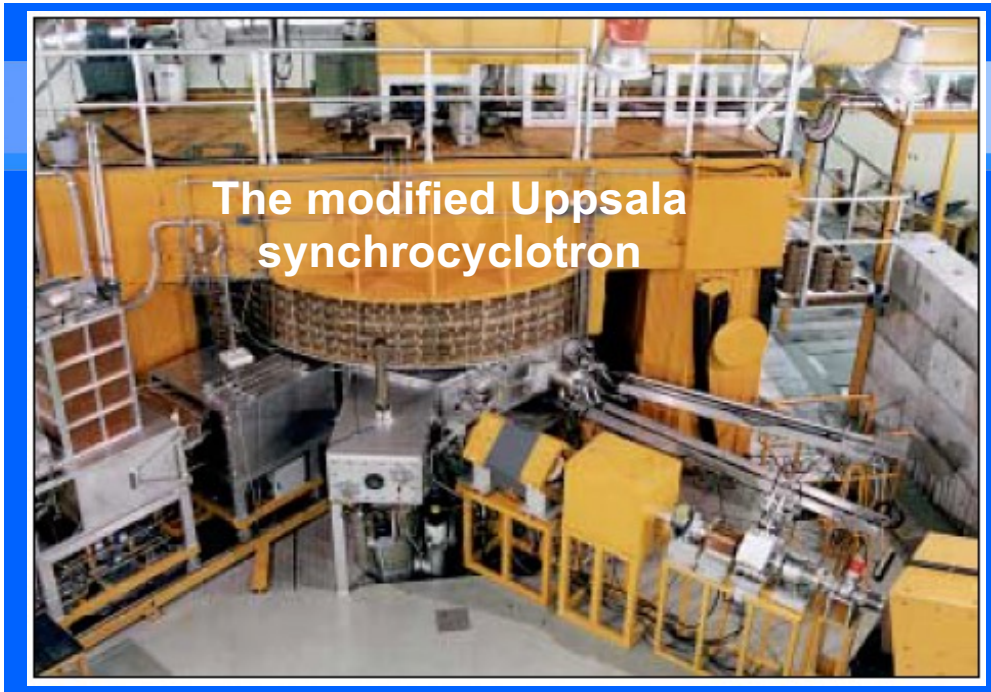
Cornelius Tobias
1918-2000

At the Berkeley Laboratory

70 years ago: First proton treatment of pituitary glands: 1954

Treatment of pituitary tumors: 1956

Uppsala - 1957

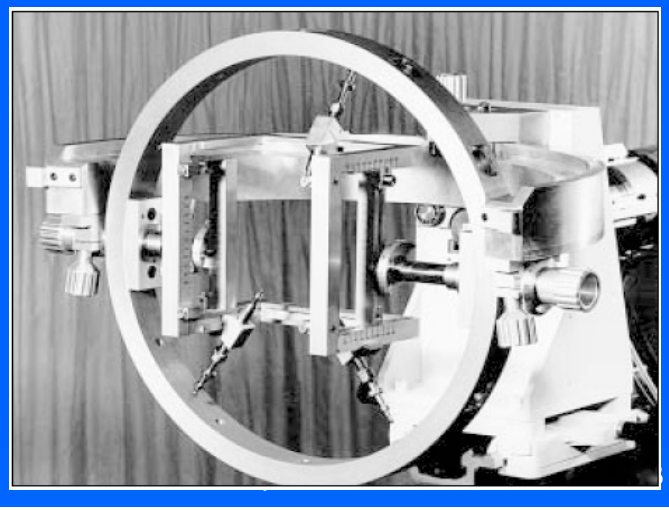


The modified Uppsala synchrocyclotron

(1931-1998)

Börje Larsson

Uppsala - Doctoral dissertation - 1962



Alignment system for the treatment of head tumours with 185 MeV protons

TERA

The Harvard cyclotron in 1949

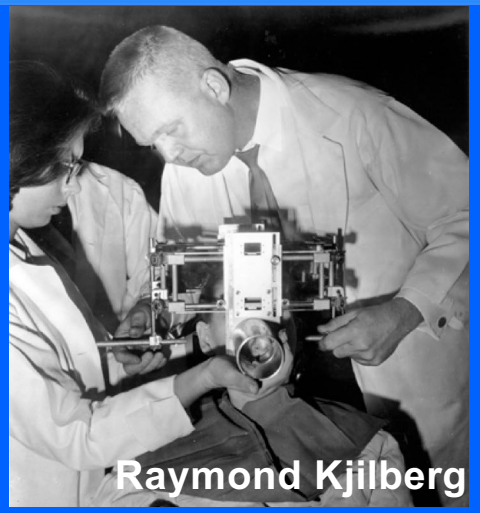
(L) Dr. Lee Davenport (R) Dr. Norman Ramsey
June 10 1949

The three programs at the Harvard cyclotron

Neurosurgery for intercranial lesions (AVMs)
(3,687 patients)
Neurosurgery Dept. of MGH
Raymond N. Kjilberg, Bernard Kliman

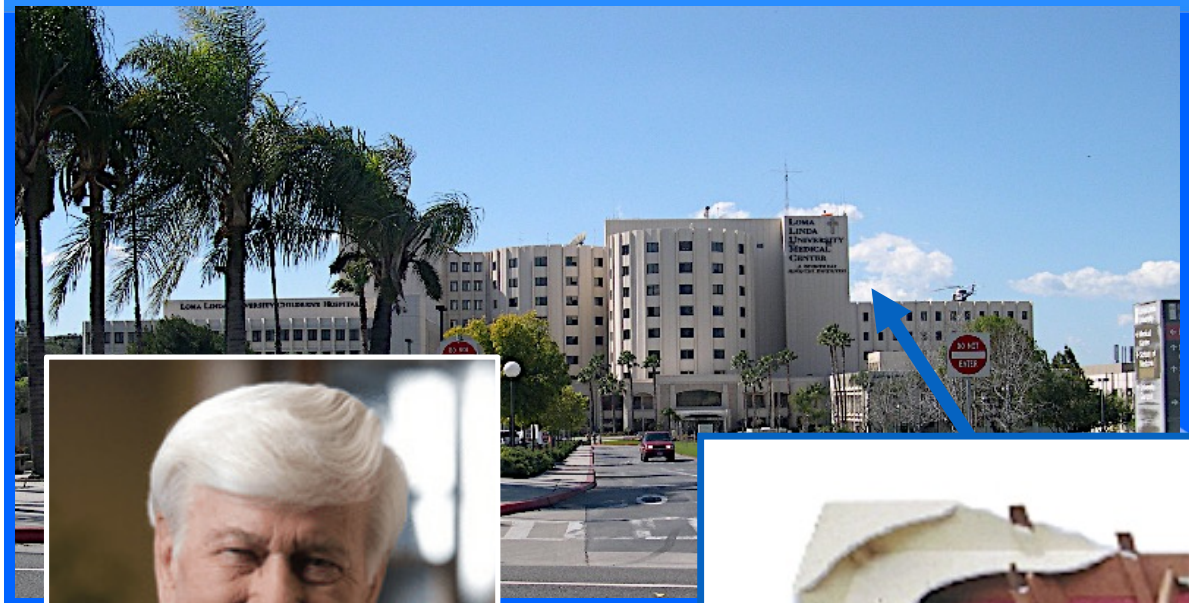
Eye tumors
(2,979 patients)
Massachusetts Eye and Ear Hospital.
Ian Constable, Evangelos Gragoudas

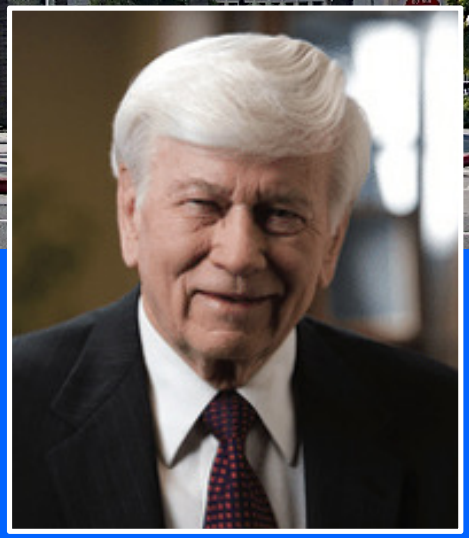
Large tumors
(2,449 patients)
Radiation Medicine Dept of MGH
Herman Suit, Michael Goitein,Joel Tepper, Lynn Verhey


Raymond Kjilberg


Michael Goitein Herman Suit

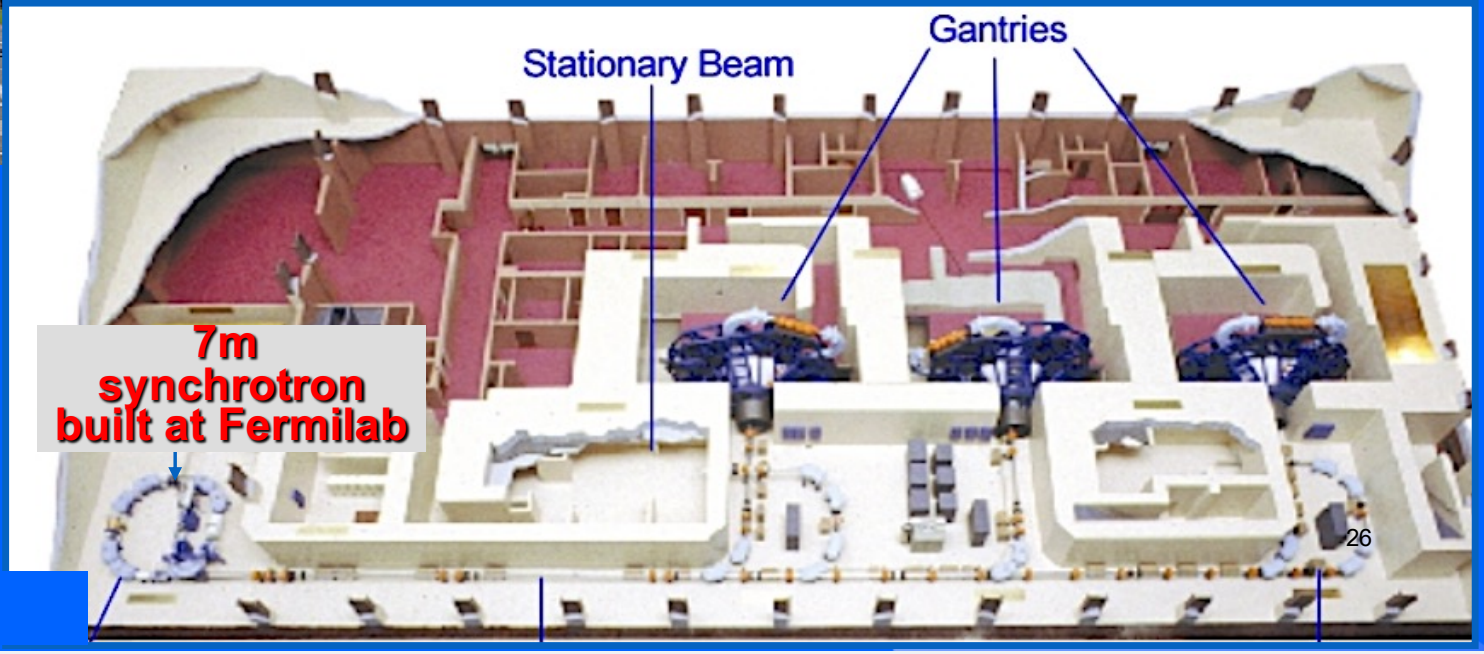
First hospital centre: Loma Linda University Medical Centre





Dr. James M. Slater MD

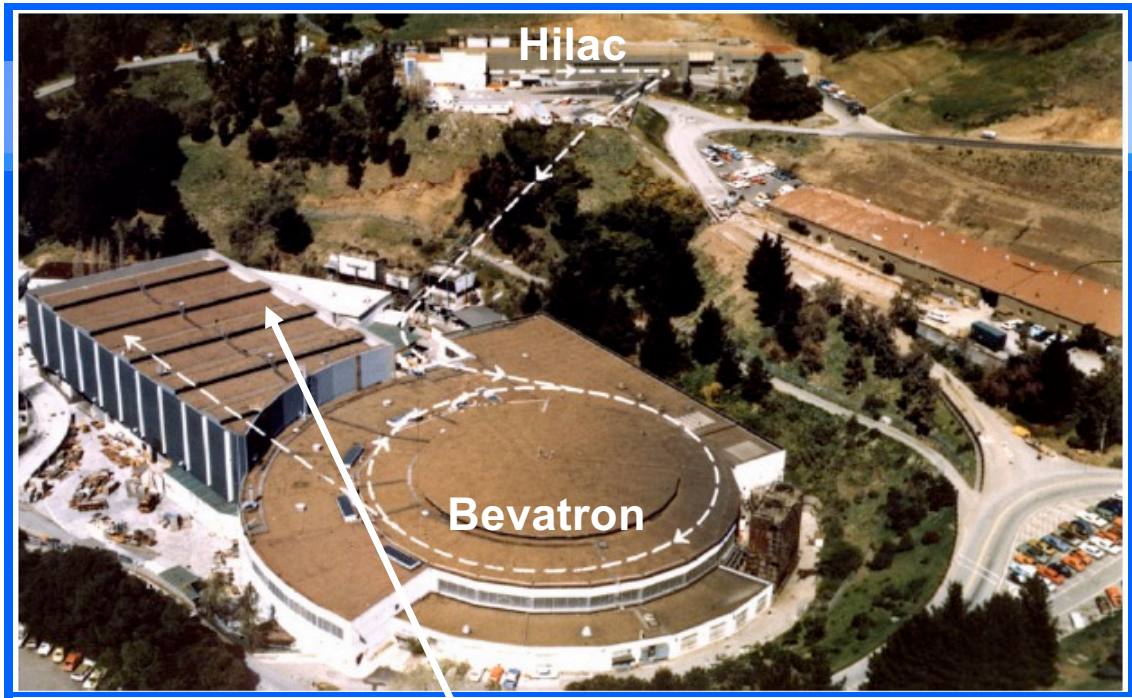
First proton patient: 1990

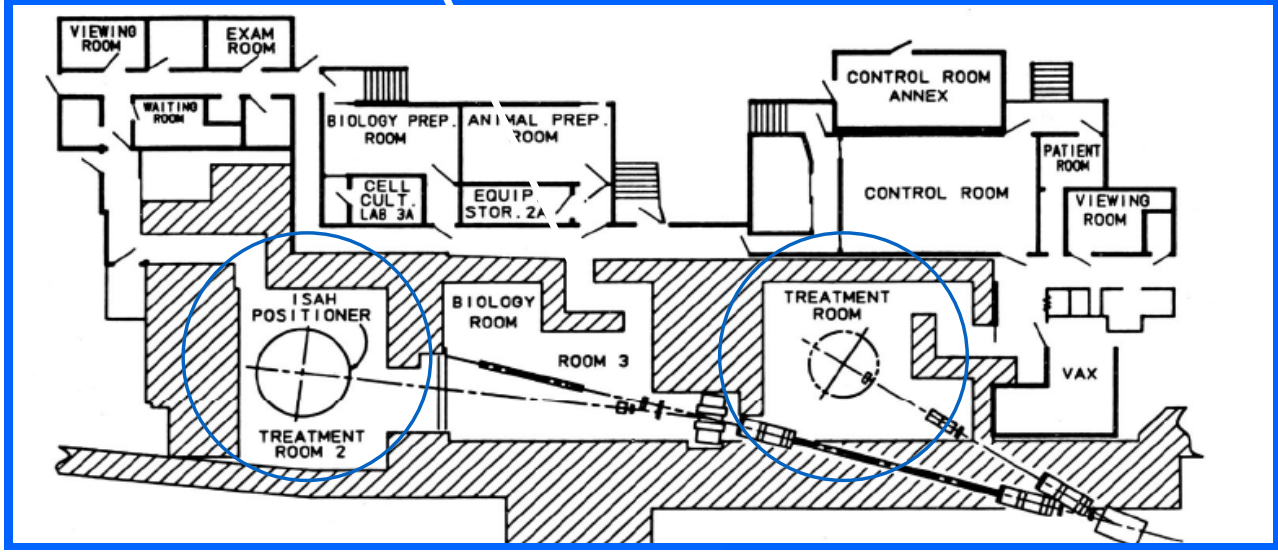


3-rooms facilities by IBA (Belgium) - market leader

Major steps in carbon ion therapy

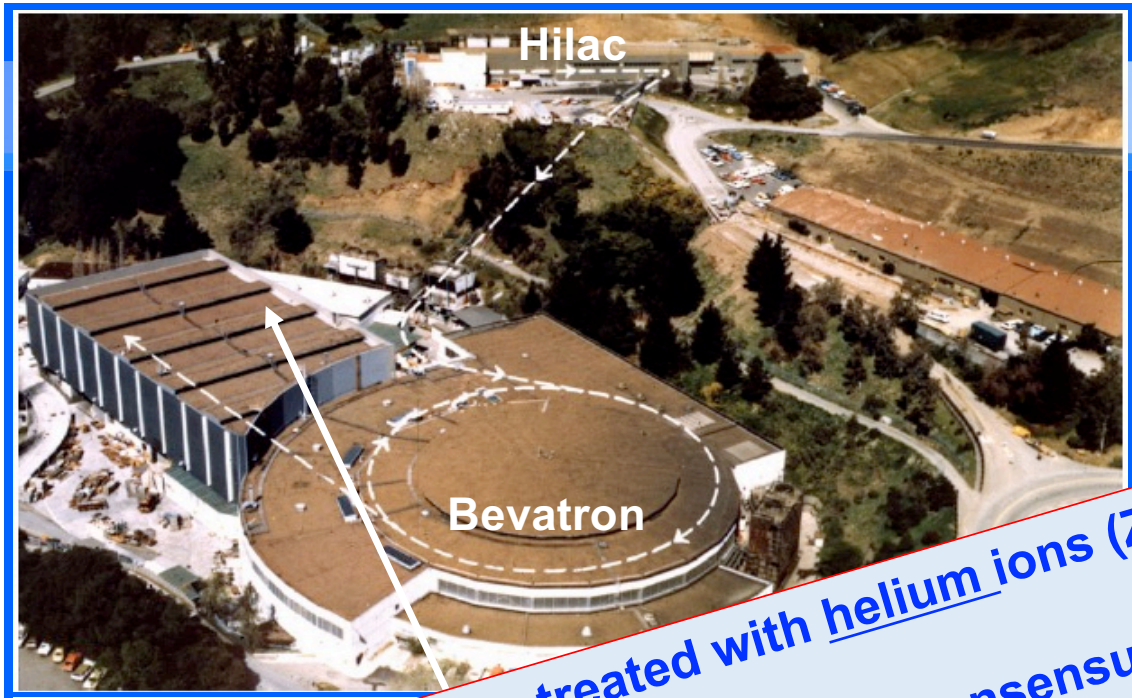
Berkeley Bevalac: 1975-92





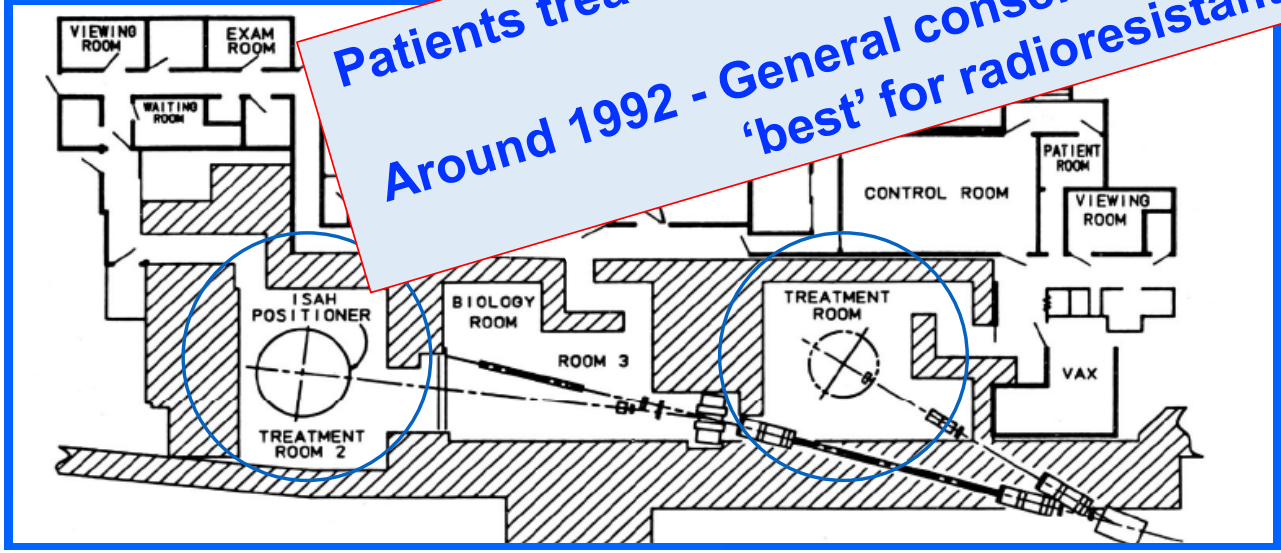
The linac HILAC injects ions in the Bevatron, which produces high-current beams of all ions

Berkeley Bevalac: 1975-92



Patients treated with helium ions (Z = 2) and neon ions (Z = 10)

Around 1992 - General consensus: carbon ions (Z = 6) are the 'best' for radioresistant tunours

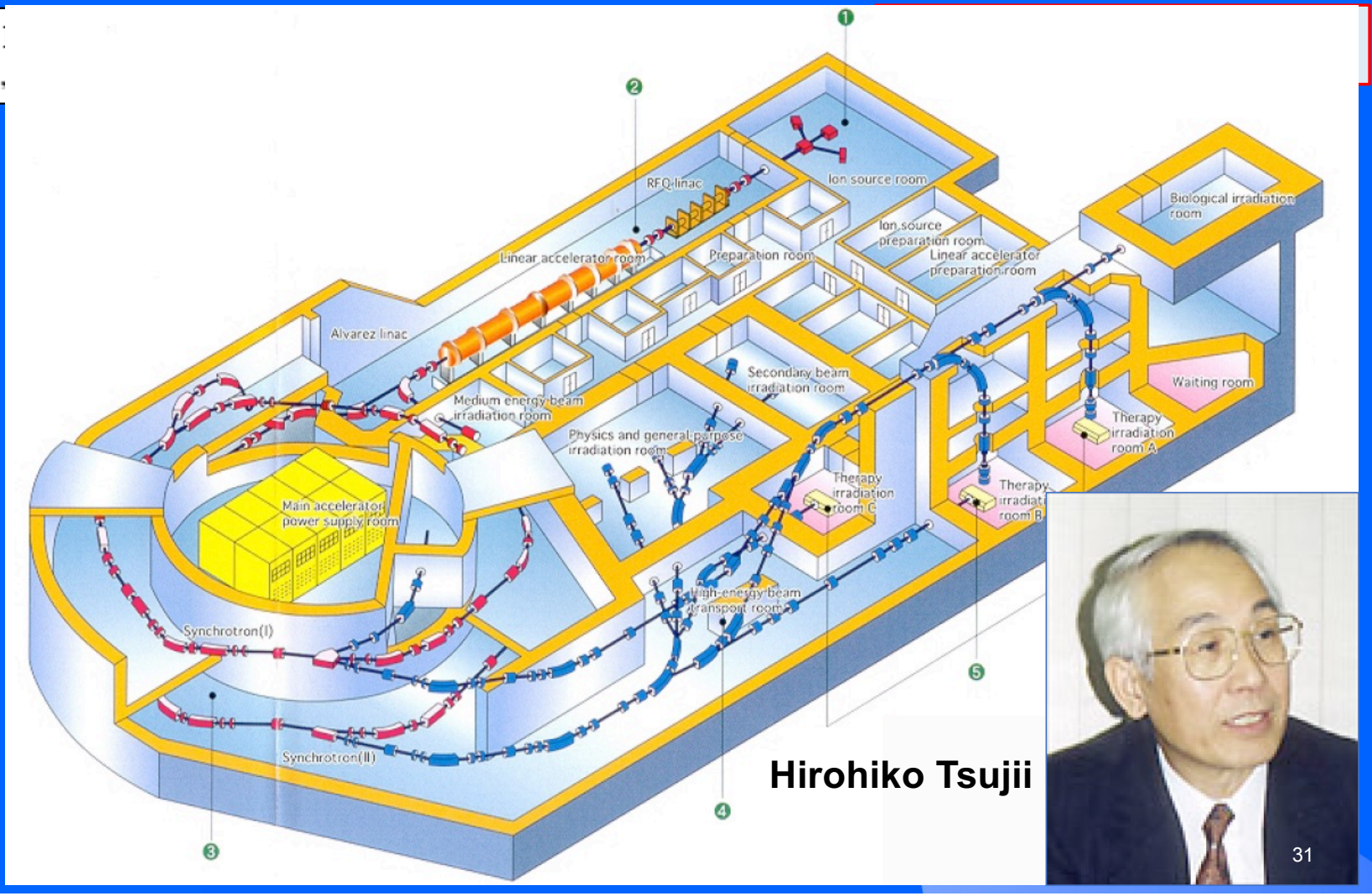


ions in the
oduces high-
beams of all ions

Heavy Ion Medical Accelerator in Chiba – 1994: 1° pt

[15] Hirao, Y. et al, "Heavy
Japan" Nucl. Phys. A538,

Yasuo Hirao



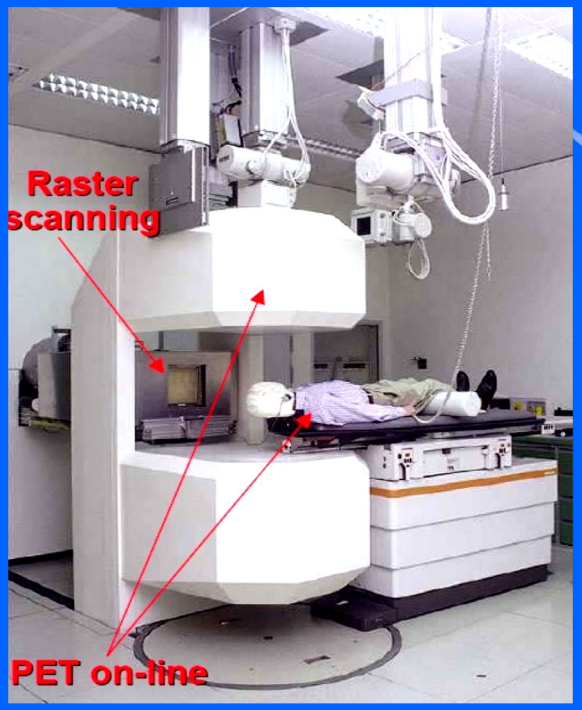
Hirohiko Tsujii

The GSI carbon ion pilot project: 1997-2008

J. Debus

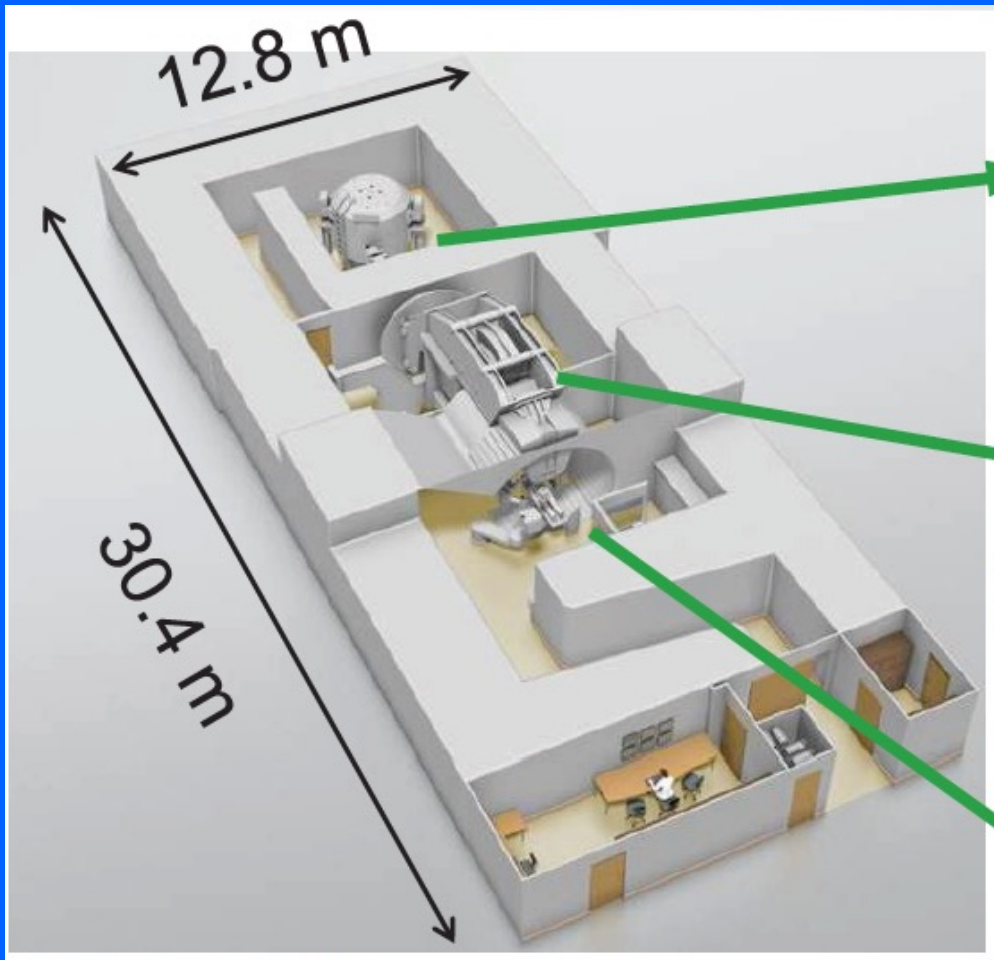
Gerhard Kraft

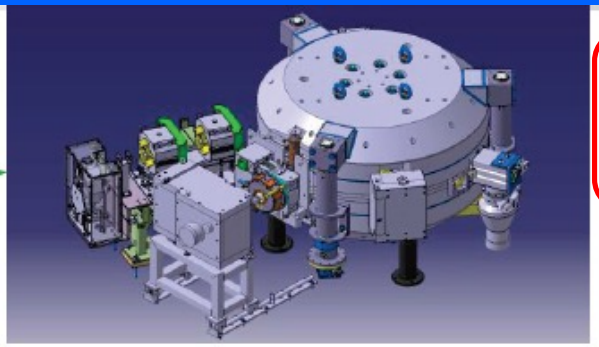
450 patients treated with carbon ions



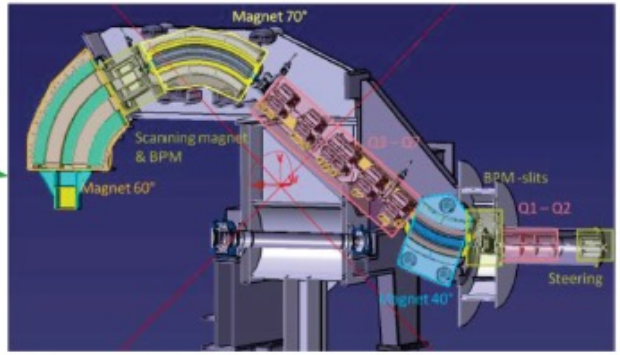
Proton single-room facilities

IBA single room facility: Proteus One





Synchrocyclotron with superconducting coil: S2C2

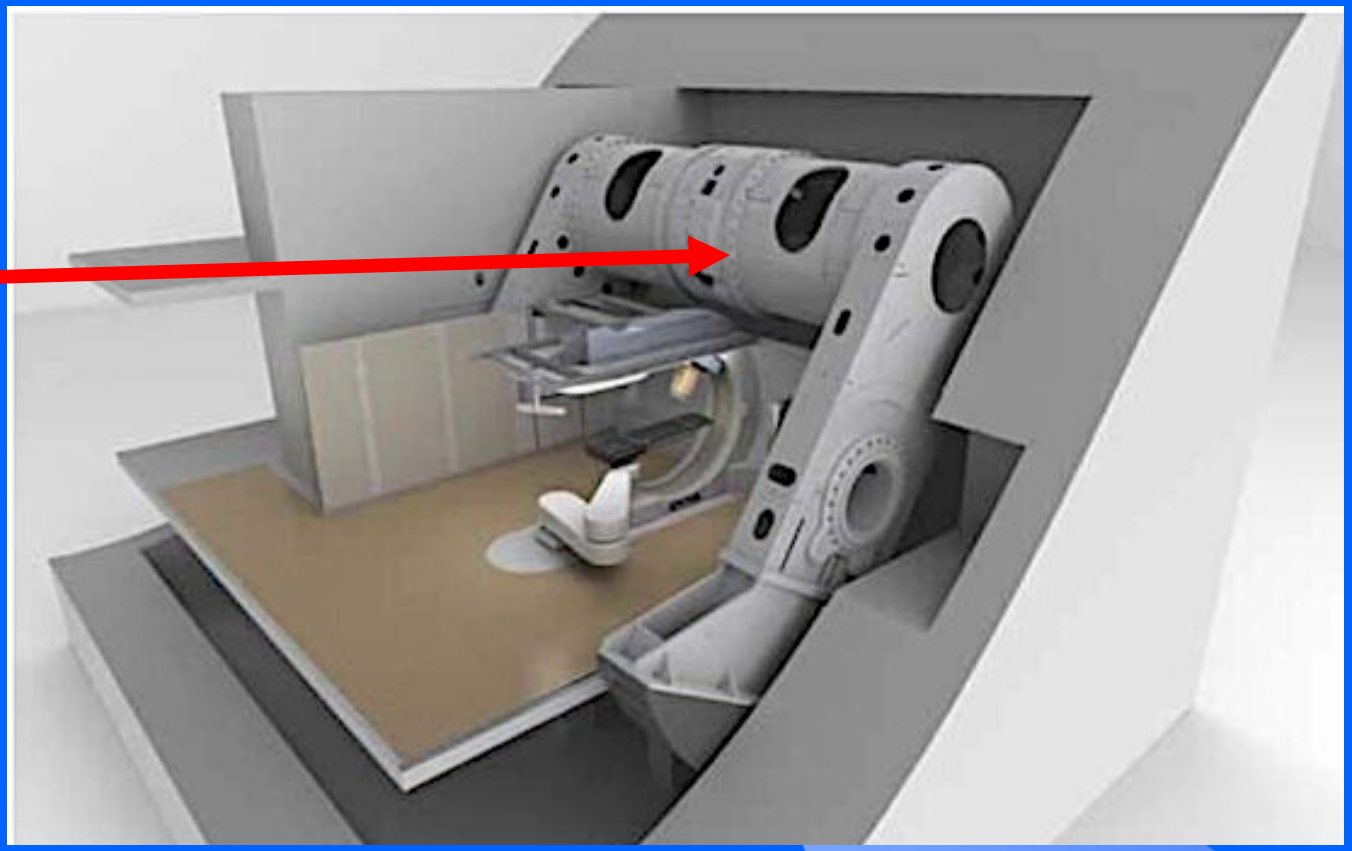


New Compact Gantry for pencil beam scanning

Patient treatment room

MeVion single-room facility

Very high field: 7 tesla

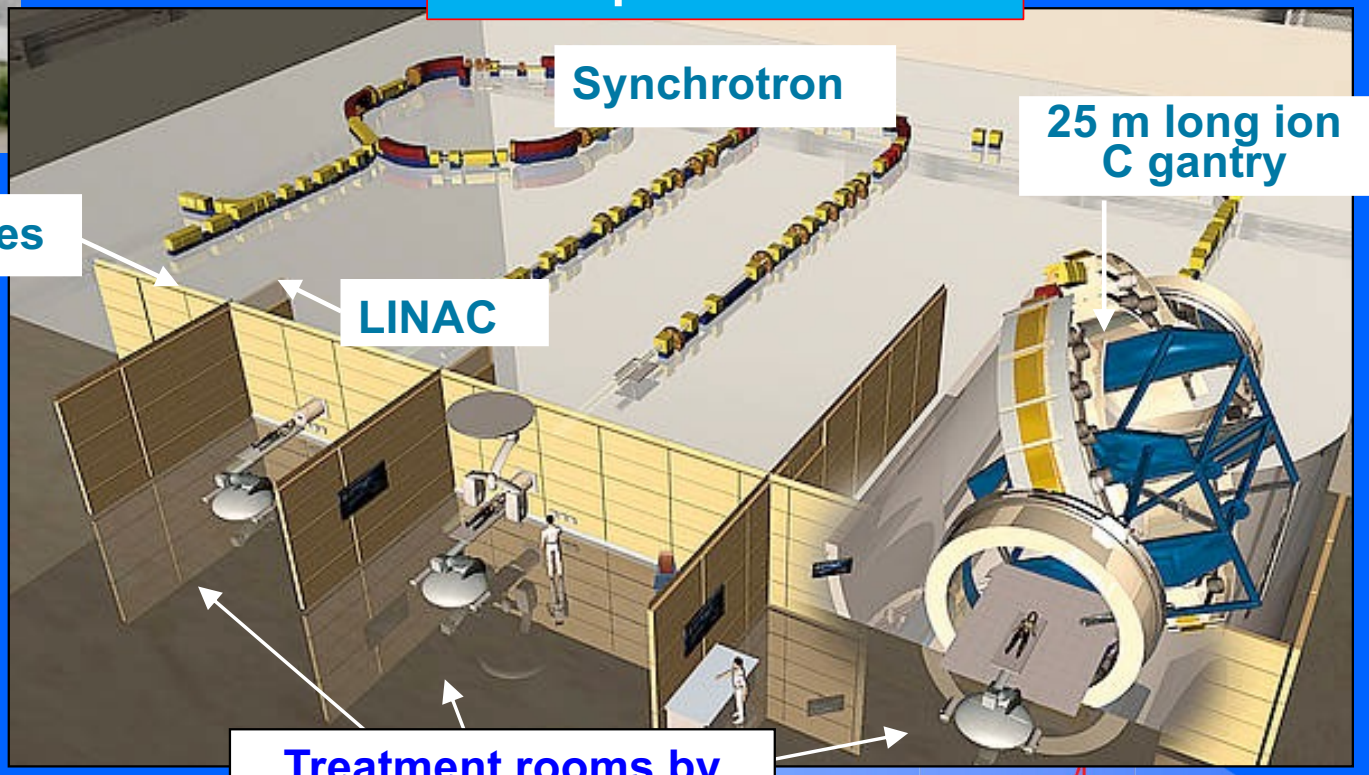


From 1995-: development of carbon ion therapy

Development of the pilot project: HIT

Beginning of the construction: 2004

First patient in 2009

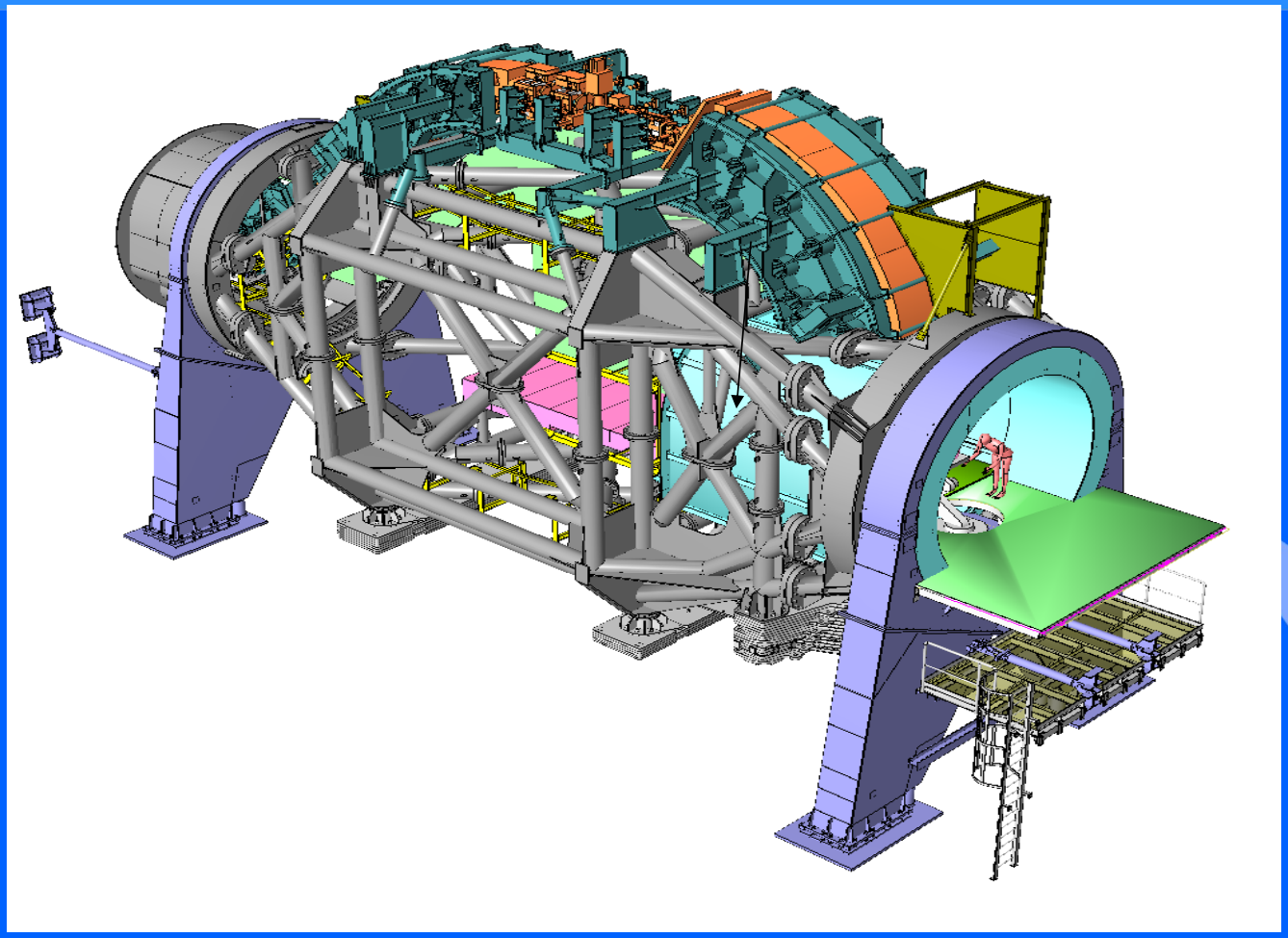


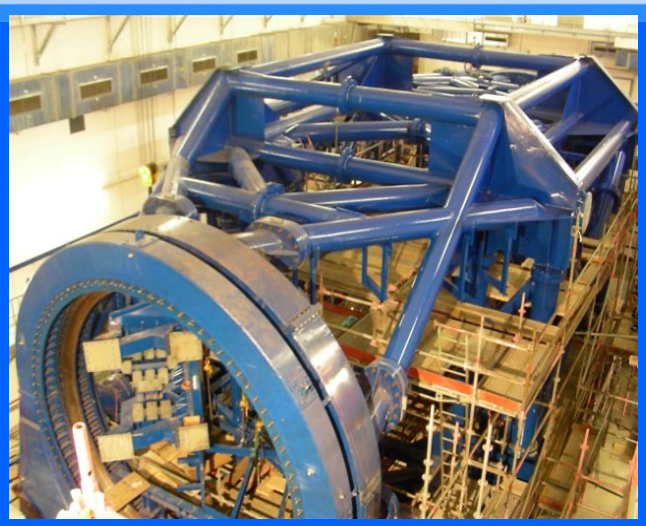
Project by GSI – Darmstadt

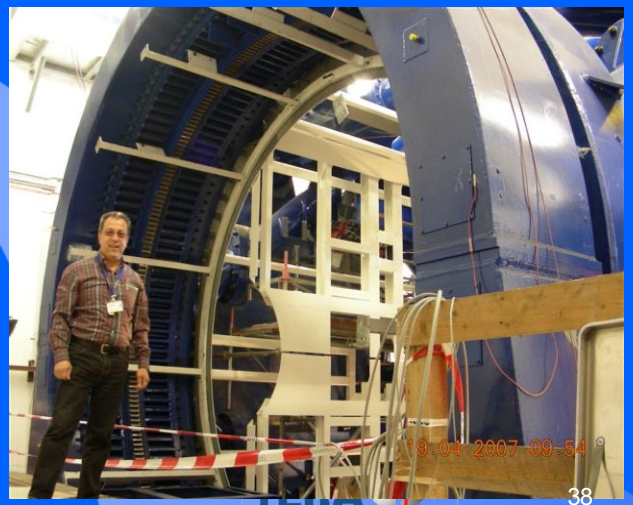
Technical Director
Thomas Haberer

Medical Directoir
Jurgen Debus

HIT: first carbon ion gantry: 25 m, 600 tons and 400 kW







In 1995 U.A. and M. Regler convinced CERN to start PIMMS

M. Regler

Proton Ion Medical Machine Study

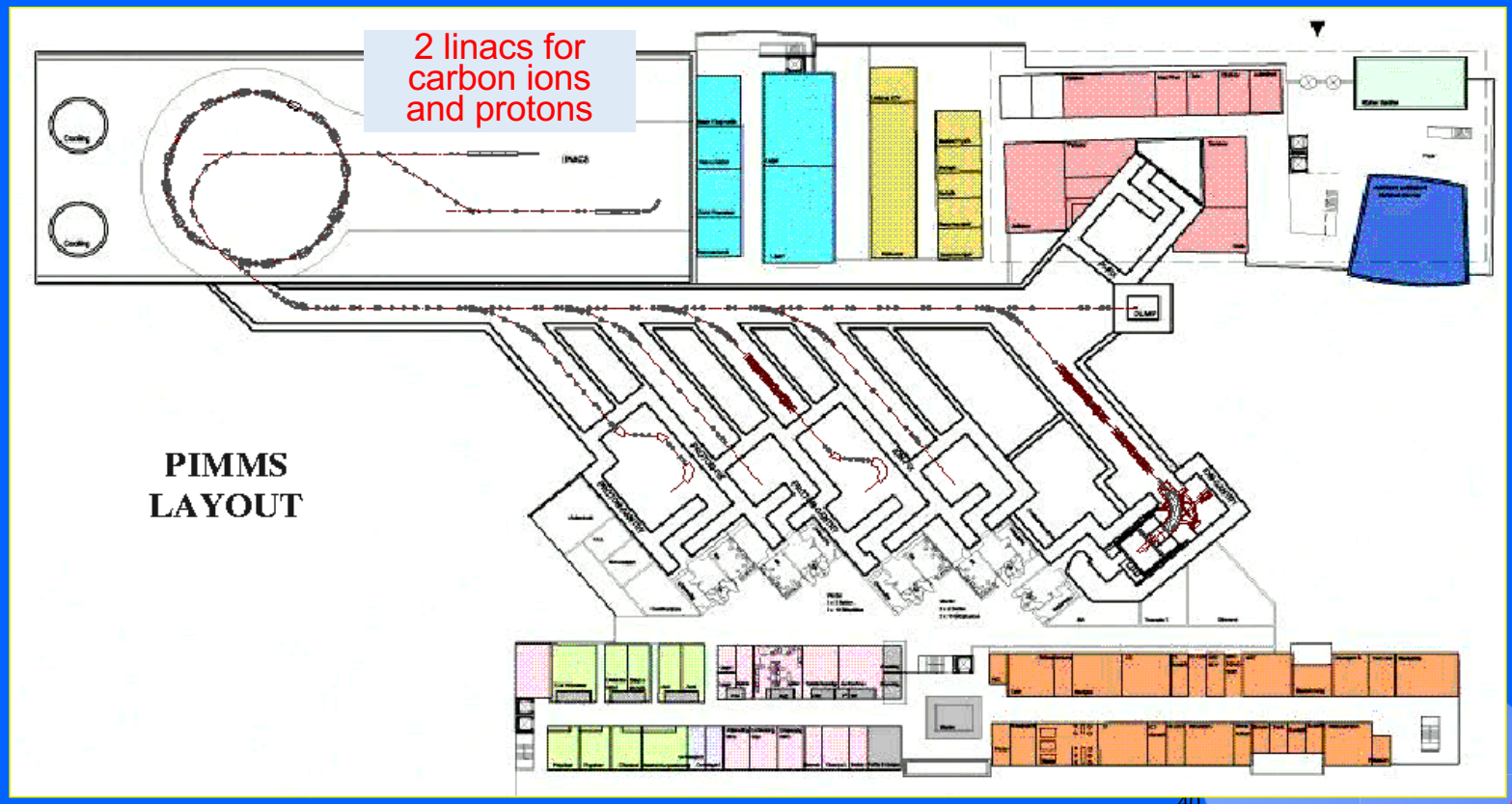
Optimized synchrotron for therapy
Project Leader: Phil Bryant
Chair of PAC: Giorgio Brianti
1996-2000

The design was conceived as a ”toolkit”
from which to take the parts of interest
for building a particular centre

In 1995 U.A. and M. Regler convinced CERN to start PIMMS

Contributors: CERN

TERA Foundation (25 man years); MedAustron Project (10 man years)

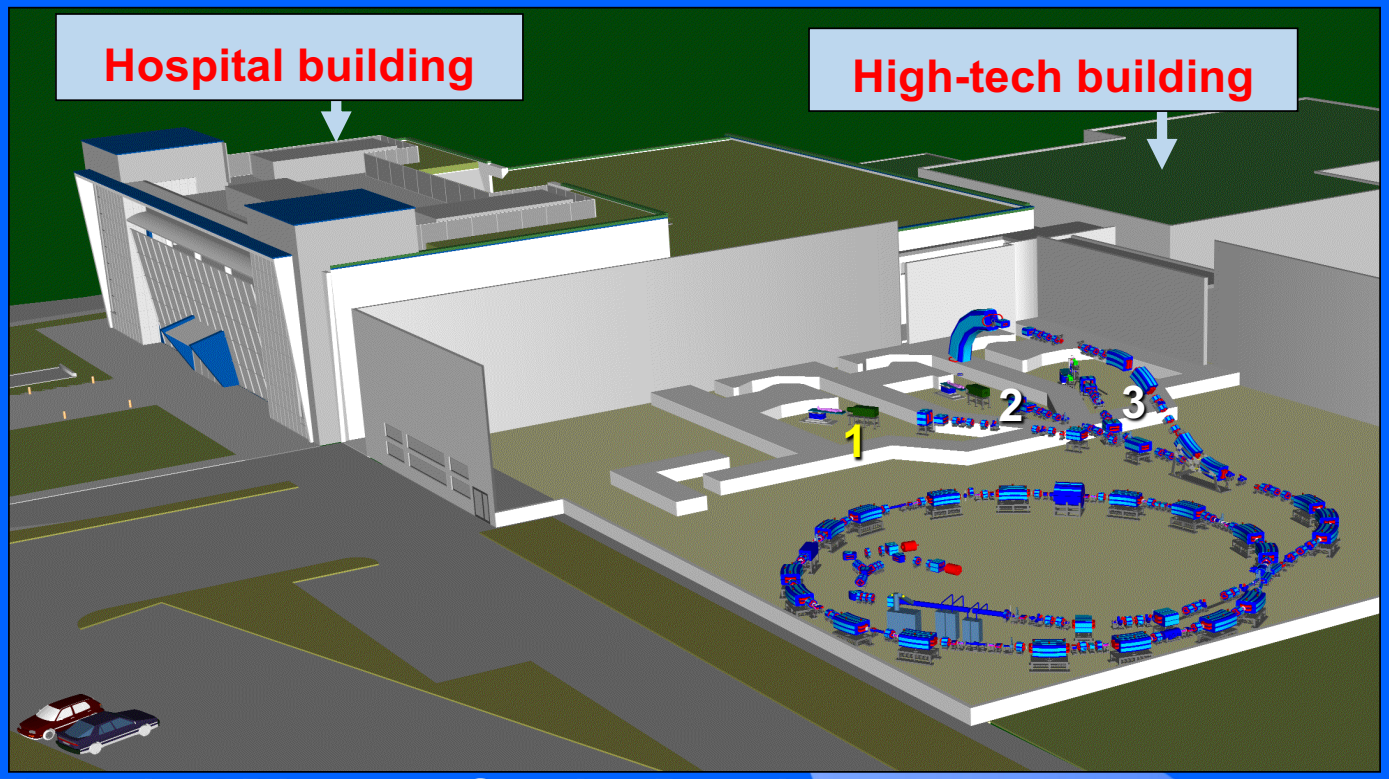


CNAO has been designed by TERA Foundation

In 2003 TERA passed to CNAO 25 people and 2000 pages

Beginning of the construction: 2005

First patient in 2011



Technical Director: Sandro Rossi

Medical Director. Roberto Orecchia

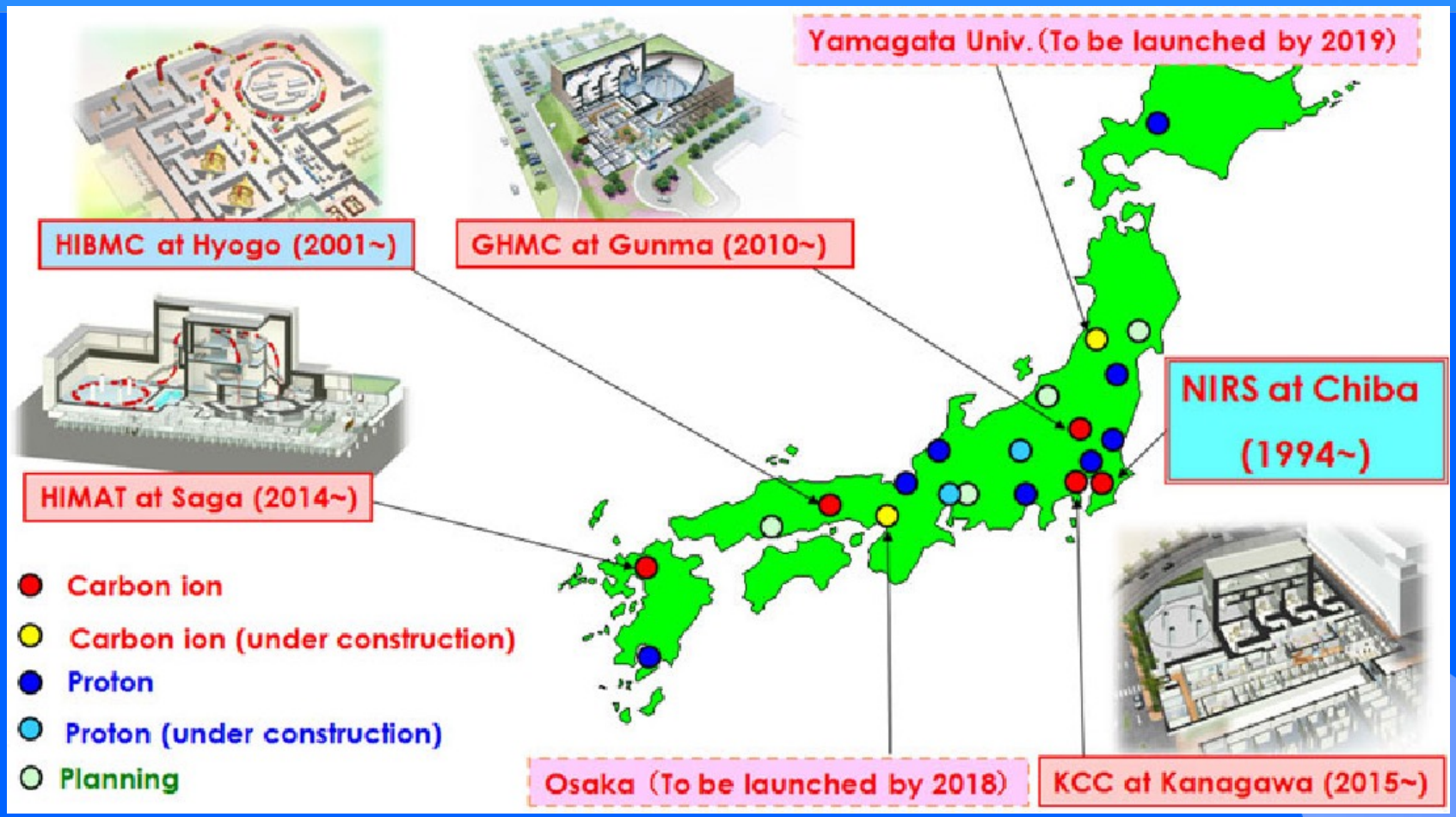
INFN: CONTRIBUTED TO THE CONSTRUCTION

The layout of MedAustron

Beginning of the construction: 2009

First patient in 2016

In 2015 the japanese network was already impressive



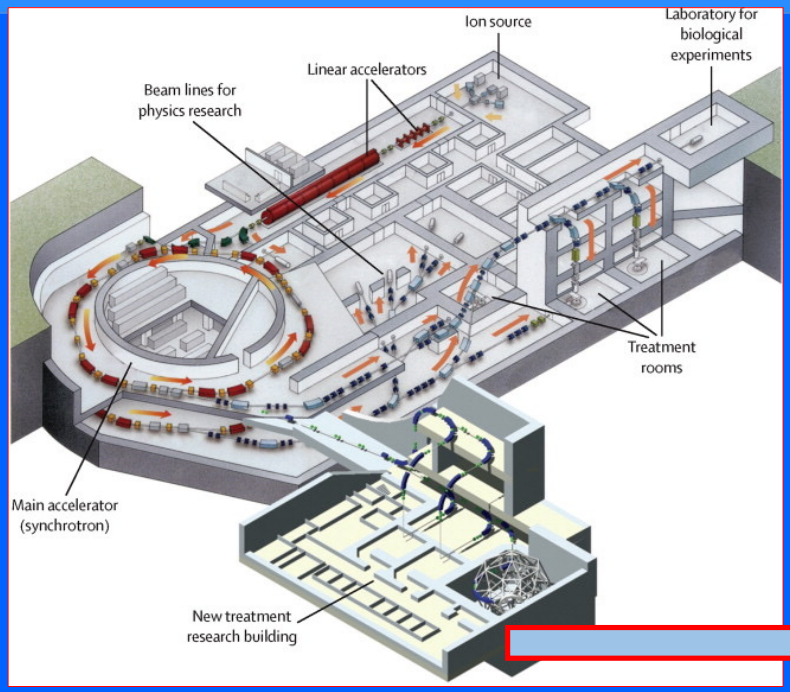
ON THE MAP
built or construction

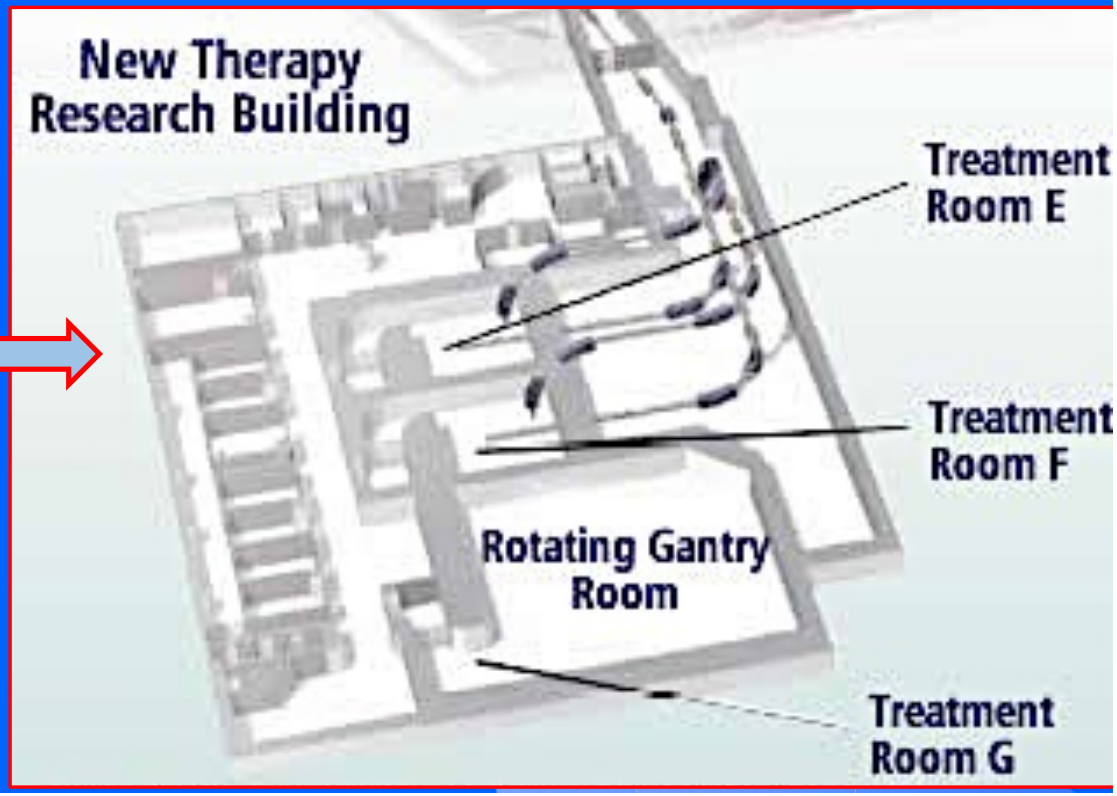
8 proton centres

11 carbon centres

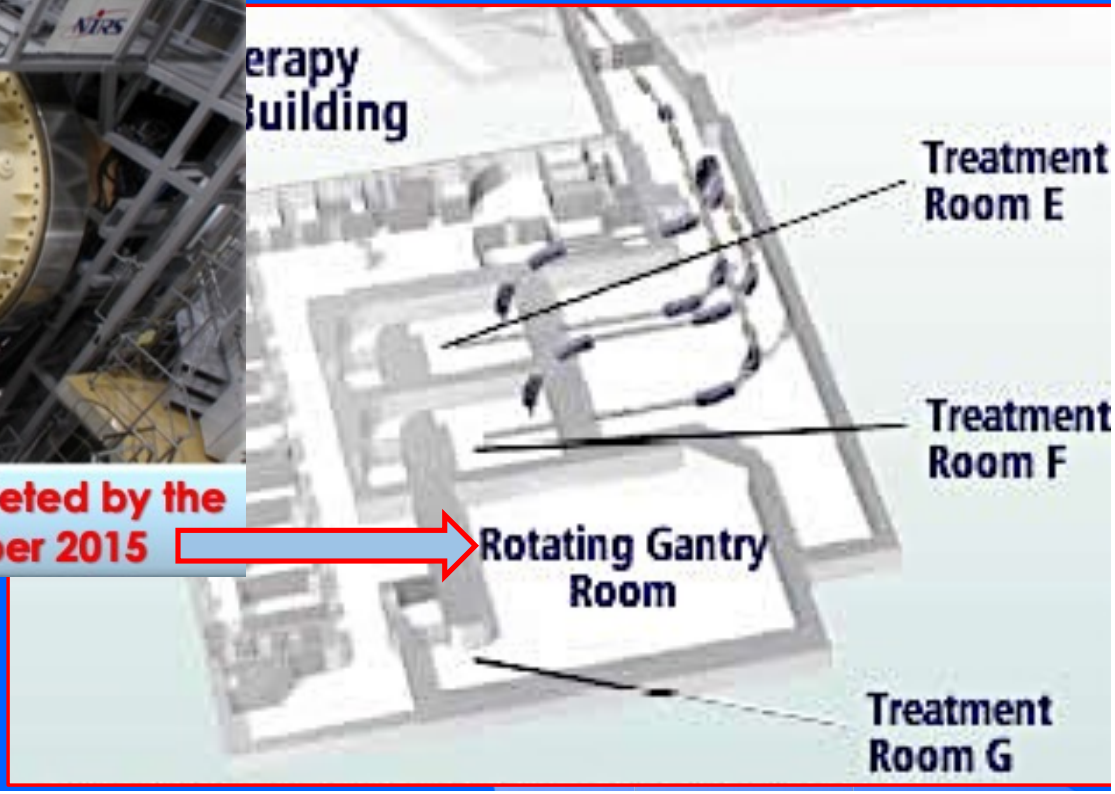
Upgrades of carbon ion Centres

HIMAC upgrades

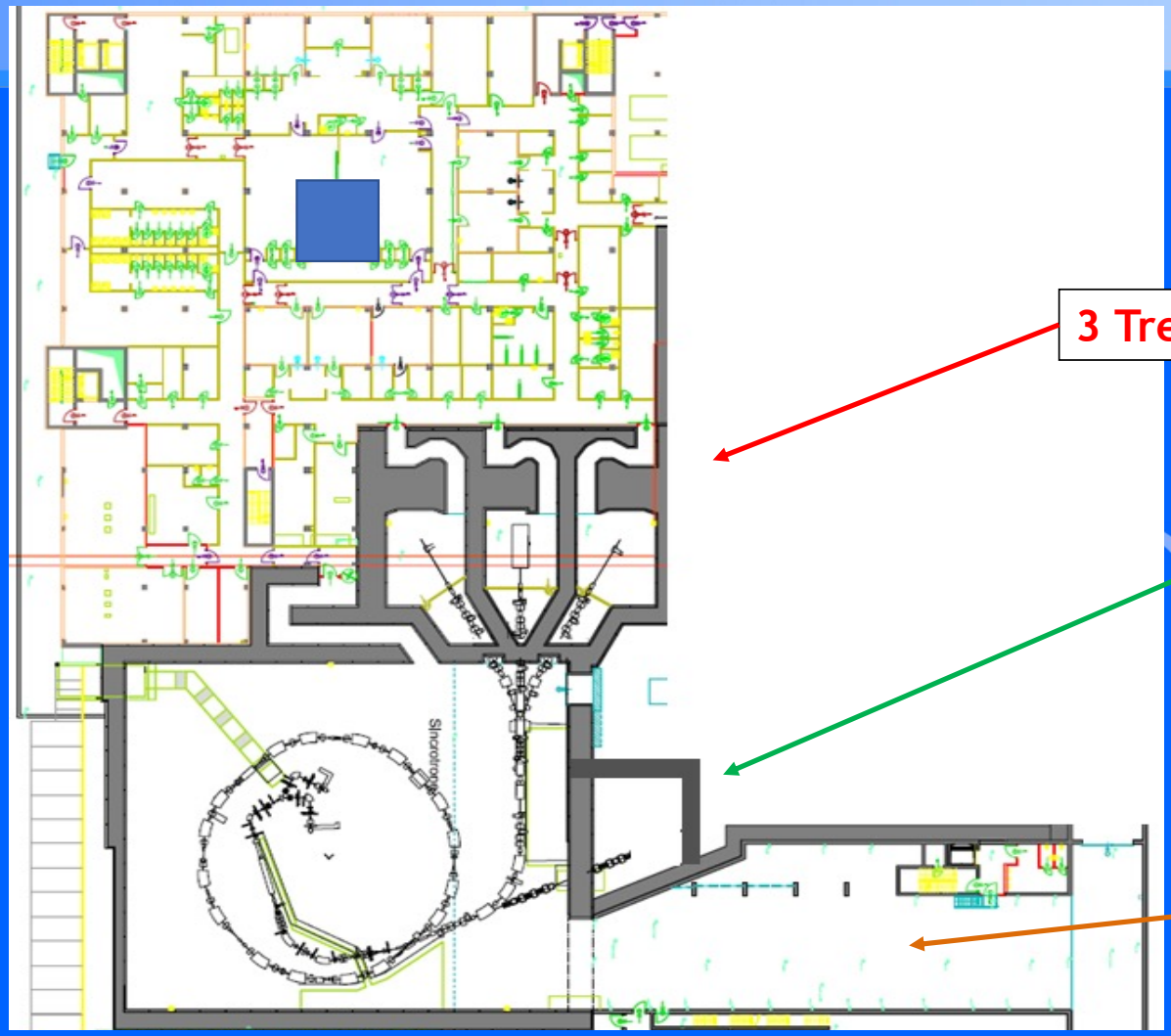




HIMAC upgrades



CNAO upgrades

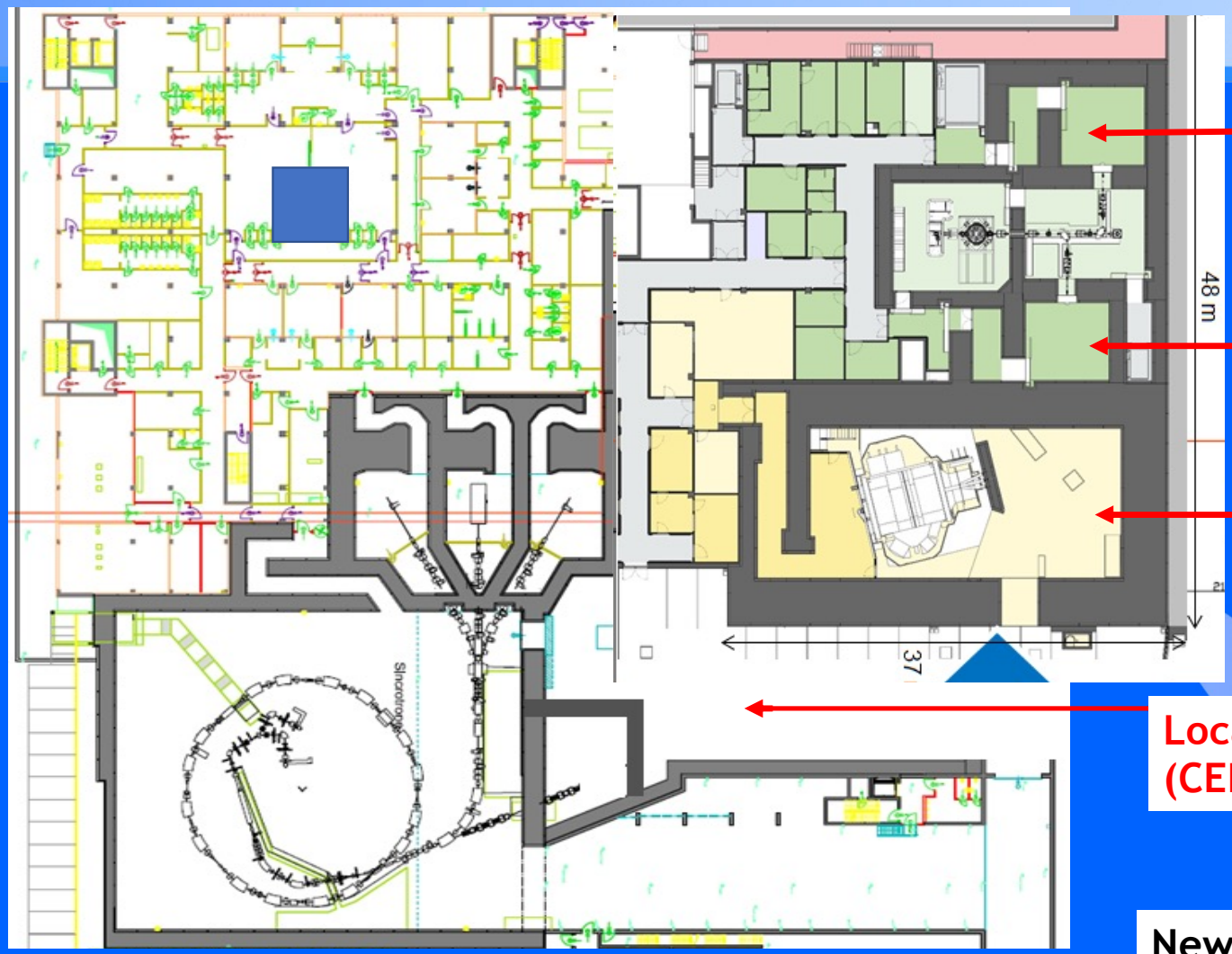


3 Treatment rooms: 3H + 1V

Experimental room

Main power supply room

CNAO upgrades



Research BNCT - 2025

Clinical BNCT

Protontherapy
with Hitachi gantry - 2025

Location of the C-ion SC gantry
(CERN-CNAO-INFN-MedAustron)

New block footprint ~1800 m²

CNAO upgrades

CNAO WILL BECOME
THE BEST EQUIPPED HADRON THERAPY CENTRE
IN THE WORLD

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CNAO @ PAVIA
THE END