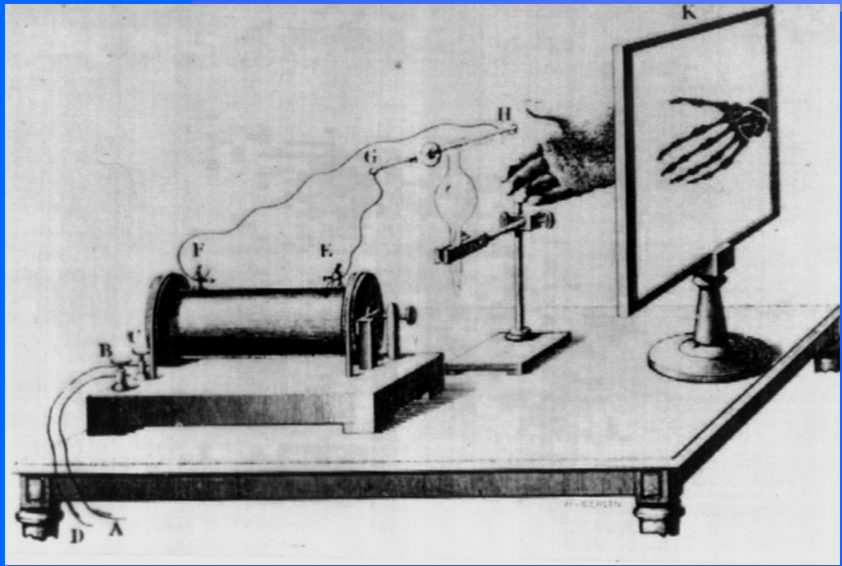
FROM THE DISCOVERY OF X RAYS TO CT/PET DIAGNOSTICS AND CONFORMAL RADIATION THERAPY

Ugo Amaldi

University of Milano Bicocca and TERA Foundation

The beginnings of modern physics and of medical physics



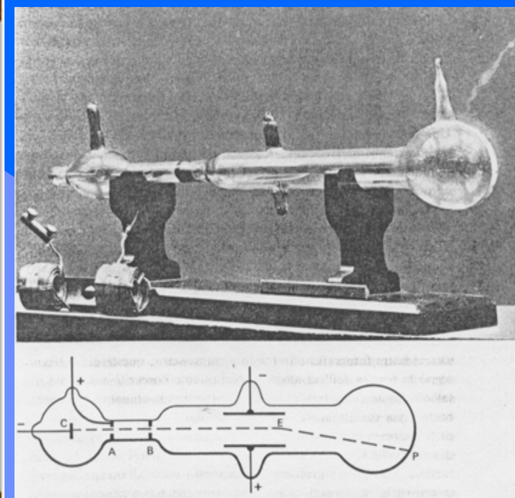
1895
discovery of X rays

Wilhelm Conrad Röntgen

J.J. Thompson

1897

"discovery" of the electron

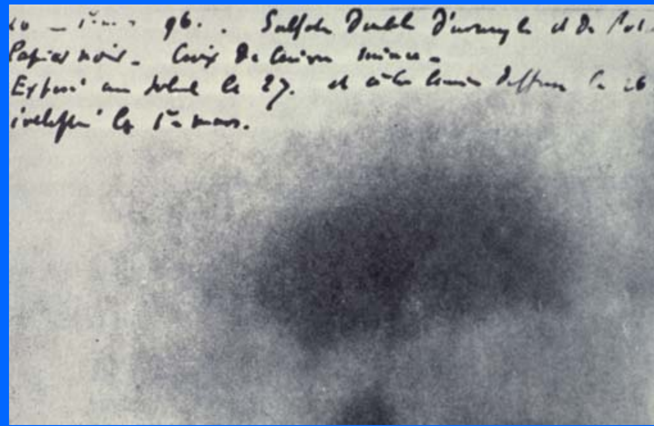


The beginnings of modern physics and of medical physics

Henri Becquerel
(1852-1908)

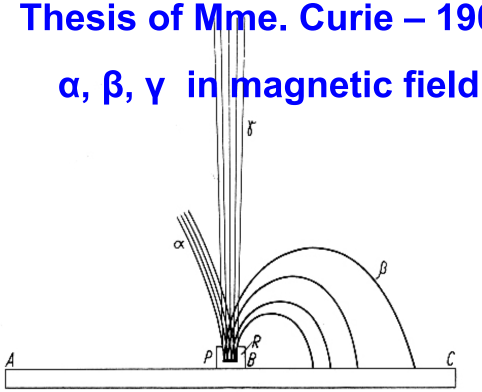
1896:

Discovery of natural radioactivity



Thesis of Mme. Curie – 1904

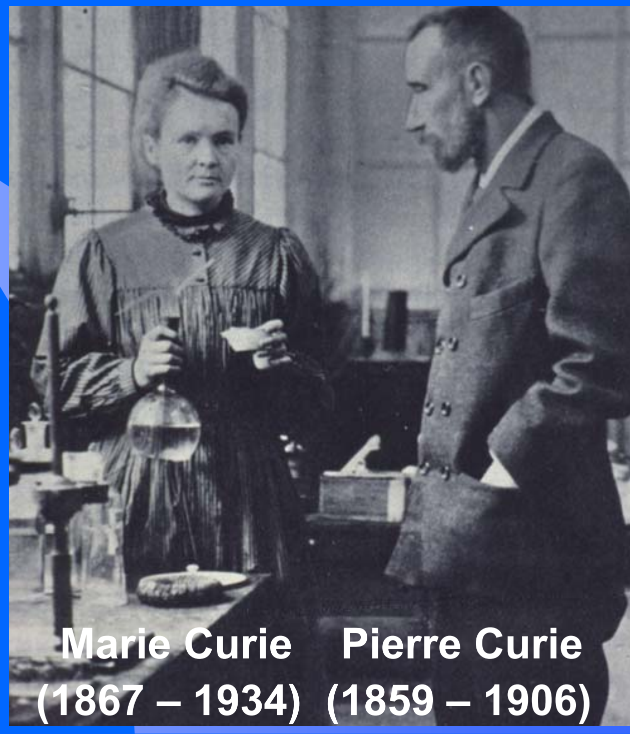
α, β, γ in magnetic field



Hundred years ago

1898

Discovery of radium

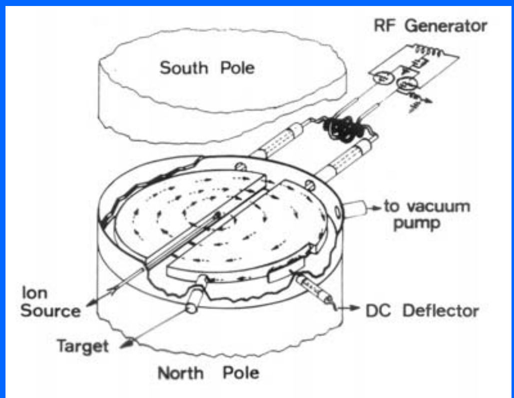


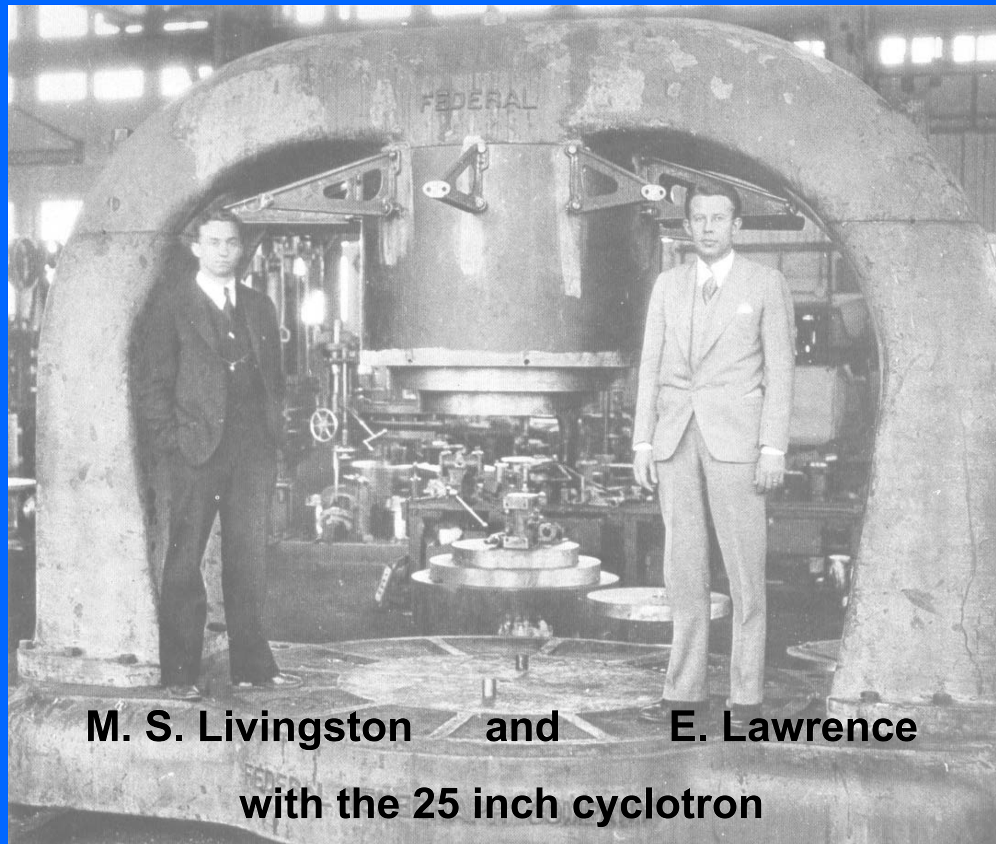
Marie Curie (1867 – 1934) Pierre Curie (1859 – 1906)

The next magnificent four years for experimental physics and medical physics

1930

Ernest Lawrence invents the cyclotron





M. S. Livingston and E. Lawrence

with the 25 inch cyclotron

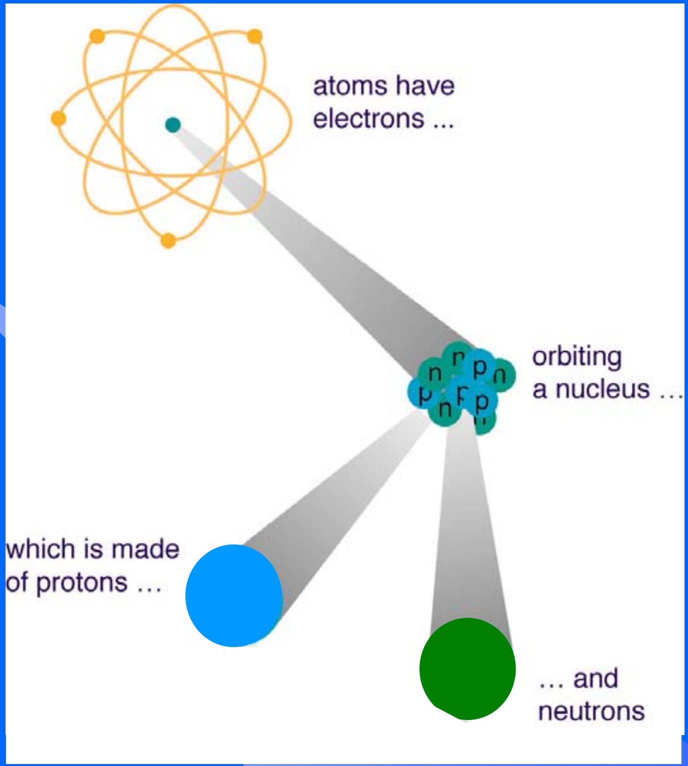
The next magnificent four years for experimental physics and medical physics

James Chadwick

(1891 – 1974)

1932

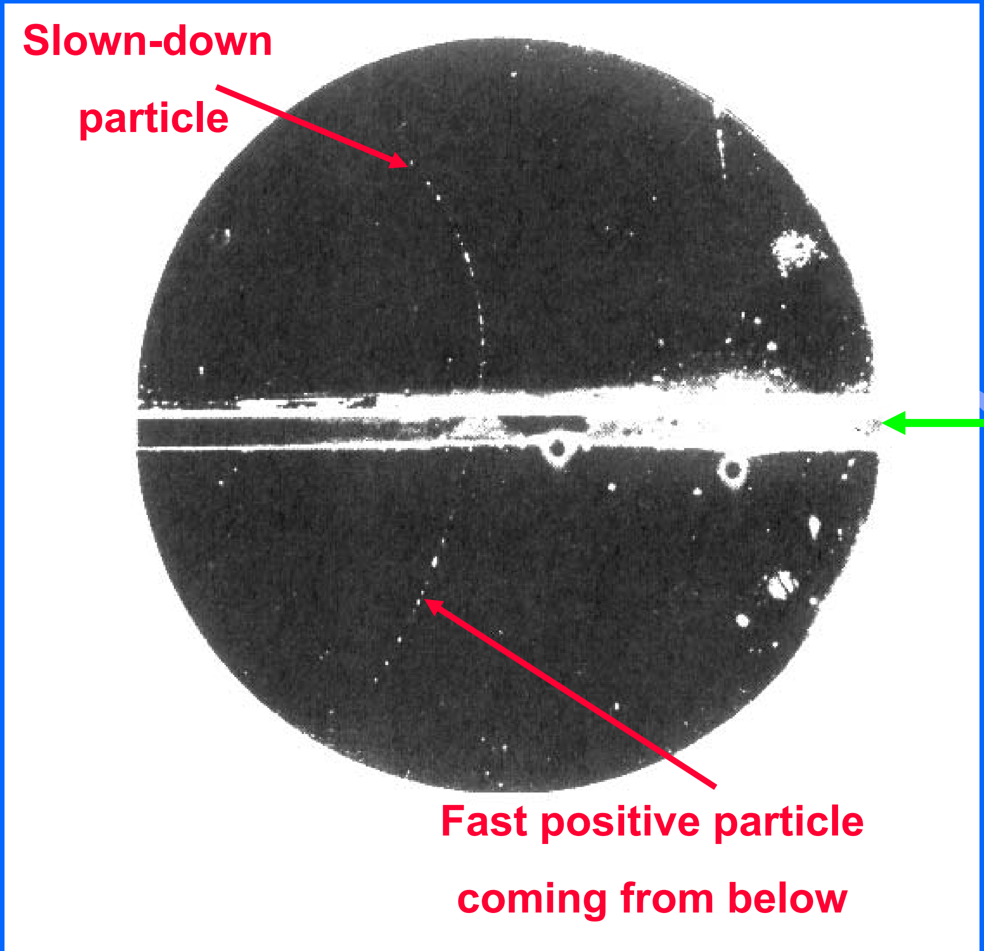
Discovery of the neutron



The next magnificent four years for experimental physics and medical physics

1932 – C. D. Anderson

Positron discovery



Layer of lead

Inserted in a cloud chamber

The next magnificent four years for experimental physics and medical physics

RADIOATTIVITÀ « BETA » PROVOCATA
DA BOMBARDAMENTO DI NEUTRONI. — III.

E. AMALDI, O. D'AGOSTINO, E. FERMI, F. RASETTI, E. SEGRÈ

« Ric. Scientifica », 5 (1), 452–453 (1934).

Sono state proseguite ed estese le esperienze di cui alle Note precedenti [1] coi risultati che ricordiamo appresso.

Idrogeno – Carbonio – Azoto – Ossigeno. – Non dànno effetto apprezzabile. Sono stati esaminati paraffina irradiata al solito modo per 15 ore con una sorgente di 220 mC, acqua irradiata per 14 ore con 670 mC e carbonato di guanidina irradiato per 14 ore con 500 mC.

Fluoro. – Il periodo del Fluoro è sensibilmente minore di quanto indicato precedentemente e cioè di pochi secondi.

Magnesio. – Il Magnesio ha due periodi, uno di circa 40 secondi e uno più lungo.

Alluminio. – Oltre al periodo di 12 minuti segnalato precedentemente ve ne è anche un altro dell'ordine di grandezza di un giorno. L'attività corrispondente a questo secondo periodo segue le reazioni chimiche caratteristiche del Sodio. Si tratta probabilmente di un Na^{24}.

Zolfo. – Il periodo dello S è assai lungo, certamente di molti giorni. L'attività si separa con le reazioni caratteristiche del Fosforo.

Cloro. – Si comporta analogamente allo S. Anche qui si può separare

corrispondente a questo secondo periodo segue le reazioni chimiche caratteristiche del Sodio. Si tratta probabilmente di un Na^{24}.

Zolfo. – Il periodo dello S è assai lungo, certamente di molti giorni. L'attività si separa con le reazioni caratteristiche del Fosforo.

Cloro. – Si comporta analogamente allo S. Anche qui si può separare
un principio attivo; probabilmente si tratta di un P^{32} identico a quello che si ricava dallo S.

Manganese. – Ha un effetto debole con un periodo di circa 15 minuti.

Cobalto. – Ha un effetto di 2 ore. Il principio attivo si comporta come Mn. Data l'identità di periodo e di comportamento chimico si tratta quasi certo di un Mn^{56} identico a quello che si forma irradiando il Fe.

Zinco. – Ha due periodi, uno di 6 minuti e uno assai più lungo.

Gallio. – Periodo 30 minuti.

Bromo. – Ha due periodi, uno di 30 minuti e l'altro di 6 ore. L'attività corrispondente al periodo lungo e probabilmente anche l'altra, seguono chimicamente il Br.

Palladio. – Periodo di alcune ore.

Jodio. – Periodo 30 minuti. L'attività segue chimicamente lo Jodio.

Praseodimio. – Ha due periodi. Uno di 5 minuti e l'altro più lungo.

Neodimio. – Periodo 55 minuti.

Samario. – Ha due periodi uno di 40 minuti e uno più lungo.

Oro. – Periodo dell'ordine di grandezza di 1 o 2 giorni.

O. D'Agostino E. Segrè

E. Amaldi F. Rasetti E. Fermi

Discovery of the effect of slow neutrons - 1934

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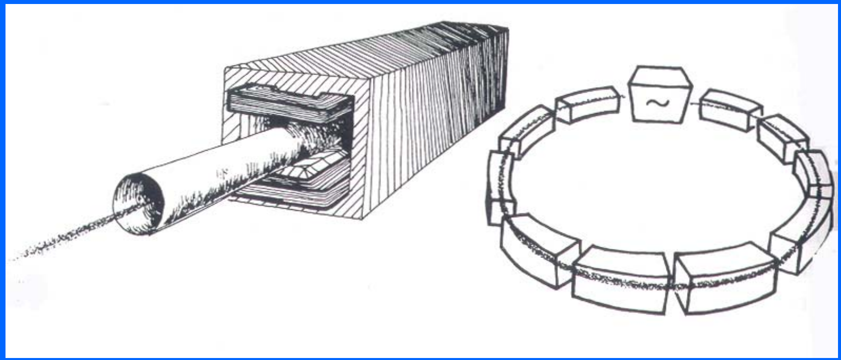
The synchrotron

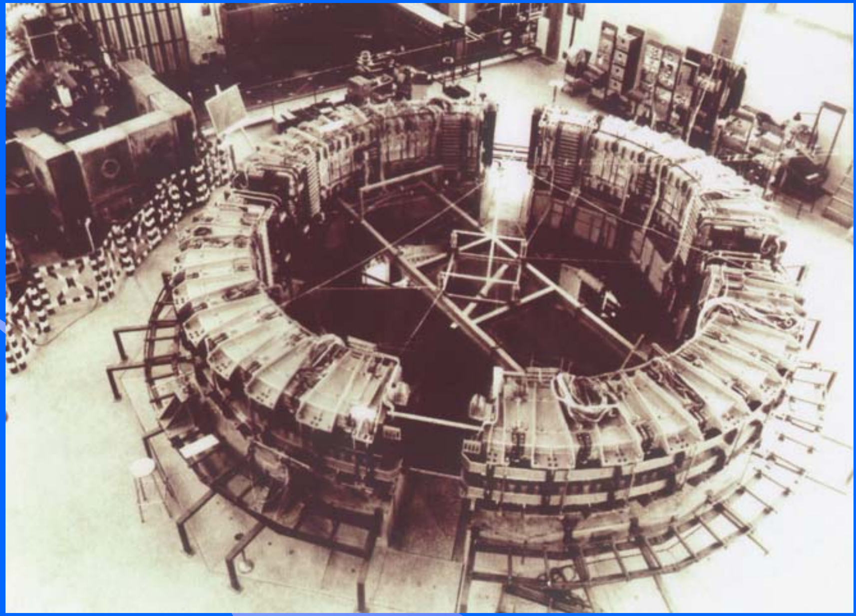
1945: E. McMillan and V.J.Veksler discover the principle of phase stability



1959: Veksler visits McMilan at Berkeley

1 GeV electron synchrotron

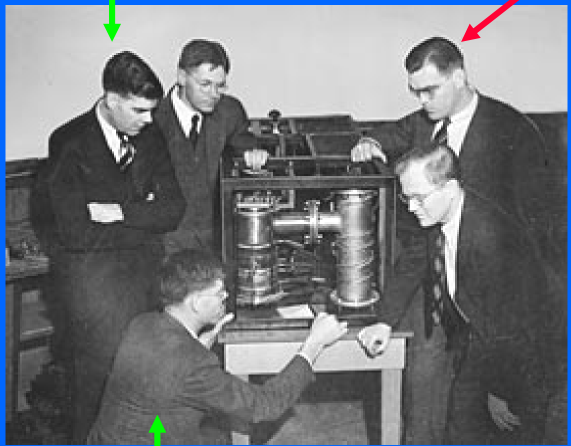
Frascati - INFN - 1959



The electron linac

Sigmur Varian

William W. Hansen



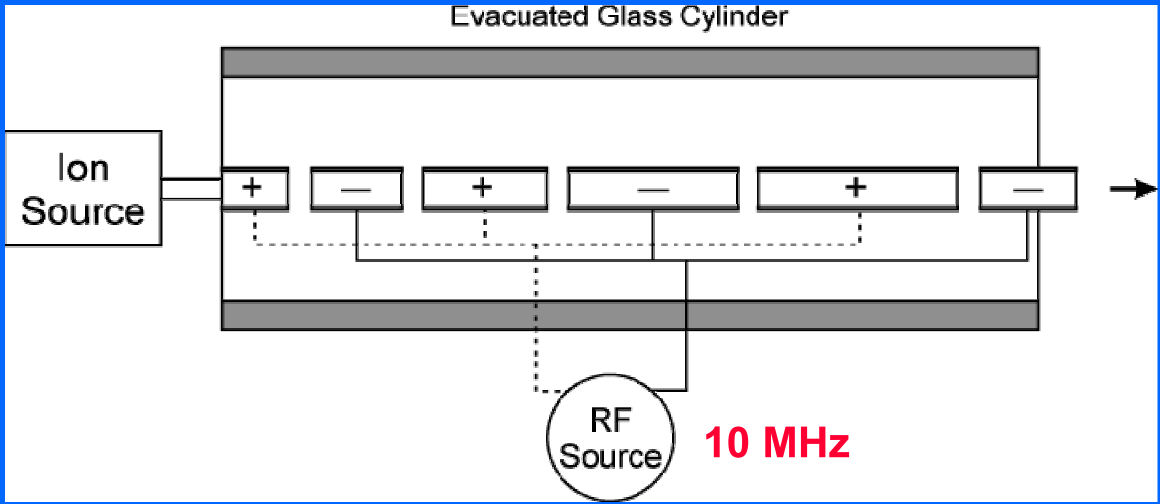
Russell Varian

1939

Invention of the klystron

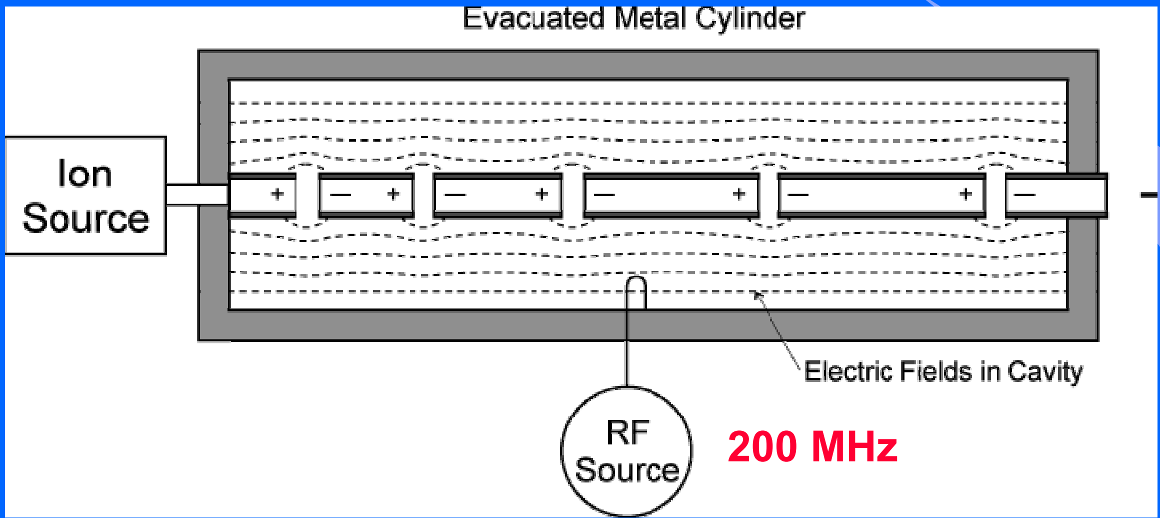
1947
first linac for electrons
4.5 MeV and 3 GHz

Linacs for protons and ions



1928 – R. Wideröe

Invention of the linac for ions



1946 – L. Alvarez

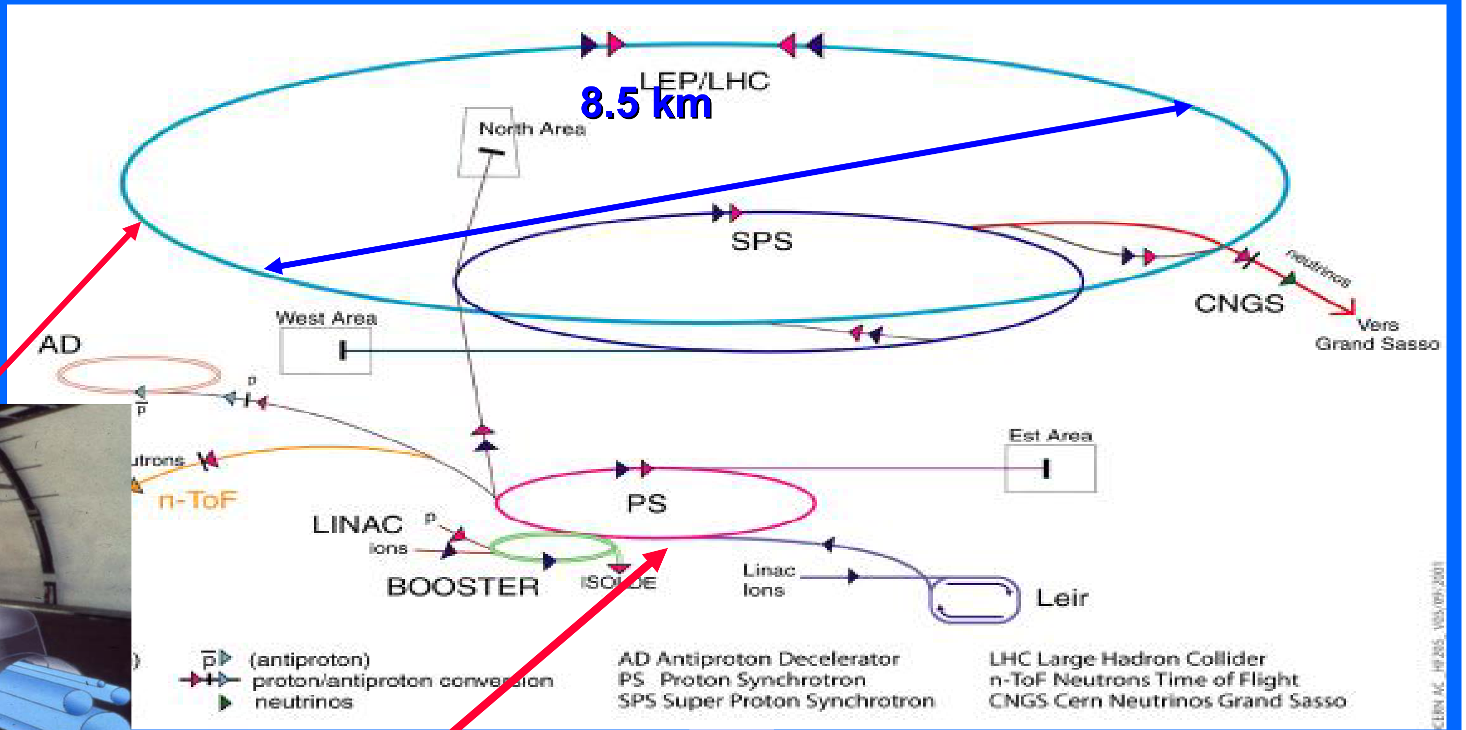
Drift Tube Linac (DTL)

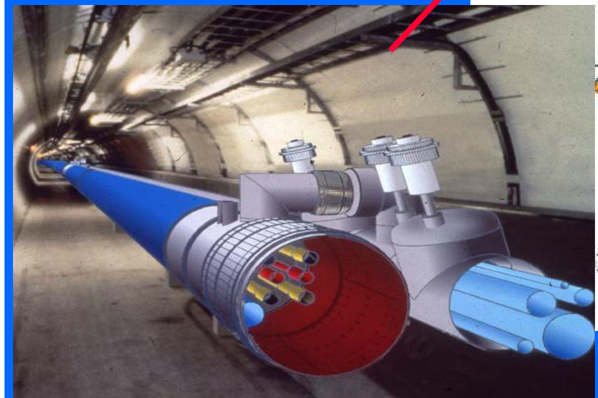
TERA

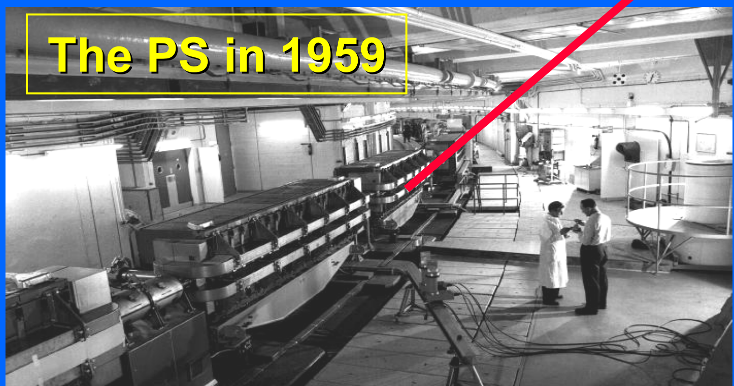
At CERN we have linacs and strong-focusing synchrotrons

Large Hadron Collider (14+14) TeV

2007







The PS in 1959

In 1952 the "strong-focusing" method invented at BNL (USA) was chosen for the CERN PS

The beginnings of CERN 50 years ago

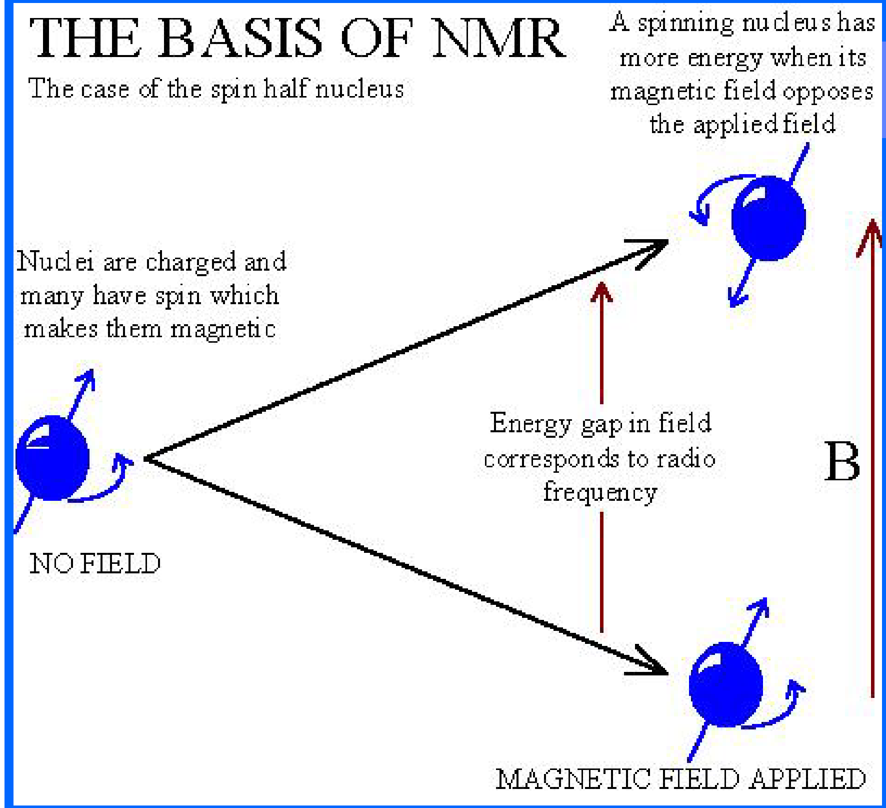
Isidor Rabi

UNESCO talk in 1950

1952: Pierre Auger Edoardo Amaldi

Secretary General

at the meeting that created the provisional CERN



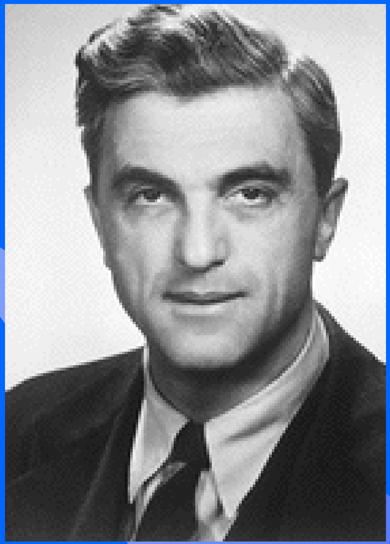
Nuclear Magnetic Resonance

1938-1945

Felix Bloch and Edward Purcell

discover and study

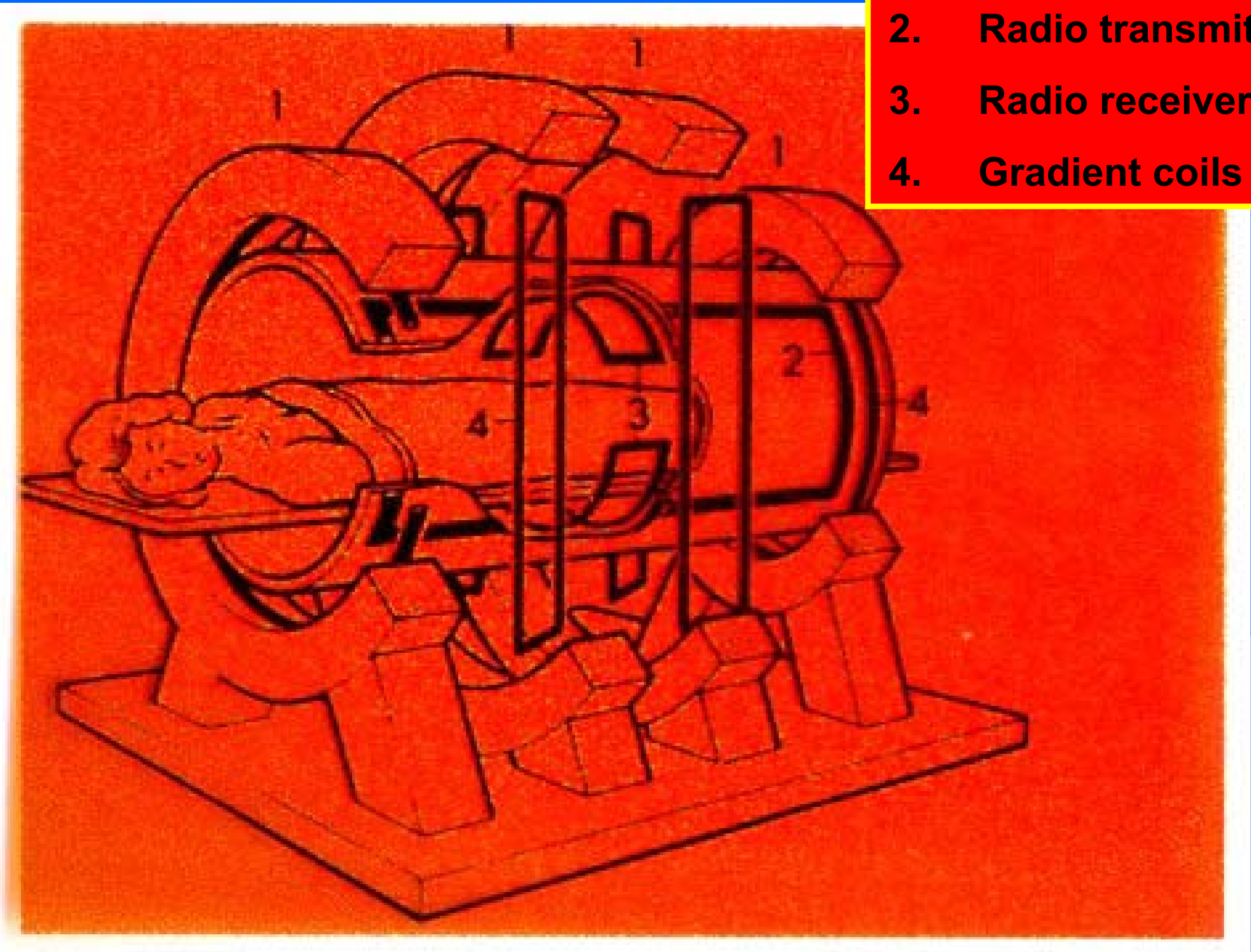
NMR



In 1954 Felix Bloch became

the first CERN Director General

MRI = Magnetic Resonance Imaging



1. Main magnet (0.5-1 T)
2. Radio transmitter coil
3. Radio receiver coil
4. Gradient coils

In diagnostics

MRI sees the protons

of the tissues

Summary of 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
Research acc. included biomedical research	~1000
Acc. for industrial processing and research	~1500
Ion implanters, surface modification	>7000
TOTAL	> 17500

(Medical radioisotope production + Radiotherapy accelerators + Research acc.: 9000)

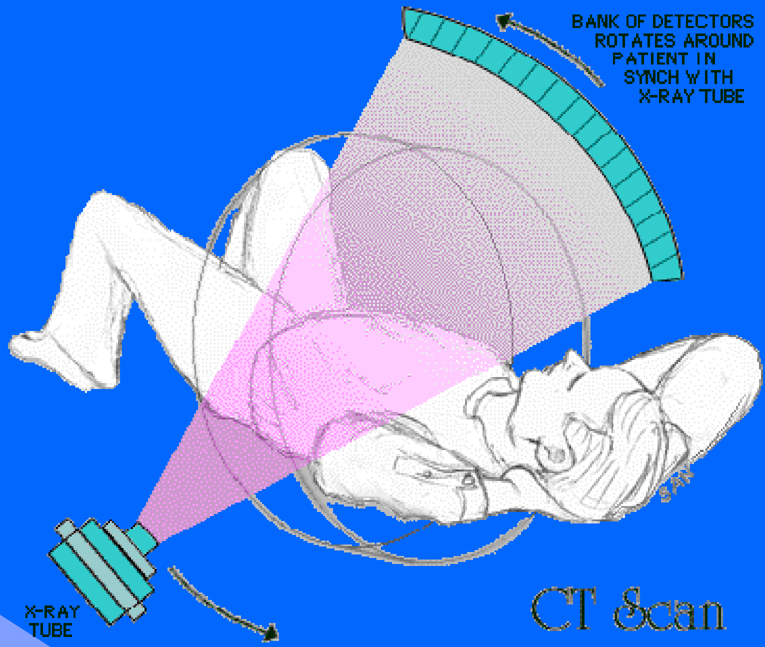
(*) W. Maciszewski and W. Scharf: Int. J. of Radiation Oncology, 2004

RADIOACTIVITY AND ACCELERATORS (*)

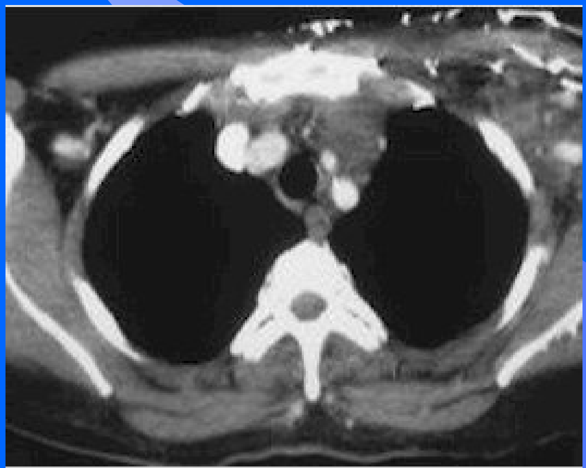
1. IN DIAGNOSTICS

(*) No time to discuss the use of detectors developed for subatomic physics

CT = Computer tomography

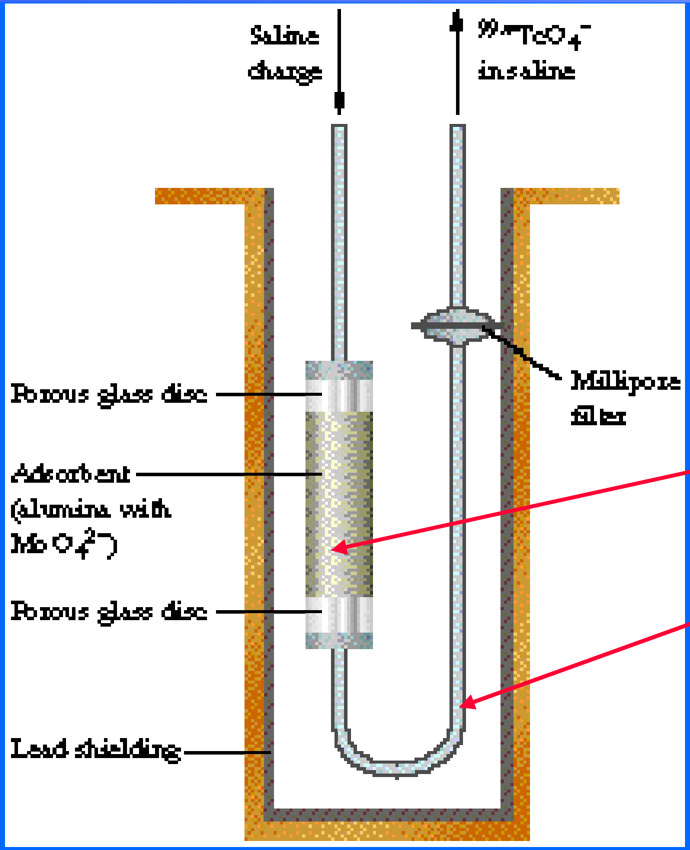


Abdomen



Lungs

SPECT = Single Photon Emission Computer Tomography

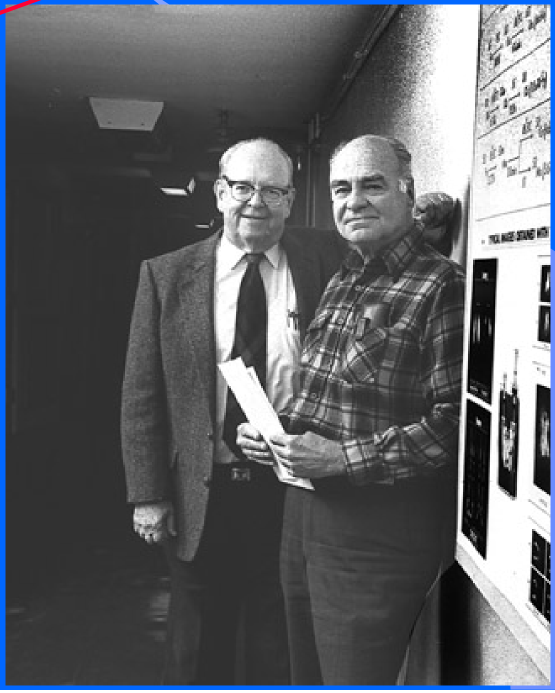


In reactors <u>slow neutrons</u> produce

$^{98}Mo + n = {}^{99}Mo + \gamma$

$^{99}Mo\ (66\ h) = {}^{99m}Tc\ (6\ h) + e^- + \bar{\nu}$

gamma of 0.14 MeV



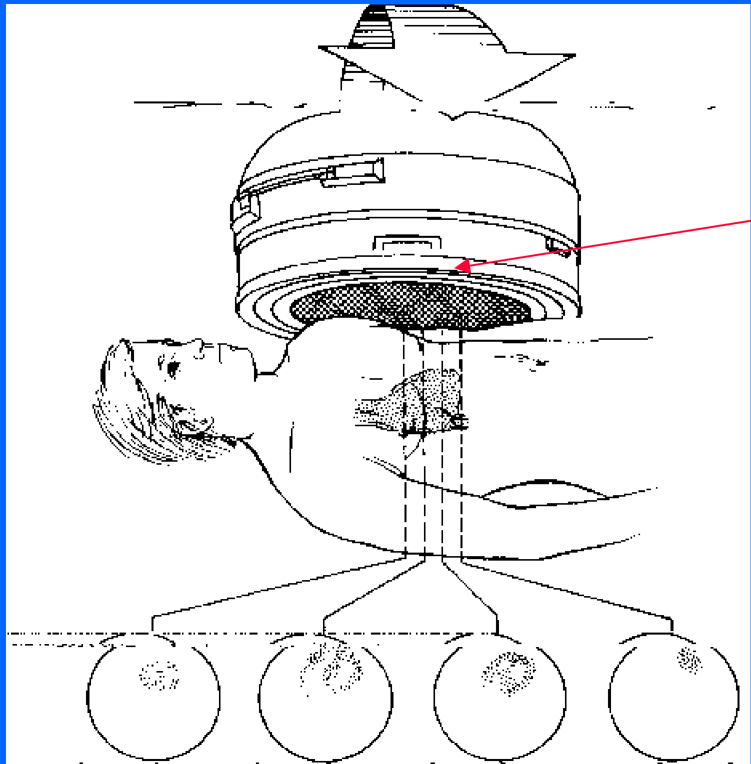
Molibdenum 'generator'

BNL - 1960

Powel Richards

and Walter Tucker

SPECT scanner



Collimators of the 0.14 MeV gammas

85% of all nuclear medicine examinations use <u>^{99m}Tc</u>

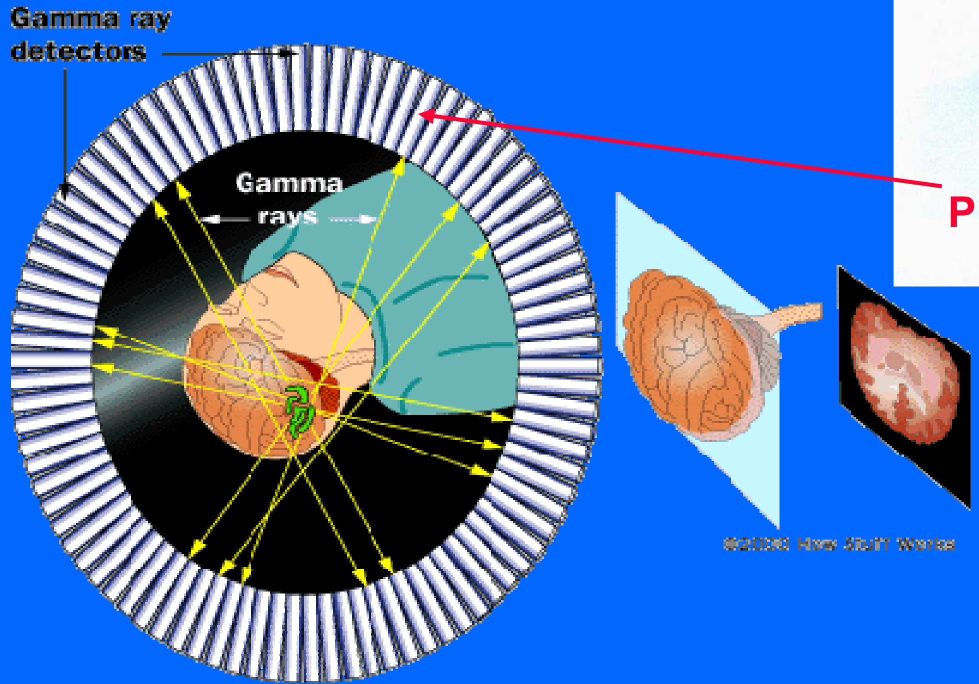
Centre for Nuclear Medicine

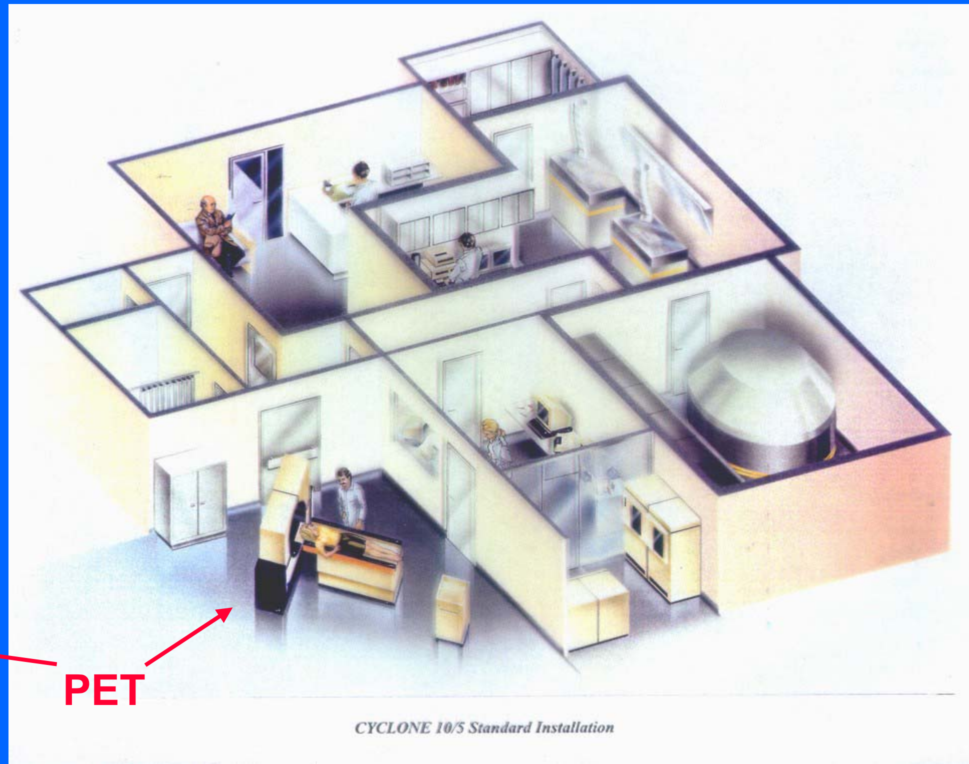
For PET the most used compound

FDG = sugar

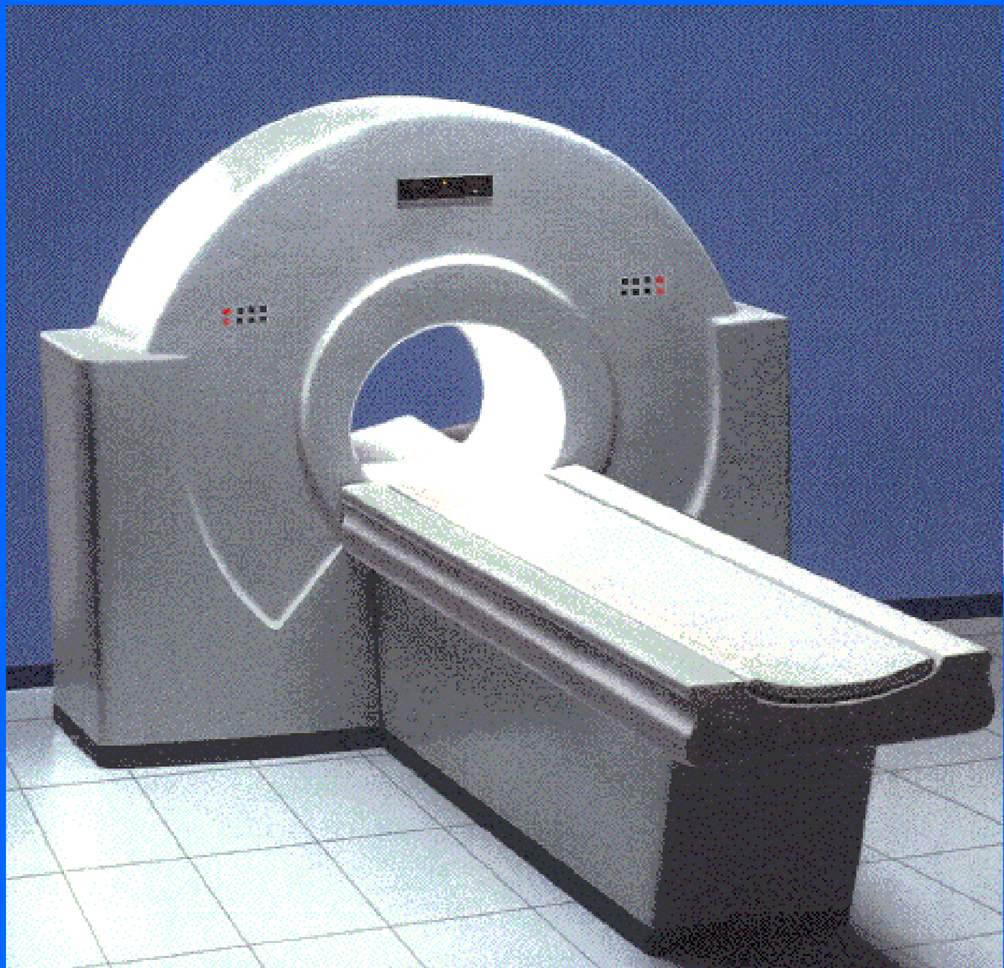
F = ^{18}F

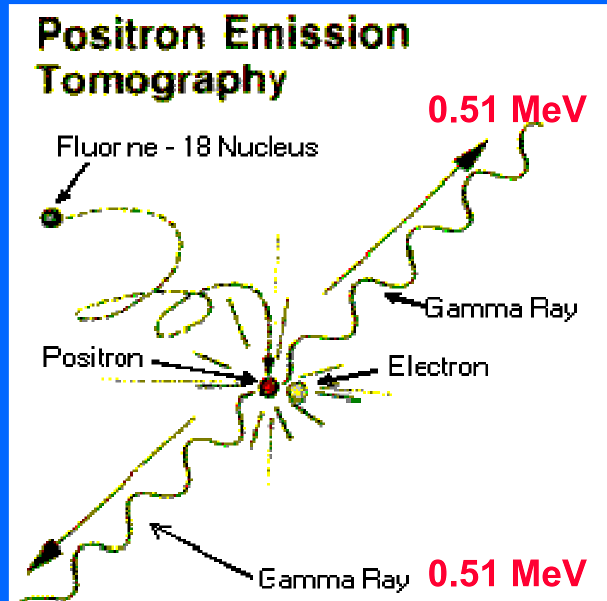
with half-life 1.6 h

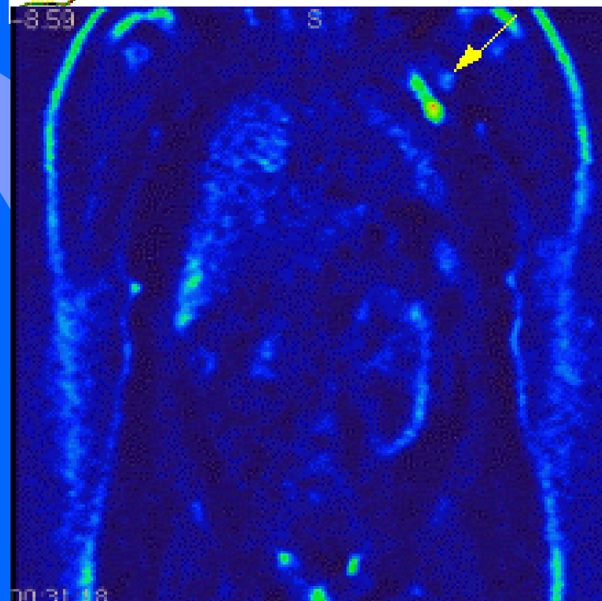




PET = Positron Emission Tomography



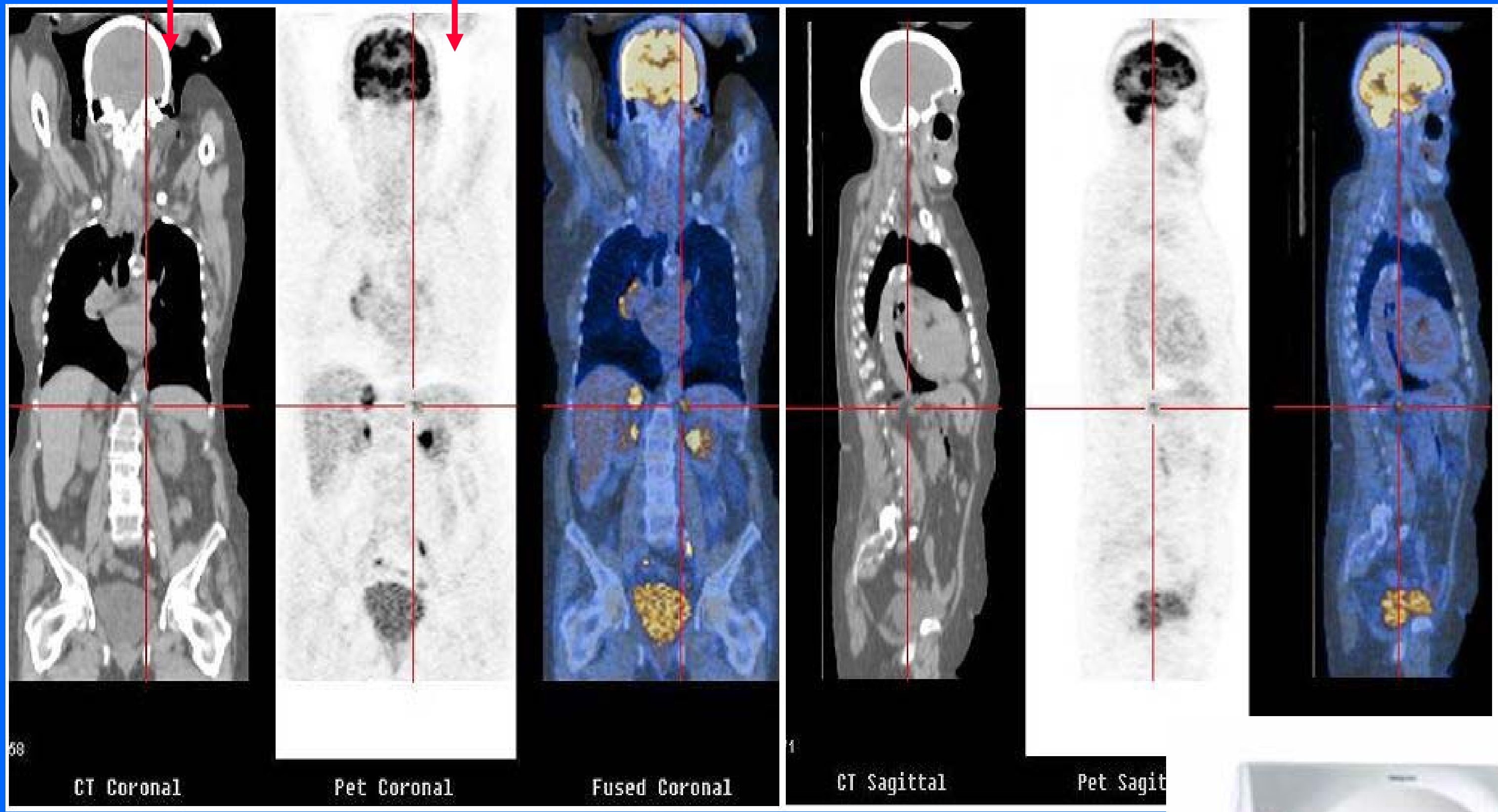




CT-PET

CT — **morphology**

PET — **metabolism**



The future of diagnostics

RADIOACTIVITY AND ACCELERATORS (*)

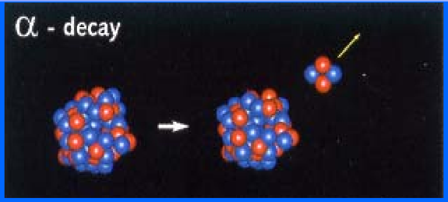
1. IN CANCER THERAPY

(*) No time to discuss the use of detectors developed for subatomic physics

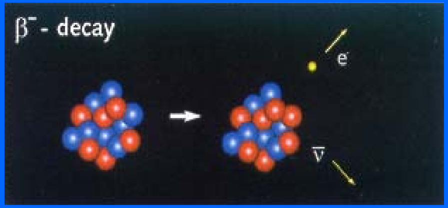
Radioactivity in cancer therapy

targeted radioimmunotherapy

α particles from Bismuth-213 for leukaemia

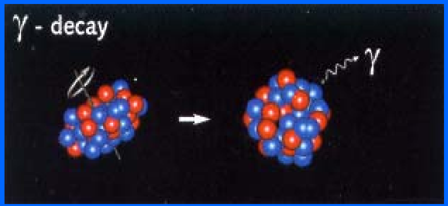


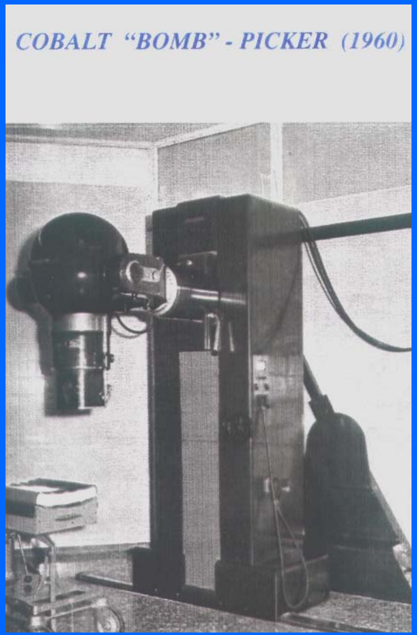
β particles from Yttrium-90 for glioblastoma



teletherapy

gammas from Cobalt-60 for deep tumours





Cobalt source 2000

Cobalt-60

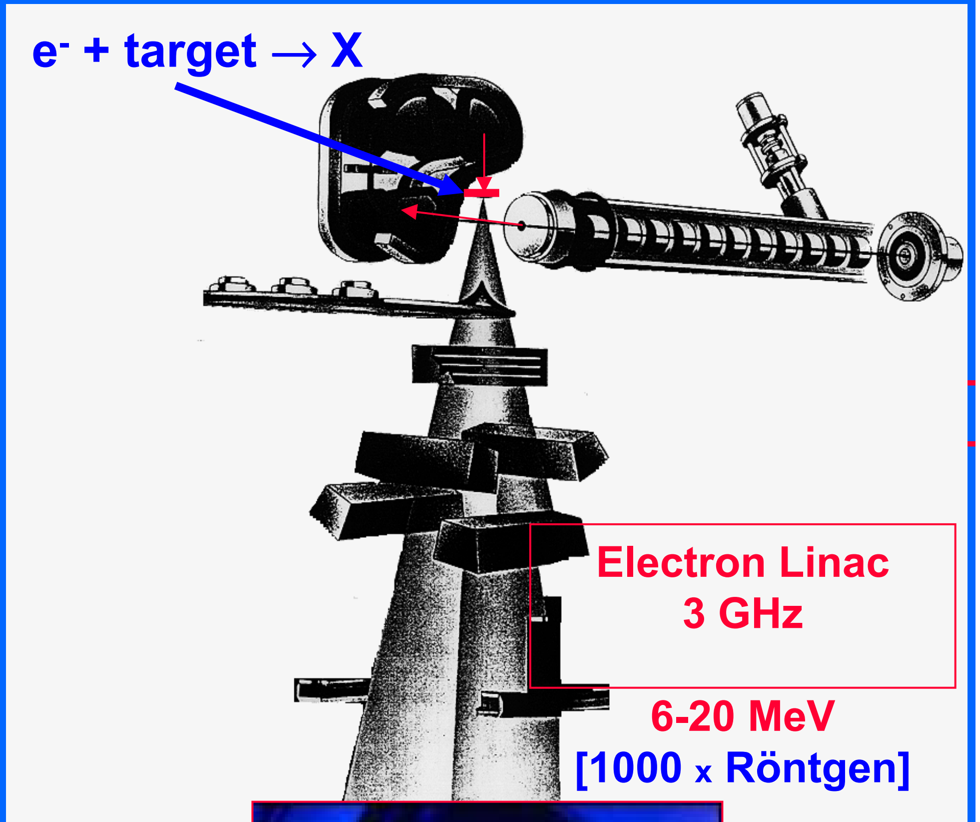
(1 MeV gammas)

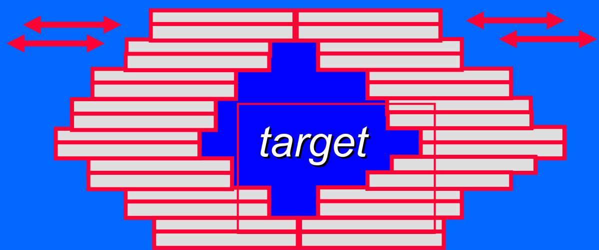
is produced in reactors

by slow neutrons

TERA

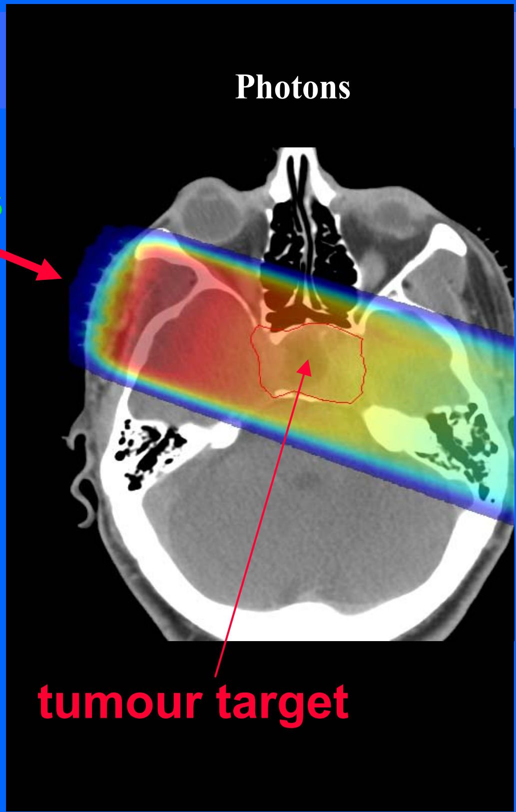
X-rays in radiotherapy: linacs



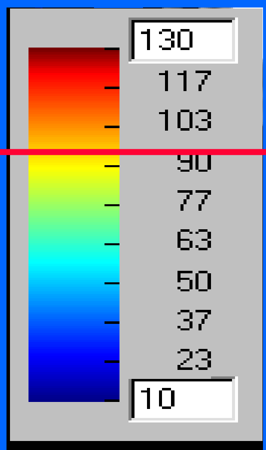


X rays have a poor energy deposition

X rays



tumour target

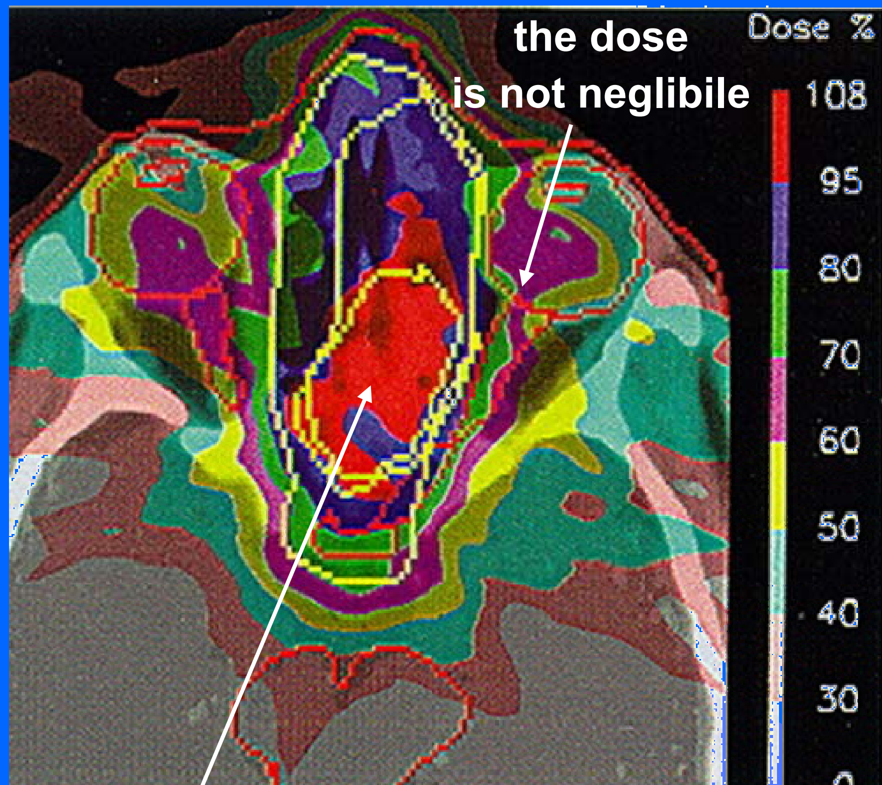


Fraction

of dose

IMRT (Intensity Modulated Radiation Therapy)

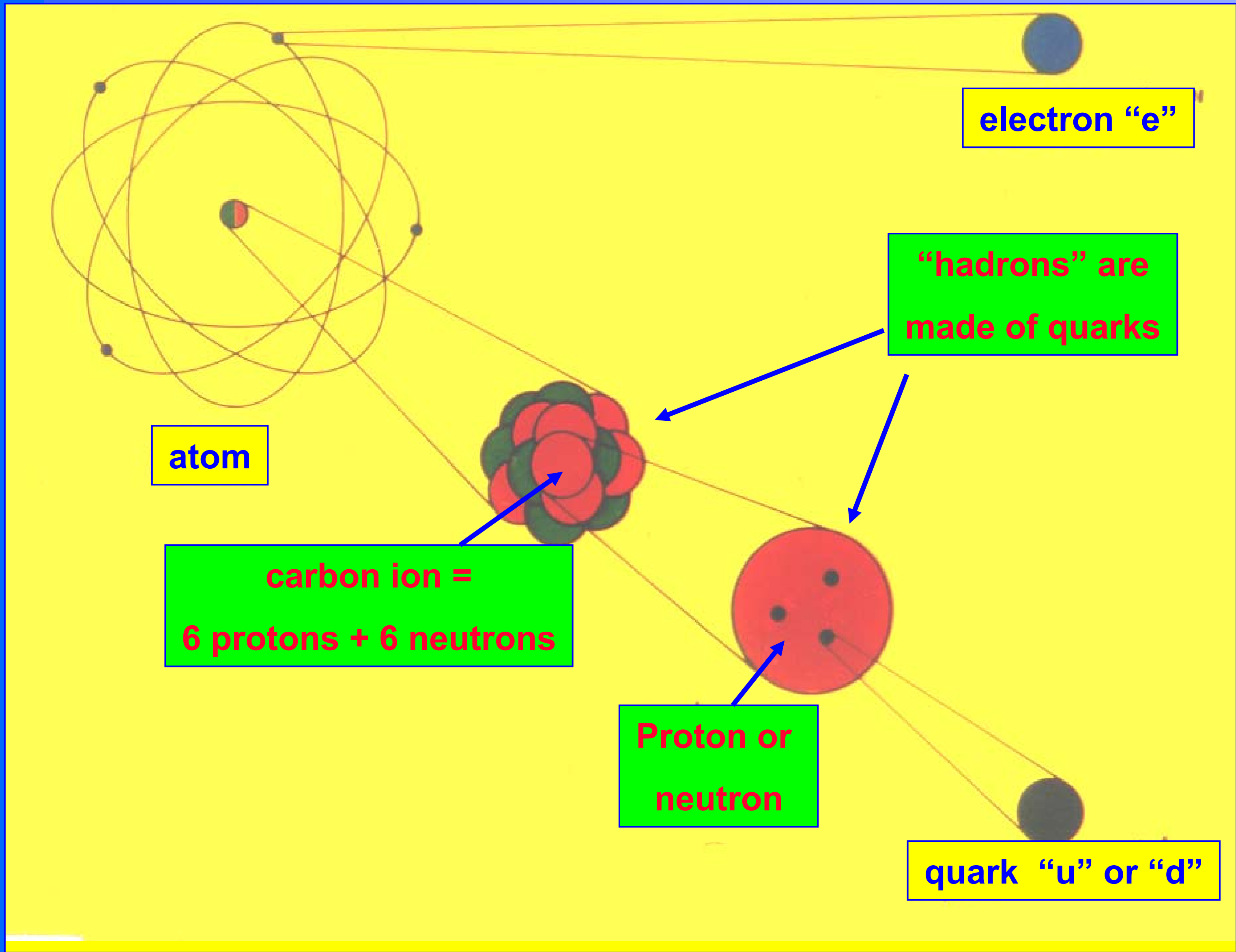
with 9 crossed beams



the dose is not neglibile

Tumour between the eyes

"Hadrontherapy" uses n, p and C-ion beams

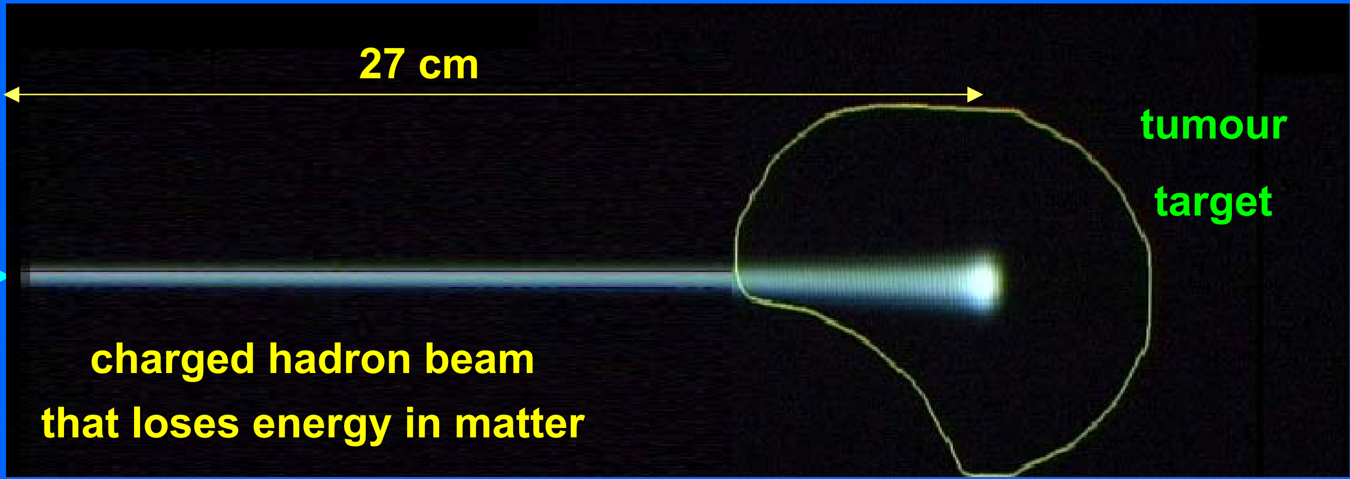


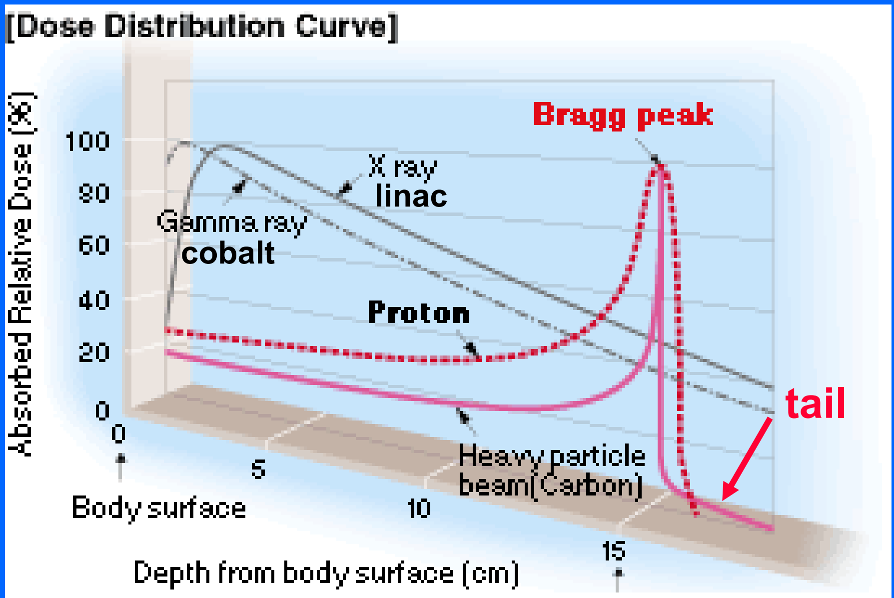
Charged hadrons have a much better energy deposition

200 MeV protons

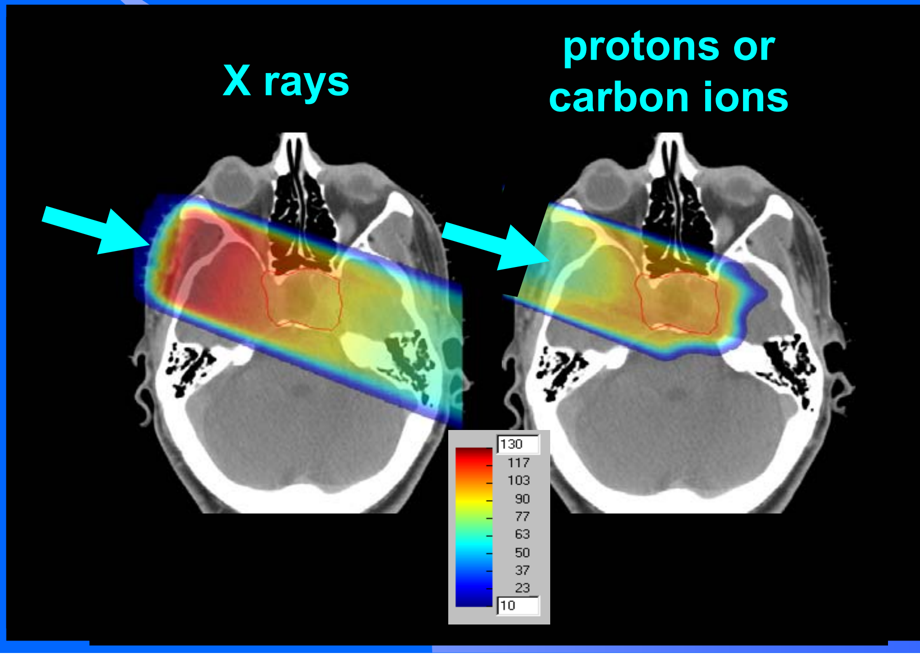
4800 MeV carbon ions

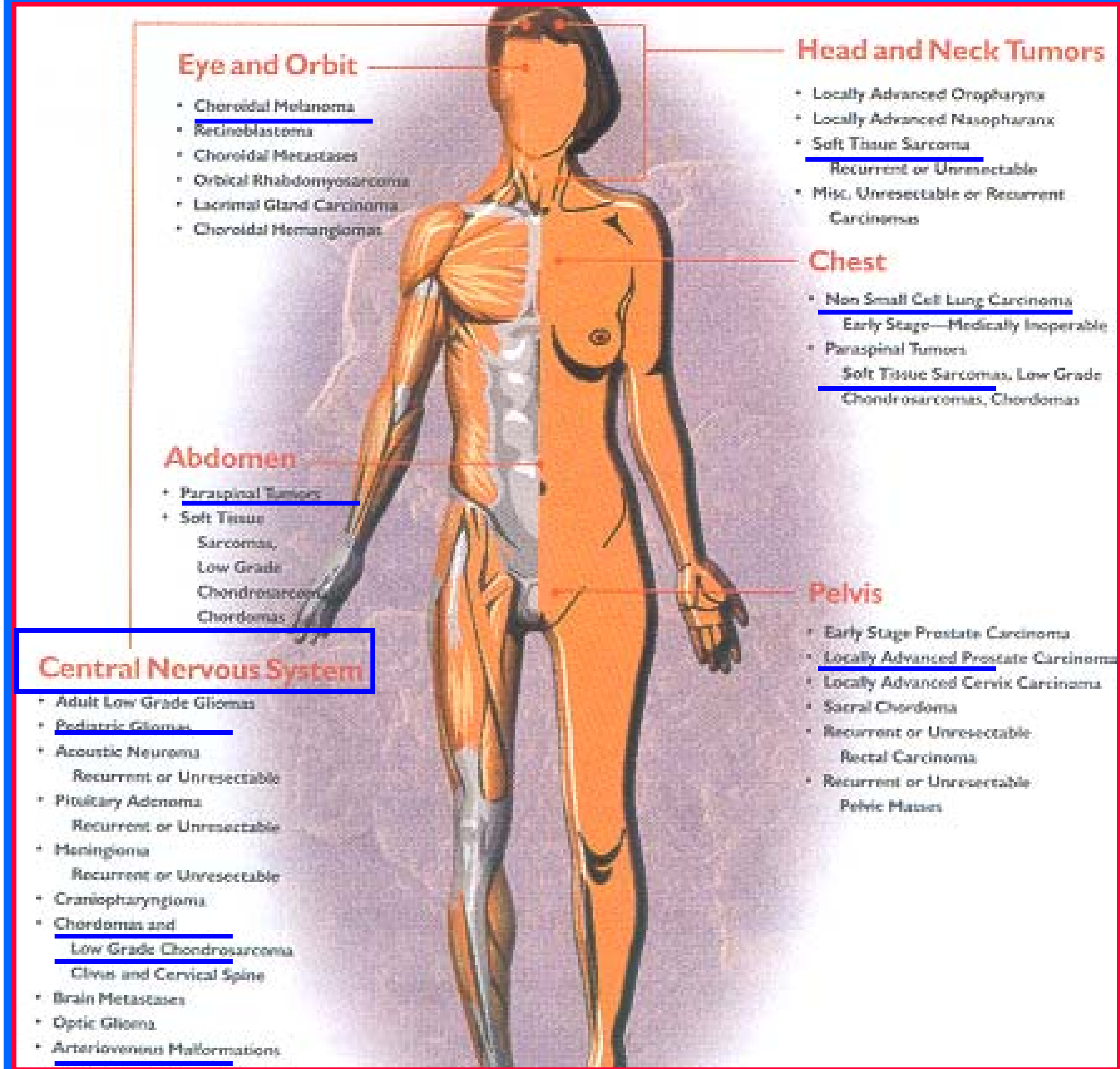
which control radioresistant tumours





http://global.mitsubishielectric.com/bu/particlebeam/index_b.html





The sites

Protontherapy:

40'000 patients

Cost about 20'000 Euro

2-3 x X-rays

If cost would be

the same

as for X-rays

90% of the treatments

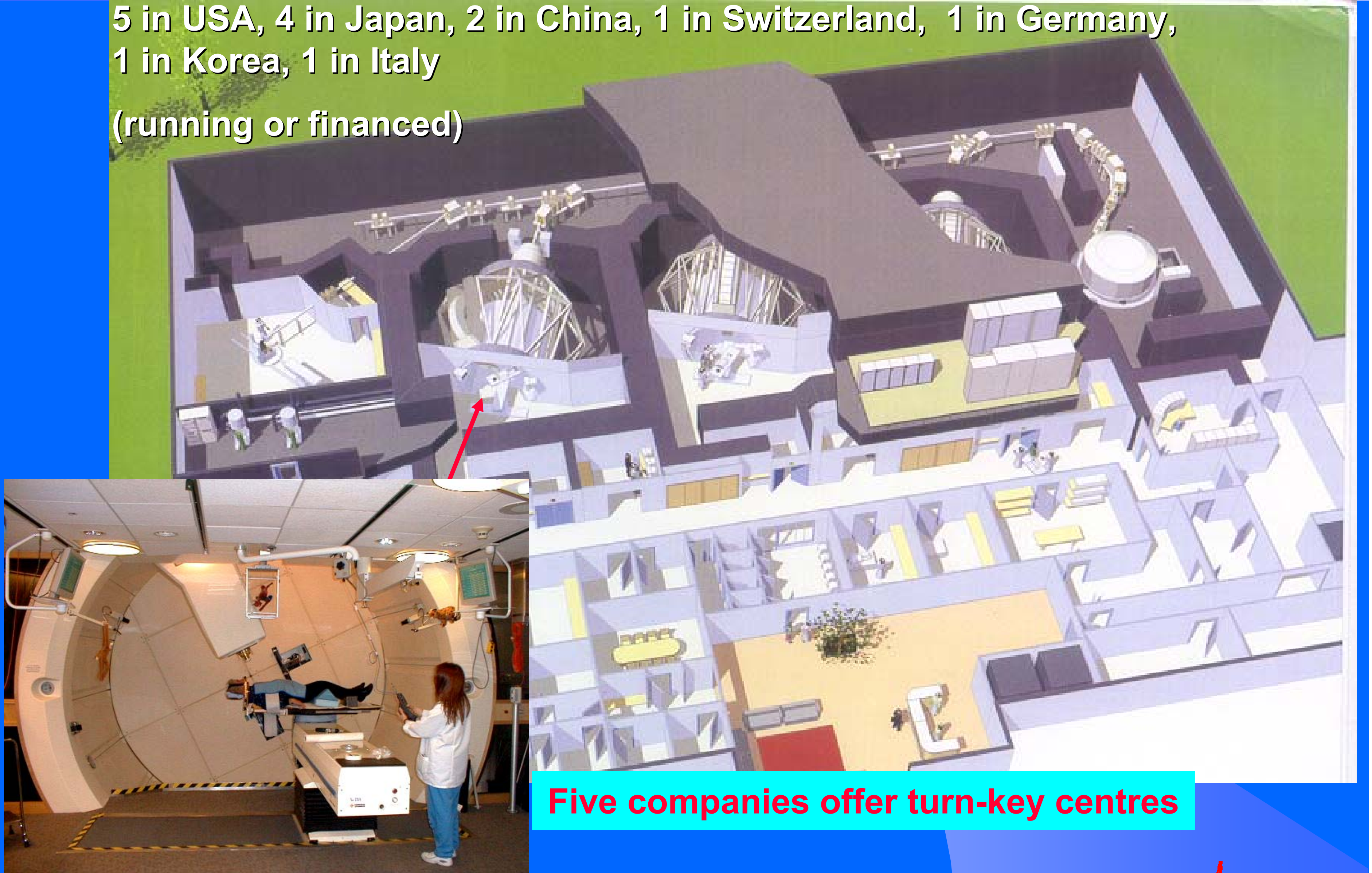
would be with

protons !

Hospital centres for deep protontherapy (>500 pts/year)

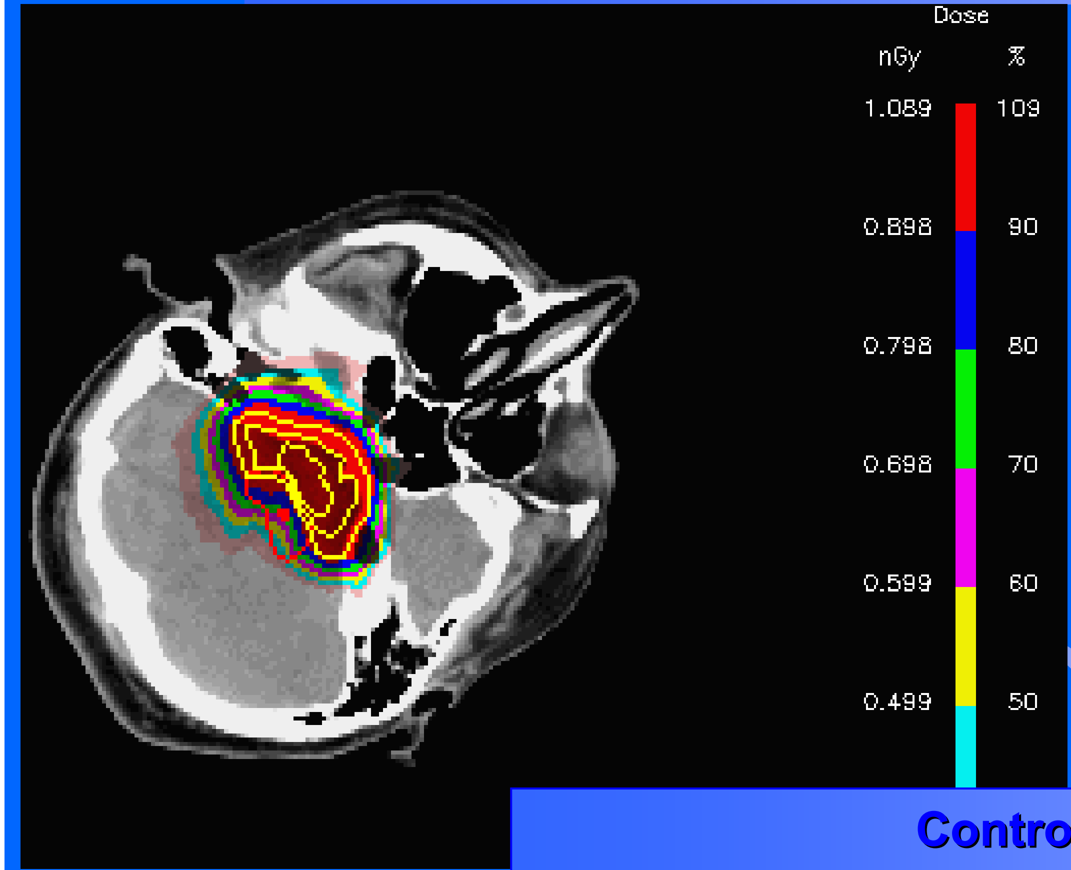
5 in USA, 4 in Japan, 2 in China, 1 in Switzerland, 1 in Germany, 1 in Korea, 1 in Italy

(running or financed)



Five companies offer turn-key centres

Tumours of the central nervous system

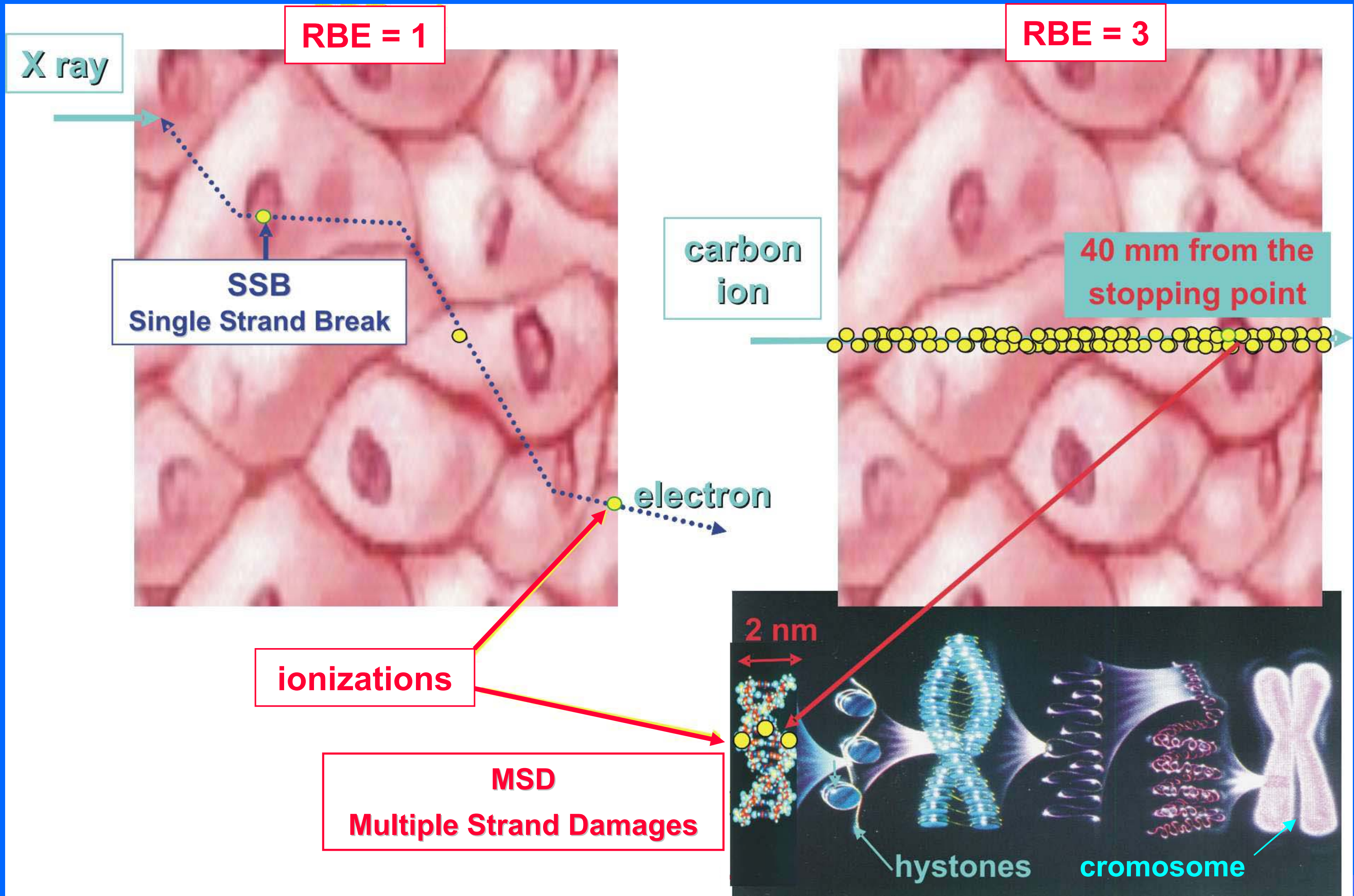


The percentages are larger with carbon ions

Control at 5 years

	RT	Protoni
Chordomas	17-50%	73-83%
Chondrosarcomas	50-60%	90-98%

Radiobiological efficiency of carbon 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

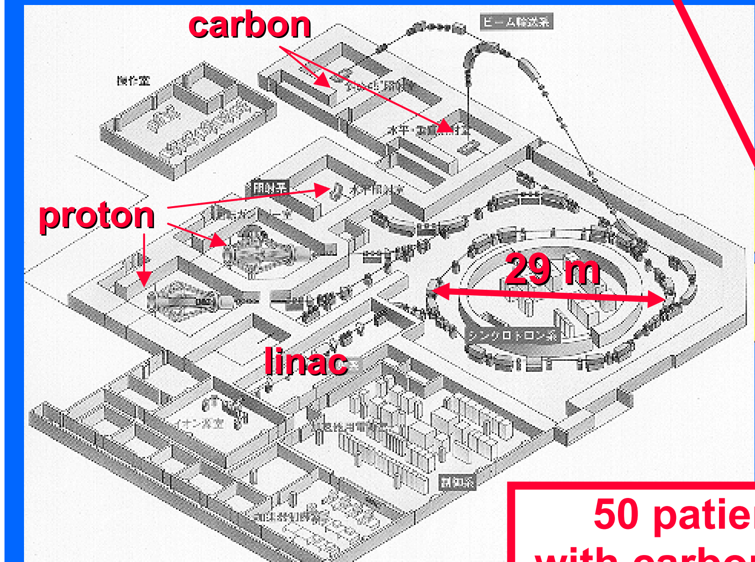
3% of X-ray patients 600 pts/year

TOTAL every 10 M about 3'000 pts/year

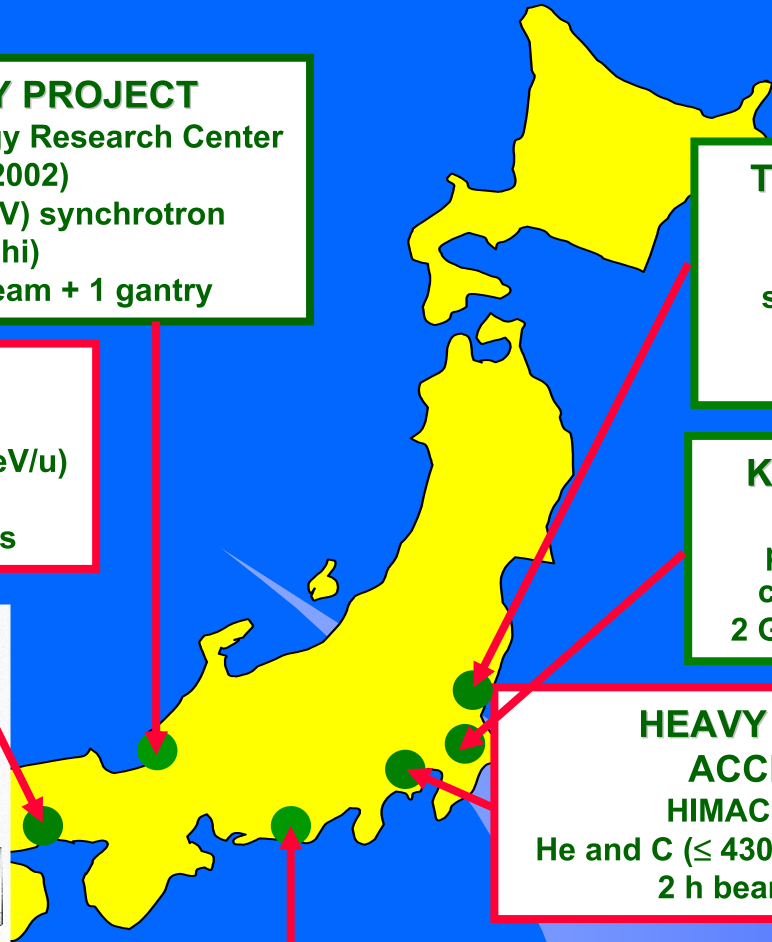
Japan: 4 proton Centres and 2 carbon ion centres

WAKASA BAY PROJECT
by Wakasa-Bay Energy Research Center
Fukui (2002)
protons (≤ 200 MeV) synchrotron
(Hitachi)
1 h beam + 1 v beam + 1 gantry

HYOGO MED CENTRE
Hyogo (2001)
protons (≤ 230 MeV) - He and C ions (≤ 320 MeV/u)
Mitsubishi synchrotron
2 p gantries + 2 fixed p beam + 2 ion rooms



50 patients
with carbon ions



TSUKUBA CENTRE
Ibaraki (2001)
protons (≤ 270 MeV)
synchrotron (Hitachi)
2 gantries
2 beam for research

KASHIWA CENTER
Chiba (1998)
protons (≤ 235 MeV)
cyclotron (IBA – SHI)
2 Gantries + 1 hor. beam

HEAVY ION MEDICAL ACCELERATOR
HIMAC of NIRS (1995)
He and C (≤ 430 MeV/u) 2 synchrotrons
2 h beams + 2 v beams

2000 patients
with carbon ions

SHIZUOKA FACILITY
Shizuoka (2002)
Proton synchrotron
2 gantries + 1 h beam

1998 - GSI pilot project

G. Kraft

200 patients treated with carbon ions
under
J. Debus (Heidelberg Univ.)

PET on-line

In collaboration with CERN

TERA (created in 1992) has proposed and designed a National Centre for carbon ions:

↓

The Italian National Centre is being built in Pavia

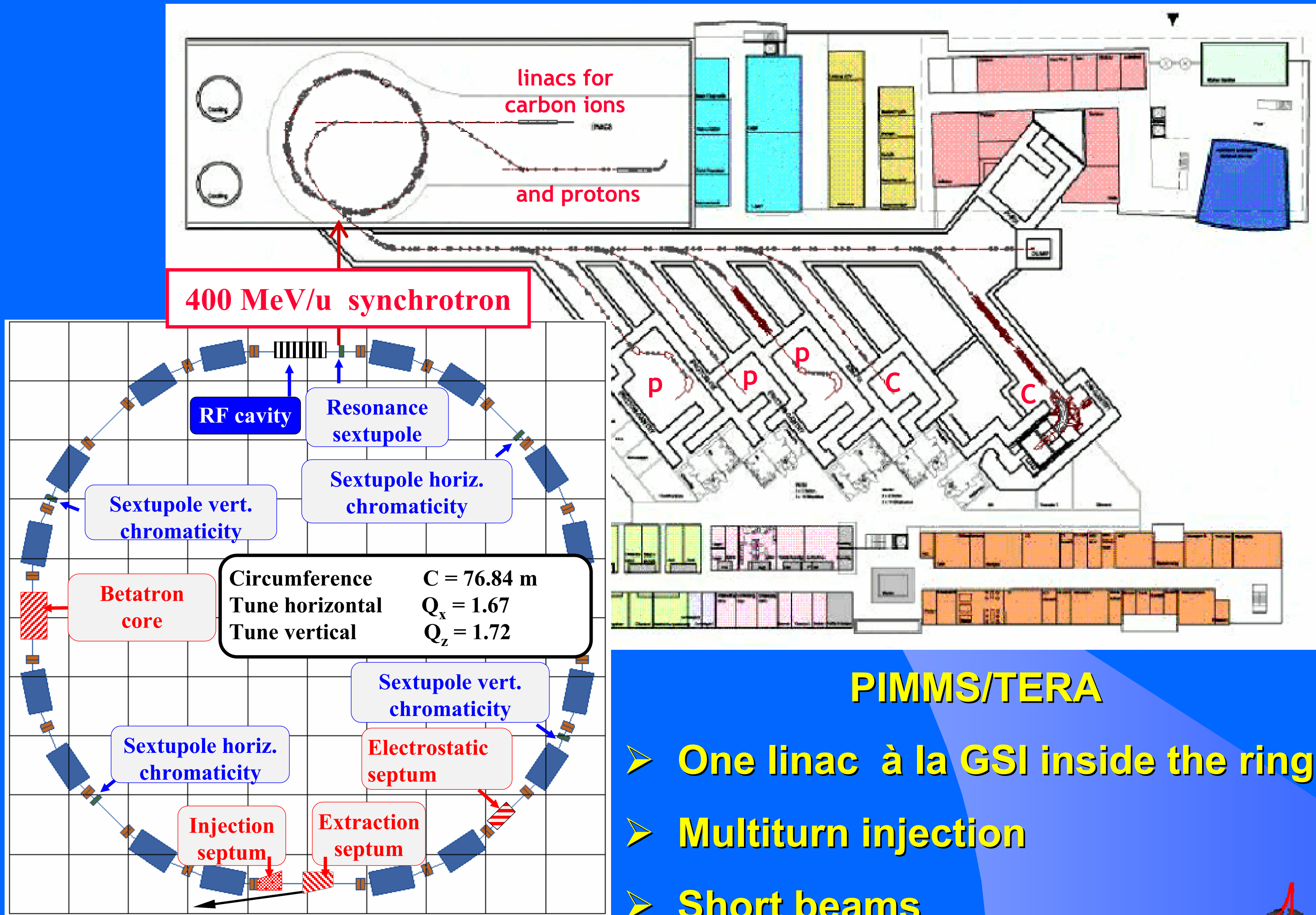
TERA has developed a novel technique for diagnostics and protontherapy

↓

The "cyclinac"

Proton Ion Medical Machine Study = PIMMS: 1996 - 2000

CERN–TERA–MedAustron-Oncology 2000 Collaboration



PIMMS/TERA

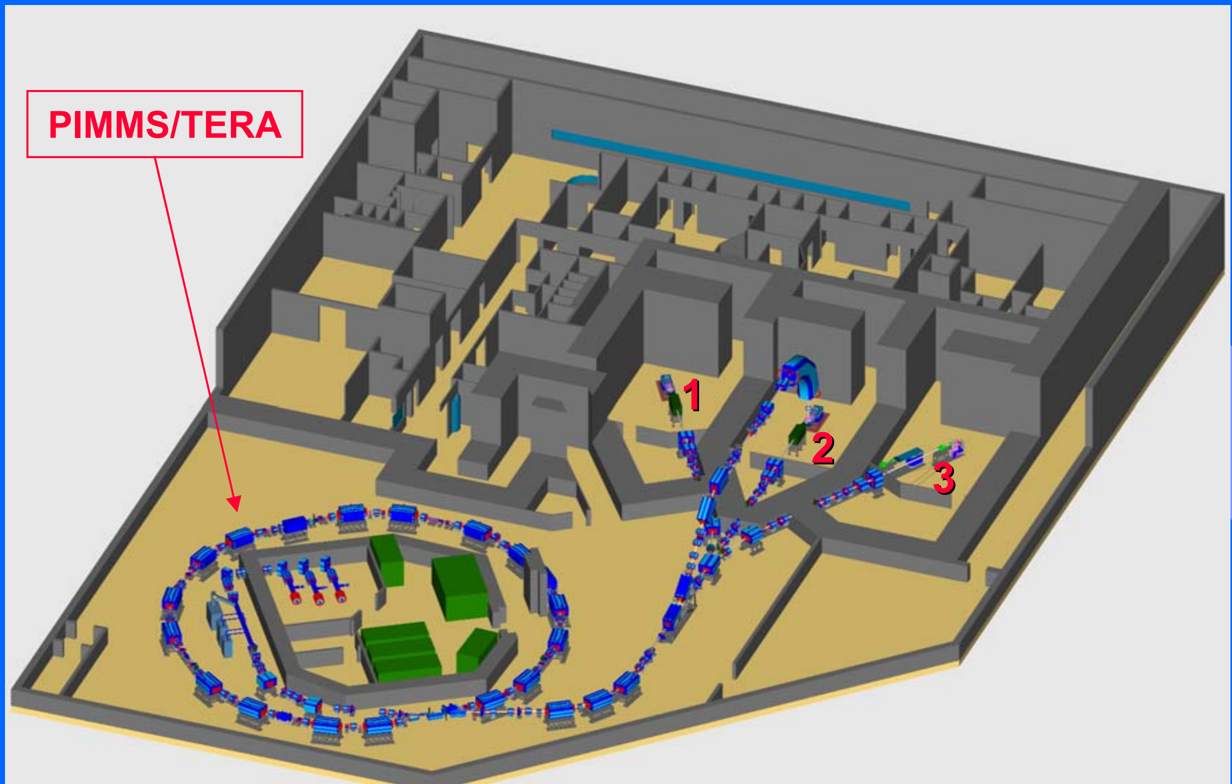
- One linac à la GSI inside the ring
- Multiturn injection
- Short beams

TERA

CNAO = Centro Nazionale di Adroterapia

CNAO Foundation was created by the Italian Government in 2001
to realize CNAO: 4 Hospitals in Milan, 1 Hospital in Pavia and TERA
Since 2003 INFN is Institutional Participant

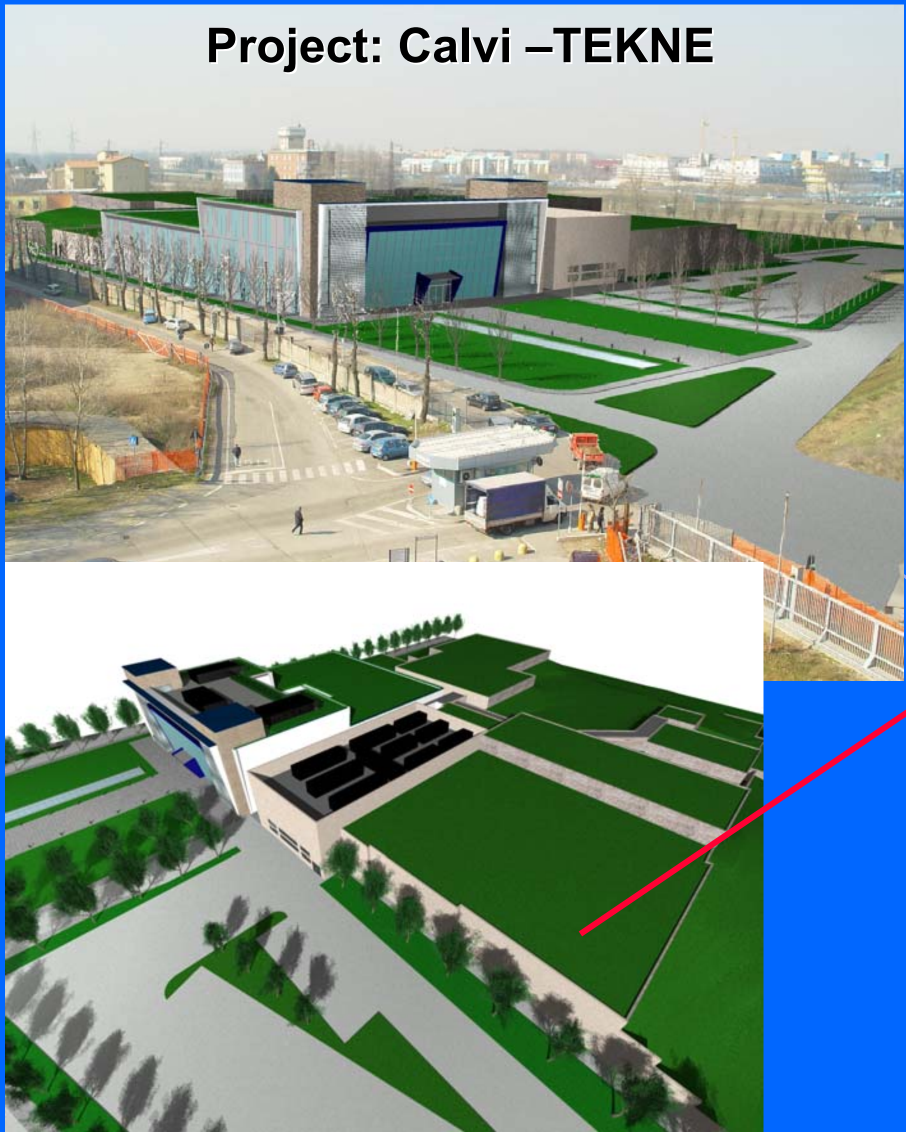
In September 2003 TERA has completed and passed to CNAO
the design of the high-tech part of CNAO and 25 people



President: E. Borloni

Med. Dir.: R. Orecchia
Tech. Dir: S. Rossi

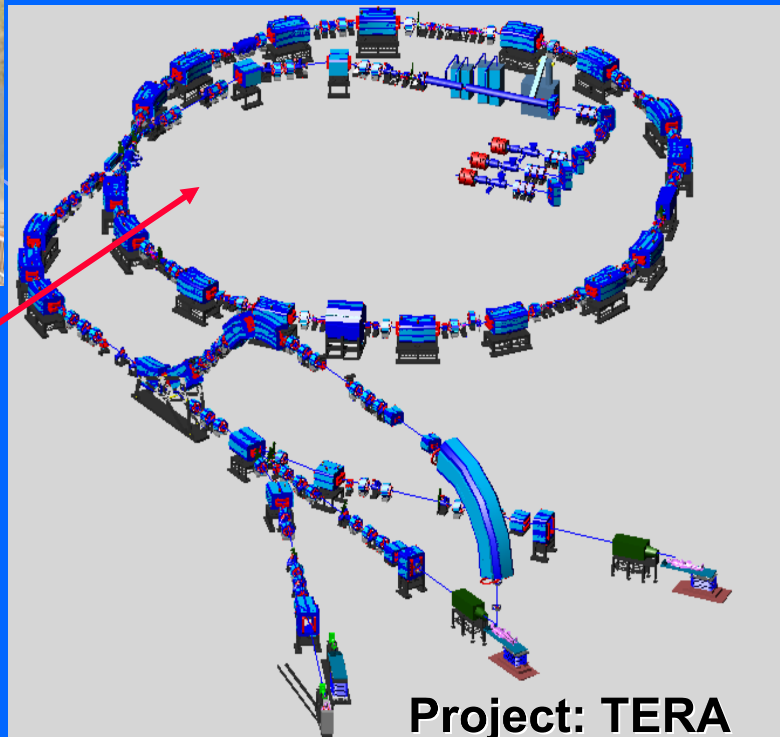
CNAO on the Pavia site



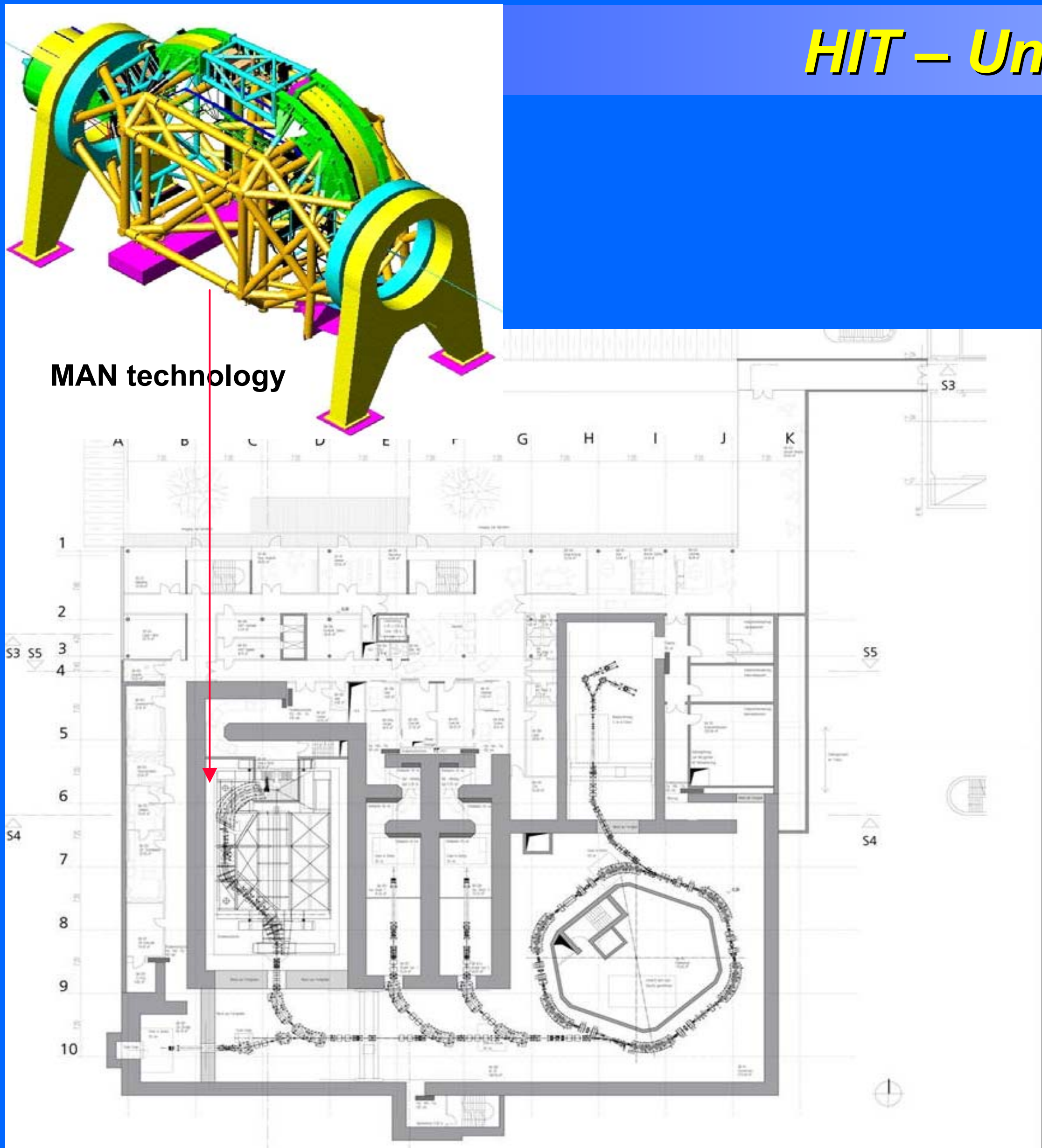
Investment: 75 M€

Main source of funds:
Italian Health Ministry

Ground breaking: 14 March 2005
Ready: end of 2007



HIT – University of Heidelberg



Financed with 72 MEuro:

Public funds: 36

loan: 36

Heidelberg: J. Debus

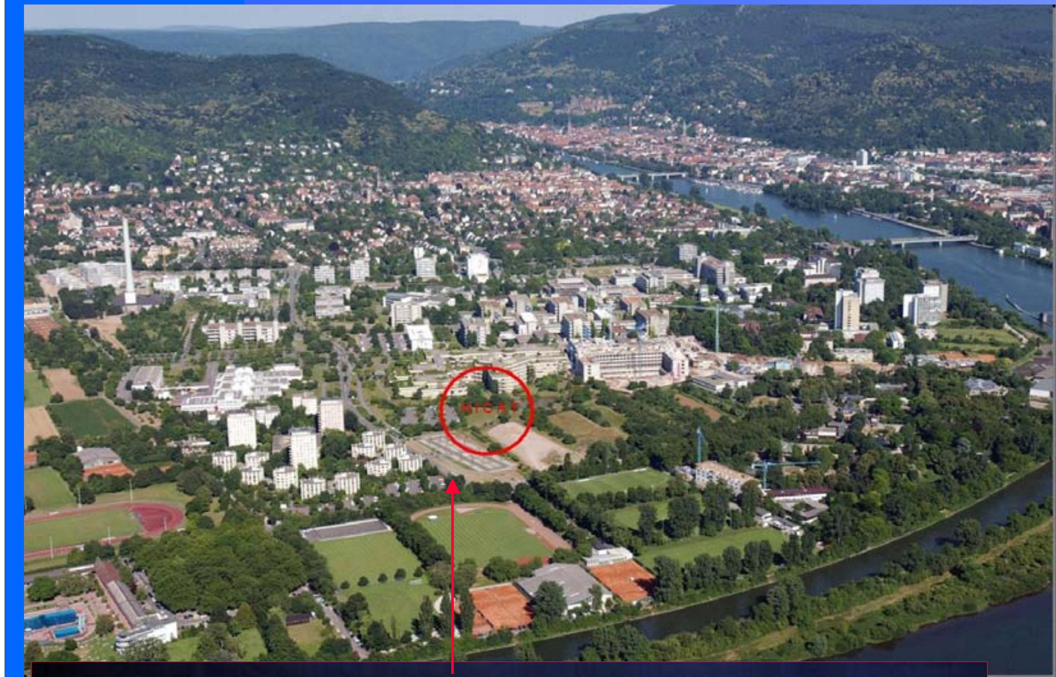
U. Weber

GSI: H. Eickhoff

Th. Haberer

Project started in 2001

The site of HIT



Sept 98 proposal

Dec 02 tendering

Mid 06 pre-clinical operation

<u>Beginning 07</u> <u>clinical operation</u>

Architects Nickl & Partner, Munich and Heidelberg University Building Authority

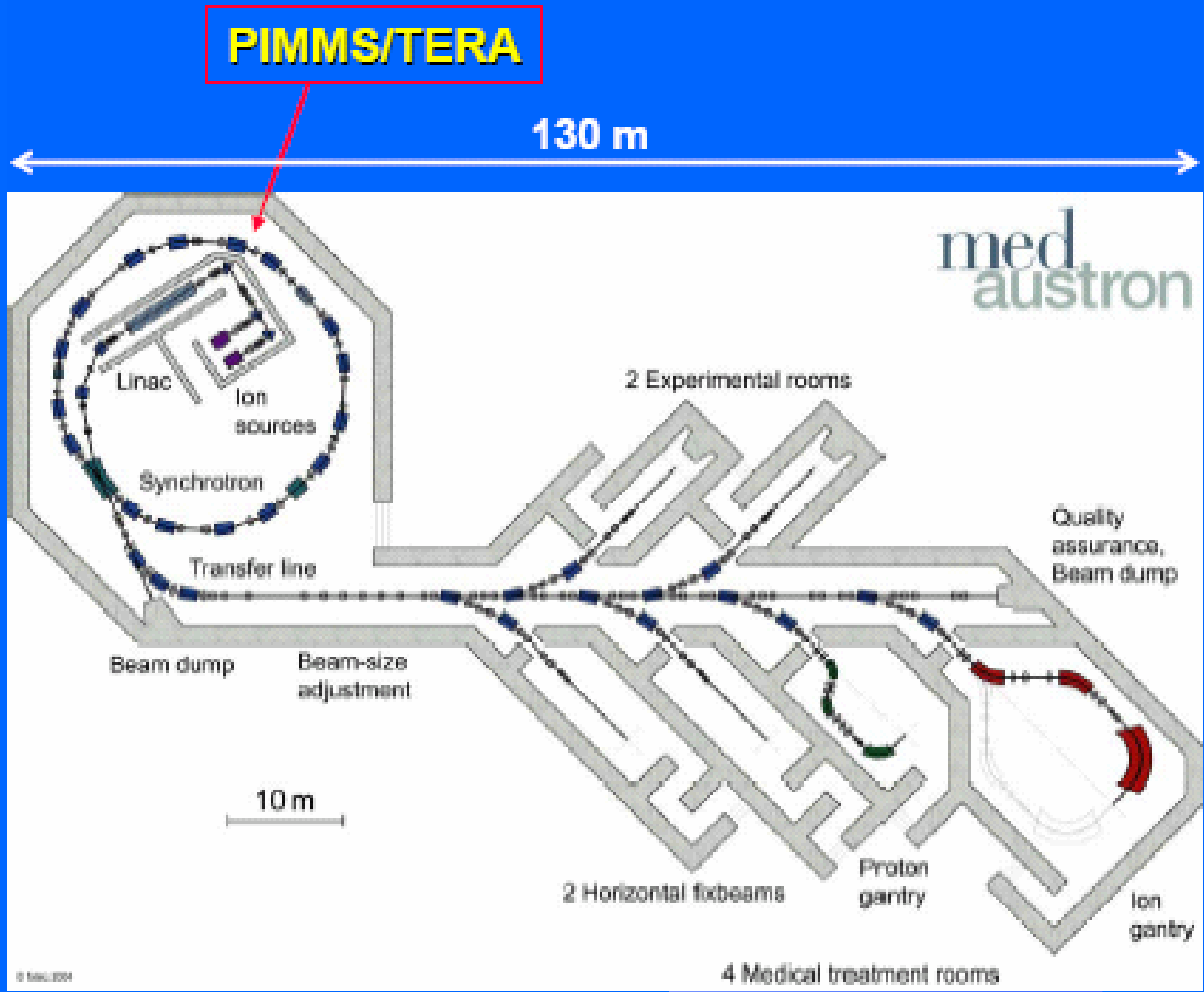
TERA

Other European projects: MedAustron in Wiener Neustadt

Approved in
November 2004

Chairman: R. Pötter

Med. Dir.: T. Auberger
Tech. Dir: E. Griesmeyer



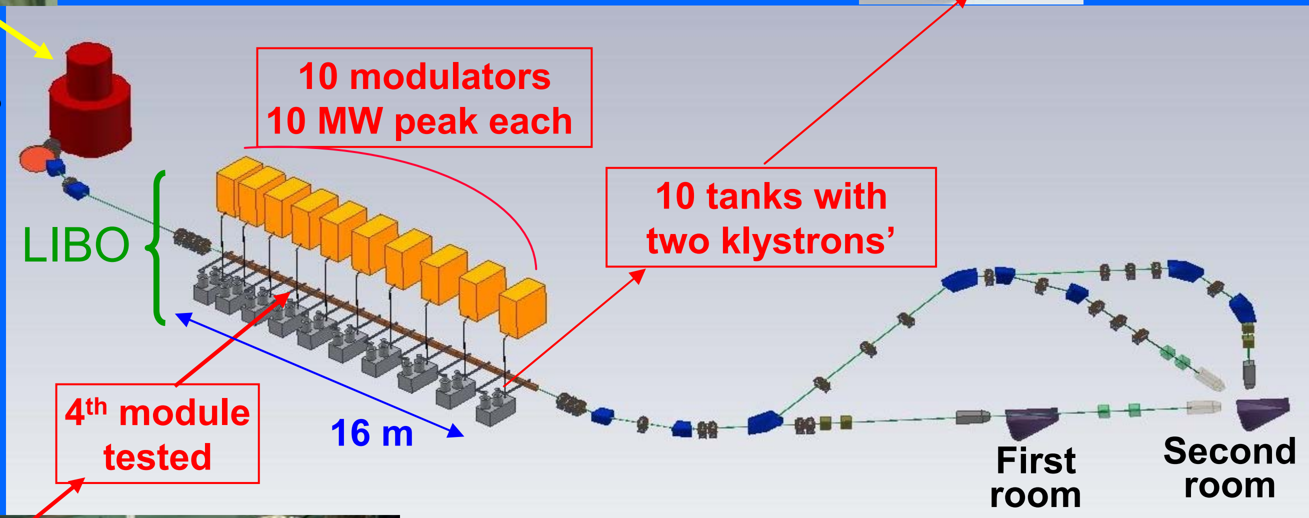
ENLIGHT and the European projects
European Network for LIGHt-ion Therapy

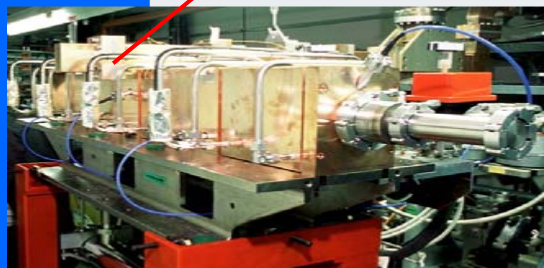
- GSI project for the University of Heidelberg Clinics } in construction
- TERA project for CNAO in Pavia } in construction
- Med-Austron for Wiener Neustadt
  partner of PIMMS since 1996
- ETOILE in Lyon (expects approval in few weeks)
  preliminary design by IN2P3 and CEA based on PIMMS/TERA

  [ASCLEPIOS in Caen in 2004]
- Baltic Centre in Stockholm
  preliminary design by TERA: NIM B184 (2001) 569

At the end: TERA new instrument for hadrontherapy: the cyclinac

IBA Cyclone 30 produces radioisotopes for diagnostics and therapy

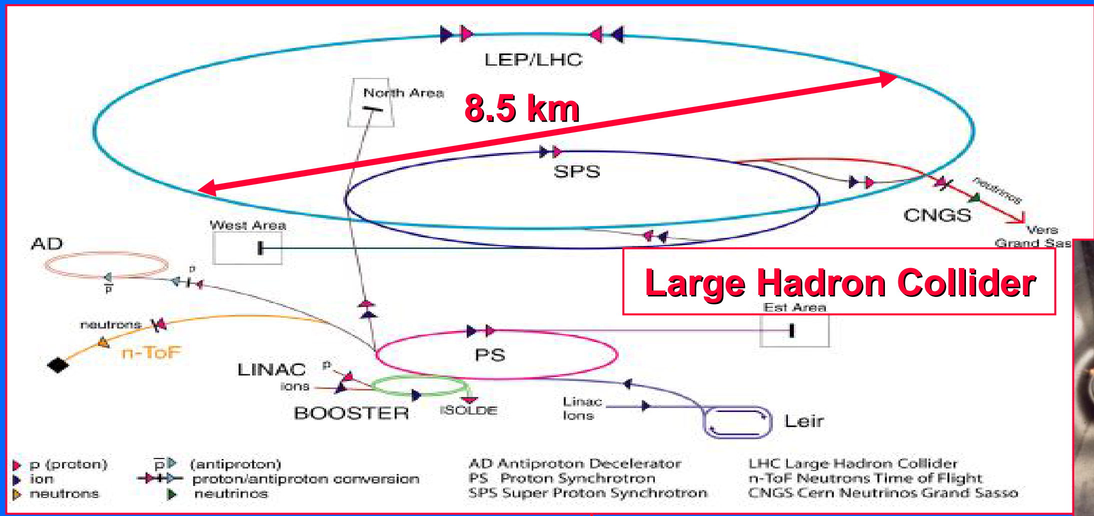




3 GHz

17 MV/m

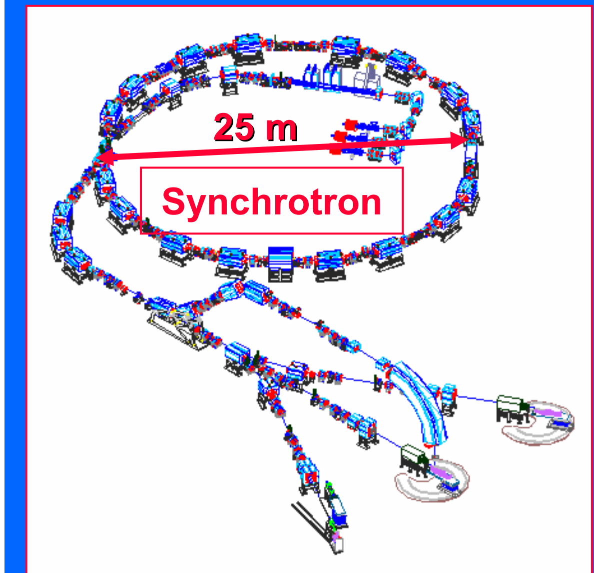
Linear accelerators have a brilliant future!

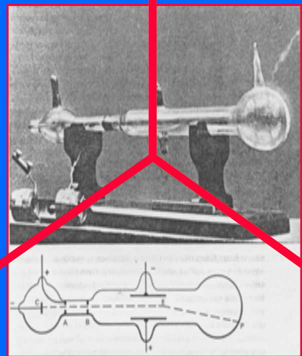


2007 – 110 years later

Research in fundamental physics

2007





1897

Therapy

Diagnostics