Radioterapia Oncologica con protoni:

Aspetti tecnico-scientifici

e

Disponibilità di acceleratori industriali

A.Lombardi

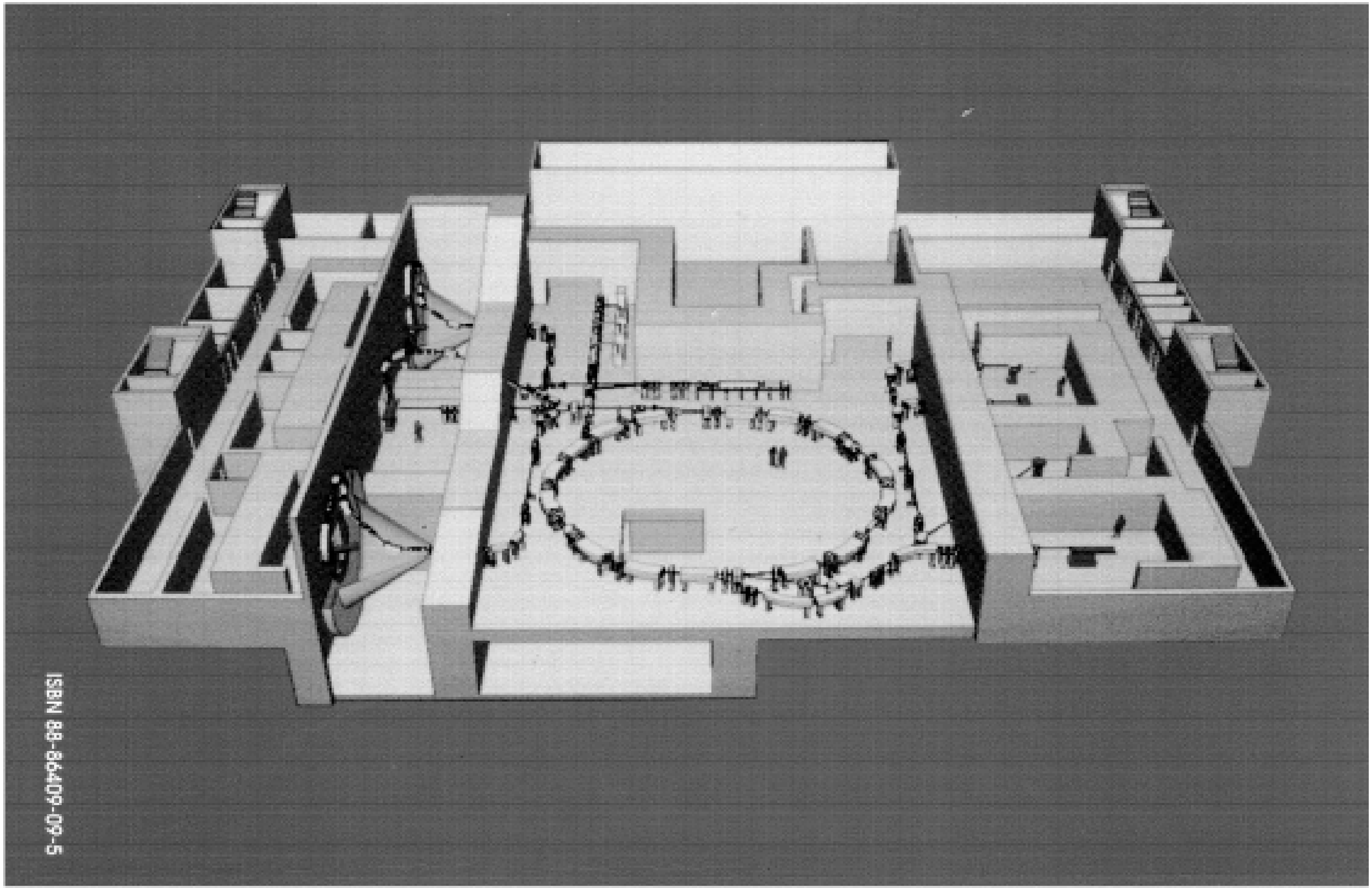
La radioterapia oncologica si pone come risultato la distruzione di cellure tumorali attraverso l'irradiazione della massa tumorale con:

- Fotoni (raggi X da fasci di elettroni)
- Protoni (energia tra 70 e 250 MeV)
- Ioni (fino al carbonio energie fino a 450 MeV/A)

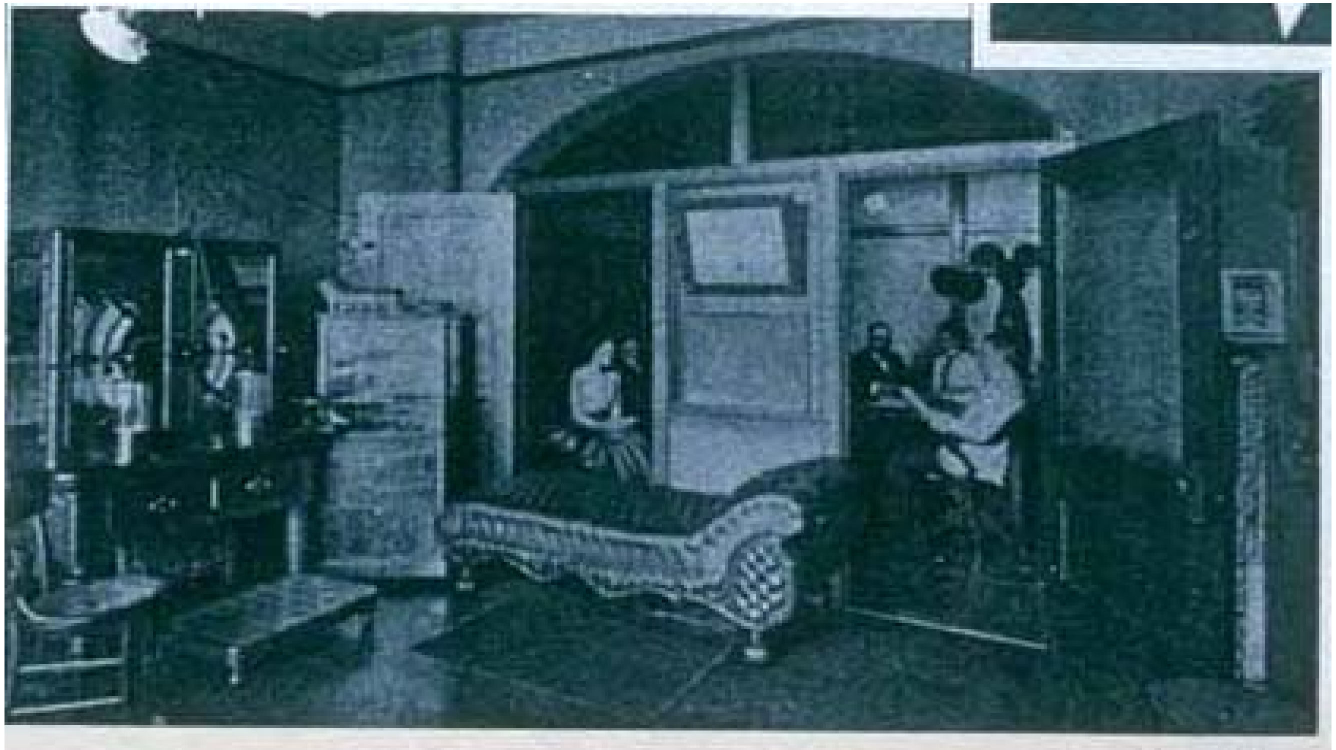
L'utilizzo degli acceleratori per le radioterapia è iniziato negli anni '40-'50

Caratteristiche di un centro di Radioterapia

- Sicurezza (Pazienti, Operatori, Pubblico)
  - Radioprotezione
  - Terapia
  - meccanica
- Affidabilità (>95%)
- Disponibilità
- Efficienza (riduzione dei costi)


ISBN 88-86409-09-5

1895. Röntgen discovers x-rays.



1896. Emil Grubbe, a Chicago electrician and metallurgist, first treated the recurrent breast cancer of a 55-year-old woman in the last days of January 1896--only weeks after the announcement of Roentgen's discovery.

1897. Note that the eyes are shielded for protection.

La radioterapia “convenzionale” utilizza acceleratori lineari di elettroni per la produzione di fasci di raggi x.

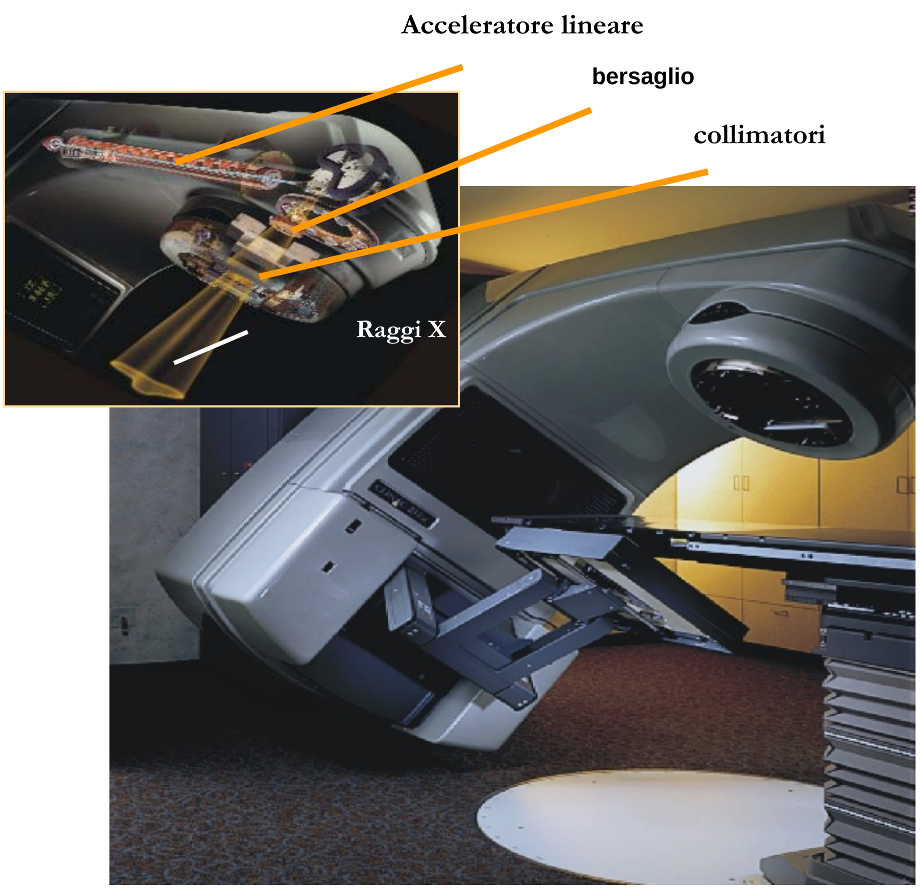


Figura 1: Una tipica moderna unità di trattamento con raggi X. (cortesia di Varian Medical Systems).

Questa tecnica può essere utilizzata anche per fare una terapia conformazionale.

Una distribuzione di dose che, utilizzando numerosi fasci da varie angolazioni e particolari schermi ad apertura variabile, segue la geometria del tumore.

Ultima nata IMRT (Intensity Modulated RT)

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 ... part, been due to the very short ...ation in tissue of protons, deut... particles from prese... ...er-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 ...

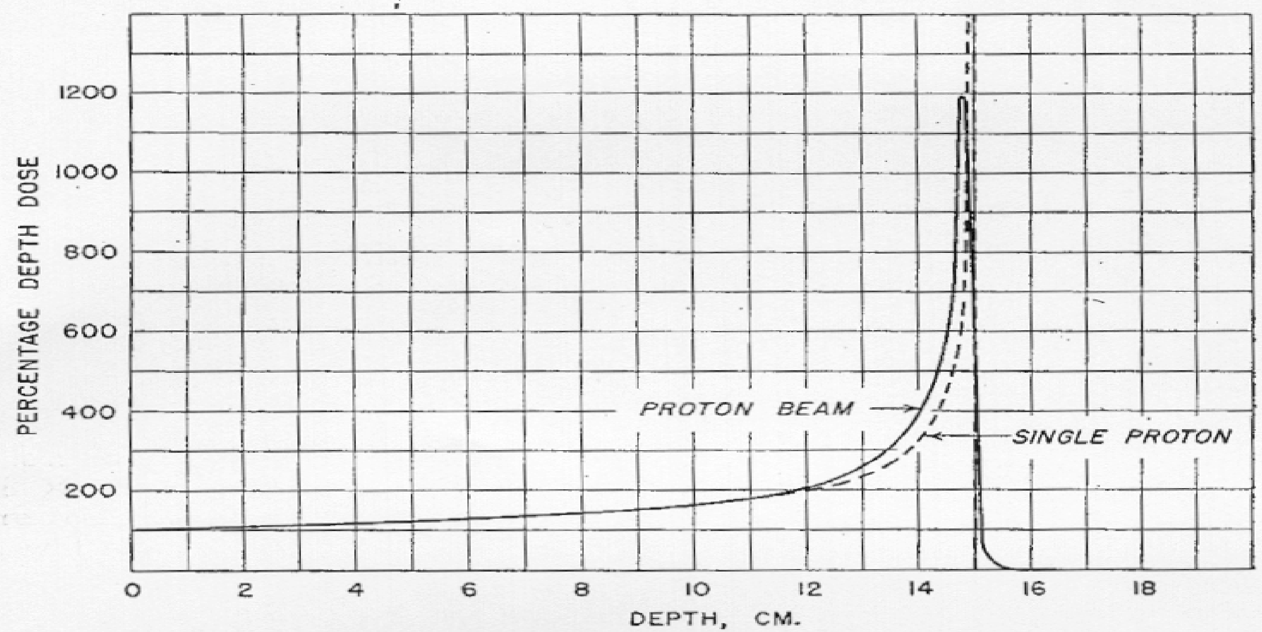
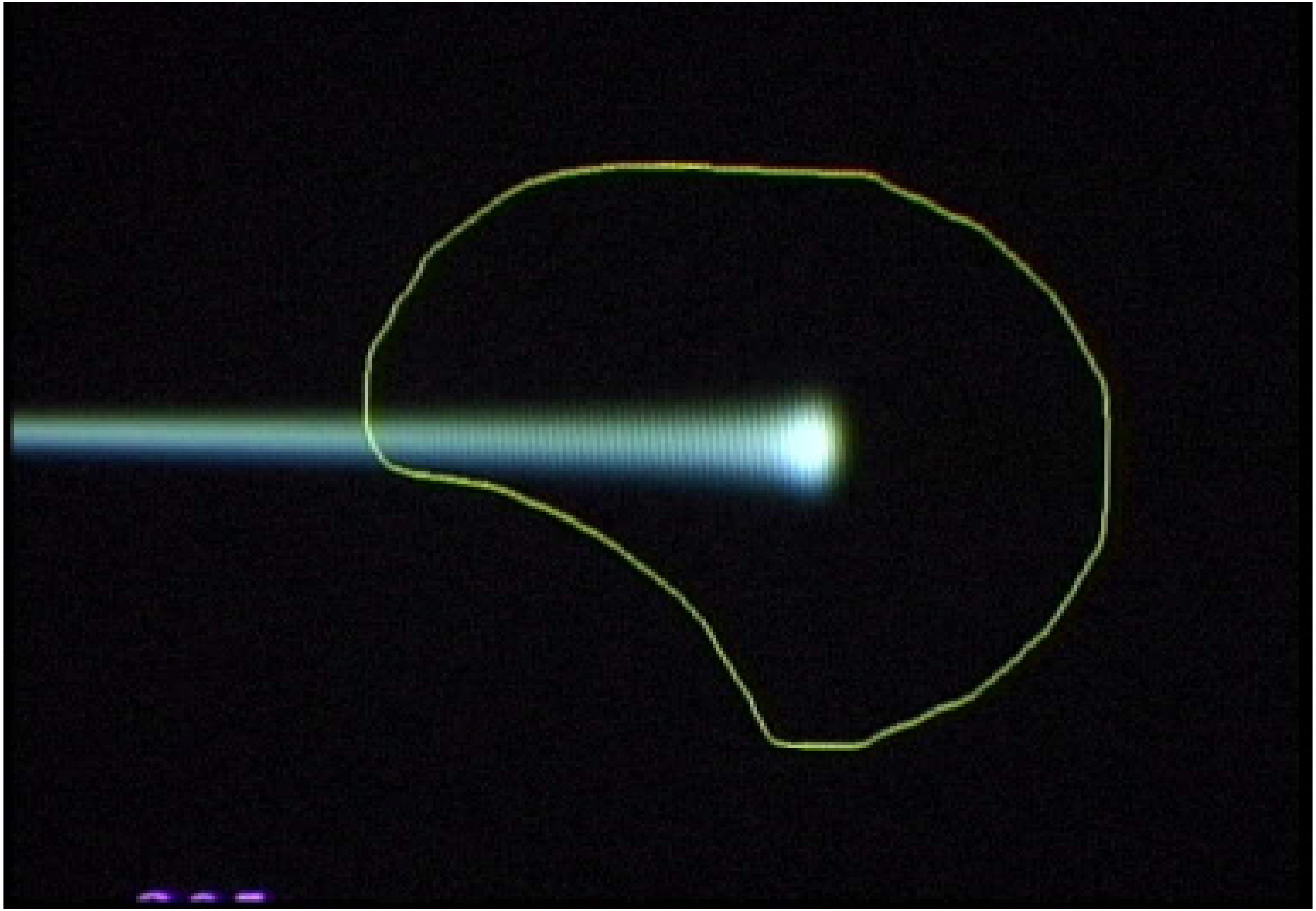
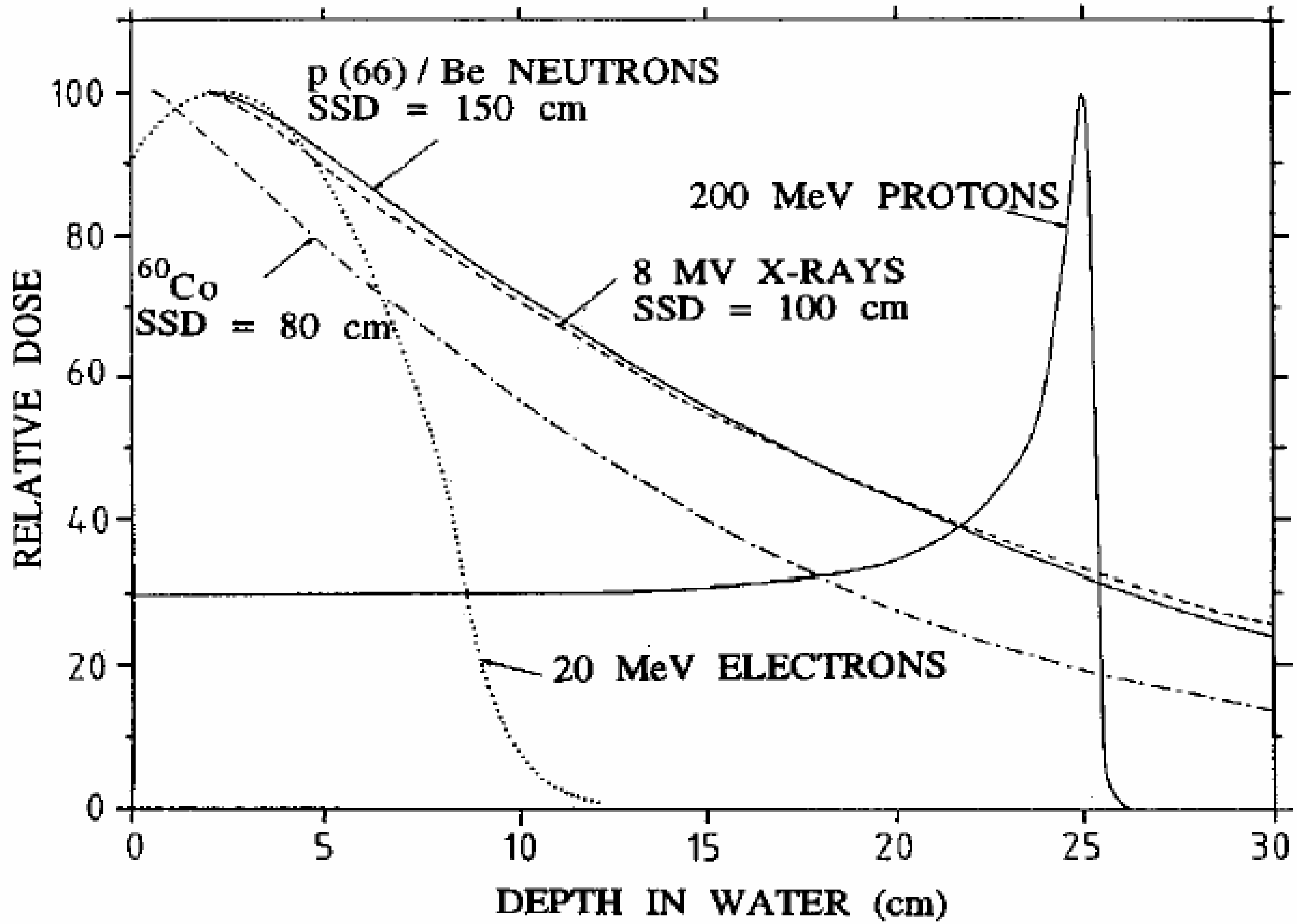
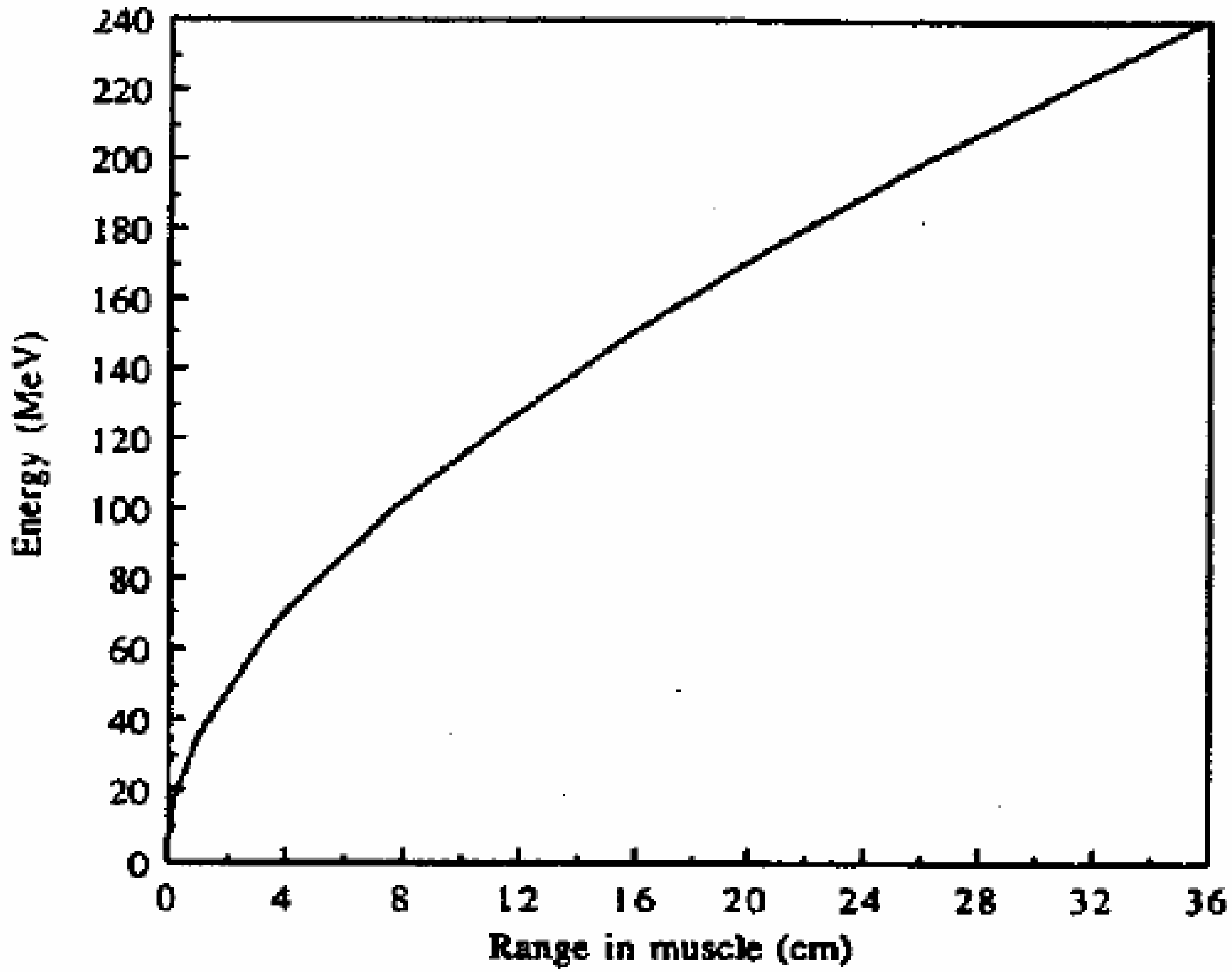


Fig. 2. The dotted curve shows the relative dose due to a single 140 Mev proton. The full curve shows qualitatively the depth dose curve for a beam of 140 Mev protons in tissue.




p (66) / Be NEUTRONS
SSD = 150 cm
200 MeV PROTONS
^{60}Co
SSD = 80 cm
8 MV X-RAYS
SSD = 100 cm
20 MeV ELECTRONS
RELATIVE DOSE
DEPTH IN WATER (cm)
0
20
40
60
80
100
0
5
10
15
20
25
30



Profondità di penetrazione di fasci di protoni in tessuto muscolare in funzione dell'energia

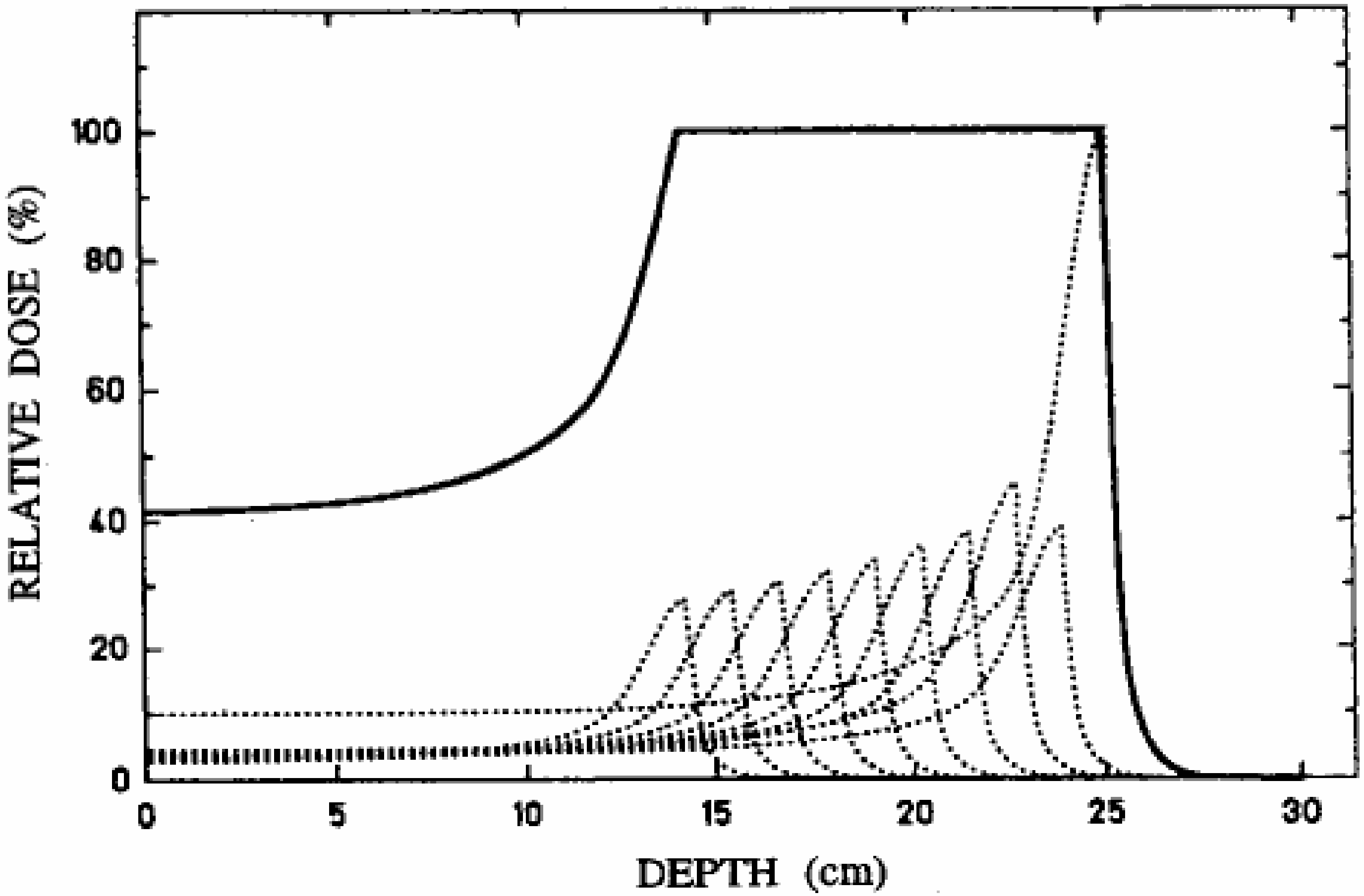


Fig. 1.11 *Un picco di Bragg allargato (SOBP) è ottenuto come sovrapposizione di molti picchi al variare dell'energia degli ioni [2.7]. I protoni mostrano un comportamento simile e lo SOBP si ottiene allo stesso modo.*

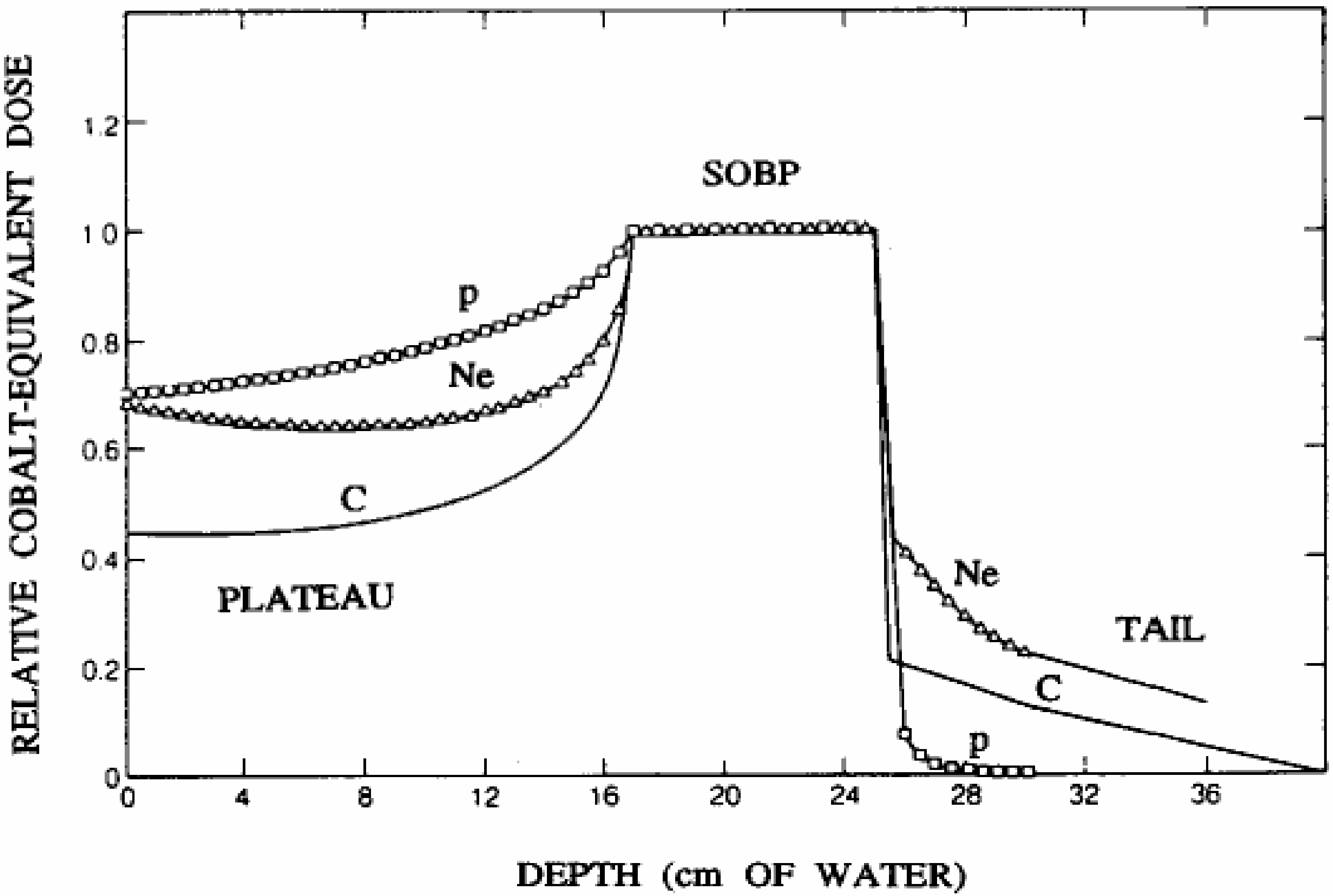
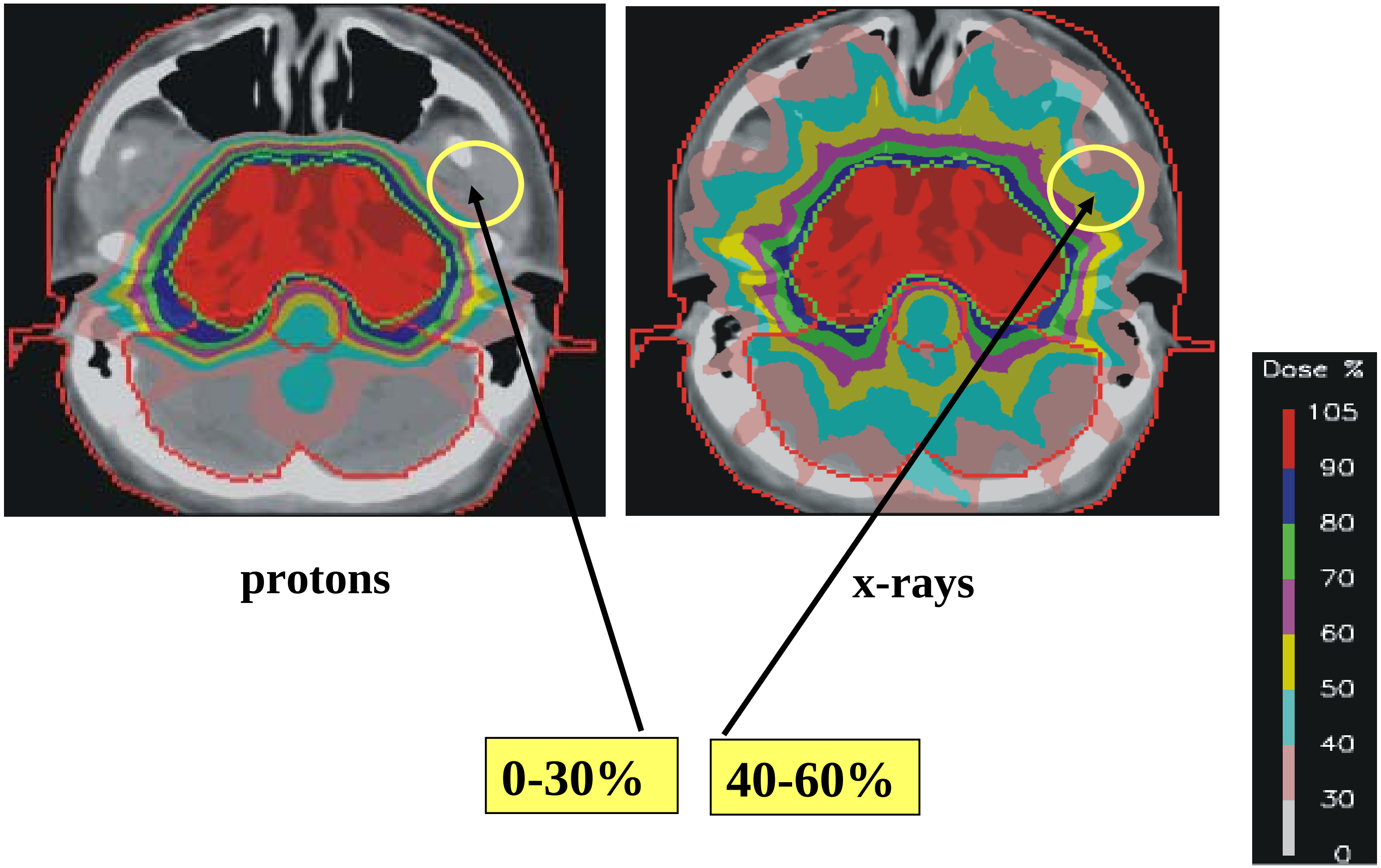


Fig. 1.13 Picco di Bragg allargato per fasci di protoni e ioni aventi lo stesso percorso [6.19].

Intensity Modulated Radiation Therapy (IMRT) with four proton beams



Slide courtesy of
Tony Lomax, PSI

Specifiche di massima

- Fascio stabile in energia (0,4MeV protoni corrispondono a 0,2cm in acqua).
- Fascio ben definito in sezione trasversa penombra non superiore a 2 mm in ogni direzione (80%-20%).
- Fascio posizionato con la precisione del mm sul paziente.
- Possibilità di modulare in energia
- Possibilità di modulare in intensità

	Clinical requirement	Dependence on
Beam range in patient	2 - 20 gr/cm2 continuously adjustable	energy: 180 Mev + 20 (?) Mev accounting for energy loss in the spreading devices to obtain a 20 x 20 cm2 field with a throw of 3 m.
Range modulation	continuously adjustable	-
Range adjustment	continuously adjustable	-
Field size	20 x 20 cm2	beam spreading beam intensity
Dose rate large fields small fields	 > 2 gy/min. >> 10 gy/min.	 beam intensity beam intensity
Field homogeneity longitudinal orthogonal	 ≤ 111% ≤ 105%	 beam spreading beam delivery system
Field simmetry	≤ 105%	beam spreading beam delivery system
Do/Dmax		energy of the beam spread of energy sad
Lateral penumbra	< 2 mm at entrance	multiple scattering spreading devices source site, sad
Distal fall-off	< 2 mm	range straggling (energy) spread of energy - sad

sad = source to axis distance

Tabella 8.3 *Richieste cliniche che hanno influenza sulla modulazione di energia (SOBP - Spread Out Bragg Peak).*

Modulazione per grandi campi	2 - 25 g/cm^2
Modulazione per trattamenti occhio	2.5 - 3.2 g/cm^2
Modulazione per trattamenti testa-collo	2 - 10 g/cm^2
Variazione dell'estensione SOBP	0.2 cm per SOBP ≤ 5 cm 0.5 cm per SOBP > 5 cm
Variazione della posizione SOBP	0.2 cm per SOBP ≤ 5 cm 0.3 cm per SOBP > 5 cm 0.1 cm per trattamenti oculari (con assorbitori meccanici)

Unità di misura della penetrazione in g/cm^2 perchè è data da:

$$\rho \times \Delta l ; \left[\frac{g}{cm^3} * cm \right]$$

ρ densità del materiale

Δl *profondità di* penetrazione del fascio

$$\frac{g}{cm^2} \Rightarrow cm$$

cm di acqua equivalente

Centro di Loma Linda

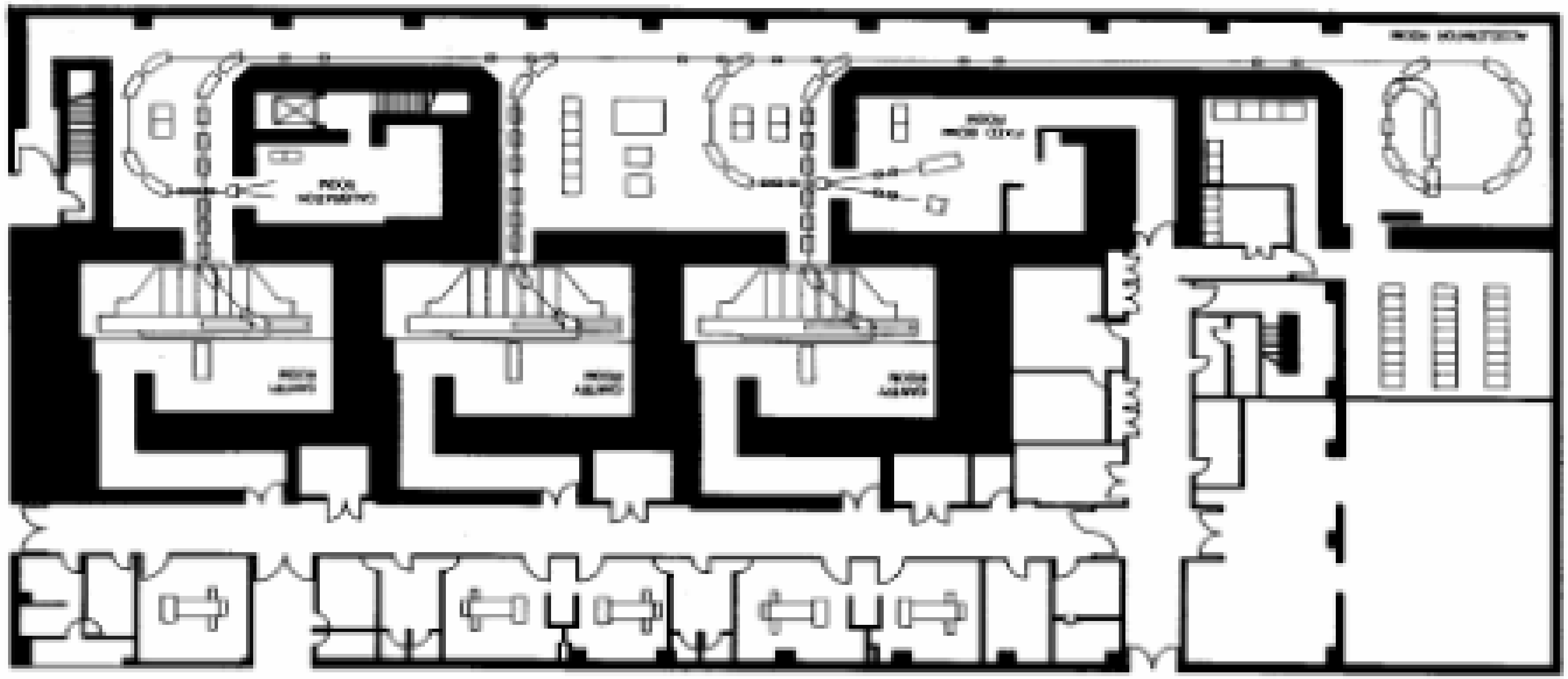
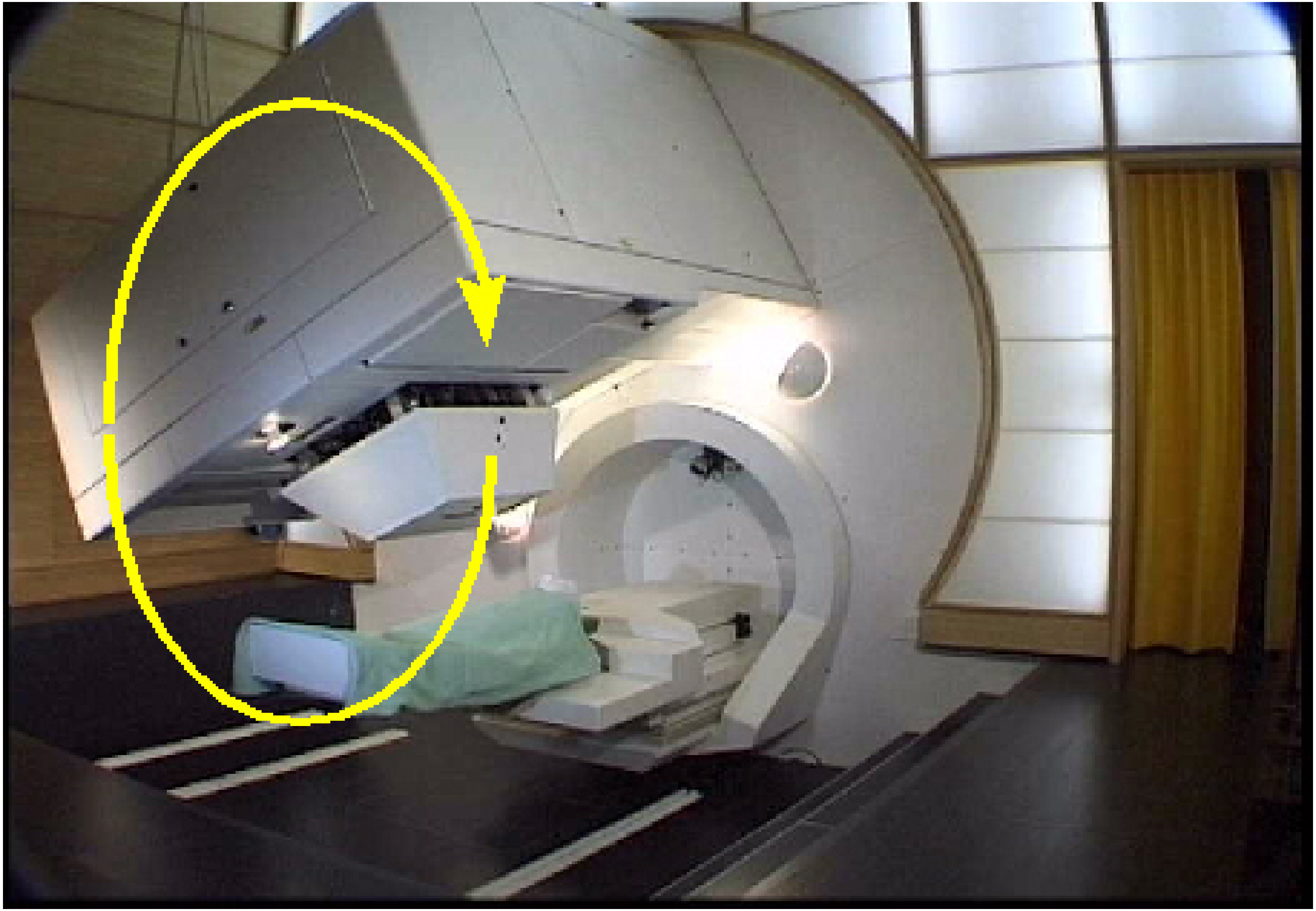
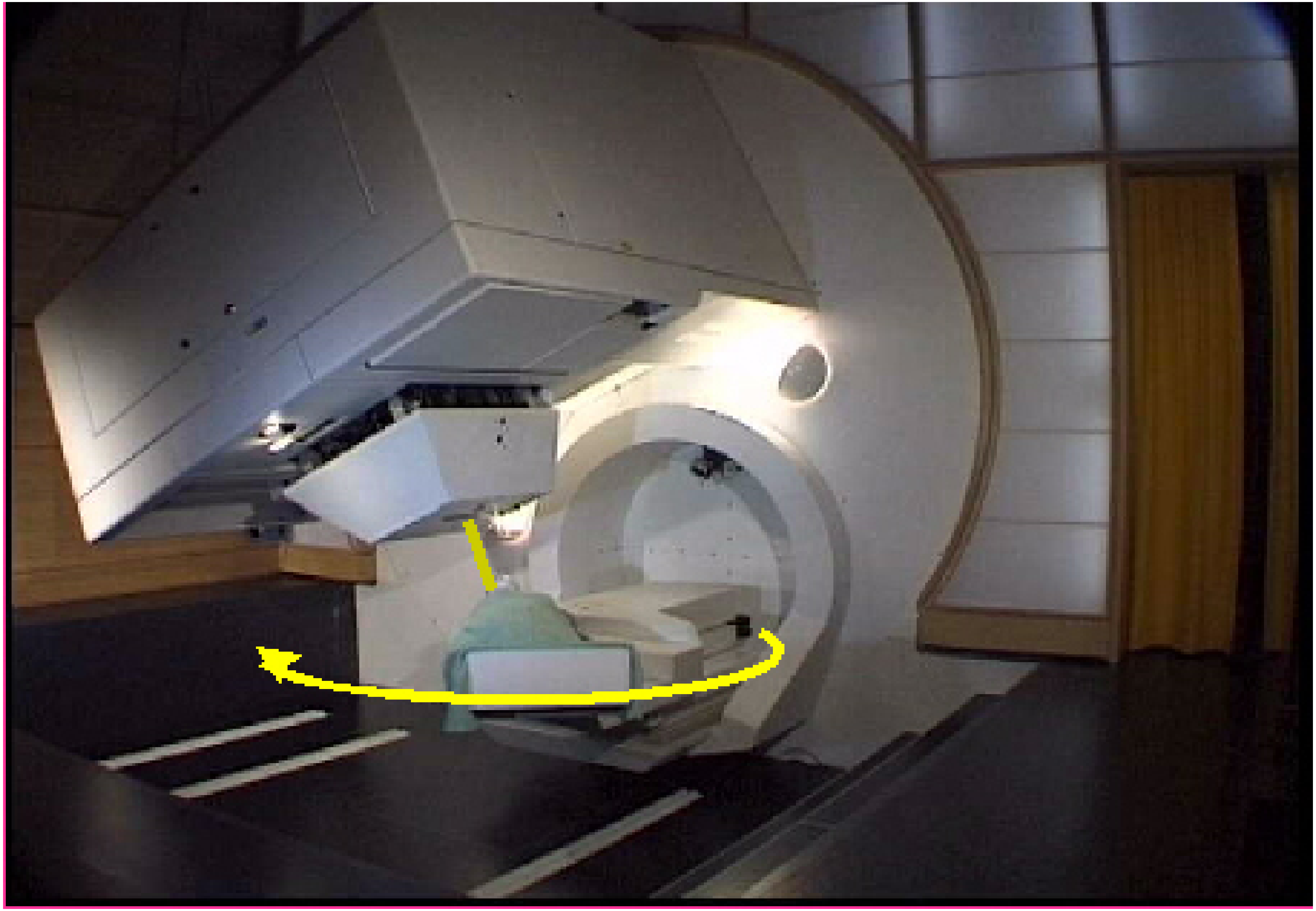
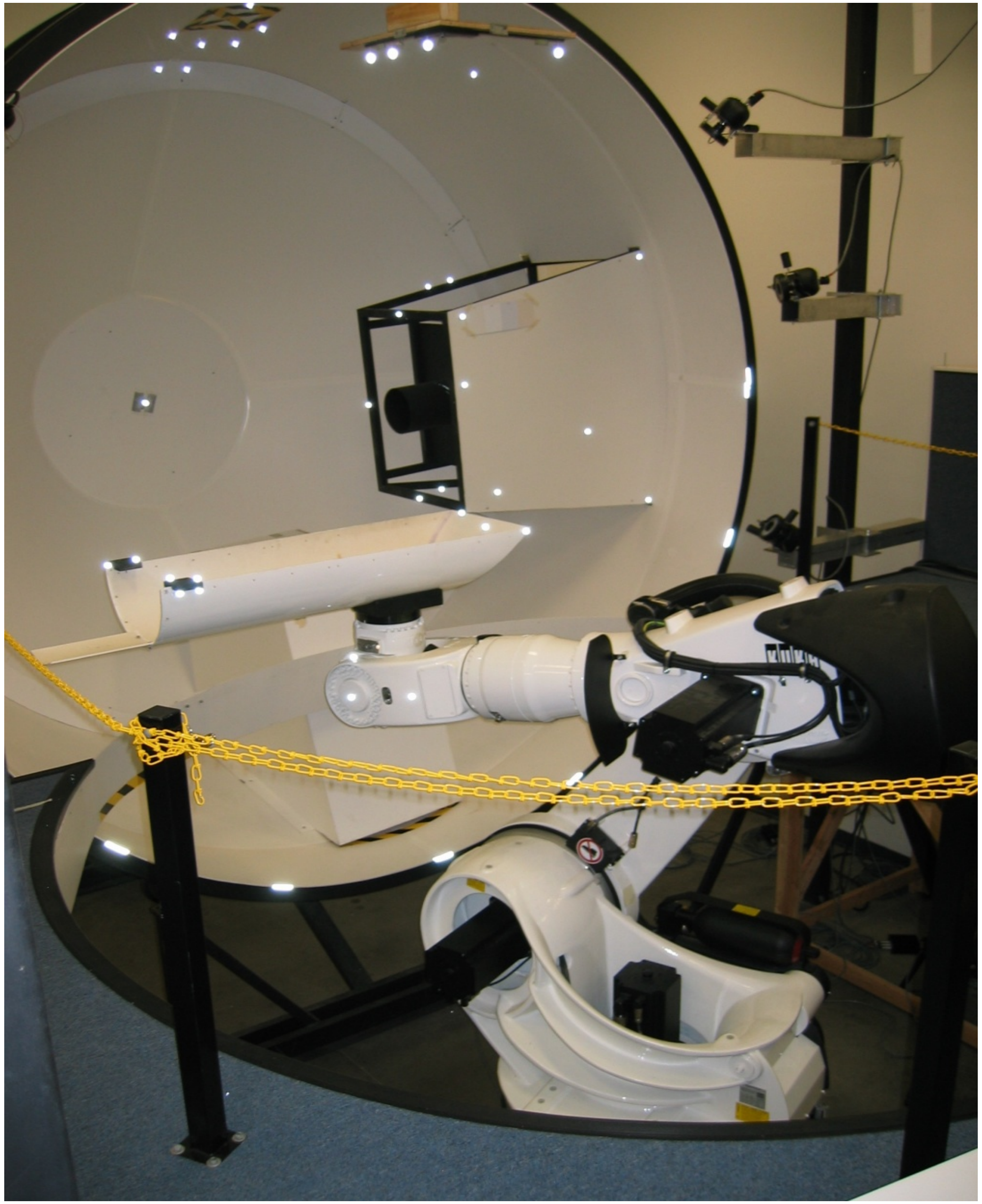


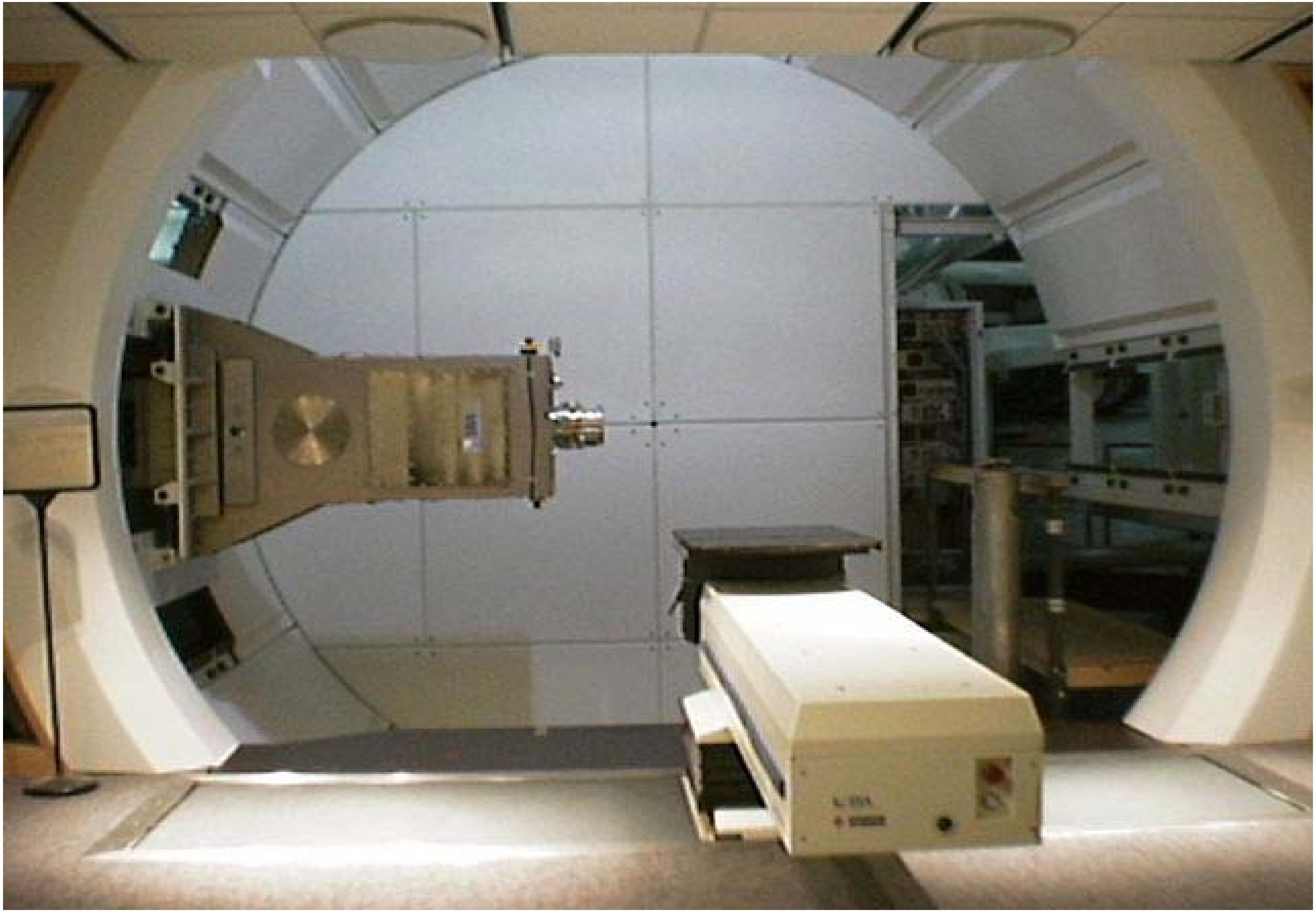
Figura 4: ***a sinistra-****la grande camera isocentrica presso lo MGH di Boston (cortesia di IBA);* ***a destra****-camera rotante compatta sviluppata ed in uso presso l'Istituto Paul Scherrer in Svizzera (cortesia di PSI)*







Per il posizionamento del paziente sulla linea del fascio c’è bisogno di un “posizionatore automatico” con 6 gradi di libertà (tre posizioni e tre angoli).
La movimentazione è ancora oggetto di ricerca e sviluppo.



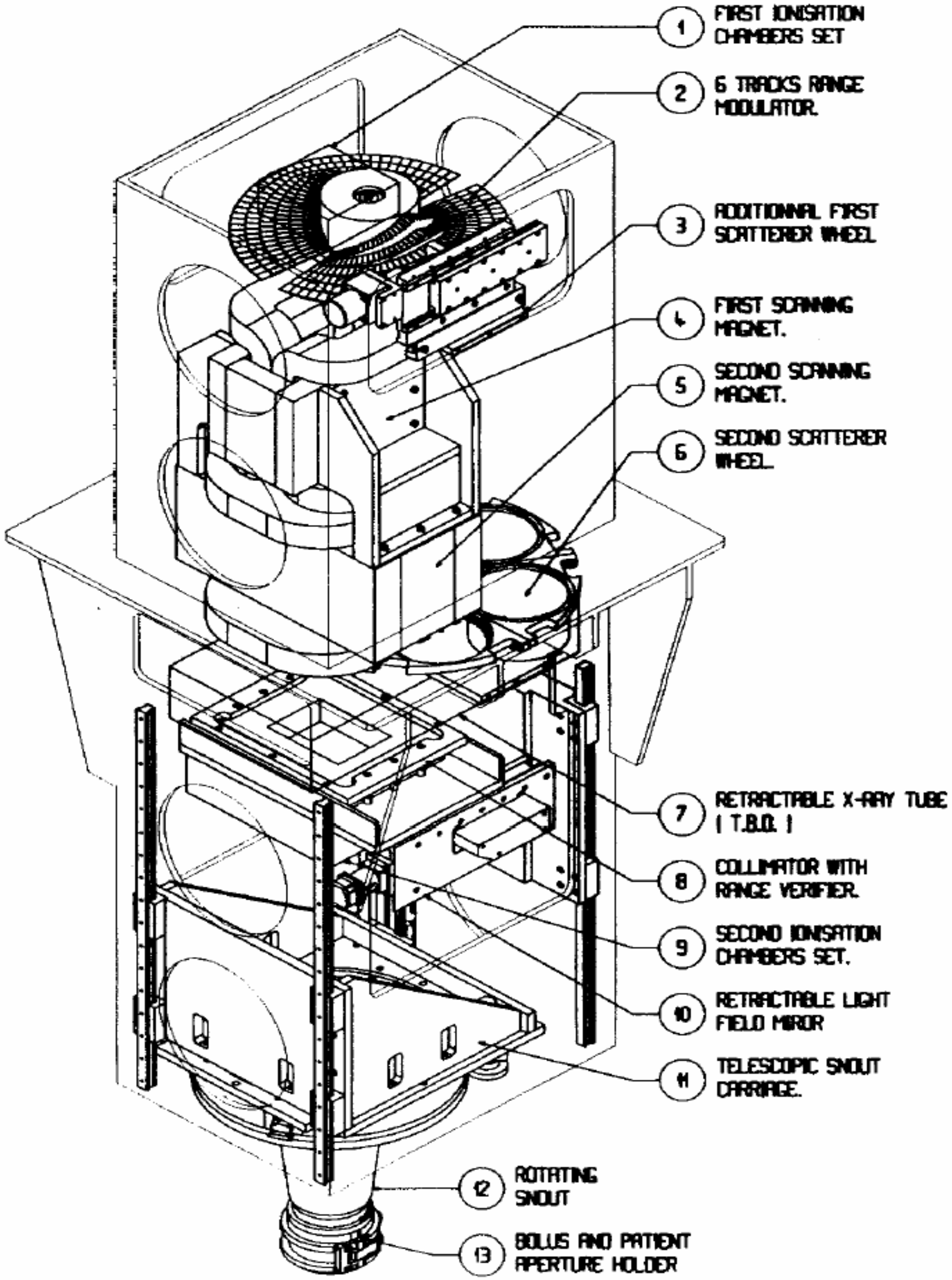
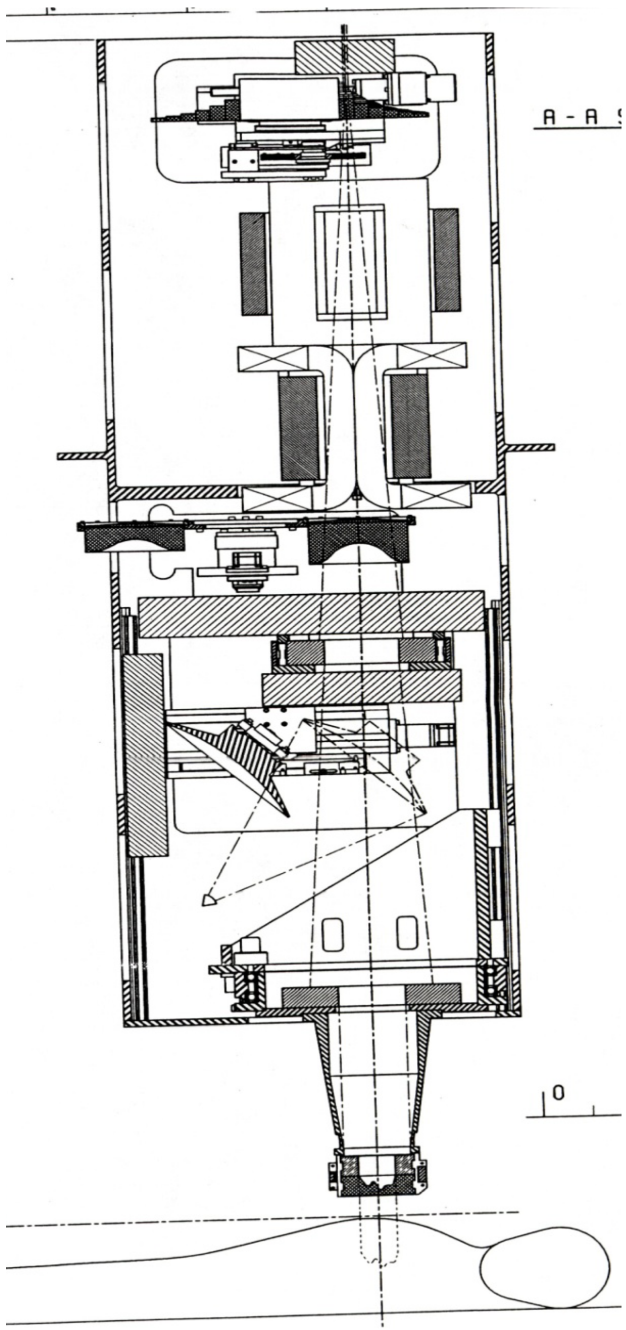


Fig. 11.14 The nozzle designed by IBA.



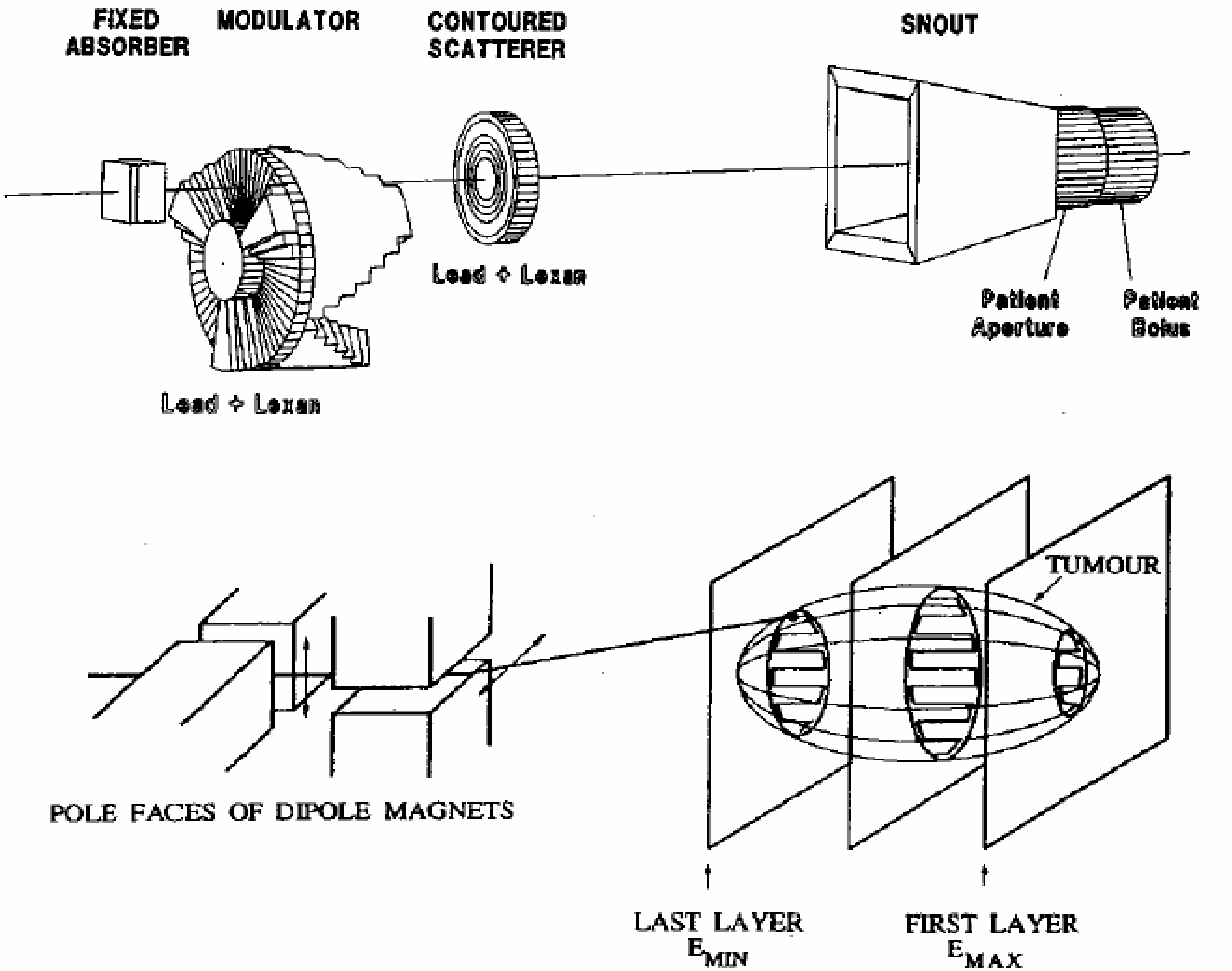
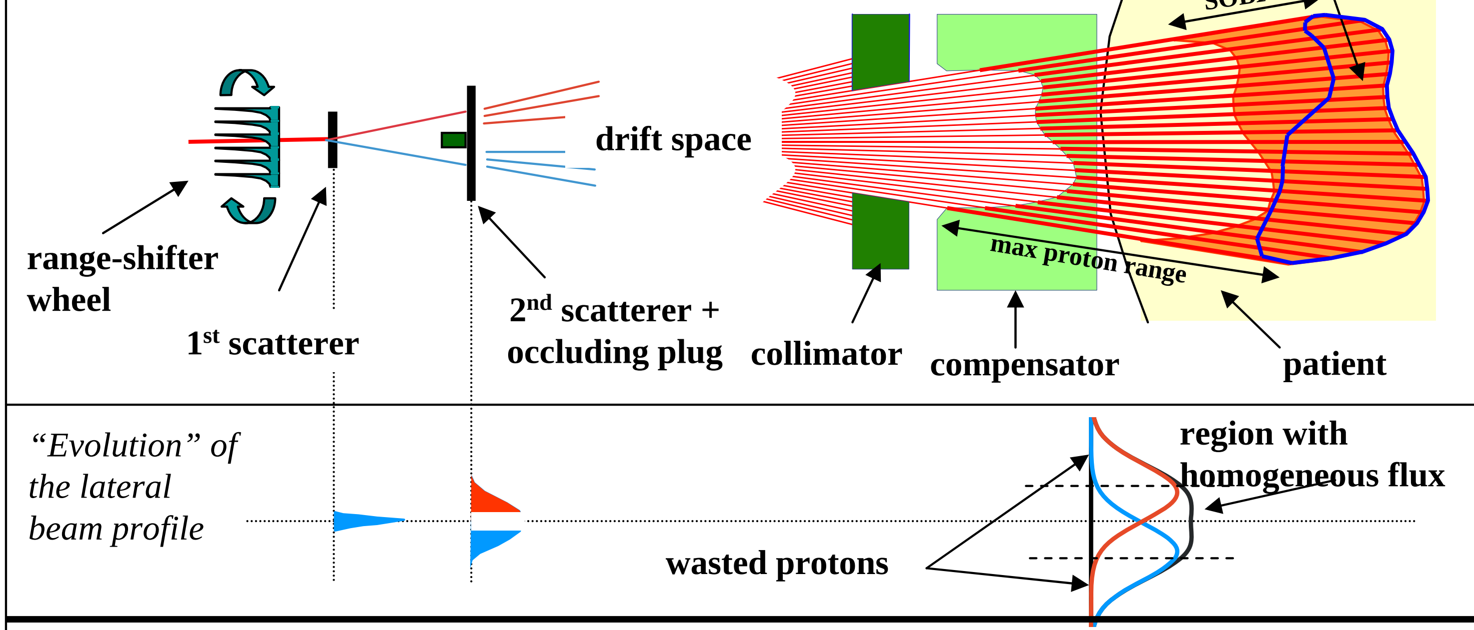


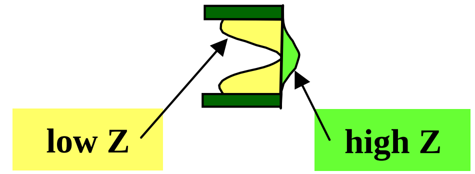
Fig. 1.5 Comparison between the working principle of a "passive" and "active" beam spreading system.

a) Passive scattering

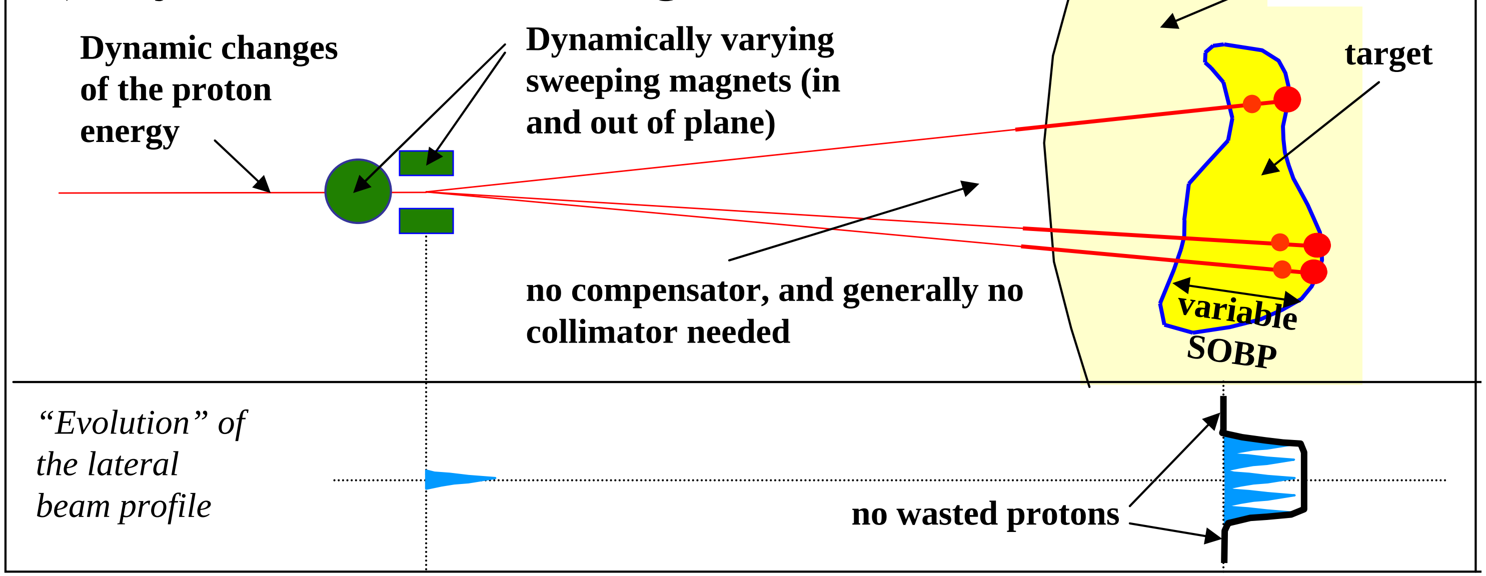


Options

- use ridge filter instead of range-shifter wheel
- use contoured two-component second scatterer (~ twice as efficient):



b) Dynamic beam scanning



Options

- use mechanical, rather than magnetic, scanning for slowest motion
- use fast-acting range shifter before patient, instead of energy variation
- discrete "spots" or continuous sweep
- modulate intensity, scan speed or both

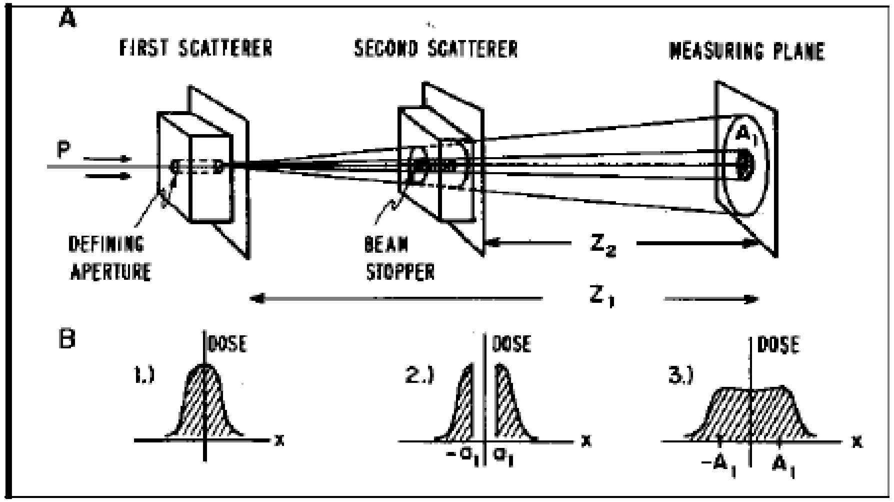


Figure 14.1: Double scattering with a beam stopper [64].

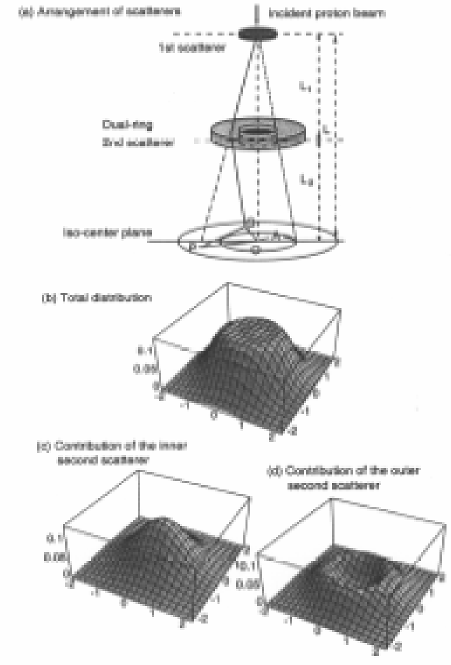


Figure 14.3: Double scattering with dual-ring scatterer [72].

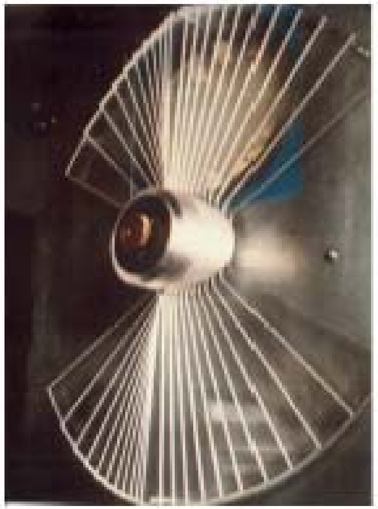


Figure 12.1: A downstream modulator.

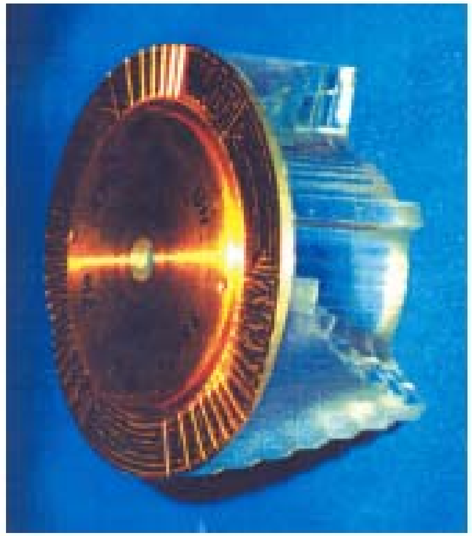
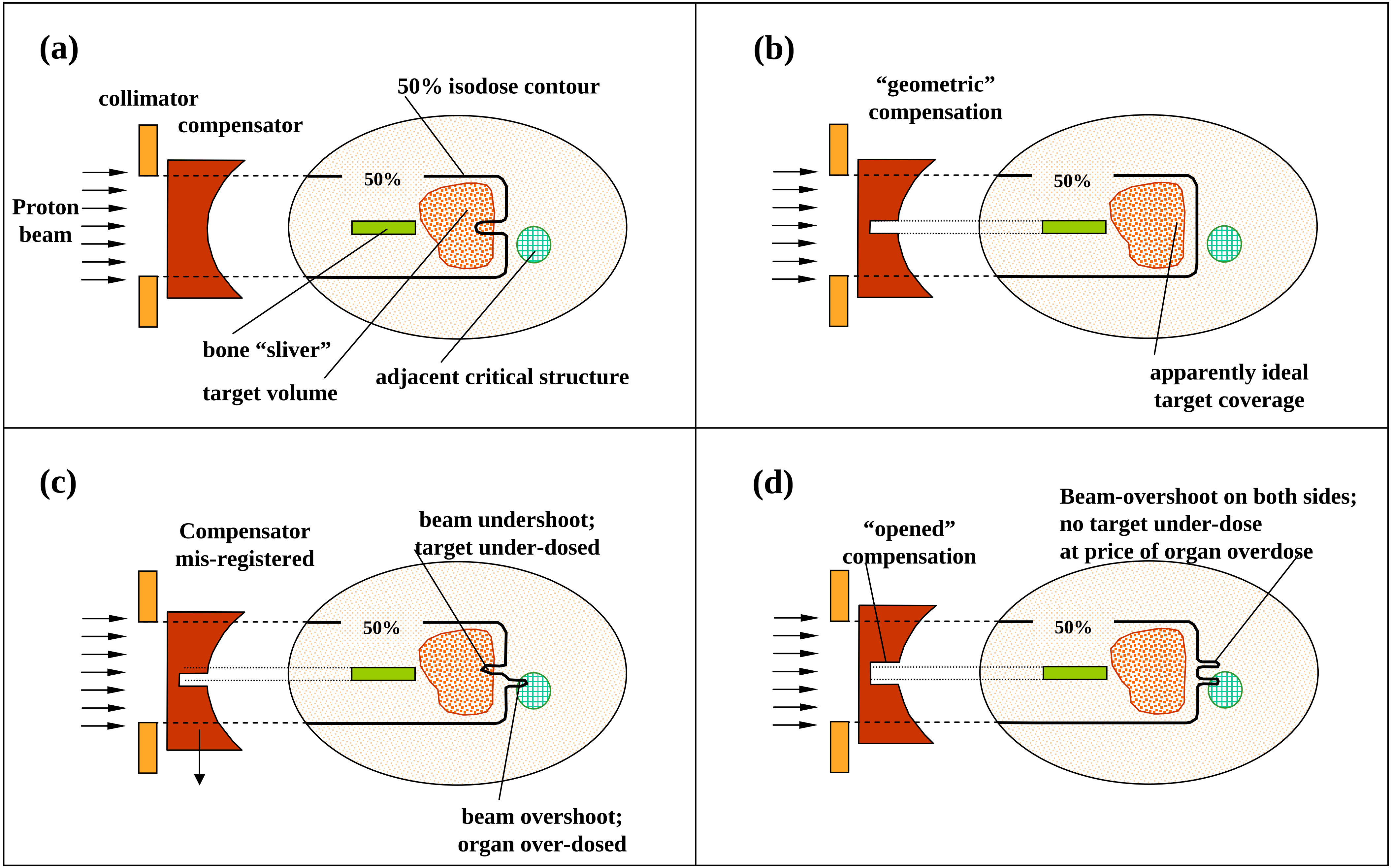


Figure 12.2: A compensated upstream modulator.


(a)
collimator
compensator
50% isodose contour
Proton beam
50%
bone “sliver”
target volume
adjacent critical structure
(b)
“geometric” compensation
50%
apparently ideal target coverage
(c)
Compensator mis-registered
beam undershoot; target under-dosed
50%
beam overshoot; organ over-dosed
(d)
“opened” compensation
Beam-overshoot on both sides; no target under-dose at price of organ overdose
50%

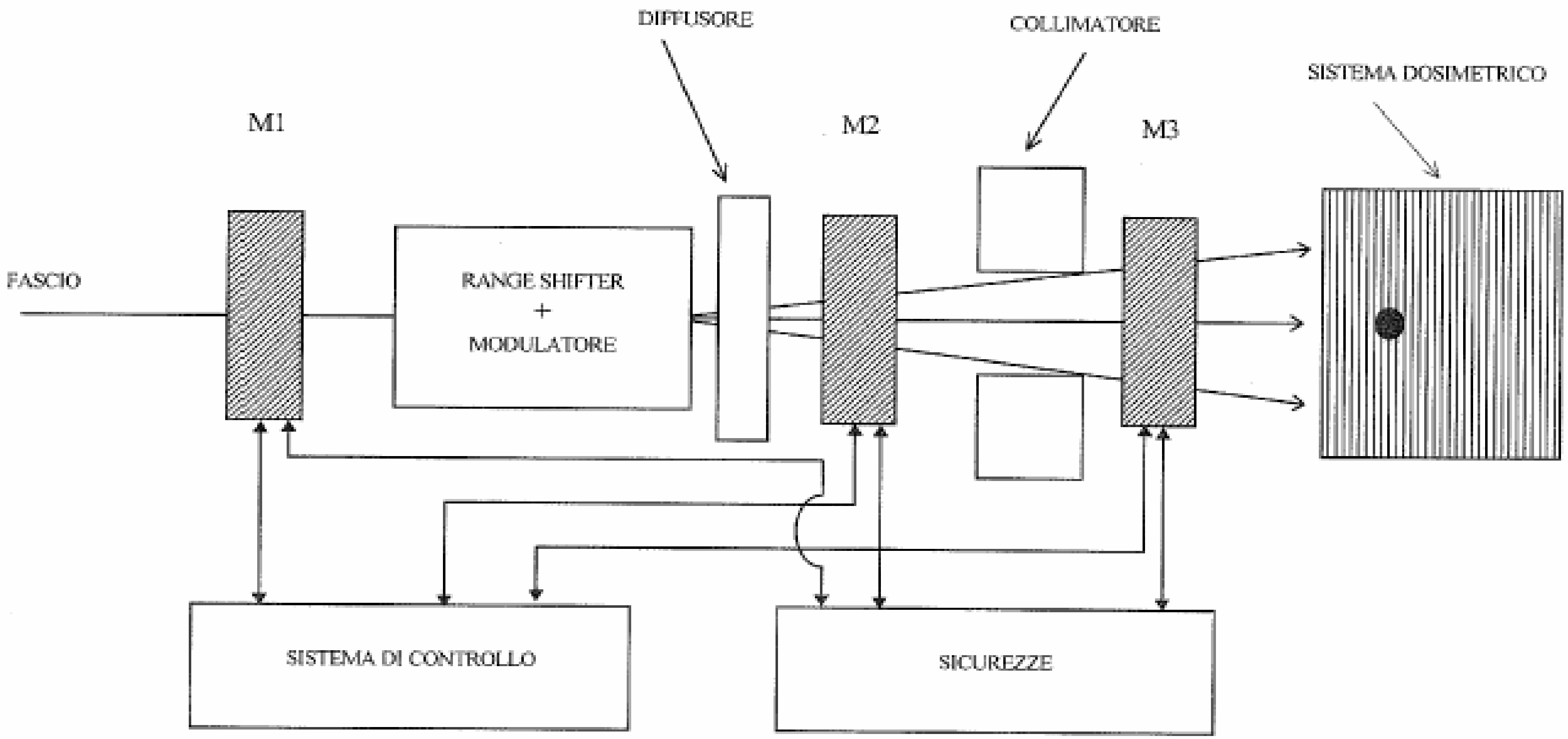


Fig. 9.2 *Sistema di monitoraggio del fascio: M1, M2, M3 sono i punti di monitoraggio.*

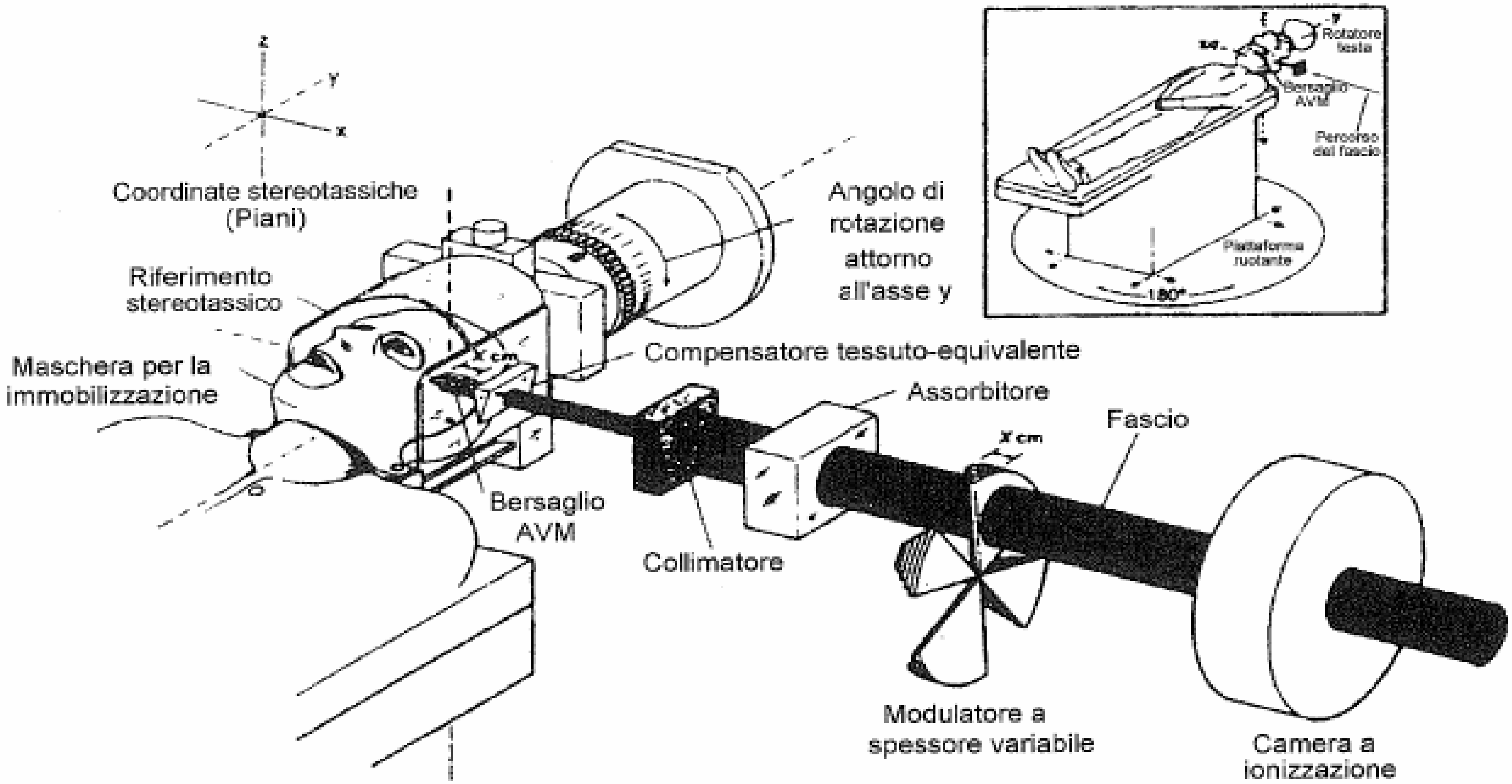


Fig. 3.9 I primi trattamenti con ioni sono stati effettuati a partire dal 1975 presso il Bevalac di Berkeley (California) con la strumentazione qui rappresentata. L'energia del fascio era fatta variare in modo passivo mediante assorbitori.

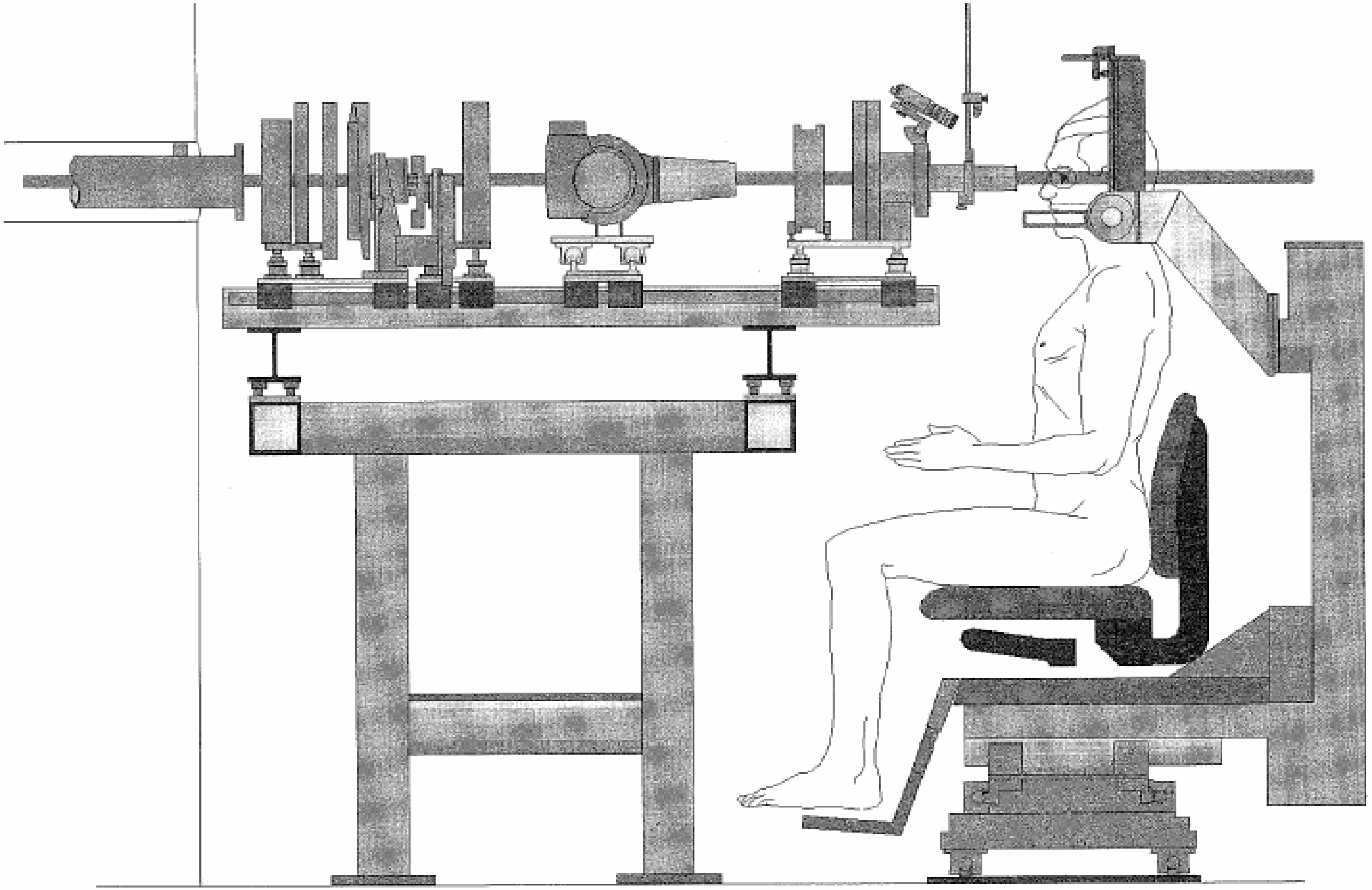
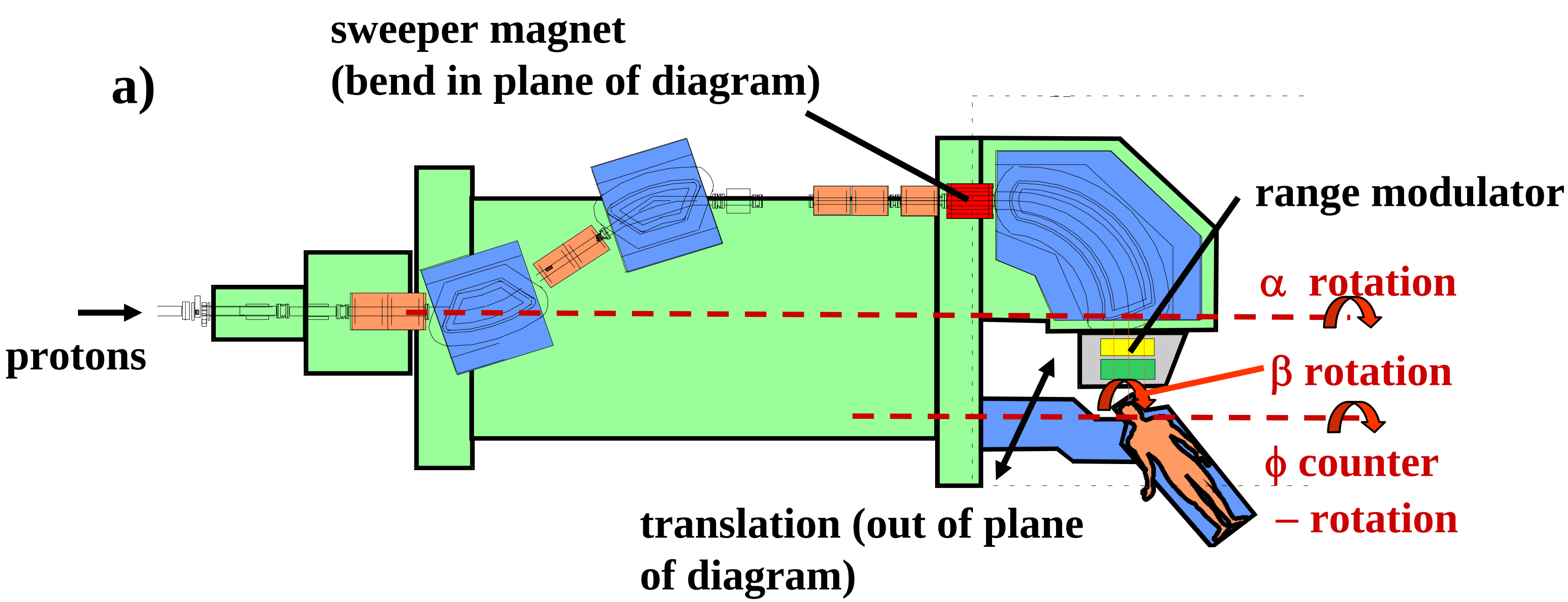
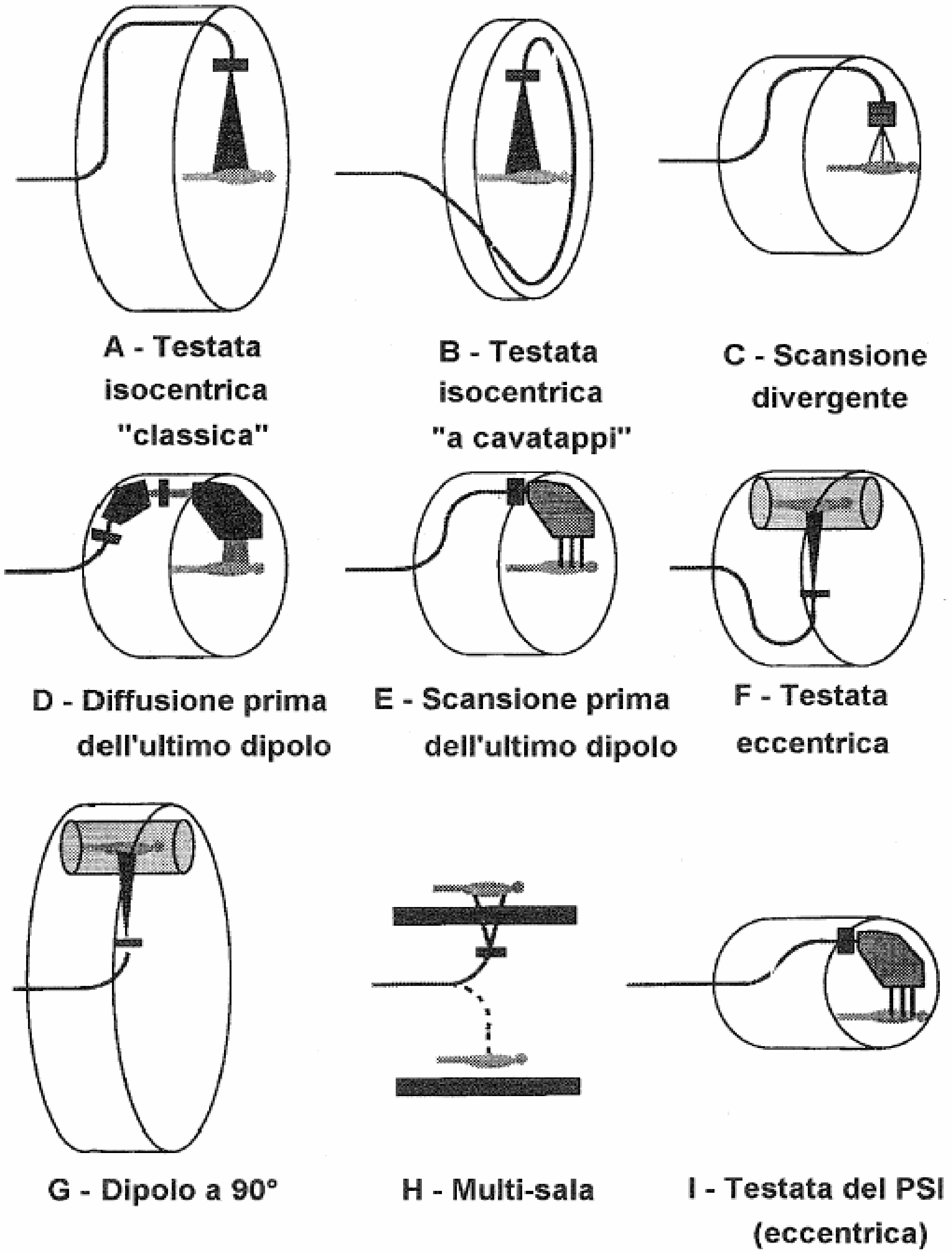


Fig. 8.9 Tratto terminale della linea e sedia utilizzata presso i laboratori TRIUMPH.

a)


sweeper magnet
(bend in plane of diagram)
range modulator
α rotation
β rotation
φ counter
– rotation
protons
translation (out of plane
of diagram)

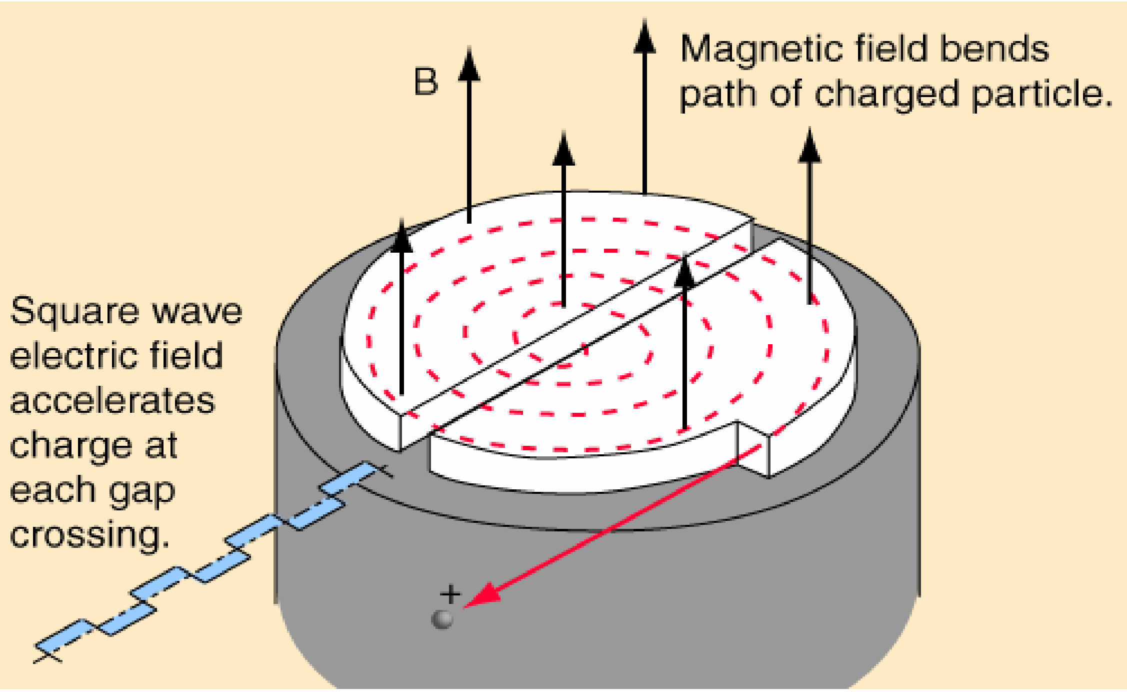
b)

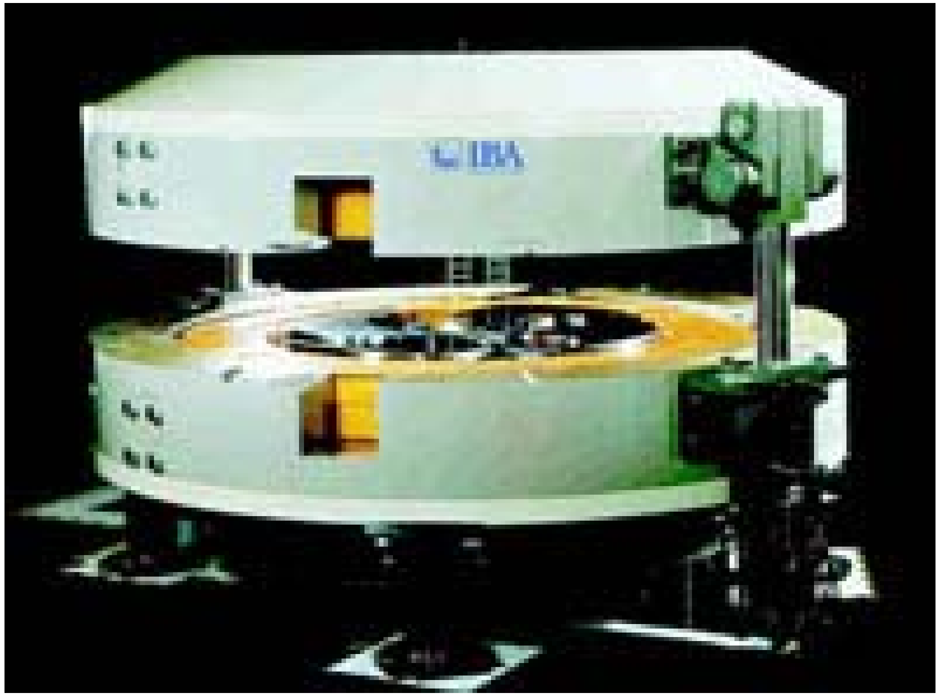


Vari tipologie di testate Rotanti dette “Gantry”

Specifiche di massima

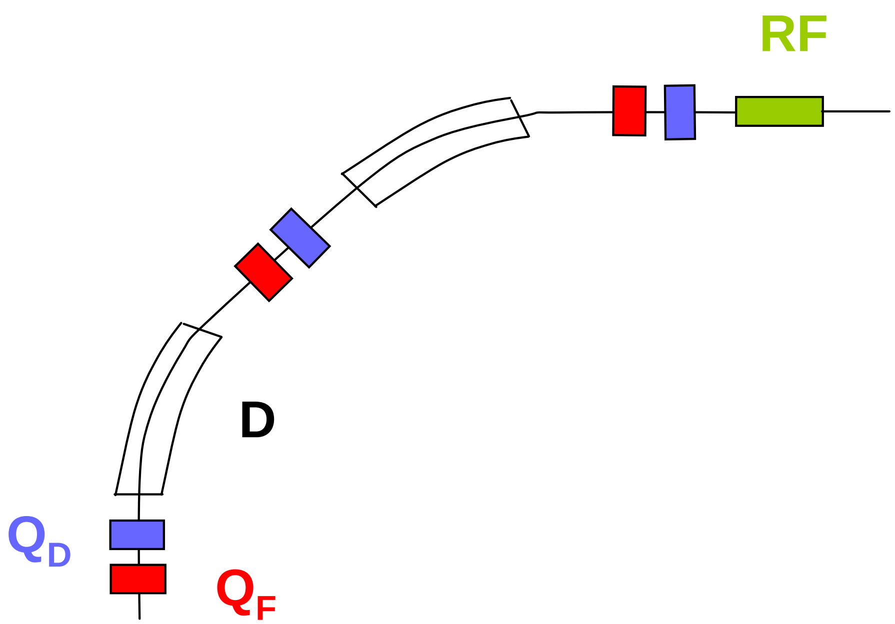
- Fascio stabile in energia (0,4MeV↔0,2cm in acqua).
- Fascio ben definito in sezione trasversa penombra non superiore a 2 mm in ogni direzione (80%-20%).
- Fascio posizionato con la precisione del mm sul paziente.
- Possibilità di modulare in energia
- Possibilità di modulare in intensità



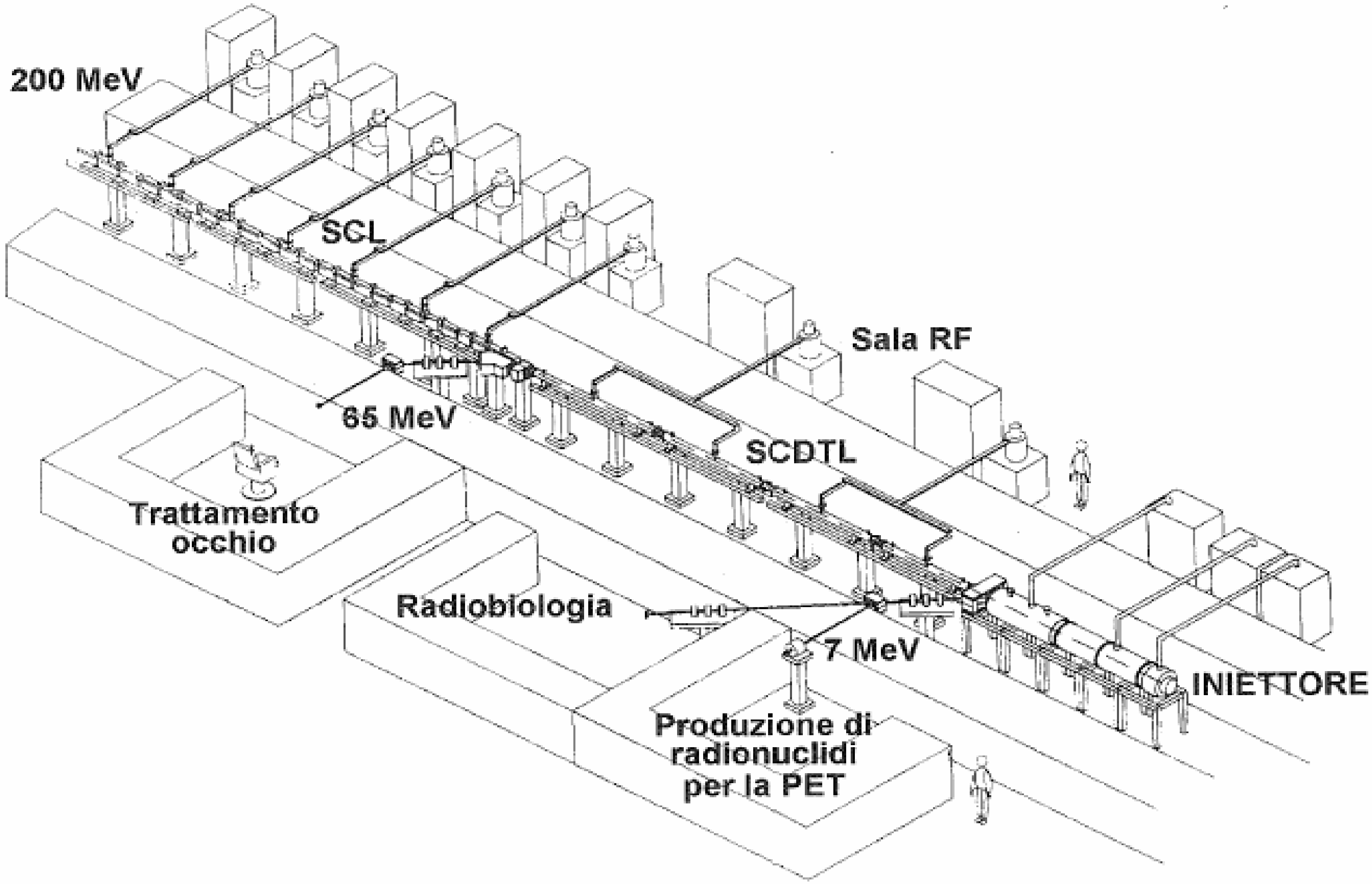


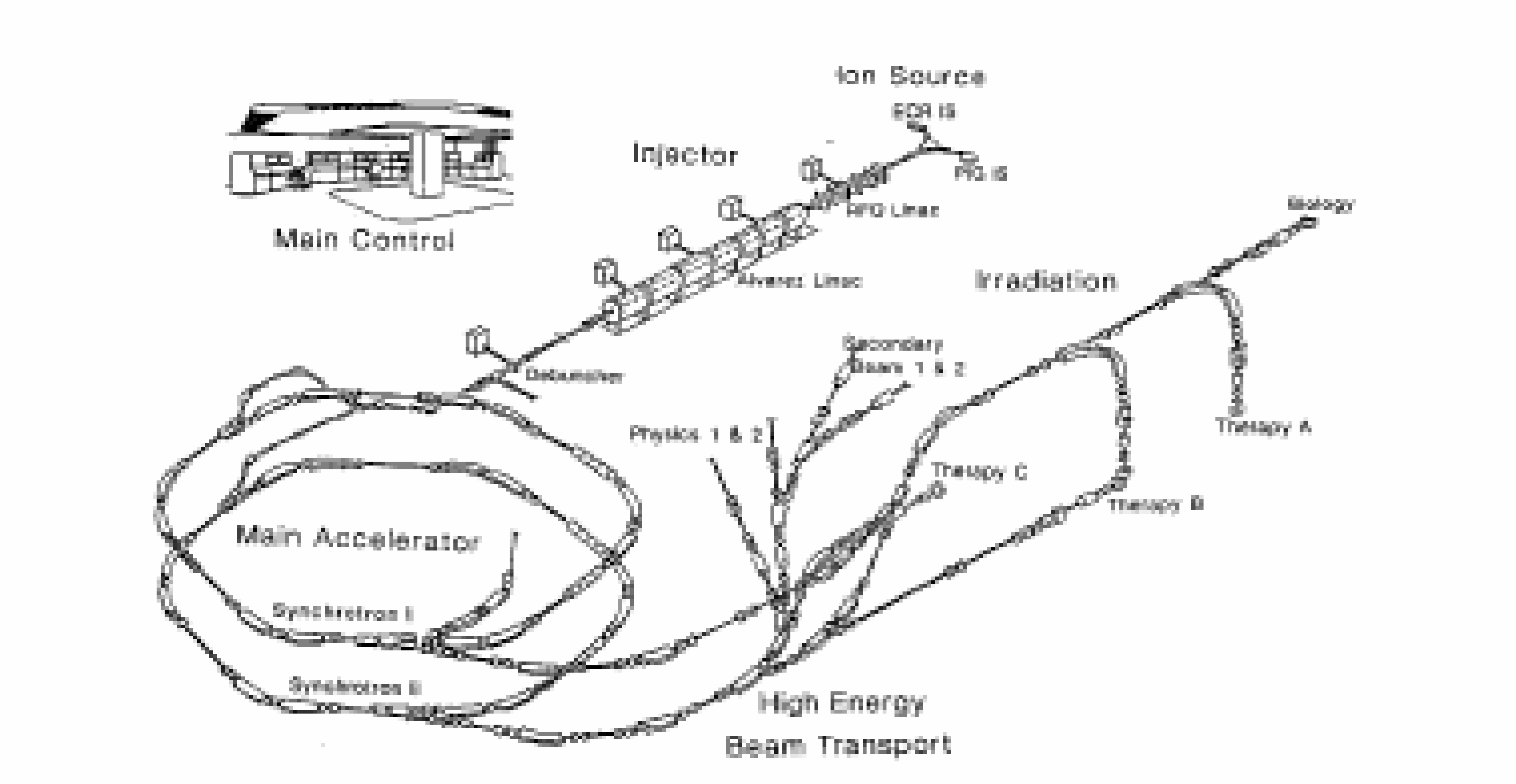
Ciclotrone: Lawrence (idea 1929, Nobel price1939)

Sincrotroni: acceleratori circolari con funzioni separate (accelerazione, focalizzazione e controllo di traiettoria)



McMillan ed indipendentemente Veksler 1944.
Courant, Livingston e Snyder 1952 focalizzazione forte.


200 MeV
SCL
Sala RF
65 MeV
SCDTL
Trattamento
occhio
Radiobiologia
7 MeV
INIETTORE
Produzione di
radionuclidi
per la PET



Presso il Centro Heavy Ion Medical Accelerator Centre (HIMAC, Chiba, Giappone) gli ioni sono accelerati da due sincrotroni aventi diametro 40 m e i pazienti sono trattati in tre sale con fasci fissi [1.36].

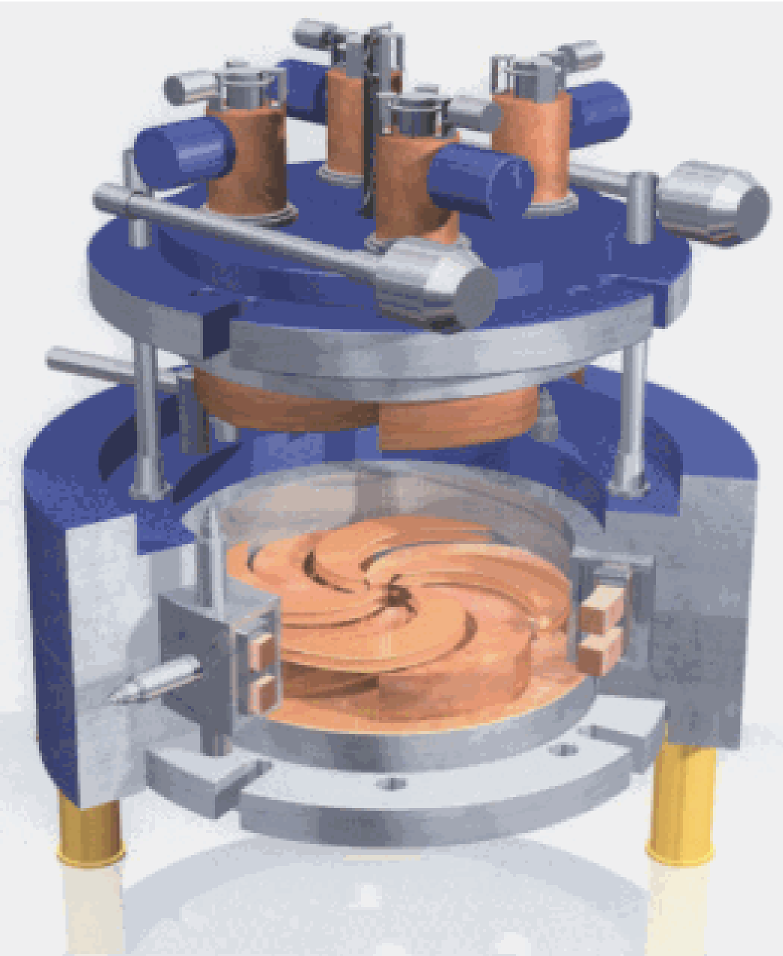
Tabella 3.1 Distribuzione dei centri di protonterapia nel mondo e numero di pazienti al giugno 1996 (da Particles Newsletter).

Centro	Data inizio terapia	Data ultima terapia	Tipo di acceleratore	Direz. del fascio	Energia massima [MeV]	Energia clinica [MeV]	Numero pazienti	Data del totale
LBL, Berkeley (USA)	1954	1957	sincrotrone	orizz.	730	70-230	30	
GWI, Uppsala (Svezia)	1957	1976	ciclotrone	orizz.	185	45-185	73	
HCL Cambridge (USA)	1961		ciclotrone	orizz.	160	160	6'785	Giu-96
JINR, Dubna (Russia)	1967	1974	sincrocicl.	orizz.	680	70-200	84	
ITEP, Moscow (Russia)	1969		sincrotrone	orizz.	10'000	70-200	2'838	Giu-96
LINPh St. Petersburg (Russia)	1975		sincrocicl.	orizz.	1'000	1'000	969	Dec-95
NIRS, Chiba (Giappone)	1979		ciclotrone	orizz.	90	70-90	86	Giu-93
PMRC Tsukuba (Giappone)	1983		sincrotrone	vert.	500	≤ 250	462	Giu-95
PSI, Villigen (Svizzera)	1984		ciclotrone	orizz.	590	< 250	2'054	Dic-95
JINR Dubna (Russia)	1987		sincrocicl.	orizz.	680	70-200	40	Giu-96
GWI, Uppsala (Svezia)	1989		ciclotrone	orizz.	200	45-200	81	Mar-96
Douglas Cyclotron Unit Clatterbridge (UK)	1989		ciclotrone	orizz.	62	62	698	Giu-96
LLUMC Loma Linda (USA)	1990		sincrotrone	1 orizz. 3 gantry	250	70-250	2'000	Giu-96
UCL Louvain-la-Neuve (Belgio)	1991		ciclotrone	orizz.	90	90	21	Nov-93
CAL, Nice (Francia)	1991		ciclotrone	orizz.	65	65	636	Nov-95
CPO, Orsay (Francia)	1991		sincrocicl.	orizz.	200	73-200	673	Nov-95
NAC, Faure (Sud Africa)	1993		ciclotrone	orizz.	200	≤ 200	130	Mar-96
IUCF, Indiana (USA)	1993		ciclotrone	orizz.	200	75-200	1	Dic-94
UC Davis, California (USA)	1994		ciclotrone	orizz.	200	≤ 200	71	Mag-96
TRIUMF (Canada)	1995		ciclotrone	orizz.		70	5	Dic-95
					TOTALE		**17'737**	

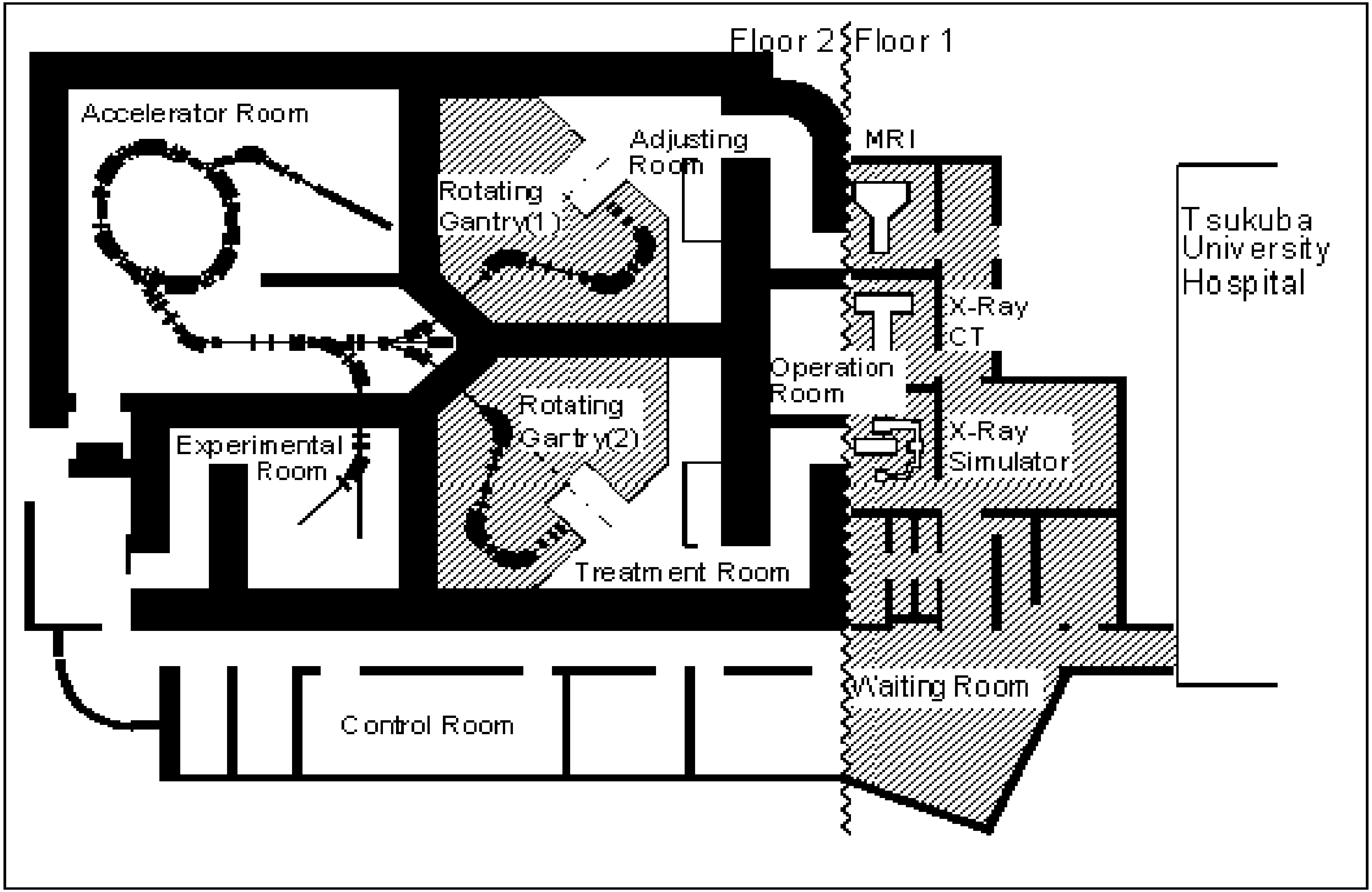
I centri di adro-terapia sono una realtà operante da decenni.

Chi, Dove	Paese	Part.	MeV	Direzione Beam	Stanze	Tratt. Prev.
RPTC, Munich	Germany	p	250 SC Cycltrn.	4 gant., scan, 1 horiz.	5	2005
PSI, Villigen*	Swizerland	p	250 SC Cycltrn.	2 gant., spot-scan, 1 hoz	3	05/06
NCC, Seoul*	Korea	p	235 Cycltrn.	2 gant., 1 horiz.	3	2005
FPTI, Florida	USA	p	230 Cycltrn.	2 gant., 1 horiz.	3	2005?
Med-Austron	Austria	p, ion	Synchrotron	2 gant., 1-2 horiz.	3	2007?
Trento	Italy	p	250 SC? Cycltrn.	1 gant., 1 horiz.	2	2008?
CNAO, Milan	Italy	p, ion	? Synchrotron	2 gant., 1-2 horiz.	3	2008?
Wanjie, Zibo*	China	p	230 Synchrotron	3 gant., 1 horiz.	4	2004
Heidelberg/GSI, Darmstadt*	Germany	p, ion	430/u, Synchrotron	1 gant., raster scan., 2 fixed beams	3	06/07
iThemba Labs	S. Africa	p	230 Cycltrn.	1 gant., 2 horiz.	3	2006?
Xi'an, Shanxi*	China	p	235 Cycltrn.	?	?	2006
RPTC, Koeln	Germany	p	250 SC Cyclotrn.	4 gant., 1 horiz.	5	2007?
MD Anderson, TX	USA	p	250 Synchroton	3 gant., 1 fixed beam	4	2006

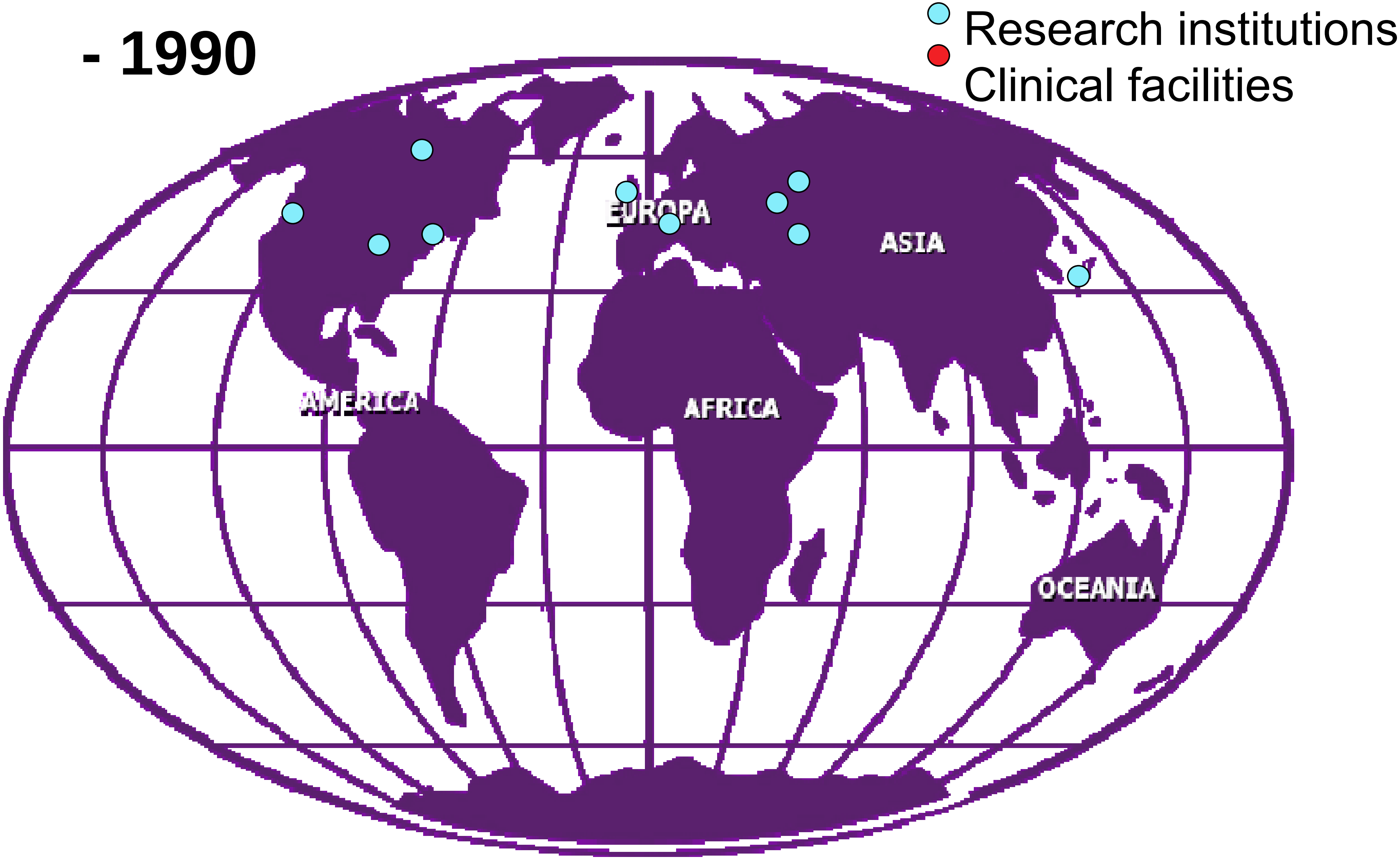

IBA




RINECKER
PROTON
THERAPY
CENTER

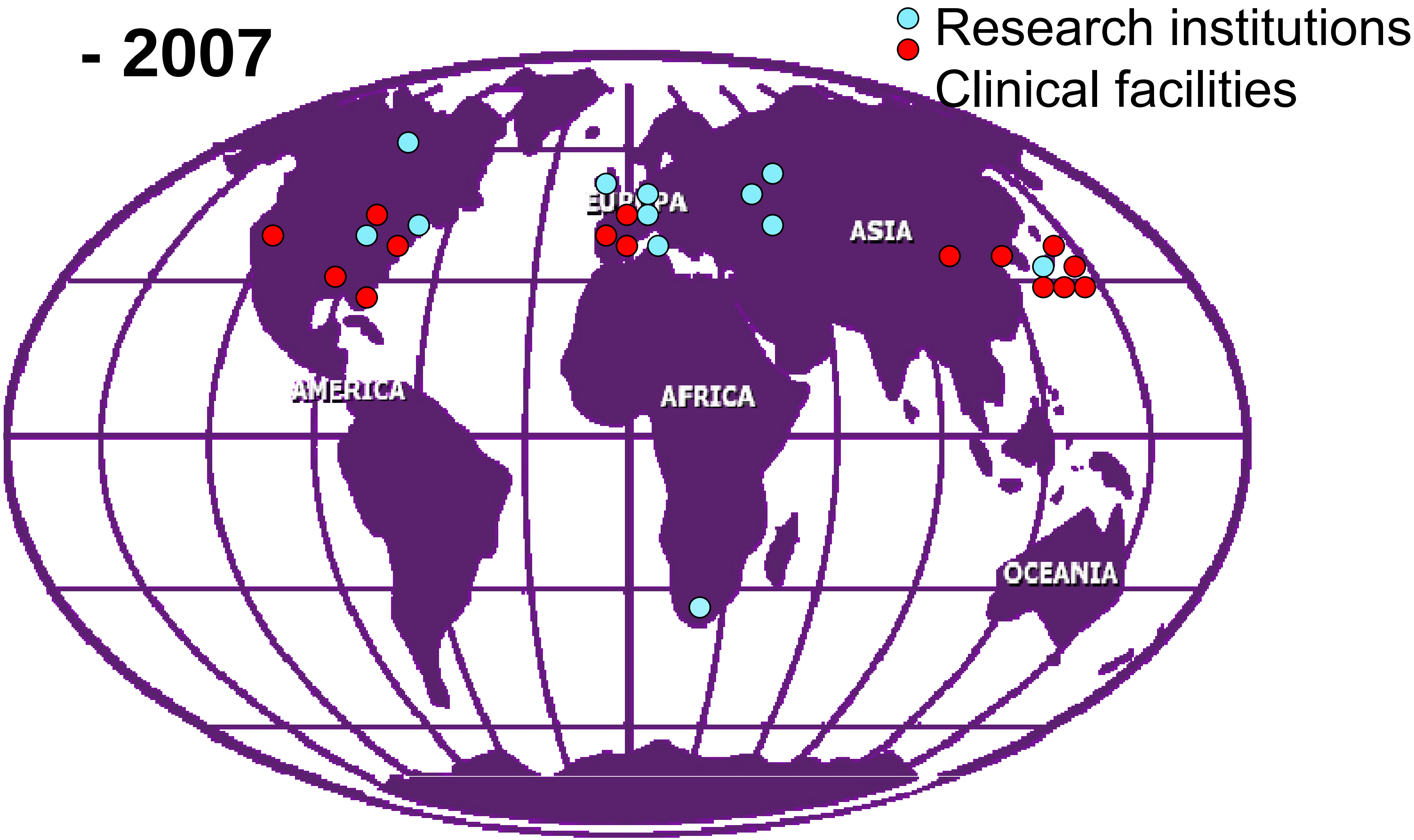

Floor 2
Floor 1
Accelerator Room
Adjusting Room
Rotating Gantry(1)
MRI
Tsukuba University Hospital
X-Ray CT
Operation Room
Rotating Gantry(2)
X-Ray Simulator
Experimental Room
Treatment Room
Waiting Room
Control Room

- 1990



Research institutions
Clinical facilities
AMERICA
EUROPA
AFRICA
ASIA
OCEANIA

- 2007


Research institutions
Clinical facilities
AMERICA
ASIA
AFRICA
OCEANIA

Evolution

Commissioning – under construction - planning stage

p	RPTC, Munich, Germany
p	PSI, Villigen, Switzerland (OPTIS2/Gantry2)
p	NCC, Seoul, Korea
p + ion	HIT, Heidelberg, Germany
p + ion	CNAO, Italy
p	UPenn, USA
p	WPE, Essen, Germany
p	iThemba Labs, South Africa
p	RPTC, Koeln, Germany
p	ICPO, Orsay, France
p	Trento, Italy
ion	Gunma Univ, Japan
P	Northern Illinois PT Res. Inst, Chicago, IL, USA
p + ion	PTC, Marburg, Germany
p + ion	ETOILE, Lyon, France
p + ion	Med-AUSTRON, Austria

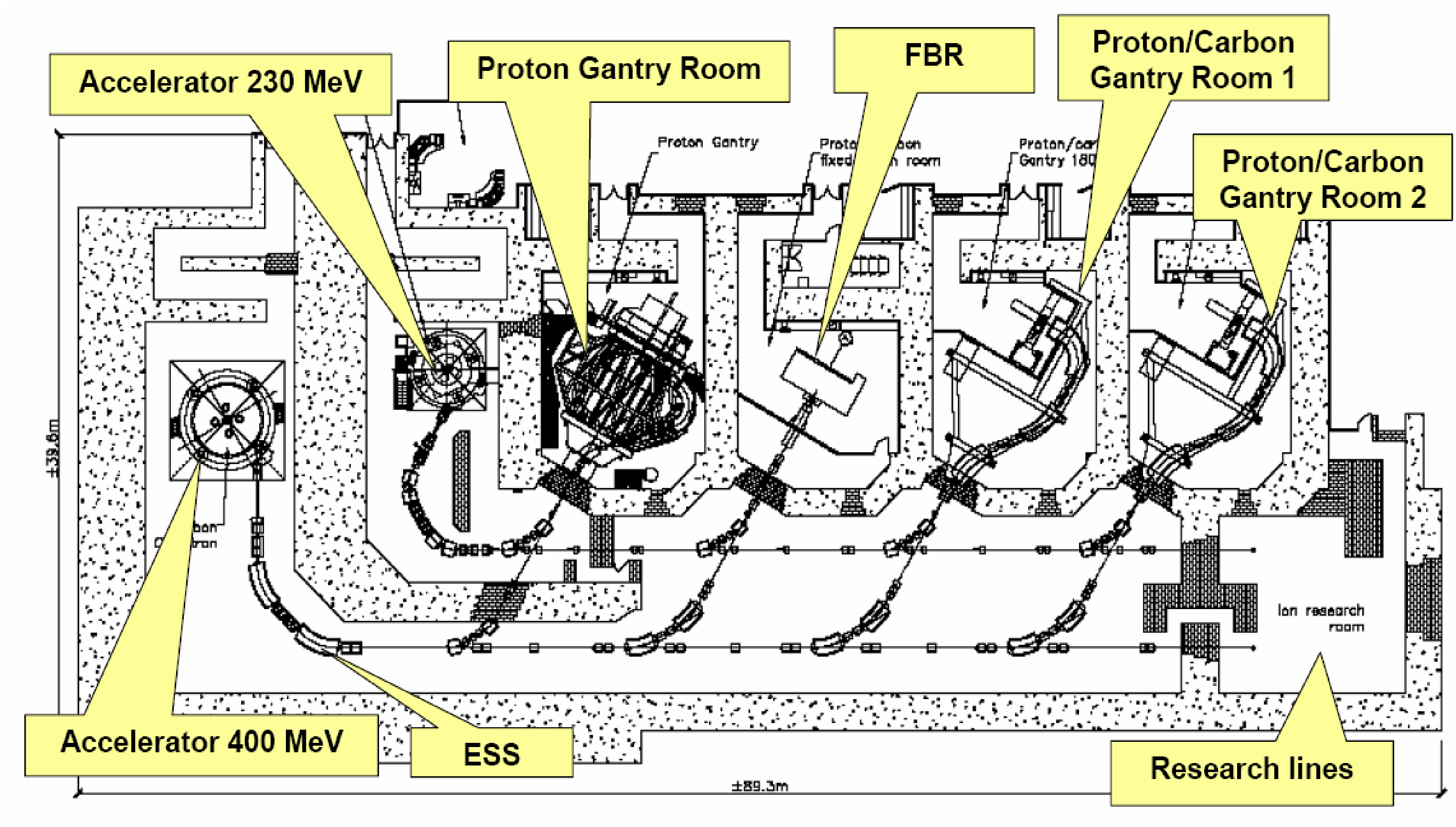
More than 16 centres over 5 years   11 in Europe   5 in Germany

Evolution ….some comments

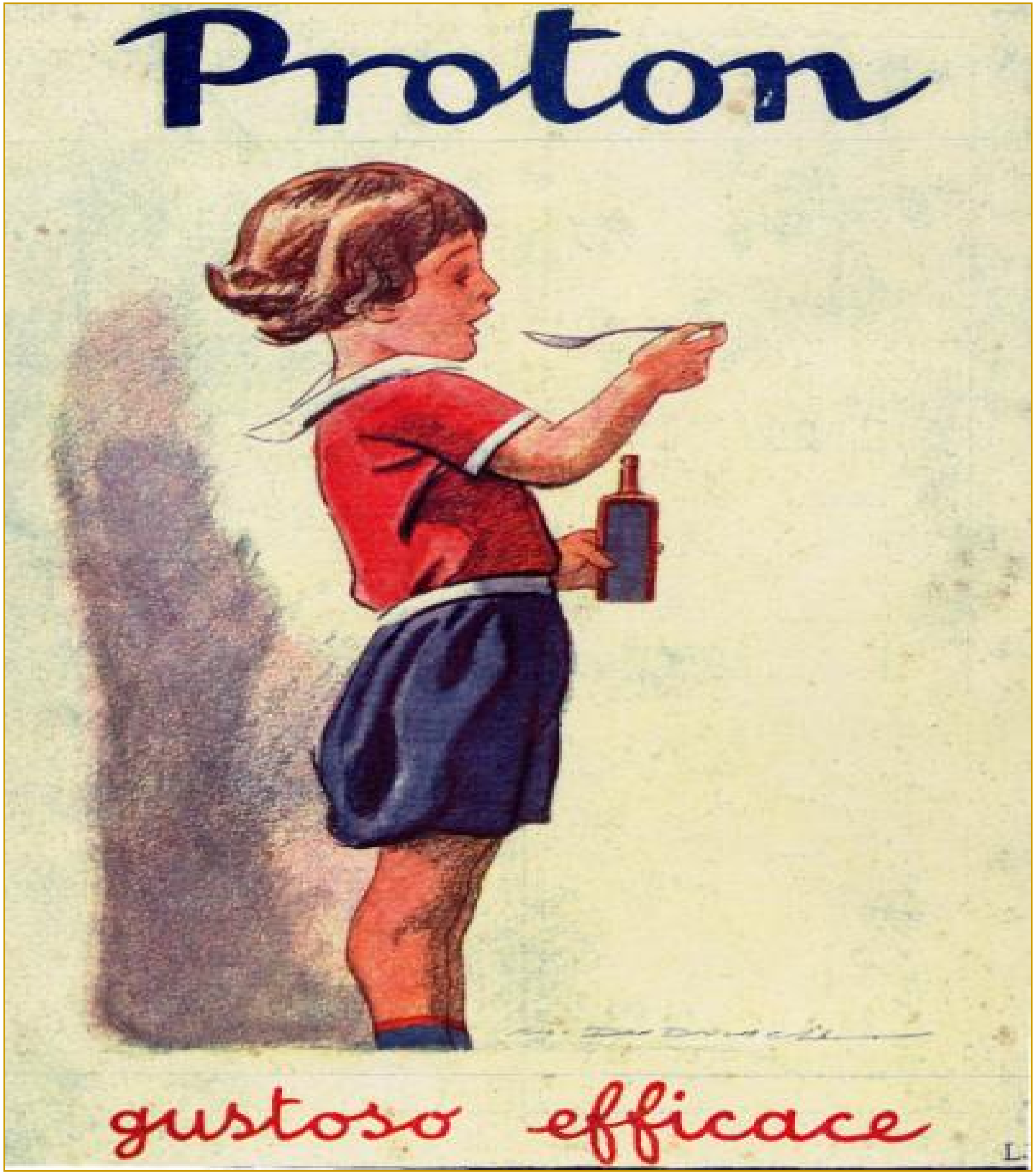
- Switch from the first generation (parasitic use) to the second generation (dedicated facilities)

- More and more turnkey constructions by specialized companies

Proton – carbon ions facilities



Superconducting isochronous cyclotron accelerating Q/M = 1/2 ions to 400 MeV/U


Proton
gustoso efficace