Accelerator Design for Proton Therapy

1. In 1998 OCPA school, Profs. **Yuzheng Lin** (Tsing-Hua Univ, China) and **Frank K.H. Ngo** (Yang-Ming Univ, Taiwan) gave three excellent LECTURES on "Medical applications" and "Radiation treatment programs in Taiwan." These lectures were useful in my preparation!

2. The particle therapy cooperative group (PTCOG) organizes yearly scientific meetings and educational workshops. Recent progresses on treatment protocol and technology are presented in the workshop. The Past and Scheduled PTCOG meetings are:

PTCOG 46	Shandong, Zibo, China *(Wanjie Hospital)*	18-23 May 2007
PTCOG 47	Jacksonville, Florida, USA	May 19 - 24, 2008
PTCOG 48	Heidelberg, Germany	Sept. 29 - Oct. 03, 2009
PTCOG 49	Gunma University - NIRS, Japan	May 17-19, 2010
PTCOG 50	Philadelphia, Pennsylvania, USA	2011
PTCOG 51	NCC, Seoul, South Korea	2012

3. The PIMMS (Proton-Ion Medical Machine Study), a collaborative study group between CERN, GSI (Germany), Med-AUSTRON (Austria), TERA (Italy) and Oncology 2000 (Czech Republic), published CERN yellow reports that aimed for a "**best**" possible design for a synchrotron-based medical treatment facility delivering protons and carbon ions. The reports are freely available online.

4. W. Chu, et al., *Performance Specifications for Proton Medical Facility*, LBL-33749 (1993)

Outline

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- Introduction and Motivations:
  - Cancer statistics
  - Physics of Radiation therapy, X-ray, proton and ion therapy
- Requirement and review of various concepts, tools & techniques
  - Proton therapy
  - Ion therapy
- Examples of Accelerator designs
- Conclusions
  - Cancer treatment facilities

Radiation dosage and its Biological effects

I. Activity: defined as the number of radioactive decay per second of a sample.
Since $dN/dt=-\lambda N$, the activity is $A=\lambda N$.

1 Bq (becquerel)	1 disintegration/s
1 Ci (curie)	3.7×10^{10} decays/s ~ the activity of 1g of ^{226}Ra.

1 g Co60 (τ~5.27y) contains about 50 Ci

II. Unit of (Absorbed) Radiation Dosage

1 **R** (Roentgen)	2.58×10^{-4} Coulomb/kg of dry air
1 **rad** (radiation absorbed dose)	1 erg/g=0.01 J/kg
1**Gy** (gray) =100 rad	1 J/kg
1 DE (dose effective)	(absorbed dose)×**RBE** (QF)
1 **Sv** (sievert) [GyE/CGE]	(absorbed dose in Gy) ×RBE (QF)
1 **rem** (rad equivalent in man)	(absorbed dose in rad) ×RBE (QF)

CGE=Cobalt Gray Equivalent; organ at risk (OAR); gross tumor volume (GTV); CTV (clinical target volume) = GTV + 5-10 mm; planned treatment volume PTV = CTV + 5~10 mm; dose volume histograms (DVH)

Background radiation is about 130 mrem/y (1.3 mSv/y), or 0.15 μ(micro)Sv/h; US regulation is 5mSv/y, radiation worker 50 mSv/y. In ICRP Publication 62, a representative value of 1.8 mSv (180 mrem) effective dose is given for a head CT.

III. Stopping power (-dE/dx) is the energy lost by a charged particle in a medium.

IV. LET is the energy absorbed in the target.

A Dosage Calculation Example

1. A 5-MeV α particle is **absorbed** by 1 gram of water, estimate the dosage in rad and rem.

$$\frac{5\text{MeV}}{1\,\text{g}}\frac{1.6\times10^{-13}\,\text{J}}{1\,\text{MeV}}\frac{10^{7}\,\text{erg}}{1\,\text{J}}\frac{1\,\text{rad}}{100\,\text{erg/g}}=8.0\times10^{-8}\ \text{rad}$$

The RBE (Q factor) is 10 for α particle, and thus the dose is 8E-7 rem or 8E-9Sv. If the α particle is absorbed by a of 10^{-9} g cell, then the dose is 10^{9} times higher (0.8 Gy, 8 Sv), exceeded lethal dose for most living beings.

2. Proton at 250 MeV are used for radiation therapy with a treatment volume of 1 kg. Assuming 70% efficiency in reaching the PTV. What is the number of protons per second needed for the dosage of 2 Grays in 2 minutes?

$$\frac{250\text{MeV}}{1\,\text{kg}}\frac{1.6\times10^{-13}\,\text{J}}{1\,\text{MeV}}\ N\times120s\times70\%=2\ \text{J/kg}$$

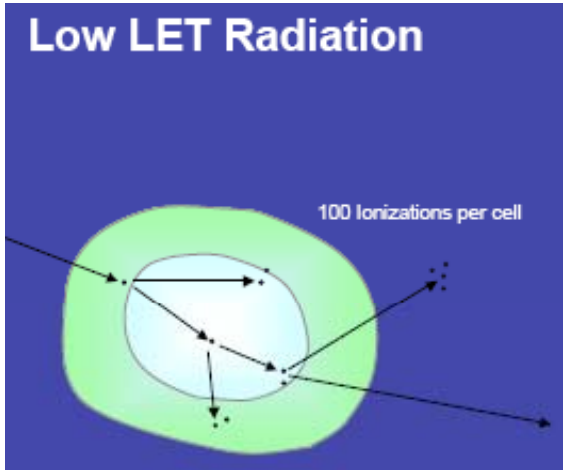
$$N=6\times10^{8}\ \text{particles/second}$$

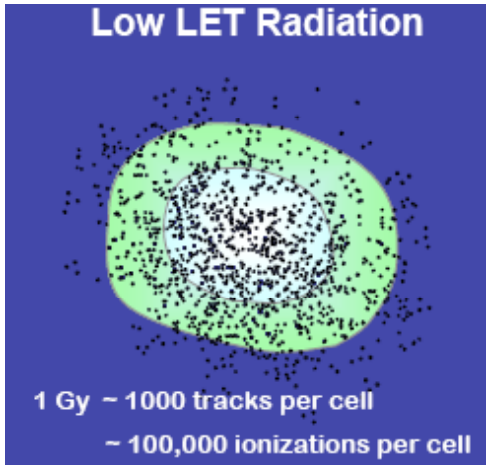
Development of Radiation Injury

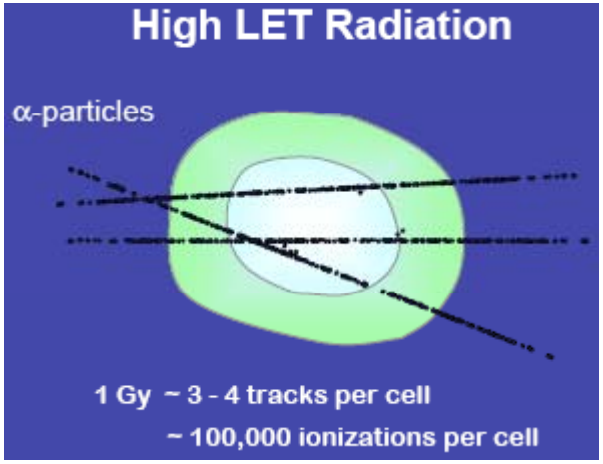
• Initial Physical Interaction	Excitation, Ionization	10^{-24} - 10^{-14} s
• Physiochemical	Free Radical Formation	10^{-12} - 10^{-8} s
• Chemical Damage	Radical Attack	10^{-7}s - hours
• Biomolecular Damage	DNA, Proteins, etc.	ms - hours
• Early Biological Effects	Toxicity, Mutation	hours - weeks
• Late Biological Effects	Cancer, Genetic Effects	years - centuries

Type	LET (keV/μm^{-1})
^{60}Co γ (1.2 MeV)	0.3
250 kV X-ray	2
150 MeV H+	0.5
10 MeV H+	4.7
14 MeV neutron	12
2.5 MeV alpha	170
2 GeV $^{56}Fe^{26+}$	1000

Processes	**units**
Radioactivity	**Bq, Ci**
Exposure dose	**Gy, rad (R)**
Quality factor	**RBE, *Q***
Biological dose	**Sv, rem, GyE, cGE**







Whole Body Dose; LD_{50} vs Body Weight

LD_{50} for Various Species from Mouse to Man and Relation Between Body Weight and Number of Cells that Needs to be Transplanted for a Bone Marrow "Rescue"

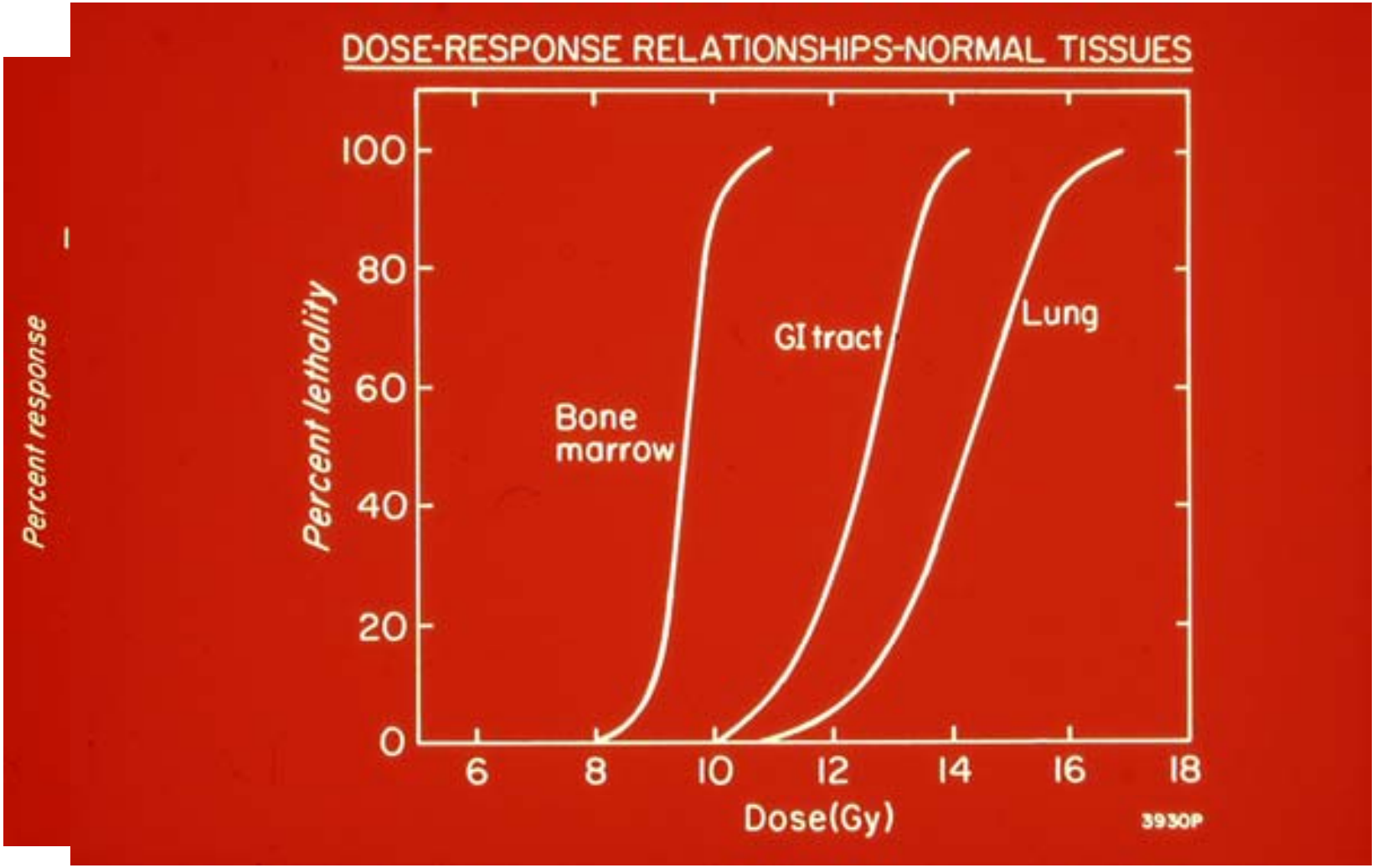
Species	Average Body Weight in kg	LD_{50} in Gy Total-Body Irradiation	Rescue Dose per kg $\times 10^{-8}$	Relative Hematopoietic Stem Cell Concentration
Mouse	0.025	7	2	10
Rat	0.2	6.75	3	6.7
Rhesus monkey	2.8	5.25	7.5	7.3
Dog	12	3.7	17.5	1.1
Humans	70	4	20	1

(Data from Vriesendorp HM, van Bekkum DW in Broerse JJ, MacVittie T (eds): Response to Total Body Irradiation in Different Species. Amsterdam, Martinus Nijhoff, 1984)

LD (Lethal Dose)

Hormesis: Evidence that a small dose of radiation produces helpful effect. Prevailing Explanation: Stimulation of hormonal and immune responses to other toxic environmental agents

Effects of ionizing radiations and the Lethal Dose (LD50)



Chemical Agents

Radiosensitivity of cells, tissues, and organs can be modified by chemical agents (Must be present during irradiation). Examples of Radiosensitizers are Halgenated pyrimidines; Methotrexate; Actinomycin D; Hydroxyurea; Vitamin K. All have effectiveness of ~2, i.e. If 90% of cell culture is killed by a 2 Gy dose, then in the presents of sensitizing agent only 1 Gy is required

Main Specifications of the Proton/Ion Therapy System

- Ability to reach the tumor

  Range in patient: up to 32 g/cm²
  Range modulation: up to full range, with steps of 0.5 g/cm²
  Field size: up to 30 x 40 cm

- Ability to reach the tumor in a supine patient from any selected direction

  Isocentric Gantry
  Precise, robotic patient positioning
  Selection of Nozzles

  In fact, Monte Carlo simulations show that 3-4 intensity modulated fixed beams can effectively and properly simulate gantry target volume.

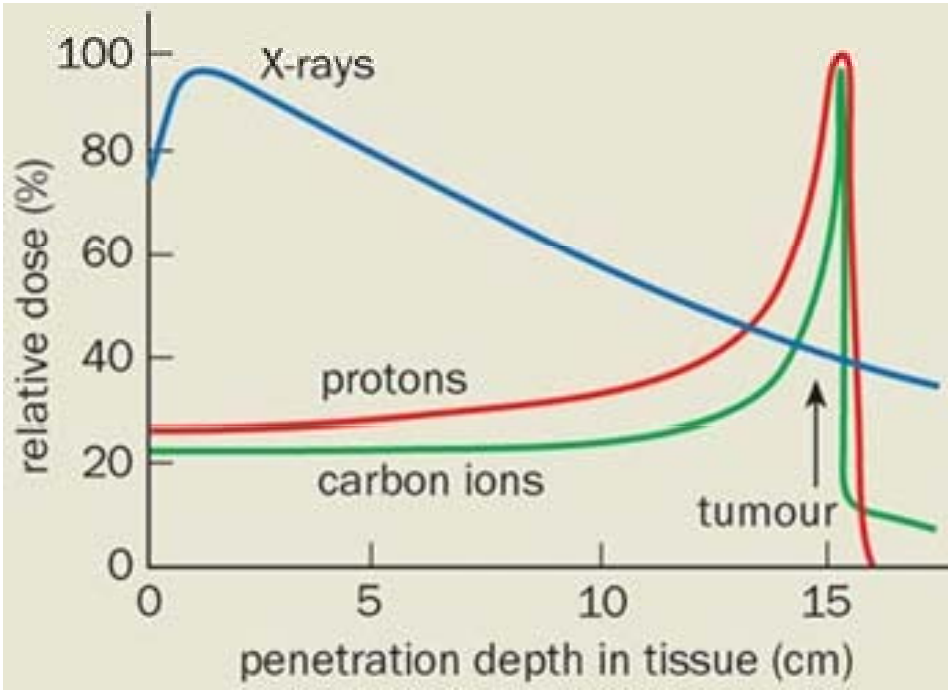
- Ability to reach the tumor accurately

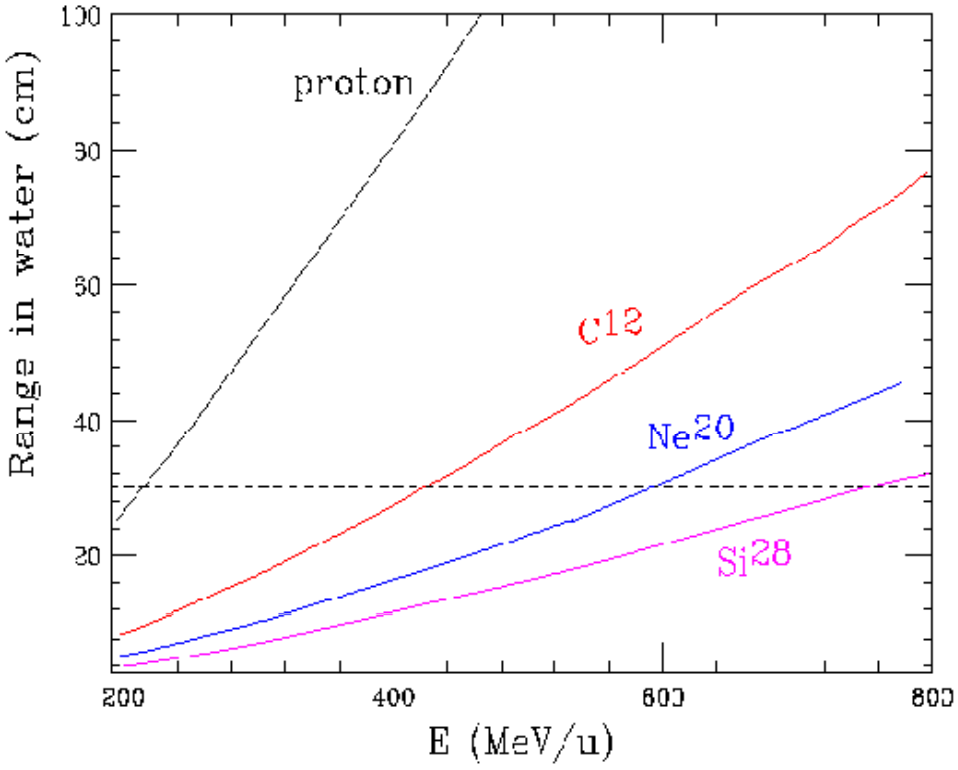
  Penumbra: maximum 2 mm at skin
  Distal dose falloff: maximum 1 mm above physical limit
  Patient position accuracy and reproducibility: 0.5 mm for small displacements
  Gantry accuracy and reproducibility: 1 mm radius circle of confusion
  Alignment methods: orthogonal Digital Radiography System (DRS), lasers etc.

- Ability to **control and verify the dose deposition**

Energy: To reach 30 cm in tissue,
protons ~250 MeV (Brho~2.5 Tm),
carbon ~ 400 MeV/u (Brho~6.5 Tm).

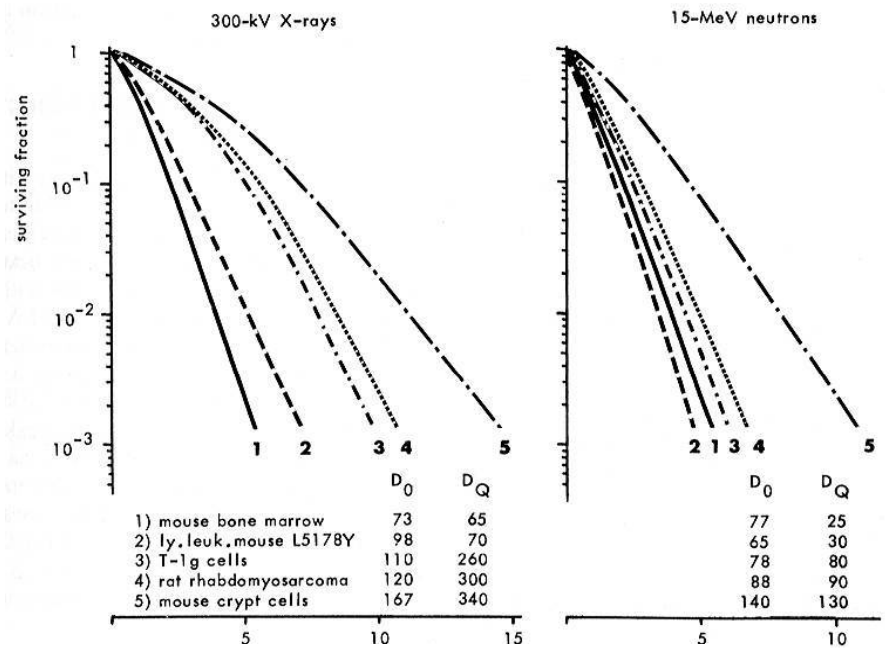
	p	C^{12}
E/u (MeV)	250	400
Brho (T-m)	2.43	6.35
L_dip (m)	11	29





$$KE\,[\mathrm{MeV/u}] \approx 150 + 85\frac{z^2}{A}$$ for a range of 30 cm in water

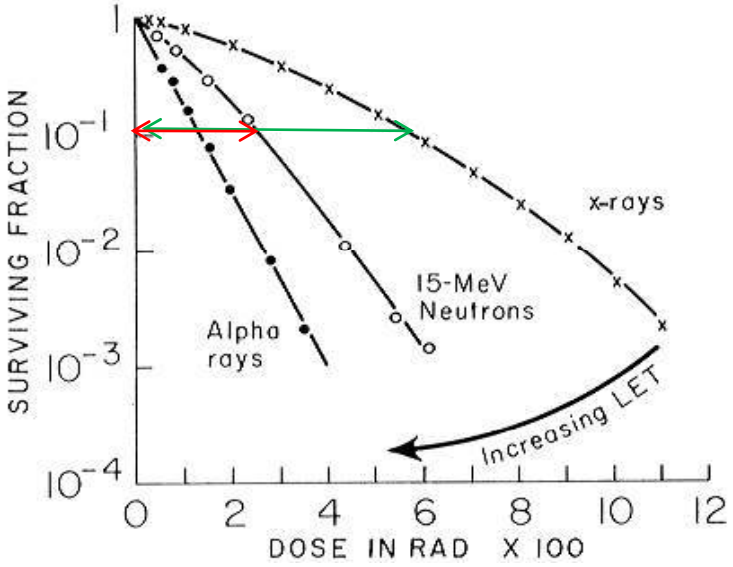
LET (RBE and OER)

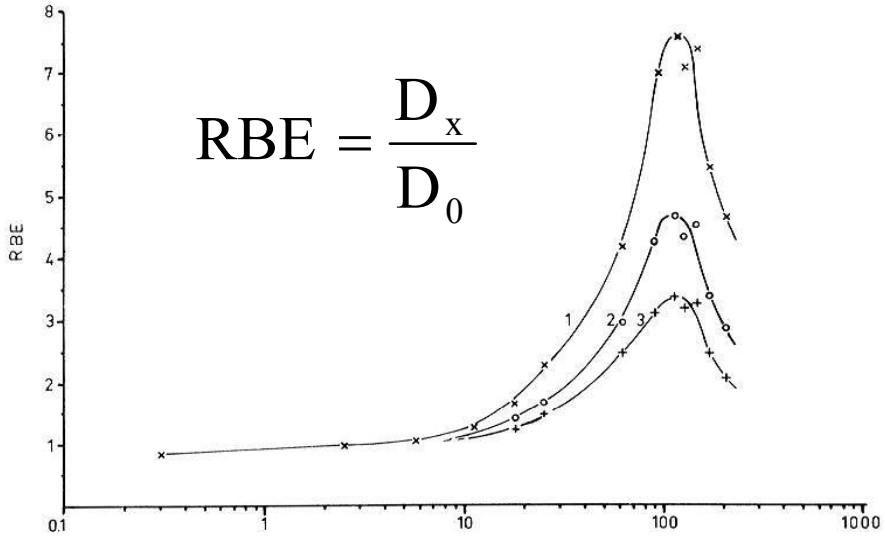


In comparing different types of radiation, it is customary to use x rays (classically 250 kVp x-rays, currently the reference standard is shifting to ^{60}Co gamma or x-rays with energy Ex>1 MeV).

linear quadratic model:

$$S = e^{-\alpha D - \beta D^2}$$



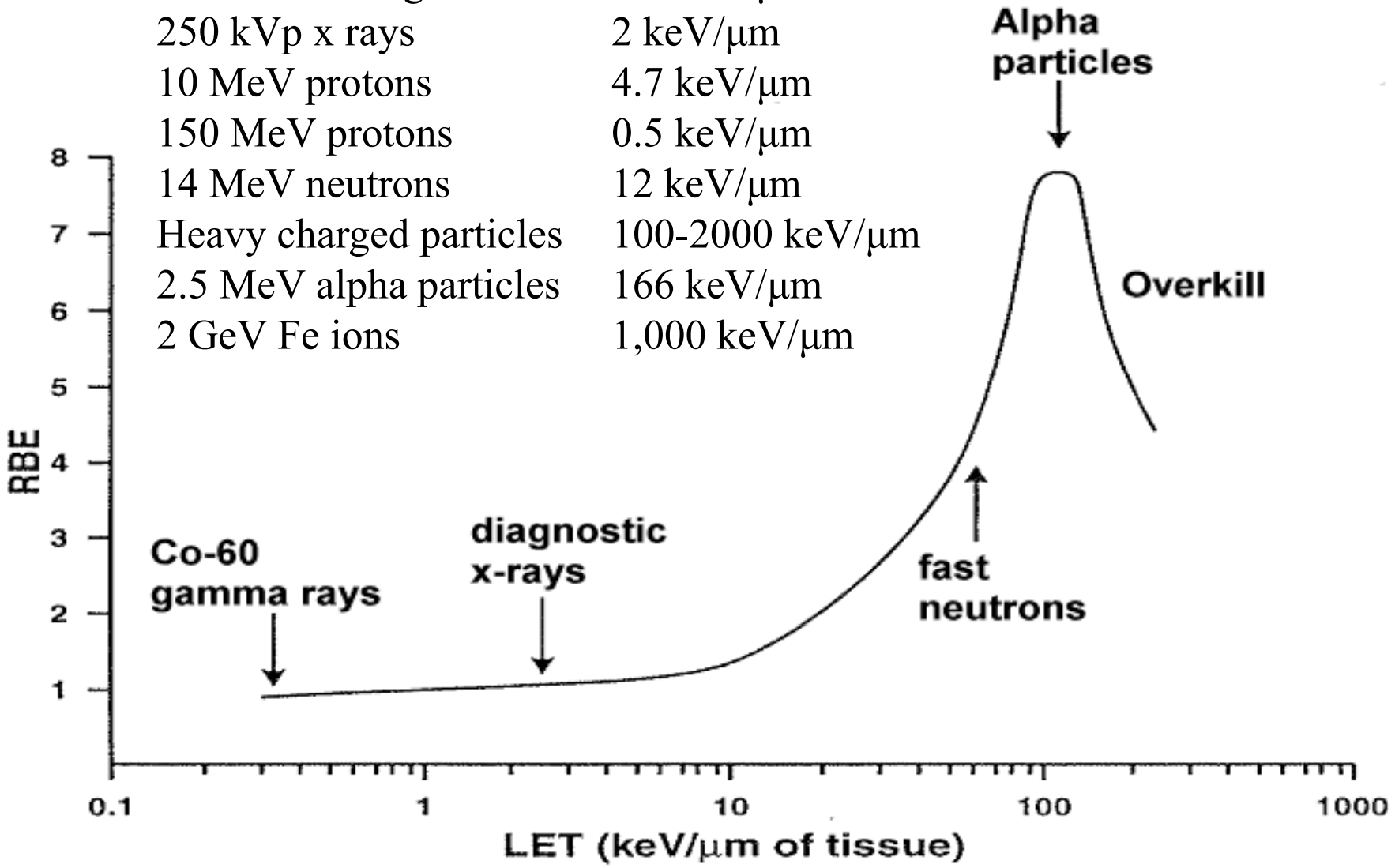


$$RBE = \frac{D_x}{D_0}$$

Biological Effect (RBE) vs LET

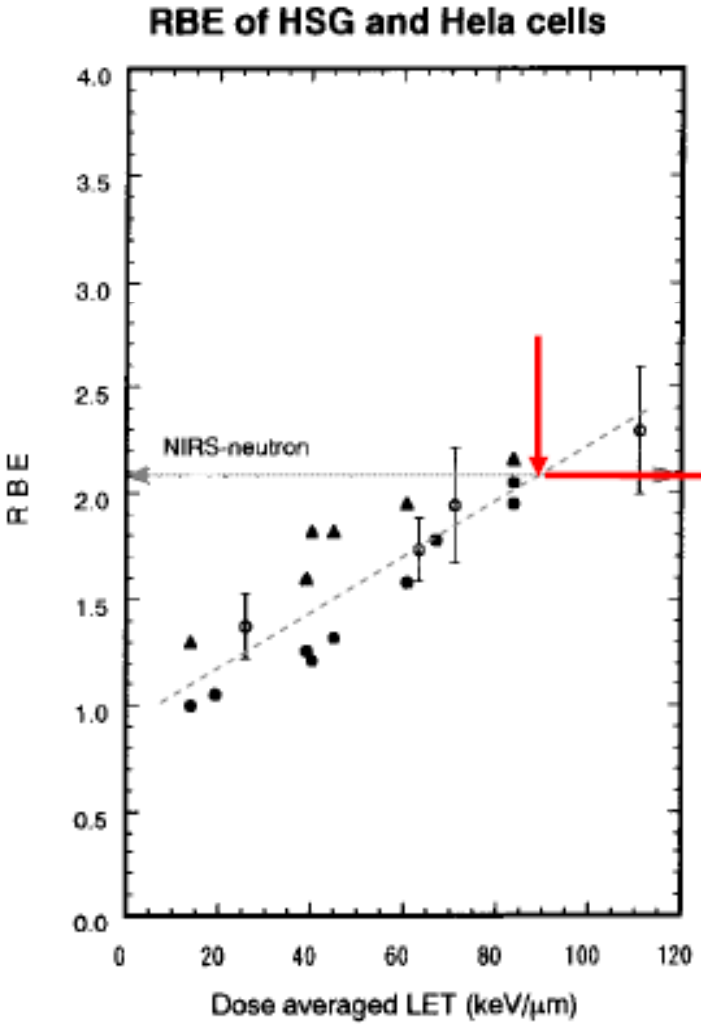
$$RBE = \frac{D_{\gamma}}{D_{\text{ion}}}$$

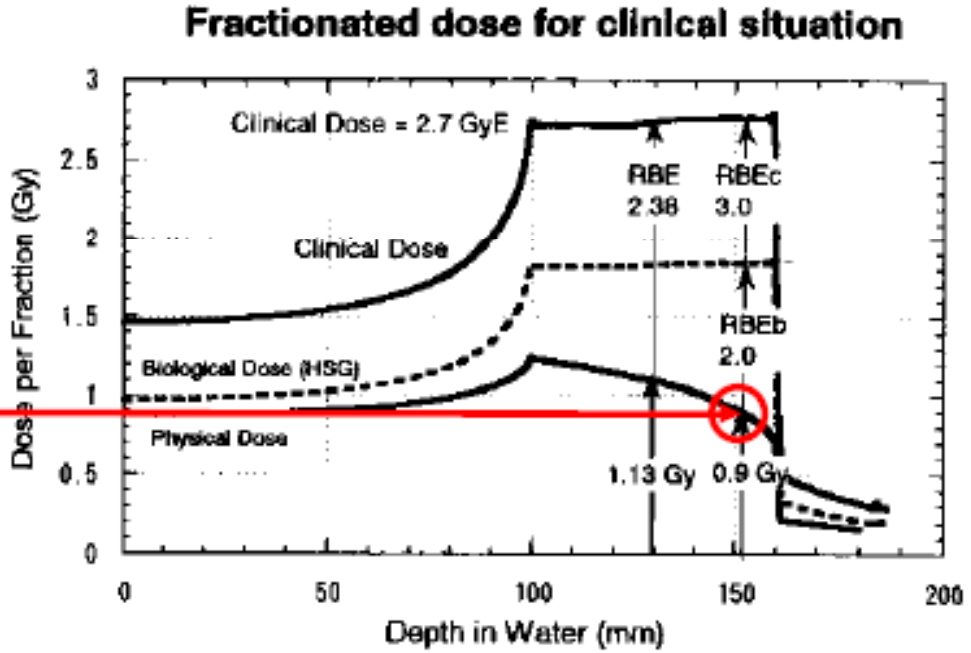
Radiation	Typical LET values
1.2 MeV ^{60}Co gamma	0.3 keV/μm
250 kVp x rays	2 keV/μm
10 MeV protons	4.7 keV/μm
150 MeV protons	0.5 keV/μm
14 MeV neutrons	12 keV/μm
Heavy charged particles	100-2000 keV/μm
2.5 MeV alpha particles	166 keV/μm
2 GeV Fe ions	1,000 keV/μm

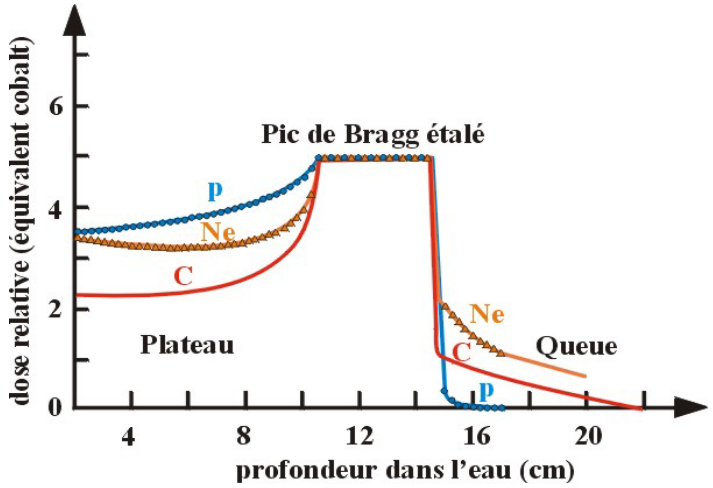


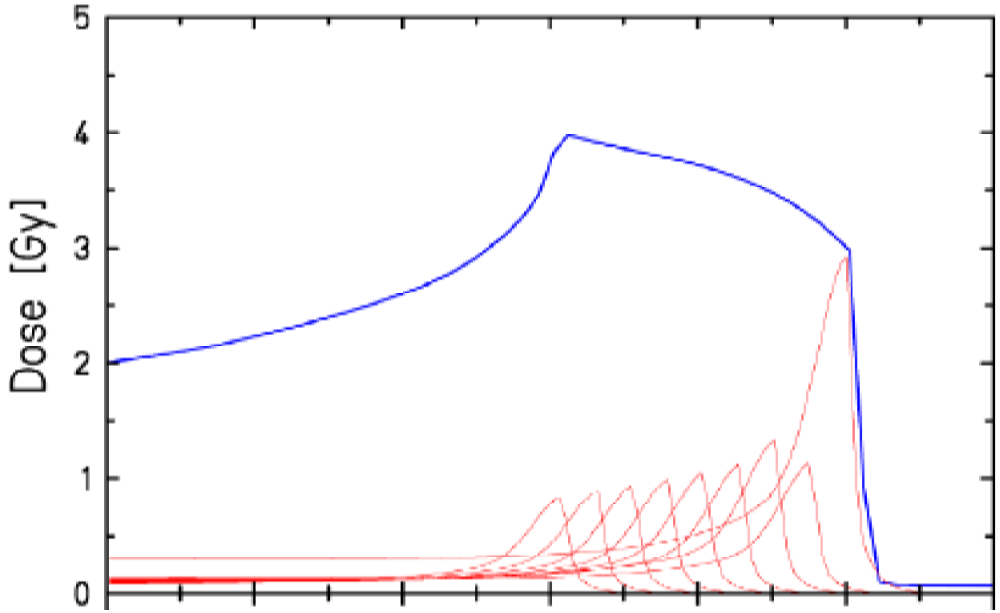
Spread Out Bragg Peak (SOBP):

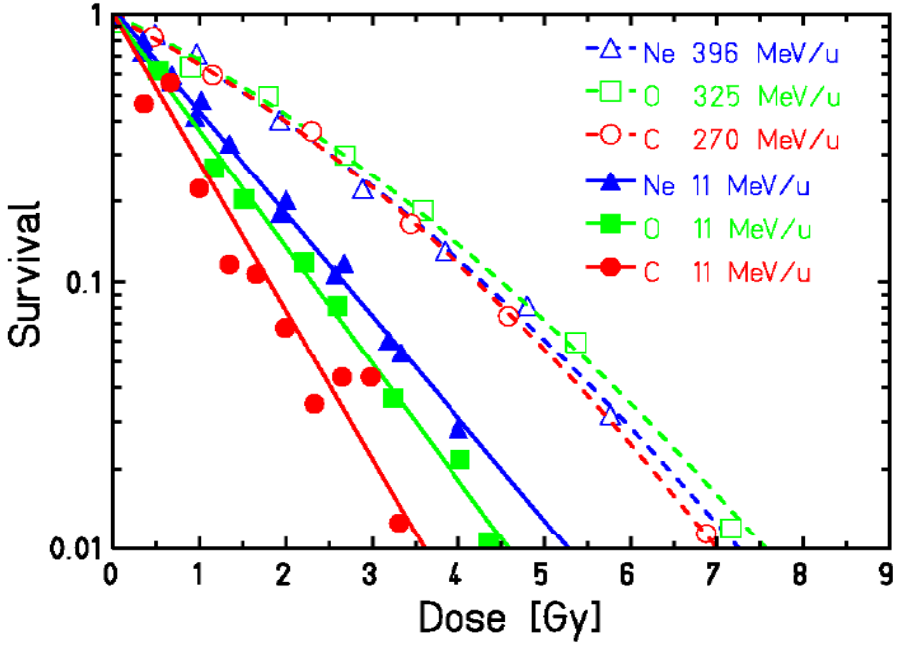
combine Energy modulation and Intensity modulation

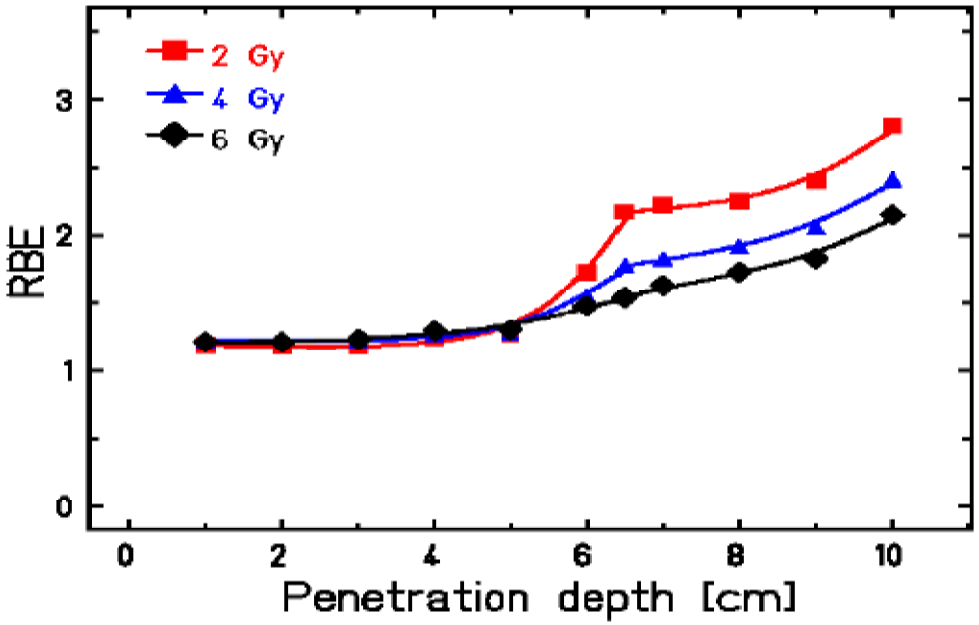


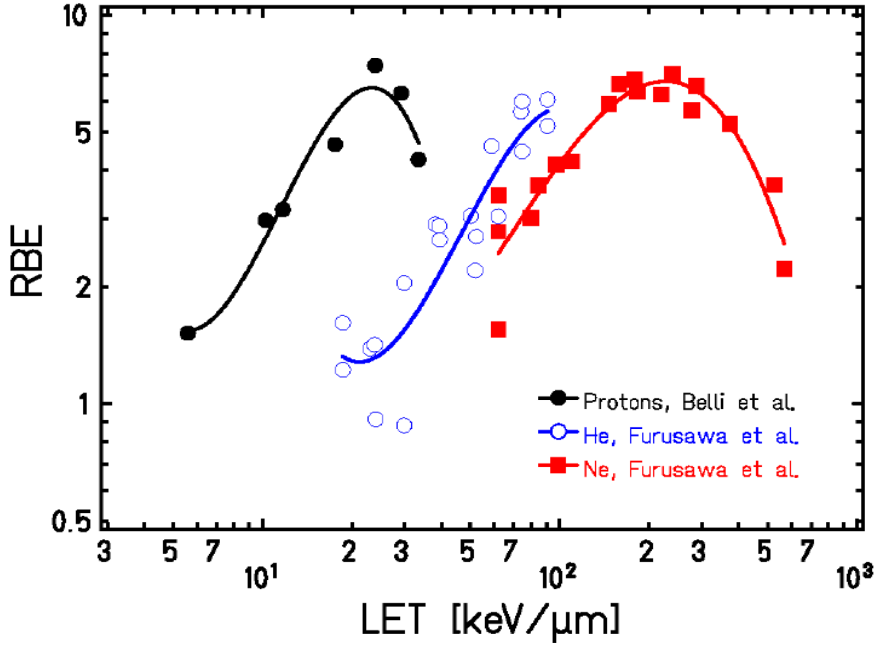




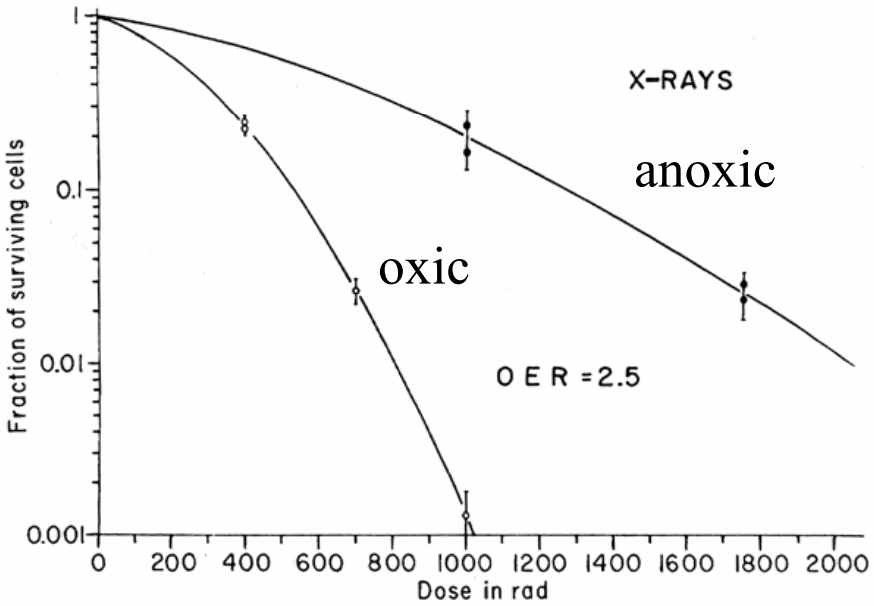








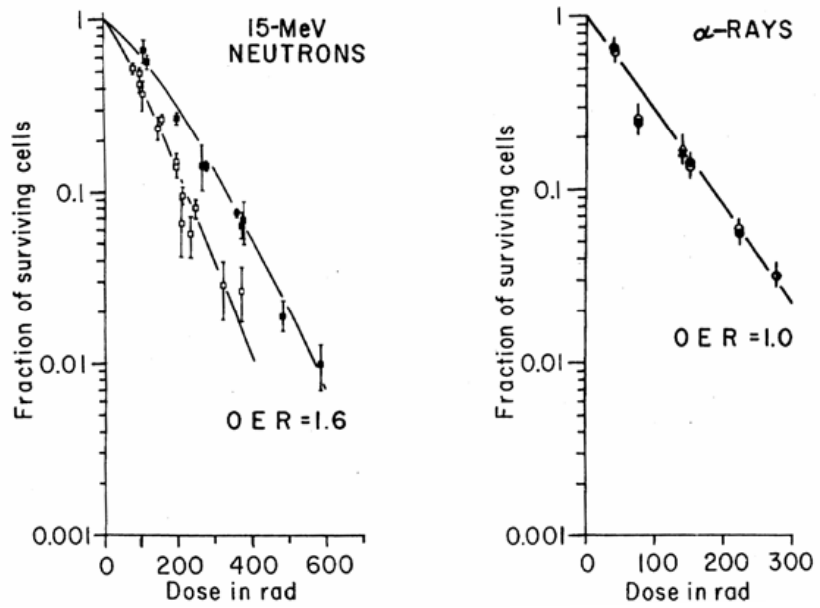
RBE maximum is shifted to higher LET for heavier particles

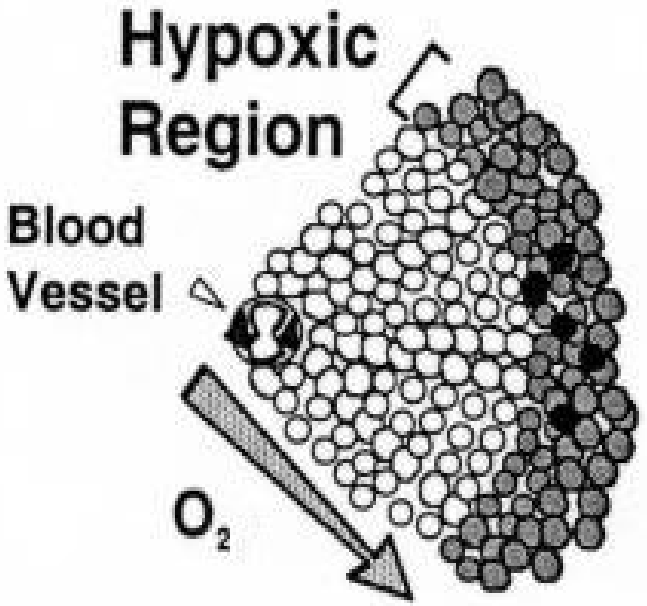


Oxygen-Enhancement-Ratio (OER)

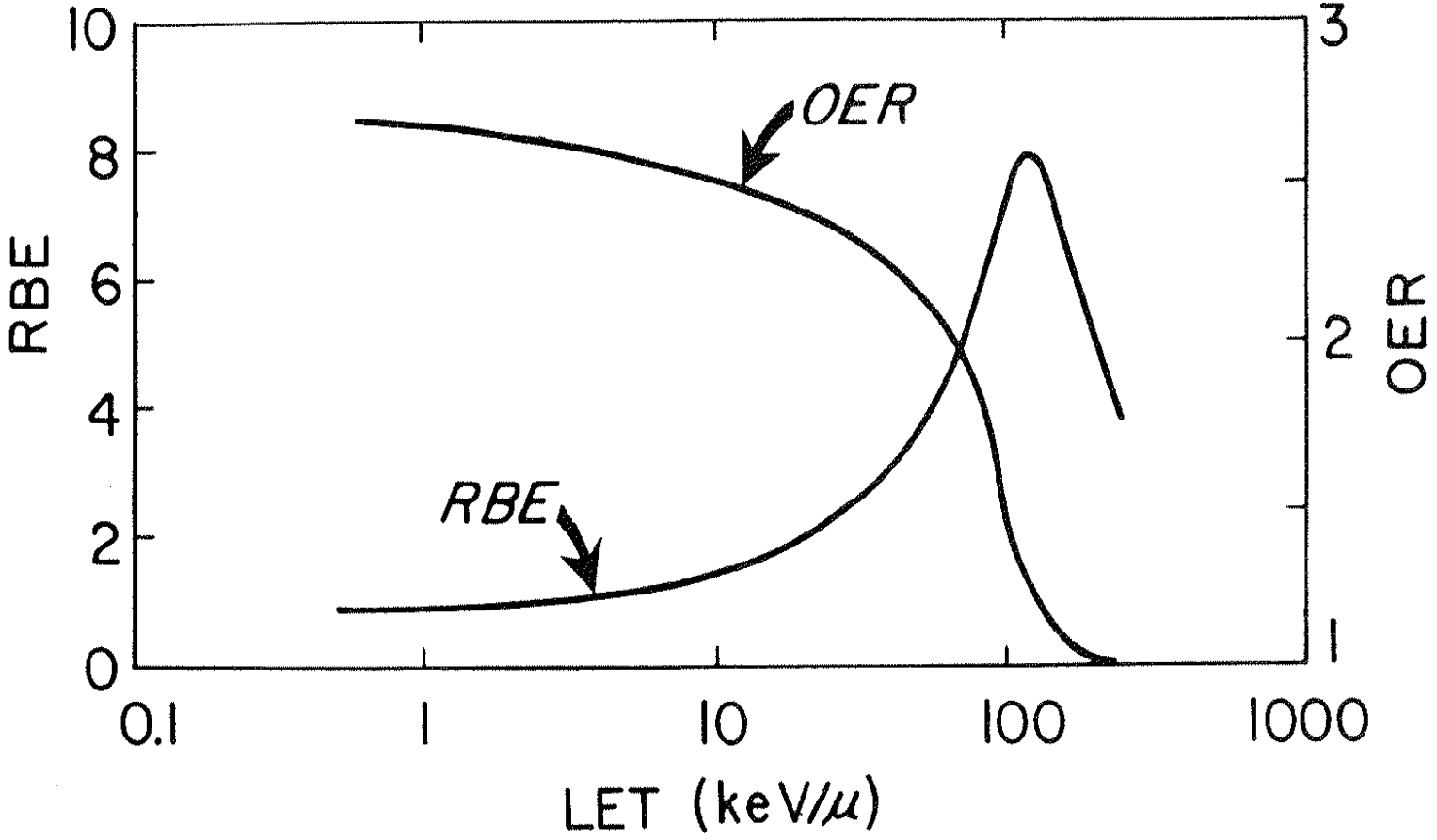
- cellular radio-sensitivity depends on oxygen concentration during irradiation in tumor regions with bad oxygen support (hypoxic / anoxic) better survival after irradiation:
  low LET: OER = 2.5 – 3
  high LET: OER=1

The differences between oxic and hypoxic/anoxic tumor is less for high LET irradiation



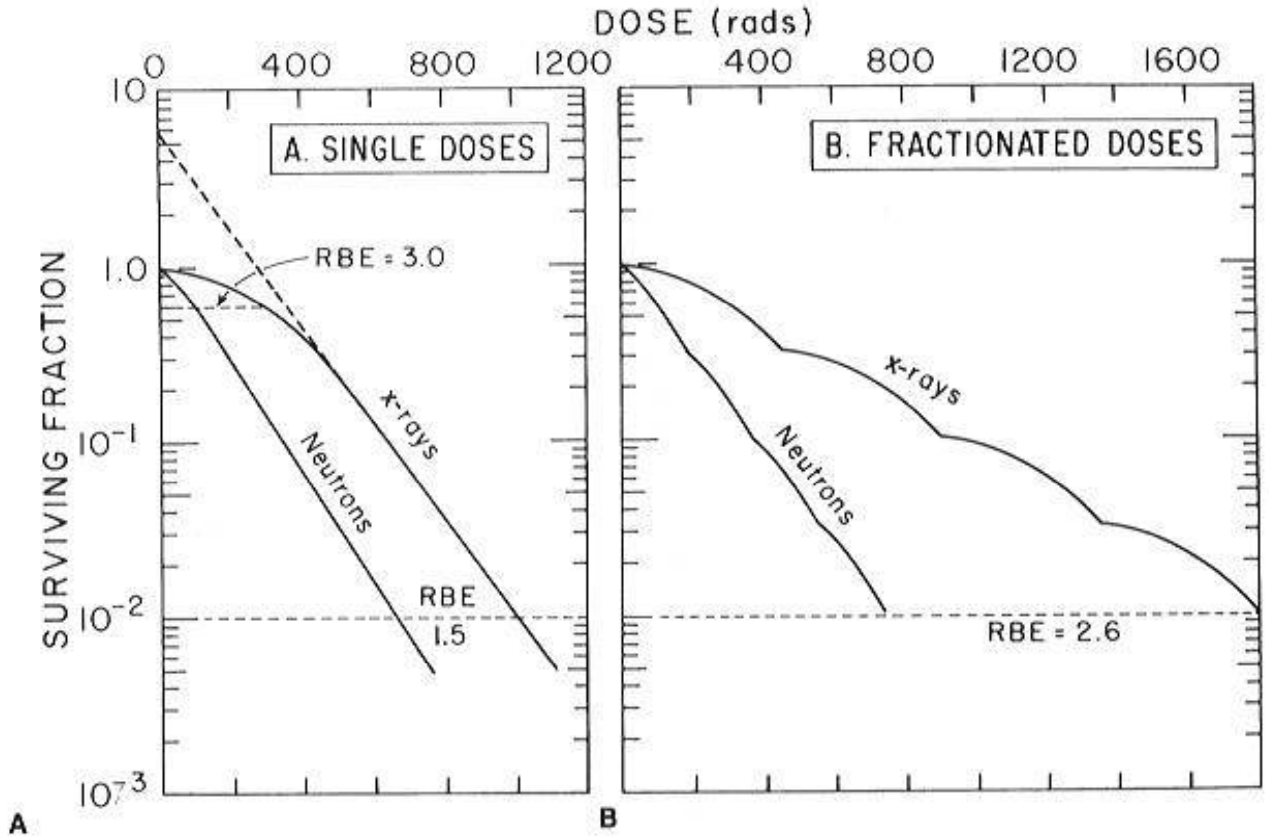


OER and RBE vs LET



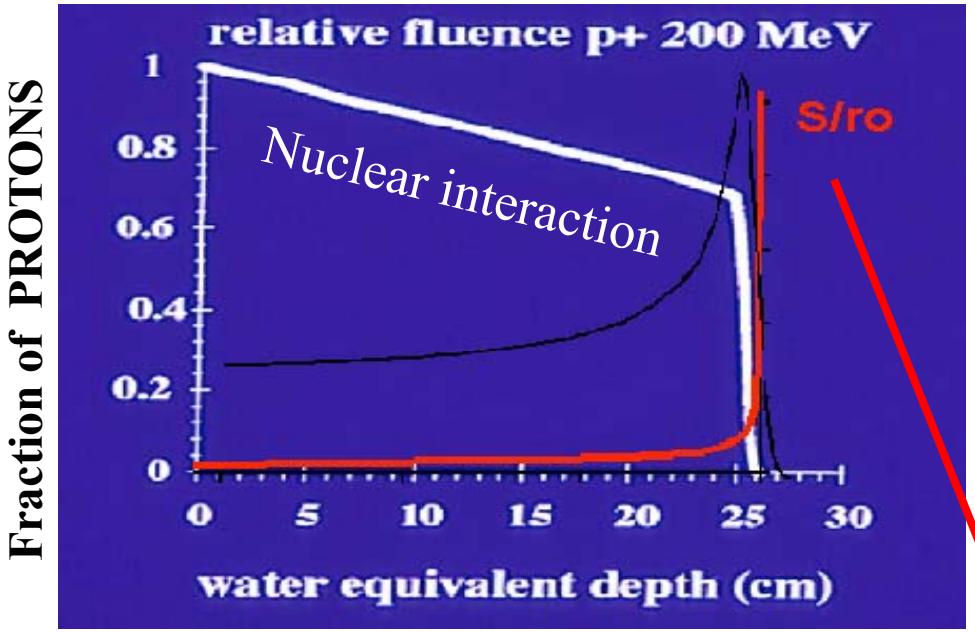
Fractionation effect

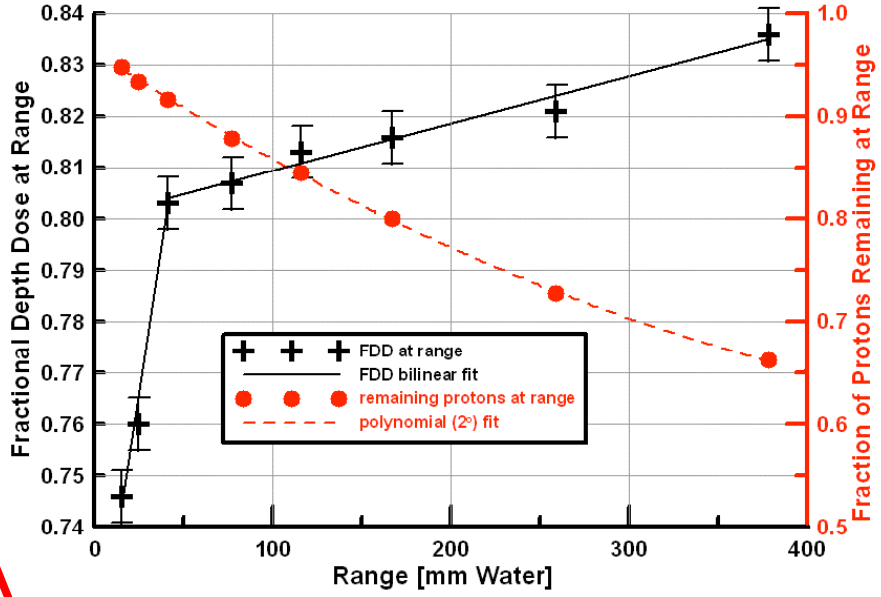
- during tumor therapy dose is split into several fractions gives normal tissue time for generation repair capacity correlates with shoulder of survival curve (low shoulder => low fractionation effect) but tumor tissue can also regenerate



- low LET: for tumor killing need of higher cumulative dose than given as single dose
- high LET: lower damage of normal tissue and lower repair capacity => lower effect of fractionation

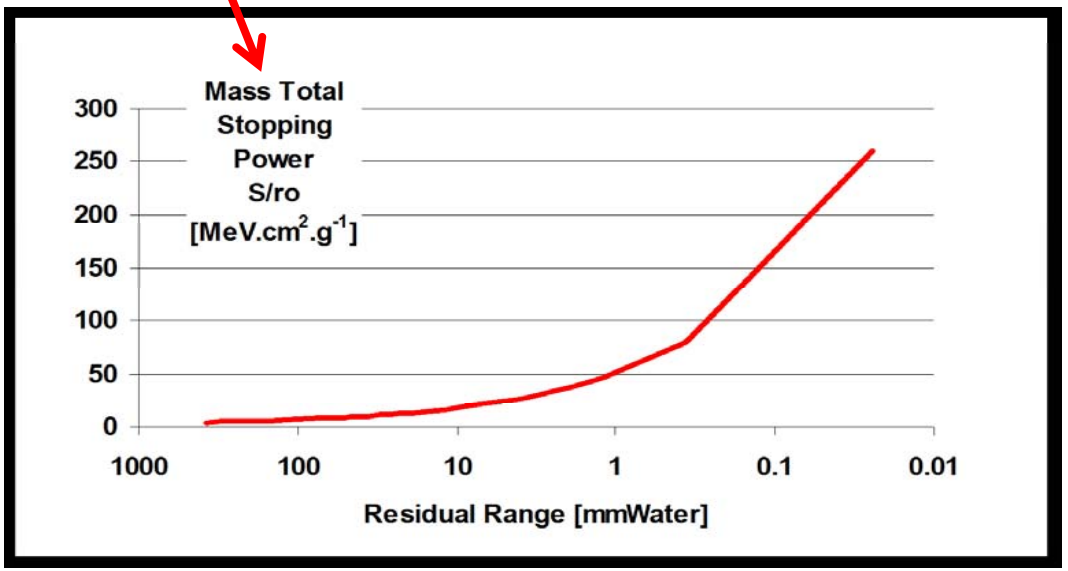
For every cm of depth, ≈ 1% of protons undergo nuclear reaction

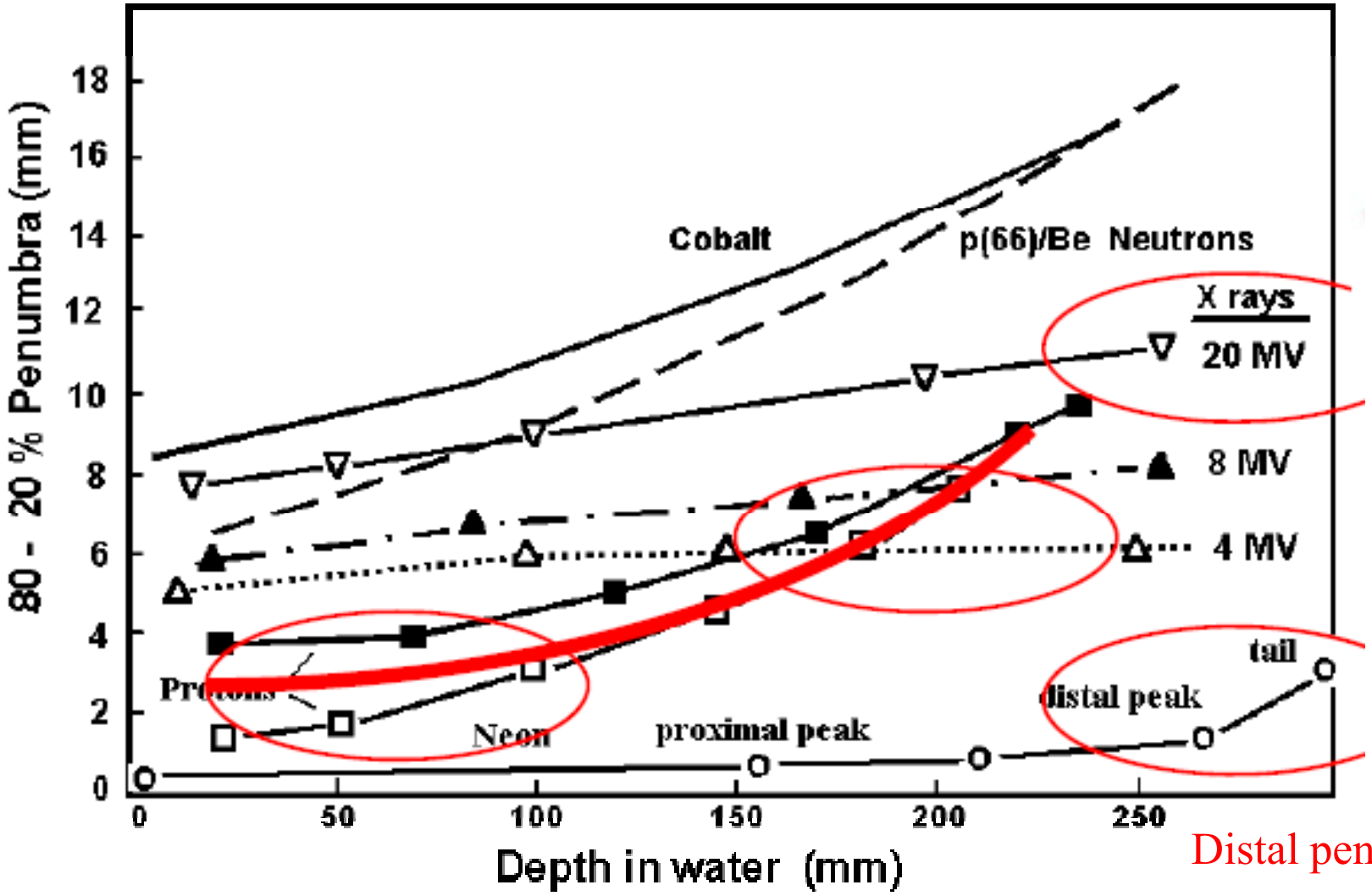




S/r0: Total mass stopping power (MeV-cm^2/g)

Effect of each proton (ionization dose)





Distal penumbra

Taken from A. Mazal et al in PTCOG46

Intensity: To treat a 20 x 20 x 10 cm volume in under 1 minute to 2 Gy:

proton >1 x 10^{10} per second,

carbon > 3 x 10^{8} per second delivered to the treatment field.

As overall efficiencies in beam utilization can be as low as 10%, accelerator capability should be about 10 times higher. The inefficiencies arises either from absorption and collimation in passive scattering systems; from reductions in intensity to minimize effect of spikes in a noisy spill, or from various gating scenarios to compensate for patient motion.

Safety: Redundancy of dosimetry and control systems, and an extremely well-trained and constantly alert staff are mandatory. The technical performance and psychological intensity levels are greater than experienced at most accelerator facilities, and require particular attention in facility designs.

Availability: An accelerator system operating in a clinical environment must have reliability > **95%.** 15~30 minutes/fraction; 8/16-hour treatment days, 6 days per week; 50 weeks per year. In addition, time for beam calibrations and QA checks.

Clinical considerations on facility design

- The most important elements defining the system performance are the **Nozzle, the Patient Positioning system and the beam delivery system**!
- The Accelerator and the Beam Transport System have much less impact on the system performance!
- ELISA (Energy, LET, Intensity, Safety, Availability)
- The **simplest accelerator** meeting the clinical specifications in a cost-effective way should be selected! The Accelerator should be transparent at treatment level. Examples of accelerator design will be given below

Beam requirements and accelerator choices

	Energy (MeV/u)	Energy stability ΔE/E for distal control	Beam Intensity	Beam current Stability for wobbling & scanning	Fast beam current control for conformal therapy
Proton	**250**		**≥5×10^{10} pps**		
Ions (C12)	**400**		**≥5×10^{8} pps**		

	Linac	Cyclotron	FFAG	Synchrotron	DWA
B-field	none	constant	constant	varying	none
F_rf	constant	constant	varying	varying	pulsed
E_Change	degrader	degrader	Acc. cycle	Acc. cycle	Pulse by pulse
Current (nA)	1600	1~100	1~100	1~10	Very high
Rep rate (Hz)	1~60	continuous	100~1000	0.5~50	< 1 Hz
Pulse length	ms	continuous	~100 ns	0.1μs~3s	ns
Scanning type	spot	all	spot	All+energy	?
cost	high	moderate	high	moderate	?

Clinical Requirements of Proton Therapy Facility

Range in Patient	3.5 – 32 g/cm^2
Range Modulation	Steps of 0.5 g/ cm^2 over full depth 0.2 g/ cm^2 for ranges < 5 g/ cm^2
Range Adjustment	Steps of 0.1 g/ cm^2 0.05 g/ cm^2 for ranges < 5 g/ cm^2
Average Dose Rate	2 Gy/min for 25 x 25 cm^2 field at 32 g/cm^2 full modulation
Spill Structure	Scanning compatible
Field Size (cm^2)	Fixed: 40 x 40; Gantry: 26 x 20
Dose Compliance	±2.5% over treatment field
Effective SAD (source to axis distance)	Scattering: 3 m from the first scatterer Scan: 2.6 m from the center of magnet
Distal Dose Falloff (80–20%)	0.1 g/ cm^2 above range straggling
Lateral Penumbra (80–20%)	<2 mm over penumbra due to multiple scattering in patient
Dose Accuracy	±2%

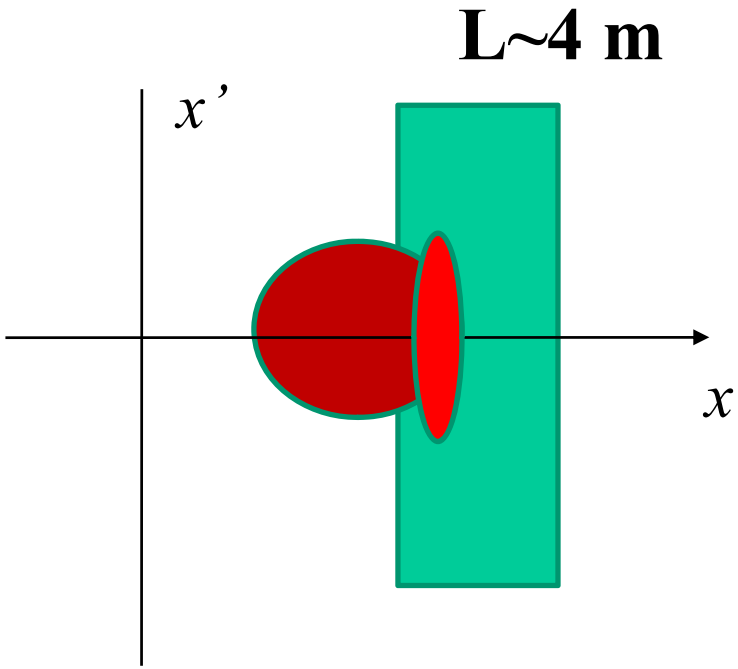
Facilities (if we find time later)

Synchrotrons: raster-scanning optimized, flexible beam extraction, fast variation of energy (range)

	LomaLinda	PIMMS	Mitsubish	Hitachi	CIS+	Carbon
C (m)	20.05	75.2		23	28.5	63.6
E_inj (MeV)/u	1.7	7	3	7	7	7
E_max(MeV)/u	250	400	250	250	300	400
Dipole length (m)	1.257	1.553		1.466	3	3.5
Dipole number	8	16	4	6	4	16
Edge angle (deg)	18.8				8.5	22.5
Quad (iron core)	4	24	5		0	16
Quad (air core)	1				1	1
sextupole	4	5	6		4	4
Qx	**0.6**	1.8		1.7	1.68	1.819
Qy	1.32	1.85		1.45	0.71	0.792

Injection

Strip-injection

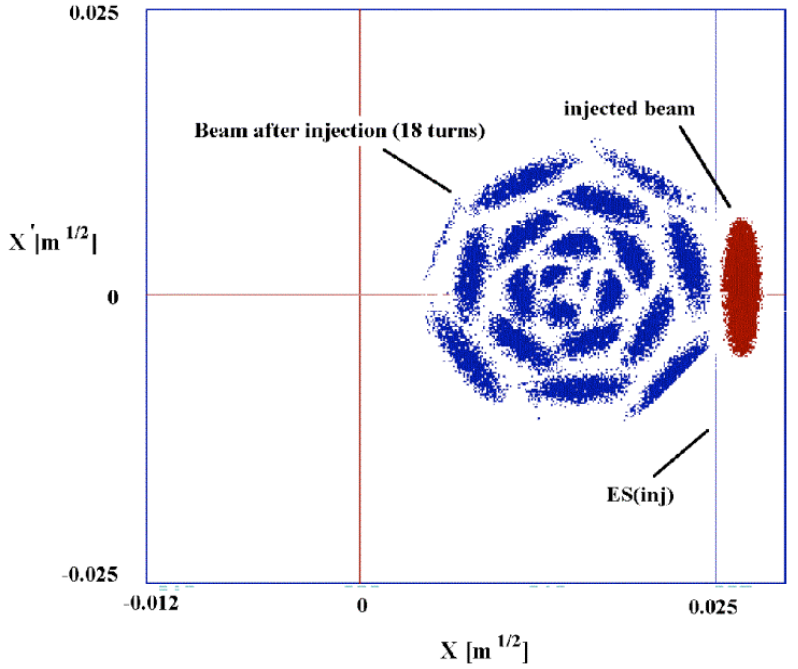


Emittance ~ 17 pi-mm-mrad

$N_B \sim 3\times10^{10}$ to 1×10^{11}

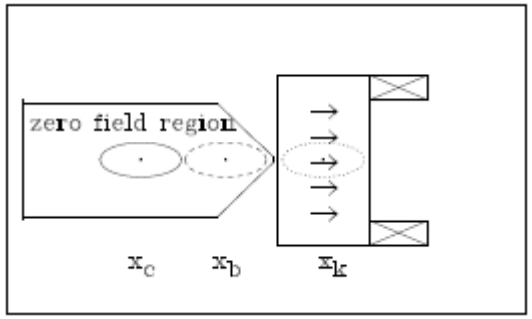
Multi-turn injection simulation

Multi-turn accumulation injection



Emittance > 100 pi-mm-mrad

$N_B \sim 3\times10^{10}$ to 1×10^{11}



Strip injection for carbon ion synchrotrons

REVIEW OF SCIENTIFIC INSTRUMENTS 78, 096104 (2007)

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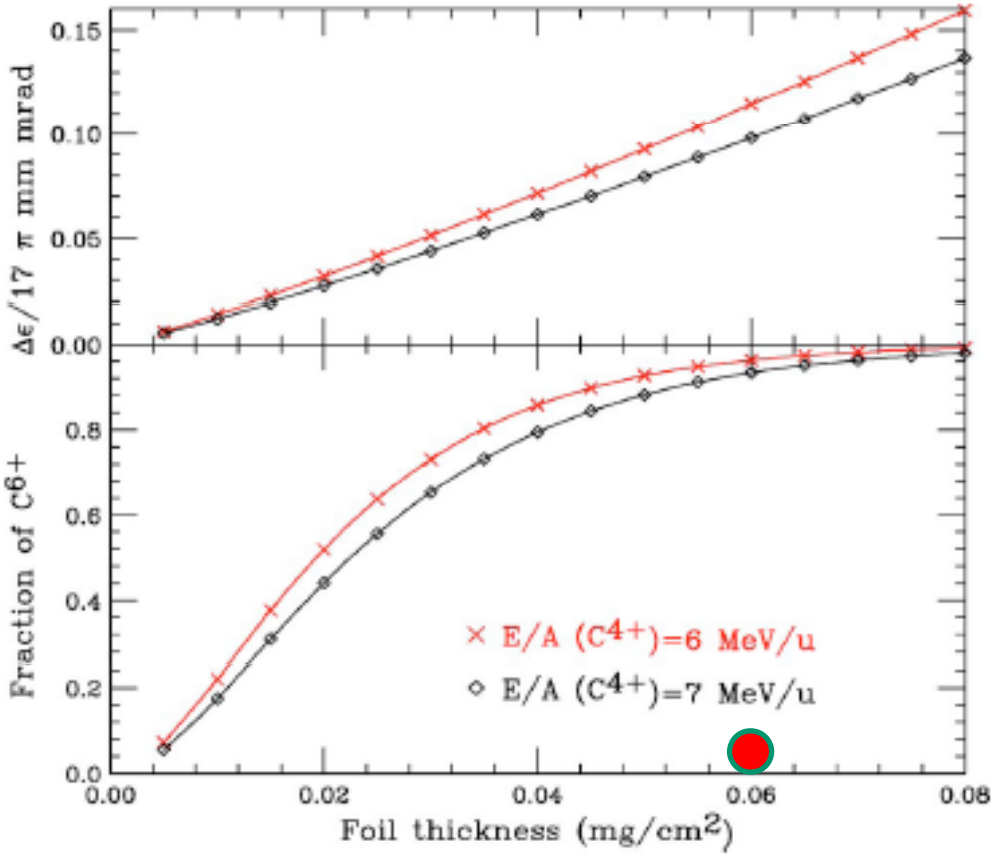
$$\frac{dF_i}{dx} = \sum_{j \neq i} \sigma_{ji} F_j - \sum_{j \neq i} \sigma_{ij} F_i,$$

$$\frac{dF_4}{dx} = -\sigma_{45} F_4,$$

$$\frac{dF_5}{dx} = \sigma_{45} F_4 - \sigma_{56} F_5,$$

$$\frac{dF_6}{dx} = \sigma_{56} F_5,$$



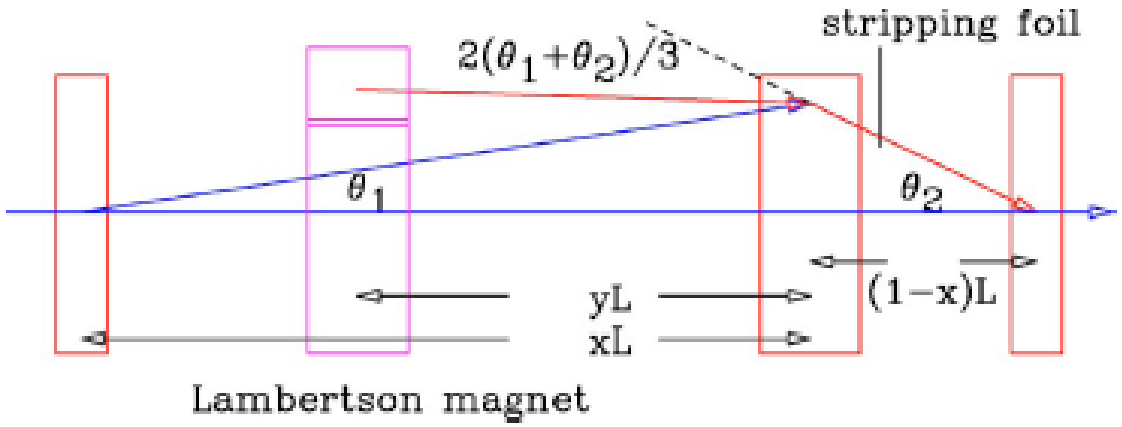
peed

(5)

data

FIG. 1. (Color online) Bottom: fraction of C^{6+} vs the foil thickness (x) for injection energies of C^{4+}:6 and 7 MeV/u, respectively. Top: fractional in- : stripping foil vs

$$F_6(x) = 1 - e^{-\sigma_{45}x} - \frac{\sigma_{45}}{\sigma_{45} - \sigma_{56}}\left(-e^{-\sigma_{45}x} + e^{-\sigma_{56}x}\right).$$



$$\frac{1}{3}(\theta_1+\theta_2)yL \geqslant 3(\sigma_{inj}+\sigma_{cir})+\Delta_{septum},$$

Septum separation

$$(x-y)L\theta_{septum} \geqslant H,$$

Injection beam clears from main dipoles

$$(1-x)L \geqslant 1\ \mathrm{m},$$

Enough space for stripping foil assembly

Using the 7 MeV/u linac or the 6 MeV/u FFAG C^{4+} sources, we can easily accumulate a beam of 10^{11} C^{6+} with an emittance of 17 π-mm-mrad in synchrotron.

	LINAC	FFAG
E (MeV/u) C^{4+}	7	6
N/pulse (10^9)	60	5.9
Emittance (πμm)	6.4	8.8
N_turn (10^9)	0.40	5.9
Pulse length (μs)	300	
Tolerable foil hits	12	10
Accumulation turns	150	19
N_total (10^{11})	0.60	1.0
Emittance (πμm)	17	17

Space charge limit: $\Delta\nu_{\mathrm{sc}} = \frac{F_{\mathrm{B}} N_{\mathrm{B}} r_0}{2\pi\epsilon_{\mathrm{N}}\beta\gamma^2} = \frac{2\pi R K_{\mathrm{sc}}}{4\pi\epsilon}$

	p	C^{12}
A	1	12
Z	1	6
Circum(m)	30	65
Einj/u (MeV)	7	7
Eext/u (MeV)	250	400
p (MeV/c)/u	729.13	951.42
Brho (T-m)	2.43	6.35
dnu_sc	0.2	0.2
N_sc	**1.01E+11**	**3.38E+10**
epsN (μm)	2	2
beta_inj	0.12	0.12
gamma_inj	1.0075	1.0075

Other instabilities?

Example: Characteristics of HIMAC

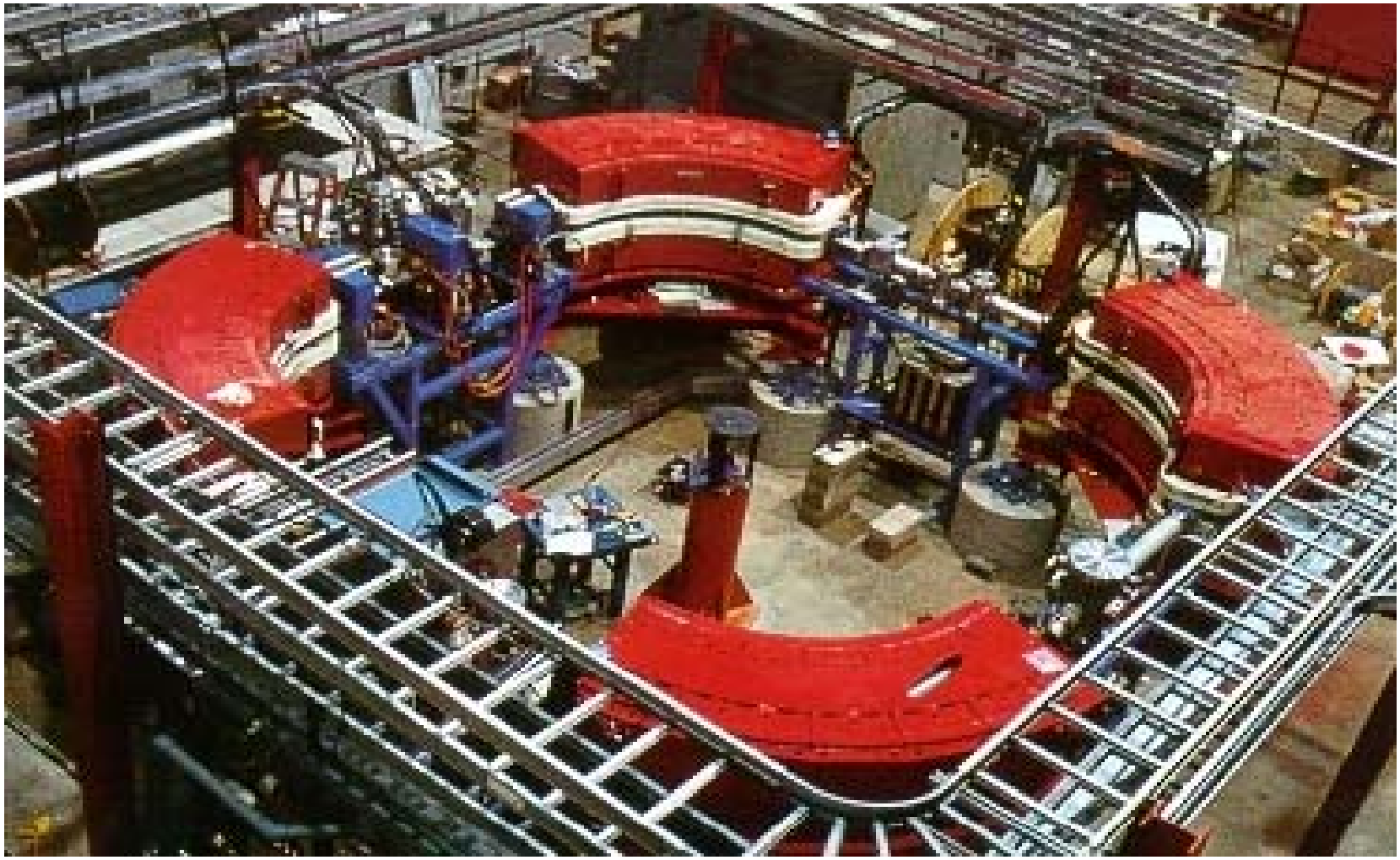
1984: Governmental 10 years strategy for cancer control
1993: Construction of heavy ion medical accelerator in Chiba(HIMAC)

ions	He to Ar
E_max (MeV/u)	800
Minimum Energy (MeV/u)	100
Beam Intensity	He: 1.2×10^{10} pps
	C: 2×10^{9} pps
	Ar: 2.7×10^{8} pps
Treatment Characteristics	Field size 22 cm
	Beam homogeneity ±2%
	Maximum range 30 cm
	Dose rate 5 Gy/min.
	Treatment rooms 3 (A,B,C)

CIS: Circumference = 1/5 C_cooler = 17.364 m

Dipole length = 2 m, 90 degree bend, edge angle = 12 deg.

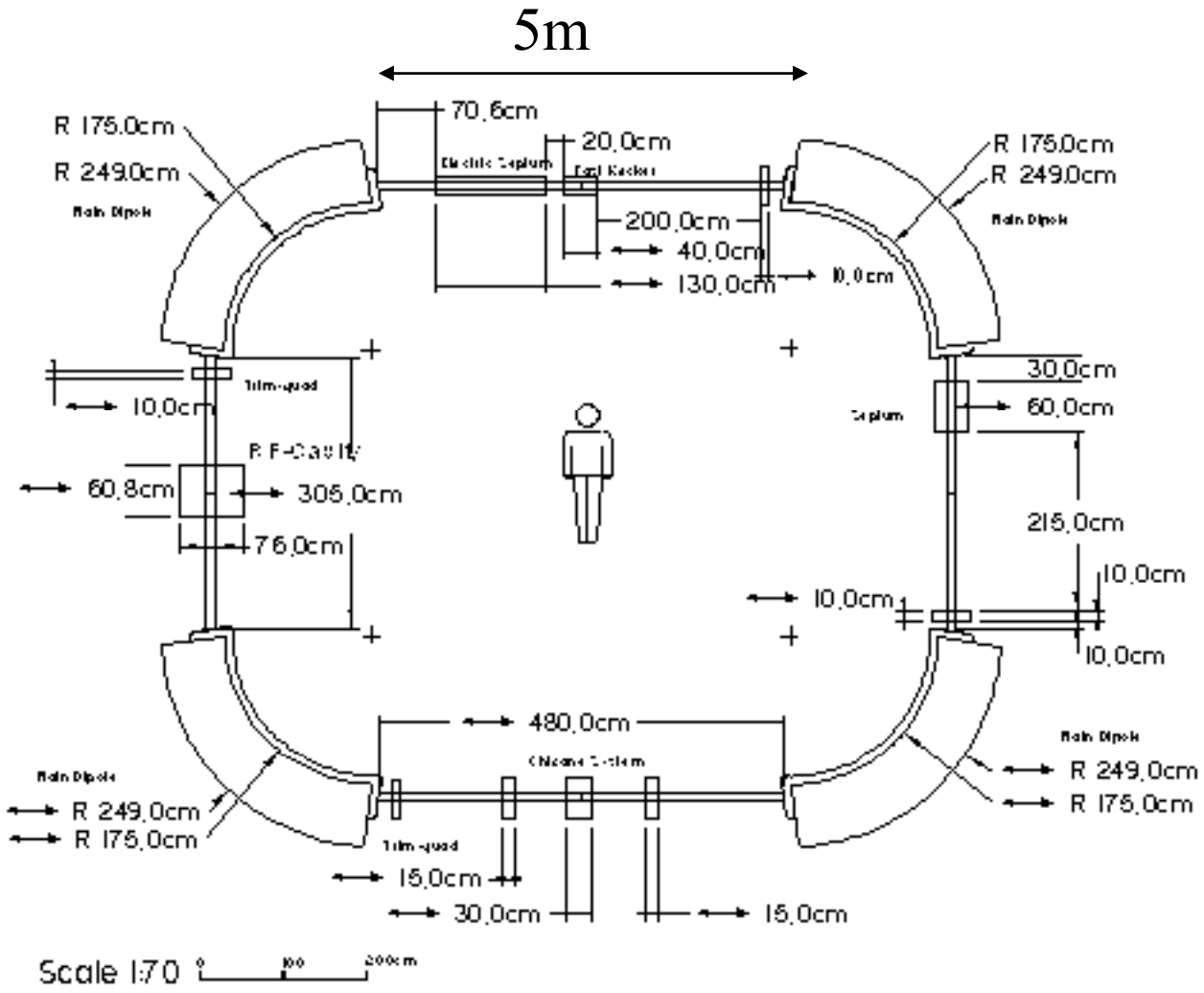
Inj KE= 7 MeV, extraction: 250 MeV



250 MeV Proton Synchrotron

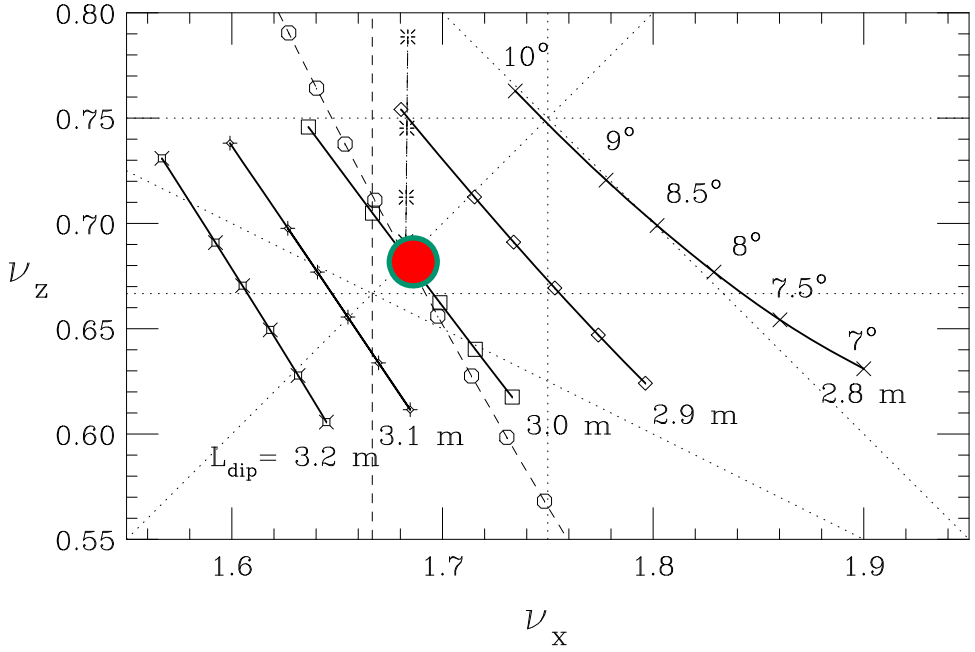
1996-1999

Example: a Compact medical **proton** Synchrotron



Ldip=3.0 m
ρ=1.91 m
Edge_angle=8.5°
Circum=28.5 m
Qx=1.68
Qz=0.71
KE_tr=356 MeV

3.25m



Ldip=3.0 m
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Qx=1.68
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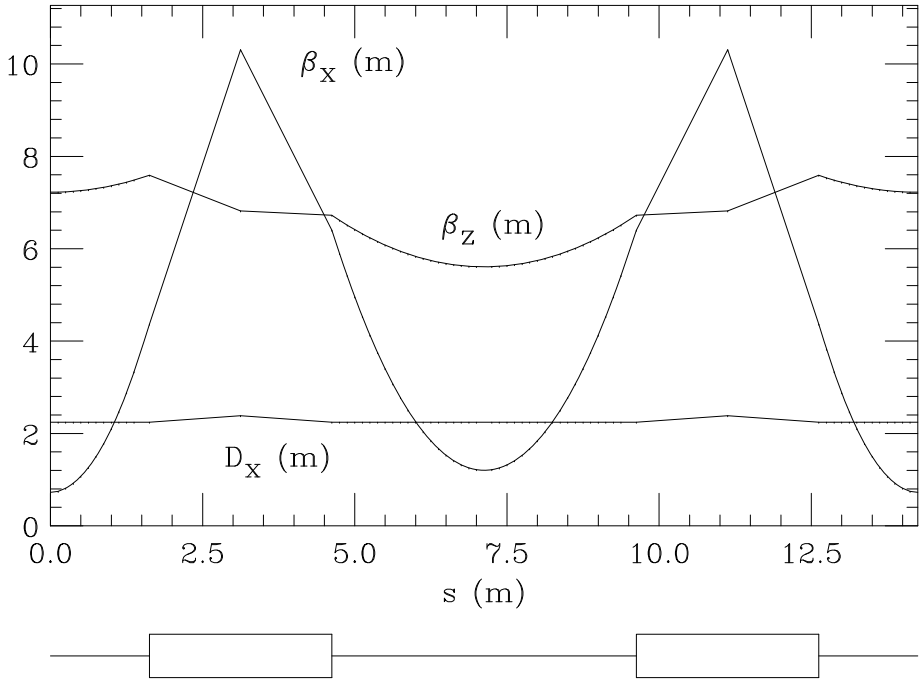
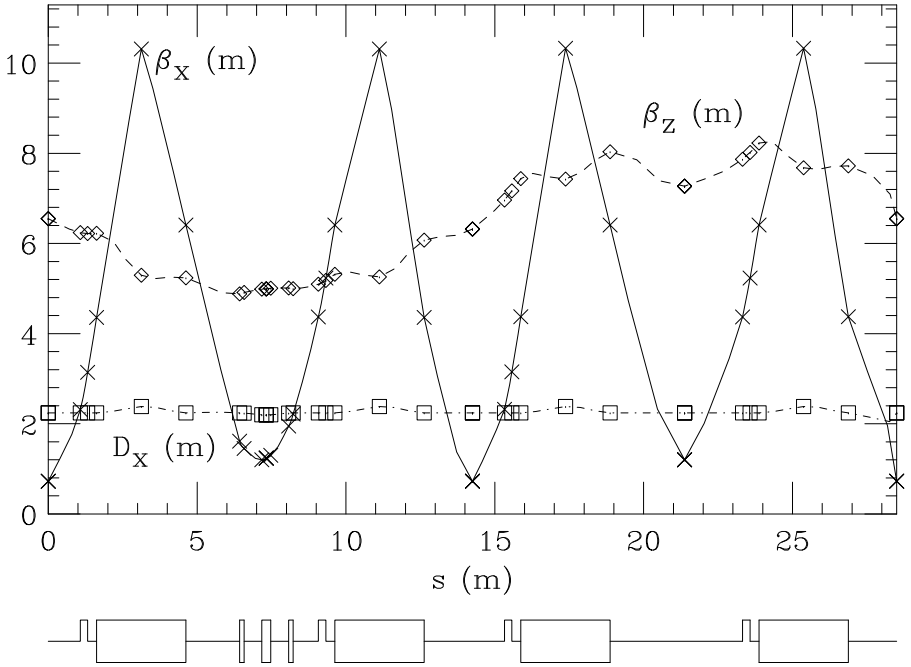
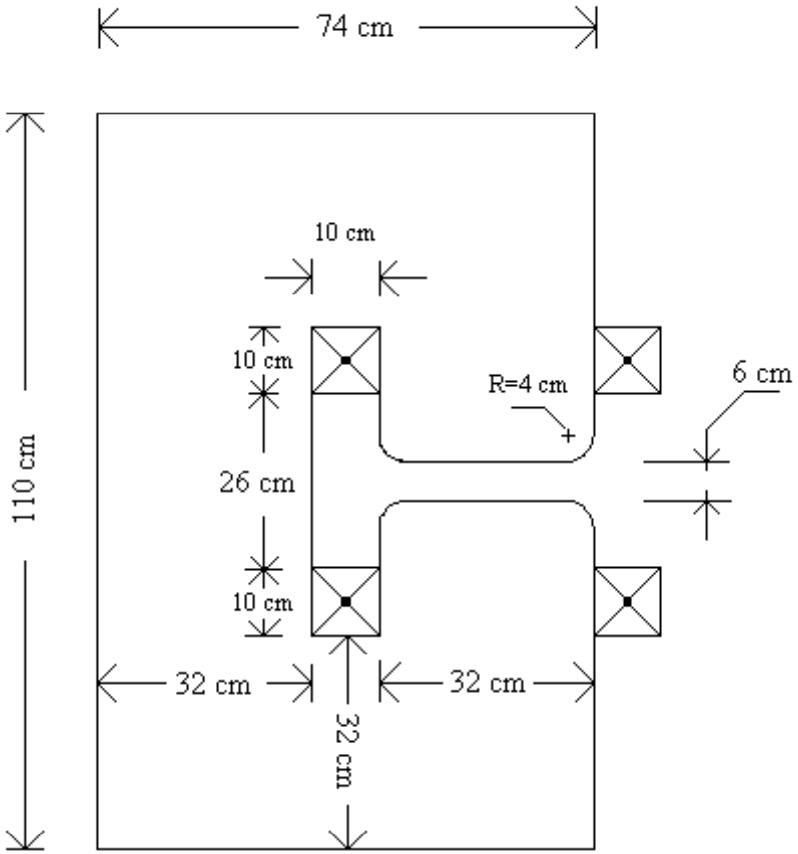
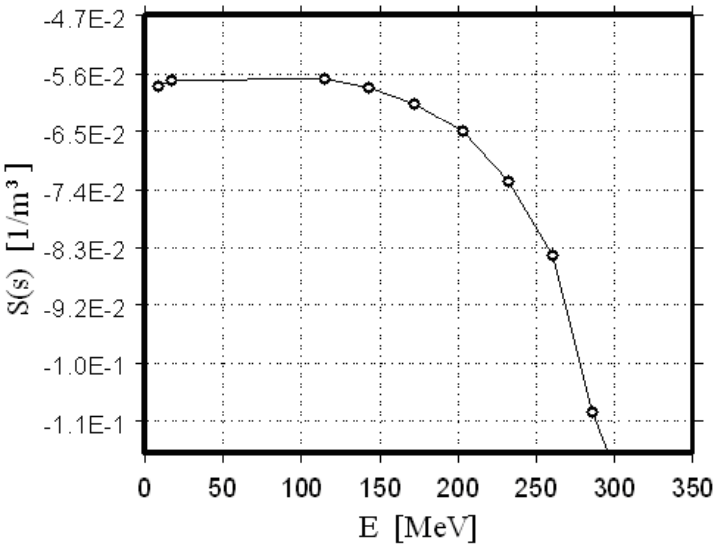
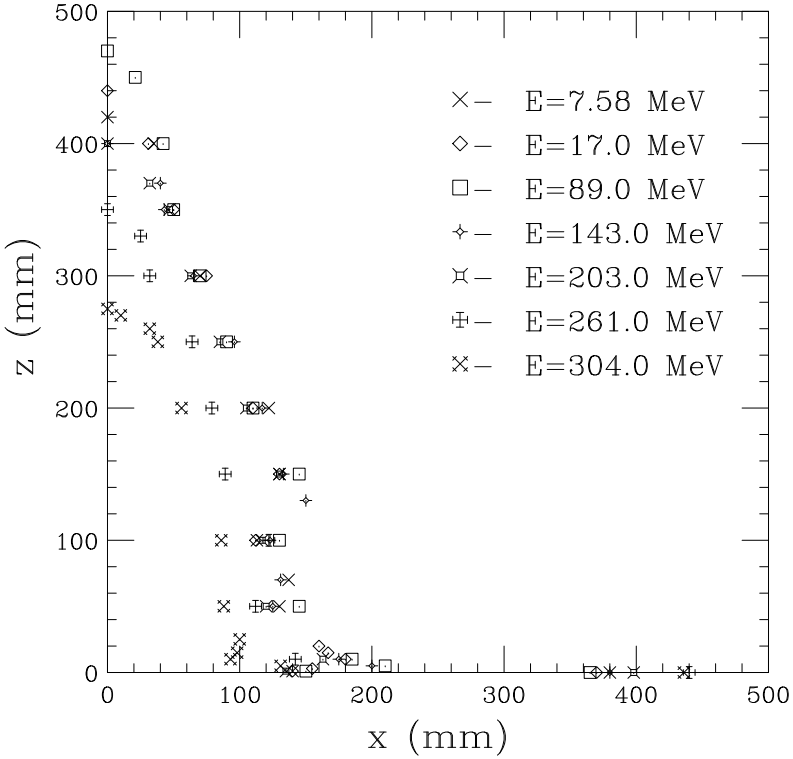




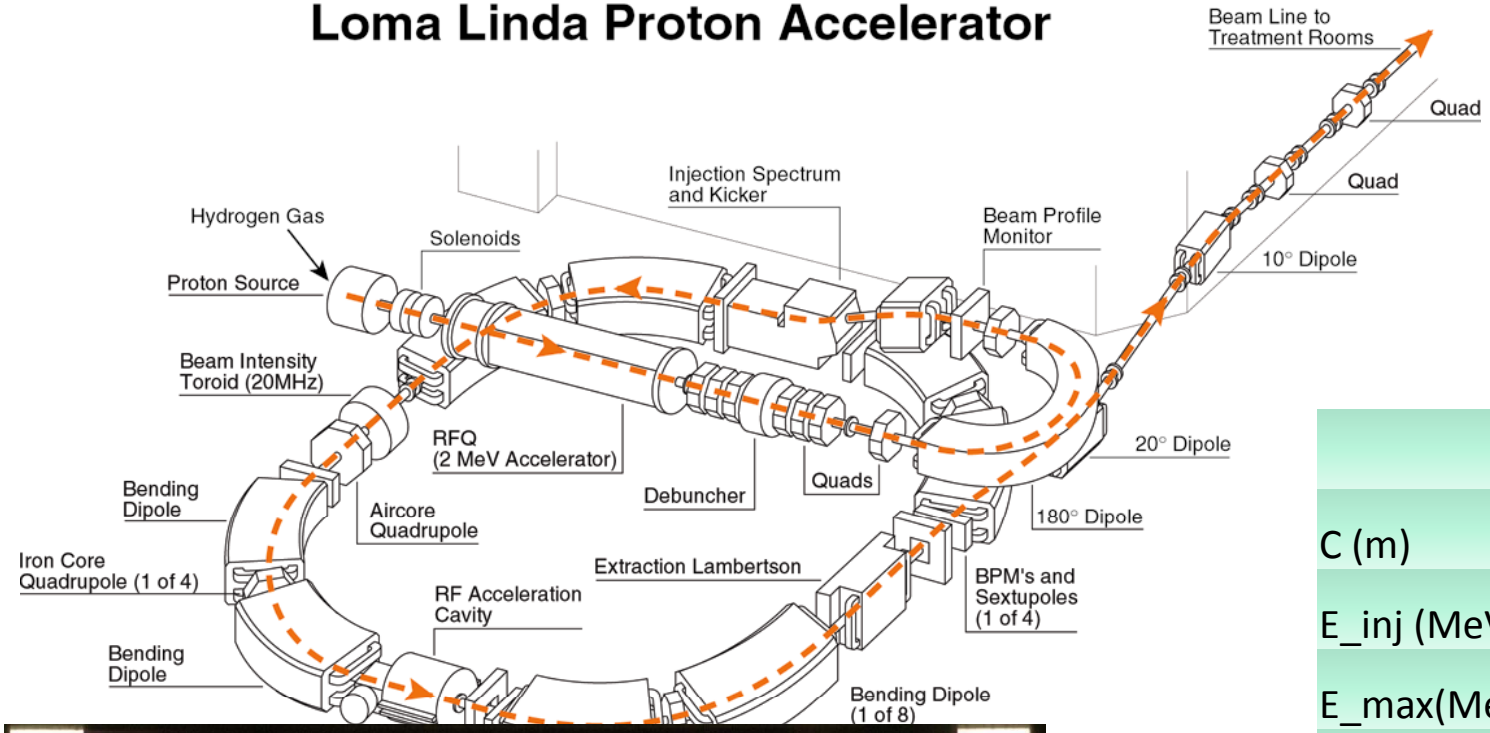


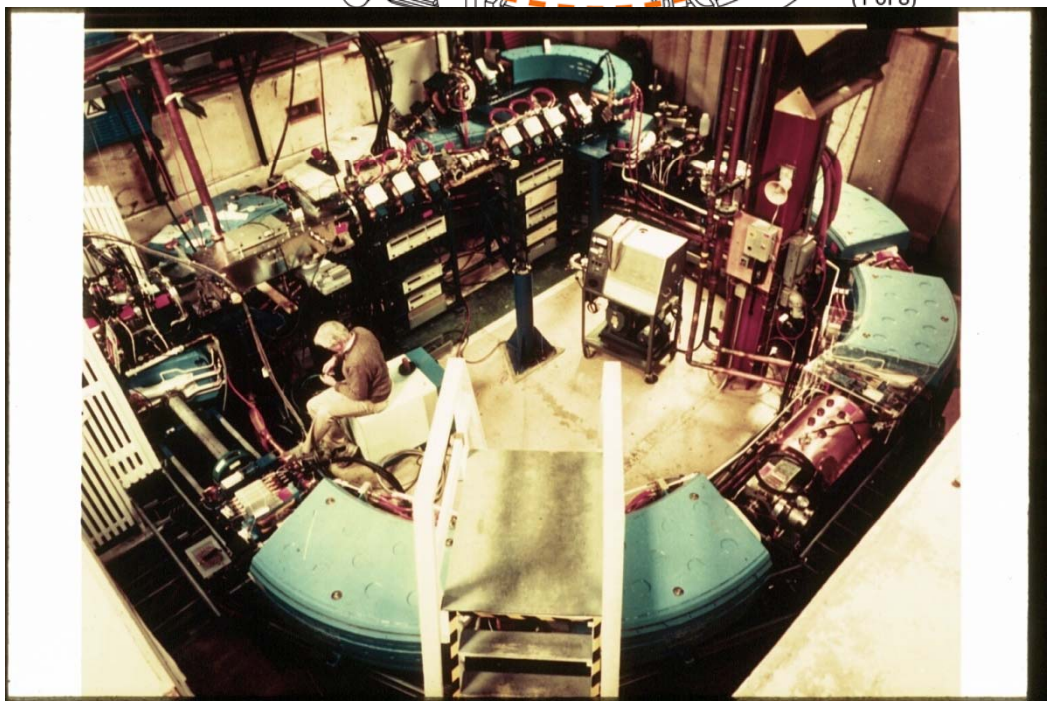




Dynamical Aperture

Loma Linda Proton Accelerator

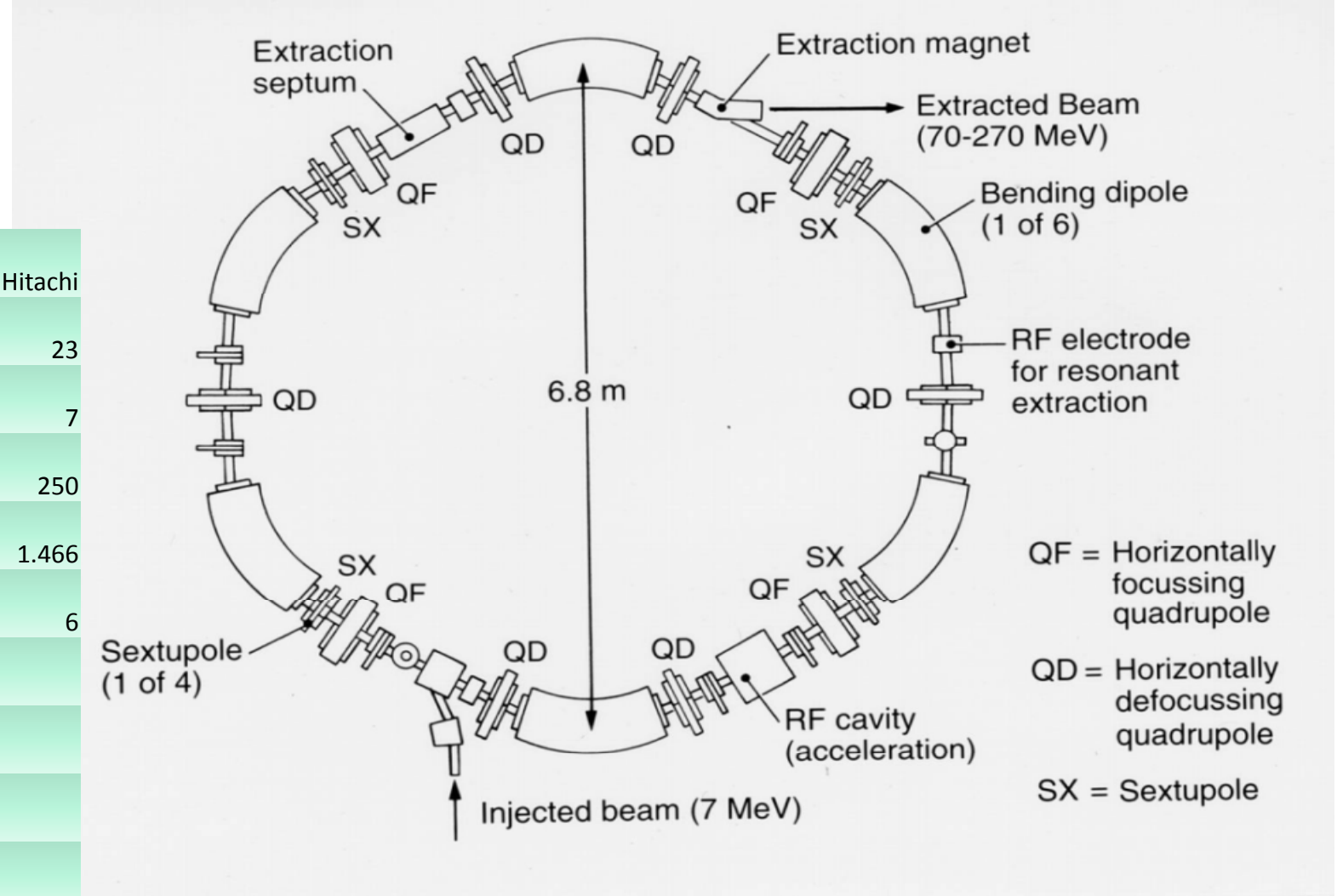




	LomaLinda
C (m)	20.05
E_inj (MeV)/u	1.7
E_max(MeV)/u	250
Dipole length (m)	1.257
Dipole number	8
Edge angle (deg)	18.8
Quad (iron core)	4
Quad (air core)	1
sextupole	4
Qx	**0.6**
Qy	1.32

Hitachi Medical Synchrotron

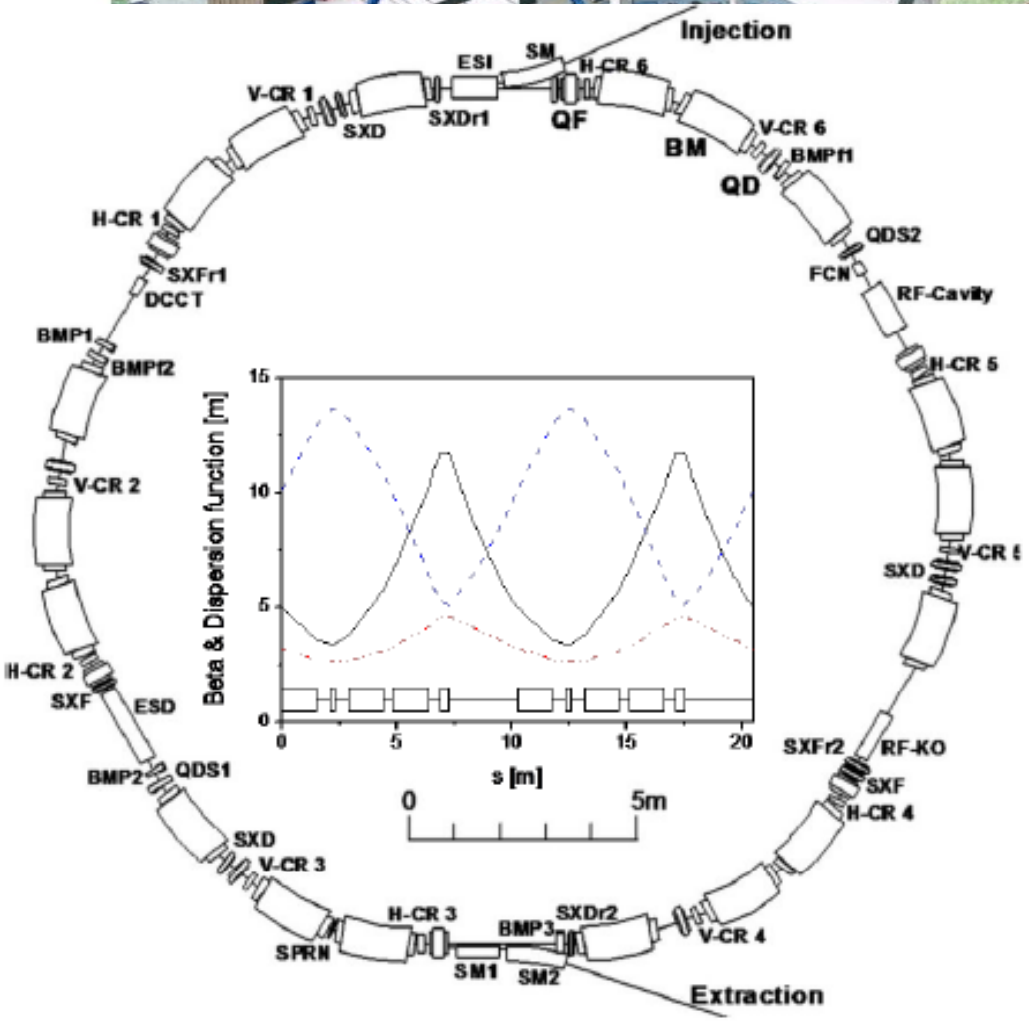
	Hitachi
C (m)	23
E_inj (MeV)/u	7
E_max(MeV)/u	250
Dipole length (m)	1.466
Dipole number	6
Edge angle (deg)	
Quad (iron core)	
Quad (air core)	
sextupole	
Qx	1.7
Qy	1.45



PMRC, Univ. of Tsukuba: P (2001)
MD Anderson Cancer Center : P (2006)
Wakasa Bay: P, He, C (Multi Purpose) (2000)

Synchrotron (70-250MeV)

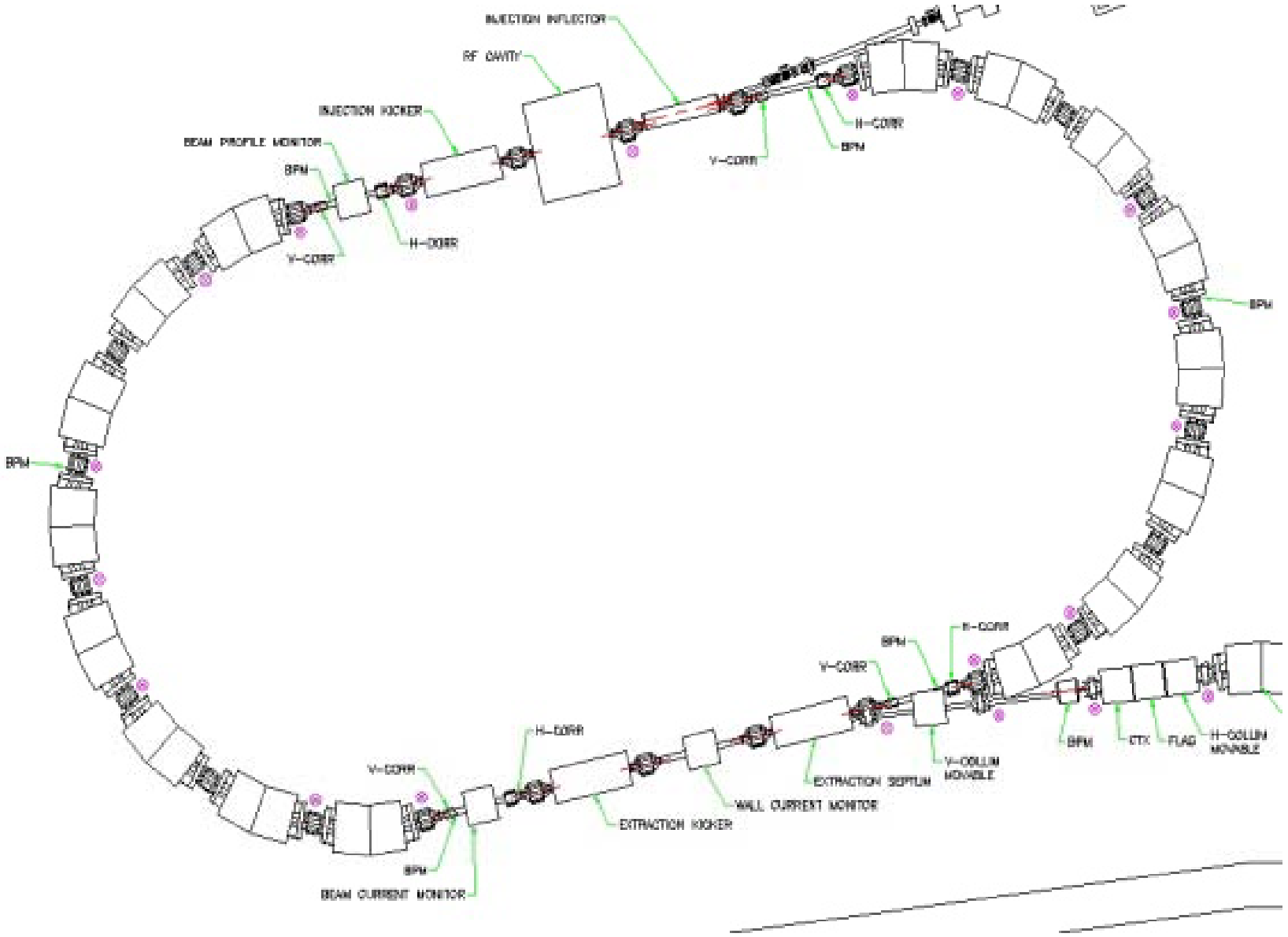
Gunma University Heavy Ion Medical Facility

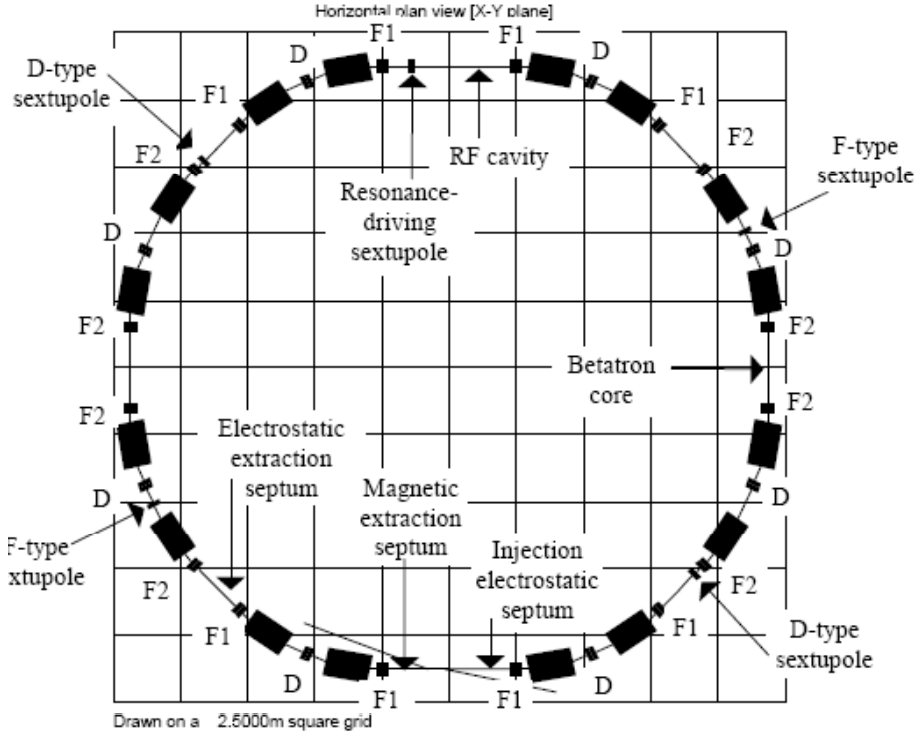


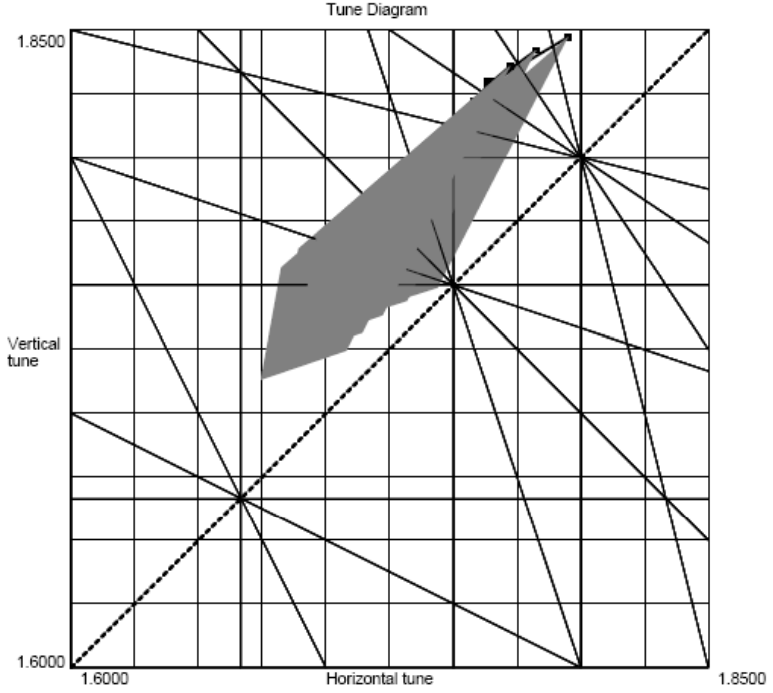
Specifications

Ions	C^{6+}
Injection	4 MeV/u
Max. Energy	400 MeV/u
Beam Intensity	2×10^9 ppp
Repetition	0.5 Hz (typical)
Circumference	62.7 m
Straight Sections	3m × 6
Max. Field	1.5 T
Acceptance:	
Momentum	±0.3%
Horizontal	200 π mm·mrad
Vertical	10 π mm·mrad
Injection Method	Multiturn

RCS, S. Peggs, et al







	PIMMS
C (m)	75.2
E_inj (MeV)/u	7
E_max(MeV)/u	400
Dipole length (m)	1.553
Dipole number	16
Edge angle (deg)	
Quad (iron core)	24
Quad (air core)	
sextupole	5
Qx	1.8
Qy	1.85

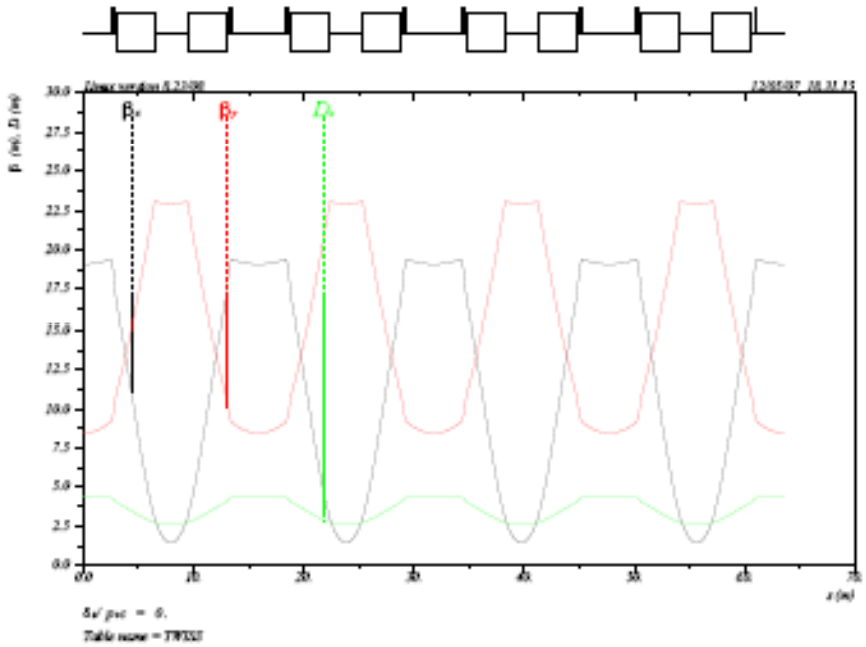
A **preliminary** design of a heavy ion therapy synchrotron

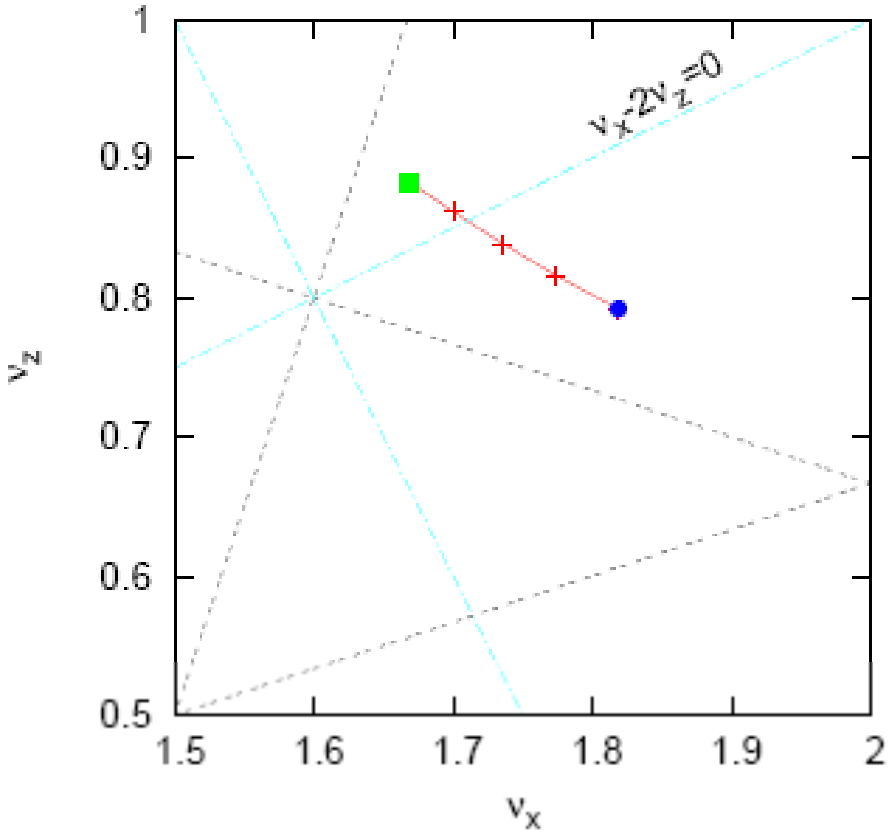
A preliminary design of a carbon ion synchrotron that can accelerate C^{6+} ions from around 6~7 MeV/u to 400 MeV/u.

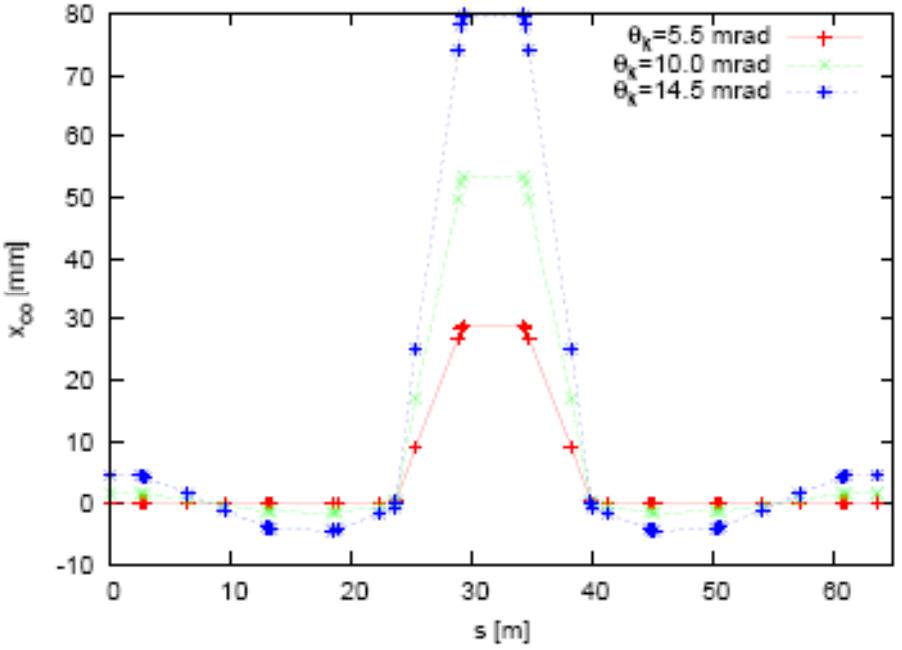
TABLE I: Lattice parameters for the Carbon Ion Synchrotron

Parameters	Symbol	Values
Circumference	C	63.6 m
Tune	Q_x	1.819
	Q_z	0.792
Dipoles:		
Length	L_b	3.5 m
Bending radius	ρ	4.244 m
Edge angle	θ_e	23.5 degrees
Quadrupoles:		
Length	L_f	0.2 m
Strength	K_f	0.99 m^{-2}
Transition energy	γ_T	1.741
Betatron functions	$\beta_{x,min}$	3.01 m
	$\beta_{x,max}$	19.41 m
	$\beta_{z,min}$	9.19 m
	$\beta_{z,max}$	23.04 m
Dispersion functions	$D_{x,max}$	6.13 m
	$D_{x,min}$	3.82 m
Chromaticity	C_x	0.370
	C_z	-2.578

The lattice function, the betatron tunes and local closed orbit bump for two injection kickers are shown. Note that a trim quad will be used to move the betatron tune for the 3rd resonance slow extraction.







The RF system

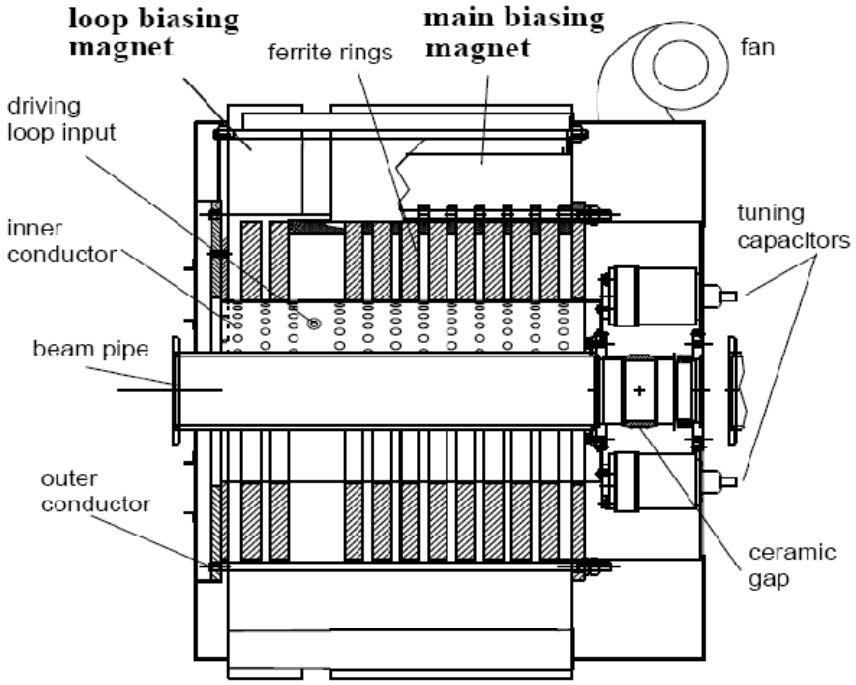
	p	C^{12}
E/u (MeV)	250	400
Brho (T-m)	2.43	6.35
L_dip (m)	11	29
C (m)	28.5	65
f_{0inj}(MHZ)	1.27	0.56
f_{0ext}(MHZ)	6.45	3.30

Requirement of rf voltage in rapid accelerating accelerators

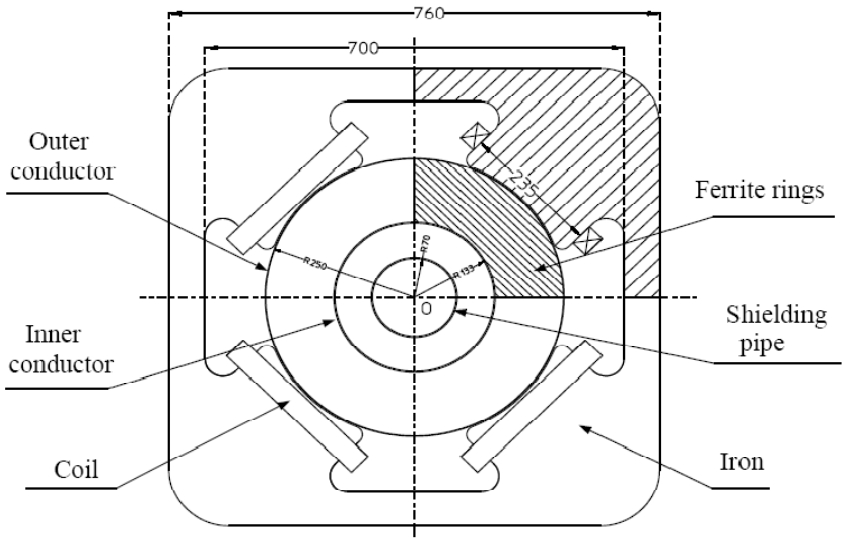
$$B\rho = \frac{p}{e}, \quad \dot{p} = \frac{1}{\beta c}\dot{E}, \quad f = \frac{\beta c}{2\pi R}, \Rightarrow V \sin\phi_s = 2\pi R\rho\dot{B}.$$

$$\omega_{\mathrm{rf}} = h\frac{\beta c}{R_0} = \frac{he\rho B}{R_0\gamma m} = \frac{hc}{R_0}\left[\frac{B^2(t)}{B^2(t) + (mc^2/ec\rho)^2}\right]^{1/2}$$

MPI cavity design



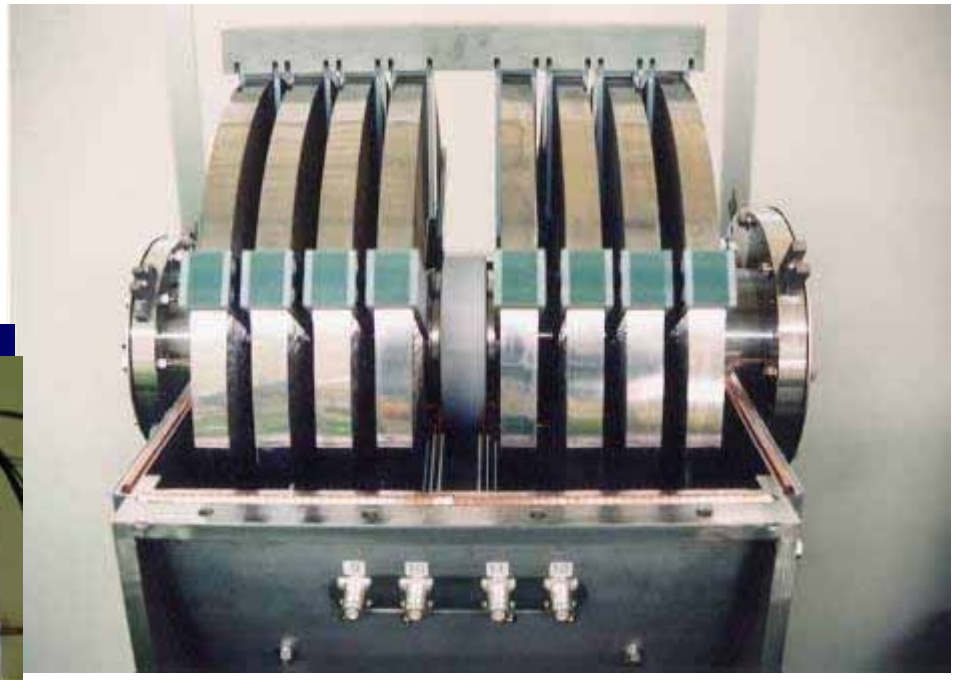
Azimuthal plan of RF cavity. Ferrite disks are divided into two groups: loop biasing magnet for the input impedance matching and main biasing magnet for biasing field.



Diameter of the cavity ~0.55m;
Length ~0.6m
10 Philips accelerator ferrite rings:
material: 8C12

Power & Industrial
Systems R&D Laboratory,
Hitachi, Ltd.
Kazuo Hiramoto

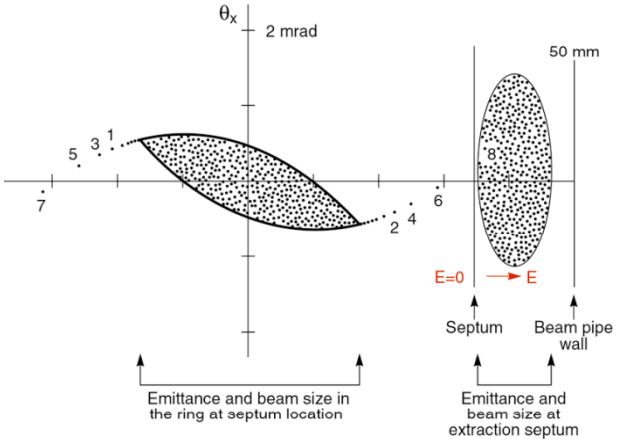
0.45 m

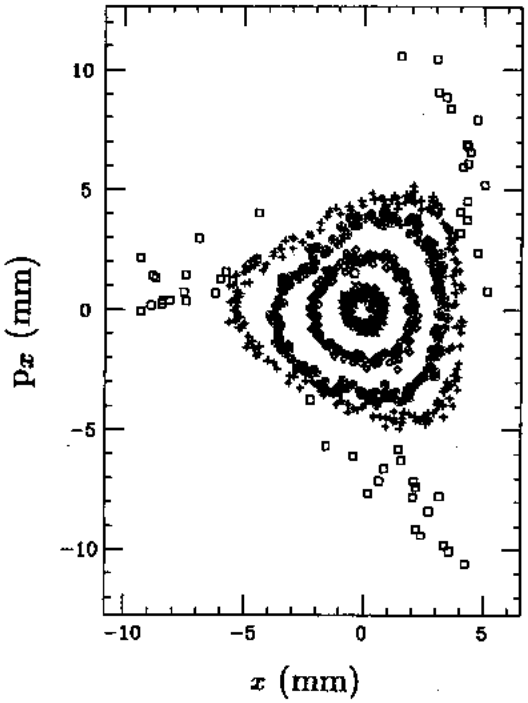


- Reliable Operation: Solid-sate Amp; Air Cooling
- Multiple Power Feeding Impedance matching between RF cavity and RF power source
- FINEMET Core
  - ✓ High complex permeability for Freq. Range 1-10 MHz
  - ✓ High Curie temperature

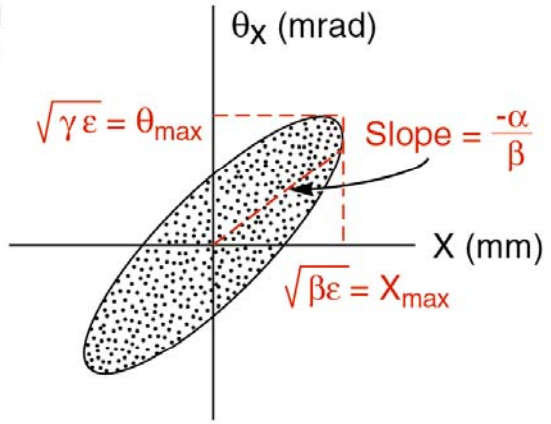
Extraction:

- Fast extraction
- **slow extraction**





$\beta\gamma - \alpha^2 = 1$
Area $= \pi\varepsilon$



The Beam Ellipse (one for X and one for Y)

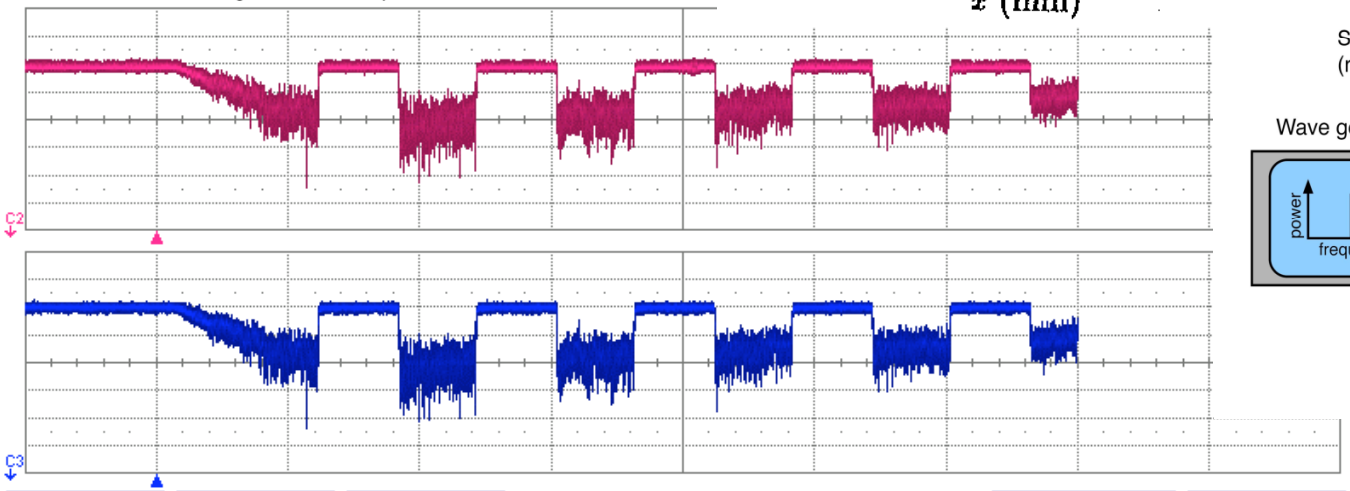
A beam is a collection of particles moving in approximately the same direction

$\sigma(1)=R\ \sigma(0)R^T$ ← 2x2 Matrix

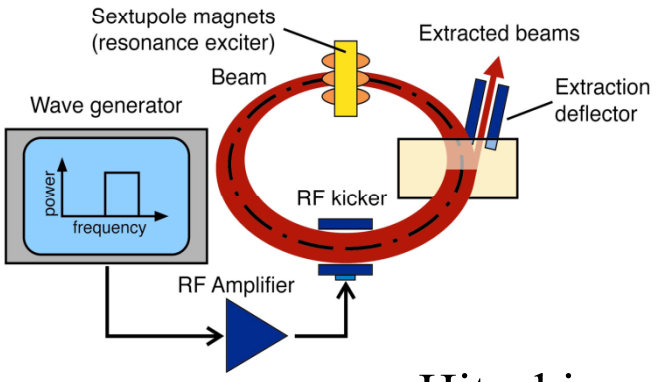
Final beam size and angles at the patient

Initial beam size and angles at extraction septum

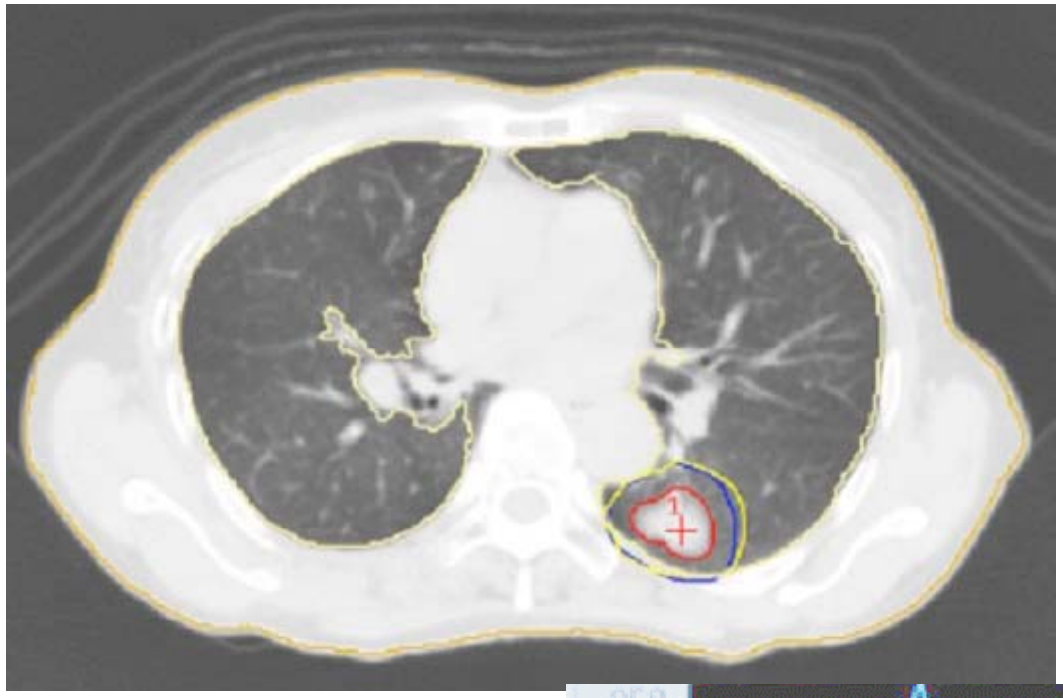
Magnet lattice



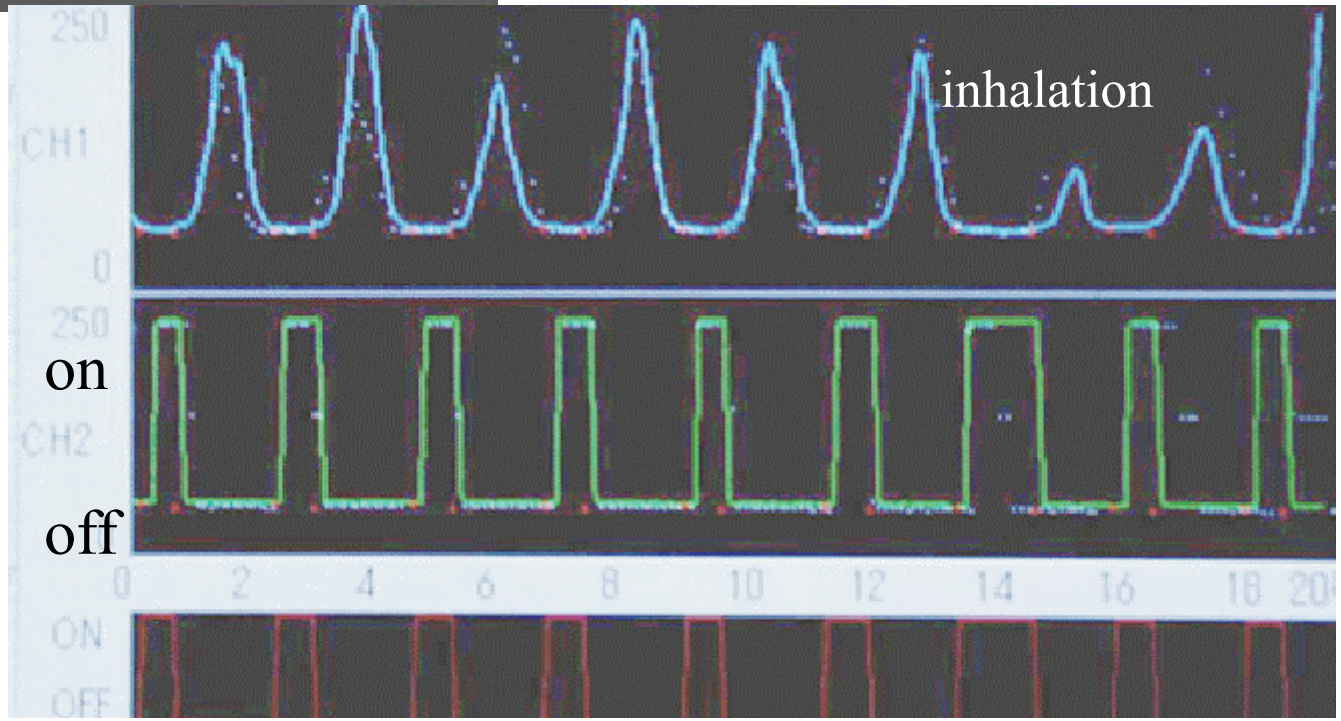
0.5 to 10 sec



Hitachi



PTV (yellow circle) is expanded from CTV + 5 mm in respiratory movement + 3 mm for set-up error



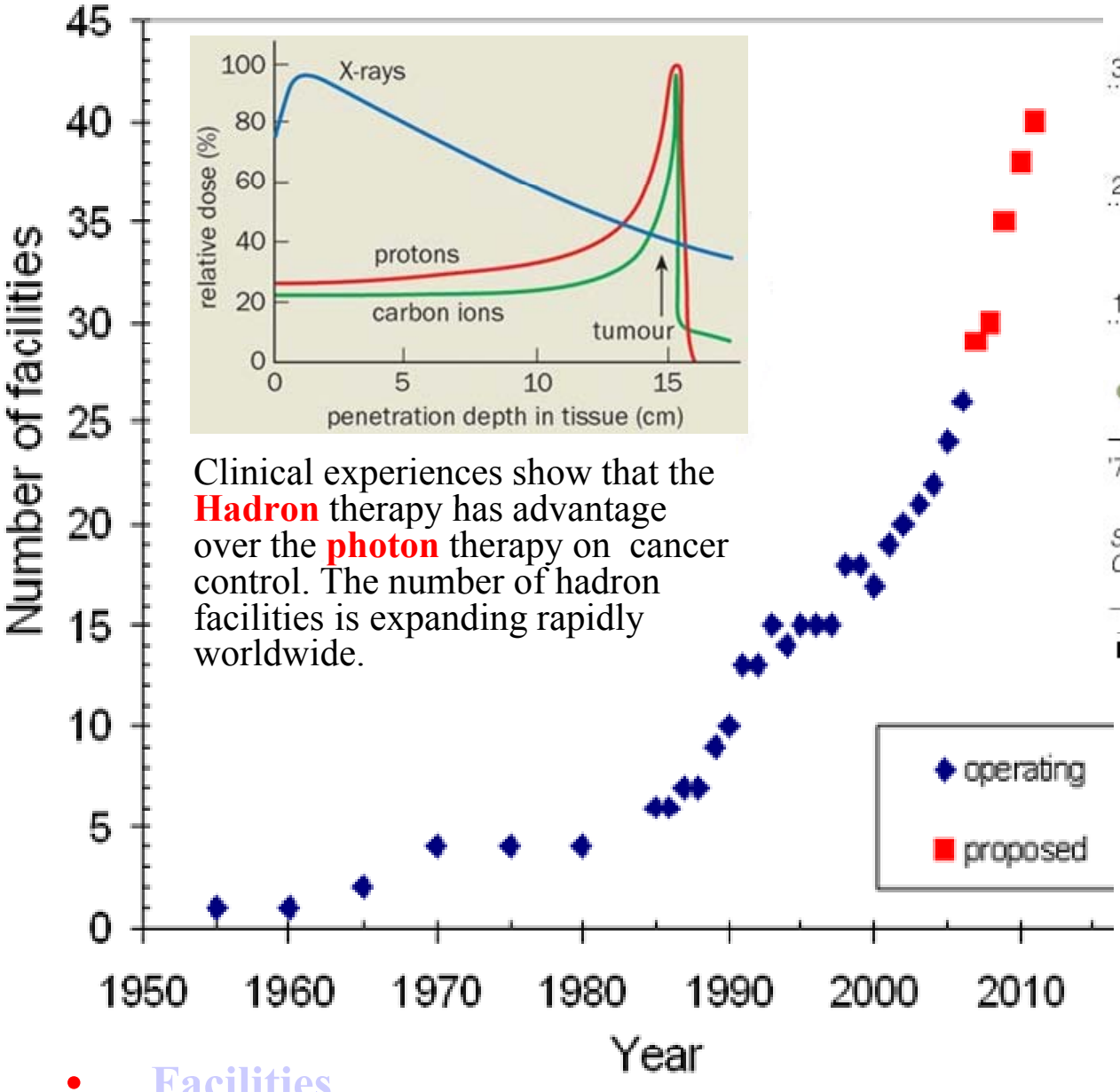
Summary

1) Energy variation for varying depth dosage -> synchrotron
2) For synchrotrons, it is better to have $\gamma \leq \gamma_T$ so that the beam can avoid negative mass instability and head-tail instability. Since $\nu_x \sim \gamma_T \geq \gamma > 1$. it is better to have a strong focusing synchrotron.
3) The wire-septum thickness becomes relatively small if the $\beta_{x(sep)}$ at the septum location is large.
4) Design $\beta_{x(sep)}$ and $\beta_{x(kicker)}$ large so that the kicker strength can be minimized
5) Design appropriate ν_x and ν_x so that dynamical aperture is large.
6) Design appropriate ν_x so that the it is easy for injection and extraction.
7) Proper locations for sextupoles and/or octupoles for increasing the extraction efficiency.
8) **Never overlook the importance of the Control system**

Conclusions

- Clinical experiences show that the **Hadron** therapy has advantage over the **photon** therapy on cancer control. The number of hadron facilities is expanding rapidly worldwide.
- Two most common accelerator designs are **synchrotron** and **cyclotron**. **Both systems work!** Technical experts are eager to work! Physicists & engineers can interact and work with medical doctors! **Medical physicists** are **well paid and in high demand**. **Dose verifiability, Beam Stability, Reliability and Reproducibility** are utmost important in a radiation therapy facility.
- Applications of accelerator, Nuclear and HEP experiences
  - Better resolution and faster **detectors**
  - Fast and compact **electronics**
  - Better and reliable beam **control systems**
  - Online controls, monitoring and fast **Data Acquisition**
  - New "in situ" imaging and dose verification technologies (in beam PET..)
  - Simulation & modeling for treatment planning
- Accelerator Design, beamline design, better uniformity of extracted beams, Control system reliability and flexibility, etc.

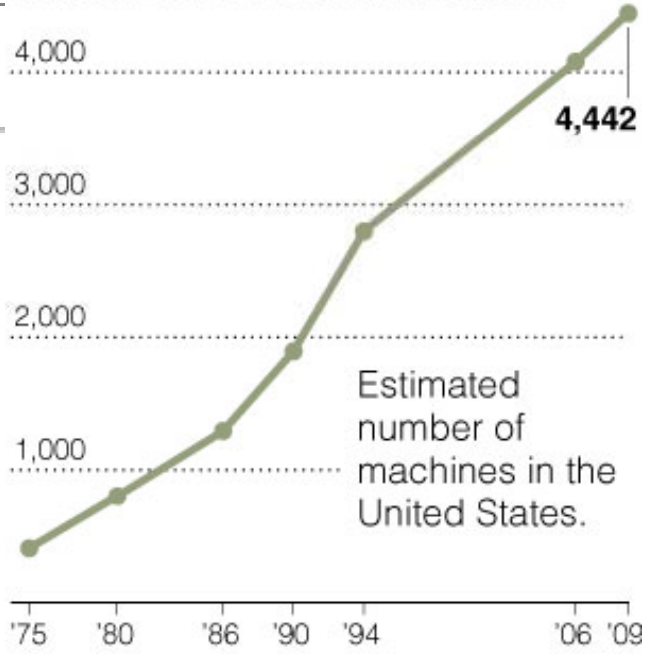
Proton Therapy Facilities



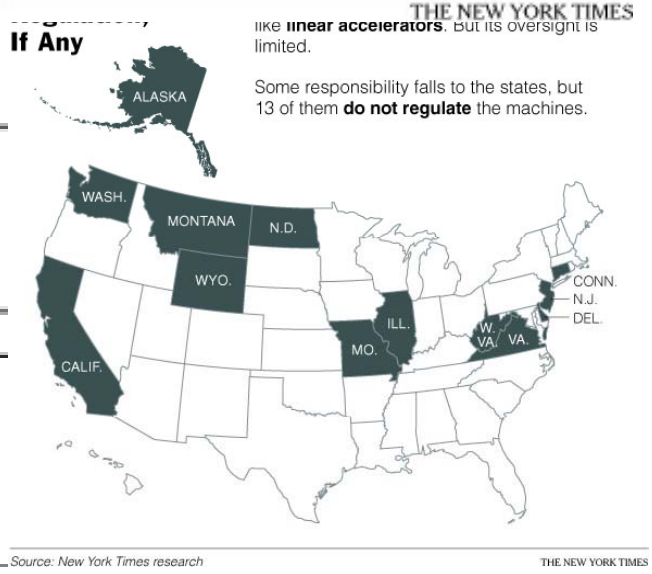
Clinical experiences show that the **Hadron** therapy has advantage over the **photon** therapy on cancer control. The number of hadron facilities is expanding rapidly worldwide.

- Facilities

More Linear Accelerators



Source: Radiological Physics Center, M.D. Anderson Cancer Center, University of Texas



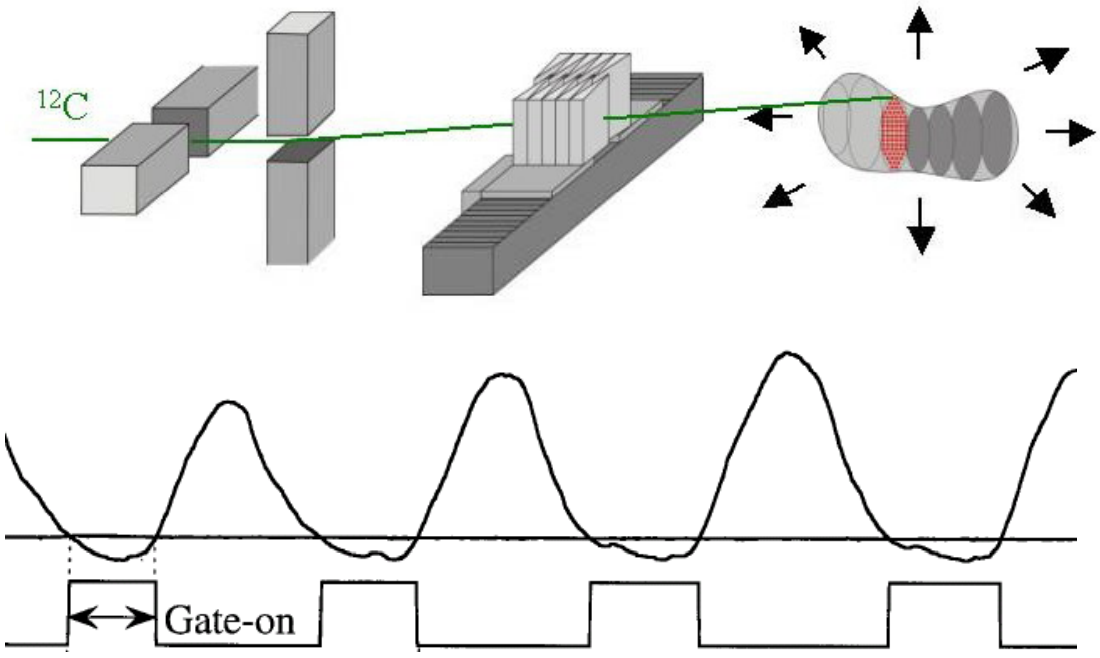
Long term:

TrackingAdaptation of beam position to follow target motion

Short term:

GatingRestrict irradiation to phases with little motion

Performed at NIRS for passively shaped C-12



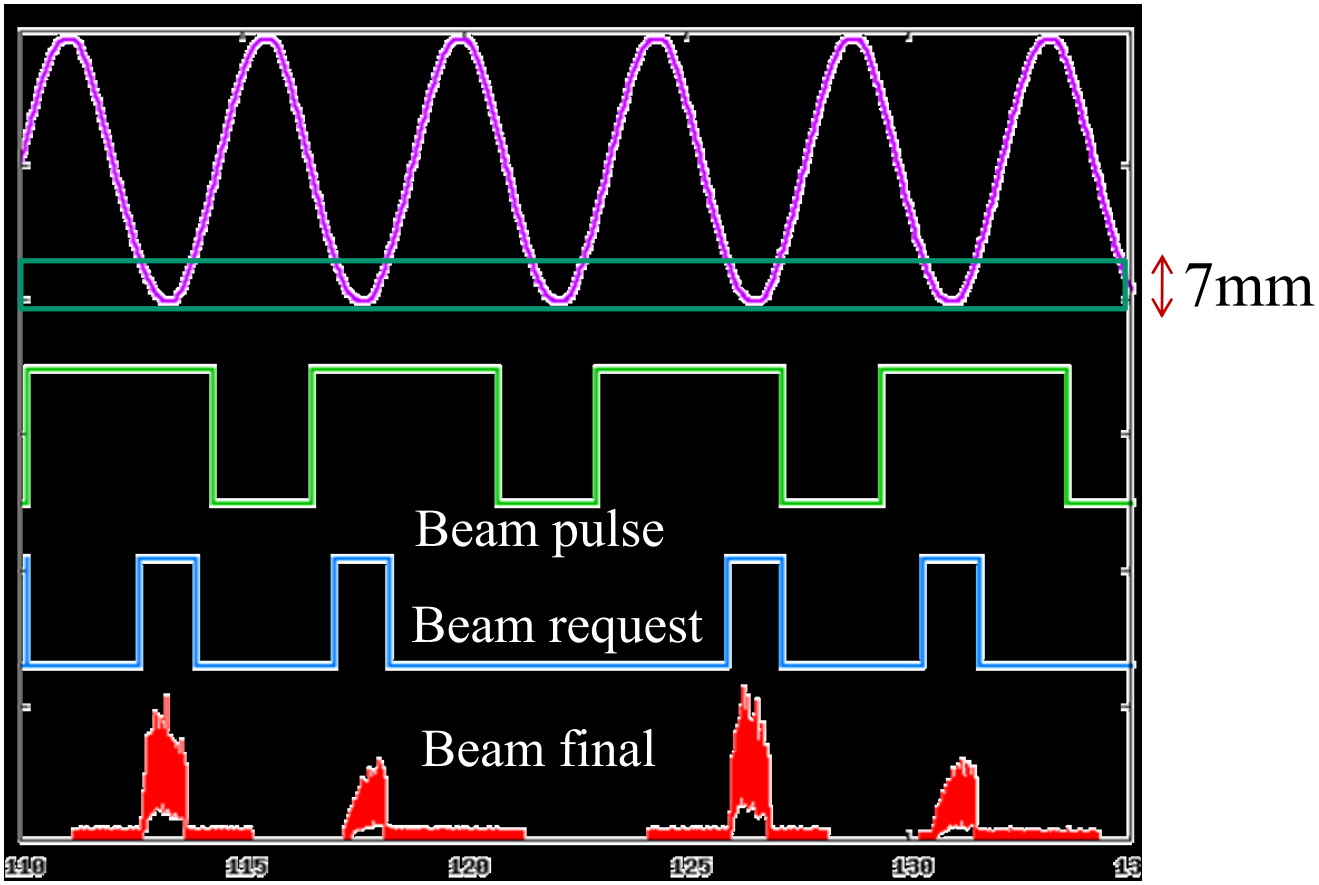

7mm
Beam pulse
Beam request
Beam final
110
115
120
125
130

Table 1
Radiation-Induced Events per 100 Patients

Variable	Hearing Loss	Hypothyroidism	Osteoporosis	GHD	Nonfatal Secondary Malignancies	Fatal Events
Conventional Radiation	11.9					
Proton Radiation	1.4					
Difference	10.5					

GHD: growth hormone deficiency
Source: Lundkvist J, Ekman M, Ericsson S,
childhood medulloblastoma: *Cancer,* 2005-

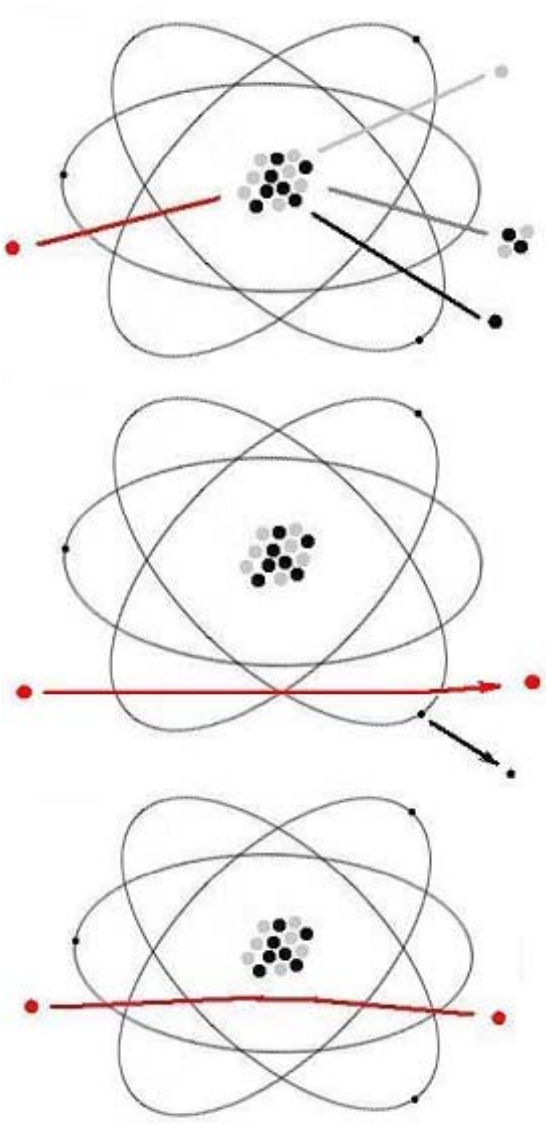
Table 2
Cost and Clinical Outcome per patient for the Base-Case Assumptions

Variable	Proton Radiation	Conventional Radiation	Difference
Radiations Cost (estimated)	10,217.9	4,239.1	5,978.8
Cost from Adverse Events (estimated)	4,231.8	33,857.1	-2,9625.3
Total cost (estimated)	14,449.7	38,096.2	-2,3646.5
LYG	13.866	13.600	0.266
QALY	12.778	12.095	0.683

LYG: life-years gained; QALY: quality-adjusted life-years
Source: Lundkvist J, Ekman M, Ericsson S, Jonsson B, Glimelius B. Cost-effectiveness of Proton Radiation in the treatment of childhood medulloblastoma: *Cancer,* 2005-103-793-801.

Proton cost ~ 2.4 fold higher than IMRT photons

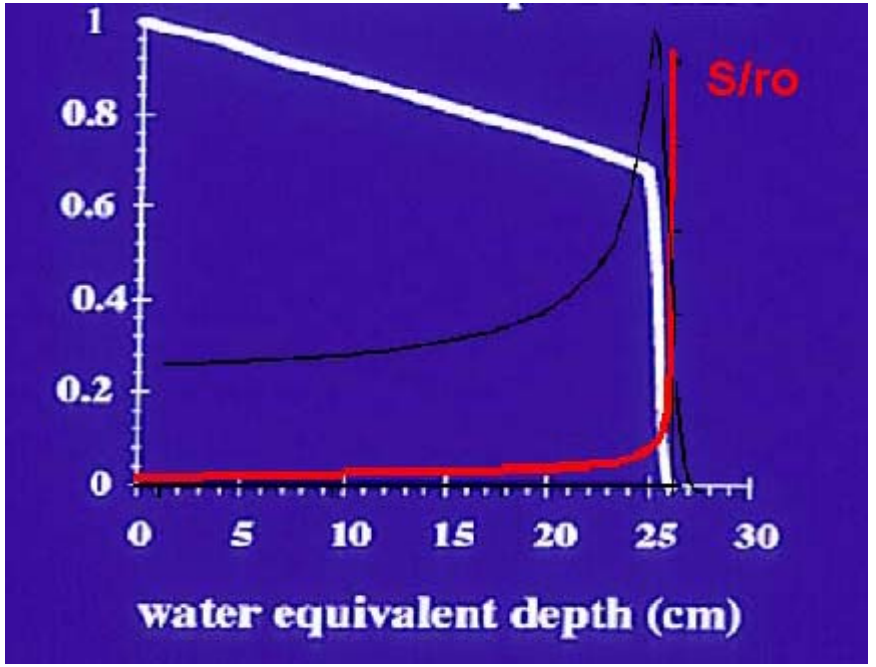
Taken from an article, by Leslie Henry Spencer***, that won first place in the Student category of the 2005* RT Image *Writing Competition.***

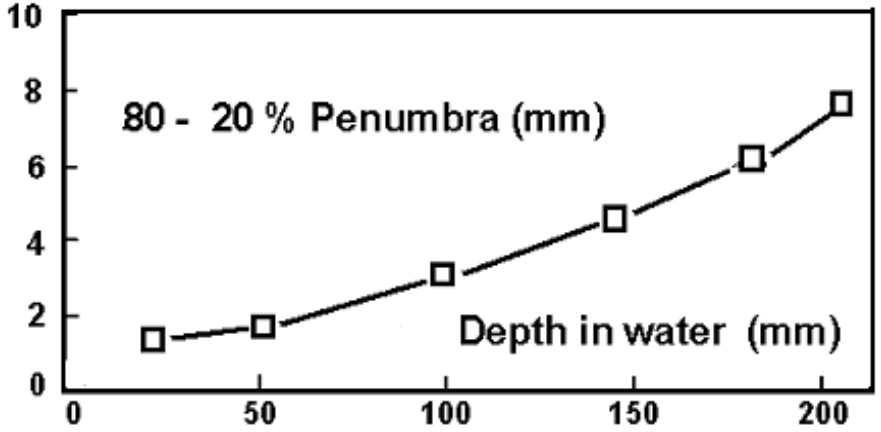


Neutrons…

Ionisation (= Dose)

Multiple Scattering





Clinical Results of Photon and C-ion Treatments

		Photons	Carbon ion	Carbon ion
Indication	**End point**		**NIRS-HIMAC**	**GSI**
Chordomas	Local control rate	30-50%	65%	70%
Chondrosarcomas	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 sinus tumors	Local control rate	21%	63%	
Pancreatic carcinoma	Av. survival time	6.5 months	7.8 months	
Liver tumors	5 year survival	23%	100%	
Salivary gland tumors	Local control rate	24-28%	61%	
Soft-tissue carcinoma	5 year survival	31-75%	52-83%	

Ref: Bill Chu, IPAC2010

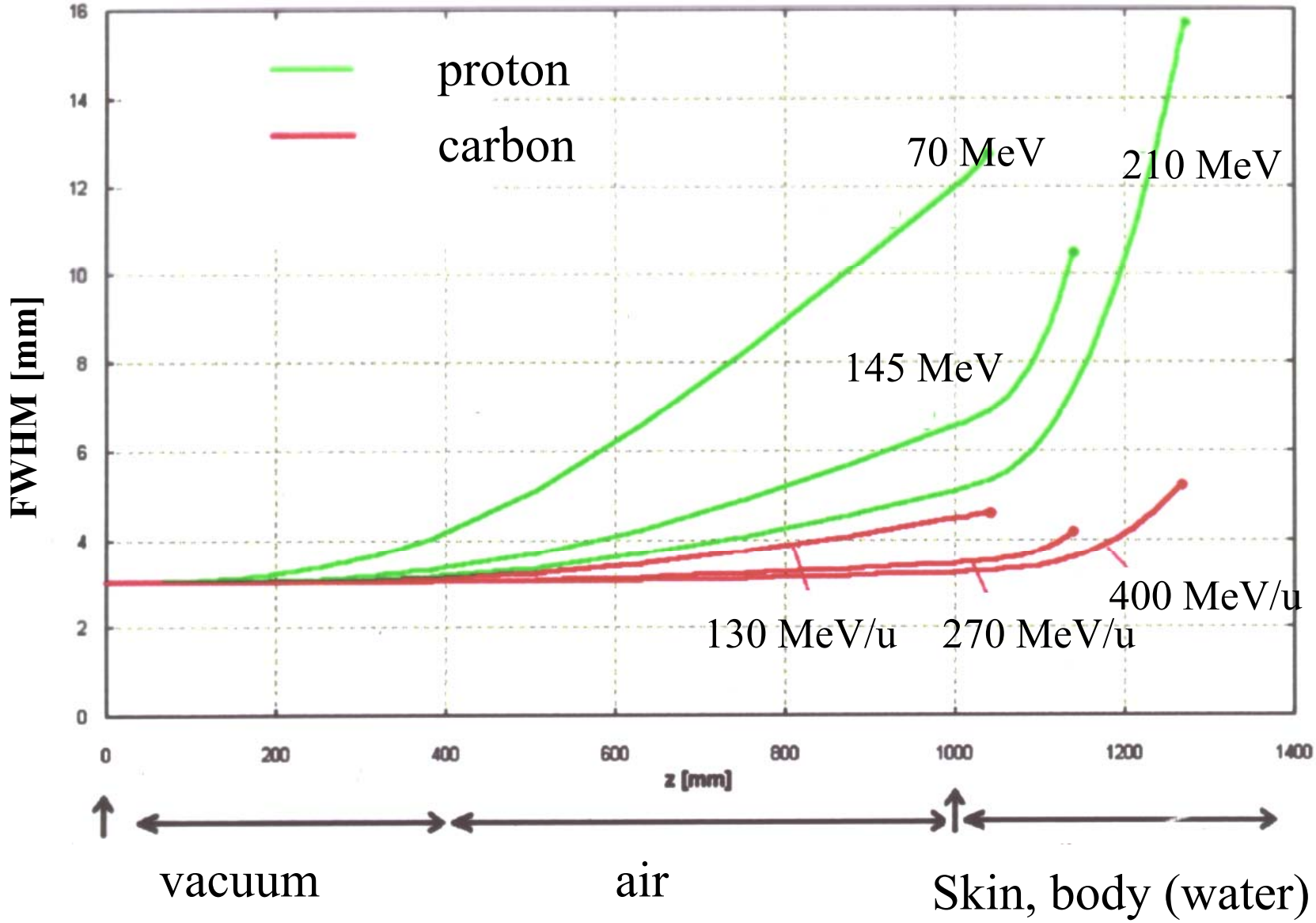
HIMAC of NIRS in Chiba, HIBMC in Hyogo, and GHMC of Gunma Univ., Gunma

Parameter	**HIMAC**	**HIBMC**	**GHMC**
Ion-source type	ECR	ECR	ECR
Ion species	C^{2+}	C^{2+}	C^{2+}
Injector type	RFQ & DTL	RFQ & DTL	RFQ & IH-DTL
Operation frequency	100 MHz	200 MHz	200 MHz
Extraction energy	6 MeV/u	4 MeV/u	4 MeV/u
Accelerator type	2 synchrotrons	synchrotron	synchrotron
Circumference	130 m	94 m	63 m
Number of Magnets	12	12	12
Deflection angle	30 deg	30 deg	30 deg
Energy at extraction	100 – 430	100 – 320	140 - 400
Beam intensity (pps)	2×10^9	1.2×10^9 2×10^{10} proton	2×10^9
Pulse repetition rate	3.3 s – 2 s	2 s	2 s
RF cavity frequency	1 – 6 MHz	1 – 6.5 MHz	0.90 - 6.97 MHz
RF power (Max)	10 kV	6 kV	2 kV

A facility treating 1000 patients per year and each patient having 30 fractions, then the facility must treat 100 patients/day (assuming 300 days/year). If the facility treats patient 16 hrs/day, then each hour needs to treat 6 patients. This means that one needs 3 treat rooms for 30 minutes per patient.

Each patient costs about $100,000, the total operation budget is about 100 M$. This is economically feasible.

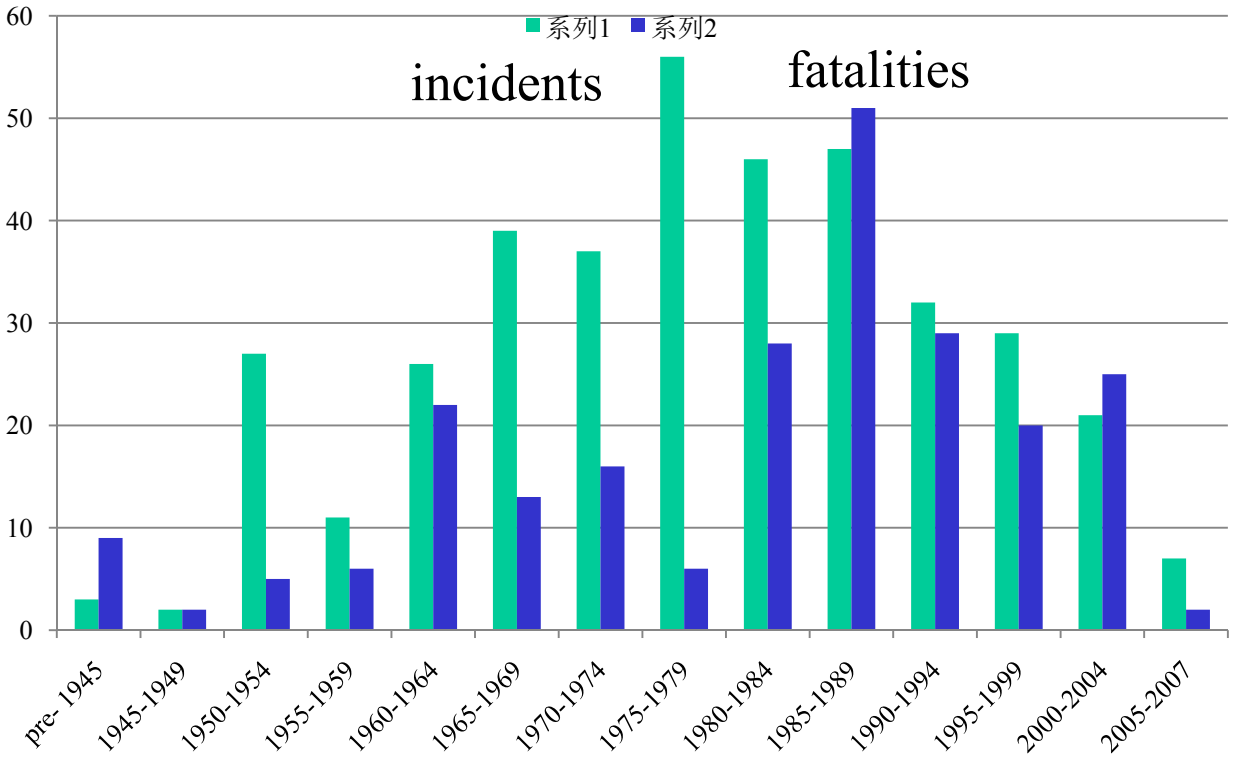
		electron		proton
		1.00E+06	3.00E+04	4.00E+06
L (keV/μm)		2.00E-01	1	10
m_nucleus	1.00E-13			
radius	5.00E-06			
V_nucleus	1.25E-16			
E_ioniz (eV)	33			
D (Gy)	1	1	1	1
N_ioniz	18915.75			
Ntracks		6.24E+02	1.25E+02	1.25E+01
		700	140	14


proton
carbon
70 MeV
210 MeV
145 MeV
400 MeV/u
130 MeV/u
270 MeV/u
FWHM [mm]
z [mm]
0
2
4
6
8
10
12
14
16
0
200
400
600
800
1000
1200
1400
vacuum
air
Skin, body (water)

A Database of Radiological Incidents and Related Events

compiled by Wm. Robert Johnston
last modified 30 May 2008
http://www.johnstonsarchive.net/nuclear/radevents/index.html#2

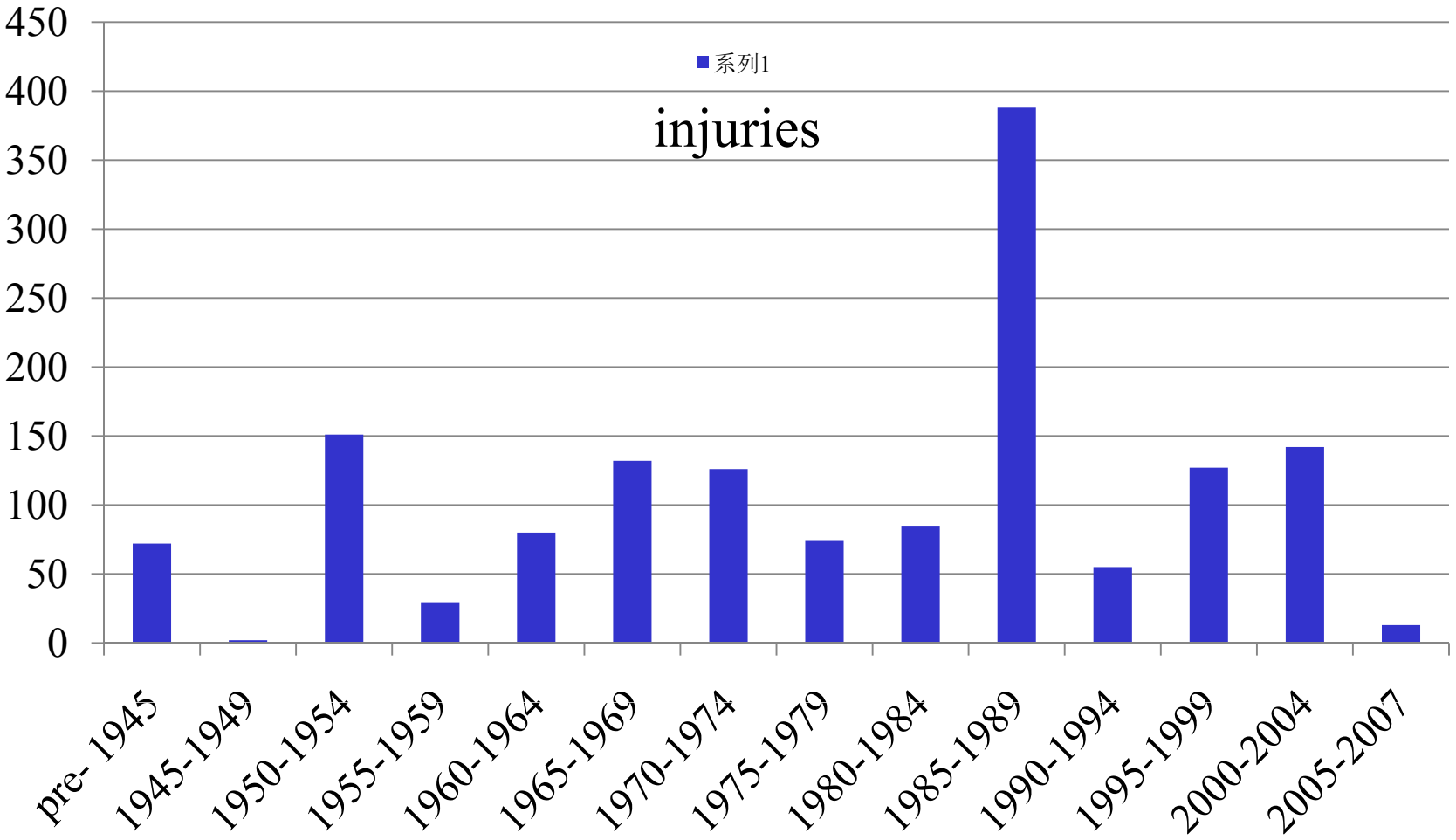
26 Apr - 06 May 1986 Chernobyl, Ukraine



Panama city: In August 2000 a **modification to the computerized treatment planning system** used to calculate shielding blocks during RTs. Unknown to the operators, the change resulted in overexposures to patients. 17 patients died.

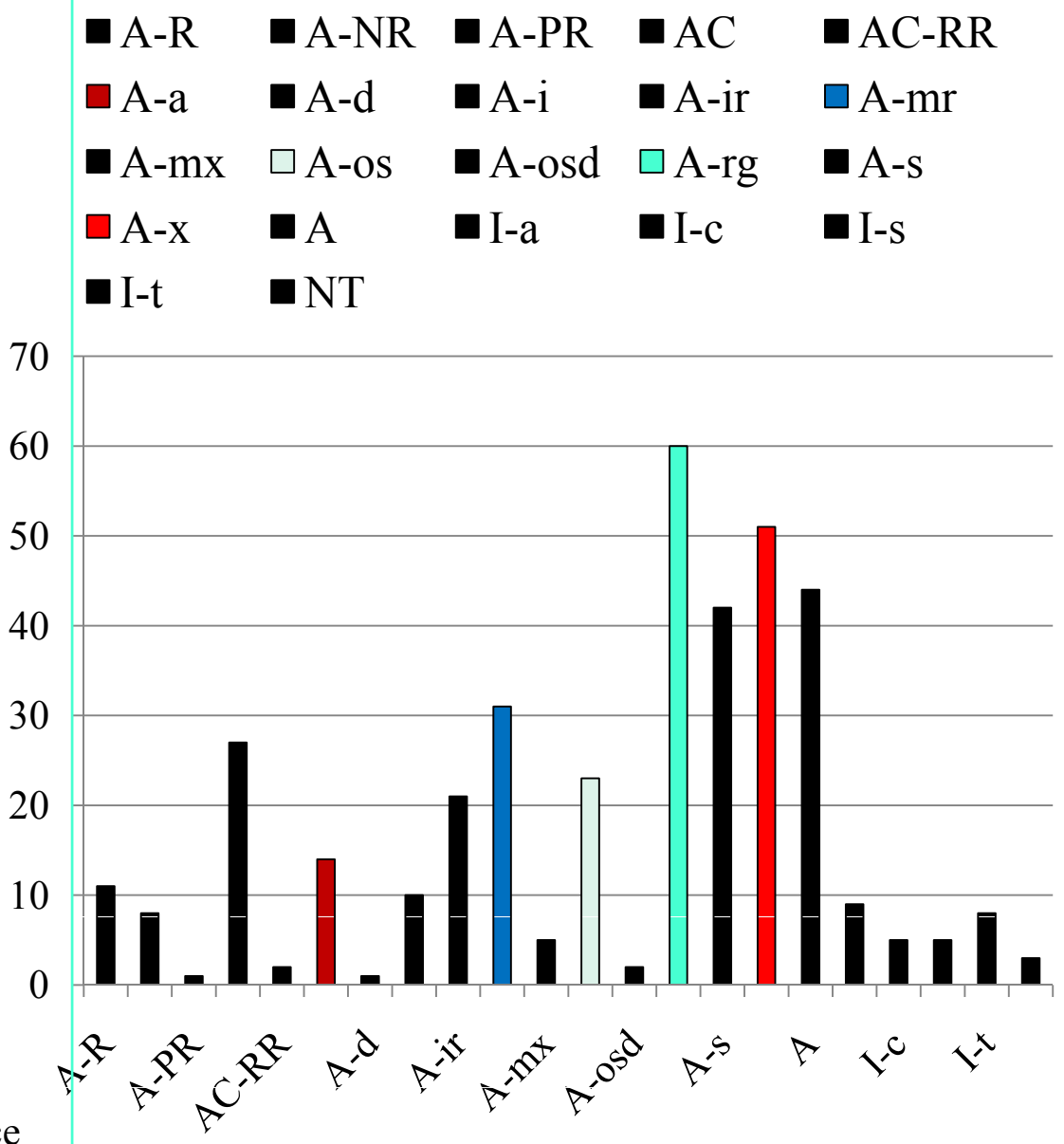
1986: East Texas Cancer Center, Tyler, Texas: A defect in the **computer program** controlling the Therac-25 radiation therapy accelerator resulted in overexposures to 2 patients.

1990: Zaragoza Clinical University, Zaragoza, Spain : An error occurred in the **maintenance and calibration** of a linear accelerator used for clinical radiotherapy; combined with procedural violations, overdosas of 200-700% occurred.

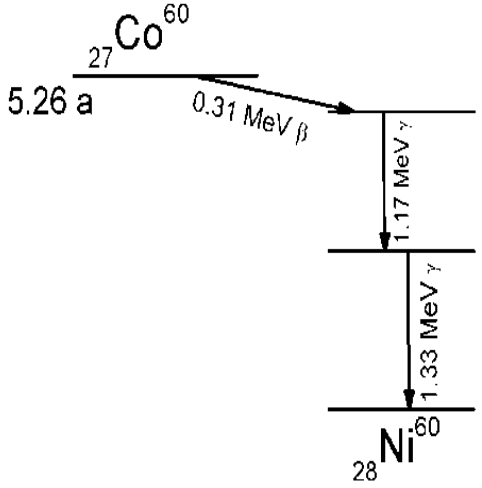


May 2002: Guangzhou: A Chinese nuclear scientist, Gu Jiming, used radioactive iridium-192 pellets in an attack on a business rival. 75 injuries

A -- radiation accident (unspecified or other)
A-R -- accident involving nuclear reactor
A-NR -- accident involving naval reactor
A-PR -- accident involving power reactor
AC -- criticality accident
AC-RR -- criticality accident involving research reactor
A-a -- accelerator accident
A-d -- accidental dispersal of radioactive material
A-i -- accidental internal exposure to radioisotope
A-ir -- irradiator accident
A-mr -- medical radiotherapy accident
A-mx -- medical x-ray accident
A-os -- orphaned source accident
A-osd -- accidental dispersal of orphaned source
A-rg -- radiography accident
A-s -- accidental exposure to source
A-x -- x-ray accident
I-a -- intentional exposure of individual (assault)
I-c -- criminal act (unspecified)
I-s -- intentional self-exposure
I-t -- exposures resulting from theft of source
NT -- nuclear weapon test
NW -- combat use of nuclear weapon



Cobalt-60 (^{60}Co) has half life of 5.2714 years. One gram of ^{60}Co contains approximately 50 curies (1.85 terabecquerels) of radioactivity. Held at close range, this amount of ^{60}Co would irradiate a person with approximately 0.5 gray of ionizing radiation per minute (also 0.5 sievert per minute. A full body dose of approximately 3-4 sieverts will kill 50% of the population in 30 days, and could be accumulated in just a few minutes of exposure to a gram of ^{60}Co. ^{60}Co has six main beneficial uses:



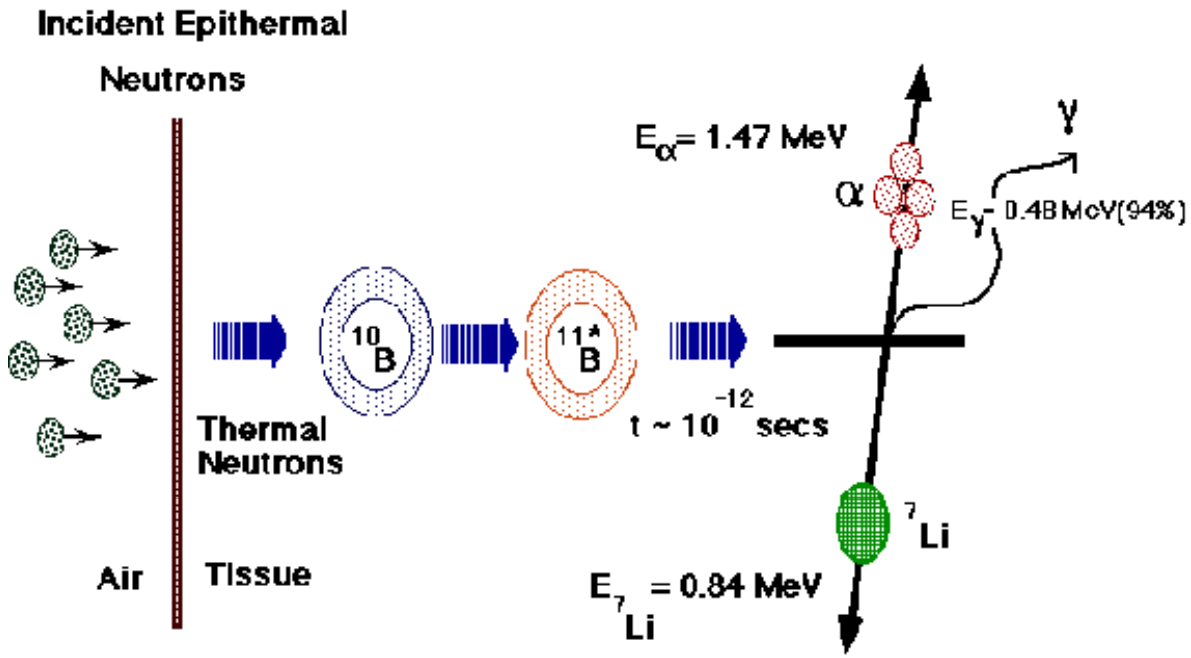
Biological: 0.5 day (transfer compartment), 6 days (0.6 in all tissues), 60 days (0.2 in all tissues), 800 days (0.2 in all tissues)
Principal Modes of Decay (MeV):
Principal Organ: Liver and Whole Body
Amount of Element in Body: 1.5 mg
Daily Intake of Element in Food and Fluids: 300 μg

- As a tracer for cobalt in chemical reactions,
- Sterilization of medical equipment,
- Radiation source for medical radiotherapy,
- Radiation source for industrial radiography,
- Radioactive source for leveling devices and thickness gauges,
- As a radioactive source for food irradiation, and
- As a radioactive source for laboratory use.

The Henry L. Stimson Center study shows that only 9 grams of Cobalt 60 (with a specific activity 1100 Curies per gram) are required to make a make a radiological explosive device or “dirty bomb” able to cause mass disruption.

BNCT: $^{10}B(n,\alpha)^{7}Li$
σ~3837 barns

$^{1}H(n,\gamma)^{2}H$ –	0.33b
$^{14}N(n,p)^{14}C$ –	1.81b
$^{14}N(n,\gamma)^{15}N$ –	
$^{16}O(n,\gamma)^{17}O$ –	
$^{17}C(n,\gamma)^{18}C$	



- ^{10}B is non radioactive and readily available, comprising approximately 20% of naturally occurring boron.
- The particles emitted by the capture reaction $^{10}B(n,\alpha)^{7}$ Li are largely high "Linear Energy Transfer", dE/dx, (LET).
- Their combined path lengths are approximately one cell diameter; i.e., about 12 microns, theoretically limiting the radiation effect to those tumor cells that have taken up a sufficient amount of ^{10}B, and sparing normal cells.
- The chemistry of boron is well understood and it can be readily incorporated into a multitude of different chemical structures.

Synchrotron vs. Cyclotron

	synchrotron	cyclotron
Energy flexibility	High (fast extract)	Fixed (need degrader)
Typical diameter	7 m	4 m
Power consumption	low	High (except scc)
Typical beam size	1-10 mm	10 mm
Typical energy spread	0.1%	0.5%
Beam intensity	Sufficient	High
Beam delivery efficiency	~95%	~50-95%
complexity	Flexible	simple
weight	Light	massive
Approximate cost	10 M$	10 M$
Other cost	Lower	Higher

No energy degrader
Small intrinsic beam size

Extraction:
EITHER -a little beam often,extract in 1 turn
OR - a lot of beam rarely, extract slowly in many turns

Also FFAG Fix Field Alternate Gradient (Japan)

(Rapid Cycling Medical Synchrotron, RCMS)

Historical Development of cyclotron principle:

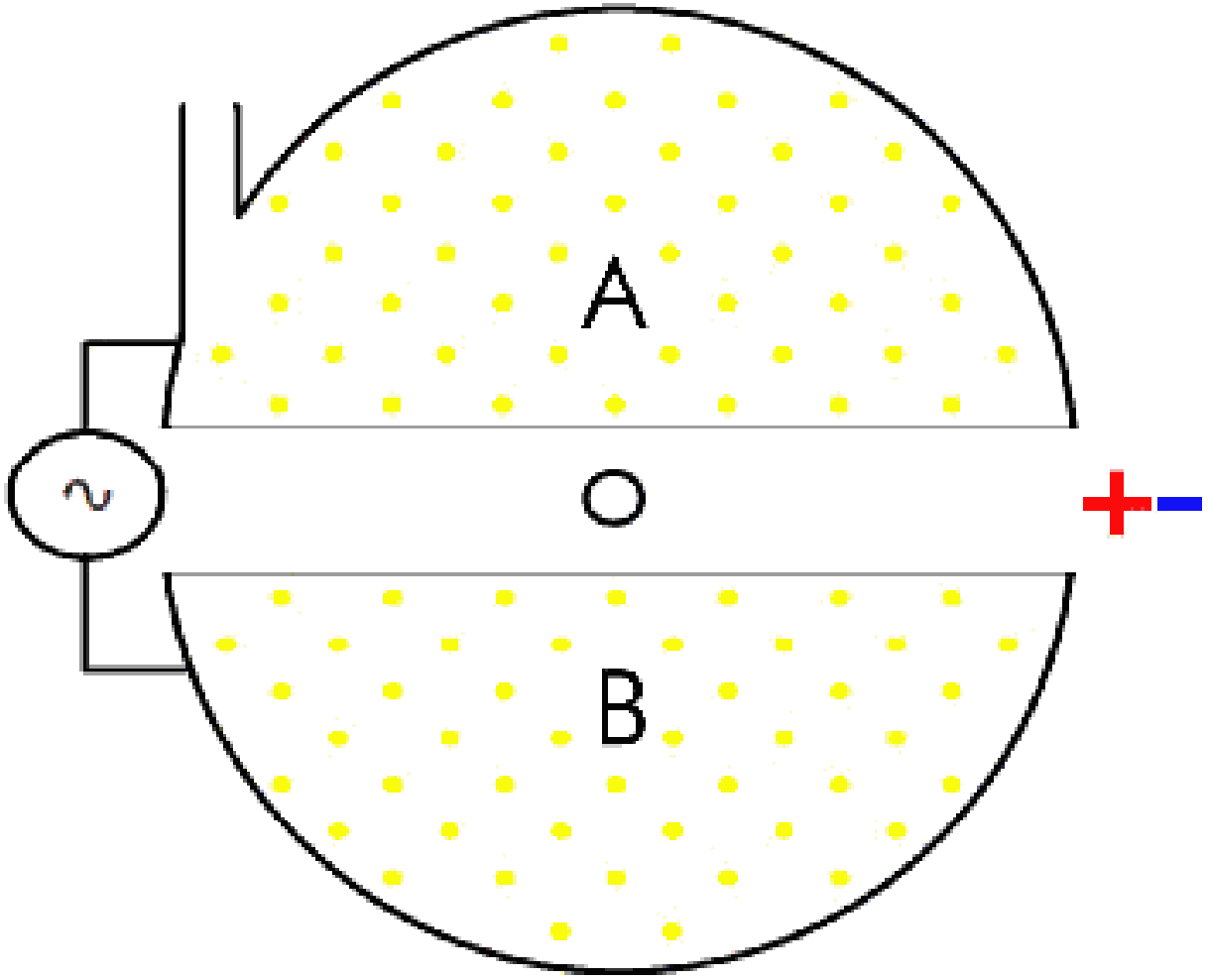
A charged particle interacts with electromagnetic field through the Lotentz force Law: $\mathbf{F}=e(\mathbf{E}+\mathbf{v}\times\mathbf{B})$, where e is the charge, **v** is the particle's velocity, **E** is the electric field and **B** is the magnetic field..

In particular, if the velocity is perpendicular to the magnetic field, the magnetic force is equal to the mechanical centrifugal force, i.e. $evB=mv^2/r$, where m is the mass and r the radius of its orbit. The particle moves in a circle with radius $r=mv/eB$. It is interesting to note that the cyclotron angular frequency $\boldsymbol{\omega=v/r=eB/m}$ is **independent** of the **radius** and **energy** of the particle!

Lawrence was surprised to find that the frequency of rotation of a particle is independent of the radius of the orbit: $\mathbf{f = v/2\pi r = eB/2\pi m}$. If the particle orbits in a circle with constant magnetic field, an electric field alternating at a constant frequency can accelerate particles to ever higher energies. As their velocities increased so did the radius of their orbit. Each rotation would take the same amount of time, keeping the particles in step with the alternating field as they spiraled outward.

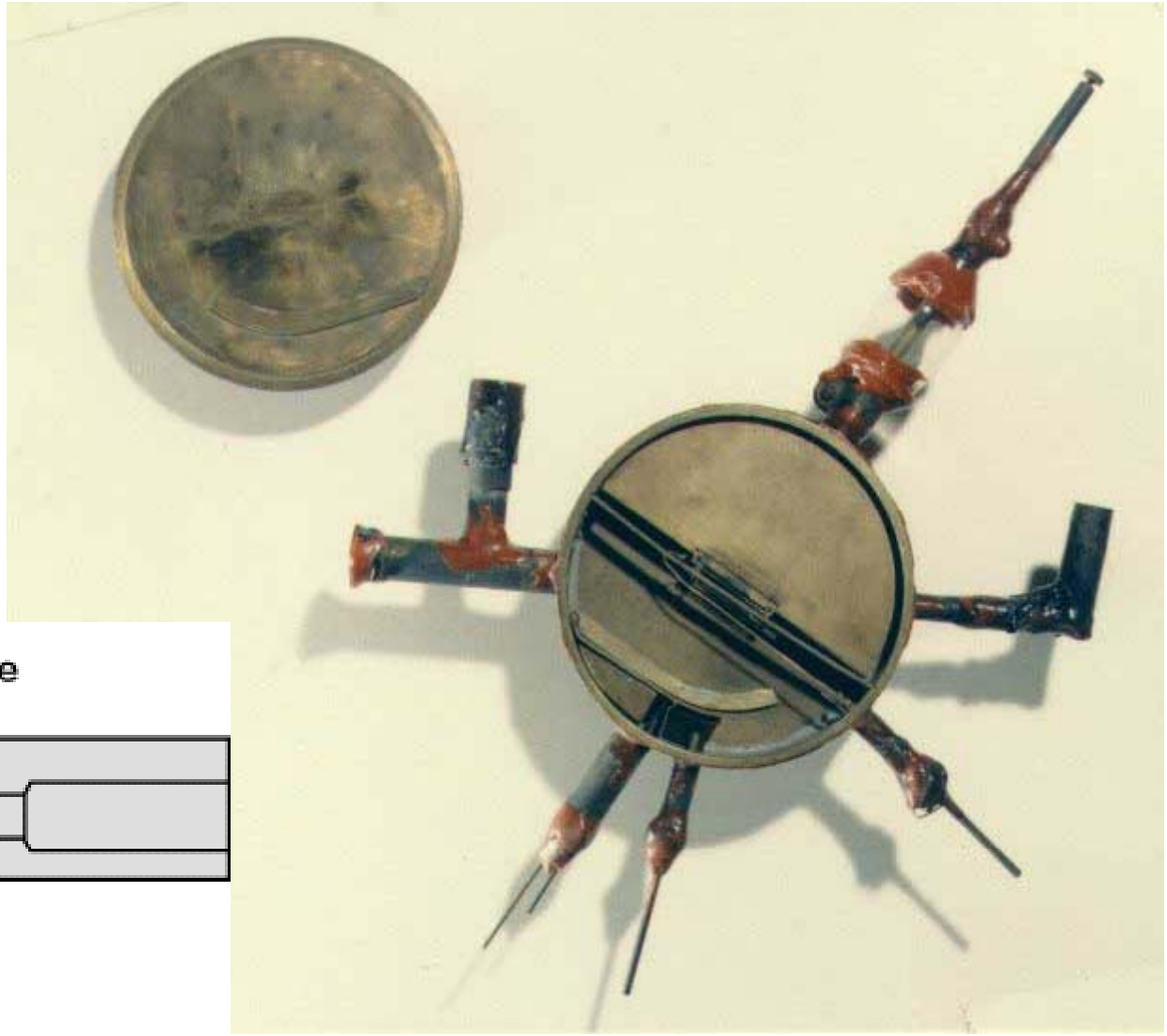
Similar to the discovery of Archimedes principle

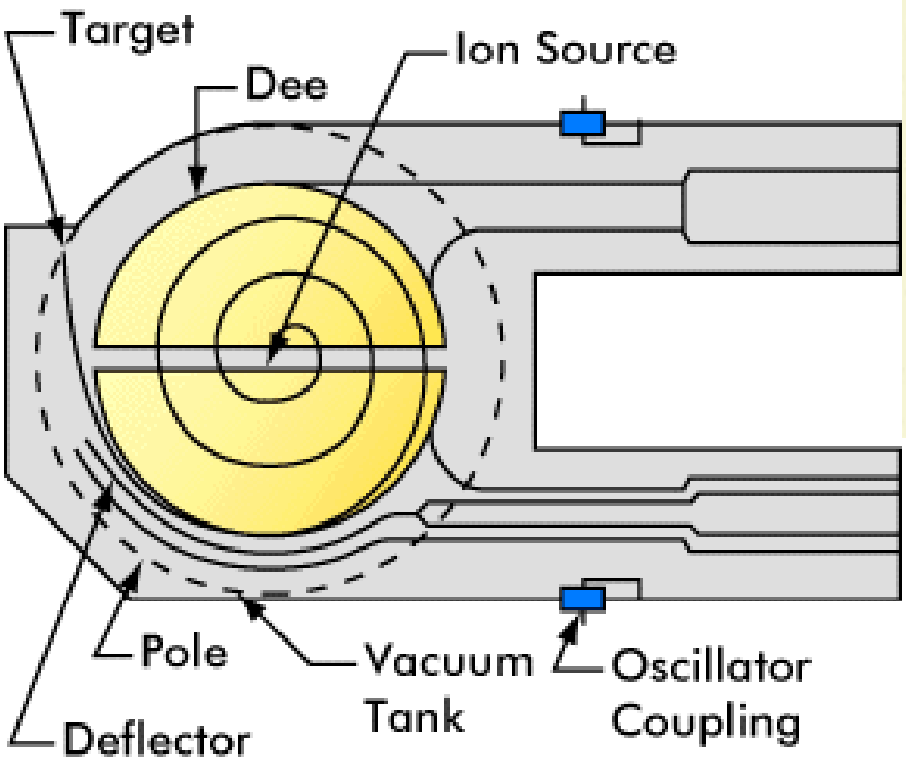
Shallow metal half-cylinders, later called Dees after their shape, serve as electrodes; charged particles injected into the gap near the center are pulled by the potential into the electrode A. The magnetic field, perpendicular to the plane of the cylinders, bends them in a semicircle back into the gap.



In the meantime the electric field has reversed and can pull them into electrode B; whence they emerge again in step with the electric field; and so on, eventually spiraling out to the edge. Each passage through the gap boosts the particles to higher energies.

The first successful cyclotron, the 4.5-inch model built by Lawrence and Livingston reached 80 keV proton energy on January 2, 1931. In 1932, Lawrence built a 11-inch cyclotron reaching 1.25 MeV and observed nuclear reaction.





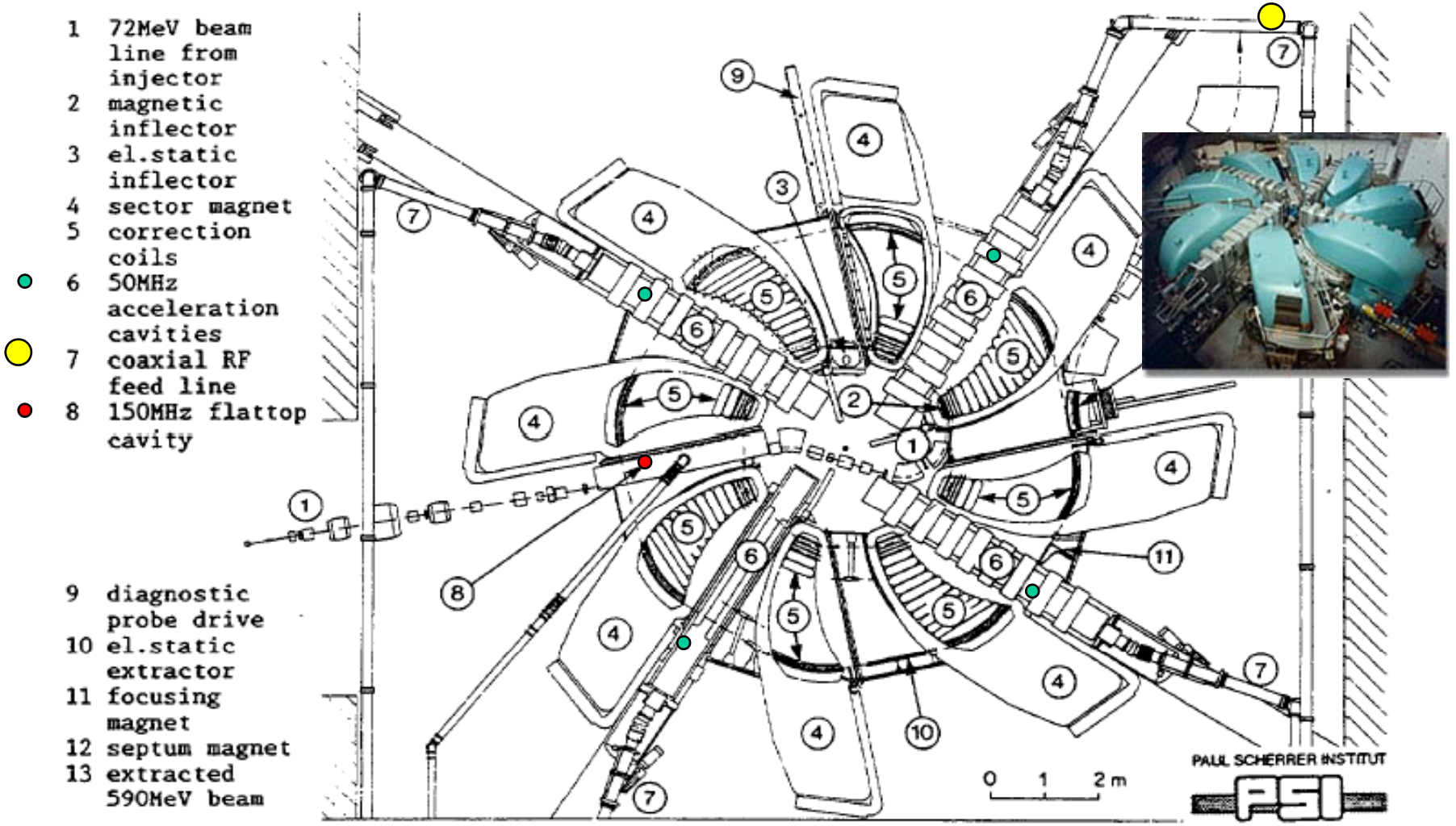
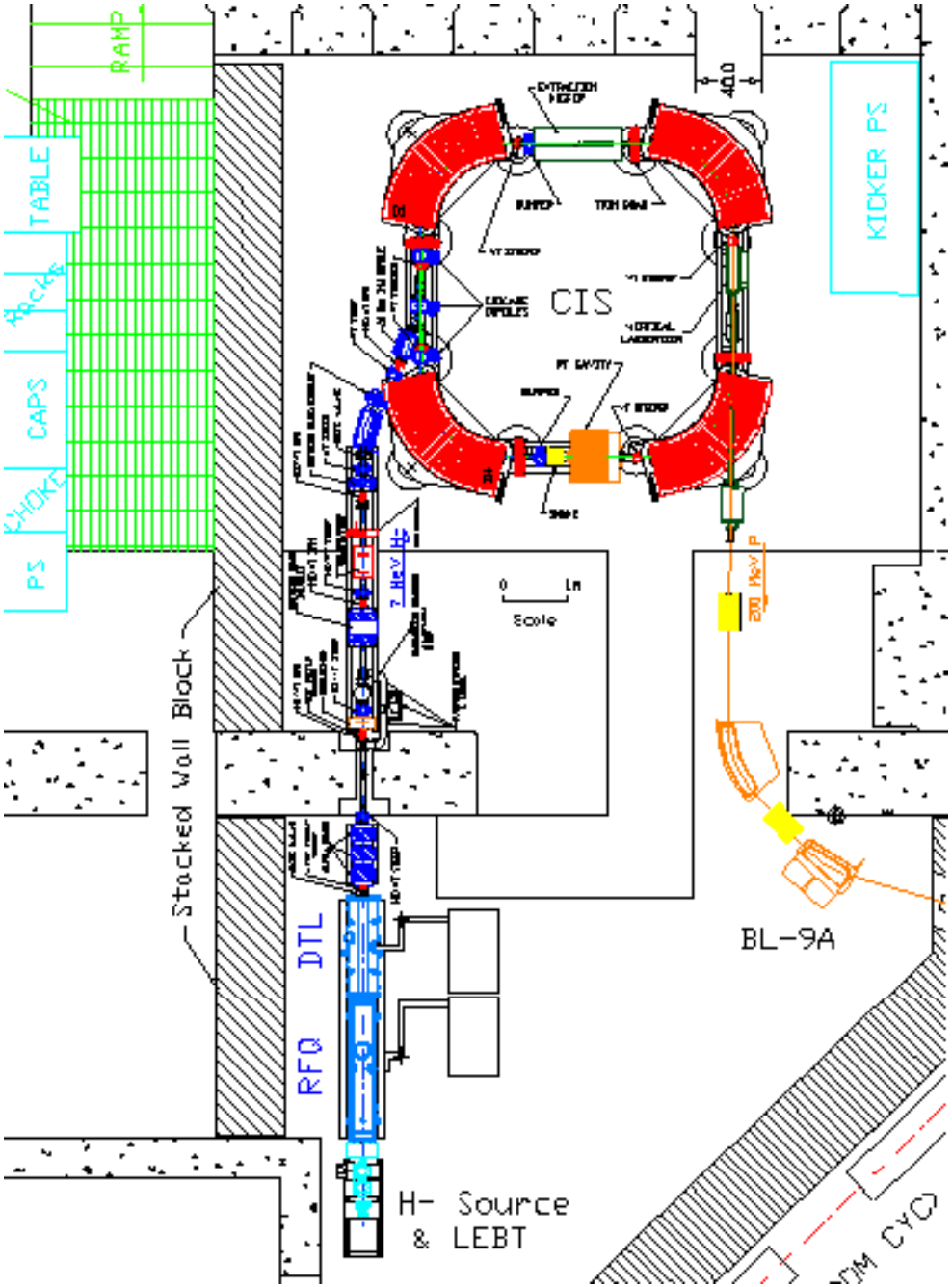


Fig.5 Layout of the Ring cyclotron at PSI. It accelerates a high intensity proton beam to an energy of 590 MeV for the production of high meson and neutron fluxes. The design makes use of eight separated magnets and four large acceleration cavities between the magnet sectors. The cavities produce a high energy gain per turn resulting in low beam loss at extraction.

Synchrotrons vs cyclotrons

In 1952, BNL built the first proton synchrotron at 3GeV, and in 1954, LBNL built a 6GeV proton synchrotron to discover the antiproton. In 1952, Courant, Snyder and Livingston discovered the alternate-gradient-focusing concept, which was patented by a US engineer working in Greece. Since then, synchrotrons are preferred for high energy accelerators. However, cyclotron can still have advantage in low energy accelerators for higher duty cycle! The largest synchrotron with a circumference of 27 km is located at CERN in Geneva.



Synchrotrons

As told by Cyclotron builders

- *Advantages*
  - Naturally variable energy
- *Disadvantages*
  - Current limited if low energy injection; Beam current stability & noise never achieved on small synchrotrons; Fast and accurate beam current control difficult to achieve
  - More expensive in capital and operation
  - More complex with negative impact on availability

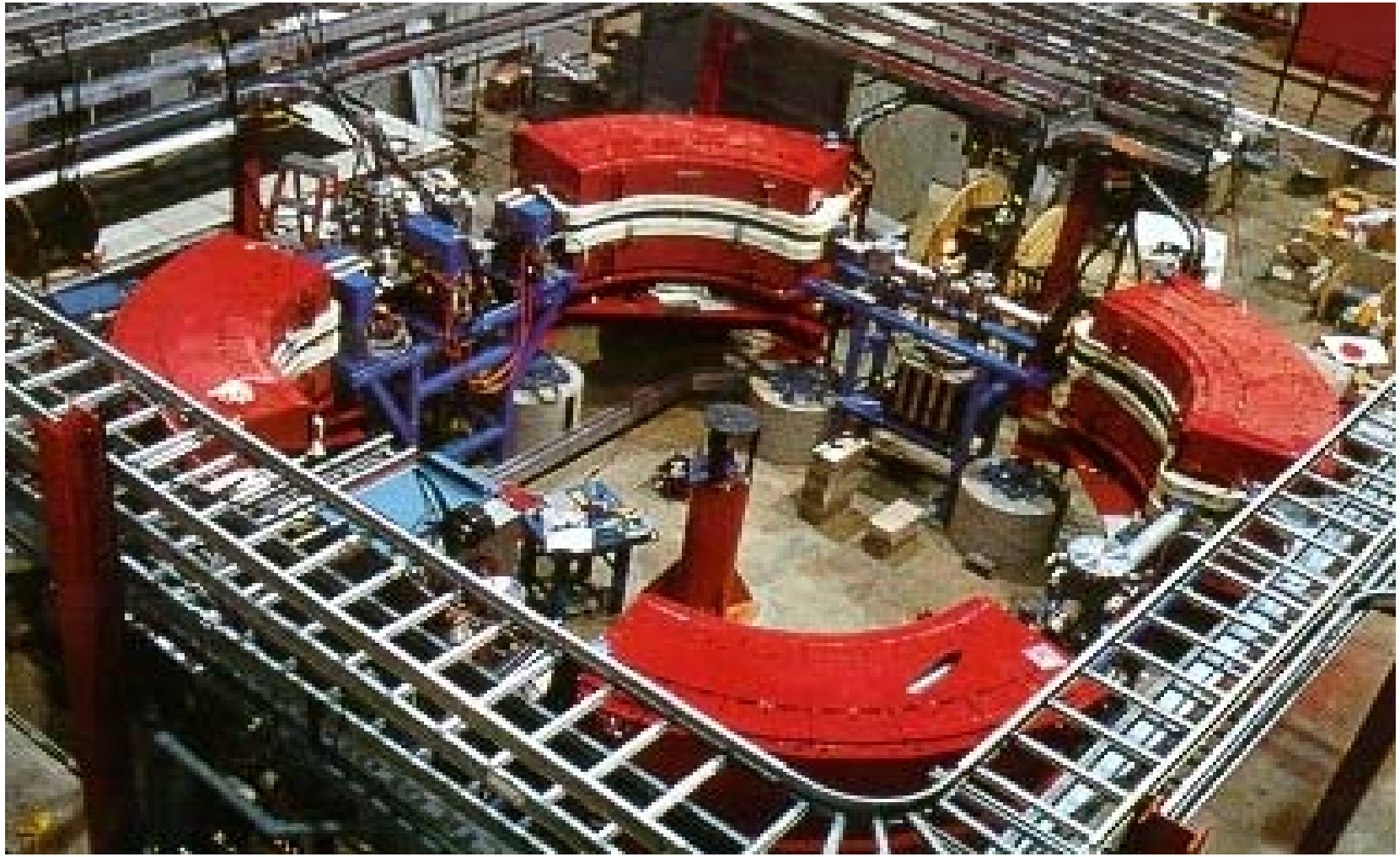
Cyclotrons

- *Advantages*
  - No physical current limitation; Beam current stability & noise specifications are currently achieved on small cyclotrons
  - Fast and accurate beam current control over 1000/1 range easy to achieve
  - Inexpensive in capital and operation; Low complexity, resulting in highest availability
- *Disadvantages*
  - Variable energy requires external Energy Selection System

Consequences of clinical considerations on facility design

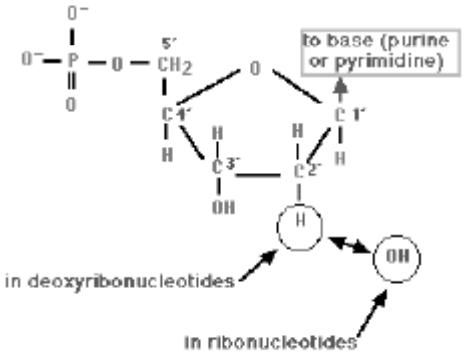
- The most important elements defining the system performance are the Nozzle and the Patient Positioner
- The Accelerator and the Beam Transport System have much less impact on the system performance
- The Accelerator should be made transparent (ignored) at treatment level
- The simplest accelerator meeting the clinical specifications in a cost-effective way should be selected

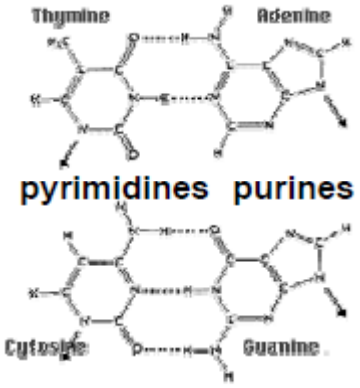
The 230 MeV cyclotron

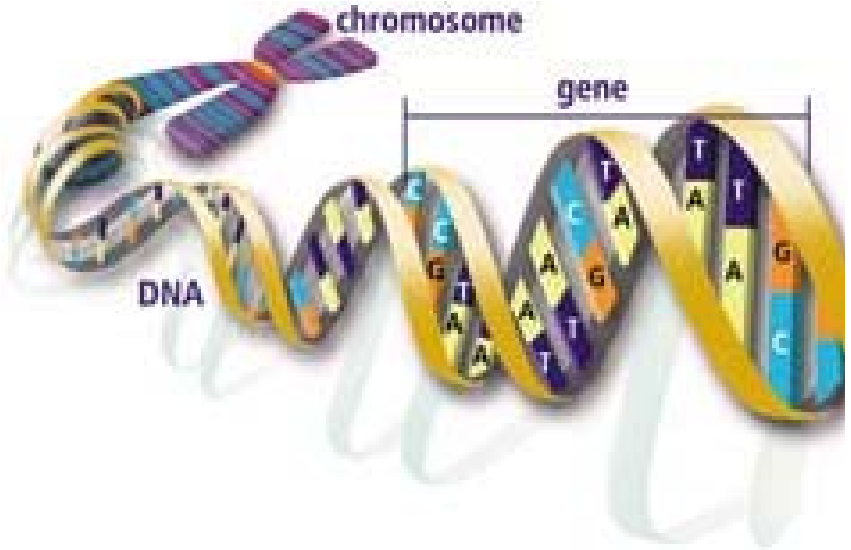


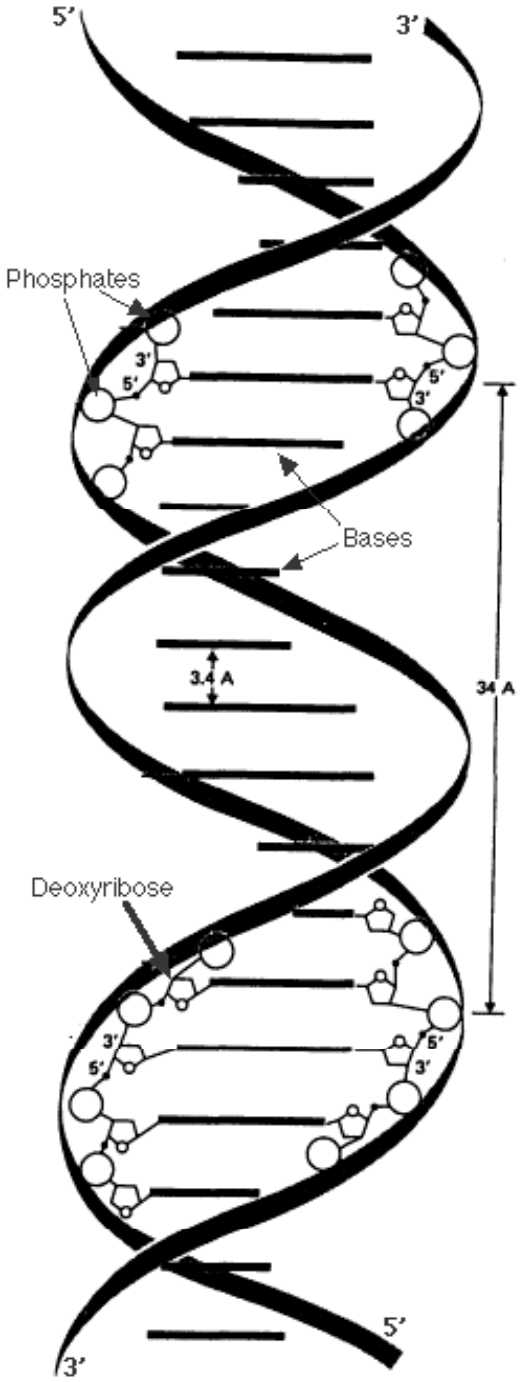
250 MeV Synchrotron

DNA





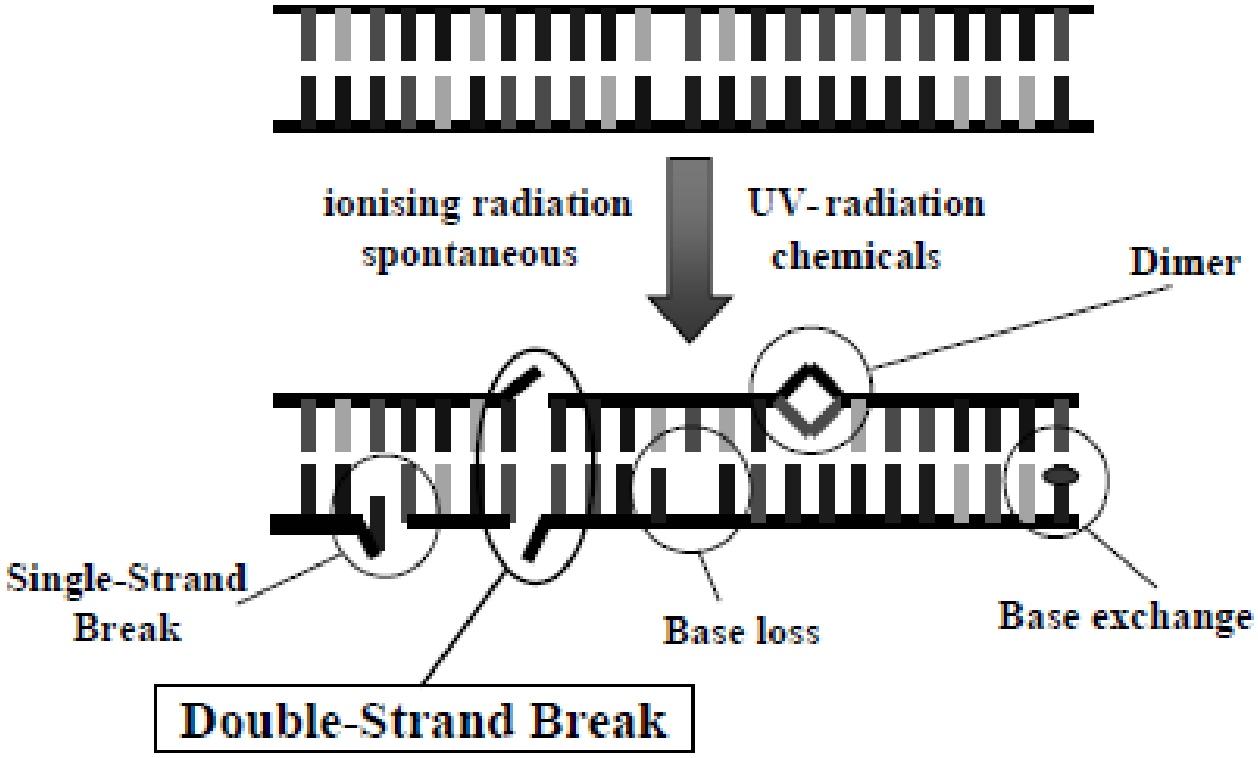




- DNA contains genetic information (non redundant)
- most critical target for ionizing radiation in a cell is DNA
- about 92 cm of human DNA is compacted in 46 chromosomes
- compaction occurs in different steps

DNA damage

DNA double helix

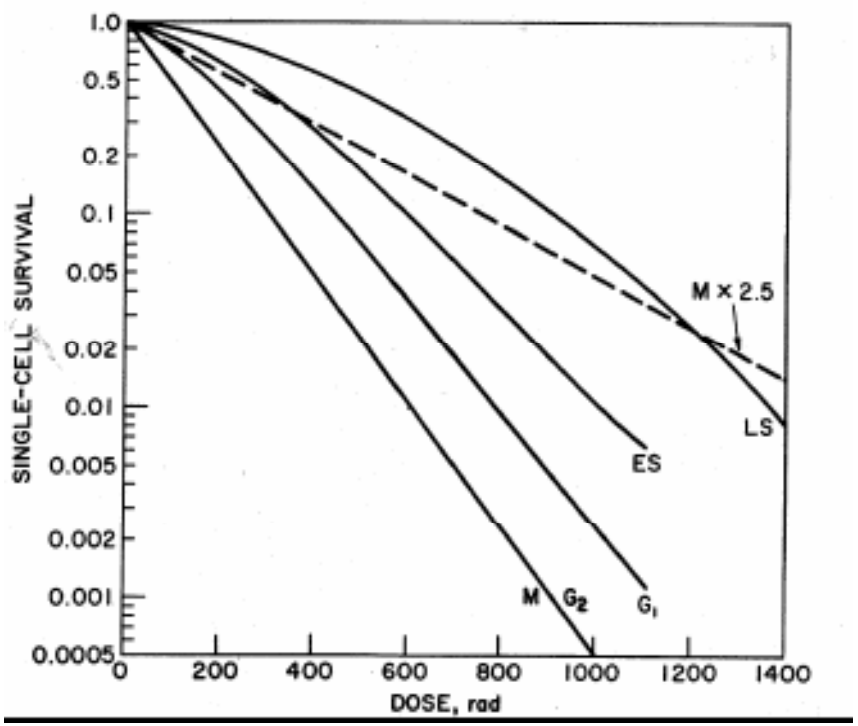


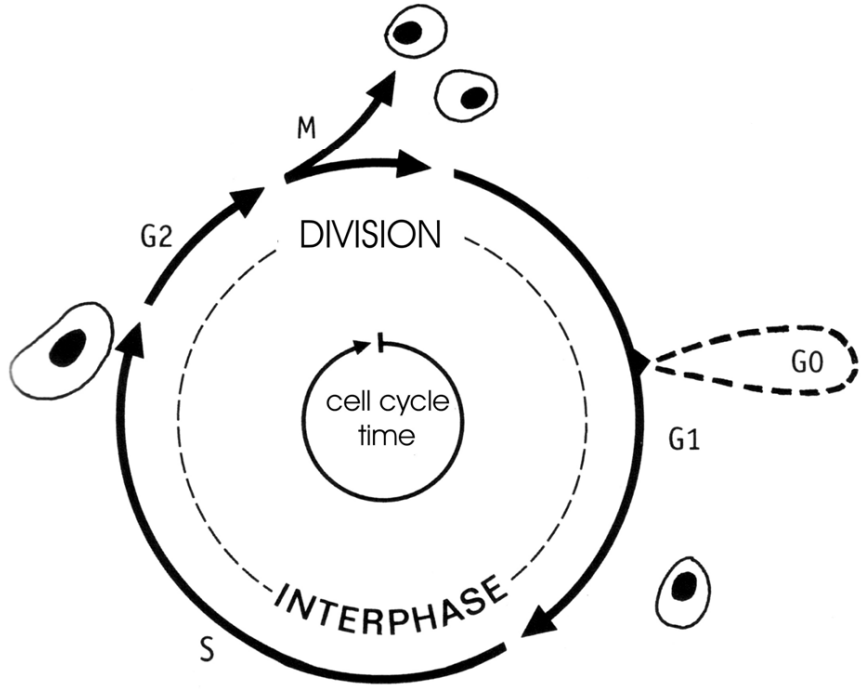
Approximate yields of DNA damage per Gy per cell:

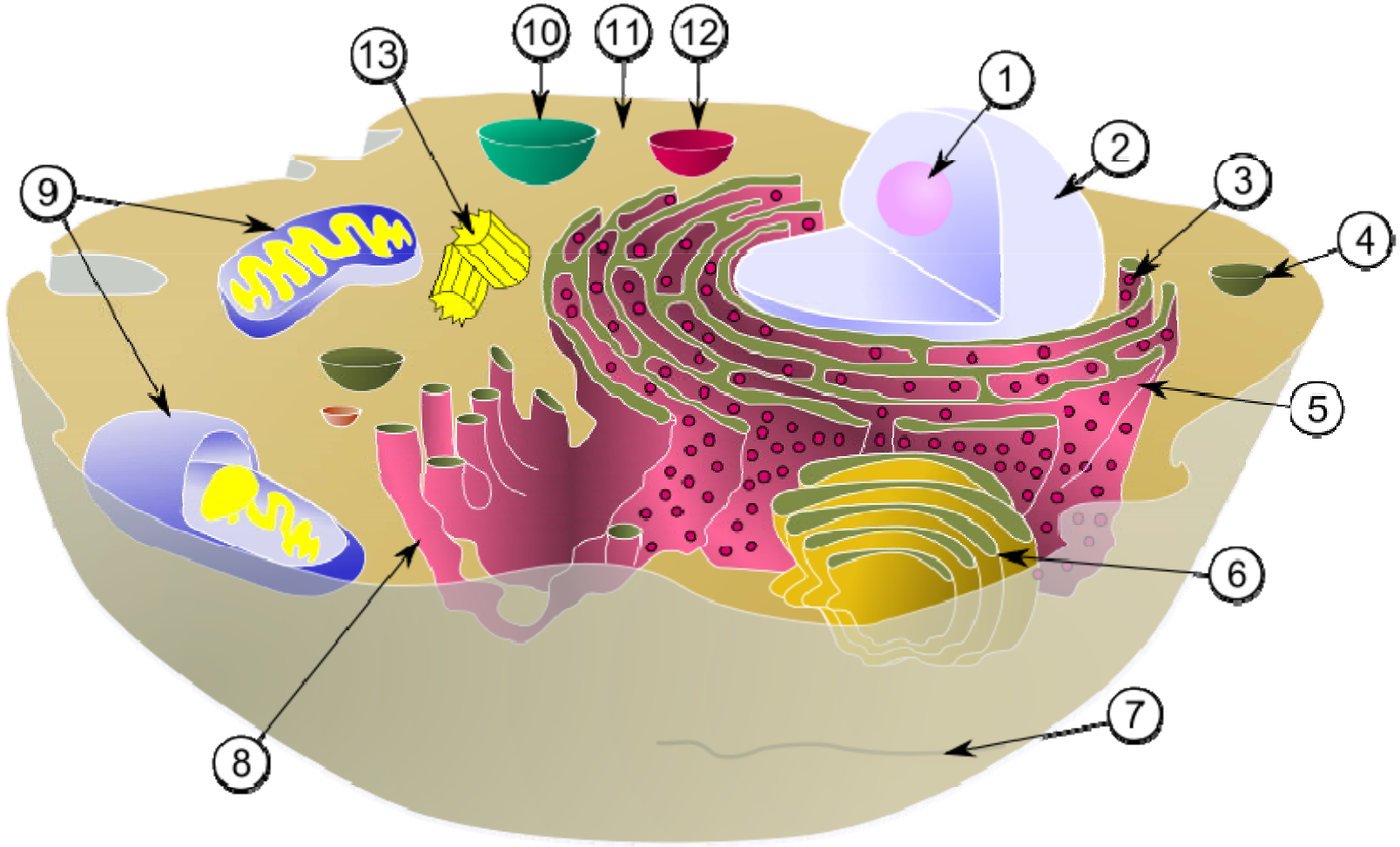
- SSB: 1000
- DSB: 30-40
- DNA-protein crosslinks: 50
- Complex damages (SSB+base lesion): 60

Cell cycle dependence of radiosensitivity

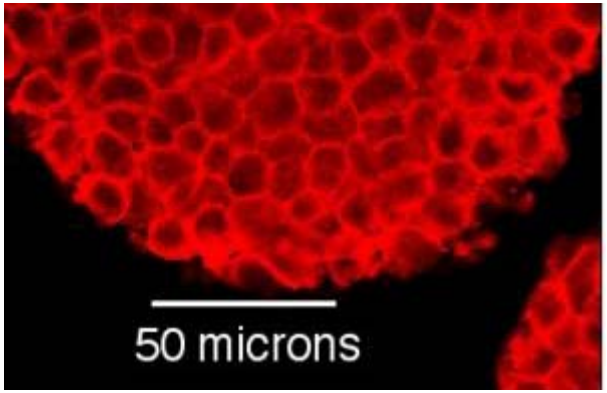
- low LET:
  - ✓ cells in late S phase most resistant
  - ✓ cells in G2/M phase most sensitive
- high LET:
  - ✓ cell cycle-specific changes in radiosensitivity disappear
  - ✓ more effective destruction of inhomogenous tumor tissue (growing and dormant)



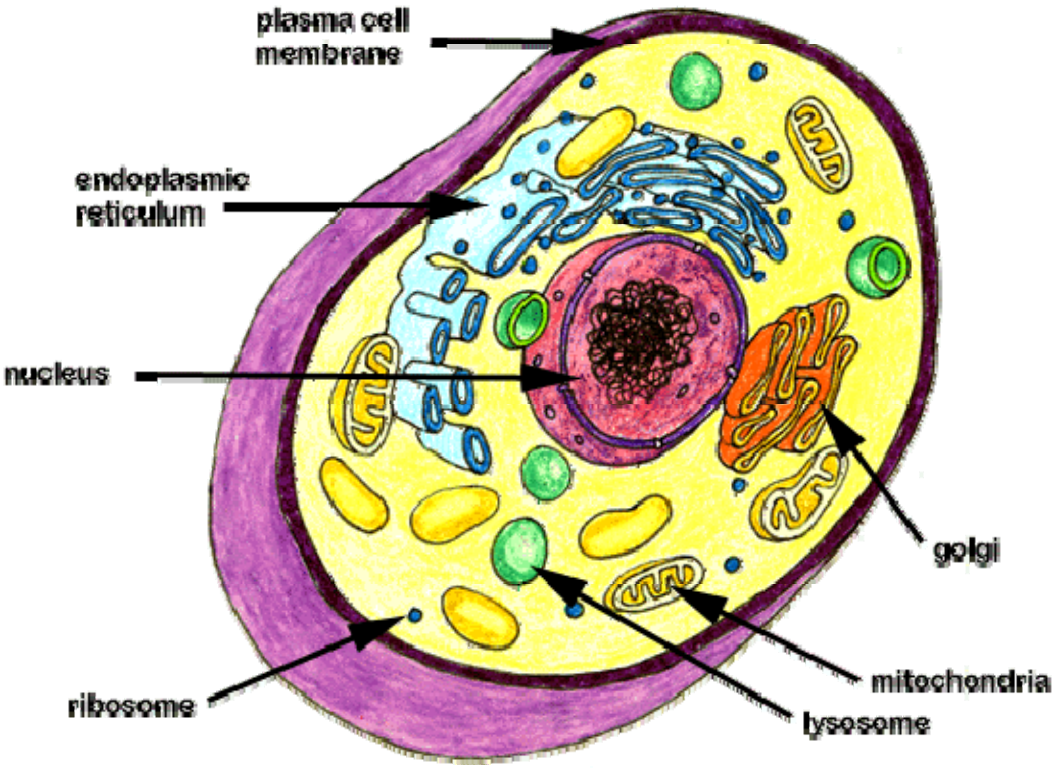




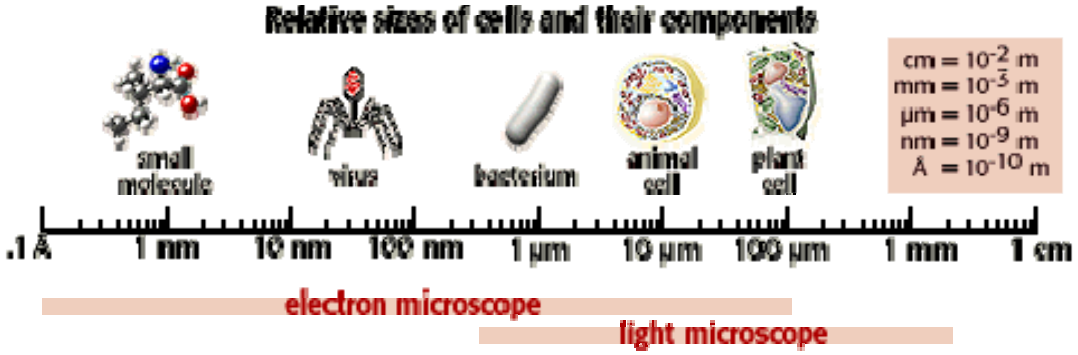
1. Nucleolus
2. Nucleus
3. Ribosome
4. Vesicle
5. Rough endoplasmic reticulum
6. Golgi apparatus (or "Golgi body")
7. Cytoskeleton
8. Smooth endoplasmic reticulum
9. Mitochondrion
10. Vacuole
11. Cytosol
12. Lysosome
13. Centriole



Mouse cells grown in a culture dish. These cells grow in large clumps, but each individual cell is about 10 µm across

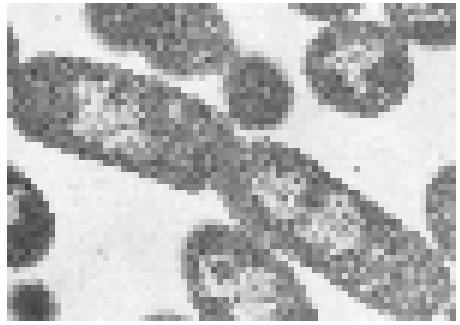


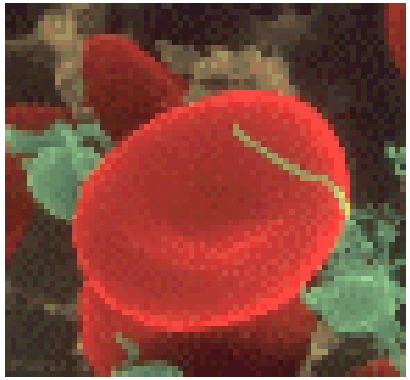
10^{14} cells/human



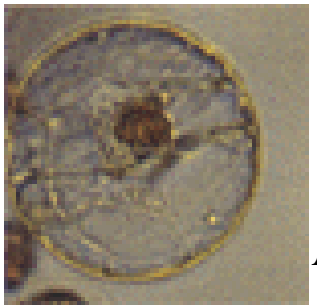
one-celled organism
amoeba proteus

single-celled
bacteria *E. coli*





A human red blood cell



Plant cell from the leaf of a tree

Tumor Hypoxia

- Preclinical Observations
  - Most animal tumor models contain significant proportions of hypoxic cells.
  - Hypoxic cells in tumors dominate their response to large single doses of radiation.

- Aggressiveness of Disease
  - Hypoxia may provide a mutant p53 growth advantage (Graeber et al., 1996).
  - In carcinoma of the cervix, patients with hypoxic tumors treated with surgery had a significantly worse disease-free and overall survival compared to patients with non-hypoxic tumors (Hoeckel et al., 1996).

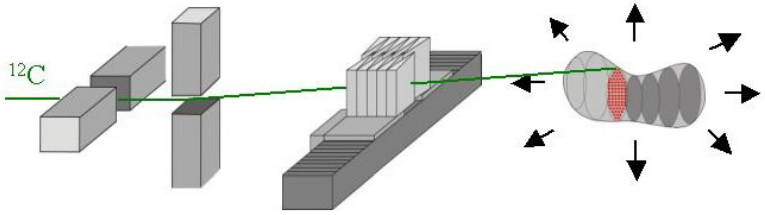
Advantages for carbon ion therapy

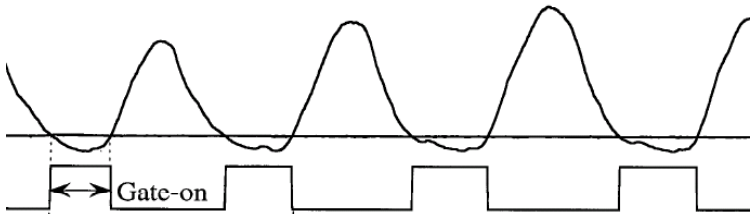
- tumor-conform irradiation – better protection of normal tissue
- higher RBE compared to X-rays – lower repair of irradiation damages
- smaller differences between cell cycle phases – growing and dormant tumor cells killed
- lower OER compared to X-rays – good and bad blooded tumor regions killed
- lower fractionation effect compared to X-rays
- Less lateral diffusion and sharper Bragg peak
- Higher RBE (~3) [may be even higher in tumor vs. normal tissue because of Lower oxygen enhancement ratio (OER)]. Relatively more effective vs. photons against hypoxic tumor More effective against slowly proliferating tumors
- Cost is higher than protons, e.g. Hyogo (2001: 28 B ¥/ $ 230 million) vs. $100 million proton accelerators.

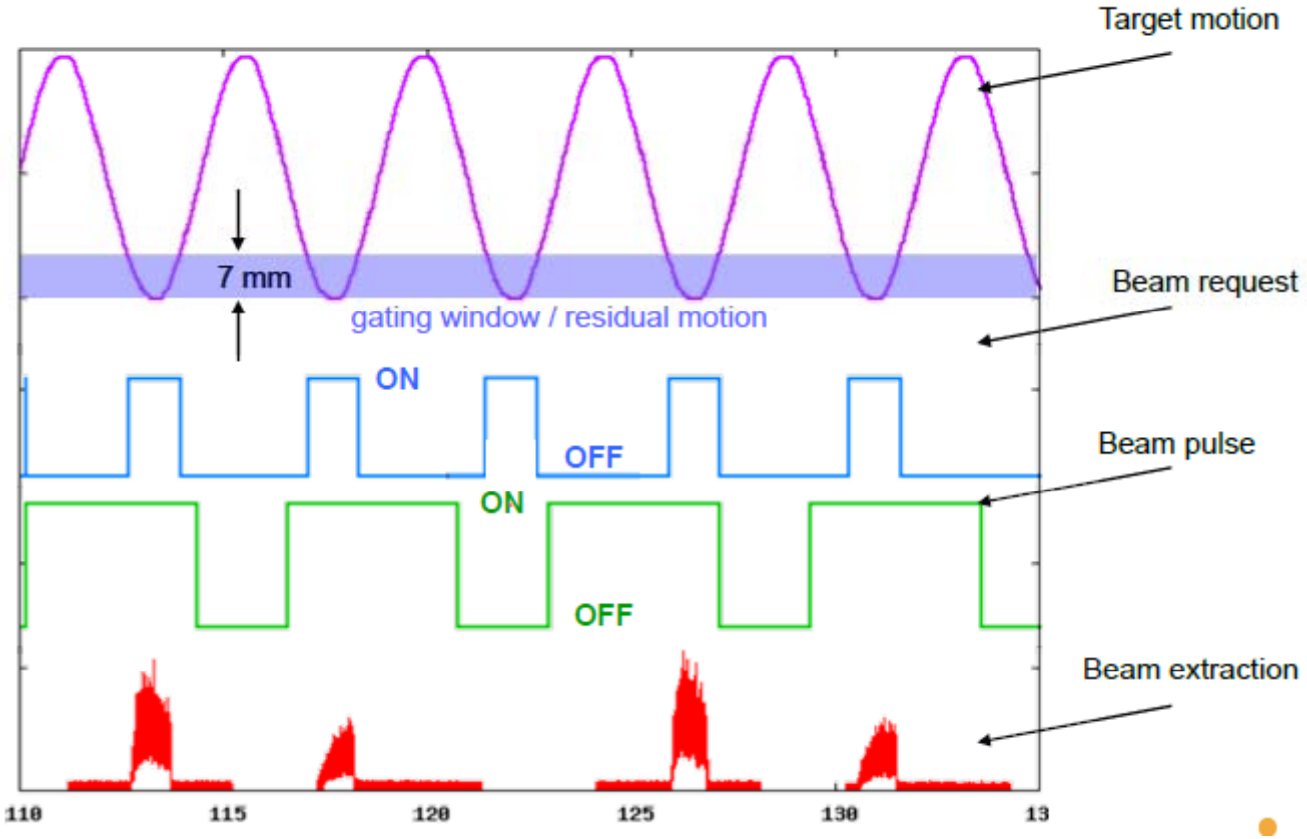
- Tumor therapy and treatment planning
- Basic research on:
  - ✓ repair mechanisms after high LET irradiation
  - ✓ cell survival studies (RBE, OER)
  - ✓ chromosome aberrations on human blood cells

Irradiation of moving targets (e.g. lung tumors)

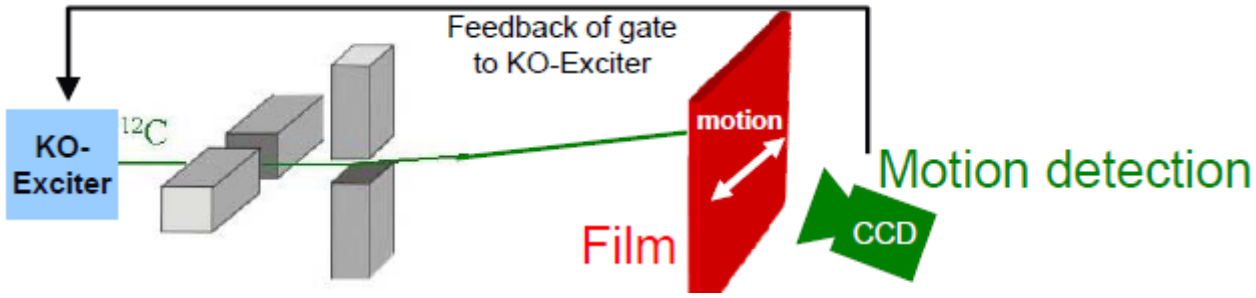
- Long term: Tracking Adaptation of beam position to follow target motion
- Short term: Gating Restrict irradiation to phases with little motion







RF-Knock-out (KO) extraction [Moritz et al. 2005]: Allows pausing and resuming within a pulse, Experimental at GSI, standard at HIT
Parameters: 2 mm grid spacing; ~18 mm spot size; 1-9 mm gating window



Radiation Effects

Somatic effects

damages to cells passed on to succeeding cell generations.

Genetic effects

damages to genes that affect future generations.
Genes are units of hereditary information that occupy fixed positions (locus) on a chromosome. Genes achieve their effects by directing the synthesis of proteins.

Somatic effects and genetic effects show no immediate symptoms

Somatic Effects

Damages to cell membranes, mitochondria and cell nuclei result in abnormal cell functions, affecting their division, growth and general heath.

Organs such as skin, lining of gastrointestinal tract, embryos, and bone marrow, whose cells proliferate rapidly are easily damaged.

Bone marrow makes blood, and its damage leads to reduction of blood cell counts and anemia.

Damage to germinal tissues reduces cell division, and induces sterility.

Genetic Effects

Human cells contain 46 chromosomes. Germ or ovum cells contain 23.

A chromosome contains a deoxyribonucleic acid (DNA) molecule.

The double-helix DNA has two strands of phosphoric-acid and sugar linked bases of Adenine, Guanine Cytosine or Thymine.

The A-T and G-C pairs stack on top of each other.

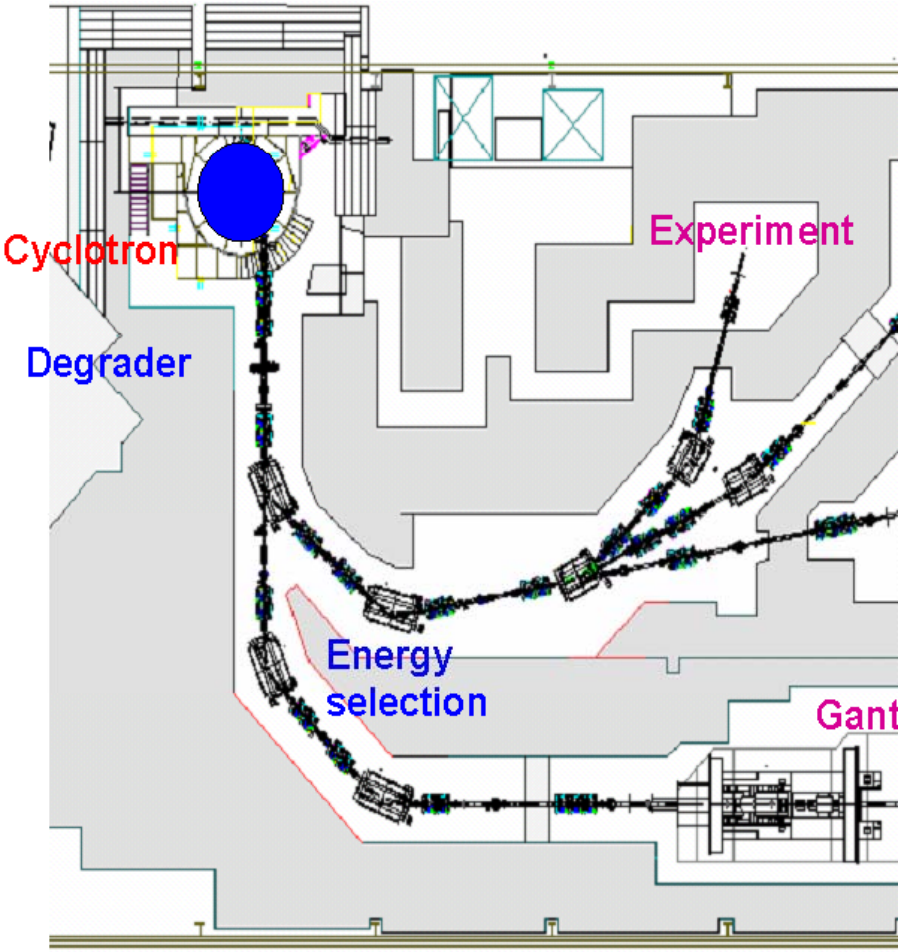
The DNA codon transcripts mRNA, which directs the amino-acid sequences of protein. DNA Damages result in somatic and genetic effects.

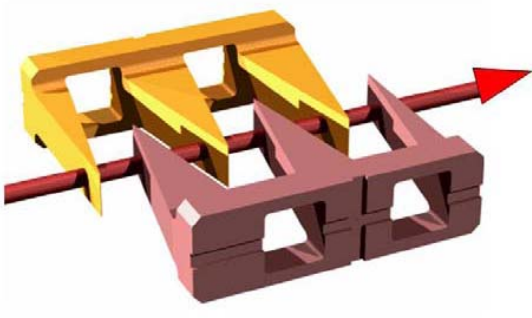
When DNA molecules replicate (pass on to next generation), they are sensitive to radiation damage. Joining wrong ends of broken DNA is called Translocation, which cause mutation and deformation at birth.

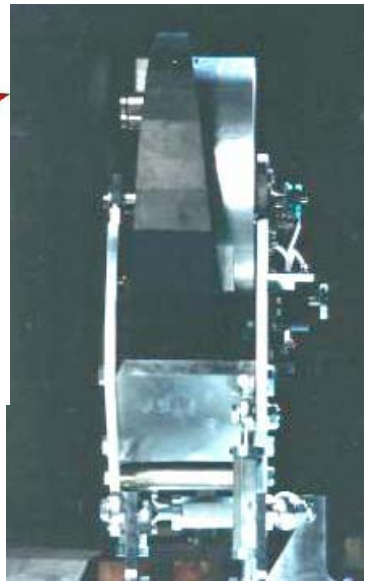
Genetic effects increase frequency of mutation.

Cyclotrons: E = 250 ± 0.1 MeV; I = 100-1000 nA; ε = 4 mm-mrad

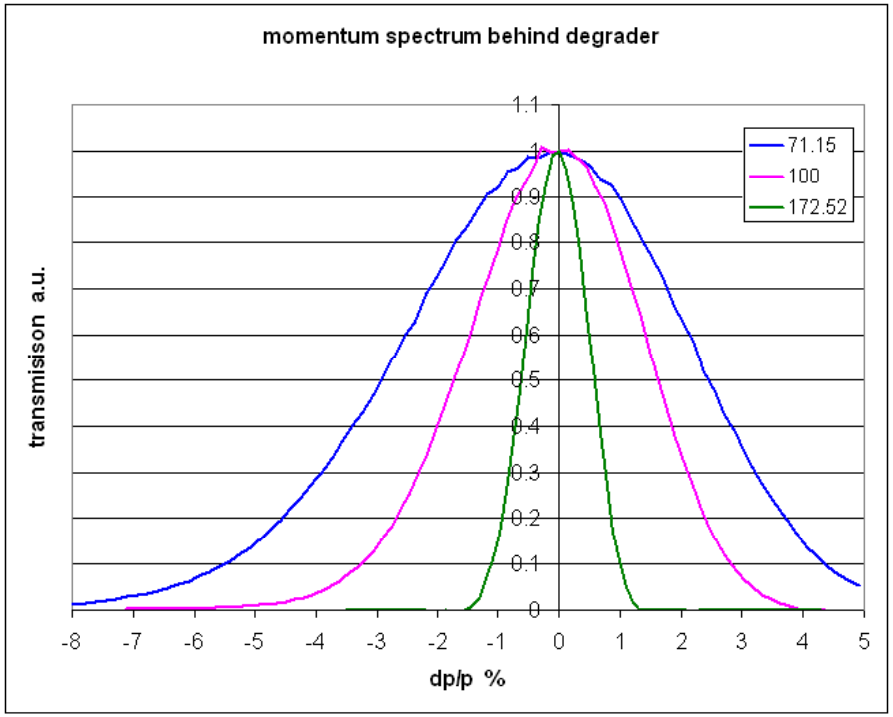
IBA, Accel/Simens



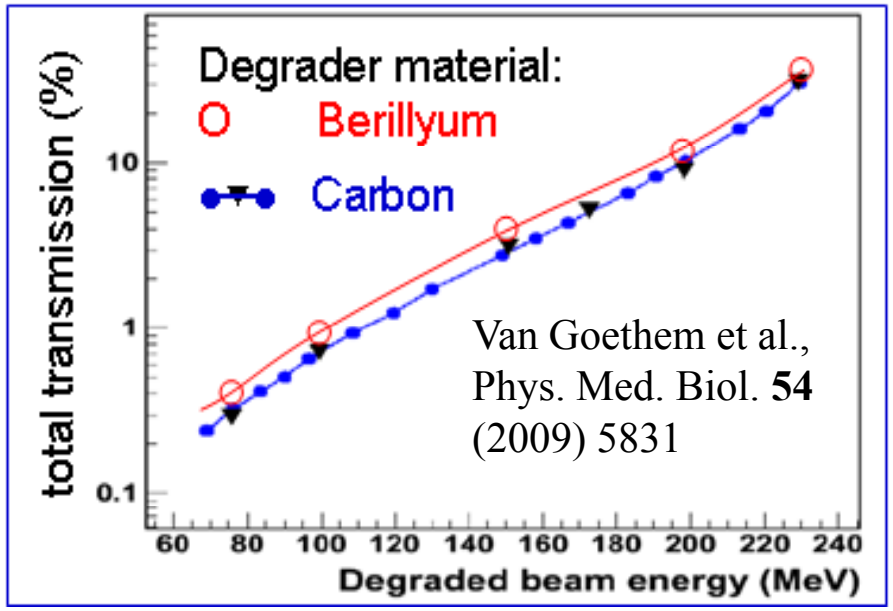




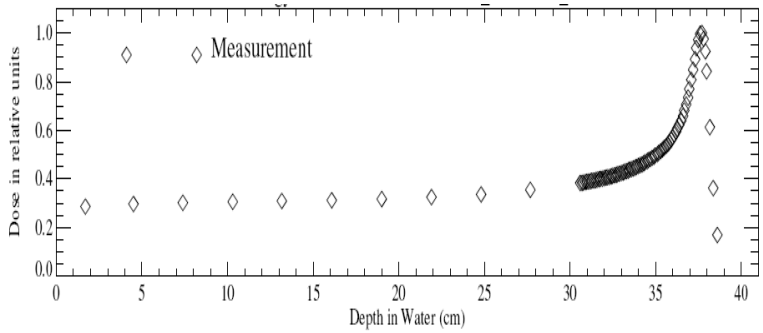
Multiple wedge degrader (PSI)
238-70 MeV **5 mm**
ΔRange in 50 ms

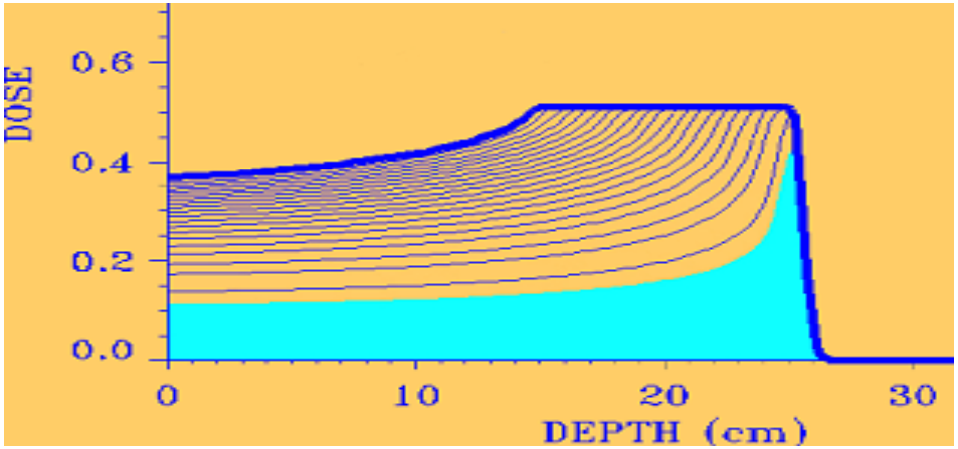


- energy spread increases
- beam loss due to nuclear reactions
- beam size increases due to multiple scattering

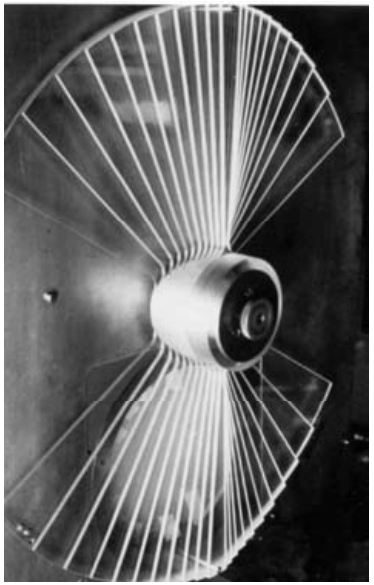


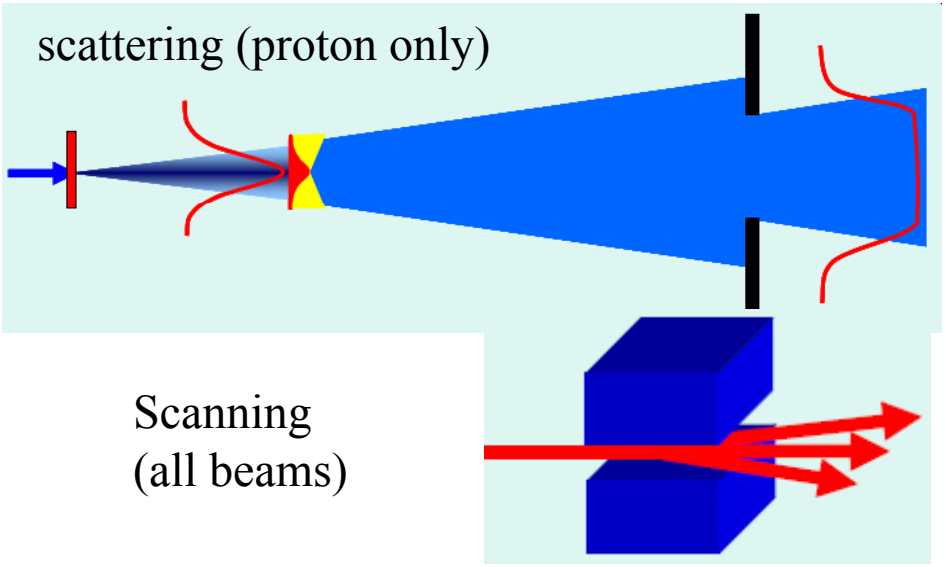
Van Goethem et al., Phys. Med. Biol. **54** (2009) 5831



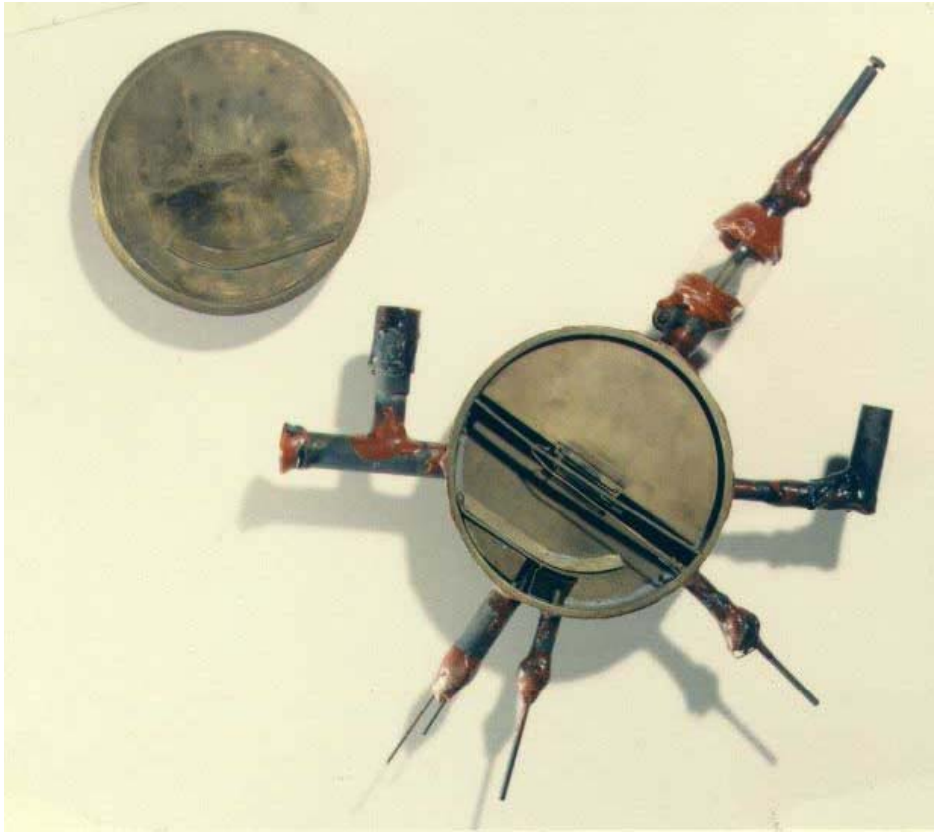


Just before the patient





Scanning
(all beams)



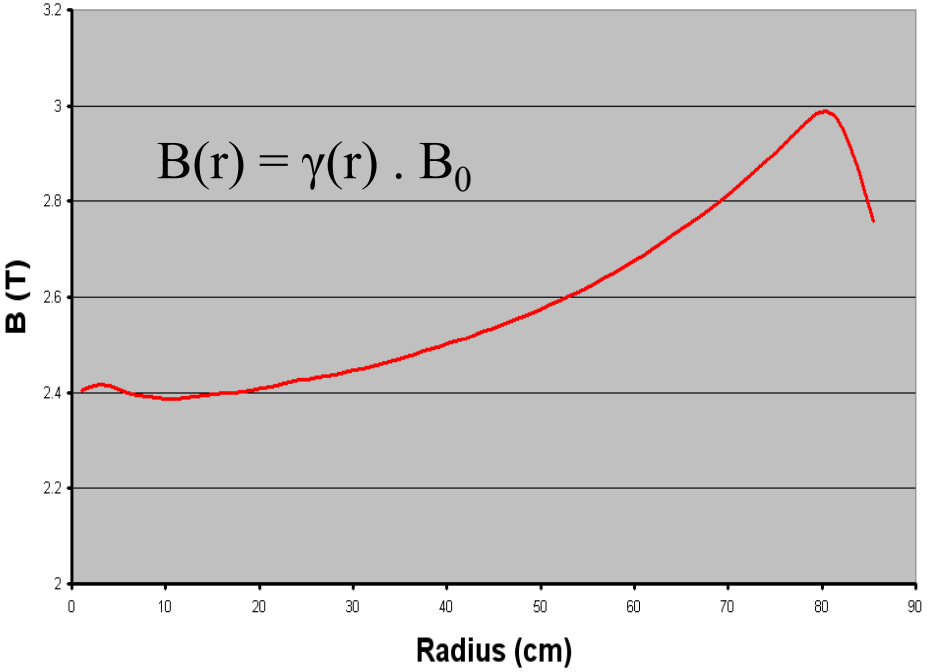
The first successful cyclotron, the 4.5-inch model built by Lawrence and Livingston reached 80 keV proton energy on January 2, 1931. In 1932, Lawrence built a 11-inch cyclotron reaching 1.25 MeV and observed nuclear reaction.

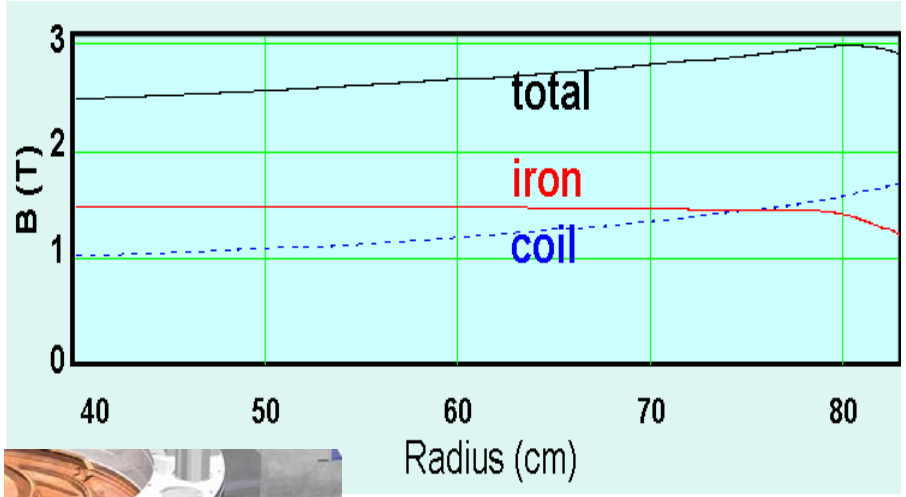
230 MeV cyclotron (IBA,1996)

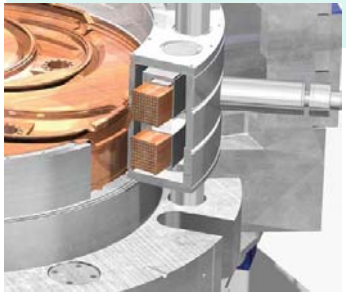
Relativity in high-Energy cyclotrons

$$r = \frac{p}{eB} = \frac{p}{\gamma m \omega} = \frac{c}{\omega}\left(1 - \frac{1}{\gamma^2}\right)^{1/2},$$

$$B = \frac{m\omega}{e}\gamma(r) = \frac{m\omega}{e\sqrt{1-(\omega r/c)^2}}$$







Azimuthally Varying Field cyclotron

- Main field increases with radius
- φ must also increase to maintain vertical focusing

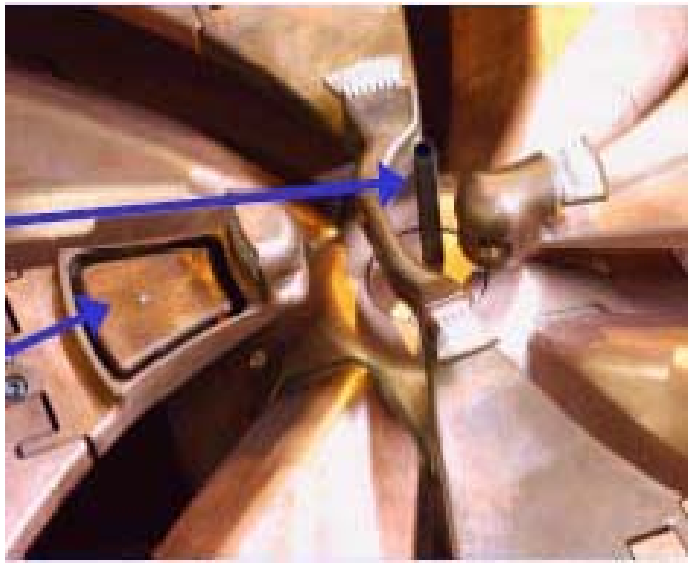
Closed He system: 4 x 1.5 W @4K

superconducting coils => 2.4 - 3.8 T

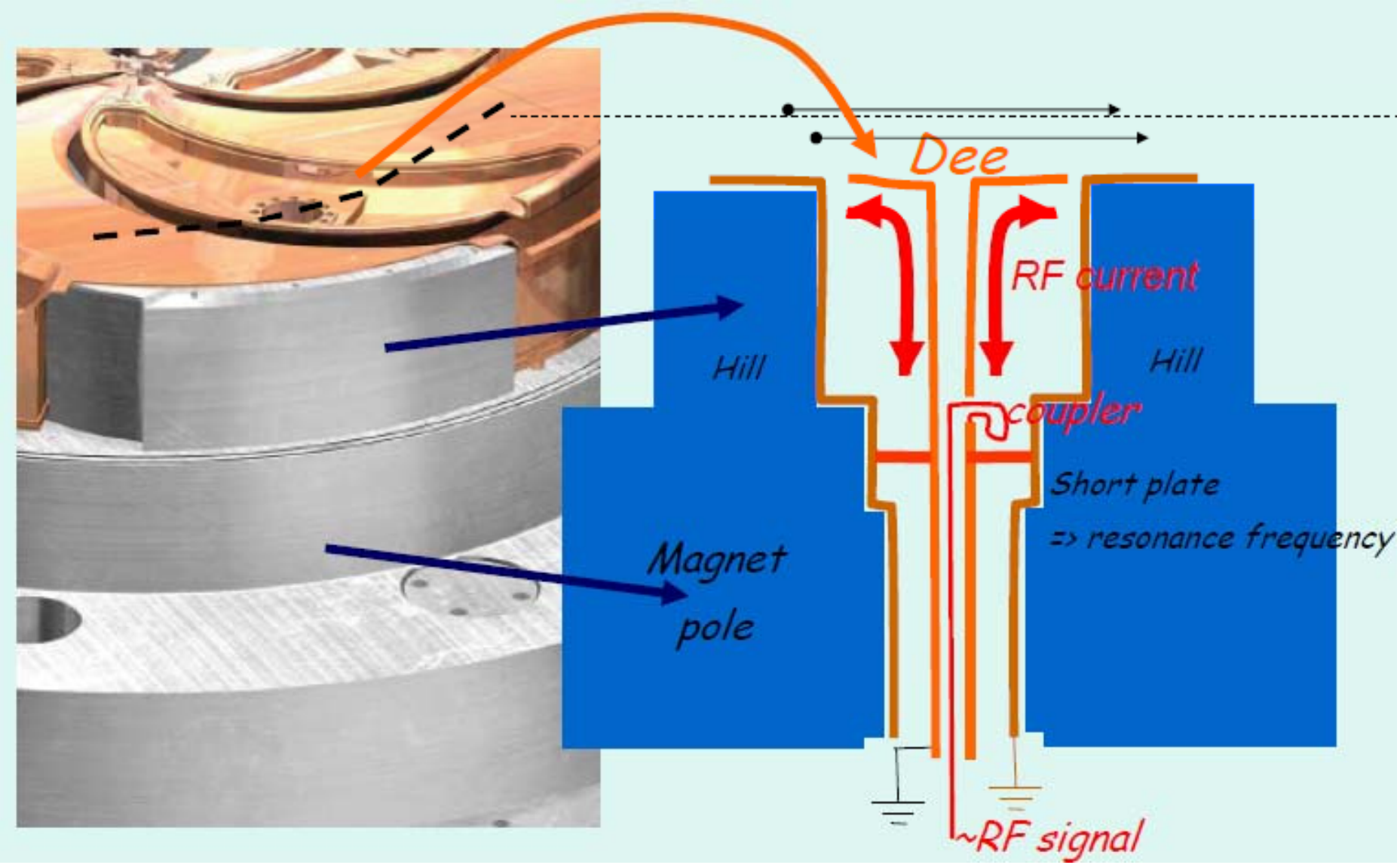
4 RF-cavities: ~100 kV on 4 Dees

250 MeV proton cyclotron (ACCEL/Varian)

Important parameters:
Voltage on Dee
Number of Dee‘s
Energy gain per turn
Orbit separation
Extraction efficiency



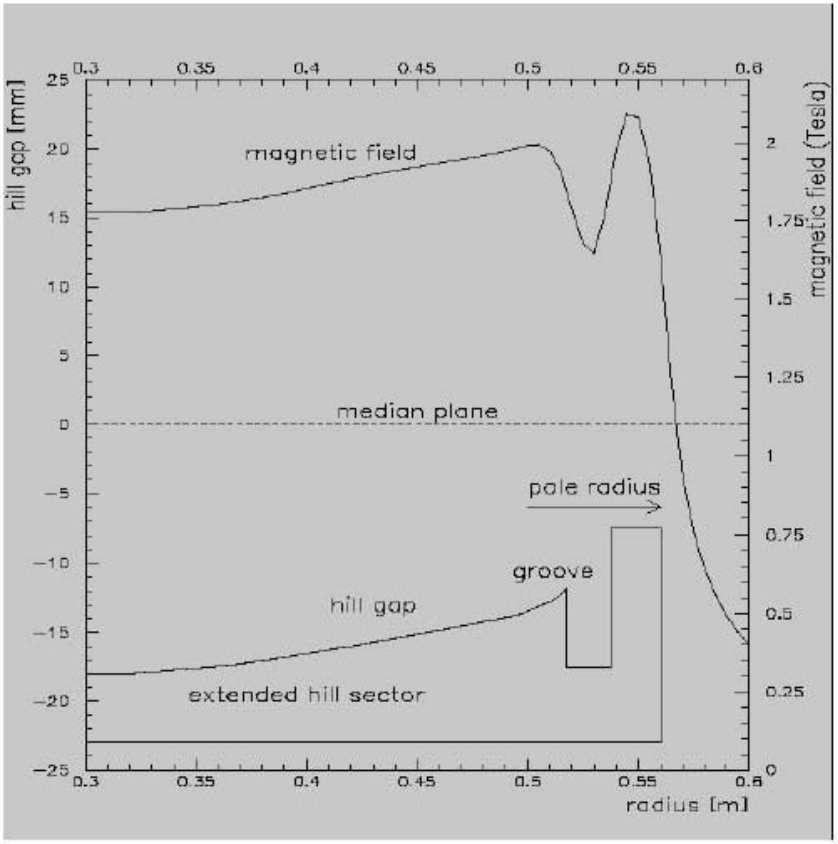
RF system: Dee



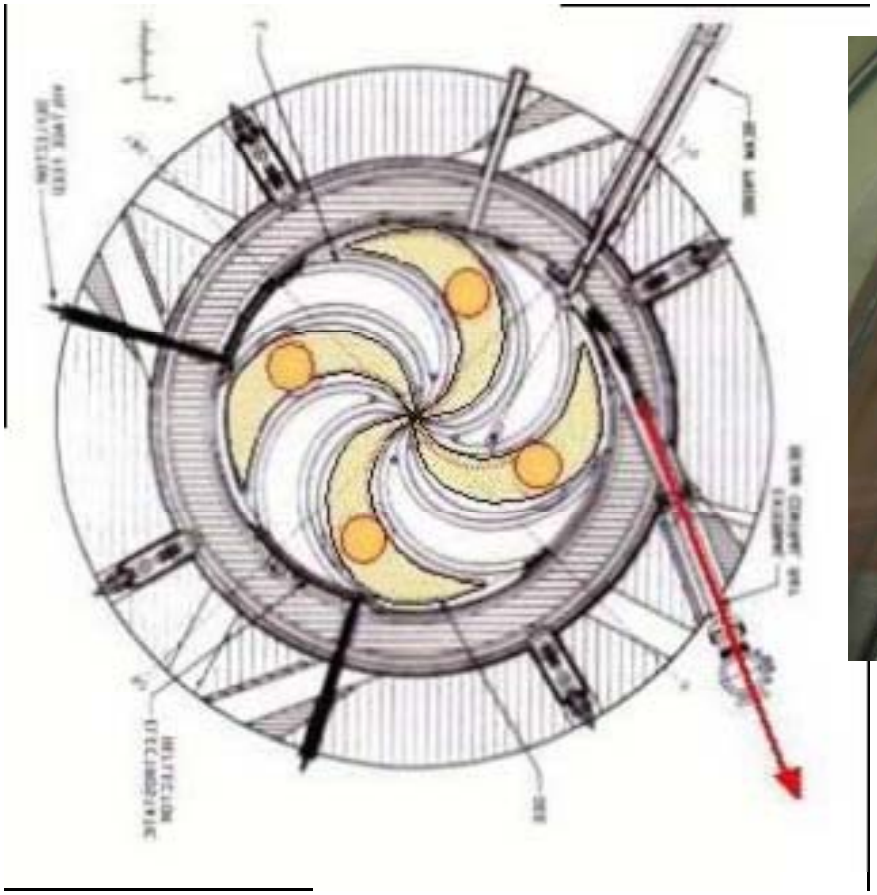
Self-extraction: Realization

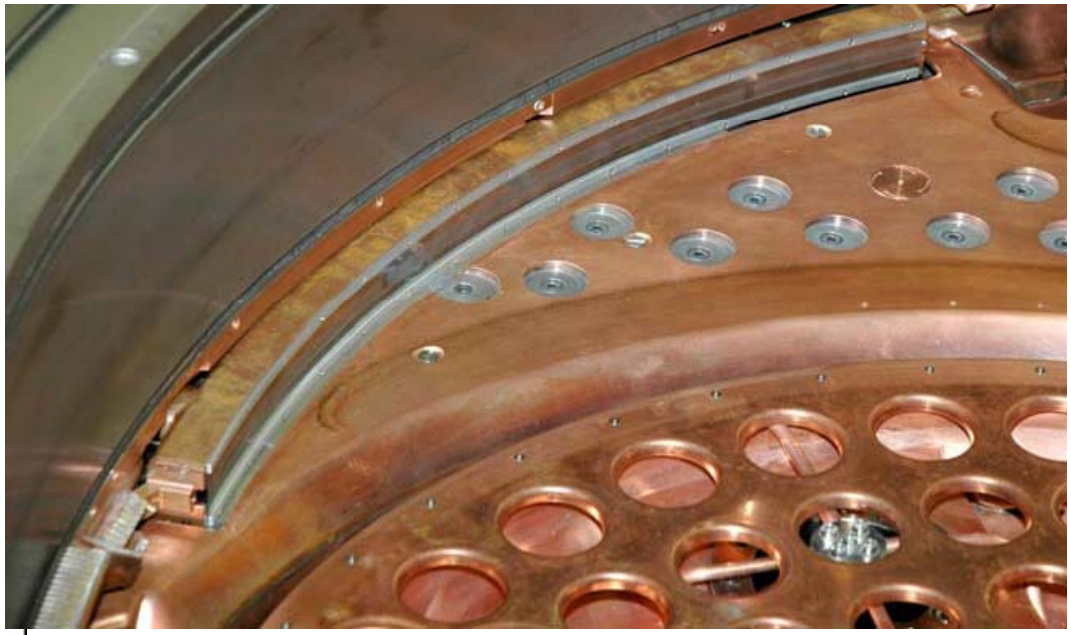
Small elliptical hill gap ⇒ allows for sharp radial gradients

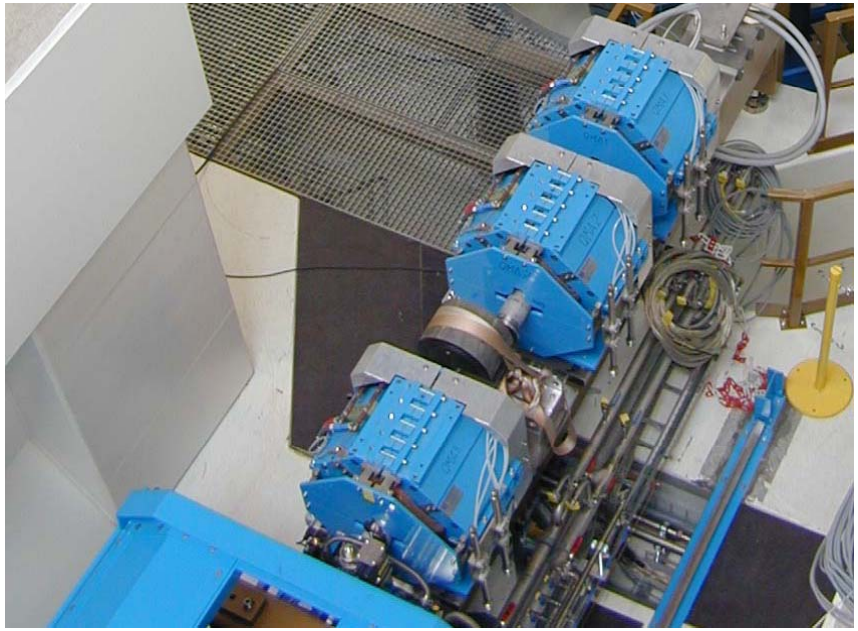
'magnetic septum' ⇒ groove machined in the pole



Pole with goove







Beam off: mechanical beam stopper in; or fast kicker magnet

Proposal of H.Blosser et al.,1989: 250 MeV; 52 tons, on gantry; B(0)=5.5T

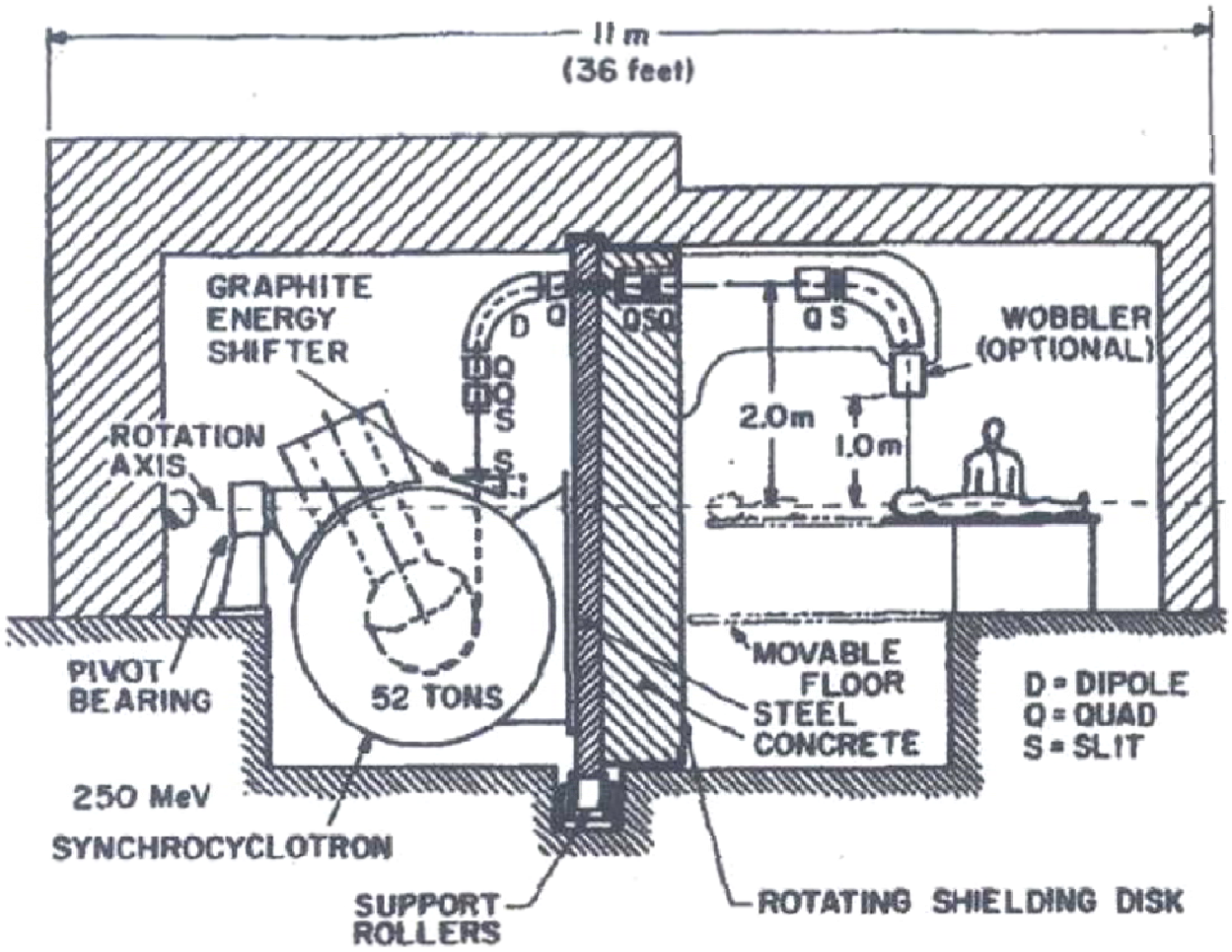
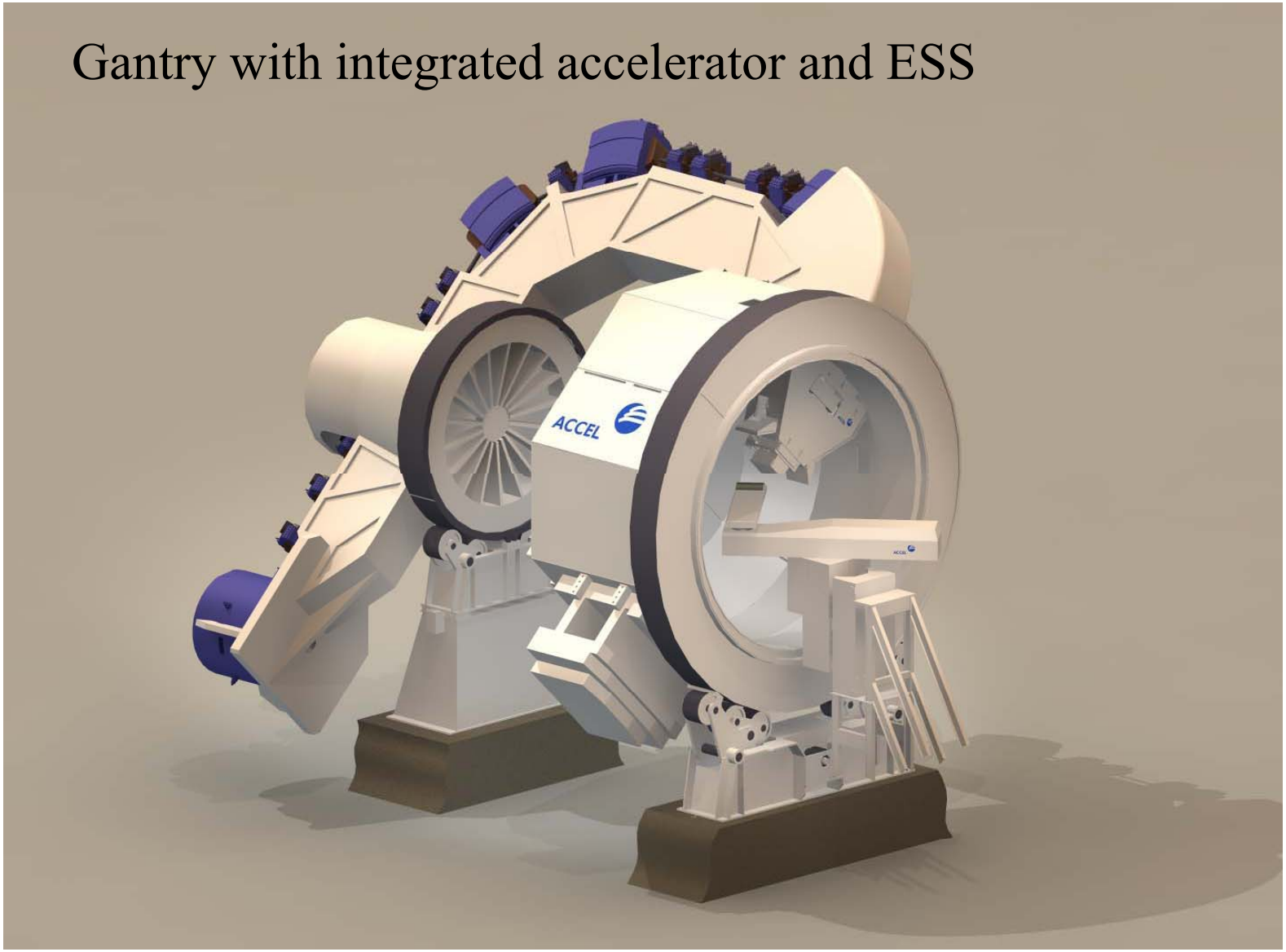
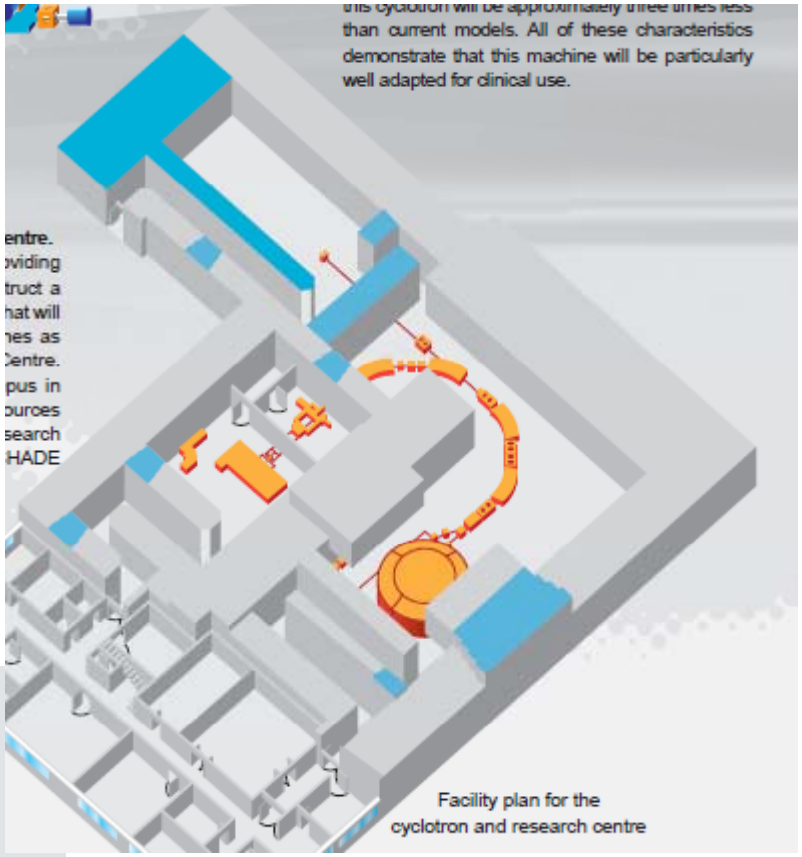
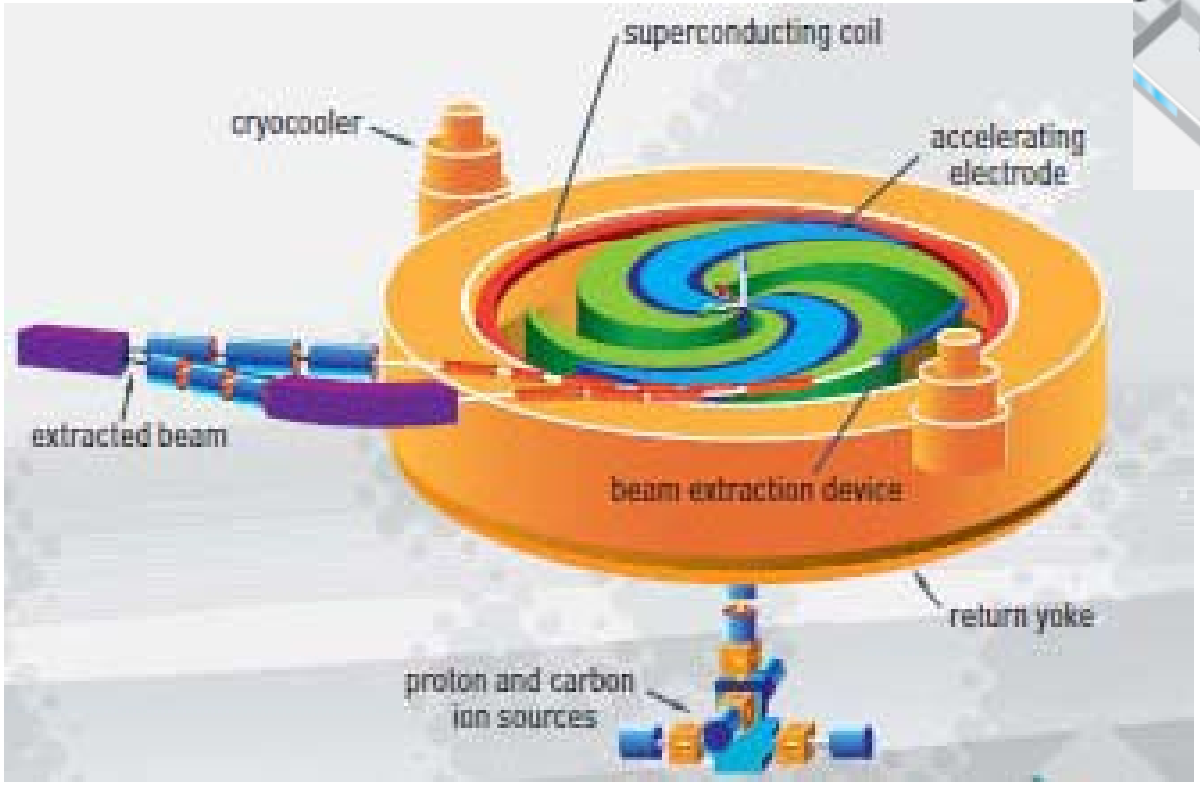


FIG. 9 -- Drawing showing synchrocyclotron rotating gantry arrangement with energy shifting wedge just after the cyclotron. Energy shifting can optionally be accomplished just ahead of the patient.

Gantry with integrated accelerator and ESS







Int. Conf. Cyclotron and appl, Tokyo 2004: IBA-C400

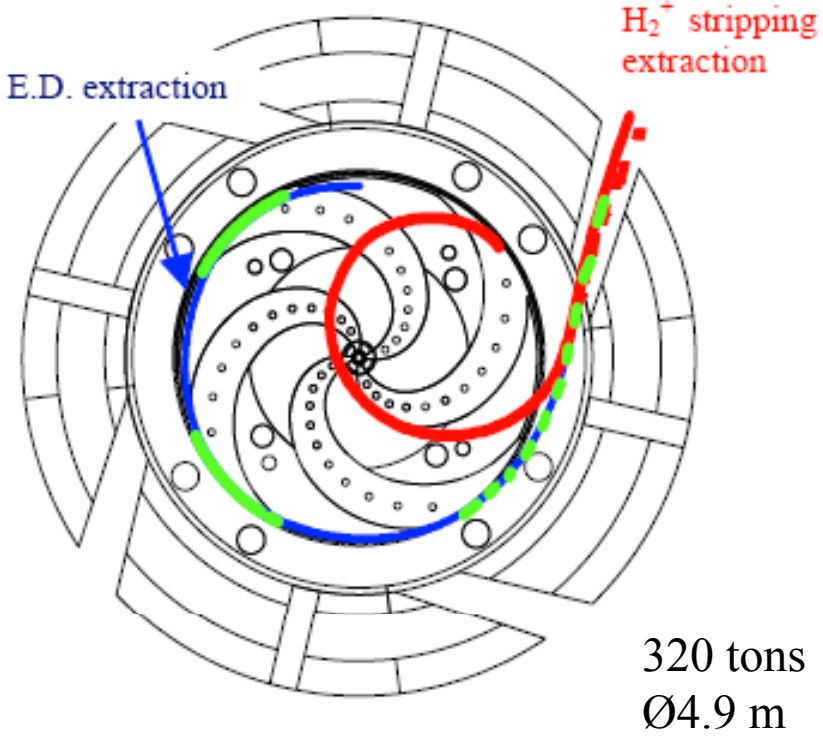


Figure 3: Layout of the cyclotron with overdrawn the extraction trajectories by E.D. and by stripper. The E.D. and the M.C. positions are also shown.

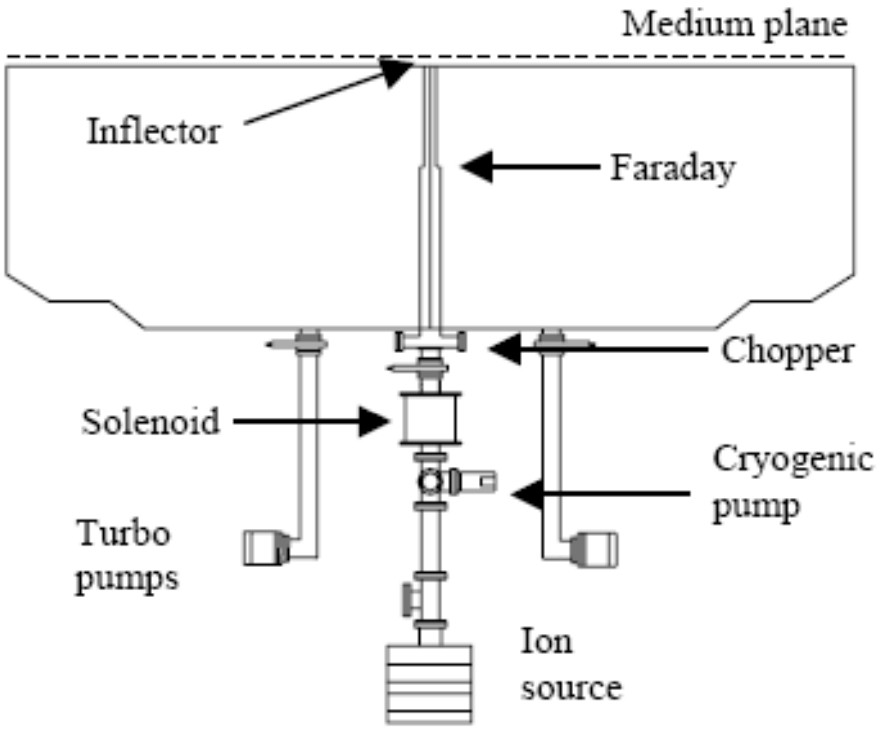
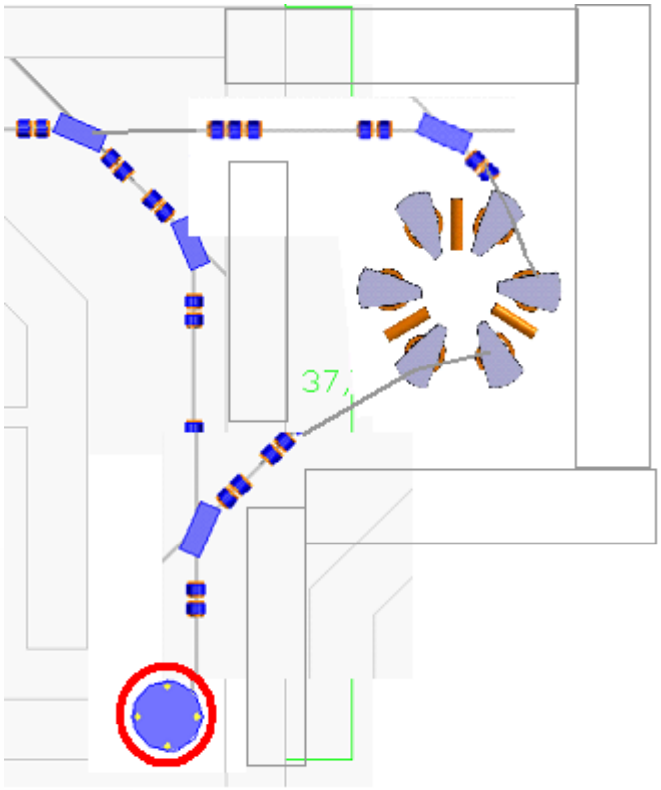
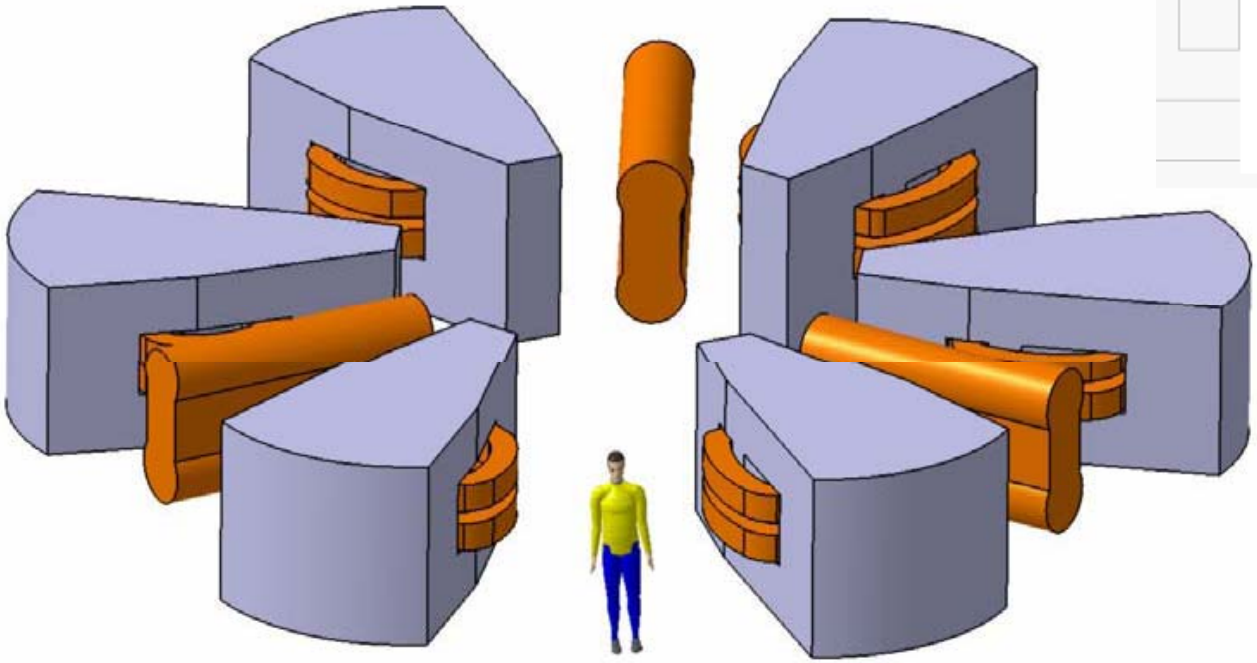


Figure 4: Layout of the axial injection line and part of vacuum plant

PSI design for 2-step approach



250 MeV/nucl.
H2+, α, C6+

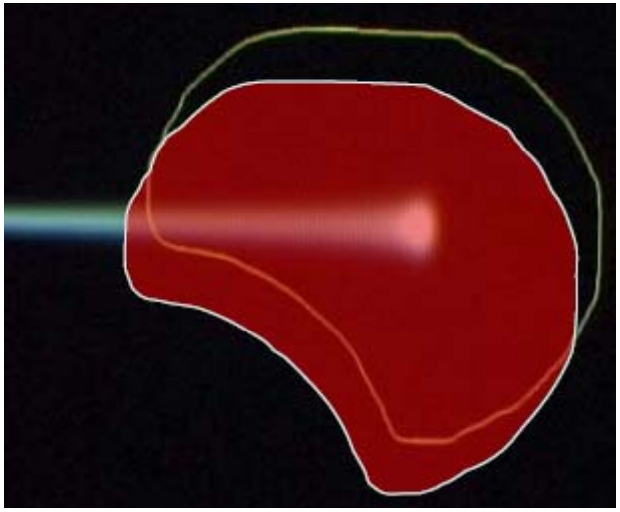


Second step: also 450 MeV/nucl Carbon

Energy + its stability
Beam size (emittance)
Beam intensity + stability (kHz) + adjustability (range, speed)
Extraction efficiency

Frequency of unplanned beam interrupts
Start up time after „off“ and after „open“
modular control systems + comprehensive user interface
Maintenance interval, maintenance time, maintenance effort
Activation level (person dose per year)

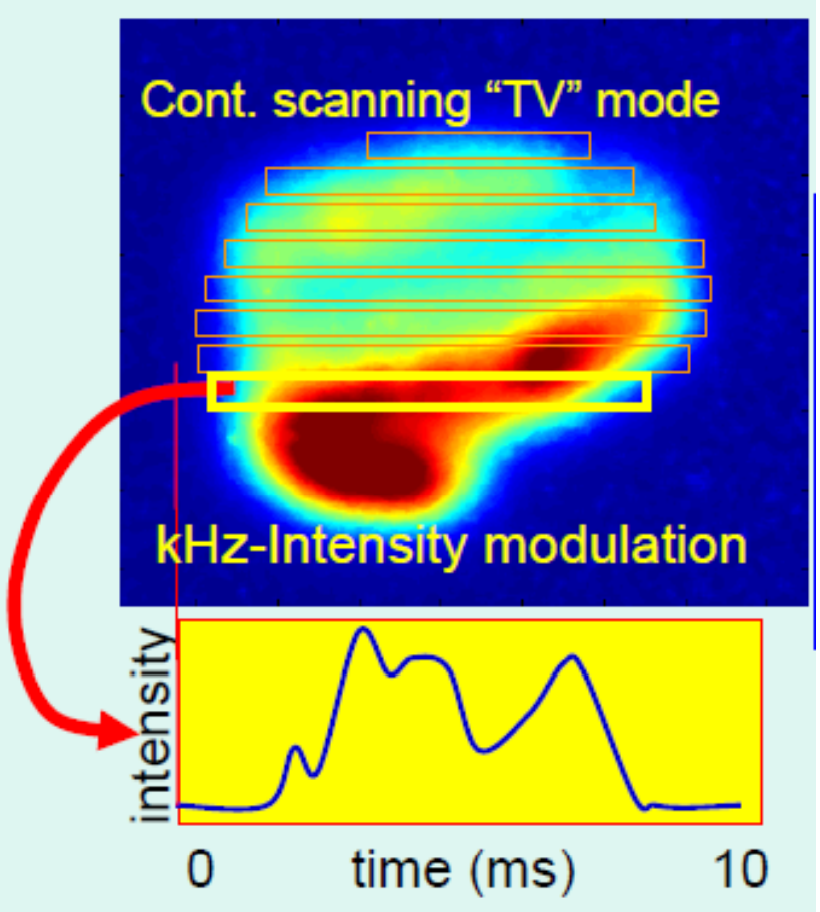
Ions: time to switch ion species
Synchrocyclotron: rep. rate, dose/pulse adjustable (scanning)?



Organ movement: Danger to underdose and overdose

Solutions: Beam gating; Multiple scans of tumor; Adaptive scanning

Fast pencil beam scanning



After each layer: Energy change in 80 ms; 7 s for a 1 liter volume.
Target repainting: 15-30 scans / 2 min.