Physics and Radiobiology of Particle Therapy

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Radiotherapy started just after the discovery of X- rays in 1895 and with discovery of Radium ^{226} in 1898 it found its use in radiotherapy. Since then in last 122 years radiotherapy has progressed rapidly as the main modality of cancer treatment.

Primary aim of radiotherapy

1. Deliver lethal dose to tumor
2. Spare normal tissue/ OAR

How to achieve
Art/ Science/Technology/Skills

Figure 2. Advances in Radiotherapy: 1900–Present

Clinical Advances
Technologic Advances
Biologic Advances

Becquerel experiences skin burn while carrying radium in vest pocket (109)
1901

Radiation intensity related to inverse square of distance from source
1903

Fractionated radiation sterilizes ram's testes without major burns (11, 12)
1911

Cellular radiosensitivity depends on mitotic activities and levels of differentiation (47)
1906

Leukemia cases reported in radiation workers (10)
1911

Hot-cathode x-ray tube invented (33)
1913

Radiosensitivity correlated with oxygen presence (52)
1923

How high-energy photons interact with tissue (Compton effect) (109)
1922

Roentgen adopted as standard exposure unit; radiation protection recommendations
1928

Head and neck cancers cured with fractionated X-rays (13)
1928

Air wall ionization chambers accurately measure radiation intensities
1924

Nobel Prize (Muller) for radiation-induced mutagenesis shown in Drosophila
1946

First self-sustaining nuclear chain reaction with uranium
1942

Plant root studies show importance of oxygen in radiotherapy (52)
1935

Dosage system for gamma ray (36)
1934

Cyclotron invented (37)
1932

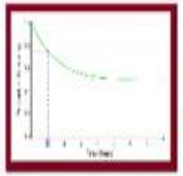
First patient treated with neutron beams
1938

Experimental quantification of the oxygen effect (109)
1952

Cobalt-60 telotherapy units first used (15)
1951

Skin iso-effects governed primarily by total dose and overall treatment time (17)
1944

1900 1905 1910 1915 1920 1925 1930 1935 1940 1945 1950



First *in vivo* radiation survival curve (19) 1967

Gamma knife for cranial radiosurgery 1968

Differential radiosensitivities of early vs. late responding tissues (112) 1980

Multi-leaf collimators developed 1980

MRI clinically available 1980

Cancer cell survival correlated with tumor control probablility after radiotherapy (21, 22) 1991

Cellular radiation damage repair shown (109) 1959

Remote after-loading in brachytherapy 1961

Metronidazole, the first hypoxic cell sensitizer (111) 1976

Model suggests metastasis occurs before detection of primary tumors (80) 1980

Sequence of the human genome completed (117) 2000

Clonogenic survival curves for irradiated cells (49) 1956

Proton beam treatment adopted (at Harvard/MGH) (45) 1961

Concept for IMRT (42) 1978

Iso-effect formula based on quadratic and linear components of radiation-induced cell kill (19) 1983

LDR and HDR brachytherapies have similar outcomes (29–32) 1993

Bystander effect first described (114) 1992

PET developed 1975

Hyperbaric oxygen in radiotherapy (110) 1966

Tumor potential doubling time (T_{pot}) (113) 1985

Hypoxia from limiting oxygen diffusion (53) 1955

Differential radiosensitivity demonstrated (109) 1963

First CT scans 1972

Survival curves for normal bone marrow (109) 1971

Nucleotron produces first computer-controlled afterloader 1985

Continuum or spectrum theory of cancer spread (81) 1994

SBRT to treat extracranial tumors (27, 28) 1995

First patient treated with proton beams (at Berkeley) (15) 1954

Cancer risk from exposure to X-rays *in utero* (109) 1970

Development of IMRT (40) 1988

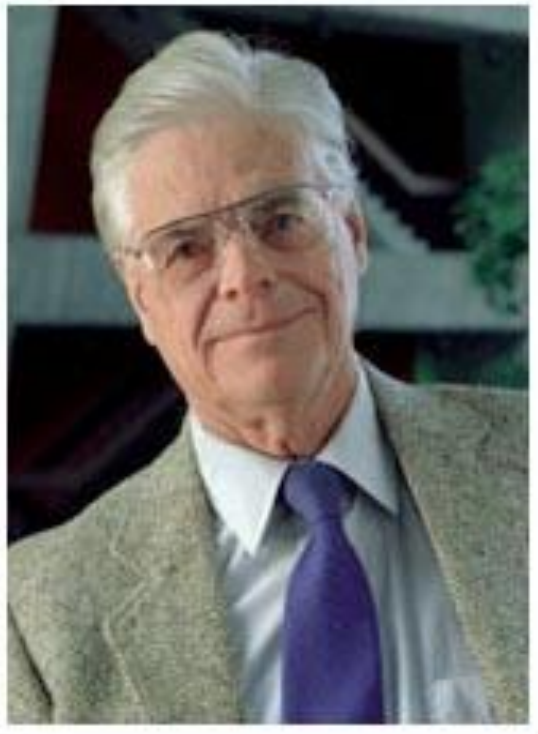
ATM gene discovered (115) 1995

Microarray technology to study expression of human genes (116) 1996

1955 1960 1965 1970 1975 1980 1985 1990 1995 2000 2005 2010

A Man - A Vision

- In 1946 Harvard physicist Robert Wilson (1914-2000) suggested*:
  - **Protons can be used clinically**
  - **Accelerators are available**
  - **Maximum radiation dose can be placed into the tumor**
  - **Proton therapy provides sparing of normal tissues**
  - **Modulator wheels can spread narrow Bragg peak**



Robert Wilson

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

- Why charged particles?
- Why heavy?
- Heavy charged particle therapy can reduce the dose load (“integral dose”) to normal tissues surrounding the tumor target volume by a factor of 2-3 (reduced “dose bath”).
- Increased “dose conformality”, i.e., dose gradient between tumor target volume and surrounding healthy tissues.

Physical Parameters of some particles of interest in radiotherapy

	Particle	charge (eu)	Mass	lifetime
Bosons ---->	photon	0	0	
Leptons ---->	electron (e)	-1	1 m_0*	stable
Mesons ---->	pion	-1	276 m_0	2 10^{-8} s
Hadrons ---->	neutron (n)	0	1835 m_0	12 min
	proton (p)	+1	1832 m_0	stable
Baryons ---->	alfa	+2	4 amu**	stable
	C-ion	+6	12 amu	stable
	Ne-ion	+10	20 amu	stable
	Ar-ion	+18	40 amu	stable

* electron rest mass

** Atomic mass unit 1 amu = 1. 6604 10^{-27} kg or 12.00000 amu is the mass of the principal isotope of Carbon ^{12}C

Linear energy transfer (LET)

"*LET of charged particles in a medium is the quotient dE/dl, where dE is the average energy locally imparted to the medium by a charged particle of specified energy in traversing a distance of dl.*"

LET < 10 keV / μm low LET
LET > 10 keV / μm high LET

- 250 kVp X rays: 2 keV/*μ*m.
- Cobalt-60 γ rays: 0.3 keV/*μ*m.
- 3 MeV X rays: 0.3 keV/*μ*m.
- 1 MeV electrons: 0.25 keV/*μ*m.

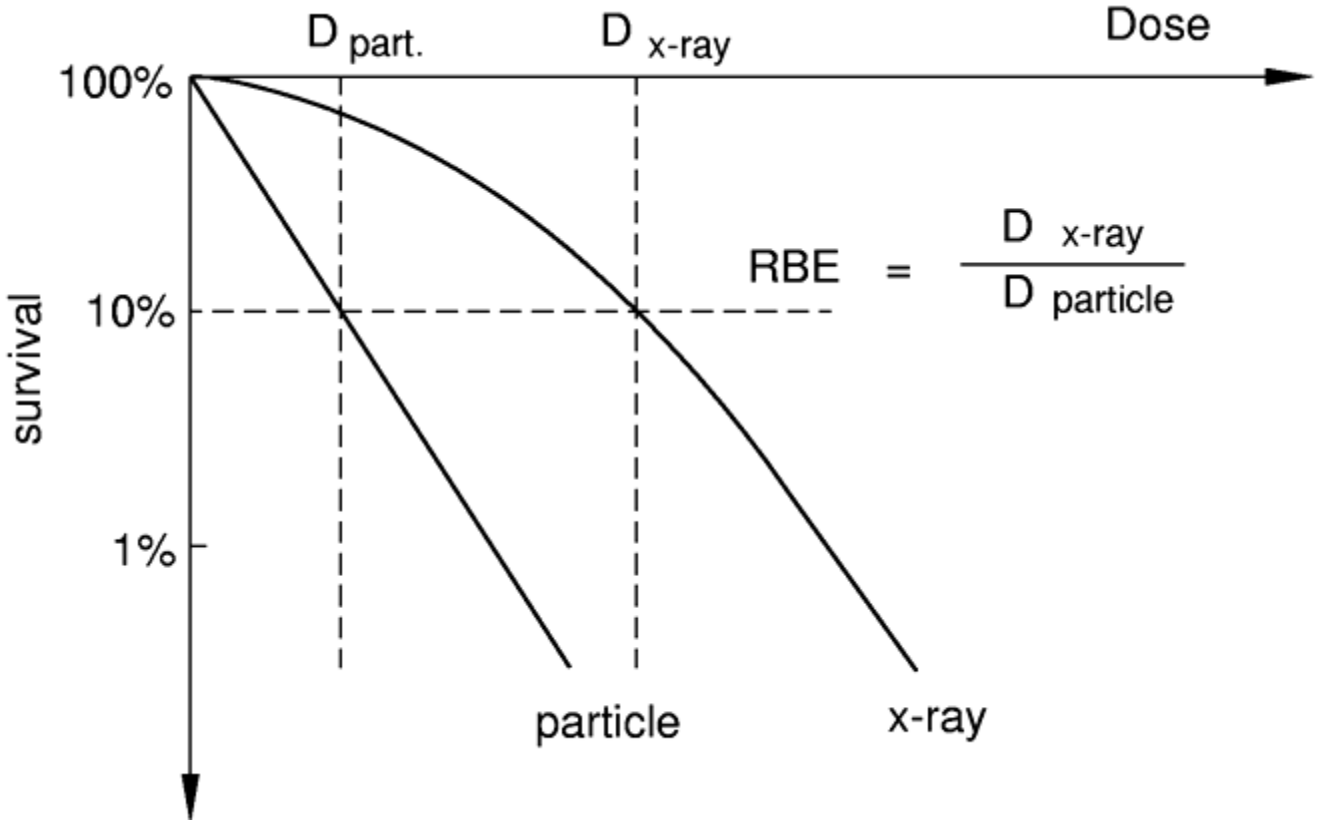
—14 MeV neutrons: 12 keV/*μ*m.

—Heavy charged particles: 100–200 keV/*μ*m.

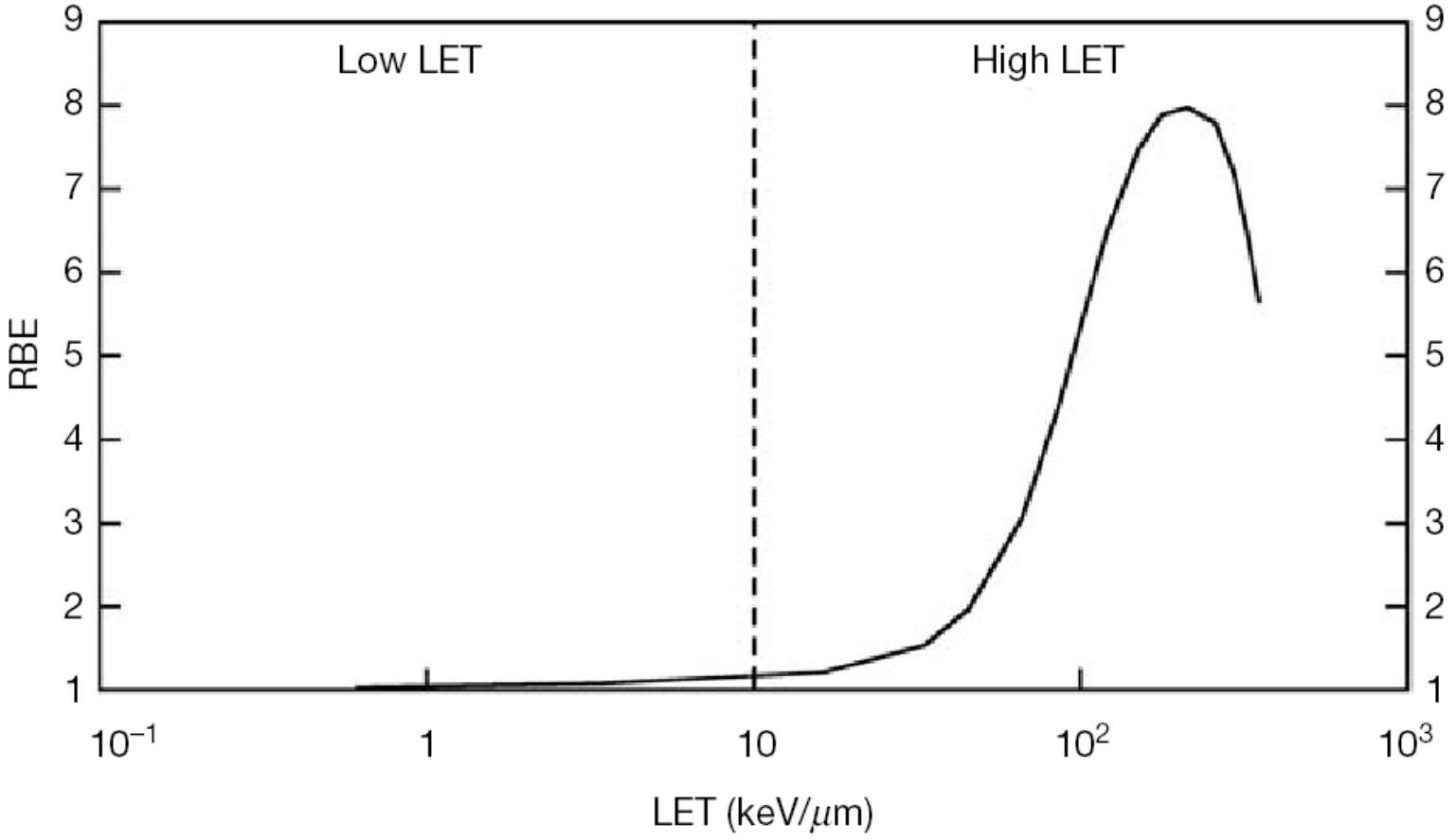
—1 keV electrons: 12.3 keV/*μ*m.

—10 keV electrons: 2.3 keV/*μ*m.

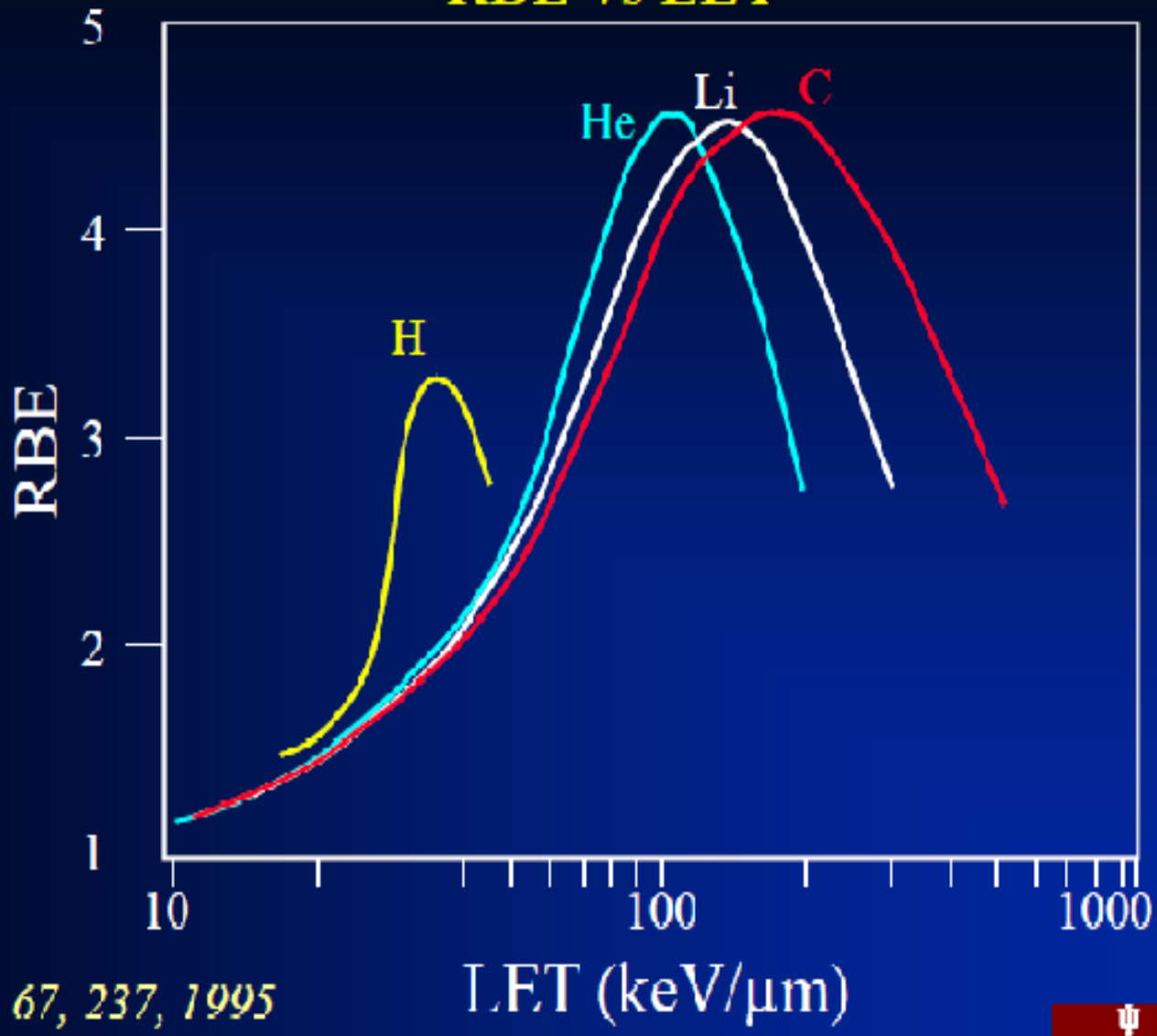
Definition of RBE



LET and RBE, “overkill”

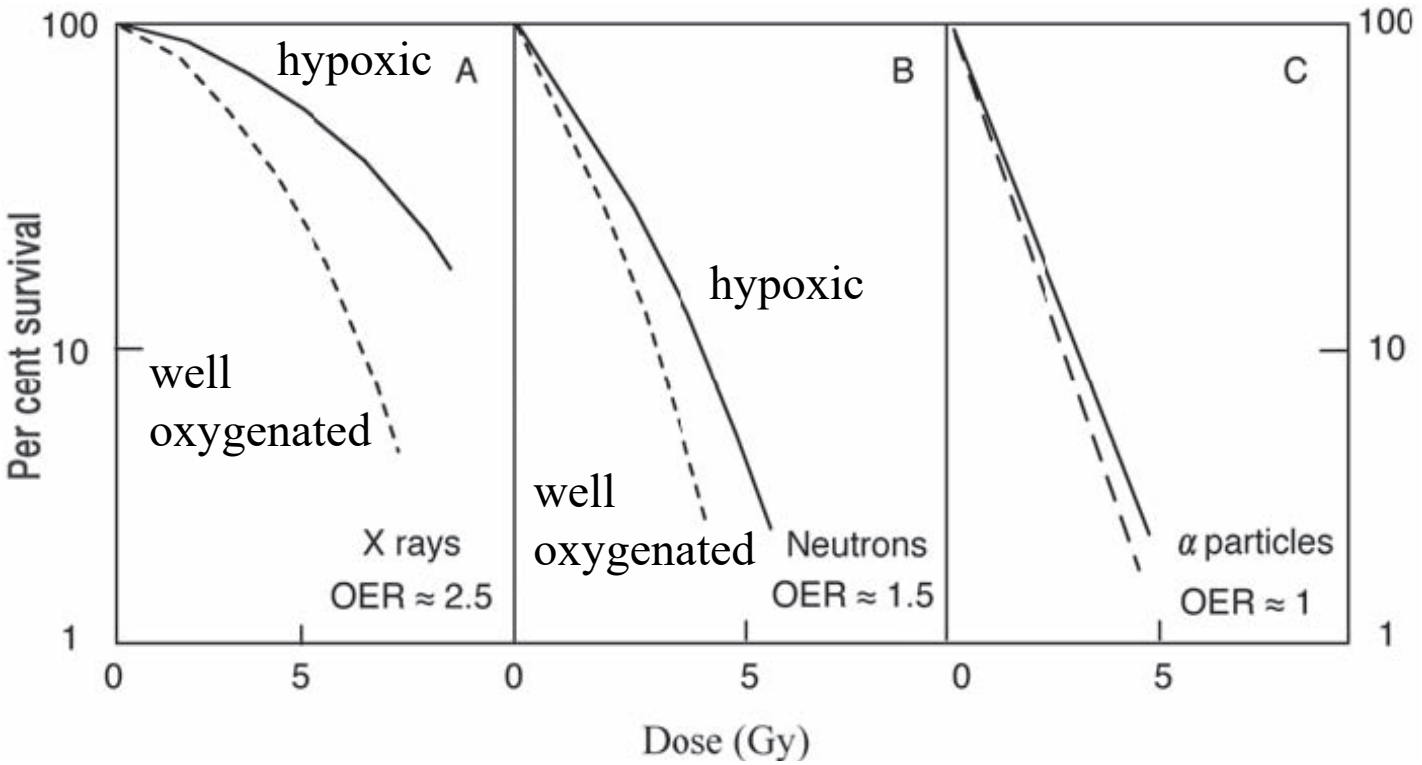


RBE vs LET



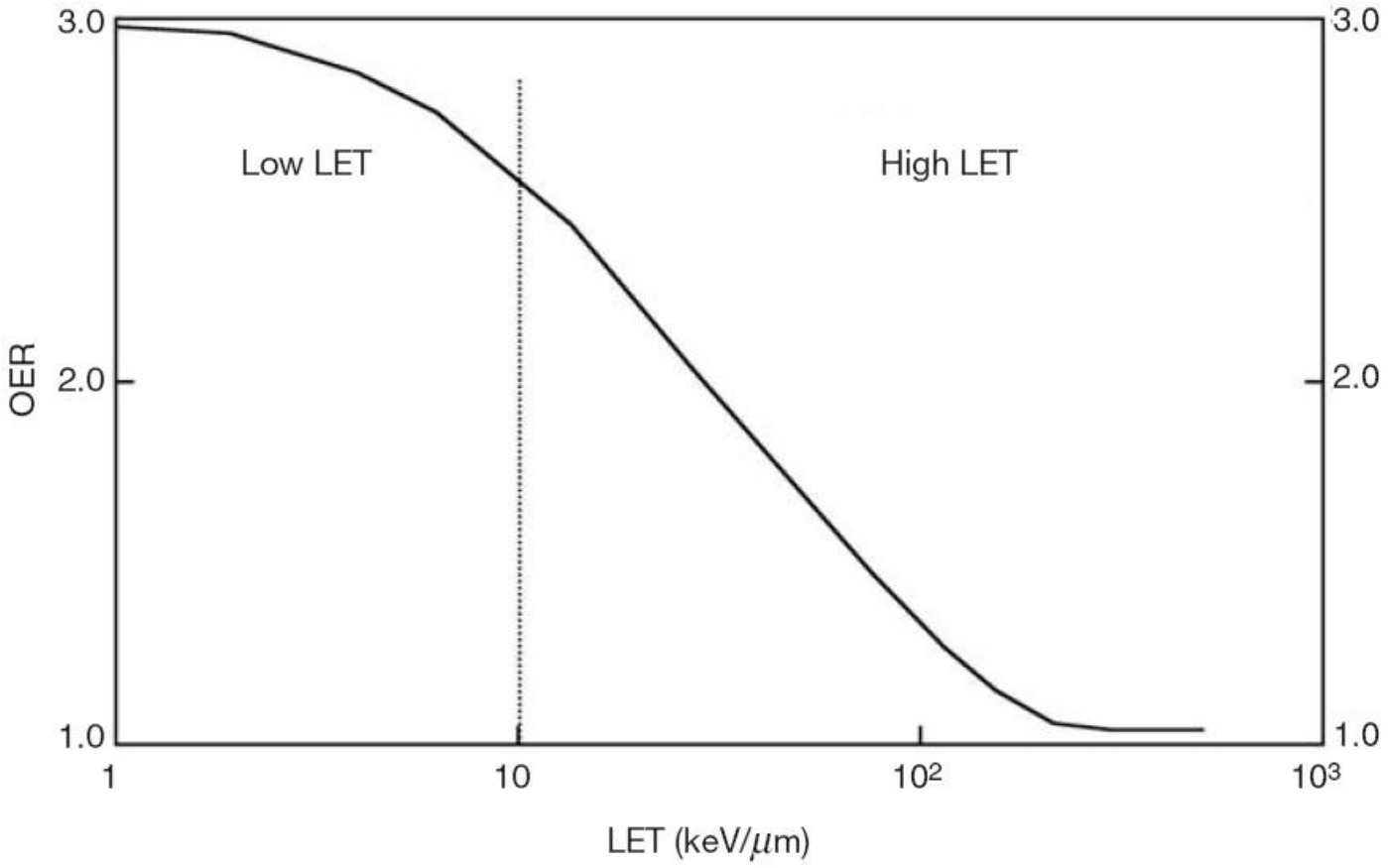
Raju, IJRB, 67, 237, 1995

Oxygen enhancement ratio (OER)

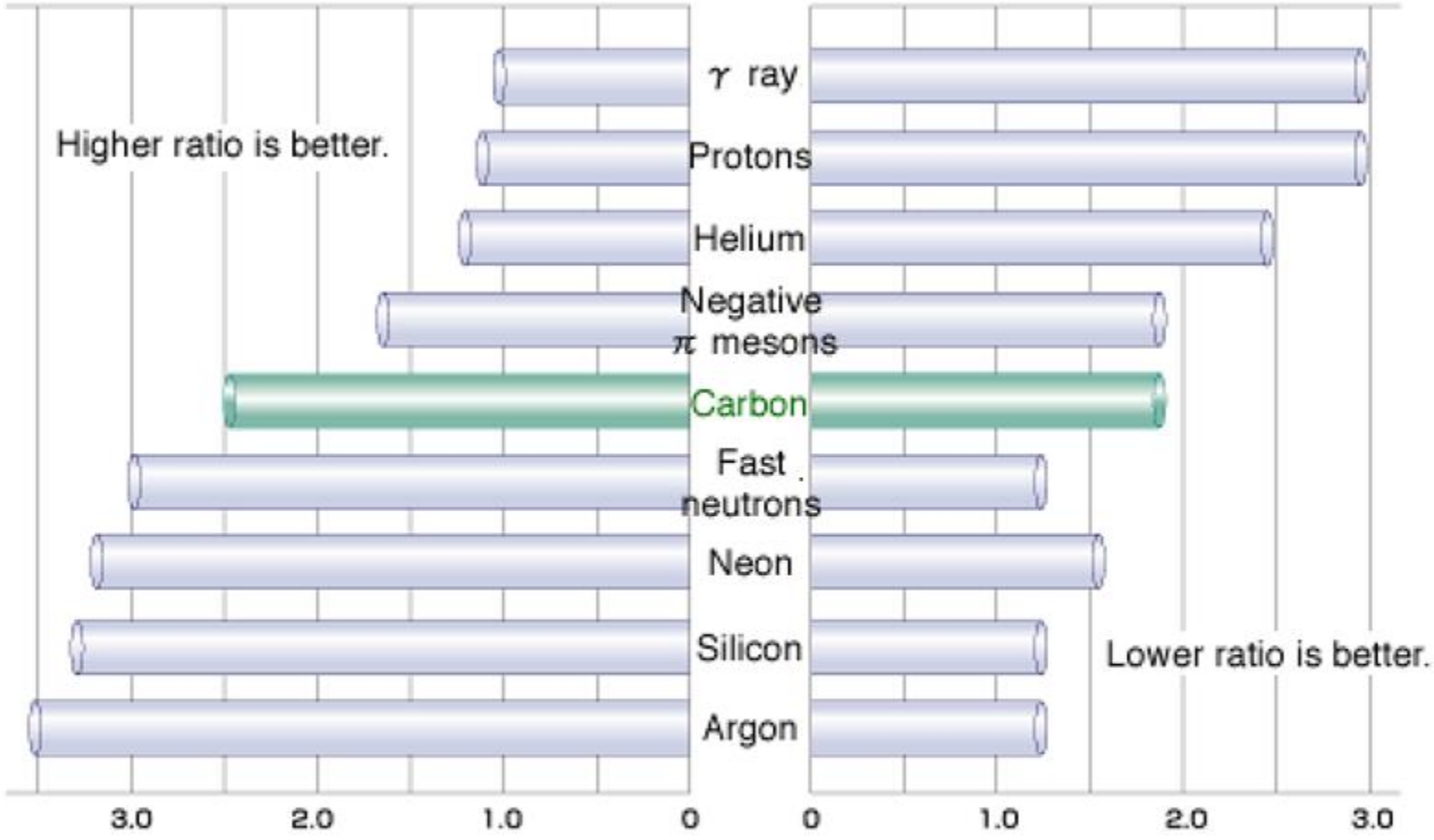


$$\text{OER} = \frac{\text{Dose to produce a given effect without oxygen}}{\text{Dose to produce the same effect with oxygen}}$$

LET and OER



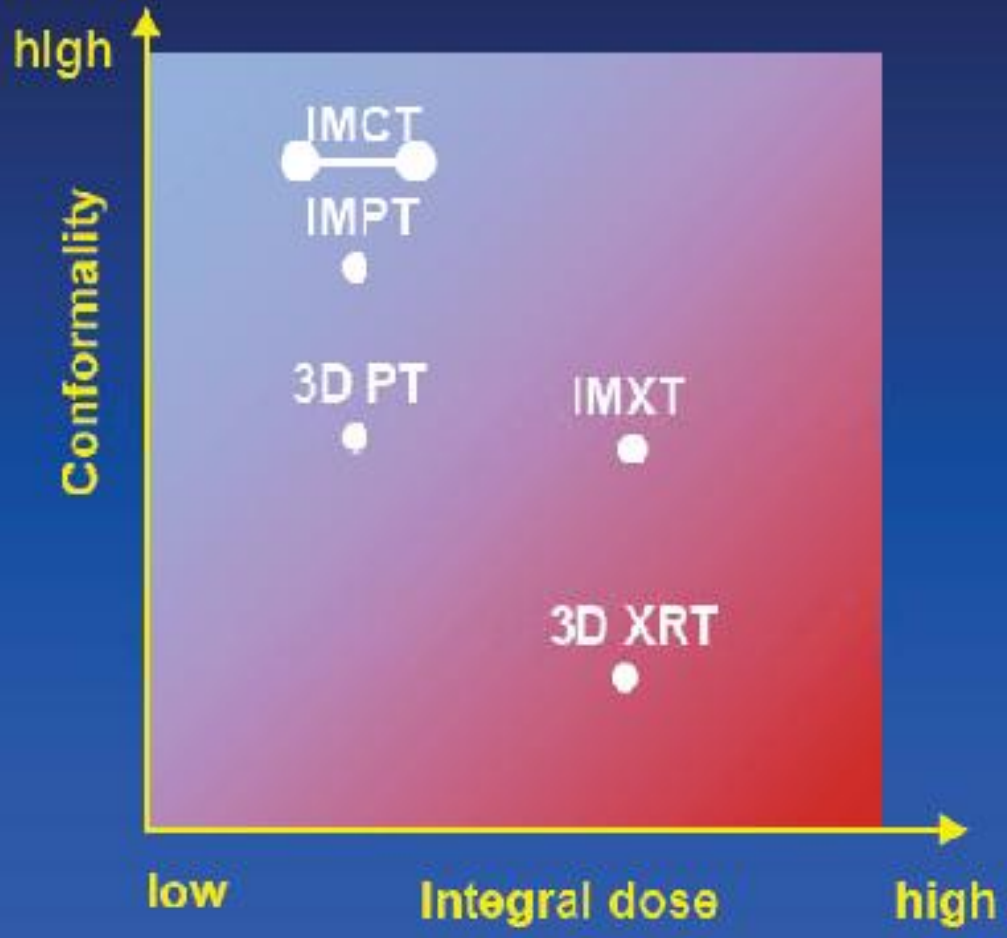
Relative biological effectiveness (RBE) and oxygen enhancement ratio (OER) of various radiation types



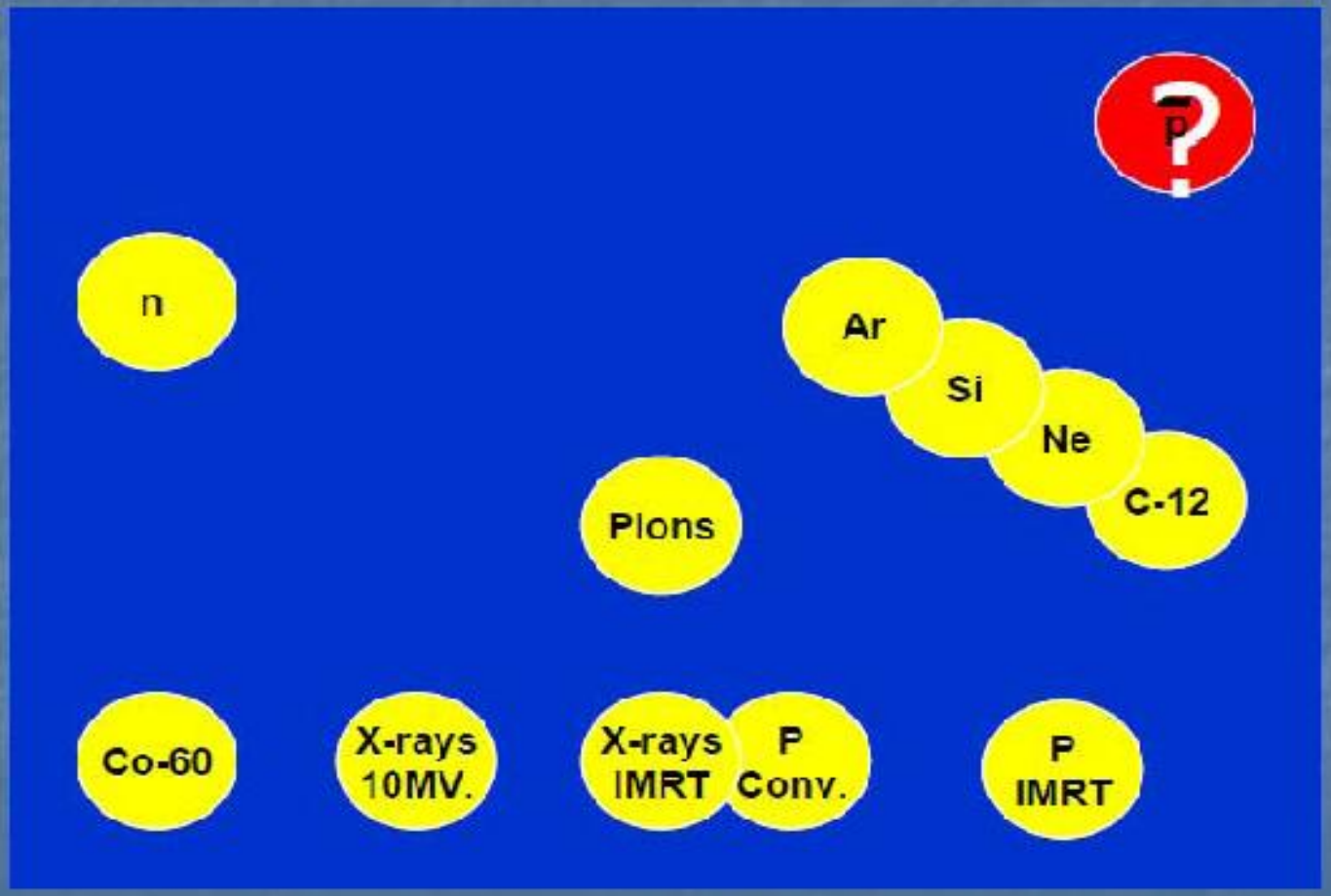
RBE represents the biological effectiveness of radiation in the living body.
The larger the RBE, the greater the therapeutic effect on the cancer lesion.

OER represents the degree of sensitivity of hypoxic cancer cells to radiation.
The smaller the OER, the more effective the therapy for intractablecancer cells with low oxygen concentration.

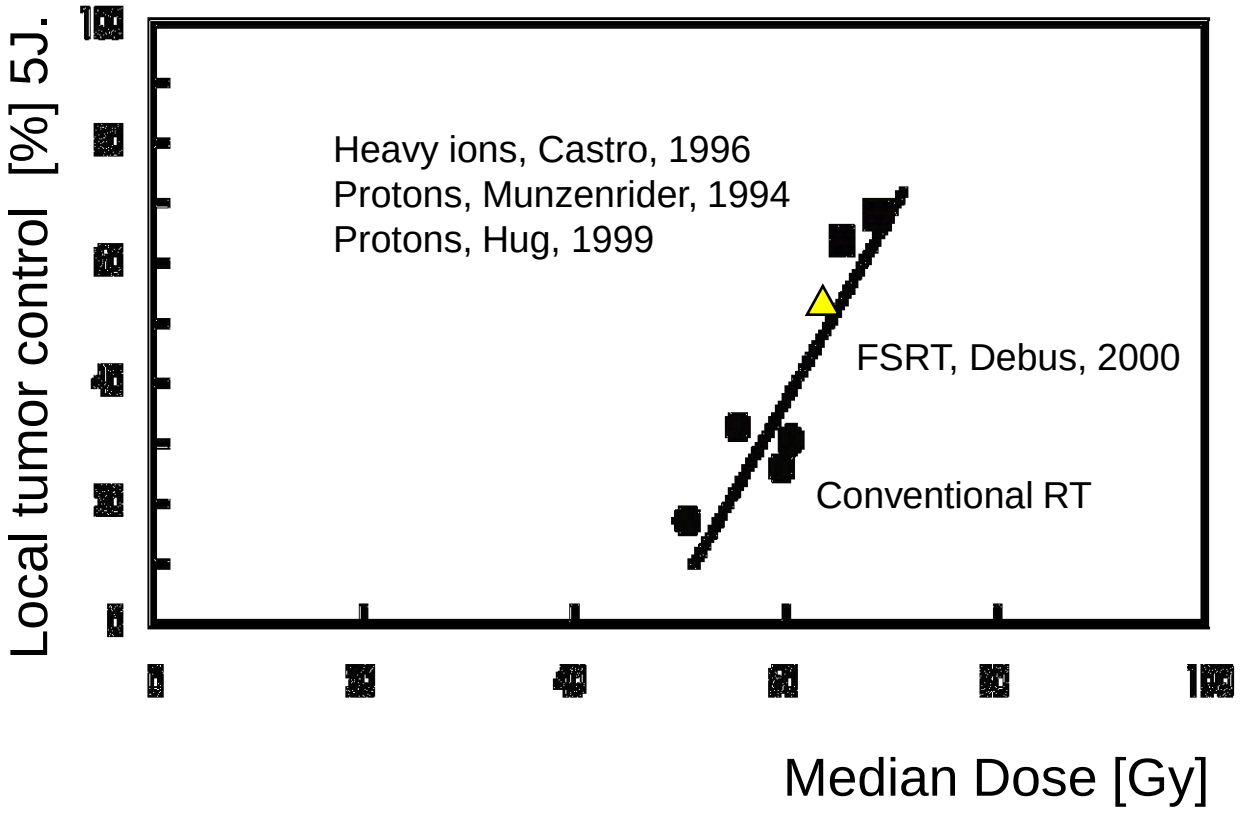
Particles vs. Photons

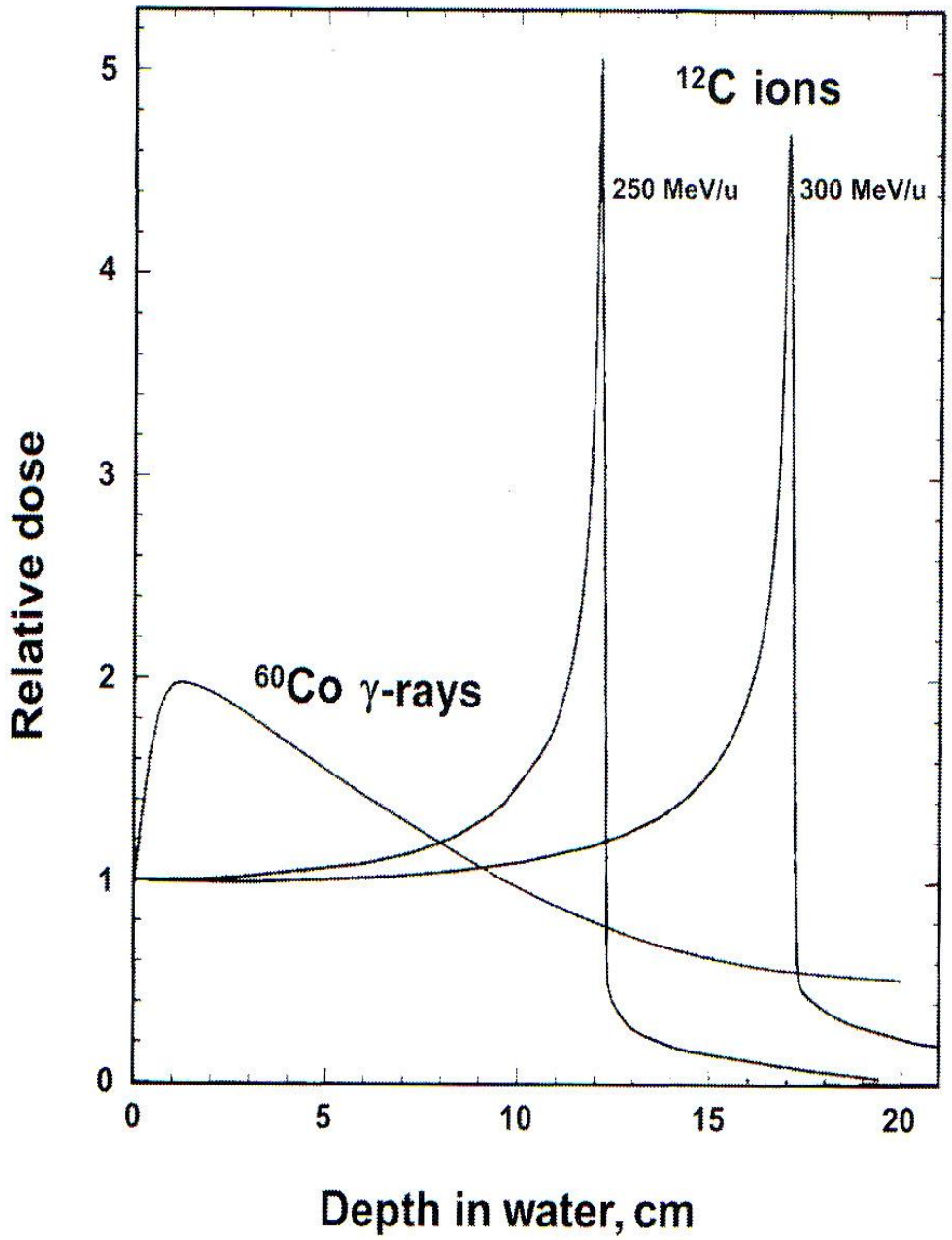


All the Particles used in Radiation Oncology



Dose response relationship for chordomas





● Comparison of the depth–dose profiles of carbon ions of two different energies with that of ^{60}Co γ-rays. (Adapted from Kraft G: Tumor therapy with heavy charged particles. *Progress in Particle and Nuclear Physics* 45:S473–S544, 2000.)

History of Hadron Therapy

J.S. Stone and John Lawrence (both MDs) used neutrons for therapy in patients, starting in late 1938, with a major program (250 patients) starting in 1940. Quoting Stone: "Distressing late effects" and "Neutron therapy…should not be continued"

No further neutron work for 25 years…

Figure 24.4. The first patient treated with neutrons at the Lawrence Berkeley Laboratory of the University of California. On the left is Dr. Robert Stone, the radiotherapist, and in the center is Dr. John Lawrence, the physician brother of the inventor of the cyclotron, E. O. Lawrence. (Courtesy of the University of California.)

A Time Line of Hadron Therapy

1938 Neutron therapy by John Lawrence and R.S. Stone (Berkeley)
1946 Robert Wilson suggests protons
1948 Extensive studies at Berkeley confirm Wilson
1954 Protons used on patients in Berkeley
1957 Uppsala duplicates Berkeley results on patients
1961 First treatment at Harvard (By the time the facility closed in 2002, 9,111patients had been treated.)
1968 Dubna proton facility opens
1969 Moscow proton facility opens
1972 Neutron therapy initiated at MD Anderson (Soon 6 places in USA.)
1974 Patient treated with pi meson beam at Los Alamos (Terminated in 1981) (Starts and stops also at PSI and TRIUMF)

A Time Line of Hadron Therapy

1975 St. Petersburg proton therapy facility opens
1975 Harvard team pioneers eye cancer treatment with protons
1976 Neutron therapy initiated at Fermilab. (By the time the facility closed in 2003, 3,100 patients had been treated)
1977 Bevalac starts ion treatment of patients. (By the time the facility closed in 1992, 223 patients had been treated.)
1979 Chiba opens with proton therapy
1988 Proton therapy approved by FDA
1989 Proton therapy at Clatterbridge
1990 Medicare covers proton therapy and Particle Therapy Cooperative Group (PTCOG) is formed: www.ptcog.web.psi.ch
1990 First hospital-based facility at Loma Linda (California)
1991 Protons at Nice and Orsay - France

A Time Line of Hadron Therapy

1992 Berkeley cyclotron closed after treating more than 2,500 patients

1993 Protons at Cape Town, SA

1993 Indiana treats first patient with protons

1994 Ion (carbon) therapy started at HIMAC (By 2017 more than 3,0000 patients treated.)

1996 PSI proton facility

1998 Berlin proton facility

2001 Massachusetts General opens proton therapy center

2006 MD Anderson opens

2007 Jacksonville, Florida opens

2008 Neutron therapy re-stated at Fermilab

2009 Lanzhou, China starts Proton Therapy

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….

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2018 – Proton Therapy in India

History of Proton Beam Therapy

- 1946 R. Wilson suggests use of protons
- 1954 First treatment of pituitary tumors
- 1958 First use of protons as a neurosurgical tool
- 1967 First large-field proton treatments in Sweden
- 1974 Large-field fractionated proton treatments program begins at HCL, Cambridge, MA
- 1990 First hospital-based proton treatment center opens at Loma Linda University Medical Center

Gantries are important even for hadrons

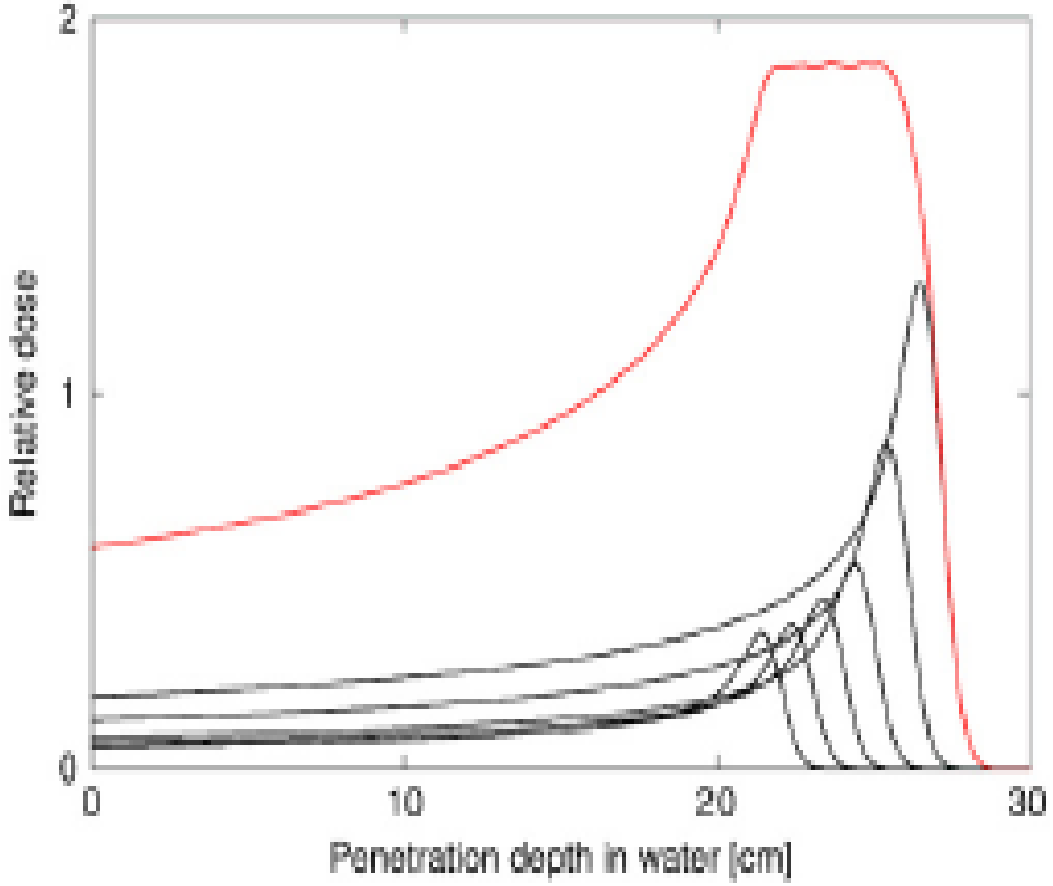
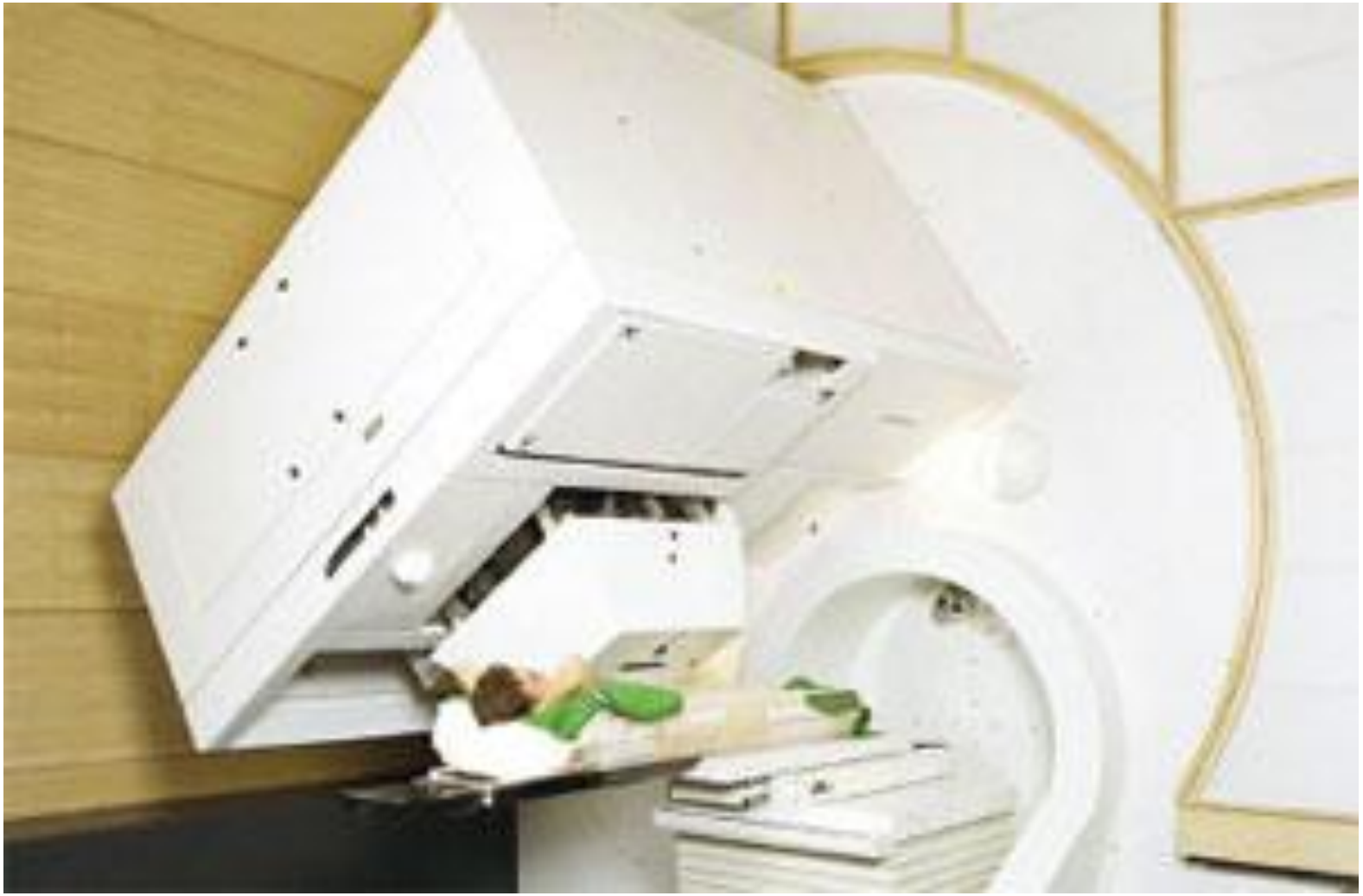


Figure 2. Range and intensity modulation of Bragg peaks to achieve a spread-out Bragg peak (SOBP). SOBPs can be produced by use of a physical device (ridge filter or modulation wheel) or by energy selection from the accelerator in conjunction with variable weighting of each individual Bragg peak. SOBPs can be produced for variable widths.

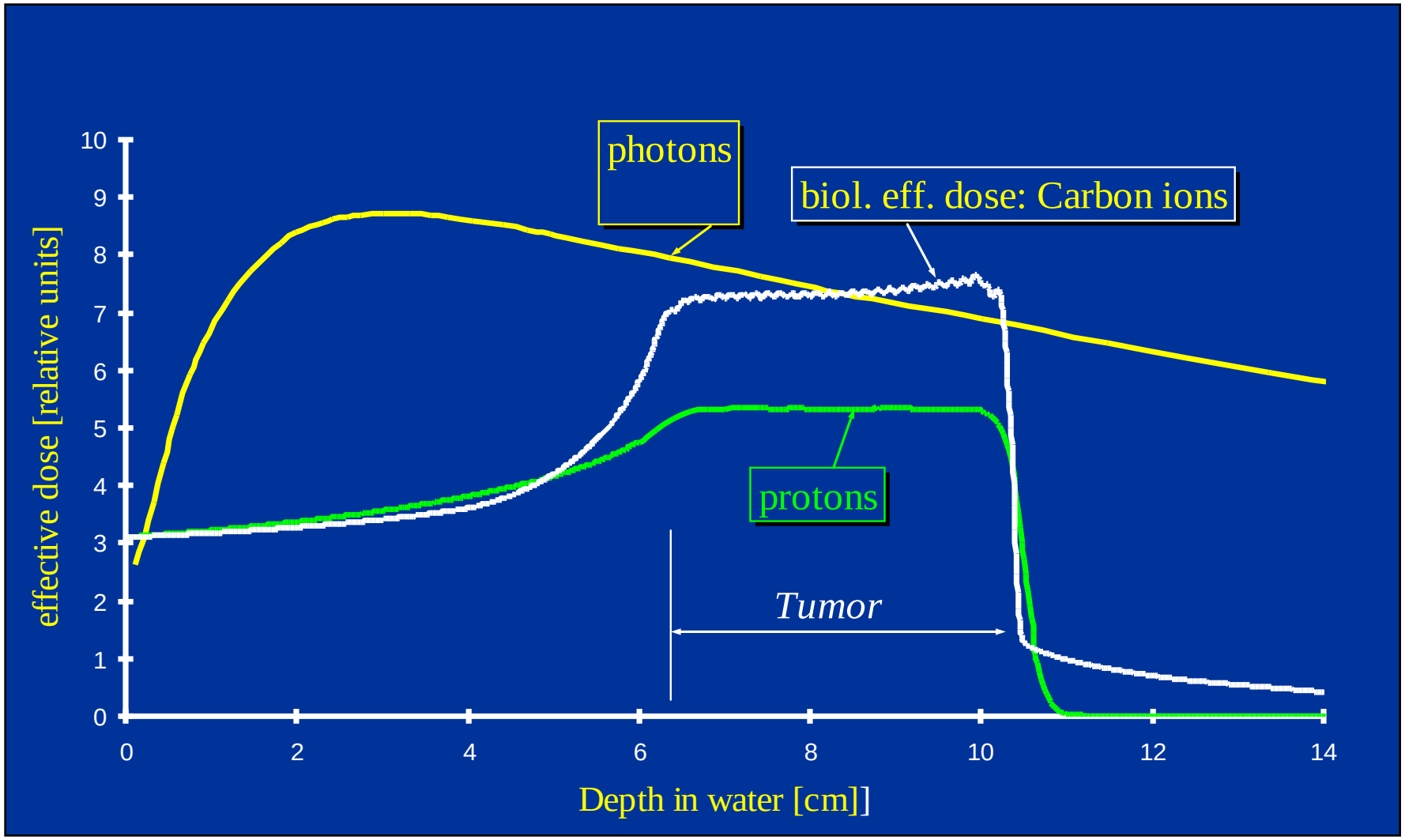


The PSI PROSCAN Gantry (100 tons)

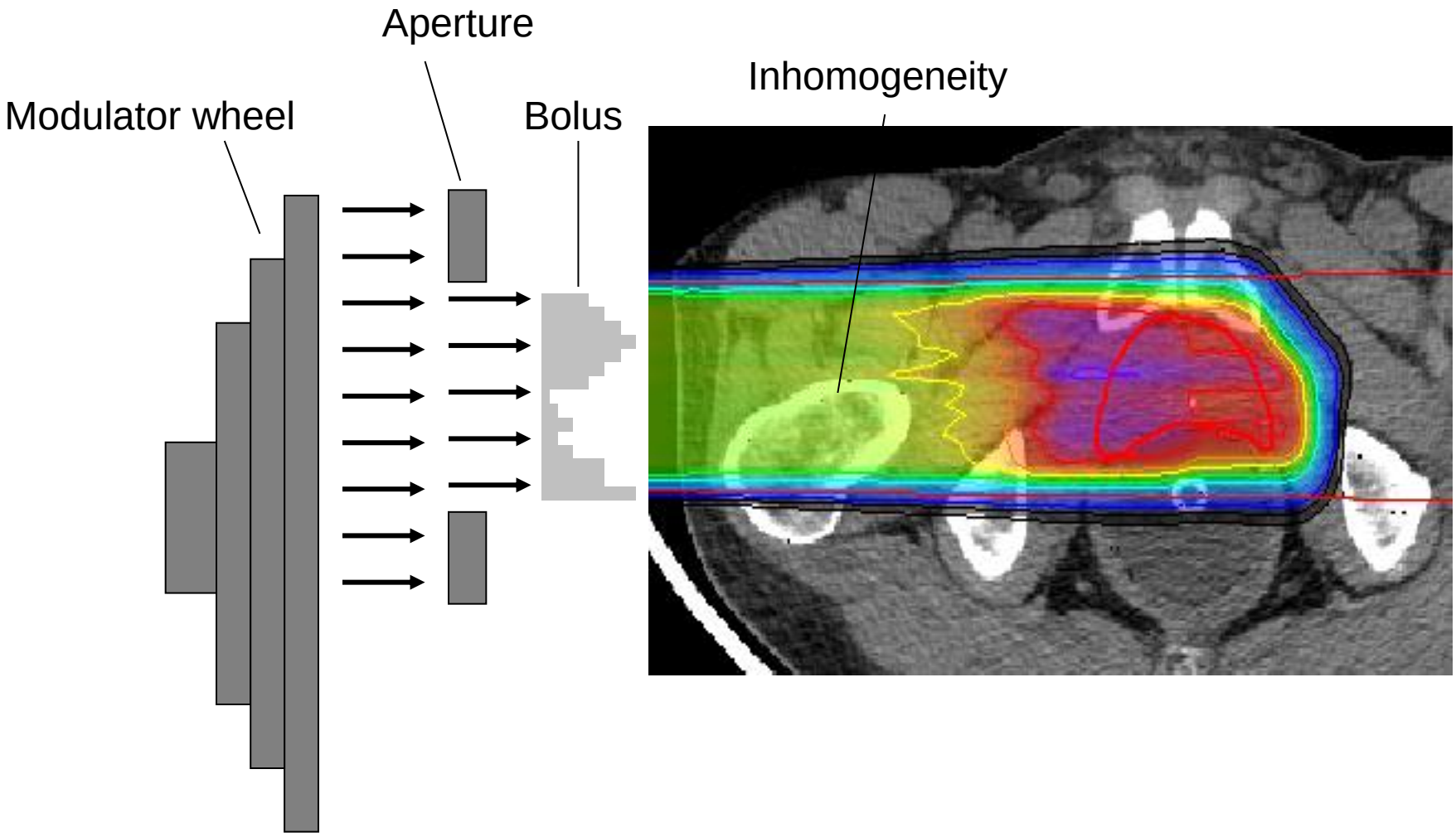
Proton Beam Shaping Devices

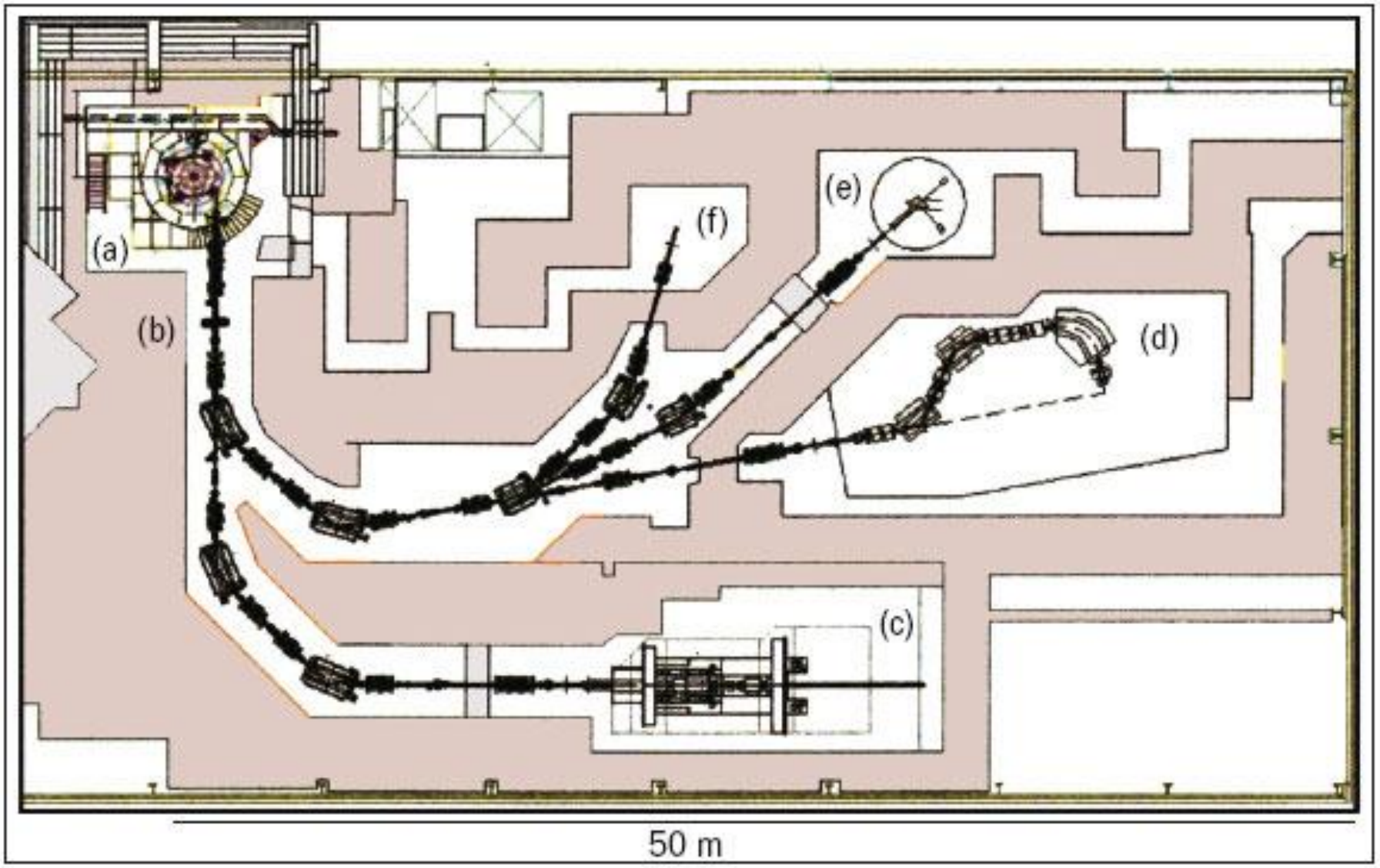
Wax bolus **Cerrobend aperture** **Modulating wheels**

Particle therapy



Proton Beam Design

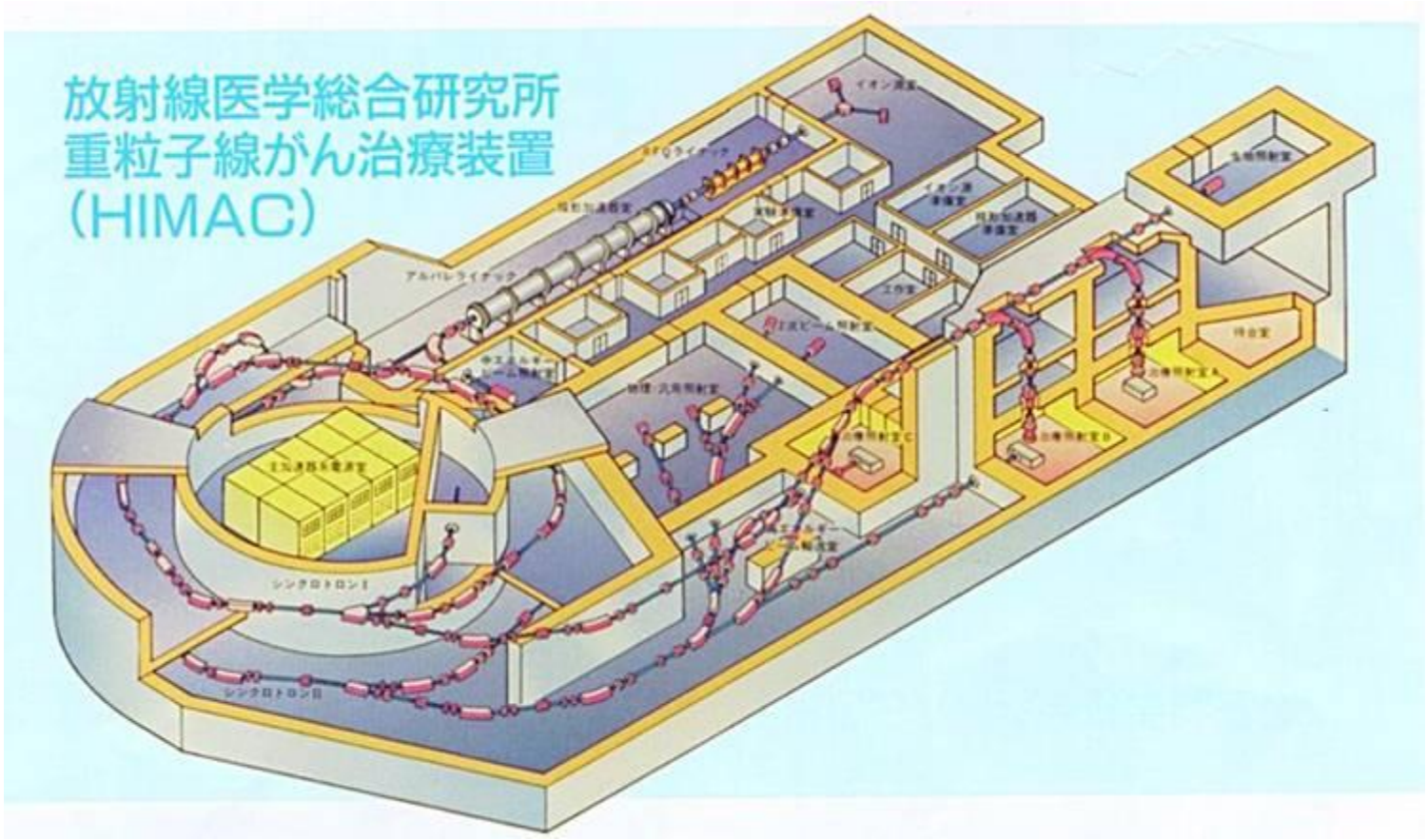




The PSI PROSCAN Facility (a) sc accelerator, (c and d) gantries, (e) Eye treatment room

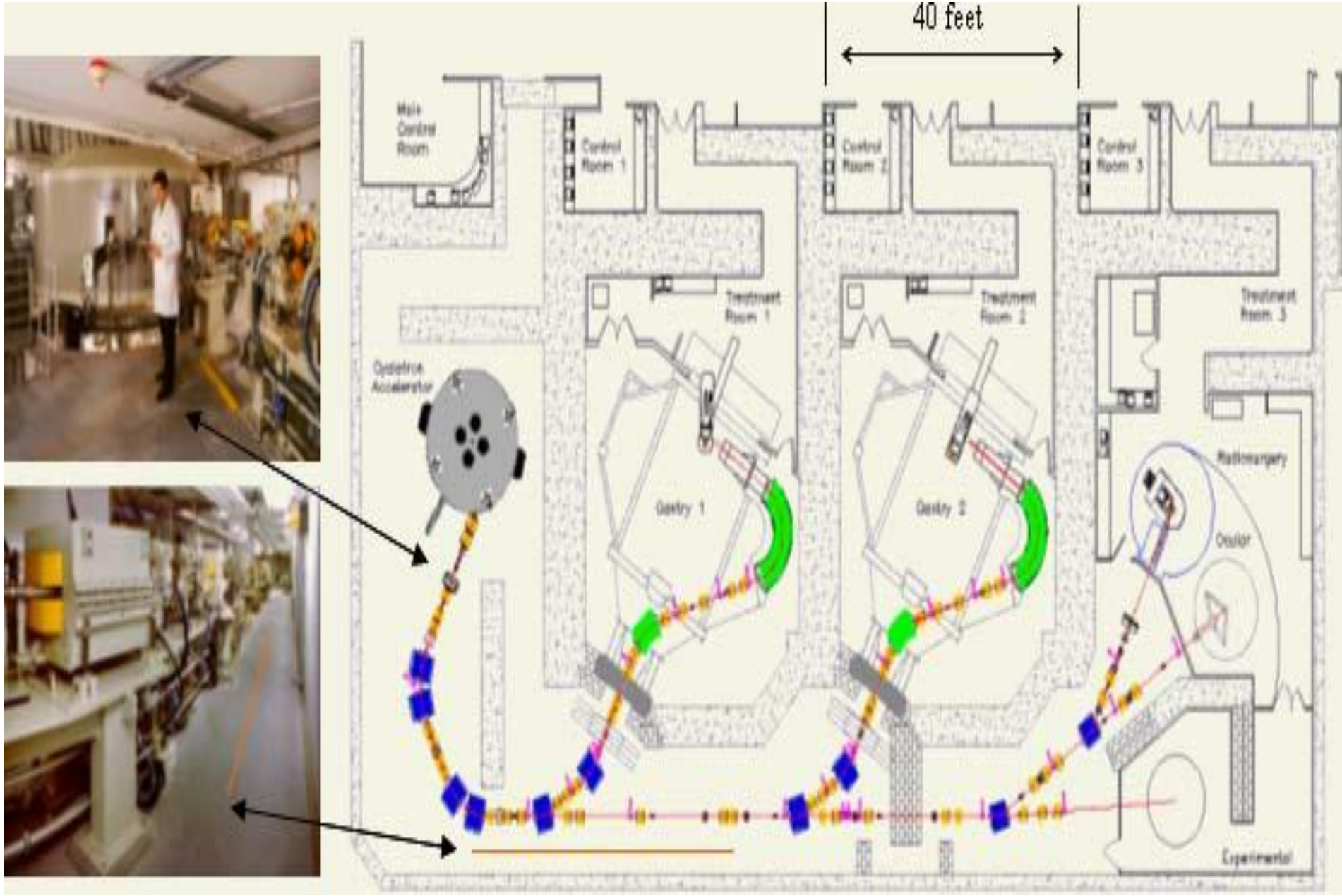
The PSI sc accelerator. Diameter 3.25 m, 250 MeV protons Built by ACCEL (based on design by Hank Blosser) ACCEL bought out by Varian on Jan 4, 2007.

Himac (Japan)

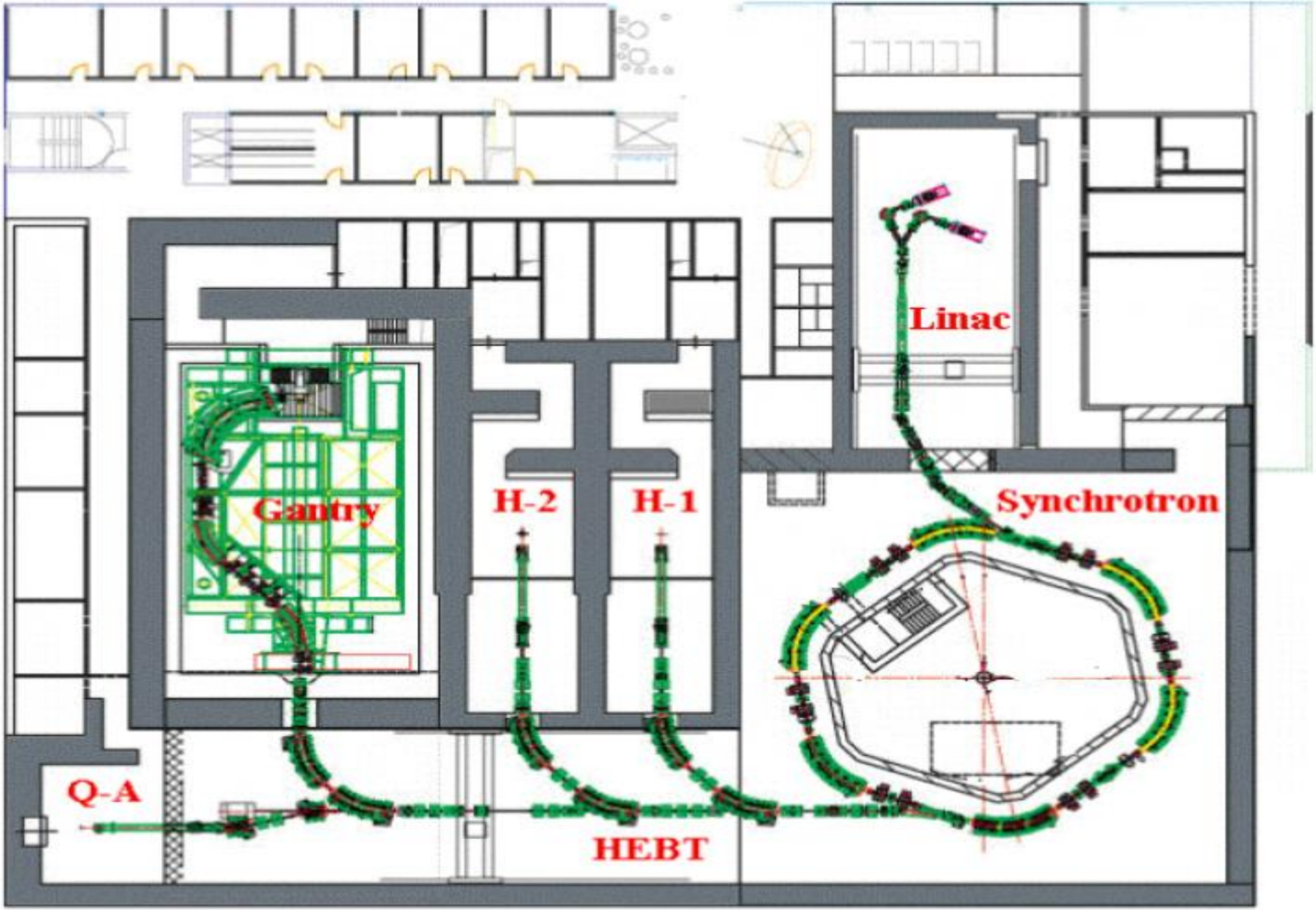


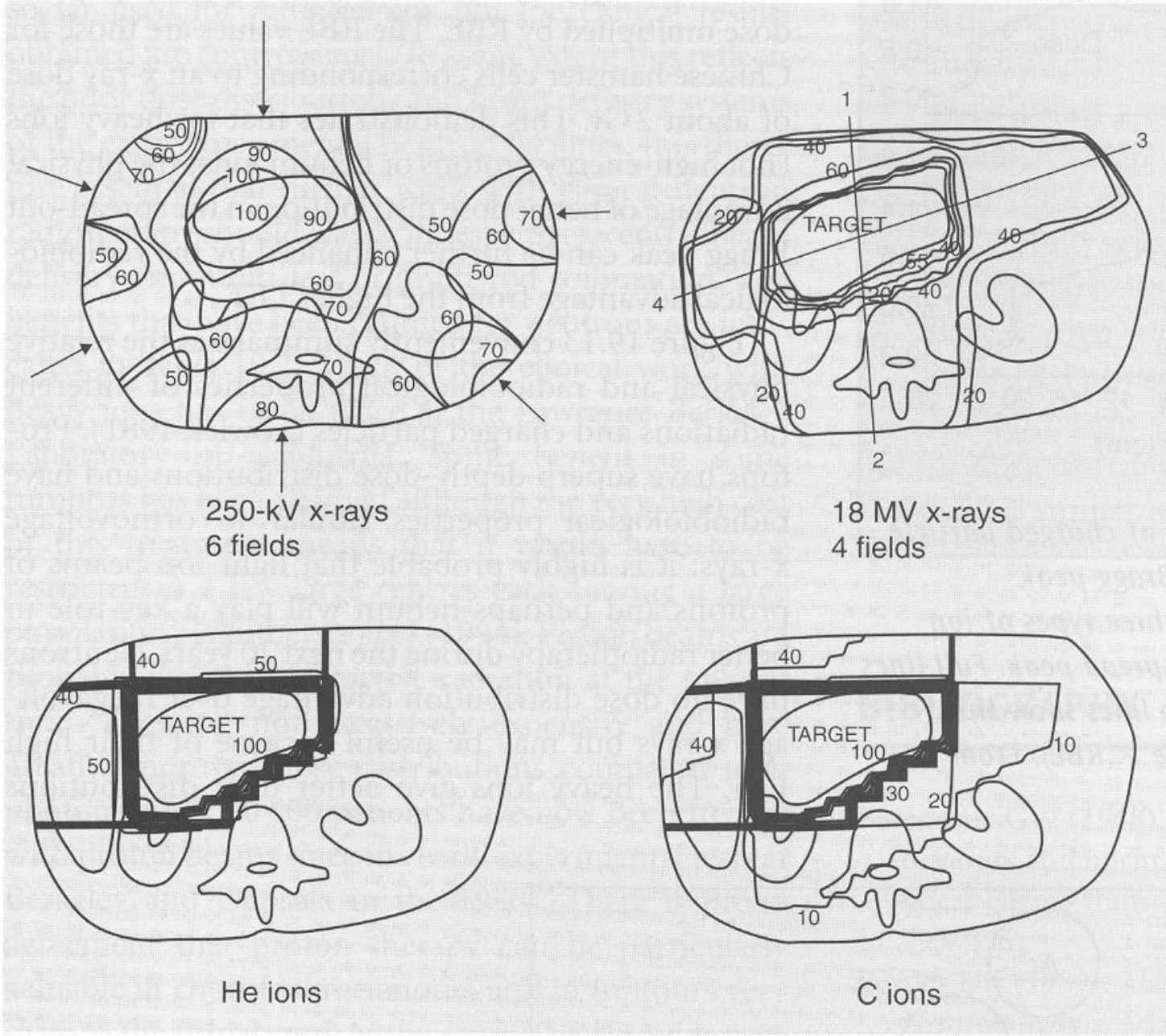
The Japanese two proton ion synchrotrons at HIMAC. The pulse of ions is synchronized with the respiration of the patient so as to minimize the effect of organ movement. The facility is being re-conditioned. A new one could be 1/3 as large.

Massachusetts General Hospital



The Heidelberg Facility

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20
18 MV x-rays
4 fields
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He ions
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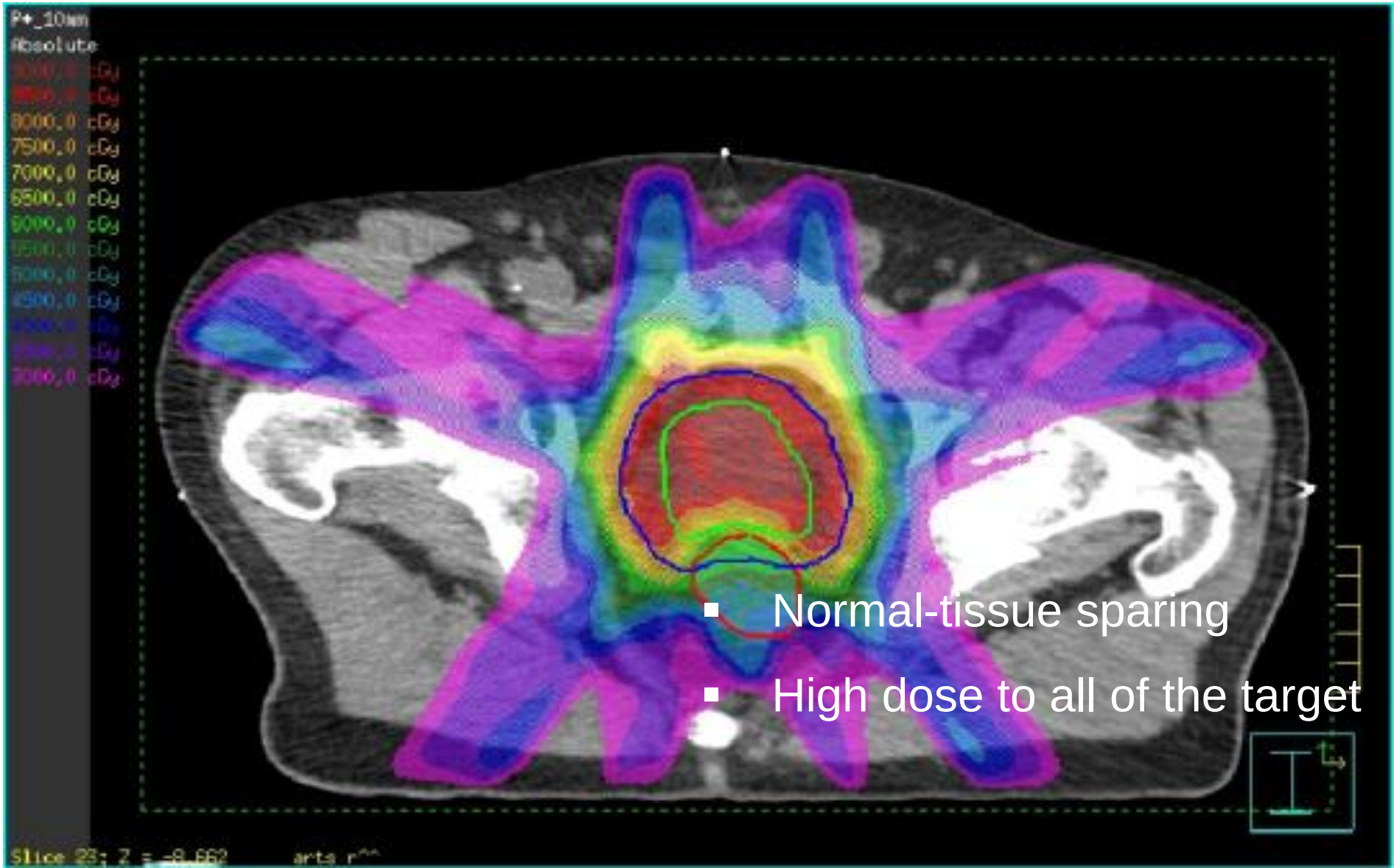
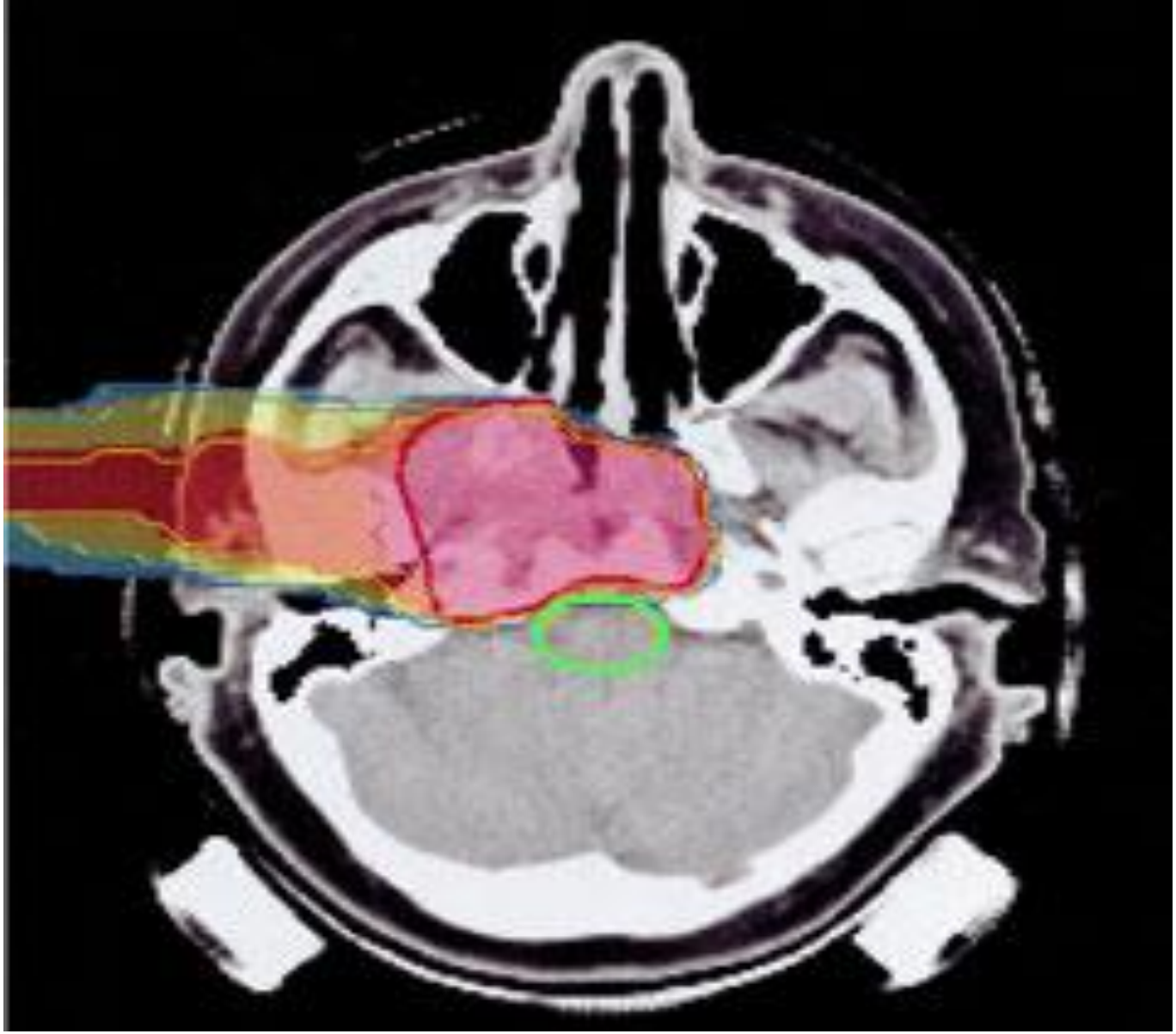
10
C ions

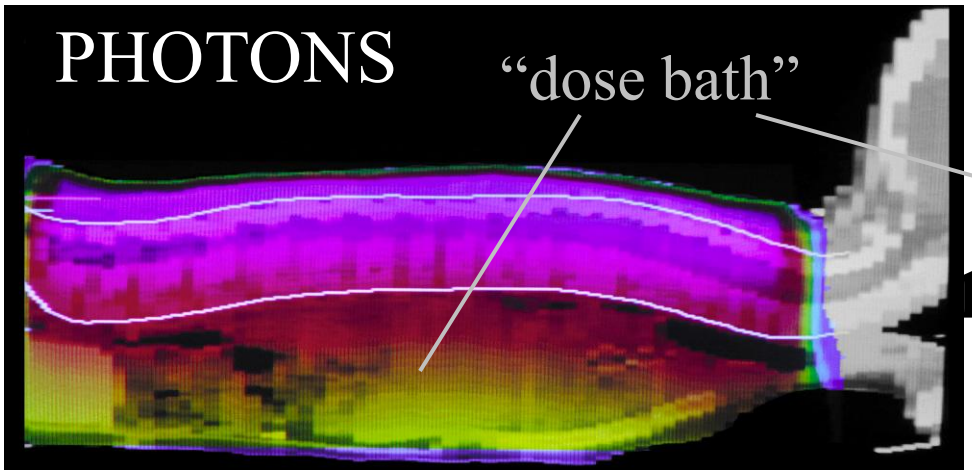
A (3D) dose distribution with photon

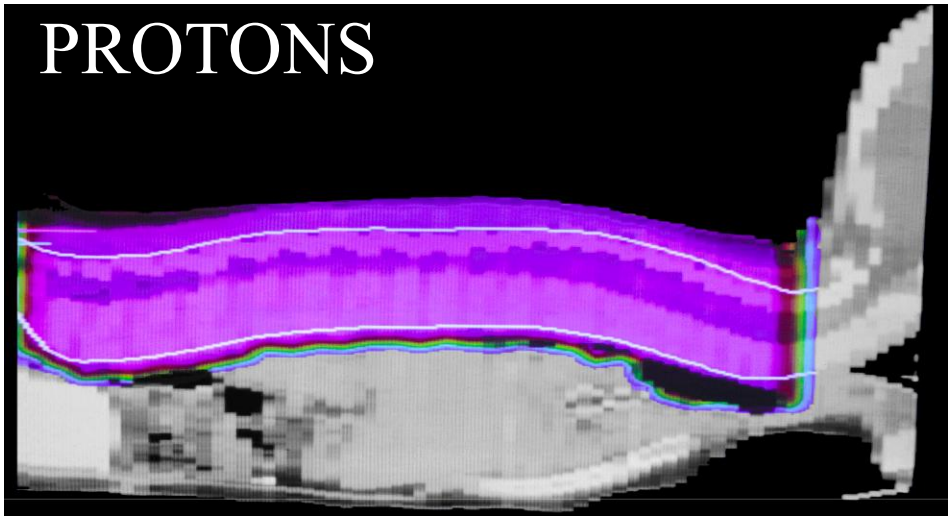


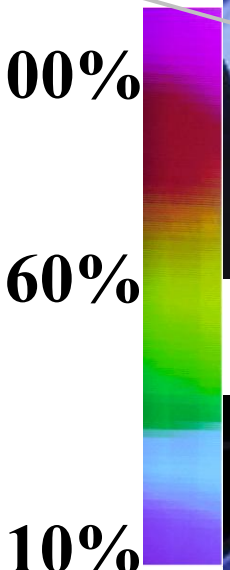


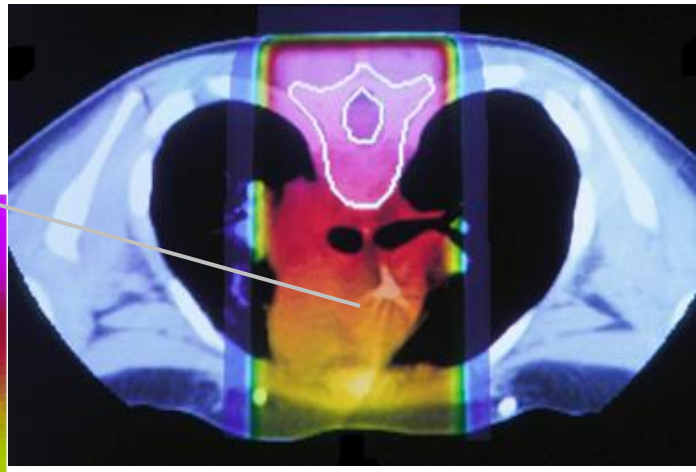
A dose plan for a carbon ion treatment of a brain tumor. The high precision allows complete sparing of the brain stem marked by the green line.

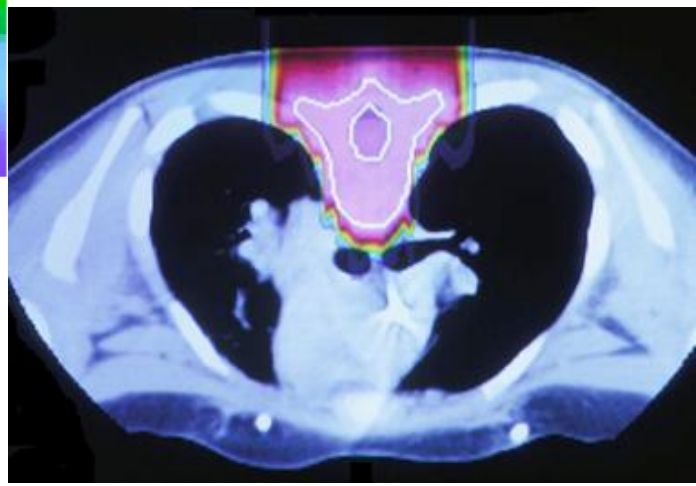
Medulloblastoma







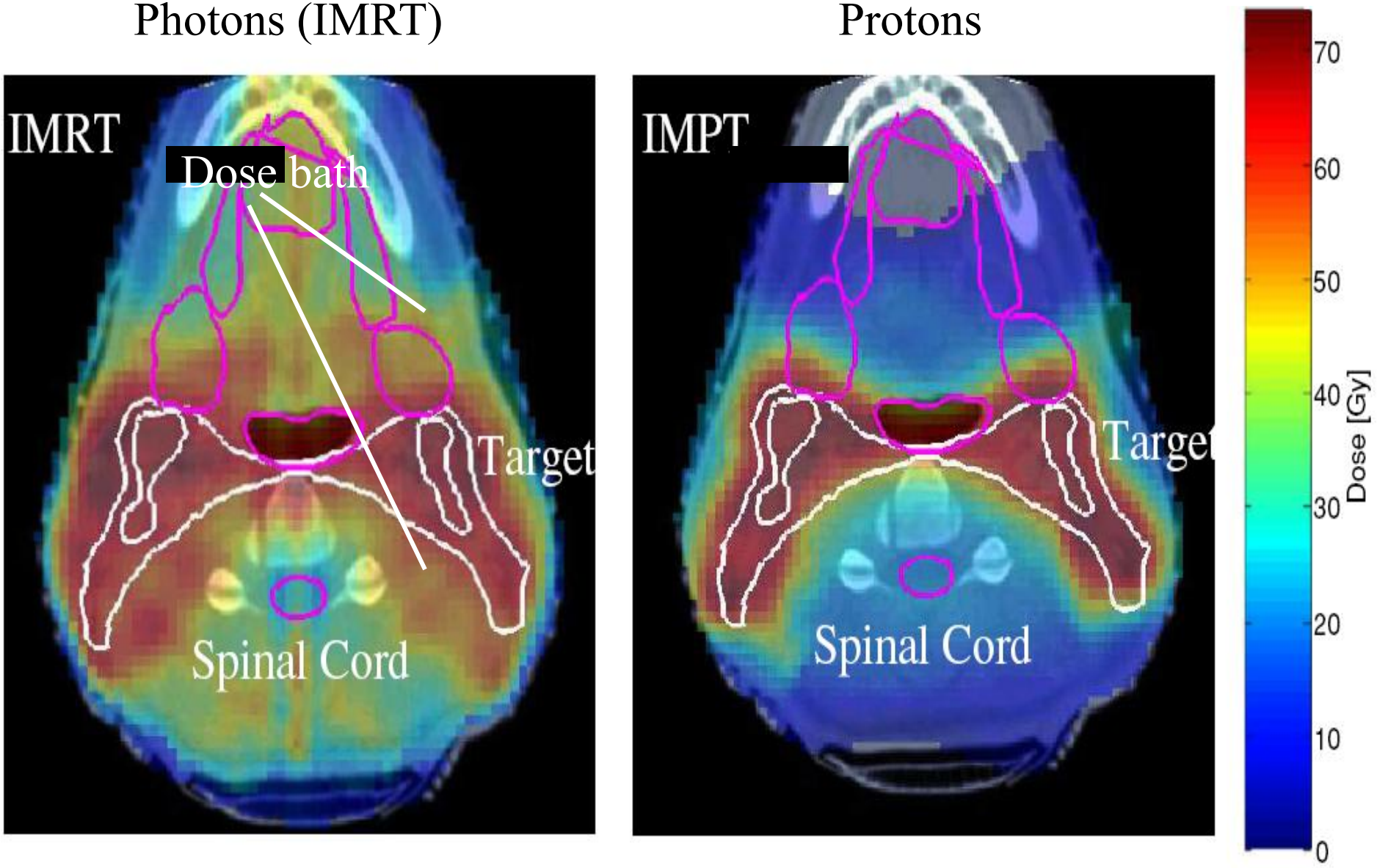




The proton advantage Nasopharynx

Photons (IMRT)

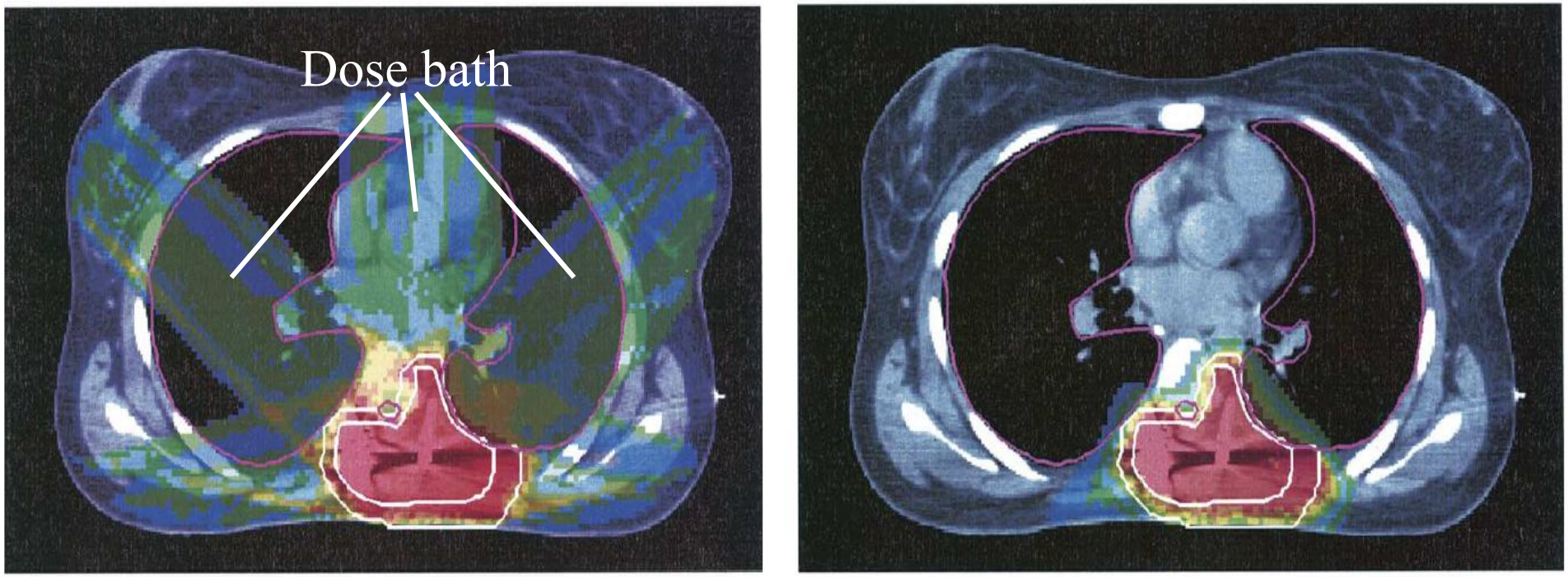
Protons

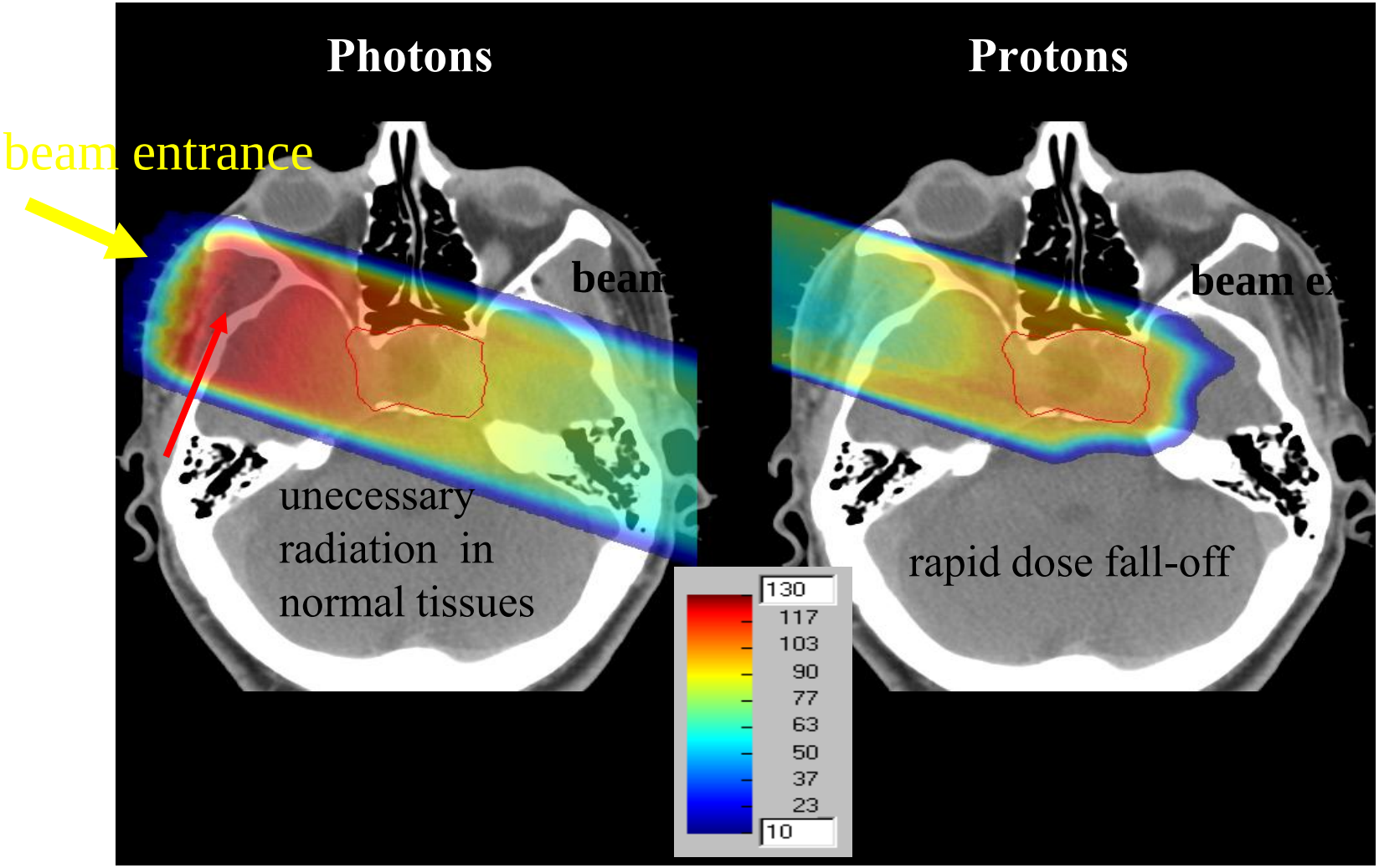


The proton advantage: Paraspinal

Photons

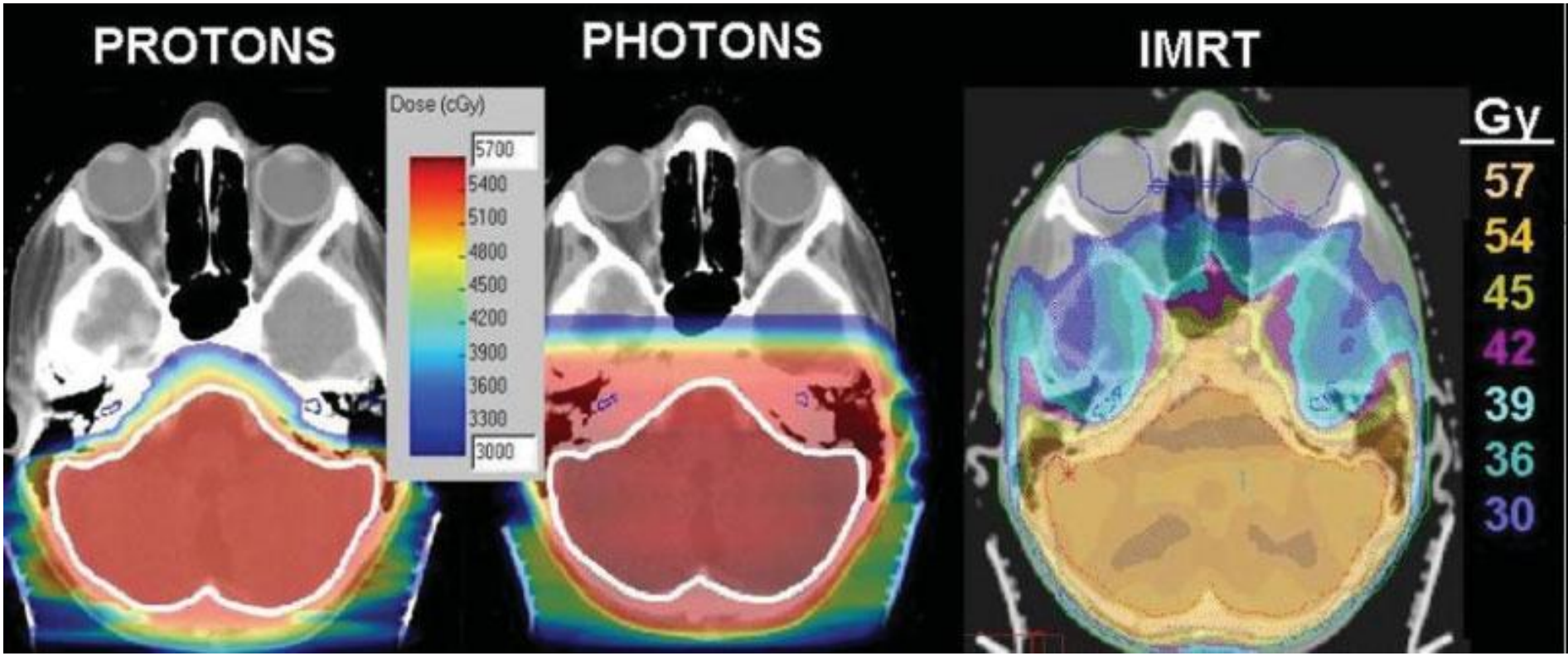
Protons





- Tissue beyond the target receives very little or no radiation

Image courtesy of Dr Annie Chan, Dept of Radiation Oncology, MGH, Boston, MA



- Improved therapeutic index
  - Irradiate smaller volume of normal tissues
- Ability to intensify dose
  - Higher doses to target zone
- Improve dose conformation

Image from Greco C. Current Status of Radiotherapy With Proton and Light Ion Beams. American CANCER society April 1, 2007 / Volume 109 / Number 7

IMRT

IMPT

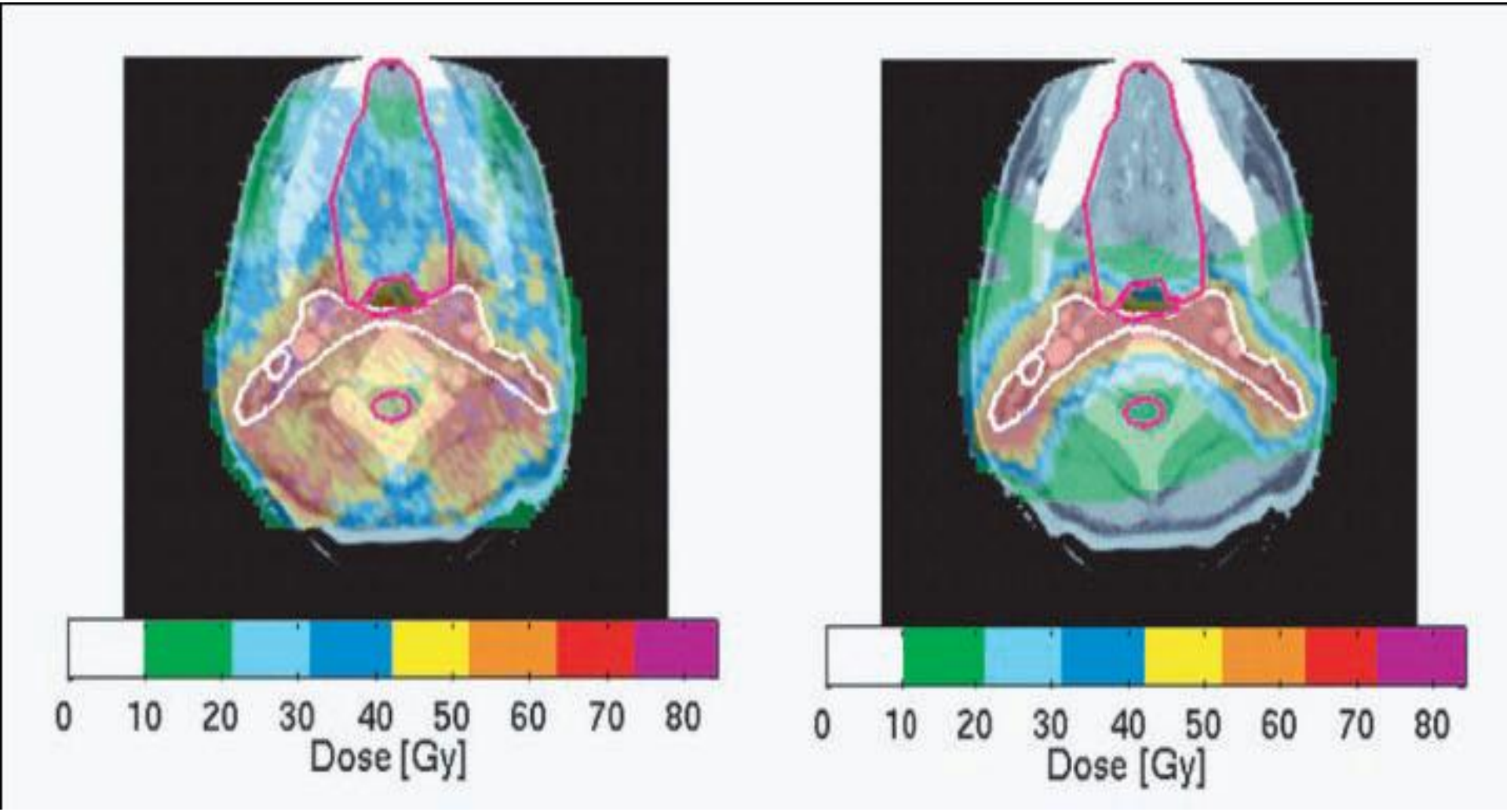
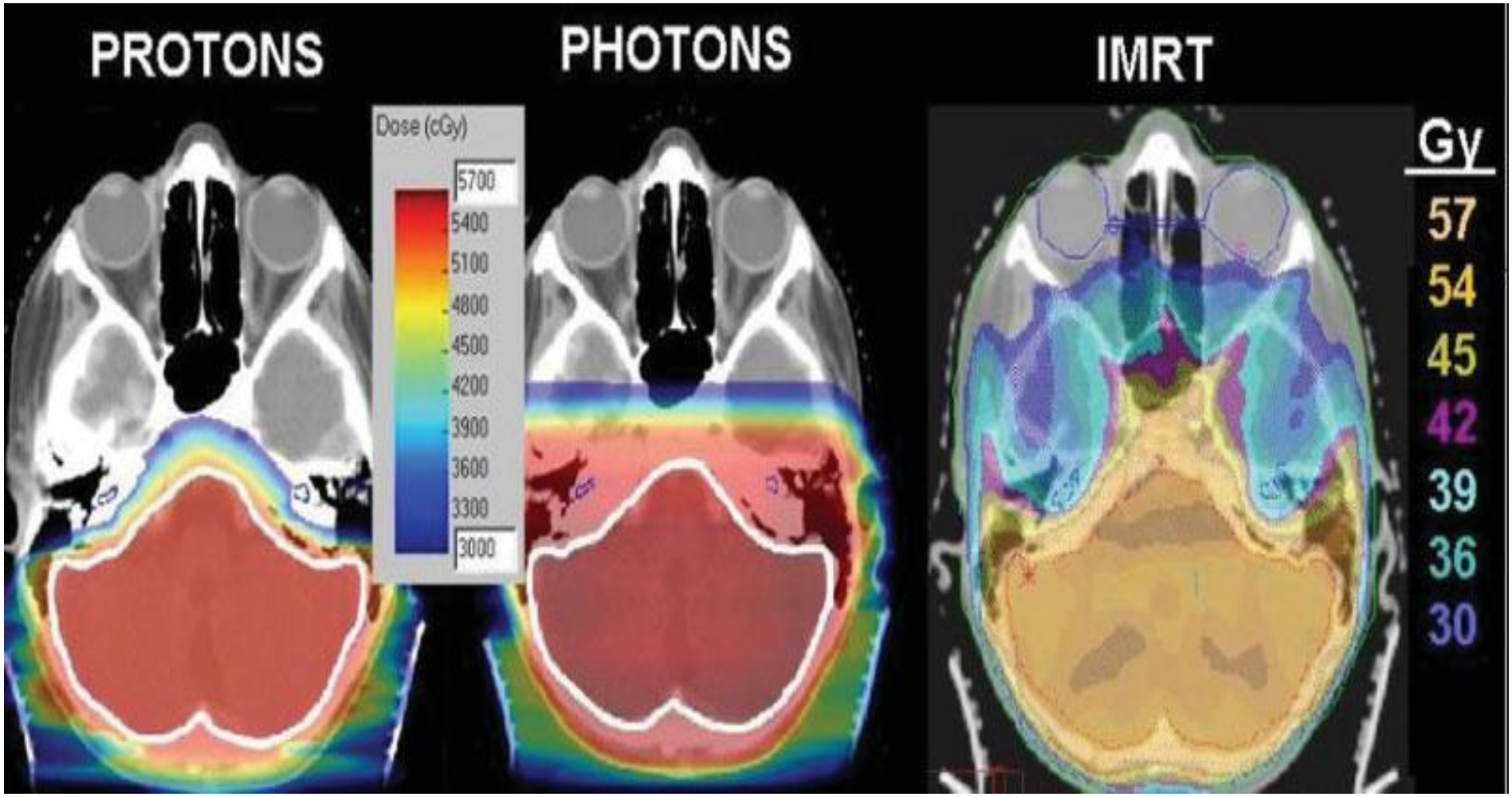


Image from CHAN A.. Proton Radiation Therapy for Head and Neck Cancer. Journal of Surgical Oncology 2008;97:697–700



- The dose to 90% of the cochlea was reduced from 101% with standard photons, to 33% with IMRT, and to 2% with protons

Image from Greco C. Current Status of Radiotherapy With Proton and Light Ion Beams. American CANCER society April 1, 2007 / Volume 109 / Number 7

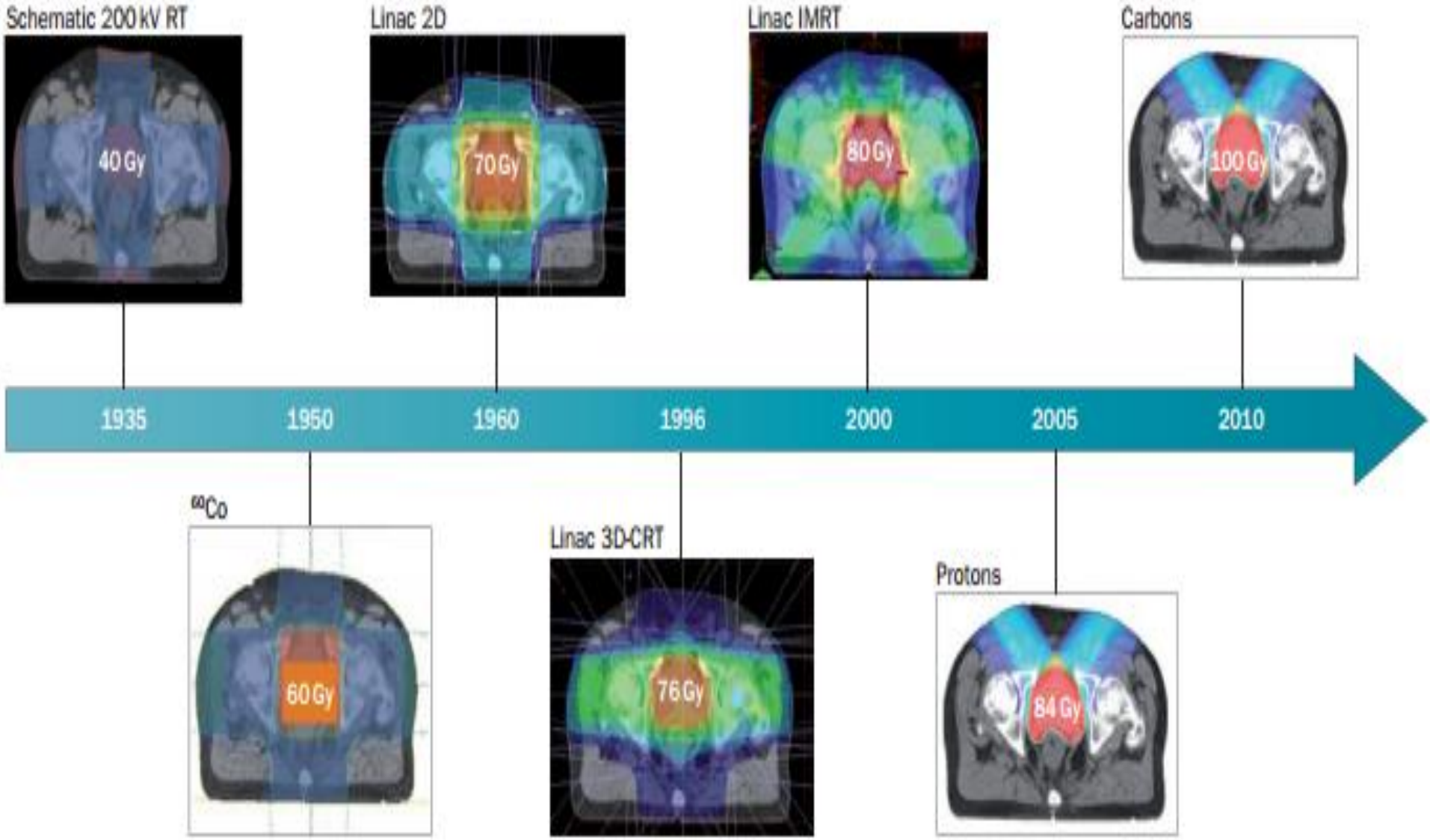
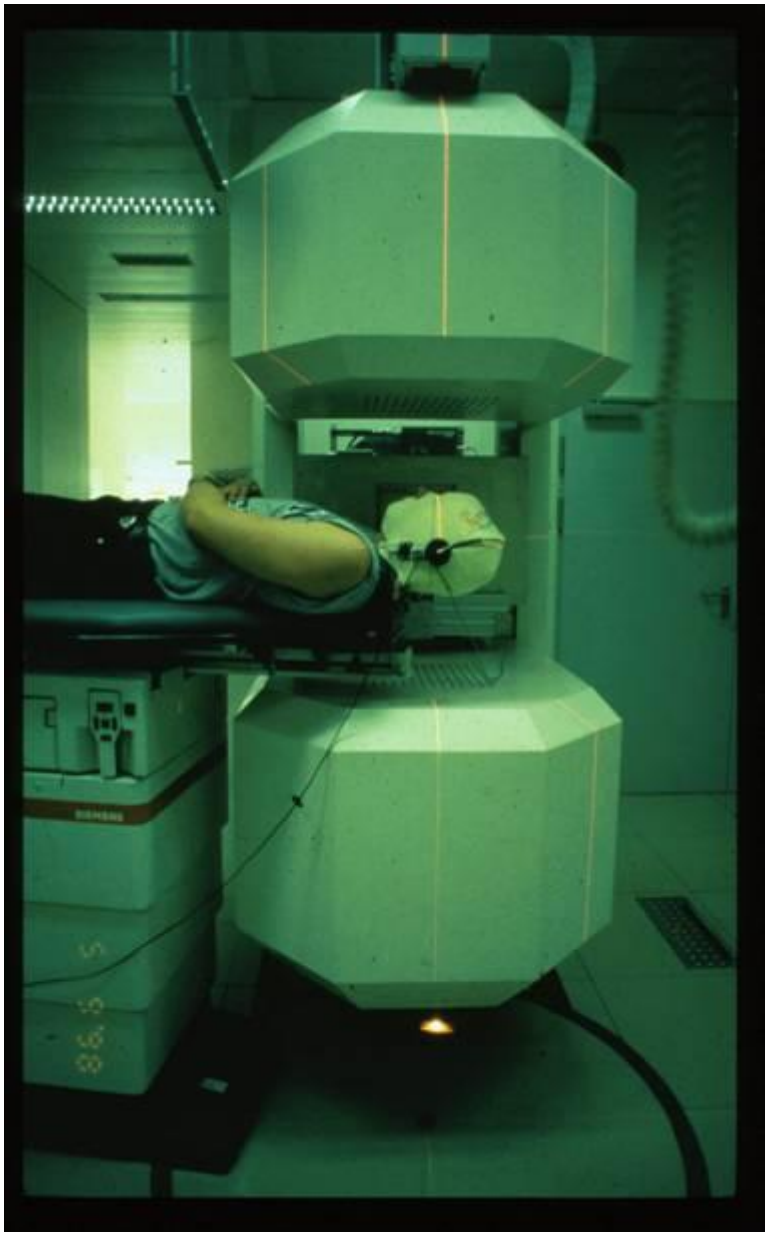
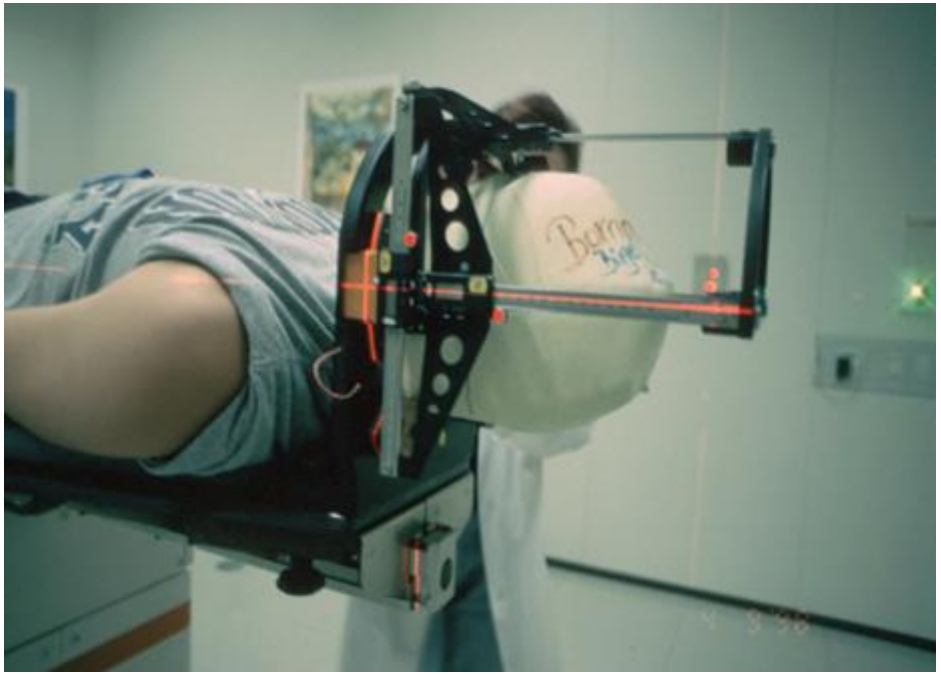


Figure 1 | Prostate cancer radiotherapy 1935–2010. Prostate cancer irradiation is a good example of the improvement of radiotherapy technology over the past decades. By increasing the beam energy and the precision of the targeting, it was possible to escalate the dose to the prostate without exceeding the tolerance dose of healthy tissues; allowing the move from palliative irradiation to curative treatment. Abbreviations: 3D-CRT, 3D conformal radiotherapy; IMRT, intensity modulated radiotherapy; RT, radiotherapy.



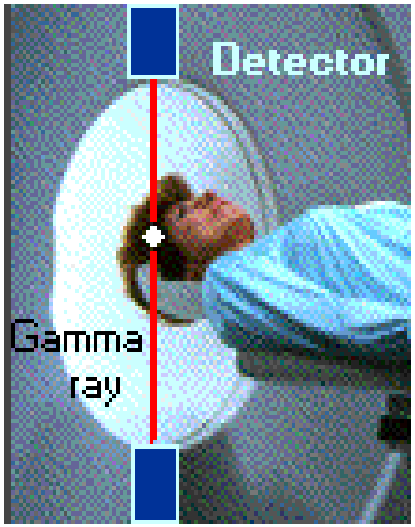
Online verification using PET



Stereotactic target point localization

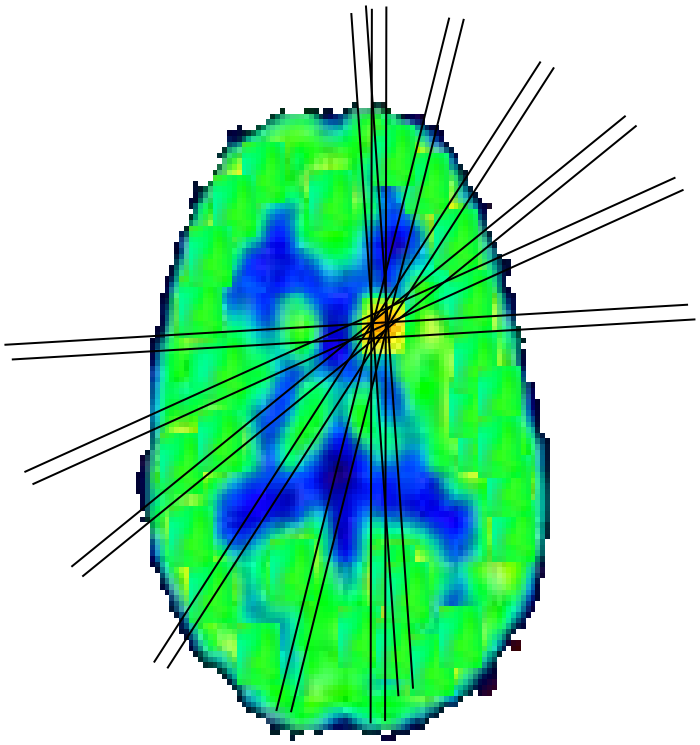
Positron Emission Tomography (PET) of Proton Beams

Reaction	Half-life	Threshold Energy (MeV)
$^{16}O(p,pn)^{15}O$	2.0 min	16.6
$^{16}O(p,2p2n)^{13}N$	10.0 min	5.5
$^{16}O(p,3p3n)^{13}C$	20.3 min	14.3
$^{14}N(p,pn)^{13}N$	10.0 min	11.3
$^{14}N(p,2p2n)^{11}C$	20.3 min	3.1
$^{12}C(p,pn)^{17}N$	20.3 min	20.3



PET Localization for Functional Proton Radiosurgery

- Treatment of Parkinson's disease
- Multiple narrow p beams of high energy (250 MeV)
- Focused shoot-through technique
- Very high local dose (> 100 Gy)
- PET verification possible after test dose



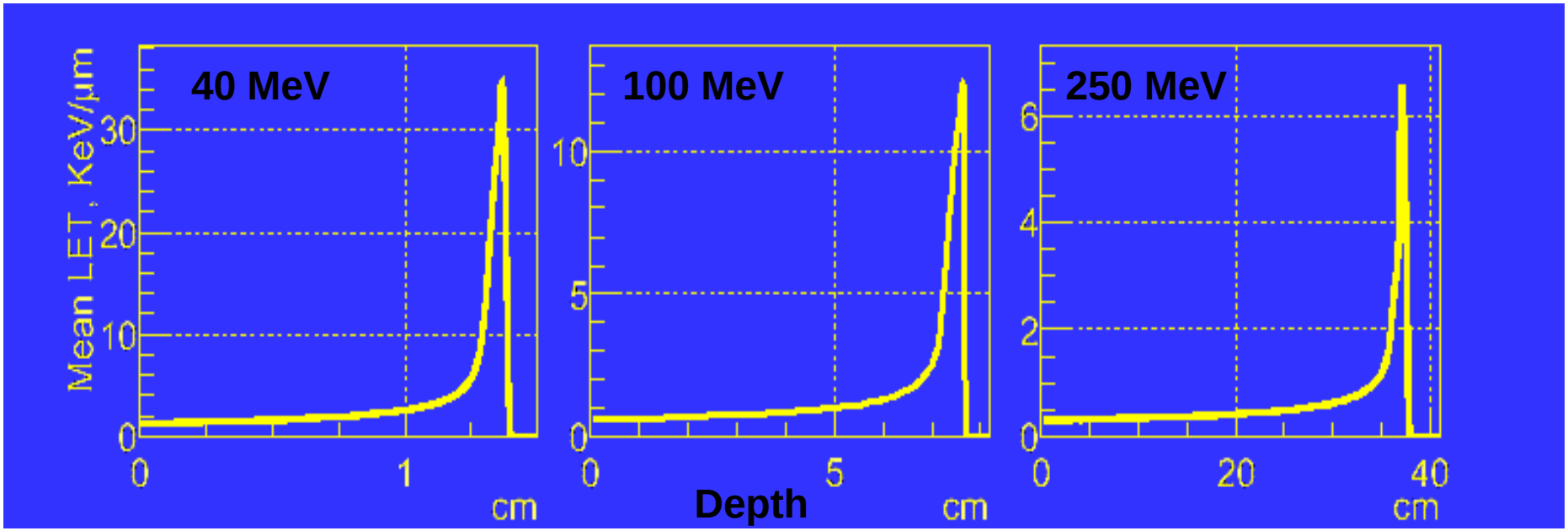
Uncertainties in Proton Therapy

- **Patient related:**
  - Patient setup
  - Patient movements
  - Organ motion
  - Body contour
  - Target definition
- **Biology related:**
  - Relative biological effectiveness (RBE)
- **Physics related:**
  - CT number conversion
  - Dose calculation
- **Machine related:**
  - Device tolerances
  - Beam energy

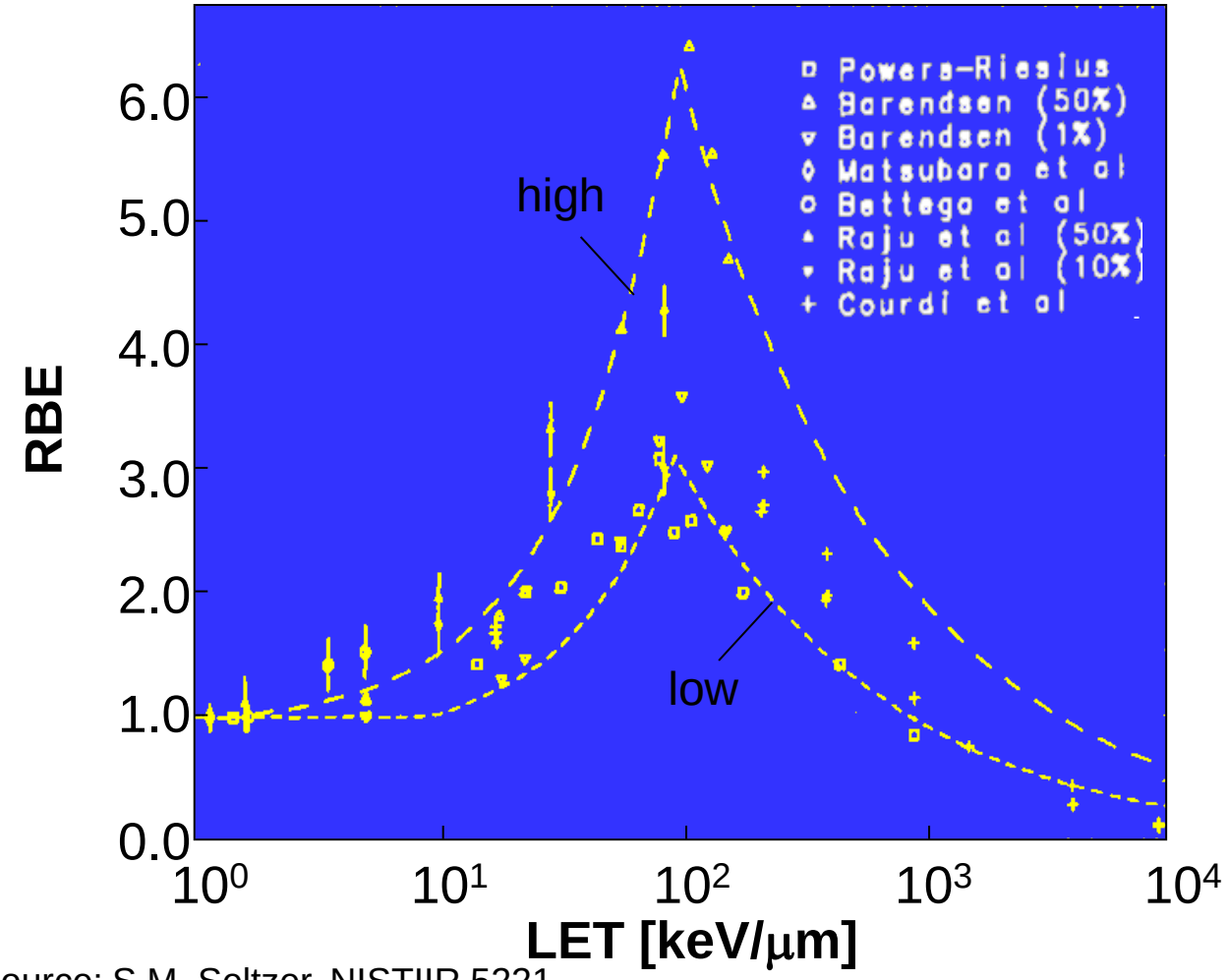
Relative Biological Effectiveness (RBE)

- Clinical RBE: 1 Gy proton dose $\equiv$ 1.1 Gy Cobalt γ dose (RBE = 1.1)
- RBE vs. depth is not constant
- RBE also depends on
  - dose
  - biological system (cell type)
  - clinical endpoint (early response, late effect)

Linear Energy Transfer (LET) vs. Depth



RBE vs. LET



Source: S.M. Seltzer, NISTIIR 5221

Treatment Planning

- Acquisition of imaging data (CT, MRI)
- Conversion of CT values into stopping power
- Delineation of regions of interest
- Selection of proton beam directions
- Design of each beam
- Optimization of the plan

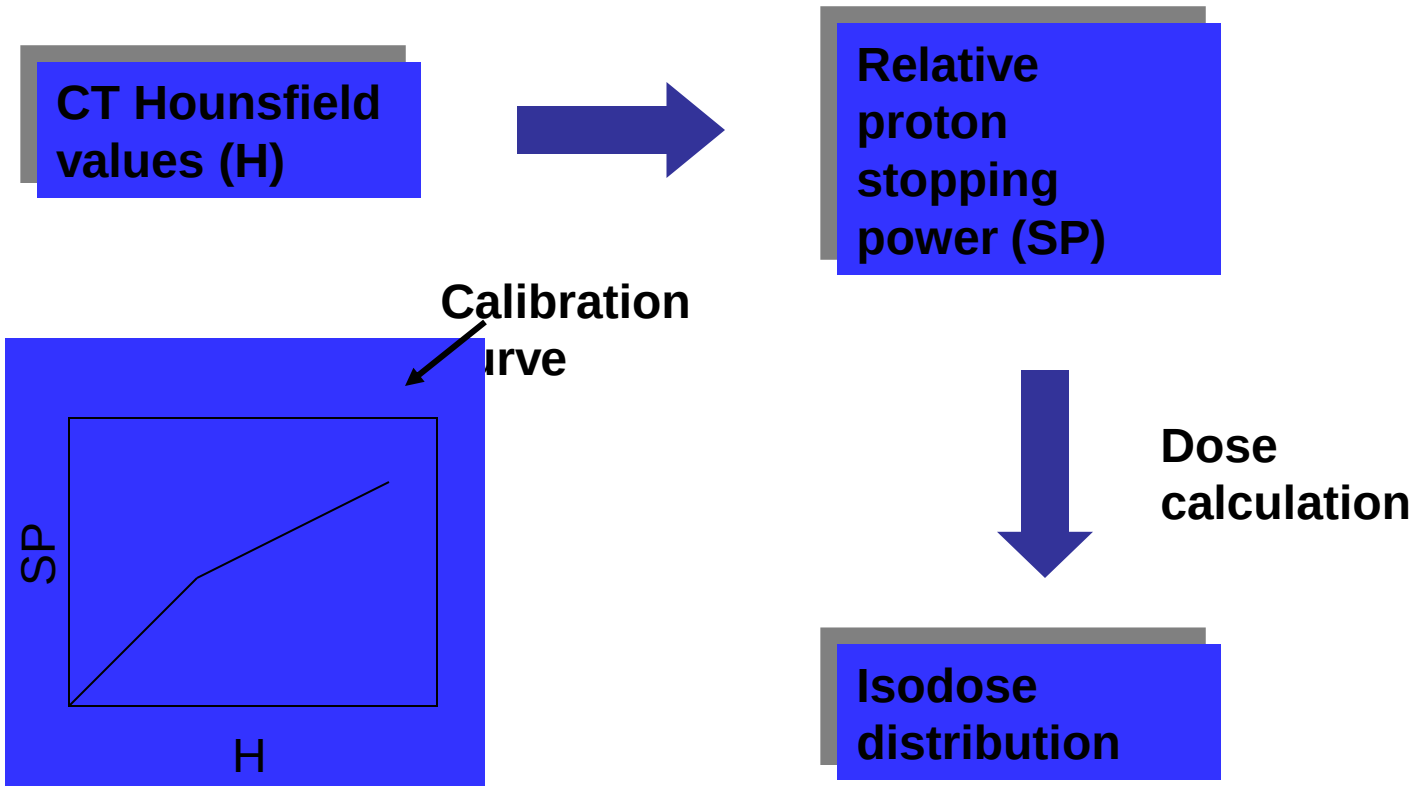
Treatment Delivery

- Fabrication of apertures and boluses
- Beam calibration
- Alignment of patient using DRRs
- Computer-controlled dose delivery

Processing of Imaging Data

$H = 1000\ \mu^{tissue} / \mu^{water}$

$SP = dE/dx^{tissue} / dE/dx^{water}$



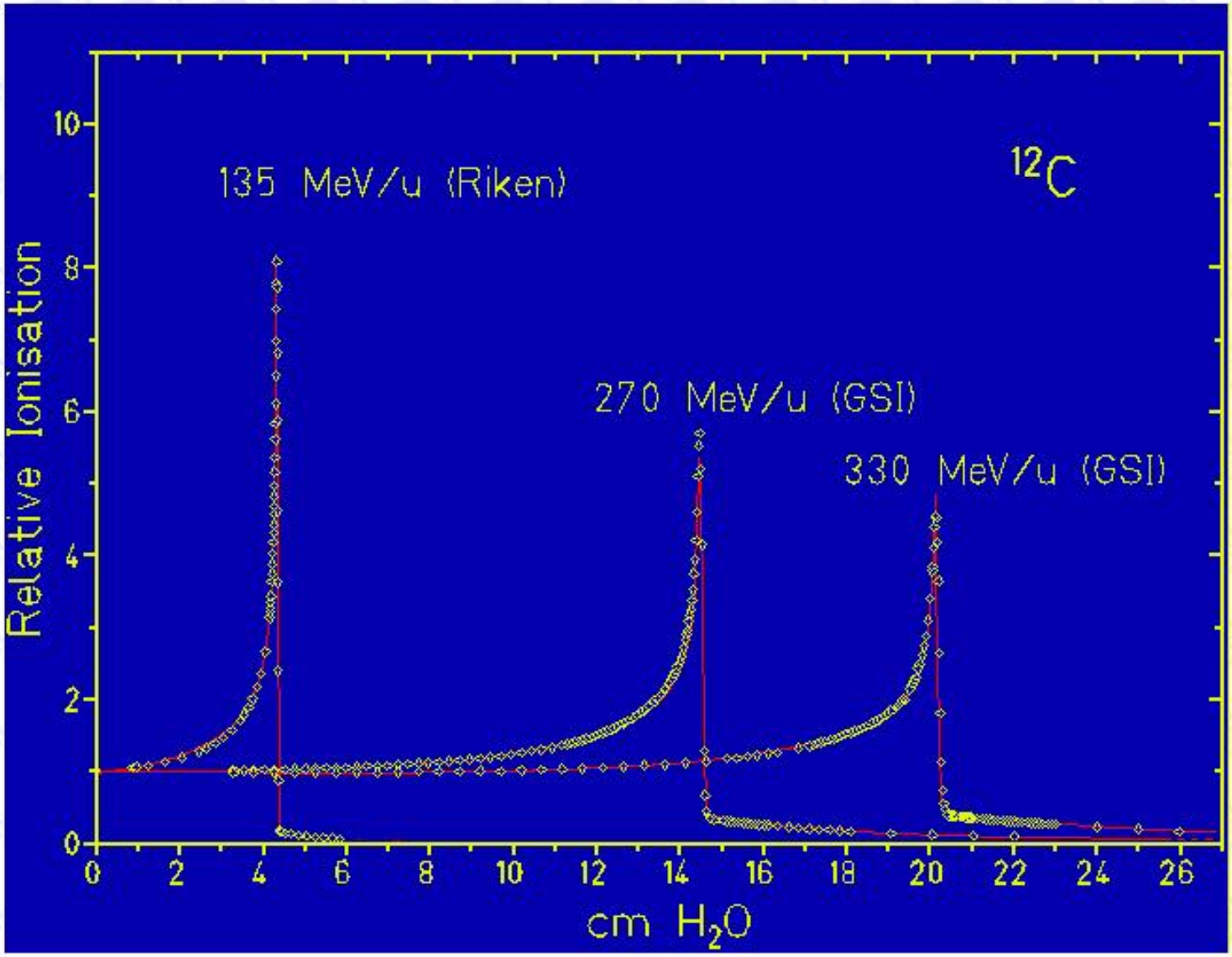
CT Calibration Curve

- Proton interaction ≠ Photon interaction
- Bi- or tri- or multisegmental curves are in use
- No unique Stopping Power values for soft tissue Hounsfield range
- Tissue substitutes ≠ real tissues
- Fat anomaly

The level of precision achievable with particle beams makes it very attractive for conforming to the tumour target. However, we still don't fully understand the biological effectiveness of particles as they decelerate within the cancer target and deposit their energy to kill the cancer cells. We need to study particle therapy not only in cell lines derived from patients with cancer, but also in 3D models of cancer and in samples grown "live" from patients. These models will allow us to study the microstructure of a cancer, with specific reference to how particle damage DNA and how the cancer cell tries to repair that damage. We are learning how cancer cells vary in their composition throughout a cancer or in a seedling that has separated from the primary cancer and grown elsewhere, and how the body's immune system might recognise the cancer in order to fight against it. The incredible advances in the science of studying single cells within the cancer, and cancer cells or cancer DNA collected in simple blood tests, and then deciphering the entire gene code from those samples will allow us to achieve this cutting edge research within the next few years.

Bragg Peaks

Physical beam model for carbon ion radiotherapy



Advantage of Carbon vs Proton

Carbon has two properties that should yield a higher tumor control probability when compared with X-rays and protons

Carbon Properties

- **Sharper knife (Sharper *Penumbra*)**
- **Higher rate of energy deposited versus depth (High *Linear Energy Transfer*)**

Consequences

- **Less dose to healthy tissue**
- **More effective against tumors resistant to X-rays and proton radiation (hypoxic tumor cells)**
- **Shorter overall treatment course**

The linear-quadratic model of cell kill

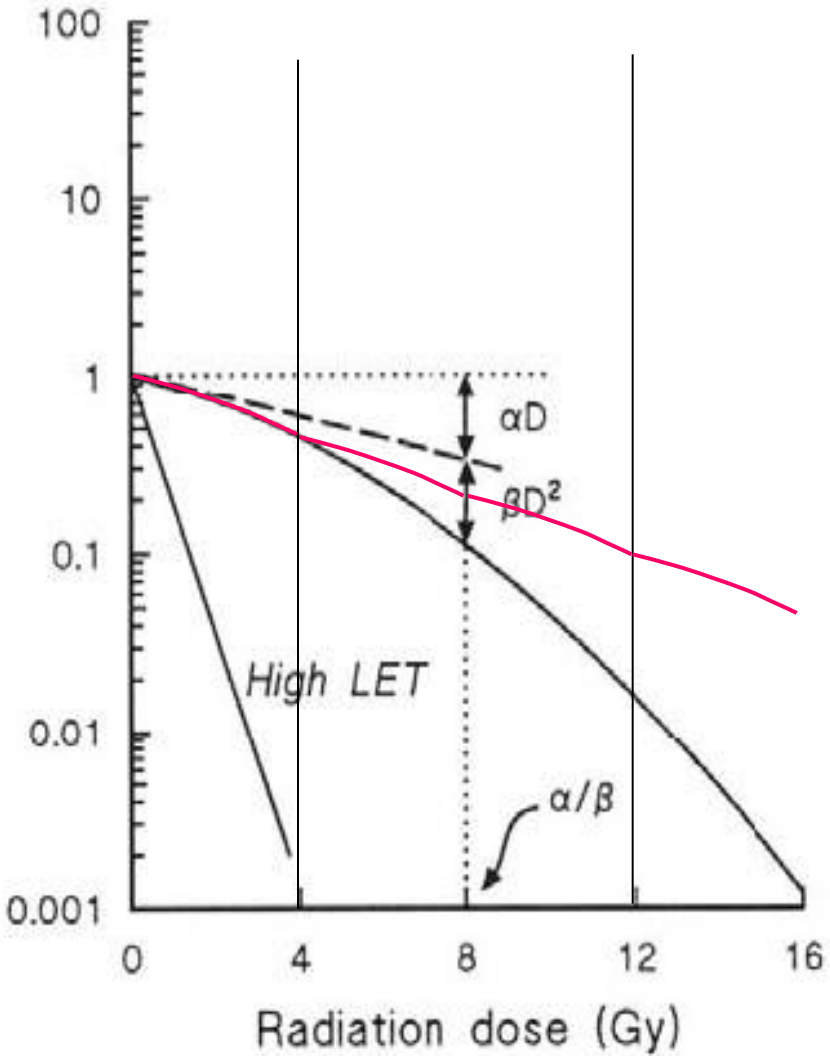
$$S(D) = e^{-\alpha D - \beta D^2}$$

$S(D)$ is the fraction of cells surviving a dose D;

α is a constant describing the initial slope of the cell survival curve;

β is a smaller constant describing the quadratic component of cell killing.

The linear-quadratic model of cell kill, fractionation



Comparison of BED for Low LET Radiation and High LET Radiation

For Low LET $BED = N_L\, d_L\, [\, 1 + d_L / (\alpha/\beta)_L]$

For High LET $BED = N_H\, d_H\, [RBE_{max} + d_H / (\alpha/\beta)_H]$

For low LET radiation 2 Gy/F 30 F 60 Gy

BED_T = 30 x 2 [1 + 2/10] = 60 x 1.2 = 72 Gy

BED_{late} = 30 x 2 [1 + 2/2.5] = 60 x 1.8 = 108 Gy

For high LET Radiation - Carbon particle RBE = 3 [Bragg Peak region] RBE = 1

4Gy/ F 6 F 24 Gy [72 GyE]

BED_T = 6 x 4 [3 + 4/10] = 24 x 3.4 = 81.6 Gy TCP = 1.33

BED_{late} = 6 x 4 [3 + 4/2.5] = 24 x 4.6 = 110.4Gy NTCP = 1.02

BED_{late} = 6 x 4/2 [1 + 2/2.5] = 12 x 1.8 = 21.6 Gy NTCP = 0.2

Carbon particle therapy - Example

1. 12.5 Gy x 2 F 12.5 x3 = 37.5GyE/F 75 GyE

BED_T = 2 x 12.5 [3 + 12.5/10] = 25 x 4.25 = 106 Gy TCP = 1.47

BED_{late} = 2 x 12.5 [3 + 12.5/2.5] = 25 x 8 = 200 Gy NTCP=1.85

BED_{late} = 2 x 12.5/2 [1+ 6.25/2.5] =12.5 x 3.5 = 43.75 Gy NTCP=0.4

2. 20 Gy Single fraction 60 GyE

BED_T = 1 x 20 [3 + 20/10] = 20 x 5 = 100 Gy TCP =1.39

BED_{late} = 1 x 20 [3 + 20/2.5] = 20 x 11 = 220 Gy NTCP=2.04

BED_{late} = 1 x 20/2 [1 + 10/2.5] = 10x 5 = 50.0 Gy NTCP=0.46

3. 2 Gy /F 20 F 40 Gy

BED_T = 20 x 2 [3 + 2/10] = 40 x 3.2 = 128 Gy TCP = 1.78

BED_{late} = 20 x 2 [3 + 2/2.5] = 40 x 3.8 = 152 Gy NTCP = 1.41

BED_{late} = 20 x 2/2 [1+ 1/2.5] = 20 x 1.4 = 28 Gy NTCP = 0.26

4. 1.5 Gy/F 35 F 52.5 Gy

BED_T = 35 x 1.5 [3 + 1.5/10] = 52.5 x 3.15 = 165 Gy TCP = 2.29

BED_{late} = 35 x 1.5 [3 + 1.5/2.5] = 52.5 x 3.6 = 189 Gy NTCP= 1.75

BED_{late} = 35 x 1.5/2 [1+0.75/2.5]= 26.25 x 1.3 = 34.13 Gy NTCP= 0.32

5. 1.2 Gy/F 40 F 48 Gy

BED_T = 40 x 1.2 [3 + 1.2/10] = 48 x 3.12= 150 Gy TCP = 2.08

BED_{late} = 40 x 1.2 [3 + 1.2/2.5]= 48 x 3.48= 167 Gy NTCP = 1.55

BED_{late} = 40 x1.2/2[1+0.6/2.5]= 24 x1.24 = 29.76Gy NTCP = 0.28

6. 1.2 Gy/F 50 F 60 Gy

BED_T = 50 x 1.2 [3 + 1.2/10] = 60 x 3.12 = 187 Gy TCP = 2.60

BED_{late} = 50 x 1.2 [3 + 1.2/2.5] = 60 x 3.48 = 209 Gy NTCP = 1.94

BED_{late} = 50 x1.2/2[1+ 0.6/2.5] = 30 x 1.24 = 37.2 Gy NTCP = 0.34

7. 1.0 Gy/F 60 F 60 Gy

BED_T = 60 x 1.0 [3 + 1.0/10] = 60x 3.10 = 186 Gy TCP = 2.58

BED_{late} = 60 x 1.0 [3 + 1.0/2.5] = 60 x 3.40 = 204 Gy NTCP= 1.89

BED_{late} = 60 x 1.0/2[1 + 0.5/2.5] = 30 x 1.2 = 36 Gy NTCP= 0.33

Tumors with low α/β i.e. Radio resistant tumors

Let $\alpha/\beta = 2$

Treated with photons 2Gy/F 30 F 60 Gy

$BED_T = 30 \times 2 [1 + 2/2] = 60 \times 2 = 120$ Gy

$BED_{late} = 30 \times 2 [1 + 2/2.5] = 60 \times 1.8 = 108$ Gy

With Carbon ion 1 Gy/F 60 F 60 Gy

$BED_T = 60 \times 1.0 [3 + 1.0/2] = 60 \times 3.5 = 210$ Gy TCP = 1.75

$BED_{late} = 60 \times 1.0 [3 + 1.0/2.5] = 60 \times 3.4 = 204$ Gy NTCP= 1.89

$BED_{lat} = 60 \times 1.0/2[1+0.5/2.5] = 30 \times 1.2 = 36$ Gy NTCP= 0.33

6Gy/F 5 F 30 Gy

$BED_T = 5 \times 6 [3 + 6/2] = 30 \times 6 = 180$ Gy TCP=1.5

$BED_{late} = 5 \times 6 [3 + 6/2.5] = 30 \times 5.4 = 162$ Gy NTCP= 1.5

$BED_{late} = 5x\ 6/2[1+3/2.5] = 15 \times 2.2 = 33$Gy NTCP= 0.31

15 Gy/F 2F 30 Gy

$BED_T = 2x\ 15 [3 + 15/2] = 30x\ 10.5 = 315$ Gy TCP=2.63

$BED_{late} = 2x\ 15 [3 + 15/2.5] = 30 \times 9 = 270$ Gy NTCP= 2.5

$BED_{late} = 2 \times 15/2 [1 + 7.5/2.5] = 15 \times 4 = 60$ Gy NTCP= 0.55

Clinical Results of Carbon ion therapy at NIRS

Head & Neck 3.6 GyE, 16 F, in 4 wks

4.4 GyE, 16F in 4 wks

BED_T = 16 x 1.2 [3 + 1.2/10] = 19.2x 3.12 = 59.9Gy TCP = 0.83

BED_{late} = 16 x 1.2 [3 + 1.2/2.5] = 19.2 x 3.48 = 66.8 Gy NTCP= 0.62

BED_{skel} = 16 x 1.2/3[1+0.4/10] = 6.4x 1.04 = 6.65 Gy NTCP= 0.1

BED_T = 16 x 1.47 [3 + 1.47/10] = 23.47x 3.147 = 73.85Gy TCP = 1.03

BED_{late} = 16 x 1.47 [3 + 1.47/2.5] = 23.47 x 3.59 = 84.21 Gy NTCP= 0.78

BED_{skel} = 16 x 1.47/3[1+0.5/10] = 7.84 x 1.05 = 8.23 Gy NTCP= 0.11

NSCL 1.67 Gy, 18 F, 5 Wks compared with 2.5 Gy , 22 F by photon

14 Gy, 1 F

BED_T = 18 x 1.67 [3 + 1.67/6] = 30.06x 3.28 = 98.55Gy TCP = 1.26

BED_{late} = 18 x 1.67 [3 + 1.67/2.5] = 30.06 x 3.67 = 110.6 Gy NTCP= 1.00

BED_{skelt} = 18 x 1.67/2[1+0.84/10] = 15.03 x 1.084 = 16.3 Gy NTCP= 0.23

BED_T = 1 x 14 [3 + 14/6] = 14 x 5.33 = 74.66 Gy TCP = 0.96

BED_{late} = 1 x 14 [3 + 14/2.5] = 14 x 8.6 = 120.4 Gy NTCP= 1.09

BED_{skel} = 1 x 14/2[1+7/10] = 7 x 1.7 = 11.9 Gy NTCP= 0.16

Prostate with Photon 3 Gy , 15 F

BED_T = 15 x 3[1 + 3/1.8] = 45 x 2.67 = 120 Gy

BED_{late} = 15 x 3 [1 + 3/2.5] = 45 x 2.2 = 99 Gy

BED_{skel} = 15 x 3[1+3/10] = 45x 1.3 = 58.5 Gy

Prostate with Carbon ion 1.1 Gy, 20 F, 5 wks

BED_T = 20 x 1.1 [3 + 1.1/1.8] = 22.0x 3.61 = 79.4Gy TCP = 0. 67

BED_{late} = 20 x 1.1 [3 + 1.1/2.5] = 22.0 x 3.44 = 75.68 Gy NTCP= 0.76

BED_{skel} = 20 x 1.1/3[1+0.37/10] = 7.33x 1.037= 7.6 Gy NTCP= 0.13

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GOVERNMENT OF INDIA
परमाणु ऊर्जा नियामक परिषद
ATOMIC ENERGY REGULATORY BOARD

Ref: AERB/DRA&C/4-1/2018/186

Date: 11.12.2018

PRESS RELEASE

FIRST PROTON THERAPY FACILITY IN THE COUNTRY CLEARED BY AERB FOR CANCER TREATMENT

Atomic Energy Regulatory Board has issued Licence on 29/11/2018 to operate the Proton Therapy facility at Apollo Hospital, Chennai for treatment of cancer patients. The Proton Therapy facility, Proteus 235, is the first of its kind facility in India and South-East Asia. There are about 78 such facilities operating all over the world. The license is issued by AERB for patient treatment with Proton beam of 226 MeV from radiation safety view point.

In the country, presently AERB has licenced around 1000 radio-therapy equipment in around 475 medical institutions. These radiation therapy equipment for patient treatment are either gamma radiation based Tele-Cobalt units or are X-ray based Linear Accelerators.

The Proton beam therapy, on the other hand is a type of radiation therapy that uses a beam of protons to irradiate diseased tissue, most often in the treatment of cancer. It uses protons, which are positively charged particles and at high energies can destroy cancer cells. The Proton beam specifically beneficial in treating paediatric cancers and deep-seated tumours more effectively than the conventional Gamma/ X-ray radiation therapy.

The AERB "Licence for Operation" for the Proton therapy facility was issued after AERB approval at each stage i.e. design, layout, construction and commissioning of the facility. The appropriate cost of Proton radiation facility is about 500 crores.

(A. U. Sonawane)

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ATOMIC ENERGY REGULATORY BOARD

संदर्भ: AERB/DRA&C/4.1/2018/186 दिनांक : 11.12..2018

प्रेस विज्ञप्ति

कैंसर के उपचार हेतु देश की पहली प्रोटॉन थेरेपी फेसेलिटी को एईआरबी ने स्वीकृति प्रदान की

परमाणु ऊर्जा नियामक परिषद ने अपोलो हॉस्पिटल, चेन्नै को कैंसर रोगियों के इलाज हेतु प्रोटॉन थेरेपी फेसेलिटी ऑपरेट करने के लिए दिनांक 29/11/2018 को लाइसेंस जारी कर दिया। प्रोटॉन थेरेपी फेसेलिटी, प्रोटियस 235, भारत तथा दक्षिण-पूर्वी एशिया में प्रयोग की जानी वाली अपने प्रकार की पहली फेसेलिटी है। पूरे विश्व में इस प्रकार की कुल 78 फेसेलिटी कार्यरत हैं। इस फेसेलिटी को विकिरण सुरक्षा के दृष्टिकोण से एईआरबी द्वारा 226 मेगावॉट के प्रोटॉन बीम के साथ रोगी उपचार के लिए लाइसेंस जारी किया गया है।

वर्तमान में एईआरबी ने देश में लगभग 475 चिकित्सा संस्थानों में लगभग 1000 रेडियोथेरेपी मशीनों को लाइसेंस प्रदान किए हैं। रोगियों के उपचार के लिए प्रयोग किए जाने वाले ये रेडिएशन थेरेपी उपकरण या तो गामा रेडिएशन आधारित टेली-कोबाल्ट यूनिट्स हैं अथवा एक्स-रे आधारित लाइनर एक्सेलरेटर्स हैं।

जबकि प्रोटॉन बीम थेरेपी, एक इस प्रकार की रेडिएशन थेरेपी है जिसमें रोगग्रस्त टिश्यूज को इरेडिएट करने के लिए प्रोटॉन बीम का प्रयोग किया जाता है, अधिकतर इसका प्रयोग कैंसर के इलाज में ही किया जाता है। इसमें प्रोटॉन का प्रयोग होता है जो कि पॉजिटिव चार्ज्ड पार्टिकिल होते हैं तथा उच्च ऊर्जा प्राप्त करने पर कैंसर सेल्स को समाप्त कर देते हैं। विशेष रूप से बच्चों के कैंसर का इलाज करने में तथा शरीर में ज्यादा भीतर स्थित ट्यूमर के इलाज के लिए प्रोटॉन बीम पारंपरिक गामा / एक्स-रे रेडिएशन थेरेपी की तुलना में अधिक प्रभावी है।

एईआरबी ने प्रोटॉन थेरेपी फैसेलिटी को "ऑपरेशन हेतु लाइसेंस" फेसेलिटी के प्रत्येक चरण जैसे कि डिजायन, लेआउट, निर्माण तथा कमीशनिंग के अनुमोदन के पश्चात जारी किया। प्रोटॉन रेडिएशन फेसेलिटी की अनुमानित लागत लगभग 500 करोड़ है ।

(ए.यू.सोनावणे)

Summary

- Physical rationale of heavy charged particle therapy
  - Reduced integral dose (by factor 2-3)
  - Potentially improved dose conformality
- Biological rationale:
  - Based on modeling studies: LET, OER, EUD, TCP/NTCP, RBE
  - Potentially increased RBE, but only for heavier particles (heavier than protons)
- Clinical rationale:
  - Do we need randomized clinical trials?

THANK YOU