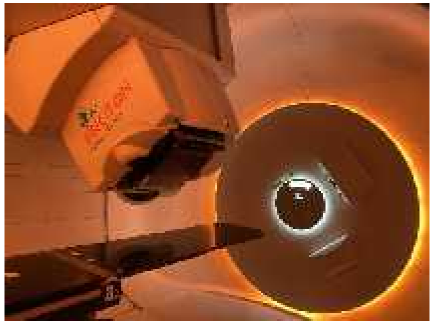

Particle beam Therapy

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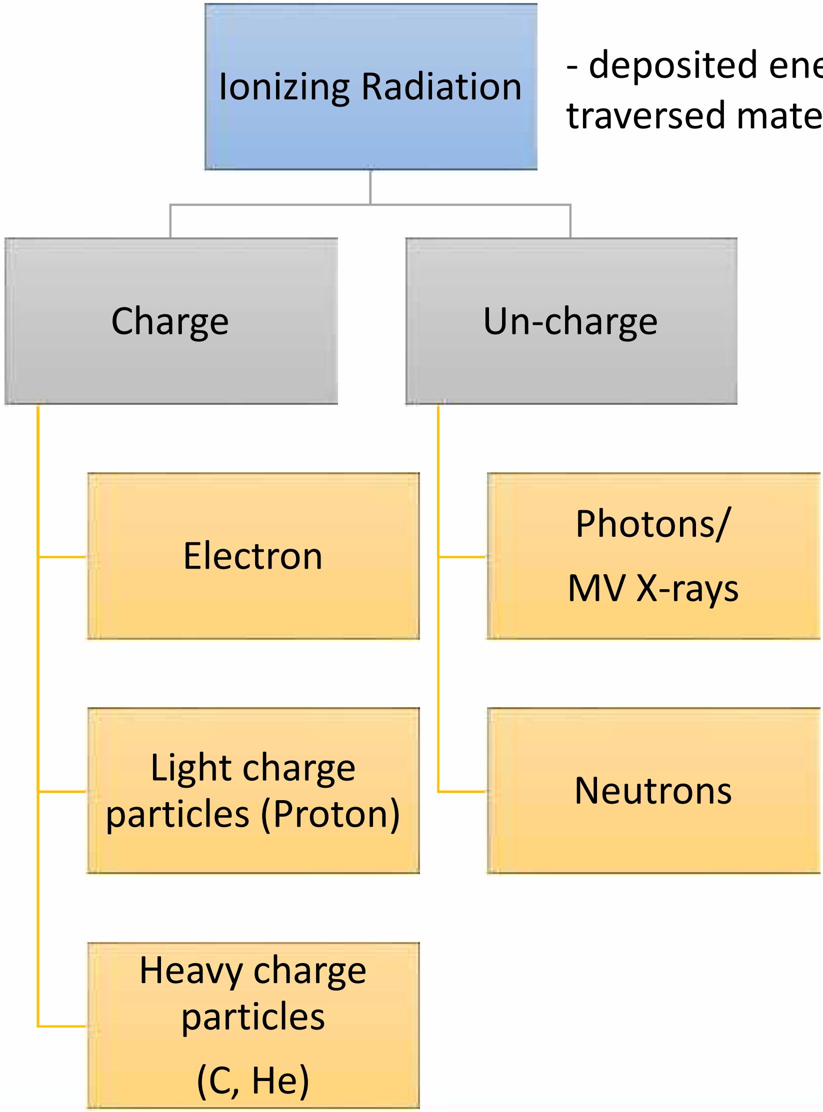
Learning objective

- Particle beam therapy ?
- Interaction of charge particle with matter
- Rational of particle beam therapy
- Carbon vs Proton
- Historical development of proton beam therapy
- How it work ?
- Accelerator technology (Cyclotron / Synchrotron)
- Passive Scattering and Pencil beam scanning
- Benefit of Proton beam therapy
- Clinical Indications

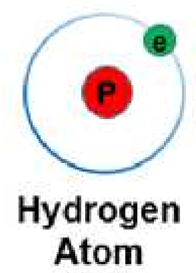


- deposited energy is high enough to ionize the traversed material

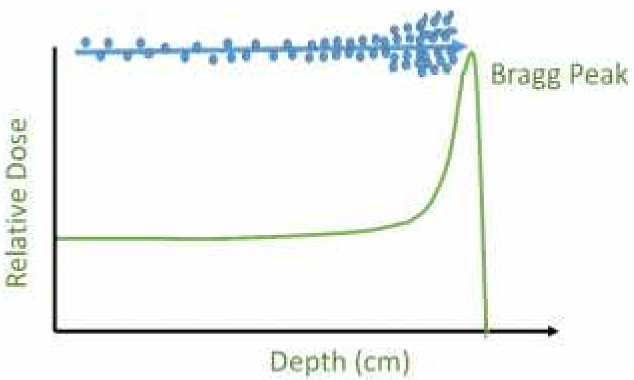
Particle / hadron / ion beam therapy

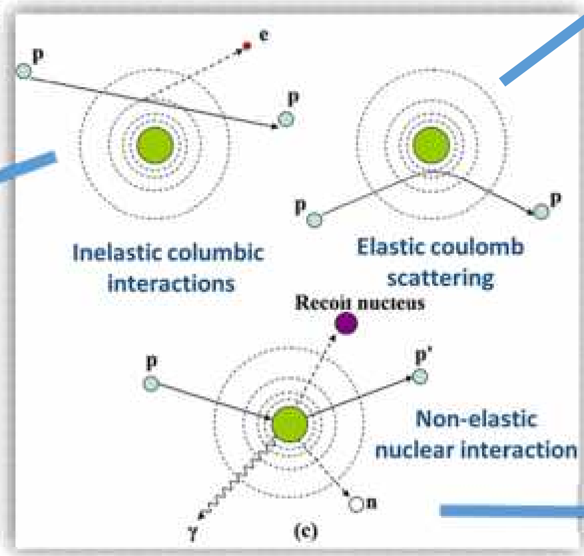
- Specific type of EXRT
- Use high energy neutron, proton, other heavy +ve ions
- Most commonly used particle in Hadron therapy
  - Proton
  - Carbon
  - Helium

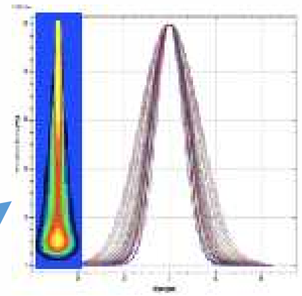
Interaction of charge particle with matter

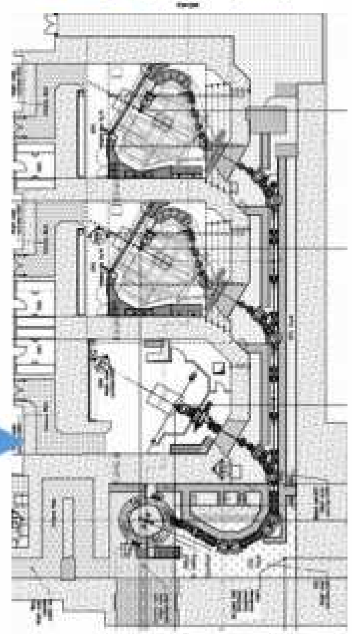


- Nucleus of the hydrogen atom.
- Unit positive charge (1.6×10^{-19} C)
- Mass of 1.6×10^{-27} kg (~1,840 times the mass of electron).









$$\frac{-dE}{dx} = 4\,\pi\, N_A r_e^2 \frac{m_e c^4}{v^2}\frac{Zz^2}{A}\rho\left[\frac{1}{2}\ln\left(\frac{2\gamma^2\beta^2 m_e c^2 E_{max}}{I_0^2}\right)\right] - \beta^2 - \frac{\varepsilon}{2} - \frac{\delta(\beta\gamma)}{2}$$

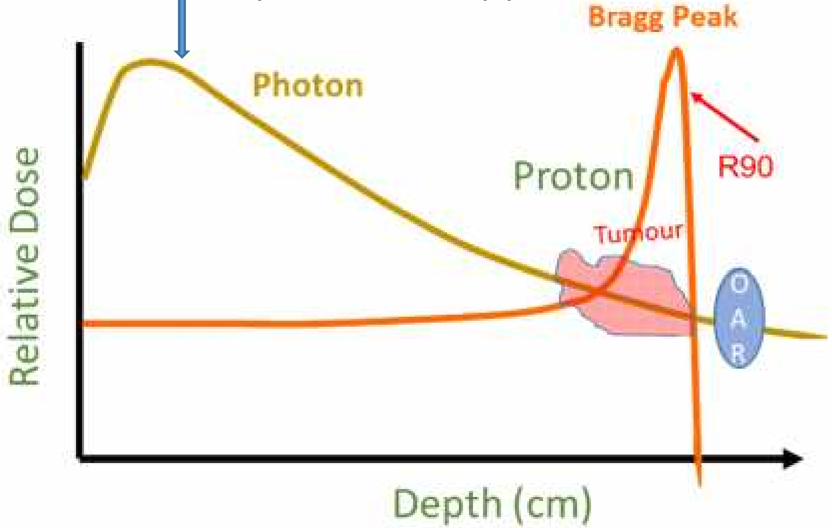
Why particle therapy ??

- Physical depth dose characteristics
  - Finite range (e.g R90)
  - No exit dose

- Radiobiology (RBE)
  - Proton = 1.1 (0.7 – 1.5)
  - Carbon = 2-5

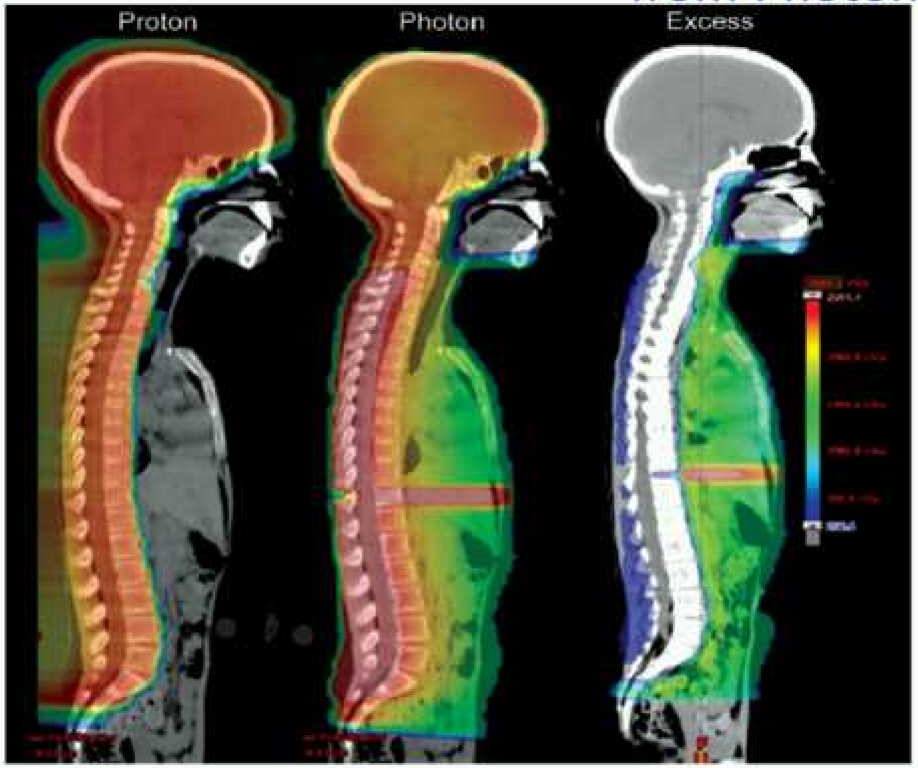
$$RBE = \frac{Dose\ of\ 150\ V\ \ X-rays\ required\ to\ cause\ effect\ x}{Dose\ of\ radiation\ required\ to\ cause\ effect\ x}$$

Exit Dose unavoidable with any form
Of photon therapy

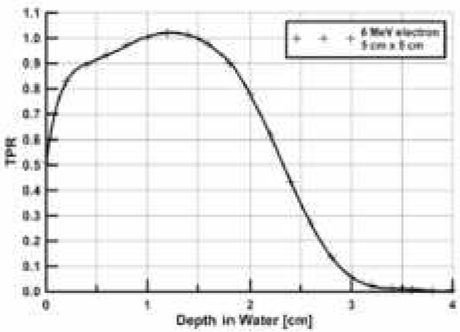


Dosimetric benefit of particle therapy

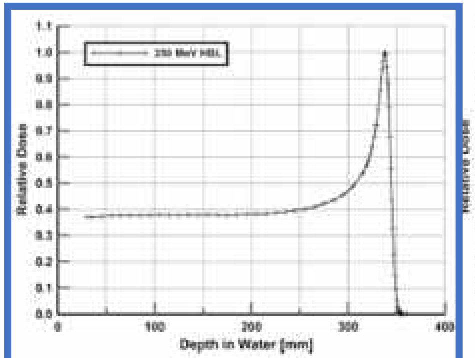
Proton Photon Excess Dose from Photon



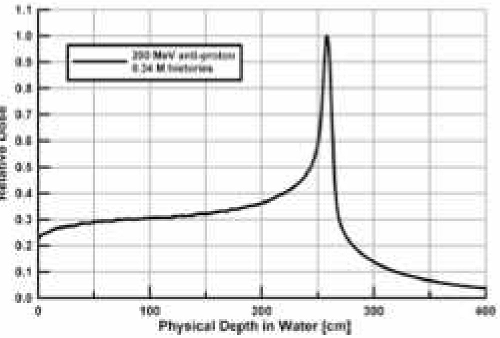
Depth dose characteristics of charge particles



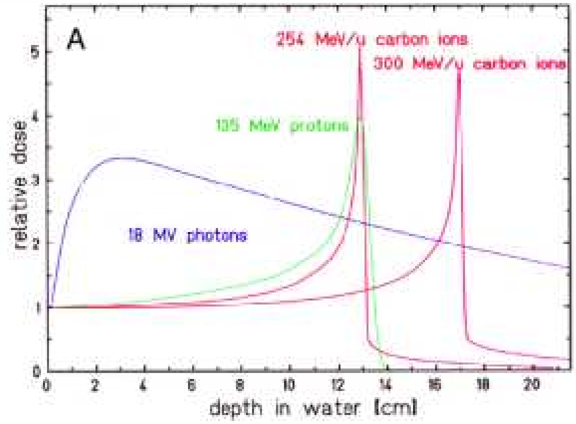
Electrons

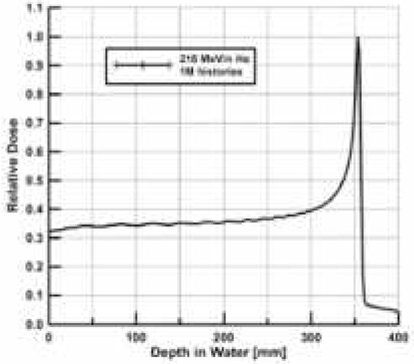


Protons

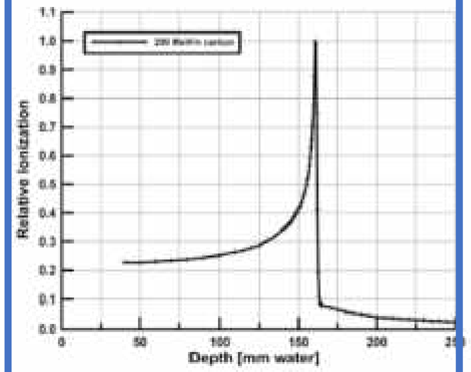


Anti-Protons

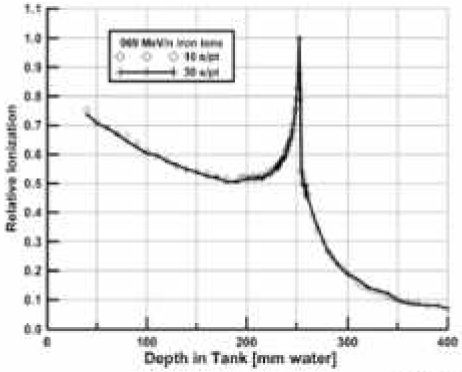




Helium



Carbon



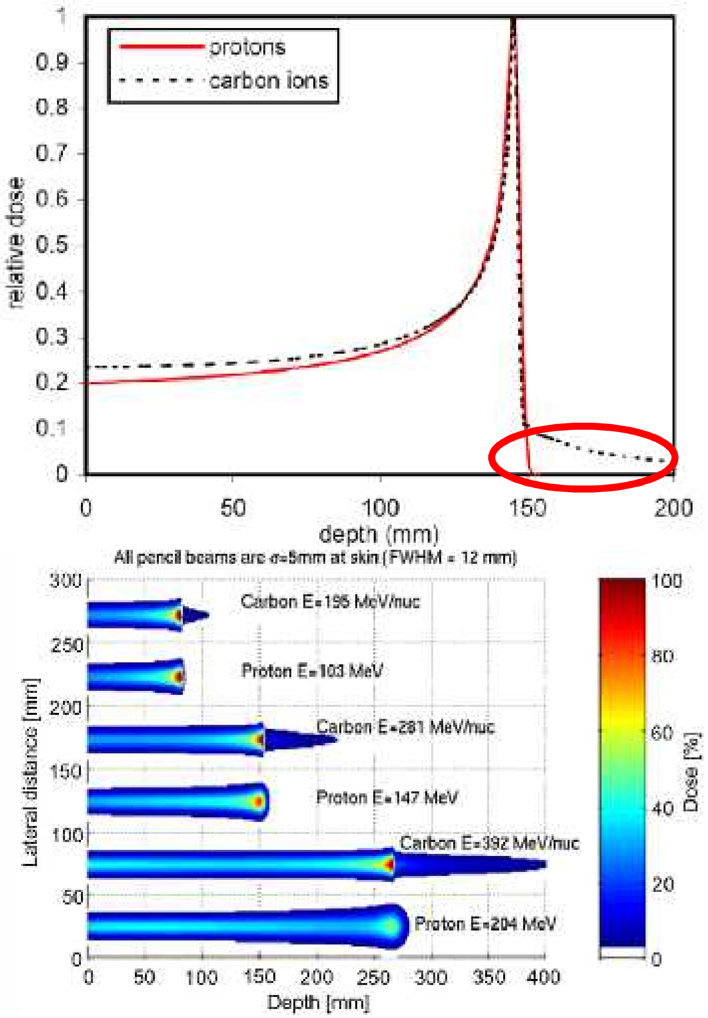
Iron

Moyers
PTCOG 2008

Carbon :

- Very high peak to plateau ratio
- Better penumbra
- Fragment tail
- Higher RBE
- Extremely high cost

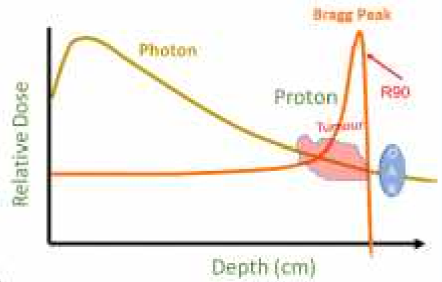
Fragment tail of Carbon

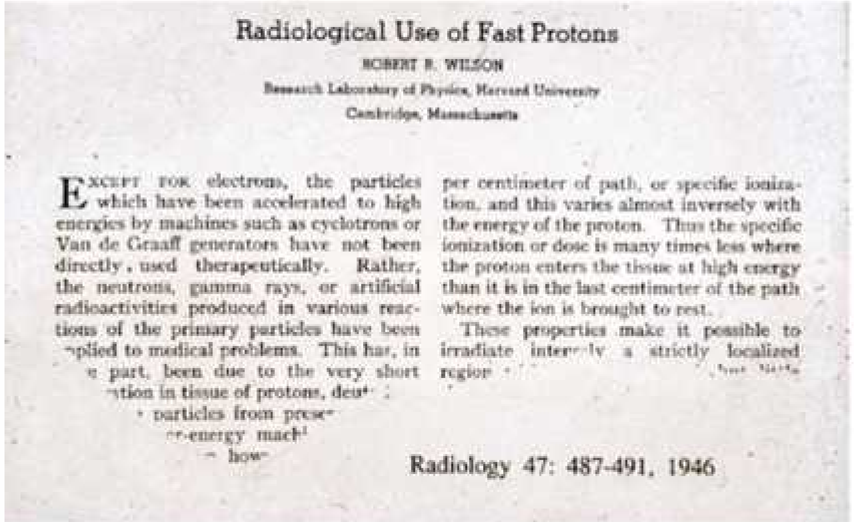


- Fragment tail beyond Bragg peak of carbon ion
- Tails are of low physical dose & relatively high RBE
- Extend up to 15 cm
- BED from fragmental tail not negligible
- Limited use of carbon in paediatric patient

Historical development

- Initial proposal by Robert Wilson in 1946
- Spread out Bragg Peak (SOBP) using range modulating wheel
  - Proton energies → Depth of the tumours
  - Number of proton energies → tumour extent in beam direction





Radiological Use of Fast Protons

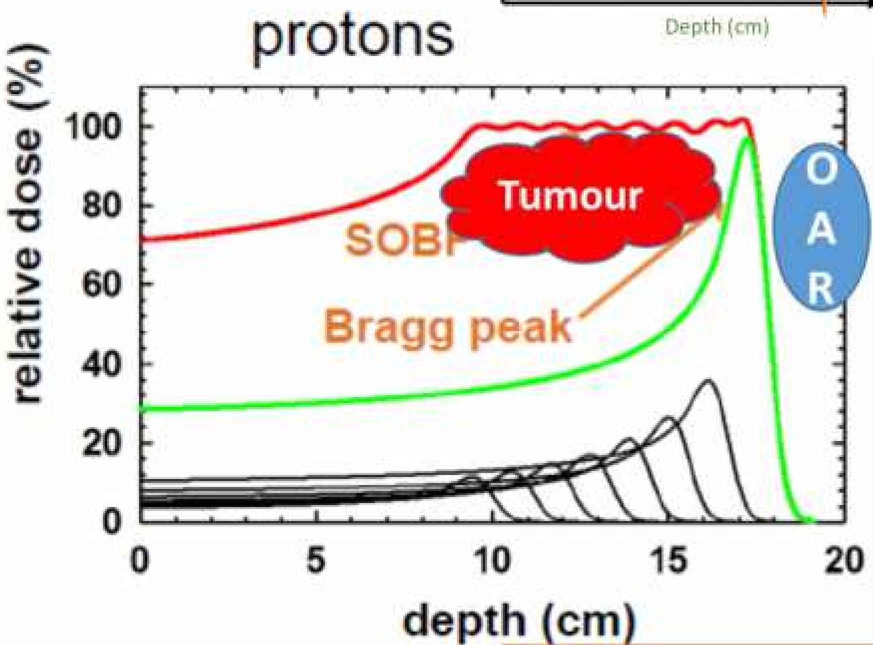
ROBERT R. WILSON
Research Laboratory of Physics, Harvard University
Cambridge, Massachusetts

EXCEPT FOR electrons, the particles which have been accelerated to high energies by machines such as cyclotrons or Van de Graaff generators have not been directly used therapeutically. Rather, the neutrons, gamma rays, or artificial radioactivities produced in various reactions of the primary particles have been applied to medical problems. This has, in part, been due to the very short ...tion in tissue of protons, deu... particles from prese... ...-energy mach... how...

per centimeter of path, or specific ionization, and this varies almost inversely with the energy of the proton. Thus the specific ionization or dose is many times less where the proton enters the tissue at high energy than it is in the last centimeter of the path where the ion is brought to rest.

These properties make it possible to irradiate inter...ly a strictly localized region ...

Radiology 47: 487-491, 1946



Courtesy : Harald Paganetti; AAPM Summer School 2015

Historical development

CANCER RESEARCH

VOLUME 18 FEBRUARY 1958 NUMBER 2

Pituitary Irradiation with High-Energy Proton Beams

A Preliminary Report*

C. A. TOBIAS, J. H. LAWRENCE, J. L. BORN, R. K. MCCOMBS, J. E. ROBERTS, H. O. ANGER, B. V. A. LOW-BEER,† AND C. B. HUGGINS‡

(Donner Laboratory of Biophysics and Medical Physics, Donner Pavilion, and the Radiation Laboratory, University of California, Berkeley, Calif.)

HYPOPHYSEAL PROTON IRRADIATION

An account is given below of the initial use of high-speed protons in human therapeutic investigations. The rationale for pituitary irradiation, the technic employed, and the initial physiological changes after proton irradiation of the pituitary gland are given in detail.

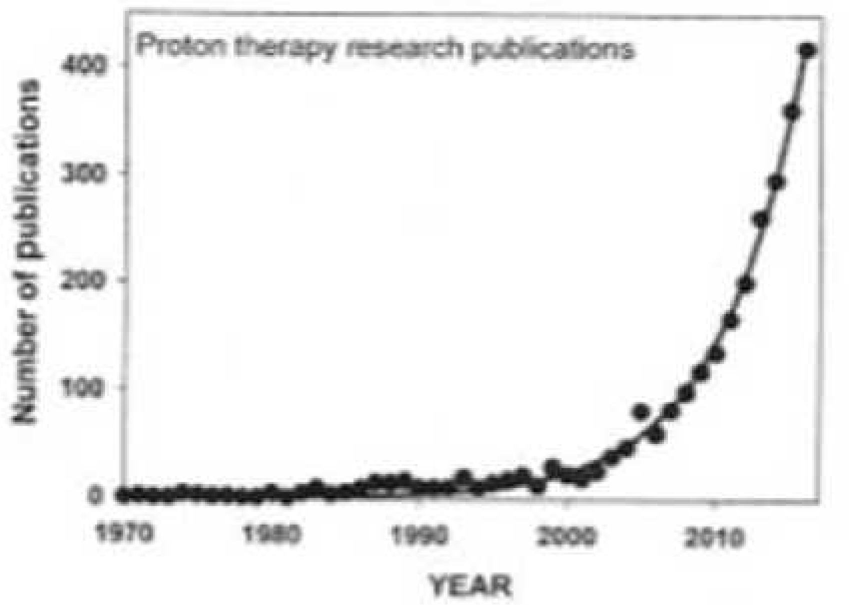
exophthalmos (4, 7). Roentgen irradiation has also been attempted for cancer in the human being, particularly by Murphy and Schwippert for prostatic carcinoma (38) and by Kelly *et al.* for mammary carcinoma (17). However, in three patients with mammary carcinoma, even 10,000 r to the region of the hypophysis was not sufficient to cause no-

- First patient treated at LBL in 1954
- Metastatic breast cancer treated for pituitary gland for hormone suppression.
- The bony landmarks made targeting of the beam feasible.
- The plateau of the depth dose curve of 340 MeV Proton
- Cross-firing technique

Courtesy : Harald Paganetti; AAPM Summer School 2015

Progress in Proton Beam Therapy

- 1990 : First Hospital based PT facility at Loma Linda University Medical center
- Present status of PT facility
  - 109 in operation
  - 37 under construction
  - 29 in planning
- Exponential increase in peer-reviewed publication
- Technological development
- Cost effective solution (Single room)



https://www.ptcog.ch/index.php/facilities-in-operation
Proton Therapy Physics (2nd Edition) by Prof Harald Paganetti

How does it work ??
Proton Therapy System Architecture

- Accelerator (Cyclotron/Synchrotron)
- Energy selection system (ESS)
- Beam Transport System (BTS)
- Beam delivery System (BDS)

Beam management system

- Positioning system
- Patient positioning and verification system

Position management system

- Therapy safety system (TSS)

TCS

TCS : Treatment control system

Proton Accelerator : Cyclotron-1932

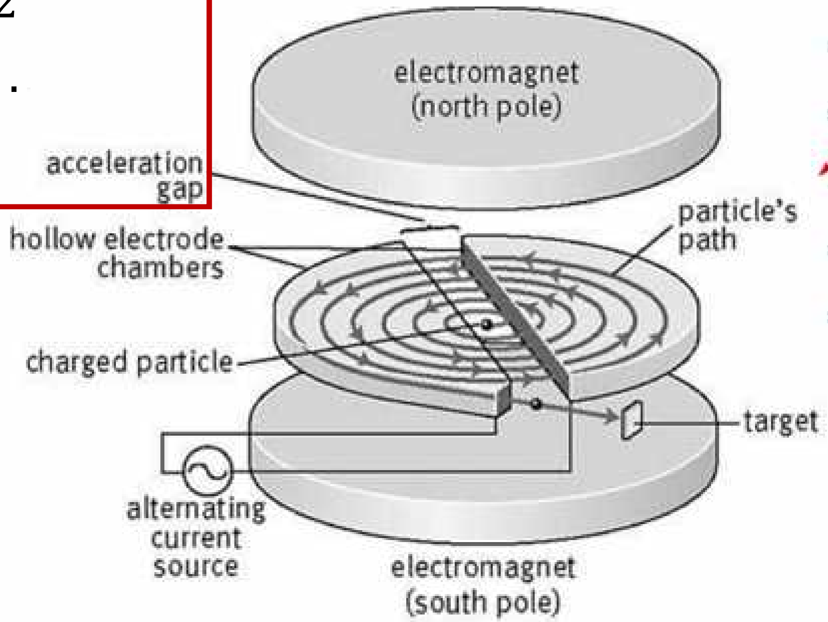
80 KeV Proton

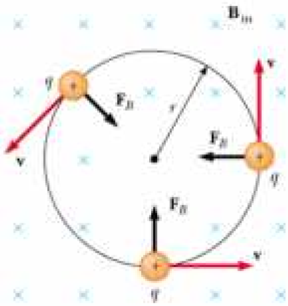
- Fixed-energy cyclic particle accelerator
- designed to generate proton beams of up to 250 MeV

Energy gain per rotation = 2

Energy = . .

$\vec{F}_{elec} = q\,\vec{E}$





$\vec{F}_{magn} = q\,(\vec{v}\times\vec{B})$

$\frac{mv}{r} = qvB$

$r = \frac{mv}{qB}$

Angular frequency

= —

Cyclotron Type

Proton revolving frequency = /2Π

Proton angular frequency = 2Π = qB/m=qB/ m_0

CLASSICAL: (original)

- Operate at fixed frequency (= qB/m) and ignore the mass increase
- Works to about 25 MeV for protons (=1.03)

SYNCHROCYCLOTRON: let the RF frequency ω decreases as the energy increases

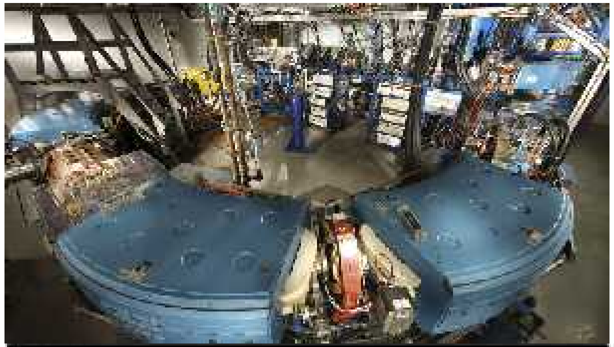
- = $_0$/ to match the increase in mass (m= m_0)
- Uses same decreasing field with radius as classical cyclotron

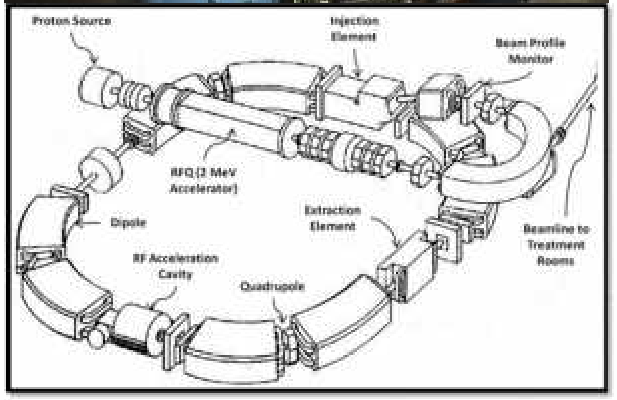
ISOCHRONOUS: raise the magnetic field with radius such that the relativistic mass increase is just cancelled

- Pick B= B_0 {this also means that B increases with radius}
- Then = qB/m = qB_0/m_0 is constant.
- Field increases with radius- magnet structure must be different
- 1.7-2.15 T in C230

Proton Accelerator : Synchrotrons

- Variable energy cyclic particle accelerator
- Suitable for both light (Proton) and heavy ions (Z>1, C12,He4, etc)
- 1st Synchrotron was Built by Fermilab and started operation in 1992 at LomaLinda University.
- Low energy proton (2-7MeV) are injected
- An alternating voltage adds energy to the proton on each rotation
- Magnetic field must be increase each cycle to keep the proton circulating on the same radius
- Commercial system
    - Hitachi
    - Mitsubishi





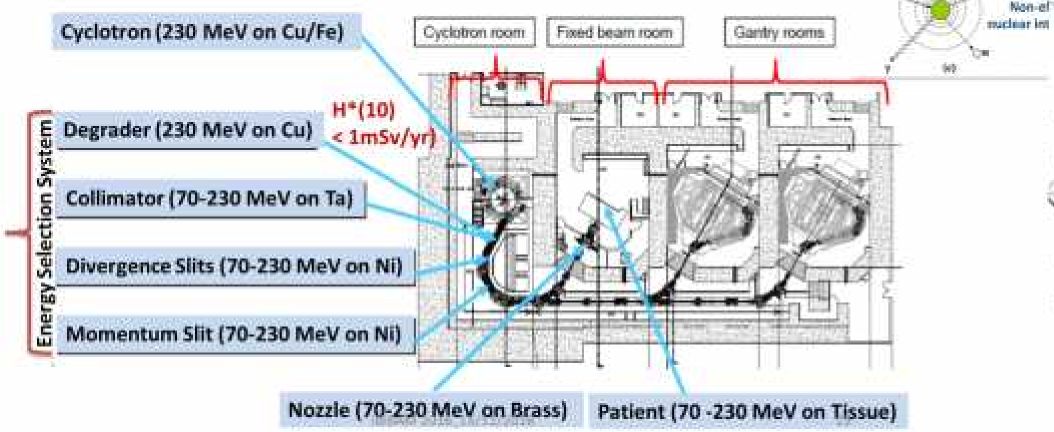
Parameter	Synchrotron	Isochronous Cyclotron	Synchrocyclotron
Mechanical Size (Dia in meter)	6 - 8 + Injection system	3.0 –4. 5 m	2.5 – 1.8
Time structure beam intensity	Spill structure	Continuous	Pulsed
Fast energy scanning	Wait for next spill During extraction	Degrader	Degrader
Activation	No problem	Degrader need shielding	Degrader need shielding
Beam intensity	Limited in magnitude & range	“Any” Adjustable within <1ms	“Any” but low on average. Adjustable within a few mS
Intensity stability	10-20%	2 - 5%	20%
Scattering	Suitable	Suitable	Suitable
Spot Scanning	Suitable	Suitable	Long time needed
Beam gating	Suitable	Suitable	Suitable
Fast continuous scanning	Difficult due to pulse structure	Suitable	Not possible due to pulse structure

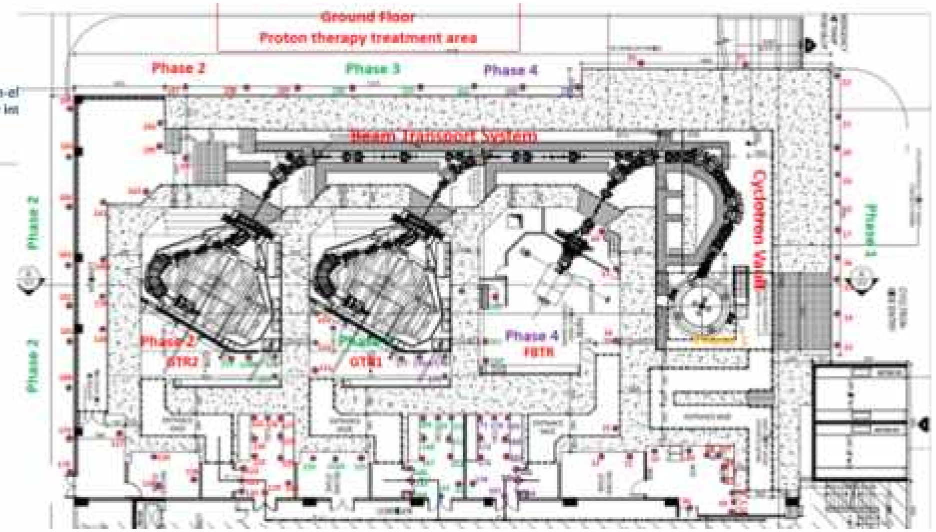
2. Energy Selection System

- Beam Degrader :
  - Degrade the beam energy to requested value up to 70 MeV
  - Scatter beam transversely & generate a spread of beam energies
- Collimate beam transverse phase space and to limit the beam energy spread
- Much of the beam is lost in ESS at lower energy

Ambient neutron and photon dose around PT facility

Neutrons and photons are produced during **beam loses** at various location along beam path when proton hits matter





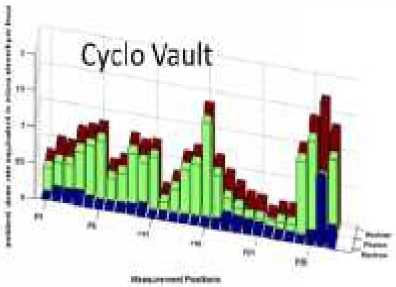
AN INTERNATIONAL JOURNAL OF RADIOLOGY, RADIATION ONCOLOGY AND ALL RELATED SCIENCES

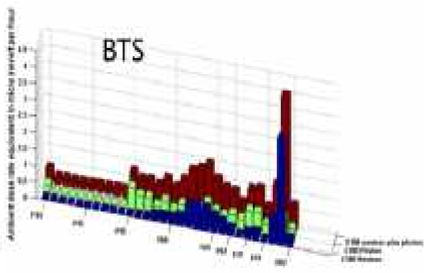
BJR

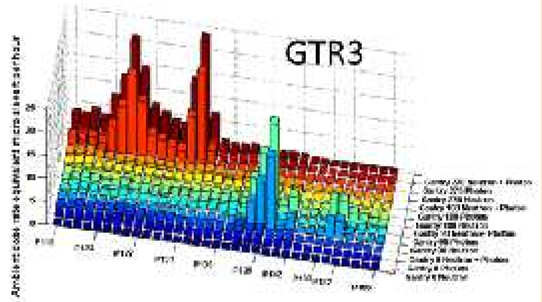
Ambient neutron and photon dose equivalent H*(10) around a pencil beam scanning proton therapy facility

[1]DAYANANDA SHAMURAILATPAM SHARMA, PhD, DipRP, [1]KARTIKESWAR CH PATRO, MSc, DipRP, [1]NOUFAL MANTHALA PADANNAYEL, PhD, DipRP, [1]MANIKANDAN ARJUNAN, MSc, DipRP, [1]GANAPATHY KRISHNAN, PhD, [1]RAJESH THIYAGARAJAN, MSc, [2]SRINIVAS CHILUKURI, MD and [2]RAKESH JALALI, MD

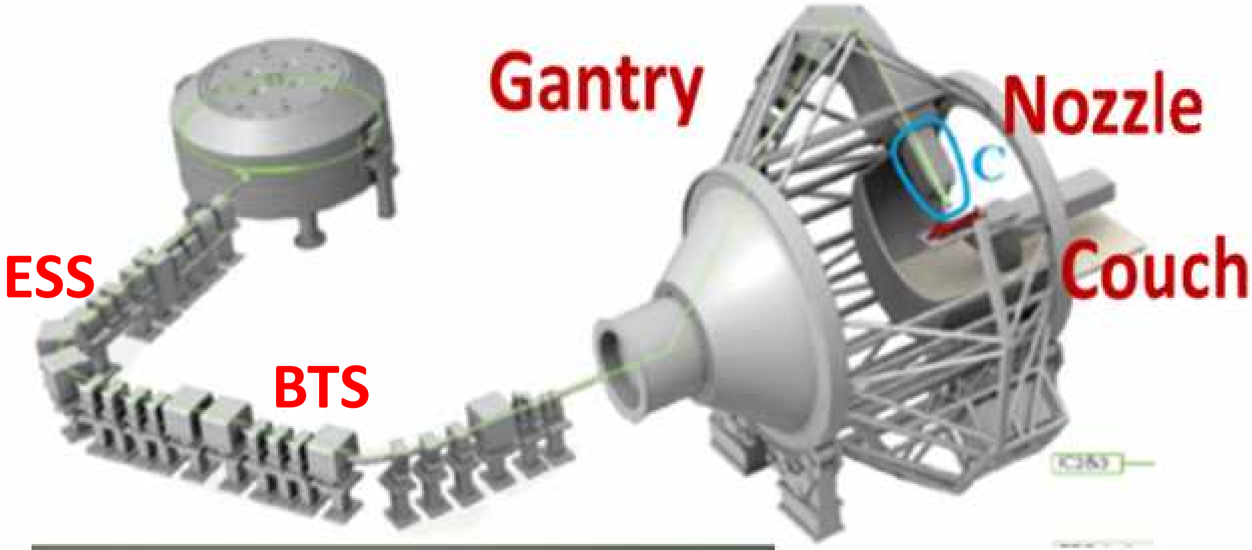
[1]Department of Medical Physics, Apollo Proton Cancer Centre, 100 Feet Road Tharamani, Chennai, Tamil Nadu, India
[2]Department of Radiation Oncology, Apollo Proton Cancer Centre, 100 Feet Road Tharamani, Chennai, Tamil Nadu, India



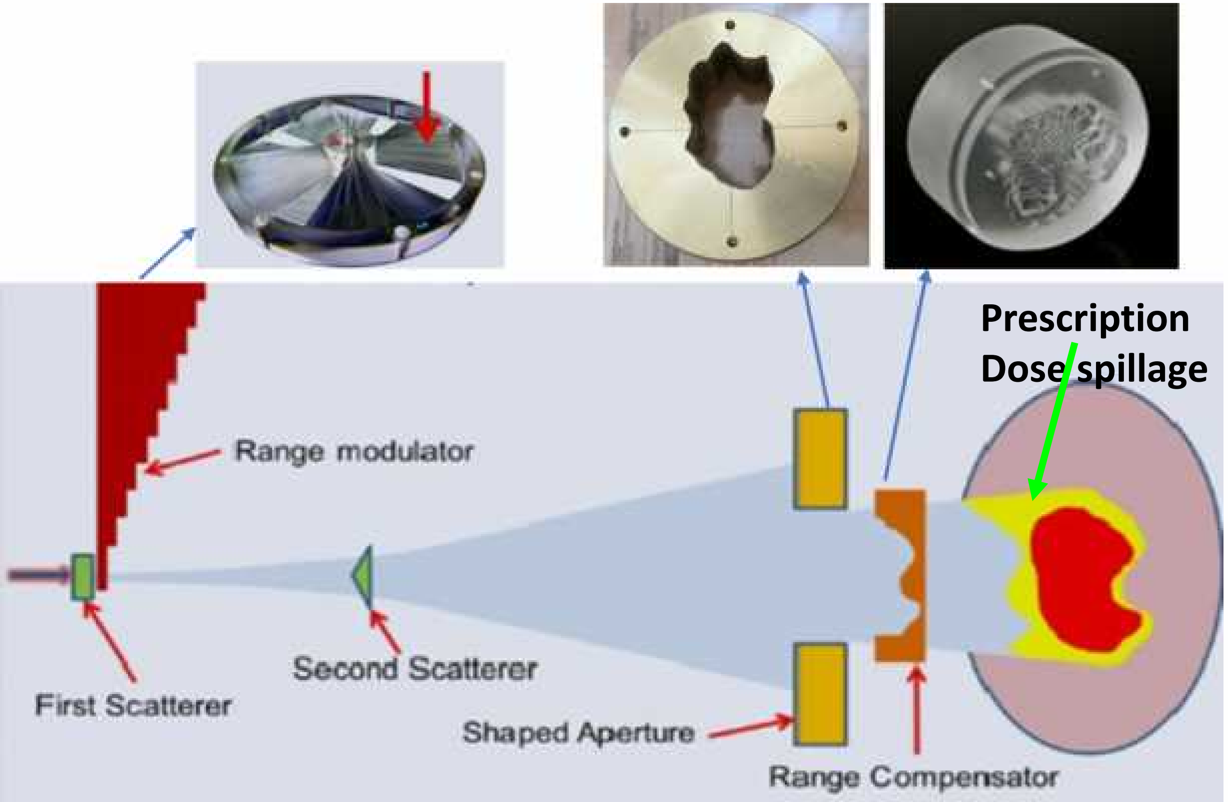


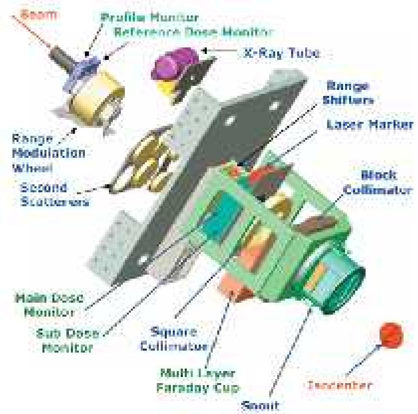


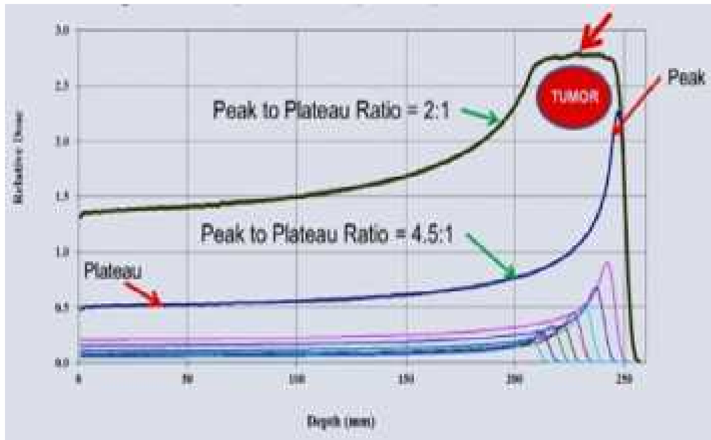
3. Beam Transport System



4. Beam delivery System : Passive scattering





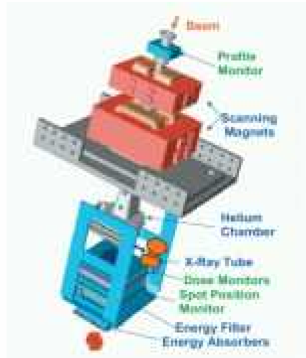


Reduced peak to plateau ratio

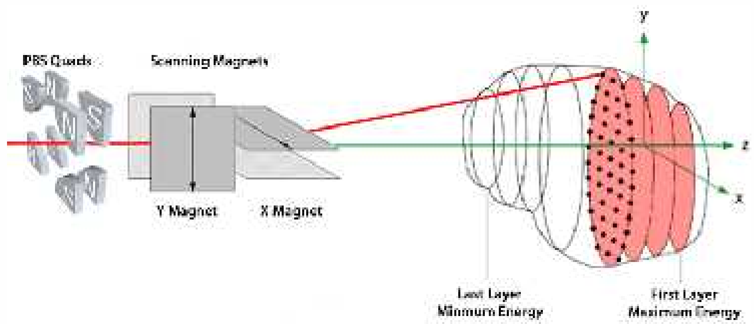
Proton beam therapy with passive scattering techniques

- Seating/sleeping position
- Planar radiograph for target localization
- Limited Clinical site
- Logistic issues
- Manpower
- Neutron contamination

Beam delivery system : Active scanning



- Reduced
  - Proximal, entrance, integral dose
  - preparation time
  - in-room therapist time
  - Easy Adaptive therapy
  - Neutron contamination
- Increase conformity
- Disadvantages
  - Sensitivity to patient motion (interplay effect)
  - Slower irradiation
  - Poorer target conformity at lower energies due to increase penumbra



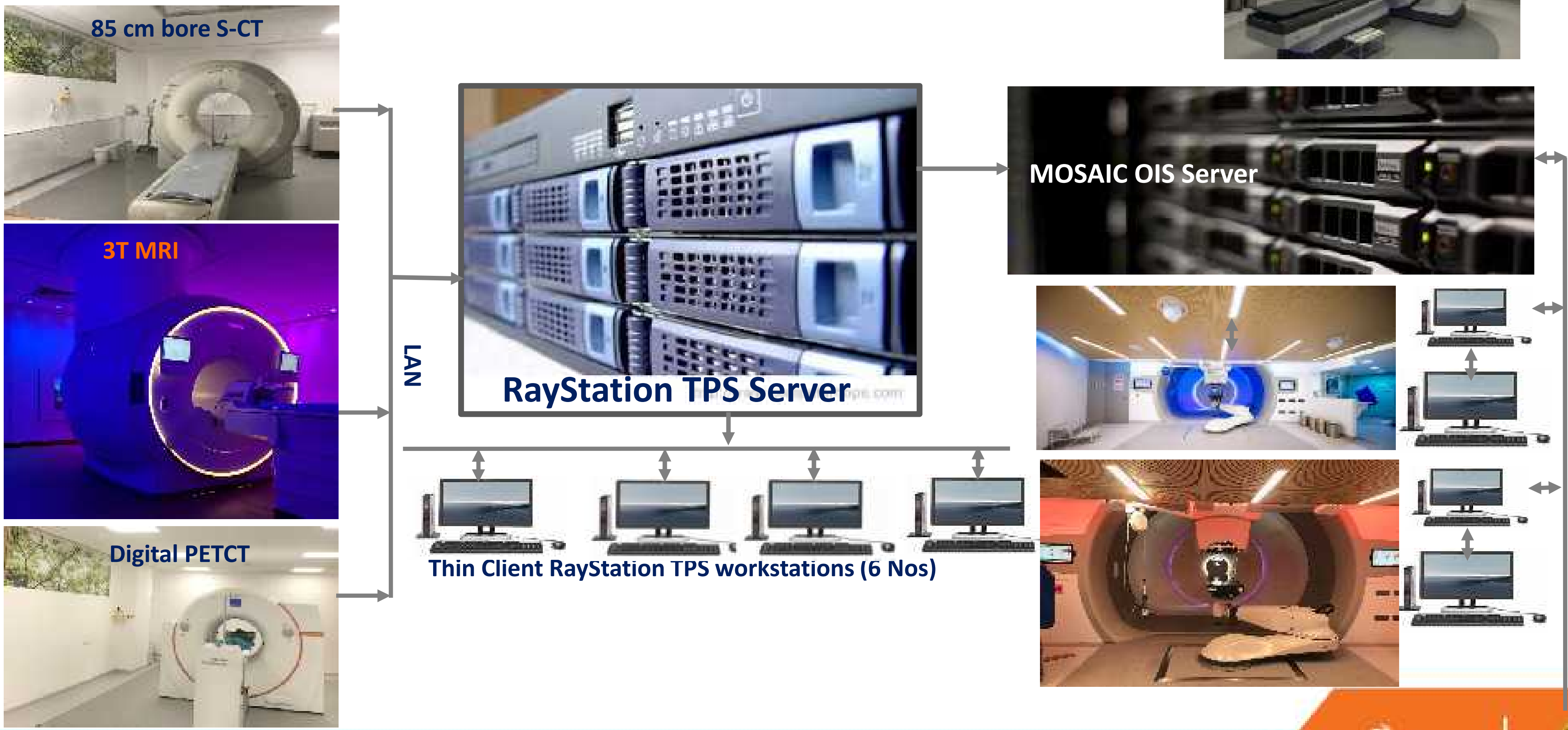
Contemporary PT

Characterization and Performance Evaluation of the First-Proton Therapy Facility in India

Dayananda Sharma Shamurailatpam, A. Manikandan, K. Ganapathy, M. P. Noufal, Kartikeshwar C. Patro, T. Rajesh, R. Jalali[1]
Departments of Medical Physics and [1]Radiation Oncology, Apollo Proton Cancer Centre, Chennai, Tamil Nadu, India

- Pencil Beam Scanning only
- Image-Guided PT (2D, 2.5D, 3D)
- 6D Robot
- Motion Management (AlignRT SGRT)
- Optimized shallow tumor treatment

Contemporary PT facility at APCC



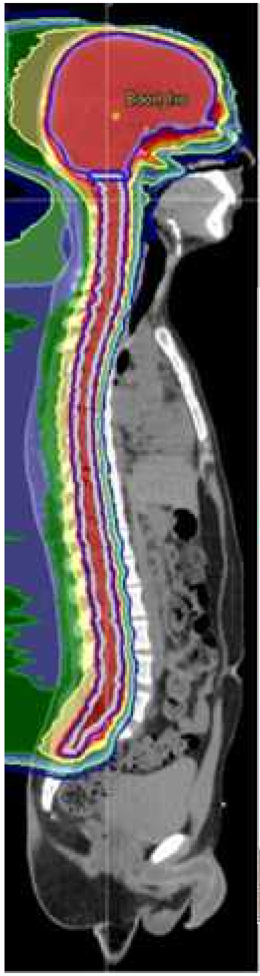
Benefit PBT

- Dosimetric benefit
  - Reduction of OAR doses
  - Reduction of Integral dose
- Impact
  - Reduction of toxicity profile
  - Possibility of dose escalation
  - Reduction or avoidance of radiation induced carcinogenesis
- Clinical outcome

Dosimetric benefit of Proton Therapy

- Reduction of Dose to OARs
- In CSI, mandible, parotid gland, thyroid gland, lung, kidney, heart, ovary, uterine, and other non-target intracranial structures (St Clair 2004 IJROBP, Lee 2005 IJROBP, Howell 2012 IJROBP)
- Models predict lower risk of second cancer, lower rate of pneumonitis, cardiac failure, xerostomia, blindness, hypothyroidism, and ototoxicity (Mirabell 2002 IJROBP, Newhauser 2009 PMB, Thaddei 2010 PMB, Brodin 2011, Acta Oncol, Zhang 2013 PMB).

Robustly optimized hybrid intensity-modulated proton therapy for craniospinal irradiation



Manthala Padannayil Noufal, Shamurailatpam Dayananda Sharma, Ganapathy Krishnan, Mayur Sawant, Utpal Gaikwad[1], Rakesh Jalali[1]

Departments of Medical Physics and [1]Radiation Oncology, Apollo Proton Cancer Centre, Chennai, Tamil Nadu, India

Website: www.cancerjournal.net

DOI: 10.4103/jcrt.JCRT_740_20

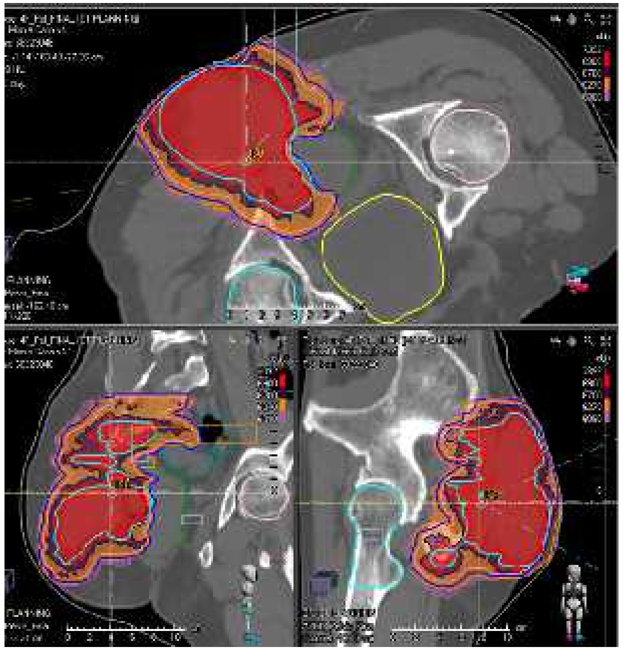
Parameter	PTV Brain	PTV Spine	CTV Brain	CTV Spine	cribriform plate
$D_{99\%}$	97.31 ± 1.65	95.10 ± 2.14	99.51 ± 0.52	99 ± 0.45	99.51 ± 0.56
$D_{98\%}$	98.11 ± 2.41	96.95 ± 1.49	99.88 ± 0.50	99.43 ± 0.5	99.00 ± 0.85
$D_{95\%}$	99.14 ± 1.61	97.67 ± 2.69	100.37 ± 0.53	100.01 ± 0.53	100.04 ± 0.57
$D_{1\%}$	104.0 ± 1.84	105.2 ± 0.68	104.93 ± 1.37	105.35 ± 0.69	105.07 ± 1.31

Structures	$D_{50\%}$ (Gy RBE)	$D_{1\%}$ (Gy RBE)
RT lens	3.72±0.92	6.17±1.06
LT lens	3.47±0.95	5.92±1.04
RT eye	10.04±2.77	24.07±5.98
LT eye	10.14±3.11	24.39±5.78
Brainstem	32.13±4.75	32.92±4.96
RT optic nerve	30.22±4.14	33.70±4.94
LT optic nerve	32.03±2.88	35.31±2.55
Chiasm	33.17±5.17	34.03±5.31
RT Kidney	1.52±1.78	20.83±10.93
LT Kidney	1.78±1.60	20.84±10.56
Thyroid	22.7±6.35	34.95±1.00
Oesophagus	24.7±16.54	27.79±16.2
Heart	0.02±0.02	14.45±12.75
RT lung	0.67±0.49	27.94±7.74
LT lung	1.14±1.37	21.45±11.68

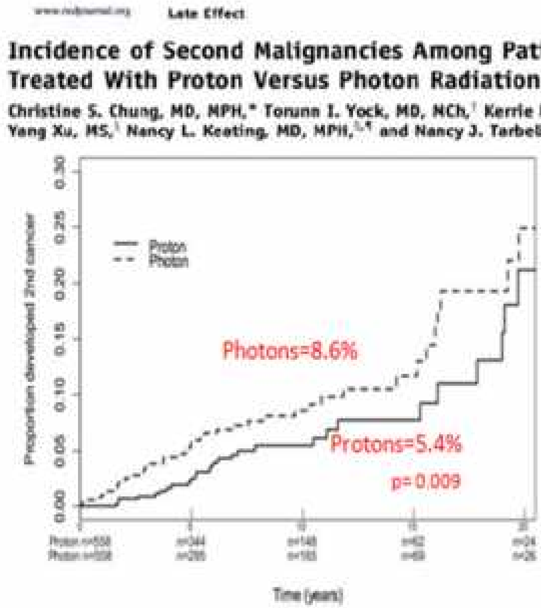
Dosimetric benefit of Proton Therapy

Dose escalation:

Sacral chordoma (Radio-resistant)



- Reduction of Second Cancer
- Expected to improve further with Pencil beam scattering Technique



558 proton pts treated from MGH (1973 to 2001) compared with 558 matched photon pts (SEER)

Hazard ratio

=0.52

(CI 0.32-0.85, p=0.009)

Mu et al 2005

Clinical benefit of proton therapy

- Datas emerging
- PSI & Orsay clinical outcome data for Chondrosarcoma : 1996 to 2015,
- **251 patients** (mean age, 42.0 ± 16.2 years)
- protons with (*n* = 135; 53.8%) or without photons (*n* = 116; 46.2%).
- Median delivered dose was 70.2 Gy_{RBE}.
- Median follow-up of 88.0 months
- 7-year Failure Free Survival was 93.1%.
- 7-year OS was 93.6%.
- 7-year Toxicity Free Survival was 84.2%.

Long term outcome of skull-base chondrosarcoma patients treated with high-dose proton therapy with or without conventional radiation therapy

D. Weber, G. Noel, L. Feuvreh et al.
Paul Scherrer Institute, Switzerland PSI and Insitute Curie, Orsay, France

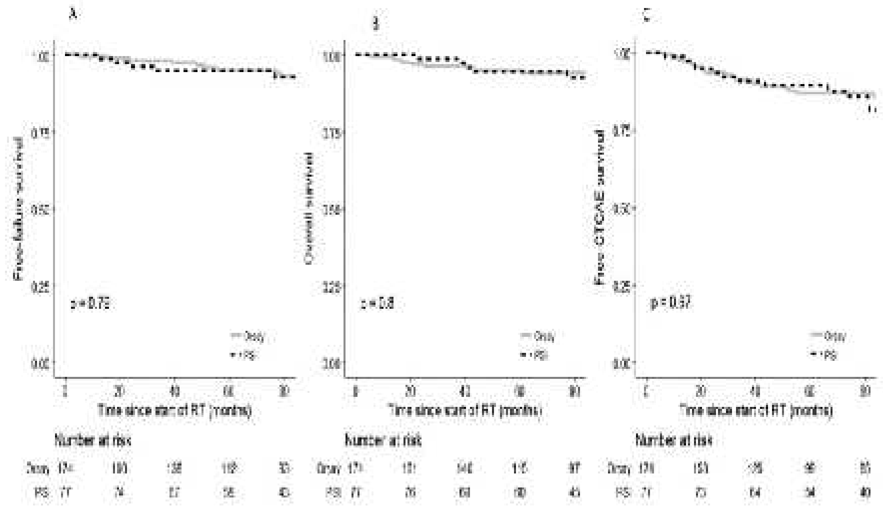


Fig. 1. Failure-free (A) overall (B) and toxicity-free (C) survival for ChSa patients treated with PT.

Recommended indications for CPT

Country	Document	Group 1 (medically necessary)	Group 2 (potential indications)
USA	ASTRO[a] Model Policy	■ Eye tumors ■ Chordoma and chondrosarcoma ■ Spine tumors[b] ■ Hepatocellular carcinoma[c] ■ Pediatric tumors[d] ■ Patients with genetic syndromes[e]	All other solid tumors, including: ■ Head and neck cancers ■ Thoracic malignancies ■ Abdominal cancers ■ Pelvic cancers
UK	Clinical indications for treatment overseas by protons	■ Skull-base and spinal chordoma ■ Skull-base chondrosarcoma ■ Spine and paraspinal soft-tissue sarcomas[f] ■ Pediatric tumors	
Italy	AIRO[g] indications for government reimbursement	■ Skull base and spine chordomas and chondrosarcomas[h] ■ Adenoid cystic carcinoma of the salivary glands[h] ■ Mucosal malignant melanoma[h] ■ Ocular melanoma ■ Osteosarcomas[h] ■ Pediatric tumors	

Recommended indications for CPT

Country	Document	Group 1 (medically necessary)	Group 2 (potential indications)
Denmark	Aarhus University, Indications for the Danish National Center for Particle Therapy	■ Chordoma and chondrosarcoma ■ Ependymoma ■ Primitive neuroectodermal tumors ■ Pituitary adenoma ■ Acoustic neuroma ■ Arterovenous malformations ■ Germinoma ■ Eye tumors ■ Lymphomas ■ Selected sarcomas ■ Nasopharyngeal cancer recurrence ■ Pediatric tumors	
The Netherlands	Health Council of the Netherlands on Proton Therapy[i]	■ Skull base and spine chordomas and chondrosarcomas ■ Meningioma ■ Pediatric tumors	■ Re-irradiations ■ Paranasal sinus tumors ■ Nasopharyngeal carcinoma ■ Retroperitoneal sarcoma
Canada	AHS[j] Proton Therapy Referral Committee Report	■ Chordomas and chondrosarcomas ■ Ocular melanomas[k] ■ Pediatric tumors	■ Benign tumors of the CNS ■ Paranasal sinus and nasal cavity tumors

Ongoing phase-III randomized clinical trials

Brief title	Sponsor	Start date	Condition	Arm 1	Arm 2
IMPT[a] versus IMRT[b] for head and neck cancers	MDACC[c], USA	August 2013	Oropharyngeal cancer	Protons[d]	X-rays[d]
Proton therapy versus IMRT[b] for prostate cancer	MGH[e], USA	July 2012	Low or intermediate risk prostate cancer	Protons	X-rays
Proton beam therapy versus IMRT[b] trial for esophageal cancer	MDACC[c], USA	April 2012	Esophageal cancer	Protons[d]	X-rays[d]
Comparing photon therapy to proton therapy to treat patients with lung cancer	RTOG[f], USA	February 2014	Stage II-III NSCLC[g]	Protons[d]	X-rays[d]
Pragmatic randomized trial of proton versus photon therapy for breast cancer	PTCORI[h], USA	2015	Post-mastectomy stage II or III breast cancer	Protons	X-rays
Trial of proton versus carbon ion radiation therapy in patients with chondrosarcoma	Heidelberg University, Germany	August 2010	Low and inter-mediate grade chondrosarcoma of the skull base	Protons	C-ions
Randomised trial of proton versus carbon ion radiation therapy in patients with chordoma	Heidelberg University, Germany	July 2010	Chordoma of the skull base	Protons	C-ions
First French prospective randomised study of the medical and financial potential of carbon ion therapy	Lyon University Hospitals	2016	Adenoid cystic carcinoma and sarcomas	C-ions	IMRT
Prospective trial comparing carbon ions to IMRT[b] in pancreatic cancer	NCI[i], USA	2016	Locally advanced pancreatic adenocarcinoma	C-ions[d]	X-rays[d]

Acknowledgement

Thank You