Particle Therapy
Physics, Biology and Clinical application

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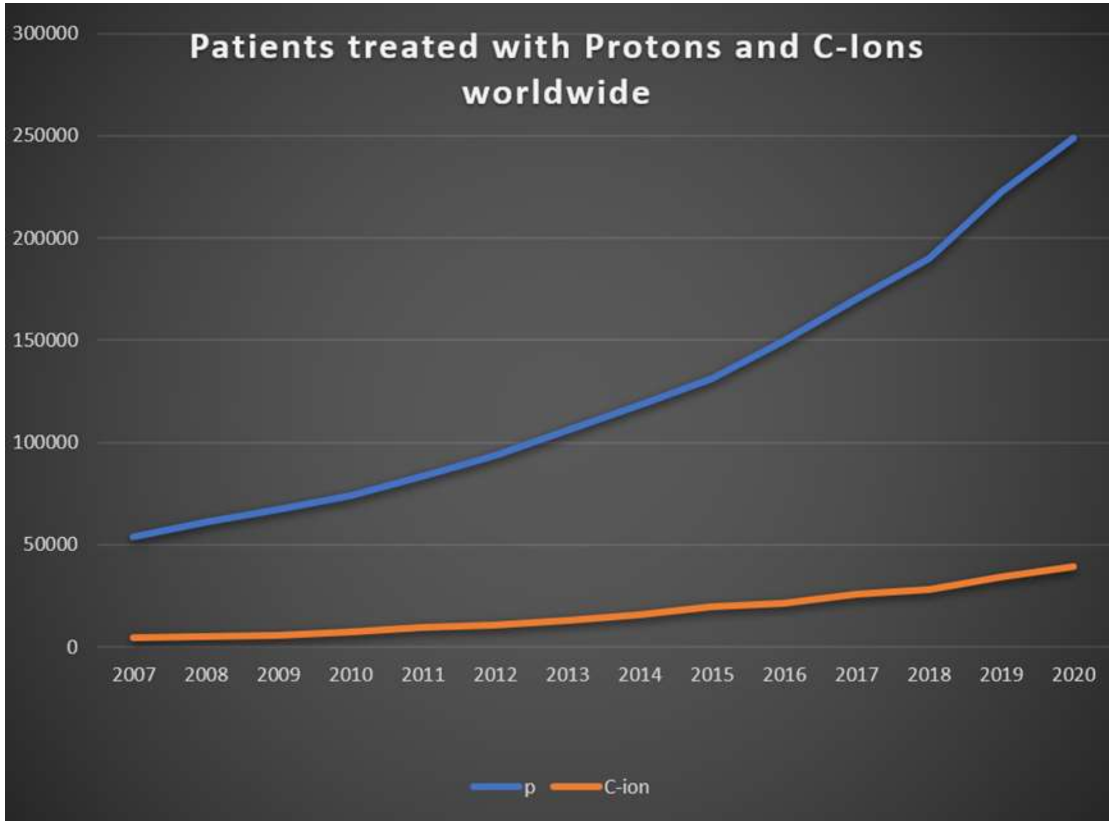
Patients treated with Protons and C-Ions worldwide
300000
250000
200000
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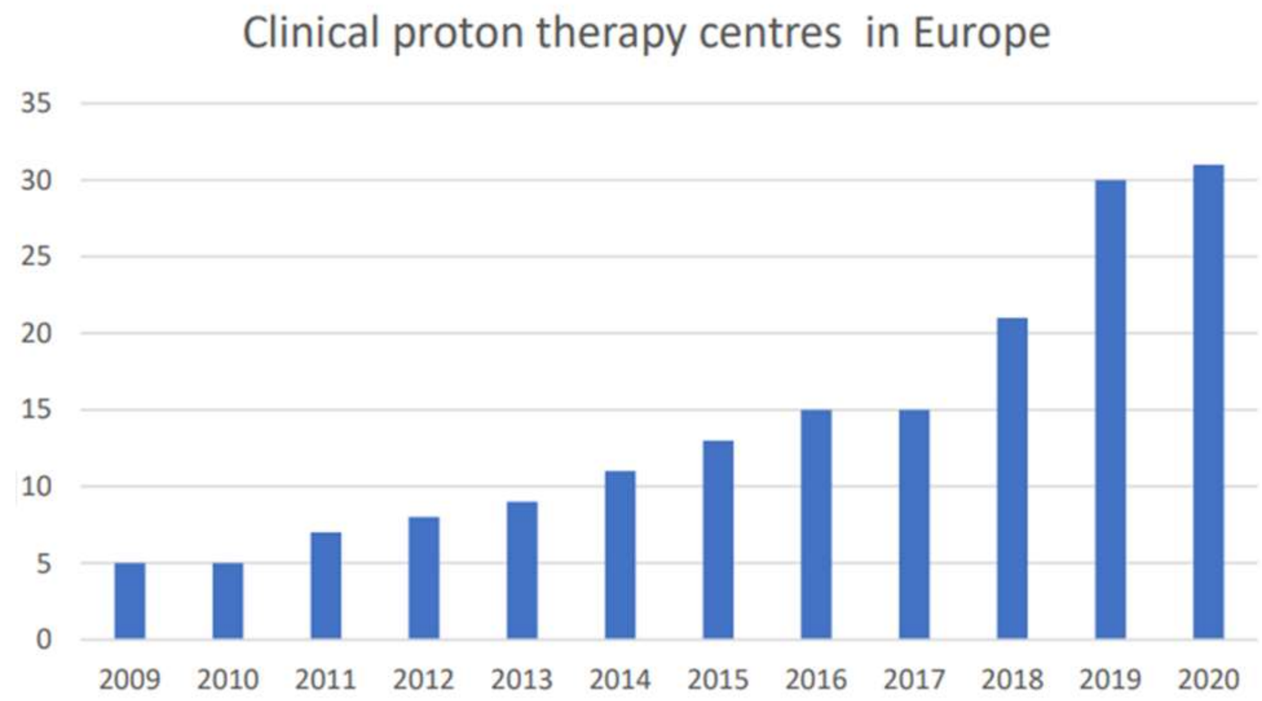
100000
50000
0
2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020
p
C-ion


Clinical proton therapy centres in Europe
35
30
25
20
15
10
5
0
2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020

Proton Centers in India

2019

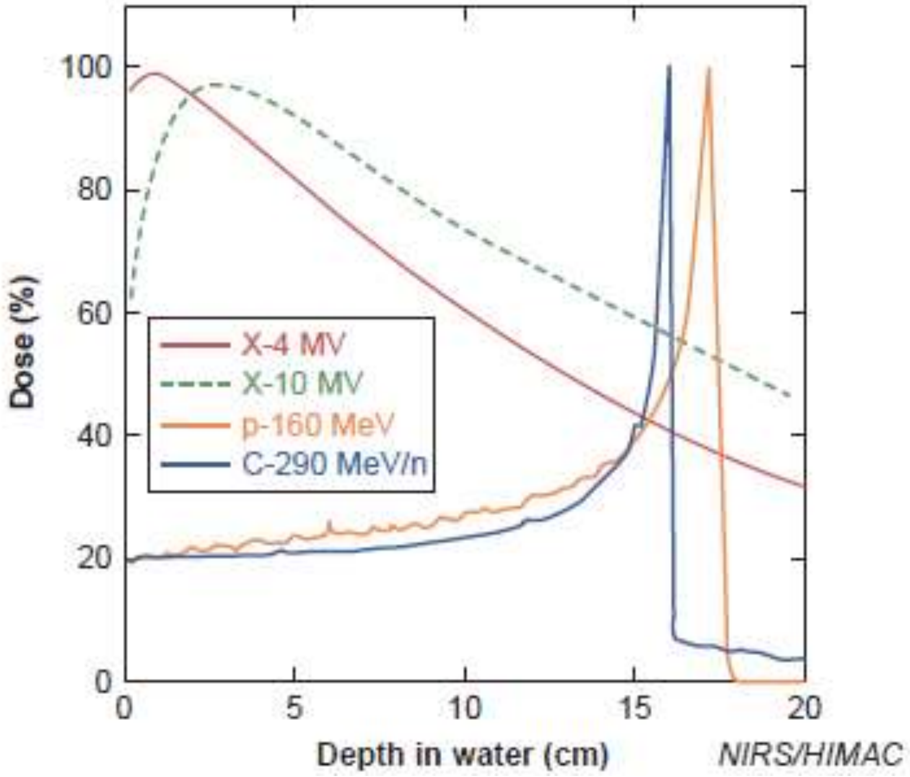
2023

Particle therapy in LMIC

- ✓ Significant variability in terms of population, resources, demography, health care infrastructure,disease presentation, and outcomes.
- ✓ Several cities now have multiple high-end linacs and advanced therapeutics comparable with HICs.
- ✓ With the improvement in purchasing power of the middle class, a large section of the population is now aspiring for world-class health care within their reach

Why Particle Therapy?

- Particles have definite range.
- Photon does not stop at a definite depth.
- Particle dose at depth(around target) is greater than the superficial dose.
- Photon dose is much less at depth as compared to D max.



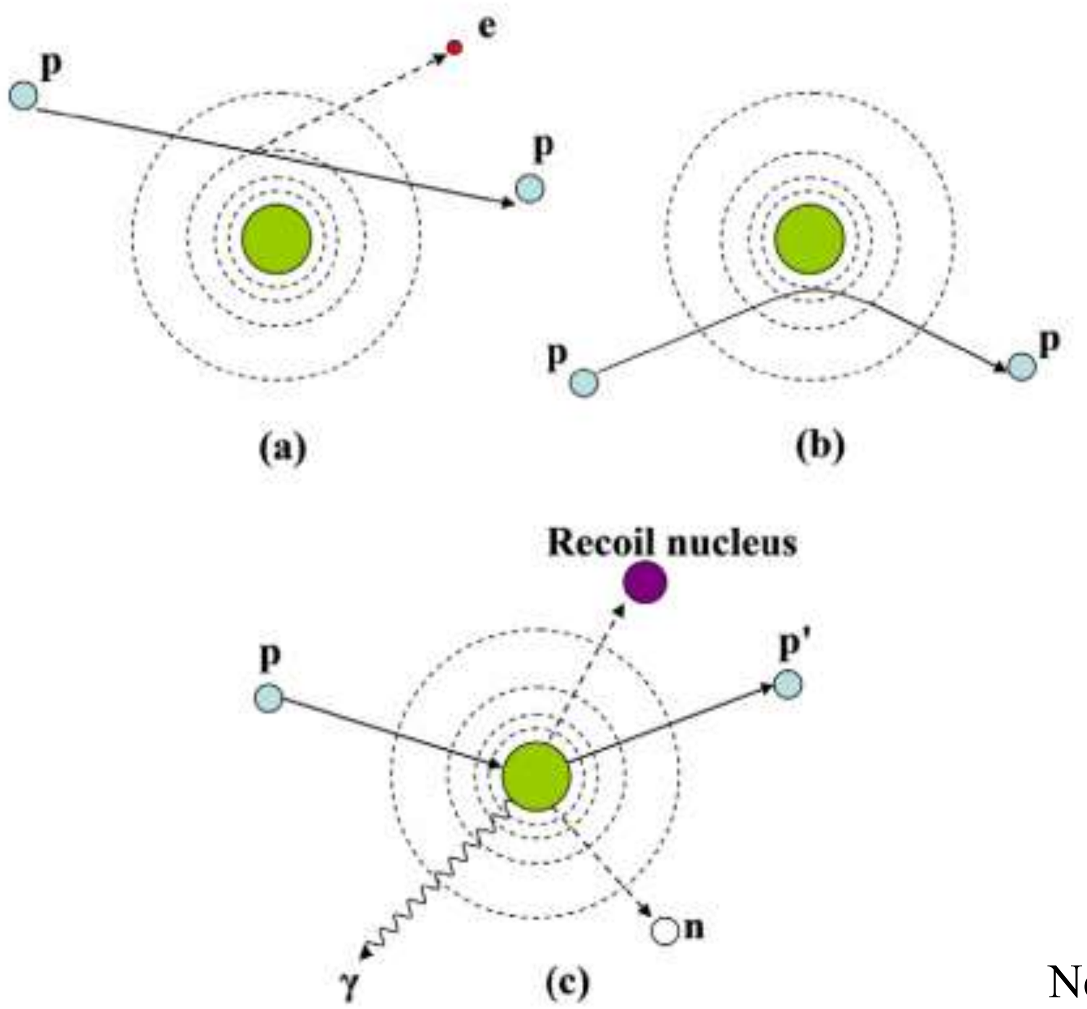
Principles and Practice of Radiation Oncology 6th edition

Interaction of photons with matter

- Photoelectric effect
- Compton Effect
- Pair production

- Photon absorbed or scattered, out of the beam.

Interaction of particles with matter



- Energy loss via inelastic Coulomb Interaction
- Elastic Coulomb interaction, owing to the large mass of the nucleus, deflects the particle from its original path
- Removal of primary proton and creation of secondary particles via non-elastic nuclear interaction
- Bremsstrahlung at therapeutic range negligible.
- Particle stays within the beam

Newhauser et al. Phys. Med. Biol. 60 (2015) R155–R209

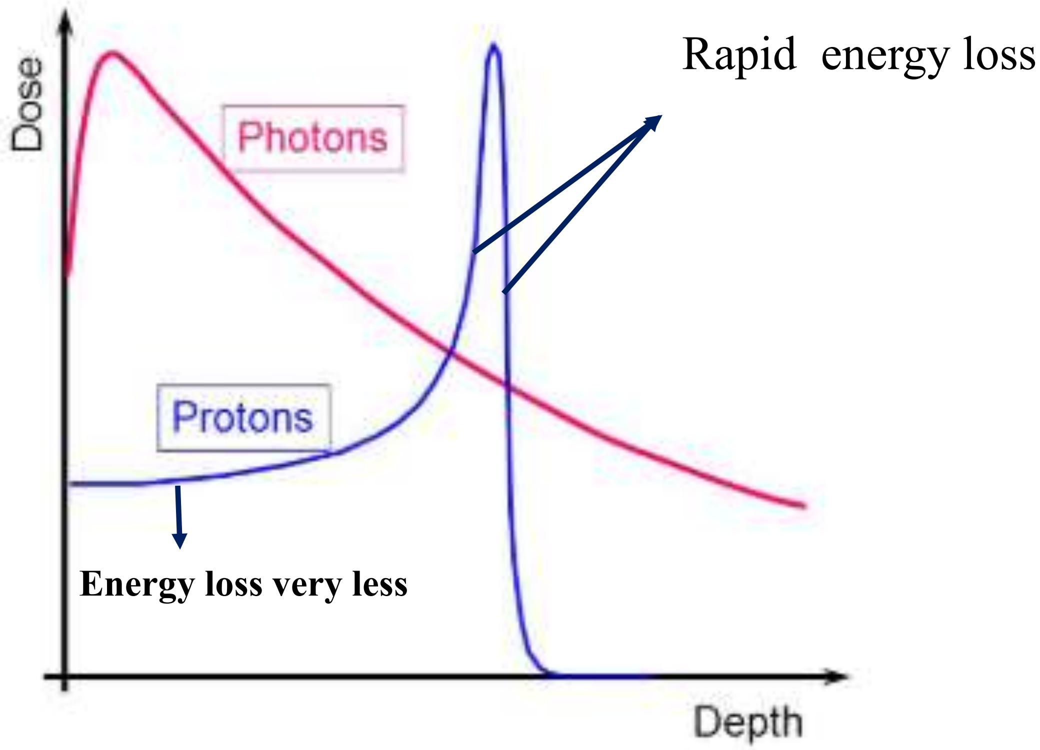
Pattern of energy deposition of particles

- Pattern of dose deposition with particles differ significantly.

- Particles are much heavier as compared to electrons.

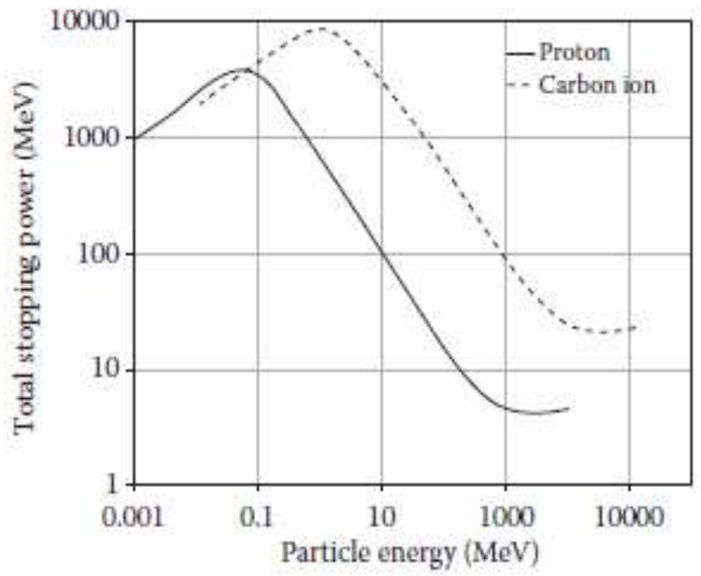
- As particles traverse matter, they lose energy primarily through interactions with atomic electrons.

- Due to the significantly larger mass of particles relative to electrons they lose only a small portion of their energy in each interaction (in contrast to x-rays) and experience only small directional changes.



Stopping power of Particle

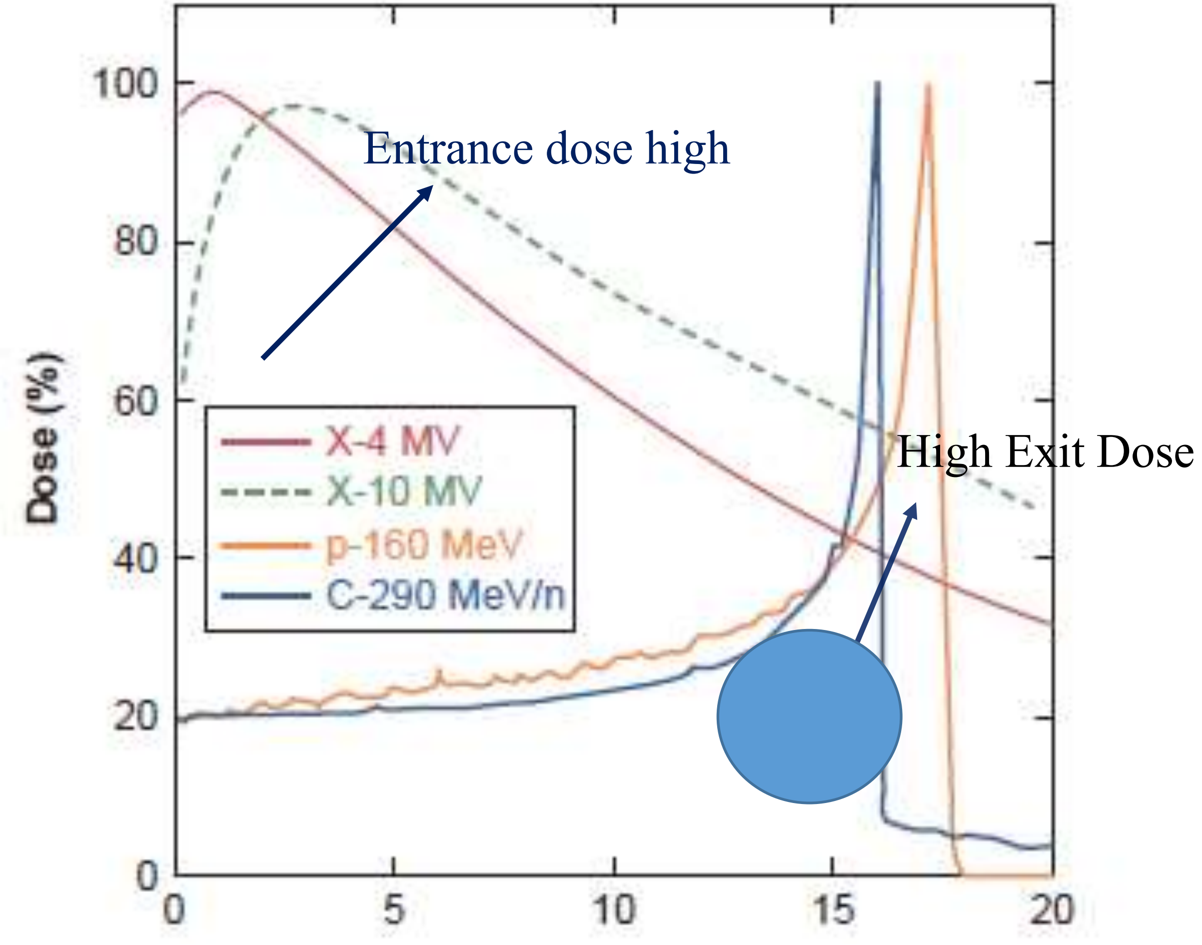
- When a fast charged particle enters a medium, it interacts with the electrons and nuclei of the medium
- Loses part of its energy in each interaction
- The rate of transfer of energy per unit distance is known as Stopping Power.
- Expressed by Bethe- Bloch Formula.
- Stopping power proportional to Z^2/V^2
- Atomic number (Z) of Carbon 6 times more than proton



Proton and Carbon Ion Therapy William R Hendee

Stopping power and Bragg Peak

- Greater the velocity of the particle, the smaller the energy deposited per unit distance
- Low energy deposition at small depths where the particles have their highest energy and velocity.
- Steep energy deposition towards the end of the range where little energy remains.
- Leads to pristine Bragg Peak.



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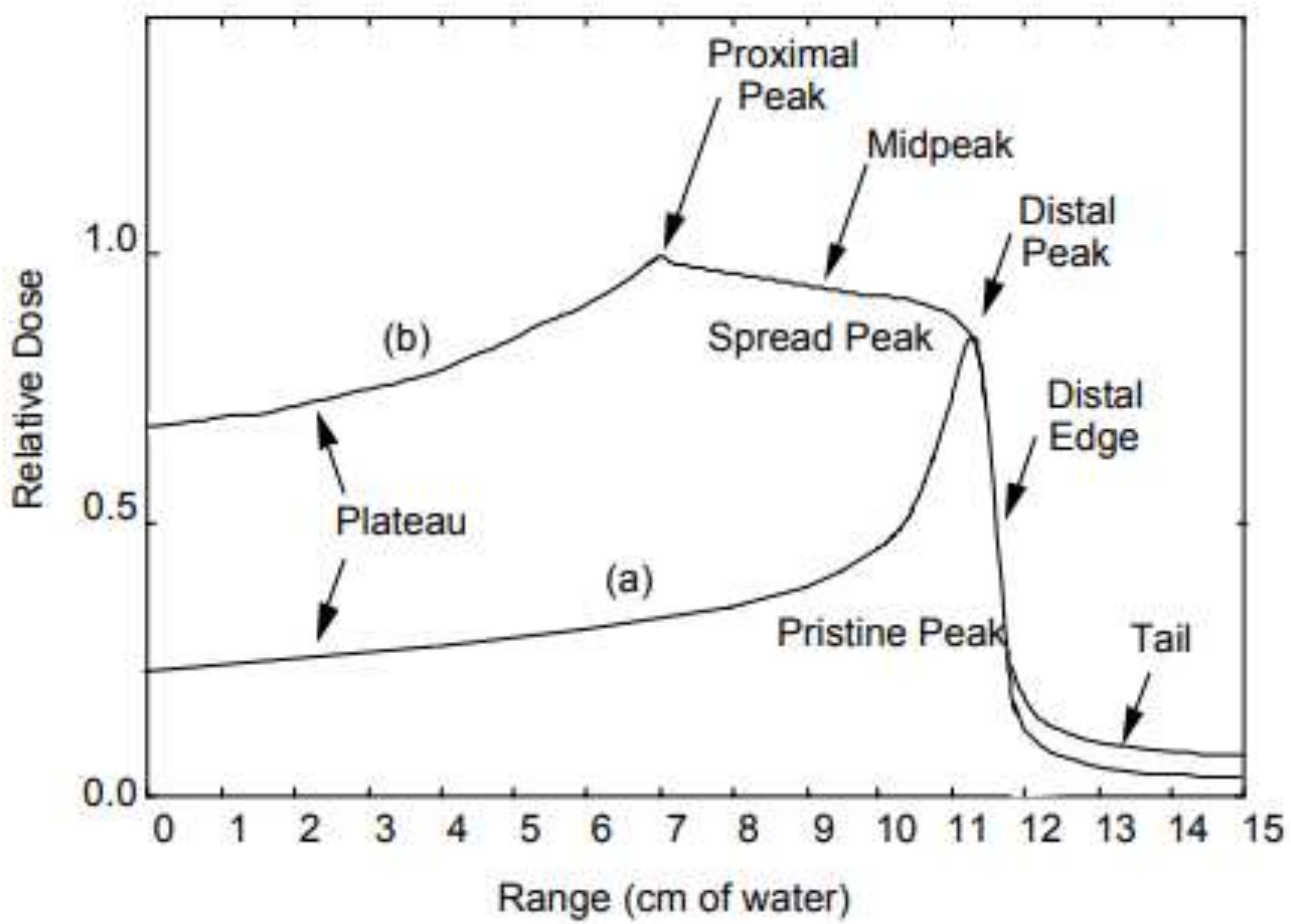
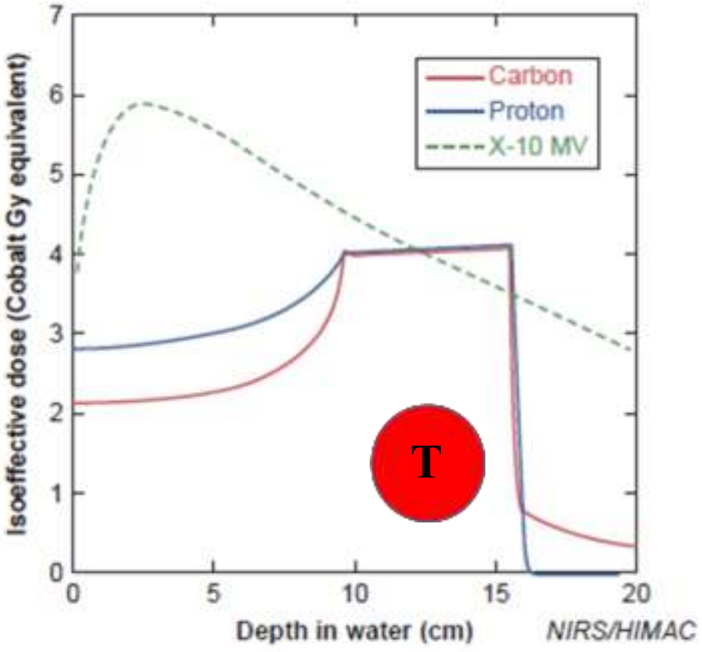
Anatomy of Bragg Peak



IAEA Dose reporting in Ion Beam Therapy 2007

Spread of Bragg Peak

- Narrow pristine Bragg Peak is not wide enough to cover the target volume.
- Need to spread the Bragg Peak.
- SOBP can be created in two ways:

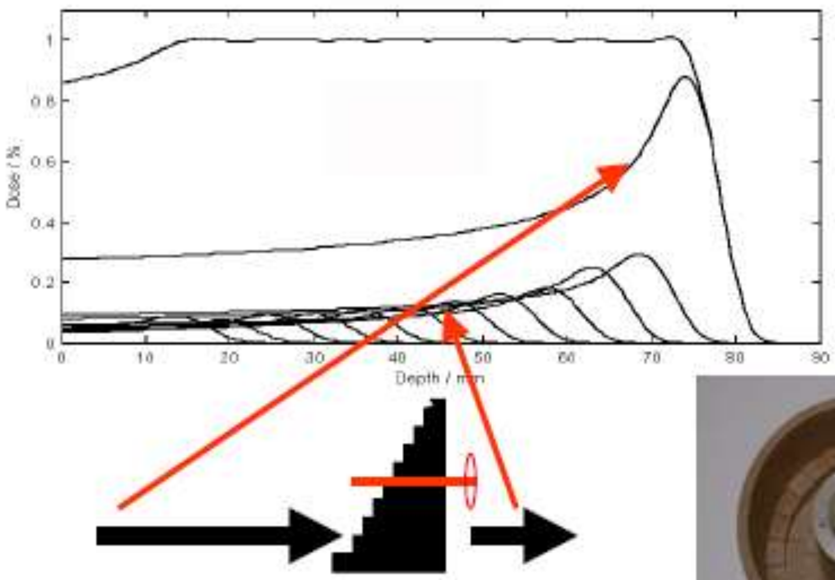


✓ Degradation of the energy by different energy degraders.

✓ Energy modulation from the accelerator and superimposition of different Bragg Peaks.

Range Modulator or Ridge filter

- The incident proton beam forms an SOBP by sequentially penetrating absorbers of variable thickness.
- Through Range Modulator or Ridge Filter.
- Each absorber contributes an individual pristine Bragg peak curve to the composite SOBP.
- A set of pristine peaks is delivered with decreasing depth and with reduced dose until the desired modulation is achieved

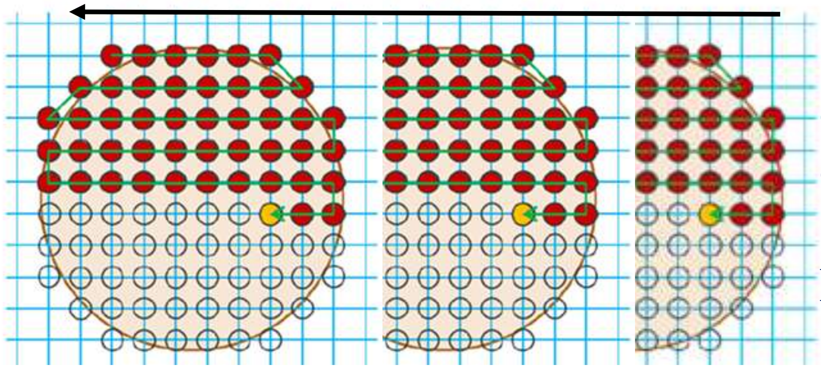


A modulator wheel combines variable thickness absorbers in circular rotating tracks that result in a temporal variation of the beam energy.

Courtesy Paganetti and Bortfield: Proton Beam Radiotherapy State of Art

Scanning and SOBP

- Generate a narrow mono-energetic "pencil" beam and to scan it magnetically across the target volume.
- The beam is scanned in a zigzag pattern in the x-y plane perpendicular to the beam direction.
- The depth scan (z) is done by means of energy variation.
- The method requires neither a collimator nor a compensator.
- One starts with the deepest layer (highest energy) and does one x-y scan.
- The energy is then reduced, the next layer is painted, and so forth until all 20-30 layers have been delivered.
- Each layer may be delivered multiple times to reduce deliverv errors and uncertainties.



Scanning from higher energy layer to lower energy layer

Deep to superficial

Paganetti and Bortfeld: Proton Beam Radiotherapy

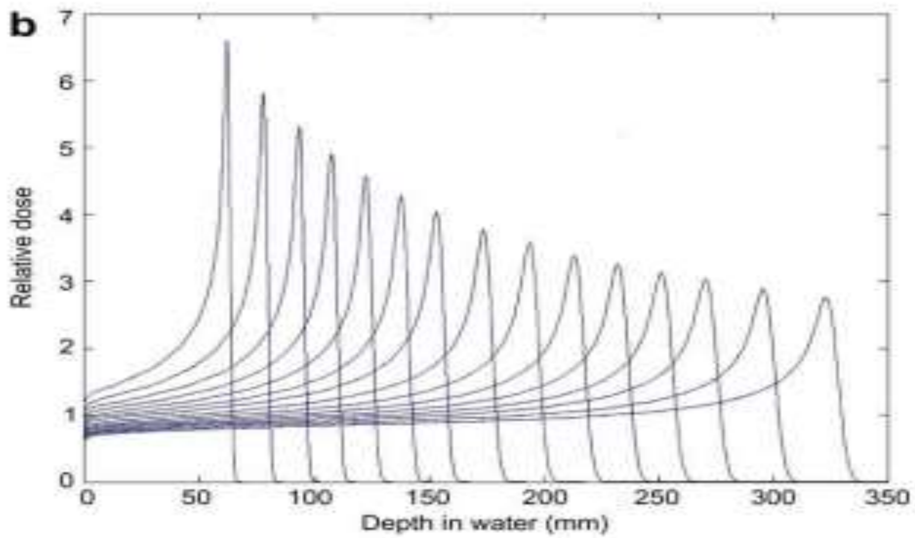
Energy Straggling and Bragg Peak

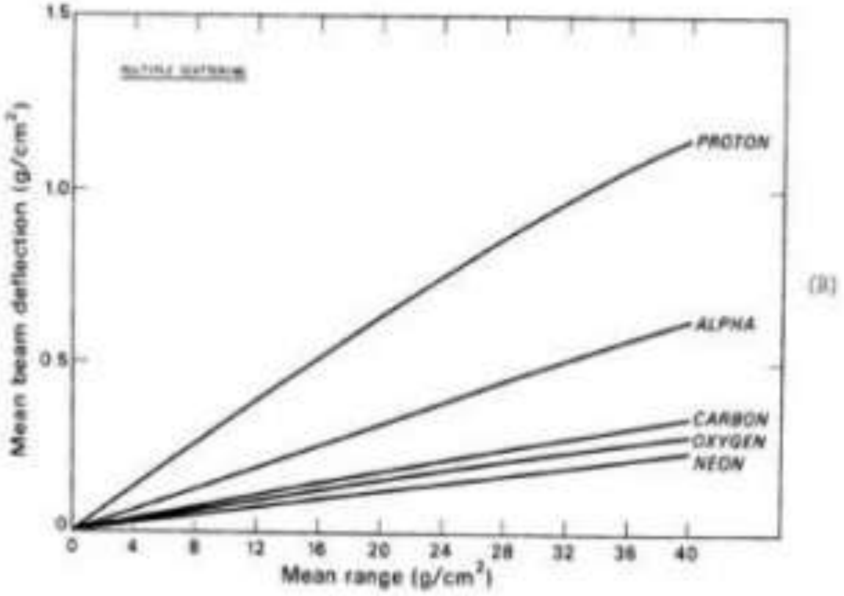
- Range Straggling is the dispersion of the path length of a particle beam due to statistical fluctuations in the energy-loss process.

- The relative height of the Bragg Peak with respect to entry dose decreases with the beam energy due to energy straggling and nuclear interactions.

- Increase in width of the Bragg Peak with beam energy.

- Proportional to range, R, and inversely proportional to the square root of the particle mass number

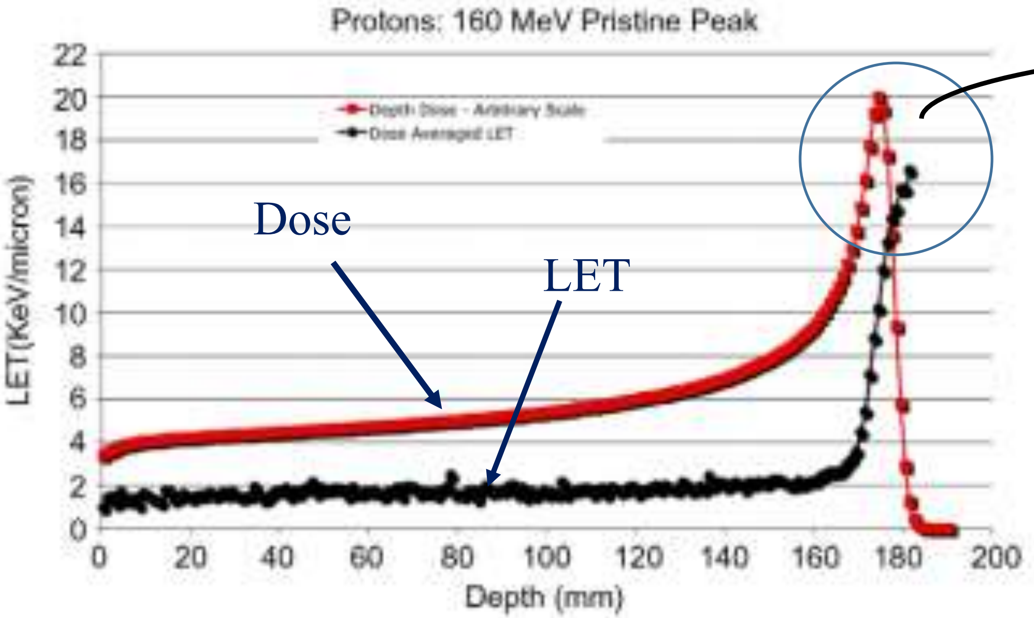




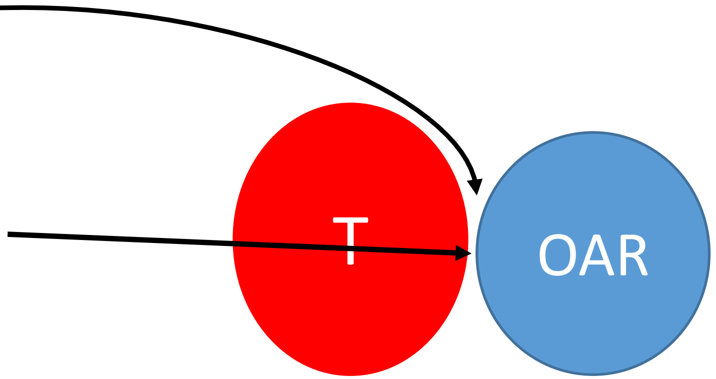
IAEA Dose reporting in Ion Beam Therapy 2007

LET and Depth Dose Relationship

- LET increases with depth on a curve similar to that of dose .
- The upswing in LET occurs at a slightly greater depth than dose and continues slightly beyond the dose peak.
- This results in an increased dose on the declining edge of the peak and a very short extension of penetration of the biologically effective dose.



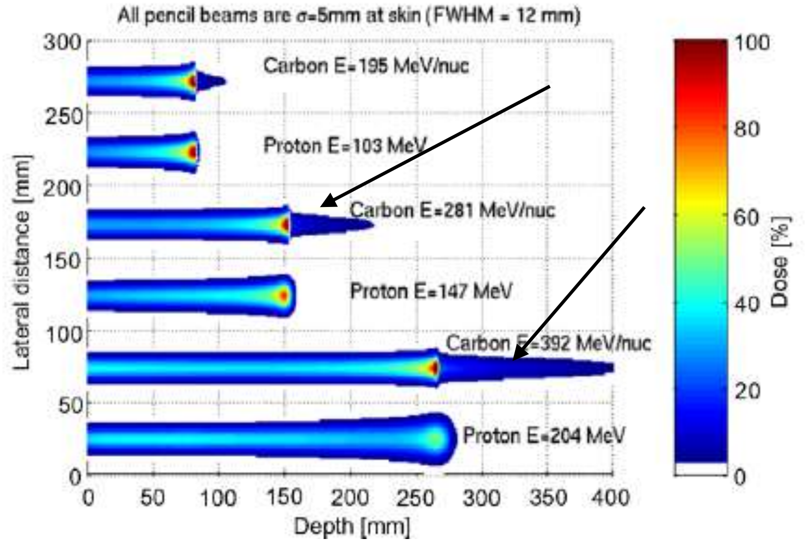
H Suit et al Radiotherapy and Oncology 95(2010) 3-22

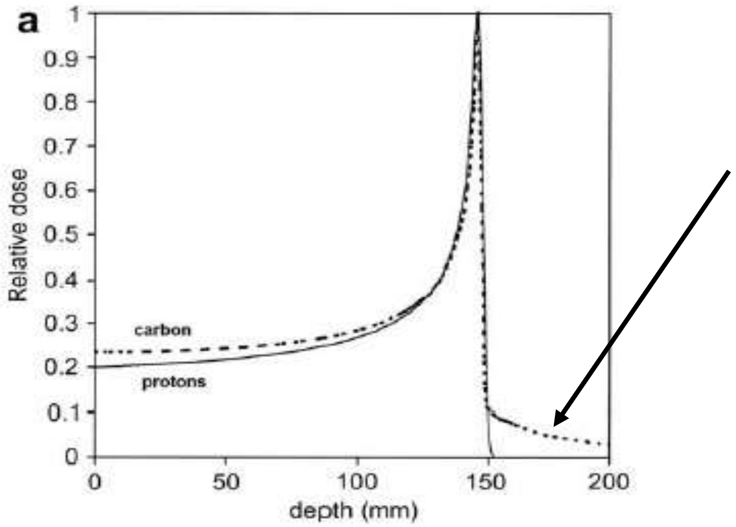


If the OAR is adjacent to the target and the beam is perpendicular to the OAR be cautious always because of high LET at target OAR interface

Fragmentation tail

- The tail exists for Carbon Ion due to the nuclear interaction with the atoms in the irradiated medium.
- These fragments are intermediate to low energy ions of boron, lithium, helium and protons.
- Tail contains very low physical dose with high RBE . Biological effective dose is low.
- Included in the Carbon Ion treatment planning system.
- Proton has no fragmentation tail.

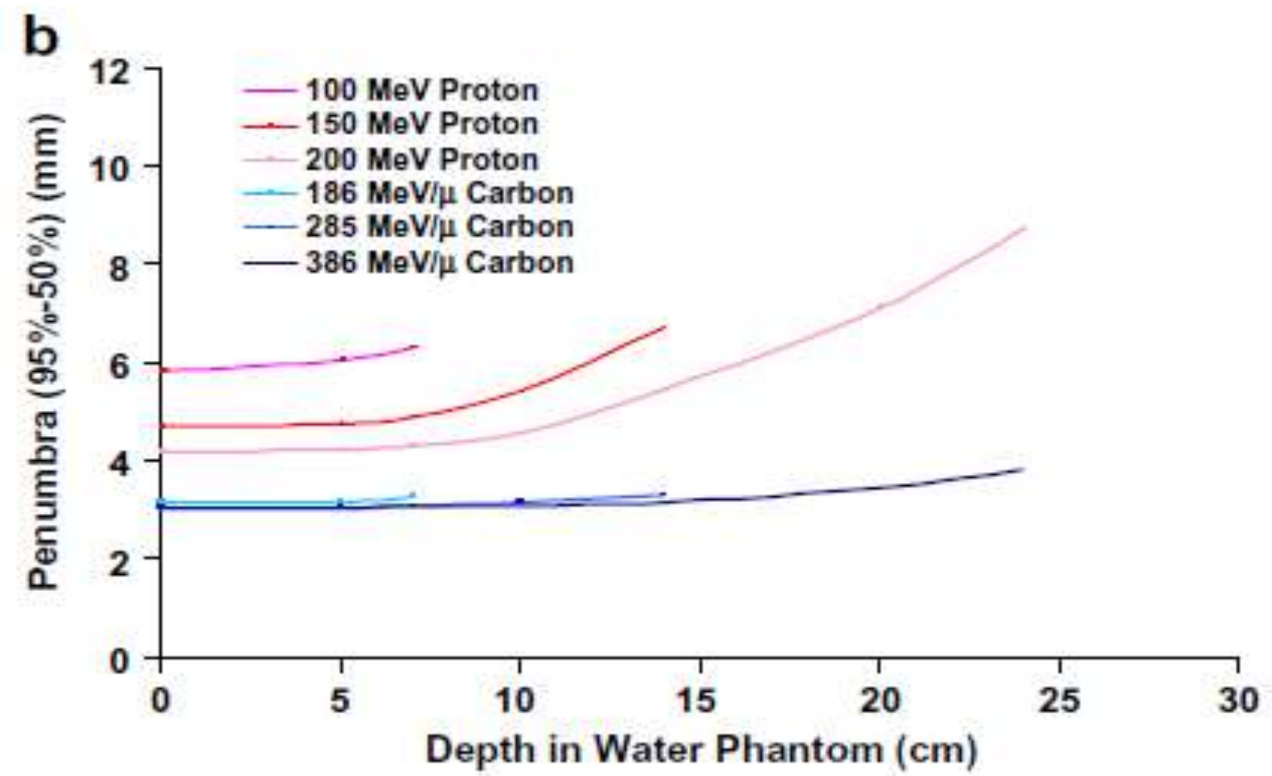




H Suit et al Radiotherapy and Oncology 95(2010) 3-22

Penumbra

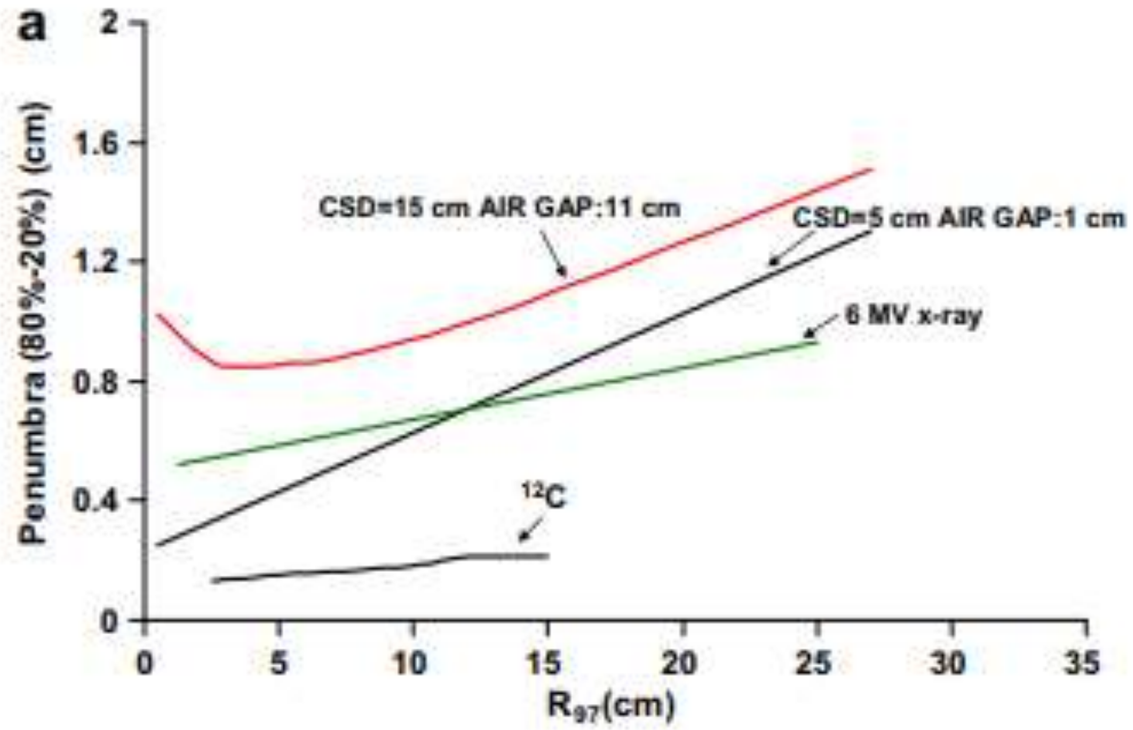
- Carbon Ion has much sharper penumbra as compared to protons.
- This advantage of CIRT increases at depth
- Carbon has 12 times higher mass than proton
- Extent of beam blurring inversely proportional to square of mass number
- Even when the range is same Bragg peak more narrowly concentrated for Carbon.

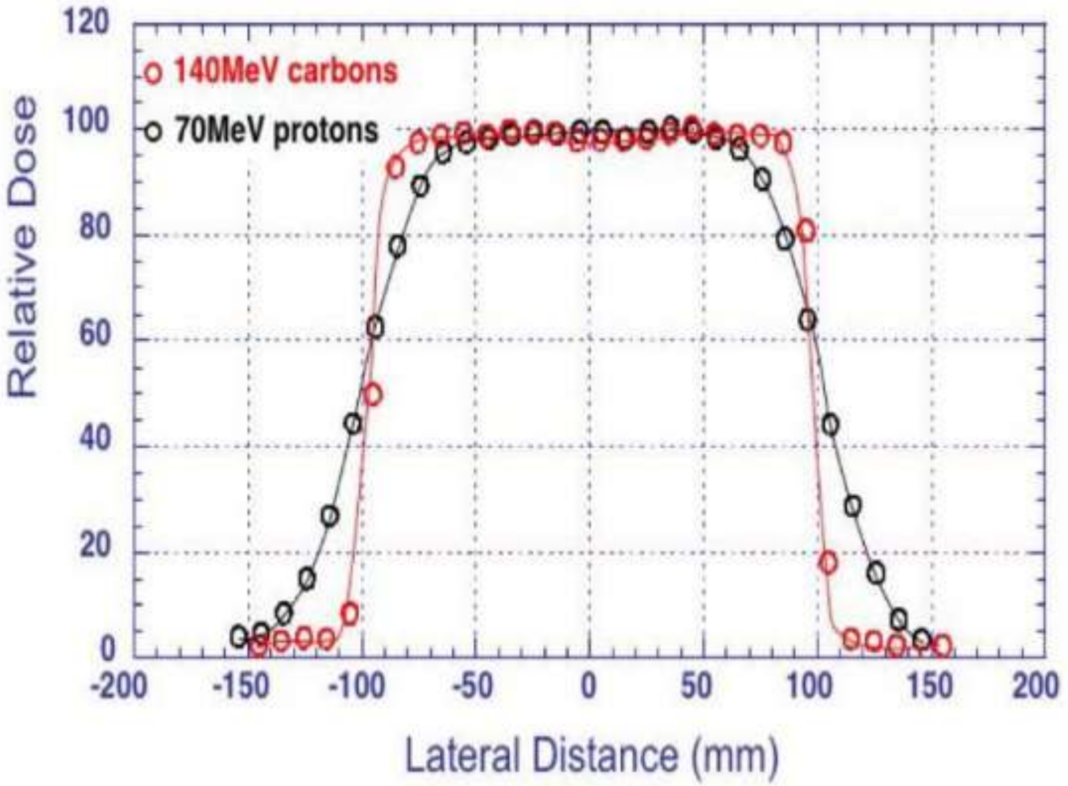


H Suit et al Radiotherapy and Oncology 95(2010) 3-22

Penumbra

- For proton 6.5 mm at 20cm depth. Dominated by multiple Coulomb Scattering.
- Carbon 1.5 mm at 20 cm depth.





H Suit et al Radiotherapy and Oncology 95(2010) 3-22

Energy and Beam Range

- For Carbon 430Mev/n- 30 cm
- For Proton 220Mev/n- 30 cm

- SOBP width for CIRT- 4-15 cm depending on the energy.

- We can treat a tumor of maximum up to 30 cm depth with particles.

Carbon vs Proton

Properties	Carbon	Proton
Charge	6	1
Mass	12x proton	1x proton
Charge to mass ratio	Less	More
LET	Mixed, 36 times more than proton	Low
RBE	2-5	1.1
Range straggling	Less	More
Bragg Peak sharpness	Sharper	Less sharp
Penumbra	Sharper	Less sharp
Dose gradient	3 times steeper than proton	Less
Fragmentation tail	Present	Absent
DNA damage	Complex clustered damage	Easily repairable
DNA Repair	Less effective	More effective
Oxygen dependence	Less	More
Cell cycle dependence	Less	More
Hypofractionation	More effective	Less effective

Accelerators for particle therapy

➢Linear Accelerator

- Beam energy is not enough high for the treatment.
- It is difficult to change the beam energy.
- It is used for the injector of the synchrotron.

➢Cyclotron

- Beam energy is not enough high for the treatment. (under development)
- It is difficult to change the beam energy. (separator prob.)
- Output beam is continuous and stable.

➢Synchrotron

- Output beam is quasi-continuous.
- Beam energy is enough high and variable.

Cyclotron

- Consists of dipole magnets designed to produce a region of uniform magnetic field.

- Dipoles are placed with their straight sides parallel but slightly separated

- An electric field is produced across the gap by an oscillating voltage.

- Particles injected into the magnetic field region move on a semicircular path until they reach the gap where they are accelerated.

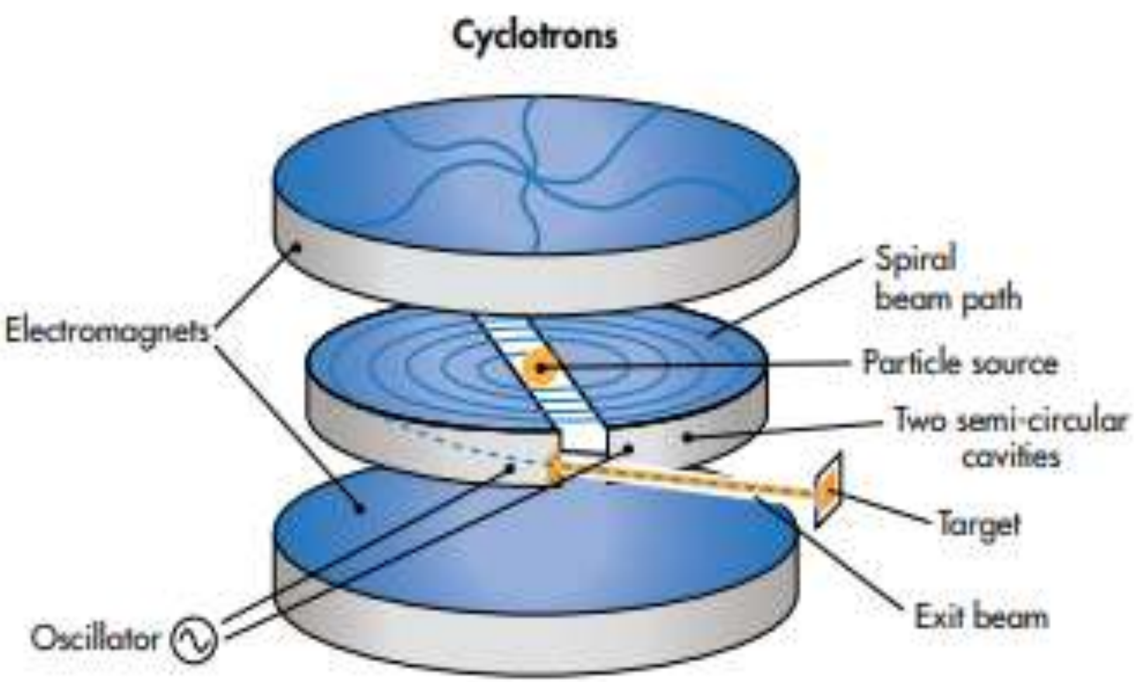


Image Courtesy Symmetry Magazine

Cyclotron

- Since the particles gain energy they will follow a semi-circular path with larger radius before they reach the gap again.

- In the meantime the direction of the field has reversed and so the particles are accelerated again.

- Cyclotron extracts particle with fixed energy.

- Able to deliver beam energy up to 230Mev.

Synchrotron

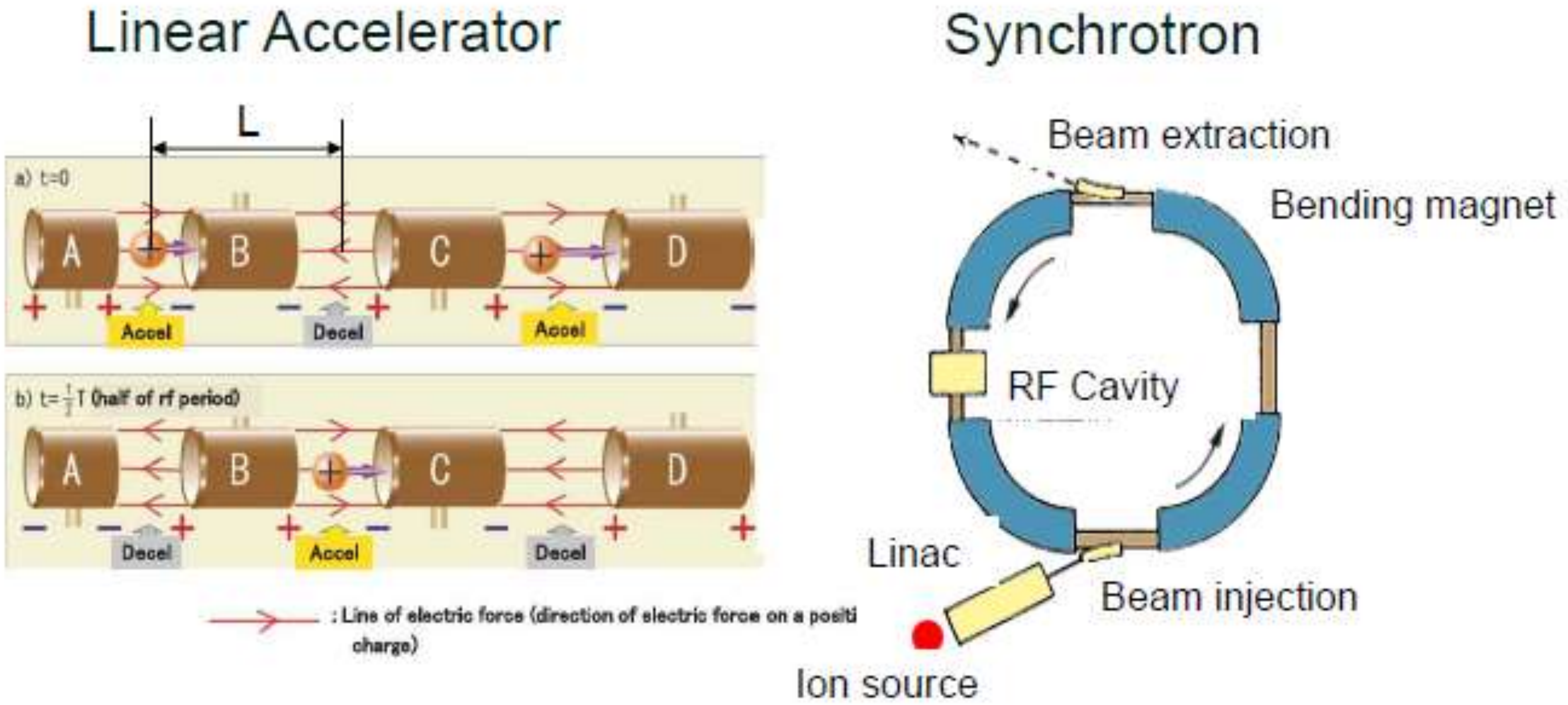
- The synchrotron is a ring (or some closed shape) of magnets.

- The beam is injected from outside the synchrotron and then circulates around the ring repeatedly through the accelerating structure.

- In order to keep the beam within the closed ring, the magnetic field of the magnets must increase in strength in conjunction with the beam energy increase.

- Thus, the beam is contained within the ring as its energy increases. When the beam reaches the desired energy, it is extracted.

Synchrotron



Because of synchronization and field strength and energy these accelerators are called synchrotrons.

This technique allows the production of particles with a variety of energies

Image Courtesy Dr Shirai NIRS

Synchrotron and Carbon Ion

- Carbon ion has charge of 6 and it is a 12 times heavier as compared to proton.
- Stopping power of Carbon more as compared to proton at a particular velocity.
- To deposit most of the energy at a certain depth carbon has to be accelerated with more energy which is possible with synchrotron .
- All facilities of Carbon Ion currently has synchrotron set up.

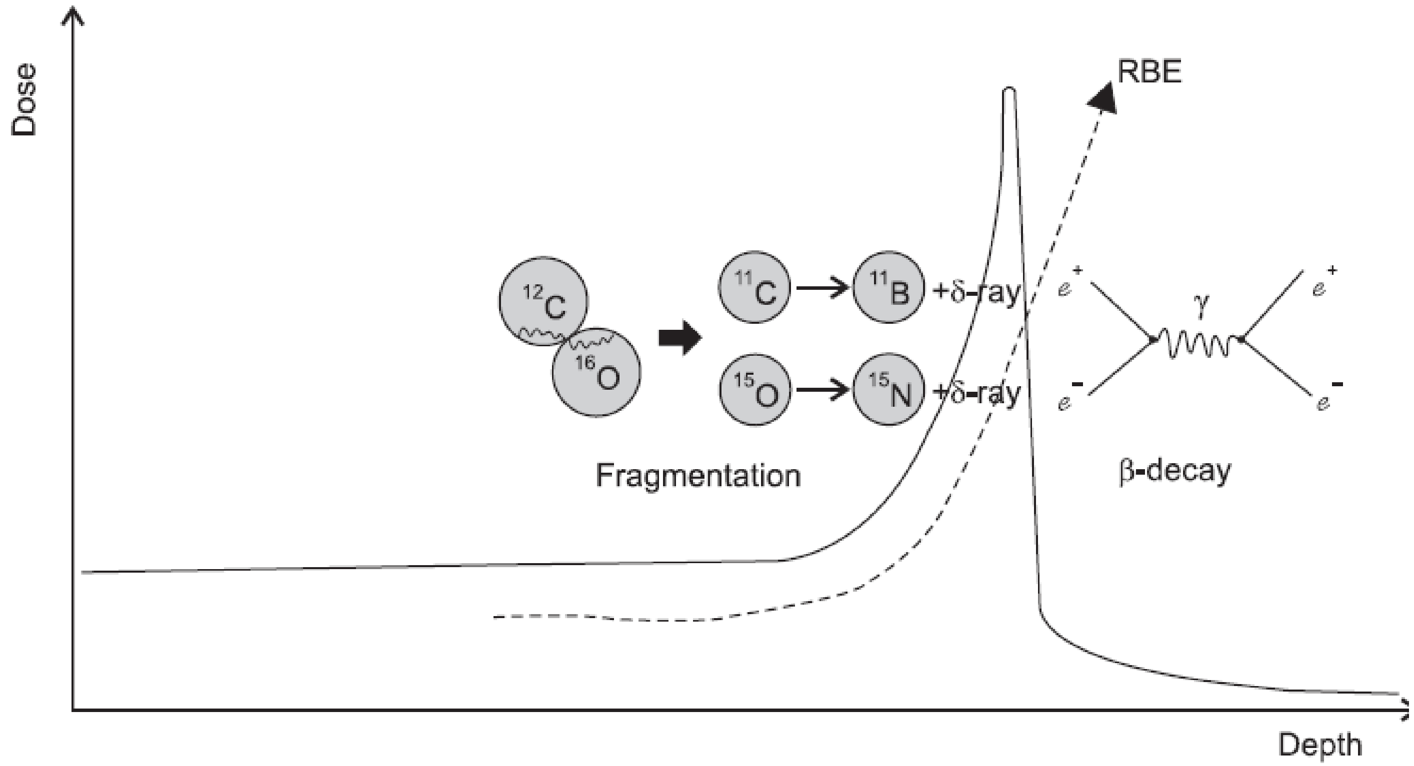
Cyclotron vs Synchrotron

Cyclotron	Synchrotron
Unable to change the energy of the particles directly	Directly can change the particle energy
Energy degradation required for changing the energy	Energy degradation not required for changing energy
Cyclotron delivers a continuous beam	Synchrotron delivers a pulsed beam
Scanning beam difficult	Scanning beam easy to deliver
Accelerates particles with less energies	Can accelerate particles with much more energies
Suitable for protons but not for carbons	Suitable for both protons and carbons

In Beam PET and in vivo Dose verification

- Unique to Carbon Ion is Fragmentation tail.
- Some of the nuclear fragment is positron emitting isotopes 10C and 11C which can be used for PET Scan.
- In beam PET can be used for verification of Carbon Ion particle range.
- In beam PET is different from normal PET.
- In CIRT in beam PET enables the range of applied dose ,quality of applied dose, to be verified from outside of the patient without applying any additional dose.

In Beam PET and in vivo Dose verification



Carbon hits oxygen and both atoms are fragmented into boron and nitrogen generating delta radiation.

The delta radiations decay to emit gamma radiation which can be used as the source of PET-CT in treatment field

Basics of particle therapy Physics   Park et al. Radiation Oncology Journal

Take Home Messages

- Characteristic Bragg Peak of particles.
- Spread of Bragg peak done by energy degradation or scanning.
- Carbon Ion has fragmentation tail which proton does not have.
- Penumbra and range straggling more for protons.
- Lateral width is also important as SOBP; follows Gaussian distribution
- Synchrotron can deliver both proton and carbon ; however cyclotron is suitable only for proton , not for carbon.
- Carbon fragmentation can be used for in beam PET which has important role in image verification, yet to be implemented in clinics.

- Questions

- What are the advantages of particles over photons?
- What are the physical advantages of carbon over proton?
- Which accelerator is preferred for Carbon Ion delivery and why?
- How is Synchrotron different from Cyclotron?
- What are the different ways of creating Spread of Bragg Peak in particle therapy?

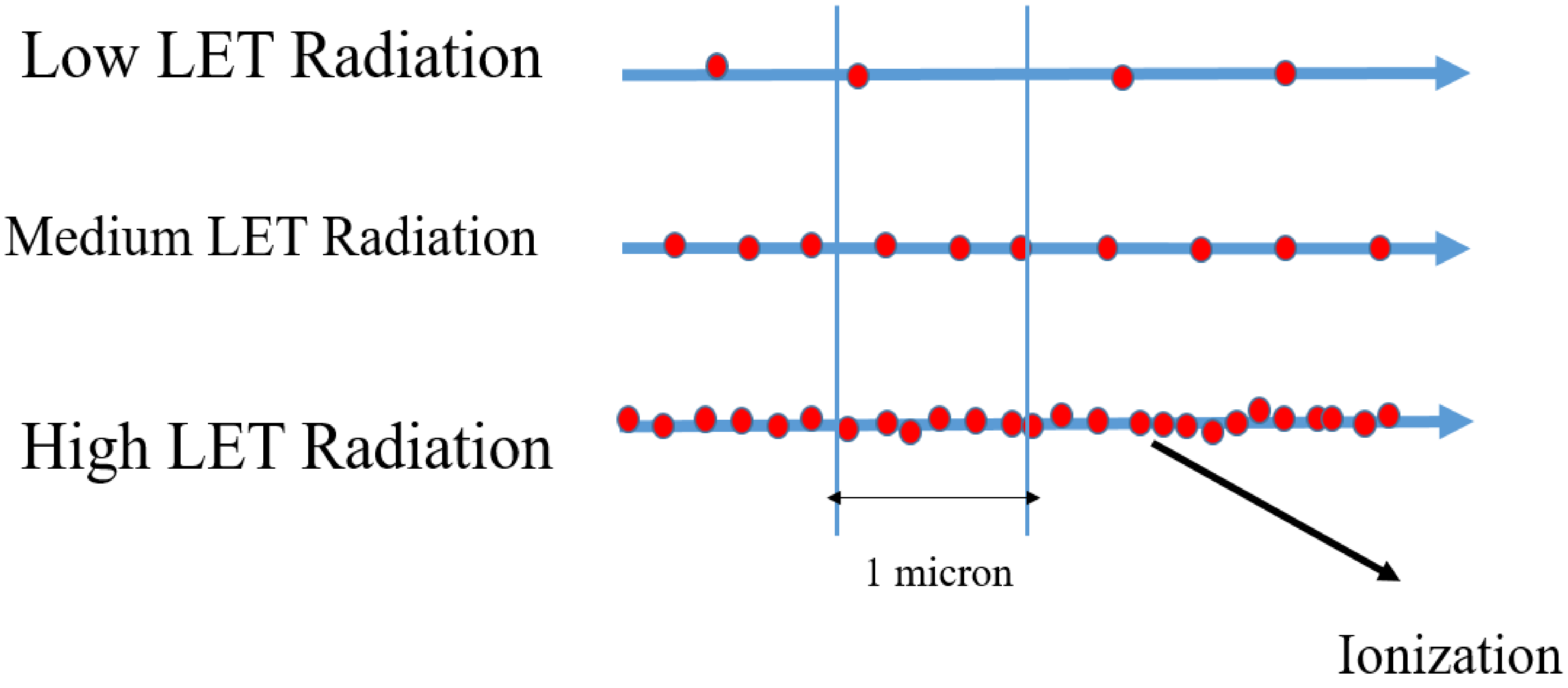
Particle Radiobiology

Biology of particle therapy: Areas to explore

- Biological efficacy increases with increase number of ionisations per distance---- Linear Energy Transfer(LET)
- Higher ionisation density for ions as for electrons/ photons---- higher relative biological efficiency (RBE)
- Ionisation density increases with atomic number---- higher RBE for heavy ions compared to protons.
- Ionisation density increases with decreasing energy-----higher RBE around the Bragg- peaks compared to the entrance channel

LET(Linear Energy Transfer)

LET: Energy deposited per unit length of track; expressed as dE /dL



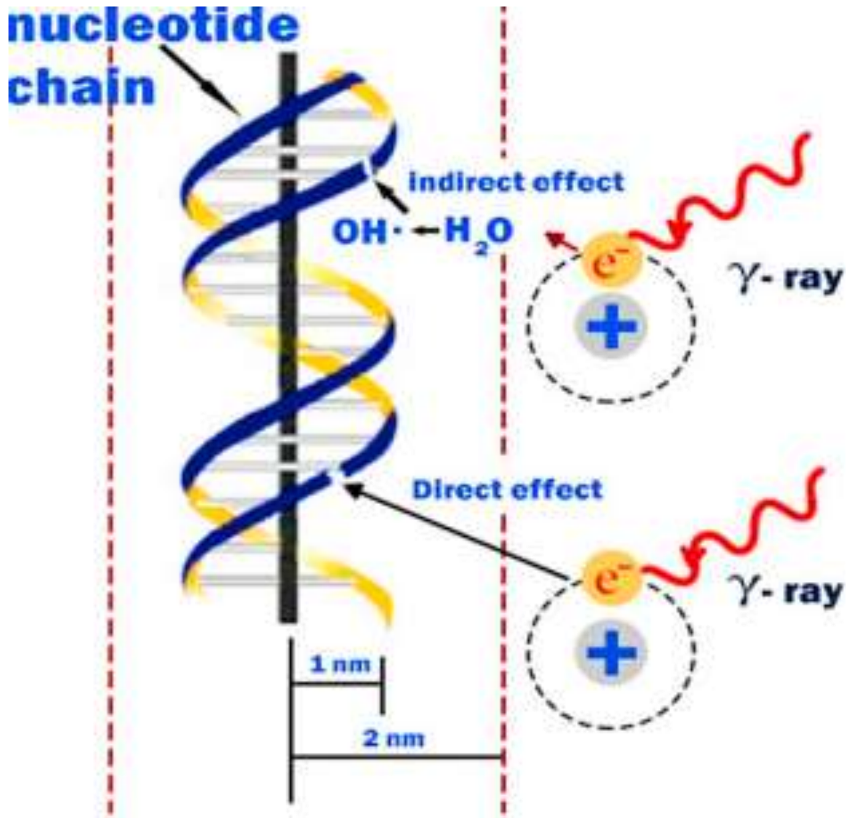
LET and Ion Beams

- Usually ion beams are classified according to their LET
- High LET >100kev/micron-Neutron
- Low LET <20 kev /micron- Proton

- Carbon has mixed LET . Low LET in the entrance channel and high LET in the target volume. Change in LET is very high.
- Carbon incorporates the good tumor response known for neutrons but without severe side effects of neutrons

Fokas et al. Biochimica et Biophysica Acta 1796 (2009) 216-219

Indirect and Direct action of Radiation



- **Indirect action**

✓Damage to DNA by free radicals formed through the ionization of water molecules.

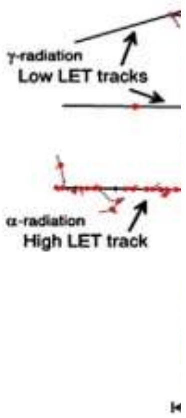
✓Dominant (2/3) for low-LET radiations

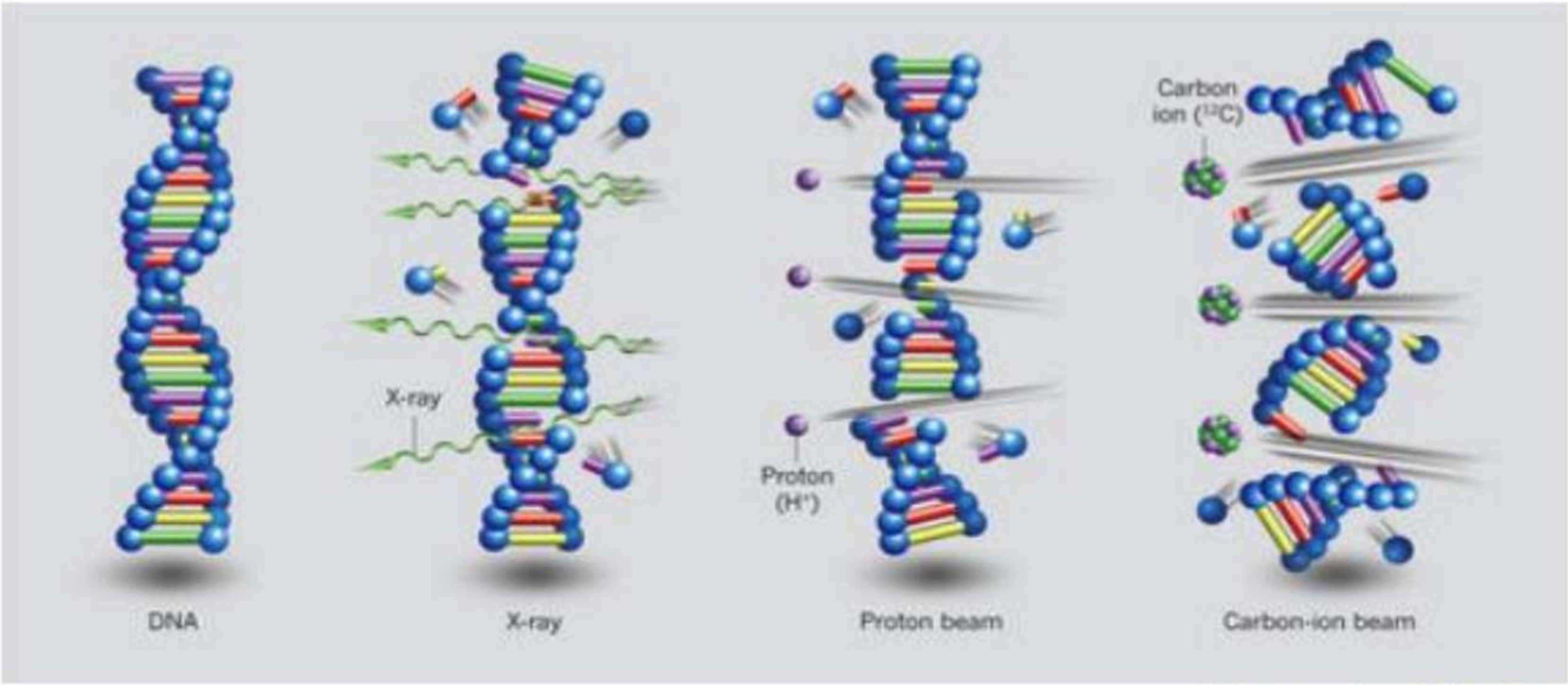
- **Direct action:**
- Damage to DNA by secondary electron resulting from absorption of radiation.
- Dominant for high LET Radiation

E.J. Hall, A.J. Giaccia, Radiobiology for the Radiologist, 7th ed., Lippincott, Philadelphia, 2012

LET and DNA Damage

DNA Damage Caused by X-ray, Proton, and Carbon





Nature, April 2014

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ced induces
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M.E. Lomax et al. / Clinical Oncology 25 (2013) 578-585

High and Low LET Radiation induced DNA Damage and its repair

- Low LET induced DSB typically repaired by NHEJ or both NHEJ and HR in GI ,S and G2 phase.

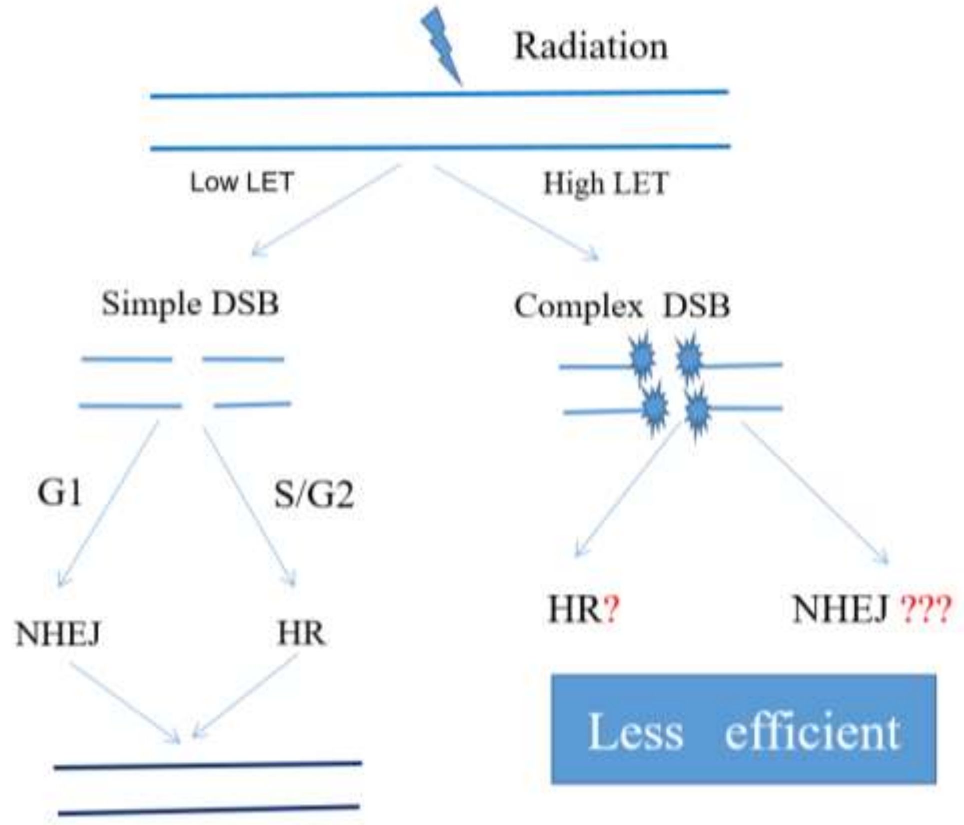
- High LET induced clustered DSB repair-

✓NHEJ suppressed

✓HR may be the preferred pathway

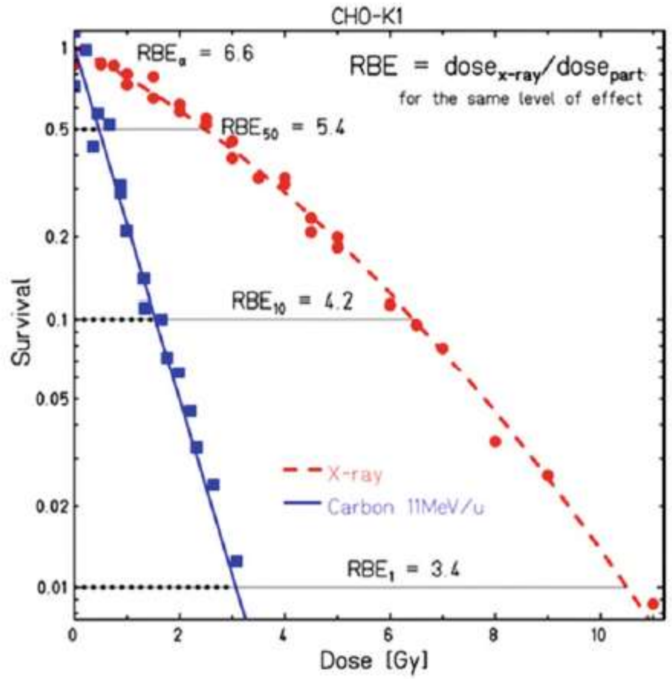
✓Less efficient repair mechanism.

✓Holds true for Protons and Carbons



Relative Biological Effectiveness(RBE)

- Ratio of the photon dose to any other test radiation dose to produce the same biological effect.
- RBE= D_{photon} / D_{ion}



Proton therapy versus Carbon Ion Therapy Advantages Disadvantages and Similarities
Marcos d Avila Nunes

LET and RBE

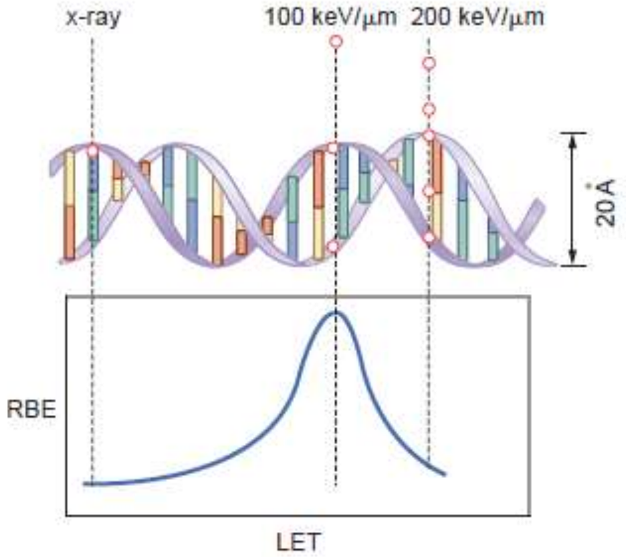
- As LET increases RBE increases
- Above 100 kev /micron overkill effect. RBE goes down with increasing LET

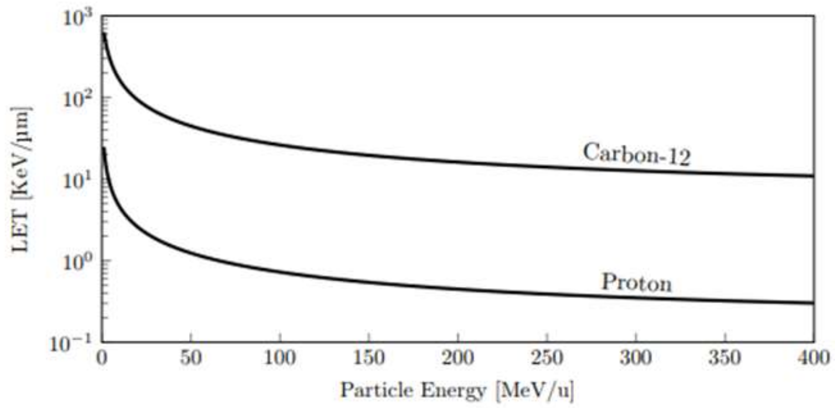
- In particle radiobiology no linear correlation between LET and RBE
- RBE depends on

✓Type of ion

✓Energy

✓Biological endpoint





A Comparison of Biological Dose Estimates in Proton and Carbon Ion Therapy Based on Averaged and Full Linear Energy Transfer Spectra E Rorvik

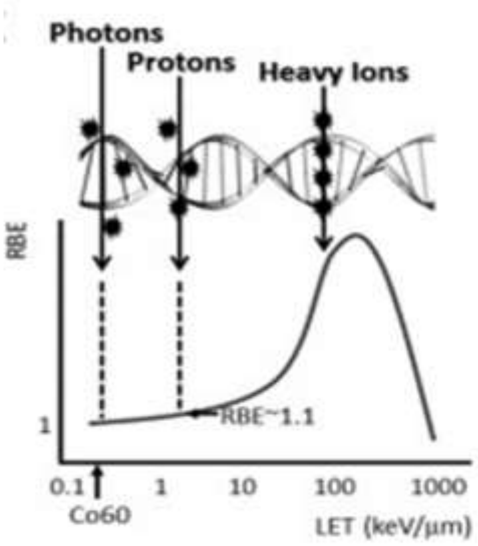
RBE of Proton and Carbon

RBE a complex function of LET, particle type, dose per fraction, tissue and cell type, oxygenation state, cell cycle phase, and the endpoint examined

PROTON

- Commonly reported RBE for Protons is 1.1
- RBE fixed
- Calculated at 10% survival
- Moving towards variable

RBE 1.1-1.8

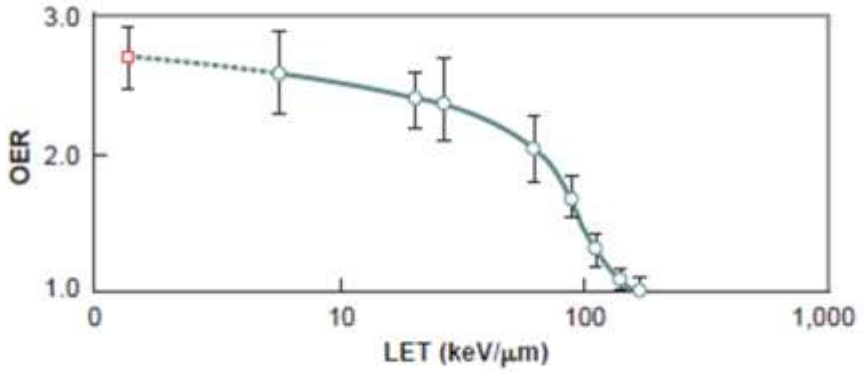


CARBON

- Accepted RBE for Carbon Ion 2-5
- Variable
- Biological end point Human salivary gland cells at 10% survival.

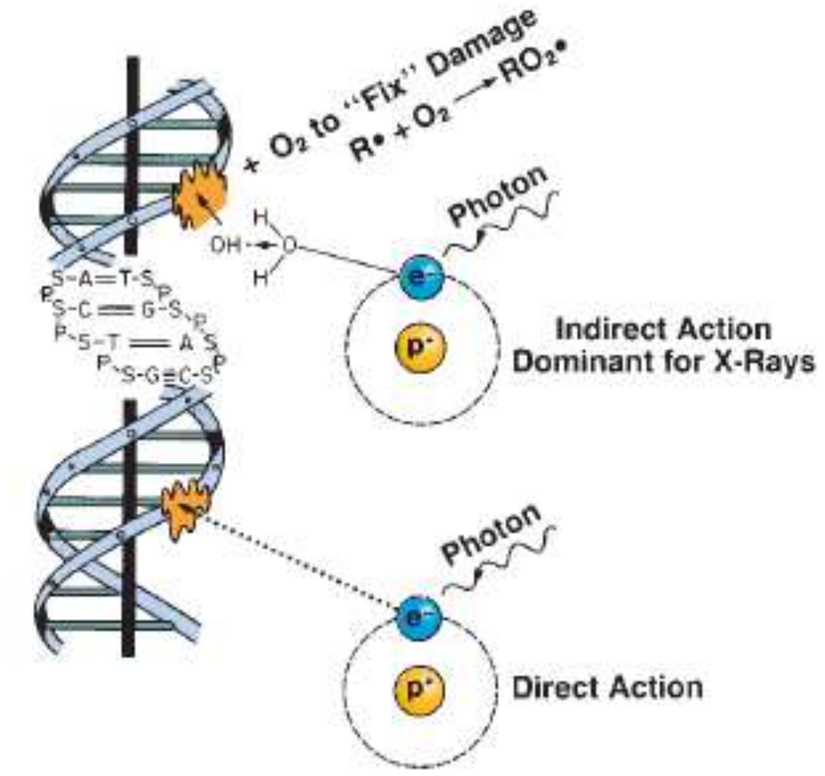
Hypoxia and Particle Therapy

- Hypoxia induced radioresistance major limiting factor for tumour control in radiotherapy.
- The increase of radioresistance quantified by OER.
- OER is ratio of isoeffective doses in hypoxic and fully oxygenated conditions.
- OER= $D_{\text{hypoxic}}/D_{\text{normoxic}}$
- LET and OER have an inverse relationship
- OER for proton =3 same as photon
- OER for carbon= 1-2.5



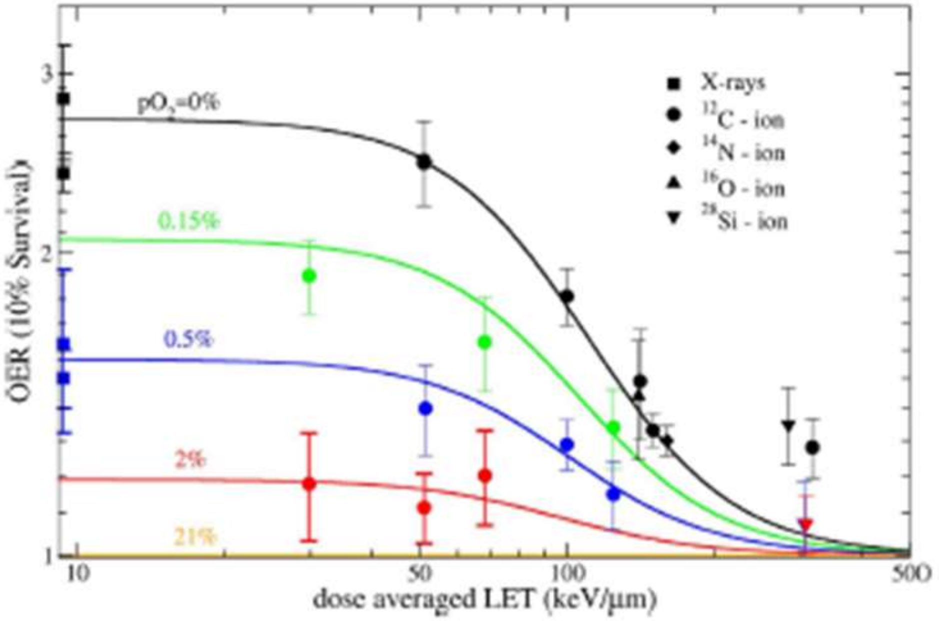
Hypoxia and Particle Therapy

- For Low LET Radiation indirect action is predominant.
- If molecular oxygen is present, organic peroxide is produced.
- Molecular O2 fixes or makes the DNA damage permanent caused by reactive oxygen species.
- Under hypoxic conditions DNA damage induced by low LET radiation can be more readily repaired.
- Direct action caused by high LET radiation (e.g. carbon) is less affected by the presence of oxygen. So OER is less.



LET,OER and LET Painting

- Particle therapy assumed to be especially effective against hypoxic tumours.
- OER drops to almost 1 when LET is over few hundreds kev/micron.
- The normal LET distribution in a typical carbon ion irradiation exceeds 100 keV/µm in a very small region of the target only.
- It is important to optimize theTPS accounting for both LET and *Po2*. Still experimental.



Walter Tinganelli Scientific Reports 2015

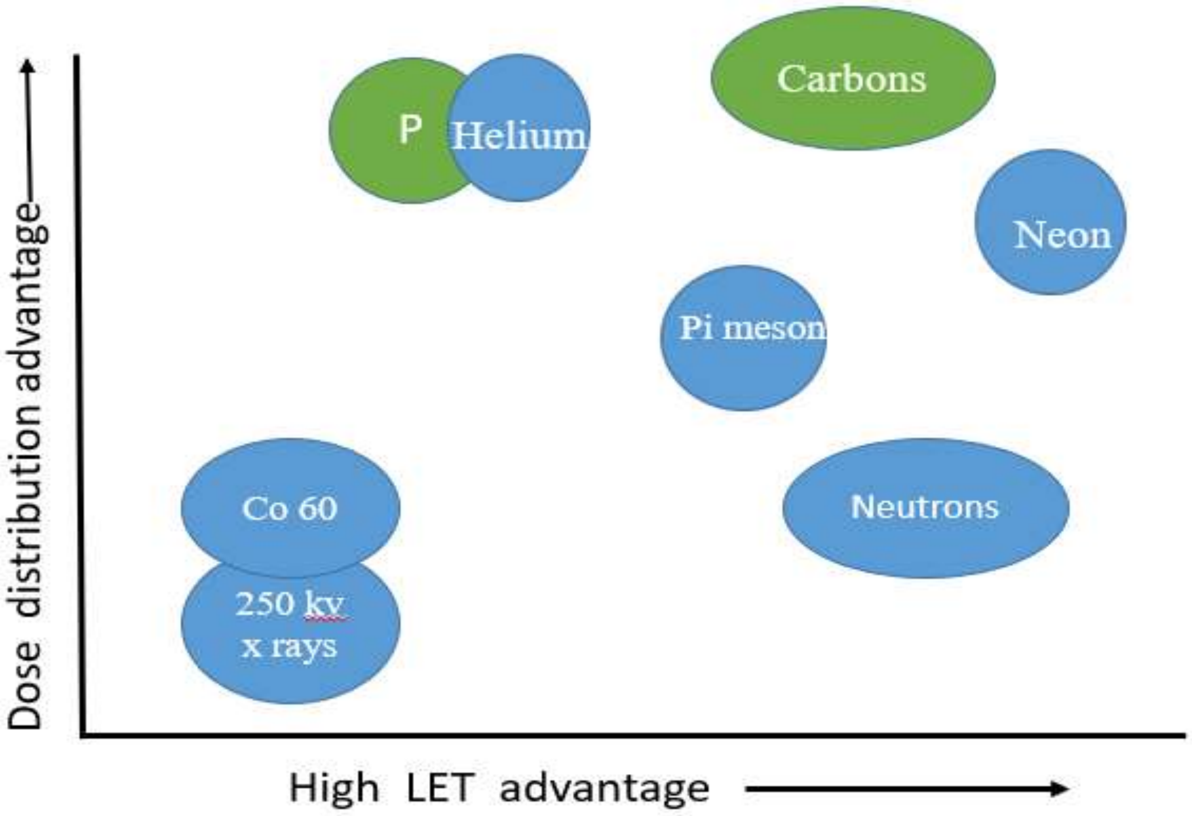
RBE Weighted Absorbed Dose

- RBE weighted absorbed dose is the product of absorbed dose D and RBE with respect to photons delivered under same conditions.
- DRBE= D X RBE
- Expressed as Gy RBE
- At present proton RBE is considered as 1.1 (fixed, variation not yet taken into consideration) , calculation is easy
- In Carbon RBE is variable ranging from 2-5, calculation is complex.
- The role of biophysical model is to take into account changeable biological effect appropriately in treatment planning.

The Different Profiles of Beams

Beams	Dose concentration	Relative Biological Effectiveness (RBE)
X-ray	poor	1.0
Proton	good	1.1
Carbon ion	good	3.0

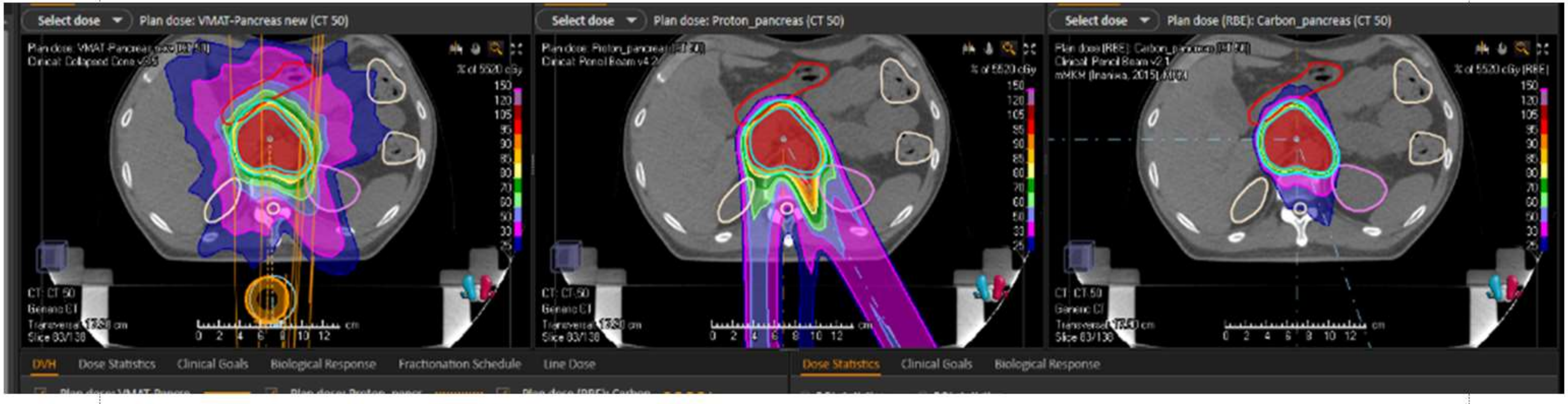
Which particle?



Raju et al 1974

Properties	Carbon	Proton
Charge	6	1
Mass	12x proton	1x proton
Charge to mass ratio	Less	More
LET	Mixed, 36 times more than proton	Low
RBE	**2-5**	**1.1**
Range straggling	Less	More
Bragg Peak sharpness	Sharper	Less sharp
Penumbra	Sharper	Less sharp
Dose gradient	3 times steeper than proton	Less
Fragmentation tail	Present	Absent
DNA damage	Complex clustered damage	Easily repairable
DNA Repair	Less effective	More effective
Oxygen dependence	Less	More
Cell cycle dependence	Less	More
Hypofractionation	More effective	Less effective

Photon Proton Carbon



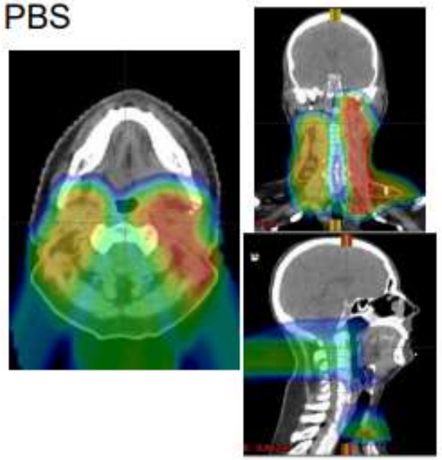
Bragg Peak matters!

Head and Neck

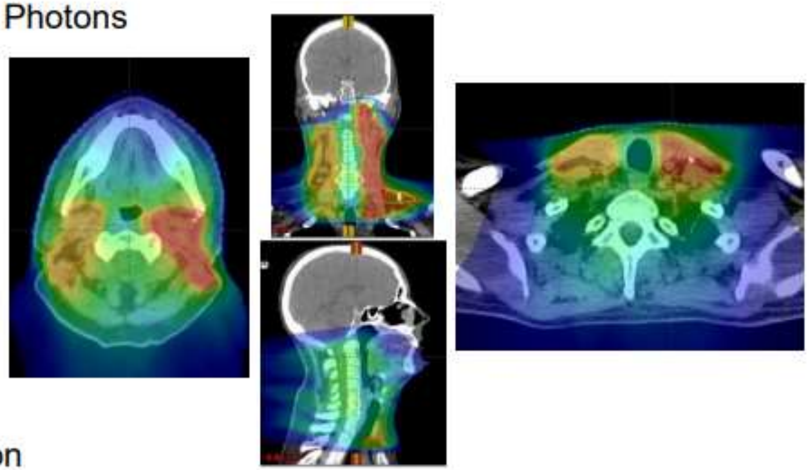
Why Proton in head and neck cancer?

- Treatment is morbid
- Increasing incidence
- Improving disease outcomes
- Many people cured, living longer after treatment
- Late toxicities are important

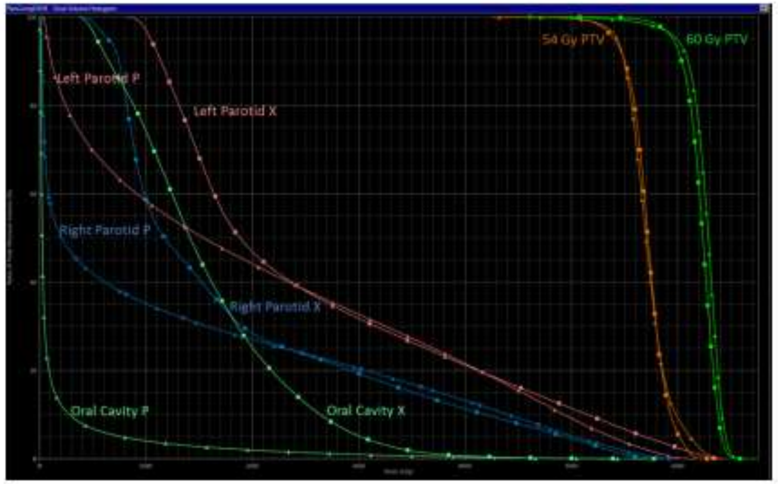
PBS



Photons



DVH Comparison



Courtesy: Dr Alexander Lin

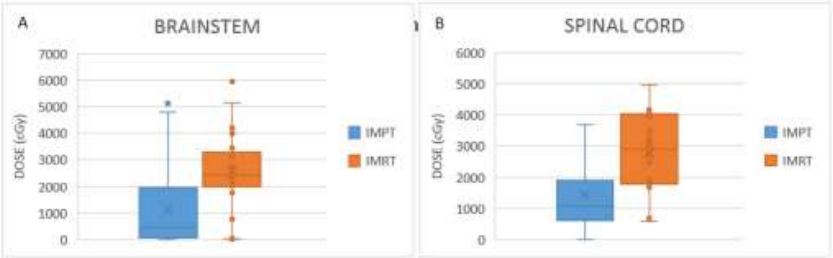


Fig. 1. Maximum DOSES FOR Brainstem (A) for 21 patients and spinal cord (B) for 21 patients.

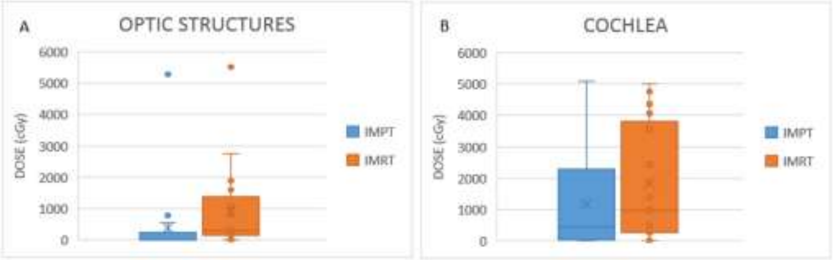


Fig. 2. Maximum doses for optic structures (A) for 21 patients and cochlea (B) for 21 patients.

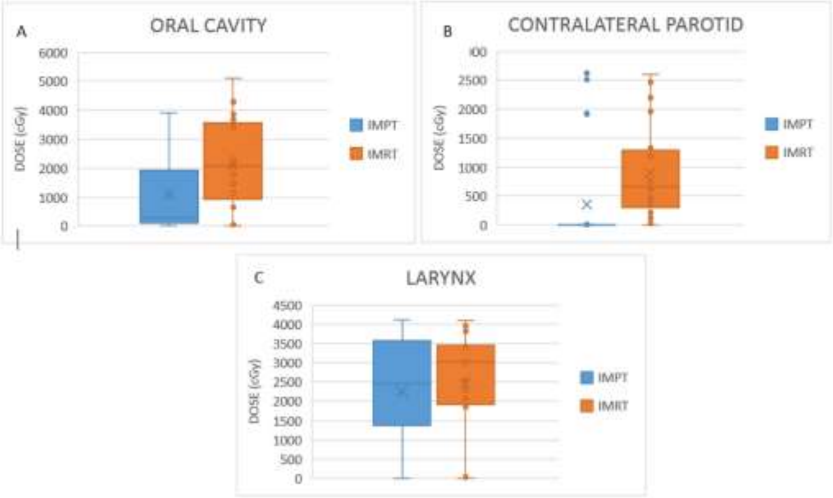


Fig. 3. Mean doses for oral cavity (A) for 21 patients, contralateral parotid (B) for 20 patients, and larynx (C) for 20 patients.

Ngeuyen et al 2021 Medical Dosimetry

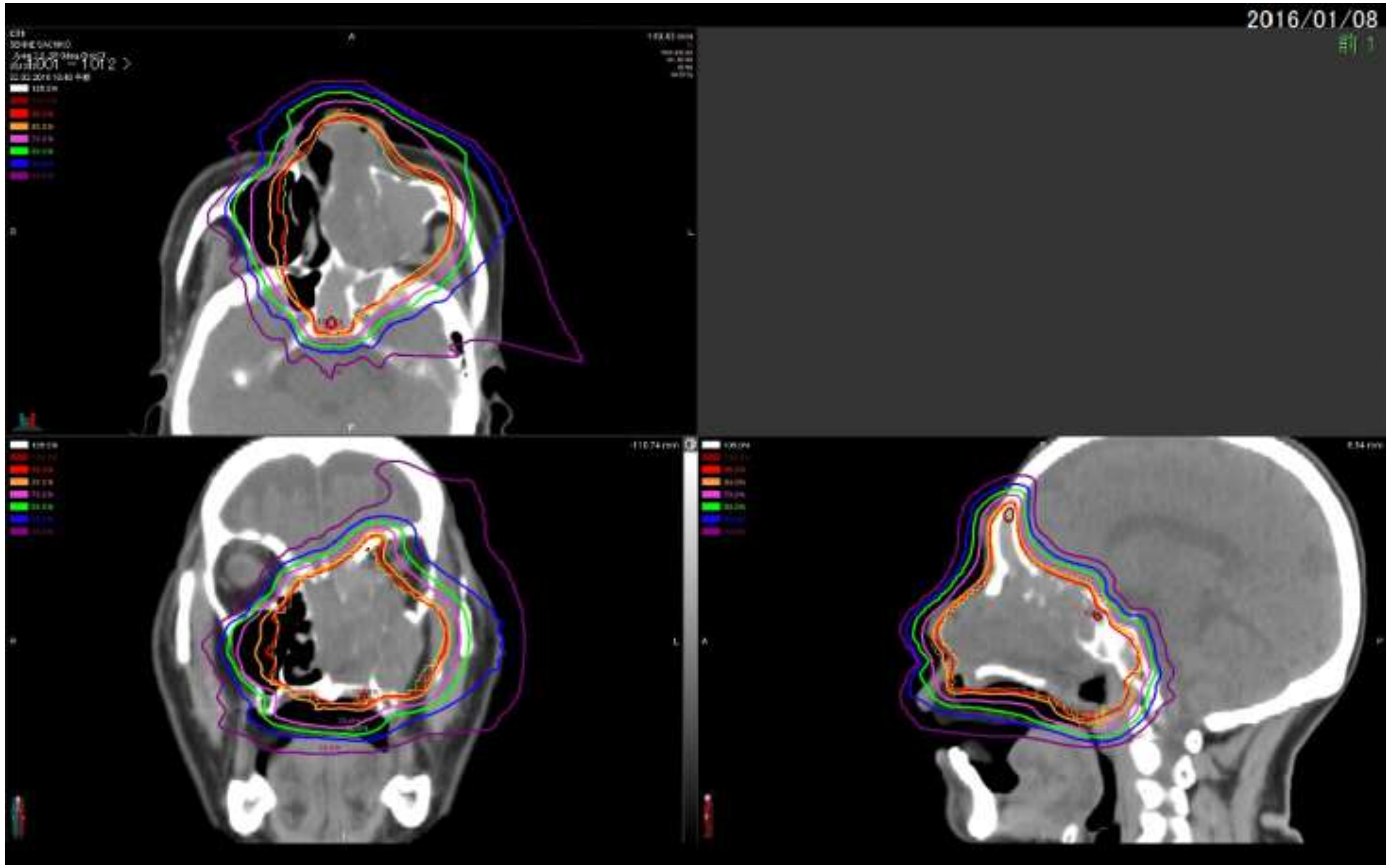
Proton in Head and Neck Cancer

- Toxicity reduction– Great advantage
- Local control and survival No different from IMRT

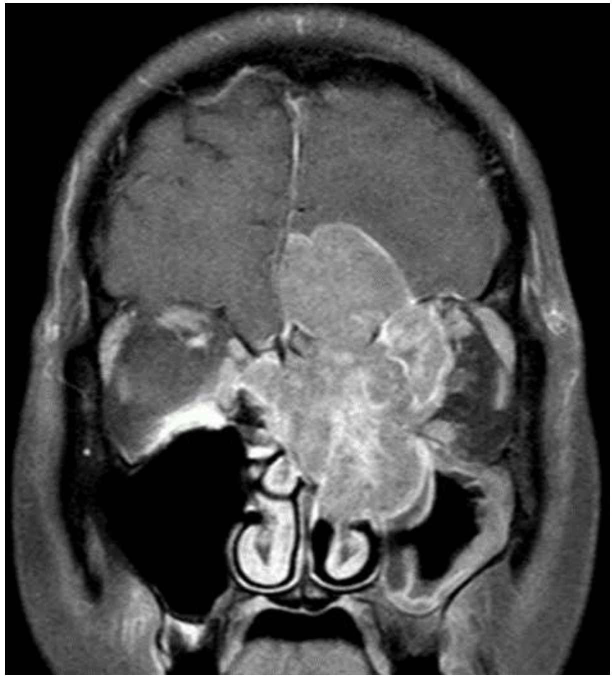
Absolute indication

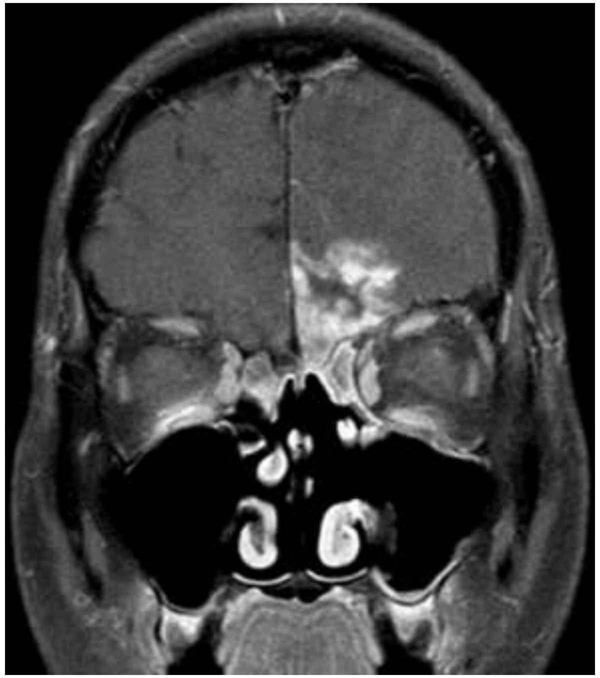
- Recurrent head and neck cancer for re-irradiation
- Tumor very close or overlapping with critical structures
- Paediatric cases
- All histologies but preferred in squamous or other radiosensitive histologies

Carbon in Head and Neck Cancer



Adenoid Cystic Carcinoma Left Ethmoid T4bN0M0

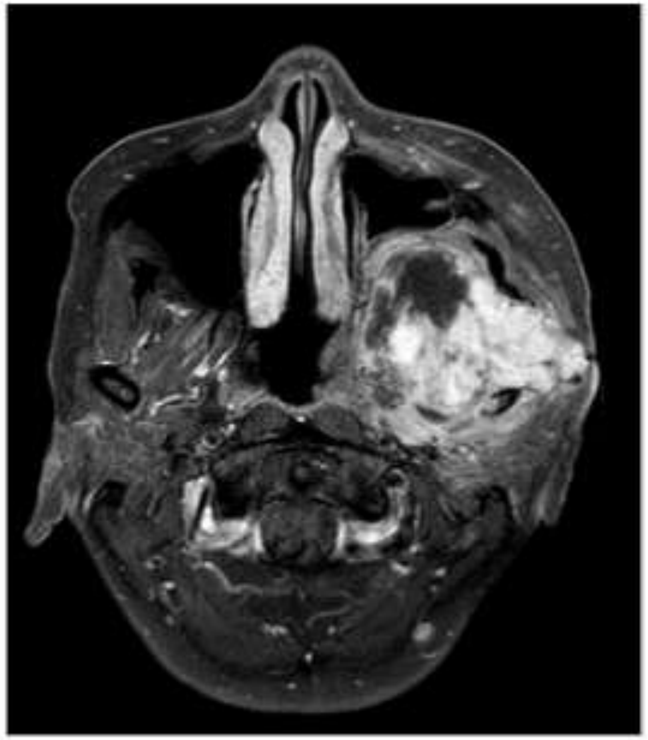




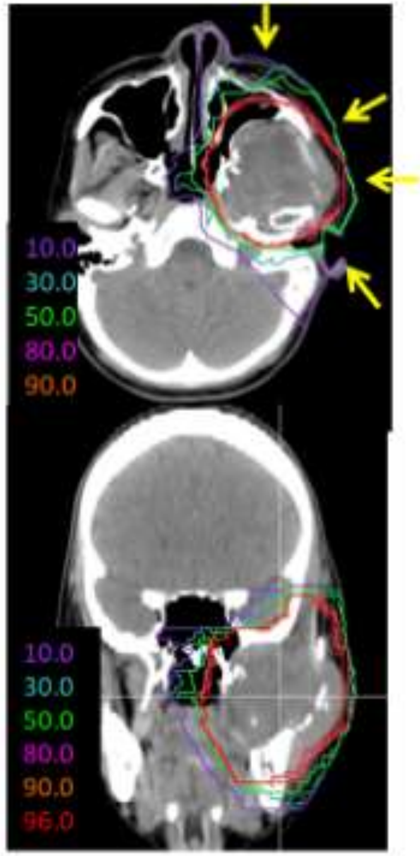
The tumor invaded the brain, orbit, and maxillary sinus. This patient received carbon ion RT of a total dose of 64Gy(RBE)

2-y after C-ion RT, this patient developed left sided blindness however eye ball was spared. Asymptomatic brain necrosis was observed but the tumor completely disappeared

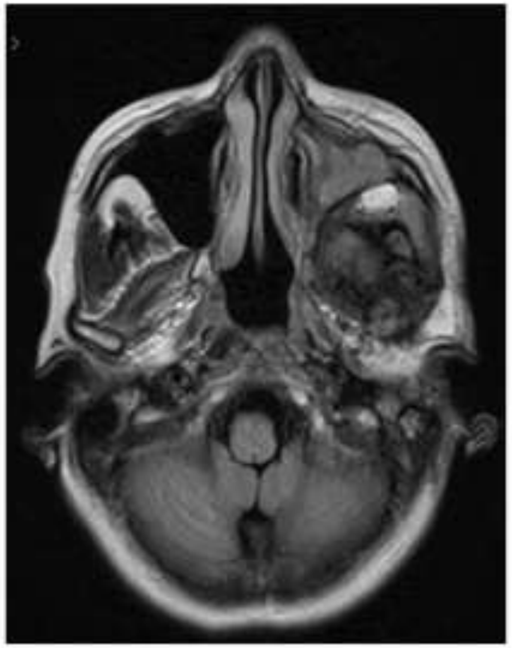
Osteosarcoma of mandible



MRI before Carbon



Carbon ion dose distribution

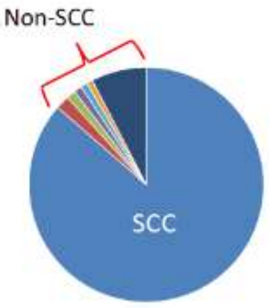


6 years after carbon

Indication of Carbon Ion in Head and Neck

- Non squamous histology
- Measurable lesion
- Recurrent disease after surgery or radiation
- Inoperable disease
- Patient preference

Carbon ion and Non SCC



- Non SCC are 10% of all Head and Neck Cancers.
- Malignant Melanomas
- Adenoid cystic carcinomas
- Sarcomas
- Adenocarcinomas
- Chordomas

Radioresistant

Chemoresistant

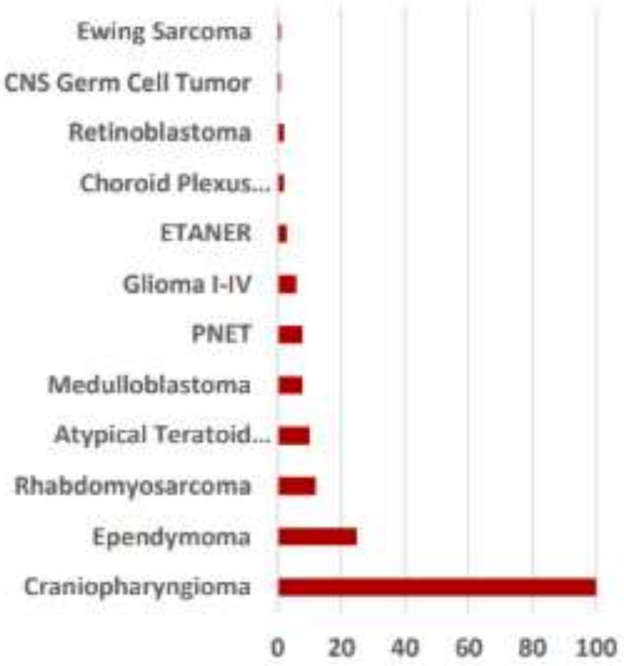
Particle Therapy in Pediatric Malignancies

- Radiation is not good for any normal tissue
- Radiation is worse for children
- Radiation has been shown to effect
- Neurocognition
- Neural development
- Normal tissue growth and function
- Secondary malignancies

Who are good candidates for Proton?

- Any child where a high dose is needed with curative intent
- Patients where the tumor volume is eccentric in the body cavity
- Where tumor volume is within or next to the sensitive organ
- Recurrent disease, in selected patients

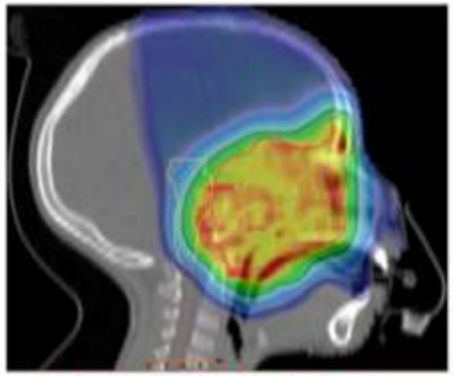
Patients by Diagnosis

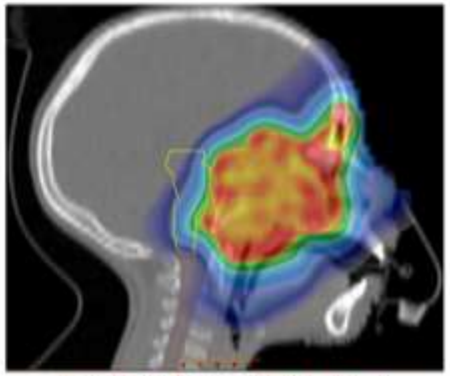


St Judes Proton Therapy referral

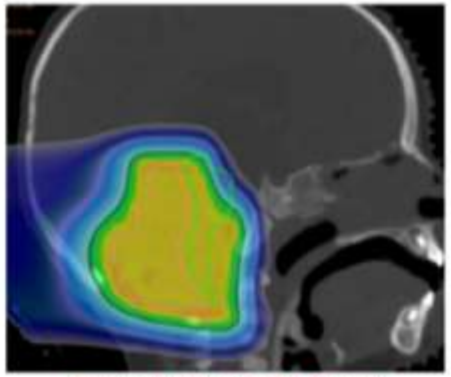
Leading Indications for Proton Therapy

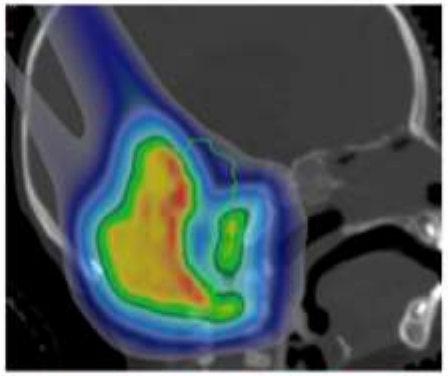
Rhabdomyosarcoma


Passive Scattering Proton Therapy

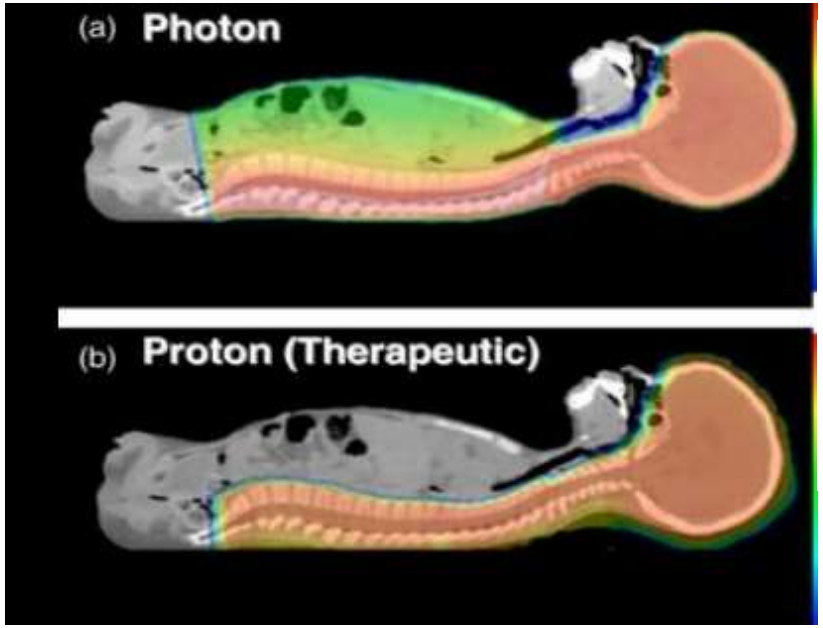

Pencil Beam Scanning Proton Therapy

Ependymoma

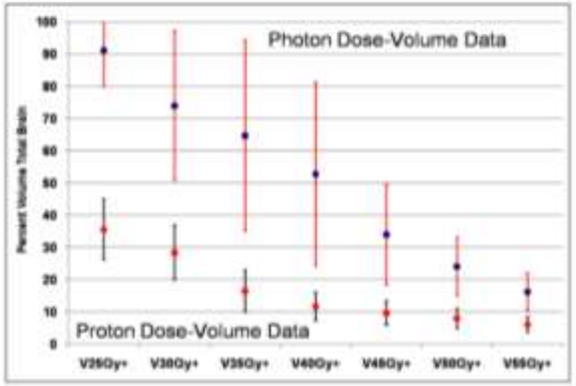

Passive Scattering Proton Therapy


Pencil Beam Scanning Proton Therapy

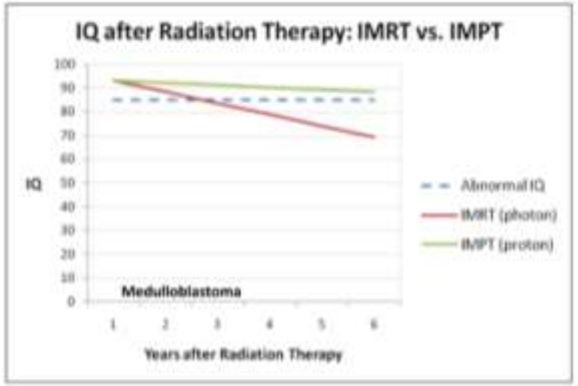
Craniospinal Irradiation



Proton-Photon Modeling
(Medulloblastoma)

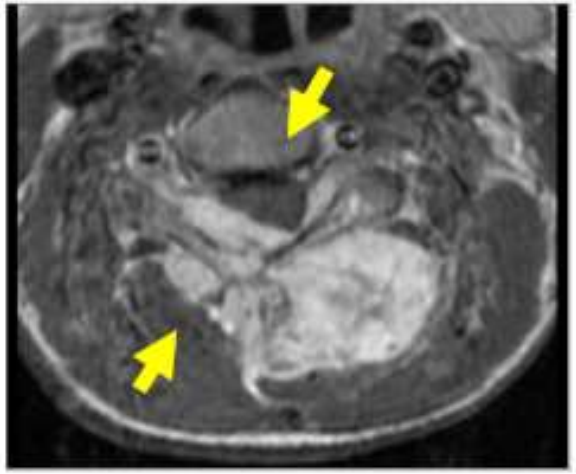


Proton-Photon Modeling
(Medulloblastoma)

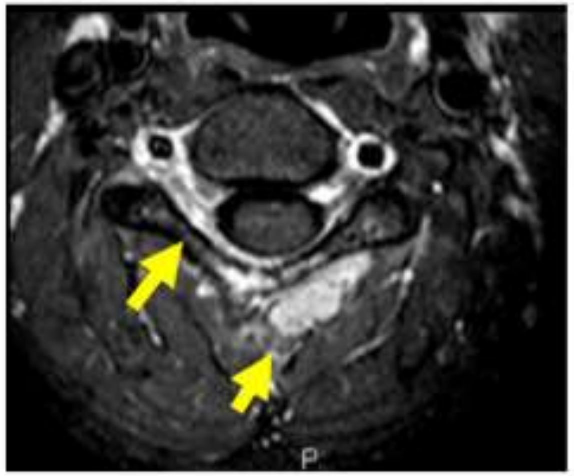


Carbon Ion in paediatrics

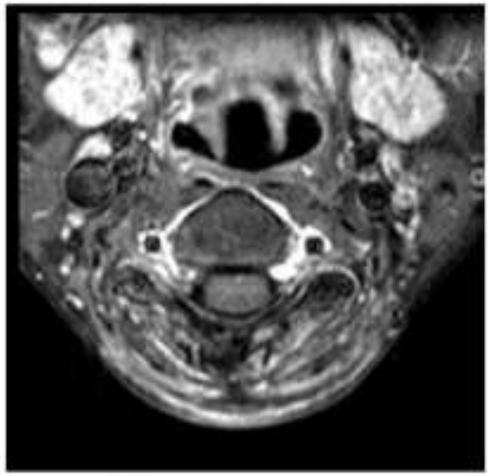
14 year old boy with high grade sarcoma treated with CIRT



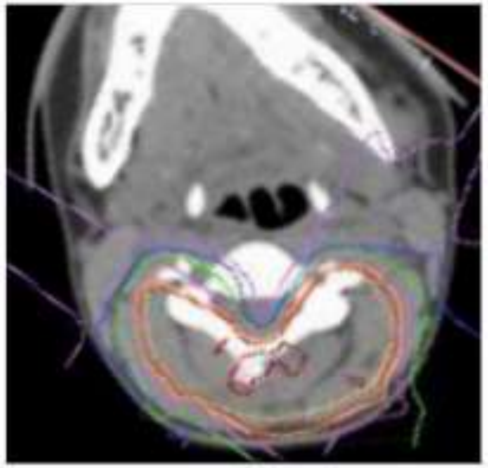
Before chemotherapy



Before CIRT

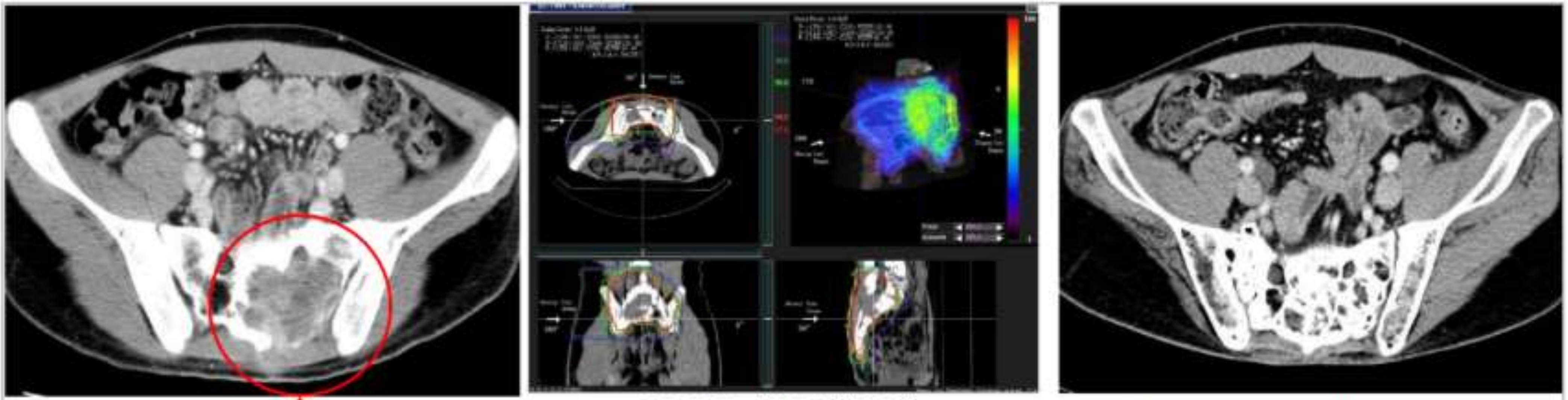


After CIRT



70.4 Gy RBE in 16 fractions

15 year old male with sacral osteosarcoma



Before CIRT

57.6 Gy(RBE)/16fr

5 years after CIRT

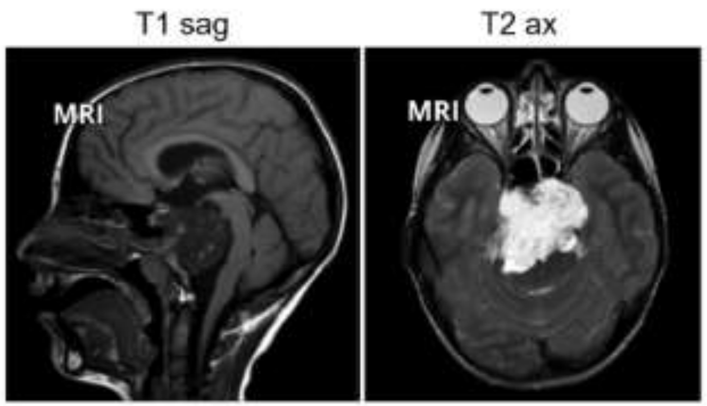
Before CIRT

5 years later

Particle in paediatrics

Proton	Carbon
Radiosensitive tumours	Radioresistant tumors
Common paediatric tumours which have been treated with Xray so far	Histologies which have not been cured by X-rays so far
Less than 10 years old	Mostly above 10 years
Craniopharyngioma, Ependymoma, Medulloblastoma, RMS, Ewings	Radioresistant sarcomas

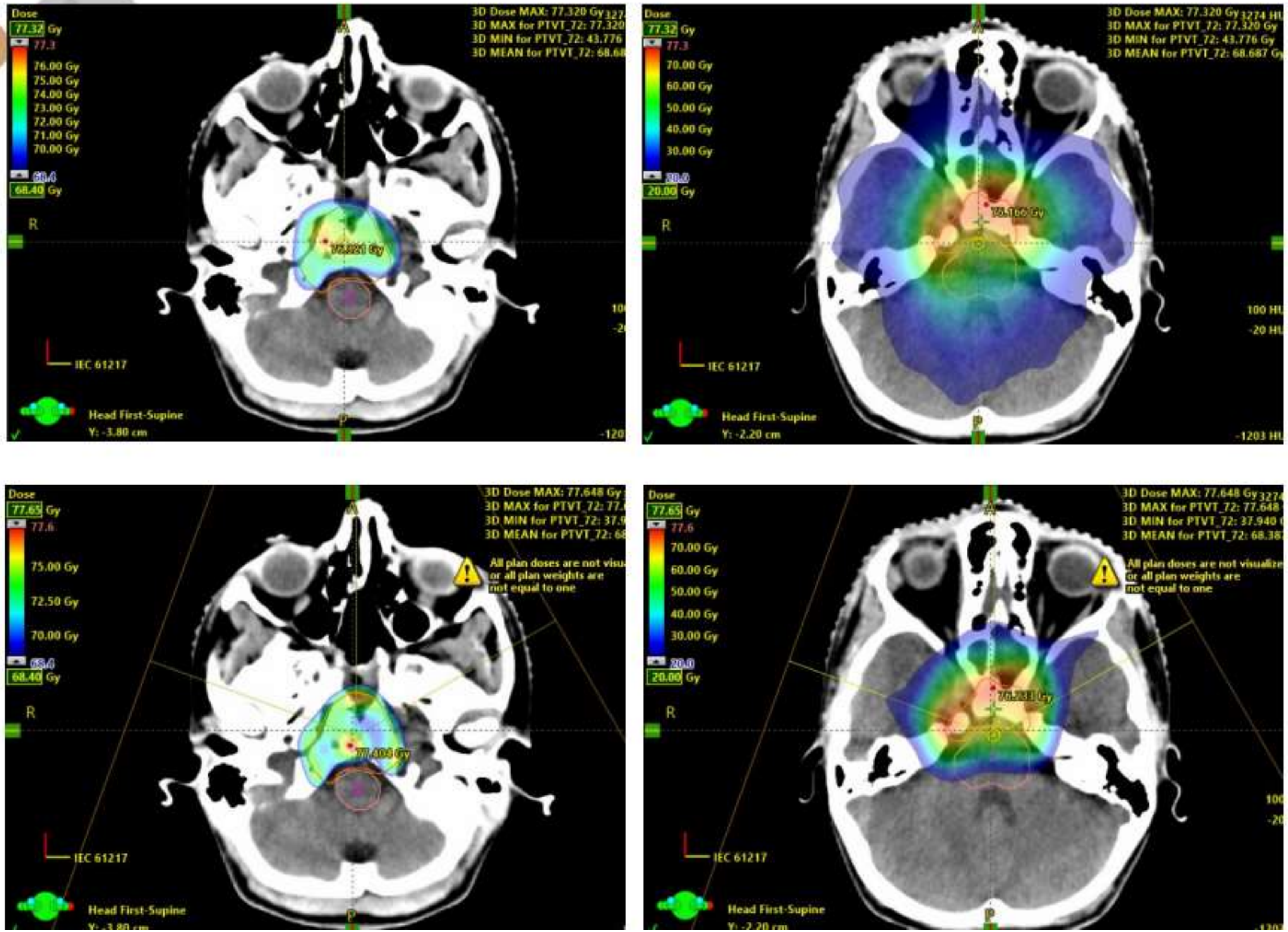
Skull base chordomas



- Chordomas are rare radioresistant neoplasms of the axial skeleton
- Close vicinity of critical structures such as the brainstem, spinal cord, and anterior optic pathways
- These anatomical structures often limit surgical access and respectability, as well as the delivery of high-dose radiations
- To achieve LC > 50%, a total dose of 70-80 Gy is required

Ph

Pr



Dose
77.32 Gy
76.00 Gy
75.00 Gy
74.00 Gy
73.00 Gy
72.00 Gy
71.00 Gy
70.00 Gy
68.40 Gy
R
IEC 61217
Head First-Supine
Y: -3.80 cm
3D Dose MAX: 77.320 Gy
3D MAX for PTVT_72: 77.320 Gy
3D MIN for PTVT_72: 43.776 Gy
3D MEAN for PTVT_72: 68.687 Gy
70.00 Gy
60.00 Gy
50.00 Gy
40.00 Gy
30.00 Gy
20.00 Gy
100 HU
-20 HU
-1203 HU
Y: -2.20 cm
77.65 Gy
75.00 Gy
72.50 Gy
70.00 Gy
3D Dose MAX: 77.648 Gy
3D MIN for PTVT_72: 37.940
All plan doses are not visualized
or all plan weights are
not equal to one
77.404 Gy

Chordoma of clivus treated with Carbon

MRI Pre carbon

Carbon dose distribution

5 years after carbon ion therapy

Heidelberg Mattke et al Cancer 2018

Chondrosarcoma Carbon vs Proton Non Randomized Sample 101

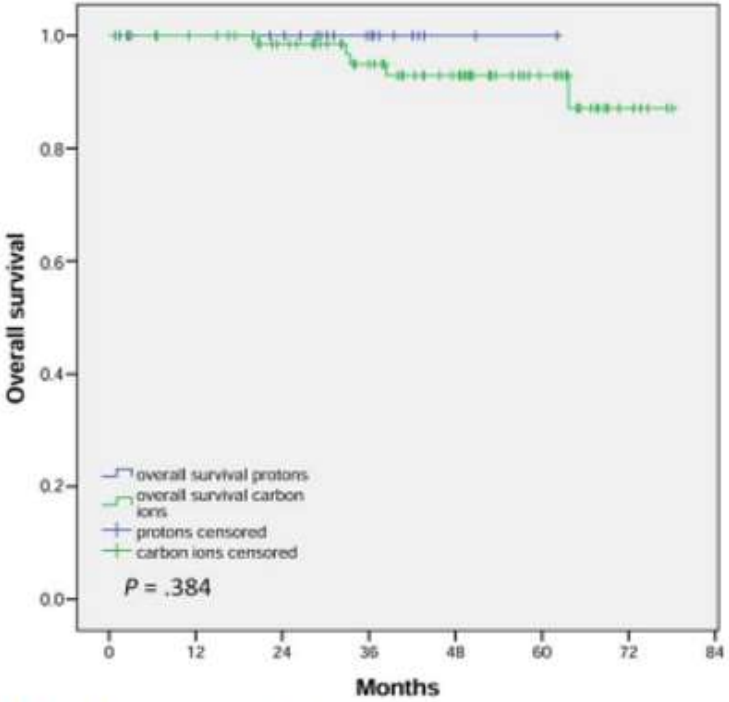


Figure 1. Overall survival with protons and carbon ions.

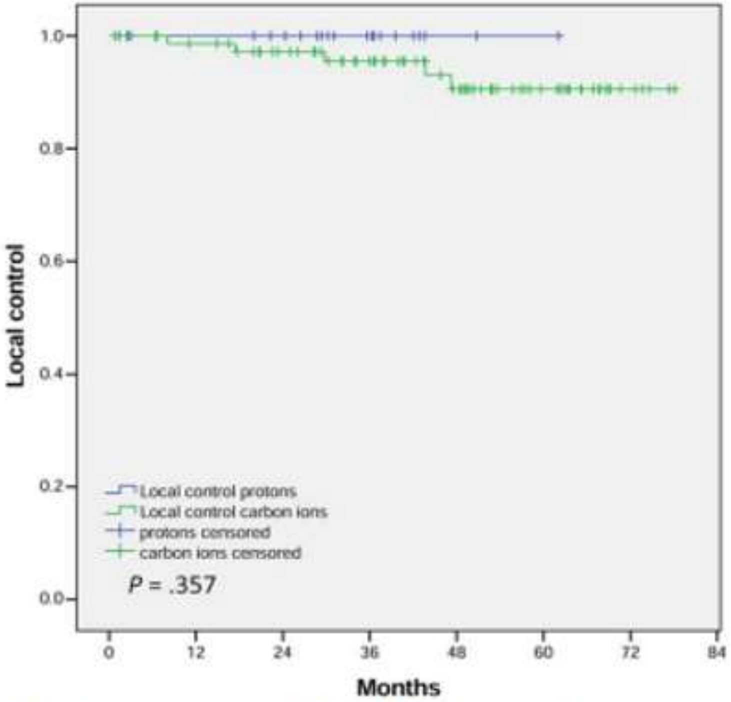


Figure 2. Local control with protons and carbon ions.

TABLE 2. Adjusted Symptoms for Carbon Ions

Adjusted Symptoms for Carbon Ions	Baseline	0-1 y	1-3 y	3-5 y
Hearing problems	25%	43%	30%	40%
Cranial nerve deficit	71%	63%	41%	19%
Abducent nerve paralysis	35%	28%	21%	9%
Double vision	42%	37%	24%	21%

TABLE 3. Adjusted Symptoms for Protons

Adjusted Symptoms for Protons	Baseline	0-1 y	1-3 y	3-5 y
Hearing problems	27%	68%	79%	33%
Cranial nerve deficit	59%	64%	63%	33%
Abducent nerve paralysis	27%	36%	21%	0%
Double vision	32%	41%	37%	33%

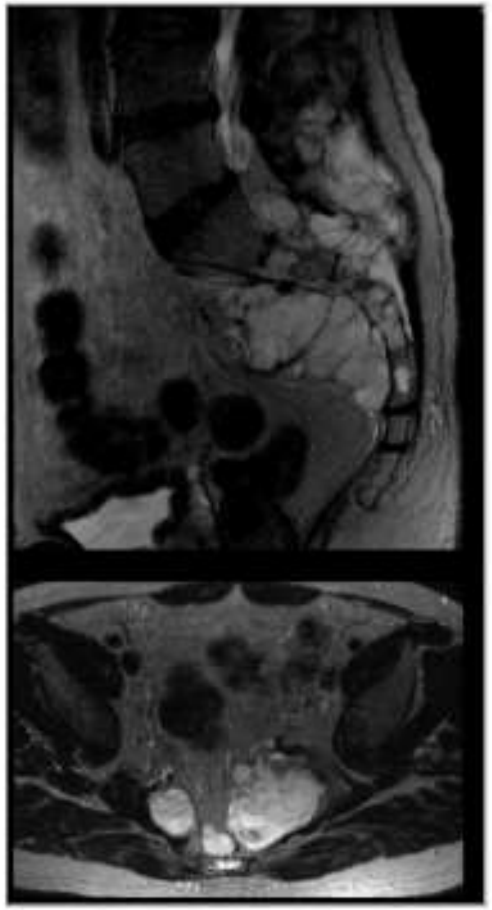
Comparable toxicity profile

No difference in Local Control or Overall Survival

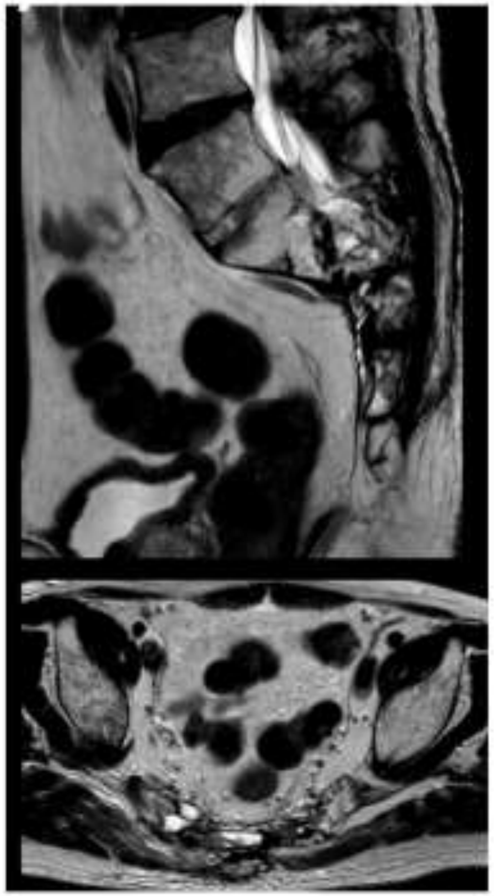
Sacral Chordoma

- Surgery mainstay of treatment of Sacral Chordoma
- Indolent nature, left undetected until they cause pain and other symptoms
- Often presents with huge mass
- Curative surgeries are morbid with bladder, bowel and gait disturbances
- Impairs quality of life
- Poor response to photon and chemotherapy
- Good physical and biological advantages of particle therapy
-

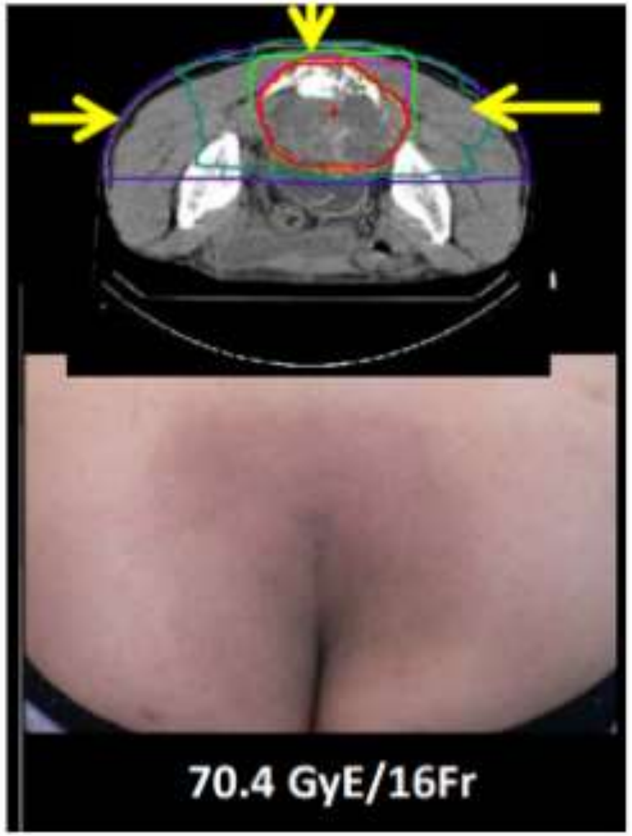
Sarcoma and chordomas



Before CIRT



10 years after CIRT



Can walk without support

International Journal of Radiation Oncology biology • physics

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Clinical Investigation

Outcomes of Patients With Primary Sacral Chordoma Treated With Definitive Proton Beam Therapy

Norihiro Aibe, MD, PhD,[*,†] Yusuke Demizu, MD, PhD,[†] Nor Shazrina Sulaiman, MD, PhD,[†] Yoshirou Matsuo, MD, PhD,[†] Masayuki Mima, MD, PhD,[†] Fumiko Nagano, MD, PhD,[†] Kazuki Terashima, MD, PhD,[†] Sunao Tokumaru, MD, PhD,[†] Tomokatsu Hayakawa, PhD,[‡] Masaki Suga, MS,[‡] Takashi Daimon, PhD,[§] Gen Suzuki, MD, PhD,[*] Yamazaki Hideya, MD, PhD,[*] Kei Yamada, MD, PhD,[*] Ryohei Sasaki, MD, PhD,[‖] Nobukazu Fuwa, MD, PhD,[¶] and Tomoaki Okimoto, MD, PhD[†]

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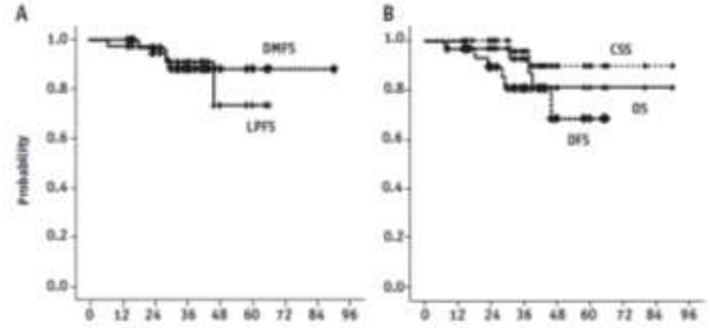

No of patients	33
Median follow up	37 months
Local progression free survival	89.6% 3 years
Disease free Survival	81.9% 3 years
Overall Survival	92.7% 3 years

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CNS, Skull Base, and Spine

Carbon Ion Radiation Therapy for Unresectable Sacral Chordoma: An Analysis of 188 Cases

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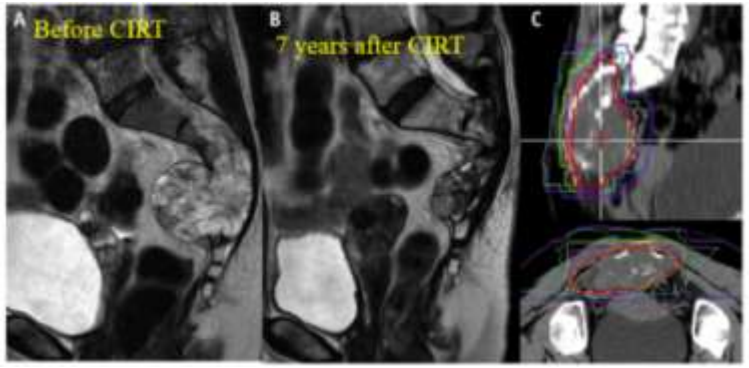
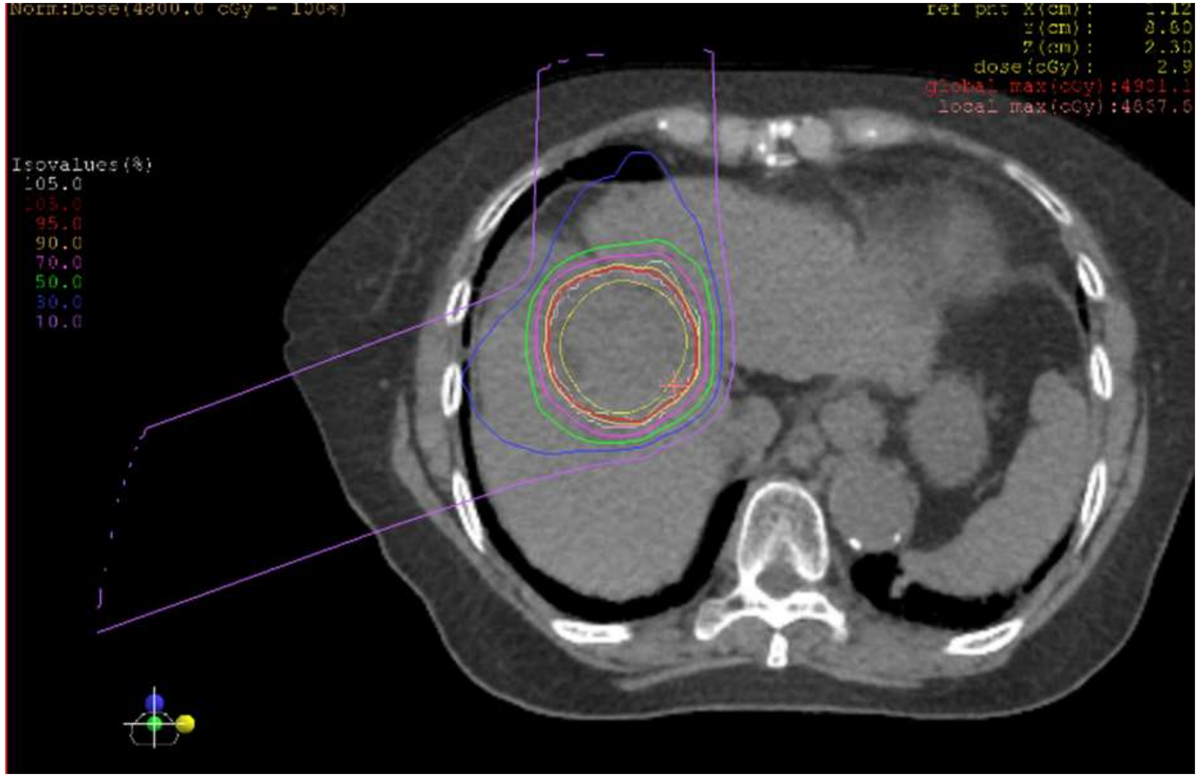
[*]Research Center Hospital for Charged Particle Therapy, National Institute of Radiological Sciences, Chiba, Japan; and [†]Department of Orthopedic Surgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka, Japan

Received Oct 1, 2015, and in revised form Jan 29, 2016. Accepted for publication Feb 1, 2016.



No of patients	188
Median follow up	62 months
Local Control	77.2% 5years
Overall Survival	81.1% 5 years
Disease free Survival	50.3% 5 years
Neurological dysfunction	6 patients
Ambulation	All patients

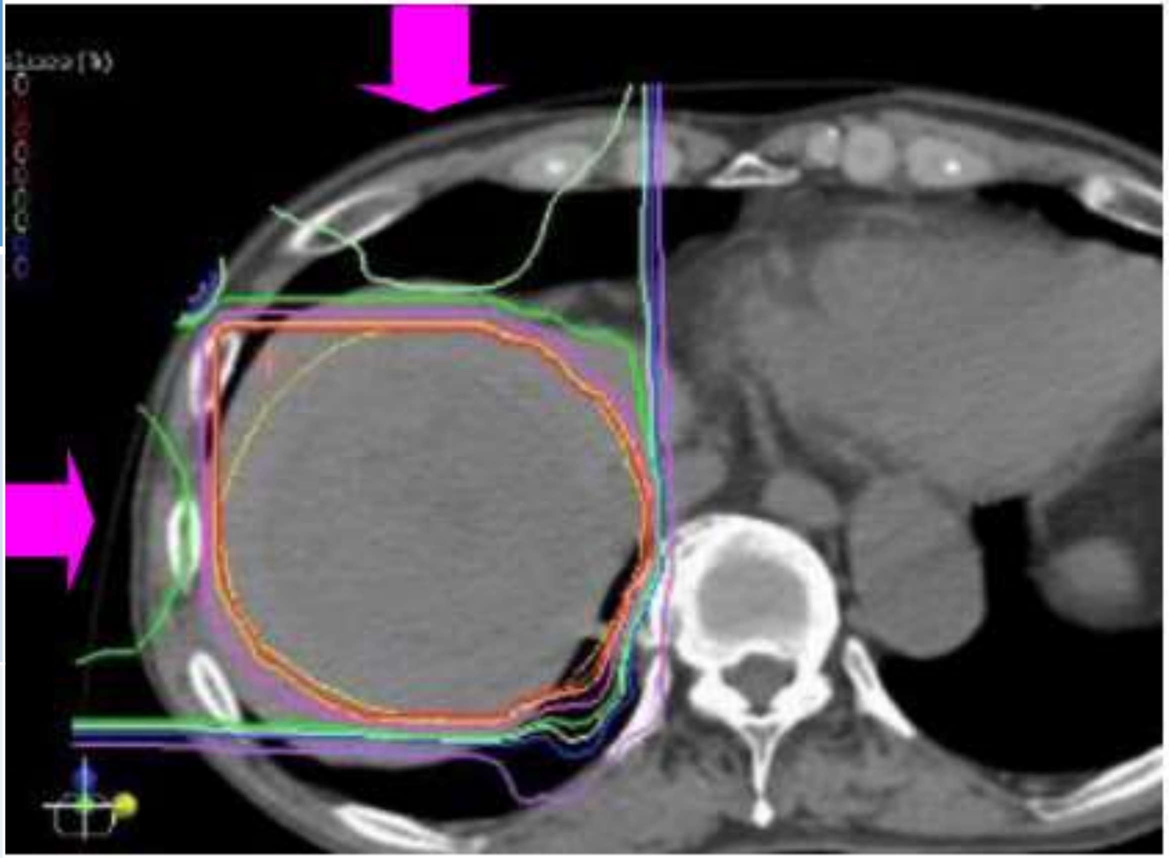


Norm:Dose(4800.0 cGy = 100%)
ref pnt X(cm):
Z(cm): 2.30
dose(cGy): 2.9
local max(cGy):
Isovalues(%)
105.0
95.0
90.0
70.0
50.0
30.0
10.0

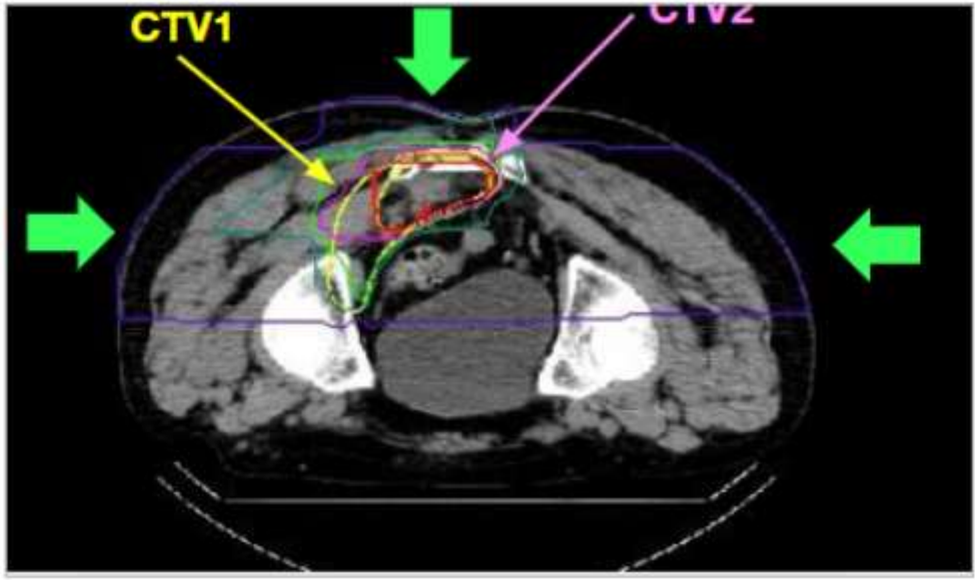
Particle Therapy in Hepatocellular Carcinoma

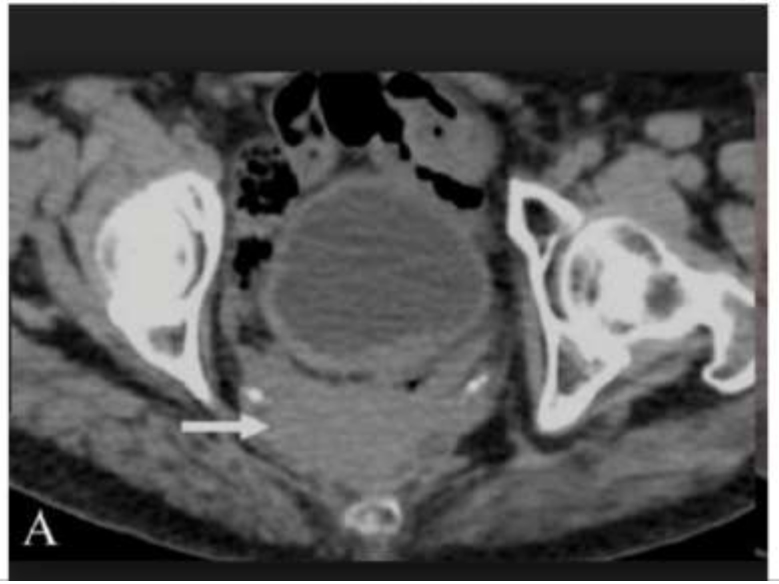
Indications	**Particle Radiotherapy**
Indications	•Histologically or Radiologically confirmed HCC •CP Class A and B •Tubular GI structures 5mm away from target preferable. •Recurrent HCC, even for infield recurrences •Can act as a bridging therapy before transplant •Post TACE residual disease •Not fit for SBRT due to size or multi centricity or not suitable for TACE due to PVTT
Contraindications	•Extra hepatic metastatic disease •GTV very close to tubular GI structures •PS-3 •Expected life expectancy less than 6 months

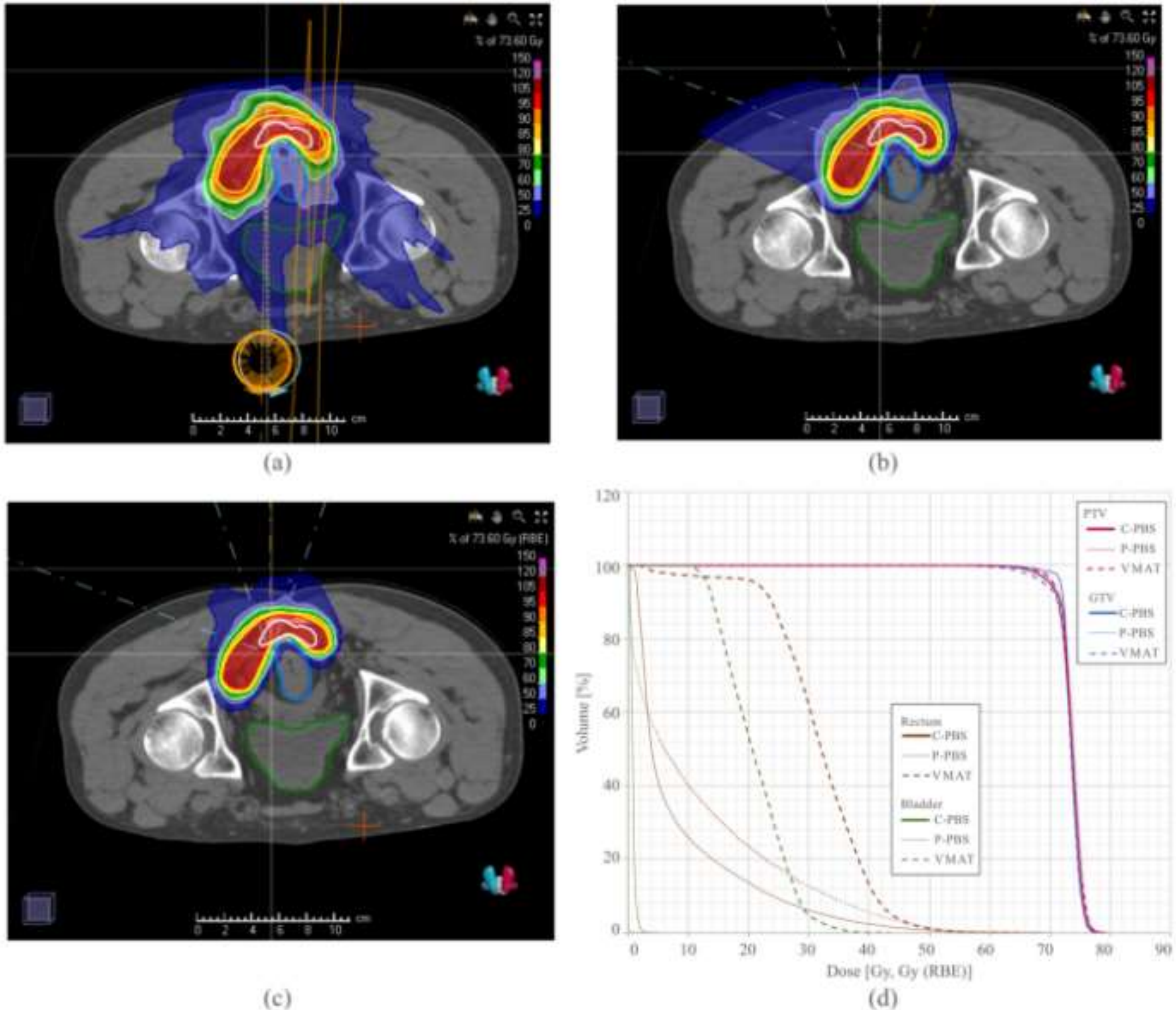
Modality	Carbon NIRS Cancer 2019	Short course Carbon Gunma Liver International 2018	Proton Tsukuba IJROBP 2011	Photon Yamashita J Rad Research
Sample size	57	174 12% CP-B Median tumour size 3 cm	47 19% CP-B	79 11% CP-B
OS	3 year OS 67% 5year OS 45%	2 years 82.5% 3 years 73.3%	3 year 50%	1 year 78%
Local control	3 year 91% 5 years 91%	2 years 87.7% 3 years 81%	3 year 88%	2 year 64%



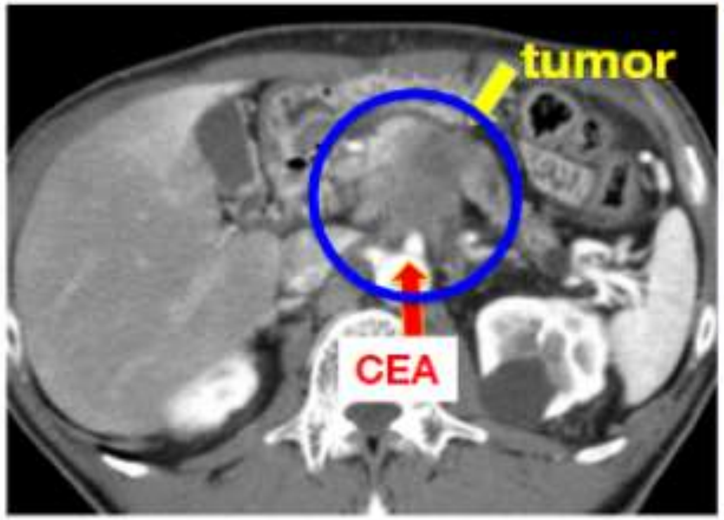
Rectal cancer





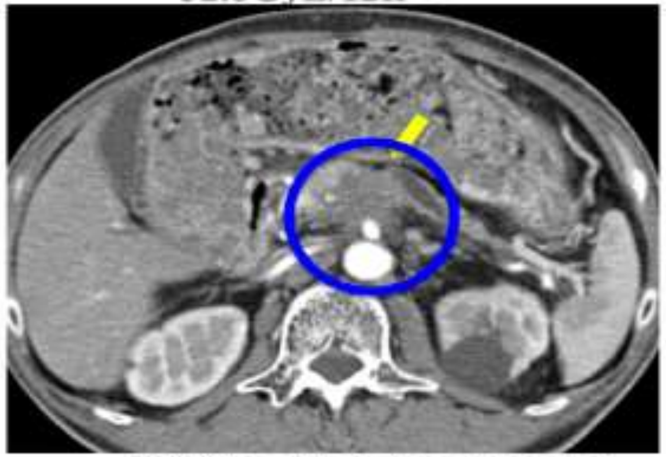

% of 73.60 Gy
150
120
105
95
90
85
80
70
60
50
25
0
cm
0 2 4 6 8 10
(a)
(b)
% of 73.60 Gy (RBE)
(c)
PTV
C-PBS
P-PBS
VMAT
GTV
C-PBS
P-PBS
VMAT
Rectum
C-PBS
P-PBS
VMAT
Bladder
C-PBS
P-PBS
VMAT
Volume [%]
Dose [Gy, Gy (RBE)]
0 10 20 30 40 50 60 70 80 90
0 20 40 60 80 100 120
(d)

Particle Therapy in Pancreatic Cancer



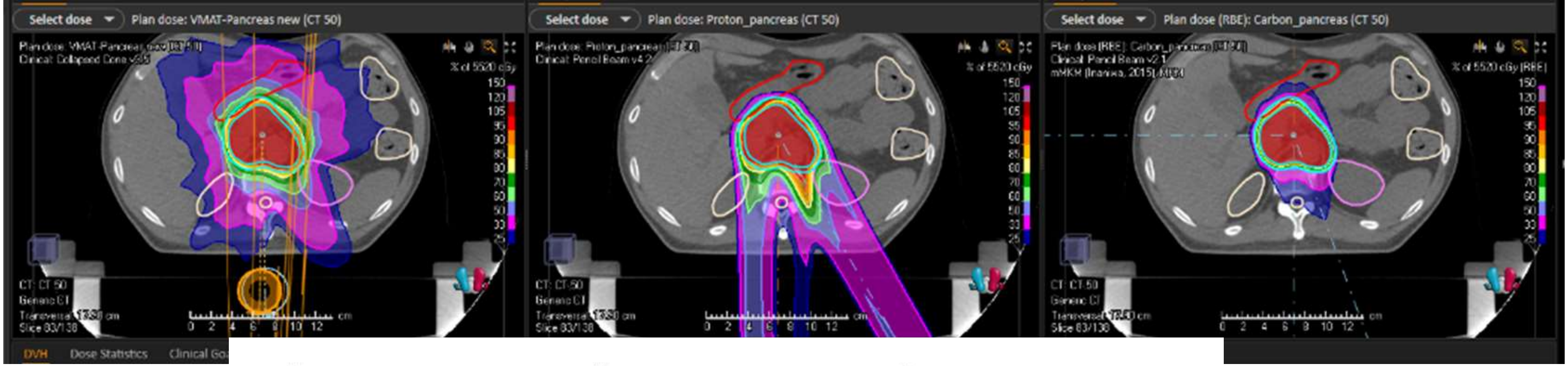
CT

52.8GyE/12fr

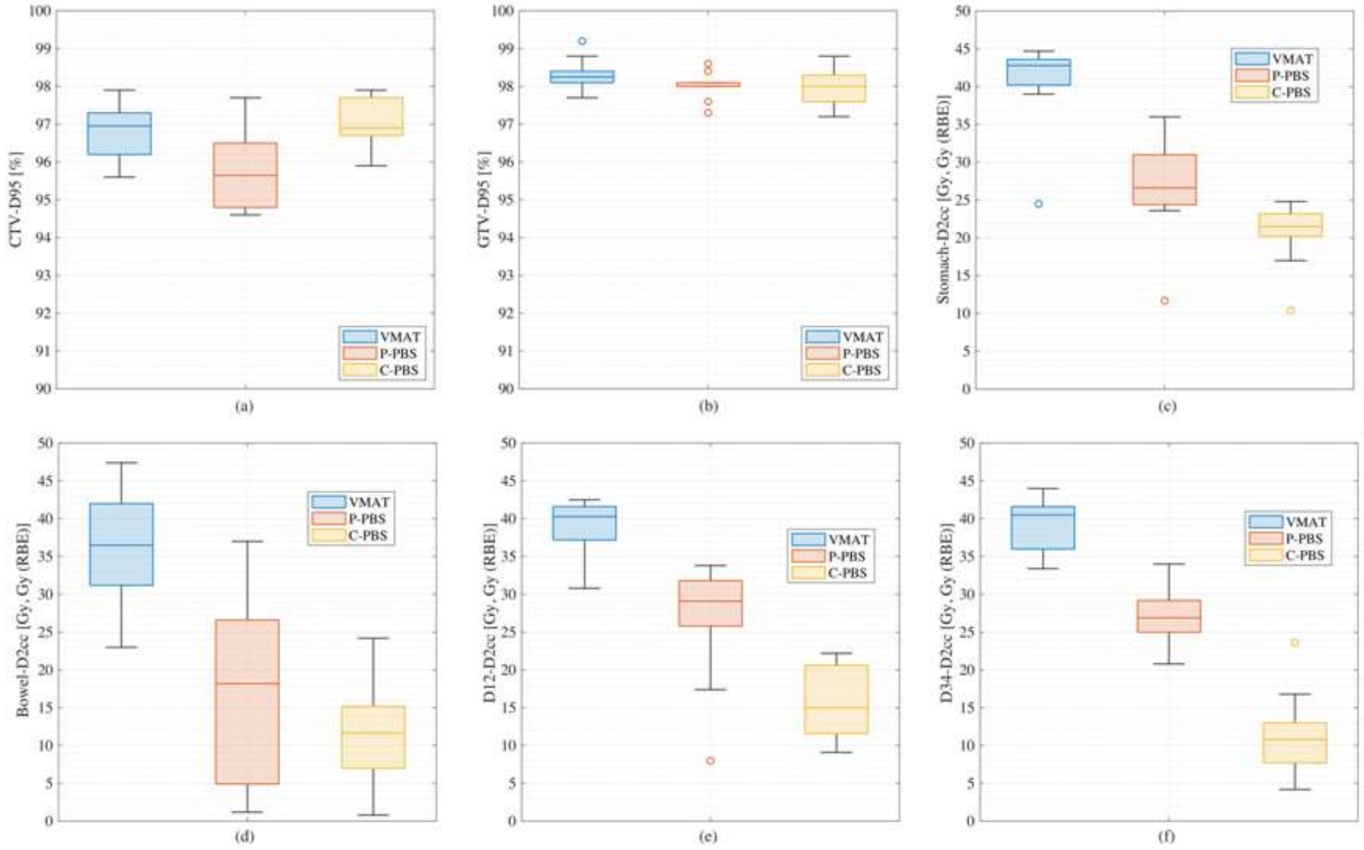


12 M after treatment

	Carbon	Proton
Eligibility	Measurable lesion Locally advanced unresectable Borderline resectable Resectable disease Non metastatic disease Recurrent disease after surgery or chemo or radiation GTV should be at least 3mm away from duodenum or stomach	LAPC BRPC
Ineligibility	Postoperative cases Metastatic disesae Tumour invading mucosa Contact length>8mm-10mm	Metastatic disease Post op cases
Dose schedule	LAPC-55.2GyRBE/12frs BRPC-55.2 Gy RBE/12frs Resectable- 36.8 Gy RBE/8 frs	

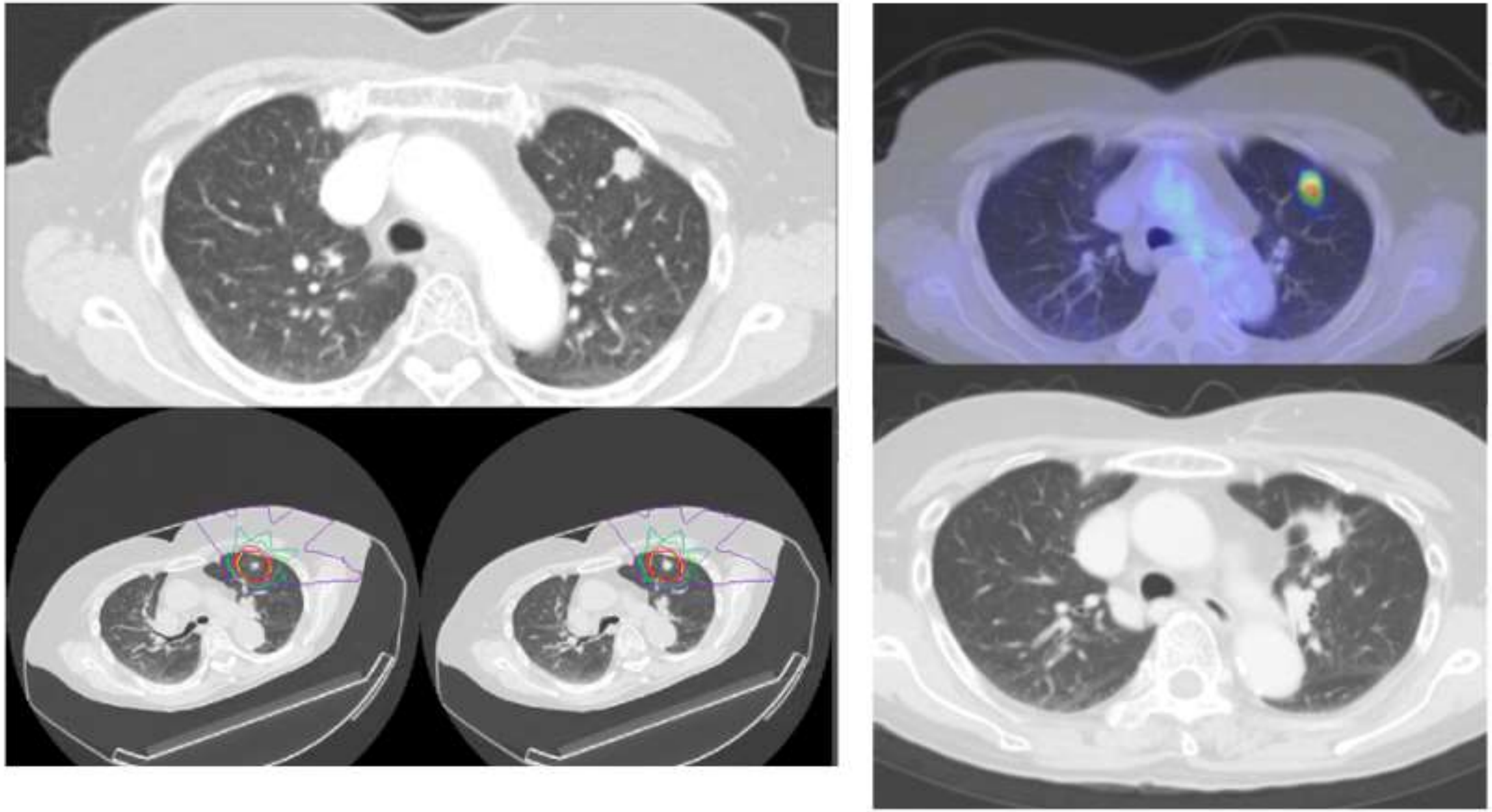


Select dose
Plan dose: VMAT-Pancreas new (CT 50)
Select dose
Plan dose: Proton_pancreas (CT 50)
Select dose
Plan dose (RBE): Carbon_pancreas (CT 50)
% of 5520 cGy
% of 5520 cGy
% of 5520 cGy [RBE]
150
120
105
95
90
85
80
70
60
50
30
25
CT: CT 50
Generic CT
Slice 83/138
cm
0 2 4 6 8 10 12
DVH
Dose Statistics



CTV-D95 [%]
(a)
GTV-D95 [%]
(b)
Stomach-D2cc [Gy, Gy (RBE)]
(c)
Bowel-D2cc [Gy, Gy (RBE)]
(d)
D12-D2cc [Gy, Gy (RBE)]
(e)
D34-D2cc [Gy, Gy (RBE)]
(f)
VMAT
P-PBS
C-PBS

Particle Therapy in Carcinoma Lung



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Meta-analysis

Comparison of the effectiveness of radiotherapy with photons, protons and carbon-ions for non-small cell lung cancer: A meta-analysis

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	CRT	SBRT	Proton	Carbon
2 year OS	53%	70%	61%	74%
5 year OS	19%	42%	40%	42%

Grade III toxicities were higher in the SBRT arm.

Carbon or Proton?

- Proton has the dosimetric advantage
- Carbon is advantageous both physically and biologically because of its high LET and variable RBE as compared the o only physical advantage of protons.
- Carbon effective in hypoxic radioresistant tumors.
- No head on randomized controlled trial.
- Barriers are
- Lack of clinical equipoise
- Ethical issues
- Funding

Is there any randomized controlled trial comparing linear accelerator vs Cobalt??