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
Technology Advances
Biologic Advances

Fractionated radiation sterilizes ram's testes without major burns (11, 12) 1911
Cellular radiosensitivity depends on mitotic activities and levels of differentiation (47) 1906
Radiation intensity related to inverse square of distance from source 1903

Leukemia cases reported in radiation workers (10) 1911
Radiosensitivity correlated with oxygen presence (52) 1923
How high-energy photons interact with tissue (Compton effect) (109) 1922
Air wall ionization chambers accurately measure radiation intensities 1924

Roentgen adopted as standard exposure unit; radiation protection recommendations 1928
Head and neck cancers cured with fractionated X-rays (13) 1928
Cyclotron invented (37) 1932

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

Skin iso-effects governed primarily by total dose and overall treatment time (17) 1944
First patient treated with neutron beams 1938
Cobalt-60 teletherapy units first used (15) 1951
Experimental quantification of the oxygen effect (109) 1952

Becquerel experiences skin burn while carrying radium in vest pocket (109) 1901
Hot-cathode x-ray tube invented (33) 1913

1900 1905 1910 1915 1920 1925 1930 1935 1940 1945 1950

AACR Centennial Series
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

• 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

<table>
<thead>
<tr>
<th>Particle</th>
<th>charge (e)</th>
<th>Mass</th>
<th>Lifetime</th>
</tr>
</thead>
<tbody>
<tr>
<td>photon</td>
<td>0</td>
<td>0</td>
<td>stable</td>
</tr>
<tr>
<td>electron (e)</td>
<td>-1</td>
<td>1 m\textsubscript{0}*</td>
<td>stable</td>
</tr>
<tr>
<td>pion</td>
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<td>1835 m\textsubscript{0}</td>
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<td>1832 m\textsubscript{0}</td>
<td>stable</td>
</tr>
<tr>
<td>alfa</td>
<td>+2</td>
<td>4 amu\textsuperscript{^*}</td>
<td>stable</td>
</tr>
<tr>
<td>C-ion</td>
<td>+6</td>
<td>12 amu</td>
<td>stable</td>
</tr>
<tr>
<td>Ne-ion</td>
<td>+10</td>
<td>20 amu</td>
<td>stable</td>
</tr>
<tr>
<td>Ar-ion</td>
<td>+18</td>
<td>40 amu</td>
<td>stable</td>
</tr>
</tbody>
</table>

* electron rest mass

\textsuperscript{^\*} Atomic mass unit 1 amu = 1.6604 \times 10^{-27} kg or 12.00000 amu is the mass of the principal isotope of Carbon 12\textsubscript{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/μm.
- Cobalt-60 γ rays: 0.3 keV/μm.
- 3 MeV X rays: 0.3 keV/μm.
- 1 MeV electrons: 0.25 keV/μm.
- 14 MeV neutrons: 12 keV/μm.
- Heavy charged particles: 100–200 keV/μm.
- 1 keV electrons: 12.3 keV/μm.
- 10 keV electrons: 2.3 keV/μm.
Definition of RBE

RBE = \frac{D_{x-ray}}{D_{particle}}
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

![Graph showing LET and OER relationship](image-url)
Relative biological effectiveness (RBE) and oxygen enhancement ratio (OER) of various radiation types

Higher ratio is better.

γ ray
Protons
Helium
Negative π mesons
Carbon
Fast neutrons
Neon
Silicon
Argon

Lower ratio is better.

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 intractable cancer cells with low oxygen concentration.
Particles vs. Photons

- IMCT
- IMPT
- 3D PT
- IMXT
- 3D XRT
All the Particles used in Radiation Oncology

- n
- Co-60
- X-rays 10MV.
- X-rays IMRT
- P Conv.
- P IMRT

Biological effectiveness

Dose conformity

Copyright ACT 2006
Dose response relationship for chordomas

- Heavy ions, Castro, 1996
- Protons, Munzenrider, 1994
- Protons, Hug, 1999
- FSRT, Debus, 2000
- Conventional RT
Comparison of the depth-dose profiles of carbon ions of two different energies with that of $^{60}$Co $\gamma$-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, 9,111 patients 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 3,000 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**

... 

... 

... 

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

![Graph showing the depth in water vs. effective dose for photons, protons, and biol. eff. dose: Carbon ions. The depth in water is on the x-axis, and the effective dose is on the y-axis. There is a highlight for the Tumor area.]
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.
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
A (3D) dose distribution with photon

- Normal-tissue sparing
- High dose to all of the target
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

PHOTONS

“dose bath”

PROTONS
The proton advantage Nasopharynx

Photons (IMRT)

Protons

Dose bath

Target

Spinal Cord

Target

Spinal Cord
The proton advantage: Paraspinal

Dose bath

Photons

Protons

Dose [Gy]

0 10 20 30 40 50 60 70 80
Tissue beyond the target receives very little or no radiation.
• 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
The dose to 90% of the cochlea was reduced from 101% with standard photons, to 33% with IMRT, and to 2% with protons.
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

<table>
<thead>
<tr>
<th>Reaction</th>
<th>Half-life</th>
<th>Threshold Energy (MeV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^{16}\text{O}(p,\text{pn})^{15}\text{O}$</td>
<td>2.0 min</td>
<td>16.6</td>
</tr>
<tr>
<td>$^{16}\text{O}(p,2\text{p}2\text{n})^{13}\text{N}$</td>
<td>10.0 min</td>
<td>5.5</td>
</tr>
<tr>
<td>$^{16}\text{O}(p,3\text{p}3\text{n})^{13}\text{C}$</td>
<td>20.3 min</td>
<td>14.3</td>
</tr>
<tr>
<td>$^{14}\text{N}(p,\text{pn})^{13}\text{N}$</td>
<td>10.0 min</td>
<td>11.3</td>
</tr>
<tr>
<td>$^{14}\text{N}(p,2\text{p}2\text{n})^{11}\text{C}$</td>
<td>20.3 min</td>
<td>3.1</td>
</tr>
<tr>
<td>$^{12}\text{C}(p,\text{pn})^{17}\text{N}$</td>
<td>20.3 min</td>
<td>20.3</td>
</tr>
</tbody>
</table>
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 ≡ 1.1 Gy Cobalt $\gamma$ 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

![Diagram showing LET vs Depth for 40 MeV, 100 MeV, and 250 MeV particles.](Image)
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

\[ H = 1000 \mu_{\text{tissue}} / \mu_{\text{water}} \]

\[ SP = \frac{dE/dx_{\text{tissue}}}{dE/dx_{\text{water}}} \]

- CT Hounsfield values (H)
- Calibration curve
- Isodose distribution
- Relative proton stopping power (SP)
- Dose calculation
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 \( D \);
\( \alpha \) is a constant describing the initial slope of the cell survival curve;
\( \beta \) 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
\[ \text{BED} = N_L \ d_L \ [1 + d_L / (\alpha/\beta)_L] \]

For High LET
\[ \text{BED} = N_H \ d_H \ [\text{RBE}_{\text{max}} + d_H / (\alpha/\beta)_H] \]

For low LET radiation
\[ 2 \text{ Gy/F} \quad 30 \text{ F} \quad 60 \text{ Gy} \]
\[ \text{BED}_T = 30 \times 2 \ [1 + 2/10] = 60 \times 1.2 = 72 \text{ Gy} \]
\[ \text{BED}_{\text{late}} = 30 \times 2 \ [1 + 2/2.5] = 60 \times 1.8 = 108 \text{ Gy} \]

For high LET Radiation
- Carbon particle
\[ 4 \text{ Gy/F} \quad 6 \text{ F} \quad 24 \text{ Gy} \quad [72 \text{ GyE}] \]
\[ \text{RBE} = 3 \quad \text{[Bragg Peak region]} \quad \text{RBE} = 1 \]
\[ \text{BED}_T = 6 \times 4 \ [3 + 4/10] = 24 \times 3.4 = 81.6 \text{ Gy} \quad \text{TCP} = 1.33 \]
\[ \text{BED}_{\text{late}} = 6 \times 4 \ [3 + 4/2.5] = 24 \times 4.6 = 110.4 \text{ Gy} \quad \text{NTCP} = 1.02 \]
\[ \text{BED}_{\text{late}} = 6 \times 4/2 \ [1 + 2/2.5] = 12 \times 1.8 = 21.6 \text{ Gy} \quad \text{NTCP} = 0.2 \]
Carbon particle therapy - Example

1. 12.5 Gy x 2 F  
   12.5 x 3 = 37.5 GyE/F  
   75 GyE

   \[ \text{BED}_T = 2 \times 12.5 \left[ 3 + \frac{12.5}{10} \right] = 25 \times 4.25 = 106 \text{ Gy} \]
   \[ \text{TCP} = 1.47 \]
   \[ \text{BED}_{\text{late}} = 2 \times 12.5 \left[ 3 + \frac{12.5}{2.5} \right] = 25 \times 8 = 200 \text{ Gy} \]
   \[ \text{NTCP} = 1.85 \]
   \[ \text{BED}_{\text{late}} = 2 \times 12.5/2 \left[ 1 + \frac{6.25}{2.5} \right] = 12.5 \times 3.5 = 43.75 \text{ Gy} \]
   \[ \text{NTCP} = 0.4 \]

2. 20 Gy  
   Single fraction  
   60 GyE

   \[ \text{BED}_T = 1 \times 20 \left[ 3 + \frac{20}{10} \right] = 20 \times 5 = 100 \text{ Gy} \]
   \[ \text{TCP} = 1.39 \]
   \[ \text{BED}_{\text{late}} = 1 \times 20 \left[ 3 + \frac{20}{2.5} \right] = 20 \times 11 = 220 \text{ Gy} \]
   \[ \text{NTCP} = 2.04 \]
   \[ \text{BED}_{\text{late}} = 1 \times 20/2 \left[ 1 + \frac{10}{2.5} \right] = 10 \times 5 = 50.0 \text{ Gy} \]
   \[ \text{NTCP} = 0.46 \]

3. 2 Gy /F  
   20 F  
   40 Gy

   \[ \text{BED}_T = 20 \times 2 \left[ 3 + \frac{2}{10} \right] = 40 \times 3.2 = 128 \text{ Gy} \]
   \[ \text{TCP} = 1.78 \]
   \[ \text{BED}_{\text{late}} = 20 \times 2 \left[ 3 + \frac{2}{2.5} \right] = 40 \times 3.8 = 152 \text{ Gy} \]
   \[ \text{NTCP} = 1.41 \]
   \[ \text{BED}_{\text{late}} = 20 \times 2/2 \left[ 1 + \frac{1}{2.5} \right] = 20 \times 1.4 = 28 \text{ Gy} \]
   \[ \text{NTCP} = 0.26 \]
4. 1.5 Gy/F  35 F  52.5 Gy

\[
\begin{align*}
\text{BED}_T &= 35 \times 1.5 \left[ 3 + \frac{1.5}{10} \right] = 52.5 \times 3.15 = 165 \text{ Gy} \\
\text{BED}_{\text{late}} &= 35 \times 1.5 \left[ 3 + \frac{1.5}{2.5} \right] = 52.5 \times 3.6 = 189 \text{ Gy} \\
\text{TCP} &= 2.29 \\
\text{NTCP} &= 1.75 \\
\text{BED}_{\text{late}} &= 35 \times \frac{1.5}{2} \left[ 1 + \frac{0.75}{2.5} \right] = 26.25 \times 1.3 = 34.13 \text{ Gy} \\
\text{NTCP} &= 0.32
\end{align*}
\]

5. 1.2 Gy/F  40 F  48 Gy

\[
\begin{align*}
\text{BED}_T &= 40 \times 1.2 \left[ 3 + \frac{1.2}{10} \right] = 48 \times 3.12 = 150 \text{ Gy} \\
\text{BED}_{\text{late}} &= 40 \times 1.2 \left[ 3 + \frac{1.2}{2.5} \right] = 48 \times 3.48 = 167 \text{ Gy} \\
\text{TCP} &= 2.08 \\
\text{NTCP} &= 1.55 \\
\text{BED}_{\text{late}} &= 40 \times \frac{1.2}{2} \left[ 1 + \frac{0.6}{2.5} \right] = 24 \times 1.24 = 29.76 \text{ Gy} \\
\text{NTCP} &= 0.28
\end{align*}
\]

6. 1.2 Gy/F  50 F  60 Gy

\[
\begin{align*}
\text{BED}_T &= 50 \times 1.2 \left[ 3 + \frac{1.2}{10} \right] = 60 \times 3.12 = 187 \text{ Gy} \\
\text{BED}_{\text{late}} &= 50 \times 1.2 \left[ 3 + \frac{1.2}{2.5} \right] = 60 \times 3.48 = 209 \text{ Gy} \\
\text{TCP} &= 2.60 \\
\text{NTCP} &= 1.94 \\
\text{BED}_{\text{late}} &= 50 \times \frac{1.2}{2} \left[ 1 + \frac{0.6}{2.5} \right] = 30 \times 1.24 = 37.2 \text{ Gy} \\
\text{NTCP} &= 0.34
\end{align*}
\]

7. 1.0 Gy/F  60 F  60 Gy

\[
\begin{align*}
\text{BED}_T &= 60 \times 1.0 \left[ 3 + \frac{1.0}{10} \right] = 60 \times 3.10 = 186 \text{ Gy} \\
\text{BED}_{\text{late}} &= 60 \times 1.0 \left[ 3 + \frac{1.0}{2.5} \right] = 60 \times 3.40 = 204 \text{ Gy} \\
\text{TCP} &= 2.58 \\
\text{NTCP} &= 1.89 \\
\text{BED}_{\text{late}} &= 60 \times \frac{1.0}{2} \left[ 1 + \frac{0.5}{2.5} \right] = 30 \times 1.2 = 36 \text{ Gy} \\
\text{NTCP} &= 0.33
\end{align*}
\]
Tumors with low $\alpha/\beta$ i.e. Radio resistant tumors
Let $\alpha/\beta = 2$
Treated with photons 2Gy/F 30 F 60 Gy

$$\text{BED}_T = 30 \times 2 \left[ 1 + \frac{2}{2} \right] = 60 \times 2 = 120 \text{ Gy}$$
$$\text{BED}_{\text{late}} = 30 \times 2 \left[ 1 + \frac{2}{2.5} \right] = 60 \times 1.8 = 108 \text{ Gy}$$

With Carbon ion 1 Gy/F 60 F 60 Gy

$$\text{BED}_T = 60 \times 1.0 \left[ 3 + \frac{1.0}{2} \right] = 60 \times 3.5 = 210 \text{ Gy} \quad \text{TCP} = 1.75$$
$$\text{BED}_{\text{late}} = 60 \times 1.0 \left[ 3 + \frac{1.0}{2.5} \right] = 60 \times 3.4 = 204 \text{ Gy} \quad \text{NTCP} = 1.89$$
$$\text{BED}_{\text{lat}} = 60 \times 1.0/2\left[1+0.5/2.5\right] = 30 \times 1.2 = 36 \text{ Gy} \quad \text{NTCP} = 0.33$$

6Gy/F 5 F 30 Gy

$$\text{BED}_T = 5 \times 6 \left[ 3 + \frac{6}{2} \right] = 30 \times 6 = 180 \text{ Gy} \quad \text{TCP} = 1.5$$
$$\text{BED}_{\text{late}} = 5 \times 6 \left[ 3 + \frac{6}{2.5} \right] = 30 \times 5.4 = 162 \text{ Gy} \quad \text{NTCP} = 1.5$$
$$\text{BED}_{\text{late}} = 5 \times 6/2\left[1+3/2.5\right] = 15 \times 2.2 = 33 \text{ Gy} \quad \text{NTCP} = 0.31$$

15 Gy/F 2F 30 Gy

$$\text{BED}_T = 2 \times 15 \left[ 3 + \frac{15}{2} \right] = 30 \times 10.5 = 315 \text{ Gy} \quad \text{TCP} = 2.63$$
$$\text{BED}_{\text{late}} = 2 \times 15 \left[ 3 + \frac{15}{2.5} \right] = 30 \times 9 = 270 \text{ Gy} \quad \text{NTCP} = 2.5$$
$$\text{BED}_{\text{late}} = 2 \times 15/2 \left[ 1 + \frac{7.5}{2.5} \right] = 15 \times 4 = 60 \text{ Gy} \quad \text{NTCP} = 0.55$$
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

\[ \text{BED}_T = 16 \times 1.2 \left[ 3 + \frac{1.2}{10} \right] = 19.2 \times 3.12 = 59.9 \text{Gy} \quad \text{TCP} = 0.83 \]

\[ \text{BED}_{\text{late}} = 16 \times 1.2 \left[ 3 + \frac{1.2}{2.5} \right] = 19.2 \times 3.48 = 66.8 \text{ Gy} \quad \text{NTCP} = 0.62 \]

\[ \text{BED}_{\text{skelet}} = 16 \times 1.2/3 \left[ 1 + 0.4/10 \right] = 6.4 \times 1.04 = 6.65 \text{ Gy} \quad \text{NTCP} = 0.1 \]

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

14 Gy, 1 F

\[ \text{BED}_T = 18 \times 1.67 \left[ 3 + \frac{1.67}{6} \right] = 30.06 \times 3.28 = 98.55 \text{Gy} \quad \text{TCP} = 1.26 \]

\[ \text{BED}_{\text{late}} = 18 \times 1.67 \left[ 3 + \frac{1.67}{2.5} \right] = 30.06 \times 3.67 = 110.6 \text{ Gy} \quad \text{NTCP} = 1.00 \]

\[ \text{BED}_{\text{skelet}} = 18 \times 1.67/2 \left[ 1 + 0.84/10 \right] = 15.03 \times 1.084 = 16.3 \text{ Gy} \quad \text{NTCP} = 0.23 \]

\[ \text{BED}_T = 1 \times 14 \left[ 3 + \frac{14}{6} \right] = 14 \times 5.33 = 74.66 \text{ Gy} \quad \text{TCP} = 0.96 \]

\[ \text{BED}_{\text{late}} = 1 \times 14 \left[ 3 + \frac{14}{2.5} \right] = 14 \times 8.6 = 120.4 \text{ Gy} \quad \text{NTCP} = 1.09 \]

\[ \text{BED}_{\text{skelet}} = 1 \times 14/2 \left[ 1 + 7/10 \right] = 7 \times 1.7 = 11.9 \text{ Gy} \quad \text{NTCP} = 0.16 \]
Prostate with Photon 3 Gy, 15 F

\[ \text{BED}_T = 15 \times 3 \left[ 1 + \frac{3}{1.8} \right] = 45 \times 2.67 = 120 \text{ Gy} \]

\[ \text{BED}_{\text{late}} = 15 \times 3 \left[ 1 + \frac{3}{2.5} \right] = 45 \times 2.2 = 99 \text{ Gy} \]

\[ \text{BED}_{\text{skeleton}} = 15 \times 3 \left[ 1 + \frac{3}{10} \right] = 45 \times 1.3 = 58.5 \text{ Gy} \]

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

\[ \text{BED}_T = 20 \times 1.1 \left[ 3 + \frac{1.1}{1.8} \right] = 22.0 \times 3.61 = 79.4 \text{ Gy} \quad \text{TCP} = 0.67 \]

\[ \text{BED}_{\text{late}} = 20 \times 1.1 \left[ 3 + \frac{1.1}{2.5} \right] = 22.0 \times 3.44 = 75.68 \text{ Gy} \quad \text{NTCP} = 0.76 \]

\[ \text{BED}_{\text{skeleton}} = 20 \times 1.1/3 \left[ 1 + \frac{0.37}{10} \right] = 7.33 \times 1.037 = 7.6 \text{ Gy} \quad \text{NTCP} = 0.13 \]
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, Proton 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 viewpoint.

In the country, presently AERB has licenced around 1000 radiotherapy 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)

Radiyopchari Ke Upchar Ke Liye Prabandh Kiyi Janye Vane Ye Radiyopchari Upkarana Vah To Gama Radiyopcharan Aapnaa Residence Ko Andhavat Dakota-lykitha 311 173 Aath Bhaba Dakshin Dakshin 311 173 Hain.

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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