HEAVY PARTICLE THERAPY

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HEAVY PARTICLES USED IN A EFFORT TO IMPROVE TUMOR CONTROL, THAT DO NOT RESPOND TO PHOTONS OR ELECTRONS

• BETTER DIFFERENTIAL EFFECT ON TUMOR CELLS VS NORMAL CELLS

• SUPERIOR LOCALIZATION CAPABILITY, THEREFORE A HIGHER DOSE TO THE TUMOR
HADRON THERAPY

• NEUTRONS
• NEGATIVE PIONS
• PROTONS
• HEAVY PARTICLES – He 2, C 6, O 8, Ne 10, Ar. 18

> MASS, RELATIVELY DIFFICULT TO PRODUCE AND CONTROL, LIMITED AVAILABILITY

ICRO 2012, Bhatinda
LET –PARAMETER TO DESCRIBE ENERGY LOSS OF THE RADIATION

ICRO 2012, BHATINDA
## CONVENTIONAL QUALITY FACTORS (RBE) TO CALCULATE EQUIVALENT DOSES

<table>
<thead>
<tr>
<th>RADIATION</th>
<th>ENERGY</th>
<th>Q FACTOR -- RBE</th>
</tr>
</thead>
<tbody>
<tr>
<td>X-RAYS, GAMMA, ELECTRON, MUONS</td>
<td>&lt; 10 KeV</td>
<td>5</td>
</tr>
<tr>
<td>NEUTRONS</td>
<td>10 KeV – 100 KeV</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>100 KeV --- 2 MeV</td>
<td>20</td>
</tr>
<tr>
<td></td>
<td>2 MeV – 20 MeV</td>
<td>10</td>
</tr>
<tr>
<td></td>
<td>&gt; 20 MeV</td>
<td>5</td>
</tr>
<tr>
<td>PROTONS</td>
<td>&gt; 2 MeV</td>
<td>2</td>
</tr>
<tr>
<td>ALPHA PARTICLES, HEAVY NUCLEI, NUCLEAR FISSION PRODUCTS</td>
<td></td>
<td>20</td>
</tr>
</tbody>
</table>
NEUTRON -- BARYON

BOTH NEUTRONS AND GAMMA RAYS --- UNCHARGED

1932 CHADWICK DEDUCED ITS EXISTENCE BY OBSERVING RECOIL PROTONS THAT WERE PRODUCED BY FAST NEUTRONS INTERACTING WITH HYDROGEN NUCLEI IN PARAFFIN
• RECOIL PROTONS & RECOIL IONS -- DUE TO NEUTRON COLLISIONS ARE THE PRIMARY ENERGY TRANSFER MECHANISMS TO THE TISSUE — ELASTIC SCATTERING.

• BIOLOGICAL EFFECT DUE TO SECONDARY ELECTRONS PRODUCED

• ENERGY DEPOSITED 30 – 80 keV/ MICRON COMPARED TO 1 KeV/ MICRON WITH COMPTON ELECTRONS

ICRO 2012, BHATINDA
NEUTRON GENERATORS

• 14.1 MeV Neutrons (DT)

For a 14 MeV neutron generator (deuterium-tritium): APPROX 250 KeV

\[ ^1D^2 + ^1T^3 \rightarrow ^2He^4 (3.5 \text{ MeV}) + ^0n^1 (14.1 \text{ MeV}) \]

• D→D NEUTRON GENERATOR, 2.5 MeV

• T→T NEUTRON GENERATOR, 0 – 9 MeV

ICRO 2012, BHATINDA
D – T GENERATOR

NEUTRON TUBE SCHEMATIC

ICRO 2012, BHATINDA
D – T GENERATOR
D – T GENERATORS

- 10 – 15 cgy/MIN
- TRITIUM CONSUMPTION
- HEAT DISSIPATION
- USUAL SSD 75 CM → PRECLUDES ADJUSTABLE COLLIMATORS
- ISOTROPIC EMISSION OF NEUTRONS → EXTN. SHEILDING
- PENETRATION ≤ CO 60. D50 = 9.5CM Vs 11.5
NEUTRON GENERATORS

• CYCLOTRONS (PARTICLE ACCELERATORS)
  → 16 MeV DEUTRONS → Be = 6MeV NEUTRON
  POOR DEPTH DOSE & FIXED BEAM GEOMETRY
• LARGER CYCLOTRONS → 22 – 50 MeV
  DEUTRONS OR 67 MeV PROTONS → Be
  ADEQUATE DOSE RATES AND GOOD DEPTH DOSES

FIXED HORIZONTAL BEAMS & IN PHYSICS
  INSTILLATIONS → INTEREST WANED BY MID 80’S

ICRO 2012, BHATINDA
P+ $\rightarrow$ Be NEUTRONS
DD % CURVES COMPARISON

![Graph showing relative dose vs depth in water for different radiation types.]

- **p (66)/Be NEUTRONS** with SSD = 150 cm
- **60Co** with SSD = 80 cm
- **200 MeV PROTONS**
- **8 MV X-RAYS** with SSD = 100 cm
- **20 MeV ELECTRONS**
CLINICAL APPLICATIONS

• **SALIVARY GLAND TUMORS** *(EXECPT SCC)* ➔ REDUCED VARIATION IN SENSITIVITY THROUGH OUT THE CELL CYCLE WITH SLOWLY CYCLING CELLS

• **ADENOID CYSTIC CA.** ➔ HIGHEST RBE (8.0) WITH # NEUTRON THERAPY. RBE > THAN FOR NORMAL TISSUE

• TREATING ADENOID CYSTIC CA. WITH 20 NEUTRON Gy = 160 Gy (PHOTONS) & =66 Gy IN EFFECT TO NORMAL TISSUE.
  THERAPEUTIC GAIN = 2.5
RESULTS

• NCI/ MRC TRIAL ---- LOW LET PHOTONS + ELECTRONS Vs NEUTRONS

• ADVANCED SALIVARY GLAND Tm. , > 7CM, UNRESECTABLE

• 10 YEAR LOCOREGIONAL TUMOR CONTROL 56 % WITH NEUTRONS Vs 17 % LOW LET RADIATION (P = .009). 10 Yr SURVIVAL NO DIFFERENCE DUE TO DEVELOPMENT OF DISTANT METASTASIS IN BOTH GROUPS
• **SCCHN CA.**---- RESULTS EQIVOCAL, NO OVERALL DIFFERENCES OBSERVED IN EITHER LOCOREGIONAL TUMOR CONTROL OR SURVIVAL.

• CERVICAL ADENOPATHY PRESENT –

<table>
<thead>
<tr>
<th>RANDOMIZED STUDY</th>
<th>LOCAL CONTROL</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>NEUTRONS</td>
<td>PHOTONS / ELECTRONS</td>
</tr>
<tr>
<td>MRC</td>
<td>22 / 38 (58%)</td>
<td>20 / 41 (49%)</td>
</tr>
<tr>
<td>RTOG</td>
<td>49 / 109 (45%)</td>
<td>23 / 87 (26%)</td>
</tr>
<tr>
<td>NCI / MRC</td>
<td>35/57 (61%)</td>
<td>33 / 67 (49%)</td>
</tr>
</tbody>
</table>
• **NSCLC** – COMBINATIONS OF NEUTRONS + PHOTONS \(\rightarrow\) INCREASED TUMOR STERILIZATION AT AUTOPSY.

• UNIV. OF WASHINGTON – 70 % LCR

• M.D.A. C.C. – 91 % LCR WITH PANCOAST TM. \(\rightarrow\) IMPROVEMENT OF SURVIVAL RATES

• NO SURVIVAL BENEFIT WITH IN LOCALLY ADVANCED, INOPERABLE NSCLC.

• MAY SHOW BENEFIT ONLY IN THE GROUP OF PATIENTS WITH GOOD PROGNOSTIC INDICATORS AND SUPERIOR SULCUS TUMORS.
• **PROSTATE CANCER** – STATISTICALLY SIGNIFICANT ADVANTAGES IN TERMS OF LRC, OS & DFS

• RTOG – 178 PTS. 5 YEAR SURVIVAL 89 % FOR NEUTRONS & 68 % FOR PHOTONS (P < 0.01)

PSA ELEVATED AT 5 YRS IN 17 % FOR PTS TREATED WITH NEUTRONS Vs 45 % FOR THOSE TREATED WITH PHOTONS
<table>
<thead>
<tr>
<th>SARCOMA</th>
<th>LOCAL CONTROL</th>
<th>LOCAL CONTROL</th>
</tr>
</thead>
<tbody>
<tr>
<td>SARCOMA</td>
<td>NEUTRONS</td>
<td>PHOTONS / ELECTRONS</td>
</tr>
<tr>
<td>SOFT TISSUE SARCOMA</td>
<td>158/ 297 (53%)</td>
<td>49 / 128 (38%)</td>
</tr>
<tr>
<td>OSTEOGENIC SARCOMA</td>
<td>40 / 73 (55%)</td>
<td>15 / 73 (21%)</td>
</tr>
<tr>
<td>CHONDROSARCOMA</td>
<td>25/ 51 (49%)</td>
<td>10/ 30 (33%)</td>
</tr>
</tbody>
</table>
Proton Therapy

- 55,000 patients have been treated with proton therapy World Wide

- In the United State there are five facilities offering this treatment

- Approximately 20,000 patients have been treated between two of this facilities
  - The Harvard cyclotron laboratory at Massachusetts General Hospital
  - The Proton Treatment Center at Loma Linda University Medical Center (LLUMC)

- The other three new centers providing this service in the US are
  - M.D. Anderson Proton Therapy Center in Houston
  - University of Florida's Shands Medical Center in Jacksonville
  - University of Pennsylvania's proton facility in Philadelphia
PROTON BEAM GENERATORS

ION SOURCE → PROTONS →

VACUM LINEAR ACCELARATOR TO, 7 MeV IN MICRO SECONDS →

ENTER THE SYCHOTRON WHERE ACCELERATED TO ENERGIES 70 MILLION – 250 MeV → BEAM TRANSPORT
235MeV proton cyclotron used for proton cancer therapy at Boshan, China

Hydrogen plasma ion source inside of the accelerator
Protons vs Photons

- Irradiate smaller volume of normal tissues
- Photon beam decreases exponentially with depth in the irradiated tissues
- Protons have a finite range
- Protons deposit most of their radiation energy in what is known as Bragg's peak

Image courtesy of Dr. Annie Chan, Dept of Radiation Oncology, MGH, Boston, MA
Bragg’s Peak

• Described by William Bragg over 100 years ago
• Depth is dependent on the energy of the proton beam
• This energy can be control very precisely

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

• Spread-out Bragg peaks (SOBP)
  – The dose peak may be ‘spread out’ to achieve a uniform dose

• Spot scanning method
  – Recently introduced
  – Small pencil beams of a certain energy deposit their peaks to obtain ‘dose-sculpting’ of the target
Dose Equivalent

- Relative biological effectiveness (RBE)
  - Ratio of the photon dose to the particle dose required to produce the same biological effect
- An RBE value of 1.1 is generally accepted for clinical use with proton beams
- Gray equivalents (GyE) or cobalt Gray equivalents (CGE) often used with protons
  - Gray multiplied by the relative biological effectiveness (RBE) factor specific for the beam used
Carbon ions

- The RBE of carbon ions has an estimated value of 3
- Carbon ion therapy attempts to capture the 'best of both worlds,'
  - Presence of the proton’s Bragg peak
  - Advantage of their high RBE to increase the tumor control probability
IMPT

- Intensity modulated proton therapy (IMPT)
  - Radiation portals which adds more accuracy to target zone
  - Also, in contrast to the two-dimensionality of IMRT, IMPT is able to modulate the Bragg peak allowing three-dimensional optimization.
• The dose to 90% of the cochlea was reduced from 101% with standard photons, to 33% with IMRT, and to 2% with protons.
CLINICAL APPLICATIONS OF PROTONS AND HEAVY IONS - UVEAL MELANOMA

EQUIVALENT OF 70 GY / 5 # / 8-9 DAYS

<table>
<thead>
<tr>
<th>5 YrS</th>
<th>PROTONS</th>
<th>HELIUM IONS</th>
</tr>
</thead>
<tbody>
<tr>
<td>LOCAL CONTROL</td>
<td>96 %</td>
<td>97 %</td>
</tr>
<tr>
<td>EYE RETAIN</td>
<td>89 %</td>
<td>83 %</td>
</tr>
<tr>
<td>MET. FREE SURVIVAL</td>
<td>80 %</td>
<td>76 %</td>
</tr>
</tbody>
</table>
SARCOMAS ADJACENT TO CNS TISSUES

CHORDOMAS OR CHONDROSARCOMA
POST OP PHOTON RADIATION LRC = 35 – 40%
HAVARD CYCLOTRON – 68.5 PHOTON Gy EQIV. @ 1.8 PHOTON Gy
5 Yr LCR = 91 % FOR CHONDROSARCOMAS AND 65 % FOR CHORDOMAS
PROSTATE CA.


• BIOCHEMICAL RELAPSE AND TOXICITY

• 30 CGE BOOST + 45 Gy PHOTONS – 4 FIELD 3 D CONFORMAL TECHNIQUE

• DFS @ 10 Yrs – 73 % AND 90 % WHEN INITIAL PSA <= 4.

• LONG TERM OUTCOMES COMPARABLE TO OTHER MODALITIES INTENDED FOR CURE
SUMMARY OF CLINICAL INDICATIONS FOR PARTICLE THERAPY

**NEUTRONS**

- SALIVARY GLAND, ADVANCED
- PROSTATE CANCER T2 – T4, N0 – 2, M0
- UNRESECTABLE SOFT TISSUE, BONE, CARTILAGE SARCOMAS
- SCCHN PRESENTING WITH LARGE NECK NODES

**PROTONS**

- UVEAL MELANOMAS
- CHORDOMAS OR CHONDROSARCOMA ADJACENT TO CNS TISSUE
THANK YOU