SBRT treatment vs Carbon Ion Planning for pancreatic Cancer

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Pancreatic Cancer

- 3.2% of all new cases in 2018.
- 55,440 new cases and 44,330 deaths.
- 4th leading cause of cancer deaths.
- 5 year survival is 4% for localized disease and 17% for resectable disease.

Pancreatic Cancer

- In the United States in years 2011-2015 : Number of deaths per 100,000 persons were 12.6 Male and 9.5 Female and the median age of diagnosis is 70 years old and age of death is 72 years old.
- Most useful diagnosis tool: CT
Our study

Four patients with pancreatic cancer treated using photon Volumetric Modulated Arc Therapy (VMAT) were replanned for carbon ion therapy to compare target coverage and normal tissue sparing.

The purpose of this study was to evaluate the dosimetric differences.

Treatment plans were evaluated based on Dose Volume Histograms (DVHs), isodose distributions, dose conformality, and normal tissue doses. The carbon ion plans were designed to achieve target dose coverage equivalent to the photon SBRT plans.

<table>
<thead>
<tr>
<th>Case</th>
<th>Rx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case A</td>
<td>35Gy/5fx</td>
</tr>
<tr>
<td>Case B</td>
<td>33Gy/5fx</td>
</tr>
<tr>
<td>Case C</td>
<td>35Gy/5fx</td>
</tr>
<tr>
<td>Case D</td>
<td>35Gy/5fx</td>
</tr>
</tbody>
</table>

Planning was done with our in-house (goCMC) fast Monte Carlo engine for therapeutic carbon ion transport.

History of Heavy Ion- Carbon-Ion

- 1954 first use protons clinically at Lawrence Berkeley National Laboratory (LBNL)
- 1973 CT
- 1990 first hospital based proton therapy with rotating gantry Loma Linda
- 1994 National Institute of Radiological Sciences (NIRS) in Japan clinical application of carbon.
  Treated more than 7300 patients by 2003
- 1997 at Gesellschaft fur Schwerionenforschung (GSI) in Germany treated 400 patients until 2005 when it was closed.
First Carbon and heavy ion studies and centers

- LBNL, California
- NIRS, Japan
- GSI, Germany

Why carbon ion therapy for pancreatic cancer

- Hypoxic Tumor vs normal oxygen concentration for healthy tissue.
- Hypoxic cells are 2-3 times less radiosensitive
- Carbon ions are more effective at killing hypoxic cells.
- Pancreatic cancer stem cells have been shown to be resistant to conventional chemotherapy and radiation
- Carbon ion beams are also safer than conventional radiological approaches.
The radiobiology of charge particle exposure is unique

The energy deposition patterns of charged particles are responsible for most of the unique radiobiology of charged particles.

Biology will drive advances in heavy charged particle radiotherapy:

- Relative Biological Effectiveness
- Complex DNA Damage
- Overcoming Hypoxia
- Combined Modalities
- Dose and Dose Fractionation
- Metastasis and Invasion
- Immunotherapy

Five unwanted issues with X-ray therapy:

1. Energy spills outside tumor
2. Same ionization in tissue & tumor
3. Substantial lateral scattering
4. Require thick collimators
5. Challenging to verify the delivered energy
2. Heavy Ions exhibit low entrance dose

Heavy ions exhibit low microscopic ionization density in healthy tissue but is high in tumors

3. Heavy Ions – have very sharp edges

Sharp
Carbon
Proton or
X-ray
4. Heavy Ions – Magnetically Controlled to Very High Precision

5. Heavy Ions – Offer Unique Verification of Energy Deposition
Heavy Ion Facility - Accelerator of Ions

Heavy Ion Facility – Treatment Room
CONCLUSION

The Physical Benefits of Heavy Ions

1. Energy stops in tumor
2. Low entrance dose
3. Dense microscopic ionization in tumor, sparse in healthy tissue
4. Razor sharp laterally
5. Magnetically controlled precise delivery
6. Straightforward in vivo deposited energy verification

Energy deposition patterns become more discrete with increasing LET.

- Photons, << 1 keV/um
- Protons @ 200 MeV, 20 keV/um
- Carbon @ 390 MeV, 112 keV/um
- Oxygen @ 468 MeV, 175 keV/um
- 1 Gy ~30 DSB
Relative Biological Effectiveness

- Increasing cell killing effect with increasing particle LET

\[ \text{RBE} = \frac{D_{	ext{ion}}}{D_{	ext{X-ray}}} \]

LET (keV/u)

The more discrete the energy deposition patterns the more complex the DNA damage

\[ \text{γ-radiation - Low LET} \]

\[ \text{High LET track} \]

damage complexity

Simple  Complex  Clustered
Reduced DNA repair capacity results in more effective cell killing

- Overcome therapeutic resistance of tumors ordinarily considered radioresistant

![Graph showing RBE vs LET (keV/u)]

Heavy charged particles can overcome the Oxygen Effect

- Hypoxia Limits the Efficacy of Radiotherapy
- Steep decline beyond ~50 keV/μm

![Graph showing OER and RBE vs LET (keV/μm)]
Heavy Ion Therapy (Carbon) has better beam profile and biologically effective than proton Therapy

Enhanced cell killing described by Relative Biological Effectiveness

Common RBE values:
- X-ray (reference) 1.0
- Protons 1.0 – 1.4
- Carbon 3 - 4
Chemoradiotherapy for Locally Advanced Pancreatic Cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>1-yr Survival Rate (%)</th>
<th>1.5-yr Survival Rate (%)</th>
<th>3-yr Survival Rate (%)</th>
<th>5-yr Survival Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crane (2002)</td>
<td>5FU alone</td>
<td>68</td>
<td>26</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Crane (2002)</td>
<td>5FU + RT</td>
<td>44</td>
<td>34</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Okusaka (2004)</td>
<td>5FU alone</td>
<td>74</td>
<td>74</td>
<td>46</td>
<td>24</td>
</tr>
<tr>
<td>Murphy (2007)</td>
<td>5FU + RT</td>
<td>50.4</td>
<td>94</td>
<td>28</td>
<td>25</td>
</tr>
<tr>
<td>NIRS (2012)</td>
<td>Carbon ion</td>
<td>45.6-52.8</td>
<td>87</td>
<td>47</td>
<td>26</td>
</tr>
<tr>
<td>NIRS (2013)</td>
<td>GEM + Carbon</td>
<td>45.6-55.2</td>
<td>74</td>
<td>54 (2yr)</td>
<td></td>
</tr>
</tbody>
</table>

GEM: Gemcitabine

More than Doubled Survival Rate!

Heidelberg Ion-Beam Therapy Center (HIT)
Our study

To test the software, I created plans with two fields.
PA and left lateral
Plans met all the constraints.
Also all VMAT SBRT plans have two full Arcs.

Used Dr. Timmerman’s constraints for 5 fx to generate the plans.

50% Isodose C-lon parallel PA and Lt Lat
Dose drop off from PTV.
Both Carbon-ion and VMAT plans were prescribed to the PTV.

<table>
<thead>
<tr>
<th>Case</th>
<th>VMAT</th>
<th>C-ion</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>1.4cm</td>
<td>0.4cm</td>
</tr>
<tr>
<td>B</td>
<td>1.7cm</td>
<td>0.35cm</td>
</tr>
<tr>
<td>C</td>
<td>1.6cm</td>
<td>0.5cm</td>
</tr>
<tr>
<td>D</td>
<td>2.2cm</td>
<td>0.4cm</td>
</tr>
<tr>
<td>Serial Tissue</td>
<td>Volume (cc)</td>
<td>Volume Max (Gy)</td>
</tr>
<tr>
<td>--------------------</td>
<td>-------------</td>
<td>-----------------</td>
</tr>
<tr>
<td>Spinal Cord</td>
<td>&lt;0.35</td>
<td>22</td>
</tr>
<tr>
<td>Duodenum*</td>
<td>&lt;5</td>
<td>26.5</td>
</tr>
<tr>
<td>Jejunum/Ileum</td>
<td>&lt;30</td>
<td>24</td>
</tr>
<tr>
<td>Colon*</td>
<td>&lt;20</td>
<td>32.5</td>
</tr>
<tr>
<td>Stomach</td>
<td>&lt;5</td>
<td>26.5</td>
</tr>
<tr>
<td>Parallel Tissue</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal cortex (R&amp;L)</td>
<td>200cc***</td>
<td>17.5</td>
</tr>
</tbody>
</table>

**Radiation Oncology**

**Duodenum Max dose**

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<th>Case</th>
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</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>22Gy</td>
<td>26.9Gy</td>
</tr>
<tr>
<td>B</td>
<td>22Gy</td>
<td>15Gy</td>
</tr>
<tr>
<td>C</td>
<td>35Gy</td>
<td>35Gy</td>
</tr>
<tr>
<td>D</td>
<td>31Gy</td>
<td>26Gy</td>
</tr>
</tbody>
</table>
Spinal Cord Max dose (0.03cc)

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<tr>
<th>Case</th>
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<th>C-ion</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>7.4Gy</td>
<td>16.7Gy</td>
</tr>
<tr>
<td>B</td>
<td>9.3Gy</td>
<td>16.5Gy</td>
</tr>
<tr>
<td>C</td>
<td>7.2Gy</td>
<td>15.3Gy</td>
</tr>
<tr>
<td>D</td>
<td>10.2Gy</td>
<td>15.3Gy</td>
</tr>
</tbody>
</table>

Maybe not a good Idea to use two beams!
50% comparison

SBRT

PA +Lt

Lats

4fld box

10% isodose VMAT SBRT treatment
10% comparison

Different beam arrangements
Spinal cord

Some structures are unapproved or rejected.

Kidneys

Some structures are unapproved or rejected.
Questions?

SO, DO YOU SMOKE?

CARBON DATING