Proton CT
Will finding a challenging solution solve a challenging problem?

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Partners

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The essence of the advantage and the problem
Why we need proton imaging?

If beam passes through 20 cm of tissue, then Bragg peak could be anywhere within +/- 7 mm. Can prohibit treatment of tumour adjacent to spinal cord.

Range uncertainties

<table>
<thead>
<tr>
<th>Tumour site</th>
<th>Median</th>
<th>90th percentile</th>
<th>95th percentile</th>
<th>Percentile with range uncertainty = 3.5%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>1.3%</td>
<td>2.5%</td>
<td>3.0%</td>
<td>98%</td>
</tr>
<tr>
<td>Lung</td>
<td>1.5%</td>
<td>2.9%</td>
<td>3.4%</td>
<td>96%</td>
</tr>
<tr>
<td>Head and Neck</td>
<td>1.3%</td>
<td>2.6%</td>
<td>3.0%</td>
<td>98%</td>
</tr>
</tbody>
</table>


Things change! Planning CT and after 5 weeks of treatment.
**Bethe equation**

\[ RSP = RED \times \frac{\ln \left( \frac{2m_e c^2 \beta^2}{(1 - \beta^2) I_m} \right) - \beta^2}{\ln \left( \frac{2m_e c^2 \beta^2}{(1 - \beta^2) I_w} \right) - \beta^2} \]

Relative Stopping Power (wrt water)

Relative Electron Density (wrt water)

Weakly energy dependent (via relativistic $\beta$)
Depends on material composition (via material I-values)

\[ \neq m + c \]

**CT calibration**

- Simple look-up-table
- Stoichiometric calibration
- Dual-energy CT
- Photon counting CT
- Proton CT

**Image guidance**

- Cone-beam CT
- Ultrasound
- MRI
- Proton CT

CT calibration Image guidance
Every proton matters

- Interaction of energetic protons chiefly through Coulomb interactions with the outer-shell electrons - **Multiple Coulomb Scattering**. Such energy losses are statistical processes.
- Fluctuation in the proton range - **range power**
- Fluctuation in the proton direction - **lateral power**
- Fraction of proton undergo non-elastic nuclear interactions - **attenuating power**

Follow the herd - use statistics

"From where we stand, the rain seems random. If we could stand somewhere else, we would see the order in it."

Tony Hillerman
The principle

Proton tracker pair (proximal) Proton tracker pair (distal) Residual energy-resolving detector

[Diagram]

Estimate entry point
Estimate maximum likely path
Estimate exit point

Repeat lots of times ...

Working specification for practical proton CT

<table>
<thead>
<tr>
<th>Category</th>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proton beam</td>
<td>Energy</td>
<td>$\geq 200$ MeV (head)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>$\geq 250$ MeV (body)</td>
</tr>
<tr>
<td></td>
<td>Flux$^a$</td>
<td>$\geq 3000$ protons cm$^{-2}$ s$^{-2}$</td>
</tr>
<tr>
<td>Imaging dose</td>
<td>Maximum absorbed dose$^a$</td>
<td>$&lt; 20$ mGy</td>
</tr>
<tr>
<td>Image quality</td>
<td>Spatial resolution, $\sigma$</td>
<td>$\approx 1$ mm</td>
</tr>
<tr>
<td></td>
<td>Relative stopping-power accuracy</td>
<td>$&lt; 1%$</td>
</tr>
<tr>
<td>Time</td>
<td>Data acquisition time</td>
<td>$&lt; 10$ min</td>
</tr>
<tr>
<td></td>
<td>Reconstruction time</td>
<td>$&lt; 10$ min</td>
</tr>
</tbody>
</table>

$^a$Quoted figure based on the scenario of 1-mm voxels and 180 projections, a target of 100 protons passing through a voxel per projection$^6$ and a 10-min acquisition.

$^b$Quoted figure based on a crude calculation of comparable stochastic risk to typical X-ray CT head scans ($\approx 40$ mGy$^7$), assuming a proton radiation weighting factor twice that of photons.$^9$
The instrument

100 – 300 MeV protons

First Proximal Strip Camera

Second Proximal Strip Camera

First Distal Strip Camera

Second Distal Strip Camera

Residual energy-Range detector (Range Telescope)

Multiple (20-30) layers of CMOS imagers, silicon strip sensors, or mixture

Record incident trajectory

 Sets of 3 strip sensors

Record exit trajectory

Record residual energy

Published patent: WO 2015/189603

“One of the most complex medical imaging instruments ever conceived”

An aside …

… other players

Fermi Lab (USA)

PRIMA (Italy)

Loma Linda (USA)
Operational Modes

Quality Assurance Mode
100 – 300 MeV protons
Beam current = 10 - 100 nA

Treatment Monitoring Mode
100 – 300 MeV protons
Beam current = 10 - 100 nA

Patient Imaging Mode
150 – 350 MeV protons
Beam current = 0.1 - 1 nA

Operational Modes

Modelling

Strip Trackers
4 banks of three 10 cm x 10 cm Silicon strip detectors
100 um pitch
150 um thickness

Range Telescope
24 layers CMOS images - each:
20 um epi
700 um substrate
200 um pitch (512 x 512 pixels)
1 mm perspex

University of Birmingham BlueBEAR HPC cluster and GridPP

Proton displacement in Range Telescope

Radiation exposure simulations
Available proton sources

- Birmingham MC40 Cyclotron – up to 36 MeV
- Clatterbridge NHS – up to 60 MeV
- iThemba LABS, South Africa – up to 192 MeV

Proton trackers

- Measures the directions of individual protons as they enter the patient and as they exit – consists of assemblies of high-speed silicon strip sensors
- Radiation-hard technology developed for the Large Hadron Collider at CERN by the University of Liverpool, and employed in the discovery of the Higgs Boson
- Counts at over 100 million times per second
- Recorded over 25 million protons per second
- Custom read-out chips (ASIC)

Imaging mode
- Every proton detected

Treatment mode
- Known fraction of protons detected
- Profile histograms to provide sufficient information for on-treatment monitoring

Double-ended 150μm thick n-in-p technology – 1024 strips at 90.8 um pitch
Proton trackers

3 rotated strip assemblies per camera
- Reduce ambiguities
- Cope with treatment level fluxes

Published patent: WO 2015/189601

Image reconstructions: Pac-man collimator (29 MeV Birmingham)

Four proton trackers
- iThemba Proton Therapy Vault

Our very first pCT
Range telescope: even more major piece of engineering

<table>
<thead>
<tr>
<th>Component</th>
<th>Quantity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Housing</td>
<td>1x</td>
</tr>
<tr>
<td>Imager Halves</td>
<td>48x</td>
</tr>
<tr>
<td>Camera Boards</td>
<td>24x</td>
</tr>
<tr>
<td>Stiffener</td>
<td>24x</td>
</tr>
<tr>
<td>Mux Boards</td>
<td>8x</td>
</tr>
<tr>
<td>Mother Boards</td>
<td>2x</td>
</tr>
<tr>
<td>Cable Interfaces</td>
<td>24x</td>
</tr>
<tr>
<td>CL Cable</td>
<td>8x</td>
</tr>
<tr>
<td>CL Cable + PWR</td>
<td>4x</td>
</tr>
<tr>
<td>Housing</td>
<td>1x</td>
</tr>
</tbody>
</table>

Sync from Strip System

Published patent: WO 2015/189602

Proton CT reconstruction: getting the data is only half the problem

- Tomographic reconstruction relies on straight rays
- Assumptions of tomography are only weakly violated but there are important consequences

\[ RSP(x, y) = i(x, y) * k(x, y) \]

Relative Stopping Power  
Backprojected image (blurred image)  
2D deblurring kernel

Published patent: WO 2016/016653

Proton CT reconstruction

And now, in 3-dimensions ...
Acknowledgements

Thank you &
Any questions