PRaVDA to OPTIma
The trials and tribulations of Proton CT

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First, apologies and a warning
I’m not a clinician
I’m not a medical physicist
I’m not a physicist
I’m an engineer

Arguing with an Engineer is a lot like wrestling in the mud with a pig. After a couple of hours, you realize the pig likes it.
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Across Europe
One new cancer diagnosis every 12 s
One death every 37 s

Estimated between 47% and 53% of cases require external beam radiotherapy for curative purposes

Most radiotherapy delivered by external x-ray beams from over 2,000 linacs across Europe

Over 30 operational proton beam therapy (PBT) centres across Europe

PBT today represents <1% of radiotherapy treatments, based on expert reports, at least 20% of patients could benefit from PBT
Proton Beam Therapy

Energy dose vs. Depth into tissue (cm)

- X-rays (15 MeV)
- Protons (200 MeV)

Beam direction

Bragg peak

Dose range
- 100%
- 95-100%
- 90-95%
- 80-90%
- 60-80%
- 40-60%
- 20-40%
- 10-20%

Proton Beam Therapy

X-ray radiotherapy

Proton radiotherapy
Why PBT?

Essence of the advantage and the problem

Protons Do stop, just not quite certain where

Photons Never stop

What makes range ‘uncertain’?

- Beam energy $[\sigma]$
- Patient positioning $[\sigma]$
- Inherent CT uncertainties (beam hardening, calibration etc) $[\Sigma]$
- Distal end RBE enhancements $[\Sigma]$
- CT artifacts $[\Sigma]$
- Variations in patient anatomy $[\Sigma, \sigma]$

Potential magnitude
Increase proton energy (ideally by about 70 MeV) and reduce intensity of beam by a factor of ~10,000.

Pair of proximal position-sensitive trackers records trajectory of individual protons, and pair of distal trackers records corresponding exit trajectory.

Residual Energy Resolving Detector (RERD) logs the residual energy of each proton \((TATE)\).

For each proton: (entry position, exit position and energy absorbed).

Rotate patient/instrument a degree or so, and repeat – require \(~10^7-8\) such triplets for full CT.
Passively scattered broad beam (85 φ mm) - 192 MeV maximum
Proton trackers

Image reconstructions – Pac-man collimator (29 MeV)

SSDs 150 μm n-in-p silicon with an active area of 93 × 96 mm² and a strip pitch of 90.8 μm. Detectors comprise 2048 split channels.

Readout by 16 custom ASICs in 0.18 μm CMOS process, with two tunable thresholds, read out at 26 MHz and up to 8 channels can be read out per readout cycle (39 ns). Translates to $2 \times 10^8$ protons/s to be detected over the full detector area.

Three equi-rotated layers in increase count rate
Ambiguity rate of 30 hits per time-slot is ~8%
Range telescope

Comprises 21 layers of SSD interleaved with 2-mm thick PMMA absorbers, providing a Water Equivalent Thickness (WET) of 2.6 mm per layer and an overall WET of 55.4 mm. Designed to stop protons in the range 30–80 MeV, as expected from a 125 MeV incident beam after passing through a 75 mm thick PMMA phantom. Thickness of a single layer optimised to allow detection of lower energy protons, while first and last layers used as veto layers.

Limitations of range telescopes

PRaVDA employed a compensator

No compensator

Many layers to preserve energy resolution

For nominal 1% energy resolution needs about 70 layers!
**PRaVDA results**

<table>
<thead>
<tr>
<th>Material</th>
<th>Density [g/cc]</th>
<th>Expected RSP</th>
<th>pCT RSP</th>
<th>Percent error</th>
</tr>
</thead>
<tbody>
<tr>
<td>PMMA</td>
<td>~1.16</td>
<td>1.15</td>
<td>1.15</td>
<td>0.0</td>
</tr>
<tr>
<td>AP7(adipose)</td>
<td>0.92</td>
<td>0.95</td>
<td>0.94</td>
<td>-0.7</td>
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<tr>
<td>WT1(water equivalent)</td>
<td>1.00</td>
<td>1.00</td>
<td>0.98</td>
<td>-1.6</td>
</tr>
<tr>
<td>RB2 rib/average bone</td>
<td>1.40</td>
<td>1.21</td>
<td>1.22</td>
<td>1.2</td>
</tr>
<tr>
<td>SB5 hard cortical bone</td>
<td>1.84</td>
<td>1.63</td>
<td>1.62</td>
<td>-0.4</td>
</tr>
<tr>
<td>LN10 lung</td>
<td>0.25-0.35</td>
<td>0.25</td>
<td>0.29*</td>
<td>-1*</td>
</tr>
<tr>
<td>AIR</td>
<td>0.00</td>
<td>0.00</td>
<td>0.09*</td>
<td>-1*</td>
</tr>
</tbody>
</table>

Comparison of film radiograph and PRaVDA radiographs

- **x-ray CT**
- **pCT**

1 mm diameter sphere
Lamb chop

Proton CT

- adipose (fat)
- muscle
- vertebrate (bone)

X-ray CT

An aside

- relative stopping-power
- relative scattering-power
- relative straggling-power
- relative attenuating-power
Current PBT delivery

• Pencil-beam (few mm dia.) scanning
• Real-time energy changes
• Full scan area typically 30 - 40 cm square
• Spot scan velocities up to 10 ms$^{-1}$
• Gantry operation!
• Certified working envelope for cyclotron
• Must integrate with clinical workflows
• Must meet clinical needs
• For commercial take-up need wide usage across different vendor’s system

OPTima

Optimising Proton Therapy through Imaging
Proton imaging beam

- Cyclotron RF frequency: 72 MHz (Varian), 106 MHz (IBA), etc.
- Incident energy: 70 MeV - 230 MeV
- Beam current: 10 pA - reasonable minimum for facility to operate within treatment envelope
- Protons/pulse: 0 - 34%, 1 – 37%, 2 – 18%, 3 – 6%, 4 - 1.5%, >4 – 0.3% (Poisson)
- Proton flux: $6.24 \times 10^7$ protons/s
- Active pulse width: 2 - 5 ns

Need to operate with more than one proton in the system!
OPTIma architecture

- **Module**: Layer 7.7 - 10 x 10^4 protons/ ms
- **Calorimeter**: 1,536 strips per layer
- **Proximal Tracker**: Up to 10 ms^{-1} 
  - Dia = 40 (at front tracker)
  - Average one proton per pulse
  - For notional 10 pA current
    - 7.7 x 10^4 protons/ ms
- **Distel Tracker**: Modular design: 60 x 60 blocks
For imaging, would like this
Need post-nozzle scatter

With nozzle, get this

Need to scan
Maximum scan velocity \(~ 10 \text{ ms}^{-1}\)
Strip sensors - how many layers?

Marked benefit of XYUV or XUV as simultaneous protons, $N$, increases and for larger phantoms.

Similar studies for layer separation and channel pitch.

SuSi 2: Geant4 Simulator
Strip ladders

Mini UV dies (30 mm) make better use of wafer

Pitch: 235 um (orthogonal to strip channel)
Thickness: 150 um
One ladder, total of 1,536 (11 bits).

Currently in fabrication by Hamamatsu
Philosophy - separate analogue and logical elements, incorporate calibration functionality, and modular

One output (selectable) per ASIC - test purposes only

All channels (buffered outputs) sampled simultaneously at 8 x system clock (e.g., 800 MHz)

Staring sensors – always active except for recovery time
Operating modes – idle, set-up, calibrate and acquire
6-bit DAC, parameters held on-chip
Die dimensions ~24 x 2.5 mm
It’s about time …

Variable number of protons arrive at regular intervals

As number of candidate protons increases then RSP becomes more uncertain
**Transit times**

Simulated Transit Time

- Trackers Transit Time: 3 – 6.5 ns
- Calorimeter Transit Time: 0.2 – 2.5 ns

Simulated Transit Time + Material Transit Time = 3.2 – 9.0 ns

Pulse period = 9.8 - 13.7 ns

Active pulse width ~ 2 - 4 ns (est.)
Transit times for Christie PBT Centre

Similar for other facilities

Full thickness phantom adds ~0.5 ns

Time bubble - need to keep these protons together
Synchronisation

Test point or RF pickup
72 - 106 MHz
Long cable
Programmable phase shift (1 ns inc.)

An on-going debate!

System Clock

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Sync time across modules using proton transit times

Beam splitter
Very fast light pulse

Say, 100 MHz

Sync time across layers using fast light pulse

Say, 100 MHz

Xstal Osc.

System Clock

Up-band 8x

System Clock (100 MHz)

All channels read at 1.25 ns intervals

ASIC

FPGA
Ambiguities

Incident beam - well collimated
Nominally 40 mm dia.

Front trackers

Rear trackers

Calorimeter

The physics does not help. Multiple Coulomb Scattering gives a fairly broad and smooth distribution. The high angle scatters are ‘cut’.

The Perils of Excess Protons
Keep protons in their bubbles

~10 ns

Super-sampling cyclic time code

800 MHz digital ‘scope

But, at the end of the day
time no meaning!

Time bubble - need to keep these protons together

Keep protons in their bubbles
System architecture

Module 1
XY Layer Board
YX Module Board
U
V

Module 2
XY Layer Board
YX Module Board
U
V

Module 3
XY Layer Board
YX Module Board
U
V

Module 4
XY Layer Board
YX Module Board
U
V

Main board

YX layer board is flipped XY layer board
V layer board is flipped U layer board

Proximal Tracker

Distal Tracker

Calorimeter
Modular design

XY-YX Ladder

Complete Tracker

Subject to change
Calorimeter

Pixellated Calorimeter
Plastic scintillating fibres/bars
Read-out Multi-anode PMT or TimePix

Scintillating elements ~30 cm long
Pre-detection gain (optional)

Energy Resolution: 230 MeV (3%), 70 MeV (1%)

Individual protons

Pixelated detector
Readout and logic

1 mm fibres
2 mm fibres

Simulations

Calorimeter is the most challenging element
General Comments

Proton and other charged particle beam therapies are relatively new and in a state of flux.

Real need for optimised and adaptive treatments.

Range uncertainties are a major challenge and proton CT can assist in several ways.

Proton CT is a challenge – evidenced by its long history.

Proton CT will only reach patients if there are confirmed clinical advantage and industry invests.

Project philosophy must be driven by the clinical professionals and developed to pre-production standards.