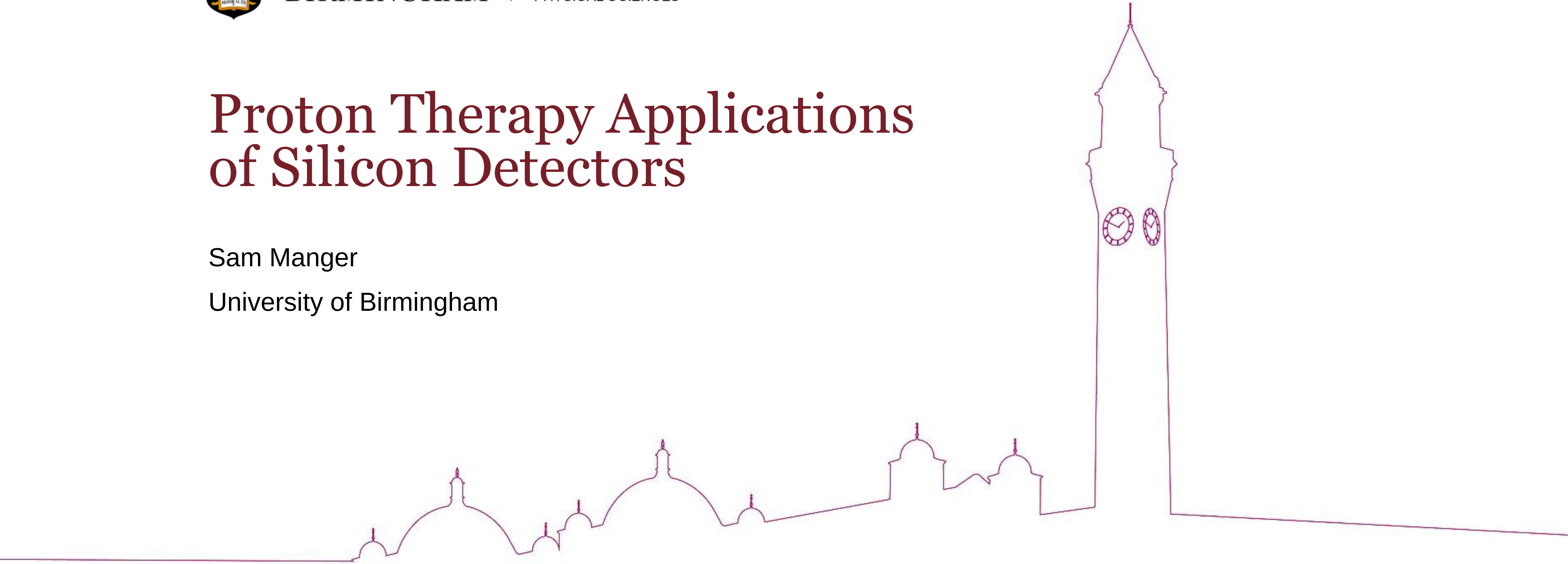
UNIVERSITY OF BIRMINGHAM

COLLEGE OF
ENGINEERING AND
PHYSICAL SCIENCES

Proton Therapy Applications of Silicon Detectors

Sam Manger

University of Birmingham



Radiation Therapy

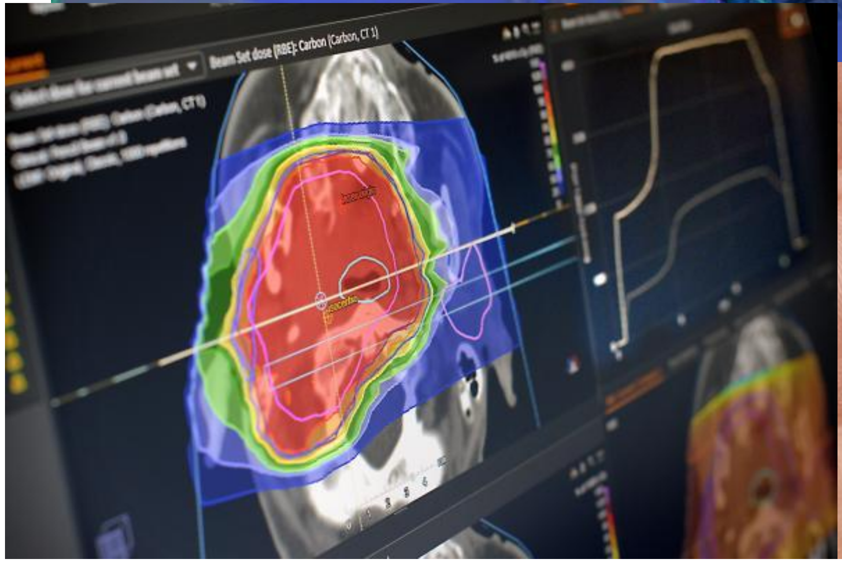
Radiation therapy involves the delivery of **ionizing radiation** in order to **damage or kill** cancer cells

Radiotherapy is used in **40%** of cancer treatments in the UK

External beam radiotherapy uses beams of x-rays, electrons, or hadrons

Brachytherapy is a form of radiotherapy using **implanted radioactive sources** to deliver treatment

The clinical goals are to deliver maximum possible dose to the target whilst **sparing healthy tissue**

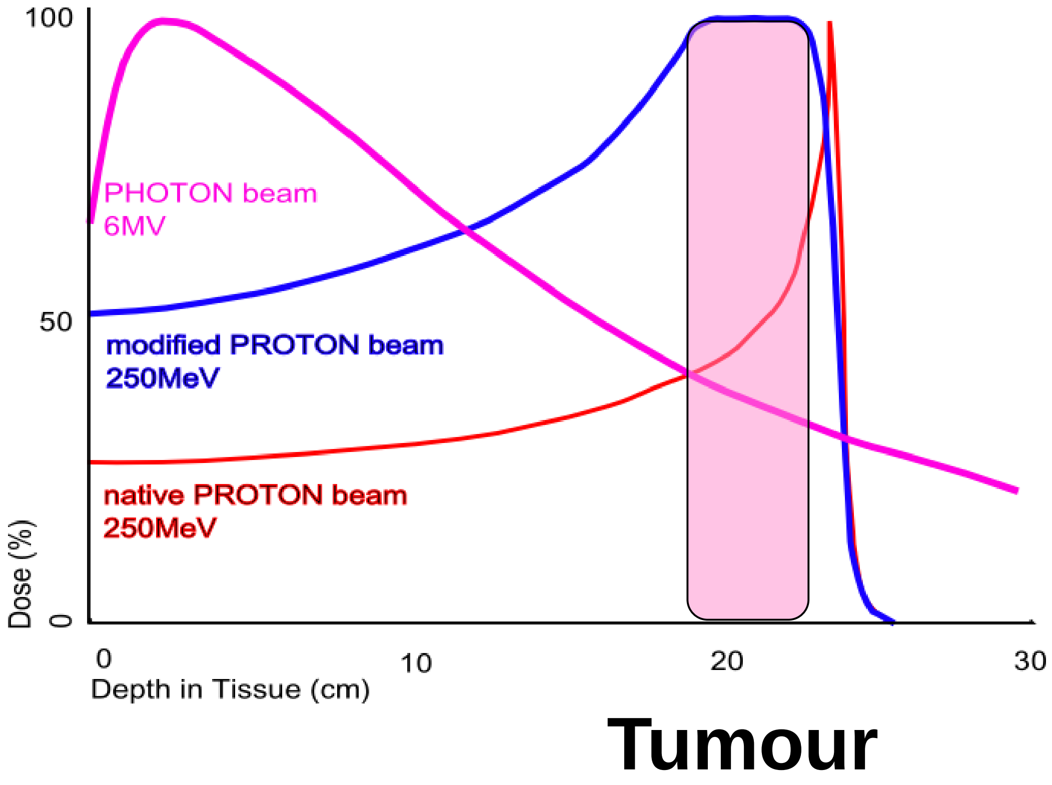


Proton Therapy

Heavy ions (protons, helium ion, carbon ion) have a much more finite range than x-rays

Ions deliver most of their dose where they stop

Principle of hadron therapy: **minimal entrance dose, maximum dose at target, no exit dose**



A brief history of proton therapy

First proposed in 1946 by Robert Wilson

First proton therapy treatment was in 1954 at Berkeley Radiation Laboratory

The world's first proton therapy treatment in a hospital occurred at the **Clatterbridge Cancer Centre** (near Liverpool) in 1989

There are currently **over 60** proton therapy sites operational worldwide with a similar number planned or under construction.

Considerable developments in the UK over recent years

- 2 NHS centres: Manchester opened and treating patients now, London delayed slightly
- Also at least 5 private proton centres in the UK recently announced

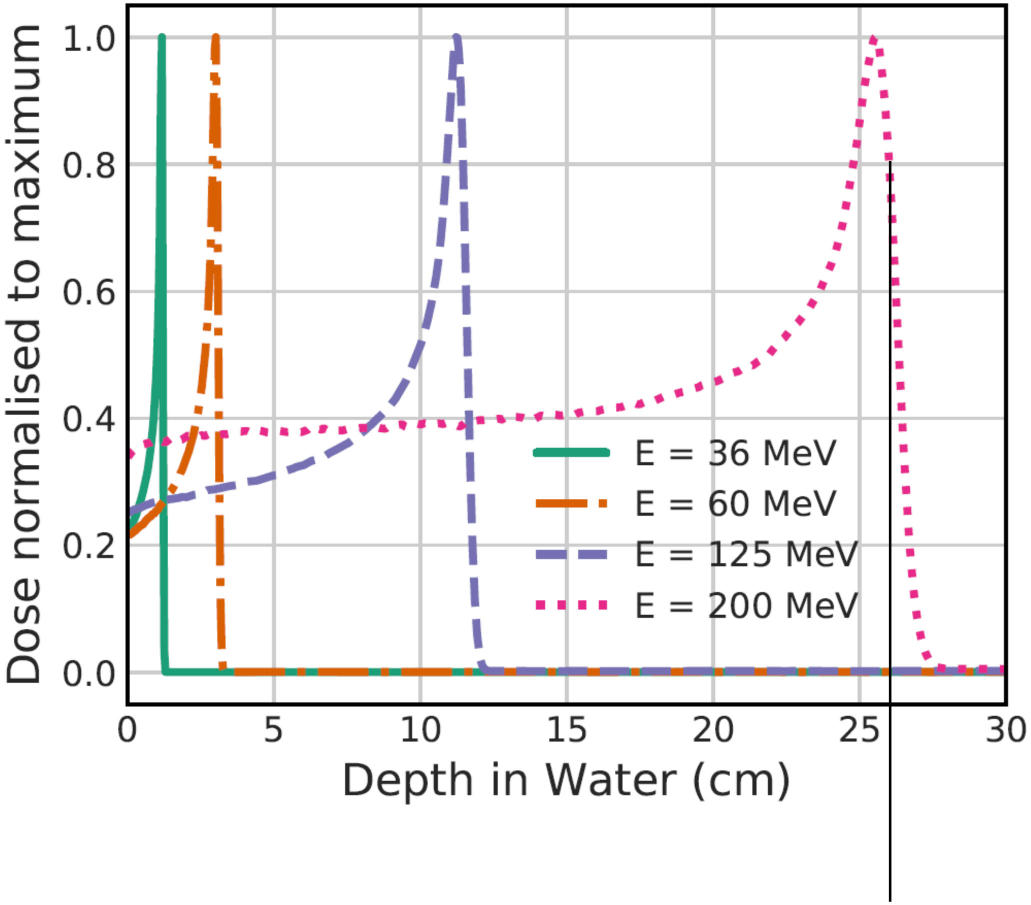
Rapidly growing and evolving field due to benefits to head and neck cancers and in paediatrics.

By the end of 2015, **131240** had received proton radiotherapy worldwide

Bragg Peak

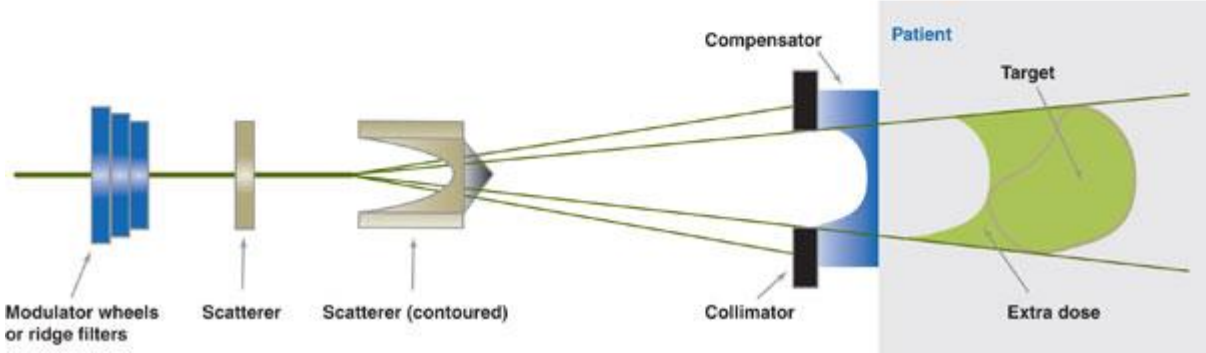
- Dose deposition of charged particle described by Bethe-Bloch formula
- Range defined as point at which Bragg peak falls to 80% of max
- We adjust the range by changing energy of the beam

$$Range[cm] \approx 0.00244 \times E[MeV]^{1.75}$$

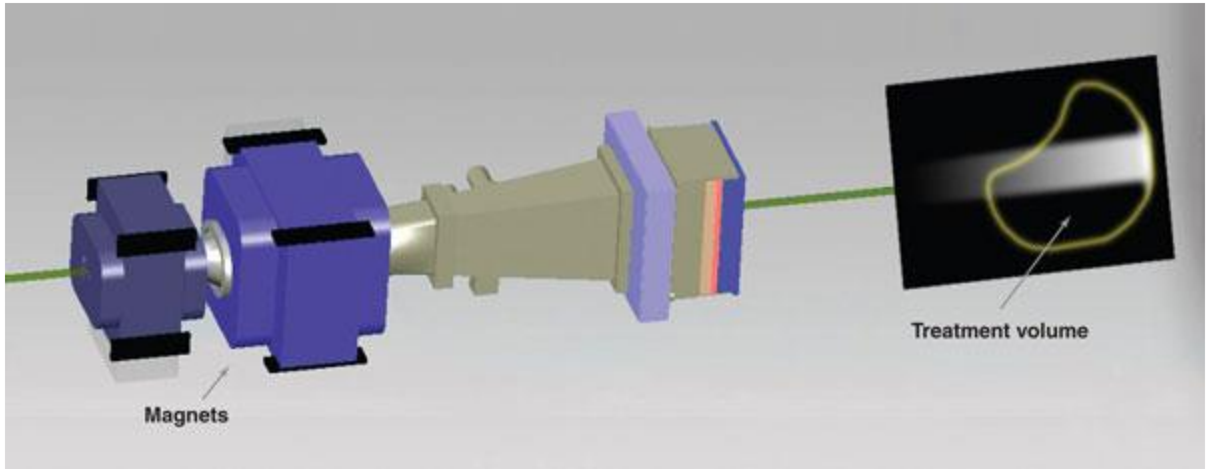


Accelerators for Proton Therapy

- Cyclotrons/synchrotrons accelerate protons to around 250 MeV
  (40 cm range in water)
- Range is modulated, typically with absorber materials
- Two methods for delivering treatment
  1. Passive scattering
  2. Pencil beam scanning

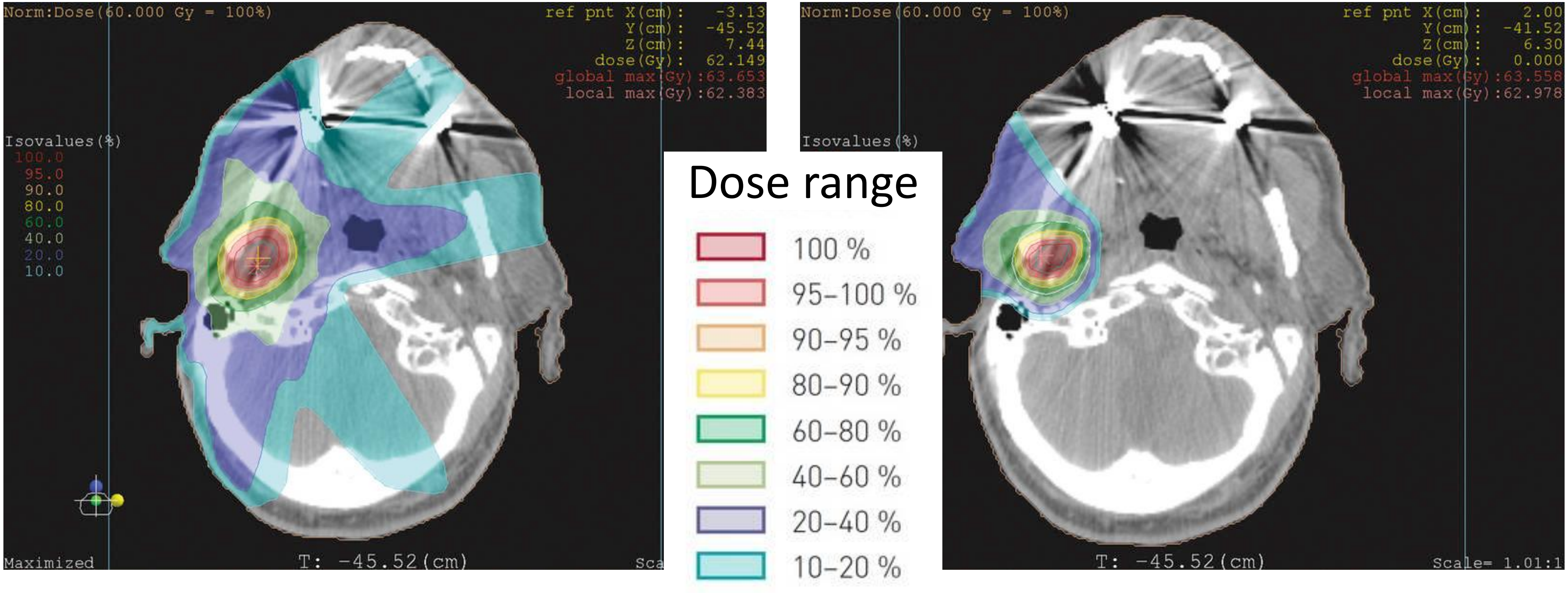


Typical proton scattering beam line



http://medicalphysicsweb.org/cws/article/opinion/42793

Treatment Plans



X-ray Radiotherapy

Proton Radiotherapy

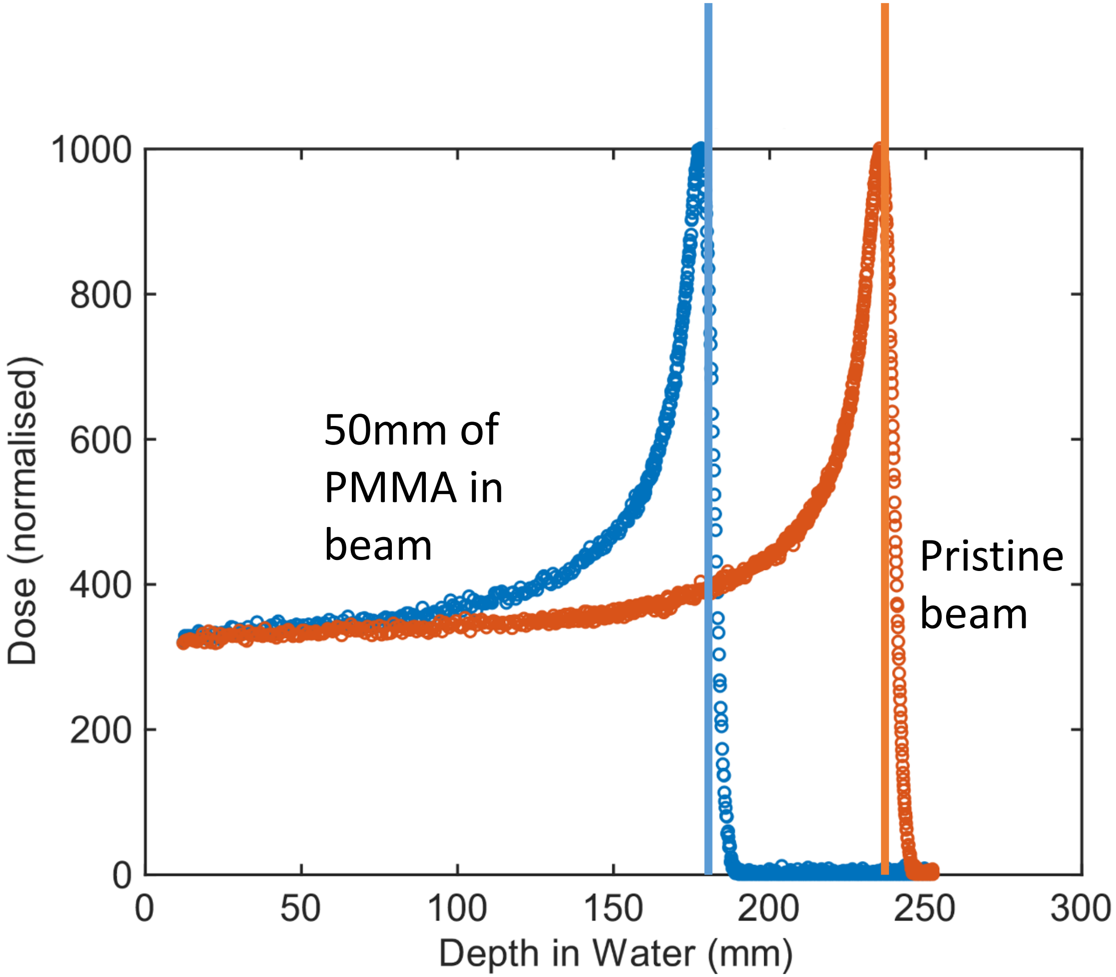
Proton Stopping Power

Human tissues contain varying quantities of **water**

Stopping power of biological tissue relative to water is almost independent of proton energy

Relative stopping power tells us the **water equivalent thickness** for a given thickness of material to allow us to plan the beam range

Range diff is 58 mm of water



PMMA RSP is 58 mm/50 mm = 1.16

X-ray Computed Tomography

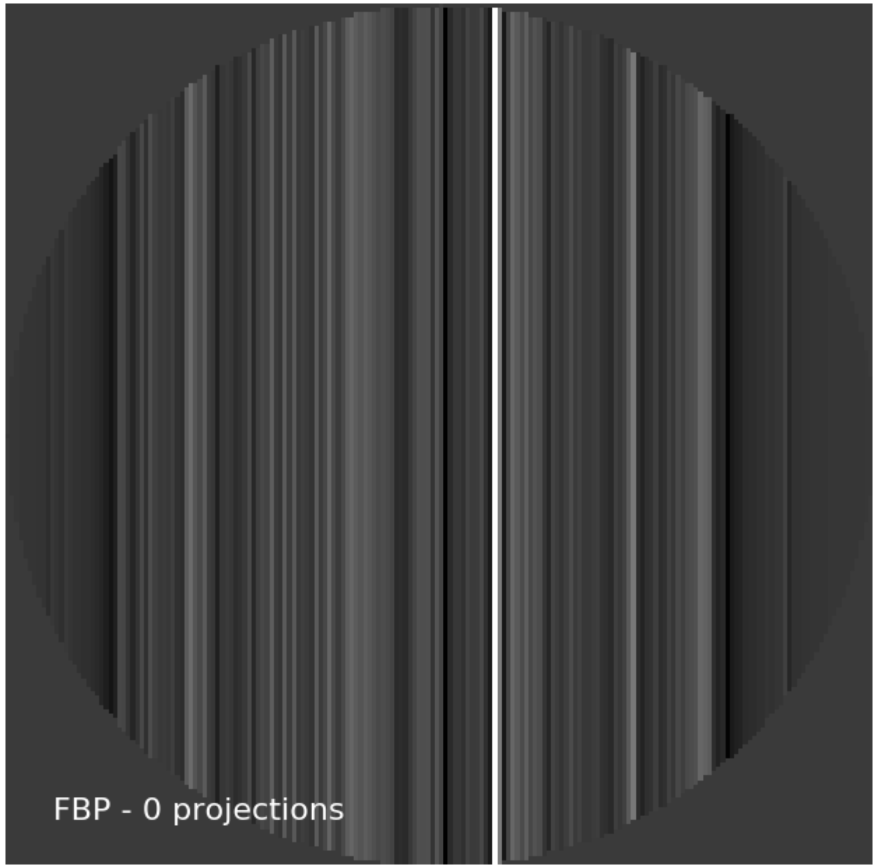
Hounsfield Units measure **x-ray attenuation** relative to water

Reconstruct using filtered backprojection

HU < 700 = **Air or Lung**

700 < HU < 1200 = **Soft Tissue**

1200 > HU = **Bone**



X-ray CT to Proton RSP

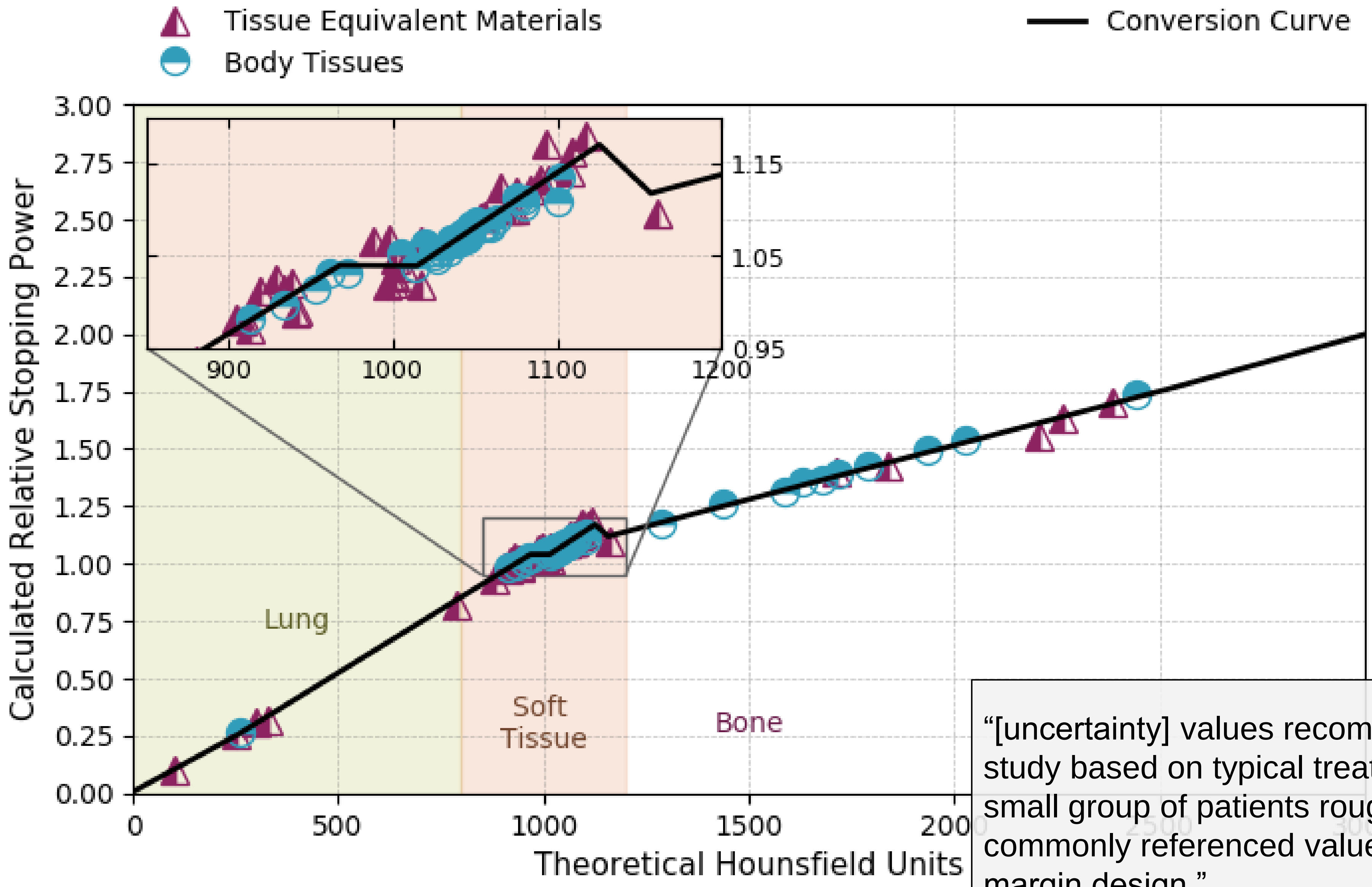
Input:
(x-ray)

$$\boldsymbol{HU = \frac{\langle \mu_x \rangle}{\langle \mu_w \rangle} \times 1000 = \rho_{e,rel} \frac{k_{ph}\widehat{Z}_{eff}^{3.62} + k_{coh}\widetilde{Z}_{eff}^{1.86} + k_{KN}Z_{eff}}{k_{ph}\widehat{Z}_{eff,w}^{3.62} + k_{coh}\widetilde{Z}_{eff,w}^{1.86} + k_{KN}Z_{eff,w}}}$$

Output:
(proton)

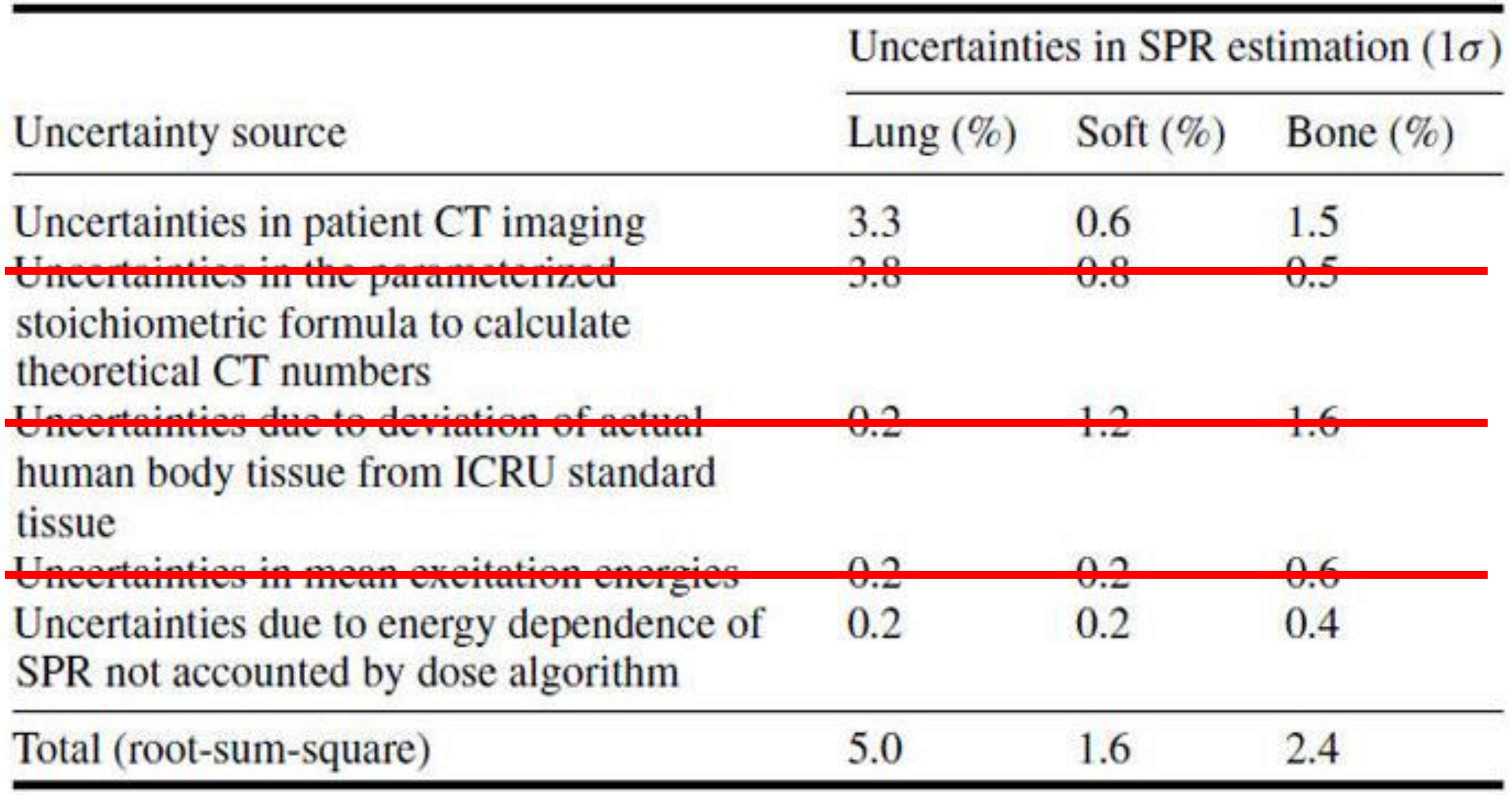
$$\boldsymbol{RSP_m = \rho_{e,rel}} \frac{\ln \frac{2m_e c^2 \beta^2}{(1-\beta^2)I_m} - \boldsymbol{\beta^2}}{\ln \frac{2m_e c^2 \beta^2}{(1-\beta^2)I_w} - \boldsymbol{\beta^2}}$$

$$\boldsymbol{I \approx 10 \times Z_{eff}}$$



> "[uncertainty] values recommended in this study based on typical treatment sites and a small group of patients roughly agree with the commonly referenced value (**3.5%**) used for margin design."
>
> M Yang *et al* PMB. 57 4095–4115 (2012)

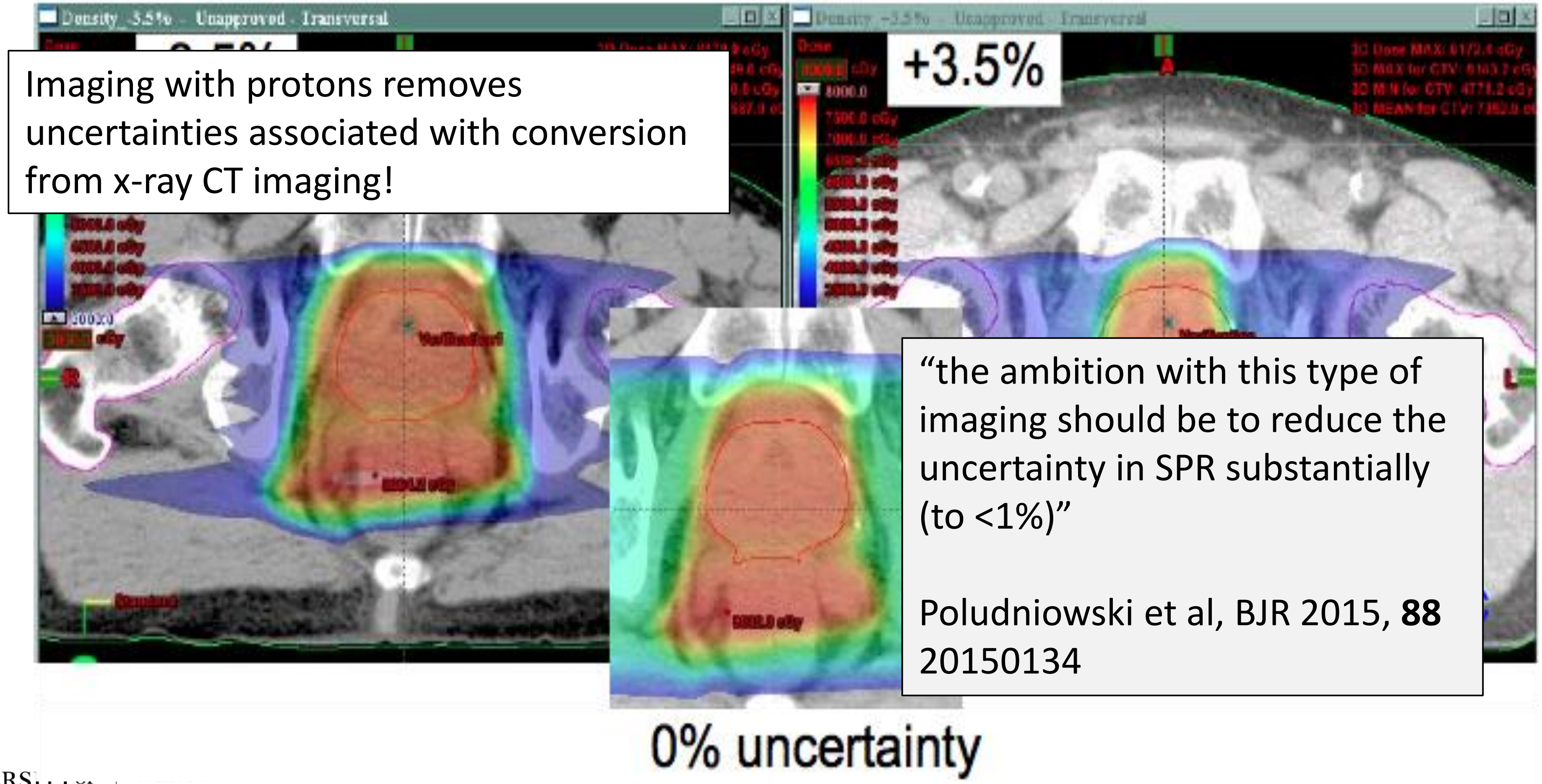
Range Uncertainties



Uncertainty source	Uncertainties in SPR estimation (1σ) Lung (%)	Soft (%)	Bone (%)
Uncertainties in patient CT imaging	3.3	0.6	1.5
~~Uncertainties in the parameterized~~ stoichiometric formula to calculate theoretical CT numbers	~~3.8~~	~~0.8~~	~~0.5~~
~~Uncertainties due to deviation of actual~~ human body tissue from ICRU standard tissue	~~0.2~~	~~1.2~~	~~1.6~~
~~Uncertainties in mean excitation energies~~	~~0.2~~	~~0.2~~	~~0.6~~
Uncertainties due to energy dependence of SPR not accounted by dose algorithm	0.2	0.2	0.4
Total (root-sum-square)	5.0	1.6	2.4

From Yang et al, 2012 Phys. Med. Biol. 57 4095

The need for Proton CT



Imaging with protons removes uncertainties associated with conversion from x-ray CT imaging!

"the ambition with this type of imaging should be to reduce the uncertainty in SPR substantially (to <1%)"

Poludniowski et al, BJR 2015, **88** 20150134

Proton CT and PRaVDA

Proton Radiotherapy Verification and Dosimetry Applications

UNIVERSITY OF LINCOLN

UNIVERSITY OF BIRMINGHAM

UNIVERSITY OF LIVERPOOL

UNIVERSITY OF SURREY

WARWICK
THE UNIVERSITY OF WARWICK

NHS
University Hospitals Birmingham
NHS Foundation Trust

NHS
University Hospitals Coventry and Warwickshire
NHS Trust

NHS
The Clatterbridge Cancer Centre
NHS Foundation Trust

NHS
United Lincolnshire Hospitals
NHS Trust

NHS
The Christie
NHS Foundation Trust

NRF
National Research Foundation
iThemba LABS
Laboratory for Accelerator Based Sciences

University of Cape Town · iYunivesithi yaseKapa · Universiteit van Kaapstad

Karolinska Institutet

aspect systems

isdi
IMAGE SENSOR DESIGN & INNOVATION

Funded by Wellcome Trust Translation Award no. 098285

wellcome

UNIVERSITY OF BIRMINGHAM
COLLEGE OF ENGINEERING AND PHYSICAL SCIENCES

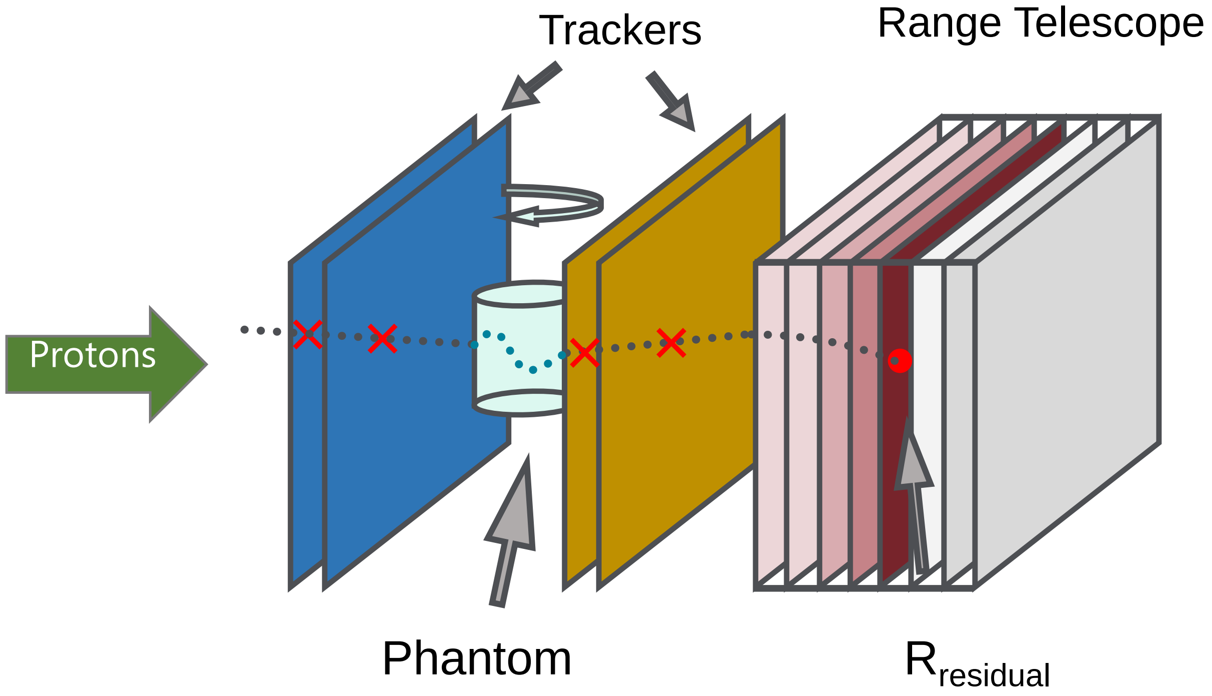
How to design a proton CT system

For proton CT we need:

1. Incident proton energy
2. Incident proton trajectory
3. Exit particle trajectory
4. Residual particle energy

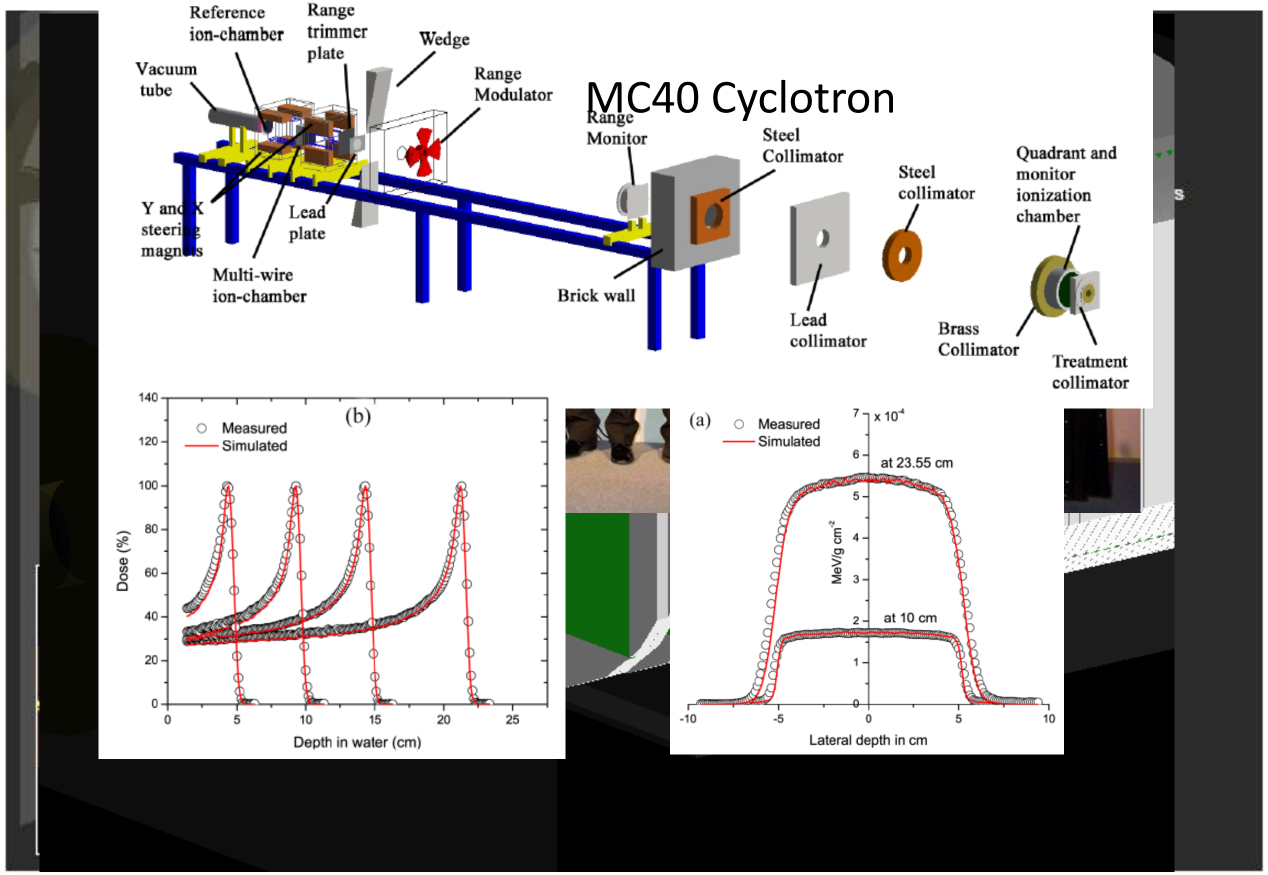
However:

- Require 10^9 protons per proton CT
- Measure position and energy of all protons
- Imaging time of few minutes
- Proton acquisition rates ~1MHz
- Detectors must be radiation tolerant



Geant4 Simulations

- PRaVDASuperSimulation (SuSi)
  - Developed and validated beamlines
  - Validated sensor responses
  - Implemented the full PRaVDA geometry
  - Generated events using of supercomputers (BlueBEAR and GridPP)
- Optimised parameters:
  - Phantom design for imaging
  - Position resolutions and sensor placement
  - Thickness of PMMA in RT for energy resolution
  - Radiation shielding

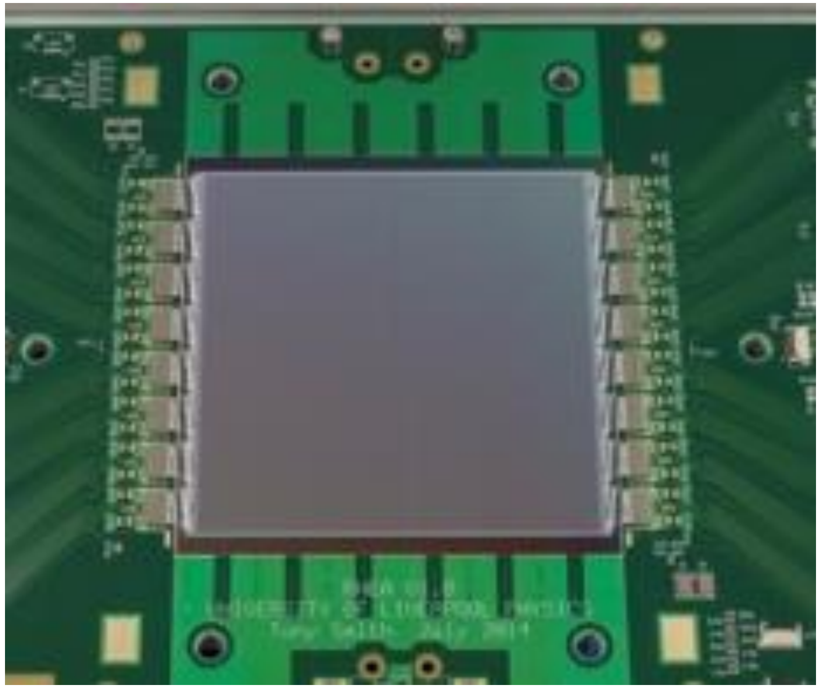


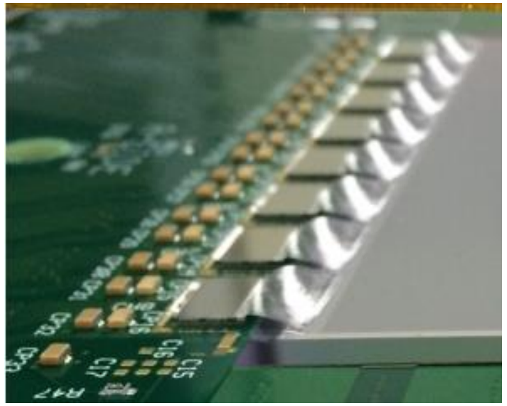
Detector technology

The detectors in PRaVDA are based on developments for ATLAS at HL-LHC and manufactured by Micron Semiconductors UK Ltd

Strip Sensor Parameters:

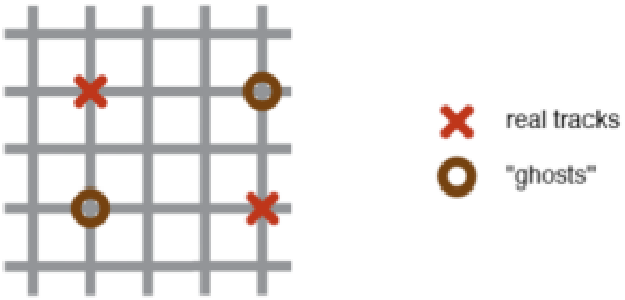
- Active area of 93x96 mm^2
- Strip pitch of 90.8 um
- 150 um thick n-in-p silicon
- Strip Length of 48 mm
- 2048 strips
- 1024 read out from each side
- 16 read out chips (8 for each strip half)
- Double threshold binary read out
- 26 MHz read out rate (synced with beam clock)



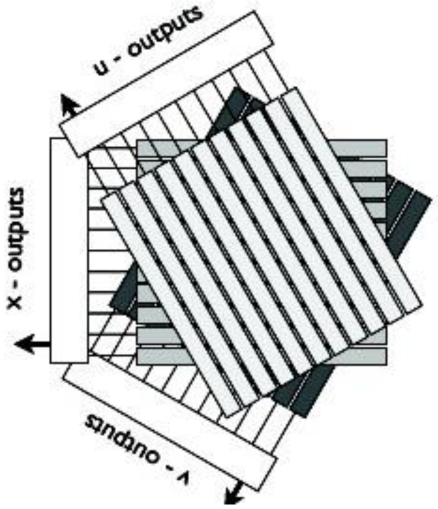


Tracking Detectors

- Strip sensors only provide information in one direction
- Need to cross alternative strips to reconstruct 2D positions
- Strip sensors suffer due to ghost hits
- XY Ghost hits = $N^2 - N$ where N = Events/Frame



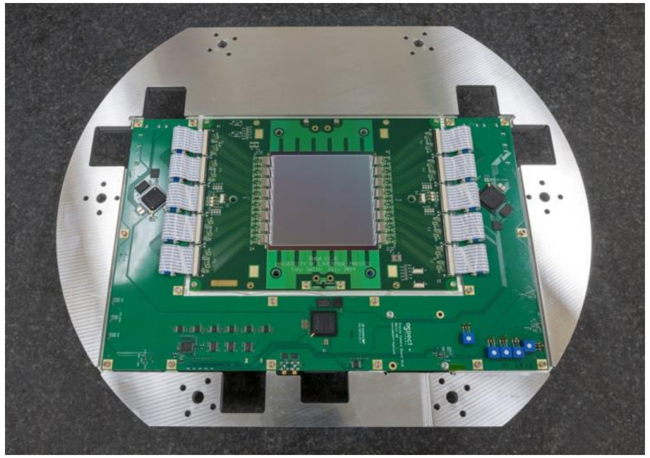
- PRaVDA use an XUV triplet of strips rotated by 60°
- Ghost hits vastly reduced -> more protons per frame -> reduced data acquisition time



Events/ Frame	XY Ghost Hits (%)	XUV Ghost Hits (%)
5	400	0.6
10	900	1.6

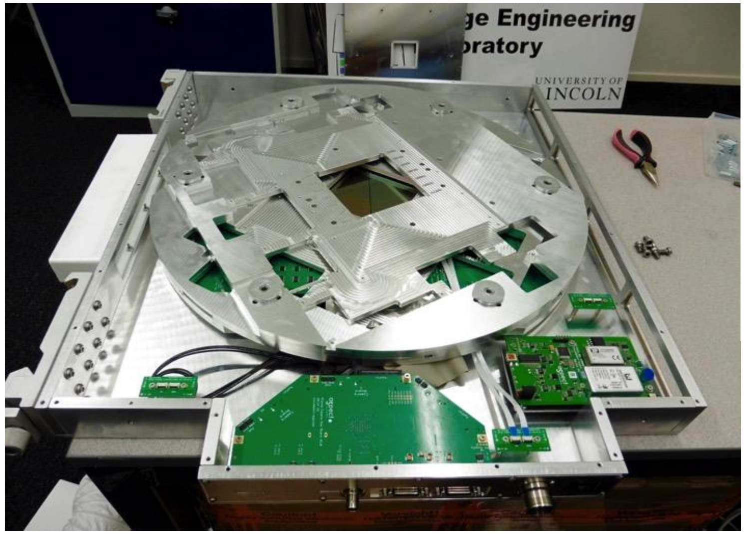
Published Patent WO2015/189601

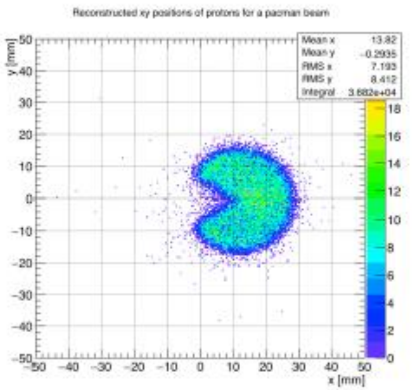
Tracker Construction and Testing

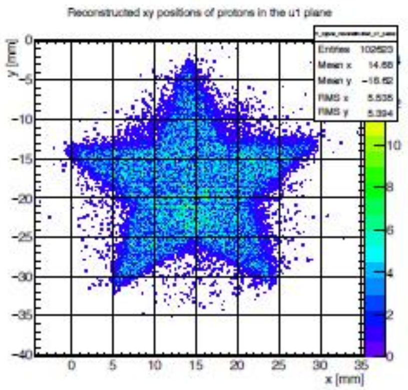


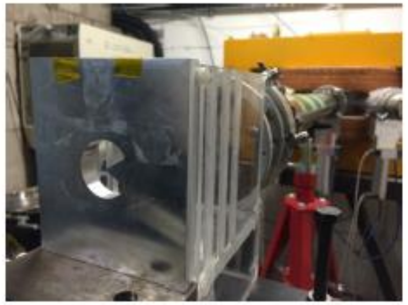
Strip sensor board paired with camera board and fixed to precision made stiffener plate

Three stiffeners mounted in custom made box, orientated by 60^o to each other









Tracking units tested using MC40 cyclotron

Range Telescope

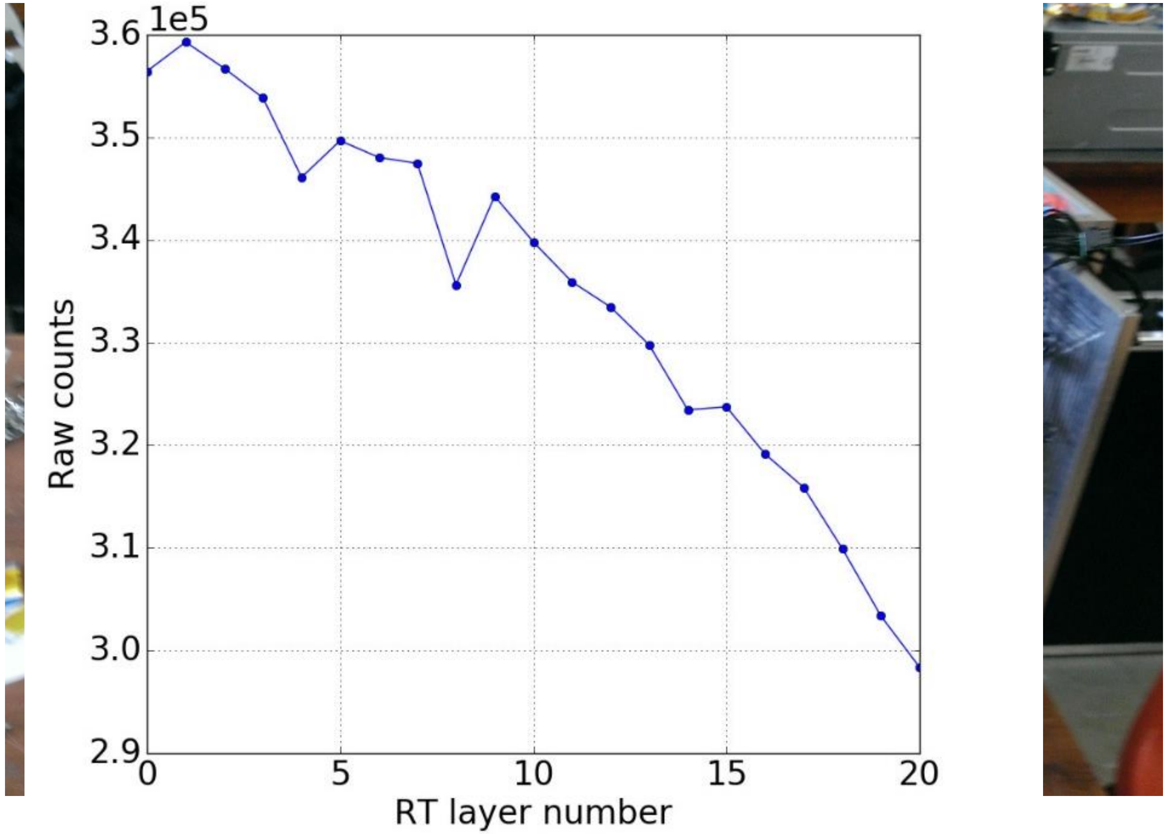
Range telescope determines the **residual range** of the proton

Knowledge of the initial range allows us to determine **change in range** in phantom and reconstruct **RSP**

21 layers of strip detectors interleaved with 1.8mm PMMA absorber

Can determine **residual range** of protons up to around 4 cm (~65 MeV)

Each proton is tracked through N layers to determine final resting point



Range Telescope Calibration

Water-equivalent thickness of calibration sheets used to calibrate RT

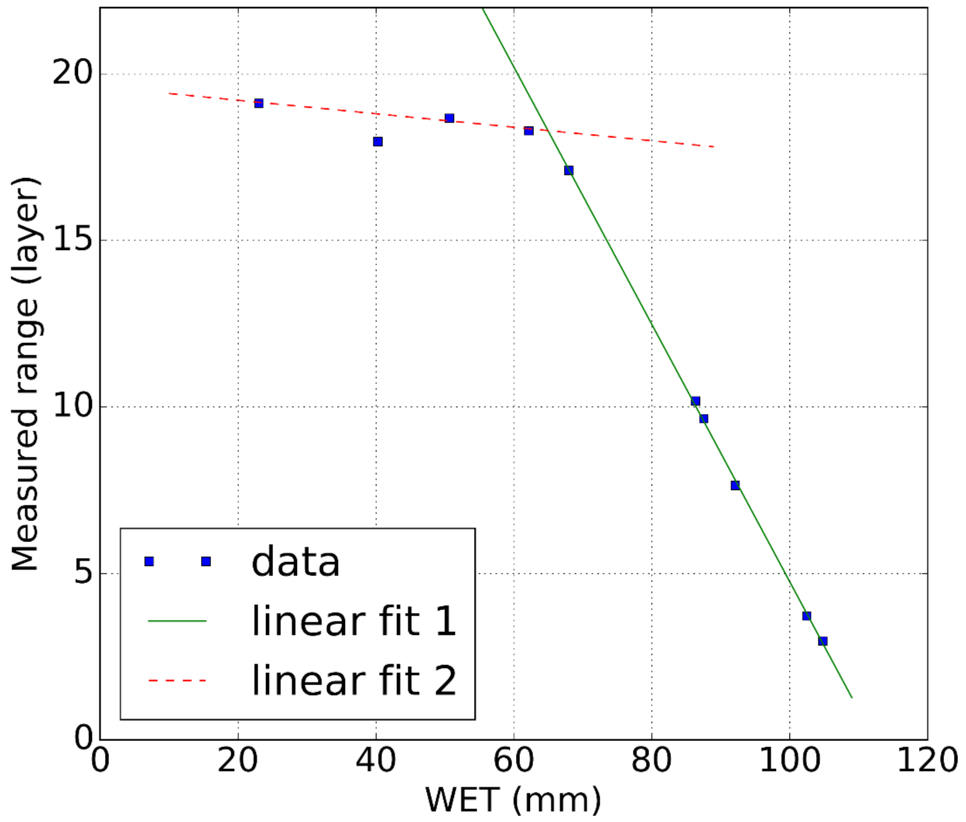
For a known WET, determine the **most-probable last layer**

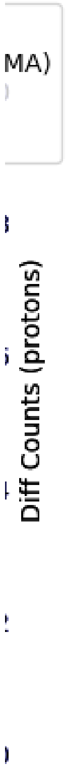
Calibration then allows us to pick a WET from **known last layer**

In practice, resolution is hindered by presence of secondaries, range straggling etc

RT **saturates** at around layer 17

We can no longer determine range due to **protons exiting the RT**





iThemba LABS

Clinical proton therapy centre near Cape Town, South Africa

Treating patients since 1993

191 MeV (240 mm range) beam from research cyclotron

Passive scattering beamline with maximum diameter of 100 mm

Energy can be degraded between 60 MeV and 191 MeV using graphite wedges

iThemba LABS

154 hours of beam time over two weekends

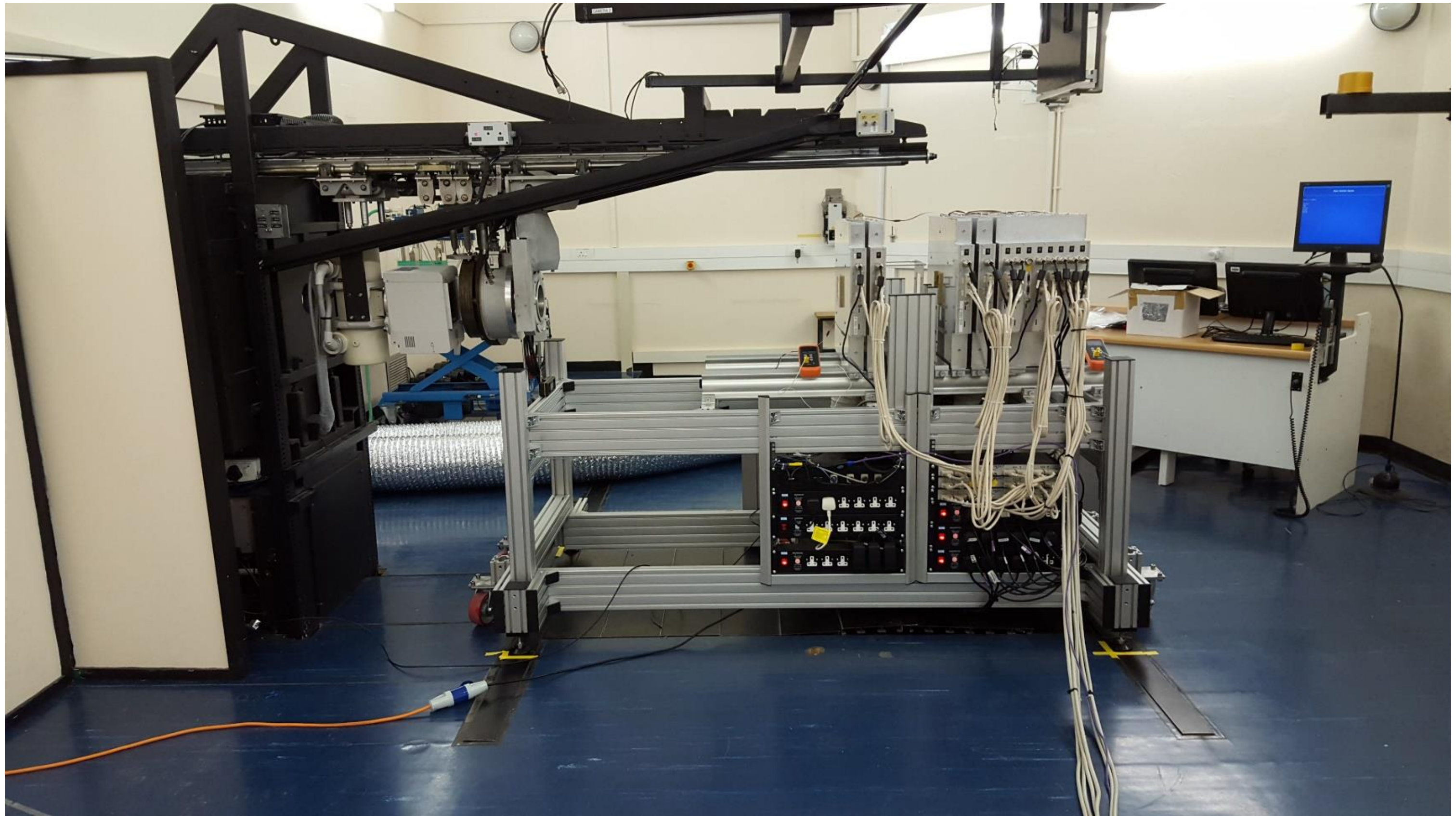
15 TB of data

Thousands of hours of CPU time

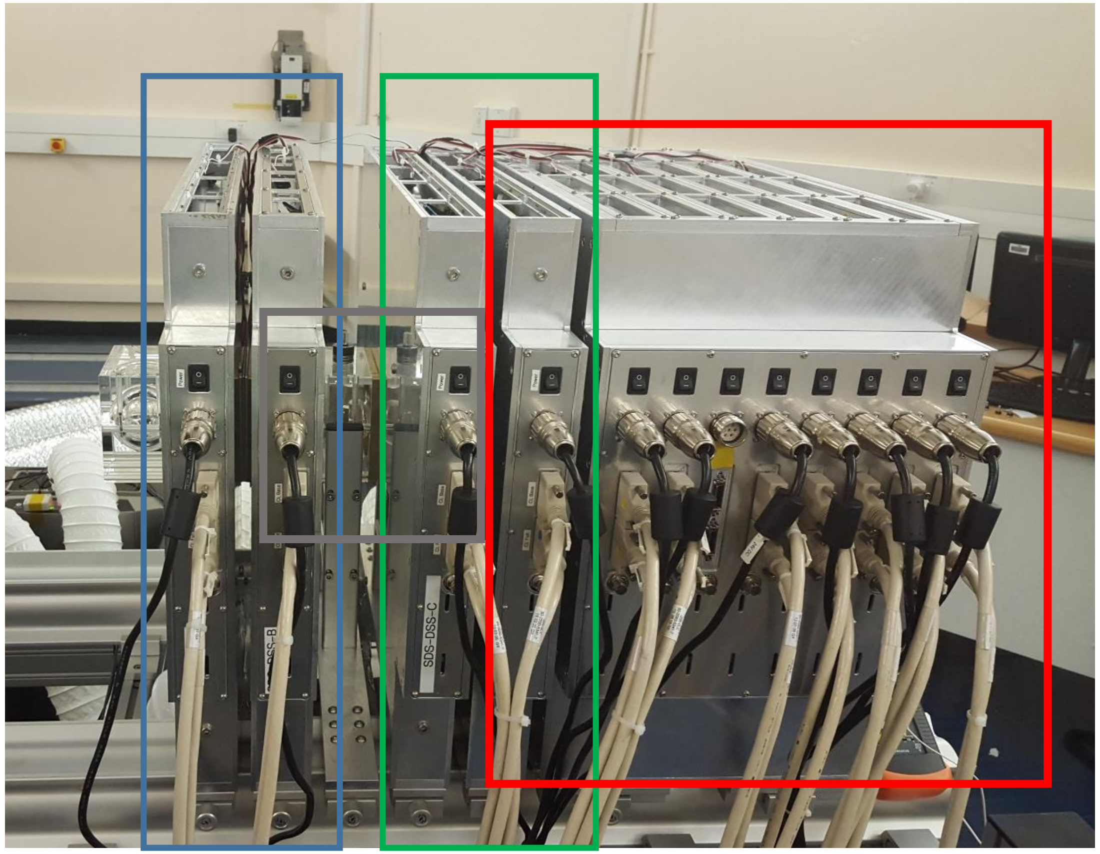
RSP measurements, calibration data, beam characterisation

3 full 3D tomographic reconstructions

iThemba LABS installation



PRaVDA proton CT instrument



Proximal trackers

Imaging Phantom

Distal trackers

Range Telescope

Imaging Phantom

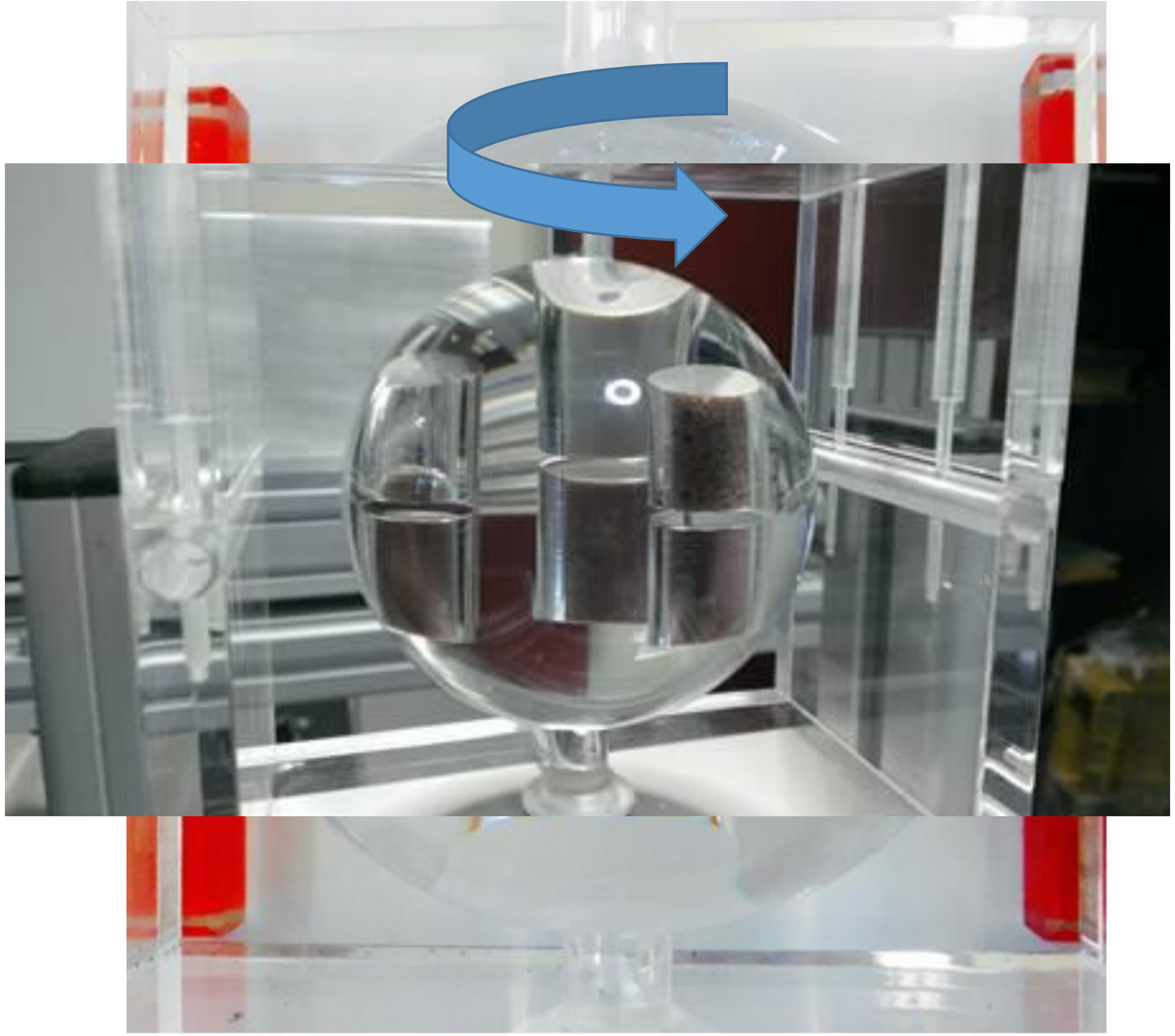
75 mm **PMMA sphere**

With compensator, provides **uniform 81 mm thickness** (93 mm WET)

Contains 6 inhomogeneites

- Adipose, Air, Lung, Cortical Bone, Average Bone, Water

Phantom rotates on a central axis in frame



Proton CT reconstructions

180 radiographs acquired in 1 degree steps

5 seconds acquisition per projection; total time around **15 minutes**

Around **280 million** individual proton histories acquired

Novel **backproject then filter** algorithm used for reconstruction

Stopping powers agree within **1.6%** of independently measured values

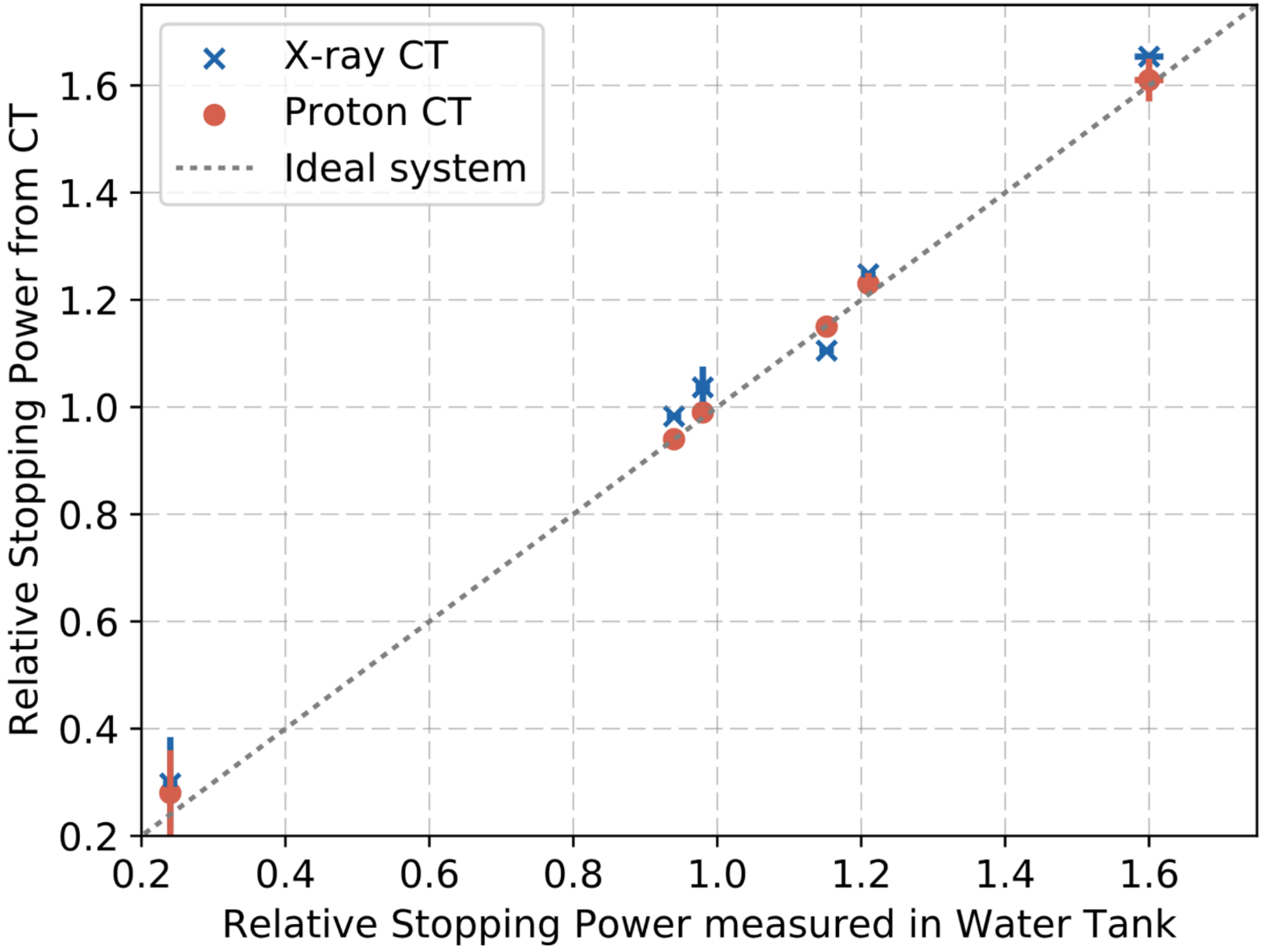


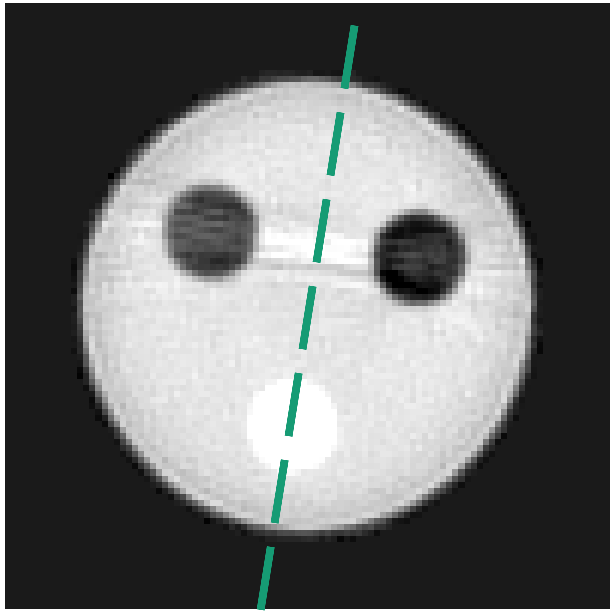
Image Artefacts

Streak artefacts appears through the centre of the phantom, parallel with lung and air

- Caused by **protons exiting the rear of the range telescope**

Ring artefact occurs at outer edge of the phantom

- Caused by **misalignment of compensator**



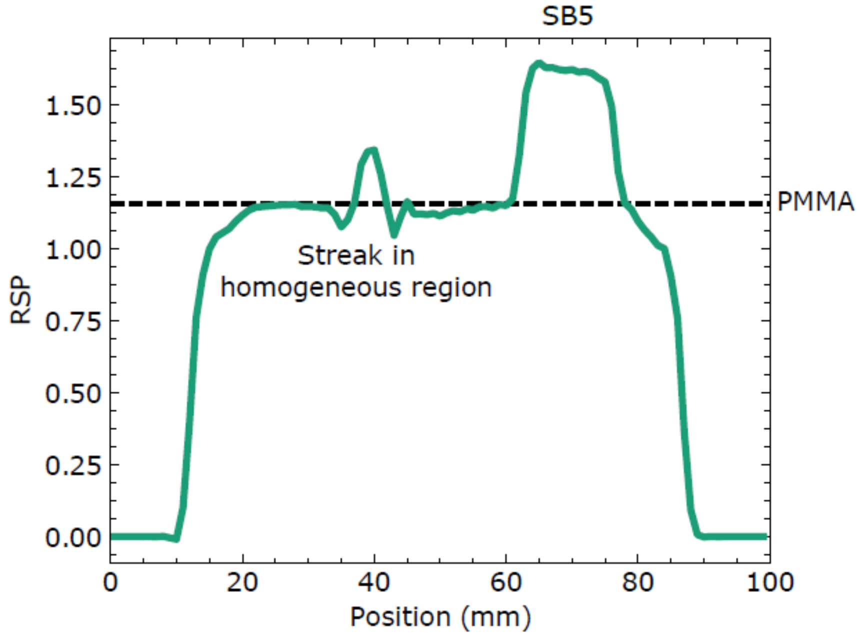


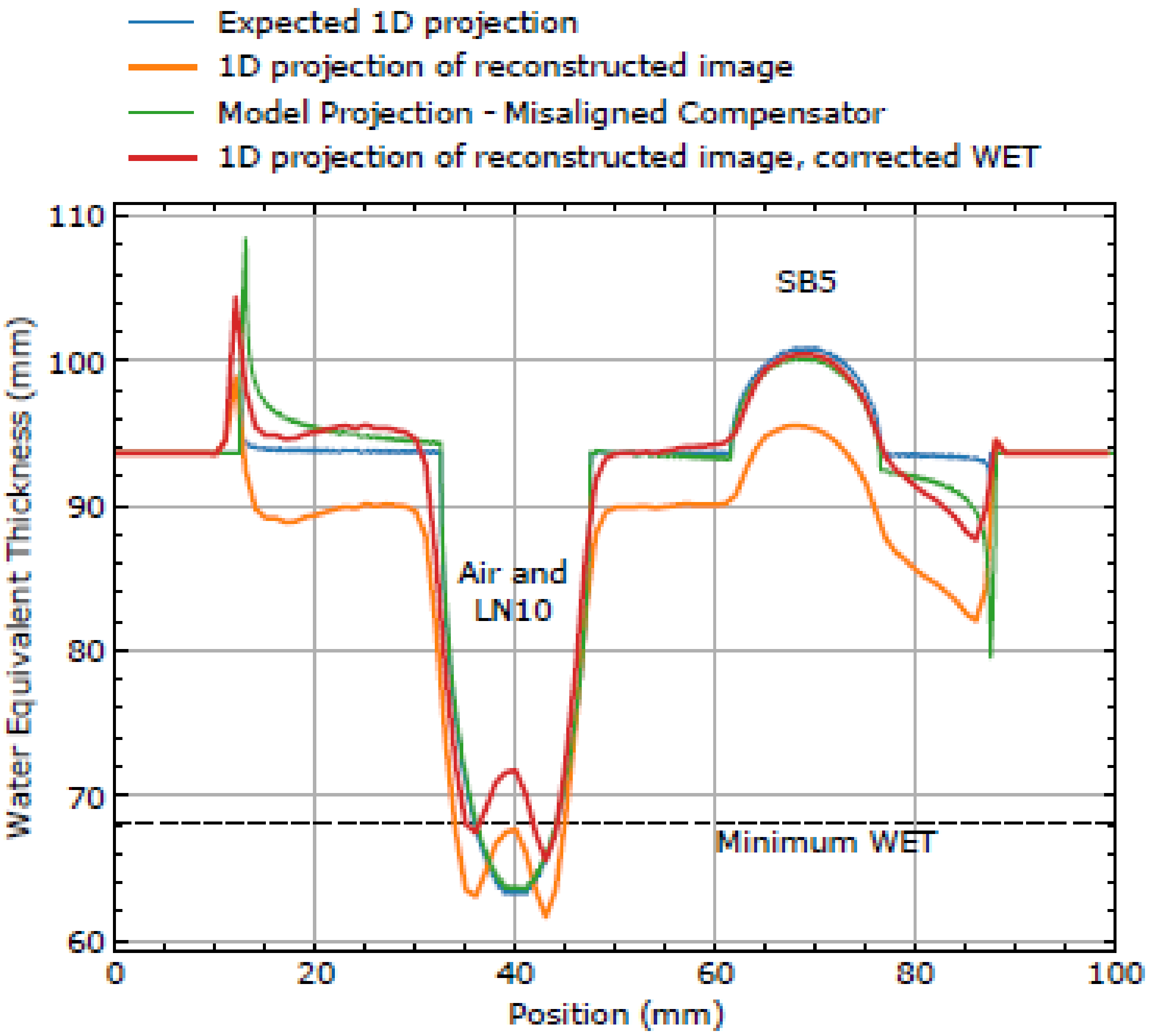
Image Artefacts

Streak artefacts appears through the centre of the phantom, parallel with lung and air

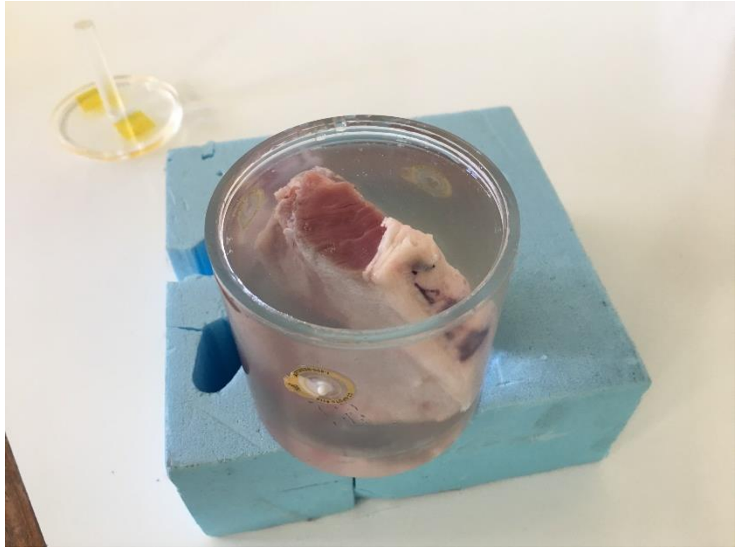
  Caused by **protons exiting the rear of the range telescope**

Ring artefact occurs at outer edge of the phantom

  Caused by **misalignment of compensator**

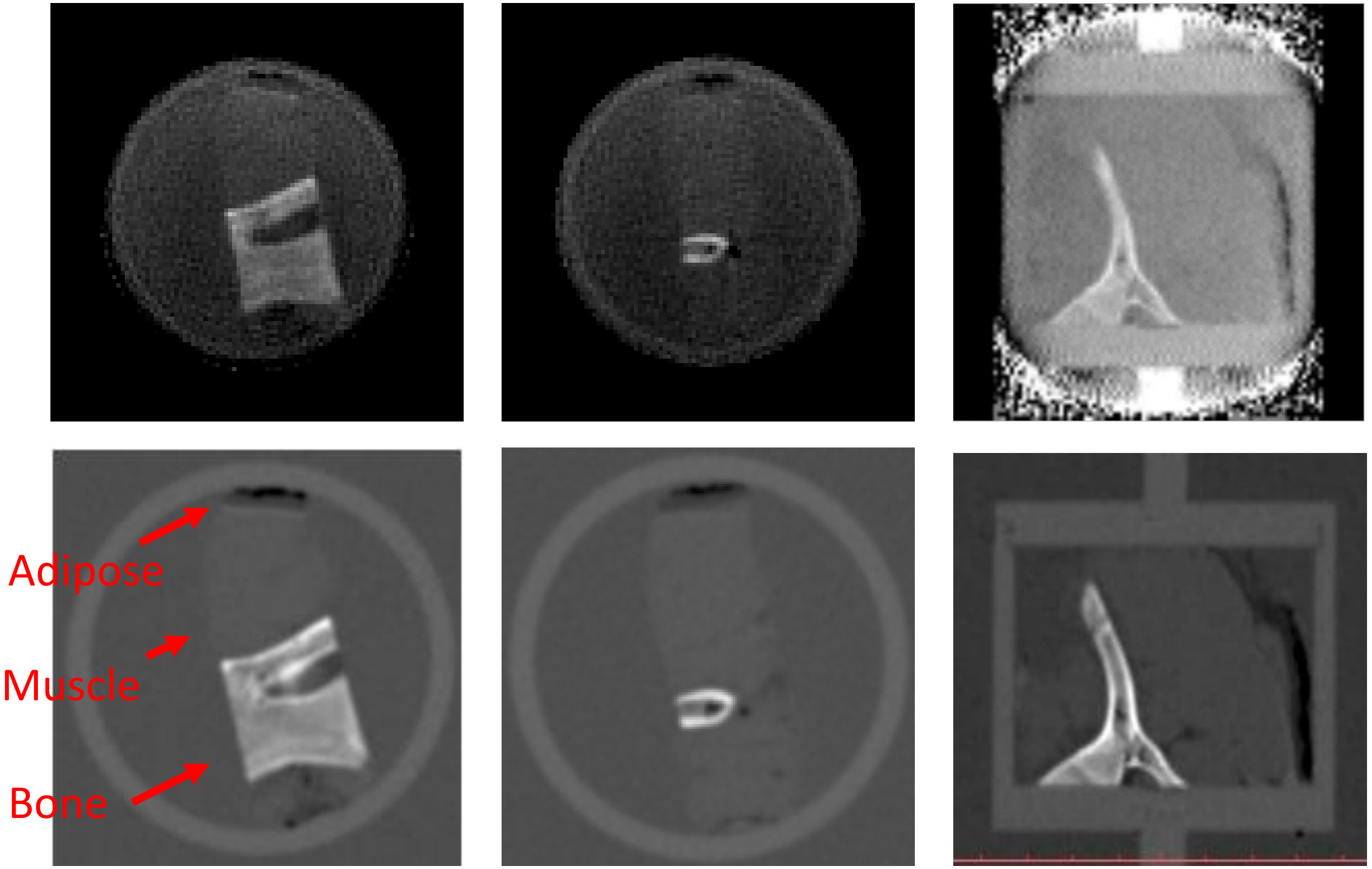


Tissue Phantom



Lamb chop chosen as first test of proton CT on real tissue due to regions of bone, soft tissue and fat

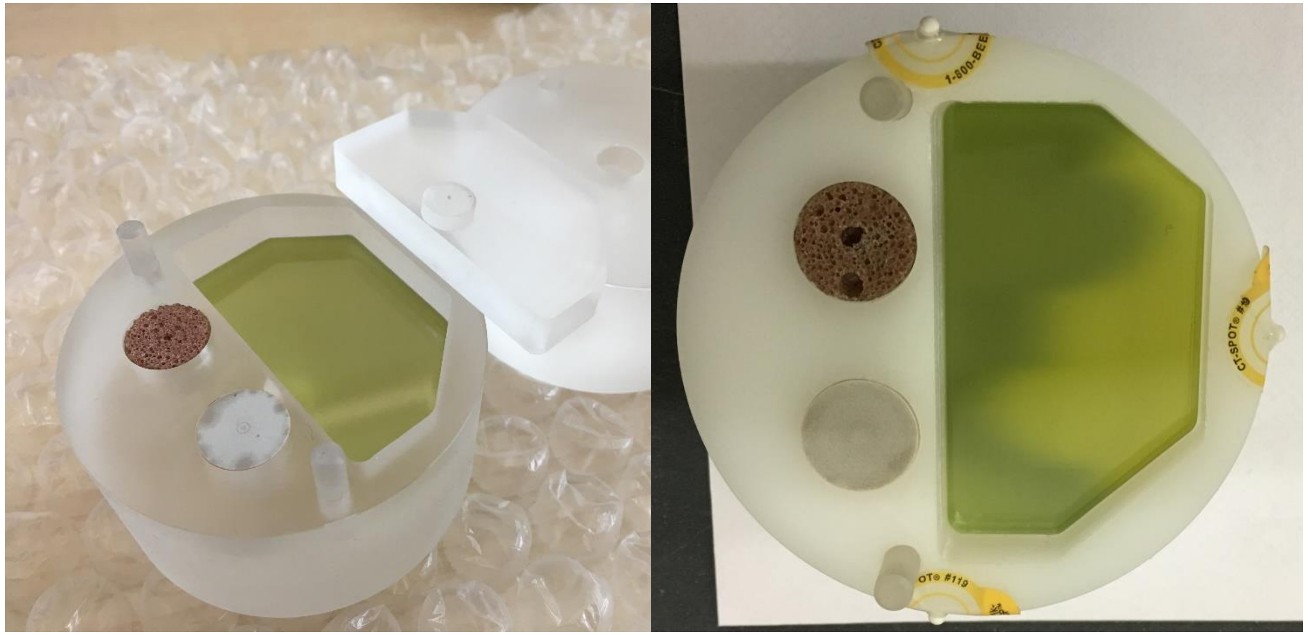
Same parameters as imaging phantom, but 2° rotation steps



Film Phantom

Film phantom allows the range of a **“treatment” beam** to be recorded

This allows comparison with **calculated proton range** on x-ray and proton CT images

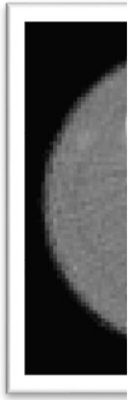


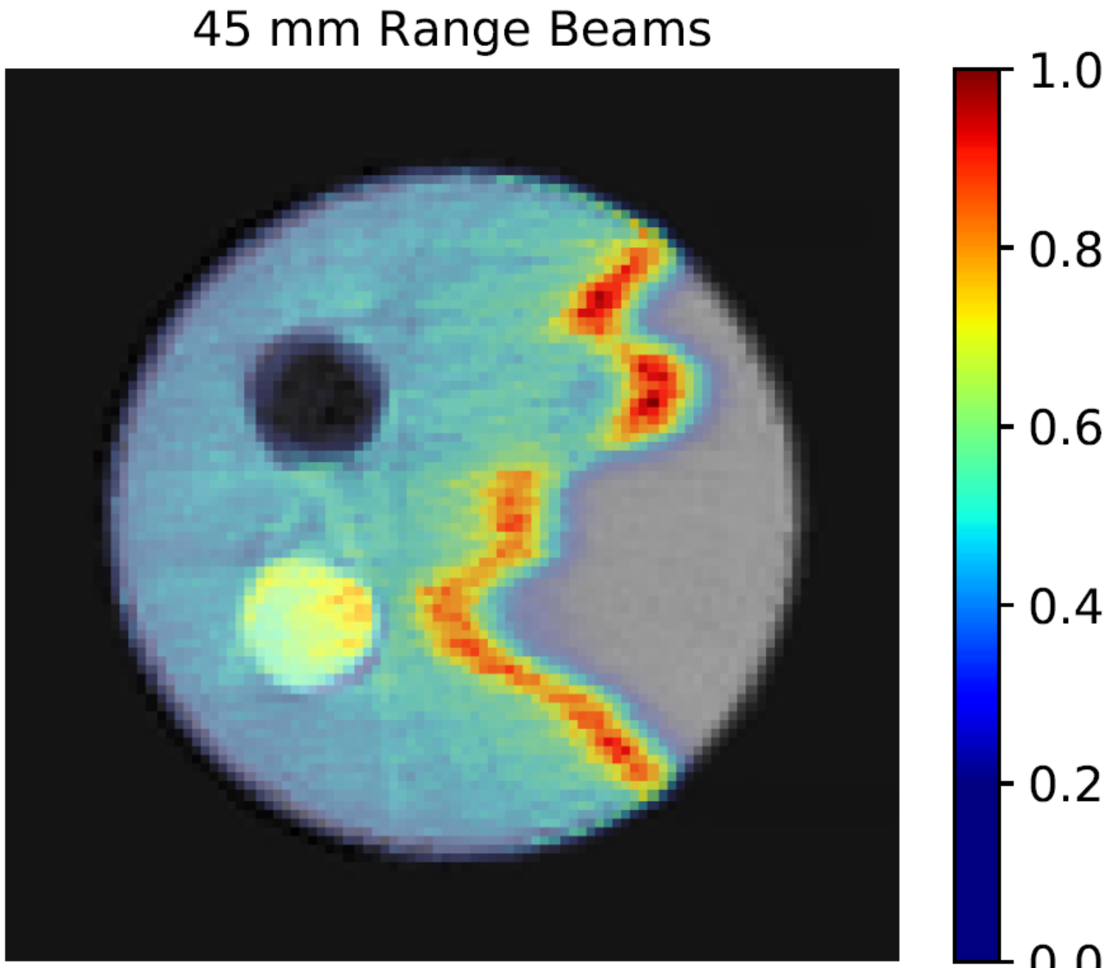
Monte Carlo Simulations

From image, to a Geant4 voxelised geometry

Monte Carlo model of iThema beam used to **calculate range** on image

This exercise could be done in a **clinical treatment planning system**





Range Uncertainties

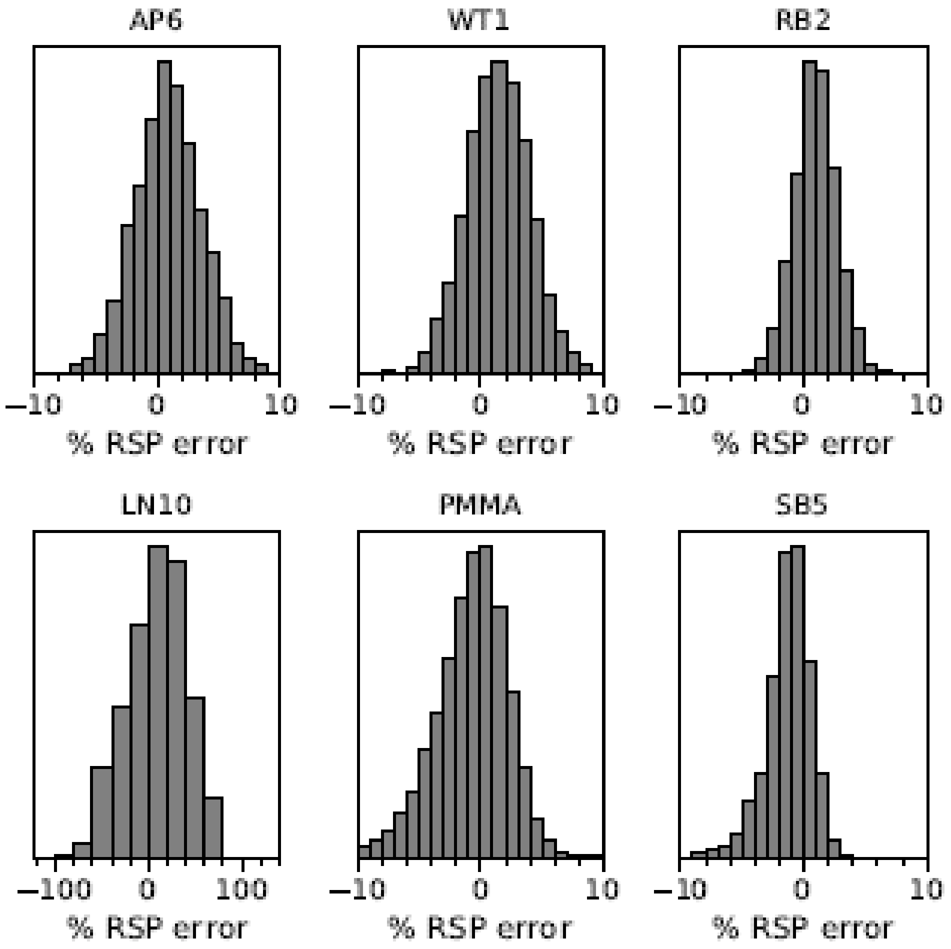
Using the imaging phantom, we wanted to calculate a new **range uncertainty**

RSP error in each voxel is calculated and an error PDF is produced

1D Bragg peaks are then modelled

Each 1 mm step has a random error applied, **sampled from the PDF**

Total range error for each Bragg peak is then calculated

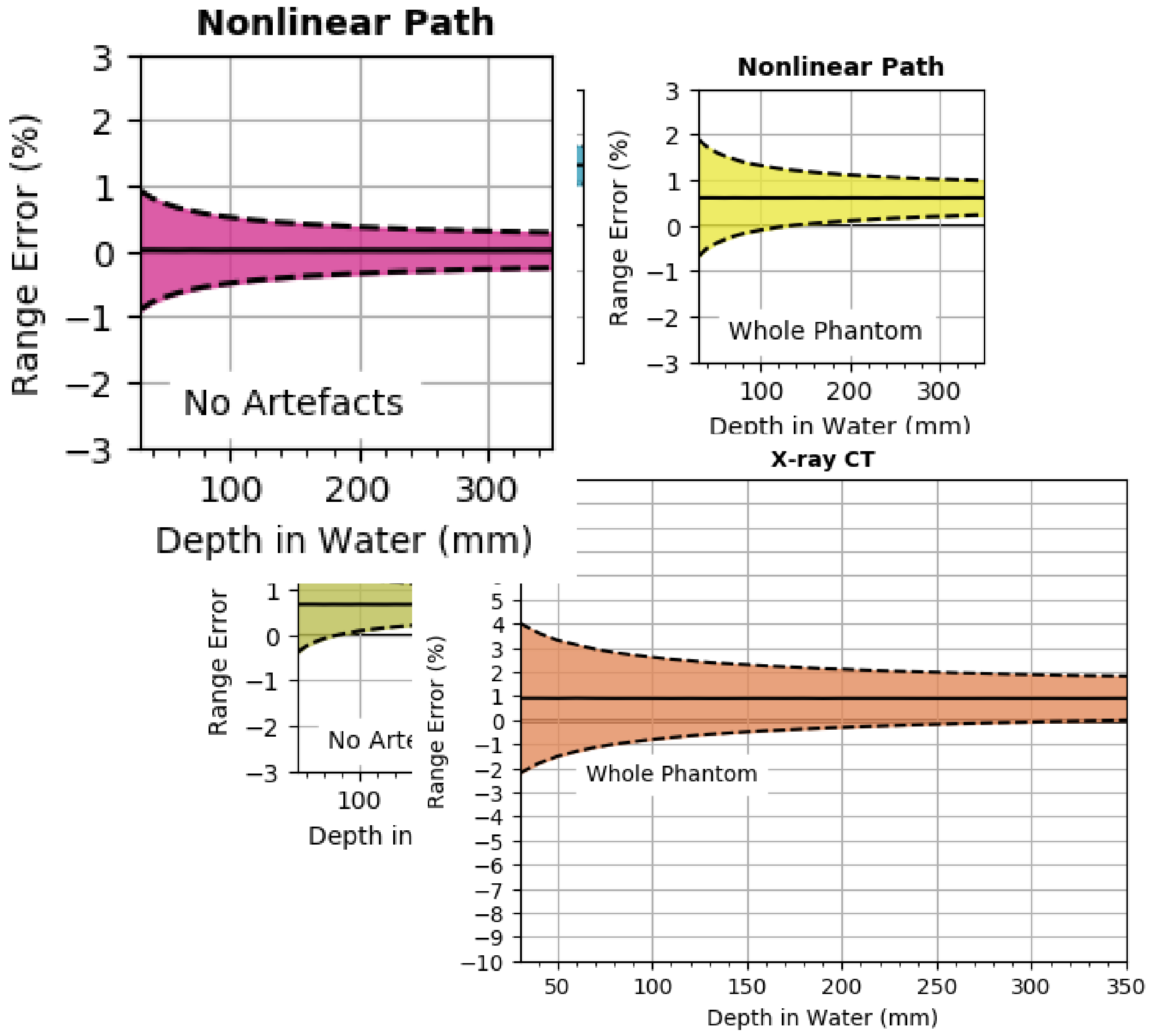


UNIVERSITY OF BIRMINGHAM | COLLEGE OF ENGINEERING AND PHYSICAL SCIENCES

Range Uncertainty Results

These results are promising when compared to range uncertainty in x-ray CT!

But still some way to go to improve images for clinical use



PRaVDA Conclusions

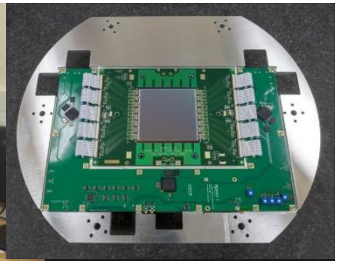
PRaVDA designed and built **first fully solid-state** pCT instrument

Acquired three pCT images of stopping power

Some images suffer from artefacts

Early results suggest that proton CT **could reduce range uncertainty to below 1%**

Design to be optimised and improved in **OPTIMA proton CT** project, based on **The Christie research beamline**



Acknowledgements

PRaVDA

University of Lincoln
Nigel Allinson
Grainne Riley
Chris Waltham
Michela Esposito

University of Birmingham
Phil Allport
David Parker
Tony Price
Ben Phoenix

University of Liverpool
Jon Taylor
Gianluigi Casse
Tony Smith
Ilya Tsurin

University of Surrey
Phil Evans
Nikos Liakos

University of Warwick
Jon Duffy

Karolinska University Hospital, Sweden
Gavin Poludniowski

University Hospital Birmingham NHS Foundation Trust
Stuart Green
Geoff Heyes
Richard Delany

University Hospital Coventry and Warwickshire NHS Trust
Spyros Manolopoulos
Pete Mulholland

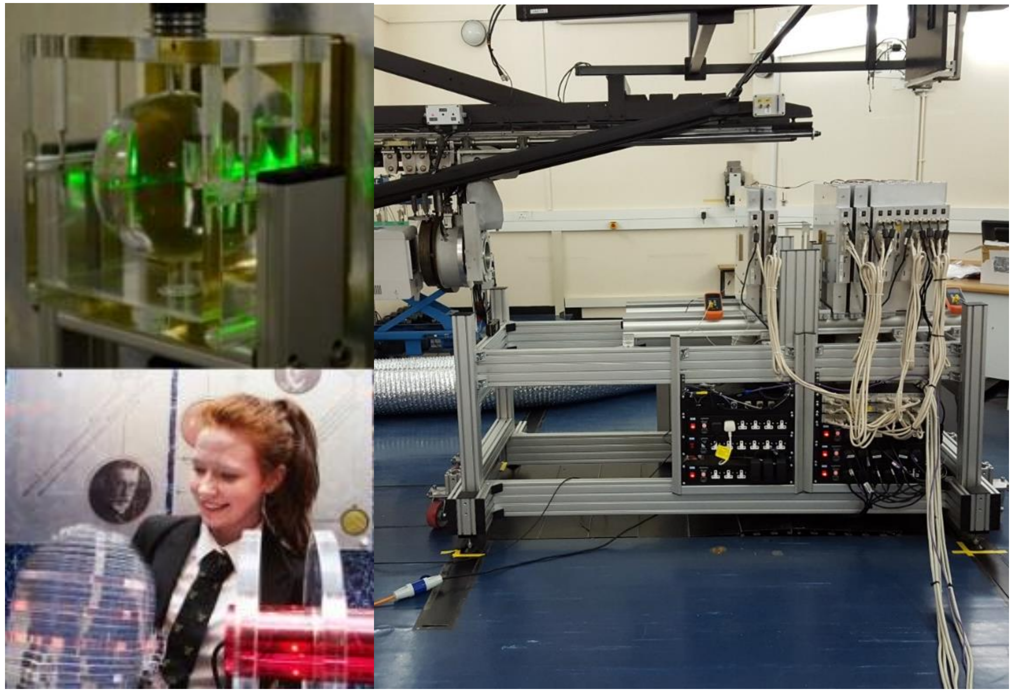
iThemba LABS, South Africa
Jaime Nieto-Camero
Julyan Symons

ISDI
Thalis Anaxagoras
Andre Fant
Przemyslaw Gasiorek
Michael Koeberle

aSpect
Marcus Verhoeven
Daniel Welzig
Daniel Schöne
Frank Lauba

Funded by Wellcome Trust
Translation Award no. 098285

wellcome



UNIVERSITY OF
BIRMINGHAM

COLLEGE OF
ENGINEERING AND
PHYSICAL SCIENCES

Thank you for listening!

- Questions?