UNIVERSITY OF BIRMINGHAM | SCHOOL OF PHYSICS AND ASTRONOMY

UK High Energy Physics developments for radiotherapy

Tony Price

University of Birmingham

PP Seminar

28th September 2016

Contents

- Brief overview of radiotherapy
- Motivation for proton therapy
- The need for proton Computed Tomography (pCT)
- The PRaVDA approach to pCT
- SuperNEMO calorimeter for proton beam QA
- CMOS MAPS for monitoring x-ray radiotherapy

UK Cancer Figures

- Cancer is responsible for 1 in 8 deaths worldwide
- In the UK alone there is 350,000 cases per year and 1 in 2 people will be affected by cancer at some point in their lives
- Most common cancers in the UK are Lung (22%), Colorectal (10%), Breast (8%), Prostate (6%)
- Overall survival rate in the UK is above 50%
- Radiotherapy is used in 40% of all cancer treatment in the UK
- In 2013 UK Gov. committed funds to build 2 proton therapy centres in the UK
- London and Manchester NHS sites to open 2018/19
- Also at least 5 private proton centres in the UK recently announced

* http://www.planningforprotons.com/overview-of-radiotherapy/

What is Radiotherapy?

- Radiotherapy uses radiation to kill the cancer cells
- Energy is deposited in the cells which damages the DNA and stops the cells from replicating
- Surrounding healthy cells are also damaged so need to plan treatment to minimise the dose to the healthy tissue and maximise to the cancer
- High energy x-rays from linear accelerators to treat cancer deep inside a patient
- Low energy x-rays and electrons to treat skin cancers
- Proton/Ion beams which are accelerated using cyclotrons/synchrotrons

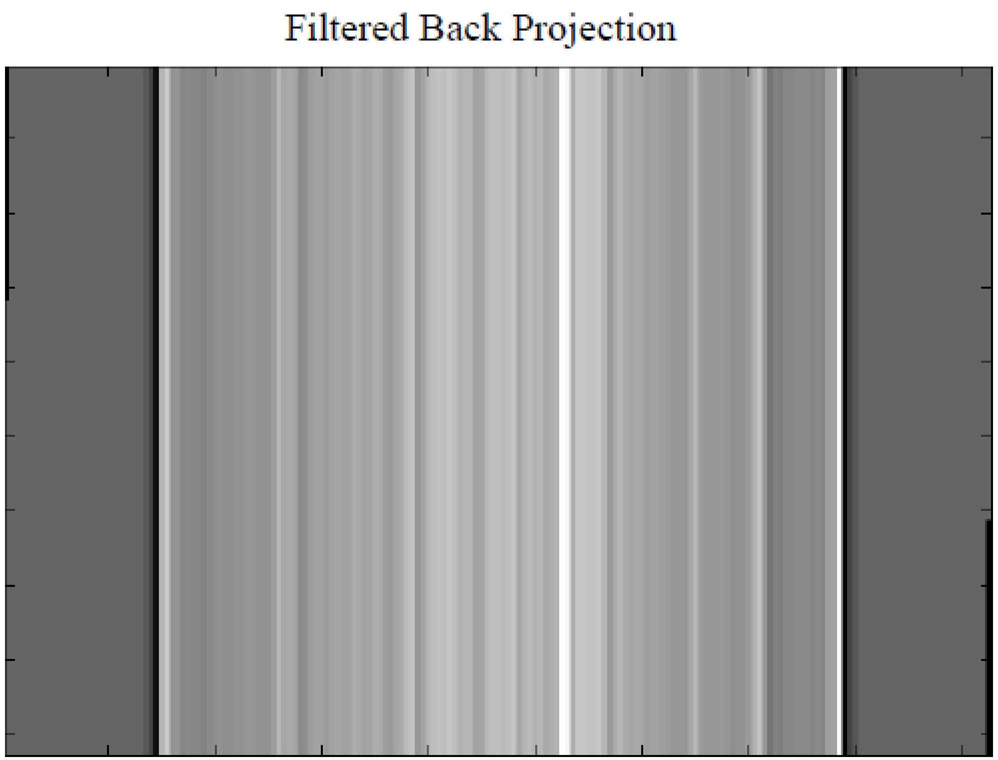
Radiotherapy: Treatment Planning

- Whilst the survival rates associated with conventional radiotherapy are excellent there is one major problem.
- The interactions of photons within the body mean there is an unavoidable dose to the healthy tissue whilst treating the tumour
- Multiple beams and treatments are required in order to spare the healthy tissue and maximise the dose to the tumour
- This requires often complex treatment plans
- To ensure that the radiotherapy is planned correctly it is essential to know
  - where the tumour is located within the body?
  - where are the essential organs which must be spared by the treatment?
  - what is the distribution and amount of various tissues in the body?

Computed Tomography

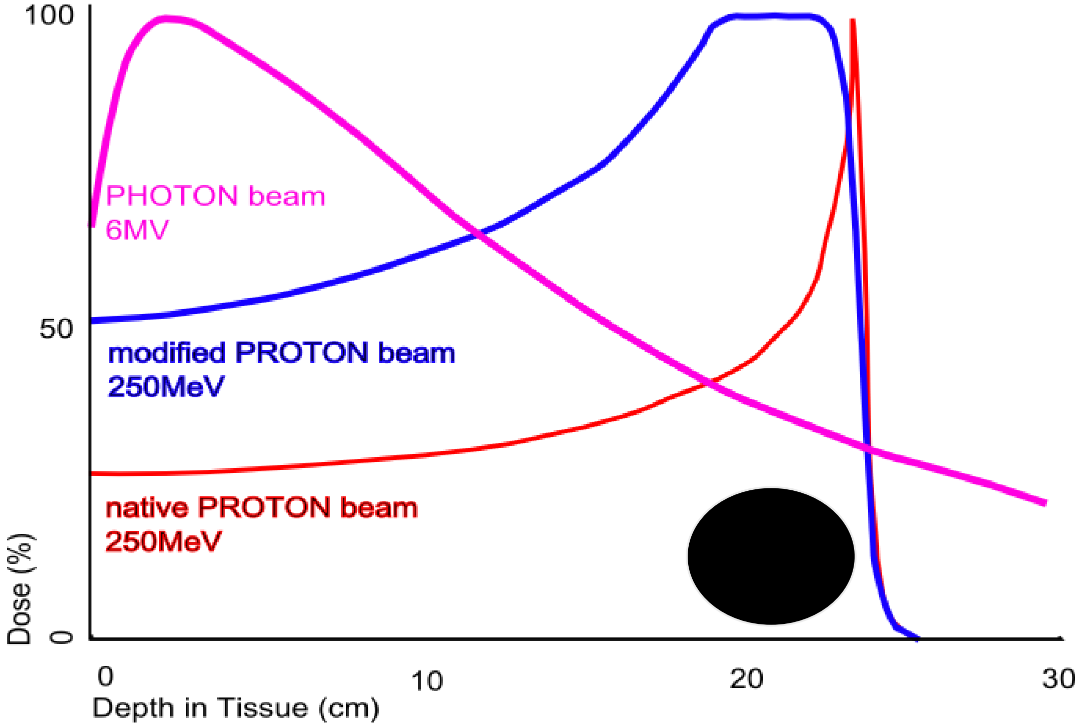
- Measure the flux of photons out of a patient as a function of position on a detector to measure the linear attenuation coefficient along that path through patient (line integral)
- Rotate the source and detectors around the patient and take another radiograph from different angles.
- Use a reconstruction algorithm to combine all of the line integrals as a function of position in the patient
- There are many ways to reconstruct the image from the line integrals
  - Filtered back projection
  - Taking Fourier transforms
  - Iterative approaches
- Many mathematicians still working on improving the CT algorithms but very good images can be reconstructed currently.

Computed Tomography



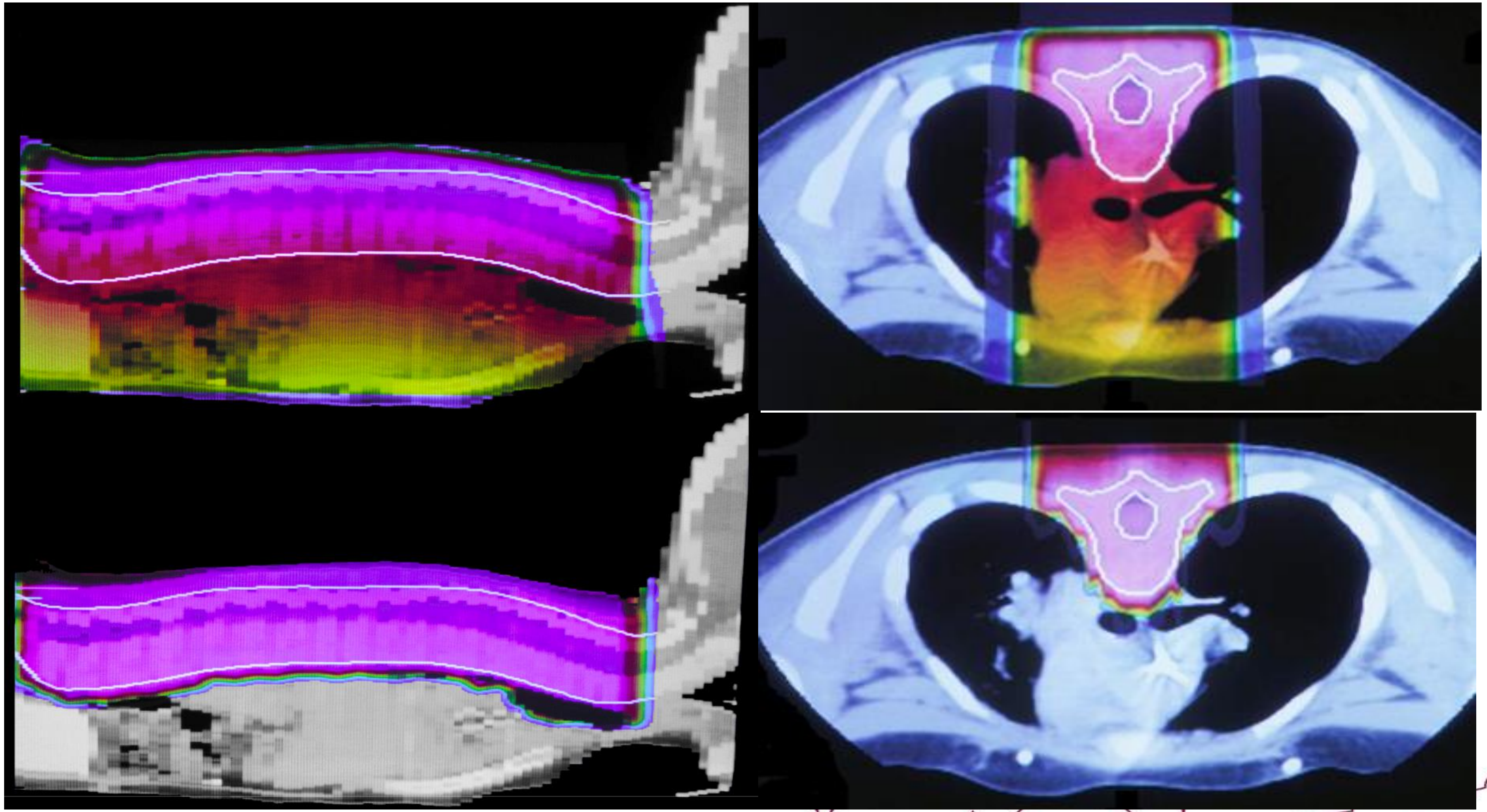
7-points filter, 1 angle (θ=0)

Proton Radiotherapy



- A beam of photons will deposit energy all along its path following an exponential law
- Charged particles lose energy via the Bethe-Bloch formula and as such exhibit a “Bragg Peak”
- Position of BP set by initial particle energy
- Most of the energy is deposited just before a proton stops, leading to an increased ratio of dose in the tumour to dose in healthy tissue
- Lower dose to healthy tissue reduces the risk of complications in later life and allows for treatment of cancers close to critical organs

Compare proton and photon



Medulloblastoma in a child

Blessing and a Curse

- Whilst the Bragg peak is a blessing with respect the sparing healthy tissue it can also be a curse
- Without accurately knowing the materials which the protons traverse the range can be set incorrectly
- This could result in a huge dose to healthy tissue or under dosing the tumour
- There are multiple sources of uncertainty in the protons range

Main uncertainty caused by imaging the patient with x-rays but treating with protons!

IOP PUBLISHING PHYSICS IN MEDICINE AND BIOLOGY
Phys. Med. Biol. **57** (2012) R99–R117 doi:10.1088/0031-9155/57/11/R99

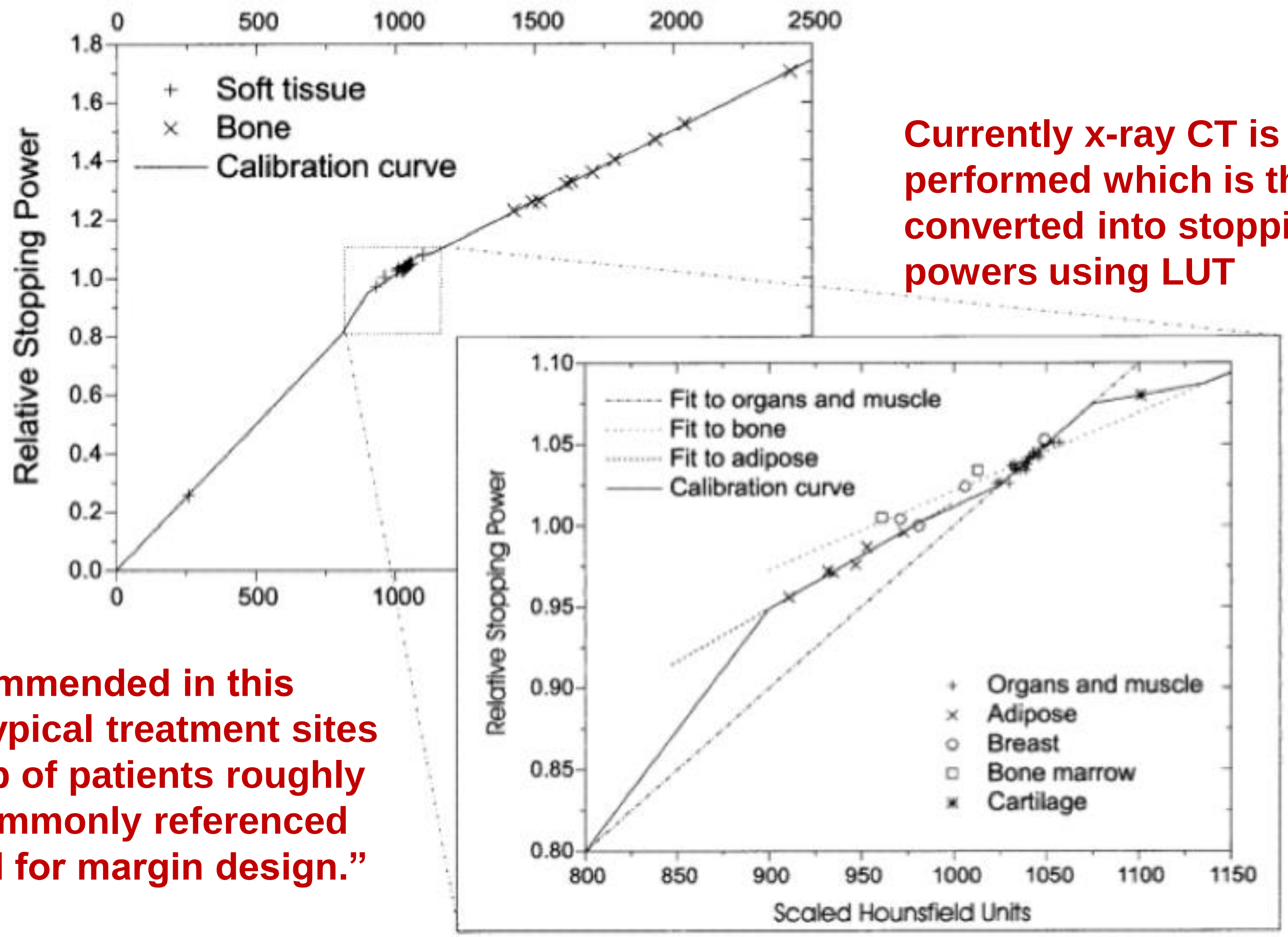
TOPICAL REVIEW

Range uncertainties in proton therapy and the role of Monte Carlo simulations

Harald Paganetti

Source of range uncertainty in the patient	Range uncertainty without Monte Carlo	Range uncertainty with Monte Carlo
Independent of dose calculation		
Measurement uncertainty in water for commissioning	±0.3 mm	±0.3 mm
Compensator design	±0.2 mm	±0.2 mm
Beam reproducibility	±0.2 mm	±0.2 mm
Patient setup	±0.7 mm	±0.7 mm
Dose calculation		
Biology (always positive) ˆ	+∼0.8%	+∼0.8%
CT imaging and calibration	±0.5% [a]	±0.5% [a]
CT conversion to tissue (excluding I-values)	±0.5% [b]	±0.2% [g]
CT grid size	±0.3% [c]	±0.3% [c]
Mean excitation energy (I-values) in tissues	±1.5% [d]	±1.5% [d]
Range degradation; complex inhomogeneities	−0.7% [e]	±0.1%
Range degradation; local lateral inhomogeneities *	±2.5% [f]	±0.1%
Total (excluding *, ˆ)	2.7% + 1.2 mm	2.4% + 1.2 mm
Total (excluding ˆ)	4.6% + 1.2 mm	2.4% + 1.2 mm

The need for pCT

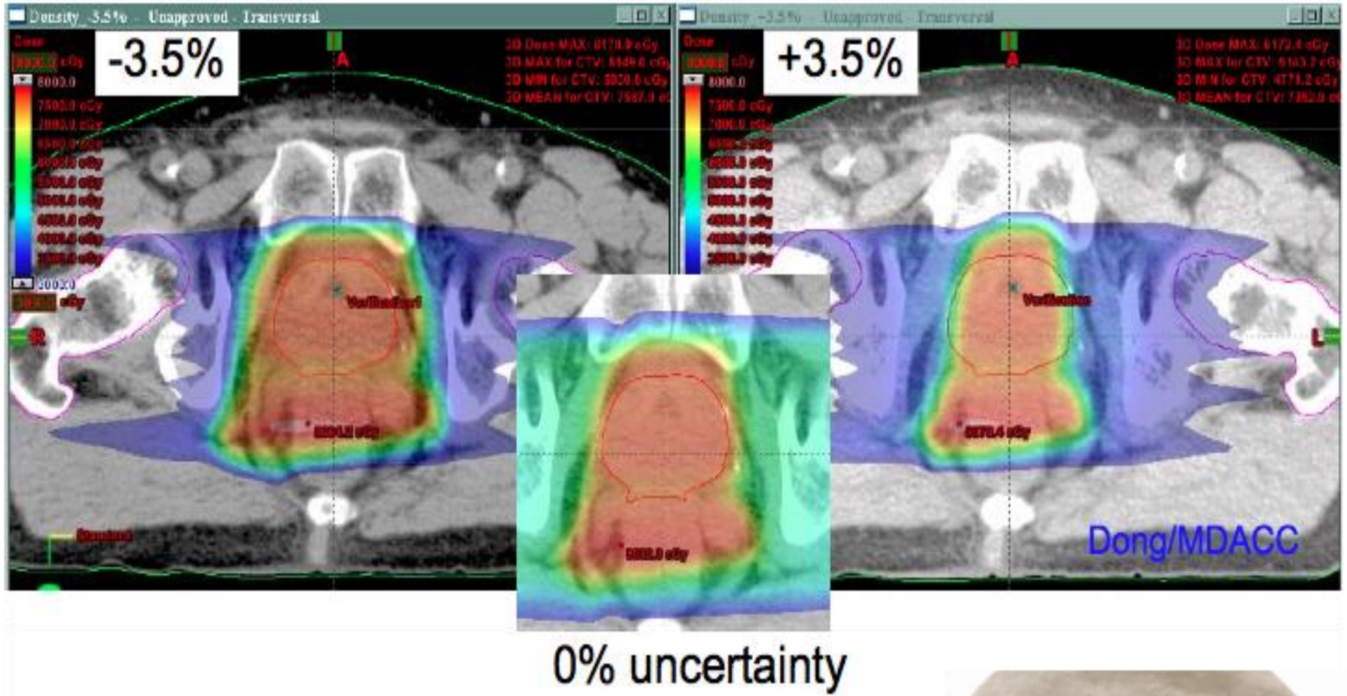


Currently x-ray CT is performed which is then converted into stopping powers using LUT

"The 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)

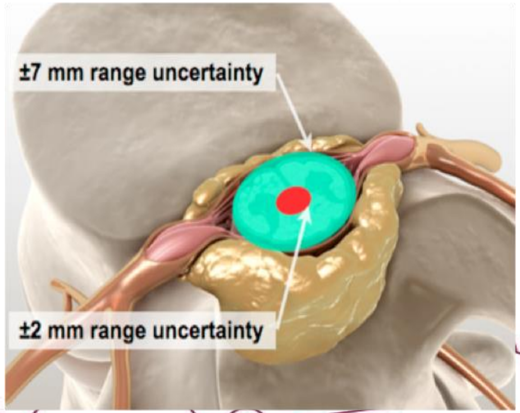
The need for pCT



Current uncertainty in proton range is ~3.5%. If beam passes through 20cm of tissue, then Bragg peak could be anywhere within +/- 7 mm

Aim to reduce proton range uncertainties to a ~1% – variation of +/- 2mm.

Simplified treatment plans – fewer beams; reduced probability of secondary cancers induced; and treatments will be shorter



Methodology

Track proton in
Track proton out
Measure residual energy

Sounds easy right?

But…
Need information on all protons
Require 10^9 protons per image
Imaging time needs to be of order minutes

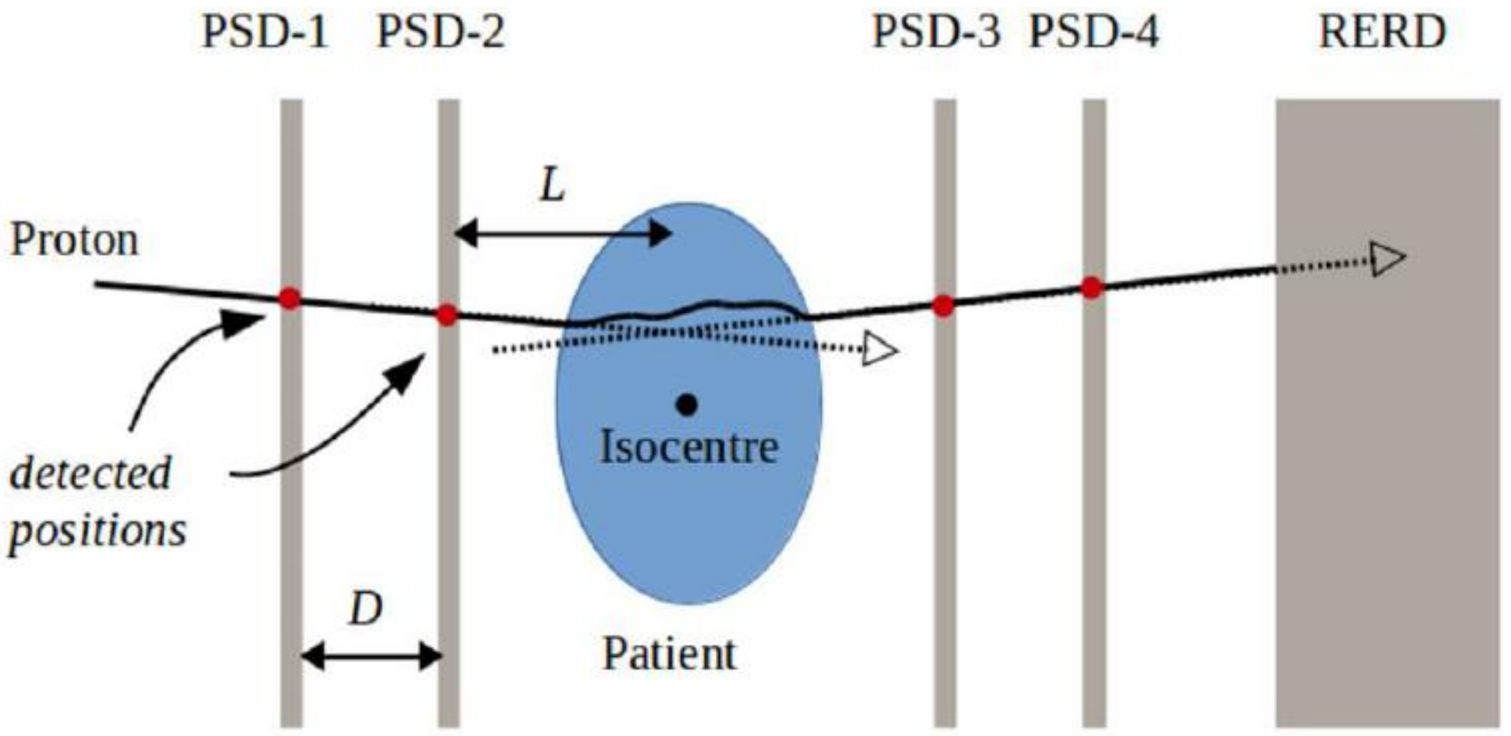


Figure 5. A schematic of the ideal proton-tracking pRG/pCT system.

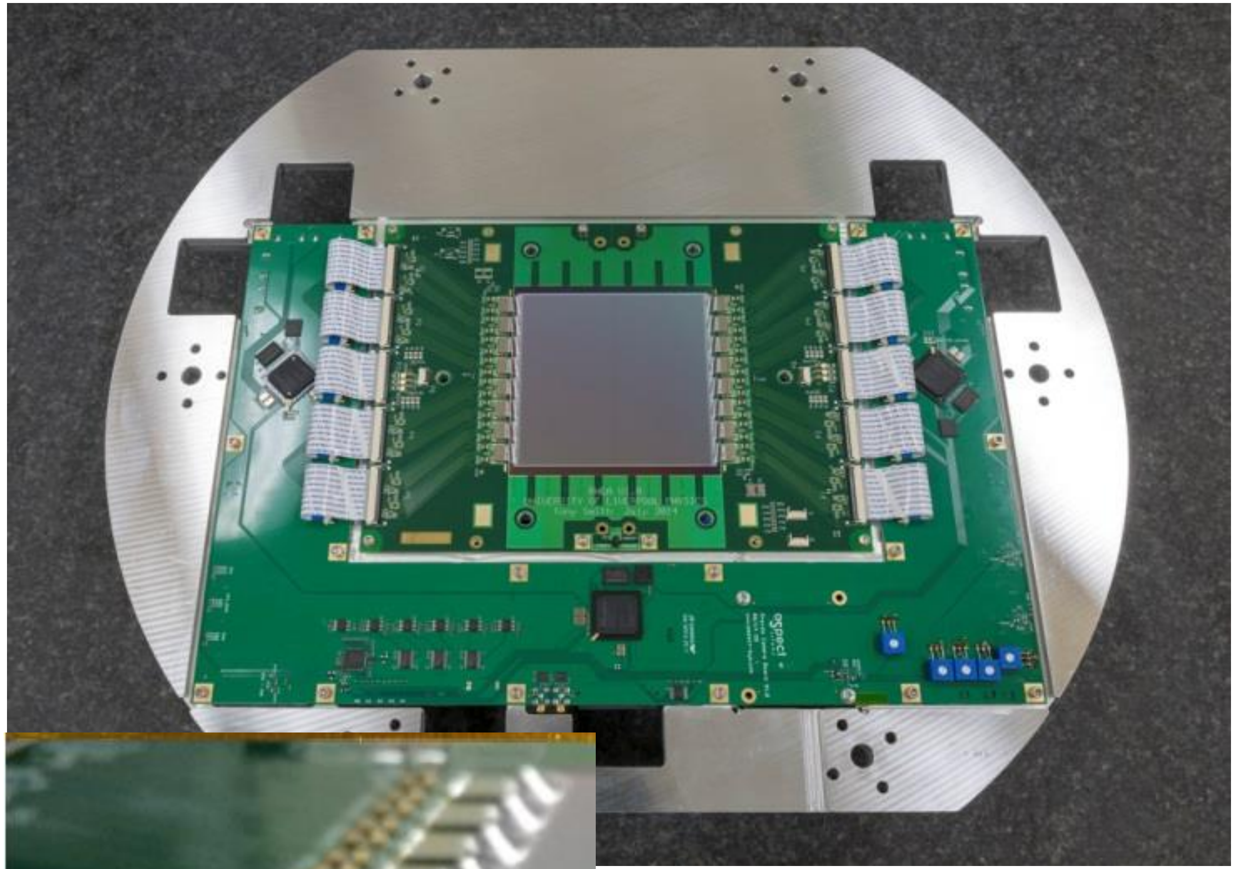
"Proton radiography and tomography with application to proton therapy", Poludniowski *et al*, BJR 2015

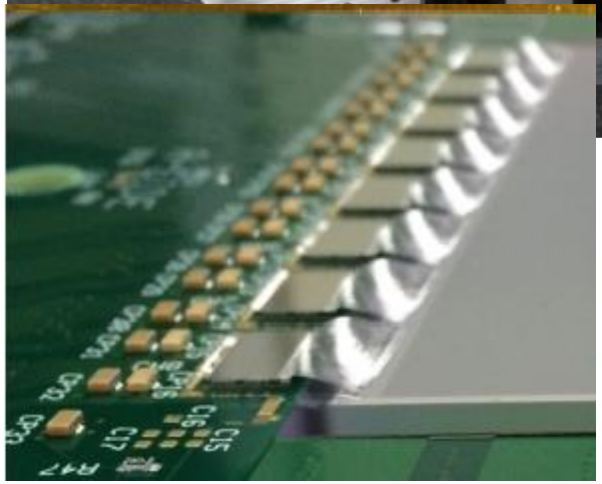
Who are PRaVDA?

- PRaVDA – Proton Radiotherapy Verification and Dosimetry Applications
- Supported by the Wellcome Translation Award Scheme, Grant 098285.
- Members from Academia, Industry, and the NHS

Silicon Strip Trackers

- The PSDs in PRaVDA were developed by University of Liverpool HEP Group
- Manufactured by Micron Semiconductor
- Strip Sensor Parameters:
  - Active area of 93x96 mm^2
  - 150 um thick n-in-p silicon
  - Strip pitch of 90.8 um
  - Strip Length of 48 mm
  - 2048 strips
  - 1024 read out from each side
  - 16 ASICs (8 for each strip half)
  - Double threshold binary readout

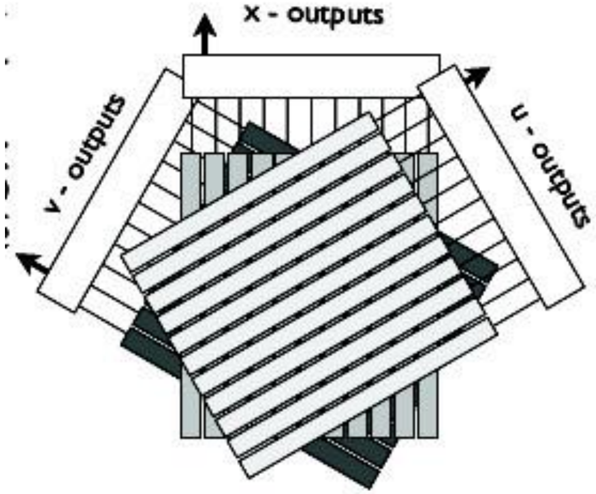


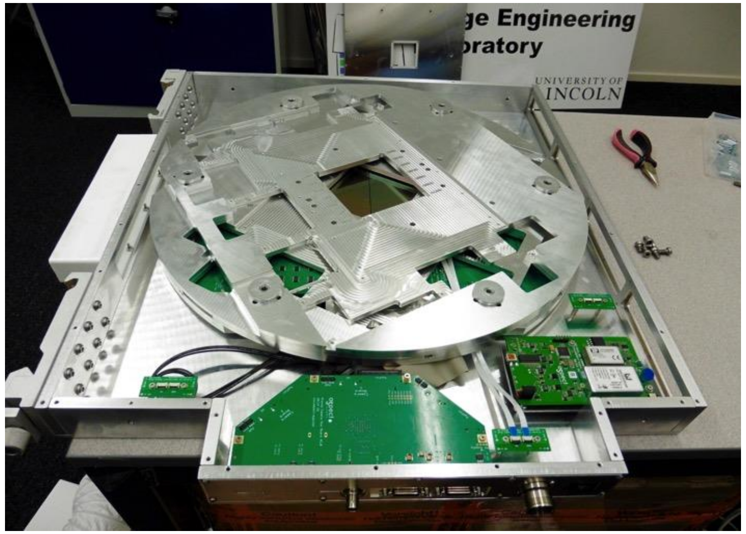


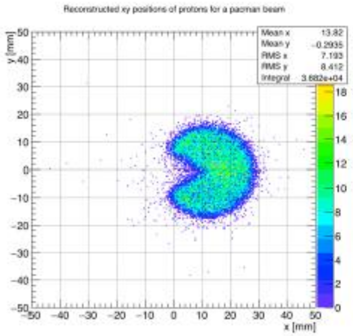
Module construction and wire bonding joint effort between Liverpool and new BILPA lab

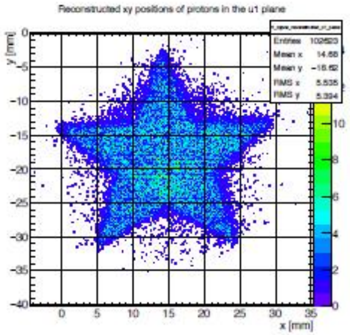
x-u-v Orientation

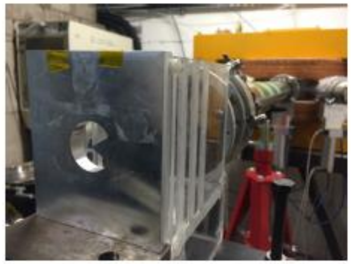
- Each tracking unit consists of 3 strip sensors, rotated at 60 degrees to each other
- The x-u-v orientation reduces ambiguities and allows for higher occupancies in the trackers
- Published Patent WO2015/189601





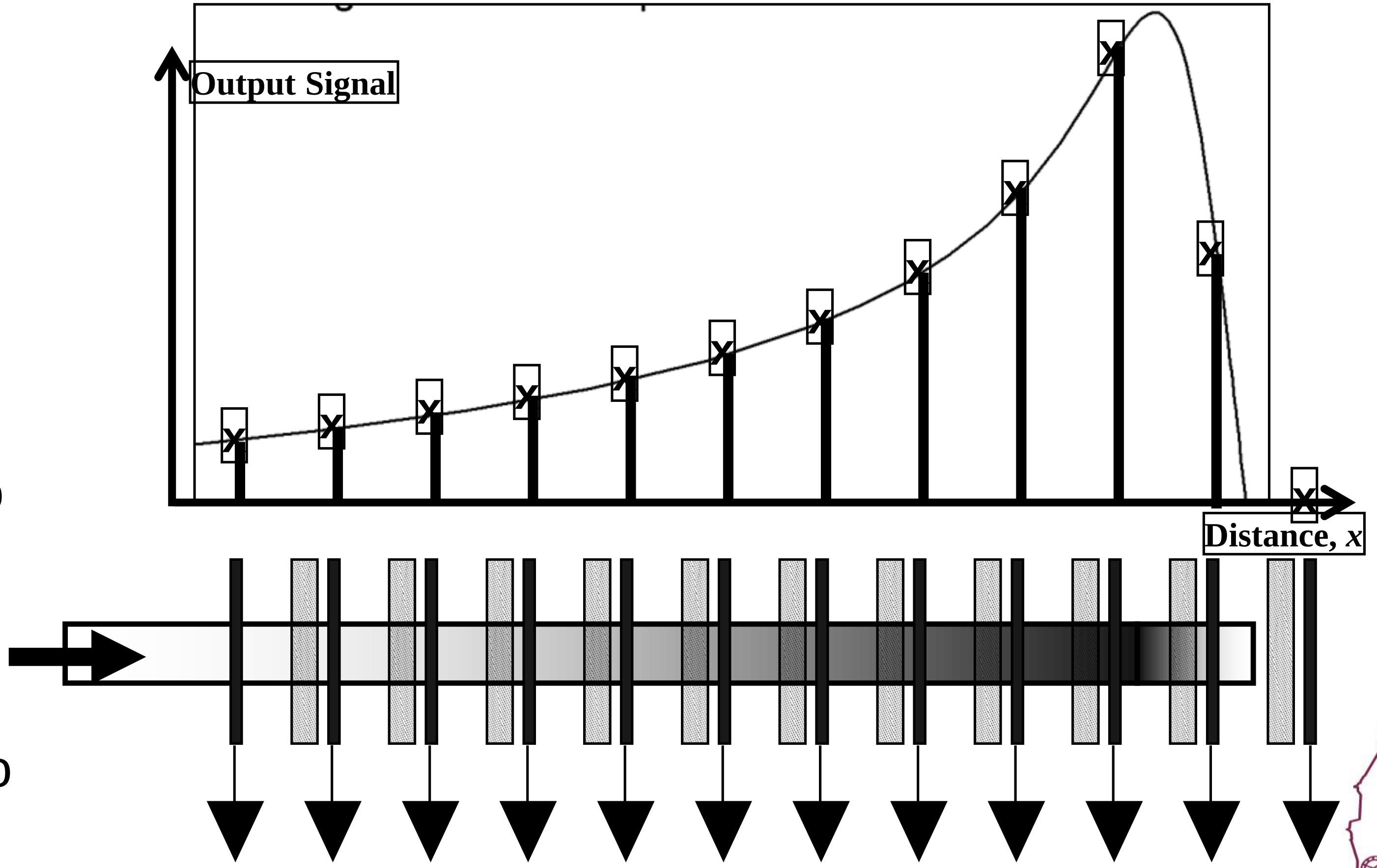






Range Telescope

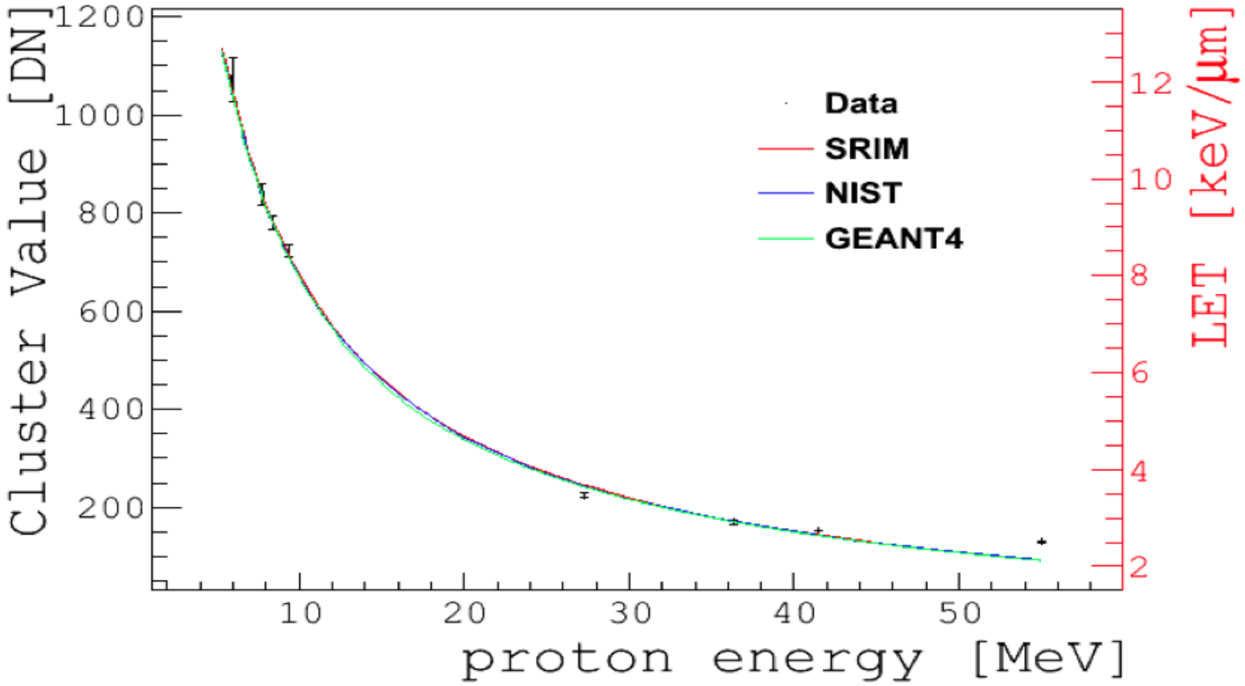
- Interweaved Si readout and PMMA sheets
- Final layer with a signal is used to calculate range
- CMOS or Strips option
- CMOS with analogue readout would allow interpolation between layers to reconstruct BP
- Strips readout at same speed as trackers so reconstruction easier
- PRaVDA constructed strip RT due to constraints within project

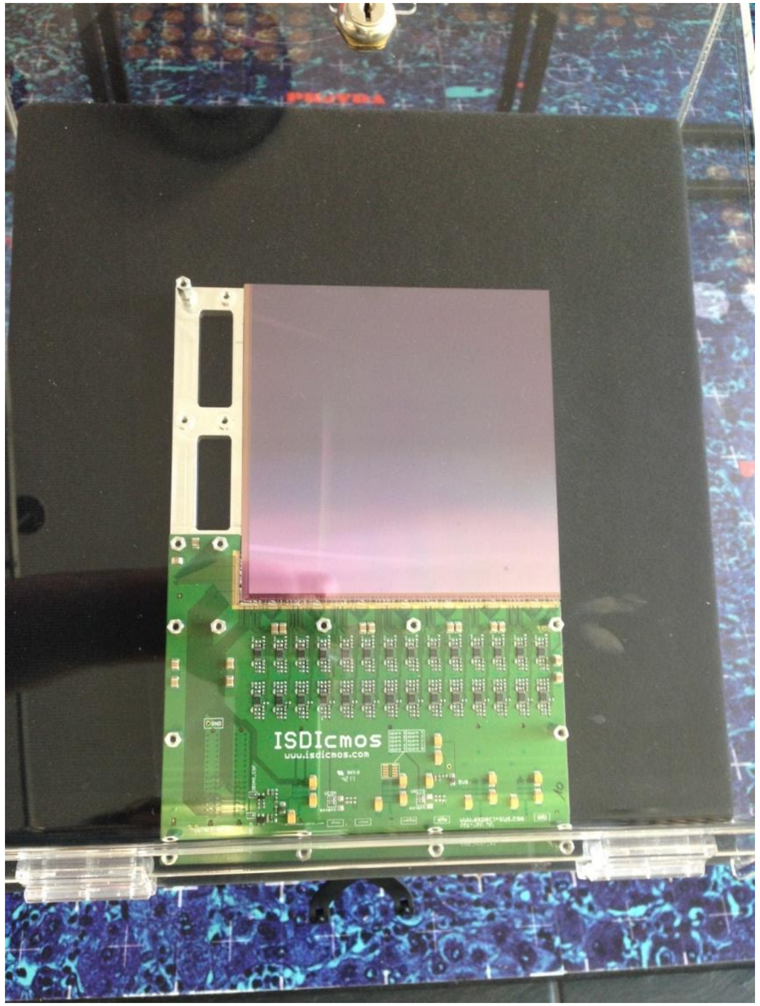


CMOS RT Measurements

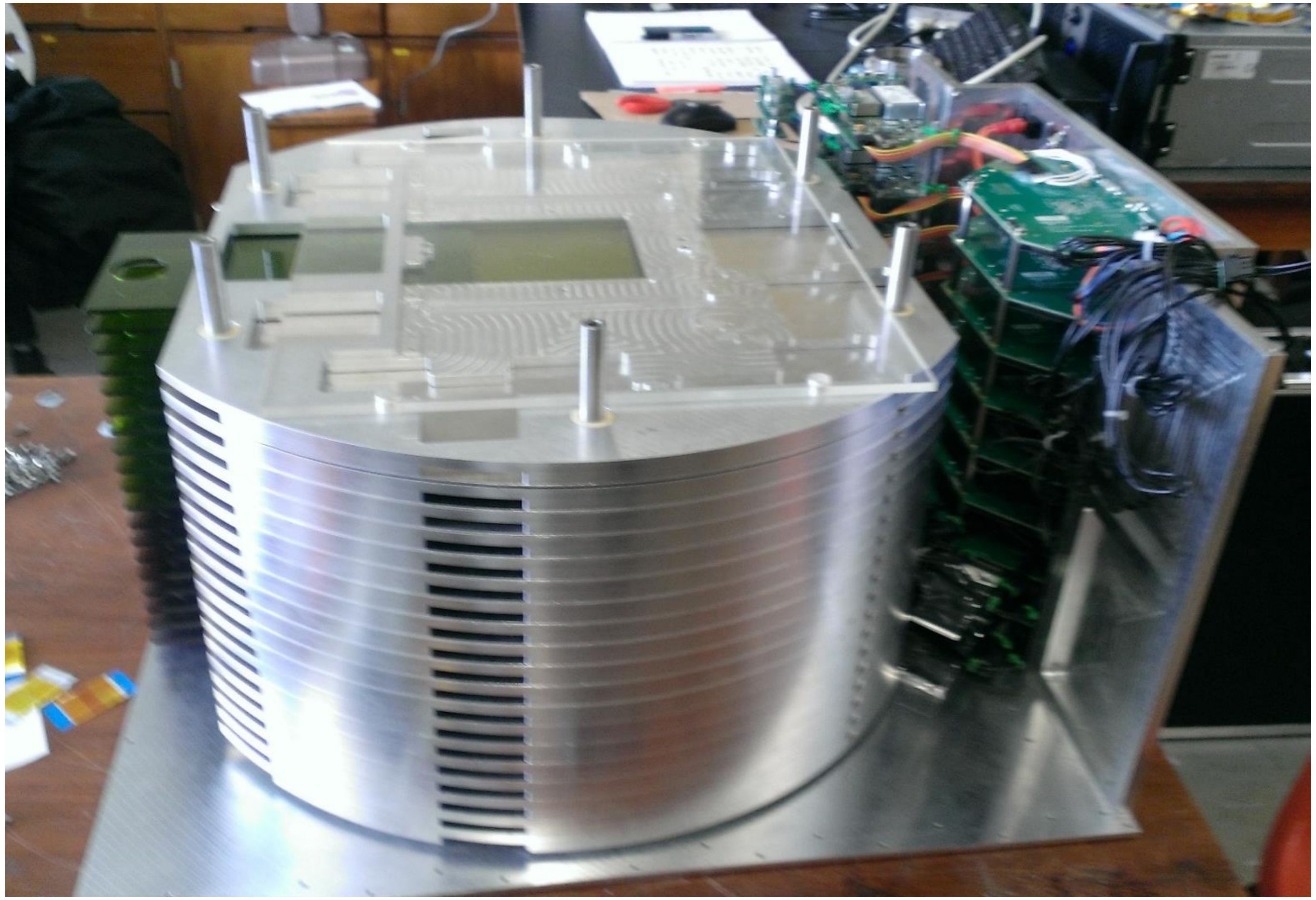
- Dynamite sensor measured at iThemba and UoB
- Changing signal size in very good agreement with theory
- Could use this to interpolate between final layers

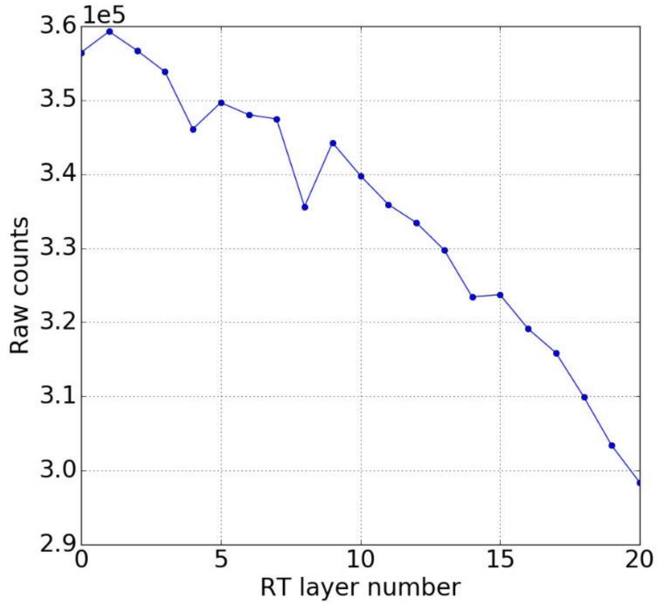
Experimental data from Birmingham and IThemba, SA



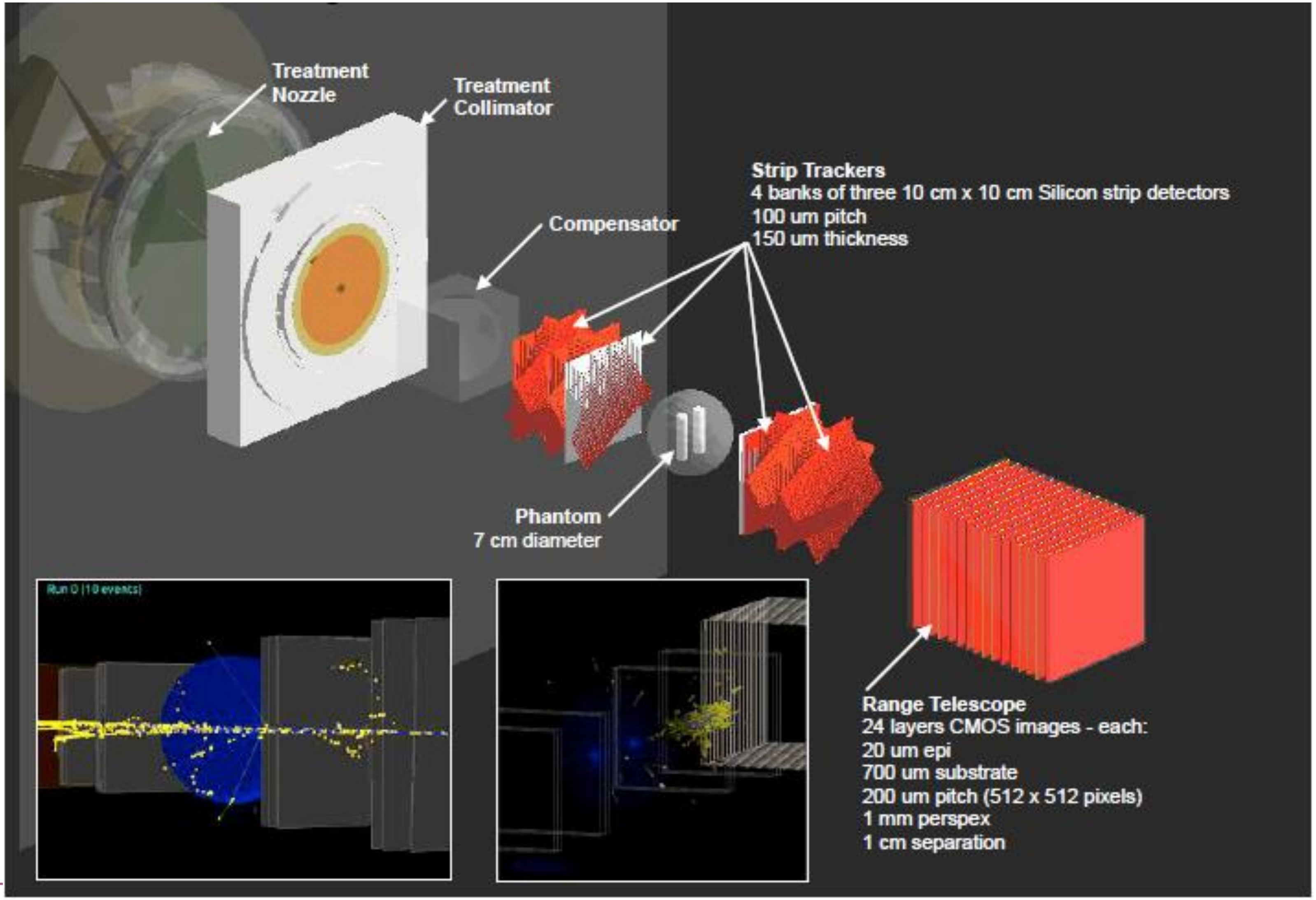


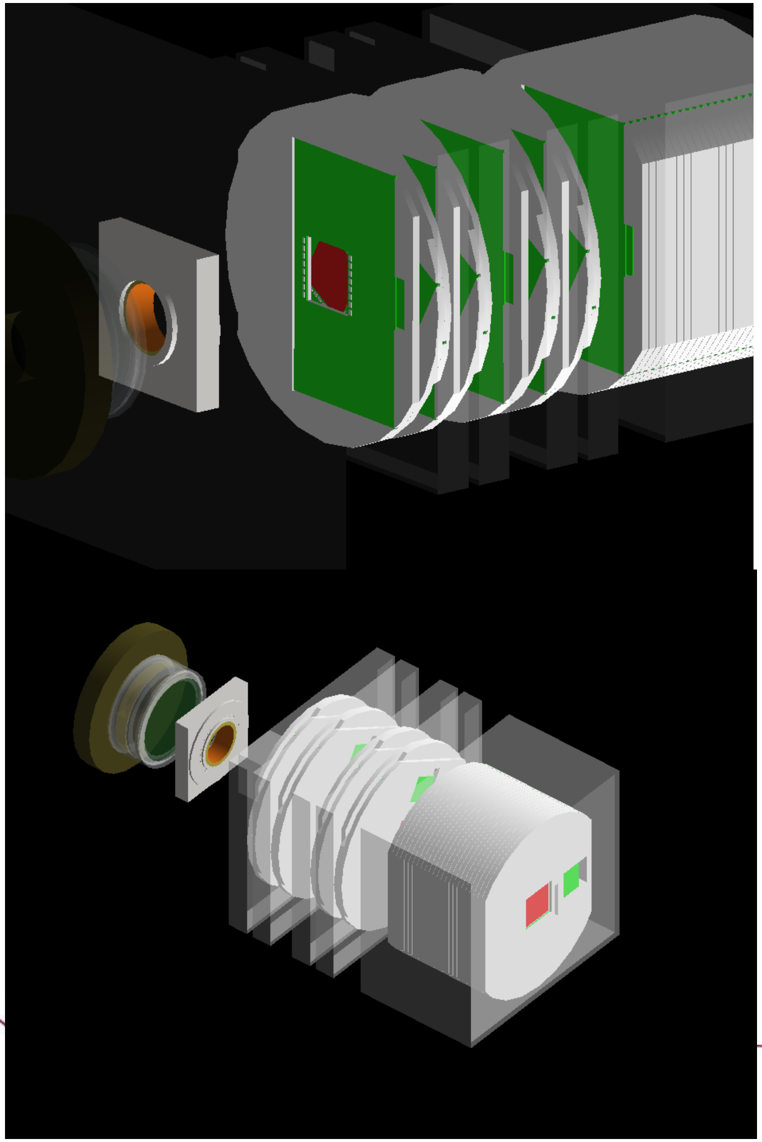
Strip RT Construction and Commisioning



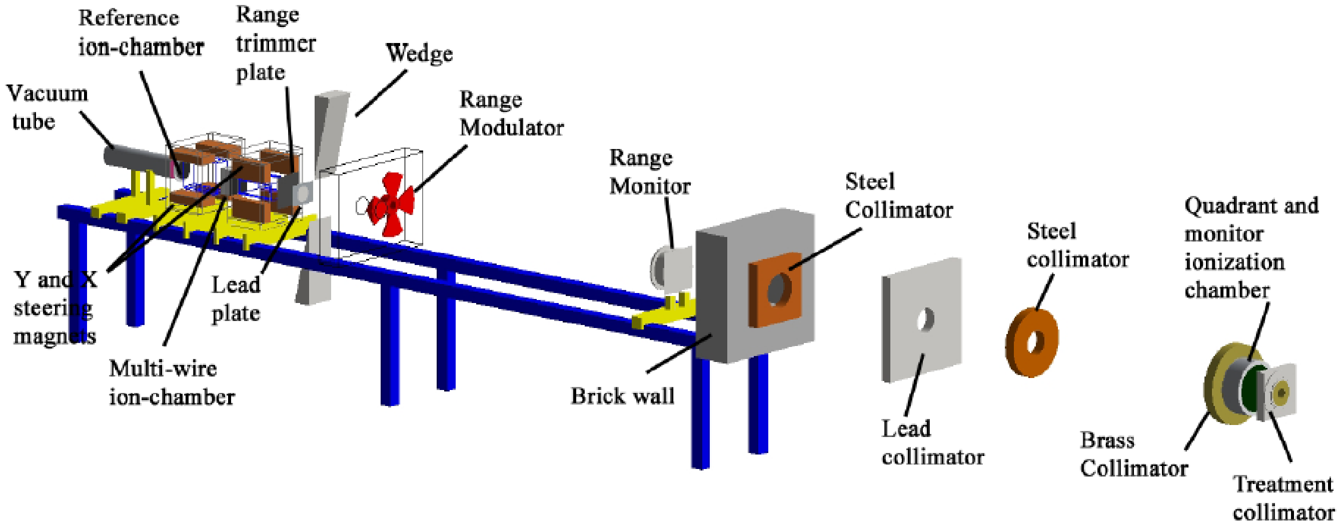


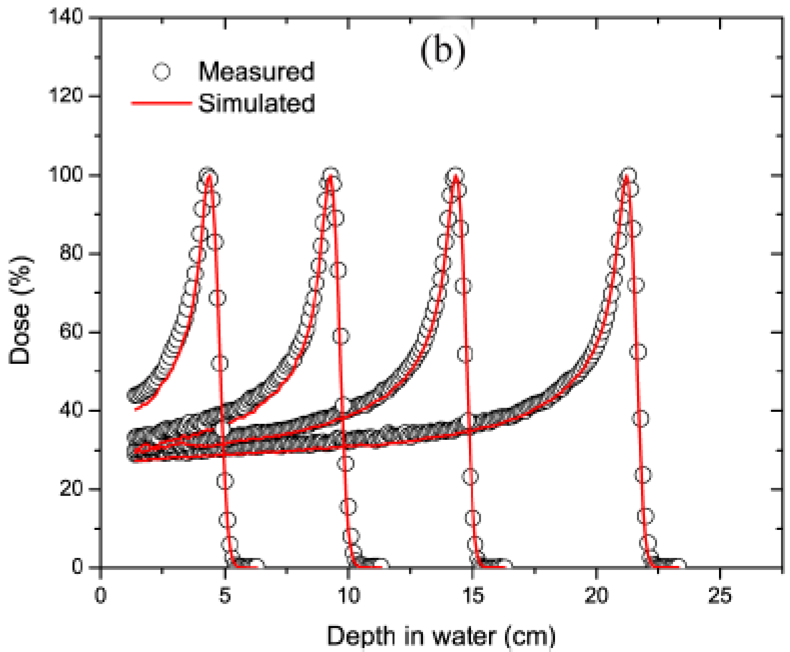
Geant4 Simulations

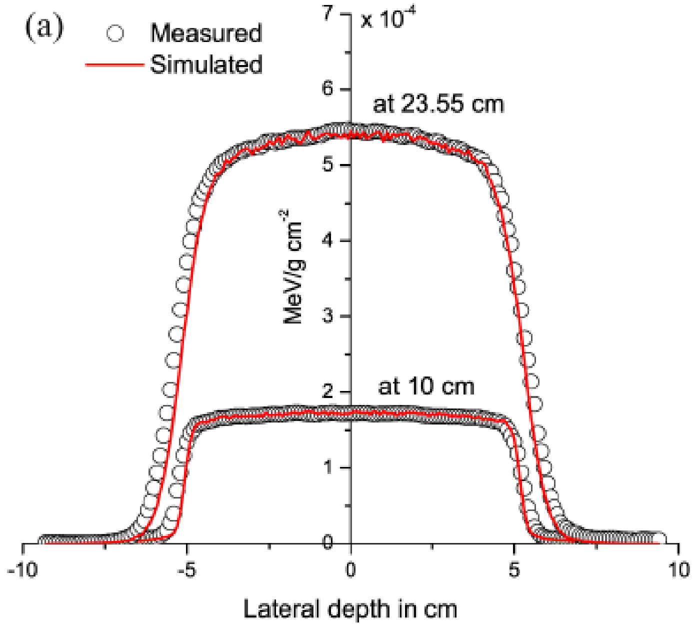




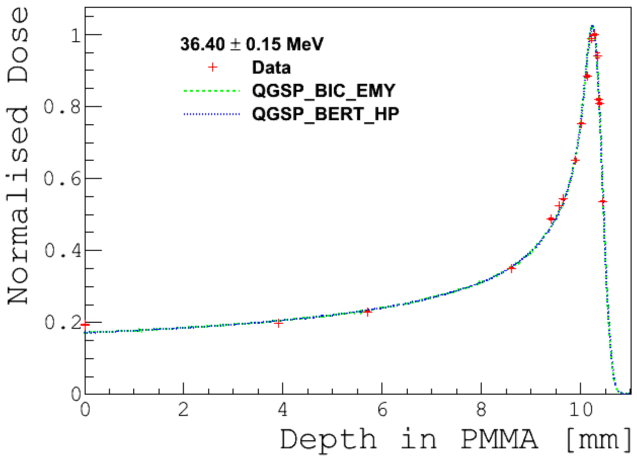
iThemba Beamline

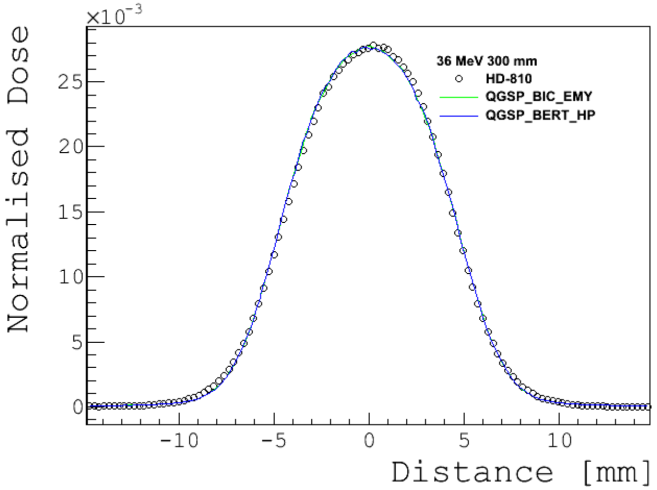




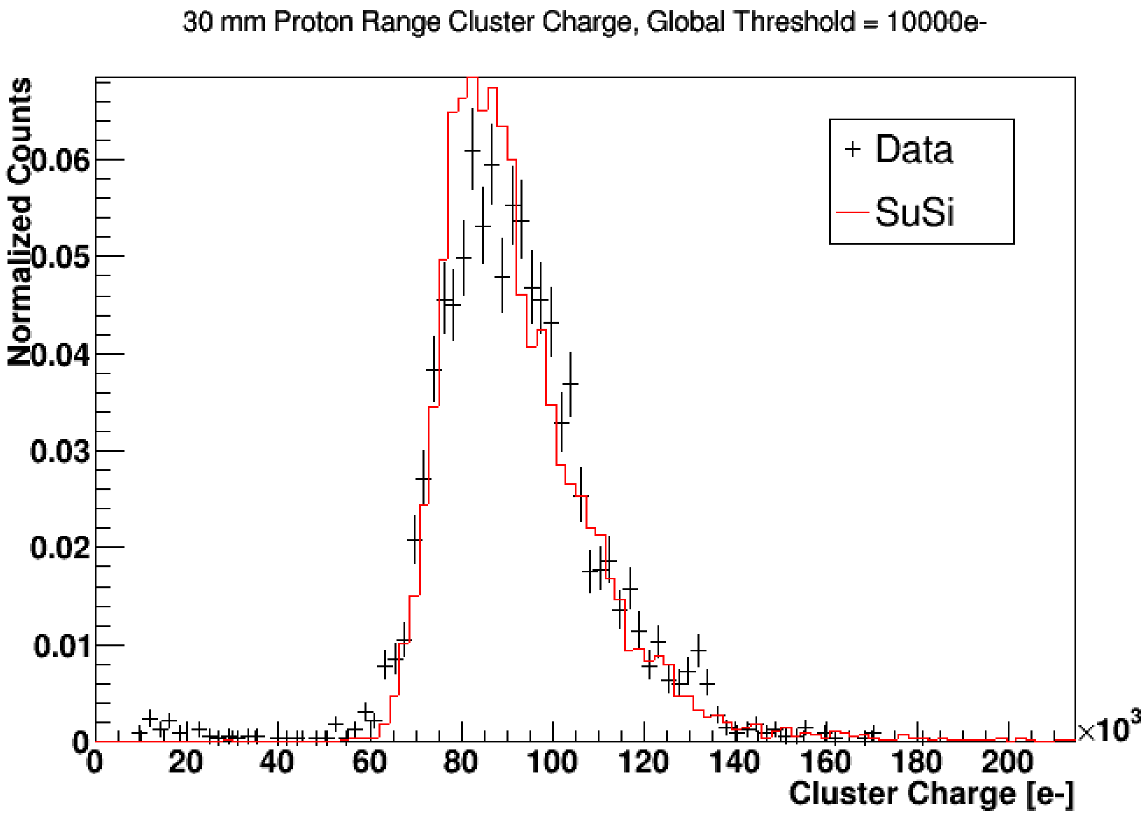


MC40 Beamline

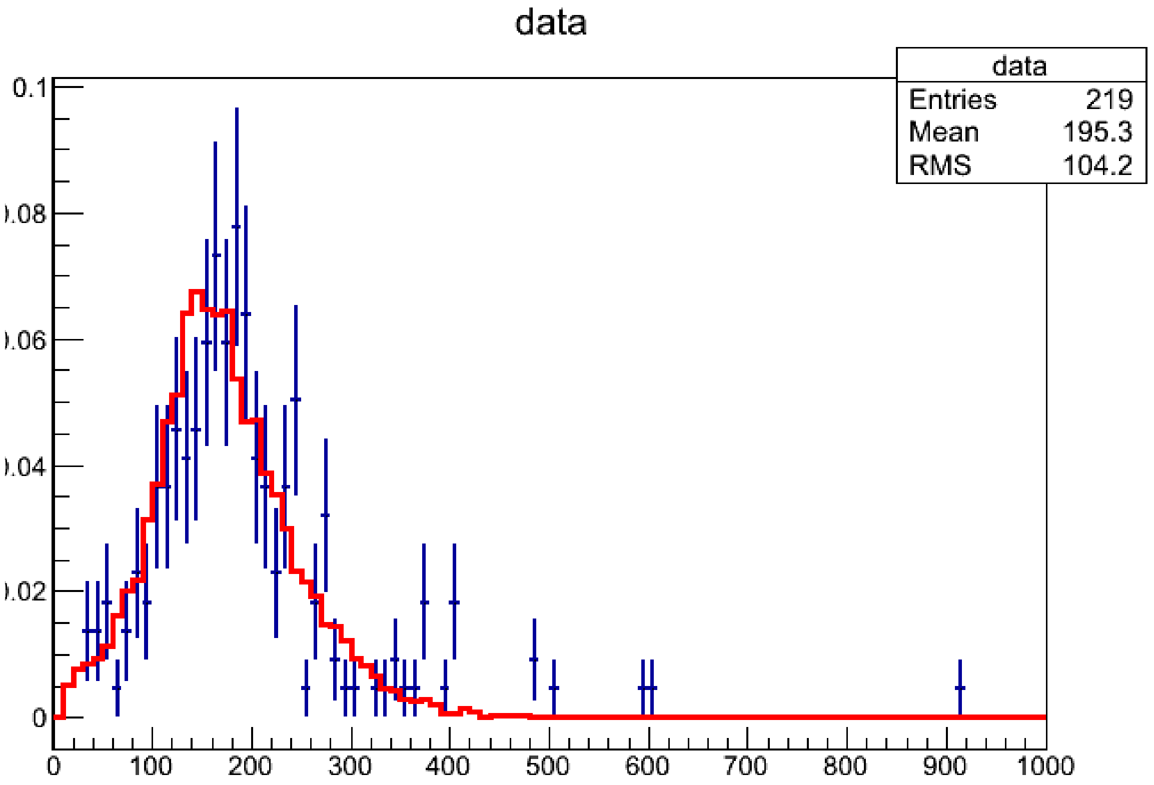




Sensor Response



60 MeV p, PRaVDA strip sensor, ALiBaVa Readout



60 MeV p, PRaVDA CMOS sensor (Dynamite)

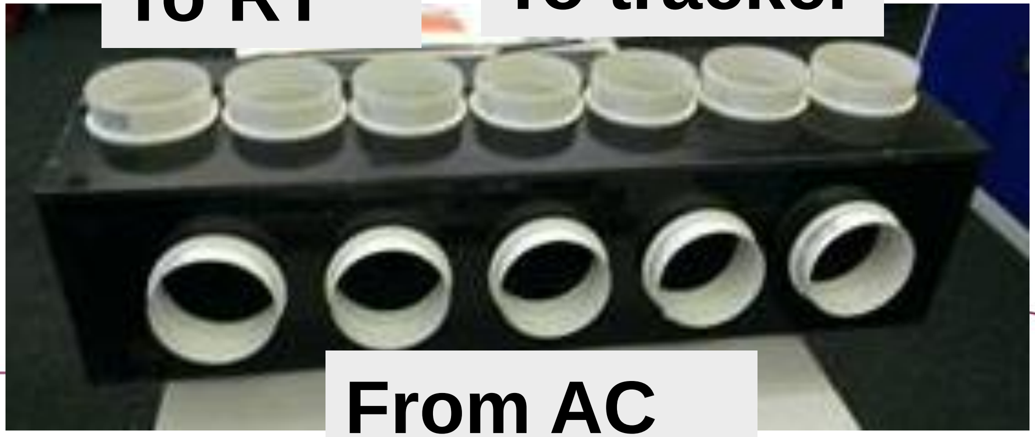
Cooling

Lot of heat to shift from boxes

Cooling system designed by Chris Waltham at Lincoln.

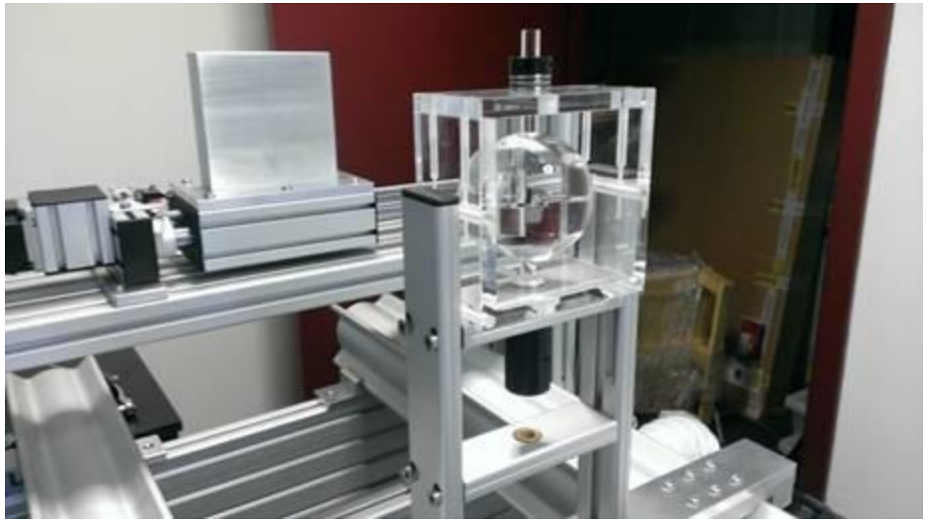
Uses 5 air conditioning units

4 running at one time whilst others defrost. Switch determines which is running

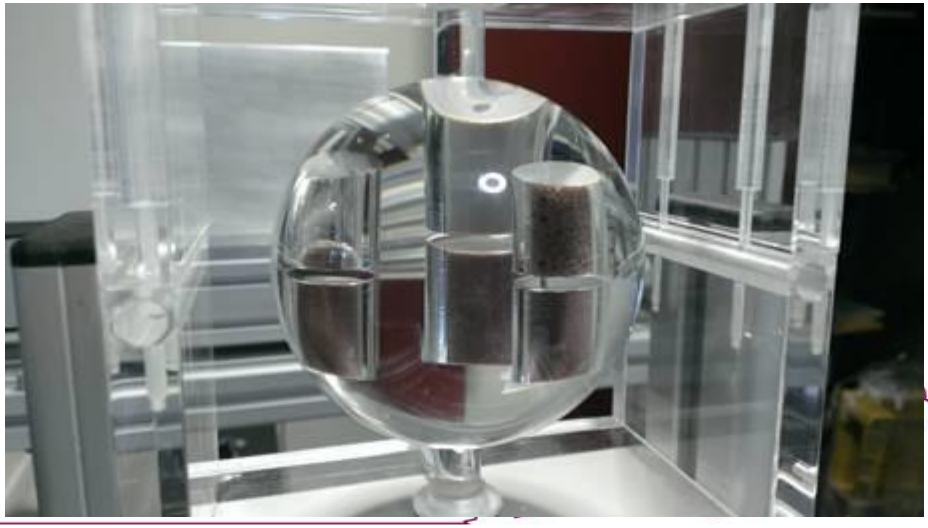


Phantoms

Phantom on rotation table



Phantom with automated beam blocker



Close up showing material inserts

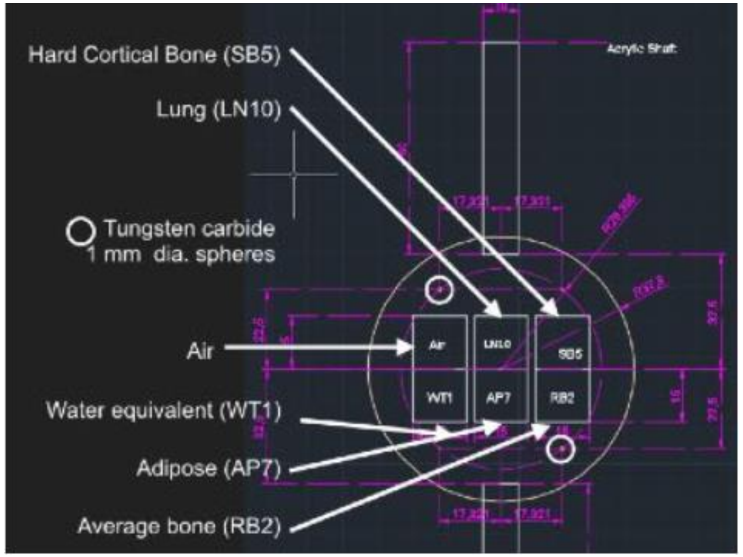
Installation in SA

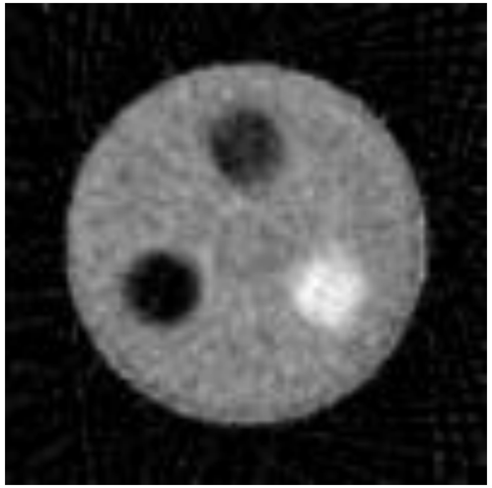
Figure

“Proton
Poludni

Scattering Power CT

- In November 2015 a reduced PRaVDA system went to beam test at iThemba consisting of the four tracking, and phantom.
- Measured the mean-square scattering angle of every proton
- Performed a CT reconstruction using novel “back-projection-then-filtering” algorithm developed within PRaVDA
- 5 degree angluar steps
- 125 MeV degraded beam
- 15M events / angle
- 80% tracking efficiency in all layers



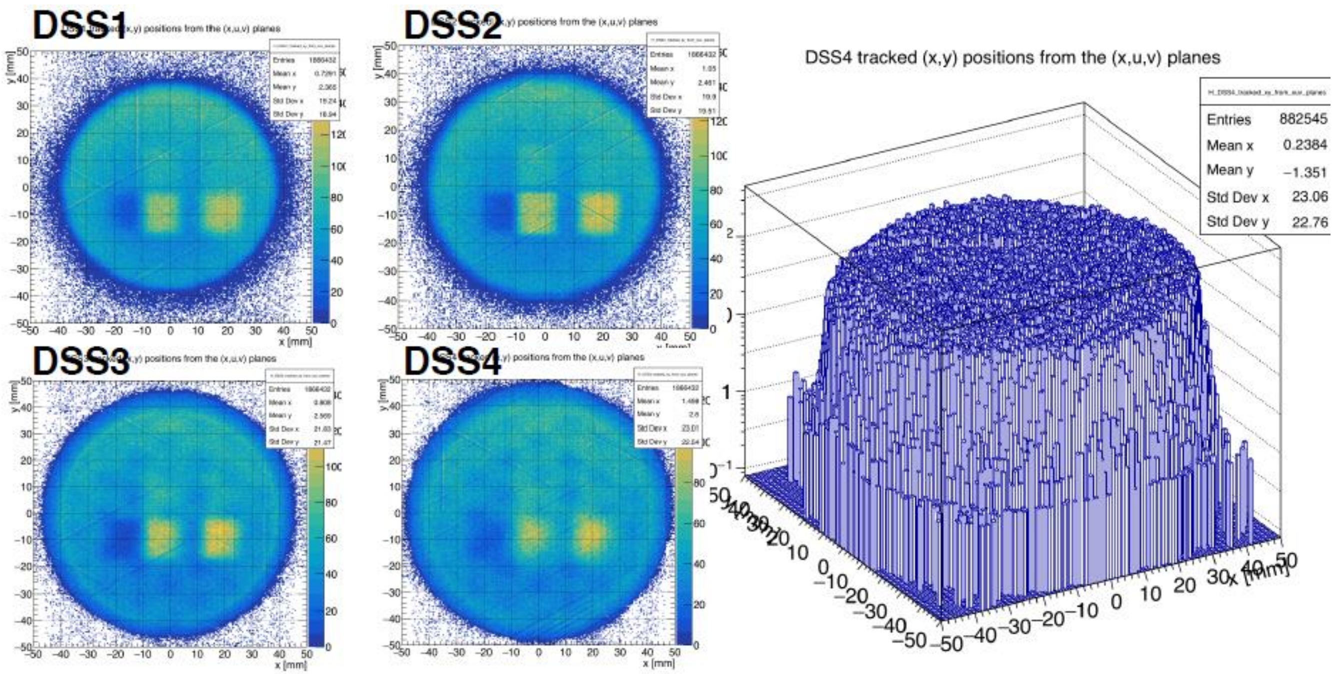


Scattering power CT

Cone beam CT

Stopping Power CT

- May 2016 the complete PRaVDA setup was used at iThemba for the first time
- All 12 tracking layers and 21 range telescope layers talked to each other!
- 125 MeV degraded beam
- Compensator in place
- 180 rotations at 1 deg steps
- ~1M protons / rotation
- Artifacts but also timing issues between system mean only 10% useable data
- Investigations since have fixed this and second pCT run coming in November 2016



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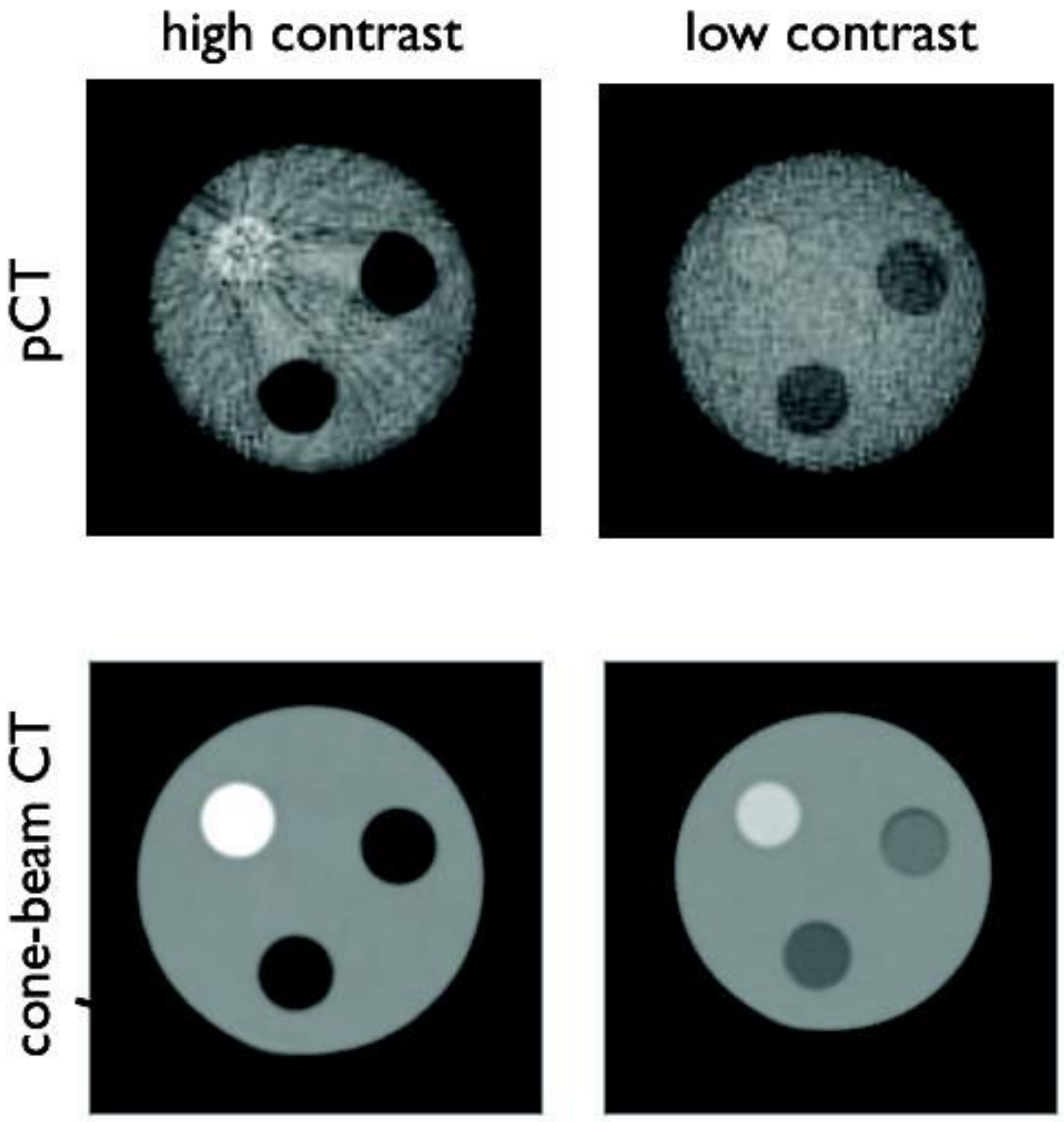
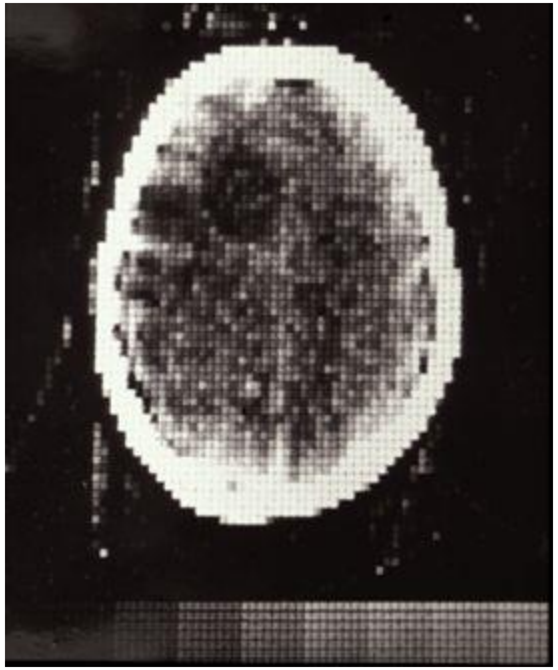
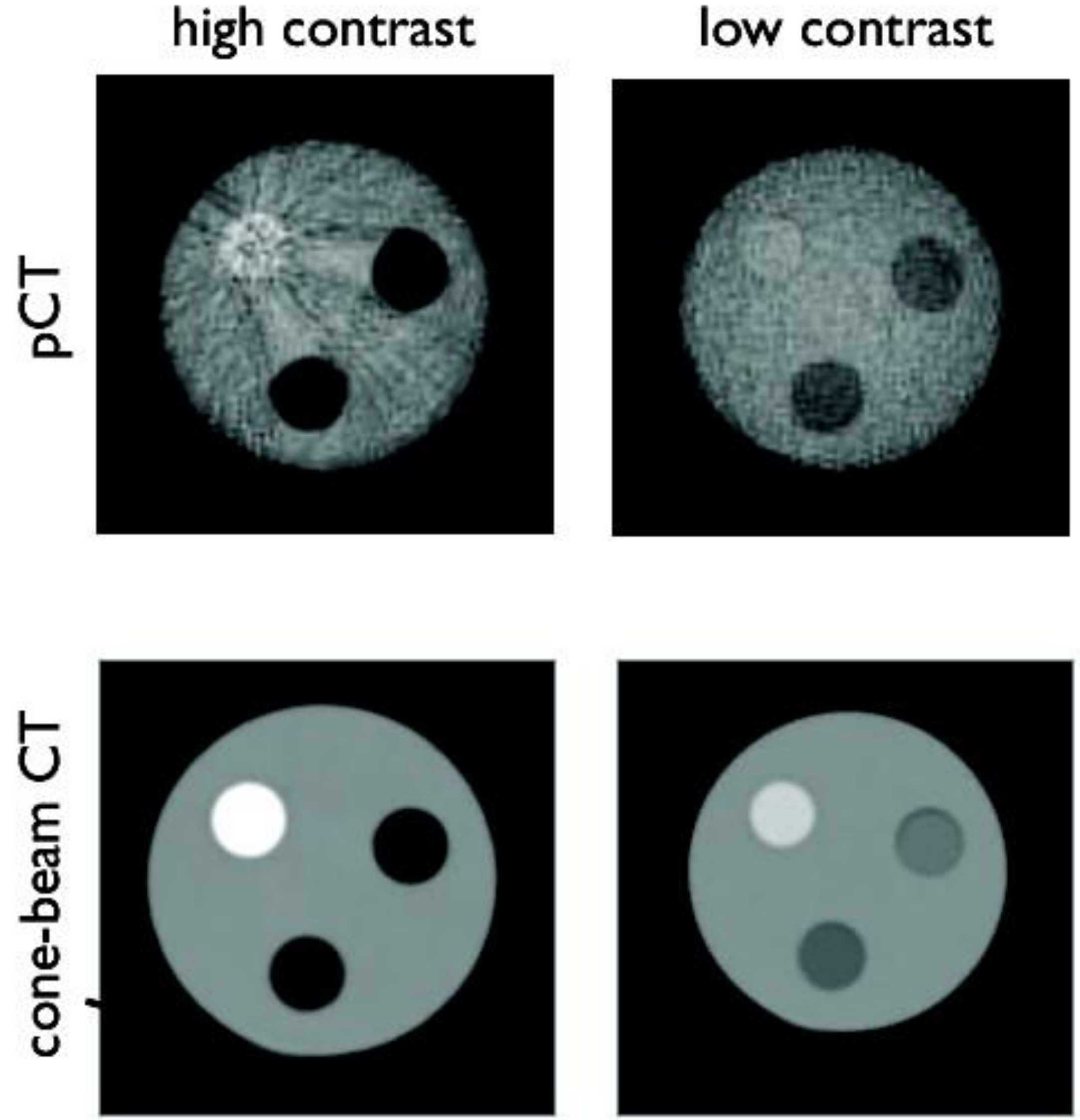


Stopping Power CT

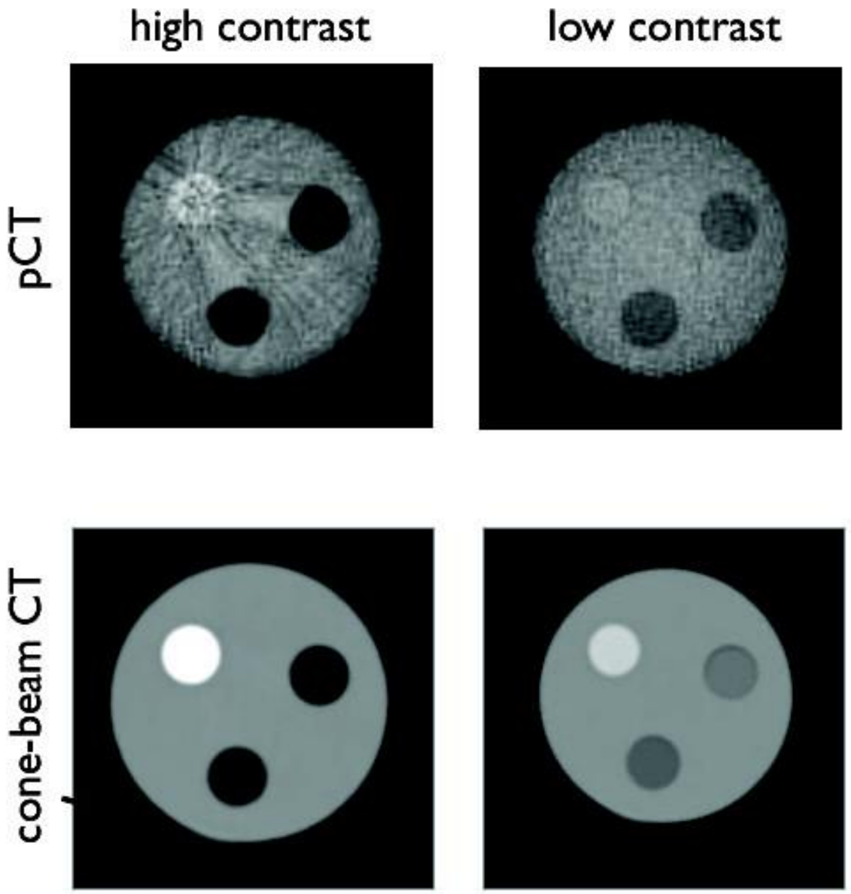


First clinical CT in 1971



PRaVDA Overview

- 4 year project, conception, construction, completion(?)
- Not quite yet, few bugs have been ironed out and then testing again to increase stats and remove artefacts
- Calibration of Range to Energy to be further investigated.
- Development of system for other facilities
- Still much work to be done!



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From SuperNEMO to Proton Therapy: Adapting the SuperNEMO Optical Module for Proton Energy QA

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[1]University College London, Physics & Astronomy, London, UK

[2]University College London Hospitals, Radiotherapy Physics, London, UK

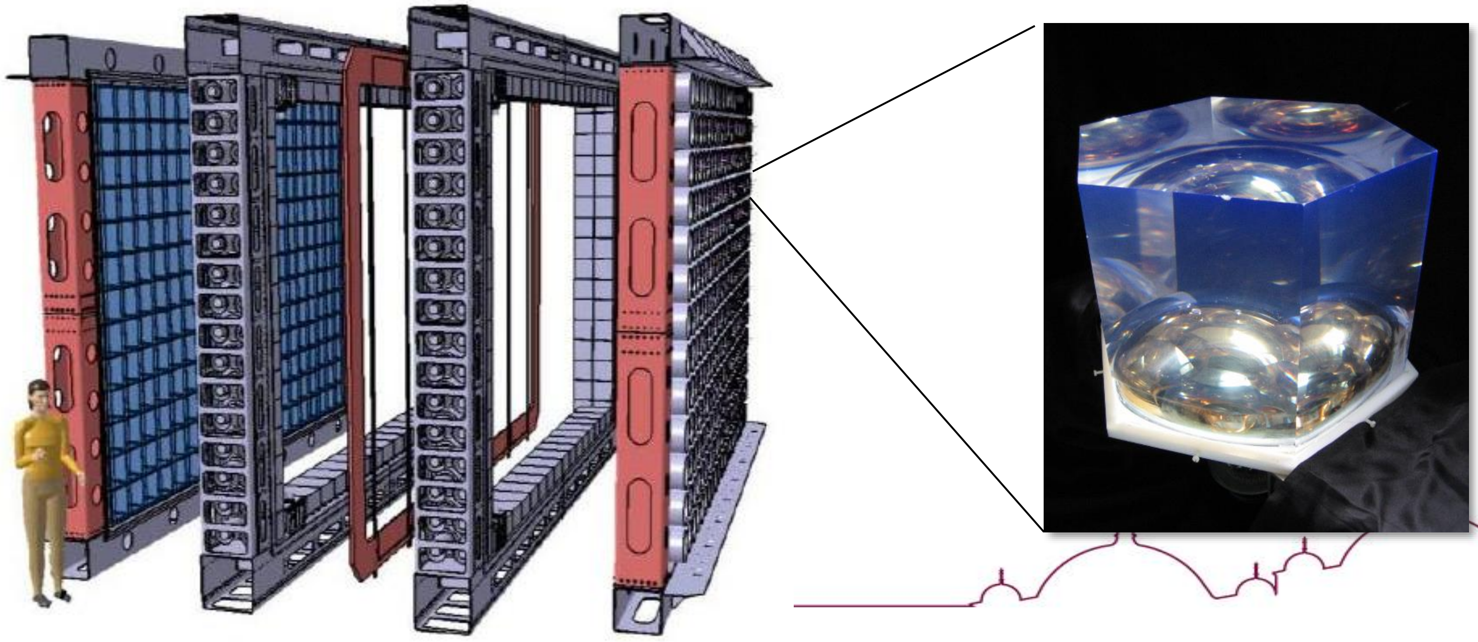
[3]Clatterbridge Cancer Centre, National Eye Proton Therapy Centre, Bebington, UK

UCL

Results shamelessly stolen (with permission) from recent poster at PTCOG (Particle Therapy Co-Operative Group)

SuperNEMO

- SuperNEMO is a next generation neutrinoless double beta decay experiment.
- Will use 100kg of Se-82 as source
- Requires a resolution of 3%/√E(MeV) to distinguish $0_{\nu\beta\beta}$ over background
- Calorimeter must be made of low Z material to minimise backscatter of low energy electrons (in the MeV range).



SuperNEMO for proton QA

- Daily QA usually at particle therapy centers use a combination of ionization chambers to measure BP
- Group at UCL are looking to adapt the SuperNEMO calorimeter scintillators to allow rapid daily QA

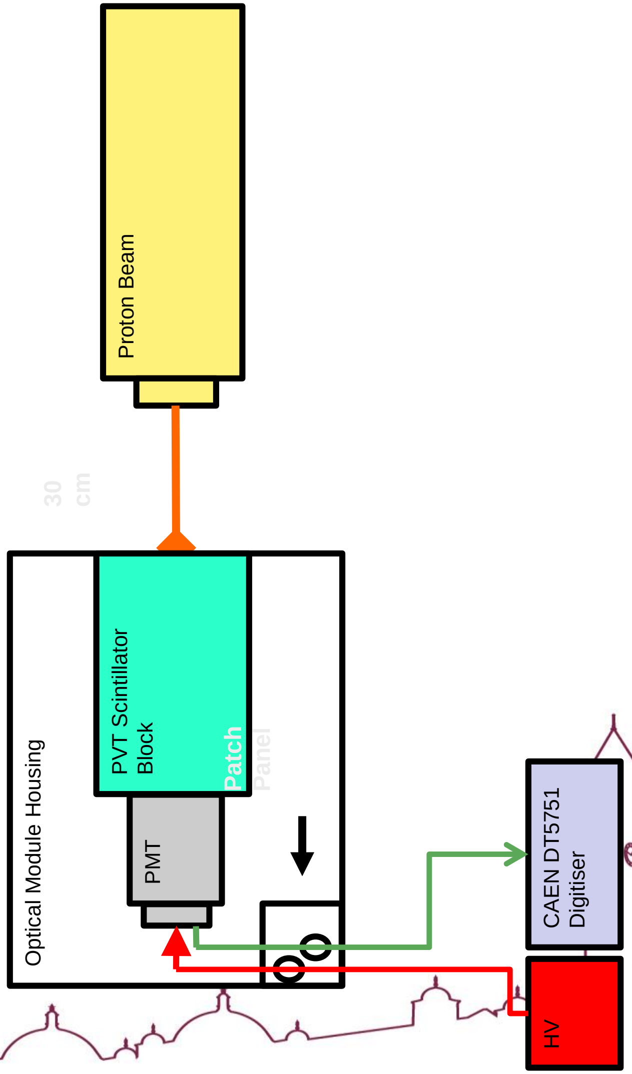
PVT scintillator

High QE PMT

- High light output
- ns response time
- Mountable on beamline
- Cheap
- PVT is water equivalent material

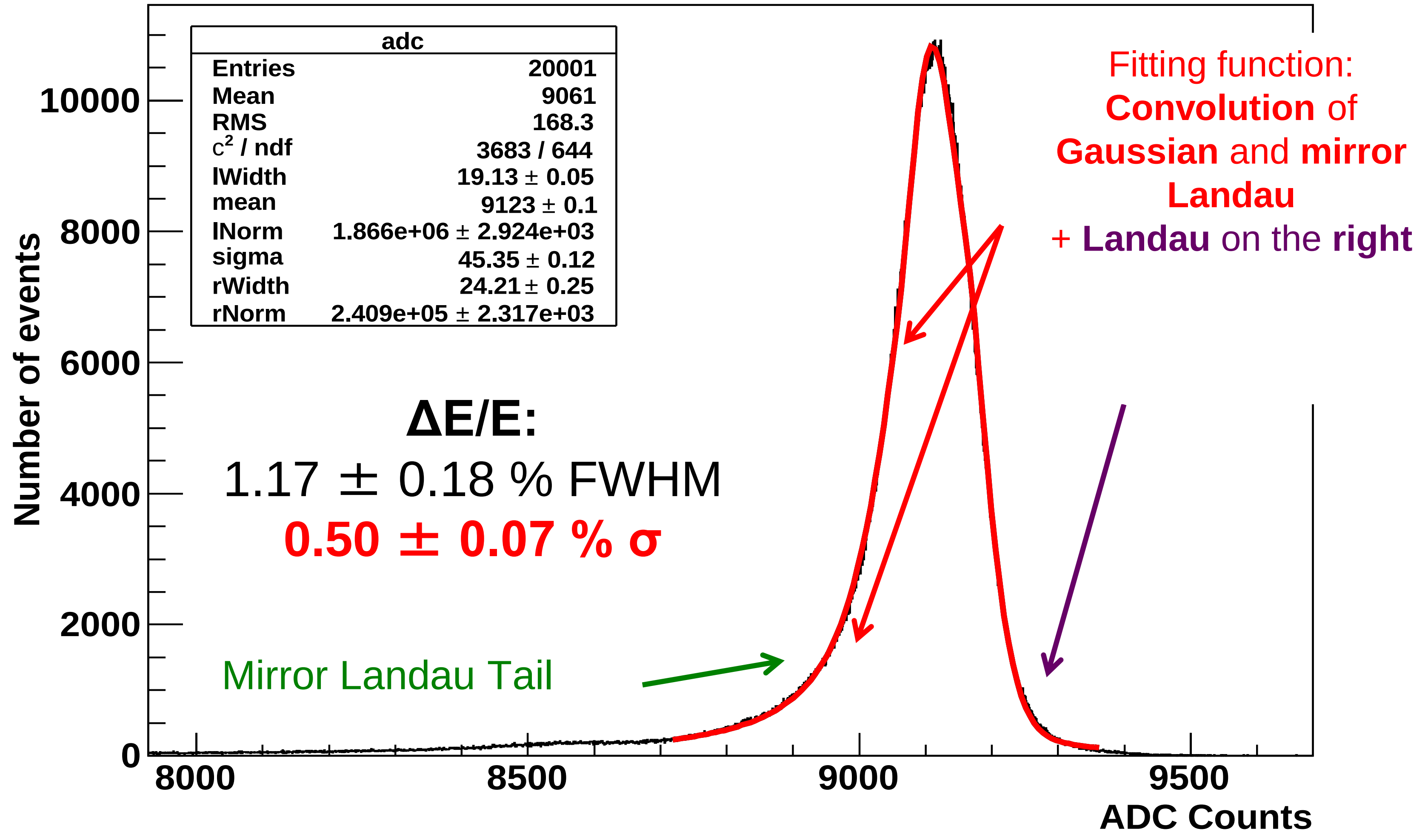
Testing at Clatterbridge Cancer Centre

- Clatterbridge is a clinical facility offering proton therapy for ocular cancers
- First clinical proton therapy centre in the world when opened in 1989
- Capable of delivering 60 MeV protons
- By the beginning of 2015 had treated 2625 patients from the UK and abroad

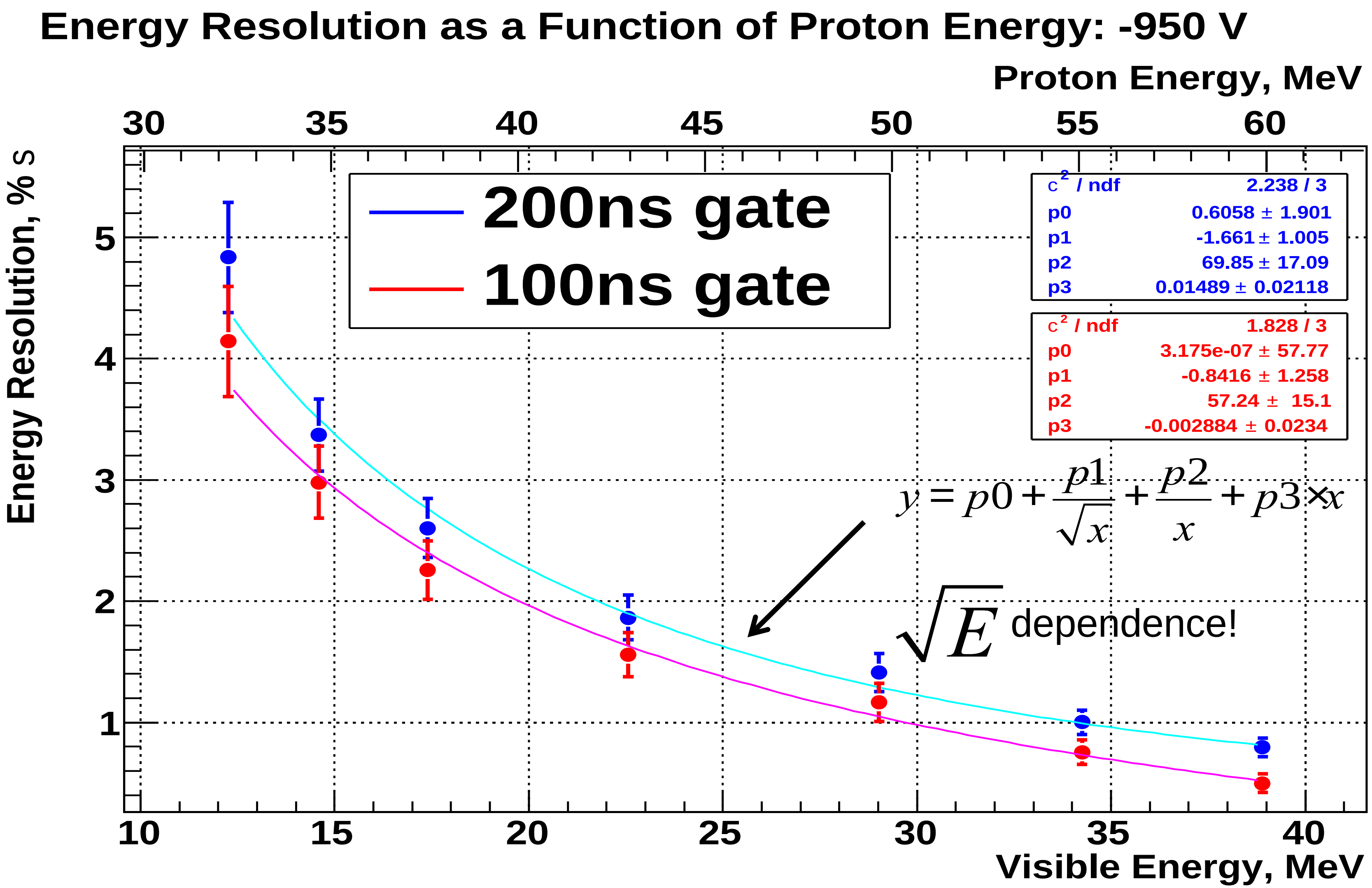


Testing at Clatterbridge Cancer Centre

60 MeV Clatterbridge Beam Test ADC Spectrum



Testing at Clatterbridge Cancer Centre



An Intensity Modulated Radiotherapy Beam Monitoring System using a Monolithic Active Pixel Sensor

Jaap Velthuis[a], Stephen Blake[b], Diane Crawford[b], Sally Fletcher[b], Richard Hugtenburg[c], Ryan Page[a], Margaret Saunders[b], Paul Stevens[b]

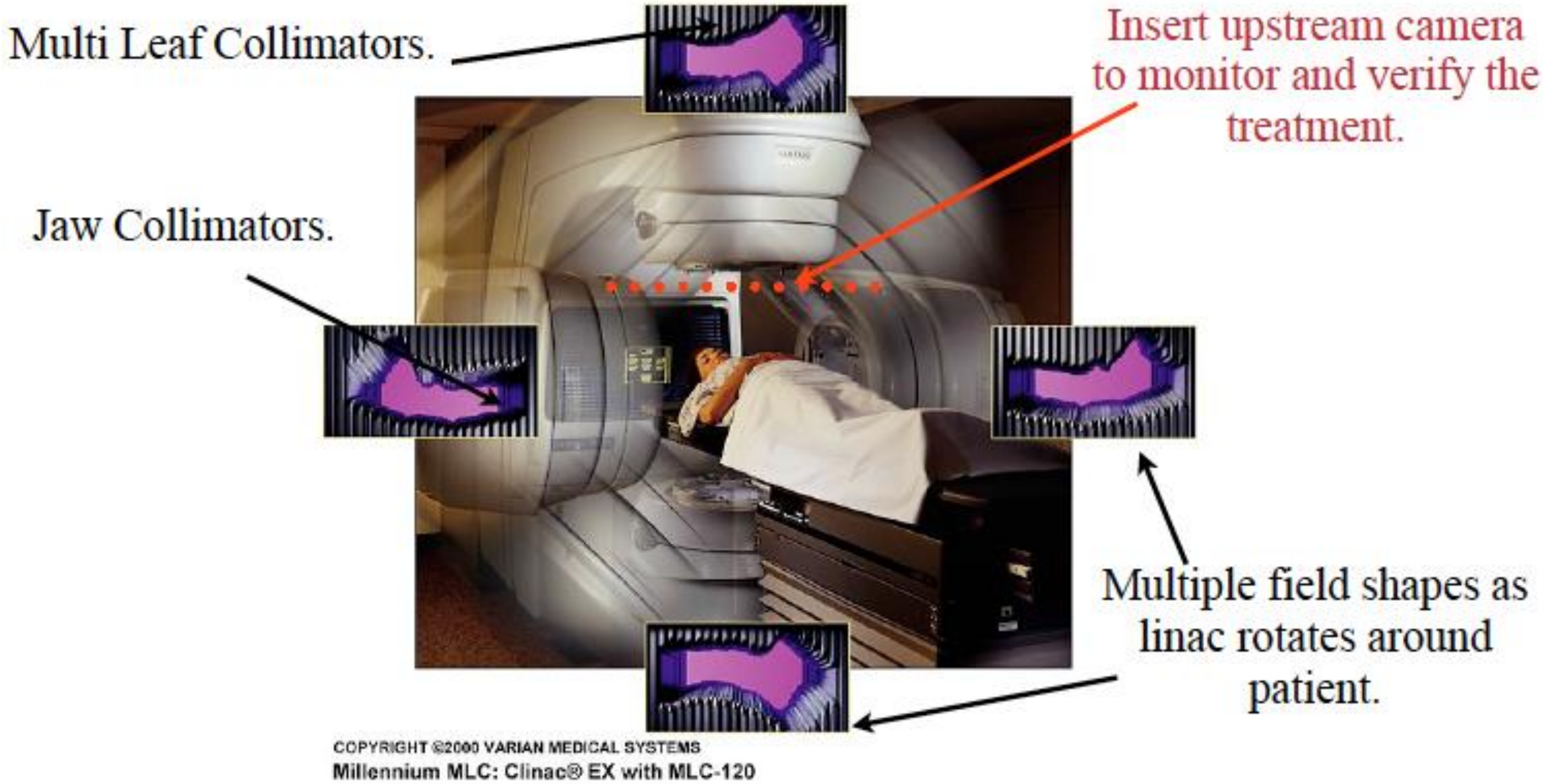
[a]University of Bristol
[b]University Hospital Bristol NHS
[c]Swansea University

The research presented here is funded by the National Institute for Health Research (NIHR) Invention for Innovation (i4i) Programme and the Elizabeth Blackwell Institute for Health Research.

Dr. Jaap Velthuis

Slides shamelessly stolen (with permission)

IMRT System

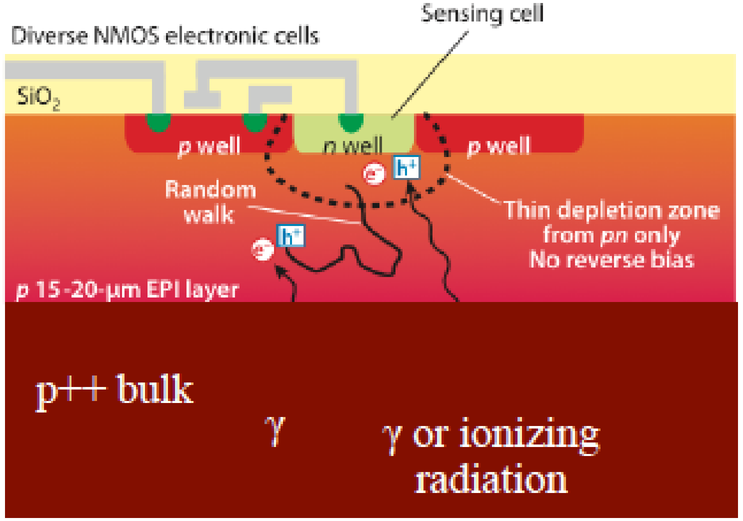


Multi Leaf Collimators.
Insert upstream camera to monitor and verify the treatment.
Jaw Collimators.
Multiple field shapes as linac rotates around patient.
COPYRIGHT ©2000 VARIAN MEDICAL SYSTEMS
Millennium MLC: Clinac® EX with MLC-120

Monolithic Active Pixel Sensors

- MAPS ideal for upstream monitoring: thin, small pixels, fast, cheap
- Signal generation in thin epitaxial layer
- Bulk for mechanical support; 30µm thick detectors easily < 0.1 % attenuation for 2MeV photons
- Charge collected at photodiode
- Each pixel has in-pixel amplification ➔ high S/N
- Fast readout of the sensor

- Using Achilles
  - 14 µm thick epitaxial layer
  - Pixel matrix dimensions 4096 x 4096
- 3T pixel architecture with 14.5µm pitch
- Readout speed of up to ~100 fps



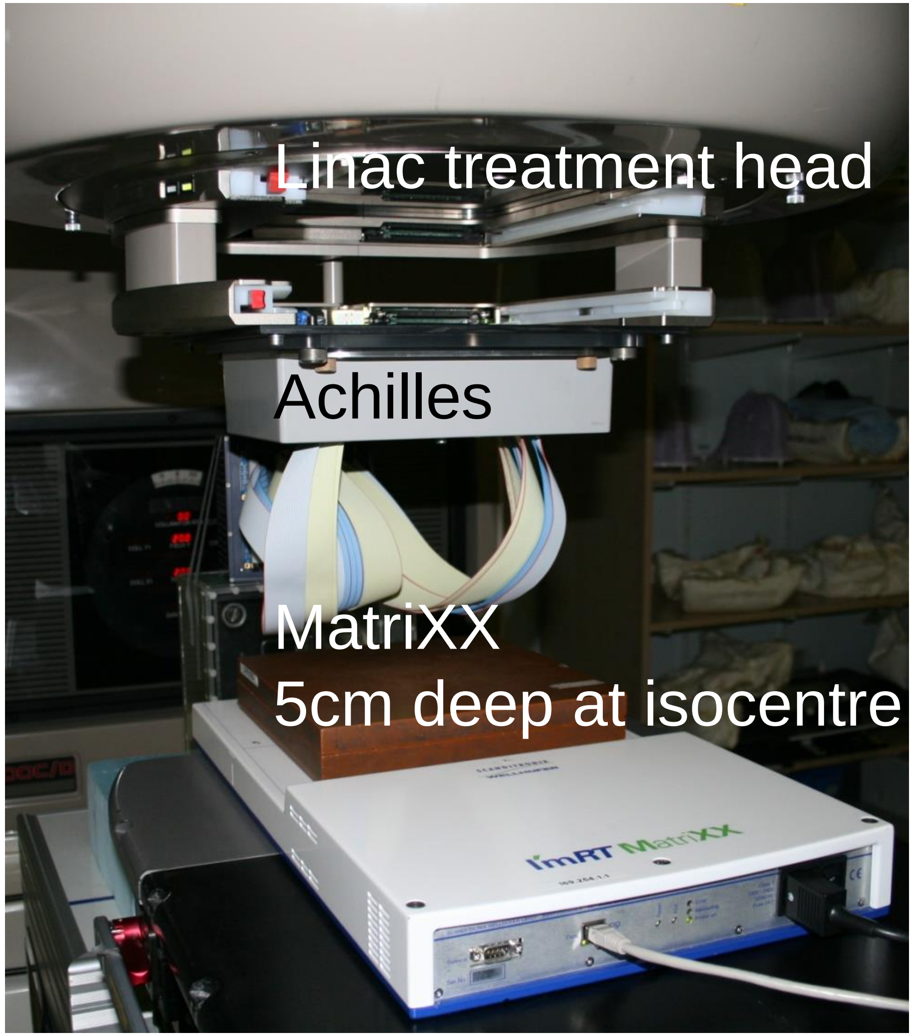
~ 6cm

N. Guerrini, R. Turchetta, and et al. A High Frame Rate 16 million pixels radiation hard CMOS sensor. Journal of Instrumentation, Volume 6, March 2011. Previously presented at IWORID, 11-15th July 2010.

Prototype system

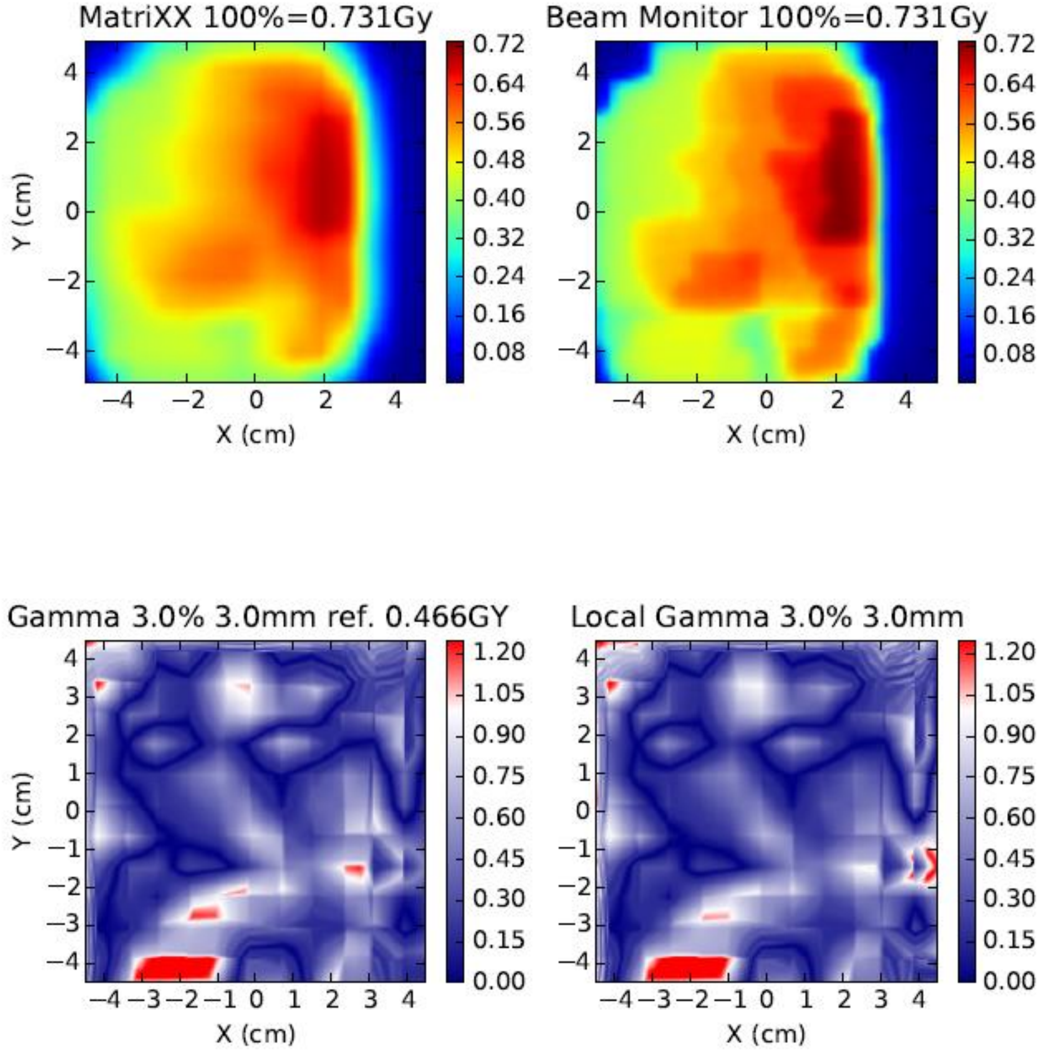
- Specific MLC fields used to allow field reconstruction to be tested
- Elekta SL22 linac operated at nominal working conditions of 400 MU/min (Pulse Repetition Frequency ~400Hz)
- Sensor running at 10 fps

- Image processing
  - Pedestal subtraction - Removes dark fixed pattern noise
  - Bad pixel averaging
  - Image resizing
  - Gaussian smoothing



Dose measurement

- 2D IMRT distributions
- Anterior Head&Neck field
- Dose measured with MatriXX 5 cm deep
- Measured fluence and used MC to determine dose at 5 cm deep
- Quantise reconstruction quality using gamma factor – 97% pass rate at 3% and 3 mm
- Excellent agreement
- Good enough for treatment verification!



Current Status in Birmingham

- PRaVDA has been extended until May 2017 with involvement from B. Pheonix,D. Parker, S. Green, P. Allport, T. Price, and J. Cotterill (new PhD student) all from Birmingham
- PRD funding to develop a radiation hard DMAPS and investigate Digital calorimetry for future colliders (FCC-hh, ILC, CLIC) etc.
- A radiation hard CMOS would have multiple uses in an ion beam environment
  - Beam monitoring during treatment
  - Beam QA
  - 2D tracking in PRaVDA RT
- Reviewers if the PRD liked the potential applications outside of HEP!

Conclusions

- The use of proton radiotherapy to treat cancers is increasing rapidly around the world
- To ensure we have optimal treatment plans we need to perform pCT
- Groups around the work have been working on this, with varying success
- PRaVDA have a fully Si device, using sensors based on HEP, which produces images in 3 years!
- But…. Still lots of work to do to refine this
- Calorimeter from neutrinoless double beta decay experiments look very promising for fast, accurate beam QA of proton beams
- CMOS devices designed by RAL can monitor beams in IMRT to the same standard as the industry leading monitors
- There are a lot of things that we do that could benefit the medical community!

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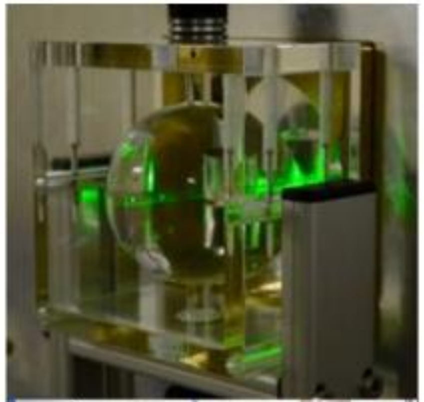

PRaVDA

University of BRISTOL

An Intensity Modulated Radiotherapy Beam Monitoring System using a Monolithic Active Pixel Sensor

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Dr. Jaap Velthuis — Slides shamelessly stolen (with permission)

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From SuperNEMO to Proton Therapy: Adapting the SuperNEMO Optical Module for Proton Energy QA

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Any questions?