PRaVDA

Enhancing Proton Beam Therapy through proton CT

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On behalf of the PRaVDA Consortium

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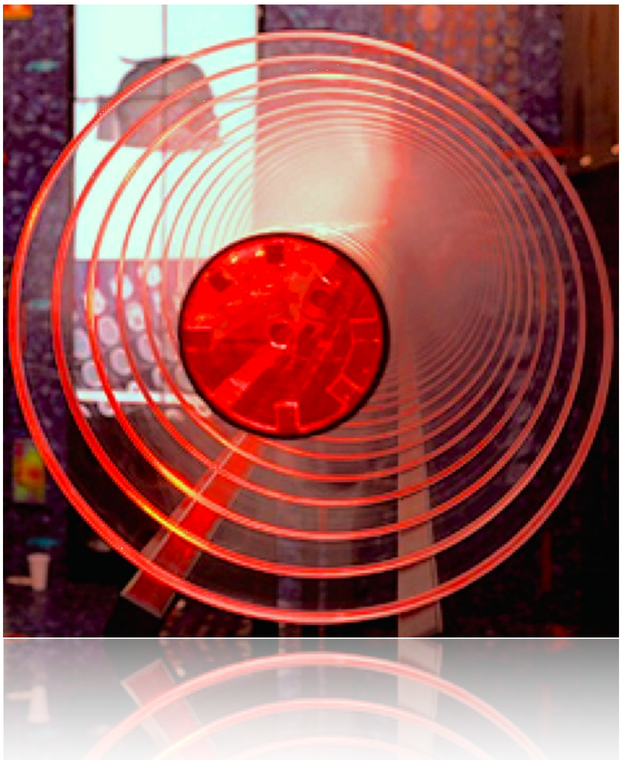
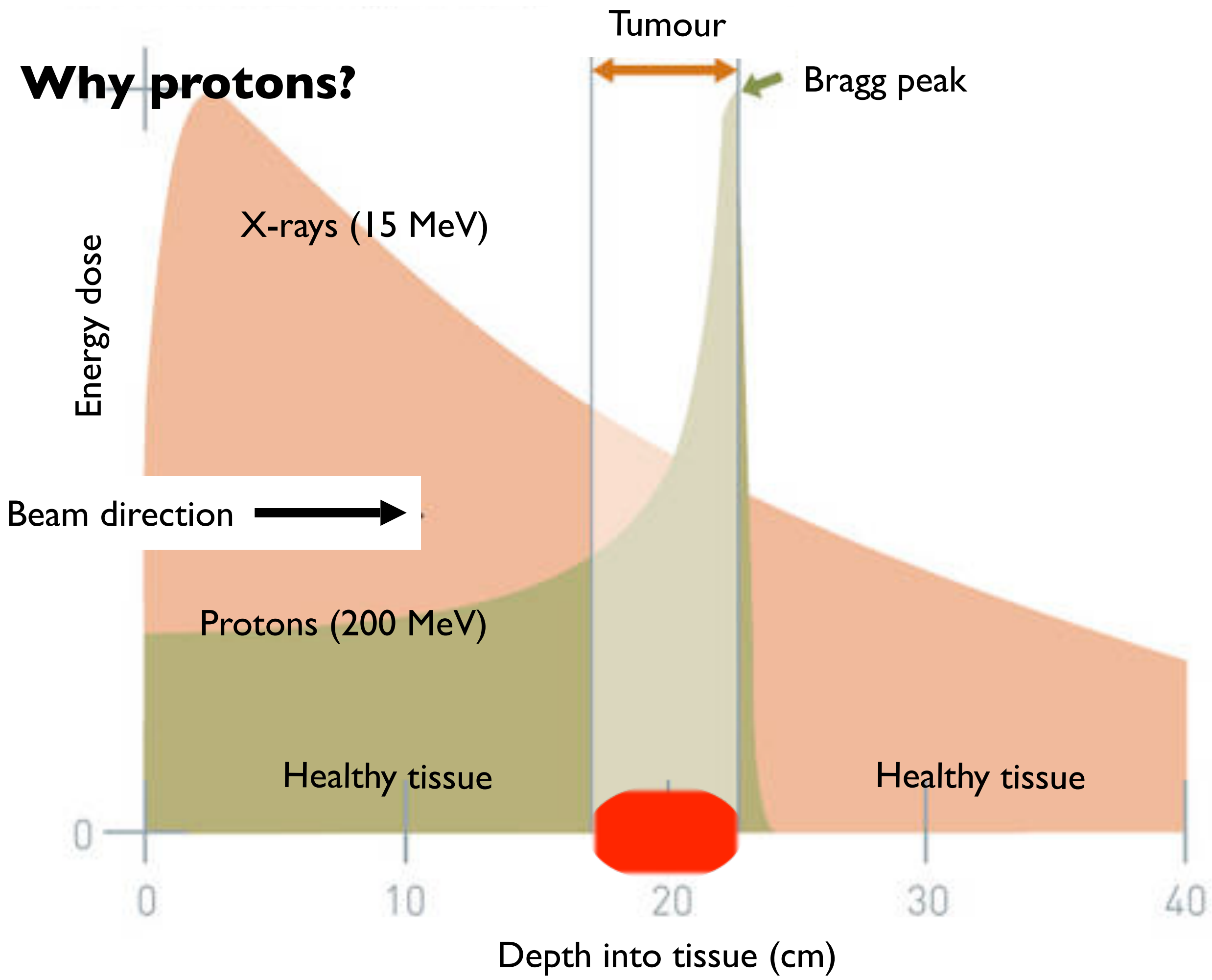
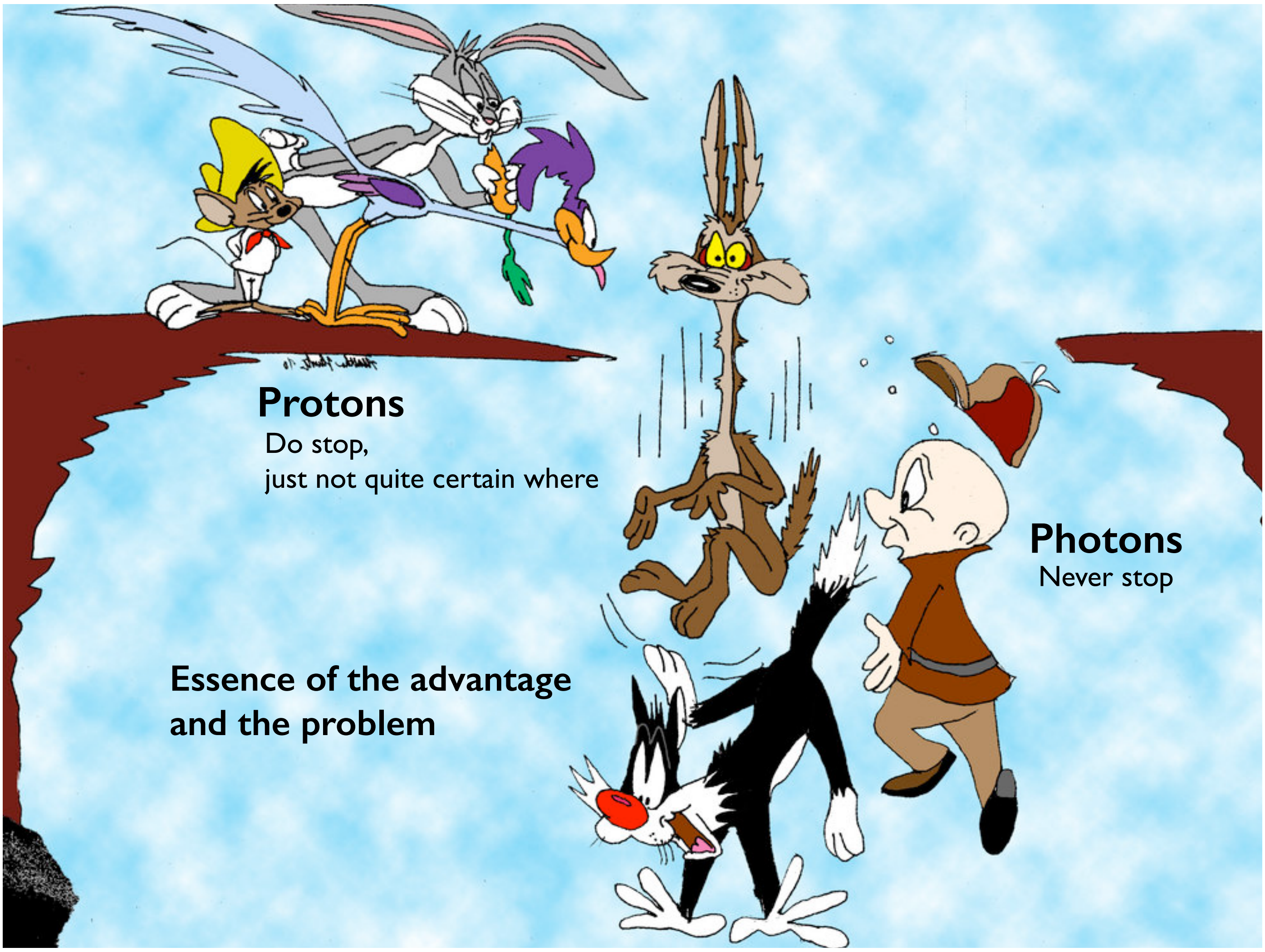
Karolinska University Hospital, Sweden
University of Cape Town
University Hospital Birmingham NHS Foundation Trust
The Christie NHS Foundation Trust
University Hospital Coventry and Warwickshire NHS Trust
iThemba LABS, SA
ISDI Ltd
aSpect Systems Gmbh



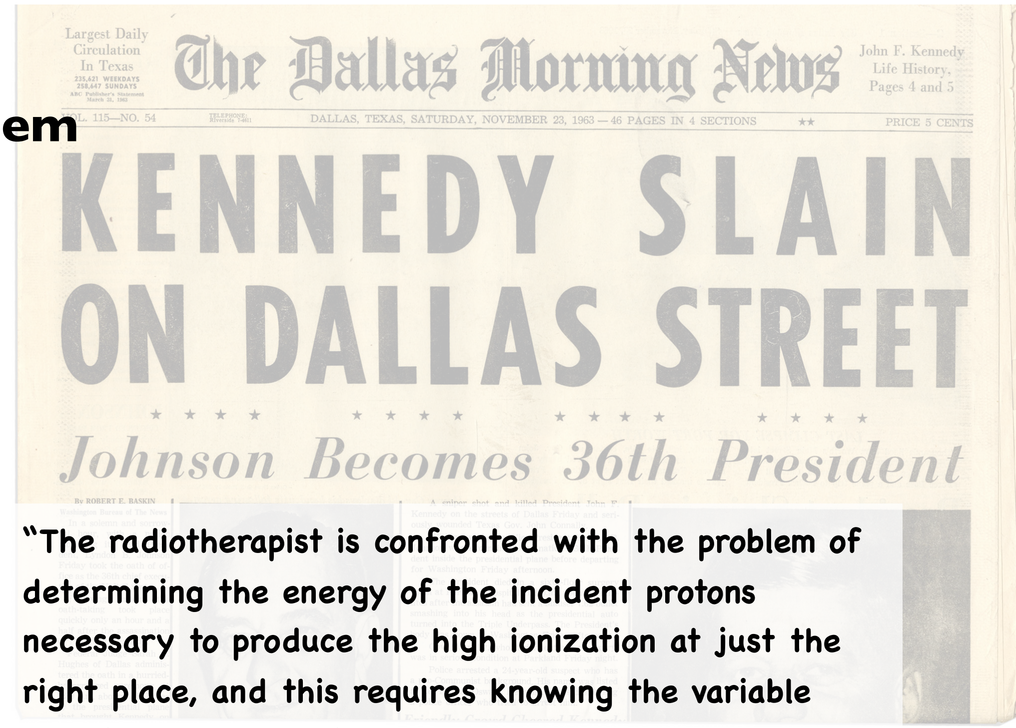
Funded by wellcome trust

Why protons?





An old problem


Largest Daily Circulation In Texas

The Dallas Morning News

John F. Kennedy Life History, Pages 4 and 5

VOL. 115—NO. 54 DALLAS, TEXAS, SATURDAY, NOVEMBER 23, 1963—46 PAGES IN 4 SECTIONS PRICE 5 CENTS

KENNEDY SLAIN ON DALLAS STREET

Johnson Becomes 36th President


Allan McLeod Cormack

"The radiotherapist is confronted with the problem of determining the energy of the incident protons necessary to produce the high ionization at just the right place, and this requires knowing the variable specific ionization of the tissue through which the protons must pass."

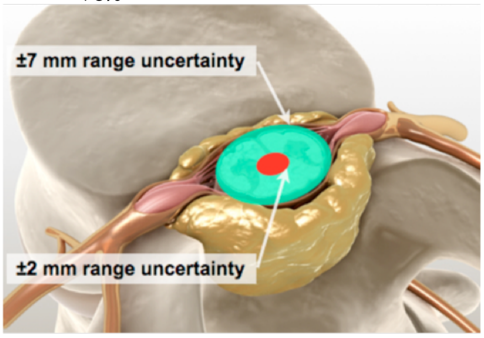
A.M. Cormack, "Representation of a Function by its Line Integrals, with Some Radiological Applications," J. Appl. Phys. 34:2722 (1963)

Range uncertainties

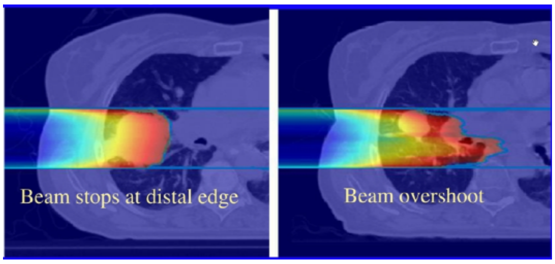
Tumour site	Median	90th percentile	95th percentile	Percentile with range uncertainty ±3.5%
Prostate	1.3%	2.5%	3.0%	98%
Lung	1.5%	2.9%	3.4%	96%
Head and Neck	1.3%	2.6%	3.0%	98%

Yang, M et al., *Comprehensive analysis of proton range uncertainties related to patient stopping-power-ratio estimation using the stoichiometric calibration*, Phys Med Biol. **57** (2012) 4095–4115.

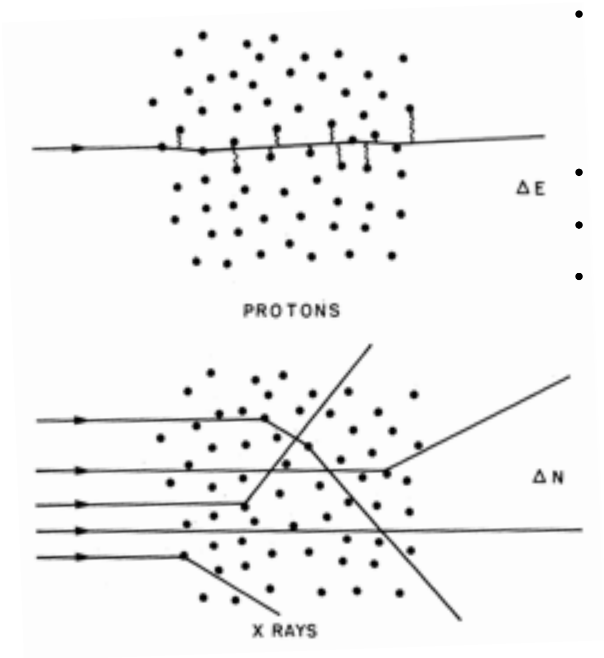
Example: 20 cm of tissue penetration



Things change! Planning CT and after 5 weeks of treatment



Why Proton CT is a challenge

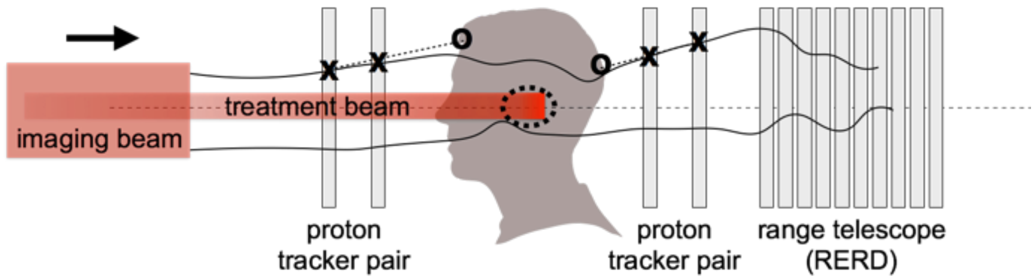


Every proton matters

- 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 protons undergo non-elastic nuclear interactions – **attenuating power**

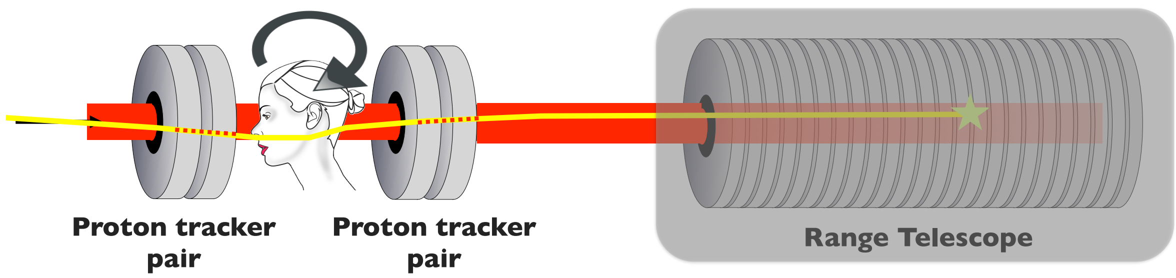
Follow the herd - use statistics

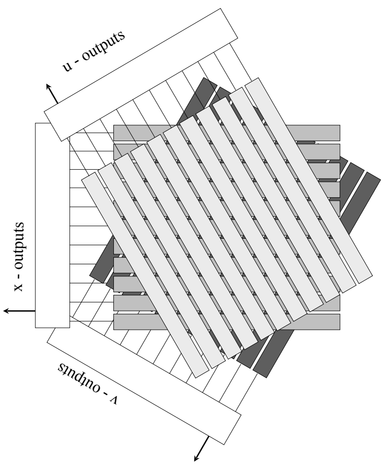
Principles of proton CT instrument



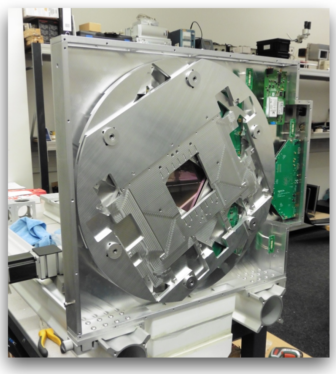
- Increase proton energy and reduce intensity of beam by a factor of ~10,000
- Pair of proximal position-sensitive trackers records trajectory of each incident proton and identical pair of distal trackers records corresponding exit trajectory
- Residual Energy Resolving Detector (RERD) logs the residual energy of each proton
- Following information for each proton: entry position, exit position and energy absorbed
- To produce a clinical-quality CT, require ~$10^{7\text{-}8}$ such triplets.

PRaVDA instrument

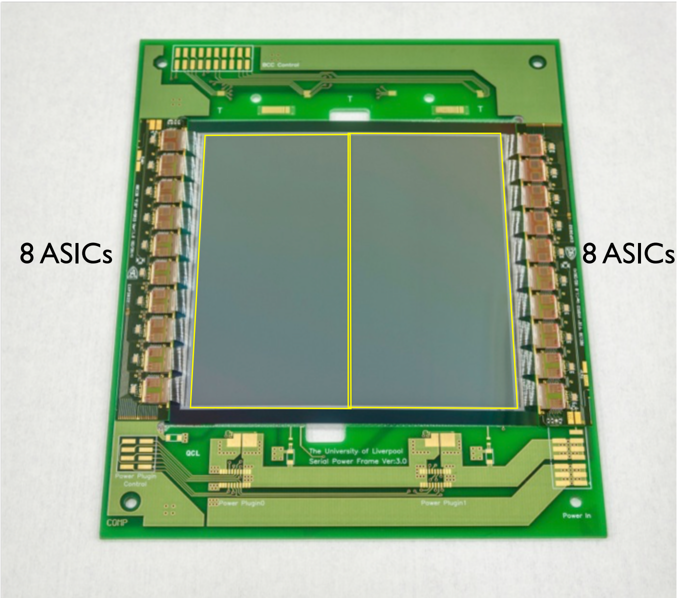




- Three equi-rotated custom silicon strip sensors – reduces anomalous events
- Copes with high flux levels (treatment beam)
- High count rate, in excess of 25 million/s
- Extremely radiation hard (developed for HL-LHC)



Custom Strip Detectors



- Double-ended 150µm thick n-in-p technology
  2,048 strips at 90.8 um pitch
- 93 mm x 96 mm active area
- Fabricated by Micron Semiconductor
- Technology choices following closely those taken for the ATLAS upgrade
- Radiation hard in a clinical environment up to doses of around 5×10^{15} n eq/cm^2

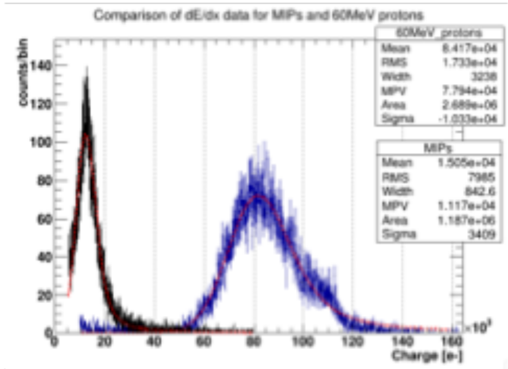
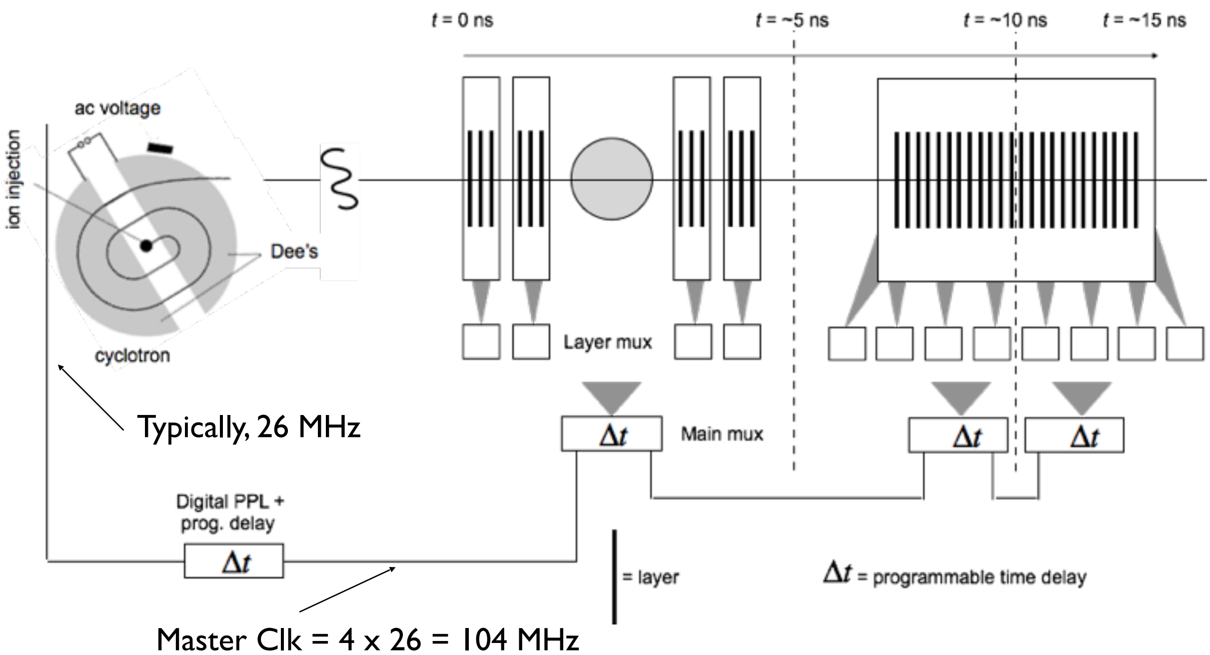


Figure 6. Energy loss of MIPs (black) and 60 MeV protons (blue) in a 155μm PRaVDA detector.

J. T. Taylor, P. P. Allport, G. L. Casse, N. A. Smith, I. Tsurin, N. M. Allinson, M. Esposito, A. Kacperek, J. Nieto-Camero, T. Price, and C. Waltham, "Proton tracking for medical imaging and dosimetry," J. Instrum. 10, C02015 (2015).

PRaVDA Clock Distribution



Rhea – ASIC

- Double programmable thresholds
- 128 channels
- Two operational modes

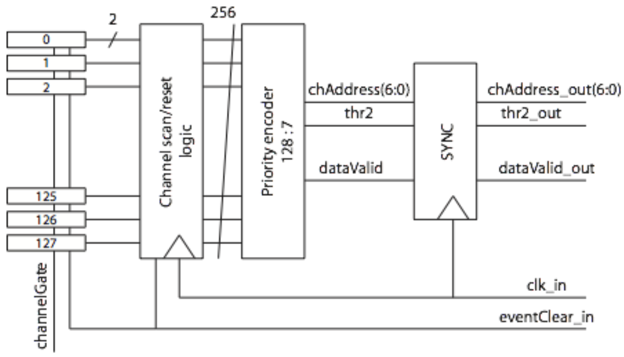
  Imaging mode

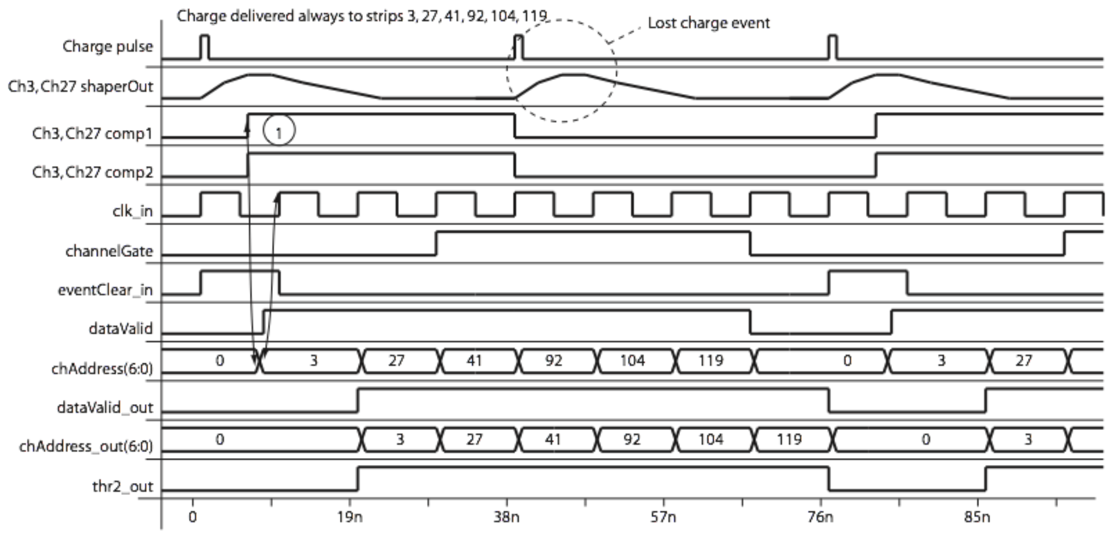
  Every proton detected

  Treatment mode

  Specified fraction of protons detected

  Profile histograms to provide information for control feedback





Proton tracker results

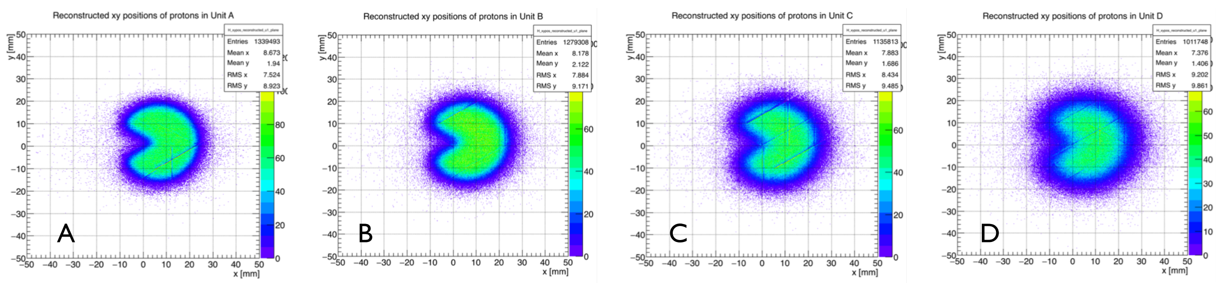
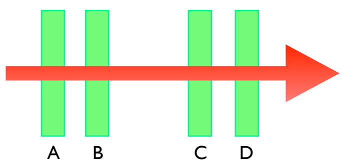
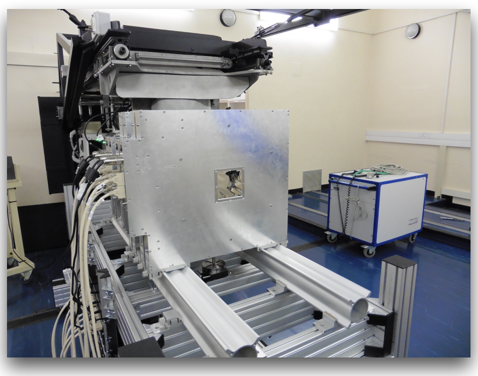
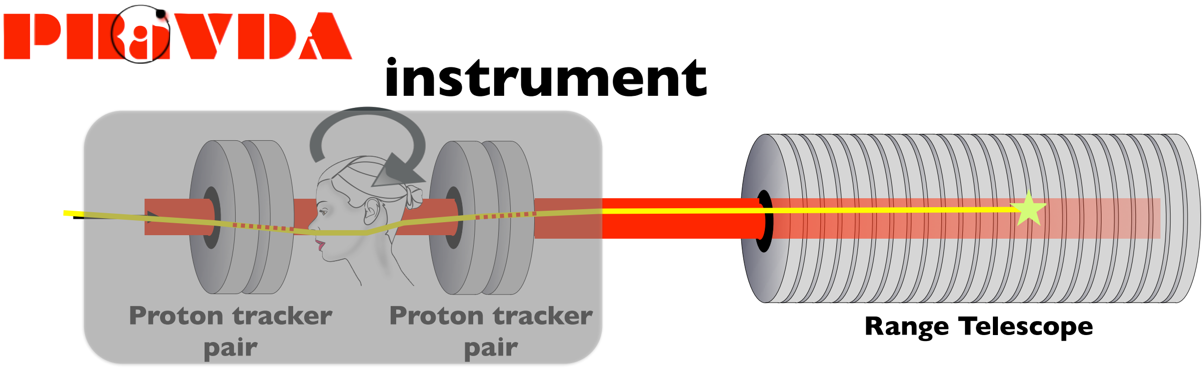


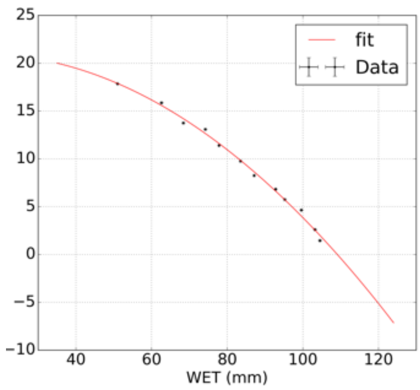
Image reconstructions – Pac-man collimator (29 MeV)



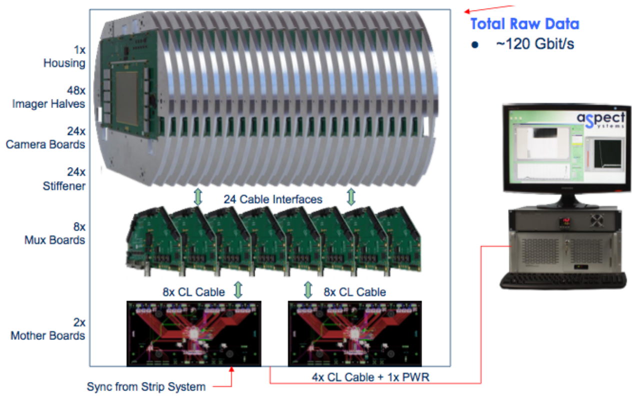


Proton trackers – iThemba LABS proton vault



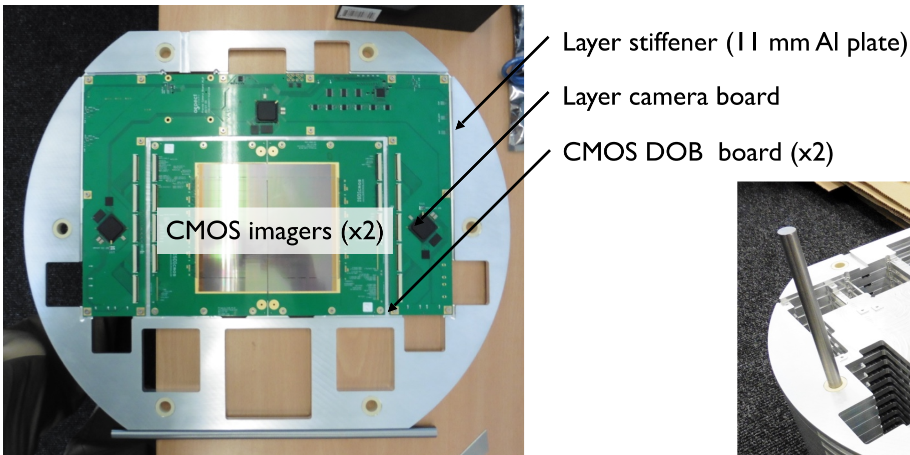


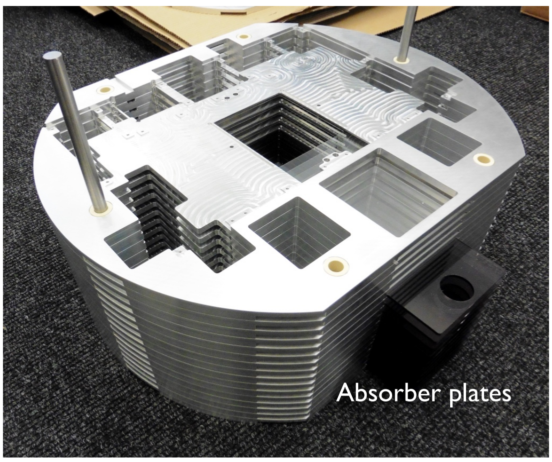
Calibration curve

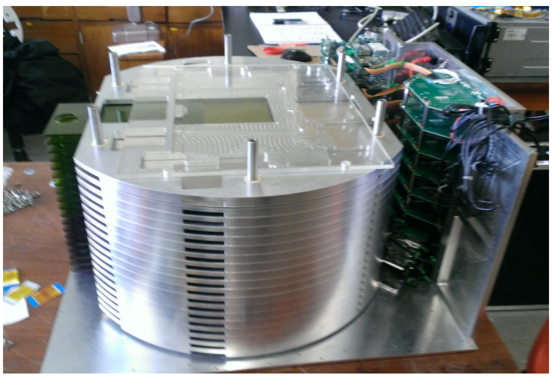


- Currently 22 layers of silicon strip sensors
- Can replace with high-speed CMOS imagers

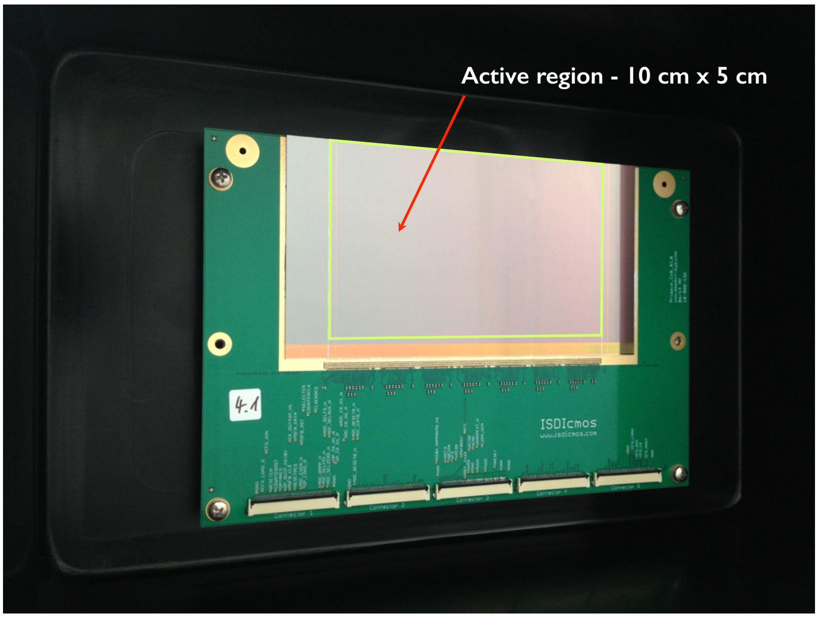
Range telescope - CMOS version



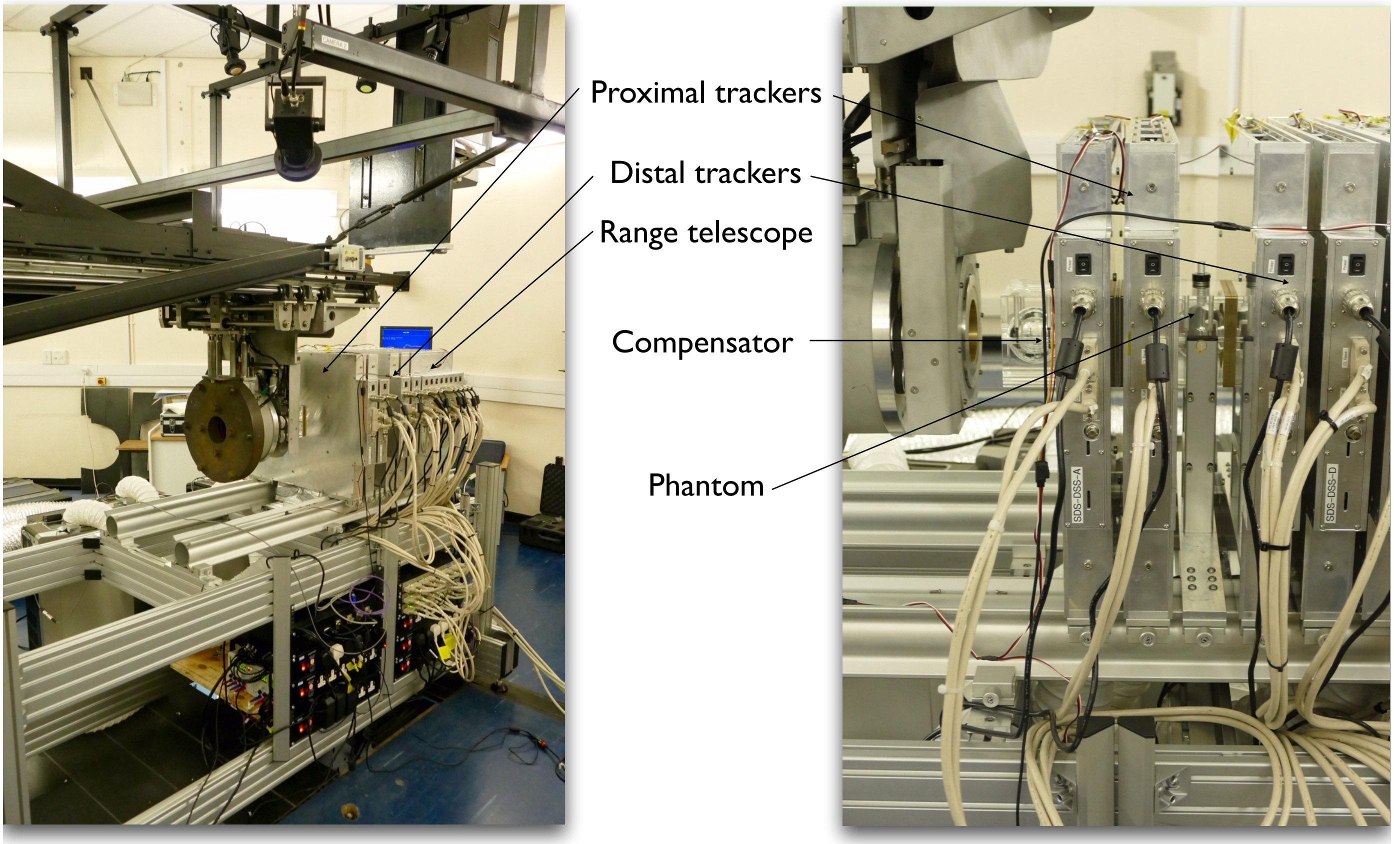




Priapus - Custom rad-hard CMOS



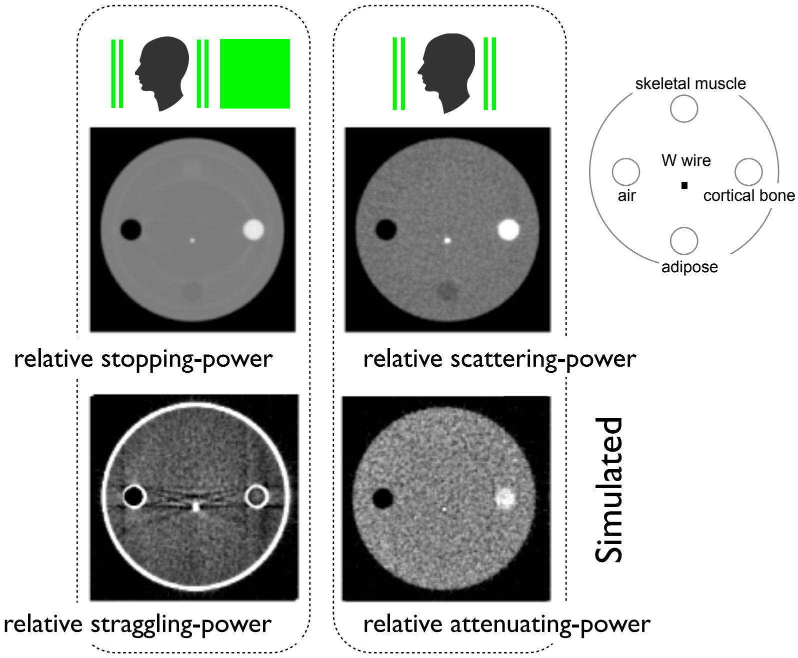
- 0.35 um CMOS Active Pixel Sensor
- Rad-hard pixels and on-chip analogue chains
- 194 um square pixels
- Column ADCs - programmable up to 16 bits
- 5 cm x 10 cm active area
- 1,000 fps at 8-bit resolution



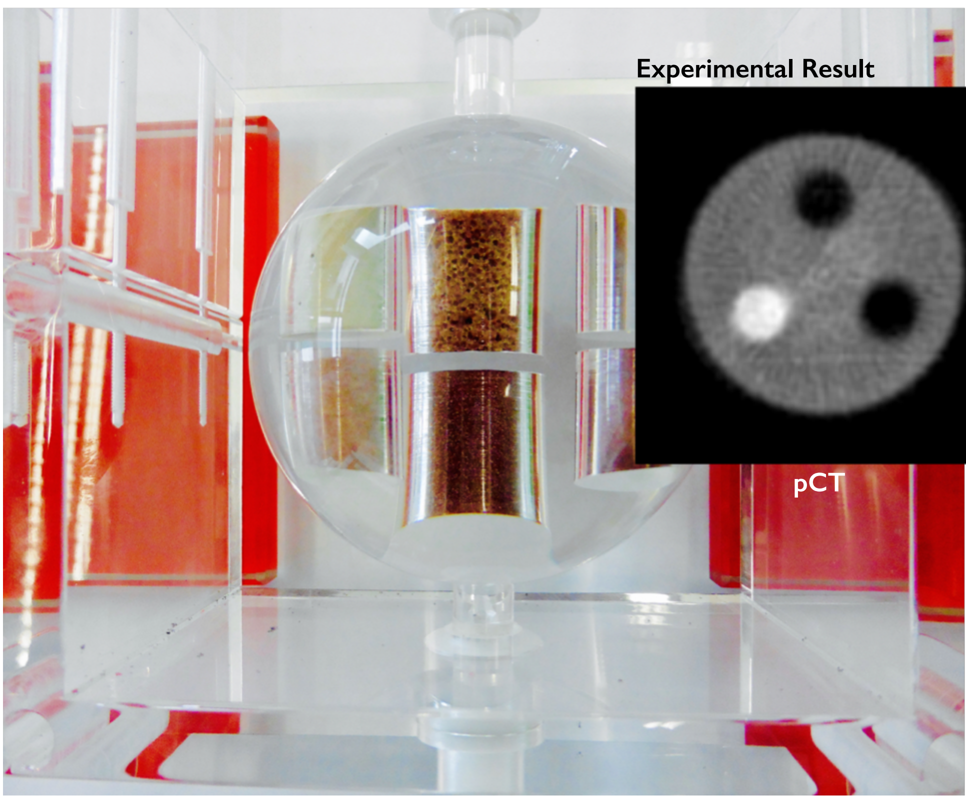
PRaVDA

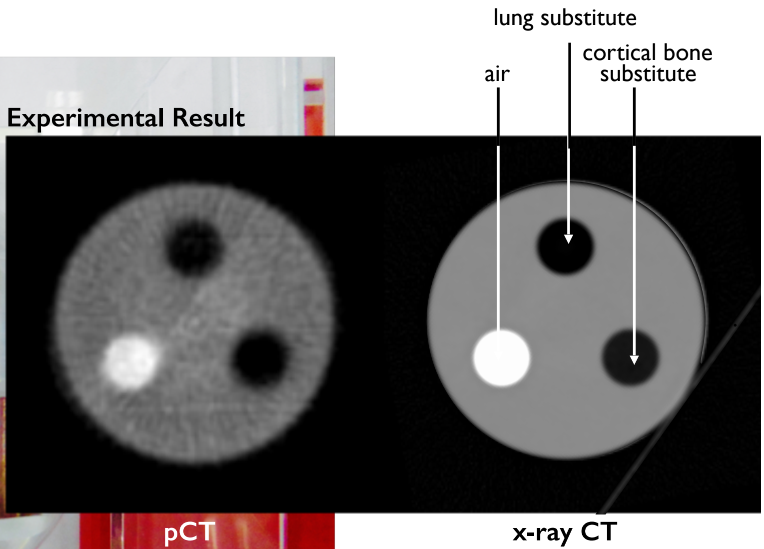
Proton CT modalities

- Stopping-power – most crucial quantity for PT planning
- For biological materials: stopping-power, scattering-power and attenuating-power can be related to electron density (Kanematsu *et al*., Medical Physics **39**, 1016, 2012)
- Scattering and attenuation power only require trackers – reduced system complexity
- Combine two or more modalities to yield improved quality pCT



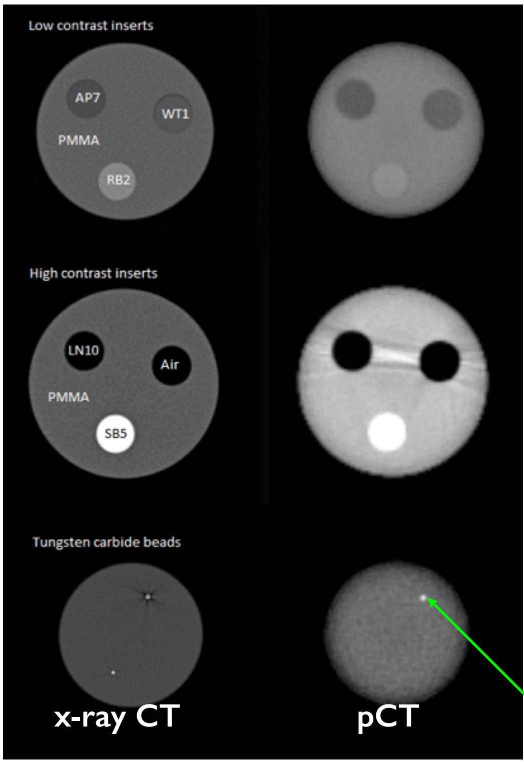
Relative scattering-power pCT





Taylor, J. T., et al., (2016), *An experimental demonstration of a new type of proton computed tomography using a novel silicon tracking detector*. Med. Phys., **43**: 6129–6136.

Relative stopping-power pCT



1 mm diameter WC sphere

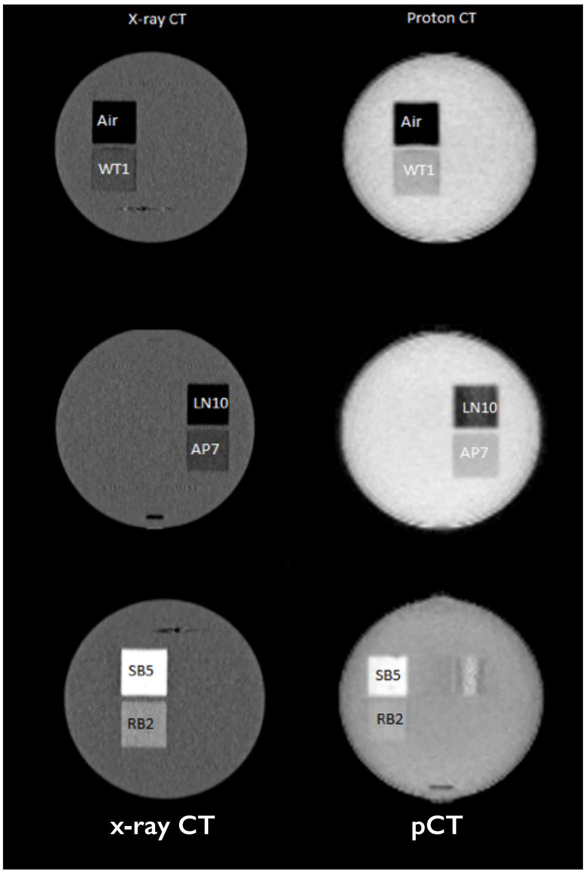
Proton CT slices of 6-insert phantom

Preliminary

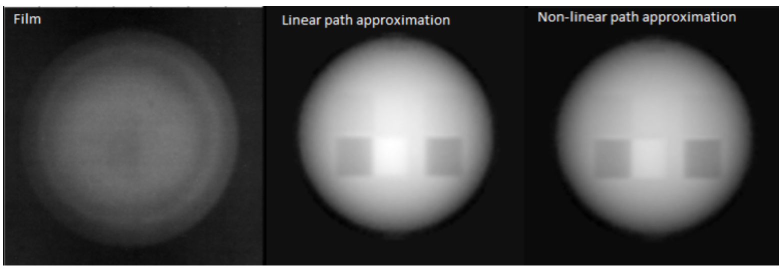
Material	Density [g/cc]	Expected RSP	pCT RSP	Percent error
PMMA	*~1.16*	*1.15*	*1.15*	*0.0*
AP7(adipose)	*0.92*	*0.95*	*0.94*	*-0.7*
WT1(water equivalent)	*1.00*	*1.00*	*0.98*	*-1.6*
RB2 rib/ average bone	*1.40*	*1.21*	*1.22*	*1.2*
SB5 hard cortical bone	*1.84*	*1.63*	*1.62*	*-0.4*
LN10 *lung*	0.25-0.35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

Comparison of known residual stopping power for Leeds Test Objects and as measured using proton CT

* Image slices containing LN10 insert and air cavity show streak artefacts that compromise quantitative accuracy. For that reason, percentages error is not shown for these two materials.



Reconstructed CT image coronal slices of the imaging phantom

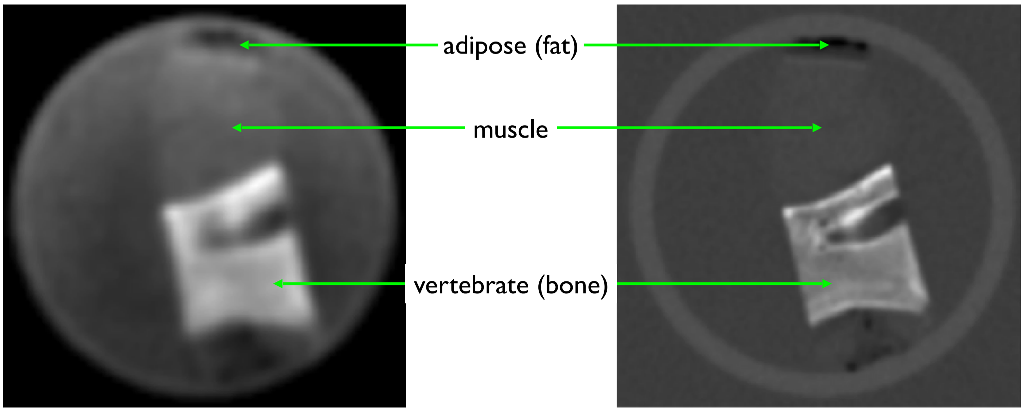


Comparison of film radiograph and radiographs from the PRaVDA system

Beam energy 125 MeV.
Overall dose ~0.5 Gy

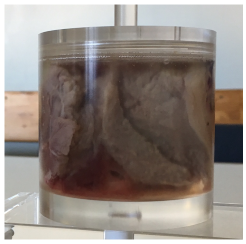
Preliminary

Proton CT biological sample



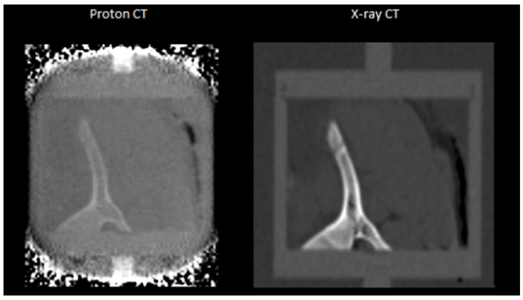
Proton CT

X-ray CT



Lamb chop in agar

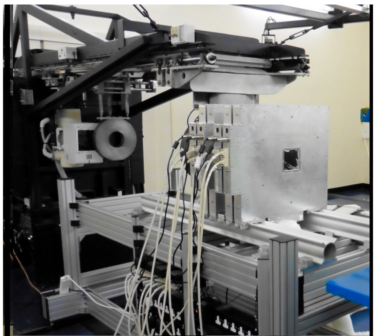
Preliminary

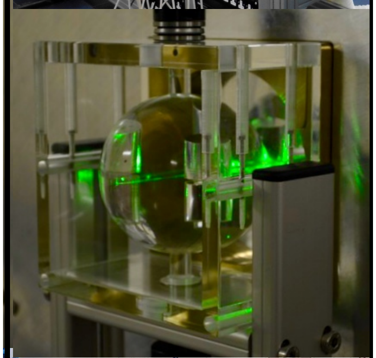


Coronal pCT and 120kV X-ray CT image slices. Fine bone structure is visible in both images. No smoothing has been applied to the pCT image

Conclusions

- Proton imaging is challenging but proven!
- Treating and imaging with the same radiation – "use the same ruler"
- Imagery will be of clinical quality – relative stopping power errors <1%
- Proton CT modalities plus combining with other modalities (e.g., x-ray CT) will open a new field of medical imaging
- System complexity will reduce
- Clinical relevant results will be near real-time – fit with radiotherapy workflows
- … and so provide robust, optimum and adaptive treatment regimes





PRaVDA

Thank you

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