Experiences with PRaVDA and future options

University of Lincoln

University of Birmingham

University of Liverpool

University of Surrey

University of Warwick

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

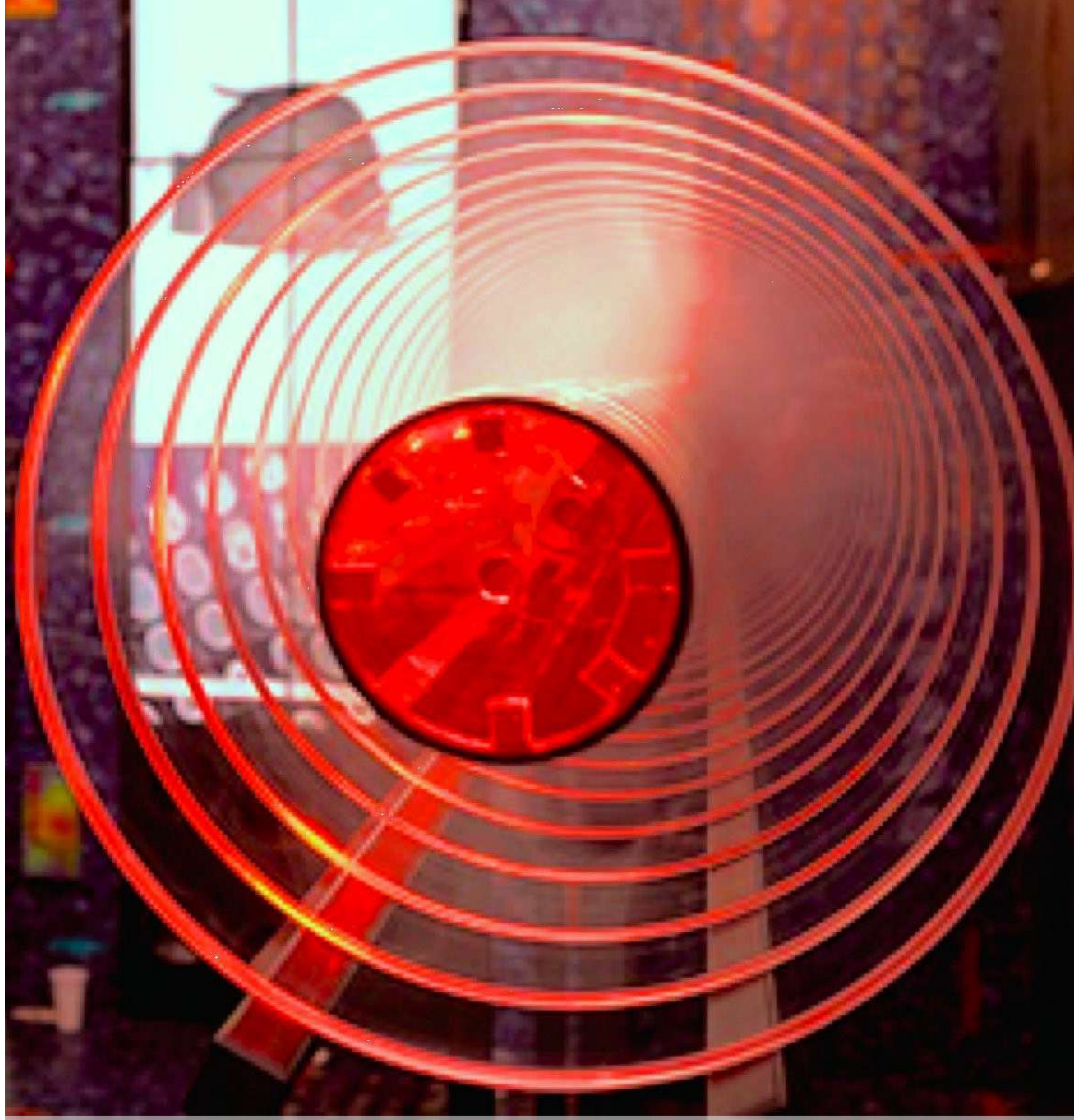
iThemba LABS, SA

ISDI

aSpect

Nigel M Allinson
University of Lincoln
On behalf of the PRaVDA Consortium

Funded by wellcome trust



Proton Imaging Workshop: Lyon 2018

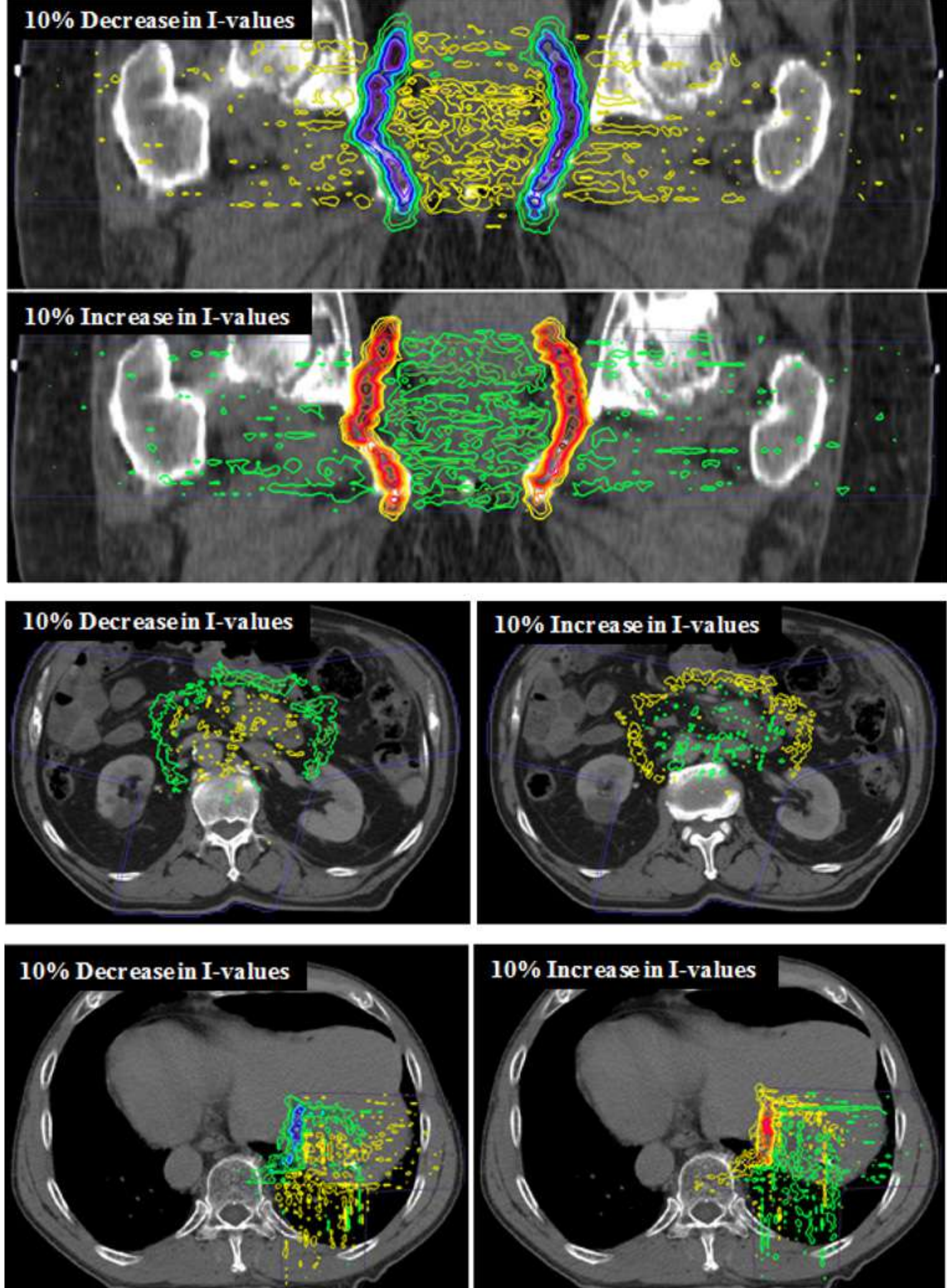
Reducing uncertainties

Not present in proton CT

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

Yang, M., Zhu, X.R., Park, P.C., Titt, U., Mohan, R., Virshup, G., Clayton, J.E. and Dong, L., 2012. *Comprehensive analysis of proton range uncertainties related to patient stopping-power-ratio estimation using the stoichiometric calibration*. *Physics in medicine and biology*, **57**, p.4095.

Besemer, A., Paganetti, H. and Bednarz, B., 2013. *The clinical impact of uncertainties in the mean excitation energy of human tissues during proton therapy*. Physics in medicine and biology, **58**, p.887.



Reducing uncertainties

Total range uncertainty

±2.4% + 1.2 mm – H. Paganetti, Physics in Medicine and Biology 57(11): R99–R117

±3.5% – M. Yang et al., *Physics in medicine and biology*, 57(13), 4095.

Dual Energy x-ray CT (DECT)

Reduce by ~ 1%

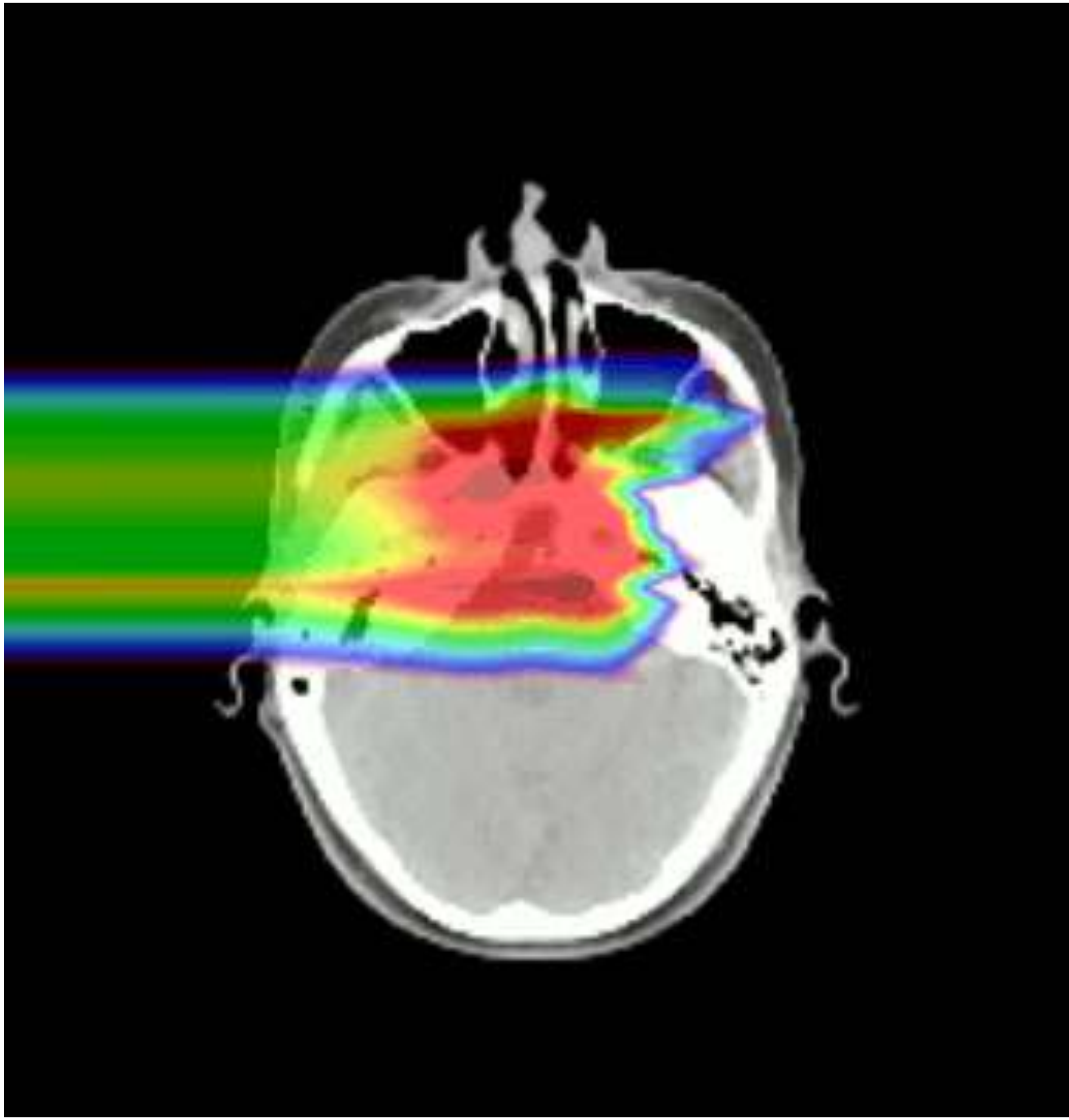
Proton CT

To <1%

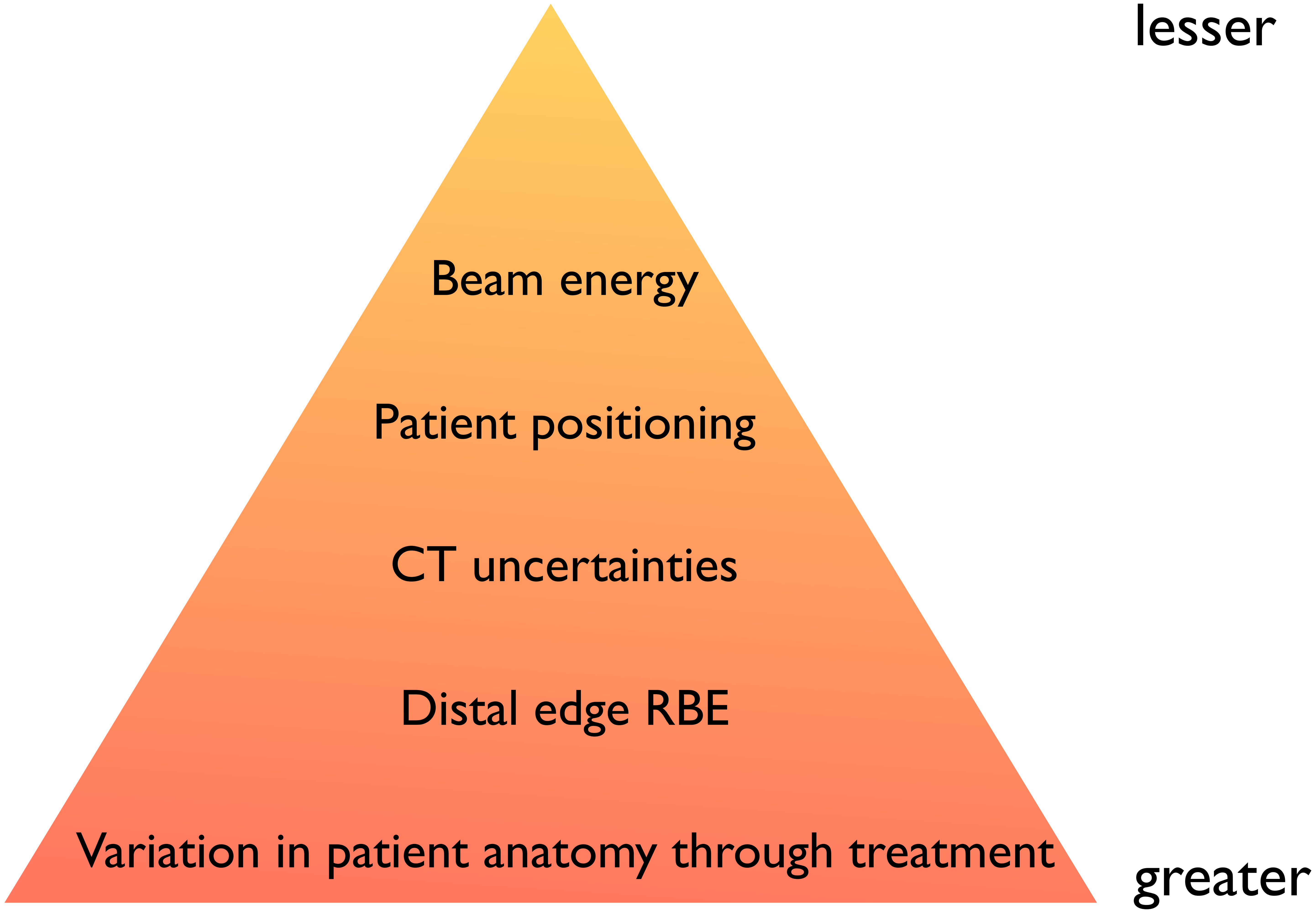
Aim to reduce range uncertainty in treatment planning to ~1%, to achieve a *percent dose difference* (ΔD) to *distance to agreement* (*DTA*) of $\Delta D/DTA$=1% per mm as prescribed for treatment QA

Effect of ±3% range error

- Never use the distal edge
- Need is to reduce exposure of healthy tissue
- To ensure target coverage, irradiate a larger volume of healthy tissue (PTV margins).
- To ensure OARs are within tolerance under patient shifts, compromise target coverage.
- The larger the uncertainty accounted for, the greater the compromise.

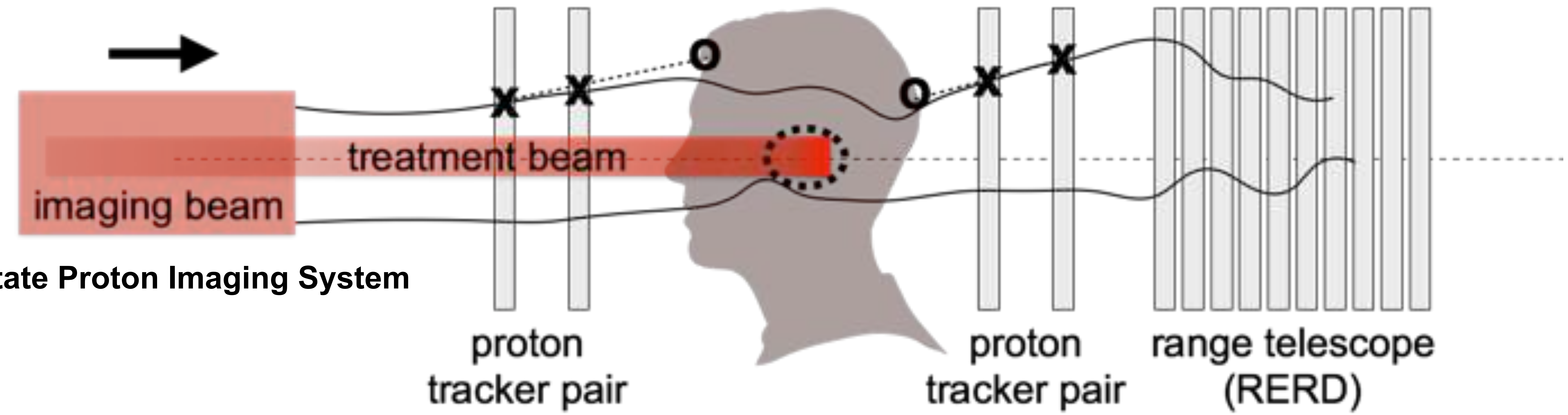


Uncertainty pyramid



Adaptive PBT pathway

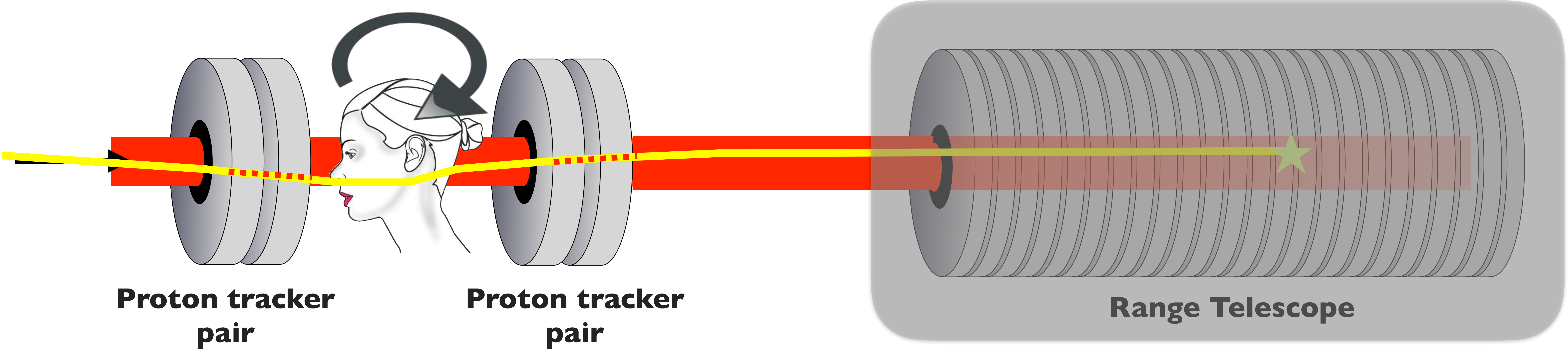
Principles of proton CT instrument

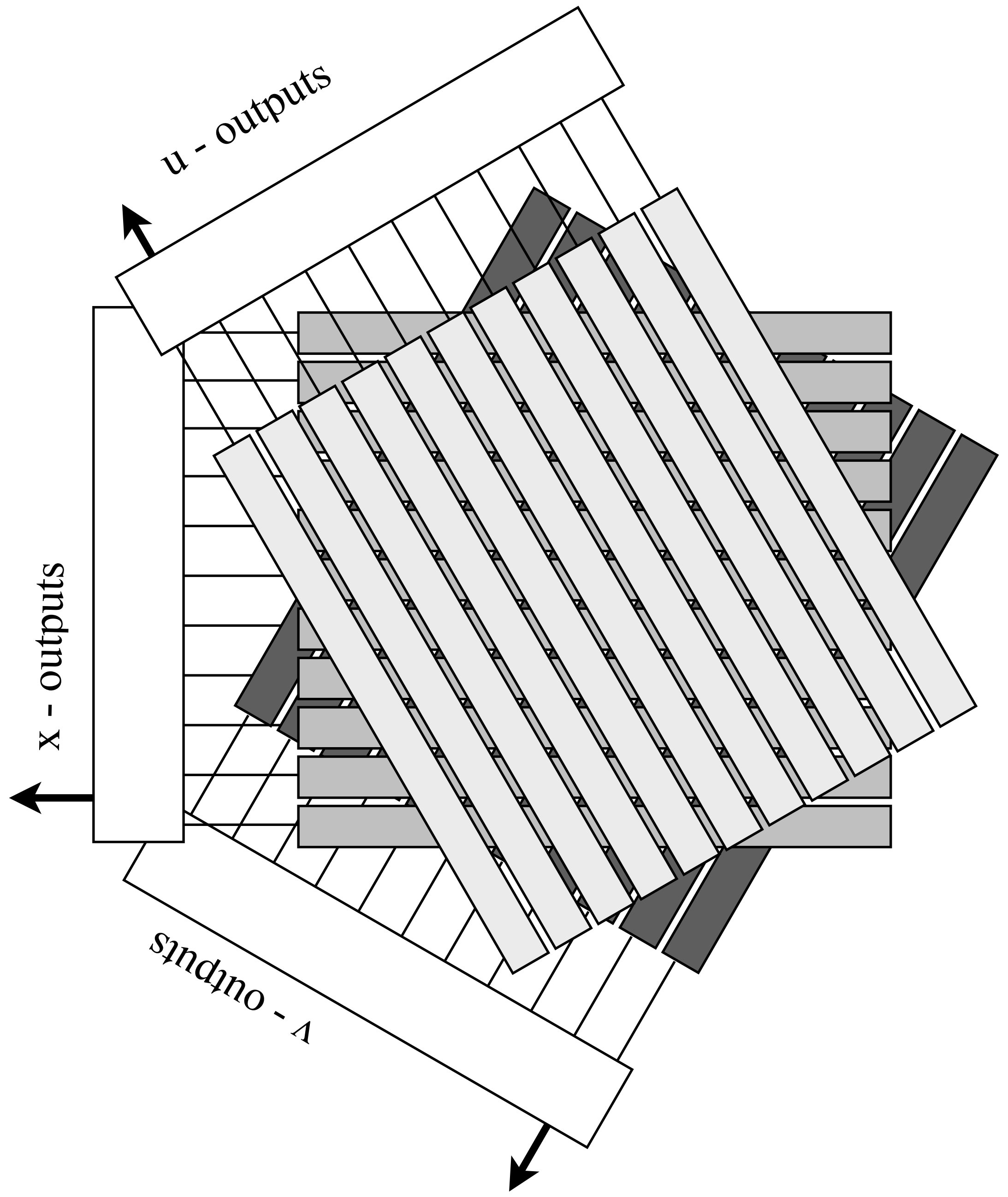


A Solid-State Proton Imaging System

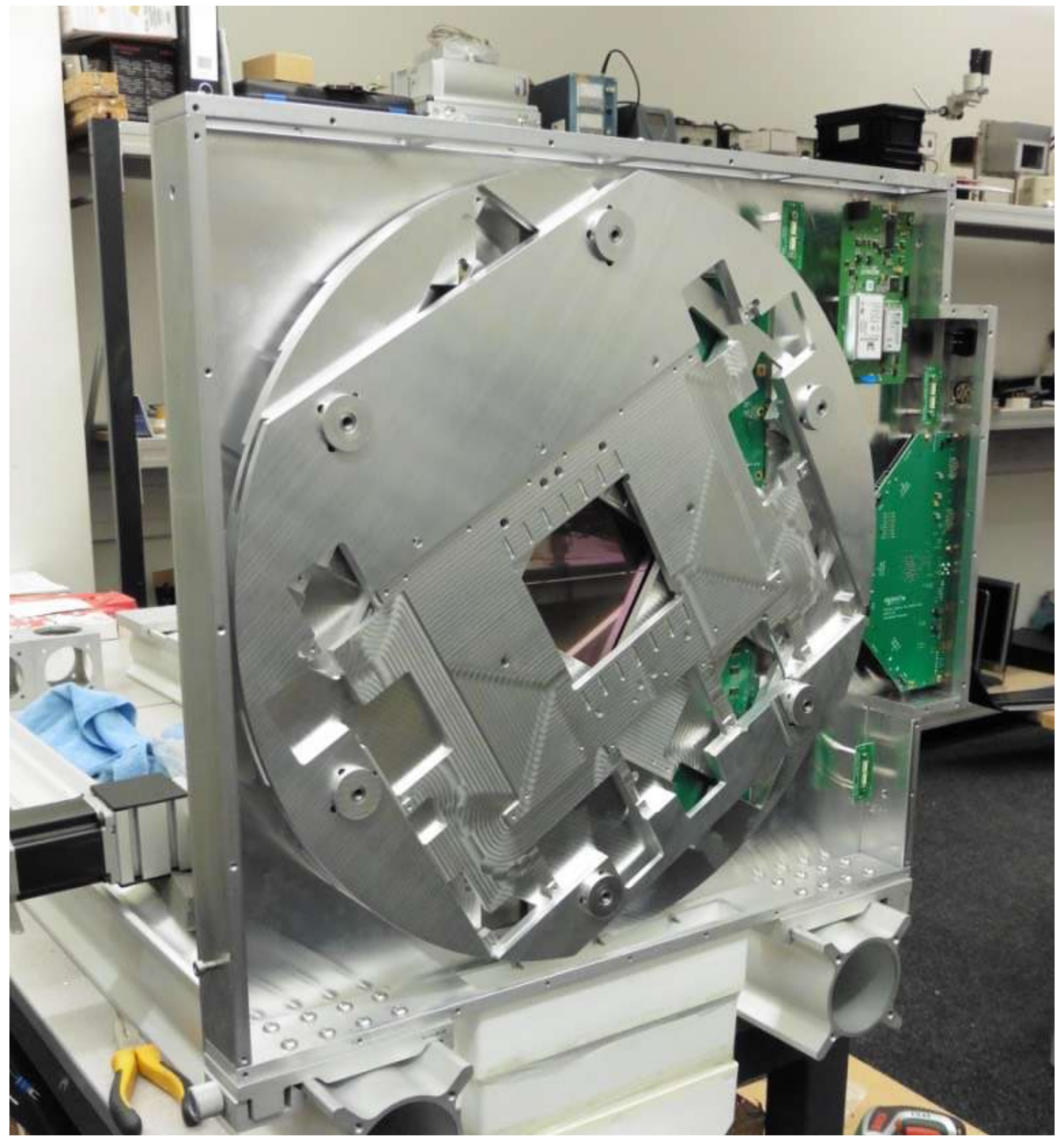
- Increase proton energy and reduce intensity of beam by a factor of ~10,000.
- Pair of proximal position-sensitive trackers records trajectory of each incident proton and identical pair of distal trackers records corresponding exit trajectory.
- Residual Energy Resolving Detector (RERD) logs the residual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

PRaVDA instrument

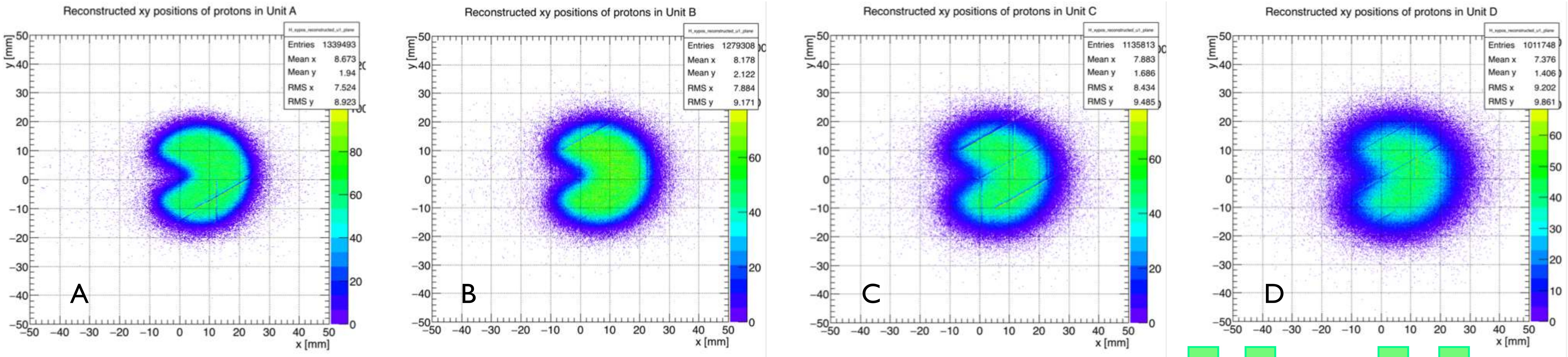




- Three equi-rotated custom silicon strip sensors – greatly reduces anomalous events
- Cope with high flux levels (treatment beam)
- High count rate – 2×10^8 protons/s detected over full detector area (@ 26 MHz spill frequency
- 150 µm-thick n-in-p silicon, active area 93 × 96 mm and strip pitch of 90.8 µm



Proton tracker results



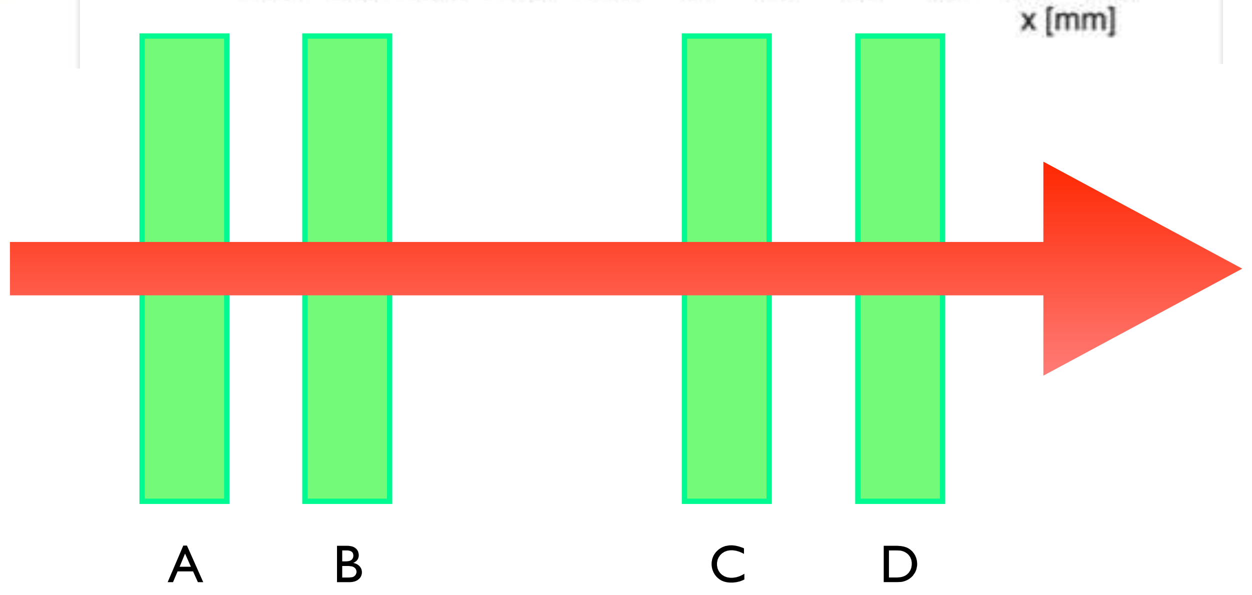
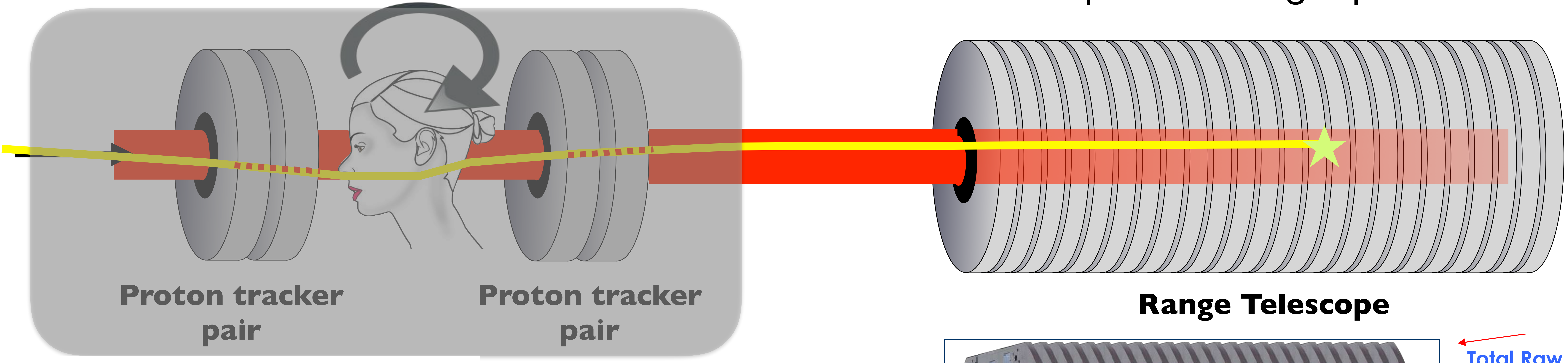


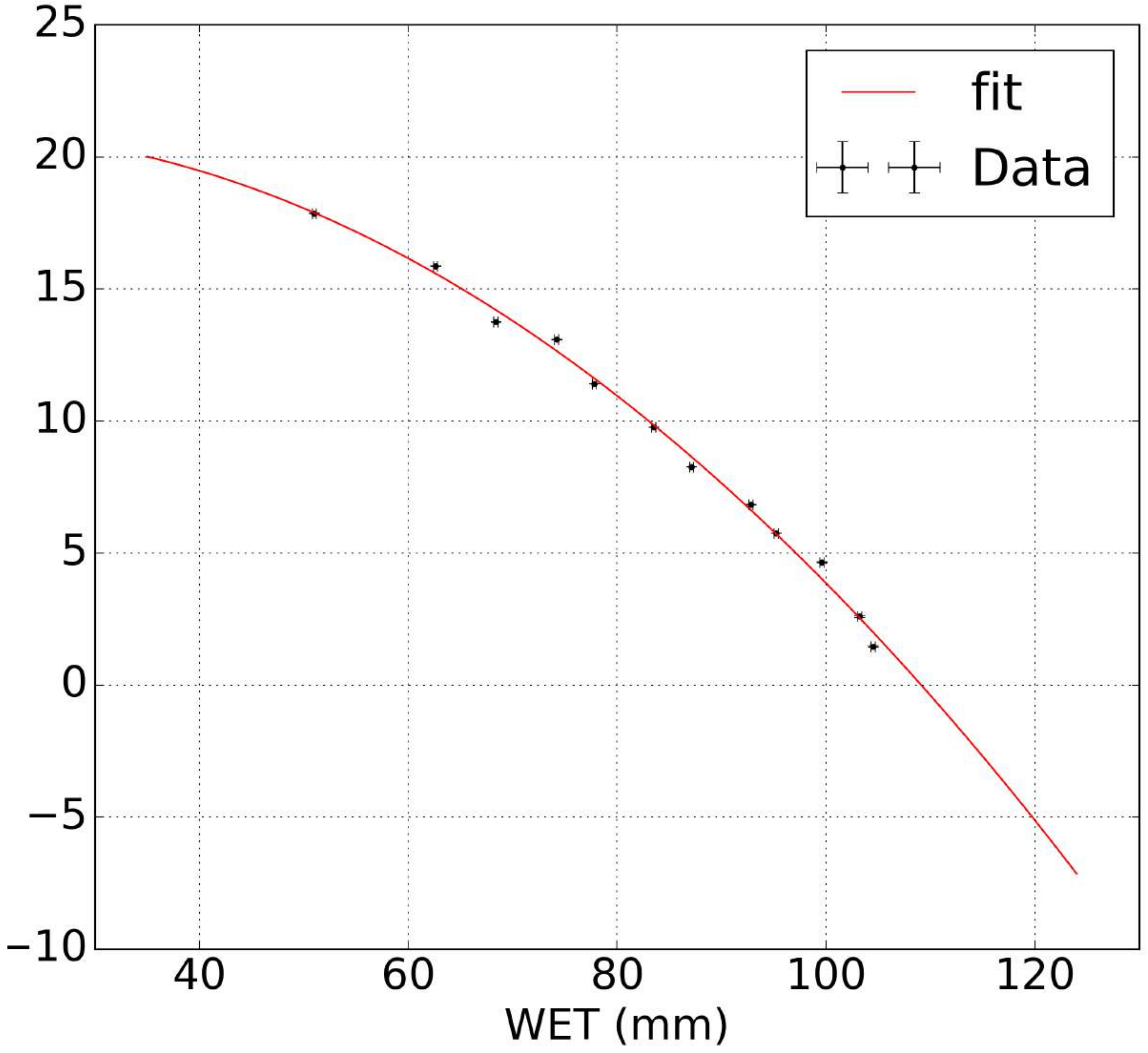
Image reconstructions – Pac-man collimator (29 MeV)

Proton trackers – iThemba LABS proton vault

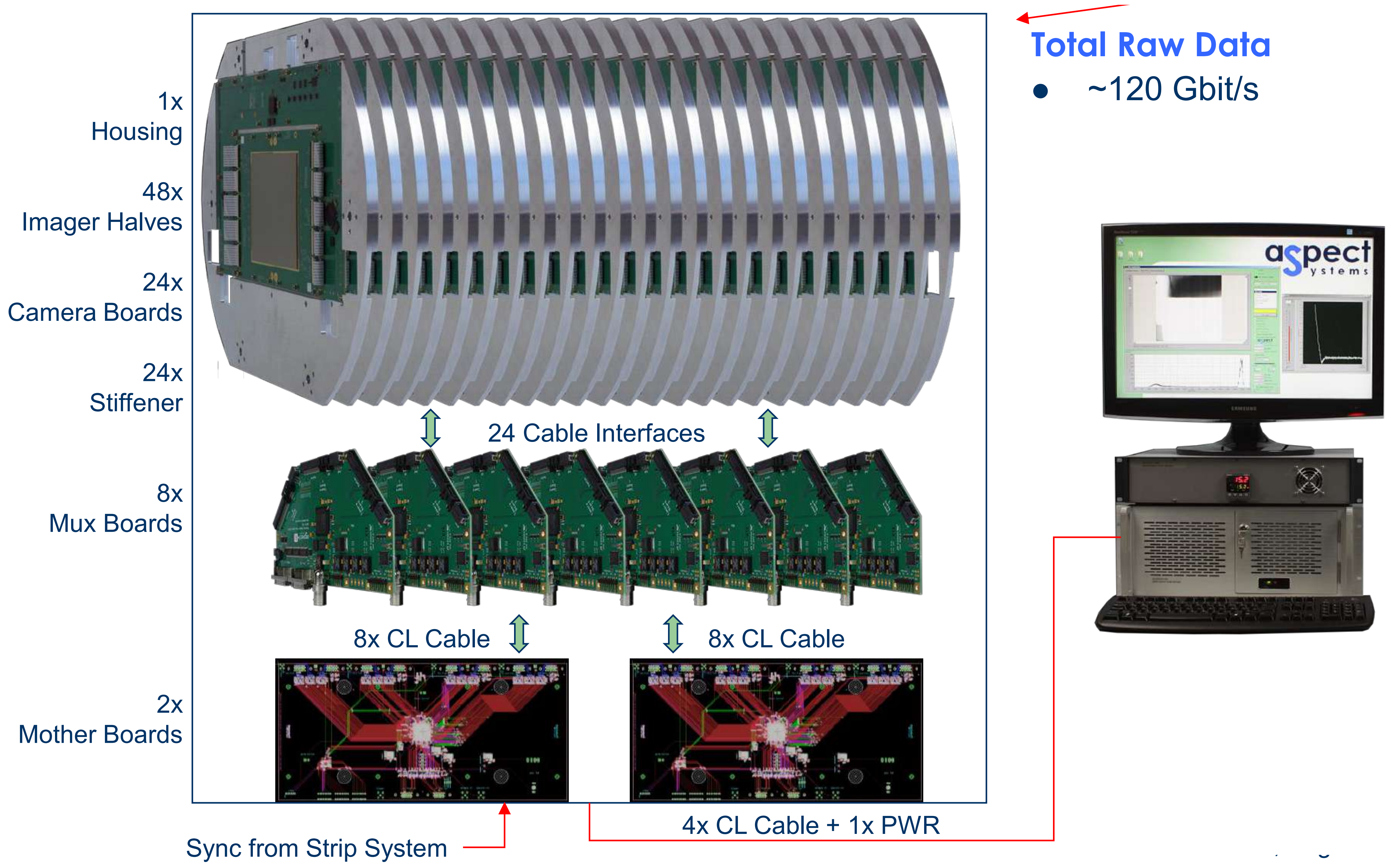
PRaVDA instrument

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





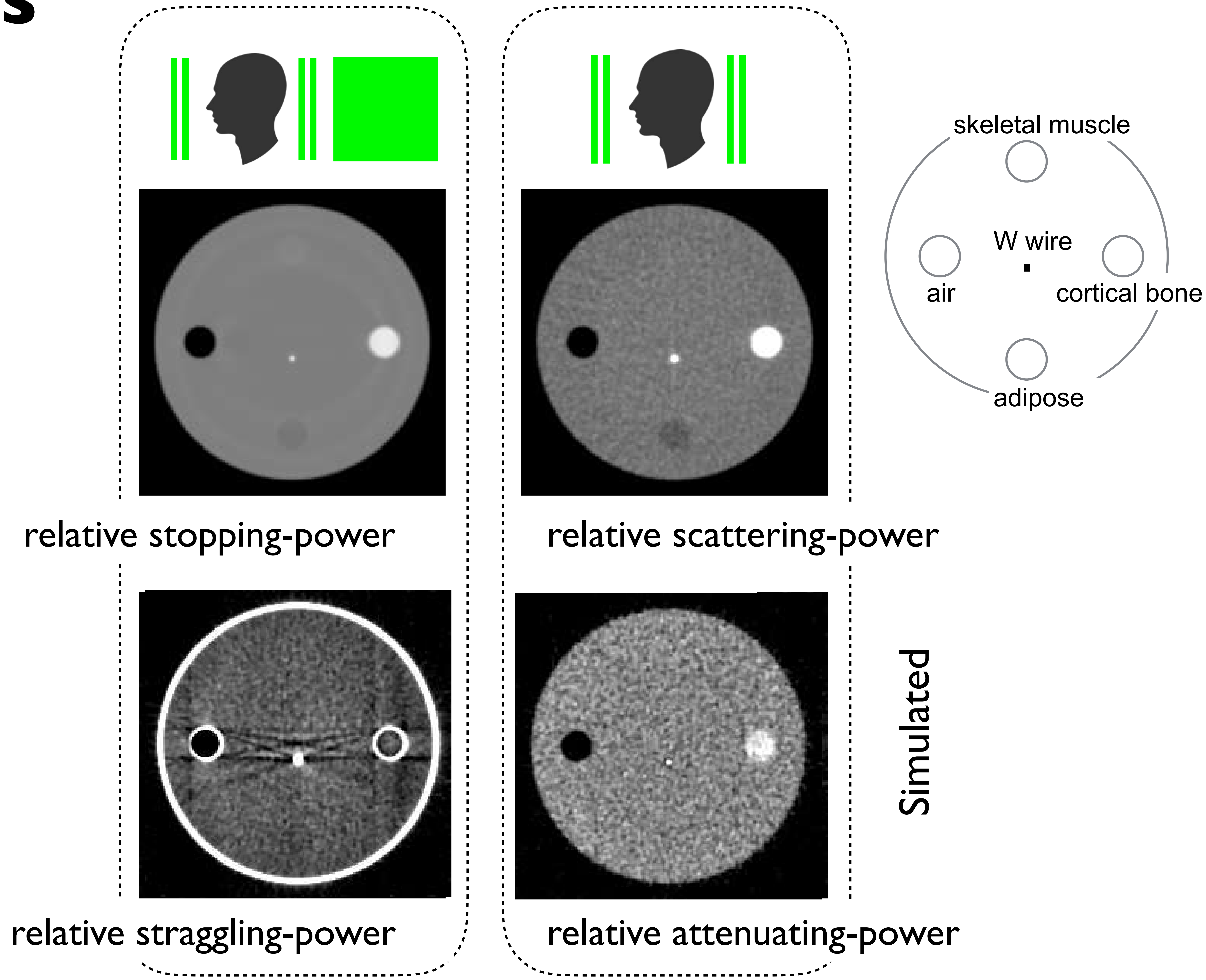
Calibration curve




Proximal trackers
Distal trackers
Range telescope
Compensator
Phantom
SDS-DSS-A
SDS-DSS-D

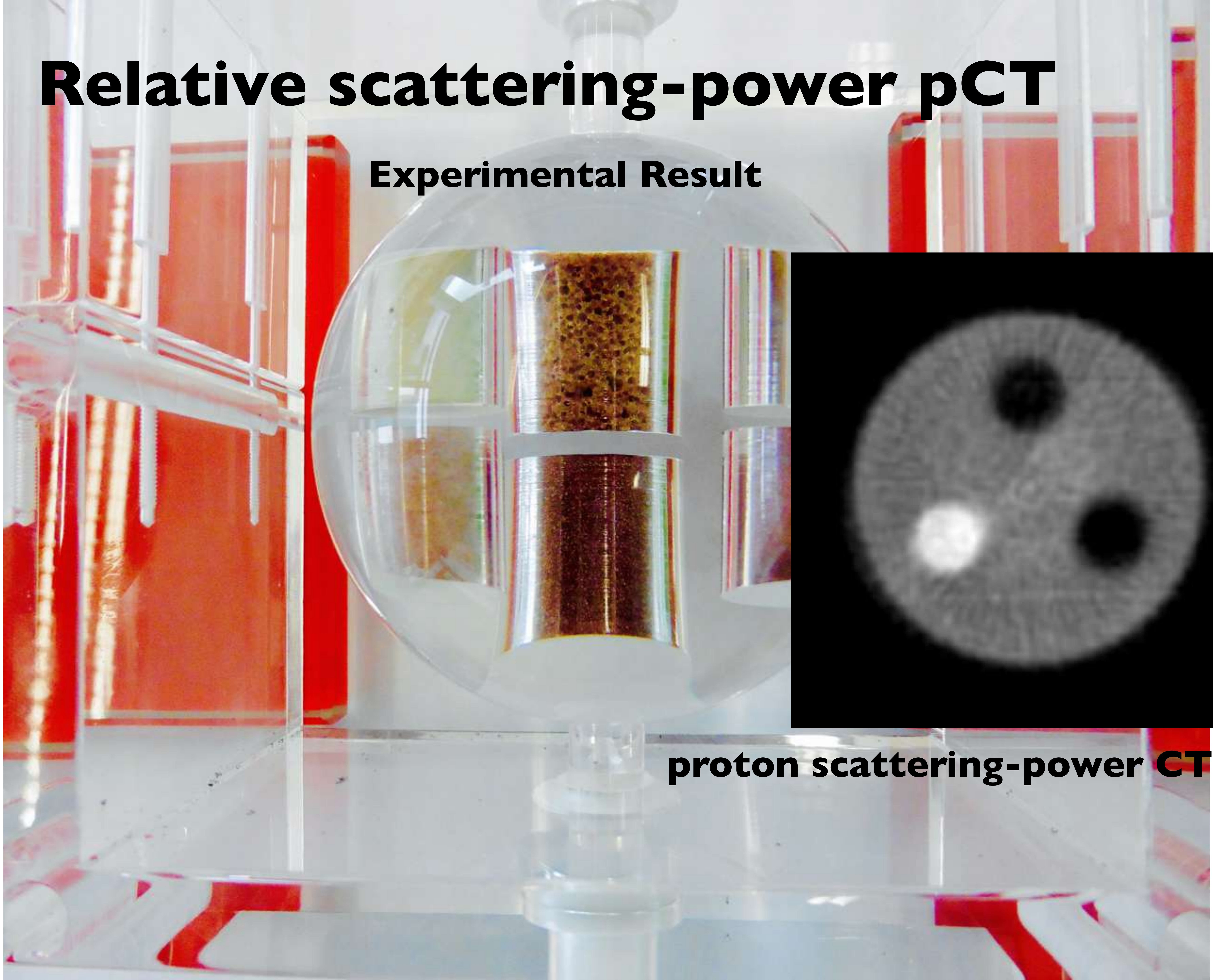
Proton CT modalities

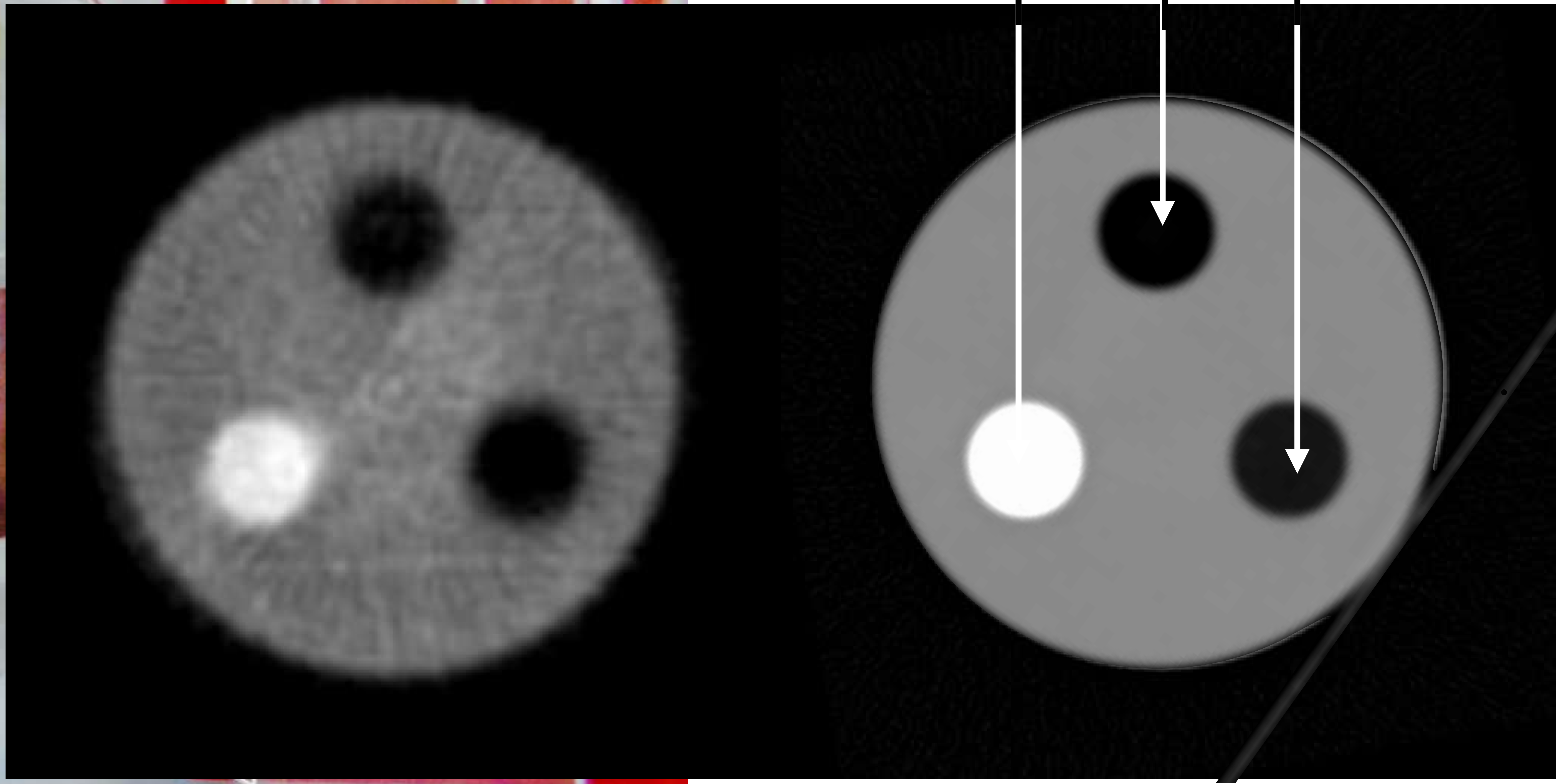
- Stopping-power – most crucial quantity for PBT planning
- For biological materials: stopping-power, scattering-power and attenuating-power can be related to electron density (Kanematsu *et al*., Medical Physics **39**, 1016, 2012)
- Scattering and attenuation power only require trackers – reduced system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



Relative scattering-power pCT

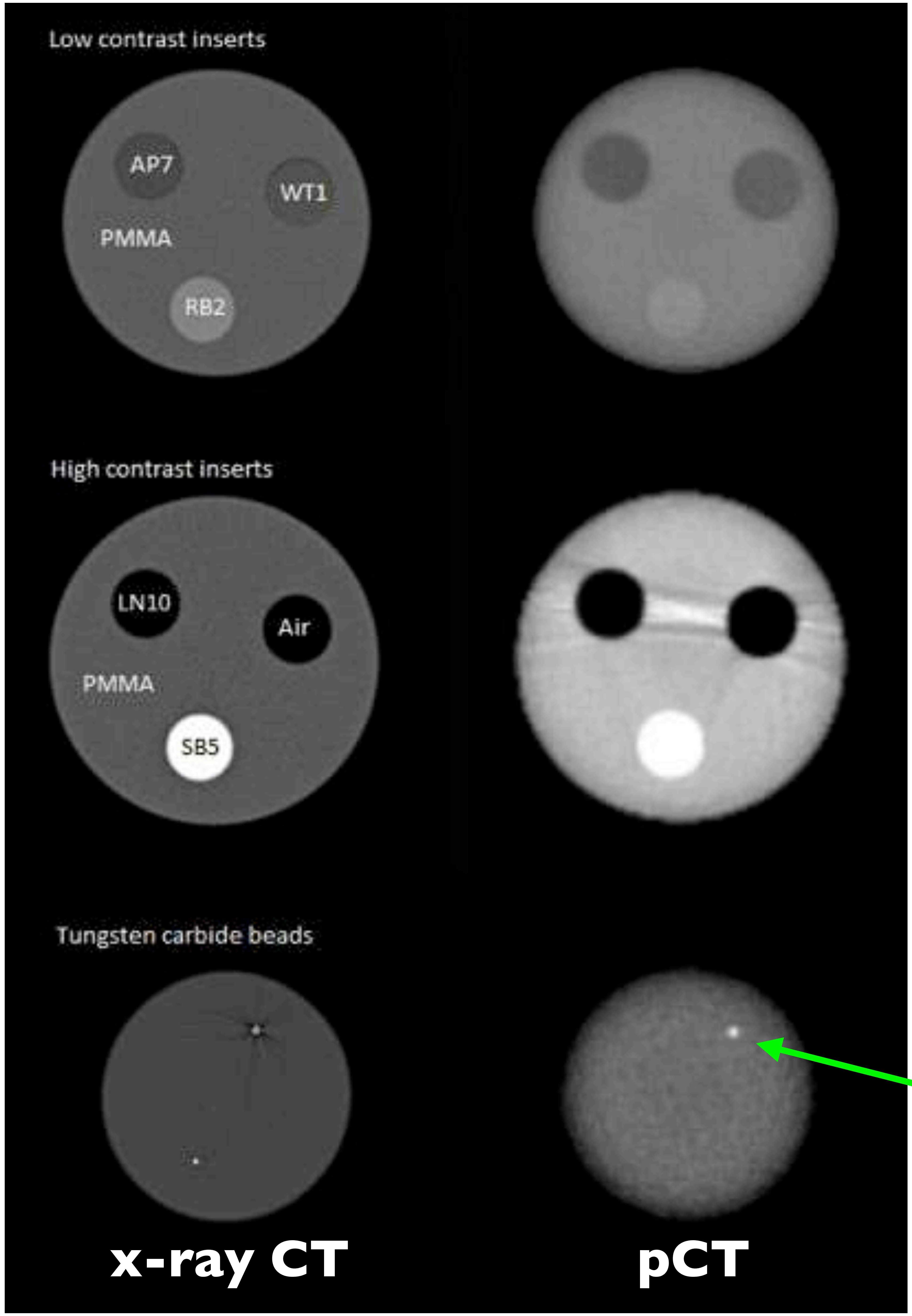
Experimental Result





proton scattering-power CT **x-ray CT**

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

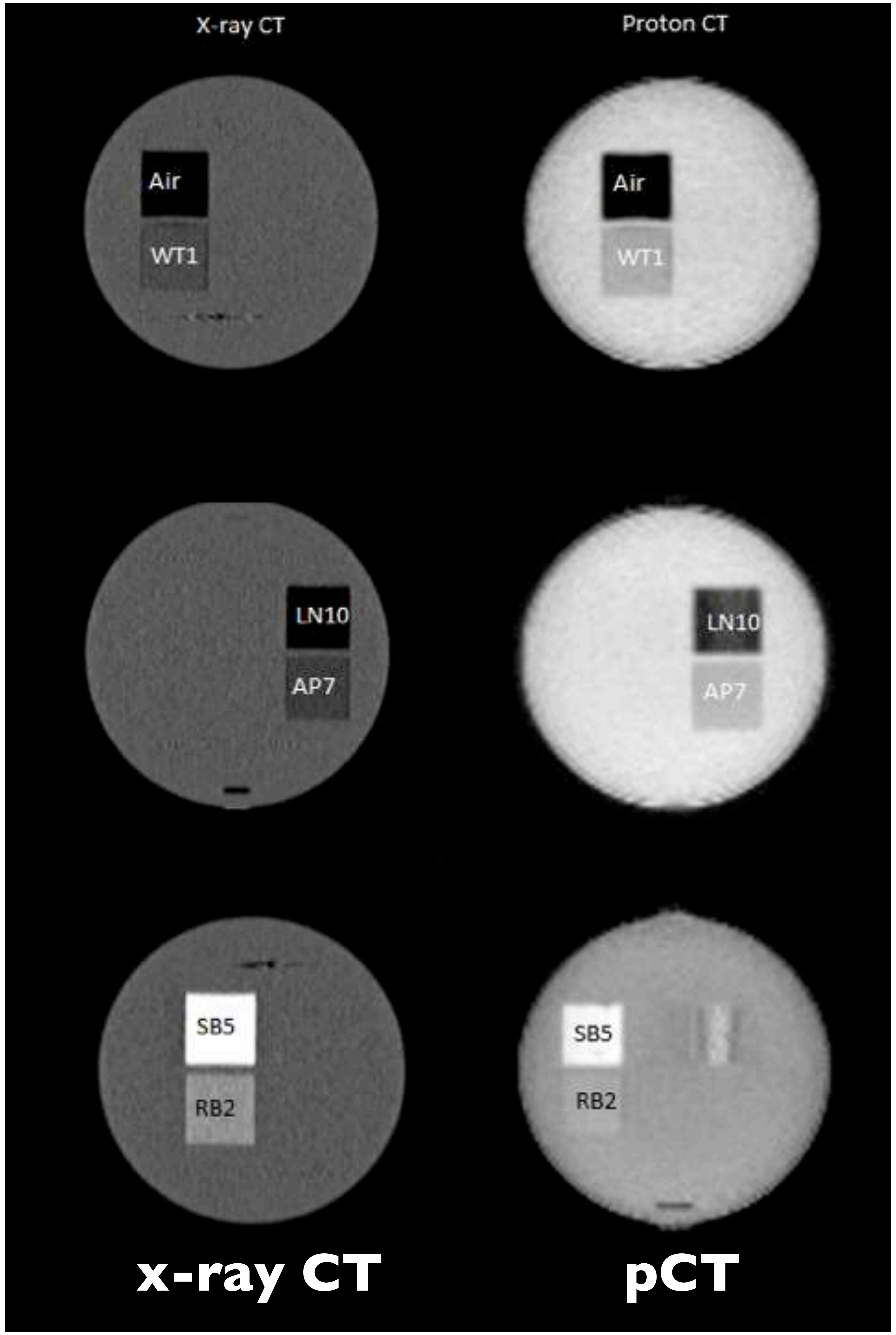
Material	Density [g/cc]	Expected RSP	pCT RSP	Percent error
PMMA	*~1.16*	*1.15*	*1.15*	*0.0*
AP7(adipose)	*0.92*	*0.95*	*0.94*	*-0.7*
WT1(water equivalent)	*1.00*	*1.00*	*0.98*	*-1.6*
RB2 rib/ average	*1.40*	*1.21*	*1.22*	*1.2*
SB5 hard cortical bone	*1.84*	*1.63*	*1.62*	*-0.4*
LN10 *lung*	0.25-0.35	0.25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

Preliminary

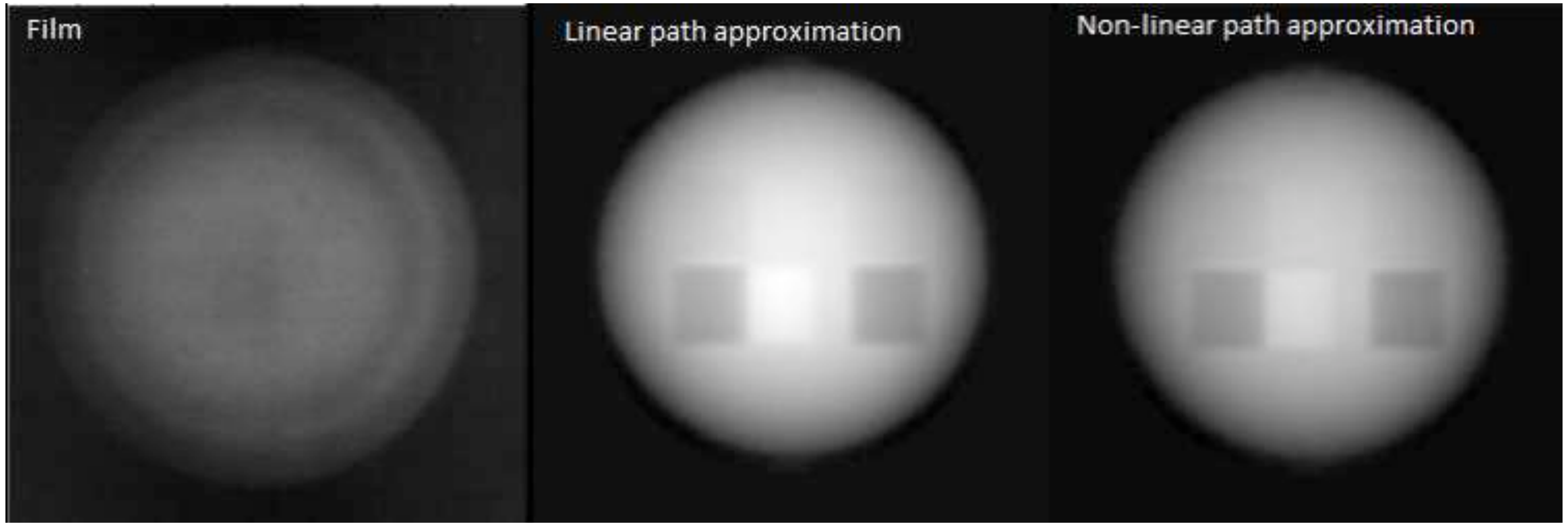
Comparison of known residual stopping power for Leeds Test Objects and as measured using proton CT

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

Proton CT slices of 6-insert phantom



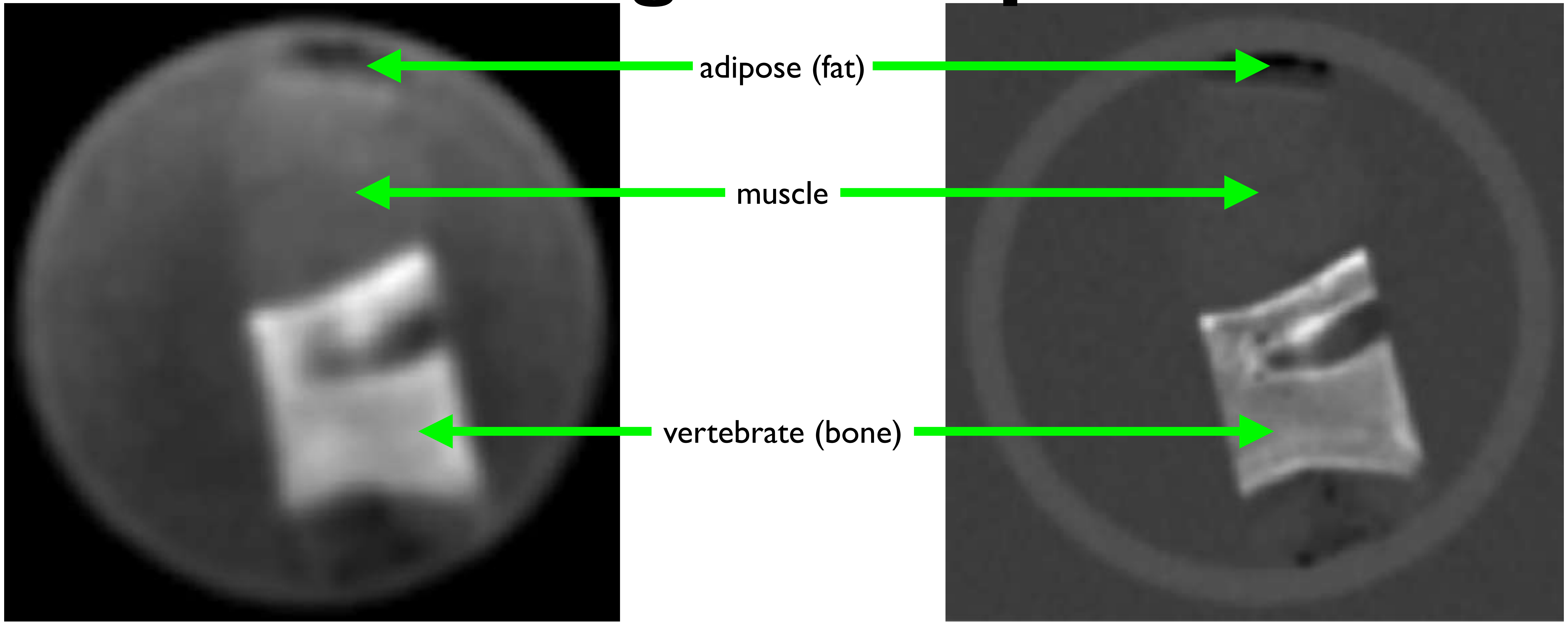
Reconstructed CT image coronal slices of the imaging phantom



Comparison of film radiograph and radiographs from the PRaVDA system

Preliminary

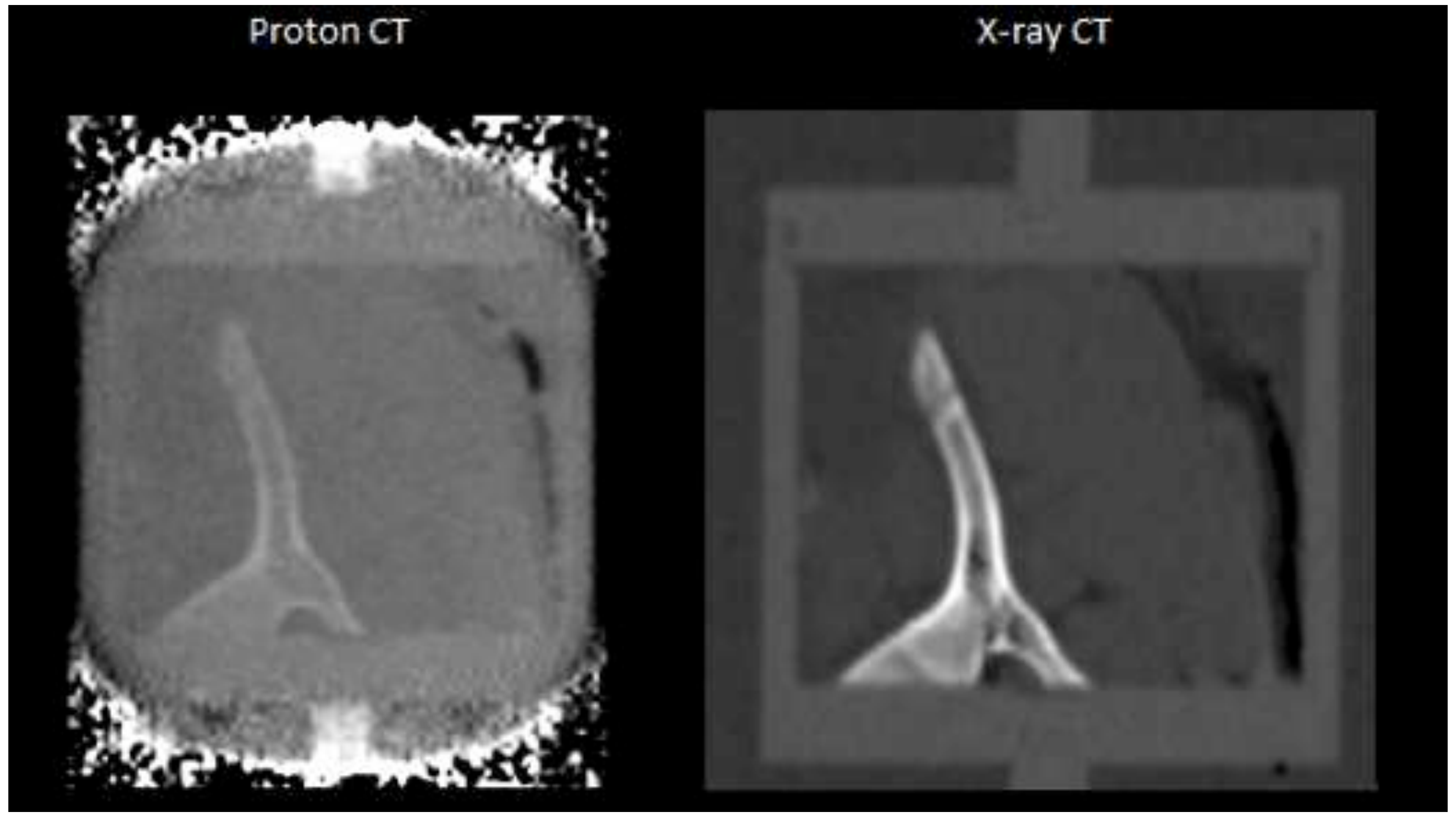
Proton CT biological sample



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

OPTima

Optimising Proton Therapy through Imaging

Funded by EPSRC Engineering and Physical Sciences Research Council

University of Lincoln

University of Birmingham

University of Manchester

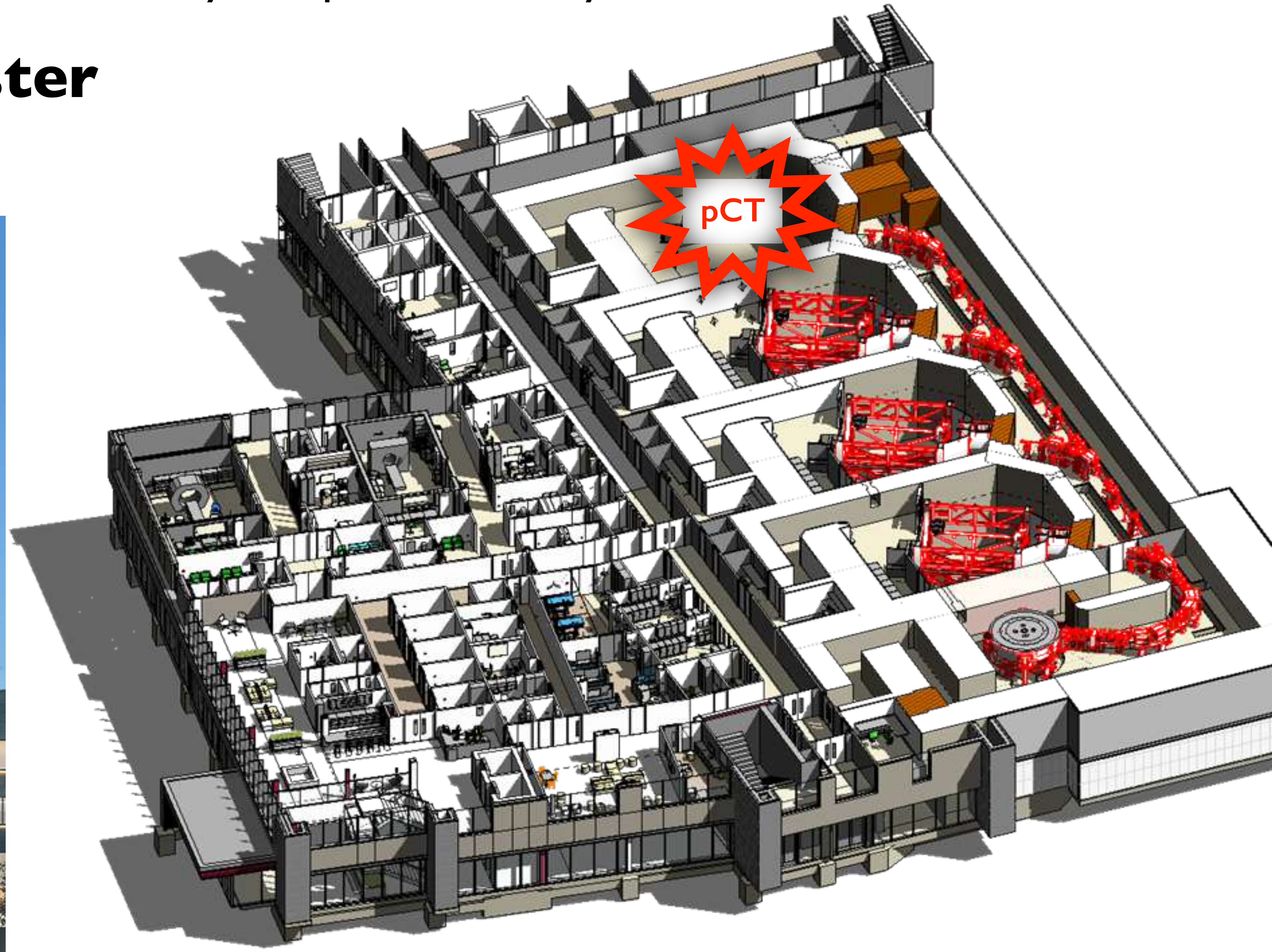
University of Surrey

University Hospital Birmingham NHS Foundation Trust

The Christie NHS Foundation Trust

University Hospital Coventry and Warwickshire NHS Trust

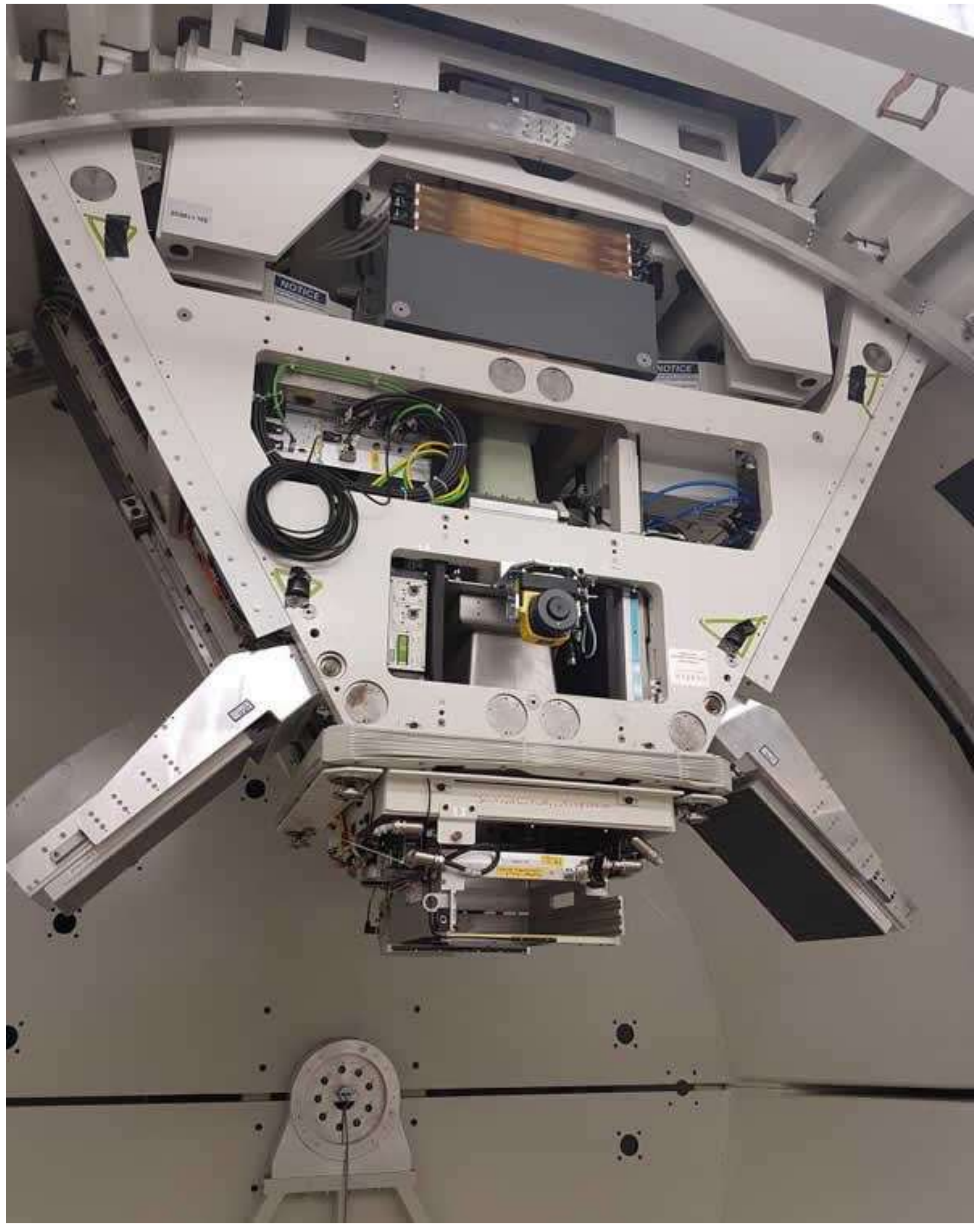
Next generation system – NHS Christie PBT Centre, Manchester



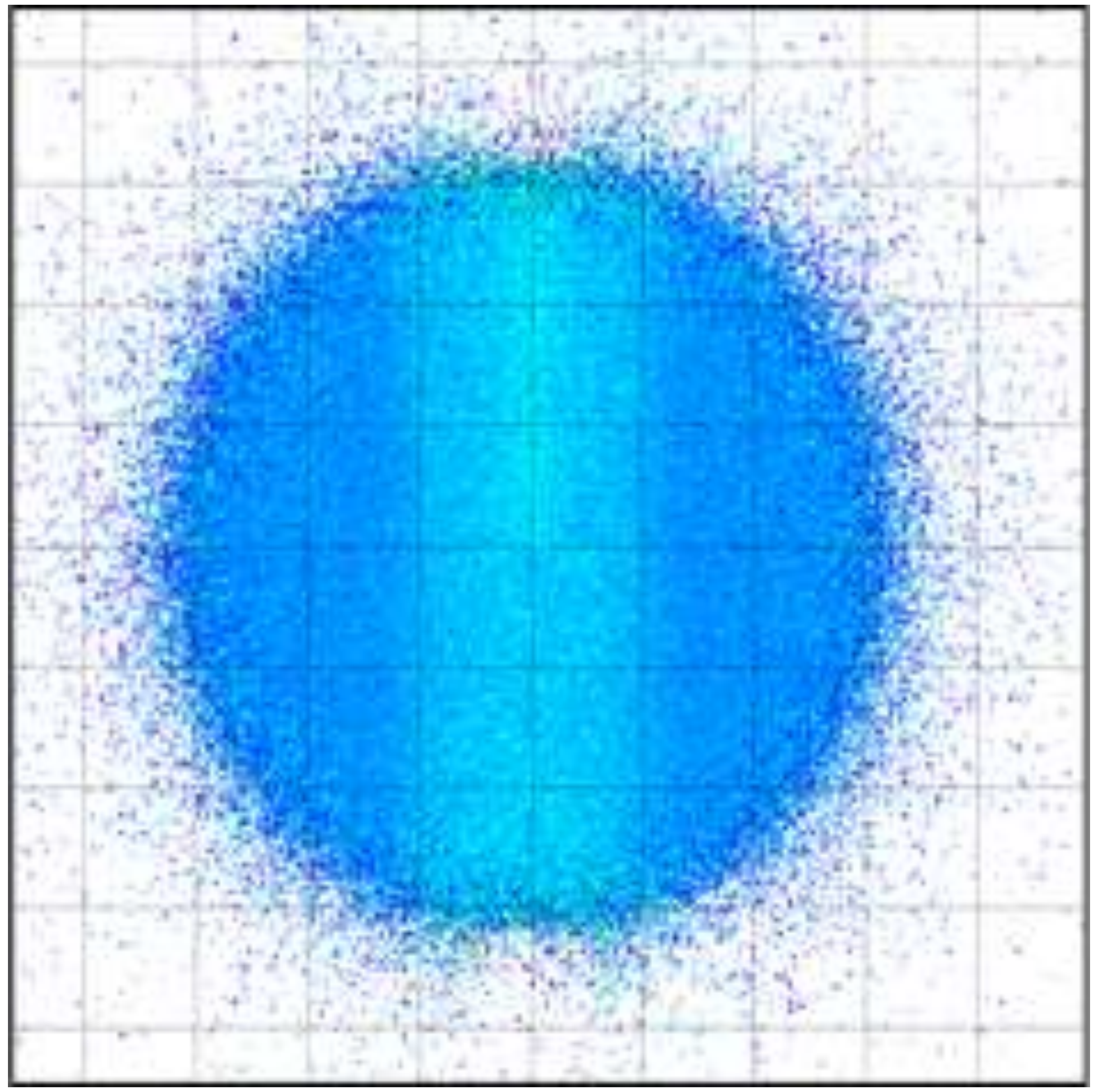
Research Room, Christie PBT Centre

- "Fourth Treatment Room"
- Horizontal scanning nozzle - no gantry
- Full independent control and beam access (out of hours!)

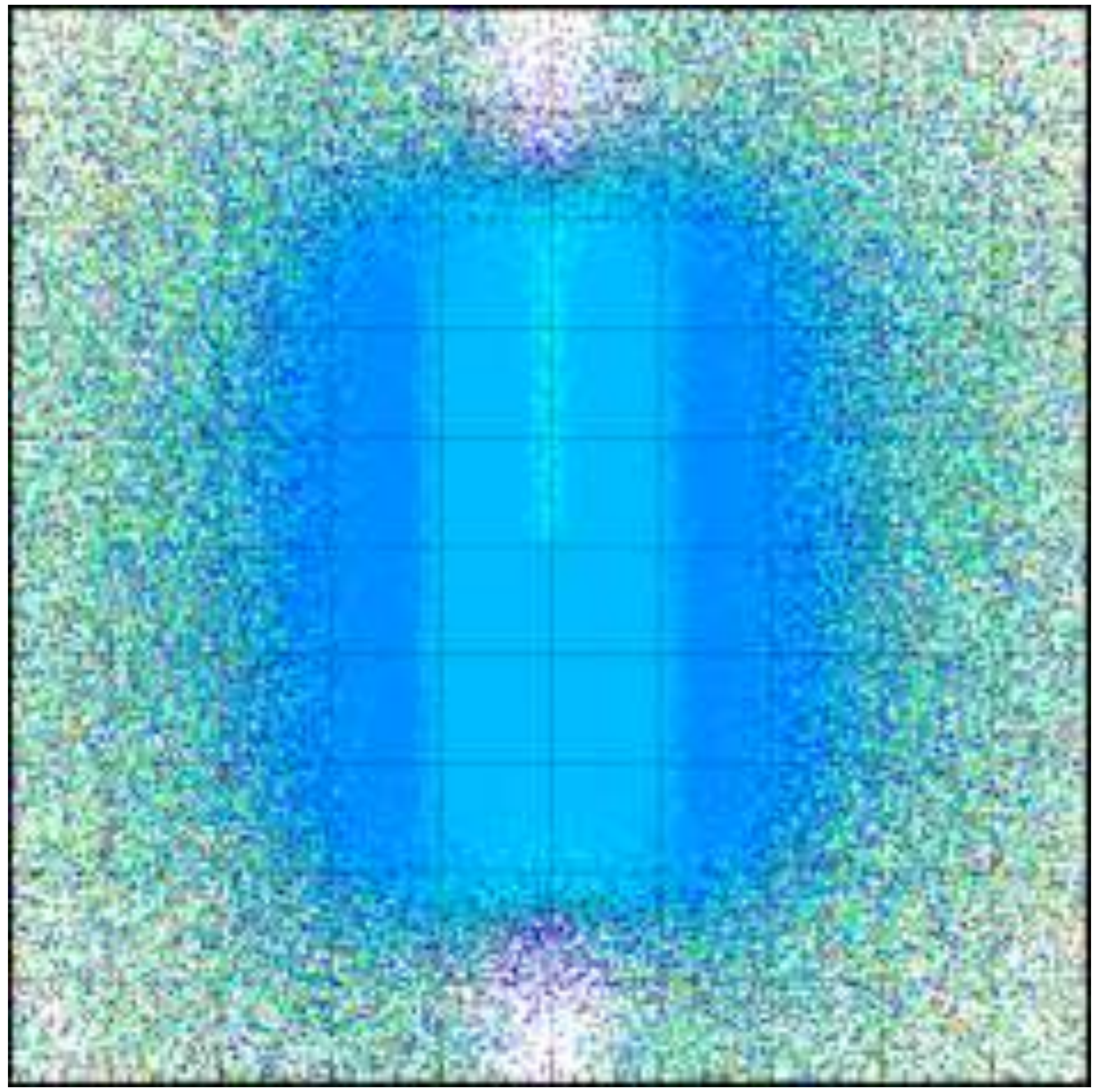
- Design for pencil beams
- Design for gantry use
- Design to match clinical needs and treatment workflows
- Design for manufacture



Advantages of Scanning



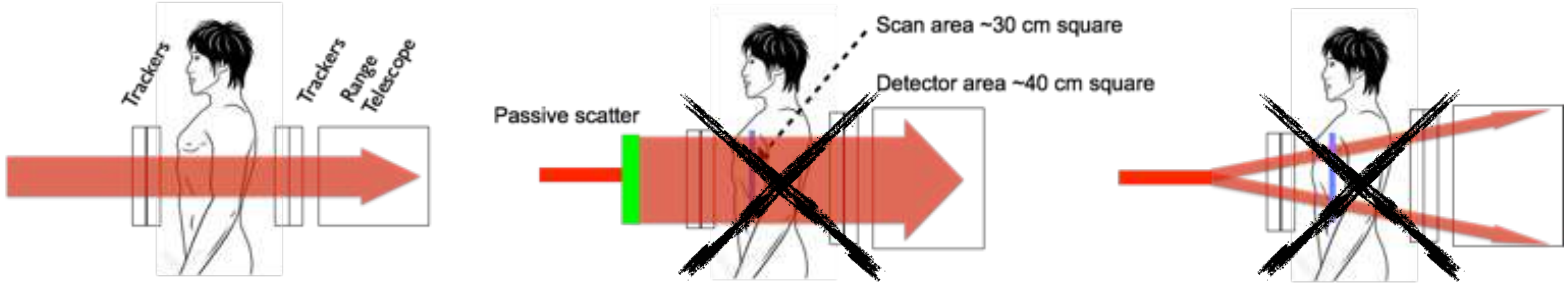
Broad beam
(scattering)



Pencil beam
(scanning)

Reduction in large-angle scattered protons and secondary radiation

Need to think differently



A. Conventional passive scattering

B. Broaden pencil beam

C. Raster scan large detector

More beam scatter
More secondary radiation

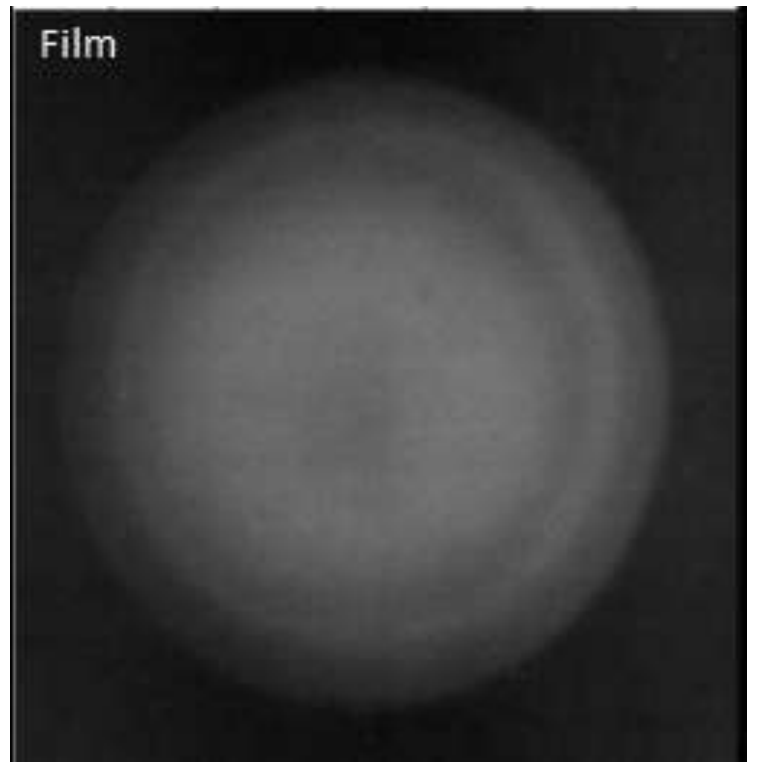
Big expensive sensors

Need smaller agile sensors: lower cost, faster readout, reduced processing power
Close integration with cyclotron/delivery system

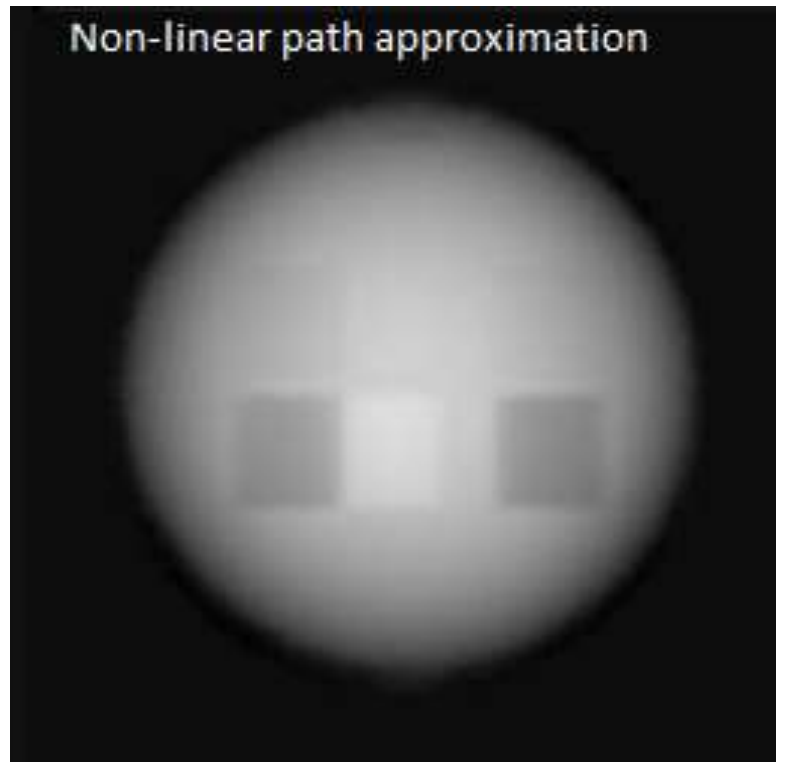
Imaging dose

Less than conventional x-ray CT

Film

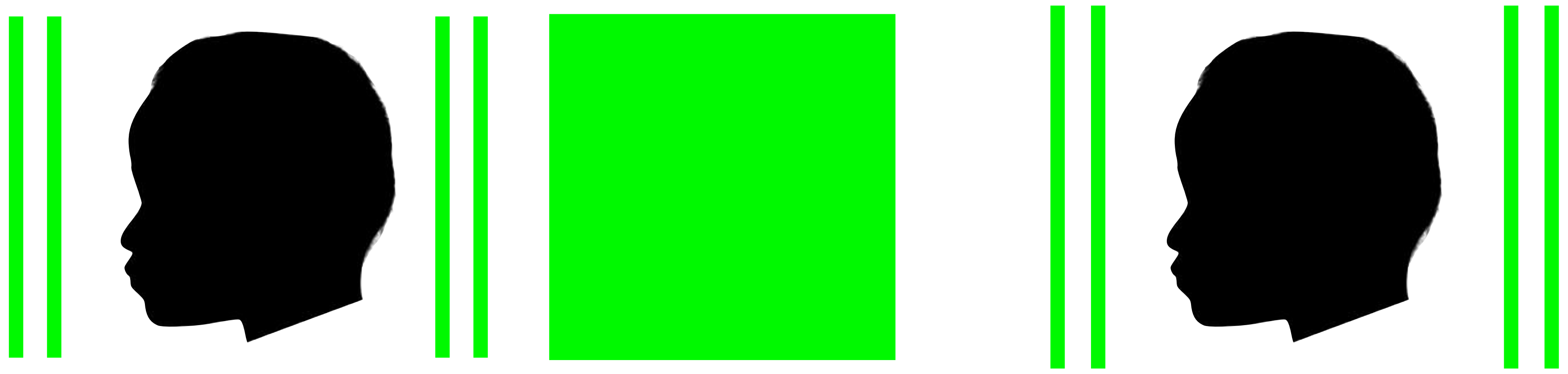


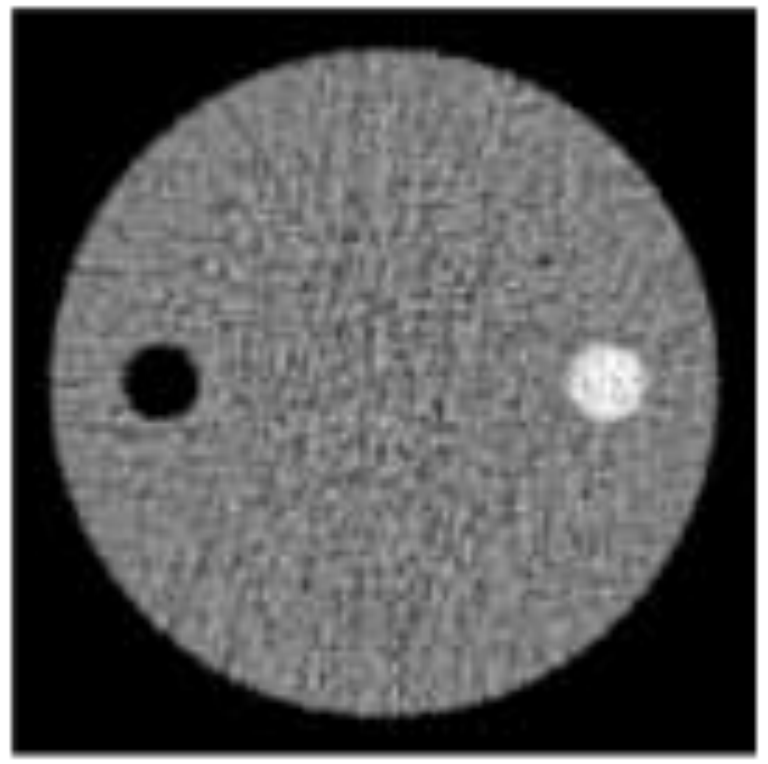
PRaVDA



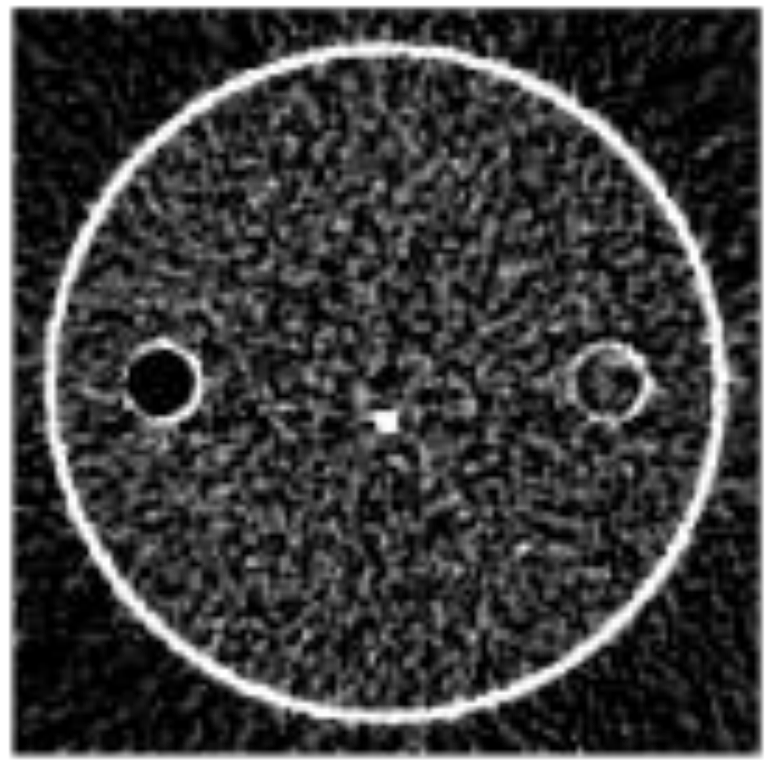
Low-dose radiographs

Overall dose ~0.5 Gy





relative stopping-power



relative straggling-power

Simulated

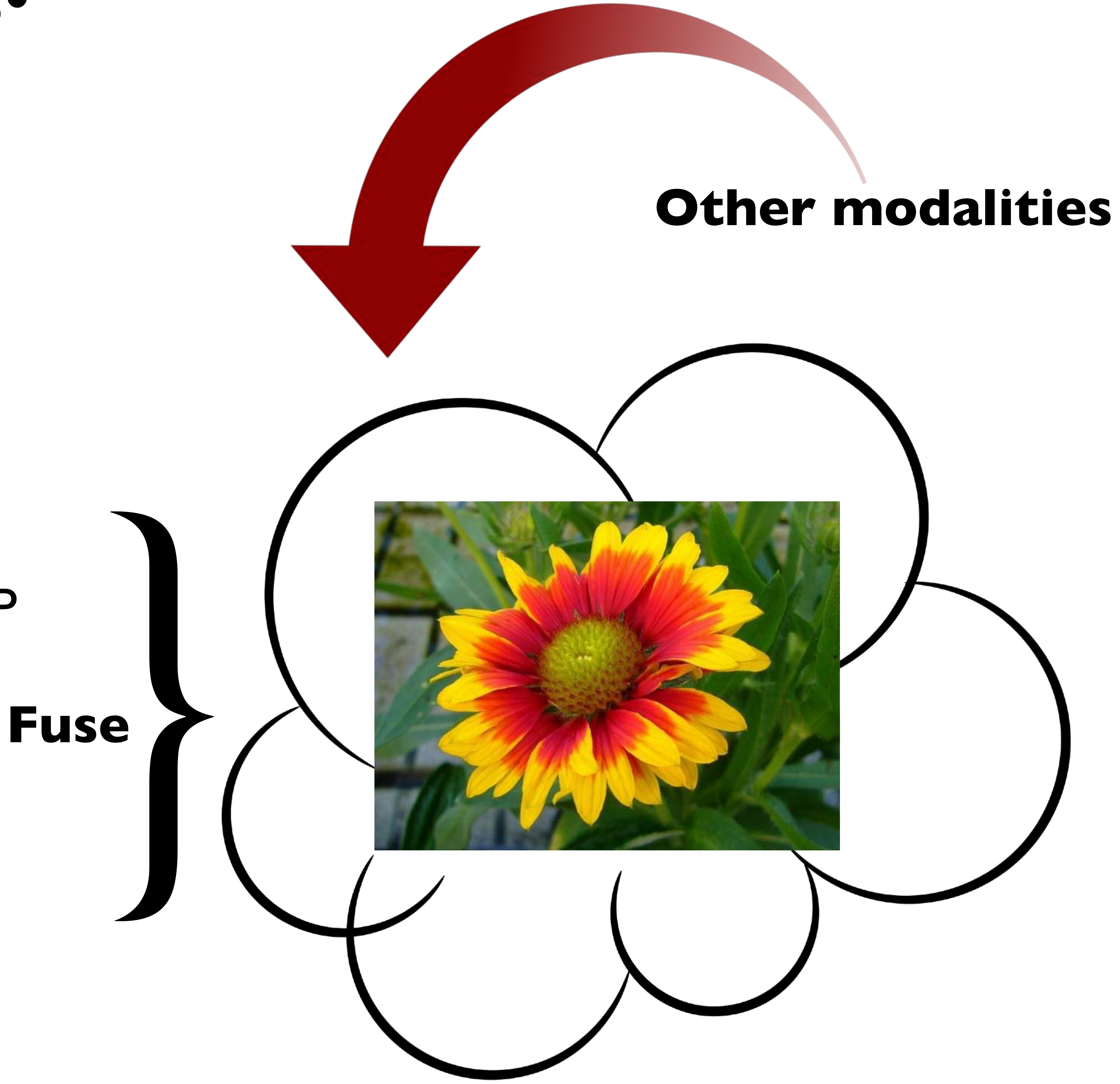
Very low dose – 80 microGy (phantom centre)
Paediatric Application

What are we really doing?

Ideal
High spatial resolution
Correct RSP, etc

X-ray CT
High spatial resolution
Calibration uncertainties in RSP

Stopping Power pCT
Low spatial resolution
Correct RSP



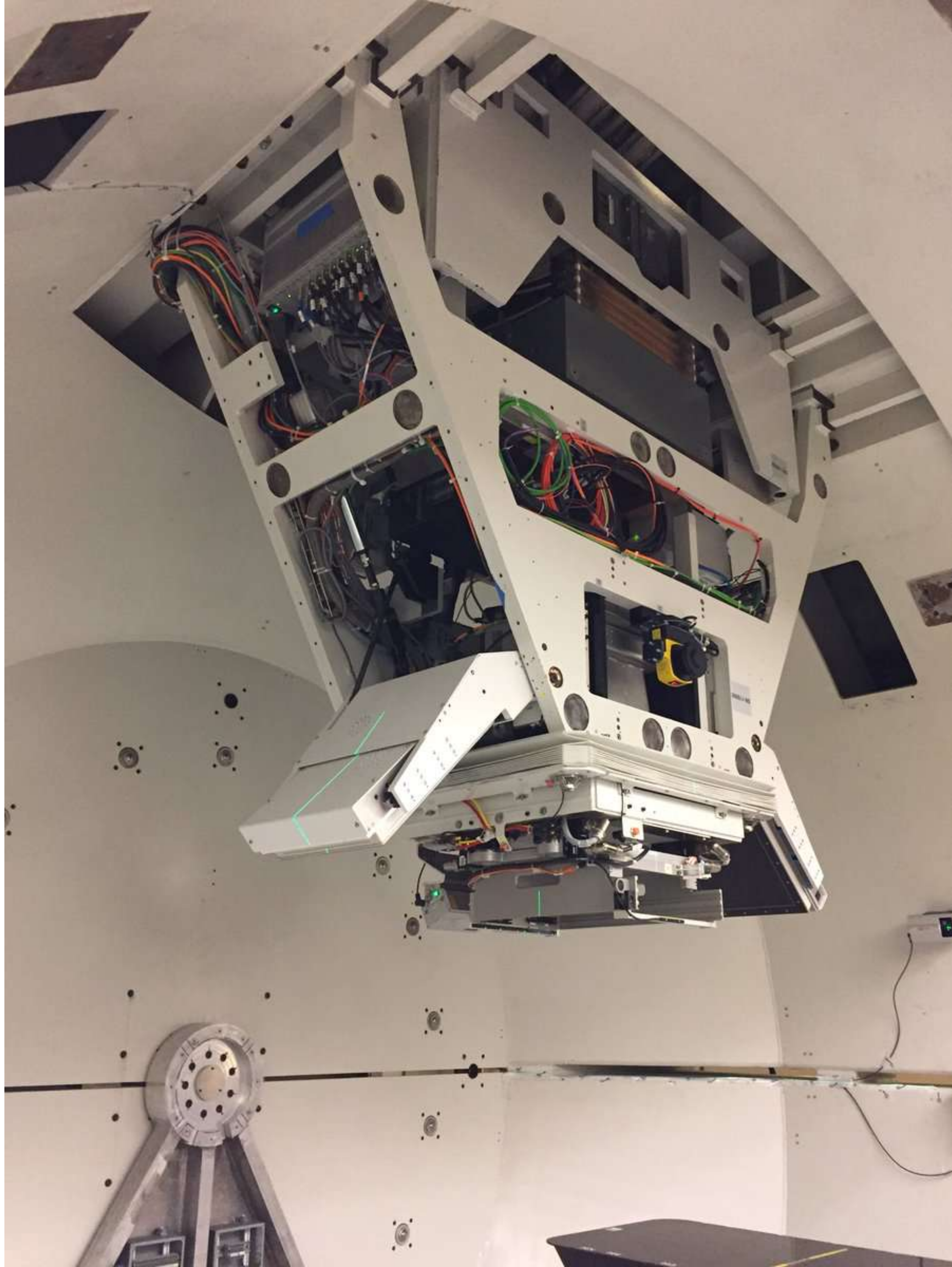
Scenarios

Replace cone-beam CT for session CT

- Image quality >= Cone-beam CT
- Reconstruction time comparable
- Acquire full pCT
- Confirm/modify plan

Augment cone-beam CT for session CT

- Image spatial quality < Cone-beam CT
- Aquire selected proton projections
- Calibrate/confirm/modify plan



What we need to do

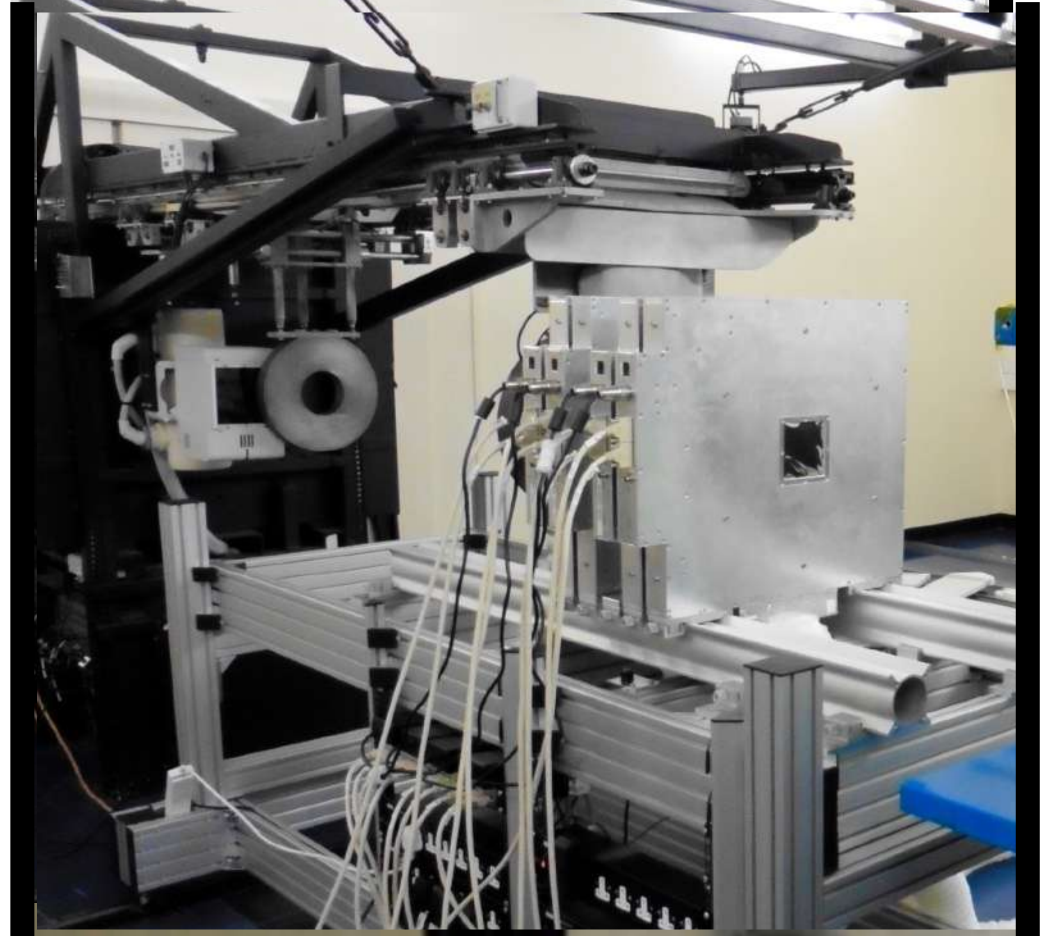
- Calibration of the planning pCT for proton beam therapy
- Calibration of phantoms, etc. for PBT - international standing
- Compare pCT with other indirect methods of reducing certainty (e.g. DECT)
- Explore potential for proton (and other charged particle) imaging
- Fusion with other modalities (e.g. X-ray, MRI, prompt-gammas)
- Develop Adaptive Optimum Treatments
- Translate, commercialise, **benefit patients**

PRaVDA

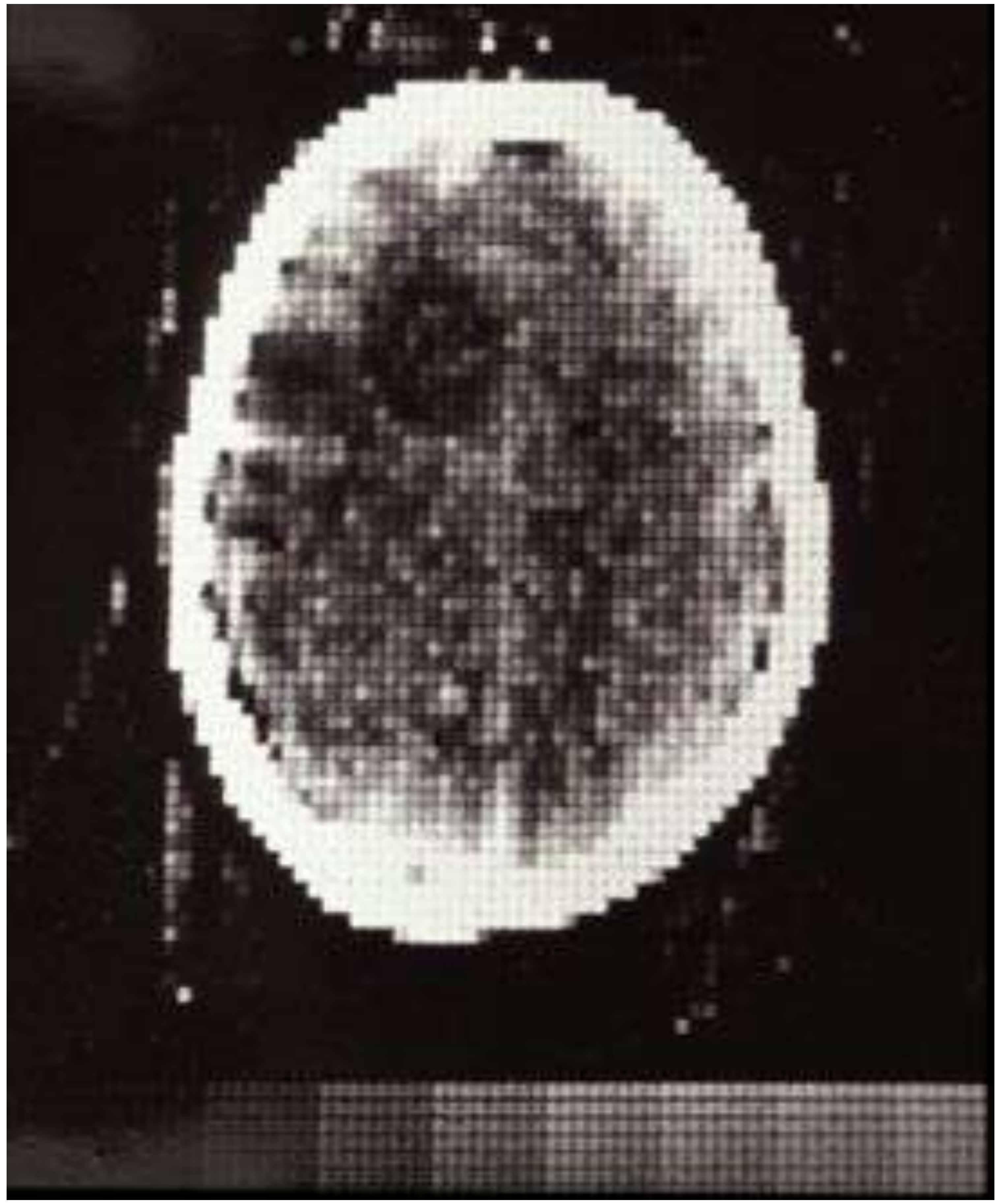
OPTima
Optimising Proton Therapy through Imaging

Thank you

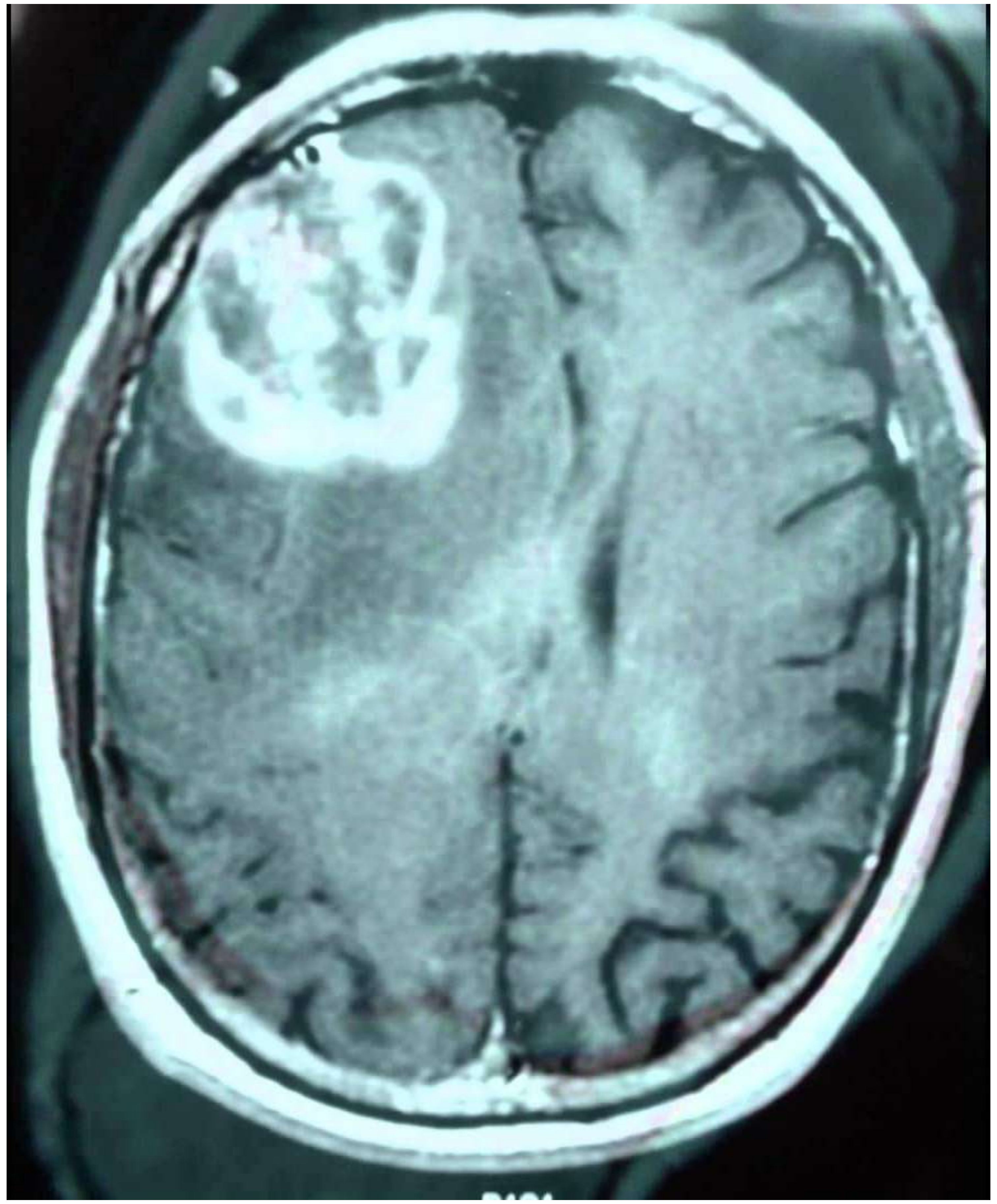
nallinson@lincoln.ac.uk



And Remember ...



October 1971
Atkinson Morley Hospital, London



Today

Any Questions?