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Design and Implementation of a Freely Moving Small Animal Imaging System

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Current Limitations of Small Animal SPECT

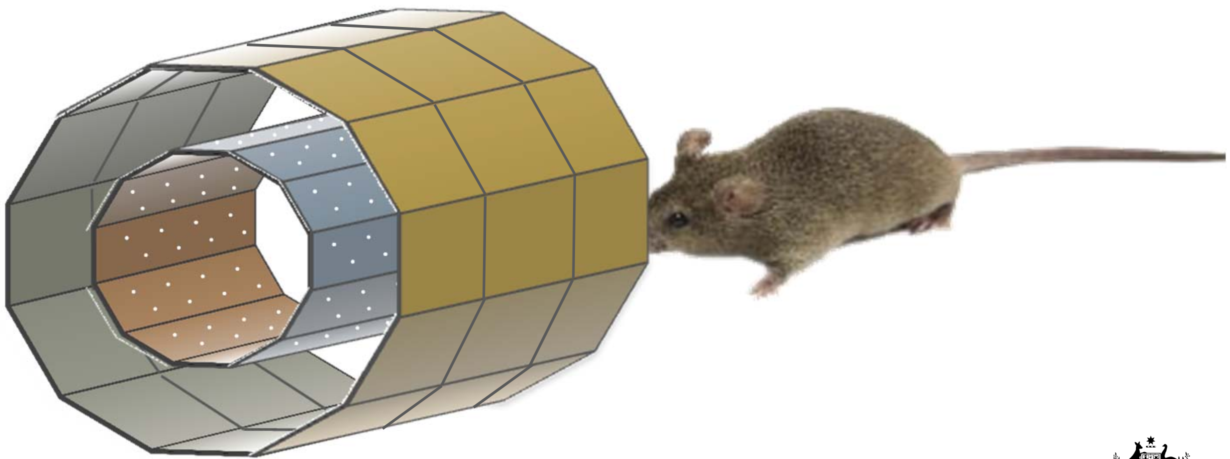
- Animal must be motionless during scan which requires **anaesthesia or restraint**

- Limits on the observation of the slow kinetics of larger molecules are due to:
  - Limited duration of anaesthesia to a few hours
  - Animal requires several hours to recover from anaesthesia

- Recording of the kinetics of the labelled molecule is only possible during a small fraction of its biological time course with limited follow up imaging times

Our Solution

- To develop an imaging system (Burrow-SPECT) capable of **pseudo-continuously** imaging the biodistribution of ^{125}I labelled macromolecules in awake, freely moving mice over **several hours or days**
  - Half life of ^{125}I = 59.38 days
  - Suited for long duration pharmacokinetic studies



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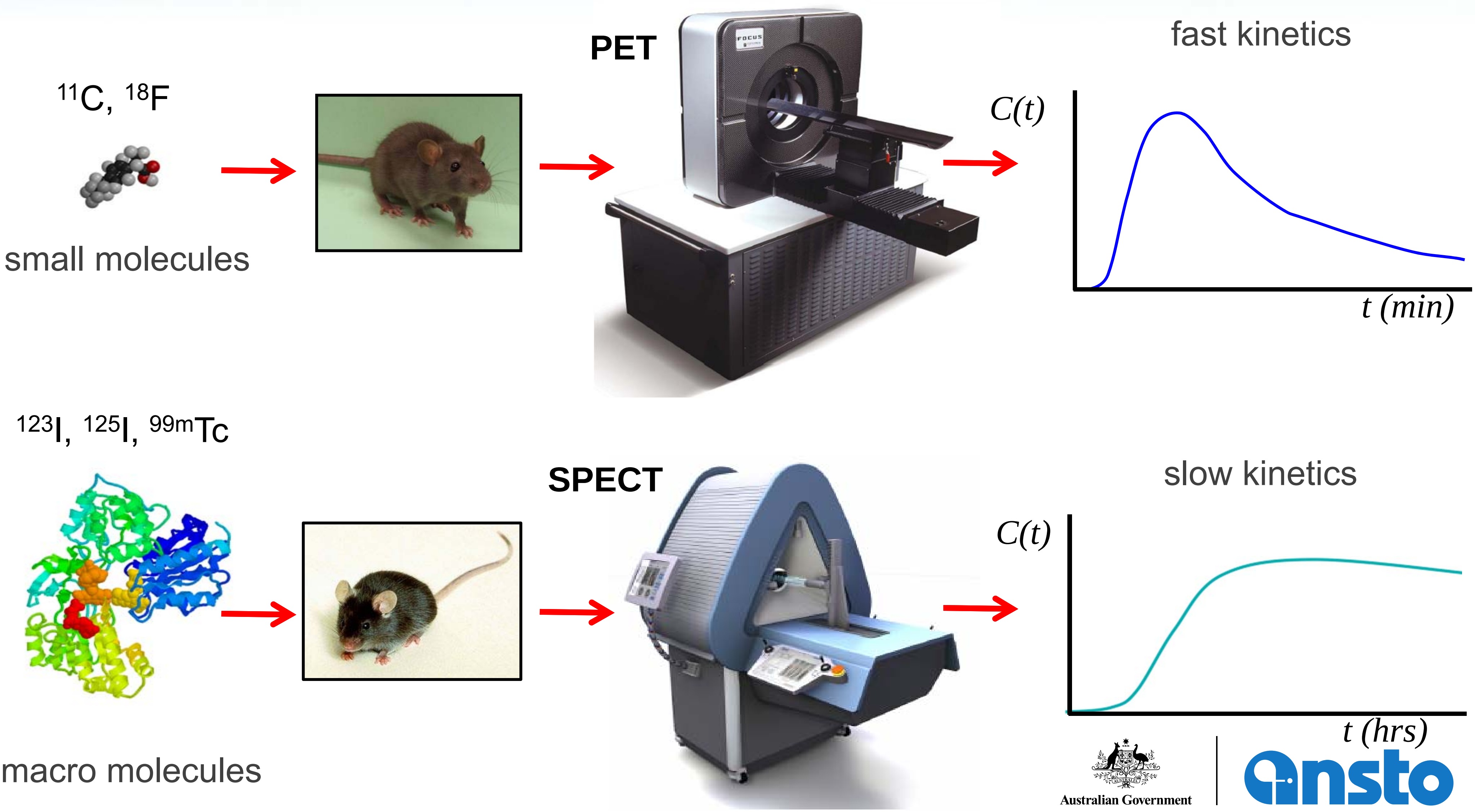
Preclinical Imaging with PET and SPECT



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Burrow-SPECT Design Considerations

- Optimised for ^{125}I (25-35 keV X-rays)
- Field of view ≈ 5 cm
- Spatial resolution 1-2 mm while maintaining high sensitivity
- Stationary detectors and collimators
- Integrated motion tracking and correction
- Detector frame rates of 30-120 fps for integration with motion capture

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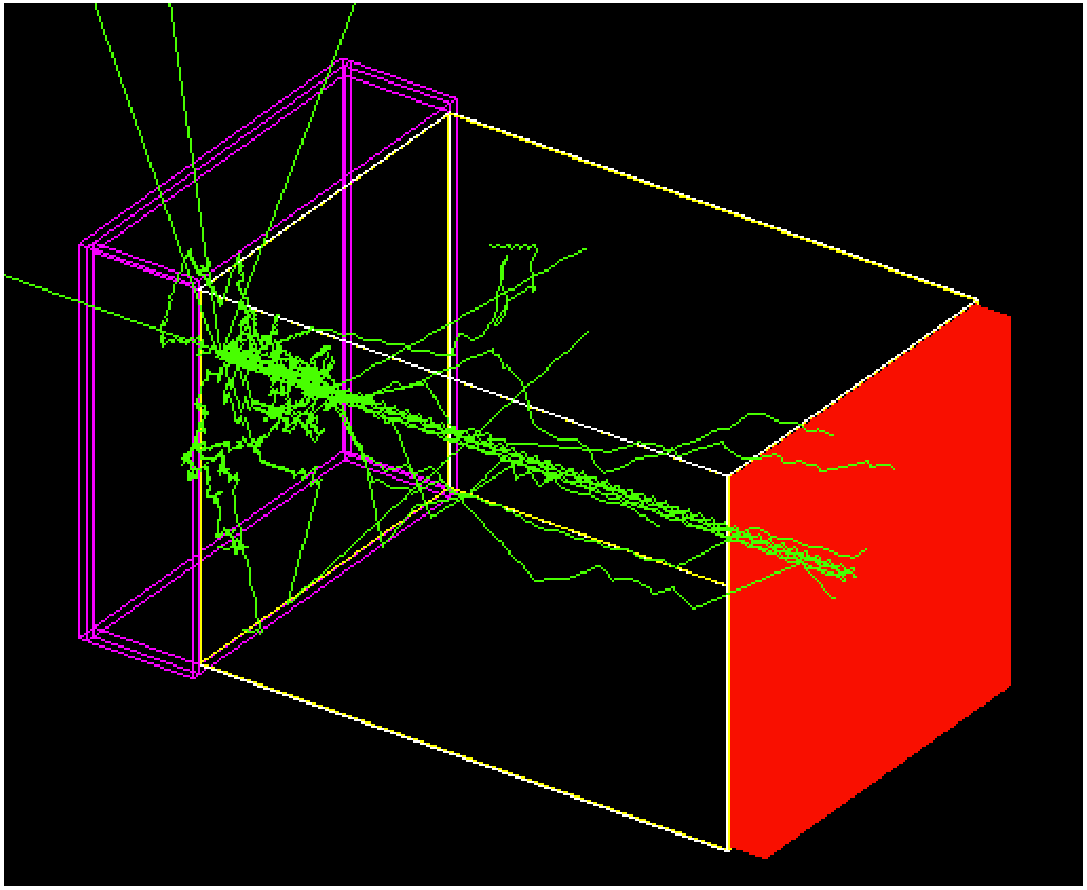
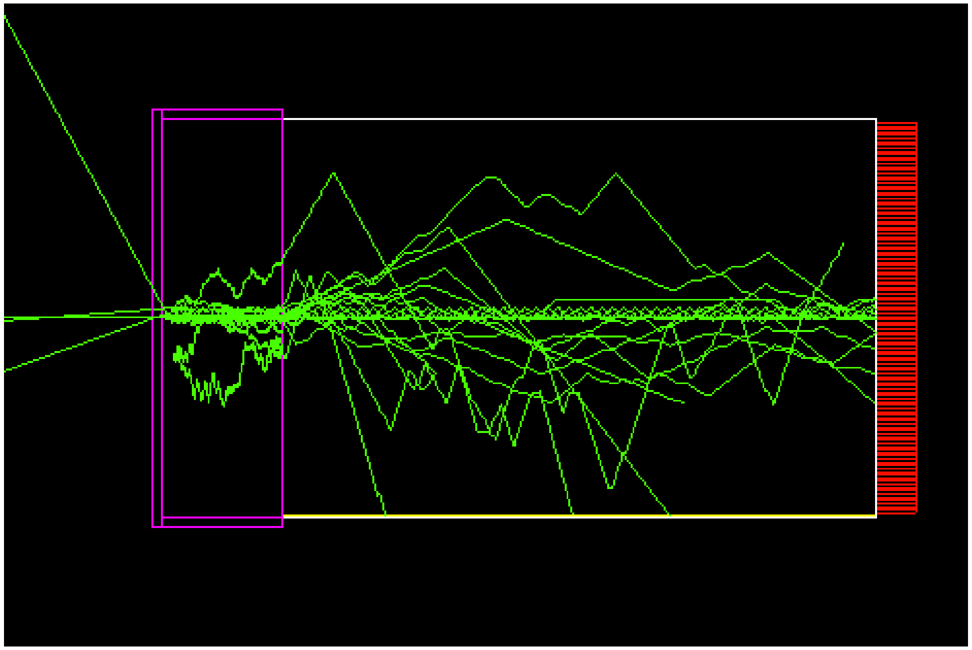
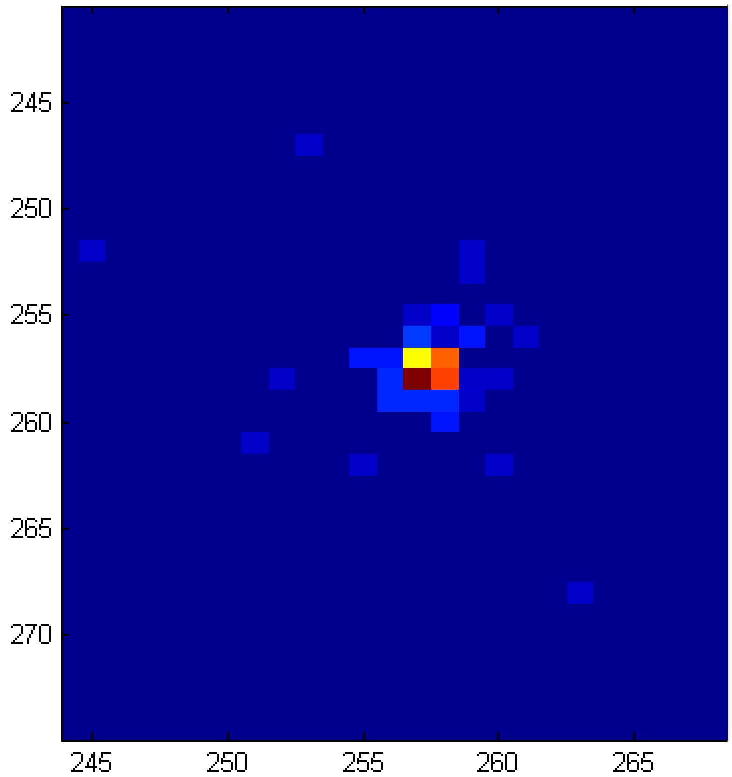
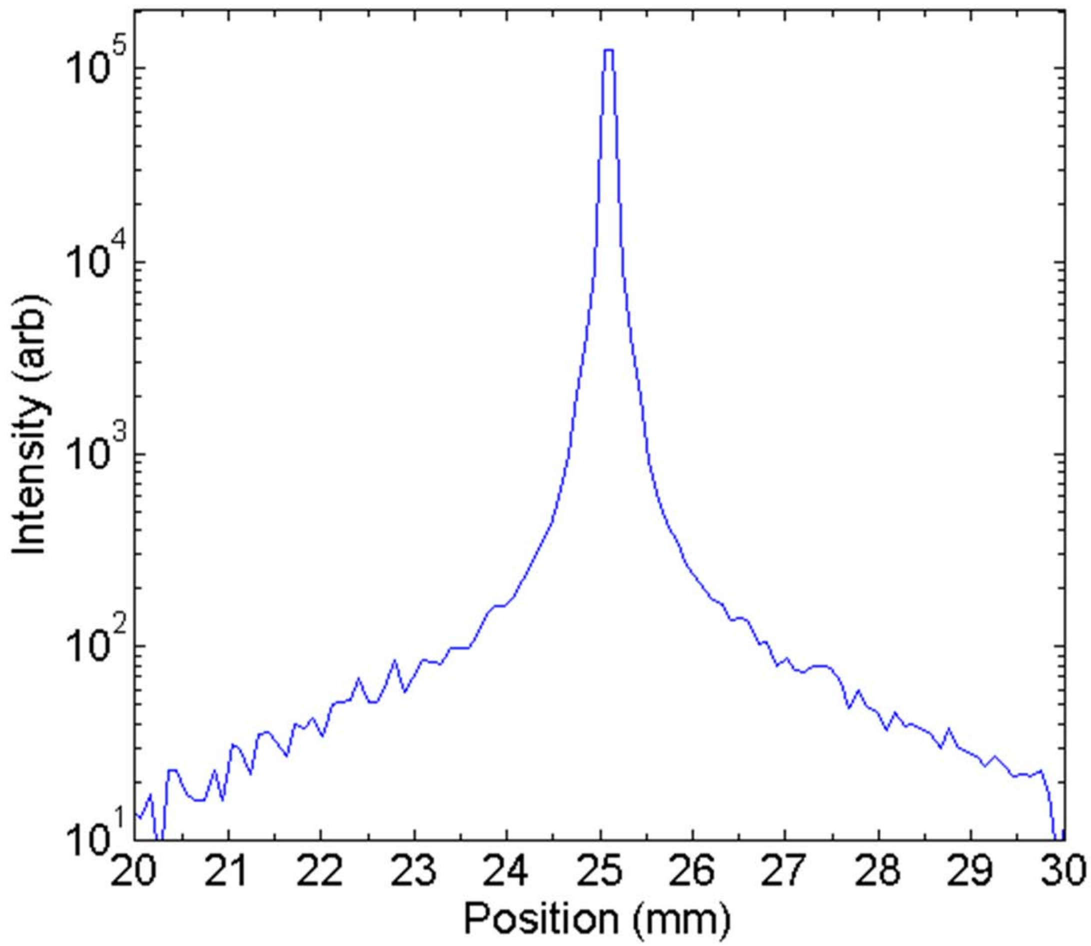
GEANT4 Simulation





GEANT4 Simulation





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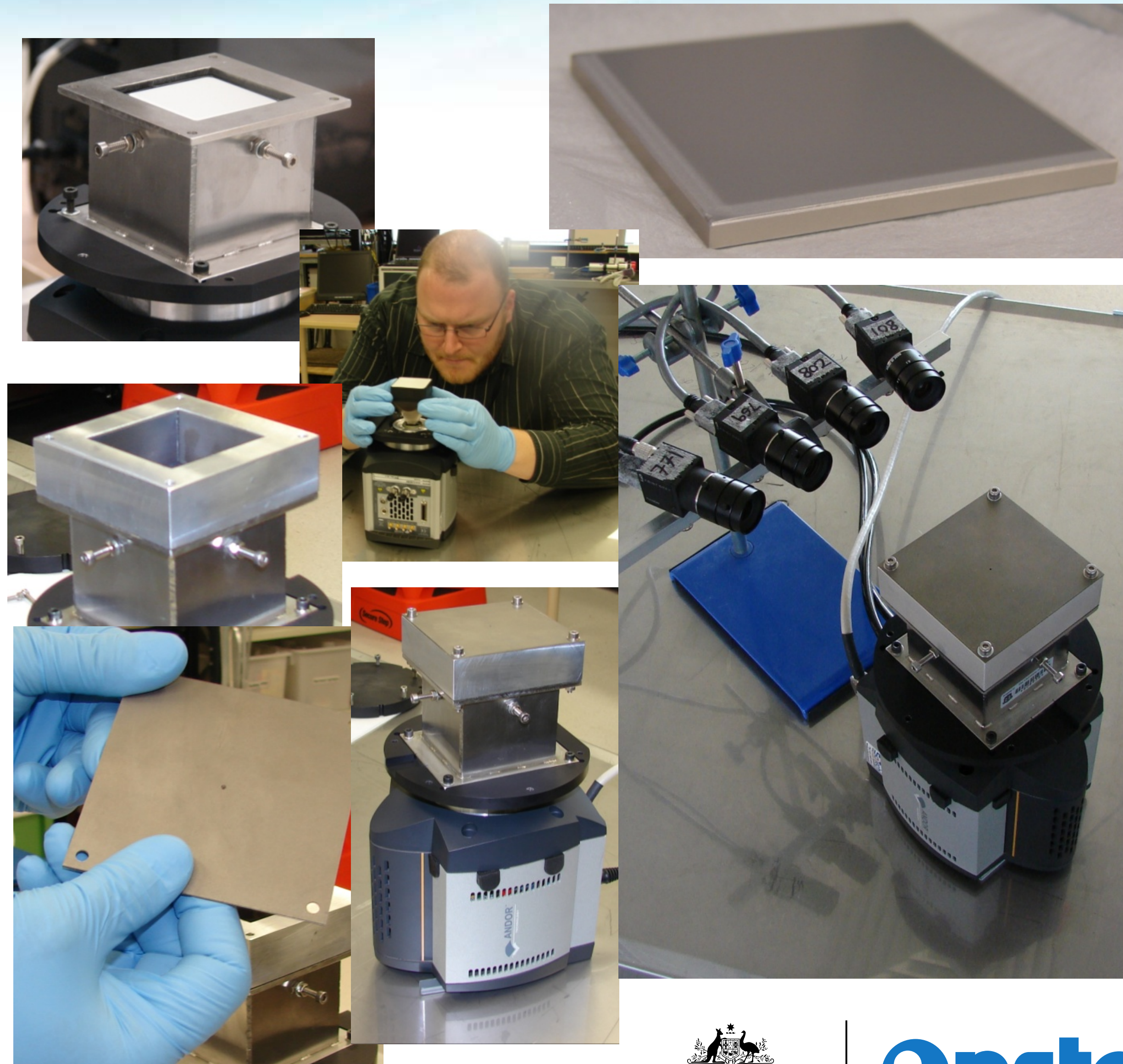
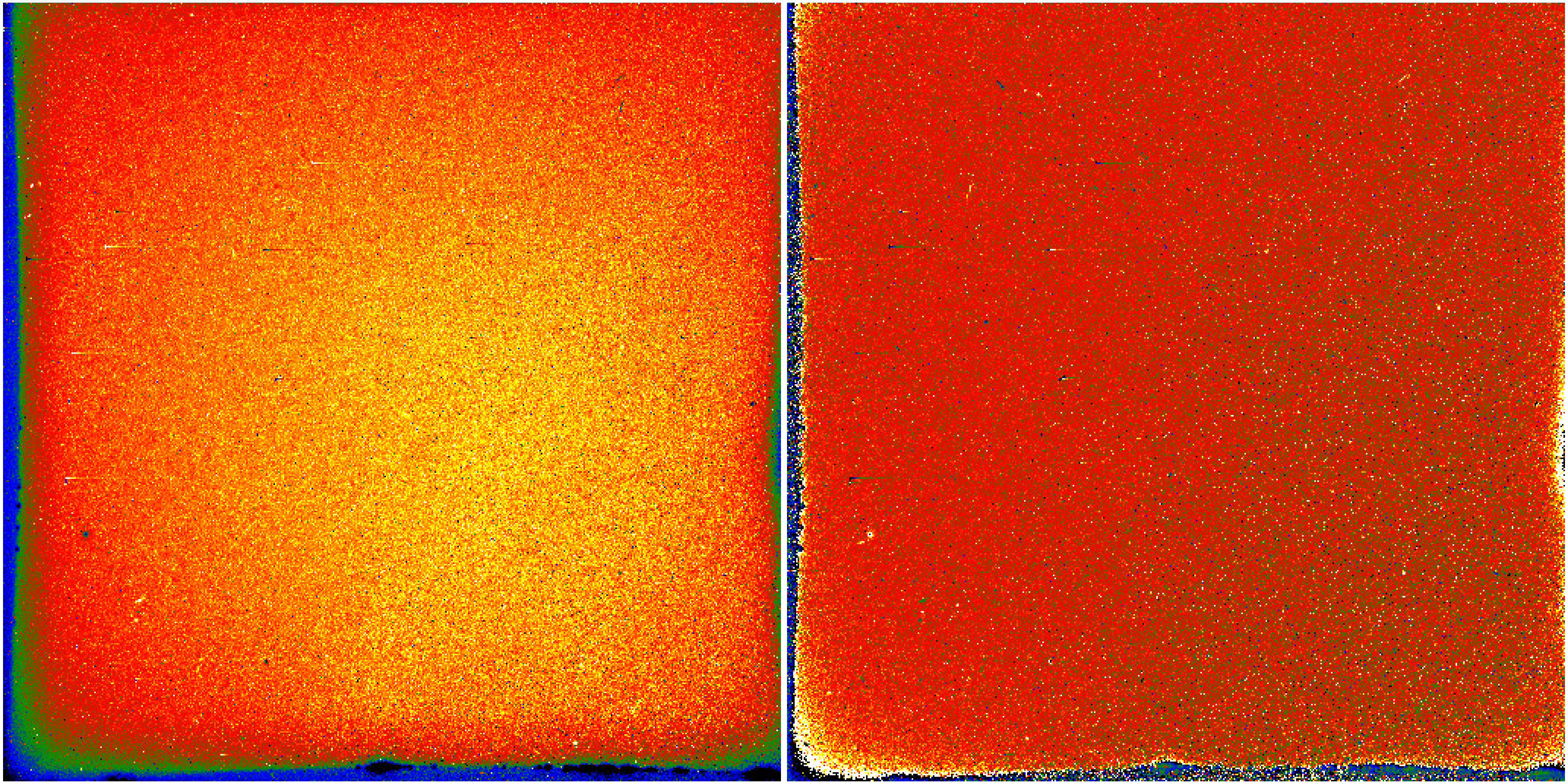
System Construction

- Andor DF897 electron multiplying CCD (EMCCD) system
  - 512 x 512 pixel rear illuminated E2V CCD97 sensor
  - peltier cooling with water or air heatsink
- Hamamatsu micro-columnar CsI(Tl)
  - Fibre optic plate (J6677)
  - 50 x 50 mm
- Schott fibre optic taper
  - 4:1 Fibre optic taper
- Stainless steel housing
  - Light tight
  - tungsten shielding
  - rigid carbon fibre entry window
  - interchangeable collimator
- Optical coupling
  - low viscosity fused silica matching fluid (refractive index 1.46 @ 550 nm, viscosity 19 cSt @ 25 ° C)
  - Bicron BC630 optical grease (refractive index 1.46 @ 550 nm)



Characterisation



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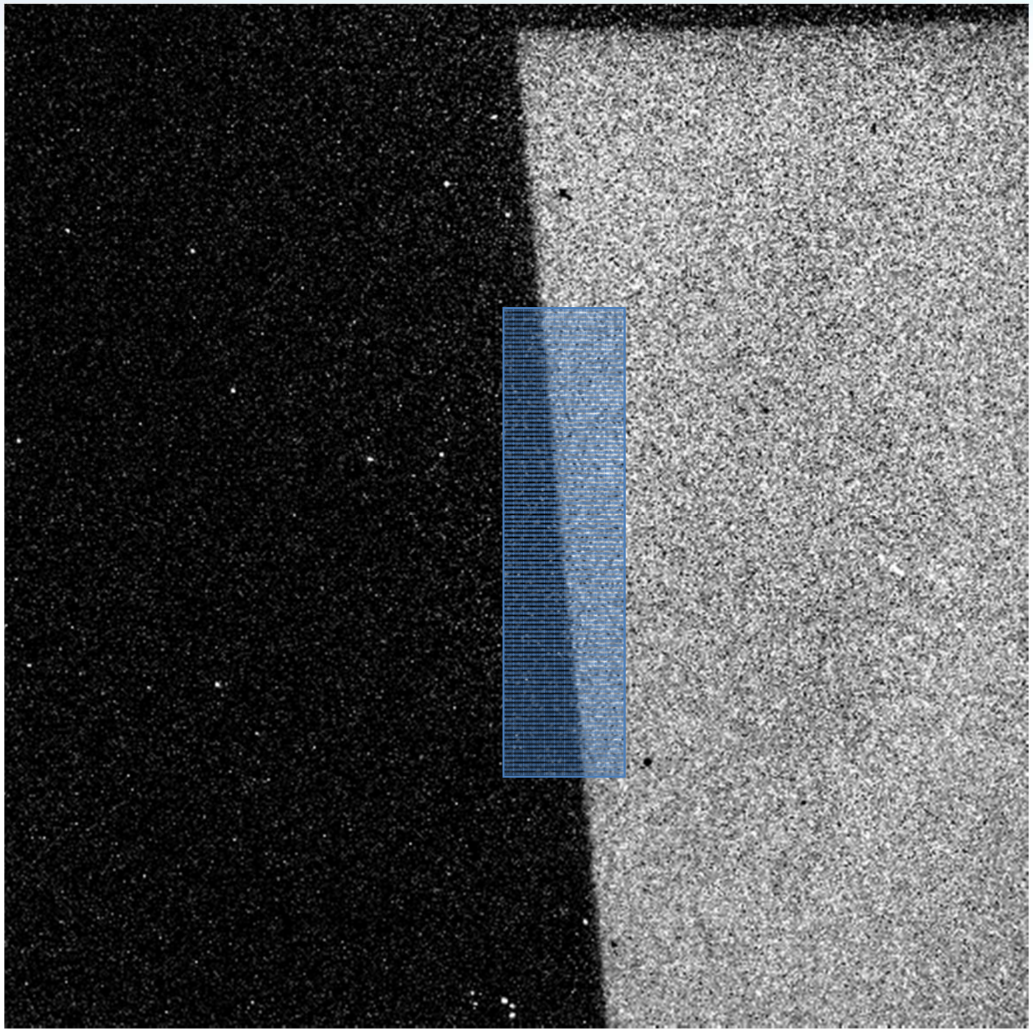
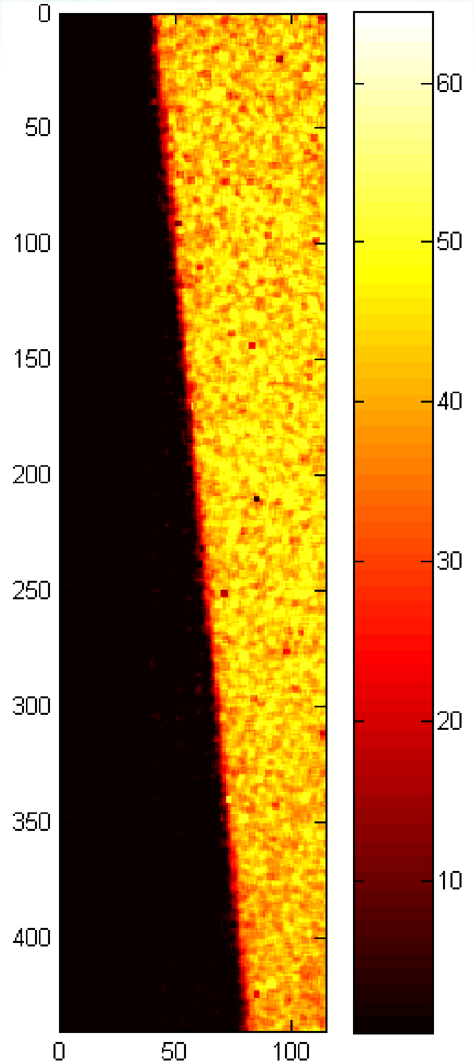
Characterisation





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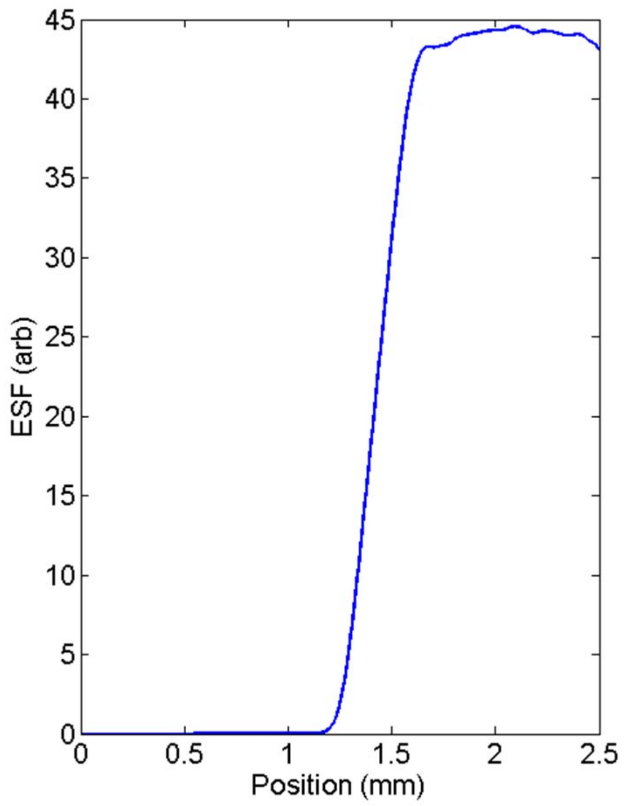
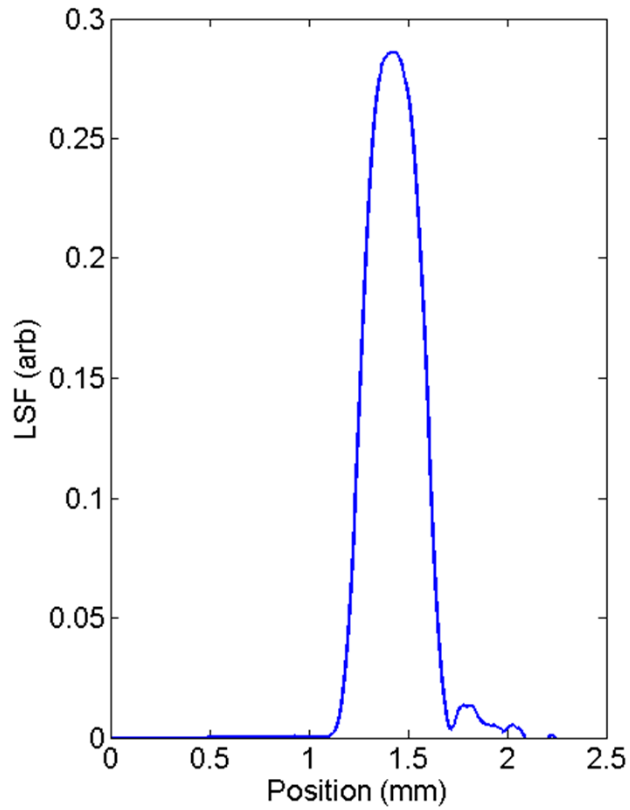
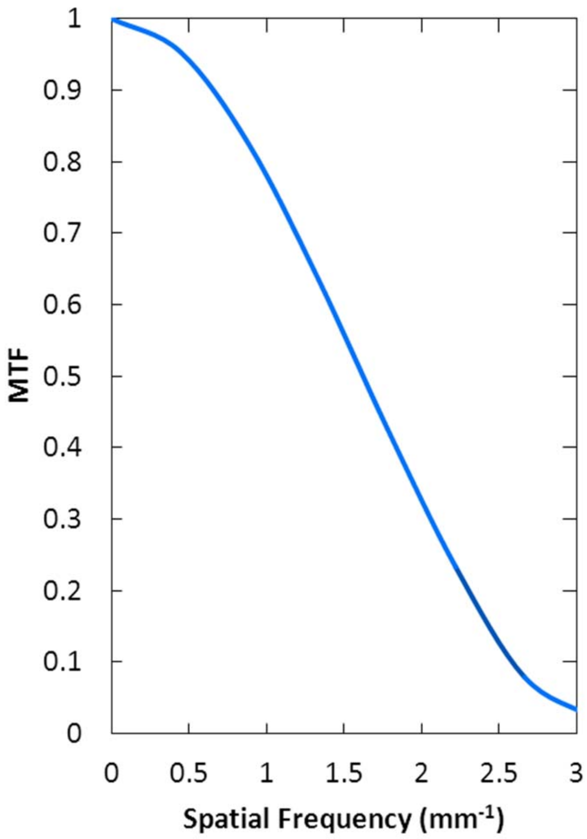
Characterisation





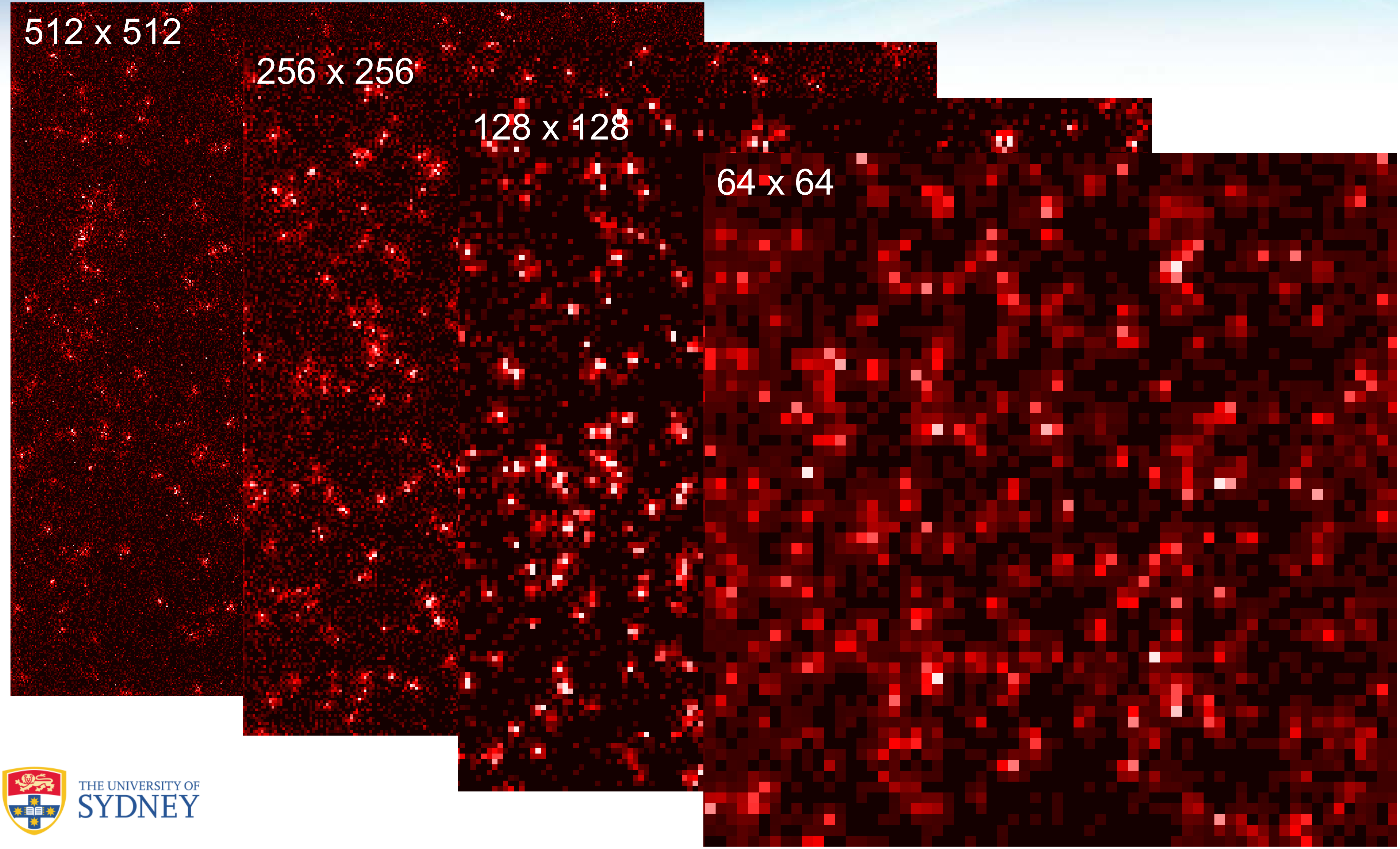


0.29 mm 10-90% edge rise width

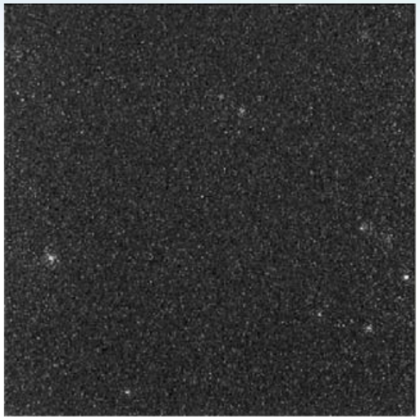
0.34 mm at Full Width Half Maximum

0.38 mm at 10%

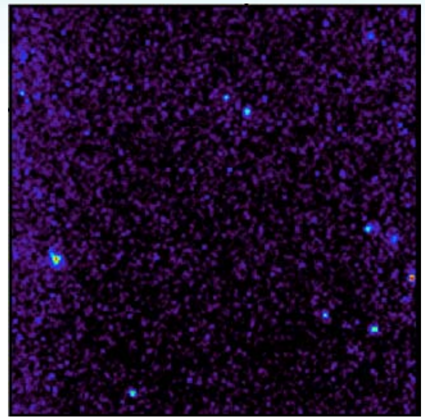
Characterisation



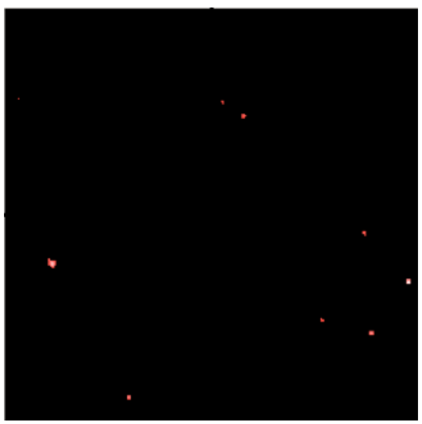
Clustering Method



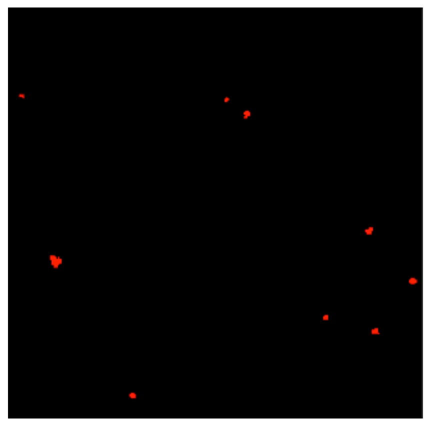
Raw Image



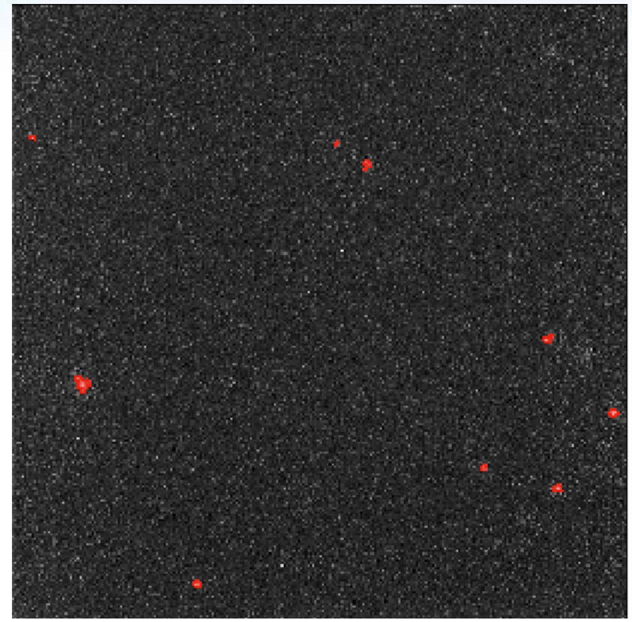
Apply Filter



Search for Seeds above $threshold_1$



Region Grow pixels above $threshold_2$



Accept clusters with n pixels

Sum cluster for incident photon energy

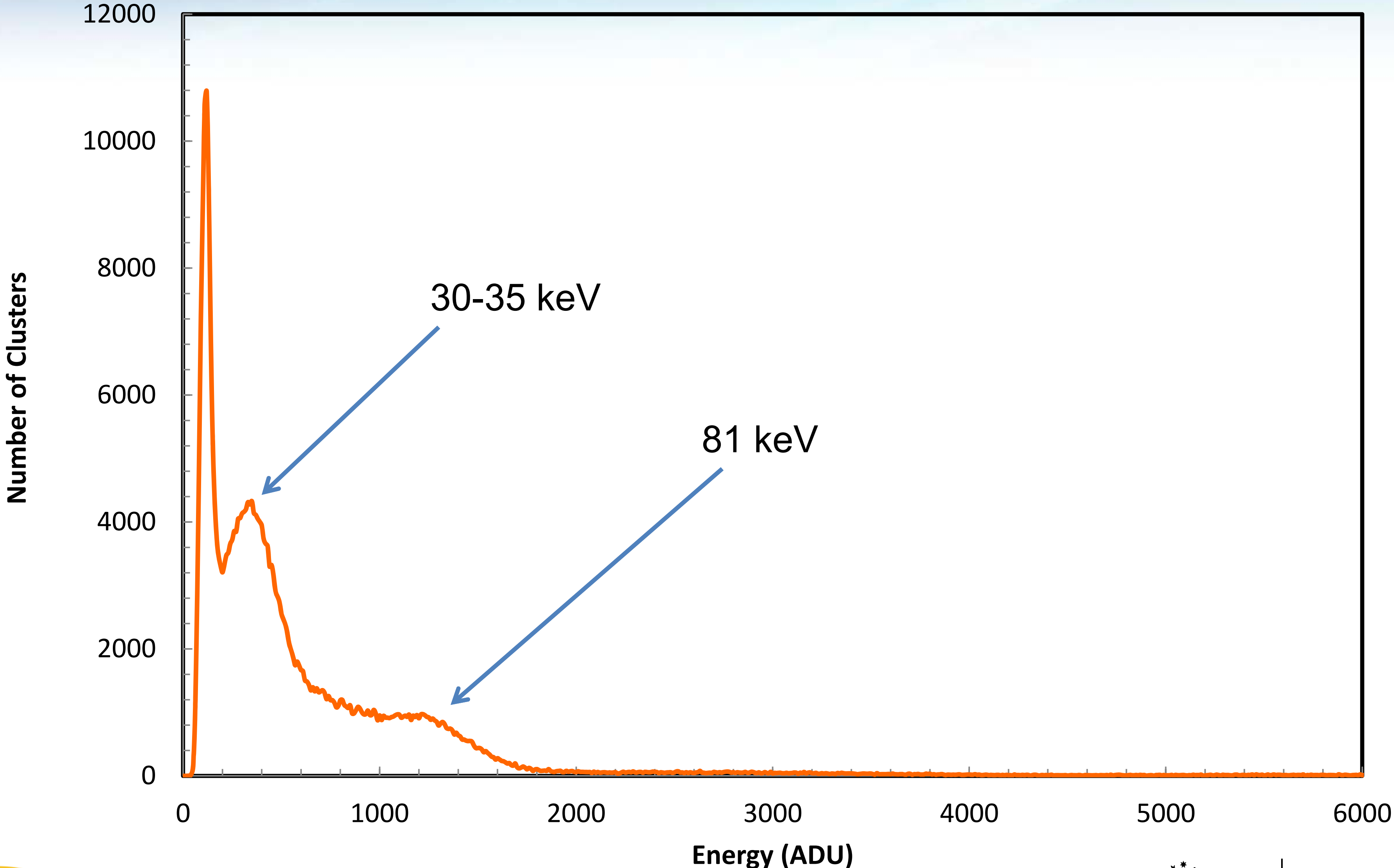
Position can be calculated by centroiding

Energy Calibration

Characterisation using ^{241}Am, ^{133}Ba and ^{57}Co isotopes

Isotope	Energy (keV)	Intensity (%)	Type
Co57	14.4	9	Gamma
	122	76	Gamma
	136	11	Gamma
Ba133	30-35	190	X-Ray
	81	32.9	Gamma
	276	7	Gamma
	302	18	Gamma
	356	62	Gamma
	384	9	Gamma
Am241	12-22	38	X-ray
	26	2	Gamma
	60	36	Gamma

^{133}Ba



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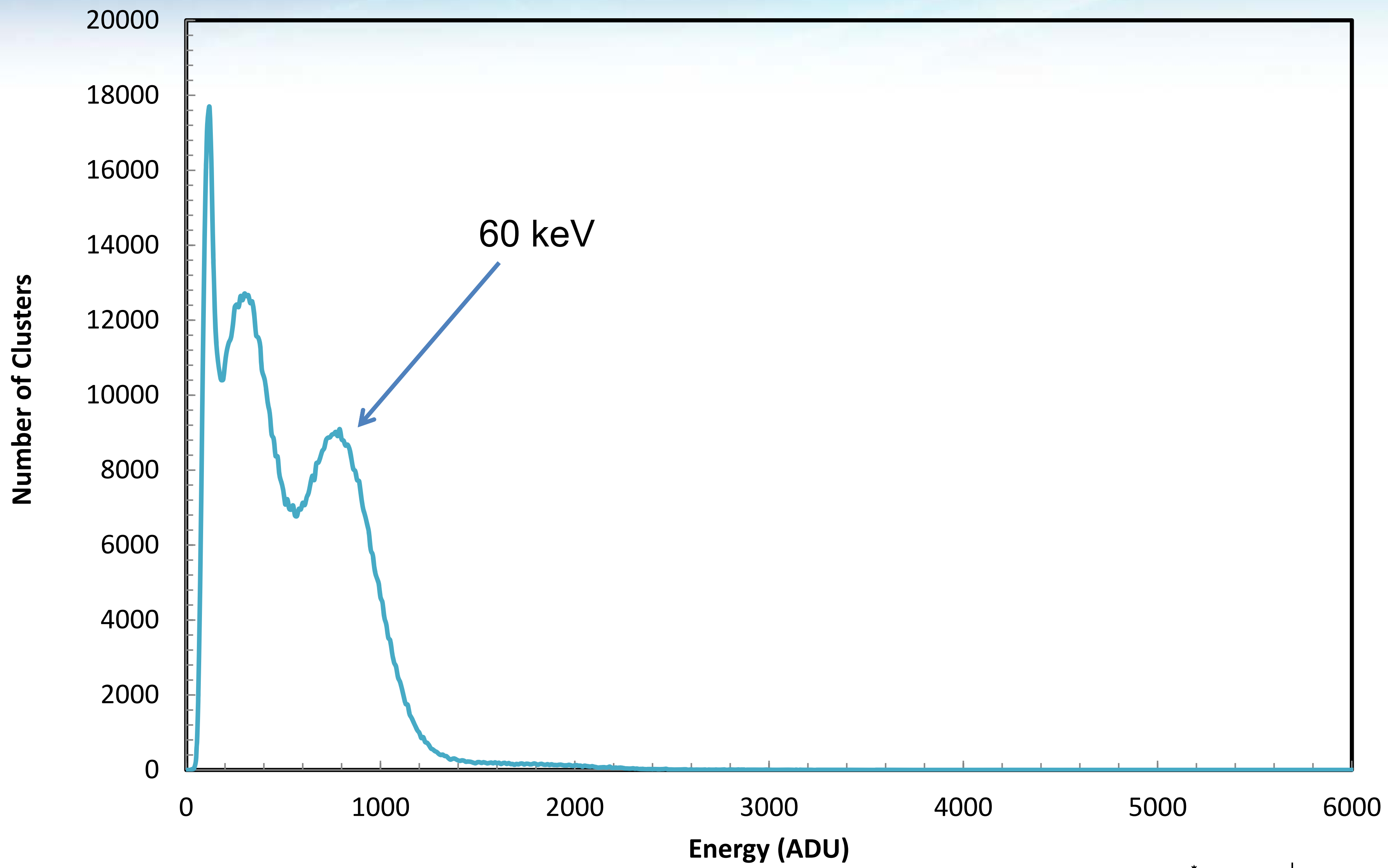
^{241}Am



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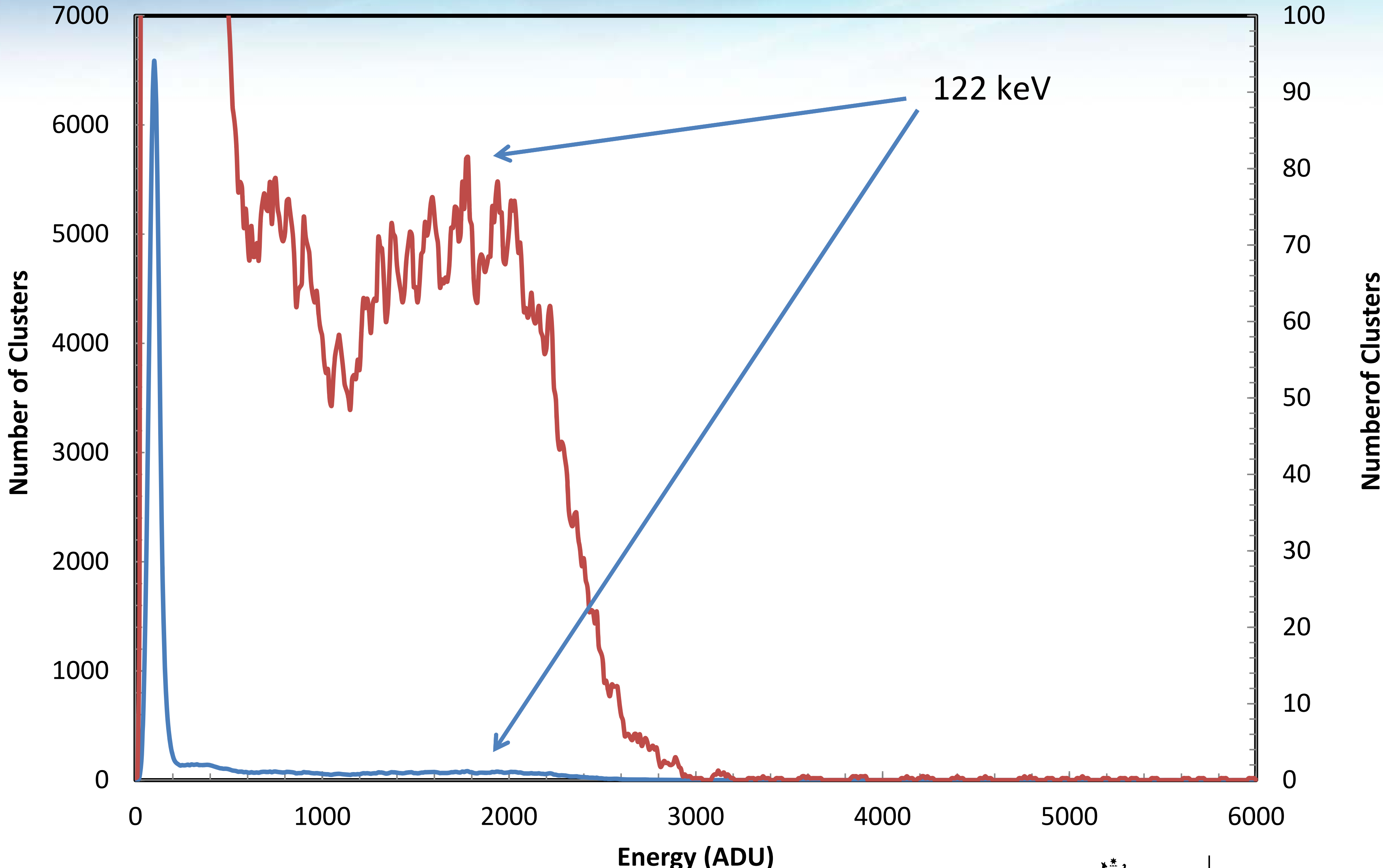
^{57}Co



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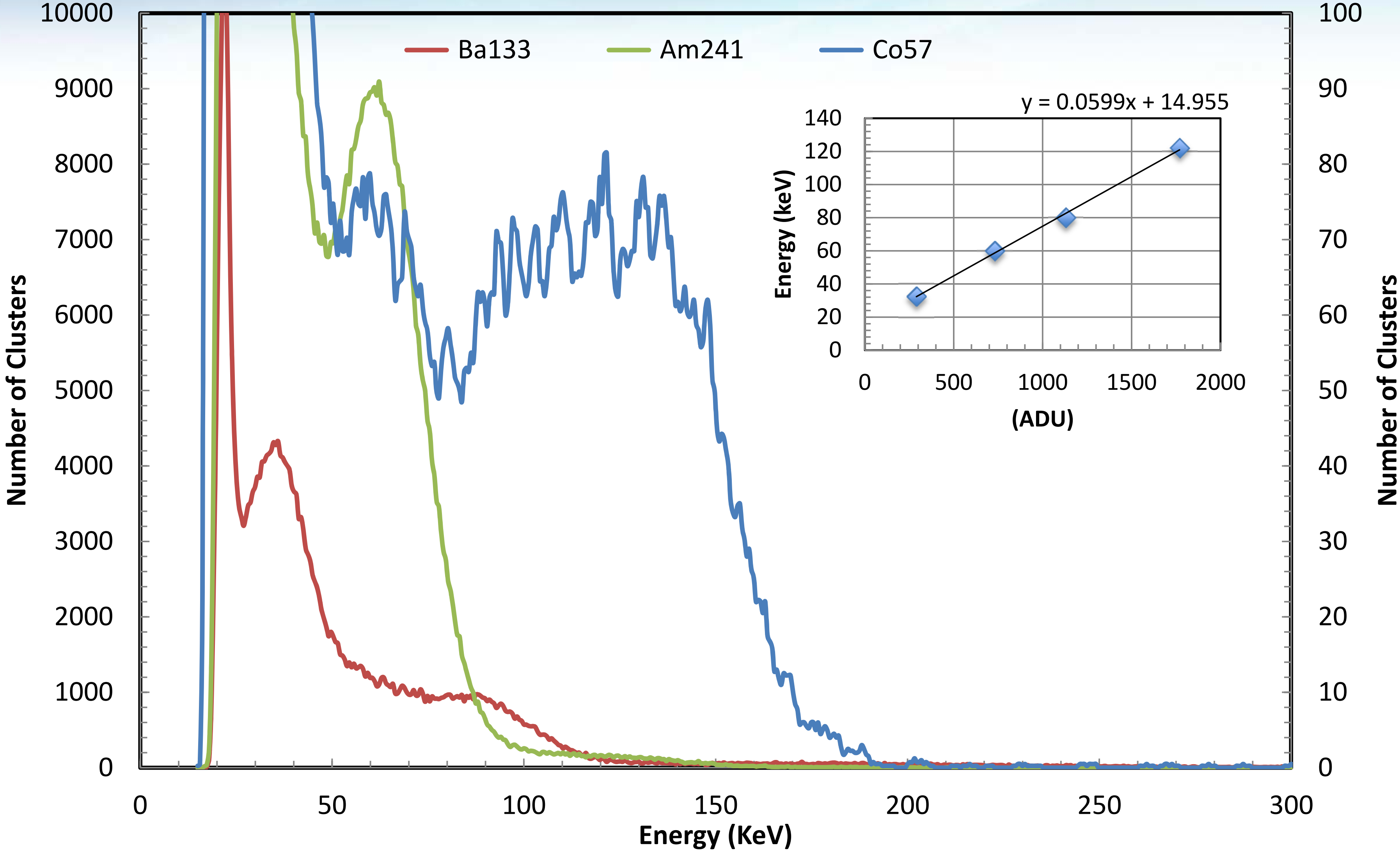
Energy Calibration



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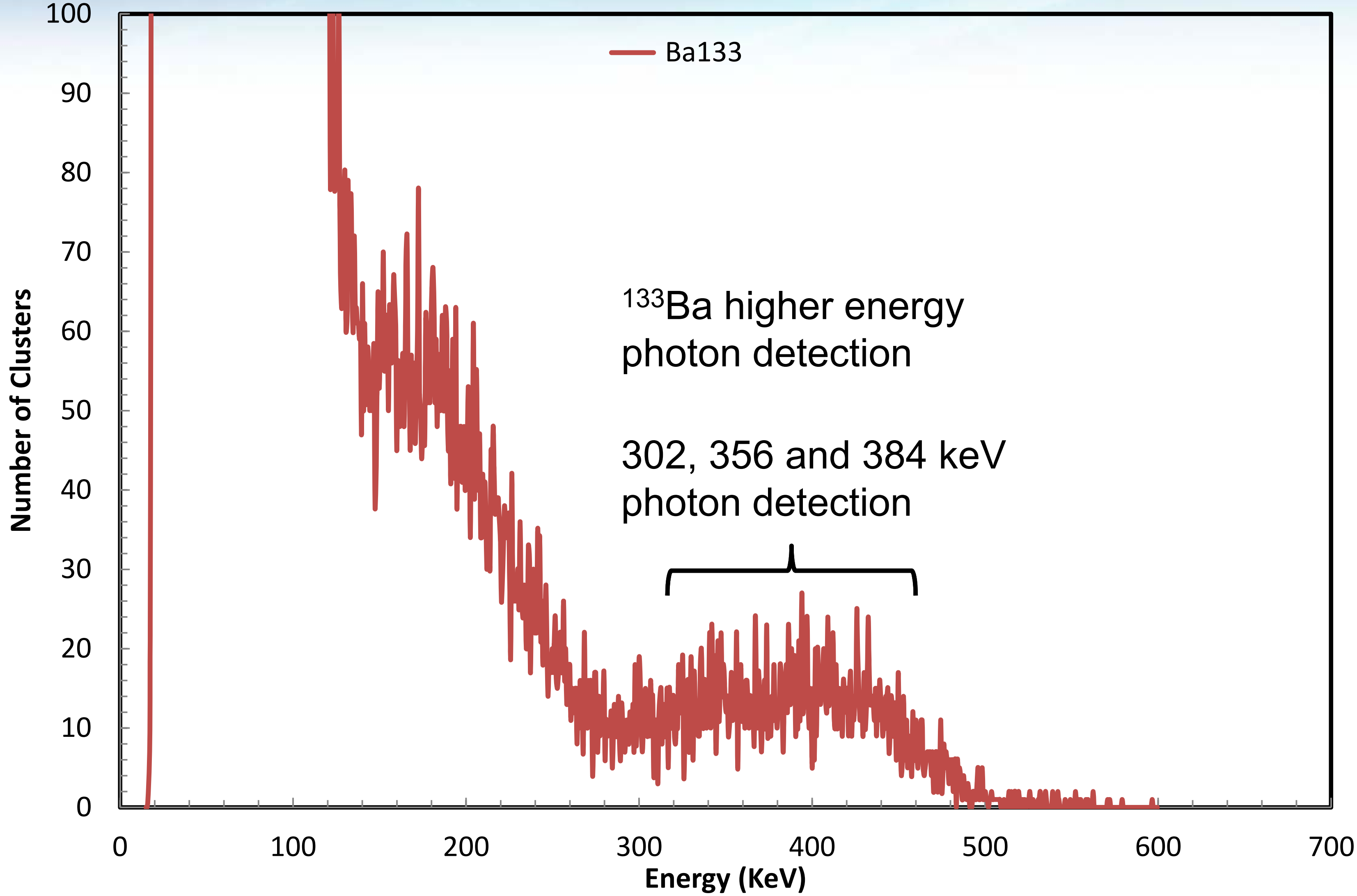
Detection of High Energy Events



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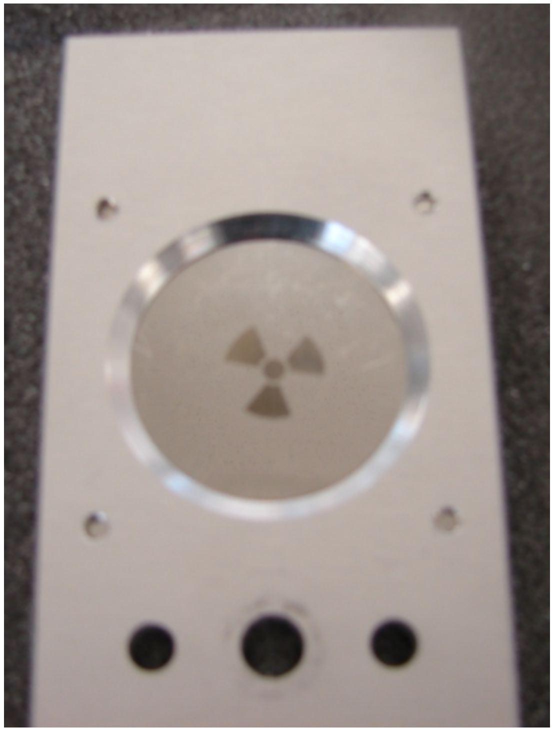
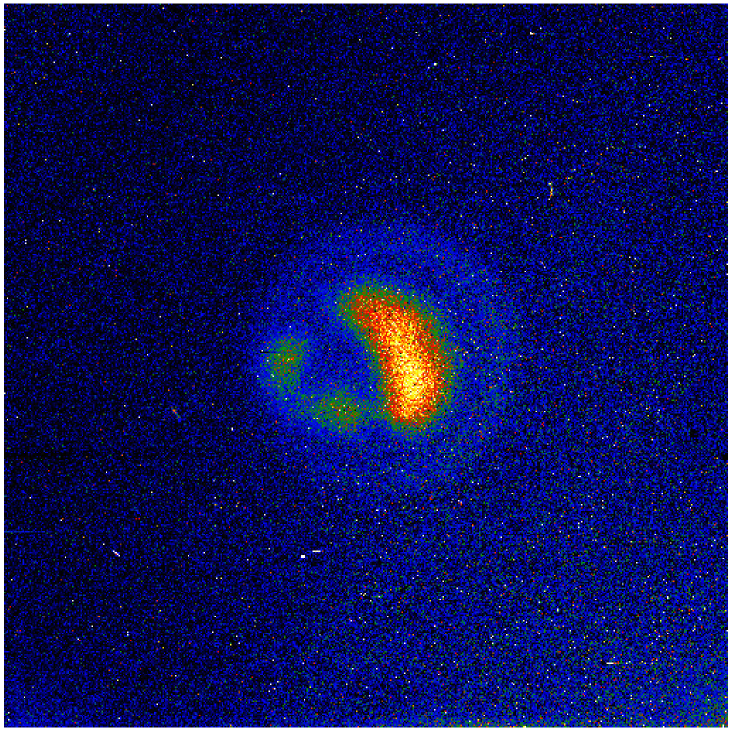
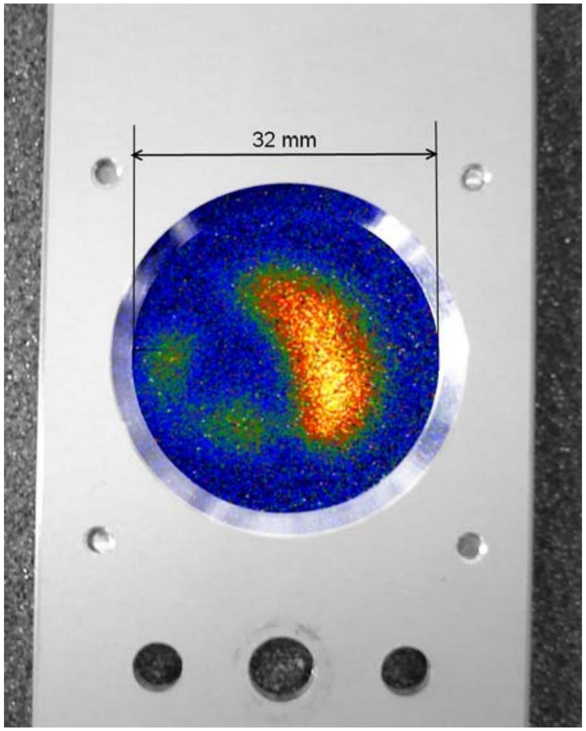
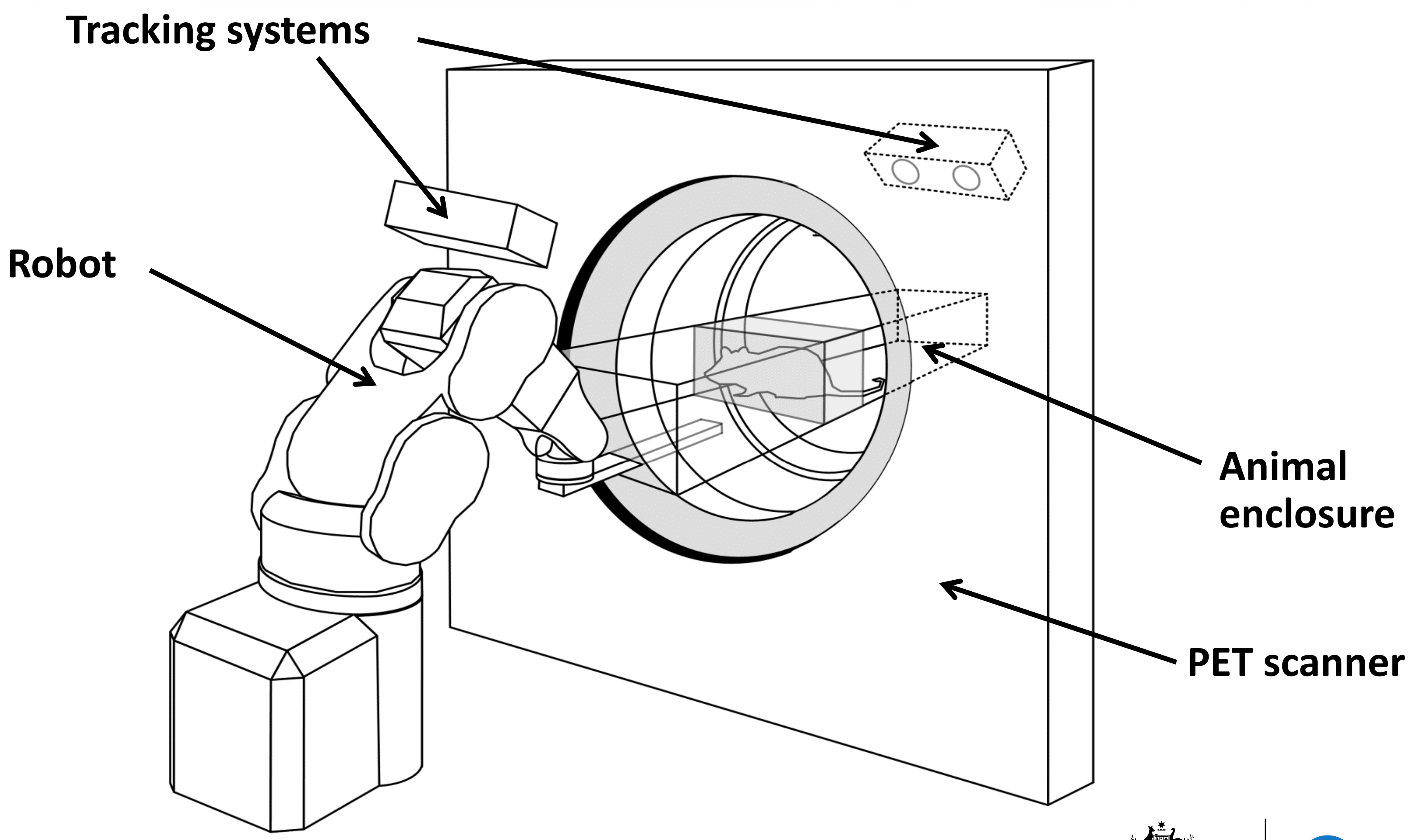
Pinhole Image Acquisition







Freely Moving Rats: System Concept



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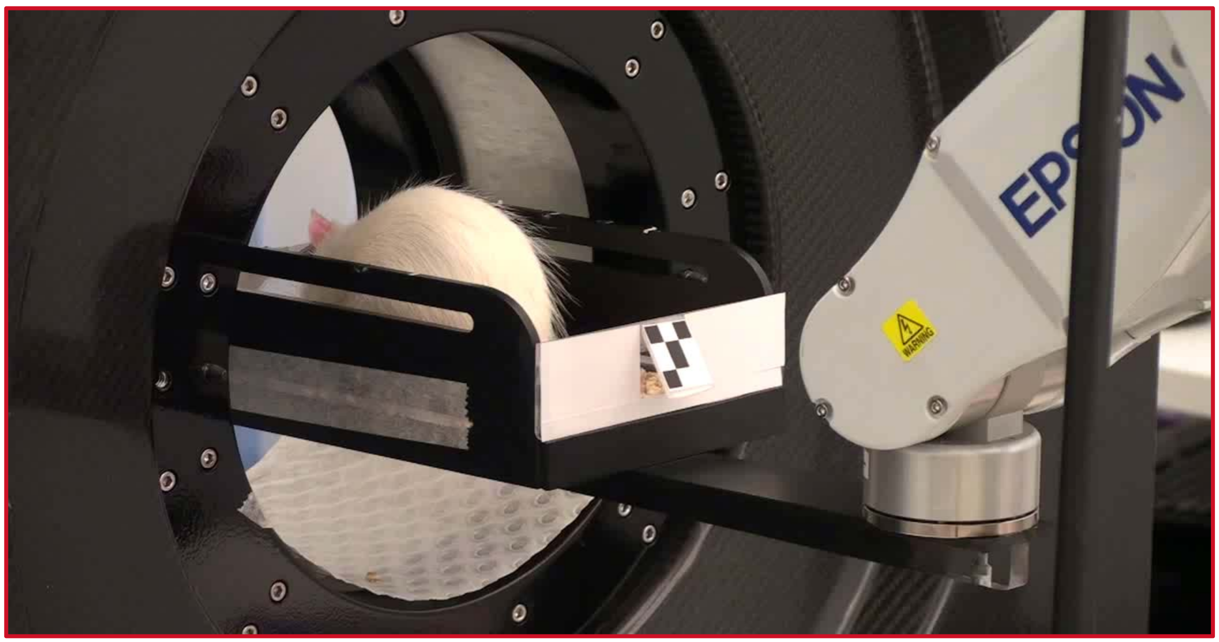
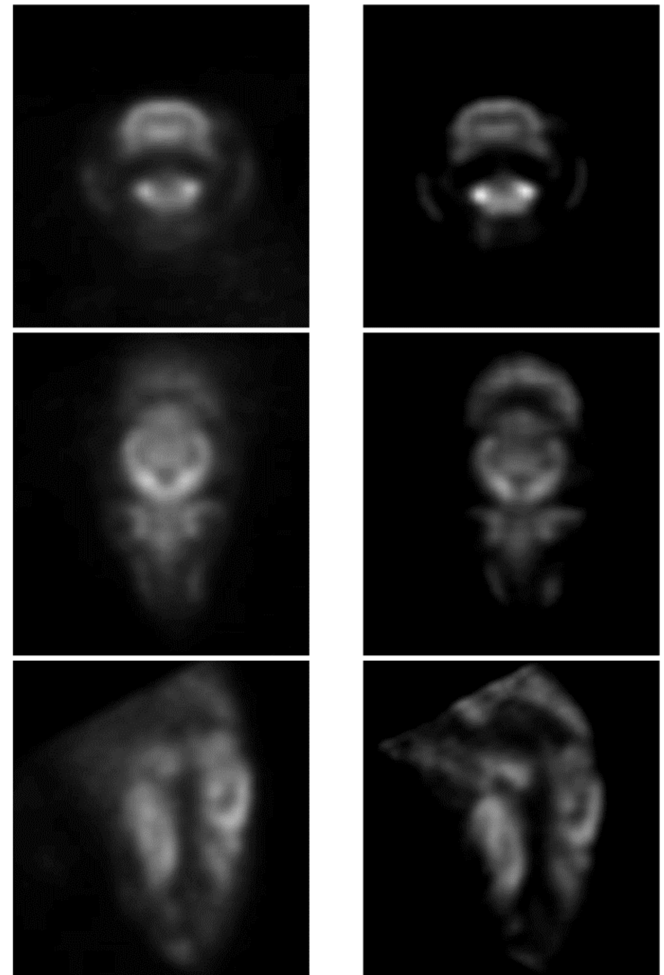
Marker-Based Tracking



Motion-Compensated | Motion-Free (Anaesthetised)



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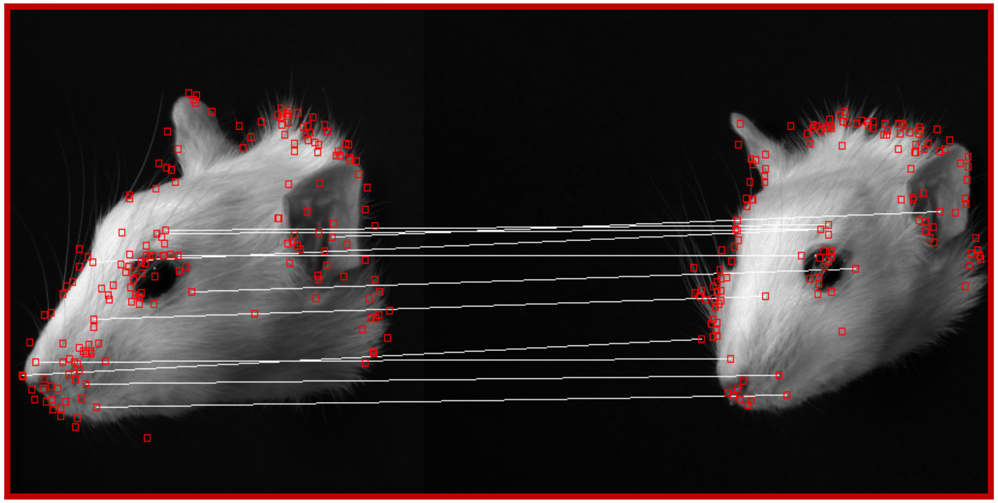
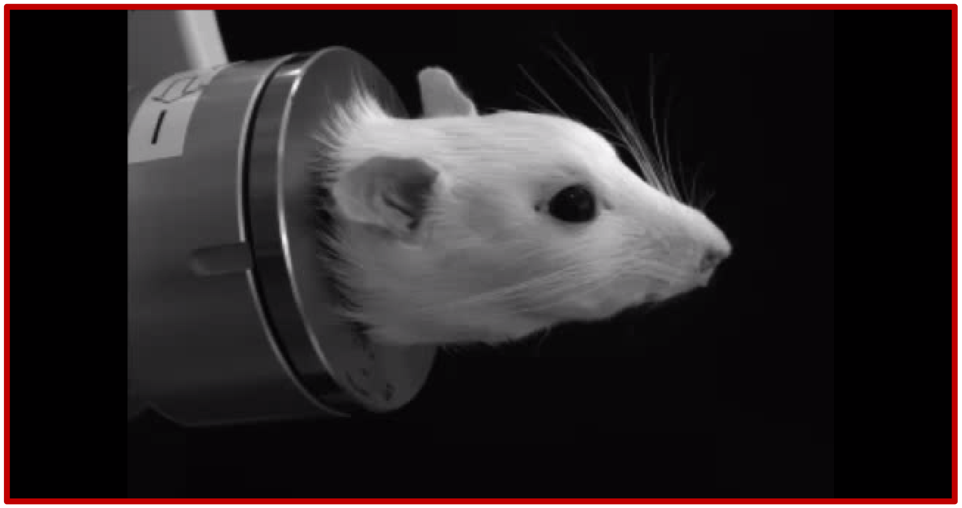
Marker-Free Tracking





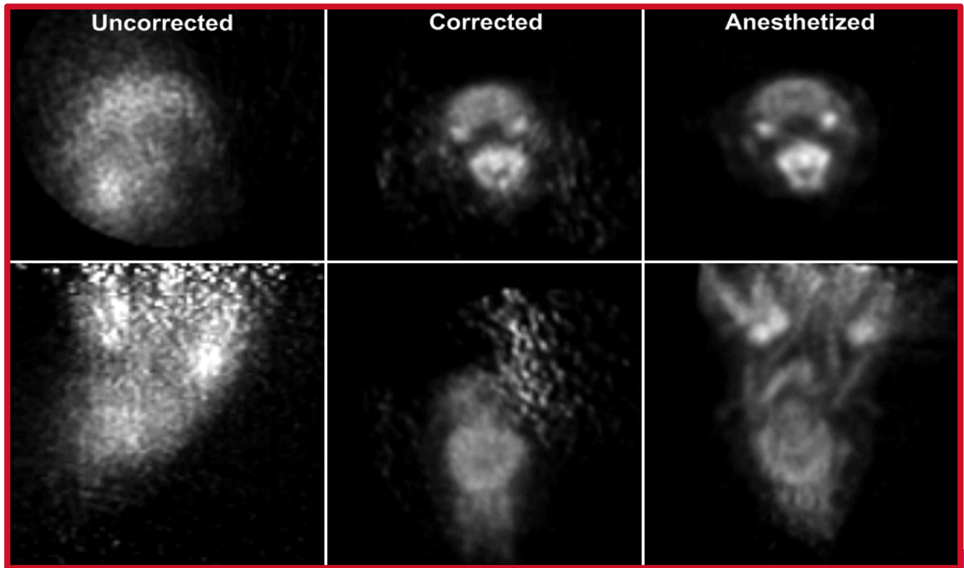


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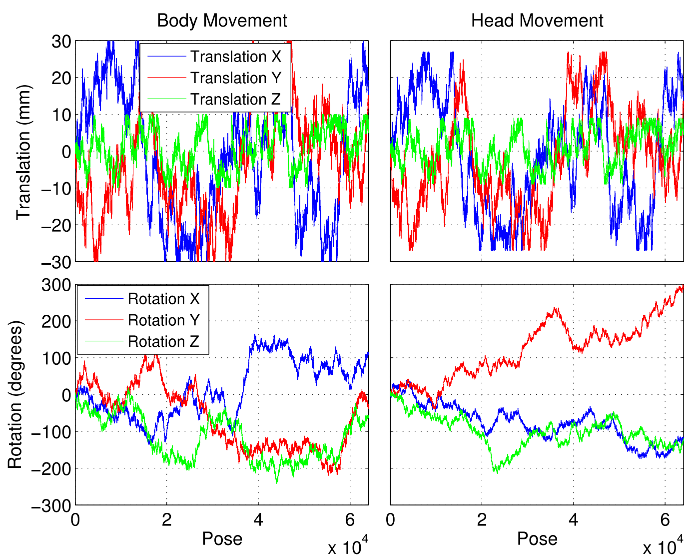
Image Reconstruction Considerations

Simulated data

- A Monte Carlo simulation package* was used to simulate a parallel-hole, single-headed SPECT camera
- Arbitrary movements of a realistic 3D digital mouse phantom# were simulated to be representative of a freely moving small animal
- Two patterns of rigid-body motion (6 degrees of freedom), were generated for the body and the head of the mouse



i. Impact of extraneous activity distribution

a. High activity in the extraneous compartment (i.e. body), compared to the activity in the head (activity ratio 4:1)
b. Low activity in the extraneous compartment compared to activity in the head (activity ratio 2:1)

i. Impact of attenuation

a. Simulate different scenarios: I. low (35 keV) and II. no attenuation
b. Due to the unknown pose of the extraneous compartment two cases of attenuation correction (AC) were considered: I. AC based on the reference μ-map and II. no AC.

i. Impact of motion-related inconsistencies in projections

a. Rotating single-headed detector geometry,
b. Full ring detector geometry.

#Dogdas *et al.* 2007, *Phys Med Biol*, **52**(3), 577-587

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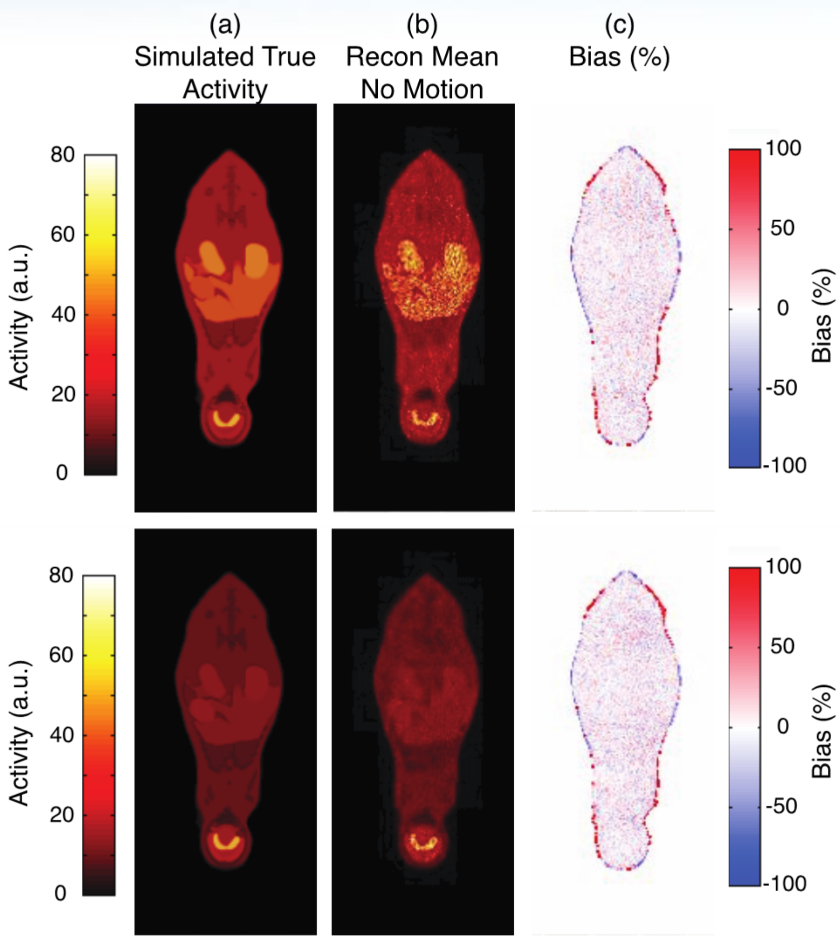
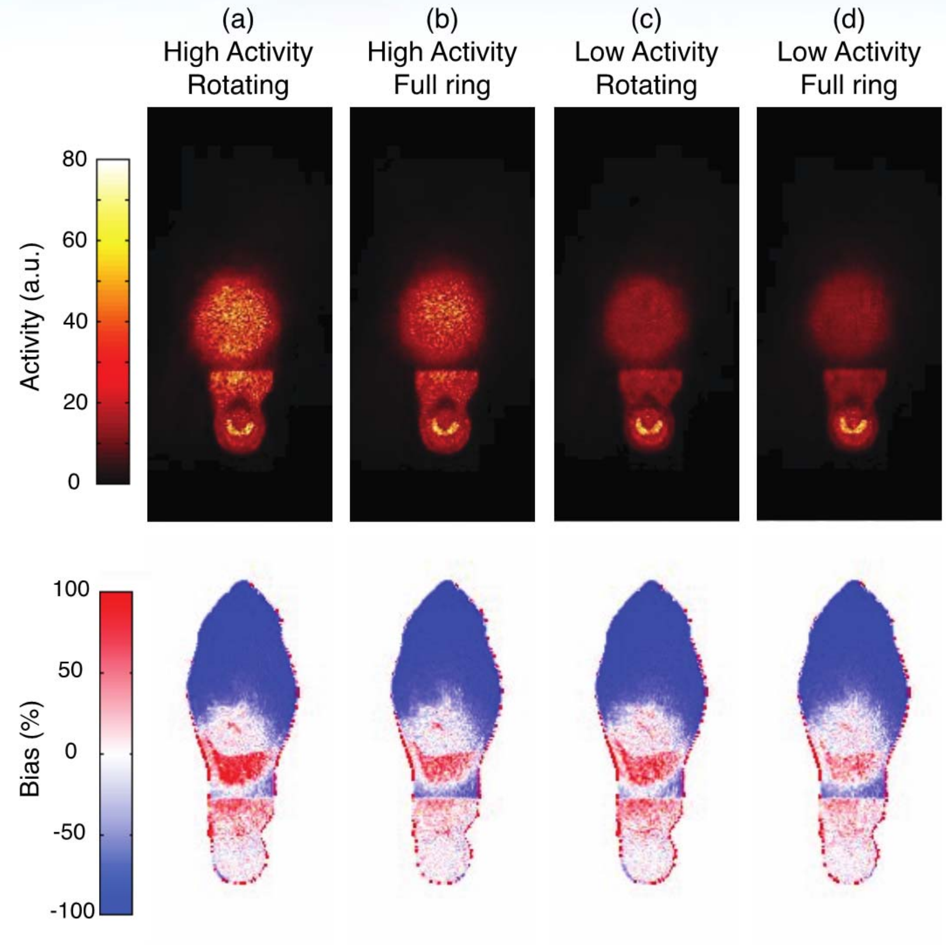
Reconstruction – No Attenuation





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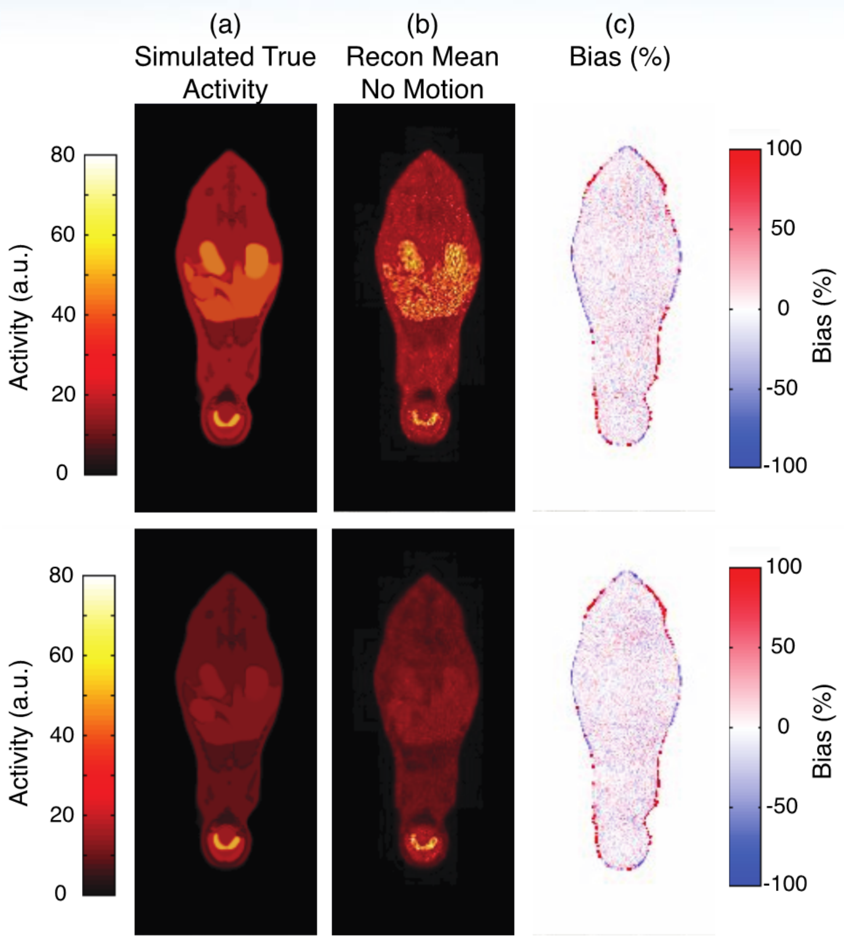
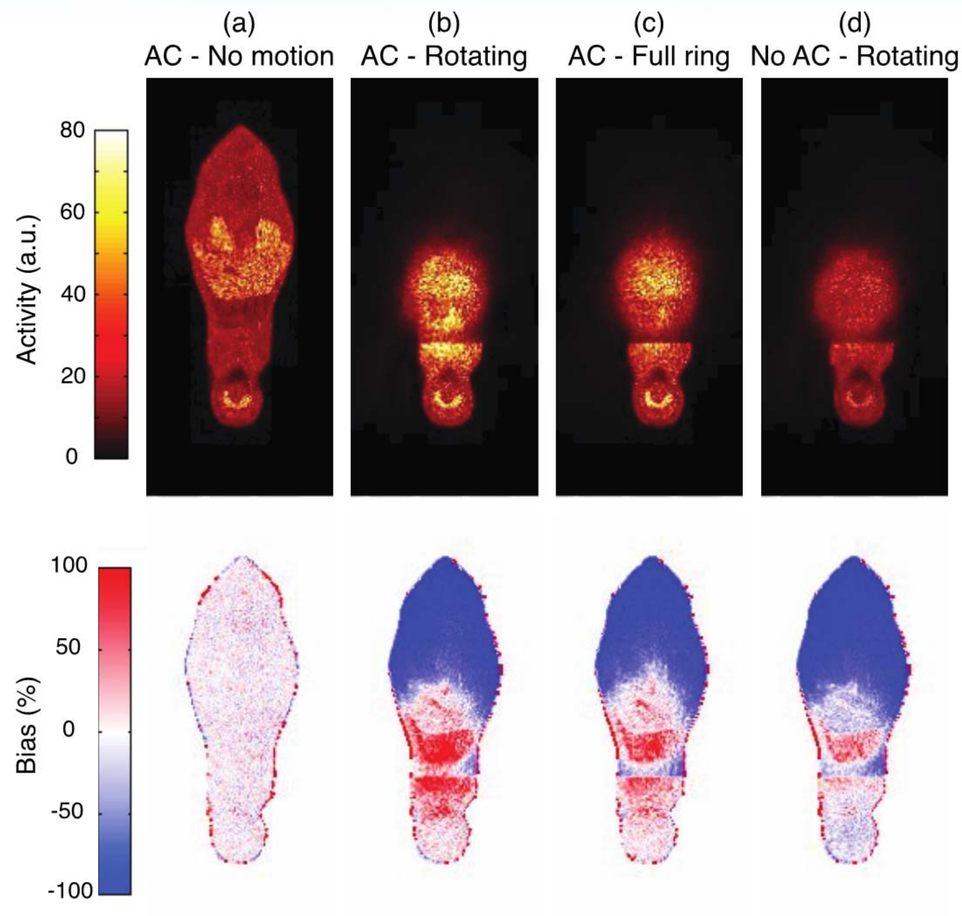
Reconstruction – Attenuation (35 keV)





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Discussion

- Successfully constructed a prototype gamma camera capable of at least 30 fps suited for coupling with motion tracking system
- Synchronised frame rates of up to 60 fps for acquisitions at 256 x 256 pixels
- Implementation of motion tracking system with investigation of markerless tracking to be investigated
- Reconstruction of the motion tracked data with future work to include reconstruction from a deformable body
- Further work will involve an investigation of alternative collimator geometries to increase the sensitivity of the detector system without compromising the minimum 30 fps requirement. Collimators to be investigated include parallel hole, slit-slat and rotating slat configurations

Acknowledgements

- The authors would like to thank Adam Sarbutt from ANSTO for the design and construction of the detector housing

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