Imaging of Ra-223 with a small-pixel CdTe detector:

potential for improved image quantification for radionuclide dosimetry

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NUCLEAR MEDICINE

Prostate Cancer

- Most prevalant cancer in men (>40,000 diagnoses per year; 13% of all cancers; 25% of new cases in men)[i]
- Highest incidence in the 75-79 age group[i]
- 81.4% survive more the 5 years[i]
- Commonly spreads to the bones in advanced disease
  (~90% of patients with castration-resistant, prostate cancer (CRPC) have bone metastases)[ii]

PROSTATE CANCER UK

i – ONS Cancer Statistics Registrations, June 2013

ii - Scher H, et al. N Engl J Med. 2012;367:1187-1197, supplemental appendix.

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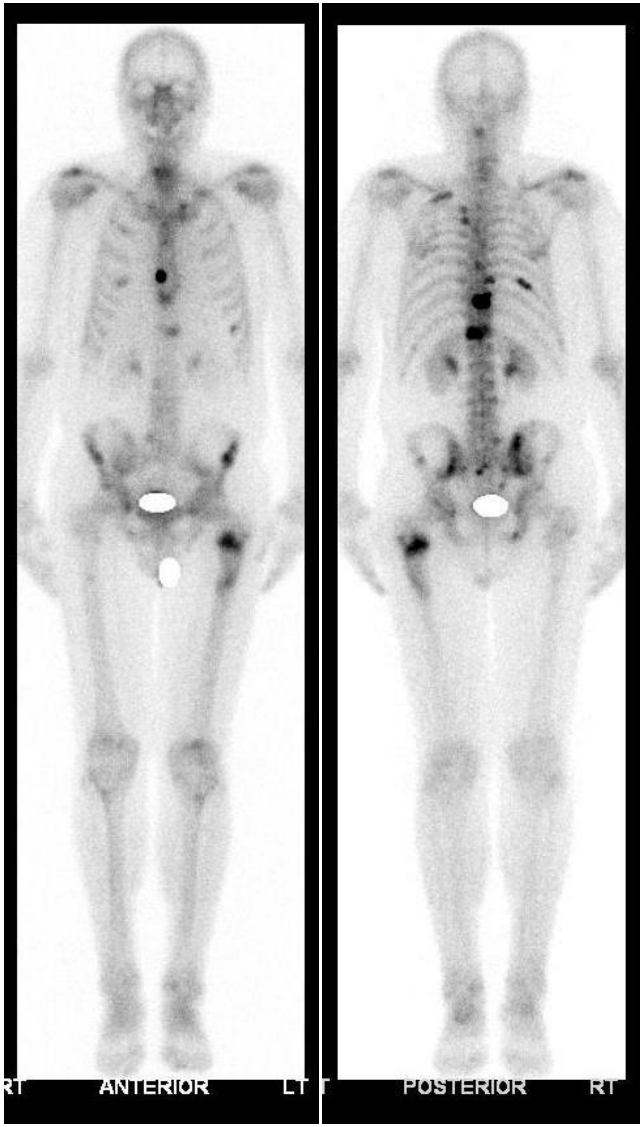
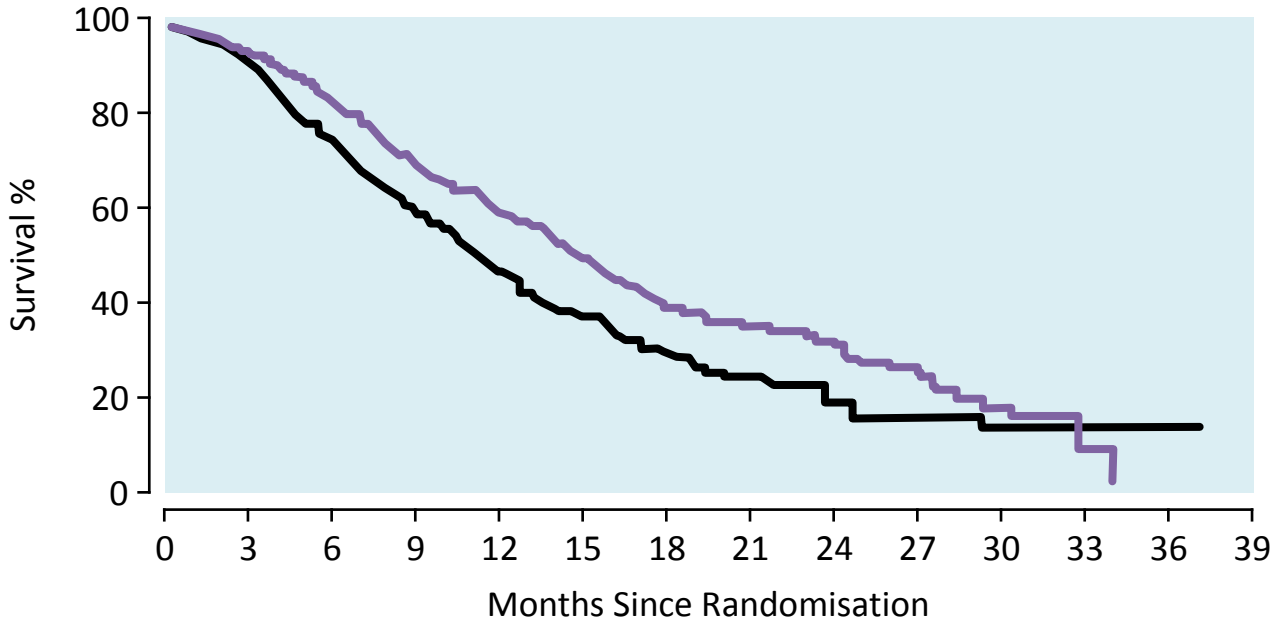
Bone metastases



- Metastases are common in the ribs, spine, pelvis and hips
- Can cause debilitating pain and severely impact quality of life
- Treatments are palliative

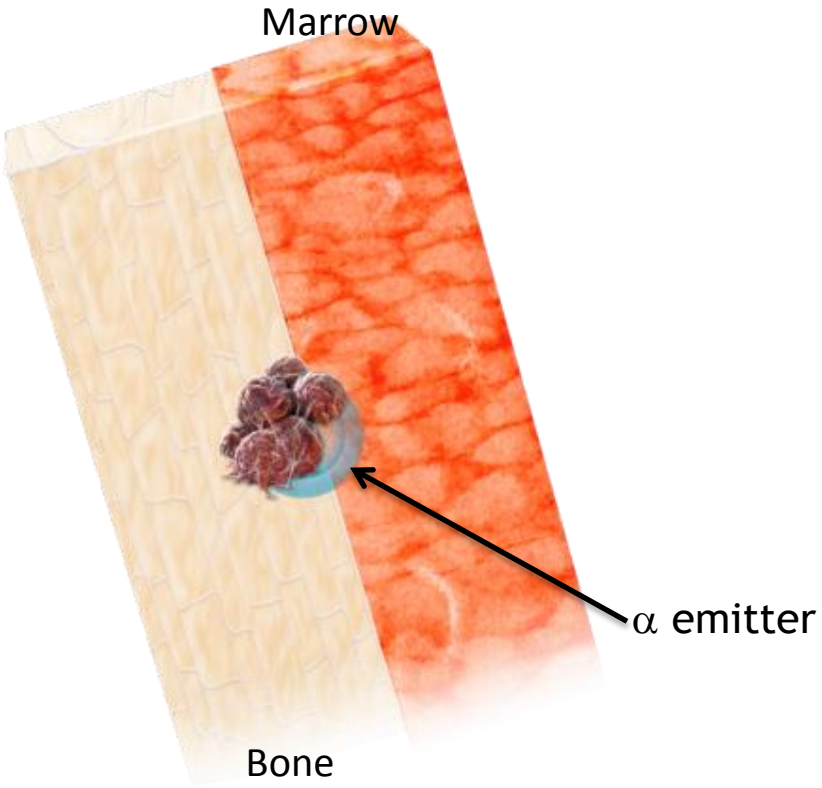
Xofigo®

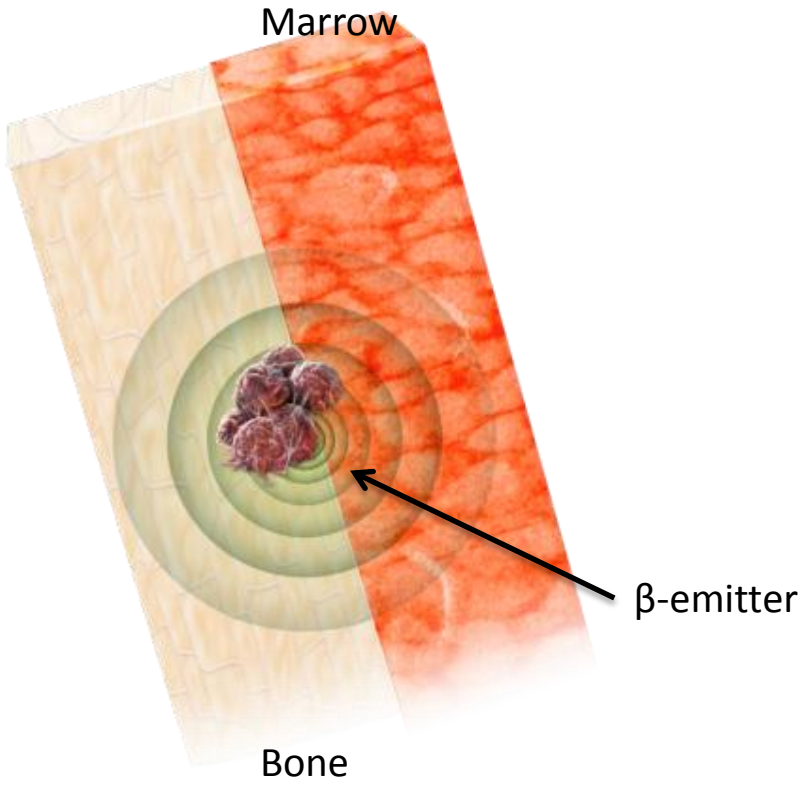
- New radiopharmaceutical ($^{223}RaCl_2$) by Bayer
- Bone-seeking alpha-emitter
- Licensed in the UK in Feb 2014 after promising clinical trial results:



- **Increased median overall survival of 3.6 months**
- Increased time to serious skeletal event (5.8 months)
- Increased time to Alkaline Phosphatase progression (3.6 months)

The Alpha Advantage



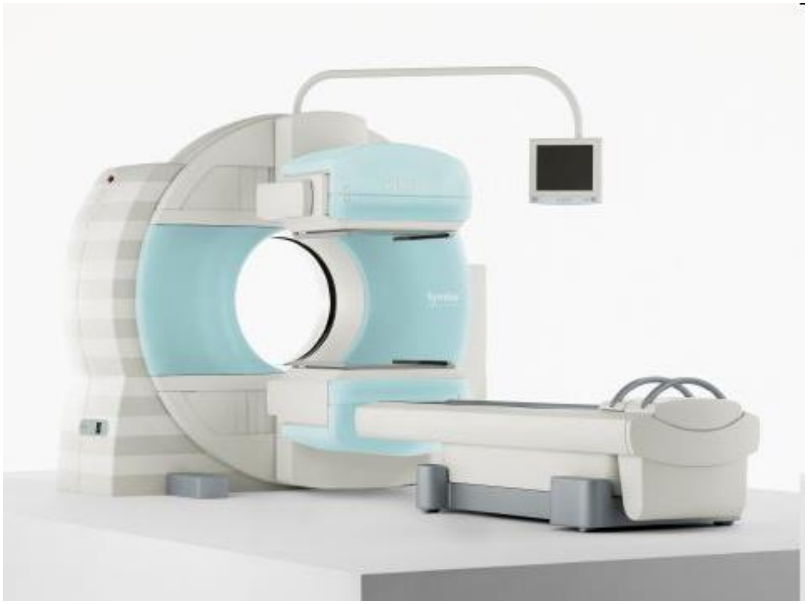


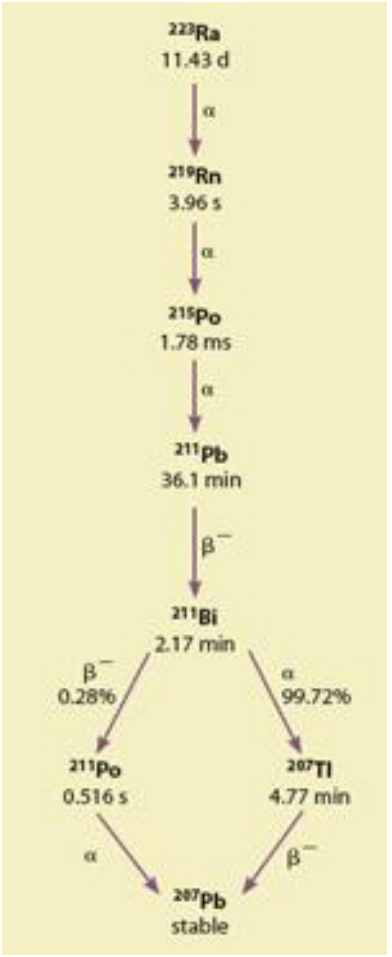
Range of α-particle:
(short range – 2 to 10 cell diameters). High LET, increased chance of double-strand DNA breaks

Range of ß-particle:
(long range – 10 to 1000 cell diameters)

The Disadvantages

- ^{223}Ra's emissions are not optimal for imaging with conventional gamma cameras





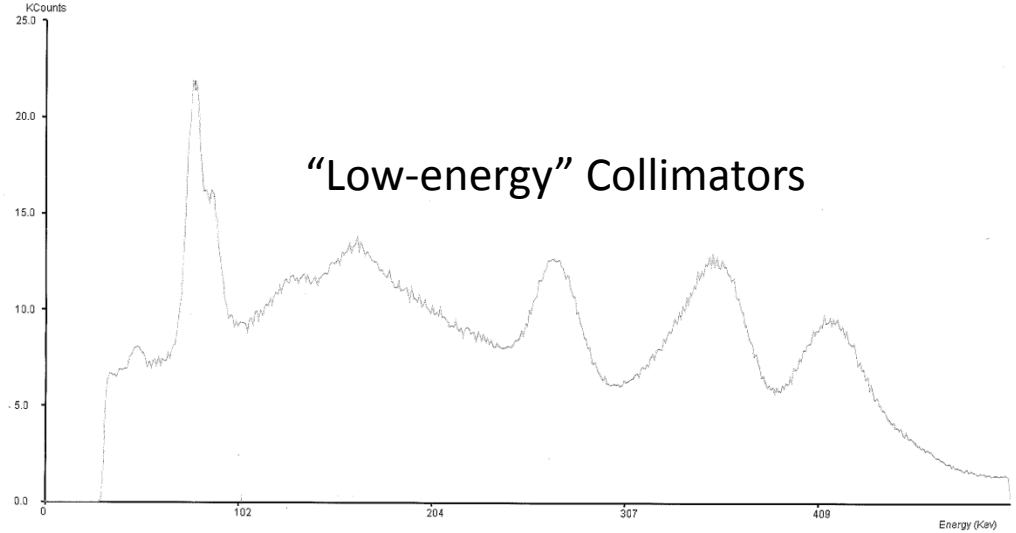
- Injected activities are generally around 6MBq → very low external dose rate (good for patients' family, not good for imaging!).

Why do we need imaging?

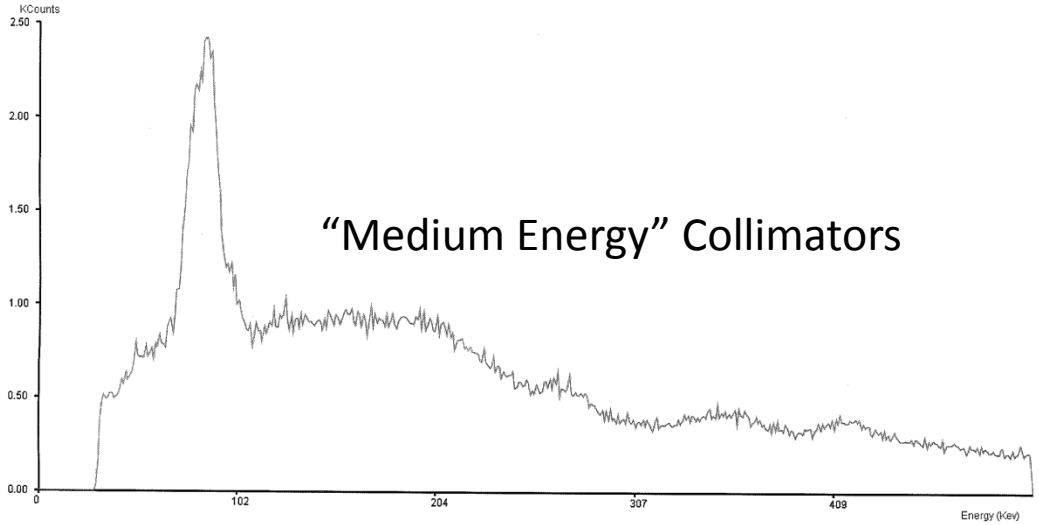
- Currently very simplistic administration regimen based on patient weight (50kBq/kg)
- BUT…patient weight does not necessarily correlate to tumour burden, radiopharmaceutical uptake, or even the patient's bone marrow reserve
- Therapy could be tailored to the individual patient by adjusting administered activity based on uptake and clearance in the bone
- Need to image the biodistribution and clearance of radiopharmaceutical, as this varies greatly between patients
- → **"Personalised medicine"**

Imaging with gamma cameras

Typical Energy Spectra:

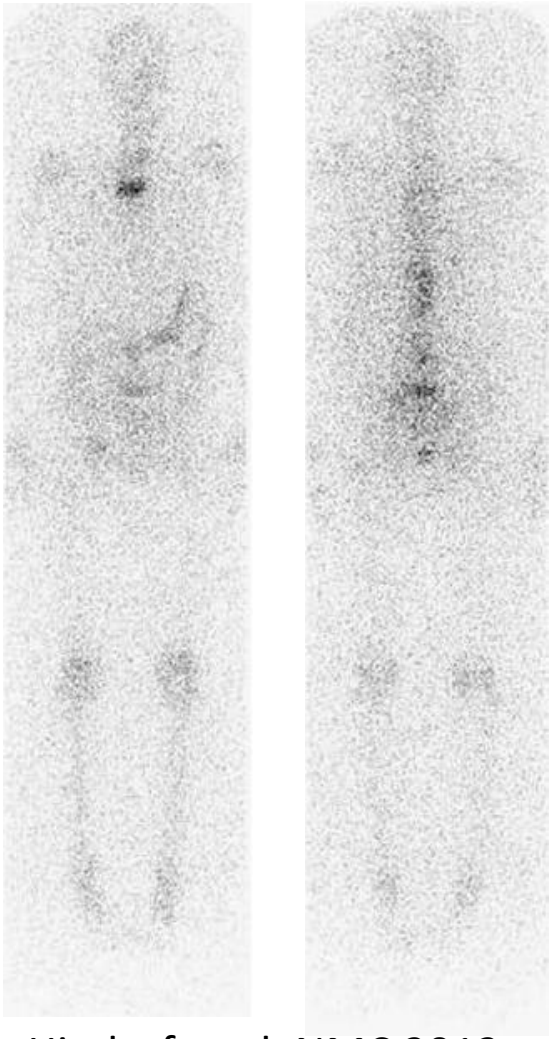


"Low-energy" Collimators



"Medium Energy" Collimators

Typical Patient Images (MEGP):

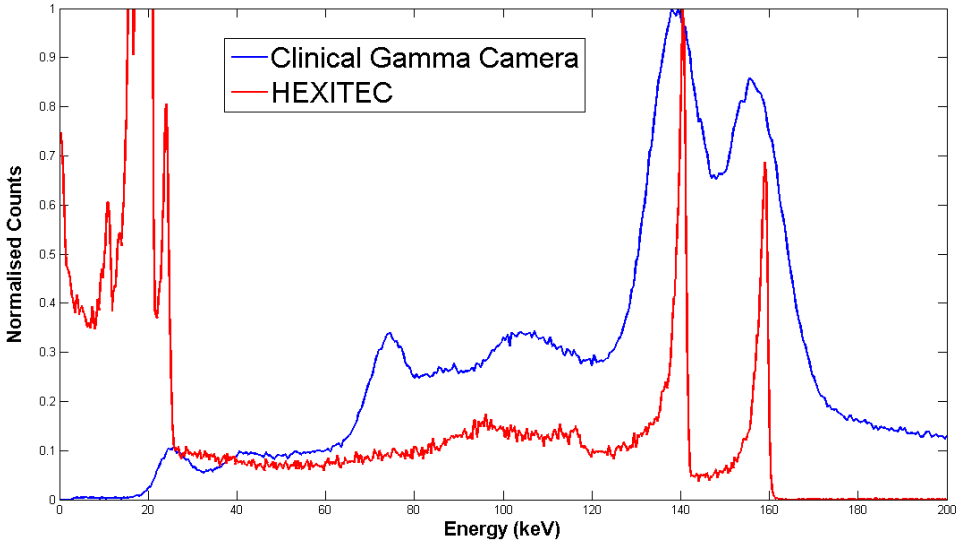


Hindorf et al, NMC 2012

The HEXITEC Detector

- 1mm thick CdTe
- 80 x 80 pixels, 250µm pitch
- 5-200keV spectroscopy per pixel
- 10000 frames per second
- -500V detector bias
- Peltier cooling, room temperature operation

- Corrections for charge sharing
- Pixelwise energy and uniformity calibrations
- Energy resolution 0.8% at 140keV (vs 9% for conventional gamma camera)



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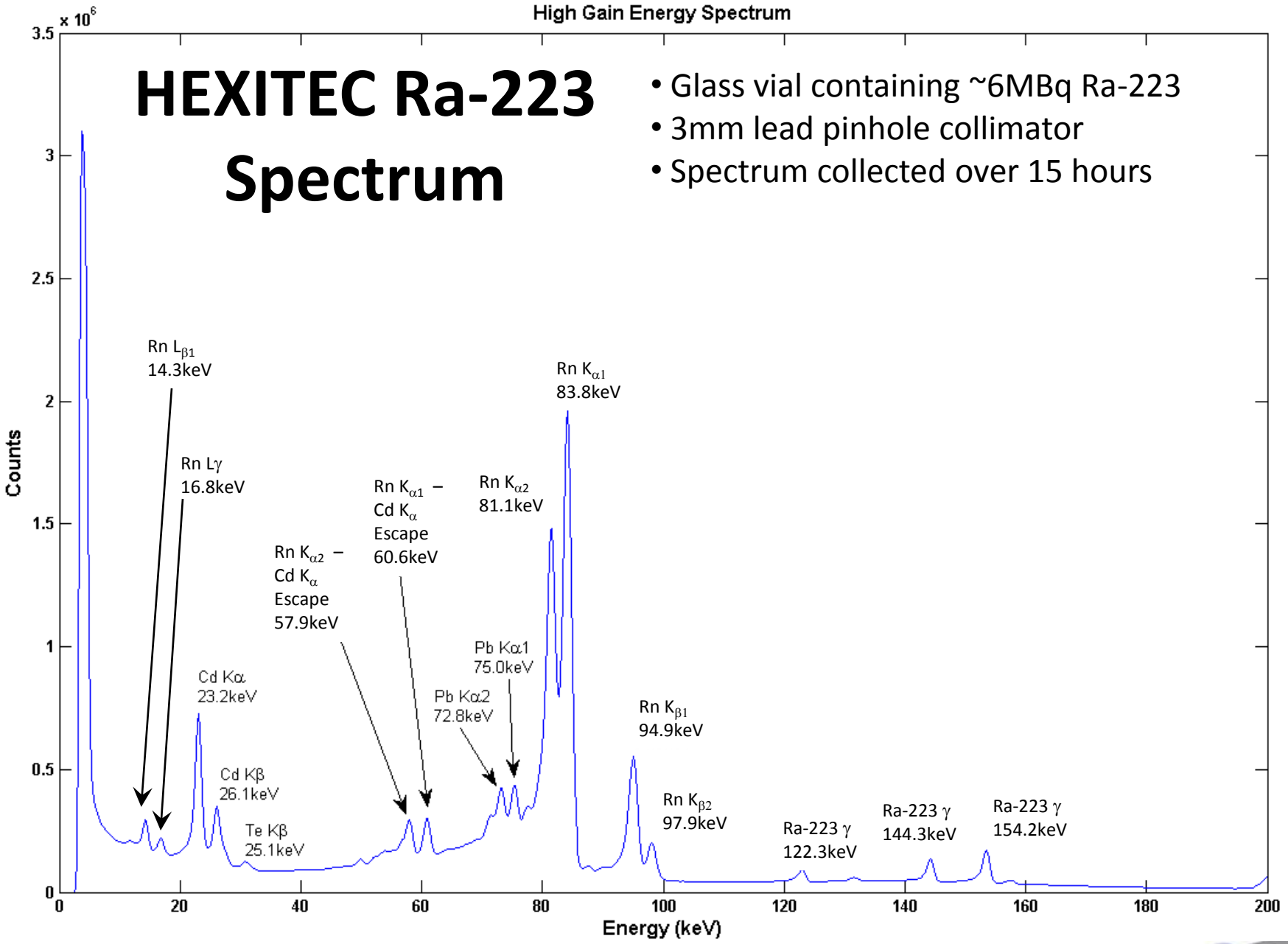
HEXITEC Ra-223 Spectrum

- Glass vial containing ~6MBq Ra-223
- 3mm lead pinhole collimator
- Spectrum collected over 15 hours



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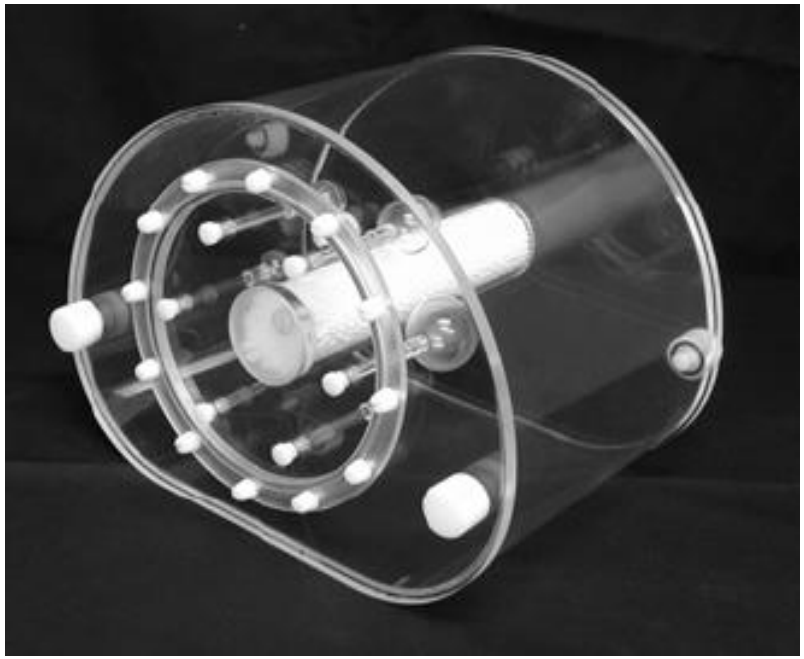
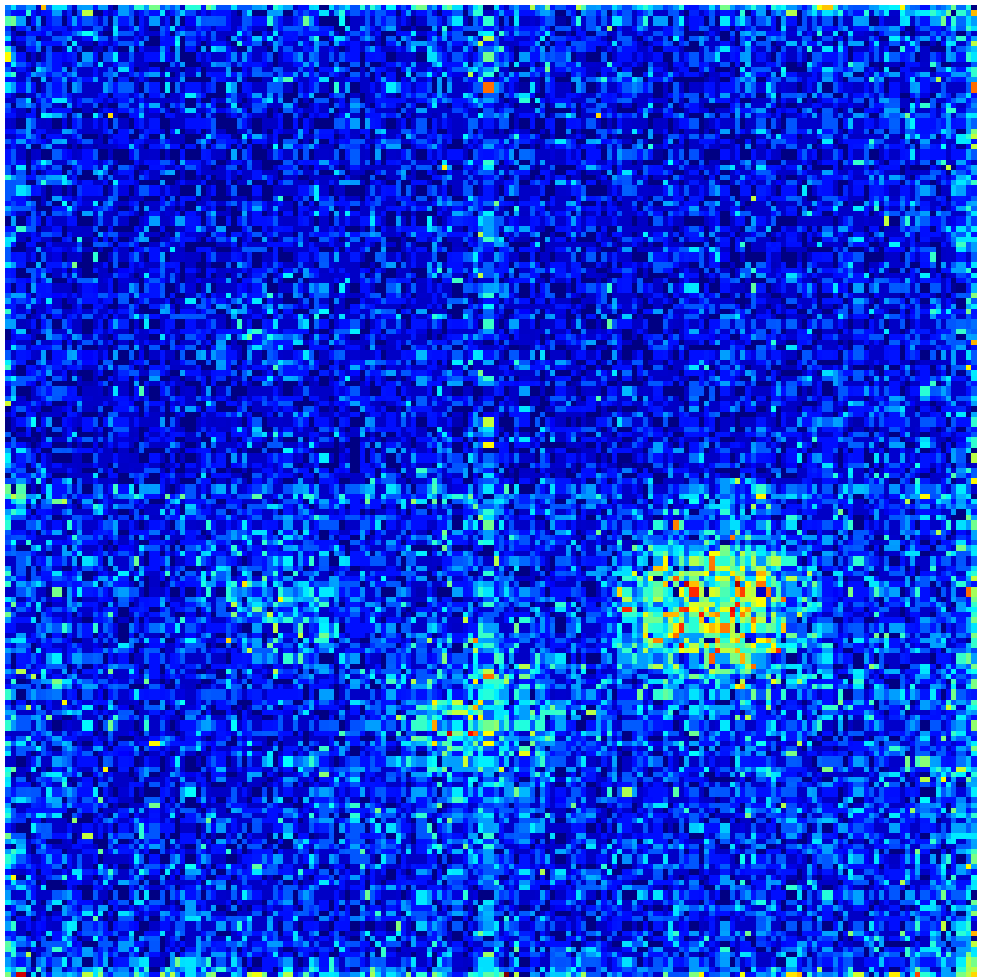
HEXITEC Imaging with Ra-223

- "Body phantom" containing 6 spheres (10, 13, 17, 22, 28, 37mm)
- Spheres: 434kBq/ml
  Cylinder: 2.4kBq/ml
  Cold background
- 3mm lead pinhole collimator at 28cm from spheres
- Planar acquisition, "tiled" with 4 stops
- 50mins "live time" per stop
- Bias refresh (60s on, 4s off, 6s settle)
- Energy calibration applied, form images with 85±5keV energy window
- Stitch 4 tiles together

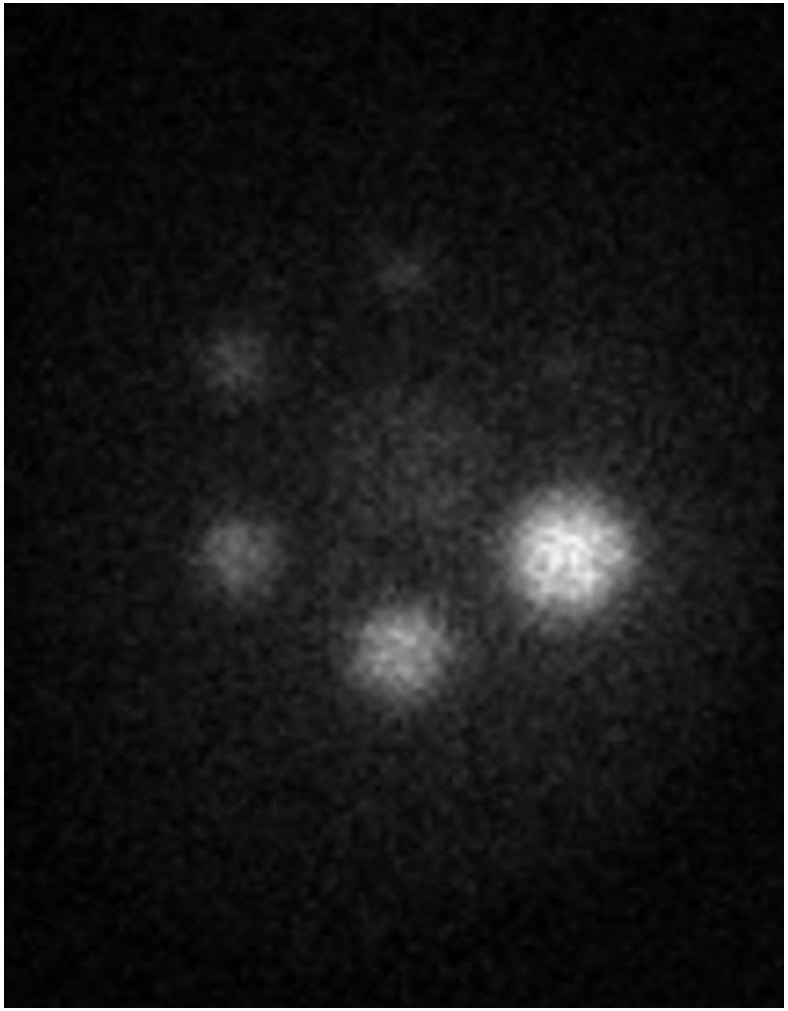


Imaging Results

- 4 (5?) spheres visible
- Low counts; noisy image
- Detector edge effects due to “stitching”.
- Efficiency limited by pinhole collimation and distance from phantom



Comparison with gamma camera



- GE Infinia SPECT/CT
- “Medium Energy” parallel-hole collimators
- 50mins, 89.5±13.4%keV
- 5 (6?) spheres visible?
- Better statistics
- Central compartment visible

HEXITEC Ra-223 conclusions

- Spectroscopy is excellent
  → potential for improved quantitative imaging due to improved scatter rejection
- Sensitivity with lead pinhole collimators too poor for clinical imaging
- Need higher sensitivity collimators
- Larger area detector would also be needed for clinical imaging

Ongoing work – RAL and Surrey

- Simulation work to optimise parallel-hole collimator design for increased sensitivity for both Tc-99m and Ra-223
- Planning to test thicker CZT detector material shortly
- Large-area detectors under development (Seller et al, this morning at PSD)