NPL
National Physical Laboratory

Radiochemistry and nuclear metrology for life sciences and health applications

Peter Ivanov

National Physical Laboratory, UK

The Lifecycles of Radionuclides in Medicine, IoP meeting, London, 7 June 2019

Overview

- Nuclear metrology at NPL
- Production and radiochemical purification
- Standardisation and nuclear data measurement
- Theranostic approach

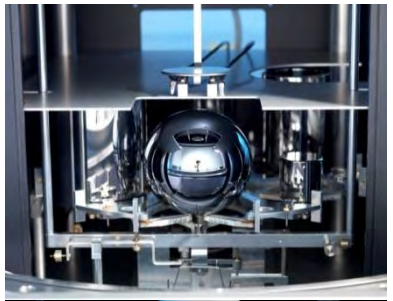
National Physical Laboratory

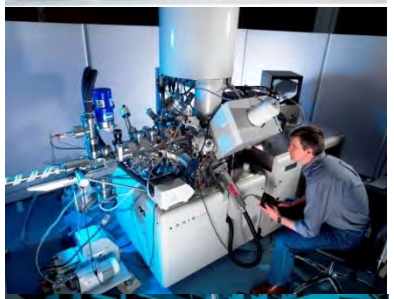
- A world leading National Measurement Institute
- UK's largest science and technology asset, engaging with government and industry
- Founded in 1900, Radioactivity since 1913
- 800+ specialists in measurement science
- Purpose built laboratory campus, state of the art facilities
- Operated and owned by the Department for Business, Energy and Industrial Strategy
- University partners – Surrey and Strathclyde

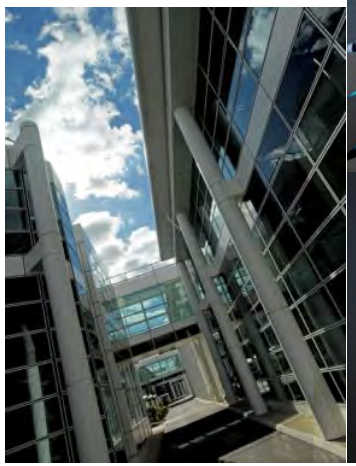
SECTORS

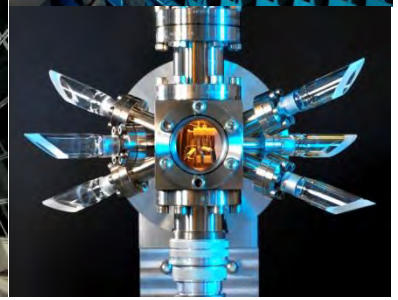
- Advanced Manufacturing
- Defence & Security
- Digital economy
- Energy and environment
- Health and life sciences
- Measurement Solutions
- Sustainability
- Training and education

All measurements of radioactivity in the UK rely on the **primary standards held at NPL**. The NPL standards are linked to the international measurement system and provide a route to demonstrate that measurements are **accurate, consistent and independent**.

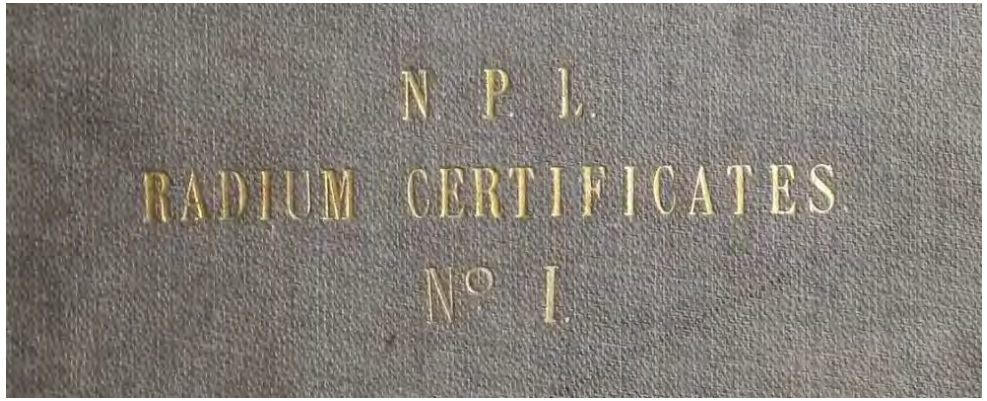








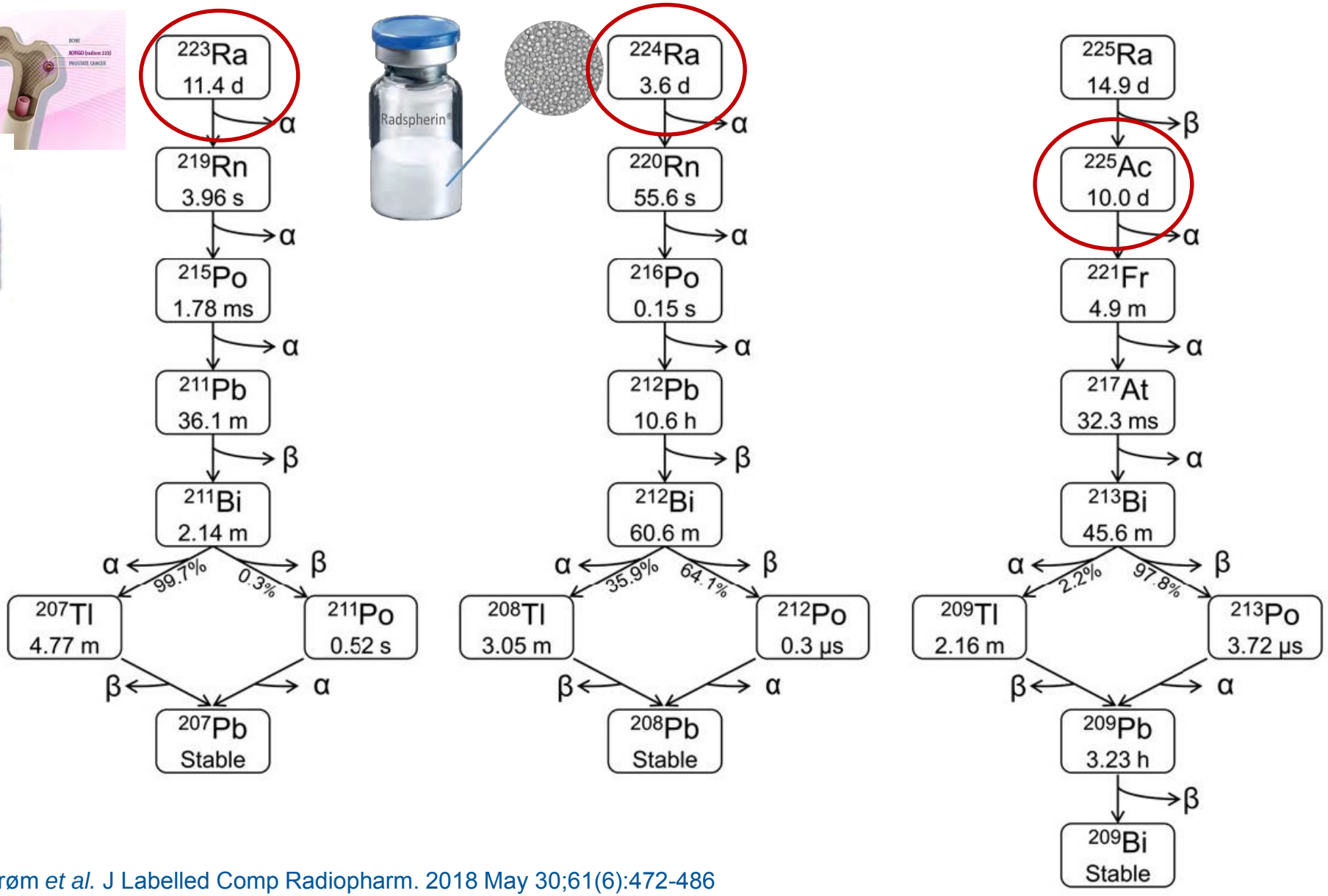
Radionuclide Metrology at NPL



The first radium standard held by NPL was prepared by Mesrs. Curie, Meyer and Rutherford.

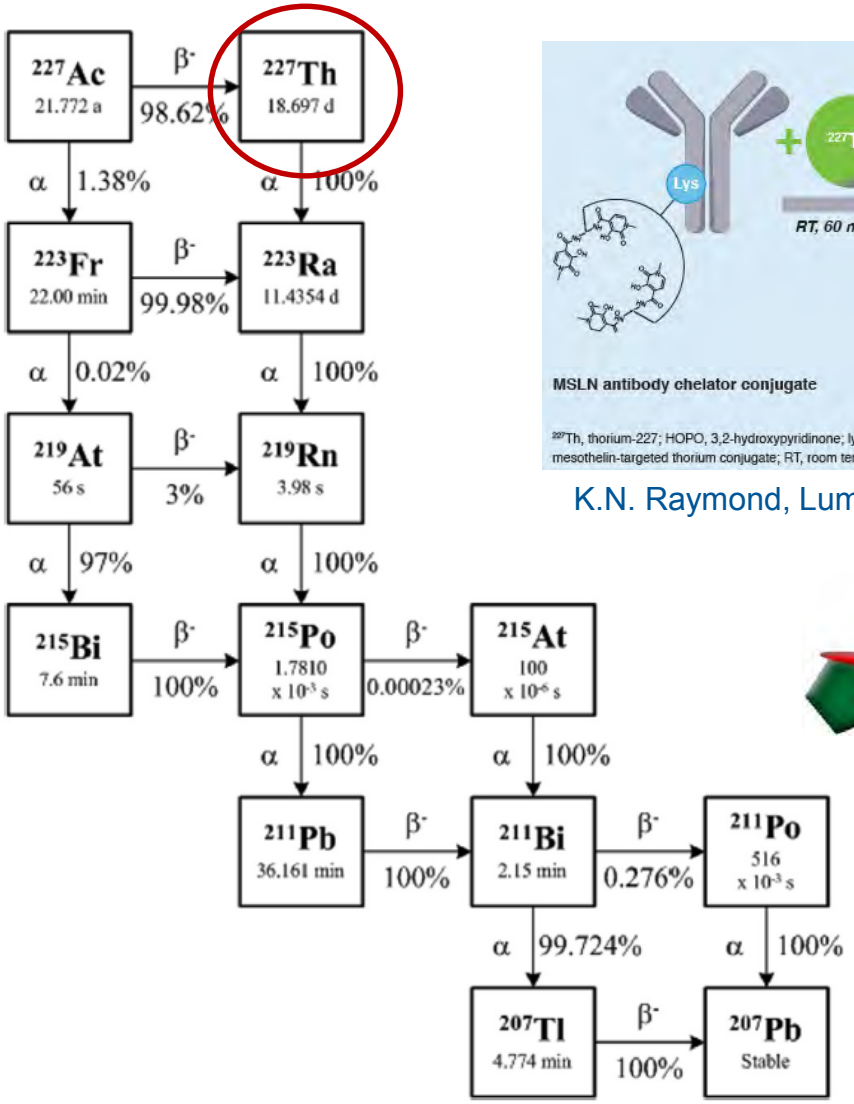
From “Radiation Science at the National Physical Laboratory, 1912-1955”, E. E. Smith.

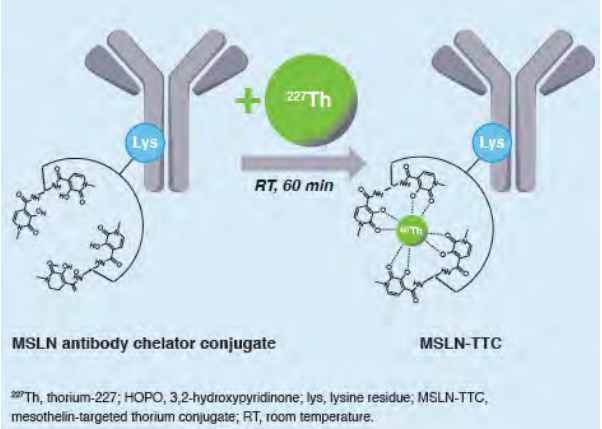
α-Emitting radionuclides for medical applications



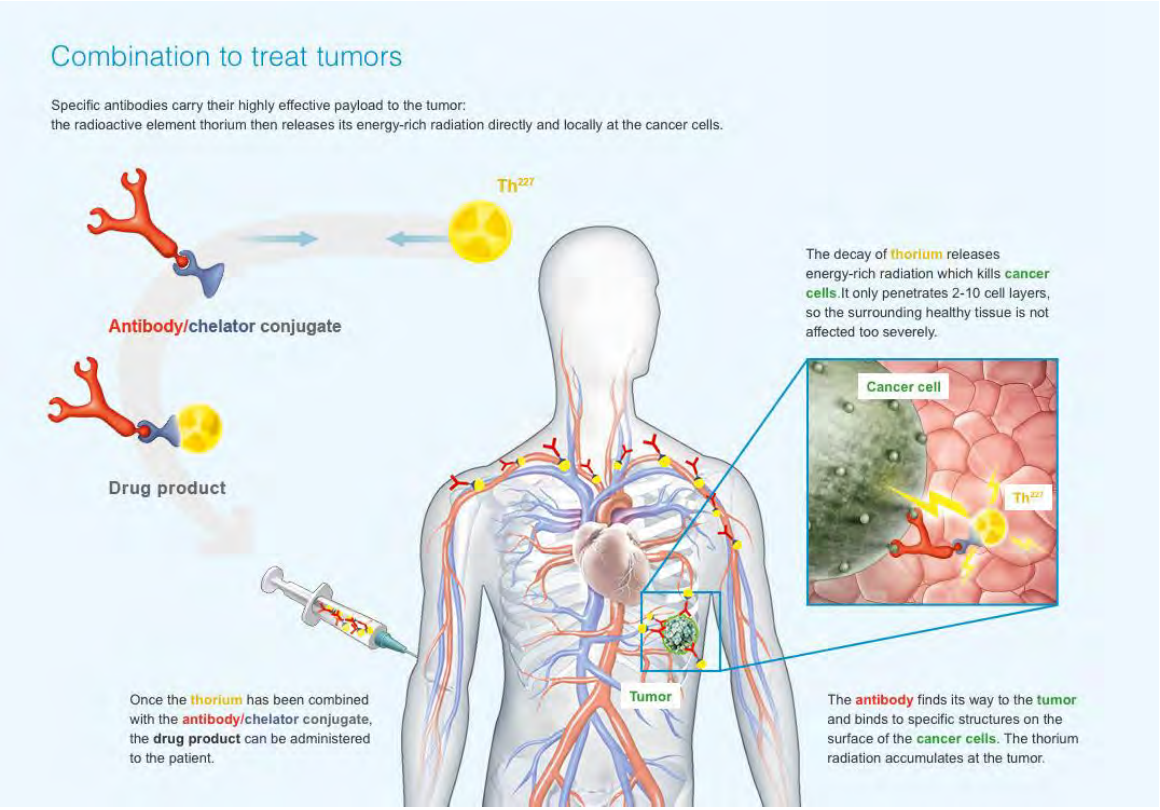
S. Westrøm *et al.* J Labelled Comp Radiopharm. 2018 May 30;61(6):472-486

^{227}Th for targeted alpha therapy

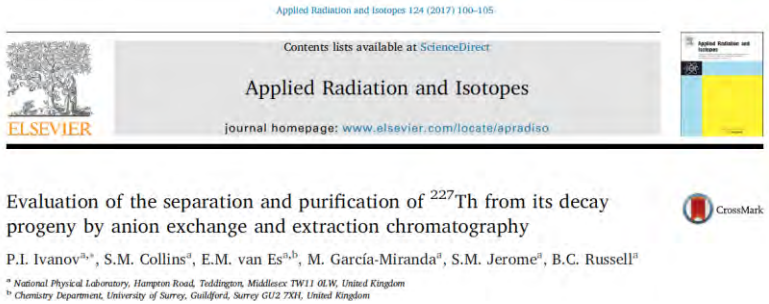




K.N. Raymond, Lumiphore, 35 (2016)



Bayer AS, https://www.research.bayer.com/en/fighting-cancer-with-radio-immunotherapy.aspx


Applied Radiation and Isotopes 124 (2017) 100–105

Contents lists available at ScienceDirect

Applied Radiation and Isotopes

journal homepage: www.elsevier.com/locate/apradiso

Evaluation of the separation and purification of ^{227}Th from its decay progeny by anion exchange and extraction chromatography

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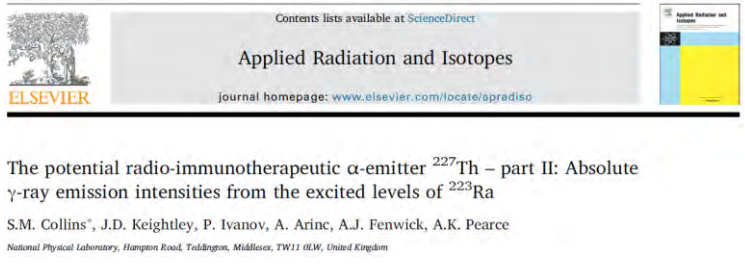
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The potential radio-immunotherapeutic α-emitter ^{227}Th – part II: Absolute γ-ray emission intensities from the excited levels of ^{223}Ra

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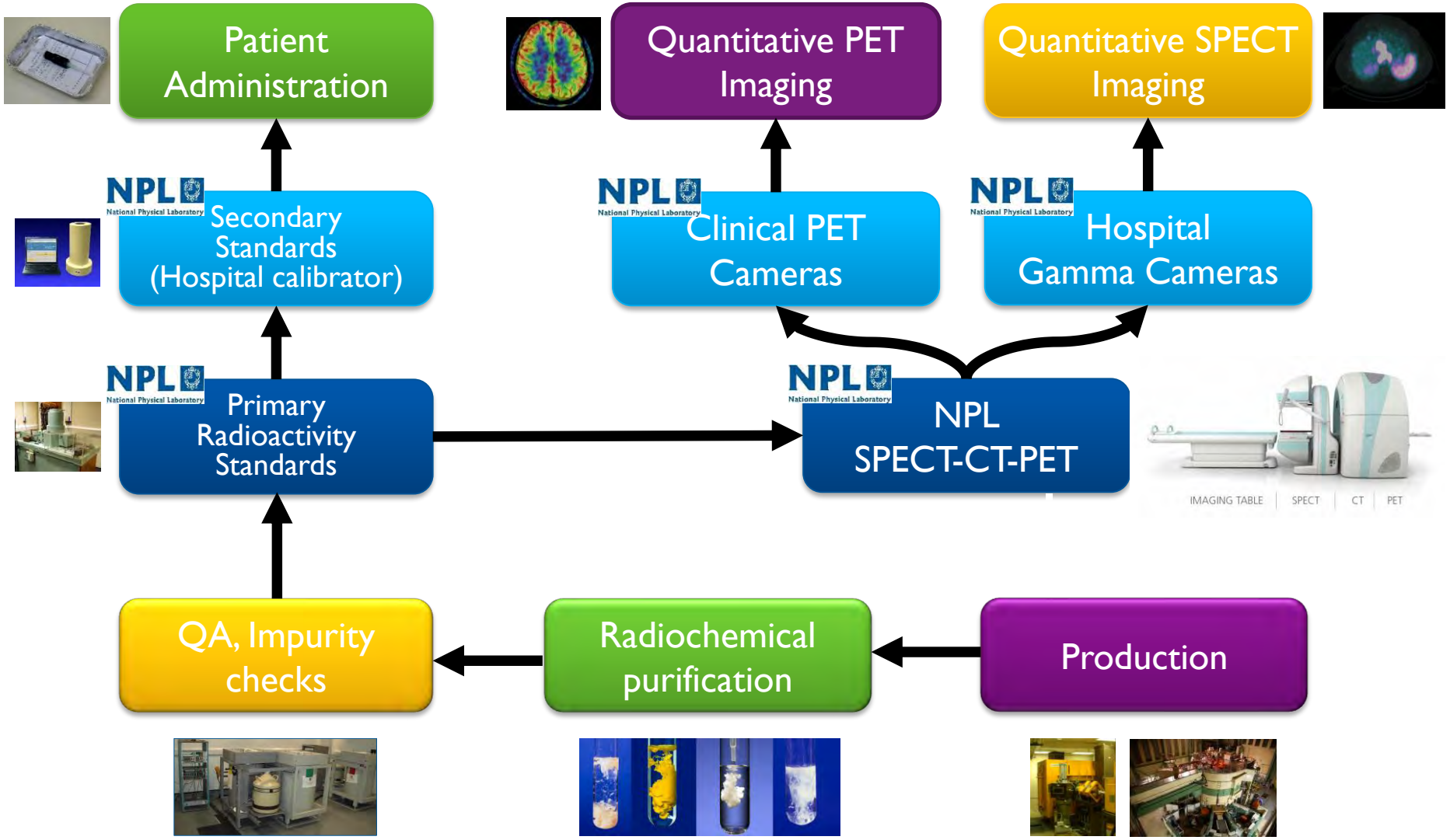
Stages towards application



Isotope production

- Neutron irradiation (high flux reactors)

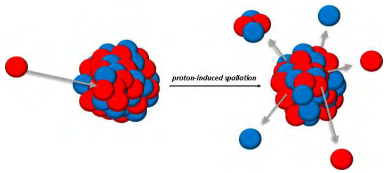
  $^{165}Ho(n, \gamma)\,^{166}Ho$ (26.8 h, β^-)

- Charged particle irradiations (cyclotrons)

  $^{89}Y(p, n)\,^{89}Zr$ (78.4 h, β^+)

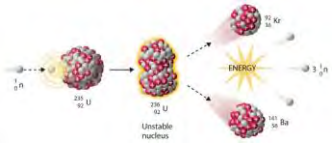
- High proton energy induced spallation (CERN)

  $^{nat}Ta(p, sp)\,^{155}Tb$ (5.3 d, EC)

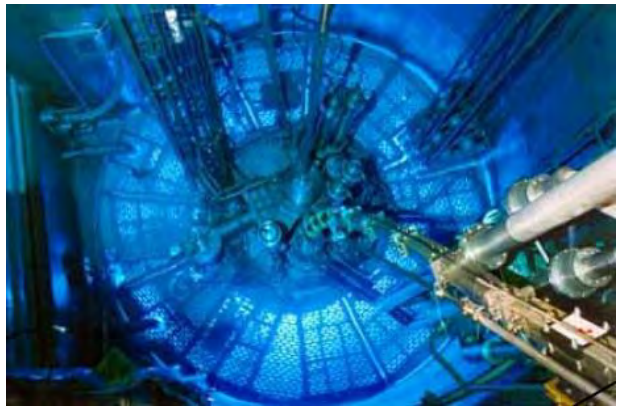


- Uranium fission (reactors or cyclotrons)

  (U-235 (n, f) FPs (^{99}Mo) (65.9 h, β^-)



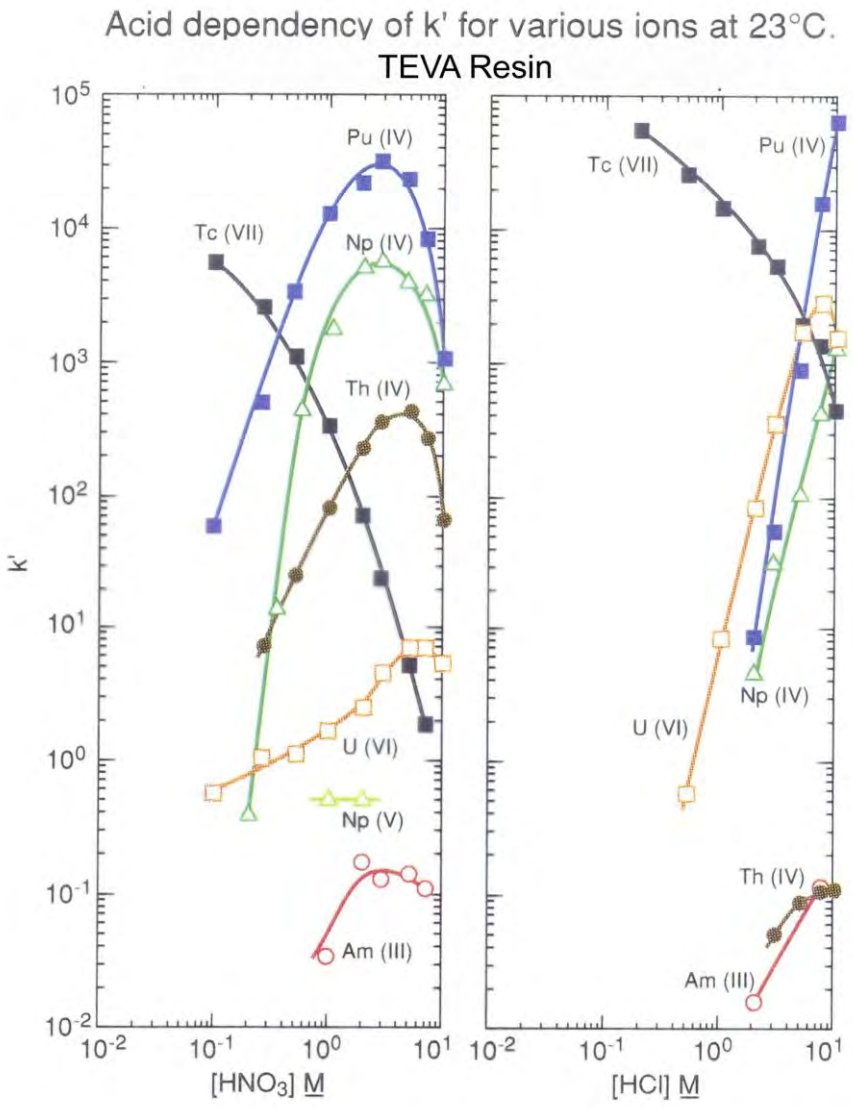
Neutron irradiation facility NPL



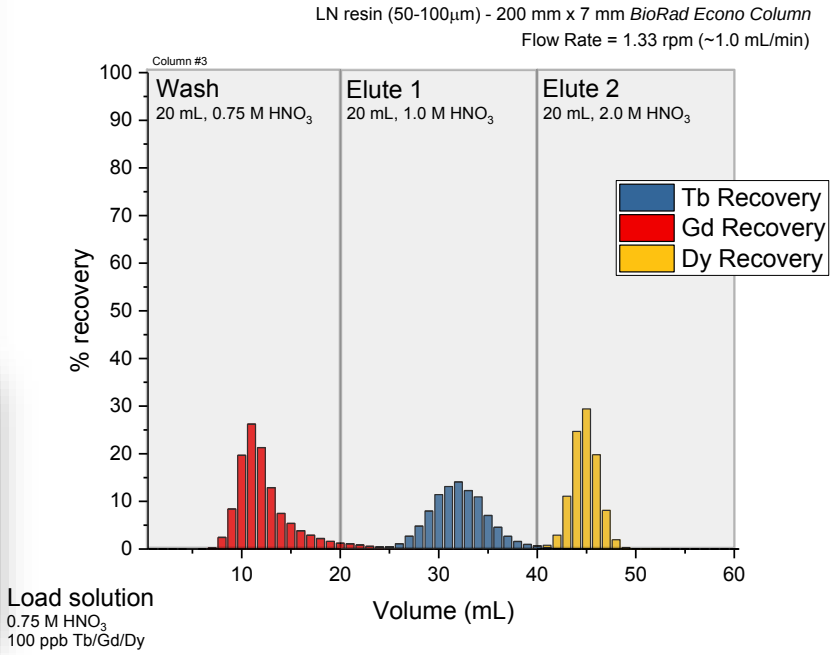
ILL Grenoble

Scanditronix MC40 Cyclotron (UoB)

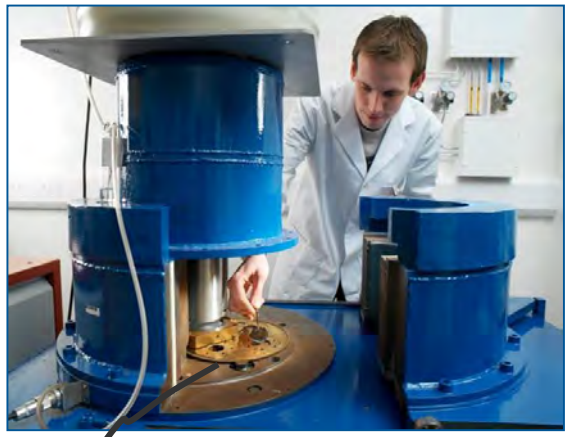
Radiochemical separation / purification

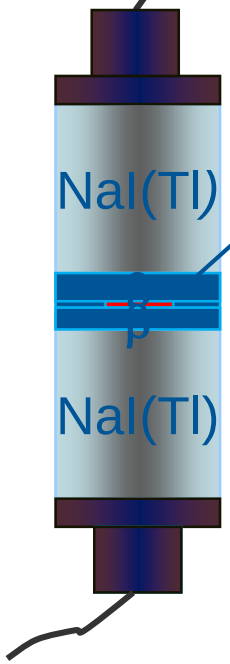


- Solvent extraction
- Ion-exchange
- Extraction chromatography
- Ion chromatography
- HPLC

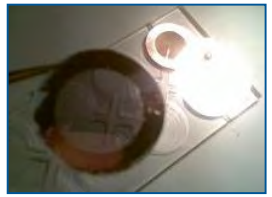


Radioactivity standards: Primary techniques (e.g. 4π β/γ coincidence counting)





Radioactive sample

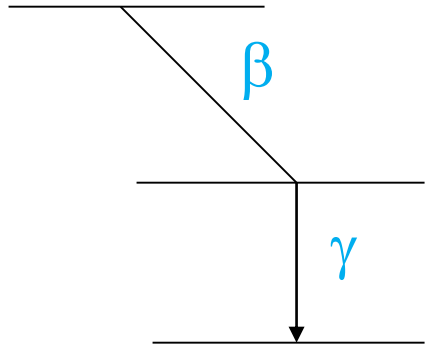


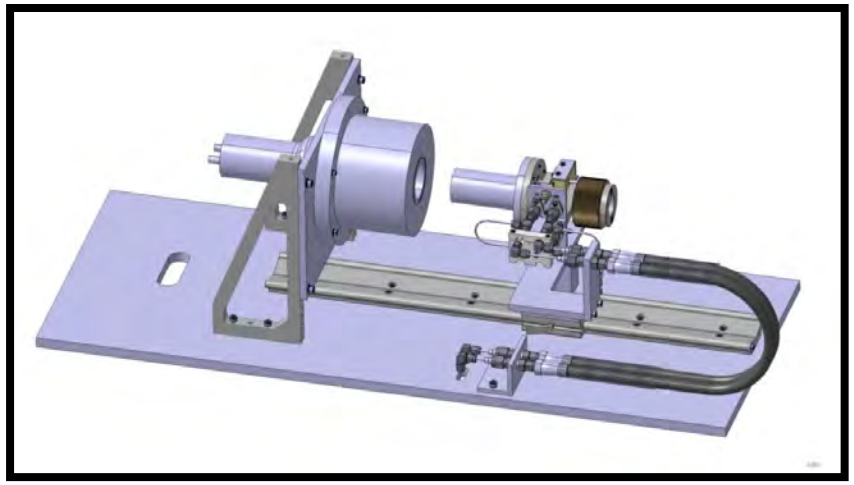
Count Rates

$N_\beta = N_o\, \varepsilon_\beta$

$N_\gamma = N_o\, \varepsilon_\gamma$

$N_c = N_o\, \varepsilon_\beta\, \varepsilon_\gamma$





Efficiencies: $\varepsilon_\beta = N_c/N_\gamma$

$\varepsilon_\gamma = N_c/N_\beta$

$$\textit{Activity}: N_o = \frac{N_\beta N_\gamma}{N_c}$$

Transfer of Primary Standards of Activity to Secondary Standard

Primary Standard (MBq/g)

↓

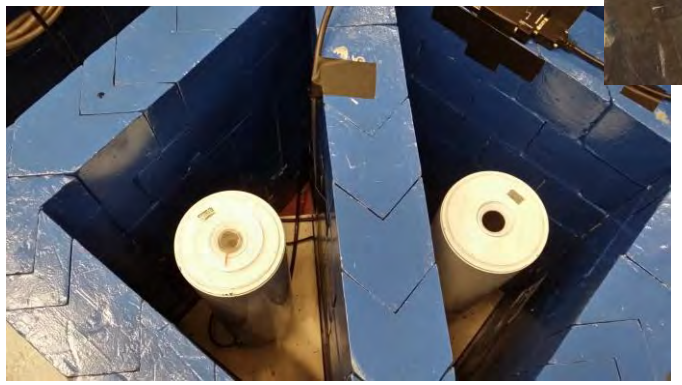
Secondary Standard Ionisation Chamber (pA/g)

↓

Calibration Factor (pA/MBq)

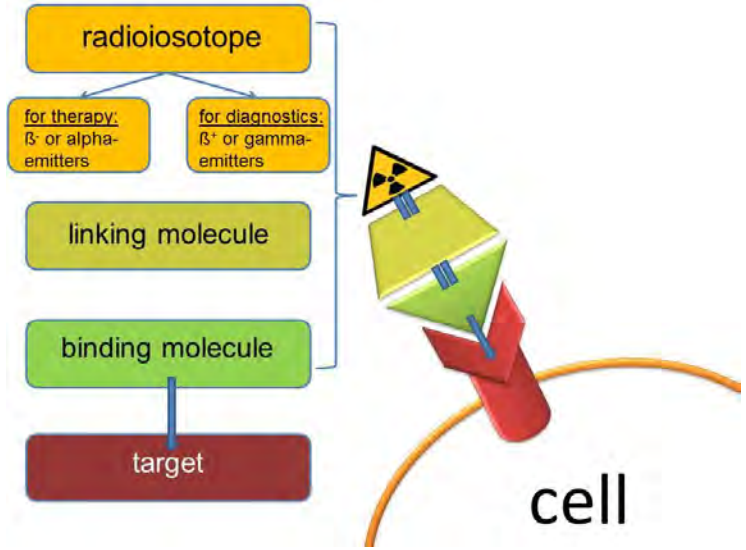
Fidelis : traceable link to NPL's Primary Standards

NPL Ion chambers



Theranostic approach

^{149}Tb	^{152}Tb	^{155}Tb	^{161}Tb
Alpha therapy	PET diagnostics	SPECT diagnostics	Beta/Auger therapy SPECT diagnostics
4.12 h	17.5 h	5.32 d	6.89 d

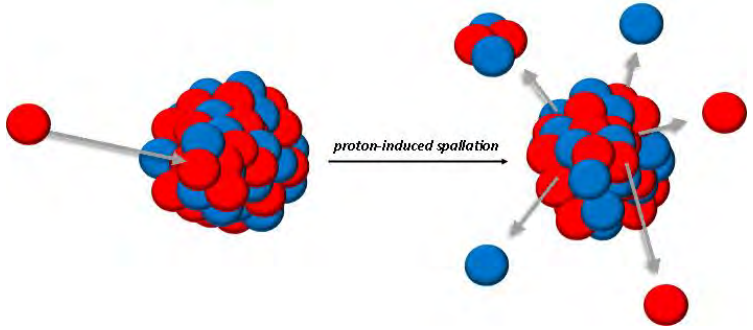


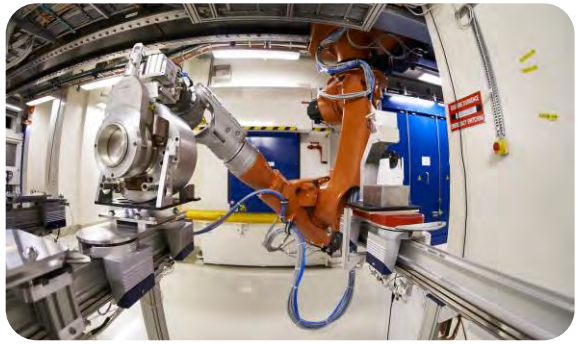
	Decay Mode	Half-life	MRT Application
^{149}Tb	α, β+ (17%, 7%)	4.12 hours	Therapy (α)
^{152}Tb	β+ (17%)	17.5 hours	PET Imaging
^{155}Tb	EC (100%)	5.32 days	SPECT Imaging
^{161}Tb	β- (100%)	6.89 days	Therapy (β-)

A. Yordanova, Theranostics in Nuclear Medicine Practice. *Preprints* **2017**, 2017 010094

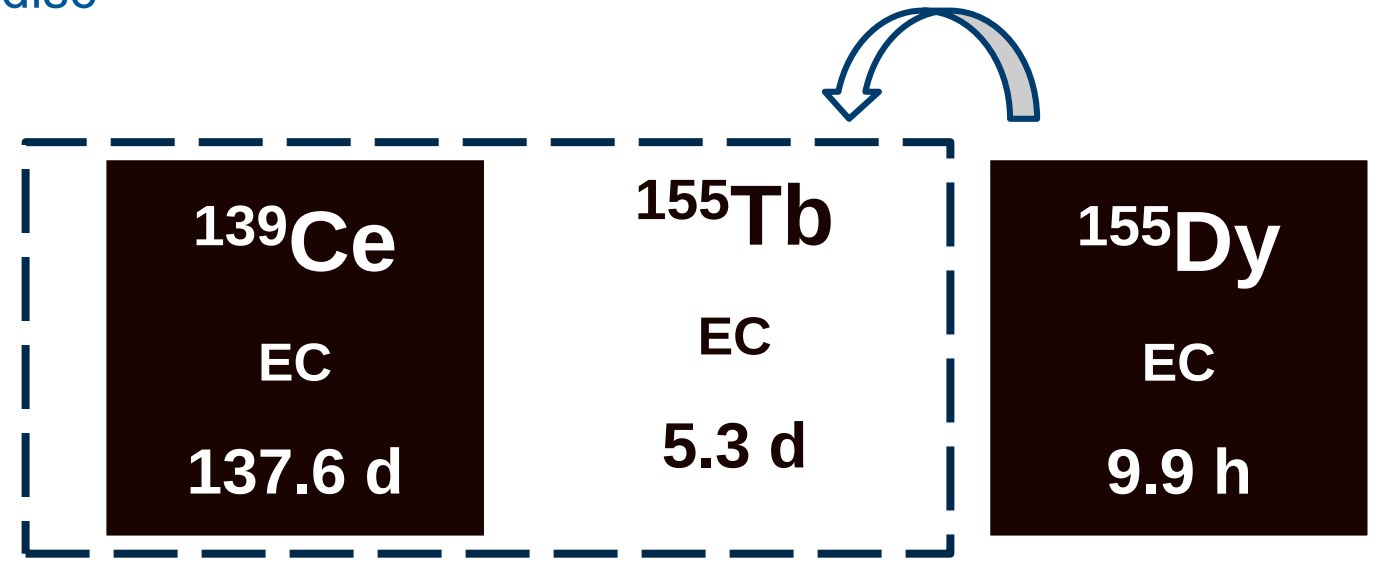
Production of ^{155}Tb at CERN

- Proton-induced spallation reaction
- Tantalum target
- On-line mass separation at 155 m/q
- Isotopes collected in a zinc-coated gold disc

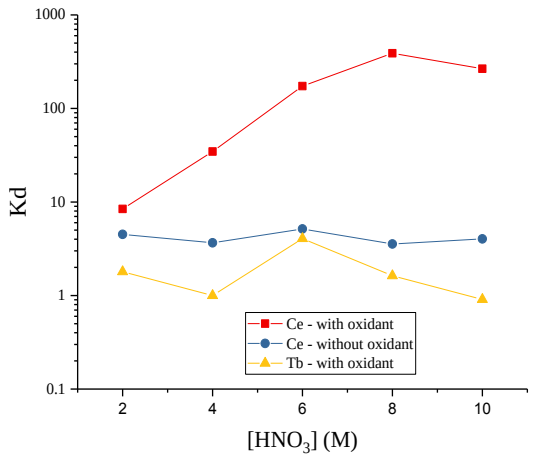


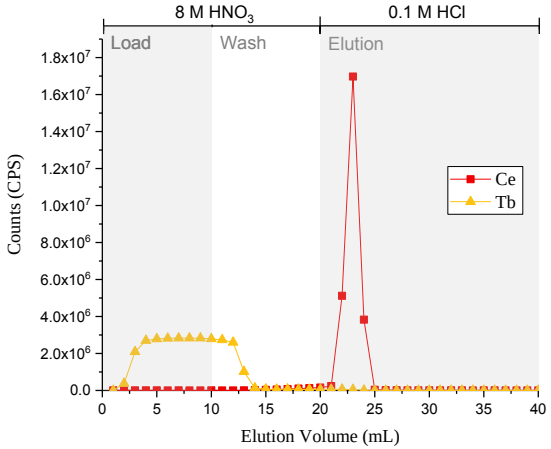


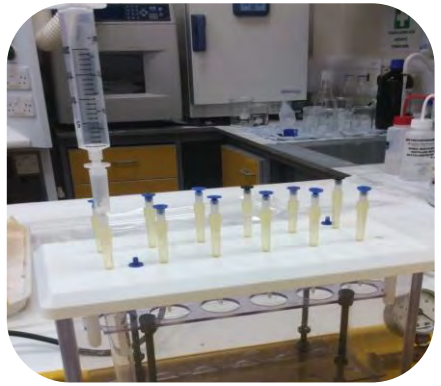
Impurities



Radiochemical purification







Supplied ^{155}Tb = ~ 8.1 MBq

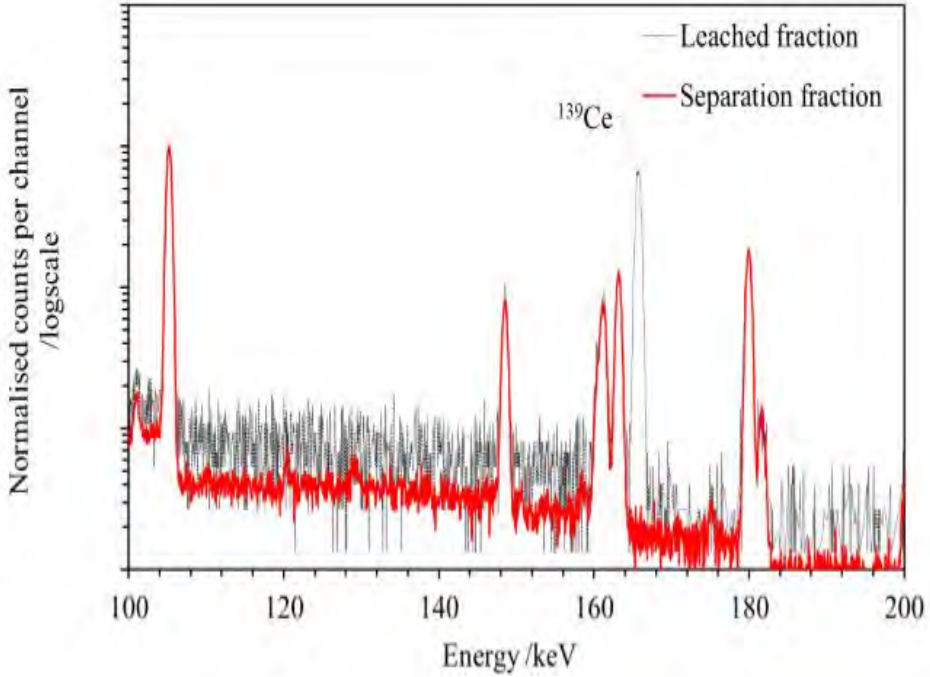
Before separation = $\frac{A_0(^{139}Ce)}{A_0(^{155}Tb)} \sim 31\%$

After separation = $\frac{A_0(^{139}Ce)}{A_0(^{155}Tb)} < 0.021\%$

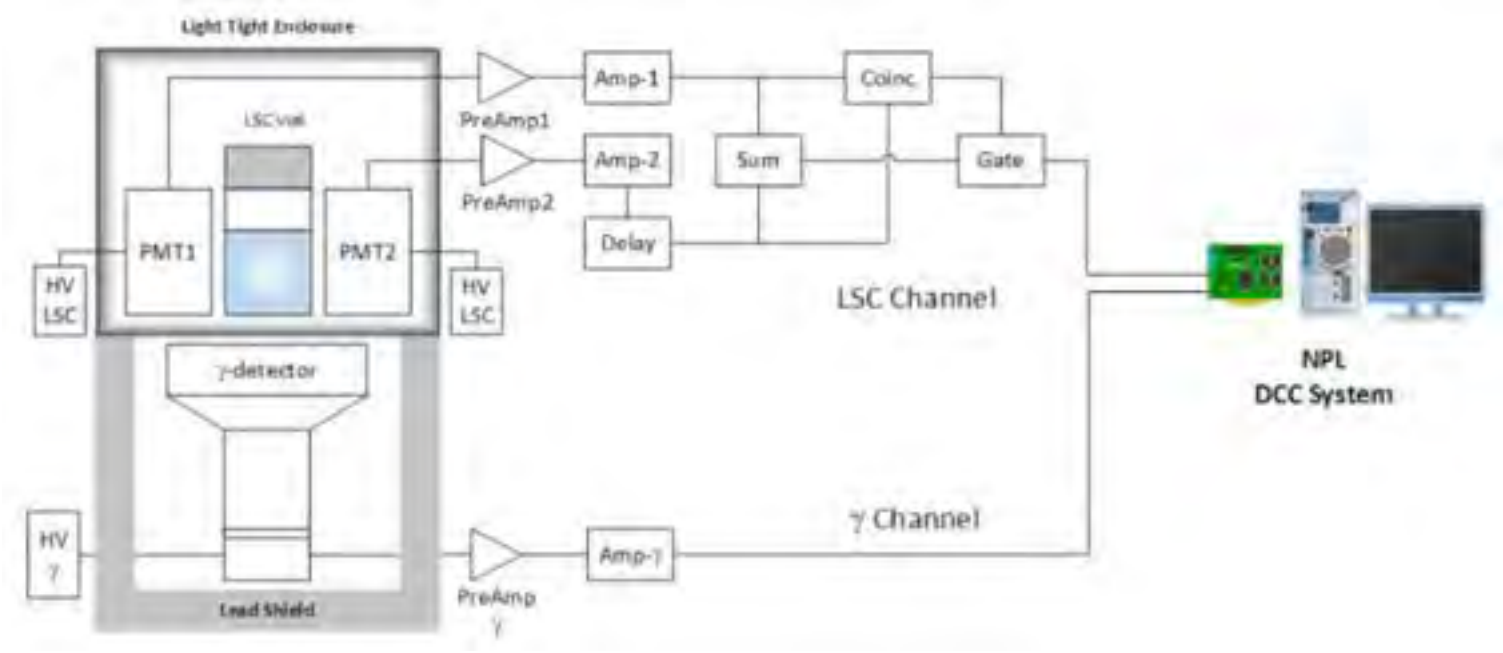
Selective oxidation of cerium:

Ce(III) → Ce(IV)

Tb(III) ~~→~~ Tb(IV)



^{155}Tb Primary standardisation



Schematic of the NPL 4π(Liquid Scintillation)-γ(HPGe) Digital Coincidence Counting system

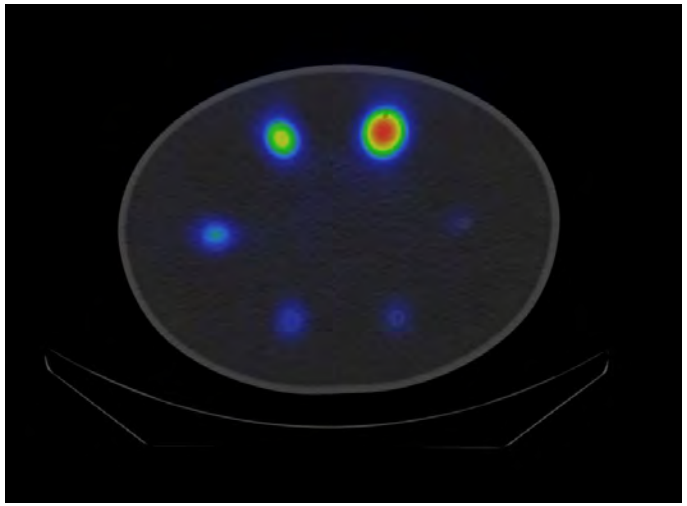
- A set of six sources measured
- For each the LSC channel efficiency varied by computer discrimination method
- The activity determined by extrapolating to 100 % efficiency

Preliminary activity at the reference time

(572.7 ± 2.9) kBq g^{-1} (k = 1)

^{155}Tb SPECT Imaging

NPL PET/SPECT camera



^{155}Tb SPECT imaging

National Physical Laboratory

National Measurement System

The National Measurement System delivers world-class measurement science & technology through these organisations

National Measurement Office | NPL National Physical Laboratory | LGC Setting standards in analytical science | nel technology for life

Thank you!

Questions?

The National Measurement System is the UK's national infrastructure of measurement Laboratories, which deliver world-class measurement science and technology through four National Measurement Institutes (NMIs): LGC, NPL the National Physical Laboratory, TUV NEL The former National Engineering Laboratory, and the National Measurement Office (NMO).