Международный семинар
«Развитие радиохимии и получение медицинских изотопов»
14 января 2022 года, Троицк-Москва, Россия

Институт ядерных исследований Российской академии наук

Стронций-82, олово-117m и актиний-225 – перспективные изотопы для получения на ускорителях протонов средних энергий

Strontium-82, tin-117m and actinium-225 – prospective isotopes for production by medium-energy proton accelerators

Stanislav Ermolaev

Production of ^{82}Sr from metallic Rb

$T_{1/2}$ = 25.55 d

A mother radionuclide for a short β^+-emitter ^{82}Rb (1.3 min) – positron emission tomography

Main nuclear route:

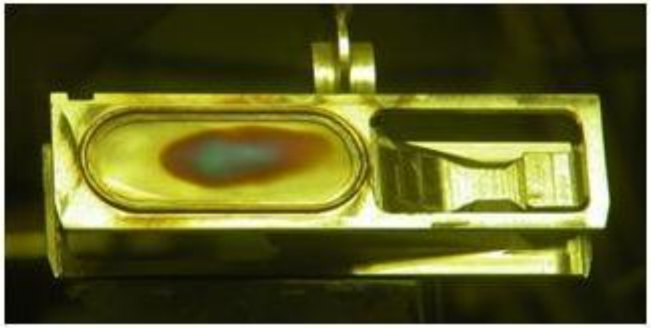
$^{nat}Rb(p,xn)$ E_p 35-100 MeV

Other approach:

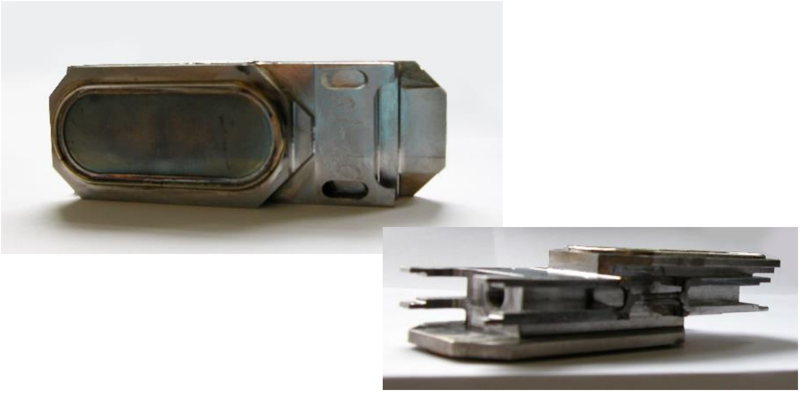
$^{nat}Mo(p,x)$ E_p 800 MeV

Metallic Rb Targets withstanding intensive irradiation

Thickness 3 cm



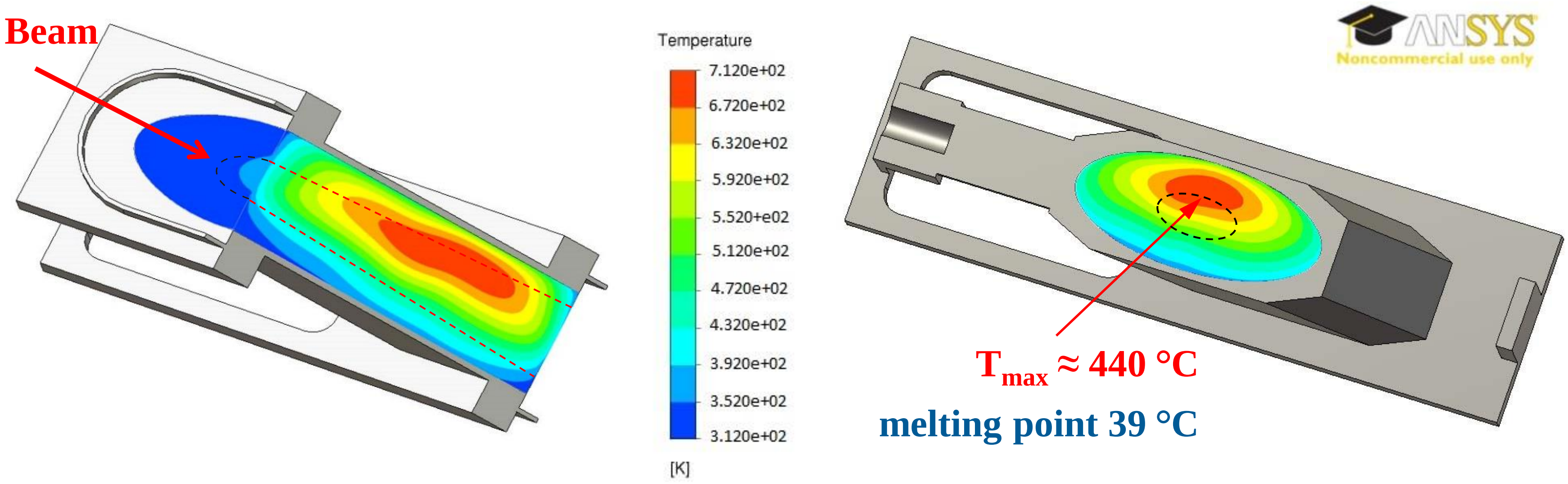
Thickness 2.3 cm



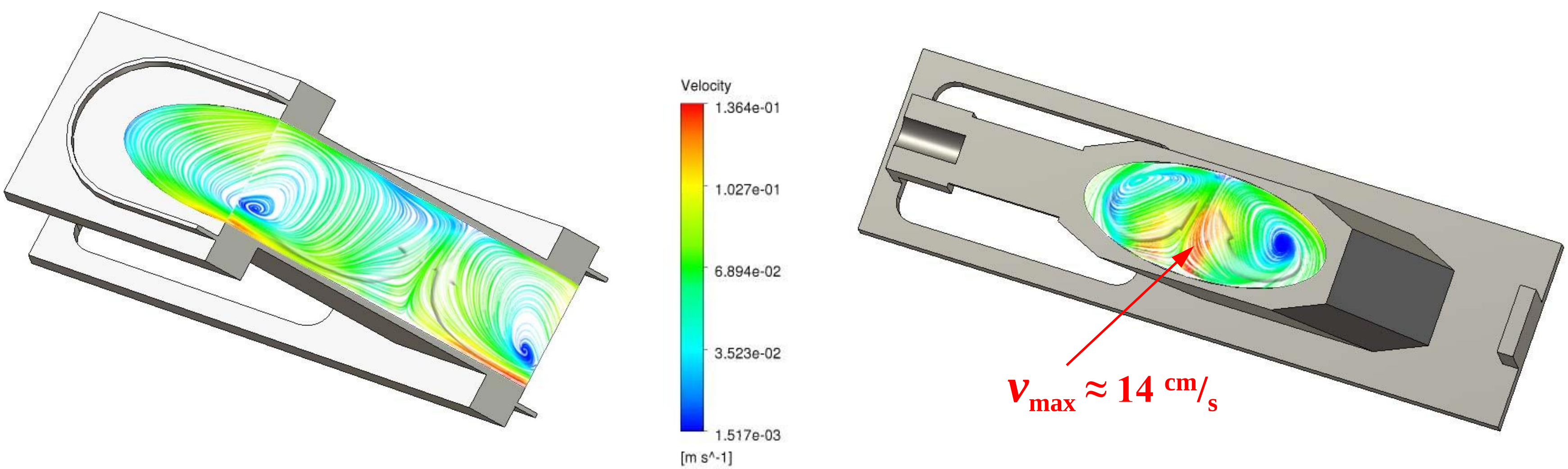
Calculated temperature and velocity distributions in liquid Rb

(at 100 μA beam current))

Temperature Distribution



Velocity Distribution

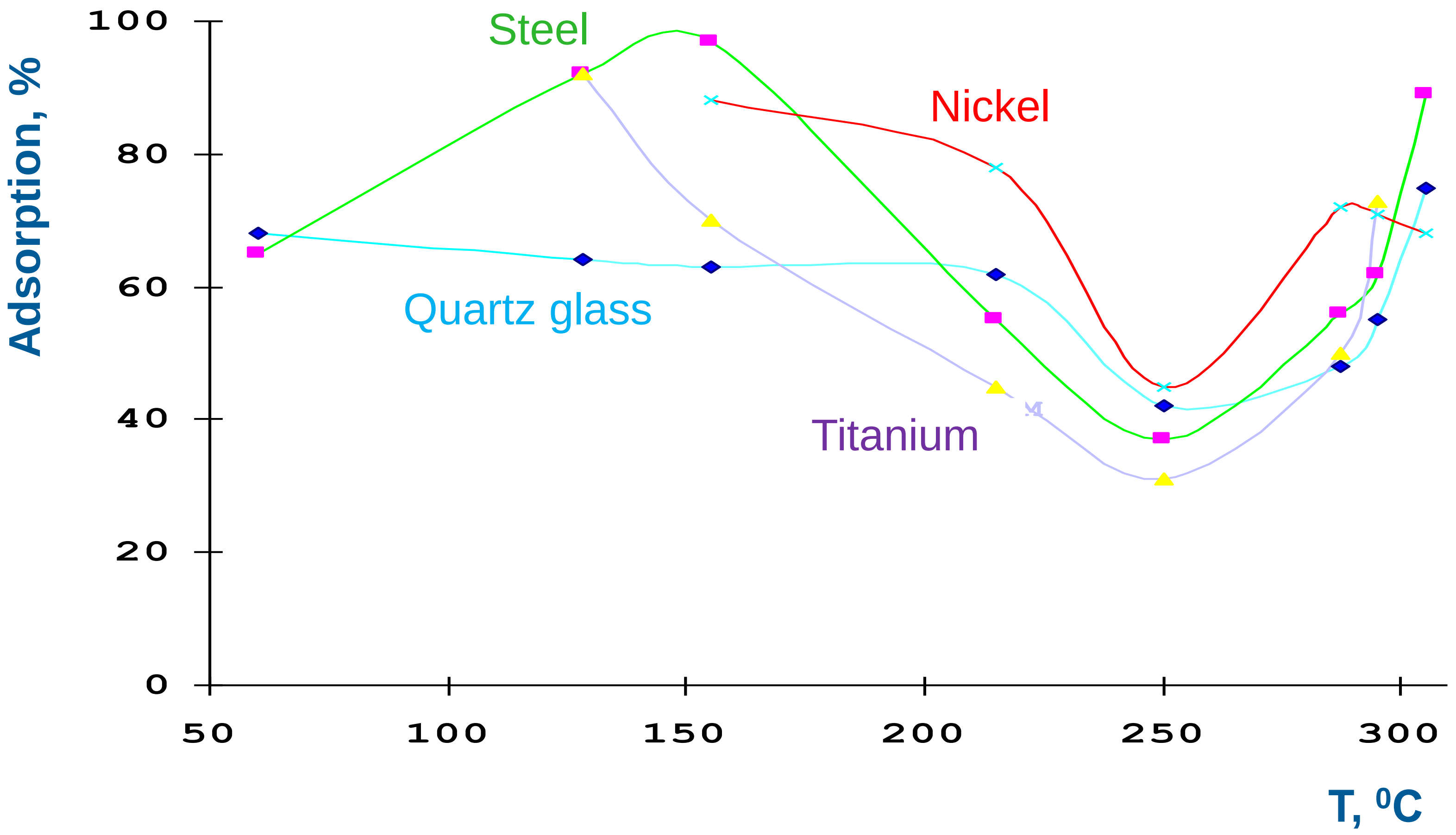


B.L. Zhuikov, S.V. Ermolaev. Radioisotope research and development at the Linear Accelerator of the Institute for Nuclear Research of RAS. *Phys. Usp.*, 2021, v. 64(12).

New approach: ^{82}Sr adsorption from liquid Rb

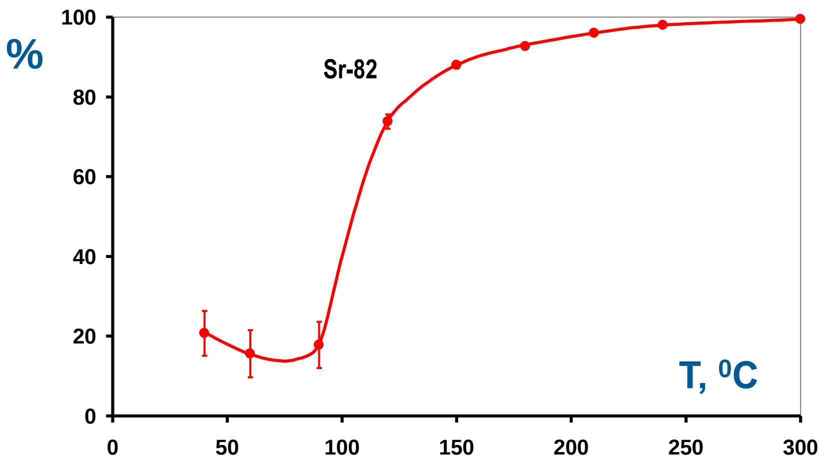
B.L. Zhuikov, V.M. Kokhanyuk, J.S. Vincent. Sorption of radiostrontium from liquid rubidium metal.

Radiochemistry, 2008, v. 50(2), p. 191-197.

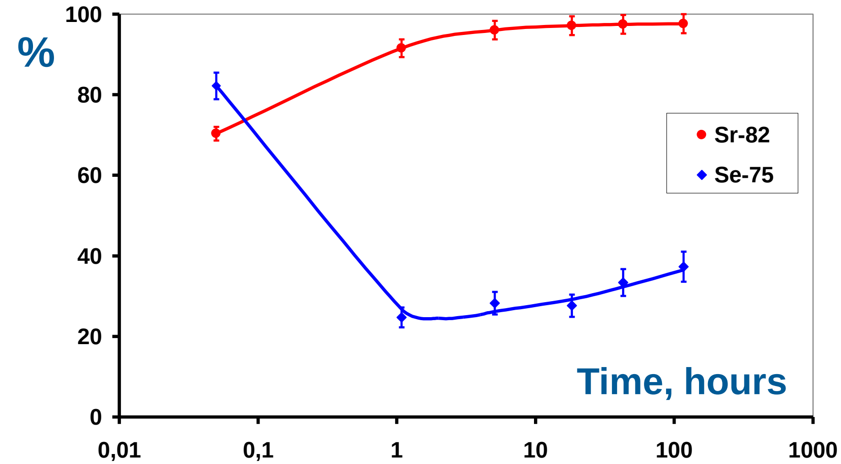


Direct ^{82}Sr adsorption inside a Rb target

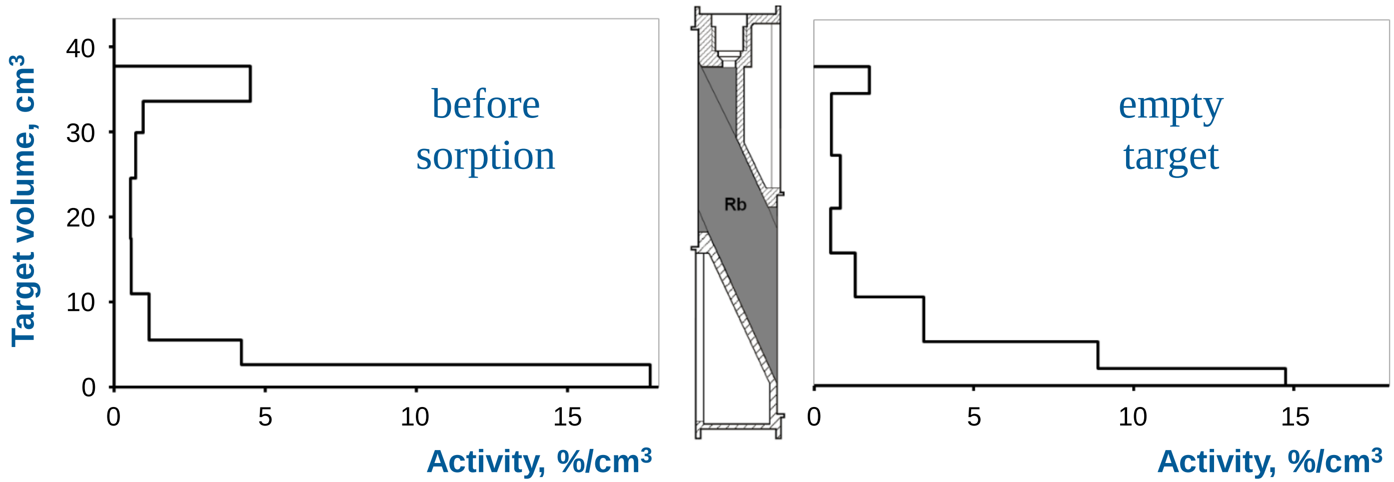
Temperature dependence



Adsorption kinetics at 270 ^{0}C



^{82}Sr Distribution Along Vertically Oriented Rb Target



Oxygen content

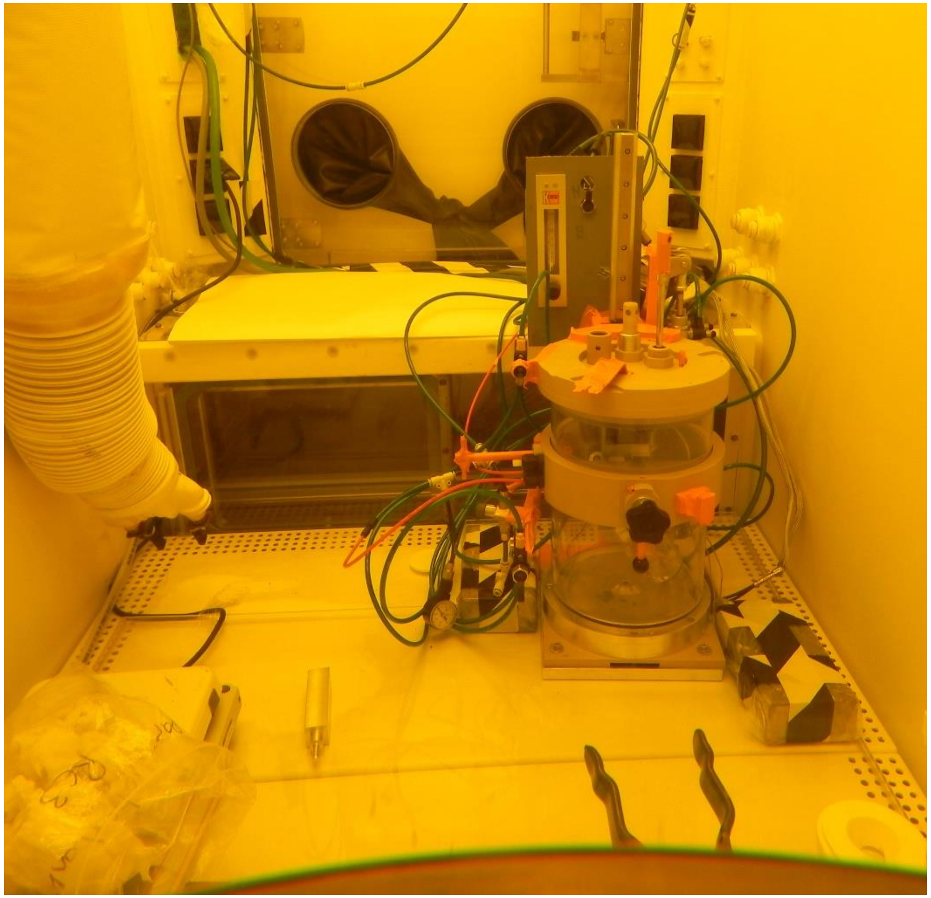
in metallic Rb

0.1 – 4 wt.%

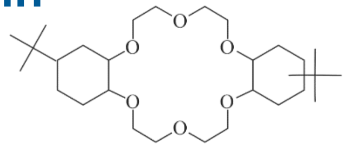
Installation of new technology of ^{82}Sr recovery

IPPE (Obninsk, RUSSIA)

ARRONAX (Nantes, FRANCE)



Final chromatographic purification using ion exchange or **Sr Resin**



Production of theranostic ^{117m}Sn from antimony

$T_{1/2}$ = 14.0 d

Therapy: conversion and Auger electrons. Diagnostics: γ-emission 159 keV

Main nuclear routes

$^{nat,121,123}Sb(p,x)$ E_p 20-70 MeV

Others:

$^{116}Cd(\alpha,3n)$

$^{116}Sn(n,\gamma)$ or $^{117}Sn(n,n'\gamma)$

Targets withstanding intensive irradiation

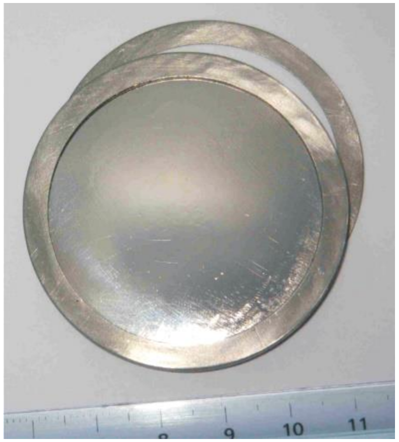
Metallic Sb

in graphite shell

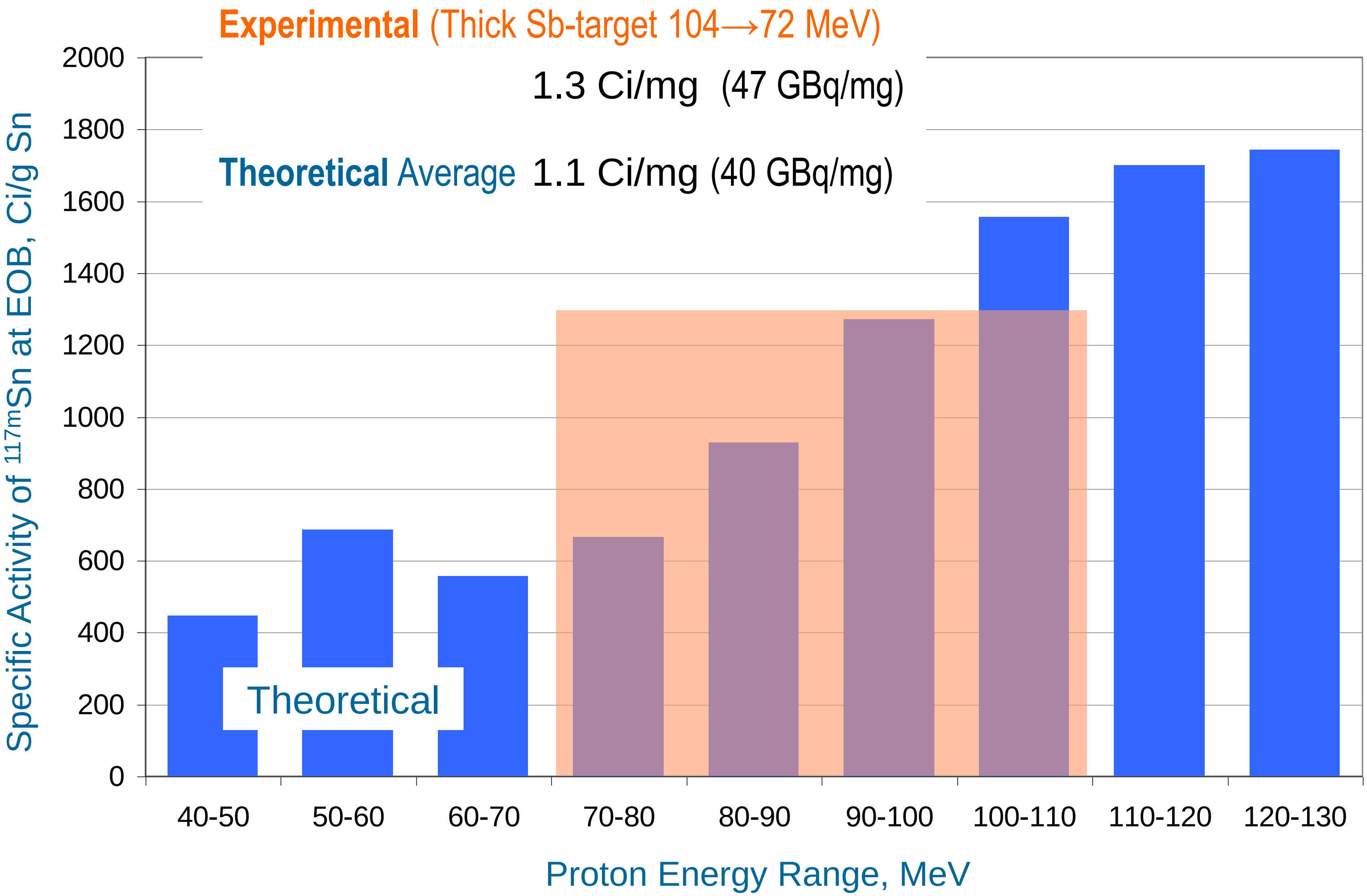
TiSb

intermetallic

compound

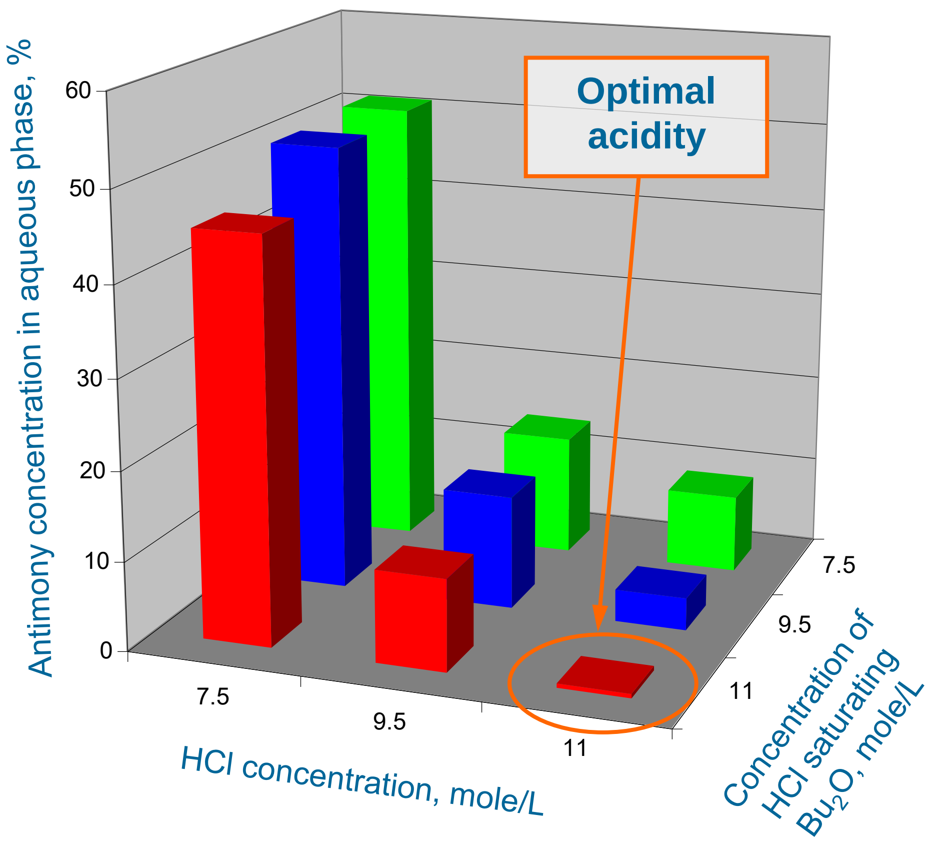


High specific activity of proton-produced ^{117m}Sn

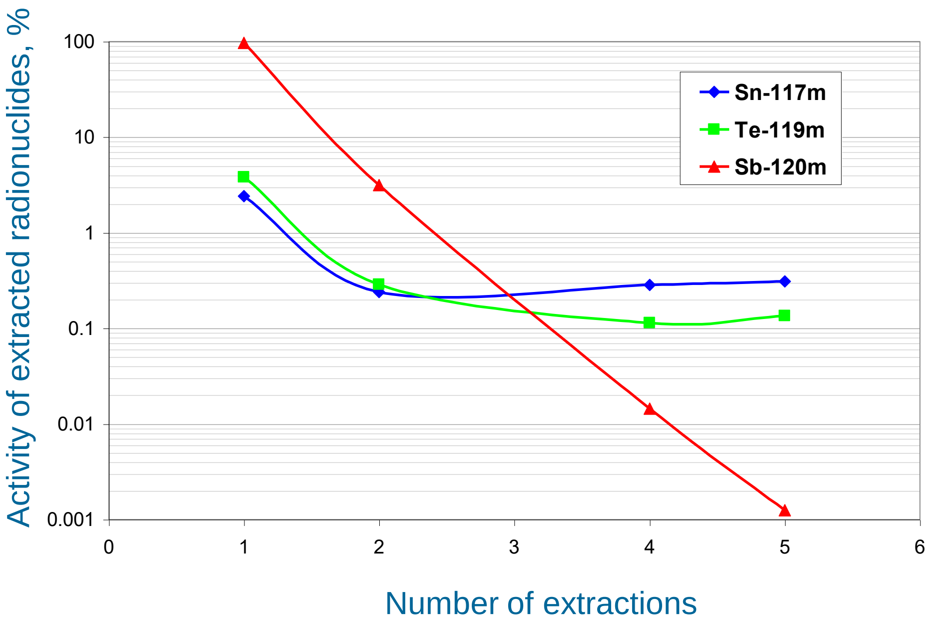


Extraction of antimony with dibutyl ether

Effect of HCl concentration



Multi-stage extraction



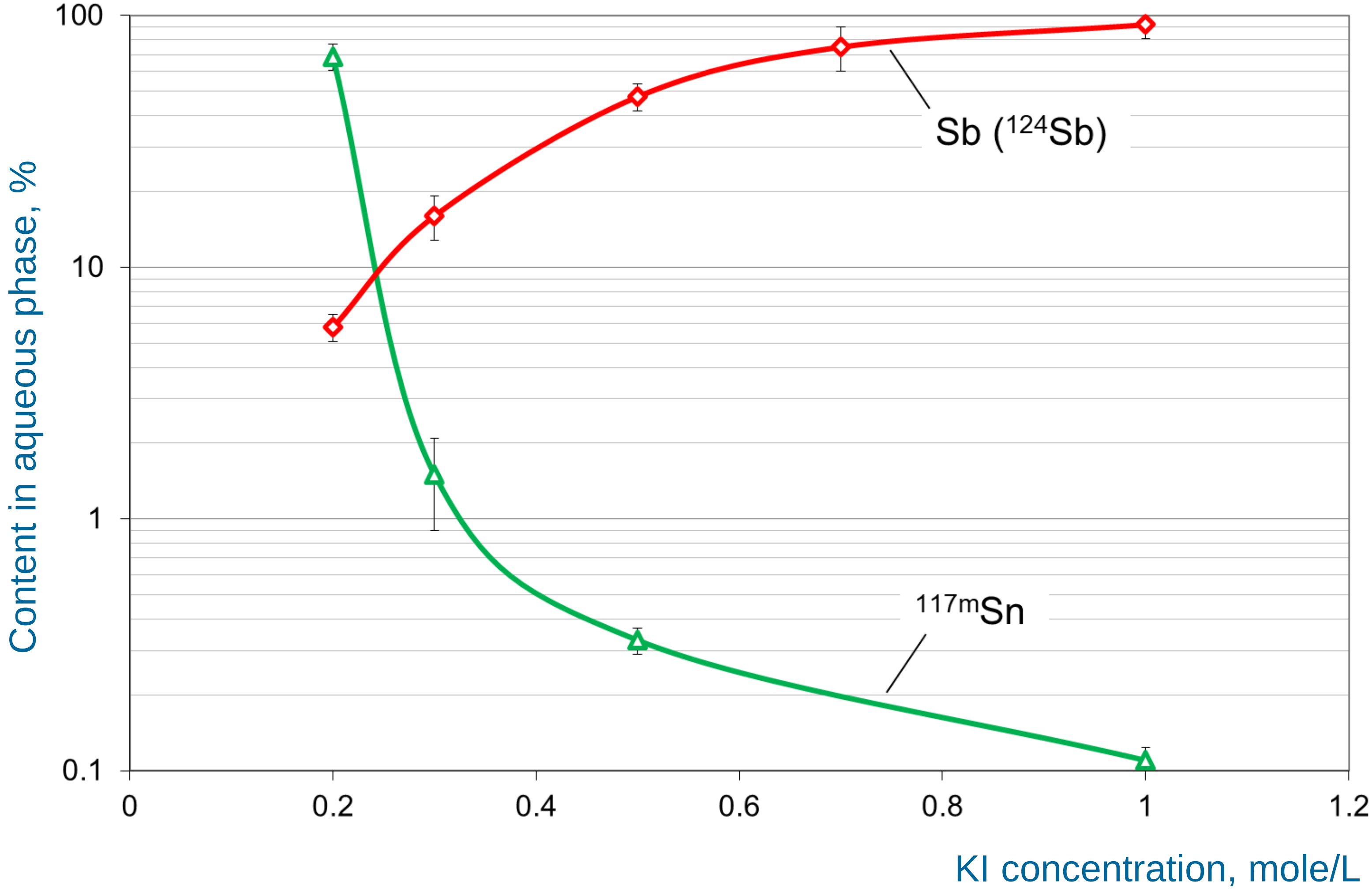
3-5 extractions remove most of Sb

Separation of ^{117m}Sn from Ti and the rest of Sb: Extraction

Organic phase: benzene

Aqueous phase: KI + mixture $HClO_4$, H_2SO_4

> 99.9% Ti remains in aq. phase



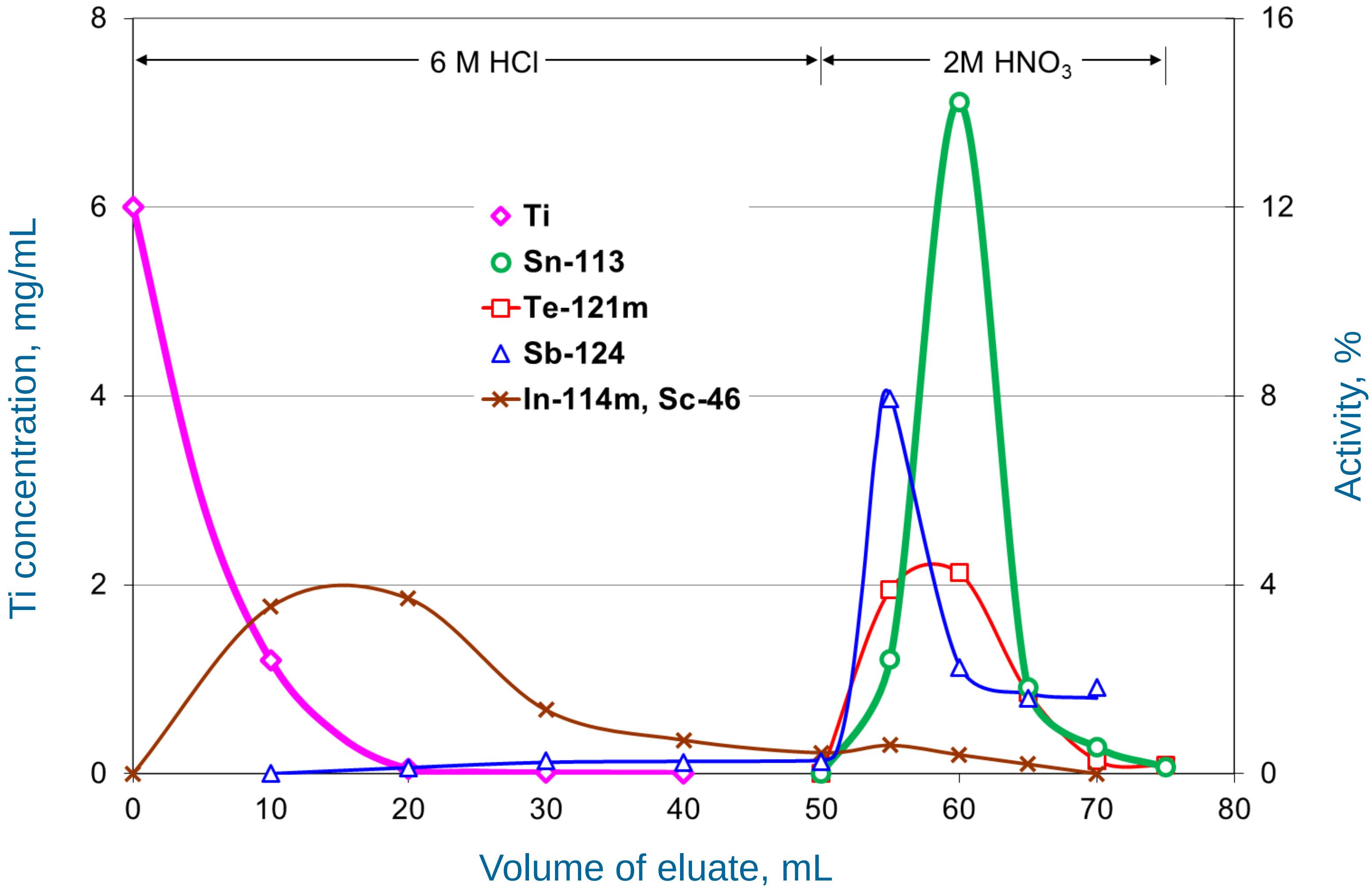
Separation of ^{117m}Sn from Ti: Ion exchange

Sorbent: AG 1x8

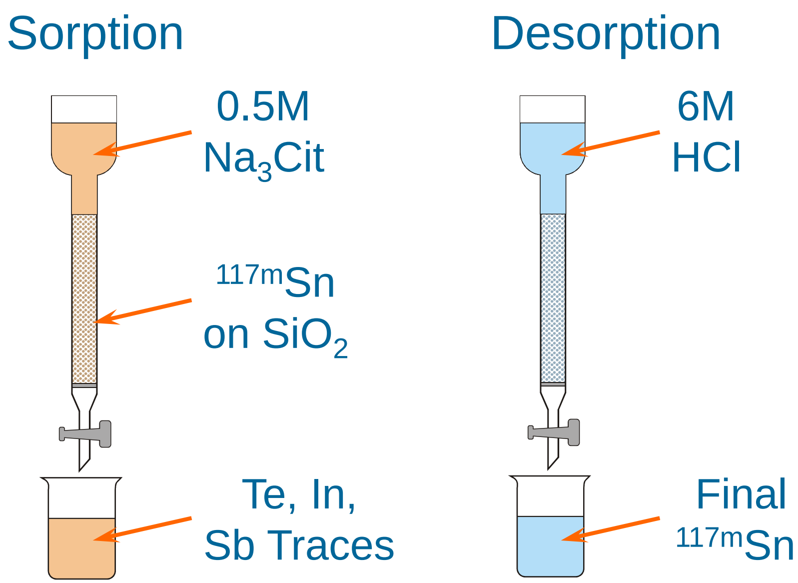
Separated ion complexes

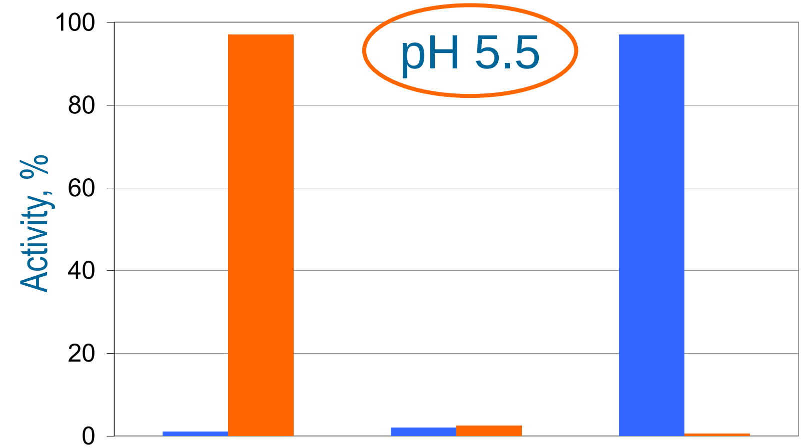
Cation: $[SnCl_6]^{2-}$

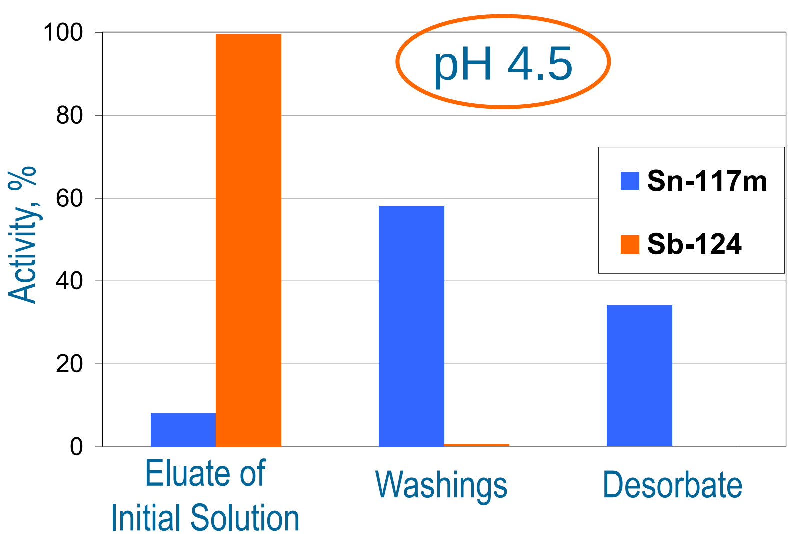
Anion: $[TiO(H_2O_2)]^{2+}$ (H_2O_2:Ti = 1.5:1)

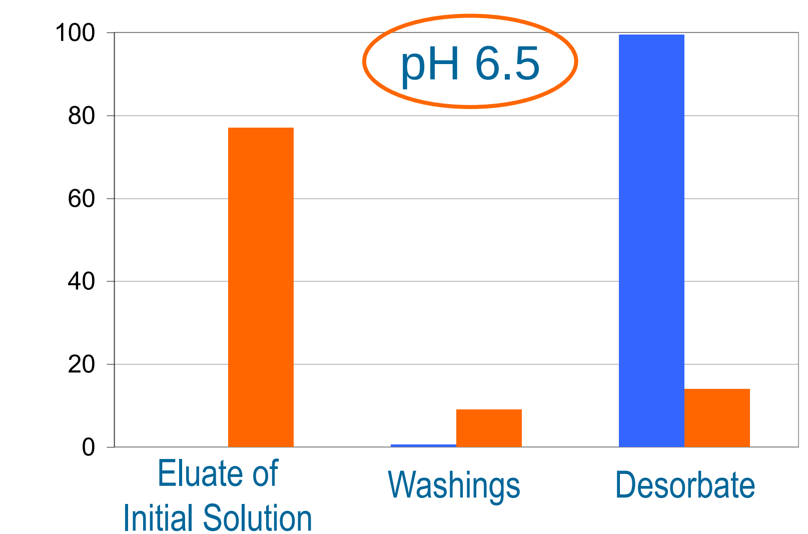


Fine ^{117m}Sn purification on a SiO_2 column from citrate solution

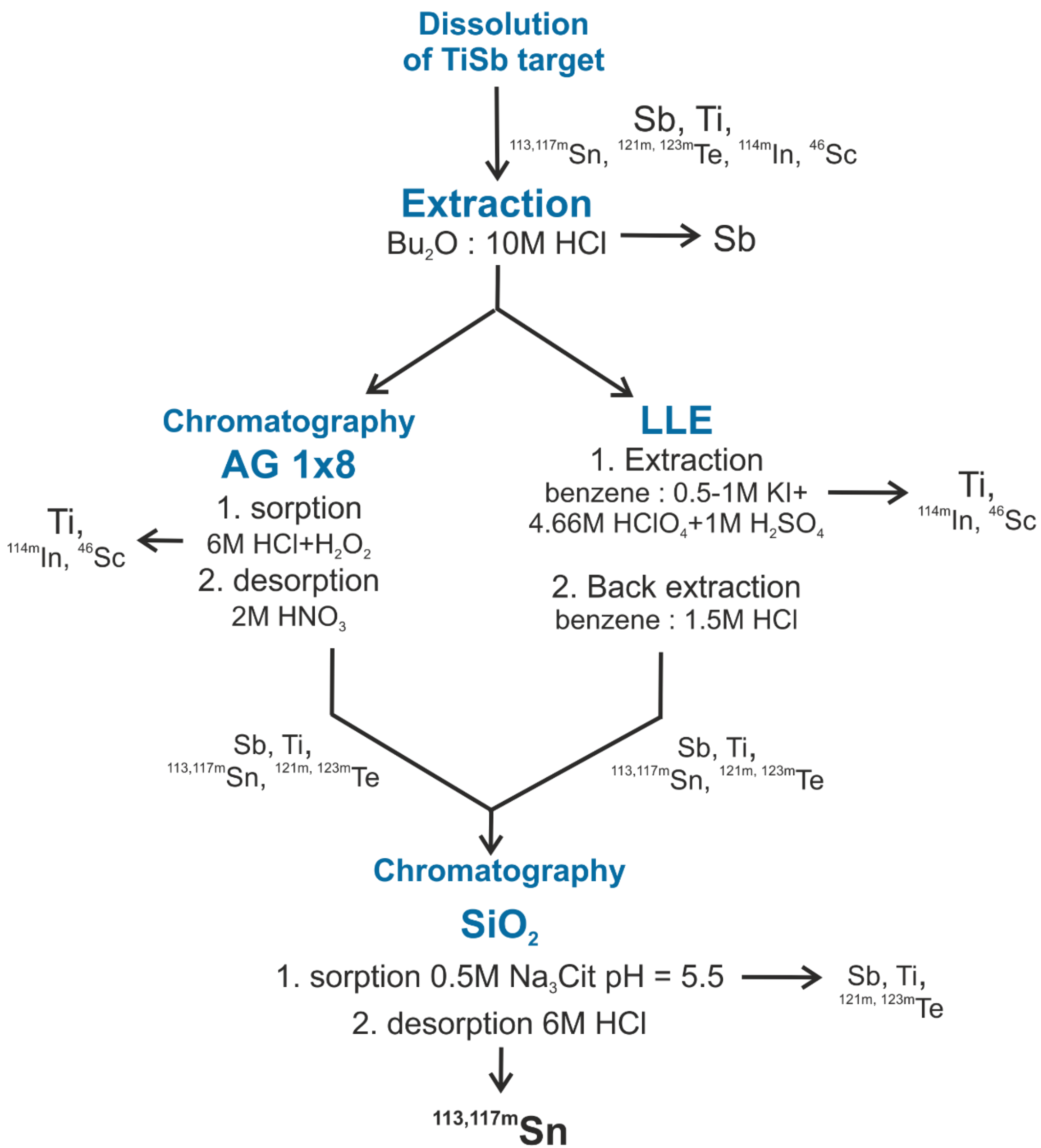








Overall scheme of ^{117m}Sn recovery



Chemical yield **75-85%**

Radionuclidic purity (excepting ^{113}Sn) **> 99.7%**

Purification from Sb and Ti **~ 10^6**

2-5 GBq samples of **no-carrier-added ^{117m}Sn** were shipped to BNL for quality analyses, biological and preclinical studies

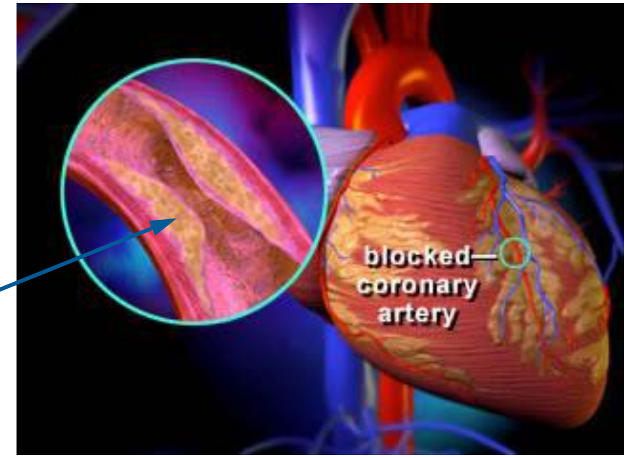
Prospective applications of theranostic ^{117m}Sn

Nigel R. Stevenson

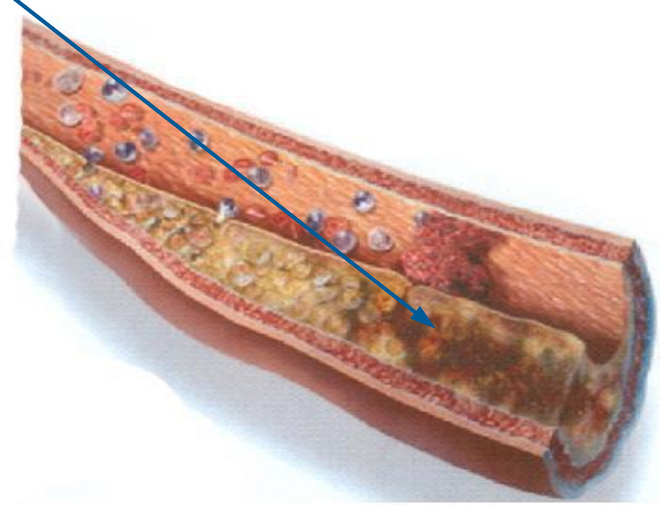
“Harnessing ^{117m}Sn for Improved Quality of Life”

10ICI, Kuala Lumpur, 2020

- Cardiology (vulnerable/unstable plaques)
- Rheumatology
- Neurology (Alzheimer’s)
- Oncology
- Veterinary



Luminal calcified plaque



Extra-luminal vulnerable plaque

Production of ^{225}Ac from thorium

$T_{1/2}$ = 9.9 d

Emission of α-particles: high LET in short range (~ 10 cell diameters). ^{225}Ac/^{213}Bi generator

Main nuclear routes

- ^{233}U (1.6·10^5 a) → ^{229}Th (7340 a) → ^{225}Ra → ^{225}Ac

- ^{226}Ra (3n, 2β$^-$) → ^{229}Th → ^{225}Ra → ^{225}Ac
- ^{226}Ra (p, 2n) → ^{225}Ac
- ^{226}Ra (n, 2n) → ^{225}Ra → ^{225}Ac
- ^{226}Ra (γ, n) → ^{225}Ra → ^{225}Ac

- ^{232}Th (p, *xpyn*) → ^{225}Ac E_p > 70 MeV

Annual production of ^{225}Ac from ^{229}Th, GBq (mCi)

Institution	JRC ITU (EC)	ORNL (USA)	IPPE (Russia)
Stock of ^{229}Th	1.7 (45.6)	5.55 (150)	5.55 (150)
Maximal annual production of ^{225}Ac	13 (350)	26 (700)	22 (600)
Maximal batch size	1.3 (35)	2.2 (60)	1.85 (50)

Totally:

60-70 GBq (1.7-1.8 Ci) ^{225}Ac → **100-200 patients per year**

USA demand for ^{225}Ac (DOE estimation) – **100-200 Ci** per year

^{225}Ac production via irradiation of ^{232}Th with medium-energy protons (200-70 МэВ)

1.5 – 2 Ci ^{225}Ac in 7-10 days (impurity ~0.1% ^{227}Ac)

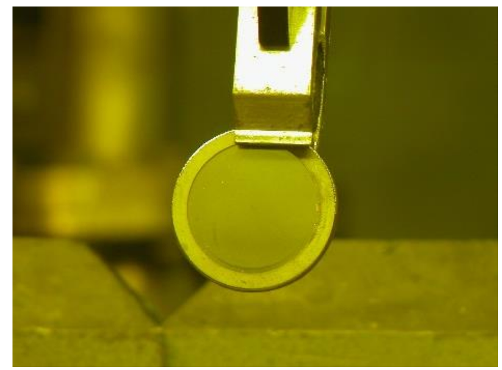
Th Targets withstanding intensive irradiation

INR Diffusion Welding facility
located at the SIA Luch (Russia)

Target of metallic thorium
encapsulated in niobium

Before irradiation

After irradiation



More than 80 radionuclides were identified in proton-irradiated thorium – products of nuclear spallation and fission and products of their decay: **^{228,229,230,232,233}Pa**, **^{227,228,231}Th**, **^{225,226,227}Ac**, **^{90,91}Sr**, **^{88,90}Y**, **^{95,97}Zr**, **^{95,96}Nb**, **^{99}Mo**, **^{103,106}Ru**, **^{105}Rh**, **^{110m,111}Ag**, **^{115}Cd**, **^{125}Sn**, **^{120,122,124,125,126,127,128}Sb**, **^{129m,131m,132}Te**, **^{126,130,131,133,135}I**, **^{132,134,136,137}Cs**, **^{140}Ba**, **^{140}La**, **^{139,141,143,144}Ce**, **^{147}Nd**, **^{148m}Pm** etc.

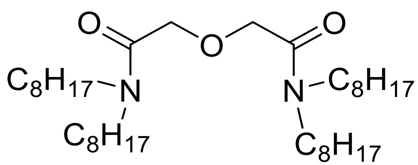
Concentration of Ac and REE fraction

Aqueous Phase

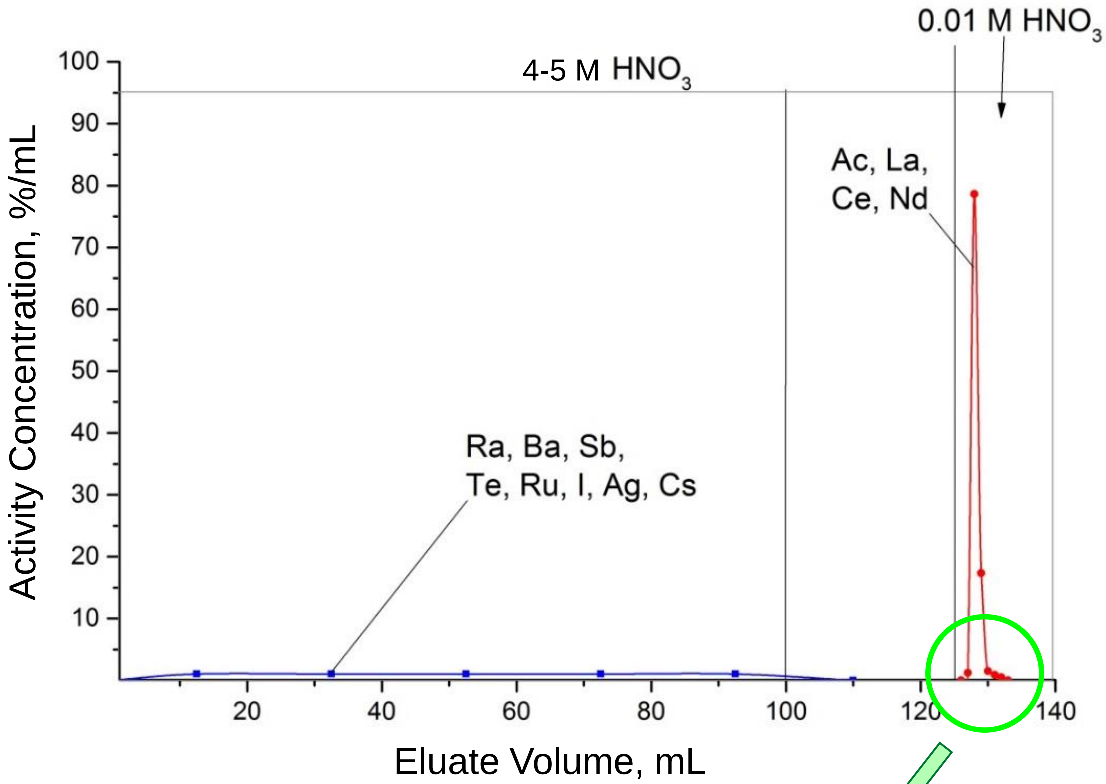
directly after Th extraction

with HDEHP solution in toluene

DGA Resin



Mode of straight flow of solutions –
outgoing solution of a step serves as incoming solution for the next step

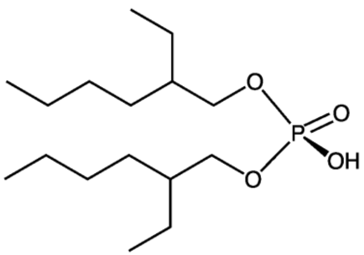


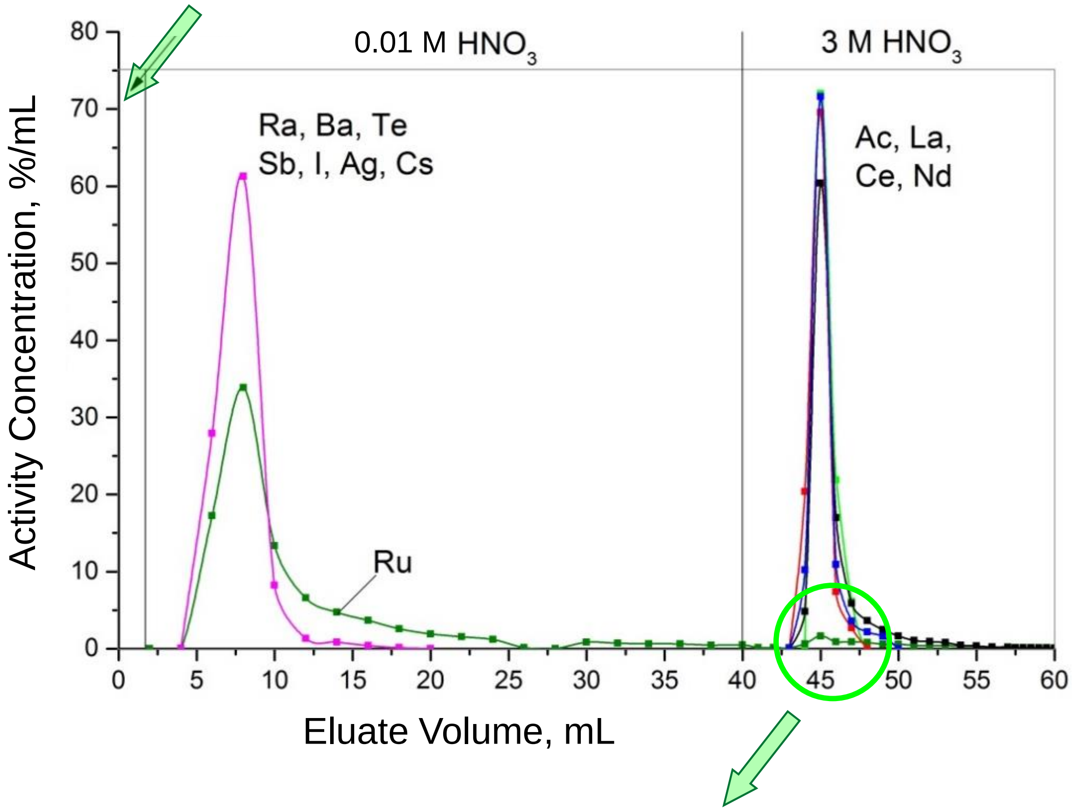
Ln Resin

Purification of Ac and REE fraction

No auxiliary steps or evaporations – an advantage for hot cell realization

Ln Resin



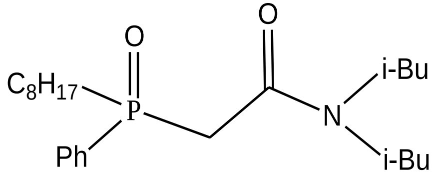


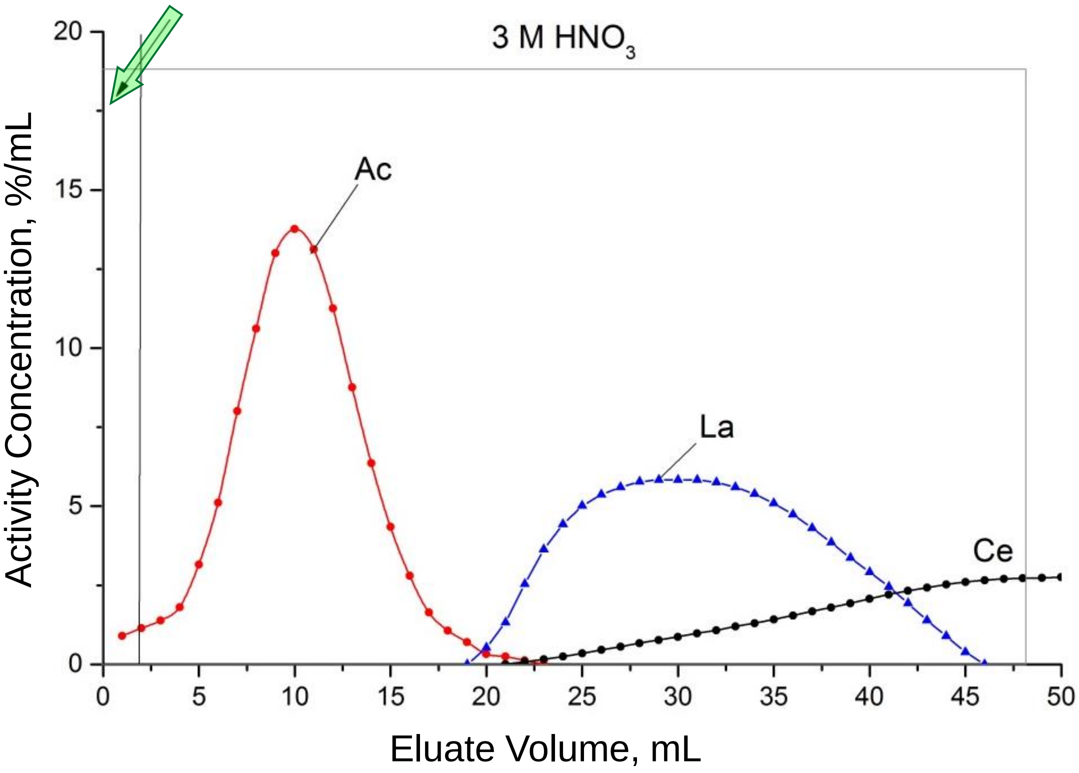
TRU Resin

Separation of Ac and REE

Three-step chromatographic separation provides high purity of final product

TRU Resin



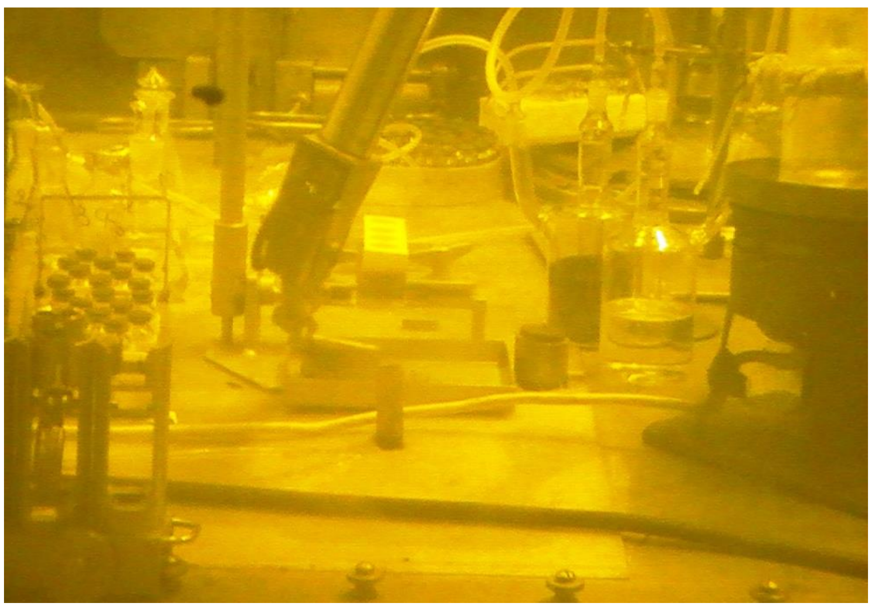


Hot cell approbation of ^{225}Ac recovery

INR RAS

Lomonosov Moscow State University

Karpov Institute of Physical Chemistry



Chemical yield	**> 85%**
Radionuclidic purity (excepting ^{227}Ac)	**> 99.8%**
^{227}Ac impurity (10th day after EOB)	**~ 0.2%**
Thorium impurity	**< 0.1 mg/L**
Stable impurities	**< 50 мг/л**

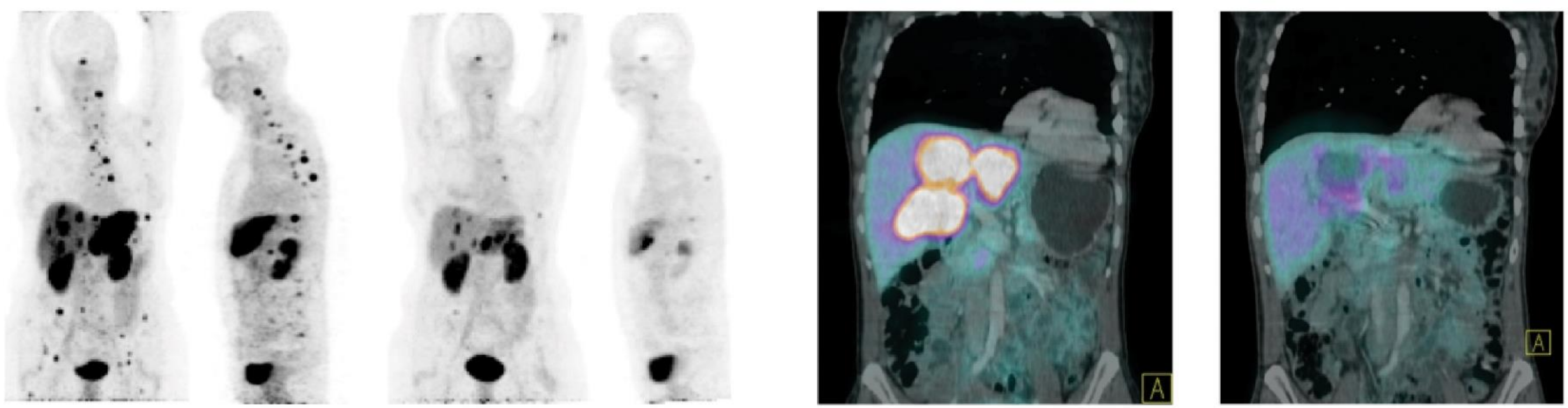
Clinical experience with ^{225}Ac- and ^{213}Bi-labeled compounds

A. Morgenstern et al. An Overview of Targeted Alpha Therapy with ^{225}Actinium and ^{213}Bismuth.

Current Radiopharmaceuticals, 2018, v. 11(2), p. 1–9.

- Leukemia
- Melanoma
- Prostate cancer
- Lymphoma
- Gliomas
- Neuroendocrine tumors

Remarkable responses to Bi-213-DOTATOC observed in tumors resistant to previous therapy with Y-90/Lu-177-DOTATOC



Case I: Shrinkage of liver lesions and bone metastases after i.a. therapy with 11 GBq Bi-213-DOTATOC

Case II: Response of multiple liver lesions after i.a. therapy with 14 GBq Bi-213-DOTATOC