LSC for Quality Control of ^{99m}TC Eluate from ^{99}Mo-^{99m}Tc Generator

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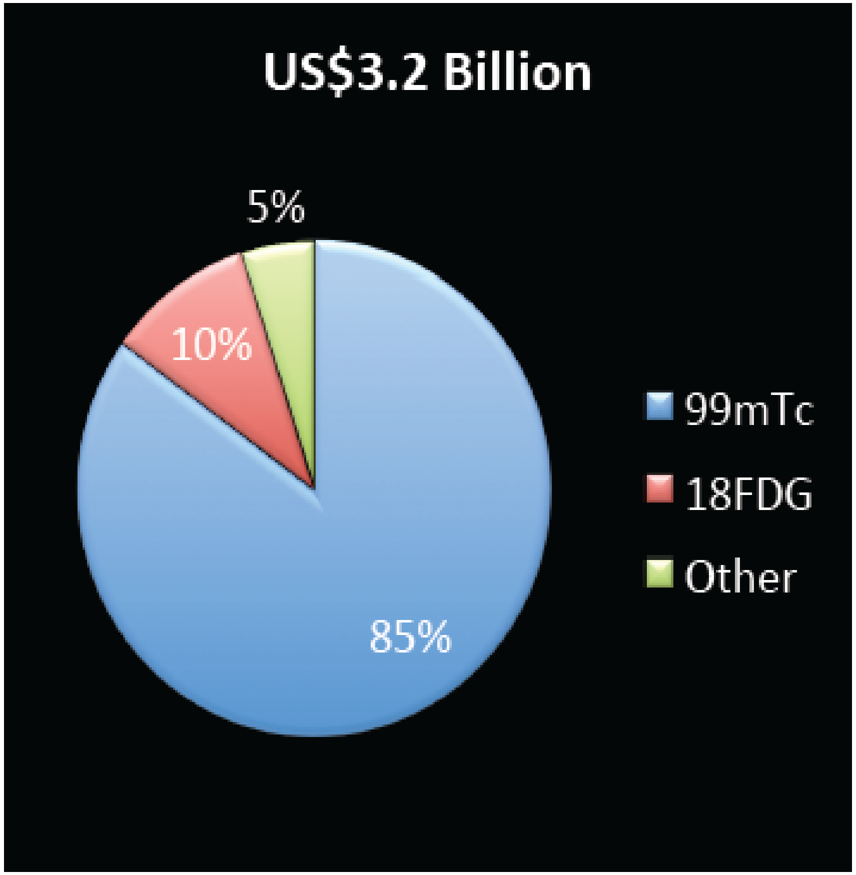
Application of ^{99m}Tc

- ^{99m}Tc is the principal radioisotope used in medical diagnostics .
- About 32 million ^{99m}Tc procedures are used per year globally and accounts for 80 to 85% of all diagnostic investigations using Nuclear Medicine techniques.

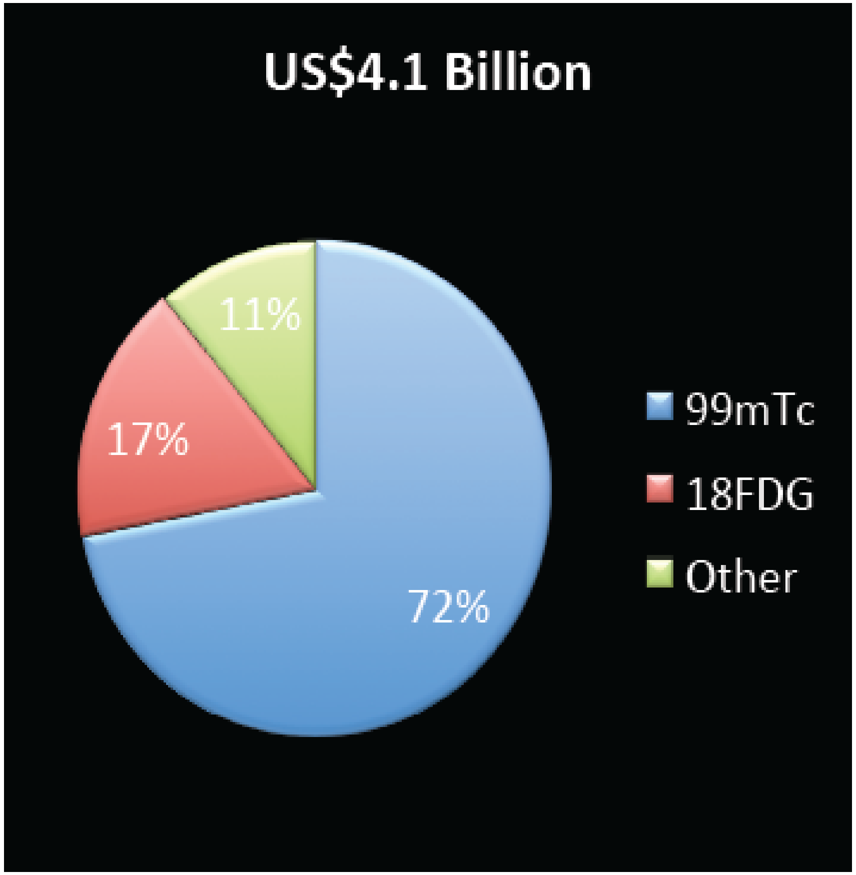
Investigation	Procedures (million)
➢ **Cardiac Imaging** Tc-99m, T- 201	**12**
➢ **Bone Investigation** Tc-99m	**10**
➢ **Lung Investigation** Tc-99m	**5**
➢ **Thyroid, Imaging** I-131 / I-123, Tc-99m	**5**

Global Radiopharmaceutical Diagnostic Market (1,2,3)

2010



2017



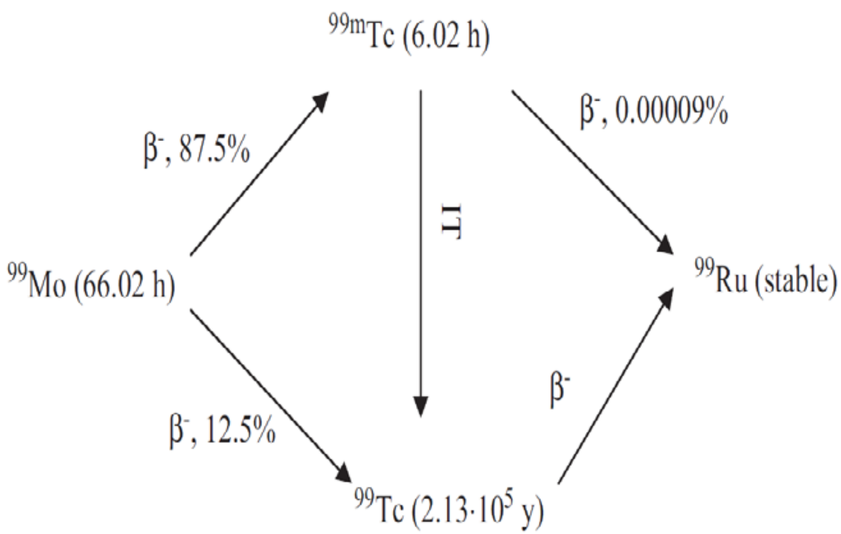
1 Global Radiopharmaceuticals Market (PET/SPECT Imaging & Therapy) – Current Trends & Forecasts (2010 – 2015); MarketsandMarkets, August 2011
2 BMI - Business Monitor International Ltd, Molybdenum-99: Privatising Nuclear Medicine, Special Report 2011
3 Interim Report on the OECD/NEA High-Level Group on Security of Supply of Medical Radioisotopes, The Supply of Medical Radioisotopes, OECD 2012

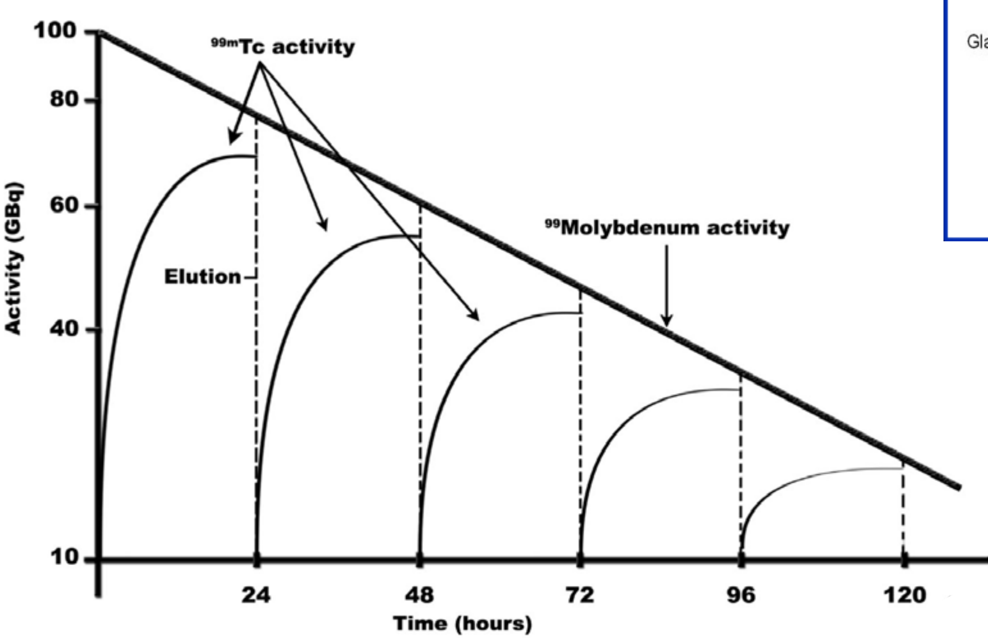
Production of ^{99m}Tc

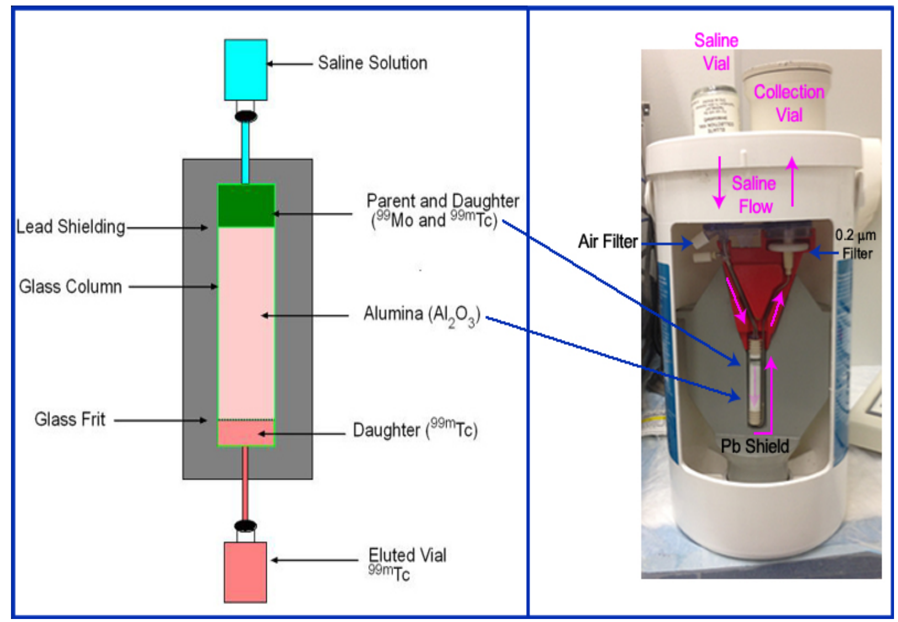
- **Direct production using cyclotron**:
  - ✓ $^{100}Mo(p, 2n)^{99m}Tc$

- **Indirect production**
  - ✓ ^{99}Mo-^{99m}Tc

Generation of ^{99m}Tc from the Decay of ^{99}Mo





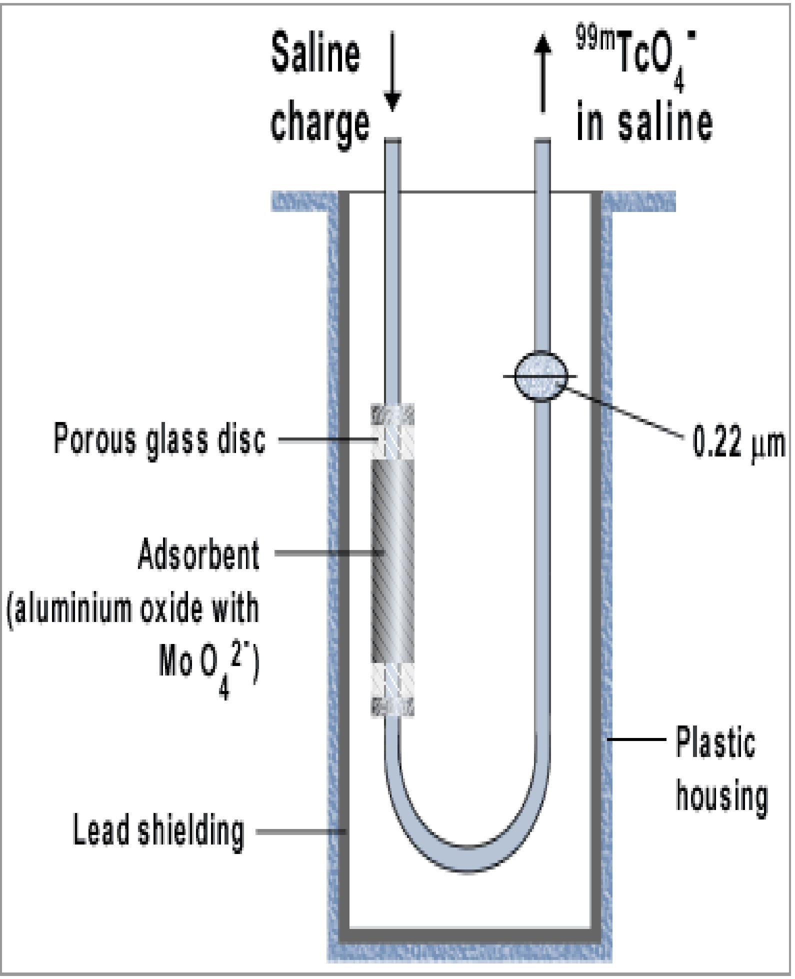


^{99}Mo production

- **Fission of ^{235}U: ^{235}U(n, f)^{99}Mo**
  - 6.2% fission yield,
  - high specific activity (no carrier)
  - ✓ Need separation from uranium and other fission products.
  - ✓ Main Impurities: fission products + activation products including actinides.

- **Neutron activation of ^{98}Mo: ^{98}Mo(n, γ)^{99}Mo**
  - Easy production, directly irradiat Mo oxides, and then dissolve irradiated Mo oxide and load it to gernerator column.
  - ✓ Main impurities: activation products
  - ✓ But, normally low specific activity and with Mo carrier

Items for the quality control of ^{99m}Tc eluate from Mo-Tc generator



- **Chemical Purity:**
  - All other elements besides technetium, the most concern is the metals which effect the application of $^{99m}TcO_4^-$, for example Al.

- **Radiochemcial Purity**:
  - Definition: For a material, the fraction of the stated isotope present in the stated chemical form.
  - The percentage of $^{99m}TcO_4$- in all ^{99m}Tc, mainly $^{99m}Tc^{4+}/^{99m}TcO_4$-

- **Radionuclidic Purity:**
  - **Definition: The proportion of the total activity that is present as a specific radionuclide.**
  - **Other radionuclides in the eluate of ^{99m}Tc**

Radionuclidic purity of ^{99m}Tc eluate from ^{99}Mo-^{99m}Tc generator

Possible impurity radionuclides:

– for fission ^{99}Mo generator)

Isotope	$t^{1/2}$	γ Energies (keV)	β_{max} Energy (MeV)
^{99}Mo	65.9 h	140.5 (4.5%)	1.350
		739.5 (12.2%)	
^{99}Tc	211 100 yr		0.294
^{131}I	8.02 days	364.4 (81.7%)	0.971
^{132}I	2.95 days	522.6 (16.0%)	3.577
^{106}Ru	373.59 days		0.039
^{90}Sr	28.74 yr		0.546
^{90}Y	64.1 h		2.282
^{89}Sr	50.53 days		1.495
^{103}Ru	39.26 days	497.1 (91%)	0.763

Radionuclidic purity of ^{99m}Tc eluate from ^{99}Mo-^{99m}Tc generator

Possible impurity radionuclides:

– Activation ^{99}Mo generator

Nuclides	Half-life	Decay model	Energy	Gamma Energy
^{60}Co	5.27 y	beta	318 keV	1173 keV, 1332 keV
^{86}Rb	18.6 d	beta	1774 keV	1076.6 keV
^{124}Sb	60.2 d	beta	1301 keV	602 keV, 1691keV
^{134}Cs	2.06 y	beta	658 keV	604.7 keV, 795.8 keV
^{235}U	703 Ma	alpha	4397 keV	185.7 keV
^{238}U	4468 Ma	alpha	4198 keV	
^{239}Np	2.35 d	beta	436 keV	106.1 keV
^{239}Pu	24110 y	alpha	5156 keV	

Limitation of radionuclidic impurity for ^{99m}Tc eluate of Mo-Tc Generator by European pharmacopoeia 7.0

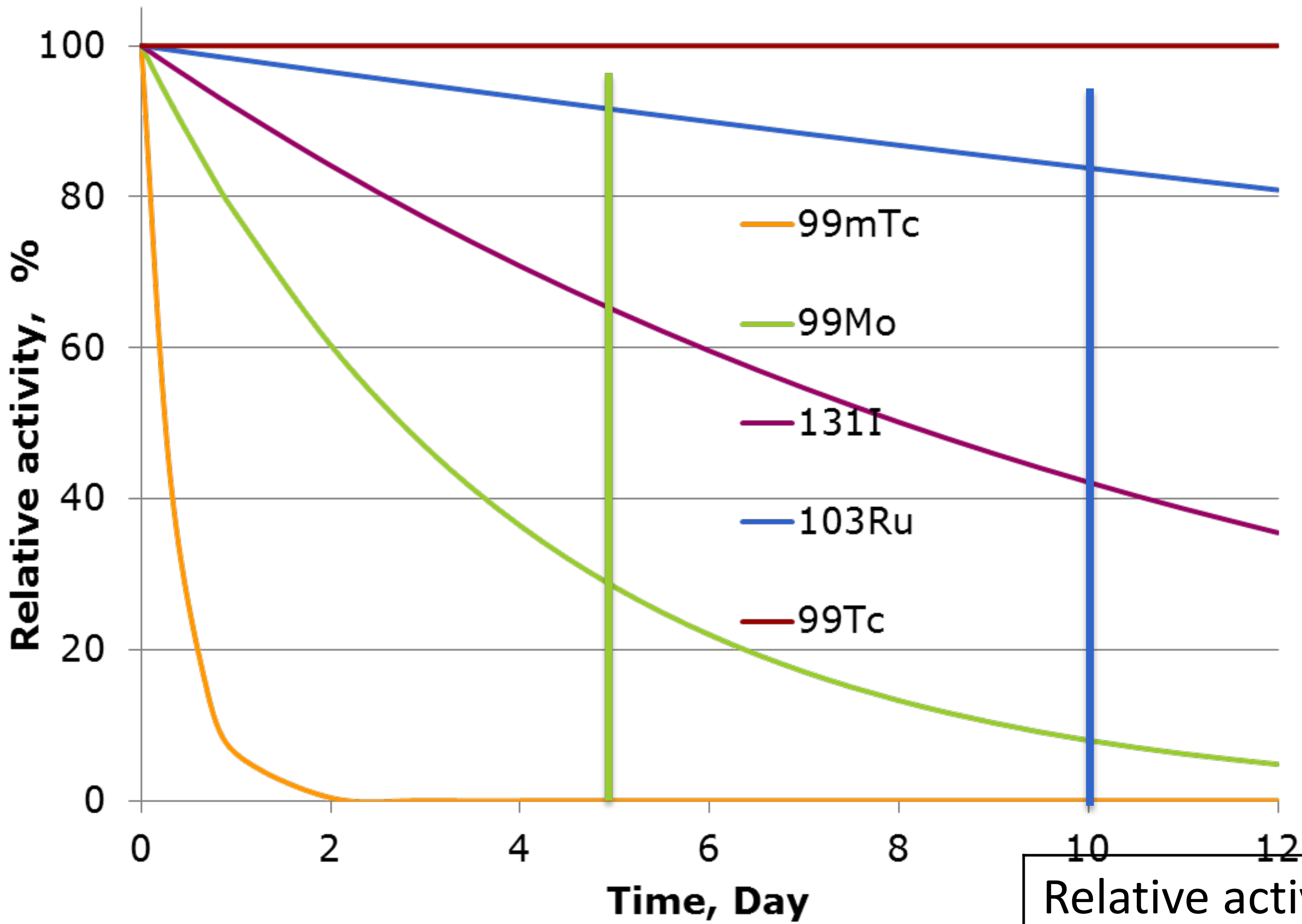
The radioactivity due to radionuclides other than technetium-99m,

- **molybdenum-99: 0.1 %**
- **iodine-131: 5×10^{-3} %**
- **ruthenium-103: 5×10^{-3} %**
- **strontium-89: 6×10^{-5} %**
- **strontium-90: 6×10^{-6} %**
- **alpha-emitting impurities: 1×10^{-7} %**
- **other gamma-emitting impurities: 0.01 %**

Strategy for determination of radionuclidic impurity in ^{99m}Tc eluate

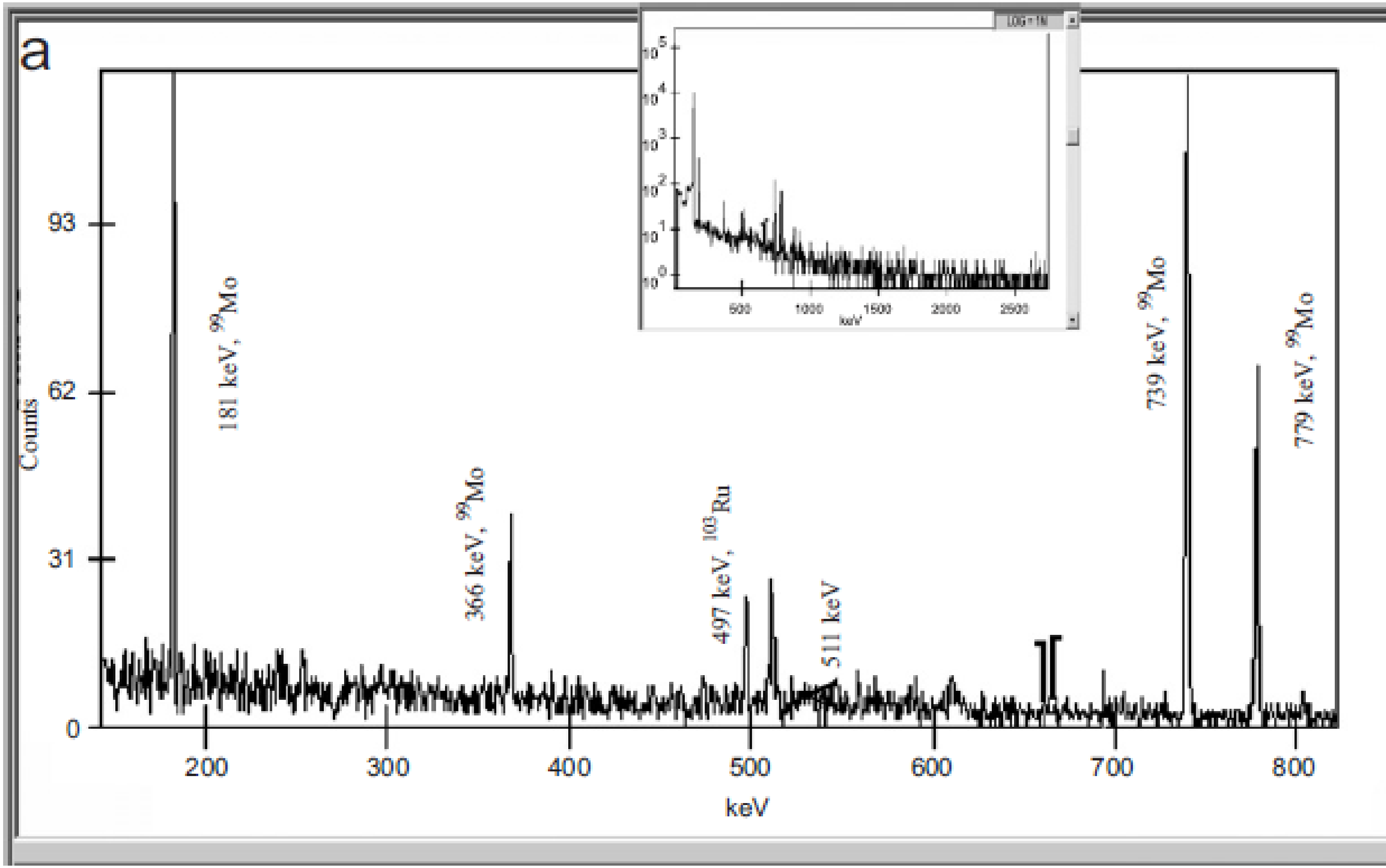
- **Direct measurement using γ-spectrometry**
  - ^{99}Mo, ^{131}I, ^{103}Ru and others
  - Removal of ^{99m}Tc by decay for more than 5 days
- **LSC for total α-emitting radionuclides**
  - Removal of ^{99}Mo, ^{99m}Tc, and ^{99}Tc
- **LSC for ^{89}Sr and ^{90}Sr**
  - Separation of Sr from all other radionuclides

Removal of ^{99m}Tc by decay



Relative activity ^{99m}Tc remained:	
Days	Remained ractivity,
5	**9.5×10^{-5}**
10	**9.1×10^{-11}**

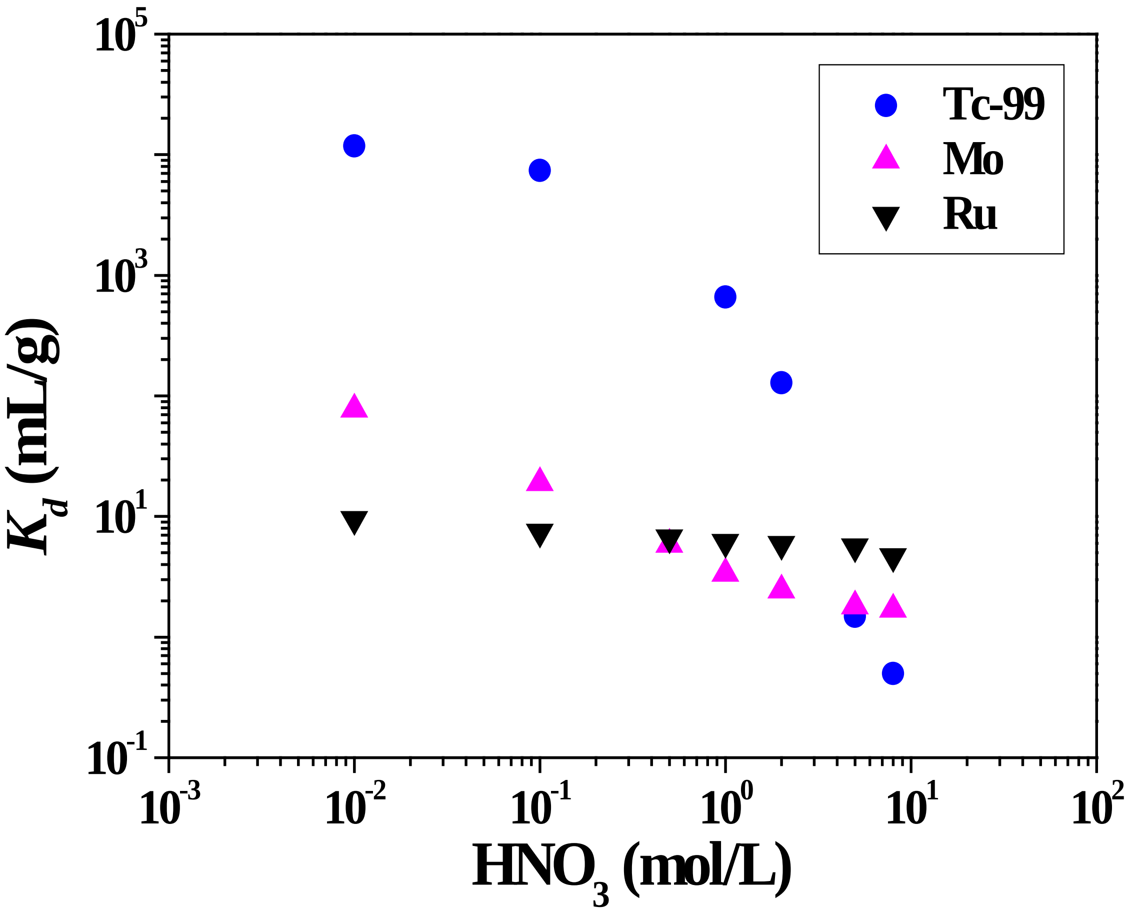
^{99}Mo and ^{103}Ru in ^{99m}Tc eluate from ^{99}Mo-^{99m}Tc Generator



Strategy on Determination of total alpha emitting radionuclides

- **Alpha spectrometry measurement**
  - Tedious separation and electrodeposition
- **Gross alpha measurement using GM counter**
  - Not discrimination from beta emitters
  - Not good accuracy
- **LSC for total α-emitting radionuclides**
  - Removal of ^{99}Mo, ^{99m}Tc, and ^{99}Tc
  - Recovery of all alpha emitters (U, Pu, Np, Am, etc.)
  - Measurement using alpha/beta discrimination

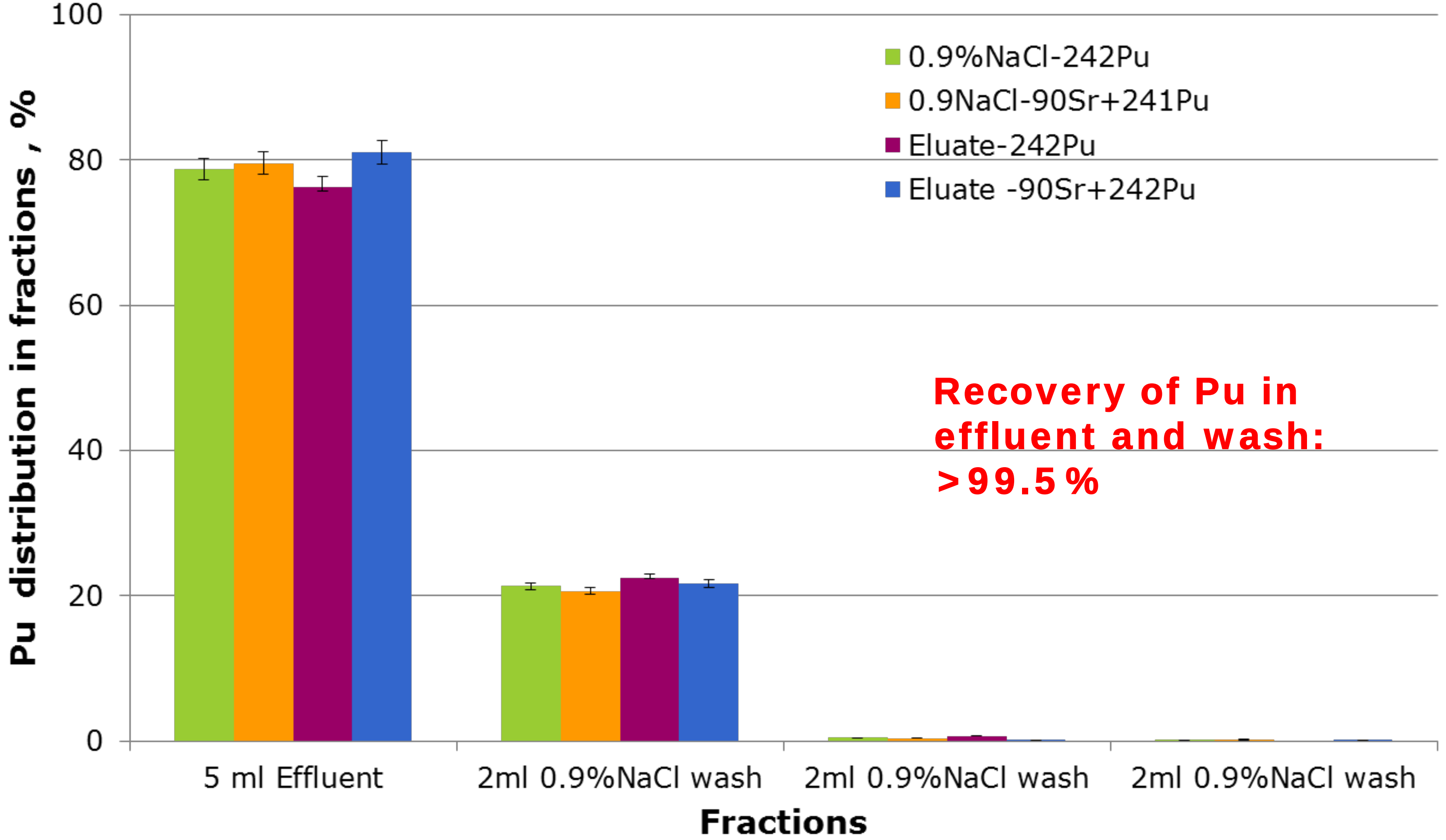
Behavior of TcO_4^-, MoO_4^{2-} and Ru on anion exchange column



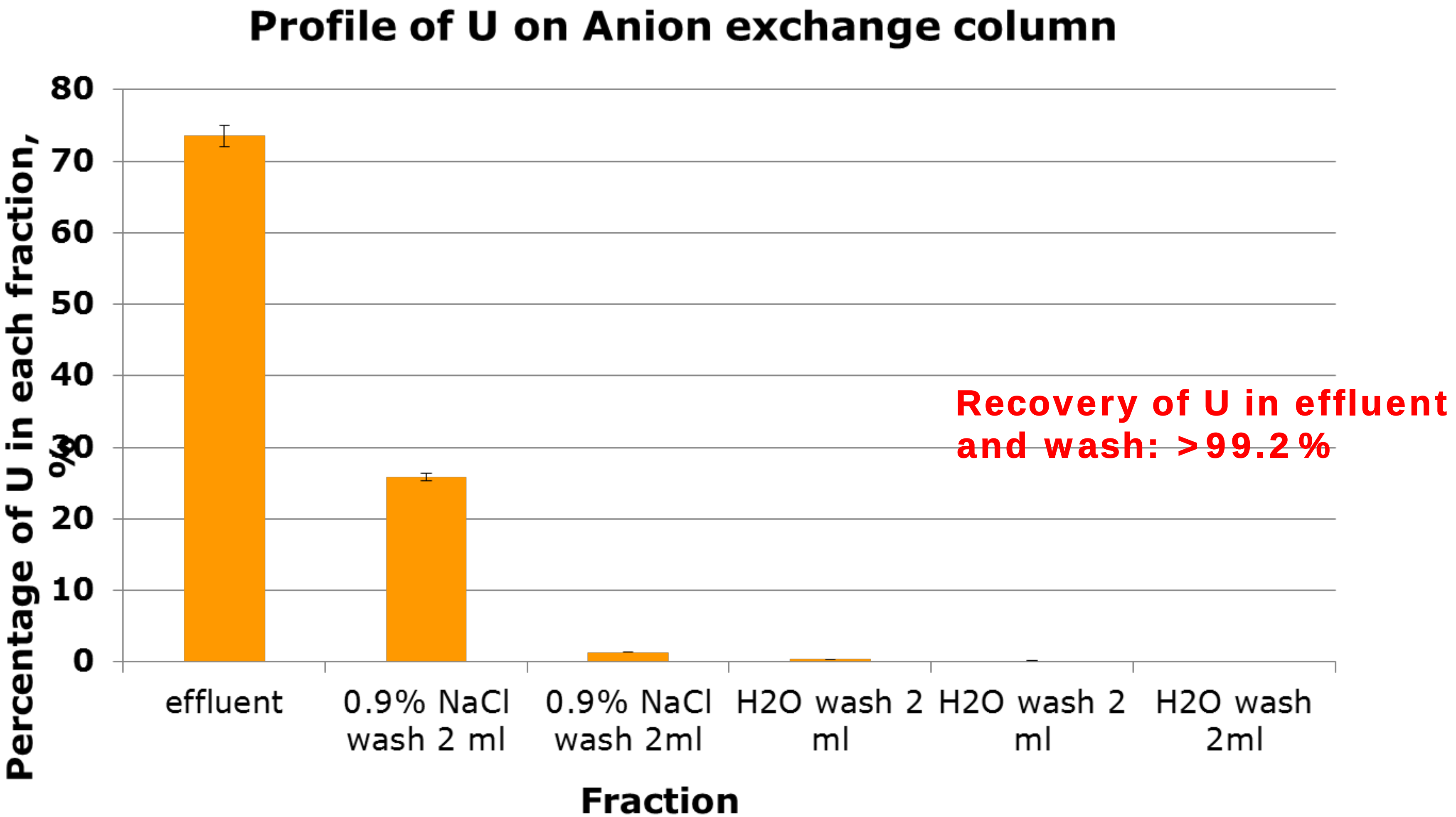
Decontamination factors on 2 ml anion exchange column (AG1-x4):

^{99m}Tc: >1x10^5
^{99}Mo: >1x10^4
Ru: > 98%

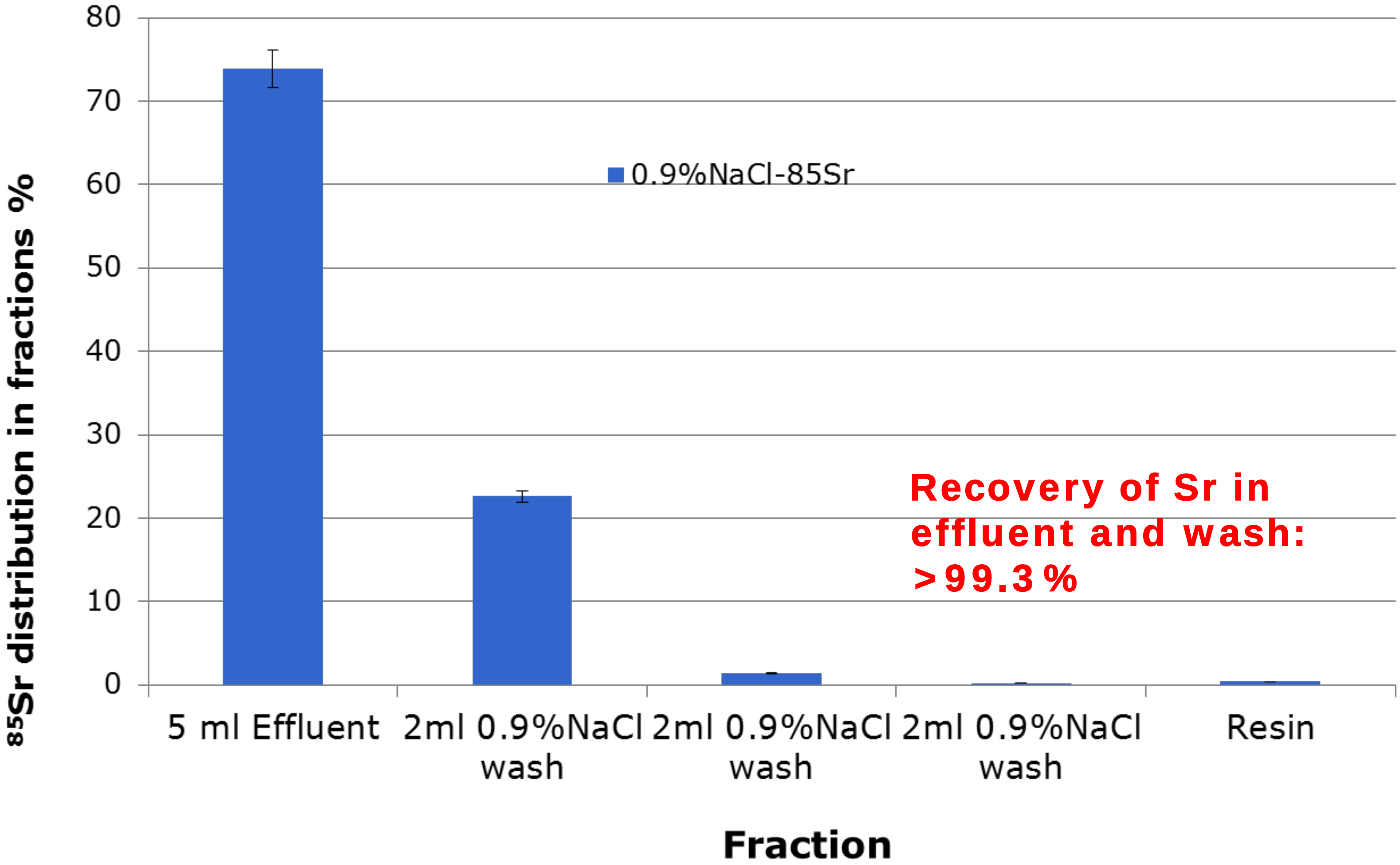
Behavior of Pu on 2 ml anion exchange column (AG1x-4)



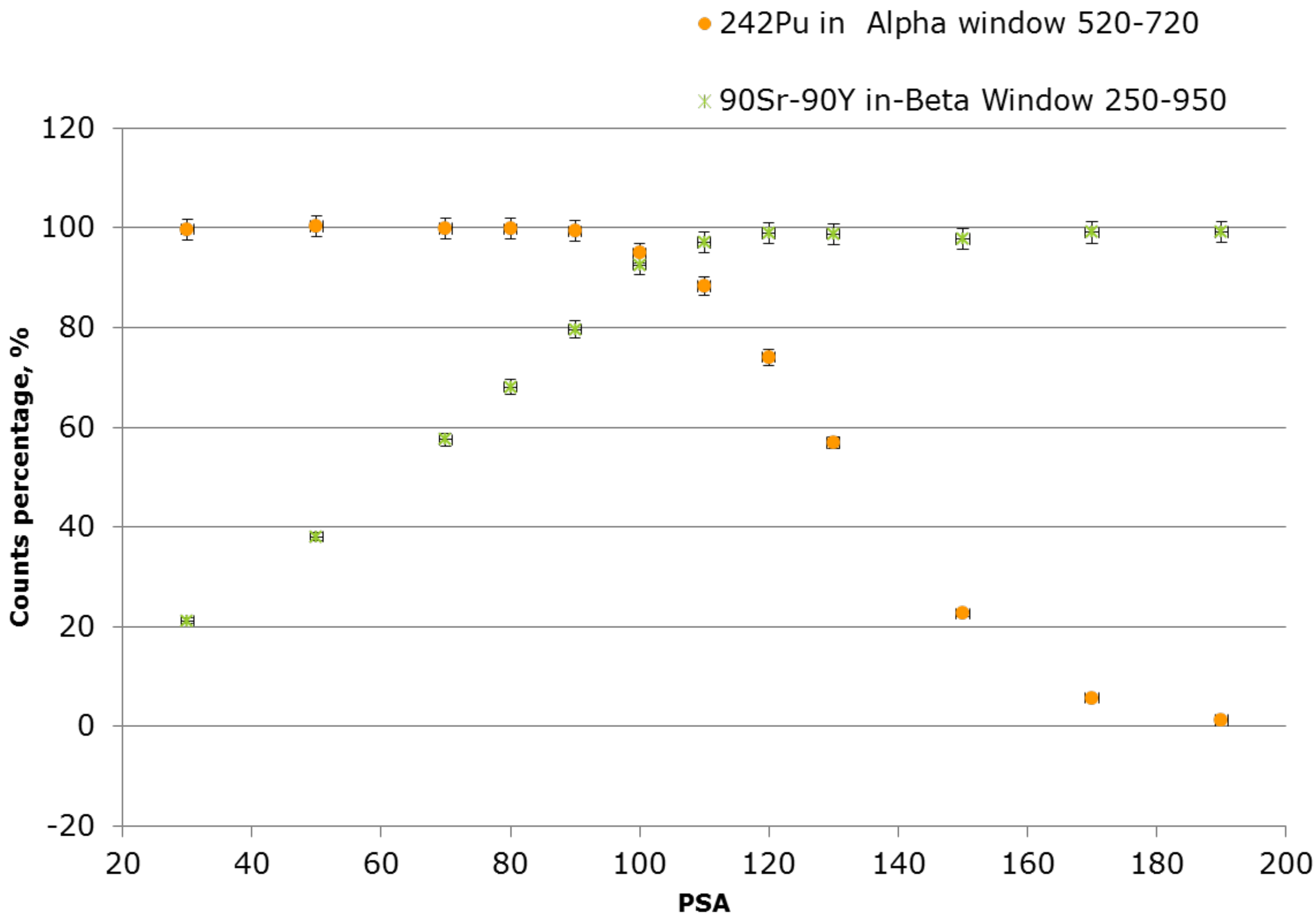
Behavior of U on 2 ml anion exchange column (AG1x-4)



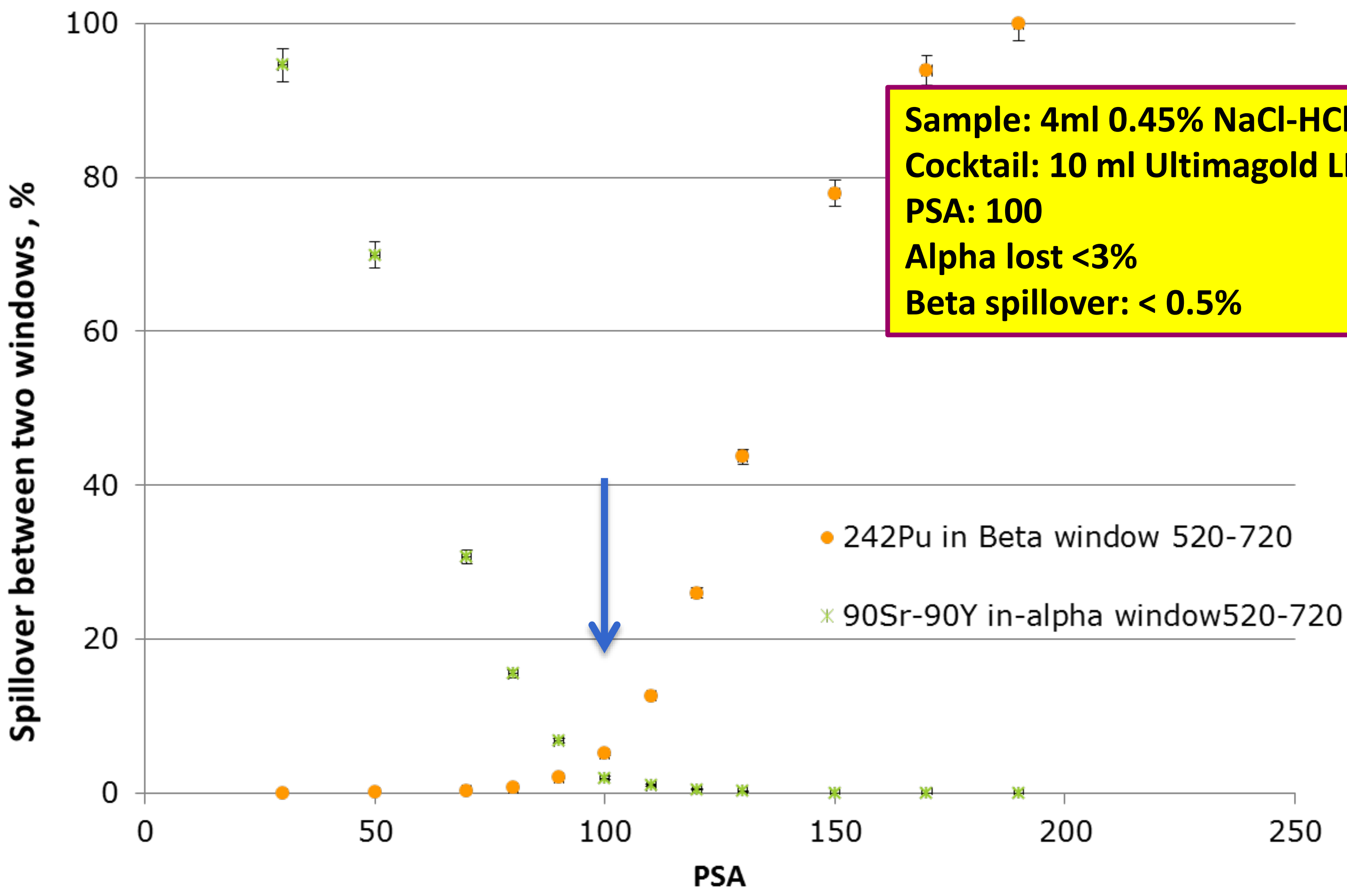
Behavior of Sr on 2 ml anion exchange column (AG1x-4)



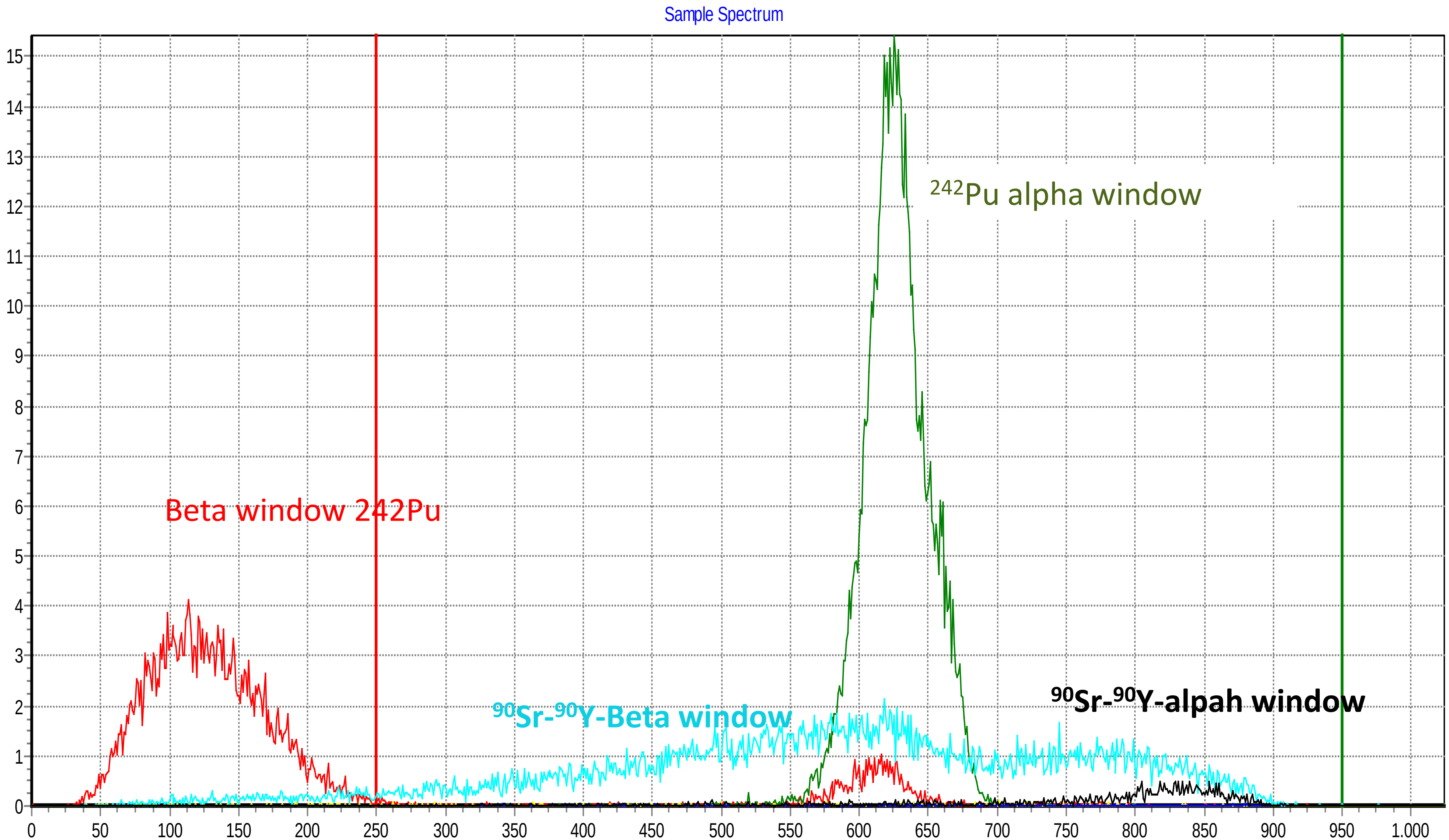
LSC measurement of concentration of total alpha emitters using α/β discrimination



LSC measurement of concentration of total alpha emitters using α/β discrimination



Sample: 4ml 0.45% NaCl-HCl pH2
Cocktail: 10 ml Ultimagold LLT
PSA: 100
Alpha lost <3%
Beta spillover: < 0.5%

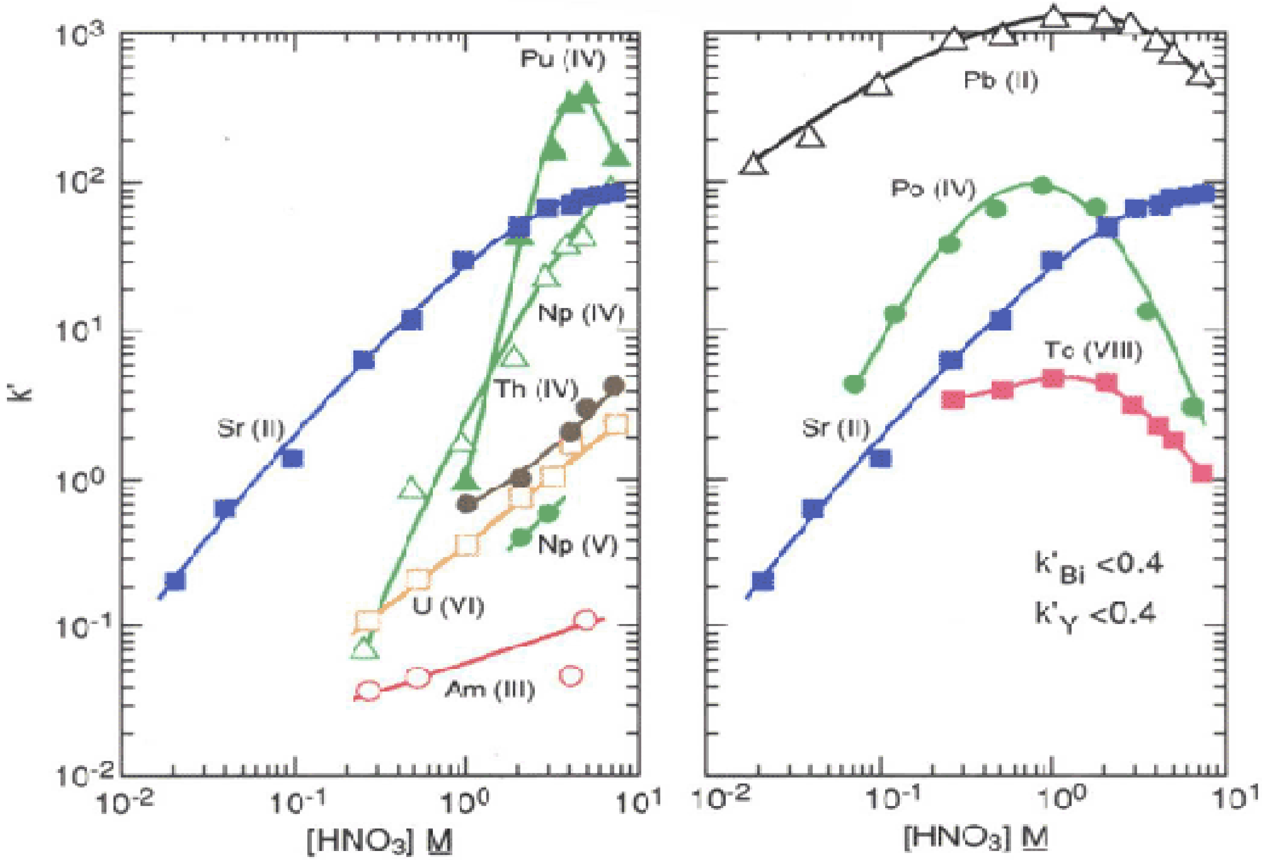

Sample Spectrum
242Pu alpha window
Beta window 242Pu
90Sr-90Y-Beta window
90Sr-90Y-alpah window
0
1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
0
50
100
150
200
250
300
350
400
450
500
550
600
650
700
750
800
850
900
950
1.000

Separation of interference for ^{89}Sr and ^{90}Sr using extraction chromatography

Sr-Resin

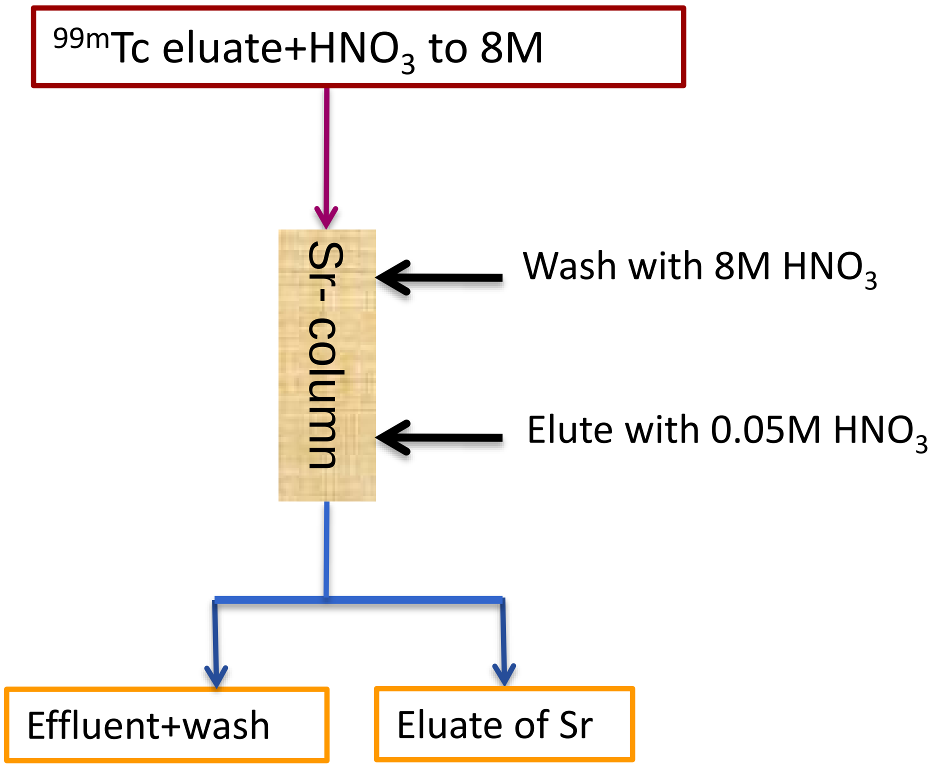
Figures 4 and 5

Acid dependency of k' for various ions at 23-25°C.
Sr Resin



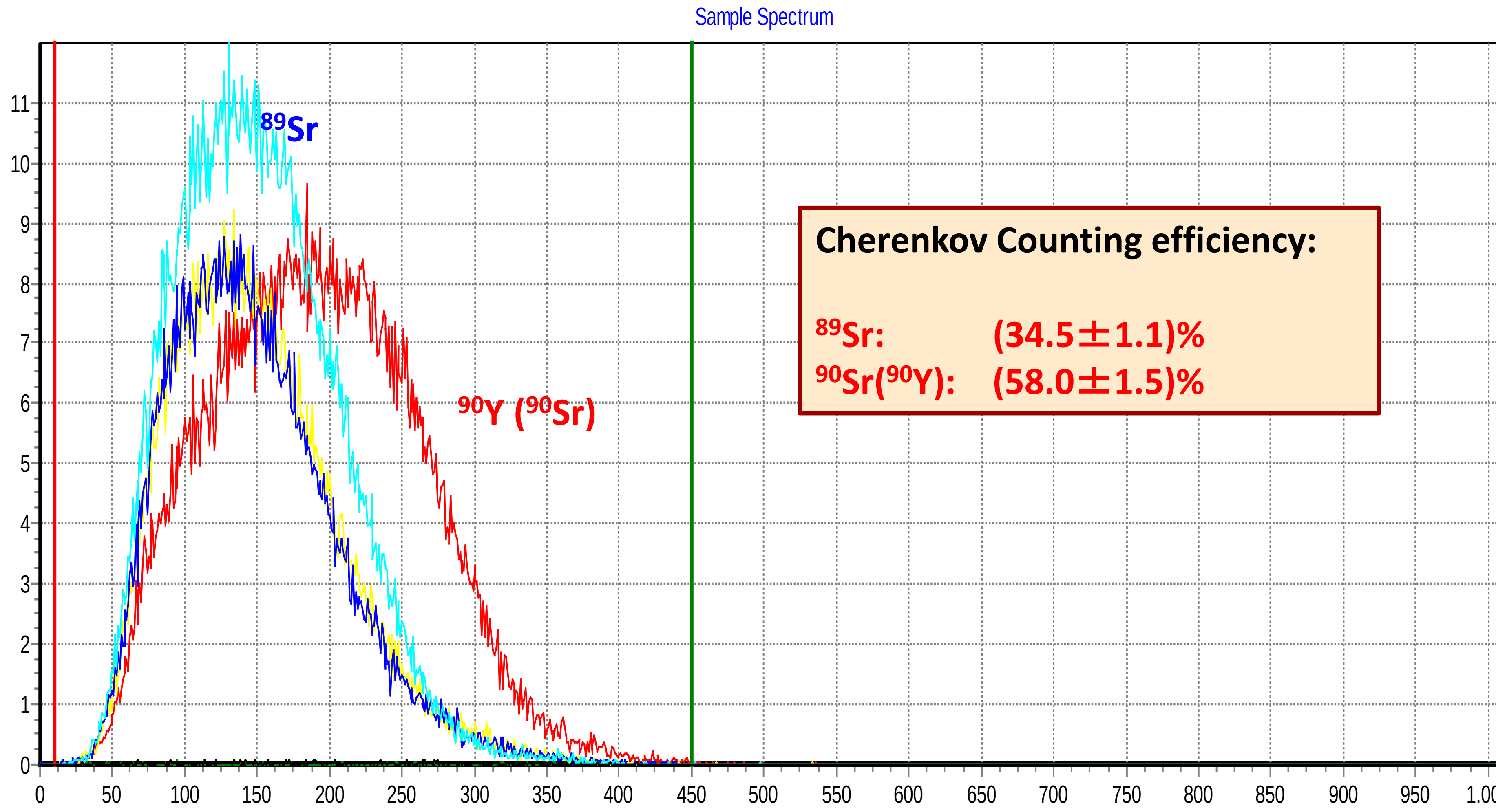
Horwitz (HP199)

Separation of ^{89}Sr and ^{90}Sr using Sr column



Chemcial recoveries of ^{90}Sr and ^{85}Sr in the extraction separation procedure using Eichrom Sr-column

Radionculide	Recoveries of Sr/decomtamiantion of ^{90}Y in eluate, %			
	No. 1	No.2	No.3	Average ± unc.
^{85}Sr	100.0	98.7	99.6	99.5±1.5
^{90}Sr	98.9	99.6	98.6	99.2±1.5
^{90}Y in eluate	< 0.5	< 0.5	< 0.5	< 0.5

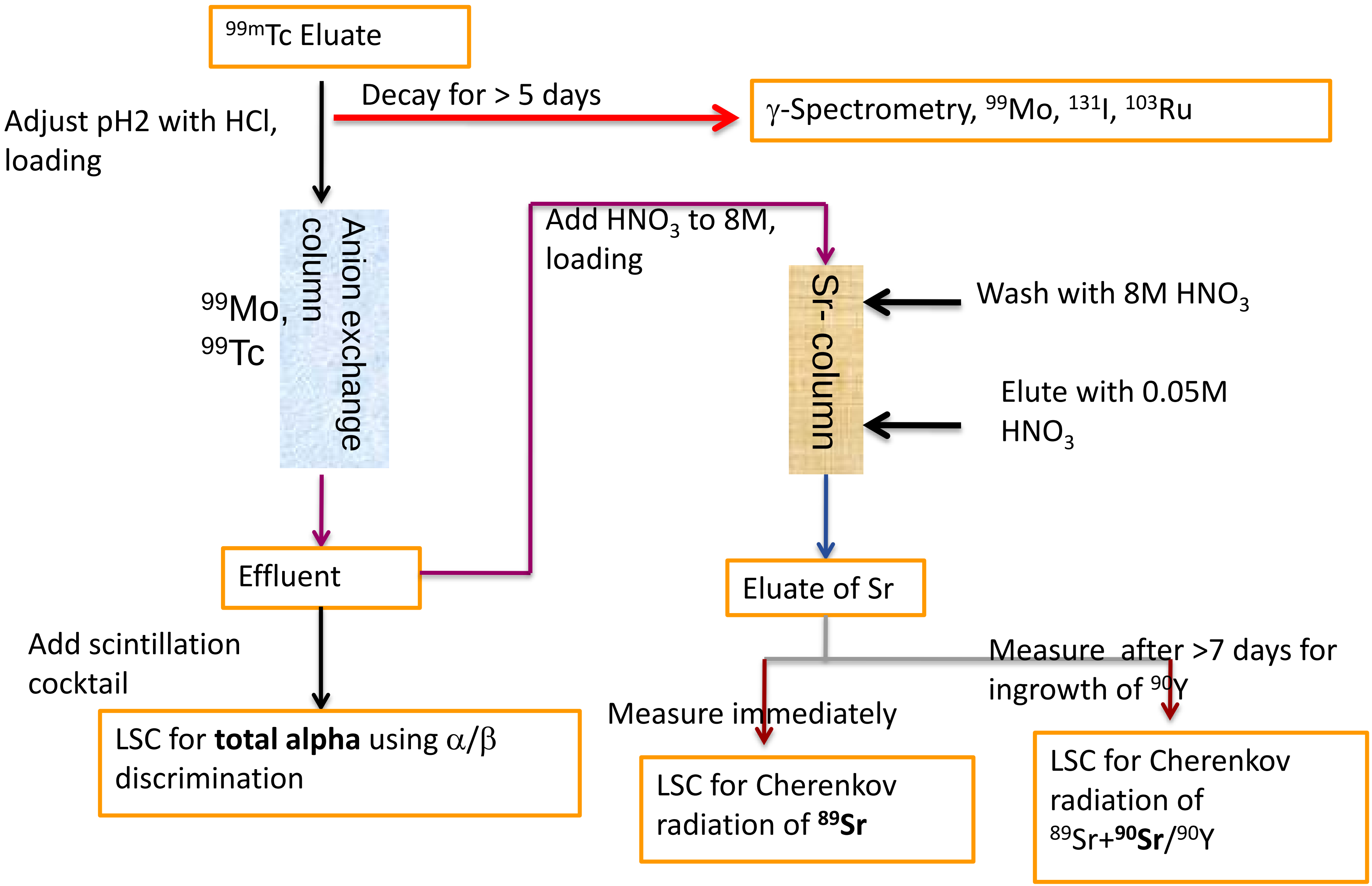


Cherenkov Counting efficiency:

^{89}Sr: (34.5±1.1)%

$^{90}Sr(^{90}Y)$: (58.0±1.5)%

Overall procedure for determination of radionuclidic impurities in ^{99m}Tc eluate



Detection limits of the method for main radionuclides

Item	Anal. method	Volume of eluate, mL	Detection limit, Bq [1)]	Limitation by Eu Ph. [2)] Bq
^{99}Mo	γ-spec.	2.0	**250**	$2x10^6$
^{131}I	γ-spec.	2.0	**20**	$1x10^5$
^{103}Ru	γ-spec.	2.0	**6.5**	$1x10^5$
Other gamma #	γ-spec.	2.0	**5**	$1x10^6$
^{89}Sr	LSC	1.0	**0.20**	600
^{90}Sr	LSC	1.0	**0.15**	60
Total beta #	LSC	1.0	**0.40**	$5x10^5$
Total alpha	LSC	1.0	**0.01**	1.0

1) Considering a decay time of 10 days from the eluting
2) For a 5 ml eluate of 10 GBq


Thank you for your attention !