TrisKem International

An overview over some new extraction chromatographic resins and their application in radiopharmacy

Steffen Happel
12/06/2021

TRISKEM
Expertise in Separation Chemistry

Overview

- TrisKem International
  - Products
  - R&D
  - Networks
- Extraction Chromatography
- Domains of application
- ZR Resin (e.g. Zr-89, Ga-68, Ge-68, Ti-44/5)
- TK200 Resin (Ga-68, Zn/Cu, Pt/Ir, Sc/Ca)
- TK201 Resin (Cu-64 from solid Ni targets)
- CU Resin (Cu from Zn and liquid Ni targets)
- Lanthanide separation (Lu-177, Tb-161)
- TK221 (LN, Ac purification)
- TBP Resin (e.g. Zr-89, Sc, Ga)
- TK400 Resin (Pa, Nb, Ga)
- CL Resin (Ag, Pa, I removal)
- TK202 (Tc/Mo)
- DGA Sheets
- PAN based resins
- TK-TcScint
- On-going developments

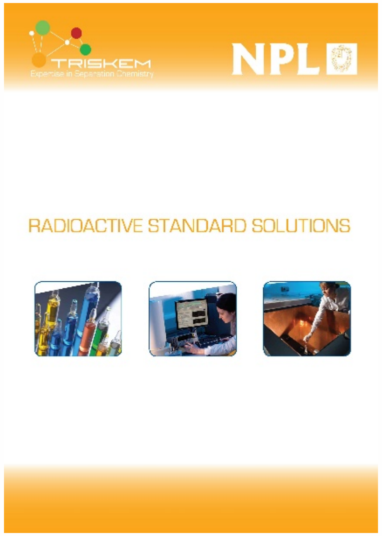
TrisKem International

- Based in Rennes (France)
- Independent company since 02/07
  - Formerly part of Eichrom Europe
  - ISO 9001 since 2007
- Staff : 20
- R&D, QC and TechSupport group:
  - 3 RadChem PhD, 2 OrgChem PhD, 5 Technicians
- R&D: Development of new resins, techniques and applications
- Several domains

TrisKem International

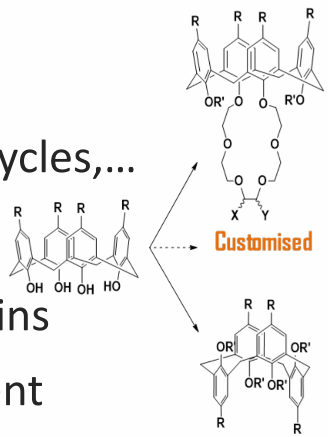
- Production and trade of selective resins and accessories
  - Mainly extraction chromatographic resins
  - PAN embedded inorganic compounds
  - Functionalized polymers and silicates
  - Analytical and chelating ion exchange resins

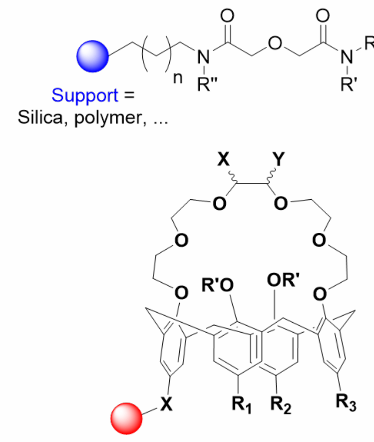
- Distribution (Europe):
  - LSC cocktails et al. (Meridian)
  - PEEK columns
  - Raddec Pyrolyser (H-3 & C-14)
  - ICP & AAS standards (Labkings)
  - New: Radioactive standards (NPL)
  - Accessories (Zr crucibles, empty columns & cartridges, funnels, vacuum boxes,…)



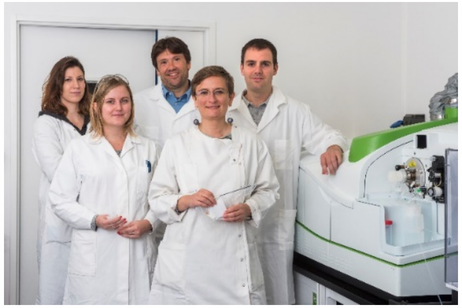
R&D TrisKem International

- Two R&D labs:
  - Synthesis Lab (new resins and extractants)
    - Incl. grafted resins (silica or polymers), macrocycles,…
  - Application Lab
    - Preparation of extraction chromatographic resins
    - Resin characterisation and method development





- Equipment:
  - ICP-MS, IC, TOC, TGA, IR, moisture analyzer, surface area and pore size/volume analyser, particle size and shape analyser, pycnometer
  - Production and packing lab with four 20L reactors



- No handling of radioactivity => R&D cooperation
  - Resin and method development "cold" => R&D partner

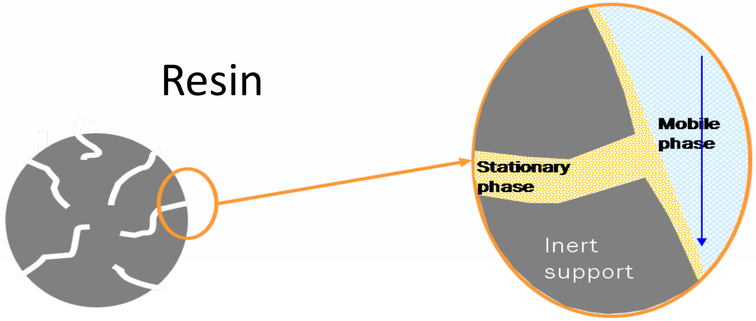
Networks

- Isotope4Life / Atlanpole Biotherapies ID2 Santé
- Nucleopolis (energy & health)
- Prometia (hydrometallurgy)
- Several projects financed by the BPI
  - Radiopharmacy (PSPC CARAT – Pb-212/LU-177)
  - Member of BPI Excellence
  - Lauréate Vague d'innovation BPI (C.L.I.P.S. 2020)

Extraction chromatography

Organic extractant impregnated onto inert support

- « Supported Solvent Extraction » / « Solvent Impregnated Resins »
  - Distribution between two non-miscible phases
  - High density of functional groups
  - Fast kinetics/small volumes => rapid separations
  - High variety of selectivities:
    - Pure extractants, synergetic mixtures, solid extractants in diluents
  - Aim: selectivity for product, no selectivity for target material
  - Combining several cartridges can allow obtaining better product quality
  - Elution under 'soft' conditions in small volume => labeling/injection
  - Bleeding might need to be adressed (Prefilter, AIX, CEX,…)



Products and applications

PRODUCTS+	APPLICATIONS*
AC Resin	Mn, Ac/Ra, gross alpha
CL Resin	Ag, Radioiodine removal, Pa, Cl, I
CU Resin	Cu from Zn and liquid Ni targets (e.g. Cu-61/7)
DGA Resin	Y, Sc-44/7, Ac-223/5/7, Co
DGA Sheets	Quality control of Ra-223, Pb-212, Ac-225/Bi-213, Ge-68/Ga-68
LN Resin Series	Lanthanide separations (Lu-177, Tb-161..)
Prefilter Resin	Organic impurities removal
Guard Resin	Organic impurities removal
RE Resin	Y
SR Resin	Sr-82, Pb, Po
TBP Resin	Zr-89, Sc, Sn-117m
TEVA Resin	Tc
TK100/1 Resin	Sr-82, Ra
TK200 Resin	Ga-67/8, Zn, Pt, Pd
TK201 Resin	Cu from solid Ni targets (e.g. Cu-64), Tc-99m, Re
TK221 Resin	Lu, Tb, Ac purification
TK211/2/3 Resins	Lanthanide separations (nca Lu-177, nca Tb-161..)
TK400 Resin	Pa, Ga-68, Nb, Mo, Po, Fe
UTEVA Resin	Zr, Sc-44/7
ZR Resin	Zr-89, Ga-67/8, Ge-68, Ti-44/5

+Resin available world wide in **orange**

*main application in **blue**

Coming soon:

TK202 (Tc from Mo)

Examples of domains and applications

- Analytical
  - Radiochemistry
    - Environmental monitoring, bioassay, waste monitoring, decommissioning
    - Actinides, fission and activation products, NORM, methods/resins for DTMs, rapid methods,…
      - » **TK100/1, TK200, TBP, CL Resin, TK201/2,** **TK300, TK-TcScint, Extractive discs,…**
  - Mass spectrometry
    - Isotope ratio determination (universities, petrol industry,…)
    - Sr, Pb, U, actinides, Cu, Sn…
      - » Dating of geological samples :**TK200, TK400,** TK300**, …**
      - » Food provenancing : **TK100,…**
      - » Nuclear forensics: **TK200, TK400,..**
      - » Biomedical (Cu),… => **CU Resin,…**

Examples of domains and applications

- Decommissioning/decontamination
  - Treatment of effluents / liquid wastes / environmental waters
    - Removal of radioactive contaminants & heavy metals (Cs, Sr, Ra, I…)
  - Inorganic compounds embedded into PAN matrix
    - ➢ **CS Resins, MnO2-PAN more under development**
  - Extractionchromatographic resins

- Hydrometallurgy
  - Recycling of critical metals
  - Purification of leachates
    - ➢ **Upscale of the production of extraction chromatographic resins**

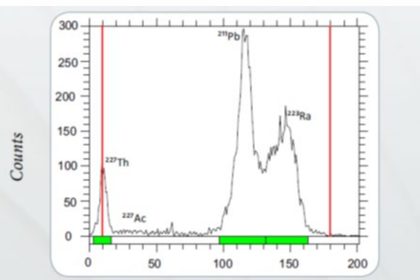
Examples of domains and applications

- Radiopharmacy/Nuclear Medicine

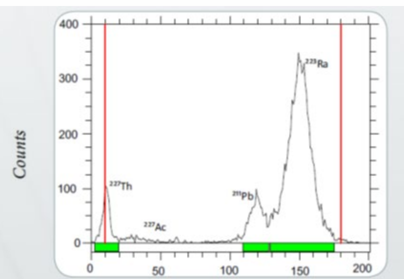
  - Radionuclide production
    - Cooperation with cyclotrons & reactors (NL, RN producers,…)
    - Equipment provider (targetry, synthesizer,…)
    - Separation of radionuclides from irradiated targets
      - » Diagnostics: Zr-89, Cu-64, Ga-68, Ge-68, Ti-44/5, Tc-99m, Sc-43/4…
        - **ZR Resin, CU Resin, TK200 Resin, TK400, TK201, TK202,…**
      - » Therapy: alpha emitters, Lu-177, Cu-67, Sn-117m, Sc-47…
        - **TK400, TK200, TBP Resin, CU Resin, TK211/2/3, TK221,…**

Examples of domains and applications

- Radiopharmacy/nuclear medicine
  - Purification of generator eluates => under development
  - Decontamination of contaminated effluents => **CL Resin,…**
  - Quality control
    - Cartridge based methods
    - **DGA sheets** (functionalized TLC, Ra-223, Ga-68, Pb-212,…. => CVUT Prague)



Radiochromatogram measured immediately after separaton. Low abundant radiatons of ^{227}Ac were not detected.



Radiochromatogram measured one hour afer separaton. Decay and ingrowth of ^{211}Pb is clearly visible.

A scheme of chromatographic separaton of mixture of ^{227}Ac and his daugther´s niclides. ^{227}Th remains on start, ^{227}Ac has the retenton factor ca 0.2, ^{211}Pb ca 0.7 and ^{223}Ra ca 0.9.

Applications in RadPharma – new resins

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Radiopharmacy

Environment
Geochemistry
Decommissioning

Separation of radionuclides for medical applications

- Rapid, highly specific separation techniques
- Separation of radionuclides from irradiated targets
- Quality control of radionuclides for medical use
- Post-generator purification
- Radioprotection and Radioanalysis
- Easily used in glove boxes or hot cells
- High active samples

Our resins are increasingly finding application in the production and quality control of radionuclides (such as Cu-64/7, Ge-68, Ga-67/8, Sc-44/7, Zr-89, alpha emitters...) for medical use, and are employed by leading radionuclide manufacturers worldwide. Further to our range of highly selective resins TrisKem is now also offering a selective chromatography paper (DGA Sheets) for quality control of radionuclides and generator effluents (Ac-225, Pb-212, Ga-68,...).

TrisKem International places a strong focus on the development of new resins and separation methods to meet your separation needs. If you'd like to receive more detailed information, or if you'd like to discuss a specific separation problem please contact us under : contact@triskem.fr

Products	Applications*
CU Resin	Cu-61/7
ZR Resin	Zr-89, Ga-67/8, Ge-68, Ti-44/5
TBP Resin	Sn-117m, Zr-89, Actinides
TK200	Ga-68, Actinides
TK201 Resin	Cu-64
TK221 Resin	Lanthanides separation and purification (e.g. Lu-177), Ac-225 purification, Actinides
TK400 Resin	Pa-230/1, Nb-90, Ga-68
DGA Sheets	Quality control of Ra-223, Pb-212, Ac-225/Bi-213, Ge-68/Ga-68
CL Resin	I removal from effluents, Ag, PGE, Cl-36/I-129
TK100 Resin	Sr-82
TK101 Resin	Ra, Pb
CS Resins	Cs, Rb
Discs	Source preparation for alphaspectrometry
MnO_2-PAN	Ra-226/8
Ra Nucfilms discs	Ra-226
LSC consumables	Liquid Scintillation Counting
Autodeposition kit	Source preparation for alphaspectrometry
Pyrolyser, Pyrolyser Mini	Total tritium, C-14, Cl-36 and I-129

*the main application is in blue

Our new developments - for information on all our products please visit our web site: www.triskem.com

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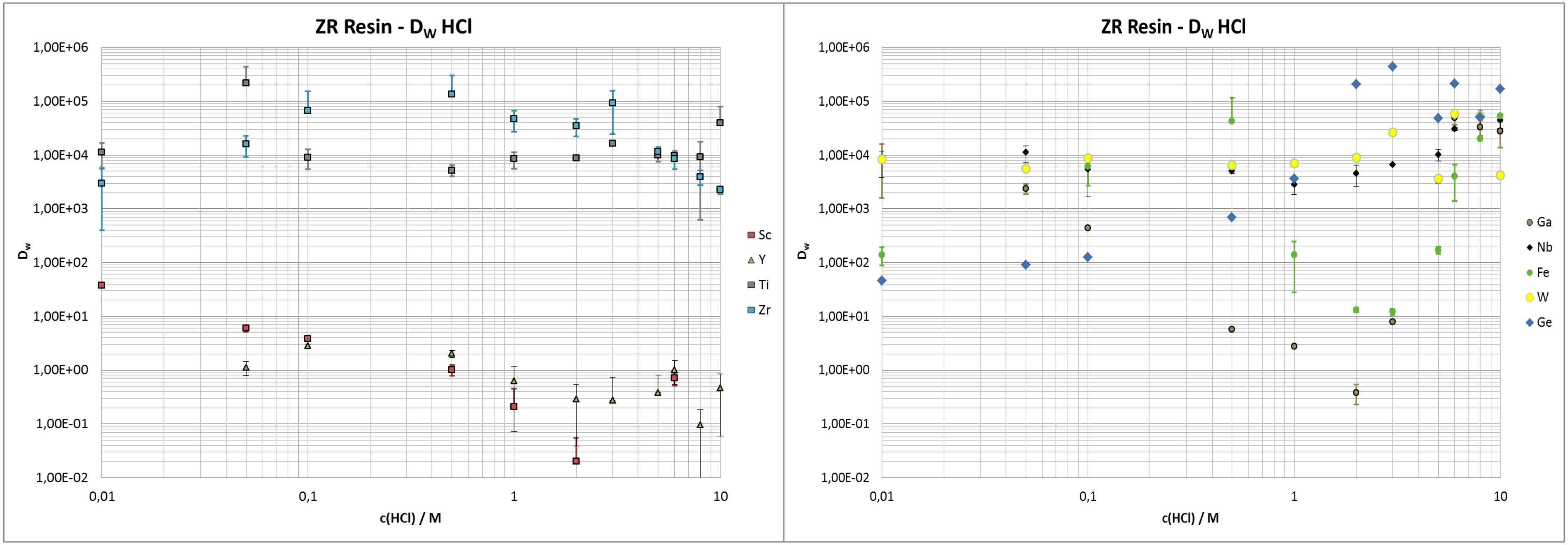
SAS au capital de 100.000 euros – SIRET 493 848 972 00029 – APE2059Z –
VAT FR05 493 848 972 - EORI FR493848972

ZR Resin

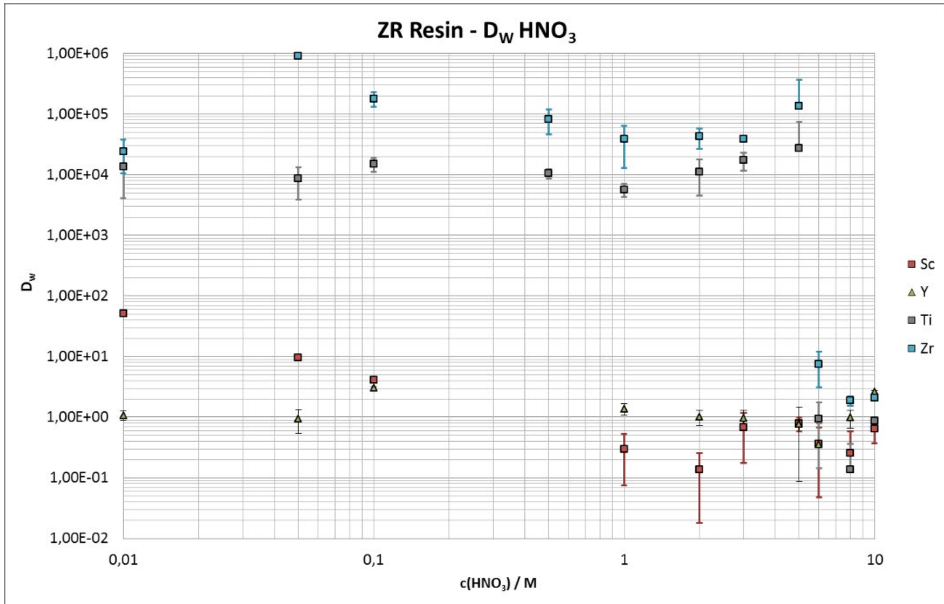
- Original scope: Hydroxamate based resin
    - Standard for Zr separation from Y targets
    - Ready to use / no activation
    - Facile Zr elution (avoid 1M oxalic acid)
- Zr-89 production via (p,n) reaction from ^{nat}Y targets
    - High Zr/Y selectivity necessary
    - Alternative e.g. TBP Resin (=> Graves et al.)
- Application for other separations: **Ti/Sc**, **Ga/Zn, Ge/Ga**

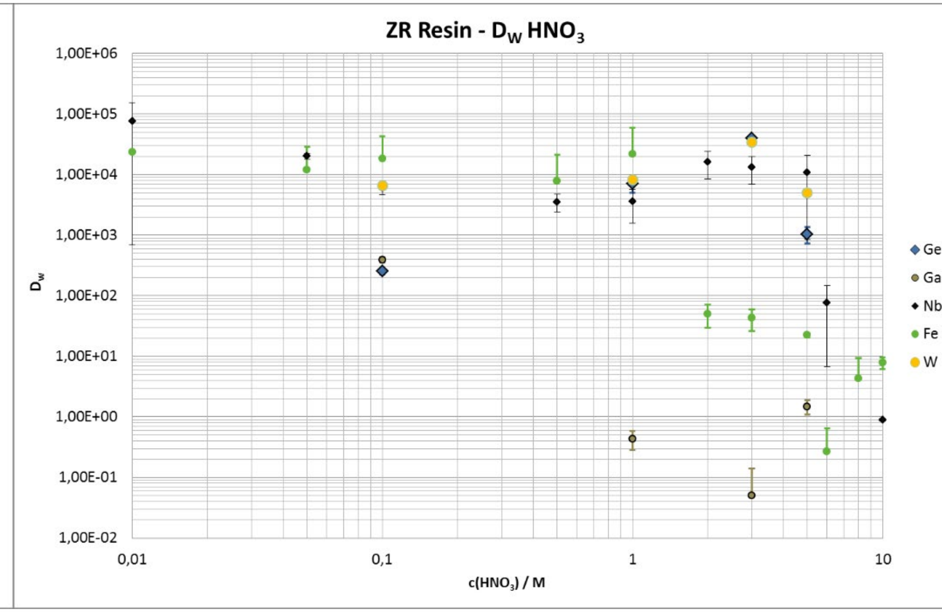
ZR Resin – HCl



- No selectivity for Y, Sc
- High Ge/Ga selectivity at elevated HCl
- High selectivity for Zr, Ti, Nb, W over wide HCl conc. range
- No selectivity for alcalines and earth alcalines
- Lanthanides not retained
- Fe retention (dip at 2 – 3M HCl)

Zr Resin – HNO_3

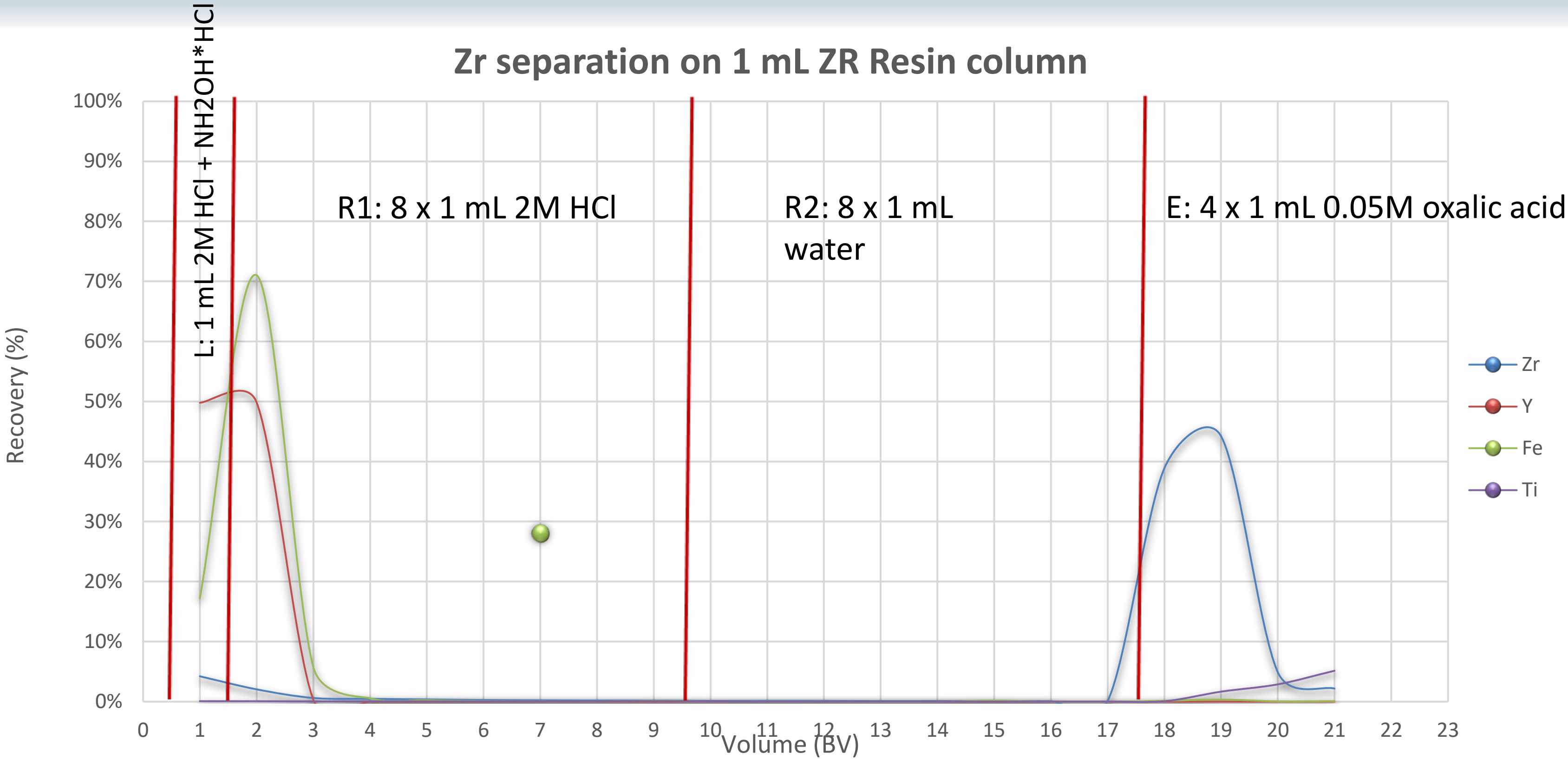




- High selectivity for Zr, Ti, Nb, W over wide HNO_3 concentration range
  - Loss of selectivity at 6M HNO_3

  => Resin shows colour change
- No selectivity for Y, Sc, lanthanides, earth alcalines, most transition metals,…
- High Ge/Ga selectivity at 3M HNO_3

Zr-89 separation from Y targets



- Load from 2 – 6M HCl
- Rinsing described by Holland may be used
- No activation with acetonitrile
- Quantitative Zr elution in 1.5 - 2 mL ≥ 0.05M oxalic acid
- Clean Fe removal
- Use in commercial systems
  - Taddeo, Pinctada,…

Ti-Sc Separation (Ti-44/5)

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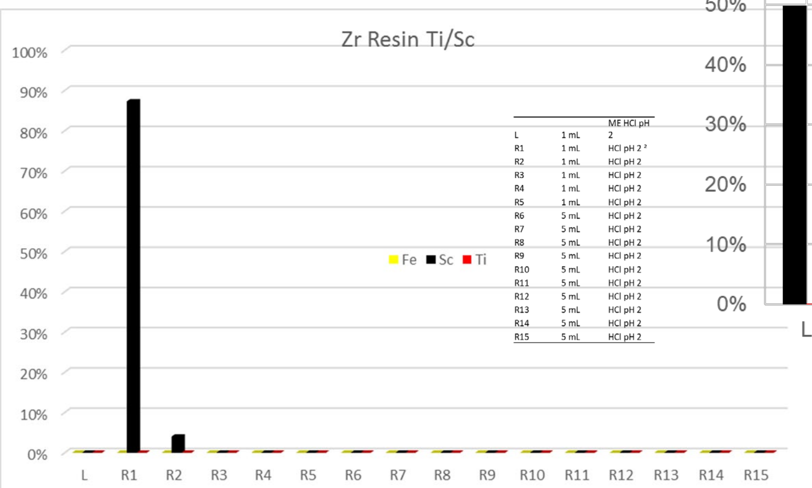
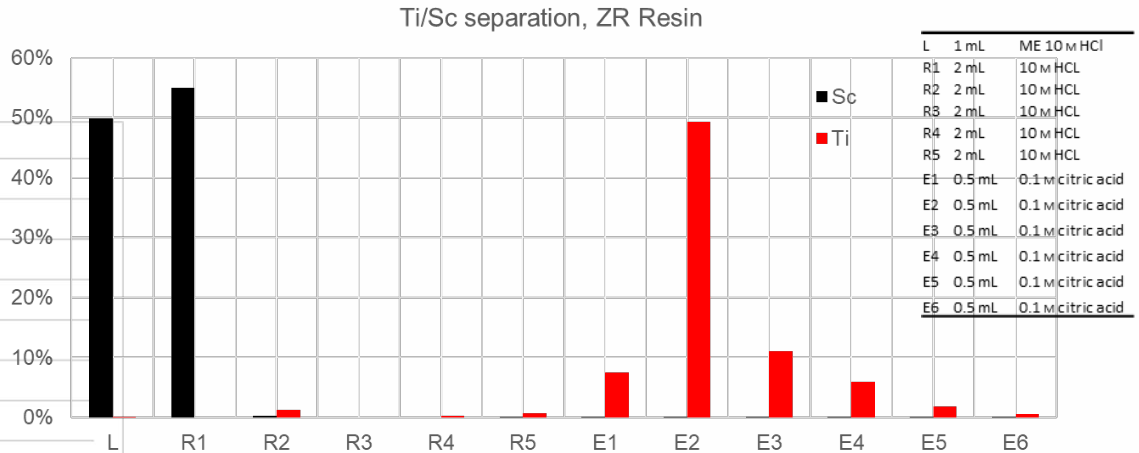
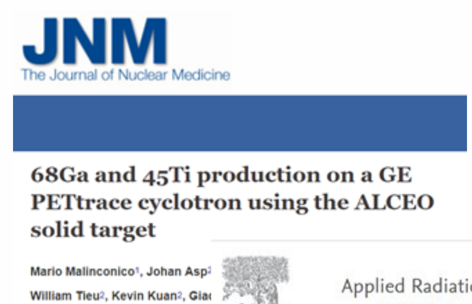
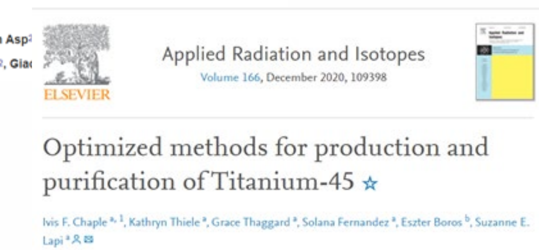





JNM
The Journal of Nuclear Medicine

68Ga and 45Ti production on a GE PETtrace cyclotron using the ALCEO solid target

Mario Malinconico[1], Johan Asp[2]
William Tieu[2], Kevin Kuan[2], Gia


ELSEVIER

Applied Radiation and Isotopes
Volume 166, December 2020, 109398

Optimized methods for production and purification of Titanium-45

Ivis F. Chaple, Kathryn Thiele, Grace Thaggard, Solana Fernandez, Eszter Boros, Suzanne E. Lapi

- Ti retained from (high) HCl, Sc not retained
- Ti also retained in dilute acid, Sc not => Ti generator?
- Ti elution with 0.1M citric, >0.2M oxalic acid, 0.1M H_2O_2
- Publications:
    - Malinconico et al.: J Nucl Med May 1, 2018 vol. 59 no. supplement 1 664)
    - Chaple et al. : Appl Rad Isot, Volume 166, December 2020, 109398

Ti-44/Sc-44

Separation of ^{44}Ti from proton irradiated scandium by using solid-phase extraction chromatography and design of $^{44}Ti/^{44}Sc$ generator system

V. Radchenko, C.A.L. Meyer, J.W. Engle, C.M. Naranjo, G.A. Unc, T. Mastren, M. Brugh, E.R. Birnbaum, K.D. John, F.M. Nortier, M.E. Fassbender*

Chemistry Division, Los Alamos National Laboratory, P.O. Box 1663, Los Alamos, NM 87545, USA

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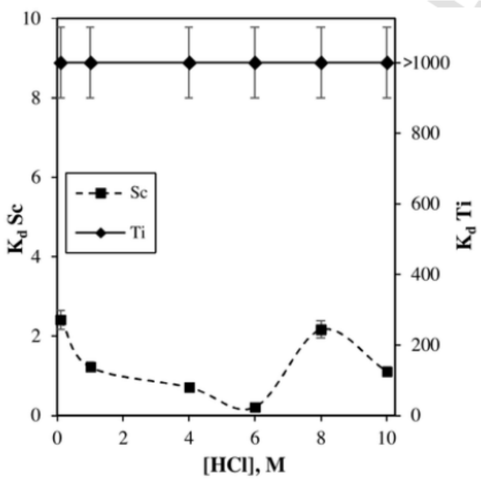


Fig. 3. HCl concentration dependency of K_d for $^{44}Ti/^{46}Sc$ on ZR hydroxamate resin.

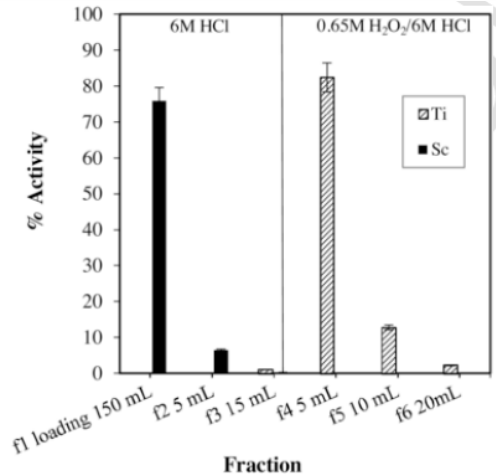


Fig. 5. $^{44}Ti/^{46}Sc$ elution profile using ZR hydroxamate resin with a load of 4 g of scandium.

- **Ti-44 production**
  - 4g irradiated Sc
  - 5 mL Zr Resin
  - Ti-44 yield >95%
  - 65.2 MBq Ti-44
  - D_f(Sc): 10^5

Use of ZR Resin as support in Ti-44/Sc-44 generators

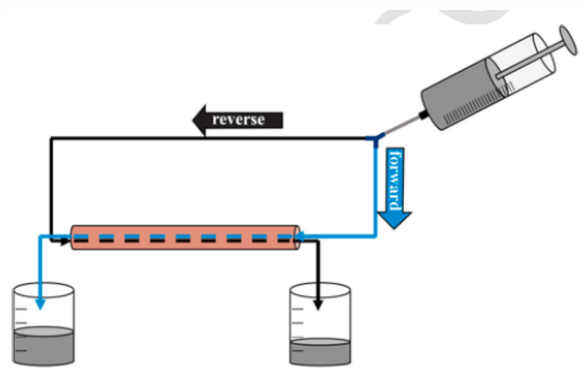
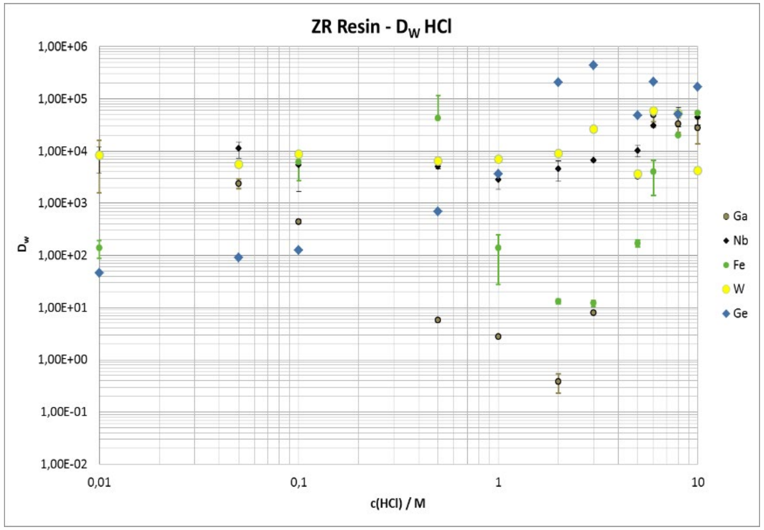


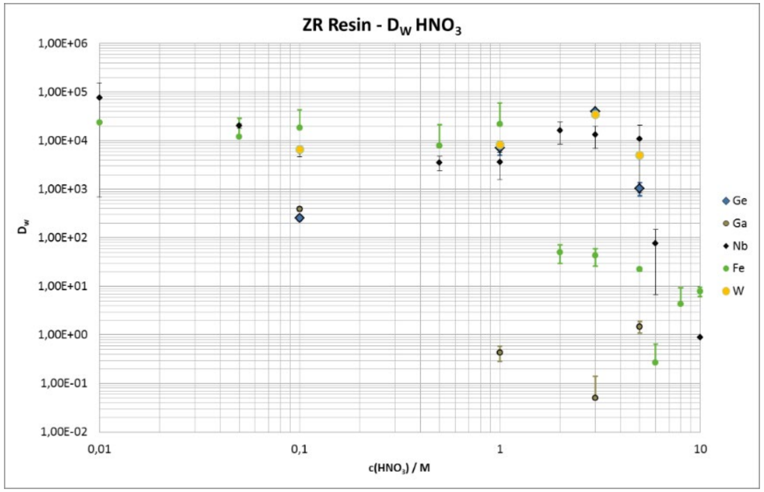
Fig. 1. Schematic concept of a forward/reverse flow radionuclide generator.

- Direct (1 mL ZR) and reverse elution (2 mL ZR)
- 65 column volumes tested up until publication
- High Sc yields, max. Ti-44 breakthrough: 4.1^{E}-4%
- Obtained Sc gave labelling yields > 94%
- Generator been set-up at BNL/SBU => Poster S. Houclier ISRS 2019

Ge-68 separation from GaNi or GaCo

- Loading from HNO_3, HCl or H_2SO_4
  - Target dissolution in HNO_3 or **H_2SO_4** often preferred => $GeCl_4$ volatile
- Ongoing: Cold test on >5g GaNi
- First cycle on ZR (**2 mL ZR Resin cartridge**):
  - Load/rinse from 5M H_2SO_4
  - High Ge retention/purification from Ga, Ni & Co
- Elution: 0.1M citric acid (pH 3)
- Second cycle on ZR (**1 mL ZR cartridge**):
  - Adjustment of eluate to 5M H_2SO_4
  - Load/rinse from 5M H_2SO_4
  - Elution with 0.1M citric acid (pH 3)
- Conversion step (**2 mL Guard Resin cartridge**):
  - Acidification to 9M HCl, load onto Guard Resin
    - Alternative: TK400
  - Rinse with 9M HCl
  - Elution with to 0.05M HCl => pH!

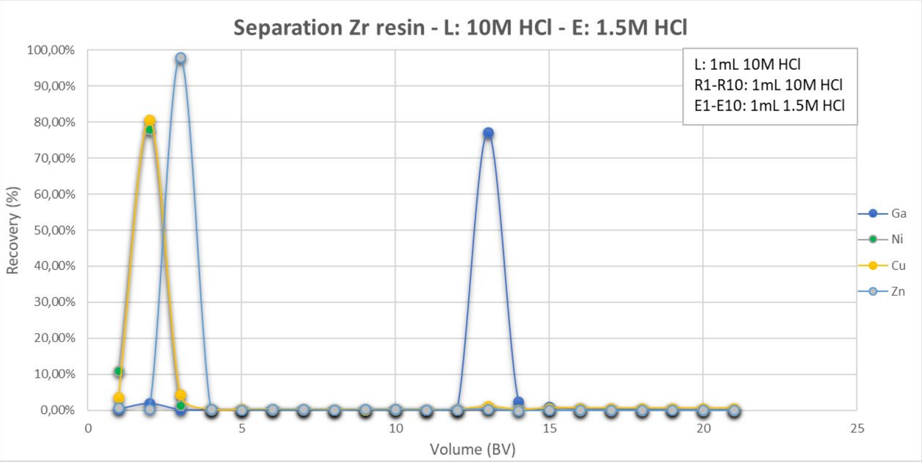


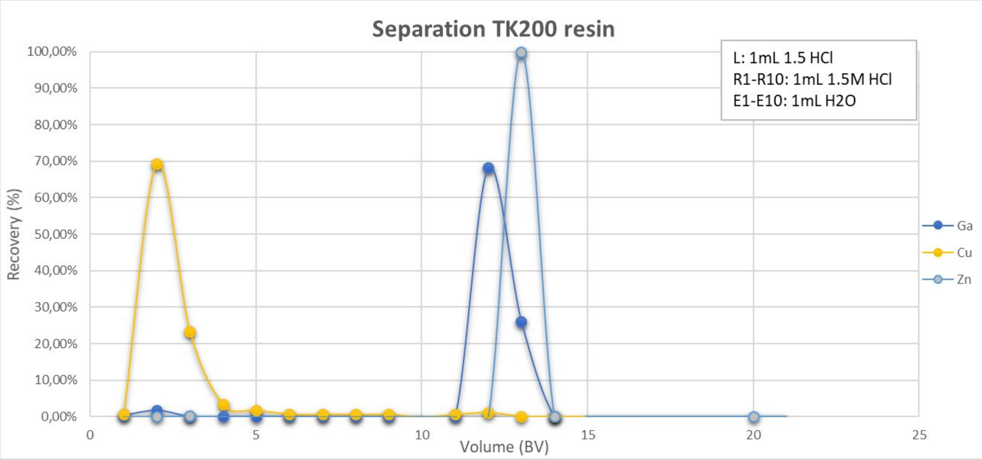


Ga-68(/Ga-67) separation from Zn targets

- **ZR Resin**
  - Loading possible from:
    - dilute HNO_3 (**liquid targets**)
    - > 6M HCl (**solid targets**)
  - Rinse under loading condition
  - Ga separation on ZR Resin
  - Elution with ~1.5M HCl

- **Ga conversion step on TK200**
  - TK200 load from 1.5M HCl
  - Rinse with 1.5M HCl
    - Better pH control of eluate via rinse with NaCl/HCl before elution=> Gagnon et al.
  - Elution in 2 – 3 BV water





⇒ **New IAEA TechDoc:**
https://www-pub.iaea.org/books/IAEABooks/13484/Gallium-68-Cyclotron-Production

Cyclotron production of Ga-68

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Rodnick et al. EJNMMI Radiopharmacy and Chemistry (2020) 5:25
https://doi.org/10.1186/s41181-020-00106-9

EJNMMI Radiopharmacy and Chemistry

RESEARCH ARTICLE Open Access

Cyclotron-based production of ^{68}Ga, $[^{68}Ga]GaCl_3$, and $[^{68}Ga]Ga$-PSMA-11 from a liquid target

Melissa E. Rodnick[1], Carina Sollert[2], Daniela Stark[3], Mara Clark[1], Andrew Katsifis[3], Brian G. Hockley[1], D. Christian Parr[2], Jens Frigell[2], Bradford D. Henderson[1], Monica Abghari-Gerst[1], Morand R. Piert[1], Michael J. Fulham[4], Stefan Eberl[5*], Katherine Gagnon[2*] and Peter J. H. Scott[1*]

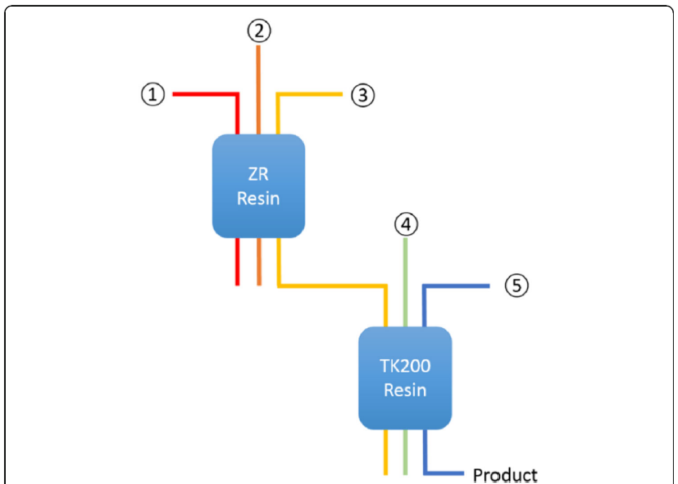


Fig. 4 Two-column approach for ^{68}Ga chemical separation

Table 1 High level schemes of $[^{68}Ga]GaCl_3$ purifications

	Scheme A*	Scheme B
1 ZR Load	< 0.1 M HNO_3	
2 ZR Wash	15 mL 0.1 M HNO_3	
3 ZR Elution / Trapping on TK200	5–6 mL ~ 1.75 M HCl	
4 TK Wash	–	3.5 mL 2.0 M NaCl in 0.13 M HCl
5 TK Elution	H_2O	1–2 mL H_2O followed by dilute HCl to formulate

*Process as reported previously (Nair et al. 2017)

- J. Kumlin et al. (preprint):
  - ZR, LN & TK200 for solid targets

ORIGINAL RESEARCH

Multi-Curie Production of Gallium-68 on a Biomedical Cyclotron and Automated Radiolabelling of PSMA-11 and DOTATATE

Helge Thisgaard, Joel Kumlin, Niels Langkjær, Jansen Chua, Brian Hook, Mikael Jensen, Amir Kassaian, Stefan Zeisler, Sogol Borjian, Michael Cross, Paul Schaffer, Johan Hygum Dam

DOI: 10.21203/rs.3.rs-70698/v1 Download PDF

  - High Ga-68 activities
  - ARTMS/Odense: 10 Ci production: https://physicsworld.com/a/cyclotron-based-gallium-68-generator-breaks-production-records/
- W. Tieu et al.: Use of single TK400 cartridge for solid Zn targets

ELSEVIER
Nuclear Medicine and Biology
Volumes 74–75, July–August 2019, Pages 12-18

Rapid and automated production of $[^{68}Ga]$gallium chloride and $[^{68}Ga]Ga$-DOTA-TATE on a medical cyclotron

William Tieu[a], Courtney A. Hollis[a], Kevin K.W. Kuan[a], Prab Takhar[a], Mick Stuckings[b], Nigel Spooner[b,c], Mario Malinconico[d]

Cyclotron production of Ga-68

- Riga et al. Physica Media 2018
- Liquid target: 1.7M $^{68}Zn(NO_3)_2$ in 0.2M HNO_3
- GE PETtrace at 12MeV, 32 min, 46 µA
- Modular Lab (EZAG)
- 4.3 ± 0.3 GBq EOB
- Separation on ZR Resin and TK200 Resin (t~40 min)
  - Loading of ZR Resin at <0.1M HNO_3,
  - Rince with 9 mL 0.1M HNO_3.
  - Ga Elution with 5 mL 2M HCl directly onto 100 mg TK200
  - Ga Elution from TK200 with water
- Chemical yield >75%,
  - 2.3 ± 0.2 GBq after separation
- Purity: 99.976 ± 0.002% => Ph. Eur.
- Target material recovery 80 – 90%

- For solid targets: single cartridge method (TK400) also under evaluation

Original paper

Production of Ga-68 with a General Electric PETtrace cyclotron by liquid target

Stefano Riga[a,*], Gianfranco Cicoria[b], Davide Pancaldi[a], Federico Zagni[a], Sara Vichi[c], Michele Dassenno[d], Luca Mora[e], Filippo Lodi[e], Maria Pia Morigi[d], Mario Marengo[a]

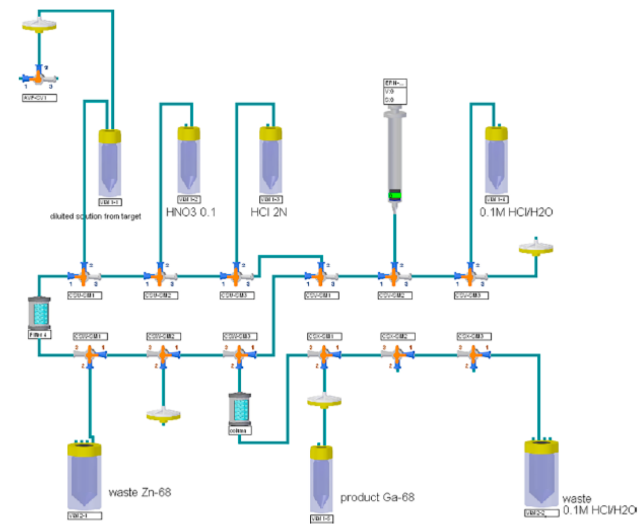
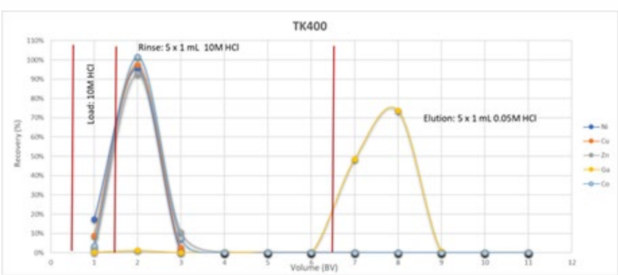
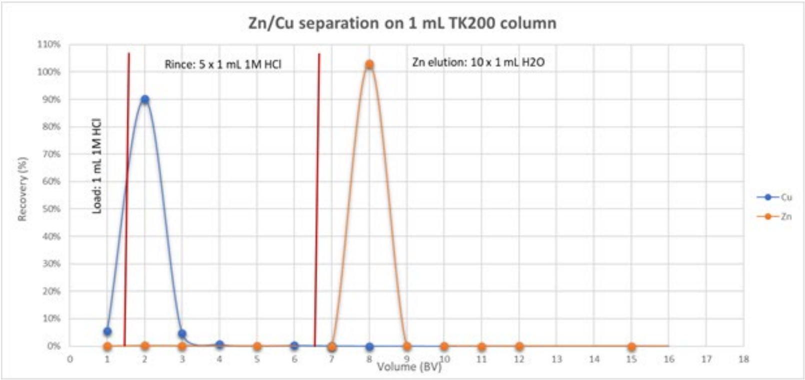


Fig. 4. Schematic diagram of the separation process (Modular Lab, Eckert & Ziegler, Berlin).

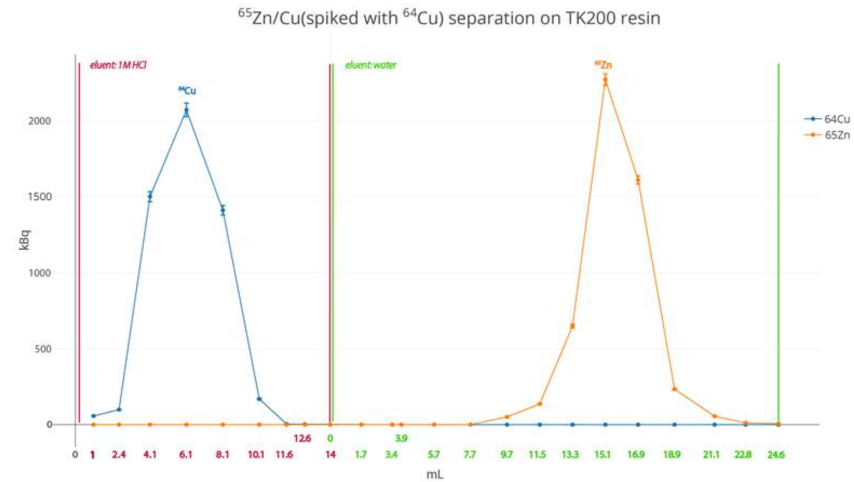


Other examples for separations on TK200 (TOPO based)

- Zn separation from Cu

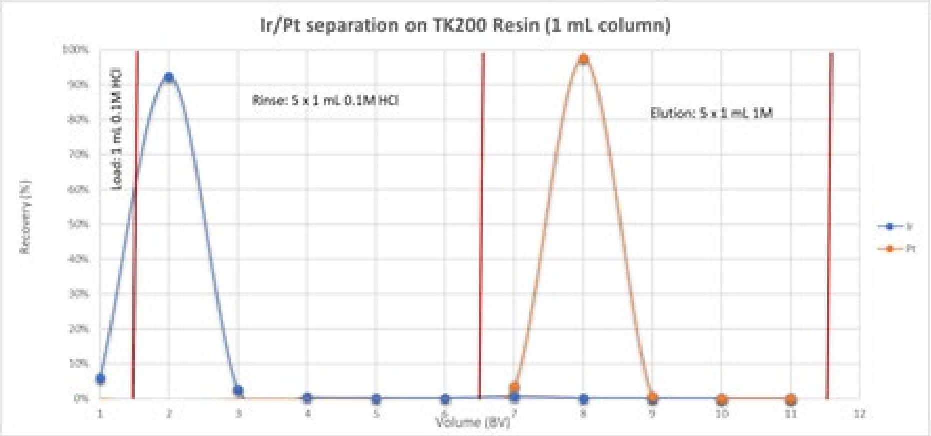


- Zn/Cu separation. Elution study, ICP-MS measurement



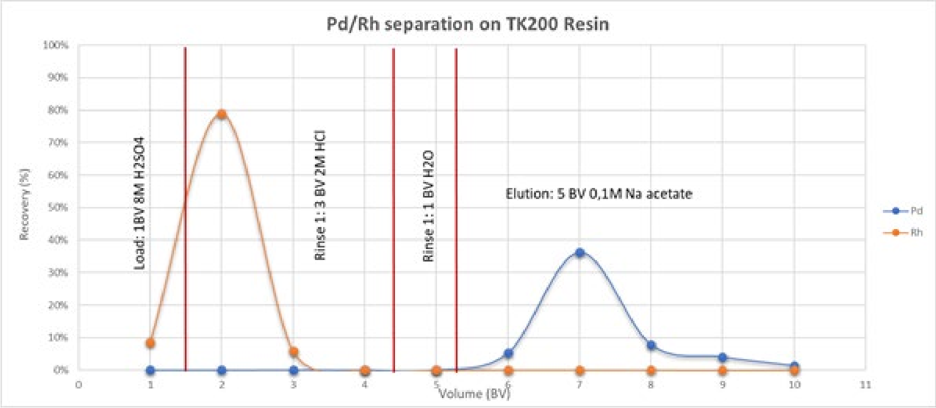
- Zn-65 separation. Data kindly provided by Fedor Zhuravlev, DTU

- Pt separation from Ir



- Pt/Ir separation. Elution study, ICP-MS measurement

- Pd separation from Rh



- Pd/Rh separation. Elution study, ICP-MS measurement

Cu-61/4 separation on TK201

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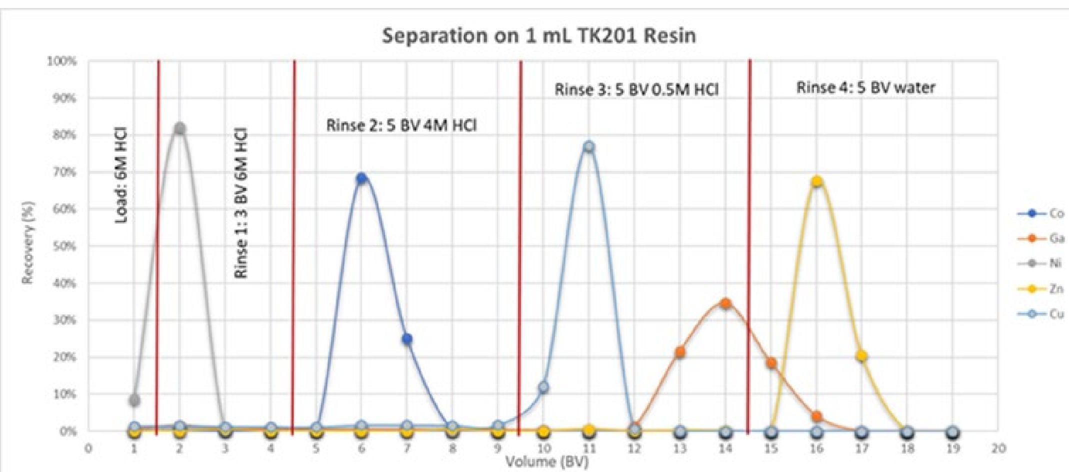
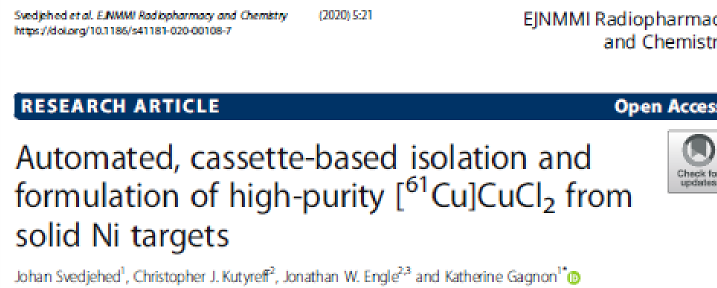
- Cu-64 separation from solid Ni targets on TK201:
  - Load and rinse at 6M HCl => Ni removal => recovery/recycling
  - Co elution with 4 – 5M HCl
  - Gagnon et al. use of NaCl/HCl for better pH control of eluate
  - Cu elution with 0.5M HCl => Fe and Zn remain retained
  - Preferred alternative: Use of TBP (or TK400) upfront for Fe/Ga removal => allows for Cu elution in 0.05M HCl




Svedjehed *et al. EJNMMI Radiopharmacy and Chemistry* (2020) 5:21
https://doi.org/10.1186/s41181-020-00108-7

EJNMMI Radiopharmacy and Chemistry

RESEARCH ARTICLE Open Access

Automated, cassette-based isolation and formulation of high-purity [^{61}Cu]$CuCl_2$ from solid Ni targets

Johan Svedjehed[1], Christopher J. Kutyreff[2], Jonathan W. Engle[2,3] and Katherine Gagnon[1*]

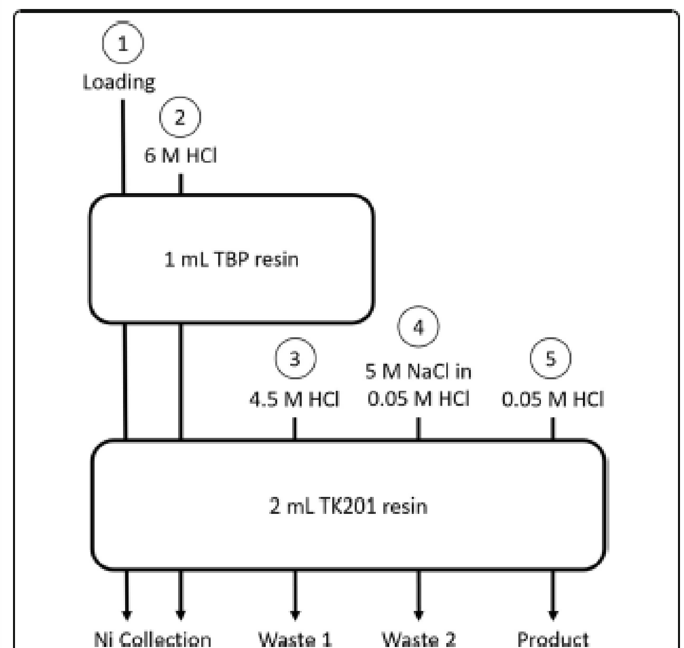
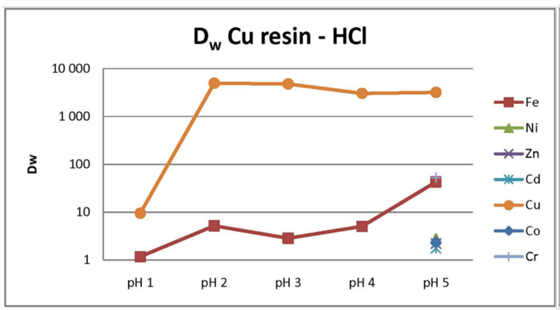
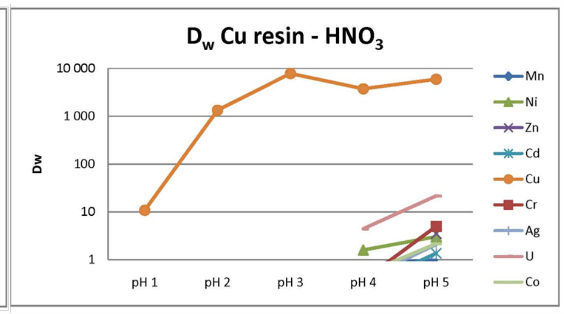


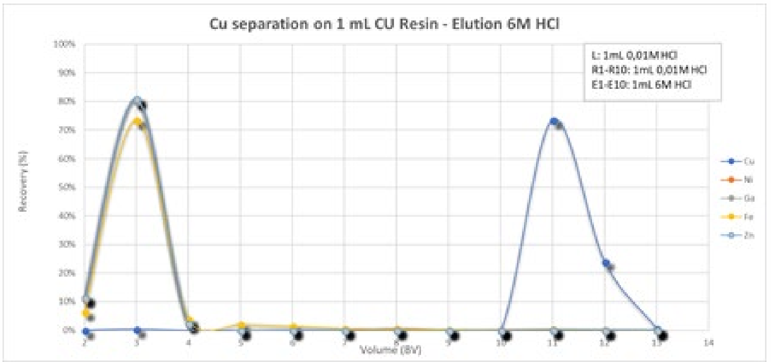
Fig. 1 Two-column approach for ^{61}Cu separation. Process steps described below

CU Resin

- Oxime based resin
- High selectivity for Cu
  - Especially with respect to Zn and Ni
  - Widely used in mass spectrometry (Cu isotope ratio measurement)







- Load from pH >2, elution in high mineral acid (0.5 – 8M)
  - Suitable for **liquid** targets
  - Used for (large) solid **Zn** targets (=> Cu-67)
  - Loading not ideal for solid Ni targets (usually high HCl) => TK201
  - Elution in high HCl not compatible with labelling/injection
    - Evaporation or conversion to dilute HCl e.g. via TK201
  - High purity and labelling yields
- Method for solid Ni targets for TK201 then CU Resin under development

Cu-67 at BNL (DeGraffenreid et al.)

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Purification of ^{67}Cu and Recovery of its Irradiated Zn Target

A.J. DeGraffenreid[a] , R. Nidzyn[a], B. Jenkins[a], D.E. Wycoff[b], T.E. Phelps[b], A. Goldberg[a], D.G. Medvedev[a], S.S. Jurisson[b], C.S. Cutler[a]
[a]Brookhaven National Laboratory, C-AD/MIRP—Upton, NY (USA)
[b]University of Missouri, Department of Chemistry—Columbia, MO (USA)

Poster presented at ISRS 2017

- 13.7g Zn metal dissolved to give 312 mg $ZnCl_2$/mL solution at pH 2
- Loading of 60,6 mL => 18.9g ZnCL2 onto 2.4g CU Resin column => 8 mL
- Rinse with 80 mL pH2 HCl
- Elution in 2 x 20 mL 6M HCl
- Evaporation to dryness
- Chemical yield ~100%
- Single column D_f for Zn ~10 000
  - Additional removal indicated
- Ideally further Zn and Co removal
- Original suggestion: AIX

Cu Resin

Nuclide	EOB Activity (mCi ± 1σ)	Recovery (%) Load w/ Quant. Transfer	pH 2 HCl Rinse	Acid #1	Acid #2
^{64}Cu	4700 ± 200	ND	ND	102	ND
^{65}Zn	41.0 ± 0.8	103	ND	0.04	ND
^{58}Co	63 ± 1	104	0.04	0.1	0.01

- Produced 143 mCi ^{67}Cu
- Quantitative recovery of radiocopper
- 99.5% radionuclidic purity—single column
- ICP-OES: 132.9 µg Cu and 1.3 mg Zn
  - Anion exchange column still needed to remove trace Zn
- Specific activity ^{67}Cu at EOB: 1.07 mCi/µg

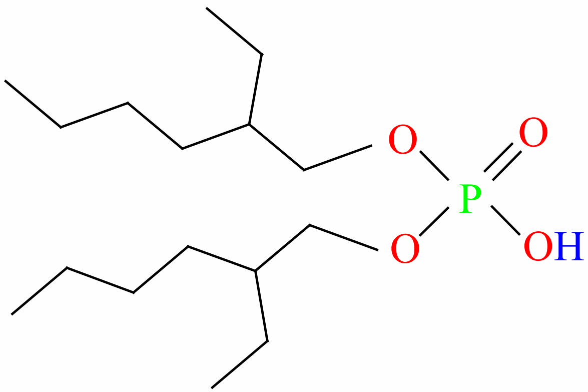
Cu Resin

Robust separation that could shorten the overall processing time to separate co-produced radionuclides and large quantities of Zn from radiocopper
Cation and anion exchange columns still needed to suitably purify radiocopper

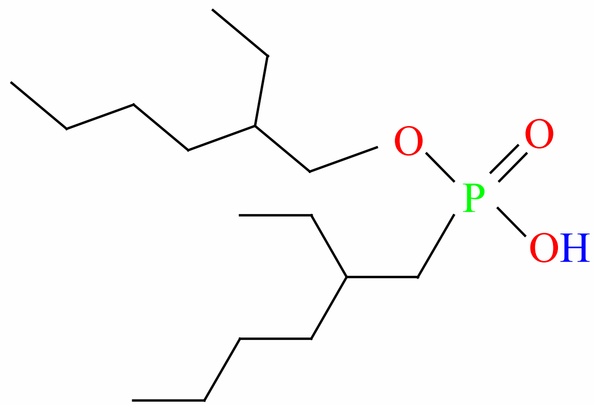
Alternatives to AIX:

- TK201: prefered option. Cu elution from CU Resin with 6M HCl directly onto TK201, followed by Cu elution from TK201 in dilute acid
- TK200: Cu eluted from CU Resin in 1 - 2M HCl, direct load through TK200 (Zn retained, Cu passes)

Lanthanide separation on TK211/2/3 or LN series

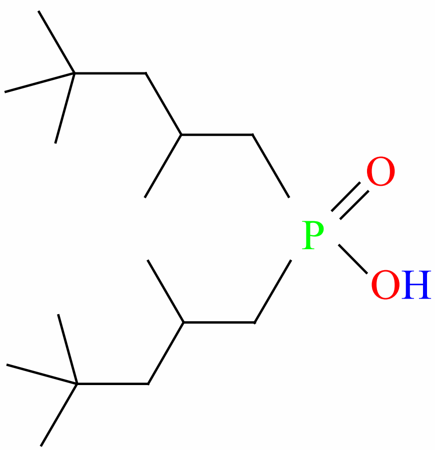


HDEHP (LN)



HEH[EHP] (LN2)

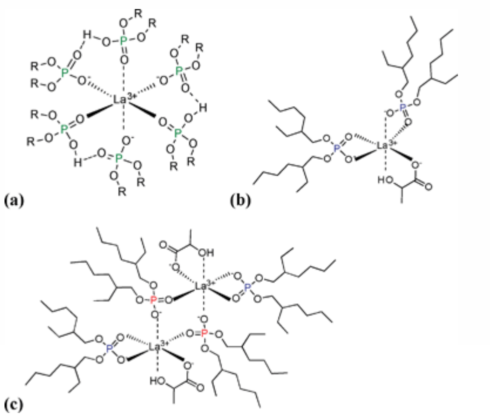
Extractants e.g. employed in **LN Resins** and **TK211/2/3**

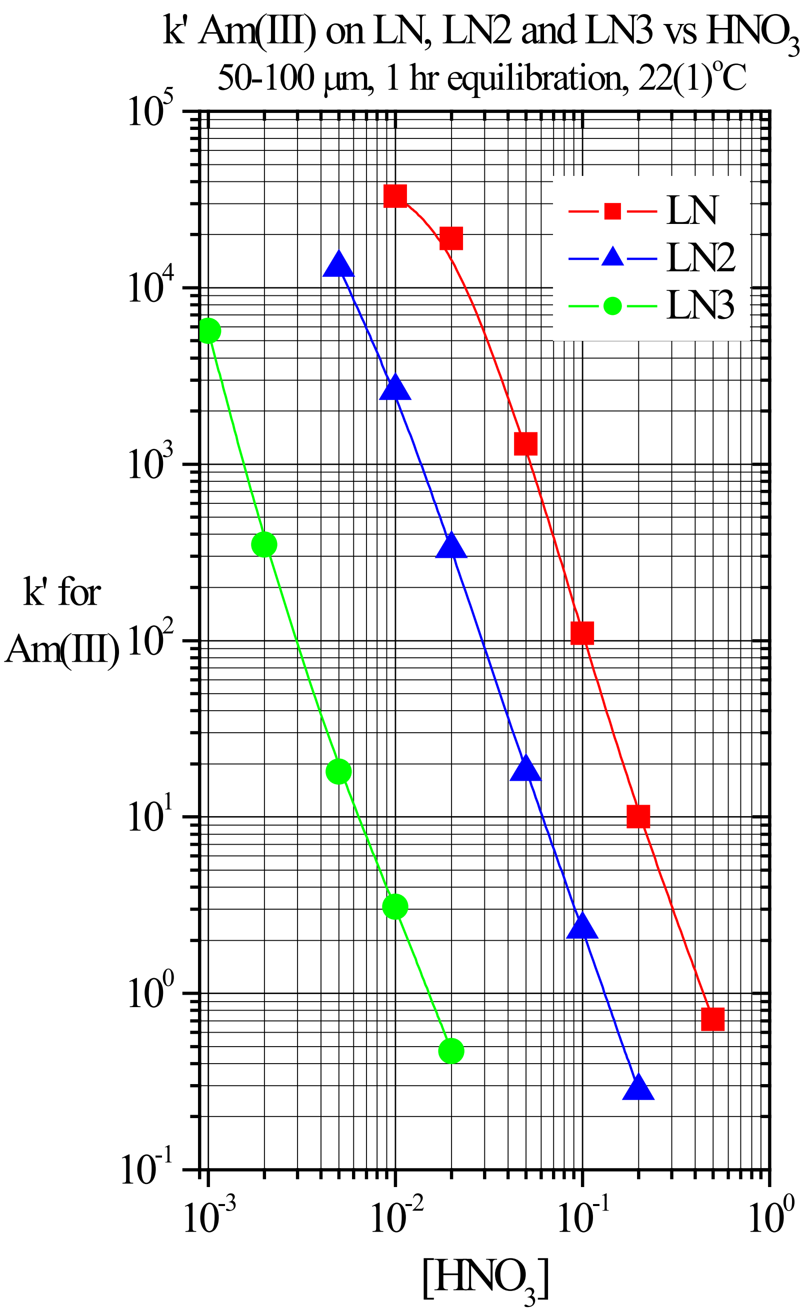


H[TMPeP] (LN3)

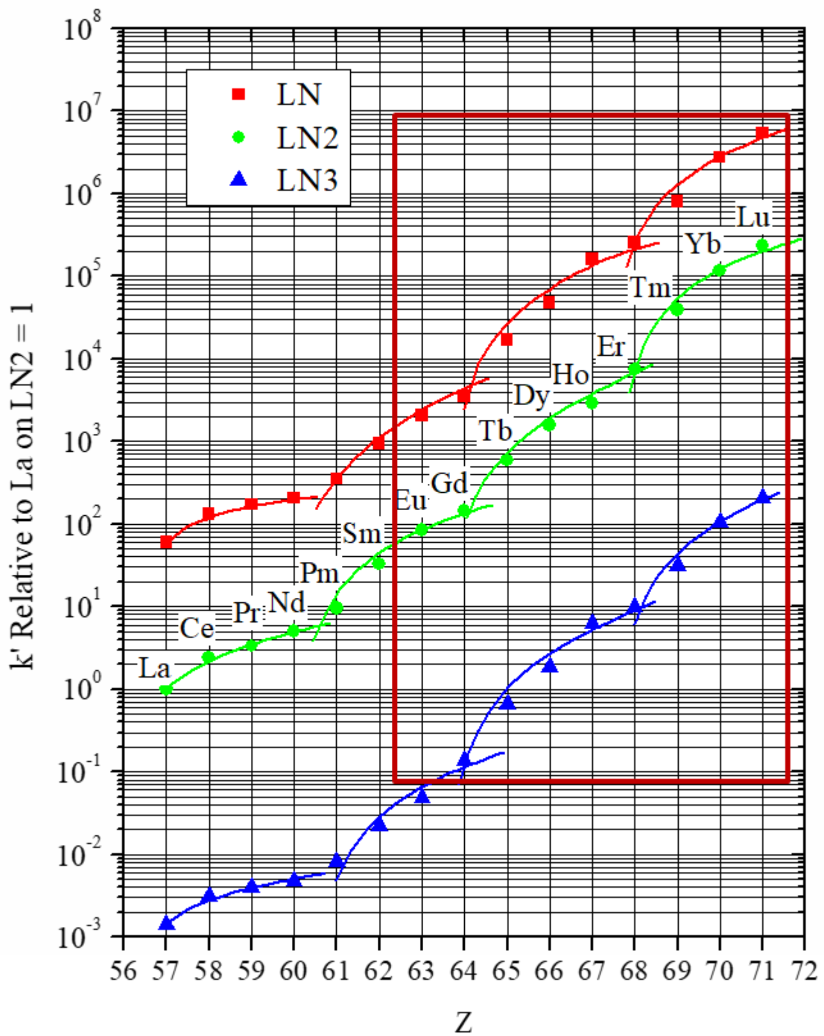
Product sheet:
http://www.triskem-international.com/scripts/files/5b0bc8955eeb28.64750263/LN_LN2_LN3%20RESINS-EN.pdf

$$M^{3+} + 3\overline{(HY)_2} \leftrightarrow \overline{M(HY_2)_3} + 3H^+$$





Main difference: acidity



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Expertise in Separation Chemistry

nca Lu-177 from Yb targets

E.P. Horwitz et al.: A Process for the Separation of Lu-177 from Neutron Irradiated Yb-176 Targets, Applied Radiation and Isotopes, Vol 63, pp 23-36, (2005)

Submitted to Applied Radiation and Isotopes 11/2004

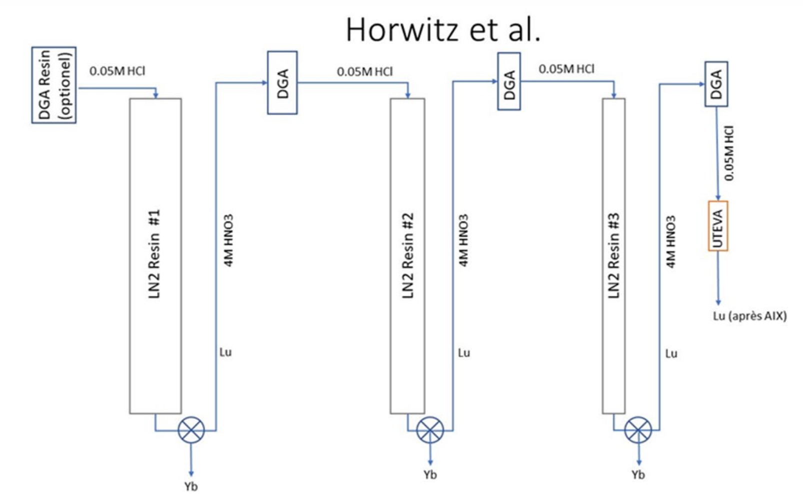
A Process for the Separation of ^{177}Lu from Neutron Irradiated ^{176}Yb Targets

E. P. Horwitz[1,]*, D. R. McAlister[1], A. H. Bond[1], R. E. Barrans[1], J. M. Williamson[2]

[1]PG Research Foundation, Inc., 8205 S. Cass Ave., Suite 106, Darien, IL 60561

[2]Eichrom Technologies, Inc., 8205 S. Cass Ave., Suite 106, Darien, IL 60561

- Allows for nca Lu-177 separation from 300 mg Yb targets
- Lu and Yb chemically very similar
- Based on LN2 and DGA, N
- Large amounts of Yb introduce peak tailing
  - The more Yb the stronger the tailing
- Multi-column method needed
- Lu yield ~73%
- Rapid (<6h) but difficult to automize method
- Under optimization and upscale



On-going developments radiolanthanides (nca Lu-177, Tb-161)

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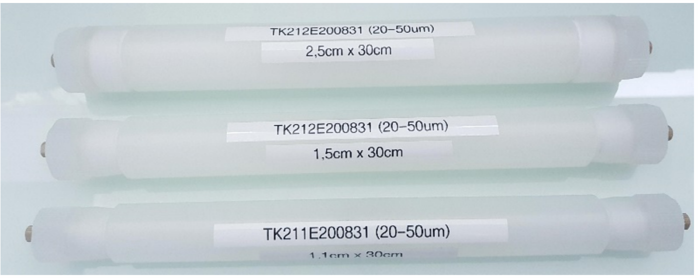
- Separation of nca Lu-177 from Yb-176 targets (500 – 2000 mg)
- Partial simplification via sequential separation steps
  - 'Sequential separations' approach also applicable e.g. to Tb separation
- New resins: TK211/2/3
  - On-bead mix of different extractants for improved selectivity
  - Higher extractant load
  - Small amount of long-chained alcohol and use of inert support containing aromatic groups => aim: improved radiolysis stability
  - 20 - 50 µm beads
    - Originally developped as 15µm beads => too small for large scale separations
  - Resins also applicable to Horwitz method
    - TK212 & TK221 instead of LN2 and DGA
- Prepacked PP columns under development
  - 29 mL, 53 mL, 150 mL, 375 mL and 750 mL
  - With CoA
- Upscale to 1g and 2g Yb targets under finalisation



• Simplified method for Lu separation from 500 mg Yb – TK211/2 & TK221

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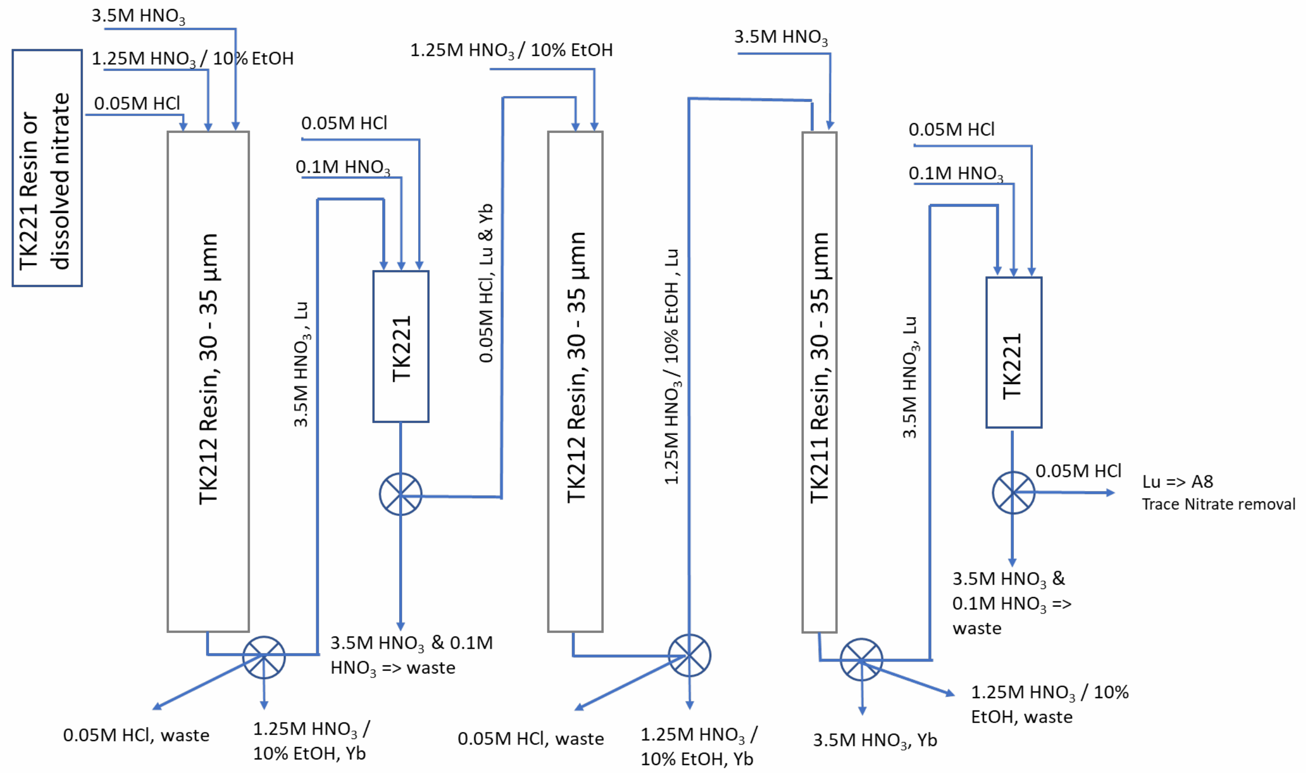
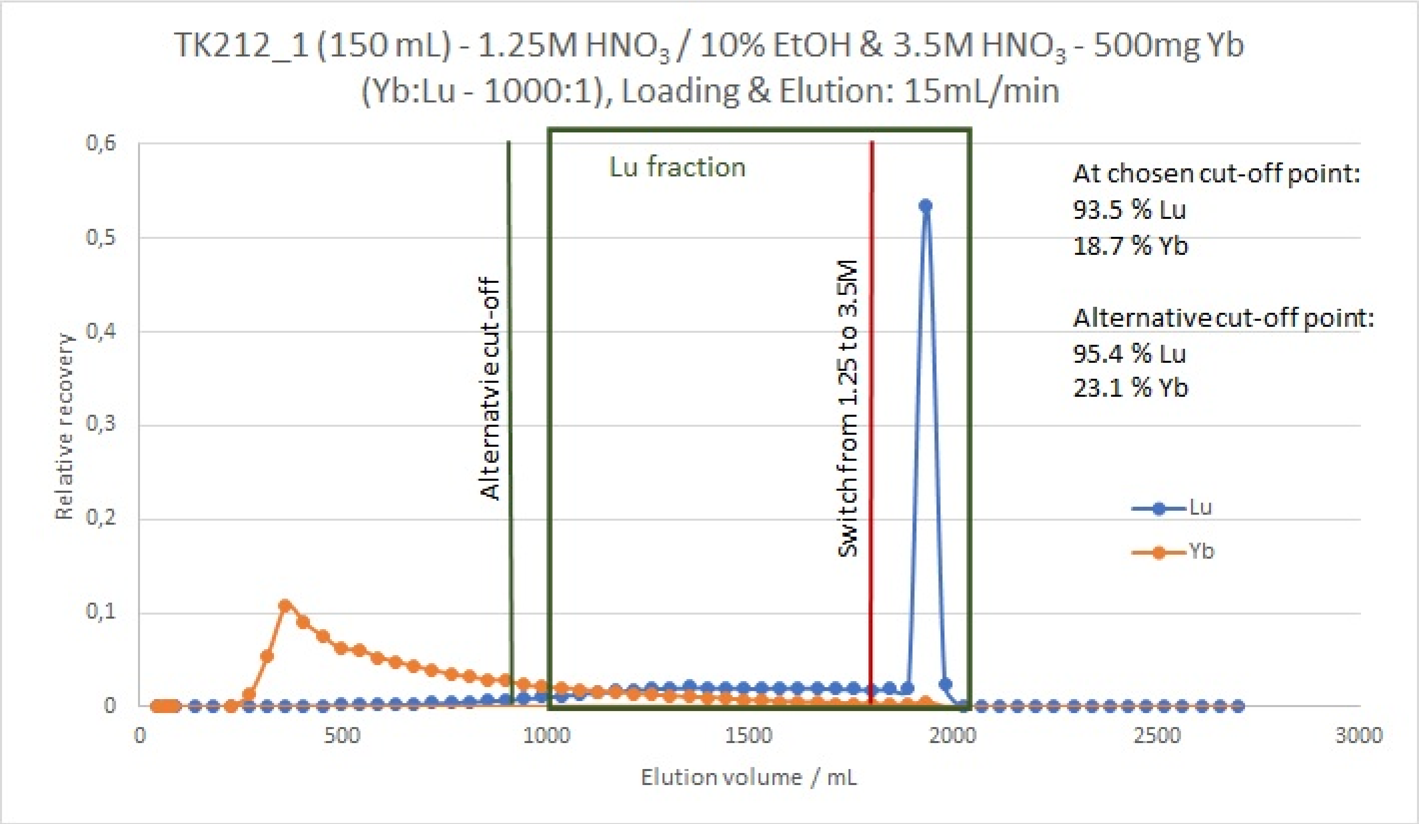


- Sequential separation step (direct load from TK212 onto TK211 for polish)
- Simplification of Horwitz method
- Can be upscaled to 1g or 2g (larger columns)

Lu separation form 500 mg Yb - **TK212**/TK221/TK212/TK211



- Large tailing due to high Yb content
- Improved separation through use of 1.25M HNO_3 / 10% EtOH (v/v)
- Higher Lu yield at similar residual Yb compared to LN2 based method (cf. LN Resins product sheet)
- Additional benefit from use of EtOH => improved radiolysis stability
- Online separation: switch at start of Lu fraction => ideally radiation detector driven

Lu separation form 500 mg Yb - TK212/TK221/**TK212**/TK211

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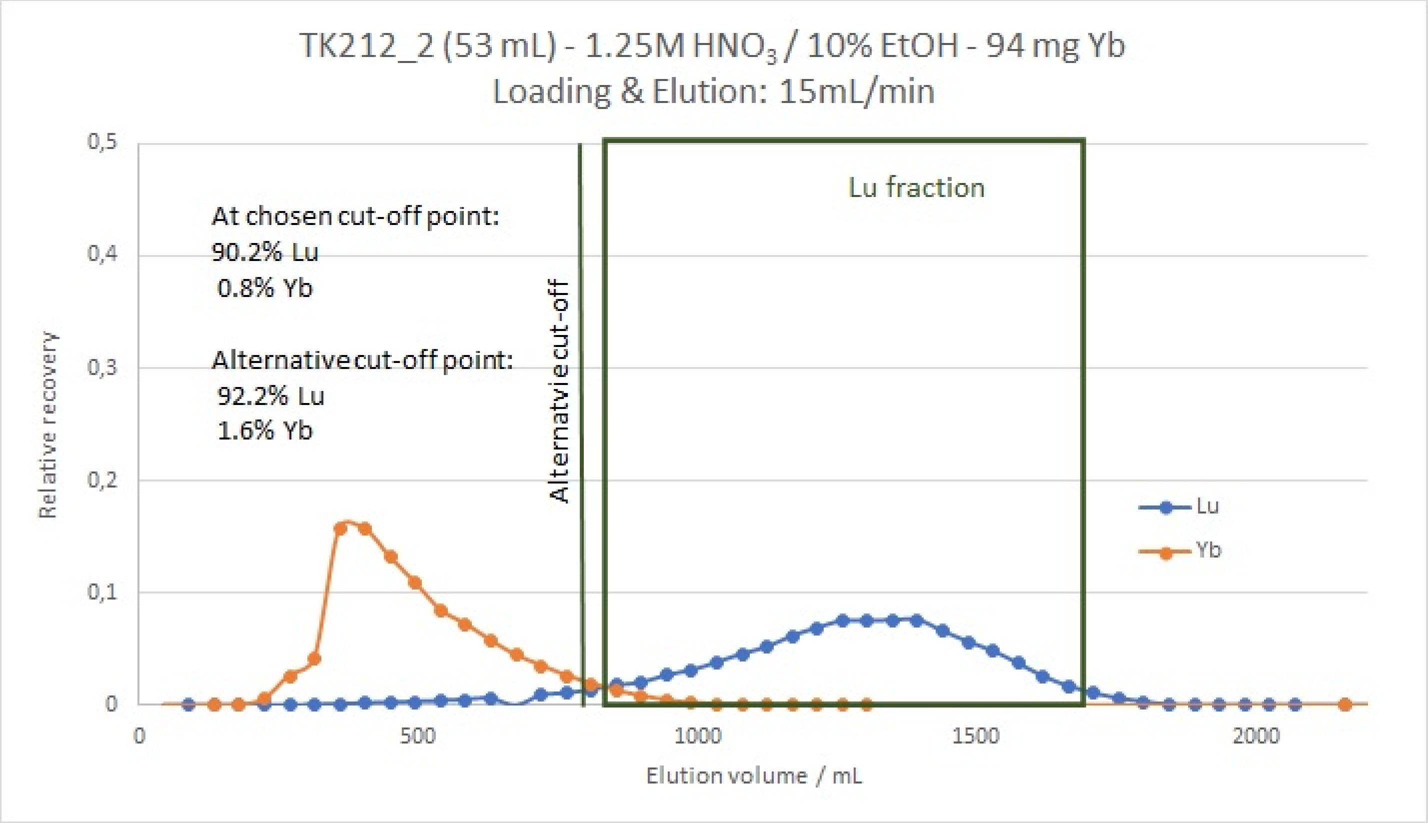
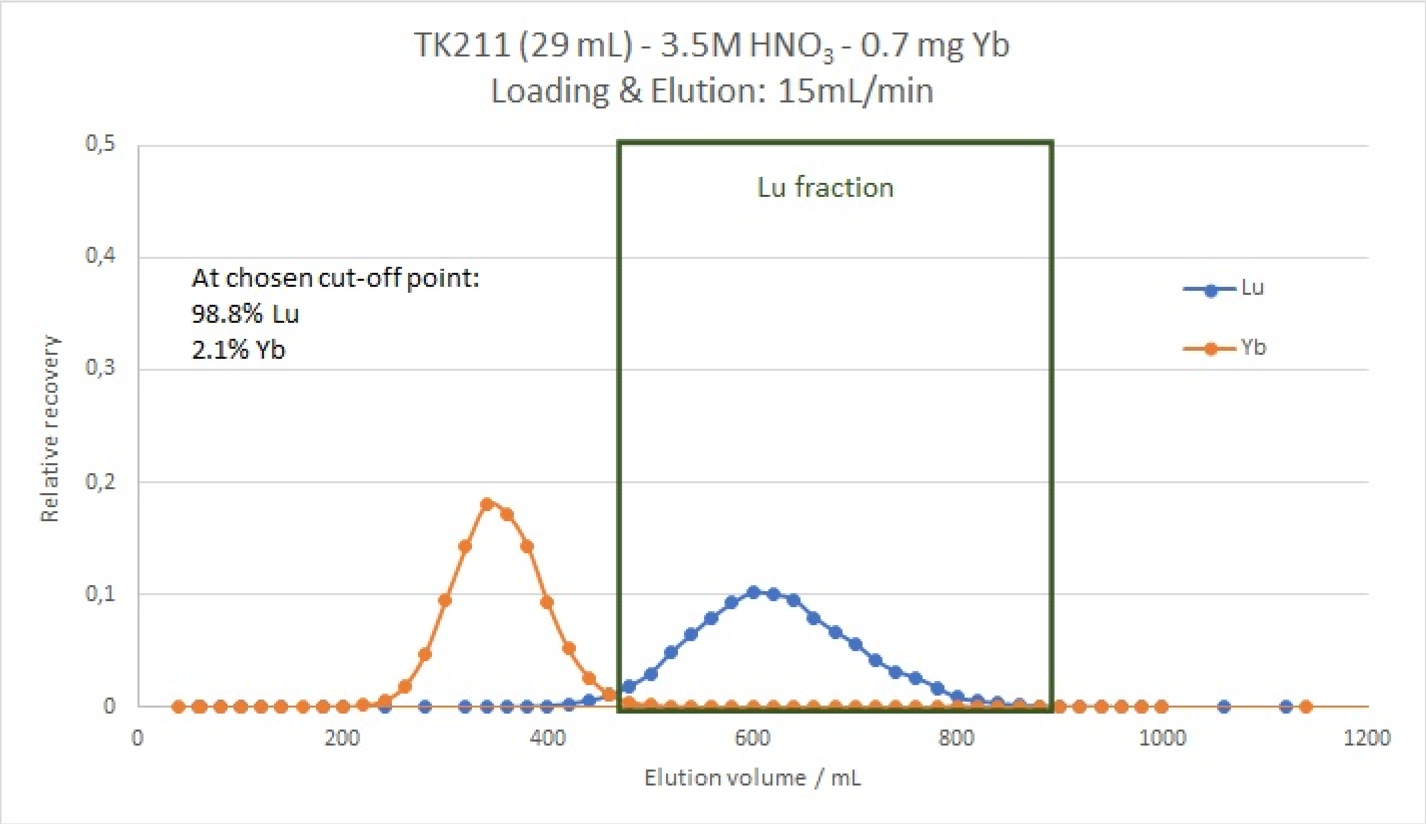


- 2nd separation step on smaller TK212 (53 mL) after TK221 for conversion from high HNO_3 to dilute HCl
- Separation with e.g. 1.25M HNO_3 (with or without 10% EtOH)
- Direct loading of obtained Lu fraction onto TK211 Resin
  - Alternatively TK221/TK212 according to Horwitze et al.

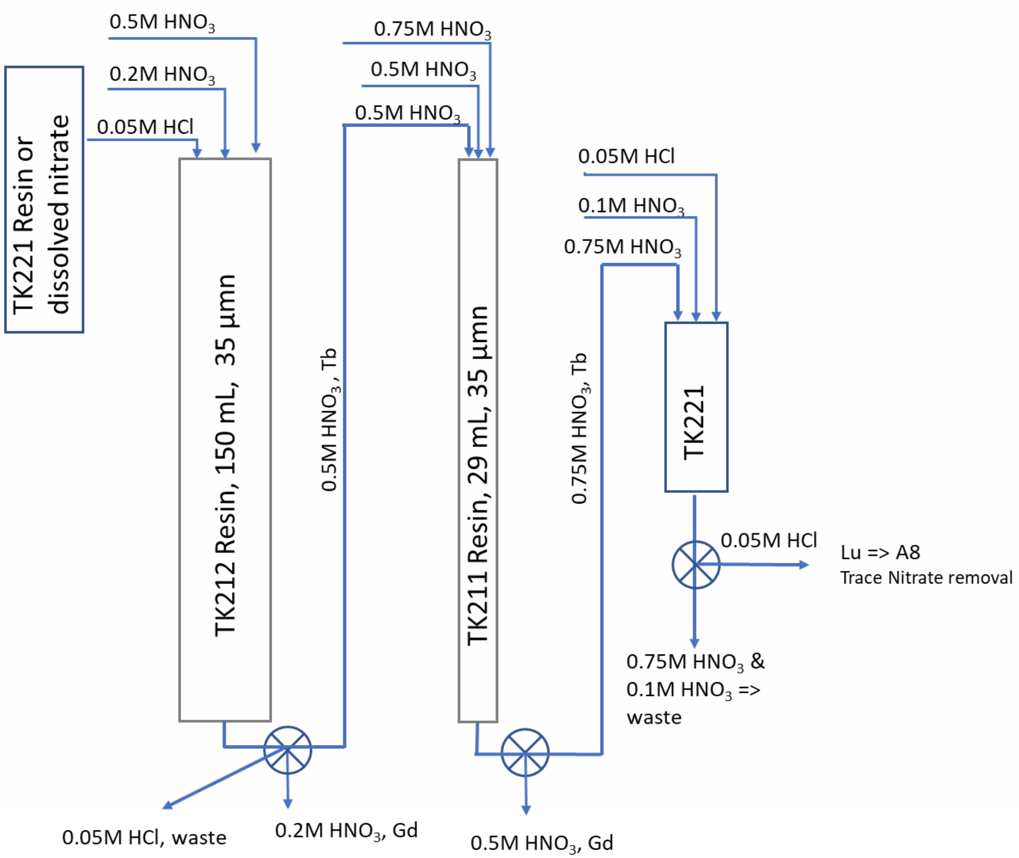
Lu separation form 500 mg Yb - TK212/TK221/TK212/**TK211**



- Lu / Yb separation on TK211 (29 mL) => Lu fraction directly loaded onto TK211 from TK212
- Overall Lu recovery of process approx 85%
- Low remaining Yb
- Flow rates may be optimized
- Final step: concentration/conversion to ≤ 0.05M HCl on TK221, nitrate removal via A8

Tb separation from 500 mg Gd targets

- Schematic view of the tested process – example HNO_3
- Further options: improvement of separation through edition of EtOH or use of HCl



Tb separation from 500 mg Gd targets

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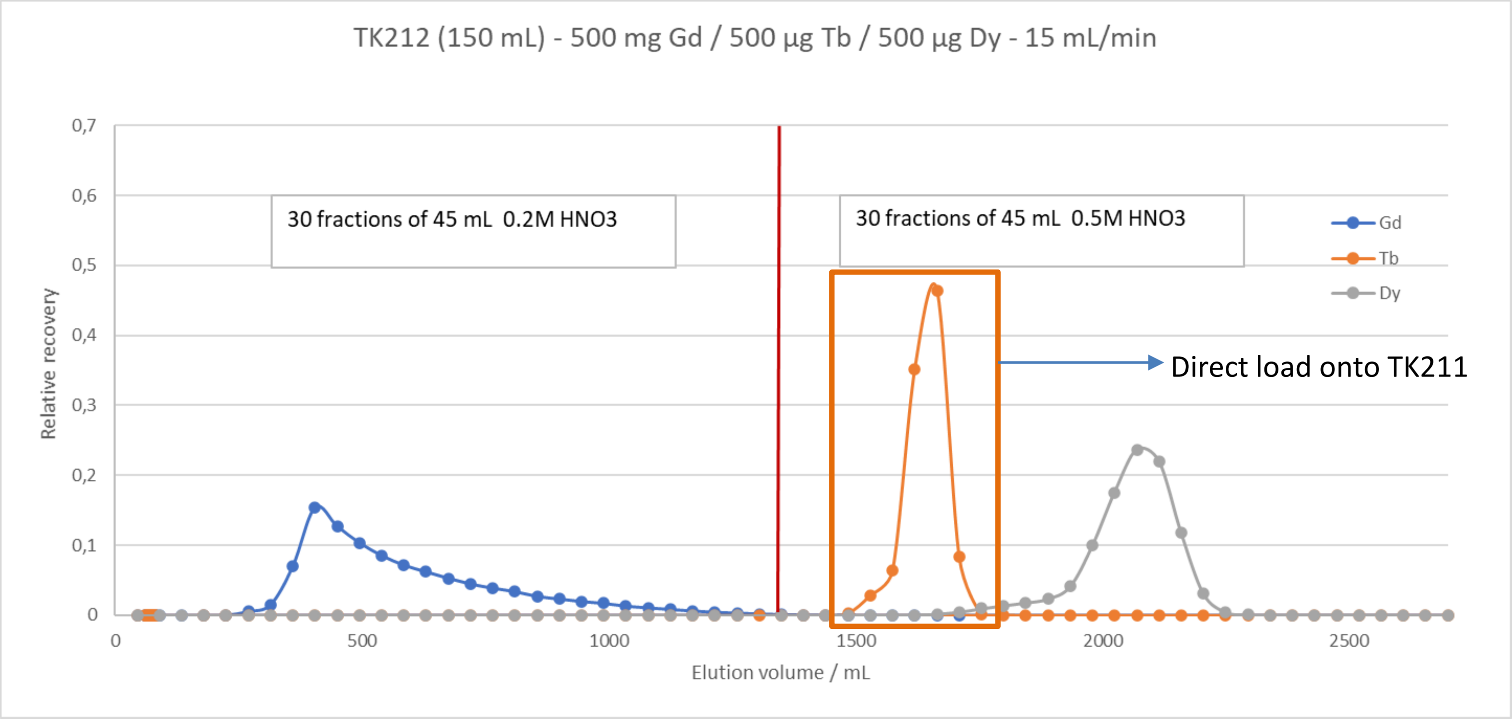
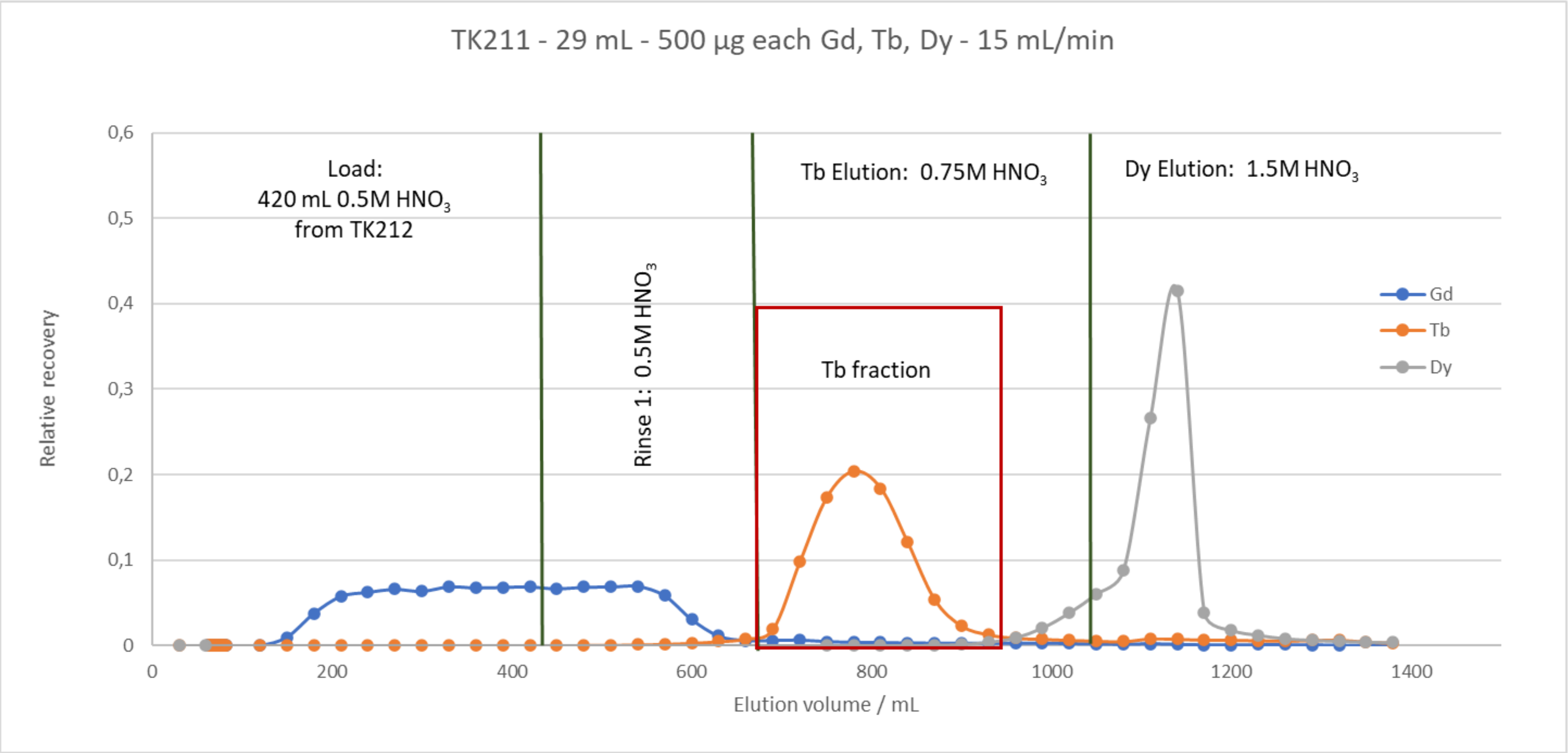
- Initial separation on TK212 – 150 mL columns / HNO_3 or HCl
- TK212 method – further fine tuning ongoing (e.g. adjustment of eluents to 10% EtOH)
- Separation easier than Lu/Yb
- Polishing via direct load ont TK211 (29 mL)



Tb separation from 500 mg Gd on TK212 (150 mL column)

Tb polish on TK211



- Direct load of Tb fraction from TK212 onto TK211 (29 mL)
- Gd breakthrough during load & rinse with 0.5M HNO_3 (alternatively HCl)
- Method optimisation on-going
- Conversion to dilute HCl via TK221, A8 for nitrate removal

• On-going developments Lu-177/Tb-161 – new TK221 Resin

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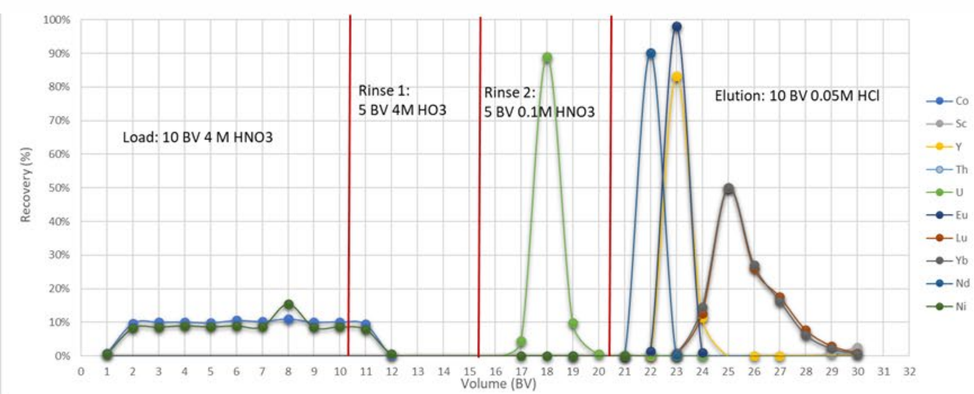
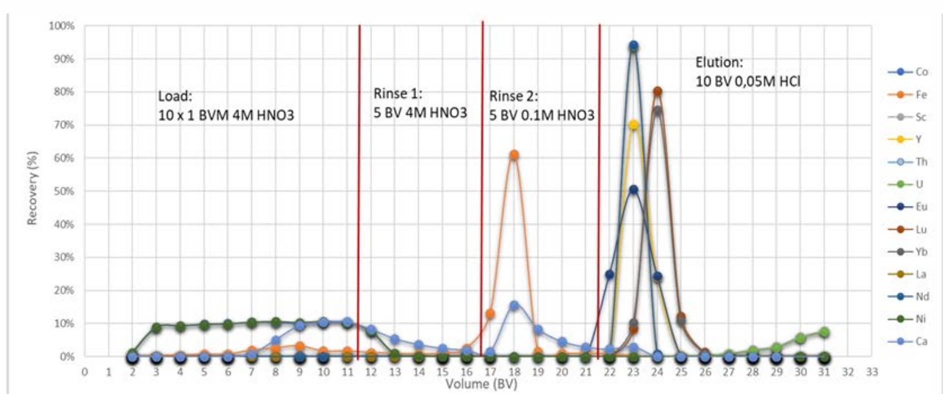
- DGA well suited for ‘conversion’ and purification (Ca, Al, Fe,… removal)
  - Convert Lu from high nitric acid to dilute HCl
- Elution of heavy lanthanides needs elevated volumes
  - small volume prefered => high activity concentration
- Optimisation of DGA Resin => new TK221 Resin
  - Lu eluted in smaller volume
  - Should also work for Ac-225 conversion/purification => better: upcoming TK222 Resin
  - Also improved U retention





Zr-89 separation on TBP Resin

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- Method published by Graves et al.
- 400mg Y foils irradiated at 14 MeV (50 µA)
- Dissolution in 10 mL conc. HCl
- Separation on 220 mg TBP Resin
- Load from 9.6M HCl, rinse with 20 mL 9.6M HCl
- Zr elution with 1 mL 0.1M HCl
- Zr yield: 89 ± 3%, Y decontamination: 1.5 x 10^5
- Zr elution with oxalate, citrate, phosphate…
- Other applications of TBP Resin:
  - Sc isotope production from Ca targets (=> presentation EANM'18, Polatom)
  - Sn-117m from Cd targets

ELSEVIER
Nuclear Medicine and Biology
Volumes 64–65, September–October 2018, Pages 1-7

Evaluation of a chloride-based ^{89}Zr isolation strategy using a tributyl phosphate (TBP)-functionalized extraction resin

Stephen A. Graves [a], Christopher Kutyreff [b], Kendall E. Barrett [b], Reinier Hernandez [c], Paul A. Ellison [b], Steffen Happel [d], Eduardo Aluicio-Sarduy [b], Todd E. Barnhart [b], Robert J. Nickles [b], Jonathan W. Engle [b]
Show more

https://doi.org/10.1016/j.nucmedbio.2018.06.003
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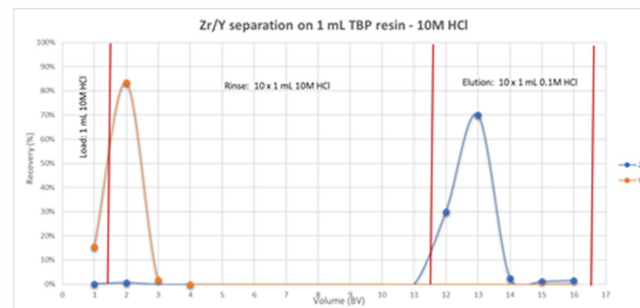
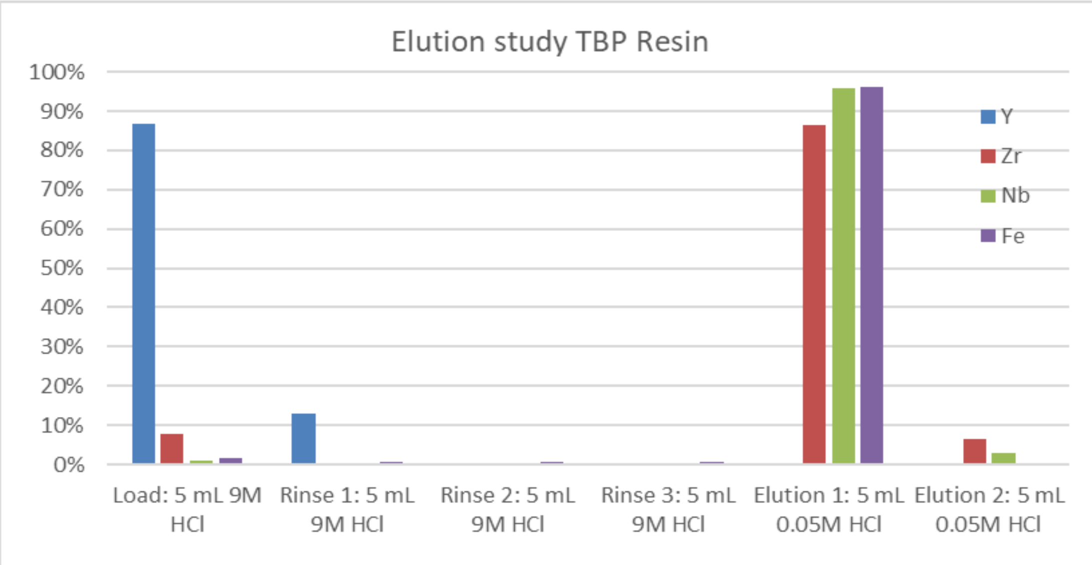
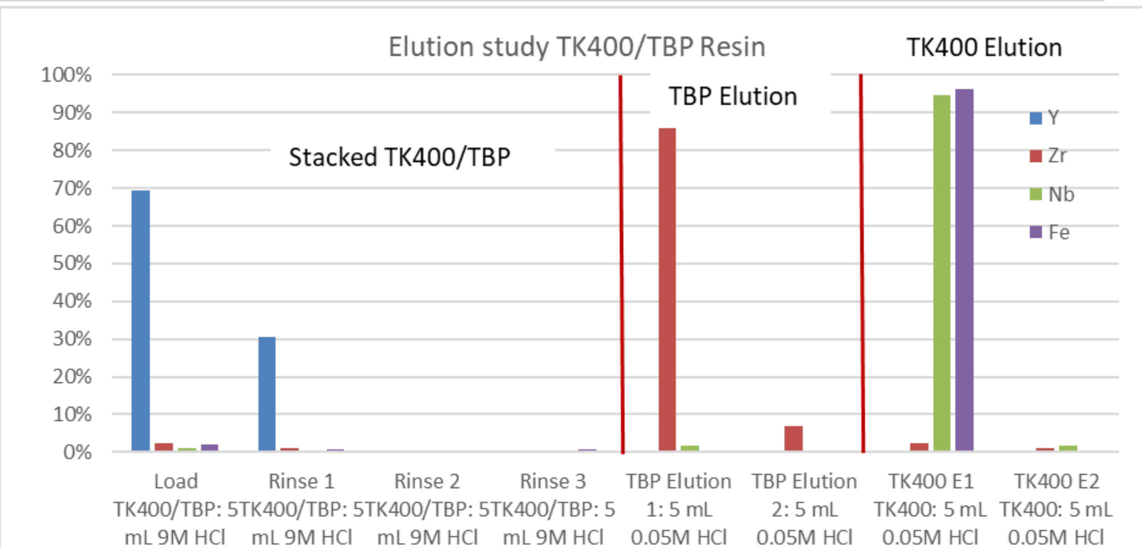


Use of TK400 for Fe/Nb removal





- On-going work – initial testing
- On TBP only:

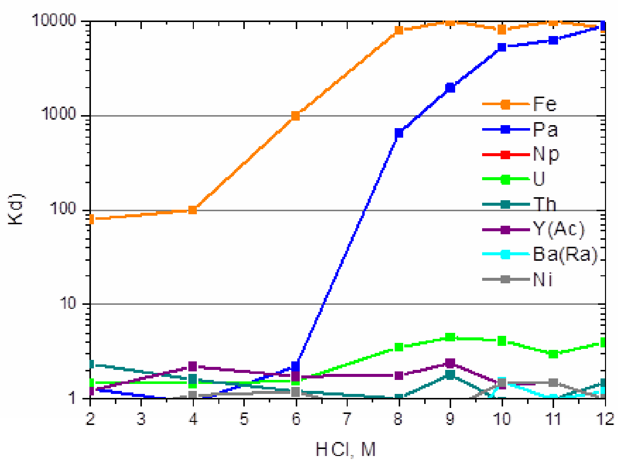
  Fe and Nb follow Zr
  - Test on vacuum box, 2 mL TBP cartridge
- Removal of Fe & Nb upfront possible using TK400 Resin
- Test with stacked 2 mL TK400/TBP cartridges
  - Load and Rinse: TK400 stacked above TBP
  - Elution: splitting of cartridges and separate elution
    - TBP => ZR
    - TK400 = > Fe & Nb
  - Use of TK400 before TBP seems efficient

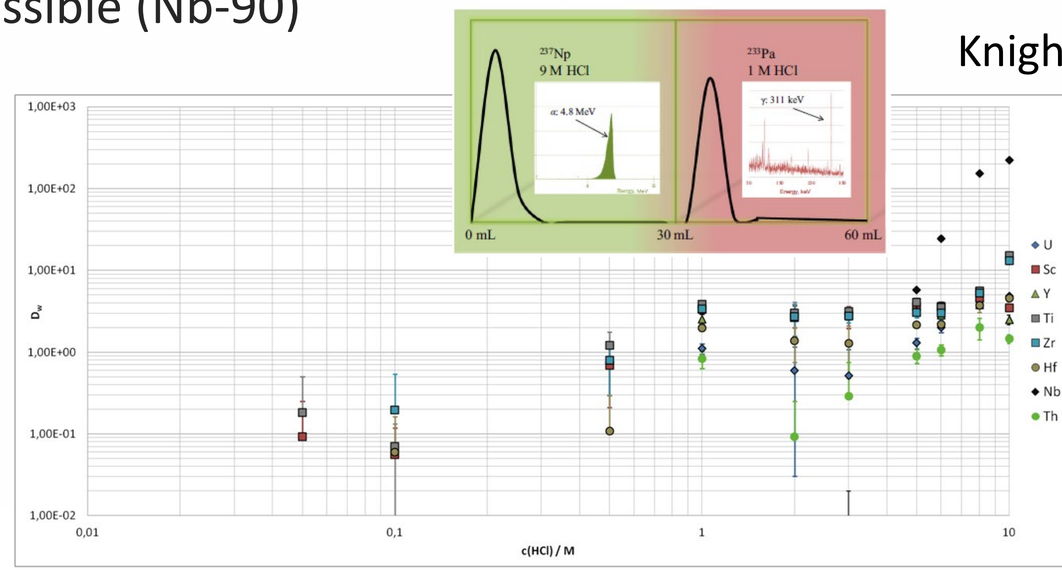
TK400 Resin

- Long chained alcohol
- Retention only at high HCl concentration, elution in low HCl, water,…
- Main application: Pa separation (Pa-231 determination by MS/Pa-230 for medical use)
  - NPL (no selectivity for actinides, Ac, Ra, Pb,…=> Pa-230 purif.)
  - Also retains Mo, Fe, Po, Ga

  => single column Ga-68 from solid targets => Tieu et al.
  - Under testing for At separation and Ge conversion to dilute HCl
  - Nb separation from Zr possible (Nb-90)

Knight et al.





CL Resin

Chromatographic separation of the theranostic radionuclide ^{111}Ag from a proton irradiated thorium matrix

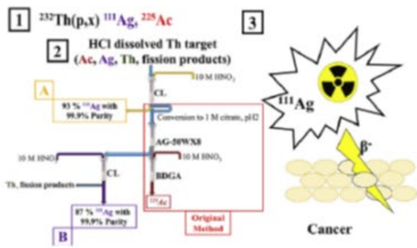
Tara Mastren [a], Valery Radchenko [a, 1], Jonathan W. Engle [a, 2], John W. Weidner [a], Allison Owens [b], Lance E. Wyant [b], Roy Copping [b], Mark Brugh [a], F. Meiring Nortier [a], Eva R. Birnbaum [a], Kevin D. John [a], Michael E. Fassbender [a, *]

[a] Chemistry Division, Los Alamos National Laboratory, P.O. Box 1663, Los Alamos, NM 87545, USA
[b] Nuclear Security and Isotope Technology Division, Oak Ridge National Laboratory, Oak Ridge, TN 37831, USA

H I G H L I G H T S

- Chromatographic recovery of medical isotope ^{111}Ag from proton irradiated thorium targets.
- First-time measured equilibrium distribution coefficients for silver and ruthenium on CL resin.
- ^{232}Th (p, fission) cross-section data for the formation of ^{111}Ag and ^{110m}Ag.

G R A P H I C A L A B S T R A C T



Anal. Chem., 2018, https://pubs.acs.org/doi/10.1021/acs.analchem.8b01380

Separation of protactinium employing sulfur-based extraction chromatographic resins

Tara Mastren[†], Benjamin W. Stein[†], T. Gannon Parker[†], Valery Radchenko[†#], Roy Copping[‡], Allison Owens[‡], Lance E. Wyant[‡], Mark Brugh[†], Stosh A. Kozimor[†], F. Meiring Nortier[†], Eva R. Birnbaum[†], Kevin D. John[†], Michael E. Fassbender[†*]

[†]Chemistry Division, Los Alamos National Laboratory, P.O. Box 1663, Los Alamos, NM 87545, USA
[‡]Nuclear Security and Isotope Technology Division, Oak Ridge National Laboratory, Oak Ridge, TN 37831, USA

[#]Current Address: Life Sciences Division, TRIUMF, 4004 Wesbrook Mall, Vancouver, BC, V6T2A3, Canada

CL Resin - Iodine removal from effluents

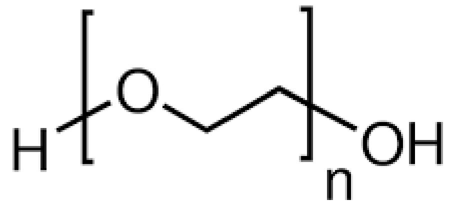
Decamp et al.: Iodine removal from elevated sample volumes[§]

- Treatment of complex process effluents
  - > 10 L radioactive effluent (1M HNO_3)
- Issues with rad. waste storage
  - Storage as liquid waste challenging
  - Preferably stored as solid waste
- Use of mixed-bed columns
  - 3g Ag loaded CL resin (plus 4g XAD-4 resin)
- Flow rate up to 180 mL/min
- Radio-iodine retention: 89% - 98%
- Retention of up to 2000 GBq radio-iodine per 7g column

- Decontamination of effluents e.g. nuclear medicine departments

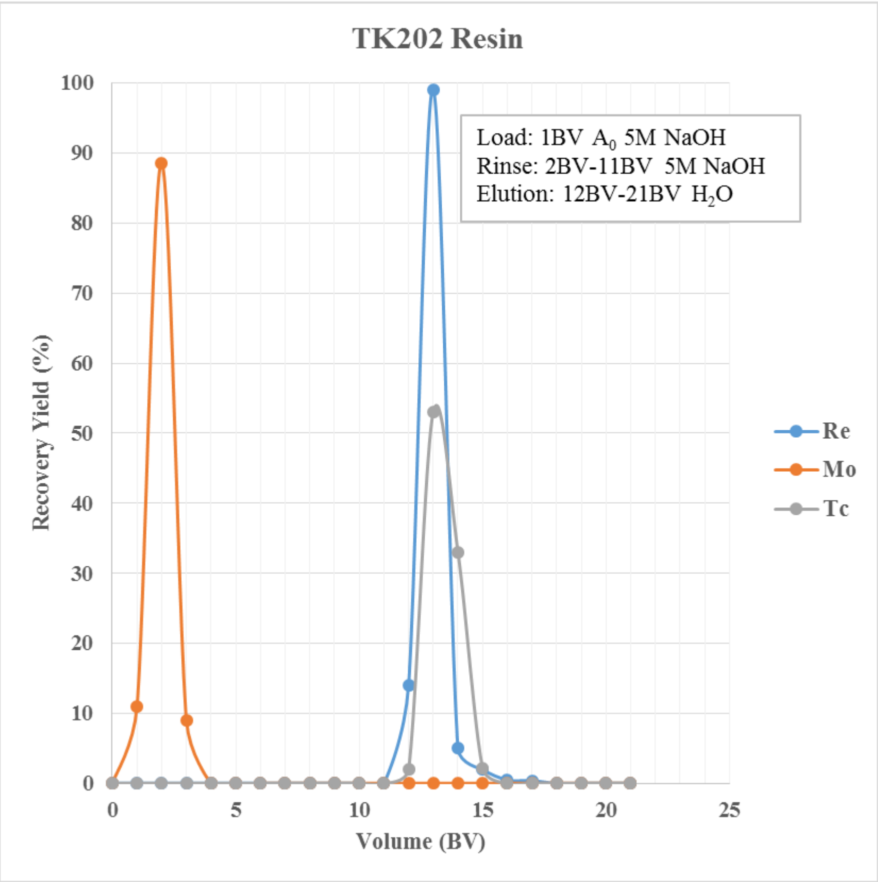
[§] C. Decamp (IRE), S. Happel: Utilization of a mixed-bed column for the removal of iodine from radioactive process waste solutions, Journal of Radioanalytical and Nuclear Chemistry, online April 2013, DOI: 10.1007/s10967-013-2503-1

Beta testing: TK202 Resin



- Based on Polyethylene Glycol (PEG) grafted on inert support
- Tc retention from high NaOH (preferably 7M NaOH)
- Tc retention increased by Mo
- Separation from high masses of Mo
- Elution with water
- Pass through CEX and aluminium oxide for trace Mo removal
- Potential uses:
  - Radiopharmacy => direct Tc-99m production by irradiation of Mo targets
    - Cyclotron or reactor
  - Decommissioning => Tc determination in decommissioning samples after sample fusion

TK202 Resin – Elution curves



- Tests show Re-Tc have similar behaviour in tested conditions
- Clean separation of Re-Tc and recovery in 5BV H2O
- Tests at Polatom with simulated Mo targets
- Poster presentation at ISTR2019, Vienna, 28/10/19 – 01/11/19
  - Tc recovery > 90% for 6 – 8g Mo per g of TK202
  - Tc recovery > 80% for 12g Mo per g of TK202

Tc-99m separation from Mo targets – suggested scheme (similar to Zeisler et al.)

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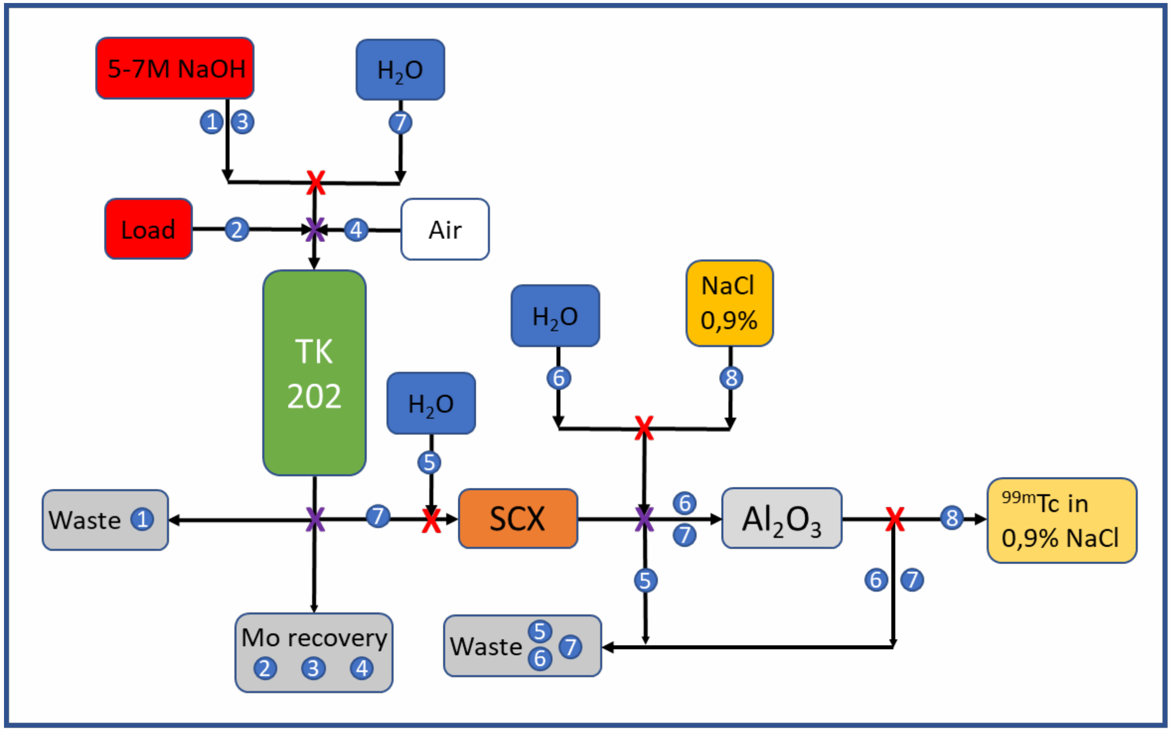
Expertise in Separation Chemistry



1. Pre-cond. TK202 – 5-7M NaOH ➔ alkaline waste
2. Load Mo/Tc on TK202 ➔ Mo recovery
3. Rinse TK202 – 5-7M NaOH ➔ Mo recovery
4. Purge TK202 – Air ➔ Mo recovery
5. Pre-cond. SCX – HCl then H_2O ➔ Aq. waste
6. Pre-cond. Al_2O_3 – H_2O ➔ Aq. waste
7. Elute Tc from TK202 on SCX and load on Al_2O_3 – H_2O
8. Elute Tc from Al_2O_3 – NaCl 0,9% ➔ Tc recovery

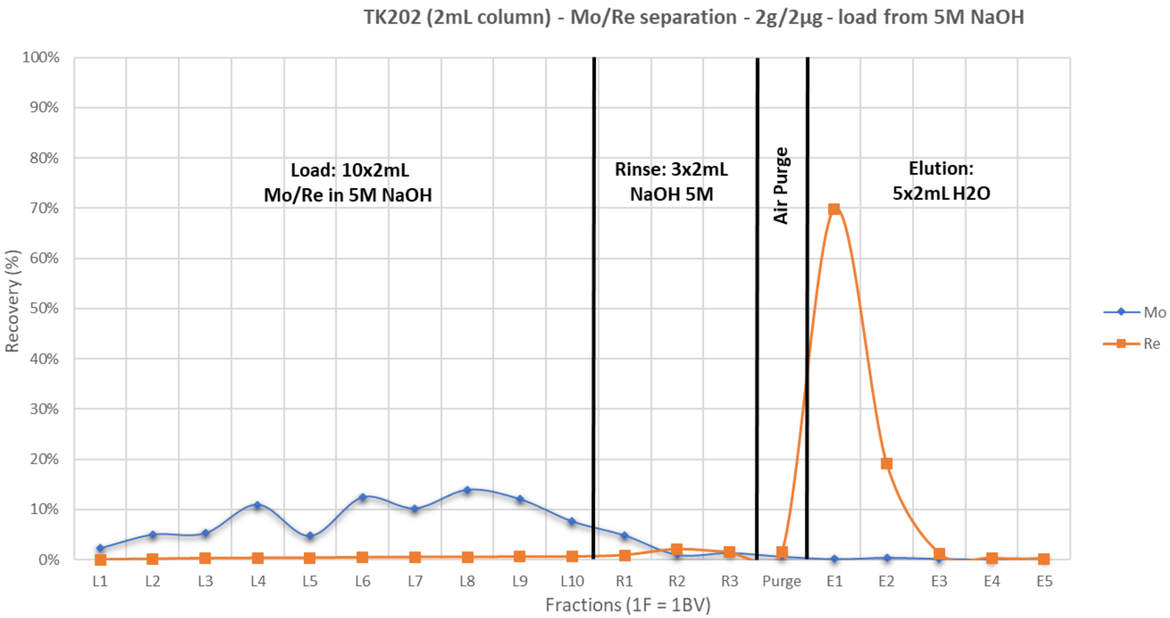
TK202 : 35-75 or 75-150µm
X : 3-ways valve
X : 4-ways valve
SCX : Strong Cation Exchange
Al_2O_3 : Acidic Alumina

Developed with ReO_4^- as TcO_4^- surrogate

Re recovered on saline solution from alkaline

Separation with 2g Mo ➔ From 20mL to 2mL
Separation with 200g Mo ➔ From 3L to 20mL

Tc-99m via cyclotron route

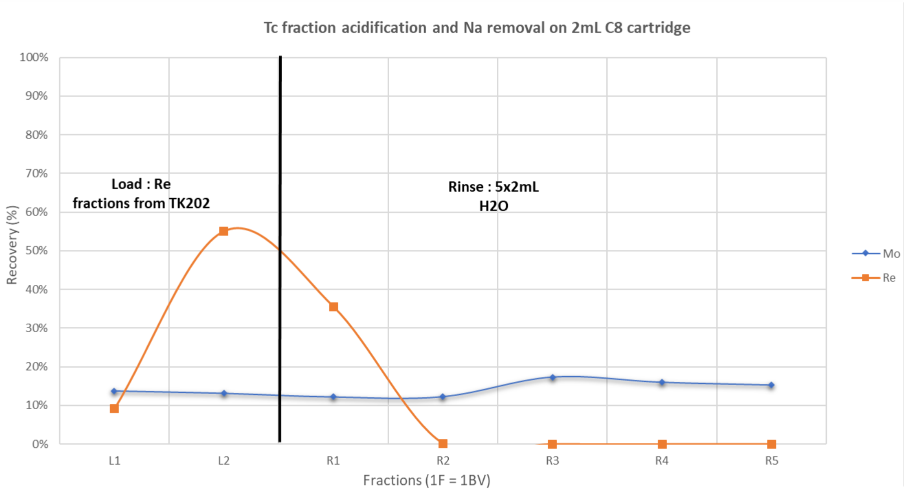


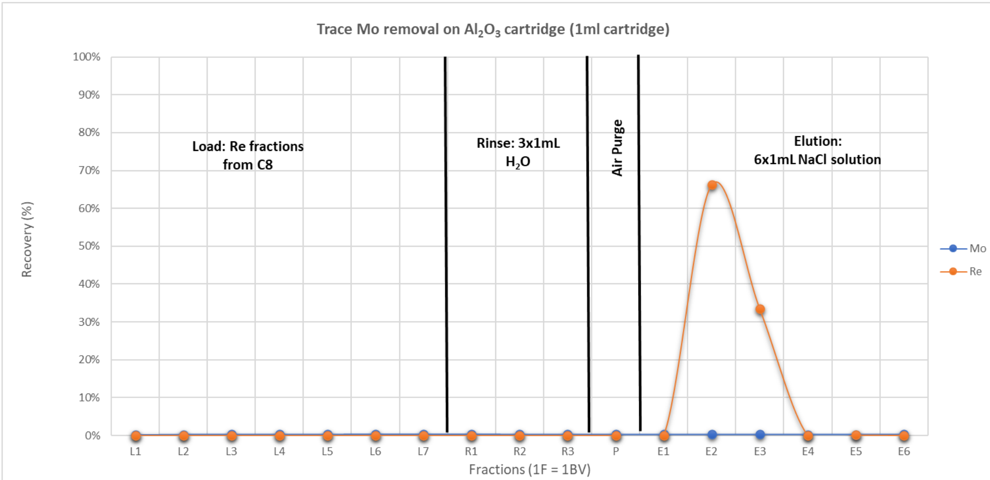
Tests performed cold with 2g Mo and 2 µg Re

- 2 mL TK202 cartridge
- 2 mL C8 cartridge
- 1 mL Al2O3 cartridge

Method similar to Zeisler et al.

High Re yield (~90%) in 2 – 3 mL 0.9% NaCl solution





On-going :Tc-99m from large Mo targets

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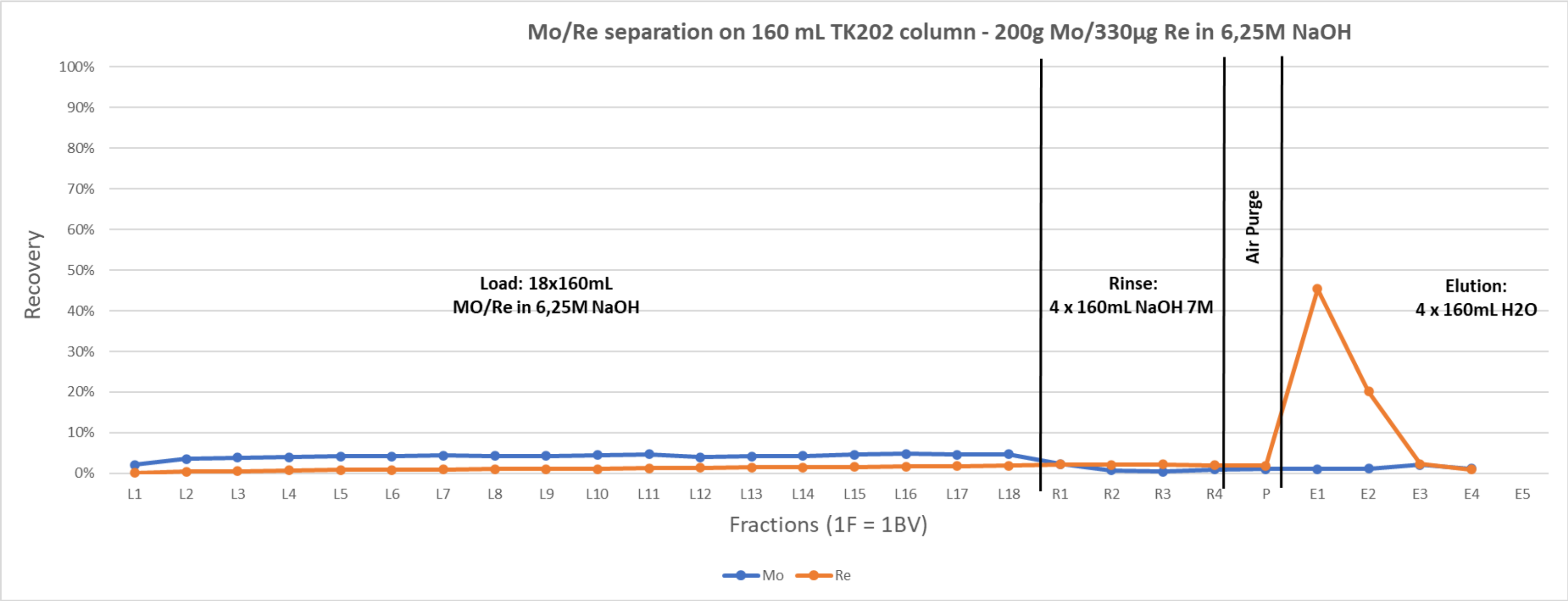
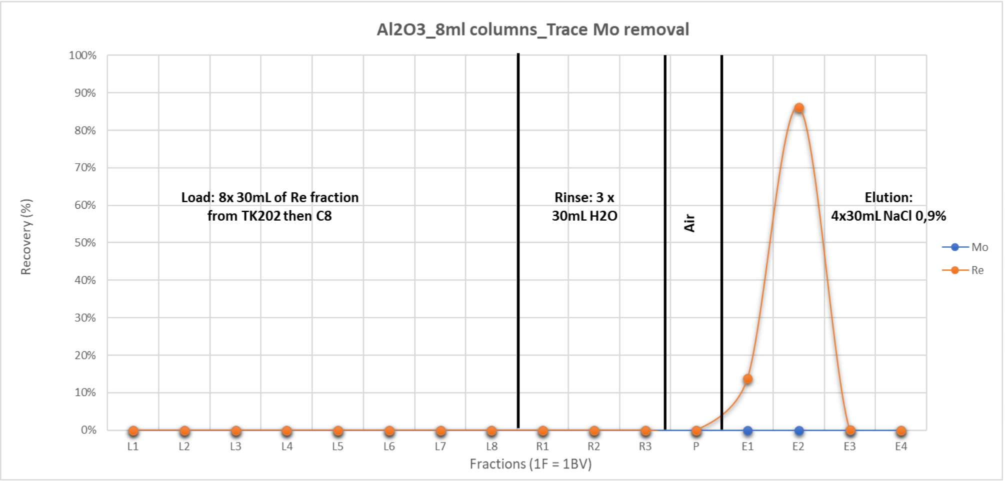
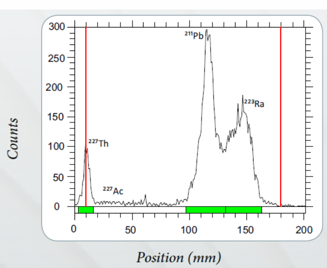


- On-going work on 200g Mo
- ~160 mL TK202 column
- Load from 6 - 7M NaOH - elution in water
- Pass through C8 cartridge for acidification and Na removal
- Final concentration/conversion to 0.9% NaCl on 8 mL $Al_2 0_3$ cartridge

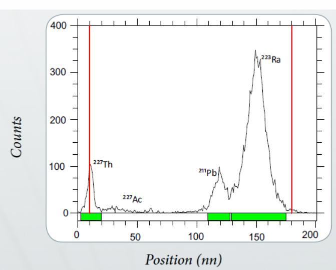


DGA Sheets

- TO-DGA (normal DGA) and TEH-DGA (branched DGA) available
- QC of radionuclides and generator eluents (p.ex. Ra-223, Ac-225/Bi-213, Pb-212, Ge-68/Ga-68 …)
  - TLC scanner or radiometer/LSC after cutting
  - Therapy: alpha emitters
  - Diagnostics e.g. generator produced Ga-68
- More types of sheets under development (selectivities, geometry)
  - TK201, LN, UTEVA,…
- 2D TLC under development => use in decommissioning
  - Quadratic sheet, two runs (90° turn in-between) with different acids => 2D pattern
  - Measurement e.g. with Ai4r Beaver system (high res α/β discrimination counting)

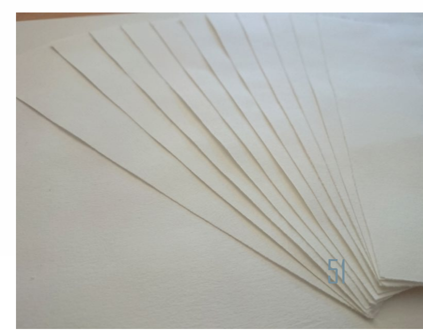


Radiochromatogram measured immediately after separaton. Low abundant radiatons of ^{227}Ac were not detected.

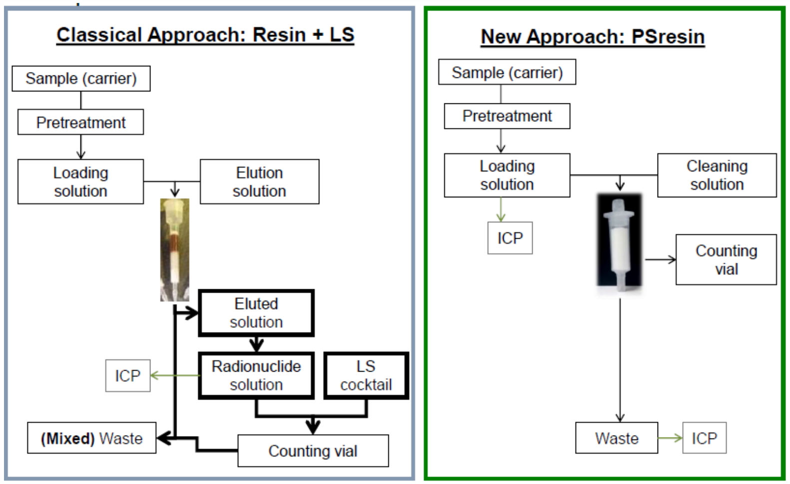


Radiochromatogram measured one hour afer separaton. Decay and ingrowth of ^{211}Pb is clearly visible.

A scheme of chromatographic separaton of mixture of ^{227}Ac and his daughter's niclides. ^{227}Th remains on start, ^{227}Ac has the retenton factor ca 0.2, ^{211}Pb ca 0.7 and ^{223}Ra ca 0.9.



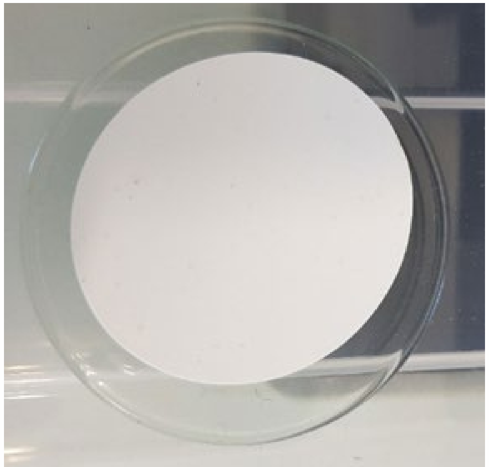
TK TcScint



- Scintillating Resins (PSm)
- Developped by Uni Barcelona (Garcia)
- « TK ELScint » range of products
- First: « TK TcScint »
  - Similar to TEVA
- Plastic scintillator beads impregnated with selective extractants
- Direct measurement of cartridges after loading on LS counter
- Environmental/decommissioing monitoring => Tc-99 by LSC
- Chemical yield preferably via Re/ICP-MS in effluents
- Use in QC?

Under development

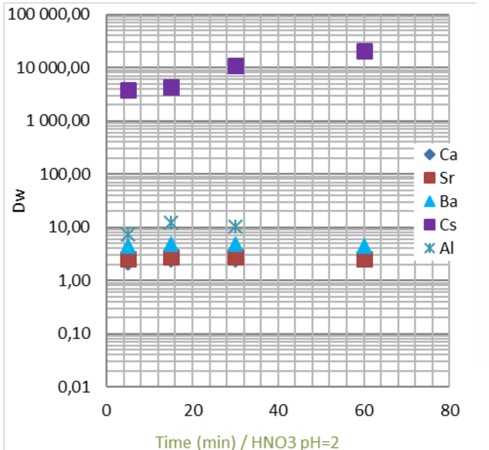
- Range of **extractive membrane filters (MF)**
- Rapid separation (up to 100 mL / min)
- Preferably for use with water samples (1 – 5L)
  - Under development:
    - TK201 (Tc)
    - TK100 (Sr), TK101 (Pb, Ra)
    - TK200 (actinides)
    - AC (gross alpha)
    - CL Resin (radio iodine)
    - Calixarenes (Ra)
    - …

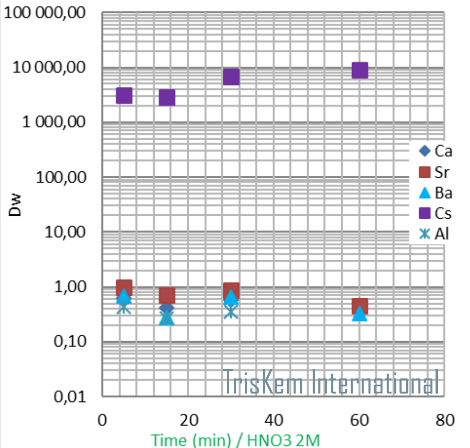


PAN based resins for decontamination

- Laureate '1. vague concours d 'innovation 2018' of the BPI
- Range of PAN based resins (other polymers possible - depending on pH)
  - Decontamination of effluents => radionuclides, heavy metals, pollutants…
  - High content of inorganic compounds (~85%)
  - Organic compounds also possible (HDEHP, TBP,…)
  - Mechanical stability
  - Control of particle shape, diameter, porosity
  - High porosity/active surface => fast kinetics

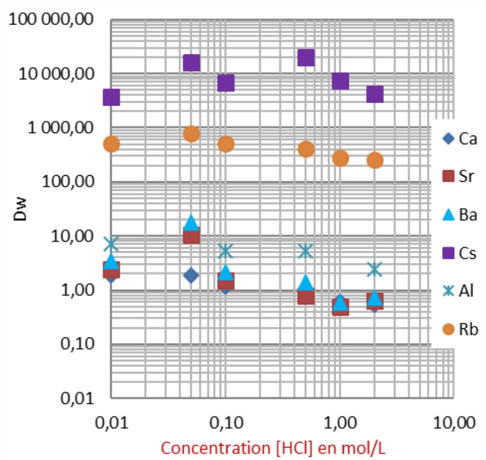
Park et al.

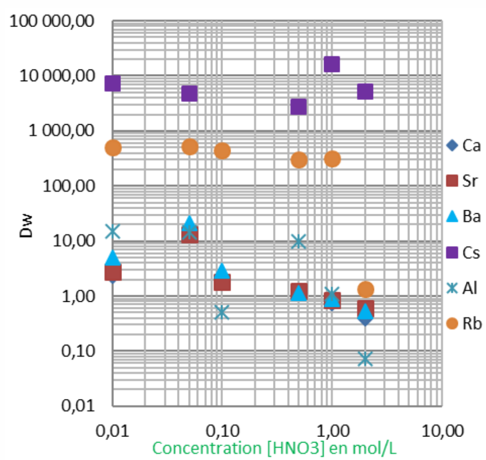




PAN based resins

- Platform technology
  - Control/choice of wide range of selectivities
  - Variety of inorganic compounds embedded in organic matrix
    - AMP & KNiFC for Cs, SbO for Sr/Y, ZrP for Sr, TiO for actinides and activation products, FeO for Se, CeO_2 or SnO_2 for Ge, $NaBiO_3$ for Am/Cm separation, MnO_2 for Ra,…
  - Organic extractants may be embedded, too





AMP-PAN selectivity in various concentrations of HNO_3/HCl

- Large scale production of resins under development

Some other on-going projects

- SE Resin
- Sc separation
- Ac separation (incl. Ra recycling)
- At separation (TK400,…)
- Tl separation
- Improvement of radiolysis stability
- Functionalised polymers & silicates,…
  - e.g. DO-DGA, DE-DGA, macrocycles,…
- Ra separation (TK100/1, CAs)
- Microfluidics
- Impregnated tube inserts/pipette tips
- Impregnated membranes
- Li Resin
- Cs/Rb separation (TK300)
- Rapid tests
  - Test sticks => Uni Southampton
  - DGA Sheets (2D TLC)
  - Spin coated discs
- DGT (Diffusive Gradients in Thin Films) => ’bio-availability’

Thank you for your attention!

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