TrisKem International

Overview and News RadPharm

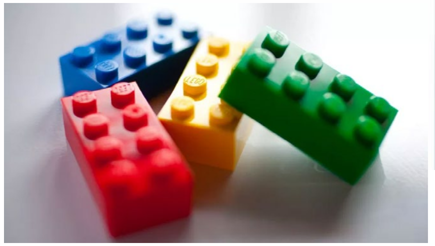
vUGM FR 2022

Steffen Happel
21/06/2022

TRISKEM
Expertise in Separation Chemistry

Research interests - Radiopharmacy

- Radionuclide production
  - Resin and method development 'cold'
    - 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…
    - Therapy: alpha emitters, Lu-177, Tb-161, Cu-67, Sn-117m, Sc-47…
  - Challenges:
    - Large excess of matrix / target material (several mg to hundreds of g)
    - Generally rapid separation and high purity (incl. radionuclidic) required
    - Elution under 'soft' conditions in small volume => labelling/injection
    - Choice of right resin particularly important
      - » No selectivity for target material, high selectivity for product
    - Combining several resins can facilitate the separation
      - » Conversion (high acid to dilute acid)
      - » Removal of impurities upfront



Research interests - Radiopharmacy

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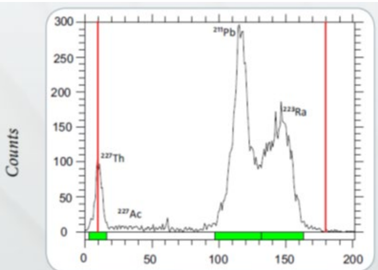
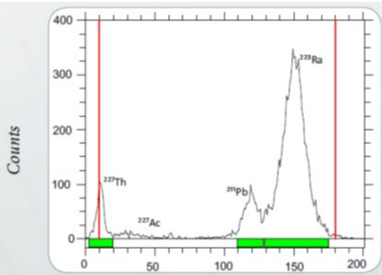
- Quality control
  - Cartridge based methods (e.g. Sr-90 in Y-90,…)
    - Use of "TK-SRScint cartridges"?
  - **"Sheets" p.ex. DGA sheets** (functionalized TLC for Ra-223, Ga-68, Pb-212,…. => CVUT Prague)



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



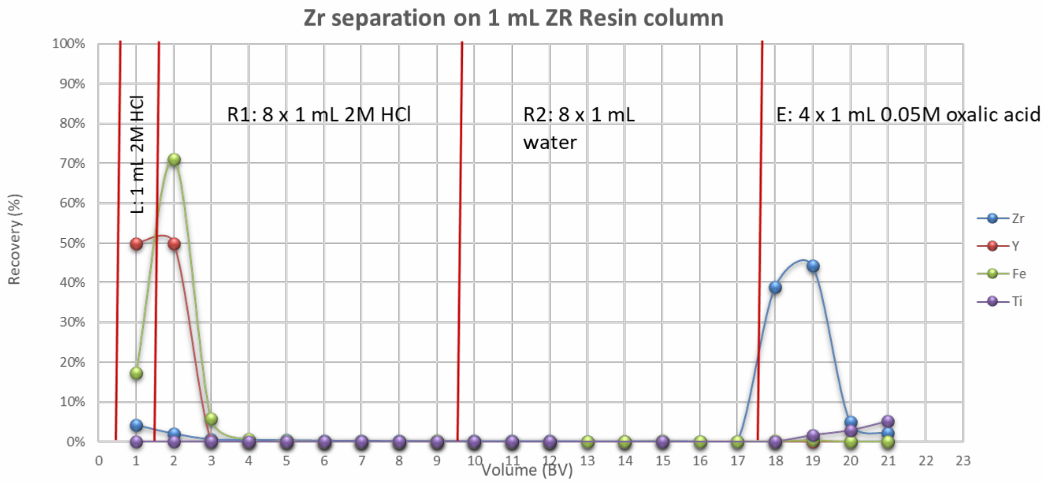
Radiochromatogram measured one hour afer separaton. Decay and ingrowth of ^{211}Pb is clearly visible.

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.

- Decontamination of effluents/waste (Ge-68, lanthanides, radioiodine,…)
- Purification/combination of generator eluates
- 'Recycling'/valorization of long-lived RNs (Ge-68,…) and target materials

ZR Resin

- Hydroxamate based resin => different from Holland publication
  - Ready to use / no activation
  - Facile Zr elution (≤ 1M oxalic acid)
  - Originally developed for Zr-89 separation from Y targets



- Alternative e.g. TBP Resin (Graves et al.) => elution as chloride
- Application for other separations: **Ga/Zn, Ti/Sc, Ge/Ga**
- **On-going question => improvement of radiolysis stability**

Zr-89 separation on TBP Resin

- Frequent request: Zr elution without oxalate
- 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 should also be possible with citrate, phosphate, oxalate…
- Fe and Nb removal not ideal

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]

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

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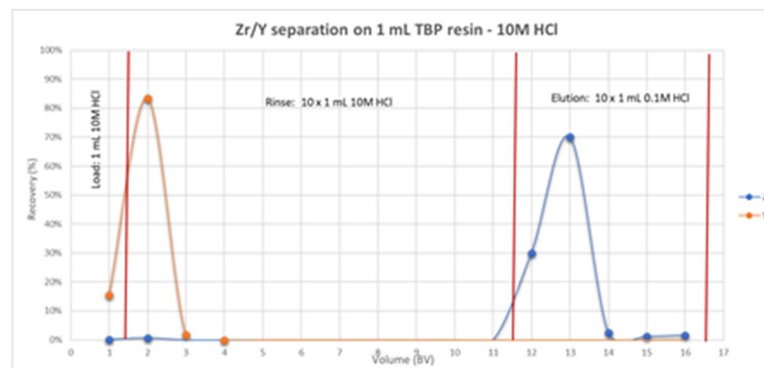
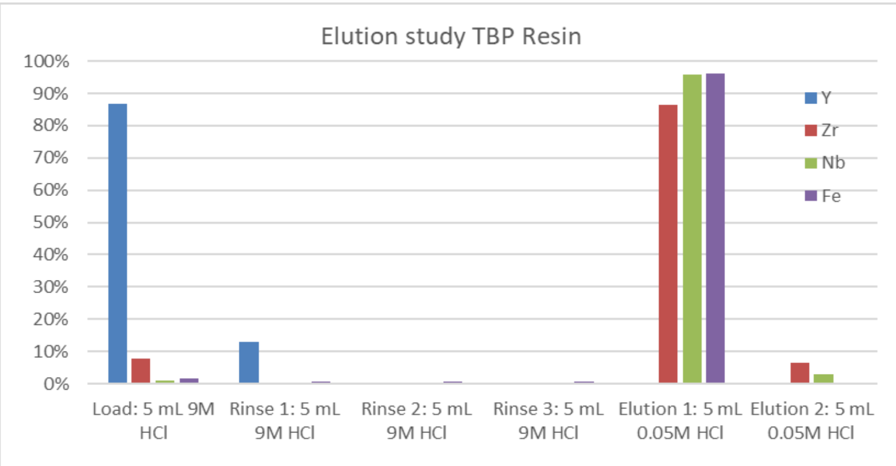
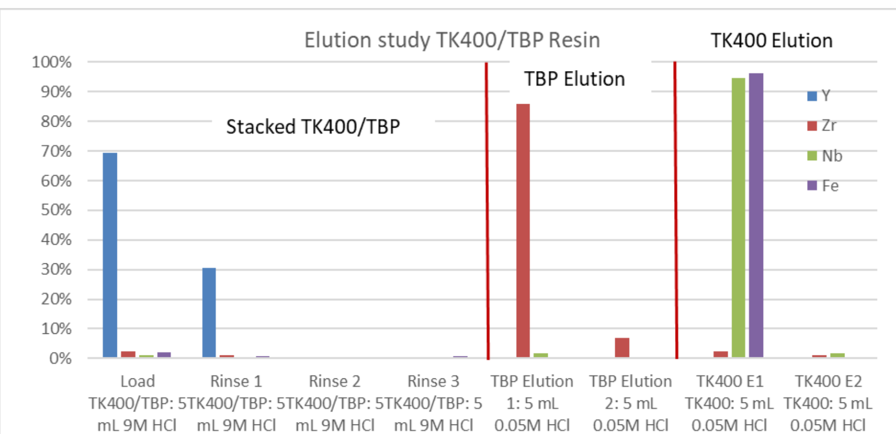


Use of TK400 for Fe/Nb removal

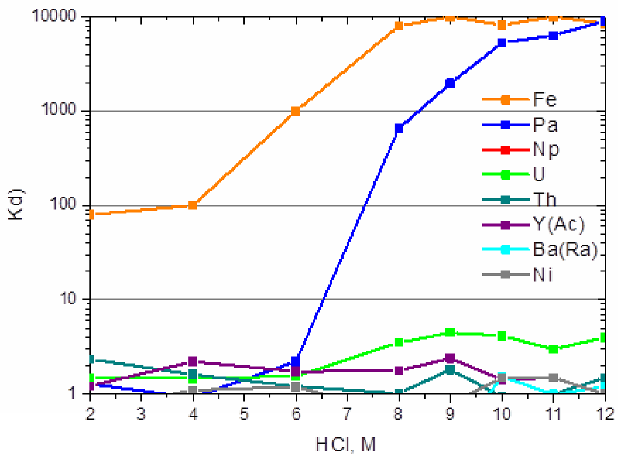


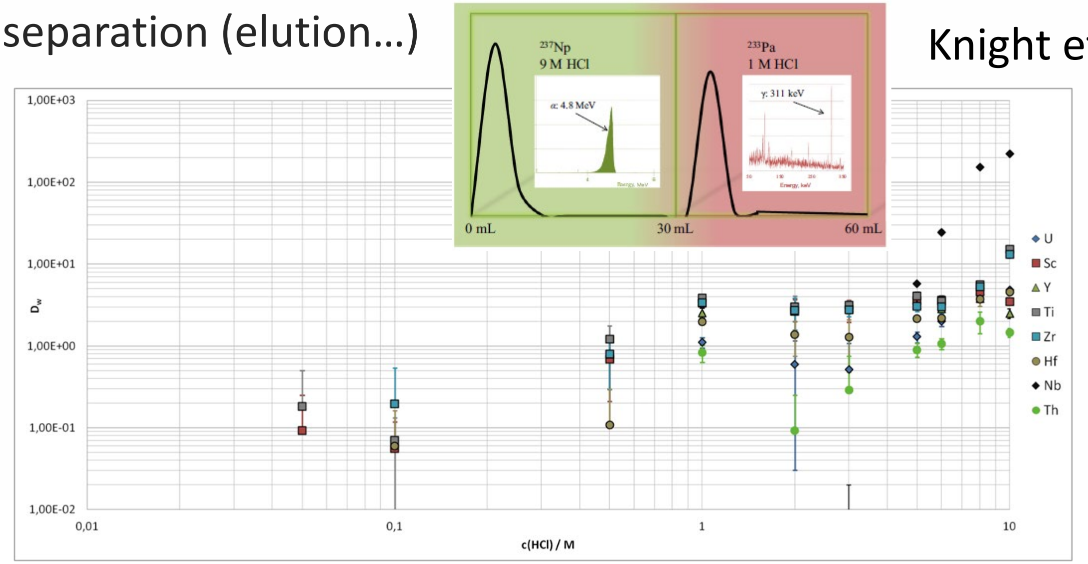


- On-going work
- On TBP only: Fe and Nb follow Zr
- Removal of Fe & Nb upfront possible using TK400 Resin
- Test with stacked 2 mL TK400/TBP cartridges
  - Load and Rinse at 10M HCl with TK400 stacked above TBP
  - Splitting of cartridges and separate elution with dilute Hcl
    - TBP => ZR only
    - TK400 = > Fe & Nb
    - Y passes through both
- Removing Fe and Nb using TK400 improves Zr purity

TK400 Resin

- Long chained alcohol – initial work by A. Knight et al.
- 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.)
- Other applications:
  - Also retains Mo, **Fe**, **Ga**, Po (=> SR Resin!)
  - Nb separation from Zr possible (Nb-90)
  - Under further testing for At separation (elution…)

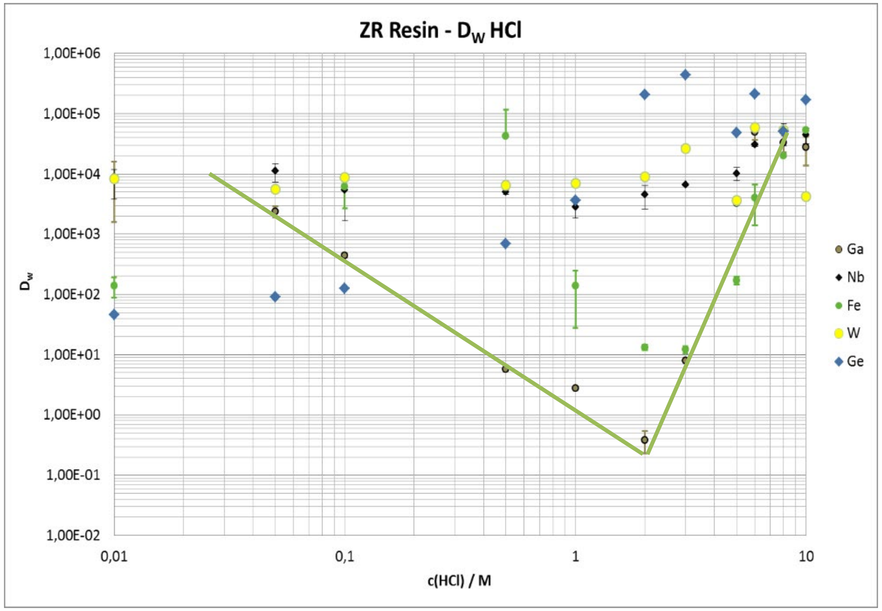


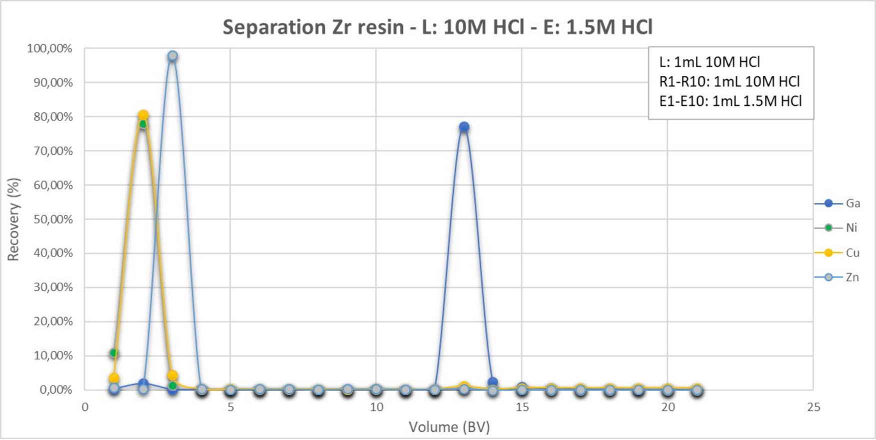


Knight et al.

Ga-68 separation from Zn targets

- Irradiation of Zn-68 targets in cyclotron
- Ga-68 separation on ZR Resin
  - No selectivity for Zn (target material)
  - Loading possible from:
    - dilute acid (**liquid targets => typically HNO_3**)
    - >6M HCl (**solid targets**)
  - Rinse under loading condition
  - Elution with ~1 - 2M HCl
  - Too acidic for injection or labelling





- Conversion necessary
  - Evaporation & dissolution difficult to automize
- Easier => use of another resin
- TK200 Resin load from 1.5M HCl
- Rinse with 1.5M HCl
- Elution in 2 – 3 BV water, dilute acid,..

Cyclotron production of Ga-68

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*]

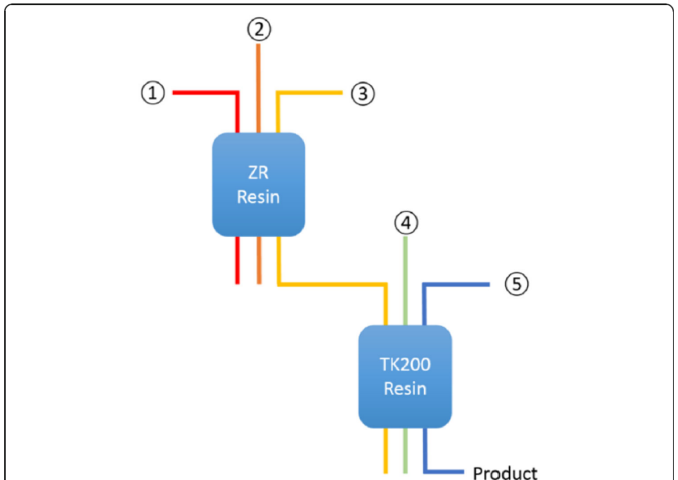


Fig. 4 Two-column approach for ^{68}Ga chemical separation

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.
- 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
- W. Tieu et al. use of single TK400 cartridge for solid Zn targets
- Svedjehed et al. use of TK400/A8/TK200 for solid Zn targets

Demystifying solid targets: Simple and rapid distribution-scale production of [^{68}Ga]GaCl$_3$ and [^{68}Ga]Ga-PSMA-11

Johan Svedjehed, Martin Pärnaste, Katherine Gagnon

Other separations on TK200

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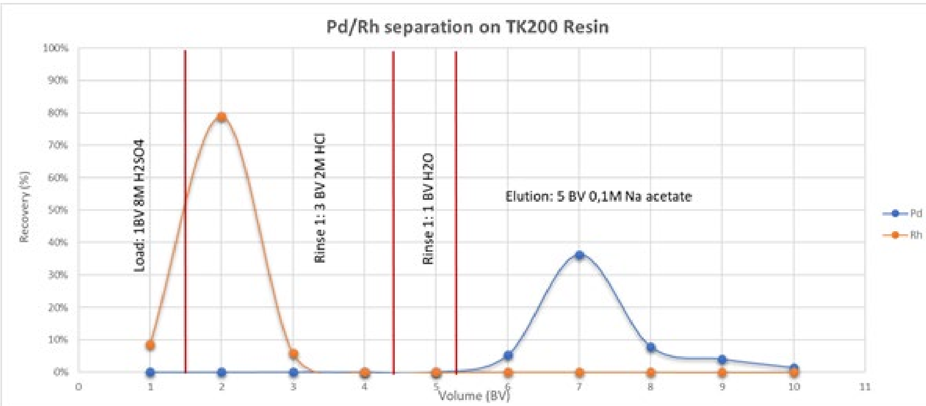
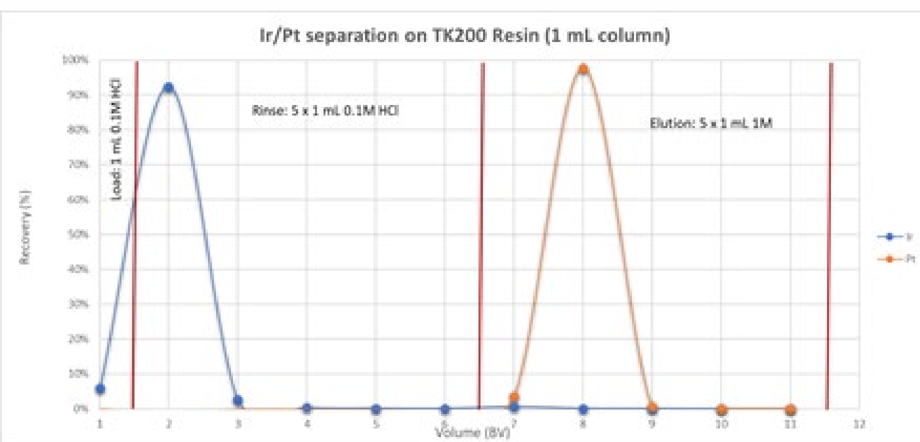
- Pd separation from Rh



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

- Pd separation form Rh targets
- Main challenge: target dissolution & oxidation states
- Request: Pd separation from high H_2SO_4
- Removal of H_2SO_4 necessary
  - Rinse with 2M HCl
- Elution in acetate possible
  - To be optimized
- Separation on TK200 possible

- Pt separation from Ir

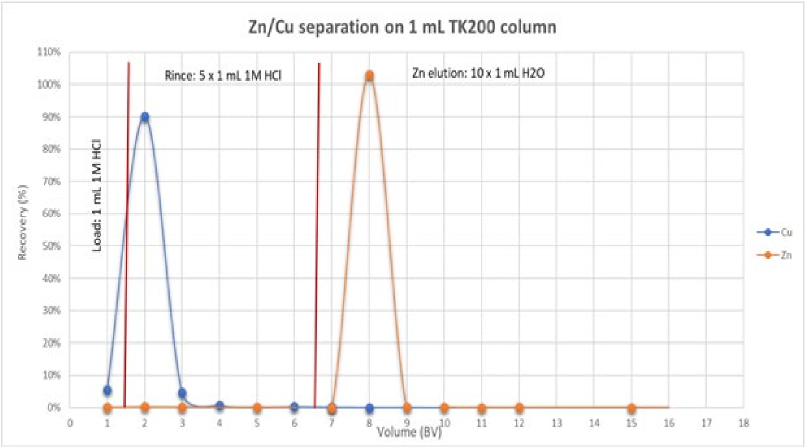


- Pt/Ir separation. Elution study, ICP-MS measurement

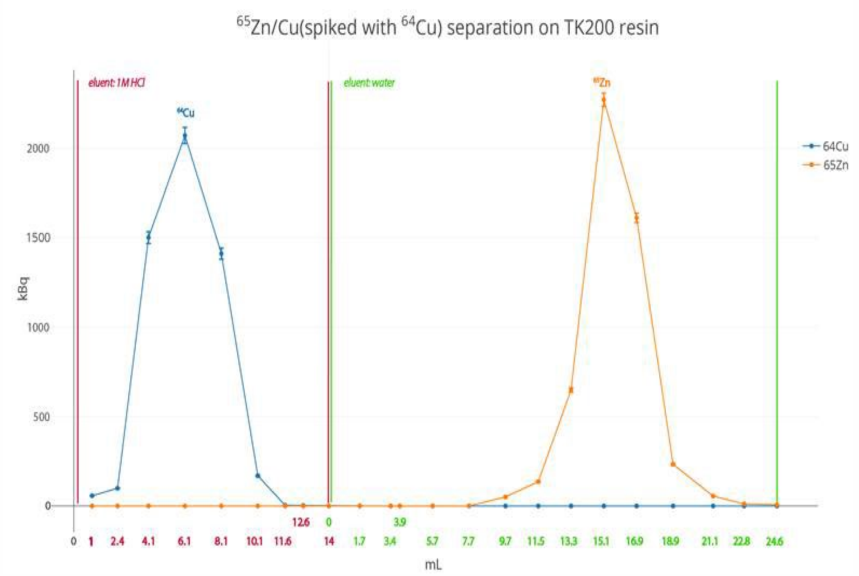
- Pt separation from Ir targets
- Challenge oxidation state control
- Separation possible on TK200
- Alternative: use of TBP => Obata et al.
- $[^{188,\ 189,191}Pt]$cisplatin
- TBP and AIX based method
  - 3x 2 mL TBP cartridges followed by QMA cartridge

Other separations on TK200

- Zn separation from Cu targets
- Load from HCl (e.g. 1M) elution in water
- 'Hot tests' by F. Zhuravlev, DTU

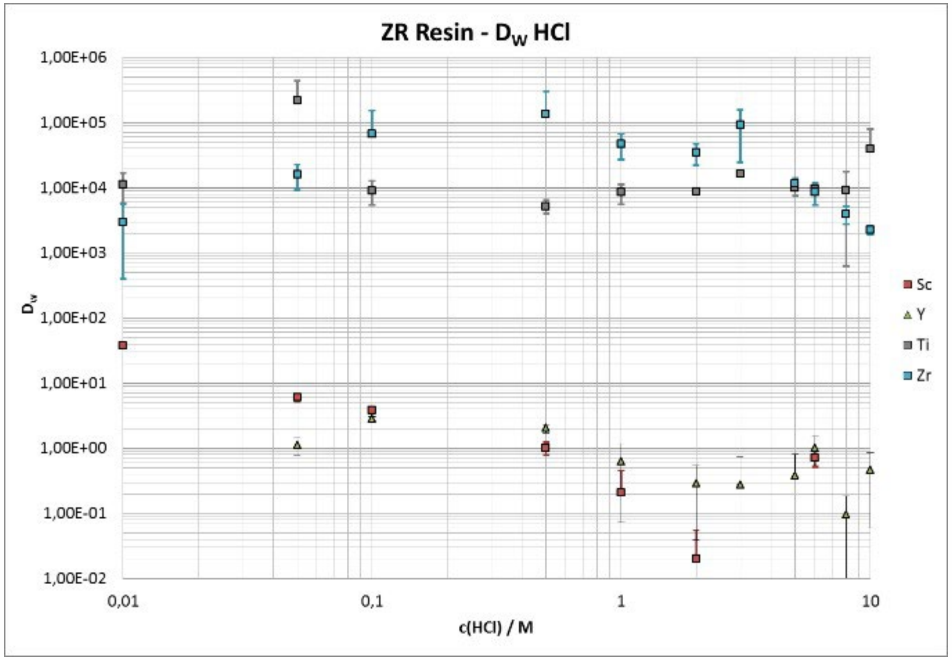


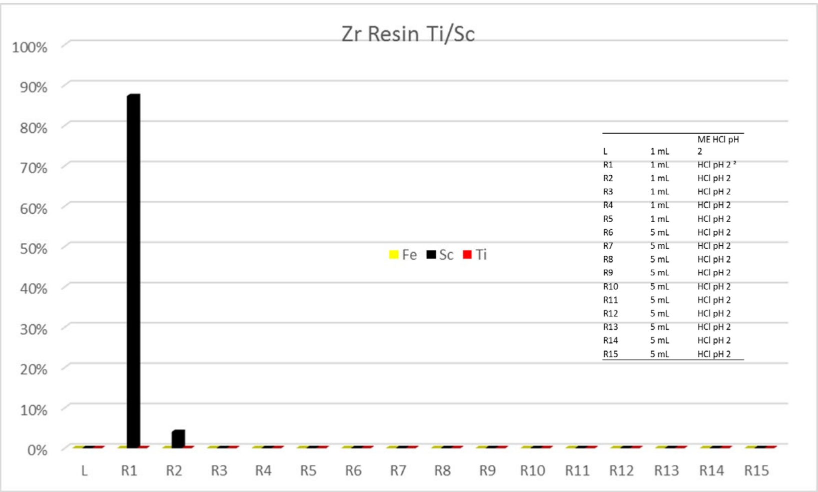
- Zn/Cu separation. Elution study, ICP-MS measurement



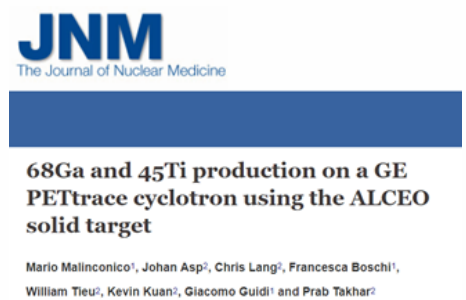
- Zn-65 separation. Data kindly provided by Fedor Zhuravlev, DTU

Ti-Sc Separation (Ti-44/5)





- Ti retained from (high) HCl, Sc not retained
- Ti also retained in dilute acid, Sc not => Ti generator?
- Ti elution with 1M oxalic acid, 0.1M citric, 0.1M H_2O_2
- Publications/presentations Ti-45:
  - Malinconico et al.: J Nucl Med May 1, 2018 vol. 59 no. supplement 1 664)
  - K. Olguin presentation vUGM 20


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], Chris Lang[2], Francesca Boschi[1], William Tieu[2], Kevin Kuan[2], Giacomo Guidi[1] and Prab Takhar[2]

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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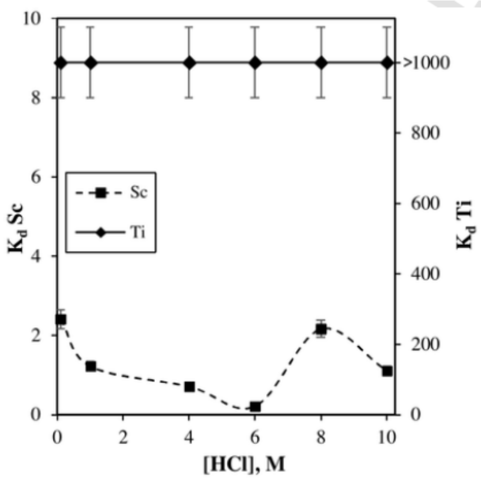


Fig. 3. HCl concentration dependency of K_d for $^{44}Ti/^{46}Sc$ on ZR hydroxamate resin.

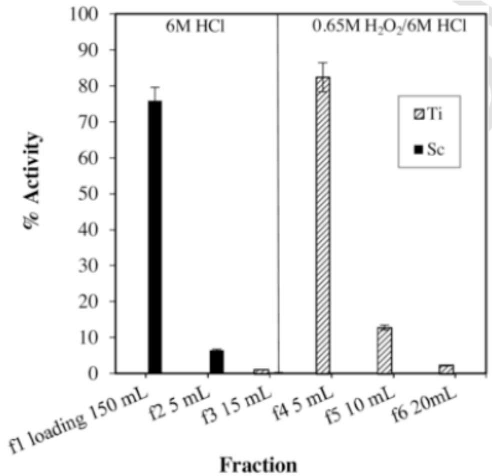


Fig. 5. $^{44}Ti/^{46}Sc$ elution profile using ZR hydroxamate resin with a load of 4 g of scandium.

- **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

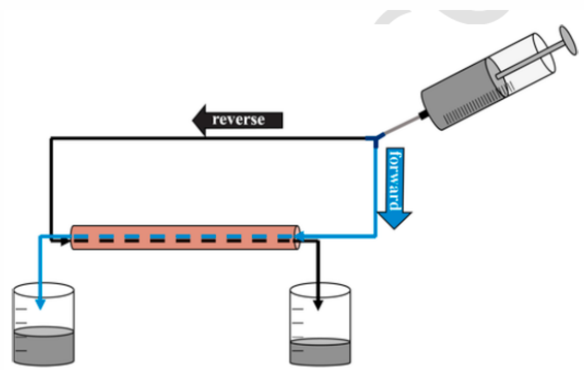
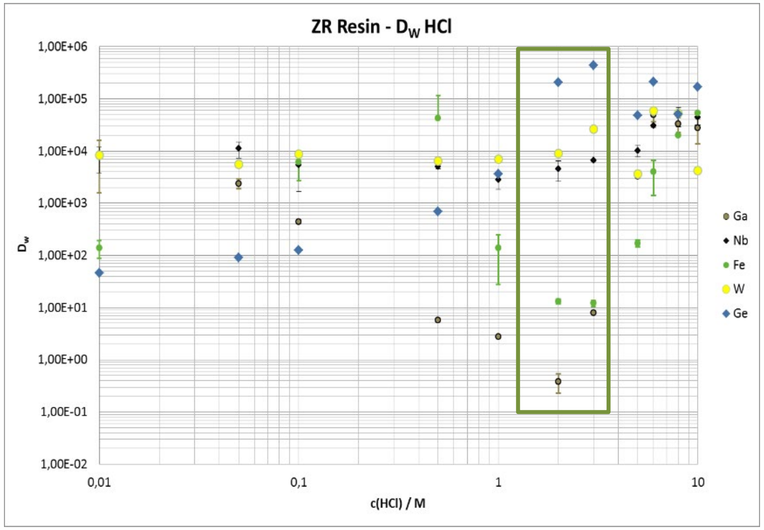


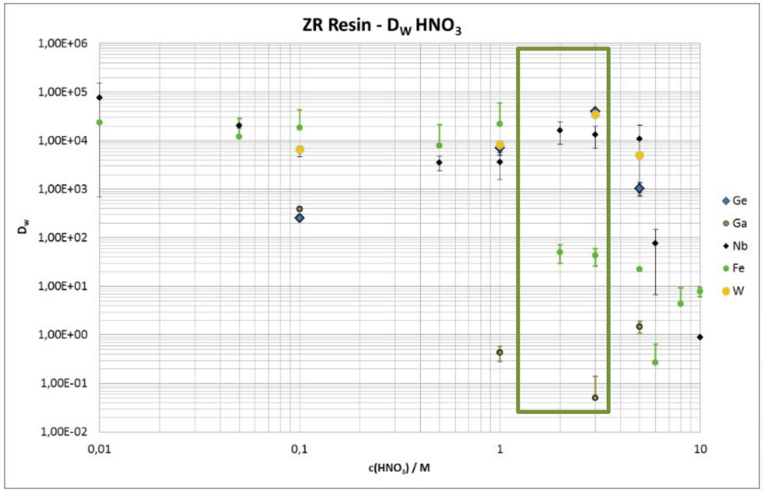
Fig. 1. Schematic concept of a forward/reverse flow radionuclide generator.

- Direct (1 mL ZR) and reverse elution (2 mL ZR)
- 65 column volumes tested up until publication
- High Sc yields, max. Ti-44 breakthrough: $4.1 \cdot 10^{-4}$%
- 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

- ZR Resin: loading from HNO_3, HCl or H_2SO_4 possible
- Cold tests on >5g GaNi, hot tests on-going
- 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
  - Ge/Ga selectivity => further purification
  - Rinse with 9M HCl
  - Elution with to 0.05M HCl => pH!





Important for high amounts of Ge: pre-rinse of GR with EtOH, then water necessary

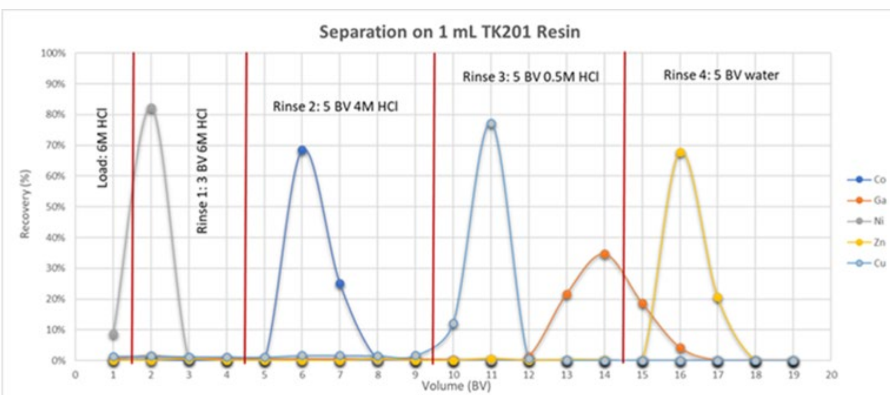
Other ongoing Ge work

- Ge removal using CeO_2-PAN (“TK-GeRem”)
  - Extracts Ge from dilute acid, seawater…
    - Decontamination of waste/effluents
    - Ge-68 removal from generator effluents?
- Ge recycling
  - Evaluation of possibility to elute Ge-68 from ‘spent’ generators
  - E.g. use of Guard Resins cartridges to collect and purify Ge…
  - Dissolution of support
- Combination of several Ge-68 generator eluents
  - Direct ZR/TK200 or
  - Acidification and load onto one TK200
  - Elution in dilute HCl

Cu-64 separation on TK201

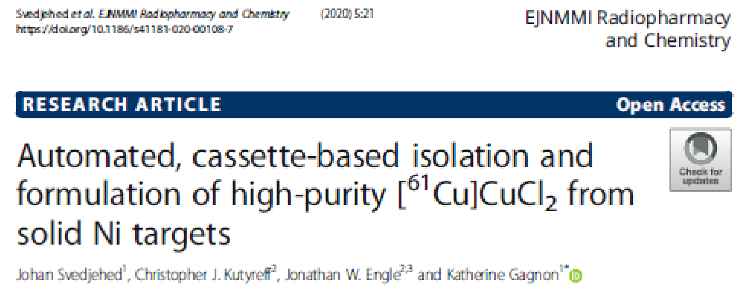
- Cu-64 separation from solid Ni-64 targets
  - Target dissolution in high HCl
  - Load and rinse at 6M HCl
    - Ni removal and recovery/recycling
  - Co elution with 4 – 5M HCl
  - Cu elution with 0.5M HCl
    - Zn remains retained (Ga and Fe partially co-elute)

    => requires further treatment



- Improvements:
  - Preferred alternative: Use of TBP (or TK400) upfront for Fe/Ga removal

  => allows for Cu elution in 0.05M HCl

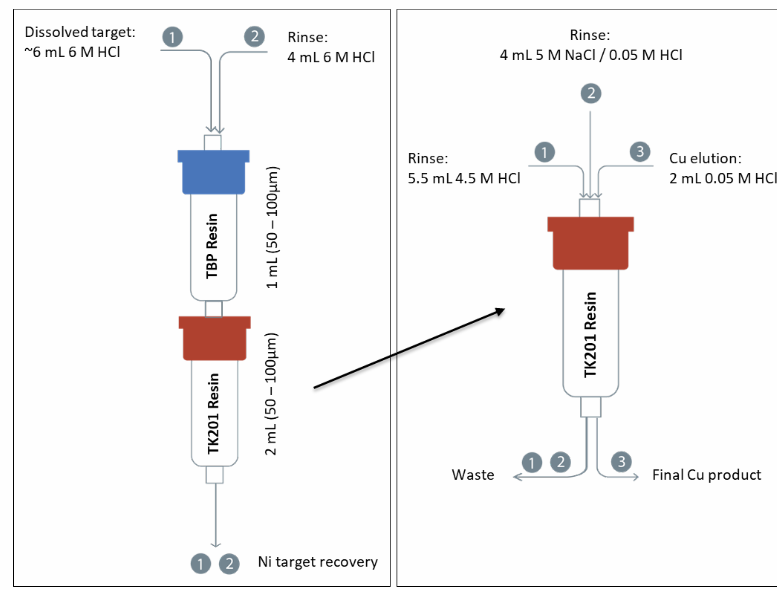

Svedjehed et al. EJNMMI Radiopharmacy and Chemistry (2020) 5:21
https://doi.org/10.1186/s41181-020-00108-7

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

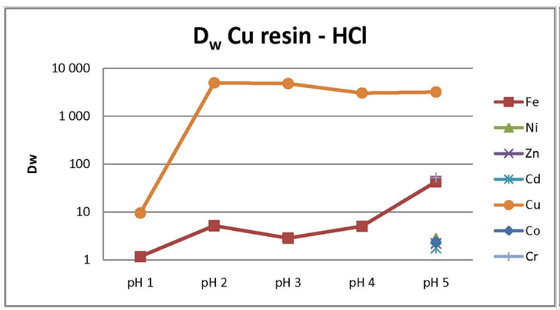
Johan Svedjehed[1], Christopher J. Kutyreff[2], Jonathan W. Engle[2,3] and Katherine Gagnon[1*]

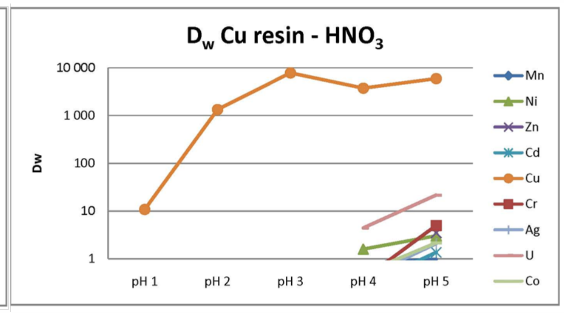


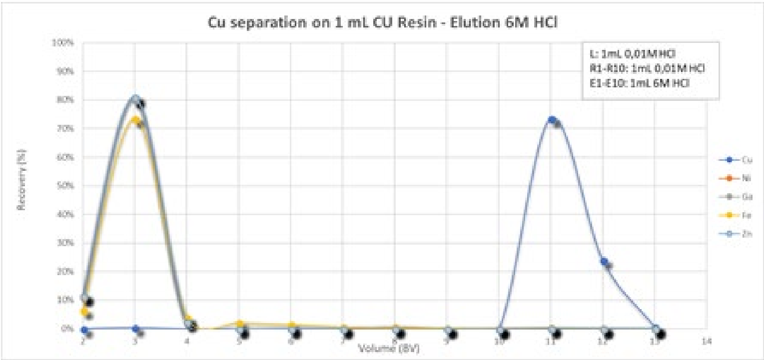
- Gagnon et al. use of NaCl/HCl for better pH control of eluate

CU Resin

- TK201 can not be used for Cu separation from Zn targets (e.g. Cu-67)
- Use of oxime based CU Resin instead
- High selectivity for Cu particularly with respect to Zn, Ni, Fe, Co,…







- Load from pH >2, elution in high mineral acid (2 – 8M)
  - Used for (large) solid **Zn** targets (=> Cu-67)
  - Not ideal for solid Ni targets (usually high HCl) => TK201
    - Works for liquid targets (pH 2 – 3) => Fonseca et al.
  - Elution in high HCl not compatible with labelling/injection
    - Evaporation/redissolution or
    - Conversion to dilute HCl e.g. via TK201 (additional Zn removal) e.g. Kawabata et al.

Article

Production of GMP-Compliant Clinical Amounts of Copper-61 Radiopharmaceuticals from Liquid Targets

Alexandra I. Fonseca [1], Vítor H. Alves [1,2], Sérgio J. C. do Carmo [1,3], Magda Silva [1], Ivanna Hrynchak [1], Francisco Alves [3,4], Amílcar Falcão [1,5] and Antero J. Abrunhosa [1,3,*]

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 $ZnCl_2$ 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- use of TK201:

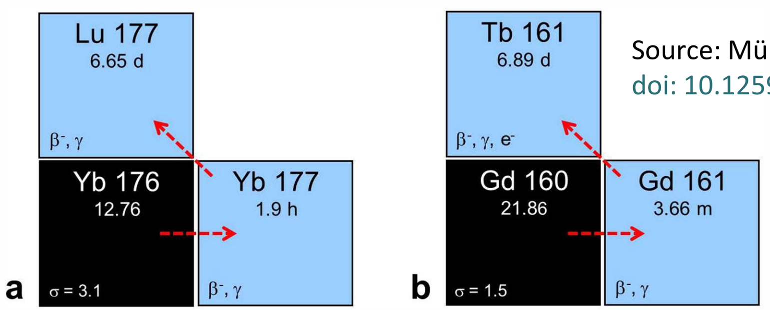
- Cu elution with 6M HCl directly onto TK201
- Cu elution from TK201 in dilute acid
- Optional: rinse with NaCl/HCl for better pH control

Ongoing: TK201/CU/TK201

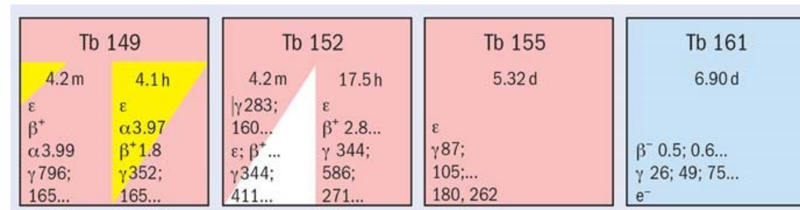
- Use of CU Resin still possible for solid Ni targets?
  - Should result in very high purity Cu…
  - TK201/CU/TK201 method…
  - Use of 2 mL TK201 for Cu 'conversion' and matrix removal
    - Ni passes through.
    - No TBP should not be needed (Fe/Ga removal on CU Resin)
    - Modified TK201 rinse (HCl/NaCl) is key!
    - Cu can be recovered in acetate buffer if modified rinse is used to lower acidity on TK201 (=> Gagnon paper on Cu-61)
  - TK201 eluate can then directly be loaded onto 1 mL CU Resin cartidge for further purification (Zn, Fe, Ga, Ni removal).
  - Cu Elution with 6M HCl onto 0.3 mL TK201 for conversion and concentration
- Proof of principle OK, now further optimisation on-going (volumes) then hot testing

Tb-161 separation

- Tb-161 currently getting strongly increasing interest
  - Part of the ‘Swiss knife of nuclear medicine’ => Tb isotopes
- Production process similar to nca Lu-177
  - Irradiation of enriched Gd-160 targets in a reactor at high neutron flux



Source: Müller et al. 2018
doi: 10.1259/bjr.20180074

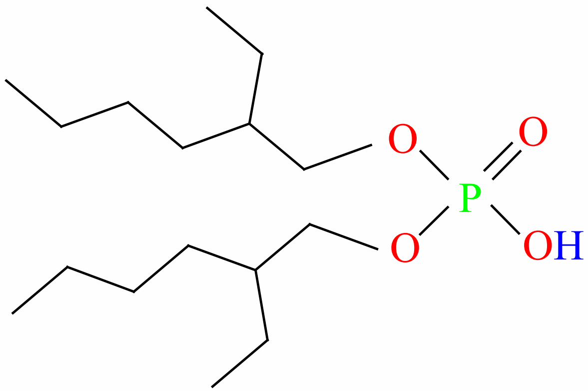


Terbium: a new ‘Swiss army knife’ for nuclear medicine
Source: https://cerncourier.com/a/terbium-a-new-swiss-army-knife-for-nuclear-medicine/

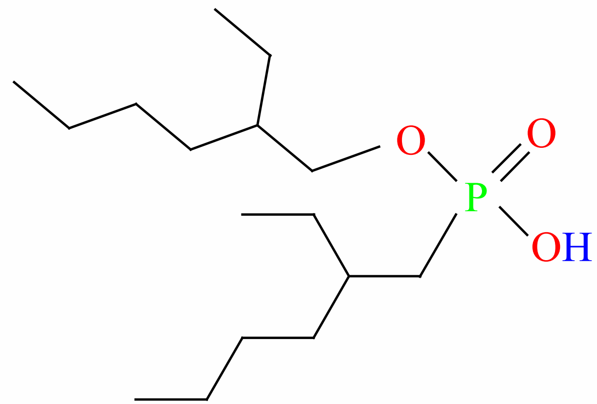
  - Irradiation of several hundreds of mg or more

- Separation method based on nca Lu-177 work (0.5 – 1g+ Yb targets)
- Separation of ultra-traces of Tb-161 from Gd-160 and by- and decay products (incl. Dy)
- Also used for Tb-155 separation (e.g. TRIUMF)

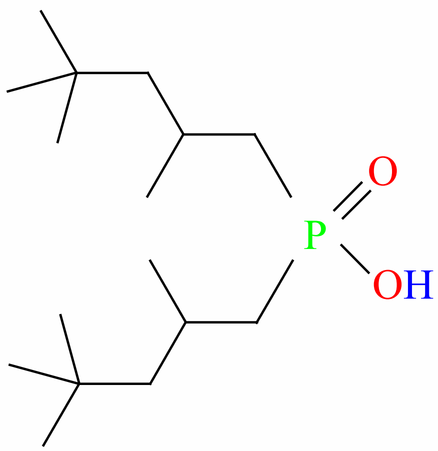
Lanthanide separation on TK211/2/3 or LN series



HDEHP (LN)



HEH[EHP] (LN2)

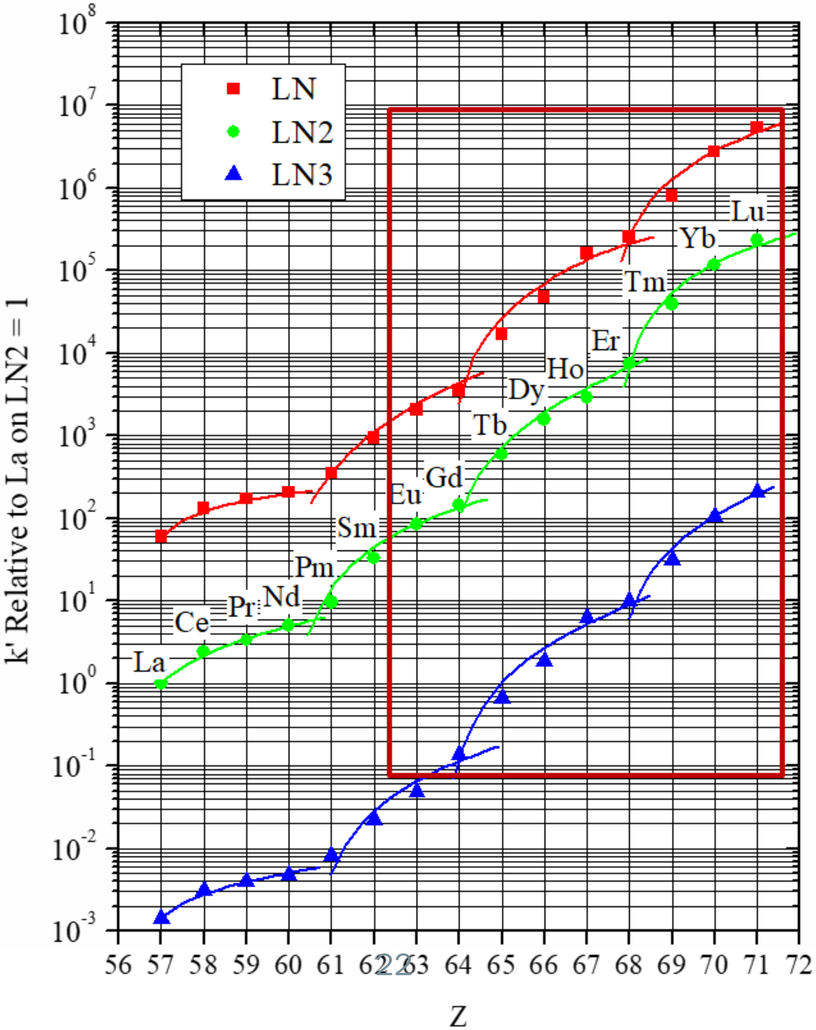


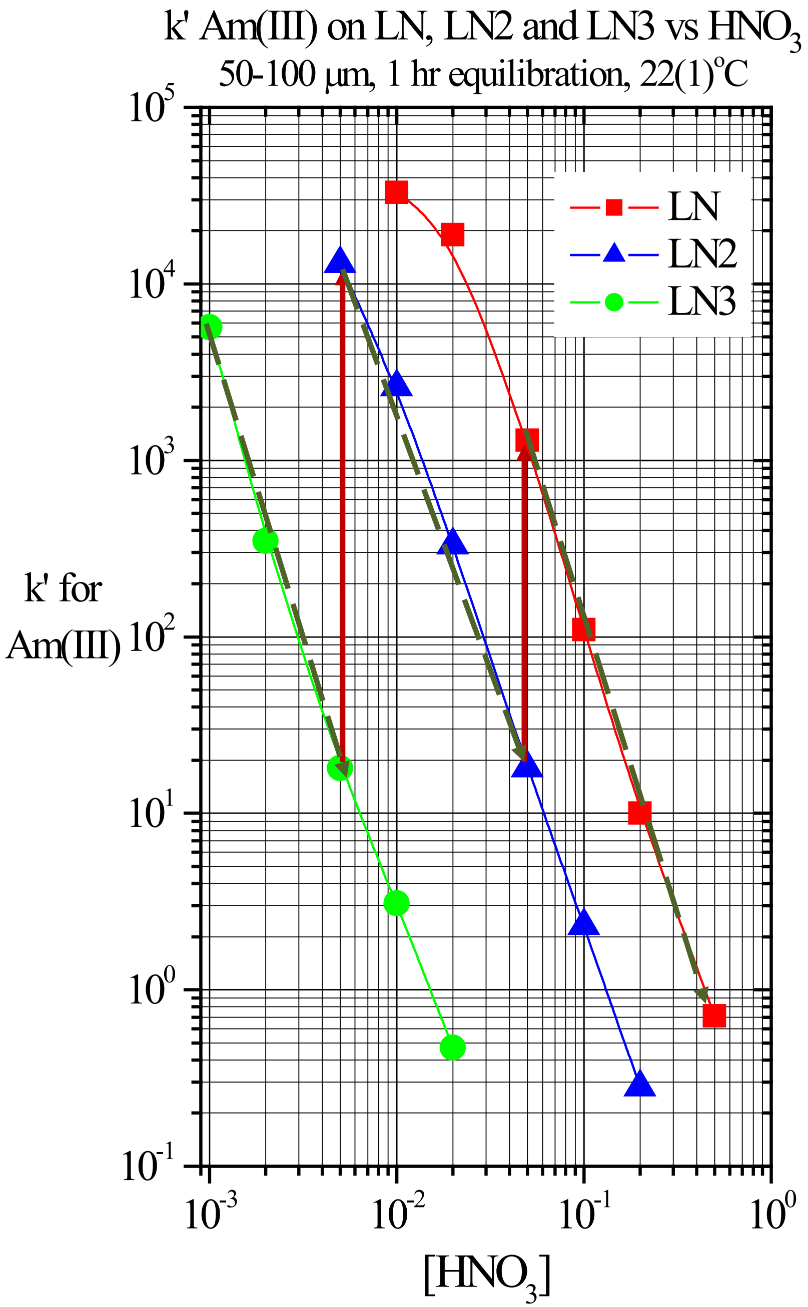
H[TMPeP] (LN3)

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

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

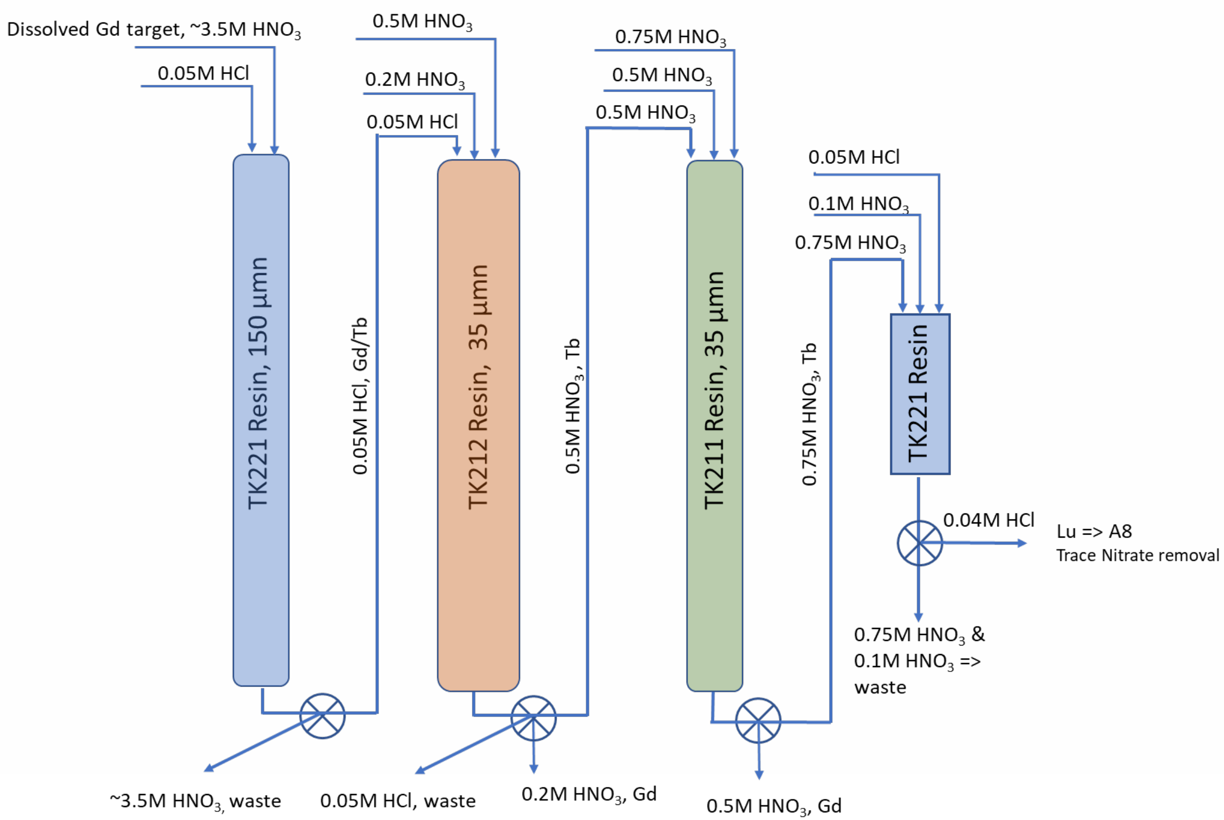
Main difference: acidity
=> Sequential separations?





Tb separation from 1000 mg Gd targets

- Irradiated target typically oxide => dissolved in >3M HNO_3
  - For separation solution needs to be dilute acid
- Conversion via TK221 Resin (i.e. TO-DGA extractant)
- Sequential separation on TK212/TK211
- Final conversion to dilute HCl on TK221 + trace nitrate removal on AIX



Tb separation from 1000 mg Gd targets

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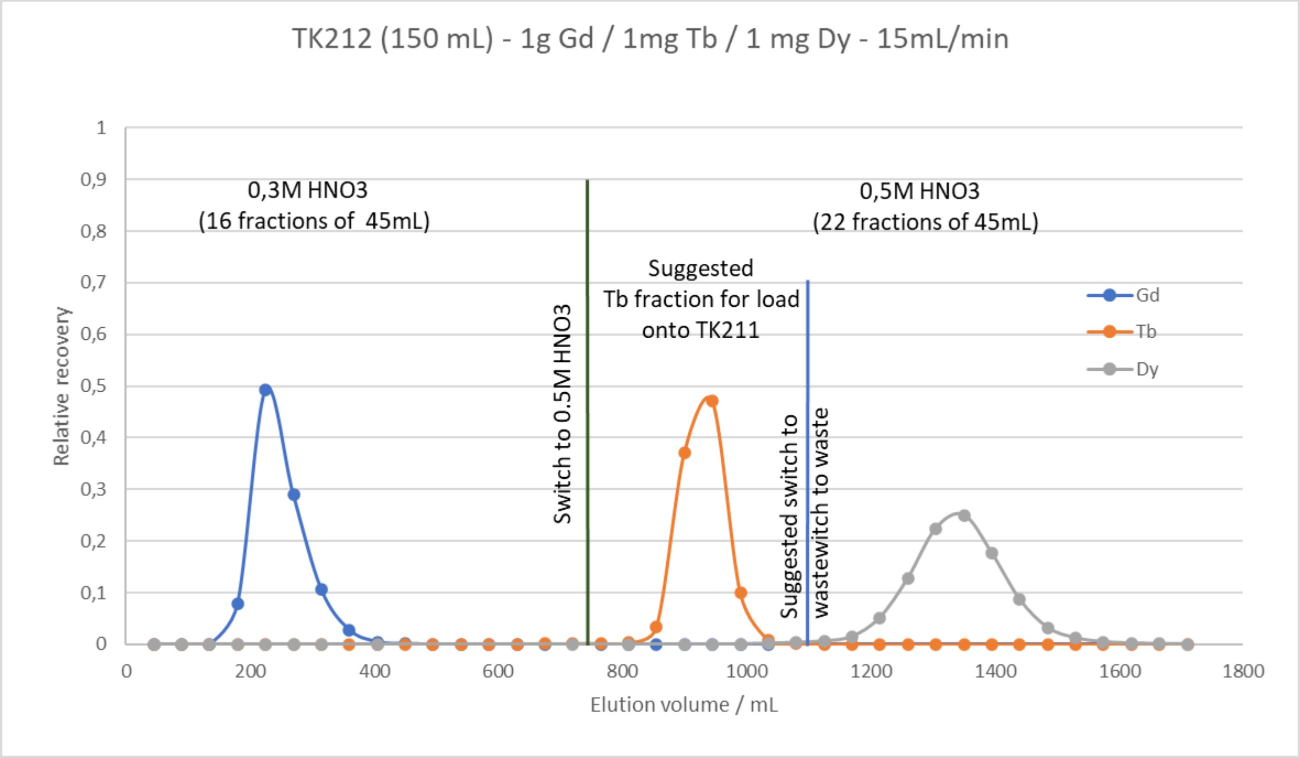
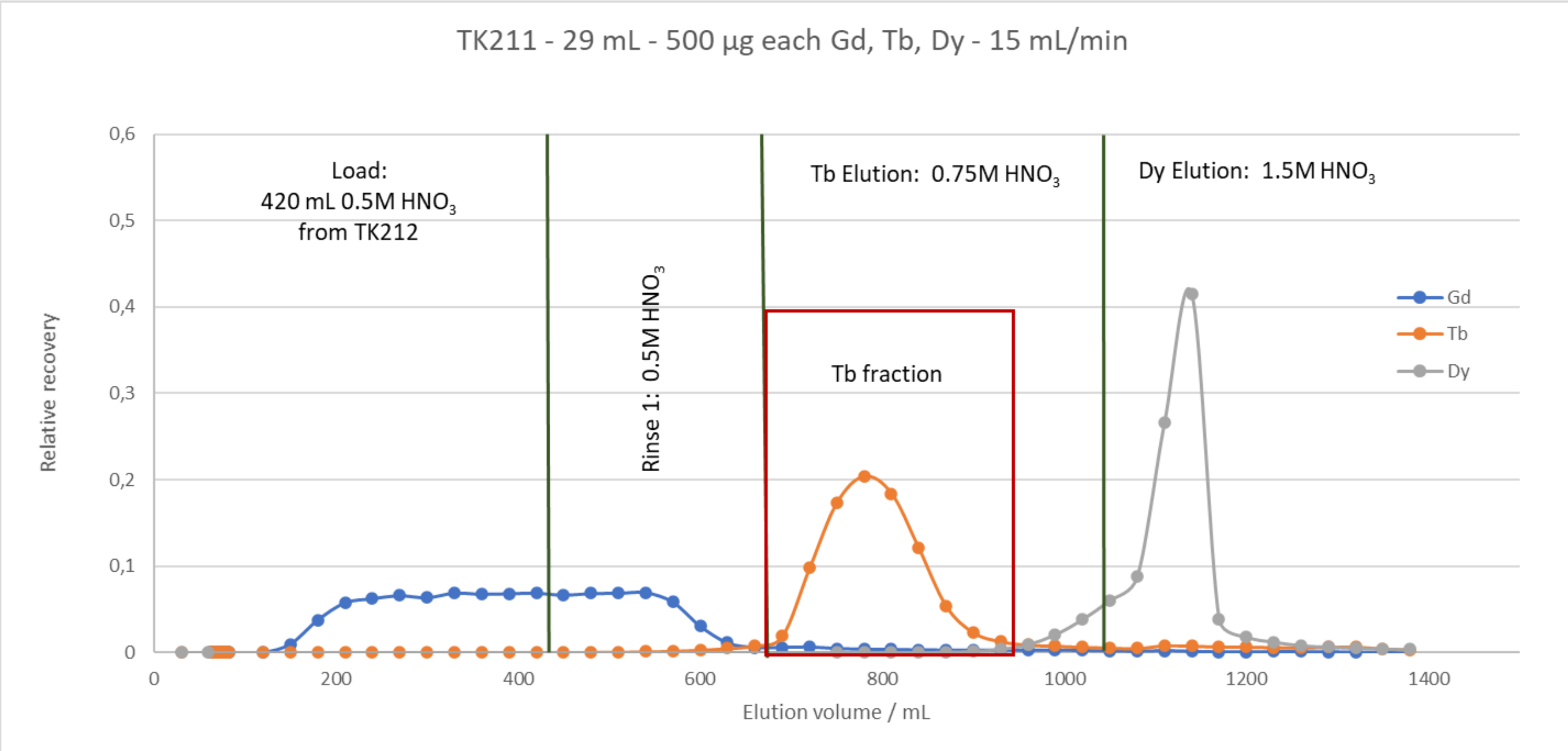
- Initial separation on TK212 – 150 mL column (30cm x 2.5cm)
- Large amount of Gd present leads to tailing
- Gd recovery => very expensive & difficult to find
- Tb separation from Gd and Dy – ideally using online detection
- Fine purification on TK211 (29 mL)



Tb separation from 1000 mg Gd on TK212 (150 mL column)

Tb purification on TK211



- Direct load of Tb fraction from TK212 onto TK211 (29 mL – 30cm x 1.1cm)
- Gd breakthrough during load & rinse with 0.5M HNO_3 (alternatively HCl)
- Tb elution (Dy sufficiently well removed before) preferably in **>3M HNO_3**
- Conversion to dilute HCl via TK221, A8 for nitrate removal

TK221 Resin

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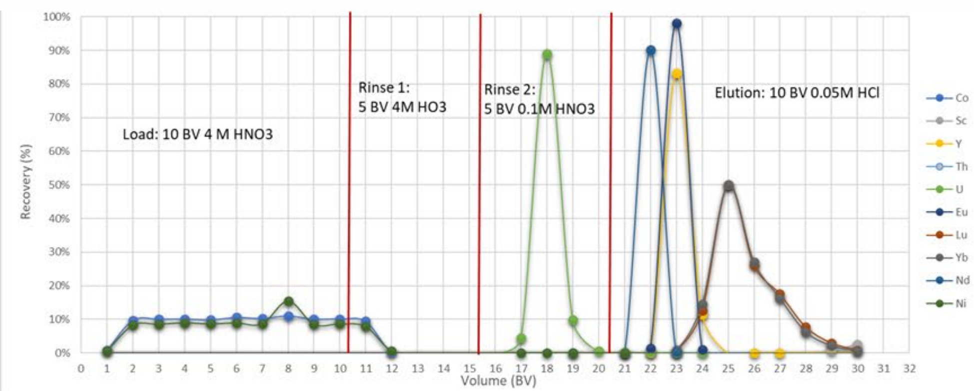
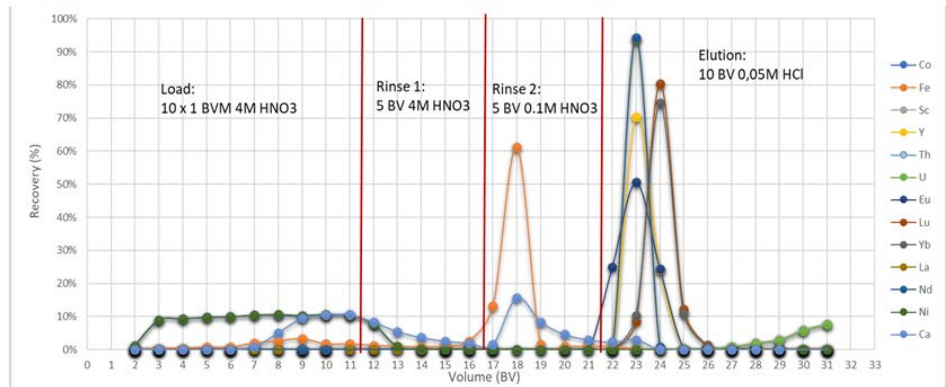
- DGA well suited for ‘conversion’ and purification (Ca, Al, Fe,... removal)
  - Convert Lu from high nitric acid to dilute HCl
- Elution of heavy lanthanides needs elevated volumes
  - small volume prefered => high activity concentration
- Optimisation of DGA Resin => TK221 Resin (TO-DGA based)
  - TO-DGA / phosphine-oxide, more radiolysis stable inert support
  - Better La and U retention
  - Lu, Tb eluted in smaller volume

DGA Resin



TK221 Resin



- **New: TK225 Resin (TO-DGA + ionic liquid) => lanthanide removal/decon**

Ac-225 from Ra-226 targets

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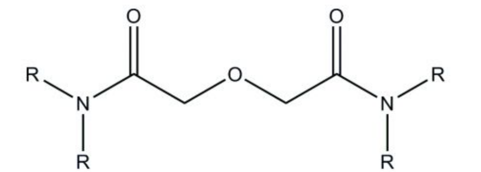
- Ac-225 separation from irradiated Ra-226 targets
- Ac separation chemistry well established
  - Reference method: DGA, B (e.g. Zielinska et al.)
    - Strong Ac retention, no selectivity for Ra
    - Smaller elution volumes compraed to DGA, N
  - Marsten, Radchenko (LANL)
    - Use of DGA (B/N) allows for Ac/LN separation
    - Ac elutes in 10M HNO_3, LN not
    - Mainly work on spallation
  - Kotaro Nagatsu et al.:
    - Use of DGA/LN cycles for Ac purification
    - Simplifies several purification cycles
  - DGA Resin availability in North America problematic
    - TK221 or TK222 options?



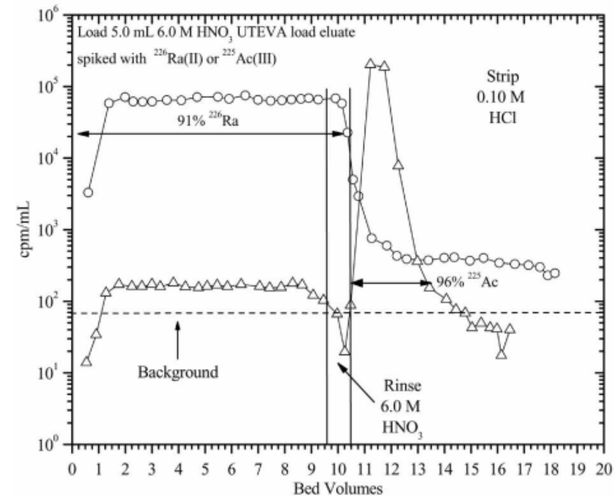


Figure 13. Separation of Ac(III) and Ra(II) on TODGA resin (50–100 µm) with 6.0 M HNO_3 and 0.1 M HCl, 0.5 mL bed volume, flow rate equals 2 mL/min load/rinse, 1 mL/min strip, 22(1)°C.

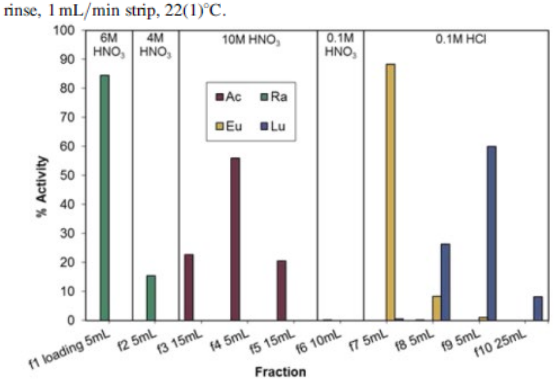
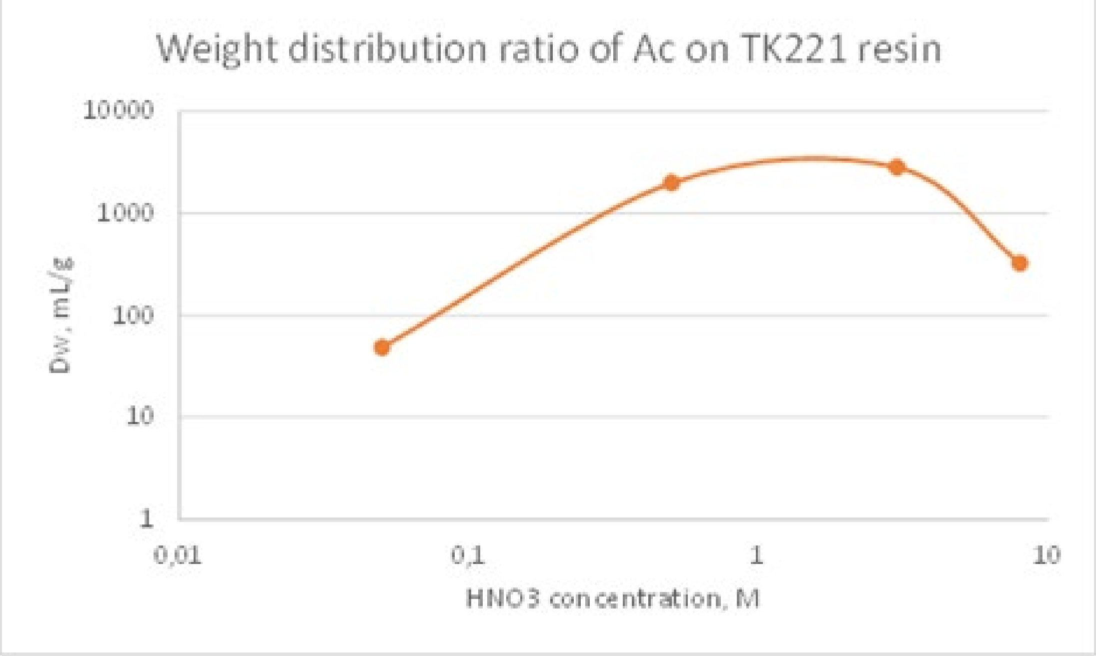


Fig. 4. Elution profile for $^{223/225}Ra$, ^{225}Ac, ^{173}Lu, and ^{155}Eu with TEHDGA resin in HNO_3 media and HCl for lanthanide elution.

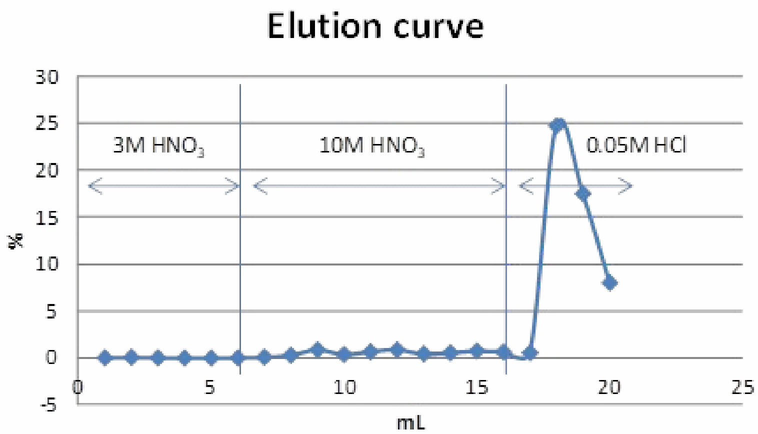
TK221 Resin – Ac separation



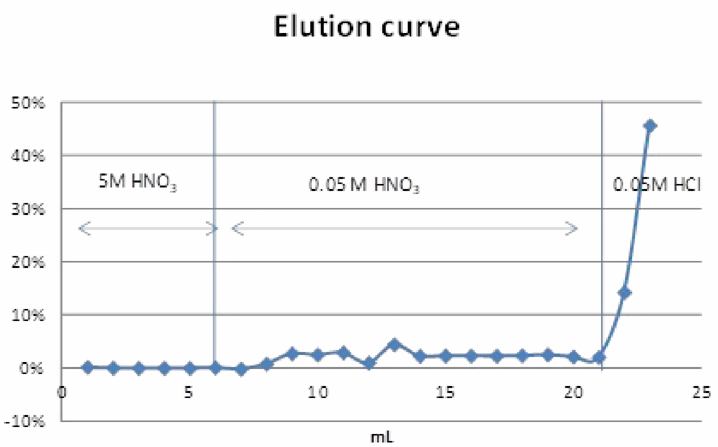
Data courtesy of N. Vajda (RadAnal)

- High Ac retention from high to low HNO_3
- Elution in 0.1 – 0.05M HNO_3 not possible
- HCl on-going, in any case low Ac retention in dilute HCl

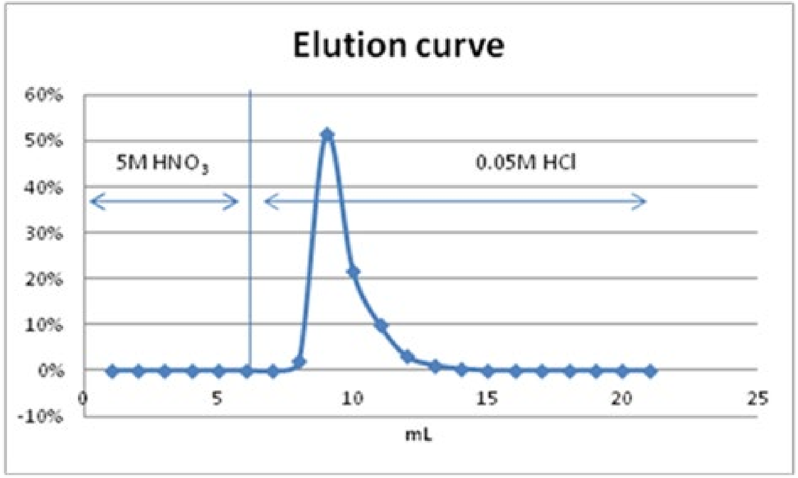
TK221 Resin – Ac separation



Elution of Ac from TK221 cartridge with 10M HNO3, 1mL TK221 column, data courtesy of N. Vajda et al.



Elution of Ac from TK221 cartridge with 0.05M HNO3, 1mL TK221 column, data courtesy of N. Vajda et al.



Elution of Ac from TK221 cartridge with 0.05M HCl, 1mL TK221 column, data courtesy of N. Vajda et al.

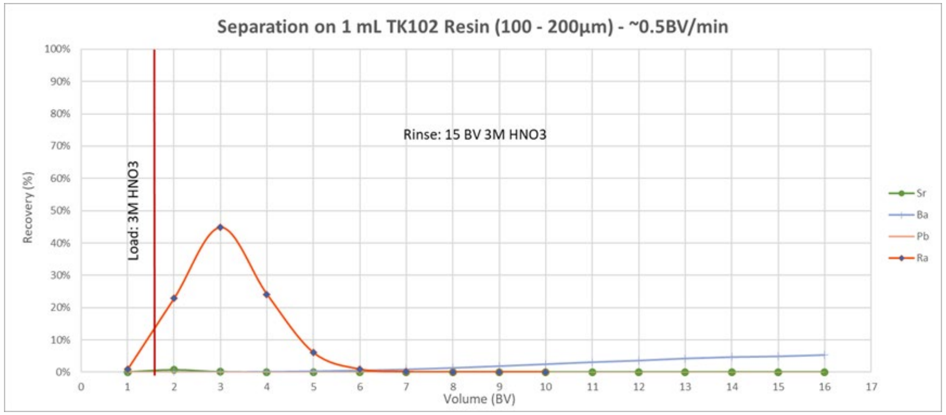
- Other than for DGA: no Ac/LN separation in 10M HNO_3 possible
  => Ac remains retained.
- No Ac elution in 0.05M HNO_3
- Elution in 0.05M HCl possible
- HNO3 => HCl conversion?
- Next steps: Dw in HCl
- TK222

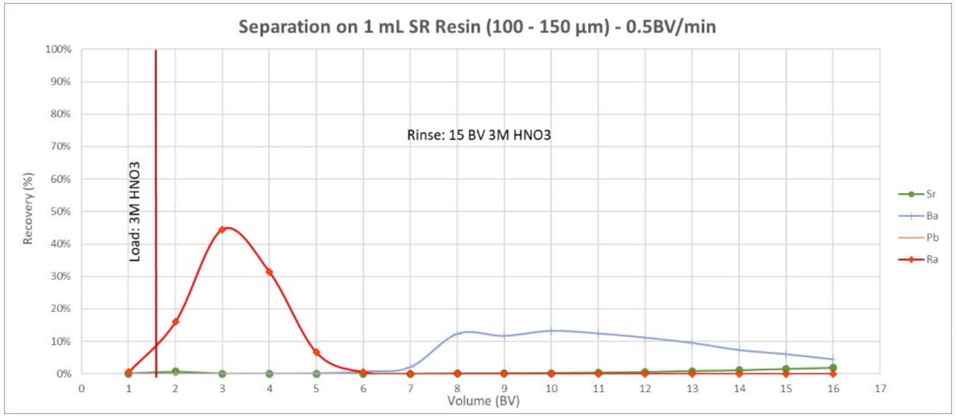
Ra purification / recycling

- Work on crown-ether based Ra Resin ongoing
  - Ra retention from acidic/high NO_3^- matrices
- Ra initial purification and recycling after irradiation
  - Depending on impurities present

  => ideal: only remove impurities

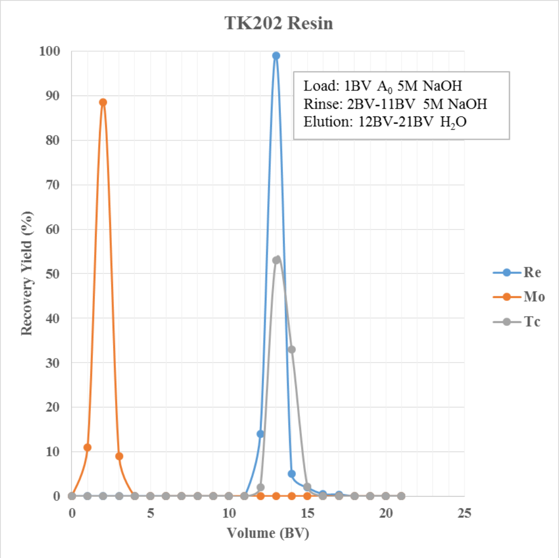
    - TK221 (or DGA) => other alpha emitters et al.
    - TK102 (or SR Resin) for Ba removal
  - In case Ra needs to be purified on-column => use of CEX or TK101



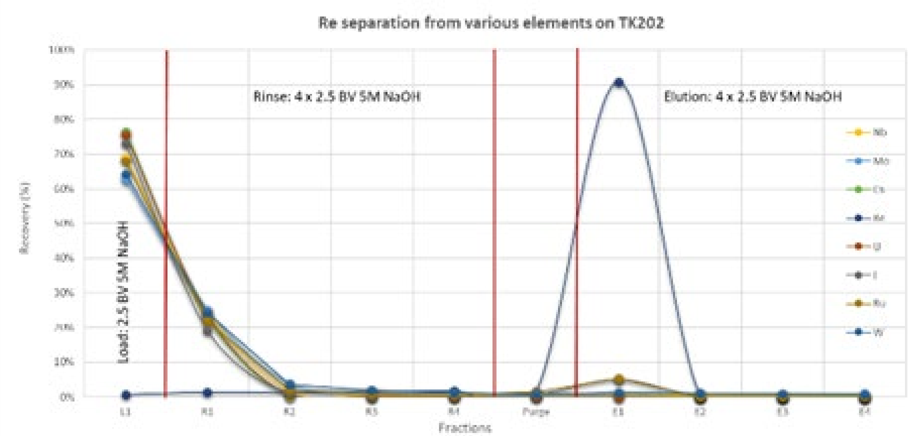


TK202 Resin

- Tc retention from high NaOH (5 - 7M)
  - Dissolved Mo targets
    - Increased Tc (Re) retention at higher Mo concentration
  - Clean separation from other elements tested
- Re used as homologue
- Elution in small volume of water
  - Eluate will still alkaline and will contain Na
  - Pass through CEX for 'neutralisation' and Na^+ removal and through
  - aluminium oxide for trace Mo removal and recovery as 0.9% NaCl solution



Re/Tc separation from Mo on TK202 Resin



Re separation from selected elements on 2 mL TK202 Resin cartridge, load and rinse at 1 BV/min, elution at 0.25 BV/min.

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

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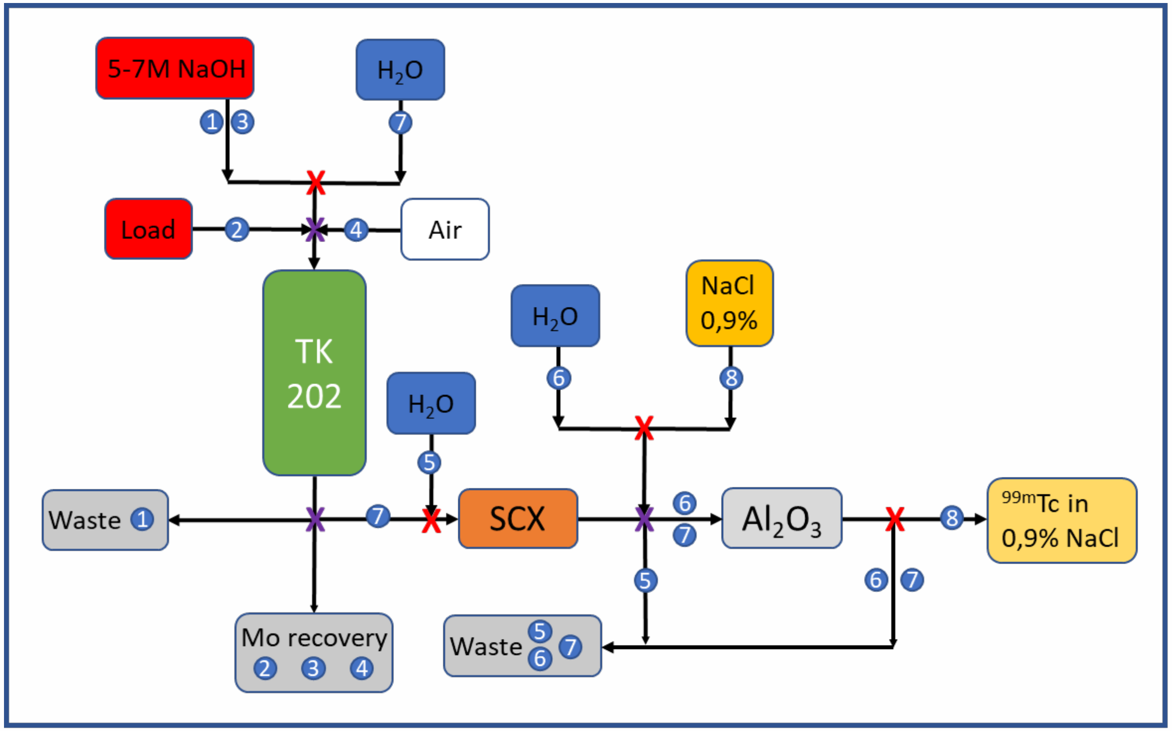


1. Pre-cond. TK202 – 5-7M NaOH ➔ alkaline waste
2. Load Mo/Tc on TK202 ➔ Mo recovery
3. Rinse TK202 – 5-7M NaOH ➔ Mo recovery
4. Purge TK202 – Air ➔ Mo recovery
5. Pre-cond. SCX – HCl then H_2O ➔ Aq. waste
6. Pre-cond. Al_2O_3 – H_2O ➔ Aq. waste
7. Elute Tc from TK202 on SCX and load on Al_2O_3 – H_2O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

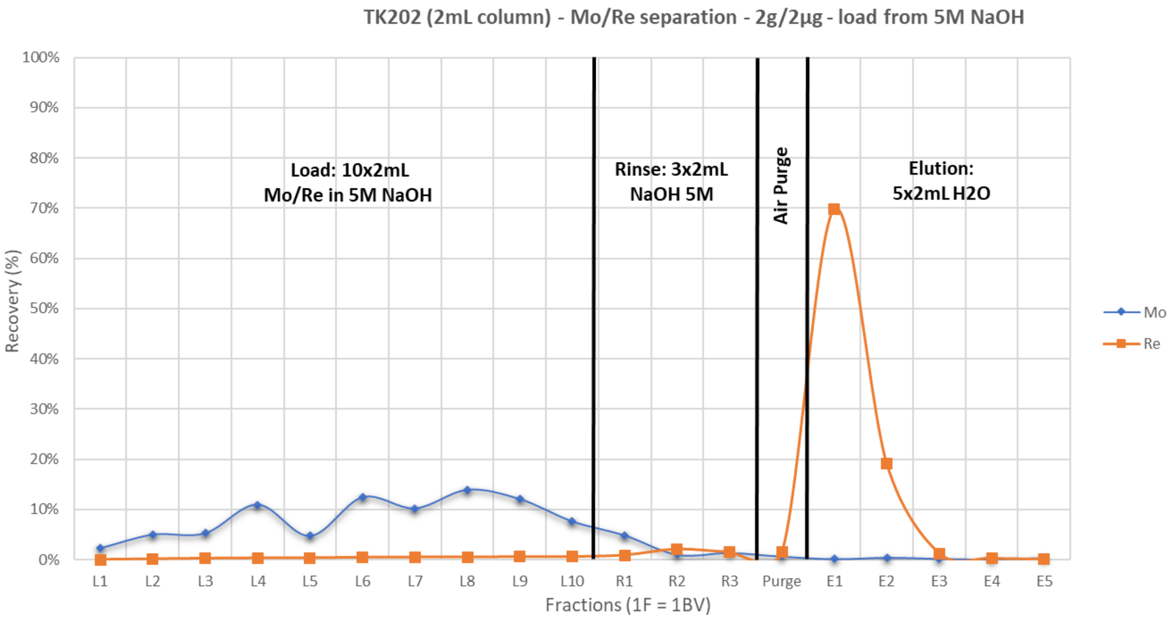
TK202 : 35-75 or 75-150µm
X : 3-ways valve
X : 4-ways valve
SCX : Strong Cation Exchange
Al_2O_3 : Acidic Alumina

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

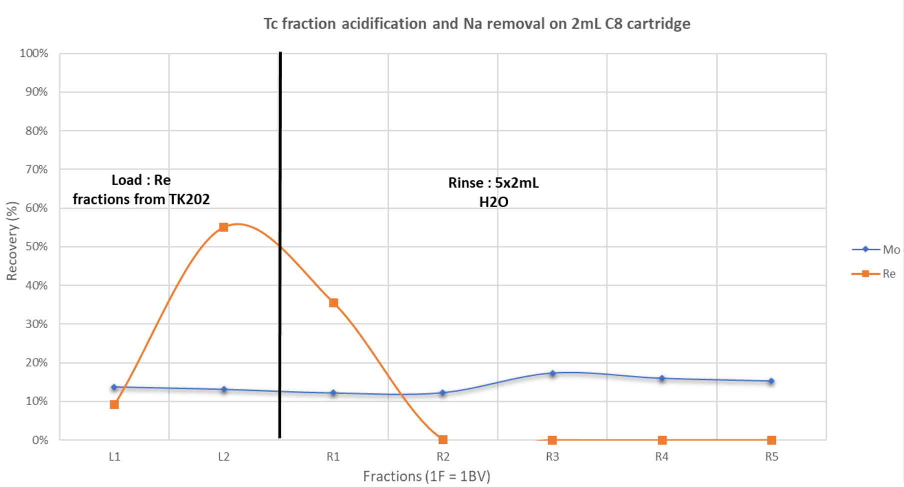


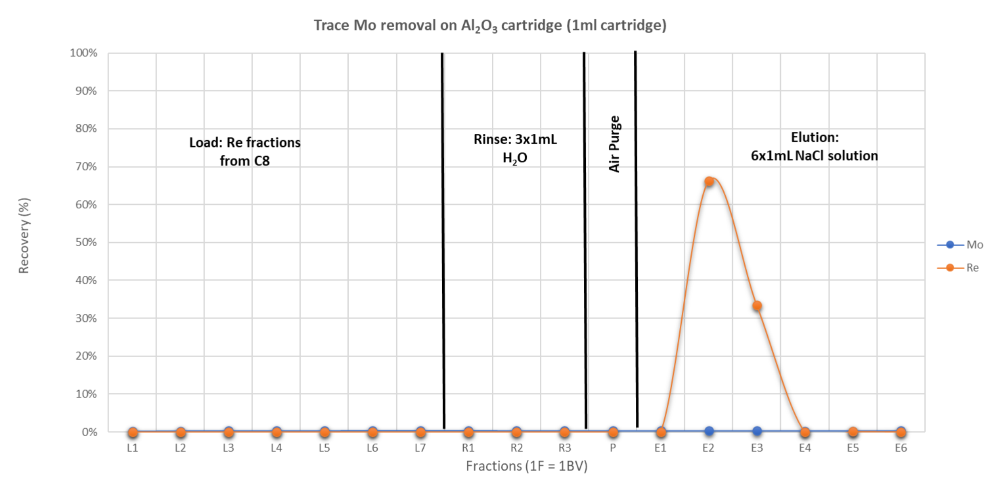
Tests performed cold with 2g Mo and 2 µg Re

- 2 mL TK202 cartridge
- 2 mL C8 cartridge
- 1 mL AlOxA 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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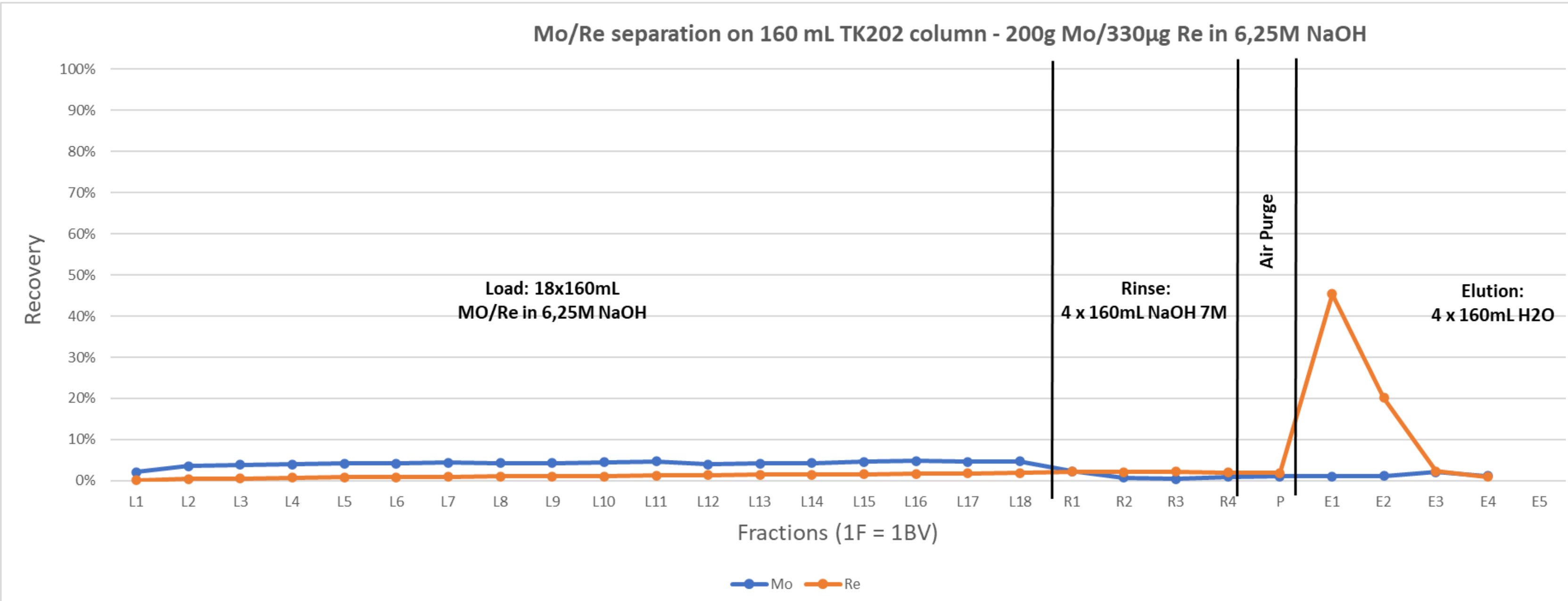
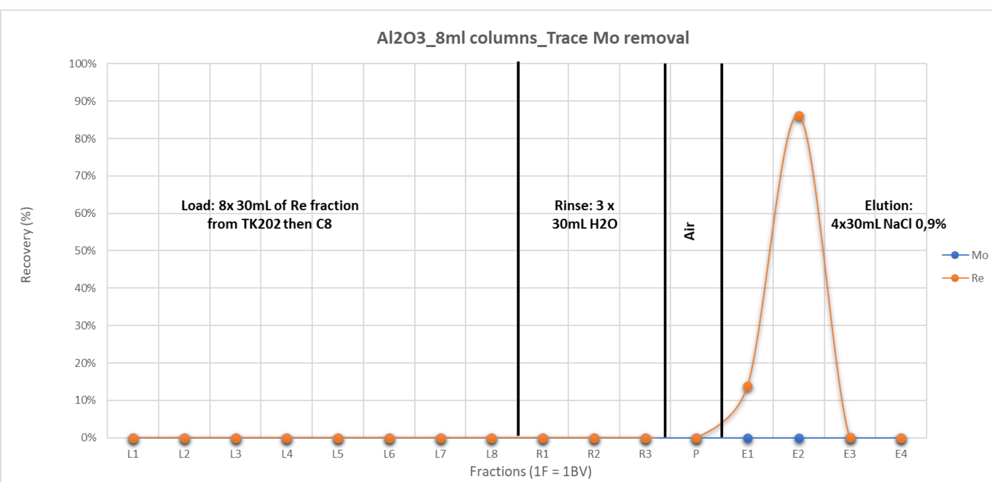


- On-going work on 200g Mo
- ~160 mL TK202 column
- Load from 6 - 7M NaOH - elution in water
- Pass through C8 cartridge for acidification and Na removal
- Final concentration/conversion to 0.9% NaCl on 8 mL AlOxA cartridge



DGA Sheets

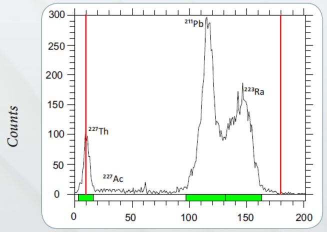
- TO-DGA (normal DGA) and TEH-DGA (branched DGA) available
- QC of radionuclides and generator eluents

(p.ex. Ra-223, Ac-225/Bi-213, Pb-212, Ge-68/Ga-68 …)

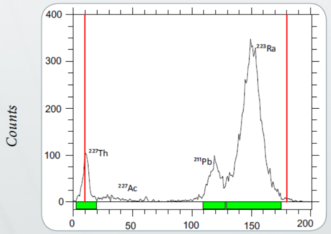
  – TLC scanner or radiometer/LSC after cutting
  – Therapy: alpha emitters
  – Diagnostics e.g. generator produced Ga-68

- More types of sheets under development (selectivities, geometry, support)

  – CU Resin, TK201, LN,, UTEVA,…

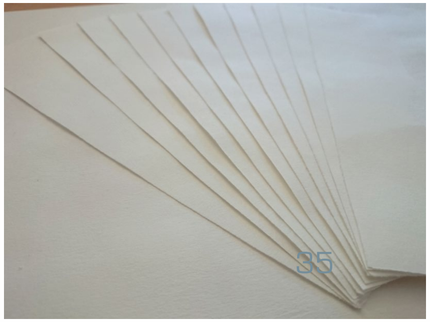


Radiochromatogram measured immediately after separaton. Low abundant radiatons of ^{227}Ac were not detected.



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.



CL Resin - Iodine removal from effluents

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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

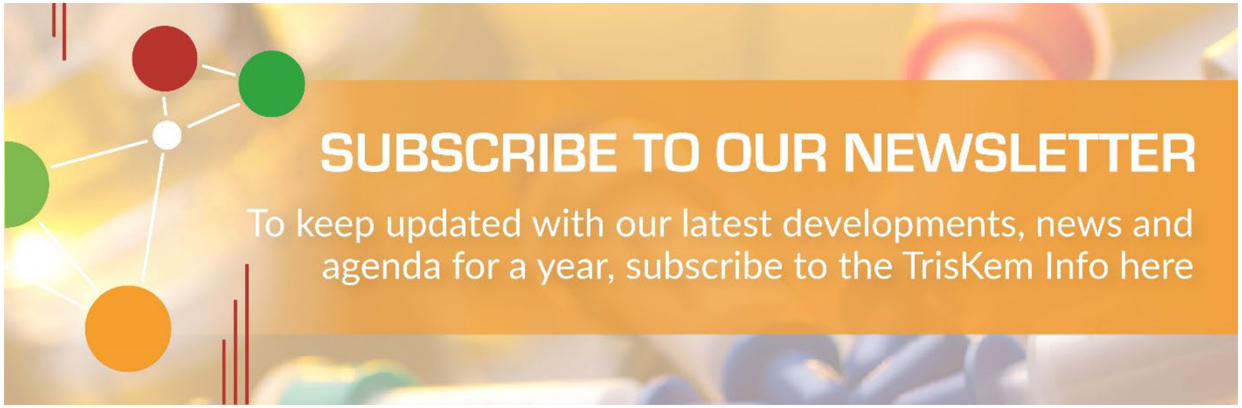
Example for decontamination of effluents

§ 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

Some other on-going projects

- Ac separation and 'resalting'
  - TK222, TK200
- Radium
  - New resins and macrocycles
- Auger emitters
  - Pd, Hg,…
- SE Resin
- Scandium separation
  - TK221, TK222
- Improvement of radiolysis stability
- At separation
  - TK400, Rn-211/At-211 generator,…
- Method development for other new, and old, radiometals
  - V, Mn, In,…
- Decontamination
  - Effluents and reaction wastes
- "Non-resin" separations
- Microfluidics
- 'Fate' of RN in the environment
  - Separation methods
  - Quantification

Thank you for your attention!



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