
# TrisKem International

## Overview and News RadPharm

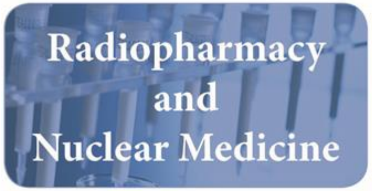
### UGM York 2022

Steffen Happel
16/09/2022

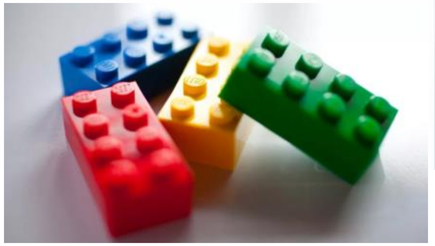
TRISKEM
Expertise in Separation Chemistry

# Research interests – Radiopharmacy

## 1. 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

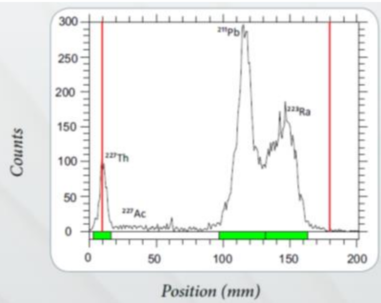


# Research interests – Radiopharmacy

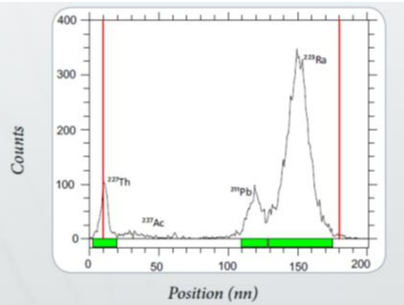
TRISKEM
Expertise in Separation Chemistry


## 2. Quality control

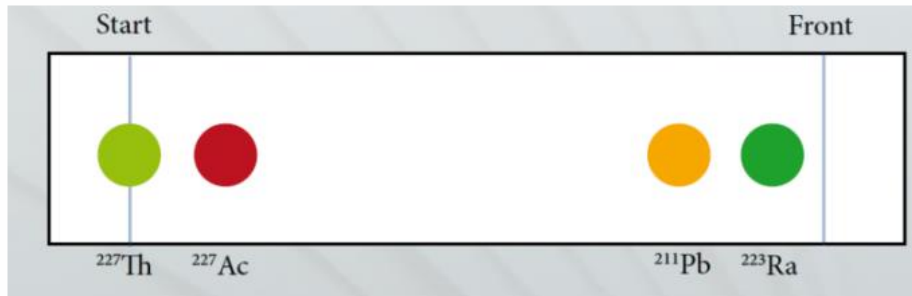
- Cartridge based methods (e.g. Sr-90 in Y-90,…)
  - Use of "TK-SRScint cartridges"?
- **"Sheets" p.ex. DGA sheets** (functionalized TLC for Ra-223, Ga-68, Pb-212,…. => CVUT Prague)




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.*

## 3. Decontamination of effluents/waste (Ge-68, lanthanides, radioiodine,…)

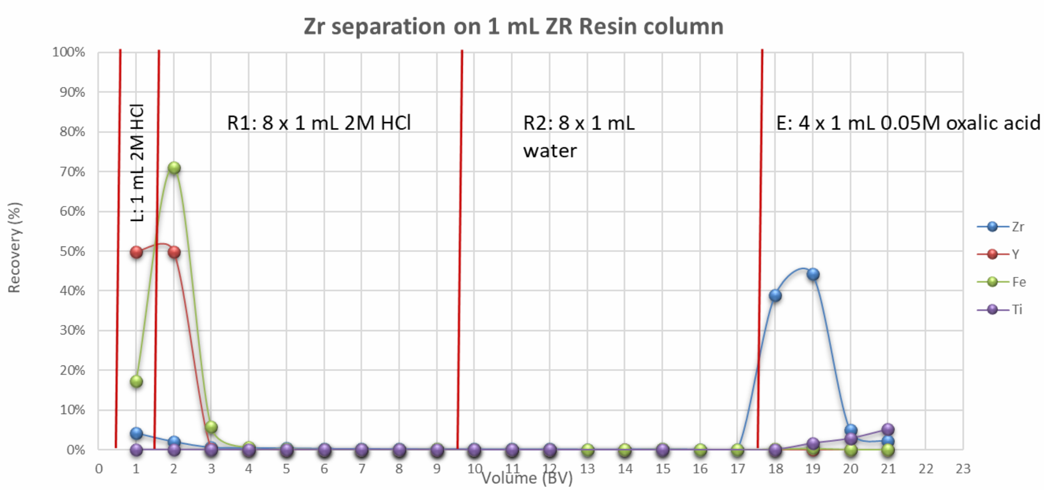
## 4. Purification/combination of generator eluates

## 5. 'Recycling'/valorization of long-lived RNs (Ge-68,…) and target materials

# Y-89/ZR-89 separation on ZR; TBP or TK400/TBP Resins

# Zr-89 separation on ZR Resin

- Hydroxamate based resin => different from Holland publication
  - Ready to use / no activation
  - Easy 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

TRISKEM
Expertise in Separation Chemistry

- 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: $1.5 \times 10^5$
- Zr elution should also be possible with citrate, phosphate, 0,01M Oxalate…
- **Limitation:** Fe and Nb removal not ideal ➔ **alternative:** use of TK400 for Fe and Nb removel before TBP resin

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

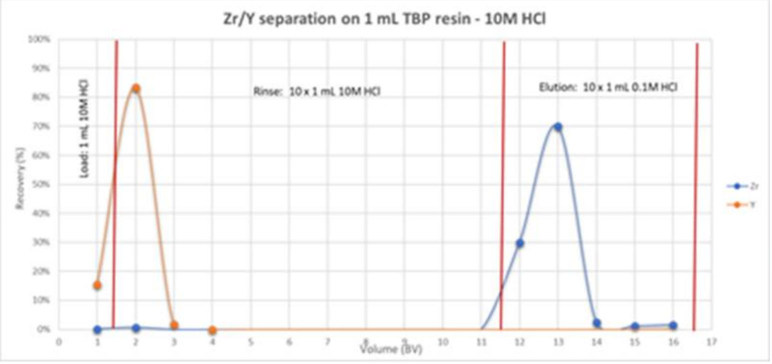
Evaluation of a chloride-based $^{89}$Zr isolation strategy using a tributyl phosphate (TBP)-functionalized extraction resin

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

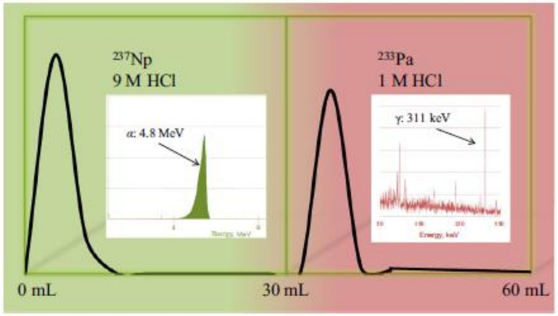
Get rights and content

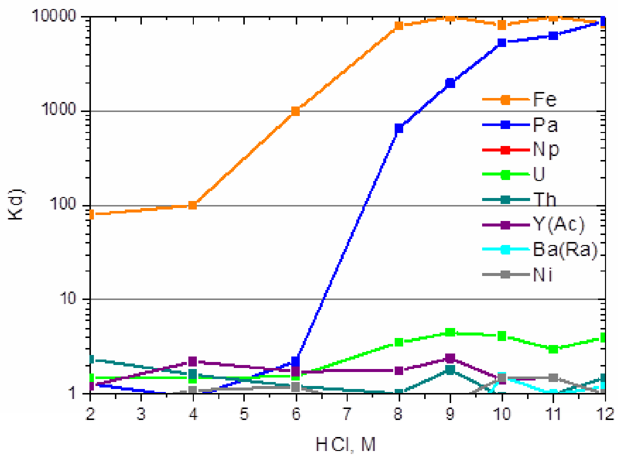


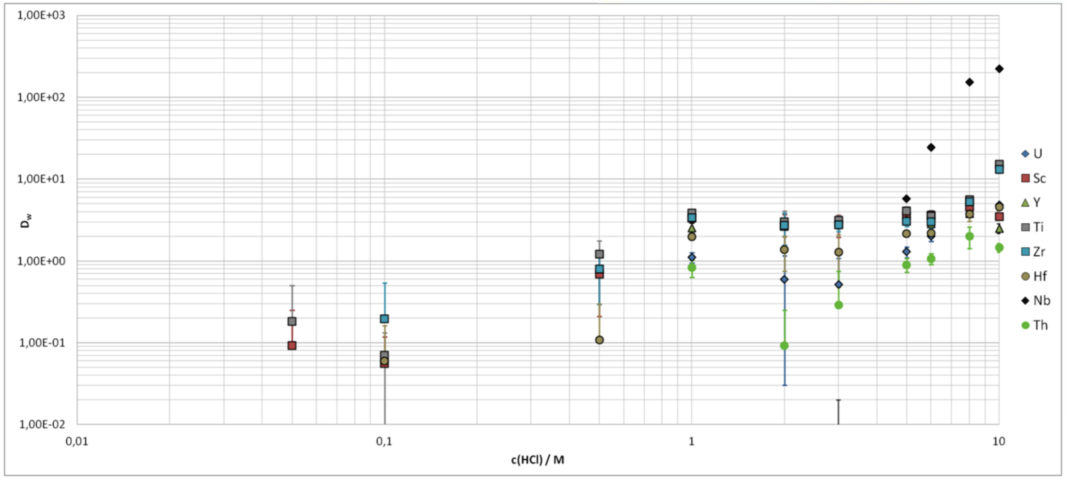
# TK400 Resin

- 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
  - Nb separation from Zr possible (Nb-90)
  - Under further testing for At separation (elution…)

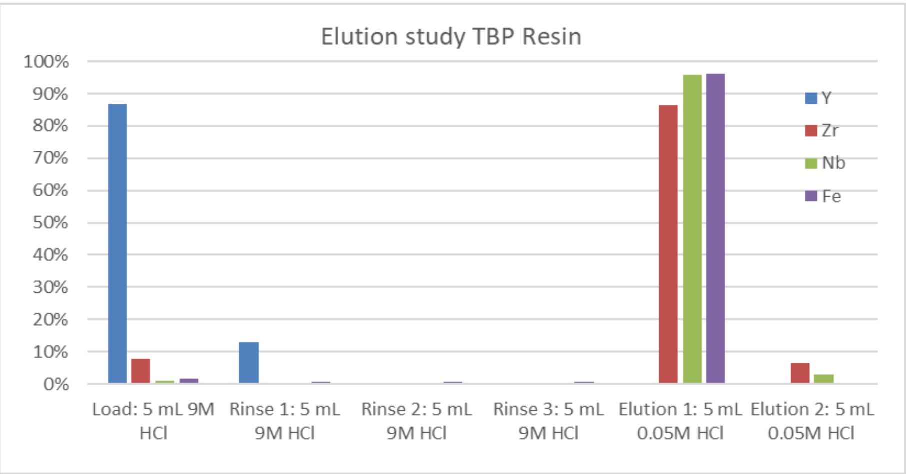
Knight et al.

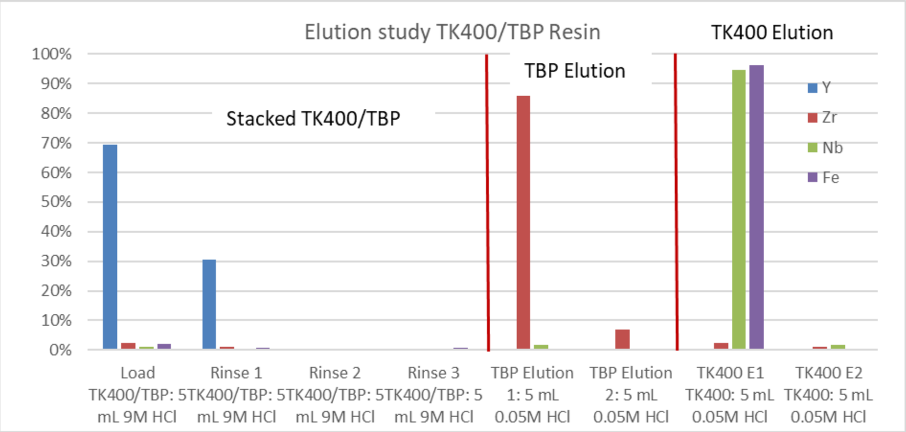


# Use of TK400 for Fe/Nb removal





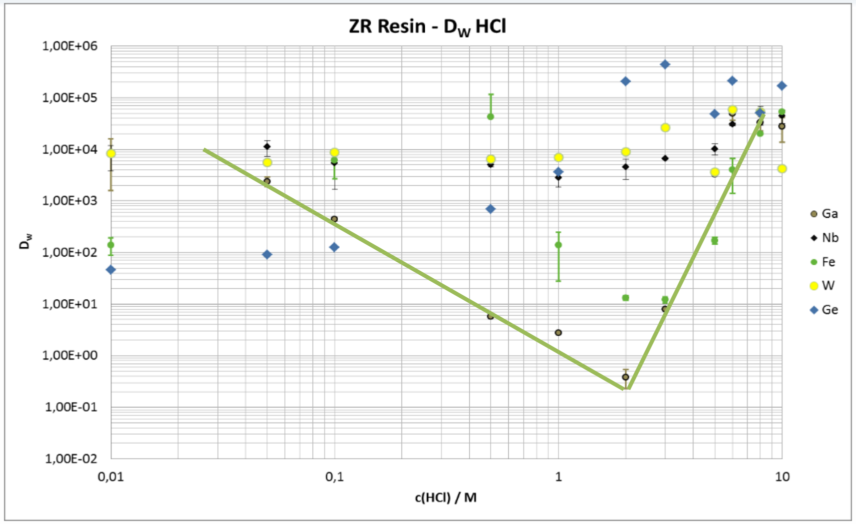
- On-going work
- On TBP only: Fe and Nb follow Zr
- Removal of Fe & Nb upfront possible using TK400 Resin
- Test with stacked 2 mL TK400/TBP cartridges
  - Load and Rinse at 10M HCl with TK400 stacked above TBP
  - Splitting of cartridges and separate elution with dilute HCl
    - TBP => ZR only
  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

➔ Removing Fe and Nb using TK400 improves Zr purity

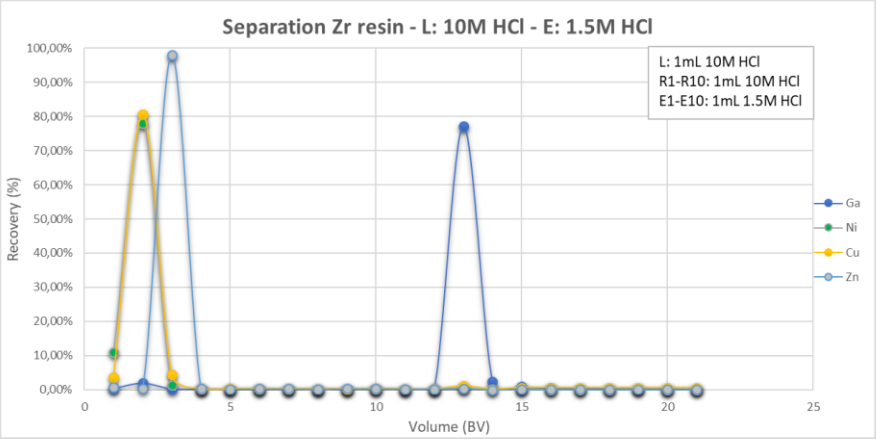
# Zn-68/Ga-68 separation on ZR; ZR/TK200 Or TK400/A8/TK200 Resins

# Ga-68 separation from Zn targets I

- 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




**Disadvantages** ➔ Too acidic for injection or labelling




**Alternatives**

1) Conversion necessary
   - Evaporation & dissolution difficult to automatize ➔ long
2) 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,..

# Ga-68 separation from Zn targets II

TRISKEM
Expertise in Separation Chemistry

## Liquid Zn targets

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*]

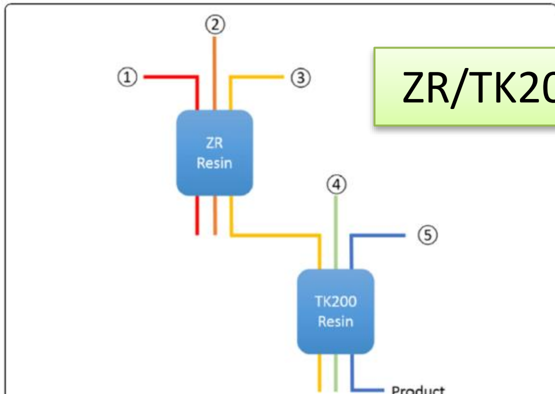


Fig. 4 Two-column approach for $^{68}$Ga chemical separation

ZR/TK200

**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$_2$O | 1–2 mL H$_2$O followed by dilute HCl to formulate |

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

## Solid Zn targets

### 1) J. Kumlin et al.

- ZR, LN & TK200

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

### 2) W. Tieu et al.

- Use of single TK400 cartridge

### 3) 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

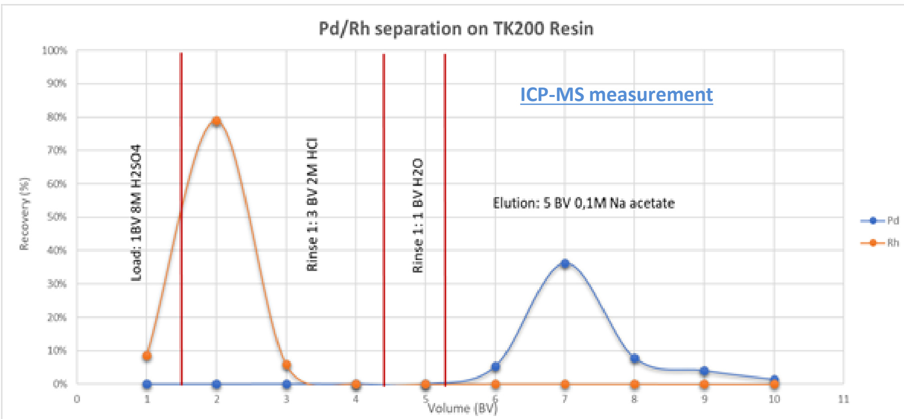
Johan Svedjehed, Martin Pärnaste, Katherine Gagnon

# Pt-194/Ir-194 and Pd-106/Rh-106 separation on TK200 Resin or TBP/AIX

# Rh/ Pd and Ir/Pt separation on TK200

TRISKEM Expertise in Separation Chemistry

**Pd separation from Rh targets**




Main challenge: target dissolution & oxidation states

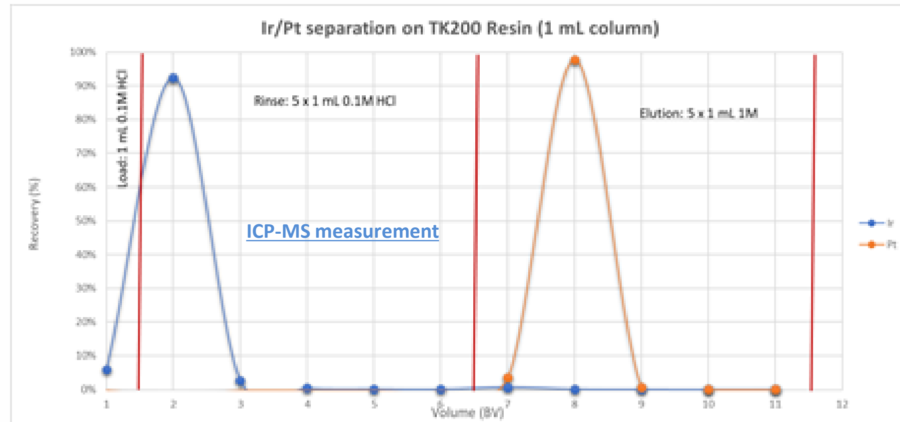
Request: Pd separation from high $H_2SO_4$

Possibility: Separation on TK200

Steps:

- Load on TK200 Pd/Rh in 8M $H_2SO_4$
- Remove of $H_2SO_4$ necessary➔ Rinse with 2M HCl
- Elution in acetate possible (To be optimized..ongoing)

**Pt separation from Ir targets**




Main challenge: oxidation state control

Possibility: Separation on TK200

Alternative:

1) use of TBP => Obata et al. [$^{188,\ 189,191}$Pt]cisplatin

2) TBP and AIX based method

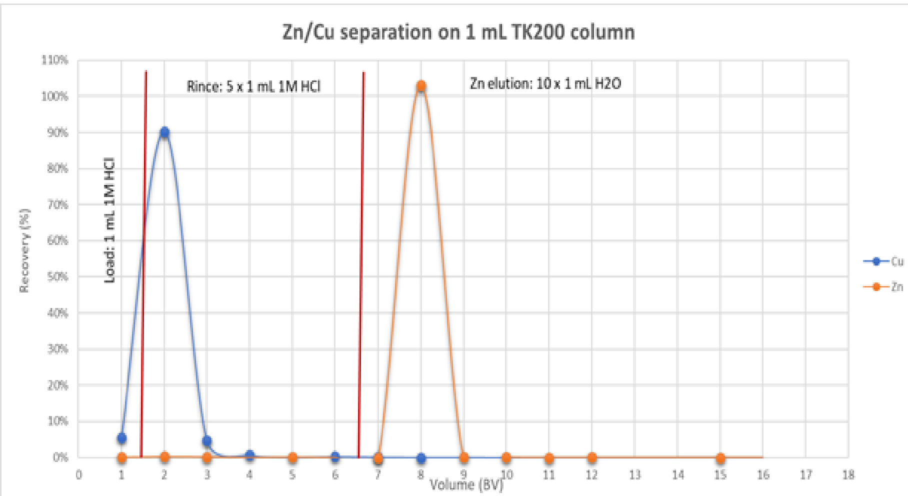
➔ 3x 2 mL TBP cartridges followed by QMA cartridge

Ongoing on TK200 : Test for Sc separation

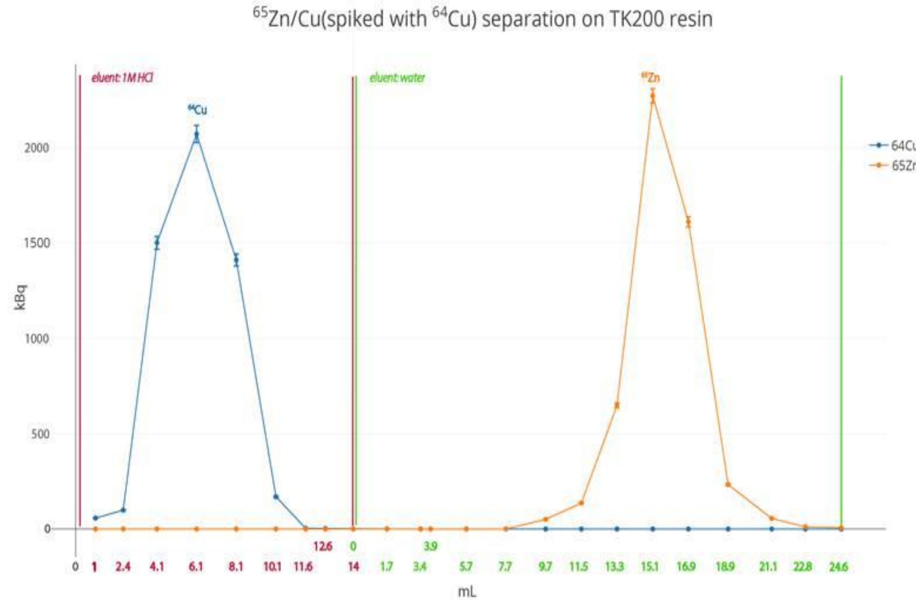
# Other separations on TK200

TRISKEM
Expertise in Separation Chemistry

## Zn separation from Cu targets




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




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

<u>Steps:</u>

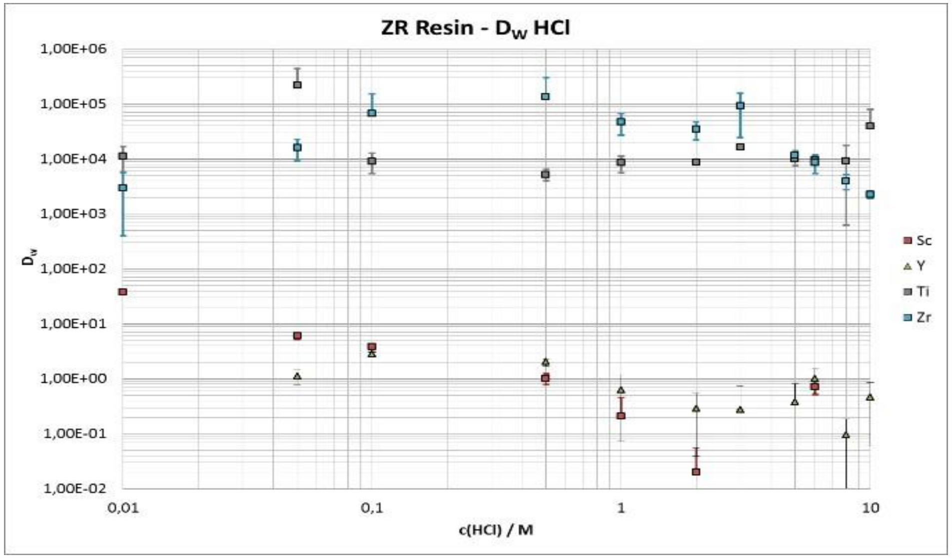
- Load from HCl (e.g. 1M)
- Rinse with 1M HCl
- Elution in water

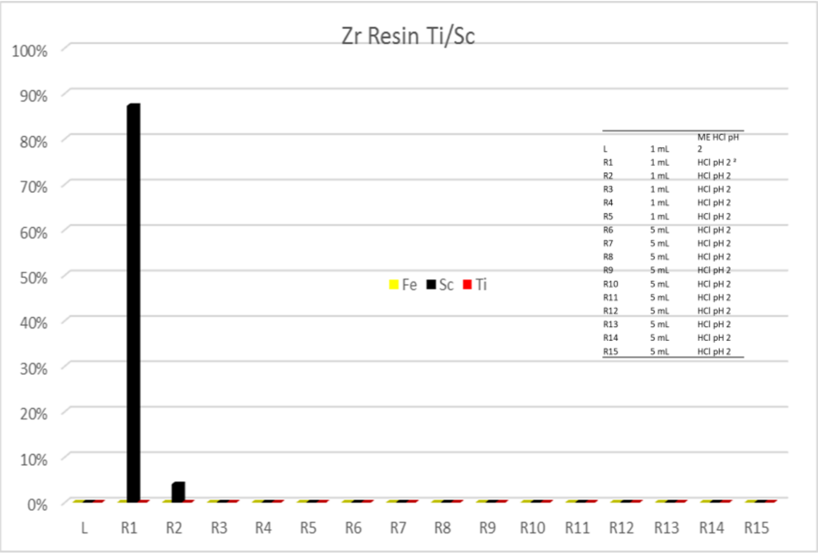
**'Hot tests' by F. Zhuravlev, DTU**

## Sc-44/Ti-44
## separation on ZR Resin

# Ti-Sc Separation (Ti-44/5) on ZR Resin I

TRISKEM
Expertise in Separation Chemistry



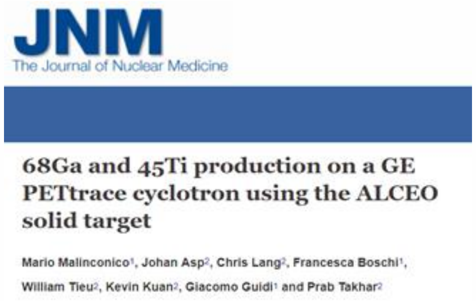




## Functionning of ZR resin:

- Ti retained from (high) HCl; Sc not retained
- Ti also retained in dilute acid; Sc not => Ti generator?
- Ti elution with 1M oxalic acid or 0.1M citric or 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-Sc Separation (Ti-44/5) on ZR Resin II

**1) Ti-44 production:**

- 4g irradiated Sc

**2) Ti-44/Sc-44 separation:**

- 5 mL Zr Resin

Results

- Ti-44 yield >95%
- 65.2 MBq Ti-44
- $D_f$(Sc): $10^5$

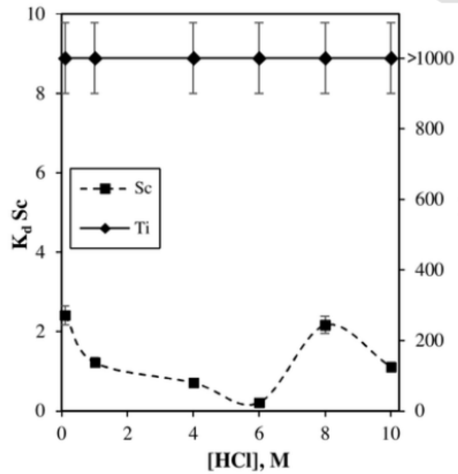



Fig. 3. HCl concentration dependency of $K_d$ for $^{44}$Ti/$^{46}$Sc on ZR hydroxamate re

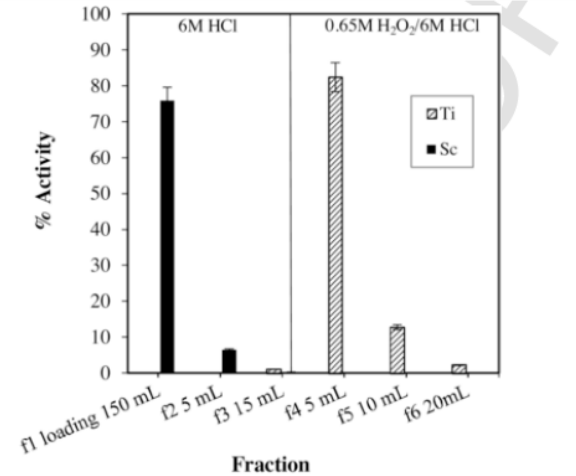



Fig. 5. $^{44}$Ti/$^{46}$Sc elution profile using ZR hydroxamate resin with a load of 4 g of scandium.

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*


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

- 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. Huclier ISRS 2019

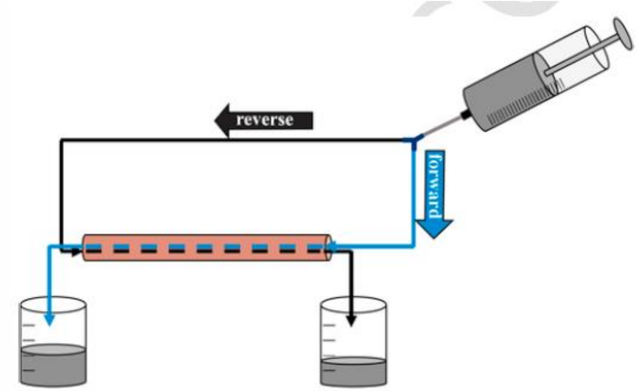
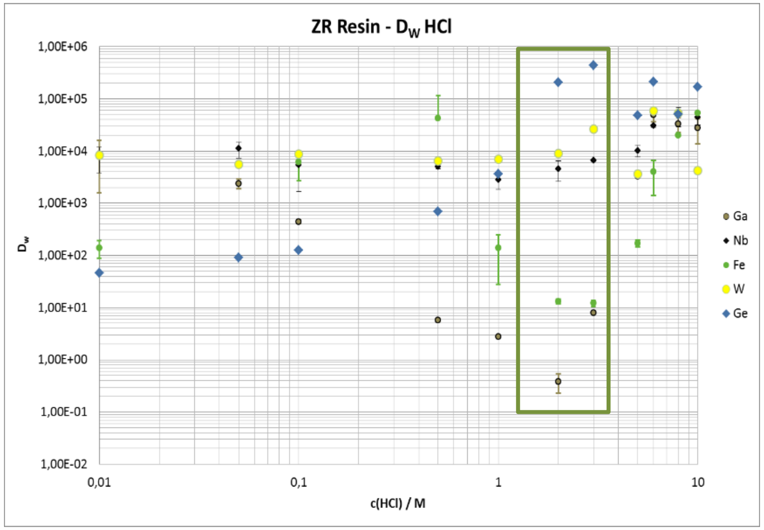


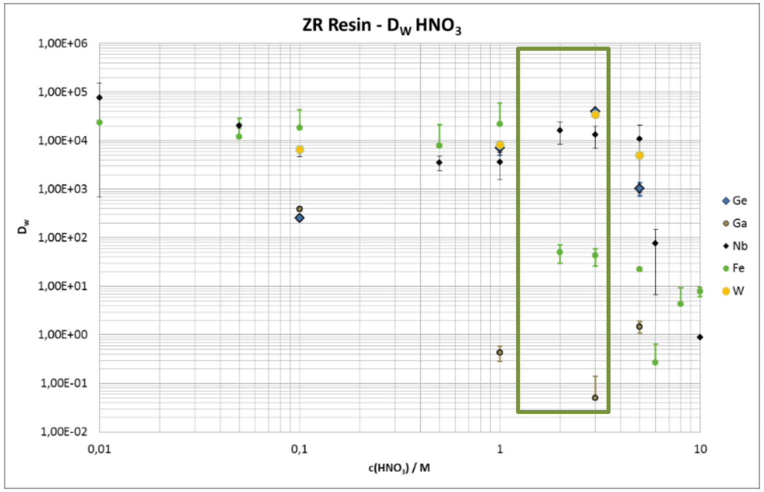

Fig. 1. Schematic concept of a forward/reverse flow radionuclide generator.

# GaNi or GaCo/Ge-68 separation on ZR Resin

# Ge-68 separation from GaNi or GaCo on ZR Resin

- **<u>ZR Resin</u>**: 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 (-GR) 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

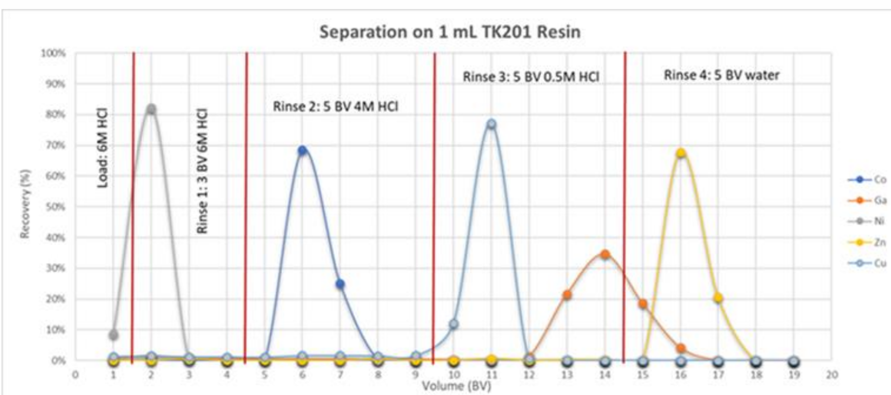
Ni-64/Cu-64 and Zn-67/Cu-67separation on

- TBP(or TK400) + TK201 Resins
- CU Resin

# Cu-64 separation on TK201 Resin

TRISKEM
Expertise in Separation Chemistry

- **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

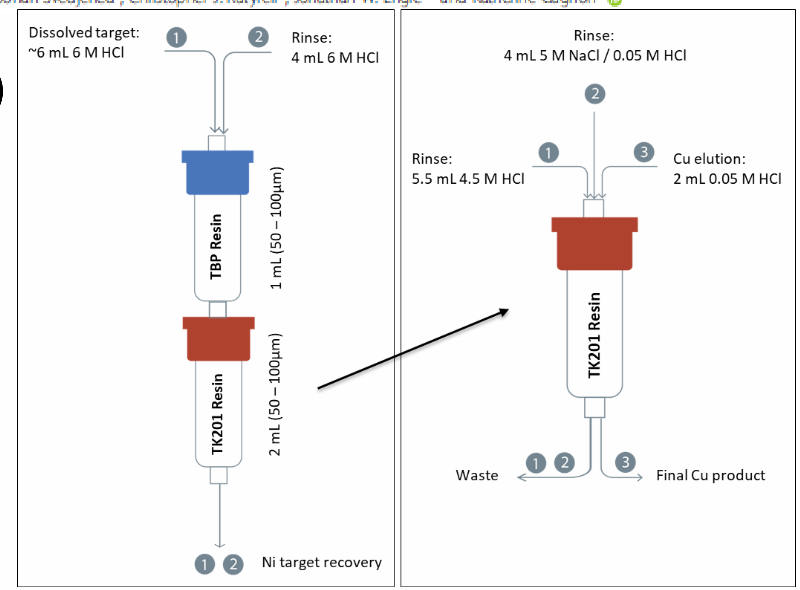



Svedjehed et al. EJNMMI Radiopharmacy and Chemistry (2020) 5:21
https://doi.org/10.1186/s41181-020-00108-7
EJNMMI Radiopharmacy and Chemistry

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

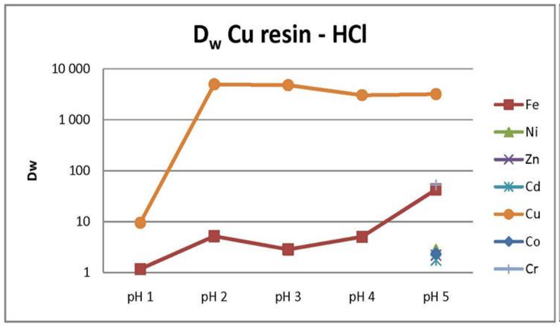
- **Improvements**:
  - Preferred alternative: Use of TBP (or TK400) upfront for Fe/Ga removal
  
  => **allows for Cu elution in 0.05M HCl**

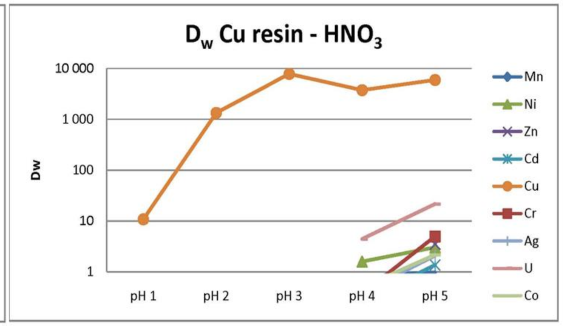
- **May be used for Zn separation combined with CU Resin**

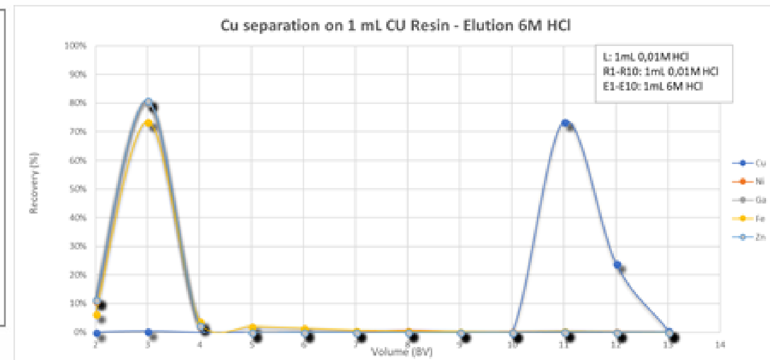
# Cu-67 separation on CU Resin

TRISKEM
Expertise in Separation Chemistry

- 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,…




- **Dissolution of target** in high mineral acid concentration then dilution to pH>2
- **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.)

TRISKEM
Expertise in Separation Chemistry

**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

## Procedure on CU Resin:

- 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

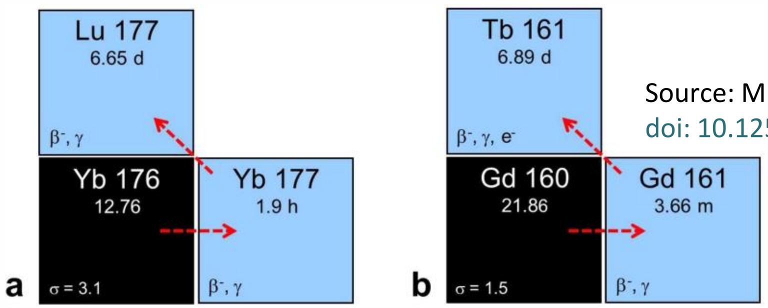
# Gd-160/Tb-161

# separation on ZR Resin

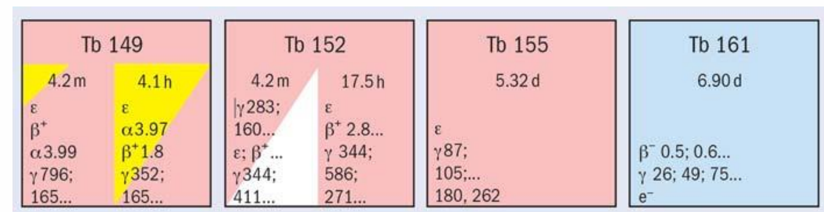
# Tb-161 separation on combined resins

TRISKEM
Expertise in Separation Chemistry

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




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

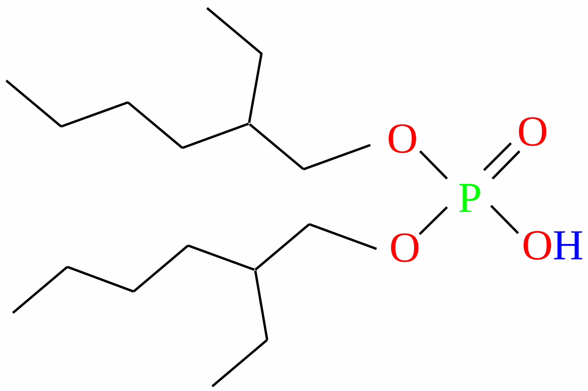



**Terbium: a new ‘Swiss army knife’ for nuclear medicine**
Source: https://cerncourier.com/a/terbium-a-new-swiss-army-knife-for-nuclear-medicine/

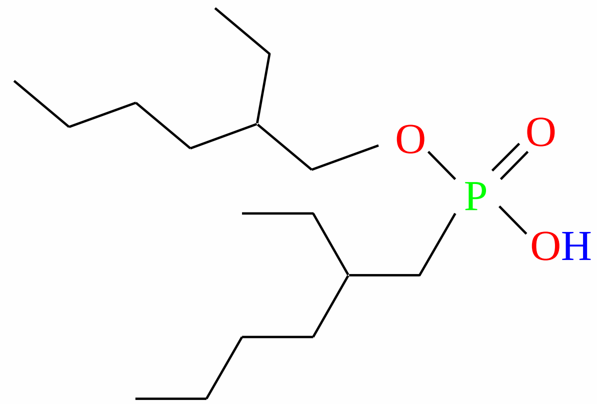
  - Irradiation of several hundreds of mg or more

- Separation method based on nca Lu-177 work (0.5 – 1g+ Yb targets)
  => TK211/2/3 product sheet
- 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)

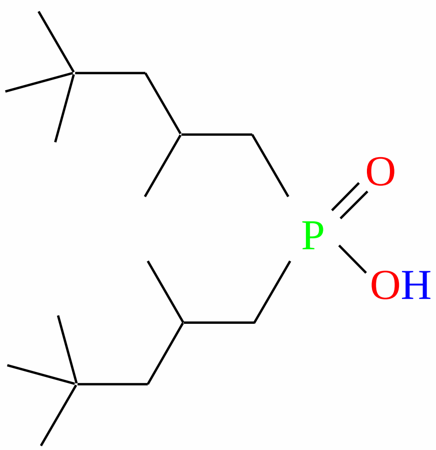
# Lanthanide separation on TK211/2/3 or LN series




HDEHP (LN)




HEH[EHP] (LN2)

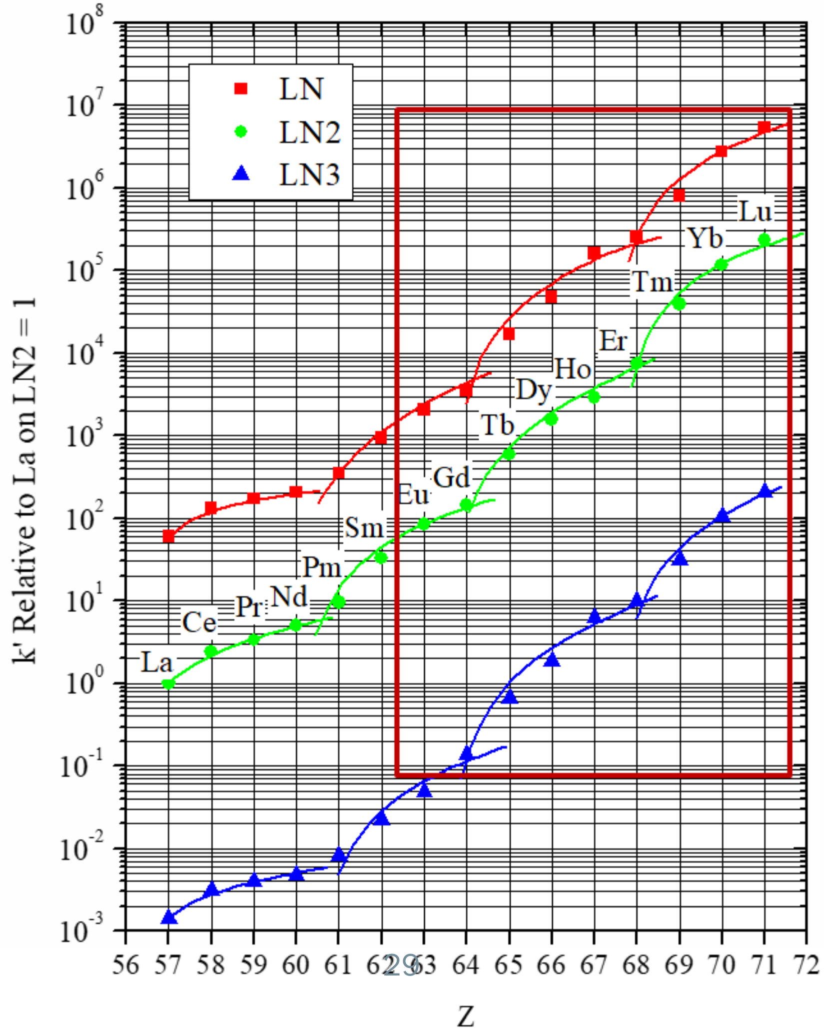


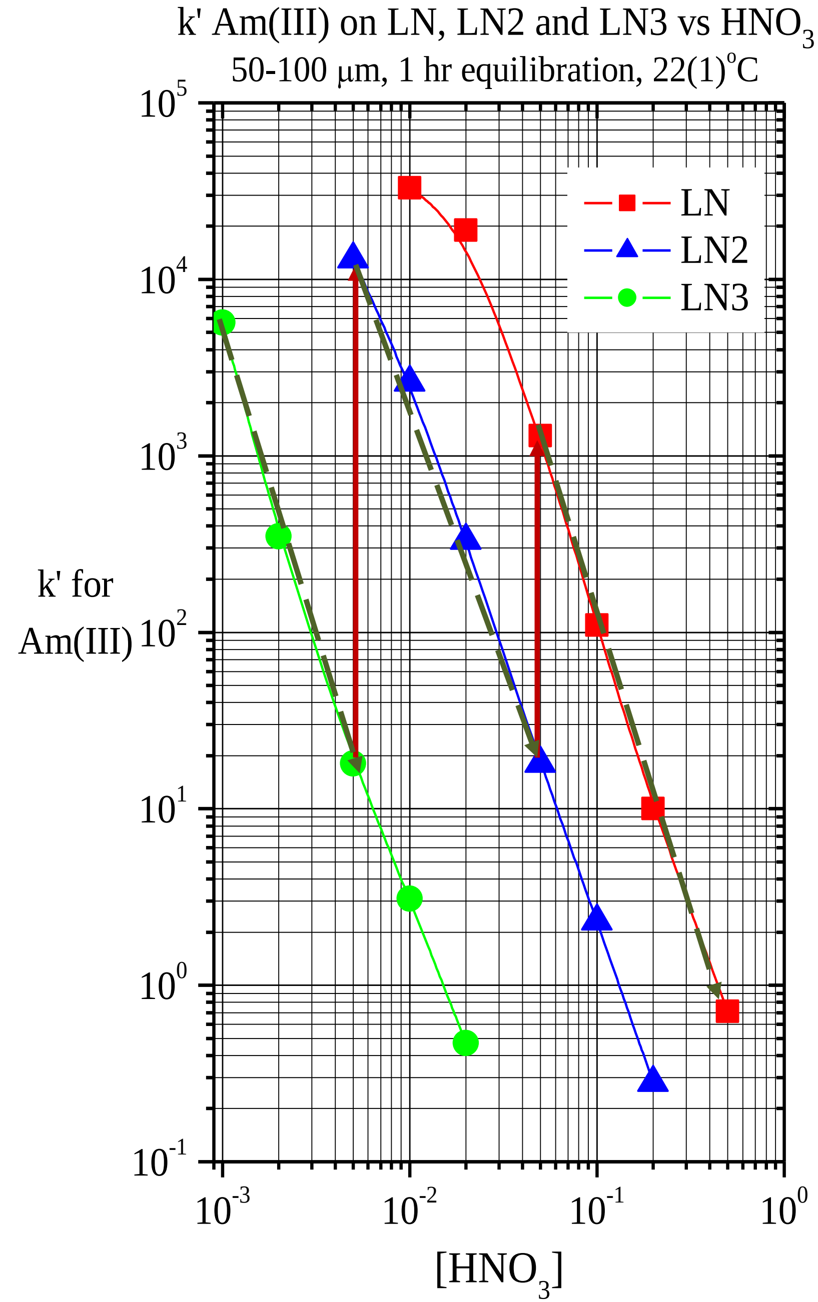

H[TMPeP] (LN3)

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?

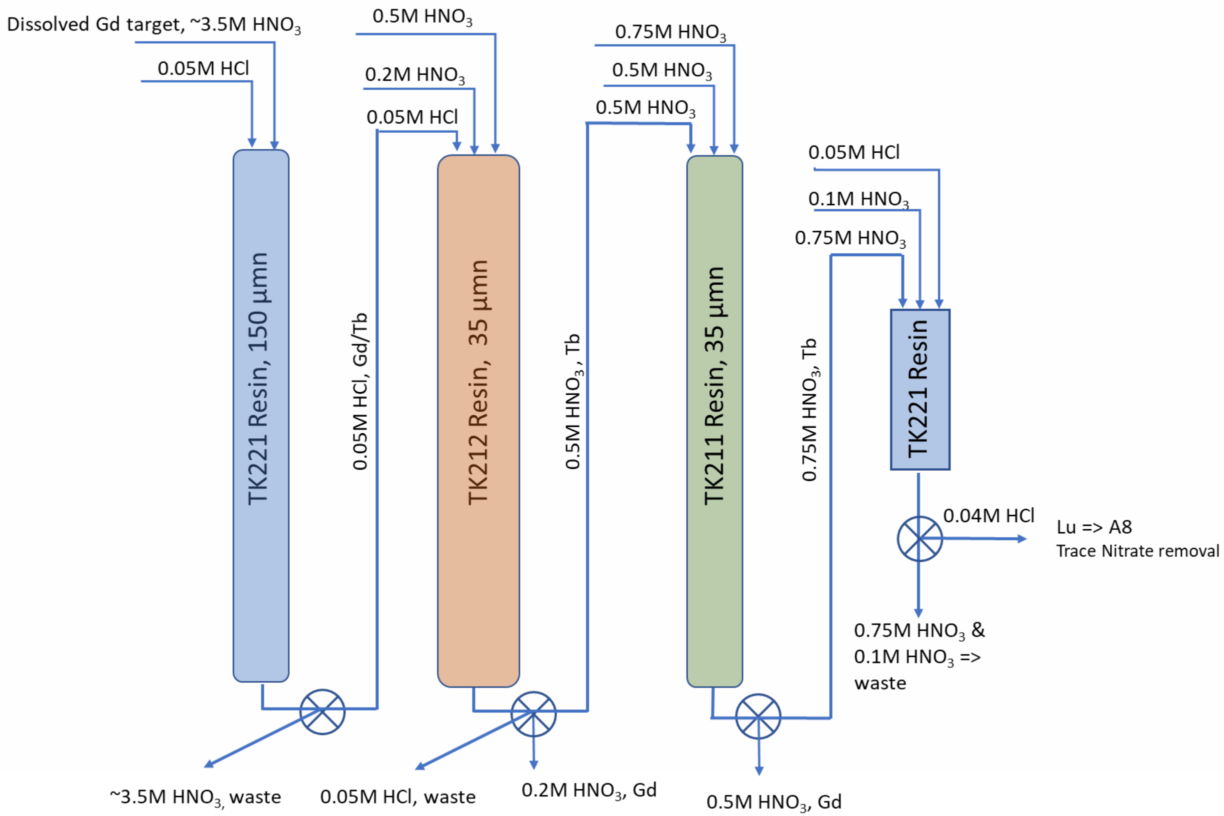


# Tb separation from 1000 mg Gd targets

TRISKEM
Expertise in Separation Chemistry

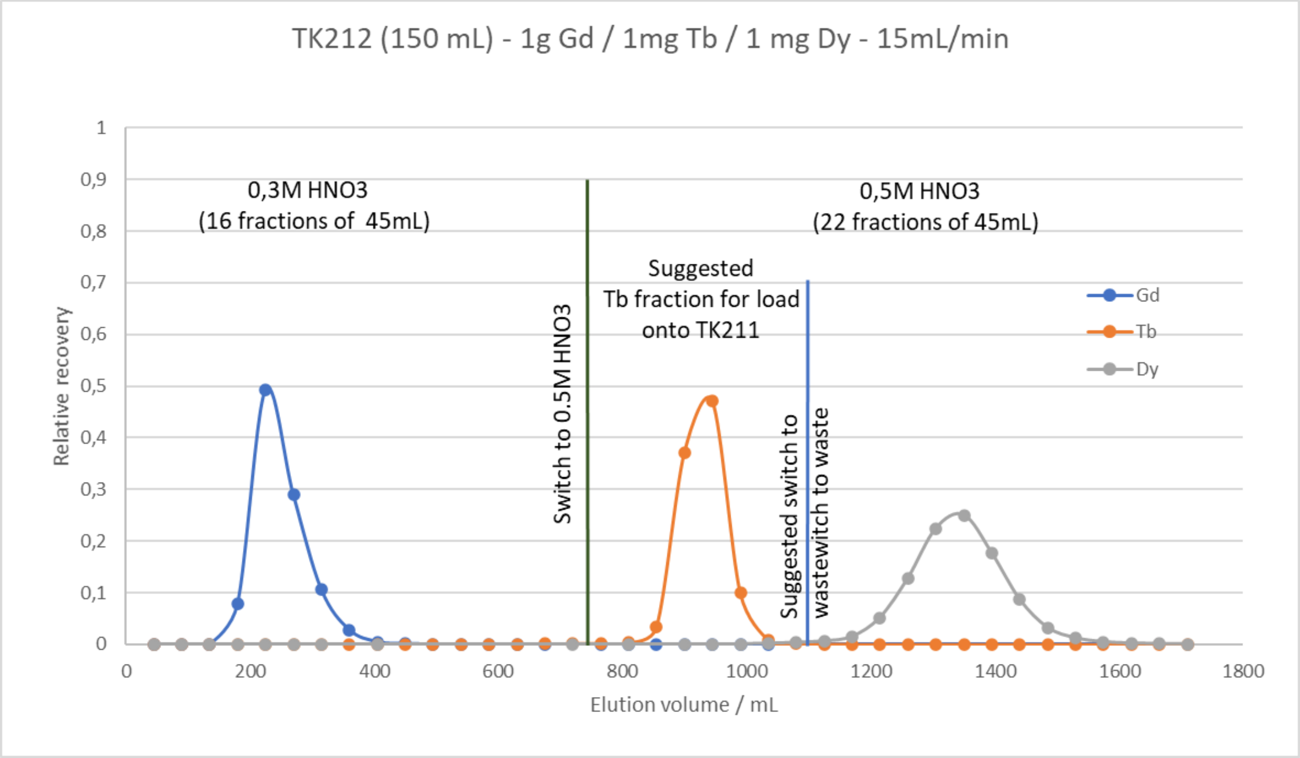
- Irradiated target typically oxide => dissolved in >3M $HNO_3$
  - For separation solution needs to be dilute acid
- Conversion via TK221 Resin (i.e. TO-DGA extractant)
- Sequential separation on TK212/TK211
- Final conversion to dilute HCl on TK221 + trace nitrate removal on AIX




# Tb separation from 1000 mg Gd targets

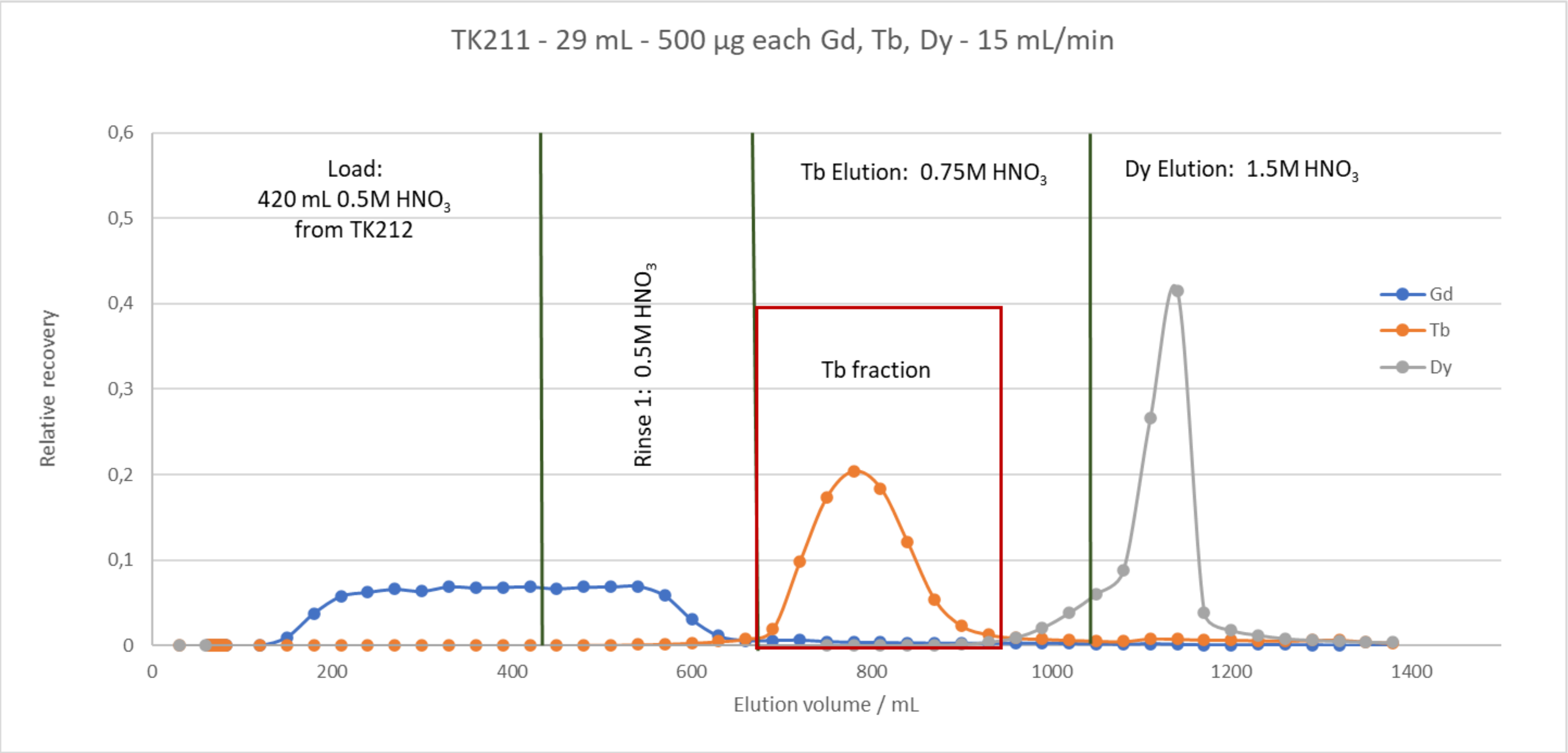
TRISKEM
Expertise in Separation Chemistry

- 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

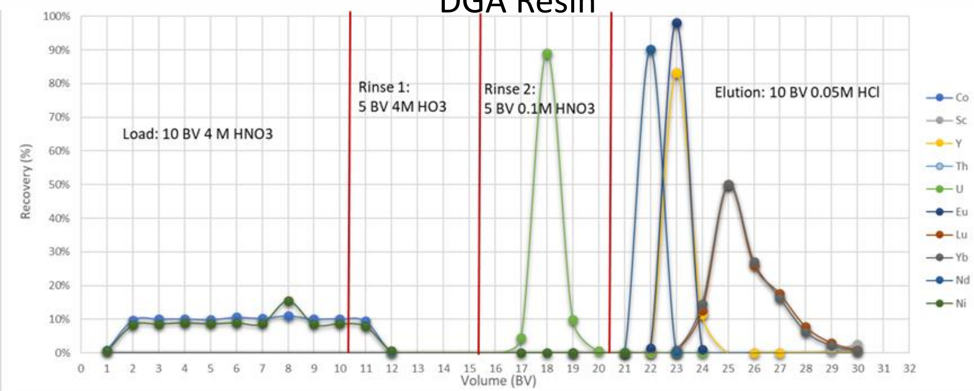



- Direct load of Tb fraction from TK212 onto TK211 (29 mL – 30cm x 1.1cm)
- Gd breakthrough during load & rinse with 0.5M $HNO_3$ (alternatively HCl)
- Tb elution (Dy sufficiently well removed before) preferably in **>3M $HNO_3$**
- Conversion to dilute HCl via TK221, A8 for nitrate removal

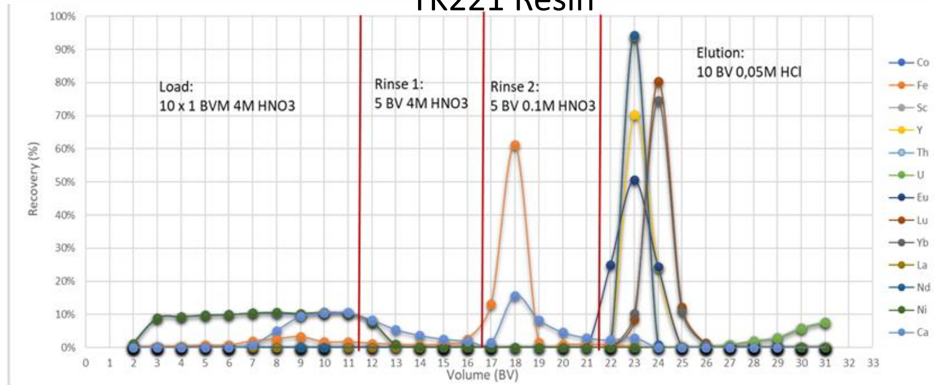
# TK221 Resin

- 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)**

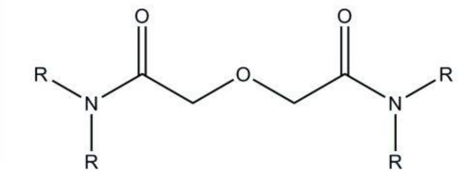
  **=> lanthanide removal / decontamination**

Ra-226 / Ac-225

separation on DGA Resins

# Ac-225 from Ra-226 targets

- 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 compared to DGA,N
  - Marsten, Radchenko (LANL)
    - Use of DGA (B/N) allows for Ac/LNs separation
    - Ac elutes in 10M $HNO_3$, LNs 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?



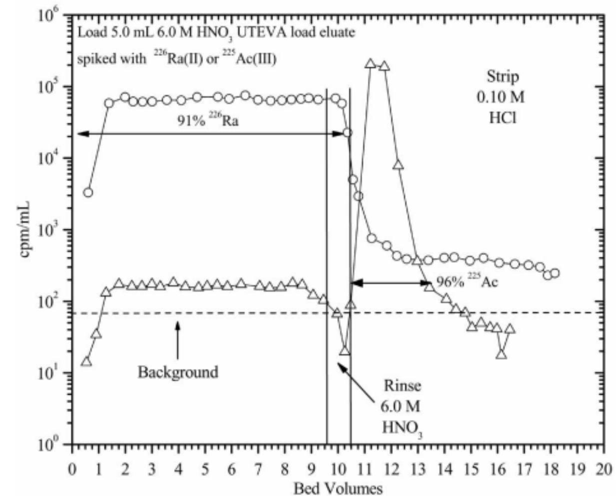




*Figure 13.* Separation of Ac(III) and Ra(II) on TODGA resin (50–100 µm) with 6.0 M $HNO_3$ and 0.1 M HCl, 0.5 mL bed volume, flow rate equals 2 mL/min load/rinse, 1 mL/min strip, 22(1)°C.

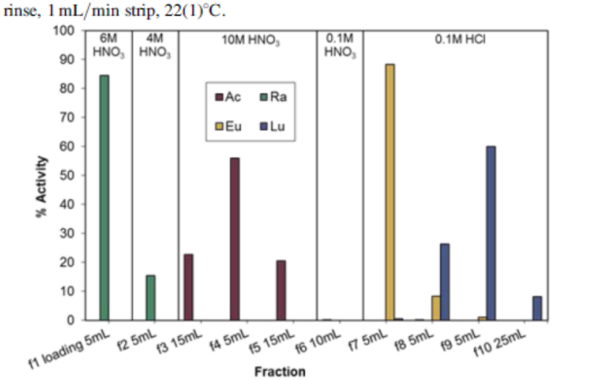
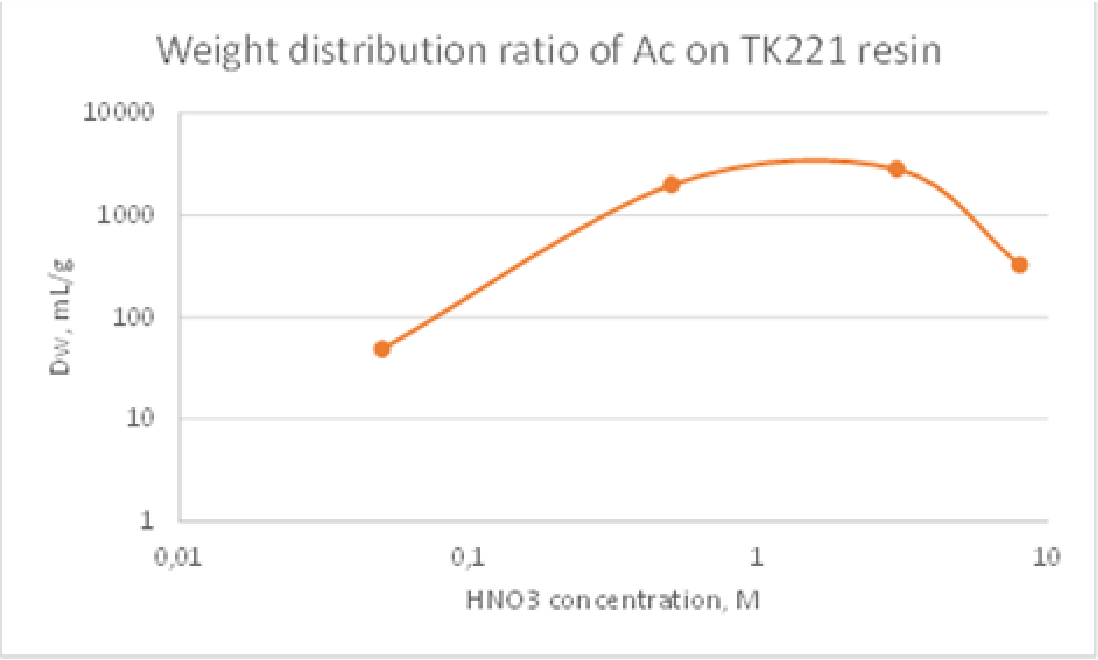



**Fig. 4.** Elution profile for $^{223/225}Ra$, $^{225}Ac$, $^{173}Lu$, and $^{155}Eu$ with TEHDGA resin in $HNO_3$ media and HCl for lanthanide elution.

# TK221 Resin – Ac separation

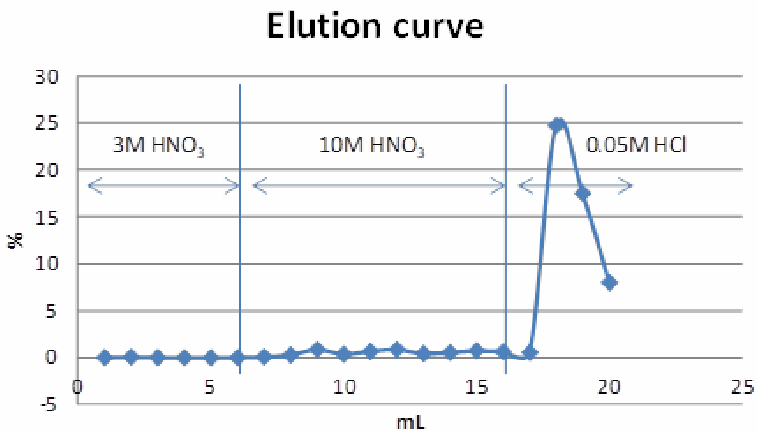



Data courtesy of N. Vajda (RadAnal)

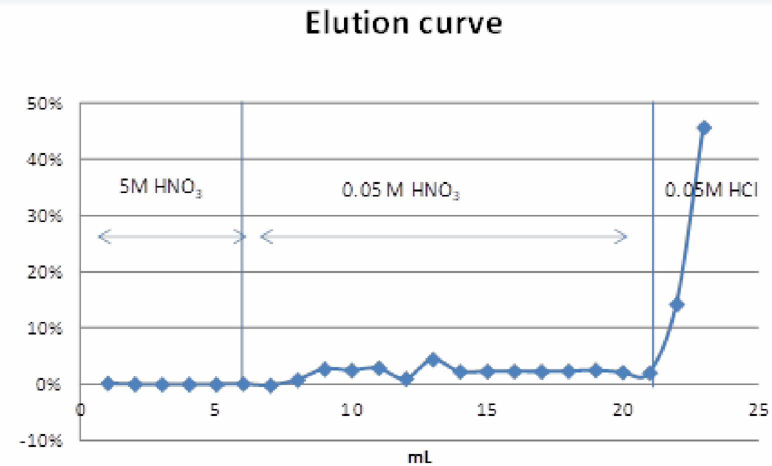
- On-going work
- High Ac retention from high to low $HNO_3$
- Elution in 0.1 – 0.05M $HNO_3$ not possible
- HCl on-going, in any case low Ac retention in dilute HCl

# TK221 Resin – Ac separation

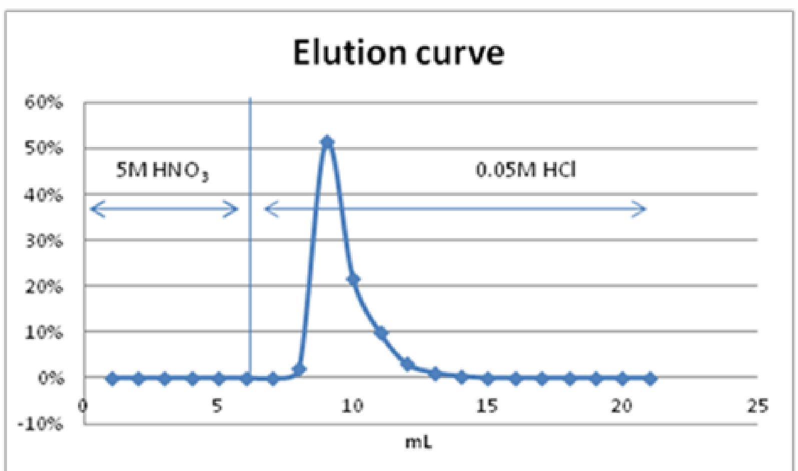
TRISKEM
Expertise in Separation Chemistry




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.



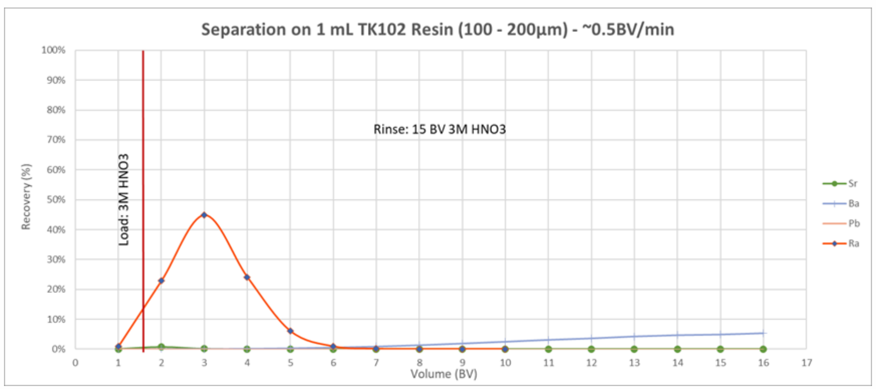

Elution of Ac from TK221 cartridge with 0.05M HCl, 1mL TK221 column, data courtesy of N. Vajda et al.

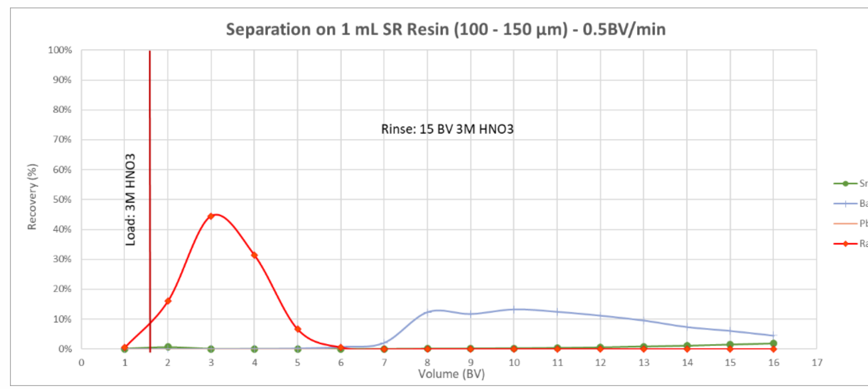
- Other than for DGA: no Ac/LNs separation in 10M $HNO_3$ possible
  => Ac remains retained.
- No Ac elution in 0.05M $HNO_3$
- Elution in 0.05M HCl possible
- $HNO_3$ => HCl conversion?
- Next steps: Dw in HCl
- TK222

# Ra purification / recycling

- Work on crown-ether based Ra Resin ongoing.
    - Aim: Ra retention from acidic/high $NO_3^-$ matrices
- Ra initial purification and recycling after irradiation
    - – Exact methods depending on impurities present

  => Ideal case: only remove impurities, leave Ra in solution
    - TK221 (or DGA) => other alpha emitters et al.
    - TK102 for Ba removal




=> In case Ra needs to be purified on-column use of TK101 for Ra retention / purification

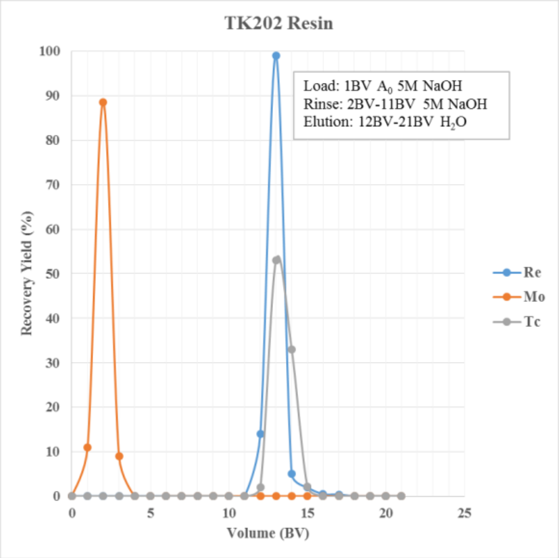
- Load and rinse from 0.01M – 0.05M $HNO_3$ or HCl => matrix removal (incl. Pt, Pd, Ir,…)
- Ra elution with 3M $HNO_3$ => Pb and most Ba remain retained

# Mo-99 / Tc-99m

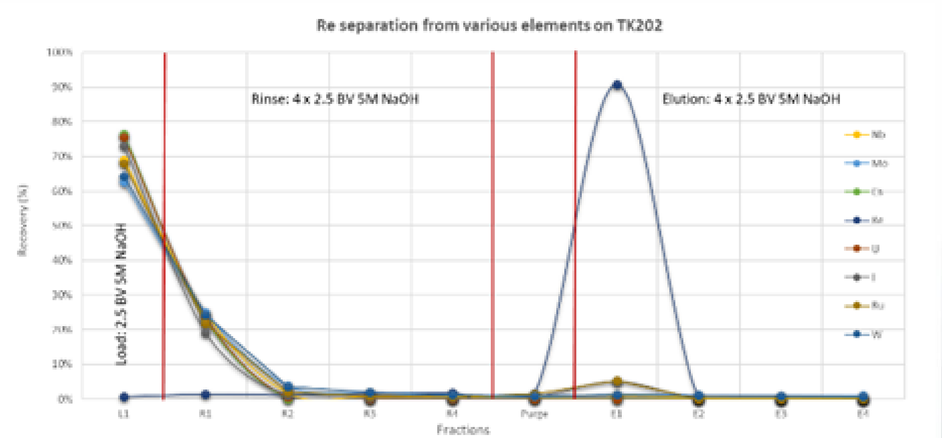
# separation on TK202 Resin

# 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 (Nb,Mo,Cs,Re,U,I,Ru,W)
- Re used as homologue
- Elution in small volume of water
  - Eluate still alkaline and containing Na
  - Pass through CEX for ‘neutralisation’ and $Na^+$ removal and through
  - aluminium oxide for trace Mo removal and recovery as 0.9% NaCl solution



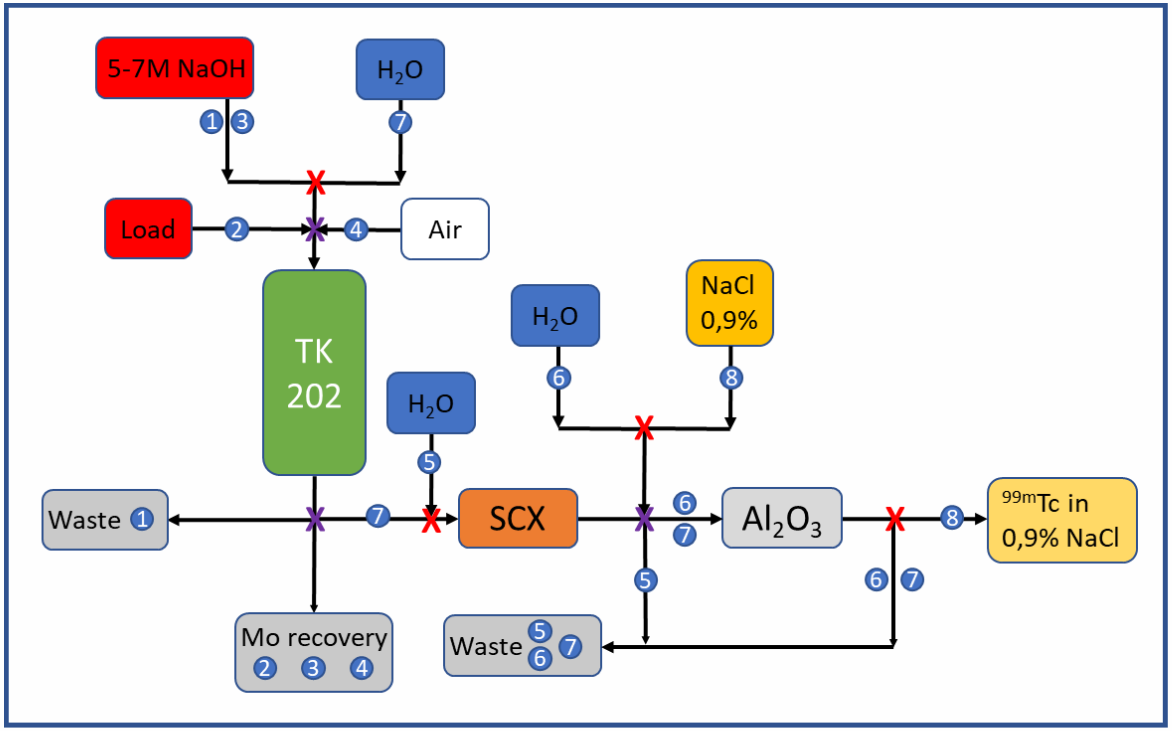

Re/Tc separation from Mo on TK202 Resin




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.)

TRISKEM
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

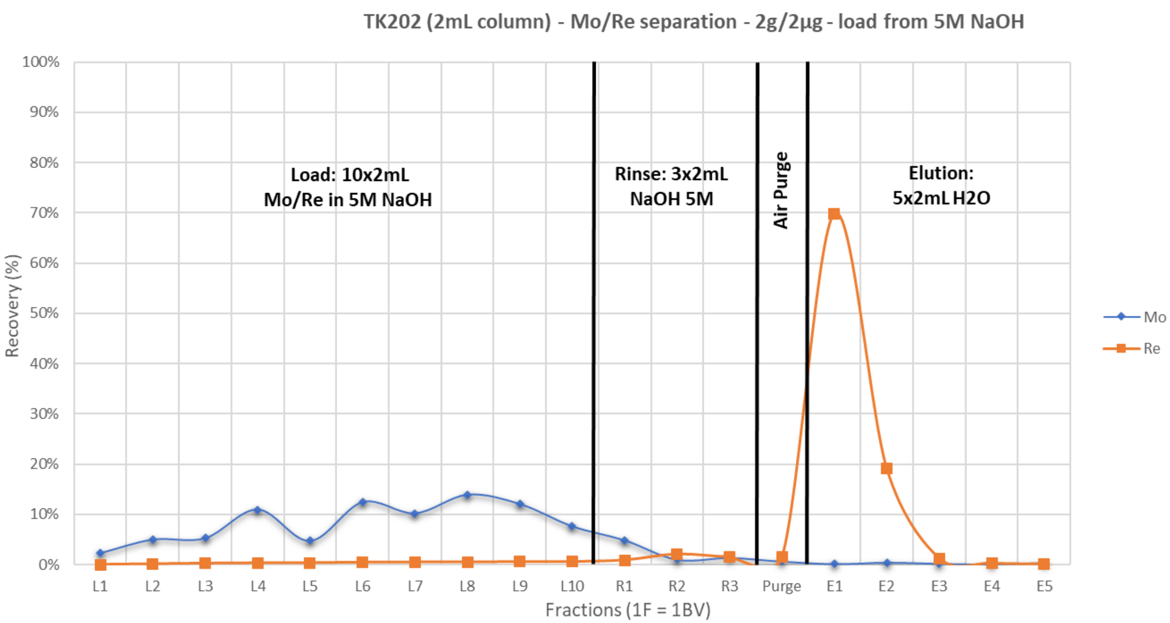
**TK202 : 35-75 or 75-150µm**
**X : 3-ways valve** (red)
**X : 4-ways valve** (purple)
**SCX : Strong Cation Exchange**
**$Al_2O_3$ : Acidic Alumina**

**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

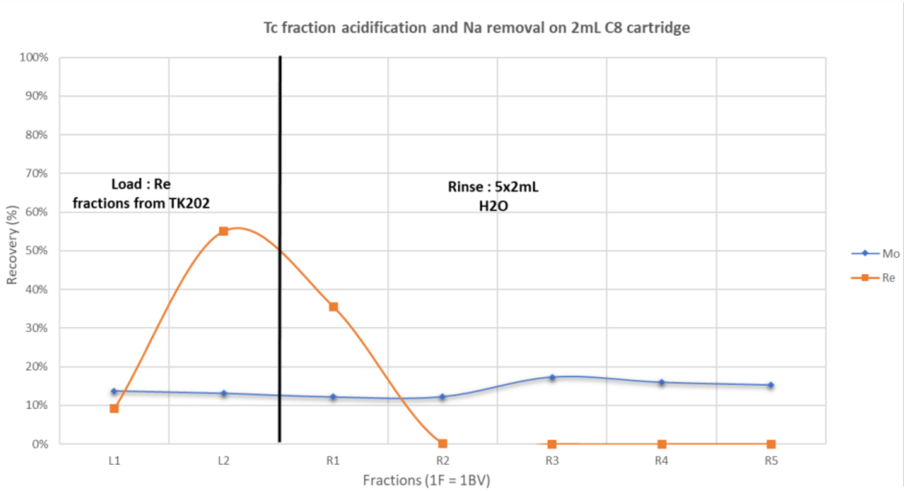


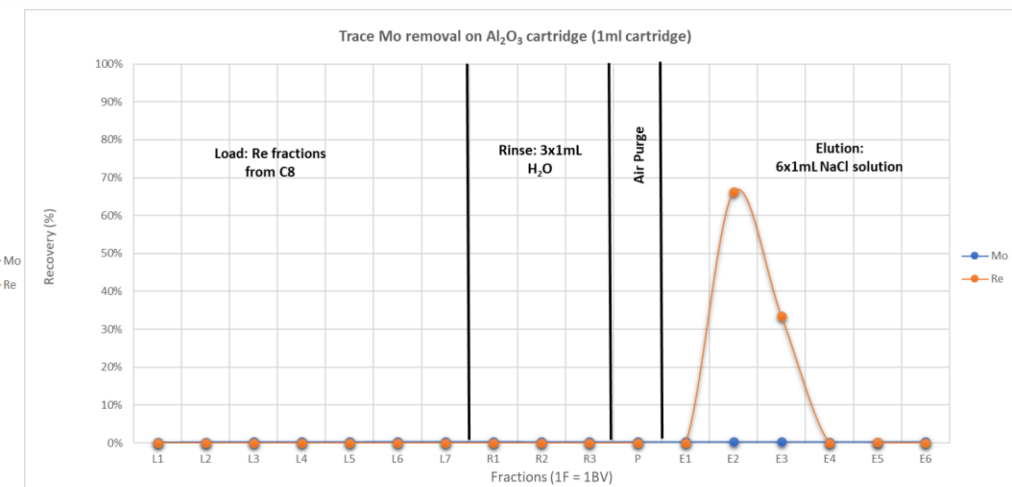

Tests performed cold with 2g Mo and 2 µg Re

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

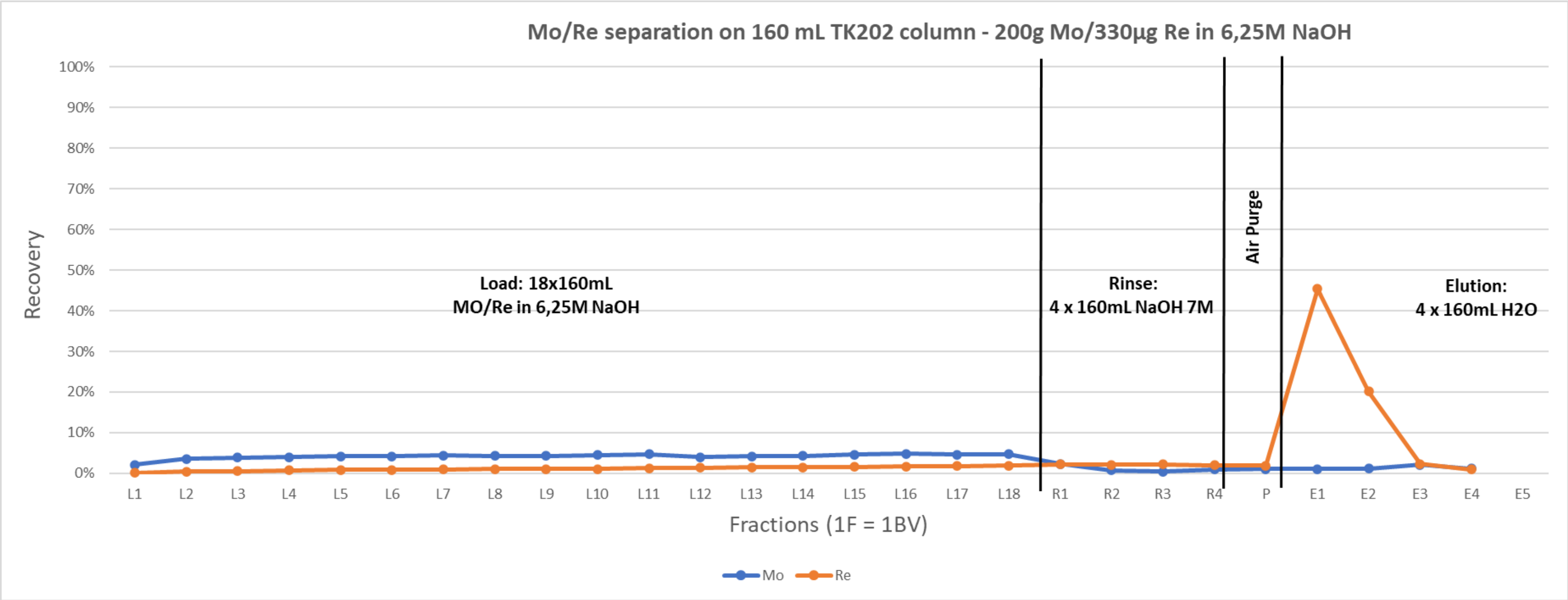
Method similar to Zeisler et al.

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

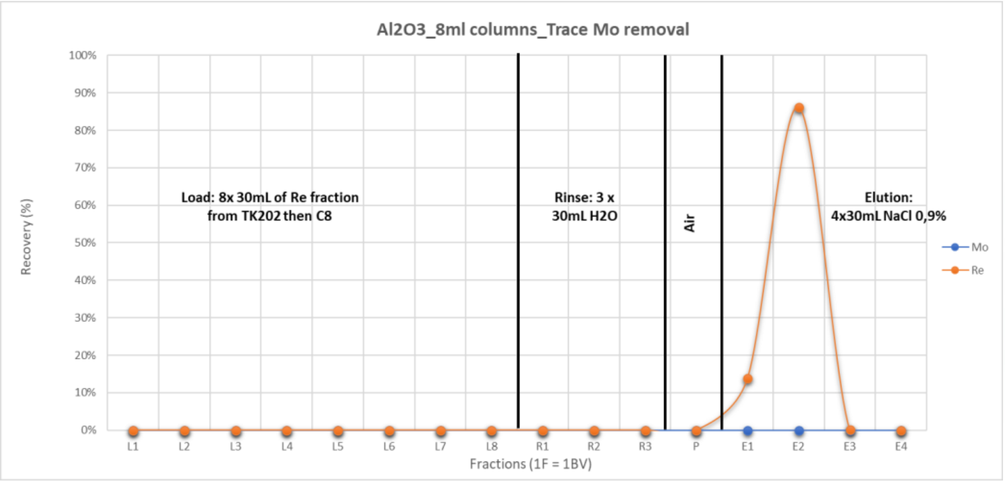


# On-going :Tc-99m from large Mo targets




- 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

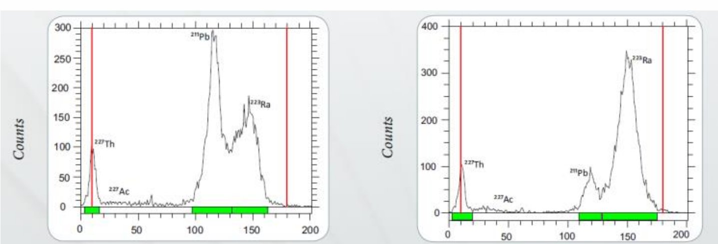


# DGA Sheets

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

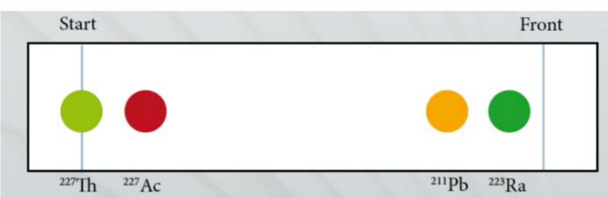
(p.ex. Ra-223, Ac-225/Bi-213, Pb-212, Ge-68/Ga-68 …)

  - 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,…

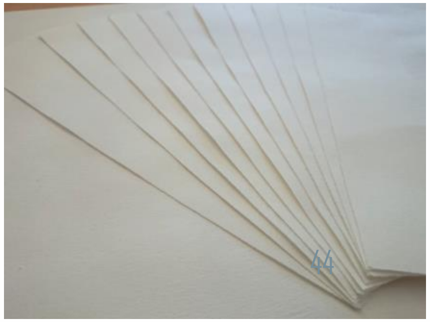



Radiochromatogram measured immediately after separaton. Low abundant radiatons of $^{227}$Ac were not detected.

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



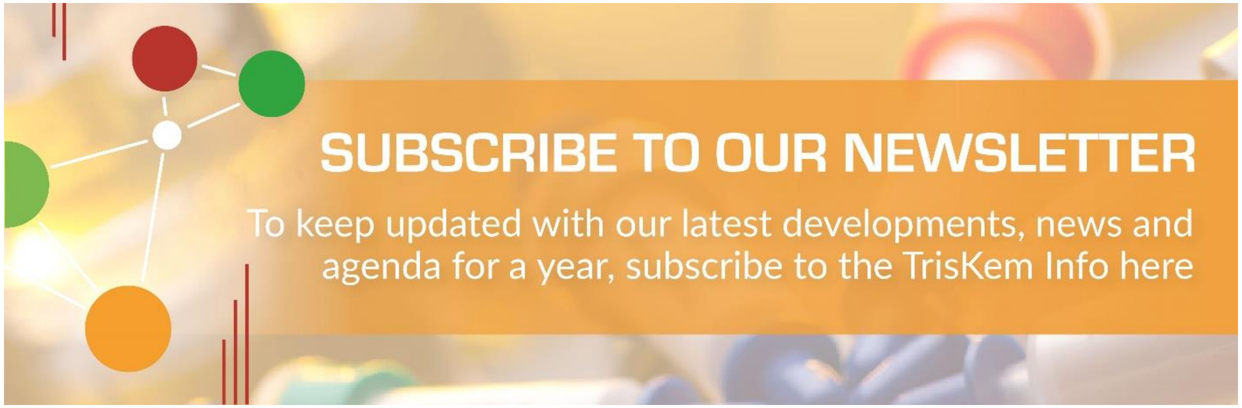

A scheme of chromatographic separaton of mixture of $^{227}$Ac and his daugther´s niclides. $^{227}$Th remains on start, $^{227}$Ac has the retenton factor ca 0.2, $^{211}$Pb ca 0.7 and $^{223}$Ra ca 0.9.



# Some other on-going projects

- Ac separation and ‘resalting’
  - TK222, TK200
- Radium
  - New resins and macrocycles
- Auger emitters
  - Pd, Hg,…
- SE Resin
- Scandium separation
  - TK200, TK221, TK222
- ‘Fate’ of RN in the environment
  - Separation methods
  - Mainly longer lived (=> therapy)
  - Quantification
- Method development for other new, and old, radiometals
  - V, Mn, In,…
- At separation
  - TK400, Rn-211/At-211 generator,…
- Decontamination
  - Effluents and reaction wastes
- Improvement of radiolysis stability
- “Non-resin” separations
  - Microfluidics
  - Rapid tests
  - New Sheets


# Thank you for your attention!




TRISKEM
Expertise in Separation Chemistry