

# Improving the chemical purity and specific activity of the $^{203}\text{Pb}/^{212}\text{Pb}$ theranostic pair

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## Background: Why $^{203}\text{Pb}$ and $^{212}\text{Pb}$ ?

- Targeted radionuclide therapy (TRT) couples a radionuclide to a chelator linked to a cancer-seeking targeting vector to deliver a radioactive payload directly to cancer cells
- Depending on the type of decay the radionuclide undergoes, it is compatible with imaging or therapy
- $^{203}\text{Pb}$  ( $t_{1/2} = 51.9$  h), a gamma-emitting diagnostic isotope, and  $^{212}\text{Pb}$  ( $t_{1/2} = 10.6$  h), an alpha-emitting therapeutic isotope, form a chemically matched theranostic pair (Fig. 1)
- $^{203}\text{Pb}$  is a cyclotron produced isotope from the proton irradiation of Tl targets (Fig. 2) while  $^{212}\text{Pb}$  is produced from a  $^{228}\text{Th}/^{212}\text{Pb}$  generator<sup>2</sup> (Fig. 3)

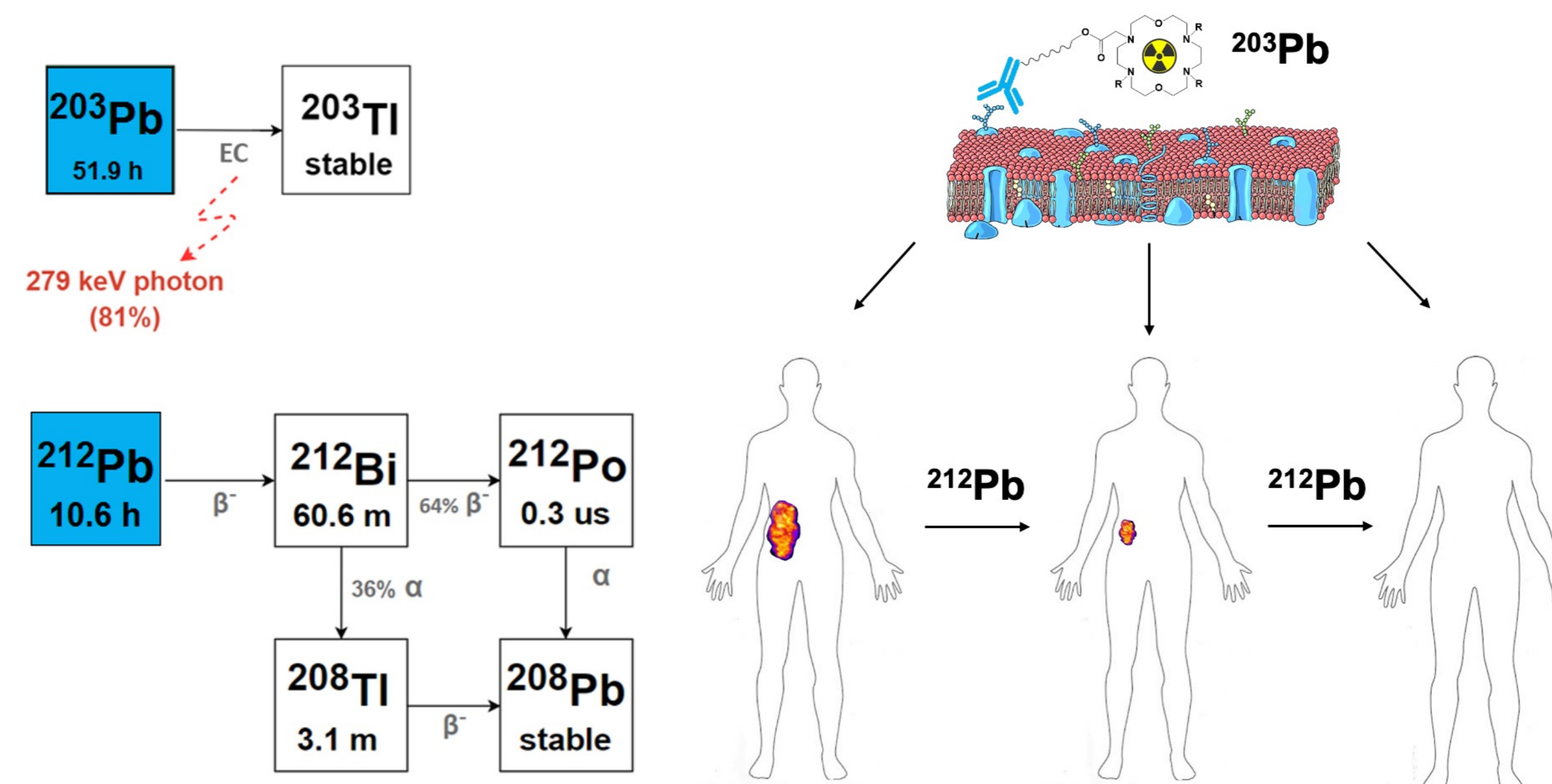


Figure 1. Decay scheme and use of the  $^{203}\text{Pb}/^{212}\text{Pb}$  theranostic pair for targeted radionuclide therapy with a bifunctional chelator labeled radiopharmaceutical.

## Challenges with Production

- High concentration of Tl and Th in elutes ( $58.2 \pm 34.5$  ppm and  $24.4 \pm 16.2$  ppm, respectively)
- $^{203}\text{Pb}$  has a stable Pb concentration of  $495 \pm 218$  ppb
- Tl target melts at currents  $> 8 \mu\text{A}$  limiting activity produced at EOB
- Large elute volume (3 mL)
- $^{212}\text{Pb}$  eluted in pH 7 buffer

## Improvement in Targetry and Dissolution

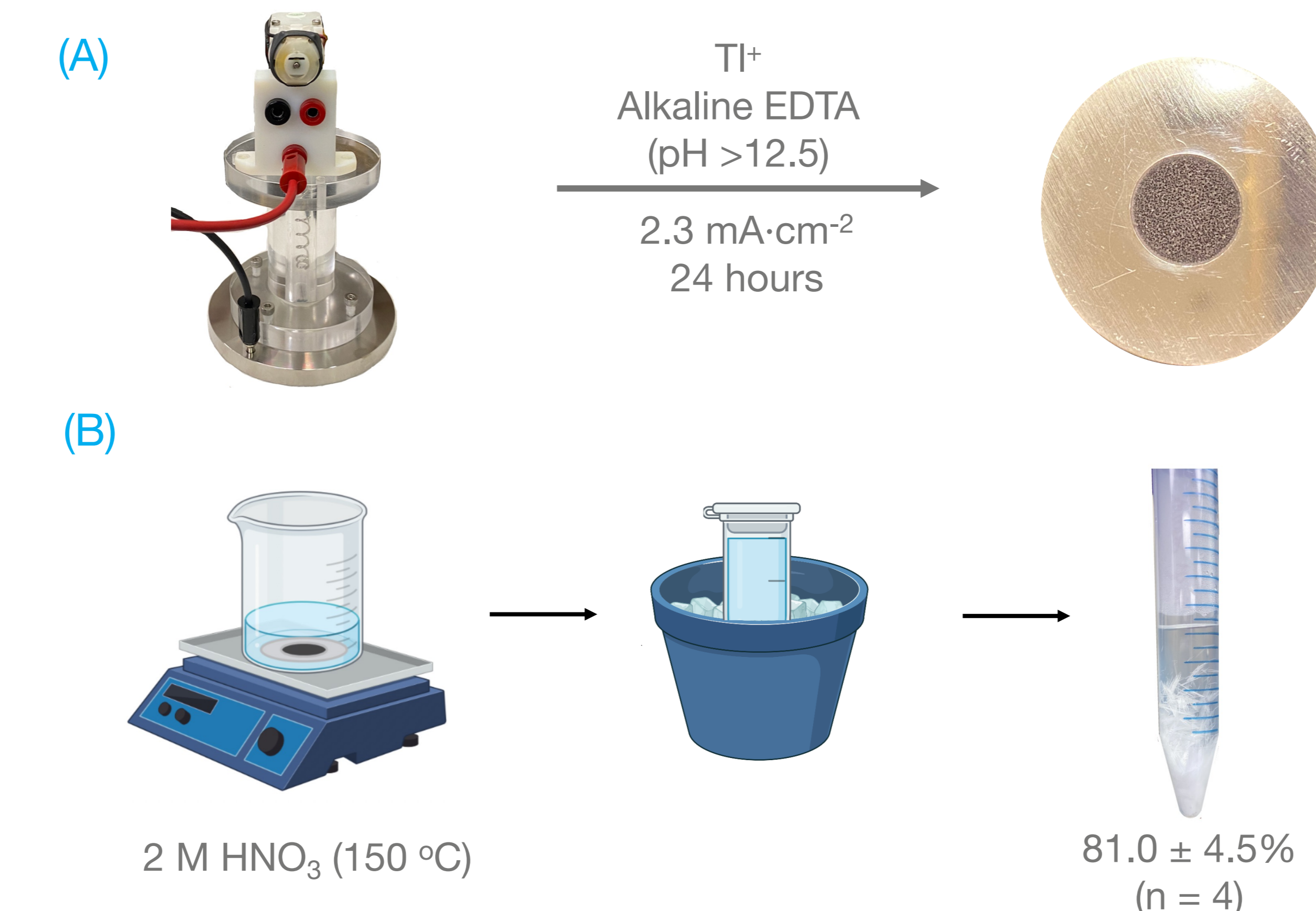


Figure 4. (A) Electroplating method for deposition of thallium onto silver. (B) Selective thallium precipitation dissolution method.

## Separation of $^{203}\text{Pb}$ from Tl

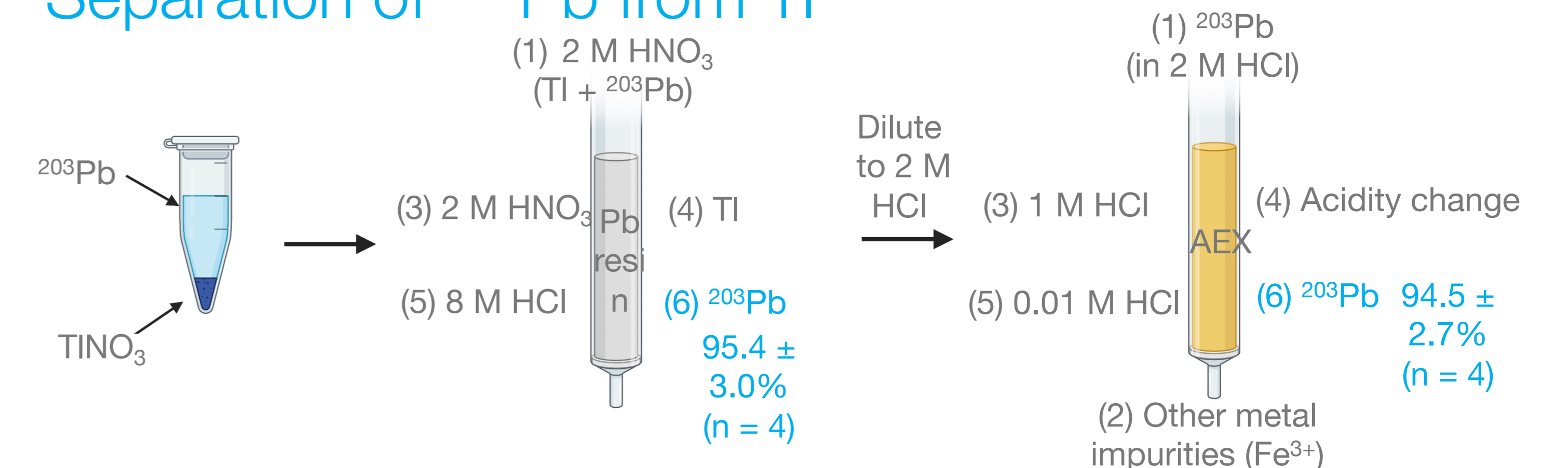


Figure 5. Separation scheme for the purification of  $^{203}\text{Pb}$  from silver-backed thallium targets.

Metal	Concentration with Old Method (ppb) (n = 3)	Concentration with New Method (ppb) (n = 3)
Al	168 ± 152	100 ± 51
Ag	N.S.	1.4 ± 0.3 (In 8 M HCl strip 3353 ± 287)
Ca	568 ± 263	N.S.
Tl	58,220 ± 35,392	26 ± 3 (In 8 M HCl strip 2236 ± 483)
Pb	495 ± 218	34 ± 6

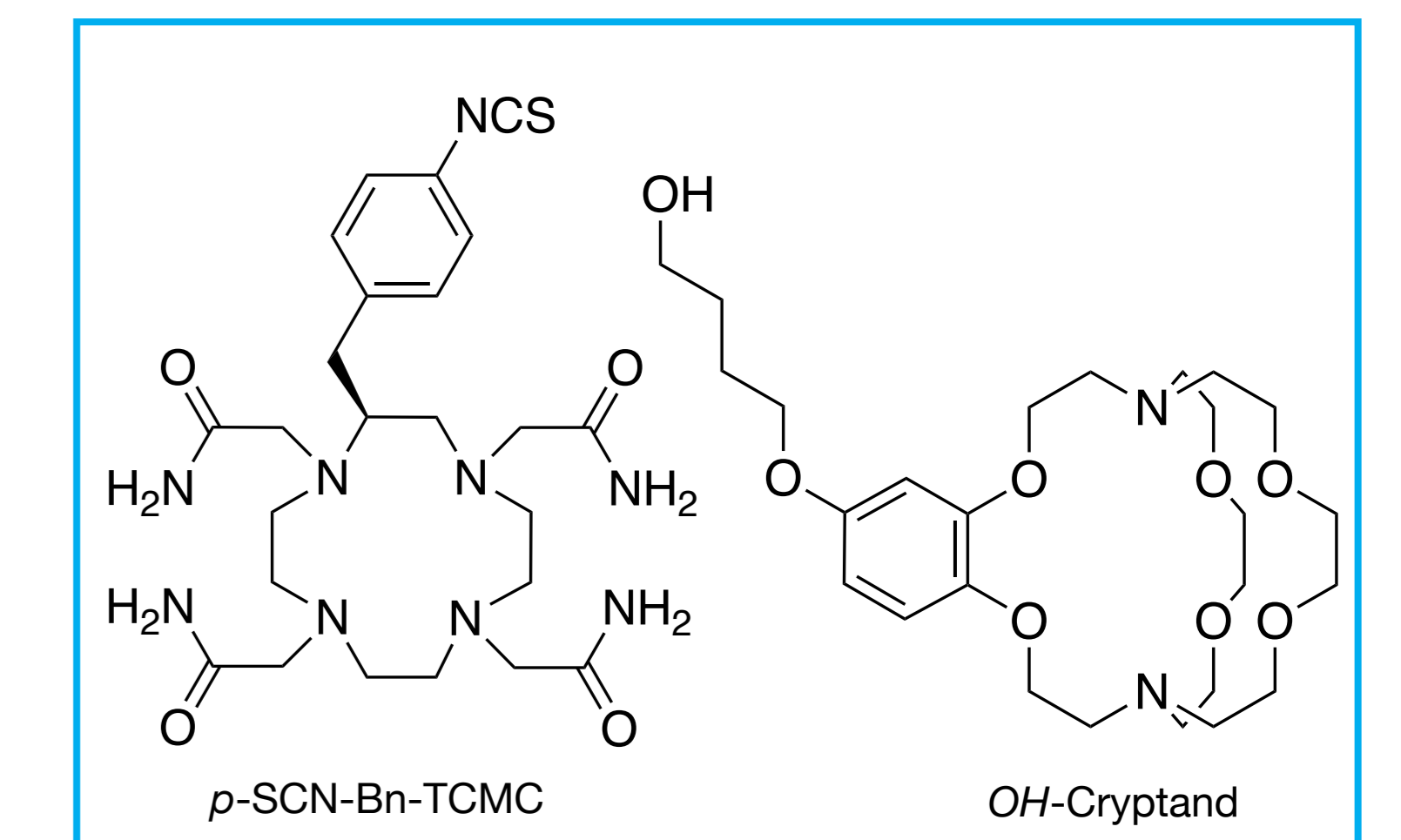
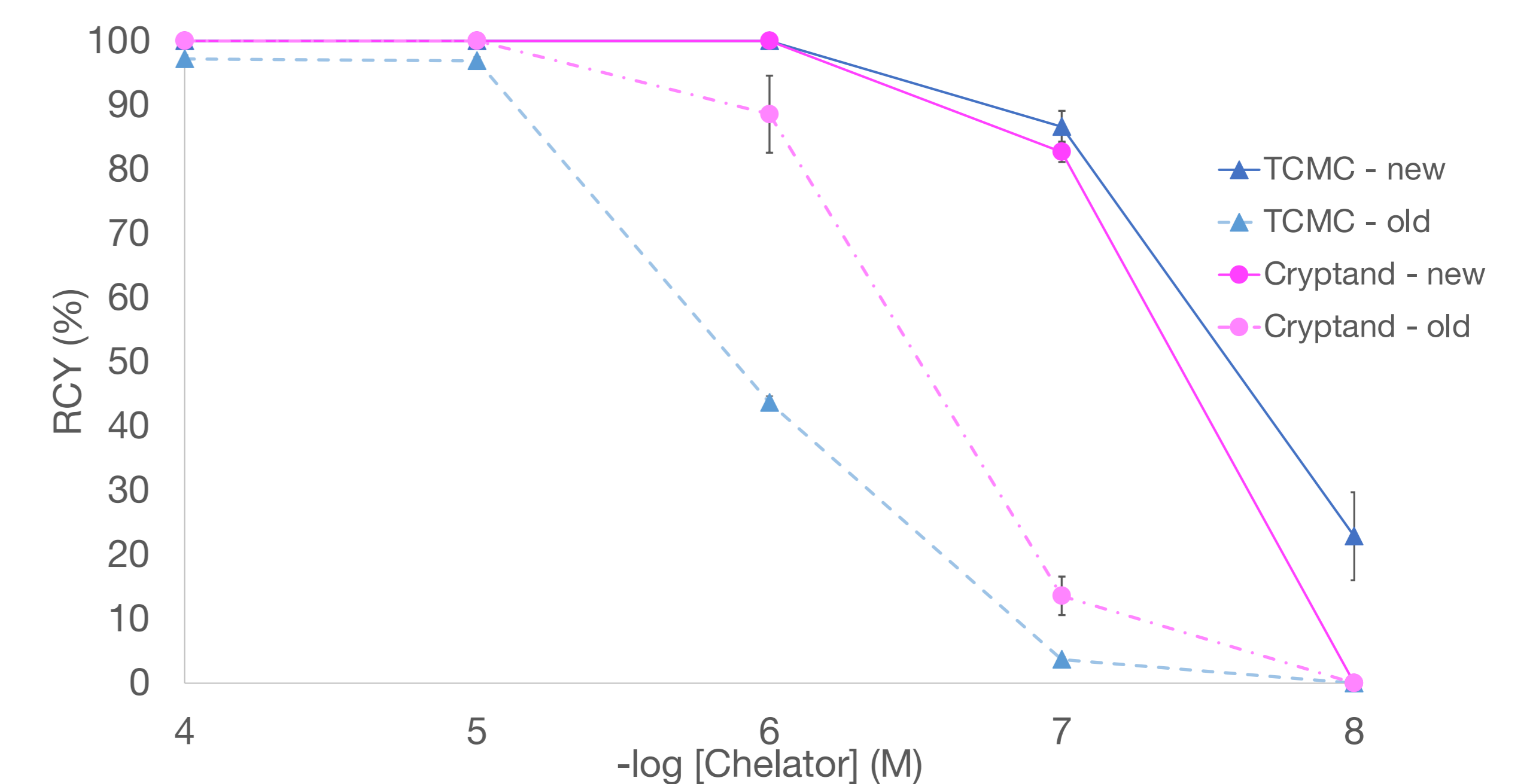


Figure 6. Pb-targeted chelators utilized for  $^{203}/^{212}\text{Pb}$  radiopharmaceuticals.

Table 1. Comparison of ICP-MS results of new and previous method<sup>2</sup>.

## $^{203}\text{Pb}$ Radiolabeling



## Conclusion

- A separation technique that utilizes selective thallium precipitation, extraction, and anion exchange chromatography produced a  $^{203}\text{Pb}$  product with 6,718 times less thallium and 44 times less stable Pb was developed, which improved chelator radiolabeling yields

## Future Work

- It will be investigated if this method is compatible with a  $^{228}\text{Th}/^{212}\text{Pb}$  generator to reduce the concentration of  $^{232}\text{Th}$  in the  $^{212}\text{Pb}$  elute fraction

## Literature Production of $^{203}\text{Pb}$

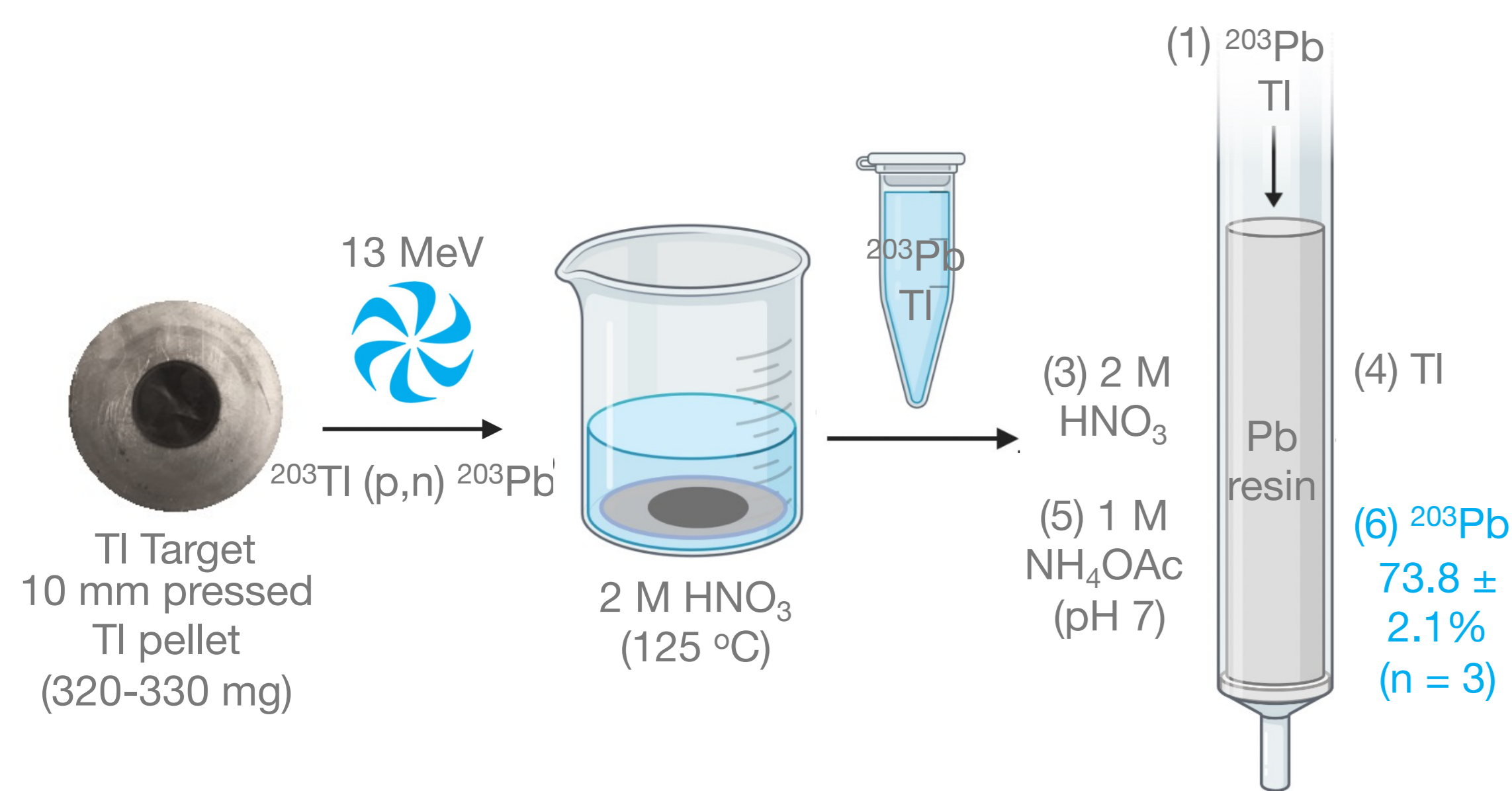


Figure 2. Literature production of  $^{203}\text{Pb}$  at TRIUMF.

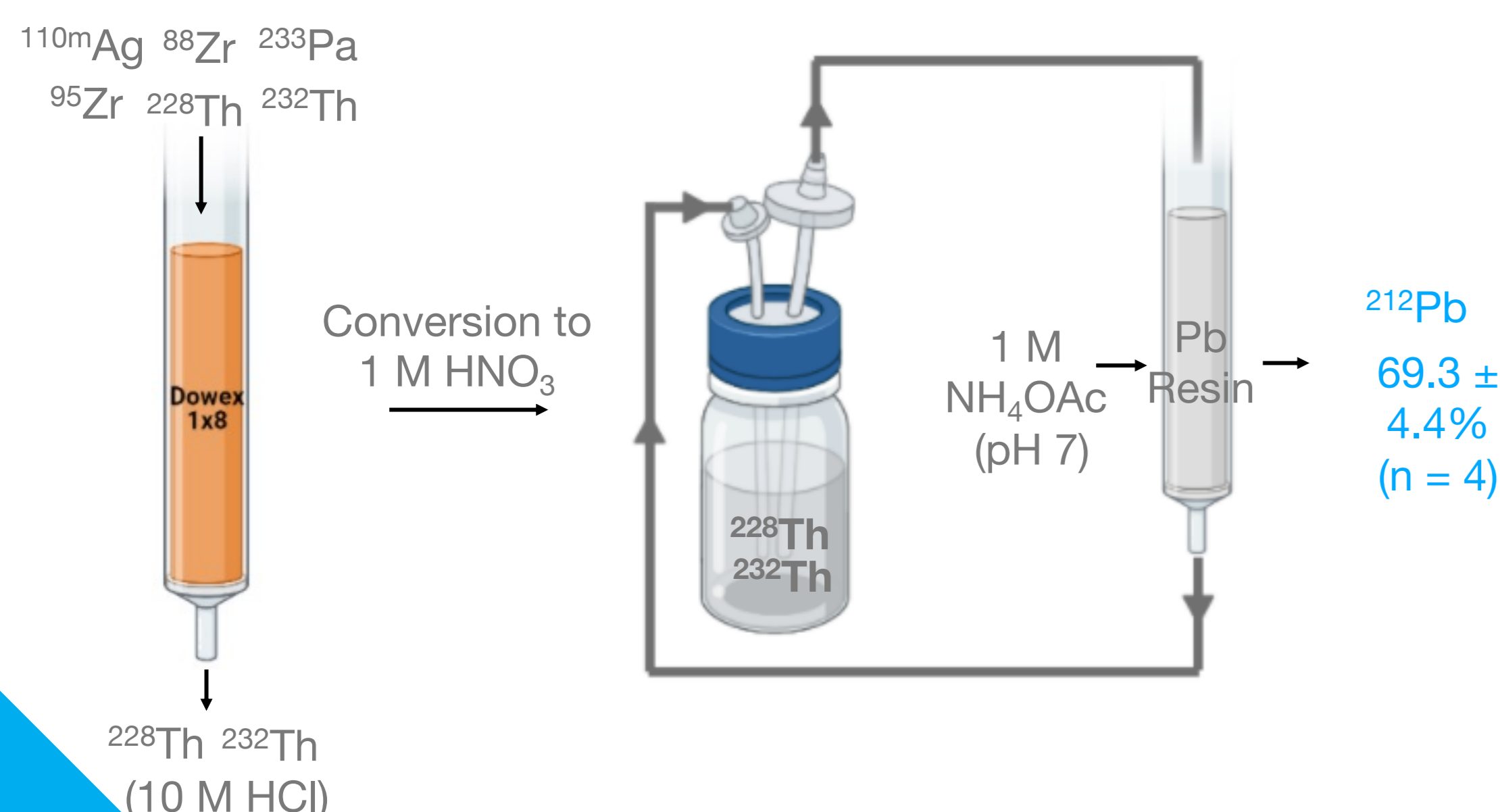


Figure 3. Literature production of  $^{212}\text{Pb}$  at TRIUMF.