Production of radionuclides for PRISMAP at the Hevesy Laboratory

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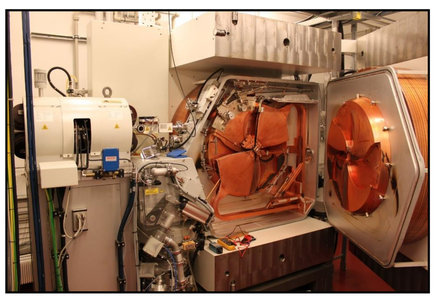
Hevesy Laboratory and Radiometals

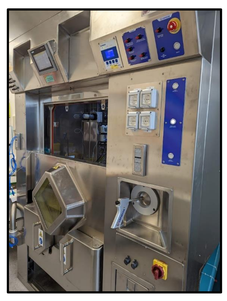
At the Hevesy laboratory, we have a strong focus on the production of non-conventional radiometals. They offer a variety of alternatives to the more mainstream radionuclides available for medical applications in term of half-life and decay properties. Some of our radionuclides such as Cu-64 and Mn-52 are mainly used for imaging. We also produce a series of β-emitters including Ag-111, Au-199, and Cu-67, and have recently developed production procedures for the Auger electron emitters La-135, Er-165 and Pd-103. These radionuclides were available for PRISMAP users, over the course of the project, and 22 batches were produced and shipped.

Target Irradiation and Handling

The targets are irradiated on one of our "medical" cyclotrons, or for neutron induced reactions at ILL. After irradiation, they are transferred to a hot cell, opened and dissolved, usually by highly acidic solutions. To speed up the dissolution process, heating or current can be applied.



GE PETtrace cyclotron 16.5 MeV protons

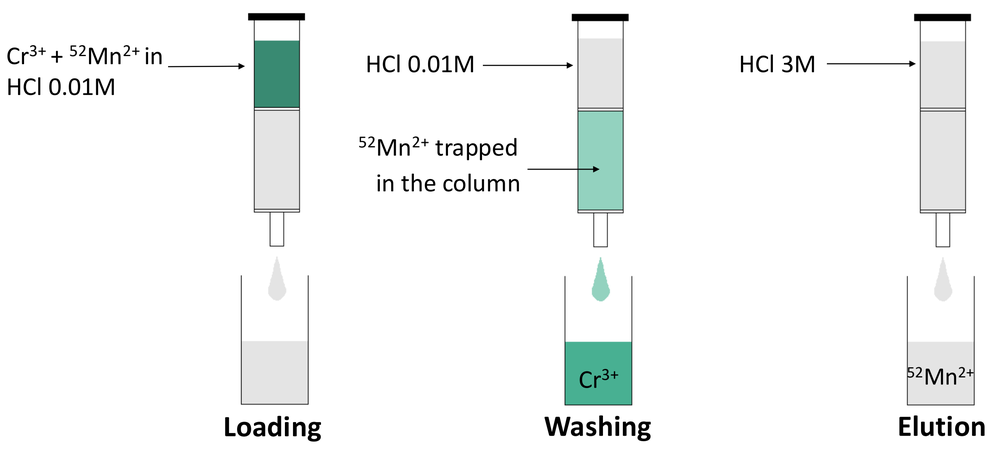


A hot cell

Target dissolution cell

Purification

The target solution contains a high amount of target material and very small amounts of radioactive material. The challenge is to separate the radionuclide from the target material as well as from all the other possible contaminants. This is done by chromatography on different commercial resins.

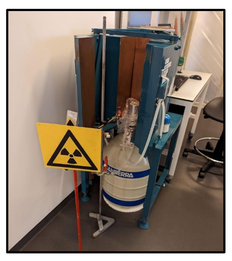


Example of purification method: the first column for ^{52}Mn purification

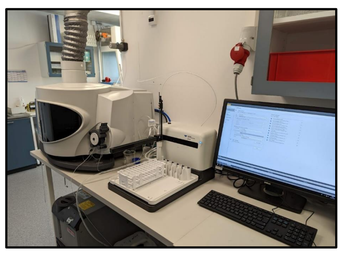
All the utensils coming into contact with the radiometal solution are metal-free and acid washed to avoid introducing impurities from the laboratory environment. When needed, evaporation is done under an argon stream, in nearly closed vials.

Quality Control Analyses

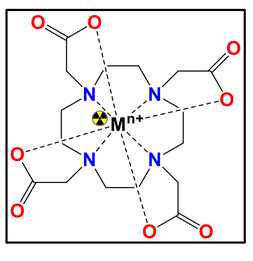
The radionuclidic purity of the processed radionuclide is measured using HPGe gamma or x-ray detectors. The chemical purity is assessed by ICP-OES analyses. The metal contents are quantified to determine the "apparent and true molar activities". The radionuclidic and radiochemical purity is important for applications in medicine. Radioactive contaminants have an influence on the dose that the patient receives especially in the case of long half-life radionuclides that are not quickly eliminated from the body. The chemical purity is very important if the radionuclide is to be used for radiolabelling.



The Ge-detector



The ICP-OES spectrometer



A radiometal-DOTA complex

Radiolabelling

The purified radiometal is usually provided in dilute HCl solutions and can be used directly for chelation. A buffer solution is chosen to adjust the pH of the radiolabelling reaction. Ligand titration and TLC analysis give access to the "effective molar activity" of the radiometal solution for that specific ligand. Once a suitable chelator has been found for a radionuclide, the stability of the complex can be studied over time in different conditions including exposure to biological material (serum). If the complex is stable enough, it is ready to be applied for preclinical experiments.

Target Material Recovery

The target material can be expensive, especially if it consists in an enriched isotope. In addition to cost saving, targets made of recycled material often have a lower content of the corresponding stable isotope, potentially leading to a better molar activity at EOP.

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Summary Table of our Radionuclides for PRISMAP

Radionuclide	Production route	Target (all solid)	Purification method	Max. activity at shipment time	Radionuclidic purity	Chemical purity (typical), ICP-OES full batch, activity recovery at EOP (d.c.)
Ag-111* (7.421 d) β^-: 100%	$^{110}Pd(n,\gamma)^{111}Pd$ $^{111}Pd(\beta-)^{111}Ag$	^{110}Pd capsule	Dowex 1x8 resin[1]	1-2 GBq	>99%	ICP-OES data not available Recovery: 60-80%
Au-199* (3.135 d) β^-: 100	$^{nat}Au(n,\gamma)^{199}Au$	^{197}Au capsule	Target dissolution only	2-3 GBq	80-90% 10-20% ^{198}Au	not analysed, but 1 GBq/µmol expected
Cu-64 (12.7 h) ε, β^+: 61% β^-: 39%	$^{64}Ni(p,n)^{64}Cu$	Electroplated ^{64}Ni Recycling >95%	Dowex 1x8 resin[2]	1-15 GBq	>99.9%	< 1 µg Ni/batch, <0.02 µmol Cu Recovery >80%
Cu-67 (61.81 h) β^-: 100%	$^{70}Zn(p,\alpha)^{67}Cu$	Electroplated ^{70}Zn Recycling >95%	Col. 1, Cu-resin Col. 2, TK200 resin[3]	200 MBq	>99%	76 nmol Al, 6.1 nmol Cu, 2.4 nmol Fe, 2.1 nmol Zn. Recovery: 93.0 ± 2.9 %
Er-165 (10.36 h) ε: 100%	$^{nat}Ho(p,n)^{165}Er$	Pressed Ho_2O_3/Al 1:1 (w/w)	Col. 1, LN2 resin Col. 2, LN2 resin Col. 3, TK221 resin	500 MBq	>99%	10-20 nmol Ho, 2 nmol Er, 2 nmol Fe, 20 nmol Pb. Recovery: 77.9 ± 21.2 %
La-135 (18.91 h) ε, β^+: 100%	$^{135}Ba(p,n)^{135}La$	Pressed $[^{135}Ba]BaCO_3$/Al 1:2 (w/w), Recycling >65%	Col. 1, DGA+TK200 resins[4]	1.5 GBq	>99%	25 nmol Al, 5 nmol Ba, 1-2 nmol Fe, Zn. Recovery 97.1 ± 3.6%
Mn-52 (5.591 d) ε, β^+: 100%	$^{nat}Cr(p,n)^{52}Mn$	Electroplated ^{nat}Cr	Col. 1 Actinide resin Col. 2, Actinide +TK200 resin Col.3, Actinide +TK200 resin	400 MBq	>99%	23 nmol Cr, 120 nmol Al, 15 nmol Pb. Recovery: 83% after col. 2 80% after col. 3
Pd-103* (c.a) (17 d) ε: 100%	$^{102}Pd(n,\gamma)^{103}Pd$	^{102}Pd capsule	Target dissolution only[5]	2-3 GBq	>99.9%	Not measured
Pd-103 (n.c.a) (17 d) ε: 100%	$^{nat}Rh(p,n)^{103}Pd$	Electroplated ^{103}Rh Recycling (data in progress)	Col. 1, DGA resin Col. 2, DGA resin	200 MBq	>99.9%	0.7 nmol Pd, 0.5 nmol Rh, 3.0 nmol Zn, 2.5 nmol Fe, 8.2 nmol Al. Recovery: 87 ± 6%

* Irradiation done in Grenoble (FR) at the Institut Max von Laue Paul Langevin (ILL) and irradiated target shipped to Hevesy Laboratory for processing.

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