Reducing Metal Contamination in Cu-64 Production

PONIGER S.S.[1,2¶], TOCHON-DANGUY H.J.[1], SACHINIDIS J.[1], ALT K.[3], HAGEMEYER C.[3], SCOTT A.M.[1,2]

Centre for PET
Austin Health

Background

Following the recent implementation of our solid target production facility, routine production of ^{64}Cu (T½=12.7 hours) was achieved with an average production yield of 11.8 MBq(0.32 mCi)/µAh. However purification of ^{64}Cu has proven to be problematic, with several metallic contaminants compromising subsequent radiolabeling. We report in this work, the step by step procedure which led us to the successful production of low metal contaminant ^{64}Cu with high specific activity and high labelling efficiency.

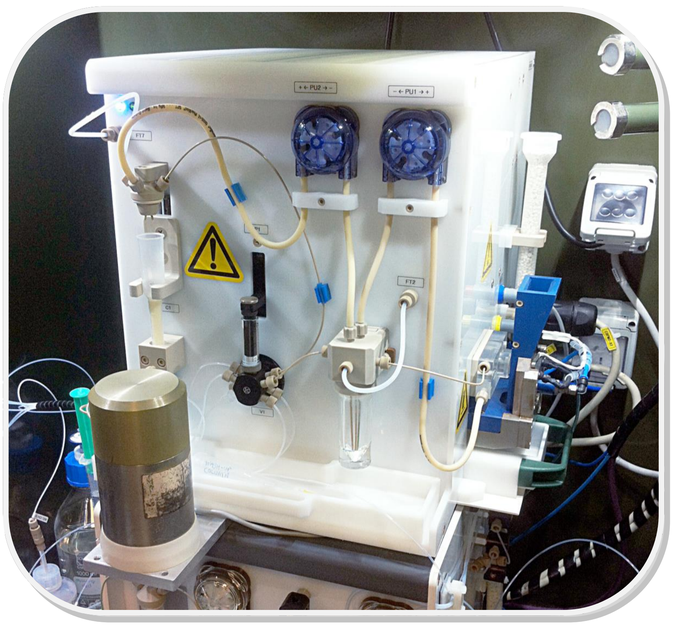

Image 1: IBA Pinctada Metal (Gen. 2) dissolution and purification module

Materials & Methods

A Nirta Solid Target from IBA was coupled to our 18/9 cyclotron using a 2-meter external beam line. A pneumatic solid target transfer system (STTS) designed by TEMA was use to deliver the irradiated target disks to a dedicated hotcell. Two separate modules developed by IBA (Pinctada metal) were used for i) electroplating ^{64}Ni onto a Ag disk and ii) acid dissolution and purification of the irradiated target material.

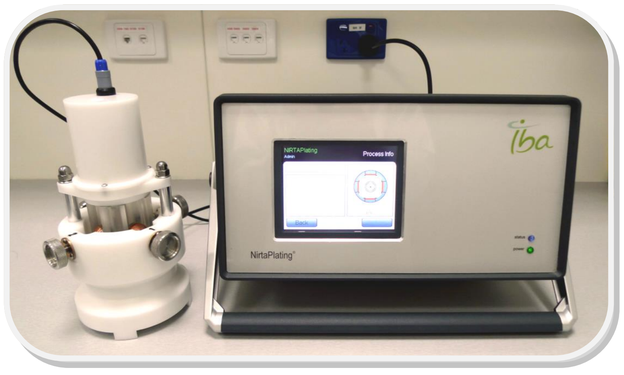

Image 2: Pinctada quad electroplating cell and controller

Electroplating: 1mm thick 24mm∅ Ag disks were electroplated with ^{64}Ni (>99%) at 5.0mA using a chopped saw tooth current for ~24 hours (Images 2&3).

^{64}Cu was produced via the ^{64}Ni(p,n)^{64}Cu nuclear reaction and typical irradiation parameters were 14.9MeV at 35 µA for 5-6 hours with ^{64}Ni plating's ranging from 10-60 µm thickness at 6-12 mm∅.

Dissolution/purification: The irradiated disk was loaded into the Pinctada dissolution module and the ^{64}Ni plating dissolved in recirculating 3mL 9M HCl at 70-80°C, and purified using an AG 1-X8 anion exchange cartridge, eluting the ^{64}Cu with 0.1M HCl in ~1.0-2.0mL. ^{64}Ni is separately collected to enable recycling for further productions.

Radionuclidic purities were evaluated by gamma spectroscopy and traces of metallic impurities were determined by ICP-MS or ICP-AES. Labelling efficiency was evaluated by measuring the amount of ^{64}Cu uptake per 20 mg of scFv-cage.

Results

Initial ^{64}Cu purifications following the manufacturers recommended method resulted in high levels of Cu, Fe and Zn metal contaminants (see Table 1, ID 1).

Visual inspection of the module after several productions revealed that the heater block used for heating the back of the Ag target disk was heavily corroded. Replacing the copper heater block with a PEEK heater block drastically reduced the levels of Cu and Fe contaminants.

In our quest for answers, ICP-MS analysis of the ^{64}Ni plating solution as well as critical stock reagents such as Milli-Q water (18 MΩ cm-1) and 30% HCl TraceSelect Ultra (Sigma) was performed (see Table 1, ID 2,3,4). From these results, it was hypothesized that the Pinctada's glass bottles (Kay 2004, BMC Physiology 4 p 4) used to store the reagents, especially concentrated acidic solutions, were the source of Zn contamination and all glass bottles were replaced by LDPE or PFA types. Subsequent ICP-MS analysis of fresh samples of HCl TraceSelect Ultra and the ^{64}Ni plating solution prepared/stored in plastic containers (see Table 1, ID 6,7), as well as a non-radioactive blank dissolution/purification test confirmed that Zn contamination was drastically reduced (see Table 1, ID 8).

Image 3: Ag disk (24mm∅) with 47.4µm thick (13.0mg, 6mm∅) ^{64}Ni plating

Finally, after implementation of the AG1-X8 resin washing protocol describe by Thieme et al. 2012 (Appl. Radiat. Isot. 70 p 602), eluting the 64Cu with 0.1M HCl rather than Milli-Q water (see Table 1, ID 9), we were able to further reduce metal contaminants especially Zn.

ID	Sample Description	Cobalt mg/L	Copper mg/L	Iron mg/L	Nickel mg/L	Silver mg/L	Zinc mg/L	Spec. Act. GBq(mCi)/µmol Cu
1	Initial Cu-64 productions (avg.; n=2)	0.0215	5.5524	7.8471	0.9322	0.3199	19.3364	0.44 (12)
2	Stock reagent, 30% HCl TraceSelect Ultra (Sigma), stored in glass bottle	0.0008	0.0135	0.1125	0.0075	0.0203	21.7500	NA
3	Milli-Q water (18MΩcm^{-1}), stored in glass bottle	0.0001	0.0001	0.0050	0.0010	0.0001	0.0060	NA
4	Ni-64 plating solution, prepared with/stored in glass bottle	0.0100	0.5000	0.5000	11000.0	0.6500	83.0000	NA
5	Cu-64 productions, replaced target disk heater block (Cu to PEEK) (avg.; n=7)	0.0101	2.3898	0.7159	1.0373	0.1078	40.7143	24.0 (649)
6	Stock reagent, 30% HCl TraceSelect Ultra (Sigma), stored in LDPE/PFA bottle	0.0008	0.0008	0.0375	0.0075	0.0458	0.0075	NA
7	Ni-64 plating solution, prepared with/stored in LDPE/PFA containers	0.0060	0.0180	0.3000	3.1800	0.4920	0.0600	NA
8	Pinctada module non-radioactive contamination test with blank PTFE target disk	0.0009	0.0891	0.2182	0.0182	0.0173	0.0909	NA
9	Cu-64 productions, LDPE/PFA reagent storage bottles, revised purification protocol (avg.; n=3)	0.0150	0.5450	0.8000	0.1500	2.3300	1.0000	163.2 (4412)

Table 1: ICP-MS/AES metal analysis

Conclusion

During the course of these experiments, a significant reduction in Cu, Fe and Zn contaminants was achieved and the true specific activity of ^{64}Cu increased from as low as 0.44 GBq (12 mCi)/µmol of Cu (n=2, Table 1, ID 1) to 24.0 GBq (649 mCi)/µmol of Cu (n=7, Table 1, ID 5) and finally to 163.2 GBq (4412 mCi)/µmol of Cu (n=3, Table 1, ID 9). In the same time, the effective specific activity increased from 1.1 +/- 0.74 MBq (0.03 ± 0.02 mCi) per 20 µg of scFv-cage, to 136.9 ± 11.1 MBq (3.7 ± 0.3 mCi) per 20 mg of scFv-cage with ^{64}Cu.

Acknowledgements: The funding provided for the construction of our solid targetry facility is an ANSTO/Austin/Ludwig partnership

[1]Austin Health Centre for P.E.T. and [2]LICR Melbourne Branch, Australia, [3]Heart & Diabetes Institute, Baker IDI, Melbourne, Australia [¶]stan.poniger@austin.org.au