## P131 PRODUCTION OF CERIUM RADIOISOTOPES FOR NANOTECHNOLOGY STUDIES: EXPERIMENTAL MEASUREMENTS OF THE EXCITATION FUNCTIONS natCe(d,x)139g/141/143Ce AND 142Pr

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**Objectives:** In recent years, the production and utilisation of nanoparticles have dramatically increased as new information about these particles and their potential applications are gained. In this respect, cerium may play an important role in the field of nanoscience as potential uses of Ce oxide nanoparticles are under evaluation in different fields. As the use of nanoparticles has increased, so also has concern about their possible detrimental effects on health or the environment, and considerable effort nowadays is devoted to their safety studies. In this respect, radiolabelling of nanoparticles can be a very useful tool for determination of nanoparticle fate, biodistribution, in vitro cellular uptake, etc. In this work, we focus on the study of the production of Ce radioisotopes and more precisely on the determination of the thin-target excitation functions for Ce radioisotope productions by deuteron-induced nuclear reactions in natural Ce, as no such data are available. Suitably radio-labelled Ce nanoparticles can be traced at different stages of their application thanks to the sensitivity of radiation measurements.

**Methods:** The Ce radioisotopes considered in this study are $^{139g}$Ce ($T_{1/2}$=137.6d), $^{141}$Ce($T_{1/2}$=32.5d), $^{143}$Ce($T_{1/2}$=33h). The detailed study of the various nuclear reactions leading to such radioisotopes was carried out using the stacked-foil technique. Thin foils of high purity natural Ce were purchased from the Goodfellow company. Care was taken for Ce handling as it is fragile and, as a lanthanide, reacts very rapidly if exposed to air or moisture. The preparation of the stacked-foils was therefore performed in a controlled atmosphere of nitrogen to avoid foil deterioration and resulting inaccuracy in the measurements of the produced activities. For this work, 5 stacked foils were prepared and irradiated under vacuum conditions using the Scanditronix MC 40 Cyclotron (K=40) of the Joint Research Centre (Ispra, Italy). The deuteron beam energies at the different Ce foils, beam current monitors and aluminum catchers were determined by the SRIM-2003 calculation code, and covered the deuteron energy range (19.5–5 MeV). The radioactive yields were measured with high resolution g-ray spectrometry.

**Results:** The excitation functions for the nuclear reactions $^{nat}$Ce(d,x)$^{139}$Ce, $^{nat}$Ce(d,x)$^{141}$Ce, $^{nat}$Ce(d,x)$^{143}$Ce and also $^{nat}$Ce(d,x)$^{142}$Pr have been determined. The maximum reaction cross sections were approximately 330, 200, 205 and 660 mbarns, at deuteron energies of 18.5, 10.4, 10.3 and 12.6 MeV respectively. We have shown that, with deuteron beam activation, high activities of various radioisotopes of Ce can be reached and data for the cross sections of the relevant nuclear reactions have been reported for the first time.

**Conclusions:** Thick target yields in the range of MBq/microA.h at the end of the deuteron beam bombardment of the different Ce radioisotopes can be obtained, which are suitable for various biological studies such as cellular uptake and biodistribution studies of Ce based nanoparticles.

## P132 SEPARATION OF MICRO AMOUNT OF SCANDIUM FROM MACRO AMOUNT OF TITANIUM USING ION EXCHANGE CHROMATOGRAPHY

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**Objectives:** The scandium-47 is a β emitter of moderate radiation energies (max. 439 and 600 keV) with a 3.35 d half life. In addition, $^{47}$Sc emits γ-rays of 159 keV suitable for imaging. Hence, its use may be considered in radiotherapy. The carrier-free $^{47}$Sc can be produced in a nuclear reactor in 2 ways, either from $^{47}$Ti by (n,p) reaction or from $^{46}$Ca by (n,γ) and consecutive β decay of $^{47}$Ca. Several methods of Sc separation from Ti have been described, including solvent extraction, ion exchange or extraction chromatography [1]. In this paper we are presenting the preliminary separation results of microgram quantities of Sc from gram quantities of Ti using the commercially available ion exchange resin DGA (N,N,N',N'-tetra-n-octyldiglycolamide) resin (EiChrom Corp), assuming similar behavior of Sc and Y. So far, the weight distribution factors for Ti were measured on DGA resin [2] while there are no data for Sc.

**Methods:** First the determination of the resin capacity factor (k') for Sc was performed as described by Horwitz et al [3]. Then experimental separation of Sc from excess of Ti was carried out with $^{46}$Sc as a tracer. The solution containing Ti (20 mg/ml) in 3.5 M $HNO_3$ was spiked with 10 MBq $^{46}$Sc (S.A. of about 2 GBq/mg Sc). The solution was loaded on 0.3 g DGA column bed weight. The flow rates ranging from 1.0 to 5.0 ml/min were used. $^{46}$Sc was eluted from the column with 0.05 M HCl and content of $^{46}$Sc was determined by gamma spectrometry.

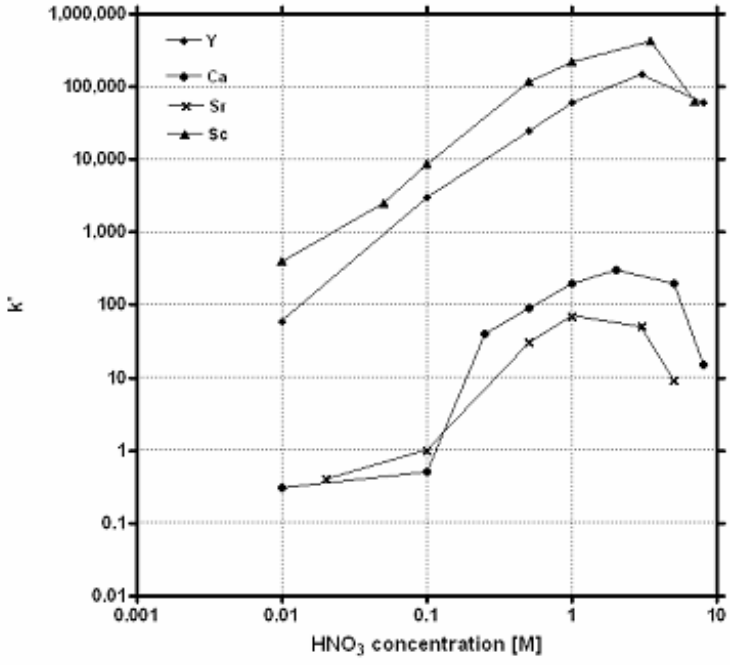
**Results:** The shape of curve presenting k' versus $HNO_3$ concentration for Sc is very similar to that for Y, as shown in Fig.1. The maximal k' value for Sc is around $4x10^5$ at 3.5 M $HNO_3$ and for Y it is around $1.5x10^5$ at 3 M $HNO_3$. The proposed method permitted relatively fast (in the process lasting about 5 h) separation of microgram quantities of Sc from about 5 g $TiO_2$. The total yield of separation was about 80% (73-85%). The $^{46}$Sc break-through from the column during loading of the Ti/Sc mixture did not exceed detection limit for $^{46}$Sc (around 1 kBq/fraction) for the flow between 1.0 and 2.5 ml/min. With the flow increased to 5.0 ml/min a significant increase in the Sc radioactivity detected was observed (10 kBq/fraction). The $^{46}$Sc was recovered from the column in about 20 ml 0.05M HCl.

**Conclusions:** The ion exchange DGA resin seems to be a promising bed for separation of Sc from Ti. The preliminary results obtained using mixed Ti and $^{46}$Sc need to be verified using in nuclear reactor irradiated targets.

Research Support: COST Actions D38 and BM0607 and the grant No: 126/N-COST/2008/0 from Polish Ministry of Science and Higher Education

**References:** 1. Kolsky K.L., Joshi V., Mausner L. F., Srivastava S.C.: Radiochemical Purifcation of No-carrieradded Scandium-47 for Radioimmunotherapy. Appl Radiat Isot. 49 (1998) 1541 2. http://www.eichrom.com 3. E.P.Horwitz, D.R. McAlister, A.H. Bond, R.E. Barrans, J.M. Williamson: A process for the separation of $^{177}$Lu from neutron irradiated $^{176}$Yb targets. Appl Radiat Isot 63 (2005) 23

Fig. 1. Comparison of DGA resin/$HNO_3$ k' values for Y, Sr and Ca [2] and these obtained for Sc.



## P133 LONG-TERM EVALUATION OF A COMMERCIALLY AVAILABE Ge-68/Ga-68 GENERATOR FOR PET IMAGING

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**Objectives:** Gallium-68 is an ideal radionuclide for positron emission tomography (PET), because the half-life of $^{68}$Ga (68 min) and its positron emission ($E_{max}$=1.92 MeV, 89%) are suitable characteristics for in vivo imaging. In addition, it can be obtained via a $^{68}$Ge/$^{68}$Ga generator which has the advantage of allowing both clinical and basic studies without an on-site cyclotron. Furthermore, the long half-life of the parent nuclide, $^{68}$Ge (270.8 days), provides a long life-span generator. The Isotope Products Laboratories Ionic Gallium Generator (IGG100) is a commercial available $^{68}$Ge/$^{68}$Ga generator. The generator is a closed system consisting of an ion exchange column containing a titanium dioxide bed on $^{68}$Ge in a borosilicate glass tube, and PEEK end plugs which are attached using PVC inlet and outlet lines via barbed fittings. The column is mounted in a tungsten/lead shielded assembly. The assembly is secured in a stainless steel outer box with two handles and recessed inlet and outlet ports. In this study, we evaluated the profile of the generator for approximately 200 elutions over a two year time period.

**Methods:** The IGG100 generator produced by Eckert & Ziegler Isotope Products GmbH (Berlin, Germany) was loaded with 1,850 MBq of $^{68}$Ge. The $^{68}$Ga was eluted with 0.1M ultrapure hydrochloric acid according to the manufacturer instructions. Elutions were carried out at 2 mL/min for 3 min using an infusion pump, and the $^{68}$Ga activity was collected every 0.5 min. The elution profile was determined by measuring the $^{68}$Ga activity in the six 1 mL fractions. The $^{68}$Ge breakthrough was calculated as a percentage of $^{68}$Ge per $^{68}$Ga in the fractions.

**Results:** The $^{68}$Ga elution yield based on loaded $^{68}$Ge was 61.0 ± 3.5 % (n=195), and 80% of the $^{68}$Ga was recovered in fractions 3 and 4. These trends were the same through the two year testing period. The breakthrough of $^{68}$Ge in all six fractions was <0.005% of eluted $^{68}$Ga at 450 days after $^{68}$Ge loaded (115th elution), and increased to 0.02% in another 200 days. The breakthrough in fractions 3 and 4 was ~0.008% at 650 days.

**Conclusions:** The results indicate that the IGG100 generator produced $^{68}$Ga with high elution yields over a two year time period. The percentage of Germanium-68 breakthrough increased slowly over the 650 day time period but was remained acceptable limits.

**Research Support:** This work was supported by NIH/NCI Grant R24 CA086307 "Radionuclide Resource for Cancer Applications."

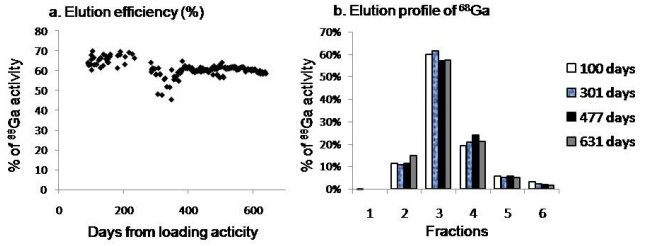


**Figure 1.** (a) The percentage of eluted $^{68}$Ga based on the activity of loaded $^{68}$Ge. Day 0 is the day of $^{68}$Ge loading on the $^{68}$Ge/$^{68}$Ga generator. (b) Elution profile of $^{68}$Ga in fraction 1 to 6. The activity in 1 mL per fraction is expressed as percentage of the total $^{68}$Ga activity.

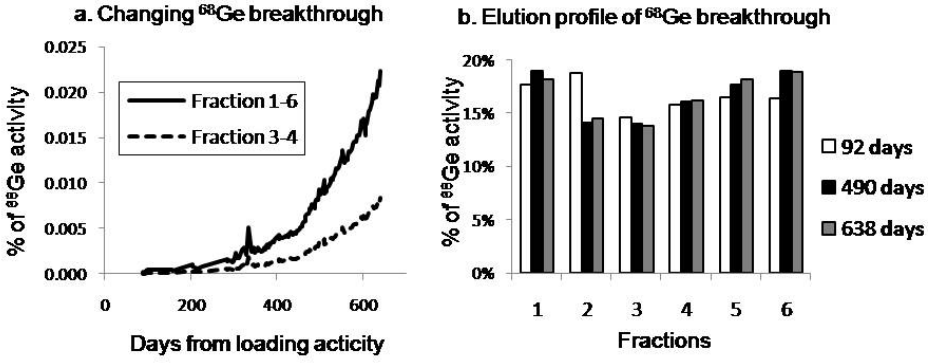


**Figure 2.** (a) $^{68}$Ge breakthrough is expressed as percentage of $^{68}$Ge/ $^{68}$Ga in total fractions (solid line), and the fraction 3 and 4 (dashed line). (b) Elution profile of $^{68}$Ge breakthrough in fraction 1 to 6. The activity in 1 mL per fraction is expressed as percentage of the total $^{68}$Ge activity.

## P134 INCREASING SPECIFIC ACTIVITY IN CU-64 PRODUCTION BY REPROCESSING THE NI-64 TARGET MATERIAL

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**Objectives:** The aim of this work is to provide high specific activity (SA) $^{64}$Cu for the preparation of high SA radiotracers for PET-based molecular imaging. $^{64}$Cu is routinely produced using 13 MeV protons via the $^{64}$Ni(p,n)$^{64}$Cu reaction with the CC 18/9 cyclotron (Efremov Institute, St. Petersburg, Russia) at the Turku PET Centre. Due to the high price of enriched $^{64}$Ni (~15□/mg) recycling of the $^{64}$Ni-target material is mandatory. The radiochemical separation process of $^{64}$Cu from $^{64}$Ni by anion exchange chromatography provides an additional purification of the $^{64}$Ni-target material from traces of Cu impurities. Our hypothesis is that the reprocessing of the enriched $^{64}$Ni is leading to a stepwise increased SA of $^{64}$Cu.

**Methods:** Ultra-pure reagents with ppt levels of metal traces are used for all preparations. Preparation of the enriched $^{64}$Ni-target, radiochemical separation of $^{64}$Cu and recovery of the enriched $^{64}$Ni is performed as previously described (1, 2). The target thickness is between 110-210 mg/cm$^2$. The effective SA (ESA) of $^{64}$Cu is determined by complexation/titration with the chelator TETA (2). Briefly, dilution series with 320-10 pmol TETA are prepared adding increasing volumes (10-160 $\mu$L) of $10^{-5}$-$10^{-6}$ M TETA stock solutions to 1.5 mL PP tubes. Aliquots (100 $\mu$L) of a diluted $^{64}$Cu stock solution (3.5-140 MBq at EOB) in 0.1 M $NH_4OAc$ buffer solution are added to each vessel. All volumes (260 $\mu$L) are kept constant by adding $H_2O$ and the mixtures are incubated at 80°C for 20 min. The percentage of the [$^{64}$Cu(TETA)] fraction in each aliquot is determined via TLC. The minimum amount of TETA required to reach >95% complexation is assumed to be equal to the amount of Cu and metal impurities which compete in the complexation with TETA. The SA is determined by analysing decayed samples from the $^{64}$Cu stock solutions for traces of metallic impurities by ICP-MS.

**Results:** Table 1 shows data from 4 production runs using and recycling the same $^{64}$Ni-target. [Table] The certificate of analysis reported 40 ppm of Cu impurities in the fresh $^{64}$Ni metal (Isoflex, San Fransisco, USA), which gives 2.9 $\mu$g of Cu impurities in the initial 72.2 mg of $^{64}$Ni in the studied target. The amount of Cu impurities decreased dramatically after the first reprocessing of the target material as determined by ICP-MS and TETA-complexation analysis. The differences between the ESA and SA of $^{64}$Cu could be explained by the presence of other metallic impurities that compete with Cu in the complexation of TETA. After the first reprocessing the concentration of Cu impurities is maintain approximately constant as confirmed by ICP-MS.

**Conclusions:** We are able to produce Cu with very high SA and also with high ESA, which is required for further labelling of high affinity tracers for PET. The results obtained showed that very high SA is achieved already after one reprocessing cycle of the target material. This is possible only by using ultra-pure reagents, Cu-free glassware and careful handling of the recovered $^{64}$Ni solution in order to maintain the SA as high as possible.

**References:** (1) McCarthy, D. W. et al. (1997) Nucl. Med. Biol. 24, 35-43. (2) Avila-Rodriguez, M. A., et al. (2007) Appl. Radiat. Isot. 65, 1115-1120.

Table 1. Results of $^{64}$Cu-production from 4 runs with the same $^{64}$Ni-batch.

| Run | Target thickness | Irradiation | Activity at EOB | Experimental yield at saturation | % of predicted sat. yield | ESA at EOB | SA at EOB | total mass (Cu) by ICP-MS |
|---|---|---|---|---|---|---|---|---|
| # | [mg/cm$^2$] | [µAh] | [GBq] | [GBq/µA] | [%] | [GBq/µmol] | [GBq/µmol] | [µg] |
| | | | | | | | | |
| 1 | 145 | 4.9 | 1.4 | 5.30 | 97 | 9 | 13 | 6.4 |
| 2 | 140 | 29.8 | 8.1 | 5.12 | 98 | 580 | 1650 | 0.2 |
| 3 | 136 | 23.0 | 3.8 | 3.09 | 61 | 750 | 1320 | 0.1 |
| 4* | 112 | 19.9 | 4.2 | 3.95 | 97 | 22 | 991 | 0.2 |

** metal contamination during processing*

## P135 CHARACTERISTICS OF GMP-PRODUCED SNO2-BASED 68GE-68GA GENERATOR

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**Objectives:** $^{68}$Ga-PET imaging is emerging in Nuclear Medicine. $^{68}$Ge-$^{68}$Ga generators provide easy access to PET radiopharmaceuticals. Currently $TiO_2$- and $SnO_2$-based generators are commercially available, and eluted with 0.1 and 1M HCl, resp. [1-3]. Fractionated elution or concentration and purification of the whole eluate by ion exchange are described [2-4]. Radiolabeling of DOTA-peptides with $^{68}$Ga are performed at pH 3.5-4 [2-4], thus requiring additions to control pH, which may contain potential competitors for $^{68}Ga^{3+}$ for the incorporation in DOTA-peptides [2-5]. [1] Loc'h C et al., JNM, 21 (1980) 171-173, [2] Meyer G-J, et al., EJNMMI, 31 (2004) 1097-1104, [3] Breeman WAP, et al., EJNMMI, 32 (2005) 478-485, [4] Zhernosekov KP, et al., JNM, 48 (2007) 1741-1748, [5] Decristoforo C, et al., EJNMMI, 35 (2008) 1507-1515.This study was to investigate $SnO_2$-based generators (iThemba Labs, Somerset West, South-Africa) in terms of fractionated elution profile, $^{68}$Ga yield and $^{68}$Ge breakthrough while lowering the molarity of Ultrapure HCl from 1M to 0.3M, in steps of 0.1M. Radiolabeled peptides like bombesin, CCK and substance P for application in humans require high specific activity, due to pharmacological side effects. By increasing specific activities when injecting a constant amount of radioactivity, the amouint of peptide can be lowered, therefore the maximal achievable specific activity of DOTA-peptides was investigated.

**Methods:** Fractionated elutions were performed in fractions of 0.25 mL, total elution volume was 6 mL. $^{68}$Ga activity was directly determined and $^{68}$Ge after $\geq$ 24h [3]. Breakthrough (as activities of $^{68}$Ge per $^{68}$Ga) and yields (as activities of $^{68}$Ga per $^{68}$Ge on the column) were determined [3]. Labeling DOTA-peptides were performed as described earlier [3]. Octreotide analogs DOTA-tate and DOTATOC were used as models. pH of the effluents from ion exchange columns were adjusted to 3.5-4 with 1M HEPES. Incorporation of $^{68}$Ga in DOTA-peptides were determined by ITLC-SG [3], and RCP (radiochemical purity of the main peak) by $C_{18}$ RP-HPLC [3]. Since ionic $^{68}$Ge has no affinity for $C_{18}$ [5] the radiopeptide-containing solution was passed over a Sep-Pak $C_{18}$ column.

**Results:** The generators have void volumes of $\approx$ 1.5 mL and a bed volume of $\approx$ 2 mL. Approximately 80% of the $^{68}$Ga is recovered in 2 mL. Elution profile of $^{68}$Ga was independent of the [HCl]. Yields were 55-60% at 1M HCl, 45-50% at 0.6M HCl, and 25-30% at 0.3M HCl. Further studies were performed at 0.6M HCl. $^{68}$Ge breakthrough was <0.1 kBq $^{68}$Ge per MBq $^{68}$Ga. SA of 0.3 GBq per nmol DOTA-peptides at >98% incorporation were achieved and confirmed by RCP. [$^{68}$Ge] was lowered with a factor of > 20 by Sep-Pak $C_{18}$ purification, ratio reduced [$^{68}$Ge] over [$^{68}$Ga] to « $10^{-3}$%.

**Conclusions:** High specific activities of $^{68}$Ga-DOTA-peptides from this new $SnO_2$-based generator are achievable. This also opens possibilities for studies with DOTA-peptides with pharmacological side effects.

## P136 PURIFICATION AND CONCENTRATION OF ELUATE FROM GMP-PRODUCED SNO2-BASED 68GE-68GA GENERATOR BY ANION OR CATION EXCHANGE

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**Objectives:** $^{68}$Ge-$^{68}$Ga generators provide easy access to PET radiopharmaceuticals. Recently a $SnO_2$-based generator became commercially available, and can be eluted with 0.6M HCl. Fractionated elution or ion exchange of the whole eluate are described [1-3]. The generator is eluted with 0.6M HCl. Radiolabeling of DOTA-peptides with $^{68}$Ga are performed at pH 3.5-4 [1-3], thus additions to control pH are required. This addition may contain compounds which also incorporate in the DOTA, and are potential competitors for $^{68}Ga^{3+}$ for the incorporation in DOTA-peptides. [1] Meyer G-J, et al., EJNMMI, 31 (2004) 1097-1104, [2] Breeman WAP, et al., EJNMMI, 32 (2005) 478-485, [3] Zhernosekov KP, et al., JNM, 48 (2007) 1741-1748. Purification and concentration of the eluate by anion and cation exchange are described for $SnO_2$-based generators [1,3]. This study was to investigate these techniques for the new $SnO_2$-based generators (iThemba Labs, Somerset West, South-Africa). Radiolabeled peptides like bombesin, CCK and substance P for application in humans require high specific activity, due to pharmacological side effects. By increasing specific activities when injecting a constant amount of radioactivity, the amouint of peptide can be lowered, therefore the maximal achievable specific activity of DOTA-peptides was investigated.

**Methods:** Either, 80% of the total eluted activity was collected in 2 mL by fractionated elution, or total elution volume was 6 mL. For application on anionic resin (e.g. AG1-X8 BioRad) the [$Cl^-$] was increased to 5M to form the anionic chloro complex $[GaCl_4]^-$ and for cationic resin (e.g. AG50W-X8 BioRad) the [$Cl^-$] was reduced to 0.1M. $^{68}$Ga activity was directly determined and $^{68}$Ge after $\geq$ 24h [2]. pH of the purified $^{68}$Ga-containing effluents from ion exchange columns was adjusted to 3.5-4 with 1M HEPES. Labeling DOTA-peptides were performed as described earlier [1-3]. DOTA-tate and DOTATOC were used as models. Incorporation of $^{68}$Ga in DOTA-peptides were determined by ITLC-SG [2], RCP (radiochemical purity of the main peak) by $C_{18}$ RP-HPLC [2].

**Results:** In the purified $^{68}$Ga-containing effluents from anion and cation exchange columns [$^{68}$Ge] was lowered by a factor of >20, resulting in <0.1 kBq $^{68}$Ge per 100 MBq $^{68}$Ga, ratio is > $10^6$. Specific activities of >0.3 GBq per nmol DOTA-peptides at > 98% incorporation were achieved and confirmed by RCP.

**Conclusions:** Purification by anion and cation exchange lowered the [$^{68}$Ge] with a factor >20. High specific activities of $^{68}$Ga-DOTA-peptides are achievable after purification and concentration of eluate by anion or cation exchange. This high specific activity also opens possibilities for studies with DOTA-peptides with pharmacological side effects.

## P137 PRODUCTION OF POSITRON EMITTING RADIONUCLIDES AT THE TURKU PET CENTRE CC-18/9 CYCLOTRON

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**Objectives:** The CC-18/9 cyclotron (18 MeV protons, 9 MeV deuterons, 100 uA, Efremov Institute, St Petersburg, Russia) installed at TPC is at present used for production of $^{11}C$, $^{18}F$ and $^{64}Cu$. These radionuclides are used for research and clinical programs on site; no regional distribution of the produced radioactivity is done. The main objectives is large scale uninterrupted availability of $[^{11}C]CO_2$, $[^{11}C]CH_4$, $[^{18}F]F$ and $[^{64}Cu]CuCl_2$. $[^{18}F]F_2$ is produced post target from $[^{18}F]F$.

**Methods:** The 18 MeV proton beam can be extracted to three different irradiation lines. One of these is attached to a beam transport tube, equipped with quadrupole pair lenses and steering magnets. The tube is connected to a switching magnet, which is capable of directing the beam to four irradiation positions at ±12° (positions B and C) and ±36° (positions A and D) angles, see figure 1. Positions B and C are equipped with target chamber changing units for four different target chambers each. At present these are identical, both having installed one target chamber for $[^{11}C]CO_2$, one for $[^{11}C]CH_4$ and two for $[^{18}F]F$. Of the $[^{18}F]F$ -production target one is static; the other utilizes circulating target water. All targets chambers have gridded front-foil windows and are water cooled. For all $^{18}F$-systems SPE situated in the cyclotron vault is used to extract the radioactivity from the irradiated target water before directing it to the appropriate hot-cell. All target chambers are operated at elevated pressures (35-70 bar). No He-cooling of target windows is used at present. Position A is used for experimental target systems and position D is used for irradiation of solid targets. At present $^{64}Ni$ targets are used for $^{64}Cu$-production. Extensive diagnostics for beam quality and target performance are in use, the diagnostic data is logged for all irradiations. The production systems at positions B and C are connected to a distribution cabinet situated in the cyclotron vault. This "switchboard" is used to direct the produced radioactivity to any of the 10 hot-cells in the laboratory. Of these hot-cells 6 are in classified clean rooms (three cubicles with two cells each). Four cells are situated in a R&D laboratory, separate from the GMP-classified radiopharmaceutical laboratories.

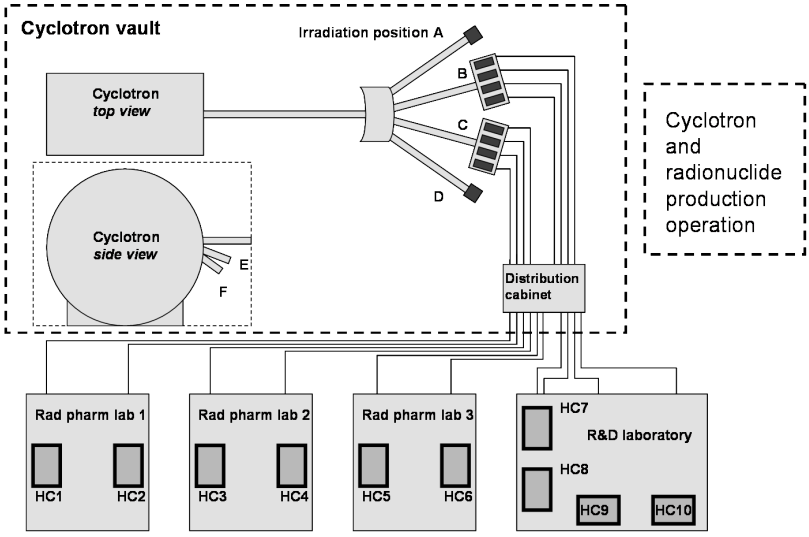


Figure 1. Schematic drawing of CC-18/9 cyclotron, beam line and radioactivity distribution system at TPC

**Results:** At present target positions A - D are in use. The $^{11}C$ and static $[^{18}F]F$ production systems are in routine use. The $^{64}Cu$- and recirculating $[^{18}F]F$ production systems are still in development.

**Conclusions:** The cyclotron with associated radionuclide production systems for PET installed at TPC has performed well according to design specifications.

## P138 EVALUATION OF A NOVEL GALLIUM-68 GENERATOR

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**Objectives:** The most common isotope used for PET scanning is Fluorine-18 which has a half-life of 110 min and a positron energy=635 MeV. However, it also has drawbacks which make PET scanning difficult and expensive. Fluorine-18 can only be produced practicallly using a cyclotron, and cannot be transported over long distances. Therefore PET medical facilities must be close to an expensive cyclotron. This makes PET scanning nearly impossible in remote medical facilities. A suitable alternative isotope, as yet not optimized for medicinal application, is Ga-68 with a positron energy=1.899 MeV, which is another positron emitting radionuclide with a half life of 68 min. Ga-68 can do for PET imaging what Tc-99m did for SPECT as it can also be obtained from a generator, thus being safe, suitable for imaging, relatively cheap and easy to use. Ga-68 ($t_{½}$ = 68 min) is obtained from a generator from decay of the long-lived parent Ge-68 ($t_{½}$ = 271 d). Ongoing studies at the University of Missouri have been developing and evaluating a novel generator and purification system of Ga-68 from Ge-68 using a metal free system. The generator's design is based on Fajan's absorption, and utilizes glass beads to selectively adsorb the Ga-68 isotope while letting the Ge-68 flow through. The goals of the studies reported here include evaluating different modifiers and support systems to lower the amount of Ge-68 breakthrough from the column and optimize the yield of Ga-68.

**Methods:** Three column substrates (silicon dioxide, borosilicate glass, and high purity borosilicate) were evaluated with and without germanium carrier, and with assorted buffers while varying pH values to optimize Ga-68 elution while minimizing Ge-68 breakthrough. Organic solvents acetone (10-98%, v/v), and $CCl_4$ (10-50% v/v), were added to the radioactive solution when passed through the column in an attempt to improve partitioning of the $Ga(OH)_3$ between the glass and aqueous medium. A water rinse was employed to rinse residual Ge-68 from the column, then followed by a dilute HCl rinse to strip the Ga-68. Later, the tests were repeated with the addition of centrifuging (at varying time and speeds) to remove any residual Ge-68.

**Results:** Of the solvents tested, the buffered solution resulted in a 0.02-0.04% Ge-68 breakthrough and a 81-92% Ga-68 yield. Neither addition of acetone or $CCl_4$ resulted in a lower % Ge-68 breakthrough or higher Ga-68 yields. The centrifuge tests gave improved results, which were however inconsistent. The High Purity BSi beads gave improved Ga-68 yields compared to the regular BSi beads (96% Ga-68), but did not result in lower Ge-68 breakthrough. Only the addition of carrier germanium resulted in lower Ge-68 breakthrough.

**Conclusions:** From our results we will continue to test the high purity BSi beads which resulted in the highest yields of Ga-68 and lowest breakthrough of Ge-68 only the additon of carrier Ge reduced the Ge-68 breakthrough.

**Research Support:** Supported by NIH P50CA103130

## P139 PREPARATION OF A 5 mCi PROTOTYPE 44Ti/44Sc RADIONUCLIDE GENERATOR

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**Objectives:** For preparation of $^{44}Ti/^{44}Sc$ radionuclide generators, several radiochemical criteria are relevant, such as effective separation strategies providing high $^{44}Sc$ yields and low $^{44}Ti$ breakthrough, high long-term stability, and type of Sc eluates useful for subsequent labelling reactions (i.e. low volume, low pH, high purity etc.) [1,2]. In the present work, distribution coefficients of Ti(IV) and Sc(III) have been determined for anion AG1x8 and cation AG 50Wx8 exchange resins and HCl / oxalic acid mixtures.

**Methods:** Distribution coefficients are summarized in Table 1. The data indicate optimum separation conditions for 0.005 M $H_2C_2O_4$ / 0.6-0.8 M HCl mixture. For the generator, a column (H=150 mm, D=3 mm, $V_0$=0.55 ml) was made of PEEK and filled with anionit AG-1×8 (200-400 mesh, $Br^-$-form). The column was washed with 20 ml 12 M HCl and 10 ml $H_2O$. Finally, it was washed with 10 ml 0.1 M $H_2C_2O_4$. The purified $^{44}Ti$ (5 mCi) was dissolved in 20 ml 0.1 M $H_2C_2O_4$. This solution was brought into the generator and the generator was washed with 0.005 M $H_2C_2O_4$ / 0.07 M HCl mixture in "reverse" direction. Two days later, the generator was eluted for first time using 20 ml of 0.005 M $H_2C_2O_4$ / 0.07 M HCl. Aliquots were selected for each 2 ml in 15 ml Eppendorf vials. One week later, the activity of $^{44}Ti$ in these samples were analysed by means of γ-spectrometry.

| N | Concentration of solution, mol/l | | $K_d$ | | | |
|---|---|---|---|---|---|---|
| | | | AG-W50x8 | | AG-1x8 | |
| | $H_2C_2O_4$ | HCl | Ti | Sc | Ti | Sc |
| 1 | 0.1 | 0 | - | - | >1000 | 184 |
| 2 | 0.1 | 0.05 | - | - | >1000 | 41 |
| 3 | 0.1 | 0.1 | - | - | >1000 | 14 |
| 4 | 0.1 | 0.15 | << 1 | 12.0 | >1000 | 5.1 |
| 5 | 0.1 | 0.20 | << 1 | 10.7 | >1000 | 1.7 |
| 6 | 0.1 | 0.30 | << 1 | 7.0 | 370 | 0.2 |
| 7 | 0.1 | 0.50 | << 1 | 11.2 | 105 | << 1 |
| 8 | 0.1 | 0.75 | ~0,5 | 14.0 | - | - |
| 9 | 0.1 | 1.0 | << 1 | 8.1 | 17 | << 1 |
| 10 | 0.025 | 0 | 1.0 | 201 | >1000 | 954 |
| 11 | 0.025 | 0.025 | 1.0 | 148 | >1000 | 168 |
| 12 | 0.025 | 0.050 | 0.6 | 129 | >1000 | 40.9 |
| 13 | 0.025 | 0.075 | 1.8 | 128 | >1000 | 14.2 |
| 14 | 0.025 | 0.125 | 3.3 | 124 | 1050 | 2.68 |
| 15 | 0.025 | 0.175 | 3.1 | 120 | 410 | 0.3 |
| 16 | 0.025 | 0.250 | 2.9 | 119 | 290 | << 1 |
| 17 | 0.005 | 0 | 32 | 7619 | >1000 | 2340 |
| 18 | 0.005 | 0.025 | 30.4 | 2378 | >1000 | 67.2 |
| 19 | 0.005 | 0.0375 | 34.2 | 2242 | >1000 | 24.0 |
| 20 | 0.005 | 0.05 | 33.6 | 2665 | >1000 | 10.9 |
| 21 | 0.005 | 0.065 | 28.2 | 1872 | >1000 | 4.0 |
| 22 | 0.005 | 0.08 | 33 | 1715 | 844 | 1.27 |
| 23 | 0.005 | 0.10 | 33 | 1646 | 688 | 0.71 |
| 24 | 0.005 | 0.125 | 25.6 | 1398 | 457 | << 1 |
| 25 | 0.005 | 0.25 | - | - | 46 | << 1 |
| 26 | 0.005 | 0.5 | - | - | 3.8 | << 1 |

**Results:** The generator was regularly eluted. A typical profile of $^{44}Ti/^{44}Sc$ radionuclide generator elution (Curie-meter measurements, relative units) is shown on the figure 1. Aliquots 4-7 contain 85±2 % of the whole Sc-activity. All fractions (20 ml) have 180 MBq of $^{44}Sc$ and $^{44}Ti$ 86±8 Bq.

**Conclusions:** After one year regular elution of $^{44}Ti/^{44}Sc$ radionuclide generator the yield of $^{44}Sc$ and $^{44}Ti$ is still stable and the breakthrough of $^{44}Ti$ is very low (<4.8 $10^{-7}$). The generator can be used in further studies for medical application.

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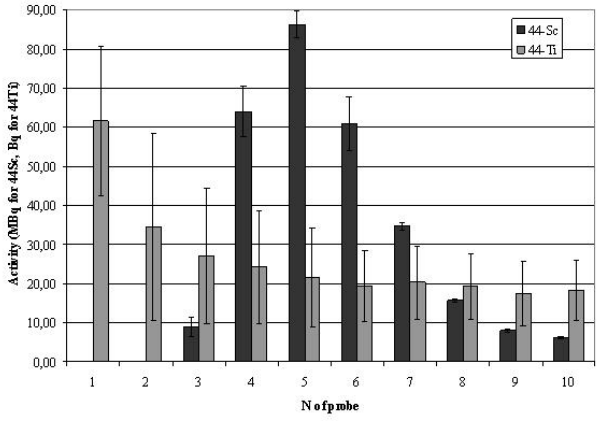

## P140 PRODUCTION OF SN-117M IN THE BR2 AND HFIR RESEARCH REACTORS

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**Objectives:** Tin-117m ($T_{½}$ 14.0 d; γ 159 keV, 86%) is a promising radionuclide for therapeutic applications. In contrast to beta emitters, $^{117m}$Sn emits low-energy conversion electrons that deposit their intense energy (127, 129, 152 keV) within a short range (0.22 - 0.29 mm) which can destroy tumors but not damage the bone marrow or other healthy tissues. The 159 keV gamma photons are ideal for imaging to monitor the cancer. This paper reports the results of $^{117m}$Sn production yield calculations and measurements for several irradiation conditions which can be achieved in both the BR2 (Mol, Belgium) and HFIR (Oak Ridge, USA) High-Flux research reactors.

**Methods:** Both BR2 and HFIR research facilities are 100 $MW_{th}$ High-Flux reactors operating currently at a power of respectively 60 and 85 $MW_{th}$. The availability of high thermal neutron flux densities of up to 1.0 (BR2) and 2.5 x $10^{15}$ n $cm^{-2}$ $s^{-1}$ (HFIR) allows important routine production of radioisotopes for medical applications. $^{117m}$Sn can be produced in a nuclear reactor by the neutron radiative capture reaction $^{116}$Sn(n,g)$^{117m}$Sn or by the inelastic scattering reaction $^{117}$Sn(n,n'g)$^{117m}$Sn. This last reaction has a threshold of 318 keV but was shown to result in greater yields and specific activities than the radiative capture reaction in a reactor with a hard neutron spectrum. Suitable irradiation conditions for the production of $^{117m}$Sn can be achieved inside thirteen BR2 fuel elements (H1/central, A, B) and in HFIR's Hydraulic Tube (HT) and Peripheral Target Position (PTP) facilities. The selected core locations are characterized by the highest fast neutron flux ($E_n$>100 keV) available in both reactors. Calculations of $^{117m}$Sn yields and specific activities were performed using LAURA, a two-group nuclear transmutation and decay code. These calculations were carried out for the irradiation of 200 mg tin metal targets with an enrichment of 92.23% $^{117}$Sn and 7.54% $^{116}$Sn in the selected irradiations positions.

**Results:** The results of the calculations shown in figure 1 have been validated by a 'test' irradiation inside a BR2 fuel element (A/B). The measured specific activity (6.1 Ci/g) was about 15% lower than the theoretically predicted value (7.1 Ci/g).

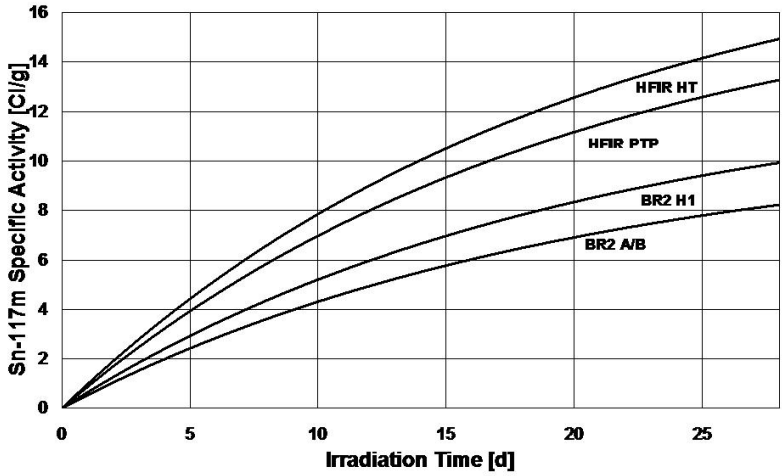


**Fig. 1. Sn-117m yield for 200 mg 92% Sn-117 enriched targets**

**Conclusions:** The specific activity of $^{117m}$Sn achieved in both the BR2 and HFIR reactors is suitable for the palliative treatment of bone metastases. These two reactors represent major resources for the production of this important therapeutic radioisotope in the frame of the development of other applications.

**Research Support:** Work supported by the Office of Nuclear Energy, US Department of Energy, at ORNL under Contract # DE-AC05-00OR22725 with UT-Battelle, LLC, and at BNL under Contract # DE-AC02-98CH10886, and in part at BNL by a research grant from Clear Vascular, Inc., New York, NY, USA.

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## P141 NEW CROSS SECTION MEASUREMENTS FOR THE PRODUCTION OF THE AUGER ELECTRON EMITTERS BR-77 AND BR-80M

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**Objectives:** The application of radioisotopes of bromine is of longstanding interest in nuclear medicine. Whereas the lighter isotopes, namely $^{75}$Br and $^{76}$Br, are already in use in the field of PET imaging [Zalutski in Radiolabeled monoclonal antibodies for imaging and therapy (Srivastava, S.C., editor) p. 195, 1988], the two Auger electron emitters investigated in this work are discussed to be useful in internal radiotherapy [Mease et al., Appl. Radiat. Isot. 42, p. 57, 1990]. The cross section data for the production of $^{77}$Br via low energy (p,n) reactions have been well determined [Hassan et al., Appl.Radiat. Isot. 60, p. 899, 2004]. In this work those measurements were extended by studying the nuclear processes $^{77,78,80}$Se(p,xn)$^{77}$Br, using enriched target materials. The excitation function of the $^{80}$Se(p,n)$^{80m}$Br reaction up to 20 MeV was determined for the first time.

**Methods:** The highly enriched Se targets were prepared by sedimentation of fine Se metal powder onto thin Al backings. The samples were irradiated in a stacked-foil arrangement together with Ni and Cu monitor foils. The irradiations up to 45 MeV were done at the compact cyclotron CV 28 and the injector cyclotron of COSY of the Forschungszentrum Jülich, Germany. Irradiations in the higher energy region were done at the Separate Sector Cyclotron (SSC) of iThemba LABS in Somerset West, South Africa. The produced radioactivity was measured non-destructively using HPGe detector g-ray spectrometry. For measurements on $^{80m}$Br, which emits only a low-energy g-ray of 37 keV, a specially calibrated solid state detector was used.

**Results:** The full excitation function of the $^{80}$Se(p,n)$^{80m}$Br reaction was determined systematically up to 20 MeV. Furthermore cross sections were measured for the first time for the reactions $^{80}$Se(p,4n)$^{77}$Br and $^{78}$Se(p,2n)$^{77}$Br between 34.5 and 80.0 MeV. The experimental results were compared with the results of nuclear model calculations based on the code ALICE-IPPE. Possible production yields of the two radionuclides were calculated. The yield of $^{77}$Br formed at intermediate energies is higher than that via low-energy (p,n) reactions.

**Conclusions:** Extended nuclear cross section data were experimentally determined for the formation of $^{77}$Br and $^{80m}$Br via proton induced reactions on enriched $^{77}$Se, $^{78}$Se and $^{80}$Se up to 80 MeV. The production possibilities of the respective radionuclides using intermediate energy reactions and the levels of impurities will be discussed.

## P142 USE OF ALPHA PARTICLE BEAM IN MEDICAL RADIONUCLIDE PRODUCTION

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**Objectives:** Medical radionuclides are now increasingly produced using small and medium-sized cyclotrons, generally having two particle beams, namely protons and deuterons. However, some radionuclides can be better produced using an α-particle beam. In several other cases an α-particle induced reaction could be a meaningful alternative to a reactor or a high-energy cyclotron production route. Our institute recently placed an order with the Ion Beam Applications S.A. to supply a Cyclone 30 cyclotron which should additionally deliver a 30 MeV α-particle beam. Apart from some fundamental nuclear chemistry work, the α-particle beam will be used for production of special radionuclides.

**Methods:** In this contribution we present a brief review of our experience over several decades in the development and production of some radionuclides using an α- particle beam of energy about 30 MeV. Furthermore, some hitherto unexplored but potentially interesting routes for production of some further radionuclides are also discussed.

**Results:** Therapeutic radionuclides: The α-particle emitting radionuclide $^{211}$At ($T_{1/2}$ = 7.2 h) has been produced for decades in many laboratories exclusively via the $^{209}$Bi(α,2n)-reaction. Similarly the most efficient method developed for the production of the Auger electron emitter $^{77}$Br ($T_{1/2}$ = 57.0 h) makes use of the $^{75}$As(α,2n)-reaction. Our recent studies have shown that two further important therapeutic radionuclides, namely $^{153}$Sm ($T_{1/2}$ = 46.3 h), a $\beta^-$ emitter, and $^{193m}$Pt ($T_{1/2}$ = 4.3 d), a pure Auger electron emitter, can be produced with much higher specific activity than presently possible. Both the radionuclides are produced to date in a nuclear reactor via the (n,γ) process and hence the resulting specific activity is low. The yields of the alternative $^{150}$Nd(α,n)$^{153}$Sm [Qaim et al., Radiochim. Acta 2007, 95: 313] and $^{192}$Os(α,3n)$^{193m}$Pt [Hilgers et al., Appl. Radiat. Isot. 2008, 66: 545] reactions leading to no-carrier-added products are high enough to make practical use of those processes. The latter process is under further technical development in our laboratory. Potentially some other radionuclides could also be produced.

**Conclusions:** Several potentially useful non-standard positron emitters like $^{52}$Fe and $^{83}$Sr, for which the α-particle induced reactions $^{50}$Cr(α,2n)$^{52}$Fe and $^{80}$Kr(α,n)$^{83}$Sr using enriched targets appear to be promising, will be discussed. The preferential formation of some Auger electron emitting high-spin isomeric states of some heavy mass nuclides in α-particle induced reactions will be discussed.

## P143 PRODUCTION OF CARRIER-FREE 86Y FOR NUCLEAR MEDICAL APPLICATION USING ENRICHED 86SrO

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**Objectives:** Due to its physical properties, $^{90}$Y is a widely used radionuclide for targeted tumor therapy. However as a pure $\beta^-$ emitter it can not be applied for dosimetry determinations. For this purpose the positron emitting radioisotope $^{86}$Y has been advanced as an imaging surrogate. It can be conveniently produced by small-sized cyclotrons via the $^{86}$Sr(p,n)$^{86}$Y nuclear reaction using enriched SrO or $SrCO_3$, and then efficiently separated and concentrated by a two-step electrochemical method.

**Methods:** Production yield of $^{86}$Y as well as applied beam current on the target was initially investigated by irradiation of 60 mg of enriched $^{86}$SrO pressed in Ø6-mm grid of Pt disc. After bombardment, the target material was dissolved in $HNO_3$ and conditioned with $NH_4OH$. The radionuclide was isolated by four electrodes in two electrolytic steps. The first electrolysis was conducted for 40 min at 2000 mA while the second electrochemical step was done with 400 mA for 15 min. After completing the electrolysis the deposited activity was then collected by immersing the Pt wire into 100 $\mu$l capillary syringe containing 70 $\mu$l of 0.2 M acetate buffer (pH 4.75). Produced $^{86}$Y was directly applied for labeling of biomolecules.

**Results:** In this work we emphasized on strontium oxide as a superior target material over strontium carbonate due to its higher thermal stability and higher content of strontium per mass unit. Using a wide range of proton currents and irradiation times, the maximum beam acceptance was determined to be 9 $\mu$A for 2h of bombardment. In those conditions we were able to produce 3 GBq of $^{86}$Y using 60 mg of $^{86}$SrO. In addition, the influence of quantities of the target material (10-60 mg) on the efficiency of the first electrochemical step was investigated and we have noticed no effect on separation yield. After irradiation, the target material was prepared for the separation of $^{86}$Y by mixing only two solutions of 3 ml 2.8M $HNO_3$ and 47 ml 0.3% $NH_4OH$. By performing electrolysis with 500-3000 mA, the first electrochemical step was optimized using 2000 mA for 40 min resulting in 98.7% of deposited $^{86}$Y on cathode. Transfer of activity on Pt wire during the second electrolysis was investigated using 200-600 mA and it was determined to be quantitative at 400 mA for 15 min. Upon completion of the electolysis $^{86}$Y re-deposited on the Pt wire was recovered in 70 $\mu$l of sodium acetate buffer resulting in an overall yield of 92.8% at EOB. Isolated in a very small volume, the final solution is directly applicable for labeling of bioactive macromolecules. The specific activity of $^{86}$Y (0.2 Ci/$\mu$mol) was determined and was found to be comparable with highly pure commercially available $^{90}$Y.

**Conclusions:** $^{86}$Y was produced by irradiation of enriched $^{86}$SrO using 14.2 MeV proton beam and a current of 9 $\mu$A resulting in yields of 167 MBq/$\mu$A•h. Improved electrochemical work-up was successfully used for separation and recovery of $^{86}$Y in a very small volume of convenient buffer solution. The isolated product was of high chemical purity what is essential for labeling of biomolecules.

## P144 A NOVEL METHOD FOR CYCLOTRON PRODUTION OF HIGH PURE 86Y

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**Objectives:** In order to predict tumor response and estimate absorbed dose in therapy, development of patient-specific dosimetry for radiolabeled compounds is essential. Yttrium-86 is a promising positron emitting radionuclide capable of serving as a PET imaging surrogate to $^{90}$Y. In addition, $^{86}$Y can be used for early detection of malignant melanoma PET imaging. It has a half-life of 14.74 hours and decays by 66% electron capture and 34% positron [1,2,3]. Yttrium-86 production via the $^{86}$Sr(p,n)$^{86}$Y reaction has gotten the most interest for the reason that it can be separated at high radionuclidic and radiochemical purity. In this method, powdered [$^{86}$Sr]$SrCO_3$ or [$^{86}$Sr]SrO have been employed as the target material. Maximum current that was applied for this aim was 15 $\mu$A [3,4]. Recently Sadeghi et al. (2009) [5] have been studied a new technique to product $^{86}$Y. In the reported method, target was prepared by sedimentation of $SrCO_3$ on the copper substrate and irradiated with a high-current beam. To separate $^{86}$Y from Sr, several techniques have been studied and used that electrolyses method done by Yoo et al. (2005) has the most separation yield of 90%. The aim of this work was to investigate the $^{86}$Y production with deposited target and separate Y from Sr by a novel technique.

**Methods:** According to calculated excitation functions from TALYS-1.0 code, entrance proton energy should be less than 16 MeV that full benefit from related excitation functions is taken and undesired radioactive impurities formation is minimized. Physical strontium carbonate deposit thickness is chosen to provide light-particle exit energy of about 6 MeV.

Results: Target was prepared by sedimenting $SrCO_3$ on the copper substrate. The thick layer of natural strontium carbonate was irradiated with 15 MeV protons at current of 30 $\mu$A. The irradiated target material was dissolved in acetone and then eluted with HCl. The obtained solution was filtered in order to remove ethyl cellulose. Then the solution was introduced on a Dowex-1x8 resin column; copper was absorbed on the resin. Separation of Y from Sr was done via a new participation method. In this technique strontium sulphate was participated and filtered.

**Conclusions:** In summary, $^{86}$Y was successfully produced by irradiation of a deposited strontium carbonate for high current bombardment for cyclotron production of Curies amounts of it. The target was bombarded at 30 $\mu$A current without any degradation. Yttrium was effectively separated from ethyl cellulose, copper and strontium. Separation yield of Y from Sr was more than 97% and the amount of strontium impurity was less than 2 ppm. To increase production yield, making use of a circulating flow of chilled helium moreover the water cooling would allow using higher beam current up to 60 mA.

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## P145 RADIOCHEMICAL SPEARATION FOR NO-CARRIER-ADDED PRODUCTION OF 68Ga

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**Objectives:** $^{68}$Ga ($T_{1/2=}$68 min, $E_{\beta^+}$=1.9 MeV, $E_{\gamma}$=0.511 MeV, $I_{\beta^+}$=89%, E.C=11%) has proposed for positron emission tomography (PET) imaging studies. $^{68}$Ga-based imaging agents to study pulmonary, myocardial and cerebral perfusion as well as renal and hepatobiliary function, to detect blood-brain barrier defect, to image tumor, brain, and bone has been investigated. It is employed for transmission measurements for encoding calibration and normalization of detector efficiencies of PET scanners.

**Methods:** $^{68}$Ga excitation function via $^{68}$Zn(p,n)$^{68}$Ga, $^{68}$Zn(d,2n)$^{68}$Ga, $^{70}$Zn(p,3n)$^{68}$Ga and $^{65}$Cu(α,n)$^{68}$Ga reactions were calculated by ALICE-ASH codes. $^{68}$Zn(p,n)$^{68}$Ga reaction was determined as the best choice for the production of $^{68}$Ga. Requisite thickness of targets were obtained by SRIM code (52 μm) and the $^{68}$Ga production yield was evaluated with attention to excitation function and stopping power calculations. Target was prepared by electroplating of Zinc-68 (97%) on a copper backing, in an alkaline cyanide bath. Bombardment of Zinc-68 plated target was performed with 15 MeV protons beams and a current of 150 μA in Cyclone30-IBA accelerator. Best conditions of precipitation method (2M NaOH, 40 ml) were obtained to separate gallium from zinc and copper. The concentration of Zn and Cu in the final product (50 ml), measured by polarography method, were 7 and 1 ppm, respectively. The chemical separation yield was 92%.

**Results:** $^{68}$Zn irradiation parameters and measured $^{68}$Ga yield for one run are in Table 1. For separation $^{68}$Ga from Zn and Cu used in this research was precipitation method. The whole chemical processing step took bout 40 minutes.

**Conclusions:** The production of yield was in agreement with previous reported. We have proposed a new method for producing $^{68}$Ga for medical purposes from enriched zinc according to the reaction (p,n) in medium-proton cyclotron. Use of 12.3 MeV proton-induced energy is mandatory, otherwise the $^{67}$Ga impurity is high. Purification of $^{68}$Ga from the proton-bombarded $^{68}$Zn target material has been achieved easily by the proposed method based on precipitation by NaOH.

Table 1. Irradiation parameters of $^{68}$Ga production

| Run | Irradiation time [h] | Beam current [μA] | $^{68}$Zn weight [mg] | $^{68}$Zn thickness [μm] | Proton energy [MeV] |
|---|---|---|---|---|---|
| 1 | 0.25 | 150 | 434 | 52 | 15 |

## P146 CYCLOTRON PRODUCTION OF Cu-64 FROM TANGENTIAL AND CUP TARGETS OF Zn-64 METAL

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**Objectives:** At the NIH, PET studies with Cu-64 ($T_{½}$=12.7 h) has relied on the use of Ni-64 internal targets [1-2]. Due to the skyrocketing cost of Ni-64 target and the publication by Abbas [3-4], we examined Cu-64 production using the $^{64}Zn(d,2p)^{64}Cu$ nuclear reaction employing the internal and external target capability of the CS30 cyclotron to determine a Cu-64 yield after separation.

**Methods:** A mixture of copper and gallium radionuclides were produced by a 1-3h bombardment of zinc metal (35±7 mg), electrodeposited on a gold internal target plate or pressed (200 mg) in an external Al cup using 10-40μA of deuteron beam. At extraction the deuteron beam energy of the CS-30 is 14.8±0.5 MeV. The irradiated zinc was dissolved in 8M HCl and Cu-64 was separated. Radionuclide mixtures were analyzed using serial count γ-spectroscopy. Periodic γ-spectra were recorded over 24 hours and the activity plotted and fitted to the decay equation $A = A_0\exp(-0.693/t_{½})t$, with the half-life ($t_{½}$) fixed for each radionuclide.

**Results:** The average Cu-64 production rate and radionuclide composition at EOB are shown in Table 1. There is a notable increase in Cu-61 production, i.e. 299% to 63% due to $^{64}Zn(d,\alpha n)^{61}Cu$ contribution with incresed Zn-64 content (48 to 99%). Ga-67 composition decreased from 20 to 1.5%. Surprisingly, there was no dramatic difference in isotope composition using an internal versus external target. For 7 runs the Cu-64 production rate for the CS-30 slant target was 9.9 and 8.5 MBq/μAh using Zn-64 metal and natural abundance Zn metal, respectively. The theoretical production rate is 12.39 MBq/μAh for natural abundance Zn at 15 MeV [3]. For 2 runs the Cu-64 production rate for the external cup target was 8.6 and 7.5 MBq/μAh using enriched and natural abundance zinc metal, respectively. Overall, there was only a 17% increase in average production rate, using an enriched metal target. However, the use of an enriched metal target reduced the exposure to Ga-67 by 90%. There was significant damage to internal plate targets and loss of Cu-64 using beam currents above 20 μAmps. This can be attributed to poor adherence of Zn on gold or to the lower melting point of zinc in vacuo compared to Ni. There was no observable target discoloration or loss using an external cup target at 20 μAmps beam current. Routinely, we produce 1 Ci of Cu-64 from Ni-64 internal target plates (40 μA x 3 h, 12.5 MeV $H^+$) with no observable target discoloration [1]. The poor experimental production rate (9.9 MBq/μAh) and target degradation over 20 μAmps precludes the use of the $^{64}Zn(d,2p)^{64}Cu$ to prepare high specific activity Cu-64. Limited quantities (~10 mCi EOB) could be prepared (10 μA x 4 h), but it is not cost efficient.

**Conclusions:** Small quantities of Cu-64 were prepared from the irradiation of Zn-64 electroplated target plates and efficiently separated. The low production rate at 14.8 MeV discourages the routine preparation of high specific activity Cu-64 for PET studies.

**References:** [1] Szajek L.P., et al. Radiochimica ACTA 93, 239-244 (2005). [2] Matasumoto K., et al. Int. J. Oncol. 30, 873-881 (2007). [3] Kozempel J., et al. Radiochimica ACTA 95, 75-80 (2007). [4] Abbas K., et al. Appl Radiat. Isot.64, 1001-1005 (2006).

Table 1: Radionuclides Normalized (±1 SD) to Cu-64 at EOB and Cu-64 Production Rates Using Zinc Internal (n=7, 14.8 MeV) and External (n=2, 14.4 MeV) Targets

| Nuclide ($T_{½}$, h) | %Cu-61 (3.33) | %Ga-66 (9.49) | %Ga-67 (78.27) | Production Rate of Cu-64 (MBq/μAh) |
|---|---|---|---|---|
| Internal (enriched) | 299 (14) | 2.1 (0.7) | 1.5 (0.4) | 9.9 (1.9) |
| Internal (natural) | 63 (21) | 0.6 (0.3) | 20 (6) | 8.5 (2.5) |
| External (enriched) | 245 (12) | 1.7 (0.8) | 1.6 (0.5) | 8.6 (0.7) |
| External (natural) | 29 (11) | 0.7 (0.1) | 15 (5) | 7.5 (1.1) |

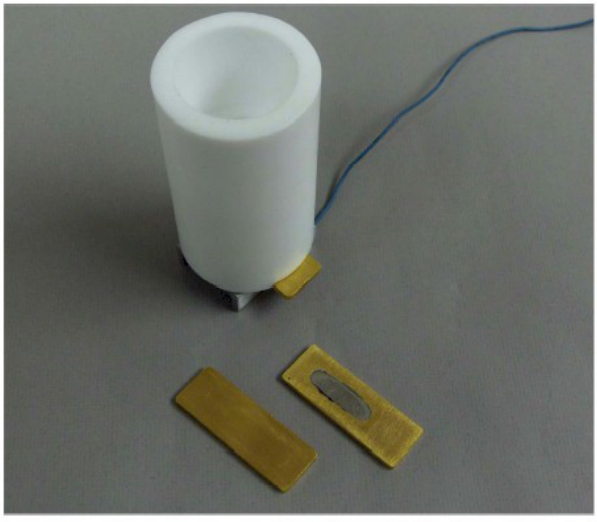

Figure 1. Simple Teflon mask for electrodepositing Zn-64 metal and internal gold target plates (5.3 cm *L* x 1.9 cm *W* x 0.3 cm *D*) with a relief (3.8 cm *L* x 0.06 cm *W* x 0.14 cm *D*) cut on one side for efficient water cooling to the rear of the target. The internal target plates are shown with and without deposited Zn-64 metal (35±7 mg).

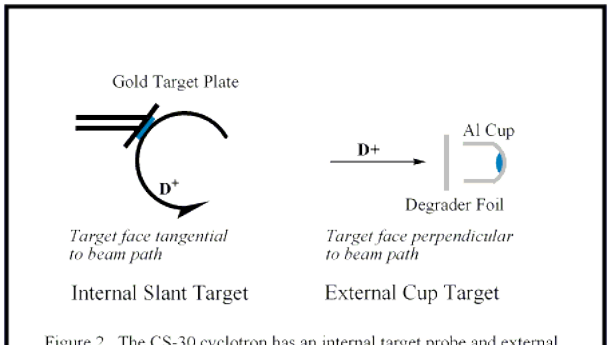


Figure 2. The CS-30 cyclotron has an internal target probe and external target station allowing for the irradiation of slant targets and aluminum cup targets over a 1-14.8 MeV deuteron beam energy range. The incident beam energy on an internal target plate is determined by its radial position from the center of the cyclotron. The extracted deuteron beam energy may be reduced using energy degrader foils of appropriate thickness before the external cup target. The internal slant target maximizes target yields because the beam path is tangential to the target material and the total length of the target material is exposed to the beam. The perpendicular incident beam on an external cup target exposes only the thickness of the target to the deuteron beam.

## P147 IMPROVING [11C]CO2 SPECIFIC ACTIVITY ON SIEMENS ECLIPSE CYCLOTRONS – THE GSK CLINICAL IMAGING CENTRE EXPERIENCE

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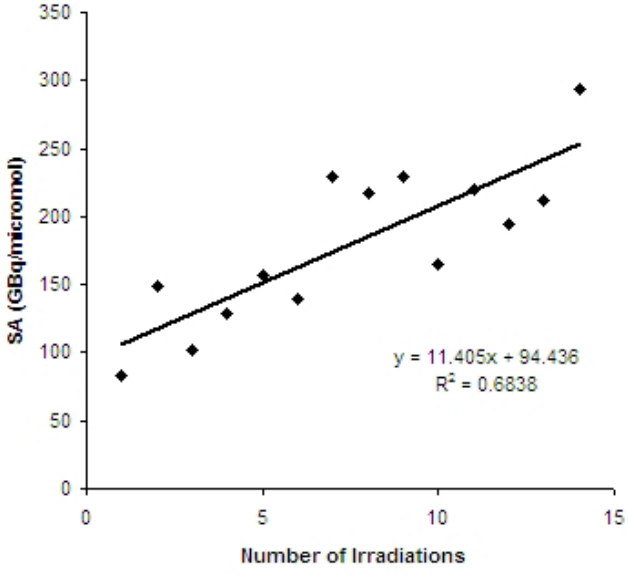
**Objectives:** The importance of imaging biological systems with PET has stressed the need for pharmacologically active compounds labelled with high specific activity (SA) radionuclides. A large proportion of $^{11}$C-labelled probes are prepared from target produced [$^{11}$C]$CO_2$ with isotopic dilution from atmospheric sources of carbon dioxide as the main contributor to decreased product SA. $^{11}$C labelling represents one of our key activities at the GSK imaging centre. We therefore systematically investigated the following factors and their contribution to $^{11}CO_2$ SA as measured by the synthesis of PHNO using Grignard chemistry: the number of consecutive irradiations on the same target and the percentage of oxygen in the nitrogen target gas.

**Methods:** [$^{11}$C]$CO_2$ was produced by the $^{14}$N(p,a)$^{11}$C nuclear reaction in a Siemens Eclipse 11Mev cyclotron using $N_2$ (6.0) containing 0.001 to 2.5% $O_2$ (5.5) as target gas in an aluminium target chamber with proton beams at currents up to 55 microAmps. Gas scrubbers were fitted between the gas cylinder and the target gas to minimise hydrocarbon based impurities entering the system. [$^{11}$C]$CO_2$ was transferred into the synthesizer module using a sweep of Helium (6N) over a distance of 30m via a 1/16 stainless steel tubing connected to a series of distribution valves. The SA was measured on the final product ([$^{11}$C]PHNO) and decay corrected to EOB.

**Results:** i) The number of consecutive irradiations on the same target: Immediately after cyclotron commissioning, PHNO SA was in the range of 100 GBq/micromole at EOB. As observed by others irradiation of the target over time reduces the cold carbon contamination and increases the SA. We observed that after 30 bombardments the SA had doubled compared to what was initially measured. IMG ii) The percentage of oxygen in the nitrogen target gas: decreasing the oxygen content in the target gas also increased the SA. Typically the average SA increased from 206 (n=8) to 380 GBq/micromole (n=9) when ratio of oxygen was reduced from 2.5 to 1%. To date the reduction of oxygen content had the biggest and most immediate impact on the SA.

**Conclusions:** Methods and procedures currently in place enable the production of batches of PHNO with SA in excess of 350 GBq/micromole at EOB (ca. 4 times better than that obtained at time of commissioning). As Grignard reagents act as natural scavengers for carbon dioxide, we feel that Grignard chemistry can represent a worse case scenario for product SA, thus in our hands, values measured for PHNO can be seen as the lower SA limit for tracers prepared via different chemistry at our site (eg methyl iodide, cyanide, carbon monoxide). Tracers labelled using [$^{11}$C]methyl iodide have been produced with specific activities of up to 1000 GBq/micromole at EOB using the above precautions.



## P148 OVERVIEW ON THE PRODUCTION OF RADIOACTIVE NANOPARTICLES FOR BIOSCIENCE APPLICATIONS AT THE JRC CYCLOTRON

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**Objectives:** Nanomaterials are already used in many applications of science and industry. Radioactive nanoparticles have the advantage that they can be accurately and precisely traced during each of the steps of their applications, thanks to the sensitivity of nuclear measurement techniques. There are already several protocols using radioactive nanoparticles, either for diagnosis or for therapeutic applications, combining the radioactivity (gamma or particle emitters) with the nanostructure in a single substance. In this paper, we give an overview of the scientific and technical activities devoted to the activation of nanoparticles. We have selected and investigated $TiO_2$, Au, $CeO_2$, Co, Ag, Re, Ho and C based nanomaterials.

**Methods:** Radioactive nanoparticles can be produced either by direct irradiation of the nanoparticles themselves or by using radioactive species as raw materials in the synthesis process. In this paper, we focus on the former production route. Direct irradiation can be performed with neutrons (in general in nuclear reactors) or with ion beams in particle accelerators (cyclotrons or LINACs). Neutron Activation: It has been observed that irradiations in nuclear reactors can damage the target nanostructure, especially if coated with organic material, due to the high gamma-radiation background. At the JRC Cyclotron, we have developed two neutron activators as an alternative to nuclear reactors for activation of nanoparticles to acceptable yields for cell/intracell uptake studies. The first activator is based on the Adiabatic Resonance Crossing concept. The neutrons are generated by protons bombarding a beryllium target. They are then slowed down in graphite and finally captured in the nanomaterial target. The second neutron activation methods is based on the thermalisation of the high neutron flux which is emitted during the daily commercial FDG production. The nanoparticles to be neutron activated are put in an appropriate neutron moderator and positioned close to the $^{18}F$ target where they can be left to increasingly activate over several days. Charged Particle Activation: The JRC cyclotron (K=40) accelerates protons, deuterons, alphas or $^3He^{2+}$ at variable energies. Neutron capture occurring in a nuclear reactor is comparable to the stripping reaction (d,p) in a cyclotron. In charged particles activation, therefore, nanoparticles/nanomaterials may be radiolabelled with a radioisotope of one of the target elements, though non-intrinsic radiolabels via (p,n) or other reactions may also be suitable.

**Results:** Table 1 gives an overview on the results of the production of a variety of radioactive nanoparticles for nanobioscience applications carried out to date using either charged particle or neutron activations.

**Conclusions:** Manufactured nanoparticles can be successfully radiolabelled by charged particles or neutrons in dedicated facilities developed for the purpose at the JRC Cyclotron. Sufficient nanoparticle activation yields have been achieved in the case of Au, $CeO_2$ and $TiO_2$ for subsequent in vitro biokinetic studies with different cell lines, and activation yields is expected to be improved.

Table 1: Result overview on the activation of nanoparticles at the JRC Cyclotron facilities

| Nanoparticles | Possible activation reactions | Half-life | Decay mode | State | Application | Tested activation routes | Achievable Yield(kBq/microA.h.g) |
|---|---|---|---|---|---|---|---|
| $TiO_2$ | $^{48}Ti(p,n)^{48}V$ | 15.97 d | b+, e | Powder | Cosmetic industry | proton | $10^3$ |
| Au | $^{197}Au(n,g)^{198g}Au$ | 2.69 d | b- | Liquid suspension | Biomedical and therapy applications | neutron | $10^3$ |
| | $^{197}Au(n,2n)^{196g}Au$ | 6.2 d | | | | | 2 |
| $CeO_2$ | $^{nat}Ce(d,x)^{139g}Ce$ | 137.6 d | e | powder | Fuel addition | deuteron | $0.4 \times 10^3$ |
| | $^{nat}Ce(d,x)^{141}Ce$ | 32.5 d | b- | | | | $4.3 \times 10^3$ |
| | $^{nat}Ce(d,x)^{143}Ce$ | 33 h | b- | | | | $1.3 \times 10^4$ |
| Co | $^{59}Co(p,pn)^{58}Co$ | 70.86 d | b+, e | Powder | Various industry and life-science applications | proton | $3.6 \times 10^4$ |
| | $^{59}Co(p,p2n)^{57}Co$ | 271.79 d | e | | | | $3 \times 10^3$ |
| Ag | $^{107}Ag(p,pn)^{106m}Ag$ | 8.3 d | e | Liquid suspension or Powder | Textile and other industries | neutron | 0.3 ($^{106m}Ag$) |
| | $^{107}Ag(n,2n)^{106m}Ag$ | | b- | | | | 0.6 ($^{110m}Ag$) |
| | $^{109}Ag(d,p)^{110m}Ag$ | 249.9 d | | | | | |
| | $^{109}Ag(n,g))^{110m}Ag$ | | | | | | |
| Carbon Black | $^{12}C(p,3d)^7Be$ | 53.29 d | e | Powder | Combustion-derived component of particulate matter | proton | $5 \times 10^3$ |
| Ho | $^{165}Ho(n,g)^{166g}Ho$ | 26.80 h | b- | Powder | Biomedical and therapy applications | neutron | $2.5 \times 10^3$ |

## P149 EVALUATION OF 67 GA-LABELED-OXYTOCIN FOR RECEPTOR

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**Objectives:** Oxytocin (OT) is a paracrine hormone with various biological activities and many sex organs in both sexes as well as many tumor cells have shown to have related receptors. There are various tissues expressing oxytocin receptors such as uterus, ovary and corpus luteum, prostate, testis etc. Notably, it has been reported that in many breast cancers oxytocin receptor is overexpression In this study development of a receptor imaging tracer for possible tumor imaging is described.

**Methods:** OT was successively labeled with [$^{67}$Ga]-gallium chloride after conjugation with freshly prepared cyclic DTPA-dianhydride. Radiochemical purity (RCP) of the labeled compound was determined using RTLC and ITLC followed by stability tests and animal biodistribution studies.

**Results:** Radiolabeling took about 60 minutes with a RCP higher than 98 % at optimized conditions (specific activity = 1000 Ci/mM, labeling efficiency 80%). Preliminary in vivo studies in normal female rat model showed ovary/blood and ovary/muscle ratio uptake of the tracer in 60 minutes to be 4.53 and 9.18 respectively which is consistent with reported OT receptor distribution in normal female mammals.

**Conclusions:** The final preparation was administered to normal rats and biodistribution of the radiopharmaceutical was checked 30 and 60 minutes later. In 30-60 minutes radiolabeled hormone is cleared from blood circulation and most of the tracer accumulates in ovaries. A more detailed study on this radiotracer is suggested using MCF-7 or other breast cancer cell lines as well as SPECT imaging studies in a bigger mammalian model in order to better demonstrate the imaging value of the tracer.

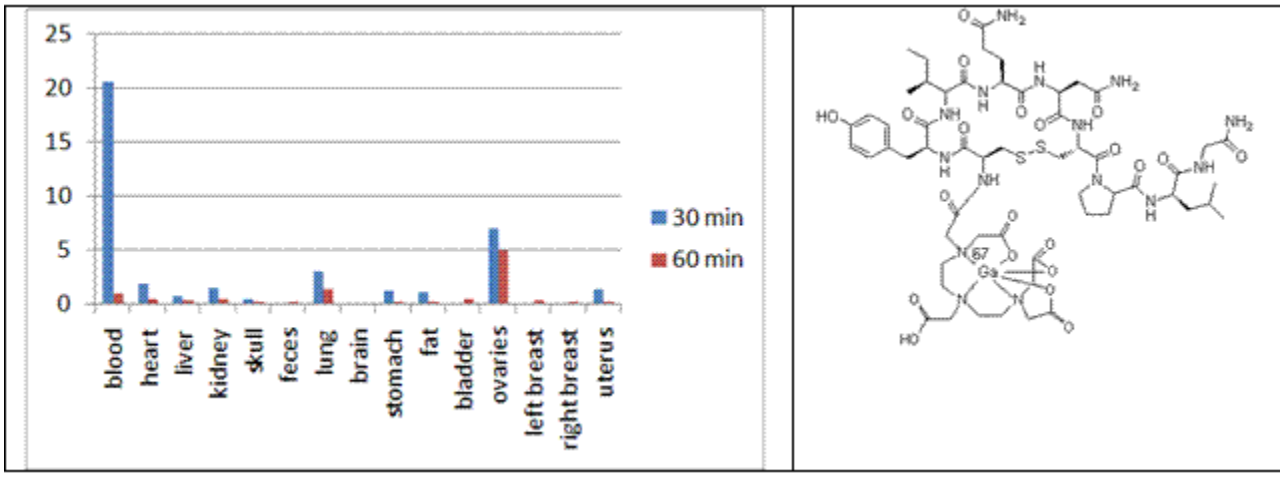


Figure: Biodistribution of $^{67}$Ga-OT in normal female rats (left) and its molecular formula (right)

## P150 INVESTIGATING WASTE STREAMS FROM 68GA CHEMISTRY

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**Objectives:** PET scintigraphy with $^{68}$Ga labeled analogs is of increasing interest in Nuclear Medicine and performed at ≈ 40 centers in Europe. $^{68}$Ge breakthrough from $SnO_2$-or $TiO_2$-based $^{68}$Ge generator varies between 0.01-0.001 % (% activity of $^{68}$Ge over $^{68}$Ga; t½ $^{68}$Ge: 9 months). European Directive 96/29/EURATOM holds for all countries in the EU and states [$^{68}$Ge] may not exceed the clearance level of 10 Bq per gram. National legislation within the EU may vary per country, but may only be more strict, e.g., Dutch legislation does not allow to store radioactive waste with half-lives of more than 100 days at local institutes for more than 2 years. It is obligatory to store this waste in a special external waste facility. In addition, in this facility waste is preferably compressed, presence of liquids is therefore limited to < 1%. Therefore, our aims were to quantify $^{68}$Ge in our waste and to concentrate and transform $^{68}$Ge-containing liquid waste to solid waste. In short: $^{68}Ge_{liq} \rightarrow {}^{68}Ge_{solid}$.

**Methods:** Several concentration techniques (Molecular Sieves (4A & 5A), cation and anion exchange) from the eluates of the generator and left-overs of labelings were evaluated, including acetone and ethanol. Sedimentation of $^{68}$Ge after the addition and homogenization of variable amounts of $TiO_2$ (325 mesh), pH range 3 – 10 was investigated time-dependently. From 1 till 24 hours mixing, the samples were centrifuged at 350 g, supernatant decanted and [$^{68}$Ge] determined. Parallel experiments were performed with $Fe_2O_3$ (500 mesh), pH range 1-10.

**Results:** Efficient methods for transforming liquid in solid waste were the addition to the solution of 1 gram $TiO_2$ per 250 mL, pH range 8 -10 and subsequent centrifugation. $Fe_2O_3$ also lowers [$^{68}$Ge] below intended10 Bq per gram, whereas $TiO_2$ reaches this level asymptotically. Preferred procedure was with $Fe_2O_3$, which eliminated >90% of the $^{68}$Ge per treatment, e.g. [$^{68}$Ge] from >10 kBq per mL to <10 Bq per mL in <6 treatments. During the last 5 years of daily practice with 4 $TiO_2$- and 4 $SnO_2$-based $^{68}$Ge generators (0.4 to 2 GBq per generator) the total amount of $^{68}$Ge was ≈ 160 MBq in 48 L and could be concentrated down to ≈ 160 MBq in <5 kgram solid waste.

**Conclusions:** $^{68}$Ge containing liquid waste from $^{68}$Ga PET chemistry can be concentrated and solidified. Developments of robotics are ongoing.

## P151 A NOVEL ELECTROCHEMICAL 90Sr/90Y GENERATOR

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**Objectives:** $^{90}$Y, a radionuclide well suited for endoradiotherapy, is distributed from specialized production sites where stocks of $^{90}$Sr are routinely processed. The state of the art of $^{90}$Sr/$^{90}$Y separation technology is not applicable to hospitals for safety reasons, thus a large portion of the cost of $^{90}$Y therapy comes from transportation. New technologies are needed in order to provide the possibility of local distribution of $^{90}$Y from remotely operated generator systems, making this therapeutic agent available at more competitive price.

**Methods:** Electrochemical separation of $^{86}$Sr/$^{86}$Y is nowadays well established and used for the production of $^{86}$Y. The same basic principle has been applied in developing an automated generator for daily $^{90}$Y supply. The generator consists of a shielded reservoir containing a stock solution of $^{90}$Sr of high purity, being in transient equilibrium with $^{90}$Y. A fraction of this stock solution is transferred to the electrochemical cell, where a two step separation is performed using platinum electrodes. After the separation the solution from the electrochemical cell is transferred back to the stock solution maintaining the total $^{90}$Sr inventory practically constant. Due to the fact that only a portion of the stock solution is processed one can milk the generator every day providing practically the same yield day after day. The operation of the generator is completely automated and computer controlled and it is suitable for installation in general purpose hotcells. Operators are required only to insert the empty and to remove the vial with the product from the hotcell and to replace the sterile filters prior to milking the generator. Small amounts of $^{90}$Sr lost during the washing procedures are collected in a dedicated reservoir and can be recovered from time to time if required.

**Results:** The separation procedure typically lasts for 60 min and the final product is formulated in 0.05 M HCl having a total volume from 0.25 to 2.0 ml. The vial with the product can be autoclaved and the preparation is suitable for labeling monoclonal antibodies and peptides. Depending on the activity concentration of the stock solution of $^{90}$Sr, batch sizes of 37 GBq $^{90}$Y can be made available on daily basis. The most critical quality factor of $^{90}$Y is its contamination with $^{90}$Sr. This generator allows for the production $^{90}$Y with radionuclidic purity complying with the applicable pharmacopoeia.

**Conclusions:** The newly developed $^{90}$Sr/$^{90}$Y generator allows for daily production of 37 GBq $^{90}$Y batches and local distribution from specialized regional centers. Widespread use of this technology could bring targeted radioimmunotherapy to a significantly larger number of patients even in developing countries.

## P152 POST-PROCESSING OF 44Ti/44Sc-RADIONUCLIDE-GENERATOR FOR MEDICAL APPLICATION

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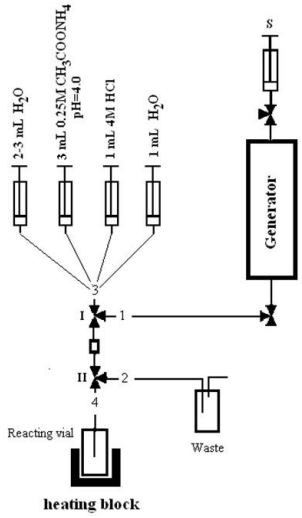
**Objectives:** The $^{44}$Ti/$^{44}$Sc generator provides cyclotron-independent access to positron-emitting $^{44}$Sc for application in PET radiopharmaceuticals. The $^{44}$Sc solution that can be obtained from generator is too diluted and too acidic for use in direct labeling procedures. The aim of this work was to design and to analyse the performance of a $^{44}$Ti/$^{44}$Sc radionuclide generator for medical application.

**Methods:** Post-elution processing studies were performed to reduce the volume and acidity of $^{44}$Sc-eluate from $^{44}$Ti/$^{44}$Sc generator and to reduce amount of $^{44}$Ti in the final product for the syntheses of $^{44}$Sc-labelled radiopharmaceuticals. It was developed, similar to the one developed for the $^{68}$Ge/$^{68}$Ga radionuclide generator [1]. The $^{44}$Ti/$^{44}$Sc generator was eluted with 20 ml mixture of 0.005 M $H_2C_2O_4$/0.07 M HCl. The retention of the $^{44}$Sc eluate was checked on micro-chromatography columns, filled with 80 mg of cation-exchange resin AG W50x8 (200-400 mesh, $H^+$-form). The columns were dried by passing air through them to remove the rest of eluate, then washed by 3 ml $H_2O$ and dried once again. Several solutions at various volumes and concentrations were used to elute $^{44}$Sc from the columns. Finally micro-chromatography column (~2 mm inner diameter, ~5 mm length) was prepared using two 3-way valves filled with 53 mg of cationit. The $^{44}$Ti/$^{44}$Sc radionuclide generator was connected to the valves via tubing. The $^{44}$Sc-eluate mixture was transferred on-line within 20 min through the column. Subsequently, the column was washed by 3 ml $H_2O$ and dried by air. Then, 3 ml of 0.25 M ammonium acetate, acidified to pH = 4.0 by drop-wise addition of acetic acid were passed slowly through the column and the $^{44}$Sc eluate was collected in a 10 ml glass vial. The aliquots of consecutive fractions were collected and measured according to the activity of $^{44}$Sc and $^{44}$Ti using dose calibrator and g-spectroscopy.

**Results:** To reduce the volume of the $^{44}$Sc eluate, a 3-valves cartridge with 53 mg of cationic resin AG W50x8 was connected with the generator on-line. Recently, the eluate passes through the cartridge and $^{44}$Sc is adsorbed on the cationic resin, from which it can be eluted by 3 ml of 0.25 M ammonium acetate, pH=4.0. This solution is ready for labelling with peptides and other biomolecules. Finally, the cartridge is reconditioned by washing with 1 ml of 4 M HCl and 1 ml of water. The scheme of the generator together with post-elution processing is presented on Figure.




**Conclusions:** On-line post-elution processing of $^{44}$Ti/$^{44}$Sc-radionoclede generator is performed on the small cationic cartridge. In the final point, around 160 MBq of $^{44}$Sc is obtained daily in 3 ml 0.25 M ammonium acetate buffer (pH=4.0). This solution can be used for labeling of biomolecules.

**References:** [1] K.P. Zhernosekov, D.V. Filosofov, R.P. Baum, P. Aschoff, H. Bihl, A.A. Razbash, M. Jahn, M. Jennewein, F. Roesch, Procesing of generator-produced $^{68}$Ga for medical application, J. Nucl. Med. (2007), 48, 1741 1748.

## P153 PRODUCTION AND QUALITY CONTROL OF HIGH SPECIFIC ACTIVITY NCA Re-186 BY CYCLOTRON IRRADIATION

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**Objectives:** The applications of the radionuclides play a fundamental role in life sciences and in particular nowadays is becoming an indispensable branch of medical science with the radionuclides and labeled compounds production for medical applications. The Re-186g is a negatron-gamma emitter presently used in metabolic radiotherapy with optimal perspectives to be used in radioimmunotherapy too, thanks to its suitable nuclear properties: $t_{1/2}$=90.64 h, main $E_\gamma$=137 keV, $E_{\beta,max}$=1 071 keV, energy range suitable to treat cancers with dimensions from few mm to a few cm. The possibility to use this radionuclide for therapeutic purposes is linked to the possibility to increase its specific activity $A_S$, substituting the common (n,γ) reaction on Re-185 with the (p,n) or (d,2n) cyclotron production on W-186 targets, followed by a selective radiochemical separation of the product in no-carrier-added form from both W target and Ta co-produced radionuclides.

**Methods:** In order to optimize the Re-186g production as by (p,n) as by (d,2n) induced nuclear reactions, the thin-target excitation functions (ttys) were measured by using the stacked-foil technique at different irradiation energies, at the MC40 cyclotron of the JRC, Ispra, Italy. The experimental thick-target yields TTYs were measured both for W-nat foils as for highly enriched W-186 pressed powder and compared with the ones obtained by integration of the experimental ttys and, if present, with literarture data . Autoabsorption corrections were taken into account for the accurate determination of TTYs. A radiochemical separation was set up. The target was solved in a $HNO_3$/HF mixture. The radioactive solution obtained contains the anions of $WO_4^{2-}$ and [$^{18x}$Re] $ReO_4^-$ . The separation was obtained by ion-exchange radiochromatography, using activated aluminium oxide as stationary phase. Quality control tests have been carried out for chemical, radiochemical and radionuclidic purities, by use of ET-AAS and HPGe spectrometries.

**Results:** The results obtained demonstate that (d,2n) production route is preferable than (p,n) one: in particular the TTY values are larger, the contamination by Ta radioisotopes is less, the RNP of the Re-186g is very high and remains higher for more time, the amount of the target requested is less, which simplify the separation of the Re-186g. In the eluted solution are presented only Re isotopes while W remains on the column. The chemical metallic impurities are generally of the order of 200 ppm exept for Al.

**Conclusions:** Even if there is a very short energy range in which proton irradiation is competitive with the deuteron one, there is no reason to prefer proton beams, as for physical as for radiochemical aspects. It was demonstarted the necessity to use high enriched target in order to obtain the high specific activity required for radiopharmaceutical applications.

**Research Support:** The present research work was funded in the mainframe of the experiment RENIO of the Commission V of INFN and the MIUR, Italy. The contributions of JRC-Ispra of European Community and ENEA-Bologna were substantial.

## P154 AUTOMATED PROCESSING OF COPPER AND HALOGEN RADIONUCLIDES AT WASHINGTON UNIVERSITY

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**Objectives:** At Washington University, we have been producing a series of non-standard positron emitting radionuclides including copper-60, copper-64, gallium-66, bromine-76, and yttrium-86, and iodine-124 for several years. These nuclides are produced for in-house studies and are distributed to many institutions throughout the United States as well. Over the past several years, we have developed and constructed automated production modules for these radionuclides, and currently, these are being operated in the Washington University School of Medicine cyclotron facility. Though the modules are in use for the production of Cu-64 and Br-76, the Br-76 module can also be utilized to produce radionuclides such as Br-77 and I-124. These systems were designed to be installed inside BBS mini-cells from Comecer that were specially adapted for use with the non-standard radionuclides. Additional shielding at the hinge door is provided with 90 mm thick lead to reduce the radiation dose.

**Methods:** The modules in use are constructed using primarily commercially available materials. Only few items are custom-made by the group. Performax digital and analog input output (I/O) controllers and Opto 22 I/O modules are used for the control logic of the synthesis. An in-house program controls both syntheses, and operator monitoring and interaction are possible throughout the process with a set of user-interface windows. Setup of the module for processing is straightforward. The copper module consists of a Teflon reaction vessel for target dissolution, a series of Teflon based solenoid valves and a vacuum to direct the flow of liquid to and from the anion exchange column, and a heater where the final copper is evaporated. The bromine module consists of a high temperature compact furnace with a tapered quartz processing tube for dry distillation, an auxiliary 200°C heater adjacent to the furnace, a valve and a vacuum to direct the flow of liquid and gas, and a heater where the bromine is evaporated under argon.

**Results:** The yields of these nuclides have been compared to those of the same nuclides prepared by a manual process, and the yields are relatively unchanged. The specific activity of Cu-64 has also been compared and was found to have improved from a mean ESA of 139.5 to 237.5 mCi/$\mu$mol. Quality control procedures are routinely carried out as these nuclides are used in biological studies, with Cu-64 being provided for several patient studies. The following table summarizes several of the important quality control results for the production of Cu-64. Br-76 is prepared in ~60% yield (n=14) with very low radionuclidic impurities.

| | n | Radionuclidic Impurities % vs. $^{64}Cu^{i}$ ($\sigma_{std}$) | | IC[ii] ppm ($\sigma_{std}$) | | EOS Yield[iii] % ($\sigma_{std}$) |
|---|---|---|---|---|---|---|
| $^{64}Cu$ | 26 | $^{55}Co$ | 0.0 | Fe | 0.296 (0.094) | 73.4 (10.7) |
| | | $^{60}Cu$ | 0.0 | Cu | 0.112 (0.105) | |
| | | $^{61}Co$ | 4.37 (2.3) | Ni | 1.144 (0.876) | |
| | | $^{61}Cu$ | 0.0 | | | |

i. QC Ge analysis performed on sample for 10 minutes
ii. n = 3
iii. recovered activity @ EOB /initial target activity @ EOB

**Conclusions:** We have shown it is possible to automate the production of a series of non-standard radionuclides using modules designed in-house. These modules have proven to be reliable and able to produce the radionuclides in yields and at specific activities comparable to those by manual processing. We are in the process of automating the other non-standard nuclides used at Washington University.

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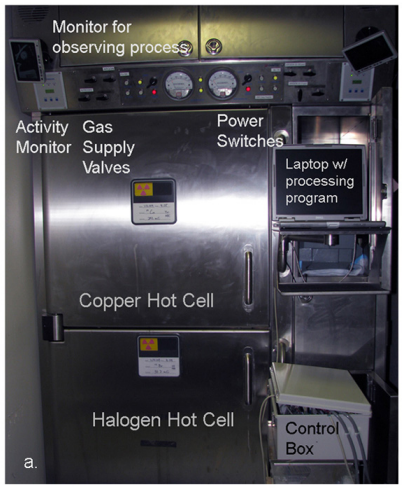


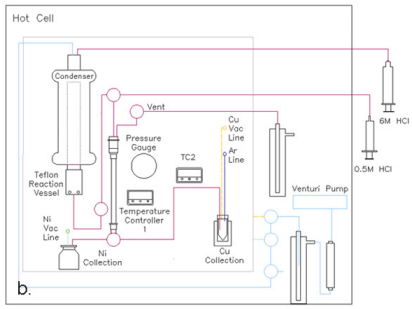


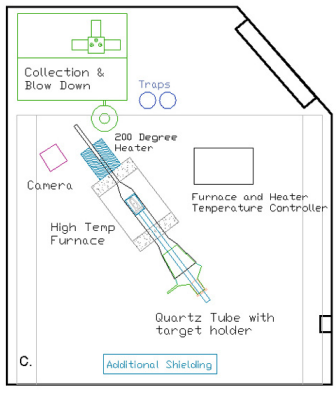


a. Comecer BBS Minicells for automated nonstandard radionuclide processing
b. Schematic of the copper module
c. Schematic of the halogen module

## P155 INVESTIGATION OF PRODUCTION OF THE MEDICAL RADIOISOTOPE 167TM VIA CHARGED PARTICLE INDUCED REACTIONS

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**Objectives:** $^{167}$Tm ($T_{1/2}$ = 9.25 d, $E_g$(average) = 147.2 keV, $E_e$(average) = 124.2 keV, $\Delta$ = 1.425 gGy/MBqday) is a candidate radioisotope both for diagnostics and therapy. Excellent tumour imaging was obtained with $^{167}$Tm-citrate. It is on the list of nuclides potentially useful for therapy by emission of Auger-electrons. The aim of the present study is to investigate charged particle induced routes for production of $^{167}$Tm directly or through decay of $^{167}$Lu ($T_{1/2}$ = 51.5 min) and $^{167}$Yb ($T_{1/2}$ = 17.5 min).

**Methods:** This work presents new experimental measurements of proton induced reactions on $^{nat}$Er, $^{167}$Er, $^{169}$Tm and $^{nat}$Yb, deuteron induced reactions on $^{nat}$Er and $^{167}$Er and alpha-particle induced reactions on $^{165}$Ho using the activation method and stacked target irradiation technique. Irradiations of metal foil targets and sedimented oxide targets were performed at the external beam of AVF 930 cyclotron of CYRIC, CGR 560 cyclotron of VUB, and MGC 20E cyclotron of ATOMKI. Activities of the irradiated samples were measured nondestructively by high resolution gamma-ray spectrometry, without any chemical separation.

**Results:** Excitation functions were measured using different bombarding beams for the $^{167}$Er(p,n)$^{167}$Tm, $^{166}$Er(d,n)$^{167}$Tm, $^{167}$Er(d,2n)$^{167}$Tm, $^{169}$Tm(p,3n)$^{167}$Yb, $^{nat}$Yb(p,x)$^{167}$Lu and $^{165}$Ho(a,2n)$^{167}$Tm nuclear reactions for the first time. Theoretical calculations were made by means of the ALICE-IPPE, EMPIRE-II and TALYS nuclear reaction model codes to predict the excitation functions. The theoretical results were compared with the experimental data. Integral yields for production of $^{167}$Tm were calculated from the experimental cross section data. Radionuclidic purities and specific activities were deduced for the investigated processes.

**Conclusions:** On the basis of the production yields, the required target technology and the easily accessible accelerator characteristics (particle type, energy) the most promising reactions are: at low energies (up to 20 MeV) $^{167}$Er(p,n)$^{167}$Tm, at medium energies (up to 40 MeV) $^{169}$Tm(p,3n)$^{167}$Yb→$^{167}$Tm and $^{167}$Er(d,2n)$^{167}$Tm. At higher energies (up to 100 MeV) the $^{nat}$Yb(p,x)$^{167}$Lu→$^{167}$Yb→$^{167}$Tm route has importance additionally allowing simultaneous production of $^{167}$Tm and the therapeutic $^{169}$Yb. Production of $^{167}$Tm via $^{167}$Er(p,n) reaction results in moderate high yield. To assure high radionuclidic purity, a highly enriched $^{167}$Er target is required (natural abundance: 22.95%). By using proton induced reactions on stable isotopes of Tm and Yb, $^{167}$Tm can be obtained indirectly in high yield through production and decay of $^{167}$Lu and $^{167}$Yb but the specific activity and the radionuclidic purity is lower compared to enriched $^{167}$Er(p,n) reaction.