FORMATION CROSS SECTIONS AND YIELDS OF ^{82}Sr AND ^{124}I IN INTERMEDIATE ENERGY REACTIONS

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The radionuclide ^{82}Sr ($T_{½}$ = 25.5 d) is the parent of the most commonly used generator system (^{82}Sr/^{82}Rb) in PET studies. It is produced either via the spallation process or the ^{85}Rb(p,4n)^{82}Sr reaction. The cross section data for the latter route were found to be somewhat discrepant [1]. We performed detailed cross section measurements [2] on the ^{85}Rb(p,xn)^{81,82,83,85m,g}Sr reactions up to 100 MeV using 99.4 % enriched ^{85}Rb as target material. The yield of ^{82}Sr calculated over the proton energy range of 40 to 60 MeV was found to be about 30 % lower than that obtained from the old literature data but is in agreement with a recent value [3] based on new measurements on ^{nat}Rb. In a further experiment we determined the thick target yield of ^{82}Sr experimentally using 1-10 g ^{nat}RbCl targets and low beam currents. Radiostrontium was radiochemically separated and the activity determined via ?- and X-ray spectrometry. The yield of ^{82}Sr and the impurity level of ^{85}Sr agreed well with the values calculated from our cross section data. The new results thus explain some of the discrepancies between theoretical and experimental yields of ^{82}Sr reported in the literature.

A second radionuclide of increasing significance is ^{124}I ($T_{½}$ = 4.18 d). It is both a diagnostic and a therapeutic radionuclide. It was originally produced via the ^{124}Te(d,2n)^{124}I reaction but now the ^{124}Te(p,n)^{124}I reaction is the method of choice [4 - 6]. Recently the ^{125}Te(p,2n)^{124}I reaction was also thoroughly studied [7]. Now we investigated the ^{126}Te(p,3n)^{124}I process in detail. Excitation functions of all the (p,xn) reactions on 99.8 % enriched ^{126}Te were measured up to 70 MeV and the theoretical yields of the products were calculated. The energy range Ep = 35 ? 25 MeV appears to be suitable for the production of ^{124}I but the finally recommended range will depend upon the levels of ^{126}I and ^{125}I impurities, which are presently being analysed. It appears that both ^{125}Te(p,2n)^{124}I and ^{126}Te(p,3n)^{124}I reactions can be used for production of large amounts of ^{124}I. However, in both cases the level of the radionuclidic impurity will be higher than in the ^{124}Te(p,n)^{124}I process.

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A SOLID TARGET FOR THE SIMULTANEOUS PRODUCTION OF CO-57 AND CD-109 WITH HIGH INTENSITY PROTON BEAM

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Keywords: Co-57, Cd-109, high intensity target

We have sought to develop a solid target for the SUNY Buffalo 30 MeV cyclotron capable of withstanding high proton beam intensity in order to simultaneously produce large quantities of the useful isotopes ^{57}Co ($t_{1/2}$ = 271.79d) and ^{109}Cd ($t_{1/2}$ = 462.6d). Short low intensity irradiations of natural nickel were used to choose the proton energy window to optimize ^{57}Co production and minimize unwanted impurities. Finite element design software was applied to mechanically and thermally model the target and choose proper material thickness, cooling channel geometry, water flow rates, desired beam intensity profile etc.

A target insert with 0.04mm layer of enriched ^{58}Ni was electroplated onto a 0.07mm silver layer electroplated on a water cooled copper backing. This scheme allows a beam exiting the nickel layer to produce ^{109}Cd and avoids copious production of unwanted ^{65}Zn in the copper backing. The high energy gamma rays emitted by ^{65}Zn and its long half-life complicate target handling and transport to BNL for processing. The high thermal conductivity of silver assures good heat transport to the cooled copper backing. The overall dimension of the insert is 8.1cm x 3.1cm x 1.5cm with nine thin cooling channels cut into the underside. The insert is compressed against a gasket in the copper target assembly to form a water/vacuum seal. The entire target assembly is tilted 7 degrees with respect to the beam axis in order to reduce power density. It can be remotely removed from the beam line vacuum system.

The best combination of ^{57}Co yield and radiopurity was achieved with an energy window of 20-15 MeV. The 15 MeV residual proton energy is ideal to make ^{109}Cd by the ^{109}Ag(p,n) reaction, and the silver layer is just thick enough to stop all protons from reaching the copper backing plate. This reduced the production of ^{65}Zn in the copper. A target with natural nickel was irradiated at 20 MeV up to 100μA beam current. There was no evidence of melting, flaking, mechanical distortion, or sputtering. A preliminary ^{57} Co yield determination measured 15.8μCi/μAh.

Further target testing up to 350μA beam current is planned. Optimization of isotope yield and radiopurity is ongoing.

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MACROSCOPIC SYNTHESES OF ARSENOORGANIC PRECURSORS AND FIRST NO-CARRIER-ADDED RADIOARSENIC LABELLING

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Keywords: arsenic, precursor, mercaptanes

The long-lived ^{72}As represents an interesting positron emitter with potential for PET. A new $^{72}Se/^{72}As$-generator based on solid phase extraction techniques delivers no-carrier-added (nca) AsI_3 [1,2]. The subsequent step for the future labelling of biomolecules with radioactive arsenic isotopes is to synthesize a small precursor molecule based on AsI_3 by inhibiting binding sites of two of the arsenic in oxidation state +III with a very stable compound while one binding site remains for coupling to a biomolecule, e.g. via nucleophilic substitution. This work describes the macroscopic and nca syntheses of dimercapto arsenic iodides and diphenyl arsenic iodides.
To simulate the behaviour of ^{72}As, ^{77}As was used as produced at the TRIGA reactor at the University of Mainz via following reaction: $^{nat}Ge(n,\ )^{77}Ge(T_{1/2}=11.3\ h) \xrightarrow{-} {}^{77}As(T_{1/2}=38.8\ h)$.

Synthesis of dimercapto arsenic iodides:
147.90 mg AsI_3 (0.325 mmol) are dissolved in 5 ml anhydrous dichloromethane. The mixture is stirred under argon, cooled with liquid nitrogen and protected against light. An equimolar amount of a dimercapto compound and 51.3 µl pyridine (0.65 mmol) are added. The mixture is then allowed to warm up and stirred for 1 hour at room temperature. Formed pyridinium salts are removed via filtration. FD-MS is performed directly with this solution. To isolate the solid yellow products, the solvent is removed in an Ar-stream.

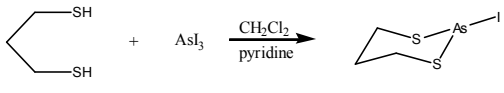

Fig.1: Reaction scheme for the synthesis of 1,3-dimercaptopropyl arsenic iodide

Synthesis of diphenyl arsenic iodide:
1 g diphenyl mercury (2.82 mmol) are dissolved in 15 ml toluene and are heated up to 60°C under stirring. 1.28 g arsenic triiodide (2.82 mmol) are suspended in 15 ml toluene and added dropwise. The mixture is refluxed for 1 h at 130°C. FD-MS is performed directly with this solution. To further proof their existence they have been derivatized to stable compounds.

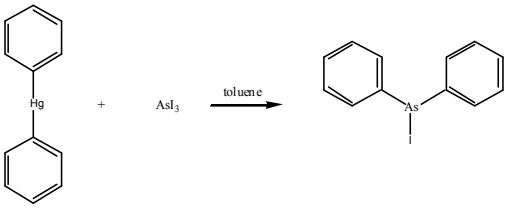

Fig. 2: Reaction scheme for the synthesis of diphenyl arsenic iodide

The nca synthesis of dimercapto arsenic and diphenyl arsenic iodides was performed according to the procedures above, using nca $^{77}AsI_3$. The radiochemical yield of the nca synthesis is above 99%. Thus, two types of arsenoorganic precursors could be synthesized for future labelling experiments. As instable reactive intermediates, they could only be analyzed by FD-MS.

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CROSS SECTION DATA AND TECHNOLOGICAL DEVELOPMENT FOR PRODUCTION OF ^{64}Cu AND ^{67}Cu VIA NOVEL ROUTES

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Keywords: Therapeutic radionuclide, ^{64}Cu, ^{67}Cu, excitation function, targetry

The radionuclides ^{64}Cu ($T_{½}$ =12.7 h, E - = 0.6 MeV, E + = 0.7 MeV) and ^{67}Cu ($T_{½}$ = 61.9 h, E - = 0.6 MeV) are finding increasing applications in endoradiotherapy. ^{64}Cu has the extra advantage of in-vivo detection via PET. For the production of ^{64}Cu the ^{64}Ni(p,n)-process is the method of choice[1,2], and for ^{67}Cu the ^{68}Zn(p,2p)-process[3-5]. For the latter, recently the ^{70}Zn(p,)^{67}Cu reaction has also been suggested[6] . In this work we report new studies in three directions.

a) Excitation function measurements via the stacked-foil technique for the ^{nat}Zn(d,x)^{64}Cu and ^{66}Zn(d,)^{64}Cu reactions from 5 to 14 MeV, for the ^{68}Zn(p, n)^{64}Cu process from threshold up to 35 MeV and for the ^{64}Ni(,p)^{67}Cu reaction from 5 to 27 MeV. Measurements on the first three reactions involved extensive radiochemical work. Some empirical yield information on a few of these reactions was available. However, for all the four reactions our data constitute the first systematic cross section measurements. Calculated yields show that for ^{64}Cu production the best route is still the ^{64}Ni(p,n)-reaction. The ^{nat}Zn(d,x)^{64}Cu reaction could be interesting if the available energy of deuterons would be a few MeV higher than 14 MeV.

b) Measurement of ^{64}Zn(n,p)^{64}Cu and ^{67}Zn(n,p)^{67}Cu reaction cross sections with 14 MeV d(Be) breakup fast neutrons using radiochemical techniques. The cross sections of both reactions with fast neutrons were found to be about six times larger than with fission neutrons.Thus the yields of both, ^{64}Cu and ^{67}Cu, in a future intense fast neutron source, e.g. a spallation source, would be much higher than in the present day fission reactors.

c) Technological development on the production of ^{67}Cu via the ^{70}Zn(p,)-process. About 70 % enriched ^{70}Zn was electroplated on a wedged target made of copper whose surface was gold plated. The target could withstand a slantig beam of 20 A intensity of 20 MeV protons falling on the target at an angle of 20°. The radiocopper was radiochemically separated and the enriched target material recovered for reuse with an efficiency of about 90 %. The product is of good radionuclidic purity, the only impurity being ^{64}Cu (< 10 %). The batch yield is not very high but the feasibility of the process is demonstrated. The yield could be considerably increased by using a thicker target and higher proton energy.

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PRODUCTION OF CARRIER FREE RADIOISOTOPES FOR RADIOTHERAPY

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Radioisotopes have different nuclear properties such as half-life and particulate emission energy that can be optimized to deliver the strength required to ablate the tumor while sparing nearby healthy tissue. We at MURR are working on the development of a class of isotopes that have similar chemical properties so they can be attached to a variety of targeting agents, but of differing strengths so that radiopharmaceuticals can be tailor-made to ablate the specific patient's cancer. Recently we have been focusing on increasing the strength or radiation impact that can be delivered. MURR researchers have been focusing on the production of radiolanthanides because their similar chemistry makes them interchangeable, and their various half-lives and beta energies make them suitable for different applications. Their high neutron cross sections allow them to be made cheaply, easily and in the large quantities required for therapeutic medical applications. Isotopes successfully developed and produced include samarium-153 (Sm-153) for the FDA-approved drug Quadramet for pain palliation; holmium-166 (Ho-166), used in clinical trials in the Skeletal Targeting Agent for treatment of multiple myeloma; and lutetium-177 (Lu-177), used in clinical trials for the treatment of a variety of cancers. MURR routinely provides these isotopes by direct production.

The specific activities of Ho-166 and Sm-153 produced by this method (0.31% and 1.4 %, respectively) are too low for use in receptor targeting agents. Due to the large production cross-section of Lu-176, the specific activity of Lu-177 produced by direct production is high enough for some applications (but not all), so MURR is now developing indirect neutron capture methods for the production of high specific activity radioisotopes suitable for receptor targeting radiopharmaceuticals. High specific activity radioisotopes such as Lu-177, Pm-149, Ho-166 and Rh-105 can be produced by indirect methods involving neutron irradiation of isotopically enriched (e.g. Ru-104) targets producing parent radioisotopes that beta decay to form the desired daughter radioisotopes. For example, Pm-149, an analog of Sm-153, can be produced by direct (n, gamma) irradiation of Nd-148. Direct irradiation of Nd-148 results in the production of Nd-149 (half-life = 1.7 hr) that beta decays to form Pm-149. Chemical separation of the Pm-149 from the Nd target results in a high specific activity Pm-149 that can then be used for radiotherapy. Separating these radionuclides from the target will enable us to provide them carrier-free and therefore suitable for developing receptor targeted radiotherapeutic agents. These radiolanthanides exhibit a wide range of half-lives and beta energies and due to their similar chemistry can be used interchangeably using the same or similar radiolabeling techniques. The successes and challenges of these separations will be presented.

NOVEL SEPARATION OF ULTRA PURE HIGH SPECIFIC ACTIVITY CU-64

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Keywords: Cu-64, Cu-67, Separation, Zn-68, co-production

Copper-64 ($T_{1/2}$ 12.7 hr) has been identified as one of the emerging PET isotopes. While ^{64}Cu may be readily produced in a reactor or a cyclotron, the limiting factor in its commercial availability appears to be the result of either poor specific activity (< 1000 Ci/gram at EOB), poor yields, contaminating isotopes, or the cost of target material.[1-9] Its routine production in an ultra pure state and at high specific activities remains a challenge.

Cu-64 and ^{67}Cu were reported to be co-produced during routine commercial production of ^{67}Ga.[10] Preliminary work by us demonstrated for the first time the separation of ^{64}Cu from the ^{67}Ga production process.[11] Since that time we have conducted a comprehensive study on the binding affinity of ^{64}Cu and ^{67}Ga as well as contaminating radioisotopes with hydrochloric acid / organic solvent mixtures with anion exchange resin AG1-X8. Solvent mixtures ranged from 0.2 – 3.0 M hydrochloric acid and 35 % to 95 % organic solvents, such as, ethanol, methanol, isopropyl alcohol and acetone.

Classical methods employed in the separation of radioisotopes usually involve binding the desired radioisotope onto a cation or anion exchange column and washing off all unwanted radioisotopic contaminants and target material. The desired isotope is then removed by a second wash. In the present study, the approach was the reverse; we sought to bind the enriched target material, ^{68}Zn, and then progressively elute the desired radioisotope/s and contaminating radioisotopes from the column. This provided an opportunity to simultaneously purify the enriched target material and also isolate a number of radioisotopes. Using the distribution coefficients for the above mentioned conditions a new separation process was designed to isolate ^{57}Ni, ^{57}Co, ^{64}Cu ^{67}Ga and ^{65}Zn from a single anion exchange column

Over 100 separations have been conducted. The production yields for ^{64}Cu are typically 1.8 mCi/ Ahr (at EOB after separation) and specific activities of up to 30,000 Ci/g are achievable. Most significant is the extremely high purity of the ^{64}Cu that allows the monitoring of ^{67}Cu (<1% contaminant at EOB) some 7 days after separation. Such high purity has allowed extensive research into copper metabolism in acquired and inherited diseases and the diagnosis and therapy of cancer[12-14]. It is felt that use of this new method should substantially increase the potential use of ^{64}Cu worldwide.

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