DEVELOPMENT OF LOW ENERGY ACCELERATOR-BASED PRODUCTION OF MEDICAL ISOTOPES

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Abstract

Here we present methods for production of new and existing isotopes for SPECT (Single Photon Emission Computed Tomography) and PET (Positron Emission Tomography) imaging using accelerator-based systems. Such isotopes are already widely used in medical diagnostics and research, and there is constant development of new drugs and isotopes. However the main production method for ^{99m}Tc, is currently in research reactors and is at risk due to scheduled and unscheduled shut downs. Therefore, a low cost an alternative accelerator-based system could provide many advantages. Various compact low energy proton machines are being proposed to enable cheap and accessible production: here we present a discussion of potential new SPECT isotopes and simulations of suitable targets for their manufacture.

INTRODUCTION

Currently the production of medical tracer isotopes for use in imaging techniques such as SPECT (Single Photon Emission Computed Tomography) and PET (Positron Emission Tomography) [1] relies principally upon an ageing fleet of nuclear reactors. For example the most common medical isotope ^{99m}Tc, used in over 80% of all radiopharmaceutical procedures, is currently produced, via its generator ^{99}Mo, by nuclear research reactors such as NRU-Canada and HFR-The Netherlands, which together produce over 60% of the worlds ^{99}Mo/^{99m}Tc supply. Both of these reactors are old (>50yrs) and close to decommissioning, and while several projects are looking at other production routes for this isotope, as yet there is no real replacement in place [2, 3]. As these reactors near their decommissioning, currently set at 2014-2016, there is considerable concern that we will soon be facing a similar situation to that of the 2010 isotope crisis, when both reactors were offline simultaneously resulting in a significant decrease in the supply of ^{99m}Tc and the postponing or cancelation of many vital radioisotope procedures [1–5]. Due to ^{99m}Tc monopolising the medical isotope market little work was done developing other isotopes and many potential isotopes fell by the wayside. The aim of this work is to resurrect some of these isotopes as alternatives to ^{99m}Tc as we head into another shortage in the hope of preventing another crisis. There are several short lived SPECT and PET isotopes that have the potential to take some of the workload from ^{99m}Tc.

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LOW ENERGY ISOTOPE PRODUCTION

We believe that the solution to this impending problem could lie in accelerator-based production methods, of both ^{99m}Tc and possible replacement isotopes. A collaboration with Siemens is focusing on the potential of a compact, low energy proton device for the generation of radioisotopes [6]. Such a machine could provide many more localised isotope production centres and allow for the use of isotopes with shorter halflives. A study of optimal target designs for such a system has been undertaken using GEANT4 simulations of low energy (<10MeV) proton induced reactions.

^{113M}INDIUM

^{113m}In is a metastable radioactive isotope that decays via a 392 keV γ into stable ^{113}In with a half life of 1.7hours [7]. In 1965 it was first proposed for use as an alternative medical tracer isotope to ^{99m}Tc for SPECT imaging in several applications such as brain and lung scanning. Trials of this isotope showed it to give results comparable to ^{99m}Tc images [7]. ^{113m}In showed several advantages over ^{99m}Tc such in terms of chemical properties. A successful generator production system for In was developed using ^{113}Sn [7, 8].

Generator Production

There are several advantages of a longer lived generator system, such as the Sn/In system. The longer gap between parent half life and daughter half life makes it easier to separate the two nuclei. It also increases the longevity of the system for example the Sn/In(parent half life approximately 118 days) system only needs replacing once every 6 months where as the Mo/Tc(parent half life approximately 3 days) system needs replacing weekly. However due the plentiful and cheap supply of Tc at the time very little serious work was carried forward with this isotope. The simplicity of the generator production system and the advantages available from such a system has prompted the exploration of a low energy method of production for this generator using the reaction:

^{113}In(p,n)^{113}Sn $\rightarrow$ ^{113m}In $\rightarrow$ ^{113}In

Preliminary simulation results from the TALYS data libraries show that such a reaction at 10 MeV gives a production cross section of 570mb. Further GEANT4 simulations have been used to study target designs and feasibility of this reaction using a <10MeV proton beam. In terms of daughter yield the most appropriate target thickness is that of just

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over the stopping distance, which from these simulations is given to be approximately 0.5mm. The generator and daughter activity for this reaction after a 30min irradiation of the target can be seen in Fig. 1.

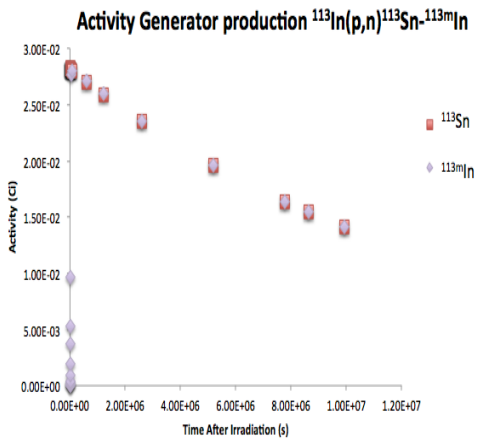

Figure 1: Activity of parent ^{113}Sn and daughter ^{133m}In produced from the generator reaction.

The lifetime of a typical Sn/In generator system is 3-6 months [9]. The activity for this time after irradiation can be seen in Fig. 1. Even after this time this small sample generator is producing an activity of 0.9 mCi which in comparison to a typical single dose of microcuries per gram [10], shows the potential of a low energy accelerator based system for the generator production of ^{113m}In.

Direct Production

Direct production of ^{113m}In appears to be less common due to the short halflife of the isotope and the lack of local facilities in which to produce it. However with the introduction of our proposed system it should be possible to make this a much more feasible production route. Both the TENDL and EXFOR libraries can be seen to agree that a cross section of just over 200mb can be obtained for the following reaction:

^{113}Cd(p,n)^{113m}In

for a proton beam between 9 and 10 MeV. The corresponding activity of In for a 0.5mm thick target after a 30min irradiation can be seen in Fig. 2.

The activity obtained for direct production is significantly larger than that of generator production. Such activity should be enough to service the needs for a local facility as is the proposed purpose of a low energy isotope production system.

^{87M}STRONTIUM

Strontium 87m is a metastable radioactive isotope that decays via a 388keV γ into stable ^{87}Sr with a half life of 2.8hours [11]. Several different strontium isotopes have an application in nuclear medicine as due to the similar

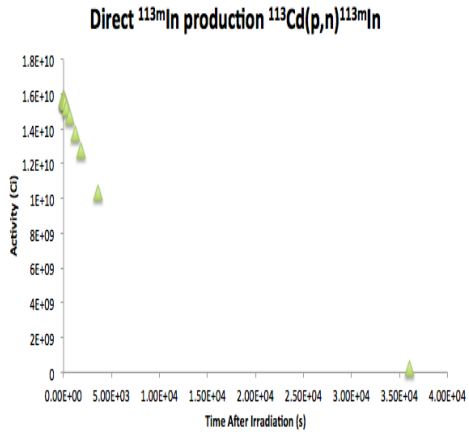

Figure 2: Activity of ^{113}In produced from the direct reaction.

chemistry to calcium it is readily taken up in bone. There are some isotopes such as ^{90}Sr which are undesirable for medial use as replace calcium in the bone and are toxic. Others however such as ^{87m}Sr can be used in both diagnostic and therapeutic techniques for various skeletal diseases [11–14].

Generator Production

^{87m}Sr is produced primarily using the ^{87}Y/^{87m}Sr generator. Literature shows many different possible methods of producing this generator. However these are all at higher energies ($>$20 MeV). This work is focusing on low energy techniques e.g. reactions such as

^{87}Sr(p,n)^{87}Y $\rightarrow$ ^{87m}Sr $\rightarrow$ ^{87}Sr

According to the TALYS/EXFOR libraries this reaction has a cross section of approximately 600mb at 10 MeV. Further study of target design were carried out using GEANT4 to obtain a suitable target that provides a viable yield for medical applications. The activity obtained from a 0.9mm thick metal target can be seen in Fig. 3.

Activity of the generator route from our simulations is of the order of curies whilst a diagnostic dose is of the order of millicurie. However from previous studied such as [11] it is apparent that this target is impractical and a compound target such as $SrCl_2$ would be more appropriate. This reduces the number of Sr nuclei within the target requiring a thicker compound target to keep the activity sufficient for the 2 week lifespan that is typical of this type of generator system.

Direct Production

It is also proposed that direct production of ^{87m}Sr is possible through the reaction:

^{87}Rb(p,n)^{87m}Sr

which according to the EXFOR libraries has a cross section of approximately 200mb in the energy range $<$10MeV. The TALYS libraries also gave a cross section of 240mb at

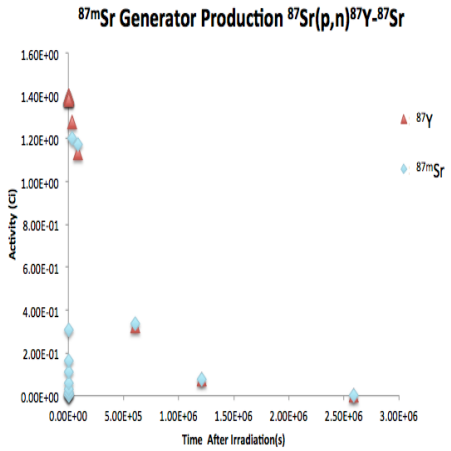

Figure 3: Activity of ^{87m}Sr produced using the ^{87}Y/^{87m}Sr generator.

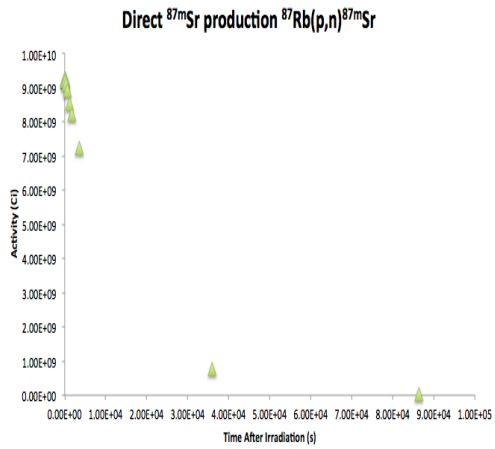

Figure 4: Activity of ^{87m}Sr produced using the direct reaction.

10MeV from which the activity of ^{87m}Sr that is produced after a 30min irradiation of a 0.5mm thick target can be seen in Fig. 4.

Even with such a simple, crude design such a large activity is obtained with this reaction. With more adjustment a suitable target could be configured so as to optimise the activity. An isotope with such a short half life is much more likely to be produced using the direct reaction on demand and so any effort to minimise the production time such as short irradiation time, from these initial results this time could be less than 30mins.

CONCLUSION

This work has shown a first test case of the feasibility and practicality of using a low energy proton accelerator system as a method of producing radioisotopes in quantities suitable for medical applications. This work will go on to optimise the low energy production routes for these isotopes in the hopes of minimising the reduction of SPECT isotopes in the predicated crisis. We will also go on to study the potential of using this system to manufacture potential isotopes to be introduced for both SPECT and PET.

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