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^{44g}Sc From Metal Calcium Targets For PET

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Abstract. A low-cost and efficient method for producing pre-clinical scale quantities of ^{44g}Sc is presented. Production involves proton irradiation of natural unenriched calcium metal followed by rapid separation of radioscandium from the target using hydroxmate functionalized resin.

Keywords: ^{44}Sc, ^{44g}Sc, Radiometal, PET, Sc-DOTA.
PACS: 29.20.dg; 87.57.un;

INTRODUCTION

^{44g}Sc is the subject of many recent papers by the group of Frank Rösch in Mainz [1- see references within]. Their interest lies in the availability of ^{44g}Sc from a ^{44}Ti (60y, EC) generator, which they have manufactured for the elution of 5 mCi fractions. As radio-metal labeling becomes more prominent in PET, it is worthwhile to explore the characteristics of ^{44}Sc to determine if it has a place in the radiochemist's toolkit. Such work may either motivate the production of more generators, or justify delving into enriched ^{44}Ca oxide powder targetry. To initiate these cursory and pre-clinical studies, we irradiated unenriched calcium metal targets, producing ^{44g}Sc from the 2% naturally abundant ^{44}Ca via the (p,n) reaction. We found that sufficient ^{44g}Sc for pre-clinical studies are available without enriched target material, at 95% radionuclidic purity, for reasonable bombardment parameters (1 hour, 20μA, 16 MeV) [2].

This brief paper describes improvements to the chemical separation and reactivity presented in [2]. The previous report outlines the simple target design, production yield, and the radionuclidic purity achieved by irradiating natural calcium metal with 16 and 13 MeV protons from a GE PETtrace. The chemical separation in [2] relies upon the insolubility and inherent 'stickiness' of scandium in near-neutral aqueous solutions, giving an overall 51% trap-and-release yield with reactivity to DOTA at roughly 50 GBq/umol. A large improvement to both figures, 63% yield and 100 GBq/umol reactivity is made by using hydroxamate-functionalized resin to separate scandium from the bulk calcium target.

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MATERIALS AND METHODS

Calcium metal (99.98% purity) and solid ammonium acetate were obtained from Sigma Aldrich. Ultrex grade HCl came from VWR, and Optima ammonium hydroxide came from Fischer. Hydroxamate resin was prepared according to the procedure outlined previously [3], using reagents from Sigma Aldrich and carboxylate-functionalized CM resin from Waters (both 300 mesh bulk resin, and 50 mg light SEP-PAK's were activated, the latter by cyclically flowing reagents through the cartridge).

Roughly 400 mg calcium was pressed with a lever-press into an aluminum holder (12 mm diameter, 3 mm deep) as shown in Fig. 1.

The holder was mounted onto an adapted PETtrace target allowing direct water cooling on the holder. The target had aluminum foil over the irradiated face of the calcium for irradiations at 16 MeV(Fig. 1), and was otherwise uncovered when used in a new target with energy degradation to 13 MeV.

Irradiated targets were dissolved in 11 ml 2 N HCl, and the pH was adjusted to 3-4 with 0.25 M sodium acetate. The solution was loaded onto a column (short Alltech Ultraclean with polyethylene frits, or activated Sep-pak lite) containing 50 mg hydroxamate resin, preconditioned with 5 ml 0.1 M HCl followed by 5 ml 0.25 M sodium acetate (pH 4-5). The loaded column was washed with 5 ml pH 4.5 0.2 M sodium acetate (adj. with HCl), and 2ml 0.01 M HCl. Activity was eluted from the column in 1 ml 0.1 M HCl.

In order to test the reactivity of the purified radioscandium, the eluted fraction was added to pre-heated (95 °C) sodium acetate buffer (pH 4), and dispensed into 10 vials containing buffered and pre-heated DOTA solutions of known concentrations from 1 to 1000 nM. The vials were incubated for 1 hour at 95 °C and then spotted onto Al-backed silica gel ITLC plates (EMD, New Jersey). The solvent was 0.75 M $NH_4OH_{(aq.)}$.

Additionally, one production was split into four fractions after the pH adjustment step, followed by four otherwise independent separation methods. One as described above, another using only inactivated CM resin, another using silica gel resin, and a last using an empty column containing only the polyethylene frits.

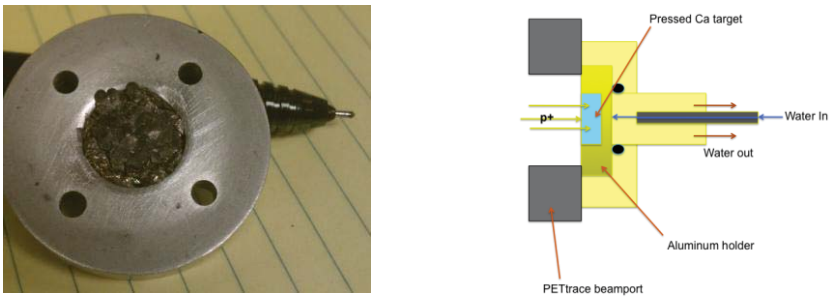

FIGURE 1. A photograph of the pressed Ca target (left) and cartoon of the simple target design (right).

RESULTS

After 1 hour of irradiation at 16 MeV, the radionuclidic purity of ^{44g}Sc was greater than 95%, with saturation production over 200 MBq/μA. ^{43}Sc, ^{48}Sc, ^{44m}Sc, and ^{47}Sc comprised the radio-impurities. It was reasonable to expect about 18 mCi of ^{44g}Sc for a one hour 20 μA irradiation at 16 MeV, and about 10 mCi for the same conditions at 13 MeV.

Overall, the hydroxamate resin trapped 87±10% of the Sc activity. Approximately, 72±11% of this retained activity was recovered in 1 ml 0.1 M HCl. Radio-TLC-measured reactivity of produced ^{44g}Sc for DOTA was roughly 100 GBq/μmol, decay corrected to end-of-bombardment (EoB). The separation procedure concluded about 30 minutes post-EoB.

The comparison of different substrates for the separation showed that the hydroxamate and carboxylate resins behaved similarly for trap and release, but the reactivity of the hydroxamate-purified scandium was higher by a factor of two. The silica gel and polyethylene frits retained activity, though not as well as the other two resins. Therefore the hydroxamate resin was selected for further study.

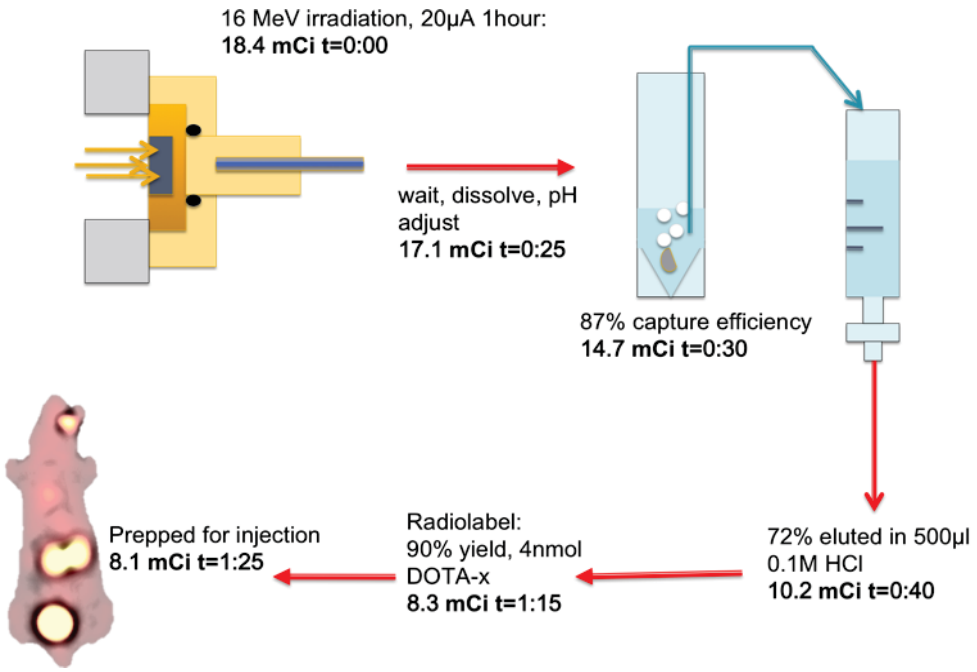

FIGURE 2. A graphical overview of the entire production procedure. The times listed are relative to EoB. The overall yield from start to finish is 24%, not decay corrected. The impurites in the 8.1mCi product are as follows: ^{44m}Sc (63 μCi), ^{43}Sc (201 μCi), ^{48}Sc (103 μCi) and ^{47}Sc (27 μCi).

ACKNOWLEDGMENTS

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