Production of radiometals in a liquid target

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Introduction

Access to radiometals suitable for labeling novel molecular imaging agents requires that they be routinely available and inexpensive to obtain. Proximity to a cyclotron center outfitted with solid target hardware, or to an isotope generator for a radiometal of interest is necessary, both of which can be significant hurdles in availability of less common isotopes. Herein, we describe the production of ^{44}Sc, ^{68}Ga, ^{89}Zr, ^{86}Y and ^{94m}Tc in a solution target which allows for the production of various radiometallic isotopes, enabling rapid isotope-biomolecule pairing optimization for tracer development. Work on solution targets has also been performed by other groups [e.g. 1, 2].

Material and Methods

Solutions containing a high concentration of natural-abundance zinc nitrate, yttrium nitrate, calcium nitrate [3], strontium nitrate or ammonium heptamolybdate [4] were irradiated on a 13 MeV cyclotron using a standard liquid target. Some of the solutions contained additional hydrogen peroxide or nitric acid to improve solubility and reduce pressure rise in the target during irradiation. Yields calculated using theoretical cross sections (EMPIRE [5]) were compared to the measured yields. In addition, we tested a thermo-syphon target design for the production of ^{44}Sc. Chemical separation of the product from the target material was carried out on a remote apparatus modeled after that of Siikanen [6].

Results and Conclusion

The proposed approach enabled the production of quantities sufficient for chemical or biological studies for all metals discussed. In the case of ^{68}Ga, activity up to 480±22 MBq was obtained from a one hour run with a beam current of 7 µA, potentially enabling larger scale clinical production, see Table 1. Considering all reactions, the ratio of theoretical saturation yields to experimental yields ranges from 0.8 for ^{94m}Tc to 4.6 for ^{44}Sc. The thermo-syphon target exhibited an increase of current on the target by a factor of 2.5 and an increase in yield by a factor of five for the production of ^{44}Sc. Separation methods were developed for all isotopes and separation efficiency ranges from 71±1% for ^{94m}Tc to 99±4% for ^{86}Y. ^{44}Sc, ^{68}Ga, and ^{86}Y were successfully used in labeling studies with a model 1,4,7,10 – tetrazacyclododecane - 1,4,7,10 -tetraacetic acid (DOTA) chelate, while ^{89}Zr coordination behavior was tested using desferrioxamine-alkyne (DFO-alkyne).

Reaction	A_{sat} (MBq/µA)	A^{theo}_{sat} (MBq/µA)	A^{theo}_{sat}/A_{sat}
^{44}Ca(p,n)^{44}Sc	4.6±0.3	21.1	4.6
syphon target	8.4±0.3	21.1	2.5
^{68}Zn(p,n)^{68}Ga	141±6	207.3	1.5
^{86}Sr(p,n)^{86}Y	31±1	52.5	1.7
^{89}Y(p,n)^{89}Zr	360±9	540.9	1.5
^{94}Mo(p,n)^{94m}Tc	40±6	32.2	0.8

TABLE 1. Reaction, experimental saturation yield A_{sat} and theoretical saturation yield A^{theo}_{sat} for all investigated radiometals. The production of ^{44}Sc in the syphon target is preliminary (n=2).

In summary, we present a promising new method to produce a suite of radiometals in a liquid target. Future work will continue to expand the list of radiometals and to apply this approach to the development of various peptide, protein and antibody radiotracers.

References

1. M. Jensen, J. Clark: *Proc. WTTC XIII*, 052, 2010.
2. M. K. Pandey, H. P. Engelbrecht, J. F. Byrne, A. B. Packard, T. R. DeGrado: *Nuc. Med. Biol.* **41**, pp. 309-316, 2014.
3. C. Hoehr, T. Morley, K. Buckley, M. Trinczek, V. Hanemaayer, P. Schaffer, T. Ruth, F. Benard: *Appl. Radiat. Isot.* **70**, pp. 2308-2312, 2012.
4. C. Hoehr, E. Oehlke, F. Benard, C. Lee, X. Hou, B. Badesso, S. Ferguson, Q. Miao, H. Yang, K. Buckely, V. Hanemaayer, S. Zeisler, T. Ruth, A. Celler, P. Schaffer: *Nuc. Med. Biol.* **41**, pp. 401-406, 2014.
5. M. Herman, R. Capote, B. Carlson, P. Oblozinsky, M. Sin, A. Trkov, H. Wienke, V. Zerkin: *Nucl. Data Sheets* **108**, pp. 2655-2715, 2007.
6. J. Siikanen, M. Peterson, T.A. Tran, P. Roos, T. Ohlsson, A. Sandell: *AIP Conf. Proc.* **1509**, pp. 206-210, 2012.

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