Cyclotron production of Ga-68 for human use from liquid targets: From theory to practice

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Introduction

Gallium-68 (^{68}Ga) is of growing interest for the production of Ga-radiolabeled compounds used as tracer molecules in positron emission tomography (PET) imaging technique.

To obtain ^{68}Ga, the most common technique is the use of a ^{68}Ge/^{68}Ga generator. Unfortunately, ^{68}Ge/^{68}Ga generators, with limited lifetime, produce limited amounts of ^{68}Ga per elution and present the risk of contaminating the final preparation with the long-lived parent nuclide ^{68}Ge.

Traditionally, ^{68}Ga is also produced in cyclotrons via the ^{68}Zn(p,n)^{68}Ga reaction in a metal (solid) target. The process, although producing high yields, requires expensive solid target irradiation, transport and processing systems, poses radioprotection issues, and is prone to contamination by metallic ions that can compromise the purification of the ^{68}Ga and subsequent labeling reaction. Although the method has been implemented in several centers, it never became a widespread solution, probably due to these drawbacks.

Alternative methods have been proposed to simplify and improve the process of ^{68}Ga production by a cyclotron, based on liquid targets [1] [2]. Recognizing the advantages of this concept, the authors developed an improved process for cyclotron irradiation of a ^{68}Zn target solution and subsequent purification in order to achieve a final solution of ^{68}Ga that can be used to label ^{68}Ga radiopharmaceuticals thus providing an economically viable alternative to ^{68}Ge/^{68}Ga generators.

Material and Methods

The different steps for the completion of a whole process to produce and separate ^{68}Ga from a liquid target have been studied and implemented in a fully integrated system.

As target material, Zinc-68 (^{68}Zn) nitrate solution diluted in low concentrated nitric acid solution has proven to be the best compromise, allowing the use of convenient amounts of ^{68}Zn, stability (including non-precipitation) of the solution over long time and better behavior (namely pressure build up) under beam.

A Nirta Conical® target system by IBA was used, benefiting from improved cooling capabilities, after confirming chemical inertness of constituent Niobium. A Niobium target window is also used. Target automatic filling system was implemented, based on peek valves and lines, thus avoiding metal contamination. Energy range to avoid ^{67}Ga production and under beam current-pressure conditions have been studied for different target material concentrations and conditioning.

Synthera® Extension IBA commercial system was used to implement the separation process based on strong cation exchanger column, and a dedicated disposable cassette was developed. The implemented method includes previous elution of ^{68}Zn, that can therefore be reused, and a final elution (with hydrochloric acid) of produced ^{68}Ga with overall yield of 85%. The purification and recovery process takes place in 30 mins.

Final ^{68}Ga was proven to be suitable for labelling radiopharmaceuticals for human use.

Results and Conclusion

A complete setup for ^{68}Ga production, separation and purification based on the irradiation of a ^{68}Zn highly enriched solution was implemented using an IBA target and a commercially available synthesis module.

A minimum of 180 mCi of ^{68}Ga was systematically produced on a 40 min irradiation at 45 uA proton beam from a conventional IBA Cyclone 18 cyclotron, using 100 mg of ^{68}Zn in a total volume of 3 ml of nitric acid solution. The implemented system and methodology has a consistent 85% yield for the recovery/purification process. ^{68}Ga obtained has been used to label (with >70% yield) peptides, namely ^{68}Ga-DOTANOC and ^{68}Ga-PSMA-11, suitable for human use, with practical and economical gains compared with the conventional methods.

References

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