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Upgrade of the equipment for production of gallium isotopes from proton-activated zinc targets

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Abstract

Two gallium isotopes, ^{66}Ga ($T_{1/2}$=9.4h, β^+ 4.2MeV) and ^{67}Ga ($T_{1/2}$=78h, EC), can serve as good models in development of new ^{68}Ga-labelled ($T_{1/2}$=68m, β^+ 1.9MeV) PET radiopharmaceuticals. In order to produce ^{66}Ga and/or ^{67}Ga from zinc targets activated in a medical cyclotron, we designed a prototype target whose external dimensions match the geometry of other standard targets, but which contains modified internal parts. Besides, we equipped our old apparatus for solvent extraction of ^{67}Ga in new, remotely controlled, electric valves. Performance of the upgraded chemical apparatus turned out good and the gas- and water-tightness of the new target at room temperature were satisfactory too. Performance of the new target in the transport lines of the PETtrace cyclotron as well as its behavior in harsh thermal conditions have to be the matter of future experiments.

Streszczenie

Dwa izotopy galu, ^{66}Ga ($T_{1/2}$=9,4h β^+ 4,2MeV) i ^{67}Ga ($T_{1/2}$=78h; EC), mogą być bardzo przydatne w badaniach nad nowymi radiofarmaceutykami krótkotrwałego ^{68}Ga ($T_{1/2}$=68m; β^+ 1,9MeV) używanego już w tomografii pozytonowej (PET). Aby móc otrzymywać ^{66,67}Ga z cynku aktywowanego protonami w cyklotronie medycznym, zaprojektowano tarczę, zewnętrznie odpowiadającą gabarytom typowych tarcz metalicznych, ale ze zmodyfikowaną strukturą wewnętrzną, zaś posiadaną szklaną aparaturę do ekstrakcji cieczowej galu wyposażono w elektrozawory oraz pulpit do zdalnego sterowania procesem. Zmodernizowana aparatura chemiczna działa bardzo dobrze, a prototyp nowej tarczy przeszedł pomyślnie próby wodoszczelności i próżnioszczelności w temperaturze pokojowej. W przyszłości należy sprawdzić zachowanie nowej tarczy w transporcie pneumatycznym do cyklotronu, a także w warunkach silnych naprężeń termicznych.

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Introduction

Among the radioactive isotopes of gallium, two play an important role in nuclear medicine. The first one, ^{67}Ga ($T_{1/2}$=78h), usually produced in ^{67}Zn(p, n) or ^{68}Zn(p, 2n) reactions, has been applied during several decades in single-photon imaging of oncological and inflammatory diseases[1]. Along with the development of positron emission tomography, ^{67}Ga got dominated by ^{68}Ga ($T_{1/2}$=68m) which is commercially available as the ^{68}Ge/^{68}Ga generator. The most common radiopharmaceutical of ^{67}Ga is gallium(III) citrate, whereas ^{68}Ga is used mainly as a label for cancer-specific peptides[2,3].

Another positron-emitting gallium isotope, ^{66}Ga ($T_{1/2}$=9.4h), easily produced in the ^{66}Zn(p, n) and ^{67}Zn(p, 2n) reactions at the energy range overlapping with the Zn(p, *x*n)^{67}Ga excitation curves, used to be regarded as an annoying contaminant because of its high energy gamma-ray emissions which deteriorate scintigraphic images of ^{67}Ga and increase the radiation burden on people. On the other hand, the relatively long half-life, good detection properties, and high production yields of ^{66}Ga made us (and not only us [4,5,6]) think that ^{66}Ga as well as ^{67}Ga might be useful tracers at least for pre-clinical research on gallium chemistry, biochemistry and radiopharmacy. Aiming at this application we decided to upgrade the glass equipment which we had used for many years to extract ^{67}Ga from proton- (or deuteron-) activated Zn targets. Aiming at production of ^{66,67}Ga in a 16MeV medical cyclotron, we also tried to design a target which would match both the existing irradiation unit and radiochemistry apparatus.

Table 1.
Nuclear properties of ^{66}Ga, ^{67}Ga, ^{68}Ga and ^{68}Ge

Nuclide	$T_{1/2}$	Decay mode and β^+ energy	Energies and intensities of main gamma rays (rounded values) keV (%)	Production route	Max cross section and the corresponding proton energy
^{66}Ga	9.4h	β^+ 4.2MeV	834 (6%); 1039 (37%); 2190 (6%); 2752 (23%); 4295 (4%)	^{66}Zn(p, n) ^{67}Zn(p, 2n)	530mb @13.0MeV 390mb @24.7MeV (rounded values)[7]
^{67}Ga	78.3h	EC	93 (39%); 185 (21%); 300 (17%); 394 (5%)	^{67}Zn(p, n) ^{68}Zn(p, 2n)	646mb @10.5MeV 732mb @20.5MeV[8]
^{68}Ga	67.63m	β^+ 1.9MeV	1077 (3%)	^{68}Ge(β+)	n. a.
^{68}Ge	270.82 d	EC	None	^{69}Ga(p, 2n) ^{71}Ga(p, 4n)	322mb @20.5MeV[9] 134mb @42.5MeV[10]

Experimental

Targetry

Our concept of target modification was based on the ALCEO Metal® (COMECER) target. The original construction is dedicated to electrochemical preparation and processing of proton-activated nickel targets[11]. The original target assembly consists of a cylindrical thin-walled platinum vessel embedded hermetically in the anodized aluminium body. The target material is electrodeposited on the bottom of the platinum support. The whole assembly works as a shuttle which is transported pneumatically from the radiochemical hot cell to the 16MeV PETtrace (GE) cyclotron, and back.

Preparation of zinc targets also requires electrochemical methods, but their processing is easier because zinc dissolves spontaneously in concentrated hydrochloric acid. Typically, zinc targets are electrochemically deposited on relatively cheap, single-use flat copper supports[12] whose additional advantage is very good thermal conductivity. Moreover, metallic copper resists rather well to hydrochloric acid. In view of the above it seemed to us reasonable to design a new target in which the multiple-use 3D platinum insert would be replaced by a copper leaf removable from the target body. To ensure compatibility of the new target with the existing pneumatic transport lines and the irradiation unit we adjusted its external dimensions to the peripheries of the PETtrace cyclotron. A sketch of the proposed target is shown at Fig. 1.

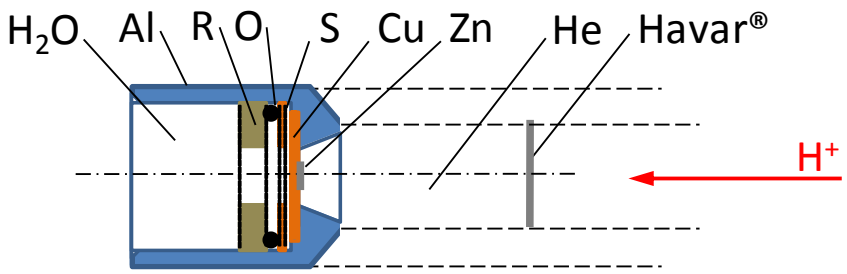

Fig. 1. A simplified drawing of the proposed target shuttle.

Two pairs of the dashed lines indicate the contour of the beam line. The external dimensions (28×35mm) and the cooling media are the same as for other metal targets in the PETtrace cyclotron.
H_2O – cooling water, Al – target body, R – threaded metal ring (aperture 12mm), O – Viton® O-ring, S – aluminium spacer, Zn – target material (7mm spot of the enriched or natural Zn), Cu – flat copper support for the irradiated material, He – cooling gas, Havar® – foil separating the cooling gas from the cyclotron vacuum, H^+ – direction of the incident proton beam.

The modified target was machined in our Institute as shown at Figs. 2-3. The whole system can be handled in a shielded box and the wrenches can be adapted for remote operation.

Fig. 2. The modified target assembly for activation of zinc at the PETtrace cyclotron.

Left: Elements of the target assembly; Right: Way of assembling or disassembling the target parts.
1 – external wrench, 2 – 28×35mm aluminum target body, 3 – 0.1×20mm copper support for the target material, 4 – O-ring, 5 – aluminum spacer, 6 – internal fixing ring, 7 – wrench to rotate the internal fixing ring.

Fig. 3. The assembled target shuttle and its two dedicated wrenches; rear (left) and front (right) views.

As a dismountable construction is more prone to leaks than a fixed one, we checked the performance of our prototype, starting from laboratory conditions at room temperature.

Water tightness of the modified target was checked as shown at Fig. 4. A stream of de-ionized water (5 bar) was supplied during 30 minutes to the back of the target, in a very similar way as in the irradiation unit of the cyclotron.

Gas tightness of the modified target was checked using an Alcatel ASM 121h leak detector, equipped with a quadrupole mass spectrometer. The assembled target was mounted in the apparatus as shown at Fig. 5. Helium gas was supplied to the front of the target shuttle during 10 minutes, which imitated the front-cooling conditions in the cyclotron.

The tests were repeated a few times, with several cycles of assembling and disassembling of the target parts in between.

Fig. 4. Water tightness check.

The target is mounted at the left-hand side of the manifold. The red line indicates the position of the target shuttle.

Fig. 5. Gas-tightness check.

The arrow shows the front part of the target shuttle. The helium gas was applied from the top.

Chemistry

As the most efficient way of separation of radioactive gallium from zinc targets is solvent extraction[13], the method was implemented in our Institute long ago[14]. Our old chemical apparatus (Fig. 6) consisted of the target dissolution vessel connected with the extraction and back-extraction vessels which are fed with diethyl ether (DIPE), 7M HCl and pure water, respectively. The last glass vessel is fed with sodium citrate, so that the radioactive product can be obtained either as ^{67}Ga(III) chloride or as ^{67}Ga(III) citrate. The activities of ^{67}Ga were up to 1MBq per batch and the shielding was 5cm of lead.

Recently, we replaced all glass stopcocks with 24 electrically-actuated valves (Fig. 7) and added a semi-automated remote control system.

Fig. 6. The old solvent extraction apparatus, custom made.

Fig. 7. Electrically actuated valve (24V DC, BIO-CHEM VALVE INC.). The valve body is PEEK (polyetherketone).

The upgraded solvent extraction apparatus and the remote control unit are shown on Figs. 8 and 9, respectively. Please note that all new valves have been mounted in the horizontal position to minimize the dead volume of liquid in the PEEK valve body.

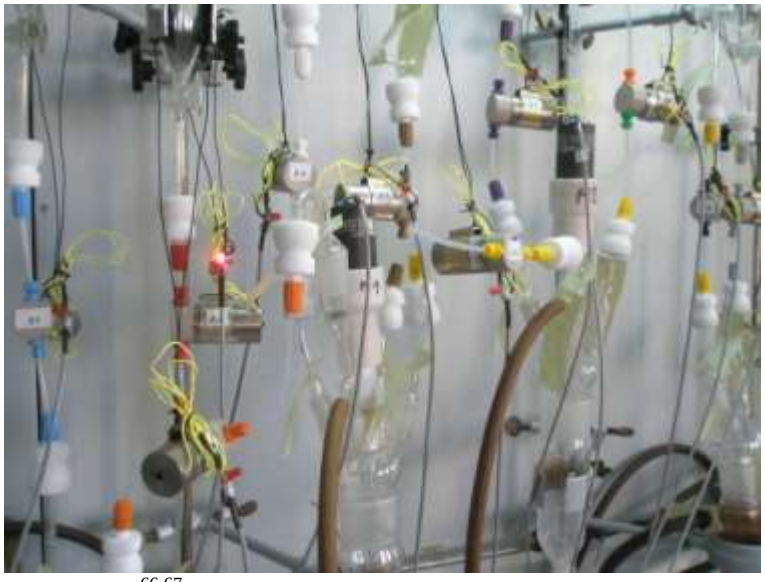

Fig. 8. The ^{66,67}Ga extraction system under construction.

Please note also that actuation of each valve is controlled by the red light lit on this valve.

Fig. 9. Remote control unit.

Results

Targetry

The freshly mounted modified target assembly passed the tests of gas and water tightness at room temperature, i.e. no leaks of helium or water were detected on either side of the virgin copper disk. However, if the target was repeatedly (5-10 times) assembled and disassembled without changing the replaceable parts, the thin copper substrate was distorting, inner threads got wearied and measurable leaks would appear.

Chemistry

The upgraded chemical apparatus works very well, starting from dissolution of the zinc target in 30% HCl, via extraction of ^{66,67}Ga from 7M HCl to diisopropyl ether, followed by back-extraction of ^{66,67}Ga to the aqueous phase, up to conversion of ^{66,67}Ga(III) chloride into citrate. Introduction of electric valves made the old equipment much easier to operate and the semi-automated remote control system reduced the radiation risk. The system is user-friendly and allows the radiochemist to tune the process parameters such as duration of contact between the reactants.

Conclusions

Targetry

The tests performed on the modified target at room temperature have shown that the assembly is water-tight and helium-tight as long as the thin copper substrate is used only once.

Since it is not known yet whether introduction of the groove on the target circumference (necessary to fix the wrench) would affect the movement of the shuttle in the pneumatic transport tubing, or what would be the behaviour of the modified target under thermal stress in the real or simulated proton beam, all these aspects must be checked in the future. Also, a safe (remotely-controlled) way of disassembling the highly active targets must be elaborated.

Chemistry

Upgrading of the target processing module made it more user-friendly and more safe than before. The apparatus can be further upgraded from semi-automated to a fully computer-controlled system. The remaining drawbacks of the apparatus are fritted glass joints and stoppers, and fragile glass capillaries. These parts should be replaced with plastic caps and joints, and polymer tubing, respectively.

General

There is an interplay between the design of the target assembly and of its processing unit. The latter works very well if irradiated zinc, electrodeposited on a thin flat copper substrate, is just dropped into concentrated hydrochloric acid, but this arrangement requires a target with removable Zn/Cu inserts. This was just the reason why we proposed a new design of the zinc target, but if the prototype does not meet the performance criteria, the device must be either re-designed or used in its original, concave form. In the latter case it would be necessary to modify the dissolution unit which ought to be adapted to the target cavity. It should be remembered that due to chemical affinity of the two reactants it may be difficult to avoid splashing of concentrated HCl during its vigorous reaction with zinc. So, it would be necessary to protect the aluminium target body from corrosion, to minimize radioactive contamination, and to prevent losses of valuable radioactive or isotopically enriched materials.

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