First experience on producing gallium-68 with liquid target at HUS Medical Imaging Center using a Cyclone KIUBE 180 cyclotron

Teija Koivula, Jyri Lehto, Tiina Lipponen, Jaana Laine, Jussi Tervonen and Kim Bergström

HUS Helsinki University Hospital, Medical Imaging Center, Cyclotron Unit

Haartmaninkatu 4, FI-00290 Helsinki, Finland

Background

HUS Medical Imaging Center at the Helsinki University Hospital provides imaging services for special and primary health care for all clinical sectors within the Helsinki and Uusimaa Hospital District (HUS) in Finland. Significant part of the services are PET-CT studies with ^{68}Ga-labelled radiotracers, such as ^{68}Ga-dotanoc. To support the in-house production of ^{68}Ga-radiopharmaceuticals, a liquid ^{68}Ga-target that enables production of ^{68}Ga with cyclotron was recently purchased. Results from the first irradiation studies are presented in this work.

Materials and methods

Gallium-68 was produced by ^{68}Zn(*p,n*)^{68}Ga nuclear reaction on the Nirta® ^{68}Ga liquid target using Cyclone® KIUBE 180 cyclotron (IBA, Belgium). The target was loaded with nitric acid solution containing enriched ^{68}Zn (Fluidomica, Portugal). Irradiated target solution was transferred to the Synthera®Extension module (IBA) containing dedicated purification kit/cassette support (Fluidomica) for separation of ^{68}Ga. Radionuclidic purity of the ^{68}Ga-solution was determined by high-purity germanium (HPGe) spectroscopy (Canberra, USA). Preliminary tests for radiolabeling of ^{68}Ga-dotanoc were also carried out using either Synthera®+ (IBA) or PharmTracer (Eckert&Ziegler, Germany) synthesis modules.

Table 1: Technical specifications of the Nirta® ^{68}Ga liquid target at the HUS Medical Imaging center.

•Target body	niobium
•Volume of the cavity	2,8 mL
•Proton beam energy	18 Mev
•Target foil	1-2 x 125 µm niobium foil
•Target solution	$^{68}Zn(NO_3)_2$ (99,5%)
•Target concentration	33 mg/ml

Results and discussion

Results from the first ^{68}Ga-productions (n=5) are summarized in Table 2. The target yield was decreased to approximately 225.7 MBq/µAsat when the Nb-foil was doubled. Both ^{67}Ga and ^{66}Ga were co-produced as expected (Alves F. *et al.* 2017); other radionuclidic impurities were not identified by the gammaspectrometric analysis of the irradiated target solution, Fig. 5. Isotopic impurities are not separated in the purification method and >4.5 h from EOB their proportion exceeded 2% of the overall activity (Fig. 6), thus the limit planned for cyclotron-produced ^{68}Ga (European Pharmacopoeia draft). As the overall time for synthesis (including dispensing) is relatively long, approximately 75 min from EOB, higher radiochemical yields would be desirable to satisfy the need for more than 4-5 patient doses. ^{68}Ga-production yield could be enhanced by increasing concentration of the zinc solution (*e.g.* to 66 mg/ml); higher beam energy would also result in higher amount ^{67}Ga impurity and thus affect self-life of the product. Optimal conditions might then be achieved by using medium-size, *e.g.* 175 µm Nb-foil as an energy degrader.

Table 2: Summary of ^{68}Ga-irradiation parameters and resulted yields at different production steps.

Beam current	45 µA
Target pressure	26 bar
Irradiation time	60-70 min
Target yield (one Nb-foil)	251.6 MBq/µAsat
Produced ^{68}Ga-activity at EOB	4.8 GBq
Activity after purification (EOP)	2.8 GBq
Activity of ^{68}Ga-dotanoc at EOS	1.5 GBq

Conclusions

Production of ^{68}Ga on the Nirta® target using the ^{68}Zn-solution was feasible. More studies are needed to find optimal production conditions with respect to radiochemical yield and shelf-life of the ^{68}Ga-labelled end-product.

Fig. 1. Helsinki and Uusimaa Hospital District (HUS) in Finland

Fig. 2. IBA Cyclone® KIUBE 180 cyclotron at the HUS Medical Imaging Center

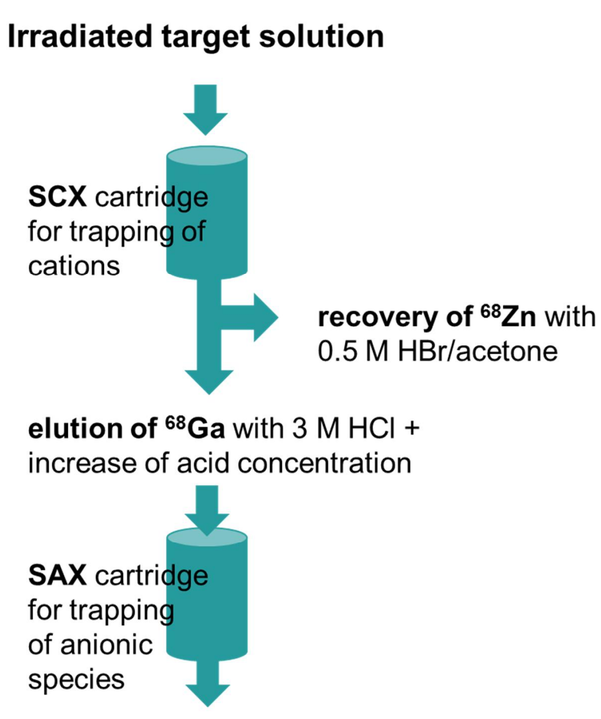

Fig. 3. Separation scheme for ^{68}Ga in $^{68}Zn(NO_3)_2$ solution. The overall time for the procedure is 35 min.

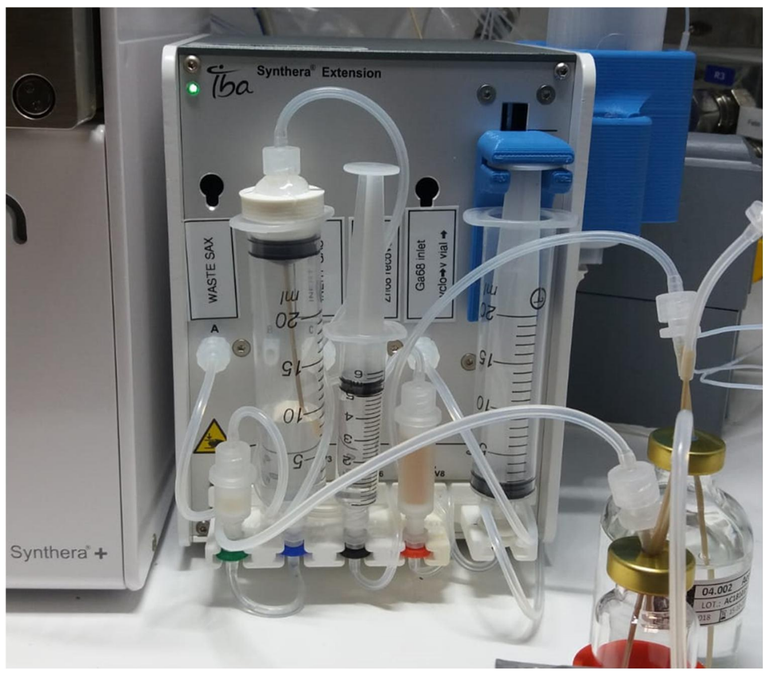

Fig. 4. IBA Synthera®Extension module equipped with Fluidomica purification kit for ^{68}Ga-target solution

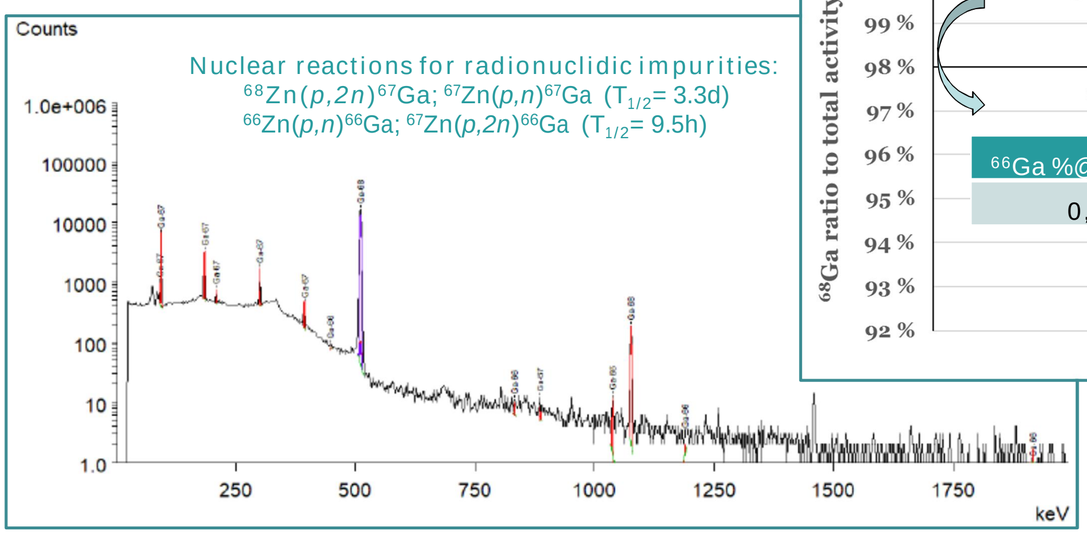

Fig. 5. Gammaspectrum of the purified ^{68}Ga-target solution at 8.5 h from EOB. The production conditions were 1 hour irradiation on 94 mg of ^{68}Zn using 40 µA beam current and approximately 14 MeV beam energy (two Nb-foils).

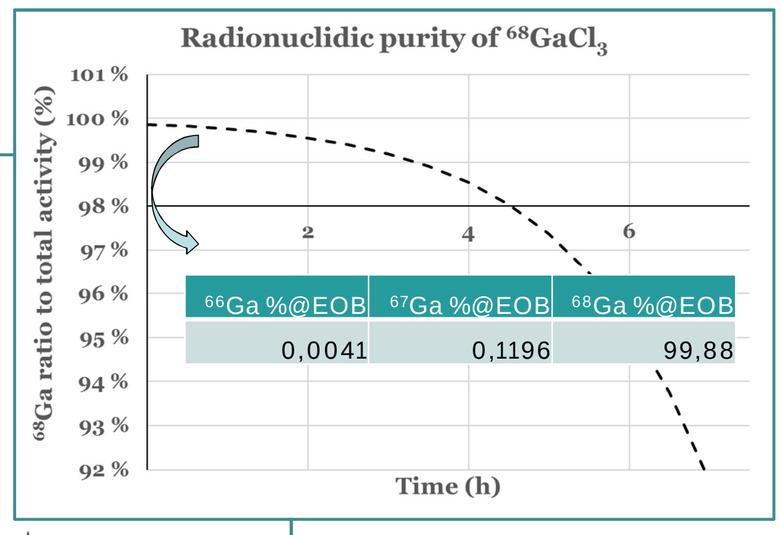

Fig.6. Radionuclidic purity of ^{68}GaCl3 at various time-points. Results are calculated from the HPGe measurements that were continued until 27h from EOB.

Acknowledgements

Dr. Liisa Porra and Dr. Eero Hippeläinen are acknowledged for their valuable help in gammaspectrometric analysis and calculation of the results.

References

(1) Alves F. et al., *Modern Physics Letters A*, 32 (17), 1740013 (2017)