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Fully automated synthesis of ^{68}Ga-labelled peptides using the IBA Synthera® and Synthera® Extension modules

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Introduction

The interest in ^{68}Ga-tracers has been growing strongly over the last years, mainly due to new developments in prostate cancer imaging and therapy.[1,2] In collaboration with IBA, we have established an automated synthesis of ^{68}Ga-labelled peptides including ^{68}Ga-DOTA-TATE, ^{68}Ga-DOTA-NOC,^{68}Ga-PMSA and ^{68}Ga-PSMA-617 on Synthera®. The process includes elution of the generator, pre-purification of the eluate over a cation exchange cartridge,[3] labelling, purification and formulation of the radiotracer. The labelling, purification and formulation steps of the process would also be applicable to cyclotron produced ^{68}Ga but is not the focus of this article.

Materials & Methods

During the tests, an IBA Synthera® and the new Synthera® Extension module were used. ^{68}Ga was obtained initially from an old iGG 100 generator in 5 mCi. The final tests were carried out in combination with a new GalliaPharm ^{68}Ge/^{68}Ga generator loaded with 50 mCi. The generators were eluted with metal-free 0.1 N hydrochloric acid. A modified standard nucleophilic IFP™ (IFP™ FDG) was designed for the synthesis process. Synthera® Extension was used for the elution of the generator. The eluate was loaded on a Macherey-Nagel Chromafix PS-H$^+$ cartridge and the hydrochloric acid waste - which contains most of the $^{68}GeCl_4$ - was transferred into the waste container. The activity was eluted from the cation exchange cartridge using a solution of 5 M sodium chloride in 0.1 N hydrochloric acid and transferred directly into the reaction vessel which was pre-loaded with precursor in 1.5 M HEPES buffer. Labelling was carried out at 95 °C for 7 minutes. The reaction mixture was taken out from the reaction vessel and the product was loaded onto a pre-conditioned Waters Sep-Pak® Light C18 cartridge. Exhaustive rinsing of the cartridge and reaction vessel with 0.9% saline removed unbound $^{68}Ga^{3+}$ and HEPES buffer. The product was then eluted with a 1:1-mixture of ethanol and water and the product was dispensed into the final vial through a sterile filter. Further dilution was

performed with 0.9% saline which was also dispensed through the sterile filter. The peptides, DOTA-TATE, DOTA-NOC, PSMA-11 and PSMA-617, were synthesized in a GMP-compliant qualified area at ABX facilities. For the DOTA-peptides, stock solutions were prepared (1 mg/ml) and freezed. For PSMA-11, vials with 10 µg of precursor were used.

Results

With 50 µg of DOTA-TATE, DOTA-NOC and PSMA-617, the final radiolabelled products were obtained in >60% uncorrected yield after 30 min of synthesis time. For PSMA-11, only 10 µg of precursor were used. The radiochemical purity was >98% in all cases. The Ph. Eur. spot test for HEPES was performed and showed HEPES < 200 µg / V with V being 12 to 14 ml. The pH of the final solution was 5 to 5.5. Ethanol content was < 10%.

Discussion/Conclusion

We have developed a dedicated disposable IFP cassette for the IBA Synthera® and Synthera® Extension modules, which delivers all common ^{68}Ga-tracers in high yield. The use of dedicated single -use Gallium-68 IFP™ allows for production of ^{18}F-FDG on the same module with no cross-contamination.

References

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