

Abstract

For the Development of new selective radiotracers which can be used for *in vivo* imaging of β -Amyloid plaques in the context of Alzheimer's Disease by positron-emission-tomography this study aimed at the application of various strategies for ^{18}F -labelling of the all-D peptide D3 (sequence: RPRTRLHTHRNR). In previous reports D3 showed promising results for the affinity to β -Amyloid.

The labelling reaction with acylation agents required an extension of the original peptide with a lysine residue at the C-terminus. The prosthetic group succinimidyl-4- ^{18}F fluorobenzoate could be produced with a radiochemical yield of 41 - 60 %. While conjugation with various model compounds gave good results the coupling with the D3-derivative was not possible.

Through the extension of D3 with cysteine instead of lysine it was possible to use thiol-reactive prosthetic groups. For this 4- ^{18}F fluorobenzylmaleimide was prepared by two different synthetic routes. But neither one of them lead to a radiochemical yield above 5% so further use was neglected. The preparation of 1-[3-(2- ^{18}F fluoropyridine-3-oxyl)propyl]pyrrol-2,5-dione succeeded by a three-step radiosynthesis within 110 minutes and lead to a radiochemical of 2-20%. The development of a new strategy via the protection of the maleimide function allowed to perform the radiosynthesis in only two steps within 60 minutes and an overall radiochemical yield of about $20 \pm 5\%$. The following coupling with the all-D peptide could be done with yields of about 95% within 15 minutes. This, the synthesis of the radiofluorinated D3-derivative including all purification steps could be achieved within 120 minutes.

The successfully ^{18}F -labelled D3-derivative was used for further preclinical *in vitro* investigation by performing autoradiography of mouse brain slices which expressed β -Amyloid plaques. Optimisation of the parameters of incubation were done in order to reduce the affinity of the compounds to the glass surface. It could be determined that the L-enantiomer of the radiofluorinated D3-derivative showed no affinity to the tissue. However the all-D peptide showed an increased uptake at some tissue regions with enrichment of β -Amyloid.