Positron emission tomography (PET) enables to detect physiological and pathophysiological processes on the cellular or molecular level. Therefore, PET has gained great importance as a diagnostic imaging technique. Thus, a number of neurological and neoplastic disordes are associated with alterations in the expression or activity of certain receptors, transporters or enzymes, which can be visualized and quantified using PET imaging. This is achieved by the application of radiolabeled probes (tracers) that selectively interact with a molecular target of interest and can be detected non-invasively based on the emission of positrons. Owing to its favorable half-live and the low energy of emitted positrons, fluorine-18 is one of the most attractive radionuclides for labeling of PET-tracers. A number of novel transition metal-mediated, late-stage radiofluorination methods have enabled an easy access to ^{18}F-labeled aromatic systems regardless of their electronic properties. In particular, Cu-mediated radiofluorination with alcohols as co-solvents has been shown to afford high radiochemical yields (RCYs) of several clinically relevant PET tracers that are hardly or not accessible by conventional methods.

The aim of the present work was to prepare ^{18}F-labeled PET tracers for different molecular targets by alcohol-enhanced Cu-mediated radiofluorination and to evaluate their properties by preclinical experiments *in vitro* and *in vivo*. The molecular targets were selected based on their pathophysiological relevance and comprised the glycine transporter 1 (GlyT1), the synaptic vesicle glycoprotein 2A (SV2A) and the A_1 adenosine receptor (A_1AR). Following identification of suitable high-affinity lead structures, the corresponding precursor compounds were synthesized and subsequently radiolabeled using copper-mediated radiofluorination.

In the first part, the potent and selective GlyT1 inhibitor ALX5407 should be labeled with ^{18}F and evaluated as a potential PET tracer for imaging of GlyT1. To this end, [^{18}F]ALX5407 was prepared via Cu-mediated alcohol-enhanced radiofluorination in RCYs of 55±7%. The experimental log$D_{7.4}$ value of [^{18}F]ALX5407 amounted to 2.2, which is in the optimal range for blood brain barrier (BBB) penetration, and experiments in human blood plasma showed its stability up to 60 min. In addition, *in vitro* autoradiography with [^{18}F]ALX5407 in rat brain slices revealed a distribution of the tracer consistent with the pattern of previous studies on the expression of GlyT1 in the brain. *In vivo* PET imaging in healthy rats injected with [^{18}F]ALX5407 alone, [^{18}F]ALX5407 together with the Pgp-inhibitor Elacridar or [^{18}F]ALX5407 together with non-radioactive ALX5407 revealed accumulation of the tracer in peripheral tissue. However, no brain uptake was observed. When the corresponding methyl ester [^{18}F]ALX5406 (log$D_{7.4}$ of 2.9) was used as a pro-drug, the corresponding PET studies showed a high brain uptake, but regional tracer distribution did neither match with the expression pattern of GlyT1 nor with the distribution of [^{18}F]ALX5407 in autoradiographic studies.

The second part of this work focused on the chiral PET tracer [^{18}F]MNI-1126, which targets SV2A and can be used to visualize synaptic integrity. Since the existing method for synthesis and HPLC purification of the enantiomeric radiolabeling precursor is cumbersome, an optimized synthetic pathway based on a chiral alcohol-modified quinidine derivative as a catalyst was developed. This approach afforded the trimethyl stannyl precursor for Cu-mediated alcohol enhanced radiofluorination over 7 steps with an overall yield of 8% and an enantiomeric excess (*ee*) of 98%. Advantageously final chiral purification by HPLC could be omitted. Transfer of the manual radiosynthesis to an automated synthesis module allowed the production of [^{18}F]MNI-1126 (RCY of 26$\pm$6%) on a preparative scale and enabled its use for preclinical studies.

Finally, in the third part of this work, radiofluorinated partial agonists for imaging of the A_1AR density via PET were prepared. To this end, four promising radioligands 2-amino-4-(3-[^{18}F]fluorophenyl)-6-{[(6-methylpyridine-2-yl)methyl]thio}pyridine-3,5-dicarbonitrile ([^{18}F]FMPD), 2-amino-4-(3-[^{18}F]fluorophenyl)-6-{[(5-methylpyridine-3-yl)methyl]thio}pyridine-3,5-dicarbonitrile (*iso*-[^{18}F]FMPD), 2-amino-4-(3-(2-[^{18}F]fluoroethoxy)-6-{[(6-methylpyridine-2-yl)methyl]thio}pyridine-3,5-dicarbonitrile ([^{18}F]FEMPD) and 2-amino-4-(3-(2-[^{18}F]fluoroethoxy)-6-{[(5-methylpyridine-3-yl)methyl]thio}pyridine-3,5-dicarbonitrile (*iso*-[^{18}F]FEMPD) with nanomolar affinities (K_i = 2.6–5.8 nM) towards A_1AR and suitable log$D_{7.4}$-values (2.6–3.4) were prepared in moderate RCYs of 8–77% and reasonable molar activities of 3.5–61 GBq/µmol (end of synthesis). For the radiosynthesis either Cu-mediated alcohol enhanced ([^{18}F]FMPD and *iso*-[^{18}F]FMPD) or conventional radiofluorination ([^{18}F]FEMPD and *iso*-[^{18}F]FEMPD) was applied. *In vitro* autoradiography in rat brain slices revealed a relatively homogenous brain distribution with higher accumulation in the cerebellum. Specific binding was determined by competitive displacement experiments with the AR antagonist DPCPX and the AR agonist NECA. Highest specific binding (40% for displacement with DPCPX) was found for [^{18}F]FEMPD, which was subsequently evaluated by *in vivo* PET imaging in a healthy rat. This experiment showed that [^{18}F]FEMPD is stable for at least one hour and displayed a binding pattern matching the binding pattern of previous A_1AR expression studies. Taken together, this ^{18}F-labeled radioligand as a representative of a partial agonist shows high potential for the visualization of the A_1AR system.