PSMA targeting agents that have been labeled with 18F-fluoride and enable radioplumbation

The development of theranostic agents has received increasing interest in recent literature. Radiolabelling of peptides with F-18 have shown its efficiency and reproducibility, and have been used extensively as PET imaging agents, for example [^{18}F]-piflufolastat. On the therapeutic side, radioligands carrying Pb-212 have shown highly promising results in recent clinical trials.[1] This study highlights our effort towards the development of a PSMA-based tracer conjugated to an ammonium methylene trifluoroborate ($AMBF_3$) radioprosthetic and which also incorporates a novel chelator, for the chelation of the medical isotopes of lead. Such combination would allow orthogonal radiolabelling of the tracer with F-18 via isotopic exchange by virtue of the $AMBF_3$ radioprosthetic group.

We developed two PSMA-based tracers, [^{18}F]-AT03 and [^{18}F]-AT05, that incorporate multiple $AMBF_3$'s alongside chelator that should be capable of accommodating $^{207/203/212}$Pb isotopes. Both candidate tracers are varied with linker arms of "medium" and "long". Both tracers yielded high quality PET images and high tumour uptake values with minimal off target uptake. These results indicate a promising future in the translation to be used as theranostic agents.

1. Delpassand et al. Targeted α-emitter therapy with ^{212}Pb-DOTAMTATE for the treatment of metastatic SSTR-expressing neuroendocrine tumors: first-in-humans dose-escalation clinical trial. J Nucl Med. 2022;63:1326–1333.