Various tracers applied for clinical routine

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A variety of PET radiopharmaceuticals with increasing importance in the clinical routine and in research have been developed during the last decade. Especially the use of short-lived radionuclides such as carbon-11 and fluorine-18 allows the synthesis of radiolabelled compounds with interesting biological properties of clinical relevance. To be a part of a clinical routine environment the radio synthesis needs to be robust and reliable in order to minimise the number of failed productions.

Fluorine-18 ($t_{1/2} = 109.8$ min) and carbon-11 ($t_{1/2} = 20.4$ min) are short lived isotopes which can be produced in a cyclotron. Fluorine-18 can be obtained as $[^{18}F]F$luoride, which can be use in nucleophilic substitution reactions. Such reactions will be exemplified by discussion of the syntheses of $[^{18}F]FDG$ and $[^{18}F]$altanserin. $[^{18}F]FDG$ is the most commonly produced radiopharmaceutical worldwide and can be distributed to PET scanners hours away from the radiochemistry facility. $[^{18}F]$altanserin is a 5-HT$_{2a}$ receptor ligand used for brain studies and is synthesised on a regular basis in Copenhagen.

For carbon-11 radiochemistry the cyclotron produced starting material offered to the radiochemist is typically $[^{11}C]CO_2$ or $[^{11}C]CH_4$. From these to compounds a variety of more reactive precursors can be synthesised and used for labelling of the molecule of interest. Due to the short half-life carbon-11 labelled compounds is not suitable for distribution over long distances and the radiochemistry laboratory must be placed next to the cyclotron and preferentially close to the PET facility. $[^{11}C]$Methyl iodide is one of the most commonly used precursor for synthesis of carbon-11 labelled compounds and can be produced via the “wet” method from $[^{11}C]CO_2$ or via the gasphase method from $[^{11}C]CH_4$. Synthesis of $[^{11}C]$flumazenil and $[^{11}C]$DASB will be discussed as examples on synthesis of carbon-11 labelled amides and amines.

For application of carbon-11 labelled tracers for human investigations the timing between the radiochemistry laboratory and the scanner personal is very important. The patient needs to be placed in the scanner and ready to received the tracer when it is released after the quality control. If the patient is supposed to receive 2 tracers on the same day the timing is even more important. Also between the cyclotron and the radiochemistry laboratory the timing is important. Especially if two tracers are synthesised in parallel. PET radiopharmaceuticals such as $[^{18}F]FDG$ and $[^{11}C]$flumazenil are described in the European pharmacopoeia and regulations for GMP have to be considered when producing PET radiopharmaceuticals. The objective of the regulations is to ensure that the quality of the product is such that the product can be safely administered to humans and experimental animals. Before initialising a clinical study the protocol for the preparation and validation of the process for producing the radiopharmaceutical have to be approved by the national authorities.