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Design and synthesis of PET-radiopharmaceuticals

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The pharmacokinetic properties of PET-radiopharmaceuticals have large influence on the in vivo behaviour of these molecules and therefore on the analysis of their PET-data using tracer kinetic modelling. This seminar aims to give insight in the properties and synthesis of PET-radiopharmaceuticals in order to design the appropriate PET-study.

Requirements for PET-radiopharmaceuticals can be discriminated at two levels, e.g. based on the application and on the radiopharmaceutical itself.

Regarding application, it is important which data are needed such as

- quantitation (receptor density, glucose consumption rate, CBF, protein synthesis rate)
- detection (mostly in oncology: sensitivity, sensitivity, TNM scoring)
- imaging of a specific target (characterization)
- therapy monitoring (either using biomarkers or specific PET-tracers, that are sensitive to physiological response)

In the seminar examples will be given on these applications and the effect on radiopharmaceutical requirements. Another aspect in this respect is the kinetics of the biological process of interest and pharmacokinetics of the lead molecule. Choice of radioisotope and class of molecules are important issues here.

Regarding the radiopharmaceutical, they should ideally interact only with the target sites of interest, and therefore show negligible non-specific binding and metabolite formation.

Selection criteria for PET-radiopharmaceuticals will be presented. These are:

- high affinity (to obtain sufficient image contrast)
- high selectivity (binding to target of interest only)
- appropriate lipophilicity (passage BBB, portion of non-specific binding)
- affinity for active transporters, such as P-glycoprotein (signal amplification or undesired efflux of PET-radiopharmaceutical)
- clearance rate of non-specific binding (washout of undesired signal for improved image contrast)
- toxicity (despite low administered amounts these data are required: acute toxicity, mutagenicity and genotoxicity)

Synthesis of PET-radiopharmaceuticals

Besides these pharmacological aspects, radiochemistry is an important player in this field. The possibilities for radiolabelling need to be considered. To be considered are: radiochemical yield, reliability, labelling position within the molecule, required specific activity, choice of radionuclide. Also aspects for clinical applications will be mentioned shortly: automation, GMP-aspects, shelf-life.

References

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