Radioactive labeling of defined HPMA-based polymeric structures: Using [^{18}F]FETos for *in vivo* imaging by Positron Emission Tomography (PET)

Matthias M. Herth[1#], Matthias Barz[2#], Markus Jahn[1], Rudolf Zentel[2*], Frank Rösch[1*]

[1]Institute of Nuclear Chemistry Johannes Gutenberg-University Mainz, Fritz-Strassmann-Weg 2, 55128 Mainz, Germany;
Institute of Organic Chemistry Johannes Gutenberg-University Mainz, Duesbergweg 10-14, 55099 Mainz, Germany

Introduction:

Polymer-based therapeutics are of increasing interest in the development of nanomedical tools for the diagnosis and treatment of many diseases. For example, micelles have been studies for drug delivery applications. Thereby, the nonspecific interaction between proteins and polymer surfaces determines the *in vivo* fate of drug carriers. Particle-sizes, compositions, physical properties and surface chemistry influences the behaviour of nanomaterials *in vivo*. To understand and fine-tune these parameters for *in vivo* therapies or diagnostics, appropriate imaging strategies are needed. In this respect, non-invasive, quantitative, and repetitive whole body molecular imaging techniques such as Positron-Emission-Tomography (PET) would provide a significant advance in the understanding of the mentioned interactions.

Methods:

Defined statistic and block copolymers were synthesized by RAFT polymerization and labeled by [^{18}F]FETos later on. The stability of the polymeric structures were determined 1 h and 2 h after the synthesis by SEC.

Results:

The polymeric structures are based on the biocompatible N-(2-hydroxypropyl) methacryl-amide (HPMA). In order to achieve these structures, functional reactive ester polymers with a molecular weight within the range of 25000-110000 g/mol were aminolyzed by 2-hydroxypropylamin and tyramin (3%) to form ^{18}F-labelable HPMA-polymer precursors. The fluoroalkylation procedure of the phenolic tyramin moieties by [^{18}F]FETos provided radiochemical yields of ~ 80% for block copolymers and > 50% for statistic polymer architectures within a synthesis time of 10 minutes and at a reaction temperature of 120 °C. Total synthesis time including synthon synthesis, ^{18}F-labeling and the final purification via size exclusive chromatography took less than 90 minutes and yielded stable ^{18}F-labeled HPMA-structures in isotonic buffer solution. Nodecomposition could be detected within 2 h.[1]

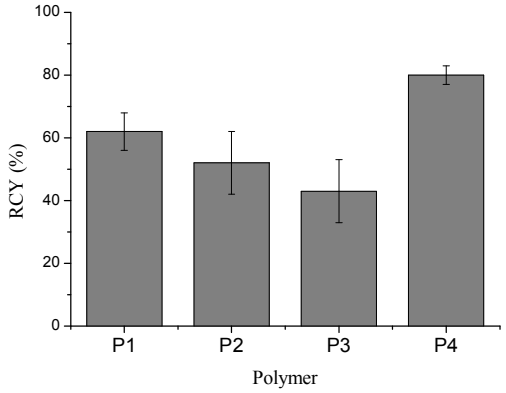

Figure 1: Corrected radioactive labeling yields (RCY) of the statistic copolymers **P1**, **P2**, **P3** and the block copolymer **P4** after 20 min at 100 °C using 3 mg of each precursor polymer

Conclusion:

A new versatile ^{18}F-labeling strategy for polymeric particles has been introduced. Defined and functional HPMA based statistic and block copolymers have been synthesized by RAFT polymerization and labeled in high RCY of > 50% using [^{18}F]FETos in a reaction time of ~ 10 min. Overall synthesis including [^{18}F]FETos synthesis, polymer labeling and polymer purification via SEC was carried out in less than 90 min. The labeled polymer showed no decomposition.

References:

[1] Herth et al. (2009); Radioactive labeling of defined HPMA based polymeric structure: Using [^{18}F]FETos for in vivo imaging by PET. Biomacromolecules (submitted)