3.2

^{99m}Tc-Hynic-Minigastrin 1: A Promising Radiopharmaceutical for Imaging Gastrin/CCK-Positive Tumours: Preclinical Evaluation

von Guggenberg E[1], Behe M[2], Behr T[2], Decristoforo C[1]

[1]Univ.Klinik f.Nuklearmedizin, Innsbruck, Austria [2]Dept.Nuclear Medicine, Marburg, Germany

Aim: Gastrin/CCK receptors are overexpressed in a number of tumours such as MTC and SCLC. Therefore Gastrin analogues binding to the CCK-B receptor are promising peptides for Nuclear Medicine imaging. Recently Minigastrin 1 has been labelled with1 ^{131}I, ^{111}In and ^{90}Y (Behr et al 1999). HYNIC as bifunctional chelator has shown favourable properties for ^{99m}Tc-labeling of small peptides. The aim of this study was the preparation, ^{99m}Tc-labelling and evaluation in vitro and in vivo of HYNIC-Minigastrin 1.
Methods: HYNIC-Minigastrin 1 was prepared by coupling protected HYNIC to Minigastrin immobilised on a resin, followed by TFA cleavage and HPLC purification. The peptide was characterised by RP-HPLC and MS. ^{99m}Tc-labelling was performed using different coligands, such as Tricine, EDDA, Tricine ternary ligand systems. In vitro stability was tested in plasma and towards cystein, plasma protein binding was determined. Receptor binding assays using a CCK-B receptor positive cellline (AR4-2J) were performed and biodistribution in normal Wistar rats was studied with a Gamma camera followed by dissection.
Results: At specific activities >1Ci/µmol HYNIC-Minigastrin 1 could be labelled with yields >95% only using Tricine as coligand. Other coligands or addition of a ternary ligand failed to give reasonable labelling yields. Two isomers of ^{99m}Tc-Tricine-HYNIC-Minigastrin 1 were observed. At higher temperature quantitative yields of a stable isomer with high hydrophilicity, low protein binding and low intestinal excretion in rat biodistribution studies was obtained. Overall biodistribution in rats was similar to ^{111}In-DTPA-Minigastrin 1 with rapid renal excretion and high kidney retention. ^{99m}Tc-Tricine-HYNIC-Minigastrin could be displaced by unlabelled Minigastrin from AR4-2J cell-membranes.
Conclusion: A Gastrin derivative could be labelled at high specific activities with ^{99m}Tc showing isomerism dependent on labelling conditions. ^{99m}Tc-labelled HYNIC-Minigastrin 1 shows promising in vitro and in vivo properties and favourable biodistribution for in vivo tumour imaging. Further evaluation of receptor binding, internalisation and tumour uptake studies are currently in progress.

3.3

Comparison of Carrier-Added [^{99m}Tc]EDTMP and Carrier-Free Preperations of [^{99m}Tc] EDTMP and [^{99m}Tc] DPD

A. Krcal, M. Mitterhauser (*),K. Kletter, R. Dudczak, and C. Pirich

Department of Nuclear Medicine, AKH Vienna
(*) Hospitalpharmacie, AKH Vienna

Aim: High uptake of bone-seeking radiopharmaceuticals in malignant bone lesions is a prerequisite for adequate bone scanning. Visual image analysis is impaired due to high soft-

tissue activity with currently available [^{99m}Tc]-EDTMP-kits. This study aimed to compare carrier-added [^{99m}Tc]-EDTMP with carrier-free [^{99m}Tc]-EDTMP and [^{99m}Tc]-DPD preparations in clinical routine.

Methods: 15µg and 150µg perrhenic acid respectively were added to [^{99m} Tc]-pertechnetate (>6GBq in 3ml phys. saline). The solution was then transferred into a vial, containing 1mg of EDTMP, 3.6mg stannous(II)chloride and 10mg ascorbic acid under inert conditions. Under vigorous stirring the reaction mixture was heated to 45°C for 10min. After cooling down to room temperature the labelling mixture was sterile filtrated (Millipore 0.22µm). Quality control was performed using radio-ITLC (Whatman SG; acetone or ethanol: R_f perrhenate/pertechnetate 0,87, colloid/product 0.05; phys. saline: R_f colloid 0.00, perrhenate/pertechnetate and product 0.9) allowing rapid and efficient assessment of the product. Carrier free [^{99m}Tc]-EDTMP and [^{99m}Tc]-DPD were prepared according to instructions of the manufacterer. Clinical studies were performed in 29 patients according to a routine bone scanning protocol by injecting 700-800 MBq of the respective tracer and whole body imaging 3h thereafter.

Results: Radiochemical purity and radiochemical yield relied on various parameters such as concentration of carrier and reducing agent and reaction conditions (pH, reaction time, temperature). Means of the labelling yield were 22% for the preperation using 150µg of carrier (5 preperations), 80% for the preperation using 15µg of carrier (10 preperations) and 91% for the carrier free products (5 preperations). Radiochemical purity was >96% in all experiments. Colloid was formed in very low amounts, and was completely removed by sterile filtration.

In clinical studies quantitative analysis demonstrated a significant ($p < 0.05$) increase in bone/soft tissue ratio and bone lesion/normal bone ratio especially for the preperation using 15µg of carrier compared to carrier-free products, resulting in a better image quality in patients. This finding of a better uptake in bone tissue could be explained by different complex-parameters such as size, polimerisation grade of the radioligand and a mixture of central atoms in the complex as well as stability parameters in the blood compartment.

Conclusion: Our new method of "co-labelling" with a different central atom allows fast and efficient preparation of Re/[^{99m}Tc]-EDTMP with high stability, good radiochemical purity and sufficent radiochemical yield. The product offers promising properties for clinical application.

3.4

A New Route for the Synthesis of O-(2-[^{18}F]Fluoroethyl)-L-Tyrosin Using Distilled 2-[^{18}F]Fluoroethylbromide

W. Wadsak[1,3], J. Schmaljohann[2], B. Keppler[3], K. Kletter[1]

[1]Department of Nuclear Medicine, University of Vienna, Austria; [2]Department of Neurology, University of Bonn, Germany; [3]Department of Inorganic Chemistry, University of Vienna, Austria

Aim: Positron emission tomography (PET) is a powerful diagnostic method for oncological questions. Therefore, the demand for new F-18 labelled radiopharmaceuticals is significant. Fluoroalkylation is a well known technique to provide no-carrier-added F-18 labelled radiotracers in high yields. The aim of this work was to establish a synthesis of O-(2-