Receptor-PET/CT of neuroendocrine tumors using the gallium-68 labelled somatostatin analog DOTA-NOC: First clinical results

R. P. Baum[1] M. Schmücking[1], A. Niesen[1], K. P. Zhernosekov[2] F. Rösch[2]
[1]Dept. of Nuclear Medicine / Center for P.E.T., Zentralklinik Bad Berka, Germany
[2]Institut für Kernchemie, Johannes Gutenberg-Universität, D-55128 Mainz, Germany

Introduction: Modification of the octapeptide octreotide in position 3 resulted in a compound [DOTA]-1-Nal[3]-octreotide (DOTA-NOC) which showed an increased somatostatin receptor (sstr) affinity for sstr2, sstr3, and sstr5. After labelling with ^{111}Indium- or ^{90}Yttrium, DOTA-NOC is superior to all somatostatin-based radiopeptides having this particular type of binding profile, and has three to four times higher binding affinity to sstr2 than In^{III},Y^{III}-DOTA-Tyr[3]-octreotide (In^{III},Y^{III}-DOTA-TOC).

In addition, [^{111}In]DOTA-NOC showed a specific and high rate of internalization into tumour cells which was about two times higher than that of [^{111}In]DOTA-TOC [1]. These very promising preclinical data prompted us to use this new radiopeptide for somatostatin receptor PET/CT imaging in patients with neuroendocrine tumours (NET) after labelling with Gallium-68, a short-lived positron emitter with a half-life of 68 min.

Experimental: 30 mCi ^{68}Ge/^{68}Ge-generators based on TiO_2-phase (Cyclotron Co., Obninsk, Russia) were used to obtained 500-750 MBq of ^{68}Ga. [^{68}Ga]DOTA-NOC was synthesised with specific activities of about 15 MBq / µg peptide as described elsewhere [2].

34 patients with histologically proven NET (mostly carcinoids) and progressive metastases were studied before peptide receptor radiotherapy (PRRT). A mean of 74 MBq (65-140 MBq) ^{68}Ga-DOTA-NOC were injected. Simultaneously, furosemide (20 mg) was injected to increase the renal elimination (patients were well hydrated). Acquisition was started 20-110 min p.i. (mean 51 min p.i.) from the femoral shaft to the head (up to 9 bed positions) using the latest generation LSO-based whole body PET/CT (biograph DUO, Siemens). Emission time ranged between 2 to 5 min per bed. Attenuation correction was performed using the low-dose whole-body spiral-CT (Somatom Emotion duo) integrated in the PET/CT scanner. CT images were acquired after injection of 100 cc iodinated contrast material.

Standardized uptake values (SUV) were determined for all tumour lesions and for normal tissue (pituitary gland, thyroid, lung, liver, kidney, spleen, gluteus muscle). Volumetry of the lesions was done using individualized iso-SUV-lines (cut-off levels) for every patient.

PET images were read indepedently by two experienced nuclear medicine physicians without knowledge of the CT results; the CT scans were read by trained radiologist (knowing the PET results).

Results: In almost all patients more lesions were detected as compared with ^{111}In-OctreoScan or ^{99m}Tc-TETOC (especially with regard to small bone metastases) or with CT or MRI (especially regarding lymph node metastases). In some patients, small lung nodules were seen on CT which were receptor negative on the PET scan (lung metastases vs. benign lesions).

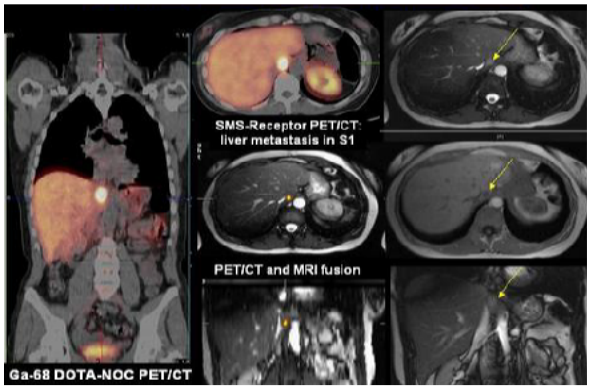

Fig.1 ^{68}Ga-PET/CT and image fusion of PET/CT and MRI for detection of a liver metastasis of a neuroendocrine carcinoma

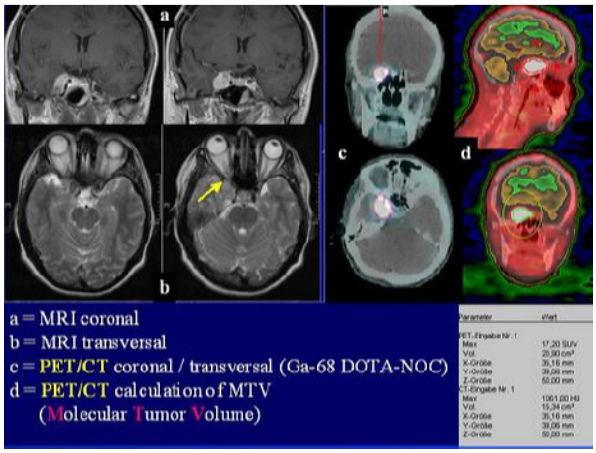

Fig. 2 Inoperable meningioma: ^{68}Ga-DOTA-NOC PET/CT of the head and MRI fusion

Brilliant PET/CT images of all known tumour lesions (see Fig. 1-2) and in addition small lymph node metastases of less than 5 mm were easily visualized as early as 20 min p.i. Receptor PET/CT using ^{68}Ga-DOTA-NOC advances as the new gold standard for imaging of neuroendocrine tumours possibly allowing also tumour dosimetry.

References

[1] Wild et al., Eur J Nucl Med Mol Imaging; **30**:1338 (2003)
[2] Zhernosekov et al., this report