Enhanced visualization of disseminated bone metastases of primary neuroendocrine tumors using ^{68}Ga-DOTATOC

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Introduction: The diagnosis of neuroendocrine tumors (e.g. carcinoides, pancreatic tumors, etc) in terms of Somatostatin-Receptor-Scintigraphy (SRS) so far is performed using the tumor-specific somatostatin-analogue ^{111}In-DTPA-D-Phe[1]-octreotide (111In-Octreoscan). However, due to the limitations of gamma camera technology, the implementation of somatostatin-analogues labelled with a positron emitting isotope and the use of PET/CT-technology is challenging because of the following reasons:

1. Spacial resolution dramatically increases from 10-20 mm to 4-6 mm.
2. (Semi-) quantitative examination of the somatostatin-receptor status per ml tumour tissue appears to be possible, which is relevant for therapy choice, prognostic outcome and therapy response control
3. Using PET/CT-technology, an exact morphological correlation is possible

^{68}Ga-DOTATOC (^{68}Ga-DOTA-DPhe[1]-Tyr[3]-octreotide) represents a biochemically most promising peptidic targeting vector for determination of human somatostatin subtype 2 expressing tumors. The potency of this ligand for molecular imaging of small metastases is currently paralleled by the implementation of PET/CT.

Experimental: ^{68}Ga-DOTATOC images were recorded with a GE DISCOVERY LS PET/CT–Scanner [PET: (GE Advance NXi): 2-D-Modus, CT-based attenuation correction, iterative reconstruction. CT: (GE LightSpeed Plus): Multislice (4-rows) Low-dose-Spiral-CT], 40 min after i.v.-injection of 106 MBq ^{68}Ga-DOTATOC, scan area: vertex to groin. ^{68}Ga-DOTATOC was synthesised using a newly developed procedure providing intrinsic minimisation of the ^{68}Ge/^{68}Ga generator eluate (volume down to < 0.5 ml), separation of metallic impurities and high-yield (> 95%) labelling in buffer-free media within an overall processing period of about 20 min. [1]

Results and Discussion: The patient illustrated here was examined using FGD, ^{111}In-OctreoScan and ^{68}Ga-DOTATOC. Whereas enhanced visualization of metastases in the whole skeleton via ^{68}Ga-DOTATOC receptor binding is obvious, these bone metastases don't show any increased FDG-uptake. ^{111}In-Octreoscan is more specific for neuroendocrine tumours than FDG, but in the patient studied shows only some metastases in the skull. The subsequent PET/CT-Scan, using ^{68}Ga-DOTATOC, reveals disseminated bone metastases, which could not be observed with any other imaging modality.

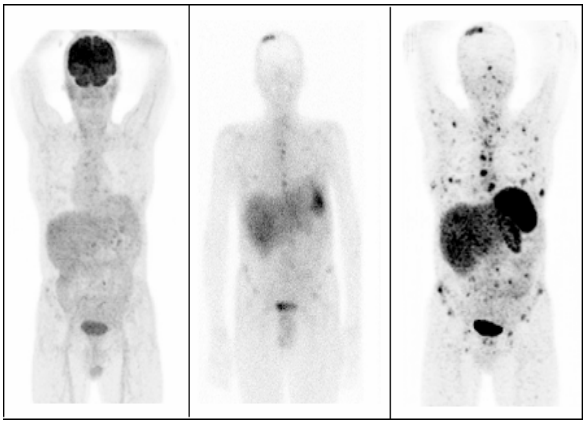

Fig. 1. Comparison of ^{18}F-FDG, ^{111}In-OctreoScan and ^{68}Ga-DOTATOC in the same patient
[Patient: male, *1939, neuroendocrine tumor with unknown primary, multiple liver and bone metastases]

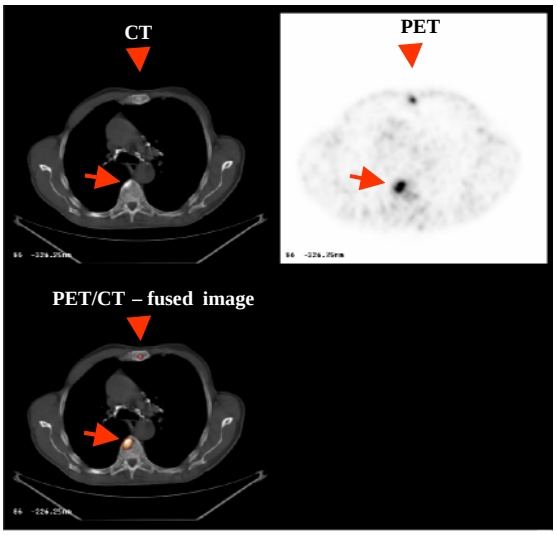

Fig. 2. osteoblastic bone metastases in sternum and spine ^{68}Ga-DOTATOC
[same patient as in Fig.1]

Conclusion: First results have been obtained regarding the diagnosis of disseminated bone metastases originating from primary neuroendocrine tumors using ^{68}Ga-DOTATOC. Visualization is dramatically enhanced compared to standard imaging modalities used to date, like e.g. ^{18}F-FDG-PET or ^{111}In-Octreoscan. Further studies with a greater number of patients should be performed.