

# Localization of Insulinoma: Comparison of Glucagon-like Peptide-1 Receptor (GLP1-R) SPECT/CT, PET/CT and MRI. Preliminary results of a prospective clinical study.

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## Objective:

The surgical removal of insulinomas is hampered by the difficulty to localize these tumors using conventional radiological procedures (MRI and CT). Angiography and intraarterial calcium stimulation and venous sampling (ASVS) has shown to improve sensitivity but is an invasive procedure with corresponding risks.

In vitro data suggest that human insulinoma cells exhibit a high density of glucagon-like peptide-1 (GLP-1) receptors that can be used as specific targets for in vivo receptor imaging (1).

In a previous study we were able to show that targeting the glucagon-like peptide-1 receptors (GLP-1R) using the specific ligand [Lys<sup>40</sup>(Ahx-DTPA-<sup>111</sup>In)NH<sub>2</sub>]exendin-4 is a very sensitive (≥ 95% sensitivity), non-invasive, method to localize benign insulinomas with SPECT (2).

However PET possesses a higher spatial resolution and sensitivity and provides accurate quantification of tracer uptake (3).

Therefore the aim of our study is to compare the detection rates of <sup>68</sup>Ga-DOTA-exendin-4 PET/CT, <sup>111</sup>In-DOTA-exendin-4 SPECT/CT and standardized contrast enhanced 3T MRI in patients with endogenous hyperinsulinemic hypoglycemia suspicious in having an insulinoma.

## Methods:

This is an IRB approved, HIPAA compliant prospective monocenter study. Only patients with confirmation of the diagnosis by histology after surgical removal were included in this interim analysis (32 patients planned).

14 consecutive patients with endogenous hyperinsulinemic hypoglycemia highly suspicious for an insulinoma (11 female; 3 male; mean 55 yrs; range 18-80 years) were included.

All patients fulfilled the following inclusion criteria: biochemically proven endogenous hyperinsulinemic hypoglycemia with neuroglycopenic symptoms, negative screening for sulfonylurea (exclusion of hypoglycemia factitia) and age above 18 years. Patients with evidence of malignant insulinoma in conventional imaging were excluded, as well as pregnant women, patients with allergies to exendin-4, and patients with renal insufficiency (blood creatinine concentrations >140 µmol/L).

Patients first underwent pancreatic MR imaging using a 3T MRI scanner (Magnetom Prisma, Siemens Healthcare) including T1w, T2w, diffusion weighted imaging (DWI) and dynamic contrast enhanced (DCE) sequences.

Afterwards <sup>111</sup>In-DOTA-exendin-4 SPECT/CT and <sup>68</sup>Ga-DOTA-exendin-4 PET/CT were performed within 24-73 hours in randomized cross-over order.

Total-body planar images and SPECT/CT of the abdomen were performed on a SPECT/CT unit (Symbia Intevo, Siemens Healthcare) 4 h and 72 h after intravenous injection of 84.1 ± 13.6 MBq (range 52-111 MBq, 10.5-14.4 µg) <sup>111</sup>In-DOTA-exendin-4.

PET/CT examination was performed on a GE Discovery ST PET/16-detector CT unit (GE Healthcare). One bed position of the upper abdomen was acquired during 8 min, 2.5 hours after intravenous injection of 82.9 ± 6.9 MBq (range 74-97 MBq, 12.0-15.3 µg) <sup>68</sup>Ga-DOTA-exendin-4.

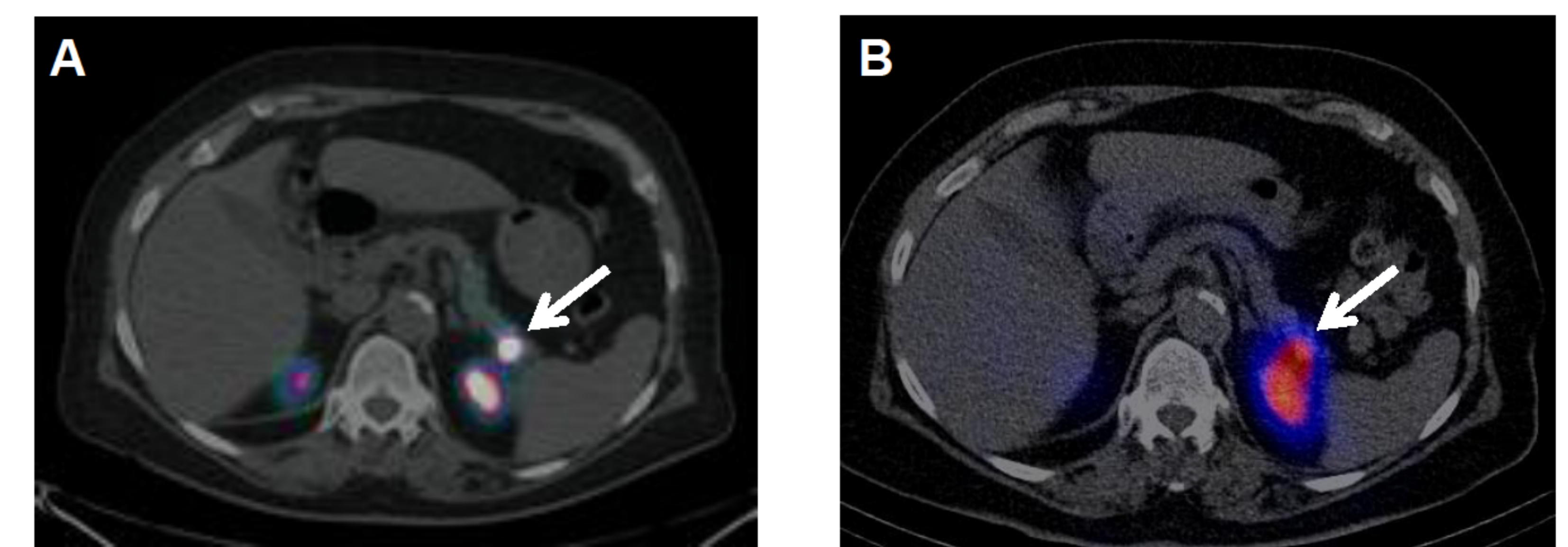
## Results:

Table 1. Comparison of <sup>111</sup>In-exendin-4 SPECT/CT, <sup>68</sup>Ga-exendin-4 PET/CT and standardized MRI (3 Tesla)

	<sup>111</sup> In-exendin-4 SPECT/CT	<sup>68</sup> Ga-exendin-4 PET/CT	Standardized MRI (3 Tesla)
Sensitivity (disease localization)	<b>79%</b> (11/14) interim analysis	<b>100%</b> (14/14) interim analysis	<b>71%</b> (10/14) interim analysis

Histology: 13 benign insulinomas and 1 nesidioblastosis

**Figure 1.** Comparison of <sup>111</sup>In-exendin-4 SPECT/CT and <sup>68</sup>Ga-exendin-4 PET/CT in patient no. 8

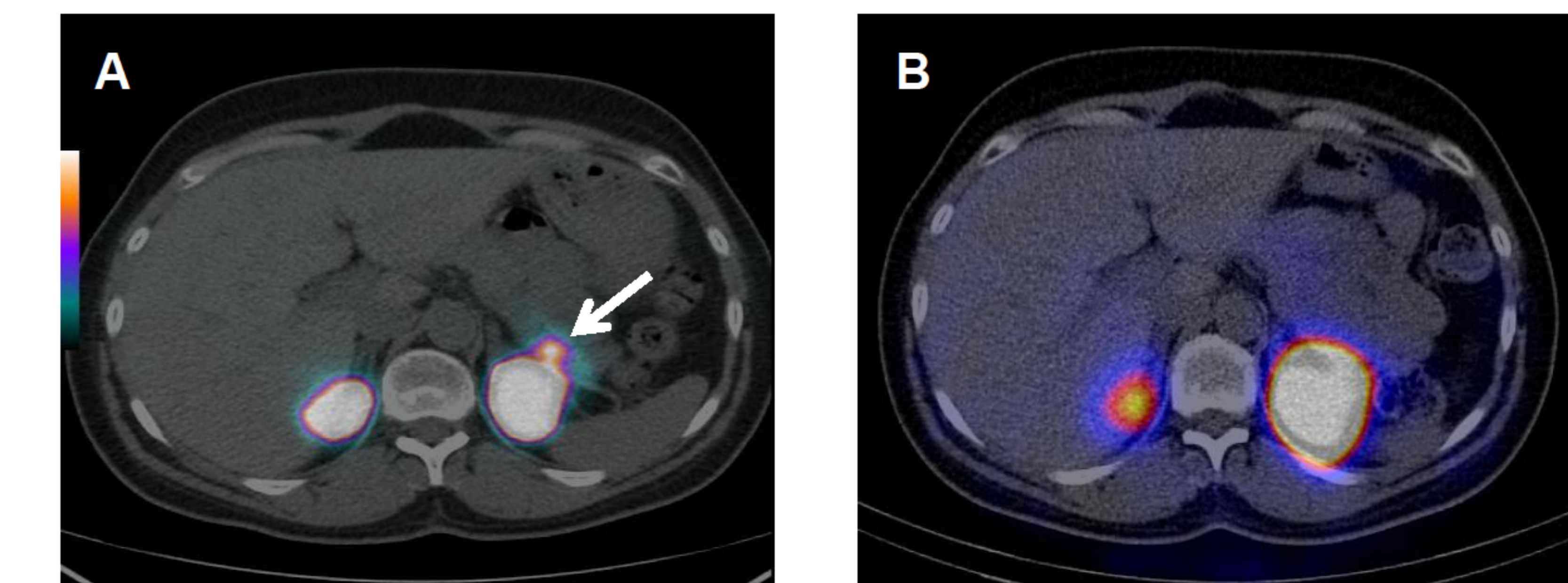


(A) Transaxial PET/CT images from patient 8, 2.5h after injection <sup>68</sup>Ga-DOTA-exendin-4.

(B) Transaxial SPECT/CT images of the same patient, 72h after injection of <sup>111</sup>In-DOTA-exendin-4.

The arrow (A+B) shows focal <sup>68</sup>Ga-DOTA-exendin-4 uptake and <sup>111</sup>In-DOTA-exendin-4 in the distal portion of the pancreatic tail consistent with the surgically removed insulinoma.

**Figure 2.** Comparison of <sup>111</sup>In-exendin-4 SPECT/CT and <sup>68</sup>Ga-exendin-4 PET/CT in patient no. 5



(A) Transaxial PET/CT images from patient 5, 2.5h after injection <sup>68</sup>Ga-DOTA-exendin-4.

(B) Transaxial SPECT/CT images of the same patient, 72h after injection of <sup>111</sup>In-DOTA-exendin-4.

The arrow (A) shows focal <sup>68</sup>Ga-DOTA-exendin-4 uptake in the distal portion of the pancreatic tail consistent with the surgically removed insulinoma. SPECT/CT did not visualize the insulinoma.

## Conclusion:

1. GLP1-R PET/CT defines a novel, non-invasive, highly sensitive tool in localizing insulinomas and performs better than standardized MRI imaging.
2. It also performs better than SPECT/CT due to the higher spatial resolution. In addition the lower irradiation dose and much shorter investigation time PET/CT may be favored over SPECT/CT

## Reference:

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