Localization of benign Insulinomas using Glucagon-like Peptide-1 Receptor (GLP-1R) SPECT/CT and PET/CT in a prospective clinical study

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Background

- In patients with benign insulinomas conventional imaging is able to detect about 60-70% of the small pancreatic lesions (1-2 cm).
- Surgery is the only curative option for this disease.
- Preoperative localisation of the tumour is critical for the surgical strategy.
- Benign insulinoma express in nearly 100% GLP-1 receptors at a high density (ca. 5x higher than in normal beta-cells).
- GLP-1R single Photon Emission Computed Tomography (SPECT) has been shown to be a valid non-invasive tool for the localisation of benign insulinoma.
- A prospective randomized study comparing GLP-1R Positron Emission Tomography (PET)/CT and GLP-1R SPECT/CT has not yet been performed.

Aim

To compare the detection rate of GLP-1R PET/CT and GLP-1R SPECT/CT in patients with a biochemically proven endogenous hyperinsulinemic hypoglycemia.

Methods

- Adult patients with with neurogylcopenic symptoms due to endogenous hyperinsulinemic hypoglycemia were enrolled (ClinicalTrials.gov: NCT02127541).
- No signs of malignancy on conventional imaging.
- Investigations included ^{111}In-DOTA-exendin-4 SPECT/CT and ^{68}Ga-DOTA-exendin-4 PET/CT in a randomized order.
- Endpoint was correct detection rate (gold standard: histology).

Results

•Thirty-three patients (25 females, 8 males, age range 18-80 years, mean 49 years) were scanned until now.

•Previously performed cross-sectional imaging (CT/MRI) was negative or not conclusive in 25/33 (76%) of patients.

•22 patients have been operated, two patients refused surgery and five patients are awaiting surgery.

•In this collective, the histopathological diagnosis of a benign insulinoma was confirmed in 19 patients, 1 patient had an adult islet cell hyperplasia. In 1 patient both intraoperative palpation and histological diagnosis did not confirm an insulinoma. In 1 patient symptoms of endogenous hypoglycemia ceased postoperative but histological diagnosis did not confirm the diagnosis. This patient was excluded from evaluation as the final diagnosis remained unclear. In 4 patients PET/CT, SPECT/CT as well as the previous performed conventional imaging did not find any suspicious lesion and were not operated up to date.

In this interim analysis:

- **PET/CT** (2.5h p.i.) showed an overall pooled sensitivity of **95%**
- **SPECT/CT** (72h p.i.) showed an overall pooled sensitivity of **73%**

•PET/CT was the only modality which correctly identified the area of islet cell hyperplasia (adult nesidioblastosis) within the pancreas.

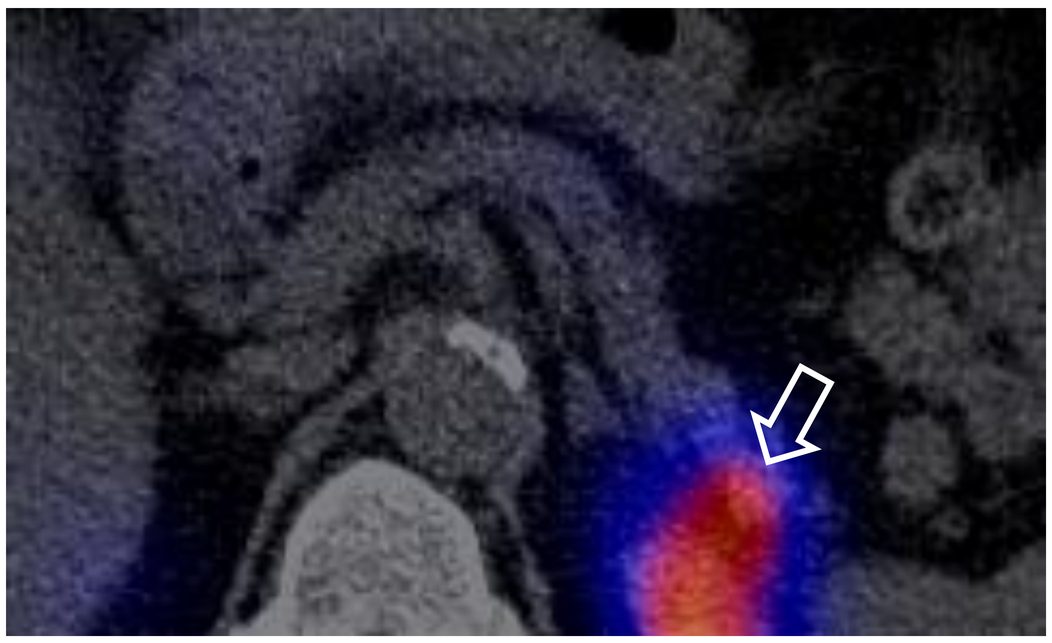

Figure 1: Transaxial ^{111}In-DOTA-exendin-4 SPECT/CT. The arrow shows focal uptake in the distal portion of the pancreatic tail.

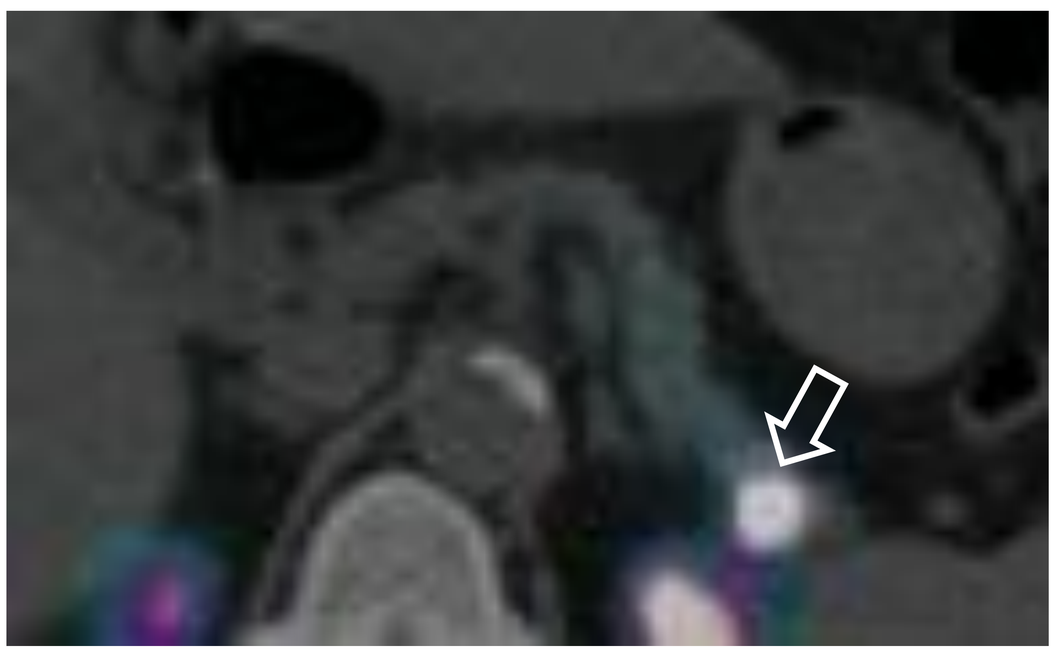

Figure 2: Transaxial ^{68}Ga-DOTA-exendin-4 PET/CT. The arrow shows focal uptake in the distal portion of the pancreatic tail (same patient).

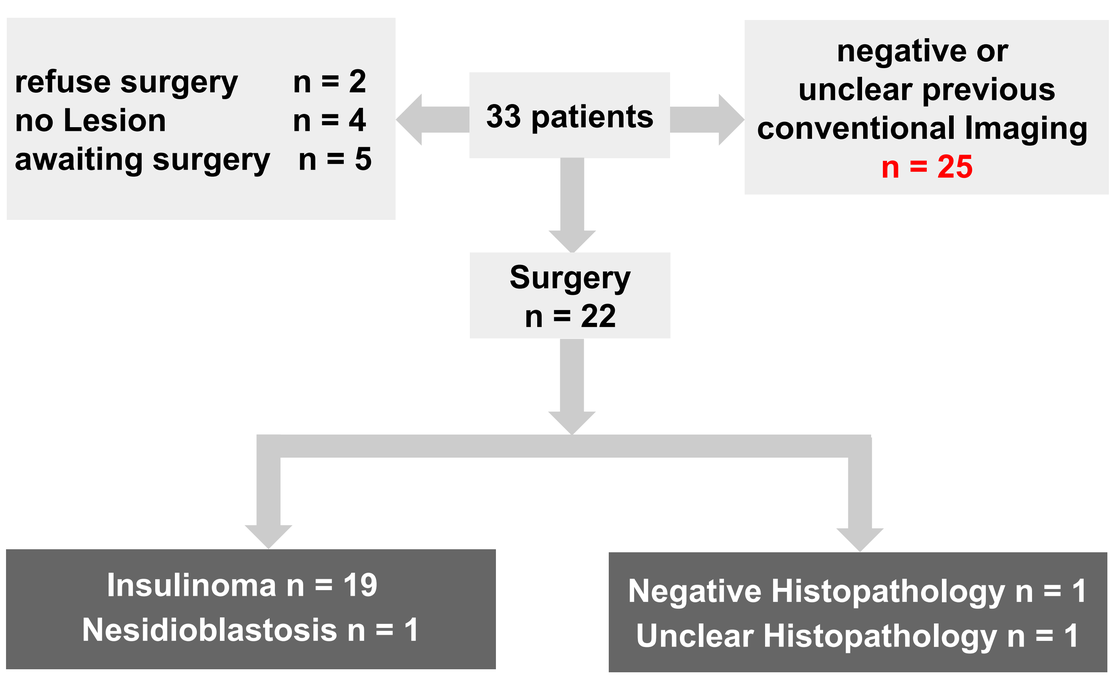

Figure 3: Results

Conclusion

1.Our interims analysis suggests that GLP-1R PET/CT performs better than GLP-1R SPECT/CT at a lower radiation dose and shorter examination time.

2.GLP-1R PET/CT will be a useful diagnostic tool in patients where cross sectional imaging (CT/MRI) fails to localize the insulinoma.