



Could ^{99m}Tc labelled Glucagon-like Peptide - 1-analogue (^{99m}Tc -GLP1) scintigraphy be an answer for patients with persistent hypoglycemia?

Alicja Hubalewska-Dydejczyk¹, Anna Sowa-Staszczak¹, Agnieszka Stefanska¹, Monika Buziak-Bereza¹, Malgorzata Trofimiuk-Müldner¹, Aleksandra Gilis-Januszewska¹, Agata Jabrocka-Hybel¹, Monika Tomaszuk¹, Romana Tomaszewska², Maciej Malecki³, Tomasz Bednarczuk⁴, Grzegorz Kaminski⁵, Aldona Kowalska⁶, Renata Mikolajczak⁷, Barbara Janota⁷

¹ Department of Endocrinology, Jagiellonian University Medical College, Krakow, POLAND ² Department of Pathology, Jagiellonian University Medical College, Krakow, POLAND ³ Department of Metabolic Diseases, Jagiellonian University Medical College, Krakow, POLAND ⁴ Department of Endocrinology, Medical University of Warsaw, Warsaw, POLAND ⁵ Department of Endocrinology and Radioisotopic Therapy, Military Institute of Medicine, Warszawa, POLAND ⁶ Department of Endocrinology and Nuclear Medicine, Holycross Cancer Center, Kielce, POLAND ⁷ Radioisotope Center POLATOM, National Centre for Nuclear Research, Otwock, POLAND

INTRODUCTION:

Surgery is the only effective therapy for insulinoma patients. While insulinomas are usually small tumors their localization with the use of majority of standard diagnostic modalities is sometimes difficult. Therefore there is a necessity to develop diagnostic strategies in cases of unknown tumour location, possibly through the use of new biomarkers. Due to the high density of receptors for glucagon-like peptide 1 (GLP1) in a benign form of insulinoma, scintigraphy with ^{99m}Tc labelled GLP1 analogue has been developed in our centre as an imaging technique of this type of neoplasm. Labelled GLP1 analogue might also be applied in diagnosis of various forms of nesidioblastosis allowing to determine the range of surgery in its focal and diffuse types, if suitable.

MATERIAL AND METHODS:

Study included: 40 patients with suspected insulinoma in whom CT/MR/EUS/SRS failed to visualize tumour thus excluding surgical intervention, 3 patients with malignant insulinoma and 3 with nesidioblastosis (to assess its type form). [Lys40(Ahx-HYNIC- ^{99m}Tc /EDDA)NH₂]exendin-4 SPECT/CT with volumetric analysis was performed.

RESULTS:

21/40 cases - true positive with focal tracer uptake in pancreas, including histopathologically confirmed bifocal insulinoma. In all operated patients symptoms resolved post-operatively

1 - false negative result appeared to be malignant insulinoma

1 - false positive result (no tumour was found)

9 - true negative with no ^{99m}Tc -GLP1 uptake (reactive hypoglycemia or Munchausen syndrome)

8 patients - lost from follow up

Sensitivity, specificity, PPV of ^{99m}Tc -GLP1 SPECT/CT were 95%, 90%, 95%, respectively.

2 patients with nesidioblastosis - diffuse tracer uptake

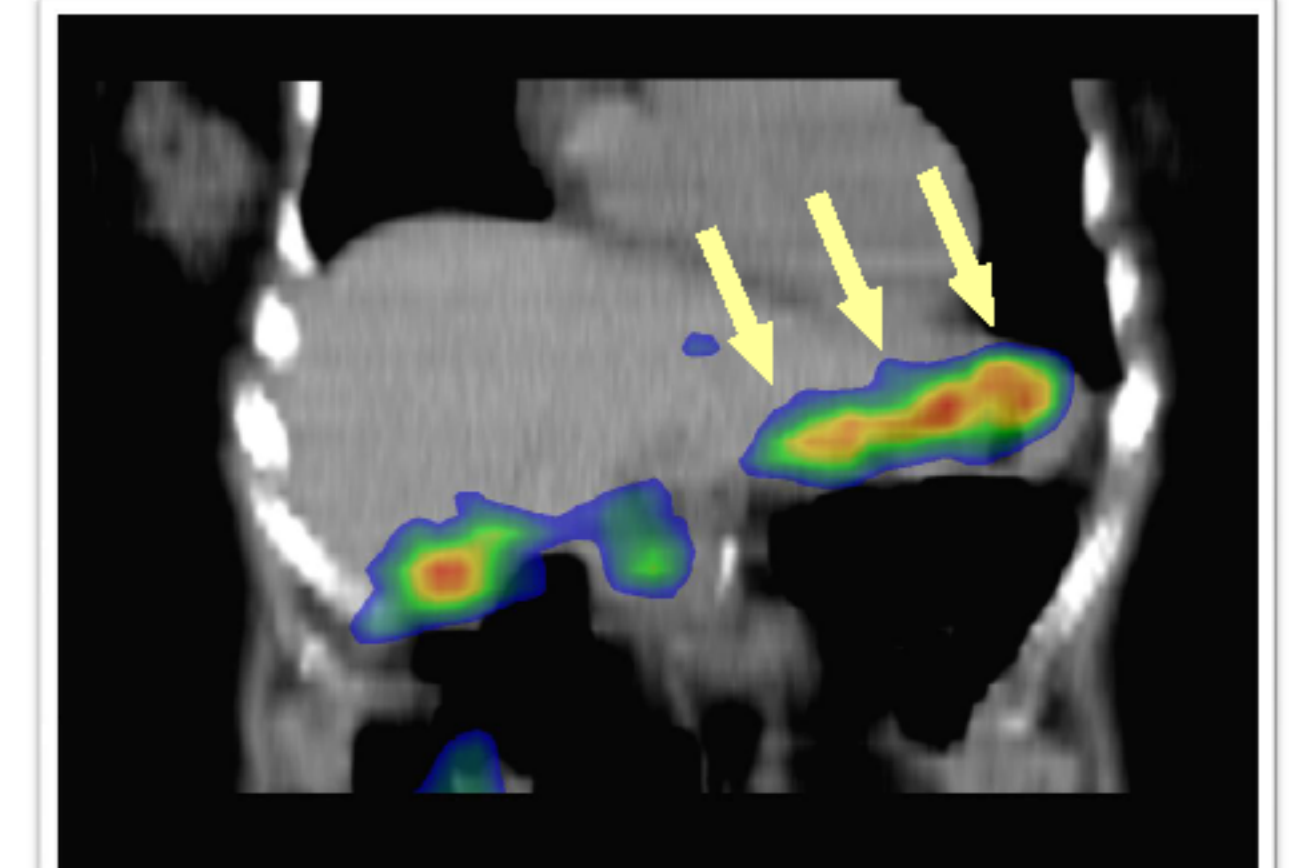
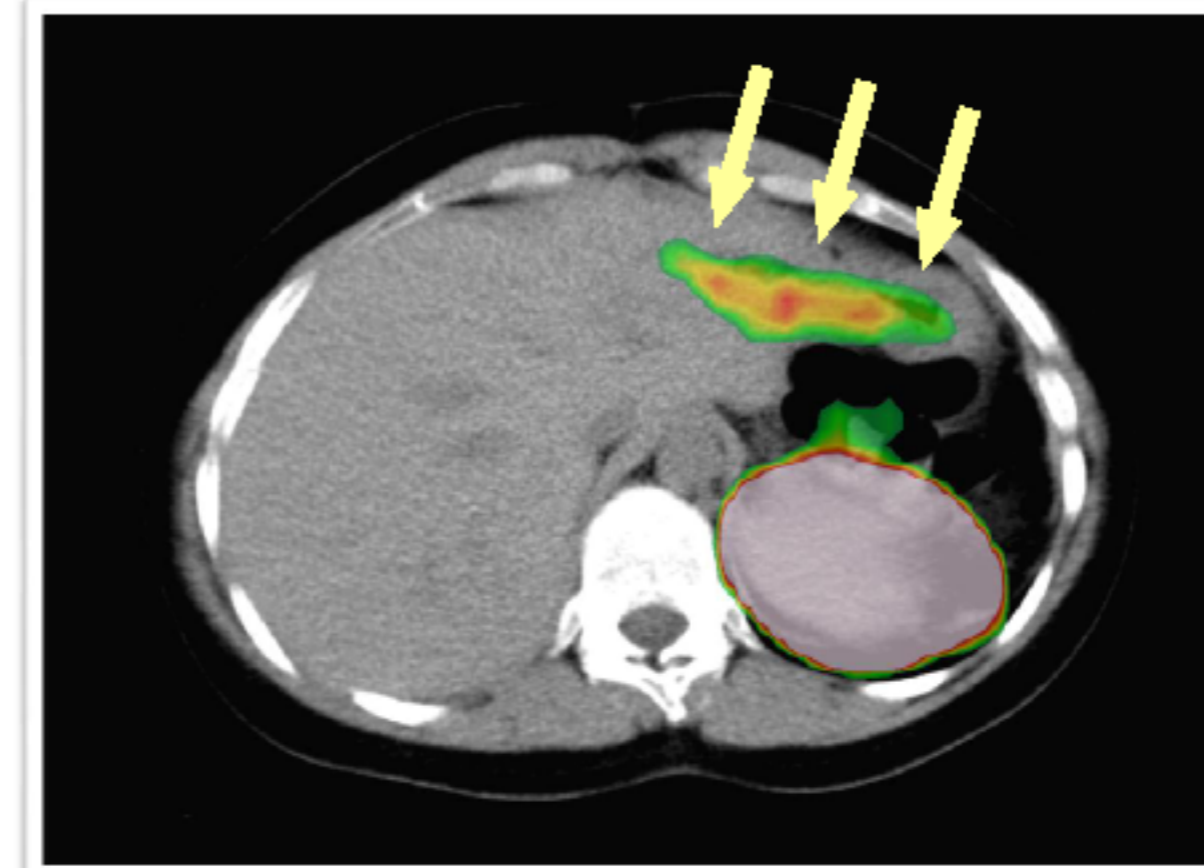
1 patient with nesidioblastosis - focal lesion (histopathological examination - coexistence of nesidioblastosis and insulinoma)

^{99m}Tc -GLP1 SPECT/CT confirmed different biology of primary tumour (PT) and metastases in malignant insulinoma (phenomenon well known in NENs)

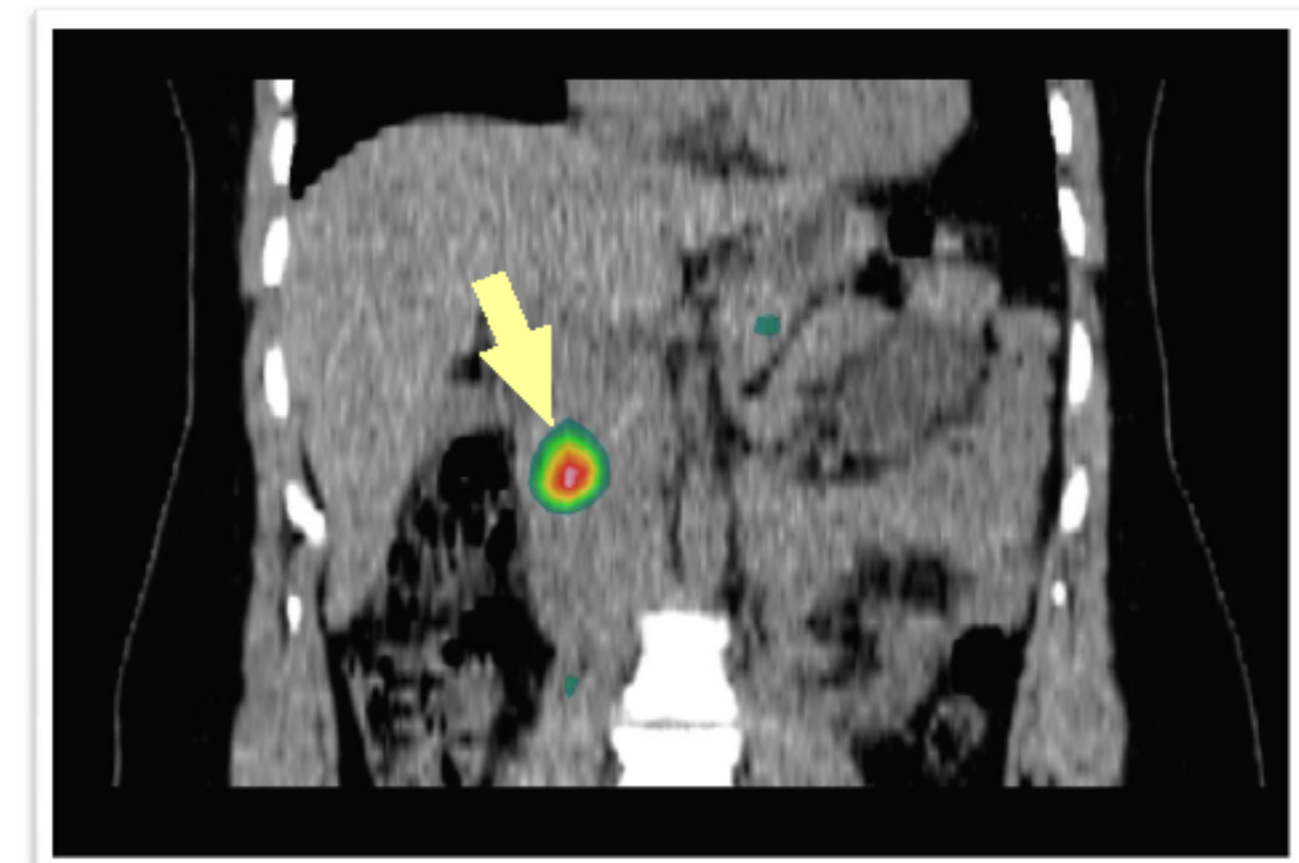
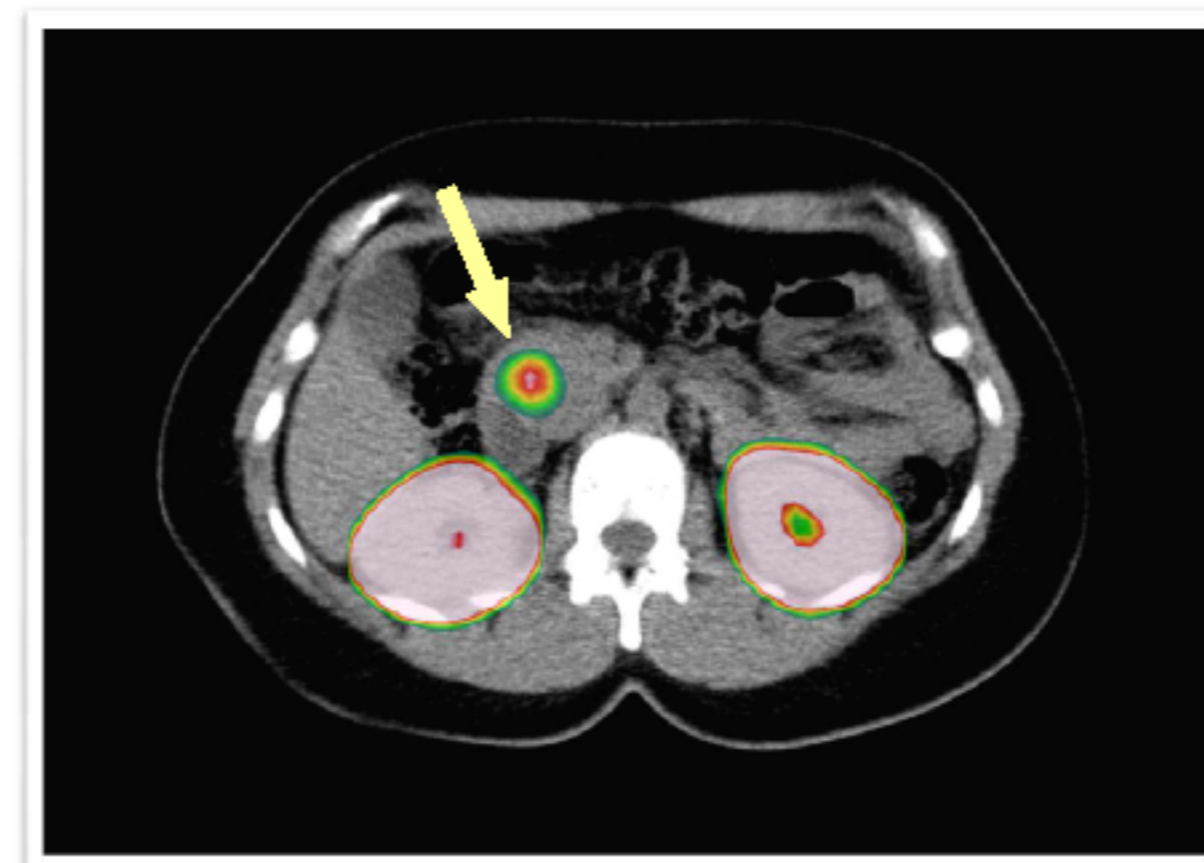
1st patient with malignant insulinoma - both primary tumor (PT) and metastases were negative

2nd patient with malignant insulinoma - PT positive and metastases negative

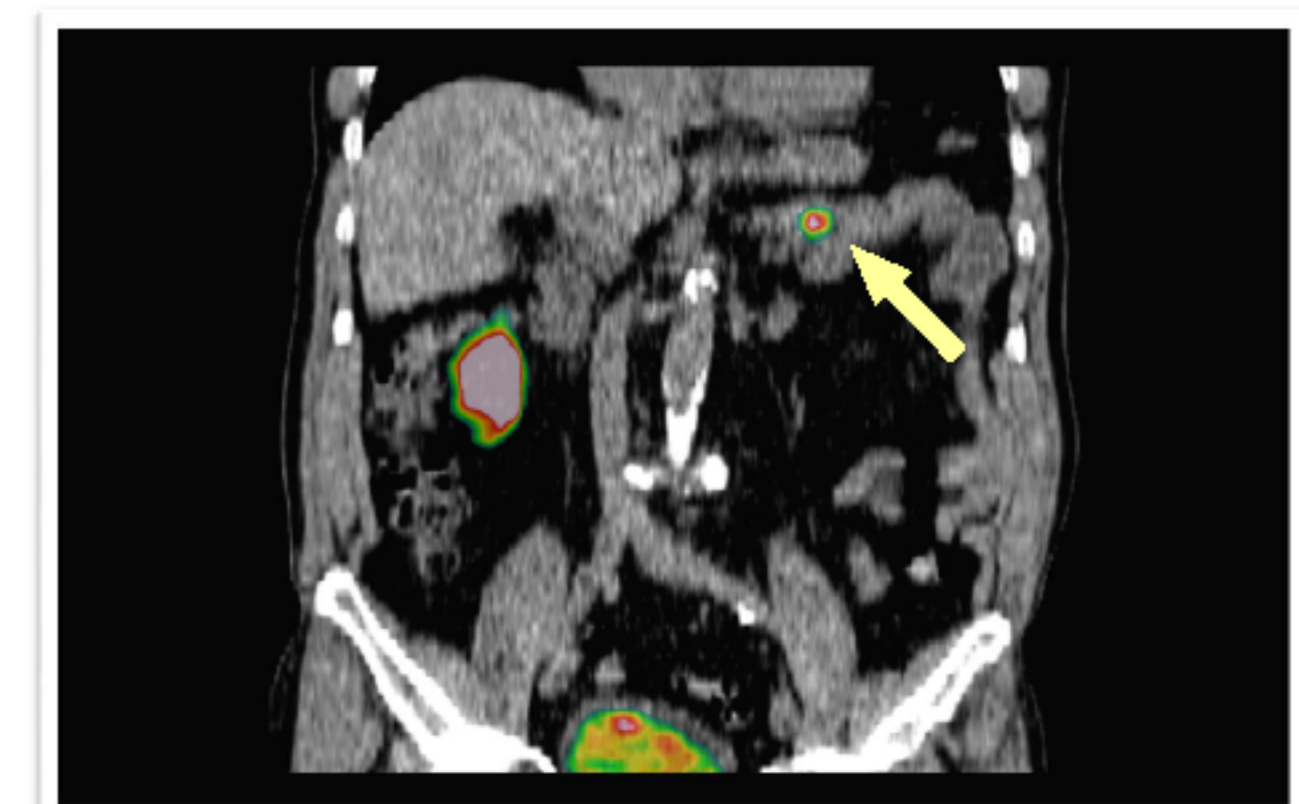
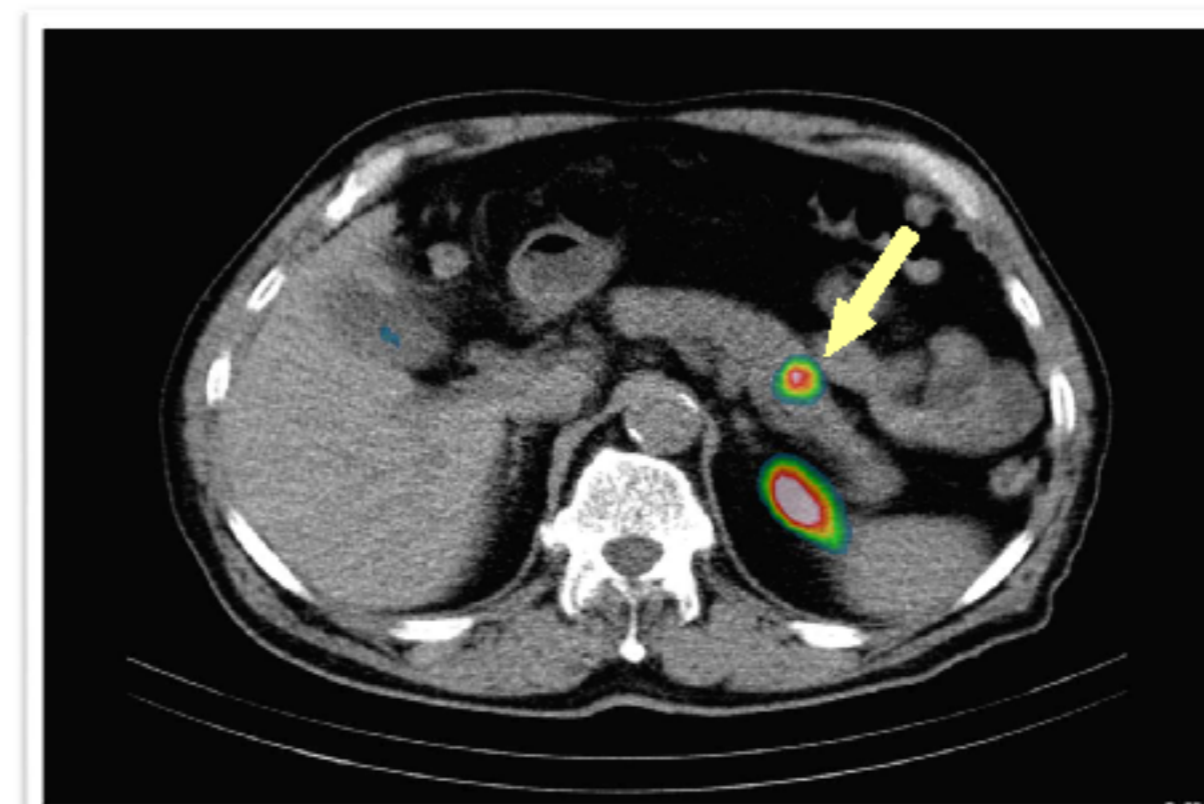
3rd patient with malignant insulinoma - PT negative and metastases positive



Figures 1 ^{99m}Tc -GLP (SPECT/CT) in 31 year old woman (U.A.) with diffuse uptake in pancreas. Histopathological examination confirmed nesidioblastosis and also a small lesion of insulinoma.



Figures 2 ^{99m}Tc -GLP (SPECT/CT) in 35 year old woman (K.E.) with focal uptake in the head of pancreas.



Figures 3 ^{99m}Tc -GLP (SPECT/CT) in 77 year old man (B.K.) with focal uptake in the anterior part of the tail of pancreas.

CONCLUSIONS

^{99m}Tc -GLP1 SPECT/CT proved to be helpful in management of patients with persistent hypoglycaemia.

GLP1 analogue labelled with ^{99m}Tc , in contrary to those labelled with ^{111}In and ^{68}Ga , is still easier available, generates lower radiation burden to patients and may be potentially useful in the intraoperative detection of insulinoma.

^{99m}Tc -GLP1 SPECT/CT could be considered in the former stages of diagnostic schemes to optimize the procedures with a more effective strategy to allow sparing operation as well as to improve the quality of life of these patients.

Lower and unhomogenous expression of GLP1 receptors on malignant insulinoma cells makes scintigraphy with ^{99m}Tc -GLP1 probably less useful than somatostatin receptor scintigraphy in malignant type of this neoplasms.

