

# 2° Convegno interregionale AME

- Emilia Romagna
- Friuli Venezia Giulia
- Lombardia
- Trentino Alto Adige
- Veneto



ASSOCIAZIONE MEDICI ENDOCRINOLOGI  
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Per la qualità clinica in Endocrinologia

## AGGIORNAMENTO IN ENDOCRINOLOGIA ONCOLOGICA: NON SOLO TIROIDE

BOLOGNA, Hotel i Portici  
Sabato, 10 Maggio 2014

## Sessione I TUMORI NEUROENDOCRINI DEL TRATTO GEP

L'iter diagnostico :  
fondamentale il gioco di  
squadra

**Dobbiamo considerare solo Octreoscan e/o PET-DOTATOC?**

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Az.Osp.S.Maria Nuova - IRCCS  
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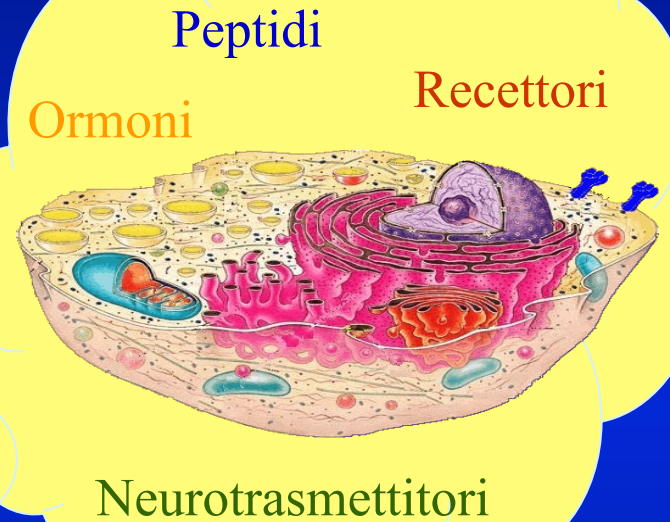
Arcispedale S. Maria Nuova

Istituto in tecnologie avanzate e modelli assistenziali in oncologia  
Istituto di Ricovero e Cura a Carattere Scientifico

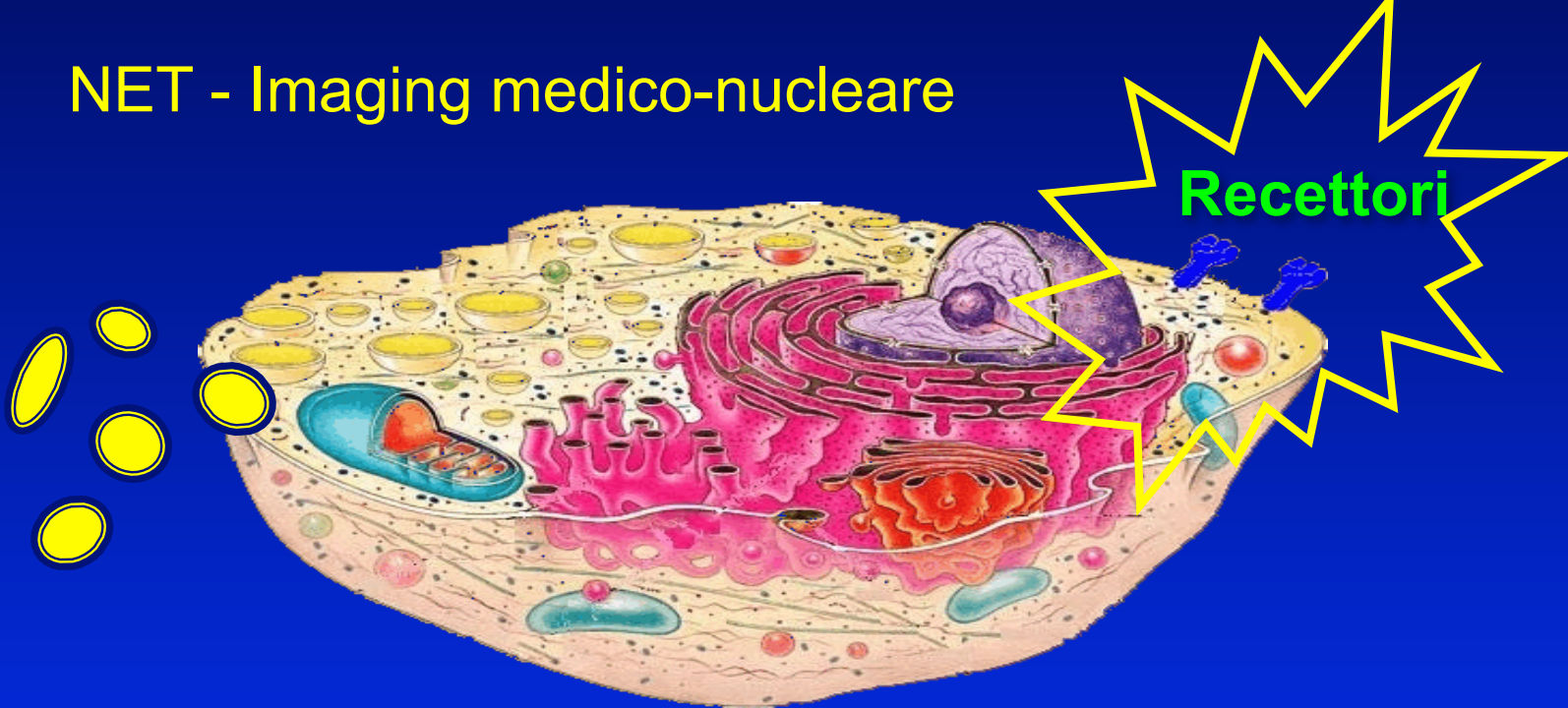


# *Imaging medico-nucleare=Imaging molecolare*

**Le immagini sono  
espressione delle  
caratteristiche  
biochimiche e  
metaboliche dei tessuti**



# NET - Imaging medico-nucleare



## *Recettori per Peptidi Espressi Preferenzialmente dai Tumori GEP*

- Somatostatina (5 sotto-tipi)
- Bombesina (3 sotto-tipi)
- Colecistochinina (2 sotto-tipi)
- VIP (2 sotto-tipi)
- Glucagone (1 principale)

# Imaging medico-nucleare

## Presupposti fisiopatologici



## Metodiche

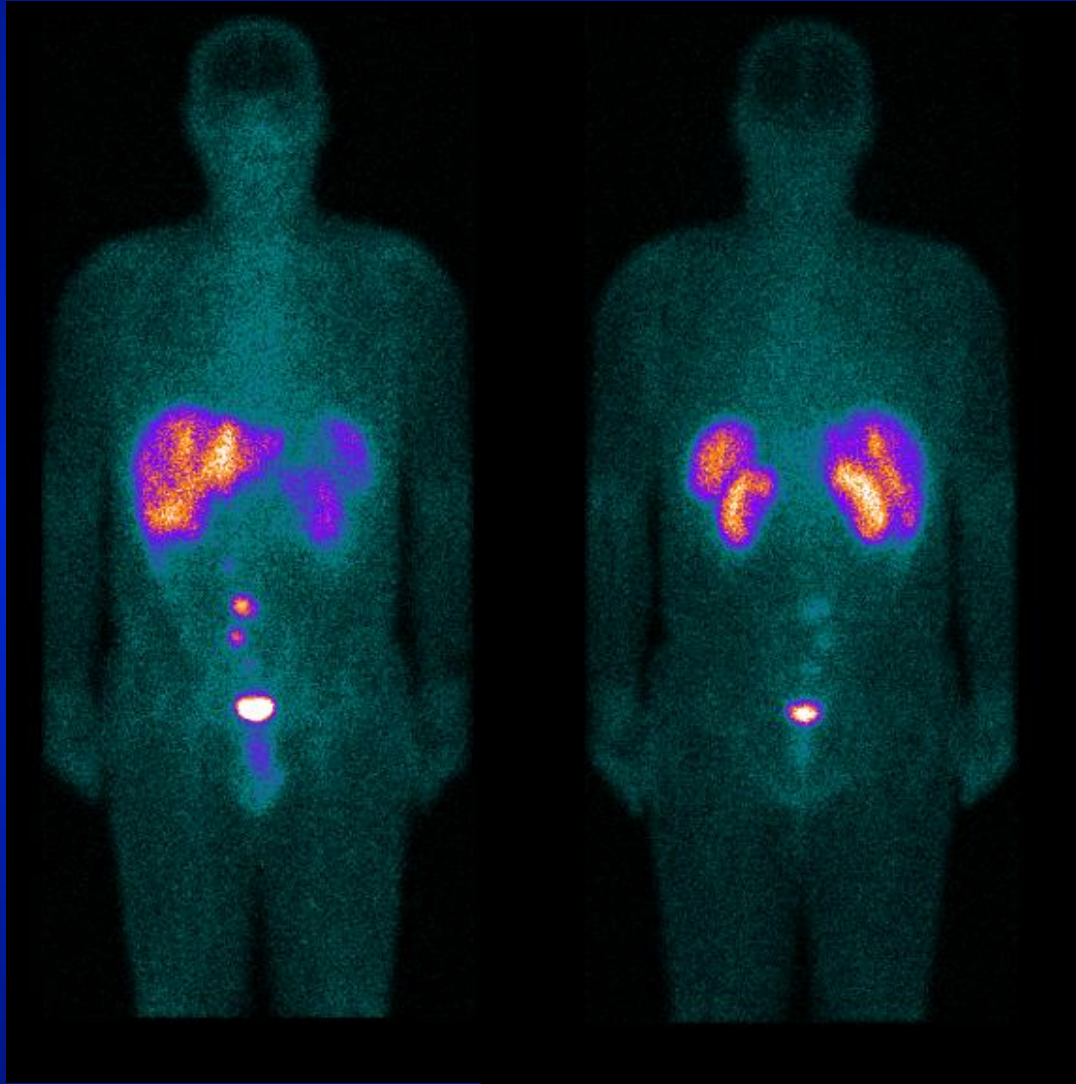
**Scintigrafia, SPECT, SPECT/CT** con

- $^{111}\text{In}$ -Octreoscan

**PET/CT** con

- $^{68}\text{Ga}$ -DOTATOC
- $^{68}\text{Ga}$ -DOTANOC
- $^{68}\text{Ga}$ -DOTATATE

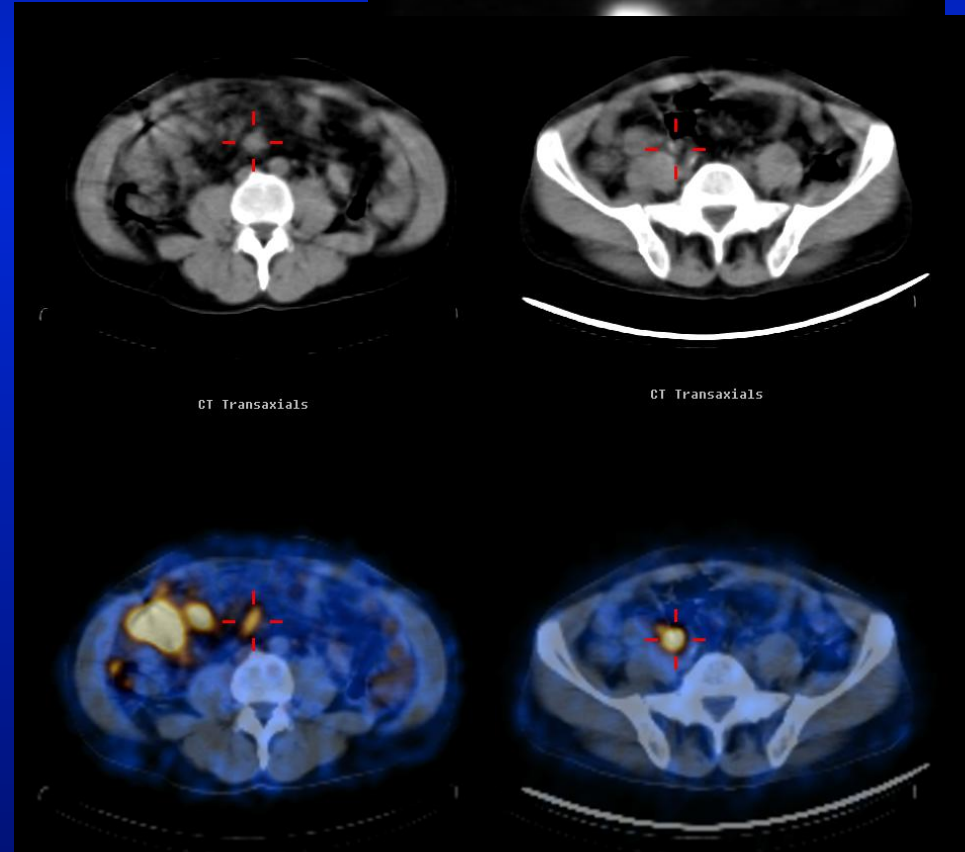
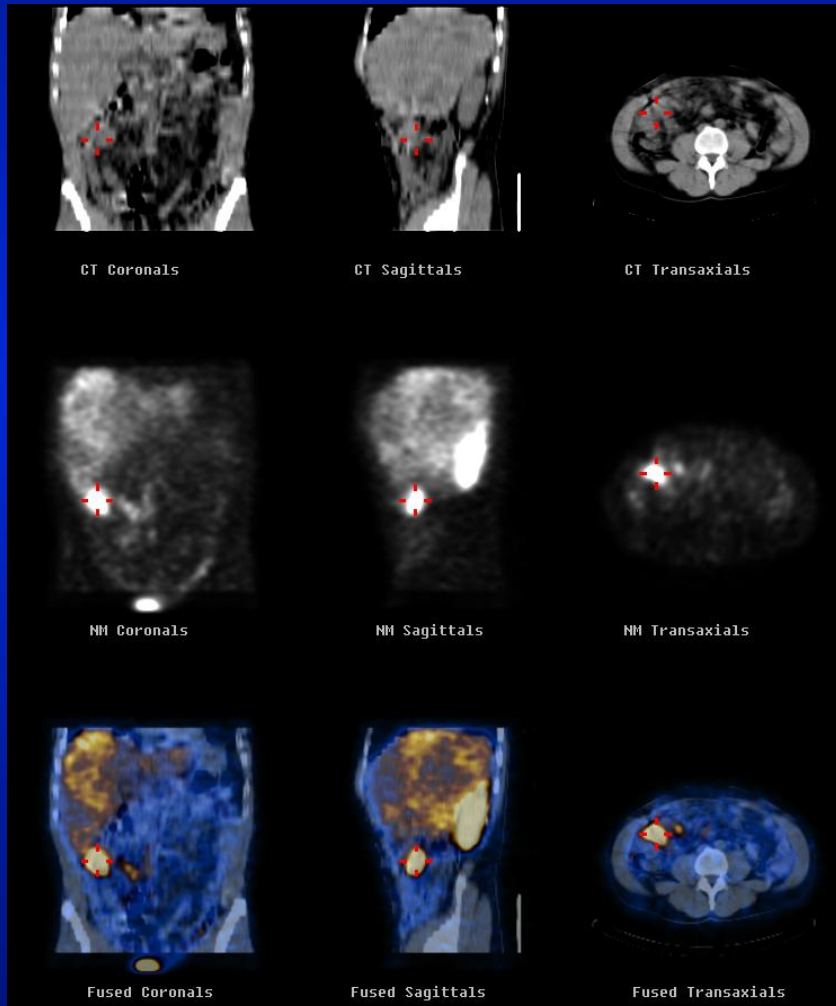
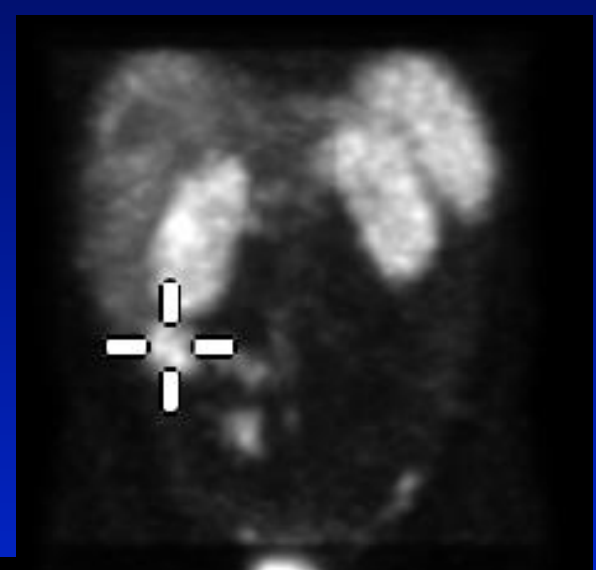
# ***Scintigrafia con $^{111}\text{In}$ -Octreoscan***



***Carcinoide Ileale***

# Octreoscan®: SPECT/CT

## Carcinoide Ileale



# Functional Imaging of Neuroendocrine Tumors: A Head-to-Head Comparison of Somatostatin Receptor Scintigraphy, <sup>123</sup>I-MIBG Scintigraphy, and <sup>18</sup>F-FDG PET

Tina Binderup<sup>1,2</sup>, Ulrich Knigge<sup>2,3</sup>, Annika Loft<sup>1</sup>, Jann Mortensen<sup>1</sup>, Andreas Pfeifer<sup>1,2</sup>, Birgitte Federspiel<sup>4</sup>, Carsten Palnaes Hansen<sup>3</sup>, Liselotte Højgaard<sup>1,2</sup>, and Andreas Kjaer<sup>1,2</sup>

<sup>1</sup>Department of Clinical Physiology, Nuclear Medicine and PET, Rigshospitalet, Copenhagen, Denmark; <sup>2</sup>Cluster for Molecular Imaging, Faculty of Health Sciences, University of Copenhagen, Copenhagen, Denmark; <sup>3</sup>Department of Surgical Gastroenterology, Rigshospitalet, Copenhagen, Denmark; and <sup>4</sup>Department of Pathology, Rigshospitalet, Copenhagen, Denmark

J Nucl Med 2010; 51:704–712

**TABLE 5.** Sensitivity of Functional Imaging Results Based on Origin of Tumor

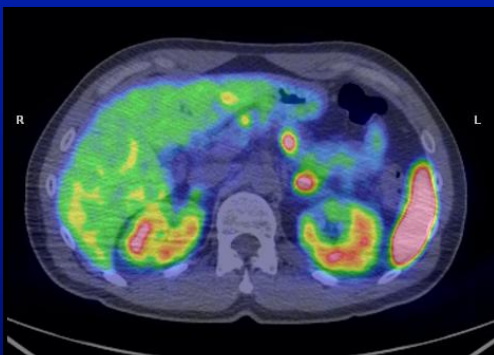
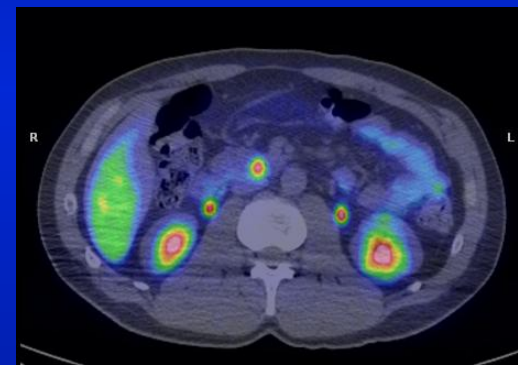
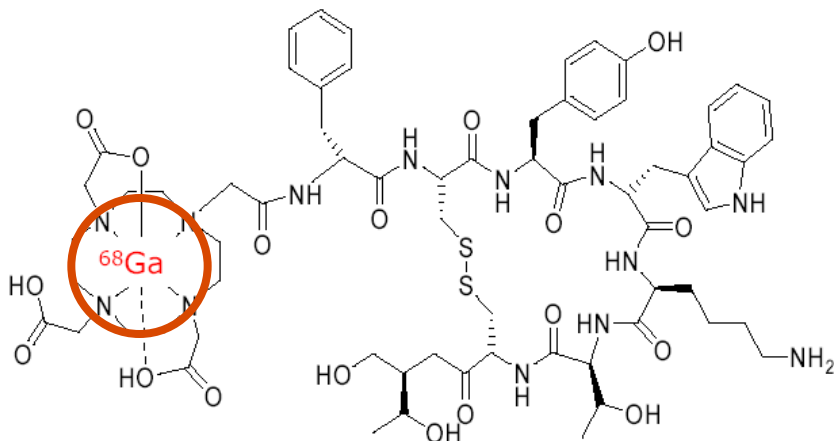
Origin of tumor	SRS	<sup>123</sup> I-MIBG	<sup>18</sup> F-FDG
Ileal neuroendocrine (n = 45)	91% (41)	71% (32)	36% (16)
Pancreaticoduodenal neuroendocrine (n = 29)	90% (26)	31% (9)	79% (23)
Neuroendocrine of lung (n = 7)	86% (6)	57% (4)	71% (5)
Colonic neuroendocrine (n = 6)	67% (4)	17% (1)	83% (5)
Unknown or rare origin (n = 9)	89% (8)	44% (4)	78% (7)
<b>Total</b>	<b>89% (85)</b>	<b>52% (50)</b>	<b>58% (56)</b>

Data in parentheses are numbers of patients.

# $^{68}\text{Ga}$ DOTATOC PET/CT



Generatore  $^{68}\text{Ge}/^{68}\text{Ga}$

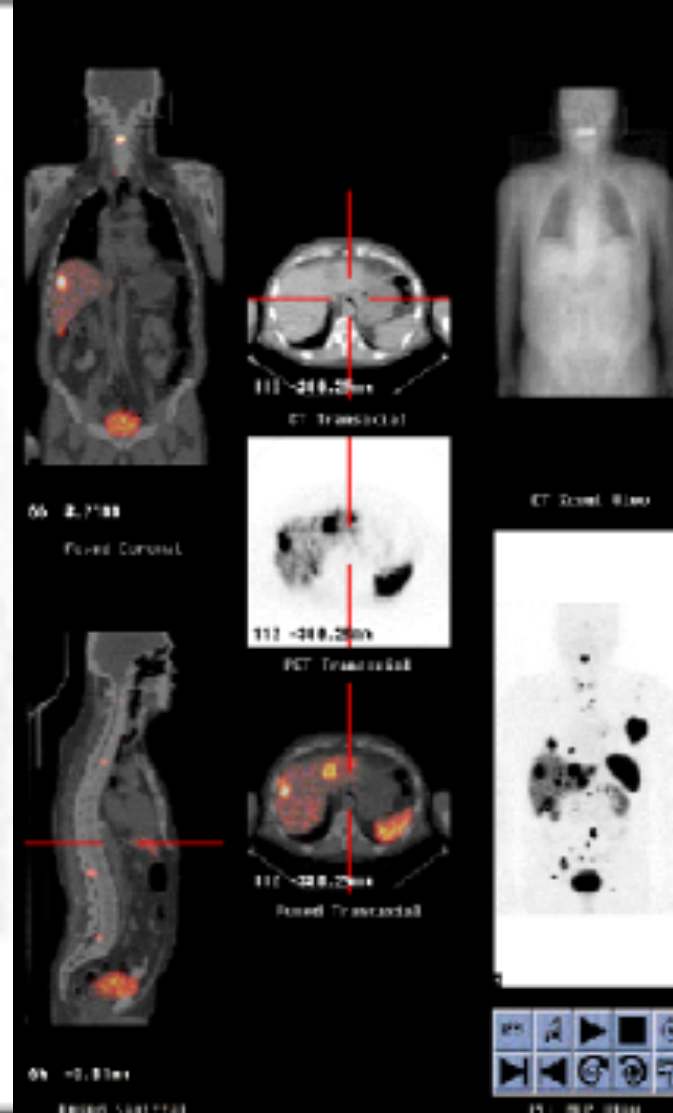
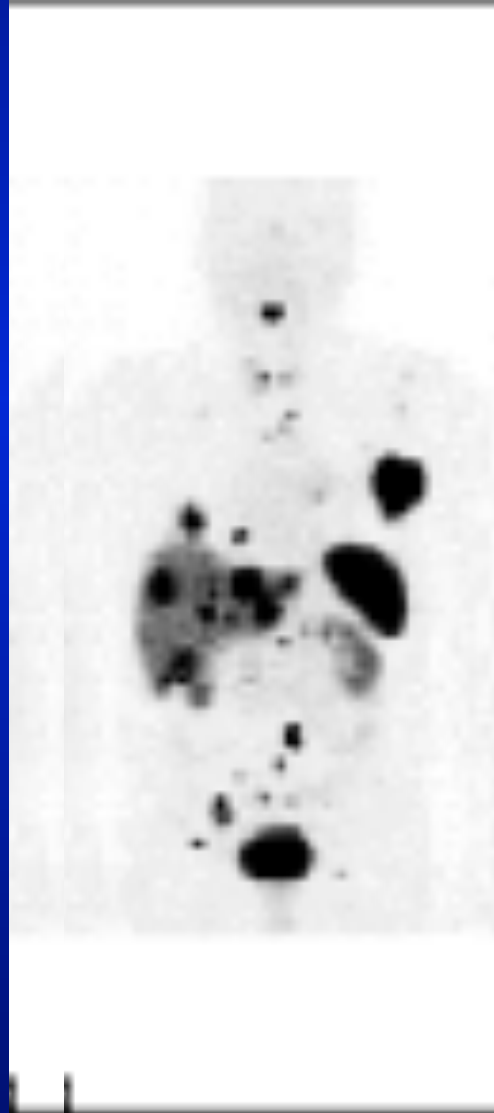
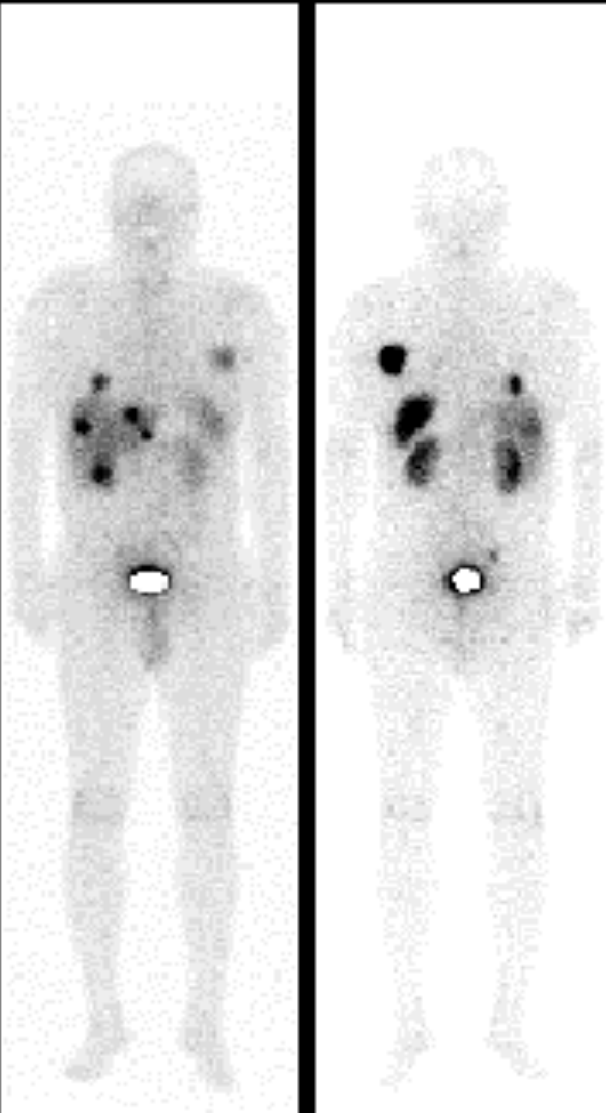




# Tumore neuroendocrino del tratto gastroenteropancreatico metastatico

**$^{111}\text{In}$ -Octreoscan**

**$^{68}\text{Ga}$ -Dotatoc PET/CT**



# $^{68}\text{Ga}$ -DOTATOC Versus $^{68}\text{Ga}$ -DOTATATE PET/CT in Functional Imaging of Neuroendocrine Tumors

Thorsten D. Poeppel<sup>1</sup>, Ina Binse<sup>1</sup>, Stephan Petersenn<sup>2</sup>, Harald Lahner<sup>2</sup>, Matthias Schott<sup>3</sup>, Gerald Antoch<sup>4</sup>, Wolfgang Brandau<sup>1</sup>, Andreas Bockisch<sup>1</sup>, and Christian Boy<sup>1</sup>

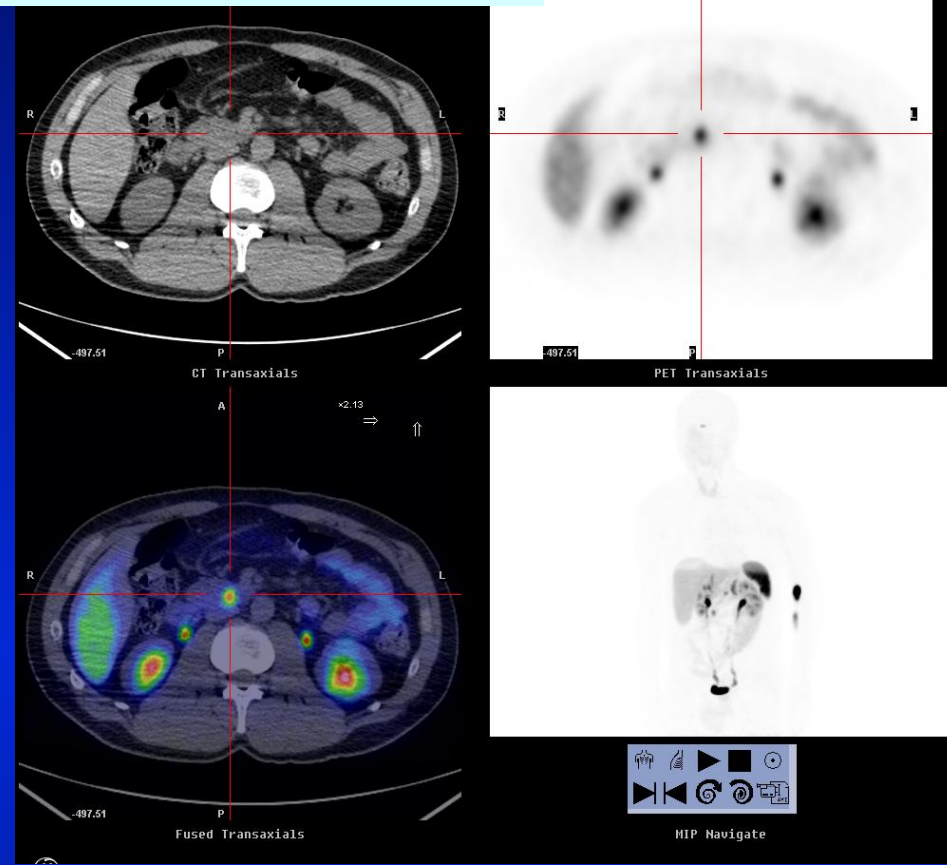
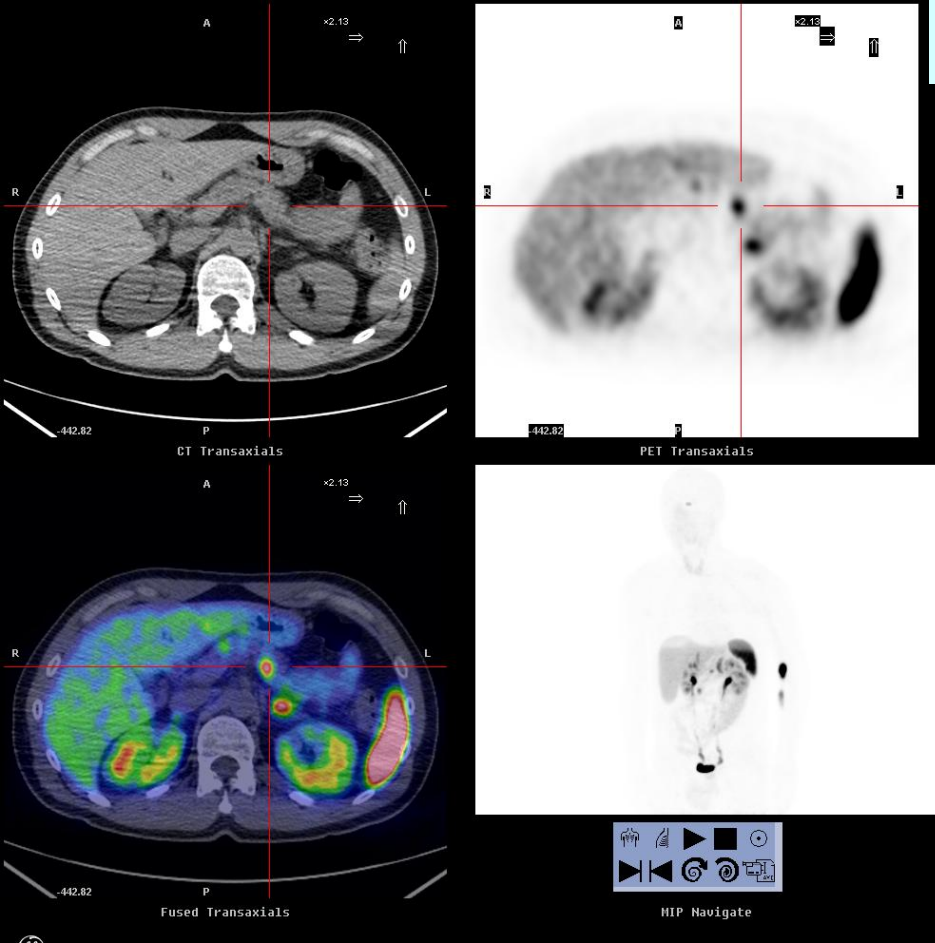
<sup>1</sup>Department of Nuclear Medicine, University Essen, Essen, Germany; <sup>2</sup>Department of Endocrinology, University Essen, Essen, Germany; <sup>3</sup>Department of Endocrinology, University Dusseldorf, Dusseldorf, Germany; and <sup>4</sup>Department of Diagnostic and Interventional Radiology, University Dusseldorf, Dusseldorf, Germany

J Nucl Med 2011; 52:1864–1870

## CONCLUSION

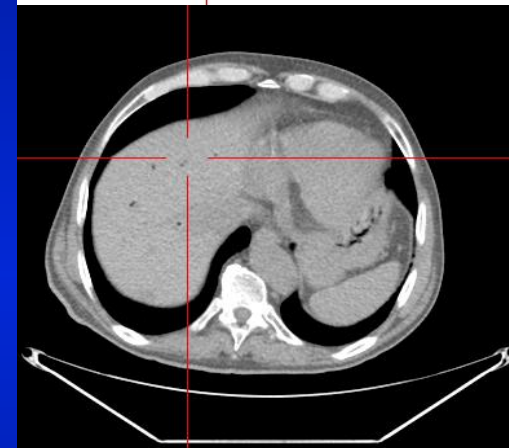
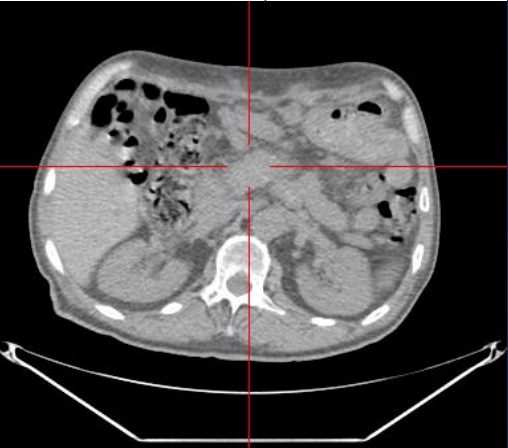
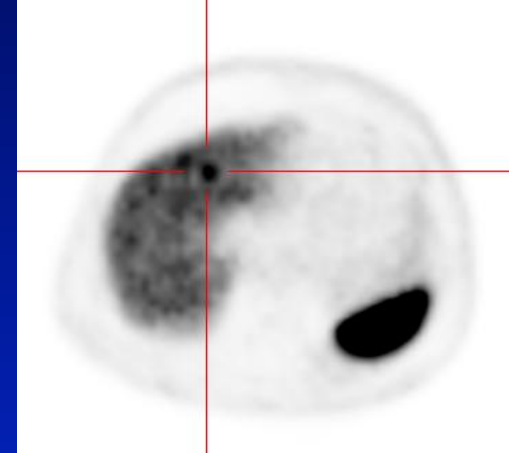
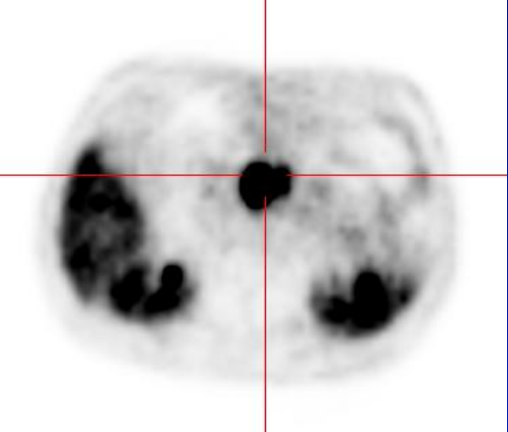
$^{68}\text{Ga}$ -DOTATOC and  $^{68}\text{Ga}$ -DOTATATE possess a **comparable diagnostic value** in the detection of lesions of NETs

# $^{68}\text{Ga}$ -DOTATOC PET



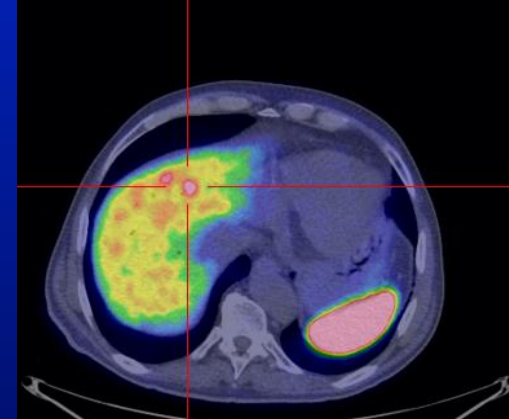
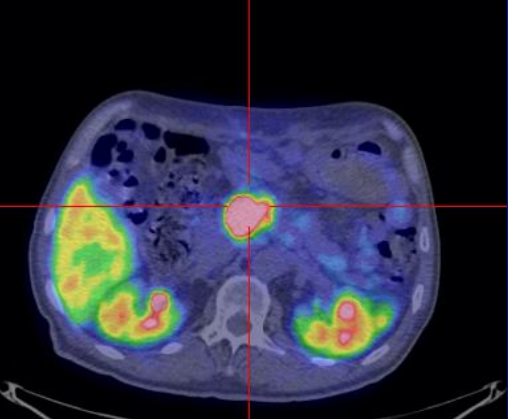
Gastrinoma del pancreas

# $^{68}\text{Ga}$ -DOTATOC PET

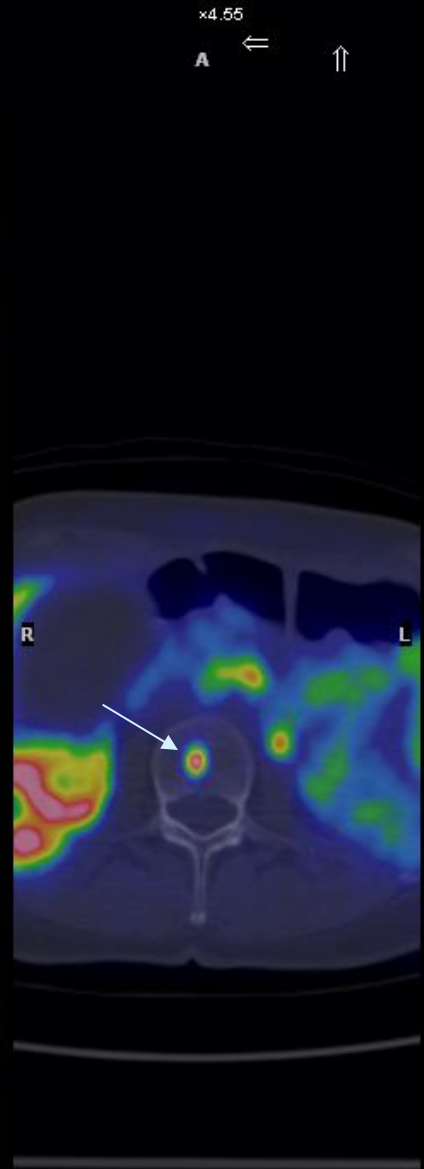
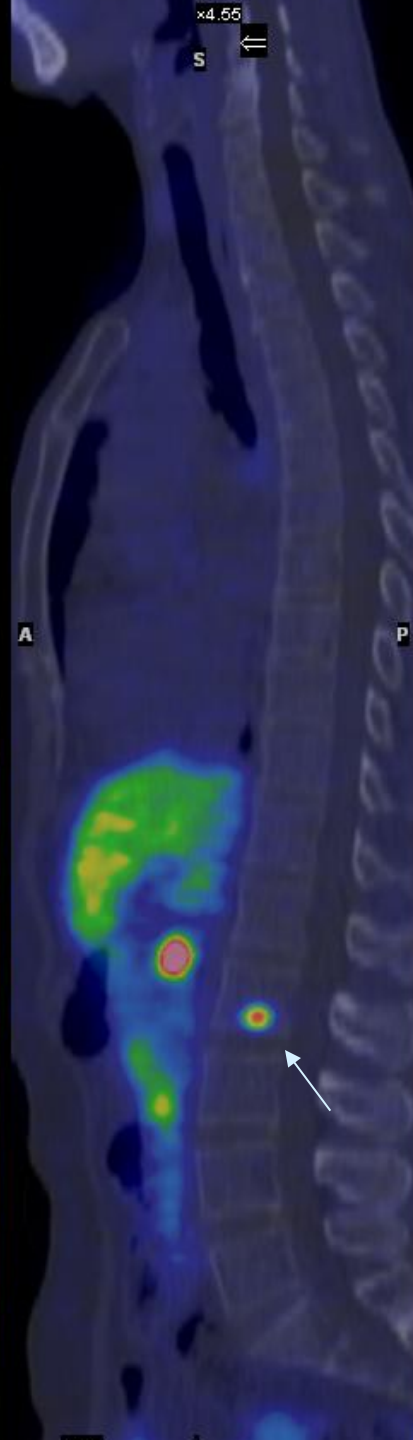
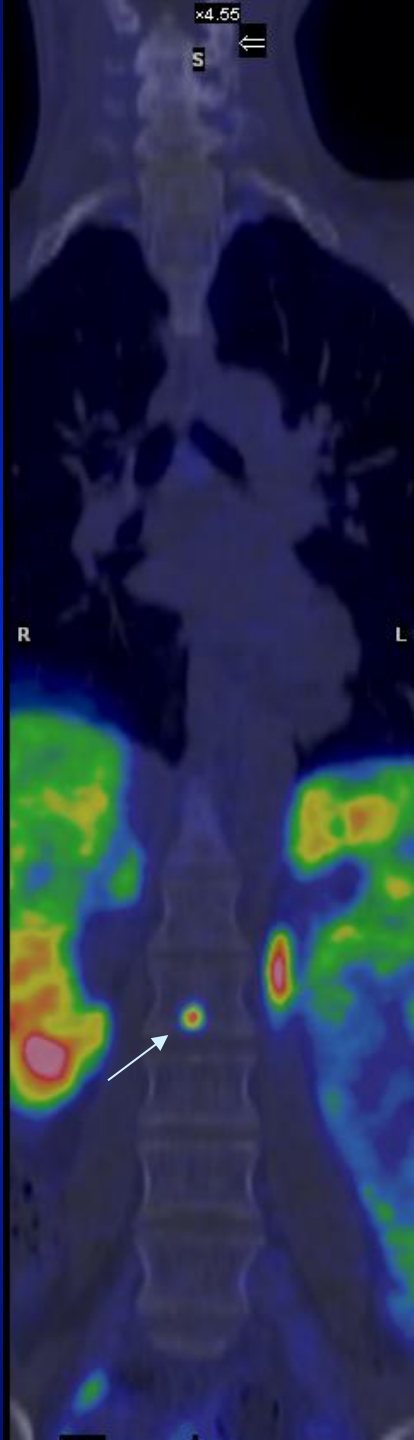
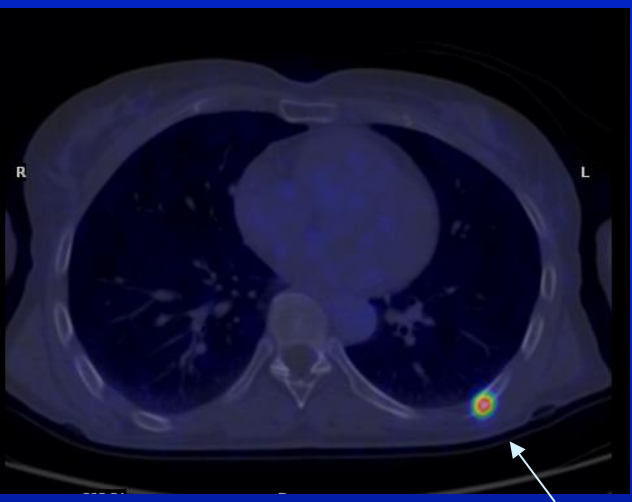
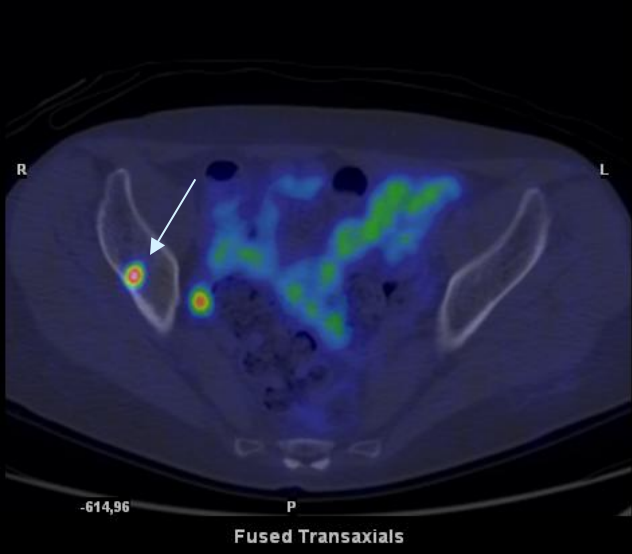


-476.29  
P  
CT Transaxials  
A  
×1.40

-383.32  
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Carcinoma neuroendocrino del pancreas  
con metastasi epatiche



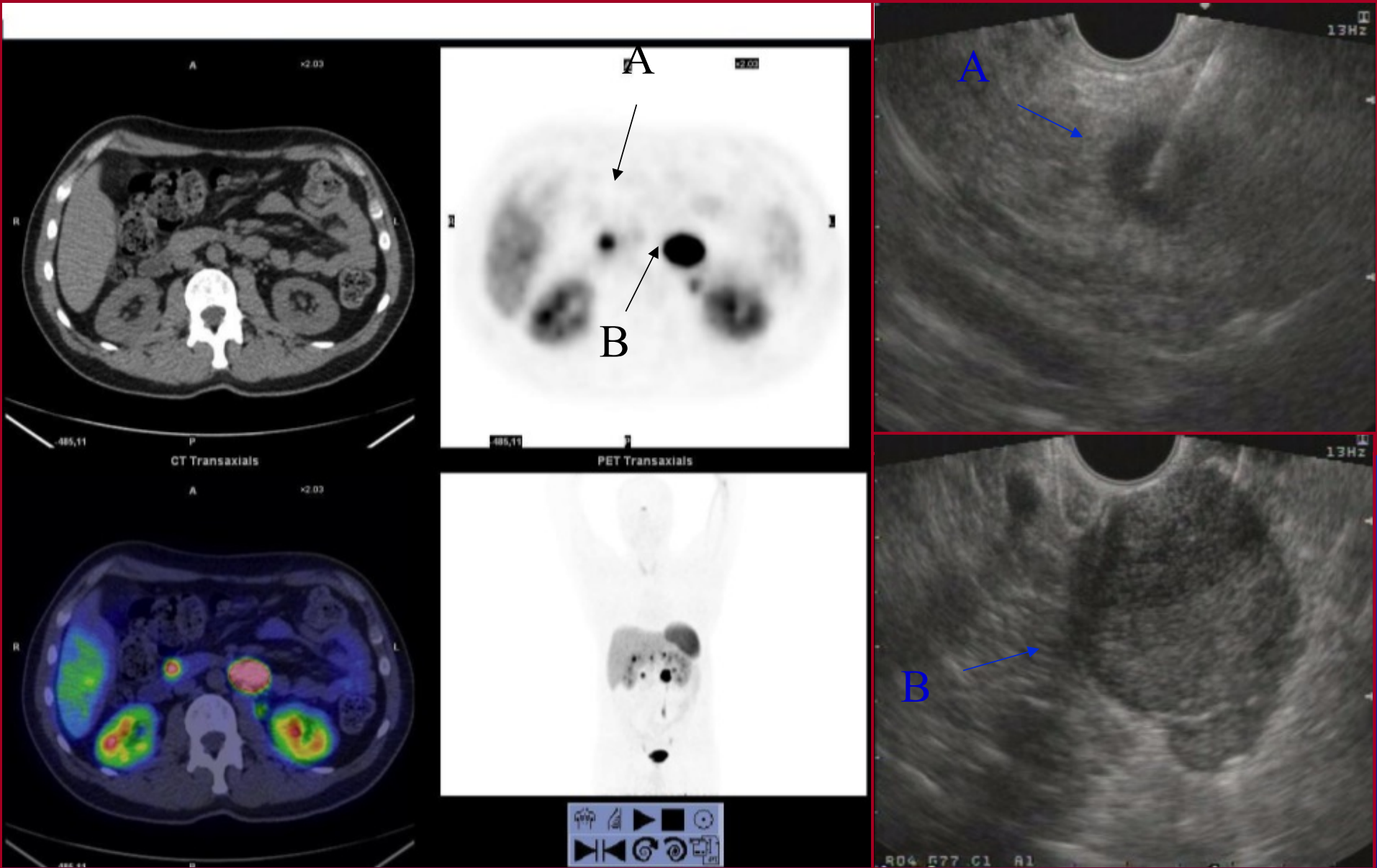
**Metastasi  
scheletriche da  
NET  
pancreatico**

# Ga-68 DOTATOC PET, Endoscopic Ultrasonography, and Multidetector CT in the Diagnosis of Duodenopancreatic Neuroendocrine Tumors

## *A Single-Centre Retrospective Study*

*Annibale Versari, MD,\* Lorenzo Camellini, MD,† Gabriele Carlinfante, MD,‡ Andrea Frasoldati, MD,\*  
Franco Nicoli, MD,§ Elisa Grassi, ●●●,¶ Carmine Gallo, MD,‡ Francesco Giunta, MD,\*  
Alessandro Fraternali, MD,\* Diana Salvo, MD,\* Mattia Asti, ●●●,\* Francesco Azzolini, MD,†  
Veronica Iori, MD,† and Romano Sassatelli, MD†*

*Clin Nucl Med 2010;*



**Head pancreatic NET (A) with lymph node metastasis (B)**

**Table 3. Comparison of results of EUS, PET, MDCT in duodeno-pancreatic NETs**

<b>19 paz</b>	patient-based analysis			lesion-based analysis		
	<b>EUS</b>	<b>PET</b>	<b>MDCT</b>	<b>EUS</b>	<b>PET</b>	<b>MDCT</b>
<b>Detection rate</b>	<b>15/19 (79%)</b>	<b>13/19 (68%)</b>	<b>11/16 (69%)</b>	<b>25/28 (89%)</b>	<b>23/28 (82%)</b>	<b>16/22 (73%)</b>
<b>True positive</b>	<b>13</b>	<b>12</b>	<b>10</b>	<b>22</b>	<b>20</b>	<b>13</b>
<b>True negative</b>	<b>4</b>	<b>5</b>	<b>4</b>	<b>4</b>	<b>5</b>	<b>4</b>
<b>False positive</b>	<b>2</b>	<b>1</b>	<b>1</b>	<b>2</b>	<b>1</b>	<b>1</b>
<b>False negative</b>	<b>0</b>	<b>1</b>	<b>1</b>	<b>1</b>	<b>3</b>	<b>5</b>
<b>Sensitivity %</b>	<b>100</b>	<b>92</b>	<b>91</b>	<b>96</b>	<b>87</b>	<b>72</b>
<b>Specificity %</b>	<b>67</b>	<b>83</b>	<b>80</b>	<b>67</b>	<b>83</b>	<b>80</b>

**CT was performed in 16 patients; in these patients 22 suspected lesions were detected by at least a method. All comparison among rates and operative characteristics in the table are not significant.**



# Ga-68 DOTATOC PET, Endoscopic Ultrasonography, and Multidetector CT in the Diagnosis of Duodenopancreatic Neuroendocrine Tumors

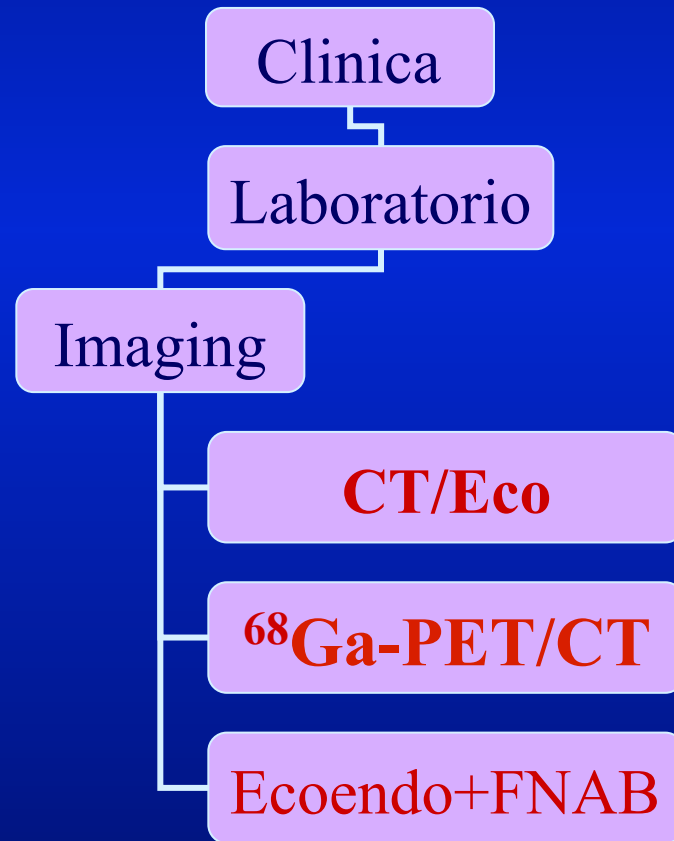
## *A Single-Centre Retrospective Study*

*Annibale Versari, MD,\* Lorenzo Camellini, MD,† Gabriele Carlinfante, MD,‡ Andrea Frasoldati, MD,\*  
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Alessandro Fraternali, MD,\* Diana Salvo, MD,\* Mattia Asti, ●●●,\* Francesco Azzolini, MD,†  
Veronica Iori, MD,† and Romano Sassatelli, MD†*

**Conclusions:** EUS, Ga-68 DOTATOC PET, and MDCT seem to have comparable accuracy in diagnosis of duodenopancreatic NET and their combination may allow an optimal preoperative diagnosis.

# Tumori neuroendocrini duodeno-pancreatici

## Proposta di percorso diagnostico



# Accuracy and clinical impact of 68-Ga-labeled octreotide analogues PET in diagnosis and staging of duodeno-pancreatic neuroendocrine tumours. A multicenter, prospective clinical trial

Proponenti:

Annibale Versari (Medicina Nucleare - PI)

Lorenzo Camellini (Endoscopia Digestiva)

Andrea Frasoldati (Endocrinologia)

Gabriele Carlinfante (Anatomia Patologica)

Pierpaolo Pattacini (Radiologia)



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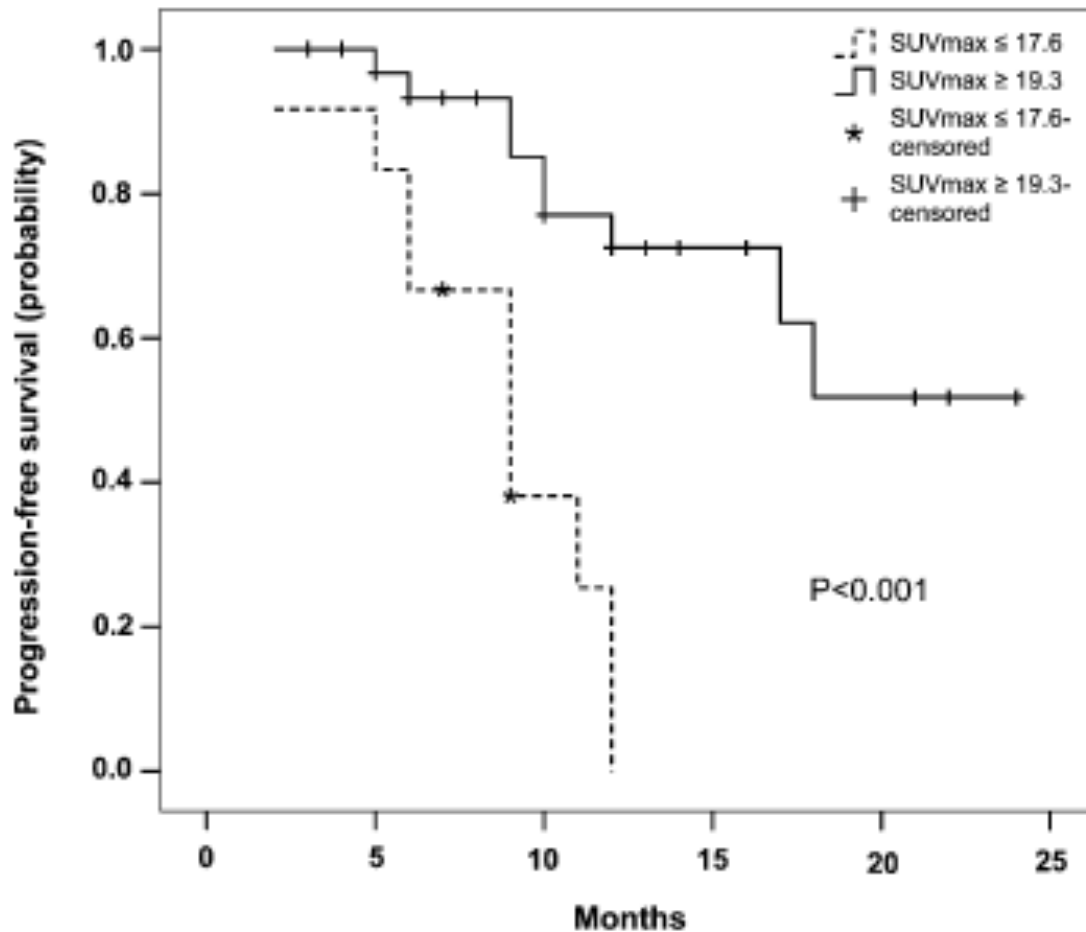
Azienda Ospedaliera di Reggio Emilia

Arcispedale S. Maria Nuova

Istituto in tecnologie avanzate e modelli assistenziali in oncologia  
Istituto di Ricovero e Cura a Carattere Scientifico

# Standardized Uptake Values of $^{68}\text{Ga}$ -DOTANOC PET: A Promising Prognostic Tool in Neuroendocrine Tumors

Davide Campana<sup>1</sup>, Valentina Ambrosini<sup>2</sup>, Raffaele Pezzilli<sup>1</sup>, Stefano Fanti<sup>2</sup>, Antonio Maria Morselli Labate<sup>1</sup>, Donatella Santini<sup>3</sup>, Claudio Ceccarelli<sup>3</sup>, Francesca Nori<sup>1</sup>, Roberto Franchi<sup>2</sup>, Roberto Corinaldesi<sup>1</sup>, and Paola Tomassetti<sup>1</sup>



# Functional Imaging of Neuroendocrine Tumors With Combined PET/CT Using $^{68}\text{Ga}$ -DOTATATE (Dota-DPhe<sup>1</sup>, Tyr<sup>3</sup>-octreotate) and $^{18}\text{F}$ -FDG

**TABLE 2**  
Numbers of Patients Showing Predominant Uptake of  $^{68}\text{Ga}$ -DOTATATE or  $^{18}\text{F}$ -FDG According to Tumor Grade

	Predominant uptake of $^{68}\text{Ga}$ -DOTATATE	Predominant uptake of $^{18}\text{F}$ -FDG	Total
High/intermediate-grade NET	3	11	14
Low-grade NET	21	0	21
Total	24	11	35

Two-tailed  $P < .0001$ . Fisher exact T-test

NET indicates neuroendocrine tumors;  $^{68}\text{Ga}$ -DOTATATE,  $^{68}\text{Ga}$ -DOTA-[SCAP]D[R]Phe<sup>1</sup>, Tyr<sup>3</sup>-octreotate;  $^{18}\text{F}$ -FDG,  $^{18}\text{F}$ -Fluorodeoxyglucose.

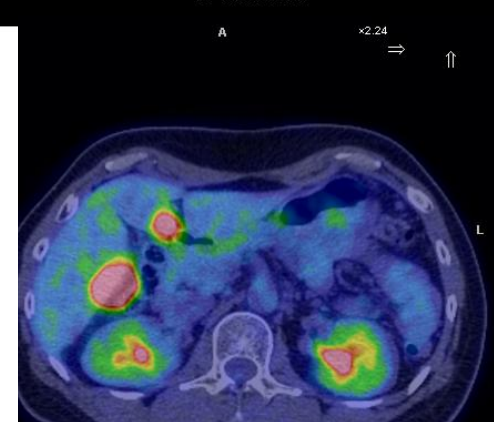
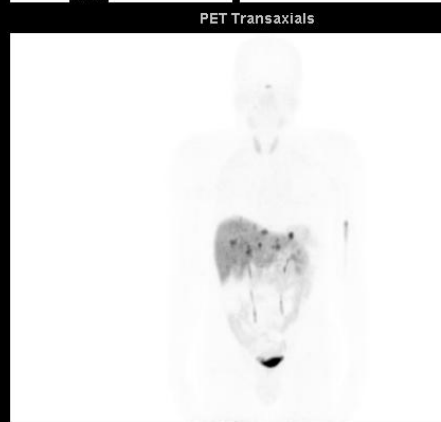
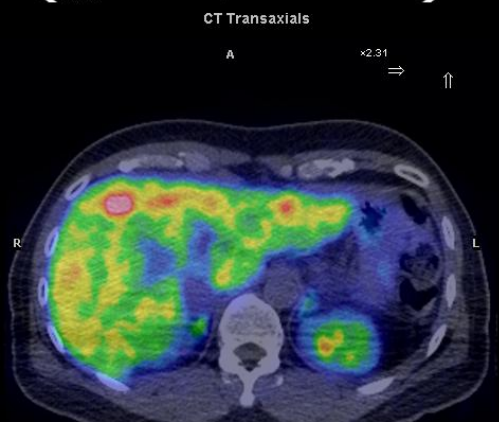
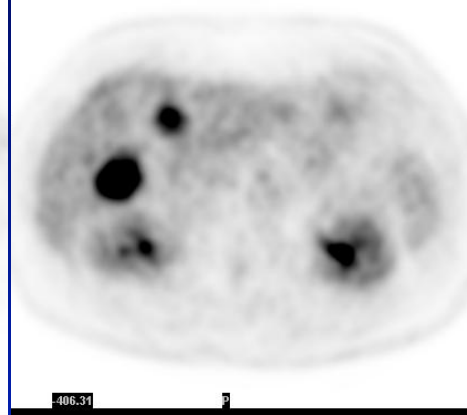
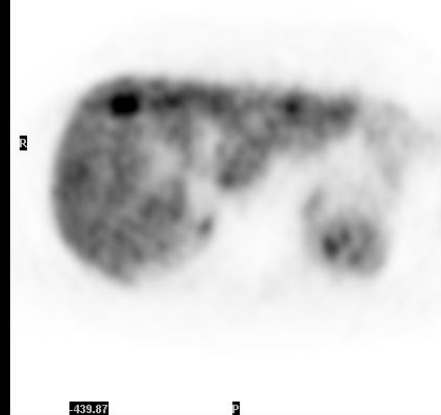
Irfan Kayani, FRCP<sup>1</sup>  
Jamshed B. Bomanji, MD, PhD, FRCP<sup>1</sup>  
Ashley Groves, MD<sup>1</sup>  
Gerard Conway, MD<sup>2</sup>  
Sveto Gacinovic, MD<sup>1</sup>  
Thida Win, MD<sup>3</sup>  
John Dickson, PhD<sup>1</sup>  
Martyn Caplin, FRCP<sup>4</sup>  
Peter Joseph Ell, FRCP, FRCP<sup>1</sup>

**TABLE 3**  
SUVmax of  $^{68}\text{Ga}$ -DOTATATE and  $^{18}\text{F}$ -FDG According to Tumor Grade

	$^{68}\text{Ga}$ -DOTATATE	$^{18}\text{F}$ -FDG	<i>P</i>
All NET	16.9 (1.6-50)	4.2 (1.4-16.4)	.005
Low-grade NET Ki67 index $\leq 2\%$	29 (3.3-45)	2.9 (1.5-12)	<.001
Intermediate NET Ki67 index 3%-20%	15.5 (1.8-50)	10.5 (2.0-13.9)	NS
High-grade NET Ki67 index $>20\%$	4.4 (1.6-8.9)	11.7 (4.1-16.4)	.03

SUVmax is the median SUVmax with range in parentheses.

SUVmax indicates maximum standardized uptake value; NET, neuroendocrine tumor;  $^{68}\text{Ga}$ -DOTA-[SCAP]D[R]Phe<sup>1</sup>, Tyr<sup>3</sup>-octreotate;  $^{18}\text{F}$ -FDG,  $^{18}\text{F}$ -Fluorodeoxyglucose.



68Ga-DOTATOC

FDG-PET/CT

Gen 2011

Feb 2011

# <sup>18</sup>F-Fluorodihydroxyphenylalanine PET/CT in Patients with Neuroendocrine Tumors of Unknown Origin: Relation to Tumor Origin and Differentiation

J Nucl Med 2014; 55:1–6

Alessio Imperiale<sup>1,2</sup>, Edmond Rust<sup>1</sup>, Sophie Gabriel<sup>3</sup>, Julien Detour<sup>4</sup>, Bernard Goichot<sup>5</sup>, Bernard Duclos<sup>6</sup>, Jean-Emmanuel Kurtz<sup>7</sup>, Philippe Bachellier<sup>8</sup>, Izzie-Jacques Namer<sup>1,2</sup>, and David Taïeb<sup>3</sup>

<sup>1</sup>Biophysics and Nuclear Medicine, Hautepierre University Hospital, Strasbourg, France; <sup>2</sup>ICube, University of Strasbourg/CNRS (UMR 7357) and FMTS, Faculty of Medicine, Strasbourg, France; <sup>3</sup>Nuclear Medicine, La Timone University Hospital, European Center for Research in Medical Imaging, Aix-Marseille University, Provence, France; <sup>4</sup>Radiopharmacy, Hautepierre University Hospital, Strasbourg, France; <sup>5</sup>Internal Medicine, Hautepierre University Hospital, Strasbourg, France; <sup>6</sup>Gastroenterology, Hautepierre University Hospital, Strasbourg, France; <sup>7</sup>Oncology, Hautepierre University Hospital, Strasbourg, France; and <sup>8</sup>Visceral Surgery and Transplantation, Hautepierre University Hospital, Strasbourg, France

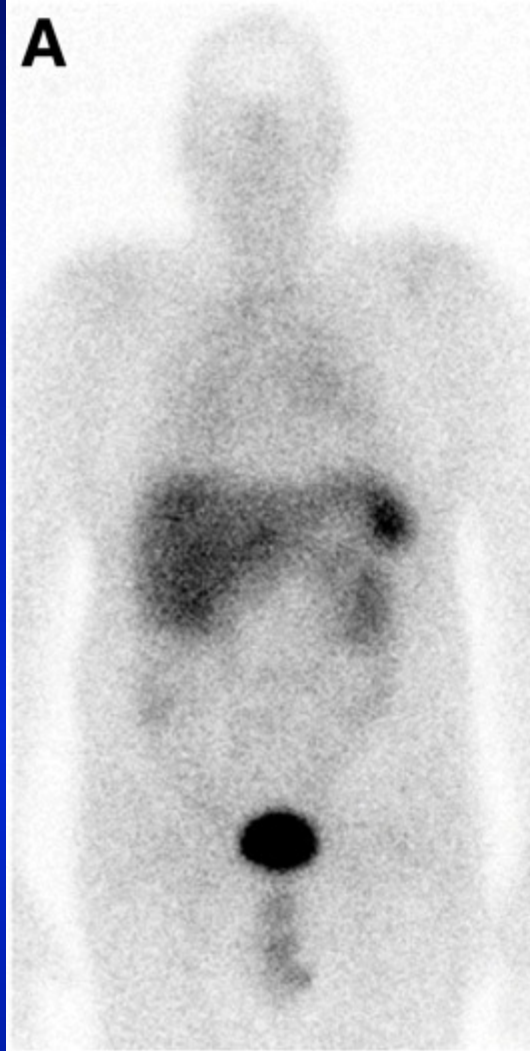
Retrospective study of NET patients with negative conventional and somatostatin receptor scintigraphy (SRS) results

**27 patients** were evaluated with <sup>18</sup>F-FDOPA PET/CT

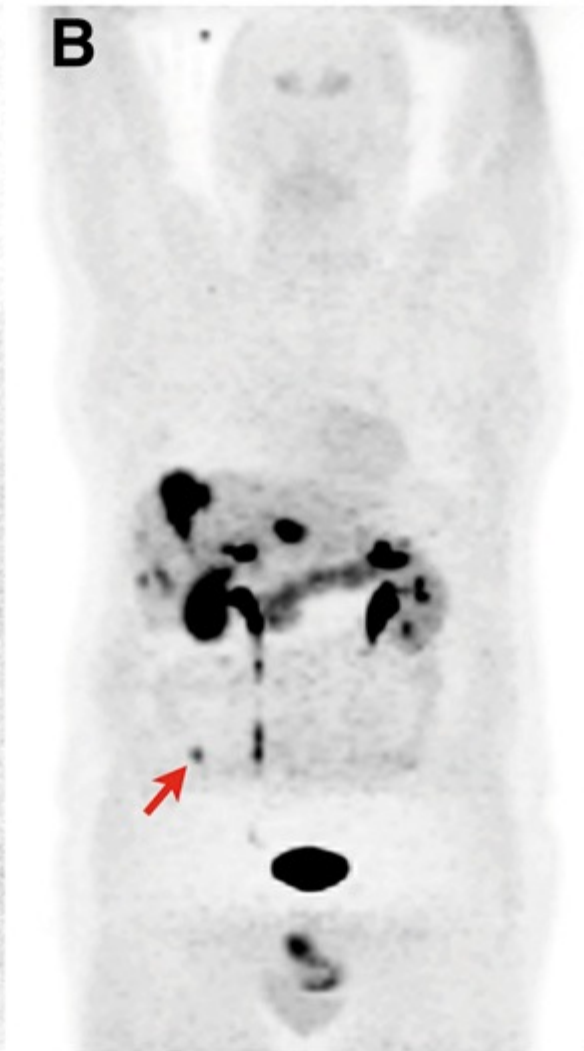
The primary occult NET was localized by <sup>18</sup>F-FDOPA PET/CT in 12 patients (overall **sensitivity, 44%**; 52% in patients evaluated at initial diagnosis)

Conclusion:

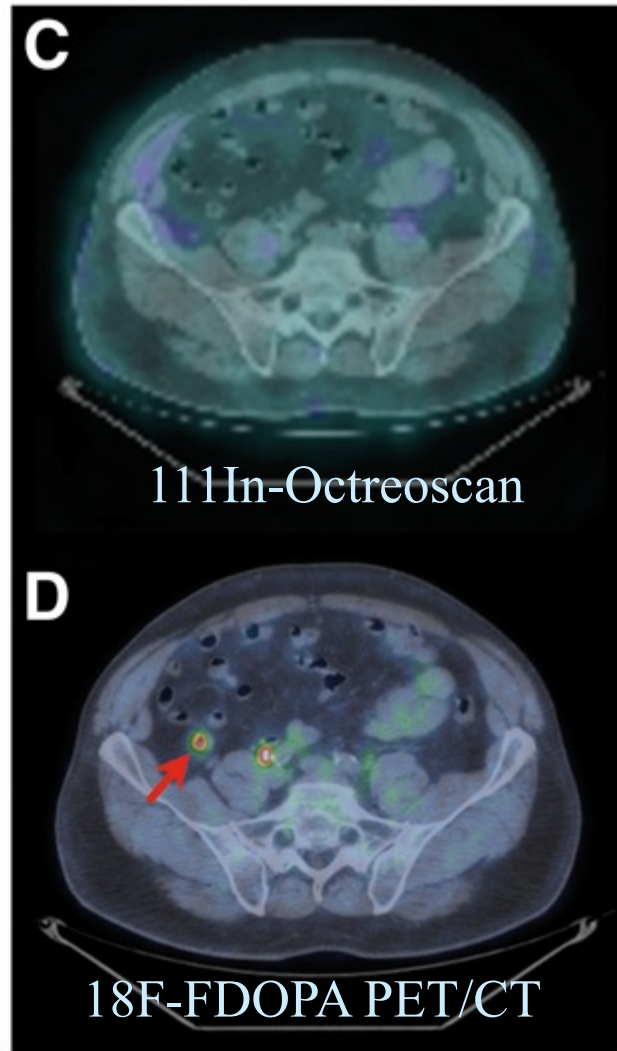
<sup>18</sup>F-FDOPA PET appears to be a sensitive functional imaging tool for the detection of primary NETs occult on SRS, **especially tumors with a well-differentiated pattern and serotonin secretion**



111In-Octreoscan



18F-FDOPA PET/CT



111In-Octreoscan

18F-FDOPA PET/CT

A 56-y-old patient with metastatic NET of unknown origin. 18F-FDOPA PET/CT confirmed presence of liver metastases and identified primary tumor in ileum occult on both conventional imaging and SRS.



# Insulinoma e diagnostica medico-nucleare

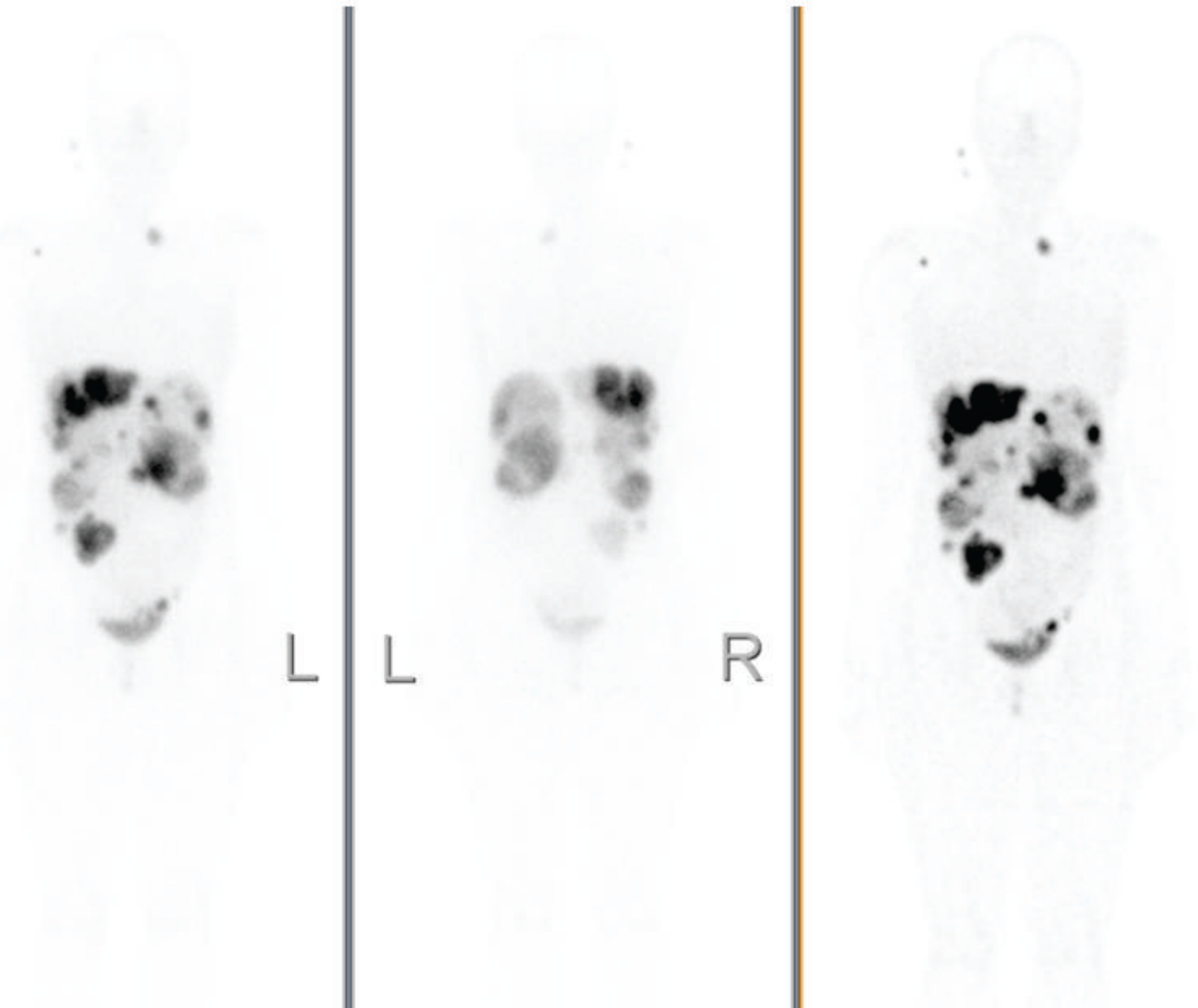
Spesso di piccole  
dimensioni

...e i recettori?

# ***Densità di Espressione del SST-R2 nei Tumori GEP e Sensibilità dell' imaging con analoghi della somatostatina marcati***

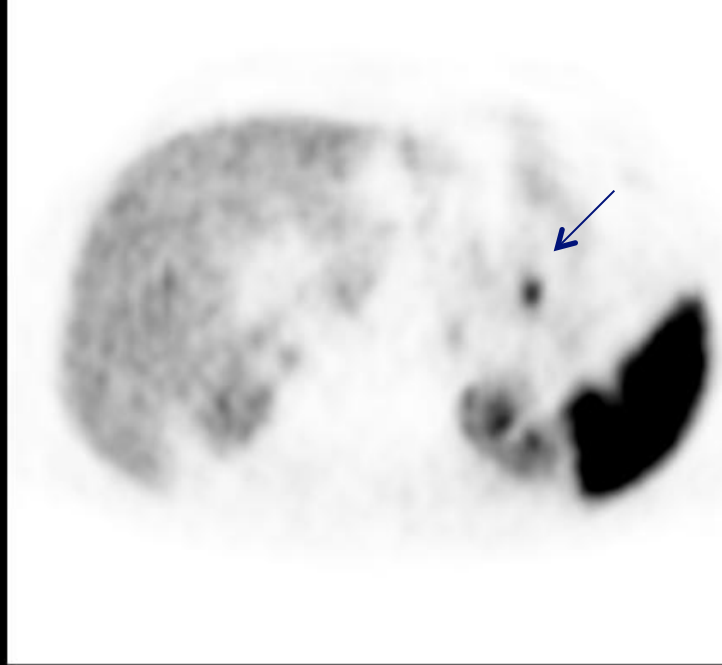
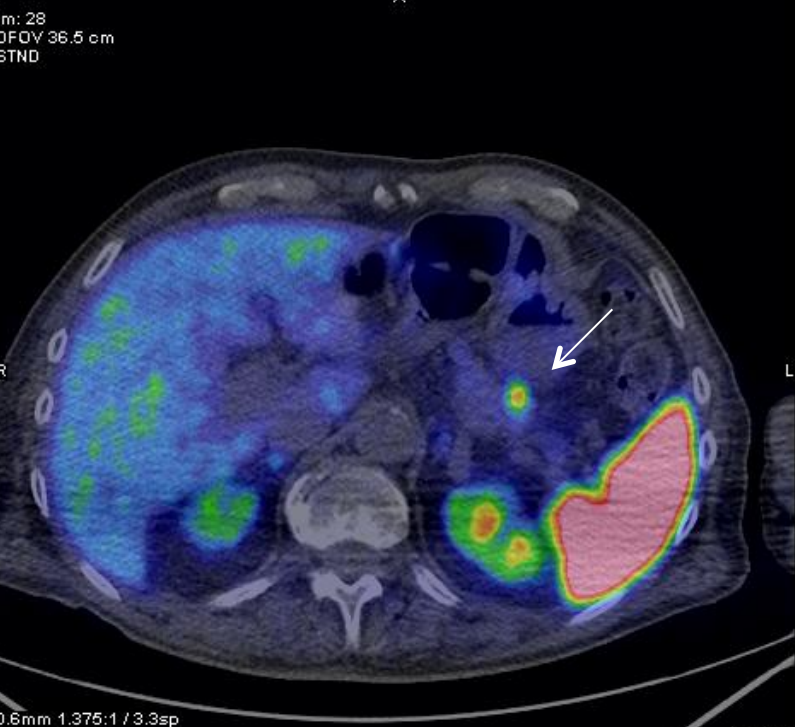


<b>Gastrinoma</b>	<b>90-95%</b>
<b>Carcinoide</b>	<b>85-95%</b>
<b>VIP-oma</b>	<b>80-90%</b>
<b>Non-funzionanti</b>	<b>75-85%</b>
<b>Glucagonoma</b>	<b>70-80%</b>
<b>Insulinoma</b>	<b>50-60%</b>



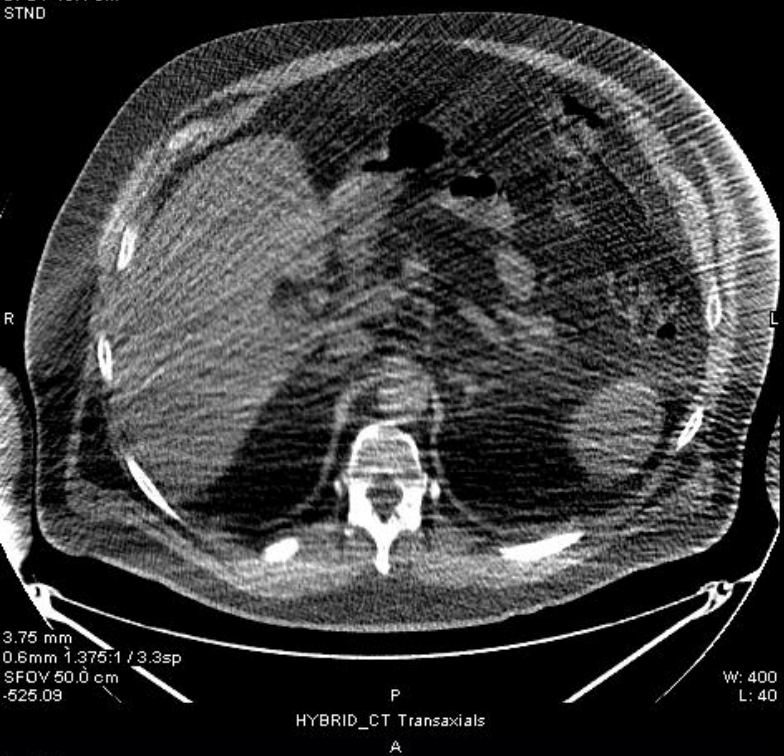
<sup>111</sup>In-  
Octreoscan

Metastatic  
insulinoma

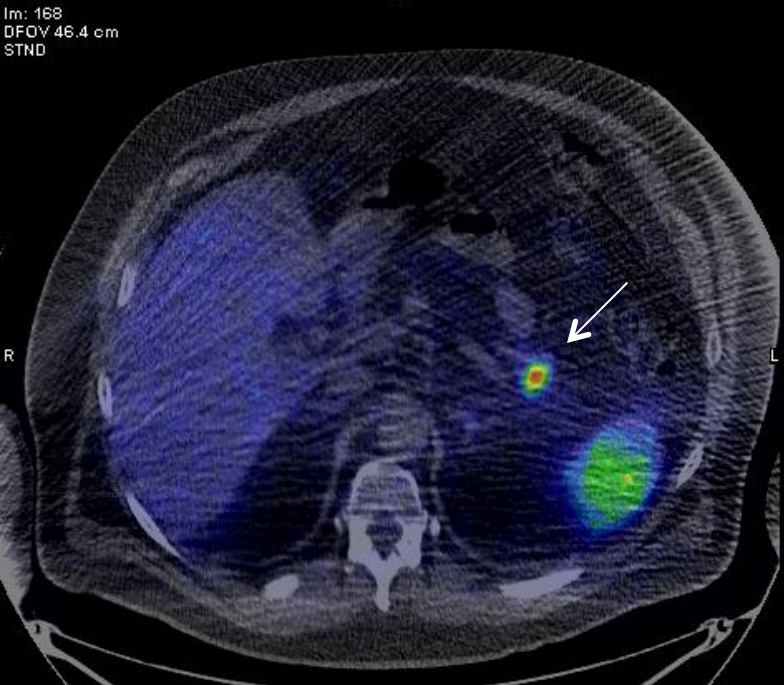


<sup>68</sup>Ga  
DOTATATE  
PET/CT

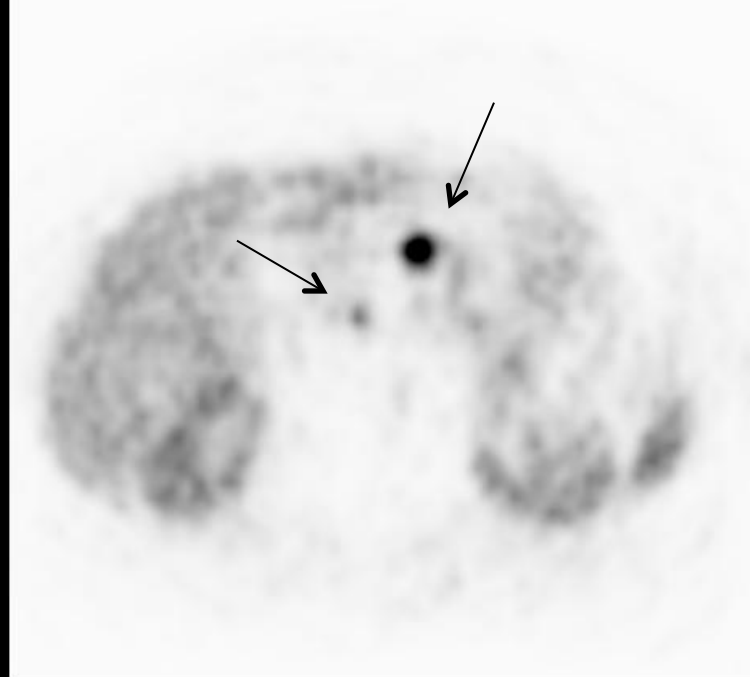
Insulinoma  
della coda  
del  
pancreas



68Ga  
DOTATATE  
PET/CT

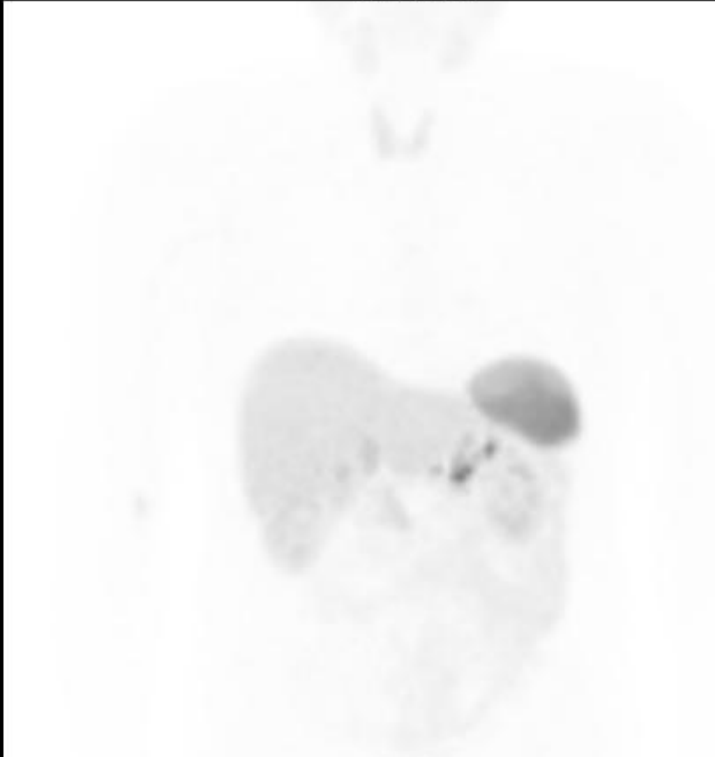
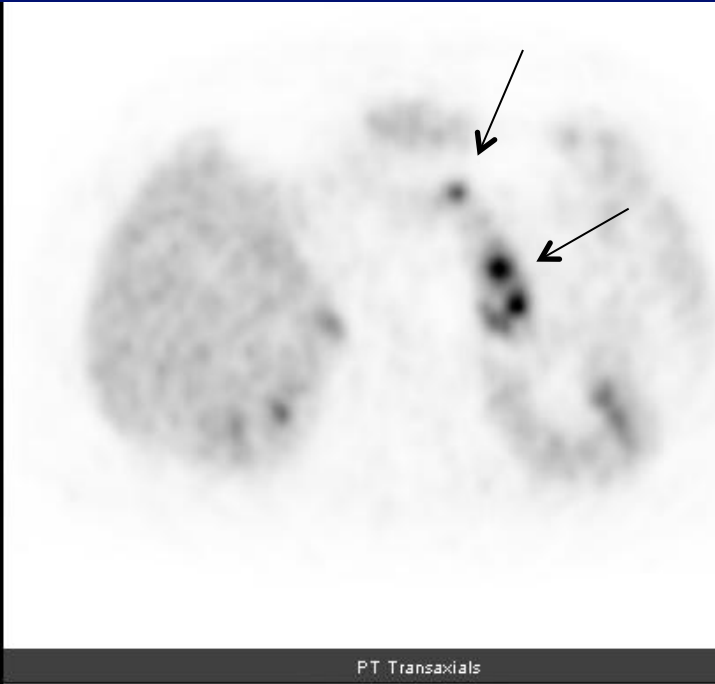


Insulinoma  
della coda  
del  
pancreas



68Ga  
DOTATATE  
PET/CT

Insulinomi  
del  
corpo  
e  
testa  
del  
pancreas



68Ga  
DOTATOC  
PET/CT

Insulinomi  
multipli  
(recidiva)

Coda  
e  
corpo  
del  
pancreas

# Somatostatin receptor based PET/CT imaging with <sup>68</sup>Ga-DOTA-Nal3-Octreotide for localisation of clinically and biochemically suspected insulinoma

Sharma P1 et al Q J Nucl Med Mol Imaging. 2014 Apr 17

- 35 patients
- Sensitivity 25,8%
- Specificity 25%
- Accuracy 25,7%
- No significant difference was seen between Conventional Imaging and PET/CT
- <sup>68</sup>Ga-DOTANOC PET/CT has limited utility for localising the primary tumor in patients with clinical and biochemical suspicion of insulinoma.
- DD benign/malignant?



# Future?

Nucl Med Commun. 2012

**Radiolabeled glucagon-like peptide-1 analogues: a new pancreatic  $\beta$ -cell imaging agent.**

Zhang Y1, Chen W.

*Grazie per l'attenzione*

