

GRAND ROUNDS CLINICI DEL MERCOLEDÌ

con il Policlinico San Matteo

Sistema Socio Sanitario



Regione
Lombardia



Fondazione IRCCS
Policlinico San Matteo

ATS Pavia

Aula Magna "C. Golgi"
& WEBINAR

Storia di un ragazzo ansioso: UN GRANDE MIMO SMASCHERATO

*Giovanna Pepe, SC Medicina Nucleare
22 febbraio 2023*



CASO CLINICO

Paz. D.L. Uomo 31 anni, anamnesi remota muta, se non per sindrome depressiva in adolescenza. Da alcuni anni sindrome ansiosa, messa in relazione a problematiche lavorative.

Eseguiva valutazione presso il MMG che consigliava esecuzione di esami ematochimici generali e funzionalità tiroidea, monitoraggio pressorio e glicemico. ECO addome. Risultati tutti nella norma.

Ma il nostro Paziente rimaneva ansioso, anche per la storia familiare che lo preoccupava...

Il nonno paterno del Paziente era deceduto durante un intervento chirurgico per asportazione di una massa surrenalica, non tipizzata.

Uno zio paterno era stato sottoposto ad asportazione di “tumore glomico” in passato e la figlia di un altro zio da parte di padre era stata sottoposta ad asportazione di un “nodulo” nel collo (dettagli istopatologici non disponibili).

Anche il padre del nostro Paziente riferiva 3 interventi chirurgici per delle lesioni peri-vascolari nel collo.

CASO CLINICO

La peculiare frequenza di neoplasie nella famiglia aveva portato il Paziente ad eseguire delle ricerche autonome, temendo una predisposizione a sviluppare egli stesso una neoplasia.

Pertanto dopo aver consultato vari specialisti addiveniva alla decisione di una **valutazione genetica**.

Così veniva identificata la mutazione del gene: SDHD c.242C>T p.Pro81Lueu

Gene coinvolto nella sindrome da paraganglioma PGL1, di cui sono portatori il Paziente, suo padre ed uno zio paterno (dato non disponibile per la cugina).

LINEE GUIDA E PDTA



National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 2.2022 Pheochromocytoma/Paraganglioma NCCN Evidence Blocks™

TUMOR TYPE

EVALUATION^{a,b,c}

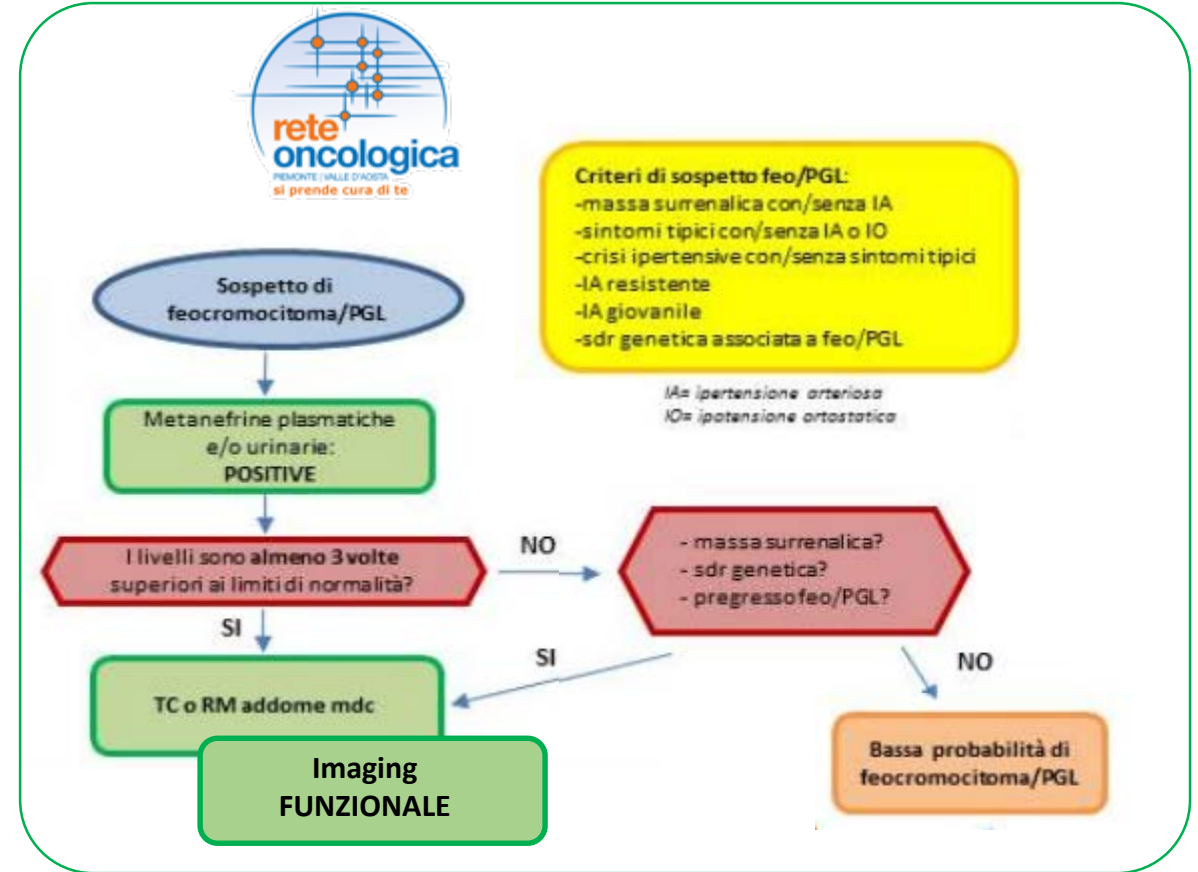
Pheochromocytoma/
paraganglioma

Recommended:

- Plasma free or 24-hour urine fractionated metanephrines and normetanephrines^{b,d,e} ± serum or 24-hour urine catecholamines^f
- Adrenal protocol CT (abdomen/pelvis)
- Genetic counseling and testing for inherited genetic syndromes^h

As appropriate, if metastatic or multifocal disease suspected:ⁱ

- Abdominal/pelvic multiphasic CT or MRI^g
- SSTR-PET/CT or SSTR-PET/MRI^{e,j,k}
- FDG-PET/CT (skull base to mid-thigh)
- Chest CT with or without contrast
- MIBG scan with SPECT/CT^l



CASO CLINICO

Il sig. D.L. veniva quindi avviato ad una serie di controlli: dosaggio catecolamine plasmatiche ed urinarie, cataboliti della catecolamine urinarie nelle 24ore, ecografia del collo.

I dosaggi di catecolamine e cataboliti erano risultati nella norma tranne in un caso di valori ai limiti superiori. L'eco del collo sempre negativa.

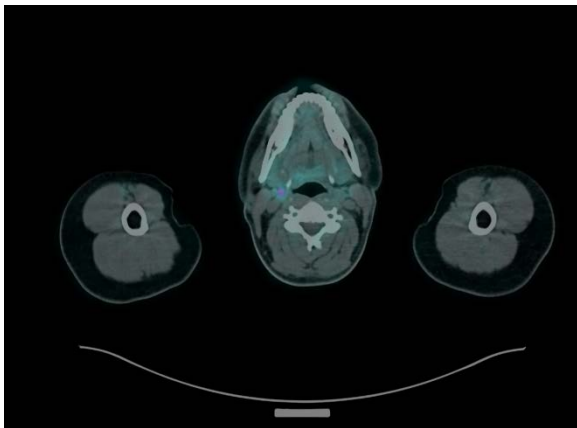
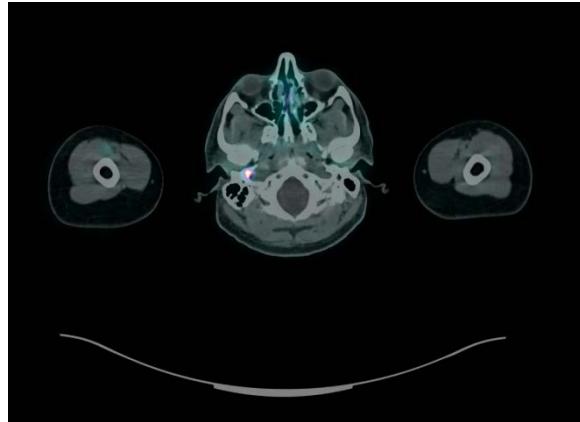
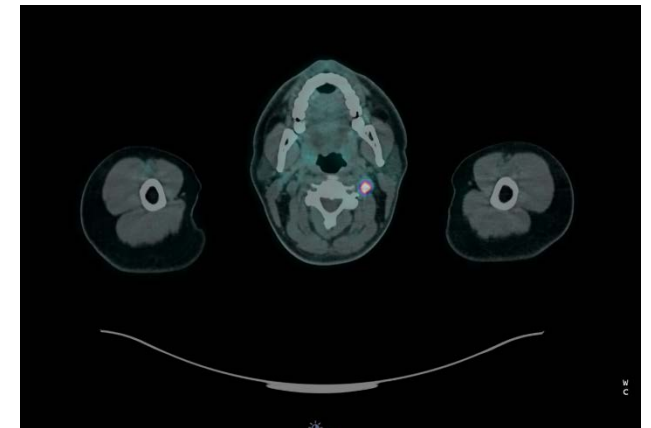
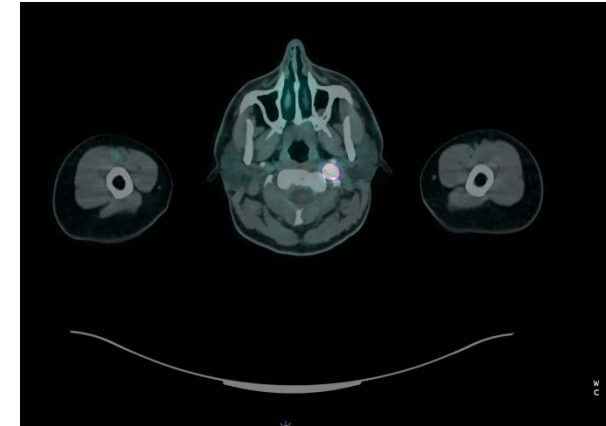
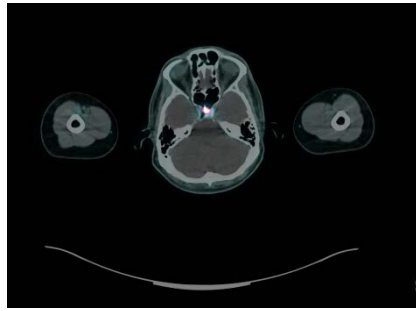
Tuttavia, sebbene i controlli risultassero sempre nell'ambito della norma, gli episodi di cefalea accusati dal Paziente stavano diventando più frequenti.

Negli ultimi due anni il sig. D.L. ha inoltre accusato qualche disturbo a vista ed udito.

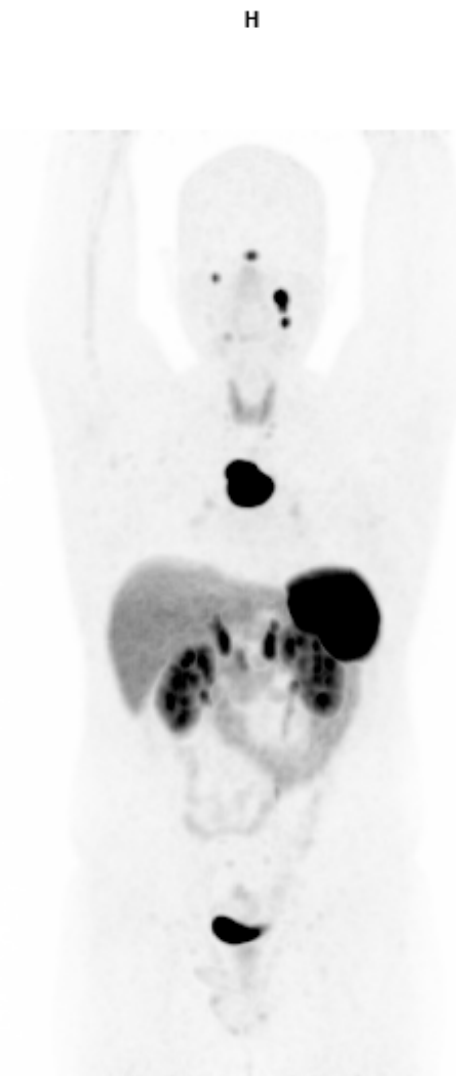
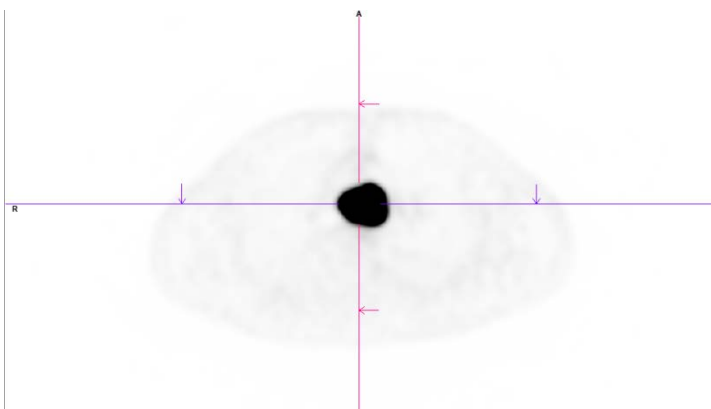
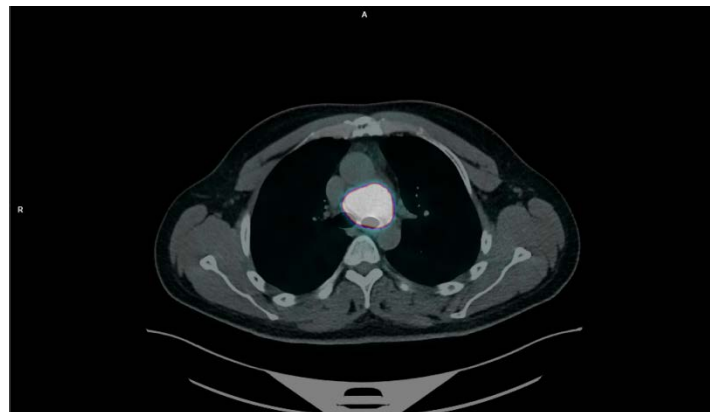
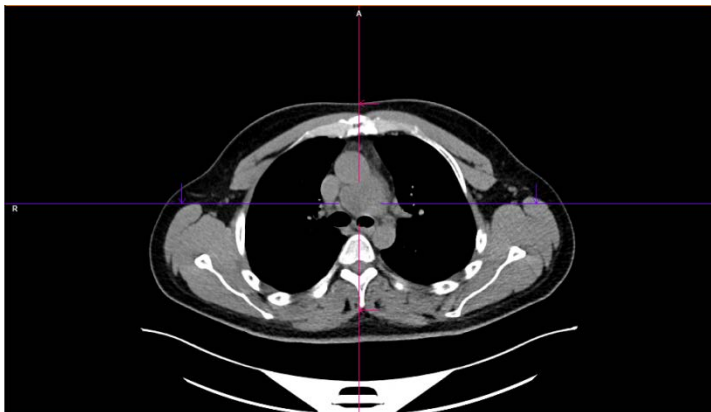
In considerazione però della negatività dei riscontri laboratoristici ed ecografici, la sintomatologia è stata sempre correlata più ad uno stato ansioso latente.

Dopo circa due anni dalla diagnosi genetica, il sig. D.L. Veniva indirizzato ad un approfondimento diagnostico mediante PET-TC con traccianti recettoriali.

CASO CLINICO, PET/CT 68Ga-DOTATOC



CASO CLINICO, PET/CT 68Ga-DOTATOC



CASO CLINICO

LA PROPOSTA TERAPEUTICA DEL SAN MATTEO

Il caso viene discusso collegialmente tra medico nucleare, endocrinologi, chirurgo toracico ed otorinolaringoiatra.

La proposta è:

- chirurgia con intento risolutivo, se tecnicamente fattibile
- radioterapia su sedi laterocervicali non (completamente) asportabili
- terapia sistemica con analogo della somatostatina

Il Paziente viene quindi ricontattato per avviare l'iter terapeutico con l'analogo della somatostatina e le valutazioni chirurgiche.

...to be continued

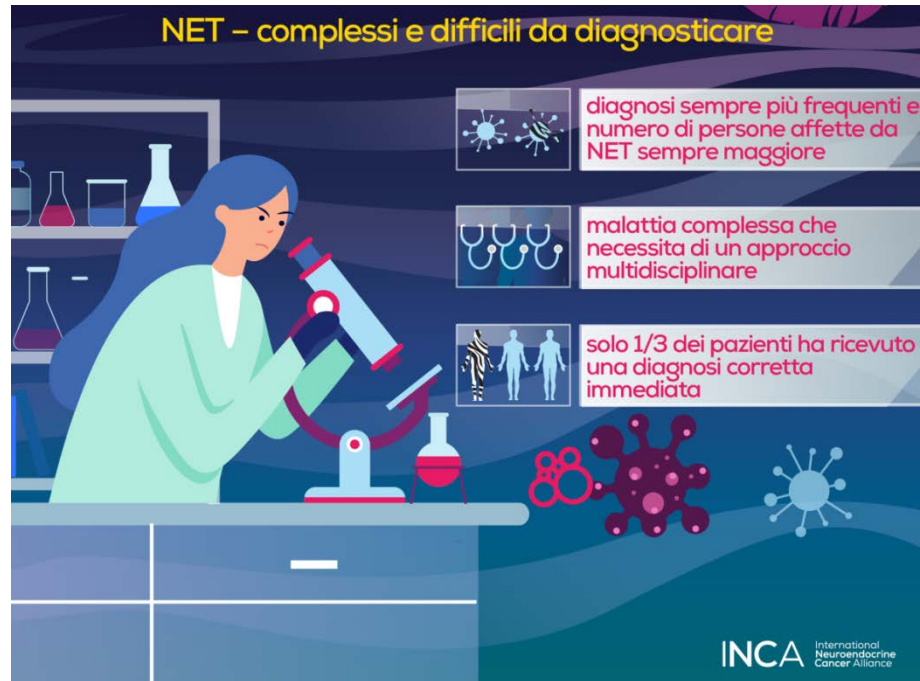


- ❑ Il “grande mimo” non è il Paziente, ma la patologia!!!
- ❑ Le patologie (rare) hanno bisogno di centri di eccellenza e multidisciplinarietà
- ❑ Il valore aggiunto dell’imaging funzionale



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“UNA” PATOLOGIA CHE NE MIMA TANTE ALTRE...



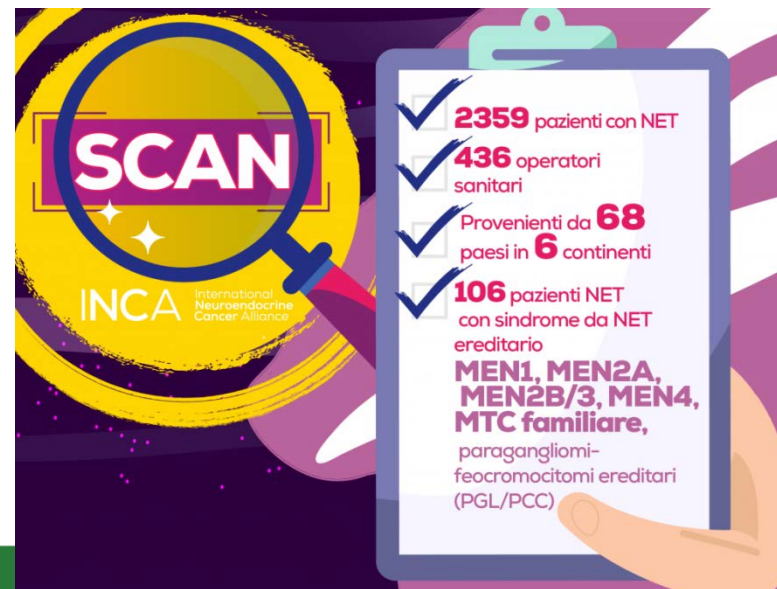
Una corretta interpretazione dei sintomi del feocromocitoma: campo minato per l'eterogeneità sul piano clinico

10% bilaterale

10% extra-surrenalico (paraganglioma)

10% maligno

Paragangliomi della regione testa-collo: spesso solo una tumefazione a livello del collo può indurre il sospetto clinico di malattia (quasi mai una sintomatologia di tipo secretivo)



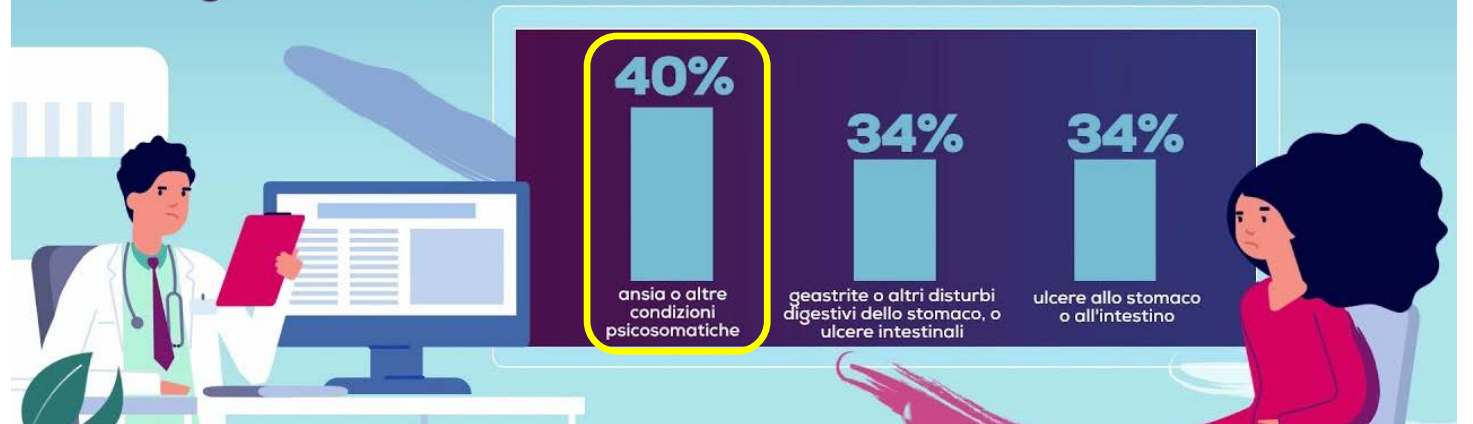
Survey of **C**hallenges in **A**ccess to Diagnostics and Treatment for **NET** Patients - **SCAN**

Survey of Challenges in Access to Diagnostics and Treatment for NET Patients

SCAN



Le 3 diagnosi errate più comuni nei pazienti affetti da NET ereditari



PARAGANGLIOMI/FEOCROMOCITOMI EREDITARI

Tumori neuroendocrini rari
circa il 30% di tutti i PGL/FEO
prevalenza del FEO è circa 1/500.000
prevalenza del PGL è circa 1/1.000.000

<https://www.orpha.net/consor/cgi-bin/index.php?lng=IT>



10% dei PGL/FEO determinati geneticamente è dovuto a una mutazione germinale di SDHx

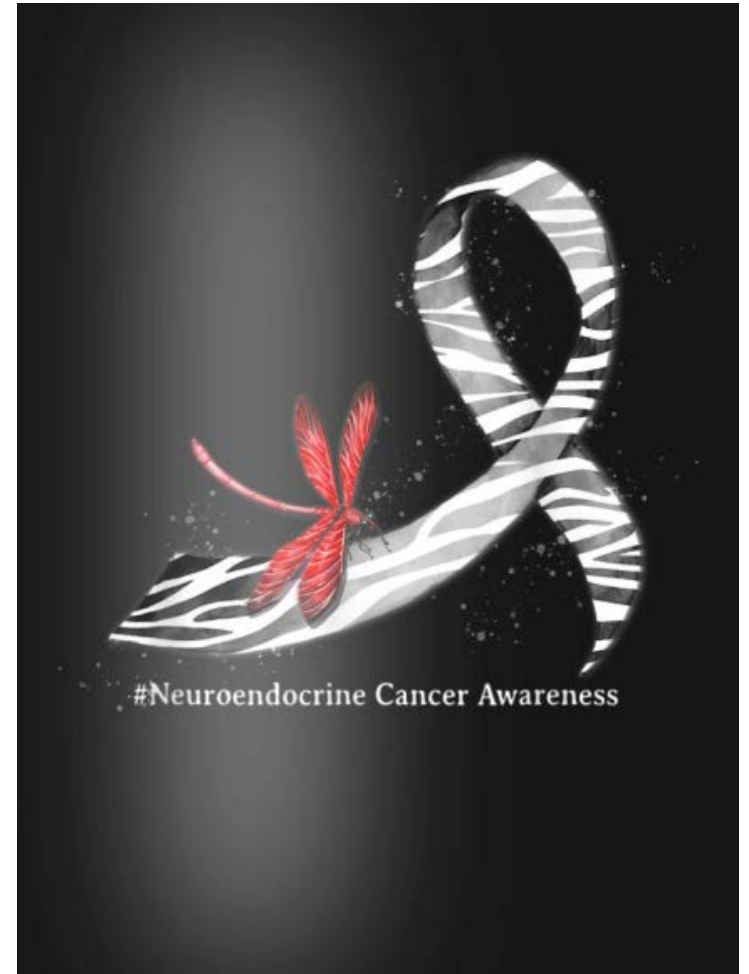
TABELLA 1

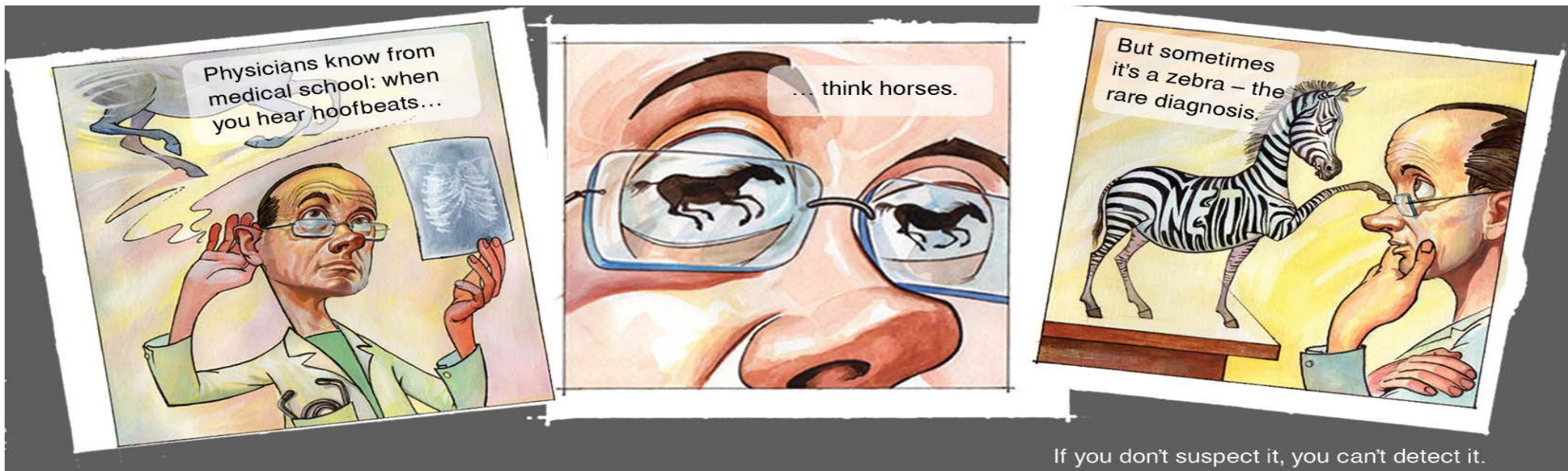
Gene	Localizzazione	Esoni	Patologia associata
SDHA	5p15	15	Sindrome di Leigh
SDHB	1p35-36.1	8	PGL4
SDHC	1q21.23	6	PGL3
SDHD	11q23	4	PGL1

Mannelli, M., Ercolino, T. & Simi, L. Sindromi feocromocitoma/paraganglioma familiari. L'Endocrinologo 10, 26–31 (2009). <https://doi.org/10.1007/BF03344642>

La trasmissione è autosomica dominante, ma si associa a imprinting genomico materno; la malattia insorge quando la mutazione è trasmessa dal padre.

Nei pazienti con mutazioni in SDHB i tumori tendono più spesso alla trasformazione maligna, rispetto a quelli causati dalle mutazioni di SDHx.





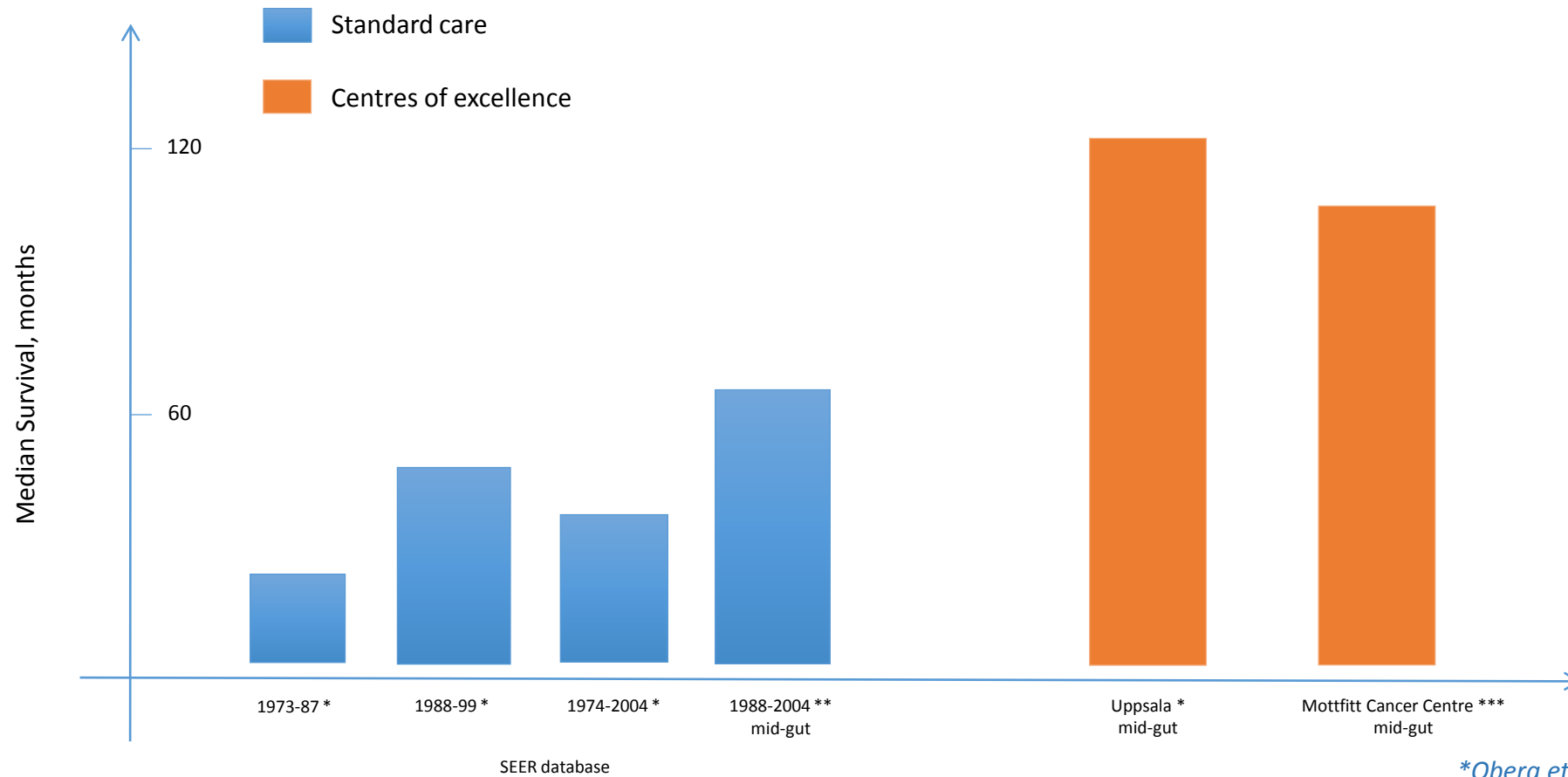
CONSAPEVOLEZZA... think of the ZEBRA!!!



- Il “grande mimo” non è il Paziente, ma la patologia!!!
- Le patologie (rare) hanno bisogno di centri di eccellenza e multidisciplinarietà
- Il valore aggiunto dell’imaging funzionale

BENEFICI DELLA GESTIONE MULTIDISCIPLINARE

Median survival of Pts affected by metastatic carcinoid



SEER = Surveillance, Epidemiology and End Results

*Oberg et al. *Annals Oncol*

** Yao et al. *J Clin Oncol* 2008

*** Stroberg et al. *Neuroendocrinology* 2009



- Il “grande mimo” non è il Paziente, ma la patologia!!!
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Radiofarmaci quali biomarkers:
from seeing to understanding.

Una nuova concezione di imaging, oltre la
diagnostica sensu strictu

Eur J Nucl Med Mol Imaging (2015) 42:535–536
DOI 10.1007/s00259-014-2981-6

EDITORIAL

Imaging biomarkers in oncology: we can get more from what we see

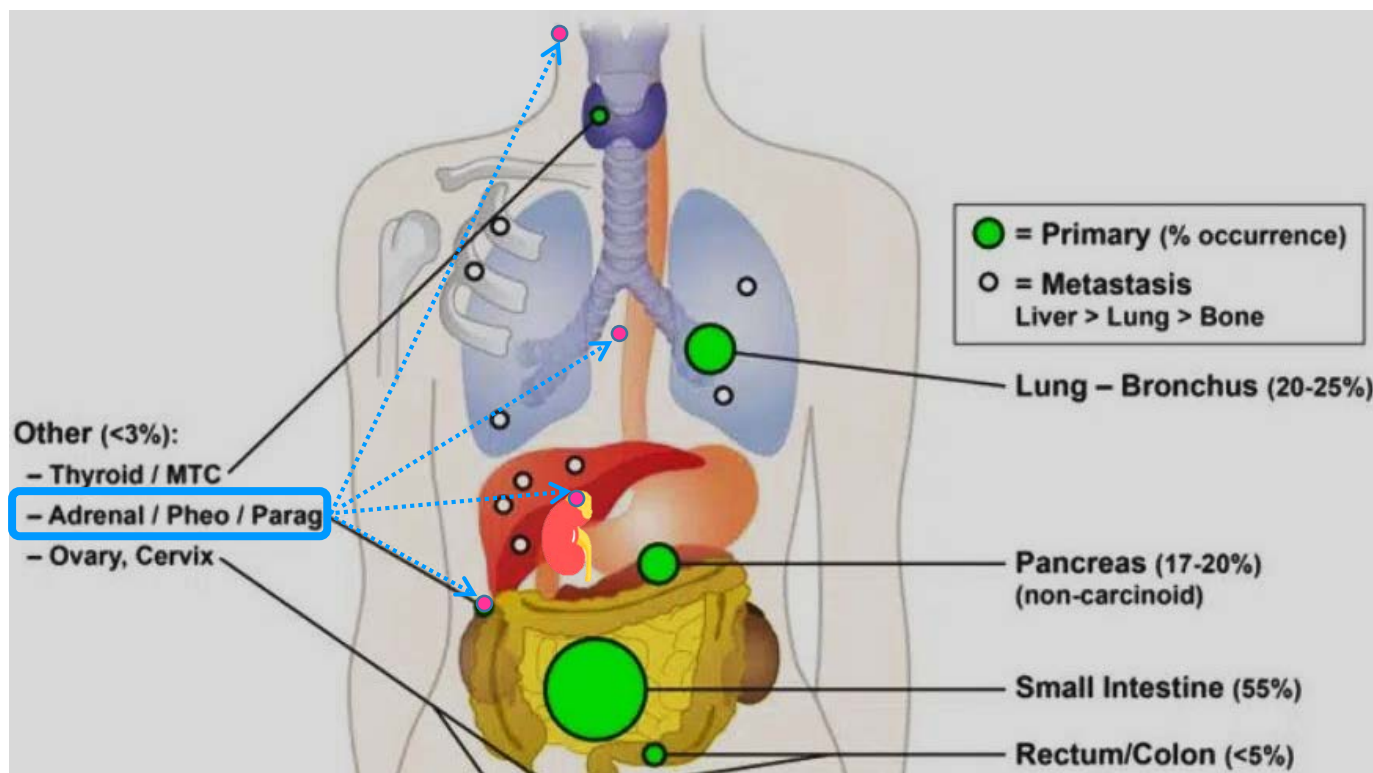
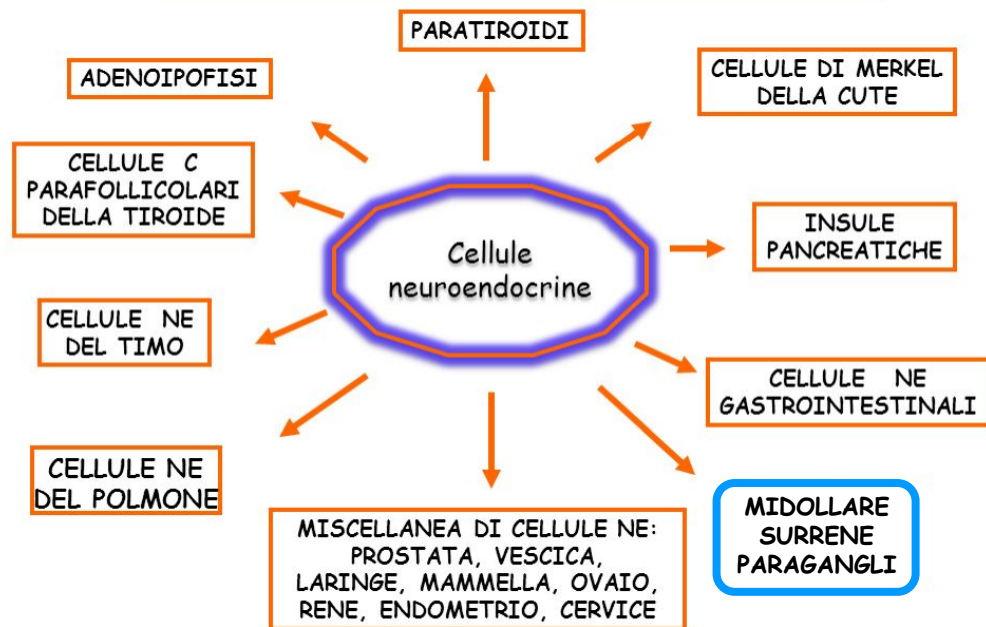
Arturo Chiti

NET, FEO, PGL

Le neoplasie neuroendocrine (NEN) sono un gruppo eterogeneo di Tumori Rari che originano da cellule di derivazione neuroectodermica che possono presentarsi in tutti i distretti corporei con un comportamento biologico variabile.

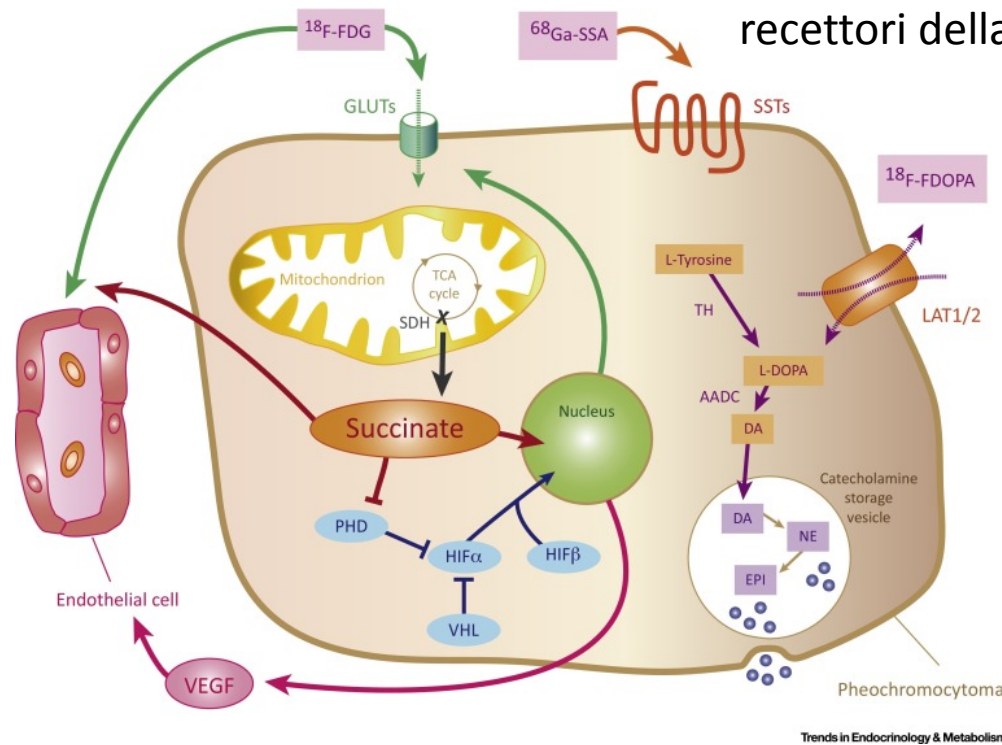


SISTEMA NEUROENDOCRINO DIFFUSO



RADIOFARMACI NELLO STUDIO DEI TUMORI NEUROENDOCRINI

18F-FDG marker surrogato del metabolismo glucidico. Entra tramite GLUT, fosforilato da esochinasi e quindi trattenuto nelle cellule per effetto Warburg

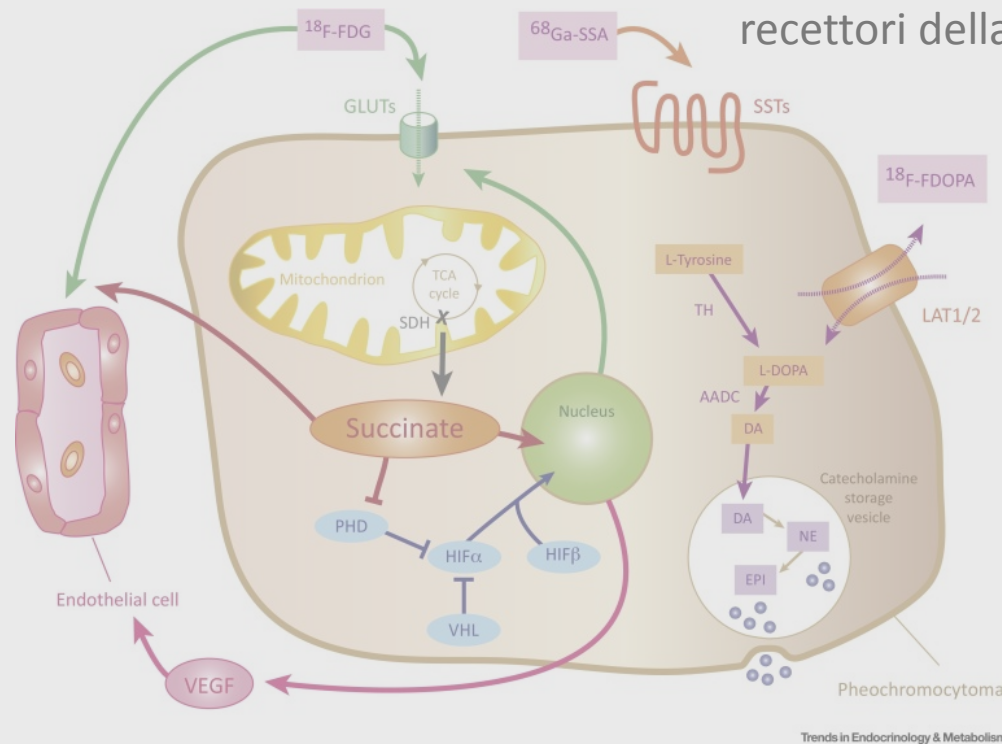


SSTR 2 and SSTR 3 sono iper-espressi in PGL e FEO. 111In-pentetreotide; 68Ga-DOTA-peptidi: imaging dei recettori della somatostatina

18F-FDOPA entra via LATs e decarbossilato a 18F-fluorodopamine, sequestrata nelle vescicole secretorie Delle catecolamine: imaging del pathways delle catecolamine -- simile a 123I-MIBG

RADIOFARMACI NELLO STUDIO DEI TUMORI NEUROENDOCRINI

¹⁸F-FDG marker surrogato del metabolismo glucidico. Entra tramite GLUT, fosforilato da esochinasi e quindi trattenuto nelle cellule per effetto Warburg



SSTR 2 and SSTR 3 sono iper-espressi in PGL e FEO.
¹¹¹In-pentetretotide; ⁶⁸Ga-DOTA-peptidi: imaging dei recettori della somatostatina

¹⁸F-FDOPA entra via LATs e decarbossilato a **¹⁸F-fluorodopamine**, sequestrata nelle vescicole secretorie Delle catecolamine: imaging del pathways delle catecolamine -- simile a **¹²³I-MIBG**

^{18}F -DOPA

F-DOPA storicamente in ambito neurologico: studio nuclei della base

Applicazioni oncologiche nelle neoplasie con accentuato metabolismo delle catecolamine.

[Ahlstrom H et al *Radiology*. 1995; 195 (2): 333-7]

Buona accuratezza diagnostica sia per la stadiazione che per ristadiatione e sospetto di recidiva.

[Kauhanen S et al *Endocr Relat Cancer*. 2009; 16(1): 255-65]

Eur J Nucl Med Mol Imaging (2017) 44:1588–1601
DOI 10.1007/s00259-017-3728-y

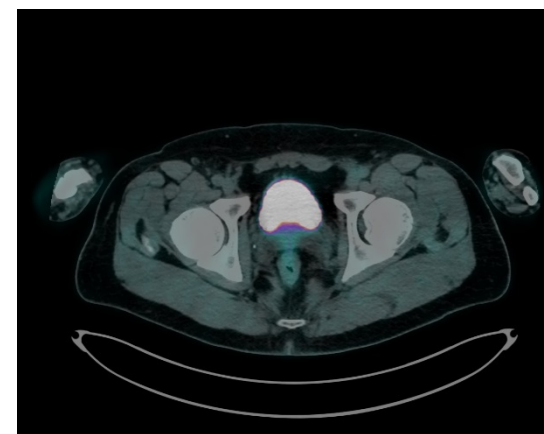
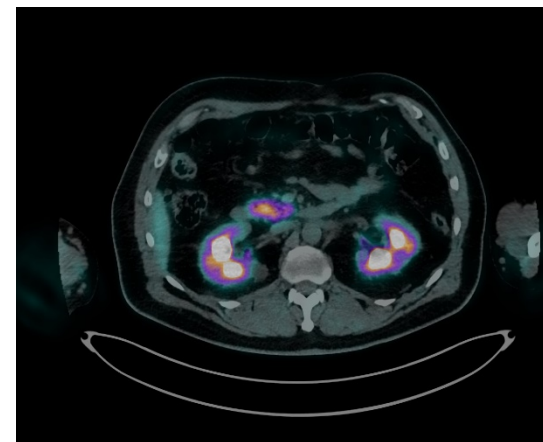
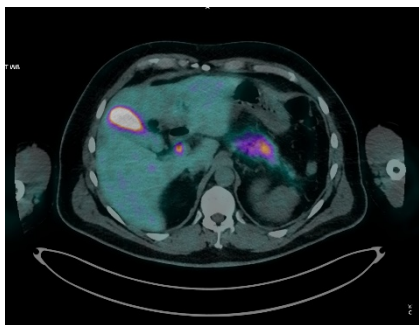
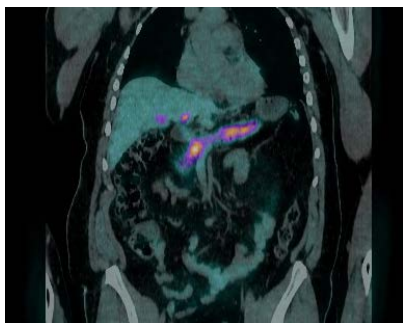
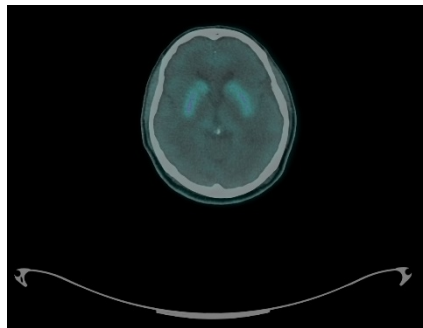


GUIDELINES

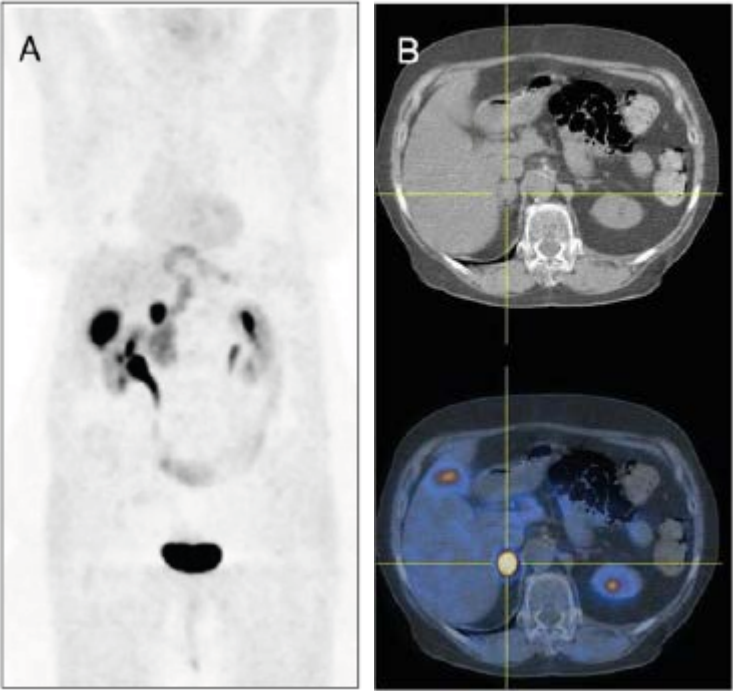
Guideline for PET/CT imaging of neuroendocrine neoplasms with ^{68}Ga -DOTA-conjugated somatostatin receptor targeting peptides and ^{18}F -DOPA

Murat Fani Bozkurt¹ • Irene Virgolini² • Sona Balogova^{3,4} • Mohsen Beheshti^{5,6} • Domenico Rubello⁷ • Clemens Decristoforo² • Valentina Ambrosini⁸ • Andreas Kjaer⁹ • Roberto Delgado-Bolton¹⁰ • Jolanta Kunikowska¹¹ • Wim J. G. Oyen¹² • Arturo Chiti¹³ • Francesco Giammarile¹⁴ • Stefano Fanti⁸

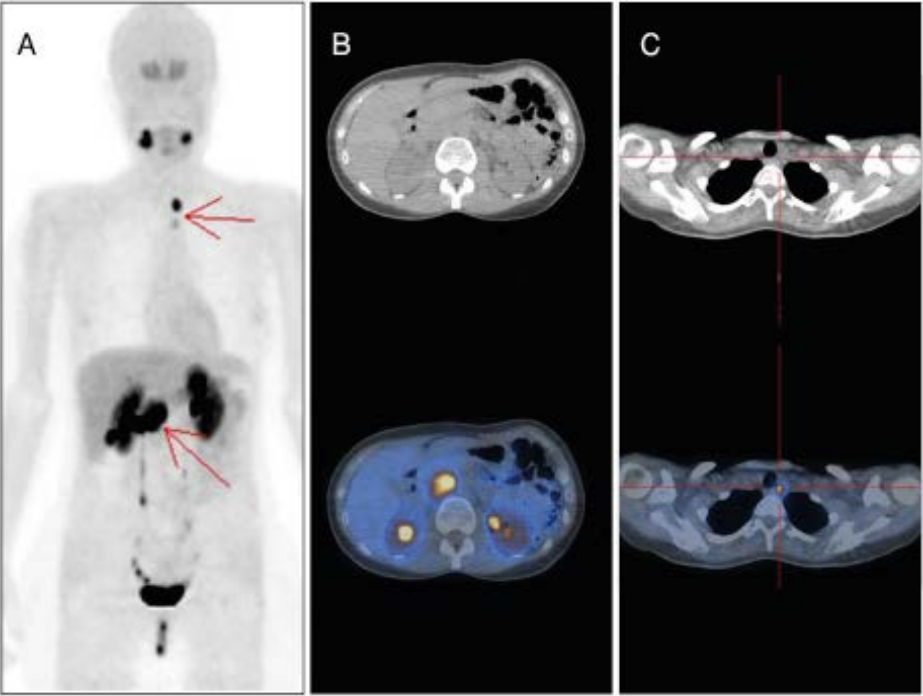
^{18}F -DOPA: NORMALE BIODISTRIBUZIONE



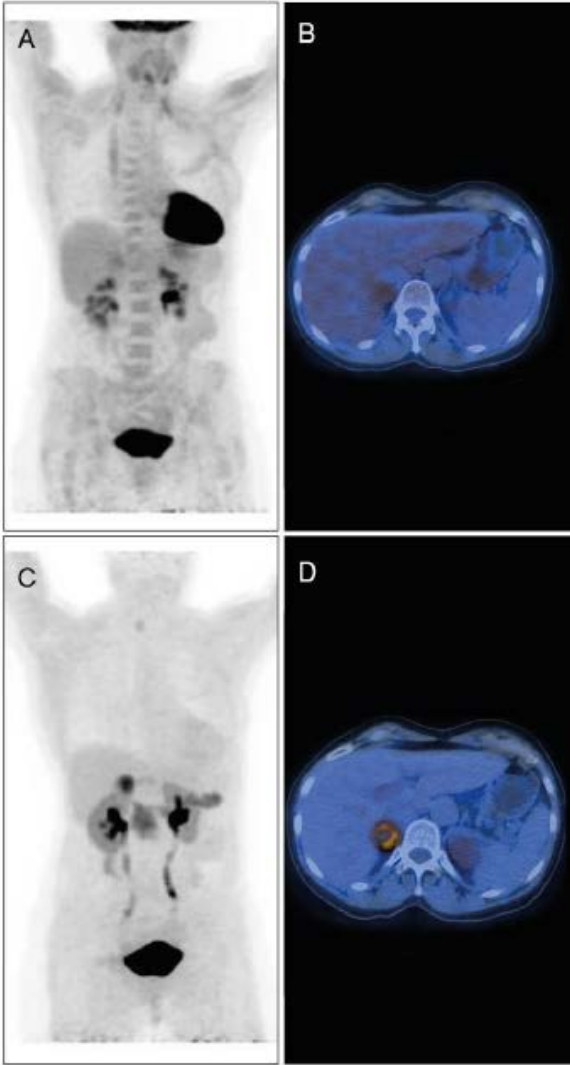
^{18}F -DOPA: FEO e PGL



FEO surrene dx

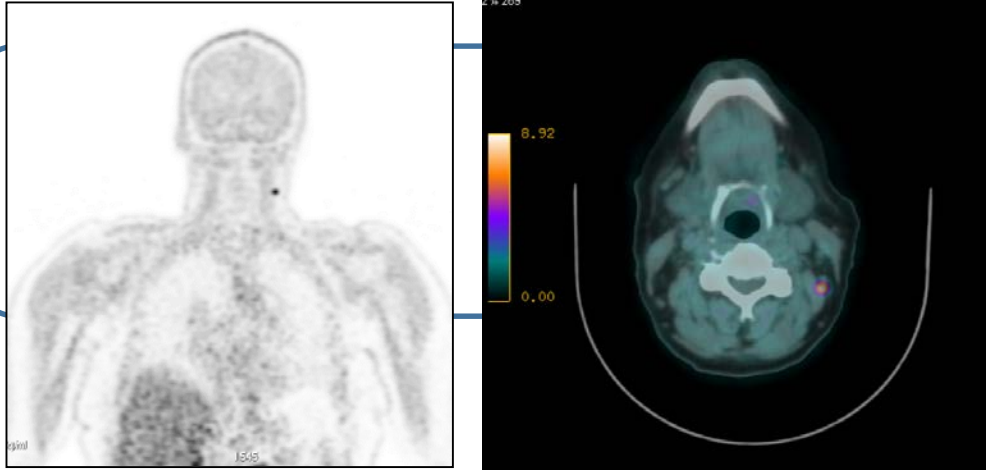


PGL addominale e paratracheale



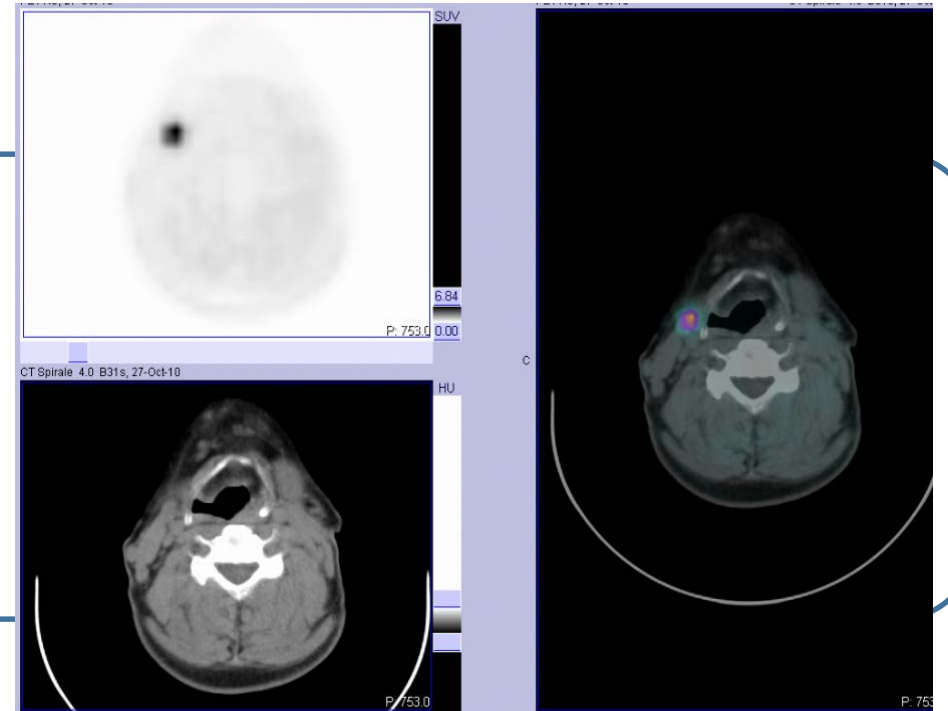
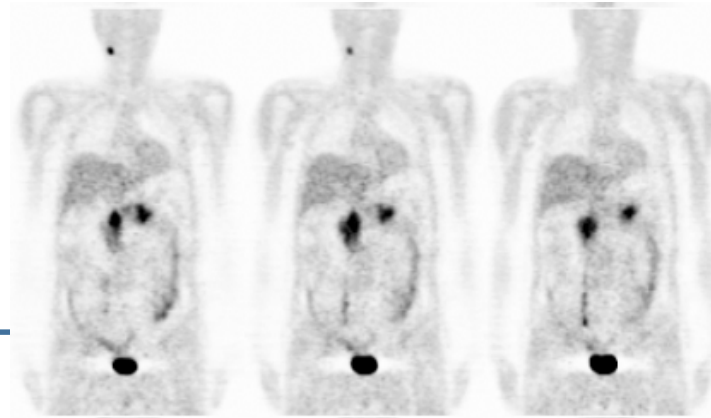
FEO surrene dx
FDG vs F-DOPA

^{18}F -DOPA: PGL



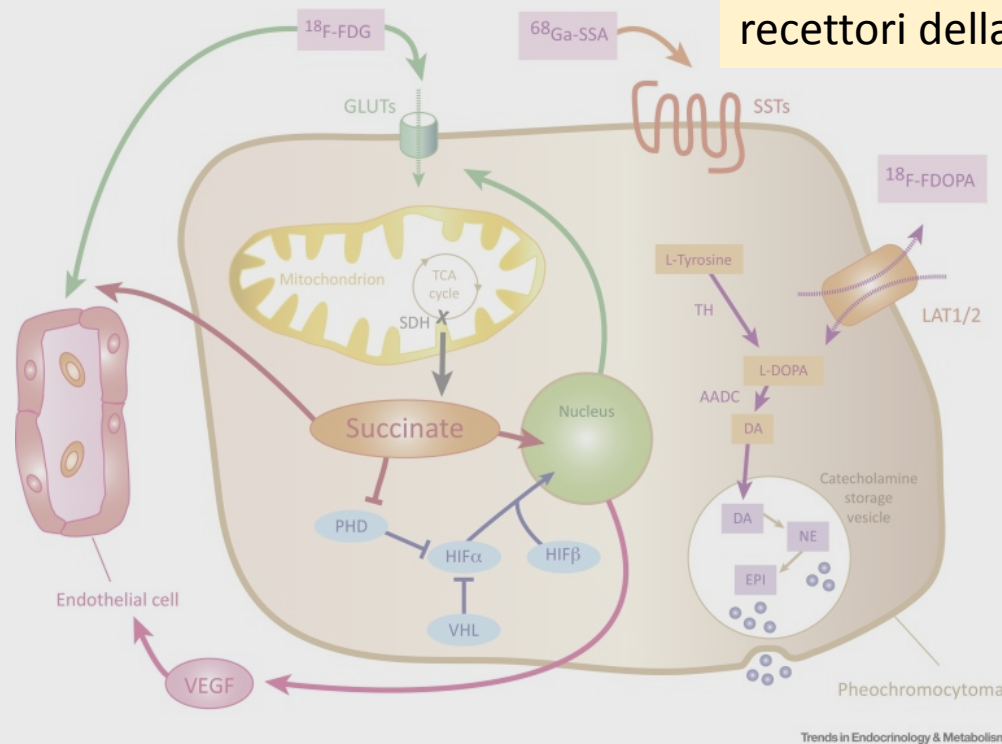
CG, M 52 anni: recidiva di paraganglioma laterocervicale a sin

LP, F 28 anni
ECO: tumefazione laterocervicale a dx
PET/CT conferma paraganglioma



RADIOFARMACI NELLO STUDIO DEI TUMORI NEUROENDOCRINI

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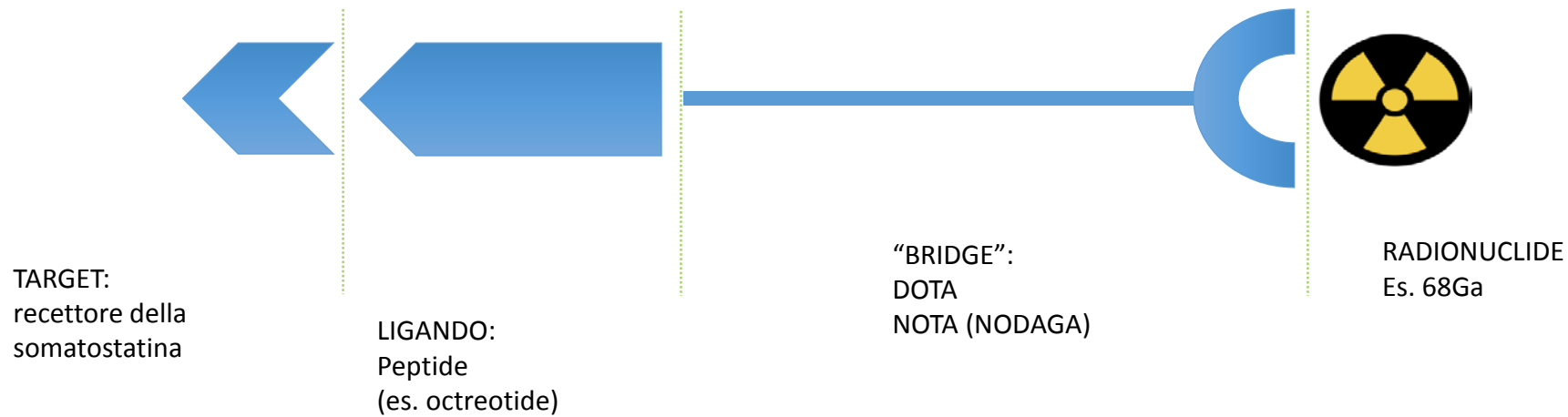
IMAGING RECETTORIALE



✓5 sottotipi:sstr 1-5

✓SOM14 e 28 legano tutti i 5 sottotipi

✓Octreotide si lega a SSTR2 e SSTR5



Gallio-DOTA-peptidi

Maggiore accuratezza diagnostica rispetto ad altre metodiche.

[Gabriel M et al. J Nucl Med. 2007; 48(4): 508-18]

Vantaggi Clinici:

✓ Identificazione delle lesioni sovra-esprimenti recettori della somatostatina, con intento diagnostico e terapeutico.

[Kwekeboom D et al. Endocr Relat Cancer. 2010 Jan 29; 17(1):R53-73]

✓ Possibile ruolo prognostico.

[Campana et al. J Nucl Med. 2010 Mar; 51(3): 353-9]

Vantaggi “Tecnici”

✓ $^{68}\text{Ge}/^{68}\text{Ga}$ Generatore, emivita 270.8 gg

✓ imaging in singola giornata (entro 180 min VS imaging tardivo in OctreoScan)

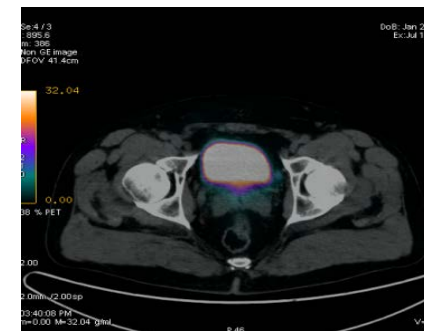
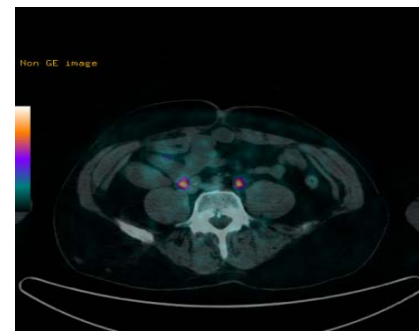
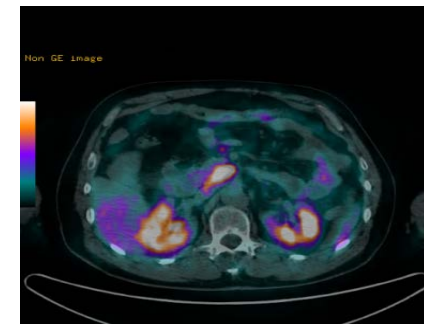
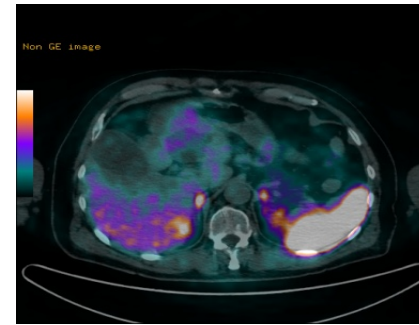
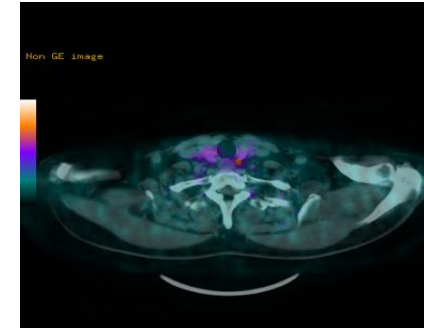
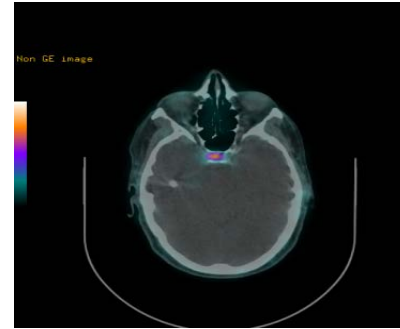
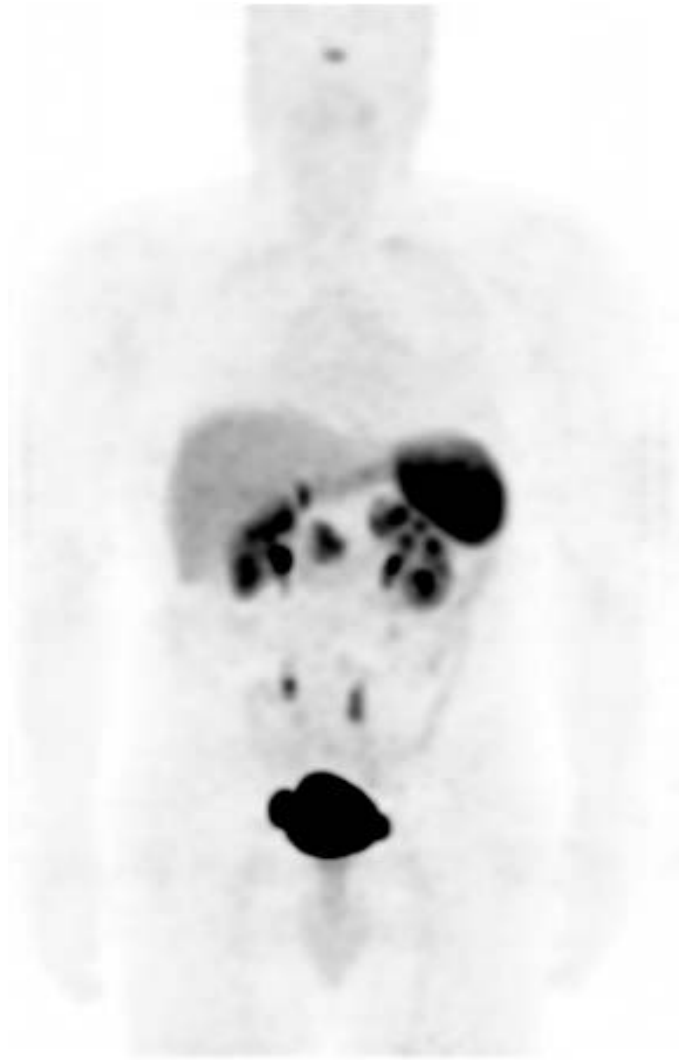
Eur J Nucl Med Mol Imaging (2010) 37:2004–2010
DOI 10.1007/s00259-010-1512-3

GUIDELINES

Procedure guidelines for PET/CT tumour imaging with ^{68}Ga -DOTA-conjugated peptides: ^{68}Ga -DOTA-TOC, ^{68}Ga -DOTA-NOC, ^{68}Ga -DOTA-TATE

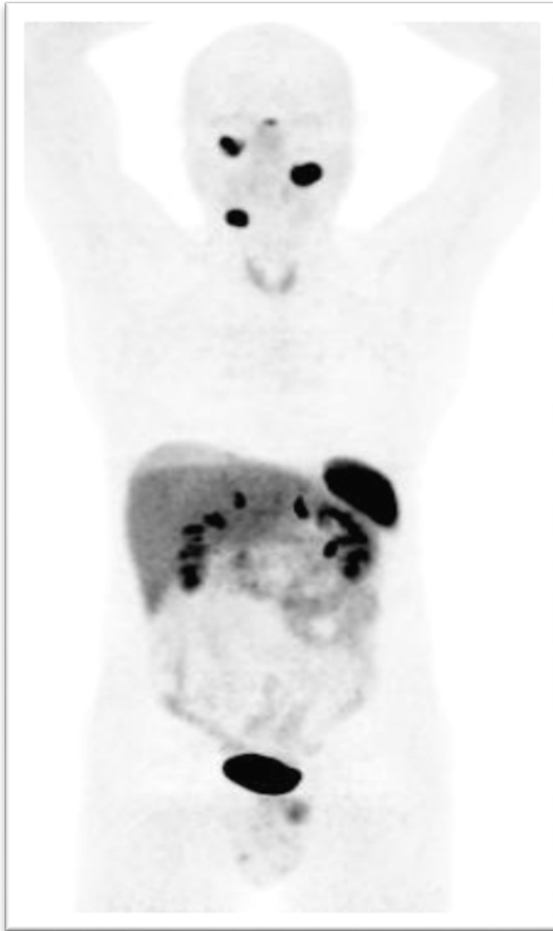
Irene Virgolini · Valentina Ambrosini · Jamshed B. Bomanji · Richard P. Baum · Stefano Fanti · Michael Gabriel · Nikolaos D. Papathanasiou · Giovanna Pepe · Wim Oyen · Clemens De Cristoforo · Arturo Chiti

68Ga-DOTApeptidi: NORMALE BIODISTRIBUZIONE



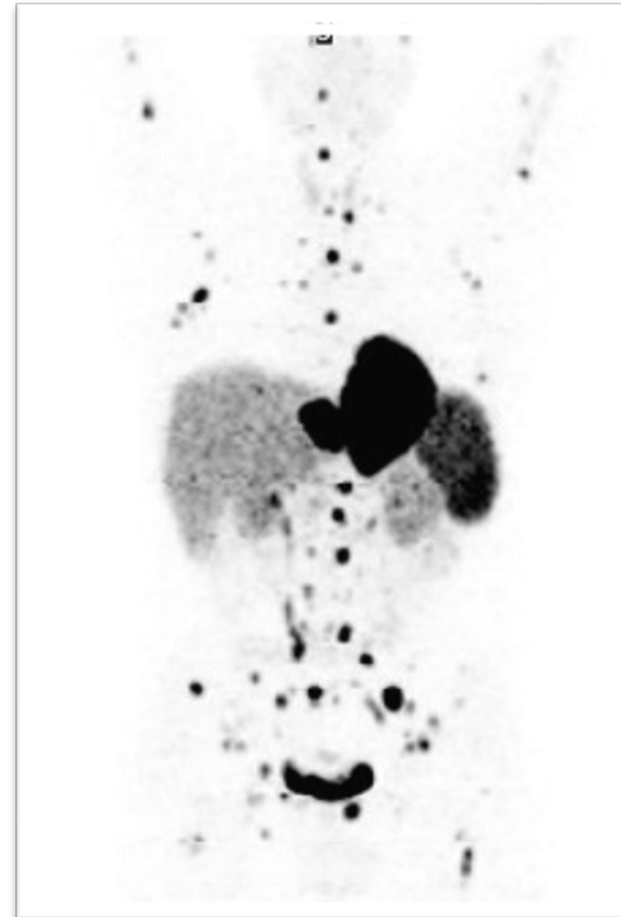
68Ga-DOTApeptidi: PGL

B.M., M 49aa, paragangliomatosi multipla cranico-cervicale bilaterale



PET/TC con ^{68}Ga -DOTATOC

R.M., M 29aa, paraganglioma del passaggio toraco-addominale metastatico all'esordio su osso e linfonodi



PET/TC con ^{68}Ga -DOTATOC

PGL: IMAGING FUNZIONALE A CONFRONTO

R.M., M 29aa, paraganglioma del passaggio toraco-addominale metastatico all'esordio su osso e linfonodi



^{111}In -OCT



PET/TC con ^{68}Ga -DOTATOC



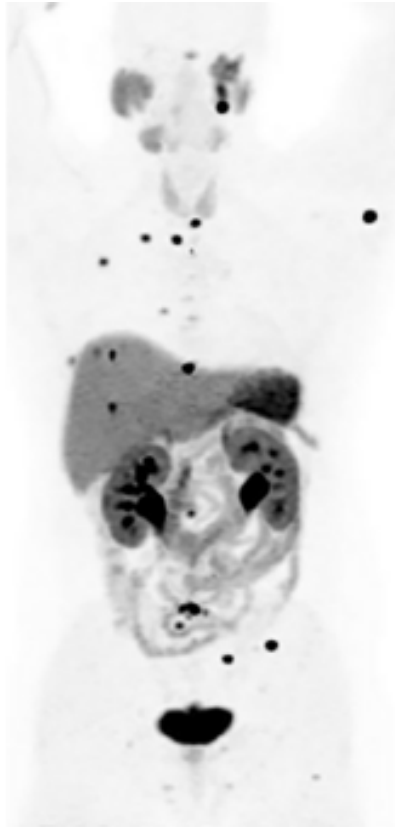
PET/TC con ^{18}F -FDG



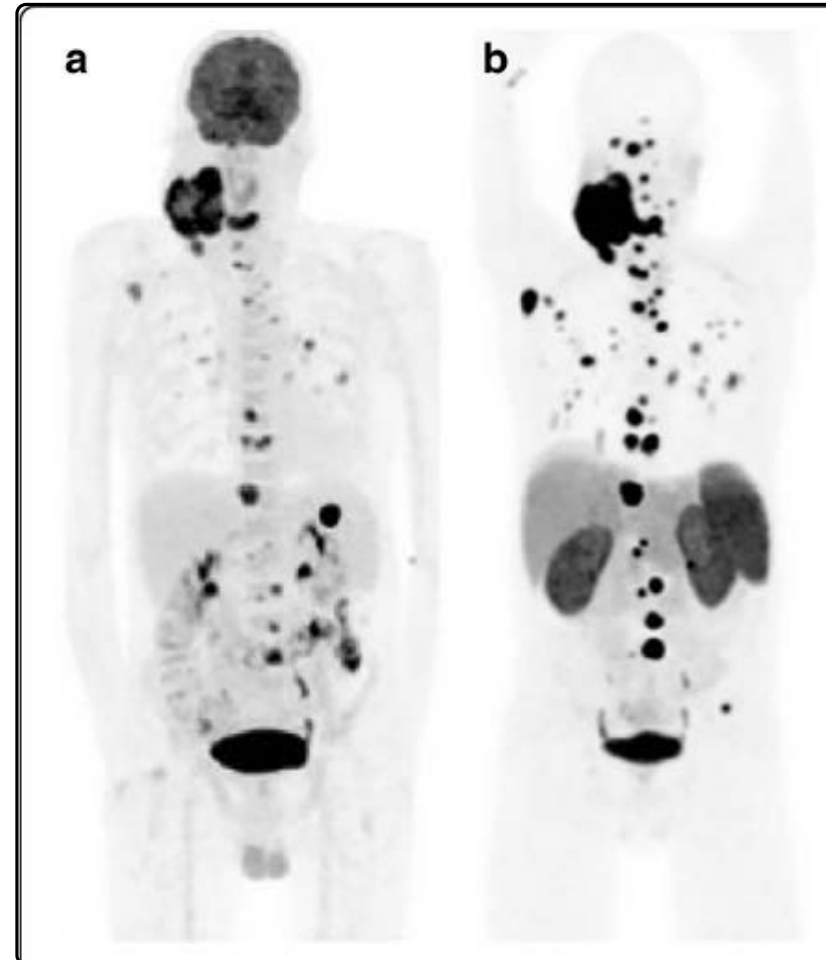
⁶⁸Ga-DOTATATE and ¹⁸F-FDG PET/CT in
Paraganglioma and Pheochromocytoma:
utility, patterns and heterogeneity

M, 20 anni, affetto da mutazione SDHB

Ga-68 DOTATATE
malattia
metastatica



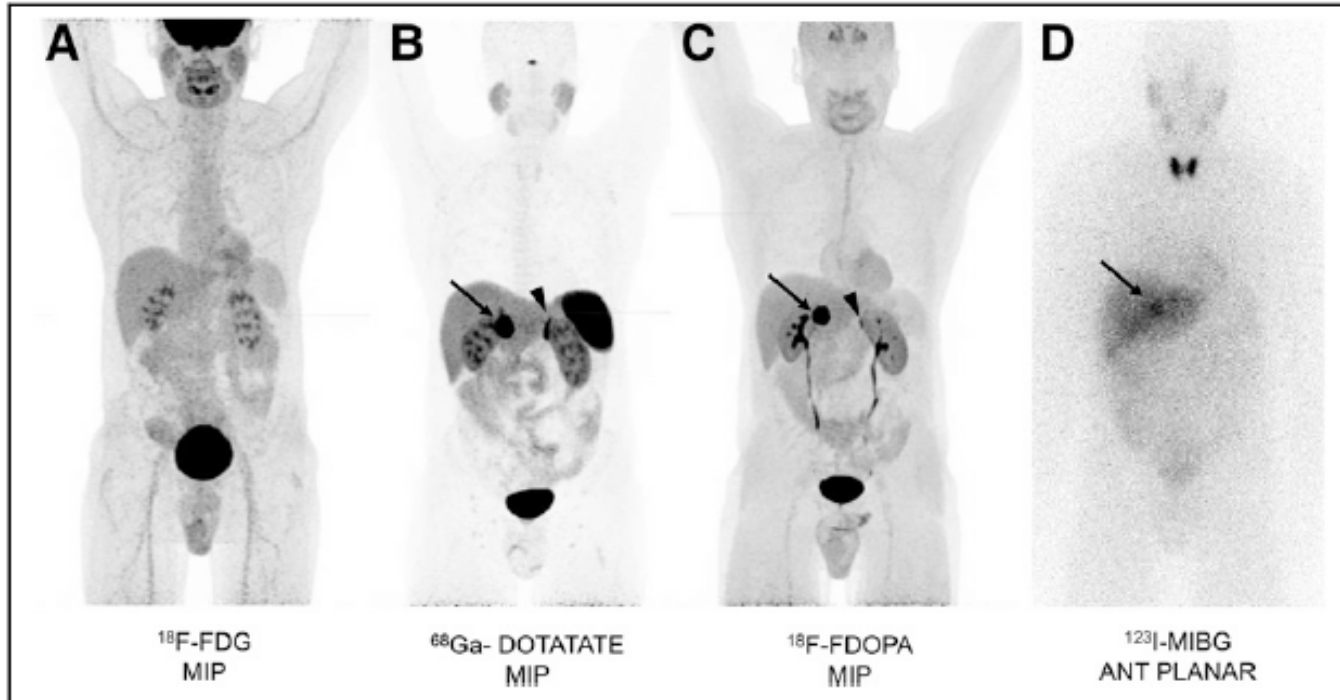
M, 65 anni, lunga storia di grossolana neoplasia peri-carotidea
in contesto di mutazione SDHD



a) ¹⁸F-FDG PET
metatasi osse massive

b) ⁶⁸Ga-DOTATATE
migliore contrasto
“tumour-to-background”
con identificazione di un
maggior numero di
lesioni rispetto all’FDG

FEO: IMAGING FUNZIONALE A CONFRONTO

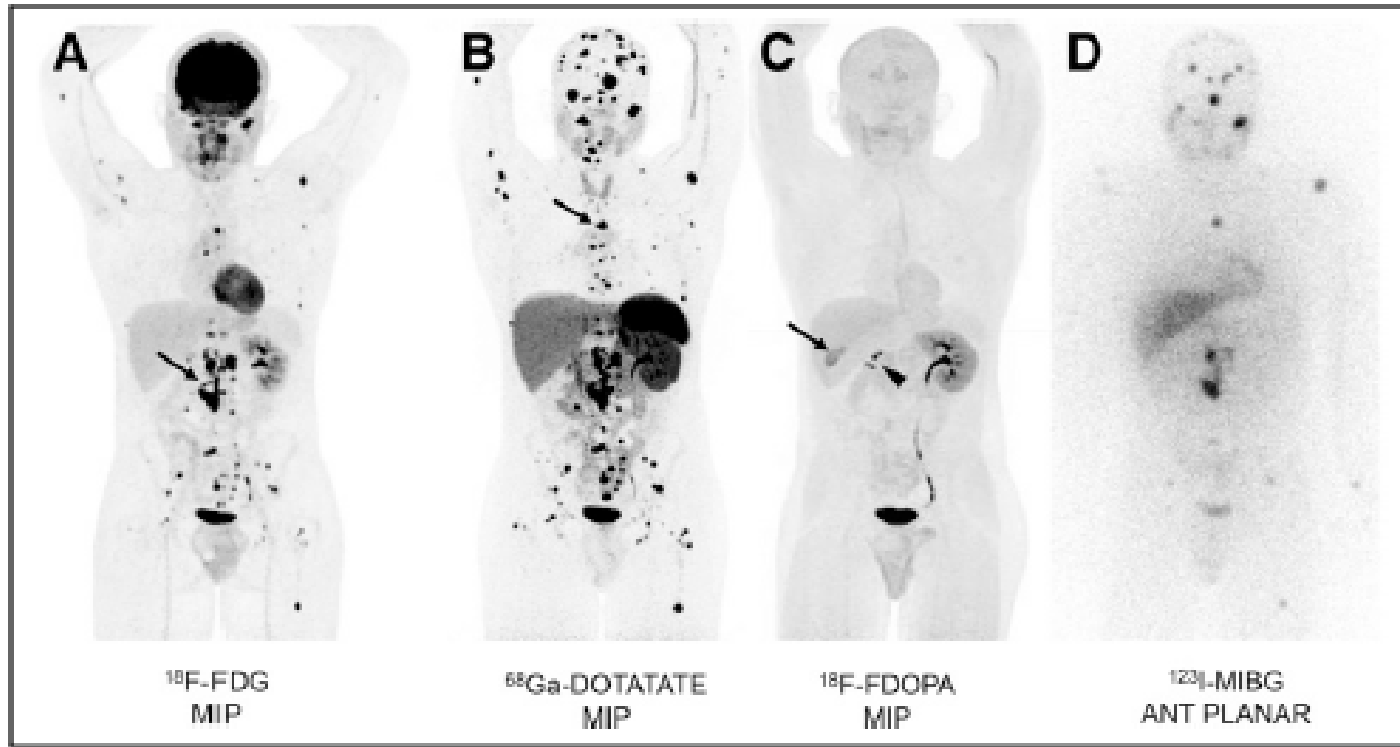


M, 54 anni affetto da FEO sporadico benigno nel surrene di destra

Carrasquillo JA, Chen CC, Jha A, Ling A, Lin FI, Pryma DA, Pacak K. Imaging of Pheochromocytoma and Paraganglioma. J Nucl Med. 2021 Aug 1;62(8):1033-1042. doi: 10.2967/jnumed.120.259689. PMID: 34330739; PMCID: PMC8833868

- (A) ^{18}F -FDG PET normale.
- (B) ^{68}Ga -DOTATATE PET ipercaptazione del surrene di destra
- (C) ^{18}F -FDOPA PET ipercaptazione del surrene di destra
- (D) Planare Anteriore ^{123}I -MIBG a 24 h moderata captazione nel surrene di destra, captazione tiroidea nonostante il blocco farmacologico

PGL: IMAGING FUNZIONALE A CONFRONTO



M, 20 anni, con PGL associato a mutazione SDHB

Carrasquillo JA, Chen CC, Jha A, Ling A, Lin FI, Pryma DA, Pacak K. Imaging of Pheochromocytoma and Paraganglioma. J Nucl Med. 2021 Aug 1;62(8):1033-1042. doi: 10.2967/jnumed.120.259689. PMID: 34330739; PMCID: PMC8833868

- (A) ¹⁸F-FDG PET massa retroperitoneale e diffuse metastasi ossee
- (B) ⁶⁸Ga-DOTATATE PET maggiore sensibilità con evidenza di un numero maggiore di lesioni
- (C) ¹⁸F-FDOPA PET sostanzialmente negativa
- (D) Planare Anteriore ¹²³I-MIBG evidenza di un numero limitato di lesioni

TABLE 1

Sensitivity of Detection of Benign Pheochromocytoma and Paraganglioma ($n \geq 20$ Patients or Prospective Studies)

Reference	Study type	Benign patients (n)	^{123}I -MIBG	Somatostatin imaging	^{18}F -FDG	^{18}F -FDOPA	CT	MRI
Lumachi (69)	P	32 PHEO/PGL 30 PHEO 2 PGL	91%				90%	93%
Timmers (11)	P	20 PHEO/PGL 12 PHEO 9 PGL	85% (77%) (86%) (67%)		95% (88%) (93%) (83%) overall	85% (81%) (93%) (67%)	(100%) [†] (100%) [†] 100% [†]	(100%) [†] (100%) [†] 100% [†]
Fiebrich (12)	P	24 PHEO	(52%)			(85%)	(70%) [†]	(70%) [†]
Timmers (19)	P	26 PHEO	(78%) (76%)*				(97%)	(92%)
Timmers (14)	R	60 PHEO/PGL 8 SDHx 9 MEN2 48 PHEO 13 PGL	(75%) 80% 100% 90% (60%)		(76.8%) 100% 40% 81% (75%)		(95.7%) [†] (97%) [†] (94%) [†]	(95.7%) [†] (97%) [†] (94%) [†]
Cerdan (70)	R	53 PHEO/PGL				(88% overall)		
Gabriel (32)	R	116 PHEO/PGL 49 PHEO 37 Sympathetic PGL 37 SDHB/D 109 HNPGL				92.2% (91.8%) (94%) (70%) (78%) (98.2%)		
Sharma (16)	R	35 PHEO		80% (90%) DOTANOC				
Tiwari (20)	P	82 PHEO/PGL 54 PHEO 28 PGL			86.6% overall (81%) (96%)			
Amodru (28)	R	56 PHEO				100%		

* ^{131}I - or ^{123}I -/ ^{131}I -MIBG.[†]Studies used either CT or MRI.

P = prospective; PHEO = pheochromocytoma; PGL = paraganglioma only; R = retrospective; MEN2 = multiple endocrine neoplasia type 2. Percentages not in parentheses are patient-based sensitivity; percentages in parentheses are lesion-based sensitivity.

Imaging of Pheochromocytoma and Paraganglioma

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TABLE 2

Sensitivity of Detection of Metastatic Pheochromocytoma and Paraganglioma ($n \geq 20$ Patients or Prospective Studies)

Reference	Study type	Metastatic patients (n)	^{123}I -MIBG	Somatostatin imaging	^{18}F -FDG	^{18}F -FDOPA	CT	MRI
Timmers (24)	R	30 PGL (SDHB)	80% (65%)	81% (59%)	100% (97%)		96% (96%)	95% (95%)
				^{111}In -pentetreotide				
Zelinka (42)	R	71 PHEO/PGL	71%*		76%		78% [†]	78% [†]
		30 SDHB,	65%*		92%		96%	96%
		41 non-SDHB	76%*		62%		65%	65%
Timmers (11)	P	28 PHEO/PGL	85% (57%)		89% (74%)	71% (45%)	86% (45%) [†]	86% (45%) [†]
		15 SDHB				(20%)		
		13 non-SDHB				(93%)		
Timmers (19)	P	34 PHEO/PGL	85%, 65%*				100%	100%
Fiebrich (12)	R	21 PHEO	(56%)			73%	(45%) [†]	(45%) [†]
Cantalamesa (39)	R	38 PHEO/PGL	79%		87%		87%	
Timmers (14)	R	95	(50%)		(82.5%)		(74.4%) [†]	(74.4%) [†]
		52 SDHx	(45%)		(92%)		(78.5) [†]	(78.5) [†]
		23 non-SDHx	(66%)		(67%)		(70%) [†]	(70%) [†]
Janssen (13)	P	17 PHEO/PGL (SDHB)	(18.7%) $n = 6$	100% (98.6%) ^{68}Ga -DOTATATE	100% (85.8%)	87.5% (61.4%)	100% [†] (84.8%) [†]	100% [†] (84.8%) [†]
Tan (15)	P	17 PHEO/PGL	46.7% (15.7%)*	93% (91.5%) ^{68}Ga -DOTATATE	90.9% (51.3%)			
Janssen (34)	P	22 PHEO/PGL (all sporadic)		100% (97.6%) ^{68}Ga -DOTATATE	91% (49%)	92% (74.8%)	100% (81.6%) [†]	100% (81.6%) [†]

* ^{131}I - or ^{123}I -/ ^{131}I -MIBG.

[†]Studies used either CT or MRI.

R = retrospective; PGL = paraganglioma only; PHEO = pheochromocytoma; P = prospective.

Percentages not in parentheses are patient-based sensitivity; percentages in parentheses are lesion-based sensitivity. In study of Zelinka (42), sensitivity of bone scan for metastasis was 82% overall, 95% for SDHB, and 70% for non-SDHB.

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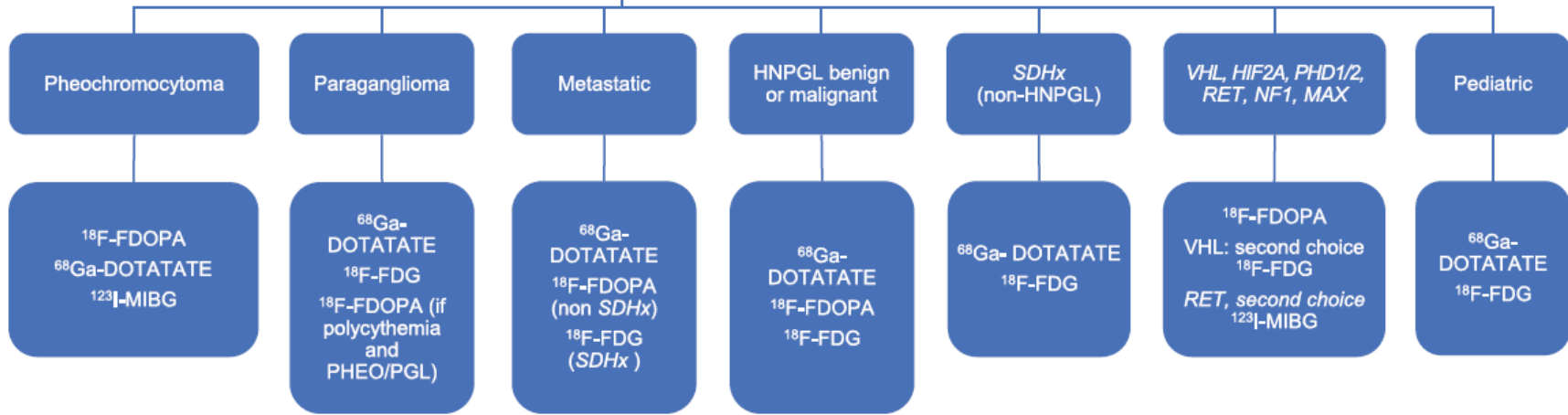
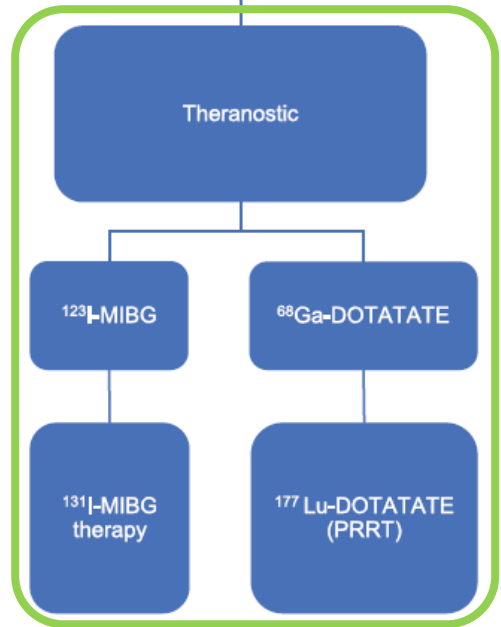
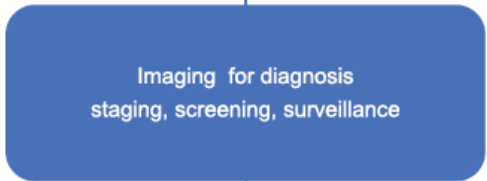
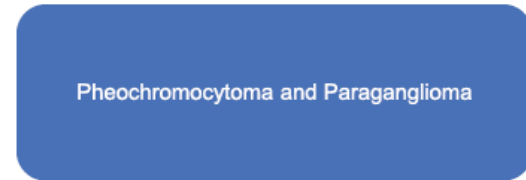
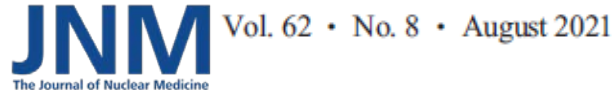
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CONCLUSION

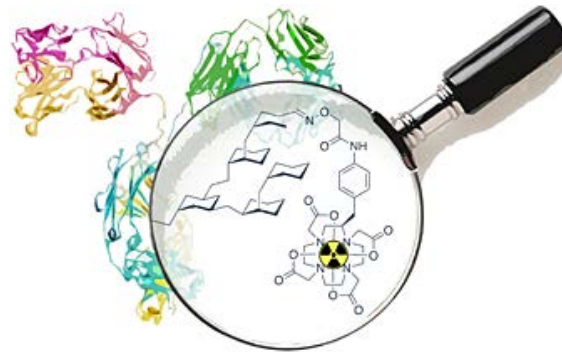
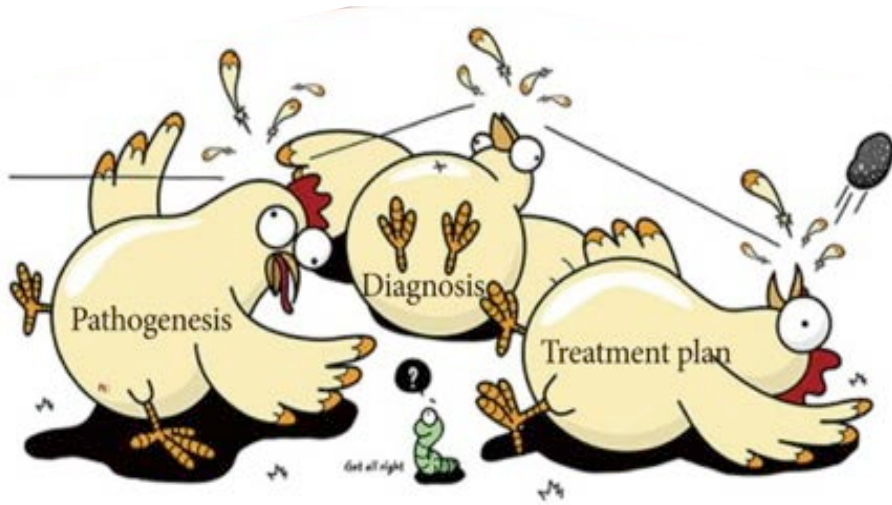
Pheochromocytoma and paraganglioma are complex molecularly driven diseases, with an increasing number of driver mutations identified. Because pheochromocytoma and paraganglioma are rare, studies are limited, typically small, and frequently retrospective. The identified pheochromocytoma and paraganglioma genotypes demonstrate imaging phenotypes that, although not perfectly predictive, offer guidance on the best functional imaging approaches. Frequently, PET/CT with ^{68}Ga -DOTA-SSA has the highest diagnostic accuracy across imaging modalities. ^{123}I -MIBG, ^{18}F -FDOPA, and ^{18}F -FDG can also be useful, especially in certain clinical presentations, in specific mutations, or for evaluating therapeutic options.

Imaging of Pheochromocytoma and Paraganglioma

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TERANOSTICA



...ma questa è un'altra storia...

GRAZIE PER L'ATTENZIONE

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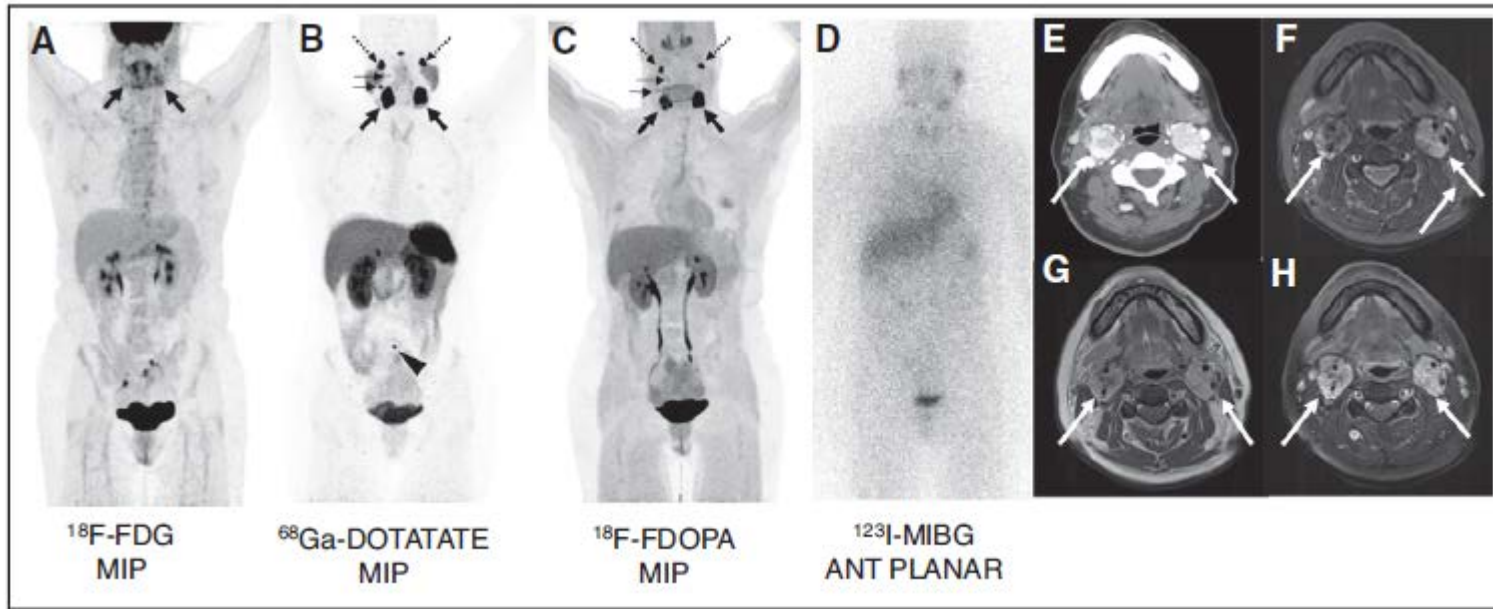
The role of imaging in pheochromocytoma and paraganglioma includes confirming the diagnosis when biochemical results are positive or borderline; defining the location, extent, and optimal approach to surgery; evaluating for multifocal or metastatic disease (staging); evaluating response to treatment (restaging); performing surveillance screening for the presence or recurrence of disease; and selecting suitable patients for theranostic applications ($^{90}\text{Y}/^{177}\text{Lu}$ -DOTA-somatostatin analog [SSA] or ^{131}I -metaiodobenzylguanidine [MIBG] therapy). Imaging modalities include anatomic imaging—principally CT and MRI—and functional imaging that relies on physiologic processes or receptor targeting

Radiolabeled MIBG ($^{131}\text{I}/^{123}\text{I}$ -MIBG, iobenguane) binds to norepinephrine transporters, which are internalized and shuttled into secretory granules via vesicular monoamine transporters (6).

^{18}F -FDOPA is transported into target cells via the large neutral amino acid transporter-1, after which it is decarboxylated to ^{18}F -fluorodopamine, which is sequestered into secretory vesicles via vesicular monoamine transporters or degraded by other enzymes.

Somatostatin, a 14-amino-acid peptide hormone, binds to somatostatin receptors (SSTRs 1, 2, 3, 4, and 5). In vitro, pheochromocytoma and paraganglioma tumors express predominantly SSTR 2 and SSTR 3. Although ^{111}In -pentetate was the first SSA approved for imaging NETs, it has been supplanted by DOTA-SSA, which has a stronger chelate and is labeled with ^{68}Ga , a positron emitter

^{18}F -FDG is a surrogate marker of glucose metabolism. Entry into tumor is mediated by glucose transporters, typically transporter-1, after which hexokinase-2 phosphorylates it and it becomes a trapped marker



A 46-y-old woman with SDHD-associated HNPGL and metastases in lymph nodes and bones.

Carrasquillo JA, Chen CC, Jha A, Ling A, Lin FI, Pryma DA, Pacak K. Imaging of Pheochromocytoma and Paraganglioma. *J Nucl Med.* 2021 Aug 1;62(8):1033-1042. doi: 10.2967/jnumed.120.259689. PMID: 34330739; PMCID: PMC8833868

- (A) ^{18}F -FDG PET scan showing carotid-body uptake (arrows) but not definitively identifying any other lesions.
- (B - C) ^{68}Ga -DOTATATE ; ^{18}F -FDOPA PET scans. Right and left carotid body tumors (horizontal solid arrows) are best identified. Bilateral uptake in glomus jugulare paraganglioma (dashed arrows), lymph node metastases (horizontal solid arrows). Highest contrast is noted in ^{68}Ga -DOTATATE scan, which also identified L5 bone metastasis (arrowhead), not identified in any other functional modality.
- (D) Anterior ^{123}I -MIBG planar scan with negative findings and showing normal salivary glands.
- (E) Axial contrast-enhanced CT scan showing enhancing right carotid body (2.1 cm) and left carotid body paraganglioma
- (F - H) Axial short-T1 inversion recovery MRI scan (F), contrast-enhanced T1-weighted MRI scan (G), and fat-suppressed contrast-enhanced T1-weighted MRI scan (H) demonstrating bilateral heterogeneous uptake

RESEARCH ARTICLE

Open Access

^{68}Ga -DOTATATE and ^{18}F -FDG PET/CT in
Paraganglioma and Pheochromocytoma:
utility, patterns and heterogeneity



Fig. 1 A 43 year-old male with *SDHD* germline mutation and prior excision of multiple paragangliomas. PET imaging was performed to characterise an equivocal mediastinal nodal abnormality identified on CT. Ga-68 DOTATATE (a) demonstrate very intense uptake in a right skull base glomus jugulare tumour (SUVmax = 90), which was not visible on F-18 FDG, in part, attributable to high uptake in physiologic cerebral activity (b). A left paratracheal abnormality in the mediastinum showed intense DOTATATE uptake and low grade uptake on FDG. This likely represented a further paraganglioma rather than a metastasis. The presence of 2 tumour suggests a probable germ-line mutation and would have warranted genetic testing if the germ-line mutation was not already known

