APPROCCIO TERANOSTICO E NUOVO APPROCCIO ALLE IMMAGINI NEI NET

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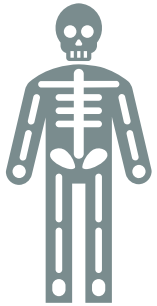
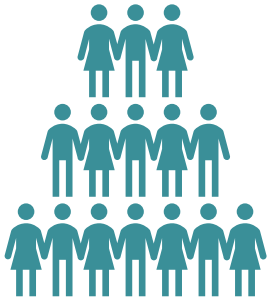
Città della Salute e della Scienza di Torino

Neuroendocrine tumors

Rare tumors



Several sites



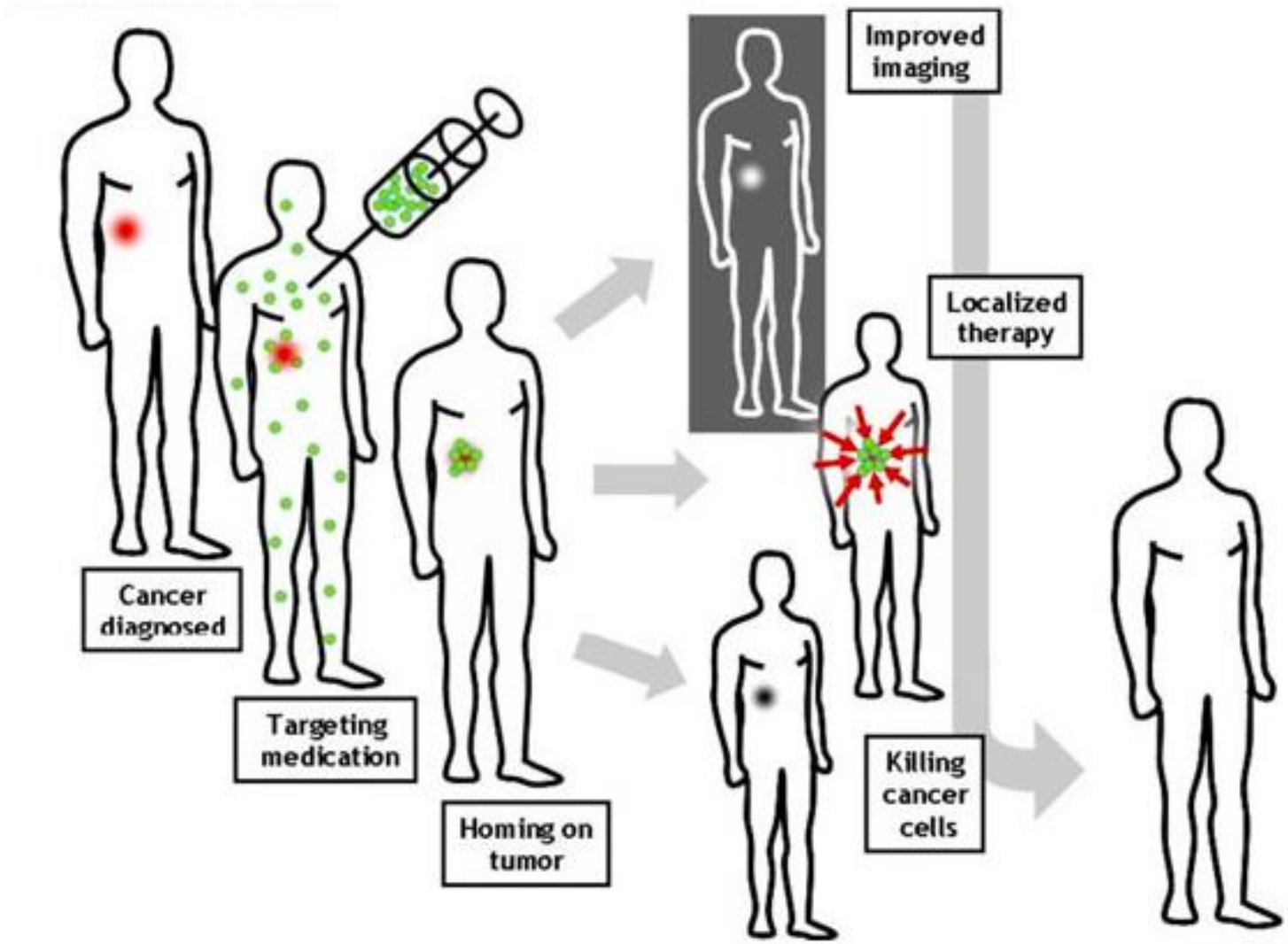
Heterogenous disease

Different treatments available

NET diagnosis

- Clinical presentation (site, functioning)
- Histology (Grade, Ki67)
- Laboratory (CgA, NSE); Molecular test
- Morphological imaging (endoscopy, CT,MRI)
- Nuclear Medicine (Molecular Imaging)

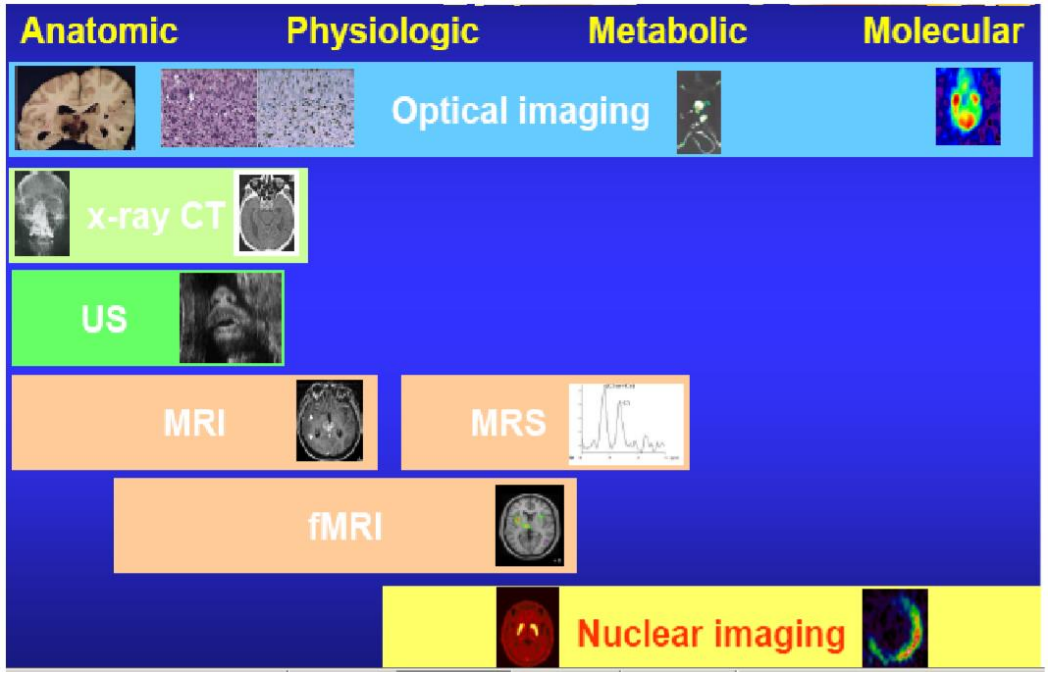
Theranostic approach: from molecular imaging to therapy



THERANOSTIC APPROACH

- ✓ Earlier detection and characterisation of disease (“molecular signature”)
- ✓ Understanding of underlying biology
- ✓ Selection of specific treatment option for targeted therapy

Molecular imaging



Tracer

Isotope

Radioactive

Gamma emittor (SPECT)
Positon emittor (TEP)

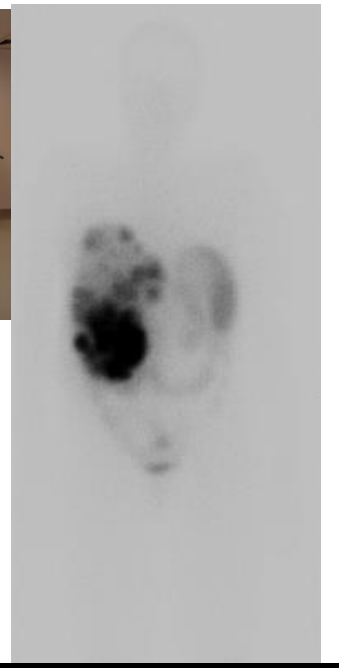
Molecule

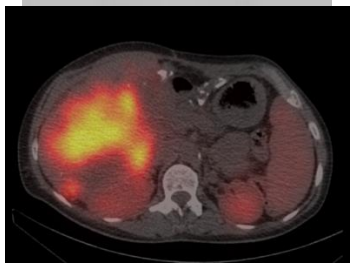
Glucose
AA
Proteine
Peptide

Not Radioactive

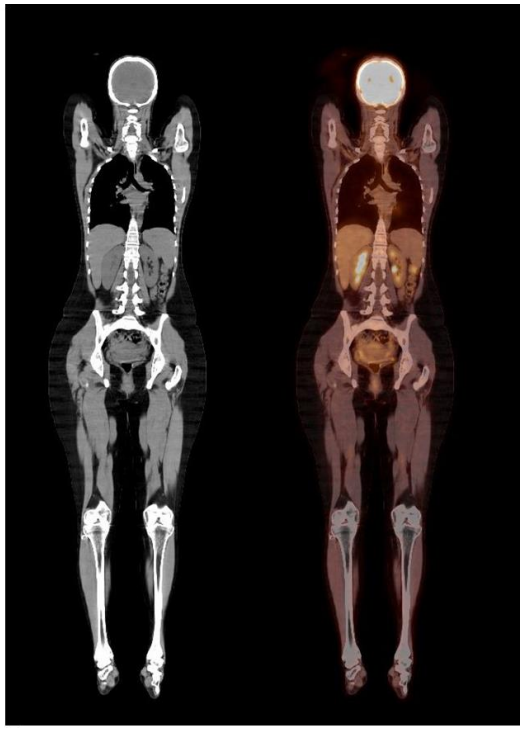
Define the Target

Hybrid Imaging



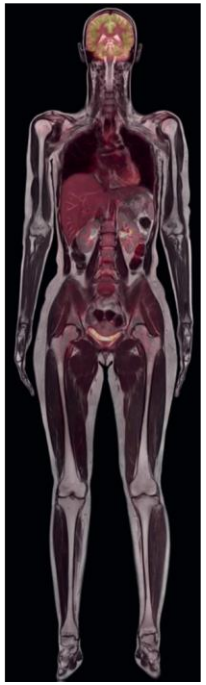


SPECT/CT



PET/CT

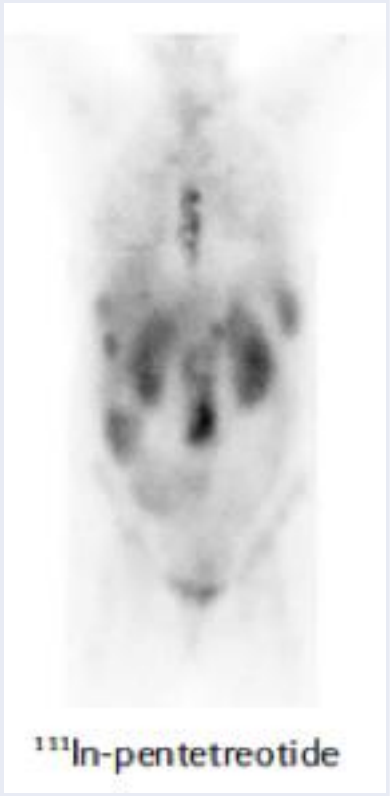
PET/MRI

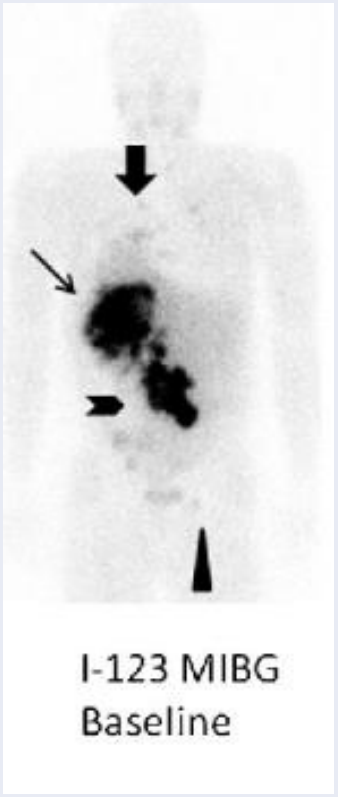


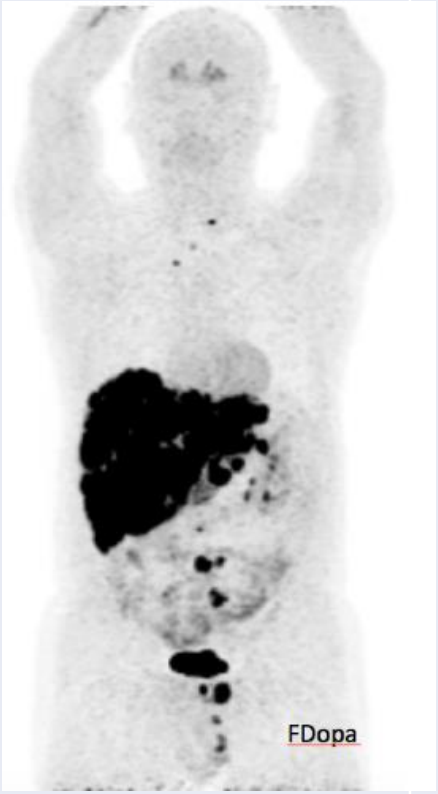
Detect and quantify the target

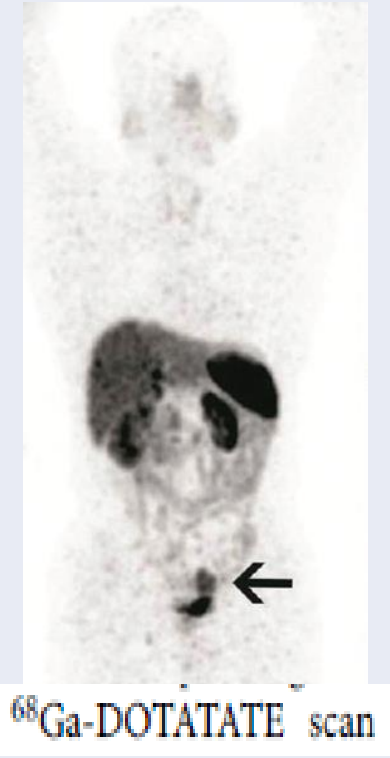
CURRENT COMMONLY UTILIZED NUCLEAR TECHNIQUE

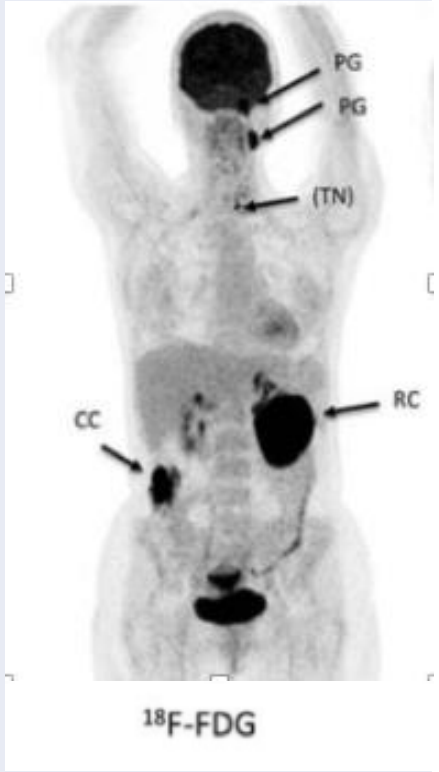
CONVENTIONAL SCINTIGRAPHY		PET/CT		
^{111}In-pentetreotide	^{123}I-MIBG	^{18}F-DOPA	^{68}Ga-SSA-peptides	^{18}F-FDG







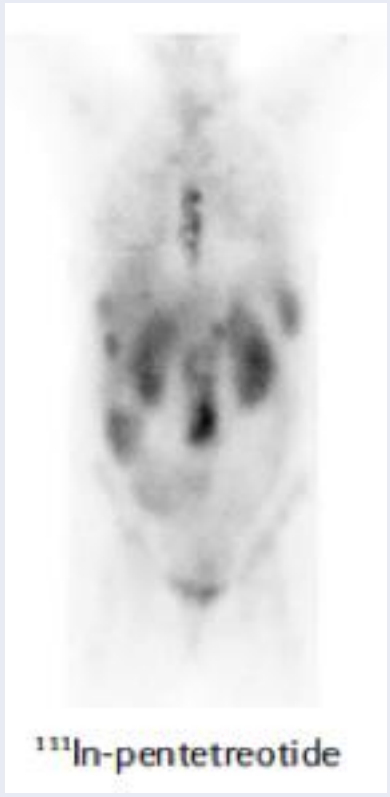




CURRENT COMMONLY UTILIZED NUCLEAR TECHNIQUE

CONVENTIONAL SCINTIGRAPHY

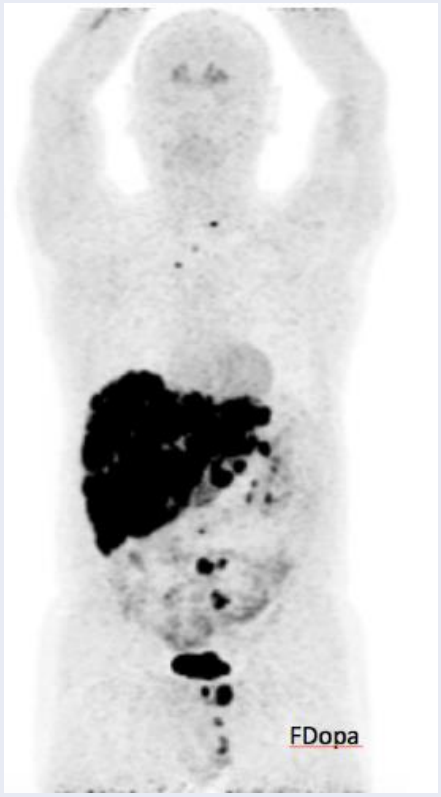
^{111}In-pentetreotide



^{131}I-MIBG

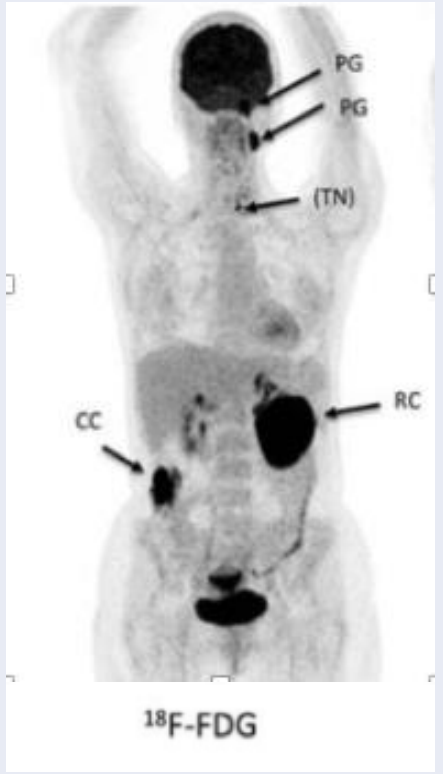
PET/CT

^{18}F-DOPA

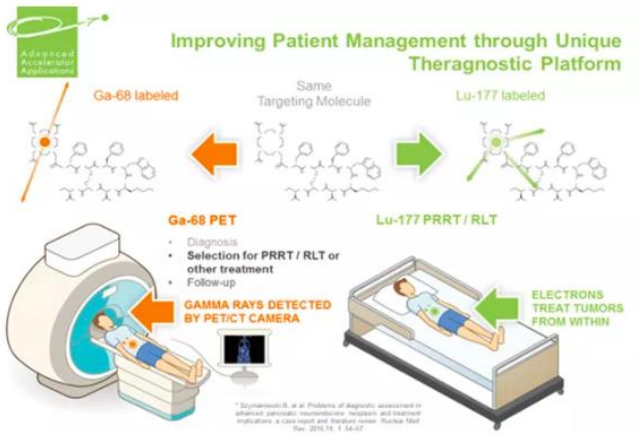


^{177}Lu-DOTATATE

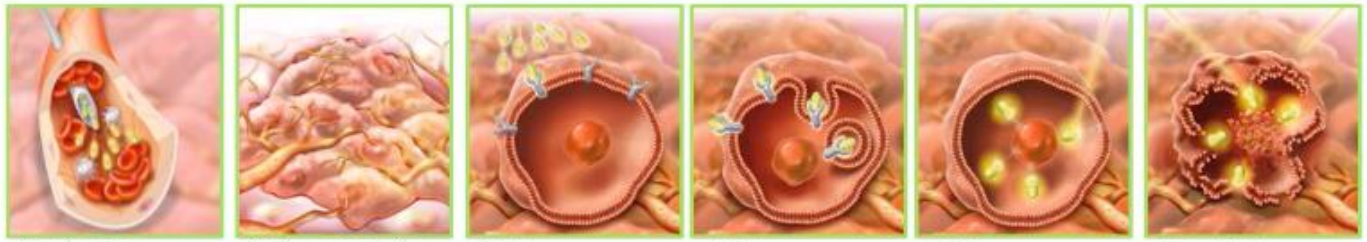
^{18}F-FDG



^{177}Lu-DOTATATE



Target	^{176}Lu
Decay product of ^{177}Lu	^{177}Hf
t½ [days]	6.71
nmoles per GBq ^{177}Lu pmoles per 37 MBq ^{177}Lu	1.39 51.3
Ci ^{177}Lu per mg GBq per mg ^{177}Lu	110 4070
Maximal achievable SA of ^{177}Lu-DOTA-peptide [GBq.nmol^{-1}]	
in Theory	0.72[a]
in Practice	0.12[b], 0.42[c] 0.5[d]



1.Injection

2.Concentration into neuroendocrine tumor (NETs) sites

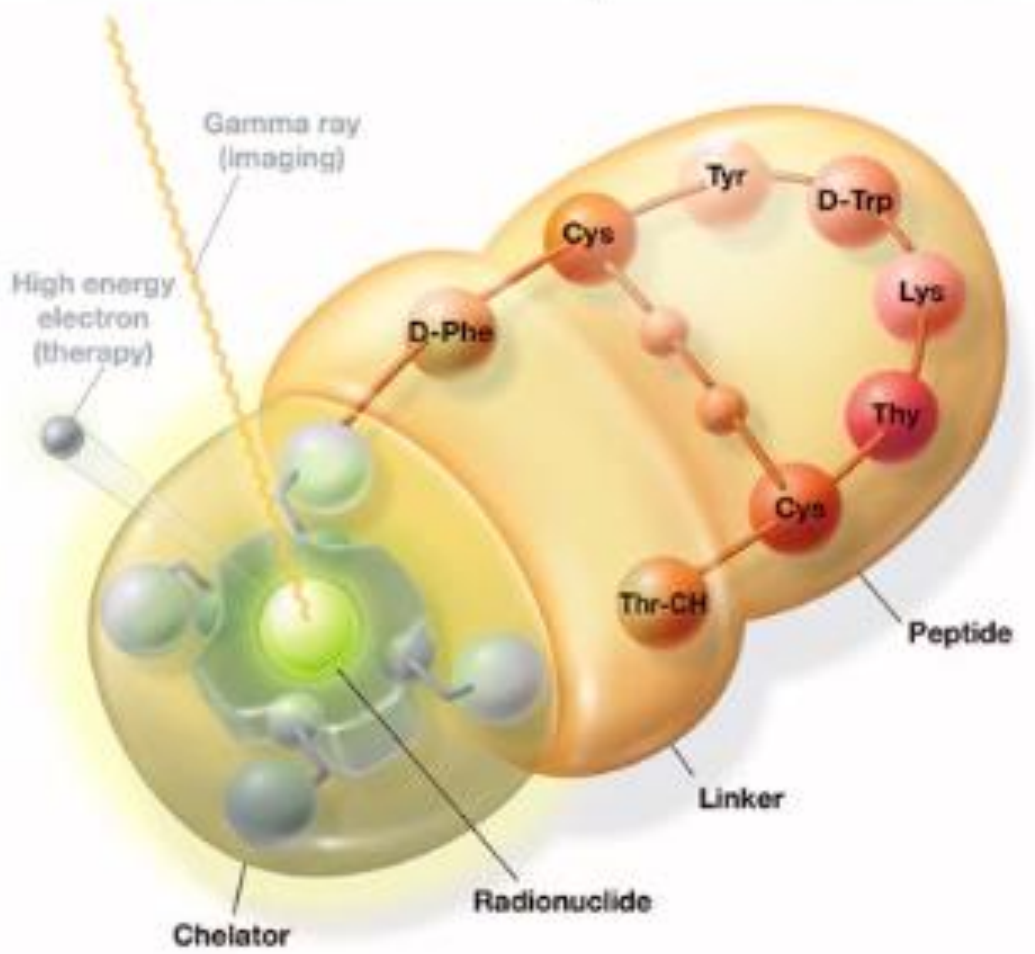
3.The radiopeptide binds to somatostatin receptors type 2 (sstr2) overexpressed by NETs

4.The radiopeptide is internalized in the NET cell

5.The radiopeptide delivers radiation within the cancer cell

6.Radiation induces DNA strands break causing tumor cell death

Structure of a radiopharmaceutical[2]

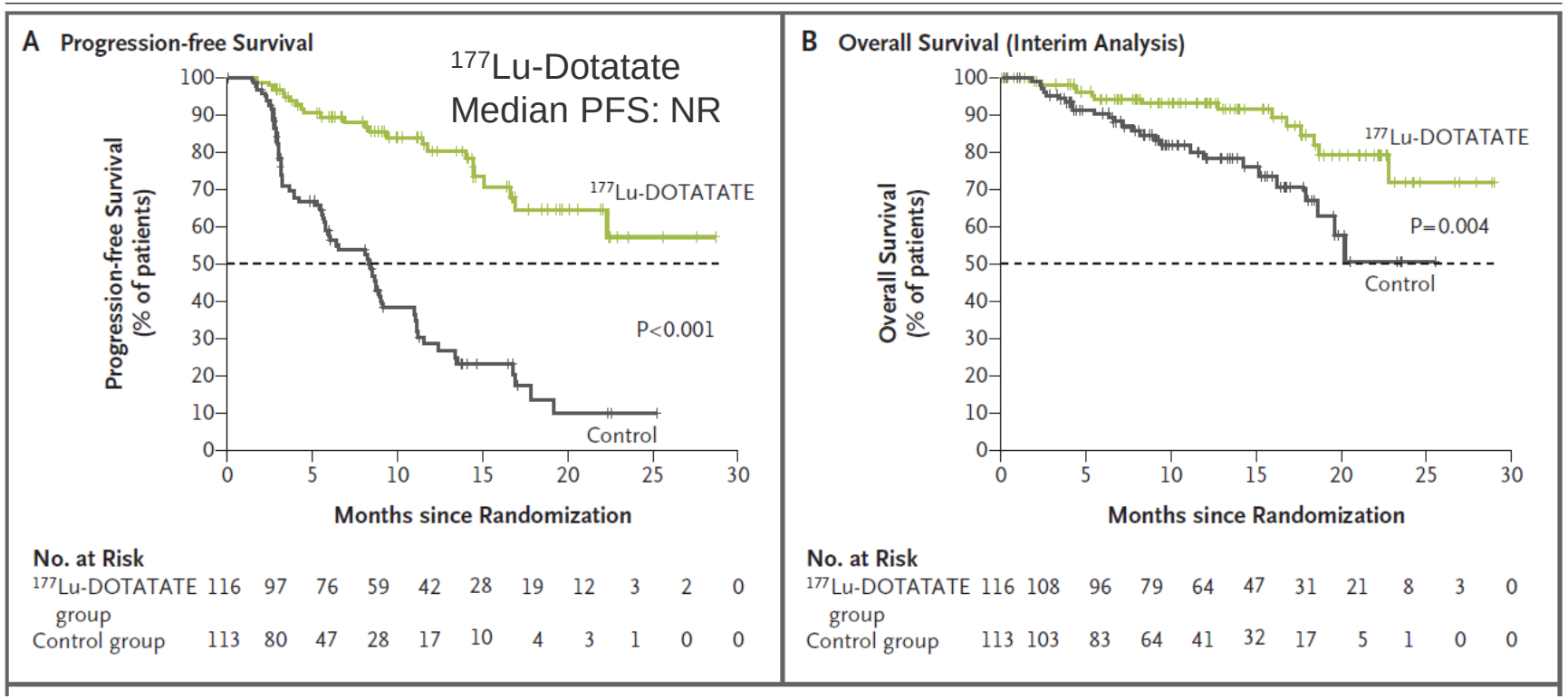


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Phase 3 Trial of ^{177}Lu-Dotatate for Midgut Neuroendocrine Tumors

Median Follow up: 14 mesi

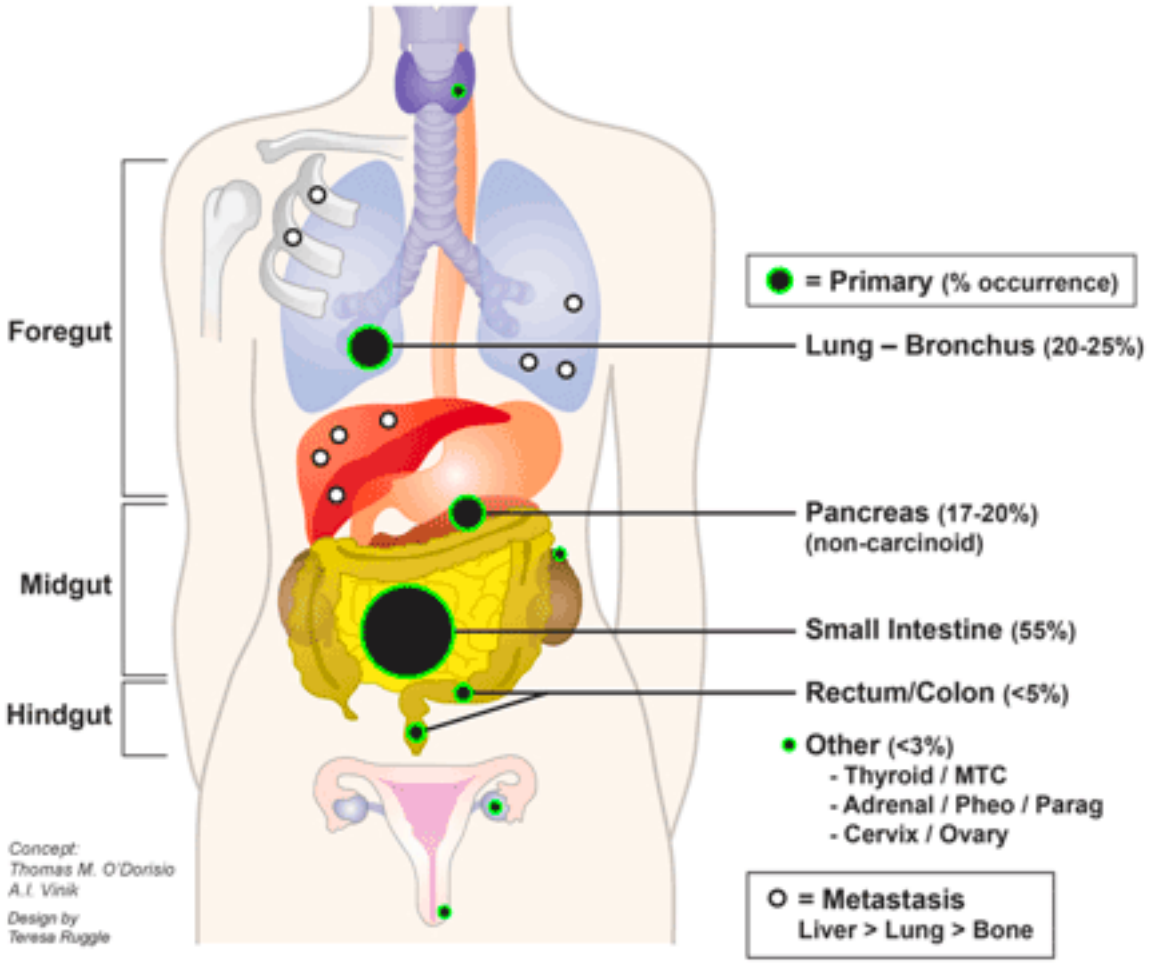


Strosberg et al 2017

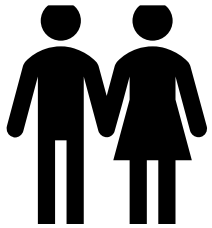
PRECISION MEDICINE

1. PRECISION DIAGNOSTIC:
   - TRACER

2. PRECISION THERAPY:
   - ^{177}Lu-DOTATATE
   - Others

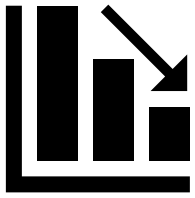


PRECISION IN NUCLEAR MEDICINE



PATIENT SELECTION

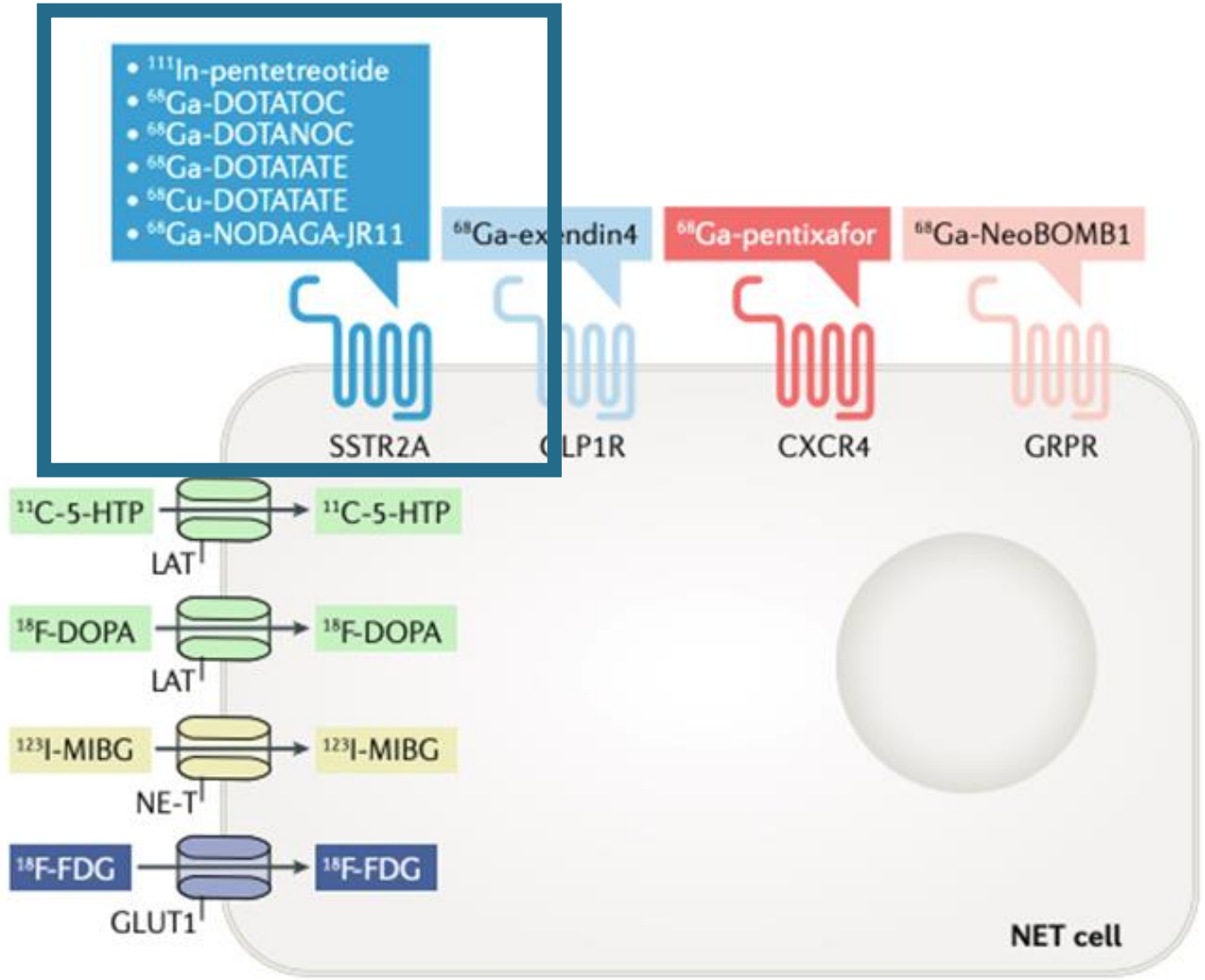
PRECISION THERAPY



RESPONSE EVALUATION CRITERIA

Molecular imaging

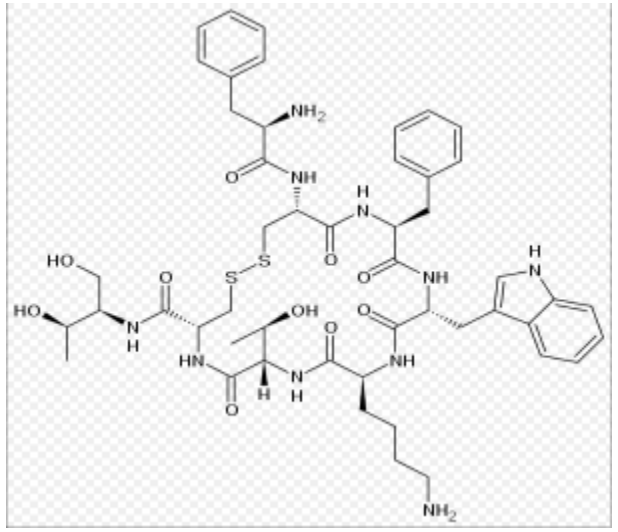
Define the target



Hofland et al 2008

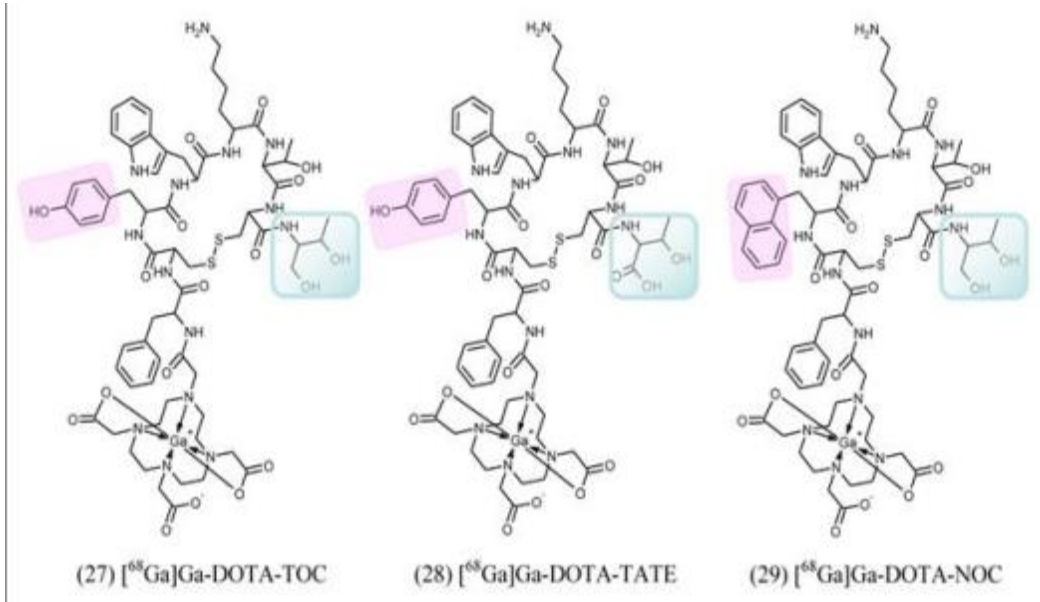
TARGET: SST-R

Octreoscan



111In DTPA octreotide

PET

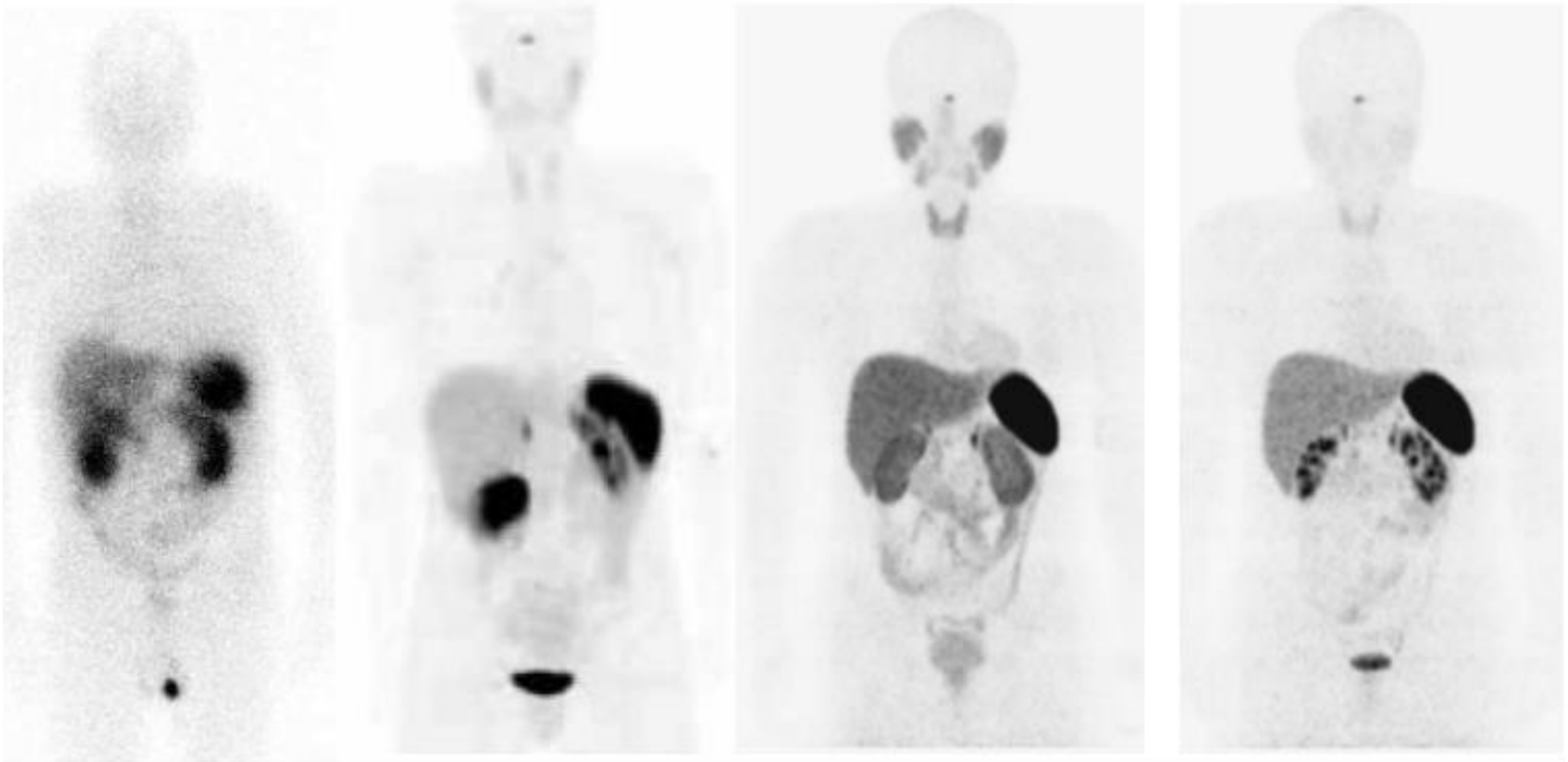


Dotatoc 68Ga DOTA(0)-Phe(1)-Tyr(3)-octreotide
Dotanoc 68Ga DOTA(0)-Phe(1)-NaI(3)-Octreotide
Dotatate 68Ga DOTA(0)-Phe(1)-Tyr3-octreotate

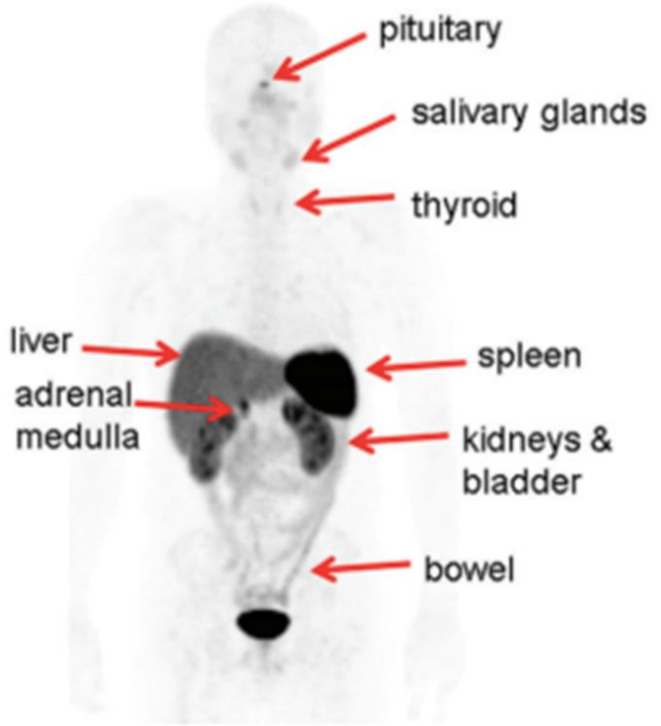
68 Ga DOTA WHAT?

BIODISTRIBUTION

Scintigraphy | PET | PET | PET

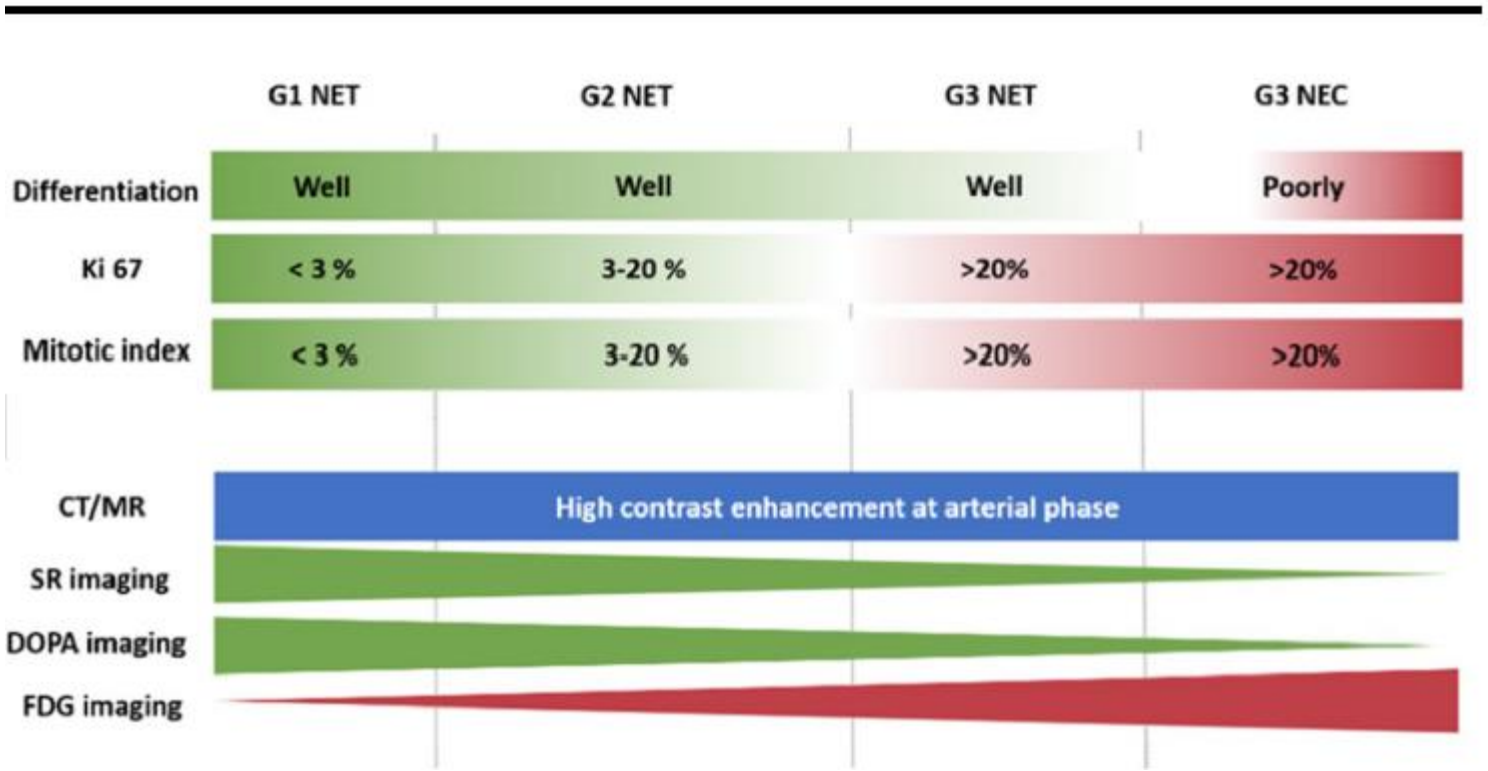


Octreoscan | Dotatoc | Dotatate | Dotanoc



POTENTIAL FALSE POSITIVE
Physiologic activity in the **pancreatic uncinate process**
Inflammation: reactive nodes, prostatitis, post radiotherapy change
Osteoblastic activity: degenerative bone disease, fracture or vertebral hemangioma
Benign **meningioma**
Epiphyseal growth plates
Intra-pancreatic accessory spleen

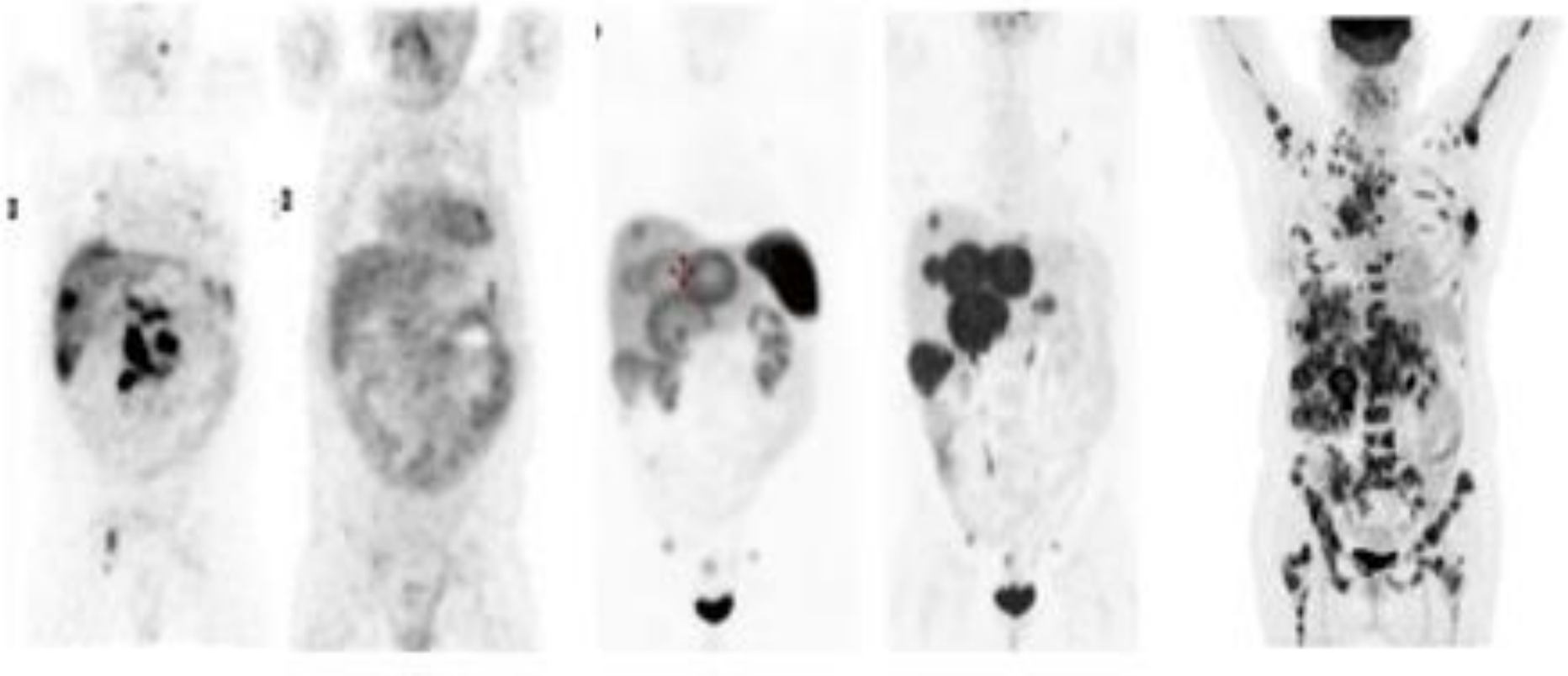
Molecular Imaging is strictly dependent on Differentiation grade and Proliferation Index



Rozenblum et al 2019

DUAL TRACER CONCEPT

NEN G1	NEN G2	NEN G3
❖ PET/CT with **^{68}Ga-DOTA-peptides**	❖ PET/CT with **^{68}Ga-DOTA-peptides**; ❖ PET/CT with **^{18}F-FDG** if ki67 is high and imaging with ^{68}Ga-DOTA-peptides is negative.	❖ PET/CT with **^{18}F-FDG**



G1
^{68}Ga-DOTA-peptide ^{8}F-FDG

G2
^{68}Ga-DOTA-peptides ^{8}F-FDG

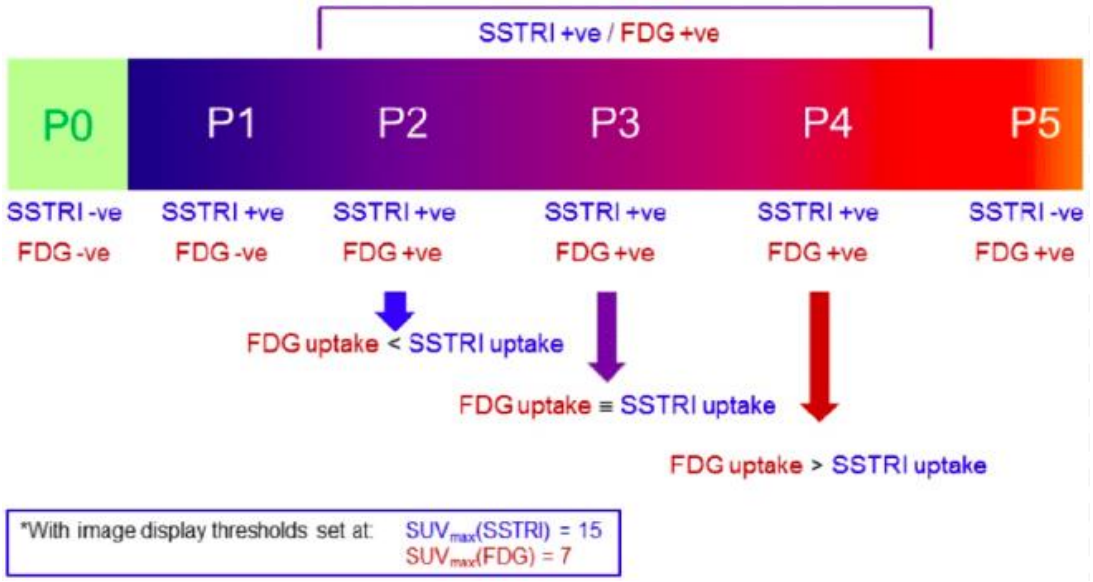
G3
^{18}F-FDG

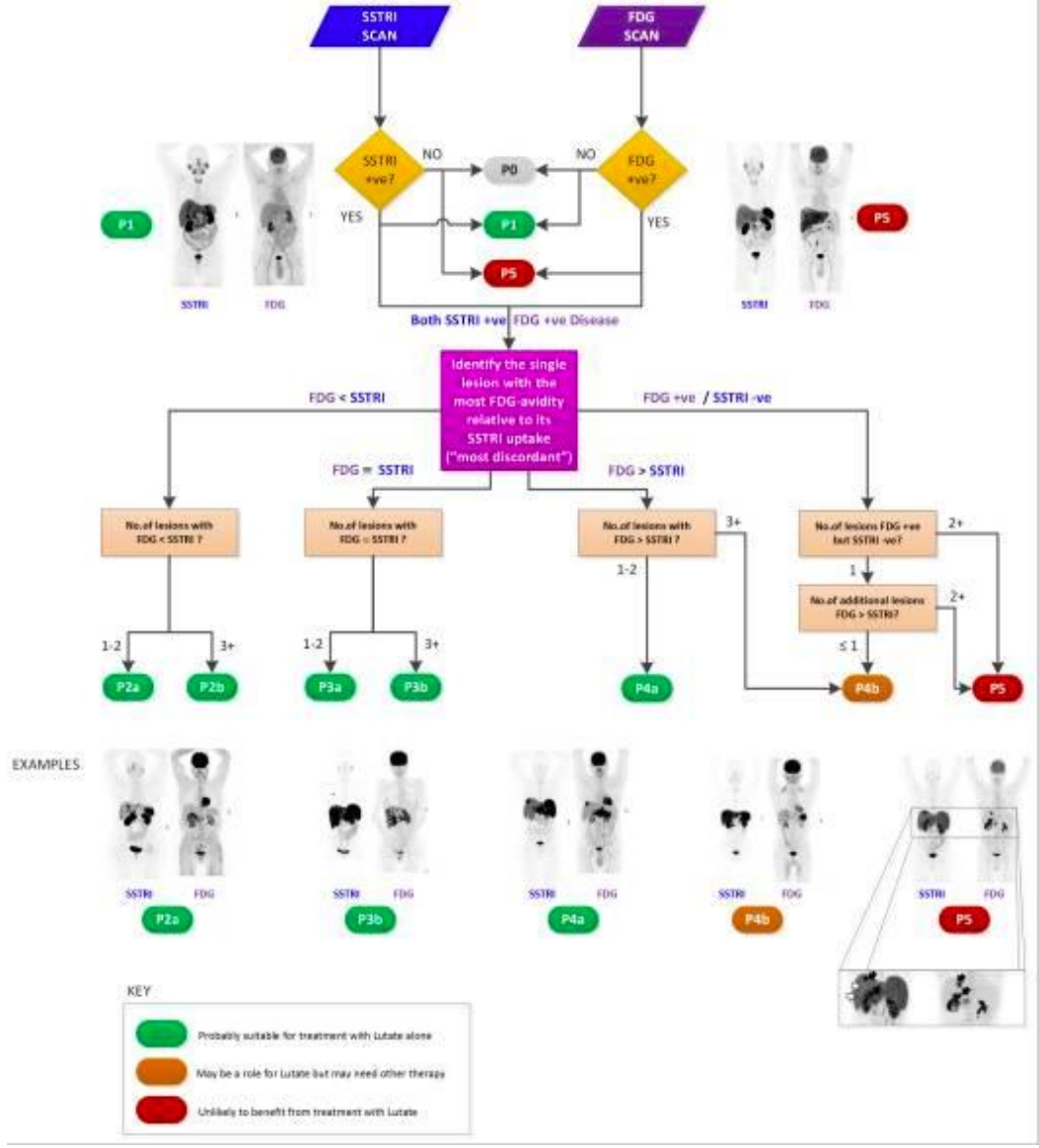
NET PET score

Theranostics. 2017 Mar 1;7(5):1149-1158. doi: 10.7150/thno.18068. eCollection 2017.

Dual Somatostatin Receptor/FDG PET/CT Imaging in Metastatic Neuroendocrine Tumours: Proposal for a Novel Grading Scheme with Prognostic Significance.

Chan DL[1], Pavlakis N[1], Schembri GP[1], Bernard EJ[1], Hsiao E[1], Hayes A[1], Barnes T[1], Diakos C[1], Khasraw M[1], Samra J[1], Eslick E[1], Roach PJ[1], Engel A[1], Clarke SJ[1], Bailey DL[1].

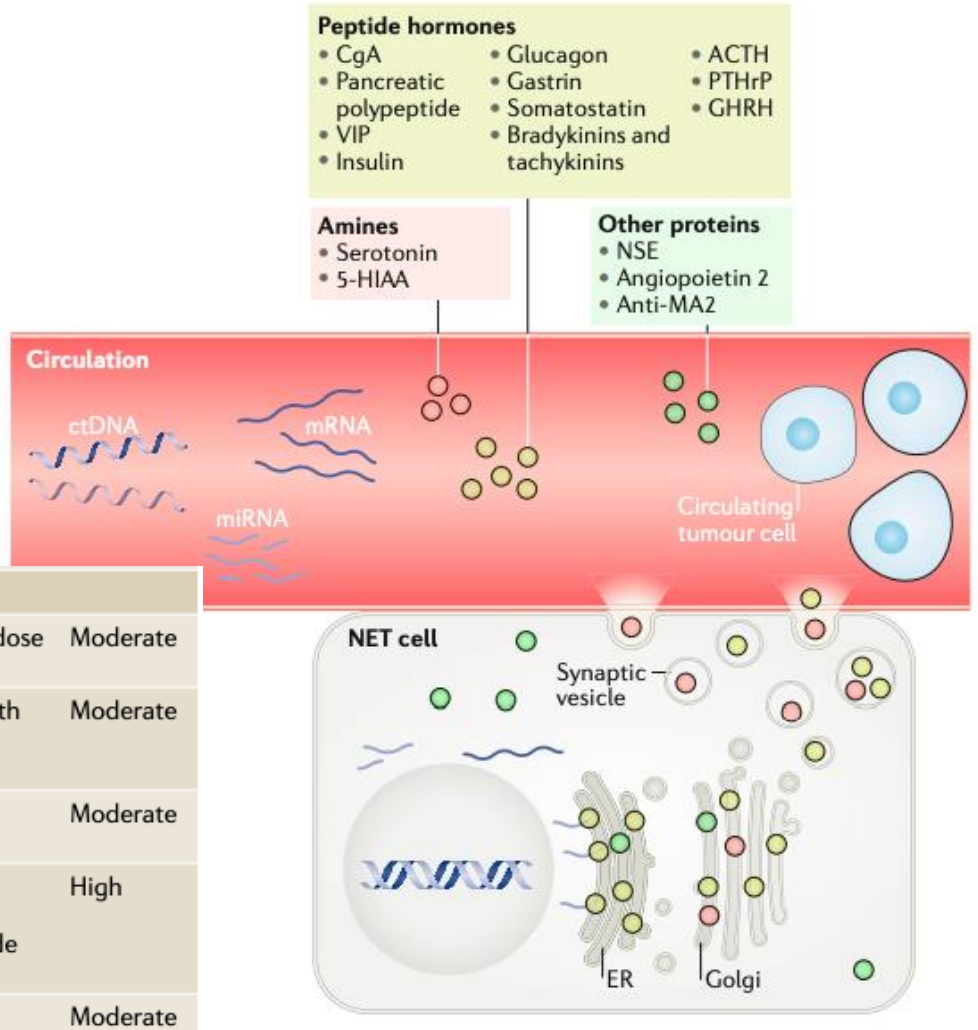




Role of biomarker tests for diagnosis of neuroendocrine tumours

Johannes Hofland, Wouter T. Zandee and Wouter W. de Herder*

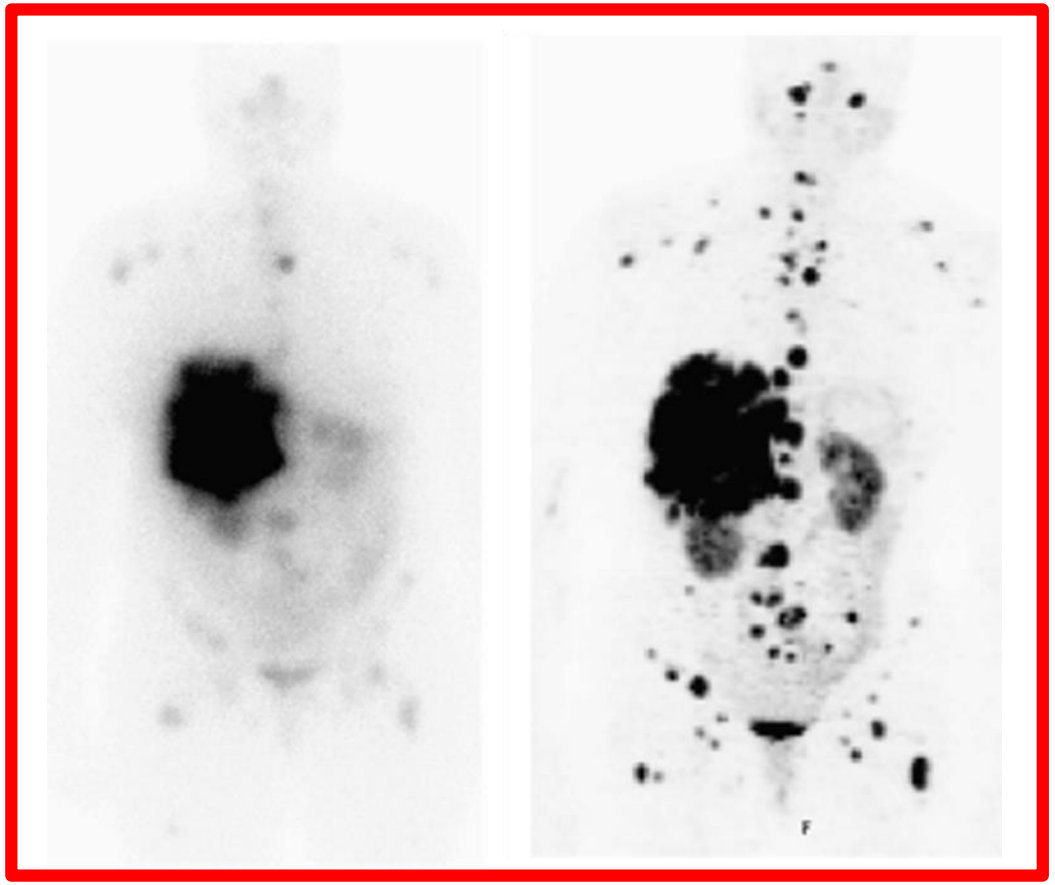
NATURE REVIEWS | ENDOCRINOLOGY



Imaging			
CT	Anatomical imaging using X-ray	Excellent availability and low cost. Limited by high radiation dose and use of nephrotoxic intravenous contrast agents	Moderate
MRI	Anatomical imaging using MRI	Good availability and intermediate costs. Limited by the length of scanning time and by the fact that patients with metal implants or severe claustrophobia are ineligible	Moderate
^{111}In-SRS	SPECT imaging of somatostatin receptor by γ-emitting radionuclide	Inferior metrics compared with those of ^{68}Ga-SRS	Moderate
^{68}Ga-SRS	PET imaging of somatostatin receptor by positron-emitting radionuclide	Extensively studied and with excellent metrics. Current gold standard for functional imaging in gastroenteropancreatic NETs. Is becoming more widely available. False positives include inflammation, lymphoma, renal cell cancer and meningioma	High
^{18}F-FDG	PET imaging of glucose metabolism by positron-emitting radionuclide	Low sensitivity in well-differentiated gastroenteropancreatic NETs. High costs	Moderate
Amine uptake	SPECT or PET imaging using amine transporters	Limited availability (^{18}F-DOPA and ^{11}C-5-HTP) and sensitivity (^{123}I-MIBG). Possible role in somatostatin receptor-negative tumours	Low

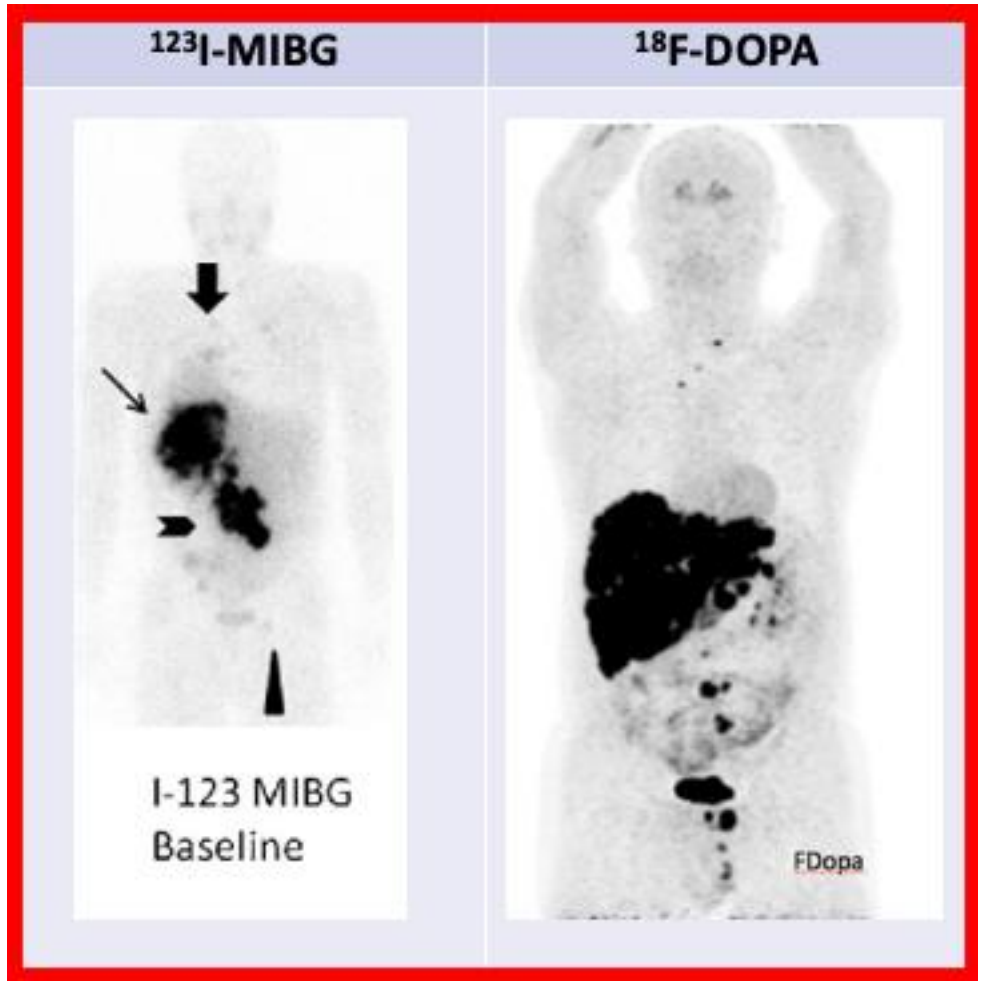
Lancet Oncol 2008; 9: 61–72

Detect the target: hybrid machine

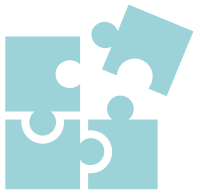


Octreoscan

SSTR PET/CT



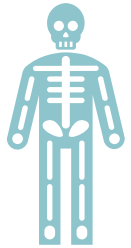
Advantages of PET



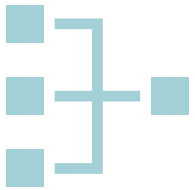
Affinity for SST- R

Image quality and resolution

Reduced time

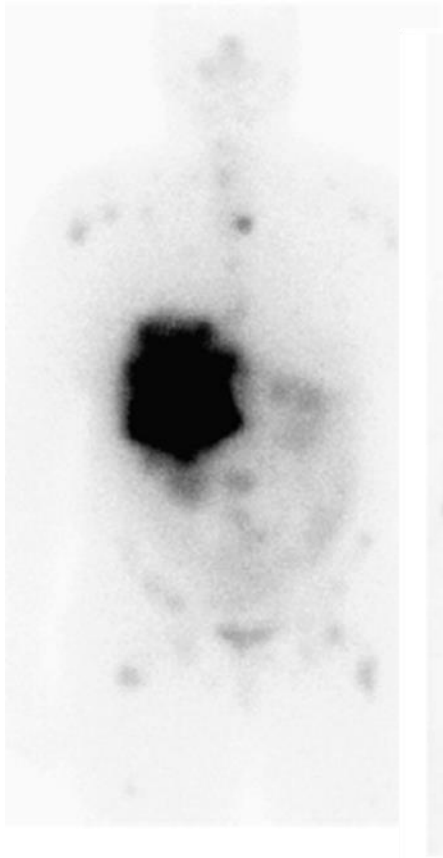


Hybrid machine with CT

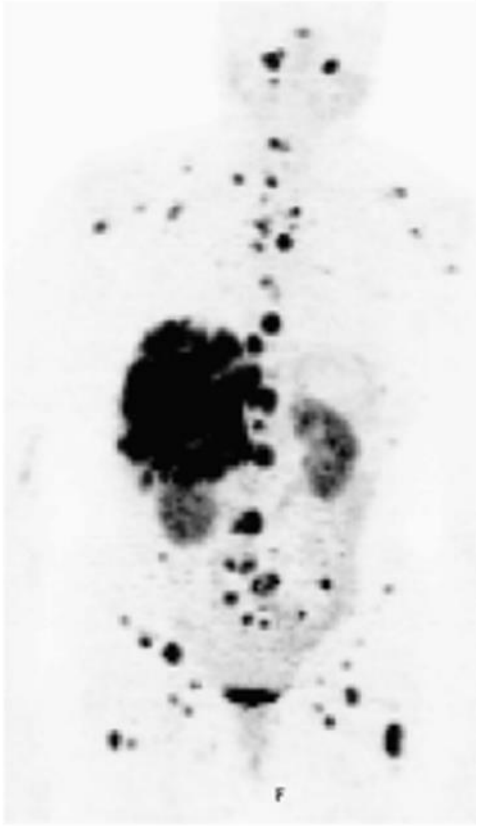


Semiquantitative analysis

IMAGE QUALITY, RESOLUTION and reduced TIME



Octreoscan



SSTR PET/CT

Advantages of SSTR PET/CT over conventional scintigraphy
+ + Sensitivity: < 5 mm lesion characterization
Fully tomographic (3D)
Multi-slice CT
- Uptake time: 45-60 min vs 24-48 hours
- Imaging time: 12-15 min vs 45-60 min
Quantitative
In-house on demand production

(SPECT) obtained after injection of 111In- pentetreotide reveals tumour lesions in over 60–80% of patients vs around 90% for PET.

Hofland et al 2008

^{68}Ga-SSA-peptides

localization, therapy selection, evaluation of response and restaging

RECCOMENDED INDICATIONS FOR ^{68}Ga-SSA-peptides PET/CT SCAN IN NET
Exclude more advanced disease **prior to surgical intervention**
Localize primary tumor in patients with biochemical suspicion of NET
Identify primary tumor in patients **with known metastatic NET**
Confirm diagnosis of NET in patients with anatomic lesions that are suspicious for NET
Identify patients who are likely to benefit from octreotide hormonal therapy or **PRRT** with **^{177}Lu-** or **^{90}Y-DOTATATE**

ENETS Consensus Guidelines for the Standards of Care in Neuroendocrine Tumors: Radiological, Nuclear Medicine and Hybrid Imaging

Detection rate[a]	Tumor type
High >75%	Primary gastroenteropancreatic NETs Gastrinomas Nonfunctioning pancreatic NETs Functioning pancreatic NETs except insulinoma Carcinoids Paragangliomas Small cell lung cancer Meningiomas
Intermediate 40–75%	Insulinomas Medullary thyroid carcinoma Differentiated thyroid carcinoma (including Hürthle cell carcinoma) Pheochromocytoma

The impact of SSTR-directed PET/CT on the management of patients with neuroendocrine tumor: A systematic review and meta-analysis

Martin Barrio[1], Johannes Czernin[1], Stefano Fanti[2], Valentina Ambrosini[2], Ina Binse[3], Lin Du[4], Matthias Eiber[1], Ken Herrmann[1,3], Wolfgang P. Fendler[1,5]

Table 1: Characteristics of Included Trials

Study	Timeline	Radioligand	Number of Patients	Change in management	Change in Management (Any or Surgical only)	Change in intended or implemented management	Response Rates	Data Acquisition (Review or Questionnaire)	Responding Entity	State of Disease (Primary or, Any)	Prior Conventional Imaging**
Frilling et al. 2010[28]	Retrospective	^{68}Ga-DOTATOC	52	31 (60%)	Any	Implemented	100%	Review	Independent expert commission	Any	Yes
Ambrosini et al. 2010[29]	Retrospective	^{68}Ga-DOTANOC	90	32 (36%)	Any	Implemented	N/A	Questionnaire	Referring physician	Any	Yes
Ruf et al. 2010[30]	Retrospective	^{68}Ga-DOTATOC	64	24 (38%)	Any	Implemented	97%	Review	Independent expert commission	Any	Yes
Srirajaskanthan et al. 2010[21]	Retrospective	^{68}Ga-DOTATATE	51	36 (71%)	Any	Implemented	16%	Review	Independent expert commission	Any	Yes
Naswa et al. 2011[23]	Prospective	^{68}Ga-DOTANOC	109	21 (19%)	Any	Implemented	100%	Review	Referring physician	Any	Yes
Krausz et al. 2011[12]	Prospective	^{68}Ga-DOTANOC	19	3 (16%)	Any	Intended	100%	Review	Referring physician	Any	Yes
Froeling et al. 2012[32]	Retrospective	^{68}Ga-DOTATOC	21	10 (48%)	Any	Implemented	N/A	Review	Referring physician	Any	No
Hofman et al. 2012[33]	Retrospective	^{68}Ga-DOTATATE	59	34 (58%)	Any	Implemented	N/A	Review	Independent expert commission	Any	Yes
Has Simsek et al. 2014[34]	Prospective	^{68}Ga-DOTATATE	27	16 (59%)	Any	Intended	100%	Review	Independent expert commission	Any	Yes
Herrmann et al. 2015[31]	Prospective	^{68}Ga-DOTATATE	88	53 (60%)	Any	Intended	88%	Questionnaire	Referring physician	Any	Yes
Ilhan et al. 2015[35]	Retrospective	^{68}Ga-DOTATATE	44	9 (20%)	Surgical Only	Implemented	N/A	Review	Independent expert commission	Primary	No
Sadowski et al. 2015[20]	Prospective	^{68}Ga-DOTATATE	130	43 (33%)	Any	Intended	100%	Review	Referring physician	Any	Yes
Skoura et al. 2016[19]*	Retrospective	^{68}Ga-DOTATATE	1,258*	515* (41%)	Any	Implemented	N/A	Review	Independent expert commission	Any	Unknown
Deppen et al. 2016[22]	Retrospective	^{68}Ga-DOTATATE	78	28 (36%)	Any	Intended	80%	Review	Independent expert commission	Any	Yes

*This study recorded the total number of scans and was analyzed on a "per scan" basis; the number of patients in their study was 728
**Conventional imaging includes bone scan, ultrasound, magnetic resonance imaging, CT, Octreoscan, and ^{18}F-FDG PET/CT

PET/CT findings resulted in managment changes in 44% of the patients

IMPACT OF ^{68}Ga DOTATOC PET/CT IN THE THERAPEUTIC MANAGEMENT OF NEUROENDOCRINE TUMORS

E. Pilati[1], M. Finessi[1], R. Passera[1], V. Liberini[1], C.G. De Angelis[2], E. Arvat[3], A. Piovesan[3], M. Gallo[3], L. Ciuffreda[4], N. Birocco[4], M. P. Brizzi[5], D. Campra[6], G. Giraudo[7], M. Bellò[1], G. Bisi[1], D. Deandreis[1]

^{68}Ga DOTATOC PET/CT finding shifted the therapeutic management in 39/103 pts (p = 0.024) *[Table 2]*: 30.8% of them were sent to **locoregional therapies, 46.2%** to **systemic therapies, 10.3%** to **PRRT** and **12.8%** to **locoregional plus systemic treatment**. [*Table 3*]

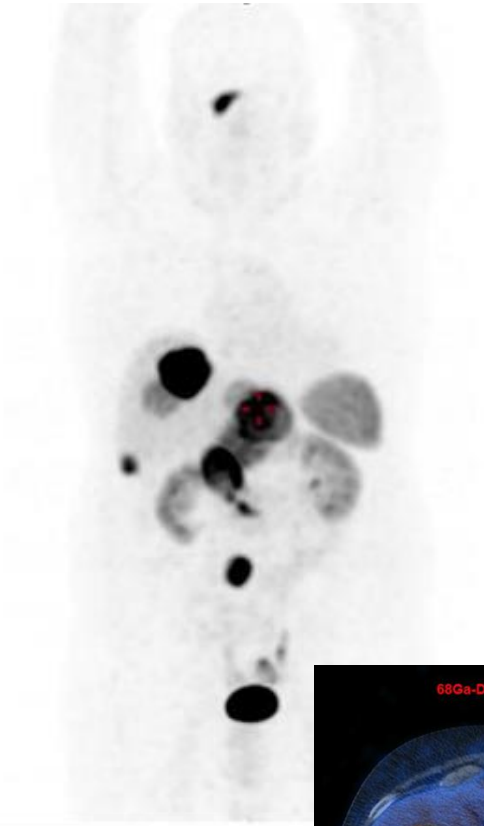
		SHIFT THERAPY		
		No	**Yes**	***Total***
^{68}Ga DOTATOC PET/CT	**Negative**	24 (80%)	**6 (20%)**	**30 (100%)**
	Positive	40 (54.8%)	**33 (45.2%)**	**73 (100%)**
	Total	64 (62.1%)	**39 (37.9%)**	**103 (100%)**

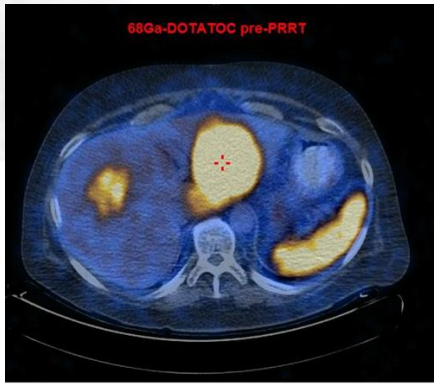
Table 2: ^{68}Ga DOTATOC PET/CT results and change management.

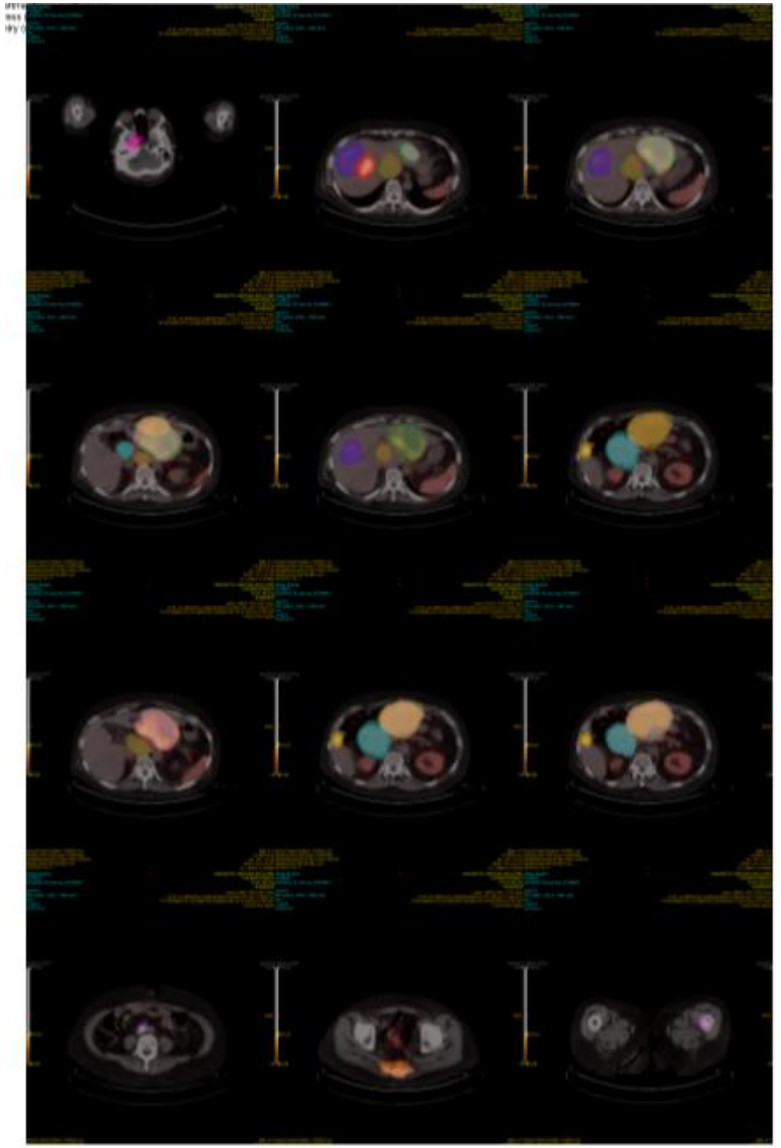
		N° PATIENTS
NEW THERAPY	**Locoregional therapy (Surgery/locoregional treatment)**	**12** (30.8%)
	Systemic therapy (chemotherapy/introduction or ↑ SStA)	**18** (46.2%)
	PRRT	**4** (10.3%)
	Locoregional + systemic treatment	**5** (12.8%)
	Total	**39/103 (37.9%)**

Table 3: Change management.

Quantify the target : SEMI QUANTITATIVE EVALUATION







- Metabolic data:
SUVmax
SUVmean
SUL peak

-Volume data:
FV
SRETV

-Integrated data:
TLSRE

68-Ga-DOTA-PET : Predictive value

Patient Selection for Personalized Peptide Receptor Radionuclide Therapy Using Ga-68 Somatostatin Receptor PET/CT

Harshad R. Kulkarni, MD*, Richard P. Baum, MD, PhD

Indications/Prerequisites for PRRT

- Well-differentiated NETs (G1 and G2)
- SSTR expression
- Documented progression of disease with metastasis (in certain cases with high tumor burden without progression might also be considered)
- Inoperability (however, also in neoadjuvant setting, to render an inoperable primary tumor operable)
- For symptomatic improvement in functional NET refractory to octreotide or lanreotide therapy
- Karnofsky index ≥60%
- Normal renal function and hematological status

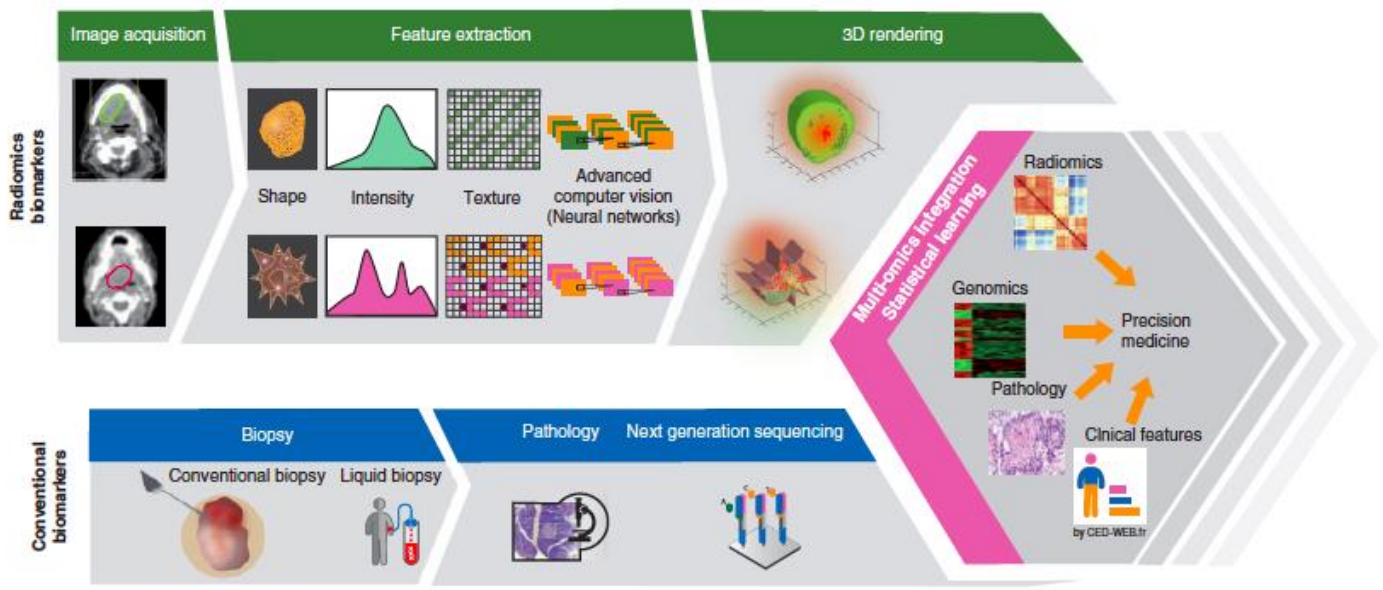
Table 2
Factors determining the Bad Berka Score for patient selection

Factor	Means of Determination
Tumor grade	Ki-67 index
Functional activity of the tumor/metastases	Biomarkers, symptoms
Time since first diagnosis and previous therapies	History
General status of the patient	Karnofsky performance score or Eastern Cooperative Oncology Group performance status scale, loss of weight
SSTR density	SUV on ^{68}Ga-receptor PET/CT
Glucose metabolism	^{18}F-FDG PET/CT
Renal functional assessment	Creatinine and blood urea nitrogen
Tubular extraction rate and elimination kinetics	^{99m}Tc-MAG3 scintigraphy
Glomerular filtration rate	^{99m}Tc-DTPA
Hematological status	Blood counts
Hepatic involvement and extrahepatic tumor burden	^{68}Ga-receptor PET/CT
Dynamics of the disease: doubling time, appearance of new lesions	Serial ^{68}Ga-receptor PET/CT

RADIOMICS

- **bioinformatic approaches** (statistical methods and *machine learning*);
- **extrapolates the quantitative variables** of the analyzed imaging (geometry, intensity and texture)
- **identifies the characteristics of the abnormal tissue**.

PURPOSE: associate the **variables** extracted from the imaging with **clinical or biological endpoint** (*whole-body histology, response to therapy, survival, etc.*) → **PERSONALIZED MEDICINE.**



Limkin et al. **Promises and challenges for the implementation of computational medical imaging (radiomics) in oncology.** *Annals of Oncology.* 2017. 28: 1191-1206.

European Journal of Nuclear Medicine and Molecular Imaging (2019) 46:2715–2721
https://doi.org/10.1007/s00259-019-04370-z

REVIEW ARTICLE

What can artificial intelligence teach us about the molecular mechanisms underlying disease?

Gary J. R. Cook[1,2] · Vicky Goh[1,3]

On a simple level, it is recognized that malignant tumours show heterogeneity of molecular and cellular features, including cellular density and proliferation, necrosis, fibrosis, metabolism, hypoxia, angiogenesis and receptor expression, factors that have been independently associated with a poor treatment response and more aggressive tumour behavioR. This variation, defined by histopathological appearance, may in turn reflect the degree of genetic clonal variation. These biological processes can be crudely determined using functional and molecular imaging methods on a global scale, and there is some evidence that **several of these adverse biological features may be reflected in medical images**

Imaging DATA ANALYSIS and INTERPOLATION = DIAGNOSIS

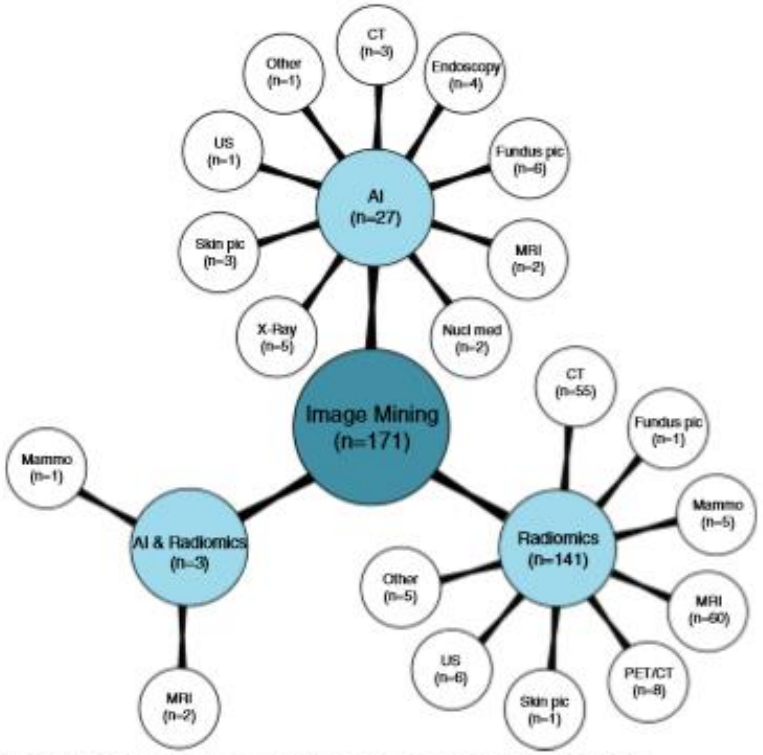


Fig. 8 Radiomics and artificial intelligence literature summary by image mining approach and imaging modality

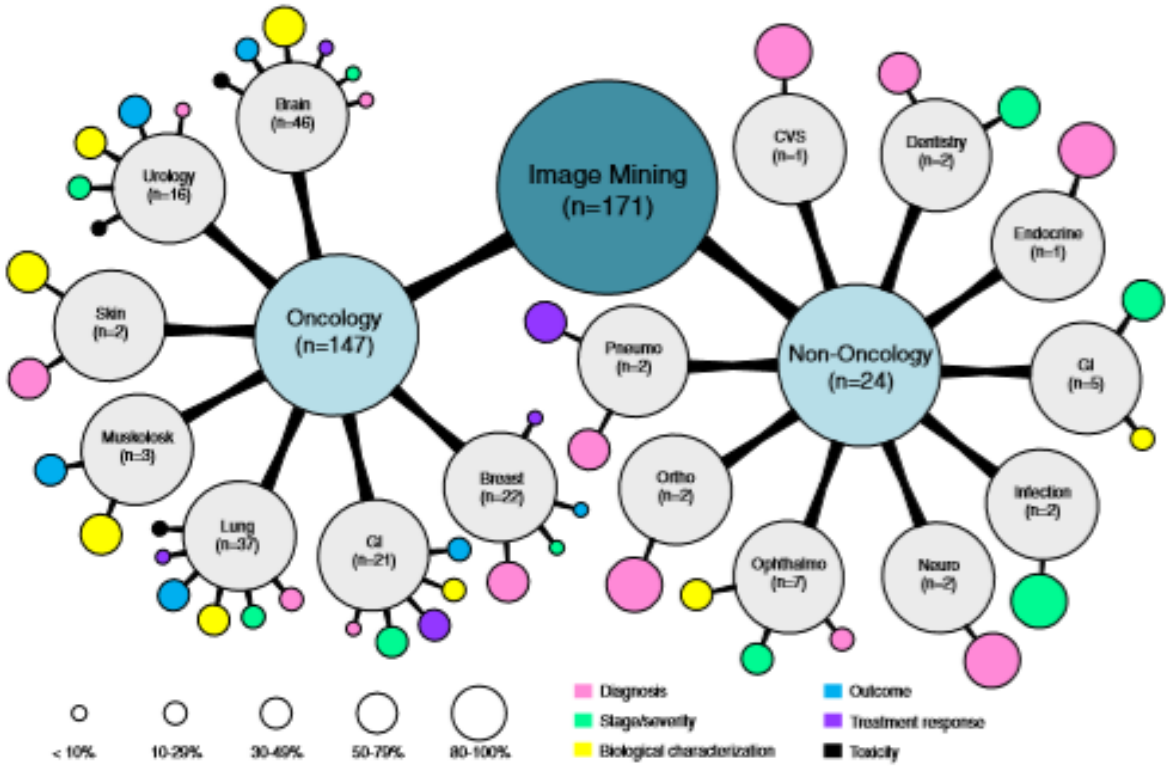


Fig. 7 Radiomics and artificial intelligence literature summary by disease and clinical setting

Sollini et al EJNM 2019

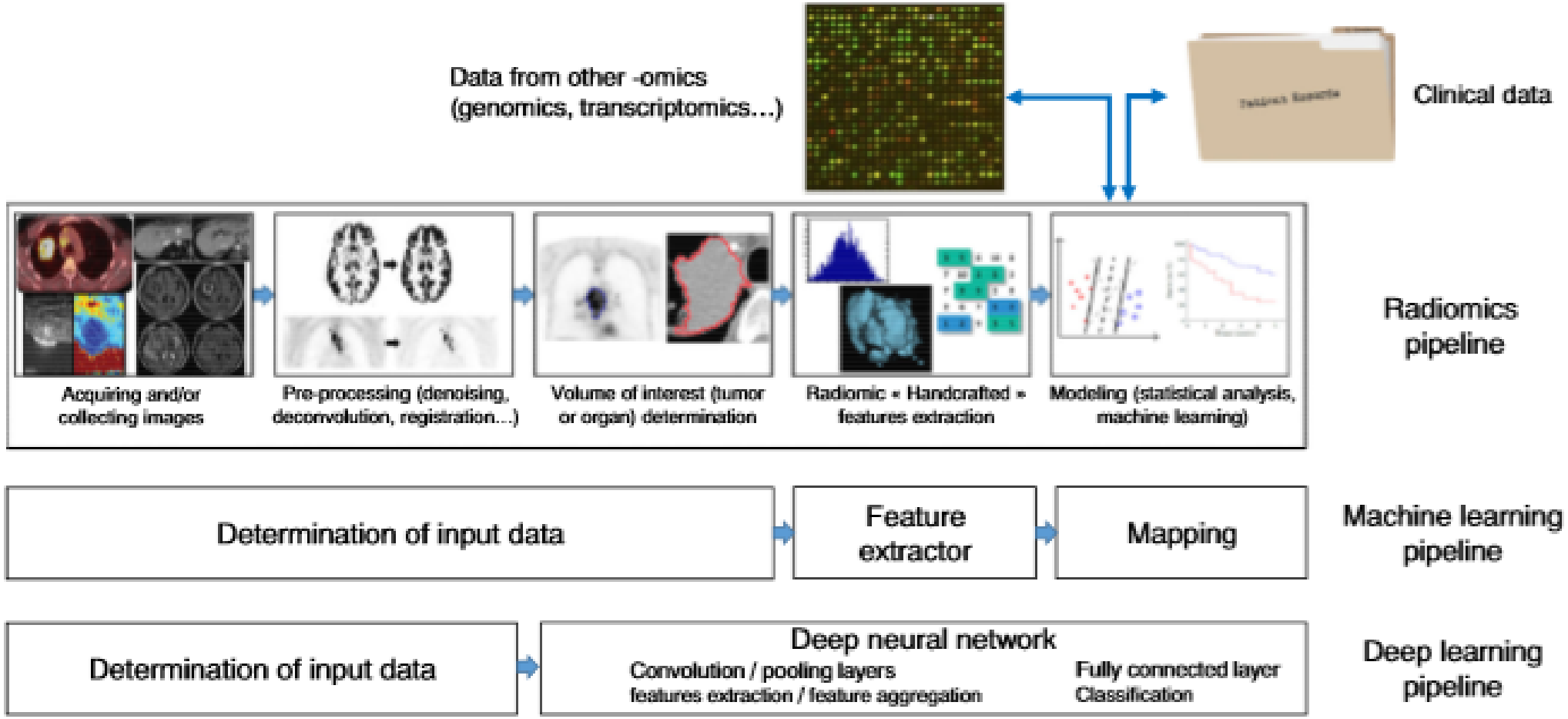


Fig. 1 The radiomics pipeline, in comparison with the usual machine learning workflow, and the deep learning workflow

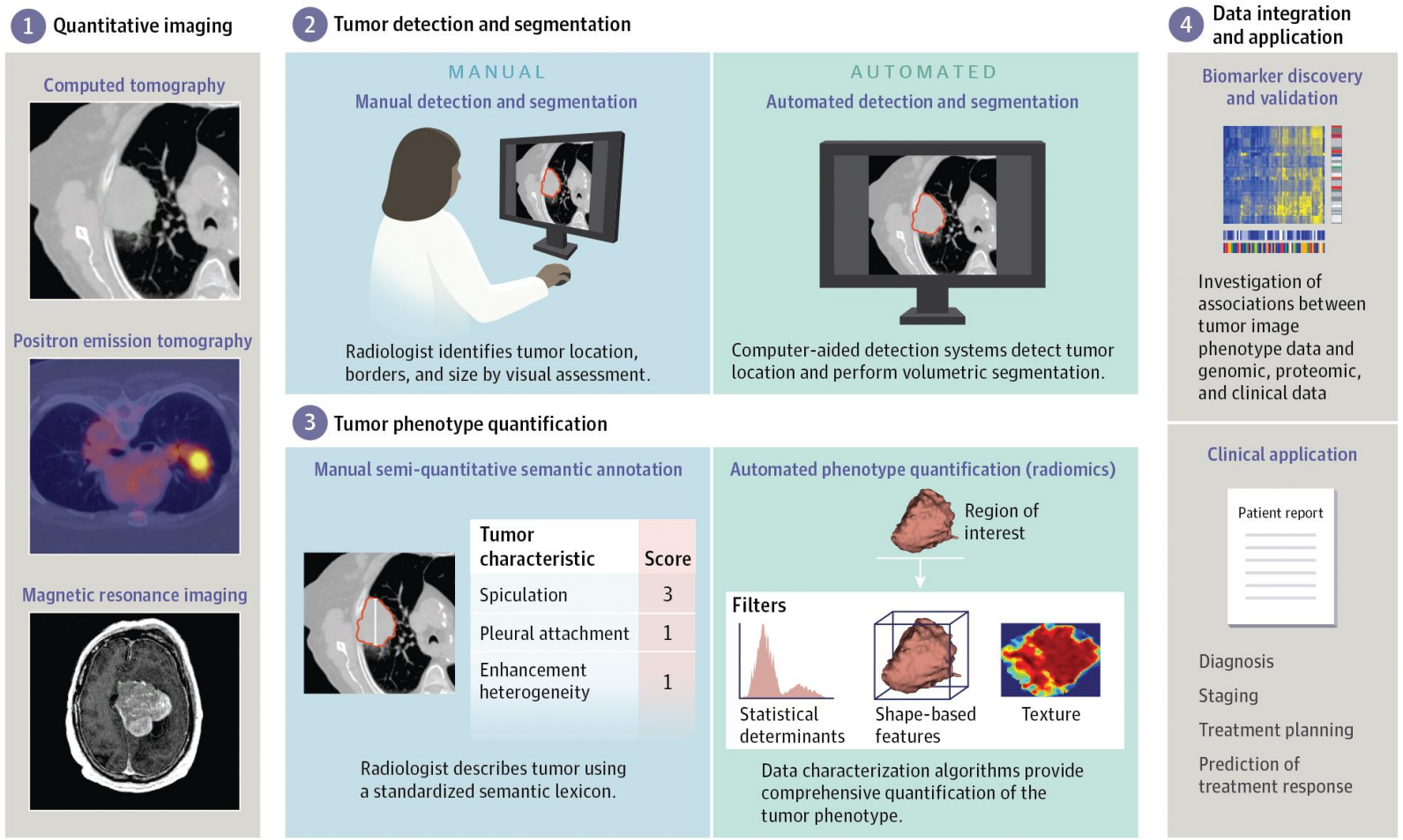
Visvikis et al EJNM 2019

AIM

texture variables
robust
^{68}Ga-DOTATOC PET/CT

DIFFERANTIATE BIOLOGICAL BEHAVIOR OF TUMOR and MTS

PERSONALIZED MEDICINE



CAN TEXTURE ANALYSIS BE USED FOR A VIVO "IMAGING BIOPSY" IN NEUROENDOCRINE TUMORS? A FIRST STEP FEASIBILITY STUDY WITH ^{68}GA-DOTATOC PET/CT

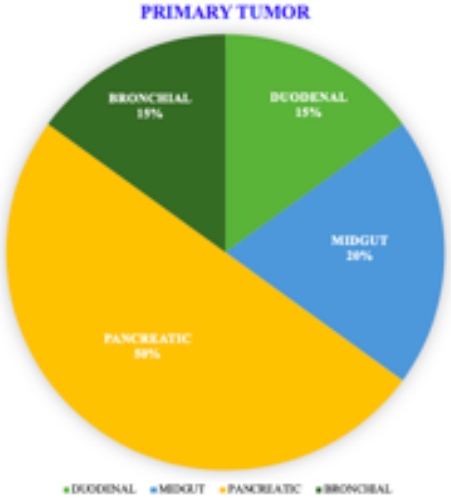
V. Liberini[1], B. De Santi[2], E. Gallio[3], E. Pilati[1], M. Finessi[1], M. Bellò[1], M.G. Papotti[4], F. Maletta[4], M. Volante[5], G. Bisi[1], F. Molinari[2], D. Deandreis[1]

1 Servizio di Medicina Nucleare, AOU Città della Salute e della Scienza, Torino
2 Biolab, Dipartimento di Elettronica e Telecomunicazioni, Politecnico di Torino
3 Servizio di Fisica Sanitaria, AOU Città della Salute e della Scienza, Torino
4 Servizio di Anatomia Patologica, AOU Città della Salute e della Scienza, Torino
5 Servizio di Anatomia Patologica, AOU San Luigi Gonzaga, Orbassano (TO)

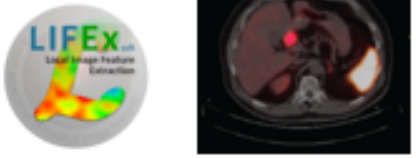
A study evaluating the correlation between the analysis of textural features at ^{68}Ga-DOTATOC PET/CT and the histological grading system in neuroendocrine tumors.

Cohort of 20 patients (treatment-naïve)

3 groups:
- **G1** (15/20): Ki67<3;
- **G2** (4/20): >3Ki67<20;
- **G3** (1/20): Ki67>20.



Lesion **segmentation** and textural features (TF) **extraction**.



Correlation between the analysis of textural features and the histological grading

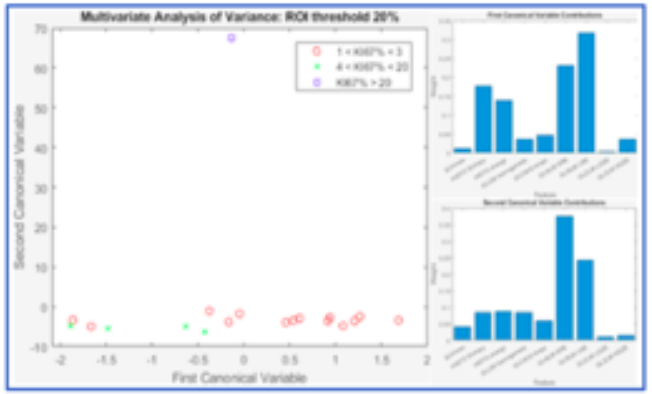
MANOVA

Distinguish the three groups according to the Ki67 index value of the primitive lesion.

CANONICAL CORRELATION ANALYSIS

Identifies the TF with greater discriminating weight (**TF** with more discriminating weight **HISTO Entropy log10**, **HISTO Energy**, **GLRLM SRE** and **GLRLM LRE**).

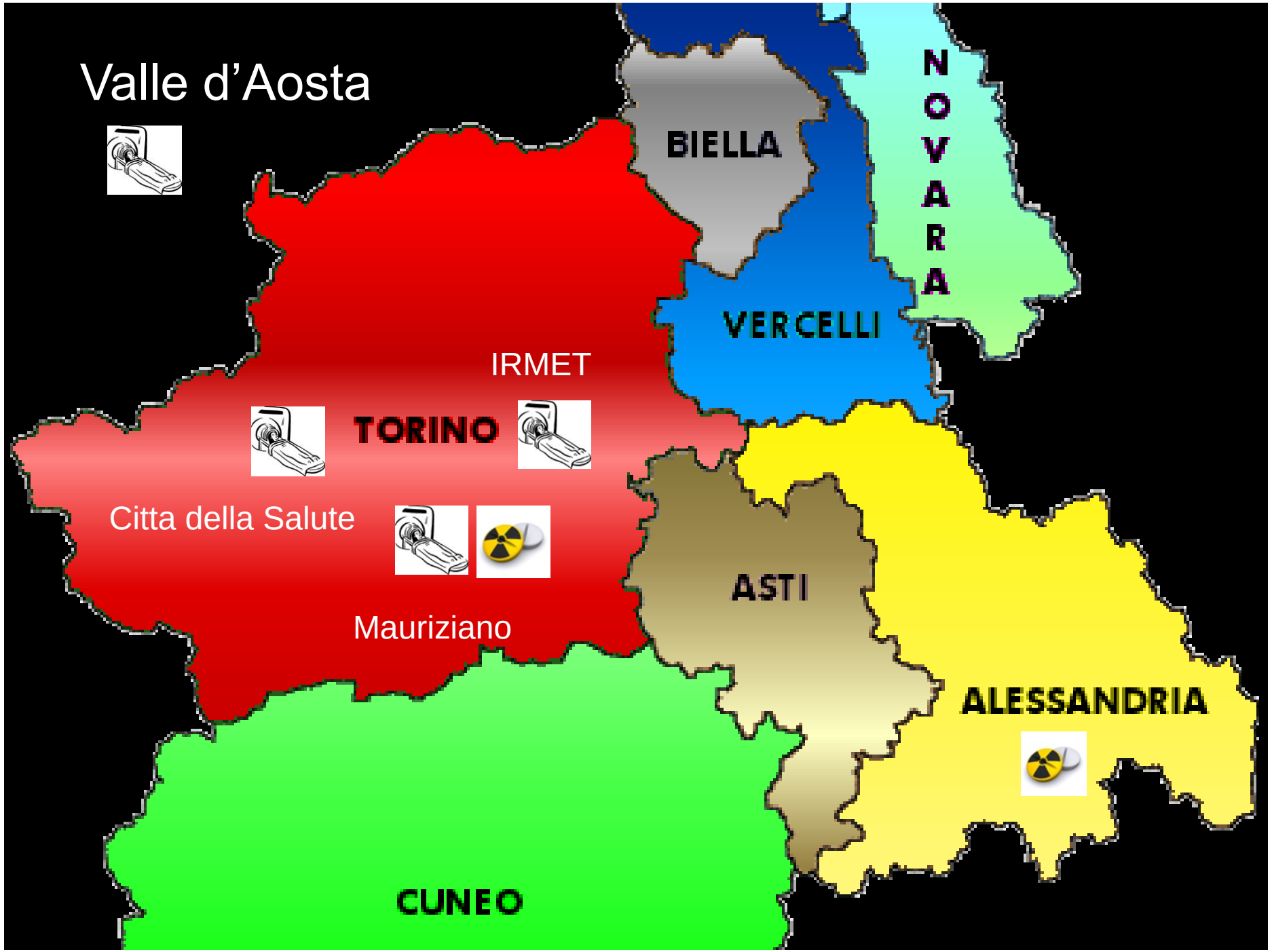
Variabili di Texture	ROI Manuale Media Gruppo 1	ROI Manuale Media Gruppo 2	ROI Manuale Media Gruppo 3	ROI Threshold 20% Media Gruppo 1	ROI Threshold 20% Media Gruppo 2	ROI Threshold 20% Media Gruppo 3
SUVmax	26.107	24.500	4.600	26.073	24.500	4.600
HISTO Entropy log10	1.119	1.190	0.520	1.095	1.148	0.500
HISTO Energy	0.120	0.085	0.340	0.124	0.093	0.340
GLCM Homogeneity	0.366	0.328	0.792	0.329	0.308	0.794
GLCM Entropy log10	1.921	2.105	0.920	1.709	1.993	0.900
GLRLM SRE	0.927	0.948	0.587	0.871	0.953	0.582
GLRLM LRE	1.443	1.235	5.690	1.308	1.193	5.760
GLZLM LGZE	0.047	0.037	0.383	0.035	0.019	0.136
GLZLM HGZE	208.293	160.825	9.700	250.373	209.275	13.200
Wilks' Lambda	0.006	(0.0000)		0.002	(0.0000)	
Pillai's Trace	1.240	(0.0997)		1.294	(0.1039)	
Lawley-Hotelling Trace	125.373	(0.0000)		320.427	(0.0000)	
Roy's Largest Root	125.043	(0.0000)		320.004	(0.0000)	



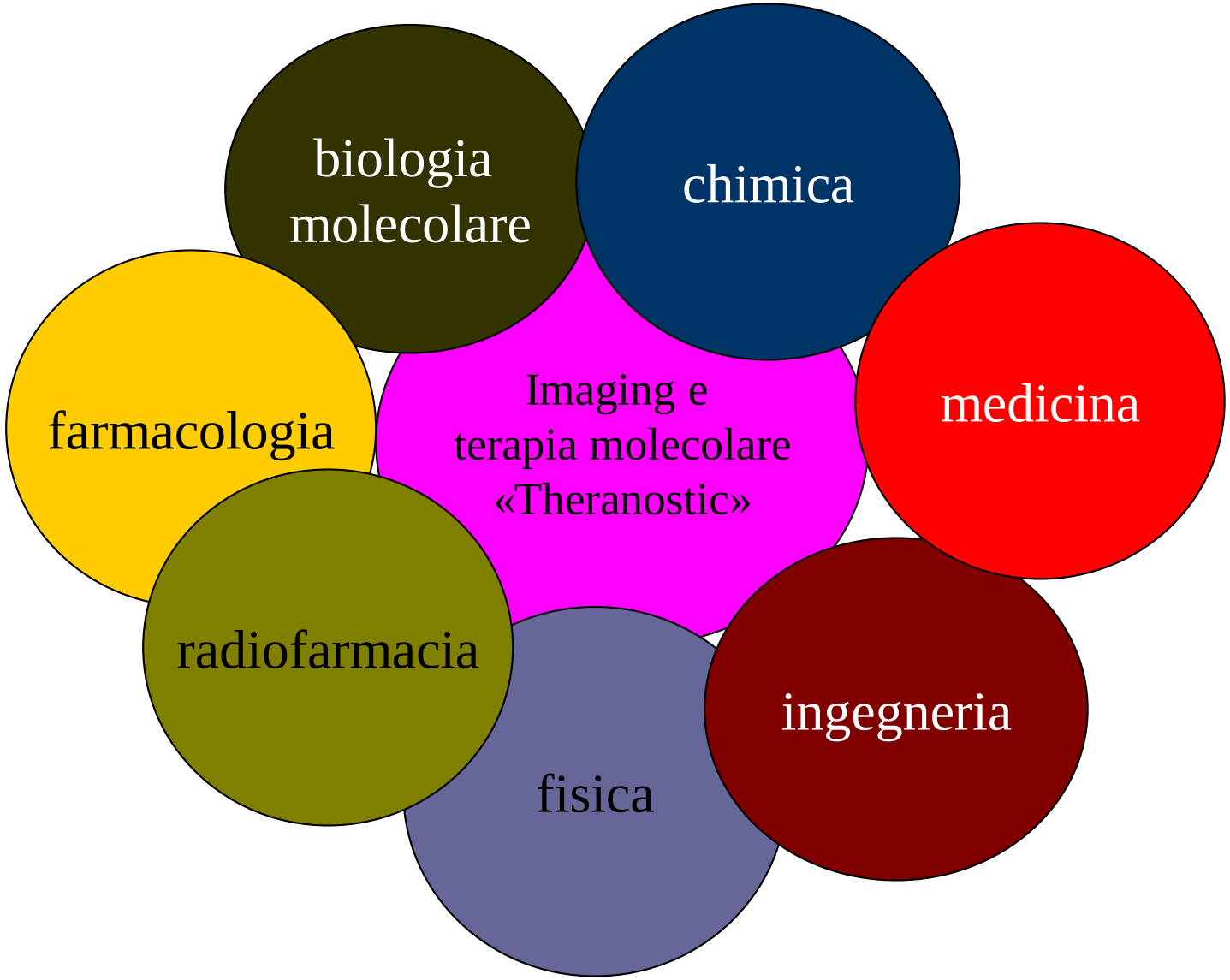
REGRESSION ANALYSIS

A linear correlation between the Ki67 index and texture features was found only for the **HISTO Energy** and the **GLRLM-LRE** features (p-value ≤ 0.05) evaluated by VOIs with threshold of 20%.

Textural features analysis with 68Ga-DOTATOC PET/CT is feasible and could in the future be used to capture the different biological behavior of NET lesions.


Valle d'Aosta
BIELLA
NOVARA
VERCELLI
IRMET
TORINO
Citta della Salute
Mauriziano
ASTI
ALESSANDRIA
CUNEO

Complessità organizzativa



Courtesy of Dr Carlo Poti

PROGETTO THERANET

CLINICAL RESEARCH/PET CENTER
Nuclear Medicine Division
Department of Medical Sciences
University of Turin
Città della Salute e della Scienza Hospital
(Prof. G. Bisi, Prof. D. Deandreis)

PET CENTER
Nuclear Medicine Division
Umberto Parini Hospital, Aosta
Dr Carlo Poti

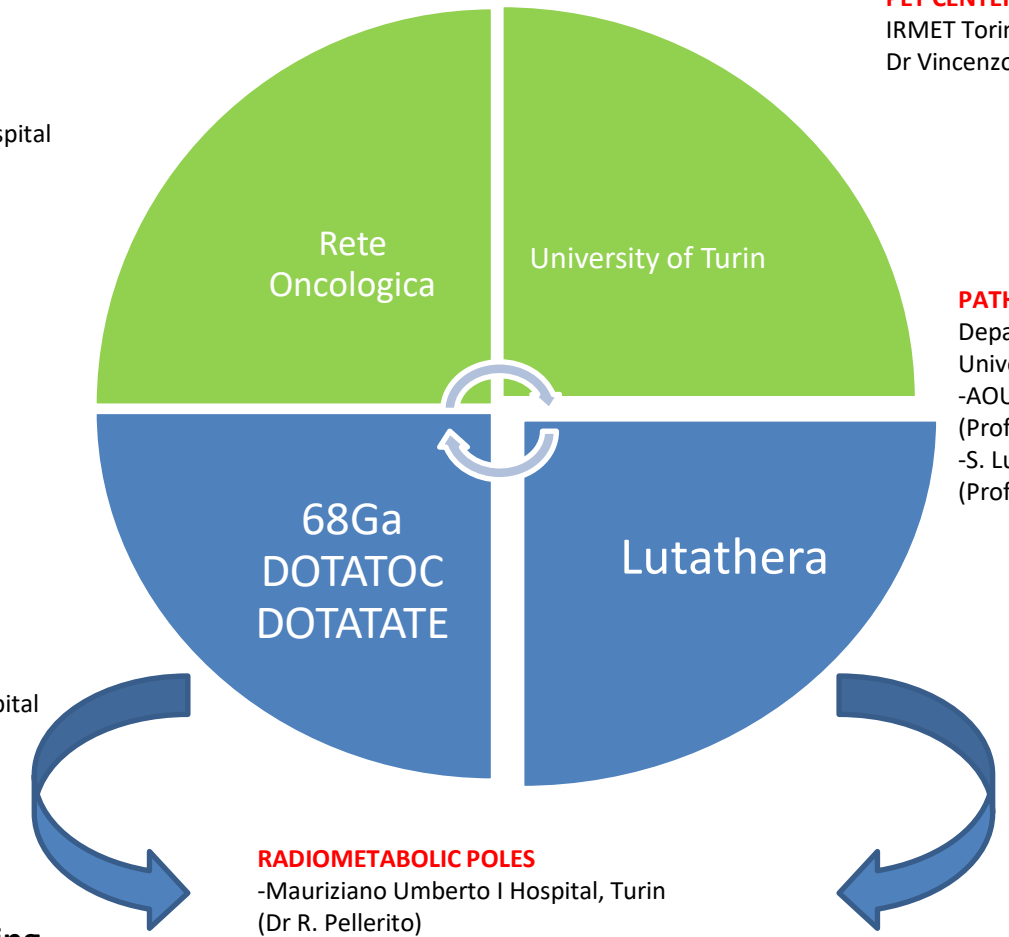
PET CENTER/
IRMET Torino
Dr Vincenzo arena

ENDOCRINE ONCOLOGY
-Department of Medical Sciences
University of Turin
Città della Salute e della Scienza Hospital
(Prof E. Arvat)
-Endocrinology Service
Mauriziano Umberto I Hospital
(D.ssa P. Razzore)

ONCOLOGY
Department of Oncology
University of Turin
- Città della Salute e della Scienza
University of Turin
(Dr. L Ciuffreda, Dr. M. Airoldi)
- S. Luigi Gonzaga Hospital
(D.ssa MP Brizzi)

GASTROENTEROLOGY
Department of Medical Sciences
University of Turin
Città della Salute e della Scienza Hospital
(Prof C. De Angelis)

Endocrino Alessandria
Laura Rossi



PATHOLOGY
Department of Oncology,
University of Turin
-AOU Città della Salute e della Scienza
(Prof. M. Papotti)
-S. Luigi Gonzaga Hospital
(Prof M. Volante)

RADIOMETABOLIC POLES
-Mauriziano Umberto I Hospital, Turin
(Dr R. Pellerito)
-SS Antonio e Biagio e C. Arrigo Hospital,
Alessandria
(Dr A. Muni)

Imaging platform sharing
UniTO start up

Dosimetry tool
Software

PERCORSO PAZIENTE

SCHEDA DI PRE-INCLUSIONE

DATA E GIC INVIANTE

1. *DATI PAZIENTE:*

Nome Cognome
Sesso F M
Data di nascita
ECOG
Peso:
Altezza
Comorbidità:
Terapie in atto : SSA SI/NO data ultima somministrazione

SCHEDA DI PRE-INCLUSIONE

2. DATI TNE

Sede di primitivo (GEP NET):
Tumore funzionante SI/NO in compenso SI/NO
Tipologia sindrome: s. carcinoide tipica SI/NO atipica SI/NO
Grading su primitivo: G1-G2; (Ki67%)
Grading su metastasi: G1-G2; (Ki67%)
Data di diagnosi primitivo
Data di diagnosi della prima metastasi:
Sede: Linfonodi Fegato Polmone Osso :
Terapie precedenti: 1.analoghi 2. Chemioterapia (linee 1.2.3)
Inoperabile (GIC): SI NO
Progressivo SI NO (3 classi 1.>12 mesi;2. < 12 mesi; 3. < 8 mesi) (GIC)
Data Progressione: tipologia di indagine utilizzata per definire progressione (TC/RMN)

SCHEDA DI PRE-INCLUSIONE

3. PATTERN METABOLICO

Data PET con 68Ga DOTATOC/DOTATATE:
PET con 68Ga DOTATOC/DOTATATE: positiva: SI NO
GRADO: 1.2.3.4.
SUVmax della lesione più captante:
Numero totale di lesioni:
Coinvolgimento epatico :1.assente 2. limitato.3. massivo

PET con FDG Disponibile (G2) SI NO;
Data PET FDG :
PET FDG: Positiva SI NO

Classe 1. DOTATOC > FDG; 2. DOTATOC =FDG; 3. DOTATOC< FDG

SCHEDA DI PRE-INCLUSIONE

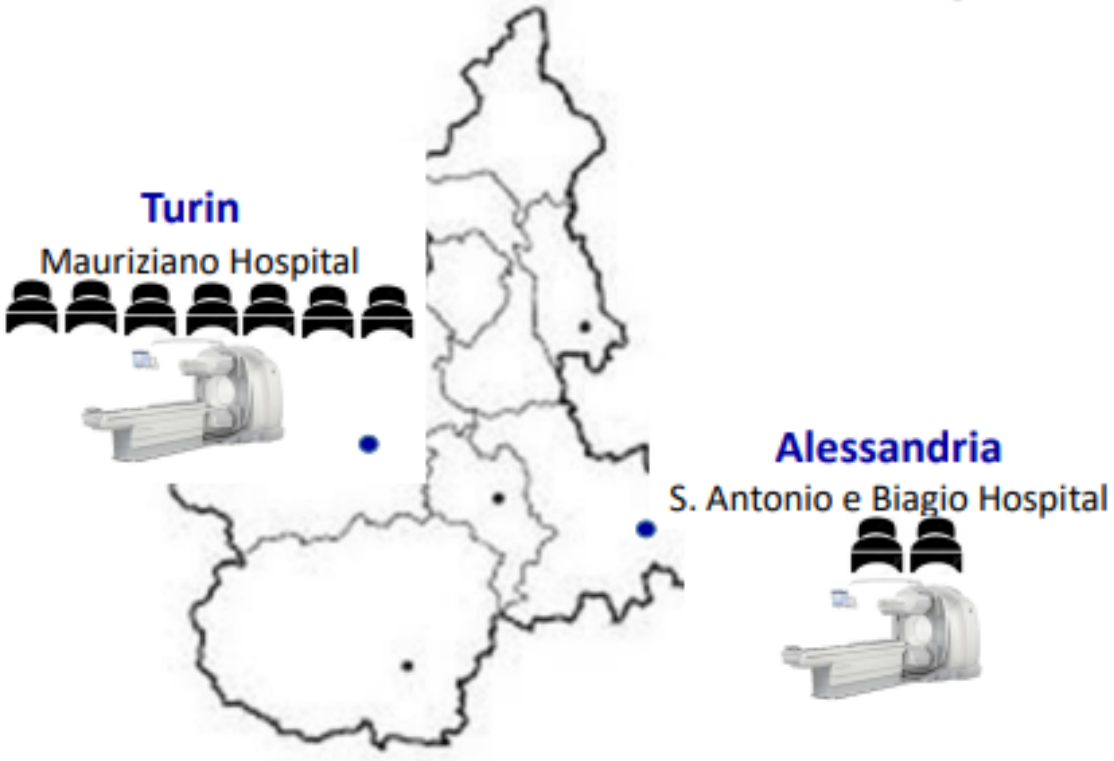
4. EMATOCHIMICI:

Emocromo nella norma SI NO (allegare)
Funzionalità renale mantenuta SI NO
Creatinina : ……. (Data) allegare
Funzionalità epatica nella norma SI NO
Bilirubina :……(Data) allegare

A. O. ORDINE MAURIZIANO TORINO

^{177}Lu TREATMENT NEUROENDOCRINE TUMOR

Piedmont Regional Oncological Net



rete oncologica

Dosimetry "Theradose" Project

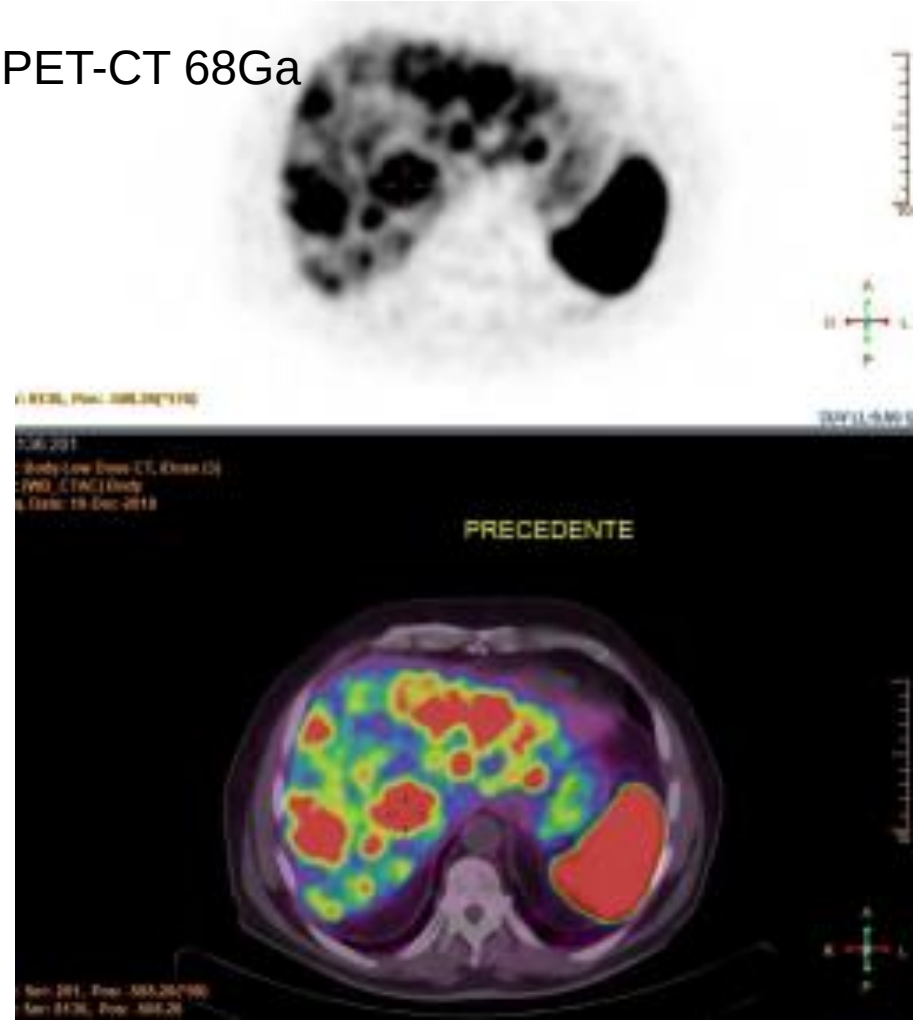
- SPECT-CT absolute calibration and verification
- Development of a MATLAB Tool for dose calculation
- Lesion and organ at risk dose dose calculation

Cortesia di E Richetta

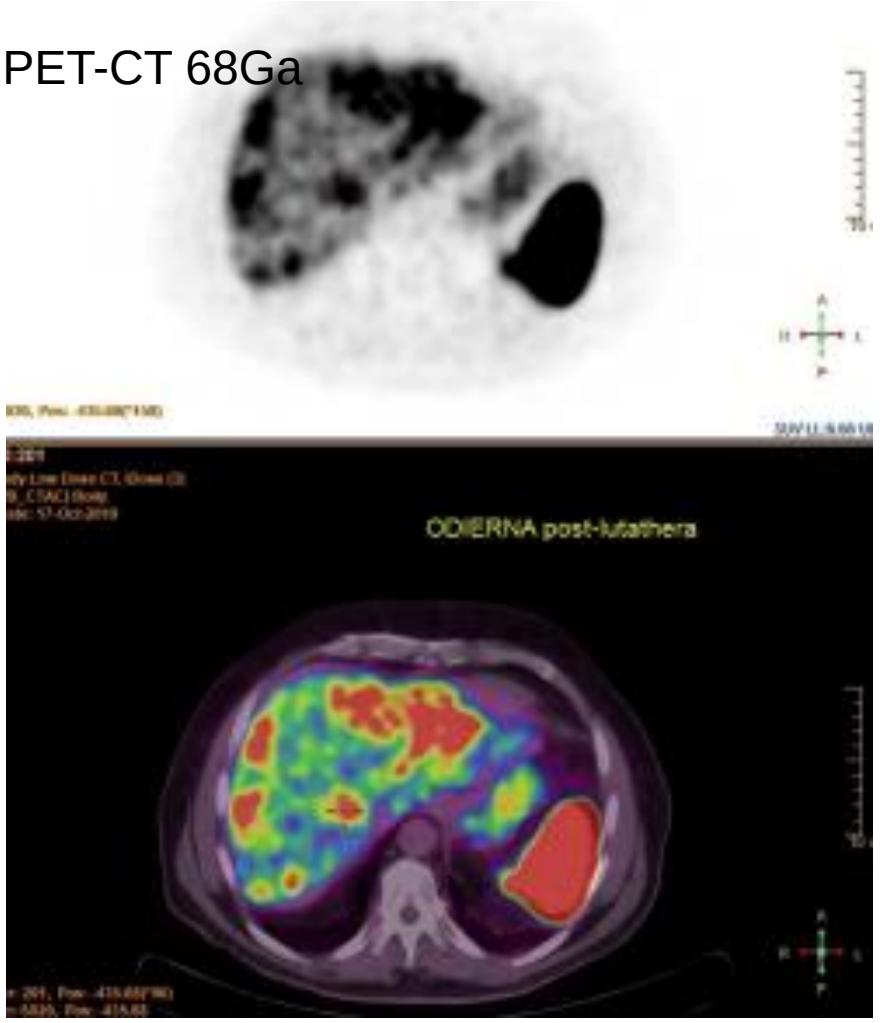
Calcolo della dose erogata post trattamento

Attività somministrata fissa: 7.4 GBq x 4 cicli

PET-CT 68Ga



PET-CT 68Ga



Cortesia di E Richetta

PRE TERAPIA

POST TERAPIA

METODO DOSIMETRICO AO Ordine Mauriziano

Lesion Activity

$$A = cts_{ROI} \cdot \frac{K_{DT}}{PVE} \cdot CF$$

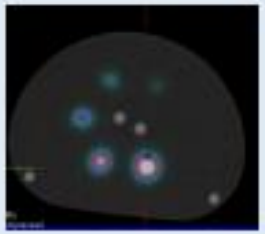
SPECT-CT Calibration

CF $\left[\frac{MBq}{cts}\right]$ Absolute calibration factor

PVE Partial Volume Effect coefficient

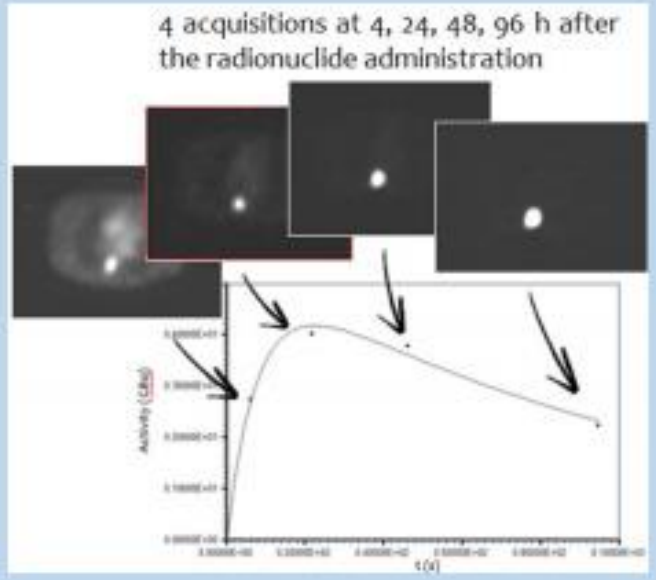
K_{DT} dead time correction factor

cts_{ROI} measured counts inside the lesion



$\widetilde{A}$ Activity-Time curve

4 acquisitions at 4, 24, 48, 96 h after the radionuclide administration



Mean Dose [Gy]

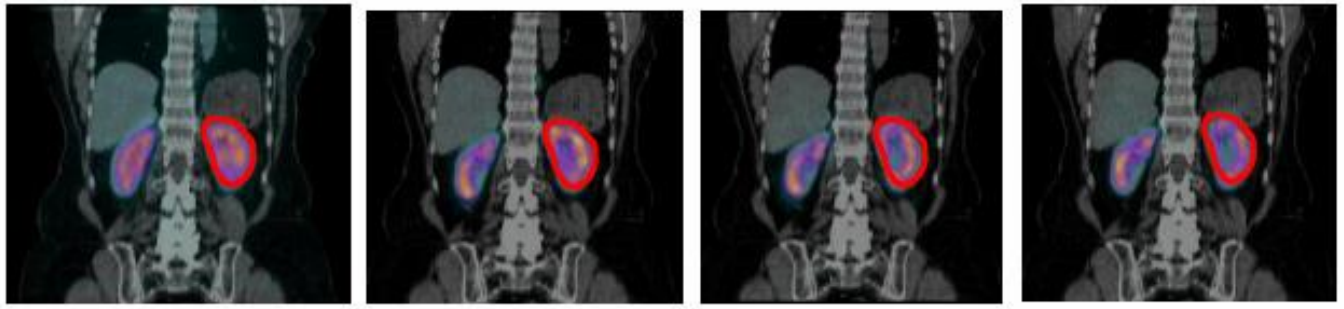
$$D = \widetilde{A} \cdot S$$

- MIRD Spheres Model S Factor
- Lesion mass estimation from volume (CT) and density curve (HU vs g/cm3)

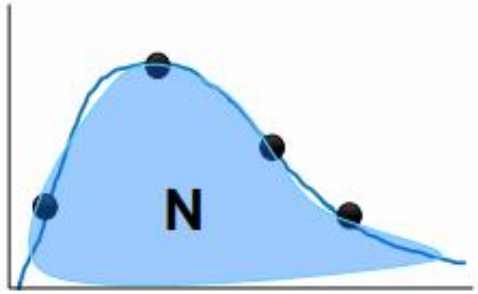
^{177}Lu DOSIMETRY - MIRD SPHERE model

METODO DOSIMETRICO

Costruzione della curva Attività/Tempo

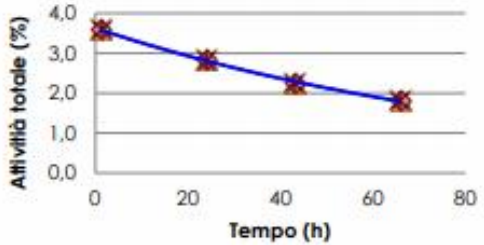


1 h p.i. 24 h p.i. 40 h p.i. 70 h p.i.

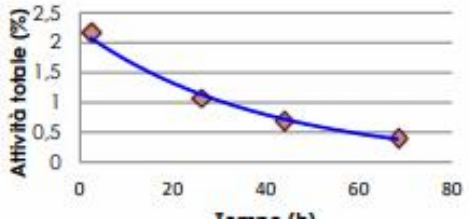


Curva attività-tempo

N = Numero di Disintegrazioni



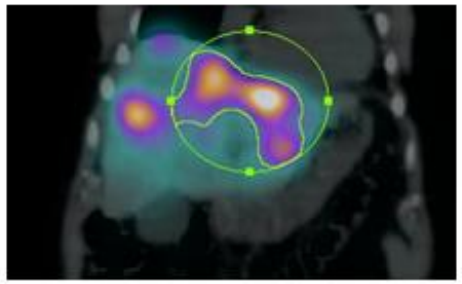
Dose al rene (^{177}Lu) = 1.22 Gy/GBq

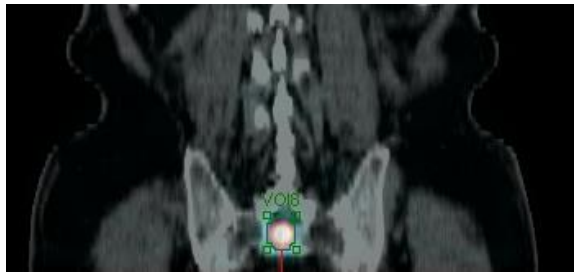


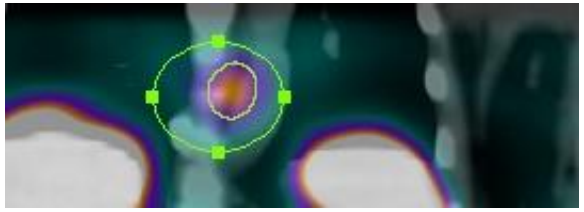
Dose al rene (^{177}Lu) = 0.15 Gy/GBq

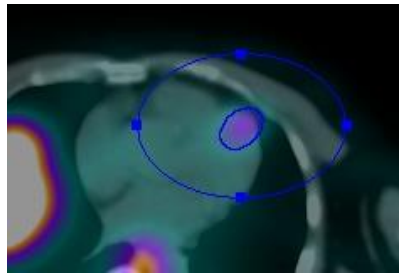
[cortesia F. Fioroni]

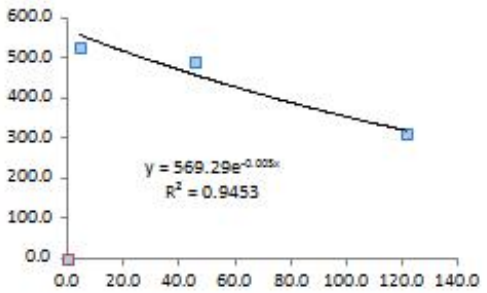
DOSE al target tumorale

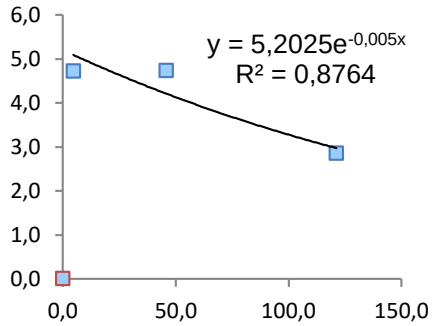


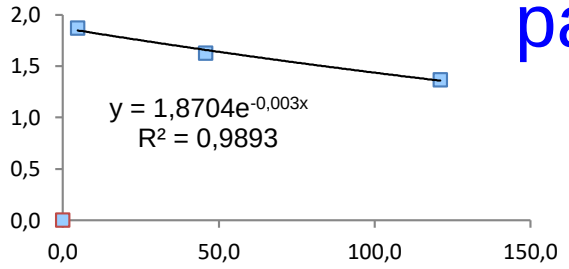


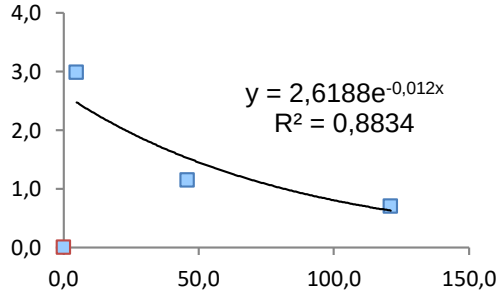












Lesioni

epatiche
117- 153 Gy

ossea
43 Gy

paraesofagea
18 Gy

pericardica
5 Gy

Perché una ATTIVITA' PERSONALIZZATA potrebbe essere meglio di una ATTIVITA' FISSA?

Dose clinicamente efficace

Sebbene i trials clinici non siano ancora numerosi, vi è una crescente evidenza che, per ottenere un beneficio clinico, sia necessario un valore minimo di dose.

Eur J Nucl Med Mol Imaging (2014) 41:1976–1988
DOI 10.1007/s00259-014-2824-5

REVIEW ARTICLE

The evidence base for the use of internal dosimetry in the clinical practice of molecular radiotherapy

Lidia Strigari · Mark Konijnenberg · Carlo Chiesa · Manuel Bardies · Yong Du · Katarina Sjögreen Gleisner · Michael Lassmann · Glenn Flux

Dose Response of Pancreatic Neuroendocrine Tumors Treated with Peptide Receptor Radionuclide Therapy Using ^{177}Lu-DOTATATE

Ezgi Ilan[1,2], Mattias Sandström[1,2], Cecilia Wassberg[1,3], Anders Sundin[1,3], Ulrike Garske–Román[1,3], Barbro Eriksson[4], Dan Granberg[4], and Mark Lubberink[1,2]

[1]Nuclear Medicine and PET, Department of Radiology, Oncology, and Radiation Science, Uppsala University, Uppsala, Sweden; [2]Medical Physics, Uppsala University Hospital, Uppsala, Sweden; [3]Molecular Imaging, Medical Imaging Centre, Uppsala University Hospital, Uppsala, Sweden; and [4]Section of Endocrine Oncology, Department of Medical Science, Uppsala University Hospital, Uppsala, Sweden

[cortesia F. Fioroni]

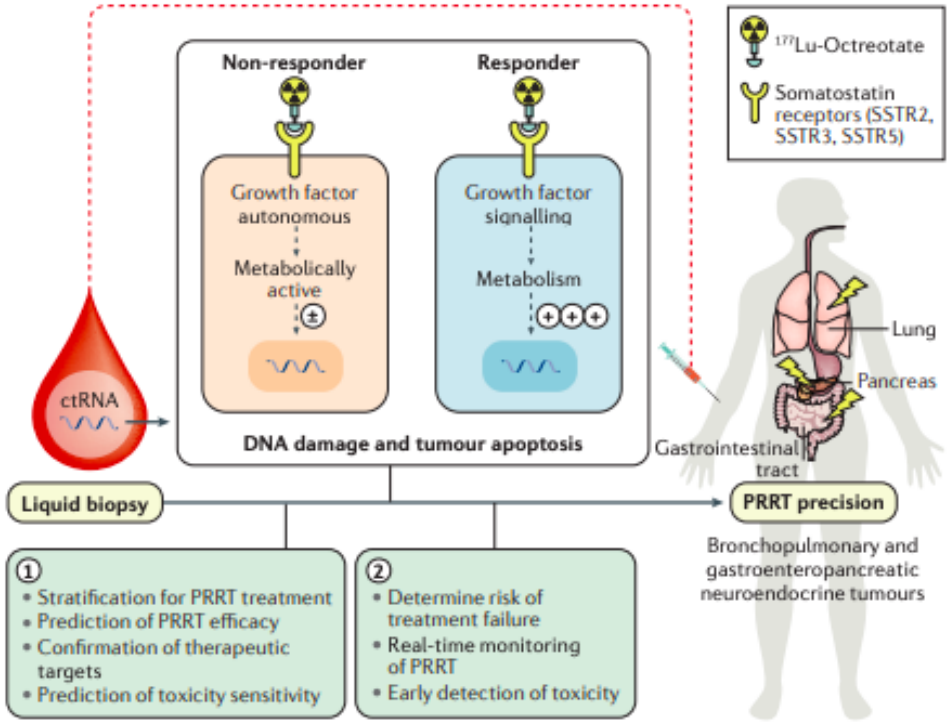
Challenge for next years … liquid biopsy

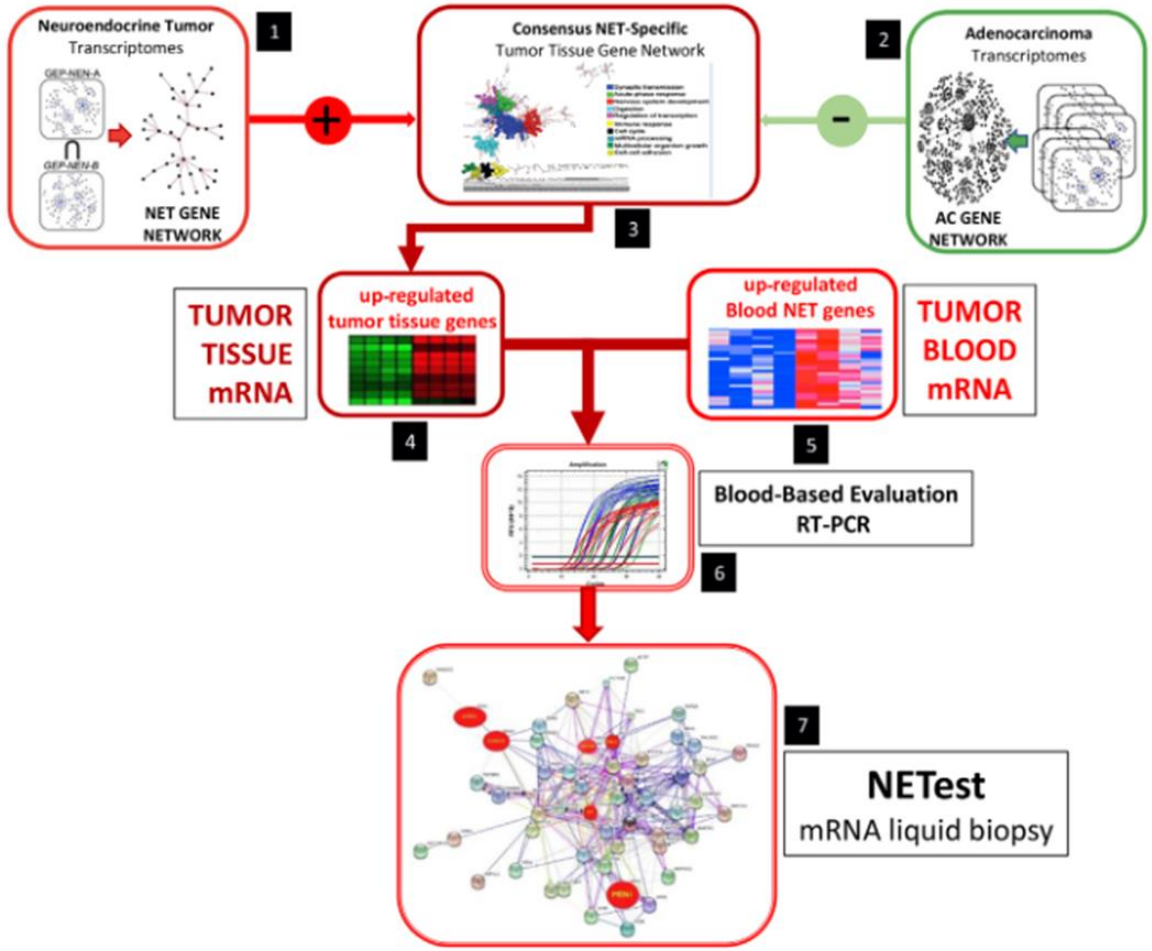
Therapy

The role of liquid biopsies to manage and predict PRRT for NETs

Mark Kidd & Irvin M. Modlin

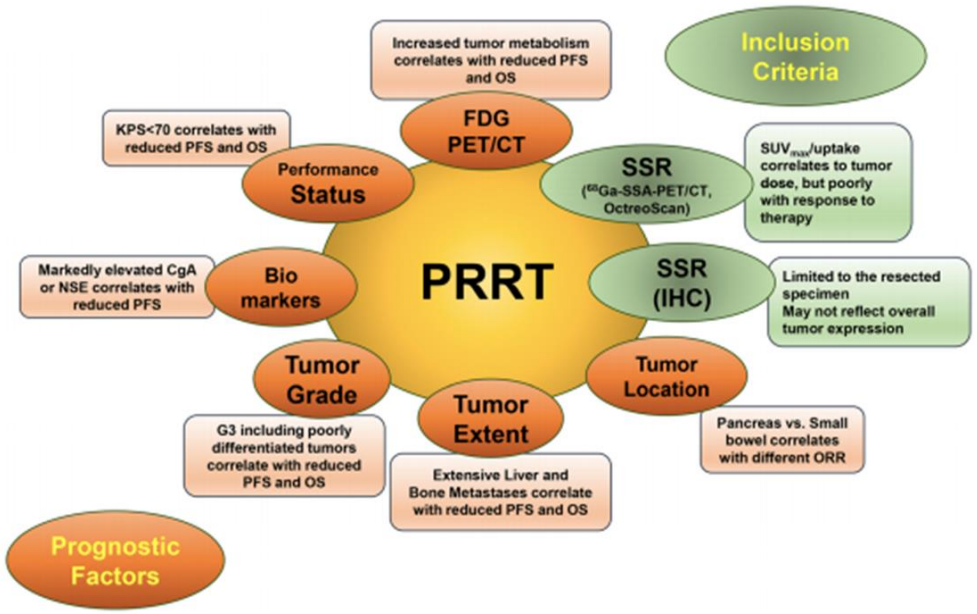
Nature Reviews Gastroenterology & Hepatology **14**, 331–332 (2017) | Download Citation

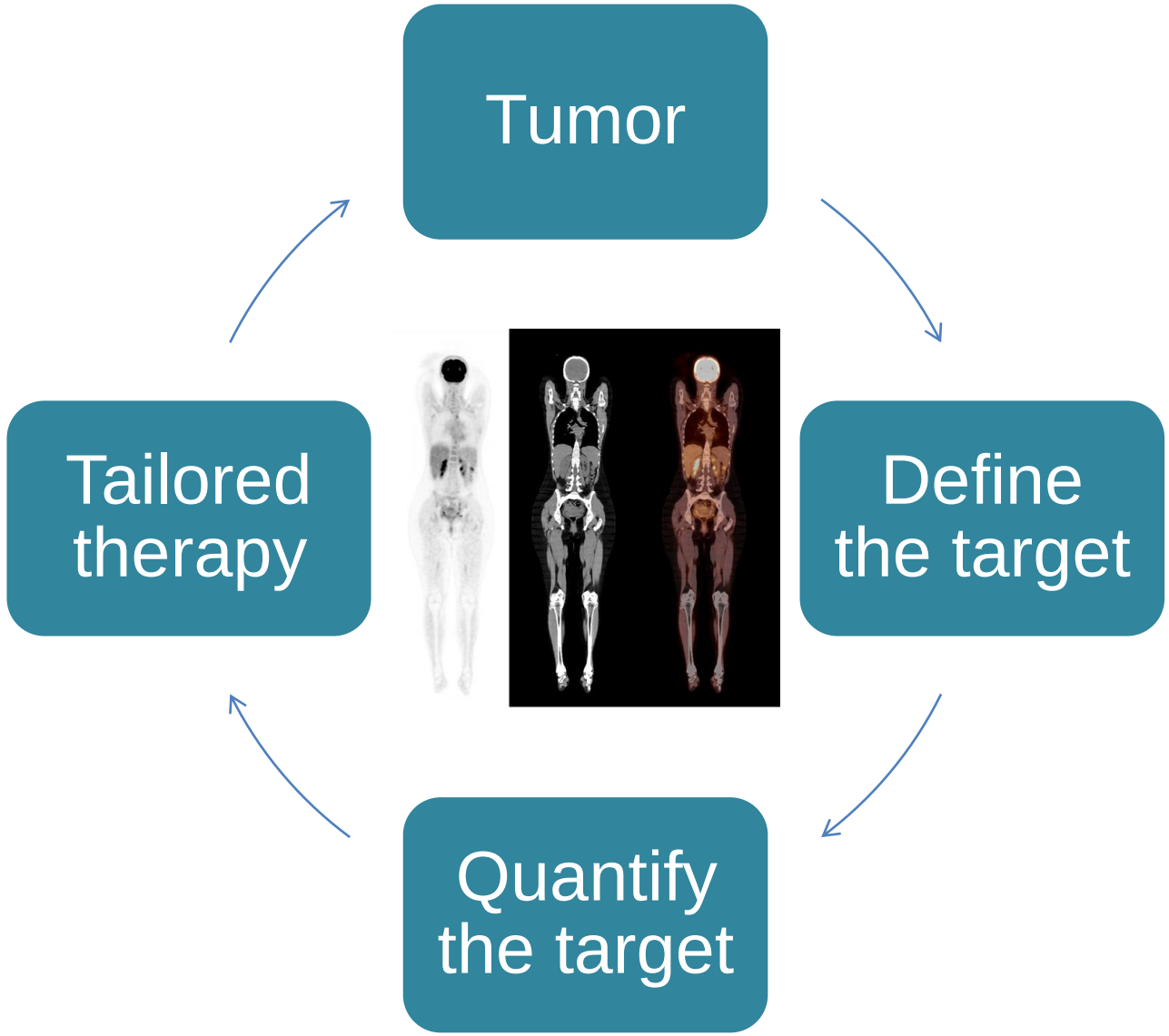




PRRT predictive quotient (PPQ)

CONCLUSION :


Inclusion Criteria
Increased tumor metabolism correlates with reduced PFS and OS
FDG PET/CT
KPS<70 correlates with reduced PFS and OS
Performance Status
SSR (68Ga-SSA-PET/CT, OctreoScan)
SUVmax/uptake correlates to tumor dose, but poorly with response to therapy
PRRT
Markedly elevated CgA or NSE correlates with reduced PFS
Bio markers
SSR (IHC)
Limited to the resected specimen
May not reflect overall tumor expression
Tumor Grade
Tumor Location
Tumor Extent
G3 including poorly differentiated tumors correlate with reduced PFS and OS
Pancreas vs. Small bowel correlates with different ORR
Extensive Liver and Bone Metastases correlate with reduced PFS and OS
Prognostic Factors


Tumor
Define the target
Quantify the target
Tailored therapy

Thank You - Think NETWORK

Condivisione e distribuzione delle risorse
Fare network

HOT POINTS

Stabilire un iter diagnostico terapeutico condiviso
Facilities: Radiofarmacia, Fisica, Tecnologia
Potenziare ricerca nel campo : progetti unito, partnership
Sviluppo per altre patologie attualmente in fase sperimentale e non rari
Sviluppo di nuovi radiofarmaci
Sviluppo nuovi trials