99mTc HYNIC TOC SPECT CT Imaging in SOMATOSTATIN expressing tumors

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NET

Neuroendocrine tumours have posed a challenge because of their rarity and heterogeneity, both from clinical and molecular perspectives.

NET

- First described in the medical literature more than a century ago.
- ‘Carcinoid tumour’ by Obendorfer in 1907.
- Rare, but are increasing in incidence, from 1.7/100,000 in 1980-89 to 3.3/100,000 in 2000-06

Steve Jobs

Islet cell NET

Nov 10 -Worldwide NET Cancer awareness Day

NET

- Origin :Enterochromaffin Neural crest cells
- Also known as APUDOMAS
- Both neural and endocrine cell features

Over expression of Somatostain receptors (SSTR)

is the hallmark of Neuroendocrine Tumors (NET)

Somatostatin

- A peptide hormone
- Known as Growth Hormone Inhibiting Hormone (**GHIH**) or Somatostatin Release Inhibiting Factor(**SRIF**)
- Produced in HT,Pituitary,Bronchus,GI tract,Pancreas
- Brain –Neurotransmitter
- Outside Brain- Inhibits GH,Glucagone,Gastrin,Serotonin,Calcitonin

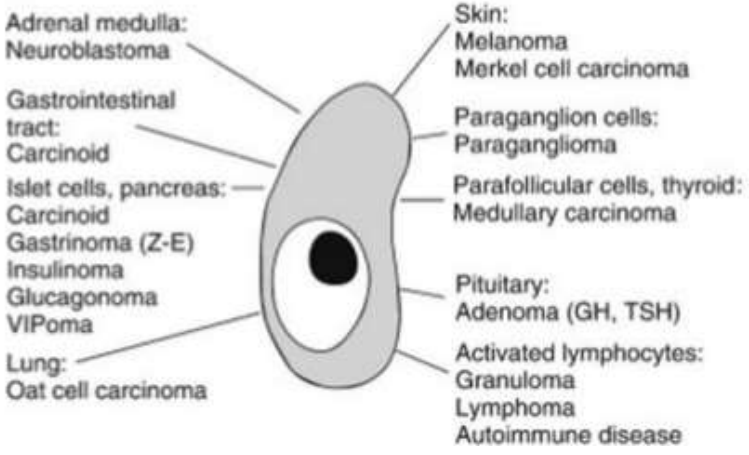
- **Angiogenesis Inhibitor, Antiprolifereative effect**

- *SST receptor activation inhibits secretary and proliferative activity*-Basis of PRRT

NET

Tumors with High Expression of SSR

1. Adrenal medullary tumors
   - pheochromocytoma, neuroblastoma, ganglioneuroma, paraganglioma
2. Gastroenteropancreatic (GEP) NETs (formerly termed carcinoid, gastrinoma, glucagonoma, vasoactive intestinal polypeptide-secreting tumor, pancreatic polypeptide-secreting tumor, etc., or nonfunctioning GEP tumors), more recently classified by the WHO as low grade, intermediate grade and high grade (G1, G2, and G3)
3. Merkel cell tumor of the skin
4. Pituitary adenoma
5. Small-cell lung carcinoma



Multiple Endocrine Neoplasia (MEN) Syndromes

Lesion	MEN-I	MEN-IIA	MEN-IIB
Pituitary adenoma	+		
Pancreatic islet cell tumor	+		
Parathyroid adenoma	+	+	
Pheochromocytoma		+	+
Medullary thyroid cancer		+	+
Ganglioneuroma			+

Radioimmunoscintigraphy (RIS) in NET

- Targeting Over expressed Somatostatin receptors (SSTR)using Somatostatin analogues

- Sensitivity of the study depends on
  1. Density of SSTR
  2. Type of the analogues used in the study

MOLECULAR HETEROGENOSITY AND CLASSIFICATION

- Aggressiveness

  1)Mitotic Index

  2)Quantification of the proliferation marker Ki- 67

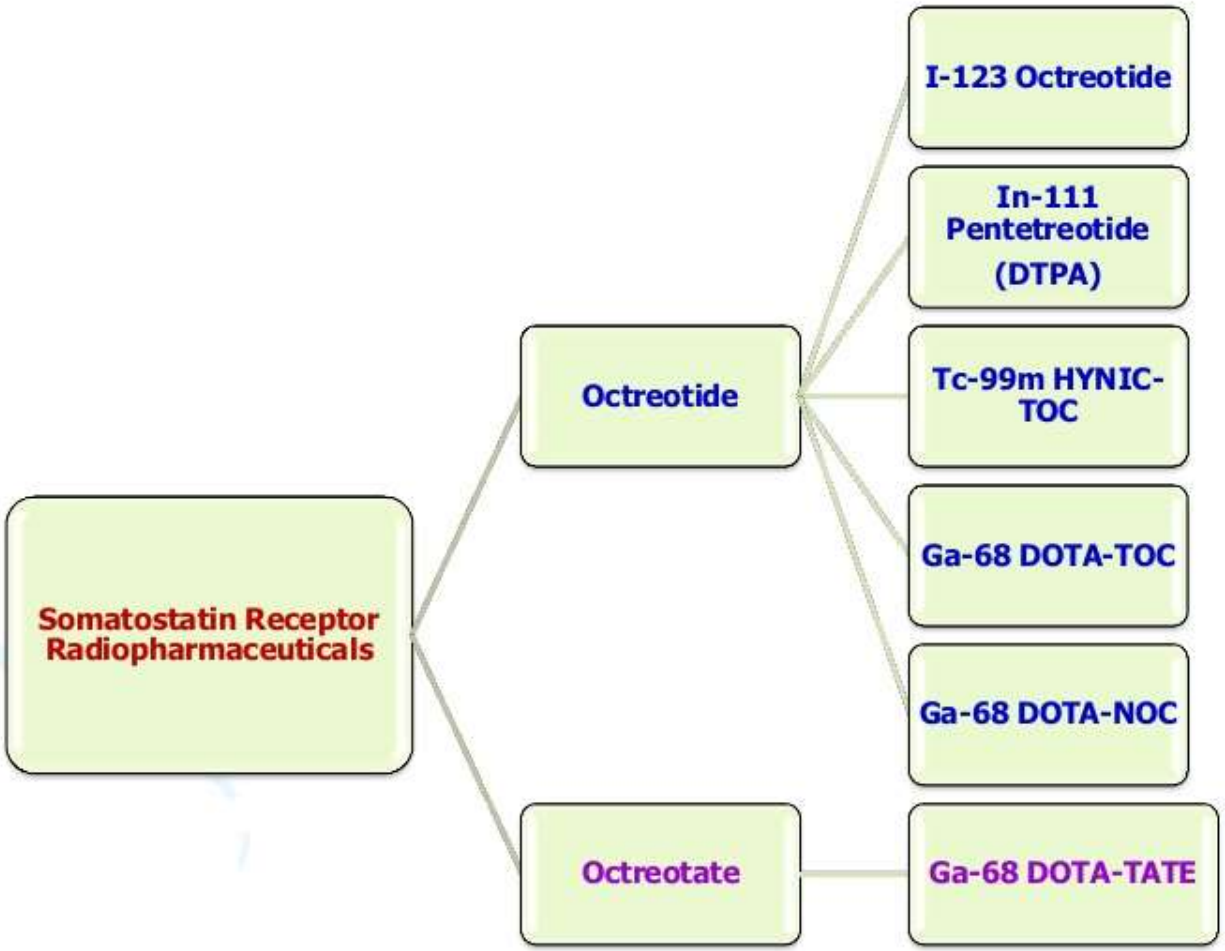
WHO classification

Table 1: *2010 World Health Organisation (WHO) classification of neuroendocrine tumours*

Grade	Mitotic count (mitoses per 10 high power fields)	Ki-67 index	Traditional nomenclature	WHO/ENETS nomenclature
Grade 1	<2mit/10HPF	<3%	Carcinoid, islet cell tumour	Neuroendocrine tumour, Grade 1
Grade 2	2-20mit/10HPF	3-20%	(Atypical) Carcinoid, islet cell tumour	Neuroendocrine tumour, Grade 2
Grade 3	>20mit/10HPF	>20%	Small cell carcinoma, large cell neuroendocrine carcinoma	Neuroendocrine carcinoma (large cell or small cell type)
Mixed adenoneuroendocrine carcinoma (MANEC)				
Hyperplastic and pre-neoplastic lesions				

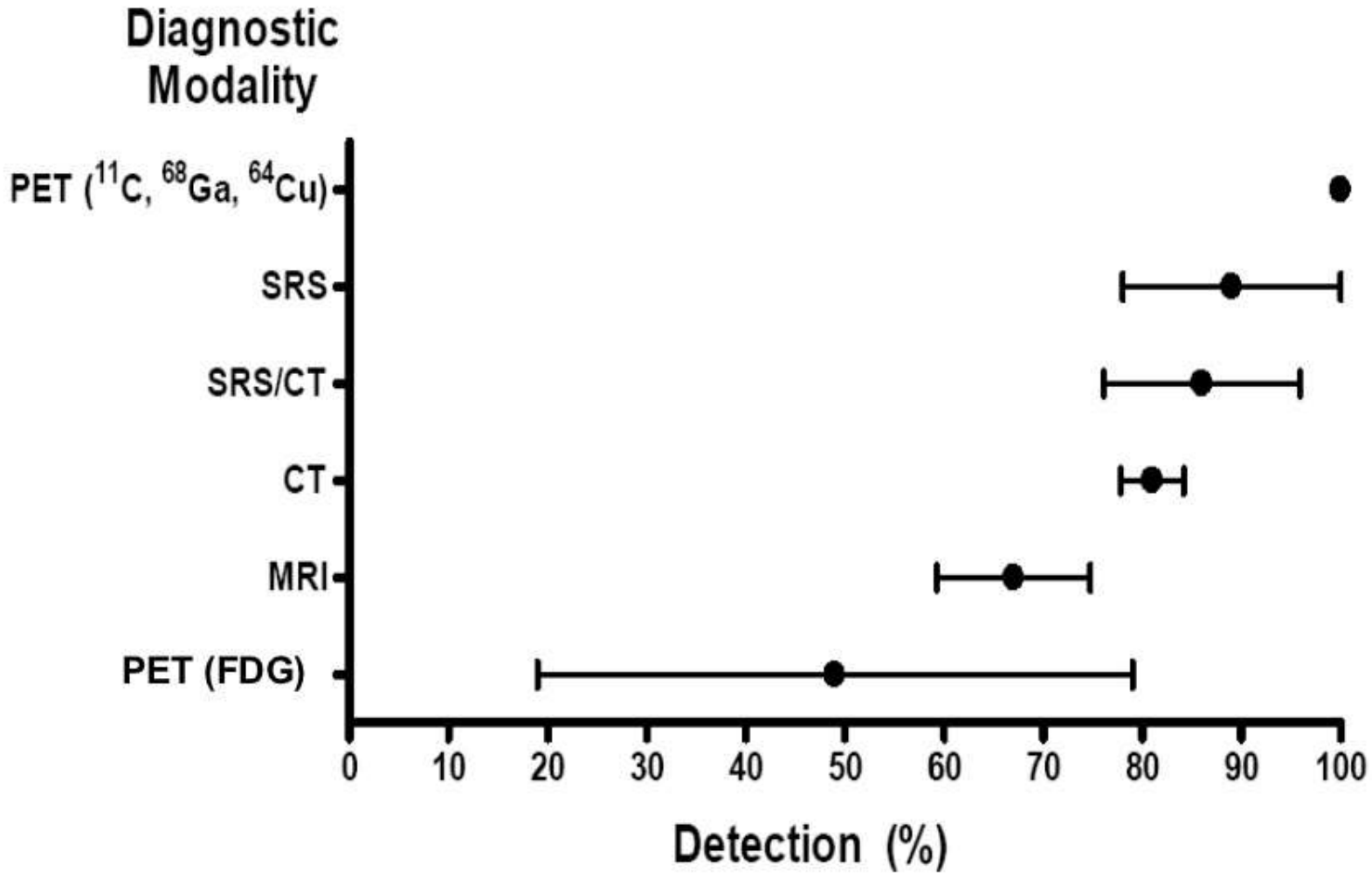
Mit: Mitoses ***HPF:*** High power fields ***ENETS:*** European Neuroendocrine Tumour Society

Somatostatin Receptor Radiopharmaceuticals



UPPSALA UNIVERSITET

Neuroendocrine tumors



Modlin 2008

99m Tc HYNIC TOC

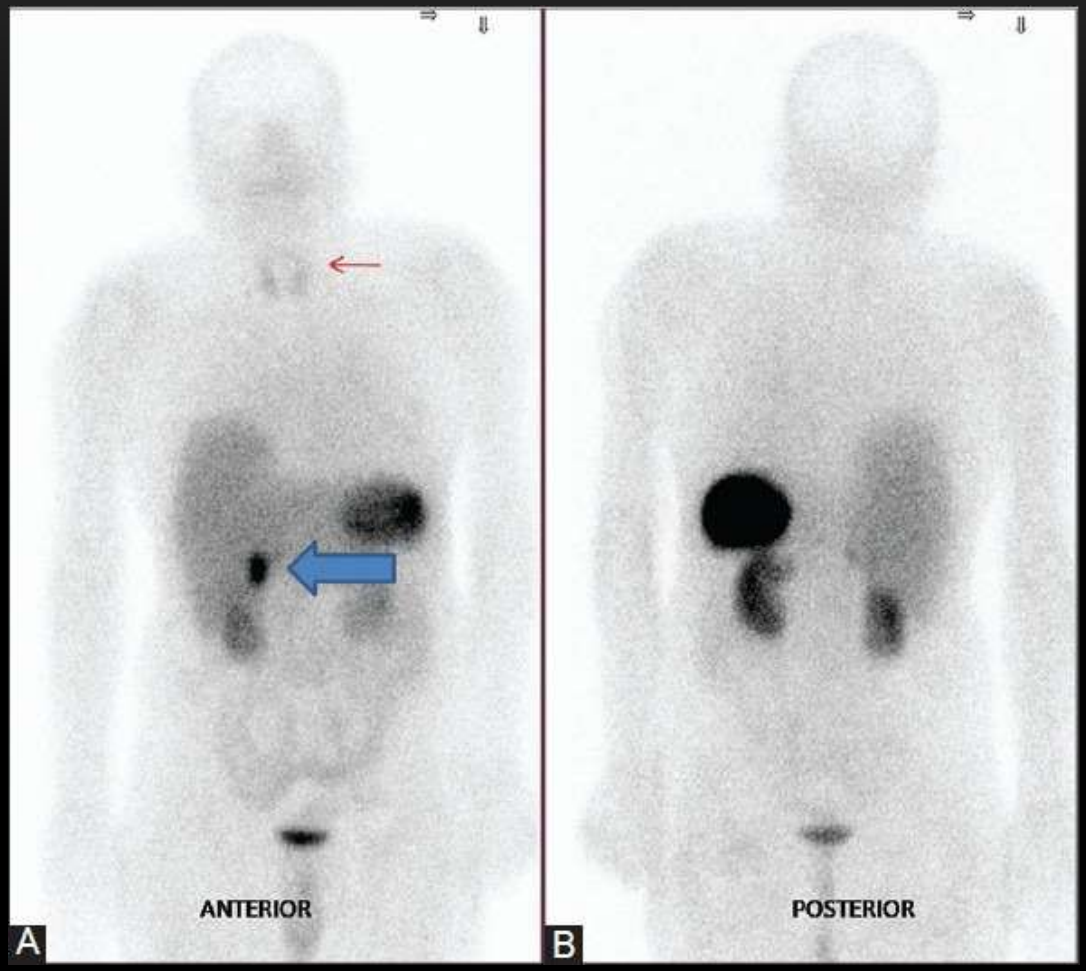
- Tc labeled Tyrosine 3 Octreotide (TOC)
- Hydrazinonicotinic acid (HYNIC)
- Better pharmacokinetic properties
- Higher target to non target ratio
- Higher absolute tumor uptake values
- Optimal acquisition time 4 hrs post injection
- Less sensitive for liver and smaller sized lesions

99Tc HYNIC TOC imaging is a time tested effective tool for the evaluation of NET in various clinical settings when Ga PET CT is not available.

99m Tc HYNIC TOC scintigraphy

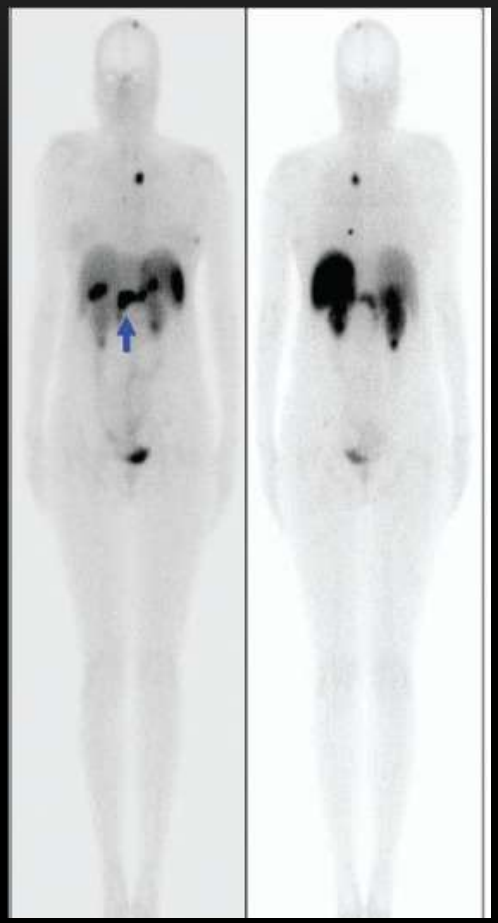
- Stop Somatostatin therapy 4 weeks
- 3 weeks post op
- 20 mci of tracer
- 2 hrs ,4 hrs , 6 hrs

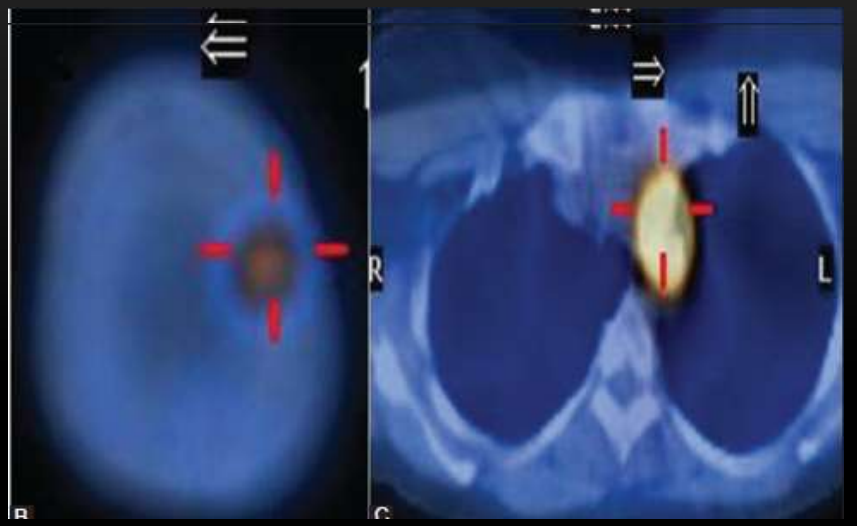
Normal Distribution of 99mTc HYNIC TOC

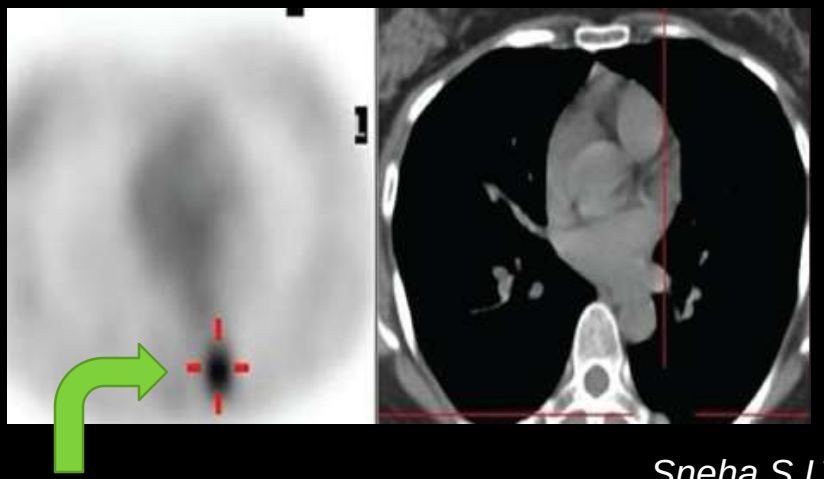


Sneha S IJRI 2012

Staging work up : Pancreatic NET

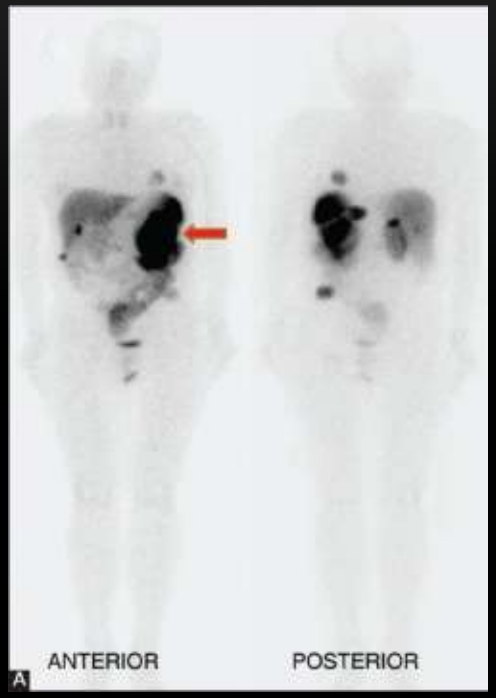


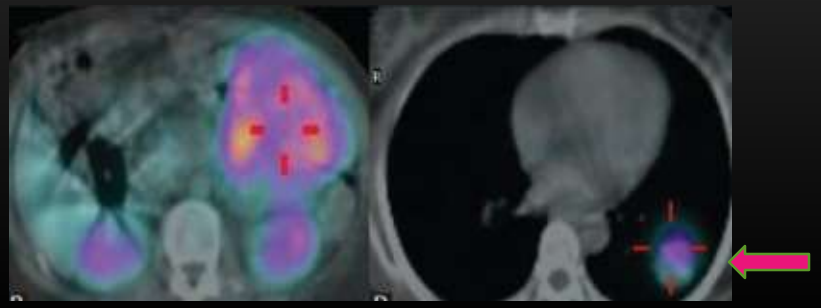


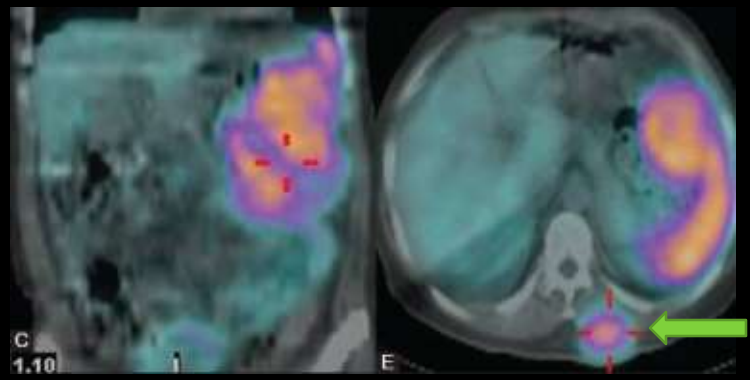


Sneha S IJRI 212

Small Cell Ca of Lung

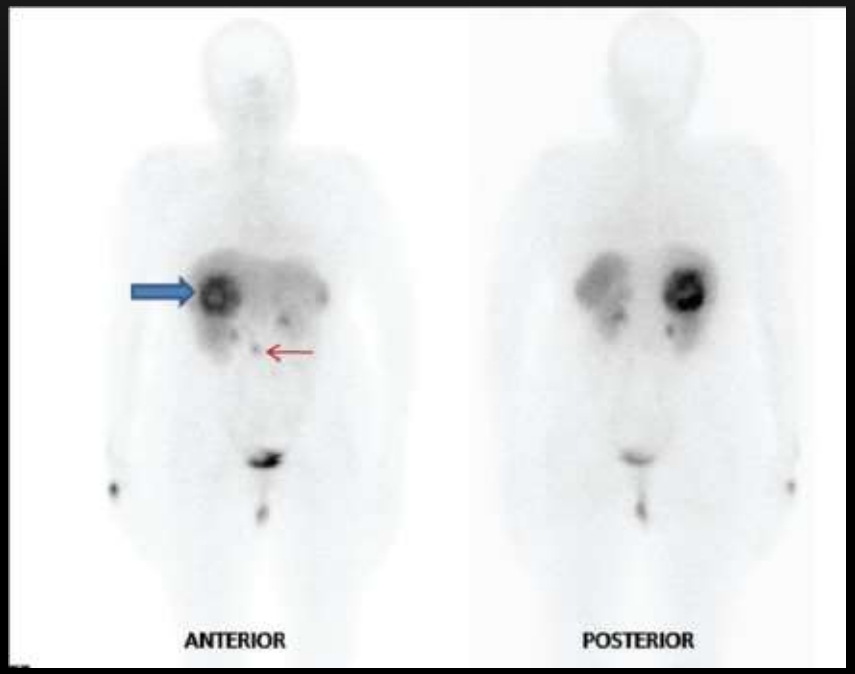


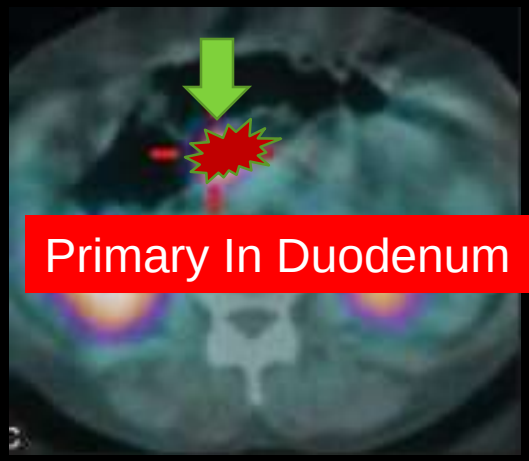




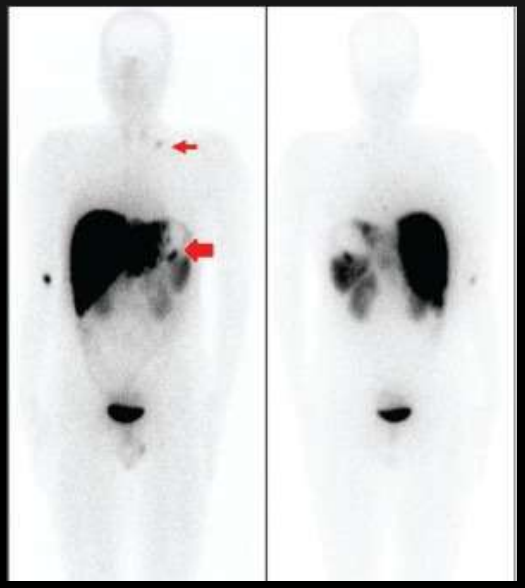
Subcutaneous mets

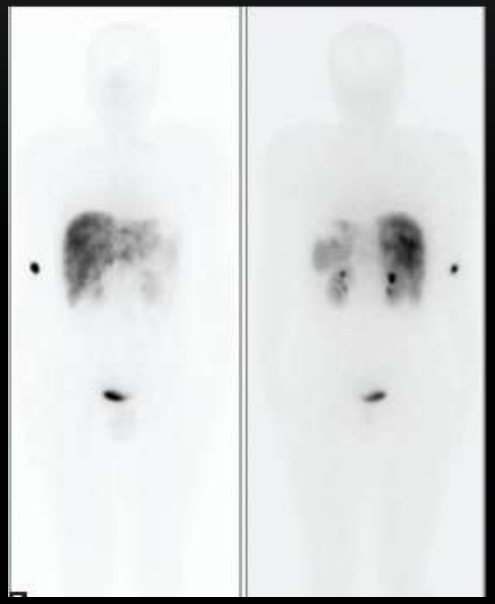
Unknown Primary



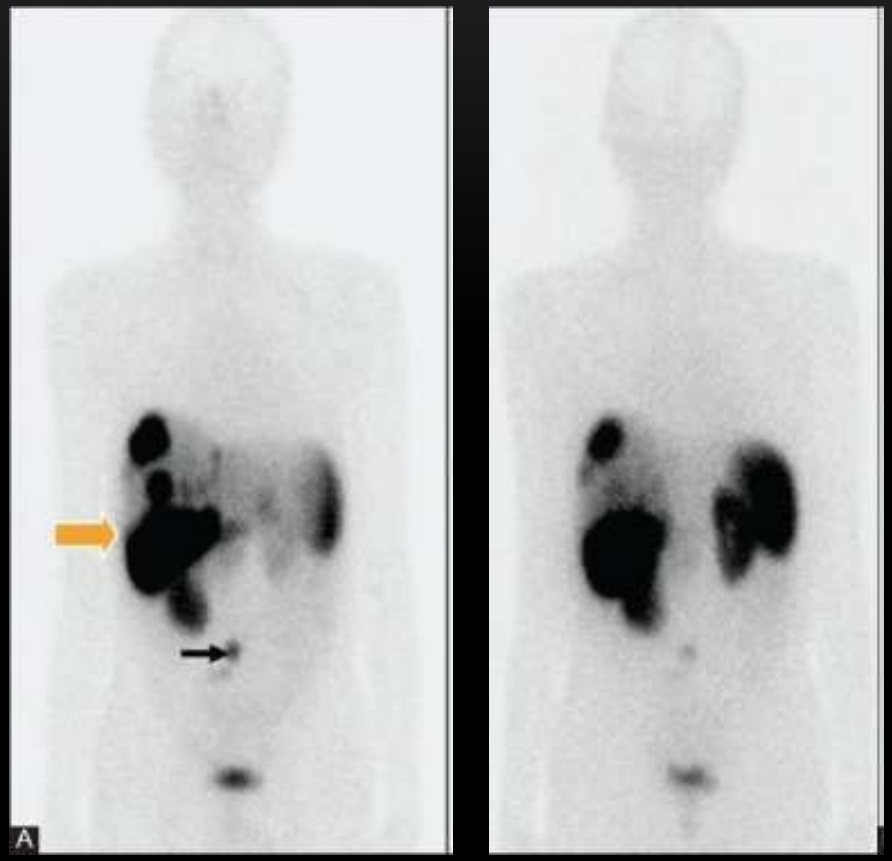


Unknown Primary-supra clavicular LN

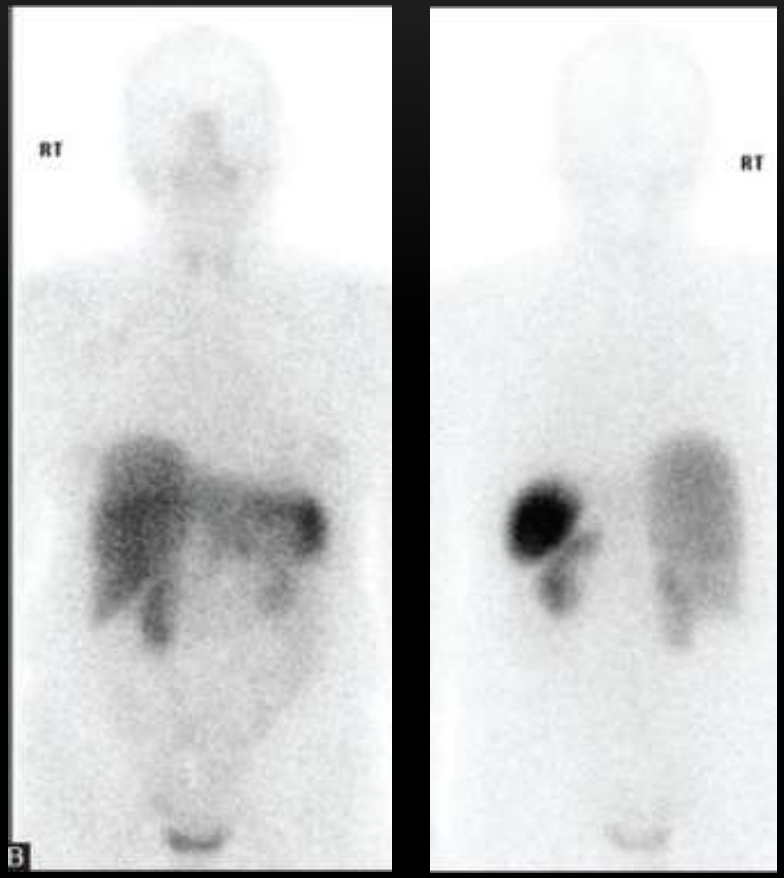




Treatment Response assessment of NET using SSTR imaging

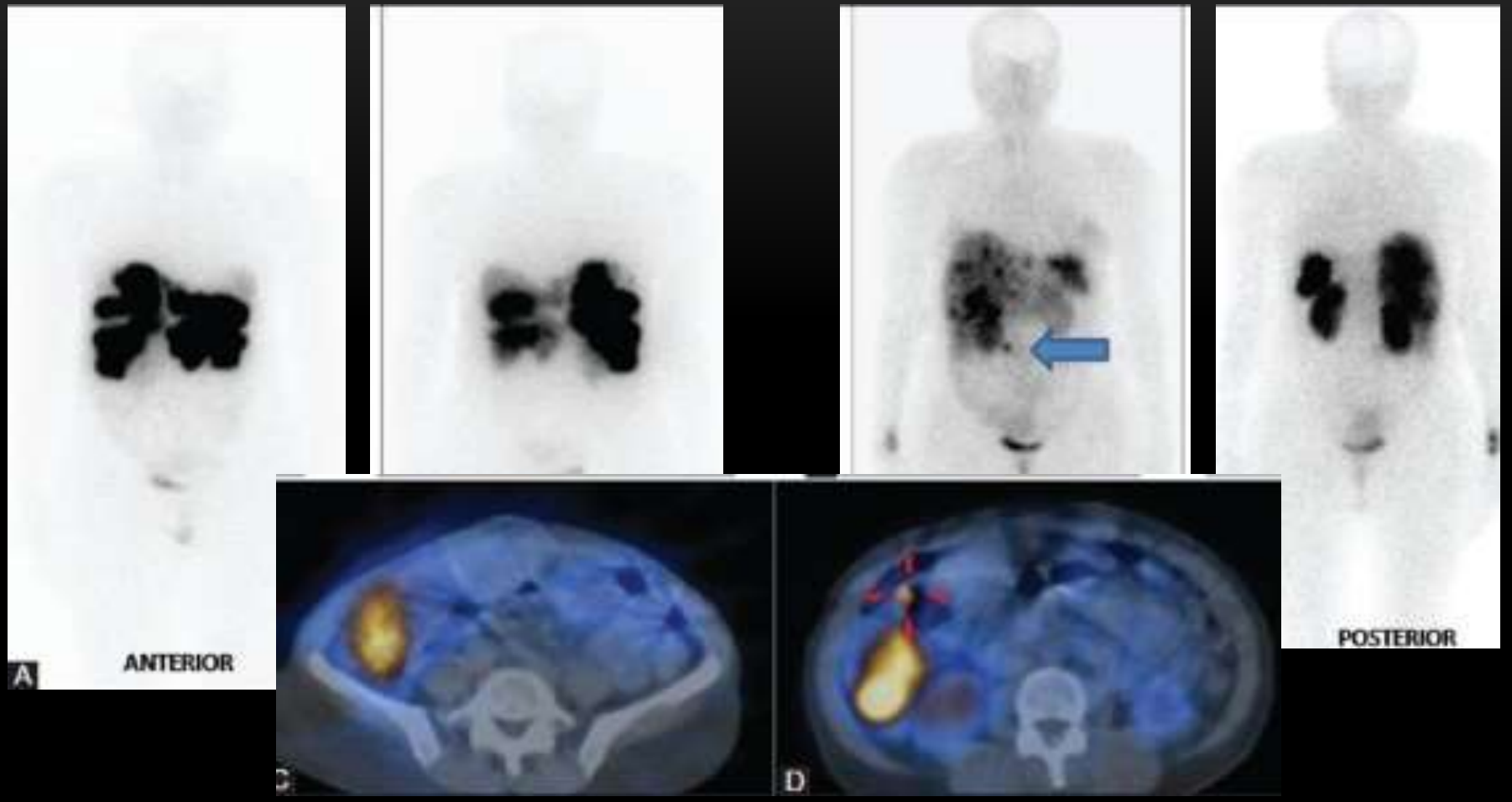


Baseline



After 3 cycles

Treatment Response assessment of NET



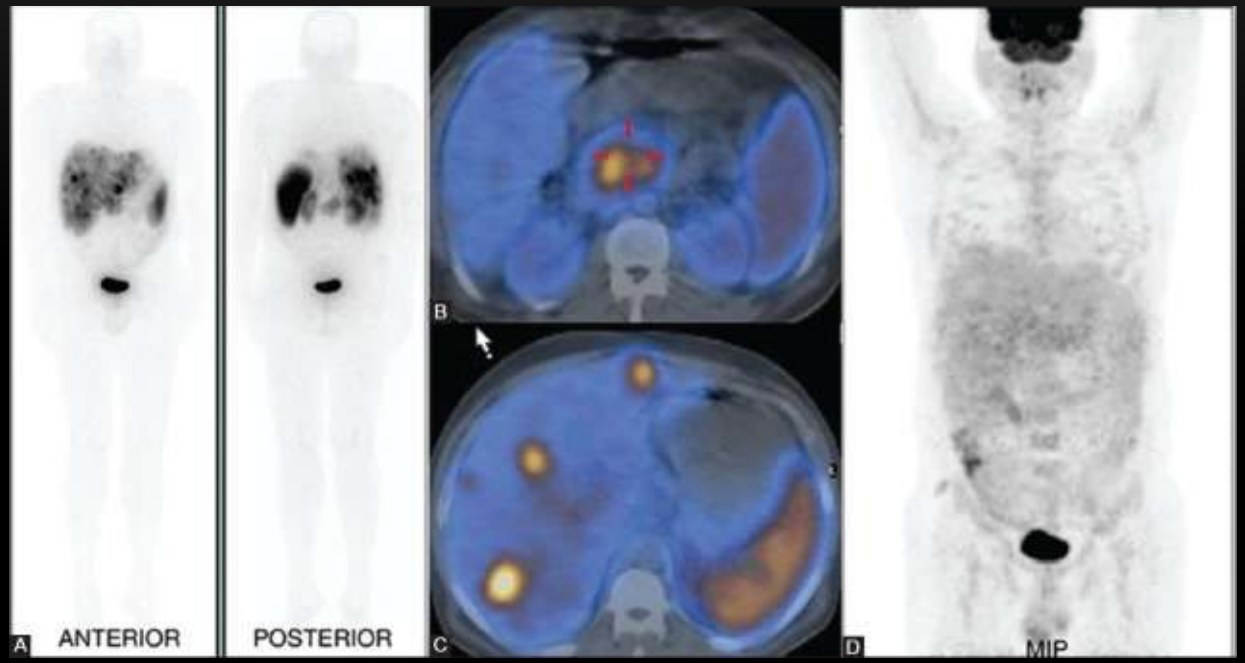
Significance of dual Imaging with 99Tc HYNIC TOC and 18F FDG PET imaging

Types of uptake in Dual HYNIC and FDG imaging

- Type I : SRS positive and FDG negative – Well differentiated tumors.
- Type II :SRS positive and Low FDG – Mixed variety of cells.
- Type III :Avid somatostatin and FDG uptake – Dedifferentiation
- Type IV :Avid FDG and low somatostatin uptake – Increasing loss of differentiation.

Type 1 Uptake pattern.

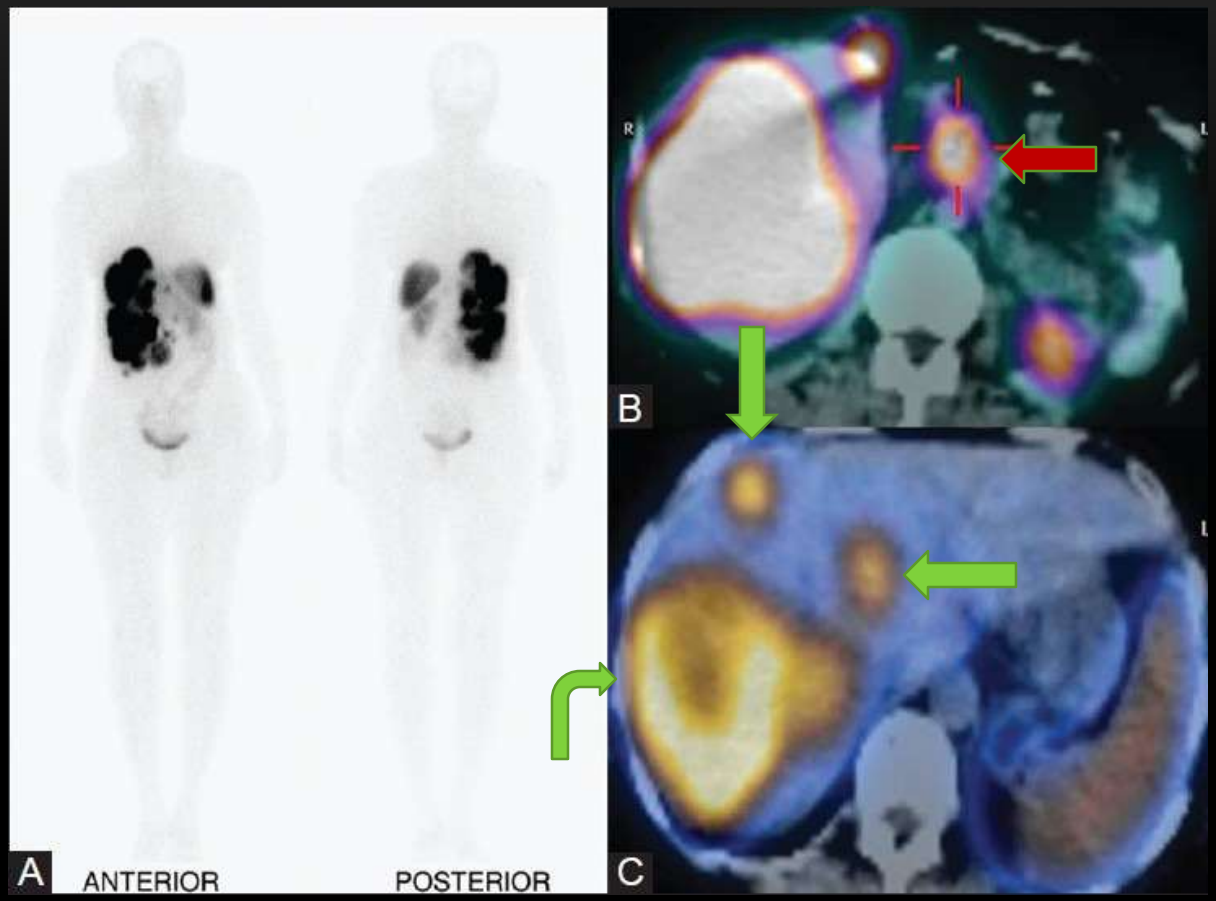
SRS Positive and FDG negative



HYNIC TOC FDG PET

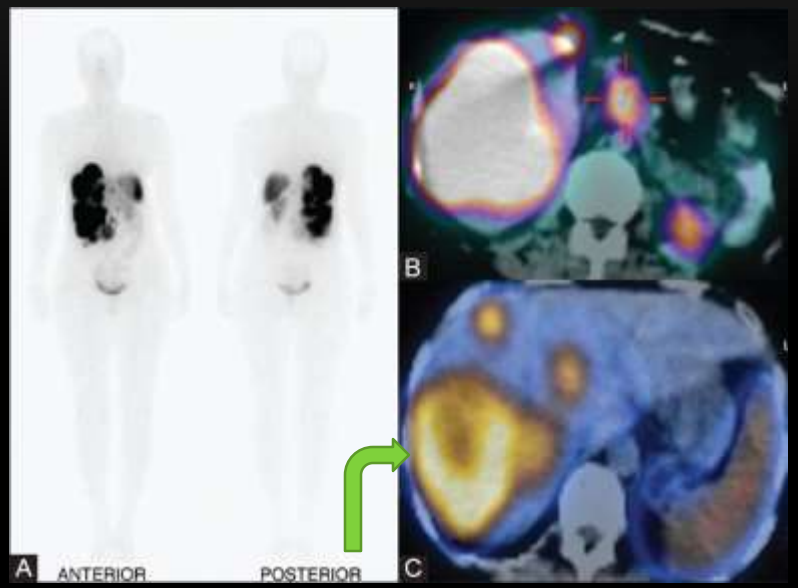
Well differentiated NET

Type 2 Uptake pattern
SRS positive and low FDG

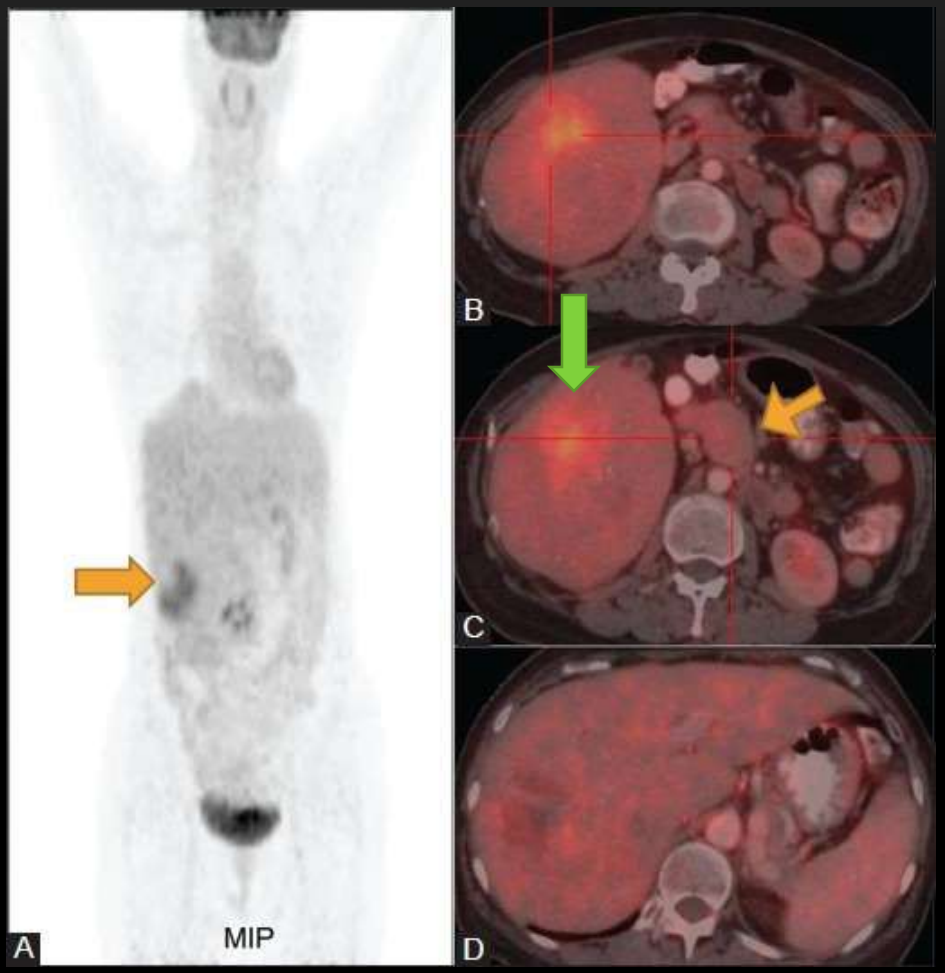


Type 2 Uptake pattern

SRS positive and low FDG



HYNIC TOC SPECT



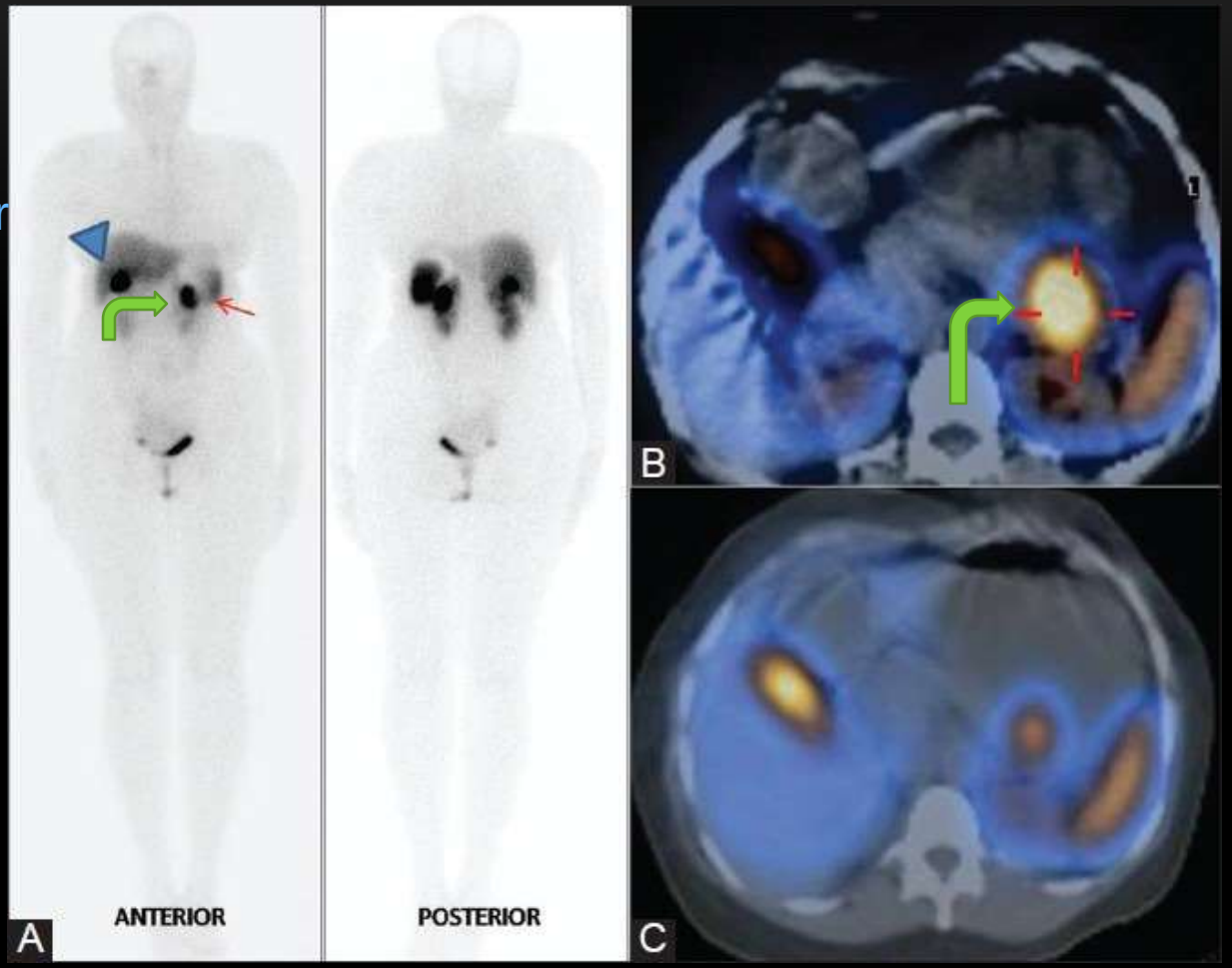
FDG PET

Mixed variety

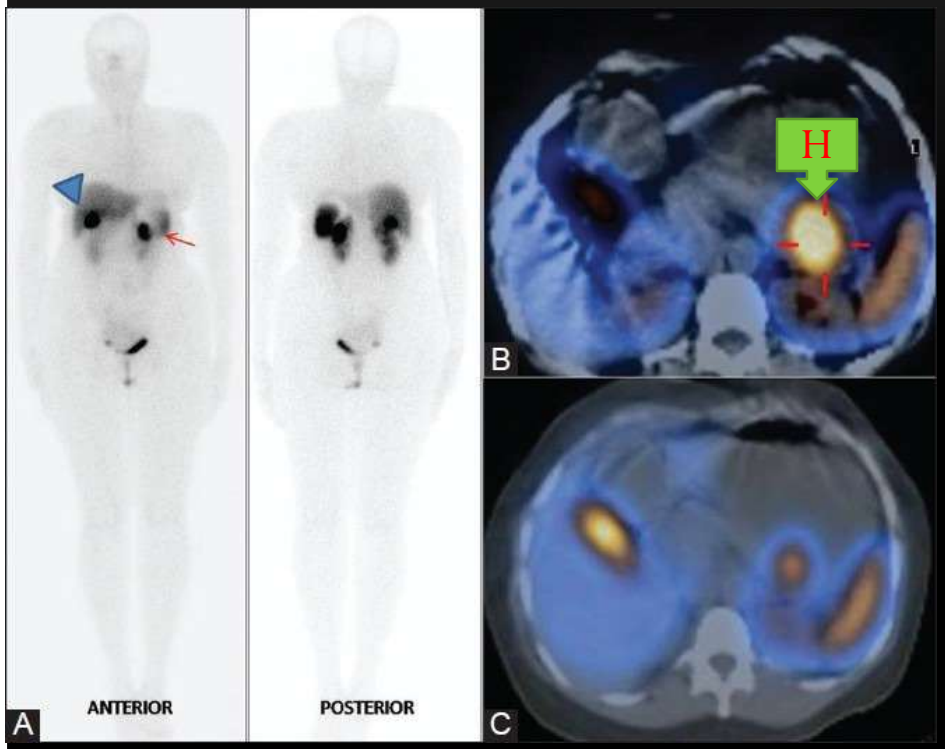
Type 3 Uptake pattern

Avid Somatostatin and FDG uptake

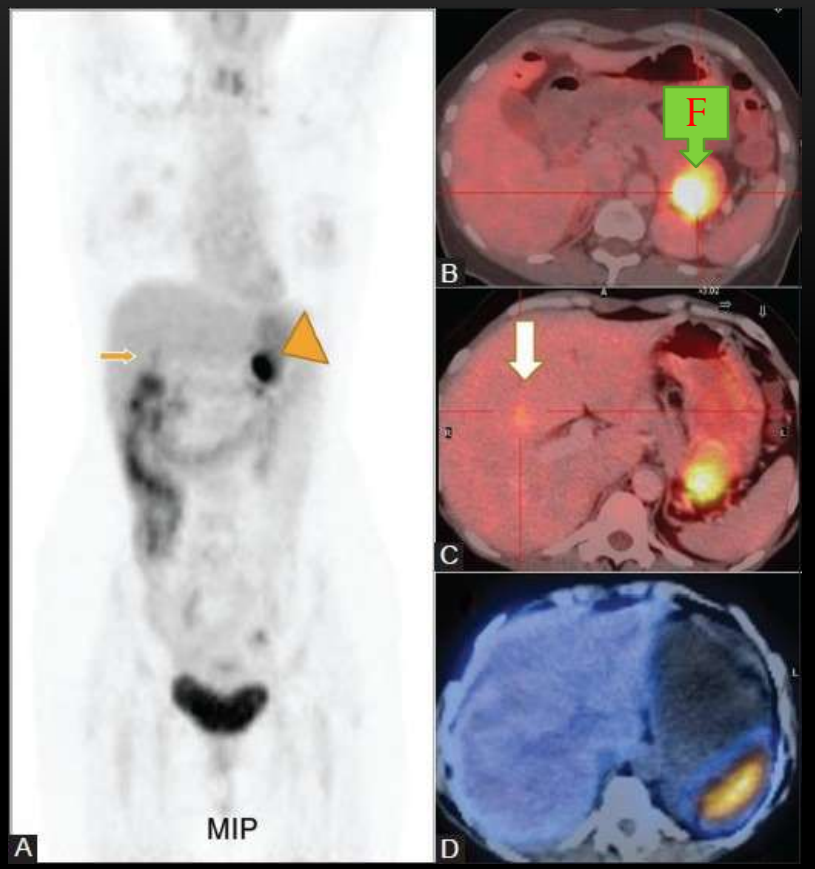
Gall bladder



Type 3 Uptake pattern
Avid Somatostain and FDG uptake



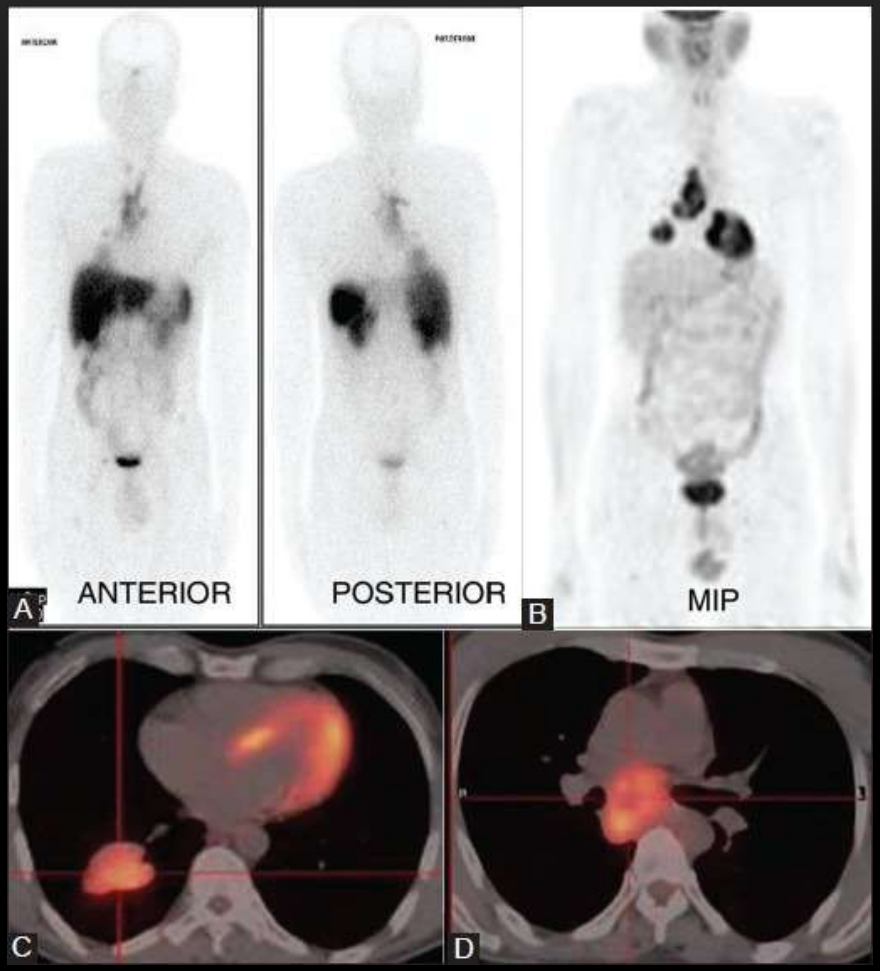
HYNIC TOC SPECT



FDG PET

Early dedifferentiated

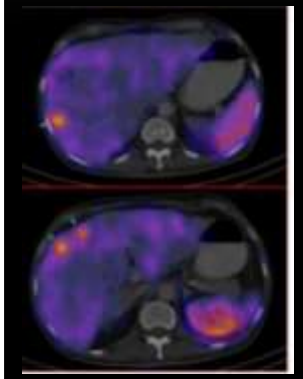
Type IV uptake pattern
Avid FDG and low somatostatin uptake

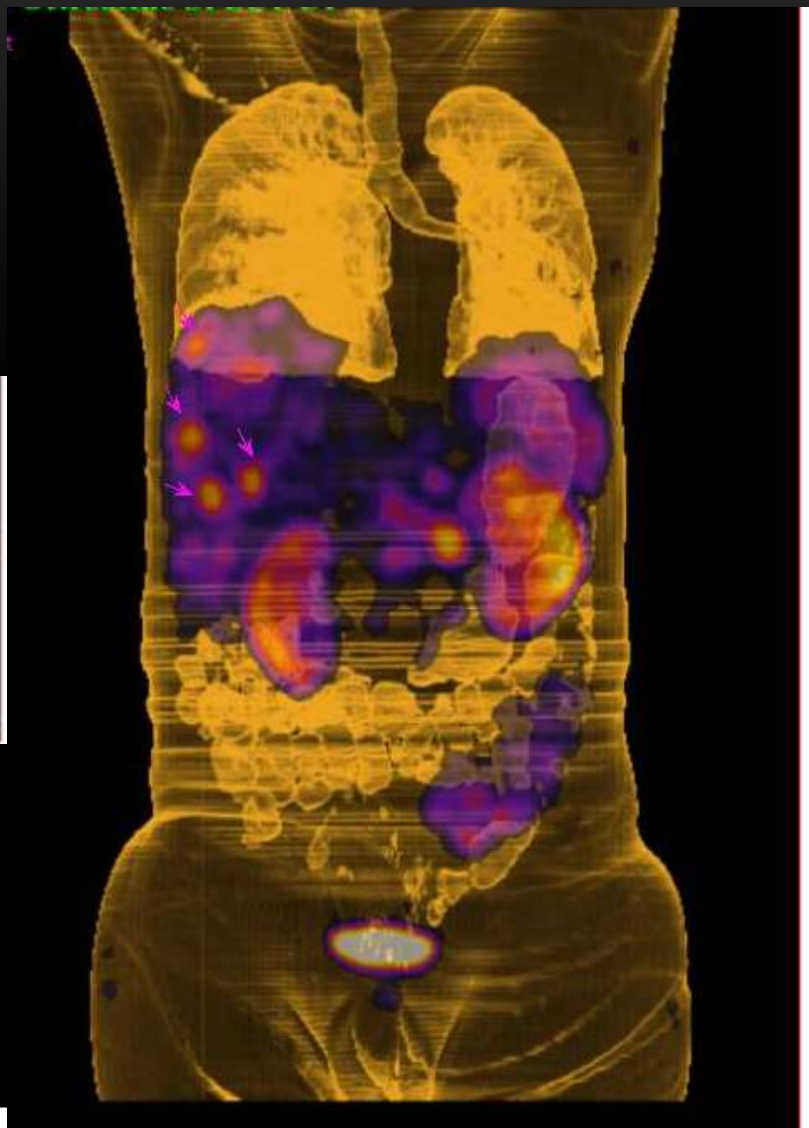


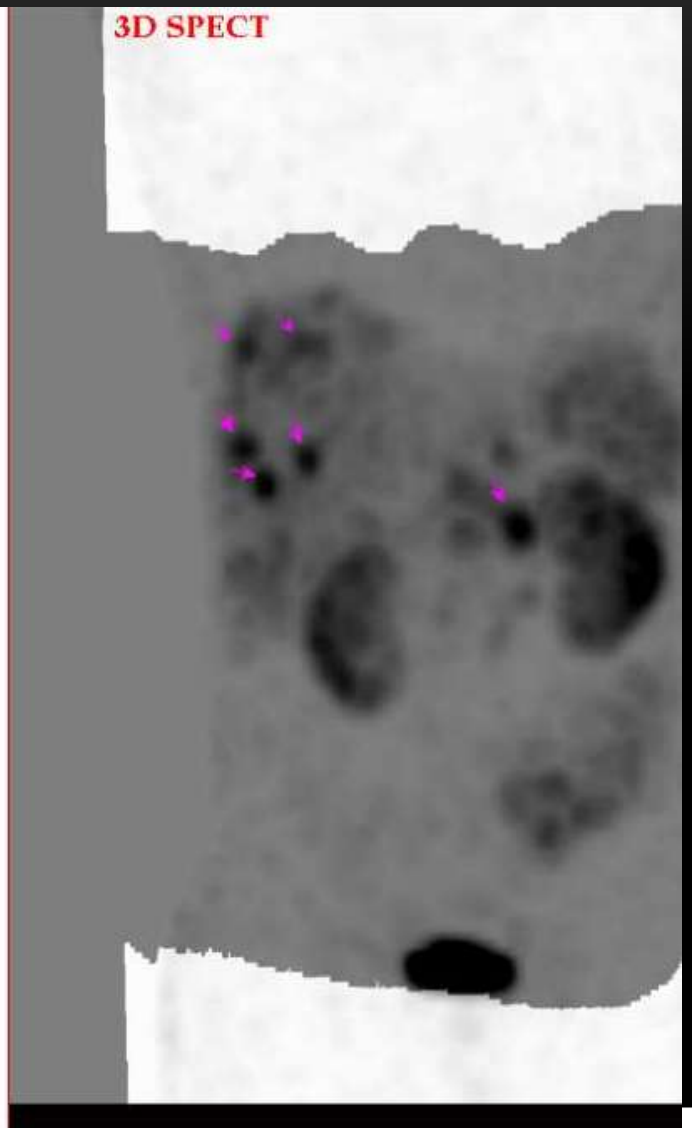
Dedifferentiated -Aggressive

Comparison Pre PRRT 99Tc HYNIC TOC and the post PRRT therapy images

Pretreatment HYNIC TOC images

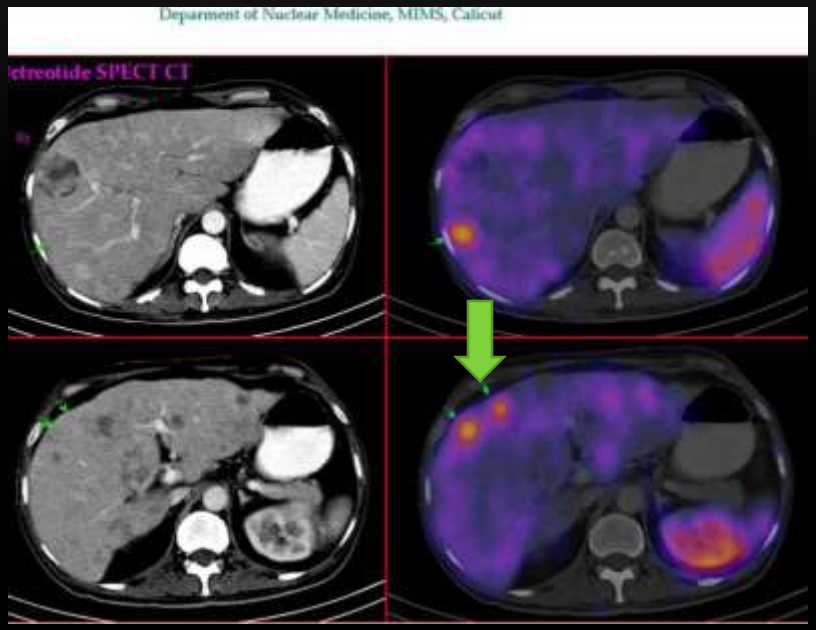




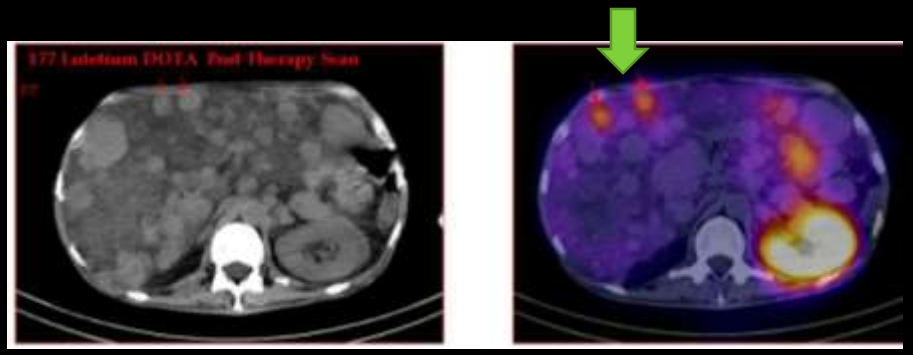


Comparison of HYNIC TOC and Lu DOTA (pre and post PRRT images)

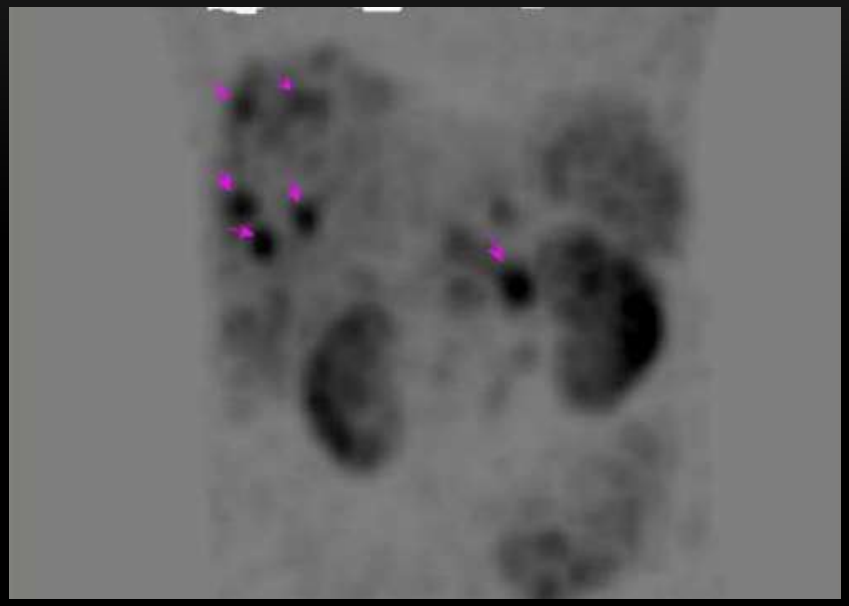
Pretreatment HYNIC TOC



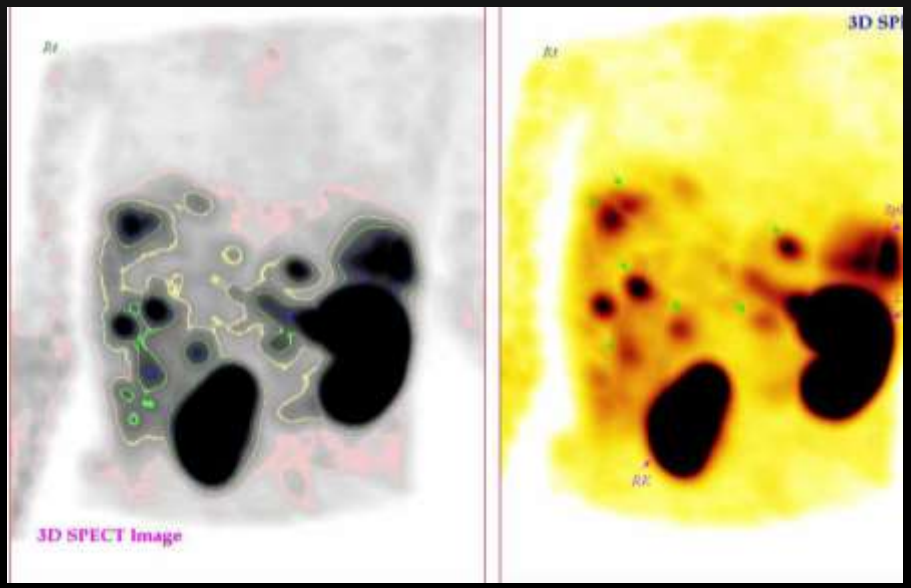
Post Lu DOTA Post Therapy Scan



Pre treatment HYNIC TOC

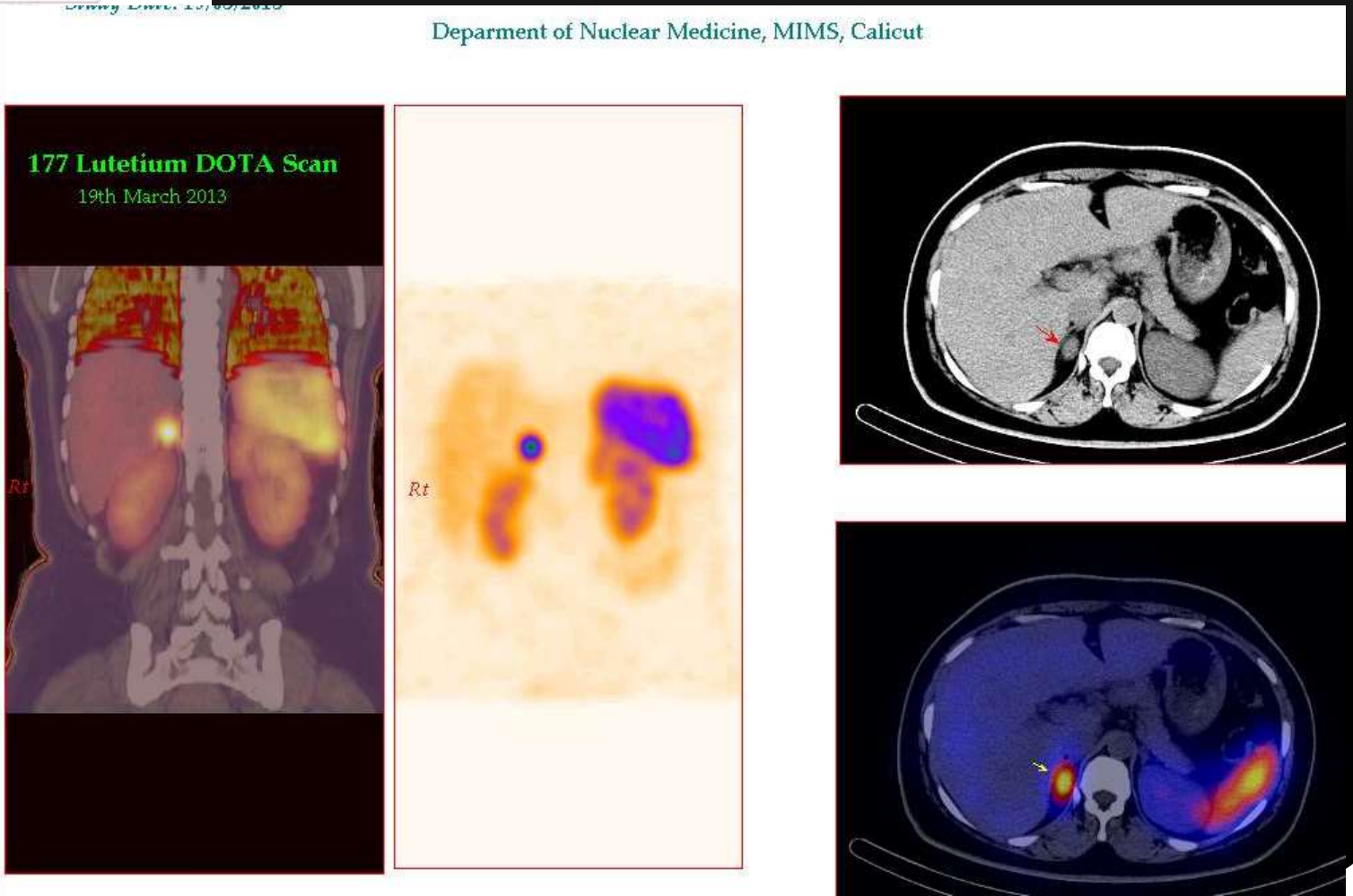


Post Lu DOTA Therapy



Intra modality imaging characteristics

177Lu DOTA Scan for Pheochromocytoma



False-positive Results

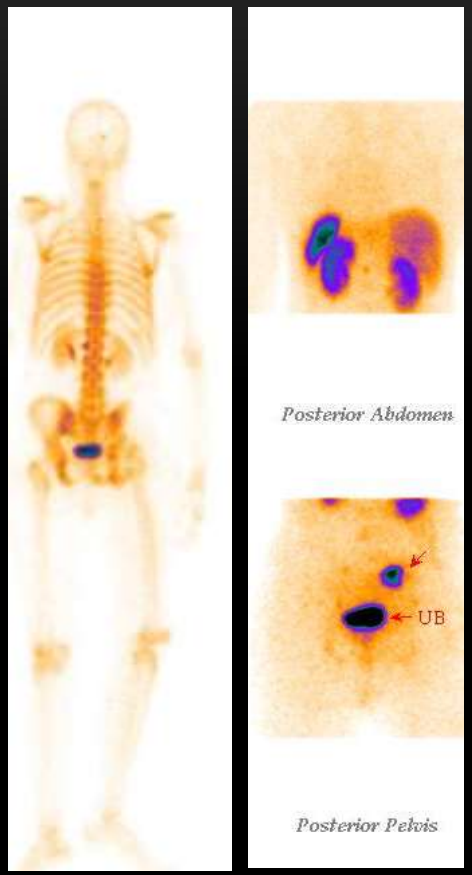
1. Autoimmune diseases (e.g., rheumatoid arthritis, Graves' disease, Graves'ophthalmopathy)
2. Bacterial pneumonia
3. CVA
4. Fibrous dysplasia
5. Granulomatous diseases (e.g., TB, sarcoidosis)
6. Post radiation inflammation

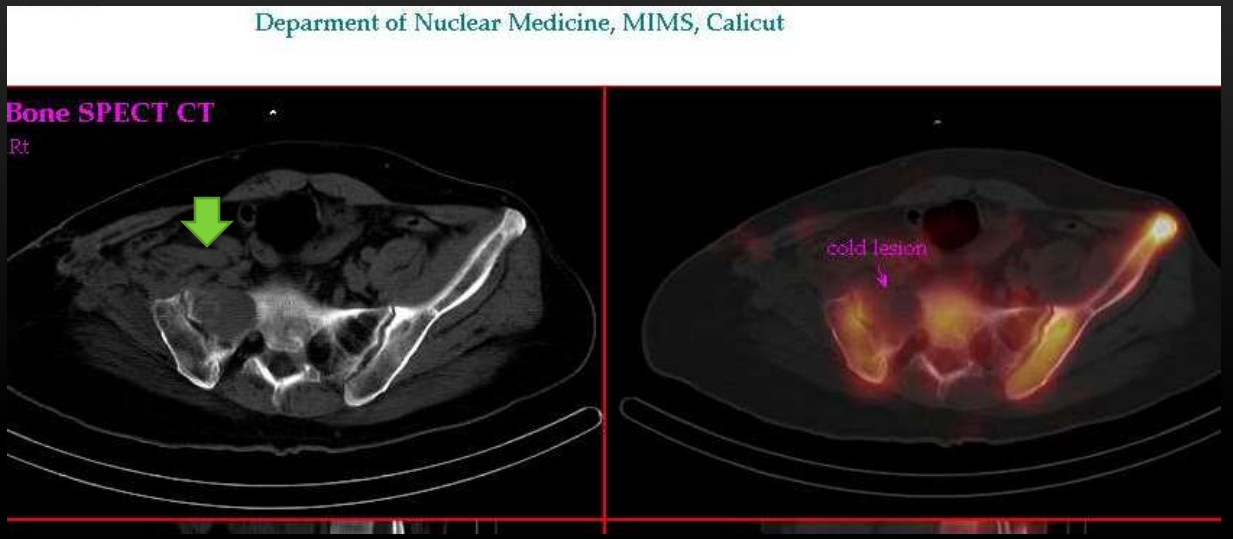
False-negative Results

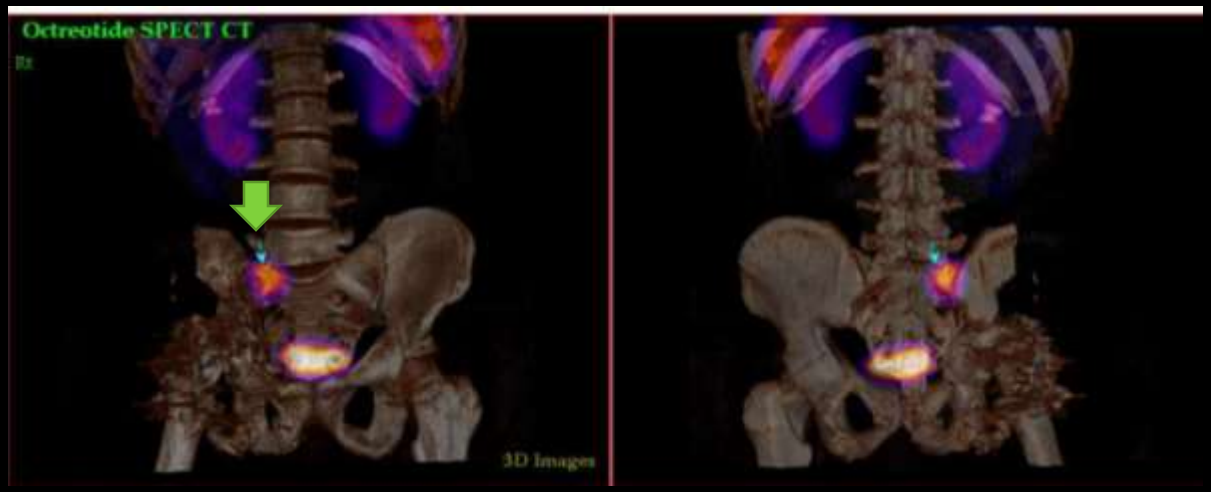
- Small size of tumors
- Tumors in adjacent area with physiologic activity
- Amount & type of SSTR present

Intra modality multiple imaging Techniques may required in some clinical cases

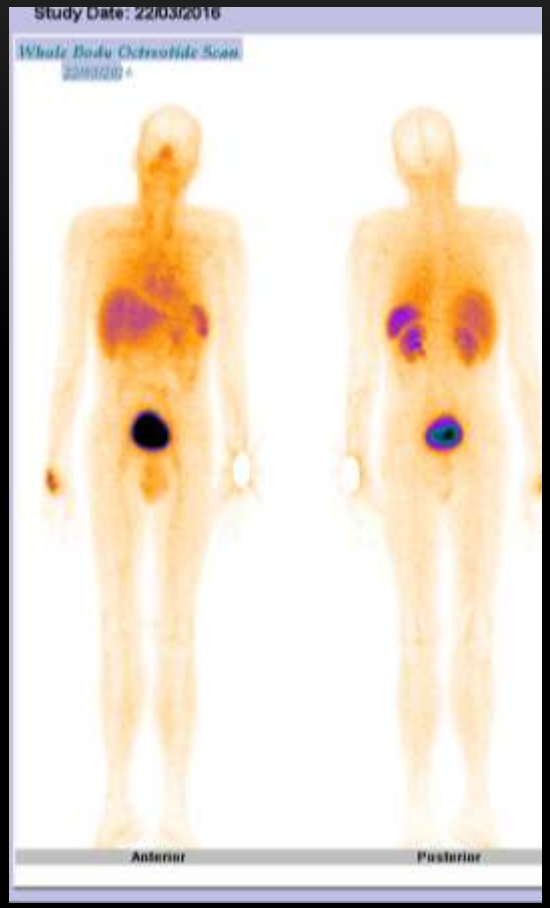
Medullary Ca Thyroid post Op recurrence- Case 1

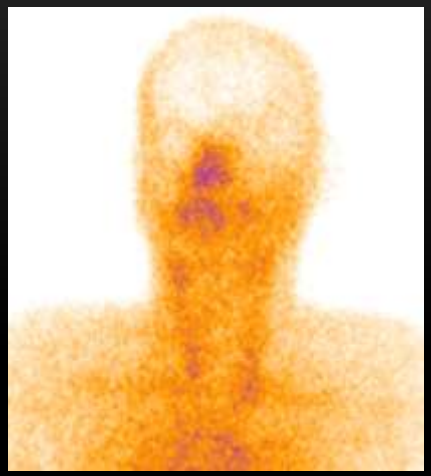




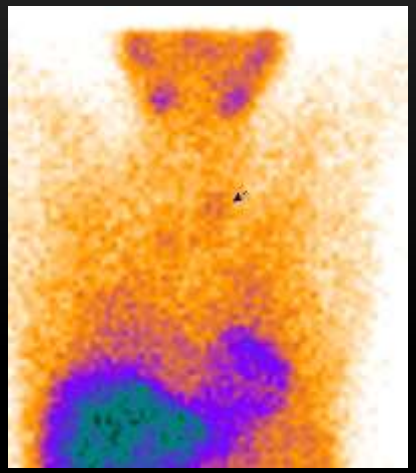


Medullary Ca Thyroid post op recurrence Case -2

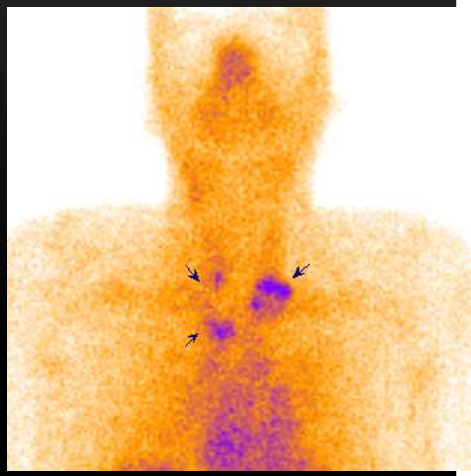




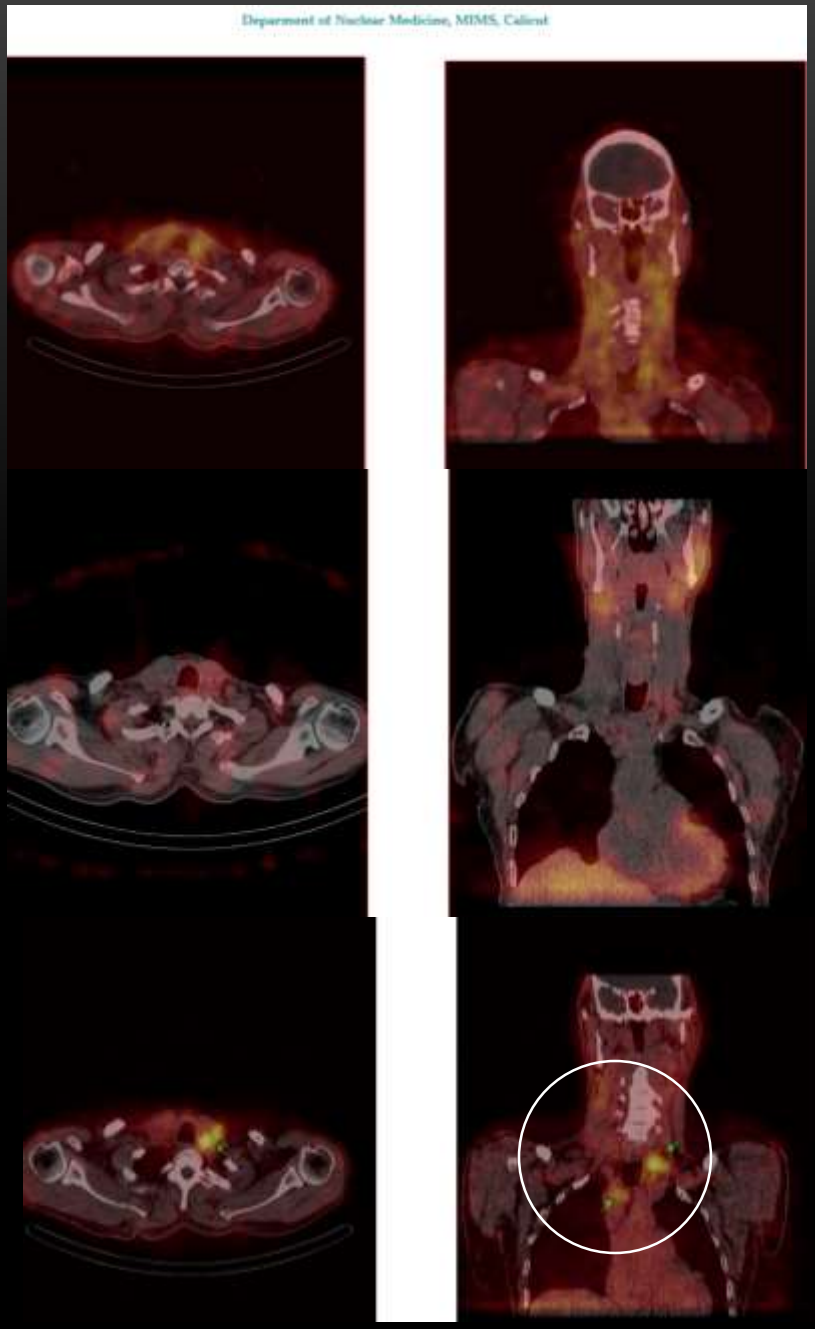
HYNIC TOC



MIBG



DMSA V



HYNIC TOC

MIBG SPECT

DMSA V

Advantages of SRS using HYNIC TOC

- Can be done all NM centers
- Can be done every day
- Superior to 111-Indium Octreotide
- Cost effective
- Lesser Radiation Dose
- Enhanced lesion detection due to SPECT CT
- Sensitivity 90%
- Quantification is possible(Target/non target) in PRRT response

Disadvantages

- Increased scan time than Ga PET
- 2 hrs,4 hrs ,6 hrs imaging
- Risk of missing small primary lesions
- Lesser sensitivity than Ga PET

Conclusion

- 99m Tc HYNIC TOC imaging is a sensitive and cost effective imaging for the early diagnosis and staging in Somatostatin expressing Tumors.
- SRS in combination with GLUT receptor imaging helps to assess the tumor receptor expression and thereby helps for prognostication.
- Helps for patient selection for PRRT
- Monitor the response of therapy
- Helps to change treatment plan in non responders at interim phase .
- Multiple intra modality methods may be needed in some conditions

Thank You..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