

# 68 Ga-DOTATATE PET/CT: TIPS AND TRICKS

- To describe radiopharmacy, normal and abnormal biodistribution of  $^{68}\text{Ga}$ -DOTATATE PET/CT;
- To review its indications;
- To describe pitfalls in interpretation and communication
- To compare it to  $^{18}\text{F}$ -FDG-PET/CT.

**<sup>68</sup>Ga-DOTATATE**

SSTRs are present on the cell surface of neuroendocrine cells and are overexpressed in some tumors, notably neuroendocrine tumors (NET).

68Ga-DOTA PET/CT is the new imaging standard of reference for the detection and characterization of NETs (particularly the well differentiated ones).

- NETs comprise a heterogeneous group of neoplasms that arise from endocrine cells within glands (adrenal medulla, pituitary, parathyroid) or from endocrine islets in the thyroid, the pancreas, or the respiratory and gastrointestinal tract;
- The majority of NETs express SSTRs, so they can be effectively targeted and visualized with radiolabelled SST analogues in vivo;
- More recently, PET with the  $^{68}\text{Ga}$ -DOTA-conjugated peptides has brought about dramatic improvements in spatial resolution and is increasingly being used in specialized centers.

## **NORMAL BIODISTRIBUTION**

This biodistribution reflects a combination of specific receptor binding and non specific tissue handling of the peptide.

## NORMAL BIODISTRIBUTION

### SSTR2-EXPRESSING ORGANS:

Pituitary

Salivary glands

Thyroid

Spleen

Liver

Adrenals/Kidney

Pancreas (uncinate  
process)

Prostate

### LOW ACTIVITY:

Lungs

### ABSENT ACTIVITY:

Cerebral Cortex

Heart

Thymus



## NORMAL BIODISTRIBUTION

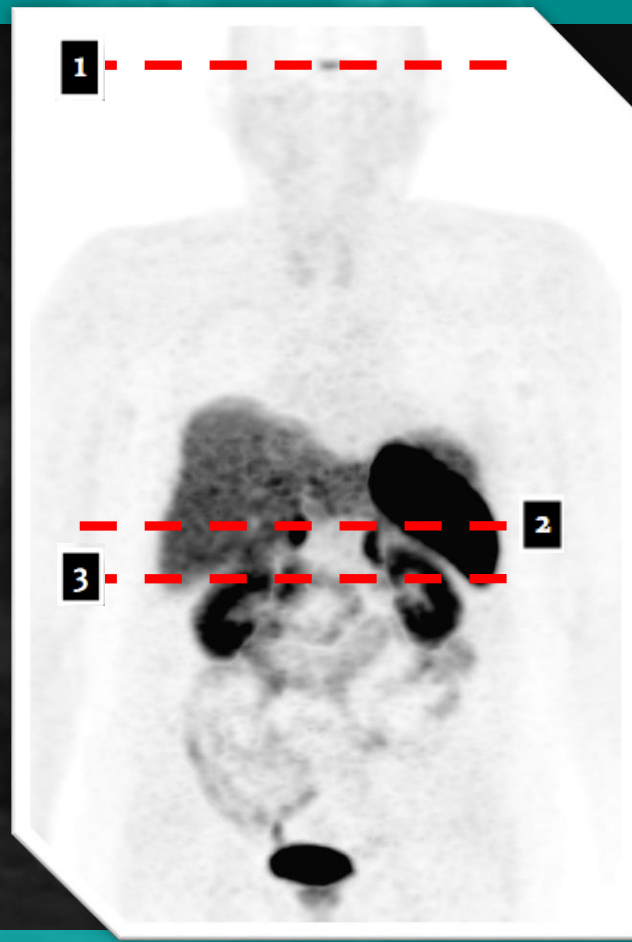
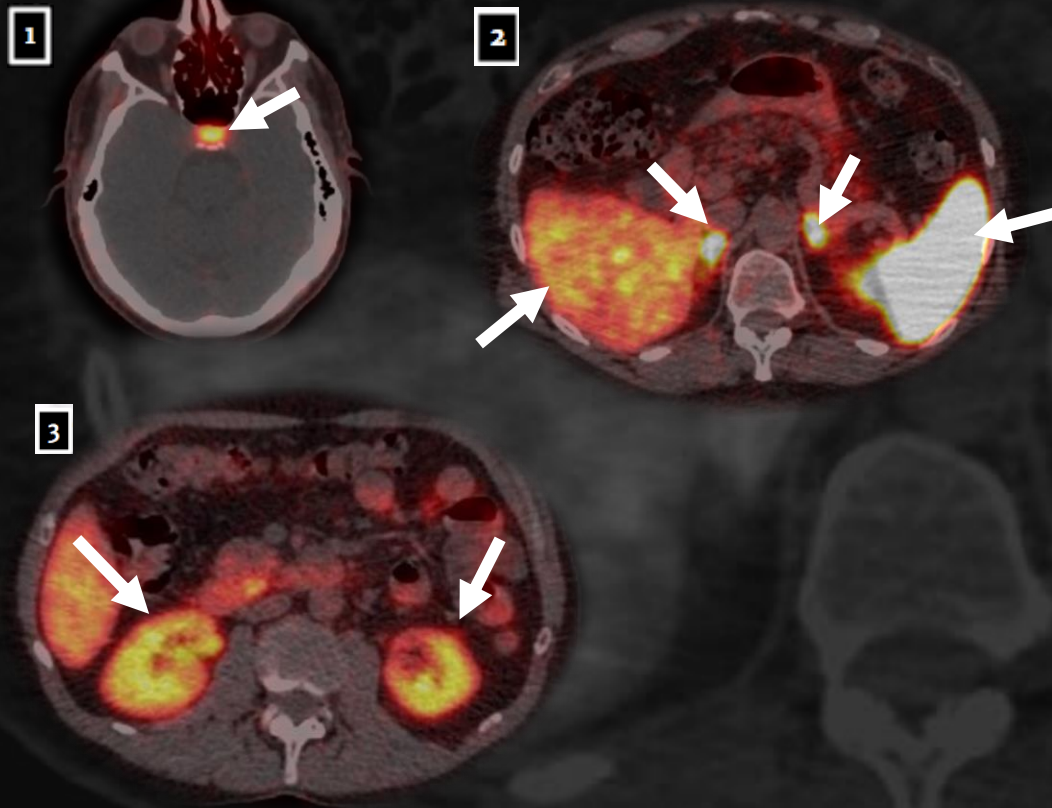
Note 1. Spleen is the highest-intensity physiologic uptake, followed by adrenal glands, kidneys and pituitary gland;

Note 2. Liver, salivary gland and thyroid have moderately intense uptake.





## NORMAL BIODISTRIBUTION

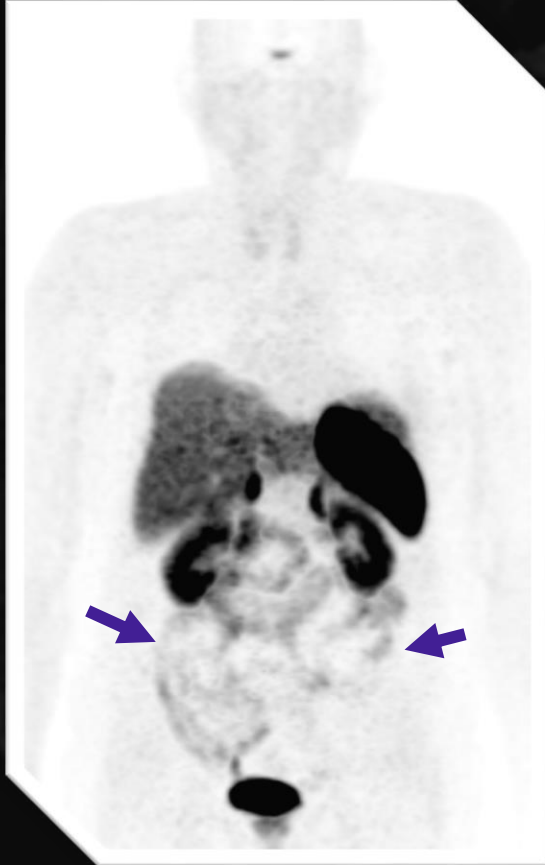






## **NORMAL BIODISTRIBUTION:** **Urinary Tract**

The peptide is small enough to be filtered through glomeruli but is also partially reabsorbed in the proximal convoluted tubule, resulting in high activity in the collecting system and bladder as well as retained activity in the renal parenchyma.



## **NORMAL BIODISTRIBUTION:** Gastrointestinal Tract

Variable physiologic uptake in the small and large intestine and gastric activity are seen, and may reflect variable degrees of neuroendocrine cell hyperplasia, since the appearance of the uptake is generally too rapid to reflect gastrointestinal excretion;

## INDICATIONS

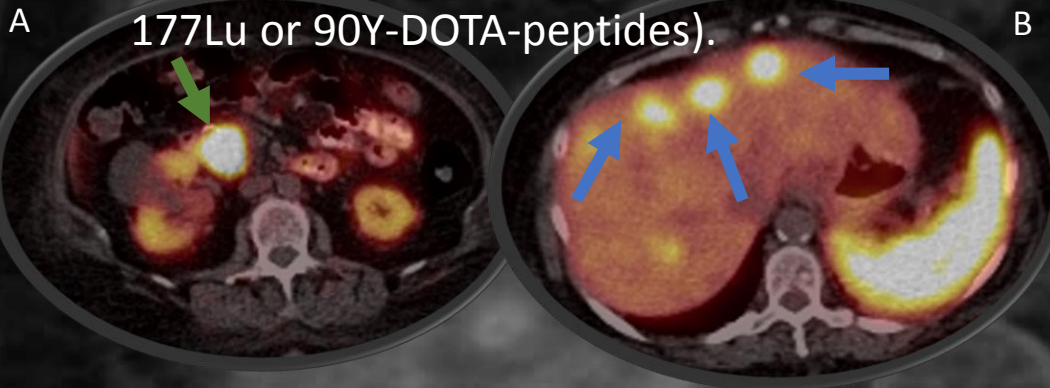
- The primary indication of  $^{68}\text{Ga}$ -DOTA PET/CT is for the imaging of NETs, which usually express a high density of SSTRs;
- It greatly impacts management by allowing identification of additional sites of disease when surgery with curative intent is being contemplated,
- There are other tumors with high levels of SSTR expression that it plays a major role: pheochromocytoma, paraganglioma, neuroblastoma, meningioma and mesenchymal tumors causing oncogenic osteomalacia.
- It can also be used in other tumors which treatment with radiolabelled therapeutic SST analogues is under consideration;

## MANAGEMENT OF NETS

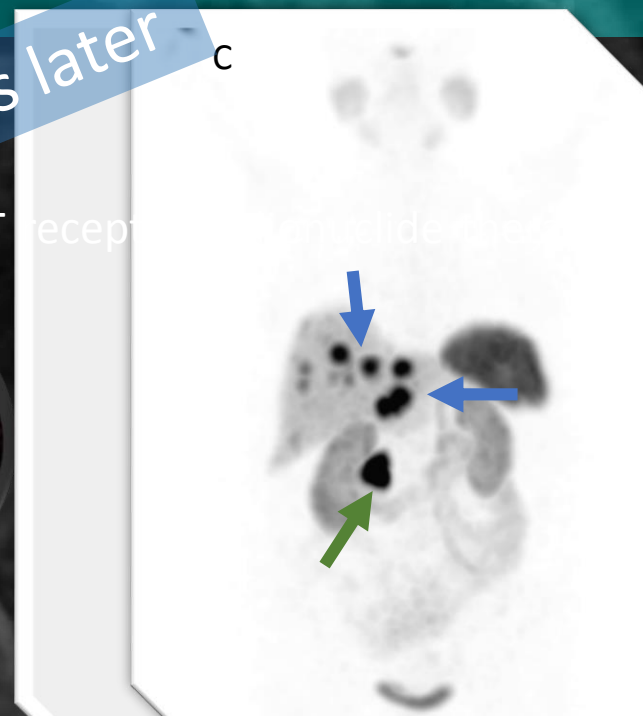
1. Localize primary tumors and metastatic disease (staging);
2. Follow-up patients with known disease to detect residual, recurrent or progressive disease (restaging);
3. Determine SSTR status visually as well by using semiquantitative parameters like standardized uptake value (patients with SST receptor-positive tumors are more likely to respond to octreotide therapy);
4. Monitoring response to therapy still needs to be assessed as the change in receptor status does not necessarily indicate therapy response and dedifferentiation with loss of receptors must be taken into account;

## MANAGEMENT OF NETS

5. Select patients with metastatic disease for SST receptor radionuclide therapy (with  $^{177}\text{Lu}$  or  $^{90\text{Y}}$ -DOTA-peptides).



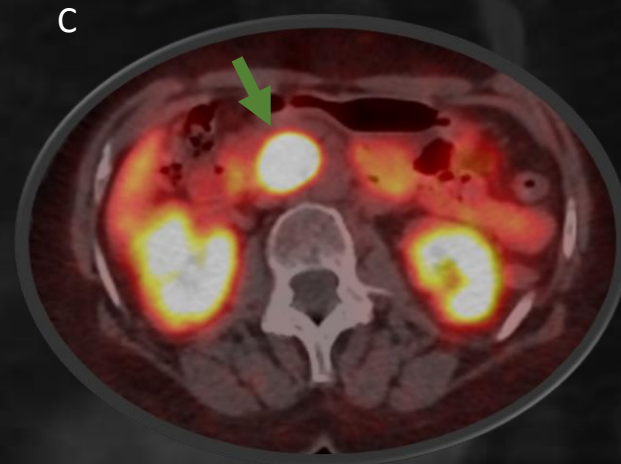
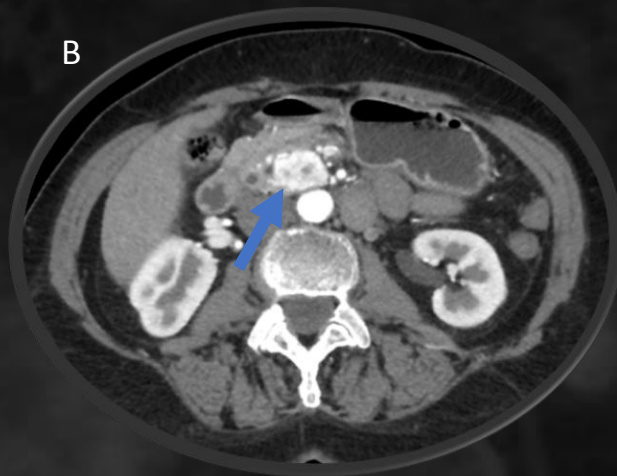
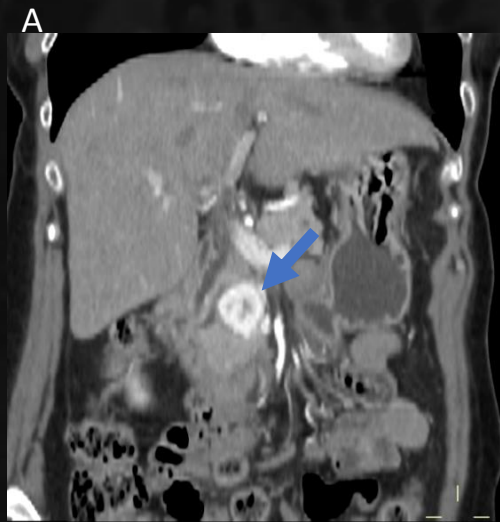
2 years later



Axial fused (a,b) and anterior maximum-intensity-projection (c) images from PET/CT scan after intravenous administration of Ga-68 DOTATATE show intense uptake of the peptide in the liver metastasis (blue arrows). The same patient two years later, after use of SST receptor radionuclide therapy, Note the good response presented here.



## MANAGEMENT OF NETS

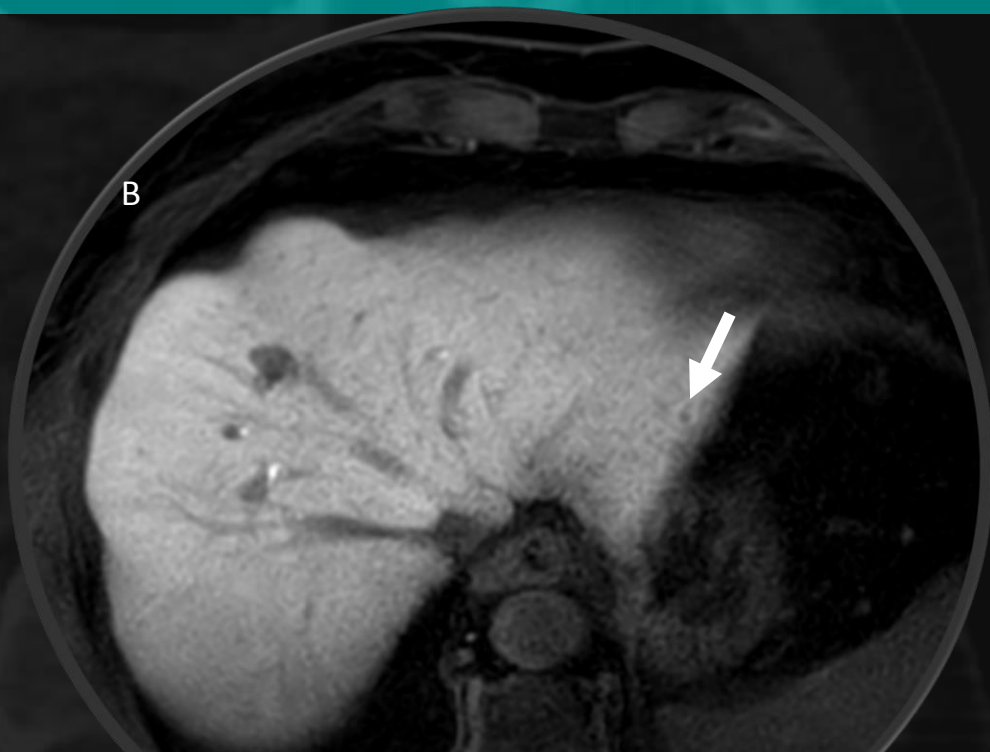
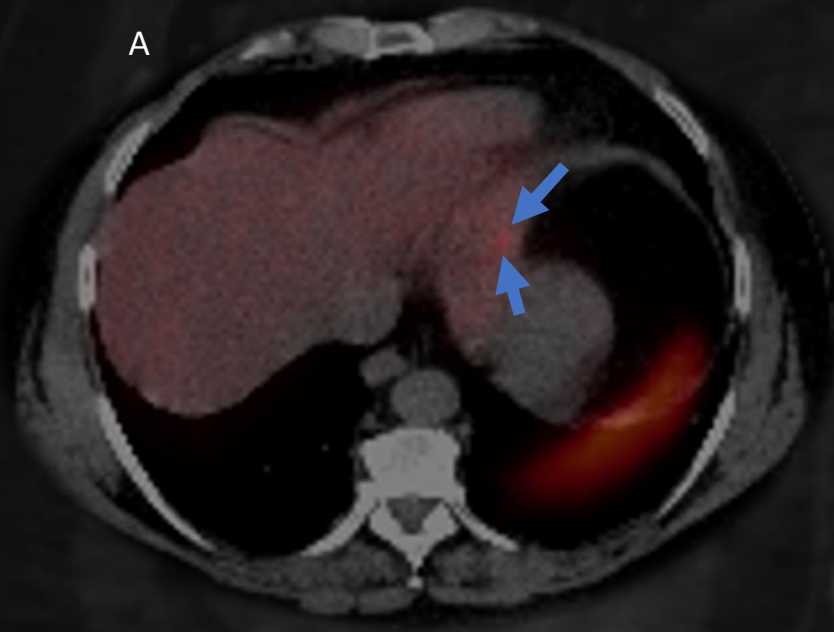


Coronal (a) and axial (b) post-contrast CT show a hypervascular pancreatic lesion (blue arrows), proved to be a NET after surgery.

Fused images from a PET scan (c) after intravenous administration of Ga-68 DOTATATE demonstrate an intense uptake of that lesion (green arrow).

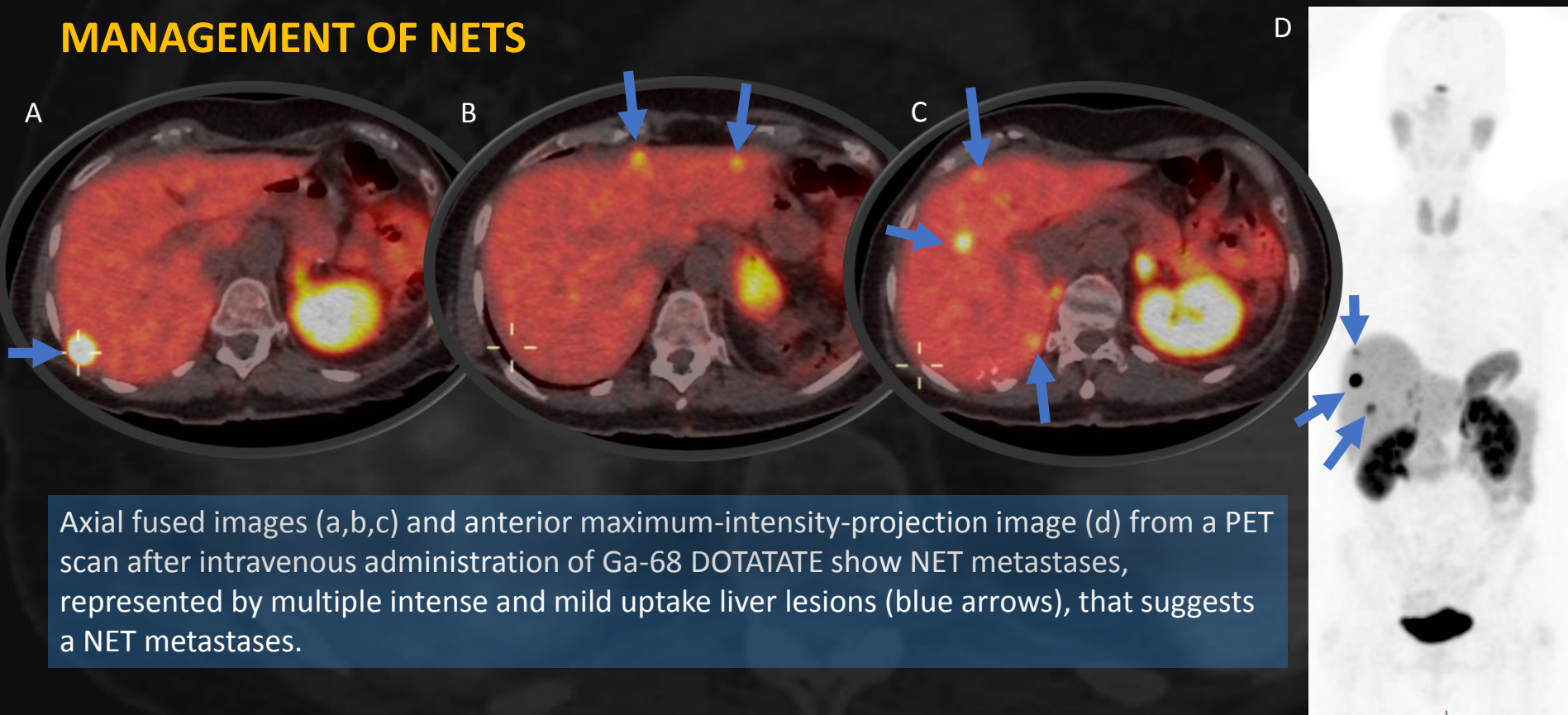


## MANAGEMENT OF NETS



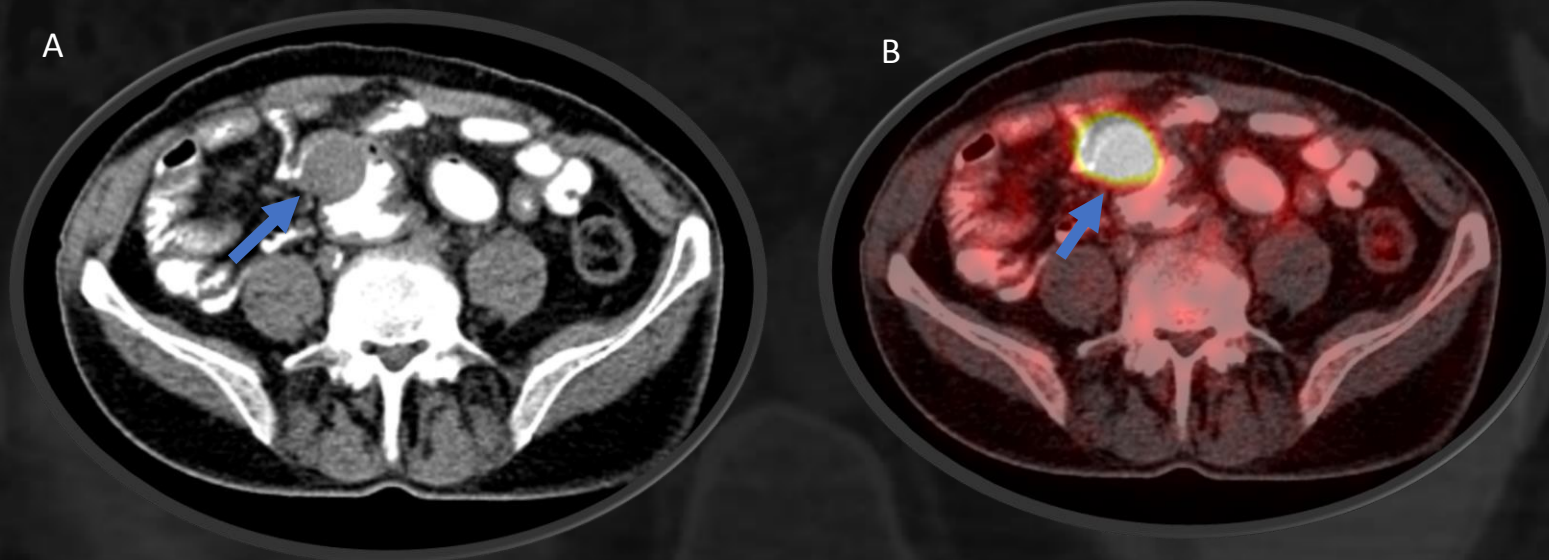
Axial fused images from a PET scan after intravenous administration of Ga-68 DOTATATE demonstrate a mild uptake within the left lobe of the liver (blue arrow), that suggests a NET metastases. Post-contrast T1W hepatobiliary phase image confirmed the small metastases (white arrow) in segment II of the liver.

## MANAGEMENT OF NETS



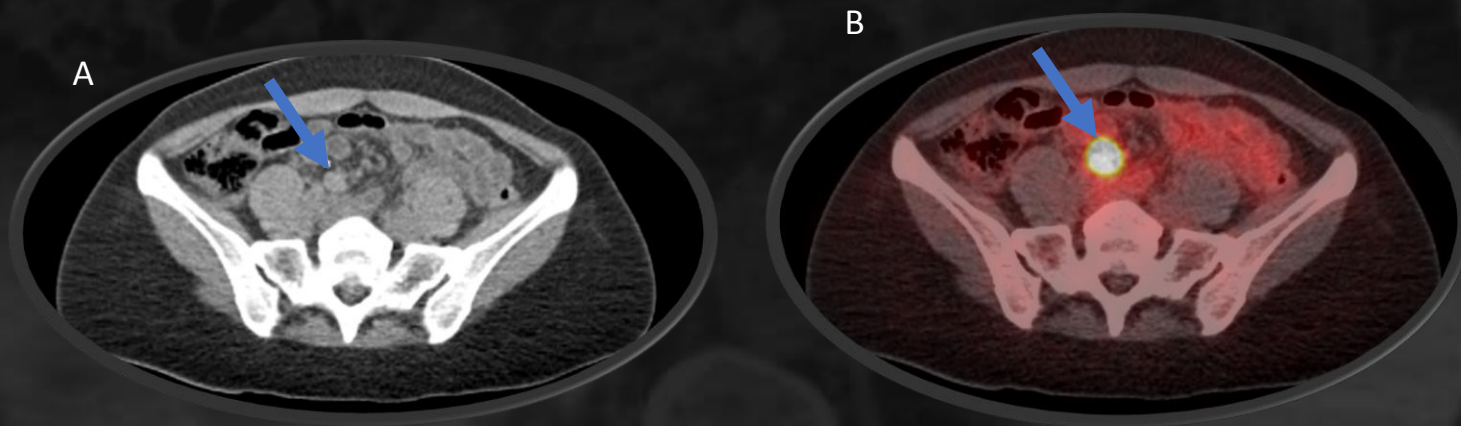
Axial fused images (a,b,c) and anterior maximum-intensity-projection image (d) from a PET scan after intravenous administration of Ga-68 DOTATATE show NET metastases, represented by multiple intense and mild uptake liver lesions (blue arrows), that suggests a NET metastases.

## MANAGEMENT OF NETS



Axial CT (a) and axial fused images from a PET scan after intravenous administration of Ga-68 DOTATATE show intestinal NET, represented by intense uptake lesion in the distal ileum (blue arrows).

## MANAGEMENT OF NETS

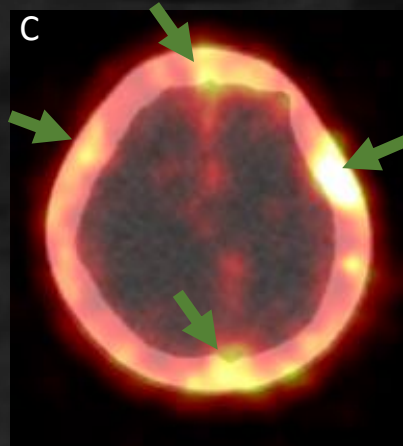
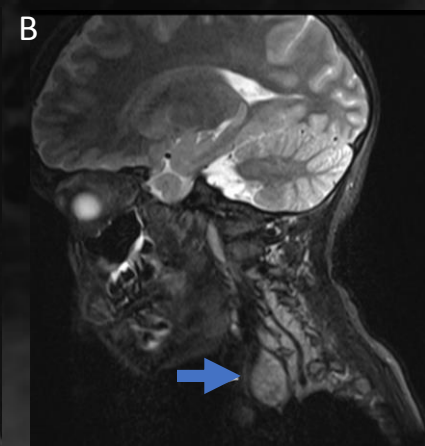
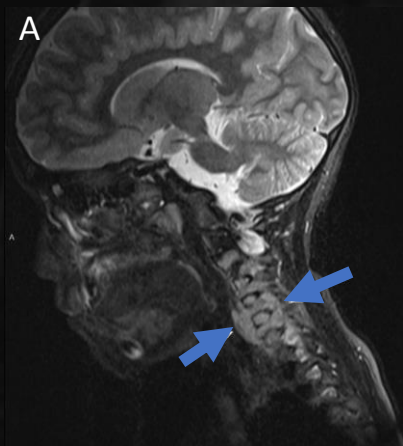


Axial CT (a) and axial fused (b) images from a PET scan after intravenous administration of Ga-68 DOTATATE show a lymph node metastasis after resection of an intestinal NET, represented by intense uptake mesenteric lymph node (blue arrows).



## TUMOURS WITH HIGH EXPRESSION OF RECEPTORS:

- Gastroenteropancreatic tumors (e.g. carcinoids, gastrinoma, insulinoma, Glucagonoma, VIPoma, etc.);
- Ewing sarcoma; and nonfunctioning sympathoadrenal system tumors (pheochromocytoma, paraganglioma, neuroblastoma, ganglioneuroma);
- Medullary thyroid carcinoma;
- Sarcoid adenoma;
- Renal cell carcinoma;
- Differentiated thyroid carcinoma & Astrocytoma;
- Spinal cord cancer (mainly primary tumors);
- Meningioma



## Multiple metastases of neuroblastoma:

- Sagittal T2W MRI (a, b) revealed two cervical masses (blue arrows).
- Axial fused (c) and anterior MIP (d, e) images from a PET scan after intravenous administration of Ga-68 DOTATATE shows extensive bone and spine metastases represented by mild and intense uptake (green arrows).



## PITFALLS

Radiologist must be aware of various **physiologic** and other **pathologic processes** in which cellular expression of SSTR can result in interpretative error.

Most of these processes demonstrate low-intensity and/or nonfocal uptake, in contrast with the focal intense abnormality encountered in NETs.

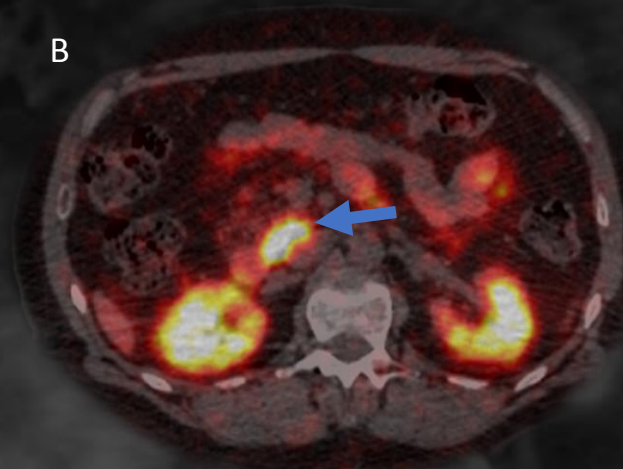
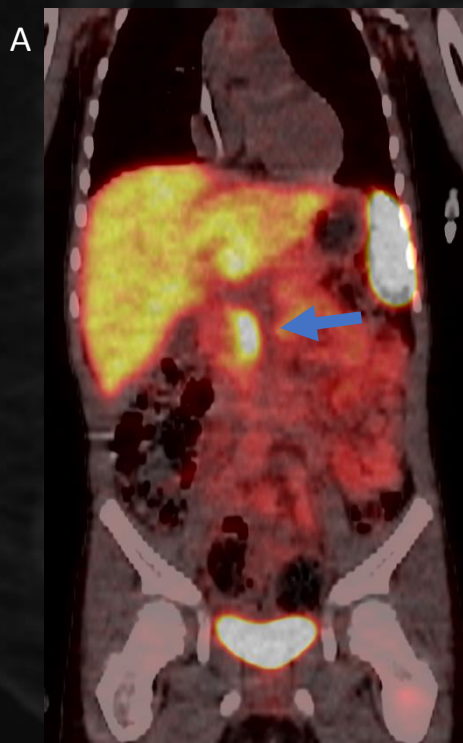
### Causes of interpretative pitfalls include:

- Prominent pancreatic uncinate process activity;
- Splenunculi or splenosis;
- Osteoblastic activity (degenerative bone disease, fracture, vertebral hemangioma);
- Inflammation;
- Benign meningioma.

## PROMINENT PANCREATIC UNCINATE PROCESS UPTAKE

- Intense physiological uptake visualized in up to one-third of patients:
- Curvilinear morphology or ill-defined edges: that help distinguish it from the focal well-defined abnormalities seen in pathologic uptake;
- Potential pitfall for radiologists or physicians who are more experienced with octreotide imaging, with which this finding is rarely seen.

## PROMINENT PANCREATIC UNCINATE PROCESS UPTAKE



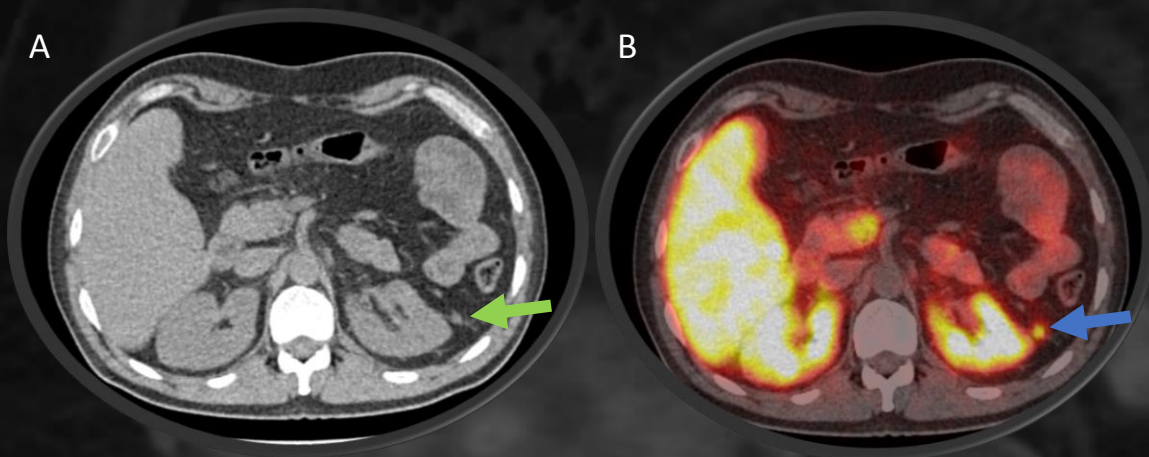
Coronal (a) and axial (b) fused images after intravenous administration of Ga-68 DOTATATE demonstrate an intense uptake of the uncinus process (blue arrows). Axial NECT image demonstrates a normal uncinus process, without any lesion.

## SPLENOSIS

- Splenectomy is commonly performed in patients with pancreatic NET (necessity of excising it when performing enbloc resection of the pancreatic tail);
- Splenosis is a common finding at restaging, and nodular splenosis can be mistaken for peritoneal metastases at anatomic imaging and 68Ga-DOTA PET/CT because, like the normal spleen, these nodules demonstrate very intense uptake;
- Thus, particularly in patients who undergo interval splenectomy, intense uptake in new, well-defined, round, peritoneal soft-tissue nodules may be due to splenosis;
- If there is uncertainty, denatured red blood cell SPECT/CT can help to characterize such lesions.



## SPLENOSIS

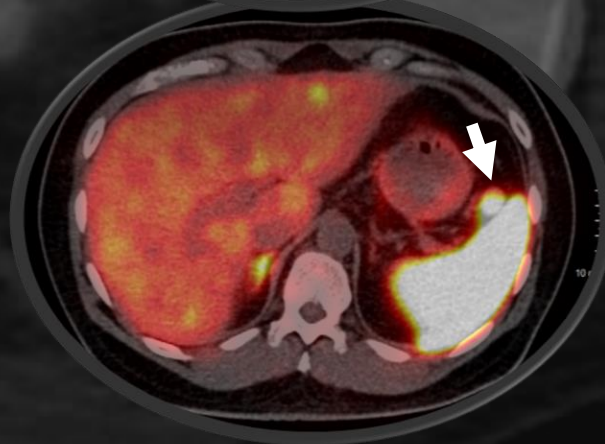


Patient who underwent distal pancreatectomy and splenectomy due to pancreatic tail NET: Axial pre-contrast CT (a), axial fused and anterior MIP images after intravenous administration of Ga-68 DOTATATE (b) demonstrate a well-defined and round nodule (green arrow), with mild focal uptake on the spleen topography (blue arrows). These findings suggest splenosis and can lead to a false-positive result.



## SPLENUNCULI

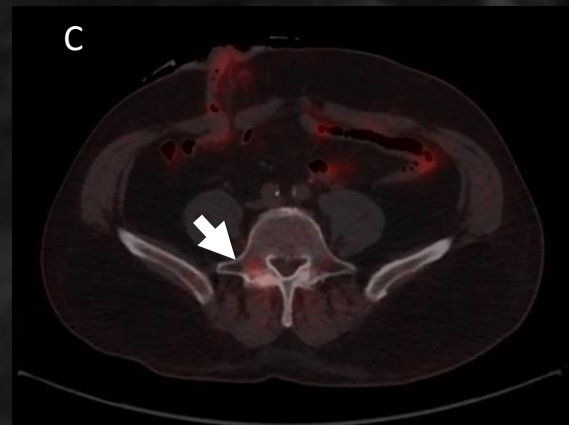
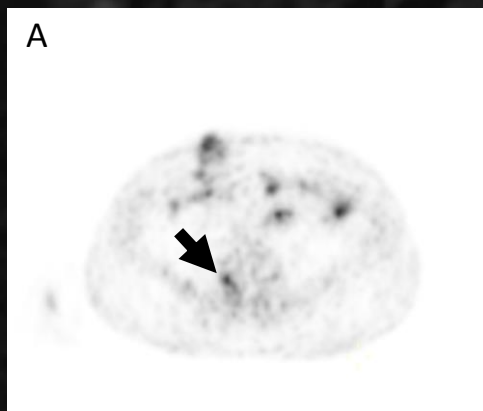
- In patients who do not undergo splenectomy, 80% of accessory spleens occur at the splenic hilum, although they may arise anywhere in the peritoneal cavity.
- Splenunculi usually have lower-intensity uptake than the spleen;
- Intrapancreatic splenunculus is another potential cause of false-positive  $^{68}\text{Ga}$ -DOTA PET/CT findings.



## OSTEOBLASTIC ACTIVITY

- Osteoblastic osseous processes demonstrate uptake at 68Ga-DOTA PET/CT, since osteoblasts express SSTR 2.
- Degenerative bone disease, fractures, fibrous dysplasia, and vertebral hemangiomas all demonstrate uptake, but these entities are readily distinguished from pathologic activity by virtue of their low- or very low- intensity uptake and consistent features on the CT component of the study.
- Epiphyseal growth plates in children also demonstrate a low to moderate increase in activity.

## OSTEOBLASTIC ACTIVITY

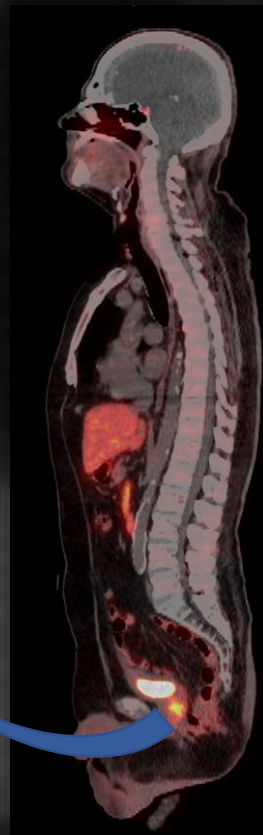
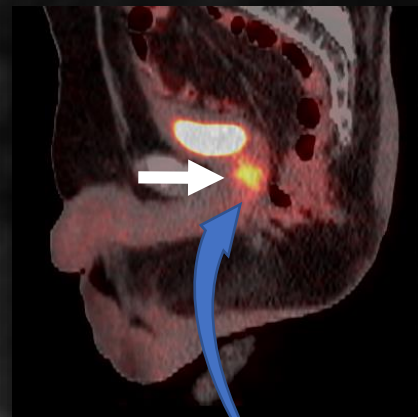
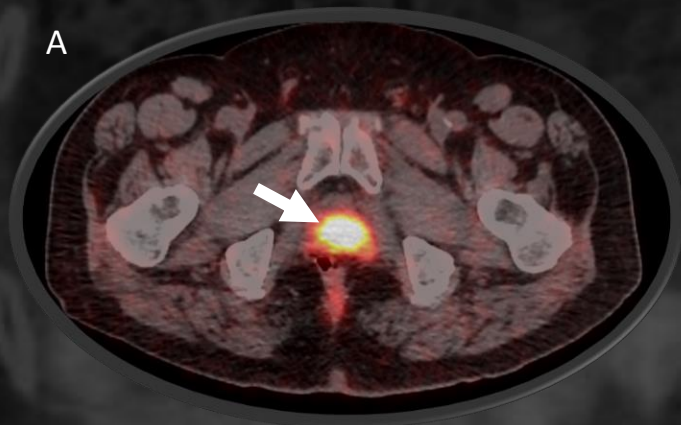


Axial (a) and axial fused (b; c) images after intravenous administration of Ga-68 DOTATATE demonstrate a low uptake of the right interapophyseal joint, degenerative.

## INFLAMMATORY PROCESSES

- White blood cells express SSTR 2, and some researchers have used this phenomenon to help image in inflammatory processes such as atherosclerotic plaques with SSTR PET/CT;
- Inflammatory uptake is invariably low or very low grade and is most commonly seen in reactive hilar, mediastinal, axillary or inguinal nodes;
- Inflammatory uptake is also commonly observed in prostatitis or post-radiation therapy change, although any inflammatory process may demonstrate some  $^{68}\text{Ga}$ -DOTA PET/CT activity.

## INFLAMMATORY PROCESSES



Axial(a) and sagital(b) fused images after intravenous administration of Ga-68 DOTATATE demonstrate a moderate uptake of the prostate due to a prostatitis.



## 68Ga-DOTA PET/CT versus FDG PET/CT

- 68Ga-DOTA PET/CT and FDG PET/CT are complementary and help to identify both well- and poorly differentiated phenotypes, thereby allowing tumor characterization, prognostication, and better selection of appropriate therapy for individual patients;
- Compared with other nuclear medicine studies, including FDG PET/CT, 68Ga-DOTA PET/CT has extraordinary target-to-background contrast, such that subcentimeter abnormalities that cannot be identified at conventional imaging can easily be identified;



## 68Ga-DOTA PET/CT versus FDG PET/CT

- In addition to helping detect disease sites, molecular imaging offers the key advantage of being able to help characterize disease;
- This high lesion contrast is reflected in high standardized uptake values (SUVs), which are significantly greater than those seen with other PET radiotracers, including FDG.

- GaTate PET/CT has an array of clinical applications in gastroenteropancreatic and other NETs, in which it is proving to represent a new standard of reference given its superior accuracy compared with conventional imaging techniques;
- The strength of 68Ga-DOTA PET/CT lies not only in its high sensitivity, but also in its ability to characterize whole-body SSTR expression, which confers a high specificity;
- This allows the selection of patients with metastatic disease for hormonal therapy or PRRT.
- FDG PET/CT plays a complementary role by helping to identify sites of poorly differentiated disease on the basis of their higher proliferation rate;
- In selected patients, the use of both techniques can elegantly demonstrate tumor heterogeneity, which can be pivotal in guiding biopsy and selecting optimal management for individual patients.

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