Ga-68 PET

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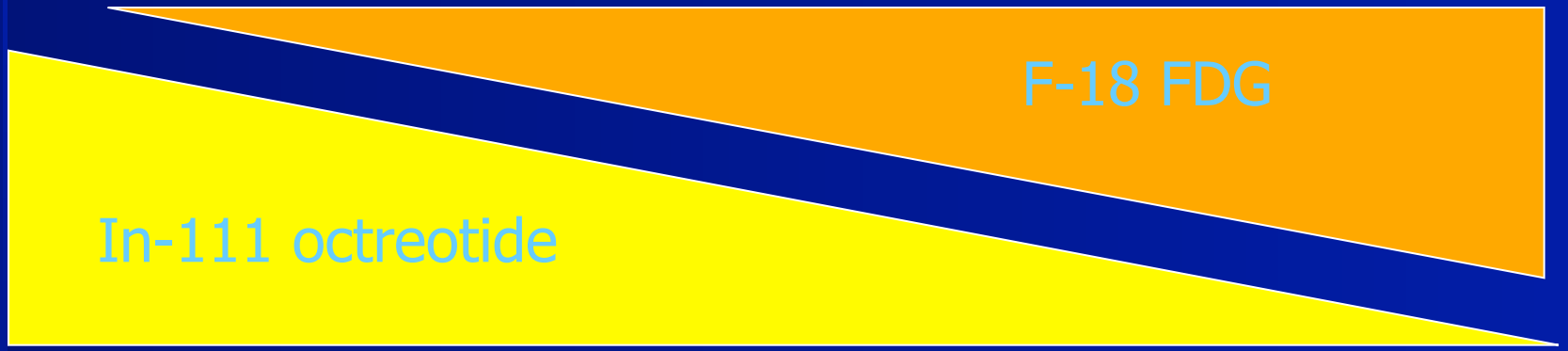
Introduction

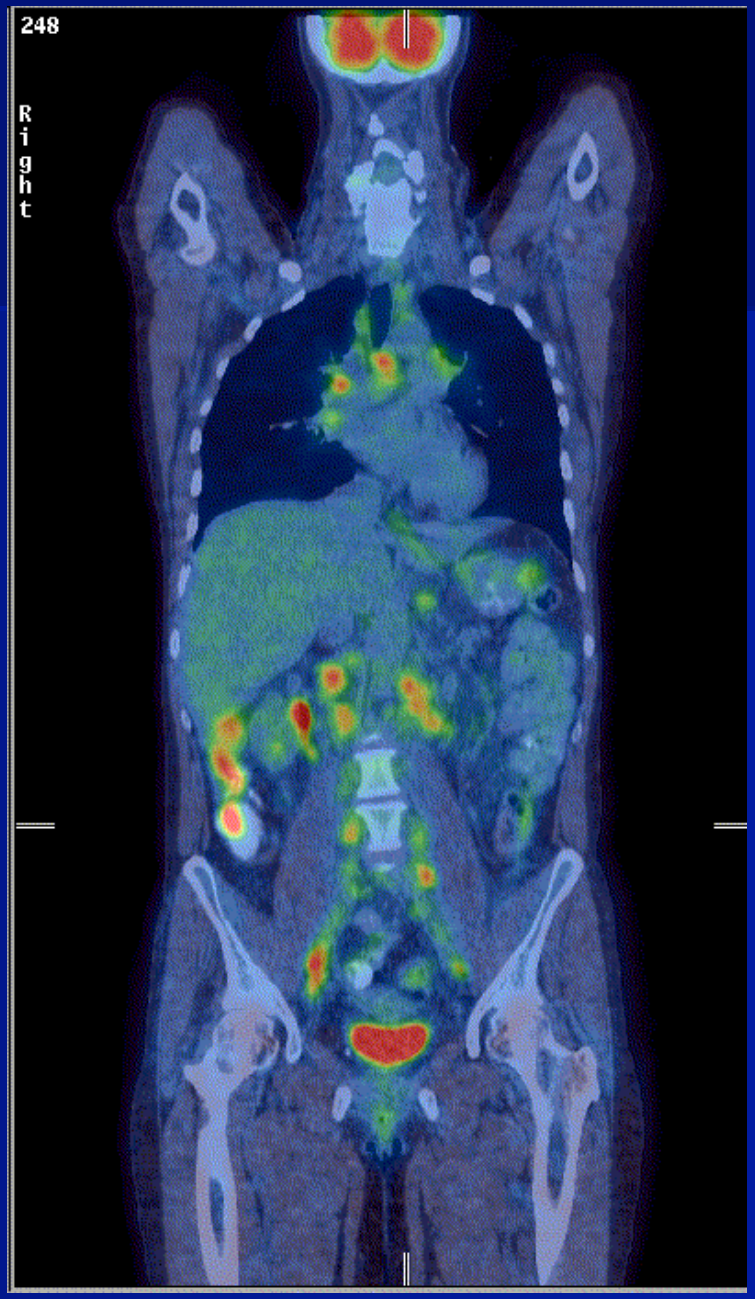
- Ga-68 a new radionuclide
- PET based
- Chemistry can be difficult
- Used primarily with DOTATATE
- Now also used with other agents

In-111 octreotide v F-18 FDG in NET patients the ying and yang of cancer



More benign ---→ More malignant

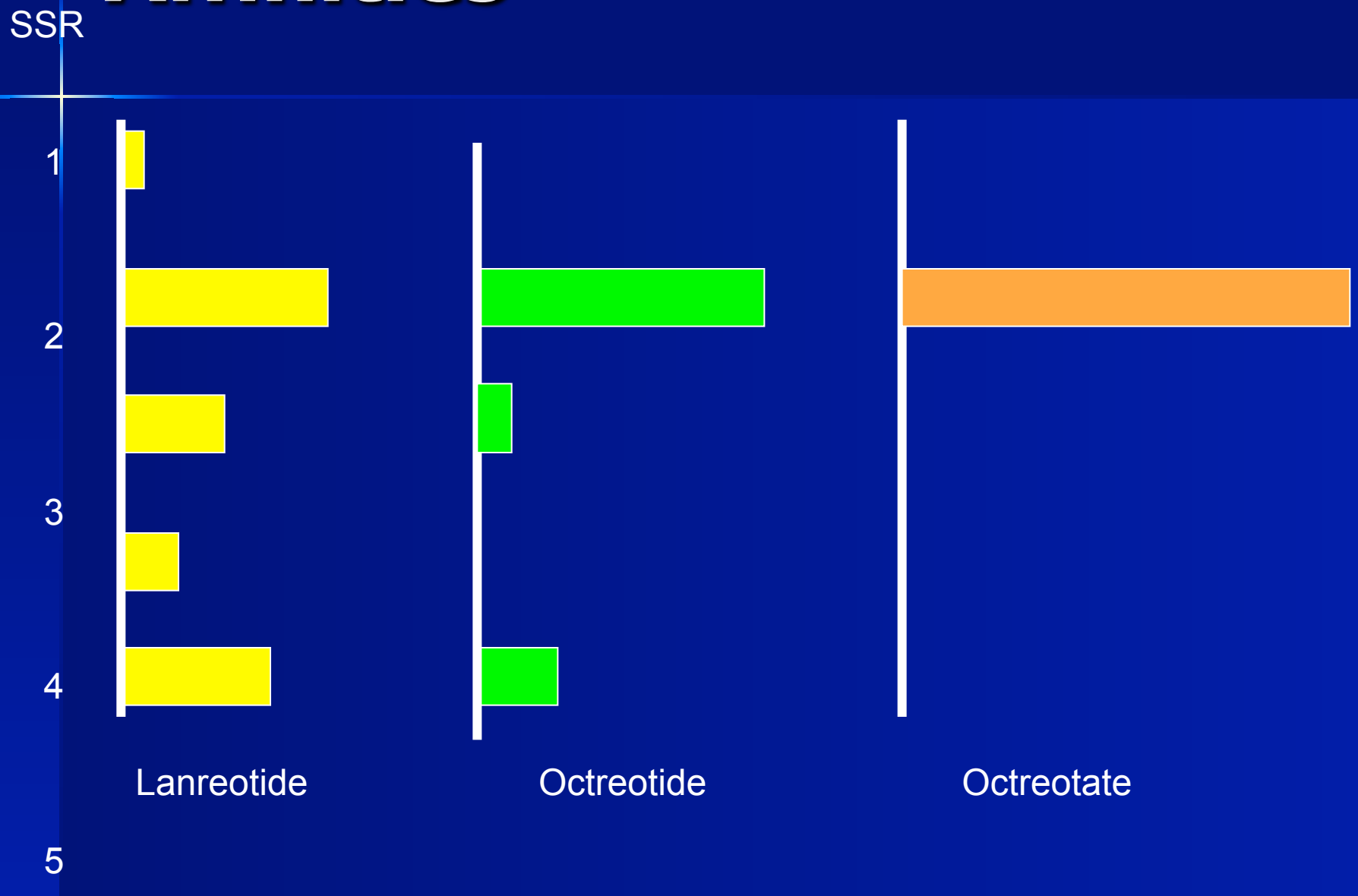
PET-CT showing multiple sites of F-18 FDG uptake in nodes involved with disseminated pancreatic non-secreting NET



How can we improve SRS

- We can improve affinity of the peptide for the tumour site
- octreoTATE >octreoTOC >octreotide >lanreotide
- Can we find a radioisotope with PET capabilities (F-18 not a stable labeller of peptides).

Affinities



What is Ga-68 DOTATATE

- Ga-68
  - Short lived daughter of Ge-68
  - Therefore generator produced
  - Half life 68 minutes
  - Positron emitter
- DOTA
  - Linker molecule
- TATE
  - Alcoholised somatostatin analogue
  - Very high affinity for SSR2 (10x-100x octreotide)

Ga-68

Development of Ga-68 DOTATATE

- Ge-68/Ga-68 used for AC for PET before CT based systems
- Ga-68 been used in-vivo since 1983
- Ga-68 IDA for PET Hidas
- Ga-68 EDTA for PET renograms
- Ga-68 mercapatobenzyl-amine for cardiacs
- Ga-68 anti-MUC1 in breast cancer

Ge-68/Ga68 generator

- Ge-68 generator 127 day half life
- Made in Russia and ?South Africa
- Can be eluted 1-2 times a day
- First eluate up to 500GBq
- Ge-68 breakthrough low (<0.02%)
- Can be eluted in 12 minutes
- Needs fast chemistry (automated machines)

iThemba generator

- Made in South Africa
- Still not in routine production
- About 10cm high and 6cm in diameter
- Still need to get DOTATATE/
- DOTATNOC

^{68} Germanium / ^{68} Gallium generator specifications

^{68}Ga

Application

^{68}Ge/^{68}Ga generator (half-life:270 days) provides an excellent source for the positron-emitting radionuclide ^{68}Ga (half-life 68 min). ^{68}Ga is mainly used for radiolabelling peptides which is used chiefly in nuclear medicine oncology for diagnostic or therapeutic applications

Manufacture of parent radionuclide (^{68}Ge)

Accelerator , ^{69}Ga(p,2n)^{68}Ge

Column material /packing

Modified tin dioxide in a polyethylene column with polyethylene tubing with no metal parts

Eluent

0.6M HCl (suprapure)

^{68}Ga yield in 5 ml of eluent

not less than 80%

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From Atom to Image

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Ga-68 somatostatins

- Since 2001 Ga-68 somatostatins used in NET and brain primaries
- Work centred on Hanover, Heidelburg and Basel
- 84 patients imaged with Ga-68 DOTATATE and In-111 pentetreotide JNM 2007 from Innsbruck
- Sensitivity 96% compared with 65% with In-111 pentetreotide

Comparison of In-111 pentetreotide with Ga-68 Dotatate PET /computed tomography uptake patterns in patients with Neuroendocrine tumours

R Srirajaskanthan, J Bomanji, A-M Quigley
I Kayani, **ME** Caplin, JNM 2010
Royal Free Hospital and University College London Hospital, London UK.

Background

- Ga-68 Dotatate is a relatively new PET tracer with affinity for SSR2
- Routine In-111 Octreotide (pentetreotide, SSR 2,5 and 3) scans performed as general work-up in our NET patients and many also have Ga-68 Dotatate PET/CT
- Impression of more lesions on Ga-68 Dotatate PET/CT

Aim

- Compare In-111 Octreotide (pentetreotide) with Ga-68 DOTATATE PET/CT uptake patterns in patients with histologically confirmed neuroendocrine tumours
- Determine whether uptake related to tumour histological grade

Methods

- Images from the two studies were retrospectively compared lesion by lesion (both scans performed within 4 month window)

- categorized accordingly

  both studies positive, Ga-68 more lesions
  both studies positive, In-111 more lesions
  both studies similar lesions
  pos Ga-68, negative In-111
  pos In-111, neg Ga-68
  both studies negative

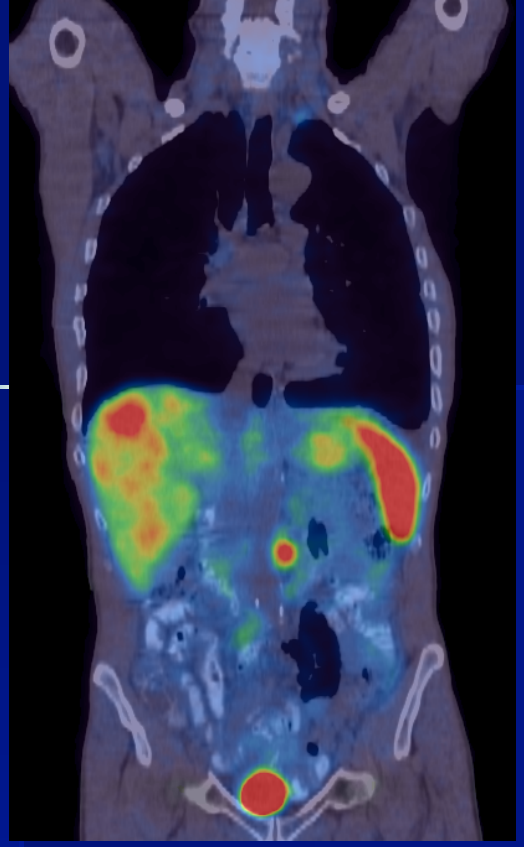
- The tumour histological grade was also recorded.

Results

- 44 patients included
  - 17 foregut
  - 21 midgut
  - 1 hindgut
  - 3 unknown origin
  - 2 other NET types
- 1 patient no SPECT performed : technical problem
- Ga-68 positive in 37, In-111 positive in 26

RESULTS

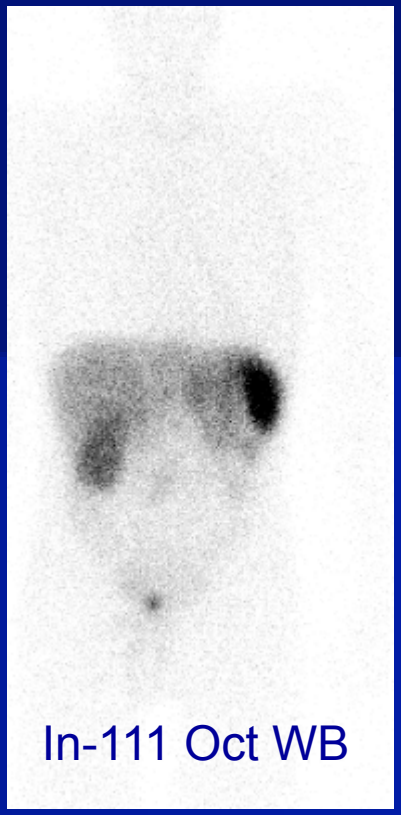
SCAN APPEARANCE	N=44
both studies positive, Ga-68 more lesions	18
both studies positive, In-111 more lesions	1
both studies similar lesions	7
pos Ga-68, negative In-111	11
pos In-111, neg Ga-68	0
both studies negative	7



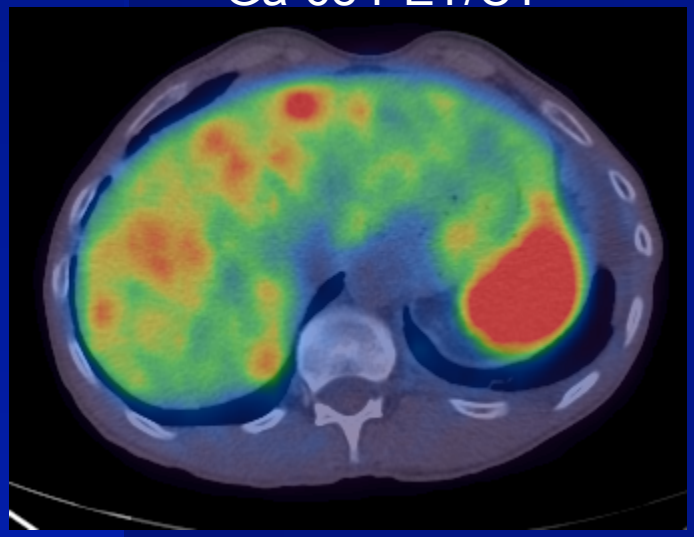
Ga-68 PET/CT

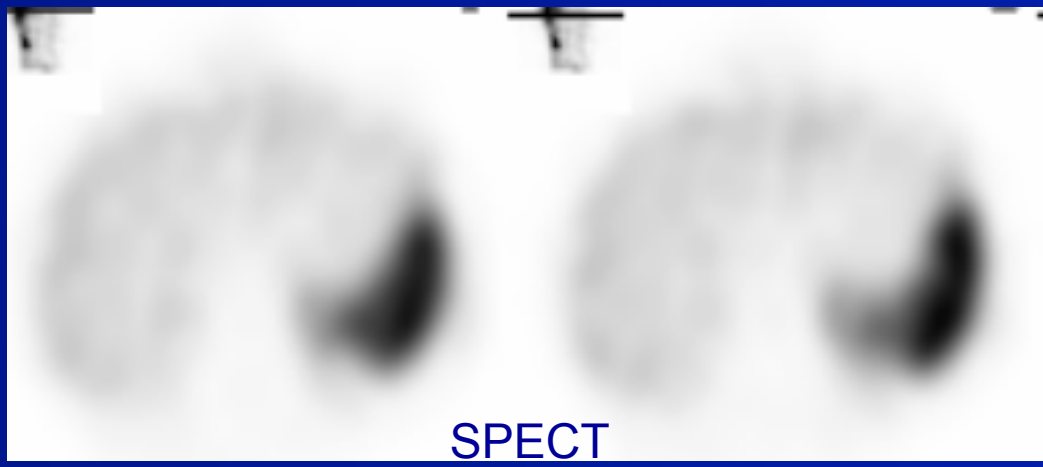
Ga-68 PET/CT more lesions than In-111 Oct

In fact 11% of patients negative of In-111 octreotide are positive on Ga-68 DOTATATE



In-111 Oct WB





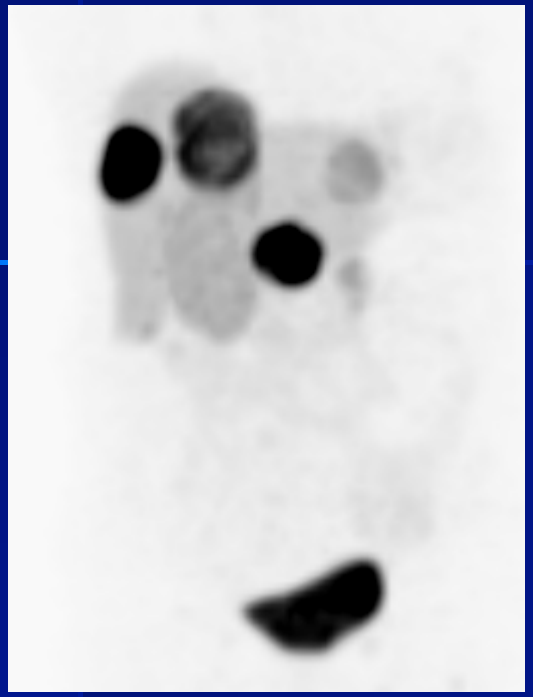
SPECT

Ga-68 PET/CT pos In-111 Oct neg

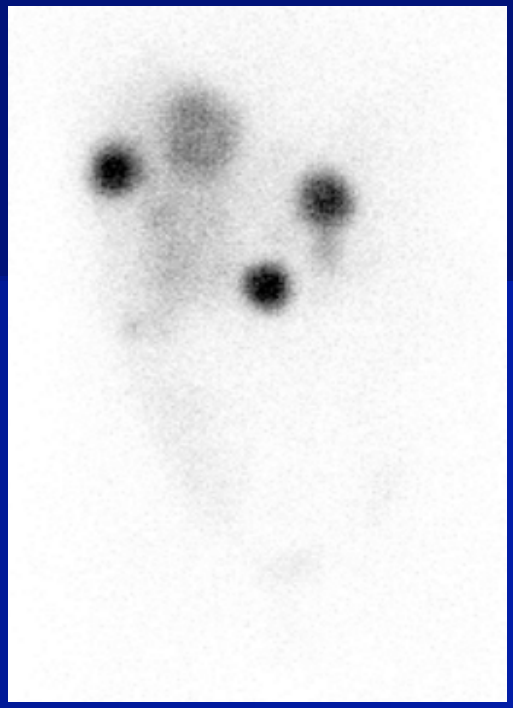
Ga-68 PET MIP

In-111 Oct WB

Similar Lesions



Ga-68 PET



In-111 Oct

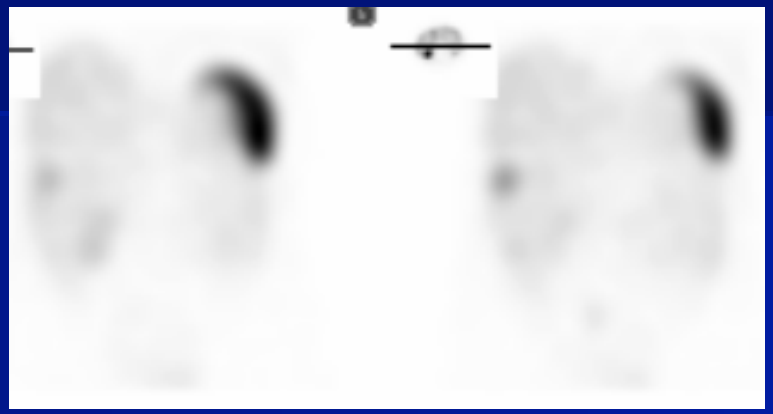
Ga-68 PET/CT more lesions than In-111 Oct

In-111 Oct

Ga-68 PET

In-111 Oct more lesions than Ga-68 PET/CT

In-111 Oct



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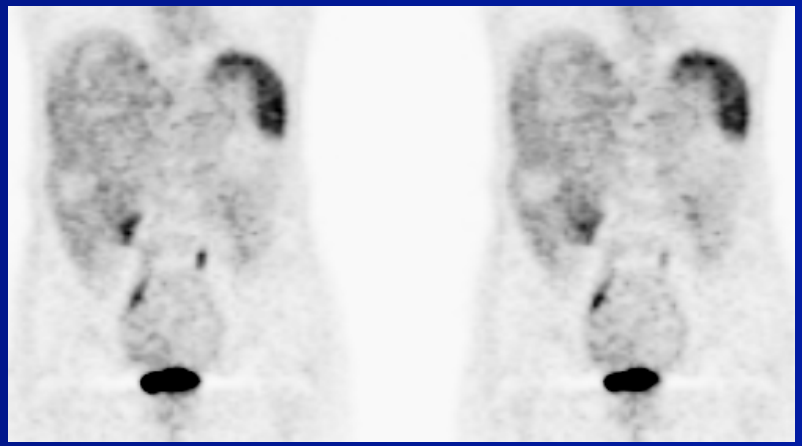


Ga-68 DOTATATE

- Normally expect uptake of Ga-68 DOTATATE *OR* F-18 FDG
- However in 18 pts Kayani et al (JNM 2005) showed uptake of both
- However more false positives with F-18 FDG
- Recommend use of Ga-68 DOTATATE
- ?Co-existent cancer

Ga-68 DOTATATE

- Compared with FDG in MTC
- Conry et al EJNM 2010
- 18 patients with raised calcitonin
  - 13 positive with Ga-68 DOTATATE
  - 15 postive with F-18 FDG
- More sites of disease seen with FDG

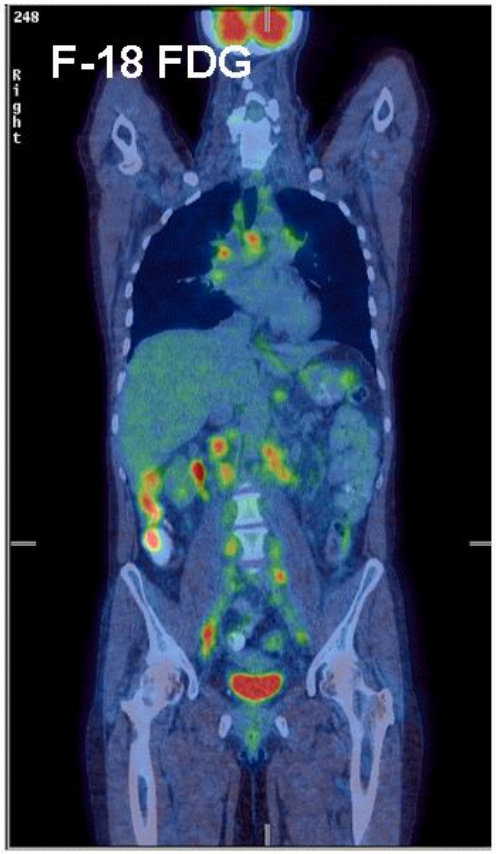
F-18 FDG measure metabolism and Ga-68 DOTATATE receptor activity

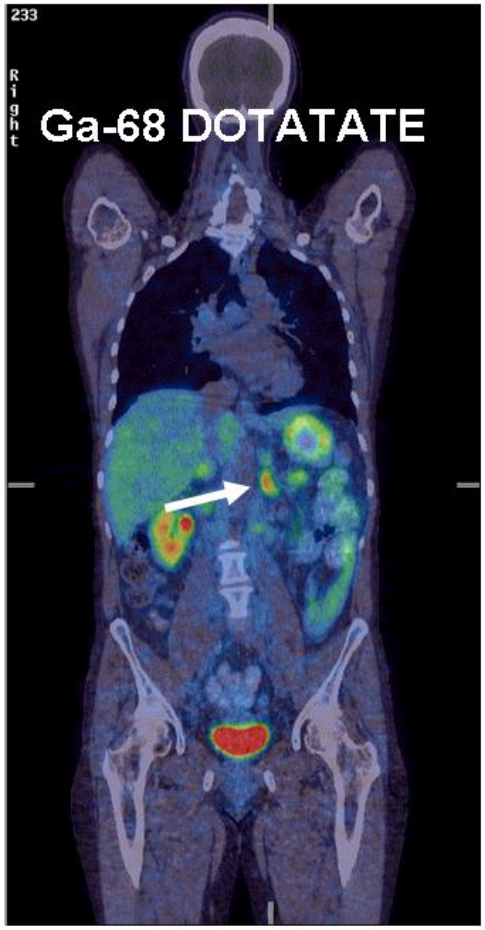
Same patient imaged with both tracers. NET unknown origin

Biopsy of F-18 FDG lesion shows Ki67 of >10%.

Biopsy of Ga-68 DOTATATE positive lesion Ki-67 1%

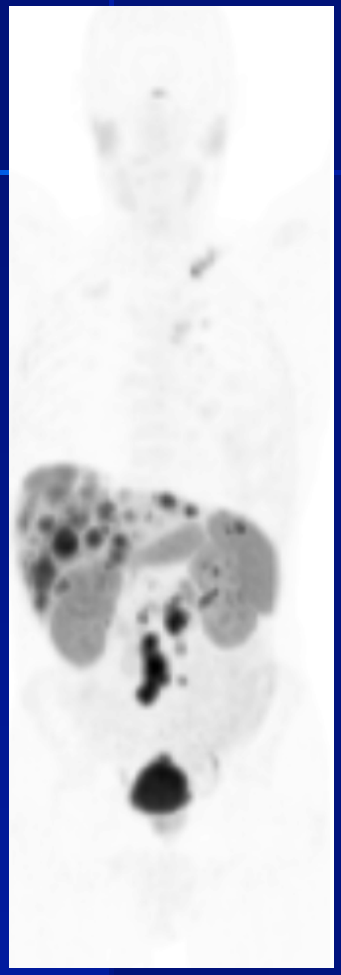
Patient responding to FCIST

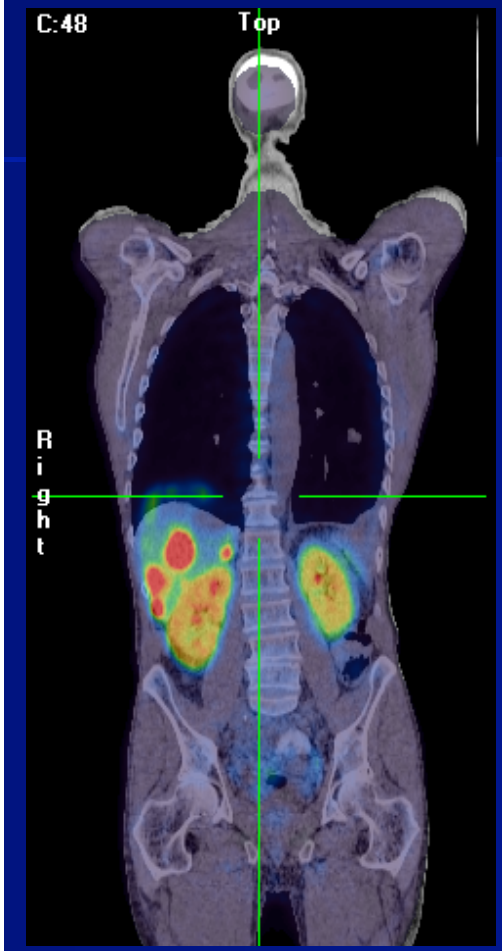




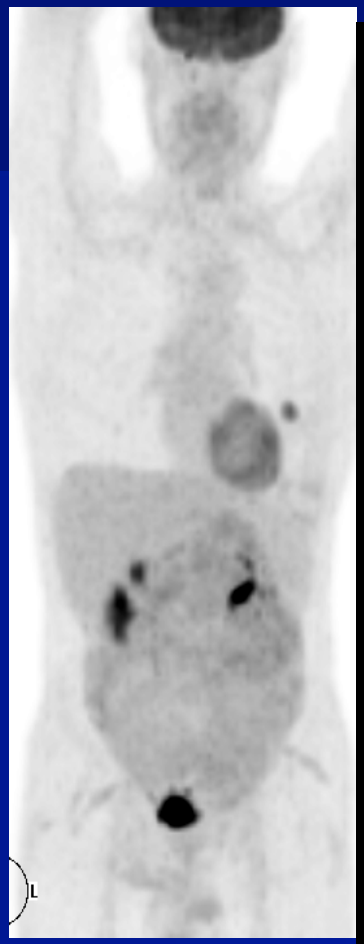
Bomanji et al JCO 2008

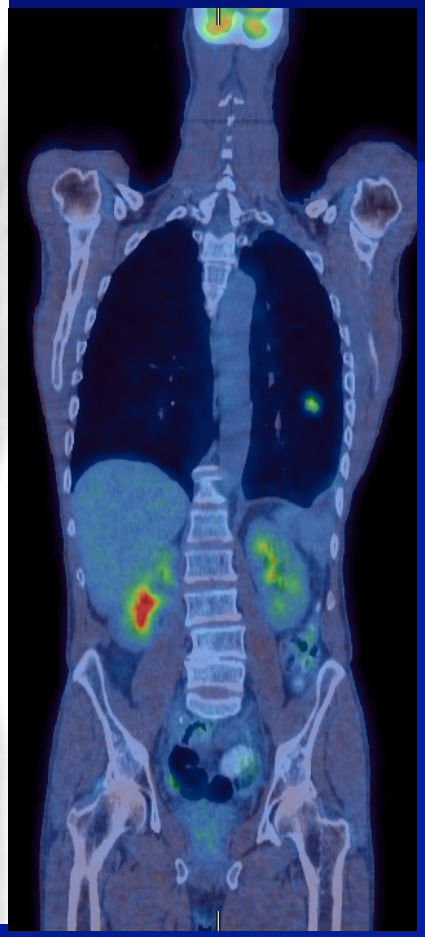
Midgut NET





New lung lesion:
Not avid on Ga-68 DOTA-octreotate



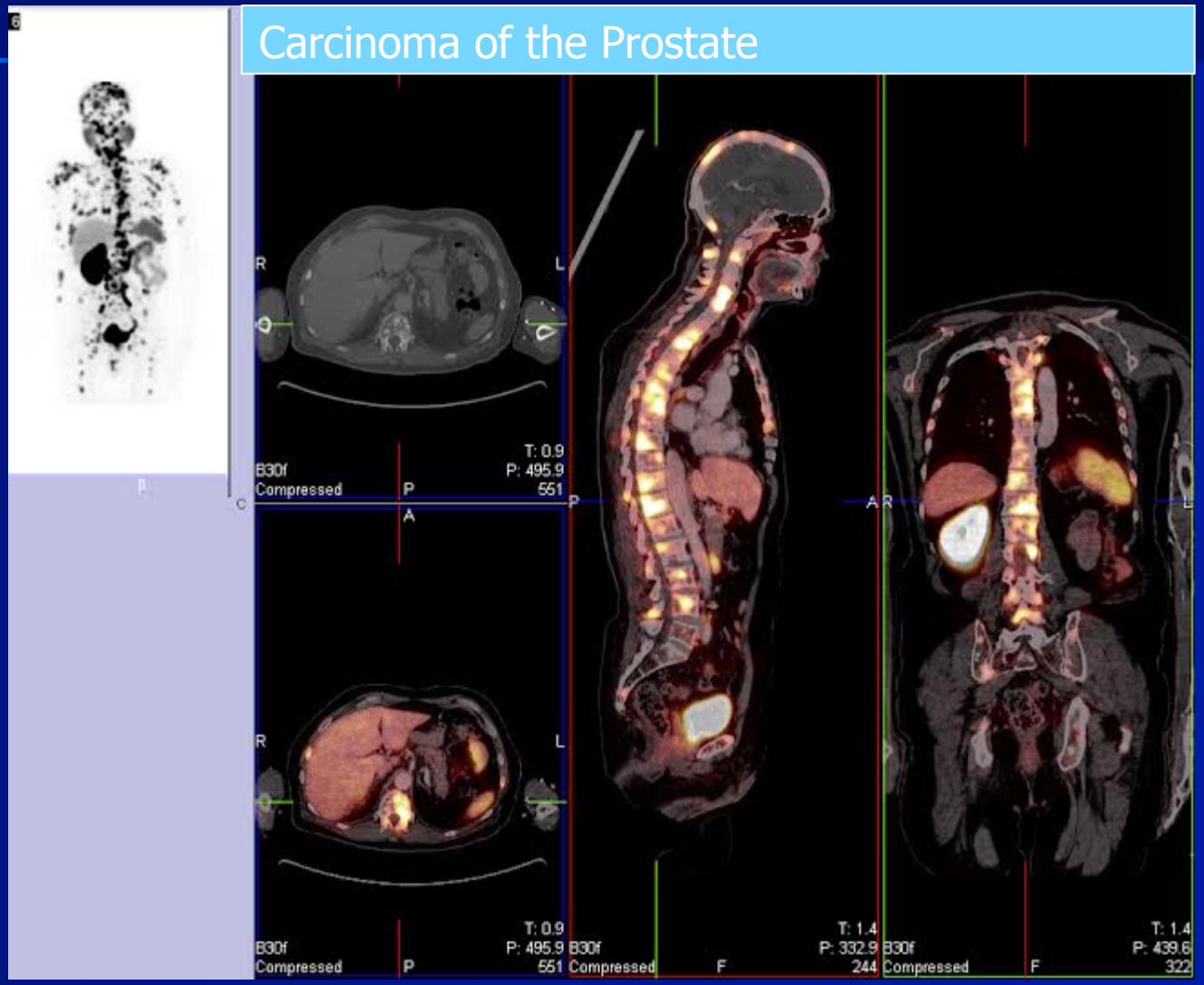


Lung Lesion: avid on FDG

Other Ga-68 derivatives

- Ga-68 DOTANOC higher affinity for SSR 3 and 5 expressed in fore-gut tumours Wild D et al
- Ga-68 minigastrin pancreatic tumours Van Googenburg Innsbruck
- Ga-68 DOTAVAP-PEG V2 looking at vascular adhesion at sites of inflammation Silova et al Turku

Ga-68 PSMA SBAH



Conclusions

- Imaging has different roles depending on what the tumour is doing
- May be used for diagnosis
- For staging and restaging
- Deciding best form of treatment
- Monitoring the effect of treatment
- Getting very complex