Ga-68 PET

John Buscombe
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

SSR

1
2
3
4
5

Lanreotide
Octreotide
Octreotate
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
Modular labs

Eckert & Ziegler

Eurotope
Ga-68 somatostatins

- Since 2001 Ga-68 somatostatins used in NET and brain primaries
- Work centred on Hanover, Heidelberg 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
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<th>SCAN APPEARANCE</th>
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<td>both studies positive, Ga-68 more lesions</td>
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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
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 more lesions than Ga-68 PET/CT
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 positive 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

Carcinoma of the Prostate
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