THE CURRENT ROLE OF PET SCAN IN UROLOGY ONCOLOGY

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Aims

• To understand the basic concepts of PET scanning
• Review the emerging role of PET scanning for urology oncology
  • Prostate cancer
  • Renal cancer
  • Bladder cancer
  • Testicular cancer
• Brief review of future research of nuclear medicine in urology oncology (radium 223)
What is a PET scan

- PET = Positron Emission Tomography
- First PET device was constructed and used for brain imaging in the 1950s.
- With an increase in radioactive isotopes available the clinically utility of PET increased
- A tiny amount of radioactive substance (radionuclide/radioactive tracer/radiopharmaceutical) is used to evaluate the metabolism of an organ or tissue.
- This provides information about the physiology and anatomy of a structure or organ
- Often fuse the PET images with CT or MRI images.

CT and MRI

- Co-registration:
- Previously PET scans were read alongside CT and/or MRI to give both anatomic and metabolic information
- They then integrated them together. Now they are done simultaneously
- This allows no change in patient position and therefore the images more precise
Radiotracers

- Radionuclides (an atom with an unstable nucleus) used in PET scans are substances (glucose, carbon, oxygen) that are normally utilized by the particular organ/tissue of interest during metabolism
- Radioactive substance is attached to this chemical. For example, the most common in clinical use is FDG (2-fluoro-2-deoxy-d-glucose). This is often used for scanning of the brain because it uses glucose for metabolism
- Shortcomings
  - Taken up by macrophages therefore false readings
  - May occur in some inflammatory conditions
  - The tracer is excreted in the urine therefore accumulates in the bladder, making assessment of the renal, bladder, prostate and pelvic nodes difficult.
  - Cancers under investigation need to be metabolically active with high glycolysis rates. This is low in prostate cancer

Radiopharmaceuticals

- Half-lives of some common isotopes.
  - Oxygen-15 2mins
  - Nitrogen-13 10mins
  - **Carbon-11** 20mins
  - **Fluorine-18** 110mins (>95% use this radiotracer)
  - Bromine-75 98mins
  - Copper-64 12.7hrs
  - Iodine-124 100hrs

- This longer half life allows FDG to be produced off site. Previously a cyclotron needed to be in close proximity to the PET scan.
- Other isotopes with shorter half-lives need onsite production resulting in a higher cost
Cyclotron

- Composed of hollow metal electrodes in a vacuum chamber between two poles of an electromagnet.
- In the centre hydrogen or deuterium gas is placed and yields the particles to be accelerated (H- or D-)
- Under a strong magnet these anions gain energy from alternating voltage between the electrodes, forcing them to travel in a spiral path
- They then hit a foil in the perimeter, removing the electrons from the anions forming positively charged particles, H+ or D+.
- This change in charge deflects the particles out of the accelerator into an isotope target, yielding positron-emitting radionuclides
Radiopharmaceuticals

- Not only do you require an expensive cyclotron but you also need specially adapted on site chemical synthesis apparatus to produce the radiopharmaceutical after radioisotope preparation.
- Because half life of fluorine-18 is approximately 2 hours it will undergo multiple half-lives of decay during the day and requires frequent re calibration of the remaining dose.
- Radiation dose usually 5-7mSv. CXR 0.02mSv. When combined with CT the radiation is up to 23-26 mSv (radiation workers up to 6mSv annually) so the use must be justified. 40% from tracer, 60% from the CT.

Mechanism of PET

- A radiolabelled isotope is given IV and becomes trapped in metabolically active cells. It is phosphorylated by hexokinase into FDG-6 phosphate which is not metabolised and accumulates intracellularly.
- As the radioisotope undergoes positron emission decay it emits a positron, an antiparticle of the electron with opposite charge.
- It travels a very short distance (<1mm) and loses kinetic energy until it decelerates to a point where it can interact with an electron. This annihilates both electron and positron, producing a pair of annihilation (gamma) photons moving in opposite directions.
Mechanism of PET

- These are detected when they reach the scintillator in the scanning device, creating a burst of light which is detected by photomultiplier tubes
- The two gamma photons are emitted in almost 180 degrees apart
- A straight line is drawn between the two simultaneous detection events, pinpointing the source in space
Attenuation

- Attenuation correction is required
- Attenuation occurs when photons emitted by radiotracer inside the body are absorbed by intervening tissue between detector and emission of the photon
- As a different line of response must transverse different thicknesses of tissue, the photons are attenuated differently
- This results in structures deep in body as having falsely lower tracer uptake. Scanners have to estimate attenuation using integrated CT equipment

Prostate cancer
Prostate cancer

- Up to 40% will have a detectable rise in their PSA level within 10 years of primary treatment
- Current clinical problems in prostate cancer include
  - Localization of tumors within the prostate.
  - Accurate detection of metastatic disease. Current staging and localization techniques are poor until the PSA is quite high. For example, there is a <5% chance finding positive bone scan until the PSA is >40ng/ml
  - Whole body bone scan and abdominal CT add little diagnostic value unless PSA serum levels are >20ng/ml
  - Detection of tumors in patients with a rising PSA and negative biopsy
  - Determining therapeutic response to treatment

1 EAU prostate cancer guidelines 2013

Radiotracers

- $^{18}$F-FDG is limited because:
  - Glucose utilisation in well-differentiated prostate cancer is lower than in other tissues and therefore low FDG uptake
  - Urinary excretion leads to high bladder activity which can mask prostate tumours
  - There is overlap of uptake between prostate cancer, BPH and inflammation
- $^{11}$C- acetate
  - Acetate uptake in tumour cells is proportional to lipid synthesis. It is metabolised and incorporated into the cellular lipid pool.
  - $^{11}$C-acetate is excreted mostly by the pancreas and intestines with little urinary excretion
Radiotracers

- **11C-Choline**
  - Choline (vitamin) is a necessary compound involved in cellular membrane phospholipid synthesis, transmembrane signaling and lipid/cholesterol metabolism and transport
  - Minimal renal excretion (predominant gastrointestinal)
  - Proliferation and up-regulated membrane lipid synthesis are some characteristic features found in cancer cells
  - There are high choline levels in prostate cancer cells (due to increased fatty acid synthesis) compared to normal prostate cells
  - Mayo clinic is currently the only location in North America where it is approved

Prostate cancer – diagnosis and staging

- **18F-FDG PET** has a low sensitivity (4, 31, 83% in 3 different trials)\(^1\)
  - 18F-FDG PET is unable to detect small foci because of low spatial resolution
  - 18F-FDG PET has no definite role for assessment of locally advanced disease or staging for nodal disease\(^2\)

- **11C-acetate**
  - Relative increase found in prostate cancer compared to BPH and normal prostate tissue
  - 11C-acetate appears to be inferior to MMRI with regard to:
    - Sensitivity 62-80% vs 82-89%
    - Specificity 82-89% vs 29-95%

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\(^1\) Kazuhiro K et al, Int Jour of Urol 2013
\(^2\) EAU guidelines 2013
Prostate cancer – diagnosis and staging

- **¹¹C-Choline**
  - Sensitivity 55-100%, specificity 43-87%
  - In the prostate it can be masked by prostatitis, BPH, normal tissue
  - Low spatial resolution of PET (approx 5mm)
  - In one of the earlier studies, Testa et al, compared to ¹¹C-Choline PET/CT with MRI and 3D MRI/S for localisation of prostate cancer in 26 men.
  - ¹¹C-Choline PET/CT MRI 3D MRS
    - Sensitivity 56% 54% 81%
    - Specificity 86% 75% 67%
  - Therefore ¹¹C-Choline PET/CT had lower sensitivity than 3D MRI alone or combined with MRI in detecting prostate cancer
  - The overall accuracy of ¹¹C-Choline PET in defining local tumour stage is approximately 70%. PET tends to under stage prostate cancer and currently has limited role in making treatment decisions in patients with clinically localised cancer.

¹Testa et al, Radiology 2007
²EAU guidelines 2013

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Prostate cancer – diagnosis and staging

- **¹⁸F – fluorocholine**
  - 64-100% sensitivity, 47-90% specificity
  - Fluorocholine PET/CT potentially useful particularly when PSA >20, poorly differentiated tumors (Gleason 8-10) or palpably locally advanced tumors

¹Beheshi M et al, Radiology 2010
Locally advanced prostate cancer using $^{18}$F-FDG PET/CT

63-year-old man (advanced prostate cancer with a PSA level of 12.6 ng/ml)
a) T2-weighted MRI. Mass measuring 3.5 × 4.5 cm, with slight hypointensity, extends through the prostate capsule in the left peripheral and transition zone
b) $^{18}$F-FDG PET/CT image shows intense $^{18}$F-FDG uptake by the mass indicated but accurate evaluation of primary local staging by $^{18}$F-FDG PET/CT is difficult.

Pre treatment prostate cancer

<table>
<thead>
<tr>
<th>Tracer</th>
<th>Authors</th>
<th>Year</th>
<th>n</th>
<th>PSA, median (range) ng/mL</th>
<th>Sen %</th>
<th>Spec %</th>
<th>Acc %</th>
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<td>Oyama et al.</td>
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<td>28–33</td>
<td>3.3 ng/mL.</td>
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<td>71%</td>
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Summary of the literature of studies using $^{18}$F-FDG, $^{11}$C- and $^{18}$F- choline, $^{11}$C-Acetate PET or PET/CT in the evaluation of detecting untreated prostate cancer.

Table 1
**Lymph nodes**

- ePLND is time consuming and adds morbidity and cost.
- $^{11}$C-choline sensitivity 60-78%, specificity 82-98%. The bigger the lymph nodes the better the detection rate
  - <2mm 0%
  - 2-4.9mm 25-30%
  - 5-9.9mm 33-43%
  - >10mm 77-90%
- $^{18}$F-flurocholine sensitivity 10-73%, specificity 80-100%
- There is a high sensitivity when there is high tumour viability (eg histological grade, high clinical stage or a tumour in a patient with a high serum PSA).
- In summary CT/PET shows better performance than conventional imaging for locoregional LN, but not as good as lymphadenectomy

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**$^{11}$C-choline PET/CT lymph node metastases**

A 60-year-old man with LN metastasis of prostate cancer after radical prostatectomy with a PSA level of 2.9 ng/mL
(a) CT image
(b) $^{11}$C-choline PET/CT image shows a left common iliac LN measuring 0.9 × 0.8 cm with intense $^{11}$C-choline uptake (arrow), consistent with LN metastasis
Biochemical failure (PSA level of 2.1 ng/mL) post external beam radiotherapy
A, B, C - 18F-FDG PET. There is no pathological uptake seen
D, E, F \textsuperscript{11}C-choline. There was a metastatic uptake in the seminal vesicle, in both external iliac lymph nodes, and right ilio-obturator

**Bone metastases – prostate cancer**

- Currently we use 99m Tc-MDP bone scan which may miss early metastases as it relies on osteoblastic turnover of cells. Findings can also be non specific (eg trauma, OA)
- PET allows ability to distinguish metabolically active lesions from non-viable bony lesions
- \textsuperscript{18}F-choline PET/CT might be superior for early detection (bone marrow) of metastatic disease\textsuperscript{1}

Bone metastasis

Multiple bone metastases from prostate cancer (PSA 18.3 ng/ml)
(a) $^{18}$F-FDG PET image
(b) CT image
(c) PET/CT image show multiple $^{18}$F-FDG avid abnormalities and sclerotic or lytic change in the spine and sternum, confirming the presence of bony metastasis.

Bone metastasis

- Bone metastasis
  - $^{11}$C-Choline PET/CT better than bone scintigraphy with sensitivity 89%, specificity 98-100%. Fuccio et al showed metastases in 18 of 123 patients (14.6%) who previously had negative results on bone scintigraphy
  - In equivocal cases of bone metastases $^{11}$C-Choline, $^{18}$F-fluoride PET/CT (or MRI) are an option

1Fuccio et al, Ann Nucl Med 2010
2EAU guidelines 2013
PSA recurrence

- PSA is the most sensitive tool to detect recurrence after primary treatment but it cannot distinguish between local, regional or distant recurrence
- What PSA cut off is appropriate to use Choline PET/CT? This is not yet defined
- $^{11}$C-Choline PET/CT for re staging post treatment: 56-100% sensitivity, 36-100% specificity
- It depends on PSA level$^{1}$. % positive scan:
  - PSA 0.23-1ng/ml 19%
  - PSA 1-3ng/ml 46%
  - PSA >3ng/ml 82%
- Husarik$^{2}$ et al confirmed that choline PET/CT is more accurate when the PSA >2ng/ml
- For example, even in patients with a PSA value >2ng/ml and previous negative imaging studies, $^{11}$C-choline PET/CT is positive in only 28% patients
- A PSA DT <3 months is a strong predictor of PET positivity$^{3,4,5}$


PSA recurrence $^{11}$C-Choline

- $^{11}$Choline PET/CT is more likely to be positive with advanced pathological stage, previous biochemical failure and advanced age
- The higher the PSA, the faster the PSADT, the better the predictability of Choline PET/CT
bladder. the pelvis without interference with tracer activity in the tines, and has little urinary excretion, allowing PET imaging of 4 gland, uptake level in primary cancer, BPH and the normal prostate synthase, have been shown in prostate cancer.

Acetate is metabolized and incorporated into the cellular lipid pool, mostly phosphatidylcholine (incorporated in the cell

Molecular biology

11 tumors. The tumors showed variable uptake of cancer. The tumors showed variable uptake of cancer.

F-FDG, PET and PET/CT represent high sensitivity and specificity for the detection of locoregional and distant metastases. Choline PET and PET/CT represent high sensitivity and specificity for the detection of locoregional and distant metastases.

11C-labeled and 18F-labeled choline have similar tumour detection rates but a longer half life of 18F makes it perhaps more practical.

Table 2: Summary of the literature of studies using 11F-FDG, 11C- and 18F-choline. 11C-Acetate PET or PET/CT in the evaluation of restaging prostate cancer

<table>
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<tr>
<th>Tracer</th>
<th>Authors</th>
<th>Year</th>
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<th>PSA, mean [range], ng/mL</th>
<th>Sens %</th>
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<td>11F-FDG</td>
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<td>26.8 (0.3–400)</td>
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<td>9 (RP 6, RT1)</td>
<td>14.1 (0.7–46.3)</td>
<td>100</td>
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<tr>
<td></td>
<td>Cisternas**</td>
<td>2006</td>
<td>LR,UN,BM</td>
<td>100 (RP 58, RT 21, AT 21)</td>
<td>0.12 (11.8)</td>
<td>98</td>
<td>100</td>
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<tr>
<td></td>
<td>Heinrich**</td>
<td>2011</td>
<td>LR,UN,BM</td>
<td>17 (RP 15, RT 22)</td>
<td>18.64 (0.5-95.1)</td>
<td>41</td>
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<td>–</td>
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<tr>
<td></td>
<td>Vees**</td>
<td>2007</td>
<td>LR</td>
<td>10 (RP 10)</td>
<td>0.35 (0.11–0.74)</td>
<td>60</td>
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<tr>
<td></td>
<td>Hausken**</td>
<td>2008</td>
<td>LR,UN,BM</td>
<td>68 (RP 47, RT17)</td>
<td>10.81 (34–100)</td>
<td>86</td>
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<td>Behnfeldt**</td>
<td>2009</td>
<td>BM</td>
<td>70 (pre 32, post 38)</td>
<td>39.7 (0.1–239)</td>
<td>79</td>
<td>97</td>
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<td>Schnellmann**</td>
<td>2012</td>
<td>LR,UN,BM</td>
<td>49 (RP 49)</td>
<td>4.13 (0.09–15.5)</td>
<td>92</td>
<td>100</td>
<td>93</td>
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<td></td>
<td>Chondrogiannis**</td>
<td>2013</td>
<td>LR,UN,BM</td>
<td>46 (RT 46)</td>
<td>6.5 (1.1–49.4)</td>
<td>80</td>
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<tr>
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<td>Marzola**</td>
<td>2013</td>
<td>LR,UN,BM</td>
<td>233 (RP 233)</td>
<td>7.4 (0.1–58)</td>
<td>54</td>
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</table>

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PET/MRI

- Combining MRI has the advantages of improved soft-tissue contrast, truly simultaneous imaging, added benefit of diffusion/perfusion imaging and functional studies
- A number of small studies indicate similar results between PET/MRI and PET/CT\(^1,2\)
- High cost involved
- Currently limited evidence


Prostate cancer summary

- PET/CT limited role in diagnosis of prostate cancer
- It is not preferred for detection and local staging of untreated cancer or for residual or local recurrence because of limited spatial resolution
- \(^1\)C-choline PET/CT has the major role in biochemical recurrence following primary treatment. This depends on PSA value, PSADT (<3 months) and PSAV (>1ng/ml/yr). The higher the PSA, faster the DT, the better the predictive value
- PSA <1ng/ml choline PET/CT is not useful\(^1\)
- Choline PET might play a role in a selected patient population with higher PSA levels and/or poorly differentiated cancer to exclude distant metastases when salvage local treatment is intended

\(^1\) Picchio et al, Eur J Urol 2011
Renal cancer

Renal cancer - primary

- FDG not very useful because of the radiotracer in urine
- Can give diuretics to aid imaging
- $^{11}$C-acetate has been tried. There are conflicting studies that renal cell carcinoma accumulates more $^{11}$C-acetate than normal renal parenchyma\(^1\), \(^2\)
- Various radiotracers have been used to correctly identify the tumour type pre operatively with mixed results
- No current role in the diagnosis of primary RCC

\(^1\)Sherve et al, J Nucl Med 1995
Renal cancer - staging

- Meta analysis in 2007 by Martinez et al\(^1\) looking at the role of \(^{18}\)F-FDG PET in RCC concluded that it is useful in the diagnosis and staging of metastatic lesions with a pooled:
  - Sensitivity of 0.87 (95% CI 0.75-0.95)
  - Specificity 0.93 (95% CI 0.86-0.97)
- Meta analysis in 2012 by Wang et al\(^2\) looking at the role of \(^{18}\)F-FDG PET/CT in RCC pooled (14 studies)
  - RCC diagnosis:
    - Sensitivity 62%
    - Specificity 88%
  - Staging diagnosis (FDG PET/CT)
    - Sensitivity 91%
    - Specificity 88%
  - For RCC FDG-PET/CT is helpful in detecting extra-renal metastases but not primary renal lesions

\(^{1}\) Martinez de Llano Sr et al, Esp Med Nucl 2007
\(^{2}\) Wang et al, Cancer Imaging 2012

(A, D) PET-FDG
(B, E) CT
(C, F) Fusion images
Previous right radical nephrectomy for RCC. 1 year post surgery. A hypermetabolic deposit is visualized (arrow) in the surgical area, compatible with local recurrence.
Renal cancer – summary

• FDG - PET has limited role in detecting primary renal lesions.
• It has a suitable sensitivity and specificity for metastases
• There is no current role for pre operative local staging
• The true role of PET in the diagnosis and follow up of renal cell carcinoma remains to be determined\(^1\) and is not currently a standard investigation\(^2\)

\(^1\)EAU guidelines 2013
\(^2\)AUA guidelines 2013

Bladder cancer
Bladder cancer - primary

- CT and MRI are currently used for pre operative staging
- These are limited by a significant false-negative rate
- There is a role for more accurate pre operative staging
- $^{18}$F-FDG PET CT is limited secondary to the urinary excretion of the radiotracer
- Intravenous fluids and diuretics can assist in removing the radiotracer
- Foley catheter insertion, flushing and subsequent filling with normal saline gave improved results to primary bladder detection using PET CT

1 Mertens, et al Nucl Med Comm Nov 2012 (Amsterdam)

Bladder cancer – pre operative staging

- Drieskens$^1$ et al reviewed the role of $^{18}$F-FDG PET in detecting lymph node and distant metastases in 55 patients pre operatively
- For diagnosis of metastatic disease:
  - Sensitivity 60% (Liu$^2$ et al found 77% but after chemotherapy, this decreased to 50% and recommended using $^{18}$F-FDG PET with caution in those post chemotherapy)
  - Specificity 88%
- Other radiotracers have been used with little success

$^2$Liu, Urol Int 2006
Meta analysis

- Lu YY et al, Meta analysis. 6 studies met the criteria for inclusion
- Pooled PET/CT data for primary lesion detection of bladder cancer (small numbers)
  - Sensitivity 0.90 (95% CI 0.70-0.99)
  - Specificity 1.00 (95% CI 0.74-1.00)
- Lu also investigated FDG PET or PET/CT versus CT alone for staging and restaging metastatic lesions of bladder cancer. PET/CT is more accurate than CT alone
  - Sensitivity 0.82 (95% CI 0.72-0.89)
  - Specificity 0.89 (95% CI 0.81-0.95)
- Yu et al concluded that FDG PET was helpful in the diagnosis of metastatic lesions in urinary bladder cancer, but the studies were limited and that its use in bladder wall tumors could not be established

Bladder cancer – neoadjuvant chemotherapy

- Neoadjuvant chemotherapy is now a standard that improves the overall survival of patients with MI UC however there are a number of non responders (up to 50%)
- Mertens et al reviewed the role of PET/CT in monitoring the response of pelvic lymph node metastases to neoadjuvant chemotherapy for bladder cancer
  - 19 patients
  - 18F-FDG PET/CT and CECT before and after median of 4 cycles (range 2-4) of neoadjuvant chemotherapy, 13 had pre operative biopsies and all underwent pelvic lymph node dissection
  - Histopathology determined a responder from a non responder
  - FDG PET/CT and CECT distinguished responders from non responders (18 of 19 vs 15 of 19). FDG PET/CT was better than CT alone
Bladder cancer – neoadjuvant chemotherapy

- The assessment of nodal response with FDG PET/CT may:
  - be considered a surrogate for survival/prognosis
  - reflect efficacy of chemotherapy regimen
    - This may allow an alternative chemotherapy regimen or early surgical intervention in poor responders
  - Avoid futile surgery in patients with rapidly progressive disease

Bladder cancer – PET/CT impact

- Mertens et al reviewed the clinical impact of PET/CT compared to CECT alone
- 96 patients (retrospective). No standard for neoadjuvant chemotherapy for T2 tumours
- Patients underwent a CECT of chest/abdomen and pelvis <4 weeks before FDG-PET/CT. The preferred treatment strategies before and after FDG-PET/CT were determined for each patient
- Treatment options were local curative intent, neoadjuvant chemotherapy, palliative treatment
- In 21.9% the stage on FDG-PET/CT and CECT were different. Upstaging by FDG-PET/CT (19.8%) was more common than downstaging (2.1%). Confirmed on fine needle aspiration
- Clinical management changed for 13 (13.5%) patients subsequent to FDG-PET/CT upstaging (6 changed to neoadjuvant therapy and 7 changed to palliative therapy)
- 8 patients incidentally detected an additional primary tumour

1Mertens, et al, BJUI Oct 2013
Bladder cancer - summary

- No role in nodal staging in muscle invasive bladder cancer due to insufficient data\(^1\)
- Detection of distant metastases is being established and PET/CT looks promising
- Monitoring a response to therapy is not established but may have an important future role like PET does in other malignancies

\(^1\)EAU guidelines March 2013

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Testicular cancer
Testicular cancer - staging

• One would expect a major role for PET because of high cell turn over rates of GCT
• 3 diagnostic dilemmas are still not solved by conventional imaging techniques
  • Correct staging of patients classified as stage 1
  • Evaluation of residual masses after chemotherapy
  • The study of rising markers without clinical evidence of disease
• 33% clinical stage 1 NSGCT have retroperitoneal nodes. 18% of clinical stage 1 seminomas relapse in retroperitoneum during surveillance\(^1,2\)
• More accurate staging would allow:
  • Confidence in advising surveillance
  • Avoidance of potential side effects of treatment in the 80% that are truly T1 N0

\(^1\)Fernandez EB et al Urology 1994
\(^2\)Horwich A et al Br J Cancer 1992

Radiotracers

• \(^{18}\)F-FDG is the only radiotracer used essentially
• Limitations of \(^{18}\)F-FDG include:
  • Inflammatory and granulomatous tissues show extensive \(^{18}\)F-FDG uptake
  • Lesions <1cm often not detected
  • Mature teratoma is indistinguishable from normal or necrotic tissue
NSGCT

- $^{18}$F-FDG is controversial in the role of staging of NSGCT
- Huddart et al in a prospective trial reviewed the role of $^{18}$F-FDG PET CT.
- 111 high risk patients with NSGCT had $^{18}$F-FDG PET within 8 weeks after orchidectomy or marker normalisation
- Of the 88 PET negative, 33 relapsed and the trial finished early.


SGCT

- Several studies indicate $^{18}$F-FDG is a standard tool in evaluating residual seminoma after chemotherapy
- It is very important to stage accurately given how technically demanding the post chemotherapy surgery can be secondary to fibrosis and desmoplastic reactions
- De Santis et al looked at 53 patients with metastatic pure seminoma. The sizes of the residual lesions on CT (>3cm or <3cm) were correlated with the presence of absence of viable residual tumour.
- All underwent a FDG PET chest, abdomen and pelvis 4 – 12 weeks after chemotherapy. There was no more than a 2 week interval between PET and CT
- PET scans were compared to histology or follow up scans which could be progressing or stable to confirm the PET scan

1. De Santis et al, J Clin Oncol 2004
2. Becherer et al, Eur J Radiol May 2005
SGCT

- All 19 lesions > 3cm (100%) and 35 of 37 (95%) lesions < or equal 3cm were correctly predicted by FDG-PET
- $^{18}$F-FDG was found to be much better post chemotherapy
  - Sensitivity 80% (95% CI 51-95%)
  - Specificity 100% (95% CI 92-100%)
  - PPV 100%
  - NNP 96%
- CT
  - Sensitivity 70% (95% CI 34-90%)
  - Specificity 74% (95% CI 58-95%)
  - PPV 37%
  - NNP 92%
- Therefore in patients with residual lesions > 3cm after chemotherapy, if PET is negative surgery can be omitted safely. If PET positive – residual lesions must be regarded as harboring viable tumour and surgery should be performed.

Testicular cancer summary

- There is currently not enough evidence to support the use FDG-PET in the routine staging of testis cancer\(^1\)
- It is recommended in the follow up patients with seminoma with any residual mass. If >3cm it should be performed, if <3cm it is optional
- Must be performed > 4 weeks after chemotherapy – limits false negative due to chemotherapy induced suppression of metabolic activity in the tumor & reduces false positives secondary to inflammation

\(^1\)EAU guidelines (2013)
Summary

- **Prostate cancer**
  - PET/CT has a limited role in prostate cancer diagnosis, local staging of untreated cancer or for residual or local recurrence
  - $^{11}$C-choline PET/CT has a major role in evaluating biochemical recurrence following primary treatment. This depends on PSA value, PSADT (<3 months) and PSAV (>1ng/ml/yr).
  - Choline PET/CT is not useful if PSA <1ng/ml

- **Renal cancer**
  - No role for local staging
  - The true role of PET in the diagnosis and follow up of renal cell carcinoma remains to be determined and is not currently a standard investigation

- **Bladder cancer**
  - No role in nodal staging in muscle invasive bladder cancer due to insufficient data
  - Detection of distant metastases is being established and PET/CT looks promising
  - Monitoring a response to therapy is not established but may have an important future role like PET does in other malignancies

- **Testicular cancer**
  - Use in patients with seminoma with any residual mass. If >3cm it should be performed, if <3cm it is optional
  - Must be performed > 4 weeks after chemotherapy

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Future research in CRPC and nuclear medicine – Radium 223
Alpha Emitter Radium-223 and Survival in Metastatic Prostate Cancer

- C. Parker et al.
- The New England Journal of Medicine July 2013
- Phase 3, randomized, double-blind, multinational study comparing the efficacy and safety of radium-223 versus placebo in patients with castration-resistant prostate cancer and bone metastases

Radium 223

- Radium-223 dichloride is a targeted alpha emitter that selectively binds to areas of increased bone turnover in bone metastases and emits high-energy alpha particles over a short range (<100 µm).
- As a bone-seeking calcium mimetic, radium-223 is bound into newly formed bone stroma, especially within the microenvironment of osteoblastic or sclerotic metastases.
- The high-energy alpha-particle radiation induces mainly double-stranded DNA breaks that result in a potent and highly localized cytotoxic effect in the target areas.
- The short path of the alpha particles also means that toxic effects on adjacent healthy tissue and particularly the bone marrow may be minimized
Radium 223

- Radium-223 has been reported to have a favorable safety profile, with minimal myelotoxicity, in phase 1 and 2 studies involving patients with bone metastases.
- Phase 2 studies have shown that radium-223 reduces pain and improves disease-related biomarkers (e.g., bone alkaline phosphatase and PSA) and they have suggested a survival benefit among patients with castration-resistant prostate cancer and bone metastases.
- This study evaluates the effect of radium-223 on survival

Radium 223

- CRPC with bone metastases
- Previous use or non use of docetaxel, baseline alk phos, current use or non use of a bisphosphonate.
- Median overall survival 14.9 months versus 11.3 months in the placebo group
- Radium-223 as compared to placebo had a 30% reduction in the risk of death (HZ 0.70)
- There was a consistent improved overall survival across all groups.
- Trial terminated early because of the overall survival improvement found at pre specified interim analysis
- Await further studies looking at combination or sequential therapy
Thank you

• BC Cancer Agency Nuclear Medicine department
  • Dr Dan Worsley
  • Dr Francois Bernard
Antibody/antigen imaging

• Antigen-based imaging
  • This screens for prostate cancer using specific antigenic targets and then develop agents capable of specific binding. Prostate specific membrane antigen (PSMA) is the most well established

• Prostate-specific membrane antigen imaging
  • Many agents being tested that target various parts of PSMA

• Monoclonal antibody targeting PSMA expression
  • Potential for imaging and/or therapeutic intervention