The Use of PET Scanning in Urologic Oncology

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Aims

- To understand the basic concepts underlying PET scanning.
- Understand the emerging role of PET Scanning for Urological Tumors.
- Future research directions in PET scanning.

History

- PET = Positron Emission Tomography
- First PET device was constructed and used for brain imaging in the 1950s.
- Newest machines fuse the PET images with CT or MRI images.
How PET Works

- A radiolabelled isotope is given IV and becomes trapped in metabolically active cells after it is phosphorylated.
- Decay of radioisotope occurs via release of positrons, or positively charged electrons.
- Gamma rays are simultaneously emitted in opposite directions and are captured by detectors in a ring.
- A straight line is drawn between the two simultaneous detection events, pinpointing the source in space.
How PET Works

[Diagram showing the process of how PET works, includingHexokinase, FDG-6P, and Trapped Glc.]
Radiopharmaceuticals

- Most common in clinical use is FDG (2-fluoro-2-deoxy-d-glucose).

Shortcomings
- Taken up by macrophages therefore false readings may occur in some inflammatory conditions.
- Excreted in the urine therefore accumulates in the bladder and makes assessment of the bladder, prostate and pelvic nodes difficult.
- Cancers under investigation need to be metabolically active with high glycolysis rates.

Radiopharmaceuticals

- Half-lives of some common isotopes.
  - Oxygen-15  2mins.
  - Nitrogen-13  10mins.
  - Carbon-11  20mins.
  - Fluorine-18  110mins.
  - Bromine-75  98mins.
  - Copper-64  12.7hrs.
  - Iodine-124  100hrs.

- FDG can be produced off site whereas isotopes with shorter half-lives need onsite production $$.
PET use in Oncology.

- PET has had a significant impact on the staging of a number of solid tumors including non small cell lung cancer, melanoma, lymphoma, oesophageal and colorectal cancers.
- Also has played a significant role in restaging following treatment and monitoring therapeutic responses.

Non small cell lung cancer

- One of the primary clinical applications of FDG PET. Used in diagnosis, staging, treatment planning and assessment of response.
- Numerous series, randomised trials and meta-analyses have shown that PET alters management in up to half of those scanned.


PROSTATE CANCER & PET

Prostate Cancer

- Current staging and localization techniques are poor.
- Current clinical problems in PCa.
  - Accurate detection of metastatic disease.
  - Localisation of recurrences in patients with biochemical failure following definitive therapy.
  - Detection of tumors in patients with a rising PSA and negative biopsy.
  - Localisation of tumors within the prostate.
  - Determining therapeutic response to treatment.
Prostate Cancer - Limitations

- Only low uptake of FDG by prostate cancer cells due to low glycolysis rates.
- Also uptake in BPH and inflammation.
- Urinary excretion of FDG.

Prostate Cancer - Localisation

- Choline used as there are high levels in prostate cancer cells compared to normal prostate cells. Limited urinary excretion.
- Farsad et al\(^1\) performed 36 $^{11}$C-choline PET/CT preoperatively on wholmount examined prostates.

Sensitivity 66%, Specificity 81% NPV 55%.

Prostate Cancer - Staging

- Local staging is poor compared to MRI\(^2\). (detection of ECE PET 22% vs MRI 63%)
- FDG-PET is not accurate at detecting occult metastases in regional lymph nodes\(^3\).
- C-acetate PET may be more useful but definitive results are awaited.

Prostate Cancer - PSA recurrence

- Limited by inability to detect disease at very low PSA levels <1.
- 22 patients with average PSA of 0.33 after RRP revealed recurrent disease in 11. MRI better with 15 of 18.

4. Vees et al: 18F-choline and/or 11C-choline PET: detection of residual or progressive disease at very low PSA values after RRP. BJU Int 2007;99:1415.

Prostate Cancer - Summary

- Limited practical role currently.
- Has theoretical potential in tumor localisation within the prostate with further development of radiopharmaceuticals and integration with MRI images.
- There is also a lot of work being done on the use of PET/CT is the monitoring of therapeutic response to treatment.
Renal Cancer - Primary Tumor

- FDG PET has not demonstrated an advantage over conventional CT. High false negative rate.
- Largest series - n=66 Sensitivity 60% compared to 91% with CT. Specificity 100%\(^5\).
- Most studies were done in the pre PET/CT era.

Renal Cancer - Staging

- Most studies suggest superiority of PET over CT.
- 4 major recent studies \(^5,6,7,8\).
  - N = (54,24,25,53).
  - Sensitivities range 47-75%.
  - Specificities
    - Bone 100%.
    - Pulmonary 80-97%.
    - Lymph Node 75 - 100%.

Renal Cancer - Summary

- FDG - PET has limited sensitivity in detecting primary and metastatic renal lesions.
- It has excellent specificity for metastases especially lesions >1.5cms.

BLADDER CANCER & PET
Bladder Cancer - Primary Tumor

- Sensitivity with FDG 55-85%.
  Enhanced by wash out with oral hydration and frusemide $^{9,10,11}$.
- All small studies in the pre dual modality era (combined PET and CT).


Bladder Cancer - Metastases.

- FDG-PET
  - Sensitivity 67-100%.
  - Specificity 86%.
- Combined PET/CT
  - More promising, but limited data.
  - Recent data 2009. N=43, Prospective, Negative conventional imaging, Positive PET were confirmed by biopsy or lymphadenectomy. Negative scans by lymphadenectomy and clinical f/u median 14.9 months. Sensitivity 70%, Specificity 94%, PPV 78%, NPV 91%.

Bladder Cancer - Metastases

- Seven of the 42 patients included in the study were found to have occult metastases who had previously had negative evaluations.

- Of the 3 patients that were negative on PET/CT but found to have nodal disease all disease < 1cm.

Bladder Cancer - Summary

- Role in staging primary disease in the new era of combined PET/CT is undefined. Limited sensitivity with PET alone.

- Role in detecting distant metastases is being established and looks promising.

- Role in monitoring therapy and restaging is not established.
Testis Cancer - Staging.

- One would expect a major role for PET because of high cell turn over rates of GCT.
- 33% clinical stage 1 NSGCT have retroperitoneal nodes. 18% of clinical stage 1 seminomas relapse in retroperitoneum during surveillance. 13, 14
- More accurate staging would allow:
  - more confidence in advising surveillance.
  - Avoidance of potential side effects of treatment in the 80% that are truly cT1 N0.

Testis Cancer - Staging.

- Several studies have shown no benefit over CT of PET in this setting because of inability to detect teratoma or low volume disease <5mm.
- These studies were generally all in the setting of stand alone PET, not integrated with CT.
Testis Cancer - Post Chemo Residual Mass.

- Has a definite role in this setting.
- Must be performed > 2 weeks after chemotherapy - limits FN due to chemo induced suppression of metabolic activity in the tumor & reduces FP secondary to inflammation.

Seminoma - Residual Mass.

- SEMPET trial
  - n=51.
  - PET correctly predicted all lesions >3cm (19).
  - Correctly predicted 35 of 37 lesions <3cms.
  - PET vs CT Specificity 100% vs 74%, sensitivity 80% vs 70%, PPV 100% vs 37%, NPV 96% vs 92%.

Non Seminoma - Residual Mass.

- Potential for teratoma. PET uptake is similar to normal tissue in teratoma.
- In the setting of residually elevated tumor markers or progression of a mass on CT PET will not add to decision making process.
- Useful in tumor marker negative disease or stable disease on CT.
  - Positive PET indicates viable cancer.
  - Negative PET indicates teratoma or fibrosis.


Future Directions

- More studies utilising PET-CT are needed to clearly define its role in uro-oncology.
- Novel radiotracers such as citrate based tracers in Prostate Ca are being trialed currently.
- Development of tracers that remain in cells beyond excretion time to get better delayed images of the renal tract.
Future Directions

- Researchers are now linking monoclonal antibodies to positron emitters to try and selectively target cell types.
- Integration of PET with MRI may give more refined images and have a role in localisation of prostate cancer within the prostate.

Future Directions

- The monitoring of therapeutic response to treatments. Its role in this setting is established in non small cell lung ca, breast ca, oesophageal ca and lymphoma. It is well correlated with clinical outcomes.
- Can and is being used in the setting of drug trials to assess response to treatment. In prostate cancer it is currently being validated in this setting.
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