PET Scanning for Malignant Melanoma: An Evidence Based Approach

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Patient SW

• 40 yo woman s/p melanoma resection on right arm, who presented in 1999, one year after chemotherapy and radiation, with a subcutaneous nodule and mass in her right axilla.
• Biopsy of the nodule indicated melanoma recurrence.
• Chest CT scan reported as “irregular soft tissue density in right axilla, . . . Presumed due to post-surgical change. Metastatic melanoma, however, cannot be excluded.”
• Head, abdomen, and pelvic CT scans were unremarkable.
CT Scan of SW Left Unanswered Questions:

- Residual tumor or scar?
- Any metastases?
FDG-PET Shows Metabolism?

- FDG (2-\(^{18}\)F-2-deoxy-D-glucose) accumulates in cells that take up glucose but do not have glucose-6-phosphatase.

<table>
<thead>
<tr>
<th>Blood</th>
<th>Tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose (GLUT1)</td>
<td>Glucose (Hexokinase)</td>
</tr>
<tr>
<td>FDG (GLUT1)</td>
<td>FDG-6-P (Hexokinase)</td>
</tr>
</tbody>
</table>

- Many malignant cells rely mostly on glycolysis and usually lack glucose-6-phosphatase.
Physiologic Positives with PET

- Brain and myocardium always positive, particularly in a fed state
- Muscle that has been recently exercised
- Excreted FDG in urinary system
- GI system: lymphoid tissue or activity
- Lactation
- Thymus
- Epiphysis
- Post-chemotherapy bone marrow hyperplasia
Other False Positives

• Inflammation
  – Post-surgery, post-radiation, or post-chemotherapy
  – Infection
  – Auto-immune
  – Stoma
  – Injury

• Benign neoplasms
Detection of FDG

Accuracy and resolution depend on:
- Electron density
- Photon scatter
- Photon attenuation
Detection of FDG

There are two positive areas in the right axilla and one positive area in the right neck.

These are all melanoma.
PET Scan of SW after 4 months of treatment

- CT scan at same time showed no change in size.
- PET scan shows no evidence of active tumor cells.

Courtesy of Dr. Kevin Donohoe, BIDMC
PET vs. CT

PET
• Physiologic resolution

CT
• Anatomic resolution

• How do you decide which to use?

• How do you assess a new imaging technology?
New Technology Assessment

1. Technical Performance
2. Diagnostic Performance
3. Diagnostic Impact
4. Therapeutic Impact
5. Impact on Health
Diagnostic Study Design

• The imaging technique under study must not influence the final diagnosis
• The final diagnosis should be based on a gold standard, particularly pathological.
• The final diagnosis and/or results of competing modalities should not influence imaging interpretation.
• Imaging should be performed in the environment in which it will be used.
• Uninterpretable test results must be reported.
• Subject number should be chosen for statistical reasons.
Technical Performance

• Does PET produce high quality images that are reliable and valid?
  – Resolution
  – Reproducibility
  – PET-Histology Correlation

• A number of studies have shown that PET can reliably show the uptake of FDG with a resolution of about 4 mm.

• Melanoma cells take up and retain FDG
Diagnostic Performance

• Do PET images allow accurate diagnoses to be made?
  – Sensitivity
  – Specificity
  – Positive predictive value
  – Negative predictive value

• There is only one published study comparing PET and a gold standard in an independent, blinded fashion.
  – Sensitivity 85%; Specificity 92%

• Recent meta-analyses found sensitivity to be 78% (CI = 70-84%) and specificity to be 88% (CI = 82-92%) for whole body and sensitivity to be 55% (CI = 40-71) for regional lymph nodes.
Diagnostic Impact

• Does PET change diagnoses and reduce the need for other tests?
  – Randomized trial with and without PET would be ideal but unlikely
  – Compare testing plans before and after PET
  – Measure diagnostic confidence before and after PET

• One complete, prospective study reported completely: PET changes stage in 22% of cases of metastatic melanoma.
Therapeutic Impact

• Do PET results change therapy?
  – Assess treatment plans with and without PET

• One complete, prospective study reported completely: PET changes management in 22% of cases of metastatic melanoma.
  – Surgery is not used if PET indicates that distant lesions are not metastases or if PET indicates need for systemic therapy because of multiple metastases (as in SW)

• Because of these changes, PET has been estimated to save about $1800 per scan in Stage II and III melanoma.
Impact on Health

• Does PET impact positively on people’s health?
  – Increased survival
  – Increased quality of life

• No studies.
References

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