Indications for Positron-Emission Tomography scans in Nova Scotia: a validation of timing rules and recorded reasons for scan in non small-cell lung cancer

June, 2014

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Background

- Canadian Partnership Against Cancer (CPAC) sponsored project to describe the use of PET in the diagnosis, staging and treatment of non small-cell lung cancer
- Not all participating provinces were able to provide an ‘indication’ variable.
- Nova Scotia’s PET database includes a standardised field for indication (‘Reason for Scan’)
- Date of PET scan, date of diagnosis, first treatment date
- Cancer registry for cases, date of diagnosis, date of RT
- Provincial discharge-abstract records for surgical dates
- GOAL: Infer ‘indication’ from timing rule
Methods

Apply Receiver Operating Characteristic (ROC) curve analysis

- Binary classification or ‘condition’
- Continuous (criterion) scale for evaluation
- Index to maximise (method of choosing ‘best’ cut-point)
- Common indices:
  - Cohen’s Kappa: a measure of agreement
  - Youden’s J: sum of sensitivity and specificity
- Weighting (‘costs’) of false negative / positive errors
# Evaluation of a single cut-point

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Condition positive</th>
<th>Condition negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Criterion above</td>
<td>A True +</td>
<td>B False -</td>
</tr>
<tr>
<td>Criterion Below</td>
<td>C False +</td>
<td>D True -</td>
</tr>
<tr>
<td><strong>True positive</strong></td>
<td>[ P_t = \frac{A}{A+C} ] sensitivity</td>
<td><strong>False positive</strong></td>
</tr>
</tbody>
</table>
Data for Validation Study

576 PET scans carried out in the investigation, diagnosis, treatment and monitoring of non small-cell lung cancer cases, diagnosed 2008 – 2011

Diagnosis and staging

- Diagnosis/Unknown Primary Tumor: To detect a primary tumor site in a patient with a confirmed or strongly suspected metastatic lesion.
- Diagnosis: To determine if a suspicious lesion is cancer.
- Initial Staging of histologically confirmed, newly diagnosed cancer.

Treatment planning and monitoring

- Radiation therapy planning.
- Monitoring Treatment Response during chemotherapy.
- Monitoring Treatment Response during combined modality therapy (e.g. chemo / radiation / surgery / biologic therapy).
- Monitoring Treatment Response during radiation therapy.
- Restaging after completion of therapy.
- Suspected Recurrence of a previously treated cancer.
### Data for Validation Study

**Indication Gold Standard:**
- Diagnosis and staging vs RT planning, post-treatment monitoring

**Continuous criterion scale for evaluation:**
- Time between diagnosis and date of PET 😊

**Other considerations:**
- Date of first treatment (surgery or RT)
- PETs to include:
  - All 576
  - First only 492
- AJCC timing rule (120 days)
## Results (all PETs)

<table>
<thead>
<tr>
<th>Any PET</th>
<th>Area Under Curve</th>
<th>Index</th>
<th>Cut point (days)</th>
<th>True positive (%)</th>
<th>False positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naïve</td>
<td>.87</td>
<td>J</td>
<td>76</td>
<td>87.2</td>
<td>24.8</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kappa</td>
<td>109</td>
<td>90.7</td>
<td>31.7</td>
</tr>
<tr>
<td>PET before tx</td>
<td>.81</td>
<td>J</td>
<td>52</td>
<td>86.1</td>
<td>38.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kappa</td>
<td>109</td>
<td>91.1</td>
<td>36.3</td>
</tr>
<tr>
<td>PET before RT</td>
<td>.85</td>
<td>J</td>
<td>76</td>
<td>87.5</td>
<td>30.0</td>
</tr>
</tbody>
</table>
## First or All PETs?

<table>
<thead>
<tr>
<th>Reason for PET</th>
<th>First PETs only</th>
<th>Subsequent PETs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis</td>
<td>201</td>
<td>11</td>
</tr>
<tr>
<td>Staging</td>
<td>216</td>
<td>3</td>
</tr>
<tr>
<td>RT planning</td>
<td>36</td>
<td>9</td>
</tr>
<tr>
<td>Monitor results of Tx</td>
<td>14</td>
<td>23</td>
</tr>
<tr>
<td>Suspected recurrence</td>
<td>25</td>
<td>38</td>
</tr>
</tbody>
</table>
## Results (first PET only)

<table>
<thead>
<tr>
<th>Any PET</th>
<th>Area Under Curve</th>
<th>Index</th>
<th>Cut point (days)</th>
<th>True positive (%)</th>
<th>False positive (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naïve</td>
<td>.80</td>
<td>J</td>
<td>18</td>
<td>47.5</td>
<td>1.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kappa</td>
<td>109</td>
<td>93.5</td>
<td>54.7</td>
</tr>
<tr>
<td>PET before tx</td>
<td>.81</td>
<td>J</td>
<td>25</td>
<td>61.3</td>
<td>25.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kappa</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PET before RT</td>
<td>.85</td>
<td>J</td>
<td>17</td>
<td>48.0</td>
<td>3.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Kappa</td>
<td>109</td>
<td>93.6</td>
<td>58.9</td>
</tr>
</tbody>
</table>
Conclusions

Most analyses supported the *a priori* rule to declare the indication of ‘Diagnosis or Staging’ if:

- within AJCC guidelines (up to 120 days after diagnosis)
- Prior to start of radiotherapy

Limitations:

- No information on chemo (relatively rare with NSLC)
- Gold standard is misclassified (gold alloy ~18k)
  ➔ prefer Kappa (?)
- Some of the later PETs may have been requested for investigation of a new primary
Condition: Diagnosis or Staging: any PET
area under curve is 0.87
Condition: Diagnosis or Staging: PET before Tx
area under curve is 0.81

52 days

52 days

True Positive Proportion

False Positive Proportion

0.0

0.2

0.4

0.6

0.8

1.0
Condition: Diagnosis or Staging: PET before RT
area under curve is 0.85
Condition: Diagnosis or Staging: first PET only
area under curve is 0.80

True Positive Proportion

False Positive Proportion

18 days

109 days
Condition: Diagnosis or Staging: first PET only, before Tx
area under curve is 0.74
Condition: Diagnosis or Staging: first PET only, PET before RT
area under curve is 0.77
Distribution of time from diagnosis to PET
All PET scans in dataset

Distribution of time from diagnosis to first PET