Accuracy of FDG-PET to diagnose lung cancer in the ACOSOG Z4031 trial


Presented at the 2012 ASCO Annual Meeting. Presented data is the property of the author.
Learning Objectives

After reading and reviewing this material, the participant should be able to:

– Describe the accuracy of FDG-PET to diagnose lung cancer in a national sample

– Identify areas of the country with differing FDG-PET results
Outline Slide

• Background / Purpose
• Population
  – ACOSOG Z4031 study
• Methods
• Results
  – FDG-PET accuracy
  – Accuracy by region
• Conclusions
Background

• NCCN guidelines recommend FDG-PET for diagnosis of suspected NSCLC

• FDG-PET highly accurate in meta-analysis
  – Sensitivity 94%
  – Specificity 83%\(^1\)

• FDG-PET performed poorly \(^2,3\)
  – Single institution case series
  – Endemic fungal lung disease

\(^1\)Gould et.al. JAMA 2001
\(^2\)Deppen et.al. Ann Thor Surg 2011
\(^3\)Croft et.al. Lung Cancer 2002
Purpose

1) To evaluate the accuracy of FDG-PET to diagnose NSCLC in patients undergoing resection for c-Stage I disease in a national population

2) To examine differences in sensitivity and specificity between enrolling cities
Population- ACOSOG Z4031 study

• “Use of proteomic analysis of serum samples for detection of NSCLC”

• Known or suspected c-Stage I NSCLC

• All underwent surgical resection
  – 2004 to 2006
  – 51 sites in 39 cities
  – 969 eligible participants
  – 80% cancer / 20% benign
Details for Z4031 study

• Inclusion / exclusion criteria
  – Clinically suspicious Stage 1 lung lesion
  – CT imaging < 60 days prior to lung resection
  – No prior malignancy < 5 years prior

• Data collected
  – Demographics
  – Imaging results / operative notes / pathology reports
  – Serum / tissue
  – Survival
Methods for current study

• Secondary analysis of prospective trial
• Population
  – Z4031 eligible patients
  – 682 patients with FDG-PET scans
• Outcome classification
  – Cancer
  – Pathology report
• FDG-PET categorization
  – Radiologists reports reviewed
Methods - cont

- FDG-PET Categorization (cont)
  - Avidity determined by:
    - Radiologist description of lesion activity
    - Reported maximum standard uptake value (SUV)
  - Avidity classification
    1) No avidity / not cancer \( \text{SUV} = 0 \)
    2) Low avidity / not likely cancer \( 0 < \text{SUV} < 2.5 \)
    3) Avid / possibly cancer \( 2.5 \leq \text{SUV} < 5.0 \)
    4) High avidity / likely cancer \( \text{SUV} \geq 5.0 \)

\[ \textbf{Avid – Category 3 and 4} \]
Methods - cont

• Analysis
  – Sensitivity, specificity, accuracy, positive predictive value and negative predictive value
    • All 682 patients with FDG-PET
    • High volume enrolling sites (>25)
  – Calculated accuracy of FDG-PET for differing lesion diameters
    • Compared accuracy based on diameter categories
Results – Z4031 participants - PET
Results - Descriptive Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Cancer N=566</th>
<th>Benign N=116</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>45%</td>
<td>47%</td>
<td>0.71</td>
</tr>
<tr>
<td>Age</td>
<td>67</td>
<td>61</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lesion Size (mm)</td>
<td>26</td>
<td>20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FDG-PET Avid*</td>
<td>465 (82%)</td>
<td>80 (69%)</td>
<td></td>
</tr>
</tbody>
</table>

*Includes avidity categories 3 and 4
Results – FDG-PET

Malignancy 566 (83%)
Accuracy (TP+TN)/N 73%
Sensitivity 82%
Specificity 31%
Positive Predictive Value 85%
Negative Predictive Value 26%
# Results – FDG-PET (2x2)

<table>
<thead>
<tr>
<th>FDG-PET Result</th>
<th>Avid</th>
<th>Non Avid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cancer</td>
<td>465</td>
<td>101</td>
</tr>
<tr>
<td>Benign</td>
<td>80</td>
<td>36</td>
</tr>
<tr>
<td><strong>True Positive</strong></td>
<td><strong>80</strong></td>
<td><strong>36</strong></td>
</tr>
<tr>
<td><strong>False Negative</strong></td>
<td><strong>101</strong></td>
<td><strong>36</strong></td>
</tr>
</tbody>
</table>

**Malignancy**

- 566 (83%)

**Accuracy**

- (TP+TN)/N = 73%

**Sensitivity**

- 82%

**Specificity**

- 31%

**Positive Predictive Value**

- 85%

**Negative Predictive Value**

- 26%
FDG-PET results

- **False positives (80)**
  - 69% granulomas

- **False negatives (101)**
  - 11 patients ≤10 mm
    - 9 adeno, 1 squamous, 1 other
  - Pathology
    - 62% Adenocarcinoma
    - 11% Squamous
    - 10% BAC
    - 9% Neuroendocrine
    - 8% Other
# FDG-PET Results by Enrolling Site*

<table>
<thead>
<tr>
<th>City</th>
<th>N</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birmingham, AL</td>
<td>111</td>
<td>89</td>
<td>15</td>
</tr>
<tr>
<td>Charlottesville, VA</td>
<td>52</td>
<td>76</td>
<td>33</td>
</tr>
<tr>
<td>Cincinnati, OH</td>
<td>31</td>
<td>73</td>
<td>33</td>
</tr>
<tr>
<td>Durham, NC</td>
<td>41</td>
<td>91</td>
<td>25</td>
</tr>
<tr>
<td>Los Angeles, CA</td>
<td>27</td>
<td>67</td>
<td>44</td>
</tr>
<tr>
<td>Philadelphia, PA</td>
<td>78</td>
<td>85</td>
<td>46</td>
</tr>
<tr>
<td>Pittsburg, PA</td>
<td>68</td>
<td>78</td>
<td>25</td>
</tr>
<tr>
<td>St. Louis, MO</td>
<td>54</td>
<td>68</td>
<td>29</td>
</tr>
</tbody>
</table>

\[ p = 0.03 \] \[ p = 0.72 \]

* > 25 participants with a FDG-PET scan
FDG-PET Results by Size

Lesion diameter

Accuracy

P < 0.001
• FDG-PET performed poorly for diagnosing NSCLC in a national sample of c-Stage I patients
  – Sensitivity - 82%
  – Specificity - 31%
• Majority of false positives were granulomas
• Sensitivity varies by enrolling city
• FDG-PET accuracy improved with lesion size
  – Accuracy < 50% for < 2cm lesions
Summary slide - Strengths

• National dataset
  – Largest series evaluating accuracy of FDG-PET in patients with known or suspected clinical stage 1 NSCLC

• Generalizable to clinical practice
  – Multiple FDG-PET scanners
  – Different radiology practices
  – Community and academic centers
Summary slide - Limitations

• Secondary analysis of a prospective study
• 67% SUV values available
  – Some centers do not report
• PET was performed for diagnosis and staging
• Did not have original images
  – Relied on written reports
Conclusions

- FDG-PET did not perform as well as previously published in c-stage 1 patients with NSCLC undergoing surgical resection
  - Should be used cautiously
  - Reasons should be explored
- Sensitivity varied across enrolling sites
  - Geographic variation
Acknowledgements

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  – Contributed patients
• Patients