PET/CT in Lung Cancer

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FDG-PET/CT in Lung Cancer

OUTLINE:

- Staging of NSCLC.
- Detection of tumor recurrence.
- Assessment of response to therapy.
- To determine prognosis.
- For RT planning.
- Small cell lung cancer.
- Mesothelioma
74 year old man that after undergoing a routine medical check up, he is found to have a mass in the left lung. The CT scan done one month before the surgical consultation was reported as “...a mass in the lingula of 3.8 cm. x 3.1 cm is noted by no evidence of mediastinal adenopathy...”. Bronchoscopy was positive, having an initial clinical staging of \textbf{T2, N0}. Which means he was \textbf{potentially a surgical candidate}. The surgeon requested an MR of the brain and a \textbf{PET/CT scan} to confirm the staging.
FDG PET/CT
Why did the PET/CT help?
Why did the PET/CT help?

It demonstrated that the disease was far more advance from what it was initially suspected. The staging increased to stage 4, and therefore, surgery was no longer indicated for this patient.

In one study with 102 lung cancer patients, considered to be resectable based on conventional imaging techniques, FDG PET increased the stage in 42 of them and decreased it in other 20.

PET/CT in mediastinal staging.

- Although the CT scan is better for T staging, PET-CT can be helpful in the characterization of other nodules, or in cases where the primary tumor may be infiltrating adjacent structures.

- FDG PET-CT is the best imaging technique for the accurate staging of disease in the mediastinum. The sensitivity is 88% and specificities of 91%. In addition, it allows detection of disease in difficult to reach (by mediastinoscopy) mediastinal regions.

- FDG PET-CT has a very high negative predictive value (NPV) in the staging of the mediastinum (92%).
PET/CT in mediastinal staging.

- Meta-analysis for FDG PET and CT:
  - Includes 14 studies (514 patients) for FDG PET and 29 studies (2,226 patients) for CT:
  - Sensitivity of FDG PET = 79%, CT = 60%
  - Specificity of FDG PET = 91%, CT = 77%

- Prospective study of 102 patients:
  - Sensitivity of FDG PET = 91%, CT = 75%
  - Specificity of FDG PET = 86%, CT = 77%
  - FDG PET detected distant metastases in 10% patients
  - FDG PET changed the stage in 60% patients

- Cost effectiveness of FDG PET has been demonstrated

  Dwamena BA et al. Radiology 1999;213:550-536
ACCP Evidenced-Based Clinical Practice Guidelines
FDG PET compared to CT for mediastinal staging

ACCP Evidenced-Based Clinical Practice Guidelines: Recommendations for FDG PET

- Stage IA being treated with curative intend
- Stage IB-IIIB treated with curative intend
- If PET is abnormal, biopsy is recommended

ESTS guideline for preoperative node staging for non-small cell lung cancer

- Due to the high NPV of FDG PET, invasive staging procedures can generally be omitted in patients with clinical stage I NSCLC with negative mediastinal PET scan. However,….

  - Central tumors
  - Central hilar N1 disease on CT scan
  - Broncho-alveolar cell carcinoma
  - Tumors with low FDG uptake
  - Mediastinal PET negative LNs≥16 mm on CT scan

- In case of positive mediastinal PET, histologic confirmation is still needed to confirm metastasis.
Since the last iteration of the staging guidelines, **PET scanning has assumed a more prominent role** both in its use prior to surgery and when evaluating for metastatic disease.

**Minimally invasive needle techniques** (EBUS-needle aspiration) to stage the mediastinum have become increasingly accepted, and are the tests of first choice to confirm mediastinal disease in accessible lymph node stations.

*If negative, these needle techniques should be followed by surgical biopsy.*

**All abnormal scans should be confirmed by tissue biopsy** (by whatever method is available) to ensure accurate staging.

*Evidence suggests that more complete staging improves patient outcomes.*
PET/CT in the assessment for distant metastases

- In one study comparing FDG PET with conventional imaging (CT of the head and thorax, or MRI of the brain + bone scan), FDG PET detected metastatic disease in 9% more patients, than the combination of all the conventional imaging modalities*.

- Other study demonstrated that FDG PET was capable of correctly detecting metastatic lesions, not depicted by conventional imaging techniques (CT of the thorax, and abdomen + bone scintigraphy) in 6.4% of patients. At the same time, in 7% of patients correctly excluded disease in equivocal lesions thought to be metastatic by conventional imaging**.

PET/CT in the assessment for distant metastases

- Common metastases to adrenals, skeleton, liver, brain.

- FDG PET is superior to conventional imaging:
  - Detect unsuspected distant metastases: ~13% of patients
  - Stage I: 7.5%
  - Stage II: 18%
  - Stage III: 24%

- Change management: 18% of these.

- In a meta-analysis from the National Institute for Clinical Excellence (NICE), the average sensitivity and specificity were 93% and 96% for detection of distant metastases. In addition, 15% of these were unsuspected.

- The use of PET-CT increased even more the specificity over stand alone PET.

- In the skeleton, FDG PET is superior to bone scans (BS= 82%, 62% vs. PET>90%)

Indeterminate Adrenal Masses

- Patients with malignancy: ~30% are malignant.
- Patients without known malignancy: rarely malignant.
- Contrast-CT with delayed washout images and MRI with T2-weighted images: accurate but requires additional imaging.
- FDG PET: high accuracy
  
  Study of 27 patients with NSCLC:
  
  Sensitivity = 100%, specificity = 80%

FDG PET/CT for Detection of Skeletal metastases

- 110 patients comparing bone scintigraphy and FDG PET
- 43 patients with metastases, 21 of which with bone metastases proven with other imaging studies or biopsy

<table>
<thead>
<tr>
<th>Modality</th>
<th>PPV</th>
<th>NPV</th>
<th>Acc</th>
</tr>
</thead>
<tbody>
<tr>
<td>BS</td>
<td>90%</td>
<td>61%</td>
<td>66%</td>
</tr>
<tr>
<td>FDG PET</td>
<td>90%</td>
<td>98%</td>
<td>96%</td>
</tr>
</tbody>
</table>

- Specificity PET (95%) > BS (61%)
- FDG PET better for lytic metastases
- Bone scintigraphy better for blastic metastases

In several studies * it is shown that by using PET-CT, there can be a reduction of futile thoracotomies in up to 51% of patients.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PET–CT</th>
<th>Conventional Staging</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>number (percent)</td>
<td>number (percent)</td>
<td></td>
</tr>
<tr>
<td>Futile thoracotomy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>39 (65)</td>
<td>35 (48)</td>
<td>74 (56)</td>
</tr>
<tr>
<td>Yes†</td>
<td>21 (35)</td>
<td>38 (52)</td>
<td>59 (44)</td>
</tr>
<tr>
<td>Total</td>
<td>60 (100)</td>
<td>73 (100)</td>
<td>133 (100)</td>
</tr>
<tr>
<td>Reason that thoracotomy was considered futile</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exploratory thoracotomy</td>
<td>5 (24)</td>
<td>4 (11)</td>
<td>9 (15)</td>
</tr>
<tr>
<td>Benign lung lesion</td>
<td>0</td>
<td>3 (8)</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Stage IV disease</td>
<td>3 (14)</td>
<td>0</td>
<td>3 (5)</td>
</tr>
<tr>
<td>Stage IIIB disease</td>
<td>4 (19)</td>
<td>8 (21)</td>
<td>12 (20)</td>
</tr>
<tr>
<td>Stage IIIA (N2) disease</td>
<td>5 (24)</td>
<td>6 (16)</td>
<td>11 (19)</td>
</tr>
<tr>
<td>Recurrence within 12 mo</td>
<td>3 (14)</td>
<td>13 (34)</td>
<td>16 (27)</td>
</tr>
<tr>
<td>Death within 12 mo</td>
<td>1 (5)</td>
<td>4 (11)</td>
<td>5 (8)</td>
</tr>
<tr>
<td>Total</td>
<td>21 (100)</td>
<td>38 (100)</td>
<td>59 (100)</td>
</tr>
</tbody>
</table>

* PET–CT denotes combination positron-emission tomography and computed tomography. Percentages may not total 100 because of rounding.
† P = 0.05 for the comparison between the two groups.
61 year old woman with NSCLC (squamous cell) in the RLL. PET/CT did not reveal any metastases. Thoracotomy was done in another hospital on September 2005, with a RLL and RML resection. Since there was evidence at the time of surgery of right hilar involvement (T1,N2), she was referred for adjuvant chemotherapy. An FDG PET/CT scan was requested to re-stage.

Pre-operative CT scan from September 2005
Why did the PET help?

CT February 2006

Biopsy March 2006
Why did the PET/CT help?

- The PET-CT scan allowed to “confirm” the presence of tumor recurrence.

- It provided valuable information as to the site to perform the biopsy.

- It ruled out the presence (at the time of the scan) of distant metastases.
PET/CT for detection of tumor recurrence

- PET and PET/CT have proven to be superior to conventional imaging techniques, for detecting tumor recurrence, changing therapeutic management in up to 63% of patients.

- Several studies demonstrate sensitivities of 98% to 100%, and specificities of 62% to 92%, for detection of tumor recurrence, after treatments with curative intention.

- PET/CT provides valuable information over stand alone CT and PET scanners, specially avoiding false positive interpretations with the use of the fused image.
Table 5. Evaluation of recurrent lung cancer using FDG-PET

<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>Reference</th>
<th>Cases</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
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<tbody>
<tr>
<td>Bury</td>
<td>1999</td>
<td>[8]</td>
<td>126</td>
<td>100</td>
<td>92</td>
</tr>
<tr>
<td>Ukena</td>
<td>2000</td>
<td>[9]</td>
<td>41</td>
<td>97</td>
<td>83</td>
</tr>
<tr>
<td>Hicks</td>
<td>2001</td>
<td>[10]</td>
<td>59</td>
<td>98</td>
<td>82</td>
</tr>
<tr>
<td>Present study</td>
<td></td>
<td></td>
<td>73</td>
<td>93</td>
<td>89</td>
</tr>
<tr>
<td>Pooled data</td>
<td></td>
<td></td>
<td>423</td>
<td>96</td>
<td>84</td>
</tr>
</tbody>
</table>

Only studies with a minimum of 35 patients were used for the pooling of data.

PET/CT for detection of tumor recurrence.

- Prospective study* evaluating the diagnostic value and management impact of PET/CT in 42 nsclc patients suspected of having tumor recurrence.

- Twenty-four of 27 positive PET/CT studies (89%) were proven to have recurrent disease. **Fourteen of 15 negative PET/CT studies (93%) had no evidence of disease.**

- The sensitivity, specificity, and positive and negative predictive values of PET/CT for diagnosis of recurrence were 96%, 82%, 89%, and 93% compared with 96%, 53%, 75%, and 90%, respectively, for PET.

- **PET/CT changed the PET lesion classification in 22 patients (52%),** by determining the precise localization of sites of increased 18F-FDG uptake.

- **PET/CT changed the management of 12 patients (29%).**

CT images of the PET/CT from June 2006

CT images of the PET/CT from September 2006
September 2006 PET/CT scan
It determined that there was a partial response to proton bean therapy.

Unfortunately, it showed that there were distant metastases in both kidneys.

Surgical management is excluded, since the patient already has stage 4 disease.
58 year old man with NSCLC (adenocarcinoma) of the right lung. Treated with initial induction chemotherapy followed by surgery in February 2005. After surgery had adjuvant RT.
Post-therapy scan: Surgery and RT. RT finished on April 2005.

January 2006 PET/CT
why did the PET/CT help?

- It accurately evaluated tumor response to therapy, excluding the presence of tumor recurrence.

- Rules out distant metastases.

- A “clean” PET/CT scan is obtained, which can serve –if needed- as the new reference for future comparison studies.
PET and PET/CT are considerably more precise than CT for assessment of tumor response to therapy, and determining the presence of tumor recurrence in lung cancer.

- **However**: There are false positive cases from post-RT pneumonitis.

- After RT is recommended to wait at least 3 to 6 months before repeating and FDG PET/CT scan.
FDG PET for prognostication in nsclc

Survival plot of 125 patients with nsclc according to the SUV of the primary tumor.
Fig. 5. Survival of patients undergoing second surgery for recurrent lung cancer. Lower FDG uptake in the recurrent tumour is a prognostic factor indicating higher probability of long-term survival ($p<0.001$)
Effect of PET/CT on Management of Patients with Non–Small Cell Lung Cancer: Results of a Prospective Study with 5-Year Survival Data

Deborah L. Gregory¹, Rodney J. Hicks², Annette Hogg², David S. Binns², Poh Lin Shum¹, Alvin Milner³, Emma Link³, David L Ball¹, and Michael P. Mac Manus¹

<table>
<thead>
<tr>
<th>Before PET/CT Management plan</th>
<th>No. of patients</th>
<th>After PET/CT Management plan</th>
<th>No. of patients</th>
<th>PET/CT impact</th>
</tr>
</thead>
<tbody>
<tr>
<td>Observation</td>
<td>1</td>
<td>Surgery</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Invasive biopsy</td>
<td>28</td>
<td>Invasive biopsy</td>
<td>9</td>
<td>19</td>
</tr>
<tr>
<td>Observation</td>
<td>1</td>
<td>Surgical</td>
<td>9</td>
<td></td>
</tr>
<tr>
<td>Radical RT</td>
<td>3</td>
<td>Palliative†</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Surgery</td>
<td>80</td>
<td>Diagnostic (invasive biopsy)</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Observation</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radical RT†</td>
<td>8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Radical RT, for both NSCLC and PET-detected pharynx cancer</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| PET/CT impact |
|--------------|--------------|--------------|--------------|--------------|
| High         | Medium       | Low          | None         |
| 2            | 26           | 50           | 4            |

| Radical RT as planned‡    | 13            |
| Radical CRT, field increased | 6            |
| Radical CRT, field decreased | 1            |
| Surgery                 | 4             |
| Induction chemotherapy, followed by surgery | 1 |
| Palliative chemotherapy or RT⁹ | 18 |
| Palliative              | 10            |
| Palliative chemotherapy or RT, as planned# | 8 |
| Palliative CRT, RT field increased | 2 |
| Total                   | 168           | 168          | 71 (42%)     | 9 (5%)  |

(299x25) EJNMMI 2012
Impact of initial PET/CT staging in terms of clinical stage, management plan, and prognosis in 592 patients with non-small-cell lung cancer.

Takeuchi S¹, Khiewvan B, Fox PS, Swisher SG, Rohren EM, Bassett RL Jr, Macapinlac HA.

¹Department of Nuclear Medicine, Unit 1483, The University of Texas MD Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX, 77030, USA, STakeuchi@mdanderson.org.

Abstract

PURPOSE:
Our objective was to determine the impact of initial (18)F-FDG PET/CT (PET/CT) staging on clinical stage and the management plan and the prognostic value of PET/CT in patients with non-small-cell lung cancer (NSCLC).

METHODS:
We retrospectively reviewed the records of 592 patients with NSCLC who were referred to The University of Texas MD Anderson Cancer Center during 2002/2011 and had both PET/CT and conventional CT for initial staging. Clinical stages and management plans were compared between PET/CT and CT. The impact of PET/CT on management plans was considered medium/high when PET/CT changed the planned treatment modality or treatment intent. PET/CT and CT stages were compared with all-cause mortality and survival rates. We also assessed potential prognostic factors for progression-free survival (PFS) and overall survival (OS).

RESULTS:
PET/CT changed the stage in 170 patients (28.7 %; 16.4 % upstaged, 12.3 % downstaged). PET/CT had a medium/high impact on the management plan in 220 patients (37.2 %). PFS and OS were significantly worse in patients with upstaged disease than in patients with no change in stage (median PFS 29.0 vs. 53.8 months, P < 0.001; median OS: 64.7 vs. 115.9 months, P = 0.006). PFS and OS were significantly worse in patients with medium/high impact of PET/CT than in patients with no/low impact of PET/CT (median PFS 24.7 vs. 60.6 months, P < 0.001; median OS 64.7 vs. 115.9 months, P < 0.001). In multivariate analysis, a medium/high impact of PET/CT was an independent predictor of worse PFS (hazard ratio, HR, 1.73; 95 % CI 1.30 - 2.29; P = 0.0002) and OS (HR 1.84; 95 % CI 1.26 - 2.69; P = 0.002).

CONCLUSION:
Initial PET/CT staging not only impacts stage and management plan but also has prognostic value.
FDG PET/CT in Malignant Pleural Mesothelioma

- Preoperative disease staging.
- Response to treatment assessment.
- Post-treatment disease surveillance of MPM.

- In all these three areas, PET-CT convincingly shows better results than conventional anatomical imaging alone and thereby can aid in exploring novel therapeutic approaches.

- Disease prognosis and radiotherapy planning are evolving areas where this modality has demonstrated significant promise, but this has to be investigated further.

Table 6. Diagnostic accuracy of $^{18}$fluorodeoxyglucose positron emission tomography for staging primary small-cell lung cancer*

<table>
<thead>
<tr>
<th>Trial (reference)</th>
<th>No. of patients</th>
<th>Eligibility</th>
<th>Method of analysis</th>
<th>Test</th>
<th>Prev %</th>
<th>Acc %</th>
<th>Se %</th>
<th>Sp %</th>
<th>PPV %</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bradley (14)</td>
<td>24</td>
<td>Histologically or cytologically confirmed limited SCLC based on conventional imaging</td>
<td>Visual and SUV</td>
<td>Staging extensive vs limited disease PET vs biopsy and additional imaging</td>
<td>8</td>
<td>96</td>
<td>100</td>
<td>95</td>
<td>67</td>
<td>100</td>
</tr>
<tr>
<td>Chin (18)</td>
<td>18</td>
<td>Newly diagnosed SCLC</td>
<td>NR</td>
<td>Staging extensive vs limited disease PET vs conventional staging</td>
<td>50</td>
<td>83</td>
<td>89</td>
<td>78</td>
<td>80</td>
<td>88</td>
</tr>
<tr>
<td>Brink (15)</td>
<td>120</td>
<td>Histologically confirmed SCLC</td>
<td>Visual</td>
<td>PET vs histology or consensus Staging extensive vs limited disease Detection of lymph node metastases Detection of distant metastases (except brain) Detection of brain metastases</td>
<td>63</td>
<td>99</td>
<td>100</td>
<td>98</td>
<td>99</td>
<td>100</td>
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<td></td>
<td>118</td>
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<td>14</td>
<td>90</td>
<td>46</td>
<td>97</td>
<td>75</td>
<td>92</td>
</tr>
</tbody>
</table>

* Prev = prevalence; Acc = accuracy; Se = sensitivity; Sp = specificity; PPV = positive predictive value; NPV = negative predictive value; SCLC = small-cell lung cancer; SUV = standardized uptake value; NR = not reported; PET = $^{18}$fluorodeoxyglucose positron emission tomography.
FDG PET in small-cell lung cancer

Fig. 3. Kaplan–Meier survival curves comparing survival in the LD/LD and LD/ED groups.

Table 2. Overall survival according to staging by conventional imaging (CI) and FDG-PET

<table>
<thead>
<tr>
<th>Group</th>
<th>CI stage</th>
<th>PET stage</th>
<th>No. of pts</th>
<th>Overall survival (median, range in days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LD/LD</td>
<td>LD</td>
<td>LD</td>
<td>22</td>
<td>557 (133–1,603)</td>
</tr>
<tr>
<td>LD/ED</td>
<td>LD</td>
<td>ED</td>
<td>4</td>
<td>172 (119–199)</td>
</tr>
<tr>
<td>ED/ED</td>
<td>ED</td>
<td>ED</td>
<td>12</td>
<td>177 (9–495)</td>
</tr>
<tr>
<td>ED/LD</td>
<td>ED</td>
<td>LD</td>
<td>8</td>
<td>328 (37–3,327)</td>
</tr>
</tbody>
</table>

CONCLUSION

Currently, there is clear evidence of the clinical benefit on the use of FDG PET/CT in lung cancer. It constitutes one of the major indications for PET/CT in Oncology.

There are several well established and cost-effective indications for PET/CT in lung cancer, while others are in evolution.
Thank You