HEAD AND NECK CANCER: ROLE OF PET/CT

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POTENTIAL ROLES OF 18F-FDG PET/CT IN HEAD AND NECK CANCER

1- Staging (N, M and Synchronous Primary Tumor)

2- Unknown Primary Carcinoma (CUP)

3- Detection of Recurrent/Residual Disease

4- Prognostic Value

5- Delineation Of Radiotherapy Target Volume
**STAGING: CERVICAL LYMPH NODE**

18F-Fluorodeoxyglucose Positron Emission Tomography to Evaluate Cervical Node Metastases in Patients With Head and Neck Squamous Cell Carcinoma: A Meta-analysis

Panayiotis A. Kyzas, Evangelos Evangelou, Despina Denaxa-Kyza, John P. A. Ioannidis


<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>79% (72-85%)</td>
<td>86% (83-89%)</td>
</tr>
<tr>
<td>(32 studies 1236 pts)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cN+</td>
<td>94% (50-99%)</td>
<td>70% (20-96%)</td>
</tr>
<tr>
<td>(3 studies 127 pts)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cN0</td>
<td>50% (37-63%)</td>
<td>87% (76-93%)</td>
</tr>
<tr>
<td>(7 studies 311 pts)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cN0/ cN+</td>
<td>82% (75-87%)</td>
<td>87% (83-90%)</td>
</tr>
<tr>
<td>(22 st. 798 pts)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No solid evidence support routine clinical application of PET in lymph node staging, mostly cN0

Better accuracy in cN2-3: detection of Nodes missed by CT or MRI → usefulness in RT (staging-BTV)
HIGH-RESOLUTION DEDICATED HEAD AND NECK PET/CT PROTOCOL

Prospective study:
- 44 patients candidate for surgery (primary tumor resection and neck dissection)
  histopatologic analysis: 9 lymph nodes per level, a total of 186 levels

**TABLE 1.** Acquisition and Processing Parameters for WB PET/CT and High-Resolution, Contrast-Enhanced HN PET/CT (Siemens Biograph PET/CT)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>WB PET/CT</th>
<th>HN PET/CT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technique CT</td>
<td>kVp, 120; mA, 240</td>
<td>kVp, 120; mA, 200</td>
</tr>
<tr>
<td>CT collimation (mm)</td>
<td>1.5</td>
<td>0.75</td>
</tr>
<tr>
<td>Bed time (min)</td>
<td>6</td>
<td>12</td>
</tr>
<tr>
<td>Matrix (PET image)</td>
<td>168</td>
<td>256, with 1.5 zoom</td>
</tr>
<tr>
<td>Pixel size (mm)</td>
<td>4.16</td>
<td>1.82</td>
</tr>
<tr>
<td>Filter FWHM (mm)</td>
<td>5 (7 if &gt;78.75 kg)</td>
<td>2.0</td>
</tr>
<tr>
<td>Iteration</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Subset</td>
<td>8</td>
<td>14</td>
</tr>
<tr>
<td>Intravenous contrast</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Interval from injection (min)</td>
<td>90</td>
<td>150</td>
</tr>
<tr>
<td>Bed</td>
<td>Cradle</td>
<td>Flat</td>
</tr>
<tr>
<td>Head position</td>
<td>In head holder</td>
<td>In head holder (chin up)</td>
</tr>
</tbody>
</table>

HIGH-RESOLUTION DEDICATED HEAD AND NECK PET/CT PROTOCOL

Nodal staging:
WB PET/CT  sens 70% spec 82%
HD PET/CT  sens 91% spec 71%
CECT      sens 57% spec 88%

ROC Analysis ➔ HD PET/CT vs WB PET/CT in N+:
level-based analysis: better performance (p<0.001)
patient-based analysis: near-significant improvement (p<0.059)

Multi-Center Prospective Study:
→ 92 patients with increased risk of M+

PET detected:
at initial staging M+ in 21% pts
synchronous primary tumors in 7% pts
within 12 months follow up M+ in 41% pts
synchronous primary tumors in 2% pts

Accuracy of CT, PET, both CT and PET in the detection of distant metastases and synchronous second primary tumors

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage with 95% confidence interval</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 92</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>39 (28–53)</td>
<td>94 (87–98)</td>
<td>83 (65–93)</td>
<td>69 (60–77)</td>
<td>72 (63–79)</td>
</tr>
<tr>
<td>PET</td>
<td>58 (45–70)</td>
<td>93 (84–97)</td>
<td>85 (70–93)</td>
<td>76 (66–83)</td>
<td>78 (70–84)</td>
</tr>
<tr>
<td>PET and CT</td>
<td>66 (52–77)</td>
<td>94 (87–98)</td>
<td>89 (76–96)</td>
<td>80 (70–87)</td>
<td>83 (75–88)</td>
</tr>
</tbody>
</table>

PPV, positive predictive value; NPV, negative predictive value.
• Early Diagnosis of Primary tumor in CUP is important to:
  - allow a targeted therapy
  - improve the prognosis (1 year vs. 2 years)

• Primary Tumor cannot be detected in 2-3% of patients:
  - small size of primary lesion
  - primary tumor may disappear after seeding the metastasis
UNKNOWN PRIMARY CARCINOMA (CUP)

Review

Role of fluorodeoxyglucose-PET versus fluorodeoxyglucose-PET/computed tomography in detection of unknown primary tumor: a meta-analysis of the literature
Meng-jie Dong¹, Kui Zhao¹, Xiang-tong Lin², Jun Zhao², Ling-xiang Ruan² and Zhen-feng Liu¹

- 28 studies (910 patients): 21 PET and 7 PET/CT

- PET/CT detected primary tumor in 31.4% of pts (PET in 28.5% pts)
  - accuracy 83% (vs 78% PET)
  - sensitivity 78% (vs 78% PET)
  - specificity 83% (vs 79% PET)

- Lower sensitivity in tumors of the base of the tongue and of tonsils
233 patients with HNSCC

1- PET Stage is more accurate \((P<0.001)\) vs Conventional Stage
   (physical examination, fibroscopic, CT of the thorax, CT/ MRI of head and neck)
   PET provides an accurate change of staging in 20% of patients \((47/ 233 \text{ pt})\)

2- Significant changes of management in 32/ 233 patients
   - 13.8% in M stage
   - 5.2% in N stage
   - 8.6% in M stage

→ Entity of management changes:
   - High impact (change in treatment intent or modality) in 20/ 233 pts (8.6%)
   - Medium impact (change within same treatment modality) in 12/ 233 pts (5.2%)
A systematic review and meta-analysis of the role of positron emission tomography in the follow up of head and neck squamous cell carcinoma following radiotherapy or chemoradiotherapy


27 studies, 914 patients (22 PET and 5 PET/CT)

• PET and PET/CT are accurate for detecting recurrence of disease

  primary site: sens 94%, spec 82%, PPV 75%, NPV 95%
  nodal metastasis: sens 74%, spec 88%, PPV 49%, NPV 96%

• The sensitivity is higher for scans performed more than 10 weeks after treatment (P=0.002)
Can PET make unnecessary elective dissection after treatment in patients with advanced nodal disease?

PET/CT performed in 65 pts after concurrent chemoradiotherapy (n=18 with neck dissection specimen)

- Overall PET/CT accuracy 88%, NPV 98%
- In residual lymphadenopathy with negative PET/CT: NPV>90%
- Adopting PET/CT before Surgery would have reduced the number of neck dissections from 18 to 13 (5TP 8FP)

ALGORITHM FOR MANAGEMENT OF HNSCC AFTER CHEMORADIOOTHERAPY

End of CRT → 4-8 wk clinical assessment as appropriate → CT/MRI if suspected disease progression

10-12 wk PET/CT*

No LN or <1 cm PET- → Observe
LN < 1 cm PET+ → Individual decision: observe** or ND
LN > 1 cm PET- → Observe** or ND:
- Patient/surgeon
- ECE?
- Initial nodal size
- Awaiting results from prospective trial
LN > 1 cm PET+ → Neck dissection

NPV>90%
PPV<50%

Kao J. et Al. Cancer 2009

“The Diagnostic and Prognostic Utility of PET/CT-Based Follow-Up After Radiotherapy for Head and Neck Cancer”

- 80 pts stage II-IVB
- serial PET/CT after 2-4 months and after 4-6 months IMRT

Negative PET/CT studies within 6 months after RT were also associated with improved

- 2 years locoregional control (97% vs 49%)
- distant disease control (95% vs 46%)
PROGNOSTIC VALUE OF 18F-FDG PET/CT

Prospective study
- 98 patients with advanced HNSCC
- PET/CT before and after Chemo+IMRT

Low post-RT Primary tumor SUVmax
Correlated with improved survival

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Survivors</th>
<th>Nonsurvivors</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pre-RT</td>
<td>19.6</td>
<td>18.0</td>
<td>0.51</td>
</tr>
<tr>
<td>Post-RT</td>
<td>4.2</td>
<td>7.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>% Chng</td>
<td>74</td>
<td>58</td>
<td>0.01</td>
</tr>
<tr>
<td>Abs Chng</td>
<td>15.3</td>
<td>10.8</td>
<td>0.07</td>
</tr>
<tr>
<td>Pre-RT</td>
<td>12.7</td>
<td>14.6</td>
<td>0.38</td>
</tr>
<tr>
<td>Post-RT</td>
<td>2.4</td>
<td>3.1</td>
<td>0.06</td>
</tr>
<tr>
<td>% Chng</td>
<td>72</td>
<td>74</td>
<td>0.81</td>
</tr>
<tr>
<td>Abs Chng</td>
<td>10.2</td>
<td>11.4</td>
<td>0.58</td>
</tr>
</tbody>
</table>

Advantages of using 18F-FDG PET/CT:

- detection of Tumor areas or Nodes missed by CI (↑ PTV)
- exclusion of areas with no metabolic activity (↓ PTV)

- identification of parts of GTV requiring an additional dose “dose painting” and “Adaptive image-guided Radiotherapy”

Geets et al. Radiother Oncol. 2007
Which is the optimal threshold in 18FDG-PET/CT segmentation for Head and Neck tumors?

More than 20% GTV\textsubscript{PET} outside GTV\textsubscript{CT}
Missed Tumor or Inflammation?

Need of Validation Studies based on histopathology

18F-FDG PET-GUIDED DOSE ESCALATION

T: right tonsil

N: oervical node

BTV
18F-FDG PET-GUIDED DOSE ESCALATION

SIMULTANEOUS INTEGRATED BOOST (SIB) → BTV 69 Gy

High sparing of OARs → $D_{\text{mean parotid}} = 25$ Gy
PET/CT Staging Followed by Intensity-Modulated Radiotherapy (IMRT) Improves Treatment Outcome of Locally Advanced Pharyngeal Carcinoma: a matched-pair comparison

Sacha Rothschild¹,², Gabriela Studer¹, Burkhardt Seifert³, Pia Huguenin⁴, Christoph Glanzmann¹, J Bernard Davis¹, Urs M Lütolf¹, Thomas F Hany⁵ and I Frank Ciernik*⁶,⁷

Radiation Oncology 2007

Case-control study:
45 pts PET/ CT and CDDP+ IMRT; 86 pts Conventional Staging and 3D-RT

Event-free survival (p=0.005)
PET/ CT+IMRT: 90% 1 yr, 80% 2 yrs
Control: 72% 1 yr, 56% 2 yrs

Overall survival (p=0.002)
PET/ CT+IMRT: 97% 1 yr, 91% 2 yrs
Control: 74% 1 yr, 54% 2 yrs
POTENTIAL ROLES OF 18F-FDG PET/CT IN HEAD AND NECK CANCER

1 - Detection of Recurrent/Residual Disease
   Isles et al. Clinical Otolaryngol 2008

2 - Delineation of Radiotherapy Target Volume

3 - Staging (N, M and Synchronous Primary Tumor)
   Lonneux et al. Journal of Clin Oncol 2010

4 - Unknown Primary Carcinoma (CUP)
   Dong et al. Nuclear Medicine Communications 2008

4 - Prognostic Value