PET/CT in Lymphoma

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PET-CT in Lymphoma

• Staging
• Response Evaluation
  – During treatment
  – End of treatment
• Surveillance
FDG PET (-CT) in Lymphoma

- PET = whole body imaging
- **Sensitivity** depends on
  - FDG avidity
  - Size
  - Background activity surrounding tissue
- **Specificity**
  - Inflammatory tissue
  - Physiological uptake in brown fat, gut, urinary system
- PET-CT
  - Combination of metabolism and anatomy
  - Increase in sensitivity and specificity
FDG avidity of lymphomas according to WHO classification

Weiler-Sagie et al. JNM Jan 2001

**TABLE 1. ¹⁸F-FDG Avidity of Lymphoma According to World Health Organization Histopathologic Classification**

<table>
<thead>
<tr>
<th>Histology</th>
<th>n</th>
<th>¹⁸F-FDG–avid</th>
<th>Negative</th>
<th>% ¹⁸F-FDG avidity</th>
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<tbody>
<tr>
<td>Hodgkin disease</td>
<td>233</td>
<td>233</td>
<td>0</td>
<td>100</td>
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<tr>
<td>Burkitt lymphoma</td>
<td>18</td>
<td>18</td>
<td>0</td>
<td>100</td>
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<tr>
<td>Mantle cell lymphoma</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Anaplastic large T-cell lymphoma</td>
<td>14</td>
<td>14</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Marginal zone lymphoma, nodal</td>
<td>8</td>
<td>8</td>
<td>0</td>
<td>100</td>
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<tr>
<td>Lymphoblastic lymphoma</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Angioimmunoblastic T-cell lymphoma</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Plasmacytoma</td>
<td>3</td>
<td>3</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Natural killer/T-cell lymphoma</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Diffuse large B-cell lymphoma</td>
<td>222</td>
<td>216</td>
<td>6</td>
<td>97</td>
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<td>Follicular lymphoma</td>
<td>140</td>
<td>133</td>
<td>7</td>
<td>95</td>
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<td>Peripheral T-cell lymphoma</td>
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<td>9</td>
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<td>90</td>
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<td>Small lymphocytic lymphoma</td>
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<td>24</td>
<td>5</td>
<td>83</td>
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<td>Enteropathy-type T-cell lymphoma</td>
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<td>2</td>
<td>1</td>
<td>67</td>
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<td>Marginal zone lymphoma, splenic</td>
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<td>2</td>
<td>1</td>
<td>67</td>
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<tr>
<td>MALT marginal zone lymphoma</td>
<td>50</td>
<td>27</td>
<td>23</td>
<td>54</td>
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<td>Lymphomatoid papulosis</td>
<td>2</td>
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<td>1</td>
<td>50</td>
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<td>Primary cutaneous anaplastic large T-cell lymphoma</td>
<td>5</td>
<td>2</td>
<td>3</td>
<td>40</td>
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<tr>
<td>All</td>
<td>766</td>
<td>718</td>
<td>48</td>
<td>94</td>
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</table>
FDG uptake and grading

Schöder et al. JCO 2005

Aggressive N=63
- DLBCL 55
- FL gr III 7
- PTCL 1

Indolent N=28
- FL gr I 11
- FL gr II 4
- MZL 4
- small cell 8
- lyPl 1

Fig 3. Box plots showing distribution of standard uptake value (SUV) among patients with aggressive and indolent lymphoma. The box represents the lower and upper quartiles and the median is marked with a horizontal line inside the box. The whiskers are the 10th and 90th percentiles with outlying observations individually plotted by squares outside the whiskers.
FDG avidity

Variability within same histological subtype: example DLBCL
PET for Staging of Lymphomas

20 studies – 854 patients – 3658 lesions

<table>
<thead>
<tr>
<th>Patient-based data</th>
<th>No. of studies</th>
<th>TPR (95% CI)</th>
<th>FPR (95% CI)</th>
<th>Maximum joint sensitivity and specificity (95%)</th>
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<tbody>
<tr>
<td>All</td>
<td>14</td>
<td>90.9 (88.0–93.4)</td>
<td>10.3 (7.4–13.8)</td>
<td>87.8 (85.0–90.7)</td>
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<td>Excluding studies with lowest sensitivity and lowest specificity</td>
<td>12</td>
<td>91.8 (88.8–94.3)</td>
<td>9.5 (6.6–13.1)</td>
<td>89.6 (87.5–91.6)</td>
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<tr>
<td>Hodgkin disease</td>
<td>6</td>
<td>92.6 (88.4–95.6)</td>
<td>13.4 (8.0–20.6)</td>
<td>89.4 (84.5–94.3)</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
<td>5</td>
<td>89.4 (82.8–94.1)</td>
<td>11.4 (5.6–19.9)</td>
<td>85.0 (78.2–82.0)</td>
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</table>

<table>
<thead>
<tr>
<th>Lesion-based data</th>
<th>No. of studies</th>
<th>TPR (95% CI)</th>
<th>FPR (95% CI)</th>
<th>Maximum joint sensitivity and specificity (95%)</th>
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<tbody>
<tr>
<td>All</td>
<td>7</td>
<td>95.6 (93.9–97.0)</td>
<td>1.0 (0.6–1.3)</td>
<td>95.6 (93.1–98.1)</td>
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<tr>
<td>Excluding study with lowest specificity</td>
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<td>95.1 (93.0–96.7)</td>
<td>1.0 (0.5–1.3)</td>
<td>95.8 (92.0–99.6)</td>
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</tbody>
</table>

upstaging: median 13.2% (7.7–17.4)
downstaging: median 7.5% (2.3–23.4)
**PET for Staging of Lymphomas**


<table>
<thead>
<tr>
<th>First author</th>
<th>Year</th>
<th>Ref.</th>
<th>Patients</th>
<th>P</th>
<th>R</th>
<th>Positive lesions</th>
<th>Type</th>
<th>Sensitivity, CT</th>
<th>Sensitivity, PET</th>
<th>Specificity, CT</th>
<th>Specificity, PET</th>
<th>Biopsy</th>
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<td>Buchmann</td>
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<td>52</td>
<td>52</td>
<td>–</td>
<td>124 regions</td>
<td>Mixed</td>
<td>84</td>
<td>99</td>
<td>100</td>
<td>100</td>
<td>30%</td>
</tr>
<tr>
<td>Jerusalem</td>
<td>2001</td>
<td>[35]</td>
<td>33</td>
<td>29</td>
<td>4</td>
<td>–</td>
<td>HD</td>
<td>73</td>
<td>79</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>Najjar</td>
<td>2001</td>
<td>[18]</td>
<td>36</td>
<td>21</td>
<td>15</td>
<td>31 sites</td>
<td>HD</td>
<td>90</td>
<td>87</td>
<td>100</td>
<td>100</td>
<td>All 31</td>
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<tr>
<td>Weihrauch</td>
<td>2002</td>
<td>[40]</td>
<td>22</td>
<td>22</td>
<td>–</td>
<td>77 sites</td>
<td>HD</td>
<td>74</td>
<td>88</td>
<td>100</td>
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<td>–</td>
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<tr>
<td>Wirth</td>
<td>2002</td>
<td>[41]</td>
<td>50</td>
<td>50</td>
<td>–</td>
<td>117 sites</td>
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<td>82</td>
<td>–</td>
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<td>–</td>
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<tr>
<td>Sasaki</td>
<td>2002</td>
<td>[22]</td>
<td>46</td>
<td>43</td>
<td>3</td>
<td>152 sites</td>
<td>Mixed</td>
<td>65</td>
<td>92</td>
<td>99</td>
<td>99</td>
<td>–</td>
</tr>
</tbody>
</table>

Three studies evaluated patients with Hodgkin’s disease (HD), the other 3 had a mix of HD and NHL. When available, the number of sites biopsied is provided.

Ref, Reference number; P, number of patients for primary staging; R, number of patients for re-staging.
PET/CT for staging HD

Raanani, Annals of Oncology 2006
Comparison of CE-CT with low-dose CT+PET

Table 3. Comparison of staging algorithms based on CT or PET/CT in 35 patients with HD

<table>
<thead>
<tr>
<th>PET/CT</th>
<th>CT</th>
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<td>I</td>
<td>II</td>
<td>III</td>
<td>IV</td>
<td>NE</td>
</tr>
<tr>
<td>I</td>
<td>–</td>
<td>2</td>
<td>–</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>II</td>
<td>1</td>
<td>14</td>
<td>1</td>
<td>2</td>
<td>–</td>
</tr>
<tr>
<td>III</td>
<td>–</td>
<td>5</td>
<td>2</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>IV</td>
<td>–</td>
<td>3</td>
<td>2</td>
<td>2</td>
<td>–</td>
</tr>
<tr>
<td>NE</td>
<td>–</td>
<td>1</td>
<td>–</td>
<td>–</td>
<td>–</td>
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</tbody>
</table>

Discordant in 45%
32% upstaging (non-enlarged LN, liver, spleen, bone, thymus)
13% downstaging
PET for staging of Lymphomas

DD lymphoma vs brown fat tissue

Kaste et al. Pediatric Radiology, 2005
PET for DD enlarged lymph nodes

Toxoplasmosis  DLBCL
PET for staging of Lymphomas

“reactive BM”

BMB+

BMB+

BMB- positive MRI
PET for Staging of Lymphomas

Conclusions

- Higher sensitivity and specificity for nodal and extra-nodal disease but false negatives do occur!!!!!!!

- Improved accuracy and “certainty of diagnosis” with PET-CT

- Complementary to contrast-enhanced CT

- Complementary to bone marrow aspiration

- Better than gallium scintigraphy

- Change in therapy management in 10%-20%, especially Stage I-II effect on outcome?

Initial staging = CE-CT + BMB + (PET)
PET-CT in lymphoma

<table>
<thead>
<tr>
<th>Description</th>
<th>Dose Details</th>
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<tr>
<td>Low dose PET-CT</td>
<td>&lt;30 mAs, no contrast, 2 mSv</td>
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<tr>
<td>“diagnostic” PET-CT</td>
<td>85 mAs, 120 ml contrast, 8 mSv</td>
</tr>
<tr>
<td>Dedicated CT</td>
<td>140 mAs, 200 ml contrast, 15-20 mSv</td>
</tr>
</tbody>
</table>
BAT regulates the body temperature by non-shivering thermogenesis. BAT is activated by stimulation of the β Adrenergic receptors and will induce oxidation of free fatty acids. The energy generated in this process is completely converted to heat.
Pattern
Methods

• Prospective study from January to March 2008
• Inclusion criteria
  – Patient scheduled for a FDG PET-CT examination (Siemens Biograph 2) were randomly assigned to the pre-treatment group or not.
• Exclusion criteria
  – Astma
  – Patients already on beta suppression
• Pre-treatment group received 20 mg Propranolol (Inderal°) 30 min prior to FDG injection.
  – No administration of Diazepam.
  – Patients were kept warm during uptake phase.
• Control of blood pressure and heart rate in all patient
  – on arrival, prior to FDG injection, prior to scan
Data analysis

- Visual scoring (- or +) for different regions
- Statistical analysis of 3 groups (Fisher exact)
  - Control group
  - Pre-treatment with Inderal 20 mg
  - Home medication
Results

330 FDG - PET – CT

- 190 males - 140 females
- mean age 58 (range 4-89)
- no significant differences between groups with regard to age, gender, diagnosis and BMI
- No effect of low dose inderal on heart rate and BP
## Results

<table>
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<tr>
<th></th>
<th>No patients</th>
<th>Brown fat</th>
<th>No brown fat</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pre-treated group</strong></td>
<td>99</td>
<td>3 (3%)</td>
<td>96 (97%)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>(propanolol 20mg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Control group</strong></td>
<td>160</td>
<td>26 (16.3%)</td>
<td>134 (83.7%)</td>
<td></td>
</tr>
<tr>
<td><strong>Beta-blocker</strong></td>
<td>71</td>
<td>1 (1.4%)</td>
<td>70 (98.6%)</td>
<td>P&lt;0.001</td>
</tr>
<tr>
<td>(home medication)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>330</td>
<td>30 (9%)</td>
<td>300 (91%)</td>
<td></td>
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</table>
Effect on one patient with Inderal without Inderal
PET for response assessment

• Literature data
  – Impact of histology, treatment, timing

• How to analyse
  – New cheson criteria vs other methods
PET at the end of therapy

Systematic review Zijlstra et al, Heamatologica 2006

Pooled sensitivity = 0.72 (95% CI 0.61 to 0.82)

Pooled specificity = 1.00 (95% CI 0.97 to 1.00)

NHL

Pooled sensitivity = 0.84 (95% CI 0.71 to 0.92)

Pooled specificity = 0.90 (95% CI 0.84 to 0.94)

HD

Systematic review Terasawa, JNM 2008, accuracy independent of residual mass
Revised Response Criteria for Malignant Lymphoma


Use of Positron Emission Tomography for Response Assessment of Lymphoma: Consensus of the Imaging Subcommittee of International Harmonization Project in Lymphoma

Malik E. Juweid, Sigrid Stroobants, Otto S. Hoekstra, Felix M. Mottaghy, Markus Dietlein, Ali Guermazi, Gregory A. Wiseman, Lale Kostakoglu, Klemens Scheidhauer, Andreas Buck, Ralph Naumann, Karoline Spaepen, Rodney J. Hicks, Wolfgang A. Weber, Sven N. Reske, Markus Schwaiger, Lawrence H. Schwartz, Josee M. Zijlstra, Barry A. Siegel, and Bruce D. Cheson
New Cheson Guidelines for end of treatment evaluation

**IWG criteria → IWC+PET criteria**

- **Complete remission (CR):** No more lesions visible
- **Complete remission unconfirmed (CRu):** reduction $>75$
- **Partial remission (PR):** reduction $>50$
- **Stable disease (SD):** reduction $<50$
- **Progressive disease (PD):** new lesion or $>50$

*Exception* New lesion $< 1.5$ cm and PET – is also PD
Guidelines on procedure and interpretation

Juweid et al, JCO 2007

• For HD and aggressive NHL at the end of treatment
  – > 3 weeks after last chemotherapy
  – > 12 weeks after end of radiotherapy

• Standardization of acquisition procedure
  – NCI guidelines Shanker et al. JNM 2006

• Visual analysis
  – Residual mass < 2cm ➔ higher than local background
  – Residual mass > 2cm ➔ higher than mediastinal blood pool
  – Special criteria for high background regions like spleen, liver, BM

• EXCLUDE increased FDG uptake in
  – Normal tissue (brown fat, Thymic rebound)
  – Inflammation

  ➔ PET-CT, baseline scan, clinical history

  ➔ EXPERIENCE
New PET-CT response criteria
Baseline
HL, Stage III

After
6x ABVD

Relapse
6 months FU
PET for detection of residual disease
Thymus Hyperplasia
inflammatory inguinal LN due to erysipelas

FL, stage III PET after 6x CHOP
Are new Cheson criteria a better predictor of outcome?
New Cheson Criteria in NHL

Brepoels, Stroobants et al., Leuk Lymphoma 2007;48:1522-1530

- **Materials and methods**
  - Data Spaepen, JCO 2000, 69 pts with NHL after CHOP like therapy
  - Revision of PET and CT images following IWG and new Cheson criteria
  - Correlation with updated outcome

- **2 analyses**
  - Potentially curable lymphoma
  - Considered incurable lymphoma

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age of diagnosis (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>52</td>
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</tr>
<tr>
<td>Range</td>
<td>15-72</td>
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<td>Ann-Arbor clinical stage</td>
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<td></td>
</tr>
<tr>
<td>I/II</td>
<td>26</td>
<td>38</td>
</tr>
<tr>
<td>III/IV</td>
<td>43</td>
<td>62</td>
</tr>
</tbody>
</table>

- **Histology**

  - **Group A**
    - Diffuse large B-cell: 41, 59%
    - Anaplastic large cell: 12, 17%
    - Burkitt’s lymphoma: 2, 3%

  - **Group B**
    - Follicle-center lymphoma: 8, 12%
    - Mantle-cell lymphoma: 4, 6%
    - Marginal-zone B-cell: 2, 3%

- **International Prognostic Index (IPI)**
  - Low: 33, 48%
  - Low intermediate: 19, 28%
  - High intermediate: 13, 19%
  - High: 4, 6%
New Cheson criteria in Aggressive NHL

Brepoels, Stroobants et al., Leuk Lymphoma 2007;48:1522-1530

Data Spaepen, JCO 2000, PET after first line R/
Updated and IWC + PET response
in 55 pts with routinely FDG-avid and potentially curable (aggressive) NHL
New Cheson criteria in Indolent NHL

Brepoels, Stroobants et al., Leuk Lymphoma 2007;48:1522-1530

Data Spaepen, JCO 2000, PET after first line R/
Updated and IWC + PET response
in 14 pts with not-routinely
FDG-avid and incurable NHL (8 FL, 4 MCL, 2 MZL)
New Cheson criteria in Hodgkin

Brepoels, Stroobants et al. Leuk Lymphoma 2007:1539-1547

Data Spaepen, Br J Haematol. 2001
Updated and IWC + PET response in 56 HD
PET at the end of first line R/ (after RT)

Table II.1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>No. of patients</th>
<th>relapse (n=5)</th>
<th>second line (n=4)</th>
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<td><strong>Age of diagnosis</strong></td>
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<td>Median</td>
<td>32</td>
<td>25</td>
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<tr>
<td>Range</td>
<td>9-70</td>
<td>15-44</td>
<td>35-39</td>
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<tr>
<td><strong>Follow-up (months)</strong></td>
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<tr>
<td>Median</td>
<td>107</td>
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<tr>
<td>Range</td>
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<td>2-20</td>
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<tr>
<td><strong>Sex</strong></td>
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</tr>
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<td>Men</td>
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</tr>
<tr>
<td>Women</td>
<td>30</td>
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<td><strong>Ann-Arbor clinical stage</strong></td>
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<td>I/II</td>
<td>24</td>
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<tr>
<td>II/IV</td>
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<td>26</td>
<td>5</td>
<td>2</td>
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<td><strong>Bulky disease</strong></td>
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<td>Lymphocyte predominance</td>
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<td>MOPP/ABV</td>
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IWC + PET

Time in years
Can RT be omitted in PET negative patients?


Patients included in HD15 trial: PET after 6 or 8 x BEACOPP in advanced HD, RT in PET+ only

Interim analysis on patient with FU >12m (n=275)

PET+ ~ new Cheson criteria

Relapse rate

PET negative 9/216 (4%)

PET positive 9/59 (15%)

NPV= 94%
Use of PET for during treatment for outcome prediction
### PET during first-line therapy


#### Table III. Prognostic value of PET for early response assessment during first-line or induction treatment.

<table>
<thead>
<tr>
<th>Author</th>
<th>Number of patients</th>
<th>Histology</th>
<th>Timing PET (cycles)</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>Accuracy %</th>
<th>PPV %</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jerusalem et al. [47]</td>
<td>28</td>
<td>NHL</td>
<td>2–5</td>
<td>42</td>
<td>100</td>
<td>73</td>
<td>100</td>
<td>67</td>
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<tr>
<td>Mikhaeel et al. [11]</td>
<td>23</td>
<td>NHL</td>
<td>2–4</td>
<td>100</td>
<td>94</td>
<td>96</td>
<td>88</td>
<td>100</td>
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<tr>
<td>Mikhaeel et al. [48]</td>
<td>32</td>
<td>HD</td>
<td>2–3</td>
<td>75</td>
<td>100</td>
<td>94</td>
<td>100</td>
<td>92</td>
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<tr>
<td>Kostakoglu et al. [49]</td>
<td>30</td>
<td>HD/NHL</td>
<td>1</td>
<td>87</td>
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<tr>
<td>Spaepen et al. [50]</td>
<td>70</td>
<td>NHL</td>
<td>3–4</td>
<td>85</td>
<td>100</td>
<td>91</td>
<td>100</td>
<td>84</td>
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<tr>
<td>Zijlstra et al. [51]</td>
<td>26</td>
<td>NHL</td>
<td>2</td>
<td>64</td>
<td>75</td>
<td>69</td>
<td>75</td>
<td>75</td>
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<tr>
<td>Torizuka et al. [52]</td>
<td>20</td>
<td>HD/NHL</td>
<td>1–2</td>
<td>87</td>
<td>50</td>
<td>80</td>
<td>87</td>
<td>50</td>
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<tr>
<td>Friedberg et al. [24]</td>
<td>22</td>
<td>HD</td>
<td>3</td>
<td>80</td>
<td>94</td>
<td>91</td>
<td>80</td>
<td>94</td>
</tr>
<tr>
<td>Haioun et al. [53]</td>
<td>90</td>
<td>NHL</td>
<td>2</td>
<td>63</td>
<td>71</td>
<td>68</td>
<td>55</td>
<td>77</td>
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<tr>
<td>Mikhaeel et al. [54]</td>
<td>121</td>
<td>NHL</td>
<td>2–3</td>
<td>5-year PFS of 16.2% when PET+, 88.8% when PET-, 59.3% for MRU</td>
<td>69</td>
<td>95</td>
<td></td>
<td></td>
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<tr>
<td>Hutchings et al. [55]</td>
<td>85</td>
<td>HD</td>
<td>2–3</td>
<td>5-year PFS of 38.5% when PET+, 91.5% when PET-, MRU considered PET-</td>
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<tr>
<td>Hutchings et al. [56]</td>
<td>77</td>
<td>HD</td>
<td>2</td>
<td>79</td>
<td>92</td>
<td>90</td>
<td>69</td>
<td>95</td>
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<tr>
<td>Gallamini et al. [57]</td>
<td>108</td>
<td>HD</td>
<td>2</td>
<td>86</td>
<td>98</td>
<td>95</td>
<td>90</td>
<td>97</td>
</tr>
</tbody>
</table>

PPV: positive predictive value; HD: Hodgkin’s disease; NHL: Non-Hodgkin’s lymphoma; PFS: progression-free survival; PET+: PET positive; PE negative; MRU: minin
PET at during first line therapy

Meta analysis Terasawa et al, J Clin Oncology 2009

HD Pooled sens= 0.81 (95% CI 0.72 to 0.89)

HD Pooled spec= 0.97 (95% CI 0.94 to 0.99)
PET at during first line therapy

Meta analysis Terasawa et al, J Clin Oncology 2009

NHL Pooled sens = 0.78 (95% CI 0.64 to 0.87)

NHL Pooled spec = 0.87 (95% CI 0.95 to 0.93)
Early Interim 2-[\(^{18}\)F]Fluoro-2-Deoxy-D-Glucose Positron Emission Tomography Is Prognostically Superior to International Prognostic Score in Advanced-Stage Hodgkin’s Lymphoma: A Report From a Joint Italian-Danish Study

Andrea Gallamini, Martin Hutchings, Caterina Patti, Annika Loft, Francesco Caterina Stelitano, Rosario Sancetta, Ivana Pierri, and Alessandro Levis
**PET in DLBCL after more intensified treatment or in combination with Retuximab**

**Haioun et al, Blood 2005**

**Induction Chemotherapy (4 cycles)**
- (R)-CHOP/3w (> 60y)
- R-ACVPB/2w
- ACVBP/ACE

**Consolidation/salvage Treatment (CT based)**
- R-ACVPB
- High Dose + AutoSTx

Comparison of PET results after 2 and 4 cycles

- 13 patients PET2 positive → PET4 negative
- Patients that were PET negative after 2 remained PET negative after 4
Poor Predictive Value of FDG-PET/CT Performed after 2 Cycles of R-CHOP standard in Patients with Diffuse Large B-Cell Lymphoma (DLCL)

Amanda Cashen, M.D., Farrokh Dehdashti, M.D.*, Jingqin Luo, Ph.D.* and Nancy L. Bartlett, MD
Washington University School of Medicine, Saint Louis, MO, USA

ASH 2008, abstract 371

PET response based on new Cheson guidelines

After 2 or 3 cycles

After 6 cycles
How to evaluate early PET

Lin, Itti, Haioun et al, JNM 2007

**Induction Chemotherapy (4 cycles)**
- (R)-CHOP/3w (> 60y)
- R-ACVPB/2w
- ACVBP/ACE

**Consolidation/salvage Treatment (CT based)**
- R-ACVPB
- High Dose + AutoSTx

Baseline → PET 2
Baseline + D 7 Mid R/ End of R/

Refactory Disease (PA+)

NED FU 29m
PET prior to stem cell transplantation

Meta analysis Poulou et al, EJNMMI 2010

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Weight</th>
<th>Hazard Ratio Exp[(O-E) / V], Fixed, 95% CI</th>
<th>Hazard Ratio Exp[(O-E) / V], Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cremerius U, 2002</td>
<td>3.8%</td>
<td>6.43 [0.78, 53.19]</td>
<td></td>
</tr>
<tr>
<td>Crocchiolo R, 2008</td>
<td>10.2%</td>
<td>4.23 [1.17, 15.27]</td>
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<tr>
<td>Derenzini E, 2008</td>
<td>18.4%</td>
<td>6.56 [2.52, 17.06]</td>
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</tr>
<tr>
<td>Hoppe BS, 2009</td>
<td>20.1%</td>
<td>2.44 [0.98, 6.08]</td>
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<tr>
<td>Schot BW, 2003</td>
<td>14.8%</td>
<td>1.25 [0.43, 3.64]</td>
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<tr>
<td>Spaepen K, 2003</td>
<td>2.4%</td>
<td>2.87 [0.21, 39.36]</td>
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<tr>
<td>Svoboda J, 2006</td>
<td>30.3%</td>
<td>3.40 [1.61, 7.16]</td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>100.0%</td>
<td>3.23 [2.14, 4.87]</td>
<td></td>
</tr>
</tbody>
</table>

Total events

Heterogeneity: Chi² = 6.12, df = 6 (P = 0.41); I² = 2%

Test for overall effect: Z = 5.61 (P < 0.000001)
PET for surveillance

- Limited data

- Jerusalem et al. (Annals of Oncology 2003)
  - 36 HD
  - PET every 4-6 months during 3y
  - 11 positive PETs – 5 relapses (FPR 55%)

- Mocikova et al. (Abstract Int. Symposium on HL, Cologne, 2007)
  - 82 HD, 301 PETs, mean FU 39 months
  - 70 patients were PET- after treatment
    - 31/70 became PET+ but transient non-specific in 19 pts (61.3%)
  - 12 patients were PET+ after treatment
    - 5 primary resistant HD
    - 7 non-specific and transient (1 biopsy: reactive changes)
PET for surveillance

- Goldschmidt et al, Ann Hematology 2010
  - Retrospective analysis of 125 patients who relapsed > 1m after end of therapy
PET and PET-CT in lymphoma
When and how to use?

- **Baseline PET**
  - PET/CT most accurate test
  - Strongly encouraged if PET response assessment will be done
  - ? Outcome

- **PET during treatment**
  - Promising but only on in trials (impact on outcome?)
  - Optimal Timing? What is PET positive?

- **End of treatment PET**
  - Routine use in aggressive NHL and HD ➔ new response criteria
  - No detection of MRD; Sensitive enough to omit radiotherapy?
  - Exclude false positive uptake!

- **PET for surveillance**
  - Limited data, high false positive rate ➔ no routine use, histology!
  - Better than clinical FU?