Response evaluation of lymphoma using PET/CT: a comprehensive review of PERCIST 1.0 and Cheson 2007

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Learning objectives

Evaluation of tumor treatment response plays an important role in oncology. Approaches to the assessment of response in lymphomas differ from those used in solid tumors. In the last decade 18F-FDG PET/CT confirmed its advantages in lymphomas and was applied in all steps of lymphomas management. As the result specific criteria for assessing lymphoma therapy, such as Cheson 2007 and PERCIST (PET Response Criteria in Solid Tumors) 1.0, were developed.

This poster follows the outlined objectives:

- to present the limitations of traditional anatomical criteria for follow-up of lymphomas;
- to discuss capabilities and disadvantages of Cheson 2007 criteria and PERCIST 1.0 on the example of follow-up of patients with different histological types of lymphomas;
- to demonstrate the applicability of the semi-automatic FDG-uptake measurement.

Background

According to the results of SEER (Surveillance, Epidemiology and End Results Program of National Cancer Institute) there are 509 065 people with the NHL and 181 928 people with HL in the USA. Distinguishing as early as possible between patients who are responding to a particular treatment and those who are not can maximize the effectiveness of patient care\(^1\). Assessment of tumor therapy response in patients with lymphomas is extremely important as the rate of response directly determines the outcomes. Due to the fact that lymphomas often do not completely regress after treatment because of residual fibrosis and necrosis, assessment of changes in anatomical dimensions may not reflect disease status precisely.

Metabolic response of lymphoma tumor may be more predictive of outcome than morphologic criteria; therefore the use of PET/CT in different types of lymphomas has increased dramatically\(^2\).

During the recent few years a necessity of developing specific treatment response criteria using PET/CT emerged. Cheson 2007 criteria and PERCIST 1.0 are commonly used for this purpose. Before 1999, response criteria for malignant lymphomas varied widely with respect to the size of a normal lymph node, the frequency of assessment and the methods used to assess response.
First created in 1997 and revised in 2007 the **Cheson response criteria** allow analysis of both: the size and the metabolic activity of lymphomas during the course of treatment\(^3\). However, only qualitative method of metabolic activity of tumor lesions assessment is used in this algorithm *(see Table 1)*.

In 2009 the **PERCIST** criteria were proposed to create an assessment tool for PET/CT tumor response. The main innovation is standardization of quantitative assessment of lesion FDG uptake, but it requires the usage of similar protocols between baseline study and follow-ups.

Thus, the measurements in our study were performed by two approaches: lymphoma-specific Cheson criteria (2007) and universal PERCIST (2009), which use qualitative and quantitative estimation of FDG uptake, respectively.

**Images for this section:**

<table>
<thead>
<tr>
<th>Criterion</th>
<th>Definition of «measurable» lesions</th>
<th>Method of measurement</th>
<th>PET technical points</th>
<th>How to choose «target» lesions?</th>
<th>New lesions</th>
</tr>
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<tr>
<td><strong>Cheson 2007</strong></td>
<td>Can clearly measure the size in 2 perpendicular dimensions at baseline; nodal lesions: &gt; 15 mm in greatest transverse diameter (GTD) regardless of short axis measurement, or &gt; 10 mm in short axis; extranodal lesions: ≥ 10 mm in the GTD; nodules within the liver or spleen: must be ≥ 10 mm in two perpendicular dimensions</td>
<td>Greatest transverse diameter</td>
<td>PET is usually performed along with CT for anatomic coregistration; post-treatment PET should be performed no less than 6-8 weeks after chemotherapy; 8-12 weeks after radiation</td>
<td>Up to 6 lesions; larger are better; lesions should be from different regions of the body; include mediastinal and retroperitoneal lesions whenever these sites are involved</td>
<td>Any new lesion which measures at least 15 mm in any axis; significant new effusions, ascites or other fluid collections; new lesions automatically mean progression has occurred</td>
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**Table 1:** Summary of Cheson 2007 criteria
Findings and procedure details

PERCIST PET/CT analysis consists of three steps: search for measurable target lesions, normalization of uptake and assessment of response.

The first step is searching for target lesions. According to Juweid et al.\textsuperscript{5}, a positive PET-scan is defined as focal or diffuse FDG uptake above background in a location incompatible with normal physiologic uptake. It should be noted that organ-specific standardized uptake value cut-offs do not exist.

Measurable target lesion is the single hottest tumor lesion SUL (lean body mass-normalized SUV [SUV\textsubscript{lbm}]) of «maximal 1.2-cm diameter volume ROI in tumor» (SUL peak). The SUL peak is determined for up to 5 tumors (up to 2 per organ) with the most intense FDG uptake (see Figure 1).

The second step is the normalization of average SUL. SUL peak is at least 1.5-fold greater than liver SUL mean + 2 SDs (spherical ROI in right lobe of liver must be # 3 cm) or > 2.0 x SUL mean of blood pool in 1-cm-diameter ROI in descending thoracic aorta (see Figure 2).

This presentation describes semi-automatic algorithm for FDG uptake measurement without using special PET/CT application. In our study maximal FDG uptake value was determined using the ROI freehand tool. The obtained values of the absorbed activity, expressed in kBq/g, were converted into SUL peak using the conversion formula by the spreadsheet software.

The third step is the assessment of tumor treatment response (see Table 2).

Quantitative assessment of FDG uptake level is the key benefit of PERCIST 1.0, which potentially may avoid false-positive results of PET/CT in patients with different types of lymphomas. In contrast, Cheson 2007 criteria provide only binary (positive or negative) classification of PET/CT results. Using PERCIST leads to increased complete and partial metabolic response rate (see Figures 3, 4).

Images for this section:
Fig. 1: Target lesion selection and measurement with PERCIST 1.0. Axial PET/CT image of a 38-year-old woman with the history of non-Hodgkin lymphoma shows multiple tumor lesions in the left axillary region and a single lesion in the right paratracheal region. According to PERCIST 1.0, FDG uptake value is determined for up to 5 tumors with the most intense FDG uptake. Measurable target lesion is the hottest single tumor lesion SUL of "maximal 1.2-cm diameter volume ROI in tumor" (SUL peak). This SUL peak ROI typically includes the maximal SUL pixel (which should also be recorded) but is not necessarily centered on the maximal SUL pixel. A. SUL peak is 5.31. B. SUL peak is 2.50.

Fig. 2: Example of liver background calculation for normalization of SUL. C. A 3-cm-diameter 3D ROI (ROI 1) is placed on normal right lobe of liver; average SUL and SD in
ROI are displayed. Liver background is calculated as follows: \(1.5 \times \text{average SUL liver} + (2 \times \text{SD average SUL liver})\). For this example, \((1.5 \times 0.96) + (2 \times 0.07) = 1.58\). Therefore, both lesions (Fig. 1; A and B) are "measurable".

<table>
<thead>
<tr>
<th>Complete Response</th>
<th>Partial Response</th>
<th>Stable Disease</th>
<th>Progressive Disease</th>
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<tr>
<td><strong>Cheson 2007</strong></td>
<td>≥50% reduction in target lesions, no growth of non-target or new lesions; if PET used, PET positive in at least one previously involved lesion; if imaging response is CR, but there is persistent bone marrow involvement or persistent clinical evidence of disease, the overall response is PR</td>
<td>None of above</td>
<td>≥50% increase from nadir in SPD of target lymph nodes, or single involved node or the size of other lesions (e.g., splenic or hepatic nodules); appearance of new abnormal nodes or any new lesion &gt; 15 mm in any axis; new FDG-positive site is only PD if confirmed with other modalities</td>
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<td><strong>PERCIST 1.0</strong></td>
<td>&gt;30% (0.8-unit) decline in SUL peak between the most intense lesion before treatment and the most intense lesion after treatment</td>
<td>None of above</td>
<td>&gt;30% (0.8-unit) increase in SUL peak or confirmed new lesions</td>
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**Table 2**: Comparison of Cheson 2007 criteria and PERCIST 1.0
Fig. 3: PET/CT images obtained before (A) and after (B) treatment of B-cell lymphoma. Note profound total decline in SUL peak (10.13#2.21; 79 %); (167.4 mm#68.3 mm; 53 % reduction in GTD) in target lesion. This decline represents metabolic partial response by PERCIST; partial response by Cheson 2007.
**Fig. 4:** Patient with Hodgkin's lymphoma before (A) and after (B) treatment (PET/CT). Note absolute decline in SUL peak (29.78% less than mean liver activity = «indistinguishable» from surrounding tissue; 100% decline), but only partial reduction (90.1 mm > 60 mm; 14.3%) in greatest transverse diameter of target lesion. On the basis of these measurements treatment response would be categorized as a stable disease by Cheson 2007 but as complete metabolic response by PERCIST 1.0.
Conclusion

The use of anatomic response criteria alone for lymphomas assessment is not sufficient. Treatment response assessment in lymphomas requires evaluation of the metabolic component. Despite the recent modification of Cheson criteria for PET/CT, application at PERCIST allows improved assessment of treatment response by quantification of FDG uptake using semi-automatic SUL calculation.

Personal information

References