Lymphoma
Read with the experts

Marc Seltzer, MD
Associate Professor of Radiology
Geisel School of Medicine at Dartmouth
Director, PET-CT Course
American College of Radiology
Recognize common pitfalls and artifacts in interpreting PET/CT in lymphoma
Discuss and apply current recommendations for performing a standardized interpretation of PET/CT in response assessment of lymphoma
Identify common patterns of spread by lymphoma and recognize subtypes of lymphoma that have variable or low FDG uptake
Case 1
22 yoM Large B-Cell Lymphoma

PET-CT performed 2 days after starting chemotherapy
On this PET-CT performed 2 days after starting chemotherapy, the most likely explanation for the low FDG uptake in the mediastinal mass is:

A. Large B-cell lymphomas are not reliably FDG avid
B. The histology of the mediastinal mass was not adequately sampled prior to starting chemotherapy
C. The bulk of the mass is comprised of inflammatory tissue
D. FDG uptake is suppressed due to 2 days of chemotherapy
On this PET-CT performed 2 days after starting chemotherapy, the most likely explanation for the low FDG uptake in the mediastinal mass is:

A. Large B-cell lymphomas are not reliably FDG avid

B. The histology of the mediastinal mass was not adequately sampled prior to starting chemotherapy

C. The bulk of the mass is comprised of inflammatory tissue

D. FDG uptake is suppressed due to 2 days of chemotherapy
22 yoM Large B-Cell Lymphoma
Restaging PET-CT after 6 cycles of chemotherapy
Restaging PET/CT after 6 cycles of chemotherapy
Baseline CT

Restaging PET/CT Post 6 cycles of chemo
The most likely explanation for the high FDG uptake in the residual mediastinal mass is:

A. Thymic hyperplasia
B. Metastatic lesion from another new primary tumor
C. Post-chemotherapy inflammation
D. Residual active lymphoma
The most likely explanation for the high FDG uptake in the residual mediastinal mass is:

A. Thymic hyperplasia
B. Metastatic lesion from another new primary tumor
C. Post-chemotherapy inflammatory tissue
D. Residual active lymphoma
Mini-sternotomy after PET-CT

• Final pathology: Rests of normal thymic tissue
• No lymphoma present in specimen
• Findings at pathology consistent with thymic hyperplasia
22 yoM Large B-Cell Lymphoma
Follow-up PET-CT 3 months post sternotomy
3 months after surgical excision with no further treatment: 
PET Interpretation: “No active lymphoma”
Case 1
Teaching Points

- FDG avid hyperplastic thymic tissue is commonly seen in children and young adults in the early months following completion of chemotherapy.

- As the thymus normally involutes with aging, the morphologic appearance of thymic hyperplasia can be quite variable ranging from homogeneous and curvilinear, to heterogenous, patchy, asymmetric, and focal.
Lymphomas can arise within or near the thymus. In such cases, residual active lymphoma cannot always be excluded as the cause of a post-chemotherapy residual hypermetabolic mass without surgical or biopsy proof.

While uncommon, high FDG uptake in a post-chemotherapy residual mass may be due to inflammation.
14 year old with anaplastic lymphoma

Baseline

4 months post-chemo (NED)
Post - Chemotherapy Thymic Hyperplasia
Post - Chemotherapy Thymic Hyperplasia
Post-Chemotherapy Thymic Hyperplasia
Recurrent Lymphoma and Thymic Hyperplasia
Recurrent Lymphoma and Thymic Hyperplasia
Recurrent Lymphoma and Thymic Hyperplasia
The degree of FDG uptake in thymic hyperplasia is variable but typically greater than or equal to liver activity.
Case 2
History

52-year-old woman with Hodgkin lymphoma referred for a restaging PET/CT after 2 cycles of chemotherapy
Baseline

Marrow Bx: +Diffuse Infiltration

Post 2 cycles chemotherapy

? Worse, Stable, Better?
Based on the images shown, the BEST interpretation of the PET findings is:

A. Worsening of active lymphoma
B. Stable active lymphoma
C. Improved but residual active lymphoma
D. Resolved, no active lymphoma
E. Indeterminate for residual active lymphoma
Based on the images shown, the BEST interpretation of the PET findings is:

A. Worsening of active lymphoma

B. Stable active lymphoma

C. Improved but residual active lymphoma

D. Resolved, no active lymphoma

E. Indeterminate for residual active lymphoma
Baseline PET/CT

Post 2 cycles chemotherapy
Baseline L2 body

Post-2 cycles chemo
Baseline
L2 body

Post-2 cycles chemo
Baseline para-aortic node

Post-2 cycles chemo
Baseline para-aortic node

Post-2 cycles chemo
Baseline para-aortic node

Post-2 cycles chemo
Based on the images shown, the BEST interpretation of the PET findings is:

A. Improved but residual active lymphoma in the left paraaortic lymph node

B. Improved but residual active lymphoma in the L4 vertebral body

C. No active lymphoma in the L4 vertebral body nor in the left paraaortic lymph node.

D. Worsening of active lymphoma (treatment failure)
Based on the images shown, the BEST interpretation of the PET findings is:

A. Improved but residual active lymphoma in the left paraaortic lymph node

B. Improved but residual active lymphoma in the L4 vertebral body

C. No active lymphoma in the L4 vertebral body nor in the left paraaortic lymph node. Reactive marrow hyperplasia in the skeleton that was not involved by lymphoma.

D. Worsening of active lymphoma (treatment failure)
Case 2
Final Diagnosis

- No active lymphoma in the L4 vertebral body nor in the left paraaortic lymph node. Marrow hyperplasia throughout the skeleton.
61F, Hodgkin Lymphoma

Baseline

Marrow Bx: +Diffuse Infiltration

Post 2 cycles chemo

Treated lesions and Reactive Marrow
“Probably no active disease”

Post 6 cycles chemo

Marrow Bx: Negative
“No active disease”
Marrow hyperplasia on PET/CT is commonly seen in patients receiving granulocyte colony stimulating factor (GCSF) which is given concurrently with chemotherapy.

Rebound marrow hyperplasia on PET/CT can also be seen in the early weeks to months after completing chemotherapy.
• The presence of diffuse marrow activity on a follow-up PET/CT should not be misinterpreted as tumor involvement, particularly when all previously known sites of disease have resolved.
Non-Hodgkin’s Lymphoma Restaging
Marrow and Splenic Hyperplasia due to colony stimulating factors
PET/CT Initial Staging NSCLC

Diffuse marrow activity presumed due to tumor GCSF production
Baseline PET/CT

Post 4 cycles chemotherapy
Baseline PET/CT

Post 4 cycles chemotherapy
Case 3
52-year-old with non-small cell lung cancer undergoing presurgical evaluation
The BEST interpretation of the PET findings is:

A. Right lung cancer and a second primary neoplastic process such as lymphoma involving the left axilla

B. Right lung cancer and unrelated inflammatory process involving the left axilla and left deltoid

C. Right lung cancer and contralateral left axillary nodal metastases

D. Right lung cancer and infiltrated dose in the left arm
The BEST interpretation of the PET findings is:

A. Right lung cancer and a second primary neoplastic process such as lymphoma involving the left axilla

B. Right lung cancer and unrelated inflammatory process involving the left axilla and left deltoid

C. Right lung cancer and contralateral left axillary nodal metastases

D. Right lung cancer and infiltrated dose in the left arm
Case 3
Diagnosis

- Right lung cancer and unrelated inflammatory process involving the left axilla and left deltoid.
- The patient had influenza vaccination in the left deltoid 3 days prior to the PET/CT.
Flu shot in left arm 3 days before PET/CT
Case 3
Teaching Points

• Recent vaccinations can result in FDG uptake at the injection site and within regional lymph nodes.

• The regional lymph nodes may or may not appear pathologically enlarged.

• Dose infiltration can result in FDG uptake within the draining sentinel lymph nodes on the side of injection. The lymph nodes are typically NOT enlarged and FDG uptake within lymphatic vessels may be seen distal to the injection site.
Dose infiltration in right antecubital fossa
Follicular lymphoma in left arm and axilla
Case 4
42 yoW Non-Hodgkin’s Lymphoma
Baseline
6 cycles
42 yoW Non-Hodgkin’s Lymphoma
Baseline
6 cycles
42 yoW Non-Hodgkin’s Lymphoma
Baseline
6 cycles
42 yo W Non-Hodgkin’s Lymphoma
Baseline 6 cycles
After 6 cycles of chemotherapy, which of the following is the BEST overall impression of the PET-CT findings:

A. No active lymphoma
B. Indeterminate for residual active lymphoma
C. Suspicious for residual active lymphoma
D. New marrow involvement by lymphoma
After 6 cycles of chemotherapy, which of the following is the BEST overall impression of the PET-CT findings:

a. No active lymphoma
b. Indeterminate for residual active lymphoma
c. Suspicious for residual active lymphoma
d. New marrow involvement by lymphoma
42 yo W Non-Hodgkin’s Lymphoma
Baseline
6 cycles
5 weeks later

“Indeterminate”
Baseline

6 cycles

5 weeks later

42 yo W Non-Hodgkin’s Lymphoma
42 yo W. Non-Hodgkin’s Lymphoma  
Baseline
6 cycles
5 weeks later
42 yo W Non-Hodgkin’s Lymphoma
Baseline
6 cycles
5 weeks later
5 weeks after the post cycle 6 PET-CT, which of the following is the BEST overall impression of the PET-CT findings:

A. No active lymphoma
B. Indeterminate for recurrent active lymphoma
C. Recurrent active lymphoma
D. New marrow involvement by lymphoma
5 weeks after the post cycle 6 PET-CT, which of the following is the BEST overall impression of the PET-CT findings:

A. No active lymphoma
B. Indeterminate for recurrent active lymphoma
C. **Recurrent active lymphoma**
D. New marrow involvement by lymphoma
NCCN recommends using which of the following PET imaging criteria to assess treatment response and determine further treatment options in Hodgkin lymphoma?

a. PERCIST
b. International working group response criteria
c. Standardized uptake value criteria
d. Deauville criteria
e. None of the above: interpretation criteria are not included in NCCN guidelines
NCCN recommends using which of the following PET imaging criteria to assess treatment response and determine further treatment options in Hodgkin lymphoma?

a. PERCIST  
b. International working group response criteria  
c. Standardized uptake value criteria  
d. Deauville criteria  
e. None of the above: interpretation criteria are not included in NCCN guidelines
Deauville Criteria for PET Guided Response Assessment of Lymphoma

### NCCN Guidelines Version 2.2014
Hodgkin Lymphoma

#### DEAUVILLE PET CRITERIA*

<table>
<thead>
<tr>
<th>Score</th>
<th>PET/CT scan result</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>No uptake above background</td>
</tr>
<tr>
<td>2</td>
<td>Uptake ≤ mediastinum</td>
</tr>
<tr>
<td>3</td>
<td>Uptake &gt; mediastinum but ≤ liver</td>
</tr>
<tr>
<td>4</td>
<td>Uptake moderately increased compared to the liver at any site</td>
</tr>
<tr>
<td>5</td>
<td>Uptake markedly increased compared to the liver at any site</td>
</tr>
<tr>
<td>X</td>
<td>New areas of uptake unlikely to be related to lymphoma</td>
</tr>
</tbody>
</table>

*For definitions of 5a and 5b as used in the NCCN Guidelines, [see MS-4](#).
Deauville Criteria for PET Guided Response Assessment of Lymphoma

Hodgkin Lymphoma

CLINICAL PRESENTATION:
Classical Hodgkin lymphoma
Stage I A, IIA Favorable
(Continued from HODG-2)
PRIMARY TREATMENT
ABVD alone

Abvd alone
ABVD x 2 cycles
including diagnostic CT of areas of initial disease

Deauville 1-2°
Restage with PET-CT
Partial response (PR) on CT

Deauville 3-4°
Deauville 5a°
Deauville 5b°

ABVD x 2 cycles (total 4)

Restage with PET-CT

ABVD x 2 cycles (total 4)

ABVD x 2 cycles (total 4)

ABVD x 2 cycles (total 6)
or ISRT

ABVD x 2 (total 6) + ISRT

See Follow-up (HODG-13)

See Follow-up (HODG-13)

See Refractory Disease (HODG-14)

See Refractory Disease (HODG-14)

Observe with short interval follow-up rt (see HODG-13)

Observe with short interval follow-up rt (see HODG-13)

Observe with short interval follow-up rt (see HODG-13)
Non-Hodgkin’s Lymphoma
Baseline
6 cycles
5 weeks later

Deauville 3 or 4
Deauville 4 or 5
Non-Hodgkin’s Lymphoma

Baseline  2 cycles  6 cycles
Non-Hodgkin’s Lymphoma
Baseline 2 cycles 6 cycles
Non-Hodgkin’s Lymphoma

Baseline  

2 cycles  

6 cycles
Non-Hodgkin’s Lymphoma

Baseline  2 cycles  6 cycles
Non-Hodgkin’s Lymphoma

Baseline

2 cycles

6 cycles
Bleomycin induced pneumonitis

Baseline | 2 cycles | 6 cycles

Deauville 2 | Deauville 2, X
The Deauville criteria is included in the NCCN guidelines for BOTH Hodgkin and Non-Hodgkin lymphoma management algorithms?

a. True
b. False
The Deauville criteria is included in the NCCN guidelines for BOTH Hodgkin and Non-Hodgkin lymphoma management algorithms?

a. True
b. False

The Deauville criteria is included in the NCCN guidelines for Hodgkin and DLBCL (2015)
The Deauville criteria is included in the NCCN guidelines for Hodgkin and DLBCL (2015).
The Deauville criteria is included in the NCCN guidelines for Hodgkin and DLBCL (2015)

However, the application of PET to responses is limited to histologies where there is reliable FDG uptake in active tumor. However, the revised response criteria have thus far only been validated for DLBCL and Hodgkin lymphoma. The application of the revised response criteria to other histologies requires validation and the original IWG guidelines should be used. Of note, the IWG response criteria may not be applicable for several of the tumor subtypes included in the NCCN Guidelines. Tumor specific response criteria are included in the guidelines for CLL/SLL, MF/SS, ATLL, HCL and T-PLL.
Which one of the following types of lymphomas is the LEAST likely to be $^{18}$F-FDG-avid?

a. Diffuse large B cell
b. Follicular
c. Marginal zone/ mucosa-associated lymphoid tissue
d. Hodgkin
e. Mantle Cell
Which one of the following types of lymphomas is the LEAST likely to be $^{18}$F-FDG-avid?

a. Diffuse large B cell  
b. Follicular  
c. Marginal zone/ mucosa-associated lymphoid tissue  
d. Hodgkin  
e. Mantle cell
Newly Diagnosed MALT Lymphoma of the Stomach
Newly Diagnosed MALT Lymphoma of the Stomach
Newly Diagnosed MALT Lymphoma of the Stomach
Case 5
60 yo male presented with increasing fatigue, night sweats and adenopathy.

Labs revealed elevated WBC with lymphocyte predominance, anemia, thrombocytopenia and elevated LDH.

Flow cytometry confirmed CLL

On exam patient had diffuse adenopathy and dominant neck mass

PET scan done to help stage disease and guide biopsy
Biopsy of neck mass confirmed transformation of CLL to DLBCL (Richter’s Transformation). Patient received 4 cycles of RCHOP with resolution of all PET avid adenopathy. Autologous stem cell transplant. In remission after 3 years. Goal of treatment was to cure the aggressive lymphoma; CLL is likely to relapse in future.
Thank you and Questions?
Bonus Cases
(Interpretation Pitfalls)
42 yo man, mediastinal adenopathy, suspected lymphoma
Final Diagnosis: Disseminated Sarcoidosis
19 yoW with fevers, night sweats, remote h/o Hodgkin’s
Acute EBV Infection (confirmed by serum titer)
Repeat (new baseline) PET-CT 6 months post EBV Infection
PET/CT Restaging Lymphoma

??Recurrence
PET/CT Restaging Lymphoma

Brown Adipose Tissue
Brown Adipose Tissue

- Exists in animals, infants, and adults.
- Mitochondria rich and highly vascular
- Sympathetic nervous system activity significantly increases glucose uptake by BAT.
- FDG uptake is felt to be due to non-shivering thermoregulation caused by sympathetic stimulation
- BAT on PET scans is more commonly seen in younger, thin, women and seen more frequently during winter months
Brown Adipose Tissue

- FDG uptake in brown adipose tissue can be dramatically reduced by pre-medication with a benzodiazepine or beta blocker
- Consider pre-medication in any young patient (up to age 40)
- Oral alprazolam 0.5 mg or diazepam 5 mg given 60 minutes prior to FDG injection
- CT part of PET-CT helps avoid misinterpretations
Thank you