Update in Lymphoma Imaging
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Lymphoma
- Heterogeneous group of lymphoid neoplasms divided into two broad histological categories
- Hodgkin's Lymphoma 15%
- Non-Hodgkin's Lymphoma 85%

Hodgkin's Lymphoma
- 15%
- Incidence is staying steady 3/100,000
- Nodular lymphocytic predominant
- Classic
- nodular sclerosis
- mixed cellularity
- lymphocyte-rich
- lymphocyte depleted
- Reed–Sternberg cells

Non-Hodgkin’s Lymphoma (NHL)
- 85% 2.6% all cancer deaths
- incidence has doubled since 1970
- Histologically more than 30 subtypes of either:
  ---B Cell neoplasm 85%
  ---T-cell neoplasms 15%
  ---natural killer (NK)-cell rare

NHL Type and Prevalence
Major Thoracic Lymphomas imaging characteristics

- Hodgkin’s Lymphoma
- DLBCL
- Primary mediastinal large B cell
- Follicular Lymphoma
- Lymphoblastic lymphoma
- T cell Lymphoma

Hodgkin's Lymphoma

- 85% have intrathoracic disease at presentation
- Mediastinum
- Lung
- Chest wall
- Pleura, pericardium
- Thymus

NHL

- 45% have intrathoracic disease at presentation
- Mediastinum
- Lung
- Chest wall
- Pleura, pericardium
- Thymus

Staging

- Defines the anatomic extent of disease
- Influences the choice of therapy
- Involves clinical, pathologic and radiologic parameters
- Includes defined prognostic indicators

PET/CT in Initial Staging

- Increased sensitivity/specificity over CT alone
- Upstaged 20%
- Downstaged 10%
- Change in treatment 15%
- (Data in DLBCL or HL)

Treatment based on:

- Histological features of the tumor
- Baseline prognostic indicators
- Stage of disease
- Important to differentiate between separate nodal/extranodal disease and contiguous spread
Extranodal Lymphoma
- Lymphomatous involvement of non-nodal tissue
- Described in every organ and tissue
- Secondary involvement as part of disseminated disease is more common than primary involvement
- HD 35%
- NHL 60%

PET/CT and biological behavior
- Indolent
  - Follicular Lymphoma 22%
  - MZBCL 6%
  - CLL/SLL 8%
  - Variable FDG avidity
- Aggressive
  - DLBCL 30%
  - MCL 6%
  - T cell 8%
  - FDG avid

What is a Positive Scan?
- Visual assessment is currently used to assess response
- If LN <2cm with FDG avidity greater than background is +
- If LN> 2 cm any activity greater than mediastinal blood pool is +
- Liver/spleen focal lesions > solid organ are +
- Spleen diffusely > than liver is +
- Focal uptake in bone marrow +

Radiologic Staging
- Description of nodal stations involved
- Representative unilinear measurements of enlarged lymph nodes in the long axis
- Identify sites of extranodal involvement
- Detect coexisting abnormalities that could affect management (ie infection)

FDG-PET/CT in Lymphomas
- Routinely PET+
  1. HL
  2. DBCNHL
  3. Follicular NHL
  4. Mrtle Cell L
- Variable FDG Avid
  1. Other aggressive NHLs
  2. Other indolent NHLs

PET correlation with clinical behavior
- Low-grade = low or variable uptake
- High grade or aggressive = high uptake
- HL treated as a separate category
Hodgkin Lymphoma

- Markedly FDG avid
- Nodular sclerosing most common
- Usually LN above the diaphragm
- PET for detecting extranodal sites
- Since residual soft tissue is common need baseline PET to prove cure

Low grade NH lymphomas

- Progress slowly
- Considered incurable
- Treatment is directed at control of symptoms (fatigue, visible LN)
- Usually variable FDG avidity
- PET/CT not always needed since the staging is less important than the symptoms

High grade NH Lymphomas

- Tend to be PET +
- DLBCL most common
- Stage change more apparent because subcentimeter nodes can be +
- Depicts unexpected extranodal sites
- Better depicts involvement of liver and spleen
- Needed for treatment planning and response are potentially curable

Low grade NH lymphomas

- Progress slowly
- Considered incurable
- Treatment is directed at control of symptoms (fatigue, visible LN)
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- PET/CT not always needed since the staging is less important than the symptoms

Pitfalls in interpretation

- If no baseline in variable FDG avid can be difficult to interpret follow up PET imaging to assess response
- CNS, testicular, gastric lymphomas difficult to detect with PET
- Bone marrow involvement frequent false positives due to reactive marrow hyperplasia, microscopic disease (sens 43% in NHL) so still need bone marrow BX

PET/CT for monitoring during therapy

- Relies on the dynamic properties of the tumor before, during and after to predict treatment
- Earlier studies suggested midtreatment PET may predict outcome but probably varies with histology

NHL Midtreatment PET/CT

- NPV high in the 90's
- PPV 40's
- Reflects variables
  - Timing
  - Patient population
  - Differences in treatment (rituximab)
  - Variable interpretations
  - So poor predictor of outcome
Midtreatment in HL
- Late stage disease more with outcome
- Early stage disease no more predictive than end-of treatment scan
- In summary no direct evidence that altering therapy on the basis of interim PET findings improves patient outcome

Goal of Therapy in Potentially curable NHL
- Complete metabolic response can be good indicator
- Need total absence of abnormal FDG
- Restage 6-8 weeks after therapy

Goal of Therapy indolent or incurable lymphomas
- Therapeutic response is measured by symptom relief
- Look for PFS
- Overall survival

HL Post treatment Scan
- Usually curable need complete PET negative response in residual soft tissue masses
- High NPV (90)
- Lower PPV (65)

Surveillance Scans
- Performed after treatment with the goal of early detection of recurrence
- Physician or patient however reports progression by clinical signs 80% of the time
- Pet has failed to show a clear benefit in surveillance (false + rate up to 40%)

Revised Response Criteria “The Cheson Criteria”
- International Working Group Recommendations 2007
- Standardized repeatable method for measuring response to therapy for lymphomas
- Response is assessed within 3 broad categories:
  1. Radiological
     - Lymph nodes/Quantitative/Qualitative masses/extra-nodal disease
  2. Clinical
     - Physical Exam Qualitative
     - Spleen/Liver Biochemical
  3. Pathological
     - Bone Marrow Semi-quantitative
Response Assessment Categories

1. Target lesions (measurable): nodes/nodal masses/lesions
2. Target lesions (measurable): extranodal lesions/spleen, liver, lung, etc.
4. Organomegaly (measured or clinical): liver and spleen
5. New lesions
6. Bone marrow
7. Other lab values and clinical symptoms

Summary of Assessable Disease

- Target lesions
  - Measured lesions: Up to 6 node/nodal masses >1.5 cm LD
  - Up to 6 extranodal masses >1 cm LD
- Non-Target lesions
  - All nonmeasurable lesions
  - Both nodal and extranodal
- Up to 6 extranodal masses >1 cm LD
- At least 1 target lesion has to be a node
- Should be representative of disease
- If PET at baseline can only chose PET + lesions

Tumor Assessment – Response Criteria

- Radiological Criteria = Lymph Nodes / Masses
  - CR
    - Large <= 1.5 cm LD if >1.5 cm at baseline, or
    - Small <=1 cm LD if between 1.1 to 1.5 cm
  - PR
    - >= 50% decrease in SPD at baseline of 6 largest dominant nodes or nodal masses
    - No increases in other nodes
  - SD
    - Less than PR but not progression
  - PD
    - >= 25% increase in SPD from nadir and/or appearance of any new lesion

Summary of FDG-PET in Assessment Criteria

- Used to differentiate PR from true CR and to eliminate the Cru category
- If PET is not available, CT/MRI are used to define response
- When PFS is the primary endpoint, FDG-PET has little added benefit
- When CR is the primary endpoint, FDG-PET could be crucial to differentiate CR from PR
- PET is still optional!

PET/CT for Lymphoma staging, treatment, and response assessment

- Has improved baseline staging for lymphomas
- Facilitates functional evaluation of disease behavior
- Evaluates metabolic response to therapy
- Can improve discrimination between residual disease and benign fibrosis
- Cannot exclude microscopic malignant change below its threshold of detectability
- Important to remember limitations/false+/False- and to interpret in context of other imaging studies and clinical information
- Poor standardization may make comparison difficult