Patients Against Lymphoma

Tests & Imaging > PET scans

Last update: 04/22/2013

TOPICS

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TOPIC SEARCH: PubMed

Recent Updates - In the News:


Includes information on protection of children, pregnant woman, breast feeding mothers and accompanying persons

Normal PET scan =>

**PET Overview:**

**PET** stands for Positron Emission Tomography. After treatment, doctors use a PET scan to see if the visible tumors are taking up the PET tracer.

The **PET tracer** is injected into the blood prior to the scan. The PET tracer has two parts: glucose, and a mildly radioactive component. As the tracer moves through the body the cells that are active take up the glucose along with the radioactive part of tracer.

Tumor cells are generally metabolically active (hungry) and will take up more sugar (glucose) than normal cells. The more glucose the cells take up, the more the cells light up. PET scans take advantage of this difference to help distinguish active from inactive tumor masses.

Injecting the PET tracer into your body allows special cameras to show cells that take up excessive glucose - cells such as malignant cells, but also reactive normal cells, that have a higher metabolic rates.

**LIMITATIONS:** While cancer cells often take up more glucose than normal cells, sometimes normal cells take up high amounts of glucose too.

Individual cancer cells that make up a visible tumor are too small to see by CT or PET scans. So we can’t know for sure if the disappearance of the majority of cancer cells (the visible tumor) or a decrease in the uptake of the glucose-based tracer in the remaining cells in the tumor area means that all the cancer cells have been killed by the treatment.

"Although CT and MRI provide high-resolution anatomic information, PET adds information on the metabolic activity of lesions."
Standardized uptake values (SUVs) are a measure of the concentration of a radiotracer in a defined region divided by the injected dose normalized for the patient's body weight at a fixed time after tracer injection.

This functional information may be particularly useful in determining response to therapy, as suggested by the European Organization for Research (25). These metabolic changes may occur even if anatomic size of the tumor does not change significantly."

Role of Positron Emission Tomography in Lymphoma

Malik E. Juweid1 and Bruce D. Cheson2

Frequently asked question - Regarding Overlap in SUV between aggressive and indolent NHL:

"FDG PET scanning in such circumstances appears justified, and it is reasonable to assume that a SUV ≥ 13 in the most intense lesion is highly indicative of aggressive histology, while a SUV ≤ 6 is much more compatible with indolent lymphoma, unless the clinical course indicates otherwise (remembering that based on the two ROC analyses provided, approximately 8% of aggressive lymphoma patients can have a SUV of < 6, whereas approximately 6% of those with indolent lymphomas can have a SUV of ≥ 13).

The occurrence and relative frequency of indeterminate SUVs, however, prompt the search for alternative approaches addressing the limitations of the FDG-based SUV method since these limitations represent the biologic basis for the observed overlap between indolent and aggressive NHL.

Clinical Use of PET-based imaging in lymphoma - "very little is actually certain and agreed upon."

Based on Lymphoma Type and Clinical Setting

<table>
<thead>
<tr>
<th>PET-based</th>
<th>Aggressive</th>
<th>Localized</th>
<th>Indolent</th>
<th>Transformed</th>
<th>Hodgkin</th>
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<td>Initial Staging</td>
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<td>Controversial, but Most do</td>
<td>Most do</td>
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<tr>
<td>Interim treatment response</td>
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<td>-</td>
<td>Investigational</td>
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<td>Predictive, but investigational</td>
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<tr>
<td>Post treatment response</td>
<td>YES</td>
<td>-</td>
<td>Controversial, but Most do</td>
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<td>Surveillance</td>
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On the clinical use of PET-based imaging in lymphoma:

**Dr. Rebecca Elstrom** shared her perspective:

"I suspect you will get different answers to these issues, which suggests that very little is actually certain and agreed upon.

I would venture that the only thing just about everyone agrees on is PET for post-treatment response assessment in Aggressive and Hodgkin lymphomas (not indolent--this is still controversial and many still argue that CT is just as good for standard care, though many patients get it anyway).

For initial staging, most do PET for aggressive and Hodgkin, though it rarely changes management and some experts argue that it is unnecessary.

PET in indolent lymphoma would be considered appropriate pre-treatment mostly in 2 settings: if thought to be localized with potential for cure with radiation, or if there is concern for transformation. Although in practice many patients get them anyway, most patients with known advanced stage, "normal" presentation indolent lymphomas do not necessarily need a PET.

Interim therapy PET is investigational in all settings. Although proven to be predictive in Hodgkin, we don't yet know what to do with the information (studies are ongoing and we should have answers soon). For DLBCL, positive vs. negative PET is not predictive, but studies are evaluating the potential utility of quantitative assessment (i.e. whether a percentage decrease in SUV, or intensity of uptake of the tracer, is predictive). For indolent lymphoma, there is minimal information.

Most would agree that PET should not be used for surveillance* due to high incidence of false positives, though
a small minority of investigators would disagree."

* Examples of surveillance would be so-called watch and wait (observation of indolent lymphoma), but also observation after therapy with curative intent such as regularly scheduled monitoring of patients with aggressive or Hodgkin lymphoma after successful therapy.

**Lack of Standard Protocols for PET**

PET protocols are **not yet standardized in regular practice** -- that is, it can be done differently at various centers, which can affect the SUV readings:

1. the dose of the tracer,
2. the length of the scan,
3. your blood sugar levels,
4. how long after therapy,
5. the type of therapy (chemo / Rituxan / RIT) …

all can influence the readings. So it's not yet an exact science.

Generally, concern increases if the SUV in one tumor region is **many times greater** than in another tumor area … but your doctor will know about this and discuss this if it is.

**Inflammation** can also cause higher SUV readings. So PET is not used to diagnose a lymphoma, but it can help guide where to biopsy. For example, the surgeon will remove (if feasible / safe) the node with the highest SUV to increase the chance of getting a reliable diagnosis.

The use of PET to judge **if a treatment is effective early** (after one or two rounds of therapy) will require standardized methods of using PET -- and clinical research to confirm that the test can be used reliably for this purpose for the different subtypes of lymphoma.

**Advocacy note**: patients **might be provided with a procedure checklist as a quality control** -- to help improve compliance with standards for administering a **PET in general practice, should this use of PET be confirmed as clinically useful by well-designed clinical trials**.

Following completion of treatment the use of PET to determine if residual masses visible by CT imaging is viable (still
lymphoma) or is scar tissue is widely considered conclusive for that region.

**More detail on the PET tracer:**

FDG (2-Fluoro-2-Deoxy-D-Glucose) is a positron emitting radio-pharmaceutical. FDG emits positrons that make gamma rays which the PET scanner detects. It’s half life is about 110 minutes. So you will pose no risk to others shortly after the test is done - about 1.2 hours.

(Corrected definition submitted kindly by Dr. Williams)

*Search for ACR accredited Diagnostic Imaging Centers*

**ACR accreditation means:**

"Your hospital, clinic or health center has voluntarily gone through a rigorous review process to be sure it meets nationally accepted standards. The personnel are well qualified, through education and certification, to perform and interpret your medical images and administer your radiation therapy treatments. The equipment is appropriate for the test or treatment you will receive, and the facility meets or exceeds quality assurance and safety guidelines."

**Preparation for PET may vary at different centers**

- You will be asked to **fast** before the PET scan.
- Regarding your **last meal** before the scan:
  
  Choose foods **high** in protein; **low** in carbohydrates, **Avoid** sweets, breads, pasta, rice, and cereals.
  
  Do not eat anything for at least 6 hours prior to your exam.

  Most medications do not interfere with this test and can be taken as usual.
Ask about the use of medication prescribed by your physician -
If required medications are taken with food, ask for instructions.

Avoid caffeine, sugar, tobacco for one day prior to your exam.
Avoid rigorous exercise for one day prior to your exam.
Avoid vigorous massage or muscle manipulations a day or two prior to your exam.

Do you have diabetes?
Discuss this with your physician and call the center staff 48 hours before your scan.
For the test to be effective, your blood sugar levels should be be low.

Are you pregnant or might be?
Generally, PET and PET/CT scans are not performed on pregnant women.

Adapted from nps.cardinal.com

PET Safety?
"Because the radioactivity is very short-lived, your radiation exposure is extremely low. The substance amount is so small that it does not affect the normal processes of the body."
Source: radiologyinfo.org

IAEA Radiation Protection of Patients:
PET/CT Scanning http://bit.ly/Sog0eu
"It is advisable not to bring children along to the PET/CT centre. Following injection of radioactive material and before the scan starts, it is important that the patient is relaxed, so that the staff can get the best scan possible. The radiation exposure to accompanying child from the patient, although small, is better avoided as far as possible."

Radiation Exposure of Patients Undergoing Whole-Body Dual-Modality $^{18}$F-FDG PET/CT Examinations

http://jnm.snmjournals.org/cgi/content/full/46/4/608

Also see Comparing Imaging for more detail on exposures.

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False Positive PET Results?

"..."fluorodeoxyglucose (FDG - PET) is not a cancer-specific agent, and false positive findings in benign diseases have been reported in active inflammation or infection, causing false-positive results (1, 2)."

FALSE POSITIVE FINDINGS

"Inflammatory cells such as neutrophil and activated macrophages at the site of inflammation or infection show increased FDG accumulation (5). Active granulomatous processes, other infectious conditions and active fibrotic lesions have also been reported to show increased FDG accumulation and cause false-positive PET scans for malignancy."


source: http://www.kjironline.org/abstract/files/v07n0157.pdf

Think Twice Before Exercising When Getting that PET Scan -
By: Society of Nuclear Medicine | Published: Mar 8, 2006 at 07:01 - yubanet.com/

"Any type of physical activity - from tapping your feet while in the waiting room to jogging the neighborhood the day before - can affect the results of a PET scan and lead to false-positive results," said Medhat M. Osman,
The study advises technologists to instruct the patients to minimize muscle activity during the uptake phase and to telephone patients ahead of their appointments to advise them to refrain from any excessive muscle activity at least 48 hours before a PET scan.

**Brown fat and false positives?**

"the phenomenon of $^{18}$F-FDG uptake in brown fat was first discovered when PET/CT fusion images showed $^{18}$F-FDG concentration in the adipose tissue rather than in muscle or lymph node as previously assumed." [http://jnm.snmjournals.org/cgi/content/full/45/1_suppl/72S#F4](http://jnm.snmjournals.org/cgi/content/full/45/1_suppl/72S#F4)

**SUMMARY by Mozartmom:**

"Reasons you might see a light up include inflammation which could be caused by radiation, chemo, an injury, or an infection. Thymic rebound (benign activity in the thymus gland) can cause a light up in the chest. So can brown fat (dense tissue filled with blood vessels) if you get cold during the scan. Muscle activity can also cause a light up. Large scar tissue masses often will have some mild degree of light up. Rarer causes could be something like even sarcoidosis."

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**Summary of potential uses of PET:**

**GUIDELINES**


"One of the most important skills in PET reporting may be to recognize its limitations and be clear when a definitive answer cannot be given to the referring physician's question."

- Barrington, O'Doherty: EJNM 2003:30, suppl. 1: S117-S127

**Notes taken from a presentation by Paul A Hamlin, MD:**

- **Staging**, such as to verify localized disease?
  (experimental; utility varies with subtype of lymphoma)

- **Distinguishing indolent from aggressive** histology based on SUV measurements?
  (experimental - not a substitute for pathologic confirmation from a biopsy)

- **Guiding location of lesion to biopsy?**
  (could be useful when transformation from indolent to aggressive is suspected)

- **PET visualizes follicular lymphoma irrespective of grading.**

- **Majority of Transformed Lymphomas Have High SUVs** on PET Scanning Similar To Diffuse Large B Cell Lymphoma (DLBCL) - ASH 2006

  "... transformation to aggressive lymphoma should be suspected in patients with indolent lymphoma found to have high SUVs on FDG PET, and biopsies should be directed to the site of greatest PET avidity whenever feasible."

- **Predicting response to treatment early?**

  (experimental; false positives are possible; probably limited to curative diseases, such as DLBCL, Hodgkins)

  CLINICAL TRIAL SEARCH: [ClinicalTrials.gov](https://clinicaltrials.gov)
**Evaluating residual masses** following treatment  
(common - biopsy may be required if aggressive interventions are to be used)

"PET is particularly valuable in delineating viable tumor tissue from areas of tumor necrosis or fibrosis after treatment of lymphoma. Because inflammatory changes after treatment can create false-positive studies, PET should not be performed for 3 weeks after the termination of chemotherapy or 8 to 12 weeks after the completion of radiotherapy."


**Bone marrow evaluations?**  
(sub optimal - MRI is better)

**Follow up/monitoring?**  
(limited information, may be useful in select patients with usual sites of disease)

Source: Paul A Hamlin, MD - presentation

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**Summary of limitations:**

- Some indolent lymphomas may show only low-grade FDG uptake,
- FDG uptake is non-specific (other pathology, inflammations, infections, HIV, etc),
- Clinical limitations of findings
- To evaluate treatment response or re-stage the disease be performed on the same scanner to be comparable

Source: Paul A Hamlin, MD - presentation
Response to treatment evaluations?

"Specifically, assessing response [with PET] may be useful in two possible situations:

(1) to evaluate tumor response at the end of a full course of treatment, or

(2) to predict tumor response early in the course of a prolonged treatment regimen [for aggressive lymphomas].

In the first instance, early detection of treatment failure may permit a physician to institute a second-line therapeutic approach.

In the second instance, accurately predicting treatment failure may allow the physician to substitute an alternative regimen, without subjecting the patient to the toxicity of the full course. " Peter E. Valk, MD

TRIAL SEARCH: ClinicalTrials.gov:

Also see PET Scan More Accurate Predictor of Outcome in [aggressive] Non-Hodgkin’s Lymphoma - cancerconsultants.com

PET: Every patient is unique: Individualized therapies for NHL eurekalert.org

PET's ability to identify patients who will respond to treatments could advance personalized medicine

"Comparison of PET data on the extent of patients' disease at relapse and their response after three months indicated a higher rate of response to the treatment in patients whose cancer was limited. In all of the cases, the findings of the PET scans at three months were consistent with the clinical findings at six months. "

... Comment: but did PET reading prior to RIT inform about response? No.

But not so fast!
Poor Predictive Value of FDG-PET/CT Performed after 2 Cycles of R-CHOP in Patients with Diffuse Large B-Cell Lymphoma (DLCL)


n = Fifty patients (mean age 58 years, range 29-80) with stage III (n=15) or IV (n=35) DLCL

End of Treatment Evaluations:

"PET is very accurate in predicting short-term treatment failure. However, it cannot detect microscopic residual disease and thus its value is hampered by false negative results in patients relapsing later.

On the other hand, a biopsy is always indicated before salvage therapy in order to exclude false positive PET results related to inflammatory lesions or to second primary tumors." ~ G. H. M. Jerusalem, et al. - ASCO presentation

Also see:


- Predictive value and diagnostic accuracy of PET treated grade 1 and 2 follicular lymphoma. Leuk Lymphoma. 2007 Aug;48(8):1548-55. PMID: 17701586

Our results indicate that PET is accurate in the diagnostic assessment of treated FL-1 and FL-2 and, post-treatment PET positive patients are likely to relapse prior to PET negative patients.

PET Standard Uptake Values (SUV) and proliferation rates in lymphoma?
Role of Positron Emission Tomography in Lymphoma

Malik E. Juweid1 and Bruce D. Cheson2

Frequently asked question -
Regarding Overlap in SUV between aggressive and indolent NHL:

"FDG PET scanning in such circumstances appears justified, and it is reasonable to assume that a SUV ≥ 13 in the most intense lesion is highly indicative of aggressive histology, while a SUV ≤ 6 is much more compatible with indolent lymphoma, unless the clinical course indicates otherwise (remembering that based on the two ROC analyses provided, approximately 8% of aggressive lymphoma patients can have a SUV of < 6, whereas approximately 6% of those with indolent lymphomas can have a SUV of ≥ 13).

The occurrence and relative frequency of indeterminate SUVs, however, prompt the search for alternative approaches addressing the limitations of the FDG-based SUV method since these limitations represent the biologic basis for the observed overlap between indolent and aggressive NHL.

"FDG uptake in indolent lymphoma appears to be lower than in aggressive lymphomas [17]. Data on the correlation between proliferative activity and glycolysis in malignant tissue, as measured by FDG uptake, are controversial [18, 19]. To date, the correlation between FDG uptake and proliferative activity specifically in indolent lymphoma has not been studied in detail."

Comparison of CT, PET, and PET/CT for Staging of Patients with Indolent Non-Hodgkin’s Lymphoma

NOTE: Differences in administration and tracers across centers may influence SUV values. That is, we don't know if the SUV values and reference ranges are comparable in different centers.

study: FDG-PET Demonstrates Different Metabolic Activities among Lymphoma Subtypes.

Results are summarized in Table 1. The highest mean SUVs were obtained in aggressive non-Hodgkin’s lymphomas (NHL) followed by Hodgkin’s disease (HD) and indolent NHL.
Majority of Transformed Lymphomas Have High SUVs on PET Scanning Similar To Diffuse Large B Cell Lymphoma (DLBCL). Session Type: Poster Session, Board #580-II

The $SUV_{\text{max}}$ for a transformed aggressive lymphoma ranged from 3.2 - 30.2, with a median of 10.8 and mean of 14.

16/28 (57%) patients had an $SUV_{\text{max}}$ above 10; and 12/28 (43%), above 13.

Review article: on PET to determine grade - Medscape free login req.

... He concludes that the SUVs are most helpful in the high and in the low ranges. an SUV > 13 is highly suggestive of an aggressive lymphoma, and an SUV < 6 is most compatible with an indolent lymphoma.

Only 8% of patients with aggressive lymphoma had SUV < 6, and 6% of patients with indolent lymphoma had SUV > 13.

However, these upper and lower cutoff values applied to only 55% of the patients studied. In other words, 45% of the patients had SUV between 6 and 13. In these, the overlap was sufficient to preclude a confident assessment of tumor type based on SUV.

Using an SUV of 10 as an absolute cutoff results in a 29% misclassification rate for aggressive NHL and 19% for indolent NHL. This could result in undertreatment of many patients with aggressive lymphomas and overtreatment of many with indolent lymphomas."

Resources:

1. Recent:
Interim FDG-PET Scan in Hodgkin's Lymphoma: Hopes and Caveats

PubMed: Utility of PET scans in mantle cell lymphoma

PET scans: when and how? James Olen Armitage

2. About PET - Cancer Help Org


4. The Role of PET in Lymphoma* ~ Yuliya S. Jhanwar1 and David J. Straus2 jnm.snmjournals.org

5. Clinical Applications of P.E.T. in Oncology Conference Vancouver, B.C. June 11, 2001 petscan.ca

6. Accuracy of end of treatment 18F-FDG PET for predicting relapse in patients with Hodgkin's disease (Hd) and non-Hodgkin's lymphoma (Nhl) ASCO

7. Assessing response to therapy:

Aggressive NHL: PET Scan More Accurate Predictor of Outcome in Non-Hodgkin's Lymphoma - cancerconsultants.com

Aggressive NHL: Early FDG-PET assessment in combination with clinical risk scores determines prognosis in relapsed lymphoma - bloodjournal.org

Assessing Therapy Response with FDG PETPET can help determine when and if additional treatment for tumors is in order. - Peter E. Valk, MD

Prognostic value of FDG-PET scan imaging in lymphoma patients undergoing autologous stem cell transplantation. Bone Marrow Transplant. 2006 Jun 12; PMID: 16770314

A positive FDG-PET scan after salvage chemotherapy and prior ASCT indicates an extremely poor chance of durable response after ASCT.

8. Lymphoma Diagnosis and Treatment: CHOP, MALT, PET, and More - Medscape (free login, req.)

9. Improving management of Lymphoma with - Dimag.com

10. Comparing PET and Gallium scans for NHL - Above

11. Frequent impact of positron emission tomography on the staging of patients with indolent non-Hodgkin's lymphoma - racp.edu.au

   Conclusion: "These findings demonstrate that 18FDG-PET has a high sensitivity for indolent NHL, and often leads to alteration of disease stage and management. This high accuracy of 18FDG-PET in assessing discordant lesions suggests a greater diagnostic utility when compared with CT."


13. PET for MALT?

   This study retrospectively enrolled 26 patients with known active disease. 18F-FDG-PET was true positive (TP) in 21/26 patients and false negative (FN) in 5/26. Sensitivity of 18F FDG-PET for extra-nodal MALT was 81%. The data show that 18FDG-PET is a useful diagnostic tool in order to stage, restage or monitor disease in patients with extra-nodal MALT lymphoma.
Positron emission tomography with PET does not visualize extranodal B-cell lymphoma of the mucosa-associated lymphoid tissue (MALT)-type

Annals of Oncology, Vol 10, Issue 10 1185-1189, Copyright 1999 by European Society for Medical Oncology - annonc.oupjournals.org

BUT a patient with MALT reports: "My most recent PET scan (last week) showed my indolent malt active in its original site; eg: stomach and a new occurrence in my mouth, sublingually. " So this finding might not apply to every situation.

FDG-PET scanning for detection and staging of extranodal marginal zone lymphomas of the MALT type: a report of 42 cases - annonc.oupjournals.org

14. Whole Body FDG PET in the Evaluation of Lymphoma -
Kavitha Vadde, MD Alan J. Fischman, MD, PhD Yr. 2000

15. Review article on PET to determine response to treatment and grade - Medscape free login req.

16. Comparison of CT, PET, and PET/CT for Staging of Patients with Indolent Non-Hodgkin\'s Lymphoma
pubmedcentral.nih.gov

17. About PET scans (2010, sponsored by LRF)

18. PET for Lung Nodules

Relation between nodule size and 18F-FDG-PET SUV for malignant and benign pulmonary (lung) nodules.
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2563015/

snips from Discussion section of the paper:

"The data of this study is collected from two PET centers, a phantom study is used to examine the SUV measurement on both scanners. The experiment indicates that SUV from different scanners under the same image protocols and same scintillation detector type (BGO for both scanners) can be quite different in value. ....we recommend that the follow up scans to evaluate treatment response or re-stage the disease be performed on the same scanner to be comparable."
"The data above support that although, the SUVmax cutoff of 2.5 is a useful tool in the evaluation of large pulmonary nodules (> 1.0 cm), it has no or minimal value in the evaluation of small pulmonary nodules (≤ 1.0 cm). However, the combination of flexible value of SUVmax cutoff according to the size of the nodule, visual assessment, and CT characteristics of the nodules, in addition to pretest probability of malignancy, is the most appropriate approach to characterize small pulmonary nodules. To increase the sensitivity of the test of SUVmax cutoff for characterizing small nodules (≤ 1 cm), we recommend reducing the cutoff of less than 2.5"

Research News:

- FDG-PET in T-cell and NK-cell neoplasms  [http://annonc.oxfordjournals.org/content/18/10/1685.full](http://annonc.oxfordjournals.org/content/18/10/1685.full)


