Clinical Area: **FDG PET for melanoma**
Keywords: **PET, lymph node, sentinel node biopsy**
Reference: **Wagner JD, Schuwecker D, Davidson D, Coleman JJ, Saxman S, Hutchins G, Love C, Hayes JT. Prospective study of fluorodeoxyglucose positron emission tomography imaging of lymph node basins in melanoma patients undergoing sentinel node biopsy. J Clin Oncol 1999; 17: 1508-15.**

Study Type: Comparison of diagnostic tests
Study Aim:. To prospectively compare PET imaging of regional lymph node basins to sentinel node biopsy in patients with stage I, II and III melanoma localized to the skin.

Outcomes

- *Primary:* Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV)

Design

- *Number of subjects:* N=70 patients (n=89 lymph node basins)
- *Description of study population:* Patients with cutaneous melanoma at a university medical center and several affiliated hospitals. 54% male, mean age=53.9 years (range=28-79). n=70 had primary cutaneous melanoma and 4 had locally recurrent melanoma.
- *Inclusion and exclusion criteria:* Inclusion: ≥18 years old, biopsy-proven primary cutaneous melanoma with Breslow's thickness greater than 1 mm or locally recurrent melanoma after prior excision. Exclusion: ocular or mucosal melanomas, any clinical evidence of regional lymph node basin metastases or distant metastatic (MI) disease; palpable lymphadenopathy; infection or inflammation in the regional node basin/s; prior wide excision greater than 4 cm in diameter; lymph node dissections; skin grafts; tissue transfers or flaps that may alter the lymphatic drainage pattern from the primary tumor site to the regional nodal basin/s; pregnancy or breast feeding; prior malignancy (except in situ lesions, stage I basal and squamous cell skin malignancies and patients without evidence of disease >5 years after treatment); allergy to isosulfan blue dye or FDG.
- *Power*: Not discussed.

Validity

- *Independent blind comparison with a gold standard or follow-up of those not receiving the gold standard test?* Yes, PET interpretation was blinded. The gold standard was histologic analysis of sentinel node biopsy specimens.
- *Was "normal" defined?* Presented several interpretations.
- *Appropriate spectrum of disease?* Yes.
- *Consecutive patients?* Not specified, do not appear to be consecutive.
- *Methods described in enough detail to enable you to replicate the test?* Yes. Two types of FDG PET imaging was done. The first 24 patients received whole-body PET scans; the remainder of the patients received a slightly different protocol to obtain a high-sensitivity scan of the regional lymph node basins.
- *Reproducible results?* Yes.

Conclusions regarding validity of methods:
Basically valid comparison. Patients were not specified as consecutive which may introduce selection bias. The study mixed patients with primary cutaneous melanoma with those who had locally recurrent melanoma. The patients with locally recurrent melanoma had little influence on the results since they represented only 5% of the sample.

Results

18 (25%) of 70 patients and 18 (20%) of 89 node basins had at least one tumor-containing lymph node at the time of PET imaging. Median aggregate tumor volume in tumor-containing basins=4.3 mm^3 (range, 0.07-523 mm^3)

FDG PET efficacy for detection of occult lymph node metastases by PET scan interpretation scenario

	%	95% confidence interval
Scenario A[1]		
Sensitivity	11.1	1.4-34.7
Specificity	100	94.9-100
PPV	100	15.8-100
NPV	81.6	71.9-89.1
Scenario B[2]		
Sensitivity	16.7	3.6-41.4
Specificity	95.8	88.2-99.1
PPV	50.0	11.8-88.2
NPV	81.9	71.9-88.5
Scenario C[3]		
Sensitivity	16.7	3.6-41.4
Specificity	94.4	86.2-98.4
PPV	42.9	9.9-81.6
NPV	81.7	71.7-89.4

PPV=positive predictive value; NPV=negative predictive value

[1]Most conservative interpretation: ROC readings of definitely positive=positive, all other readings considered to be negative
[2]More liberal interpretation: ROC readings of definitely positive and probably positive=positive, all other readings considered to be negative
[3]Most liberal interpretation: ROC readings of definitely positive, probably positive and uncertain=positive, all other readings considered to be negative

FDG-PET results by prestudy melanoma stage[1]

Stage	No. patients	Patients with metastases No. (%)	Sensitivity	Specificity
I	16	2 (12.5)	0	100
II	42	11 (26.2)	9	93
III	12	5 (41.7)	40	100

[1]ROC readings of definitely positive and probably positive=positive, all other readings considered to be negative

Authors' Conclusions
Previous studies of FDG PET with melanoma patients are flawed by the comparison of FDG PET to conventional imaging studies known to be inadequate for detection of metastatic melanoma rather than to lymphatic mapping and sentinel node biopsy. PET imaging with FDG is an "insensitive indicator of occult melanoma lymph node metastases because of the minute tumor volumes encountered in this population. PET imaging does not have a primary role in regional lymph node staging in patients who present with AJCC stage I, II or III melanoma localized to the skin."

Reviewer's Conclusions
The sensitivity of FDG PET to detect occult lymph node metastases in patients with stage I, II or III cutaneous melanoma was relatively low. This was a reasonably well-done study comparing FDG PET images to histologic analysis of sentinel node biopsy results.