Clinical Area: **FDG PET for breast cancer: Monitoring primary chemotherapy**
Keywords: **FDG PET, breast cancer, chemotherapy**
Reference: **Smith IC, Welch AE, Hutcheon AW, Miller ID, Payne S, Chilcott F et al. Positron emission tomography using 18-F-Fluorodeoxy-D-glucose to predict the pathologic response of breast cancer to primary chemotherapy. J Clin Oncol 2000; 18: 1676-1688.**

Study Type: Comparison of diagnostic tests
Study Aim:. To determine whether FDG PET can be used to predict pathologic breast cancer response to primary chemotherapy.

Outcomes
- *Primary:* FDG uptake after one pulse of chemotherapy, sensitivity and specificity.
- *Secondary:* FDG uptake after additional pulses.

Design

- *Number of subjects:* N=30 (n=31 primary breast cancers).
- *Description of study population:* Mean age=49 years (range=31-72 years).
- *Inclusion and exclusion criteria:* Inclusion: newly diagnosed, noninflammatory, large (>3 cm) or locally advanced (T3, T4 or TXN2) breast cancers; willingness to participate in a larger study evaluating different chemotherapy regimens. Exclusion: Not specified.
- *Procedure*: All patients received eight doses of primary chemotherapy over a mean of 157 days (range, 135-184) days). FDG PET imaging was performed before the first, second and fifth doses of chemotherapy and before surgical excision of the primary tumor and axillary lymph nodes. Not all patients received the same chemotherapy regimen.

Validity
- *Independent blind comparison with a gold standard or follow-up of those not receiving the gold standard test?* Yes. Gold standard was surgical resection specimens. Assessors were blinded to details of tumor and lymph node response—they were aware of the location of the primary breast lesion.
- *Was "normal" defined?* Yes, clinical response or lack of response was defined.
- *Appropriate spectrum of disease?* Yes.
- *Consecutive patients?* Not specified.
- *Methods described in enough detail to enable you to replicate the test?* Yes.
- *Reproducible results?* Likely.

Conclusions regarding validity of methods:
Other than the relatively small sample size, it appears to be a relatively well-done study of diagnostic tests. Not all patients received all of the scheduled PET scans (2 patients did not receive a scan before their second pulse of chemotherapy, 11 patients did not receive a scan before their fifth pulse and nine patients did not receive a scan before their last pulse).

Results
Measure of responsiveness to chemotherapy:
Complete clinical response (cCR)= complete resolution of a palpable mass within the breast
Partial clinical response (pCR)= tumor size reduced by at least 50%.
Clinical progression of disease= increase in tumor size of at least 25%
Static disease= all other responses

Partial pathologic response (pPR)= macro- and microscopically evident residual neoplastic tissue demonstrated features consistent with chemotherapy-induced damage.
Microscopic complete pathologic response (pCR-micro)= histological absence of invasive tumor cells.
Macroscopic complete pathologic response (pCR-macro)= absence of macroscopically visible tumor.

Measures of FDG PET uptake:
Influx constant (K)
Dose uptake ratio (DUR)=activity in image voxel x body surface area / injected area

Differences in FDG uptake by primary breast cancers (all lesions, n=31)

	Mean pretreatment DUR	p-value	Mean change in DUR after 1st dose	p-value
Clinical response after 4th dose[1]				
Yes	0.095	0.452	-0.026	0.076
No	0.081		0.003	
Clinical response after 8th dose[1]				
Yes	0.087	0.295	-0.021	0.017
No	0.120		0.051	
Pathologic response pCR-macro				
Yes	0.106	0.222	-0.082	0.003
No	0.088		0.001	
pCR-micro				
Yes	0.123	0.037	-0.057	0.001
No	0.079		-0.003	

[1]Complete clinical response (cCR) or partial clinical response (cPR)

Differences in FDG uptake by locally metastatic breast cancer

	Mean pretreatment Value	p-value	Mean change after 1st dose	p-value
DUR				
pCR	0.230	0.076	-0.102	0.038
No pCR	0.094		-0.023	
K				
pCR	0.051	0.037	-0.025	0.012
No pCR	0.021		-0.051	

Sensitivity and specificity of PET findings after 1st dose of chemotherapy by percentage reduction in DUR (prediction of overall pathologic response: pPR, pCR-macro or pCR-micro)

	Cutoff, % reduction in DUR	
	10%	20%
Sensitivity	82.4%	66.7%
Specificity	90%	74%

Authors' Conclusions

Primary breast cancers that achieved a pPR or pCR (macroscopic and microscopic) demonstrated a significantly greater reduction in the rate of FDG uptake after a single pulse of chemotherapy than those cancers that failed to achieve a pathologic response. These results suggest that FDG PET may be useful in predicting a pathologic response to chemotherapy at an early stage in the treatment regimen. Further studies, involving larger patient numbers, are currently underway in an attempt to validate this hypothesis.

Reviewer's Conclusions

Support authors' conclusions. This small study provides a preliminary indication that FDG PET may be useful at identifying patients who might benefit from chemotherapy. Sensitivity and specificity were higher using a 20% decrease in DUR as the cutoff. Further work on appropriate cutoff values for PET results needs to be done.