

Evidence Table

Clinical Area: ^{18}F Fluoro-Estradiol PET (FES-PET) to measure estrogen receptor expression in advanced breast cancer.
Reference: Linden HM, Stekhova SA, Link JM et al. Quantitative fluoroestradiol positron emission tomography imaging predicts response to endocrine treatment in breast cancer. *J Clin Oncol* 2006; 24: 2793-2799.

Study Type: Case Series

Study Aim: To evaluate the ability of FES-PET to predict response to hormonal treatment among patients with recurrent or metastatic breast cancer.

Outcomes

- *Primary:* Association between qualitative FES-PET results and response to treatment.

Design

- *Number of subjects:* n=47.
- *Description of study population:* Mean age=55.5 years (range 35-76); n=3 male; median time from primary breast cancer to FES imaging=58 months; median number chemo regimens=3.
- *Inclusion criteria:* Recurrent or metastatic breast cancer; estrogen-receptor (ER)-positive primary tumor confirmed by immunohistochemistry; underwent endocrine treatment without cytotoxic chemotherapy close to the time of FES-PET; at least one site of disease ≥ 1.5 cm maximal dimension that could be imaged; at least 6 months of follow-up after FES-PET.
- *Exclusion criteria:* Patients with liver metastasis.
- *Consecutive patients?* Not reported.
- *Intervention:* Patients were required to discontinue tamoxifen for ≥ 2 months before FES imaging. FES-PET and FDG-PET imaging was performed either before starting hormonal therapy, or shortly after initiating hormone treatment. The physician selected the type of hormone treatment. PET results were not used to select or direct treatment.
- *Source of outcome data:* Imaging results (PET and conventional imaging), clinical data.
- *Length of follow-up:* At least six months after PET imaging. Did not report average follow-up time.

Validity

- *Was population homogenous?* Variable disease characteristics and treatments received.
- *Potential selection biases:* Possible bias from excluding patients with less than 6 months of follow-up.
- *Were intervention/ care/follow-up similar in each group?* No standard regimen of hormonal therapy.
- *Did an objective observer assess outcomes?* Blinded evaluation of response to treatment and blinded qualitative analysis of FES-PET.
- *Completeness of follow-up:* Only included patients with sufficient follow-up.

- **Conclusions regarding validity of methods:**

The study was small and there was not a consistent hormonal regimen after FES-PET. Advantages were clear inclusion criteria and blinded outcome assessment.

Results

Clinical characteristics and treatments

	No. (%) (n=47)
Site of disease	
Bone only	19 (40)
Soft tissue only	6 (13)
Bone and soft tissue	20 (43)
Visceral only	2 (4)
Histological characteristics, primary tumor	
Invasive ductal	35 (74%)
Invasive lobular	11 (23%)
Mixed ductal and lobular	1 (2%)
Immunochemical characteristics, primary tumor	
Estrogen receptor+	47 (100%)
Progesterone receptor+	40 (85%)
HER2+	10 (21%)
Prior treatment	
Metastatic chemotherapy	13 (28)
Metastatic hormonal therapy	20 (43)
Metastatic radiation therapy	20 (43)
Treatment regimen after FES-PET	
Tamoxifen	5 (11)
Aromatase inhibitor	36 (77)
Aromatase inhibitor and fulvestrant	6 (13)
Trastuzumab	5 (11)

Clinical response to endocrine therapy*

	No. (%) (n=47)
Complete response	0
Partial response	11 (23)
Progressive disease	18 (38)
Stable disease	18 (38)

*Response=30% or greater decline in the average diameter of the measurable tumor side; Progressive disease=20% of greater increase in average measurable tumor diameter; stable disease=all others not meeting criteria for response or progression.

Qualitative FES-PET¹ results versus response, No. patients

	Response (R)	Stable (S)	Progression (P)	p-value
FES+	11	16	14	R vs. S vs. P = 0.21
FES-	0	2	4	R vs (S or P ²) = 0.14

¹FES-positive was defined as FES uptake above background level at all sites of known disease within the imaging field.

²Response vs. Stable or Progression, aka response vs. no response

Dichotomized quantitative FES-PET¹ results versus response, No. patients

	Response (R)	No Response (Stable or Progression)	p-value: R vs (S or P)
SUV>1.5	11	21	0.01
SUV<1.5	0	15	
Flux >0.2	10	14	0.005
Flux <0.2	0	14	

SUV=standardized uptake value; Flux is another way of measuring uptake that takes into account variable FES blood clearance.

Authors' Conclusions

“Quantitative FES-PET can predict response to hormonal therapy and may help guide treatment selection. Treatment selection using quantitative FES-PET in our patient series would have increased the rate of response from 23% to 34% overall, and from 29% to 46% in the subset of patients lacking Her2/neu overexpression. A multi-institutional trial would permit definitive assessment of the value of FES-PET for therapeutic decision making.”

Reviewer's Conclusions

Quantitative but not qualitative analysis of FES-PET significantly predicted response to hormonal therapy among patients who ER-+ breast tumors. None of the patients who were FES-negative responded to treatment. The study did not address the ability of FES-PET to identify ER-positive vs. ER-negative tumors.