

The Diagnostic Accuracy of ¹⁸F-FDG PET and ¹⁸F-FES PET for Staging Grade 1-2 Estrogen Receptor–Positive Breast Cancer



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Objective

To determine prospectively whether ¹⁸F-fluoroestradiol (FES) positron emission tomography (PET) improves staging for patients with grade 1 or 2, estrogen receptor (ER)–positive breast cancer (BC) compared with standard of care ¹⁸F-fluorodeoxyglucose (FDG) PET

Study Design

Prospective multicenter pilot study

- Participants:



41 consecutive women (44 primary tumors) with clinical stage II/III or local-regional recurrent, grade 1 or 2, ER-positive BC who were candidates for treatment with curative intent. Patients with recent surgery or unexpected stage II/III disease were eligible.

- Exclusion criteria:



Other malignancies within the past 5 years or ongoing BC treatment

- Staging:



- Conventional imaging plus FDG PET and FES PET
- Determined twice in multidisciplinary team meetings
- Suspect lesions verified by histopathology

Key Results

1. Overall Staging Detection Rates

	FDG PET (95% CI)	FES PET (95% CI)	P-Value
Per patient level (n = 41)	71% (56-82)	83% (69-91)	0.18
Per primary tumor (n = 44)	70% (56-82)	84% (71-92)	0.12

CI, confidence interval.

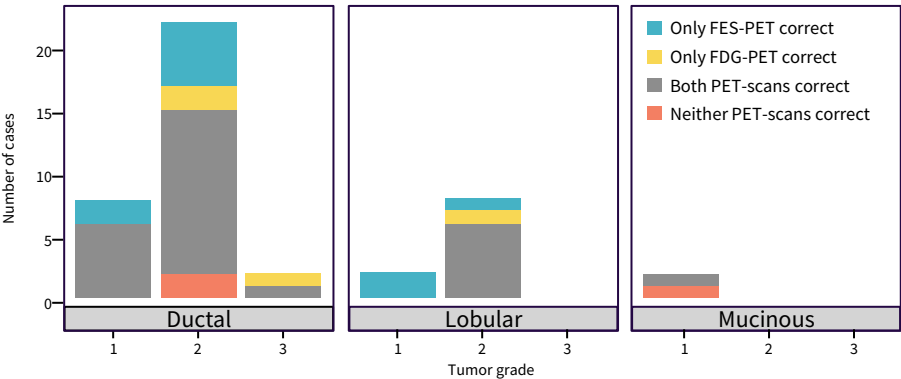
2. Staging Detection Rates by Histologic Subtype and Tumor Grade

	FDG PET (95% CI)	FES PET (95% CI)	P-Value
Lobular carcinoma (n = 10)	70% (40-89)	90% (60-98)	0.38
Ductal carcinoma (n = 32)	72% (55-84)	84% (68-93)	0.23
Grade 1 tumors (n = 12)	58% (32-81)	92% (65-99)	0.06
Grade 2–3 tumors (n = 31)	77% (60-89)	81% (64-91)	0.75

CI, confidence interval.

Numerically, more participants were correctly staged with FES PET than with FDG PET (34 of 41 vs 29 of 41).

Number of BC Cases Correctly Staged at FDG and FES PET, Presented According to Histologic Subtype and Tumor Grade



3. Primary Tumors

FDG	FES
Missed 7/44 tumors (16%)	- Missed 4/44 tumors (9%) - Detected residual tumor + 2 malignant lymph nodes (LN) missed by FDG, prompting neoadjuvant chemotherapy and planned re-resection - Detected a second primary tumor in the contralateral breast that was missed by FDG

4. Regional Lymph Nodes

FDG	FES
Incorrect staging in 6/44 cases (14%)	- Correct staging in all cases (100%) - Detected more LNs in 10 patients, changing staging and treatment plans - Identified supraclavicular LN missed by FDG

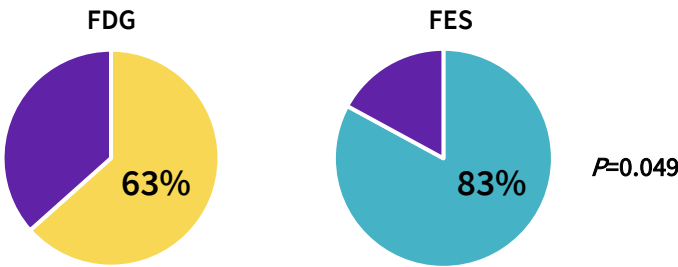
5. Distant Metastases

Both detected all metastatic cases (7/7) and false positives in 3 patients:

- Sensitivity: 100% (95% CI: 59-100)
- Specificity: 91% (95% CI: 76-98)

In one oligometastatic case, FDG PET detected 1 bone metastasis, whereas FES PET detected 2, leading to additional curative-intent radiation therapy.

6. Diagnostic Understanding Improvement by Adjudication Committee



Findings from FES PET led to changes in disease management for 22% of participants (9 of 41).

Limitations

- Small sample size, limiting statistical power and generalizability
- Selection bias, with some participants undergoing FDG PET before inclusion, potentially introducing bias if inconclusive results motivated participation
- Incorporation bias, with additional diagnostics influenced by PET scan results, potentially overestimating diagnostic accuracy

Considerations

- Larger, full-scale studies are needed to confirm findings and determine the optimal role of FES PET in BC staging.
- Sequential diagnostic strategies should be explored, where a second PET scan is performed only if the first is equivocal. Especially in grade 1 and lobular tumors, FES PET could be the optimal first choice for staging.



Clinical Implications

Although there was no statistically significant difference in diagnostic accuracy of FES PET and FDG PET in staging participants with grade 1 or 2 ER-positive BC (P=0.18), numerically, more participants were correctly staged with FES PET than with FDG PET.

- FES PET demonstrated especially high accuracy in regional N staging, correctly identifying nodal status in 100% of cases compared with 86% for FDG PET (P=0.02).
- FES PET provided a more comprehensive assessment of metastatic lesions in patients with metastatic disease, potentially reflecting the selection of grade 1–2 BC.

CERIANNATM (fluoroestradiol F18) injection is indicated for use with PET imaging of ER-positive lesions as an adjunct to biopsy in patients with recurrent or metastatic BC, with limitations including the need for biopsy confirmation and lack of utility for other receptors (eg, HER2, PR). FES has not been approved for use in early-stage ER-positive BC, and its safety and effectiveness in this setting have not been established. CERIANNA has no listed contraindications; warnings include risk of misdiagnosis and radiation exposure. For full prescribing information, visit https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/212155s000lbl.pdf.