Title: Optimizing Resource Utilization and Personalizing Therapy in ER-Positive Breast Cancer: The Potential Role of 18F-FES PET/CT

Purpose: To evaluate the potential value implications of 16α-[18F]-fluoro-17β-estradiol positron emission tomography (FES PET/CT) in patients with histologically ER-positive breast cancer by assessing its impact on staging, treatment decisions, and diagnostic performance.

Materials and Methods: This retrospective study included 67 patients with biopsy-proven ER-positive breast cancer who underwent FES PET/CT at a single institution from February 2023 to February 2024. Electronic medical records were reviewed for primary/metastatic lesion histopathology, changes in staging and treatment plans, and time to treatment adjustment.

Results: FES PET/CT identified ER-positive disease in 73.1% (n=49/67) of patients. Scans led to upstaging in 43.2% (n=29/67) of patients, resulting in treatment changes as outlined in Figure 1 for 58.4% (n=39/67). These changes included therapy escalation (n=14), de-escalation (n=4), and initiation of systemic therapy, including chemotherapy (ACT n=4/ADC n=4), aromatase inhibitors (AI) (n=3), AI with cyclin dependent kinase 4/6 inhibitor (CDK4/6) (n=4), CDK4/6 with Selective Estrogen Receptor Downregulator (n=3). The median time to therapy change post-FES PET/CT was 12 days (range 1-61 days).

Metastatic disease was present in 49 patients (73.1%). Significant discordance was observed between primary and metastatic lesions in ER (17/41, 41.5%), PR (9/20, 45%), and Ki-67 (3/10, 30%) expression. In our study, FES PET/CT demonstrated a sensitivity of 64.6% for detecting malignant ER+ lesions in patients with >10% ER expression on recent biopsy, aligning with prior studies that have reported sensitivities for detection primary or metastatic lesions ranging from 66% to 85. However, FES PET/CT maintained a high specificity of 100% for ER+ disease, consistent with the established literature. This suggests that while FES PET/CT may not always detect all ER+ lesions, a positive FES PET/CT finding is highly indicative of true ER+ disease. Most imaging indications aligned with Society for Nuclear Medicine and Molecular Imaging guidelines, as noted in Table 1.

Conclusion: FES PET/CT may contribute to value-based care in ER-positive breast cancer by potentially reducing unnecessary treatments, expediting personalized therapy, and improving diagnostic accuracy. Further research is needed to quantify the economic and patient-reported outcome benefits associated with FES PET/CT.

Clinical Relevance Statement: This study highlights the potential of FES PET/CT to optimize resource utilization and improve patient care in ER-positive breast cancer, aligning with the goals of value-based and equitable radiology.
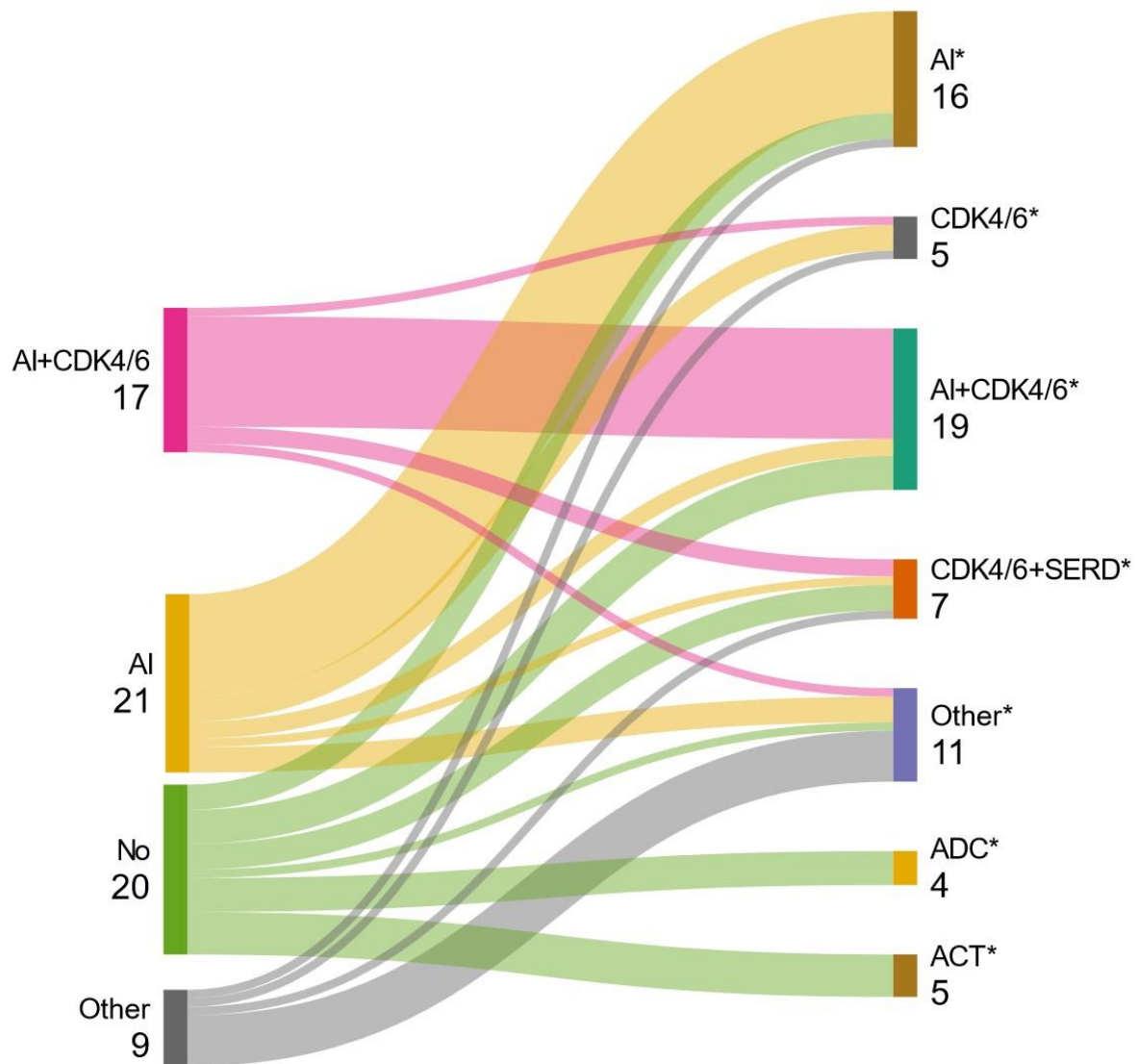
Figure 1 (above): Sankey diagram of treatment changes for patients in study. AI = Aromatase Inhibitor, CDK4/6 = Cyclin dependent kinase 4/6, No = treatment naïve, SERD = Selective Estrogen Receptor Downregulator, ADC = Antibody Drug Conjugate, ACT = Doxorubicin Cyclophosphamide Paclitaxel.

Sr. No.	Indications	Patients of 67
1	Confirm ER+ metastasis	22
2	Confirm disease progression	12
3	Confirm disease stage	10
4	Confirm disease ER status	8
5	Avoid biopsy	6
6	Other	3
7	Assess for disease recurrence	3
8	Assess for disease response	3

Table 1 (above): Physician documented indications for FES PET/CT scan in medical record.