The impact of 16α-18F-fluoro-17β-estradiol (FES) positron emission tomography (PET) on the staging and management of invasive lobular carcinoma (ILC) of the breast: A Case Series

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Background

- Despite advances in imaging and detection, ILC remains a diagnostic challenge because of its weak enhancement, linear growth pattern, and lack lymph node (LN) architecture disruption on metastasis.[2]
- Contemporary imaging for initial workup and re-staging of ILC often underestimates the burden of disease.[3,4]
- Subsequently, these patients are often upstaged at the time of surgery and may receive suboptimal initial management.
- 16α-18F-fluoro-17β-estradiol (FES) positron emission tomography (PET) has shown utility in assessment of ER-positive disease.[5,6]
- Given the diagnostic challenge of ILC, FES-PET may have a potential role during initial work-up and restaging.

Objective

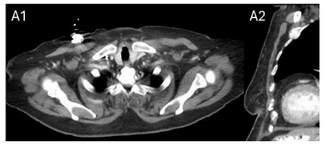
- Here, we present a case series elucidating the potential role of FES-PET on the staging and multi-disciplinary management of ILC.

Methods

- An institutional retrospective case series of six patients with newly diagnosed ILC between 4/2024-4/2025 was conducted.
- Three patients underwent FES-PET, which altered or confirmed management, and three patients did not undergo FES-PET but were upstaged at the time of surgery.
- Data on patient demographics, standard of care and FES-PET imaging, and pre-and post FES-PET management plans were collected.

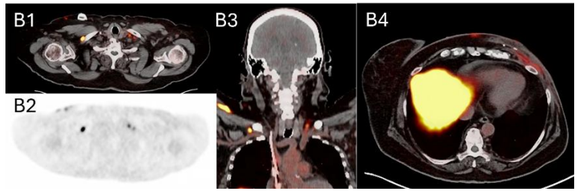
Results

Case 1 77-year-old, post-menopausal female with clinical stage IIIB(cT4bN0), pathologic stage IIB(ypT3N0), grade 3, ER-positive (100%)/progesterone receptor(PR)-negative/human epidermal growth receptor 2(HER2)-negative ILC underwent FES-PET prior to radiation, following paclitaxel, doxorubicin, cyclophosphamide (ACT) neoadjuvant chemotherapy (NAC), with a partial response of the primary tumor and resolution of biopsy confirmed skin involvement, followed by lumpectomy with a positive margin, re-resection with a positive margin, and mastectomy with a positive margin.

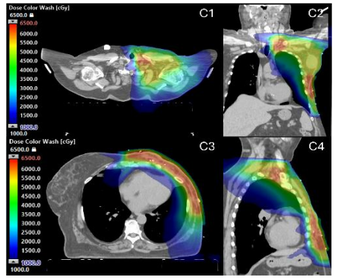


Pre-operative mammography, breast and axillary ultrasounds (US), CT chest, abdomen and pelvis (CAP), bone scintigraphy (BS), MRI, and F-18 FDG-PET showed focal breast disease with enhancement extending to skin and pectoralis, and no evidence of nodal or distant involvement. Post-operative MRI demonstrated enhancement at the post-mastectomy site with difficulty in discerning residual disease from postoperative enhancement, and no evidence of nodal involvement on patient's CT simulation (**Figure 1, A1-2**).

Results

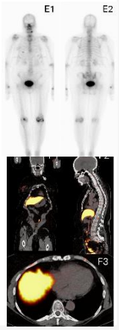


FES-PET revealed supraclavicular (SCL) avidity (SUV_{max}3.3) and left chest wall (CW) avidity (SUV_{max}5.4) (**Figure 1, B1-3**), consistent with residual disease and occult nodal involvement, upstaging the patient to pathologic stage IIIC(ypT3N3c).



A 1000 cGy in 5 fraction sequential boost to residual CW disease and FES-PET avid SCL-LN (**Figure 1, C1-6**) was subsequently included in her radiation treatment plan. She has no progression or metastatic disease on 1-year post-treatment follow-up and continues on anastrazole (AI) and zoledronic acid (BSP), after not tolerating 4 months of abemaciclib (CDK4/6i).

Case 2 72-year-old, post-menopausal female completed FES-PET for initial workup and staging of a grade 1, ER-positive (91-100%)/PR-positive/HER2-negative invasive mammary carcinoma with ductal and lobular features. Prior to FES-PET she had completed mammography, breast US, CT CAP, and MRI which detected a breast mass, bulky level 1-3 axillary lymphadenopathy, an asymmetric internal mammary (IM) LN, and focal osseus enhancement of two right anterior ribs, interpreted as suggestive of post-traumatic pathology on BS (**figure 2, E1-2**), consistent with clinical stage IIIC(cT3N3bM0). FES-PET was performed given the increased BS uptake within the right anterior fifth rib, which revealed avid subpectoral, axillary (SUV_{max}16.6), and IM-LNs (SUV_{max}8.5), avid 5th rib metastasis (SUV_{max}3.5), and diffuse osseus metastases (SUV_{max}8.8) (**figure 2, F1-3**). Biopsy confirmed metastatic breast cancer. The patient's treatment plan was changed from curative intent multi-modality therapy to metastatic first-line therapy with AI-BSP-CDK4/6i.



Results

Case 3 59-year-old, post-menopausal female with pathologic stage IIIC(pT3N3a), grade 2, ER-positive (100%)/PR-positive/HER-negative ILC managed with mastectomy, axillary lymph node dissection (ALND), and adjuvant ACT, underwent FES-PET for post-chemotherapy re-staging. Previous CT CAP and BS prior to chemotherapy reported no evidence of disease. FES-PET showed no evidence of disease. Following FES-PET, she subsequently proceeded with adjuvant CW and regional nodal irradiation (RNI) 5000 cGy in 25 fractions with a sequential scar boost, 1000 cGy in 5 fractions. She continues on BSP and has no evidence of recurrence 5 months following FES-PET.

Case 4 64-year-old, post-menopausal female with grade 2, ER-positive (100%)/PR-positive/HER2-negative ILC completed mammography, breast US, MRI, and CT CAP demonstrating multicentric breast masses, slightly enlarged, asymmetric level 1 axillary LNs, and no level 2 or 3 axillary lymphadenopathy. She was determined to be clinical stage IIA(cT2N1M0). She underwent mastectomy and sentinel lymph node biopsy (SLNB) which demonstrated a 7.8 cm tumor and 4/4 positive LNs. She then received adjuvant ACT. A delayed ALND was performed with 11/12 LNs involved. Her surgical pathology was consistent with pathological stage IIIC(pT3N3a). She was treated with CW and RNI, 4256 cGy in 16 fractions, with a sequential boost to mastectomy scar, 1000 cGy in 4 fractions. She continues on AI-BSP-CDK4/6i.

Case 5 68-year-old, post-menopausal female with grade 2, ER-positive (100%)/PR-positive/HER2-negative ILC underwent mammography, breast US, CT CAP, BS, and MRI during initial workup which showed a breast mass and no lymphadenopathy consistent with clinical stage IA(cT1cN0M0). She underwent lumpectomy and SLNB with 4/4 positive LNs. A delayed ALND was performed with 4/25 LNs positive, consistent with pathologic stage IIIA(pT2N2a). She then completed adjuvant TC and is currently undergoing hypofractionated breast and RNI, planned for 4256 cGy in 16 fractions with a 1000 cGy in 4 fraction sequential boost. She is planned for AI-BSP-CDK4/6i following completion of radiation.

Case 6 64-year-old, post-menopausal female with grade 2, ER-positive (100%)/PR-positive/HER2-negative ILC completed mammography, MRI, CT CAP, and BS during initial workup which showed a breast mass, level 1-3 LNs with suspicious but non-enlarged morphology, consistent with clinical stage IIA(cT1cN1M0). She underwent lumpectomy, ALND and prophylactic lymphovenous bypass which demonstrated a 2.1 cm tumor with 28/31 LNs positive, consistent with pathologic stage IIIC(pT2N3a). She then received adjuvant ACT. She subsequently completed right breast and RNI 4256 cGy in 16 fractions followed by 1000 cGy in 5 fractions sequential boost to the lumpectomy cavity. She continues on AI-BSP-CDK4/6i with no evidence of recurrence.

Discussion

- In case 1, after FES-PET showed ER-avidity in non-enlarged, non-FDG avid SCL-LNs, and residual CW disease, the patient's radiation plan was modified to include a sequential 1000 cGy in 5 fraction boost to the CW disease and SCL-nodes.

Discussion

- Case 2 describes the utility of FES-PET during initial workup which identified osseus metastatic disease not identified on previous SOC imaging. The patient's management was transitioned to palliative systemic therapy alone.
- FES-PET, ordered following modified radical mastectomy, ALND, and adjuvant chemotherapy given extensive locoregional involvement and concern for residual or occult disease, confirmed no evidence of disease, supporting the initial plan for local therapy in Case 3.
- In cases 4- 6, if the degree of LN involvement was accurately predicted, NAC may have been considered and a delayed ALND may have been avoided. Given the burden of disease in cases 4-6, it is possible metastatic disease could be missed, and the patient may be unnecessarily treated with more aggressive therapy.
- FES-PET has shown superiority to contemporary imaging in evaluation of ER-positive recurrent or metastatic disease and is now recommended during the work-up for recurrent or metastatic ILC in the National Comprehensive Cancer Network guidelines. [5,6,7]
- FES-PET can lead to management changes in up to 35% of patients with recurrent or metastatic breast cancer.[8] **We hypothesize that this impact may be even more pronounced in newly diagnosed ILC cases.**
- Baseline, treatment-naïve FES-PET may be of particular benefit in radiation treatment planning, as additional information regarding suspicious LNs or identification of occult disease prior to neoadjuvant systemic therapy and surgery may change management to include extended radiation volumes or dose escalation.

Conclusion

- FES-PET has potential as a valuable tool in the initial workup and re-staging of ER-positive LA-ILC, potentially reducing the need for subsequent therapy modifications and improving treatment outcomes.

Future Directions

- Prospective studies with upfront FES-PET staging in all cases of ILC are warranted to investigate the potential significance in clinical management, decision-making and outcomes.

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