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

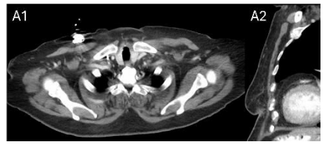
- Here, we present a case series elucidating the potential role of FES-PET on the staging and multi-disciplinary management of ILC.

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 (Cases 1-3, **Table 1**), and three patients did not undergo FES-PET but were upstaged at the time of surgery (Cases 4-6, **Table 2**).
- Data on patient demographics, standard of care and FES-PET imaging, and pre-and post FES-PET management plans were collected.

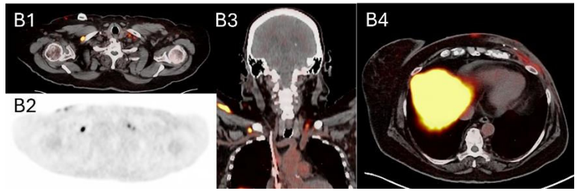
Results

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.

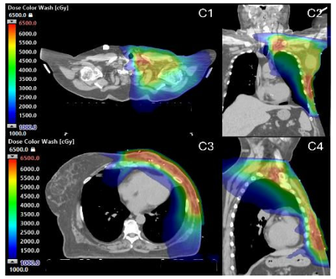


Pre-operative mammography, breast and axillary ultrasounds (US), CT chest, abdomen and pelvis (CAP), bone scintigraphy (BS), MRI, and F-18 FDG-PET showed focal breast disease with enhancement extending to skin and pectoralis, and no evidence of nodal or distant involvement. Post-operative MRI demonstrated 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

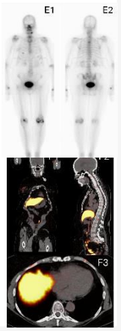


FES-PET revealed supraclavicular (SCL) avidity (SUV_{max}3.3) and left chest wall (CW) avidity (SUV_{max}5.4) (**Figure 1, B1-3**), consistent with residual disease and occult nodal involvement, upstaging the patient to pathologic stage IIIC(ypT3N3c).



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

	Histology	Prior Imaging	Disease on prior imaging	Staging prior to FES-PET	FES-PET avid disease	Staging following FES-PET	Significance	Management plan prior to FES-PET	Management after FES-PET	Management sigificance
Case 1	Grade 3 ILC: ER+(100%)/PR-(0%)/HER2- (IHC 1+)	Bilateral screening mammogram, left breast ultrasound, left axillary ultrasound, CT chest, abdomen and pelvis with contrast, nuclear bone scan, bilateral breast MRI with and without contrast, F-18 FDG PET	Infiltrative enhancement at post-mastectomy site, no evidence of nodal disease	Pathologic anatomic stage IIB / prognostic stage IIA (ypT3 ypN0,sn (+))	Fat stranding and cutaneous nodularity (SUV 5.4) in left chest wall, left supraclavicular lymph node avidity (SUV 3.3)	Pathologic anatomic stage IIIC / prognostic stage IIIB (ypT3N2c)	Residual chest wall disease and supraclavicular nodal involvement following neoadjuvant chemotherapy	Regional nodal irradiation 5000 cGy / 25 fractions	Regional nodal irradiation 5000 cGy / 25 fractions with 1000 cGy sequential boost in 5 fractions to avoid lymph supraclavicular lymph node and residual chest wall disease	Escalation of radiation therapy with sequential supraclavicular lymph node and residual chest wall disease boost
Case 2	Grade 1 invasive mammary carcinoma with ductal and lobular features ER+(91-100%)/PR+(31-40%)/HER2- (IHC 2+)	Bilateral screening mammogram, right breast ultrasound, CT chest abdomen and pelvis with contrast, bilateral breast MRI with and without contrast	Right breast mass, bulky right level 1-3 axillary lymphadenopathy, an asymmetric internal mammary/lymph node, focal osseus enhancement of 2 right anterior ribs suggestive of post-traumatic pathology on nuclear bone scan	Clinical anatomic stage IIIC / prognostic stage IIIA (cT3N3bM0)	Axial (SUV 8) and appendicular (SUV 5.2) osseus lesions	Clinical anatomic / prognostic stage IV (cT3N3bM1)	Clinical upstaging	Neoadjuvant chemotherapy, right modified radical mastectomy, regional nodal irradiation	Ribociclib, anastrozole, zoledronic acid	Conversion to systemic therapy alone for management of metastatic disease
Case 3	Grade 2 ILC: ER+(100%)/PR+(90%)/HER- (IHC 1+)	Bilateral screening and diagnostic mammogram with tomosynthesis, left axillary ultrasound, CT chest, abdomen and pelvis with contrast, nuclear bone scan	Left breast mass, left axillary lympadenopathy	Pathologic anatomic stage IIIC / prognostic stage IIIA (pT3N3a) followed by 4 cycles of adjuvant doxorubicin/cyclophosphamide followed by 4 cycles of dose-dense paclitaxel, post chemotherapy staging	Negative for disease	Negative for disease	Possible negative in setting of adjuvant chemotherapy	Left chest wall and regional nodal irradiation 5000 cGy / 25 fractions with sequential scar boost 1000 cGy / 5 fractions	Left chest wall and regional nodal irradiation 5000 cGy / 25 fractions with sequential scar boost 1000 cGy / 5 fractions	Confirmation of management decision

Table 1*: Cases 1-3 in which FES-PET changed or confirmed management*

	Histology	Imaging prior to surgery	Disease on imaging prior to surgery	Clinical Staging	Surgical pathology	Pathologic Staging	Disease on imaging following surgery	Significance	Potential difference in management
Case 4	Grade 2 ILC: ER+(100%)/PR+(100%, strong)/HER2- (IHC 1+)	Bilateral screening mammogram with tomosynthesis, left breast ultrasound, bilateral breast MRI with and without contrast, CT Chest, abdomen and pelvis with contrast, MRI abdomen with and without contrast	Multicentric left breast masses, slightly enlarged asymmetric level 1 left axillary lymph nodes, no level 2 or 3 left axillary lymphadenopathy	Clinical anatomic stage IIA / prognostic stage IIB (cT2N1M0)	Left mastectomy and sentinel lymph node biopsy: 7.8 cm, 4/4 lymph nodes positive Delayed left axillary lymph node dissection: 11/12 lymph nodes positive	Pathological anatomic Stage IIIC / prognostic Stage IIIA (pT3N3a)	Nuclear bone scan and MRI abdomen with and without contrast: no evidence of disease	Upstage at the time of surgery	Neoadjuvant chemotherapy, avoidance of delayed completion axillary lymph node dissection
Case 5	Grade 2 ILC: ER+(100%)/PR+(95%, strong)/HER2- (IHC 1+)	Bilateral screening mammogram with tomosynthesis, diagnostic left breast MMG with tomosynthesis, left breast ultrasound, CT Chest, abdomen and pelvis with contrast, MRI brain with and without contrast, nuclear bone scan, bilateral breast MRI with and without contrast	Left breast mass, no axillary lymphadenopathy	Clinical anatomic / prognostic Stage IA (cT1cN0M0)	Left lumpectomy and sentinel lymph node biopsy: 2.3 cm, 4/4 lymph nodes positive Delayed left axillary lymph node dissection: 4/25 lymph nodes positive	Pathologic anatomic stage IIIA / prognostic stage IB (pT2N2a)	CT chest abdomen and pelvis, nuclear bone scan: no evidence of disease	Upstage at the time of surgery	Neoadjuvant chemotherapy, avoidance of delayed completion axillary lymph node dissection
Case 6	Grade 2 ILC: ER+(100%)/PR+(100%)/HER- (IHC 1+)	Bilateral screening mammogram, right diagnostic mammogram, bilateral breast MRI with and without contrast, CT chest, abdomen and pelvis with contrast, nuclear bone scan	Right breast mass, right level 1, 2, and 3 lymph nodes with suspicious morphology, non-enlarged	Clinical anatomic stage IIA / prognostic stage IB (cT1cN1M0)	Left lumpectomy and axillary/lymph node dissection with prophylactic lymphovenous bypass: 2.1 cm tumor, 28/31 lymph nodes positive	Pathologic anatomic stage IIIC / prognostic stage IIIA (pT2N2a)	PET: no evidence of disease	Upstage at the time of surgery	Neoadjuvant chemotherapy, avoidance of delayed completion axillary lymph node dissections

Table 2: *Cases 4-6 in which FES-PET may have changed management*

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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