2026 ASCO ANNUAL MEETING

Modern Imaging of Metastatic Invasive Lobular Carcinoma: Anatomic and Molecular

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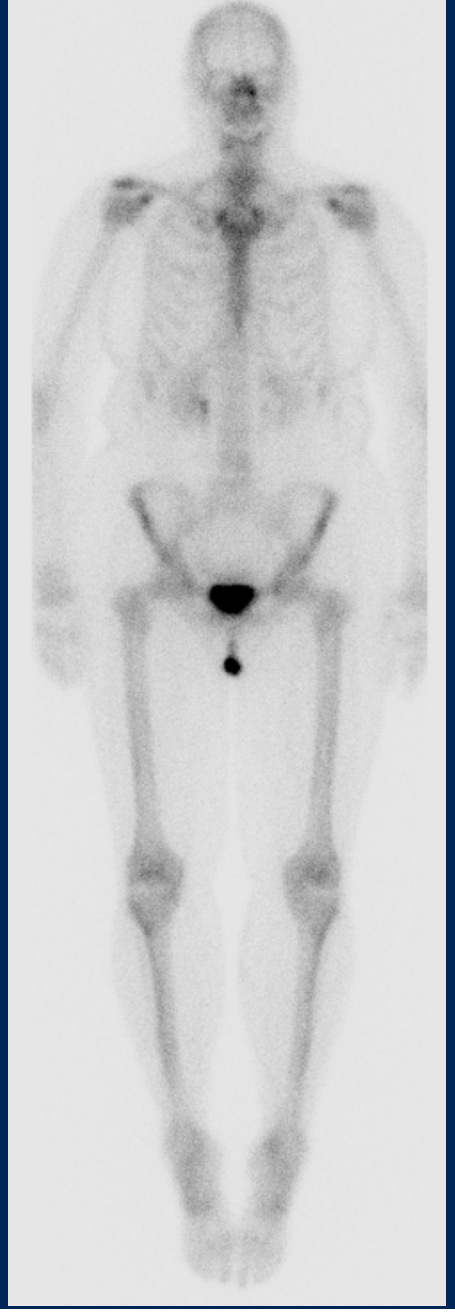
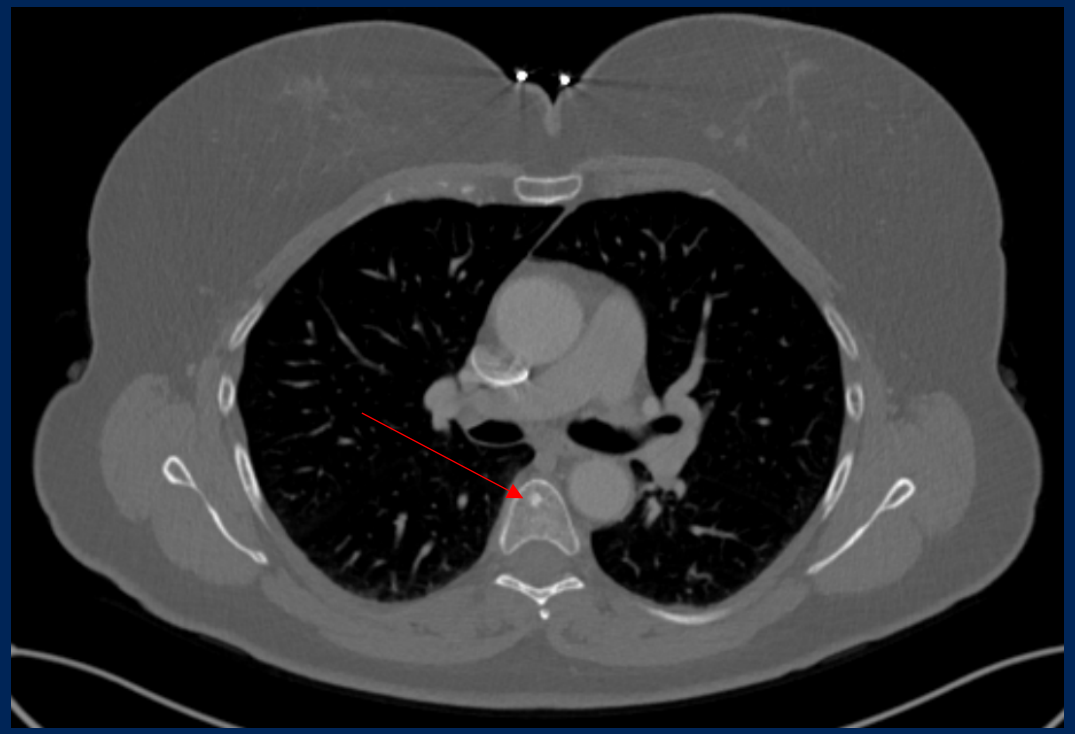
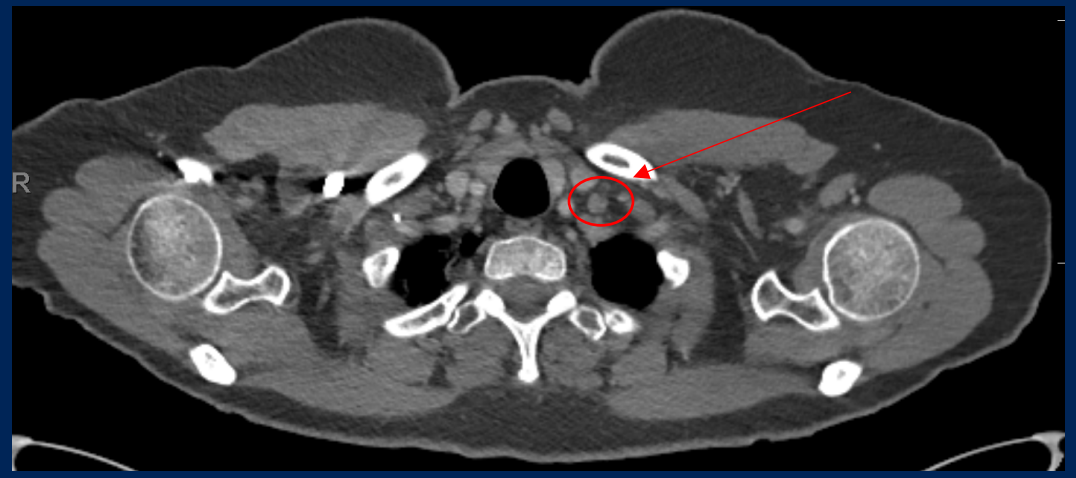
Teaching Case

61 year old female with recent screening detected right breast ILC, ER/PR+, HER2-, conventional imaging including MRI with a right breast 0.7 cm mass and right axillary nodal metastasis

- Underwent initial staging with CT chest, abdomen, pelvis, and bone scan







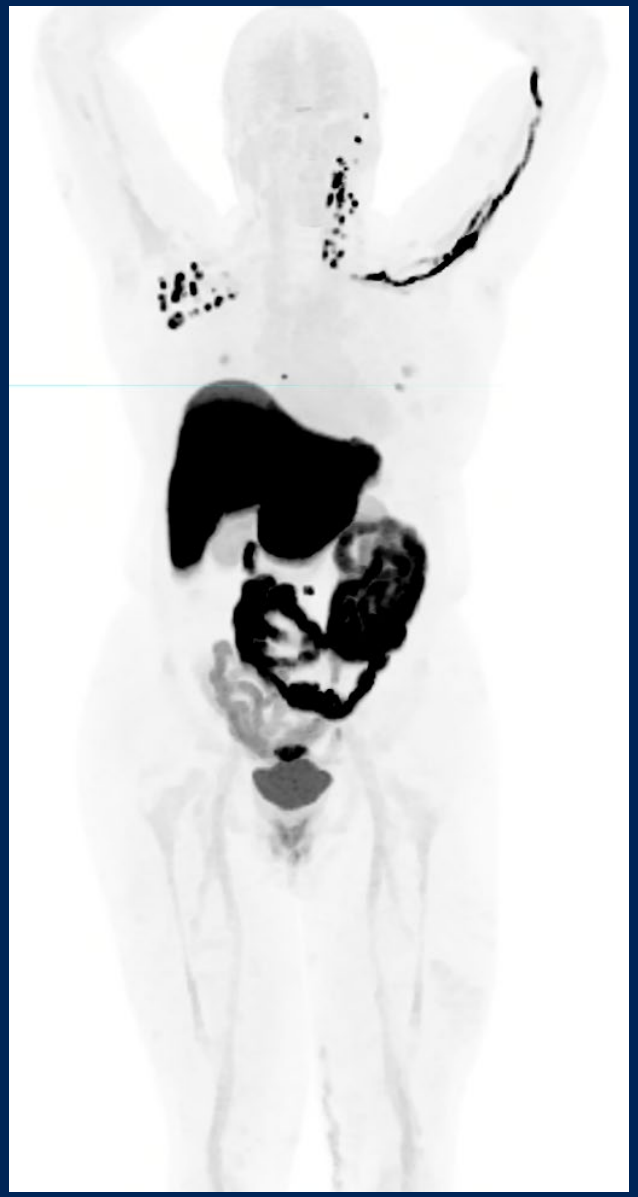
CT chest, abdomen, and pelvis and nuclear medicine bone scan for systemic staging

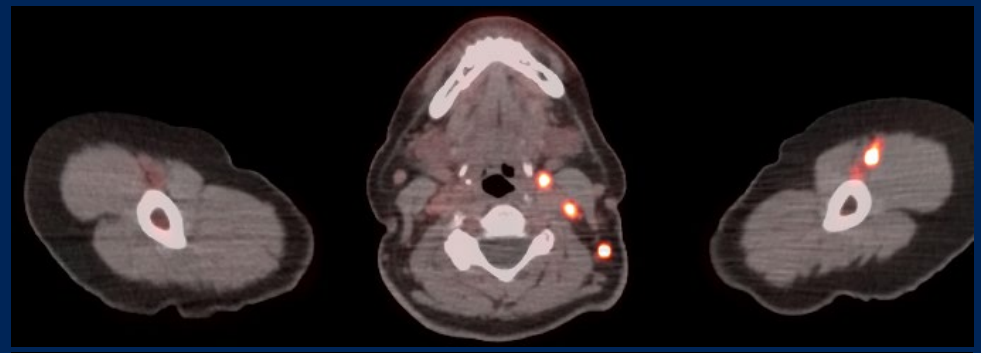
- Bone Scan:
  - “No definite scintigraphic evidence for osseous metastatic disease.”
- CT:
  - “Nonspecific sclerotic focus within the T7 vertebral body.”
  - “Prominent subcentimeter left supraclavicular and right subpectoral nodes measuring up to 8 mm. Recommend attention on follow-up imaging.”

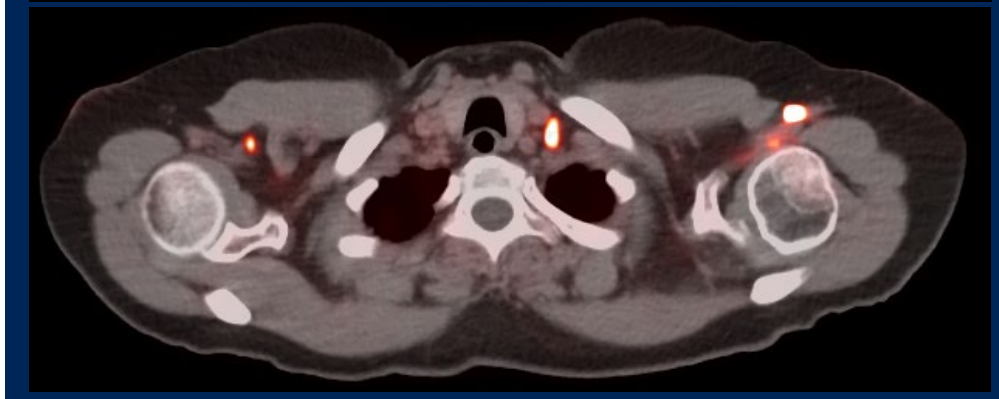
Clinical management plan

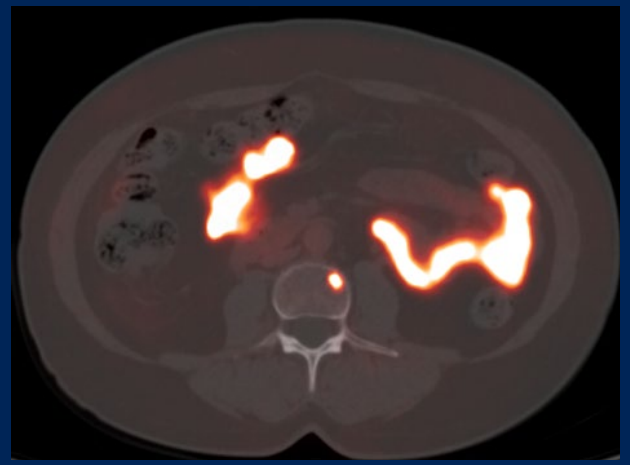
- “Has an unusual presentation with a small 0.6 cm mass with positive nodal disease”
- “Her CT abdomen pelvis and bone scan indicate there may be distant contralateral supraclavicular nodal involvement. Her insurance company denied a PET/CT”
- *Plan:*
  - *“Neoadjuvant endocrine vs chemotherapy TBD”*
  - *“Lumpectomy with radiation therapy”*
  - *“Standard of care would be full axillary node dissection.”*
  - *“Plastic surgery consult for potential lymphovenous bypass”*
  - *“Potential right axillary SAVI scout placement”*

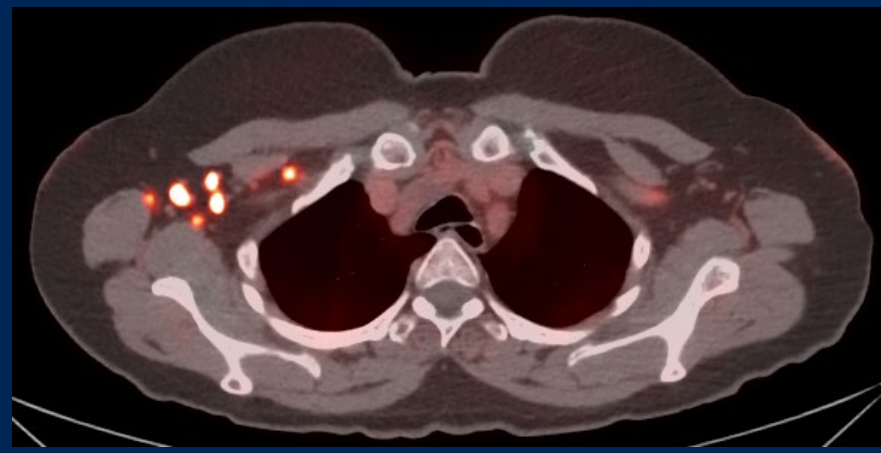
FDG and FES-PET/CT obtained on ILC-specific clinical trial at Huntsman Cancer Institute in Salt Lake City, Utah.

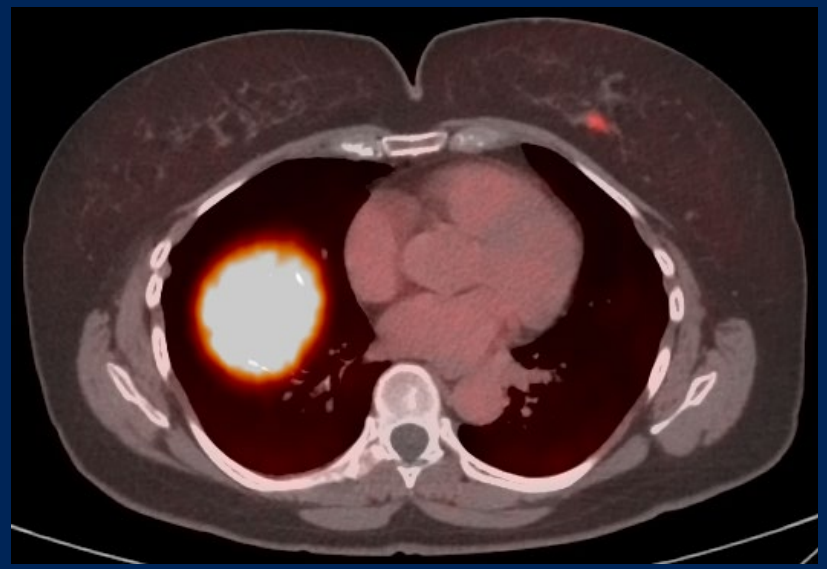












New management plan

- “Pursue histologic confirmation of metastatic disease by performing cervical lymph node biopsy”
- Plan for aromatase inhibitor (letrozole) with CDK 4/6 inhibitor

- **Plan no longer includes:**
  - **Lumpectomy**
  - **Radiation therapy**
  - **Right axillary dissection with lymphovenous bypass**
  - **Right axillary savi scout placement**

- ***This shows why advanced imaging matters for ILC***

Key Takeaway Points/Conclusions

1

Conventional Imaging and Standard FDG PET/CT Have Limitations in Detecting ILC

2

Receptor-Targeted and Advanced Imaging Modalities May Improve Detection

3

The Future: More PET agents, Improved MRI, Radioligand Therapy for Breast Cancer Including ILC

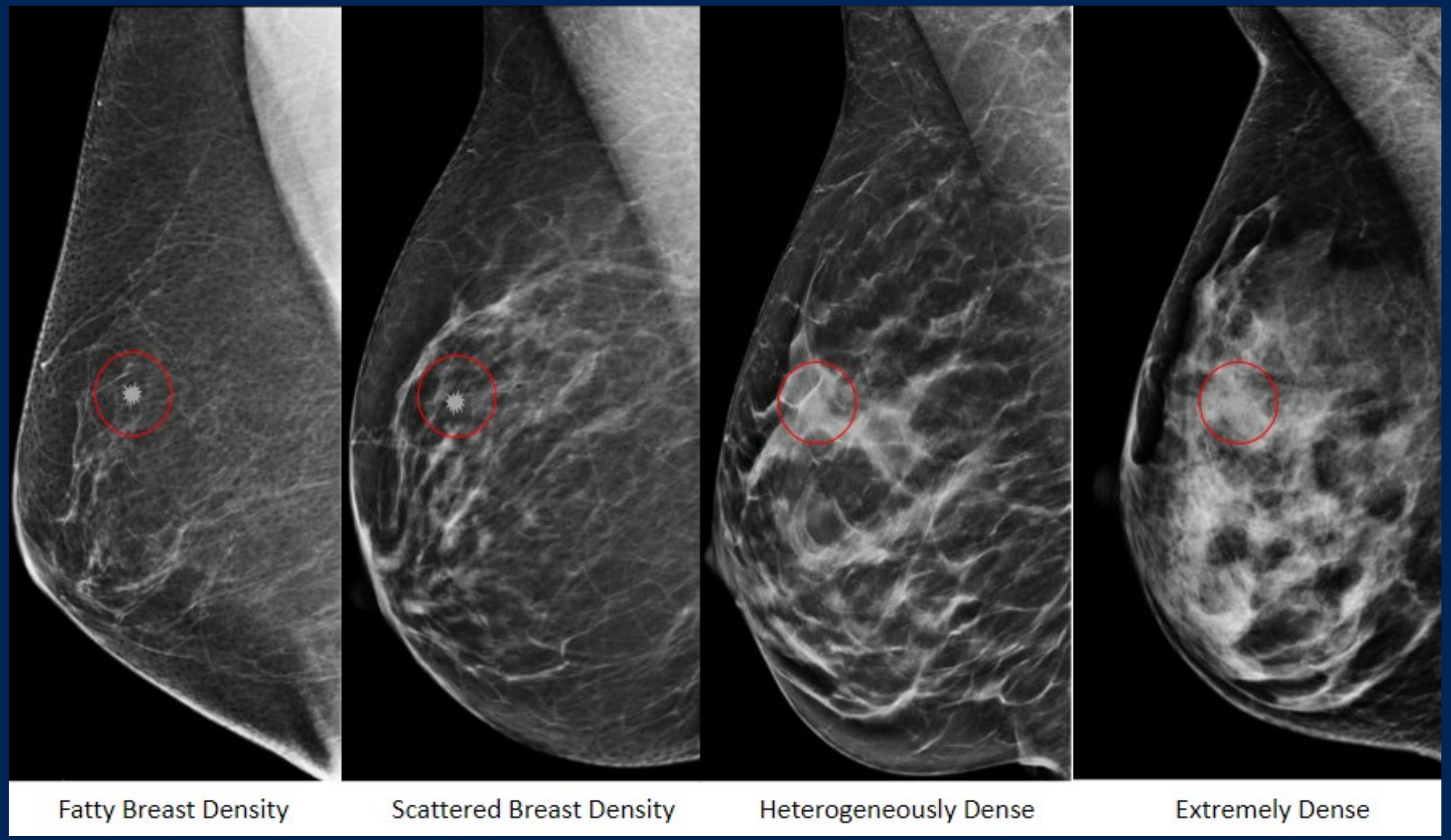
Why ILC Evades Conventional Imaging

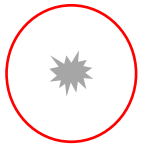
Primary Problems

- **Minimal Mass Effect:** Infiltrative growth causes subtle anatomic changes rather than distinct masses.
- **Atypical Metastatic Patterns:** Spreads to "hidden" sites (e.g., GI tract, peritoneum, leptomeninges) often missed on standard anatomic imaging.
- **Low FDG Avidity:** Frequent false negatives on FDG PET due to low metabolic glucose uptake.

Primary Problems

- **The "Masking" Effect:** Breast density on mammography significantly degrades sensitivity for all cancers but creates a "perfect storm" for occult ILC.
- *Why does this matter for a presentation on metastatic ILC?*
  - By evading screening detection ILC has more opportunity to spread before we intervene





Hypothetical cancer in red circle, also placed in the mammograms above. This is easily seen in the breasts with fatty and scattered density but is obscured on the heterogeneously and extremely dense breasts.

ILC lines rather than enlarges. It infiltrates rather than pushes. It coats rather than obstructs.

It whispers rather than shouts.

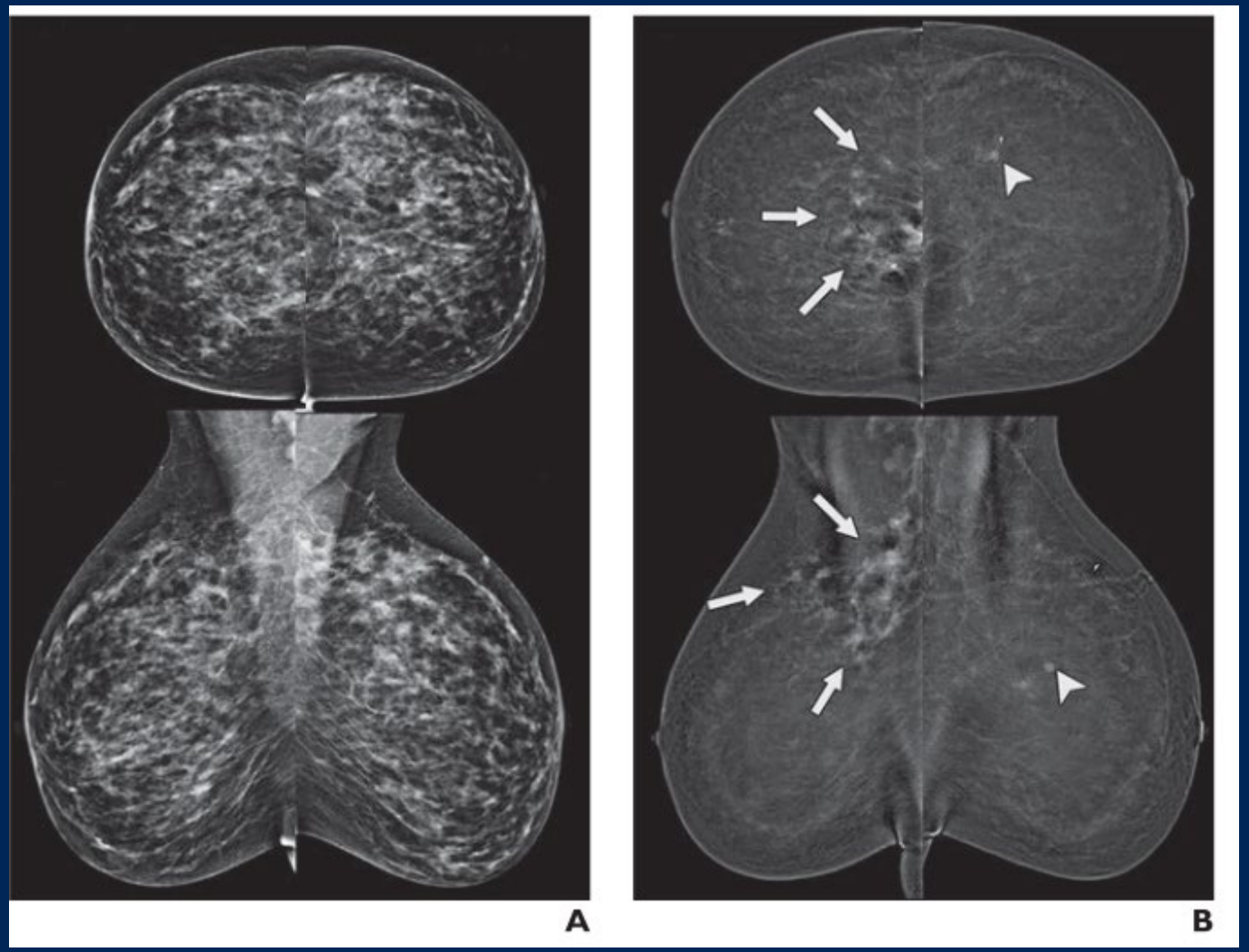
Matching ILC's Challenges with Advanced Imaging Modalities

Beyond the Workhorses: Redefining ILC Imaging

Challenge the Standard	Optimize Local Evaluation	Improve Systemic Staging
Recognize that traditional workhorses (Mammography, CT, FDG-PET) frequently miss and under-stage ILC	Integrate high-sensitivity tools like breast MRI, CEM, and MBI for screening and diagnostic breast imaging evaluation	Leverage FES-PET and WB-MRI beyond standard CT or FDG-PET to map disease burden more accurately

Match the best tools for the task at hand

Don’t eat soup with a fork



Mammography

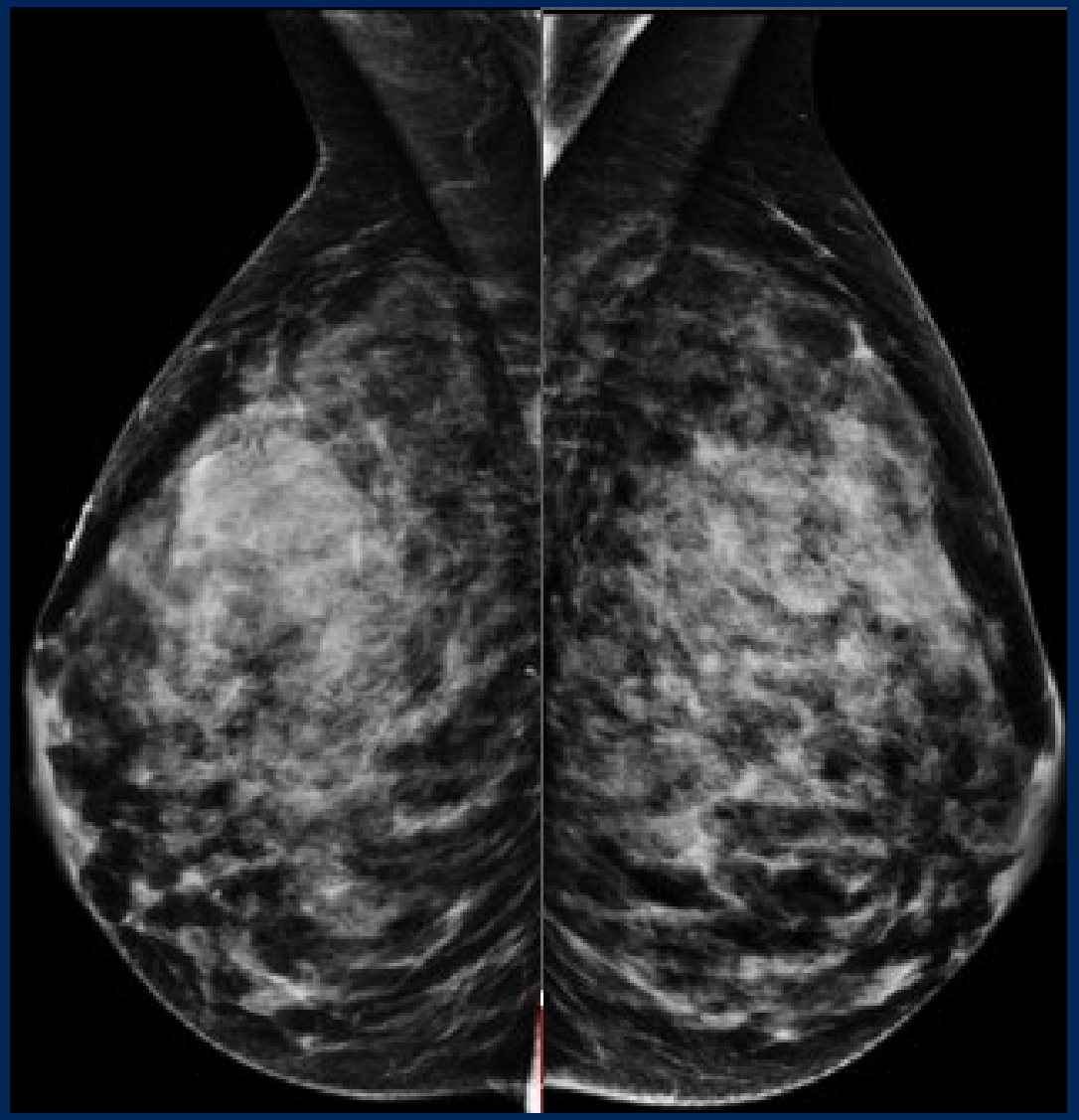
Contrast Enhanced Mammography

Options exist beyond breast MRI

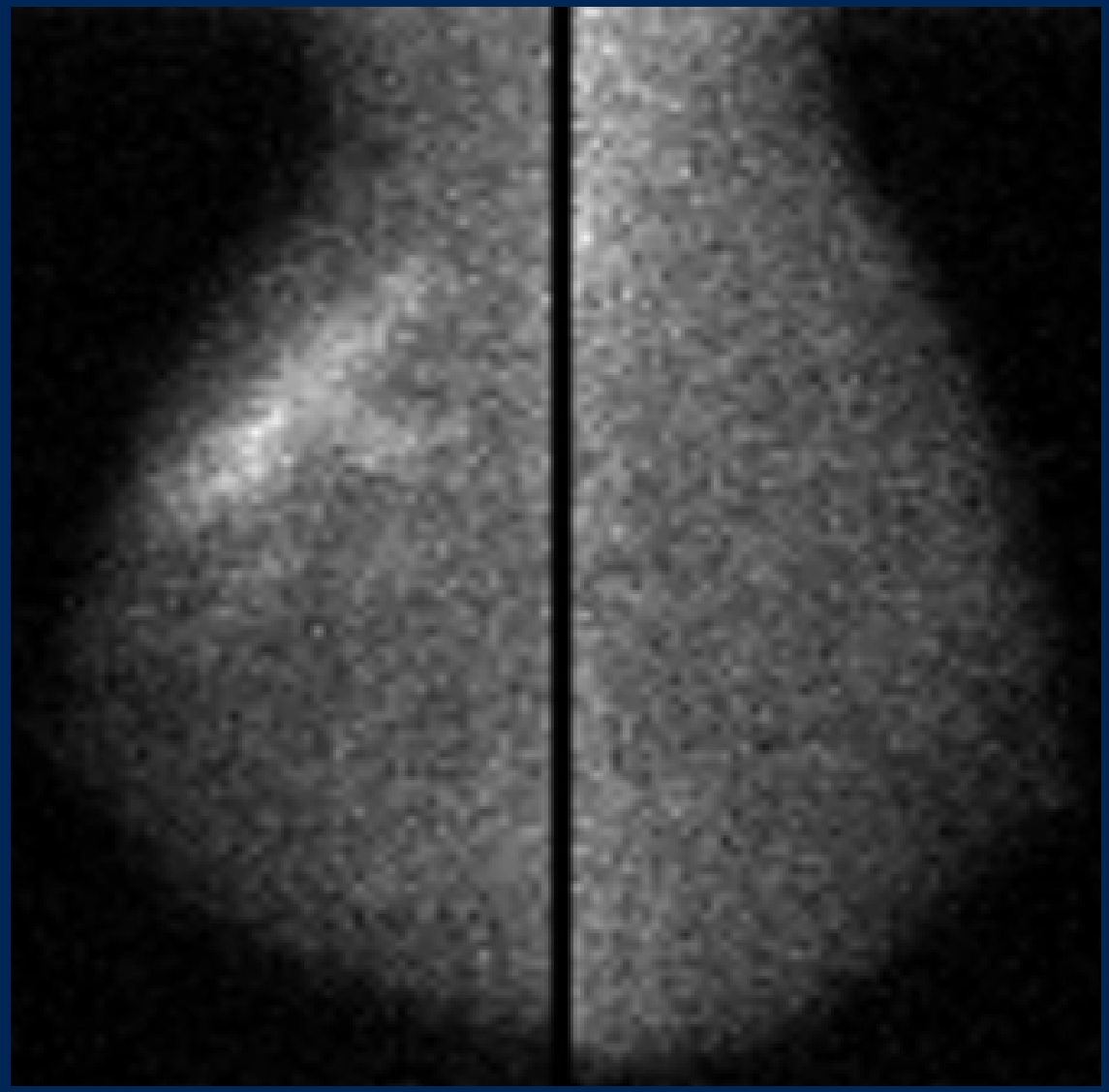
AJR Am J Roentgenol. 2018 Feb;210(2):292-300. doi: 10.2214/AJR.17.18749. Epub 2017 Oct 24.

The Future of Contrast-Enhanced Mammography.

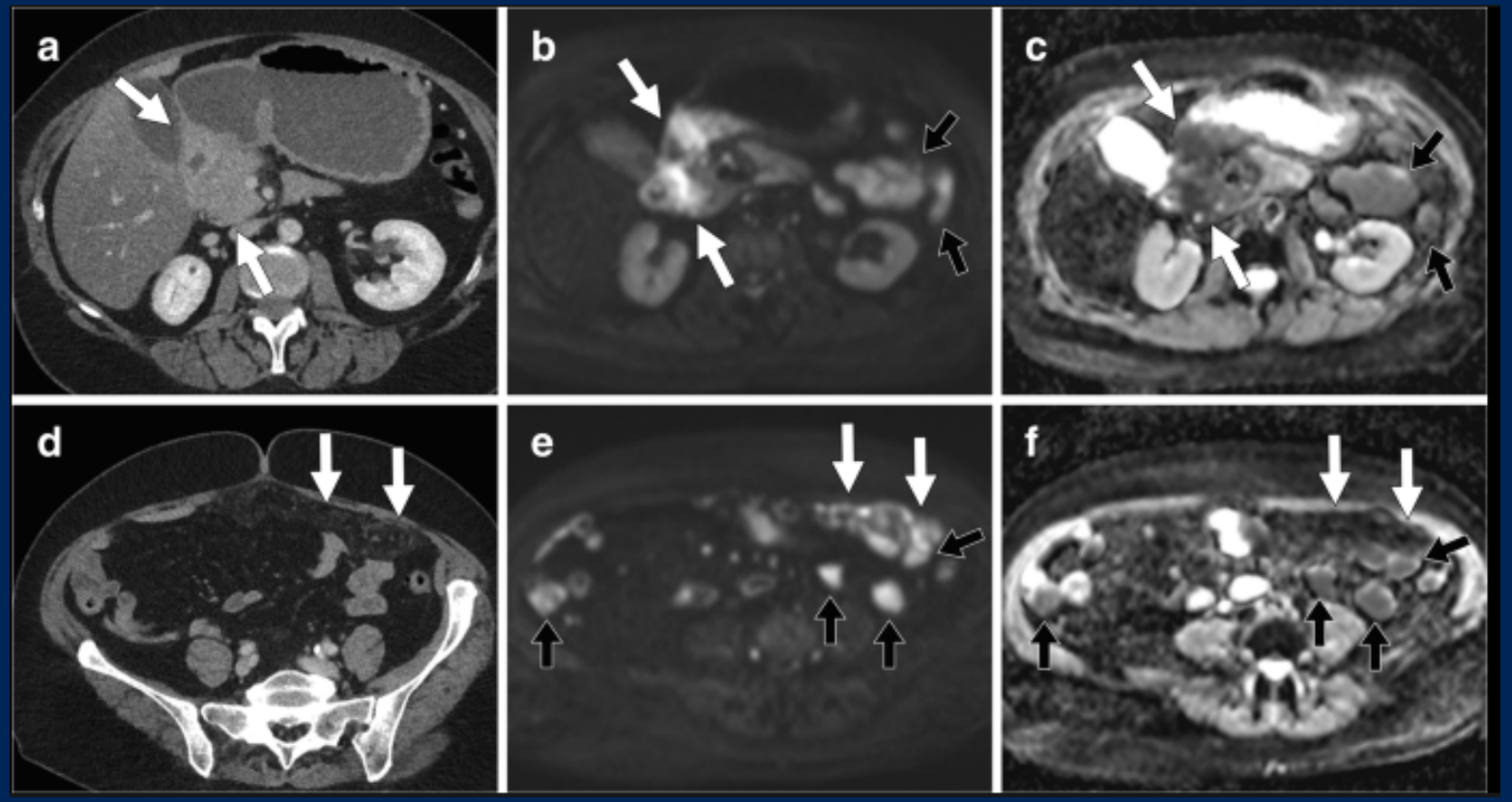
Covington MF[1,2], Pizzitola VJ[1], Lorans R[1], Pockaj BA[3], Northfelt DW[4], Appleton CM[2], Patel BK[1].



Mammography



Molecular Breast Imaging



Options exist beyond PET for systemic staging

Home › European Radiology › Article

A review on the added value of whole-body MRI in metastatic lobular breast cancer

Magnetic Resonance | Published: 06 April 2022 | **32**, 6514–6525 (2022)

Overview of FES-PET Imaging

- Approved by the FDA as an adjunct to biopsy for:
  - Identification of estrogen receptor (ER)-positive lesions
  - Identification of biopsy target(s)
  - Assessment of ER heterogeneity among sites of malignancy
  - Clarify equivocal findings on FDG-PET or other imaging modalities

Overview of FES-PET Imaging

- Before administering FES, discontinue drugs that bind to the ER, such as SERMs and SERDs, for at least 5 biological half-lives
  - Elacestrant for 11 days (oral SERD)
  - Tamoxifen for 8 weeks
  - Fulvestrant for 28 weeks

Summary: Appropriate Use Criteria for Estrogen Receptor–Targeted PET Imaging with 16α-^{18}F-Fluoro-17β-Fluoroestradiol

Gary A. Ulaner[1], David A. Mankoff[2], Amy S. Clark[3], Amy M. Fowler[4], Hannah M. Linden[5], Lanell M. Peterson[6], Farrokh Dehdashti[7], Brenda F. Kurland, Joanne Mortimer[8], Jason Mouabbi[9], Dae Hyuk Moon[10], and Elisabeth G.E. de Vries[11]

TABLE 1
Clinical Scenarios for ER–Targeted PET with ^{18}F-FES

Scenario number	Description	Appropriateness	Score*
Diagnosis			
1	Diagnosing primary breast cancer	Rarely appropriate	2
2	Diagnosing malignancy of unknown primary when biopsy is not feasible or is nondiagnostic	May be appropriate	5
Staging			
3	Routine staging of primary tumor (T staging)	Rarely appropriate	1
4	Routine staging of axillary nodes	Rarely appropriate	3
5	Routine staging of extraaxillary nodes and distant metastases	May be appropriate	5
6	Staging ILC and low-grade IDC	May be appropriate	5
Biopsy			
7	Assessing ER status, in lieu of biopsy, in lesions that are easily accessible for biopsy	May be appropriate	5
8	Assessing ER status in lesions that are difficult to biopsy or when biopsy is nondiagnostic	Appropriate	8
Selection of therapy			
9	After progression of metastatic disease, for considering second line of endocrine therapy	Appropriate	8
10	At initial diagnosis of metastatic disease, for considering endocrine therapy	Appropriate	8
11	At initial diagnosis of primary breast cancer, for considering endocrine therapy	Rarely appropriate	1
Other			
12	Measuring response to therapy	Rarely appropriate	1
13	Detecting lesions in patients with suspected/known recurrent or metastatic breast cancer	May be appropriate	5
14	Detecting ER status when other imaging tests are equivocal or suggestive	Appropriate	8

6	Staging ILC and low-grade IDC	May be appropriate	5
Biopsy			
7	Assessing ER status, in lieu of biopsy, in lesions that are easily accessible for biopsy	May be appropriate	5
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14	Detecting ER status when other imaging tests are equivocal or suggestive	Appropriate	8

AJR Online First Accepted Manuscript

Prospective Pilot Study of ^{18}F-Fluoroestradiol PET/CT in Patients With Invasive Lobular Carcinomas

Matthew F. Covington, MD, John M. Hoffman, MD, Kathryn A. Morton, MD, Brandon Buckway, PhD, Kenneth M. Boucher, PhD, Regina Rosenthal, MD, Jane Porretta, MD, Kirstyn E. Brownson, MD, Cindy B. Matsen, MD, Christos Vaklavas, MD, John H. Ward, MD, Mei Wei, MD, Saundra S. Buys, MD, Namita Chittoria, MD, Ellen D. Yakish, BS, CNMT, ARRT(CT), Zane G. Archibald, BS, RT, ARRT(N)(CT), Lance D. Burrell, MS, CNMT, PET, NCT, RT(CT), Regan I. Butterfield, BS, CNMT, ARRT(CT), Jeffrey T. Yap, PhD

https://doi.org/10.2214/AJR.22.28809
Accepted: March 1, 2023
Article Type: Original Research

Conclusions from pilot study

- FES-PET/CT
  - Showed abnormal uptake in 83% of sites of histologically known ILC (88% on per-patient basis)
  - Detected additional breast and/or axillary lesions with respect to standard-of-care evaluation in 24% of patients
  - Changed the clinical stage in 18% of patients
- Study shows potential for assisting ILC staging

Clinical Breast Cancer

ORIGINAL ARTICLE · Volume 26, Issue 1, P36-46, January 2026

Staging Invasive Lobular Carcinoma: A Prospective Study on the Efficacy of 18F-Fluoroestradiol (FES)-PET/CT

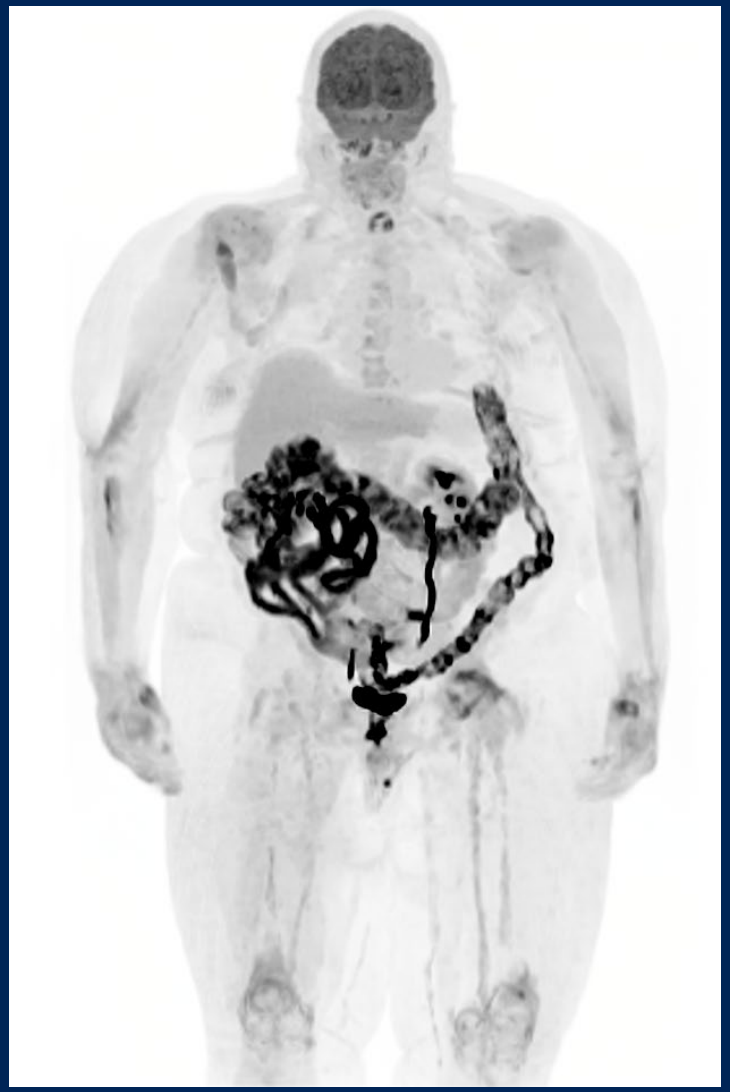
Matthew F. Covington [1,2,#] · Samantha Salmon [2] · Andrew Kozlov [2] · ... · Brandon Buckway [1] · Angela Meite [1] · Jeffrey Yap [1,2] ...

Show more

FES-PET/CT

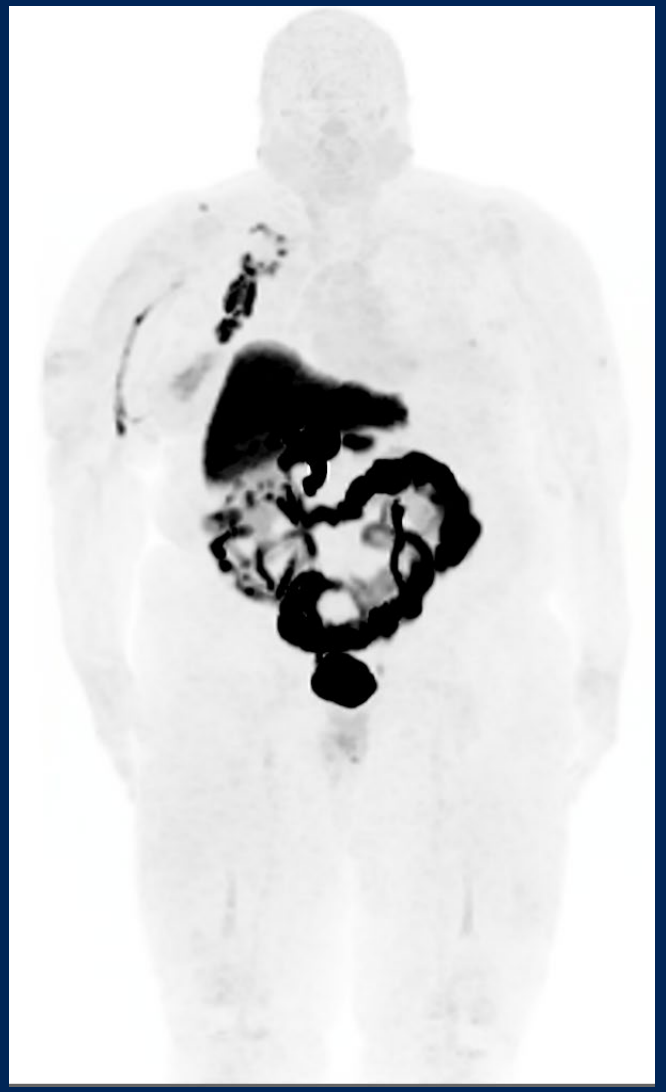
- Altered the clinical staging in **32% of patients** (P=.036) compared to standard-of-care (SOC) imaging
- Identified previously undetected Stage IV (metastatic) disease in **12.5%** of cases and histologically confirmed axillary lymph node metastases in **8%** of cases
- Failed to detect axillary metastases in **28%** of cases when compared to traditional surgical staging

In the subset of 15 participants who also received an FDG-PET/CT, there was a **40% discordance** in findings between the two imaging modalities.



FDG

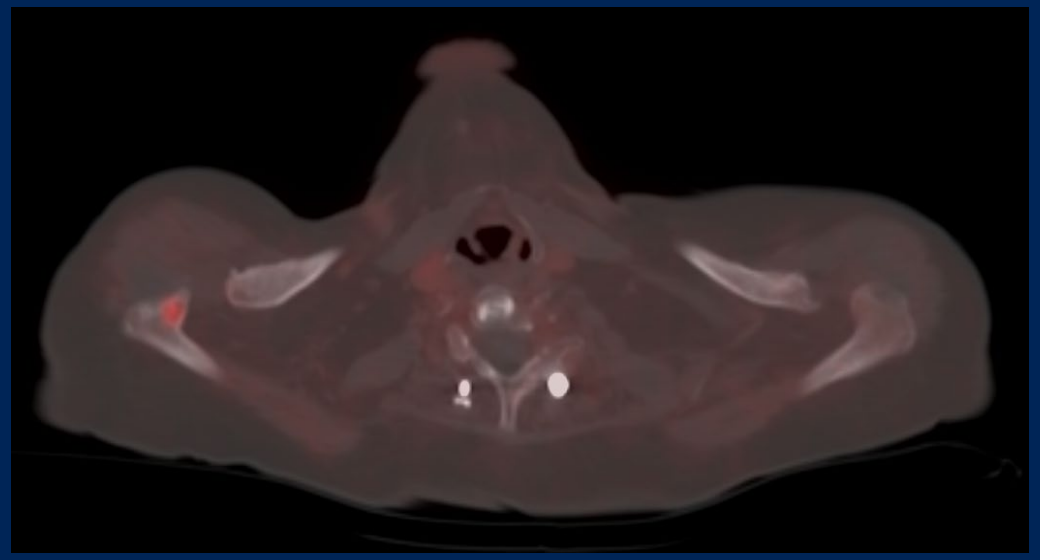
No disease

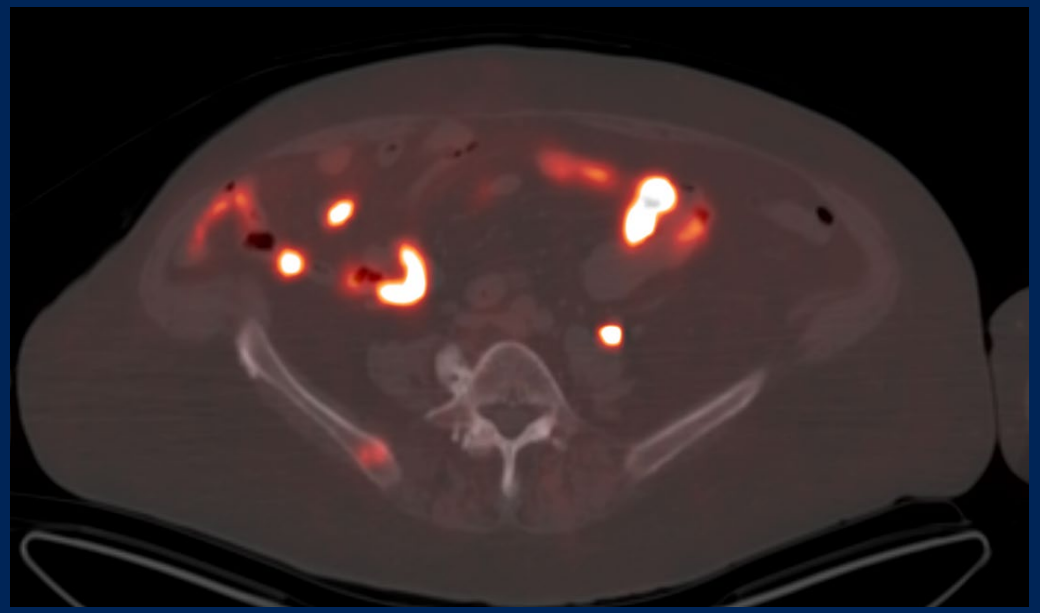


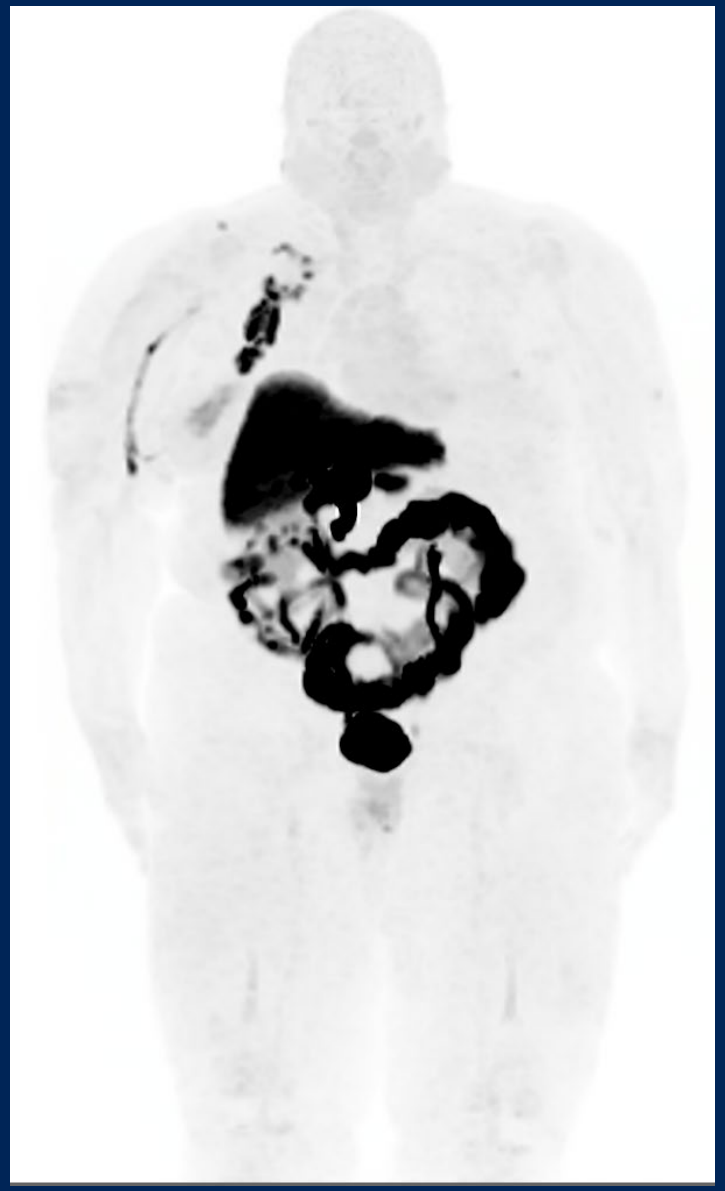
FES

Extensive nodal metastatic disease

Osseous metastatic disease

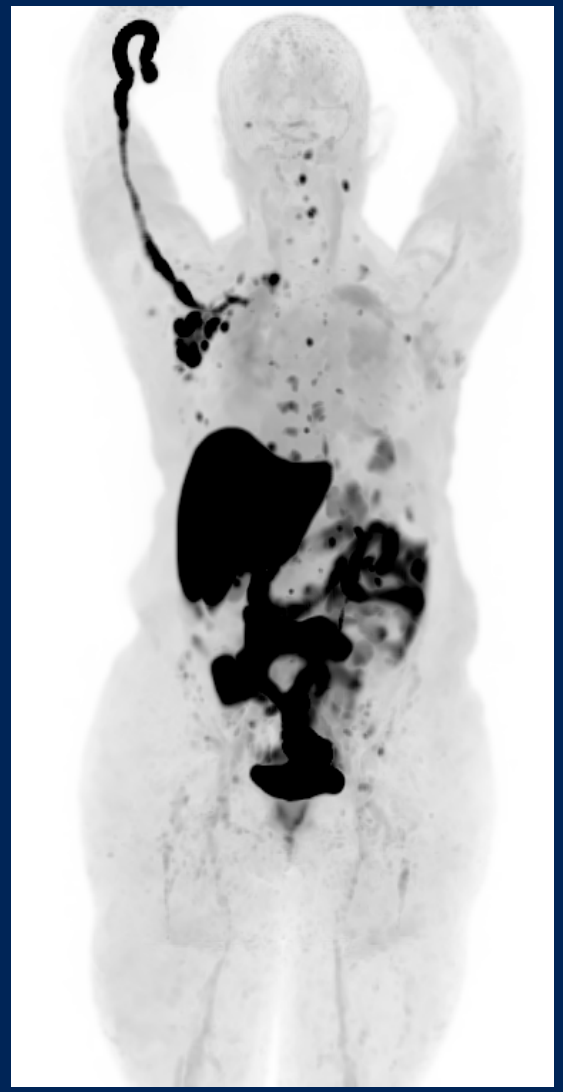




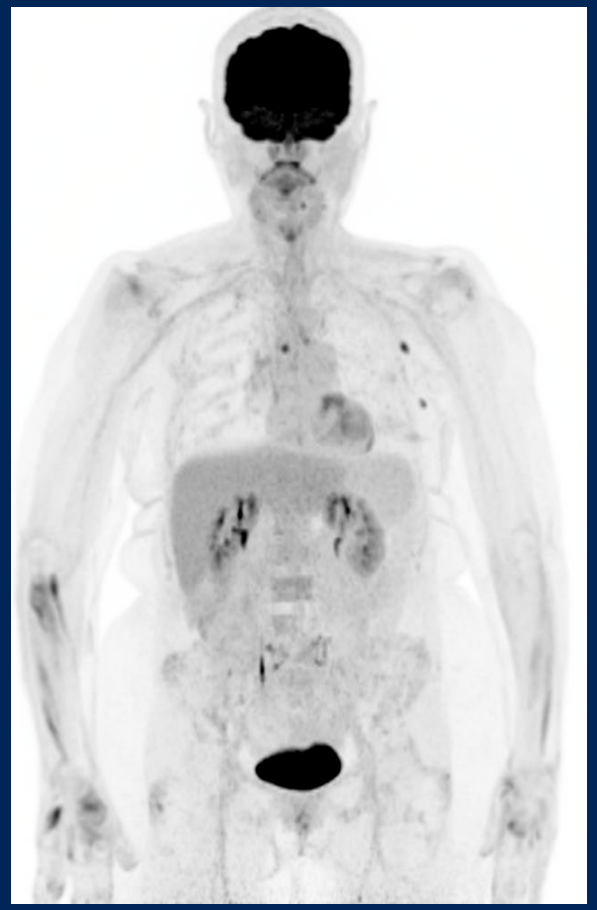


FDG

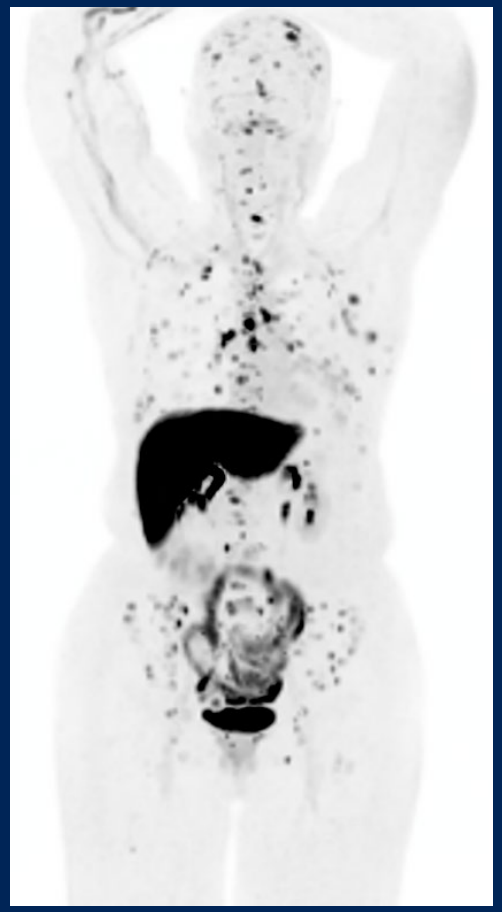
FES



FDG



FES



75-year-old with prior ILC, prior bilateral mastectomies, recurrence biopsy-proven in left chest wall

FDG revealed 2 left chest wall masses and some indeterminate mediastinal lymph nodes

FES revealed additional disease:

- >100 bone metastases
- Metastatic lymph nodes (left axilla, mediastinum, left internal mammary)

The future of breast cancer PET extends beyond FDG and FES

- Many potential (and even surprising) radiopharmacuetical candidates include
  - Fibroblast activating protein (FAPI)
  - Trastuzumab (HER2)
  - FFNP (PR)
  - NeoB
  - PSMA
  - SSTR

^{68}Ga-FAP-2286 PET of Solid Tumors: Biodistribution, Dosimetry, and Comparison with ^{18}F-FDG

Brad Kline, Surekha Yadav, Youngho Seo, Robin Cumming Ippisch, Jessa Castillo, Rahul R. Aggarwal, Robin Kate Kelley, Spencer C. Behr, Robert R. Flavell, Courtney Lawhn-Heath, Michelle Melisko, Hope S. Rugo, Victoria Wang, Sue S. Yom, Patrick Ha, Fei Jiang and Thomas A. Hope

Journal of Nuclear Medicine June 2024, 65 (6) 938-943; DOI: https://doi.org/10.2967/jnumed.123.267281

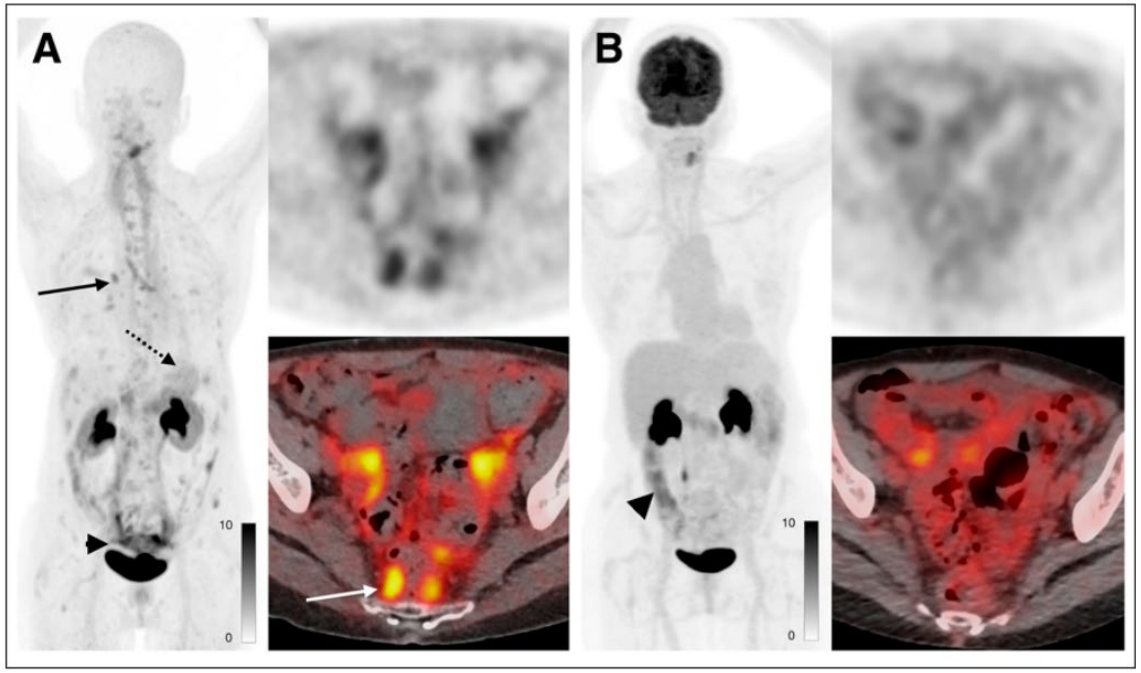


FIGURE 4. A 72-y-old woman with metastatic invasive lobular breast cancer. ^{68}Ga-FAP-2286 PET (A) revealed extensive metastatic disease not seen on ^{18}F-FDG PET (B), including small mediastinal and hilar lymph nodes (A, solid black arrow), diffuse gastric mucosal disease (A, dotted black arrow), and extensive peritoneal disease (SUV_{max}, 7.1; A, black arrowhead and white arrow). Uptake seen on ^{18}F-FDG PET in abdomen reflects physiologic uptake in bowel (B, black arrowhead) rather than tumor.

Theranostics

- **DIAGNOSE → TARGET → TREAT**
- **Step 1: See It:** PET imaging detects specific cancer cell receptors.
- **Step 2: Treat It:** Radioligand therapy delivers targeted radiation to those exact receptors.
- **The Hoped for Outcome:** Maximum precision. Minimal side effects.

Theranostics

- Current clinical applications:
  - PSMA for prostate therapy
  - SSTR for neuroendocrine therapy
- Numerous breast cancer theranostic trials currently underway
- **Need for ILC-specific theranostic research!**

Key Takeaway Points/Conclusions

1

Conventional Imaging and Standard FDG PET/CT Have Limitations in Detecting ILC

2

Receptor-Targeted and Advanced Imaging Modalities May Improve Detection

3

The Future: More PET agents and Radioligand Therapy for Breast Cancer Including ILC

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- Key questions for future study:
  - Which ILC patients should get FDG only, FES only, or both for staging, treatment monitoring, recurrence evaluation, etc
  - If imaging struggles, will liquid based screening assays (ctDNA) fill gaps for breast cancer screening, treatment monitoring, etc
  - Can we do better at predicting which patients are at risk for ILC specifically so we can offer advanced screening up front?
    - Currently we only tailor breast MRI for those at elevated lifetime risk of all breast cancers, and/or those with dense breast tissue on mammography

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