



# 18F-Fluoroestradiol (FES) and 18F-Fluorodeoxyglucose (FDG) PET imaging in metastatic lobular breast cancer.



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## ABSTRACT

**Background:** The histology and pattern of spread in lobular breast cancer has presented challenges in estimating extent of disease by traditional imaging methods<sup>1</sup>. <sup>18</sup>F-FES is an estrogen analogue PET imaging tracer which measures tumor ER expression at multiple tumor sites simultaneously<sup>2</sup>. It is FDA approved in the US and will be available in 2021, pressing clinicians to define the role of FES in patients with breast cancer before use in practice. We compared quantitative FES-PET and clinical FDG-PET SUV uptake between patients with metastatic lobular carcinoma.

**Methods:** We retrospectively evaluated FES SUV uptake in ER+ lobular metastatic breast cancer patients (n = 38) enrolled in various studies at our institution. Up to ten lesions in each patient were evaluated by FES SUV<sub>max</sub> for a total of 192 lesions and matched pairwise with FDG images. Linear mixed effects models were used to assess the difference between FES and FDG lesions while controlling for within patient correlation. Overall survival (OS), from time of FES-PET scan to death, and progression-free survival (PFS), from FES scan to death or relapse, was evaluated using Kaplan-Meier curves.

**Results:** Among metastatic breast cancer patients with lobular histology, 87% of patients had a positive FES scan. The majority of positive scans demonstrated uptake in all sites, with only a small percentage (6%) lacking FES uptake in at least one lesion. Uptake was noted in various metastatic tumor sites including bone (78%), soft tissue/lymph node (17%), breast (4%) and lung (1%). After averaging scans within a sample, the mean (range) of average SUV<sub>max</sub> in FES and FDG respectively was 3.38 (0.88, 9.06) and 4.14 (1.25, 9.49). Paired lesion analysis shows concordance between the two imaging modalities in lesions with low SUV uptake, however as the average SUV uptake increases, there is variability and discordance between FES and FDG. The average difference between paired FES and FDG lesions is -0.60 (95% CI: -0.97, -0.23, p = 0.0018). Specifically, in bone lesions the difference between paired FES and FDG was -0.74 (95% CI: -1.18, -0.30, p = 0.0011), with greater difference noted at higher SUV values (Difference of -0.91, 95% CI: -1.68, -0.15, p = 0.02 when either FES or FDG SUV was >5). Following FES-PET imaging, patients with lobular carcinomas had median survival time of 3.14 years (95% CI: 2.6, 6.4) and progression free survival of 1.3 years (95% CI: 0.7, 2.5).

**Conclusions:** FES and FDG scans demonstrate similar uptake in metastatic lobular breast cancer, suggesting that both scans have utility in detecting lobular histology. Our data suggests that at higher SUV values, FES may provide additional information to FDG. Large prospective trials are needed to define the clinical utility of FES-PET in metastatic lobular breast cancer.

## OBJECTIVES

- To quantitatively analyze FES-PET and FDG-PET uptake in patients with metastatic lobular breast cancer.

## METHODS

- Retrospective review of FES and FDG scans in patients with metastatic lobular breast cancer (n = 38) enrolled in various studies at UWMC from 1996-2015.
- Up to 10 lesions evaluated per patient. Total of 192 lesions in both FES and FDG.
- Statistical Analyses: Linear mixed effects models, Kaplan-Meier curves.

## RESULTS

TABLE 1. Baseline Characteristics

Characteristic	Lobular Breast Cancer (N = 38)
Median Age (Range)*	59 (34-80)
Prior Therapies (%)	
Endocrine	25 (66%)
Chemotherapy	26 (68%)
Radiation	20 (53%)
Metastases Location (by total lesions)**	
Bone	150 (78%)
Soft Tissue	33 (17%)
Breast	8 (4%)
Lung	1 (1%)

All primary tumors were ER positive.  
 All patients were female.  
 \*Age is calculated at the time of FES scan.  
 \*\*192 Total lesions evaluated

TABLE 2. Summary of FES and FDG Uptake

Outcome	Lobular Breast Cancer (N = 38)
FES SUV <sub>max</sub>	
Mean (SD)	3.38 (1.96)
Median (Q1,Q3)	3.03 (1.84, 4.25)
Range	0.88 – 9.06
FDG SUV <sub>max</sub>	
Mean (SD)	4.14 (2.00)
Median (Q1,Q3)	3.64 (2.07, 5.15)
Range	1.25 – 9.49

Table shows summary statistics of average scans within each sample, i.e., we average up to ten lesion scans within a sample and then summarize these averages across all samples.

- Average difference between paired FES and FDG lesions was -0.60 (p = 0.002)
  - Concordance between FES and FDG with low SUV uptake.
  - Discordance between FES and FDG with higher SUV values
- In bone, average difference between paired FES and FDG was -0.74 (p = 0.001)

FIGURE 1. Comparison of FDG SUV<sub>max</sub> and FES SUV<sub>max</sub>

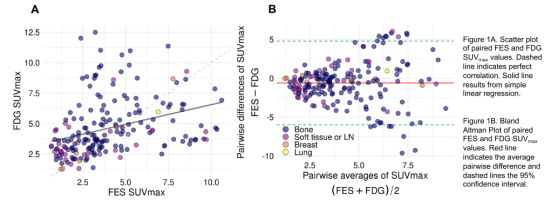


Figure 1A. Scatter plot of paired FES and FDG SUV<sub>max</sub> values. Dashed line indicates perfect correlation. Solid line results from simple linear regression.

Figure 1B. Bland-Altman Plot of paired FES and FDG SUV<sub>max</sub> values. Red line indicates the average pairwise difference and dashed lines the 95% confidence interval.

FIGURE 2. Overall Survival

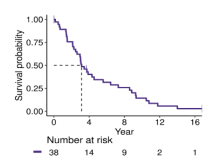


Figure 2. Kaplan-Meier curves for overall survival (OS). Time is calculated from date of FES scan to last day of follow-up or death. Dashed line indicates median survival time.

FIGURE 3. Progression Free Survival

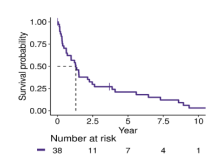


Figure 3. Kaplan-Meier curves for progression free survival (PFS). Time is calculated from date of FES scan to last day of follow-up, death, or relapse. Dashed line indicates median survival time.

- Following FES-PET imaging, patients with lobular carcinomas had:
  - Median Overall Survival time of 3.14 years
  - Median Progression Free survival of 1.3 years.

## CONCLUSIONS

- Both FES and FDG can be used to identify metastatic lobular breast cancer.
- Our study suggests that at higher SUV values, FES may provide additional information to FDG.

## REFERENCES

- Hogan et al. Comparison of 18F-FDG PET/CT for Systemic Staging of Newly Diagnosed Invasive Lobular Carcinoma Versus Invasive Ductal Carcinoma. *J Nucl Med.* 2015;56(11):1674-1680.
- Lindström LS, Yau C, Czene K, et al. Intratumor Heterogeneity of the Estrogen Receptor and the Long-Term Risk of Fatal Breast Cancer. *J Natl Cancer Inst.* 2018;110(7):726-733.