BRAIN FES PET STANDARDIZED UPTAKE VALUE ASSOCIATION WITH ESR1 AND PIK3CA GENOMIC ALTERATIONS

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Objective

Breast cancer (BC) is the second most common cancer linked to brain metastases (BM), with 70% of patients having estrogen receptor-positive (ER+) disease[1].
Brain metastases represent a major clinical challenge, second in frequency only to those arising from lung cancer[1].
[F18]-Fluoroestradiol ([F18]-FES) PET is an FDA-approved molecular imaging tool that targets ER with high specificity (>90%) and allows whole-body assessment of ER expression[2].
Brain FES PET has shown promise as an adjunct diagnostic tool in BC BM[3].
Liquid biopsies, including circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and exosomes, are emerging non-invasive diagnostic and monitoring tools.
Our purpose was to combine FES PET with liquid biopsy in a pilot cohort to assess the potential of this multi-modal biomarker in evaluating response to endocrine and radiotherapy in patients with ER+ BC BM.

Method

Following informed consent, patients with ER+ BC and known or suspected BM who underwent dedicated brain FES PET/CT and blood ctDNA analysis were included in this IRB-approved retrospective study. Clinical and demographic data were collected via chart review.
Dedicated dynamic brain PET/CT acquisition was performed from 0–90 minutes.
FES PET was co-registered to post-gadolinium contrast 3D T1 MRI.
Two 10-mL blood samples were collected and analyzed using the Guardant360 next-generation sequencing platform to detect genetic alterations.
Codon variants of ESR1 and PIK3CA mutations were analyzed, and mutant allele frequency was assessed for personalized treatment.
The average of maximum standardized uptake values (SUV) in ESR1 and PIK3CA-positive and ESR1 and PIK3CA-negative groups was compared separately.
Mann-Whitney and Spearman correlation tests were performed.

Results

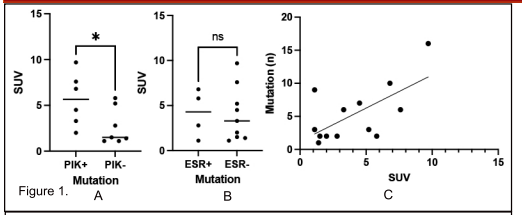


Figure 1.

13 patients with FES-positive lesions were stratified by PIK3CA and ESR1 mutations. 6/13 (46%) were PIK3CA-positive, and 4/13 (31%) were ESR1-positive.
The median FES PET SUV was 5.65 in the PIK3CA-positive and 1.50 in the PIK3CA-negative subgroup ($p = 0.049$*) (Figure 1A).
The median FES PET SUV was 4.30 in the ESR1-positive and 3.30 in the ESR1-negative subgroup (p = ns)(Figure 1B).
Positive correlation was found between FES PET SUV, and mutation count, demonstrating statistical significance ($r = 0.65$, $p = 0.02$) (Figure 1C).

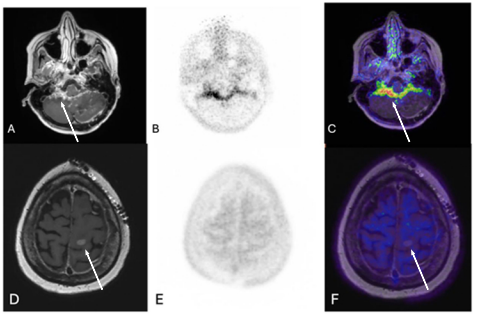


Figure 2. FES PET brain images in two patients with PIK3CA-positive (top row) and PIK3CA-negative (bottom row) ER+ BCBM, illustrating variability in estrogen receptor expression based on PIK3CA mutation status. Patient with ER+ BCBM post left suboccipital craniotomy, treated with a combination of SRS and systemic therapy, presenting with heterogeneous leptomeningeal thickening and enhancement involving the bilateral cerebellum on axial T1 postcontrast MRI (A). Corresponding FES PET (B) and fused axial PET/MR (C) demonstrate mild to moderate avidity along the right superior cerebellar folia, SUV 5.1. Patient with ER+ BCBM, treated with a combination of SRS and systemic therapy, presenting with enhancing lesion centered in the left postcentral gyrus on axial T1 postcontrast MRI (D). Corresponding FES PET (E) and fused axial PET/MR (F) demonstrate low FES avidity fusing to the enhancing lesion in left postcentral gyrus, SUV 1.1. FES PET and fused images windowed at 0–5 SUV.

Conclusion

Our preliminary analysis demonstrates higher FES PET SUV in patients with PIK3CA and ESR1 mutations, as well as a trend for greater SUV in patients with a greater number of mutations, noting limitations of small sample size.
Integrating brain FES PET with liquid biopsy has the potential to optimize treatment response in patients with ER-positive BC BM.
This multi-modal approach may enhance our understanding of therapy resistance mechanisms by integrating biologically targeted PET with molecular profiling to guide treatment decisions in patients with ER+ BC BM.

References

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