CASE REPORT
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The impact of PET-FES on changing therapeutic conduct in bilateral luminal phenotype breast cancer

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ABSTRACT

Positron emission tomography with ^{18}F-fluoroestradiol (PET-FES) is a functional imaging exam that assesses the expression of estrogen receptors and is highly sensitive in detecting metastases in luminal tumors, which represent the majority of breast cancer cases. We report the case of a 75-year-old patient with bilateral breast carcinoma, whose initial treatment would be adjuvant chemotherapy based on positron emission tomography/computed tomography (PET-CT) with fluorodeoxyglucose (FDG), which showed no evidence of metastases. However, PET-FES identified metastatic involvement in lymph nodes and the skeleton, reclassifying the disease to stage IV. This new assessment made it possible to replace chemotherapy with endocrine therapy associated with cyclin-dependent kinase 4 and 6 (CDK4/6) inhibitors, a more effective and less toxic approach for the metastatic scenario. The unavailability of PET-FES in the public system and in several private health insurance plans constitutes an ethical imperative, as it limits access to precision diagnostics. This reality highlights structural inequalities in Brazilian oncology, representing a dilemma that requires public policies and evidence-based solutions to ensure equity in cancer treatment.

KEYWORDS: breast neoplasms; positron emission tomography; neoplasm staging; access to health services; health equity.

INTRODUCTION

Breast cancer is the most common malignant neoplasm in women in Brazil, with a predominance of luminal subtypes, which express hormone receptors and account for about 70% of cases. Accurate staging is the cornerstone for defining the therapeutic strategy, whether curative or palliative. In this context, functional imaging tests such as positron emission tomography (PET) are crucial. However, PET-CT with fluorodeoxyglucose (FDG), which is widely used, has known limitations in luminal tumors, which often have low glycolytic metabolism, resulting in false-negative tests for metastatic disease[1].

To overcome this gap, positron emission tomography with fluoroestradiol-18F (PET-FES) emerges as a highly accurate tool, capable of altering staging and, consequently, the therapeutic plan[2,3]. Its unavailability in the Unified Health System (SUS) and restricted coverage in supplementary health insurance plans raise a relevant ethical dilemma, highlighting structural inequalities in access to technologies that embody advances in precision oncology.

This study was conducted in accordance with all ethical and regulatory requirements established by Resolution 466/2012 of the National Health Council[4]. The project was submitted to and approved by the Research Ethics Committee (CEP) of Santa Casa de Misericórdia de São Paulo, receiving the Certificate of Presentation for Ethical Review (CAAE) number 90831025.8.0000.5479.

CASE REPORT

A 75-year-old patient diagnosed with bilateral breast carcinoma. In February 2025 she underwent surgical procedures. The anatomopathological examination of the right breast revealed mixed invasive carcinoma (non-special and lobular), grade 2, pT2N3a, with an immunohistochemical profile of estrogen receptors (95%), progesterone (80%), and Ki-67 of 12%. The left breast presented non-special invasive carcinoma, grade 2, pT3N1a, with a similar profile.

Due to locally advanced disease, initial staging with FDG PET-CT was performed and showed no evidence of metastatic disease. The proposed course of action was adjuvant chemotherapy with curative intent. However, considering the high clinical risk and the possibility of micrometastases undetected by conventional methods, it was decided to perform PET-FES for definitive staging. The exam revealed multiple foci of radiopharmaceutical

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uptake in supraclavicular lymph nodes and multiple costal arches and vertebrae, findings consistent with disseminated metastatic disease (stage IV).

This new information radically changed the prognosis and treatment. The disease was reclassified from potentially curable to incurable, and the therapeutic proposal was changed from adjuvant chemotherapy to first-line targeted therapy for metastatic disease, with cyclin-dependent kinase 4/6 (CDK4/6) inhibitor associated with hormonal blockade. This change prevented the toxicity of inappropriate chemotherapy treatment and instituted the most effective therapy for controlling the disease at its actual stage (Figure 1).

DISCUSSION

The case highlights the emerging role of PET-FES as a decisive tool in staging and therapeutic decision-making in luminal tumors, particularly those with low glycolytic metabolism. In RH+ neoplasms, especially invasive lobular carcinoma (ILC), the accuracy of PET-FDG is limited, with false-negative rates exceeding 30–40% for bone, serosal, and lymph node metastases[1]. This limitation is accentuated in ILC due to diffuse dissemination through the gastrointestinal tract, retroperitoneum, and serosal surfaces, exposing patients to understaging, therapeutic delays, and suboptimal clinical decisions[1].

Although Brazilian experience with PET-FES is limited to small series, our case demonstrates that the exam can directly alter therapeutic conduct. Unlike immunohistochemistry, which only assesses the static expression of the estrogen receptor, PET-FES measures the functional activity of the estrogen pathway

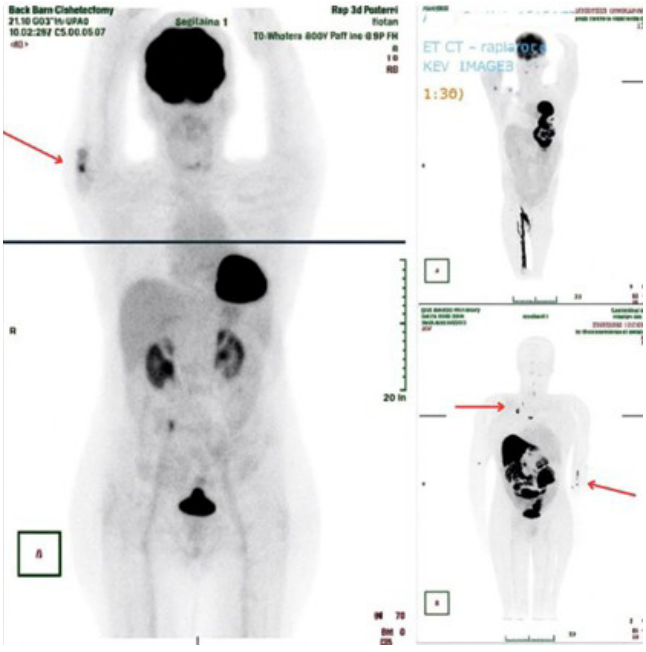

Figure 1. PET-FES in tumor detection.

in vivo, detecting tumor heterogeneity and providing essential dynamic information for clinical management[2,3]. Studies indicate 80–90% sensitivity for detecting ER+ lesions, surpassing FDG in tumors with reduced glycolytic metabolism, such as ILC. Heterogeneous uptake in FES correlates with early resistance to endocrine therapy, allowing for the anticipation of therapeutic failure and guiding precise interventions[2,3].

In the reported case, PET-FES corrected the initial understaging by false-negative PET-FDG, redefining the clinical condition as metastatic from the outset and completely changing the therapeutic plan. Trials such as MONALEESA-2, MONARCH-3, and PALOMA-2 demonstrate that early introduction of endocrine therapy combined with CDK4/6 inhibitors at the first metastatic event provides substantial gains in overall survival and a relative risk reduction of 24–35%[4-6].

Internationally, the FDA has approved PET-FES for the evaluation of ER+ tumors, and the 2024–2025 NCCN guidelines recommend its use in cases of clinical-radiological discordance, ambiguous staging, or suspected metastatic disease not detected by FDG[5]. Countries such as France, Canada, and the United Kingdom have already integrated FES into their diagnostic algorithms, especially in the ILC.

In Brazil, experience remains limited. A small series in a private center (12 exams, August 2022–March 2024, mean age 62.2 years) demonstrated the contribution of PET-FES to clinical reasoning in 40% of cases, mainly in lymph nodes without FDG hypermetabolism[7]. There are no robust national series on sensitivity, specificity, therapeutic impact, or clinical follow-up, limiting the extrapolation of international results.

Restricted access to PET-FES highlights technological inequality, creating an ethical dilemma: oncologists have superior technology that could modify clinical outcomes, but face institutional limitations. This creates a conflict between beneficence, by offering more effective evidence-based treatment, and distributive justice, by acting within the constraints of the SUS and supplementary health care.

Emerging clinical implications include: detection of tumor heterogeneity and clones resistant to hormone therapy; improved staging, especially in ILC; accurate selection of candidates for CDK4/6 use; definition of target volume in oligometastatic disease; and early monitoring of endocrine response, reducing unnecessary interventions. This case demonstrates that PET-FES allows for "the right treatment at the right time," reinforcing its impact on personalized medicine, equity, therapeutic decision-making, and patients' quality of life.

CONCLUSIONS

This case clearly demonstrates how PET-FES can redefine staging and therapeutic management in luminal breast cancer, enabling the indication of a more rational and effective treatment. The adoption of targeted therapy instead of chemotherapy

not only improved the patient's prognosis but also spared her from unnecessary toxicity. The lack of access to this technology in Brazil represents a structural failure that widens inequality in cancer care. It is imperative that managers, regulatory agencies, and medical societies work together to develop policies that accelerate the incorporation of cost-effective technologies, ensuring that the benefits of science reach all patients.

AUTHORS' CONTRIBUTIONS

MMM: Conceptualization, Formal analysis, Methodology, Project administration, Supervision. APL: Data curation, Writing – review & editing. GMV: Data curation, Writing – review & editing. PHAD: Resources, Validation. GDS: Investigation, Visualization, Writing – original draft. MSR: Investigation, Visualization, Writing – original draft.

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