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Incidental hip lesions on fluorodeoxyglucose-positron emission tomography during breast cancer staging: Addressing false positives in clinical practice

Ahmed R Awad, Erin J Pearson, Cristina A Moldovan, Louise M Nott, Jane K Mills, Gavin C Mackie

ABSTRACT

Introduction: Fluorodeoxyglucose-positron emission tomography-computed tomography (FDG-PET/CT) is increasingly used in breast cancer (BC) staging due to its high sensitivity for detecting extra-axillary lymph nodes and distant metastases. This hybrid imaging modality is particularly valuable for its ability to identify metastases not readily detected by conventional methods like CT and whole-body bone scan (WBBS). However, FDG-PET/CT has limitations, especially with lower-proliferative, low-grade tumors, and well-differentiated luminal BC subtypes, which may show reduced FDG uptake. Although FDG-PET/CT generally has significantly fewer false positives (FPs) than standard imaging, FPs on FDG-PET/CT can still cause patient anxiety and treatment initiation delays.

Case Series: In our case series, we highlight three breast cancer patients who presented with FDG-PET/CT avid hip lesions which were reported as possible metastatic disease but on further investigation were all found to be histologically proven benign false positives (FPs). These findings underscore the need for careful interpretation, as solitary FDG-avid lesions can mimic metastatic disease, potentially leading to unnecessary anxiety, additional diagnostic procedures, and delays and significant alterations in treatment. When clinical history, examination, and imaging modalities like magnetic resonance imaging (MRI) cannot definitively diagnose a lesion, histopathological confirmation becomes crucial. Accurate diagnosis and staging, including biopsy, if necessary, are essential for determining the appropriate first-line systemic treatment for each patient.

Conclusion: Ultimately, FDG-PET/CT enhances BC staging by improving detection accuracy across tumor phenotypes and grades; however, it requires careful interpretation and a multidisciplinary approach to prevent overtreatment and ensure the best patient outcomes.

Keywords: Bone metastases, Breast cancer, Diagnostic accuracy, False positives, FDG-PET/CT, Hip lesions, Histopathological confirmation, Staging

Ahmed R Awad[1], Erin J Pearson[1], Cristina A Moldovan[1], Louise M Nott[1,2], Jane K Mills[3], Gavin C Mackie[2,4]

Affiliations: [1]Medical Oncology Unit, Royal Hobart Hospital, Tasmania, Australia; [2]Icon Cancer Centre, Hobart, Tasmania, Australia; [3]General Surgery Unit, Royal Hobart Hospital, Tasmania, Australia; [4]Nuclear Medicine Unit, Royal Hobart Hospital, Tasmania, Australia.

Corresponding Author: Louise M Nott, Medical Oncology Unit, Royal Hobart Hospital, Tasmania, Australia; Icon Cancer Centre, Hobart, Tasmania, Australia; Email: louise.nott@ths.tas.gov.au

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INTRODUCTION

Breast cancer (BC) is the most frequent type of cancer diagnosed in women. Survival is dependent on the stage at diagnosis and the subtype of BC [1].

Clinical staging of BC is based on the American Joint Committee on Cancer's Tumor-Node-Metastasis (TNM) staging system [2], in which imaging plays a central role. Accurate clinical staging at diagnosis is important in determining prognosis and the most appropriate local and systemic treatment. Patients with locoregional breast malignancy have 5-year survival rates of 76–99%, but for those with distant metastases, this rate decreases to 20–28% [3]. Mammography, ultrasound, and breast magnetic resonance imaging (MRI) help accurately stage local disease extent, whereas whole-body bone scan (WBBS), computed tomography (CT) or MRI of the chest, abdomen, and pelvis, and fluorodeoxyglucose-positron emission tomography-computed tomography (FDG-PET/CT) are used to determine systemic staging.

Fluorodeoxyglucose-positron emission tomography-computed tomography's sensitivity for detecting unsuspected distant metastases tends to increase with the clinical stage of the disease [4]. In early-stage breast cancer (stages I and II), the likelihood of asymptomatic distant metastases is low, and guidelines generally advise against comprehensive systemic imaging in the absence of clinical symptoms or abnormal laboratory findings [5]. However, in patients with positive axillary lymph nodes or stage III disease, FDG-PET/CT can reveal occult metastases in approximately 10–29% of cases [6], underscoring its utility in more advanced stages of breast cancer. This evidence suggests that FDG-PET/CT plays a critical role in tailoring treatment plans by identifying metastatic disease that might otherwise go undetected, thus influencing both prognosis and treatment intent.

Fluorodeoxyglucose-positron emission tomography-computed tomography has been shown to be a cost-effective modality for radiologic staging of clinical stages II and III BC in comparison to standard imaging modalities in the United States and Netherlands but has not been universally adopted in all guidelines [7, 8]. In Australia, FDG-PET/CT is reimbursed for the staging of locally advanced BC and for the evaluation of suspected metastatic or recurrent BC [9].

While FDG-PET/CT imaging offers high sensitivity in detecting both local and distant metastases, it also has limitations that may result in FPs. False positives can arise from benign conditions such as inflammatory processes, infections, or degenerative changes, especially in bone or lymph nodes, which may appear as FDG-avid and mimic metastatic disease [10]. In the context of BC FPs can lead to incorrect upstaging, unnecessary biopsies, delay in treatment, and altered treatment course, as well as increased anxiety for patients. Lobular breast cancers, for instance, often have lower FDG uptake and may be missed or underestimated, while other benign conditions with higher FDG uptake may be mistakenly identified as malignancies [11].

To mitigate these effects, careful interpretation of FDG-PET/CT findings is critical, particularly when ambiguous solitary lesions are detected. When necessary, follow-up imaging, histopathological confirmation, or correlative MRI can provide additional specificity to clarify uncertain findings.

In this case series, we outline three cases of women with BC who were found to have FP bony lesions on FDG-PET during their initial staging workup.

CASE SERIES

Case 1

A 57-year-old woman being evaluated for recurrent fever due to aspiration pneumonitis secondary to a laparoscopic adjustable gastric banding procedure was incidentally found on CT to have a 34 × 27 mm irregular mass in the medial left breast, accompanied by mild nipple retraction and suspicious axillary lymph nodes. Fine-needle aspiration (FNA) confirmed a grade 3, triple-negative, basal phenotype invasive adenocarcinoma of the left breast. Fluorodeoxyglucose-positron emission tomography-computed tomography prior to neoadjuvant therapy showed an intensely FDG-avid breast lesion (SUV_{max} 7.9), a mildly avid left axillary node (SUV_{max} 1.9), and an intensely avid lesion in the anterior left femoral head (SUV_{max} 7.07) with lytic changes suggestive of possible bony metastasis (Figure 1). To clarify the femoral lesion for accurate staging, a hip MRI was obtained, revealing that the FDG uptake likely corresponded to synovial hypertrophy associated with an anterior superior labral tear, without any aggressive features.

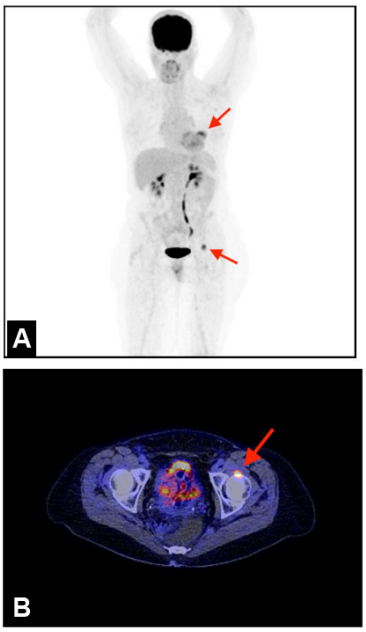

Figure 1: Maximum intensity projection (MIP) image (A) and axial fused FDG PET CT image (B) from case 1—a 57-year-old female's staging PET/CT demonstrating an intensely FDG-avid left breast lesion (arrow—SUV_{max} 7.9), a mildly avid left axillary node (SUV_{max} 1.9), and an intensely avid lesion in the anterior left femoral head (arrow—SUV_{max} 7.07) with lytic changes suggestive of possible bony metastasis. Subsequent biopsy-confirmed to be nodular tenosynovitis (GCTTS).

A subsequent surgical biopsy of the left hip revealed a nodular histiocytic process, histologically consistent with nodular tenosynovitis [giant cell tumor of the tendon sheath (GCTTS)]. The patient then underwent curative-intent neoadjuvant chemotherapy with dose-dense doxorubicin and cyclophosphamide, followed by weekly paclitaxel (ddAC-T). This was followed by wide local excision of the breast mass and excision of five sentinel lymph nodes. Pathology revealed ypT1cN0 residual disease with a Ki-67 index of 45–50%, and no nodal involvement. Germline testing for breast cancer genes was negative. She completed her treatment with adjuvant capecitabine and radiotherapy and remains in remission.

Case 2

A 55-year-old woman who with a screen-detected left sided breast grade 3 estrogen receptor (ER), progesterone receptor (PR) positive, HER-2 negative mixed invasive ductal and lobular carcinoma. She underwent a wide local excision and sentinel lymph node biopsy confirming a pT2pN1 disease with the same phenotype as initial biopsy. A post-operative staging FDG-PET/CT identified a moderately FDG avid (SUV_{max} 5.1) right proximal lytic femoral lesion with sclerotic margins extending into the right femoral neck (Figure 2), raising the possibility of a skeletal metastasis. The sclerotic margins appeared relatively well-circumscribed within a part of the lesion.

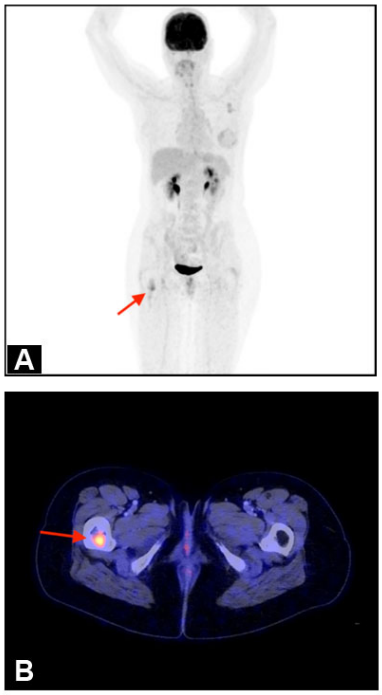

Figure 2: Maximum intensity projection (MIP) image (A) and axial fused FDG PET CT image (B) from case 2—a 55-year-old female's post-operative staging FDG-PET/CT identifying a moderately FDG avid (SUV_{max} 5.1) right proximal lytic femoral lesion with sclerotic margins extending into the right femoral neck (arrows). The sclerotic margins appeared relatively well-circumscribed within a part of the lesion. This lesion was later confirmed to be fibrous dysplasia on biopsy.

Magnetic resonance imaging (MRI) described a heterogenous 25 × 23 × 89 mm enhancing lesion within the right proximal femur, with internal sclerotic septations and a sclerotic rim. The MRI findings could not exclude a solitary metastasis, although the differential included a liposclerosing myxofibrous tumor (LSMFT)—a variant of fibrous dysplasia, or a degenerated (stage III) intraosseous lipoma. A CT-guided core biopsy of the femoral lesion was performed; pathological assessment confirmed fibrous dysplasia, a benign condition.

The clinical stage was therefore pT2N1M0 and the patient commenced curative intent adjuvant ddAC-T chemotherapy followed by endocrine therapy and radiotherapy. She remains in clinical remission.

Case 3

A 47-year-old woman with a self-detected, triple-negative, grade 3 invasive ductal carcinoma of the right breast underwent staging with FDG-PET/CT. The scan showed a 22 × 20 × 23 mm circumscribed intensely FDG avid mass in the right breast consistent with the known carcinoma (SUV_{max} 13.5). Activity within several small right axillary lymph nodes measuring up to 6 mm in diameter is at most extremely mild (SUV_{max} 1.6), likely within normal limits. An FNA later revealed no lymph node malignancy. The scan also identified an FDG-avid focus adjacent to the right femoral neck (SUV_{max} 6.2), appearing to involve the obturator internus or gemellus muscle and associated with focal soft tissue thickening (Figure 3).

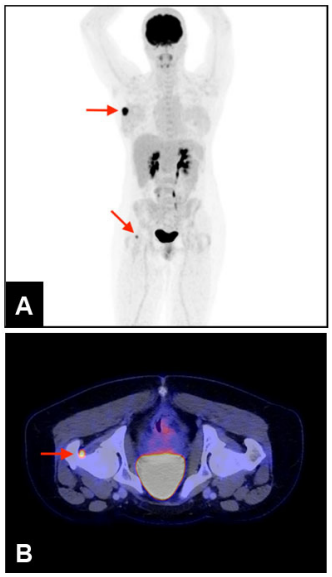

Figure 3: Maximum intensity projection (MIP) image (A) and axial fused FDG PET CT image (B) case 3—a 47-year-old female's staging FDG-PET/CT showing 22 × 20 × 23 mm circumscribed intensely FDG avid mass in the right breast (arrow) consistent with the known carcinoma (SUV_{max} 13.5). Extremely mild activity within several small right axillary lymph nodes measuring up to 6 mm in diameter (SUV_{max} 1.6) was within normal limits consistent with the findings at biopsy. An FDG-avid focus adjacent to the right femoral neck (arrow—SUV_{max} 6.2), appearing to involve the obturator internus or gemellus muscle and associated with focal soft tissue thickening was found on biopsy to be PVNS.

A subsequent MRI of the right hip revealed a 7 mm intra-articular enhancing nodule at the superior aspect of the femoral neck, corresponding to the FDG-PET finding. The nodule displayed diffuse contrast enhancement and a thin, low-signal capsule on T2 imaging, raising concern for possible synovial metastasis. However, excisional biopsy of the hip capsule lesion confirmed pigmented villonodular synovitis (PVNS).

The patient began curative-intent neoadjuvant ddAC-T chemotherapy, showing an initial favorable response. Shortly after starting paclitaxel, however, the primary breast tumor began to enlarge. Repeat FDG-PET revealed increased activity in the right breast lesion, with no new metastatic findings.

A wide local excision of the breast tumor was performed, revealing residual basal phenotype invasive ductal carcinoma, 24 mm in size, without sentinel lymph node involvement and no significant neoadjuvant therapy-induced changes. The patient completed adjuvant radiotherapy and capecitabine and enrolled in an adjuvant vaccine therapy trial.

DISCUSSION

Accurate staging of BC is essential for developing individualised treatment plans and providing precise prognostic estimates. Guidelines, including those from the National Comprehensive Cancer Network, outline specific situations in which FDG-PET/CT is recommended, particularly as a supplement to standard imaging in clinical stage II or operable stage III BC. These recommendations aim to enhance detection accuracy, particularly for de novo stage IV disease, which has substantial prognostic and therapeutic implications. Accurate staging in this context can prevent unnecessary surgeries or radiation treatments and enable the selection of the most appropriate systemic therapies for metastatic BC.

Fluorodeoxyglucose-positron emission tomography-computed tomography has demonstrated superior sensitivity in identifying regional and distant metastases, particularly in the bone, lymph nodes, and liver, compared to conventional imaging such as CT and WBBS. However, FDG-PET/CT has limitations, especially with certain histologic subtypes like lobular breast cancer, which tend to have lower FDG avidity and may not be as readily detectable as ductal carcinoma, even when sizable [12].

Bone is the main site of metastasis in patients with BC, accounting for 20% of the distant metastasis [13]. Fluorodeoxyglucose-positron emission tomography-computed tomography scan more accurately detects bone metastases, than other modalities [14]. Fluorodeoxyglucose-positron emission tomography-computed tomography showed higher accuracy and sensitivity (98.0% and 93.83%) than WBBS (95.61% and 81.48%) in detecting BC bone metastases [15]. Despite improved accuracy with FDG-PET/CT, FPs can occur, which may negatively impact patient outcomes by leading to incorrect upstaging in patients who might otherwise be candidates for curative treatment. A meta-analysis evaluating the diagnostic performance of FDG-PET in detecting BC metastases showed a FP rate of 12.5% and a false negative rate of 10% [16]. Several FDG-avid bone tumor mimickers can lead to FPs on FDG-PET/CT, including bone marrow repopulation from colony-stimulating factors, fractures, avascular necrosis, Paget's disease, benign neoplasms, hypermetabolic bone lesions (such as bone islands and Schmorl's nodes), systemic inflammatory diseases, and iatrogenic injuries [4]. Notably, it is well-recognized that GCTTS and PVNS are FDG avid entities [17]. Colby et al. reported that FPs were more frequently observed in younger breast cancer patients (≤45 years). False positives can cause significant anxiety for patients by raising concerns about potential metastatic disease and may lead to delays in initiating anticancer treatment, which can be particularly detrimental for patients at high risk of recurrence. Prompt investigation of FPs and the development of staging strategies aimed at reducing FP rates are essential goals to optimize patient care [10]. In the case of FDG avid bone lesions which may represent solitary metastases, a biopsy should be strongly considered.

It is extremely important that FDG-PET findings are correlated with clinical history and findings on correlative CT. Histopathological confirmation of suspicious solitary lesions where possible is also essential, as solitary findings may mimic metastases but can be benign or unrelated. This can ensure accurate staging and prognosis, and most importantly, prevents a potentially curative treatment plan being overlooked.

In summary, FDG-PET/CT should be carefully applied to selected BC populations to maximize its diagnostic benefit and while minimizing the risks of FPs. Incorporating FDG PET/CT for staging when appropriate improves patient outcomes by offering the most tailored treatment options, avoiding unnecessary procedures, and ensuring precise therapeutic planning in the evolving field of breast cancer management.

CONCLUSION

Fluorodeoxyglucose-positron emission tomography-computed tomography is a valuable tool for staging breast cancer, particularly in detecting distant metastases and tailoring treatment strategies. However, its limitations include the potential for false positives, the risk of overtreatment, and the potential adverse outcomes associated with this. By adopting a multidisciplinary approach and refining staging practices, clinicians can minimize unnecessary interventions, reduce patient anxiety, and optimize outcomes in breast cancer management.

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Author Contributions

Ahmed R Awad – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Erin J Pearson – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Cristina A Moldovan – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Louise M Nott – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Jane K Mills – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

Gavin C Mackie – Conception of the work, Design of the work, Acquisition of data, Analysis of data, Interpretation of data, Drafting the work, Revising the work critically for important intellectual content, Final approval of the version to be published, Agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved

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Authors declare no conflict of interest.

Data Availability
All relevant data are within the paper and its Supporting Information files.