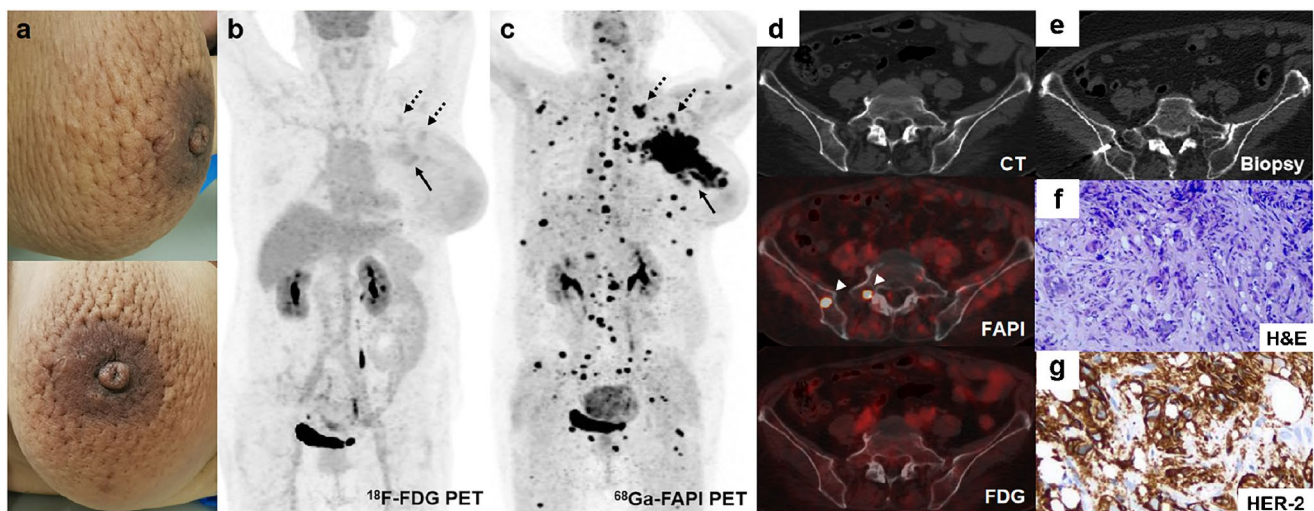




^{68}Ga -FAPI PET/CT detected non-FDG-avid bone metastases in breast cancer

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A 71-year-old woman presented with a 6-month history of a noticeable masses in the left breast. “Orange peel” skin was observed on the left breast (a). Biopsy of the breast masses and axillary lymph nodes (LNs) revealed invasive ductal carcinoma of the breast. Immunohistochemistry was positive for HER2 (3+), but negative for ER and PR. PET/CT was performed for tumor staging, and the patient was enrolled in the prospective trial on the comparison of [^{18}F]FDG and ^{68}Ga -labeled fibroblast-activated protein inhibitor-04 ([^{68}Ga]

Ga-FAPI-04) PET/CT in various cancers. This study was approved by the institutional review board and was registered at clinical-trials.gov (NCT04416165). Written informed consent was obtained from this patient. [^{18}F]FDG PET/CT showed mild radiotracer uptake in the left breast masses (solid arrow, SUV_{max} 4.3) and enlarged axillary LNs (dotted arrows) (b). [^{68}Ga]Ga-FAPI-04 PET/CT was performed 2 days after [^{18}F]FDG PET/CT. Intense [^{68}Ga]Ga-FAPI-04 uptake was observed in the left breast masses (solid arrow, SUV_{max} = 48.9) and axillary LNs (dotted arrows). Surprisingly, [^{68}Ga]Ga-FAPI-04 PET/CT showed numerous foci of intense activity in the skeleton (arrowheads, SUV_{max} = 34.9), suggesting bone metastases (c). However, the bone lesions showed no abnormal uptake on [^{18}F]FDG PET and no morphological changes on CT (d). PET/CT-guided biopsy was performed in the FAPI-avid bone lesions (right ilium) (e). Histopathology revealed metastatic breast cancer with positive HER-2 expression (f–g).

Fibroblast activation protein (FAP) is highly expressed in cancer-associated fibroblasts (CAFs) in over 90% of epithelial carcinomas. FAP is also involved in the processes

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of many non-cancerous conditions, including wound healing, tissue remodeling, fibrosis, and inflammation [1, 2]. FAP-directed PET tracers show excellent imaging characteristics and added diagnostic value in breast cancer [3, 4]. FAP-targeted radionuclide therapy is also used in refractory breast cancer [5]. This case provides evidence that [⁶⁸Ga]Ga-FAPI-04 PET/CT may have higher sensitivity in breast cancer staging than [¹⁸F]FDG, especially in detecting bone metastases.

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Declarations

Ethics approval and consent to participate This study was approved by the Clinical Research Ethics Committee of the First Affiliated Hospital of Xiamen University, and written informed consent for publication of this report was obtained from the patient.

Conflict of interest The authors declare no competing interests.

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