Emerging role of ¹⁸FDG PET/CT in breast cancer

Breast cancer (BC) is the most common cancer in women worldwide and unfortunately Pakistan is one of the countries having the highest rate.¹ BC related mortality is higher in patients having advance disease at the time of diagnosis. Various therapeutic strategies are available which include surgery (from radical to breast conserving options), radiation therapy, hormonal therapy and targeted therapy. Precise staging of the disease and information about the phenotype of tumor (ER: estrogen receptor; progesterone receptor: PR; Human epidermal factor receptor2: HER2) is very important for selection of proper therapeutic options. Epidemiological data have shown that young BC patients have more aggressive tumors with potential for early metastases than older patients.² Similarly patients with triple negative breast cancer (ER, PR and HER2 negative) have the worst while ER+/HER2- have the best prognosis.³ Studies have also shown that patients with triple negative and HER2+ BC have a higher predilection for extra-skeletal metastases.⁴

Although 18-Flourodeoxy Glucose (18FDG) is a non-specific imaging agent but using PET/CT hybrid imaging scanner allows accurate localization of functional abnormalities and also minimizes falsepositive and false-negative interpretations.⁵ In low risk BC patients (tumor up to 3 cm and clinically non-palpable axillary nodes), ¹⁸FDG PET/CT is not included in the paradigm for initial staging in BC cancer patients due to low incidence of distant metastasis.⁴ Furthermore, sensitivity of ¹⁸FDG PET/CT for axillary nodal metastasis in clinically negative axilla is lower than sentinel node biopsy.6 So use of ¹⁸FDG PET/CT in early stage BC is not justified due to its high cost, radiation exposure. potential false positive findings resulting in unjustified further investigations and delay in care as well. Although few recent studies have suggested that ¹⁸FDG PET/CT could also be valuable in stage II BC patients, especially in stage II-B for detecting unexpected distant metastasis.7 Data from Memorial Sloan Kettering Cancer Centre, New York suggested that ¹⁸FDG PET/CT might be valuable in young patients with stage II-B and III disease. Studies have also shown that 18FDG uptake was found higher in triple negative BC and 18FDG PET/CT may be used in staging patients with this phenotype.9 Patients with triple negative and HER2+ BC are found to have higher proportion of extra-skeletal metastases. 10 Similarly patients with histopathological Grade-III tumor are more prone to have extra-axillary nodal metastasis but rate of distant metastasis does not differ between low and high grade tumors.9 Patients with invasive lobular cancer are considered not good candidates for staging with 18FDG PET/CT due to low avidity of primary tumor for 18FDG as compared to invasive ductal cancers.¹¹ Furthermore, patients with invasive lobular cancers are prone to have ¹⁸FDG nonavid sclerotic bony metastasis and predilection for metastasis in peritoneum and hollow viscera.10 However, there is mounting evidence that, in high-risk BC patients (locally advanced and inflammatory BC - Stage III according to AJCC classification) 18FDG PET/CT plays an important role by modifying staging and management in a substantial percentage of patients.4 Many studies have shown that ¹⁸FDG PET/CT outperformed conventional imaging modalities for detecting metastases in extraaxillary nodes, chest, abdomen and bones in a single session.¹² Based on these facts and analysis of current literature, ¹⁸FDG PET/CT should be the first imaging modality used for restaging in BC patients with known or suspected recurrence. ¹⁸FDG PET/CT has a promising role in response evaluation of neoadjuvant chemotherapy. Presently data have shown variable findings due to use of non-standardized imaging protocols, heterogeneity in phenotypes and interpretation criteria. Therefore, it is imperative to adopt standardized imaging protocols upon properly selected BC phenotypes and homogenous interpretation criteria to make ¹⁸FDG PET/CT more valuable tool in assessing response to neoadjuvant chemotherapy.

Conflict of Interest: None

References

- 1. Fatima N, Zaman M, Fatima T. Increased risk of breast cancer in multiparous and lactating women attending a breast care clinic in Pakistan: a paradigm shift? Asian Pac J Cancer Prev 2010; **11**: 1219-23.
- 2. Riedl CC, Slobod E, Jochelson M, Morrow M, Goldman DA, Gonen M, et al. Retrospective analysis of 18F-FDG PET/CT for staging asymptomatic breast cancer patients younger than 40 years. J Nucl Med. 2014; **55:** 1578-83.
- 3. Groheux D, Giacchetti S, Espié M, Rubello D, Moretti J-L, Hindié E. Early monitoring of response to neoadjuvant chemotherapy in breast cancer with (18)F-FDG PET/CT: defining a clinical aim. Eur J Nucl Med Mol Imaging. 2011; **38:** 419-25.
- 4. Ulaner GA, Castillo R, Goldman DA, Wills J, Riedl CC, Pinker-Domenig K, et al. (18)F-FDG-PET/CT for systemic staging of newly diagnosed triple-negative breast cancer. Eur J Nucl Med Mol Imaging. 2016; **43**: 1937-44.
- 5. Groheux D, Espié M, Giacchetti S, Hindié E. Performance of FDG PET/CT in the Clinical Management of Breast Cancer. Radiology 2013; **266(2)**: 388-405.
- 6. Veronesi U, De Cicco C, Galimberti VE, Fernandez JR, Rotmensz N, Viale G, et al. A comparative study on the value of FDG-PET and sentinel node biopsy to identify occult axillary metastases. Ann Oncol. 2007: **18:** 473-8.
- 7. Groheux D, Cochet A, Humbert O, Alberini J-L, Hindié E, Mankoff D. 18F-FDG PET/CT for staging and restaging of breast cancer. J Nucl Med. 2016; **57(1):** 17S-26S.
- 8. Riedl CC, Slobod E, Jochelson M, Morrow M, Goldman DA, Gonen M, et al. Retrospective analysis of 18F-FDG PET/CT for staging asymptomatic breast cancer patients younger than 40 years. J Nucl Med. 2014; **55**: 1578-83.
- 9. Basu S, Chen W, Tchou J, Mavi A, Cermik T, Czerniecki B, et al. Comparison of triple-negative and estrogen receptor-positive/progesterone receptor-positive/HER2-negative breast carcinoma using quantitative fluorine-18 fluorodeoxyglucose/positron emission tomography imaging parameters: a potentially useful method for disease characterization. Cancer. 2008; **112**: 995-1000.
- 10. Ulaner GA, Castillo R, Wills J, Gönen M, Goldman DA. (18)FFDG-PET/CT for systemic staging of patients with newly diagnosed ER-positive and HER2-positive breast cancer. Eur J Nucl Med Mol Imaging. 2017; **44(9):** 1420-27
- 11. Groheux D, Giacchetti S, Moretti J-L, Porcher R, Espié M, Lehmann-Che J, et al. Correlation of high (18)F-FDG uptake to clinical, pathological and biological prognostic factors in breast cancer. Eur J Nucl Med Mol Imaging. 2011; **38:** 426-35.
- 12. Koolen BB, Vrancken Peeters M-JTFD, Aukema TS, Vogel WV, Oldenburg HSA, van der Hage JA, et al. 18F-FDG PET/CT as a staging procedure in primary stage II and III breast cancer: comparison with conventional imaging techniques. Breast Cancer Res Treat. 2012; **131**: 117-26.

Maseeh uz Zaman,¹ Nosheen Fatima,¹ Areeba Zaman,² Sidra Zaman,² Unaiza Zaman²

- ¹ Department of Radiology, Aga Khan University Hospital (AKUH), Karachi, Pakistan
- ² Dow Medical College / Dow University of Health Sciences (DUHS), Karachi, Pakistan.