# Developing a personalized treatment model based on molecular biomarkers and imaging in breast cancer: Has the time come?

Risk stratification in breast cancer can be done with either bio markers which are quite helpful in predicting the risks associated with development of loco regional recurrence and distant metastasis or 18F-fluorodeoxyglucose (18F-FDG) which is a marker of glucose metabolism and evaluates the glucose utilization by the tumour which is a way to demonstrate tumor aggressiveness. Standardized uptake value (SUV) is a semi quantitative parameter which can be measured in all disease sites with whole body positron emission tomography-computed tomography (PET-CT) imaging using this radiopharmaceutical. There are many studies in the literature which have related SUV to prognostication and co-relating it with progression-free survival and overall survival (OS). However, prediction of response to treatment, whether local or systemic has not been well or widely studied. In order to have more accurate quantification other parameters like total lesion glycolysis (TLG) and/or metabolic tumor (MTV) burden seems to be better. TLG signifies total metabolic burden of the tumor which requires parameters like SUV max SUV mean and MTV. This will represent both tumor volume and the glucose utilization rate. Few studies in other malignancies have shown encouraging results. Multi variate analysis have shown MTV and TLG are independent prognostic factors for DFS and OS whereas high MTV and TLG were significantly associated with reduced DFS and OS. It has also been shown that only high SUV max is not a prognostic factor for recurrence or survival. These volumetric parameters also have a predictive value for outcome in patients undergoing external beam radiation therapy. Co-relation between molecular markers of breast cancer and the outcome has also been recognized.[1] The receptor status also plays an important role in predicting outcome as well as have a significant role in personalizing treatment protocols. *In vivo* receptor imaging has also made an inroad from the bench to the bed side. Hormone positivity has an impact on both treatment planning and prognosis and therefore imaging the estrogen receptor (ER) plays an important role. In this context 16-α-(18F)-fluoro-17-β-estradiol PET 18F-FES PET-CT is supposed to play a crucial role in resolving diagnostic dilemma and also planning further management.[2] Measurement of ER expression is by biopsy at the time of primary diagnosis. Estrogen is involved in the growth of both normal and cancerous breast tissues. Its activity is mediated by ER receptor and its positivity in breast cancer cells has a profound impact on treatment and patient outcome. With the background knowledge of tumor heterogeneity, a uniform expression of receptor is an exception rather than a rule. At the same time the expression in primary tumor and the metastatic sites may be different which may further prompt the need for imaging. 16-α-17β estradiol is a synthetic estrogen and showed good affinity for ER receptor in *in vivo* studies. FES PET-CT scan in combination with FDG PET-CT scan can be used as a problem solving modality in deciding the regimen. Our initial results point to this and highlights the spectrum of metastatic sites which can be resolved by this radiopharmaceutical. A common rule of thumb could be well differentiated hormone positive tumor with FDG uptake less than FES uptake is unlikely to benefit from cytotoxic chemotherapy and would be an ideal candidate to be treated with hormone or vice versa where a poorly differentiated tumor with higher FDG uptake in comparison to FES will need cytotoxic chemotherapeutic regimen. In the coming years and in future we hope that the treatment of breast cancer has a very high potential to be personalized based on PET scan (both FDG and FES) and other molecular bio markers giving early and clear indications to the treating oncologist as to where the disease is heading and how the treatment regimen needs to be modified.

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