Preoperative PET/CT in early-stage breast cancer: is the TNM classification enough?

We have read with interest the paper by Bernsdorf et al. [1], examining the role of PET/CT in the preoperative evaluation of patients with early breast cancer.

The authors subjected 103 patients with newly diagnosed operable breast cancer ≥2 cm to [^{18}F]2-fluoro-2-deoxy-D-glucose-positron emission tomography/computed tomography (FDG-PET/CT) and to conventional assessment. PET/CT detected distant metastases in 6 patients, extra-axillary lymph node involvement in 12 patients and new primary cancer in 2; PET/CT was the only procedure able to detect extra-axillary malignancy in 15 patients, leading to an upgrade of initial staging in 14 and to a change in subsequent treatments in 8.

These data confirm the utility of PET/CT even in the case of a supposed early-stage breast cancer, providing the base for a proper definition of the stage and of the subsequent therapeutic strategy, including the real aim (curative versus palliative). Nevertheless, in this study patients were selected only according to the size of the tumor and the authors evaluated the results in terms of change in the TNM stage [TNM (tumour–node–metastasis)] before and after the execution of PET/CT scan [2].

However, each TNM subgroup does not consider the biology of tumors cells and includes tumors with very different behaviors. Breast cancer is indeed a heterogeneous disease in terms of histology, dissemination modality, therapeutic response and prognosis. The tumors can be classified into subtypes distinguished by pervasive difference in their gene expression patterns [3]. These differences can be defined by genetic array testing or by a common histopathological determination of the expression of estrogen receptors, progesterone receptors, c-erbB2 and Ki67, that are actually considered sufficient to guide the systemic therapeutic plan [4].

The decision to carry out an FDG-PET/CT scan in the initial evaluation of patients with early breast cancer should probably take into account these biological differences as it is quite well established that some more aggressive subtypes of breast cancer have a greater probability to develop systemic disseminations even in the case of a relative small tumor. This could make the imaging procedure more useful, further improving its impact on the management of patients. Obviously, this is an impression that should be validated through a targeted prospective study with a large number of patients.

Finally, some novel PET tracers that have been already tested in human, such as ^{18}F-fluoroestradiol (that binds to ER), ^{18}F-FFNP (a progesterone analog) and ^{68}Ga-ABY-002 (a molecular imaging agent with high specificity and affinity for HER2), may provide additional useful information about tumors' heterogeneity and about their responsiveness to therapy, in particular in the case of stage IV disease at the diagnosis.

In vivo molecular imaging with PET can indeed be regarded as a true classifier of the different tumor cell lines, as it can provide a global assessment of a given tumor and of all its sites in the patient body through the characterization of the subpopulations of the cell [5].

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disclosure

The authors have declared no conflicts of interest.

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doi: 10.1093/annonc/mdt004

Reply to 'preoperative PET/CT in early-stage breast cancer: is the TNM classification enough?'

The letter by Gilardi et al. [1] raises the overall important question in staging early-stage breast cancer with positron emission tomography/computed tomography (PET/CT): who should be evaluated initially with PET/CT?

We, as well as others [2, 3], demonstrated a more precise staging of early-stage breast cancer patients with PET/CT compared with the conventional methods, ultimately leading to a change in planned therapy in 8% of patients [4]. However, the influence of PET/CT on changes in therapy was limited to a small percentage of patients reducing its feasibility with respect to cost utility. So far, studies have focused on TNM staging for identifying patients that are at a higher risk for advanced disease and thus, would benefit from a PET/CT scan. A recent study suggests recommending PET/CT in patients with breast cancer stage IIb and higher as distant metastasis was reported in 11%–47% in those groups [3].

A different approach is suggested by Gilardi et al. namely that the different molecular subtypes of breast cancer [5] should be taken into account when assessing whether a breast cancer patient should be offered a PET/CT scan in the initial evaluation. These molecular subtypes can roughly be identified