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 [18F]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 [18F]fluoroestradiol (that binds to ER), [18F]FFNP (a progesterone analog) and 68Ga-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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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 Ib 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...
by the hormone receptors: estrogen and progesterone and HER2 and Ki67 status. However, even though only 8% of patients had their treatment altered in our study, baseline tumor characteristics with regards to estrogen receptor, progesterone receptor and HER2 status, from patients with no change in stage or treatment after PET/CT did not differ substantially from patients with change in treatment/stage. Furthermore, in our study we failed to identify a subgroup of patients based on the baseline characteristics that could identify a group that was more likely to benefit from a PET/CT scan (data not shown). Ki67 was not evaluated as part of our study. Based on our results, it is somewhat difficult to see why the suggestion by Gilardi et al. would identify a subgroup of patients that would benefit from a PET/CT scan. On the contrary, the fact that no such subgroup has been identified and, as mentioned, the number of patients with change in treatment in our study was small should encourage further investigations into this issue.

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Clinical complete response in locally advanced rectal cancer: can we offer a wait-and-see policy?

After neoadjuvant treatment in locally advanced rectal cancer, and based on the current evidence, patients undergo surgery, which includes total mesorectal excision [1], sometimes with a definitive ostomy, regardless of achieving a clinical complete response (cCR), due to the lack of correlation between clinical and pathological responses [2]. A recent publication has raised a debate whether in some cases patients who get a cCR could go into a wait-and-see policy in order to avoid a mutilating surgery [3], although it is true that the criteria of cCR, with or without the excision of the residual scar, has not been validated yet.

The recent publication in this journal of the ESMO Consensus Guidelines for Management of Patients with Colon and Rectal Cancer [4] offers, beyond the standard approach, the possibility of a conservative management in selected patients in this scenario (e.g. young patients who need a definitive ostomy), including the recommendation of the use of a nomogram to establish the risk of locoregional relapse [5]. Until now, current nomograms for predicting the risk of local recurrence after achieving a cCR include pathological response of the primary tumor and node involvement, data that could not be known without going for a surgery. This is why we do not have information a priori of the risk of relapse in our patients. However, in our opinion, the wait-and-see approach in selected patients with rectal cancer who have achieved a cCR after neoadjuvant treatment might be offered taking into account present data and after a discussion on risk benefits with the patient.

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