Breast Cancer Staging: To Which Women Should ^{18}F-FDG PET/CT Be Offered?

TO THE EDITOR: We read with interest the article by Riedl and colleagues (*1*), who retrospectively investigated the yield from ^{18}F-FDG PET/CT staging in 134 breast cancer patients younger than 40 y. PET/CT allowed detection of unsuspected extraaxillary lymph nodes in 11% of patients and distant metastases in 15% (*1*). This important report adds to other recent studies emphasizing the role of PET/CT staging in patients with clinical stage II or III breast cancer (*2–6*). The study by Riedl et al. focused on patients younger than 40 y, a population at higher risk for cancer mortality (*7*). However, their results should not be taken as an indication that PET/CT should be restricted to this age group. Indeed, the study did not compare the yield of PET/CT in young women to that in patients older than 40 y, who represent most breast cancer patients. Interestingly, retrospective findings from Riedl and colleagues in women younger than 40 y agree with our findings in a prospective evaluation of 254 patients unselected for age (*4*). The yield according to initial clinical stage in the study by Riedl et al. was quite similar to ours, with the detection of distant metastases in 50% of stage IIIC patients (vs. 47% in our study), in 50% of stage IIIB (vs. 36.5%), in 31% of stage IIIA (vs. 17.5%), in 17% of stage IIB (vs. 10.7%), and in 5% of stage IIA (vs. 2.3%). As also observed by Segaert et al. (*2*), these results show that ^{18}F-FDG PET/CT has a substantial yield in breast cancer patients with clinical stage IIB or higher.

It is well known that younger patients with breast cancer have a poorer prognosis (*7*). On ^{18}F-FDG PET/CT imaging, the SUVs of the primary breast cancer are higher in premenopausal women (*8*). One explanation for the poorer outcome in young women is the higher incidence of biologically unfavorable factors such as high-grade and estrogen receptor–negative tumors (*7*). However, Riedl and colleagues found that the rates of distant involvement did not differ according to tumor grade or phenotype. This is in agreement with our findings in 254 patients unselected for age (*4*). We observed that triple-negative breast cancers were more ^{18}F-FDG–avid, with a higher proportion of extraskeletal metastases compared with bone metastases. We also found that triple-negative breast cancer patients had poorer survival. However, the overall rate of distant metastases on baseline ^{18}F-FDG PET/CT was similar to that in other phenotypes (HER2+ and ER+/HER2−) (*4*).

In conclusion, there is mounting evidence of a high yield offered by ^{18}F-FDG PET/CT staging in patients with clinical stage III or IIB breast cancer.

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David Groheux*
Elif Hindié
**Saint-Louis Hospital*
1 Avenue Claude Vellefaux
Paris 75475, France
E-mail: dgroheux@yahoo.fr.

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REPLY: We thank Drs. Groheux and Hindié for their comments on our article (*1*). Their position and ours are quite similar. We both support the growing evidence for using ^{18}F-FDG PET/CT for systemic staging of patients with newly diagnosed stage III or IIB breast cancer (*1,2*), because the detection of unsuspected distant metastases in these patients would alter treatment from neoadjuvant or surgical to palliative systemic. Although our study specifically examined the yield of ^{18}F-FDG PET/CT for patients less than 40 y old, the study that Drs. Groheux and Hindié cite was unselected for age. It is of course difficult to compare studies that vary in design and are from regions that may potentially encompass different patient populations, but we note that the yield of ^{18}F-FDG PET/CT for detecting distant metastases for each initial stage was higher in the cohort of patients less than 40 y old than in the cohort unselected for age. For example, the rate of upstaging to distant metastatic disease (stage IV) in initially stage IIB patients was 17% for patients less than 40 y old (*1*) and 10.7% for patients unselected for age (*2*). Thus, although ^{18}F-FDG PET/CT may be considered for any patient with newly diagnosed stage IIB or III breast cancer, the value of the examination may be higher for younger patients.

We caution that further evaluation is still warranted. There are still several patient and tumor factors that have not been adequately addressed. For example, tumor histology may influence the utility of ^{18}F-FDG PET/CT for systemic staging

of patients with breast cancer. Indeed, on ^{18}F-FDG PET both primary (*3*) and metastatic (*4*) lesions from invasive lobular carcinoma are less apparent than comparable lesions from invasive ductal carcinoma. Thus, the utility of ^{18}F-FDG PET/CT for systemic staging of patients with newly diagnosed invasive lobular carcinoma may not be as strong as for patients with invasive ductal carcinoma. The histologic subtype of breast cancer may also affect the evaluation of prognosis in initial (*5*) and metastatic (*6,7*) breast cancer, as well as the evaluation of treatment response (*8*).

Although there is growing evidence in support of offering ^{18}F-FDG PET/CT to all patients with newly diagnosed stage IIB or III breast cancer, we must continue to investigate this issue.

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Gary A. Ulaner*
Christopher C. Riedl
**Memorial Sloan Kettering Cancer Center*
1275 York Ave., Box 77
New York, NY 10065
E-mail: ulanerg@mskcc.org

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