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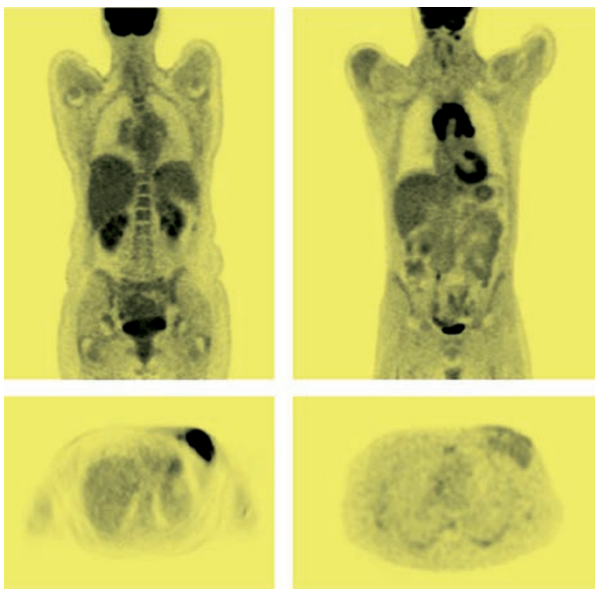
IMAGING

Follow your PET for guidance

Changes in ^{18}F-fluorodeoxyglucose (FDG) uptake measured using PET have shown considerable promise in evaluating the early response of different types of cancer to therapies. Now, a study involving patients with Hodgkin lymphoma, led by Peter Johnson from the University of Southampton, UK, and another study involving patients with oestrogen receptor-positive (ER+) breast cancer, led by Brenda Kurland from the University of Pittsburgh, USA, have shown that PET scans performed early in the course of treatment can guide the selection of different therapeutic approaches.

> "We now expect to see more use of early PET scanning to guide therapy"

Johnson and collaborators aimed "to determine whether we can use early PET scanning to modulate treatment for patients with advanced-stage Hodgkin lymphoma: reducing treatment for those responding well to conventional ABVD (doxorubicin, bleomycin, vinblastine and dacarbazine) chemotherapy, and escalating it for those with an unfavourable initial response. The underlying reason to follow this strategy is to reduce the risk of long-term adverse effects by using treatments tailored to patients' needs."



Images courtesy of Sally Barrington (top) and David A. Mankoff (bottom). Top: Coronal PET images with negative (left) or positive (right) findings in patients with Hodgkin lymphoma. Bottom: axial PET emission images of the breast showing ^{18}F-FDG (high uptake; left) and ^{18}F-FES uptake (right).

In this study, 1,135 patients underwent PET–CT imaging after receiving two cycles of ABVD. Negative imaging results indicated a good response, and those patients (n = 937) were randomly assigned to either continue ABVD therapy or initiate de-escalation therapy omitting bleomycin (AVD). Conversely, patients with positive PET–CT scan results were assigned to receive BEACOPP (bleomycin, etoposide, doxorubicin, cyclophosphamide, vincristine, procarbazine and prednisone). The overall survival rates at 3 years were 97.2%, 97.6% and 95.8% in the ABVD, AVD and BEACOPP groups, respectively, indicating that stopping the administration of bleomycin after detecting a good initial response is safe and effective. As Johnson explains, "by reducing the total amount of treatment being given we hope to see fewer long-term adverse effects. We now expect to see more use of early PET scanning to guide therapy." In the opinion of Dimitris Visvikis, from the INSERM unit at the University of Brest, France, assessing the value of an earlier evaluation (after one cycle) might be useful. He adds, "the power of ^{18}F-FDG-PET–CT scan might not simply lie within the evaluation of differences during treatment, but also directly by exploiting newly proposed biomarkers on baseline scans, such as heterogeneity of uptake."

The study conducted by Kurland and collaborators involved patients with ER+ metastatic breast cancer who, for many years, can have indolent disease that needs to be managed by a series of therapies, for which there is no evidence-based standard for selection and sequencing. ^{18}F-fluoroestradiol (FES)–PET was previously validated as a measure of ER activity; low ^{18}F-FES uptake is predictive of a poor response to endocrine therapy. Kurland explains, "Failing to establish an association between ^{18}F-FES-PET and survival, we explored the combined value of ^{18}F-FDG-PET and ^{18}F-FES-PET for predicting outcomes for patients receiving endocrine therapy."

Patients enrolled in this study underwent PET scans to evaluate both ^{18}F-FES and ^{18}F-FDG uptake before initiating endocrine therapy. Of 84 patients, 24 had low ^{18}F-FDG uptake, indicating indolent disease. Of the remaining 60 patients (with more-metabolically active disease), 50 had high and 10 had low ^{18}F-FES uptake. The median PFS for these groups of patients was 26 months, 8 months and 3 months, respectively.

Kurland and collaborators expect that evaluating "^{18}F-FES-PET in concert with ^{18}F-FDG-PET might help to identify a minority of patients who would be unlikely to have clinical benefit from endocrine therapy, despite a diagnosis of ER+ cancer". Visvikis comments that, "again, one future direction might be the exploitation of newly proposed biomarkers on the baseline scan because such biomarkers can be combined not only with other tracers, but also with features extracted from anatomical modalities, such as radiomics."

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ORIGINAL ARTICLES Johnson, P. *et al.* Adapted treatment guided by interim PET-CT scan in advanced Hodgkin's lymphoma. *N. Engl. J. Med.* http://dx.doi.org/10.1056/NEJMoa1510093 (2016) | Kurland, B. F. *et al.* Estrogen receptor binding (FES PET) and glycolytic activity (FDG PET) predict progression-free survival on endocrine therapy in patients with ER+ breast cancer. *Clin. Cancer Res.* http://dx.doi.org/10.1158/1078-0432.CCR-16-0362 (2016)