

Getting the Most out of ^{18}F -FDG PET Scans: The Predictive Value of ^{18}F -FDG PET-Derived Blood Flow Estimates for Breast Cancer

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Prior studies have shown that breast cancer patients experienced higher mortality and recurrence risks when their tumors failed to show a decline in blood flow (BF) after neoadjuvant therapy, as measured directly from ^{15}O -water PET scans (1) or indirectly from dynamic ^{18}F -FDG PET scans using changes in ^{18}F -FDG transport (K_1), which can be estimated via kinetic image analyses (1,2). The gold standard BF PET tracer, ^{15}O -water (3), is only available at PET imaging centers that have a cyclotron on-site because of the short 2-min half-life of ^{15}O . ^{18}F -FDG is a more widely available radiotracer, with a half-life that allows regional supply to clinical centers. However, the 60-min dynamic ^{18}F -FDG PET imaging protocol used by Dunnwald et al. that enabled estimates of ^{18}F -FDG transport (K_1) and metabolic flux (K_i) to predict disease-free survival and overall survival (2) is impractical in a busy clinical setting (4).

image analysis software and personnel capable of performing kinetic analyses have limited dynamic ^{18}F -FDG PET protocols to larger PET imaging centers.

An alternative method for estimating BF from ^{18}F -FDG PET uses the first-pass extraction model of Mullani et al. (5), which assumes highly extracted tracers can be used to estimate BF with a 1-compartment model during the first pass of the tracer through the tissue that in practice requires only a 2-min dynamic PET scan starting simultaneously with injection of ^{18}F -FDG (6–8). The average first-pass ^{18}F -FDG BF (first-pass BF) estimates using this method were found to correlate with ^{15}O -water ($R^2 = 0.74$), with first-pass BF estimates being on average 14% below BF estimates from ^{15}O -water PET scans (6). In this issue of *The Journal of Nuclear Medicine*, Humbert et al. report that low overall survival is associated with triple-negative breast cancer patients whose tumors experienced a less than 30% drop in tumor first-pass BF after neoadjuvant therapy (8). Humbert et al. also found their first-pass BF estimates capable of stratifying between patients with 87% versus 48% overall survival ($P < 0.001$) in women without a pathologic complete response (8). The results of Humbert et al. support using first-pass ^{18}F -FDG PET scans as an alternative to ^{15}O -water PET scans for estimating BF to tumors.

In Humbert et al., results are reported from analyses of a 2-part imaging protocol in which patients were positioned prone followed by a 1-bed-position ^{18}F -FDG 2-min dynamic PET scan, which was followed by an additional PET scan starting 90 min after injection that was completed over prone patients in a region that included the first scan's imaging area (8). The Humbert et al. 2-part image acquisition and analysis protocol (8) is similar to a 2-part protocol previously published by 8 coauthors of Humbert et al. in Cochet et al. (7), and it is possible that results from up to 10 patients analyzed by Cochet et al. were included in the Humbert et al. analysis of 46 women with triple-negative breast cancer. The Cochet et al. scan protocol was performed only on women before any treatment (7) whereas the Humbert et al. protocol was completed in patients undergoing neoadjuvant therapy before and after the first course of chemotherapy (8). Analyses of the Humbert et al. 2-part set of PET images (2-min dynamic and 90-min static) yielded estimates of BF (first-pass BF from ^{18}F -FDG scans) and tumor metabolism (SUV) in a manner analogous to the kinetic analysis of a single 60-min dynamic ^{18}F -FDG scan yielding estimates of tracer transport (^{18}F -FDG transport) and tumor metabolism (flux, metabolic rate of ^{18}F -FDG, or SUV). A disadvantage of the 2-part ^{18}F -FDG PET scan image analysis method is the inability to distinguish between free and phosphorylated (i.e., trapped) ^{18}F -FDG tracer at later time

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New imaging protocols more compatible with typical ^{18}F -FDG PET clinical workflows (4) might enable routine BF or ^{18}F -FDG transport measures. In current clinical practice, patients are injected with ^{18}F -FDG in an uptake room before being brought to the PET/CT room, where the PET scan starts approximately 60 min after injection. This workflow allows a busy clinic to average 2 or more ^{18}F -FDG PET scans per hour because one patient can undergo image acquisition while other patients are injected with ^{18}F -FDG in an uptake room. A dynamic ^{18}F -FDG PET scan of 60 min is considered disruptive to the clinical workflow because a patient remains on the scanner much longer than the duration of a standard ^{18}F -FDG PET whole-body scan. The longer required use of the PET/CT room, patients' ability to lie still in the PET scanner for a longer period, specialized equipment, need for technicians trained to conduct more complex image acquisitions, and limited access to

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points, which could lead to overestimation of first-pass BF (6) and limitations in the ability to measure change in metabolism with therapy (9). An advantage of a 60-min dynamic ^{18}F -FDG PET scan over the Humbert et al. 2-part ^{18}F -FDG scan protocol is the ability to measure SUVs without PET tracer injection-to-acquisition time variation, which can occur in a busy clinic, because an increase in uptake time variation has been reported to decrease the sensitivity for detecting response in clinical trials using ^{18}F -FDG PET endpoints (10). On the other hand, the 2-part ^{18}F -FDG scan protocol proposed by Humbert et al. could have an advantage over a single 60-min dynamic ^{18}F -FDG scan because it may be more compatible with a clinical workflow if the 0- to 2-min dynamic PET/CT and the second 90-min static PET/CT scan for one patient can be interleaved with other patient scans to accommodate a busy clinical setting. However, the Humbert et al. 2-part ^{18}F -FDG PET/CT scan protocol would have the disadvantage of requiring patients to receive a slightly higher radiation dose due to the requirement for a second, limited field-of-view CT attenuation scan.

The intriguing results of the study of Humbert et al. (8) support ^{18}F -FDG first-pass BF estimates as a viable alternative to BF estimates from ^{15}O -water PET scans, with the major advantage that first-pass BF imaging protocols could be conducted at PET imaging centers without an on-site cyclotron. Although the Humbert et al. first-pass 2-min ^{18}F -FDG dynamic PET scan protocol could be implemented in many clinics, it is unclear whether clinics would also accept the logistic complication of adding a second scanning time to the current standard of a single delayed uptake scan. However, innovative PET quantitative methods such as first-pass BF estimation (5) and integrated imaging protocols such as the one proposed by Humbert et al. that allow measurement of orthogonal phenomena (e.g., BF and metabolism) are important steps forward in translating validated research methods into practical imaging protocols for a busy clinical PET practice.

DISCLOSURE

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