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REPLY: We would like to thank Dr. Salavati and his coauthors for the interesting comment on our study (*1*). As they mentioned, dynamic PET and PET/CT are more time-consuming and at the moment are therefore confined to research projects for scientific purposes. Furthermore, dynamic PET/CT requires dedicated evaluation software. However, the introduction of new-generation PET/CT scanners has reduced the total acquisition time because of, for example, new detector materials such as lutetium oxyorthosilicate, which improves the counting rate performance, as well as 3-dimensional acquisition protocols. Moreover, new-generation PET/CT scanners also allow dynamic (list-mode) multibed acquisitions. In the future, this technologic improvement will allow for dynamic partial-body PET/CT studies without the need for additional bed positions in static mode, with a shorter acquisition than in our study (*2*). We agree that an additional limitation hampering the use of dynamic protocols in a clinical environment is the lack of operator-friendly and robust evaluation software—an omission that will hopefully be addressed by manufacturers. The existing software for calculation of transport rates is based on a 2-tissue-compartment model for oncologic studies. This software is not robust enough because it is based on an iterative fitting, like the Levenberg–Marquardt algorithm. We presented a solution that is based on the use of an oncologic reference database and a support vector machine algorithm (*3*). Routine use of dynamic PET/CT requires that the calculated rates be reproducible—a problem that should be solved in the future.

Ludwig Strauss proposed at the end of the 1980s the use of the standardized uptake value (SUV) as a robust value that can easily be calculated for the evaluation of PET data (*4*). SUVs are widely used and lead to good results, provided that the values are acquired under standardized conditions, such as at a defined time point after tracer injection, with glucose levels within the normal range, and with the same reconstruction algorithms. John W. Keyes, Jr., wrote an interesting paper in *The Journal of Nuclear Medicine* in 1995 titled "SUV: Standard Uptake or Silly Useless Value?" In this paper he doubted the usefulness of SUV and discussed the limitations of this semiquantitative approach in detail (*5*). Nineteen years later, everybody uses the SUV or its derivatives (such as SUVmax, SUVlean, or even total lesion glycolysis) as a first quantitative approach. It remains to be seen how silly or useless dynamic multibed PET/CT (including parametric imaging) in oncology will be in the future.

Dynamic imaging allows the registration of tracer kinetics over time instead of at only one time point after the tracer injection as static images do. Pharmacokinetic studies are helpful not only for the evaluation of new tracers but also for the evaluation of small therapeutic effects, such as the use of ^{18}F-FDG early after the onset of chemotherapy. Furthermore, the use of kinetic parameters may help to differentiate between benign and less aggressive tumors (e.g., lipomas from low-grade liposarcomas) (*6*). In a recent paper, we demonstrated a correlation between k_1 and angiogenesis-related genes (*7*). Based on dynamic datasets, parametric imaging can be applied using different algorithms. Parametric images allow the visualization of dedicated parameters of radiopharmaceutical kinetics, such as perfusion, transport, or phosphorylation in the case of ^{18}F-FDG. Karakatsanis et al. recently presented some aspects of the use of whole-body PET parametric imaging and, for example, Patlak analysis in addition to SUVs for tumor diagnosis and therapy response monitoring (*8*).

We agree that several approaches available today may be used for the evaluation of oncologic ^{18}F-FDG imaging, including metabolic tumor volume and total lesion glycolysis. We decided to use an analysis based primarily on the pharmacokinetic data, and this proved to be successful. We hope our colleagues will succeed as well in future using any other approach they may wish to choose.

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Understanding SUV Variability in Reference Tissue for ^{18}F-FDG PET with a Simple Measurement Model

TO THE EDITOR: In their interesting research, Boktor et al. (*1*) report variabilities of widely used reference tissue standardized uptake values (SUVs). But underlying causes of these should also be important. A simple 2-random-processes model proposed below supplements the scope of these authors' research. An excellent feature of the latter is having both same-patient paired data and serial data.

A series of paired (j = 1 and 2) reference tissue SUV measurements in patients i is modeled in Figure 1. Measured results can be algebraically represented as $Q(i,j) = Q_{avg} + s(i,j) + p(i)$. Here, random zero mean s(i,j) represents lumped scan-associated random processes encountered in obtaining the SUV. p(i) represents zero mean lumped patient-to-patient randomness—but having the same value for each within a pair of scans. In this model, the coefficient of variation (COV) for a group of measurements, such as Q(i,1) or Q(i,2), is $COV_{group} = [SD_s^2 + SD_p^2]^{1/2}/Q_{avg}$. For Q(i,2) − Q(i,1) paired measurements, $COV_{dif} = [SD_s^2 + SD_s^2]^{1/2}/Q_{avg} = \sqrt{2} \times SD_s/Q_{avg}$ since p(i) is the same in pair i.

This model may be applied to a reference blood-pool activity Q having several measurement noise sources. But a dominating one explored here is the variability caused by a substantial imaging time SD of 21.3 min (*1*) in a busy clinic. Just the scan-encountered variability of Q that this causes may be computed as $SD_s/Q_{avg} = |dQ/dt| \times (21.3 \text{ min}) \div Q_{avg} = |(dQ/dt/Q)| \times (21.3 \text{ min}) = 0.0125 \times 21.3 = 0.266$. Here, the ^{18}F-FDG instantaneous clearance parameter (a fractional time–activity curve slope), 0.0125 min^{-1}, is an available reported average (*2*) for a single exponential representation of Q centered on a time of 45 min after injection. Thus, a - prediction for a pair of blood-pool scans is $COV_{dif} = \sqrt{2} \times 0.266 = 0.38$. This may be compared with the direct measurement of Boktor et al. (*1*), though at an average time of 69.75 min, COV_{dif} = (SD of 0.42)/(Q_{avg} of 1.565) = 0.27.

An expected SD_p/Q_{avg} of 0.254 can be computed directly from analytic expressions for ^{18}F-FDG blood-pool time–activity curves of 26 patients (*2*) evaluated at 69.75 min. This variability is a direct consequence of the fact that the ^{18}F-FDG clearance differs somewhat among patients. Using this and the above SD_s/Q_{avg} leads to the expectation: $COV_{group} = [0.266^2 + 0.254^2]^{1/2} = 0.37$. For comparison, Boktor et al. (*1*) directly measure COV_{group} = (SD of 0.375)/(Q_{avg} of 1.565) = 0.24.

Curiously, $SD_s/Q_{avg} = 0.266$ and $SD_p/Q_{avg} = 0.254$ are fortuitously almost equal in this example despite unrelated origins. The former depends on customs specific to an institution regarding allowable departures from a nominally desired scan time. The latter on the other hand depends on the average scan time experienced. These two protocol features are used in a model here also having ^{18}F-FDG dynamic behavior parameters from another investigation (*2*). With customs at other institutions not the same as here, SD_s/Q_{avg} and SD_p/Q_{avg} would have different values from here.

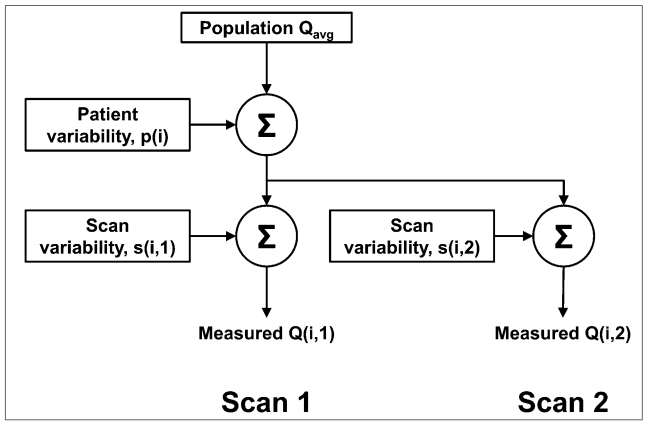

FIGURE 1. Simplified measurement model for serial and paired scans. Scan 1 (or 2) pathway, alone as a sequence of separate patient scans, shows influences of both interpatient and intrapatient (i.e., scan) variability. But if same-patient, that is, paired, scans are also done, then its Q(i,2) − Q(i,1) is influenced only by scan variability.

Model results above would in fact be even slightly higher if other lesser scan measurement noise effects were included. But more importantly, the used ^{18}F-FDG instantaneous clearance parameter at just 45 rather than 69.75 min after injection is known (*2*) to be significantly too large. Thus, the model overestimates COV as 0.37 versus the directly measured 0.24. A better understanding of variability influences must come from further research. The latter, investigating impacts of imaging time and other effects including scan measurement noise, would logically use appropriate scan durations, and on the same patient group, for all types of data required. Meanwhile, a normal liver reference tissue, also studied by Boktor et al. (*1*), has an advantage of a time–activity curve known to change very little over the time range in which ^{18}F-FDG imaging typically occurs.

In summary, a simple measurement model is illustrated. When applied to a blood-pool example, important contributions to its SUV variability are imaging time variations regarded as scan effect and variations of the ^{18}F-FDG clearance as an interpatient effect. Although these can have comparable influences, the more important at a particular institution can be determined from model evaluation using its average scan time and associated SD experienced. It is believed that model analyses, more extensive than here, explaining variability can be beneficial and possibly improve quantitative PET investigations. One motivation stems from a model's ability to identify the dominant features in a protocol that affect a quantifier's variability. Another could be identifying unimportant protocol features when it could be more economical or clinically convenient to be less stringent, yet with little effect on precision of results.

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