In a previous publication (*2*), we demonstrated a distinctly improved linear correlation between tumor-to-blood SUV ratio (SUR) and K_m, the metabolic rate of ^{18}F-FDG, in comparison to SUV versus K_m correlation. In a later publication (*3*), we provided strong evidence that SUR possesses a distinctly improved prognostic value in comparison to SUV.

Our results, together with other data (*4,5*), support the notion that SUV normalization (either to body weight or lean body mass) does not reduce interscan blood SUV variability below 20%–30% (single SD). This implies an equally large test–retest variability of SUV parameters (SUV_{peak}, SUV_{mean}, SUV_{max}) since tracer uptake is proportional to the scaling of the arterial input function. This variability can be eliminated by replacing SUV by SUR, that is, by normalizing tumor SUV to arterial blood SUV.

Weber et al. (*1*) did not detect a notable influence of uptake time differences on the SUV variability coefficients although irreversible binding of ^{18}F-FDG will cause continuously increasing SUVs over time in the presence of nonnegligible residual blood SUVs. We have quantitatively investigated this effect and were able to demonstrate that a variation in uptake time from T_0 to T might be corrected approximately (*6*) according to $SUV_0/SUV_T \approx (T_0/T)^{1-b}$, where $b \approx 0.31$ is determined by the given (essentially invariant) shape of the arterial input function. Since Table 1 of the present paper yields some 15%–20% (SD) uptake time variability for the respective scan groups in both trials, one arrives at roughly 12% SUV variability (SD). Together with a conservative low estimate of 22% for the variability of tracer supply (blood SUV), one then can estimate by gaussian error propagation that both (uncorrelated) effects lead to a cumulative variability of about $\Delta SUV/SUV \approx \sqrt{(22^2 + 12^2)} \approx 25\%$. Since the uptake time variability is moderate in the investigation of Weber et al., the predicted tumor SUV variability is thus mostly due to interscan blood SUV variation, which might explain that the uptake time effect alone does not clearly manifest itself in the investigation of Weber et al.

Overall, comparing the 25% estimate given above with the actual SUV variability reported by Weber et al., we conjecture that a large part of the observed variability might be a consequence of blood SUV variability (plus an additional component due to uptake time variability). On top of this approximately 25% effect, other factors are operational such as imperfect scanner calibration and inaccuracies of body weight and dose information (all of which should also be accounted for when moving from SUV to SUR since they cancel out from the ratio computation).

If our conjecture is correct, one would expect that the test–retest stability of tracer uptake quantification would be distinctly improved if instead of SUV the SUR corrected for uptake time were used. SUR (which equals the left-hand side of the Patlak equation) can be shown to have a better linear correlation to K_m than SUV theoretically as well as experimentally (*2*), which has rather obvious consequences for the prognostic value of both quantities (*3*). We would therefore find it highly desirable to test the hypothesis of superior performance of SUR in the valuable data of Weber et al. This could be done retrospectively by performing an image-based determination of the blood SUV in a suitable 3-dimensional region of interest placed in the aorta.

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Published online Jun. 25, 2015.
DOI: 10.2967/jnumed.115.161570

REPLY: My coauthors and I thank Drs. van den Hoff and Hofheinz for their comment. Our paper (*1*) focused on commonly used parameters for quantifying tumor ^{18}F-FDG uptake (SUV_{peak} and SUV_{max}). However, we fully agree that there are several other potential ways to normalize tumor ^{18}F-FDG uptake. Normalizing tumor SUV by arterial blood SUV is supported by tracer kinetic analysis as described by Drs. van den Hoff and Hofheinz in their letter and their previous publications. One caveat, however, is that defining a second region of interest to measure the blood activity concentration introduces an additional source of variability. Also, tumor-to-blood ratios will be more dependent than tumor SUVs on the time after injection, because the activity concentration in the blood steadily decreases with time whereas that in the tumor typically increases.

Therefore, it needs to be determined whether the repeatability of tumor-to-blood ratios is better than the repeatability of SUVs. The image data of our trial are stored at the American College of Radiology Imaging Network, and data access can be requested to evaluate the repeatability of other quantitative parameters of tumor glucose metabolism. We encourage Drs. van den Hoff and Hofheinz to apply their interesting approach to our data and compare the repeatability of SUVs and tumor-to-blood ratios.

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Published online Aug. 6, 2015.
DOI: 10.2967/jnumed.115.162271