REPLY: We would like to thank the authors of the letter for their interest in our contribution (*1*).

Our study was aimed at evaluating the technical feasibility of administering intravenous contrast agents as part of whole-body PET/CT protocols based on PET/CT tomographs with multislice-CT technology. Although the use of intravenous contrast material in PET/CT has been debated for several years now with respect to potential image distortions and biases of the reconstructed PET activity distribution (*2–4*), few studies have addressed the diagnostic need to tailor the administration of intravenous contrast material for improved CT and PET/CT image quality (*5*).

With the availability of multislice-CT technology in PET/CT, modified contrast administration becomes feasible in whole-body oncology imaging. At the Department of Diagnostic Radiology of the University Hospital of Tuebingen we were fortunate enough to have a combined PET/CT tomograph with 16-slice CT components installed about 2 y ago. Since then, we have operated the PET/CT scanner jointly with our colleagues from the Department of Nuclear Medicine. Our objective is to enhance the diagnostic power of PET/CT through contrast enhancement. This was reflected in our study (*1*).

With multislice CT, intravenous contrast administration for whole-body oncology studies typically is performed in 3 phases: a native CT scan of the liver is obtained first, followed by an arterial-phase scan covering the upper thorax and liver and a venous-phase scan covering the abdomen and pelvis. Contrast-enhanced CT scans may be triggered automatically by monitoring arterial enhancement during repeated CT scans of a single axial image plane intersecting the artery. It is standard practice in radiologic CT to combine phase scanning with breath-hold instructions in order to minimize motion artifacts from patient respiration. Although a full-inspiration breath-hold on CT is ideal from a radiologic perspective (fully extended lung tissue, improved contrast in air-filled lung tissue and pulmonary vessels, limited blurring of anatomic structures from motion artifacts), combined PET/CT requires that the anatomy from the CT scan matches the anatomy during the emission scan. This is the case also for standard PET examinations, in which CT is replaced with a lengthy PET transmission scan. We therefore agree with the statement made in the letter that, after attenuation correction, the corrected emission data are no longer independent. This, however, relates both to positional artifacts and noise propagation.

Because a full-inspiration breath-hold is not an option for whole-body PET/CT if the breath-hold CT is used for attenuation correction, we have looked at shallow breathing and normal expiration as 2 alternative approaches to acquiring the CT portion of the PET/CT protocol. The normal-expiration protocol, in particular, has been recommended by other PET/CT users as the protocol yielding minimum PET/CT misregistration averaged over larger whole-body PET/CT patient cohorts (*6,7*).

Using the liver dome as the point of reference on CT and PET, Goerres et al. (*8*) reported an average misregistration of 1 ± 14 mm for the normal-expiration protocol, compared with 3 ± 12 mm for normal respiration during the CT scan portion of combined PET/CT scans. In an earlier publication, Goerres et al. (*9*) reported an average misregistration of 0.4 ± 11.7 mm for the normal-expiration protocol, compared with -12 ± 13 mm for normal respiration during CT. Osman et al. (*10*) reported cold (i.e., undercorrected) artifacts with an average width of 14–16 mm as an indicator of respiration-induced mismatches of CT and emission activity distribution in the area of the diaphragm for normal-breathing protocols. Nakamoto et al. (*11*) reported a craniocaudal misregistration of 10 mm in shallow-breathing patients.

Although we agree in principle with the authors of the letter on the benefits of using the uncorrected emission data as correlate markers for CT, such correlations will be affected by the low and inhomogeneous contrast of the dome of the liver and the lower thorax on uncorrected emission images. This contrast worsens toward the central/dorsal portion of the images. In our experience, the contrast of the thorax and abdomen on uncorrected emission images is not predictable and does not correlate well with the injected activity or patient size, making this parameter an uneasy option for routine assessment of misregistration in PET/CT.

We agree that using the appearance of the diaphragm on attenuation-corrected PET/CT images as a measure of image registration accuracy is debatable. However, CT-based masking effects on the attenuation-corrected emission images of whole-body PET/CT studies become less frequent in normally breathing patients when using PET/CT tomographs with a CT component of 6 detector rings or more, as shown by Beyer et al. (*12*). These authors demonstrated that the average axial extent of respiration artifacts of the upper diaphragm in normally breathing patients is limited to less than 10 mm for PET/CT tomographs incorporating 6- to 16-slice CT technology. The same study also showed that the extent of the artifact, which is synonymous with the misregistration of CT and PET, is about twice as much for CT systems with 4 or fewer detector rings. All these studies (*8–11*) used 4-slice CT technology, and the misregistration is similar to the results of the study by Beyer et al. (*12*). Of course, respiration artifacts and misregistration in individual patients may exceed these average values by far, but these instances can likely be limited by proper patient coaching.

It was not the intent of our study to evaluate the effect of lesion localization on attenuation-corrected CT (*13*). Also, we believe that the clinical significance of missing a lesion on attenuation-corrected PET because of mismatches between the anatomy on CT and the emission data is less serious than expected. Allen-Auerbach et al. (*14*) have shown that the diagnostic accuracy of ^{18}F-FDG PET/CT for small lung lesions can be increased by acquiring a separate (low-dose) CT scan of the thorax in addition to the whole-body PET/CT scan. Although it is fair to assume that the location of potential lesions on full-inspiration CT is different from that on standard whole-body PET/CT (shallow breathing or normal expiration), misdiagnosis of these findings is unlikely because of the availability of the CT and PET/CT images from the same scan without moving the patient in between.

We concluded, from our study, that the alignment quality will be degraded for multiphase protocols as described in our methodology. It is important to realize that accurate coregistration of all regions covered by a whole-body PET/CT protocol is not feasible, just as it is not feasible to obtain perfect coregistration with retrospective image registration. However, PET/CT provides the best intrinsic coregistration possible and thus limits the chance of misdiagnosis through false localizations of lesions. Nevertheless, the coregistration accuracy of PET/CT data may need further improvement for more accurate diagnosis or therapy planning (*15*).

In conclusion, the focus of our study was to assess the flexibility and performance of different PET/CT protocols involving multiphase intravenous contrast enhancement. Our intention was not to evaluate previously published methods for the detection of misalignment. Therefore, we used the simplified approach of assessing potential PET/CT misregistration with respect to the dome of the liver. Nevertheless, we feel confident that for the purpose of our study this singular parameter assesses PET/CT

alignment well, in particular given the results from Beyer et al. (*12*) that indicate a reduced significance of CT masking effects in PET/CT with 16-slice CT.

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