SPECT/CT

TO THE EDITOR: We read with interest the article "SPECT/CT" by Buck et al. (*1*). The authors nicely summarize the benefits of multimodality imaging. Furthermore, the issue of software based image coregistration is mentioned in this continuing education paper. Until recently, the software to fuse images from different modalities has remained a problem and certainly has not been easy to deal with. In our daily routine work, we experienced 2 difficulties. First, the registration tools were not available in the image-processing workstations that we use in our routine work. Second, the algorithms were not fully automatic and required manual adjustments.

Since January 2008, our nuclear medicine department has been clinically evaluating a new software tool (Volumetrix Suite; GE Healthcare) that incorporates a fully automatic rigid registration algorithm into our image-processing workstation and also enables the creation of dual-modality, fused, 3-dimensional, volume rendered images. With this software tool, we can register a low-dose CT scan with a high-dose CT scan, register scans obtained of the same patient but with different radiopharmaceuticals, and monitor a patient's response to treatment and the evolution of the disease. The registration and segmentation is performed using the National Library of Medicine Insight Segmentation and Registration Toolkit, an open-source software system to support the Visible Human Project (*2*). The algorithm implemented for the image registration protocol consists of a preprocessing step (initial reformatting of target and reference images, optimization by applying 1 of 3 thresholds [bone, soft tissue, or brain], and resampling of the datasets) followed by the registration of the datasets. The datasets are registered by minimizing the cost function using a least mean squares approach in the x, *y,* and *z* directions, followed by applying the final rotation and translating to the target hybrid CT image and to the SPECT/PET image. Furthermore, the software package provides us with the tools to enable a 3-dimensional review of volume datasets by using rendering software that applies OpenGL (Silicon Graphics, Inc.) libraries and a flexible graphical user interface. Predefined anatomic presets (abdomen and bone, among others) allow the easy creation of dual-modality, fused, 3-dimensional, volume rendered images (SPECT/CT or SPECT/external CT).

To validate this software tool, we performed more than 50 SPECT/CT acquisitions of different organs, using different radiopharmaceuticals. After visual registration with an external CT scan, the fused datasets were examined by 3 nuclear medicine specialists. In 50 patients, additional clinical data were obtained or clinical information was improved, whereas in 6 other patients no additional clinical information was obtained. Furthermore, an additional advantage of the 3-dimensional visualization of fused volume datasets was the fact that the clinical findings were easily visible to clinicians not used to SPECT data interpretation. Because the implemented algorithm is rigid, some misregistration could not be avoided, especially if the patient could not be positioned identically in the 2 examinations to be registered (e.g., different arm positions). We solved this problem by visually finding the optimal translation position for the organ of interest or even for only part of this organ.

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REPLY: We thank Dr. Knoll and coworkers for their comments regarding our recent continuing education article on hybrid imaging with SPECT/CT (*1*). In their letter to the editor, they report on their experience with a new software tool for image fusion (Volumetrix Suite; GE Healthcare). In more than 50 patients examined with this new tool, Knoll et al. observed an improvement of the diagnostic information in more than 89% (50/56) of imaging studies. As outlined in our article, software-based image fusion is still attractive. It would be highly interesting to learn how this new software approach affects various imaging situations in SPECT. The authors are therefore encouraged to submit an original article reporting their results in more detail.

Current software algorithms already allow the highly accurate coregistration of anatomic and functional images, therefore representing a regular component in daily clinical practice, for example, for image-guided surgery or radiation treatment planning. Whereas software-based image fusion seems appropriate in certain clinical situations, we hypothesize that hardware image fusion using integrated SPECT/CT scanners outperforms software-based algorithms in several scenarios. It has been previously demonstrated that motion artifacts arising from separate acquisition of CT and SPECT may seriously affect the accuracy of image fusion in the thorax, abdomen, or pelvis (*2,3*). Typical functional images of the thorax or the abdomen contain insufficient anatomic landmarks for their correlation to anatomic reference points. Differences in patient positioning and respiratory motion make the correct alignment of anatomic and functional images from separate devices even more complicated. Because of these issues, software algorithms did not reach widespread clinical use for

image coregistration of the abdomen or the thorax. In the future, however, this technology may play an important role in allowing correction of misregistration due to patient motion or breathing artifacts, which may also arise from integrated SPECT/CT.

Besides anatomic referencing, the added value of CT coregistration is also based on the attenuation correction capabilities of CT. Cardiac imaging poses a particular problem in attenuation correction because of respiratory and cardiac motion in the thorax. Individual CT-based attenuation correction of brain studies using SPECT may also lead to improved image quality and more accurate data evaluation. Furthermore, radionuclide treatment planning using attenuation correction of imaging data and assessment of organ or target volumes derived from simultaneously performed CT may be more accurate and potentially allows safe and effective therapy.

A similar discussion on the need for integrated hybrid scanners has already been raised after the introduction of hybrid PET/CT systems to clinical medicine. As indicated for PET/CT, image fusion is faster, more reliable, and more accurate using an integrated scanner than using separately performed imaging modalities (*4*). In addition to these technical issues, hybrid image acquisition of both modalities in a single clinical visit (1-stop) offers apparent logistic advantages and is obviously more comfortable for the patient. PET/CT scanners represent the imaging modality with the most rapid growth worldwide and play an increasing role in routine patient care, especially in oncologic applications. Yet, there is a lack of evidence that the same holds true for hybrid SPECT/CT systems. CT coregistration, however, has been recognized to result in higher specificity and sensitivity of scintigraphic imaging and to markedly reduce the number of indeterminate findings. The superiority of SPECT/CT over planar scintigrams or SPECT has been clearly demonstrated for imaging skeletal diseases, parathyroid adenomas, and neuroendocrine cancers and for mapping sentinel lymph nodes in various cancers (*1*). Studies demonstrating superiority in other clinical applications are lacking; however, pilot studies encourage the use of SPECT/CT in cardiac and neurologic imaging.

Regarding the growing number of studies demonstrating an added value of hybrid SPECT/CT over separately performed imaging modalities (*1*), it appears likely that this promising technique will gain an important role in clinical routine practice. The broad spectrum of existing SPECT tracers and their widespread availability suggests SPECT/CT as a complementary imaging modality to PET/CT procedures. In summary, we agree with Knoll and colleagues that advanced software-based coregistration procedures do have a legitimate relevance for image fusion, particularly if no hybrid technology is available. However, we believe that hardware-based hybrid acquisition offers several apparent advantages regarding accuracy, reliability, logistics, and comfort for the patient, which cannot be easily outweighed by software-based image fusion approaches.

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Tumor Metabolic Phenotypes on ^{18}F FDG PET

TO THE EDITOR: With great interest, we have read the article by Iagaru et al. (*1*) in the November issue of *The Journal of Nuclear Medicine*. The paper raises several issues on the use of functional imaging in oncology. The study assumed that refractory or relapsed non-Hodgkin lymphoma always maintains the same tumor phenotype as at the initial diagnosis and had been treated correctly before ^{90}Y-ibritumomab therapy. The authors suggested that the bulky disease revealed by pretreatment ^{111}In-ibritumomab imaging showed a less favorable response, although there are no well-cited references to suggest that ^{111}In-ibritumomab accumulation is proportional to tumor load. Furthermore, ^{111}In-ibritumomab imaging is usually for biodistribution only, as the authors have pointed out in the paper. Figure 1 is convincing for complete response because it shows negative PET findings after treatment. However, no quantitative parameters such as standardized uptake value (SUV) tables (*2–4*), glucose sensitivity calculations (*2*), or tumor load assessments (*5*) to characterize tumor phenotype are reported for the initial pretreatment PET. On the basis of our clinical experiences, the tumor load appears visually to be in the low to medium range and the ^{18}F-FDG uptake is moderately intense in Figure 1, suggesting an intermediate grade of lymphoma by the presented pretreatment PET findings. Figure 2 shows an increased extent and magnitude of metabolically active foci on PET after treatment. On the corresponding pretreatment PET scan, tumor load appears to be in the medium range and the degree of uptake appears to be less intense than that in Figure 1. Thus, it would be of interest to readers from both the nuclear medicine/radiology and the oncology disciplines for the authors to clarify and characterize tumor metabolic phenotypes and tumor load assessment on PET. These 2 pieces of additional biologic information from PET have gradually been found to be useful in various cancers, including many types of lymphoma, for systemic and organ-directed or regional therapies (*4–6*).

The lack of response on PET could be due to the following causes: invalid assumption of the tumor phenotype before treatment, lack of chemosensitivity, or possible transformation or grade migration (as in Fig. 2, with more diffuse disease and higher ^{18}F-FDG uptake after treatment). Thus, the suggestion of progression alone in Figure 2C may not be entirely accurate. The additional