

advantageous. In addition, ^{99m}Tc -HMPAO labeled leukocytes may give the same type of distribution activity in the marrow and thus may be used in these situations (2,9). Lastly, what about the possible consequences of repeated injections of such antibodies—one of the most interesting utilizations of marrow imaging is management and follow-up of patients under treatment (5,6).

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REPLY: We thank Drs. Bourgeois and Fruhling for their interest in our work. Regarding our staging of patients, as explained in the Methods section (1), Table 1 presents the stage of the patients when they were referred to our laboratory (before bone studies). Table 1 also presents the extension of the disease disclosed in addition to bone involvement, including extension revealed by the work-up performed simultane-

ously, bone studies. For example: Patient 10 was referred for evaluation as Stage III. Axillary nodes were apparent at palpation. The bone scan was interpreted as primarily benign (degenerative disease). Bone marrow imaging revealed two cold foci, which turned out to be metastases at follow-up. A CAT scan of the abdomen performed at the same time as the bone studies revealed liver metastases.

Bone scans in cancer patients can be interpreted as primarily benign if only abnormalities more likely to correspond to benign disease are observed (i.e., aligned hot foci in the ribs, hot patella, increased uptake in the periarticular regions in patients with chronic arthritis) (2).

In breast cancer, a patient who presents with a single metastatic bone lesion may benefit from local treatment (radiation therapy) with or without endocrine therapy or chemotherapy (3). If this is the case, more aggressive chemotherapy regimens are kept as second line treatment to be applied if there is progression of the disease or subsequent relapse. This therapeutic strategy has been shown to improve survival of these patients (3). Patients presenting with widespread bone metastases are prompted into aggressive chemotherapy.

We did not use the presence of marrow activity in the skull as a criterion for bone marrow expansion. We used the classical criteria based on the presence of bone marrow in the distal femoral shafts (4–5).

Bourgeois and Fruhling seem to state in their letter that all benign bone diseases affect bone marrow and, therefore, produce cold defects in marrow scans. It seems possible to us that injuries to the bone starting from the cortical bone, i.e., degenerative arthrosis, may in their time course first involve the cortical bone, and later produce marrow injury (6). We have observed patients with peripheral increased uptake in adjacent vertebrae corresponding to degenerative disease in their bone scans who had normal marrow scans. In any case, further studies directed to assess bone marrow involvement in benign conditions have to be undertaken.

Bone marrow expansion may be multifactorial in origin (4). The cause of this frequent finding was out of the scope of our work. Silent micrometastatic disease may be one possible cause for marrow expansion even if hard to prove. We agree in that the possible development of antimouse antibodies may limit the use of this intact antibody for repeated injections (1). Marrow scans are not used to assess liver involvement in breast cancer; liver assessment is usually performed with CAT or ultrasonography.

We understand that Bourgeois et al. have had excellent results with colloidal agents in cancer patients. This has not been our experience. However, comparison between the antigranulocyte antibody and any other bone marrow imaging agent was not the aim of our study. We have shown that bone marrow scans performed with the antigranulocyte antibody detect more patients with metastatic bone disease than bone scans in primary breast cancer with suspected bone metastases. Furthermore, in patients with metastatic bone tissue invasion, bone marrow scans detect more metastatic sites than bone scans.

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Design and Use of PET Tomographs: The Effect of Slice Spacing

TO THE EDITOR: Miller et al. (1) have elegantly explained and demonstrated the requirements of axial sampling in PET. Their findings are consistent with the work done by Mullani (2,3) with theoretical and phantom studies and with Senda et al. (4) with clinical PET studies except in their conclusions.

As a designer of PET cameras with considerable experience in three-dimensional imaging camera design (5), I have to disagree with Dr. Miller's conclusion, which is stated as follows. "Thus, for typical objects, the slice spacing of the tomograph should be approximately 50%-75% of the z-axis resolution (FWHM)." My reasons for disagreeing with this conclusion are discussed below.

1. The Nyquist sampling criteria for repetitive functions such as a sine function is to sample at twice the frequency of the function, which could be interpreted as slice separation divided by slice resolution (S/FWHM) ratio of 0.5 (50%). However, for non-repetitive functions such as a Gaussian function, accurate recovery of information requires the sampling frequency to be greater than twice the "resolution frequency," which is approximated by 1/FWHM. In the transaxial direction, most PET designers have found it necessary to sample between two to three times the "resolution frequency" (33%-50% ratio for sampling distance to resolution) in order to avoid spatial artifacts in the image due to aliasing. I have found similar spatial artifacts in the axial direction when imaging a special partial volume phantom (3), if the axial sampling is inadequate. Dr. Miller's conclusion that the sampling/resolution ratio can be reduced to 0.75 (75%) is much coarser than that specified by Nyquist sampling criteria

and certainly not consistent with the sampling requirements in the transaxial direction.

2. Dr. Miller's simulations were carried out with highly symmetric and smooth objects—spheres. The frequency content of the sphere as contrasted to a bar of radioactivity across the field of view is quite different and the aliasing effects will be quite smaller for the spheres than for the bar of radioactivity. Undersampling a bar of radioactivity will certainly result in greater aliasing which in turn will result in greater underestimation of the recovery coefficient. Therefore, his estimate of 10% acceptable error in recovery coefficient by under sampling may be higher for objects such as the myocardium and the cortical areas of the brain which are closer in geometry to a bar of radioactivity than a sphere.
3. Acceptable error in recovery coefficient is arbitrary and will depend significantly on the clinical application. A 10%-15% error in quantitation may not be significant for a moving heart application where there is considerable smearing of radioactivity from one slice to another due to the motion of the heart. However, for gated heart images, where the motion is minimized, it could be interpreted as a mild defect since a 10%-15% change in a physiologic condition such as myocardial perfusion can be clinically significant. Similarly, in oncology where one might encounter spherical objects, a 10% error may not be acceptable in a serial study where a tumor is studied pre- and post-treatment to assess changes in metabolism or shape of the tumor. A 10% change in tumor quantitation may be clinically significant in the treatment strategy for the patient. It must also be remembered that undersampling causes spatial artifacts which will result in an error in the estimation of the size of the tumor. Again, for a serial study in which the size of the tumor is an important measure of the effect of treatment, an error of 10% may not be acceptable.

I have been a proponent of finer axial sampling in PET for several years and have deliberated a great deal about the compromise between the optimum and the acceptable number of slices and slice separation. I agree with Dr. Miller that finer sampling puts a great deal of burden on the finite number of photons collected in a PET study. Fewer number of photons per slice will result in poorer image quality and a greater uncertainty in quantitation within the slice. Finer axial sampling will decrease the number of photons per slice and the temptation to decrease the number of slices by decreasing the sampling distance between slices is very strong for a PET camera designer. However, for the best three-dimensional imaging, the sampling criteria for the transaxial and the axial directions must be satisfied in a similar fashion. It is not appropriate to arbitrarily apply a different sampling criteria in the axial direction than the transaxial direction. For that reason, the S/FWHM ratio cannot be higher than 0.5 (50%) and in a practical sense should not be much higher than 0.4 (40%) for accurate three-dimensional reconstructions in PET.

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