worsening of the disease. In the last patient, marrow scintigraphy suggested the complete healing of the medullary metastases despite a still pathological (although improved) bone scan but with later worsening of the disease. Our patients' results differ thus from those of Berna et al., except for our last patient. We do not wish to discuss yet again the differences between colloids, leukocytes or antibodies for imaging bone marrow (*4,5*), but we definitely conclude that in such patients with extensive or multifocal metastatic disease from prostate or breast carcinomas (data to be published), marrow scintigraphy using nano-sized colloids represents the simplest and least expensive way—not excluding its possible superiority to bone scanning—to evaluate these patients' responses to treatment.

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The Localization of Indium-111-Leukocytes, Gallium-67-Polyclonal IgG and Other Radioactive Agents in Acute Focal Inflammatory Lesions

TO THE EDITOR: With great interest, we have read the results of the excellently designed animal study presented by McAfee et al. in a recent issue in which eight different radiotracers for localizing experimental abscesses in dogs were investigated and the local uptake ratio was calculated (*1*).

The final results of the study demonstrated the superior quality of ^{111}In-oxine-labeled granulocytes especially in comparison to the other investigated radiopharmaceuticals. A comparison with monoclonal mouse antibodies directed against the human granulocyte epitope NCA-95, labeled with ^{99m}Tc (Mab BW 250/183, Granulozyt^{R}, Behringwerke AG) or ^{123}I (Mab 47, Granuloszint^{R}, Mallinckrodt), was impossible due to species-specificity.

At our institutions, like in many others in Europe, ^{99m}Tc-labeled Mab BW 250/183 is frequently used for clinical applications concerning infection and inflammation. The simple in-vivo use, a ^{99m}Tc label, the logistic advantages and the lower radiation burden are important facts that emphasize this modality from a clinical point of view. The sensitivity, specificity and accuracy are similar to the reported data from studies with ^{111}In-oxine granulocytes (*2–9*). Those studies include infections of the musculoskeletal system.

In regard to the limitation in transferring data from animal experiments to humans and the clinical results of anti-NCA-95, we cannot agree with the general conclusion of the authors that ^{111}In-granulocytes are superior to all other agents for localization of infectious lesions and that other options only play the part of a substitute. In our opinion, isolation and labeling procedures become more unpopular, because they are time-consuming procedures and there is the risk of infection from the AIDS virus.

Indium-111-oxine-labeled granulocytes have been the gold standard for many years, but the development of new monoclonals has become successful and seems to be as effective in clinical routine. An important future task will be to list the different available radiopharmaceuticals and to evaluate their various indications for localizing foci of infections.

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REPLY: We thank Dr. Sciuk for his interest and kind remarks about our manuscript. Many of us in the U.S. have been following the interesting literature on the Behringwerke AG ^{99m}Tc-monoclonal antibody (Mab) BW 250/183 originally developed by Bosslet et al. (*1*). Although other anti-granulocyte Mabs are under development in Europe and in the U.S., none are available

clinically in the U.S.; hence, they are not a viable option for imaging foci of infections in our country. Moreover, no radiolabeled Mab has been approved for any clinical use as yet in the U.S., although a few are under serious consideration.

Few comparisons of ^{111}In in-vitro labeled leukocytes with in-vivo ^{99m}Tc-anti-granulocyte Mab in the same group of patients seem to be available. In 33 patients with positive endoscopies indicating active inflammatory bowel disease, the sensitivity of ^{111}In-leukocytes was 95%, compared with 79% for ^{99m}Tc-Mab at 24 hr (*2*). At that time, the liver and spleen activity was higher with ^{111}In-leukocytes and the marrow activity higher with ^{99m}Tc-Mab. Some authors have observed ^{99m}Tc bladder activity in normal subjects, suggesting that this may not be the ideal agent for urinary infections.

Fortunately, no functional impairment has been detected when this anti-granulocyte Mab becomes bound to granulocytes (*3,4*), and there has been no change in the circulating neutrophil count (*5*). However, the recovery rate of the ^{99m}Tc activity in circulating granulocytes observed by Becker et al. (*5*) at 90 min was not higher than 15%, a value much lower than that with leukocytes labeled in vitro with either ^{111}In-oxine or ^{99m}Tc-HMPAO. Therefore, it is conceivable that the detection of foci of infection with this Mab may not be primarily due to in-vivo binding to the NCA-95 glycoprotein in the circulation. Perhaps the free Mab may migrate to an infectious focus and bind to viable or damaged neutrophils already localized there. Some of the localization may be nonspecific, similar to that of polyclonal IgG or serum albumin. With another ^{99m}Tc-labeled antigranulocyte Mab against lacto-N-fucopentose (alpha-stage specific embryonic antigen or alpha-SSEA), an IgM, Thakur et al. (*6*) obtained a higher level of in vivo binding to circulating neutrophils ranging from 14% to 44%.

Elicitation of antibodies in humans directed against murine monoclonal antibodies (HAMA) rarely results in harmful symptomatic reactions, but the half-life of the murine Mabs is greatly shortened, and their efficacy is reduced or nullified. This is the most serious problem remaining in human immunotherapy (*7*). HAMA has limited response to treatment with Mabs in over half of the patients in whom treatment with murine Mabs has been attempted. Current progress in the development of human Mabs to overcome the HAMA problem includes utilization of B cells from human peripheral blood mononuclear cells pretreated with lysosomotropic agents (such as amino acid or peptide methyl esters), SCID mice that accept and proliferate human B cells producing human immunoglobulin and gene amplification technology, including the polymerase chain reaction.

Until human monoclonal antibodies become available, how widely should we use murine Mabs for the diagnosis of nonmalignant diseases? Seybold et al. (*8*) did not consider another antigranulocyte Mab suitable for general use, partly because the antigenicity should be examined in more detail. The therapeutic use of unlabeled murine monoclonals gained impetus with the approval of Orthoclone OKT3 targeted against the CD3 receptor T-cell complex. This is now widely used not only for the prophylaxis and treatment of transplant rejection, but in other conditions such as refractory rheumatoid arthritis and collagen vascular disease (*7*). Other murine monoclonals are undergoing human therapeutic trials for refractory inflammatory bowel disease, graft versus host disease in marrow transplantation, other organ rejection episodes and in certain lymphoid malignancies (*7*). It is possible that future potential treatment of life-threatening sepsis with Mabs could be jeopardized by a previous exposure to a diagnostic murine immunoglobulin (*9*). HAMA so far has developed infrequently from the BW 250/183 Mab (*10,11*). According to Joseph et al. (*4*), only 10%–20% of the patients developed HAMA of the IgG type with blocking potential and transient HAMA response of the IgM type was somewhat more common.

As Dr. Sciuk concludes in his letter, we should continue to evaluate the different radiopharmaceuticals (both old and new) available for localizing foci of infection and define the indications of each.

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Standardized Tests of PET Performance

TO THE EDITOR: In deciding whether an imaging device might be appropriate for particular nuclear medicine studies, user-specific tests of the device and examination of any relevant performance data available from vendors can be helpful. After selection of an imaging device, additional measurements are necessary as part of acceptance testing and of good quality control procedures. Tests may also be performed to assist in defining and improving image quantitation. Therefore the standardization of performance tests requires careful consideration of the imaging