Journal, describe difficulty in obtaining early images using indium-111-labeled granulocytes to detect occult infection (*1*). In this study they used autologous granulocytes for labeling and imaging in patients with normal or elevated granulocyte counts. The early images, at 1-4 hr, had a sensitivity of only 33%. They therefore question our previous report of the rapid localization of activity to sites of infection, which were seen in granulocytopenic patients with known infections when given indium-111-labeled donor cells (*2*). However, I would like to reaffirm our observation of the rapidity with which labeled cells migrate in granulocytopenic patients. As a continuation of the previous report, studies done in nuclear medicine at our institution confirm this. The localization is clearly apparent, without computer manipulation of the image, as early as 30 min after injection of labeled donor cells.

I do not doubt that they are observing less localization at 1 hr in their autologous studies, but suggest that this difference is not a function of the technique, but is related to granulocyte kinetics and the differences in the marginating pool of granulocytes available in patients with a normal white-cell count contrasted with granulocytopenic patients. There may be a dilutional effect in patients with normal counts so that proportionally fewer labeled granulocytes migrate to sites of infection initially, because unlabeled granulocytes are also migrating there. In contrast, in granulocytopenic patients, the only circulating granulocytes are often the labeled donor cells, and they respond rapidly and in larger proportion to the chemotactic stimulus of an infection. This, in part, I believe explains the differences between these two studies.

Furthermore, in our study, we were imaging clinically apparent infections for purposes of evaluating transfusion response. It is possible that this involved a greater chemotactic stimulus than that in an occult, clinically nonlocalized infection.

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Reply

We thank Dr. Dutcher for her comments. Since we studied only patients with normal or elevated white counts whereas Dr. Dutcher's patients were granulocytopenic, a difference in leukocyte kinetics certainly could explain the disparity between her findings and ours.

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Re: Does Bone Measurement on the Radius Indicate Skeletal Status?

I read with interest the paper by Mazess et al. (*1*) and the statement that the "limbs . . . did not reflect the preferential osteopenia in the spine". I-125 absorptiometry of the distal third of the radius is chiefly a measurement of cortical bone, and thus a comparison has been made of cortical bone at one site with mainly trabecular bone in the spine.

The distal end of the radius contains significant amounts of trabecular bone and special-purpose I-125 CT scanners have been built that can measure the trabecular bone density very precisely (*2,3*). The distal radius is not only convenient and accessible for bone-density measurement but in osteoporotic patients is associated with fracture. In women approximately one third of all fractures occur at this site, and after age 55 the incidence of fracture in women is six times that in men (*4*).

For monitoring the course of osteopenia or its treatment, the method should have a reproducibility of greater than 1%, and there should be few obstacles to repeat measurements. We have built a low-dose CT scanner that uses an I-125 source (Hosie CJ, Richardson W, Gregory N, unpublished data). This is a self-contained unit, with image reconstruction carried out by a multiprocessor microcomputer. Trabecular bone density in the distal radius has been measured with a reproducibility of 0.5% in normal subjects and osteoporotic patients. Other groups have reported similar reproducibility with an I-125 computed tomograph (*2,3*) and have obtained good correlation between trabecular bone density of the distal radius and trabecular bone density of excised vertebrae (*2,5*). Our preliminary results indicate that in osteoporosis there is a preferential decrease of trabecular bone (45%) compared with that for cortical bone (30%).

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Reply

Hosie correctly notes that measurements of compact bone on the limbs do not reflect the trabecular bone of the axial skeleton, but suggests that measurement of trabecular bone of the distal radius may be clinically useful. Of course, absorptiometric scans on the distal radius are usually done at a site (10% of the forearm length) that is only about 10-15% trabecular, and even more distal sites are not more than 20-40% trabecular (*1*). We have found that shaft and distal sites on the radius are highly correlated (r = 0.95), and consequently absorptiometric scans at both locations must be equally poor indicators of spinal status (2). Computerized scanners based on x-rays and I-125 emission, such as those pioneered by the Zurich group cited by Hosie, provide precise measurements at the distal radius and other limb locations (proximal tibia). Rüegsegger (*3*) reported that trabecular bone of the distal radius was significantly diminished in osteoporotic patients. Nevertheless, there are two perplexing problems in addition to the high cost of these specially engineered systems. First, a technical difficulty is caused by the "environmental density" artifact (*4*). The trabecular bone on the distal radius (or tibia) is surrounded by a layer of much denser

compact bone that profoundly influences the CT results. Second, the trabecular bone of the limbs does not reflect changes in the axial skeleton; it has been characterized as metabolically inactive.

It might be difficult for readers to reconcile the latter point with Hosie's contention that there is a good correlation between trabecular bone density of the distal radius and that of the spine. In the first report cited by Hosie (*3*), the CT determinations in both locations were made on macerated specimens from normal subjects. Even with one highly deviant case excluded, the predictive error was 10–15%. In the second study (*5*) the predictive error appeared to be closer to 20%, or about the error one sees in predicting vertebral density from compact bone. In another study by Bydder et al. (*6*) the predictive error again was 15–20%. Moreover, there was a far lower correlation, with a considerably different (and lower) slope, in osteoporotics compared with normals. This closely parallels the findings in our report. Prospective studies have shown that several drugs used in osteoporosis positively influence the axial skeleton without concomitant effects on the distal radius.

Given the relatively high cost of specially constructed CT scanners, their technical problems, and the apparent differences between axial and appendicular trabecular bone, it would be prudent for interested investigators to await further reports from existing units using this exciting but unproven method.

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Re: Improved Intrinsic Resolution: Does it Make a Difference?

The recent paper by Hoffer et al. (*1*) suggests that an improvement in the intrinsic resolution of an Anger camera from <4.9 mm FWHM at 140 keV to <3.8 mm FWHM has no observable effect on lesion detection in liver or bone images. The authors use ROC analysis to compare observer performance. We have used ROC analysis in our department to compare hard-copy imaging formats (*2*). In an unpublished part of our study we compared analog (Polaroid) images from a Union Carbide Cleon 720 Anger camera (intrinsic resolution 5.3mm FWHM at 140 keV) and a Nuclear Enterprises Mark 4 (intrinsic resolution 7.1mm), each fitted with a high-resolution low-energy collimator. The images, each of 1 million counts, were formed by placing an absorber (20mm diam) between the Anger camera face and a flood source for different periods of time and at different sites to simulate photon-deficient lesions of varying contrast. Seven observers studied a set of 100 images from each camera, and ROC and LROC curves wer produced. Using the methods detailed in our paper (*2*), we derived from these curves two sets of seven areas for each camera. The areas were then compared using the Wilcoxon Matched Pairs Signed Ranks test. No significant difference was found in observer performance between the images from the two Anger cameras.

This study shows that improved intrinsic resolution from 7.1mm to 5.3mm FWHM did not significantly improve detectability for the size of photon-deficient lesion selected for investigation. Whereas metastatic lesions in the liver are likely to be of varying size and at varying depths, it has been observed at autopsy that superficial lesions are present in 90% of cases, and in 70% of cases the lesions are greater than 20mm in diameter (*3*). Thus for practical purposes, improvements in intrinsic resolution from 7mm to 5mm or so would not be expected to have a major effect on lesion detectability. The results of our simple study, however, lend support to the more detailed investigations of Hoffer et al. (*1*). The findings are also in keeping with an impression that recent advances in instrumentation and radiopharmaceuticals have not improved the diagnostic accuracy of conventional radionuclide liver imaging (*4*).

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Reply

While the results obtained by Eadie and Hilditch are certainly compatible with our own, we do note that two different imaging instruments were used in their study. These instruments may have differed not only in intrinsic resolution, but also in energy resolution. Although both were equipped with "high-resolution" collimators, we have also observed marked differences in performance characteristics of collimators designated as "high-resolution" by various manufacturers. Moreover, and most importantly, the 20-mm test "lesion" used by Eadie and Hilditch would definitely militate against the observation of any difference in lesion detection between two systems with intrinsic resolutions of 7.1 and 5.3 mm FWHM.

Although we feel that the importance of improvement in intrinsic resolution has perhaps been overemphasized, it should not be disregarded. There is obviously some point at which degradation