

Nanocolloid Imaging in Early Bone or Marrow Metastatic Spread

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As bone marrow is richer in blood supply than bone, it seems likely that the initial spread of metastatic disease is to marrow rather than bone. In order to explore this possibility and, hopefully, the rate at which the cortex becomes affected, 20 patients have undergone bone marrow imaging as well as conventional bone studies. The bone and marrow images were compared for each patient and the number and sizes of the lesions noted. Results suggest that marrow lesions are often larger or more numerous than corresponding bone lesions, indicating that bone involvement may well follow marrow. Accurate positioning and experienced interpretation of the images are vital as it is difficult to detect "cold" lesions in areas of poor count rate, and obscuring liver and spleen uptake. The immediate benefit to patients has been to confirm the diagnosis of secondary disease in equivocal bone images.

This study was initiated with the hope of answering two questions. First, whether the initial spread of metastatic disease from primary tumors which metastasize by blood borne transmission was to bone marrow rather than cortical bone and, hence, whether the bony involvement followed that of the marrow. This seemed likely since red marrow is by comparison much richer in blood supply than bone. Yellow marrow's lesser blood supply renders it less susceptible to secondary disease and, therefore, the inability to image it by this method was not seen as significant. Second, we wished to see whether bone marrow imaging was significantly more positive than conventional imaging in cases of early bone/marrow spread and whether it might present a more positive indicator for early disease if the rate of progression was fairly slow.

Several approaches to imaging have been used in many centers (1). Magnetic resonance imaging (MRI) has many advantages. It can image yellow marrow, distinguish between diseased and normal marrow as well as show sites of replaced marrow. MRI does not utilize ionizing radiation (1). It is, however, very expensive, even when available, in most countries.

Radionuclide marrow imaging can be approached in two ways. First, by identifying hemopoietic tissue with materials that bind in vivo to transferrin. Iron-52 (^{52}Fe) citrate and

indium-111 (^{111}In) chloride have been used and while these methods avoid the problem of liver and spleen uptake obscuring other structures, they are relatively expensive and deliver a high radiation dose. The second method, locating the macrophages in the reticuloendothelial system by the phagocytosis of radiolabeled colloids, is relatively inexpensive, readily available and, by using technetium-99m ($^{99\text{m}}\text{Tc}$) as the tracer, provides good counting statistics as well as a relatively low effective dose equivalent (2).

A newer method of imaging combines both bioroutes by using white blood cells labeled with $^{99\text{m}}\text{Tc}$ -HMPAO (hexamethylpropaleneamineoxine). This has the advantage of a relatively lower liver and spleen uptake than the colloids. Work is now in progress at this center to evaluate this technique (3). It is, however, more time consuming and requires cell labeling facilities. We, therefore, chose the colloid method as suitable for this study despite the technical drawbacks.

Nanocoll* is a human serum albumin prepared to contain 95% of its particles at less than 80 nm. About 15% of the injected dose is estimated to go to marrow.[†]

MATERIALS AND METHODS

To date twenty patients all with abnormal bone scans have been studied. Included in the study population were 15 females (range 34–70 yr) and 5 males (range 50–80 yr). All patients had documented malignant disease including lymphoma ($n = 5$), bronchial carcinoma ($n = 2$) and breast cancer ($n = 13$). Each patient had a conventional bone scan using ~740 MBq of $^{99\text{m}}\text{Tc}$ -labeled MDP (methylene-diphosphonate) and a marrow scan using 555 MBq $^{99\text{m}}\text{Tc}$ -labeled Nanocoll within 2 wk of the bone scan. Whole body images were acquired with extra views as indicated (3 hr postinjection of MDP, 2 hr postinjection of Nanocoll). Equivalent views were obtained on the marrow scans.

The marrow scans were set up using the posterior thorax excluding liver and spleen to assess the speed or time per view which would give an information density over the marrow equivalent to that obtained on the bone images.

For individual views, the liver/spleen uptake was excluded from the images as far as possible by careful positioning and lead masking as appropriate. Thoracic spine and rib views were acquired erect (patient condition permitting) so that the lower position of the liver would reveal more of the bony

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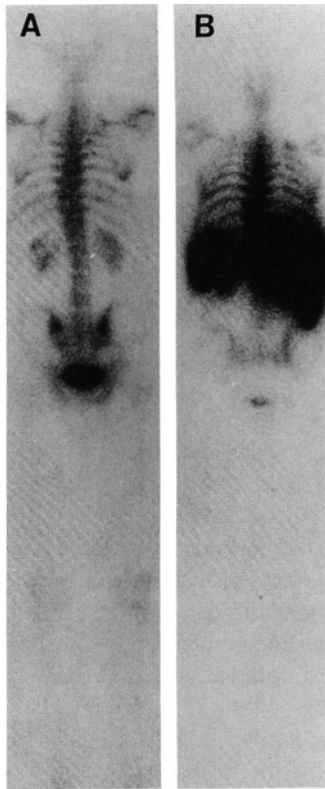


FIG 1. Whole-body images of (A) bone and (B) bone marrow in which the posterior ribs were suspicious of abnormality.

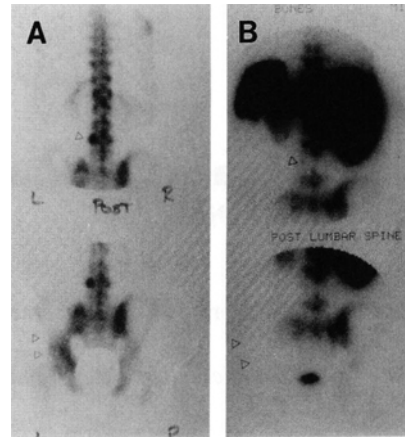


FIG 3. The small bony lesions seen on this bone image (A) (arrows) are seen as larger marrow lesions (B).

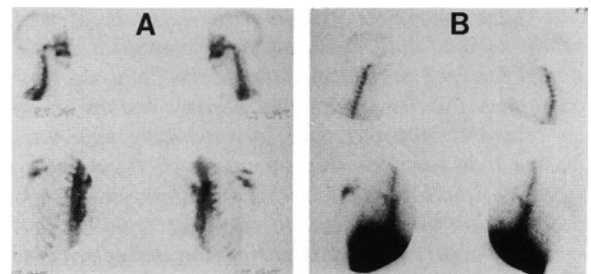


FIG 4. Bone images (A) which show a normal right shoulder where the corresponding marrow uptake (B) is reduced due to radiation fibrosis.

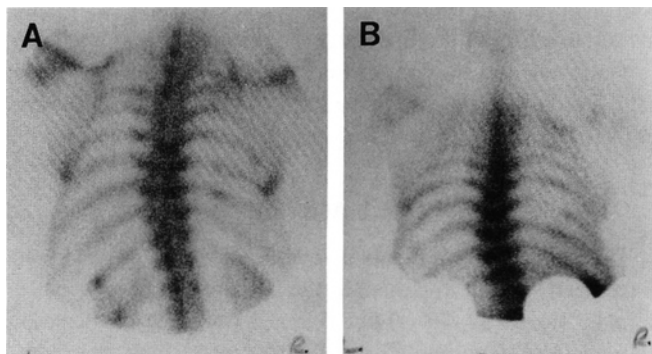


FIG 2. Localized rib views in the same study with lead masking show clearly the matched defects.

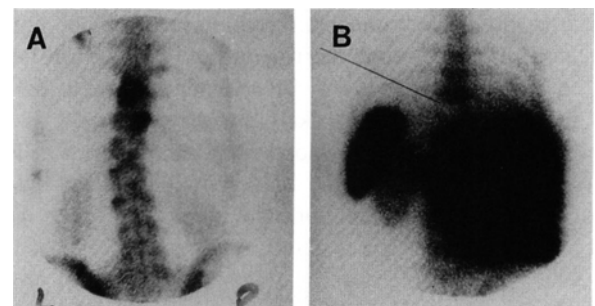


FIG 5. A bone image (A) showing two lesions of which only one can be seen in the marrow image (B) due to obscuring hepatic uptake.

structures (Figs. 1 and 2).

The scans were routinely reported and subsequently reviewed by a second nuclear medicine physician who estimated the relative sizes of lesions and tabulated their number and position.

RESULTS

Results shown in Table 1 indicate that in all but one case, lesions seen on bone imaging were demonstrated on marrow studies. Clearly as bone lesions are seen as "hot spots" and will, therefore, appear to be larger than is in fact the case and

marrow as "cold spots" which will to some extent "fill in," the relative sizes were hard to assess (4). We were, however, reasonably certain that overall the marrow images showed concordant or larger marrow lesions than the corresponding bone images (Fig. 3).

In the breast cancer category, of the two cases which demonstrated further marrow lesions, one was thought to be due to fibrosis from local radiotherapy. Three had no corresponding marrow lesions and it was, therefore, decided that the bone lesions seen represented degenerative disease only as fitted with their appearance, position and intensity of uptake. One patient had one bone lesion with corresponding larger

TABLE 1. Results of Bone Imaging

	Lymphoma	Ca* bronchus	Ca* breast	Total
Concordant	3	1	7	11
Greater marrow lesions	2	1	2	5
Lesser marrow lesions	-	-	3	3
Discordant	-	-	1	1

* Ca = cancer.

marrow lesion and another with no marrow lesion which was thought to represent mixed pathology.

DISCUSSION

These results reflect the limitations of the technique which we have found. First, that bony lesions cannot be confirmed in areas in which, on the marrow scan, the liver obscures the spine and ribs (Fig. 4). Second, that radiation fibrosis and consequent infiltration of the destroyed marrow space with fat gives a false-positive result (Fig. 5). Third, the difficulty in identifying cold lesions is well known, although we feel that this can be, to some extent, overcome by reporting these images alongside a bone scan.

CONCLUSIONS

In spite of the difficulties and the small sample size, we feel that the evidence so far is that the majority of the marrow

images are as positive or more positive than the corresponding bone studies in cases of confirmed metastatic disease, indicating that the marrow lesions do predate the cortical bone lesions in any one site.

Second, as the marrow studies did not show greatly increased abnormalities over the bone and would be harder to report in isolation, they are not likely to prove more useful as an "early warning" indicator of secondary disease than conventional bone imaging.

Third, given the very high coincidence rate of lesions in paired studies, we do feel that as a means of deciding with confidence between diagnoses of malignant or degenerative disease, marrow imaging is a very useful adjunct to conventional bone studies.

NOTES

* Solco-Nuclear, Birsfelden, Switzerland

† Instruction packet produced by Solco-Nuclear.

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