The Scintigraphic Investigation of Sacroiliac Disease

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Bone scintigraphs obtained with both Technetium-99m polyphosphate and Technetium-99m pyrophosphate have been abnormal at the sacroiliac joints of 44 patients with definite ankylosing spondylitis (AS). Because of the normal registration of the sacroiliac joints on bone scintigraphy, it has been necessary to develop a profile-scan technique to quantify the abnormality that proves to be significantly different from the normal finding. In 17 patients with a strong clinical suspicion of AS but normal radiographs, the sacroiliac joints have frequently been abnormal. This finding is meaningful because there is a common occurrence in this group of the histocompatibility antigen HL A-B27, known to be a marker of AS. We also note the frequency of abnormal sacroiliac scintigrams in 26 patients with rheumatoid arthritis and in a group of other diseases—Crohn's disease, uveitis, psoriasis, ulcerative colitis, and Reiters' disease—all of which share some of the manifestations of AS.

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The recognition of disease of the sacroiliac joints by radiologic methods has been shown to be subjective and uncertain (*1,2*). A new generation of bone-seeking radiotracers has been developed (*3*). These agents are safe and acceptable for the investigation of benign disease. We have explored their application to the diagnosis of sacroiliitis.

The abnormal accumulation of strontium-85 and strontium-87m at the sacroiliac joints of patients with AS has been reported (*4–8*). We have described the increased efficacy of bone scanning in comparison with radiologic methods in the diagnosis of sacroiliac disease (*9*). Technetium-99m polyphosphate (Tc-99m PP_x) and its analogues are not associated with either toxicity or idiosyncrasy. The radiation dose to the skeleton of 54 mrads/mCi (*10*) is acceptable.

Because of the normal registration of the sacroiliac joints on a scintigram, and of the subjective nature of an assessment of increased activity in such a situation, we have devised a simple, objective technique for the measurement of sacroiliac activity. We report here in detail the use of this technique in patients with and without other evidence of sacroiliac disease. We find that a similar technique has been used with strontium-85 (*4*) given in microcurie doses. Because of the safety of Tc-99m PP_x it is possible to use relatively large doses (of the order of 15 mCi) which yield a large photon flux, with the potential for high information densities in the resulting scintigraphs. Thus there is a suitable statistical sampling size for the design of techniques involving measurements of the kind described here.

PATIENTS AND METHODS

The patients of interest are those with, or with a suspicion of, AS or with a variety of diseases known to be associated with sacroiliitis, or with the presence in the blood of the histocompatibility antigen HLA-B27 (*11–14*)—diseases such as Reiter's disease, Crohn's disease, ulcerative colitis, and uveitis. The patients have been clinically evaluated and investigated by radiography, bone scintigraphy, and HLA-B27 measurement, the latter having been known formerly as HLA-W27.

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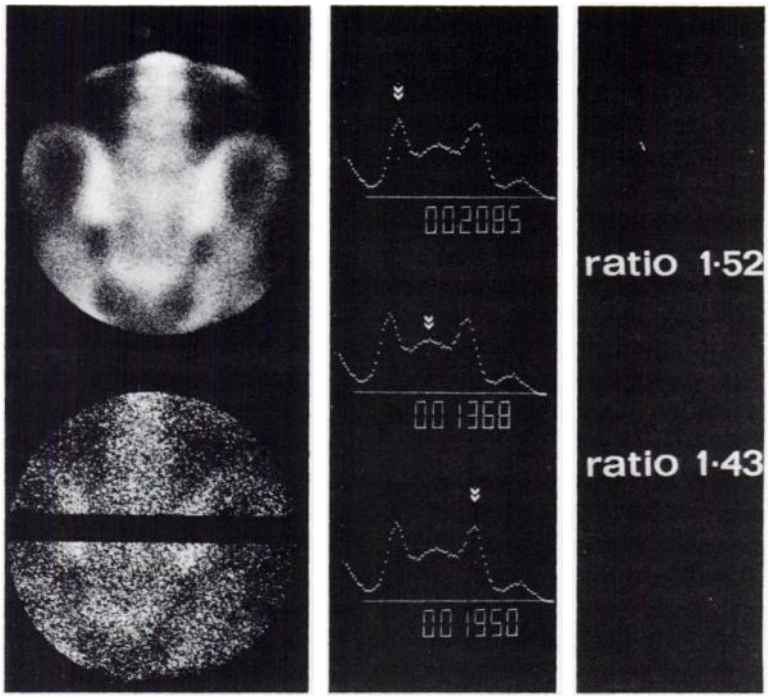


FIG. 1. Scintigram of sacroiliac joints (Tc-99m PP_1, posterior view), in patient with AS. Location of profile and counts are at arrowed points along profile of scan. Counts are used to obtain ratio of activity between sacroiliac joints and sacrum.

The microdroplet lymphocyte cytotoxicity test was used to identify HL-A antigens (*15*).

The radiotracer used has been either Tc-99m polyphosphate, "T-99m PP_x," or Tc-99m pyrophosphate, "Tc-99m PP_1," in doses of 170–180 μCi/kg. Scintigrams are obtained 4 hr after injection of Tc-99m PP_x, or 3.5 hr after Tc-99m PP_1, to minimize blood–background concentrations.

Bone scintigrams of the whole body have been obtained with either a 5-in. dual-probe, rectilinear scanner, operated in 1:5 minification mode, or a scintillation camera with whole-body imaging accessory, using the low-energy, all-purpose collimator. These scintigrams have been made at an information density of 400 counts/cm^2 over normal bone.

Immediately after completion of the whole-body scan a scintillation camera image of the lumbosacral area is obtained posteriorly (Fig. 1). These data are recorded to a minimum total information density of 2000 counts/cm^2 onto an off-line videotape store/playback system. The tape's replay system is then used in conjunction with the camera's data-processing system to place an electronic cursor over the mid part of the sacroiliac joints and related sacrum, and to generate a profile sweep of this anatomic region (Fig. 1). The data processor may then be used to measure the counts accumulated at the sacroiliac joints and sacrum. The ratio of activity at these joints with reference to central sacrum is used here in assessing the normality or otherwise of the joints.

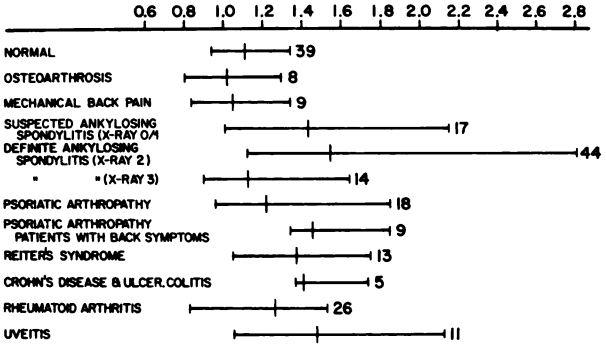
No field nonuniformity correction is applied, but routine flood-field checks are performed and, under the circumstances described, a maximum difference of 5% of activity is identifiable between any two points on the effective crystal face. This represents the possible experimental error in the technique we are describing.

Conventional radiographic examination of the sacroiliac joints has been undertaken on all but the normal control patients. The findings have been graded according to the standard method (*16*) as follows:

Grade 0: Normal.
Grade 1: Early sclerotic stage with an increase in the radiodensity of the joint margins, particularly on the iliac border.
Grade 2: Marked irregularities of the joint margins and widening of the joint space associated with definite sclerotic changes.
Grade 3: Bony bridging of the sacroiliac joint with solid ankylosis, and resolution of the sclerotic changes.

The statistical methods used depend upon a comparison of more than two groups, so that an analysis of variance was applied followed by Scheffé's multiple-comparison test where there proved to be a possible significant difference. The comparison of groups was otherwise accomplished using a paired t-test since each patient provided two observations, one from each sacroiliac joint. In those patients investigated more than once, a Pearson correlation

TABLE 1. THE SACROILIAC/SACRAL RATIOS IN A NUMBER OF GROUPS



coefficient was determined to evaluate the reproducibility of the sacroiliac ratios in a given patient.

RESULTS

In 39 patients between 20 and 45 years of age, investigated for other reasons and without clinical or scintigraphic evidence of an arthropathy, the sacroiliac-joint ratios have measured less than 1.34, with a mean of 1.11. In nine patients with musculoskeletal back pain the mean ratio was 1.05, and in eight patients with osteoarthrosis the mean ratio was 1.02. In neither of these groups were the means significantly different from the normal group ($p > 0.5$).

In 44 patients with definite clinical evidence of AS and radiologic Grade 2 sacroiliitis, the mean sacroiliac-to-sacral ratio (si/s) was elevated (Tables 1 and 2) and significantly greater than in normal controls ($p < 0.0001$). In 14 patients with Grade 3 radiologic sacroiliitis, the mean si/s ratio proved not to be significantly different from normal controls ($0.8 < p < 0.7$) consistent with the radiologic picture of end-stage obliterative disease.

There were 17 patients with a strong clinical suspicion of AS but with normal or equivocal (Grade 1) sacroiliac joints upon radiographic examination; in these there was evidence of increased uptake of the radiotracer at the joints on scintigraphy (Tables 1 and 2). The uptake was significantly greater than normal in this group as a whole ($p < 0.001$). It is of note that 9 of 15 patients in this group had HLA-B27 in the blood, a much higher incidence than normal.

Of the 26 patients with rheumatoid arthritis examined, two had both radiologic and scintigraphic evidence of sacroiliitis. This finding was not the rule, but the mean si/s ratio measured 1.26, and was significantly greater than normal ($p < 0.001$).

Patients with psoriatic arthropathy varied in the extent of uptake of radiotracer at the sacroiliac joints. However, those with clinical evidence of a stiff back had uniformly increased si/s ratios (Tables 1 and 2), with a mean significantly greater than normal ($p < 0.001$).

Many patients with uveitis, ulcerative colitis, Crohn's disease, or Reiter's syndrome had scintigraphic evidence of sacroiliitis, with radiographic findings normal in some and abnormal in others (Tables 1 and 2). An unusual feature of the patients with Reiter's syndrome was the striking asymmetry between the sacroiliac joints. This was encountered occasionally but less consistently in the other diseases mentioned.

Whatever its conceptual significance might be, we

TABLE 2. THE MEAN, RANGE, AND STANDARD DEVIATIONS OF THE SACROILIAC RATIOS IN THE PATIENT GROUPS*

	Numbers of patients	Sacroiliac/sacral ratios		Standard deviation	% of observations greater than 95% of normal range
		Mean	Range		
Normal	39	1.11	0.94–1.34	0.064	0
Nonspecific mechanical back pain	9	1.05	0.84–1.34	0.095	0
Osteoarthrosis	8	1.02	0.81–1.29	0.059	0
Suspected AS (x-ray 0/1)	17	1.43	1.01–2.14	0.230	80
Definite AS					
X-ray Grade 2	44	1.54	1.12–2.80	0.287	81
X-ray Grade 3	14	1.12	0.90–1.64	0.141	15
Psoriatic arthropathy	18	1.21	0.96–1.84	0.246	47
Psoriatic arthropathy with back symptoms	9	1.45	1.34–1.84	0.150	94
Reiter's syndrome	13	1.37	1.05–1.74	0.121	67
Crohn's disease and ulcerative colitis	5	1.40	1.36–1.73	0.060	100
Rheumatoid arthritis	26	1.26	0.83–1.52	0.157	53
Uveitis	11	1.47	1.05–2.12	0.276	68

* The percentage of observations in each group differing from 95% of normal observations is also tabulated together with the number of patients in each group.

considered the possibility that scintigraphic evidence of sacroiliac disease might be a physical marker associated with the presence of HLA-B27 itself. In 49 patients having HLA-B27 in the blood, the mean si/s ratio appeared to be 1.43 against 1.40 in those who did not. This difference, however, is not significant. In making this analysis patients with radiologic Grade 3 sacroiliitis were excluded, since this represents end-stage disease not necessarily characterized by a scintigraphic abnormality.

In 38 of the patients described, repeat observations were made and the si/s ratios thus obtained correlated significantly ($p < 0.001$).

DISCUSSION

The advent of a newer series of bone imaging agents that are associated with acceptable radiation doses to the skeleton has led to their evaluation in nonmalignant diseases of bone and joint.

In this study we report a technique for the objective evaluation of sacroiliac disease. The subjective difficulties in the radiologic evaluation of sacroiliitis have been referred to (*1,2*). Our scintigraphic findings have been consistently abnormal in patients with definitely active AS. As might be expected, end-stage ankylosis of the sacroiliac joint is not always associated with an abnormal degree of uptake of the radiotracer at these joints. Thus the scintigram, if it is to contribute to diagnosis, will do so in the diagnosis of early or indeterminate disease.

Where repeat examinations have been possible, the ratios derived have been found to be reproducible. This was in some respects a surprising fact, since the group of patients included some in whom the si/s ratios fell towards normal accompanying the development of end-stage obliterative sacroiliac disease as observed radiologically. It is this aspect of the natural history of the disease that has made us cautious about the use of the si/s ratio as a measure of the efficacy of a particular treatment, although this had been one of our original intentions. It cannot be too strongly stated, however, that data analysis, such as we have used, requires the most careful attention to the many variables contributing to a bone scan—including dose, time of imaging, and radiopharmaceutical quality control (*17,18*). It is equally important that any laboratory anticipating use of this technique should determine a normal range of si/s values under the operating conditions prevailing therein.

Abnormal scintiscan findings observed in patients with the clinical suspicion of early AS are of interest. Such patients with normal x-rays have nevertheless, in many cases, been shown to possess the histocompatibility antigen HLA-B27. There is, therefore, a strong presumption that the technique will prove to be of value in early diagnosis, and the present patients are being followed to determine this. Indeed, in one patient presenting with a long history of low-back pain and limited movement with no progressive disability, scintigraphic examination of the sacroiliac joints was abnormal yet the x-rays have remained normal for more than 5 years. It may be that bone scintigraphy will allow the definition of a group of patients with clinical but not radiological sacroiliitis which, although recognized, has hitherto been difficult to categorize (*19*).

Regarding the use of strontium-87m, van Laere (*5*) has pointed out some diagnostic limitations of scintigraphy, in that in the very young there is a normal increase in uptake of the radiotracer at the sacroiliac joints, presumably reflecting the immaturity of the joint, which can be appreciated radiologically and which has been elegantly described by Jacobs (*1*). This is also our experience, and the numerical values reported here would not be applicable below about age 20, the age of maturation of the sacroiliac joint.

For any quantitative laboratory technique each laboratory needs to define specific values for normal and abnormal, with respect to detection equipment, radiotracer, and other variables. We have not recognized, however, any difference between Tc-99m PP_x and Tc-99m PP_i when due allowance is made, in the time between injection and scintigraphy, for the slight differences in clearance from the blood. It has been pointed out that not only is Tc-99m PP_i probably the breakdown product of Tc-99m PP_x in vivo (*20*), but that all the many analogues of this generation of bone-scanning agents are sufficiently alike and efficacious (*21*) that the technique will be readily adaptable to any particular laboratory practice.

As our experience with this technique enlarges, we also recognize that a further limitation of the method we propose is its nonspecificity. Thus abnormal findings have been encountered in certain patients with osteoarthrosis as well as in the several diseases described (Tables 1 and 2). In these situations the abnormalities are often asymmetrical, and there are other findings to indicate the correct diagnosis. Indeed it is one of the characteristics of bone scintigraphy in all its applications that the findings are not specific. Nevertheless the value of a technique that can support or modify the clinical impression that a patient suffers from sacroiliac disease, and possible early AS, does not need emphasis.

We have concerned ourselves here with the pragmatic application of bone-scanning methods to diagnosis. A firm understanding of the implications of altered uptake of the radiotracer at the sacroiliac

joint must await a clearer understanding of the factors involved in producing an abnormal bone scan (*22–24*). Suffice it to say that currently the evidence suggests that hyperemia may contribute to the abnormal accumulation of radiotracer, but that the deposition itself is in relation to the larger surface area of immature crystal in new bone. Whatever the cause of AS, there is radiographic evidence that new-bone formation is an epiphenomenon associated with the disease in the axial skeleton and this is presumably, at least in part, being reflected in the abnormal scintigram.

SUMMARY

Bone scintiscans obtained with either Tc-99m PP_x or Tc-99m PP_i have proven to be consistently abnormal at the sacroiliac joints of patients with radiologically confirmed, active AS. A profile sweep of the sacroiliac joints and sacrum has been used to detect and measure the degree of abnormality at the sacroiliac joints in an objective manner.

The finding of increased sacroiliac-to-sacral ratios in patients who are clinically suspected to have AS or Reiter's syndrome, but who have normal pelvic x-rays, is of note. In both groups of patients we have found an association between the detection of sacroiliitis and the presence of the histocompatibility antigen HLA-B27. In addition, sacroiliitis was detected in patients with psoriasis, uveitis, and Crohn's disease, some of whom had normal x-rays. These diseases are also known to be associated with sacroiliac involvement. This suggests that the radionuclide approach is more sensitive than conventional radiography in the detection of sacroiliac disease.

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