# Bone Scanning of Limited Value for Diagnosis of Symptomatic Oligofocal and Multifocal Osteonecrosis

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***ABSTRACT.*** ***Objective.*** Bone scintigraphy has been advocated as a useful diagnostic tool for patients with suspected osteonecrosis or in screening for multifocal disease. We evaluated the sensitivity of bone scanning relative to magnetic resonance imaging (MRI) in the diagnosis of osteonecrosis.

***Methods.*** Forty-eight patients presented with suspected osteonecrosis of the shoulder, hip, knee, or ankle. All patients underwent simultaneous (< 3 months apart) bone scans and MRI studies as part of diagnostic investigations. Histological confirmation of osteonecrosis was obtained for all suspected lesions. The diagnostic result for each imaging modality was then assessed and compared.

***Results.*** All 163 (100%) histologically confirmed lesions were identified by MRI, while only 91 lesions (56%) were identified by bone scan. There was complete congruency of bone scans with MR images in only 38% of patients (18/48). Bone scanning identified 72% of lesions (47/65) in oligofocal patients (≤ 2 joints involved) compared with 45% of the lesions (44/98) in multifocal patients (≥ 3 joints involved). Sensitivity of lesions was highest for the knee and hip and lower for the shoulder and ankle. Larger and later-stage lesions had a higher bone scan sensitivity.

***Conclusion.*** Our results demonstrated the low sensitivity of bone scintigraphy for diagnosing symptomatic osteonecrosis. It is least sensitive for early-stage lesions where it might be most useful to diagnose the disease. Our study also confirms that this test is less sensitive for joints other than the hip and is also not useful as a screening tool. Our study does not support the use of bone scans as a diagnostic or screening tool for osteonecrosis. (First Release June 1 2008; J Rheumatol 2008; 35:1629–34)

*Key Indexing Terms:*
OSTEONECROSIS BONE SCAN MAGNETIC RESONANCE IMAGING
AVASCULAR NECROSIS OUTCOME DIAGNOSIS

Osteonecrosis is a devastating disease that typically afflicts a young patient population. The disease can affect various joints such as the knee, shoulder, and ankle, although it most commonly involves the hip. Radiographs are often initially used to diagnose osteonecrosis. If disease is apparent radiographically, then often no other imaging or screening tests are necessary. However, disease often may not be detectable in early stages because radiographic abnormalities appear only after prolonged changes in ischemic tissue. As a result, other diagnostic methods including bone marrow pressure measurements, intramedullary venography, and biopsies have been utilized for detecting early ischemic changes in bone[1]. As imaging technology developed, investigators recorded varying degrees of success at detecting osteonecrosis with multiple imaging techniques, including bone scanning, computed tomography (CT), single-photon emission CT, and magnetic resonance imaging (MRI)[2-5]. These additional tests are needed to investigate early changes of the contralateral hip or to investigate other symptomatic joints. If these joints can be diagnosed early, there is the best chance for treatment aimed at saving the bone from collapse and requiring joint replacement.

Bone scanning has been advocated as a useful diagnostic tool for patients with suspected osteonecrosis of the femoral head. Before the advent and utilization of MRI, scanning was believed to be a more sensitive diagnostic test than standard radiographs for early detection of the disease[6-14]. MRI has been shown in multiple studies to be more sensitive than bone scanning for detection of osteonecrosis, some authors reporting 99% or higher sensitivity for this disease[2,15-18]. Despite this, many practitioners still use bone scans as an initial screening modality for detection of symptomatic or asymptomatic disease. Additionally, various authors have advocated the use of bone scanning for early detection of

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osteonecrosis of other joints or to screen for multifocal disease[3,9,11,19,20].

In clinical practice, we found that bone scintigraphy often missed lesions that were diagnosed on radiographs and MR images. This led us to investigate the utility of bone scanning in diagnosis or screening of osteonecrosis. Specifically, we compared the diagnostic sensitivity of bone scanning with that of MRI in patients presenting with suspected atraumatic osteonecrosis in various joints who also had confirmed osteonecrosis on bone histological evaluation after surgical procedures.

## MATERIALS AND METHODS

*Study design and inclusion criteria.* Between January 1, 1994, and November 23, 2005, 48 patients presenting to 2 institutions who underwent simultaneous (i.e., within 3 months) radiographs, bone scans, and MRI studies as part of diagnostic investigation for possible symptomatic osteonecrosis of the hip, knee, shoulder, or ankle were included in the study. There were 33 women and 15 men, mean age 39 years (range 20–76 yrs). All patients had histological confirmation of osteonecrosis from tissue obtained by various surgical procedures (core decompression, bone grafting, joint replacement) within 3 months of the imaging studies as well. We retrospectively assessed the diagnostic result for bone scanning and compared it to MRI results.

Patients were selected for diagnostic imaging and inclusion in the study based on a number of inclusion and exclusion criteria. The patient had to be at least 18 years of age and have had deep joint pain associated with either 2 or more known risk factors for osteonecrosis or prior radiographic evidence of osteonecrosis in at least one other joint. Patients who had trauma-associated lesions were excluded. Patients were also excluded if all diagnostic imaging was not completed within a 3-month period from the date of the first test procedure. Patients with endstage osteoarthritis (Ficat and Arlet; stage IV) with femoral head collapse and acetabular involvement were not included. Patients were later stratified into 2 cohorts: oligofocal osteonecrosis ($\leq$ 2 joints involved) and multifocal osteonecrosis ($\geq$ 3 joints involved).

From the outset, we did not use positive MRI scans as the key to the diagnosis. Seventeen of the patients had MRI scans (to delineate locations of lesions) after the diagnosis had been made with radiographs, bone scans, and clinical measures. Since we found that all lesions had a positive MRI (no false-positives), we retrospectively reanalyzed the cases to determine if there was an MRI bias that would clarify them as cases of osteonecrosis (positive radiographs, clinical factors, bone scans, histological confirmation). Therefore, for the initial selection of patients and further analysis, we do not believe there was a selection bias for only MRI-positive patients.

A clinical and radiographic review was performed to assess whether any variables were associated with positive bone scans. Hospital outpatient records were analyzed with respect to demographic data, including patient's age at presentation, sex, associated diseases, and other factors known to increase the risk of osteonecrosis such as alcohol abuse (> 400 ml of 100% absolute ethanol per week), tobacco use, and use of prednisone (or equivalent other corticosteroid medication) in doses exceeding 2 g[3,21-25]. Associated diagnoses included systemic lupus erythematosus (SLE) in 10 patients, inflammatory bowel disease in 3, breast carcinoma in 2, connective tissue disorders in 2, renal disease in 3, and one patient each with idiopathic thrombocytopenic purpura, arteriovenous malformation, Hodgkin's lymphoma, T-cell acute lymphoblastic leukemia, and asthma. Nine patients had a history of alcohol abuse and 8 patients smoked more than 1 pack of cigarettes per day.

*Radiographic and histological assessment.* All MR imaging was performed using T1-weighted spin-echo images [echo time (TE) 15–20 ms; repetition time (TR) 150–200 ms] and T2-weighted spin-echo images (TE 80–90 ms; TR 2000–2500 ms) obtained in the coronal, sagittal, and axial planes. MR images were interpreted by a radiologist, with equivocal cases interpreted by another radiologist specializing in bone diseases. Images were considered positive for osteonecrosis if areas of low signal intensity in the weight-bearing portion of the affected bone were noted.

For bone scans, all patients were injected intravenously with 20 to 30 mCi $^{99m}$technetium methylenediphosphonate. Immediate flow images as well as static images of the skeleton were obtained. Anterior and posterior planar whole-body delayed images were obtained 3 h after injection. Findings by bone scan were considered compatible with a diagnosis of osteonecrosis when increased or decreased activity was observed in the humeral or femoral head, distal femur, proximal or distal tibia, or talus.

Histological confirmation of osteonecrosis was obtained for each suspected lesion, and this was considered the "gold standard" for comparison purposes. Histological material was obtained from bones during one of the following procedures: core decompression (n = 122), total hip arthroplasty (n = 13), limited femoral resurfacing (n = 14), various bone grafting procedures (n = 6), total knee arthroplasty (n = 3), shoulder hemiarthroplasty (n = 3), or ankle arthrodesis (n = 2). Specimens were fixed in 10% neutral buffered formalin and decalcified in a solution of formic acid and sodium citrate. Sections were cut at 4 μm thickness and were stained with routine hematoxylin and eosin. All specimens were classified by a bone pathologist as Type III or IV osteonecrosis by the classification system of Arlet and Durroux[26]. This represents medullary and trabecular necrosis without repair (Type III) and bone formation in apposition to dead trabeculae (Type IV).

Anteroposterior and lateral plain radiographs obtained at presentation were used to stage all symptomatic-positive joints by the Ficat and Arlet system, which was originally described for use in the hip but can be applied to any joint (Table 1)[1,27]. All positive lesions were stratified by lesion size by the radiographic method of Kerboul and co-workers[28] or by MRI volumetric analysis as described[29]. Lesions were classified as small (< 15%), medium (15% to 30%), and large (> 30%). Ficat and Arlet staging and size of lesion analysis were performed to evaluate if there was an association of the size of the lesion with positive bone scans.

*Statistical methods.* The data were compiled utilizing an Access 7.0 database (Microsoft, Redmond, WA, USA). Descriptive statistics were calculated. Histological diagnosis of osteonecrosis was used as the gold standard for assessing sensitivity of the imaging studies. Sensitivity was calculated with 95% confidence intervals and defined as the number of true-positives divided by the sum of the number of true-positives plus the number of false-negatives. Chi-square analysis with Yates' correction was performed to determine if differences between frequencies for different groups were statistically significant. All analyses were performed using Program for Epidemiologic Analysis (PEPI) software, version 2.03 (USD Inc., Stone Mountain, GA, USA).

## RESULTS

We identified 48 patients who met the inclusion and exclusion criteria. Overall, 163 lesions were identified by MRI and histology, while only 91 lesions were identified by bone scan ($p = 2.56 \times 10^{-21}$). The sensitivity of the bone scan was 55.8%. None of the lesions were identified by bone scanning

*Table 1.* Ficat and Arlet staging system.

| Stage | Radiographic Findings |
|---|---|
| I | None (only evident on MRI) |
| II | Diffuse sclerosis, cysts (visualized on radiographs) |
| III | Subchondral fracture (crescent sign; with or without head collapse) |
| IV | Femoral head collapse, acetabular involvement, and joint destruction (osteoarthritis) |

that were not observed on radiographs or MRI. All positive bone scans revealed increased flow and delayed activity, and no lesion was diagnosed on the basis of photopenic areas. There was complete consistency of bone scans with MR images in only 38% of patients (18/48).

Bone scanning identified a greater proportion of lesions (47/65, 72%) in oligofocal patients as compared to the multifocal patients (44/98, 45%; p = 0.001). In only 13 of 28 oligofocal patients and in only one of 19 multifocal patients were all of the lesions identified by bone scan. Stratification by joints involved revealed the highest yields for the knee (37/58 lesions, 64%) followed by the hip (37/61 lesions, 61%), with lower yields for the ankle (7/14 lesions), and shoulder (10/30 lesions, 33%) (p = 0.038; Figure 1).

A higher Ficat-Arlet stage led to a higher percentage of positive lesions. Overall, radiographic Stage I lesions had 19% positive bone scans (5/27), Stage II lesions had 56% positive scans (53/95), and Stage III lesions had 80% positive bone scans (33/41) ($p = 3 \times 10^{-6}$; Figure 2). Combining radiographically evident lesions (Stage II and III), of 136 cases, only 86 (63%) were positive on bone scans. Larger lesions also led to a higher percentage (41/58 positive scans, 71%) of positive bone scans versus medium-size (42/79 positive scans, 53%) and small (8/26 positive scans, 31%) lesions (p = 0.002; Figure 3).

There was no statistical difference in percentage of positive bone scans when lesions were subcategorized by patient sex, use of corticosteroids, diagnosis of SLE, or alcohol and tobacco use.

## DISCUSSION

The use of radionuclides in diagnosing femoral head osteonecrosis was introduced in the 1950s by Tucker and Boyd and associates using phosphorus-32[30,31]. Later investigation used strontium-85 in the late 1960s and early 1970s[10]. $^{99m}$Technetium was introduced in 1971 and continues to be used for standard 3-phase bone scans. These can show both deficient uptake in the femoral head (usually in posttraumatic cases of osteonecrosis) and increased uptake in the later stages of osteonecrosis[1]. Before the advent of MRI, studies compared bone scans to plain radiographs and found that bone scanning was more sensitive for early lesions. Conklin and co-workers compared the sensitivities of the 2 modalities in diagnosing osteonecrosis in patients with SLE. They found sensitivities of 89% (24/27) for bone scanning and 41% (11/27) for standard radiographs (the gold standard)[9]. A reason for the higher sensitivity in their study compared to ours is that their patients had SLE, which presents at later stages of disease and differed from the many earlier-stage (I and II) lesions as in our study.

Recently, studies have shifted to comparison of the diagnostic capabilities of MRI with those of bone scanning and other techniques. MRI was found to be more sensitive than bone scans and CT in scanning for early lesions by Mitchell, *et al* in a controlled statistical study[18]. Similarly, in a comparison by Markisz, *et al*, MRI had an overall sensitivity of 100% compared with 81% for bone scanning (37/37 and 30/37 hips, respectively)[17]. MRI was found to be better than bone scanning for the diagnosis of early osteonecrosis in 25 patients with suspected lesions by Bassett, *et al*, who reported that no false-negative MR images were found, but diphosphonate scans were negative in 9 hips with normal radiographic and abnormal MR images[15]. Hauzeur, *et al*[2] studied MRI, radiographs, and bone scans in 25 patients with suspicion for osteonecrosis in 49 hips. Thirty-three hips were confirmed positive by histological examination. Among these, every MRI test was always positive, while only 77% (24/31) of available bone scans showed any signs of osteonecrosis. Additionally, 22 (67%) radiographs and 18/29 (62%) available CT scans were positive[2]. Thus, these

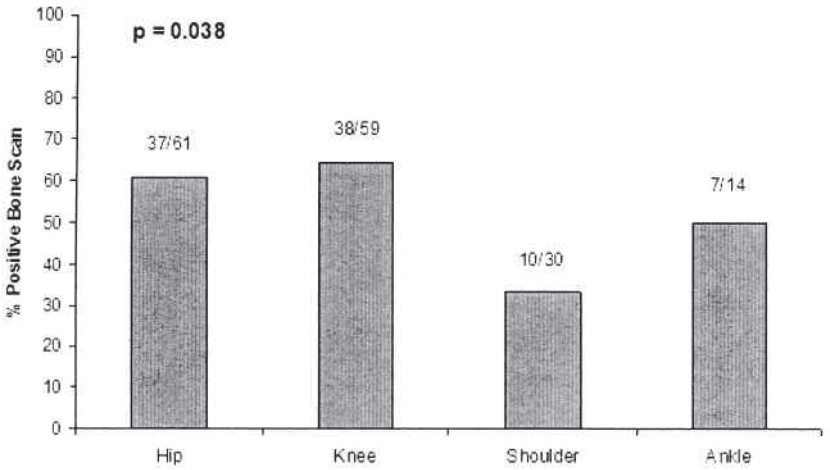


*Figure 1.* Bone scan findings classified by joints. Percentage of positive bone scans was lower for shoulders and ankles than for hips and knees. Nevertheless, each group had low sensitivity compared to MRI scanning (100%), ranging from 33% to 64%.

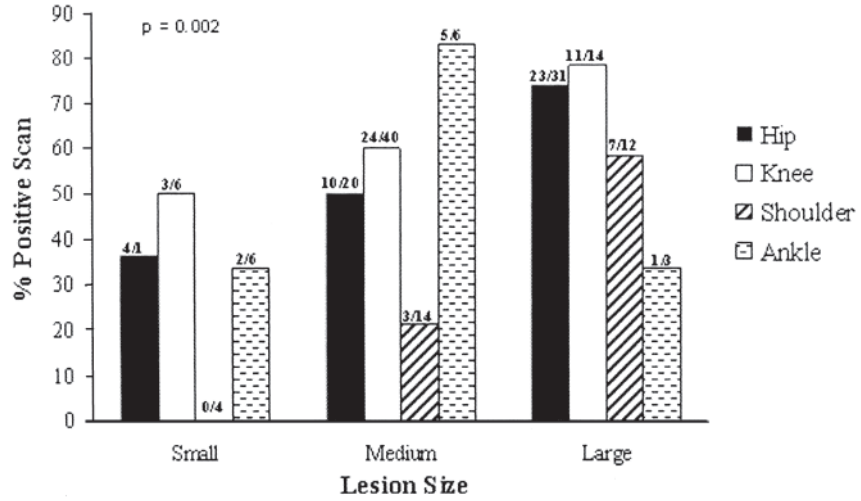


*Figure 2.* Positive bone scan results classified by lesion size. Larger lesions in general led to higher percentages of positive bone scans compared to medium-size or small lesions.

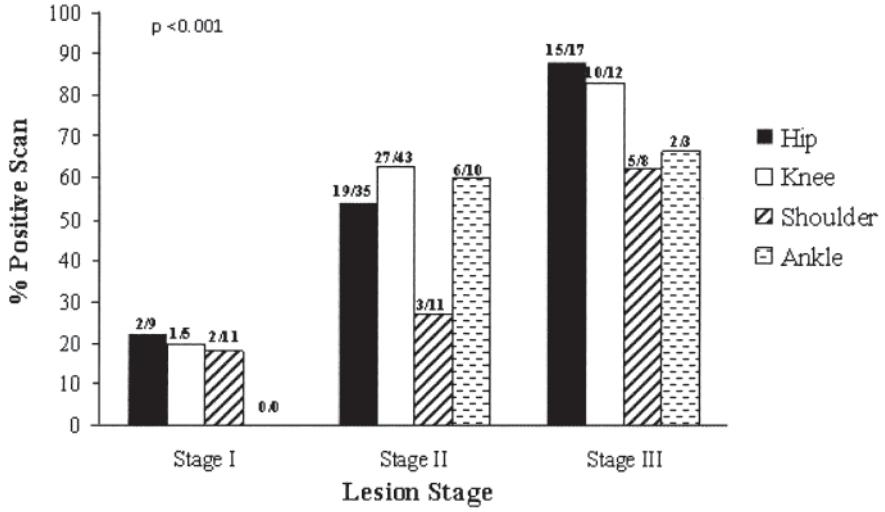


*Figure 3.* Positive bone scan findings stratified by the Ficat and Arlet stage. Higher stages of disease led to higher percentages of positive bone scans.

2 studies were similar to ours, in which MRI scans were 100% sensitive for osteonecrosis, with lower sensitivities for bone scanning. Other studies have found similar low-sensitivity bone scintigraphy results for the hip[16,32] or knee[20].

Some studies have reported bone scanning results more comparable to those of MRI. In a study by Steinberg of biopsy-proven hip osteonecrosis, the sensitivity, specificity, and accuracy of MRI were calculated to be 96%, 71%, and 91%, respectively, which were still superior to technetium scans (86%, 79%, and 85%), although neither test was completely accurate[4]. These results were not found in our study, in which MRI was 100% sensitive, with bone scanning detecting only 56% (91/163) of confirmed lesions. This may be because many tests in the Steinberg study involved MRI techniques and scanners from the 1980s. In a prospective study, Stulberg and co-workers[5] compared the multiple diagnostic modalities and calculated their respective sensitivity, specificity, and predictive values (positive and negative; Table 2). They concluded that since no imaging modality evaluated was completely accurate and since bone scanning was less expensive than MRI, the most cost-efficient initial method would be bone scans. Stulberg suggested performing MRI studies on all patients with symptomatic hips who had negative bone scans. However, since our data demonstrated that bone scanning did not detect 44% of the 163 lesions identified by MRI and histology, we disagree with this algorithm as a means of reducing the cost of a diagnostic investigation.

We believe that in our study many lesions were diag-

*Table 2.* Diagnostic modality comparison[5].

| Modality | Sensitivity | Specificity | Predictive Value (positive/negative) |
|---|---|---|---|
| Bone scan | 83 | 83 | 96/48 |
| MRI | 87 | 83 | 96/55 |
| SPECT | 87 | 83 | 96/55 |
| Interosseous pressure | 80 | 60 | 95/25 |
| Biopsy | 88 | 100 | 100/25 |

MRI: magnetic resonance imaging; SPECT: single photon emission computed tomography.

nosed in early stages of the disease (especially for joints other than the hip), which may be why the sensitivity is much lower than in previous reports where lesions were diagnosed at later stages. This is important because early diagnosis is imperative, as multiple studies have shown that femoral head preservation treatment in the early stages has the most efficacy.

Some limitations of our study are that it is a retrospective review of a small population of patients. Additionally, although all imaging tests were completed within a 3-month period for each patient, durations of time between the bone scans and MRI studies varied. These limitations can be corrected in the future with a prospective study on a larger patient cohort that minimizes variability in the diagnostic investigations. Despite these limitations, we believe our conclusions concerning bone scans are accurate.

Bone scintigraphy might be justified in regions where MRI scans are not available. It could possibly be used as a screening tool for the entire body, with caution (many joints missed), but we prefer to obtain MR images of the multiple symptomatic joints to rule out this disease. Claustrophobic patients might consider this test if "open-air" MRI are not available. Bone scintigraphy might be useful in situations where metal hardware or fixation would make MRI interpretation difficult. We cannot comment on the role of bone scanning in the diagnosis of asymptomatic patients.

We observed a lower sensitivity of bone scintigraphy than MRI in diagnosing symptomatic osteonecrosis and do not support its use for diagnosis of this condition. It was least sensitive for early stage I lesions, where it might be most useful to diagnose the disease for early treatment. The utility was less effective for joints other than the hip and we do believe it is useful as a screening tool.

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