

Comparison of Indium-111-labeled leukocyte scintigraphy and Technetium-99m joint scintigraphy in rheumatoid arthritis and osteoarthritis

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This study was undertaken to evaluate the use of Indium-111-labeled leukocyte (^{111}In -WBC) imaging compared with Technetium-99m pertechnetate ($^{99\text{m}}\text{TcO}_4^-$) imaging in 19 patients with rheumatoid arthritis (RA) and 8 with osteoarthritis. Knee and wrist joints were evaluated for both radionuclides. The results indicated a good correlation of the clinical assessment of pain and swelling with joint uptake ratio (JUR) between ^{111}In -WBC and $^{99\text{m}}\text{TcO}_4^-$ in RA and osteoarthritis patients. We observed a discrepancy in both imagings in "burned out" cases. It was concluded that a JUR of ^{111}In -WBC could distinguish active RA from inactive RA or osteoarthritis at a value of 1.15 and that the use of ^{111}In -WBC was a more reliable procedure than $^{99\text{m}}\text{TcO}_4^-$.

Key words: Indium-111-labeled leukocyte, Technetium-99m pertechnetate, rheumatoid arthritis, osteoarthritis, comparative studies

INTRODUCTION

VARIOUS METHODS have been used to assess inflammation in patients with rheumatoid arthritis (RA), both with regard to the severity of the disease and response to treatment. Joint imaging employing radiopharmaceuticals has been used as one such adjunctive tool for the detection of inflammatory joint disease. Historically, the first radiopharmaceutical employed was I-131 HSA,¹ followed by Tc-99m phosphate compound. Although imaging may show increased uptake in RA joints and may prove to be the most sensitive^{2,3} for the evaluation of RA, these cases must already have advanced to a stage where

there is involvement of the periarticular bone.⁴ These compounds are non-specific as increased periarticular accretions are found in degenerative osteoarthritis, metabolic bone disease and trauma.⁵ Tc-99m pertechnetate ($^{99\text{m}}\text{TcO}_4^-$) could be used to reflect the degree of inflammatory involvement.⁶ $^{99\text{m}}\text{TcO}_4^-$ is a blood pool and extracellular-fluid space tracer and its accumulation consists of diffusion into intracellular water and selectively in inflammatory exudate because of its increased protein content.⁷ With the introduction by Thakur et al.⁸ of an In-111 label for leukocytes, a new tool became available for the evaluation of suspected inflammatory processes. In 1986 we introduced In-111 labeled leukocyte (^{111}In -WBC) imaging. This method utilized autologous peripheral blood leukocytes, and provided results consistent with known acute cellular exudation and rapid turn over of leukocytes in rheumatoid synovial fluid on the images.⁹ This study was designed to assess the utility of ^{111}In -WBC imaging compared

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with $^{99m}\text{TcO}_4^-$ for the detection of inflammatory joints and for the differentiation of joints with RA and osteoarthritis.

MATERIALS

Nineteen patients (3 male and 16 female) with classical or definite RA (American Rheumatism Association (ARA) criteria) and eight patients with osteoarthritis were investigated. The age range with RA was 37 to 73 years (average 57 years). The radiographic stage of disease by ARA criteria ranged between I and IV.¹⁰ All patients had had drug treatment; 9 had received steroids and 10 had non steroidal therapy prior to imaging. The criteria of active RA was defined clinically from the clinical assessment of pain and swelling, leukocytosis and promotion of ESR. None of these patients had an infected joint as determined by their clinical course, laboratory data and/or synovial fluid culture.

METHODS

The leukocyte harvesting and labeling were prepared by the following method.¹¹ Forty milliliters of heparinized whole blood was obtained from each patient. The red blood cells were allowed to sediment for 30 min to 1 hour. The resultant leukocyte rich plasma was removed and centrifuged at 450 G for 5 min. The leukocyte pellet was washed twice in saline, resuspended and incubated with In-111 oxine or tropolone for 20 min at room temperature.

The condition of wrist and knee joints was evaluated by the accumulation of both ^{111}In -WBC and $^{99m}\text{TcO}_4^-$. Anterior and posterior joint images of each patient were taken for 200 sec at 15 min after the intravenous administration of 37–111 MBq (1–3 mCi) of $^{99m}\text{TcO}_4^-$ using a low-energy parallel-hole collimator. This was followed by the administration of 11.1–18.5 MBq (0.3–0.5 mCi) of ^{111}In -WBC without plasma. Imaging of ^{111}In -WBC was performed for 400 sec at 24 hours using a medium-energy parallel-hole collimator and dual energy settings at the 173 and 247 keV photopeaks of Indium with a 10% window.¹² The images obtained were analysed by computer (Toshiba GMS-80, Nova-3) and the amount of activity in a similar area of the proximals of both the thigh and arm to the joint, and an area over the knee and wrist joints, was measured in counts/pixel providing a joint/thigh or arm ratio; namely the joint uptake ratio (JUR) (Fig. 1).

RESULTS

The incidence of pain and swelling in wrist and knee joints was compared with the accumulation of ^{111}In -

WBC and $^{99m}\text{TcO}_4^-$. The accumulation of ^{111}In -WBC showed better correlation with the activity of inflamed joints determined by the clinical signs of both pain and swelling than $^{99m}\text{TcO}_4^-$. Two wrist joints without pain and swelling revealed false positive images of ^{111}In -WBC and their JURs were border line abnormal (JUR: 1.16, 1.17). There seemed to be little correlation between the radiographic stage of the disease and the accumulation of ^{111}In -WBC and $^{99m}\text{TcO}_4^-$ (Fig. 2).

JURs of wrist and knee joints in RA and osteoarthritis patients, excluding burned out joints, showed correlation coefficients of $r=0.697$ and $r=0.534$ between ^{111}In -WBC and $^{99m}\text{TcO}_4^-$ respectively. We could clearly distinguish active RA or osteoarthritis with a minimum JUR of 1.15 using ^{111}In -WBC (Figs. 2, 3).

This value was set as a matter of convenience to divide patients clearly into two groups. A burned out case of classical RA (Stage III, class 3) showed a discrepancy in accumulation between ^{111}In -WBC and $^{99m}\text{TcO}_4^-$, with JURs of 1.07 and 1.62 on the right knee, respectively and 0.98 and 1.41 on the left knee, respectively. An X-ray examination of both knee joints revealed a narrowing of the joint space with bone atrophy, marginal erosion, and destructive change (Fig. 4).

DISCUSSION

This study was designed to assess the utility of ^{111}In -WBC imaging compared with $^{99m}\text{TcO}_4^-$ for the detection of inflammatory joints and for the differentiation of joints with RA and osteoarthritis. We therefore chose both wrist and knee joints for contrast since the former is not a weight bearing joint, and the latter is. From the results of JURs, wrist joints showed better correlation coefficients than knee joints (Figs. 3, 4). We thought the accumulation of $^{99m}\text{TcO}_4^-$ in knee joints was largely due to an increased vascular pool, and extravascular accumulation in the thickened and inflamed synovium was higher in knee joints with osteoarthritic changes than in wrist joints.

On the other hand, ^{111}In -WBC provided results consistent with known acute cellular exudation and rapid turn over of leukocytes in rheumatoid synovial fluid on the images. Hence ^{111}In -WBC was more accurate for the detection of inflammatory joints (Fig. 2). Al-Janabi et al.¹² demonstrated that white cell uptake is a specific phenomenon in the rheumatoid knee joint and not just a blood pool effect. We support these results from our data. Of course there was a difference in the uptake of $^{99m}\text{TcO}_4^-$ and ^{111}In -WBC in patients with burned out stages of RA or osteoarthritis. In view of these results, ^{111}In -WBC

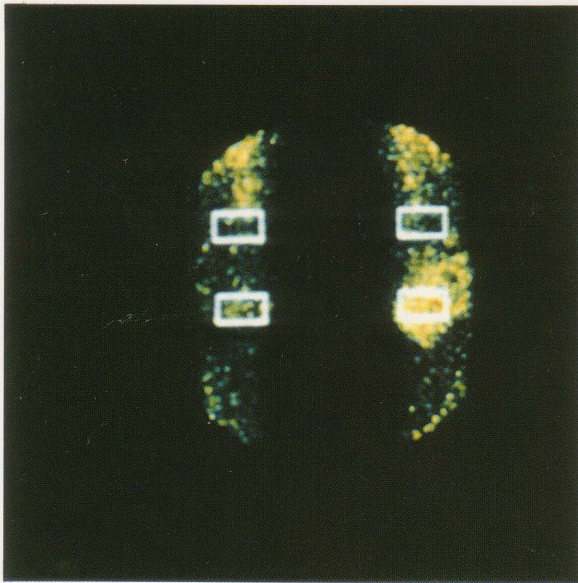


Fig. 1 JUR was obtained by comparing the amount of activity within regions of interest over the knee and wrist joints and an area of the arm and the proximal thigh.

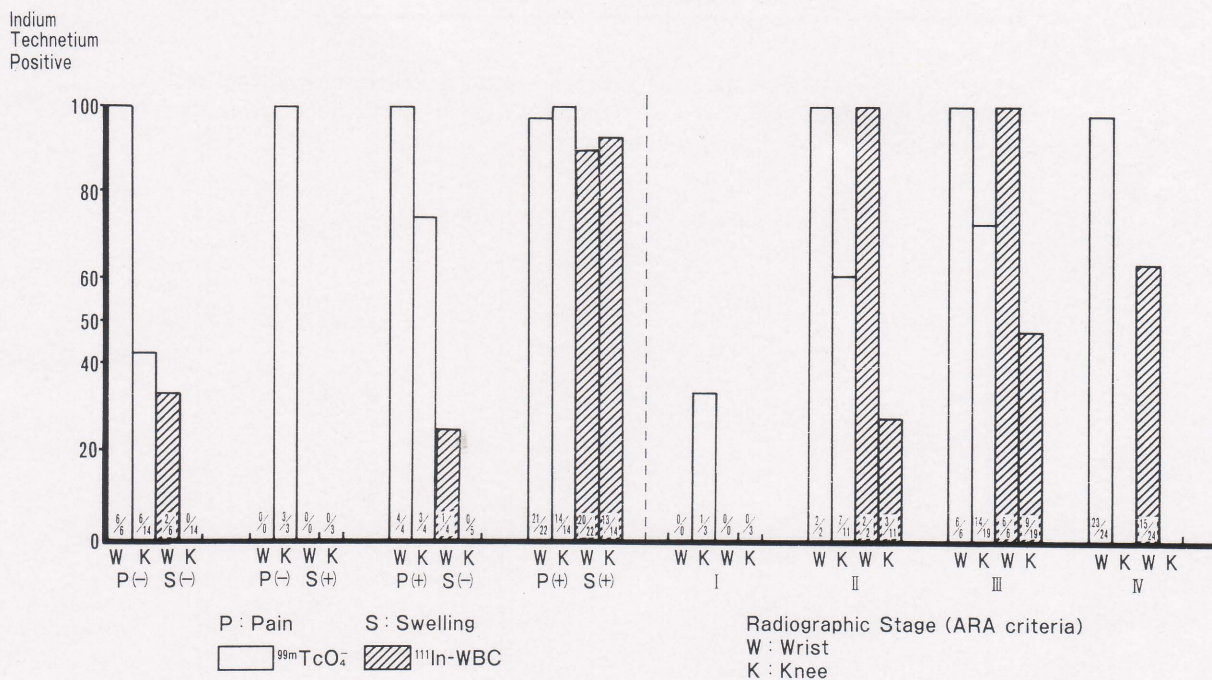


Fig. 2 Clinical signs, bone changes and accumulation of ¹¹¹In-WBC and ^{99m}TcO₄⁻. Accumulation of ¹¹¹In-WBC showed greater correlation with the activity of inflamed joints determined by the clinical signs of both pain and swelling than ^{99m}TcO₄⁻. Accumulation of ¹¹¹In-WBC and ^{99m}TcO₄⁻ showed similar distribution by radiographic stage.

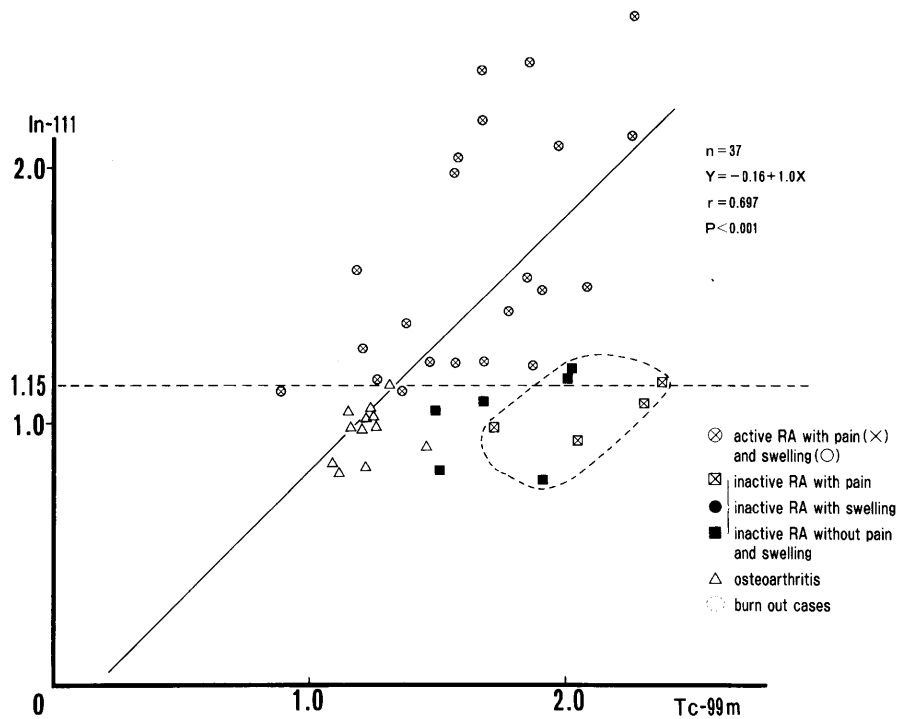


Fig. 3 Distribution of JUR of the wrist is dependent on the clinical assessment of pain and swelling for ^{111}In -WBC and $^{99\text{m}}\text{TcO}_4^-$. There was a good correlation between them in both RA excluding burned out cases, and osteoarthritis.

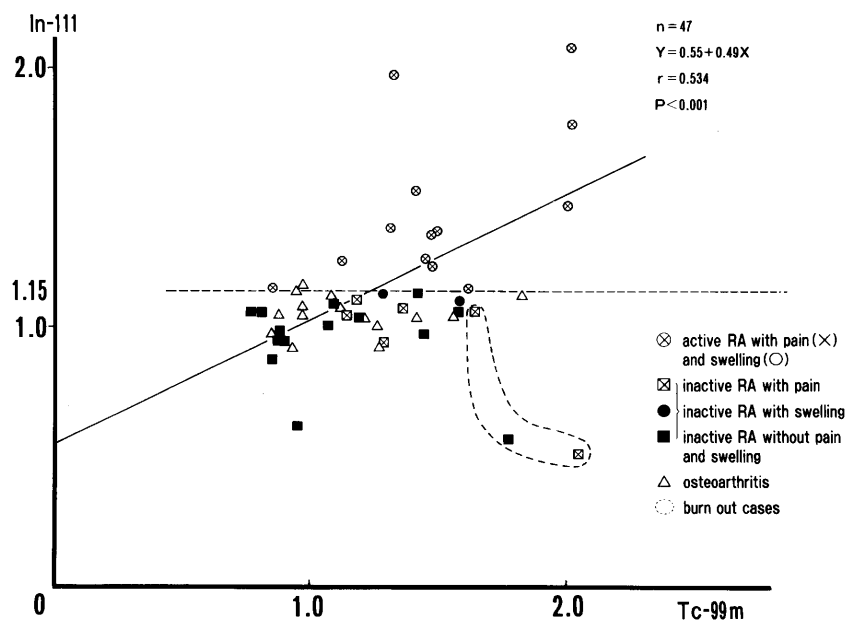


Fig. 4 Distribution of JUR of the knee is dependent on the clinical assessment of pain and swelling for ^{111}In -WBC and $^{99\text{m}}\text{TcO}_4^-$. There was a fair correlation between them in RA excluding burned out cases and osteoarthritis. We could clearly distinguish active RA from inactive RA or osteoarthritis by the JUR of ^{111}In -WBC at a point of 1.15.

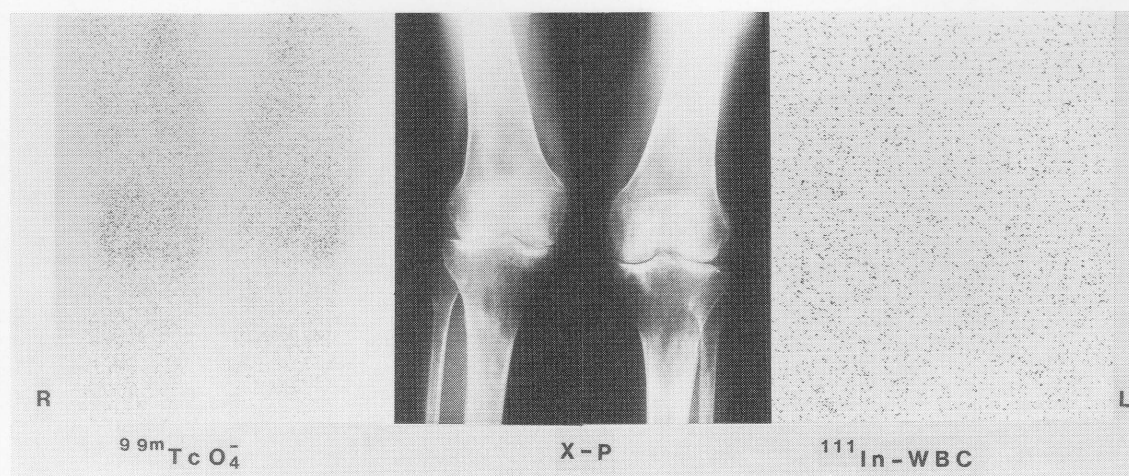


Fig. 5 A burned out case of classical RA (Stage III, class 3). A difference in the accumulation of $^{111}\text{In-WBC}$ and $^{99\text{m}}\text{TcO}_4^-$ could be seen.

was thought to reflect the presence of leukocytes, and was a more specific procedure to use in estimating the activity of RA, in spite of being a more complex procedure than $^{99\text{m}}\text{TcO}_4^-$ imaging. It also aided in differentiating between osteoarthritis and active RA with pain and swelling. The leukocytes used here were mixed, but most of the labeled leukocytes were granulocytes. A limitation of $^{111}\text{In-WBC}$ imaging is considered to be the high radiation dose to the spleen, and many repeated examinations for follow up should be avoided. $^{99\text{m}}\text{Tc}$ labeled leukocyte imaging appears to be a promising procedure, but there may remain problems related to taking quantitative measurements of joints inflammation.¹³

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