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Tc99m Methotrexate (MTX) A Novel Complex for Imaging of Rheumatoid Arthritis (RA): First Clinical Trials

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Abstract

Introduction: Methotrexate (MTX) is being used for treatment of rheumatoid arthritis (RA) and a variety of other inflammatory joint diseases.

Methods: The aim of the present study was to use Tc^{99m} labeled MTX as imaging agent in rheumatoid arthritis. Labeling efficiency was studied with paper chromatography (PC) and Instant thin layer chromatography (ITLC) and found it to be 99.8%±0.2. We then tested the radiopharmaceutical on five diagnosed patients of RA. Percentage of ID (%ID) uptake in the major joints was evaluated in all patients. For this we first developed normal %ID data for major joints in 14 volunteers who underwent conventional Tc^{99m}-MDP bone scintigraphy. Then normal %ID data was calculated in five normal subjects for Tc^{99m}- MTX as well for future comparison with patient data.

Results: Scintigraphic results showed excellent selective tracer uptake of Tc^{99m}-MTX in all effected joints of patients which correlated well with the conventional bone scan data as well. High T/NT ratios were highest for Tc^{99m}-MTX when compared with Tc^{99m}-MDP.

Conclusions: Tc^{99m}-MTX is a promising imaging agent for RA and it also predicts sensitivity of disease to Methotrexate. This agent can also be used for follow up of disease as it can pick active disease or residual disease even during the course of treatment.

Implications for patient Care: This method will help to identify the patient who shall be sensitive to MTX treatment and further will help for response evaluation during therapy.

Introduction

Methotrexate (MTX) is an antimetabolite and antifolate drug. It is used in the treatment of **cancer**, **autoimmune diseases**, **ectopic pregnancy**, and for the induction of medical **abortions [1]**. It acts by inhibiting the metabolism of **folic acid**. In the 1970's, methotrexate was considered an experimental treatment for rheumatoid arthritis, it is now an FDA-approved drug for patients with RA [2].

Rheumatoid arthritis (RA) is a chronic, inflammatory type of arthritis. The primary symptoms associated with rheumatoid arthritis include joint pain, joint swelling or effusion, joint stiffness, redness and/or warmth near the joint and restricted range of motion. Morning stiffness lasting more than an hour, involvement of the small bones of the hands and feet, extreme fatigue, rheumatoid nodules, and symmetrical joint involvement (i.e. both knees not one knee) are all characteristics of rheumatoid arthritis [3]. Methotrexate is known as a disease-modifying anti-rheumatic drug (DMARD), because it not only decreases the pain and swelling of arthritis, but it can also decrease damage to joints and long-term disability. Improvements in arthritis and other conditions usually are first seen in 3-6 weeks with full benefits often seen after 12 weeks of treatment. There is no single laboratory test or x-ray which can diagnose rheumatoid arthritis. A combination of test results, a clinical examination, and patient medical history together can help determine a diagnosis of rheumatoid arthritis. Laboratory tests which are commonly ordered to help diagnose rheumatoid arthritis include rheumatoid factor, erythrocyte sedimentation rate, anti-CCP test and C - reactive protein. X-rays and MRIs are also ordered early on to help with the diagnostic process and throughout the course of the disease to check on the effectiveness of treatment. There is a little role of bone scan imaging of RA nevertheless to localize the affected joint however clinical examination correlates well the results of bone scan [3].

Materials and Methods

All chemicals used for this research were analytically derived from the following sources: Methotrexate, stannous chloride, ascorbic acid and sodium citrate were purchased from Aldrich, USA. Technetium-^{99m} generator was purchased from Pakistan Institute of Nuclear Science and Technology (PINSTECH), Pakistan and saline from Ostuka, Pakistan. Kits were prepared using modified method developed at INOR to increased stability, shelf life and labelling efficiency of MTX with Tc^{99m} especially for rheumatoid arthritis. Affinity and specificity of MTX of earlier method has already been validated in the published [4].

Patient Selection

Fourteen normal volunteer subjects with mean age of 53.5 and a range of 40 to 62 years were selected to study normal percentage injected dose (%ID) of ^{99m}Tc-MDP bone scan in various joints, Five

normal volunteers with mean age of 47 years and a range of 25 to 62 years were selected to study normal biodistribution and %ID of ^{99m}Tc-MTX in various joints of body. These volunteers served to develop normal %ID data for each joint with ^{99m}Tc-MTX, allowing for comparison with patients of the local population. Five patients with mean age of 47 years ranging from 26 years to 60 years and diagnosed Rheumatoid Arthritis were selected for this study at Institute of nuclear medicine oncology and radiotherapy (INOR) according to the guidelines published in 2010 by the American College of Rheumatology (ACR).

Disease score of more than 6 as defined by ACR was taken as gold standard. The selected patients were diagnosed cases and patient no 2 and 3 were already receiving treatment. None of the patients had history of allergy. The study was approved by our ethical review board according to international guidelines and in accordance with the precepts established by the Helsinki Declaration. Each patient gave his/her written consent after being fully informed about the procedure. Patient's history is shown in (Table 1).

	History
Patient 1	A 54 year old male with history of pain in multiple joints and morning stiffness for last one year. X-ray showed mild arthritic changes in wrists, knee joints and bilateral ankle joints. Qualitative RA factor was positive. ACS scoring done by rheumatologist was 08. No treatment was yet started.
Patient 2	A 42 year old female, diagnosed case of Rheumatoid Arthritis was on treatment i.e. methotrexate, steroids and intra-articular injection of hyaluronic acid. Qualitative RA factor was positive. ACS score done by rheumatologist was 06.
Patient 3	A 60 year old female with history of pain in all major joints for last 18 months. Qualitative RA factor was positive and she was on oral Methotrexate treatment. ACS score done by rheumatologist was 06.
Patient 4	A 26 year young female presented with pain in multiple joints. RA factor was positive. Took methotrexate for 1 year and improved significantly but left treatment for last six months and presented with tender wrist, shoulders and knee joints. ACS score done by rheumatologist was 08.
Patient 5	Middle aged female of 52 diagnosed case of RA and took NSAIDs only for pain relief. ACS score done by rheumatologist was 07.

Table 1: Patient history

Study Protocol

Before starting imaging studies (X-ray of involved joints), routine blood and biochemical lab tests of all patients including complete blood count (CBC), ESR, liver function tests (LFTs), urea and creatinine were determined. Besides these clinical investigations, the blood pressure and blood sugar level of all patients were also monitored along with RA factor status. Urine samples were collected for routine chemical and microscopic examination. All these investigations were considered as baseline. A dose of 555MBq of ^{99m}Tc-MTx (total dose of 1mg-kit/patient) was given i.v. over 30sec. During the study, vital signs were monitored for any significant change from baseline. Scintigraphic results were co-evaluated with conventional Tc^{99m}-MDP bone scan and x-rays as well.

Imaging Protocol

Anterior and posterior whole body images were acquired at 60min, 120min and 180min post injection (p.i.) for normal subjects undergoing MTX imaging to evaluate optimal time of imaging. Highest target to non-target (T/NT) ratios were observed at 120min p.i. Therefore protocol was optimized especially for patient group and patients were scanned at 120 min p.i. MDP bone scan images were taken 120min p.i. as well. Images were recorded by using a large field-of-view (LFOV) dual head gamma camera ECAM by Siemens, Germany, equipped with a low-energy, all-purpose collimator for acquisition. Data processing was done on ECAM work station using ESOFT, SYNGO™.

Pharmacokinetics and Biodistribution

Imaging studies were performed with five patients showing different stages of the disease. A region of interest was drawn around the whole body on anterior and posterior views, and counts with geometric mean method were considered 100% of the injected dose at that particular time. Region of interest (ROI) was also drawn around important areas like shoulder joints, wrist joints, knee joints and ankle joints. The background regions were placed close to the region of interest for background correction. Scans were analyzed semi quantitatively by calculating the percentage of injected dose (%ID) per joint at 120min. Percentage injected dose at these times was calculated using the following formula: percentage injected dose in an organ=100× (organ counts at particular time)/ (total-body counts at that time). To evaluate the clinical objective difference in uptake percentages among ^{99m}Tc MTX and ^{99m}Tc MDP, target to non-target ratios (T/NT) were calculated. It was achieved by dividing %ID values of ^{99m}Tc MDP scan of patients with normal %ID values of ^{99m}Tc MDP scan of normal subjects. Same procedure was adopted for calculation of T/NT ratios for ^{99m}Tc MTX scan as well.

Statistical Analysis

Statistical analysis was done in 14 normal subjects. Mean and standard deviations were calculated. The volunteer patients were only five, thus no statistical results, such as sensitivity, specificity and accuracy could be determined. Nevertheless correlation with the clinical data and diagnostic results from radiology was certainly crucial and proved to be accurate.

Results

Scintigraphic biodistribution of Tc^{99m}-MTX

Scintigraphic results showed excellent selective tracer uptake of ^{99m}Tc-MTX in the effected joints of patients (Figure 1,2,3). An important finding was that ^{99m}Tc-MTX has negligible uptake in the normal bones or joints and shows selective uptake only in inflamed

joints. Main routes of excretion were kidneys with liver to a lesser extent. No tracer uptake was noted in lungs or spleen.

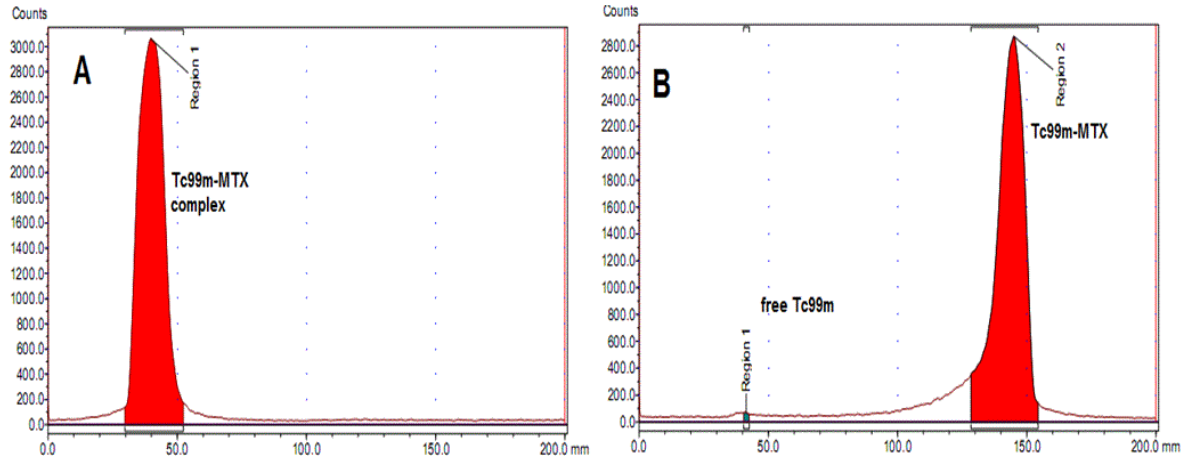

Figure 1: QC results of Tc^{99m} –MTX A) PC B) ITLC, 1. PC in acetone 2. ITLC in saline

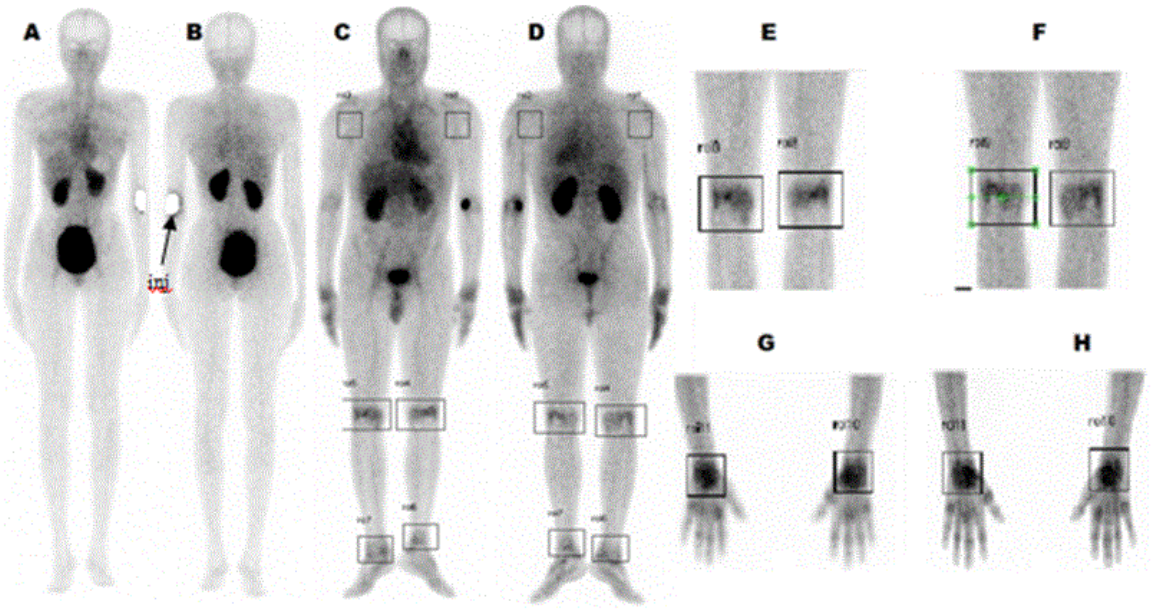

Figure 2: Scintigraphic biodistribution of 555MBq ^{99m}Tc-MTX at 120min where a) and b) are anterior and posterior whole body scans of normal subject taken at 2h p.i. c), d) Anterior and posterior views of ^{99m}Tc-MTx scan in patient no1showing remarkable tracer uptake in the wrist and knee joints (e-h) show the static views at 2hr p.i.of both knee joints and wrist joints.

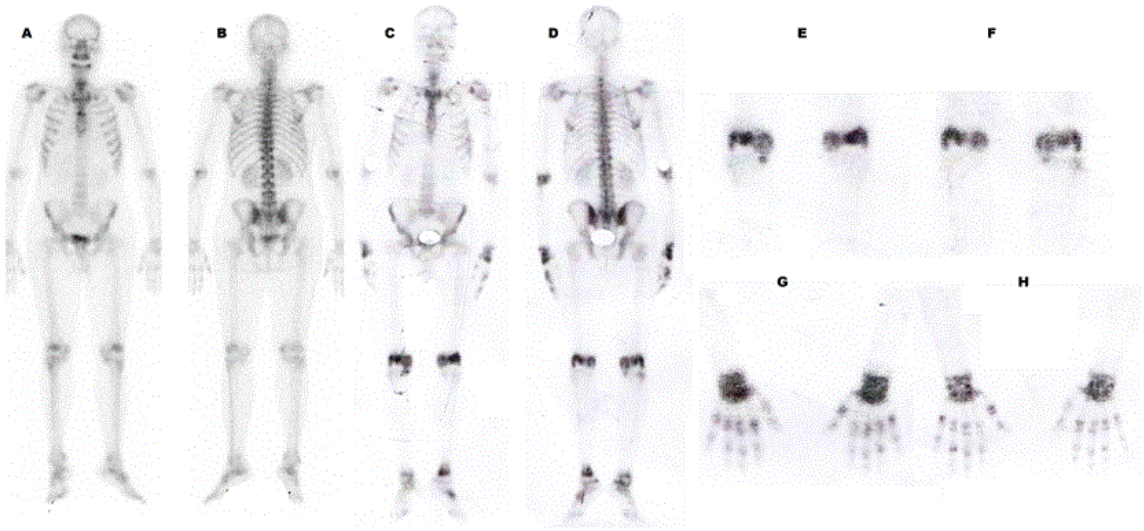

Figure 3: Scintigraphic biodistribution of 555MBq ^{99m}Tc-MDP at 120min (a,b) anterior and posterior whole body scan of normal subject (c,d) Anterior and posterior views of ^{99m}Tc-MDP scan of patient 1 showing significant tracer uptake in the wrist, knee joints and left ankle (e-h)shows static spot views of knee and wrist joints

Safety and quality control

Labeling efficiency was determined using paper chromatography (PC) and instant thin layer chromatography (ITLC) and it was calculated to be 99.8% ± 0.2 as shown in the figure 1. Quality control and clinical results showed that the complex is safe and non-toxic with high labeling efficiency and showed selective uptake in inflamed joints only. No adverse reaction was noted in any subject after four weeks of follow-up.

Objective analysis of %ID data

Normal values of %ID in major joints were calculated for shoulder, wrists, knee and ankles for both ^{99m}Tc-MTX and ^{99m}Tc MDP as shown in table 2 and 3 respectively. Normal %ID for shoulder, wrist, knee and ankle for ^{99m} Tc-MTX were calculated to be 0.06288 ±0.026689, 0.02624 ±0.036182, 0.06212 ±0.022888and 0.03664 ±0.043685 respectively and 1.65±0.61, 0.68±0.36,1.30±0.51 and 0.66±0.32 respectively for ^{99m}Tc MDP scan (Table 2,3). Very low values of normal %ID of ^{99m}Tc MTX scan shows insignificant uptake in the bone/joints hence above values represent blood levels of tracer in the bone/joint tissue which is well supported by normal biodistribution study already published [12].

Joint	1	2	3	4	5	Mean ± StDev
shoulder	0.0847	0.0224	0.0829	0.0493	0.0751	0.06288 ±0.026689
wrist	0.0034	0.002	0.0361	0.0857	0.004	0.02624 ±0.036182
knee	0.0845	0.0607	0.0854	0.046	0.034	0.06212 ±0.022888
ankle	0.0088	0.0689	0.005	0.0974	0.0031	0.03664 ±0.043685

Table 2: Normal biodistribution data of ^{99m}Tc-MTX in joints of five normal subjects, expressed as mean of percentage injected dose (%ID) in the both sided joints

	Mean %ID of normal MDP bone scan														
Joint	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Normal Mean ±STDEV
Shoulder	1.8	2.5	1.5	1.8	1.9	1.7	0.3	1.7	1.8	1.6	2.2	2	1.9	0.3	1.65 ±0.61
wrist	1	1.1	0.4	0.8	0.1	1	0.1	1	0.9	0.4	0.9	0.8	0.8	0.1	0.68±0.36
knee	1.4	1.5	1.1	1.4	1.8	1.6	0.3	1.4	2	1.1	1.2	1.6	1.6	0.3	1.30±0.51
ankle	1	0.8	0.5	0.7	0.9	1	0.2	0.8	0.9	0.5	0.5	1.1	0.1	0.2	0.66±0.32

Table 3: Normal biodistribution data of ^{99m}Tc-MDP in joints of 14 normal subjects, expressed as mean of percentage injected dose (%ID) in the both sided joints

Results of 45 year male diagnosed RA with pre-treatment ACS score of 08 showed significant tracer uptake of ^{99m}Tc MDP in clinically tender joints with %ID values of shoulders, wrist, knee and ankle as 1.782, 3.445, 3.055 and 0.666 for right sided joints and 1.677, 3.279, 3.0 and 0.632 for left sided joints respectively. %ID uptake of ^{99m}Tc MTX in same joints i.e. shoulders, wrist, knee and ankle was found to be as 0.8496, 2.5007, 1.7544 and 1.0249 for right sided joints and 0.8647, 2.4401, 1.6344 and 0.8616 for left sided joints respectively. To evaluate significance of difference among %ID of both scans T/NT ratios were developed. T/NT ratio were significantly higher for ^{99m}Tc MTX in shoulders, wrist, knee and ankle as 13.51, 95.30, 28.24 and 27.97 for right sided joints and 13.75, 92.99, 26.31, and 23.52 for left sided joints whereas T/NT ratios of ^{99m}Tc MDP for shoulders, wrist, knee and ankle were 1.08, 5.03, 2.34 and 0.87 for right sided joints and 1.02, 4.79, 2.30 and 1.20 for left sided joints .

Another patient was selected who was a diagnosed case of RA and was on second line drugs for last 2 months ^{99m}Tc MTX scan was done to evaluate the efficacy of this imaging probe in a patient on treatment. Data showed significant tracer uptake of ^{99m}Tc MDP with %ID values of shoulders, wrist, knee and ankle as 2.1364, 1.1155, 1.9981, and 0.6658 for right sided joints and 2.0385, 1.0112, 3.2217 and 0.6315 for left sided joints respectively. %ID uptake of 99mTc MTX in same joints i.e. shoulders, wrist, knee and ankle was found to be as 1.0030, 0.5020, 0.9290 and 0.3300 for right sided joints and 1.0240, 0.5000, 1.1540 and 0.3260 for left sided joints respectively. T/NT ratio were again significantly higher for ^{99m}Tc MTX in shoulders, wrist, knee and ankle as 15.95, 19.13, 14.95 and 9.01for right sided joints and 16.28, 19.05, 18.58 and 8.90 for left sided joints whereas T/NT ratios of ^{99m}Tc MDP for shoulders, wrist, knee and ankle were 1.29, 1.63, 1.53 and 1.01for right sided joints and 1.23, 1.48, 2.47 and 0.96for left sided joints.

Discussion

Our study provides the first clinical evidence for ^{99m}Tc-MTx as a possible imaging agent in rheumatoid arthritis at different stages of disease (early disease as in patient no 1and 5 and chronic disease as in patient no 2, 3 and 4, and at different scenarios of treatment i.e. pre-treatment as in patient no 1and 5 and during treatment as in patient no 2, 3 and 4. Published results for quality control of ^{99m}Tc-MTX showed that the drug was easily radiolabeled. The scintigraphic procedure was used to evaluate the normal biodistribution and biogenetics of the said radiopharmaceutical [4].

Safety clinical trial tests are essential for any drug before it is widely used and our study was also initially approved from our Ethical Committee then the entire project was started. Safety tests include preparation of drug under sterile conditions and applying it to animals for evaluation of affinity of this probe and to study its normal biodistribution which we already published in the international journal [4,5,12]. After publishing the results in the international journal we proceeded to the present study.

Methotrexate is effective in reducing the signs and symptoms of RA, as well as slowing or halting radiographic damage. Methotrexate is effective in many other forms of inflammatory arthritis including psoriatic arthritis and other spondyloarthopathies, and is used in many autoimmune diseases. The anti-inflammatory effects of Methotrexate in rheumatoid arthritis appear to be related to blockage of adenosine pathway and possible blockage of other inflammatory and immunoregulatory pathways. The immunosuppressive and toxic effects of methotrexate are due to the inhibition of an enzyme involved in the metabolism of folic acid, dihydrofolate reductase [6].

In the past other methods to image RA like Anti-CD3,^{99m}Tc-anti-TNF-a [7], ^{99m}Tc-anti-E-selectin-Fab scintigraphy and (111) In-1.2B6-F(ab')(2) [8], quantitative ^{99m}Tc-labeled nanocolloid (NC) scintigraphy detecting wrist joint inflammation in early rheumatoid arthritis (RA) [9], Comparison of Tc-^{99m} MDP, Tc-^{99m} HSA and Tc-^{99m} HIG uptake in rheumatoid arthritis [10] were studies for its imaging and treatment. 111In-WBC was studied as well to distinguish active RA from inactive RA or osteoarthritis at a value of 1.15 and showed that the use of 111In-WBC was a more reliable procedure for this purpose [11].

MTX has been used to treat RA as a first line drug, so the author wanted to evaluate this specific drug for imaging of RA so as to evaluate the sensitivity of RA to MTX treatment. Another vital benefit expected is that the same radiopharmaceutical will be used as follow-up agent for interval response evaluation of treatment.

In the start of study normal values were developed for local population in terms of %ID for ^{99m}Tc MTX and ^{99m} Tc MDP as well. Normal data was developed by calculating %ID in each joint of 14 normal subjects who underwent Tc^{99m}-MDP bone scan (Table 3) and five subjects who underwent Tc^{99m}–MTX scan (Table 2). Single normal mean of %ID for both joints was taken as reference for our population and %ID in each joint of the patients for both scans i.e Tc^{99m}-MDP and Tc^{99m} –MTX were compared with this normal data.

Our results showed that Tc^{99m} labeled MTX is a promising radiopharmaceutical to image RA. Scintigraphic and numerical data of %ID in the joints of patients was compared to the image and numerical data of a normal volunteer subjects (Table 4 and 5). Normal scan data of this study (Figure 2A,B) and the study already published [12] show that in the absence of any disease, Tc^{99m}-MTX is freely filtered from blood without any nonspecific uptake (Figure 2a, b). Negligible or no uptake was noted in any bone or joint. Tc^{99m}-MTX study in patient no 1 showed that there is remarkable tracer uptake in the large inflammed joints of the body especially shoulder joints, wrist joints, knee joints and ankle joints bilaterally. Same patient underwent Tc^{99m}-MDP bone scan for comparative study which also confirmed significant tracer uptake in the same joints as mentioned above. Scintigraphic images of Tc99m-MDP scan of patient were also compared to the normal Tc^{99m}-MDP bone scan images for visual comparison (Figure 3 a-h and Figure 4). The advantage of the Tc^{99m}-MTX scan is evident that it showed selective uptake only in the inflammatory joints which explains and justifies why it is being used as first line anti-rheumatic drug therefore keeping in view the unique property of this novel probe, same may be used as follow up agent to evaluate the response to methotrexate therapy. Bone scan equally shows tracer uptake but as it is taken up in the non-inflammatory lesions like old healed trauma it lack specificity for inflammatory bone diseases [13]. T/NT ratios for ^{99m}Tc MTX were subjectively higher than with ^{99m}Tc MDP bone scan and were decisive regarding comparison of both techniques (Table 6). Tc^{99m} –MTX did not show any uptake in rest of the normal bone which is an excellent advantage over MDP.

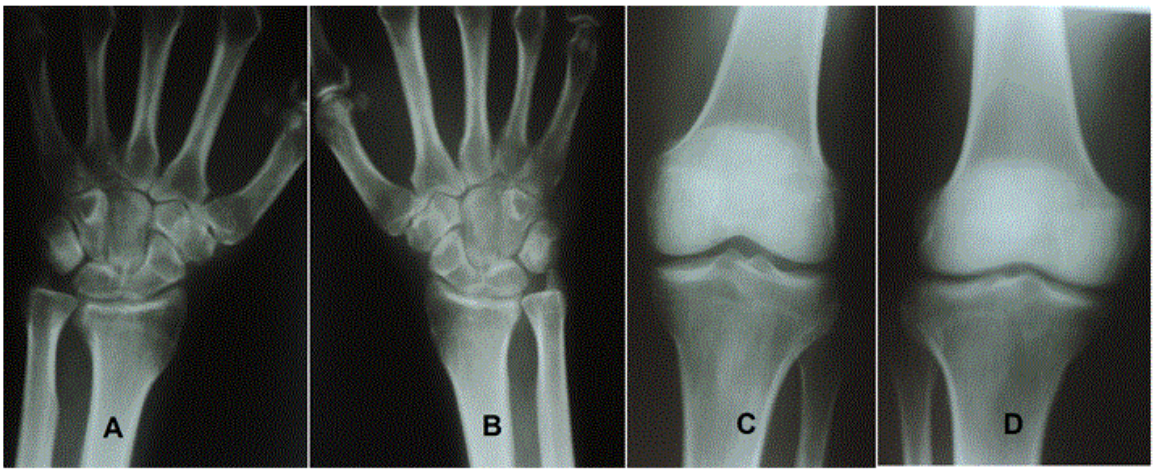

Figure 4: X-rays showing mild sclerotic changes A,B) Left and right wrist joint respectively C,D) Left and right knee joints respectively

Joint	Normal %ID MDP scan	MDP Scan Results of Patient 1		Normal %ID of MTX scan	MTX Scan Results of Patient 1	
	Mean Value	RT side	Left Side	Mean Value	RT side	Left Side
Shoulder	1.65 ±0.61	1.782	1.677	0.06288 ±0.026689	0.8496	0.8647
wrist	0.68±0.36	3.445	3.279	0.02624 ±0.036182	2.5007	2.4401
knee	1.30±0.51	3.055	3	0.06212 ±0.022888	1.7544	1.6344
ankle	0.66±0.32	0.666	0.632	0.03664 ±0.043685	1.0249	0.8616

Table 4: Comparison of %ID biodistribution data of ^{99m}Tc -MDP and 99mTc-MTX of patient no 1 with normal %ID data of normal population

	%ID mean from both sided joints of Tc^{99m} –MTX scan in normal subjects	%ID Tc99m –MTX scan Patient no 2		Normal %ID Tc^{99m}-MDP	%ID Tc^{99m}-MDP Patient no 2	
Joint	Mean± Stdev	RT side	Left Side	Mean	RT side	Left Side
shoulder	0.06288 ±0.026689	1.003	1.024	1.65	2.1364	2.0385
wrist	0.02624 ±0.036182	0.502	0.5	0.68	1.1155	1.0112
knee	0.06212 ±0.022888	0.929	1.154	1.3	1.9981	3.2217
ankle	0.03664 ±0.043685	0.33	0.326	0.66	0.6658	0.6315

Table 5: Comparison of ^{99m}Tc-MTX patient no 2 data with normal biodistribution data of ^{99m}Tc-MTX scan of 05 normal volunteer's joints and intercomparison of ^{99m}Tc-MTX and ^{99m}Tc-MDP

Patient no 2 was a diagnosed case and was on treatment (Table 1) but again Tc^{99m}-MTX bone scan showed significant tracer uptake in the left sided joints especially knee joints which effectively showed the active disease (Figure 5,6,7).

As patient no 2 was on previous treatment with methotrexate a scintigraphic study with ^{99m} Tc labeled MTX was done to evaluate active and residual disease areas. %ID data showed that there was active disease in wrist and knee joints especially left knee joints (Figure 6,7 c-f) and (Table 5). Graphical analysis of MDP data showed that there was no significant difference of %ID from normal values in shoulders, wrists and ankle joints (Figure 6). However analysis of %ID data of ^{99m}Tc MTX scan shows subjective difference from normal values which is more effectively reflected in the T/NT ratios of ^{99m}Tc MTX scan (Table 6) and Figure 8-B. Hence T/NT ratios for early or less active disease in shoulders, wrists and ankle joints of patient no 2 are well depicted up to satisfactory difference by ^{99m}Tc MTX scan rather than ^{99m}Tc MDP scan.

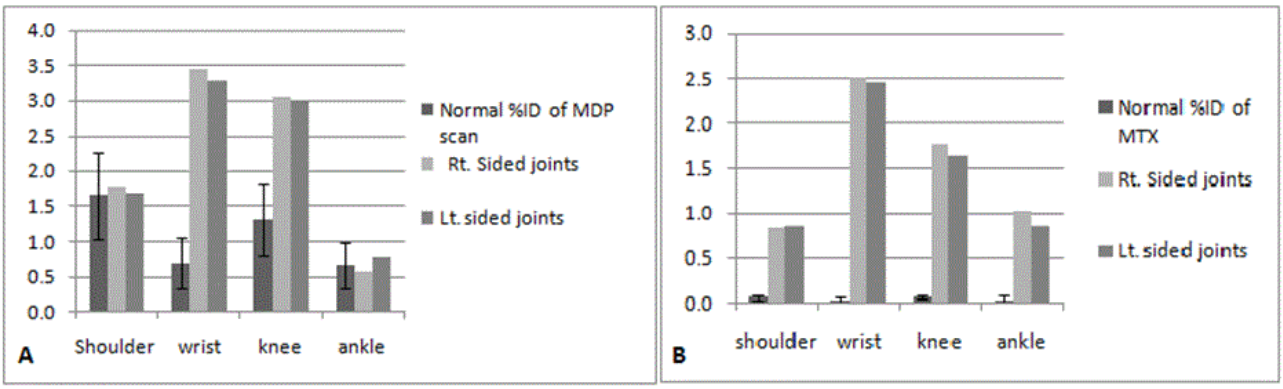

Figure 5: A) Comparison of %ID data of patient no 1 with normal population %ID data of Tc^{99m}-MDP B) Comparison of %ID data of patient no 1 with normal population %ID data of Tc^{99m}-MTX

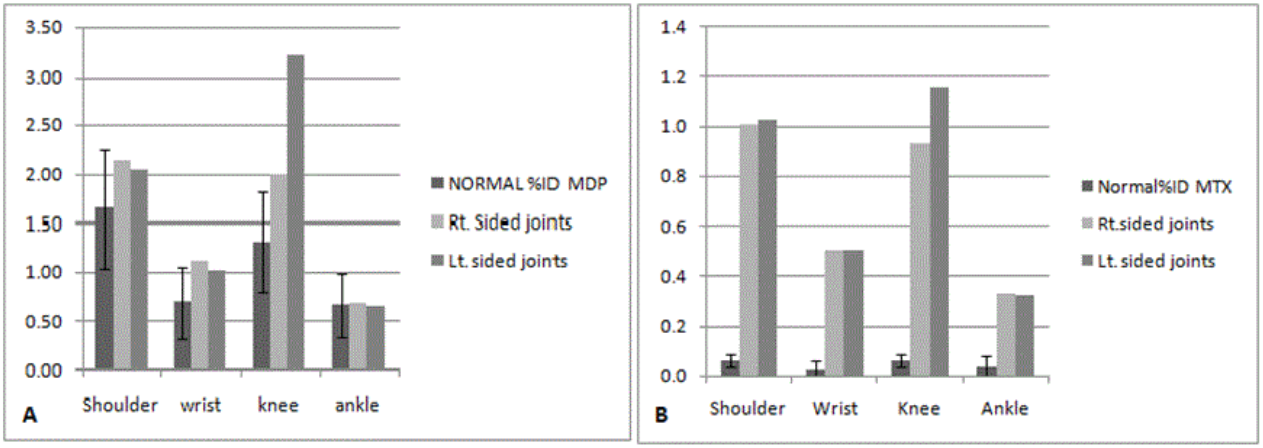

Figure 6: A) Comparison of %ID data of patient no 2 with normal population %ID data of Tc^{99m}-MDP B) Comparison of %ID data of patient no 2 with normal population %ID data of Tc^{99m}-MTX

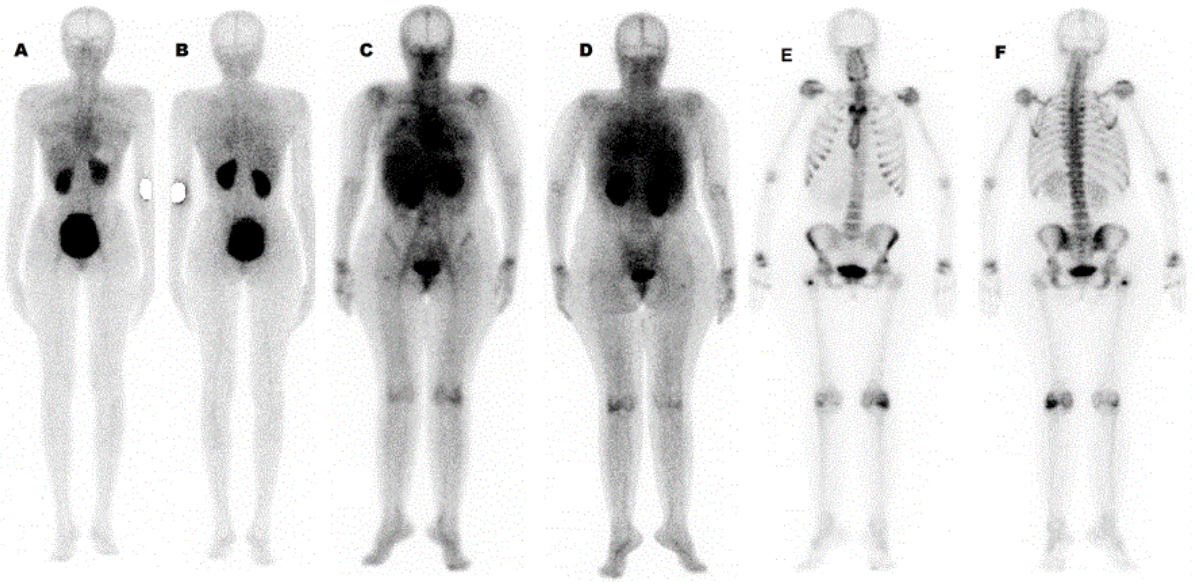

Figure 7: Scintigraphic comparison of joint uptake at 120 min (A,B) Normal scintigraphic biodistribution of 555MBq of ^{99m}Tc-MTx (C,D) Scintigraphic biodistribution of 99mTc-MTX in the joints of patient no 2 (E,F) Scintigraphic biodistribution of 555MBq of ^{99m}Tc-MDP in the joints of patient no 2

	Patient No 1				Patient No 2			
	T/NT ratios with ^{99m}Tc MDP		T/NT ratios with ^{99m}Tc MTX		T/NT ratios with ^{99m}Tc MDP		T/NT ratios with ^{99m}Tc MTX	
	RT side	Left Side	RT Side	Left Side	RT Joints	LT Joints	RT Side	Left Side
Shoulder	1.08	1.02	13.51	13.75	1.29	1.23	15.95	16.28
wrist	5.03	4.79	95.3	92.99	1.63	1.48	19.13	19.05
knee	2.34	2.3	28.24	26.31	1.53	2.47	14.95	18.58
ankle	0.87	1.2	27.97	23.52	1.01	0.96	9.01	8.9

Table 6: T/NT ratios of patients

^{99m}Tc-MDP localizes to entire bone and uptake is increased on blood pool and delayed images especially in inflammatory conditions however Tc^{99m}-diphosphonates are taken up by all joints to a variable degree, making interpretation difficult. The number of false positives is unknown but it is clear that MDP scans are unable to reliably distinguish between 'active' and 'inactive' rheumatoid arthritis [13] and in case of Tc^{99m}-MDP bone scan, non-specific uptake may lead to further investigation rather than patient reassurance but as evident in our study where patient no 2 images show that after treatment of a year, active RA in clinically tender joints is well predicted by Tc^{99m}-MTX scan with high T/NT ratios when compared to conventional ^{99m}Tc MDP bone scan (Figure 8).

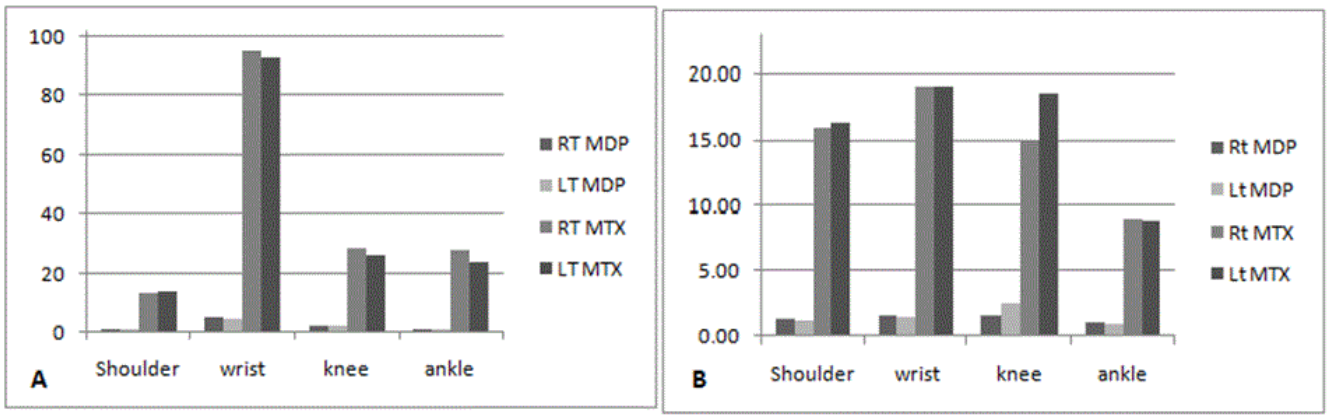

Figure 8: Comparison of T/NT ratios of %ID data of patient with normal A)Patient no1 B) Patient no 2 showing promising advantage of ratios of MTX scan over MDP scan in imaging RA.

In conclusion Tc^{99m}-MTX is a promising imaging probe for RA and it may be used for detection of early rheumatoid arthritis and to evaluate sensitivity of this disease to Methotrexate treatment as well. This probe may also be used for follow up of disease as it can pick active or residual disease even during the course of treatment.

References

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