Proximal interphalangeal arthroscintigraphy in rheumatoid arthritis

J. REMANS, H. BERGHS, L. DRIESKENS, L. KIEBOOMS,
AND J. POLDERMAN

From the Centre of Rheumatology and the Department of Nuclear Medicine, Genk, Belgium

SUMMARY Quantitative scintigraphy of proximal interphalangeal joints was performed by a reproducible method using ^{99m}Tc in the hands of 40 normal controls and 20 patients with rheumatoid arthritis (RA). The range of the mean uptake varied considerably between proximal interphalangeal (PIP) joints in normal subjects. The mean uptake over PIP joints was not significantly different either between normal controls and RA patients, nor between those rheumatoid arthritis patients with and those without clinical signs of inflammation in the PIP joints. However, the variation in the PIP counts was significantly greater in the rheumatoid hands than in the normal hands. There was no clear correlation between the technetium uptake and the clinical parameters of inflammation in the PIP joints.

Pain, swelling, and limitation of motion are clinical parameters of inflammatory activity in rheumatoid arthritis, while technetium (^{99m}Tc) scanning is a physical method of measuring inflammation in joints (Dick *et al.*, 1970). The aim of this study was (1) to determine a 'normal range' for PIP joint scanning performed in 'normal controls'. (2) To compare ^{99m}Tc -pertechnetate PIP joint quantitative scintigraphy in rheumatoid arthritis patients and in normal controls. (3) To compare the inflammatory state of the joints (synovitis) assessed by clinical and scintigraphic methods.

Materials and methods

CLINICAL

Forty 'normal controls' and 20 patients with rheumatoid arthritis were submitted to quantitative PIP scintigraphy. The normal controls consisted of healthy persons without any clinical or radiological abnormalities of the hands. Laboratory investigations confirmed the absence of abnormal serological and immune factors, and normal erythrocyte sedimentation rates and haemoglobin values.

All RA patients had 'classical' or "definite" RA. They belonged to the functional classes II or III and the anatomical stages II or III according to the ARA criteria. They had suffered from the disease for

more than 2 years and were all receiving therapy. Eleven of the RA patients had clinical signs of active inflammation (pain, swelling, tenderness on palpation or motion) in at least one PIP joint. The remaining 9 RA patients had no clinical signs of active inflammation at the PIP level.

ARTHROSCINTIGRAPHY

The counting apparatus consisted of a sodium iodide crystal and a photomultiplier system connected to a scaler and channel analyser. The entire crystal-photomultiplier system was encased in lead 8 mm thick, so that the background count rate with the patient in position was reduced to the order of 5% of that recorded with the finger joint in place.

A good definition of each PIP joint was obtained by positioning the PIP joint in a lead chamber on the surface of the collimator mounted over the crystal (Sturrock *et al.*, 1974).

Approximately 500 μCi of ^{99m}Tc -pertechnetate was injected into the cubital vein. The technetium for injection was made up to 2 ml with physiological saline in a 5 ml syringe. This was fixed over the crystal by an attachment to the collimator for counting the injected dose under the same conditions as the PIP joints. This allowed accurate calculation of the difference in counts between the filled syringe before and the empty syringe after the intravenous injection of technetium.

Hands were rested for 1 hour before carrying out

the test. Twenty minutes after injection, PIP joint counts were measured in a standard order from the thumb to the little finger, first in the right hand and then in the left hand. The counting time was 30 s over each PIP joint. The ^{99}Tc uptake was expressed as a percentage ($\% \times 10^{-3}$) of the administered dose.

The reproducibility of the counts on individual PIP joints was of the order of 5%.

Results

In the 40 normal controls, uptakes for the same finger showed a mean variability as expressed by coefficients of variation from 25 to 27%. The mean value for each finger increased from little finger to thumb on both hands (Table 1).

The analysis of variance (Table 2) shows that the uptake differs significantly for each of the 5 fingers (a) and among the different patients (b).

A significant difference exists in the evolution of the counts from little finger to thumb (c = finger $\times$

patient interaction). There is however no significant difference between right and left hand (d) and no significant difference between the two hands in the evolution from little finger to thumb (e). For each finger, using the mean and standard deviations, a tolerance interval is calculated (Table 3) giving a tolerance probability of 0.95 and a confidence probability of 0.95. This tolerance interval is taken as the 'normal range'. (Sokal and Rohlf, 1969).

Comparison (Student's *t* test) of the 20 normal controls and 40 RA patients (Table 4) shows no significant differences between the mean values of normal controls and of RA patients, though the values of RA patients always lie a little higher. Fig. 1 illustrates the results for the left little finger. It is obvious that the values of many RA patients lie within the normal range.

The variances of the PIP counts are significantly higher (F variance ratio—Snedecor and Cochran, 1967) in RA patients than in normal controls (Table 4).

Comparing 11 RA patients with and 9 RA patients

Table 1 Count rate ($\% \times 10^{-3}$ of injected dose) of each PIP joint in 40 normal controls

	Little finger	Ring finger	Middle finger	Forefinger	Thumb
Right hand	2.80 $\pm$ 0.73* (26)†	3.10 $\pm$ 0.83 (27)	3.41 $\pm$ 0.90 (26)	3.51 $\pm$ 0.93 (26)	4.54 $\pm$ 1.19 (26)
Left hand	2.73 $\pm$ 0.69 (25)	3.08 $\pm$ 0.83 (27)	3.36 $\pm$ 0.90 (27)	3.51 $\pm$ 0.90 (26)	4.54 $\pm$ 1.13 (25)

*Mean $\pm$ SD.

†Coefficient of variation.

Table 2 Three-way analysis of variance on the counts of the PIP joints in 40 normal controls

Source of variation	Degree of freedom	Sum of squares	Mean square	Variance ratio (with indication of the sum of squares used)	Significance
(a) Between fingers	4	143.451	35.863	a/g = 199	P < 10 ⁻⁵⁰
(b) Between patients	39	285.352	7.317	d/g = 143	P < 10 ⁻¹⁰
(c) Finger $\times$ patient interaction	156	28.046	0.180	e/g = 3.53	P < 10 ⁻¹⁰
(d) Between hands	1	0.064	0.643	b/f = < 1	NS
(e) Finger $\times$ hand interaction	4	0.096	0.240	c/g = < 1	NS
(f) Hand $\times$ patient interaction	39	5.711	0.146	f/g = 2.86	P < 10 ⁻⁵
(g) Residual interaction (finger $\times$ hand $\times$ patient)	156	7.906	0.051		
(h) Total	399	470.626			

NS = not significant.

Table 3 Tolerance* interval for the counts ($\% \times 10^{-3}$) of each normal PIP joints

	Little finger	Ring finger	Middle finger	Forefinger	Thumb
Right hand	1.00–4.60	1.06–5.14	1.20–5.61	1.22–5.78	1.63–7.44
Left hand	1.05–4.40	1.06–5.10	1.16–5.56	1.30–5.72	1.76–7.32

*Tolerance probability = 0.95. Confidence probability = 0.95.

Table 4 Counts ($\% \times 10^{-3}$) of each PIP joint (mean $\pm$ SD). Comparison of 40 normal controls and 20 RA patients

	Right hand					Left hand				
	Little finger	Ring finger	Middle finger	Fore-finger	Thumb	Thumb	Fore-finger	Middle finger	Ring finger	Little finger
Controls (n=40)	2.80 $\pm$ 0.73	3.10 $\pm$ 0.83	3.41 $\pm$ 0.90	3.51 $\pm$ 0.93	4.54 $\pm$ 1.19	4.54 $\pm$ 1.13	3.51 $\pm$ 0.90	3.36 $\pm$ 0.90	3.08 $\pm$ 0.83	2.73 $\pm$ 0.69
RA patients (n=20)	2.87 $\pm$ 1.27	3.68 $\pm$ 1.89	3.96 $\pm$ 1.93	4.28 $\pm$ 2.04	4.59 $\pm$ 2.07	4.49 $\pm$ 1.92	3.73 $\pm$ 1.80	3.92 $\pm$ 2.18	3.59 $\pm$ 2.07	3.24 $\pm$ 1.46
Student's two sample <i>t</i> test: mean difference	0.22	1.31	1.21	1.60	0.10	-0.10	0.51	1.10	1.06	1.48
P	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Snedecor's F variance ratio	3.02	5.18	4.59	4.81	3.02	2.88	4.00	5.86	6.21	4.47
P	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01	<0.01

without clinical signs of inflammation in at least one PIP joint (Table 5), there is no significant difference between the mean values (Student's *t* test) nor between the variances (F variance ratio) of the counts.

Fig. 1 Count ($\% \times 10^{-3}$ of injected dose) for one PIP joint. Example of a left finger.Table 5 Counts ($\% \times 10^{-3}$) of each PIP joint (mean $\pm$ SD). Comparison of 11 RA patients with clinical signs of inflammation in at least one PIP joint and 9 RA patients with no signs of inflammation

	Right hand					Left hand				
	Little finger	Ring finger	Middle finger	Fore-finger	Thumb	Thumb	Fore-finger	Middle finger	Ring finger	Little finger
Patients with signs of inflammation (n=11)	2.94 $\pm$ 1.14	3.84 $\pm$ 2.09	3.64 $\pm$ 1.99	4.35 $\pm$ 2.13	4.64 $\pm$ 2.31	4.27 $\pm$ 2.03	3.72 $\pm$ 1.86	3.80 $\pm$ 2.05	3.56 $\pm$ 2.23	3.22 $\pm$ 1.27
Patients without signs of inflammation (n=9)	2.78 $\pm$ 1.47	3.48 $\pm$ 1.73	4.13 $\pm$ 1.96	4.19 $\pm$ 2.06	4.52 $\pm$ 1.86	4.76 $\pm$ 2.02	3.75 $\pm$ 1.84	4.16 $\pm$ 2.37	3.62 $\pm$ 1.98	3.27 $\pm$ 1.76
Student's two sample <i>t</i> test: mean difference	0.29	0.42	0.56	0.17	0.11	0.56	0.045	0.36	0.055	0.084
P	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Snedecor's F variance ratio*	1.66	1.46	1.03	1.06	1.53	1.009	1.03	1.33	1.26	1.92
P	8 & 10df NS	17 & 8df NS	10 & 8df NS	10 & 8df NS	10 & 8df NS	10 & 8df NS	10 & 8df NS	8 & 10df NS	10 & 8df NS	8 & 10df NS

df=degrees of freedom.

Table 6 Number of fingers involved per patient

No. of fingers involved (r)	Frequency of patients with r fingers showing clinical signs of inflammation	Frequency of patients with r fingers with elevated scanning-counts	Frequency of patients with r fingers with elevated scanning-counts and with clinical signs of inflammation
0	9	12	16
1	5	0	2
2	2	2	0
3	0	0	0
4	1	2	1
5	1	1	1
6	2	1	0
7	0	0	0
8	0	1	0
9	0	0	0
10	0	1	0
Mean	1.50	2.05	0.55
Variance	4.26	9.52	1.94
$q = \frac{\text{variance}}{\text{mean}}$	2.17	4.65	3.53
Positive binomial distribution	Rejected since $9 > 1$	Rejected since $9 > 1$	Rejected since $9 > 1$
Poisson distribution	Rejected since $9 > 1$ and by a test for Poisson series	Rejected since $9 > 1$ and by a test for Poisson series	Rejected since $9 > 1$ and by a test for Poisson series

Table 7 Concordance between scan results and clinical state of joints in 20 RA patients

Clinical state	Scan results		
	Too high once	Always within norms	Total clinical state
At least one PIP joint with inflammation	4	7	11
No PIP joint with inflammation	4	5	9
Total scan results	8	12	20

patients are not significantly different. This can be attributed to the overlap of numerous RA values within the 'normal range'. The significant difference between the variances of these 2 groups adds some weight to this assumption.

Regarding the inflammation assessed by clinical methods or by scintigraphy, the fingers are not affected by RA at random. Clusters of involved fingers exist in some patients. For our 20 RA patients,

the scan results and the clinical signs of joint inflammation are not related. Dick *et al.*, (1970), Green and Hays (1972), and Weiss and Schuler (1974) found that technetium uptake over rheumatoid joints correlated with disease activity, though these workers demonstrated also that the joint scans could be positive when clinical examination is unremarkable; the reverse situation was less frequent. Huskisson *et al.* (1973) have reported that in an individual joint with arthritis, the ^{99m}Tc uptake correlated neither with the clinical inflammatory signs nor with the thermography of the same joint.

Using a quantitative method, we observed (Remans *et al.*, 1976) no significant correlation between the clinical evolution and the scanning evolution of rheumatoid hand joints under treatment with an anti-inflammatory drug.

This lack of correlation could be explained by the hypothesis that radioisotope assessment measures something related to, but not identical with, the clinical parameters of rheumatoid synovitis.

References

Dick, W. C., Neufeld, R. R., Prentice, A. G., *et al.* (1970). Measurement of joint inflammation. A radioisotopic method. *Annals of the Rheumatic Diseases*, **29**, 135-137.

Green, F. A., and Hays, M. T. (1972). The pertechnetate joint scan. II. Clinical correlations. *Annals of the Rheumatic Diseases*, **31**, 278-281.

Feinstein, A. R. (1974). Clinical biostatistics XXXI: On the sensitivity, specificity and discrimination of diagnostic tests. *Clinical Pharmacology Therapeutics*, **17**, 104-115.

Huskisson, E. C., Berry, H., Browett, J. P., and Wykeham Dalme, H. (1973) Measurement of inflammation Part II: Comparison of Technetium clearance and thermography with standard methods in a clinical trial. *Annals of the Rheumatic Diseases*, **32**, 99-102.

Remans, J., Berghs, H., Drieskens, L., Kiebooms, L., and Polderman, J. (1976). Scintiscan evaluation of rheumatoid hands for monitoring the anti-inflammatory effects of drugs. *Journal Belge de Rhumatologie et de Médecine Physique*, **31**, 211-218.

Snedecor, G. W., and Cochran, W. G. (1967). Analysis of independent samples when $O^1 \mid O^2$. In *Statistical Methods*, 6th Edition, pp. 114-116. Iowa State University Press USA.

Sokal, R. R., and Rohlf, F. J. (1969). Graphic test for normality — Rankit method for small samples. In *Biometry—the Principles and Practice of Statistics in Biological Research*, p. 124. Freeman: San Francisco.

Sturrock, R. D., Nicholson, R. and Wojtulewski, J. A. (1974). Technetium counting in rheumatoid arthritis. Evaluation in the small joints of the hands. *Arthritis and Rheumatism*, **17**, 417-420.

Weiss, T. E., and Schuler, S. E. (1974). Joint imaging as a clinical aid in diagnosis and therapy of arthritic and related diseases. *Bulletin on the Rheumatic Diseases*, **25**, 791-793.