Influence of Radiation Synovectomy on Articular Cartilage, Synovial Thickness and Enhancement as Evidenced by MRI in Patients with Chronic Synovitis

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Radiation synovectomy is a safe and effective treatment for chronic synovitis that is refractory to the repetitive, intra-articular application of glucocorticosteroids in patients with rheumatoid or seronegative arthritis. Short-term and long-term effects of radiation synovectomy on articular cartilage, synovial enhancement and thickness were assessed in a prospective, clinical trial by MRI. **Methods:** Thirteen patients (mean age 39 ± 13 y) were treated with a median activity of 8.4 GBq ^{165}Dy ferric hydroxide, a radionuclide with favorable physical properties and a well-documented clinical safety and efficacy profile. MRI was performed on a 1.5-T MR unit using a circular polarized knee coil. **Results:** After a mean observation period of 13 mo, a marked reduction in synovial enhancement was observed in 10 patients. The mean reduction in baseline synovial thickness (mean 7.6 ± 3.0 mm) was 24% ($P = 0.03$) at 1 wk and 42% ($P = 0.01$) about 1 y after treatment, respectively. Clinically, 9 of 13 patients (69%) exhibited persistent response to radiation synovectomy. The local clinical score, as defined by the reduction in pain, pannus, joint effusion and by the increase in the range of motion, improved significantly ($P = 0.01$), from a median of 7 (range 4–10) to a median of 2 (range 0–9). One year after treatment, changes in the local clinical score were related to the decrease in synovial enhancement in MRI ($r = 0.7$, $P = 0.008$, n = 12). There were no persistent adverse effects, nor was there evidence for any severe radiation-induced damage to the articular cartilage. On later follow-up images, the structure of the articular cartilage remained unaltered in all but 3 patients, who had new, superficial erosions most likely attributed to an active disease with persistence of inflammation. **Conclusion:** This study suggests that radiation synovectomy with ^{165}Dy-ferric hydroxide is effective in terms of reducing chronic synovitis without causing detectable harm to the articular cartilage, as shown by MRI.

Key Words: radiation synovectomy; cartilage; synovial enhancement; synovial thickness; MRI

J Nucl Med 1999; 40:1277–1284

An effusion of any joint is a painful sign of acute or chronic inflammation. Pannus formation and the consequent destruction of the articular cartilage result from chronic inflammation, of which rheumatoid arthritis is a frequent but not sole cause. All forms of chronic synovitis lead to the progressive loss of joint function and significant disability (*1*). Treatment of chronic synovitis using radiation synovectomy aims to control the inflammatory process that causes pain, disability and severe structural damage to the joint (*1*). Radiation synovectomy was introduced more than 30 y ago (*2,3*), primarily as an alternative to surgical treatment (*4*). Meanwhile, radiation synovectomy of locally active rheumatoid arthritis and other forms of chronic arthritis has gained clinical acceptance in Europe (*5*). ^{90}Y-silicate colloid (*6*) is the radionuclide most commonly used for the treatment of chronic synovitis of the knee and has been shown to be safe and effective. This also applies to the short-lived (half-life 2.4 h) lanthanoid ^{165}Dy bound to ferric hydroxide (FH) macroaggregates. In previous studies, ^{165}Dy-FH was at least as effective as the ^{90}Y-silicate colloid but caused even less exposure and cumulative radiation dose to nontarget organs (*7–10*). Radiation synovectomy using ^{165}Dy-FH has been performed routinely for 6 y in our department (*11,12*). The advantageous safety profile of ^{165}Dy-FH is well documented and supports theoretical concepts suggesting that ^{165}Dy-FH has near-ideal characteristics for radiation synovectomy of the knee, with a maximum soft-tissue penetration of 5.7 mm, which is deep enough to ablate the synovium without potential harm to the articular cartilage and the bone (*13*). However, chronic synovitis exhibits great variability in its clinical course even within a single joint, underlining the need to validate the local effects of radiation synovectomy with one of the most sensitive techniques available. Radiation synovectomy has been reported by Larsen et al. (*14*) to be effective in more advanced stages (II and III) of arthritis, but there are increasing (although never validated) concerns about its effects on articular cartilage (*13*). MRI allows

Received Aug. 14, 1998; revision accepted Feb. 4, 1999.

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distinct imaging of articular morphology required to validate the safety and efficacy of radiation synovectomy, as assumed in theoretical concepts based on the physical properties of current radionuclides. MRI is more sensitive than radiography in detecting and localizing any changes in synovial thickness, and is a method of choice for evaluating articular cartilage in any form of synovitis. Monitoring the structure of the articular cartilage is of particular importance in chronic synovitis, because articular cartilage relates directly to joint damage and functional ability. Whether any local treatment modality prevents articular cartilage from degradation has not been resolved until today, because controlled studies using MRI with an extended period of observation are rare (*15*). Long-term results are missing even for the evaluation of radiation synovectomy.

We are reporting a prospective clinical trial using MRI to assess the effects of radiation synovectomy with ^{165}Dy-FH on articular cartilage and synovial thickness and enhancement in patients with rheumatoid or seronegative arthritis.

MATERIALS AND METHODS

^{165}Dy-FH Preparation

^{165}Dy-FH is a precipitate of ^{165}Dy-hydroxide on Fe(II)Fe(III) hydroxide used as carrier (Research Center, Seibersdorf, Austria). The improved preparation of the carrier was published in detail (*12*).

Study Protocol and Patients

This study was approved by the Ethical Committee of the University of Vienna, and all patients gave their written consent to participate. Thirteen knees were investigated in 13 patients (6 women, 7 men) with rheumatoid arthritis (n = 6) (*16*), psoriatic arthritis (n = 4) or other forms of seronegative arthritis (n = 3) (Table 1). Patients' knees were classified according to Larsen et al. (*14*), with stages ranging from 0 to III. Patients underwent MRI enhanced with gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA) before, 1 wk and approximately 1 y after radiation synovectomy. Mean age of the patients was 39 ± 13 y, and the duration of disease ranged from 1 to 21 y (median 3 y). Patients were eligible if suffering from persistent synovitis of the knee refractory to systemic and local pharmacological treatment without any evidence of infection, trauma or joint instability. All patients had undergone multiple arthrocenteses or diagnostic arthroscopies of the affected knee, with subsequent synovial fluid analysis. Systemic pharmacotherapy was defined as the use of nonsteroidal anti-inflammatory drugs, glucocorticosteroids and disease modifying antirheumatoid drugs for at least 4 mo. Patients were included when they fulfilled the criteria mentioned above but showed no evidence of an acute, polyarticular exacerbation of the underlying disease. Local management included only those drugs that were injected intra-articularly. None of the patients had received intra-articular glucocorticosteroids within 2 mo before the study, but all patients had been treated orally with nonsteroidal anti-inflammatory drugs. No patient was treated with intra-articular glucocorticosteroids or any other locally acting therapeutic agent during the study period. Radiographs were taken before admission to the study and approximately 1 y after treatment and were classified according to Larsen et al. (*14*). The patients were followed up clinically by two orthopedic surgeons and two rheumatologists. Clinical evaluations were performed before and 1 d, 1 wk and in 3-mo intervals after radiation synovectomy and in-between when necessary for the monitoring of drug therapy. Beside the assess-

TABLE 1
Demographic and Clinical Patient Data

Patient no.	Sex	Age (y)	Diagnosis	Duration of disease (y)	Medication	C-reactive protein* (mg/dL)	Local clinical score		Patient satisfaction†
					T_0	T_0	T_0	T_2	T_2
1	M	22	PA	1	None	<0.5	4	0	1
2	F	31	RA	3	Chloroquine	1.5	10	1	1
3	F	38	RA	11	MTX, SS	2.7	10	9‡	4
4	M	48	RA	10	SS	4.4	8	1	1
5	M	33	RA	2	MTX	1.2	7	1	1
6	F	69	RA	21	AP, AZT	1.5	5	1	2
7	F	37	PA	1	Etretinate	<0.5	8	6	3
8	M	42	PA	2	MTX	0.9	7	3	2
9	F	54	RA	4	MTX	2	8	2	2
10	F	27	SA (M. Still)	2	CyA, MTX, AP	3.1	7	6	4
11	M	40	SA	3	None	<0.5	7	2	2
12	M	28	PA	1	None	<0.5	6	4	3
13	M	33	SA	6	None	<0.5	6	0	1

*C-reactive protein reference range < 0.5 mg/dL.
†Patient satisfaction classified as excellent (1), good (2), fair (3) or poor (4).
‡Before arthroplasty.
PA = psoriatic arthritis; RA = rheumatoid arthritis; SS = sulfasalazine; MTX = methorexate; AP = aprednisolone; AZT = azathioprine; SA = seronegative arthritis; CyA = cyclosporine A.
T_0 represents time before treatment.
T_2 represents 1 y after treatment.

ment of standard clinical parameters (i.e., joint count, joint index, morning stiffness, global assessments of arthritis activity, erythrocyte sedimentation rate or C-reactive protein), the evaluation included assessment of local pain, pannus, range of motion and joint effusion of the treated knee joint (clinically or sonographically). A score was derived from each of the clinical symptoms and signs for the assessment of treatment. Each parameter was classified into a scale ranging from normal (0) to severe (3 points). Using this point scale, the range of motion of the treated knee could be classified as normal (>130°, i.e., 0 point), good (115°–130°, i.e., 1 point), fair (90°–115°, i.e., 2 points) or poor (< 90°, i.e., 3 points). Patients' assessments were graded as excellent (complete relief of symptoms), good (almost complete relief of pain, little or no joint effusion and improved or maintained range of motion), fair (only partial improvement in the majority of the parameters) or poor (no improvement in most parameters).

The use of any accepted form of contraception was obligatory for fertile women when treated with ^{165}Dy-FH. Exclusion criteria for treatment with ^{165}Dy-FH were pregnancy, any life-threatening or infectious disease or the presence of a Baker's cyst of the respective joint.

Each patient was admitted to the application room at calibration time. Arthrocentesis was performed in this room, with the patient in a supine position under strictly aseptic conditions. ^{165}Dy-FH was injected into the joint space using a 1.2-mm-gauge needle. Approximately 3 mL 1% lidocaine hydrochloride were instilled into the joint space before the application of activity when the effusion was small. The knee was then moved for a few times through a flexion/extension arc and immobilized in extension. The patient was confined to rest for 5–6 h to minimize movement.

Estimation of Activity for Therapy

Earlier experience demonstrated a target dose of approximately 100 Gy to be necessary for the therapeutic effect of radiation synovectomy. The activity to be applied to obtain a dose of 100 Gy was derived from the equation for estimation of radiation for the evaluation of the dose (D) due to β-emitting sources distributed in a volume V (*17*). The contribution of γ rays to the energy dose is less than 0.1% and therefore negligible. Injected activities (Table 2) were sometimes lower than calculated activities, as a result of the time gap between calibration and application and of small amounts of radioactivity remaining in the syringe (<3%).

Biokinetics and Biodistribution. Determination of Leakage

Gamma Camera Imaging. Imaging of the ^{165}Dy-distribution was performed using a large-field-of-view (FOV) gamma camera adjusted to 94.7-keV ^{165}Dy-rays (3.6%). A low-energy collimator was used. Data were stored by a computer for subsequent analysis and review. Patients were scanned 1 and 3 h after intra-articular injection of ^{165}Dy-FH.

Whole-body Counter Measurements. The method of whole-body counter measurements was published previously (*12*). Patients were scanned after 2, 4 and, in case of leakage, 6 h after intra-articular injection of ^{165}Dy.

Measurement of Blood Activity. Levels of blood activity were determined from 8-mL blood samples taken before and 1 and 3 h after therapy, using a gamma counter calibrated for ^{165}Dy.

MRI

MR examinations were performed on a 1.5-T MR unit (Magnetom SP 63; Siemens, Erlangen, Germany) using a circular polarized knee coil. The following sequences were applied: A sagittal (axial) T1-weighted spinecho sequence (repetition time [TR]/echo time [TE] 600/15 ms; acquisitions: 4, FOV: 200, matrix: 256 × 256, thickness: 4 mm) and a T1-weighted three-dimensional gradient-echo sequence with frequency selective fat saturation (TR/TE 45/10 ms, flip angle 40°; acquisitions: 1, FOV: 200, matrix: 192 × 256, thickness: 1.6 mm). From the three-dimensional data set, axial reformations for the patellar cartilage layer were performed. The addition of frequency selective fat suppression to T1-weighted three-dimensional gradient-echo sequences results in a significant increase in contrast-to-noise ratios between cartilage and subchondral bone, demonstrating articular cartilage as a band of high signal intensity. After suppression of fat signal, intensities are rescaled by the MR unit to render articular cartilage as the brightest structure in the joint (Fig. 1), with joint fluid and subchondral bone comparatively lower in signal intensity. The advantage of fat-suppressed three-dimensional gradient echo sequences is a relatively high signal intensity of articular cartilage

TABLE 2
Biokinetics and Biodistribution After Administration of ^{165}Dy-Ferric Hydroxide

Patient no.	Applied activity (MBq)	Blood*	Leakage to urinary bladder*	Leakage to lymph nodes*	Liver	Local adverse reactions
1	9544	0.029	None	None	None	+
2	8900	0.009	None	0.29	None	+
3	7050	0.074	None	None	None	+
4	7553	<0.001	None	None	None	–
5	9012	<0.001	None	None	None	+
6	6436	0.220	0.28	None	None	–
7	6405	<0.001	None	None	None	–
8	11100	<0.001	None	None	None	–
9	8444	<0.001	None	None	None	–
10	6298	0.020	None	None	None	–
11	8906	0.007	None	None	None	+
12	8033	0.092	None	None	None	–
13	9998	0.001	None	None	None	–

*Activities in blood, urinary bladder and lymph nodes are given as percentage of injected activities (3, 2 and 4 h after injection).

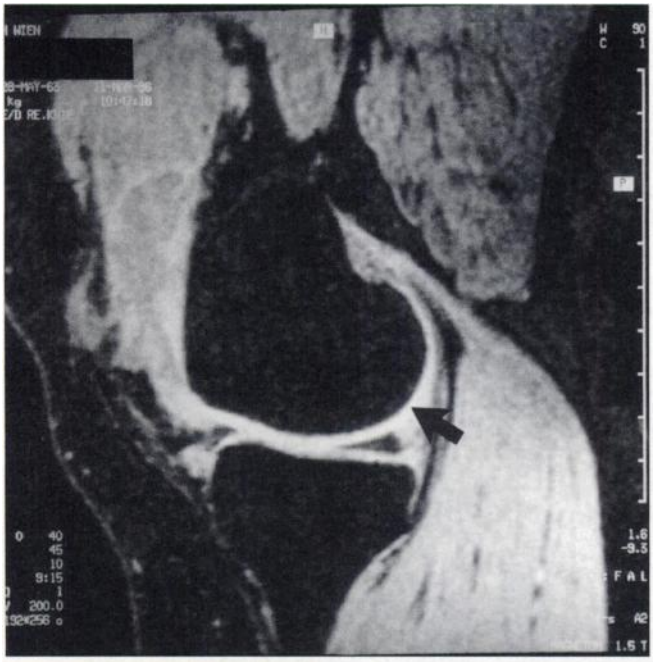

FIGURE 1. Normal articular cartilage thickness and structure (arrow) on T1-weighted three-dimensional gradient-echo sequence with fat saturation MR images approximately 1 y after treatment.

contrasting to the low signal intensity from the surrounding tissue. Three-dimensional acquisition yields images with higher resolution and contrast-to-noise ratio than two-dimensional acquisitions. Thin imaging sections allow high- quality multiplanar reconstructions, which are useful in evaluating the patellar and trochlear surfaces with images perpendicular to facets where the articular surface is curved (*18,19*).

After intravenous injection of 10 mL Gd-DTPA (Omniscan; Nycomed, Linz, Austria), sagittal and axial T1-weighted spinecho sequences were performed (*20*). Examples of pre- and postcontrast media MR images are shown in Figures 2A and B, respectively. Synovial enhancement during the first minute after injection was graded as: +++ = very intense; ++ = intense; + = moderate; and no enhancement.

MRI studies were evaluated by three observers, who were unaware of the clinical results. Synovial measurements were performed in each patient three times in three regions (retropatellar, lateral and medial), using the slice with the maximum thickness of the synovium on pretreatment images as the reference site for follow-up measurements. The intercondylar distance was measured on that particular slice to identify the same region at follow-up measurements. The means of three measurements of synovial thickness at each reference site were calculated. Intraobserver and interobserver variations were 6% and 11%, respectively.

Articular cartilage thickness and homogeneity were assessed visually in all slices. Comparisons of pre-and post-treatment images were performed at the above mentioned reference sites. A semiquantitative classification of normal, decreased (−) and loss of cartilage (−−) was used. In accordance with the classification of in vitro studies used by Hayes et al. (*21*), articular cartilage lesions were classified as indicative of superficial or basal degeneration. Cohen κ was 0.84, indicating strong interobserver agreement on classification of articular cartilage and synovial enhancement.

Pathological Evaluation of Articular Sections and Effusions

Synovial layer sections were obtained by routine diagnostic arthroscopy (medial and lateral approach) at least 6 wk before radiation synovectomy. Pretherapeutic effusions were drawn using a 1.2-mm-gauge needle followed by the injection of ^{165}Dy-FH. Post-therapeutic effusions were obtained from those 3 patients requiring post-therapeutic arthrocenteses for clinical reasons, i.e., to resolve effusion causing pain and tenderness. Post-therapeutic articular sections were obtained from 1 patient undergoing arthroplasty because of rapid disease progression.

The sections were examined twice by one of the authors, who was blinded to the clinical, radiological and MRI findings. The following microscopic features were assessed in paraffin-embeded sections after staining with hematoxylin and eosin: fibrin exsudation, polymorphonuclear cell infiltration, mononuclear cell infiltration, multiplication of synoviocyte lining layer, villous hypertrophy of synovial surface, proliferation of blood vessels, formation of granulation tissue and fibrosis within the synovium. We examined at least three microscopic fields per section, with a magnification of 100× and, when necessary, confirmed the findings at a higher magnification. Presence or absence of each microscopic feature was recorded for every microscopic field. Cytological analysis was performed after Giemsa staining using a magnification of 400×.

Statistical Analysis

Data are given as mean ± SD unless otherwise stated. Wilcoxon nonparametric test or Student *t* test was used to analyze changes in synovial thickness and clinical score for statistical significance. Bonferroni's correction was used to adjust the significance level for

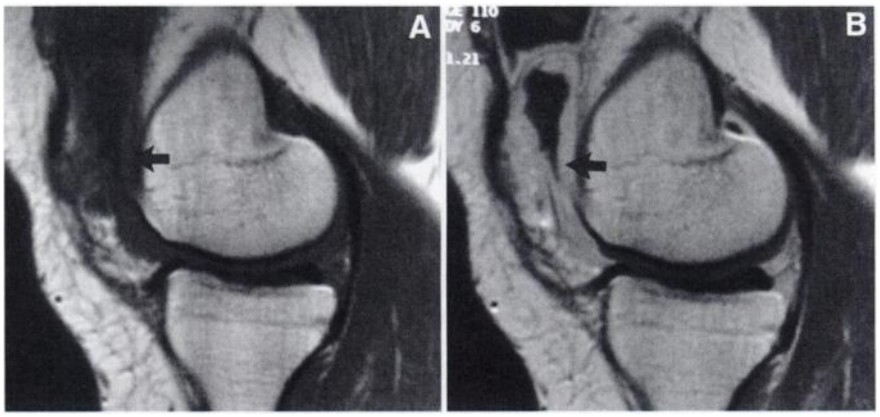

FIGURE 2. Examples of synovial membrane (arrows) on T1-weighted MR images before (A) and after (B) injection of Gd-DTPA. Intense synovial enhancement can be seen after contrast media application.

multiple measurements. Spearman's rank coefficient of correlation was calculated to relate the changes in synovial thickness and enhancement to the local clinical score before and after treatment. Chi-square analysis was used for categorical data, i.e., comparisons of responders with nonresponders. Nonresponders were defined clinically by an unchanged or negligibly improved local clinical score (<3 points) or by means of MRI by the absence of decreased synovial enhancement. Statistical difference was assumed if the null hypothesis could be rejected at 0.05 probability level.

RESULTS

Biokinetics and Biodistribution: Determination of Leakage

In no patient was any leakage to bladder or to the local lymph nodes detected by gamma camera imaging. Blood activity levels were negligible (Table 2).

Whole-body Counter Measurements Dosimetry

Whole-body counter measurements revealed some leakage to the bladder in 1 patient and to the local lymph nodes in another. The doses to the nontarget organs were about 0.28 and 0.29 Gy in these cases, respectively (Table 2).

Clinical Course

Nine of 13 patients (69%) exhibited persistent responses to radiation synovectomy (Table 1). The local clinical score improved significantly ($P < 0.001$), from a median of 7 (range 4–10) before treatment to a median of 2 (range 0–9) after treatment. In detail, effusions decreased from a pretherapeutic median of 2 (range 1–3) to a median of 0.5 (range 0–2) after treatment. One year after treatment, 7 patients did not suffer from any effusions and 7 suffered from no pannus. All but 2 patients showed an increase in range of motion in the affected knee joint (median improvement 20°, range 0°–95°). Nine patients felt no local pain in the treated knee joint 1 y after treatment. Treatment failed to induce any relevant clinical improvement in 4 patients (Table 1). Among those 4 nonresponders, 1 patient underwent knee arthroplasty because of disease progression.

Adverse Effects

A moderately increased effusion and local tenderness were observed in 5 patients within a few days after treatment, with a maximum duration of 7 d. Arthrocentesis was performed in 3 patients to resolve the symptoms.

MRI

Articular Cartilage. There was no evidence of any immediate damage to the articular cartilage (Table 3). After a mean observation period of 13 mo, the thickness and homogeneity of the articular cartilage was unaltered in all but 3 patients, whose MR images revealed previously undetectable superficial erosions.

Synovial Thickness and Enhancement. All patients except 3 exhibited significant reduction in synovial thickness, with

TABLE 3
Results of MRI Before and After Radiation Synovectomy

Patient no.	Synovial thickness (mm)			Synovial enhancement*			Cartilage thickness†			Cartilage lesions‡		
	T_0	T_1	T_2	T_0	T_1	T_2	T_0	T_1	T_2	T_0	T_1	T_2
1	4.9	4.8	3.4	++	++	None	− (Rp)	− (Rp)	− (Rp)	None	None	None
2	7.2	6.0	5.1	+++	+	+	Normal	Normal	Normal	None	None	None
3	6.6	5.4	NA	++	++	NA	−−	−−	NA	II	II	NA
4	9.9	6.8	4.9	+++	++	+	−−	−−	−−	II	II	II
5	4.8	3.2	2.4	++	+	None	Normal	Normal	Normal	None	None	None
6	6.0	3.7	2.2	+++	+	+	−	−	−	None	None	None
7	5.4	4.8	5.2	+++	++	++	Normal	Normal	Normal	None	None	None
8	12.0	9.8	4.3	+++	++	+	−	−	−	None	None	I (1)
9	3.8	3.7	3.8	+++	+	None	−	−	−	I	I	I (1)
10	7.2	4.8	4.9	+++	+++	+++	−−	−−	−−	II	II	II
11	7.0	5.7	7.0	++	+	+	Normal	Normal	Normal	None	None	None
12	13.2	7.8	7.2	++	++	++	−	−	−	I	I	I
13	11.7	9.0	1.9	++	+	None	− (Rp)	− (Rp)	− (Rp)	None	None	I (1)
Mean	7.7	5.8	4.4	None 0	0	4	Normal	4	4	None 8	8	6
SD	3.0	2.0	1.7	+ 0	6	5	4	−6	−6	I 2	2	4
				++ 6	6	2	−6	−−3	−−3	II 3	3	3
				+++ 7	1	1	−−3					

*Synovial enhancement is graded in: +++ very intense, ++ intense, + moderate and none.
†Articular cartilage thickness is classified as normal, decreased (−) and loss of cartilage (−−).
‡Cartilage lesions are classified as superficial degradation (I) and basal degradation (II); number of new lesions is in parentheses.
Rp = retropatellar; NA = not applicable.
T_0 represents time before treatment.
T_1 represents 1 wk after treatment.
T_2 represents 1 y after treatment.

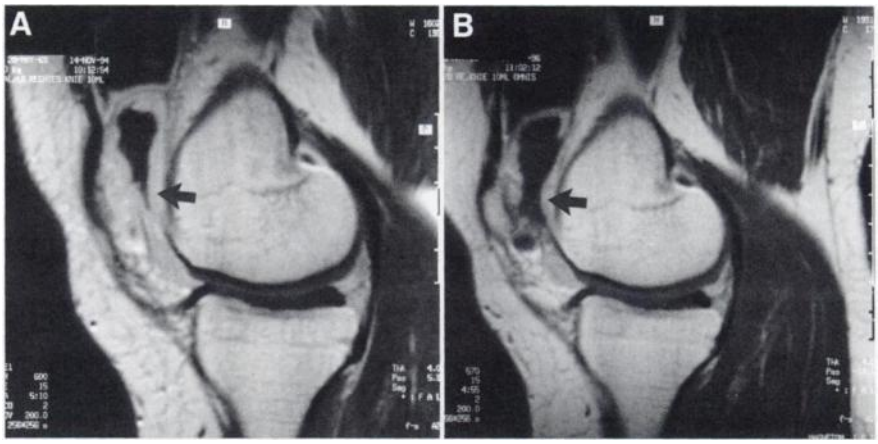

FIGURE 3. Decrease in synovial thickness (arrows) and enhancement on sagittal T1-weighted MR images after contrast media application before (A) and after (B) treatment.

a median reduction of 24% ($P = 0.03$; range 0%–40%) after 1 wk and 42% ($P = 0.01$, range −83% to −8.7%) after 1 y (Fig. 3). Synovial enhancement was significantly decreased in most patients. However, 2 patients exhibited substantial reduction in synovial thickness without any decreased enhancement or clinical improvement. Two patients had no decrease in synovial thickness but in synovial enhancement with concomitant clinical improvement. Changes in the local clinical score were significantly related to the gradual decrease in synovial enhancement in MR images after 1 wk ($r = 0.621$, $P = 0.024$, n = 13) and 1 y ($r = 0.7$, $P = 0.008$, n = 12; scatter plot shown in Figure 4). In other words, a response to therapy as defined by a decrease in synovial enhancement in MRI 1 wk or 1 y after treatment was significantly ($P = 0.007$) associated with a favorable clinical outcome after 1 y.

DISCUSSION

Radiation synovectomy is an alternate, locally acting treatment for chronic synovitis refractory to intra-articular glucocorticosteroids and systemic pharmacological treatment. It is unknown whether the reduction of the synovial thickness and inflammatory activity is achieved at the price of any damage to the articular cartilage. This MRI study demonstrates that radiation synovectomy is effective in reducing synovitis without evidence of severe harm to the articular cartilage during the 1-y observation period. The clinical results are also in agreement with those of many trials (*5–10*) and reveal reductions in joint pain and effusion as well as an increased range of motion in most patients. A benefit of radiation synovectomy at advanced stages of disease (Larsen III) has been claimed but with concerns about possible harm to the articular cartilage (*9*). Similar concerns have been expressed arguing that chronic synovitis affects different regions in the same joint to a varying extent. We demonstrate the absence of relevant articular cartilage reaction by MRI at early follow-up studies in all 13 patients and in all but 3 patients after a mean follow-up of 13 mo, although some patients had basal articular cartilage lesions before treatment. Three patients exhibited new, isolated superficial lesions of articular cartilage on later follow-up MR images. It is quite plausible that the course of the underlying disease, rather than the treatment, caused these changes. Radiation-induced damage leads to a diffuse reduction in the volume of articular cartilage, whereas only isolated erosions were found in the retropatellar region. Moreover, radiation-induced damage should be detectable a

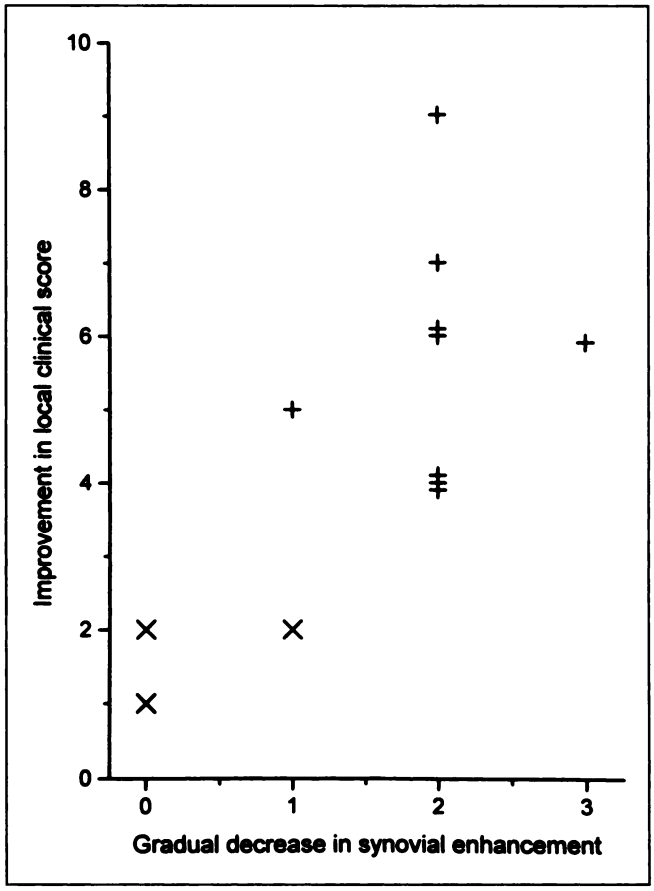

FIGURE 4. Association between improvement in local clinical score and decrease in synovial enhancement in 12 patients approximately 1 y after radiation synovectomy. + = responder (improvement in local clinical score > 3 points); x = nonresponder. All responders reveal persistent decrease in synovial enhancement after therapy.

few days after treatment, particularly when considering the fact that we used high activities of a short-lived radionuclide (half-life 2.4 h). The lesions were seen some months after treatment, which argues against a causal relationship. Finally, it should be kept in mind that the clinical course of both psoriatic and rheumatoid arthritis is associated with a high frequency of spontaneously developing lesions of the articular cartilage (*23*). It is notable, however, that the inflammatory activity could be reduced in all but 2 patients, as demonstrated by a substantial reduction in synovial enhancement associated with clinical improvement.

MRI is well suited to the imaging of patients with chronic synovitis. Not only is this technique capable of depicting joints in multiple planes without manipulation, but it is a noninvasive method with some potential for directly depicting articular cartilage and synovial tissue in the early course of synovitis. Differentiation of inflammatory tissue from effusion, cartilage and bone is possible with the intravenous administration of Gd-DTPA (*24–27*), increasing the signal intensity of hypervascular synovial tissue on T1-weighted images and thus improving the contrast between synovium and adjacent joint effusion. MRI has been used to assess the activity of rheumatoid arthritis and its response to therapy. Synovial enhancement is dependent on the severity of pathological findings (*28–29*). Assoun et al. (*30*) are thus far alone in reporting the effectiveness of nonsurgical synovectomy by the use of an MRI protocol. They suggested, in abstract form, that the synovial thickness determines the probability of therapeutic success of chemical synovectomy with osmic acid. Their treatment was successful in 86% of patients in whom MRI showed moderate synovial thickness of <2 mm and no bone or cartilage lesions (*30*). The mechanism of action of radiation synovectomy is different, because the particles are phagocytized by the surface layer of synovial lining cells, presumably by macrophages. The β-emitting nuclides irradiate the target tissue of chronic synovitis, leading in months to local fibrosis (*13,22*). Synovial thickness was reduced by radiation synovectomy by a mean of 24% after 1 wk, improving to 42% after 1 y. The mean thickness of the inflamed synovium was 7.7 mm, whereas the maximum range of ^{165}Dy in soft tissue is 5.7 mm. The results fit well into the hypothesis about the mode of action and make the superiority of radiation over chemical synovectomy plausible, though some patients were included with advanced stages of the disease (Table 3). The results may be comparable to the reported reduction in synovial membrane volume by 49% after intra-articular injection of glucocorticosteroids (*15*), which had failed to induce remission in all our patients. Though the number of patients in our study was rather small, our results confirm the efficacy of radiation synovectomy shown in previous trials (*9,10,22*). Clinically, the short-term outcome does not always reflect long-term outcome, because signs of local inflammation were found in some, but not all, patients shortly after radiation synovectomy. The histological and cytological findings in sections and effusions obtained before and shortly after application of the radionuclide in 3 patients might support this assumption by indicating relevant changes in cellular composition within a few hours. Signs of an acute inflammatory response with an excess of neutrophils were seen in effusions aspirated immediately after treatment, while lymphocytes predominated in the pretreatment sections or effusions, which is typical for a chronic inflammatory process (Fig. 5). It is notable that, although validity is restricted by the limited number of patients in this study, an acute, clinically manifested inflammatory response does not seem to predict the clinical outcome. However, MRI shortly after radiation therapy might be predictive for long-term results when indicating a substantial reduction in synovial enhancement, whereas synovial thickness often takes months to decrease. Again, this fits well into the presumed mechanism of action that suggests the development of synovial fibrosis several months after treatment (*22*).

The conclusions of this study may be limited by the fact that rheumatoid arthritis and psoriatic arthritis are polyarticular systemic diseases in which the disease activity may spontaneously fluctuate within a single joint. According to

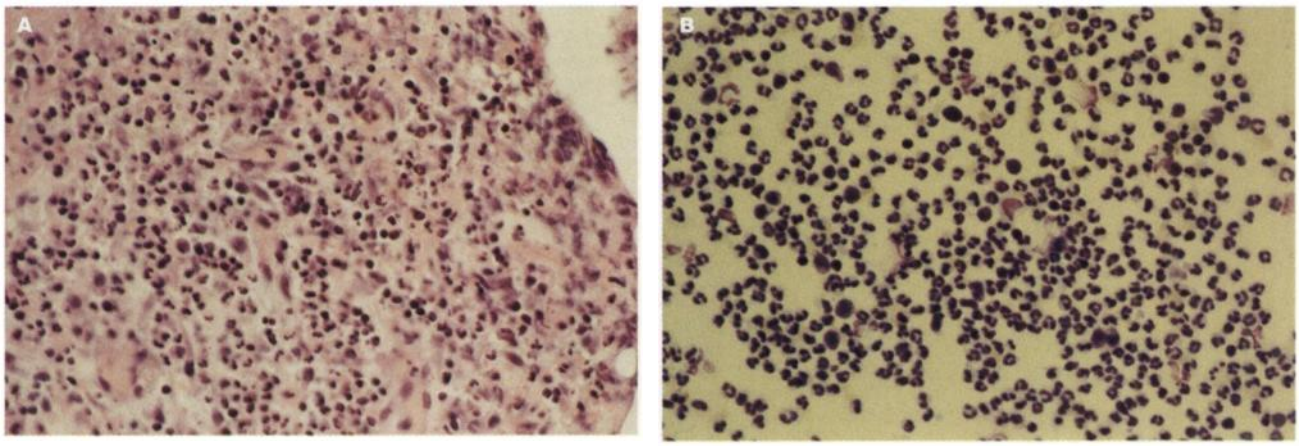

FIGURE 5. (A) Histological section of synovial membrane with predominance of lymphocytes and plasma cells over neutrophils, before treatment. (B) Cytological analysis of effusion punctured 1 d after treatment, with a predominance of neutrophils.

Tamai et al. (*29*), maximum enhancement, in addition to pathological findings and microscopy scores, varies substantially within an individual knee joint. The quantitative assessment of the severity of synovitis is feasible with dynamic MRI, although the rate of signal enhancement may vary from day to day within an individual joint. We did not quantify the enhancement of the synovium, but the visual evaluation has been demonstrated to be accurate. The use of a protocol that assessed synovial thickness, enhancement and cartilage structure in patients with locally active but systemically stable disease just before and 1 wk and 1 y after treatment reduced the probability that the observed changes occurred spontaneously.

CONCLUSION

This MRI study provides morphological evidence for the clinical efficacy of radiation synovectomy and suggests that there is no severe short-term or long-term harm to articular cartilage.

ACKNOWLEDGMENTS

This research project was supported in part by a grant from the Österreichische Nationalbank—Jubiläumsfondsprojekt 6248. We thank F. Kainberger, MD, for his comments on the manuscript.

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