The effect of radiation synovectomy in patients with persistent arthritis: A prospective study

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Abstract

Objective

To investigate and compare the effects of radiation synovectomy of various joints in a rheumatological practice.

Methods

Consecutive patients referred for radiation synovectomy to Medical Center Alkmaar from 1993 till 1996 were analyzed (n = 138). Patients had to have persistent arthritis despite at least two intra-articular glucocorticoid injections with 20 mg triamcinolone hexacetonide. The knees were treated with 185 MBq Yttrium-90; shoulders, elbows, wrists, hips and talocrural joints received 185 MBq Rhenium-186 and meta-carpophalangeal joints and proximal interphalangeal joints 37 MBq Erbium-169. The radionuclide injection was followed by injection of 20 mg triamcinolone in order to prevent flare-up of synovitis (due to chemical irritation) and needle-track burn. The clinical effect was assessed by evaluating VAS pain (0-10 point scale), functional disability, tenderness and swelling of the treated joint and patient's and physician's global assessments of the effect of therapy (each on a 4-point scale).

Results

The overall success rate for radiation synovectomy one year after treatment was 70% with a significant improvement in the variables VAS pain, functional disability and joint tenderness and swelling, when compared to baseline values ($p < 0.000001$). Moderate to considerable satisfaction of patients and physicians one year after treatment was found for > 50% of cases. Wrists and shoulders were the joints with highest success rate of treatment, followed by the elbows. Lowest success rates were found for hips and ankles. In RA treatment was effective in 76% of cases whereas patients with OA exhibited a success rate of 50%. In RA all treated joints, except the ankles, exhibited a success rate of ≥ 75%. No short-term clinical adverse side effects were noted.

Conclusion

Radiation synovectomy seems to be a successful treatment for persistent arthritis when other therapeutic modalities have failed.

Key words

Radiosynovio-orthesis, radiation, synovectomy, synoviolysis, arthritis, therapy, yttrium, radionuclide.

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Introduction

Radiation synovectomy or radiosynovectomy or radiosynovio-orthesis is a local therapy for persistent arthritis, especially monarthritis or oligo-arthritis (1,2). It is an alternative to surgical (open or arthroscopic) synovectomy, in which the inflamed synovium is removed mechanically or by means of a laser, and chemical synovectomy, in which the amount of inflamed synovium is reduced by chemicals such as osmic acid (3-7). Good effect of radiation synovectomy correlates with a reduction in the amount of inflamed synovium (8). Indications for synovectomy are symptoms of persistent inflammation such as pain; furthermore, theoretically progression of joint damage might be inhibited (9, 10). However, this latter beneficial effect of radiation synovectomy has not yet been proven (11, 12).

In the literature, data on the efficacy of radiation synovectomy vary widely; some authors claim very good results (predominantly in open studies) (13, 14); other authors are less positive or conclude that radiation synovectomy is not superior to treatment with intra-articular triamcinolone (15-17). In our retrospective study on radiation synovectomy with yttrium-90 (^{90}Y) for arthritis of the knee, prolonged remission of synovitis was only achieved in 29% of the subset of joints with an initially good response during a follow-up period of 8 years (18). Theoretically, the effect of radiation synovectomy of the knee could be different from the effect of this therapy in another joint. The knee is a weight-bearing joint; frequently in osteoarthritis (OA) of the knee there are signs and symptoms of arthritis, e.g. increased amounts of fluid in this joint in contrast to other (non-weight-bearing) joints with OA. It is possible that monoarthritis of the knee is based more frequently on OA than monoarthritis of other joints. It is known that the beneficial effect of radiation synovectomy is less in OA than in inflammatory arthritis (19).

To investigate and compare the effects of radiation synovectomy in various joints in a rheumatological practice, this prospective study was performed.

Patients and methods

Consecutive patients referred to Medical Center Alkmaar for radiation synovectomy between 1993 and 1996 (n = 214) were included in the present study. The referring rheumatologists were asked to record follow-up data on the treated patients according to a predefined protocol. Data on 138 patients with a complete follow-up were analyzed. The indication for radiation synovectomy was an insufficient reaction twice to an intra-articular injection of 20 mg triamcinolone hexacetonide. Insufficient reaction was defined as recurrence of arthritis within 4 months of the injection.

Excluded were patients younger than 18 years, pregnant patients or fertile women with inadequate contraceptive measures, patients with a Baker's cyst and patients with joint destruction (clear reduction of the joint space, indicating damage to the cartilage and/or bone erosions, i.e. Steinbrocker radiological stage >2).

In all joints, radiation synovectomy was performed with arthrographic control of the needle position. The knees were treated with 185 megabequerel (MBq) ^{90}Y; shoulder, elbow, wrist, hip and talocrural joints with 185 MBq Rhenium-186; and the meta-carpophalangeal joints and proximal interphalangeal joints with 37 MBq Erbium-169 (1, 20). After injection of the radionuclide, 20 mg triamcinolone hexacetonide was injected into the joint through the same needle to prevent a flare-up of arthritis (chemical irritation of the joint) and a needle tract burn. The treated joints were splinted for 3 days and patients were instructed to rest the treated joint (8). If the hip, knee or ankle had to be treated, the patient was admitted to the hospital for bedrest for 3 days. Assessments were performed at the start and the end of the study; the follow-up period per patient was 1 year.

In Table I the characteristics of patients (those analyzed in the present study, n = 138) and patients with missing follow-up (n = 76) are shown. Of the patients analyzed, 97 were women (70%). The mean (SD) age was 58 (13) years and the mean (SD) disease duration

Table I. Patient characteristics.

	Analyzed patients (n=138)		Patients with missing follow-up (n=76)	
Mean age in years (SD, range)	58	(13, 20-84)	58	(13, 29-83)
Gender, M/F (% female)	41/97	(70)	15/61	(80)
Mean disease duration in years (SD, range)	10	(9, 1-44)	11	(10, 1-44)
Mean duration of synovitis in months (SD, range)	17	(13, 1-60)	14	(12, 3-60)
Diagnosis: Number of patients (%)				
- Rheumatoid arthritis	104	(75)	56	(74)
- Psoriatic arthritis	13	(9)	4	(5)
- Ankylosing spondylitis	5	(4)	1	(1)
- Osteoarthritis	4	(3)	6	(8)
- Other diagnoses#	3	(2)	2	(3)
- *E causa ignota*	9	(7)	7	(9)
Joint: Number of treated joints (%):				
- Knee	40	(29)	27	(36)
- Wrist	28	(20)	12	(15)
- Elbow	26	(19)	8	(11)
- Ankle	15	(11)	11	(14)
- Hip	13	(9)	5	(7)
- Finger	11	(8)	4	(8)
- Shoulder	5	(4)	7	(9)

Other diagnoses: haemophilia,pigmented villonodular synovitis and calcium pyrophosphate deposition disease.

Table II. Number of treated joints versus diagnoses.

	Diagnosis*						
Joint	RA	APs	AS	OA	other	eci	Total
Knee	23	7	3	3	1	3	40
Wrist	26	1	0	0	1	0	28
Elbow	24	2	0	0	0	0	26
Ankle	13	0	0	1	1	0	15
Hip	5	1	1	0	0	6	13
Finger	8	2	1	0	0	0	11
Shoulder	5	0	0	0	0	0	5
Total	104	13	5	4	3	9	138

*RA: rheumatoid arthritis, APs: psoriatic arthritis, AS: ankylosing spondylitis, OA: osteoarthritis, other:other diagnoses (haemophilia,pigmented villonodular synovitis or calcium pyrophosphate deposition disease), and eci: *e causa ignota*, i.e. arthritis of unknown cause.

was 10 (9) years. The duration of synovitis of the treated joints was on average (SD) 17 (13) months. The baseline characteristics of the patients with a missing follow-up versus those of the patient group did not differ. Most patients suffered from rheumatoid arthritis (RA): 104/138 (75%); the most frequently treated joint was the knee: 40/138 (29%) (Table II). Shoulders were least frequently treated: 5/138 (4%).

Clinical evaluation

The clinical variables evaluated were:

a) a visual analogue scale (VAS) of pain for the treated joint, assessed by the patient, ranging from 0 (no pain) to 10 (maximal pain) in centimeters, rounded off to integers;

b) functional disability of the treated joint on a 4-point scale: 0 representing no, 1 slight, 2 moderate and 3 severe disability (assessed by the patient representing the perception of the patient);

c) joint tenderness, assessed on a 4-point scale, 0 representing no tenderness, 1 pain on pressure, 2 pain and wincing on pressure, and 3 wincing and withdrawing on pressure;

d) joint swelling on a four point scale, 0 representing no, 1 slight, 2 moderate and 3 severe swelling (excluding the hip joint) (13);

e) patient's global assessment of the effect of therapy on a 4-point scale, 0 representing dissatisfaction, 1 little, 2 moderate, and 3 considerable satisfaction;

f) physician's global assessment of the effect of therapy on a 4-point scale identical to that used for the patient's global assessment.

Statistical methods

For the variables pain, functional disability, joint tenderness and swelling intra-group changes from baseline were evaluated and for the variables patient's and physician's global assessment mean values at 12 months. For each variable, the percentage of improved patients, according to the treated joints and diagnosis was calculated, to gain insight into possible differences in effect due to the kind of joint or diagnosis. Two cut-off points for improvement (moderate and good improvement) were defined for each variable: a post-treatment amelioration of at least 3 or 5 cm for the VAS, at least 1 or 2 points on the scales of functional disability, joint tenderness and joint swelling, and at least 2 or 3 points on the scales of the patient's and physician's global assessment.

To evaluate individual patient improvement, a composite effect scale ranging from 0 (failure) to 10 (maximal effect) was composed using all variables. Each of the variables added 0-2 to the effect scale, except for the patient's and physician's global assessments which, being summary measures, each added only 0 or 1 point. For the pain score: deterioration or improvement in the VAS < 3 cm added no points, an improvement of 3-5 cm added 1 point and an improvement of 5 cm or more added 2 points. For functional disability deterioration or no change added no points, a positive change of 1 point on the 4-

point scale added 1 point, and improvement of 2 or 3 points on the 4-point scale added 2 points. For joint tenderness and swelling, the same approach as for functional disability was used. For the patient's and physician's global assessment of the effect of therapy, dissatisfaction or little satisfaction added no points and moderate or considerable satisfaction added 1 point. For the hip joints (n=14), joint swelling could not be assessed; to obtain the same range for the composite effect scale as for the other joints, the score of the remaining 5 variables was multiplied by 1.2. To calculate the number of patients with improvement after 12 months of follow-up, improvement or success of treatment was defined as a score of at least 5 on the composite effect scale. For all diagnoses, the percentages of effectively treated patients were calculated and for RA (n = 104) the percentages of effectively treated joints at 12 months were also calculated. In addition, the effect scale was used in regression analysis (step-wise) as a dependent variable to investigate the influence of the clinical parameters of age, gender, disease duration, duration of synovitis of the treated joint, rheumatological diagnosis, and the kind of treated joint (independent variables) on the effect of radiation synovectomy.

We only could use data on 138 patients for the analysis, because the follow-up of other patients (36%) was missing due to inadequate registration of follow-up data by different rheumatologists from different centers during their busy daily practice. Because of the amount of missing data, no attempt was made to estimate missing values. The statistical analyses were performed using the Number Cruncher Statistical System (NCSS) and SPSS/PC+ Statistical Packages (NCSS, Kaysville Utah and SPSS Inc, Chicago, Illinois, respectively).

Table III. Effect of treatment one year after synoviorthesis (n=138), means (SD).

	Baseline	1 year after treatment
VAS pain	5.3 (2.4)	2.4 (2.7) *
Functional disability	1.8 (0.9)	0.7 (0.9) *
Joint tenderness	1.8 (0.9)	0.5 (0.8) *
Joint swelling	1.9 (0.8)	0.7 (0.9) *
Patient's global #		2.3 (1.0)
Physician's global #		2.1 (1.0)

*$p < 0.000001$ compared to baseline
global assessments of the effect of therapy one year after treatment on a four-point scale, 0 representing dissatisfaction, 1 little, 2 moderate and 3 considerable satisfaction.

Results

In Table III the effect of radiosynoviorthesis one year after treatment is shown. The variables VAS pain, functional disability, joint tenderness and swelling showed statistically significant improvement one year after treatment when compared to baseline values ($p < 0.000001$).

Data on joints with improvement at one year are shown in Table IV; percentages of effectively treated patients (pa-

Table IV. Percentages improved patients for each variable at one year, according to treated joint.

	All joints n=138	Knee n=40	Wrist n=28	Elbow n=26	Ankle n=15	Hip n=13	Finger n=11	Shoulder n=5
VAS pain								
(≥ 3 cm)	54	49	64	58	40	39	73	60
(≥ 5 cm)	31	23	39	46	27	15	27	40
Functional disability								
(≥ 1 point)	70	73	82	73	47	62	55	80
(≥ 2 points)	40	38	50	42	27	39	27	60
Joint tenderness								
(≥ 1 point)	75	75	82	85	60	62	73	80
(≥ 2 points)	45	50	57	46	47	23	27	20
Joint swelling								
(≥ 1 point)	76	70	82	89	60		91	20
(≥ 2 points)	42	45	46	46	13		64	0
Patient's global assessment*								
(≥ "moderate")	83	74	89	96	60	92	82	100
(≥ "much")	59	48	61	81	47	54	64	60
Physician's global assessment*								
(≥ "moderate")	77	74	82	77	60	92	82	80
(≥ "much")	49	45	43	62	33	46	82	40

* Global assessments of the effect of therapy one year after treatment: moderate = moderate, much = considerable satisfaction.

tients with clinically relevant improvement) are presented in Table V. The overall success rate for radiation synovectomy, regardless of the treated joint or diagnosis, was 70%. Treatment was most effective among patients with RA (success rate 76%) and least effective for patients with arthritis of unknown origin (*eci*): their success rate was 22%. The success rates for patients with ankylosing spondylitis (AS) and OA were 60% and 50%, respectively. Generally speaking, the wrists (86%) and shoulders (80%) were most frequently treated effectively, followed by the elbows (77%). Least frequent improvement was seen in the hips (46%) and ankles (53%). For the knee joints the success rate was 68%. However, the number of joints with an improvement in VAS ≥ 5 cm or good improvement in the other variables (≥ 2 points) was small in nearly all categories. Improvement in VAS pain (≥3 cm) after one year was obtained for ≥ 50% of all joints, except for the ankles and hips (40%), while an improvement of ≥ 5 cm was found for only 30% of all joints. Improvement in VAS pain occurred most frequently in the finger joints (73%) and least frequently in the hips (39%). Functional disability, joint tenderness and joint swelling improved after one year by ≥ 1 point in at least 70% of all joints, while improvement of ≥ 2 points was found for only about 40% of these joints. After one year, improvement in functional disability was most frequent in the wrists (82%) and least in the ankles (47%). Elbows were the joints with the most frequent (85%) reduction in joint tenderness and ankles the joints with the least frequent reduction (60%). Reduction of joint swelling occurred most frequently in the finger joints (91%), whereas shoulders exhibited the least frequent amelioration (20%). This latter fact could be due to the difficulty of examining clinically swelling of the shoulder. At least moderate satisfaction of both patients and physicians after one year was found in about 80% of the cases and considerable satisfaction in about 50%.

Data on the patients, categorized according to the diagnosis, who improved after one year is presented in Table VI. The most frequent improvement in VAS pain (≥ 3 cm) occurred in RA and ankylosing spondylitis (AS) (about 60%), the least frequent in OA (25%). An improvement of ≥ 5 cm was clearly less common (RA: 40%). Functional disability improved most frequently in patients with RA or OA (75%), least in patients suffering from AS or arthritis

Table V. Percentages of effectively treated patients after 12 months, according to the diagnosis and according to the treated joint*.

	Number of treated patients	% Effective
Diagnosis		
Rheumatoid arthritis	104	76
Psoriatic arthritis	13	54
Ankylosing spondylitis	5	60
Osteoarthritis	4	50
Other diagnoses	3	100
Arthritis *e causa ignota*	9	22
Joint		
Knee	40	68
Wrist	28	86
Elbow	26	77
Ankle	15	53
Hip	13	46
Finger	11	64
Shoulder	5	80

* Of all 138 patients,70% was treated effectively (a score of at least 5 on a composite effect scale, ranging from 0 (failure) to 10).

Table VI. Percentages of improved patients for each variable at one year, according to the diagnosis*.

	All joints n=138	RA n=104	APs n=13	AS n=5	OA n=4	Other n=3	Eci n=9
VAS pain							
(≥ 3 cm)	54	58	54	60	25	0	38
(≥ 5 cm)	31	39	15	0	0	0	13
Functional disability							
(≥ 1 point)	70	74	62	40	75	67	44
(≥ 2 points)	40	43	23	20	75	67	11
Joint tenderness							
(≥ 1 point)	75	81	62	80	75	67	33
(≥ 2 points)	45	50	23	40	50	67	11
Joint swelling#							
(≥ 1 point)	76	77	75	50	75	100	67
(≥ 2 points)	42	42	42	50	25	67	33
Patient's global assessment**							
(≥ 2 "moderate")	83	86	75	80	50	100	78
(≥ 2 "much")	59	62	62	40	25	67	44
Physician's global assessment**							
(≥ "moderate")	77	80	62	80	50	100	78
(≥ "much")	49	52	46	40	25	67	33

*RA: rheumatoid arthritis; APs: psoriatic arthritis; AS: ankylosing spondylitis; OA: osteoarthritis; other:miscellaneous (pigmented villonodular synovitis,haemophilia or calcium pyrophosphate deposition disease); and *eci*: arthritis *e causa ignota*, i.e. arthritis of unknown cause.
Hip joints excluded; ** Global assessments of the effect of therapy one year after treatment.

Table VII. Percentages effectively treated joints after 1 year in RA patients (n=104).

Joint	Number of joints treated	% Effective
Knee	23	78
Wrist	26	85
Elbow	24	79
Ankle	13	46
Hip	5	80
Finger	8	75
Shoulder	5	80

"e causa ignota" (*eci*) (40%). Joint tenderness decreased markedly in all patients (> 60%), except for those with arthritis *eci* (33%). Reduction in joint swelling occurred frequently in all disease categories (range 70-100%), except for patients with AS (in 50%). In each disease category 60-100% of patients and physicians were moderately satisfied one year after treatment, except for OA (50%); however, there were only 4 OA patients.

In RA one year after treatment ≥75% of all joints proved to have been treated effectively, except for the ankle (46%) (Table VII). The best response was found for the wrist (success percentage of 85).

In all cases the effect of treatment could only be predicted by the rheumatological diagnosis, not by age, gender, disease duration, duration of synovitis of the treated joint or the kind of joint treated. For RA patients, a good effect of treatment was only predicted by a short disease duration, not by age, gender, duration of synovitis of the treated joint or the kind of joint treated.

No short-term adverse effects were seen.

Discussion

Radiation synovectomy is performed throughout the world, especially in Europe, but it is unknown exactly how often this therapy is applied (21). Radiosynoviorthesis is a less invasive method compared to surgical synovectomy and may provide long-term relief of pain and swelling as well as improvement in joint function. It has primarily been applied among patients with some form of inflammatory arthropathy, since the mode of action is to retard or stop deleterious proliferation of the inflamed synovial membrane. Generally speaking, radiation synovectomy is less successful in controlling the symptoms of patients suffering from OA, probably because synovial proliferation is absent in these patients (22, 23).

Depending on the joint treated, different radionuclides are used. In large joints, such as the knee, ^{90}Y is used because of the deep penetration of its energetic beta particles (mean tissue penetration 3.6 mm). An average activity of 185 MBq ^{90}Y (5 mCi) has been calculated to give an absorbed radiation dose of approximately 100 Gy to 100 grams synovial tissue (24). Yttrium has been proven to be superior in effect to placebo; however, it was not superior to triamcinolone or other therapeutic modalities (15). A provocative idea is that triamcinolone hexacetonide might be more effective than ^{90}Y therapy (16). We chose to flush the needle with 20 mg triamcinolone hexacetonide after injection of ^{90}Y because of several reasons that are discussed further on in this paper. We expected triamcinolone hexacetonide to have only a small and very short-lived therapeutic effect, if any, after radiosynoviorthesis as in these patients it was impossible to induce sufficient remission of arthritis with two previous injections with the same dose triamcinolone.

Rhenium-186 agents are used for intermediate-sized joints such as the wrist (mean tissue penetration 1.2 mm), while *erbium-169* agents are applied to the smallest joints, i.e. finger joints (mean tissue penetration 0.3 mm).

Evaluation of the therapeutic effects of radiation synovectomy is based largely upon improvements in clinical parameters, as used in our study. Patients who are treated at earlier stages of the disease are known to respond invariably more favorably than those with late to end-stage disease. Radiological staging has been shown to have prognostic significance. Patients with Steinbrocker radiological stages ≤ 2 exhibit significantly better success than those with stage 3 changes (25, 26). In the present study, patients with Steinbrocker radiological stage >2 were excluded from treatment. Radiation synovectomy with ^{90}Y, regardless of the diagnosis, has an overall success rate of approximately 50% (improvement in different parameters) (25, 27). In our previous retrospective study prolonged remission of synovitis after ^{90}Y synovectomy was only achieved in 29% of the subset of patients with joints with a good initial response, during a follow-up period of up to 8 years (18). The success rate at one year was 25%, defined as complete remission of synovitis. The mean duration of remission of synovitis was 21 months (median 16 months), whereas recurrent synovitis occurred after a mean (SD) duration of remission of 3.3 (5.9) months, range 0-22. In the present study the overall success rate for radiation synovectomy with ^{90}Y was 68% (success rate for treated knees) one year after treatment. This discrepancy with our previous study can be explained by different definitions of a treatment response and the different study designs (retrospective versus prospective). Regardless of the radionuclide, the diagnosis or the type of treated joint, the overall success rate for radiosynoviorthesis in the present study was 70% one year after treatment (Table V). The majority of patients and physicians (80%) was satisfied one year after treatment (Tables IV and VI). Generally speaking, the majority of patients is treated for symptoms of RA, as in our study (75%) (Table II). Overall good to excellent response rates for radiation synovectomy in RA, regardless of the radionuclide used, vary from 50-90% (14,28). In the present study the response rate for RA patients was 76%, which is comparable with previous studies.

The second most prevalent diagnosis in our study was psoriatic arthritis (n=13, 9%) with a success rate of 54%. Only 3% of patients suffered from osteoarthritis with a success rate of 50% one year after radiation synovectomy. This success rate is in accordance with data from previous studies (22, 23). The highest percentage of effectively treated patients one year after radiation synovectomy was found for patients with pigmented villonodular synovitis, hae-

mophilia or calcium pyrophosphate deposition disease (100%) (Table V). However, the latter diagnosis involved only 3 joints (2%). Radiosynoviorthesis of haemophilic arthropathic joints apparently changes the bleeding pattern of articular tissues, without arresting the destruction and deformation of joints (29). The reduction in joint haemorrhages and factor usage after synovectomy is most obvious in elbow joints, although the other joints as a group also show a significant reduction (30). In the present study there was only one haemophilia patient and this patient underwent treatment of the ankle.

The number of knees treated in other studies far exceeds the number of other joints. In a European prevalence study the knees were found to be the most frequently treated joints (46%) (21). In the present study as well the most frequently treated joint was the knee (n= 40); of all knees 58% were affected by RA and the success percentage 1 year after treatment was 78 (Table VII). For RA patients treatment of the wrist was the most effective (in 85%). These results are in accordance with those of other investigators who obtained good results in 75% of knees and 100% of wrists in RA patients during a follow-up period of 8 to 60 months (31).

Finger joints were the second most frequently treated joints in the European prevalence study (20%) (21), whereas in the present study the second most frequently treated joint was the wrist (20%). Eight percent of all treated joints in our study were finger joints; 73% of all finger joints were affected by RA and the success percentage one year after treatment was 75.

In previous studies the elbows of RA patients responded significantly better than shoulders and ankles (25). Treatment of the elbow with RA led to a "good" result in 72% of the cases (32). In the present study the success rates for the shoulders and elbows in RA patients were similar 1 year after treatment (approximately 80%) and were significantly higher than the success rate for ankles (46%) (Table VII).

Immobilization of the treated joint seems to be essential, since a significantly higher absorbed radiation dose to the lymph nodes and lower dose to the synovial tissue due to leakage is observed in the absence of immobilization. There is a strong correlation between the reduction in blood pool activity and synovial swelling versus improvement in pain (8, 9, 33). Also, immobilization could lead to a better clinical result (34).

Leakage to the lymph nodes and liver is less if the needle has been flushed with saline or triamcinolone hexacetonide after administration of the radionuclide (35). Furthermore, the occurrence of radiation necrosis of the needle tract burn, due to leakage of the radionuclide back into the needle tract when withdrawing the needle, is avoided (36). In our hospital the needle is always flushed with 20 mg triamcinolone hexacetonide after injection of the radionuclide to avoid needle track burns, to prohibit a flare up of arthritis due to chemical irritation of the joint by the radionuclide, to inhibit leakage from the joint by reducing arthritis associated increased vascularity and perfusion of the inflamed synovium, and to bridge the lagtime before onset of the effect of the radionuclide.

Although in the present study no short-term clinical adverse effects were noted, long-term effects cannot be excluded. However, in literature no serious long-term side-effects like malignancies are reported (25).

Treatment of the hips and ankles was least frequently successful. This cannot be attributed to a lower dose to the synovial tissue due to leakage, because after treatment of these joints the patients were immobilized for 3 days in the hospital. Repeated therapy for a previous non-responder is associated with a high failure rate (25). In our previous study a second injection with a double dose of ^{90}Y after an initial failure had no beneficial effect (15). Treatment with arthroscopic synovectomy followed by radiation synovectomy within 2 weeks leads to a success rate of 40% only, suggesting no benefit of this combination (25). In cases of failure, perhaps diagnostic arthroscopy is of value to explore further treatment modalities.

A major drawback of this study is the large amount of missing data, resulting from the inadequate registration of follow-up data by the referring rheumatologists, despite frequent reminder notes from the primary investigator. The busy daily practice of the rheumatologist remains the main reason why the registration of data for prospective clinical studies is experienced as a burden. The fact that these data are missing could have led to selection bias. However, the baseline characteristics of the patients with missing follow-up did not differ from those of the patient group.

We conclude that radiation synovectomy seems to be a successful, moderately effective method for treating persistent arthritis for up to one year if other local therapies have failed.

Whether the final effect of this treatment depends mainly upon the radionuclide injected or its combination with a corticosteroid is unknown. In order to evaluate and compare the individual effects of the two therapeutic compounds we have started a multicenter randomized double-blind, placebo-controlled study in which patients with arthritis of the knee are treated intra-articularly either with corticosteroids and placebo or with corticosteroids and ^{90}Y. In this study the knee joint is immobilized and rest is prescribed (i.e., a hospital stay of 3 days) in order to optimize the effect and to prevent leakage from the knee joint. We hope to complete the inclusion of patients in this study by the end of the year 2001.

References

1. GUMPEL JM: The role of radiocolloids in the treatment of arthritis. *Rheumatol Rehabil* 1974; 13: 1-9.
2. BOUSSINA I, TOUSSAINT M, OTT H, HERMANS P, FALLET GH: A double-blind study of erbium169 synoviorthesis in rheumatoid digital joints. Results after one year. *Scand J Rheumatol* 1979; 8: 71-4.
3. NISSILA M, ANTTILA P, HAMALAINEN M, JALAVA S: Comparison of chemical, radiation and surgical synovectomy for knee joint synovitis. *Scand J Rheumatol* 1978; 7:225-8.
4. SHEPPEARD H, ALDIN A, WARD DJ: Osmic acid versus yttrium-90 in rheumatoid synovitis of the knee. *Scand J Rheumatol* 1981; 10: 234-6.
5. JANIS LR, KRAVITZ RD, WAGNER SS: The pulsed holmium: yttrium-aluminum-garnet laser. Applications to ankle arthroscopy. *Clin Podiatr Med Surg* 1994; 11: 483-98.

6. OGILVIE HARRIS DJ, WEISLEDER L: Arthroscopic synovectomy of the knee:Is it helpful? *Arthroscopy* 1995; 11:91-5.
7. O'DUFFY EK,ELL PJ: The practice of medical and surgical synovectomy: A UK survey. *Nucl Med Commun* 1999; 20: 21-4.
8. GRATZ S, GOBEL D, BEHR TM, HERRMANN A,BECKER W: Correlation between radiation dose, synovial thickness, and efficacy of radiosynoviorthesis. *J Rheumatol* 1999; 26: 1242-9.
9. GOBEL D, GRATZ S, VON ROTHKIRCH T, BECKER W: [Chronic polyarthritis and radiosynoviorthesis:A prospective, controlled study of injection therapy with erbium 169 and rhenium 186]. *Z Rheumatol* 1997; 56: 207-13.
10. GOBEL D, GRATZ S, VON ROTHKIRCH T, BECKER W, WILLERT HG: Radiosynoviorthesis with rhenium-186 in rheumatoid arthritis: a prospective study of three treatment regimens. *Rheumatol Int* 1997; 17:105-8.
11. SZANTO E: Long-term follow-up of 90 Yttrium-treated knee-joint arthritis. *Scand J Rheumatol* 1977; 6: 209-12.
12. TEIGLAND JC, TJONNFJORD GE, EVENSEN SA, CHARANIA B: Synovectomy for haemophilic arthropathy:6-21 years of follow-up in 16 patients. *J Intern Med* 1994; 235: 239-243.
13. DEUTSCH E, BRODACK JW, DEUTSCH KF: Radiation synovectomy revisited. *Eur J Nucl Med* 1993; 20: 1113-27.
14. ASAVATANABODEE P, SHOLTER D, DAVIS P: Yttrium-90 radiochemical synovectomy in chronic knee synovitis:A one year retrospective review of 133 treatment interventions. *J Rheumatol* 1997; 24: 639-42.
15. ARTHRITIS AND RHEUMATISM COUNCIL MULTICENTRE RADIOSYNOVIORTHESIS TRIAL GROUP: Intra-articular radioactive yttrium and triamcinolone hexacetonide: An inconclusive trial. *Ann Rheum Dis* 1984; 43:620-3.
16. JONES G: Yttrium synovectomy: a meta-analysis of the literature. *Aust NZJ Med* 1993; 23: 272-5.
17. HEUFT LLJ, DE VET HCW, VAN DER LINDEN S: Yttrium radiosynoviorthesis in the treatment of knee arthritis in rheumatoid arthritis: a systematic review. *Ann Rheum Dis* 2000; 59: 583-6.
18. JAHANGIER ZN, JACOBS JW, VAN ISSELT JW, BIJLSMA JW: Persistent synovitis treated with radiation synovectomy using yttrium-90: A retrospective evaluation of 83 procedures for 45 patients. *Br J Rheumatol* 1997; 36: 861-9.
19. TAYLOR WJ, CORKILL MM, RAJAPASKE CN: A retrospective review of yttrium-90 synovectomy in the treatment of knee arthritis. *Br J Rheumatol* 1997; 36: 1100-5.
20. WANG SJ, LIN WY, HSIEH BT, SHEN LH, TSAI ZT, TING G, KNAPP FF JR: Rhenium-188 sulphur colloid as a radiation synovectomy agent. *Eur J Nucl Med* 1995; 22: 505-7.
21. CLUNIE G, ELL PJ: A survey of radiation synovectomy in Europe, 1991-1993. *Eur J Nucl Med* 1995; 22: 970-6.
22. WILL R, LAING B, EDELMAN J, LOVEGROVE F, SURVEYOR I: Comparison of two yttrium-90 regimens in inflammatory and osteoarthropathies. *Ann Rheum Dis* 1992; 51:262-5.
23. TANAKA S, UEO T, OHNISHI N: Clinical effects of radiation synovectomy. *J West Pac Orthop Assoc* 1978; 15: 83-92.
24. ZUCKERMAN JD, SLEDGE CB, SHORTKROFF S, VENKATESAN P: Treatment of rheumatoid arthritis using radiopharmaceuticals. *Int J Rad Appl Instrum B* 1987; 14:211-8.
25. STUCKI G, BOZZONE P, TREUER E, WASSMER P, FELDER M: Efficacy and safety of radiation synovectomy with Yttrium-90: A retrospective long-term analysis of 164 applications in 82 patients. *Br J Rheumatol* 1993; 32: 383-6.
26. SAVASER AN, HOFFMANN KT, SORENSEN H, BANZER DH: [Radiosynoviorthesis in the treatment plan of chronic inflammatory joint diseases]. *Z Rheumatol* 1999; 58: 71-8.
27. RAU R, SCHUTTE H: [Results of radiosynoviorthesis with yttrium 90 in chronic synovitis: a long-term prospective study. I. Total results and effect of local factors]. *Z Rheumatol* 1983; 42: 265-70.
28. MULLER BRAND J: [Principles of radiosynoviorthesis]. *Schweiz Med Wochenschr* 1990; 120: 676-9.
29. VAN'T PAD BOSCH PJ, VAN DE PUTTE LB, BOERBOOMS AM, GEERDINK PJ: Radiosynoviorthesis in haemophilic joint disease. *Z Rheumatol* 1981; 40: 237-9.
30. DAWSON TM, RYAN PF, STREET AM, ROBERTSON PL, KALFF V, KELLY MJC-F: Yttrium synovectomy in haemophilic arthropathy. *Br J Rheumatol* 1994; 33:351-6.
31. AGUILERA S, PIZZI T, DONOSO I: [Radiation synovectomy with yttrium 90 and rhenium 186 in rheumatoid arthritis,long term follow-up and effects on synovial membrane]. *Rev Med Chil* 1994; 122: 1283-8.
32. GREGOIR C, MENKES CJ: The rheumatoid elbow: Patterns of joint involvement and the outcome of synoviorthesis. *Ann Chir Main Memb Super* 1991; 10:243-6. [published erratum appeared in *Ann Chir Main Memb Super* 1991;10:540].
33. JAWORSKI R, MCLEAN R, CHOONG K, SMART R, EDMONDS J: Re-evaluating the need for hospitalization following synovectomy usingYttrium-90 silicate. *Br J Rheumatol* 1993; 32: 1012-7.
34. CHAKRAVARTY K, PHAROAH PD, SCOTT DGI: A randomized controlled study of post-injection rest following intra-articular steroid therapy for knee synovitis. *Br J Rheumatol* 1994; 33: 464-8.
35. VAN SOESBERGEN RM, HOEFNAGEL CA, MARCUSE HR, DIJKSTRA PF, BERNELOT MOENS HJ: Radiosynoviorthesis of the knee: a double-blind trial of 1 versus 5 mCi Gold-198. *Clin Rheumatol* 1988; 7: 224-30.
36. PETERS W, LEE P: Radiation necrosis overlying the ankle joint after injection with yttrium-90. *Ann Plast Surg* 1994; 32: 542-3.