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ORIGINAL ARTICLE

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# Yttrium$^{90}$ synovectomy in the management of chronic knee arthritis: a single institution experience

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**Abstract** Radiation synovectomy (RS) has been used to treat chronically inflamed joints refractory to treatment using conventional agents. In RS, the radioactive isotope is concentrated in the synovial membrane from the injected colloid suspension, where it exerts its activity. However, despite numerous reports confirming its safety and efficacy, this procedure is not widely practised. In the Singleton Hospital NHS Trust, yttrium$^{90}$ ($Y^{90}$) RS has been practised since 1990 for refractory synovitis. In this study, we analyse the results of therapy and complications in 38 joints so treated. Doses of 10 mCi were used in the majority of patients. Most responses were apparent by 6 months following the procedure. Altogether, 68% of the treated joints showed satisfactory response at 3 years, with 29% having all symptoms under control beyond 3 years. In three patients, there was evidence of minor pigmentation at the injection site. Two patients had extravasation of the isotope and needle track ulcers, which were recorded as major toxicity. We find $Y^{90}$ radiosynovectomy to be safe, quick, and effective in the management of patients with refractory synovitis. The efficacy of RS should be tested in randomised clinical trials involving large numbers of patients.

**Keywords** Arthritis · Radiation · Synovectomy · Yttrium$^{90}$

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## Introduction

Radiation synovectomy (RS) is used in the treatment of chronically inflamed joints refractory to treatment using conventional agents such as nonsteroidal anti-inflammatory drugs (NSAIDs), antirheumatoid drugs, or intra-articular corticosteroids. The technique is useful in delaying or, in some instances, avoiding surgical synovectomy.

Whilst the use of radioisotopes in managing chronically inflamed joints has been known for over three decades, RS is not commonly performed due to cost, difficulty in administration, and concerns of safety and effectiveness [1, 2]. There is reportedly a high dose delivery to surrounding normal structures and a high incidence of chromosomal aberrations following RS using certain radioisotopes. However, there are no reports of malignancy resulting from RS [3]. Yttrium$^{90}$ ($Y^{90}$) is a pure beta emitter with a mean tissue penetrance of 3.6 mm and mean half-life of 2.7 days. The use of this isotope in RS minimises the risk of irradiating the surrounding normal structures [1, 4].

In our hospital we have used $Y^{90}$ RS since 1990 for inflammatory arthritis and synovitis that persists in one or both knees or recurs despite antirheumatoid drugs and several local corticosteroid injections. In this study, we analyse the results of therapy and complications in a group of patients so treated.

## Materials and methods

All patients treated with RS to their knee joints at the Singleton NHS Trust between January 1990 and June 1999 were included in the study (Table 1). A total of 28 patients were referred for RS during this period, and a total of 38 joints were treated (including ten patients who had both knees treated). There were 11 males and 17 females in the study group, with a mean age of 55.9 years (range 32–80). The most common diagnosis (18 patients) was rheumatoid arthritis. Other varieties included ankylosing spondylitis, psoriatic arthritis, and seronegative inflammatory arthritis. The mean duration of treatment prior to RS was 6.7 years

**Table 1** Patient characteristics

| | |
|---|---|
| Total *n* joints | 38 |
| Total *n* patients | 28 |
| *N*female | 17 |
| *N*male | 11 |
| Female age | Mean 59 years (39–80) |
| Male age | Mean 51 years (32–71) |
| Rheumatoid arthritis | 18 |
| Seronegative arthritis | 5 |
| Ankylosing spondylitis | 3 |
| Psoriatic arthritis | 2 |

**Table 2** Previous systemic treatment

| Previous treatment[a] | *N* patients |
|---|---|
| Gold | 8 |
| Sulphasalazine | 6 |
| Methotrexate | 3 |
| D-penicillamine | 2 |
| Gold and sulphasalazine | 5 |
| Gold and methotrexate | 2 |

[a]All patients received corticosteroids and nonsteroidal anti-inflammatory agents as part of systemic therapy

(range 1–20). All five patients with seronegative arthritis had involvement of only one joint, while the majority ($n = 23$) showed evidence of polyarthritis.

All patients had been treated unsuccessfully with NSAIDs and intra-articular corticosteroids. Antirheumatoid drugs used included methotrexate, gold, and sulphasalazine (Table 2). One patient had had a partial surgical synovectomy prior to referral for RS. All patients continued their systemic drug therapy during and after the RS. Seventeen patients also had involvement of other joints at the time of $Y^{90}$ therapy.

The joints treated were assessed before and after RS by the rheumatologist and clinical oncologist separately. Clinical assessments included joint pain, swelling, and range of movement. Follow-ups were also performed separately by the rheumatologist and oncologist, and response assessments by the different specialists were blinded. There was no disagreement on the assessments.

Radiation synovectomy was performed as an inpatient procedure in all patients jointly by the clinical oncologist and the rheumatologist. The joint was infiltrated with lidocaine anaesthetic with aseptic precautions. Synovial fluid was aspirated to ensure correct positioning of the needle within the joint space and, when a large effusion was present, to reduce its volume. A 10-mCi dose of $Y^{90}$ was instilled through a three-way tap into the joint space, after which the needle was flushed with normal saline. Topical corticosteroid was not administered along with RS. The needle was removed and the wound sealed with sterile gauze. The treated joint was immobilised in a fibreglass shell for 72 h. Bed rest was not enforced.

Patients were followed up at 3-month intervals for 1 year and at 6-month intervals thereafter. Review of patients prior to 3 months was performed only for toxicity and not for response assessment. Response to therapy was first assessed at 3 months and performed clinically using a simple scoring system. Responses were recorded as good, very good, excellent, or none, based on assessments of pain, joint tenderness, joint swelling, and joint mobility (Table 3). An excellent or very good response to treatment was considered a satisfactory outcome. The endpoint for the study was relapse of symptoms. Patients were followed up for a minimum of 3 years after treatment or till relapse of symptoms.

## Results

Treatment outcomes are summarised in Table 4 and Table 5.

### Response to treatment

Assessment of response to treatment began at 3 months, and 29 of 30 joints showing response to RS had done so by 6 months (Table 4). Nine joints failed to show any response within this period, of which one showed response by 9 months. The maximum observed responses were achieved within 18 months and recorded as excellent in ten patients, very good in nine, and good in 11. Eight patients failed to show any response to treatment. No differences in response were noted, depending on the duration of arthritis, therapy before RS, or the number of joints involved.

**Table 3** Response to radiation synovectomy

| | |
|---|---|
| Nil | No improvement of symptoms |
| Good | Reduction in pain and joint tenderness<br>Reduction in joint swelling |
| Very good | Minimal residual pain<br>Minimal joint effusion and moderate improvement in joint movement |
| Excellent | No residual pain<br>No residual joint effusion or swelling and normal or nearly normal joint movement |

**Table 4** Time to response of radiation synovectomy

| Follow-up time | No response | Good | Very good | Excellent | Failures after initial response |
|---|---|---|---|---|---|
| 3 months | 17 | 17 | 2 | 2 | 0 |
| 6 months | 9 | 15 | 10 | 2 | 2 |
| 9 months | 8 | 6 | 7 | 4 | 13 |
| 1 year | 8 | 7 | 5 | 6 | 12 |
| 3 years | 6[a] | 2[b] | 7[b] | 4 | 15 |
| >3 years (long-term) | – | 2 | 7 | 4 | 15 |

[a]Two patients lost to follow-up in this period
[b]One patient lost to follow-up in this period

**Table 5** Outcome of radiation synovectomy

| Total numbers | Follow-up status | Response[a] | Long-term control (> 3 years) ($n = 13$) | Failures ($n = 21$) |
|---|---|---|---|---|
| Patients 28<br>Joints 38 | Available: 34 joints<br>Lost to follow-up: 4 (median 21 months) | No response: 6<br>Good: 2 Satisfactory:26 (15 very good, 11 excellent) | Good:2 Satisfactory:11 (7 very good, 4 excellent) | No response: 6<br>Following initial response: 15 recorded as satisfactory (8 very good, 7 excellent) |

[a]Response in the four lost to follow-up was noted as good and very good in one each and nil in two at last follow-up

### Long-term control

Four patients were lost to follow-up after a mean of 21 months. Two of these patients had control of symptoms at the time of last follow-up; one was recorded as 'good' and the other as 'very good'. The other two patients had no response to treatment when last assessed.

Follow-up status at 3 years was available for the remaining 34 joints. Of these, six joints showed no response to the treatment, and in two joints the response was recorded as 'good'. The remaining 26 joints (68%) showed a satisfactory response to treatment (15 very good and 11 excellent) at 3 years. Of these, 11 joints (29%) showed control of all symptoms beyond 3 years. Their responses were scored as excellent and very good in four and seven joints, respectively. Two joints continued their 'good' response beyond 3 years.

In all, 15 joints showed recurrence of symptoms after a period of initial control (mean 13.6 months, range 9–36). The best response before relapse was recorded as very good in eight patients and excellent in seven.

The mean duration of response in patients showing a satisfactory outcome after RS was 28.4 months (range 10–84). The mean duration of long-term control of symptoms in the 11 joints was 48.6 months (range 36–84). The mean duration of symptom control observed in the entire patient group was 24.4 months (range 0–84).

### Management of failures

Fifteen joints failed after an initial period of response following RS, and eight joints showed no response at all, making a total of 23 failures. Eleven of these failures were treated by surgery and six were treated using other agents. Two patients were lost to follow-up. Retreatment with $Y^{90}$ was performed in four patients who showed no response to initial therapy. All these patients were treated with 10 mCi of $Y^{90}$. Two showed an excellent response to reinjection which was maintained after 28 months and 34 months of follow-up, respectively. The other two patients did not respond.

### Toxicity

The RS was well tolerated in all patients, with no evidence of acute pain, tenderness, or swelling. Two patients had extravasation of the isotope and needle track ulcers, which were recorded as major toxicity. One of these patients showed a necrotic area of skin and subcutaneous tissue which required skin grafting. In three other patients, there was evidence of minor pigmentation at the injection site.

## Discussion

Patients with chronic arthritis refractory to standard drug therapy and intra-articular corticosteroid injections are sometimes managed with surgical synovectomy. The procedure is costly and may be associated with surgical complications including joint stiffness resulting from prolonged joint immobilisation [5]. Radiation synovectomy is an easy and relatively cheap alternative for delaying or, in many instances, avoiding surgical synovectomy [3, 6].

Radioactive gold ($Au^{198}$) was commonly used in RS, but currently the silicate colloid of yttrium$^{90}$ ($Y^{90}$) is preferred. $Y^{90}$ is a pure beta emitter with a mean tissue penetrance of 3.6 mm and mean half-life of 2.7 days. Studies have shown very little migration of this isotope (especially the silicate colloid) from the joint space, and therefore minimal uptake occurs into regional lymph nodes [7, 8]. Thus, the substitution of $Y^{90}$ for $Au^{198}$ minimises the risk of irradiating normal tissues and reduces chromosomal aberrations and damage to normal tissues [1, 4, 9].

Following instillation, the radioactive isotope is concentrated in the synovial membrane from the injected colloid suspension, where it exerts its activity. It is common practice to drain synovial fluid prior to instilling $Y^{90}$ for better contact of the radioactive isotope with the inflamed synovial membrane. It is estimated that, following an injection of 6 mCi to the joint space, a total radiation dose of between 5,500 rad and 11,000 rad is delivered to the synovium over 3 days [10]. Radiation synovectomy is performed as an inpatient or day-case procedure. Rigid splinting of the joint is advised following the procedure, but prolonged bed rest or inpatient stay is not mandatory [11]. These procedures help to prevent extravasation of the isotope from the joint space and reduce uptake by the lymphatics [12].

Most studies used a dose of 5 mCi for RS. Menkes [13] reports that 4 mCi may be sufficient to produce acceptable control of symptoms. It is advisable to limit the total dose of isotope to less than 15 mCi, especially in younger patients, for fear of long-term effects on

normal tissues. Doses of 10 mCi were used in 35 of the treated joints in our series. Three patients receiving treatment in the initial period of the study were treated with 5-mCi doses, and their outcomes were not satisfactory. Our decision to use a higher, 10-mCi dose was based on this personal experience.

Intra-articular injection of $Y^{90}$ is useful in reducing pain, tenderness, and swelling of the joints and improving mobility. In the series reported by Asavatanabodee et al., 82% of joints treated with $Y^{90}$ showed improvements in clinical status at 6 months after injection [2]. Most other studies reported results ranging between 50% and 80% after $Y^{90}$ synovectomy [14, 15, 16, 17, 18]. In a long-term retrospective study by Stucki et al. [6], an overall success rate of 50% was noted for 164 $Y^{90}$ treatments. Their 3-year success rate was reported to be 30%.

Patients with established radiological abnormalities of the joints generally respond less well than those with less damage as seen on radiology [2, 17, 19, 20, 21]. Patients with short duration of disease generally respond better to $Y^{90}$ RS than those with longer disease, in which there is likely to be greater irreversible joint damage. It is also reported that response to RS worsens in the presence of multiple joint involvement and active systemic disease.

Pain, swelling, febrile reactions, malaise, local tenderness, and infection are reported complications of RS [2, 19, 22]. Extravasation of the isotope, needle tract ulcers, and soft tissue necrosis are less frequent [8, 23]. In our series, no pain, fever, or joint swelling was reported despite routine avoidance of corticosteroids. However, in the initial period of the study, two patients developed extravasation of the isotope and needle tract ulcers. In one, the needle track ulcer was managed conservatively, while skin grafting was required in the other. By improving our technique using the three-way system and with adequate joint immobilisation, we were able to prevent further complications.

Responses to treatment were recorded by 6 months following therapy in most studies [2, 20]. Menkes et al. report that responses could be reliably assessed 6 months after therapy and that late responses are unlikely to occur [20]. Also in our study, 29 out of 30 joints which responded to therapy had done so by 6 months following RS. However, outcome of treatment continued to improve beyond 6 months to a maximum of 18 months. Response to RS was reported to be maintained for 24–49 months following therapy [16, 17, 24]. This is in agreement with the mean response duration of 28.4 months observed in the patients who responded to $Y^{90}$ in our series.

Several studies have looked into the factors determining outcome with RS. Patients with established radiological abnormalities of the joints generally respond less well than those with less damage as seen on radiology [2, 15, 19, 21]. Patients with short duration of joint involvement also do better with RS [2]. It is likely that with a prolonged history of joint involvement, there may be more pronounced damage of the joint architecture, thereby accounting for worse response to therapy. Patients with multiple joint involvement and active systemic disease are also known to respond badly to local therapy [25]. It has also been attempted to study the outcome of RS by type of arthritis; psoriatic joints generally are reported to show a poor response [2, 16]. It should however be noted that most studies have too few patients to make any statistically significant comparison of outcome. In our study, too, a valid comparison of outcome based on number of affected joints, duration of arthritis, and nature of arthritis was not possible due to the limited number of patients within the different subgroups.

The role of reinjecting radioactive yttrium in relapsing or nonresponding patients is another matter of debate. Stucki [6] and Asavatanabodee [2] reported response rates of up to 53% following reinjection. In the series reported by Winfield et al., 20% and 63% of the patients undergoing retreatment with the isotope showed complete and partial response, respectively [26]. In our series, only four patients were reinjected with $Y^{90}$, and there were two responses.

Nonresponders and patients who fail after a period of symptom control are managed by arthroscopic synovectomy, surgical synovectomy, or joint replacement. By the time of reporting, 13 patients in our series had been referred for surgical intervention and nine had undergone knee replacement. The RS helped to delay the procedure in several patients and gave long-term control of symptoms in 29% of the patients in this series.

Few randomised clinical trials examine the role of $Y^{90}$ RS in the management of refractory arthritis [27]. Besides, randomised trials comparing RS with placebo or intra-articular steroid injection have used limited numbers of patients or short duration of follow-up [28, 29]. We find $Y^{90}$ RS to be a safe and quick procedure with a favourable long-term outcome that can be useful in the management of patients with refractory synovitis. We feel its use is justified until its role is prospectively evaluated in a randomised clinical trial involving a large number of patients.

## References


1. Prichard HL, Bridgman JF, Bleehan NM (1970) An investigation of radioactive yttrium for the treatment of chronic knee effusion. Br J Radiol 43:466–470
2. Asavatanabodee P, Sholter D, Davis P (1977) Yttrium-90 radiochemical synovectomy in chronic knee synovitis: a one-year retrospective review of 133 treatment interventions. J Rheumatol 24:4 639–642
3. Lee P (1982) The efficacy and safety of radiosynovectomy. J Rheumatol 9:165–168
4. Gumpel JM (1973) Clinical application and investigations—review of published and personal results. Ann Rheum Dis 32:29–33
5. Nissila M, Antilla P, Hamalainen M, Jalava S (1978) Comparison of chemical, radiation and surgical synovectomy for knee joint synovitis. Scand J Rheumatol 7:225–228

6. Stucki G, Bozzone P, Treuer E, Wassmer P, Felder M (1993) Efficacy and safety of radiation synovectomy with yttrium-90: a retrospective long-term analysis of 164 applications in 82 patients. Br J Rheumatol 32:383–386
7. Williams ED, Caughey DE, Hurley PJ, John MB (1976) Distribution of yttrium$^{90}$ ferric hydroxide colloid and gold$^{198}$ colloid after injection into knee. Ann Rheum Dis 35:512–520
8. Gumpel JM (1979) $Y^{90}$ colloids in chronic synovitis of the knee: a review 1970–1977. Rheumatol Rehabil [Suppl]:38–41
9. Stevenson AC, Bedford J, Dolphin GW, Purrott RJ, Lloyd DC, Hill AGS, Hill HFN, Gumpel JM, Williams D, Scott JT, Ramsey HW, Bruckner FE, Fearn CBA (1973) Cytogenetic and scanning study of patients receiving intra-articular injections of gold$^{198}$ and yttrium$^{90}$. Ann Rheum Dis 32:112–123
10. Nemec HW, Fridrich R (1977) Retention and dosage in radiation synovectomy with yttrium$^{90}$ silicate colloid. Nuklearmedizin 16:113–118
11. Williams PL, Crawley JC, Freeman AM, Lloyd DC, Gumpel JM (1981) Feasibility of outpatient management after intra-articular yttrium-90: comparison of two regimes. BMJ 282: 13–14
12. Oka M, Isomaki AM, Rekonen A, Ruotsi A, Seppala O (1972) Intraarticularly injected $Y^{90}$ resin colloid: clinical effect changes in joint fluid, autoradiographic and electron microscopic findings. Rheumatologie (Baillieres Clin Rheumatol) 2:49
13. Menkes CJ (1979) Radioisotope synoviorthesis in rheumatoid arthritis. Rheumatol Rehabil [Suppl] 45–46
14. Jones G (1993) Yttrium synovectomy: a meta-analysis of the literature. Aust N Z J Med 23:272–275
15. Oka M (1975) Radiation synovectomy of the rheumatoid knee with yttrium 90. Ann Clin Res 7:205–210
16. Szanto E (1977) Long-term follow-up of yttrium-90-treated knee-joint arthritis. Scand J Rheumatol 6:209–212
17. Tueber J, Baenkler HW, Regler G (1978) Treatment of rheumatoid arthritis with yttrium-90. Follow up studies. Immunität und Infektion 6:106–109
18. Gumpel JM, Beer TC, Crawley JW, Farran EA (1975) Yttrium 90 in persistent synovitis of the knee—a single centre comparison. The retention and extra-articular spread of yttrium 90 colloids. Br J Radiol 48:377–381
19. Spooren PF, Rasker JJ, Arens RP (1985) Synovectomy of the knee with Y-90. Eur J Nucl Med 10:441–445
20. Menkes CJ, Aignan M, Galmiche B, Le Go A (1972) Le traitement des rheumatismes par le synoviorthesis. Rheumatologie 2 [Suppl 1]:61–80
21. Boerbooms AM, Buijs WC, Danen M, van de Putte LB, Vandenbroucke JP (1985) Radiosynovectomy in chronic synovitis of the knee joint in patients with rheumatoid arthritis. Eur J Nucl Med 10:446–449
22. Wilson AP, Prouse PJ, Gumpel JM (1984) *Listeria monocytogens* septic arthritis following intra-articular yttrium-90 therapy. Ann Rheum Dis 43: 518–519
23. Wiss DA (1982) Recurrent villonodular synovitis of the knee. Successful treatment with yttrium-90. Clin Orthop 169:139–144
24. Hagena FW (1982) Radiosynoviorthesis with yttrium 90 of the knee joint in polyarthritis. Fortschritte der Medizin 100: 1673–1677
25. Schutte H, Rau R (1983) Results of radiosynoviorthesis with yttrium 90 in chronic synovitis: a long-term prospective study. II. Effect of general disease parameters. Zeitschrift für Rheumatologie 42:271–279
26. Winfield J, Gumpel JM (1979) An evaluation of repeat intra-articular injections of yttrium-90 colloids in persistent synovitis of the knee. Ann Rheum Dis 38:145–147
27. Heuft-Dorenbosch LLJ, de Vet HCW, Van der Linden S (2000) Yttrium radiosynoviorthesis in the treatent of knee arthritis in rheumatoid arthritis: a systematic review. Ann Rheum Dis 59:583–586
28. Bridgman JF, Bruckner F, Eisen V, Tucker A, Bleehen NM (1973) Irradiation of the synovium in the treatment of rheumatoid arthritis. Q J Med 42:357–367
29. Grant EN, Bellamy N, Fryday-Field K, Dinsey T, Driedger A, Hobby K et al (1992) Double-blind randomised controlled trial and six-year open follow-up of yttrium-90 radiosynovectomy versus triamcinalone hexacetonide in persistent rheumatoid knee synovitis. Inflammopharmacology 1:231–238