A REVIEW ON RADIOSYNOVECTOMY A MINIMALLY INVASIVE REVALUATION IN RHEUMATOID ARTHRITIS TREATMENT

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Abstract:

Radiosynovectomy (RSO) has emerged as a highly effective, minimally invasive therapeutic modality for the management of chronic synovial inflammation, particularly in rheumatoid arthritis and other inflammatory arthritides. By delivering targeted β-radiation through intra-articular radiocolloids, RSO induces selective ablation and subsequent fibrosis of the diseased synovial membrane, thereby reducing pain, swelling, and recurrent effusions. Advancements in radiopharmaceutical development—from early colloidal gold to modern joint-specific agents such as ^{90}Y, ^{186}Re, and ^{169}Er—have significantly improved the precision, safety, and durability of clinical outcomes. Contemporary evidence demonstrates that RSO consistently achieves symptom control in a majority of treated joints and often outperforms or complements alternative local treatments, including corticosteroid injections and chemical synovectomy. Owing to its minimal systemic exposure, short recovery time, and suitability across a wide range of joint sizes, RSO is increasingly recognized as a valuable adjunct to disease-modifying therapies. This review synthesizes current knowledge on the principles, indications, contraindications, procedural techniques, radiopharmaceutical selection, efficacy outcomes, and safety considerations of radiosynovectomy, highlighting its evolving role as a cornerstone in the non-surgical management of persistent synovitis.

KEYWORDS: Radiosynovectomy, Rheumatoid arthritis, Yattrium-90, Rhenium-186, Erbium-169.

INTRODUCTION:

Rheumatoid arthritis is a chronic inflammatory disease managed through systemic and local therapies. Common treatments include DMARDs, NSAIDs, biologics, and corticosteroids. For persistent synovitis, local steroid injections or synovectomy procedures—surgical, chemical, or radiation based are considered. While steroid injections offer quick relief and surgery ensures effectiveness but at a high cost, chemical synovectomy is often painful and less durable. Among these, radiosynovectomy stands out as a safe, effective, and minimally invasive local treatment for controlling arthritis inflammation.[1]

The use of radioactive substances in the treatment of arthritis dates back to 1963, when radioactive gold (^{198}Au) was first introduced for managing persistent knee effusions.[2] However, its clinical application was limited due to a high leakage rate, attributed to the small particle size of the radiocolloid. During the 1970s and 1980s, significant progress was made with the introduction of other radionuclides such as yttrium-90 (^{90}Y),[3]colloidal

chromic phosphate (^{32}P)[4], and rhenium-186 sulfide colloid (^{186}Re), which became widely used for radiosynovectomy. Over the past two decades, the technique has experienced a renaissance, with tailored radiopharmaceuticals now being selected based on joint size: erbium-169 citrate (^{169}Er) for small joints, ^{186}Re or ^{32}P for medium joints (such as the wrist, elbow, ankle, and shoulder), and ^{90}Y for larger joints like the knee. This evolution highlights the growing precision and effectiveness of radiosynovectomy in the modern management of arthritis.[1]

For over four decades, Radiosynovectomy (RSO), sometimes called radiosynoviorthesis, has served as a powerful, time-tested tool in the rheumatologist's arsenal, offering significant relief from the persistent pain and swelling associated with rheumatoid arthritis and other inflammatory joint conditions. The genius of RSO lies in its precision.[5] The procedure involves carefully introducing a beta-emitting radionuclide directly into the affected joint capsule. By cleverly binding the radioactive material to a large, non-diffusible colloid, the radiopharmaceutical is trapped either within the synovial fluid or is taken up by the overactive cells lining the joint.This delivers a highly localized, intense dose of radiation right where it's needed to the inflamed synovial membrane while sparing surrounding healthy tissue from high exposure. This focused radiation effectively calms the inflammation, leading to desirable sclerosis and fibrosis of the troublesome lining, ultimately alleviating chronic joint symptoms.[6] While the basic concept of intra-articular radiation therapy existed earlier, the procedure gained its formal, recognized identity in 1968. This was a pivotal year when Delbarre and colleagues published their seminal clinical experience and introduced the specific term 'radio-synoviorthesis.[7] This term perfectly captures the technique’s objective: the functional restoration and normalization of the chronically inflamed and synovial membrane. Consequently, this technique has earned its position in clinical practice as a highly valuable, non-surgical alternative to early surgical synovectomy.[8]

The success of Radiosynovectomy hinges on a crucial clinical decision: selecting the right radionuclide for the specific joint. This choice is carefully calibrated based on the radionuclide's energy and its corresponding depth of penetration—matching the therapeutic agent's power to the joint's size.For delicate, small joints, such as those in the hand, the agent of choice is typically the low-energy Erbium-169 citrate (max. penetration: 1 mm), offering highly localized treatment. Moving up to medium-sized joints, the slightly more energetic, though still low-energy, Rhenium-186 sulfide (max. penetration: 3.6 mm) is employed. Finally, for large joints like the knee, the procedure demands a higher energy agent: Yttrium-90 citrate (max. penetration: 11 mm).[9]This tiered approach ensures maximum therapeutic effect on the synovial membrane while minimizing the radiation dose to surrounding healthy tissues. Importantly, safety guidelines dictate that the maximum activity for adults should not exceed 370 MBq in any single intra-articular delivery.[1,9]

PRINCIPLE:

• Radiosynovectomy uses beta-emitting radioactive isotopes in colloidal form to treat inflamed joints.

• After entering the joint, colloids are recognized as foreign particles and are phagocytosed by synovial membrane cells.

• Yttrium colloids localize mainly in the superficial and deeper synovial layers, with very little reaching the bone.

• The localized beta radiation causes selective necrosis of inflamed synovial cells and reduces abnormal cellular proliferation.

• Arthroscopic findings show smaller and fewer synovial villi and a marked reduction in hyperemia.

• Over time, the synovial membrane undergoes progressive fibrosis, with only rare minimal damage to bone.

• This leads to loss of mononuclear cell infiltration and reduced synovial fluid filtration/reabsorption.

• The newly formed fibrotic tissue does not react to immune stimulation, preventing recurrence of inflammation.

• As a result, long-term remission and protection against further joint destruction are achieved.[10,11,12,13,14,15]

RADIOSYNOVECTOMY IN RHEUMATIC DISEASES:

Radiosynovectomy (RS) has emerged as an important therapeutic option in various rheumatic diseases, particularly rheumatoid arthritis (RA). Multiple studies consistently highlight that RS offers better outcomes than chemical synovectomy or intra-articular corticosteroid injections. A meta-analysis by Kresnik et al. reported clinical improvement in nearly two-thirds (66.7%) of RA patients, while Matryba et al. observed notable responses in 68.7% of treated knee joints and even higher rates in hand joints, though the latter finding requires cautious interpretation due to the limited sample size. Interestingly, treatment efficacy appeared more pronounced in patientsover 50 years of age, with men experiencing greater reduction in joint effusions, whereas women reported better pain relief. Further evidence from Menkes et al. showed that RS provided good to very good outcomes in 69.6% of RA cases, outperforming both chemical synovectomy (54.4%) and steroid injections (38.9%). Beyond RA, RS has also demonstrated promising results in other rheumatic conditions: Jahangier et al. documented significant improvement in 76% of patients with psoriatic arthritis and 75% with ankylosing spondylitis, while Gazda et al. reported clinical, biochemical, and ultrasound improvement in 66% of children with juvenile idiopathic arthritis, with an average symptom remission lasting around 20 months. Overall, the growing evidence underscores radiosynovectomy as a safe, effective, and durable treatment option across a spectrum of antiinflammory joints. [16,17,18]

Table 1: Commonly Used Radiopharmaceuticals ForRadiosynovectomy

Joint	Yttrium - 90 MBq	Rhenium-186 MBq	Erbium-169 MBq	Phosphorus-32 MBq
Shoulder		111		
Acromioclavicular joint			37	
Elbow		74		37
Wrist		74		
Thumb base, MCP I			30	
MCP (Others)			22	
PIP			18.5	
DIP			15	
Hip		111		
Knee	185			55.5
Ankle joint		74		37
Subtalar joint		37		
Articulation			37	
Cuneonaviculare				
MTP I			30	
MTP (Others)			22	

CLINICAL INDICATIONS FOR RADIOSYNOVECTOMY:[20,21,22]

1. Rheumatoid arthritis.
2. Haemolytic arthritis and haemophilicarthropathy.
3. Spondyloarthropathies.

4. Crystalopathies, including gout and pseudogout (calcium pyrophosphate dihydrate arthritis, CPPD).
5. Recurrent effusions following arthroplasty.
6. Recurrent effusions following arthroscopy.
7. Undifferentiated arthritis.
8.Pigmente villonodular synovitis (PNVS).

CONTRAINDICATIONS FOR RADIOSYNOVECTOMY:

Absolute contraindications include:[20,21,22]

1) Pregnancy.

2) Local joint or skin infection.

3)A waiting period of up to six weeks after joint surgery is recommended to avoid the risk of theradiopharmaceutical leaking outside the joint.

4) A ruptured popliteal cyst or semimembranosus bursa increases the risk of the radiotracer escaping outside the joint.

5) A two-week gap after joint puncture is advised to prevent the radiotracer from leaking outside the joint.

Relative contraindications include:

1)A minimum recovery time—six weeks after arthroscopy or joint surgery, and two weeks after joint puncture—is recommended before proceeding.

2) The time just before hip replacement surgery is avoided because the procedure could increase the risk of bone damage and implant loosening.

3) The period right before reconstructive joint surgery is avoided, as it may interfere with proper tissue healing and regeneration.

4) Severe joint instability or deformity with cartilage and bone damage raises the risk of bone irradiation and possible osteonecrosis, so the benefits must be weighed carefully against the potential harms.

SIDE EFFECTS:

Overall, radiosynovectomy is considered a safe procedure, with side effects reported only rarely. Published data note a joint infection rate as low as 1 in 35,000 treated joints, while extra-articular leakage—particularly with ^{90}Y—may cause skin necrosis [23]. A German survey of 36 centers over six years found very low complication rates: 23 centers reported no adverse events, and insurance data documented only a few issues, including 28 cases of skin necrosis, 13 intra-articular infections, and 12 thromboses, the latter largely preventable with appropriate heparin prophylaxis during immobilization. Importantly, available evidence shows no increase in tumor risk after radiosynovectomy[24,25] and no detrimental effects on cartilage, as confirmed by animal studies showing no histological or genetic changes [26]. Given the short tissue penetration of β-particles and the low radiosensitivity of bone, induction of osteoarthritis is considered unlikely.In our own experience with over 15,000 treated joints, only a single early joint infection was observed, with no cases of skin necrosis. Occasional, mild, and reversible erythema occurred mainly in small joints due to minor radiotracer reflux.

TECHNICAL PREREQUISITES:

According to the European Association of Nuclear Medicine (EANM) guidelines, β-emitting radionuclides must be administered only in specially designated rooms that support sterile techniques and are approved for β-emitter use [27]. Because direct quantification of β-emitters is challenging, dose calibrators are typically used to measure their Bremsstrahlung radiation, provided that the setup ensures a fixed and reproducible geometry for the syringe holder. Strict safety measures are essential, as accidental contact with the radionuclide zone on a syringe can expose fingers to extremely high radiation doses. Acrylic shielding is recommended for safe handling, significantly lowering exposure: fingertip doses as high as 22.1 μSv/MBq have been reported without shielding, whereas the use of an acrylic shield and clamp reduced this to just 0.4 μSv/MBq[28].This highlights the critical need for proper protective equipment in β-emitter procedures.

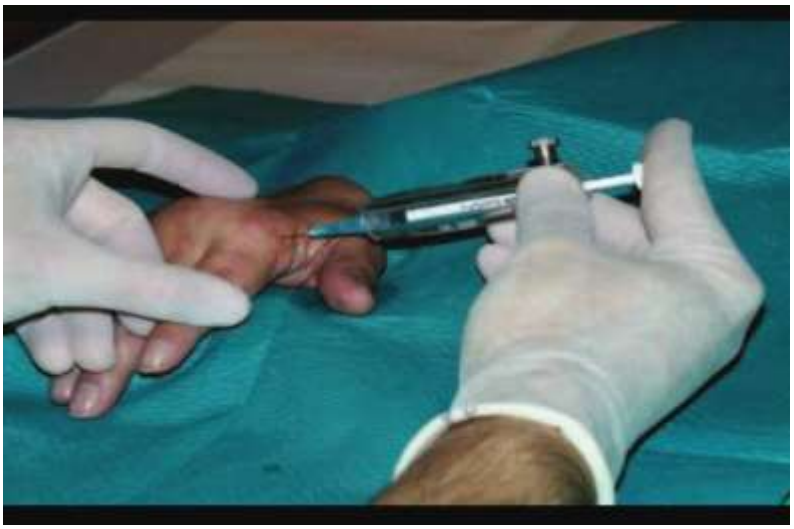

Fig.no.1 Injection of 169Er-citrate into proximal interphalangeal joint.

PROCEDURE:

Radiosynovectomy must be performed under strict sterile conditions by trained medical staff, with support from radiation-qualified physicists to ensure safe handling of radioactive materials. Sterile gloves, proper skin disinfection, and local anesthesia are essential before joint puncture. Accurate intra-articular placement of the needle is the most important step: in large joints such as the knee, this is usually confirmed easily by aspirating synovial fluid, typically using a 7.6-cm, 20-gauge needle. In contrast, smaller joints often require fluoroscopic guidance, where a 22-gauge needle and a small amount of contrast medium help verify correct needle position (as shown in Fig. 1). To minimize radioactive spills, the needle is held firmly in place with a clamp while the tubing is removed and replaced with the β-emitter syringe.

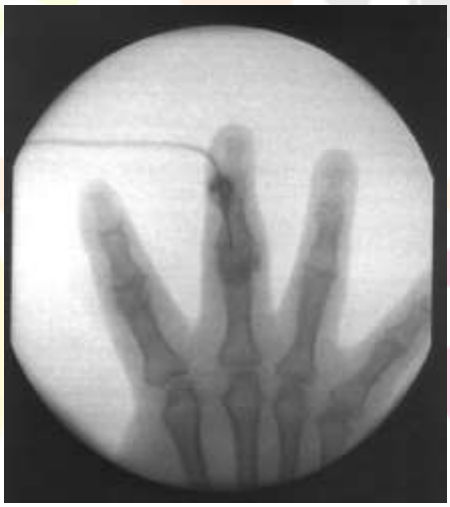

Fig.no.2 Radiography of the interphalangeal joint clearly shows proper needle placement inside the joint and a smooth, even spread of the contrast medium.

Once the needle position is confirmed, the radiocolloid is injected—often together with 0.9% saline to improve its distribution volume, as summarized in Table 2. A long-acting glucocorticoid may also be co-administered to reduce the risk of acute post-injection synovitis. Before withdrawing the needle, the puncture tract is flushed with saline to prevent β-emitting particles from depositing along the channel, although this is less feasible in very small joints due to limited space. After injection, a sterile compression dressing is applied, and the treated joint is immobilized for approximately 48 hours using splints or similar supports.

When multiple joints are treated in a single session, short hospitalization is recommended. Before discharge, post-therapy imaging is performed when γ-emitting 186Re is used, and Bremsstrahlung imaging is obtained after 90Y injections to confirm correct intra-articular location of needle and good distribution of the radiopharmaceutical (as illustrated in Fig. 2).

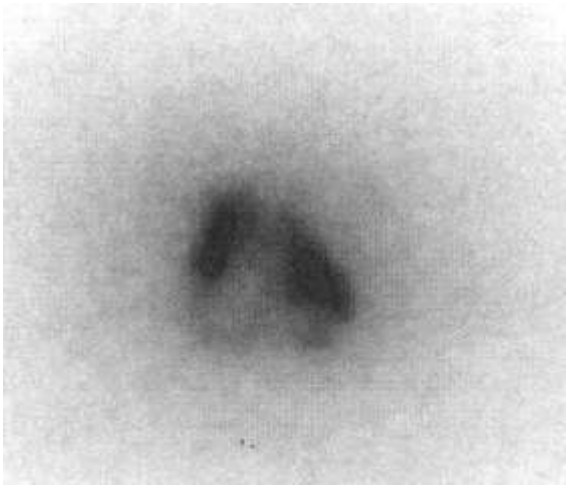

Fig no.3 Bremsstrahlung scintigraphy taken 30 minutes after the 90Y-silicate injection shows excellent distribution within the knee joint, with no leakage outside the joint or along the injection track

Table no.2Success Rates for Radiosynovectomy of Different Joints[29]

Joint	No. of treated patients	Success rate (%)		
		6 mo	1 y	2 y
Knee	196	77	66	73
Shoulder	56	62	65	54
Elbow	60	51	50	50
Wrist	202	79	67	50
MCP	208	54	38	44
PIP	164	53	47	39
Hip	14	43	40	44
Ankle	58	76	100	96
Total	958	66	58	54

CONCLUSION:

Radiosynovectomy stands as a mature, evidence-based intervention that fills an important therapeutic gap in the management of persistent synovitis unresponsive to systemic therapy. Its ability to deliver localized radiation with minimal collateral damage makes it a superior option for patients who require long-lasting control of inflammation without undergoing invasive surgical procedures. The broad spectrum of indications—including rheumatoid arthritis, spondyloarthropathies, hemophilic arthropathy, and crystal-induced arthritis—demonstrates its versatility and clinical relevance. Modern radiopharmaceuticals, combined with improved imaging guidance and stringent safety protocols, have further reduced procedural risks and enhanced therapeutic predictability. Available long-term data confirm that RSO does not increase cancer risk, rarely causes complications, and preserves joint function without damaging cartilage. As rheumatology increasingly embraces targeted, organ-specific interventions, radiosynovectomy is positioned to remain a pivotal treatment option, complementing systemic therapies and offering durable symptomatic relief. Continued research, refinement of guidelines, and broader clinician awareness will further strengthen its integration into routine care and reinforce its role as a minimally invasive, safe, and effective strategy for controlling chronic joint inflammation.

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