

# Radiosynoviorthesis in Painful Total Knee Replacement

38

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## Keynotes

1. Radiosynoviorthesis or radiation synovectomy (RSO) is a local radionuclide therapy using radiolabelled yttrium-90-labelled colloids for patients with chronic synovitis.
2. The indication for RSO is persistent knee pain, effusion and swelling.
3. RSO should only be used as a salvage procedure in patients with unidentified cause of the persistent pain. In these patients, RSO leads to attenuation of the symptoms in 50 % of patients.

Radiosynoviorthesis or radiation synovectomy (RSO) is a local radionuclide therapy and targets the inflamed synovial tissue in patients with chronic synovitis. It has an anti-inflammatory and analgesic effect.

The first preclinical intra-articular use of radionuclides was described in 1924 by Ishido and colleagues [7]. In 1952, Fellingner and Schmid [5] were the first to use radionuclides in patients with rheumatic diseases. The term RSO was first used by Delbarre et al. in 1968 [3]. Currently, half of all RSO procedures are performed on the knee joint [2].

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Radiosynoviorthesis or radiation synovectomy is a local radionuclide therapy using radiolabelled yttrium-90-labelled colloids for patients with chronic synovitis.

The main effects of RSO are necrosis, anti-inflammatory and antiproliferative, reduction of detritus development, reduction of joint effusion and fibrotic effect on the synovial joint.

### 38.1 Mechanism of Action

Radiolabelled colloids are injected into the knee joint. For the knee, yttrium-90 citrate or silicate is typically used. After injection these colloids are resorbed by the inflamed synovial tissue. The radioactive colloid-synovial tissue complex is phagocytized by type A macrophage-like synoviocytes. Through its locally high-energy radiation, a coagulation necrosis of the superficial synovial layers occurs. The resulting inflammatory reaction then leads to a demarcation of the necrotic tissue, and finally new synovial tissue is regenerated.

RSO can be considered as a true local therapy with very limited radiation burden to the whole body. The main effects of the beta radiation on the synovial cells are:

- Necrosis, anti-inflammatory and antiproliferative effect
- Reduction of detritus development
- Reduction of joint effusion
- Fibrotic effect on the synovial membrane

### 38.2 Indications and Contraindications

The indication for RSO should be established in close interdisciplinary collaboration with the orthopaedic surgeon and/or rheumatologist. RSO should be considered in patients after TKR if other treatment options are not available or have failed to improve the patient's symptoms or if possible side effects outweigh the expected benefit.

Indications and contraindications for intra-articular radionuclide treatment are presented in Table 38.1.

In young patients (<20 years) RSO should be performed with all due caution. The main indications in infants and adolescents are haemophilic joint disease and pigmented villonodular synovitis. The time interval between arthroscopy or open knee surgery and RSO should be at least 4–6 weeks to minimize any risk of protracted wound healing.

**Table 38.1** Indications and contraindications for intra-articular radionuclide treatment

Indications	Relative contraindications	Absolute contraindications
Reactive arthritis	Gravidity and breastfeeding	Haemarthrosis
Arthritic Lyme disease		
Chronic pyrophosphate arthropathy [4]		
Seronegative spondyloarthropathy psoriatic arthropathy [19]	Local skin infection at the injection site	Conditions that increase the risk of radionecrosis in case of unintentional leakage, for example, Baker's cyst [15]
Haemophilic arthropathy for prophylaxis of chronic bleeding [18]	Recently ruptured synovial cyst communicating with the articular cavity	
Pigmented villonodular synovitis (PVNS)	Periprosthetic joint infection	
Osteoarthritis with proven synovitis [9, 19]		
Undifferentiated chronic arthritis [21]		
Synovitis in painful arthroplasty [21]		
Crystal arthropathy [6, 8]		

A good indication for RSO is persistent knee pain, effusion and swelling. In young patients (<20 years) RSO should be performed with all due caution. The time interval between arthroscopy or open knee surgery and RSO should be at least 4–6 weeks to minimize any risk of protracted wound healing.

mean and by 11 mm in the maximum. The half time is 64 h, and the maximum energy emitted is 2.27 MeV [20].

90-Yttrium (Y-90) is the radionuclide of choice for RSO of the knee joint. It is available as Y-90 citrate and Y-90 silicate.

### 38.2.1 Pre-RSO Diagnostics

As RSO is a second- or even third-line treatment. All patients need undergo extensive diagnostic workup before RSO to exclude other causes such as mechanical loosening, instability, TKR malposition or infection.

### 38.4 Therapeutic Procedure

The tracer is injected intra-articularly under aseptic conditions. Fluoroscopy is used to facilitate the correct needle position (Figs. 38.2, 38.3 and 38.4). In addition to the tracer, 10–20 mg of a glucocorticoid suspension like triamcinolone acetate is injected (Figs. 38.4 and 38.5). This glucocorticoid aims to reduce the radiation-induced synovitis and the risk of leakage by reduction of hyperperfusion and vascular permeability [10]. It also avoids tracer backflow into the needle. If there are any reasons not to apply steroids, it is necessary to flush the needle with saline solution to prevent backflow and to minimize the risk of radionecrosis.

### 38.3 Radiopharmaceuticals

Based on its physiochemical properties, 90-yttrium (Y-90) is the radionuclide of choice for RSO of the knee joint (Fig. 38.1). Y-90 is available as Y-90 citrate and Y-90 silicate. Both radiopharmaceuticals show different stability and drainage from the joint. Due to longer deposition in the knee, some authors like Gumpel et al. recommended Y-90 silicate [6]. Y-90 is a pure  $\beta$ -emitter. The therapeutic  $\beta$ -radiation penetrates the synovial membrane by 3.6 mm in the

After the injection a consequent immobilization of the knee for 48 h is mandatory. It aims to reduce the risk of leakage and fast drainage, which could be caused by motion-related hyperperfusion (Fig. 38.6). After 48 h the knee can be normally mobilized. The decision whether to perform an in- or outpatient regimen should be based on the patient's compliance. RSO can be repeated after 6–12 months. However, in that case a lower response rate is assumed.



**Fig. 38.1** Based on its physiochemical properties, 90-yttrium (Y-90) is the radionuclide of choice for RSO of the knee; Y-90 is available as Y-90 citrate and Y-90 silicate

### 38.5 What Is the Evidence for RSO?

Despite the high number of published papers dealing with the clinical application of RSO, there is only scarce evidence for the use of RSO (evidence level III). Most studies included patients with a variety of different joints, different medications and sometimes different entities



**Fig. 38.2** The knee joint is palpated, and the necessary portals are marked. Then the knee joint is disinfected and sterile draped

which alters the comparability. A meta-analysis from Heuft-Dorenbach et al. dealing with Y-90 RSO found only one well-designed randomized study demonstrating the efficiency of Y-90 RSO against placebo [1].

### 38.5.1 Inflammatory Disease

In inflammatory joint diseases, RSO is a well-established form of “nonsurgical” synovectomy. It is used as a monotherapy or in combination



**Fig. 38.3** This image shows the interventional radiologist or nuclear medicine specialist performing the knee joint injection, which is fluoroscopy guided



**Fig. 38.4** In addition to the tracer, 10–20 mg of a glucocorticoid suspension like triamcinolone acetate is injected. This glucocorticoid aims to reduce the radiation-induced synovitis and the risk of leakage



**Fig. 38.5** After injection the knee is flexed and extended to achieve sufficient distribution of the radiopharmaceutical substance

with surgical synovectomy, e.g. in pigmented villonodular synovitis (PVS) following incomplete arthroscopic synovectomy.



**Fig. 38.6** After the injection a consequent immobilization of the knee for 48 h is necessary to reduce the risk of leakage and of fast drainage caused by motion-related hyperperfusion

Prospective studies in patients with rheumatoid arthritis (RA) showed positive effects on range of motion and significant reduction of pain, joint effusion and swelling. Response rates of 42–91 % and 61–80 % have been reported in retrospective studies [11, 13, 14]. In a placebo-controlled trial, Bridgman et al. [1] reported a significant improvement of the range of motion and swelling after Y-90 RSO. The combination of surgical synovectomy and Y-90 RSO in patients with PVS showed reduction of all clinical symptoms 1 year after therapy [11]. Another study using RSO in an adjuvant setting in PVS patients lowered the rate of recurrence compared to operation in up to 40 %. Other studies showed good therapeutic response in 75 % in psoriasis arthropathy and 76 % in ankylosing spondylitis [8].

### 38.5.2 Patients with Pain After Knee Replacement

In TKR cases with unexplained pain after an extensive and thorough diagnostic evaluation, RSO is a therapy option [12] with an overall response rate of 50 % [16]. In the same study, a subgroup analysis in patients without need of any additional interventions after primary TKR showed improved symptoms in up to 84 %. On the other hand, patients who needed revision of the knee replacement presented complications such as low-grade infection, loosening and metal

allergy that was not diagnosed previously. This fact emphasizes the importance of careful patient selection. Recurrent effusion induced by particle disease RSO seems to be a potent adjuvant therapy option [17].

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