Radionuclide synovectomy – essentials for rheumatologists

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Abstract

Radionuclide synovectomy is a minimally invasive method of treating persistent joint inflammation. It involves intra-articular injection of radioactive colloids which induce necrosis and fibrosis of hypertrophic synovial membrane. The most common indication for radiosynovectomy is rheumatoid arthritis, although patients with seronegative spondyloarthropathies, unclassified arthritis, haemophilic arthropathy and other less common arthropathies can also benefit from this method. Radiosynovectomy is safe, well tolerated and efficacious. About 70–80% of patients respond well to the therapy. However, the therapeutic effects are considerably worse in patients with co-existent osteoarthritis and advanced joint degeneration. Despite its advantages, radionuclide synovectomy is not performed as often as it could be, so greater knowledge and understanding of this method are needed. The authors present the most important facts about radiosynovectomy that may help rheumatologists in their daily clinical practice.

Key words: rheumatoid arthritis, radiosynovectomy, hypertrophic-exudative synovitis.

Introduction

Radionuclide synovectomy (radiosynovectomy – RS) is a minimally invasive method of treating persistent join inflammation. The basic idea of this procedure is to destroy hypertrophic synovial membrane with ionizing radiation. In the long term, its effects are comparable to arthroscopic or open synovectomy, without all the side effects of surgery or need for rehabilitation [1].

The first concepts of joint radiotherapy date back to as long ago as 1924 [2], but the first large clinical trial with intra-articular radioactive agents was performed in 1963, when injections of colloidal gold-198 were used to treat knee joint effusions [3]. Since the late 1960s yttrium-90 citrate has remained a state-of-the-art joint therapy agent up to this day [4]. In Poland it has been possible to perform RS since 2004, when the radiopharmaceuticals manufactured in the European Union became commercially available.

Mechanism of action

The joint is punctured using ultrasonographic or fluoroscopic guidance and a solution of colloidal radio-

active agent is intra-articularly injected. The diameter of the colloid particle is between 2 and 5 μ m, which is small enough to be phagocytised, but big enough not to enter bloodstream via capillary fenestrations [5, 6]. Immediately after the injection, most of the radiocolloid is phagocytised by type 2 synoviocytes (synovial macrophages) and captured in the external cell layers of the synovial membrane. The radioisotopes employed in RS emit high energy β^{-} radiation, which induces water hydrolysis, production of reactive oxygen species and cell apoptosis due to oxidative stress [7]. With a half-life ranging from 3 to 10 days, radionuclides used for RS continuously emit radiation for several weeks. In time, this leads to necrosis and subsequent fibrosis of the synovial membrane, a decrease in synovial fluid production and, clinically, reduction of inflammation symptoms. β^{-} radiation has very limited tissue penetration, depositing more than 90% of energy within 10 mm from the point of origin, thus affecting almost exclusively the joint cavity [8]. Most of the radiation is absorbed by the synovium, synovial fluid, superficial layers of cartilage and articular capsule. Subchondral bone and other para-articular tissues, in turn, receive negligible doses of radiation [8].

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Indications

Radiosynovectomy is intended for treating joint inflammation with synovial hypertrophy, especially in the course of connective tissue diseases. Rheumatoid arthritis (RA) is the most common indication [9], followed by seronegative spondyloarthropathies (mainly psoriatic arthritis [10] and ankylosing spondylitis with peripheral joint involvement) and juvenile idiopathic arthritis (JIA) [11]. Less common indications include reactive arthritis, enteropathy-associated arthritis, other systemic diseases with joint involvement (e.g. Sjögren's syndrome, Behçet's disease), calcium pyrophosphate dehydrate deposition disease (CPPD) and pigmented villonodular synovitis (PVNS) [11]. International guidelines also list idiopathic joint effusion and persistent inflammation associated with a joint prosthesis (foreign body reaction, polyethylene disease) [12, 13]. However, in such cases special care is advised, and every measure should be taken to rule out occult, chronic joint infection. In patients with progressive synovial proliferation in a single joint and no obvious diagnosis of rheumatic disease, malignancy should be definitely excluded before performing RS.

Radiosynovectomy can also be performed in haemophilic arthropathy, often yielding excellent results, greatly reducing the number of bleeding episodes and even preventing further joint damage [14].

It should be duly noted that osteoarthritis is not an indication for RS and it is not listed as such in national or international guidelines. As stated above, the only effect of ionizing radiation is partial destruction of the synovial membrane. No beneficial effect can be expected in the scope of pre-existing joint degeneration, i.e. cartilage loss, osteophyte formation and joint space narrowing. In case of severe joint inflammation and synovial hypertrophy secondary to osteoarthritis, performing RS may be justified, but response rates are low and long-term effects discouraging [15, 16].

Similarly, post-traumatic joint effusions without synovial hypertrophy, e.g. after meniscus or ligament tear, are unlikely to respond to RS and should not be considered a valid indication.

Contraindications

Contraindications for performing RS are listed in Table I.

Preliminary qualification

Radiosynovectomy should never be considered the first line of treatment. Before being qualified for RS, patients should undergo full rheumatologic evaluation and at least six months of standard therapy with disease-modifying antirheumatic drugs (DMARDs). In the case of osteoarthritis, where no targeted pharmacotherapy is available, the patient should fail to respond to at least one intra-articular glucocorticoid injection after six months of observation [12].

In practice, patients rarely require RS within the first years of rheumatic disease, since it is recommended to attempt treatment with various available DMARDs or biological agents. Patients referred for RS should have at least a partial response to DMARDs with limited joint involvement and low to moderate disease activity, as determined based on commonly used scoring systems (e.g. DAS28, SDAI). In most cases, it is not recommended to qualify patients with high disease activity and highly elevated parameters of systemic inflammation (sedimentation rate - SR, C-reactive protein - CRP), since continuous stimulation of the synovial membrane by inflammatory cells may lead to its rapid regeneration and low rate of clinical response. However, patients who for some reason have contraindications for all the DMARDs and biological agents and receive only glucocorticoid treatment may still benefit from RS [17].

Patients with inflammation persisting in only one joint despite DMARD and biological treatment require particular attention. In such cases successful RS of the problematic joint may lower levels of SR and CRP, and help to achieve clinical remission (based on DAS28 or SDAI scoring systems) (authors' own experience, data yet to be published).

The rheumatologist referring a patient for RS should objectively confirm active inflammation of the joint.

Table I. Contraindications for radiosynovectomy [11]

Absolute contraindications

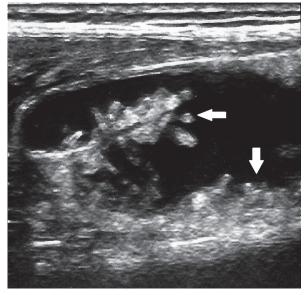


Fig. 1. Extensive synovial hypertrophy (arrows) in course of JIA in the suprapatellar recess of the knee joint. Ultrasound, longitudinal cross-section.

The simplest and readily available method is ultrasonography (US) with the power Doppler (PD) option [18]. Joint effusion, synovial thickening/hypertrophy and PD signal indicating increased blood flow in the synovium are hallmarks of active inflammation. If marked effusion and synovial hypertrophy are present, but there is no PD signal, the patient may still be considered a viable candidate for RS. On the other hand, patients with no signs of inflammation, with old fibrotic synovial membrane, especially in the metacarpophalangeal and proximal interphalangeal joints, are unlikely to experience any positive effect of radioisotope treatment.

Diagnostics before radiosynovectomy

The nuclear medicine physician performing RS is responsible for the final qualification. Like before any invasive procedure, obtaining the medical history and performing a physical examination are mandatory.

Detailed information about certain conditions unrelated to rheumatic disease should be collected, since they may influence the performance of RS. These include:

- diabetes (in some cases steroids are administered simultaneously with the radioisotope – in diabetic patients this should be avoided due to the possibility of prolonged hyperglycaemia),
- deep vein thrombosis (DVT) and pulmonary embolism (immobilisation after RS is an independent risk factor of DVT),
- hyperthyroidism and allergy to iodine agents (in such cases use of iodine contrast agents during fluoroscopy is contraindicated),

• oral contraception and hormone replacement therapy (other risk factors of DVT).

In equivocal situations, it may be advised to test the β -HCG level in women of reproductive age in order to rule out pregnancy.

Imaging studies performed before RS that confirm the presence of inflammation include US (Fig. 1) and three phase bone scintigraphy (Fig. 2) [15]. US is again the method of choice because scintigraphy provides no information on anatomical aspects of the joint, degree of effusion or synovial membrane morphology. In special cases, however (for example, patients with an endoprosthesis), scintigraphic imaging has to be performed in order to rule out infection.

Plain radiographs of the treated joints are not obligatory, although they can provide information on the degree of joint degeneration and damage, which helps predict the final outcome of the therapy.

Patient preparation

Radiosynovectomy is performed on an outpatient basis and does not require any special preparations. The patient should be well informed about the nature of the procedure and the need of continuous pharmacotherapy with DMARDs. There are no known interactions between RS radiopharmaceuticals and any drugs, so that discontinuation of other forms of treatment is not necessary. Contrary to surgical synovectomy, RS does not require withdrawal of biological therapy with anti-TNF agents, since it is not associated with increased risk of infection (authors' own experience, data yet to be published).

In the lower limb joints, prolonged immobilization might cause DVT. Inflammatory joint diseases and prolonged steroid therapy in rheumatic patients are both independent risk factors of DVT [19], so with additional immobilization prescribing anticoagulation therapy is strongly advised [20]. Usually, a prophylactic dose of low molecular weight heparin for 3–5 days is sufficient. However, there are no official guidelines as to that matter, so the type and duration of therapy remain at the responsible physician's discretion. If the patient already receives oral anticoagulant drugs (acenocoumarol, warfarin, rivaroxaban, etc.), no additional intervention is needed. It should be noted that in patients receiving oral anticoagulants, joint punctures do not increase the risk of bleeding and haemarthrosis [21].

Performing radiosynovectomy

Radiosynovectomy has to be performed in a room intended for handling open sources of ionizing radiation, with lead shielding of the walls as required by the national provisions of Atomic Law.

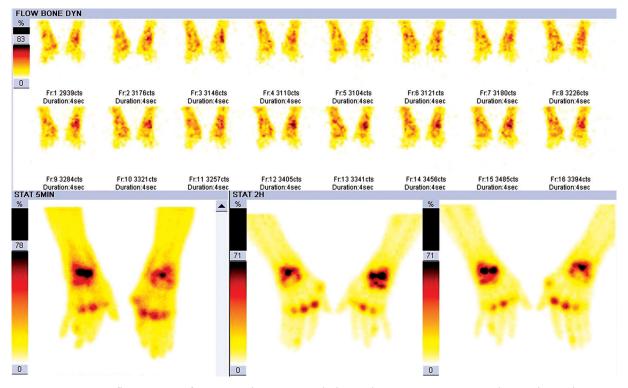


Fig. 2. Active inflammation of wrists and metacarpophalangeal joints in a patient with RA. Three phase bone scintigraphy with ^{99m}Tc-methylene diphosphonate.

Strict adherence to rules of aseptic technique is mandatory, with sterilization of the patient's skin and use of sterile drapes and gloves. However, the actual risk of infection is minimal, since β^- radiation is a potent antiseptic [6].

Application of local anaesthetics is advisable before RS, e.g. a 1% solution of lidocaine, especially when treating small joints of the hands and feet.

During the actual joint puncture, all means should be taken to ensure the correct position of the needle tip and complete intra-articular injection. Extra-articular injection or leakage can cause extensive damage to healthy tissues since β^- radiation can induce necrosis not only of the synovial membrane, but also of any other soft tissue. This makes 'blind' joint puncture unacceptable, and RS should be performed using imaging guidance (Fig. 3) [6].

When treating large and medium-sized joints, direct ultrasonographic guidance is usually sufficient. However, fluoroscopic guidance, with injection of contrast agent and performing arthrography, may be necessary when treating small joints of the hands and feet.

Before injecting the radiopharmaceutical, any excess fluid should be removed from the joint. In the case of large joints (knee, hip, shoulder), a small amount of glucocorticoid is injected during RS. This is done in or-



Fig. 3. RS of the elbow joint under fluoroscopic guidance. Contrast medium is injected before the actual radiopharmaceutical (tip of the needle is visible in the humeroradial joint).

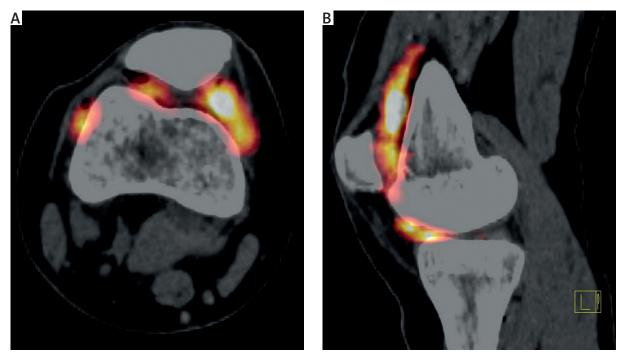


Fig. 4. PET/CT with 90Y after knee RS. Coronal (A) and sagittal (B) cross-sections show diffuse distribution of the radiopharmaceutical in the joint, without any extra-articular leakage.

Parameter	Yttrium-90	Rhenium-186	Erbium-169
T _{1/2} (days)	2.7	3.7	9.5
Energy (MeV)	2.26	0.98	0.34
Tissue penetration (mm) Max.	11.0	3.7	1.0
Mean	3.6	1.2	0.3
Joints	knee	shoulder, elbow, wrist, hip, ankle	small joints of hands and feet

 Table II. Radionuclides used in radiosynovectomy

der to reduce inflammation induced by radiation in the course of tissue damage (radiosynovitis), which can clinically manifest as a transient pain flare [6]. Some authors argue against use of glucocorticoids, advising intra-articular administration of a 1–2% solution of lidocaine instead [22].

Following the injection of the radiopharmaceutical and glucocorticoid/lidocaine, the needle should be flushed with saline solution during withdrawal. This removes the excess radiopharmaceutical from the puncture canal and reduces the risk of skin irradiation.

After RS, it is recommended to immobilize the treated joint for at least 48 hours, to minimize the risk of radioactive leakage to para-articular tissues. In the case of lower limb joint treatment (hip, knee, ankle), the patient is advised not to walk and thus requires the assistance of third parties [6].

Finally, to confirm proper execution of the procedure, post-therapeutic imaging can be performed. Classical scintigraphy or PET/CT (the latter in the case of yttrium-90 agents) can show radioactivity distribution inside the joint cavity up to several days following RS (Fig. 4) [23].

For one month after RS, the patient should refrain from any kind of strenuous activity, rehabilitation or physical therapy of the treated joint.

For four months after RS women in reproductive age should avoid pregnancy and use effective contraception if needed.

Radiopharmaceuticals and dosing

There are several radiopharmaceuticals suitable for treating joint conditions. The three most commonly used in Europe are colloidal solutions of yttrium-90 citrate, rhenium-186 sulphide and erbium-169 citrate (Table II). They differ in radiation energy, range and tissue penetration [6, 15]. Each radiopharmaceutical is intended for treatment of specific joints and should not be used for treating other joints (e.g. yttrium-90 injected into joints other than the knee may cause severe radiation burns and necrosis). The dose (activity) of radiopharmaceuticals is measured in becquerels (Bq; megabecquerel – MBq), which represent the number of radioactive decays occurring every second. Doses range from 12 MBq of erbium-169 (for interphalangeal joints) up to 220 MBq of yttrium-90 (for knee joints).

It is possible to treat many joints at once, e.g. wrist, metacarpophalangeal and interphalangeal joints of one hand, but one should not exceed the dose of 400 MBq per treatment [8, 24]. The total annual dose should not exceed 750 MBq [24].

Different radionuclides are routinely used outside Europe, such as phosphorus-32 (USA) and dysprosium-165 (Australia), with many others investigated in clinical trials (e.g. holmium-166, rhenium-188, tin-117m).

Efficacy and assessment of effects

The response to RS is not immediate, and the 'lag phase' can last from weeks to months. Bigger joints respond more quickly than the small ones, with effects in the knee joint seen as soon as 4–6 weeks later and in the interphalangeal joints as late as 4–6 months afterwards. Regardless of the size of the joint treated, final effects of RS should be evaluated 6 months after the therapy. Apart from clinical examination, the presence or absence of inflammation should be objectively confirmed, preferably with ultrasound or bone scintigraphy [6, 15, 24].

If the effects of RS are satisfactory, the patient continues essential DMARD therapy and remains under the rheumatologist's supervision. When the inflammation relapses, RS may be repeated in the same joint several times, provided that each procedure gives a good clinical outcome lasting at least 6 months.

If the patient fails to respond to the first RS after 6 months, a second procedure may be performed. However, failure of two successive radiosynovectomies is a contraindication for further radionuclide joint therapy, and in such cases other modalities of treatment should be explored [24].

There are numerous research papers assessing response rates to RS. Unfortunately, they evaluate different radiopharmaceuticals, joints and diseases and lack a uniform method for assessing effects. This results in conflicting reports regarding the effectiveness of RS, with estimates of a good response ranging from 40% to 90%. The limited number of meta-analyses and prospective studies allows for a conclusion that up to 75% of patients correctly qualified for the procedure will have a good response to therapy, lasting from a few months to several years [25]. The most important negative outcome predictors include pre-existing joint damage and degeneration, advanced stage of osteoarthritis and long duration of an underlying inflammatory disease [26]. Thus, the best responders would be patients with limited joint damage and short disease duration, in whom all the complaints can be attributed to joint inflammation. In contrast, patients with coexistent advanced osteoarthritis may feel no clinical effects of RS despite cessation of the inflammatory process, since their major source of pain is structural joint damage, not inflammation.

Adverse effects and complications

When performed properly, RS has a very low rate of side effects and complications [6, 15]. The most common adverse effect is intensification of inflammatory symptoms (radiosynovitis) within 2–4 weeks after RS. The patient may feel greater pain, increase in oedema and joint effusion. In rare cases (< 2% of patients), a flulike syndrome may develop, with high fever and malaise. The initial worsening of symptoms may be considered a natural course of the treatment, being a clinical manifestation of rapid and extensive synovial tissue necrosis.

Even if the needle is properly flushed after RS, trace amounts of radiopharmaceutical may remain on the skin or inside the injection canal, causing a local reaction to radiation ("beta burns"). This can be seen as skin discoloration, thickening or formation of a small scar at the site of injection, usually with no clinical consequence [6]. Very rarely, the patient may experience a burning sensation in the general area of the injection, most likely due to irritation of small nerve fibres.

The risk of infection after RS is very small (1: 35 000) [24], and septic arthritis is an uncommon complication. Kisielinski et al. [27] reported an increased rate of infection after RS in patients with a knee endoprosthesis. This may likely be attributed to occult infection already present prior to RS and emphasizes the need for detailed diagnostics before the procedure.

The most dramatic complication of RS takes the form of extensive skin and muscle necrosis due to extra-articular injection or leakage. The possible treatments include hyperbaric oxygen therapy, surgical debridement and autologous skin transplant. If necrosis occurs, surgery should be delayed, because, as in the case of beneficial effects of RS, it may take some time for the damage to reach its full extent [6]. Yttrium-90 is the most potent in inducing tissue damage, possibly even full thickness skin necrosis [28]. Beta burns after rhenium-186 are much more limited, usually self-healing within 3-4 weeks, but in severe cases they may require hyperbaric chamber treatment. Erbium-169, with its low energy and small tissue penetration, is unlikely to cause necrosis, and beta burns associated with its use require only conservative treatment [15]. Fortunately, severe burns and skin necrosis after RS are extremely rare and can be avoided with the proper injection technique and the patient's cooperation.

The potential risk of deep vein thrombosis resulting from joint immobilization has already been highlighted. DVT can be prevented with proper anticoagulation prophylaxis.

Recent studies suggest that in patients with endstage osteoarthritis and extensive cartilage erosion, β^{-} radiation may cause aseptic necrosis of the exposed subchondral bone [28]. While the immediate sequelae of this condition may be clinically silent, presence of aseptic osteonecrosis might compromise the outcome of future surgical joint replacement.

There are no allergic or hypersensitivity reactions to RS radiopharmaceuticals described in the literature. However, since RS agents are solutions of metallic ions, premedication with antihistamines may be considered in patients with known severe allergies to metals (e.g. chromium, cobalt).

Radionuclide synovectomies have been performed for more than half a century, and it is a well-established fact that the procedure does not carry a risk of malignancy, infertility or permanent chromosomal damage. Large studies involving thousands of participants showed that in patients after RS, the risk of developing a malignant neoplasm was no greater than in a matched population untreated with ionizing radiation [29–31]. Moreover, previous history of malignancy is not a contraindication for RS.

Radiation safety issues

In terms of radiation exposure, RS is a very safe procedure. With proper joint immobilization, radioisotope leakage to the systemic circulation does not exceed 2% of the injected dose. Since most of the radiation is absorbed by the articular structures and does not reach the skin surface, the patient does not need to be isolated from third parties [32]. It is customary, however, to avoid physical contact with pregnant women and small children for the first 2 weeks after RS.

In daily practice, a rheumatologist may encounter a patient who has recently undergone RS and complains of growing effusion which limits his joint mobility. If necessary, the joint can be punctured and the fluid removed, but only in the nuclear medicine department. For over one month after RS, the joint fluid is highly radioactive, and the physician untrained in handling open sources of radiation might contaminate the patient and himself. Moreover, the joint fluid, together with the contaminated syringe, needle and drapes, is considered radioactive waste, and as such requires appropriate processing, available only in specialized facilities. Although small, the amounts of radiation emitted outside the joint can be detected by specialized Geiger-Müller counters at airports, border crossings and other places with high security levels. In such situations, the patient should be prepared to present a relevant radiotherapy certificate to the authorities.

Finally, since RS radiopharmaceuticals contain a very high dose of radiation in a very small volume, spilling even a single drop can cause a so-called 'radiation incident'. Such a situation requires contacting local and/ or national authorities followed by decontamination of the area and the personnel. Consequently, RS should be performed only by a nuclear medicine specialist trained in handling open sources of radiation [16].

Controversies

Co-injection of glucocorticoids

As in many other rheumatologic therapies, both local and systemic, use of steroids should be limited or avoided if possible. Before performing RS, it should be established whether the patient actually needs steroid co-injection or it can be spared.

The main reason for co-injecting glucocorticoids is to prevent or limit the initial worsening of inflammation symptoms due to radiosynovitis. Additionally, by reducing inflammation, steroids also decrease systemic radioisotope leakage through dilated capillaries of the synovium [6, 24]. Accordingly, it is advised to co-inject steroids in patients with high activity of the inflammatory process and an extensive power Doppler signal in the synovial membrane. Glucocorticoids are also routinely injected into large joints (knee, shoulder, and hip), since radiosynovitis in these joints not only is common, but may even incapacitate the patient. On the other hand, medium and small joints with low to moderate inflammatory activity and PD signal do not require co-administration of steroids.

If the patient has contraindications for glucocorticoid use (e.g. unstable diabetes or hypertension), intra-articular local anaesthetics can be used instead [22]. Bupivacaine may be preferred to lidocaine because of its more prolonged effect (author's own observation).

Popliteal cyst

A popliteal cyst (Baker's cyst) is an expanded, fluidfilled semimembranous bursa which often accompanies persistent knee arthritis. In terms of definition, it is not a 'true' cyst, since it typically maintains communication with the intra-articular space. This fact is crucial for RS, since any agent injected into the main joint space will probably penetrate into the popliteal cyst. The cyst is a point of decreased resistance, prone to rupturing, especially when exposed to radiation after RS, and as such requires preparation before radionuclide treatment of the knee joint.

Two to three days before RS, the cyst should be punctured under ultrasonographic guidance and completely drained of fluid. Some authors advise injecting small amounts of steroids after the fluid is removed. A pressure exerting dressing is applied on the popliteal fossa and removed just before the actual RS [33].

The procedure described above should be mandatory in large, high pressure popliteal cysts, especially with a valve mechanism, in which the risk of rupturing is significant. Small (< 1 cm) low-pressure cysts or cysts completely filled with synovial tissue usually do not require any preparation.

Before treatment of knee joints, all patients should undergo ultrasonographic screening for popliteal cysts, because even a small cyst may rapidly dilate following RS, causing pain and increasing the risk of rupture [33].

Influence on the cartilage

Concerns exist regarding potential harmful effects of radiation on the cartilage. Most of the studies, however, do not support these fears, ruling out a direct link between RS and chondrocyte damage or acceleration of osteoarthritis [34]. Moreover, RS may lead to a significant decrease in numbers of inflammatory cells, levels of proteolytic enzymes and metalloproteinases harmful to the cartilage, to some extent preventing further joint damage.

In animal models, transient radiation effects were observed only in young, growing cartilage [34]. Consequently, potential risks and benefits should be carefully evaluated before treating patients below 20 years of age.

Radionuclide synovectomy of 'unusual' joints

Radionuclide synovectomy can be performed on all the joints of the appendicular skeleton. Acromioclavicular and sternoclavicular joints can also be injected with radiopharmaceuticals, although inflammation of these joints is rarely severe enough to justify RS. It is universally agreed that joints of the spine should not be injected with radioisotopes, because of the close proximity of radiation-sensitive neural structures. There are individual reports of sacroiliac joint RS in spondyloarthropathies, but there are no reliable data on the safety and efficacy of these procedures.

In theory, temporomandibular joints are a good target for RS, especially in patients with JIA, in whom involvement of these joints is common. However, the proximity of the facial nerve raises safety concerns, and

currently there is not enough evidence to routinely recommend this type of treatment.

Radiosynoviorthesis

The term 'radiosynoviorthesis' was first used in 1968 and was meant to underline the positive, restorative effect of the therapy on the joint [35]. Indeed, removal of inflammatory cells and cytokines may create conditions which slow down joint damage and promote healing. However, the only direct impact of the radiation is tissue necrosis and destruction, with no rejuvenating effects on the joints whatsoever. 'Radiosynovectomy,' which, in parallel to appendectomy or cholecystectomy, stresses the fact of physical tissue removal, seems to be a more appropriate term than 'radiosynoviorthesis'. What is more, the term 'radiosynoviorthesis' might be confusing for both the patient and the referring physician, since it may imply that RS can cure osteoarthritis or substitute for joint replacement, which it cannot.

Summary

Radionuclide synovectomy is a safe, potent and cost-effective method of treating joint inflammation. Combined with modern DMARD therapy it remains a powerful tool to treat persistent inflammation and an attractive alternative to surgical synovectomy, even in the era of biological agents [17]. Despite its advantages, radionuclide synovectomy is not performed as often as it could be, so greater knowledge and understanding of this method are needed. At each stage of radionuclide joint therapy, an interdisciplinary approach is essential and close cooperation of a rheumatologist with a nuclear medicine specialist is indispensible.

The authors declare no conflict of interest.

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