REVIEW ARTICLE

Radiation Synovectomy: an effective alternative treatment for inflamed small joints

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Abstract

An inflamed painful joint is one of the most common indications for the patient to be referred to a rheumatologist or an orthopedician. In relation to the aetiology, the therapeutic approach might be systemic, local or a combination of them in some cases, always with the thought of balancing risk with benefit for the patient. In all cases, independently of the cause, the goal of therapy is to improve the quality of life through the reduction of pain, improvement of mobility and preservation of function. Nuclear Medicine has to offer Radiosynoviorthesis, an effective alternative procedure for treating inflamed small joints. Various radionuclides are available for radiosynoviorthesis. Their selection depends on the size of the joint to be treated. Small joints are mainly treated with [^{169}Er] erbium under a fluoroscopic or sonographic guidance, usually with a simultaneous instillation of a corticoid. Candidates for radiosynoviorthesis should have been under a six-month systemic treatment without encouraging results or should have undergone at least one unsuccessful intra-articular injection of a long acting glucocorticoid. Since 1973, when [^{169}Er] erbium was firstly suggested as a therapeutic agent for radiosynoviorthesis of the finger joints, there has been quite enough experience in its' application. It has been found to be cost effective in providing long term relief of pain and deformity of the inflamed joints in comparison to other therapeutic approaches. Additionally, there is no radiation risk and can be performed on an out patient basis. Therefore it can stand as an effective alternative procedure for treating early stages of chronic synovitis in RA (rheumatoid arthritis) patients, with minor damage of the cartilage and the adjacent bones, and for synovitis secondary to inflammatory arthropathies. Hippokratia 2010; 14 (1): 22-27

Key words: radiosynoviorthesis, inflamed small joints

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A painful joint may appear as a musculosceletal presentation of a systemic disease, or as a local degenerative procedure. Small joints' arthritis concerns mainly the peripheral joints of hand and foot. It appears usually as a result of degenerative diseases such as osteoarthritis, of rheumatologic diseases such as rheumatoid arthritis, SLE or scleroderma, of diseases characterized by crystal deposition such as gout, of autoimmune diseases such as psoriatic arthritis and might also be of traumatic aetiology1. Therefore, in relation to the aetiology, the therapeutic approach might be systemic, local or a combination of them in some cases, always with the thought of balancing risk with benefit for the patient.

While feet are mostly affected by a degenerative joint disease, through an imbalance between stress bearing capacity and actual stress (occupational or sport overuse of the joints, overweight, posttraumatic axial deviation, ligamentous instability)[2], hands seem to be present many different joint involvement patterns, characteristic of specific diseases. For example, in rheumatoid arthritis[3] the metacarpophalangeal (MCP) and the proximal interphalangeal (PIP) joints are most frequently, symmetrically affected, whereas, in psoriatic arthritis[4] there is an asymmetrical ipsilateral involvement of the joints of the fingers, which look like sausages, or a transverse involvement of the distal interphalangeal (DIP) joints. Furthermore, in finger polyarthrosis[2] the DIP joints (Heberden's polyarthrosis) and/or the PIP joints (Bouchard's polyarthrosis) and/or the first carpometacarpal joint (rhizarthrosis) are affected.

In all cases, independently of the cause, the goal of therapy is to improve the quality of life through reduction of pain, improvement of mobility and preservation of function. The usual treatment programms[5] consist of medication, radiopharmaceutic or surgical intervention, rehabilitation, patient instruction, psycological support and social advice. Given the potential toxicity of the systemic therapy (disease modifying drugs, immunosuppressive drugs, corticosteroids, nonsteroidal anti-inflammatory drugs), local joint therapy[6] (intraarticular corticosteroid injection, radiosynoviorthesis, chemosynovectomy[7], surgical treatment) is becoming an increasingly attractive option. Surgical measures cost a lot of effort and financial expenses and have mainly disappointing results at finger joints[2] (eg. Swanson endoprosthesis as replacement for the PIP joints, arthrodesis with Kirschner wires

of the DIP joints). On the other hand, radiosynoviorthesis has a favourable cost to benefit ratio, due to its' low rate of side effects, its' availability as an outpatient procedure and its' application to all joints, especially to the small, peripheral ones[8].

Principles of Radiosynoviorthesis

Radiosynoviorthesis[9] (RSO) is the restoration (orthesis) of the synovia by the local application of radioactive agents (radiolabelled particulates and radionuclide-loaded colloid particles), which emit beta rays. In the different types of arthritides, as well as in the activated arthrosis (osteoarthritis), the main cause of pain and discomfort is the underlying synovitis. Therefore, through radiosynoviorthesis one tries to influence the synovial process favorably as an alternative to early surgical synovectomy, especially when a surgical approach is contraindicated[10].

The injection of the radiopharmaceutical into the joint cavity is followed by phagocytosis[11] of it's' molecules by the outermost cellular layer of the synovial membrane (Figure 1A). Due to this selective irradiation, the result is apoptosis and ablation of the inflamed synovial membrane. A reduction in the number and the size of the synovial villi is observed and a decrease of the involved hyperaemia (thrombotic occlusion of capillaries) as well.

There is also a reduction in the filtration and reabsorption of the synovial fluid. After a few months the synovial membrane is fibrosed without signs of mononuclear infiltration (Figure 1B). In this way, further destruction of the joint cavity by immunological reactions is prevented and a long term remission is achieved[12].

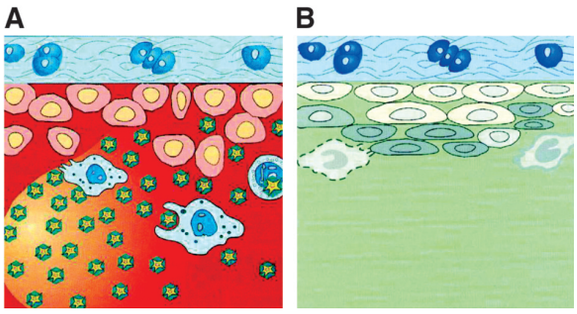

Figure 1: Mechanism of Action of RSO
(A) í-Emitting colloidal particles (yellow stars) phagocytized by inflamed hypertrophic synovial lining with proliferating synoviocytes (pink). Top cartilage layer remains unaffected. **(B)** Subsequent cell damage and sclerosis of synovial membrane

Indications

According to the guidelines of the European Association of Nuclear Medicine, candidates[9] for radiosynoviorthesis should have been under a six-month systemic treatment without encouraging results or should have undergone at least one unsuccessful intra-articular injection of a long acting glucocorticoid. The earlier in the course of the disease[14], the better results are expected from the application of the procedure (Table 1). Among common indications for RSO stand rheumatoid arthritis, spondyloarthropathy (reactive or psoriatic arthritis), hemarthrosis or synovitis in the hemophiliac, chronic pyrophosphate arthropathy, pigmented villonodular synovitis, persistent effusion after joint prosthesis, osteoarthritis (with mild or moderate radiographic changes) and inflammatory joint diseases such as Lyme disease or Behcet's disease[15].

Table 1: Groups for RSO[14].

Group	Clinical response rate	Disease	Pre-existing morphological changes
A (Appropriate)	> 80%	Rheumatoid arthritis Haemarthrosis in haemophilia Haemarthrosis in Willebrand's disease Villonodular synovitis	No changes
B (Acceptable)	60%-80%	Rheumatoid arthritis Seronegative arthritis Osteoarthritis Repeating injection in previous responder	Steinbrocker I, II Minimal or moderate
C (Helpful)	< 60%	Rheumatoid arthritis Osteoarthritis	Steinbrocker III, IV Severe destruction
D (Not indicated)	No response	Need for surgical interventions Previous non-responder Deformed joints Unstable joints	

Table 2: Steinbrocker functional classification of arthritis[18].

Class I	Complete functional capacity with ability to carry on all usual duties without handicaps.
Class II	Functional capacity adequate to conduct normal activities despite handicap of discomfort or limited mobility of one or more joints.
Class III	Functional capacity adequate to perform only few or none of the duties of usual occupation or of self-care.
Class IV	Largely or wholly incapacitated with patient bedridden or confined to wheelchair, permitting little or no self-care.

Contraindications

The procedure should not be used[9] in case of pregnancy, breastfeeding, ruptured baker's cyst (concerning the knee joint) or local skin infection. It should be applied in children and young patients (‹20 years) only if the benefit of treatment is likely to outweigh the potential hazards. Extensive joint instability and osteoarthritis with severe joint destruction are relatively contraindicated.

Radiopharmaceutical selection for RSO of the small joints

Various radiopharmaceuticals are available for radiosynoviorthesis, in a colloidal or particulate form. The most commonly used worldwide are [^{90}Y] ytrium silicate/citrate colloid, [^{186}Re] rhenium sulfur colloid, [^{169}Er] erbium citrate colloid and [^{32}P] chromic phosphate. Their selection depends on the physical half live of the radionuclide, the mean tissue penetrance of the emitted b-particles, the size of the particles in use, their biodegradability and irreversible binding of the radionuclide to them, as well as the size of the joint to be treated. The smaller the joint, the shorter the range of the emitted beta particles should be. Besides, the thickness of the synovium and the amount of the synovial fluid affect radiation delivery[16]. For radiosynoviorthesis of the small joints[2,9] as the MCP, PIP and metatarsophalangeal (MTP), [^{169}Er] erbium citrate colloid is used. Other joints, that can be treated with [^{169}Er] erbium as well, are DIP, tarsometatarsal (TMT), the proximal tibiofibular joint and the thumb base joint or first carpometacarpal (CMC I).

[^{169}Er] erbium decays under emission of beta particles[17] to stable [^{169}Tm] thulium. It has a physical half life of 9.5 days and the maximum energy of the b particles is 0.34 MeV. The maximum range in soft tissue is 1mm, whereas the mean range lies between 0.2 and 0.3mm. The fraction of gamma rays is negligible; therefore a distribution posttherapeutic scintigraphy is not possible. The administered activity and the injected volume vary according to the volume of the joint to be treated. Usual applications[9] consist of 20-40 MBq in 1ml for MCP joints, 30-40 MBq in 1ml for MTP joints and 15-20 MBq in 0.5 ml for PIP and DIP joints. As many joints can be treated at the same session, the total activity of erbium injected should not exceed 750 MBq at a single session.

Pretreatment evaluation

Before proceeding to a radiosynoviorthesis, careful history and physical examination are of fundamental importance. X-ray films or magnetic resonance imaging of the affected joints, ultrasound and scintigraphy are also necessary to obtain optimal results[2]. In evaluating the patient the clinical stage classification and the functional classification of rheumatoid arthritis according to Steinbrocker et al[18] has proved to be useful (Table 2). However, an increasing preference of the radiologic stage classification according to Larsen[19,20] has been observed within recent years, not only for rheumatoid arthritis, but also for psoriatic arthritis and Behcet's disease with peripheral joint involvement (Table 3). Although x-ray examination is an indespensible diagnostic tool, the most decisive examination for the detection of arthritis is the joint soft tissue scintigraphy[21].

This is the second phase of the triple phase bone scintigraphy; in which joint images are produced approximately 5-10 minutes post injection.

The images represent the distribution in the blood pool and the soft tissues. Only with the proof of a clear synovitis through scintigraphy does radiosynoviorthesis seem promising and therefore indicated. As for sonography[22], it helps the physician evaluate the structure and the thickness of the synovial membrane (Figure 2). Especially, in hands and feet tenovaginitis and tenosynovitis are differentiated easily this way.

Technique

At every joint there are usually various puncture sites available. To avoid an injury of the related structures (vessels, nerves, tendons, tendon sheaths) or an extra artricular administration, it is advisable to proceed under a fluroscopic or sonographic guidance[2,9]. Injection into a joint must be performed under sterile conditions, after application of local skin anesthesia. The position of the needle in smaller joints may easily be controlled by radiography under fluoroscopic guidance, using a 22-gauge needle. A joint should be punctured with one single plunge through the joint capsule, without searching around with the needle[2,24]. Administration of just enough contrast medium to document that the needle is intraarticular is helpful.

The volume of the injected contrast agent should be as small as possible[25], because the stabilizing agent of ethylenediaminetetraacetic acid (EDTA), that it includes, causes

Table 3: Larsen radiologic stage classification of arthritis[19].

Grade 0	Normal conditions. Changes not related to arthritis, may be present.
Grade I	Slight abnormality. One or more of the following changes are present: periarticular soft tissue swelling, periarticular osteoporosis and slight joint space narrowing. When possible, use for comparison a normal contralateral or a previous radiograph of the joint in the same patient sa grade 0, as demonstrated in standard films. Soft tissue swelling and osteoporosis are sometimes reversible changes. This is an early, uncertain phase of arthritis. The compatible changes may occur without arthritis in old age, in traumatic conditions or in Sudeck's atrophy.
Grade II	Definitive early abnormality. Erosions and joint space narrowing corresponding to the standards. Erosion is obligatory except in the weight-bearing joints (in standard films erosion is present in all joints except tarsus).
Grade III	Medium destructive abnormality. Erosion and joint space narrowing corresponding to the standards.
Grade IV	Severe destructive abnormality. Erosion and joint space narrowing corresponding to the standard. Bone deformation is present in the weight-bearing joints.
Grade V	Mutilating abnormality. The original articular surfaces have disappeared. Gross bone deformation is present in the weight-bearing joints.

destabilization of the radiopharmaceutical. Simultaneously with the radiopharmaceutical a glucocorticosteroid is administered[26,27], in order to bridge the lag phase between the time of the injection and the time of the effect of RS, to lower the risk of radiation-induced synovitis and to inhibit a possible extraarticular leakage of the radiopharmaceutical. Triamcinolone[26] is often used at a dosage of 8mg (0,2ml) for MCP and 4mg (0,1ml) for PIP joints. What seems of great significance is the fact that overpressure during administration should be avoided. For this reason a dose of small volume and high specific activity is preffered[2]. Sometimes, due to the synovial hypertrophy and the joint space narrowing, there is hardly any inner space for the administration of the radiopharmaceutical.

Then, it is preferable to inject a few drops of the activity (followed by air) and proceed to a re-radiosynoviorthesis a few months later[2]. Before removal of the needle, flushing with saline solution is recommended to keep the puncture channel free of beta emitting particles. After removing the needle, the puncture site is squeezed off with a gauze, fixed with an elastic bandage and the joint, under manual pressure upon the puncture site, is carefully moved a couple of times.

Then a splint or a cast is formed to the physiologic position of the joint and the joint is immobilized for 48-72 hours[2,9,26]. The treated joint should be at a state of mild relaxation for approximately 1 week. When toe joints are treated, the patient leaves on a wheelchair and is advised to walk only to the restroom for the aforementioned period of time[28].

After RSO

The patient should be urged to report by telephone about 4-6 days after the radiosynoviorthesis for possible side effects. After this period, a follow-up visit at 3-4 months, 6 months and 1 year post therapy is recommended[2,9,12]. Pain reduction typically occurs 1-3 weeks post injection, but occassionally may delay a couple of weeks more . Patients should be informed[9] that the procedure is 60%-80% effective and that there is the possibility of a temporary increase in synovitis. Active training of the periarticular soft tissue apparatus is recommended in order to achieve the maximum functional capacity of the joint[28]. A tingling sensation or stabbing pain in the joint might appear, for which a cold compress or ice directly to the joint and not through the bandage could be applied. Potential complications[9,29] of treatment are local haemorrhage, bruising, extravasation and radiation necrosis, and very rarely infection or allergic reaction. Thrombosis due to immobilization and lymphoedema may occur. Since the radionuclide is applied in form of a colloid of appropriate size, it remains mostly within the joint, with no significant radiation exposure to other organs or parts of the body. The risk for induction of a future malignancy is estimated as exceptionally small[30-33]. Patients who have failed to respond to the first radionuclide injection report pain reduction and improvement of joint function follow-

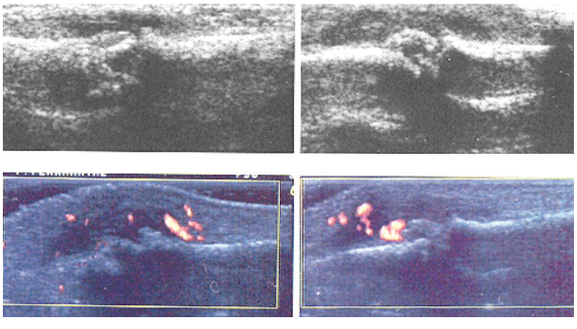

Figure 2: Woman 60 years old, with soft tissue swelling and RA test (+)
Synovitis and bone erosions of the PIP II[23]

Table 4: Comparison of isotope properties[17].

Isotope	Particle size (μm)	Emission	Halph-life (days)	Soft tissue penetration mean/max (mm)
169-Erbium	2-3	beta	9.5	0.30 / 1.0
177-Lutetium	2-10	beta, gamma	6.73	0.67 / 2.0

ing re-treatment 6 months later. The simultaneous instillation of a corticoid often brings permanent recovery in contrast to steroidal ineffectiveness before radiosynoviorthesis[12,34].

Clinical effect

Since 1973, when [^{169}Er] erbium was firstly suggested as a therapeutical agent for radiosynoviorthesis of the finger joints[35], there has been quite enough experience in its' application. Although there is no uniform, validated system for scoring the effect of RSO, which makes comparison between different studies difficult, reported success rates range from 40% to 95% for the different joints and underlying pathology[2,12]. At the early years of RSO, good to very good results leading to restoration of normal function have been reported in 54% 6 months after treatment in a study consisting of 1261 finger joints by Menkes et al[36], as well as in a study by Rampon et al[37]. Boussina et al reported good to excellent results concerning pain relief and joint mobility in 71.5% and 79.4% 6 months and 12 months after RSO, respectively[38]. At that time, another study by Tubiana et al. reported 62.5% good and very good results 1 year post RSO treatment of MCP and PIP joints[39]. In later years, Gamp found good and satisfactory results 6 months after RSO in 70% of MCP joints and 54% of PIP joints.

These results were noticed in 68% of both MCP and PIP joints 1 year after treatment and 64% and 41% respectively at 2 years follow-up[40]. More recently, according to a double-blind, randomized, placebo-controlled, international multicentre study in patients with RA and recent (≤24 months) ineffective corticosteroid injections into their finger joints, there has been reported, a six months follow-up with a 92% decrease in pain, a 82% decrease in swelling and a 64% increase in mobility of the MCP and PIP treated joints in comparison to the placebo-injected joints, which showed 72%, 53% and 42% respectively[41]. Best results come from a study of Mödder et al, who report 95% good results, concerning pain relief and 83% total improvement, concerning joint mobility and swelling, in patients with rheumatoid arthritis and corticosteroid resistant small joints (MCP, PIP, DIP, MTP) six months post therapy[2].

These relatively good results are attributable to optimal injection parameters such as high specific activity, small injection volume and fluoroscopic control[2]. In overall, after the application of RSO, a reduction of pain, swelling and stiffness of the joint is observed, as well as an improvement in the range of movement and quality of life[42,43]. The effect rate of the procedure is estimated at about 79% for the upper and 60% for the lower extremities at a period of six months[44]. The higher effect rate of the upper extremities, which is in accordance with another randomized, double-blind, placebo-controlled study of the upper extremity joints[45], is attributed to the absence of weight-bearing mechanical forces in them. A less favorable outcome for RS has been reported in more severely damaged joints and in diseases other than RA, especially osteoarthritis[13,43,46].

According to a survey[47] undertaken by PJ Ell and G Clunie, radiosynoviorthesis is practiced in about 24% of nuclear medicine centres in Europe. Rheumatoid arthritis is the most prevalent disease (71% of treated patients) and the most frequently treated joints are knee (46%) and finger joints (20%). Corticosteroid is routinely co-injected in 60% of cases.

Conclusion

With a 35 year record of use, radiosynovectomy of the small joints is an effective alternative procedure for treating early stages of chronic synovitis in RA patients, with minor damage of the cartilage and the adjacent bones, and for synovitis secondary to inflammatory arthropathies[9,13,48]. It has been found to be cost effective in providing long term relief of pain and deformity of the inflamed joints in comparison to other therapeutical approaches[12,49,50]. Additionally, there is no radiation risk and can be performed on an out patient basis[9]. As for the future prospects of the technique, Lutetium-177 (^{177}Lu) labeled hydroxyapatite particles[51] (Table 4) are considered a promising radiopharmaceutical in radiation synovectomy of small-sized joints, owing to its favorable decay characteristics and feasible and cost-effective production route in comparison to Erbium. Nevertheless, further investigations are yet to come.

References

1. Heisel J. Entzuendliche Gelenkerkrankungen. Stuttgart: Verlag; 1992.
2. Mödder G. Radiosynoviorthesis. Involvement of Nuclear Medicine in Rheumatology and Orthopaedics. Warlich Druck und Verlagsgesellschaft mbh 2001.
3. The American Rheumatism Association revised criteria for the classification of rheumatoid arthritis. Arthr Rheum. 1987; 31: 315-324.
4. Dihlmann W. Bildgebende Verfahren in der Rheumatologie. Internist. 1993; 34: 825-830.

5. Miehlke K. Medikamentoese Therapie und Prophylaxe der Arthrose. Internist. 1989; 30: 643-645.
6. Bird HA. Intra-articular and intralesional therapy S8/16.5 in Klippel JH, Dieppe PA: Rheumatology. London: Mosby; 1994; p. 163-165.
7. Dahmen G. Possibilities and dangers of chemical synovectomy. Hippok. 1971; 42: 251-252.
8. Gamp R. Die Radiosynoviorthese im Handbereich. Akt Rheumatol. 1983; 8: 165-167.
9. Clunie G, Fischer M. EANM procedure guidelines for radiosynovectomy. Eur J Nucl Med Mol Imaging. 2003; 30: BP12-BP16.
10. Dunn AL, Busch MT, Wyly JB, Abshire TC. Radionuclide synovectomy for hemophilic arthropathy: a comprehensive review of safety and efficacy and recommendation for a standardized treatment protocol. Thromb Haemost. 2002; 87: 383-393.
11. Valotassiou V, Wozniak G, Demakopoulos N, Georgoulias P. Radiosynoviorthesis-indications, side effects. Hell J Nucl Med. 2006; 9: 187-188.
12. Pirich C, Schwameis E, Bernecker P, et al. Influence of radiation synovectomy on articular cartilage, synovial thichness and enhancement as evidenced by MRI in patients with chronic synovitis. J Nucl Med. 1999; 48: 1277-1284.
13. Schneider P, Farahati J, Reiners C. Radiosynovectomy in rheumatology, orthopedics, and hemophilia. J Nucl Med. 2005; 46: 48s-54s.
14. Kresnik E, Mikosch P, Gallowitsch HJ. Clinical outcome of radiosynoviorthesis: a meta-analysis including 2190 treated joints. Nucl Med Comm. 2002; 23: 683-688.
15. Siegel HJ, Luck VJ Jr, Siegel ME. Advances in radionuclide therapeutics in orthopaedics. J Am Acad Orthop Surg. 2004; 12: 55-64.
16. Farahati J, Schulz G, Wendler J. Multivariate analysis of factors influencing the effect of radiosynovectomy. Nuklearmedizin. 2002; 41: 114-119.
17. Cherry S, Sorenson J, Phelps M. Physics in Nuclear Medicine 3rd ed. Philadelphia: Saunders; 2003; p.20-21.
18. Steinbrocker O, Traeger CH, Batterman RC. Therapeutic criteria in rheumatoid arthritis. J Am Med Ass. 1949; 140: 659-663.
19. Larsen A. A radiological method for grading the severity of rheumatoid arthritis. Helsinski: Thesis; 1974.
20. Dale K, Eek M. Preliminary experiences with Larsen's radiological method for grading rheumatoid arthritis. Scand J Rheumatol. 1975; 4/8 abstr. 27-02.
21. Ziessman H, O'Malley J, Thrall J. The Requisites. Nuclear Medicine 3rd ed. Philadelphia: Mosby Elsevier; 2006; p.115-116.
22. Sattler H, Harland U. Arthrosonographie. Berlin-Heidelberg: Springer-Verlag; 1988.
23. Raphailidis D. Ultrasound of the musculosceletal system and soft tissues. Rotonda; 2006.
24. Kaiser H, Fischer W. Technicken der Injektion. Selecta-Verlag; 1985.
25. Schomäcker K, Dietlein M, Mödder G, et al. Stability of radioactive colloids for radiation synovectomy: influence of X-ray contrast agents, anaesthetics and glucocorticoids in vitro. Nucl Med Comm. 2005; 26: 1027-1035.
26. van der Zant FM, Jahangier ZN, Gommans GM. Radiation synovectomy of the upper extremity joints: does leakage from the joint to non-target organs impair its therapeutic effect? Appl Rad Isotopes. 2007; 65: 649-655.
27. Noble J, Jones AG, Davis MA. Leakage of radioactive particle systems from a synovial joint studied with a gamma camera: its application to radiation synovectomy. J Bone Joint Surg. 1983; 65: 381-389.
28. Móller-Brand J. Grundlagen der Radiosynoviorthese. Schweiz Med Wochenschr. 1990; 120: 676-679.
29. Das BK. Role of radiosynovectomy in the treatment of rheumatoid arthritis and hemophilic arthropathies. Biomed Imaging Interv J. 2007; 3: 45.
30. Lóders C, Kopec M, Morstin K. Die Radiosynoviorthese. Anwendung und Durchfuehrung unter besonderer Berueckssichtigung dosimetrischer Aspekte. Akt Rheum. 1992; 17: 74-81.
31. Johnson LS, Yanch JC, Shortkoff CL, Barnes AI, Sledge CB. Beta-particle dosimetry in radiation synovectomy. Eur J Nucl Med. 1995; 22: 977-988.
32. Liepe K, Andreeff M, Mielcarek J. Beta radiation exposure at the finger tips during the radionuclide synovectomy. J Nucl Med. 2003; 42: 104-108.
33. Johnson LS, Yanch JC. Calculation of beta dosimetry in radiation synovectomy using Monte Carlo simulation (EGS4). Med Phys. 1993; 20: 747-753.
34. Fischer M, Mödder G. Radionuclide therapy of inflammatory joint diseases. Nucl Med Commun. 2002; 23: 829-831.
35. Delbarre F, Menkes CJ, Aignau M. La synoviorthese par les radioisotopes a la main et au poignet. Rev Rheum. 1973; 40: 205.
36. Menkes CJ, Verrier P, Le Go A. Radio-isotopic synoviorthesis of finger joints in rheymatoid arthritis. Ann Chir. 1974; 28: 883-889.
37. Rampon S, Bussiere TZ, Prim P. Synoviorthese par les radioisotopes. Rheumatologie. 1976; 6: 123-135.
38. Boussina I, Toussaint M, Ott H. A double-blind study of erbium 169 synoviorthesis in rheumatoid digital joints. Results after one year. Scand J Rheumatol. 1979; 8: 71-74.
39. Tubiana R, Menkes CJ, Galmiche B, Delbarre F. Die intraartikulaere Injektion von B-Strahlern. Ihre Anwendung zur Behandlung der rheumatoiden Veraenderungen an der Hand. Therapiewoche. 1979; 29: 507-513.
40. Gamp R. Die radiosynoviorthese im Handbereich. Akt Rheumatol. 1995; 8: 165-167.
41. Kahan A, Mödder G, Menkes CJ. 169 Erbium-citrate after failure of local corticosteroid injections to treat rheumatoid arthritis affected finger joints. Clin Exp Rheumatol. 2004; 22: 722-726.
42. Srivastava S, Dadachova E. Recent advances in radionuclide therapy. Semin Nucl Med. 2001; 31: 330-341.
43. Kampen WU, Hellweg L, Massoudi-Nickel S, et al. Clinical efficacy of radiation synovectomy in digital joint osteoarthritis. Eur J Nucl Med Mol Imaging. 2005; 32: 575-580.
44. Jahangier ZN, Moolenburgh JD. The effect of radiation synovectomy in patients with persistent arthritis: a prospective study. Clin Exp Rheumatol. 2001; 19: 417-424.
45. van der Zant FM, Jahangier ZN, Moolenburgh JD. Clinical effect of radiation synovectomy of the upper extremity joints: a randomised, double-blind, placebo-controlled study. Eur J Nucl Med Mol Imaging. 2007; 34: 212-218.
46. Deutsch E, Brodack JW, Deutsch KF. Radiation synovectomy revisited. Eur J Nucl Med. 1993; 20: 1113-1127.
47. Clunie G, Ell PJ. A survey of radiation synovectomy in Europe, 1991-1993. Eur J Nucl Med. 1995; 22: 970-976.
48. Kat S, Kutz R, Elbracht T, Weseloh G, Kuwert T. Radiosynovectomy in pigmented villonodular synovitis. Nuklearmedizin. 2000; 39: 209-213.
49. Gobel D, Gratz S, von Rothkirch T. Chronic polyarthritis and radiosynoviorthesis: a prospective, controlled study of injection therapy with erbium 169 and rhenium 186. Z Rheumatol. 1997; 56: 207-213.
50. Kampen WU, Brenner W, Kroeger S. Long-term results of radiation synovectomy: a clinical follow-up study. Nucl Med Commun. 2001; 22: 239-246.
51. Chakraborty S, Das T, Banerjee S. Preparation and preliminary biological evaluation of 177 Lu labelled hydroxyapatite as a promising agent for radiation synovectomy of small joints. Nucl Med Comm. 2006; 27: 661-668.