29 Radiosynoviorthesis (Radiation Synovectomy)

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29.1 Introduction

Radiosynoviorthesis (RSO) is a proven important instrument for local treatment of chronic inflammatory joint diseases in the context of medical and orthopaedic efforts. The term radiosynoviorthesis was created by Delbarre et al. 1968, meaning the restoration (*orthesis*) of the *synov*ium by means of *radio*nuclides. By local administration of radioactive agents an attempt is made to influence the synovial process favourably as an alternative to surgical synovectomy. In the Anglo-American literature the term "radiosynovectomy" or "radiation synovectomy" came into use.

The first descriptions of the method go back to Ishido (1923) and Fellinger and Schmid (1952).

In Germany, RSO nowadays is performed in about 63,000 joints per year, as much as radioiodine therapy in thyroid diseases.

29.2 Indications

Basically RSO is indicated for the local treatment of almost all kinds of chronic synovitis (Mödder 2001a, b; Kampen et al. 2001). The *main indications* for radiosynoviorthesis are (modified according to German and European guidelines: Farahati et al. 1999; Clunie and Fischer 2003):

- Rheumatoid arthritis
- Seronegative spondyloarthropathy (i.e., reactive arthritis, psoriatic arthritis)
- Haemarthrosis in haemophiliacs
- Recurrent joint effusions (i.e., after arthroscopy)
- Pigmented villonodular synovitis (PVNS)
- Osteoarthritis (activated arthrosis)
- After joint prosthesis: persistent effusions, polyethylene disease
- Undifferentiated arthritis (where the arthritis is characterized by synovitis, synovial thickening or effusion)

Absolute contraindications:

- Pregnancy
- Breast feeding
- Local skin infection
- Acute rupture of popliteal cyst (Baker's cyst)

Relative contraindications:

- RSO should only be used in children and young patients (< 20 years) if the benefit of treatment is likely to outweigh the potential hazards. But it is routinely applied in haemophilic children.
- Extensive joint instability with bone destruction

29.3 Radiopharmaceuticals

The most common and approved radiopharmaceuticals used for RSO are:

- [^{90}Y]yttrium citrate or silicate ([^{90}Y]colloid), only used for RSO of knee joints
- [^{186}Re]rhenium sulphide ([^{186}Re]colloid), used for RSO of middle sized joints
- [^{169}Er]erbium citrate ([^{169}Er]colloid), used for RSO of small joints

Table 29.1. Proven dosages for the most frequently treated joints

Joint	Radioisotope	Dose (MBq)
Knee joint	Yttrium-90	185 – 222
Glenohumeral joint	Rhenium-186	74
Elbow joint	Rhenium-186	74
Wrist joint	Rhenium-186	55 – 74
Hip joint	Rhenium-186	111 – 185
Ankle joint	Rhenium-186	74
Talonavicular/subtalar joint	Rhenium-186	55
Metacarpophalangeal joint (MCP)	Erbium-169	20 – 40
Proximal interphalangeal joint (PIP)	Erbium-169	10 – 20
Distal interphalangeal joint (DIP)	Erbium-169	10 – 15
Metatarsophalangeal joint (MTP)	Erbium-169	30 – 40
Thumb base	Erbium-169	30

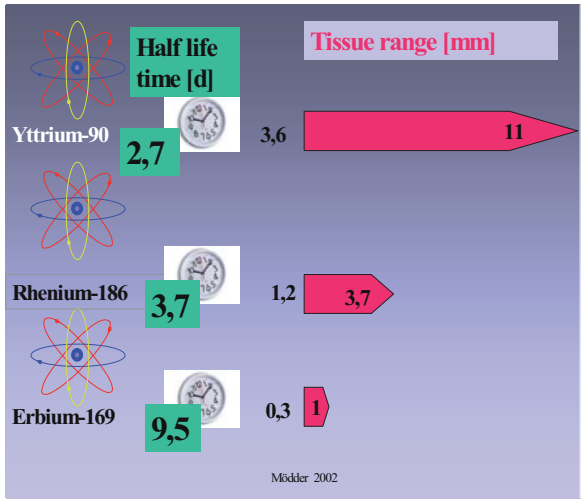

Fig. 29.1. Radioisotopes for radiosynoviorthesis

The physical characteristics of these radioisotopes are shown in Fig. 29.1. Proven dosages are listed in Table 29.1. These radiopharmaceuticals are β-emitters in colloidal suspensions.

Other radiopharmaceuticals rarely used for RSO are dysprosium-165 ferric hydroxide, holmium-166 hydroxyapatite and samarium-153 hydroxyapatite.

29.4 Mechanism of Action

"Synovitis is the villain of the drama" (Mannerfeldt), in rheumatic diseases causing brutal destruction of cartilage, bone, tendons and ligaments correlated with pain, swelling and loss of function. After intra-articular administration the radioactive particles in colloidal form are taken up by phagocytosis in synovial macrophages. A particle size of about 5 ± 10 nm is essential to avoid leakage and provide homogenous distribution on the surface of the synovium. β-radiation leads to coagulation necrosis, sclerosis and fibrosis of the synovial tissue including vessels and pain receptors, resulting in reducing effusion, swelling and pain of the joint. Due to the fact that cartilage has no ability to phagocytose, this tissue is not a target for the radiation effects (Ishido 1923).

The remark "synovitis is the villain of the drama" is not only valid for rheumatic diseases but also for osteoarthritis (activated arthrosis). Arthrosis with typical joint space narrowing as a result of cartilage defects is not associated with pain because cartilage has no nerves and vessels. Only after detritus leads to synovitis does simple arthrosis escalate to inflammation (activated arthrosis = osteoarthritis) with pain, swelling and effusions (Otte 2002; Mödder 2001a; Mödder 2006). The rather good effects of RSO in osteoarthritis (i.e., knee joint) will be lacking if mechanical problems such as severe instability and axe deviation predominate.

Simultaneous intra-articular injection of corticosteroids (i.e., triamcinolone hexacetonide or triamcinolone acetonide) is recommended because this might reduce local inflammation due to radionuclide instillation and prolong residence time of the radiopharmaceutical agent in the joint (11). An additional reason is the reduction of the often superposed layer of oedema on the synovium so that the thin film of radioisotopes gets closer to the destructing pannus – resulting in improvement of the effect of RSO.

29.5 Side Effects

Early: Temporarily increased synovitis (rapid relief by local application of ice)
Late: Local radionecrosis (rare)

29.6 Methodology

29.6.1 Patient Selection

Rheumatic patients need systemic treatment with antirheumatoid drugs because rheumatism is a systemic disease. If after at least 6 months a few joints do not show adequate improvement even after corticosteroid injections into the affected joints, these joints are selected for RSO, thus avoiding escalation of systemic therapy with its possible side effects. In monarthritis or oligoarthritis RSO could be the therapy of first choice, after failure of locally administered corticosteroids (Mödder 2001b; Fischer and Mödder 2005).

Orthopaedic patients should be selected after failure of local corticoid injection and/or ineffective conservative treatment. But also after plenty of surgical interventions RSO might improve the complaints of the patient, i.e., after total knee replacement (Mödder and Mödder-Reese 2001) or effusions after arthroscopy. Some authors recommend RSO after arthroscopy as a routine method to improve results (Kerschbaumer and Herresthal 1996; Thabe 1997). The time interval between arthroscopy or joint surgery (i.e., villonodular synovitis) and RSO should be planned as (4–)6 weeks.

29.6.2 Diagnostic Studies Prior to RSO

- Medical history, clinical inspection, examination of joint function.
- *X-ray images* provide basic information about the joint.
- *Ultrasound study* evaluates joint space, synovial structure and thickness and extent of effusion, and assesses tenosynovialitis or rotator cuff tear (shoulder). Ultrasound is obligatory prior to performing RSO to rule out a Baker's cyst (Fig. 29.2).
- *Multiphase scintigraphy* with ^{99m}Tc-MDP (or similar radiopharmaceuticals) is the best diagnostic tool for detecting and demonstrating inflammation of the synovium, thus – including findings of the clinical examination – selecting joints for RSO. In the first step (10 min p.i.) *soft tissue scintigraphy* detects the degree of active inflammation of synovium. In the second step (3 h p.i.) *bone scintigraphy* assesses the bone involvement in the painful process. The study reveals nearly indispensable information in activated arthrosis (osteoarthritis) and gives the best overview over multiple joint involvement especially in (also seronegative) polyarthritis (Mödder 2001a) (Figs. 29.3, 29.4).
- Magnetic resonance imaging might be suitable for additional information in a few patients (i.e., bone oedema, femur head necrosis).

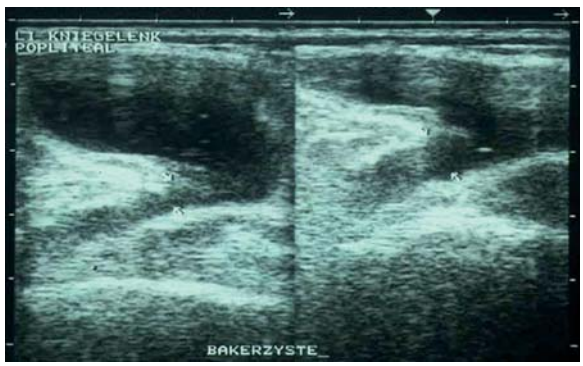

Fig. 29.2. Ultrasound of a Baker's cyst (transverse). Check for valve mechanism. *Left* The connecting duct between the knee joint (*below*) and Baker's cyst is seen. *Right* By soundhead pressure the cyst is decreased in size and the duct dilates. There is no valve mechanism

Fig. 29.3. The hands as the "visiting card" of the rheumatic patient. Soft tissue scintigram with ^{99m}Tc-MDP shows a typical pattern in psoriatic arthritis

29.6.3 Performance of RSO

29.6.3.1 Joint Puncture

A suitable room and strict asepsis are necessary. A good puncture technique is essential (for details see Mödder 2001a). The best puncture technique for the knee joint is shown in Fig. 29.5.

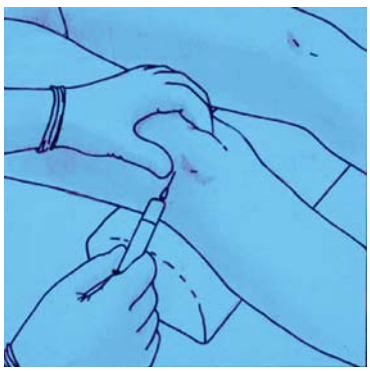

Fig. 29.5. Injection technique for the knee joint. Beware of injecting beside the ligamentum patellae with the patient in the sitting position, because then there is the danger of injecting yttrium-90 into the crucial ligaments or into Hoffa's fat body

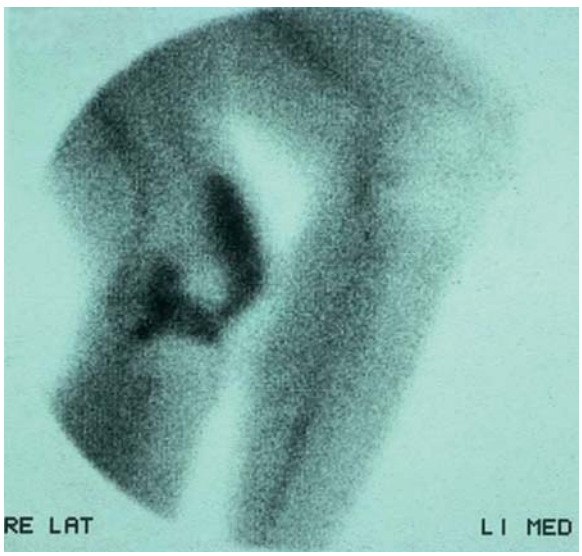

Fig. 29.4. Non-specific but highly sensitive synovitis – typical increased accumulation above the right knee joint in a patient with knee osteoarthritis. In rheumatoid arthritis the scintigram would look identical

29.6.3.2 Fluoroscopy

Apart from the knee, all joints have to be punctured for RSO by fluoroscopy and often by arthrography. Dye distribution predicts the distribution of radionuclide which is injected immediately afterwards. Using this procedure perfect needle position in the cavity of the joint is ensured (Fig. 29.6a, b).

Examples of the importance of fluoroscopic control for an absolutely exact injection technique are given in Figs. 29.7 and 29.8.

Figure 29.9 illustrates (a) a soft tissue scintigram, (b) an arthrogram and (c) a distribution scintigram as a proof for a perfect performance.

29.6.3.3 Radiation Safety Considerations

For the patient: Very late radiation induced stochastic hazards have not been observed (Vuorela et al. 2003). The effective dose to the whole body is estimated to be 30 times lower than in iodine-131 therapy of benign thyroid diseases (Manil et al. 2001).

For the personnel: To avoid high radiation exposure for the fingers during preparation and administration of yttrium-90 radiation, protection has to be provided by use of acrylic syringe protectors, nitrile or vinyl gloves, β-fingerdosimeters, etc. (Brenner 2006) (Fig. 29.10).

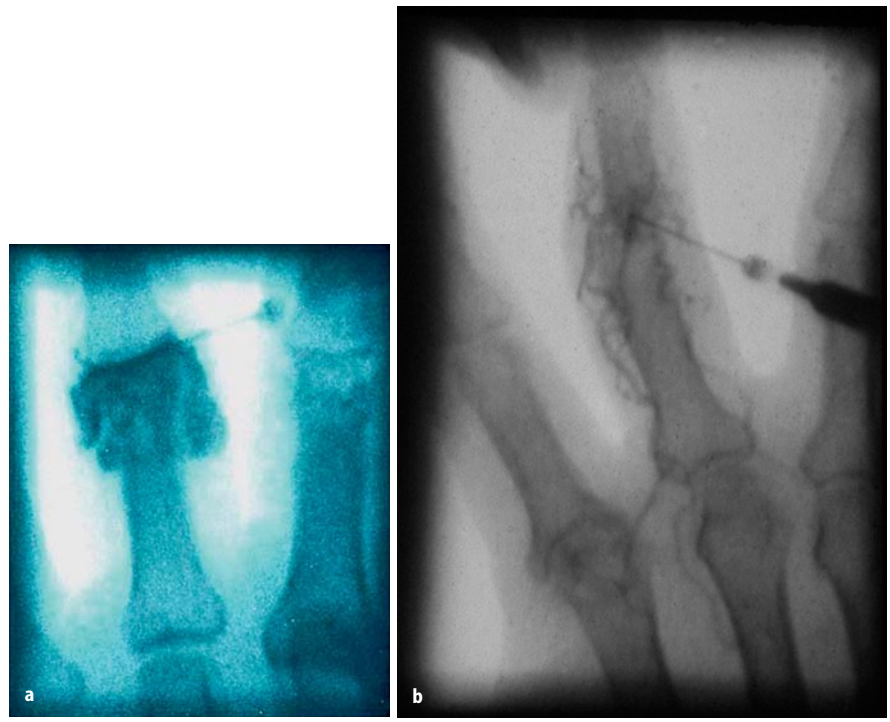

Fig. 29.6. a Arthrogram after perfect injection into a proximal interphalangeal joint (PIP) joint. **b** Arthrogram of a PIP joint. Intra-articular position of the needle, but *not in the cavity*. The contrast medium is injected into a villus with transportation by vessels. If this occurred with injection of erbium-169, it would be followed by side effects

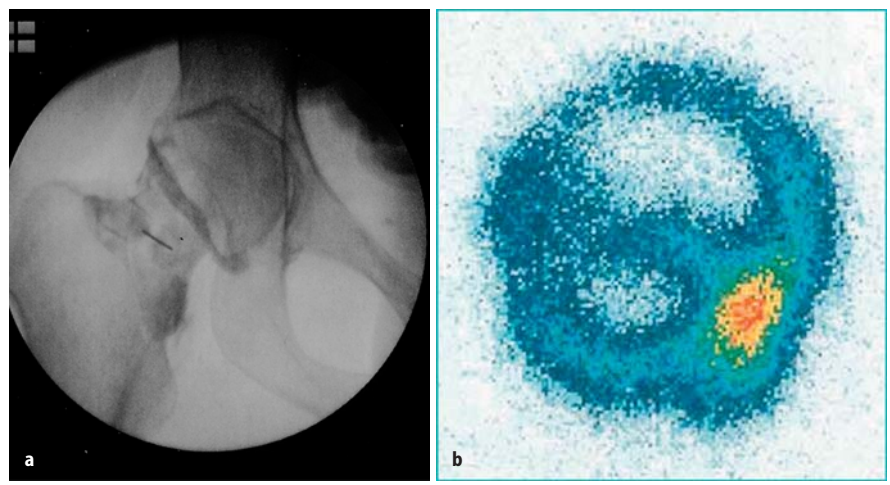

Fig. 29.7. a Arthrogram of a hip joint. The image shows the perfect and safe needle position. Beware of injecting into the joint space as usually recommended! You would risk destroying the ligamentum capitis femoris and thus cause femur head necrosis. **b** Distribution scintigram after injection of rhenium-186 colloid into the hip joint

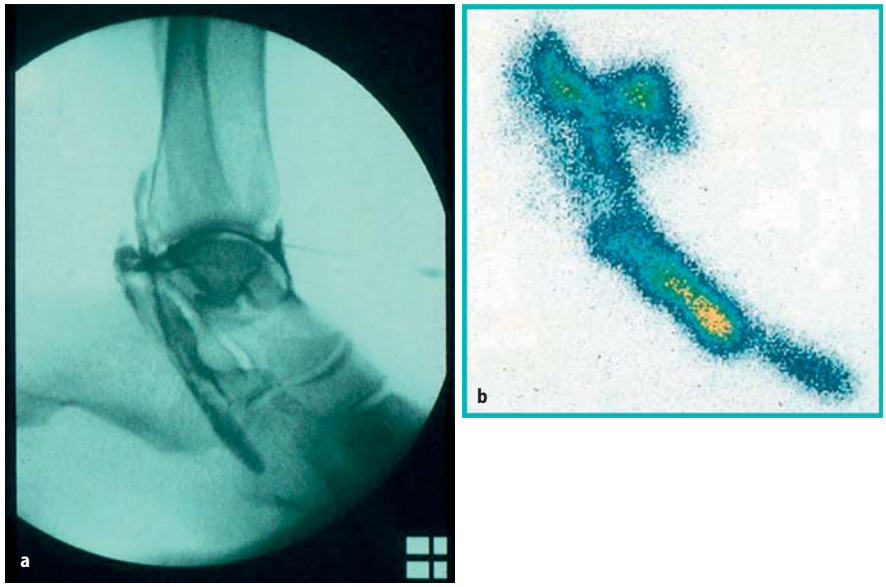

Fig. 29.8. a Arthrogram during RSO of ankle joint. Also a peroneal tenosynovialitis is involved in the psoriatic process. **b** The distribution scintigram demonstrates distribution of rhenium-186 within the ankle joint and within the peroneal sheet, indicating a good RSO effect for both structures

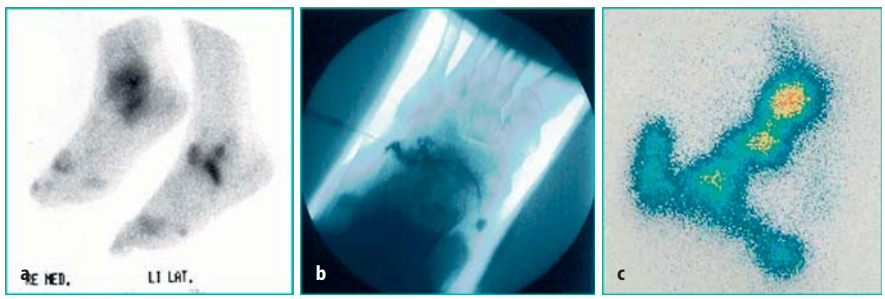

Fig. 29.9. Patient with rheumatoid arthritis was submitted for RSO of the left ankle. **a** Soft tissue scintigram detected no inflammatory involvement in the ankle but in the talonavicular, subtalar and calcaneocuboid joint. **b** Arthrogram after injection in the calcaneocuboid joint. **c** Distribution scintigram demonstrating perfect distribution in all joints marked in the diagnostic scintigram (**a**)

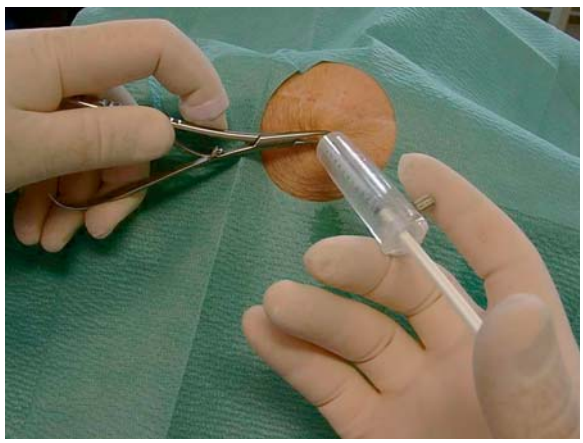

Fig. 29.10. Radiation protection for the RSO performing doctor: sterile gloves, forceps, and finger ring dosimeter (see text)

29.6.4 After RSO/Follow-up

- *A distribution scintigram* confirms the appropriate intra-articular distribution of the radiopharmaceutical. Scintigraphy is enabled after use of yttrium-90 by its *Röntgenbremsstrahlung*, after use of rhenium-186 by its gamma portion (140 keV). After the use of erbium-169 no scintigram is available.
- The joint has to be immobilized to avoid necrosis of injection channel or skin caused by reflux and to avoid transport of radioactive particles through the lymphatic vessels (leakage). A splint is required for 48 h. After removal of the splint the joint should be treated with care for 1 week, but then the patient should go into training of the joint and muscles.
- In our experience, the first *follow-up* is recommended about 6 months after RSO, or of course earlier when problems (reactive inflammation, suspected infection, swelling of Baker's cyst) occur. Clinical evaluation, possibly ultrasound scans of the joints and also checking that sufficient active joint training has been done, belong to the basic control steps.

Sometimes an effusion fluid or a Baker's cyst has to be punctured before the development of the definitive effect of RSO. Clinical examination and ultrasound scans, sometimes control of scintigraphy, should take place 12 months after treatment.

29.7 Repetition of Radiosynoviorthesis

Radiosynoviorthesis should be performed at an early stage of the disease, when cartilage damage is minimal. Reasons for non-satisfactory results of RSO might be, e.g., rapidly recurrent effusions, strongly developed thickness of synovial villus, enlargement of the joint cavity by additional cavities (Baker's cyst, bursa subdeltoidea), unfavourable Larsen stage, etc. Then a repetition of RSO (Re-RSO) may be indicated, normally not earlier than 6 months after the previous procedure (Mödder 2001a). Re-RSO of the wrist will not only treat the proximal wrist joint but will additionally reach the intercarpal compartments. And after total knee replacement the deeper layers of polyethylene disease can be attacked by Re-RSO. A new fraction is more effective than a primarily enhanced dose (Pinkert 2006) (Fig. 29.11a, b).

29.8 Results

Response rates reported in an abundant literature range from about < 60 % to > 80 % for all joints, often with greater success for rheumatoid diseases than for osteoarthritis. Most of the studies relating to RSO in the last 40 years do not fulfil the criteria of modern evidence based medicine, but recently a number of well designed trials have been carried out in order to evaluate the efficacy of RSO. In a multicentre prospective study an improvement of 78 % without a significant difference in rheumatoid arthritis or osteoarthritis was found (Farahati et al. 1999). In a prospective study on rheumatoid arthritis, Göbel et al. (1997) found a significant improvement in terms of pain and swelling after 3 years and a reduced progression of radiological destruction compared to triamcinolone. More recently two prospective multicentre studies carried out under strict evidence based medicine criteria demonstrated a significant improvement (pain, swelling, joint mobility) for erbium-169 versus placebo (Kahan et al. 2004) and after 2 years for rhenium-186 versus high dose corticosteroid (Tebib et al. 2004).

In a recent study, Jahangier et al. (2005) drew unfavourable conclusions about the performance of RSO with yttrium-90. But it could be demonstrated that their conclusions were wrong because the results in fact provided evidence for the efficacy of RSO with yttrium-90 (Kampen and Czech 2006; Mödder and Langer 2006).

Kresnik et al. (2002) investigated the clinical outcome of radiosynoviorthesis in a meta-analysis including 2,190 treated joints. They found an overall response rate of 72.5 ± 17 %. In rheumatoid arthritis RSO was successful in 66.7 ± 15.4 %. There was a difference according to the Steinbrocker stages (Steinbrocker I: 72.8 ± 12.3 %; Steinbrocker II: 64 ± 17.3 %; Steinbrocker III and IV: 52.4 ± 23.6 %). The response rate in osteoarthritis was 56 ± 11 %, with better results in the case of

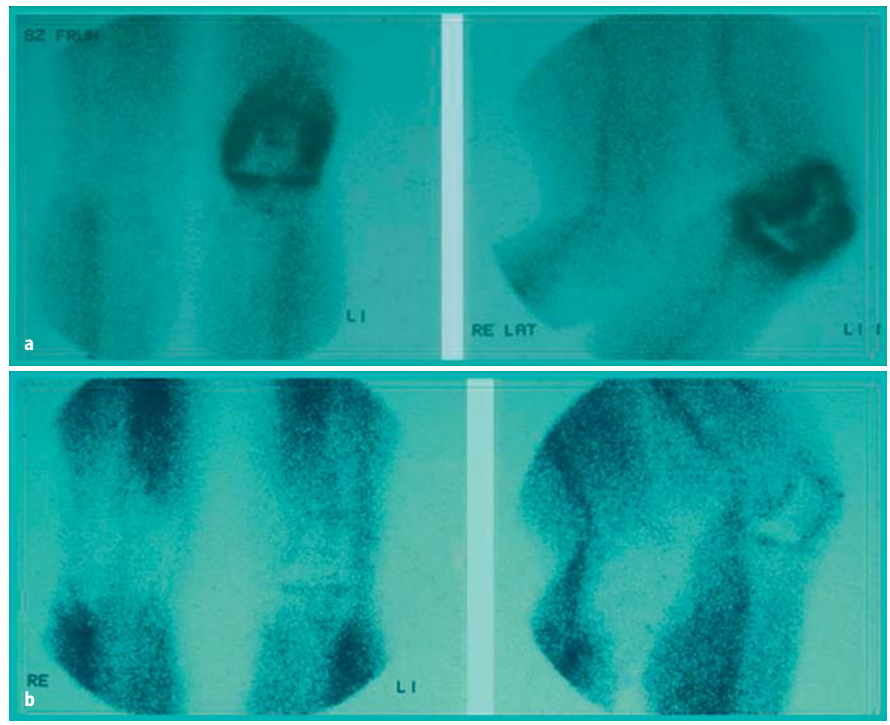

Fig. 29.11. a Prior to RSO: left knee joint with polyethylene disease, pain and recurrent effusions. **b** After RSO: improvement with regard to symptoms and scintigraphic findings

minimal radiological changes. Improvement in haemophilia and Willebrand's disease was 91 ± 4.3 %, and in pigmented villonodular synovitis it was 77.3 ± 25.3 %.

The conclusion of this study was that radiosynoviorthesis provides better results in rheumatoid arthritis than in osteoarthritis. Minimal or moderate changes according to Steinbrocker stages I and II respond better to radionuclide therapy than do stages III and IV. Deformed or unstable joints might fail treatment and therefore surgical interventions should be considered. Close cooperation with orthopaedists and rheumatologists is necessary in the consideration of RSO for each patient to ensure optimal medical care.

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