Serious complications after radiosynoviorthesis

Survey on frequency and treatment modalities

Gravierende Komplikationen nach Radiosynoviorthese: Überblick zu Häufigkeit und therapeutischen Optionen

W. U. Kampen[1], E. Matis[1], N. Czech[1], Z. Soti[1], S. Gratz[2], E. Henze[1]
[1]Clinic of Nuclear Medicine (Director: Prof. Dr. E.Henze), University Hospital Schleswig-Holstein, Campus Kiel
[2]Practice for Radiology and Nuclear Medicine, Stuttgart, Germany

Keywords
Radiosynoviorthesis, synovitis, necrosis, thrombosis, infection

Summary
Aim: Radiosynoviorthesis using intraarticular injection of beta-emitting radiocolloids is increasingly performed throughout Europe in patients with inflammatory joint disease. It is a cost-effective and safe treatment, local complications are very rare with only eight cases mentioned in the literature so far. No recommendations for therapy of tissue necrosis, infection or thromboembolism after radiosynoviorthesis are available. **Methods:** Using a standardized questionary, 260 nuclear medicine physicians and 20 medical liability insurances were asked for the kind and frequency of complications after radiosynoviorthesis between 1998 and 2003. The survey was terminated after nine months with a response of only 25.7%. **Results:** A total of 53 severe complications were documented (28 necroses, 12 thromboses, 13 joint infections). Eight other complications were seen but difficult to correlate directly with radiosynoviorthesis. Tissue necroses from yttrium-90 were successfully treated by surgical excision and closure of the defect. Rhenium-186-induced ulcers healed by hyperbaric oxygen therapy in two cases. Lesions from erbium-169 showed restoration by conservative treatment. Thromboembolic events happened after radiosynoviorthesis in joints of the lower limb only, mostly treated by conventional anticoagulation. Intraarticular infections showed restoration after intraarticular antibiotics in the majority of cases. **Conclusion:** Severe complications after radiosynoviorthesis seem to be rare. However, because of the low return rate, a reliable frequency cannot be calculated. Nevertheless, important advices regarding treatment concepts can be taken from our data.

Nuklearmedizin 2006; 45: 262–8

Schlüsselwörter
Radiosynoviorthese, Synovalitis, Nekrose, Thrombose, Infektion

Zusammenfassung
Die Radiosynoviorthese (RSO) mittels intraartikulärer Injektion kolloidaler Betastrahler wird zunehmend als Lokaltherapie der Arthritis angewandt. Schwere Komplikationen (z. B. Weichteilnekrose, Infekt, Thrombose) sind sehr selten. Acht Fälle sind dokumentiert, Erfahrungen bei der Behandlung sind nicht verfügbar. **Ziel** war es, die Häufigkeit der Komplikationen abzuschätzen und eine möglichst große Fallzahl mit den Therapien zu dokumentieren. **Methode:** 260 Nuklearmediziner und 20 Versicherungsgesellschaften wurden nach Häufigkeit und Art der Komplikationen der Jahre 1998 bis 2003 befragt. Die Erhebung wurde nach neun Monaten bei einer Rücklaufquote von 25,7% beendet. **Ergebnisse:** Insgesamt wurden 53 gravierende Komplikationen dokumentiert: 28 Weichteilnekrosen, 12 Thrombosen und 13 Gelenkinfekte. Acht weitere Fälle waren kausal nicht auf die RSO zurückzuführen. Gewebenekrosen durch ^{90}Y wurden durch chirurgische Resektion mit Defektdeckung erfolgreich behandelt. Ulzerationen durch ^{186}Re konnten in zwei Fällen mit hyperbarem Sauerstoff therapiert werden, Läsionen durch ^{169}Er heilten häufig unter konservativer Therapie ab. Thrombosen traten nur nach posttherapeutischer Immobilisierung von Gelenken der unteren Extremität auf und wurden konventionell durch Antikoagulation behandelt. Gelenkinfekte waren häufig nur mit intraartikulärer Antibiose beherrschbar. **Schlussfolgerung:** Die Rate schwerer Komplikationen nach RSO erscheint sehr niedrig; eine genaue Angabe der Häufigkeit ist aufgrund der geringen Rücklaufquote und der vermutlich hohen Dunkelziffer unmöglich. Dennoch erlaubt diese Dokumentation der bislang größten Fallzahl wichtige Rückschlüsse auf therapeutische Optionen.

More than fifty years ago intracavitary treatment of inflammatory-rheumatic joint disease using intraarticular injection of colloidal beta-emitters was developed (9). The term radiosynoviorthesis (RSO) was introduced in 1968 (6). RSO is increasingly applied throughout Europe, reaching a stable number of approx. 63 000 treatments per year 2001 to 2003[1].

Three beta-emitting radiopharmaceuticals, Erbium-169-, Rhenium-168- and Yttrium-90-colloid are approved in the EU for radiosynoviorthesis. Except for Rhenium-186, which emits an additional gamma-radiation, all radionuclides are pure beta-emitters with a tissue penetration depth of a few mm depending on their kinetic energies. To avoid radiation damage to other diarthrodial tissues, ^{90}Y with its maximum beta energy of approx. 2.2 MeV should be used for treatment of the knee joint only, ^{186}Re in mid-sized joints and ^{169}Er with its low energy of 340 keV is administered to small finger and toe joints. Because of the different joint sizes, the activity to be injected in a respective joint is recommended in both national and international guidelines (5, 8) (Tab. 1).

After intraarticular injection, the radiocolloids are phagocytized by the synovial lining cells. Most of the kinetic energy is deposited within a few mm to one cm of the synovium. A reduction in volume of the synovial folds and finally their fibrinoid necrosis together with a marked reduction of the inflammatory pannus is seen within a few weeks (20). Thus, a significant reduction of pain and joint effusion is achieved because of a marked decrease in secretory activity (19).

Serious local complications after RSO are very rare and, thus, literature data are hardly available. Superficial skin or needle track ulceration may occur if drops of the radionuclide flush back out of the needle during retraction from the joint. This is normally avoided by flushing the needle with corticosteroids or saline solution prior to retraction. Necrosis of juxtaarticular tissues may result from an incorrect, paraarticular injection. Intraarticular infection is another possible complication after arthrocentesis and finally, thromboembolic complications may happen due to the man-

[1] Information from CIS bio international and Amersham Buchler as the only two supplier of RSO radionuclides in Europe.

Received: May 30, 2006; in revised form: September 25, 2006

datory immobilization of the treated joint after radiosynoviorthesis.

Due to the lack of data and recommendations for treatment, we conducted a survey on frequency and type of the mentioned severe complications seen in Germany between 1998 and 2003. Using a standardized questionary, the type of therapy and the clinical course in those cases was additionally evaluated.

Tab. 1
Radionuclides and activities used for radiation synovectomy (5)

parameter	Erbium-169	Rhenium-186	Yttrium-90
physical half life (d)	9.5	3.7	2.7
radiation type	β	β and γ	β
max. β-energy (MeV)	0.34	0.98	2.26
γ-energy (keV)	---	137	---
mean particle size (nm)	approx. 10	5-10	approx. 10
tissue range (mm), mean/max.	0.3/0.7	1.2/3.6	3.6/11.0
joints to be treated	finger and toe joints	shoulder, elbow, wrist, hip, ankle, subtalar joint	knee
activities (MBq)	10-40	37-185	185-222

Material, methods

A standardized questionary was sent to both 260 nuclear medicine physicians performing radiosynoviorthesis throughout Germany and 20 insurance companies engaged in medical liability.

Type and number of complications were asked (e. g. necrosis, infection, thrombosis or others) documented between 1998 and 2003. Biographical data of the respective patient, the joint and informations on the application process (e. g. injection under fluoroscopy or ultrasound-guided, pretherapeutic sonography, arthrography, MRI or X-ray) were collected. We asked for the radionuclide and its injected activity, the use of contrast media and both method and extent of immobilization after treatment. Finally, specific features of the patient like varicosis, coagulopathy, preexisting infections or any joint surgery, diabetes or a Baker's cyst should be documented.

In a second part of the questionary, important questions referred to the onset of symptoms, the type of therapy that was chosen to treat the respective complication, the clinical course and the final result.

Results

The survey was terminated after nine months with an over-all response of only 25.7%. A total of 61 responses from 260 physicians included 38 answers with 52 reports on complications after radiosynoviorthesis. 23 collegues never saw any side-effects. In three responses obtained from 20 insurance companies, nine complications were documented. Eight companies have had no reports in this respect (Tab. 2). Any repeated entries were excluded as far as possible this could be noticed from the data. Thus, a total of 61 complications were documented.

The most serious complications consisted of 28 necroses, 13 intraarticular infections and 12 thromboses (Tab. 3). Eight other minor complications were reported: Two cases of a transient effusion and a restricted movement in another patient with no need for further treatment since all these disorders were self-limiting. One case of a carpal tunnel syndrome, one transient fibular nerve paresis and one Sudeck's dystrophia were debatable due to a too tight bandage and were not strictly related to the RSO. One radiogenic dermatitis was probably attributed to a long duration of fluoroscopy in a seriously mutilated joint. One case of cystoid ostitis multiplex during follow-up could not be related to RSO.

A clinical course of a severe tissue necrosis is documented in Figure 1. A circumscript redness appeared at the medial aspect of the knee 1.5 weeks after injection of 165 MBq ^{90}Y-colloid and progressed to a deep and painful necrosis five weeks after RSO. The conventional lateral approach was used for injection but probably with a penetration of the needle through the suprapatellar recessus into the medial joint capsule. Several surgical debridements and 40 sessions of hyperbaric oxygen therapy were performed but did not yield satisfying results. Granulation tissue was noticed from three to four months after injection but the defect was not closed by conventional treatment. Six months after RSO, the wound decreased in inflammatory activity but increasing hypersensitivity of the surrounding skin was noted. The patient agreed to surgical excision not until two years after RSO. The defect showed scarred closure three months after surgery.

A focal skin necrosis and joint swelling after injection of 15 MBq ^{169}Er-colloid in a proximal interphalangeal joint is shown in Figure 2a. A complete restoration without specific treatment was noted within nine months. Figure 2b demonstrates a rare case of scarry healing of a tissue necrosis from ^{90}Y one year after RSO of a knee joint but without any further treatment.

Discussion

Local complications after radiosynoviorthesis are very rare. A transient radiogenic effusion is seen in 2% of patients (10). This is frequently self-limiting and can be

Tab. 2
Response rates nine months after mailing of the questionnaires. The intermediate column shows the number of complications, reported in 38 answers of NMP and in 3 answers of IC.

consignees	n	respose rate [%]	complications	
			yes	no
nuclear medicine physicians	260	61 [23.5%]	38 (52)	23
insurance companies	20	11 [55%]	3 (9)	8
total	280	72 [25.7%]	41 (61)	31

Tab. 3 Documented cases of complications

complication	joint	diagnosis	radionuclide, activity	RSO	documentation	particularities	onset of symptomes	treatment, result
necrosis (n = 28)	knee	others*	^{90}Y, 222 MBq	inpatient	1	superficial joint replacement prior to RSO	8 weeks	conservative, n.d.
			^{90}Y, 222 MBq	under flouroscopy, outpatient	1,3	state after several arthroscopy and RSO	n.d.	conservative, ad integrum
			^{90}Y, n.d.	n.d.	1	total joint replacement	n.d.	surgical, n.d.
		osteoarthritis	^{90}Y, 180 MBq	under flouroscopy, outpatient	1	n.d.	3 weeks	conservative, n.d
		others*	^{90}Y, 37 MBq	ultrasound guided	2	n.d.	1 week	conservative; surgical, ad integrum
		n.d.	^{90}Y, 185 MBq	n.d.	n.d.	no strict immobilization	n.d.	conservative, ad integrum
		n.d.	^{90}Y, n.d.	n.d.	n.d.	no compression of needle track	n.d.	conservative; surgical, partly spontaneous healing
		others*	^{90}Y, 185 MBq	under flouroscopy, outpatient	1	no strict immobilization	2 weeks	surgical, scar formation
		n.d.	^{90}Y, 165 MBq	outpatient	1	n.d.	1–2 weeks	conservative; HBO; surgical, scar formation
		others*	^{90}Y, 185 MBq	inpatient	1	state after arthroscopy; no immobilization	8 weeks	surgical, ad integrum
		rheumatoid arthritis	^{90}Y, 185 MBq	inpatient	1	no immobilization	8 weeks	surgical, ad integrum
		osteoarthritis	^{90}Y, 200 MBq	outpatient	1	n.d.	2 weeks	surical;debridement, ad integrum
			^{90}Y, 185 MBq	outpatient	1	n.d.	8 days	conservative, scar formation
			^{90}Y, 222 MBq	outpatient	1,2,3	Baker's cyst	8 weeks	surgical, ad integrum
		n.d.	^{90}Y, 259 MBq	under fluoroscopy, outpatient	1,2	n.d.	10 days	conservative, scar formation
		n.d.	^{90}Y, 185 MBq	n.d.	n.d.	n.d.	5 days	conservative, n.d.
		rheumatoid arthritis	^{90}Y, 185 MBq	outpatient	1	probably no immobilization	1 week	surgical, n.d.
			^{90}Y, n.d.	n.d.	1	n.d.	n.d.	conservative, ad integrum
	ankle	others*	^{186}Re, n.d.	under fluoroscopy, inpatient	1	n.d.	2 weeks	surgical, ad integrum
		n.d.	^{186}Re, n.d.	n.d.	n.d.	no strict immobilization	n.d.	conservative; HBO ad integrum
		rheumatoid arthritis	^{90}Y, 148 MBq	under fluoroscopy, inpatient	1	state after several RSO using ^{169}Er; no immobilization	8 weeks	surgical, improved, not ad integrum
	shoulder	rheumatoid arthritis	^{186}Re, 74 MBq	under flouroscopy, outpatient	1,3	highly inflammatory, insufficient pharmacotherapy	2 months	conservative; surgical; debridement, ad integrum
	PIP 3	n.d.	^{169}Er, 15 MBq	n.d.	n.d.	n.d.	2 weeks	n.d.
	MCP I	psoriatic arthritis	^{186}Re, 37 MBq	under flouroscopy, outpatient	3	no immobilization	8 weeks	debridement; HBO, scar formation; restricted movement
	finger (4x)	n.d.	^{169}Er, n.d.	n.d.	n.d.	n.d.	n.d.	n.d.,spontaneous healing

avoided in most cases by intraarticular co-injection of a corticosteroid (11).

More serious complications are skin and needle track ulceration or even necrosis of periarticular tissues. Savaser et al. report on one needle track ulceration after radiation synovectomy of an ankle joint with ^{186}Re (22) which showed healing by scar formation after a few weeks without any further treatment. A very low frequency of two necroses out of 11 000 treatments was reported by Kolarz and Thumb 1982 (17). However, the true number of radionecroses is probably higher and is not documented. The use of an inappropriate radionuclide is another possible reason for a radionecrosis and was demonstrated after injection of ^{90}Y into an ankle joint, which would normally be

Tab. 3 Continued

complication	joint	diagnosis	radionuclide, activity	RSO	documentation	particularities	onset of symptomes	treatment, result
infection (n=13)	knee	rheumatoid arthritis	^{90}Y, 245 MBq	outpatient	1	total joint prosthesis	17 days	antibiotics; surgical, n.d.
		osteoarthritis	^{90}Y, 250 MBq	under flouroscopy, outpatient	3	prior RSO	3 days	antibiotics; surgical, ad integrum
		osteoarthritis, others*	^{90}Y, 177 MBq	under flouroscopy, outpatient	1,3	Baker's cyst; state after Borrelia infection	5 days	surgical, n.d.
		others*	^{90}Y, 185 MBq	under flouroscopy, outpatient	1	state after synovectomy and two RSO	3 weeks	antibiotics; joint lavage, ad integrum
		osteoarthritis	^{90}Y, 185 MBq	under fluoroscopy	1	n.d.	hours	antibiotics; endoscopic synovectomy, total joint prosthesis after 4 weeks
			^{90}Y, 185 MBq	under fluoroscopy	1	n.d.	1 day	aspiration; endoscopic joint lavage, ad integrum
			^{90}Y, 185 MBq	under fluoroscopy	1	n.d.	hours	aspiration; endoscopic joint lavage, ad integrum
		n.d.	^{90}Y, 185 MBq	n.d.	n.d.	total joint prosthesis	8 days	antibiotics; surgical, ad integrum
		rheumatoid arthritis	^{90}Y, 185 MBq	under fluoroscopy	1,2	n.d.	-5 days	antibiotics; surgical, scar fomation
	wrist	rheumatoid arthritis	^{186}Re, 70 MBq	under flouroscopy, outpatient	1	n.d.	6 days	conservative; surgical; debridement; synovectomy, severly restricted movement
	subtalar	n.d.	^{186}Re, n.d.	n.d.	n.d.	n.d.	n.d.	n.d.
	ankle	rheumatoid arthritis	^{186}Re, n.d.	under flouroscopy, outpatient	1	n.d.	2 days	antibiotics, ad integrum
	shoulder	osteoarthritis	^{186}Re, 60 MBq	under fluoroscopy	1,3	n.d.	2-3 days	antibiotics; surgical ad integrum
thrombosis (n = 12)	knee	osteoarthritis	^{90}Y, 185 MBq	under flouroscopy, outpatient	1	post-traumatic osteo-arthritis	1 week	anticoagulation, ad integrum
		others*	^{90}Y, 185 MBq	under flouroscopy, outpatient	1,3	n.d.	22 days	n.d.
		osteoarthritis, others*	^{90}Y, 148, 222 MBq	outpatient	1,3	Baker's cyst	7 weeks	anticoagulation, ad integrum
			^{90}Y, 185 MBq	under flouroscopy, outpatient	1	varicosis both legs	1-2 days	anticoagulation, n.d.
			^{90}Y, 250 MBq	under flouroscopy, outpatient	3	massive obesity	3 days	anticoagulation ,n.d.
		others*	^{90}Y, 190 MBq	under fluoroscopy	1,3	massive joint effusion, no prophylactic anticoa-gulation	1 day	only partial restitution, suspected paresis
		n.d.	^{90}Y, 185 MBq	n.d.	n.d.	known coagulopathy	4 days	anticoagulation ad integrum
		n.d.	^{90}Y, n.d.	under fluoroscopy	1	no prophylactic anticoa-gulation	n.d.	n.d.
		osteoarthritis	^{90}Y, 222 MBq	under fluoroscopy	1,2	n.d.	1-2 days	anticoagulation, ad integrum
			^{90}Y, 222 MBq	under fluoroscopy	1,2	n.d.	1-3 days	anticoagulation,ad integrum
		n.d.	^{90}Y, 259 MBq	n.d.	n.d.	n.d.	n.d.	n.d.
	knee hip	n.d.	^{90}Y, 185 MBq ^{186}Re, n.d.	n.d.	1	no prophylactic anticoa-gulation	n.d.	anticoagulation, ad integrum

n.d.: not determined; *reactive arthritis, peripheral joint involvement in ankylosing spondylitis, chronic synovitis after surgery, etc
documentation: 1: distribution scan after RSO; 2: photo documentation; 3: other imaging modalities (ultrasound, arthrography, MRI, x-ray, etc.)

treated with ^{186}Re (21). Therapy was performed by surgical excision of the necrotic tissue; closure was achieved with a fasciocutaneous lap. In a retrospective study on 83 RSO in 45 patients, one local „skin burn lesion" was described (15) and one skin necrosis was seen at the site of injection of ^{90}Y-colloid in a patient with severe bone destruction (18). However, no details are mentioned regarding treatment or the clinical course.

We documented a total of 28 necroses with the majority of Yttrium-90-induced le-

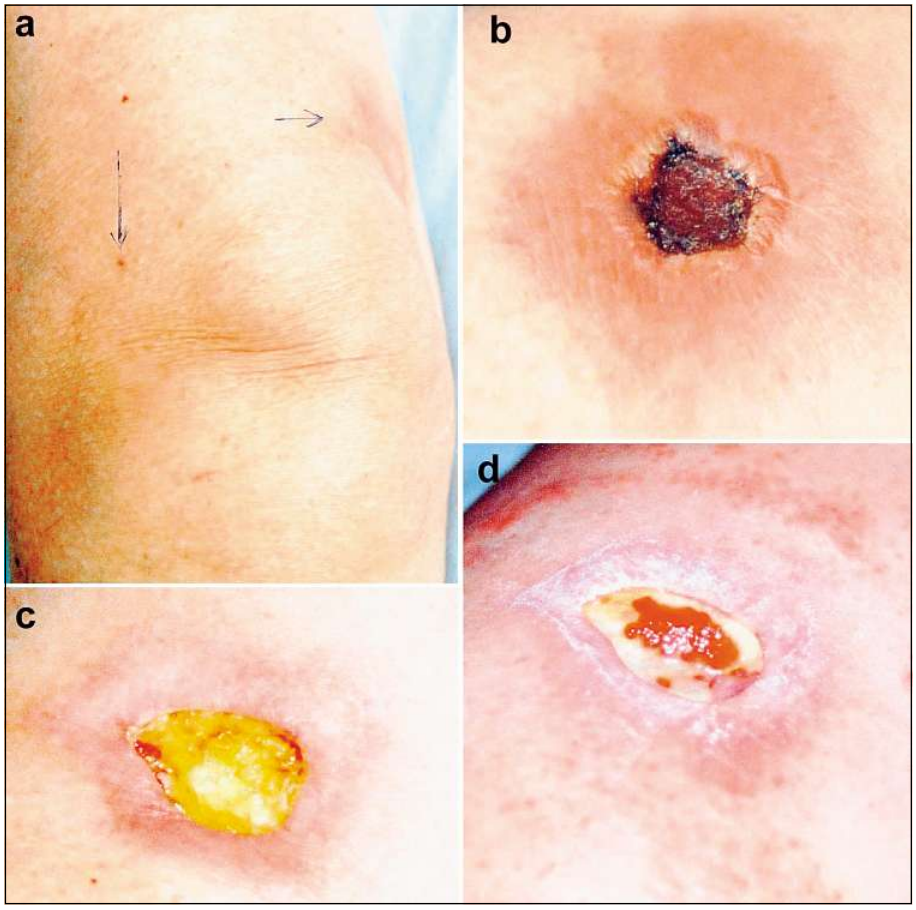

Fig. 1 Clinical course of a necrosis at the medial aspect of a knee joint after injection of 165 MBq Yttrium-90
a) initial redness 1.5 weeks after injection (horizontal arrow); vertical arrow: injection site on the lateral part of the supra-patellar bursa
b) necrosis (diameter 1.8 cm) with inflammatory margin five weeks after RSO
c) 12 weeks after RSO, after debridement and 40 sessions hyperbaric oxygen
d) approx. six months after RSO: increasing granulation and hypersensitivity of the surrounding skin

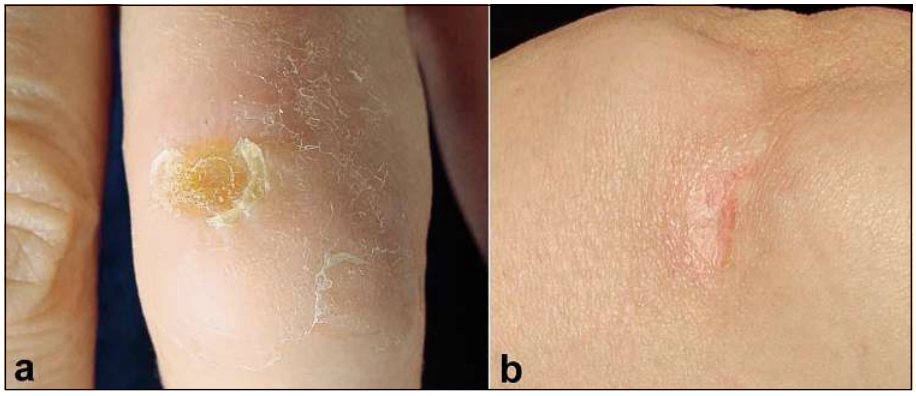

Fig. 2 Skin necrosis after RSO
a) with joint swelling of a PIP joint two weeks after injection of 15 MBq ^{169}Er
b) scar tissue at a knee joint approx. one year after spontaneous healing (^{90}Y, unknown activity)

sions in 19 cases. This is not surprising since ^{90}Y has a penetration depth up to 11 mm and is thus expected to be the most hazardous radionuclide. An inappropriate radionuclide was used in two cases, ^{90}Y in one ankle joint and ^{186}Re in one metacarpophalangeal joint. Using ^{90}Y in finger joints, two cutaneous necroses were documented (14). This urges the use of the appropriate radionuclide recommended for each joint in the guidelines for RSO. Thus, to our knowledge a total of only eight cases of local tissue damage after radiosynoviorthesis are mentioned in the literature.

Referring to the treatment of radiation-induced necroses, there is only little knowlegde from lesions seen after external beam radiation therapy. Radiation induces parenchymal stem cell and vascular damage, leading to a reduced tissue regeneration and local hypoxia, finally resulting in necrosis (25). Apart from a „wait and see" strategy, surgical treatment and hyperbaric oxygen therapy were used for treatment in those cases. For a successful surgical therapy, the damaged tissue must completely be resected and the defect is closed with well-vascularized, non-irradiated tissue. Complications are frequent and range from local dehiscence or seroma to vessel thrombosis and complete flap loss in some cases (12). In our series of documented necroses, 12 of 23 cases after application of ^{90}Y or ^{186}Re were treated surgically. Spontaneous healing of necroses from ^{90}Y or ^{186}Re was shown (Fig. 2b) but was not the normal course. Skin necroses from ^{169}Er showed spontaneous healing as far as detailed informations were available.

Hyperbaric oxygen (HBO) is reported to eradicate anaerobic bacteria and to promote re-vascularization of irradiated tissue with an increase of tissue oxygen tension (2). Success rates up to 93% were published for therapy of radiation induced oedema, ulceration and bone necrosis (25). However, all data obtained from the literature refer to soft tissue necroses caused by percutaneous radiation therapy only, the majority of studies do not comprise of a control group and thus, detailed descriptions or even guidelines for the treatment of necroses from local beta-irradiation are not available. In our data pool, hyperbaric oxygen was

used in three cases after tissue necrosis from RSO with success in two of them, both after application of ^{186}Re, whereas in one case of a necrosis caused by ^{90}Y, even 40 sessions of HBO treatment did not yield satisfying results as documented in Figure 1.

Apart from excellent improvement of osteoradionecroses after radiotherapy in patients with head and neck cancers, even soft tissue or mucous membrane necroses were shown to improve in roughly 50% in a retrospective study (4). No serious side effects of HBO therapy were noted in contrast to a literature review containing more than 2000 patients where seizures and pressure-related traumas like pneumothorax, including a few deaths were documented (27). To abstain from exclusive HBO therapy, a combined approach with a debridement of the necrotic tissue and a skin graft was successfully performed in the abovementioned study in some patients after radiotherapy of head and neck cancer (4). 20 to 30 sessions of HBO therapy, consisting of five sessions per week with 2.4 atmosphere absolute for 100 min each were followed by surgery and another 10 to 15 HBO sessions postoperatively. Due to the advantage of an additional excision of the severely damaged tissue after interstitial beta-radiation, this approach should be discussed for treatment of necroses after RSO.

The costs for HBO treatment average approximately 200 € per session. However, due to the lack of any reliable data on the number of sessions needed to treat a respective patient, every calculation or comparison with surgical therapies will remain hypothetical. Thus, HBO treatment may be applied to patients with soft tissue necroses as a complication after RSO with ^{186}Re or ^{169}Er, especially if surgery should be avoided, although detailed treatment schedules based on controlled clinical trials are not available.

It must be emphasized that only the high-energy β-radiation is responsible for any possible local skin damage. The concomitant bremsstrahlung from absorption of the β particles in the surrounding tissue does only account for a minor radiation load of the gonads. In case of ^{90}Y, which has the highest β-energy of all radionuclides used in RSO, the radiation dose for the gonads from ^{90}Y bremsstrahlung was calculated to be 1.1 µGy/MBq, corresponding to 0.000244 Gy from the maximum recommended dose of 222 MBq ^{90}Y (26).

Intraarticular infection is another possible, yet unspecific complication and only one case of a septic arthritis after repeated radiosynoviorthesis is described in the literature so far (24). In our data, 13 intraarticular infections were documented with seven of them treated by intraarticular antibiotics and additional four cases in which an endoscopic joint lavage was performed. It is known from the treatment of septic arthritis, that early and aggressive therapy is necessary to prevent severe joint damage and ankylosis. Initial parenteral antibiotics should be followed by surgical treatment if the symptoms increase within 24-48 hours (13). In other studies, early surgical therapy was recommended because of the lower intraarticular bacterial count rate and the excellent decompression after joint lavage (7). In two cases, the symptoms of joint infection were described to develop only hours after injection of the radionuclide which seems to be very unusual for primary infection. Thus, it may be speculated about a clinically silent intraarticular bacterial infection prior to RSO or a concomitant and intense radiogenic inflammation with joint effusion occasionally seen after RSO (10).

The frequency of joint empyema after arthrocentesis is estimated to be 1 : 30 000 (1). The majority of patients eligible for RSO might be at a higher risk for intraarticular infection due to systemic or local immunosuppressive pharmacotherapy like methotrexate, anti-TNFα-drugs or corticosteroids. Moreover, rheumatoid arthritis, degenerative joint disease or even a state after endoprosthetic joint replacement were described as risk factors (23). However, a concluding statement cannot be drawn from our data due to the lack of statistical significance caused by a low response rate as mentioned.

The question of a possible burst of necroses or infections due to the application of local anaesthetics (LA) prior to RSO can not be answered on the basis of our data. Only two complications, one infection and one case of restricted joint movement were reported with concomitant application of LA and a causal coherence could not be found. However, the injection of LA prior to RSO may only be useful in joints with severe bone destruction or in anxious patients but is not routinely applied.

Due to the mandatory immobilization of the treated joint, thromboembolism may occur after RSO. This holds especially true for old and immobile patients or for those with a high risk of thrombosis. However, there is no documented case of a thromboembolic complication which is definitely linked to prior radiosynoviorthesis. 12 cases of thrombosis after a total of 13 RSO treatments (one patient with RSO of hip and knee joint) of lower limb joints were documented in our survey. In six out of 12 patients, an elevated risk profile was described or no prophylactic anticoagulation was performed. The majority of eight patients was treated successfully with routine anticoagulation pharmacotherapy. A recent guideline for effective treatment of venous thromboembolic disease recommended short-term treatment with subcutaneous low molecular weight heparin or unfractionated heparin given intravenously (3).

Like after surgical interventions, early mobilization of the patient is the best prophylaxis against thromboembolism. However, a strict immobilization of the treated joint must be assured to avoid any unwanted leakage of radioactivity outside the joint cavity. In this respect, any bending of the joint seems to be more dangerous than physical upright joint load. Thus, with respect to thromboembolic prophylaxis, it seems more advisable to use a very rigid splint with which the patient is even allowed to walk and to load the treated leg instead using a more flexible splint and to rule bed rest (16).

Apart from necrosis, infection or thrombosis, eight other complications were documented in our series but were either self-limiting or were not related to radiosynoviorthesis.

Referring to the overall frequency of severe complications after RSO, a statistically reliable quantitative analysis cannot be done due to the low response rate of only 25.7% and the estimated number of unknown cases may be higher. However, we documented a total of 61 cases which is more than sevenfold the number mentioned in the literature by now.

Conclusion

Due to the experience with several treatment methods chosen for each complication, the following advices may help to decide about the further procedure in such cases:

- Early surgical excision of the necrotic tissue and closure of the defect should be aspired in case of local tissue damage from ^{90}Y.
- Hyperbaric oxygen therapy may be sufficient for ^{186}Re-induced necroses. However, a surgical treatment seems advisable, if no improvement is noted.
- Necroses from ^{169}Er will probably heal by conservative treatment.
- Intraarticular infections after RSO should be secured by immediate fluid aspiration and bacterial culture. If an initial oral antibiotic treatment does not improve the situation significantly within 24-48 hours, the joint should be treated by joint lavage or endoscopy together with the local application of intraarticular antibiotics.
- Due to the risk of thromboembolism caused by immobilization of joints of the lower limb, prophylactic anticoagulation is recommended, especially in patients with elevated risk profile.

Acknowledgement
The authors like to thank all those collegues and insurance companies who supported our survey by their honest statements and photo documentations – we wished there would have been some more.
Special thanks to Prof. Dr. Moedder, Cologne, Dr. C. Franke, Hamburg, and Dr. M. Troglauer, Wiesbaden, for their fruitful discussions.

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Correspondence to:
Priv.-Doz. Dr. med. Dipl.-Biol. Willm Uwe Kampen
Assistant Medical Director, Clinic of Nuclear Medicine
University Hospital Schleswig-Holstein, Campus Kiel
Arnold-Heller-Str. 9, 24105 Kiel, Germany
Tel: 0049 – 431 – 597 3060
Fax: 0049 – 431 – 597 3065
Mail: ukampen@nuc-med.uni-kiel.de