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Research Article

Treatment of Chronic Knee Synovitis with Radiosynoviorthesis After Failure of Surgical Interventions

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Abstract

Objective: Authors make a long-term evaluation of patients treated with radiosynoviorthesis (RSO), including patients having formerly unsuccessful surgical interventions of the knee. Aim was also, to evaluate the effectiveness of RSO after these ineffective surgical interventions.

Methods: From the patient pool of N = 205 patients: 115 had rheumatoid arthritis (RA), 17 had spondylarthritis ankylopoetica (SPA), 13 other seronegative spondylarthritis (SNSA, as arthritis psoriatica, M. Crohn, Colitis ulcerosa), 47 inflammed osteoarthritis (OA), 1 hydrops articulorum intermittens (HAI), and 1 pigmented villonodular synovitis (PVNS); respective 11 patients were with chronic synovitis following trauma. From the total of 205 patients treated there were 6 patients in radiological stage I, 107 patients in stage II, and 92 patients in stage III.

From the n = 39 patients who had surgical interventions: 14 had RA, 5 had SPA, 4 SNSA, 1 PVNS, 6 had previous trauma, and 9 had OA. Regarding the radiological grading: 15 patients had grade II and 24 patients had grade III, based on the Steinbrocker respective Kellgren and Lawrence classification. Before the radiosynoviorthesis was performed in the n = 39 patients: 22 patients had surgical synovectomy, 4 patients had chemical synovectomy, 9 patients' meniscectomy, 3 patients had operation for popliteal (Baker's) cyst, and 1 had anterior cruciate ligament (ACL)-reconstruction.

Results: From the total 205 patients treated with 90-Yttrium RSO, in the first 4-years there was a 70% "excellent/good" success rate. The excellent/good classified patients rate decreased to 65% in the 5th year. The decrease was not significant. Those 39 patients who underwent formerly surgical interventions, the success rate in the 5th year was between 68-70%. There was no significant difference between the two groups: so, even that several patients were treated earlier with surgical interventions, the later (> 6 weeks) administered RSO was successful on long term (2-5 year).

Conclusion: For both groups (surgical intervention and not operated) the administration of the RSO was considered 65-70% effective within the first 5 years. The surgical intervention group reacted as well, there was no difference, so RSO is indicated to be applied in this group also. We analysed the long-term determinants of the effectiveness of the RSO, and we had the conclusion that the primary diagnosis (i.e. rheumatoid or other arthritides), respective the preliminary radiological staging was influencing the final results. There were no major correlations regarding the age, gender, duration of the background disease and the persistence of the synovitis, respective the intra-articular number of punctions and surgical interventions in the joints.

Keywords: *Radiosynoviorthesis; Yttrium-90; Chronic Synovitis; Surgical Synovectomy*

Introduction

The aim of this study was to assess the long-term effectiveness of radiosynoviorthesis using Yttrium-90 colloid in knee, including patients who formerly underwent unsuccessful surgical intervention. Surgical and RSO methodologies being used for the resolution of painful synovitis and recurrent joint effusion of knee joints in RA, SPA, SNSA, OA, respective other degenerative and painful arthropathies. The initial concept of treating inflamed joint with radiation dates back to 1924, Ischido C [1]. Intra-articular radiocolloids were first time applied in clinical setting by Fellinger and Schmidt in 1952 [2]. However, the first clinical trial looking for the efficacy of intra-articular administration of radioactive agents was performed by Ansell., *et al*. in 1963, when colloidal gold-198 was administered to treat chronic knee effusion [3]. Beginning from the 70s several radiocolloids entered in daily practical use, like 90-Yttrium silicate/citrate, 186-Rhenium sulphide, 169-Erbium citrate, later 166-Holmium phytate by Szentesi., *et al*. [4-7]. Phosphate-32 is used mainly in developing countries, being cost effective. (8) Related to these radiopharmaceuticals several clinical studies and reviews were published, by Kampen., *et al*, Deutsch., *et al*, Knut., *et al*. [9-11], respective systematic reviews and meta-analyses made by Jones, Kresnik, Heuft-Dorenbosch., *et al*. [12-14]. The effects of radiosynoviorthesis on long-term (5-8-10 years) were published by Kampen [15] and Szentesi [16]. Radionuclide treatment guidelines started to appear from 2003 [17-19].

The main objective of the radiosynoviorthesis being the introduction of beta-ionizing radiocolloids intra-articularly (i. a.) and in this way facilitating the ablation of the inflamed synovial membrane, resulting in subsequent fibrosis and reduction of joint effusion [20]. The ideal agents for radiation synovectomy are around 1-10 μm, and in this way are enough small to be phagocytized, but enough big not to leak out from the cavity before emitting the radioactive dose necessary for the targeted membranes [21]. In addition, the radiocolloid particles should be bio-degradable, and the biological half-life should be relatively short to prevent leakage and necrosis [22].

Radiologic and surgical/arthroscopic synovectomy is mainly indicated for rheumatoid arthritis (RA), however other arthritides can be treated also [23-25]. Rheumatoid arthritis is a chronic autoimmune disease that is characterized by symmetric erosive synovitis, affecting peripheral joints of the fingers and foots [26]. Current treatment for RA is based on pharmacological approach (DMARDs, biologicals), physical therapy and patient education [27]. Synovectomy through the use of radiation and surgical/arthroscopic intervention are ultimate modalities in the treatment of chronic, therapy-resistant, persistent joint inflammations. Before these modalities, intra-articular injection of glucocorticoids is applied, respective the patient should be resistant to DMARDs/biologicals. After these options, it is decided the intervention with surgical/arthroscopic or radiocolloid-based synovectomy. These methodologies relieve joint pain, improve joint flexibility and reduce effusion in about 60-80% of cases [28,29]. In case of chronic persistent synovitis the synovial membrane is inflamed, producing effusion, invades the adjacent tissues, and pannus is developed. In case the process advances, a severe destruction of the cartilage and bone results. The objective of the treatments is to stop or slow-down this process. To have an effect on these, different interventions are applied, like glucocorticoid injections, chemical (osmic acid) synovectomy, arthroscopy, radiosynoviorthesis or surgical "open" synovectomy [30]. Deciding which methodology is the best for the patient depends on several factors, like the diagnosis and activity of the basic disease, the radiological status of the joint, other comorbidities (i.e. coagulation disorders), or the presence of other risk-factors (i.e. deep venous thrombosis) [31]. In general, radiosynoviorthesis is indicated for chronic persistent joint inflammation, when it is outstanding for more than 4-6 months, is not reacting to the general administered systemic or local treatments, inclusive the i.a. administration of 3-6 long lasting glucocorticoid injections. The patient is not under 20 years-old and is not pregnant. We have to take in consideration other contraindications like severe cartilage and bone destruction, (as stated in EANM, Hungarian and German Guidelines), respective local joint infection (septic arthritis, severe joint instability, communicating Baker's cyst) [17-19]. More and more reports appear regarding the combined application of the RSO and arthroscopy, considering the combination more effective than the other methods and superior in terms of patient satisfaction [32-34]. Sometimes the RSO is administered first, but the synovium is not reactive due to different reasons, and in this case arthroscopic or surgical synovectomy is performed as a second step [35,36]. However, these two interventions can complete each other, and the RSO can be applied before and after the surgical/arthroscopic synovectomy.

To answer the question if RSO is effective after the unsuccessful surgical interventions, we analysed the 205 patients treated with RSO, inclusive the 39 patients who underwent former surgical interventions, and the additional factors which could have an influential effect.

Materials and Methods

Patients and ethical considerations

The study was approved by the Research and Ethics Committee of the Polyclinic of the Hospitaler Brothers of St. John in God, Semmelweis University Budapest on 2nd of September 2008, confirmed on the 27th of March 2019. All procedures performed in the study involving human participation were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration, and its later amendments. Informed consent was obtained from all individuals participants in the study. The medical records of the patients are filed in the Polyclinic of the Hospitaler Brothers of St. John. Patients data were collected from the period from April 1995 to July 2014 inclusive. All patients had chronic, painful, recurrent synovitis of the knee, despite 6 months of conservative therapy consisting of NSAIDs, DMARDs, biologicals and intra-articular steroid injections. Patients were divided in groups based on initial diagnosis, age, former therapies (i.e. surgical interventions). In addition to the former open synovectomy, patients were evaluated for the increase of activity in the clinical signs, ultrasound, plain radiographies, and via scintigraphy. Exclusion criteria were younger than 20 years of age, pregnancy, breastfeeding, infectious arthritis, severe knee instability, advanced degenerative joint findings. Knee score (see attached) and visual analogue scale (VAS) was completed for patient and physician based setting, and pre-interventional ultrasound had to exclude popliteal cyst.

Surgical synovectomy

Was performed in the Orthopedic Department of the Polyclinic of the Hospitaler Brothers of St. John in God, Semmelweis University, in general or spinal/epidural anaesthesia. Synovial biopsy was performed during the operation, to confirm the diagnosis and to analyse the degree of inflammation. Synovial tissues with inflamed appearance were removed.

Methodology of radiosynoviorthesis

The knee joint of the lying patient was punctured, in case of effusion this was drained prior to the injection of 188-222 MBq 90 Yttrium and a mixture of 40 mg triamcinolone-acetonid + 1ml lidocaine. Slowly withdrawing the needle, it was flushed with this mixture. The outside point of the puncture was compressed with a sterile tampon and the joint carefully moved to improve tracer distribution in the joint capsule. To avoid extra-articular radionuclide leakage, the joint finally was immobilized for 48 hours with a bandage and the patient confined to bed. After taking off the bandage, its contamination with activity was measured in all patients. Before the treatment in all patients' knee-joint-scintigraphy (with 99m-Tc-pertechnetate). For the evaluation of the effectiveness of the radiosynovectomy the treating physician had to fill in the point system for objective assessment (Table 3) and the patients the point system for subjective assessment of pain (VAS). (Table 4) In some cases, a control knee-joint scintigraphy has been performed to demonstrate the effectiveness after radiosynovectomy after 5 years.

Radiological evaluation

In evaluating the radiological stage, for the patients with RA the classification according to Steinbrocker [37], and for other synovitis (i.e. OA) according to Kellgren-Lawrence [38,39] was used (Table 1, 2).

Scintigraphy assessment

In all patients included into this study soft tissue scintigraphy with 99m-Technetium-pertechnetate of both knee joints was performed before the radiosynoviorthesis to confirm acute synovitis of the affected joint. After intravenous injection of 100-150 MBq Tc-99m-pertechetate one day before the RSO we perform planar images within 10-20 minutes after injection upon the knees in AP projection and

Stage I	Juxta-articular osteoporosis and soft tissue swelling (minimal damage)
Stage II	Destruction, loss of joint space, erosions, cysts
Stage III	Erosions and joint space narrowing or subluxation
Stage IV	Total joint destruction, either lysis or ankylosis (severe damage)

Table 1: *Steinbrocker radiologic stage classification of rheumatoid arthritis (RA).*

Grade 0 (none)	Absence of x-ray changes of osteoarthritis
Grade 1 (doubtful)	Minute osteophyte, positive joint space narrowing (doubtful significance)
Grade 2 (minimal)	Definite osteophyte formation, unimpaired joint space narrowing
Grade 3 (moderate)	Multiple osteophytes, moderate joint space narrowing, sclerosis and possible bony deformity
Grade 4 (severe)	Large osteophytes, marked joint space narrowing, severe sclerosis and definite bony deformity

Table 2: *Grading of morphological joint changes for radiographic osteoarthritis (OA) after the classification of Kellgren-Lawrence.*

another lateral image about the involved knee. Processing of the images: two regions of interest (ROIs) were targeted on the AP images for both knees. One is on the knee, the other is under the knee, as background for each leg. We calculated the synovial index for both knees, according to the count numbers within the same sized ROIs. The lateral images are only to predict an eventual Baker's cyst, which is in contact with the knee. This does not replace the ultrasound examination but can demonstrate the communication grade with the knee joint.

Regarding the scintigraphy assessment 1 day before RSO with Tc-99m-pertechnetate, it does not figure in the guidelines but according to the normal biodistribution of the injected Tc-99m-pertechnetate, the uptake is only in the muscles of the lower limbs. If we see an uptake in the knees its pathological. Therefore, the normal value of the synovial index is maximum 1 or less. According to the ultrasound results sometimes the value of the synovial index can be low as 1.10 – 1.20. Usually in these cases there is an aseptic liquid accumulation in the knee. If there are no laboratory evidences about the synovial liquid, we still can demonstrate an eventual infection with our examination. If the synovial index is over 2 there is a severe infection and can be a preview for the rheumatologist, that the RSO may be done only later. These are the main reasons for performing this examination before the RSO. In our Hospital we are performing this examination for more than 25 years and the rheumatologists require this method. It's simple to perform, but helps in the RSO decision, better than a 3-phase bone scintigraphy. Seventy-two hours after the RSO, we perform an additional gamma camera examination with the injected isotope for each patient, mainly for the eventual leakage investigation.

Sonographic assessment

Mainly for the exclusion of Baker's cyst, this being a contraindication and a place of leakage and necrosis. Also, the structure and the thickness of the synovial membranes can be evaluated before and after the treatments. We measure the synovial thickness in the following locations: in the midline, in the condylus of medial femur, and in the condylus of lateral femur.

Statistical analysis

SPSS for Windows version 5.0 software (SSPS Inc., Chicago Ill., USA) was used for statistical analysis. with two-sided Student *t* test, correlation test, respective multifactorial regression analysis, and $p < 0.05$ was considered statistically significant.

Clinical scoring system

For the evaluation of the effectiveness of 90-Yttrium-synovectomy, a points system (Table 3, 4, 5) was developed for the objective assessment, and all patients received a questionnaire for the subjective assessment of pain; representing the clinical changes compared to the situation before the intervention.

The evaluation of the efficacy was done 6 months, 1-2-3 and 4-5 years after the radiopharmaceutical therapy by the physician. Patients were asked to rank their subjective assessment of pain alteration compared to their pre-treatment status in a 10-cm visual analogue scale (VAS). In the physician's questionnaire the joint pain scale was evaluated for each patient twice (at rest and under lead); also, other symptoms such as changes in joint movements, walking capacity, and the number of arthrocentesis before the RSO were reported. In this way the total objective (physician) and subjective (patient) assessment of 90-Yttrium colloid intervention was found to be 31 points, and +4 points from VAS self-evaluation of the patient. The maximal point to be obtained was: 35 points. The grading was according to the obtained: excellent (no complains) = 29-35 points, good (major improvement) = 22-28 points, medium (moderate improvement) = 15-21, weak (minor improvement) = 8-12, bad (no change/worsening) = 0-7 points. The effectiveness of the intervention was analysed using this scoring system, comparing the obtained values to the initial (baseline/pre-treatment) values.

Parameters	Objective	Points	Parameters	Objectives	Points
Decrease of joint circumference (cm)	>7 cm, no more swelling	4	Joint hyperthermia	No	1
	5.1-7.0 cm	3		Yes	0
	3.1-7.0 cm	2	Ability to walk	Yes	1
	0.1-3.0 cm	1		No	0
Improvement of joint function (flexion)	Over 20^0 total function is kept	4	Walking capacity	Unlimited	5
	15^0	3		5-10	4
	10^0	2		2-5	3
	5^0	1		1-2	2
	0^0 or worsening	0		0.5-1	
Contracture after RSO (measure of fixed flexion)	0^0/total extension	4		0-0.5	1
	1^0-5^0	3	Joint punctures post RSO (n =)	0	2
	6^0-10^0	2		1-2	1
	11^0-15^0	1		>2	0
	over ≥ 16^0-20^0	0	Surgery post RSO	no	2
Improvement of pain in load VAS 1-10 cm scale	8-10 or no pain	4		yes	0
	5-7	3			
	3-4	2			
	1-2	1			
	0 or worsening	0			
The resting and loaded pain score was taken separately – the objective maximal score is: 31.					

Table 3: *Clinical scoring system of the functional parameters.*

Subjective point number (based on VAS score)	
Excellent	4
Good	3
Medium	2
Weak/no change	1
Worsening	0

Table 4: *Subjective patient scoring system.*

Overall evaluation	
Maximal point number for radiosynoviorthesis evaluation (31+4=35)	
Excellent	29-35
Good	22-28
Medium	15-21
Weak	8-14
Bad	6-7

Table 5: *Overall evaluation.*

Methodology of investigations

Radiosynoviorthesis is a daily used methodology in our institute since 1985 [40,41]. We included 205 patients in our analyse: from these N = 205 patients 115 were diagnosed with RA, 17 with SPA, 13 were other SNSA, 47 with inflammed osteoarthritis (OA), 1 hydrops articulorum intermittens (HAI), 1 pigmented villonodular arthritis, and 11 patients with posttraumatic synovitis.

The total number of patients based on their age and diagnosis are shown in Table 6 and 7. Can be seen that more than half of the patients were over the age of 60 years.

Age	Number of patients	Average score	Variance	Level of significance
40-45	15	27.45	7.832	0.176NS
46-50	30	27.52	8.417	0.100NS
51-55	20	27.958	6.779	0.463NS
56-60	36	25.188	8.106	0.163NS
61-65	44	24.469	7.692	0.679NS
66-70	26	24.366	7.031	0.911NS
71-90	34	24.489	7.063	0.107NS
	205			

Table 6: *Y-90 radiosynoviorthesis total number of patients by age (N=205).*

Diagnosis	
RA II	55
RA III	55
RA IV	5
SPA	17
SNSA	13
OA	47
PVNS	1
Hydrops articulorum intermittens	1
Chronic traumatic synovitis	11
	205

Table 7: *Y-90 radiosynoviorthesis total number of patients by diagnosis (N = 205).*

From these 205 patients there were n = 39 who underwent surgical intervention before RSO Table 8. From diagnostic point: 14 patients were treated with RA, 5 with SPA, 4 SNSA, 1 PVNS, 6 traumatic-based, and 9 with OA synovitis. Chronic synovitis could have a recurrence rate after the surgical synovectomy due to the insufficient removal of all pathological tissues, as demonstrated by Akmese., *et al*. [42] In our database the radiological grading was: 15 patients stage II, and 24 patients stage III. The respective n=39 pre-treated patients: 22 patients had surgical synovectomy, 4 patients had arthroscopical synovectomy, 9 patients' meniscectomy, 3 patients had enucleation of the Baker's cyst, and 1 patient had ligament reconstruction (Table 9).

After the surgical intervention all patients had chronic persistent synovitis, so there was need for the additional administration of radiosynoviorthesis. From 39 patients there were 20 male and 19 female patients, the age of the patients was between 42-82, average 63 years in the first group. There were 3 males and 1 woman between 41-45 years, and 19 interventions for the age group of 55-65 years. Two patients were over 70 years old. In general, the synovitis was more persistent than the initially expected 3-6 months. There was one patient who had persistent synovitis of more than 1 year; 9 patients had 1-3 years persisting, 4 patients had 4-5 years, 12 patients having

Diagnosis	Number of patients according to diagnosis
RA II	6
RA III	8
OA	9
SPA	5
SNSA	4
Chronic traumatic synovitis	6
Synovitis villonodularis	1
Total patients with interventions	39

Table 8: *Distribution diagnosis of patients undergone surgery before Yttrium-90 radiosynoviorthesis (n=39).*

Interventions	Number of patients 39
Surgical synovectomy	22
Arthroscopical synovectomy	4
Meniscectomy	9
Baker cyst enucleation	3
Operation on ligaments	1

Table 9: *Orthopedic-surgical interventions in n=39 patients before Y-90 RSO.*

6-10, seven patients 11-20 and 6 patients had chronic synovitis outstanding more than 20 years. Regarding the knee punctures before RSO: a wide range from 3 to 150 punctures were registered, in average 18.95.

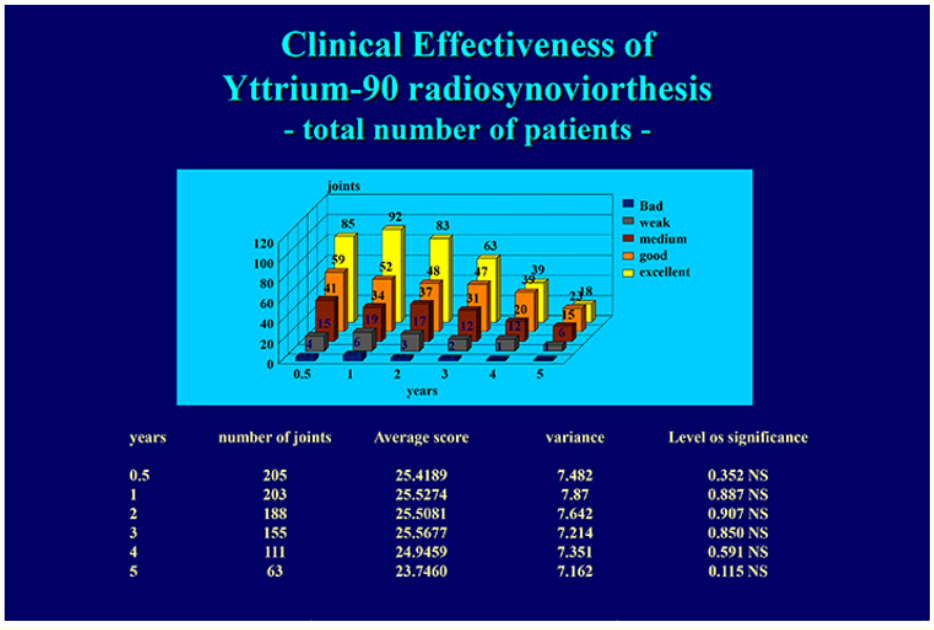
Results

Results after radiosynoviorthesis (total number of patients, N=205)

We considered the effectiveness of the radiosynoviorthesis according to the "excellent/good/moderate/weak/worse" scoring system presented over. At 6-months evaluation from the 205 subjects: 85 patients (41.46%) were excellent, 59 (28.78%) were good, 41 (20%) were medium, 15 (7.32%) were weak, 4 patients (1.95%) were bad reported.

- At 1 year from the 203 patients: 92 (43.52%) were excellent, 52 (25.62%) were good, 34 (16.75%) were medium, 19 (9.36%) were weak, 6 patients (2.96%) were insufficient resulted.
- After 2 years from 188 patients 83 (44.15%) were excellent, 48 (25.53%) were good, 37 patients (19.68%) medium, 17 patients (9.04%) weak, and at 3 patients (1.6%) bad results were observed.
- At 3 years 155 patients were evaluated: 63 patients (40.65%) were excellent, 47 patients (30.32%) good, 31 patients (20%) medium, 12 patients (7.74%) weak, and 2 patients (1.29%) were bad reported.
- At 4 years 111 patients were observed, from which 39 (35.14%) were excellent, 39 patients (35.14%) were good, 20 patients (18.02%) were medium, 12 patients (10.81%) were weak and 1 patient (0.9%) was bad.
- At 5 years only 63 patients were still ongoing: 18 patients (28.57%) were excellent, 23 patients (36.51%) were good, 15 patients (23.81%) were medium, 6 patients (9.52%) were weak, and 1 patient (1.59%) was bad reported.

In the first 4 years the results are similar, the excellent and good results reported have a total of 70%. In the 5th year the reported success rates decreased to 65%, however the decrease was not significant. We consider successful the intervention if additional punctures after the radiosynoviorthesis are not needed, and we can see that 65% of the patients (132 from 205) did not needed additional punctures in the 5th year, so the intervention could be considered successful (Figure1).



years	number of joints	Average score	variance	Level os significance
0.5	205	25.4189	7.482	0.352 NS
1	203	25.5274	7.87	0.887 NS
2	188	25.5081	7.642	0.907 NS
3	155	25.5677	7.214	0.850 NS
4	111	24.9459	7.351	0.591 NS
5	63	23.7460	7.162	0.115 NS

Figure 1: *Clinical effectiveness of Yttrium-90 RSO - total number of patients.*

Results of the patients with previous surgical intervention treated with radiosynoviorthesis (n=39)

As reported, n=39 patients (Figure 2) underwent surgical intervention, which after 6-months had the next results: 7 patients (17.95%) were excellent, 18 patients (46.15%) were good, 10 patients (25.64%) were medium, 3 patients (7.69%) were weak, and 1 patient (2.56%) was bad reported.

- At 1 year from the 39 patients: 11 (28.82%) patients were excellent, 16 patients (41.03%) were good, 7 patients (17.95%) were medium, 5 patients (12.21%) were weak reported.
- During the second-year control from the 35 patients: 11 (31.43%) were excellent, 13 patients (37.14%) were good, 8 patients (22.86%) were medium, 3 patients (8.57%) were weak reported.
- At the 3rd year control the remaining 29 patients: 10 (34.85%) were excellent, 12 (41.38%) were good, 5 patients (17.24%) were medium, 2 patients (6.9%) were reported weak.
- At the 4-year control the appearing 25 patients were: 4 (16%) excellent, 13 (52%) good, 5 patients (20%) medium, 3 patients (12%) weak reported.
- During the 5-year control only 17 patients appeared: 2 patients (11.76%) were excellent, 8 (46.06%) were good, 4 patients (23.53%) were medium, 3 subjects (17.65%) were weak reported.

So, the excellent and good reported patients together were 64% after the first half-of-year, at 1 year were 70%, at 2 year 68%, at 3 year 76%, at 4 year 68%, and 5th year 58%. There was no significant difference between the yearly controls, for the 5th year the excellent + good patients success rate deceased, but this was not significant.

From the surgical (n=39) treated patients: 24 (61.5%) needed no additional punctures at the end of the 5th year, so this procedure was considered successful. Twelve patients needed 1-3, three patients needed 4-6 punctures, due to the lack of the efficacy of the RSO. From these 15 unsuccessful patients 6 needed repeated interventions: 3 had surgical synovectomy, 1 patient received prothesis, 1 patient had ligament plastic, and the RSO was repeated in case of 1 patient.

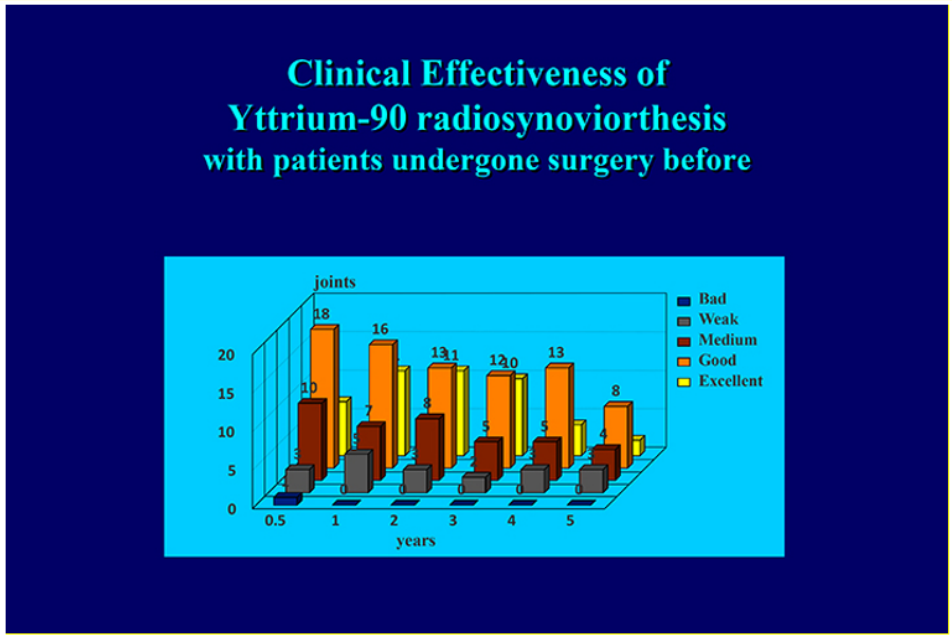


Figure 2: *Clinical effectiveness of Yttrium-90 RSO – with patients undergoing surgery before RSO.*

In case we compare the effectiveness of the surgical intervention of these n=39 patients with the effectiveness of total patients who underwent RSO (N=205): there is no significant difference; both methodologies were considered successful. So, RSO can be applied, and it is indicated for patients who formerly underwent surgical interventions.

Efficacy based on the radiological stage

From the n=15 patients classified in radiological stage II, at 6-months 11 (73%) patients, at 1 year 12 patients (79%), at 2 years from total of n=13 patients: 10 patients (77%), at 3 years 10 patients (77%), at 4 year from the remaining 10 patients 8 (80%) were evaluated "excellent" and "good". Similar, at 5 years from the remaining 8 patients 6 were (75%) evaluated in the "excellent + good" class.

The n=24 patients classified in the radiological stage III at 6-months 14 (58%), at 1 year 15 (62%), at 2 years from the 22 remained patients 14 (63%) were considered excellent or good, at 3-years from the 16 remaining 10 patients (62%), and for the 4 year from 15 the 9 (60%), at 5 year from the remaining 9 the 4 subjects (44%) were considered excellent/good. Between the efficacy significance of stage II and III patients there was a difference of p=0.00001.

With 2-sided Student t-probe and multifactorial regression analysis we searched the question which factors influence the success of the RSO. There was no correlation with the patients age and gender, and the persistence of the synovitis also did not influence the results (Table 10), respective the number of previously received i.a. steroid injections. The analysis has shown that the initial radiological stage of the joint (in case of the knee): is influencing the final results (p=0.00001), however the basic disease (diagnosis) in the final results shows no correlation (p=0.001).

Discussion

There are several comparative evaluations in the literature regarding the effectiveness of the RSO and surgical/arthroscopic synovectomy. Bauer [43] compared 46 patients treated with RSO to 50 patients with surgical synovectomy and reported success rates of 78% for surgical synovectomy, and 52.2% for RSO. The patients treated with surgical synovectomy were radiological Grade I in 33%, Grade II in 45%, Grade III in 22%, however the RSO patients were only 2.3% Grade I, 46.5% Grade II, 51,5% Grade III. The difference of patients

Influence of different factors on the effectiveness of Yttrium-90 radiosynoviorthesis					
Multifactorial regression analysis					
	Beta in	SE B	Beta	T	Sig T
X-ray stadium	-5.57358	0.95527	-0.41183	-5.835	0.00001 S
Diagnosis	-0.37686	0.15154	-0.17553	-2.487	0.01390 S
Sex	-0.08546	-0.09385	0.92171	-1.189	0.2364 NS
Age	-0.11604	-0.12949	0.95671	-1.647	0.1016 NS
Duration of synovitis	-0.06885	-0.07739	0.95464	-0.979	0.3292 NS
Number of punctions before	0.03160	0.03244	0.80405	0.409	0.6829 NS
Number of punctions before	0.04713	0.05210	0.94803	0.658	0.5116 NS

Table 10: *Regression Analysis - influence of different factors.*

in radiological grading could influence the final difference between the two methodologies. Beatson [44] reached better results with the radiosynoviorthesis as Paradies [45] with surgical synovectomy. Nisilla [46], Gumpel [47] and Lee [48] reached similar results as with surgical synovectomy. Delbarré considers that the radiosynoviorthesis methodology can substitute the surgical synovectomy [49]. Formerly, Combe., *et al.* [30] reported the results of arthroscopic synovectomy applied after the failure of RSO with Yttrium-90. Patients after the surgical intervention needed a rehabilitation period of 6-36 months (in average 17.7 months), all patients having a significant improvement in the range of motion of the knee. There was no detectable radiographic evidence of disease progression at 1 and 2 years after the intervention. Bauer [43] considers one of the advantages of the radiocolloid administration that these radiopharmakon's reach the posterior recesses of the joint synovium, places which are extremely hard accessed by the surgical synovectomy operations. Another advantage of the RSO is that can be applied in elderly, bad cardiovascular and general status patients, or for subjects whose collaboration and compliance is not satisfactory. Otherwise, in case of young good collaborative patients, but with advanced proliferative (chronic) synovitis the surgical, or arthroscopic synovectomy would be the first choice. General experience is that after an unsuccessful surgical intervention the radiation synovectomy is indicated only in those cases when there is no ruptured or multicystic Barker's cyst, or the joint space had not too many recesses. In these cases, the uniform colloid distribution can be assured. The RSO has its effectiveness in stage III synovitis also, if there are no severe cartilage and bone destructions. Hagena [50] considers surgical synovectomy longer lasting. Muller [53] is on the opinion that RSO is an alternative of surgical synovectomy for elderly people with risk factors. All investigators consider that the preliminary surgical and orthopedic interventions decrease the later effectiveness of the RSO. However, there are only a few reviews regarding the efficacy of RSO after surgical synovectomy from Göbel and Rittmeister [24,25] respective Oztemür, Jha, and Gumpel [28,29,31].

Applying the RSO in earlier radiological stages is more effective, and better results can be obtained as shown earlier by Jones and Kampen [12,15].

Arthroscopic and surgical synovectomies can be unsuccessful in case a proliferative synovitis is showing heterogenous conditions, with inflammatory areas, necrotic zones, and cicatricial areas covered with fibrin [51]. In these cases, the histologic examinations demonstrate an irregular active synovitis; however, the radiographic findings are not always prominent. There can be debris in the joint or small parts from the meniscus; cruciate ligaments can be atrophied. Satisfactory results cannot be obtained in these extensive damaged joints, however RSO may be useful for such patients and even can postpone the total knee prosthetic replacement surgery [52]. There are rheumatoid arthritis patients with chronic synovitis who are not responsive to RSO and only "satisfactory" short-term (3-6 months) results can be obtained, and there is need for additional interventions, like arthroscopy or "open" surgical synovectomy. On the other side, even a well performed surgical intervention was leaded, the progressive changes of the degenerative disease are ongoing, and patients progress from stage I-II to higher stages, and there is need again for intervention. Both methodologies are more effective in early stages of destruction, because advanced stages are more difficult to be treated in an effective way [53,54]. Both methodologies have their advantages, a low

morbidity rate, a minimal interventional pain (i.e. radiation synovitis after RSO), the joint function is early restored, respective there is no need for a long postoperative rehabilitation [55]. Both methodologies can be repeated in case of recurrence of synovitis. Both appears to be of value in the treatment of chronic knee synovitis and could be performed if other procedures are ineffective [56].

Conclusion

The application of radiocolloids in chronic painful joints remains an effective, simple and acceptable methodology. The effect was long-lasting, and even after 5-years the patients didn't require additional intra-arterial punctures with NSAIDs or glucocorticoids. Both interventions (radiosynoviorthesis and surgical synovectomy) had their indication and they were complementary each to the other. The success is dependent from the basic disease and the radiological grading of the targeted joint. In case of unsuccessful surgical or arthroscopic synovectomy the joint can be re-treated with radiosynoviorthesis.

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