The effect of P32 radioactive synoviorthesis in hemophilic synovitis: How long does it last?

Abstract

Introduction: Radioactive synoviorthesis, used as a local treatment for hemophilic arthropathy, causes the ablation of sub-synovial vessels. Previous studies have indicated that this procedure is effective in reducing the frequency of hemarthrosis in patients with recurrent episodes. However, it remains unclear how long this effect lasts and whether it has any impact on radiographic changes. We are reporting on the impact longevity of synoviorthesis on recurrence of hemarthrosis, in hemophilia and the also clinical and radiographic changes of the joint.

Materials & Methods: Synoviorthesis using 32P that had been performed one time on 56 target joints in 56 patients. The pre-treatment radiographic changes were compared with post treatment changes using Arnold-Hilgartner grading, and the clinical change was compared with Fernandez-Palazzi grading. The time period of follow-ups was grouped into below and over 36-months periods.

Results & Discussion: 56 joints in 56 patients were studied. Thirty cases (29 males, one female) with an average age of 15.55 (±6.17) years and a follow-up duration of 21.8 months (range: 3–36 months) were compared with 26 males with an average age of 17.71 (±8.33) years and an average follow-up duration of 43.6 months (range: 38–102 months). The average reduction in the rate of hemarthrosis was 56.4% in the group with up to 36-month follow-up ($p<0.05$) and 35.9% in over 36-months follow-up group ($p<0.05$) but with non- significant difference. Additionally, the mean improvement in clinical grade (Fernandez-Palazzi) was 0.56 (SE: 0.21) in shorten ($p<0.05$) and 0.65 (SE: 0.28) in longer follow-up group ($p<0.05$), with the slightly better but non-significant results in the former group. The mean increase in radiographic grade (Arnold-Hilgartner) was 0.25 (SE: 0.15) in the shorter follow-up and 0.78 (SE: 0.14) in the longer follow-up group, with a significant difference.

Conclusion: The beneficial clinical effect of 32P synoviorthesis in hemophilic arthropathy persists over time. Despite an initial reduction in its effectiveness, longer follow-up demonstrated that synoviorthesis remains as a durable procedure. However, it is unable to halt the radiologic progression of joint destruction.

Keywords: Hemophilia, Arthropathies, Hemarthrosis, Synovitis, Radioactive Isotope.

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Introduction

The joints are the most common sites of bleeding in patients with hemophilia(1,2). Recurrent hemarthrosis can lead to the accumulation of excess iron, which triggers synovitis by damaging synoviocytes, releasing chondrolytic enzymes and inflammatory mediators(3). This process can result in progressive hemophilic arthropathy and eventually arthrofibrosis(4,5). Although prophylactic replacement of coagulation factor is the preferred treatment for preventing bleeding and its associated arthropathy(5,6), challenges such as limited accessibility to coagulation factors in some countries and complications from repeated injections (such as development of inhibitors and the risk of infection from continuous intravenous catheters) have led to the exploration of alternative modalities. These include therapeutic factor replacement after each hemarthrosis, open or arthroscopic synovectomy, and synoviorthesis(7-9). Synoviorthesis, which is used to disrupt the vicious cycle of synovitis caused by inflammation and bleeding in the synovium, can be performed chemically or with radioactive agents(10).

According to previous studies, synoviorthesis treatment has demonstrated significant improvements in various symptoms. These include a reduction in joint bleeding, decreased pain and swelling, and enhanced joint mobility. Additionally, there have been observed reductions in coagulation factor consumption and, in some cases, notable clinical and radiological changes in the treated joints[11-14]. Some studies have reported the duration of its effectiveness typically ranges from 6 months to 2 years, with some patients experiencing benefits for up to 3 years[10,15]. However, the durability of the improvement was inconsistent across these studies, with initial reductions in bleeding rates often followed by an increase in bleeding over the subsequent years after radio-synoviorthesis[16,17].

The aim of this study was to evaluate whether the time elapsed since synoviorthesis for hemophilic arthropathy influences the clinical and radiological effects of ^{32}P radio-synovectomy. To achieve this, outcomes were compared between two groups with follow-up periods of less than and more than 36 months.

Materials & Methods

This study was a retrospective cohort study, which was performed on hemophilic patients with recurrent hemarthrosis in a target joint at Tehran University of Medical Sciences between May 2002 and March 2009. Our inclusion criteria were: (1) hemophilic patients who had experienced more than three episodes of hemarthrosis in a target joint in the previous six months, or (2) those with at least clinical stage II hemophilic arthropathy based on the Fernandez-Palazzi classification. Our exclusion criteria were: (1) patients with less than three months of follow-up, (2) those who received more than one intra-articular ^{32}P injection in the same joint, (3) patients with advanced joint degeneration (Arnold-Hilgartner stage V) or clinical grade IV based on the Fernandez-Palazzi classification, (4) individuals with prior surgical synovectomy of the treated joint, and (5) those with active infection or non-hemophilia-related inflammatory joint diseases.

After an acute hemarthrosis, a conservative treatment protocol was applied, which included coagulation factor replacement, immobilization, and analgesics. It was followed by a rehabilitation program consisting of physical therapy and orthotic support. If indicated, radioactive synoviorthesis was performed once the acute stage of hemarthrosis had subsided. The clinical diagnosis of hemophilic arthropathy was confirmed by Magnetic Resonance Imaging (MRI) prior to synoviorthesis. The protocol followed was the same as described in our previous publication[13]. Briefly, patients received two bolus doses of FVIII (to provide 100% activity), one just before and another 8–12 hours after the procedure. For patients with positive inhibitors, factor VIIa was administered.

Under aseptic conditions, an intra-articular injection of ^{32}P (1 mCi for the knee and 0.5 mCi for other joints, with half the adult dose for children under 12 years) was performed. After the injection, the needle was flushed with 2 cc of saline, and the injection site was dressed. The joint was then immobilized with a compression bandage and a plaster of Paris splint for 1–2 weeks, depending on the patient's age. Only one injection was administered per affected joint, and joints that received more than one injection of ^{32}P were not included in the study. Patients were evaluated after one week, then every three months for up to one year, and annually thereafter.

In this study, the rate of hemarthrosis, clinical score (Fernandez-Palazzi classification), and radiological score (Arnold-Hilgartner scale) based on anteroposterior and lateral radiographs were assessed for each joint before synoviorthesis and at the final follow-up[18]. Joints with a follow-up duration of less than three months were excluded from the study. The study was conducted under a protocol approved by the ethics committee of Tehran University of Medical Sciences, and informed consent was obtained from the patients or their parents.

Wilcoxon signed-rank tests, ANOVA, and paired t-tests were conducted to compare pre- and post-synovectomy results. A p-value of <0.05 was considered significant, and SPSS version 13 (Chicago, IL, USA) was used for statistical analysis.

Results

^{32}P synoviorthesis procedures were performed on 78 joints. Out of these, 56 joints in 56 patients received a single injection and were followed for more than three months, thus qualifying for inclusion in the study. To assess the results based on the duration of follow-up, data analysis indicated that approximately 36 months was a critical threshold for observing significance of different outcomes. Therefore, the results were compared between these two groups:

those followed for 36 months or less (≤36m) and those with a follow-up duration of more than 36 months (>36m). The ≤36m group consisted of 30 patients (age: 6-36 years) with a mean follow-up of 21.83 months (SD: 12.12; range: 3-36 months), while the >36m group included 26 patients (age: 2.5-35 years) with a mean follow-up of 43.63 months (SD: 20.60; range: 38-102 months). The patients' demographic data, as well as the type of hemophilia and presence of inhibitors, are summarized in Table 1. The ≤36m group included 21 knees, 3 elbows, and 6 ankles, while the corresponding numbers for the >36m group were 24, 1, and 1, respectively. There was no significant difference between the two groups regarding variables such as sex, age, type of hemophilia, presence of inhibitors, and injected joints.

The average reduction in the rate of hemarthrosis was 56.4% in the ≤36m group and 35.9% in the >36m group, with both being statistically significant (p=0.001 and p=0.002, respectively) (Table 2). The clinical reduction was also graded as described in Table 3[13]. Although the comparison of hemarthrosis reduction grades between the two groups was not statistically significant (p=0.90), there was a trend toward a better response to radio-synovectomy in the short-term follow-up group (mean reduction grade: 1.8 in ≤36m versus 1.65 in >36m). During the follow-up period, new target joints were identified in 10 patients (33.3%) in the ≤36m group and 13 patients (50%) in the >36m group. We observed a 91.2% and 77.2% reduction in mean coagulation factor consumption per month for the ^{32}P-injected joint in the ≤36m and >36m groups, respectively (p<0.001 within each group, but p>0.05 p=0.065 between groups).

Tables 2 and 4 present the frequency of clinical grades (Fernandez-Palazzi scale) and comparisons of means before and after ^{32}P injection within and between the two groups. These tables also show the Δ clinical score, defined as the difference between the grade at the last follow-up and the pre-injection grade. ^{32}P radio-synovectomy significantly improved the mean clinical score in both groups. Although this improvement was clinically more significant in both groups, the comparison of the Δ clinical score between the two groups was not statistically significant (p=0.8). Furthermore, while no patient had a clinical grade of 0 before ^{32}P synovectomy, this intervention improved the clinical score to grade 0 (indicating no clinical signs of arthropathy, except for radiological findings) in 23.3% of patients in the ≤36m group and 26.9% in the >36m group at the last follow-up (Table 4).

Similar data on radiographic grades (Arnold-Hilgartner scale) are presented in Tables 2 and 5. As these tables show, the mean radiological grade worsened in both follow-up groups, with a significant p-value in the >36m group (p=0.001). At the last follow-up, 4% (1 case) of the ≤36m group showed improvement in the radiological score, 58% (17 cases) showed no change, and 28% (7 cases) worsened. In the >36m group, no cases (0%) showed improvement, 34.7% (8 cases) showed no change, and 65.2% (15 cases) experienced worsening of the radiological score. Additionally, the comparison of Δ radiological grades (difference between the last follow-up radiological grade and the pre-injection grade) between the two groups (Table 2) showed that the radiological grade deteriorated to a greater extent in the >36m group (0.78 versus 0.25, p=0.013). This statistically significant worsening of the radiological grade with longer follow-up duration may suggest that ^{32}P synoviorthesis is unable to halt the joint destruction associated with hemophilic arthropathy.

Table 1: The demographic and hemophilia data of the patients

Group (follow-up duration)	Number of patients	Sex (male/female)	Age (mean ± SD)	Type of coagulation disorder frequency (%)			Inhibitor frequency (%)	
				Severe A (factor VIII ≤1%)	Moderate A (factor VIII 1-5%)	Von Willebrand type 3	Positive	Negative
≤36m	30	29/1	15.55±6.17	27 (90%)	2 (6.7%)	1 (3.3%)	4 (13.3%)	26 (86.6 %)
>36m	26	26/0	17.71 ± 8.33	25 (96.2%)	1 (3.8%)	-	6 (23.1%)	20 (76.9%)

		P= 1.00 (Fischer's Exact test)	P=0.27 (independent samples t-test)	P= 1.00 (Fischer's Exact test)	P=0.48 (Fischer's Exact test)

Table 2: Comparing variable within and between ≤36 months and > 36 months follow-up groups

A: Rate of hemarthrosis per month					
		Pre-injection		Last follow-up	Grade of hemarthrosis reduction
≤36 m	N:30 Miss:6	Mean: 7.30 SE: 1.54	P: 0.001	Mean:3.17 SE:0.79	Mean: 1.80 SE: 0.28
		P: 0.078		P: 0.574	P: 0.90
>36 m	N:26 Miss:3	Mean: 4.85 SE: 1.13	P: 0.002	Mean: 3.11 SE: 1.05	Mean:1.65 SE: 0.30
C: Clinical grade (Fernandez-Palazzi)					
		Pre-injection		Last follow-up	Δ clinical score
≤36 m	N:30 Miss: 0	Mean: 2.73 SE: 0.09	P: 0.027	Mean: 2.17 SE: 0.23	Mean: -0.56 SE: 0.21
		P: 0.57		P: 0.39	P: 0.8
>36 m	N:26 Miss:0	Mean: 2.65 SE :0.12	P: 0.028	Mean: 2 SE: 0.26	Mean: -0.65 SE: 0.28
D: Radiological grade (Arnold–Hilgartner scale)					
		Pre-injection		Last follow-up	Δ Radiological score
≤36 m	N:30 Miss:5	Mean: 3.16 SE: 0.16	P: 0.130	Mean:3.41 SE:0.19	Mean: 0.25 SE: 0.15
		P: 0.61		P: 0.017	P: 0.013
>36 m	N:26 Miss:3	Mean: 3.26 SE: 0.21	P: 0.001	Mean: 4.04 SE: 0.15	Mean: 0.78 SE: 0.14

Table 3: Grading of hemarthrosis reduction after radiosynovectomy

Grade	Definition	Frequency (%)	
		F/U≤ 36m	F/U>36m
0	no bleeding episode	9 (30%)	5 (19.2%)
1	>75% reduction in bleeding episodes	11 (36.7%)	6 (23.1%)
2	>50% reduction in bleeding episodes	2 (6.7%)	5 (19.2%)
3	>25% reduction in bleeding episodes	2 (6.7%)	2 (7.7%)
4	No change in the frequency of bleeding episodes	6 (20%)	8 (30.8%)
Total		30 (100%)	26 (100%)
Mean of decrease in hemarthrosis rate/month Standard error		1.80 0.28	1.65 0.30
		P value = 0.90	

Table 4: The effects of radiosynovectomy on clinical grade (Fernandez-palazzi scale) before and after 32P radiosynovectomy.

	Definition	F/U≤36m		F/U>36m	
		Before	after	Before	After
0		-	7 (23.3%)	-	7 (26.9%)
1	Transitory synovitis with no post-bleeding sequelae	1 (3.3%)	1 (3.3%)	2 (7.7%)	1 (3.8%)
2	Permanent synovitis with persistent synovial thickening and limited range of motion	6 (20%)	2 (6.7%)	5 (19.2%)	3 (11.5%)
3	As for Grade 2 plus muscular atrophy and axial deformity of the limb	23(76.7%)	20(66.7%)	19(73.1%)	15(57.7%)
4	Fibrous or osseous ankylosis	-	-	-	
Total		30 (100%)	30 (100%)	26 (100%)	26 (100%)

Table 5: The effects of radiosynovectomy on radiological grade (Arnold–Hilgartner scale) before and after 32P radiosynovectomy.

	Definition	≤36m		>36m	
		Before	after	before	after
0	Normal joint	-	-	-	-
1	No skeletal abnormalities: soft tissue swelling present	-	1 (3.7%)	-	-
2	Osteoporosis and overgrowth of epiphysis; no erosions; no narrowing of cartilage space	6 (24%)	3 (11.1%)	7 (30.4%)	-
3	Early subchondral bone cysts; squaring of patella; intercondylar notch of distal femur or humerus widened; cartilage space remained preserved	9 (36%)	10 (37%)	5 (21.7%)	7 (26.9%)
4	Findings of Stage III more advanced: cartilage space narrowed	10 (40%)	10 (37%)	9 (39.1%)	11(42.3%)
5	Fibrous joint contracture; loss of joint cartilage space; marked enlargement of the epiphysis and substantial disorganization of the joint	-	3 (11.1%)	2 (8.7%)	8 (30.8%)
Total		25 (100%)	27 (100%)	23 (100%)	26 (100%)

Discussion

Similar to our study, several research studies have investigated the use of radioactive ^{32}P synoviorthesis for treating hemophilic arthropathy and have found that it effectively reduces the rate of hemarthrosis, decreases coagulation factor consumption, and improves the patient's clinical condition[12,13,17,19]. The primary difference between synoviorthesis using P-32 and previous methods lies in the type of radionuclide used and its specific properties. P-32, a beta-emitting radionuclide, offers a higher energy emission compared to earlier radionuclides like Y-90 or Re-188. This higher energy emission allows for a more effective penetration and treatment of the synovial lining, potentially leading to better outcomes in terms of pain relief and reduction of joint effusion. Additionally, P-32 has a shorter half-life, which may result in a more localized effect and reduced risk of systemic radiation exposure. However, further studies are needed to fully understand the long-term benefits and potential risks associated with P-32 synoviorthesis compared to previous methods[19]. However, an important question concerns the durability of this effect. When radioactive synoviorthesis targets sub-synovial vessels by ablating and occluding them , the angiogenesis and revascularization eventually lead to the formation of new bleeding vessels, thereby causing recurrent hemarthrosis? This possibility could be inferred from a decrease in the efficacy of synoviorthesis in reducing hemarthrosis, coagulation factor consumption, and clinical grades over a longer

follow-up period. Another critical question is whether the destructive nature of hemophilic arthropathy can be reversed or halted by synoviorthesis.

Eraghi and colleagues found that patients with fewer than 36 months of follow-up required less factor compared to those with more than 36 months of follow-up. However, they did not determine whether the increased factor consumption in the over -36 - months group was due to the treatment of the original joint or the development of new target joints(14). In another study, Silva et al. observed that 75% of cases showed a decrease in hemarthrosis within 6 months to 8 years following 115 primary ^{32}P synoviortheses. The reduction in hemarthrosis decreased over time, from 93% three months after the injection to 73.7% after 8 years(17). In a previous study, Mortazavi et al. examined 66 cases of ^{32}P synoviorthesis in 53 patients, some of whom were included in the >36 months follow-up group of the present study. They found that the percentage of cases with no bleeding episodes after the ^{32}P injection tended to decrease, particularly during the first six months post-injection, dropping from 39% at the third month to 26% at the sixth month. This decline was attributed to factors such as synovial regrowth and ongoing inflammation, the increased physical load as patients became less cautious and more active, and the lack of post-injection physical therapy to enhance muscular strength(13).

In the present study, while there was a significant decrease in the hemarthrosis rate in both the ≤36 and >36 months follow-up groups (Table 2), consistent with previous studies, we did not find any significant difference in the efficacy of synoviorthesis between the two groups when comparing the grade of hemarthrosis reduction (Table 3). At the last visit, a complete cessation of hemarthrosis (grade 0 of hemarthrosis reduction) was observed in 30% of the ≤36 months group and 19.2% of the >36 months group (Table 3). Although the difference was not statistically significant ($p=0.574$), it suggests that there may be a higher likelihood of curing hemarthrosis after ^{32}P synoviorthesis in In our study Regarding clinical grade, we found an improvement trend in both groups (0.65 in the >36 months group ($p=0.028$) and 0.56 in the ≤36 months group ($p=0.027$)), with no significant difference between these improvements ($p=0.8$). As shown in Table 4, although no patients had a clinical grade of 0 before ^{32}P radio-synovectomy, this intervention improved the clinical score to grade 0 (indicating no clinical signs of arthropathy, except for radiological findings) in 23.3% of patients in the ≤36 months group and 26.9% in the >36 months group at the last follow-up. This finding, which could be viewed as synonymous with the cessation of hemarthrosis (grade 0 of hemarthrosis reduction) and has been reported in previous studies, represents a significant opportunity for patients to be fully cured by a simple procedure(13,17).

During follow-up, new target joints were identified in 10 patients (33.3%) in the ≤36 months group and 13 patients (50%) in the >36 months group in the present study ($p>0.05$). As follow-up duration increases, the involvement of a greater number of joints by hemophilic arthropathy may progressively occur. The emergence of new target joints indicates that synoviorthesis is a focal, rather than systemic, treatment and has no therapeutic or preventive effect on other joints. This also explains the continued factor consumption in patients who otherwise responded well to synoviorthesis, making it difficult to directly correlate factor consumption with the success of synoviorthesis.

Similar to our findings, a radiographic follow-up study of 29 joints over 1 to 14 years (median 8 years) demonstrated deterioration in the radiological score in 23 (79%) of the joints. Rivard et al. evaluated the radiographic grade of 92 joints in 48 hemophiliacs treated with 32P synoviorthesis. Compared to joints that had not been injected with ^{32}P, they concluded that once initiated, hemophilic arthropathy progresses regardless of the treatment(11). In our study, 63% of joints in the >36 months follow-up group showed deterioration in radiological grade, with a mean deterioration of 0.78. This was significantly worse than in the ≤36 months follow-up group, where only 28% of cases showed deterioration, with an average deterioration of 0.25 ($p<0.05$). These findings reinforce the notion that, despite improvements in the hemarthrosis rate and clinical grade of the joint, the destructive nature of hemophilic arthropathy continues, even after ^{32}P synoviorthesis. However, our case study is limited to a 36-month period, which constrains our ability to fully evaluate the inhibitory effects of radioactive P32 synoviorthesis on joint cartilage destruction.

Our study had some limitations. The relatively small sample size may have affected our results, particularly in terms of a type II error, where some differences that appeared non-significant might have been significant with a larger sample. Additionally,

we compared follow-up results between two groups of different patients, rather than following the same patients over different periods. Although matching groups before the ^{32}P injection was done to minimize selection bias, this approach is less robust than within-patient comparisons.

Calculating the rate of hemarthrosis was based on a subjective variable, which may not have been sufficiently precise. Although the same referral center was used for treatment in all patients, incorporating objectively recorded clinical scores could have served as a double check to ensure the accurate diagnosis of hemophilic arthropathy. Furthermore, while the primary goal of radioactive synoviorthesis is to reduce the burden of coagulation factor consumption, the calculation of factor use—given the possibility of treatment at home or other centers for joint and non-joint bleeding—may not have been exact. This potential inaccuracy precluded a detailed discussion of this aspect in our study.

In the context of synoviorthesis using P32 radioactive for hemophilic joints, our findings indicate a significant reduction in hemarthrosis. However, it is premature to conclusively state that this reduction is constant over time. While the initial results are promising, indicating a notable decrease in joint bleeding, long-term follow-up studies are essential to ascertain the durability of this effect.

The current study's limitation to a 36-month observation period constrains our ability to definitively conclude the permanence of hemarthrosis reduction. Further research with extended follow-up durations is necessary to evaluate the sustained efficacy of P32 synoviorthesis in maintaining reduced hemarthrosis levels. Additionally, monitoring potential long-term adverse effects will be crucial in determining the overall viability and safety of this intervention for chronic management in hemophilia patients.

Conclusion

^{32}P synoviorthesis is an effective and durable procedure for managing hemophilic synovitis, particularly in reducing hemarthrosis and improving clinical scores. However, this treatment modality does not appear to halt the radiologic progression of joint destruction associated with hemophilic arthropathy.

References

1 Hanley J, McKernan A, Creagh M, Classey S, McLaughlin P, Goddard N, et al. Guidelines for the management of acute joint bleeds and chronic synovitis in haemophilia: a United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) guideline. Haemophilia. 2017;23(4):511-20. doi.org/10.1111/hae.13201

2 Rodriguez-Merchan EC. Radiosynovectomy in haemophilia. Blood Reviews. 2019;35:1-6. doi.org/10.1016/j.blre.2019.01.002

3 Stein H, Duthie R. The pathogenesis of chronic haemophilic arthropathy. Journal of Bone & Joint Surgery, British Volume. 1981;63(4):601-9. doi.org/10.1302/0301-620x.63b4.7298694

4 van Vulpen LF, Thomas S, Keny SA, Mohanty SS. Synovitis and synovectomy in haemophilia. Haemophilia. 2021;27:96-102. doi.org/10.1111/hae.14025

5 Hoots W, Rodriguez N, Boggio L, Valentino L. Pathogenesis of haemophilic synovitis: clinical aspects. Haemophilia. 2007;13(s3):4-9. doi.org/10.1111/j.1365-2516.2007.01533.x

6 Rodriguez-merchan e. Haemophilic synovitis: basic concepts. Haemophilia. 2007;13(s3):1-3. doi.org/10.1111/j.1365-2516.2007.01532.x

7 Rodriguez-Merchan E, Wiedel J. General principles and indications of synoviorthesis (medical synovectomy) in haemophilia. Haemophilia. 2001;7(s2):6-10. doi.org/10.1046/j.1365-2516.2001.00102.x

8 odriguez-Merchan EC. Surgical approaches to hemophilic arthropathy. Blood Coagulation & Fibrinolysis. Haemophilia and Other Congenital Coagulopathies. 2019;30: 11-13. doi.org/10.1097/MBC.0000000000000824

9 Ernstbrunner L, Hingsammer A, Catanzaro S, Sutter R, Brand B, Wieser K, et al. Long-term results of total knee arthroplasty in haemophilic patients: an 18-year follow-up. Knee Surgery, Sports Traumatology, Arthroscopy. 2017;25:3431-3438. doi.org/10.1007/s00167-016-4340-6

10 Rodriguez-Merchan EC, De la Corte-Rodriguez H, Alvarez-Roman MT, Gomez-Cardero P, Jimenez-Yuste V. Radiosynovectomy for the treatment of chronic hemophilic synovitis: an old technique, but still very effective. Journal of Clinical Medicine. 2022;11(24):7475. doi.org/10.3390/jcm11247475

11 Rivard GE, Girard M, Belanger R, Jutras M, Guay JP, Marton D. Synoviorthesis with colloidal 32P chromic phosphate for the treatment of hemophilic arthropathy. The Journal of bone and joint surgery American volume. 1994;76(4):482-488. doi.org/10.2106/00004623-199404000-00002

12 Zhang W-Q, Han S-Q, Yuan Z, He Y-T, Zhang H, Zhang M. Effects of intraarticular 32 P colloid in the treatment of hemophilic synovitis of the knee: A short term clinical study. Indian Journal of Orthopaedics. 2016;50:55-58. doi.org/10.4103/0019-5413.173507

13 Mortazavi S, Asadollahi S, Farzan M, Shahriaran S, Aghili M, Izadyar S, et al. 32P colloid radiosynovectomy in treatment of chronic haemophilic synovitis: Iran experience. Haemophilia. 2007;13(2):182-188. doi.org/10.1111/j.1365-2516.2006.01424.x

14 Eraghi AS, Kaseb MH, Espandar R, Mardookhpour S. The long-term effects of radioactive phosphorous synoviorthesis on hemophilic arthropathy. Blood Cells Mol Dis. 2015;55(1):68-70. doi.org/10.1016/j.bcmd.2015.03.011

15 Rodriguez-Merchan E, De la Corte-Rodriguez H, Jimenez-Yuste V. Radiosynovectomy in haemophilia: long-term results of 500 procedures performed in a 38-year period. Thrombosis Research. 2014;134(5):985-90. doi.org/10.1016/j.thromres.2014.08.023
16 Heim M, Goshen E, Amit Y, Martinowitz U. Synoviorthesis with radioactive Yttrium in haemophilia: country experience. Haemophilia. 2001;7(s2):36-9. doi.org/10.1046/j.1365-2516.2001.00108.x
17 Silva M, Luck J, Siegel M. 32P chromic phosphate radiosynovectomy for chronic haemophilic synovitis. Haemophilia. 2001;7(s2):40-9. doi.org/10.1046/j.1365-2516.2001.00109.x
18 Gualtierotti R, Solimeno LP, Peyvandi F. Hemophilic arthropathy: current knowledge and future perspectives. Journal of Thrombosis and Haemostasis. 2021;19(9):2112-21. doi.org/10.1111/jth.15444
19 Knut L. Radiosynovectomy in the therapeutic management of arthritis. World Journal of Nuclear Medicine. 2015;14(01):10-5. doi.org/10.4103/1450-1147.150509