



**NATIONAL HEMOPHILIA FOUNDATION**  
*for all bleeding and clotting disorders*

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## **MASAC RECOMMENDATIONS REGARDING RADIONUCLIDE SYNOVECTOMY**

*The following recommendations were approved by the Medical and Scientific Advisory Council (MASAC) of the National Hemophilia Foundation on April 18, 2010, and adopted by the NHF Board of Directors on June 26, 2010.*

Radionuclide synovectomy (RS) utilizing phosphorous 32-sulfur colloid (P32) has been performed in Canada since 1977 and in the United States since 1988 for rheumatoid arthritis. (1) In individuals with hemophilia and chronic synovitis, the procedure is used to reduce recurrent joint bleeding. In contrast to surgical synovectomy options, RS is relatively inexpensive and requires little factor coverage. Extensive post-procedure rehabilitation is not required to maintain good joint range-of-motion.

P32, the only isotope currently utilized for RS in North America, was chosen for its larger particle size, pure beta emission, and longer half-life. A review of the efficacy and safety of this procedure published in 2002 found no reports of malignancy associated with P32 RS. (2) Since this initial review, there have been two cases of acute lymphoblastic leukemia (ALL) reported in children with hemophilia after RS: one with precursor B-cell ALL and another with T-cell ALL.(3,4) Both patients developed leukemia within one year after uncomplicated RS, much earlier than the expected peak of radiation-induced leukemia. (5, 6) Also, both patients manifested a history of an unusual immunologic/inflammatory or autoimmune disorder prior to the development of leukemia. The patient with precursor B-cell ALL has been in remission for 10 years; the patient with T-cell ALL had a relapse and died.

There have been approximately 1100 RS procedures performed in 700 patients with hemophilia, both adults and children, in the United States since 1988. The overall cancer rate in persons with hemophilia is not known, but in one NIH-funded prospective study of malignancy in over 3,000 individuals with hemophilia in the U.S., the rate of leukemia was low, less than 1 in 33,000 person-years.(7) Pediatric ALL has a yearly incidence of 1 in 2500 children under age 15. Estimates from the CDC (number of hemophilia patients; HSS data) and the NCI (incidence of leukemia; SEER data) would suggest that there should have been 1.5 cases of ALL in the hemophilia population over the last 10 years. These 2 cases are the only reported cases of malignancy among persons with hemophilia or rheumatoid arthritis who have received the isotope P32. Due to the low frequency and the short interval between exposure and development of leukemia in these two cases, the casual relationship between radiation exposure and malignancy cannot be established conclusively, but possible causality cannot be ruled out. Additionally, the biology and epidemiology of pediatric acute lymphoblastic leukemia and adult ALL differ greatly. The majority of RS procedures have been performed in adults, so it is unclear whether these 2 pediatric ALL cases have significance for radionuclide synovectomies done in adults with hemophilia.

Accordingly, MASAC recommends the following guidelines when considering this procedure in hemophilia patients with chronic synovitis:

1. RS should be considered for patients with chronic synovitis or chronic joint bleeds not responsive to replacement therapy in whom a surgical synovectomy might pose excessive risk due to associated co-morbidities and for patients who are a post-surgical rehabilitative risk due to non-compliance.
2. Discussion about the risk/benefit ratio of RS, including the potential risk of cancer, should be undertaken with all individuals considering the procedure.
3. Written informed consent should be obtained and should clearly document that these two cases of malignancy were discussed.
4. A standard RS protocol published in the literature (2, 3) should be utilized. It should include arthrogram documentation of intra-articular needle placement and P32 distribution. There should be concomitant steroid administration to decrease leakage and inflammation.
5. All patients undergoing RS should be enrolled in a nationwide registry. Malignancy data in persons with hemophilia and a registry of all patients undergoing RS should be collected by ATHN.

References:

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4. Dunn AL, Manco-Johnson M, Busch MT, Balark KL, Abshire TC. Leukemia and P32 radionuclide synovectomy for hemophilic arthropathy. J Thromb Haemost 2005; 3:1541.
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6. Kleinerman RA. Cancer risks following diagnostic and therapeutic radiation exposure in children. Pediatr. Radiol. 2006; 36 (Suppl 2): 121-5.
7. Ragni MV, Belle SH, Jaffe RA, Duerstein SL, Bass DC, McMillan CW, Lovrien EW, Aledort LM, et al. Acquired immunodeficiency syndrome-associated non-Hodgkin's lymphoma and other malignancies in patients with hemophilia. Blood 1993; 81:1889-97.

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