

The American College of Radiology, with more than 30,000 members, is the principal organization of radiologists, radiation oncologists, and clinical medical physicists in the United States. The College is a nonprofit professional society whose primary purposes are to advance the science of radiology, improve radiologic services to the patient, study the socioeconomic aspects of the practice of radiology, and encourage continuing education for radiologists, radiation oncologists, medical physicists, and persons practicing in allied professional fields.

The American College of Radiology will periodically define new practice parameters and technical standards for radiologic practice to help advance the science of radiology and to improve the quality of service to patients throughout the United States. Existing practice parameters and technical standards will be reviewed for revision or renewal, as appropriate, on their fifth anniversary or sooner, if indicated.

Each practice parameter and technical standard, representing a policy statement by the College, has undergone a thorough consensus process in which it has been subjected to extensive review and approval. The practice parameters and technical standards recognize that the safe and effective use of diagnostic and therapeutic radiology requires specific training, skills, and techniques, as described in each document. Reproduction or modification of the published practice parameter and technical standard by those entities not providing these services is not authorized.

Revised 2019 (Resolution 41)\*

## **ACR–ACNM–ASTRO–SNMMI PRACTICE PARAMETER FOR THE PERFORMANCE OF THERAPY WITH UNSEALED RADIOPHARMACEUTICAL SOURCES**

---

### **PREAMBLE**

This document is an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. Practice Parameters and Technical Standards are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care<sup>1</sup>. For these reasons and those set forth below, the American College of Radiology and our collaborating medical specialty societies caution against the use of these documents in litigation in which the clinical decisions of a practitioner are called into question.

The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the practitioner in light of all the circumstances presented. Thus, an approach that differs from the guidance in this document, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in this document when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations of available resources, or advances in knowledge or technology subsequent to publication of this document. However, a practitioner who employs an approach substantially different from the guidance in this document is advised to document in the patient record information sufficient to explain the approach taken.

The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. Therefore, it should be recognized that adherence to the guidance in this document will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of this document is to assist practitioners in achieving this objective.

<sup>1</sup> Iowa Medical Society and Iowa Society of Anesthesiologists v. Iowa Board of Nursing, \_\_\_ N.W.2d \_\_\_ (Iowa 2013) Iowa Supreme Court refuses to find that the *ACR Technical Standard for Management of the Use of Radiation in Fluoroscopic Procedures* (Revised 2008) sets a national standard for who may perform fluoroscopic procedures in light of the standard's stated purpose that ACR standards are educational tools and not intended to establish a legal standard of care. See also, Stanley v. McCarver, 63 P.3d 1076 (Ariz. App. 2003) where in a concurring opinion the Court stated that "published standards or guidelines of specialty medical organizations are useful in determining the duty owed or the standard of care applicable in a given situation" even though ACR standards themselves do not establish the standard of care.

## I. INTRODUCTION

This practice parameter was revised collaboratively by the American College of Radiology (ACR), the American College of Nuclear Medicine (ACNM), the American Society for Radiation Oncology (ASTRO), and the Society of Nuclear Medicine and Molecular Imaging (SNMMI).

This practice parameter is intended to guide appropriately trained and licensed physicians who perform therapy procedures with unsealed radiopharmaceutical sources. Such therapy requires close cooperation and communication between the physicians who are responsible for the clinical management of the patient and those who determine the appropriateness and timing, administer radiopharmaceutical therapy, manage the attendant safety and side effects. Adherence to this parameter should help to maximize the efficacious use of these procedures; maintain safe conditions for patients, medical personnel, and others possibly exposed; and ensure compliance with applicable regulations.

Application of this parameter should be in accordance with the [ACR–AAPM–SPR Technical Standard for Therapeutic Procedures Using Radiopharmaceuticals](#) [1], as that standard also relates to the handling of radiopharmaceuticals, radiation safety, and radiation protection of patients, personnel, and the public. There must also be compliance with applicable state and federal laws and regulations.

Therapy with unsealed radiopharmaceutical sources entails the use of ionizing radiation, delivered internally via oral, parenteral, intra-articular or intracavitary methods to effectively treat cancer and other diseases. Such therapy requires detailed attention to personnel, equipment, patient and personnel safety, and continuing staff education along with close cooperation and communication between the physicians who are responsible for the clinical management of the patient. Because the practice occurs in a variety of clinical environments, the judgment of a qualified authorized user (AU) should be used to apply these practice parameters to individual practices.

This practice parameter addresses the overall role of the applicable AU (generally a nuclear radiologist, nuclear medicine physician, or radiation oncologist), the Qualified Medical Physicist, and other specialized personnel involved in the delivery of radiopharmaceutical therapy. It includes detailed discussion of several therapeutic agents that hold a long-standing, well-defined role in cancer treatment (strontium-89, samarium-153 lexidronam, yttrium-90 ibritumomab tiuxetan), whereas separate practice parameters and standards define the appropriate use of novel radiopharmaceuticals or radiopharmaceuticals whose appropriate use are evolving.

AUs are specifically trained to weigh the benefits with the risks associated with exposure to ionizing radiation and should always follow the guiding principle of limiting radiation exposure to the patient while accomplishing the therapeutic goal.

## II. DEFINITION

Therapy with unsealed sources may involve the oral, parenteral, intra-articular, or intracavitary administration of radiopharmaceuticals for the treatment of malignant and benign medical conditions.

## III. INDICATIONS

Examples of therapy with unsealed radiopharmaceutical sources include, but are not limited to, the following:

- A. Alpha emitters: Alpha emitters emit a helium nucleus upon decay (two protons/two neutrons) at very high velocity. The combination of heavy particles and high speed make for highly energetic particles capable of substantial tissue damage. Alpha particles have short tissue penetration, usually in the range of 40 to 90  $\mu\text{m}$  [2]. The limited penetration of alphas mitigates the risk of adverse side effects. The linear energy transfer (LET) of alpha particles is approximately 80 to 100 keV/ $\mu\text{m}$ , 100- to 1,000-fold higher than that of beta particles, translating into high rates of biologic damage [3]. Tissue damage is predominantly in the form of DNA strand breaks, with a propensity for the alpha-induced breaks to be double stranded and lethal. In general, double strand breaks are difficult to repair via normal DNA repair mechanisms [4]. Additionally, there is a potential role for immunologic factors to augment radiation-induced cell death [5].

- Radium-223 (more detailed information can be found in the [ACR–ACNM–ASTRO–SNMMI Practice Parameter of Therapy with Radium-223](#)).

B. Beta emitters: Beta particles are negatively charged electrons emitted from the nucleus of decaying radioactive atoms with the conversion of a neutron to a proton. They have various energies and thus a distribution of ranges from approximately 1  $\mu\text{m}$  to 10 mm. The LET of these energetic and negatively ( $-1$ ) charged particles is very low, approximately 0.2 keV/ $\mu\text{m}$ , making them sparsely ionizing [6]. Consequently, a very high radionuclide concentration is required in the targeted tissue, but the long range of beta particles leads to the production of cross-fire of the bystander effect, potentially destroying additional cells within the range of the decaying atoms that were not directly targeted by the radiopharmaceutical.

1. Iodine-131 (more detailed information can be found in the [ACR–ACNM–ASTRO SNMMI-SPR Practice Parameter for Treatment of Benign and Malignant Thyroid Disease with Iodine 131](#))
2. Iodine-131 MIBG (FDA approved July 2018, practice parameter in development)
3. Strontium-89 (strontium chloride) for adjuvant and palliative treatment of painful skeletal metastases
4. Samarium-153 lexidronam ethylene diamine tetra methylene phosphonic acid (EDTMPA), for adjuvant and palliative treatment of painful skeletal metastases
5. Lutetium-177 DOTATATE (FDA approved January 2018, practice parameter in development)
6. Yttrium-90 ibritumomab tiuxetan (murine monoclonal antibody targeting the CD20 antigen) for treatment of patients with CD20-positive follicular B-cell non-Hodgkin lymphoma (NHL).
7. Yttrium-90 microspheres. These are considered brachytherapy sealed sources and devices. (for further information see the [ACR–ABS–ACNM–ASTRO–SIR–SNMMI Practice Parameter for Radioembolization with Microsphere Brachytherapy Device \(RMBD\) for Treatment of Liver Malignancies](#)) [7].

Additional unsealed radiopharmaceuticals for therapy include phosphorus-32 (sodium phosphate) for treatment of myeloproliferative disorders, phosphorus-32 (colloidal chromic phosphate) for treatment of malignant ascites/effusions, and iodine-131 radio immunotherapy for NHL. These radiopharmaceuticals are not currently available and will not be discussed further.

#### IV. QUALIFICATIONS AND RESPONSIBILITIES OF PERSONNEL

The qualifications and responsibilities of physicians and other personnel performing these therapeutic procedures should be in accordance with the [ACR–AAPM–SPR Technical Standard for Therapeutic Procedures Using Radiopharmaceuticals](#) [1] and/or the [ACR–ASTRO Practice Parameter for Radiation Oncology](#) [8]. In addition, training and experience must be in compliance with the applicable laws and regulations, including 10 CFR 35.390 [9].

#### V. SPECIFICATIONS OF THE EXAMINATION AND TREATMENT

The written or electronic request for a radiopharmaceutical procedure should provide sufficient information to demonstrate the medical necessity of the examination and allow for its proper performance.

Documentation that satisfies medical necessity includes 1) signs and symptoms and/or 2) relevant history (including known diagnoses). Additional information regarding the specific reason for the procedure or diagnosis would be helpful and may at times be needed to allow for the proper performance of the procedure.

The request for the procedure must be originated by a physician or other appropriately licensed health care provider. The accompanying clinical information should be provided by a physician or other appropriately licensed health

care provider familiar with the patient’s clinical problem or question and consistent with the state’s scope of practice requirements. (ACR Resolution 35, adopted in 2006 - revised in 2016, Resolution 12-b)

#### A. General Procedures

1. Clinical evaluation – In concordance with the [ACR–ASTRO Practice Parameter for Radiation Oncology](#) and the [ACR–ASTRO Practice Parameter for Communication: Radiation Oncology](#) [8,10]. The treating physician’s initial evaluation of the patient must include review of the patient’s history, physical examination, and pertinent diagnostic studies and reports, including a complete history of all previous radiotherapy and radiopharmaceutical therapy. These findings should be communicated to the referring physician and other physicians involved in the patient’s care in a timely manner. For radiopharmaceutical treatments that are potentially marrow-toxic, a complete blood count obtained within the previous 7 to 10 days, and including differential and platelet count, should be part of the initial assessment and of each pretreatment evaluation.
2. Quality management – In order to use therapeutic unsealed radiopharmaceuticals, a “quality management” program must be in place as required by the US Nuclear Regulatory Commission (NRC) or by Agreement State regulations. Key elements of such a program include: written directives; specified procedures for shipment acceptance, handling, and storage; duplicative procedures for patient identification; careful record-keeping to ensure prescribed administered activity; procedures to minimize the possibility of infiltration for radiopharmaceuticals that are administered intravenously; procedures for minimizing radiation exposure or radiopharmaceutical contamination of personnel, family members of patients, and the public (eg, alerts regarding possible current or future pregnancy); procedures for containment of radioactivity; and an audit mechanism to ensure compliance with the program.
3. Informed consent – Informed consent must be obtained and documented. Given the unique nature of therapy with unsealed sources, the informed consent should ideally address known potential near and long-term radiation risks to patient. It is also encouraged that the consent and instructions include a statement regarding risk of exposing caregivers and family members to unnecessary radiation if radiation precautions are not appropriately followed. See the [ACR Practice Parameter on Informed Consent – Radiation Oncology](#) [11].
4. Treatment – The procedure and follow-up should be performed according to predetermined facility policies and procedures that may be unique for each type of application.
5. The decision to provide therapy in a pregnant, breastfeeding, or lactating patient should only be made with full understanding and provided with careful patient and provider dialogue. Pregnancy should be excluded prior to radiopharmaceutical administration by one of the following: negative human chorionic gonadotropin test, documented hysterectomy, postmenopausal state (absence of menstrual bleeding for 2 years), or by premenarche (patient age 10 years or younger).
6. Radiation precautions – Radiation precautions and patient release criteria may be regulated by the NRC or by the Agreement State. The radiation safety officer, medical physicist, or health physicist for the local facility should follow the applicable federal or state regulations. Details on the federal regulations can be obtained at the NRC website, [www.nrc.gov](http://www.nrc.gov).

Under the guidelines of federal code 10 CFR 35.75 [12,13] and key sections of NUREG 1556 [14], the patient may be released if the total effective dose equivalent to any other individual (including any caregiver or family member) who is exposed to the patient is not likely to exceed 5 mSv (0.5 rem). If the total effective dose equivalent is likely to exceed 1 mSv (0.1 rem) to any individual, written instructions must be provided to the patient on actions to maintain doses to others by utilizing the “as low as reasonably achievable” (ALARA) [15] principle. Agreement States may have specific rules and regulations regarding release of patients with significant residual activity.

The dose limits specified by the National Council on Radiation Protection & Measurements (NCRP) differ somewhat from the NRC regulations [16]. Because the fetus and children are more sensitive to radiation injury than adults, the NCRP specifies that children and pregnant women, whether or not they are members of the patient's household, should be limited to 1 mSv (0.1 rem). Any individual who has no familial connection to the patient and for whom there is no emotional benefit should also be limited to 1 mSv, which is also the NRC dose limit to a member of the public.

Many radiation survey meters measure exposure rates in milliroentgens/hour (mR/h). For purposes of radiation protection and for low LET radiation (including beta particles and most x-rays and gamma rays), the organizations that developed this consensus document accept the approximation that 1 mR, 0.01 mSv, and 1 mrem are equivalent. Thus, an exposure rate of 7 mR/h at 1 m is an adequate approximation to the dose rate, 0.07 mSv/h (7.0 mrem/h) at 1 m.

All routine blood work and laboratory specimens should be obtained prior to treatment with the radiopharmaceutical. If confinement in a health care facility is needed, it is not usually necessary to store body effluents, such as urine, stool, or vomitus. For effluent disposal, where acceptable under state or federal regulations, the toilet should be flushed two or three times after each use to ensure sufficient dilution and disposal of radioactivity. Food trays and linens should be stored in the patient's room until monitored and cleared by radiation safety staff. The patient must remain in the room except in a medical or nonmedical (eg, fire) emergency, and access by personnel and visitors must be limited. All trash and residual nondisposable items must be monitored after the patient's release and stored until radiation levels reach the statutory level defined for safe disposal or reuse. (In some jurisdictions, items in decay storage must be contained in safe storage for 10 half-lives or when radiation levels are indistinguishable from background.) Once all known contamination is removed from the room, the room must be surveyed to verify that the radiation levels and removable contamination are sufficiently low to permit its general use. The room may not be used until the survey is performed [16]. Room and contents release survey must be documented in the patient and facility records.

If the physician responsible for the patient's care during their confinement (eg, hospital admission) is different from the physician who is responsible for and administers the radiopharmaceutical, there must be a mechanism to prevent premature discharge or release of the patient from confinement.

## B. Specific Procedures Beta Emitters for Palliation of Bone Metastases

### 1. Strontium-89

#### a. Background

Strontium-89 was one of the first bone-seeking radiopharmaceuticals approved for the treatment of painful bone metastases. It has a physical half-life of 50.6 days and emits a beta particle with a maximum energy of 1.46 MeV and an average soft-tissue range of 2.4 mm. As a calcium analog, strontium-89 is taken up in the skeletal system in proportion to osteoblastic activity, with osteoblastic metastatic bone lesions accumulating the radiopharmaceutical up to 10-fold greater than normal bone [17]. The radiopharmaceutical can remain in these lesions for an extensive period, with 20% of injected activity present in the skeleton after 90 days [18]. Strontium emits a comparatively small fraction of gamma photons (0.01%) and hence poses minimal radiation risk to those in contact with the patient while also precluding imaging or dosimetry studies.

#### b. Summary of selected data

Strontium-89 has been investigated primarily in the context of osseous metastasis in prostate cancer. The use of this radiopharmaceutical in other malignancies, including breast and lung cancer, has also been investigated.

i. A phase III placebo-controlled randomized controlled trial evaluated conventional palliative radiotherapy ± strontium-89 as a single injection of 10.8 mCi or placebo in 126 patients with metastatic castration-resistant prostate cancer (CRPC) [19].

1. Complete pain relief at 3 months was achieved in a greater number of patients treated with strontium-89 compared with placebo (40% versus 23%).

2. There was a significant reduction in the need for subsequent and continued analgesic use in the strontium-89 group ( $P < .05$ ).
  3. Significantly fewer patients in the strontium-89 group experienced new sites of pain compared with placebo ( $P < .002$ ), which translated into a longer disease-free interval and subsequent retreatment with radiotherapy (35 weeks versus 20 weeks).
  4. Quality-of-life analysis demonstrated superiority of strontium-89 with alleviation of pain and improvement in physical activity being statistically significant ( $P < .05$ ).
- ii. A study including 284 patients with symptomatic bone metastases from prostate cancer who were randomly assigned to either conventional palliative radiotherapy or 5.4 mCi of strontium-89 treatment found [20] that:
1. The analgesic effect was similar in both treatment groups, but fewer patients developed new sites of pain in the strontium-89 group ( $P < .05$ ).
  2. Significantly fewer patients required local radiotherapy to new sites following strontium-89 treatment compared with the local radiotherapy group ( $P < .01$ ).
  3. Platelet and leukocyte counts fell by approximately 35% after strontium-89 treatment, but functional sequelae were rare.
  4. There was no significant difference in overall survival between groups ( $P = .10$ ).
- c. Clinical results  
Approximately 57% to 92% of patients respond to therapy. Pain relief onset typically begins in 2 to 4 weeks after administration, and its effect is maintained for 4 to 15 months with an average 6-month duration [21,22]. A small percentage of patients may experience a transient flare phenomenon 2 to 3 days after injection. This flare is usually mild, controlled well with analgesics, and heralds a good response [23].
- d. General treatment recommendations  
For strontium-89, the current standard administered activity is 1.48 to 2.22 MBq (40-60  $\mu$ Ci per kilogram of body weight, approximately 4 mCi [148 MBq] for standard weight) given by intravenous infusion over several minutes.
2. Samarium-153 lexidronam
- a. Background  
Samarium-153 is a radiopharmaceutical indicated for metastatic bone pain palliation. The isotope is bound to ethylenediamine tetramethylene (EDTMP) with the phosphonate groups present in the EDTMP providing its biologic properties, accumulating in skeletal tissue in association with hydroxyapatite in an identical manner to technetium-99m-methyl diphosphonate-MDP [23]. Bone metastases accumulate five times more samarium-153 than healthy bone tissue. Compared with strontium-89, samarium-153 has a physical half-life of only 46.3 hours. Samarium-153 emits both beta particles and gamma radiation. The beta particles have a maximum energy of 0.81 MeV and an average soft-tissue range of 0.8 mm. The beta decay is accompanied by 28% emission of gamma rays of 103.2 keV, which can be detected using gamma camera for a low-resolution bone scan and dosimetry.
- b. Summary of selected data  
Samarium-153 has primarily been investigated in the context of osseous metastatic prostate cancer.
- A phase III randomized controlled trial of 152 patients with CRPC randomized patients to radioactive samarium-153 at 1 mCi/kg versus nonradioactive samarium-152 [24].
- i. There was a significant improvement in pain descriptor scale scores by week one and in pain intensity visual analogue scale scores by week two for patients treated with samarium-153.
  - ii. There was significant reduction in opioid consumption by week 3 with samarium-153 use.
  - iii. Grade 3 thrombocytopenia and leukopenia developed in 3% and 5% of patients, respectively, in the samarium-153 treatment arm. Counts returned to baseline after approximately 8 weeks. No grade 4 hematologic toxicity was noted in either platelets or white blood cells.
  - iv. There was no significant difference in overall survival between groups.

- c. Clinical results
 

Approximately 62% to 84% of patients respond to therapy [22]. Pain relief usually commences within 1 week of administration and as early as 2 days in some individuals. The palliative effect endured anywhere from 4 to 35 weeks, with an average of 8 weeks [25].
  - d. General treatment recommendations
 

The recommended samarium-153 lexidronam activity is 37.0 MBq (1.0 mCi) per kilogram of body weight, given intravenously over several minutes. If desired, imaging may be performed between 2 and 24 hours postinjection.
3. General recommendations for all radiopharmaceuticals used to treat skeletal metastases
    - a. Patient
 

Patients with multiple osseous metastases that show increased tracer uptake on bone imaging, who are obtaining diminishing relief from other methods of pain management (eg, analgesics, bisphosphonates, external-beam irradiation), and whose bone marrow is competent, are candidates for radiopharmaceutical therapy. Complete blood cell count with platelets should be obtained within 7 to 10 days prior to therapy. Platelet count should be greater than 60,000 to 100,000/ $\mu$ L, leukocyte count greater than 2,400 to 5,000/ $\mu$ L, and absolute granulocyte count greater than 2,000/ $\mu$ L. Patients with disseminated intravascular coagulation (DIC) must be excluded from therapy. Other patients may be treated after a case-specific evaluation, as adjuvant therapy to delay symptomatic skeletal metastases. Urinary incontinence is not a contraindication to treatment, but the patient or caregiver should be instructed on how to minimize radiation contamination from spilled urine. For samarium-153 lexidronam and strontium-89, bladder catheterization should be considered for patients incontinent of urine, to minimize the risk of radioactive contamination.
    - b. Complications
 

A “flare” phenomenon occurs in some patients with transient worsening of pain within several days after treatment. This flare is a self-limited process, although it can occasionally be severe. Patients should be counseled concerning the possibility of a flare phenomenon. The pain associated with the flare phenomenon can usually be managed with analgesics or corticosteroids. For intravenously administered radiotherapy, extravasation of the radiopharmaceutical should be avoided by secure intravenous access confirmed prior to isotope administration. Although local skin damage is rare, some clinicians believe it is prudent to follow a vesicant protocol for radiotherapy infusion [26]. For both samarium-153 and strontium-89, bone marrow depression may occur transiently, with a nadir at about 3 to 6 weeks, with recovery in about 3 to 6 additional weeks. Complete blood and platelet counts should be followed routinely for 8 to 12 weeks.
    - c. Interactions with other forms of treatment
      - i. Hormone administration need not be discontinued before the administration of radiopharmaceutical therapy because it does not interfere with the mechanism of action and does not potentiate any side effects.
      - ii. External-beam radiation therapy may be used synchronously with radiopharmaceutical therapy for local treatment of selected sites, especially those in which pathologic fracture or cord compression might occur. Careful evaluation of complete blood and platelet counts is required when these potentially myelosuppressive therapies are combined.
      - iii. Caution should be exercised when delivering concomitant myelosuppressive chemotherapy to these patients.
  4. Radiation precautions
 

No special precautions are required for strontium-89 as long as the patient is continent of urine and feces. Because samarium-153 lexidronam has a gamma-ray emission, the patient may be released if the total effective dose equivalent to any other individual who is exposed to the patient is not likely to exceed 5 mSv (0.5 rem) per year. Applicable state or NRC/federal regulations and facilities policies must be followed.
  5. Retreatment
 

Retreatment may be administered if initial treatment fails or if symptoms recur. Special consideration should be given to recovery of bone marrow and blood counts. Retreatment may be given after adequate bone marrow recovery, typically in 2 to 3 months.

6. Management should be coordinated with clinical services and with other health care providers involved in management of the patient, especially radiation oncology, if external beam irradiation has been used or is being considered.

### C. Specific Procedures Yttrium-90 Ibritumomab Tiuxetan for Radioimmunotherapy of Non-Hodgkin's Lymphoma

#### 1. Radiopharmaceuticals

The marker CD20 is expressed in the pro-B-cell stage as the B-cell evolves from the stem cell precursor and throughout the life of the mature B-cell, but is neither present in the stem cells nor in plasma cells derived from B-cells. CD20 is also expressed on many of the B-cell lymphomas: follicular lymphoma and diffuse large B-cell lymphoma. Thus, CD20 is an attractive target, potentially sparing stem cells and allowing regeneration of normal B-cells.

Yttrium-90 ibritumomab tiuxetan consists of ibritumomab, the murine IgG1 kappa monoclonal antibody from which rituximab was developed, and tiuxetan, which stably chelates yttrium-90 for therapy. Iodine-131 tositumomab is a murine IgG2a lambda monoclonal antibody covalently linked to iodine-131. Both antibodies are directed against the CD20 antigen.

#### 2. Patients

- a. Patients with CD20-positive follicular B-cell NHL, including patients who are refractory to rituximab, are candidates for radioimmunotherapy. The radiopharmaceutical is indicated for the treatment of relapsed or refractory low-grade or follicular B-cell NHL [27] as well as the treatment of previously untreated follicular NHL in patients who achieve a partial or complete response to first-line chemotherapy [28].
- b. Summary of selected data
  - i. One study evaluated ibritumomab tiuxetan in the treatment of rituximab-refractory follicular NHL [27].
    - Fifty-seven patients were treated. The median age was 54 years, 74% had tumors that were  $\geq 5$  cm. All had been extensively pretreated.
    - The overall response rate for the 57 patients with follicular NHL was 74% (15% complete response [CR] and 59% partial response [PR]).
    - The Kaplan-Meier-estimated time-to-progression was 6.8 months for all patients and 8.7 months for responders.
    - Adverse events were primarily hematologic; the incidence of grade 4 neutropenia, thrombocytopenia, and anemia was 35%, 9%, and 4%, respectively.
  - ii. An international, randomized, phase III trial evaluated the efficacy and safety of consolidation with yttrium-90 ibritumomab tiuxetan in patients with advanced-stage follicular lymphoma in first remission [28].
    - A total of 414 patients (consolidation, n = 208; control, n = 206) were enrolled at 77 centers.
    - Yttrium-90 ibritumomab tiuxetan consolidation significantly prolonged median progression-free survival (PFS) regardless of whether patients achieved PR, CR, or unconfirmed CR.
    - The most common toxicity was hematologic; grade 3 or 4 infections occurred in 8% of patients.
- c. The principal toxicity of anti-CD20 radioimmunotherapy is hematologic. A careful hematologic evaluation must be performed prior to therapy. Because lymphomatous involvement of the bone marrow will increase the radiation dose to the marrow, a bone marrow biopsy within 6 to 12 weeks of anticipated isotope therapy must be evaluated by an experienced hematopathologist to document less than 25% bone marrow involvement by tumor. A recent complete blood count obtained 7 to 10 days prior to anticipated isotope therapy should be reviewed, to confirm absolute neutrophil count (ANC) greater than 1,500 and platelet count greater than 100,000.

#### 3. Dosimetry and assessment of biodistribution

- a. When clinical circumstances warrant and the isotopic emission creates the opportunity, individual patient dosimetry and/or biodistribution can be considered by appropriate imaging or other techniques.

4. Administered activity
  - a. According to manufacturer's instructions, the therapeutic dose of yttrium-90 ibritumomab tiuxetan is administered on days 7 to 9, with day 1 being the day of the administration of the cold antibody (see below).
  - b. Biodistribution of radiolabeled antibody is improved by concurrent administration of unlabeled radiopharmaceuticals in order to saturate readily accessible CD20-positive sites, including circulating B-cells and cells in the spleen. Biodistribution of radiolabeled ibritumomab tiuxetan is improved with the prior administration of rituximab (cold antibody).
  - c. The therapeutic dosage of yttrium-90 ibritumomab tiuxetan, after an infusion of rituximab, is 14.8 MBq/kg (0.4 mCi/kg) for patients with a platelet count greater than 150,000 cells/ $\mu$ L and 11.1 MBq/kg (0.3 mCi/kg) for patients with platelet count of 100,000 to 149,000 cells/ $\mu$ L. The maximum allowable dosage of yttrium-90 ibritumomab tiuxetan is 1.184 GBq (32.0 mCi).
  - d. Because yttrium-90 is a pure beta emitter, on-site administered-dose measurement can be difficult. A standard operating procedure for evaluation, administration, and follow-up should be established with the help of a radiopharmacist and Qualified Medical Physicist.
  
5. Complications
  - a. Hypersensitivity reactions may occur and may be severe. Patients who have previously received murine proteins should be screened for human anti-mouse antibodies (HAMA). Patients who are positive are likely to be at increased risk of anaphylaxis and serious hypersensitivity and may show altered biodistribution of the antibody. Known hypersensitivity to rituximab or murine proteins is considered a contraindication to administration of yttrium-90 ibritumomab tiuxetan. Premedication with acetaminophen and diphenhydramine is recommended and should be considered prior to infusion, but patients should be carefully monitored. Reactions to the infusion of unlabeled rituximab are common. Although reactions to subsequently infused ibritumomab tiuxetan are uncommon, a physician must be present during the infusion. Medications for the treatment of hypersensitivity reactions (eg, epinephrine, antihistamines, and corticosteroids) and equipment for resuscitation must be immediately available.
  - b. The most common serious adverse reactions associated with yttrium-90 ibritumomab tiuxetan are severe or life-threatening cytopenias. Retrospective studies showed grade 3 or 4 thrombocytopenia in 57% of patients. The percent decline in platelets was 79% ( $\pm$ 17%). The ANC nadir for yttrium-90 ibritumomab tiuxetan was  $\pm$ 36 days [29]. Precautions include delay or avoidance of treatment of patients who have more than 25% of bone marrow involved, or who have poor bone marrow reserve (including but not limited to prior stem-cell or bone marrow transplant, ANC less than 1,500 cells/ $\mu$ L, or previous failure of stem-cell collection). The radiation dose is modified according to the pretreatment platelet counts. Blood counts should be monitored weekly for at least 10 to 12 weeks, or more frequently as needed until recovery occurs. Stem-cell support and/or transfusions are provided as necessary, and cases of febrile neutropenia or infection are treated as appropriate.
  
6. Interactions with other forms of treatment
  - a. A time interval sufficient to allow for bone marrow recovery after cytotoxic chemotherapy is recommended. Concomitant use of chemotherapy with yttrium-90 ibritumomab tiuxetan has not been fully evaluated and should be considered with caution when not performed in conjunction with a defined research protocol.
  - b. Prior to radiopharmaceutical therapy, external beam radiation therapy may be necessary for local treatment of selected sites, especially with life-threatening or function-threatening presentations (such as fracture or spinal cord compression). Careful consideration must be given to the amount of bone marrow treated, as treatment of a large percentage of the patient's bone marrow is likely to significantly affect the ability to tolerate radioimmunotherapy.
  - c. The concern that patients treated with yttrium-90 ibritumomab tiuxetan may have severe marrow impairment rendering them ineligible for further therapy is not substantiated by the results of several studies comparing retreatment with chemotherapy, stem-cell mobilization, and successful autotransplantation of treated patients to otherwise matched control groups [30].

- d. Adding ibritumomab tiuxetan to marrow-ablative CT regimens is also being tested in poor risk NHL and diffuse large B-cell lymphoma (DLBCL) as well in patients  $\geq 60$  years. Data from phase II trials are encouraging, with acceptable toxicity (<http://dx.doi.org/10.1016/j.critrevonc.2016.07.008>).

7. Radiation precautions

- a. No special precautions are necessary for yttrium-90 ibritumomab tiuxetan beyond the usual care taken to minimize radiation exposure to patients and medical personnel, consistent with institutional radiation safety practices, patient management procedures, and applicable regulations. Yttrium-90 is a pure beta emitter, and safety precautions for medical professionals include universal precautions, with the addition of acrylic shielding for the yttrium-90 ibritumomab tiuxetan. Patients may be released immediately after administration of yttrium-90 ibritumomab tiuxetan, with basic instructions.
- b. Applicable federal or state regulations and facility policies must be followed.

8. As with all other forms of therapy with unsealed sources, patient management should be coordinated with other involved health care providers.

#### D. Posttherapy Follow-Up

Physicians using unsealed radiopharmaceutical sources for therapy should participate with the patient's primary physician in the follow-up and management of all patients treated with curative, adjuvant, or palliative intent and should document the outcome of therapy, including results of treatment (tumor control, survival, degree of palliation, time to retreatment) and significant sequelae [31]. Because the effect of radionuclide therapy may require time to be evident, patients should be seen in follow-up within intervals appropriate for the specific agent and therapeutic intent.

## VI. DOCUMENTATION

Reporting should be in accordance with the [ACR–ASTRO Practice Parameter for Communication: Radiation Oncology](#) [10].

The report should include the radiopharmaceutical used, the dose and route of administration, as well as any other pharmaceuticals administered, also with dose and route of administration.

## VII. STATEMENT ON THERAPEUTIC USE OF UNSEALED RADIOPHARMACEUTICAL SOURCES

On the basis of their education, training pathway(s), experience, initial board certification(s), subsequent fellowship training, and maintenance of certification(s), NRC AU status, and clinical work experience, diagnostic radiologists (DRs), interventional radiologists (IRs), nuclear radiologists (NRs), nuclear medicine physicians (NMs), and radiation oncologists (ROs) may have the necessary qualifications to supervise and perform therapies using unsealed radioisotopes. Although it is recognized that individual physician variations and state and federal regulatory requirements may, of necessity, dictate site-specific practice patterns, these physicians may best participate in the practice according to their special interests and qualifications. In most clinical settings, one of the following common practice paradigms generally applies:

- Physicians who are board-eligible or board-certified in DR, NR, NM, IR/DR, or RO but do not hold AU status: These physicians may participate in the practice of therapy with specific unsealed radiopharmaceuticals under the supervision of an AU for the specific therapeutic radiopharmaceutical. Although they may not issue written directives for those specific radiopharmaceuticals, they may administer such a dosage as designated by an AU.
- Physicians who are board-certified in DR, NR, NM, IR/DR or RO and hold AU status based on that certification and site-specific credentialing: These physicians may practice radioisotope therapy under their own AU and facility license qualifications.

## VIII. RADIATION SAFETY

Radiologists, medical physicists, registered radiologist assistants, radiologic technologists, and all supervising physicians have a responsibility for safety in the workplace by keeping radiation exposure to staff, and to society as a whole, “as low as reasonably achievable” (ALARA) and to assure that radiation doses to individual patients are appropriate, taking into account the possible risk from radiation exposure and the diagnostic image quality necessary to achieve the clinical objective. All personnel that work with ionizing radiation must understand the key principles of occupational and public radiation protection (justification, optimization of protection and application of dose limits) and the principles of proper management of radiation dose to patients (justification, optimization and the use of dose reference levels)

[http://www-pub.iaea.org/MTCD/Publications/PDF/Pub1578\\_web-57265295.pdf](http://www-pub.iaea.org/MTCD/Publications/PDF/Pub1578_web-57265295.pdf).

Facilities and their responsible staff should consult with the radiation safety officer to ensure that there are policies and procedures for the safe handling and administration of radiopharmaceuticals and that they are adhered to in accordance with ALARA. These policies and procedures must comply with all applicable radiation safety regulations and conditions of licensure imposed by the Nuclear Regulatory Commission (NRC) and by state and/or other regulatory agencies. Quantities of radiopharmaceuticals should be tailored to the individual patient by prescription or protocol

Nationally developed guidelines, such as the [ACR Appropriateness Criteria](#)<sup>®</sup>, should be used to help choose the most appropriate imaging procedures to prevent unwarranted radiation exposure.

Additional information regarding patient radiation safety in imaging is available at the Image Gently<sup>®</sup> for children ([www.imagegently.org](http://www.imagegently.org)) and Image Wisely<sup>®</sup> for adults ([www.imagewisely.org](http://www.imagewisely.org)) websites. These advocacy and awareness campaigns provide free educational materials for all stakeholders involved in imaging (patients, technologists, referring providers, medical physicists, and radiologists).

Radiation exposures or other dose indices should be measured and patient radiation dose estimated for representative examinations and types of patients by a Qualified Medical Physicist in accordance with the applicable ACR Technical Standards. Regular auditing of patient dose indices should be performed by comparing the facility’s dose information with national benchmarks, such as the ACR Dose Index Registry, the NCRP Report No. 172, Reference Levels and Achievable Doses in Medical and Dental Imaging: Recommendations for the United States or the Conference of Radiation Control Program Director’s National Evaluation of X-ray Trends. (ACR Resolution 17 adopted in 2006 – revised in 2009, 2013, Resolution 52).

- A. Whenever possible, removal of bodily fluids and/or tissue should be avoided following therapeutic instillation of unsealed radioactive sources into any body area until such time as permitted by the facility radiation safety officer or responsible provider.
- B. Patient instructions should specify a time interval for safe removal of body fluids and/or tissues based on the therapeutic isotope employed in the procedure.
- C. For in-patient facilities, patient orders should specify procedures for handling of removed bodily fluids and/or tissues as well as notification of the responsible radiation safety officer or provider.
- D. In the unlikely event of a patient death following instillation of unsealed therapeutic radionuclides, the responsible radiation safety officer or provider should be notified immediately of the death; and handling of the body, including cremation, should be directed by that individual.

## IX. QUALITY CONTROL AND IMPROVEMENT, SAFETY, INFECTION CONTROL, AND PATIENT EDUCATION

Policies and procedures related to quality control and improvement, patient education, infection control, and safety should be developed and implemented in accordance with the ACR Policy on Quality Control and Improvement, Safety, Infection Control, and Patient Education appearing under the heading *Position Statement on QC & Improvement, Safety, Infection Control, and Patient Education* on the ACR website (<https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/Quality-Control-and-Improvement>).

Equipment performance monitoring should be in accordance with the [ACR–AAPM Technical Standard for Nuclear Medical Physics Performance Monitoring of Gamma Cameras](#) [32].

## ACKNOWLEDGEMENTS

This practice parameter was revised according to the process described under the heading *The Process for Developing ACR Practice Parameters and Technical Standards* on the ACR website (<https://www.acr.org/Clinical-Resources/Practice-Parameters-and-Technical-Standards>) by the Committee on Practice Parameters – Nuclear Medicine and Molecular Imaging of the ACR Commissions on Nuclear Medicine and Molecular Imaging and the Committee on Practice Parameters – Radiation Oncology of the ACR Commission on Radiation Oncology, in collaboration with the ACNM, the ASTRO, and the SNMMI.

Collaborative Committee – members represent their societies in the initial and final revision of this practice parameter

### ACR

Kevin P. Banks, MD, Co-Chair  
Bassem I. Zaki, MD, Co-Chair  
Paul E. Wallner, DO, FACR

### ACNM

Bital Savir-Baruch, MD

### ASTRO

Adam P. Dicker, MD, PhD  
Zoubir Ouhib, MS, FACR  
James S. Welsh, MD

### SNMMI

Hossein Jadvar, MD, PhD, MPH, MBA  
Erik Mittra, MD, PhD  
Rathan M. Subramaniam, MD, PhD, MPH

Committee on Practice Parameters and Technical Standards – Nuclear Medicine and Molecular Imaging  
(ACR Committee responsible for sponsoring the draft through the process)

Kevin P. Banks, MD, Co-Chair  
Richard K. J. Brown, MD, FACR, Co-Chair  
Alexandru C. Bageac, MD, MBA  
Twyla B. Bartel, DO, MBA  
Murray D. Becker, MD, PhD, FACR  
Erica J. Cohen, DO, MPH  
Joanna R. Fair, MD  
Erin C. Grady, MD

Edward D. Green, MD  
Jeffrey S. Kempf, MD, FACR  
Jennifer J. Kwak, MD  
Charito Love, MD  
Syam P. Reddy, MD  
Levi Sokol, MD  
Rathan M. Subramaniam, MD, PhD, MPH  
Stephanie P. Yen, MD

Committee on Practice Parameters – Radiation Oncology  
(ACR Committee responsible for sponsoring the draft through the process)

Alan C. Hartford, MD, PhD, FACR, Chair  
Naomi R. Schechter, MD, Vice Chair  
Nathan H. J. Bittner, MD  
Samuel T. Chao, MD  
Chee-Wai Cheng, PhD, FAAPM  
Neil B. Desai, MD  
Nancy A. Ellerbroek, MD, FACR  
Beth A. Erickson, MD, FACR  
Mark Hurwitz, MD  
Lesley A. Jarvis, MD, PhD

Join Y. Luh, MD  
Matthew Poggi, MD  
Helen A. Shih, MD  
Nikhil Thaker, MD  
Paul E. Wallner, DO, FACR  
Kristina L. Woodhouse, MD  
Ying Xiao, PhD  
Sue S. Yom, MD, PhD  
Bassem I. Zaki, MD

Don C. Yoo, MD, FACR, Chair of the Commission Nuclear Medicine and Nuclear Medicine  
Seth A. Rosenthal, MD, FACR, Chair, Commission on Radiation Oncology  
Jacqueline Anne Bello, MD, FACR, Chair, Commission on Quality and Safety

Matthew S. Pollack, MD, FACR, Chair, Committee on Practice Parameters and Technical Standards  
Mary S. Newell, MD, FACR, Vice Chair, Committee on Practice Parameters and Technical Standards

#### Comments Reconciliation Committee

Darlene F. Metter, MD, FACR, Chair  
Ralph P. Lieto, MS, FACR, Co-Chair  
Kevin P. Banks, MD  
Jacqueline A. Bello, MD, FACR  
Richard K. J. Brown, MD, FACR  
Adam P. Dicker, MD, PhD  
Richard Duszak, Jr., MD, FACR  
Michael L. Goris, MD  
Alan C. Hartford, MD, PhD, FACR  
Hossein Jadvar, MD, PhD, MPH, MBA  
Paul A. Larson, MD, FACR  
Erik Mittra, MD, PhD  
Mary S. Newell, MD, FACR

Zoubir Ouhib, MS, FACR  
Matthew S. Pollack, MD, FACR  
Seth A. Rosenthal, MD, FACR  
Bital Savir-Baruch, MD  
Naomi R. Schechter, MD  
Rathan M. Subramaniam, MD, PhD, MPH  
Timothy L. Swan, MD, FACR  
Paul E. Wallner, DO, FACR  
James S. Welsh, MD  
William Wong, MD  
Don C. Yoo, MD, FACR  
Bassem I. Zaki, MD

#### **REFERENCES**

1. American College of Radiology. ACR–AAPM–SPR technical standard for therapeutic procedures using radiopharmaceuticals. 2016; Available at: <https://www.acr.org/-/media/ACR/Files/Practice-Parameters/RadioPharm.pdf>. Accessed October 24, 2018.
2. Sartor O, Sharma D. Radium and other alpha emitters in prostate cancer. *Translational andrology and urology*. 2018;7(3):436-444.
3. Aghevlian S, Boyle AJ, Reilly RM. Radioimmunotherapy of cancer with high linear energy transfer (LET) radiation delivered by radionuclides emitting alpha-particles or Auger electrons. *Advanced drug delivery reviews*. 2017;109:102-118.
4. Wieder HA, Lassmann M, Allen-Auerbach MS, Czernin J, Herrmann K. Clinical use of bone-targeting radiopharmaceuticals with focus on alpha-emitters. *World journal of radiology*. 2014;6(7):480-485.
5. Gameiro SR, Jammeh ML, Wattenberg MM, Tsang KY, Ferrone S, Hodge JW. Radiation-induced immunogenic modulation of tumor enhances antigen processing and calreticulin exposure, resulting in enhanced T-cell killing. *Oncotarget*. 2014;5(2):403-416.
6. Kassis AI. Therapeutic radionuclides: biophysical and radiobiologic principles. *Seminars in nuclear medicine*. 2008;38(5):358-366.
7. American College of Radiology. ACR–ABS–ACNM–ASTRO–SIR–SNMMI practice parameter for radioembolization with microsphere brachytherapy device (RMBD) for treatment of liver malignancies. 2014; Available at: <https://www.acr.org/-/media/ACR/Files/Practice-Parameters/RMBD.pdf>. Accessed October 24, 2018.
8. American College of Radiology. ACR–ASTRO practice parameter for radiation oncology. 2018; Available at: <https://www.acr.org/-/media/ACR/Files/Practice-Parameters/RadOnc.pdf>. Accessed March 26, 2018.
9. United States Nuclear Regulatory Commission. § 35.390 training for use of unsealed byproduct material for which a written directive is required. 2009; Available at: <https://www.nrc.gov/reading-rm/doc-collections/cfr/part035/full-text.html#part035-0390>. Accessed October 17, 2018.
10. American College of Radiology. ACR–ASTRO practice parameter for communication: radiation oncology. 2014; Available at: <https://www.acr.org/-/media/ACR/Files/Practice-Parameters/Communication-RO.pdf>. Accessed March 26, 2018.
11. American College of Radiology. ACR practice parameter on informed consent - radiation oncology. 2017; Available at: <https://www.acr.org/-/media/ACR/Files/Practice-Parameters/InformedConsent-RO.pdf>. Accessed March 26, 2018.
12. United States Nuclear Regulatory Commission. § 35.75 release of individuals containing unsealed byproduct material or implants containing byproduct material. 2007; Available at: <http://www.nrc.gov/reading-rm/doc-collections/cfr/part035/part035-0075.html>. Accessed May 13, 2014.

13. United States Nuclear Regulatory Commission. NRC policy on release of iodine-131 therapy patients under 10 CFR 35.75 to locations other than private residences. RIS 2011-01. 2011; Available at: <http://pbadupws.nrc.gov/docs/ML1036/ML103620153.pdf>. Accessed September 2, 2014.
14. United States Nuclear Regulatory Commission. Consolidated guidance about materials licenses: program - specific guidance about medical use licenses (NUREG-1556, Volume 9, Revision 2, Page 8-73 and Appendix U) 2008; Available at: <http://www.nrc.gov/reading-rm/doc-collections/nuregs/staff/sr1556/v9/r2/>. Accessed May 27, 2014.
15. United States Nuclear Regulatory Commission. ALARA. 2018; Available at: <https://www.nrc.gov/reading-rm/basic-ref/glossary/alara.html>. Accessed October 17, 2018.
16. National Council on Radiation Protection and Measurements. NCRP No. 155, management of radionuclide therapy patients. 2006; Available (for purchase) at: [http://www.ncrponline.org/Publications/Press\\_Releases/155press.html](http://www.ncrponline.org/Publications/Press_Releases/155press.html). Accessed September 2, 2014.
17. Blake GM, Zivanovic MA, Blaquiere RM, Fine DR, McEwan AJ, Ackery DM. Strontium-89 therapy: measurement of absorbed dose to skeletal metastases. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine*. 1988;29(4):549-557.
18. Bos SD. An overview of current clinical experience with strontium-89 (Metastron). *The Prostate. Supplement*. 1994;5:23-26.
19. Porter AT, McEwan AJ, Powe JE, et al. Results of a randomized phase-III trial to evaluate the efficacy of strontium-89 adjuvant to local field external beam irradiation in the management of endocrine resistant metastatic prostate cancer. *International journal of radiation oncology, biology, physics*. 1993;25(5):805-813.
20. Quilty PM, Kirk D, Bolger JJ, et al. A comparison of the palliative effects of strontium-89 and external beam radiotherapy in metastatic prostate cancer. *Radiotherapy and oncology : journal of the European Society for Therapeutic Radiology and Oncology*. 1994;31(1):33-40.
21. Sciuto R, Festa A, Pasqualoni R, et al. Metastatic bone pain palliation with 89-Sr and 186-Re-HEDP in breast cancer patients. *Breast cancer research and treatment*. 2001;66(2):101-109.
22. Paes FM, Ernani V, Hosein P, Serafini AN. Radiopharmaceuticals: when and how to use them to treat metastatic bone pain. *The journal of supportive oncology*. 2011;9(6):197-205.
23. Pandit-Taskar N, Batraki M, Divgi CR. Radiopharmaceutical therapy for palliation of bone pain from osseous metastases. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine*. 2004;45(8):1358-1365.
24. Sartor O, Reid RH, Hoskin PJ, et al. Samarium-153-Lexidronam complex for treatment of painful bone metastases in hormone-refractory prostate cancer. *Urology*. 2004;63(5):940-945.
25. Das T, Banerjee S. Radiopharmaceuticals for metastatic bone pain palliation: available options in the clinical domain and their comparisons. *Clinical & experimental metastasis*. 2017;34(1):1-10.
26. Williams G, Palmer MR, Parker JA, Joyce R. Extravazation of therapeutic yttrium-90-ibritumomab tiuxetan (zevalin): a case report. *Cancer biotherapy & radiopharmaceuticals*. 2006;21(2):101-105.
27. Witzig TE, Flinn IW, Gordon LI, et al. Treatment with ibritumomab tiuxetan radioimmunotherapy in patients with rituximab-refractory follicular non-Hodgkin's lymphoma. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2002;20(15):3262-3269.
28. Morschhauser F, Radford J, Van Hoof A, et al. Phase III trial of consolidation therapy with yttrium-90-ibritumomab tiuxetan compared with no additional therapy after first remission in advanced follicular lymphoma. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2008;26(32):5156-5164.
29. Berlin NI. Treatment of the myeloproliferative disorders with 32P. *European journal of haematology*. 2000;65(1):1-7.
30. Ansell SM, Schilder RJ, Pieslor PC, et al. Antilymphoma treatments given subsequent to Yttrium 90 ibritumomab tiuxetan are feasible in patients with progressive non-Hodgkin's lymphoma: a review of the literature. *Clinical lymphoma*. 2004;5(3):202-204.
31. Schraml FV, Parr LF, Ghurani S, Silverman ED. Autopsy of a cadaver containing strontium-89-chloride. *Journal of nuclear medicine : official publication, Society of Nuclear Medicine*. 1997;38(3):380-382.
32. American College of Radiology. ACR–AAPM technical standard for nuclear medical physics performance monitoring of gamma cameras 2018; Available at: <https://www.acr.org/-/media/ACR/Files/Practice-Parameters/Gamma-Cam.pdf>. Accessed March 27, 2018.

---

\*Practice parameters and technical standards are published annually with an effective date of October 1 in the year in which amended, revised, or approved by the ACR Council. For practice parameters and technical standards published before 1999, the effective date was January 1 following the year in which the practice parameter or technical standard was amended, revised, or approved by the ACR Council.

Development Chronology for this Practice Parameter

1996 (Resolution 11)

Revised 2000 (Resolution 27)

Revised 2005 (Resolution 21)

Amended 2006 (Resolution 35)

Revised 2010 (Resolution 26)

Amended 2014 (Resolution 39)

Revised 2015 (Resolution 49)

Revised 2019 (Resolution 41)