

ACR–ACNM–ARS–SNMMI–SPR PRACTICE PARAMETER FOR TREATMENT OF BENIGN AND MALIGNANT THYROID DISEASE WITH I-131 SODIUM IODIDE

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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 care¹. 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 considering 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 variables such as the condition of the patient, limitations of available resources, or advances in knowledge or technology after publication of this document. However, a practitioner who employs an approach substantially different from the guidance in this document may consider documenting in the patient record information sufficient to explain the approach taken.

The practice of medicine involves the science, and 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 purpose of this document is to assist practitioners in achieving this objective.

¹ *Iowa Medical Society and Iowa Society of Anesthesiologists v. Iowa Board of Nursing*, 831 N.W.2d 826 (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 developed collaboratively by the American College of Radiology (ACR), the American College of Nuclear Medicine (ACNM), the American Radium Society (ARS), the Society of Nuclear Medicine and Molecular Imaging (SNMMI), and the Society for Pediatric Radiology (SPR).

This practice parameter is intended to guide appropriately trained and licensed physicians treating thyroid disease with I-131 sodium iodide. Therapy with I-131 sodium iodide involves its oral administration for the treatment of benign and malignant thyroid diseases.

I-131 is used for the treatment of hyperthyroidism and differentiated thyroid cancer based on sodium-iodine symporter expression in normal and neoplastic thyroid tissue. Symporter expression permits trapping and organification of iodine (including its radioactive isotopes). Once taken up by thyroid tissue, the therapeutic effect of I-131 sodium iodide is achieved by the emission of ionizing radiation in the form of high-energy beta particles, which cause DNA damage, culminating in cell death.

I-131 sodium iodide is both a beta particle and gamma ray emitter, with a physical half-life of 8.02 days. Its primary means of decay is via beta particle emission, which provides cytotoxic properties. The principle beta particle emitted by I-131 sodium iodide has a maximum energy of 0.61 MeV, an average energy of 0.192 MeV, and a tissue range of 0.6–2 mm [1]. I-131 sodium iodide also emits gamma rays, with its principal gamma ray having an energy of 364 KeV, which allows for imaging using high-energy collimators.

Therapy requires close cooperation and communication between the clinicians who are responsible for the clinical management of the patient and the physicians who administer radiopharmaceutical therapy and manage the attendant side effects (treating physician). Adherence to this parameter should help to maximize the efficacious use of these procedures, maintain safe conditions, 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](#) as that standard relates to the handling of radiopharmaceuticals, radiation safety, and radiation protection of patients, personnel, and the public [2]. There must also be compliance with applicable laws and regulations.

II. DEFINITION

I-131 therapy refers to therapeutic administration of I-131 for the treatment of benign or malignant thyroid disease.

In 2009, Cooper et al [3], and Van Nostrand [4] proposed terminology for I-131 therapies for differentiated thyroid cancer with further confirmation by the Martinique Working Group in 2019 [5]. This included definitions and objectives of (1) remnant ablation, (2) adjuvant treatment, and (3) treatment. Remnant ablation has the objective to destroy postoperative residual, presumably benign, thyroid tissue to facilitate initial staging and follow-up studies. Adjuvant treatment has the objective to destroy subclinical tumor deposits that may or may not be present after surgical resection of all known primary tumor tissue and metastatic foci. The goals of adjuvant treatment are to improve disease-specific survival and decrease recurrence rates, as well as to improve progression-free survival [6]. Treatment has the objective to destroy biochemically or structurally known locoregional and/or distant metastatic disease and has a goal of destroying persistent or recurrent differentiated thyroid cancer to improve progression free, disease specific, and overall survival [6].

III. INDICATIONS

The most common indications for therapy with I-131 sodium iodide are:

1. Benign Disease:
 - a. Treatment of hyperthyroidism/thyrotoxicosis in patients with Graves disease
 - b. Treatment of hyperthyroidism/thyrotoxicosis caused by a toxic single thyroid nodule in adults

- c. Treatment of hyperthyroidism/thyrotoxicosis caused by a toxic multinodular goiter
- d. Treatment of volume effects caused by a nontoxic nodular goiter

2. Malignant Disease:

- a. Thyroid remnant ablation
- b. Adjuvant treatment of differentiated thyroid cancer
- c. Treatment of known locoregional or distant metastatic differentiated thyroid cancer
- d. Treatment of recurrent differentiated thyroid cancer (to include suspected recurrence based upon elevated thyroglobulin levels)

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](#) and/or the [ACR–ASTRO Practice Parameter for Radiation Oncology](#) [2,7]. In addition, training and experience must be in compliance with the applicable laws and regulations.

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)

For further information on benign thyroid disease, thyroid uptake measurement, and thyroid scintigraphy see the [ACR–SPR Practice Parameter for the Performance of Scintigraphy and Uptake Measurements for Benign and Malignant Thyroid Disease](#) [8].

V. SPECIFICATIONS OF THE EXAMINATION AND TREATMENT

A. General Procedures

1. Clinical evaluation

In concordance with the [ACR–ARS Practice Parameter for Radiation Oncology](#) and the [ACR–ARS Practice Parameter for Communication: Radiation Oncology](#) [7,9], the treating physician’s initial evaluation of the patient must include physical examination, review of the patient’s history (including symptoms of hyper/hypoparathyroidism and if these symptoms occurred before or after surgery surgery was done before radiotherapy and before radiopharmaceutical therapy), medications, pertinent diagnostic studies (including dates of most recent administration of last iodinated contrast material), and laboratory and pathology reports. Pregnancy test (serum preferred) should be performed in patients of reproductive potential. Likewise, inquiring about breastfeeding is recommended.

2. Quality Management

Key components relevant to safe clinical use of radiopharmaceuticals, including 1-131 include:

- i. All radiopharmaceuticals dispensed and administered must be pursuant to an order (ie, prescription)

- by an authorized user.
- ii. Treating physicians are responsible for the safety, quality, and correctness of all radiopharmaceuticals prepared and dispensed for administration under their direction.
 - iii. Nuclear pharmacists are responsible for the safety, quality, and correctness of radiopharmaceuticals prepared and dispensed under their supervision.
 - iv. The preparation, quality control, dispensing, and administration to patients of radiopharmaceuticals and adjunctive drugs may be delegated to qualified personnel, in accordance with applicable state and local laws.
 - v. There must be a signed and dated written directive for each patient for I-131 sodium iodide in activities of 1.1 MBq (30 μ Ci) or more and for all therapeutic doses.
 - vi. The identity of the radiopharmaceutical and patient and the route of administration must be verified before administration. Outer shields or containers must be labeled for verification of contents.
 - vii. The activity of each radiopharmaceutical dose must be determined before administration to patients and must be consistent with that ordered by the treating physician or as stipulated in the applicable standing orders in the nuclear medicine procedure manual. The activity of radioactivity dispensed should be within 10% of the prescribed dose or dose range, and the actual activity administered should be within 20% unless otherwise directed by the authorized user and recorded in the patient's medical record.
 - viii. Radiopharmaceuticals should not be used beyond the expiration date or time recommended by the manufacturer unless quality control testing demonstrates that the product still meets the specifications of the US Pharmacopeial Convention at the time of use.
 - ix. Any discrepancies must be resolved before administration.

3. Therapy

The treating physician must discuss the risks, benefits, and alternatives of I-131 therapy with the patient in detail and obtain informed consent. The treating physician must confirm the ability of the patient to comply with prescribed radiation precautions.

Specific precautions and caution should be used when treating patients with ophthalmopathy, large thyroid glands, or significant postthyroidectomy residual or metastatic disease to the brain or spine. The patient must not be pregnant, breastfeeding, or lactating at the time of I-131 sodium iodide therapy. Pregnancy must be excluded before radiopharmaceutical administration by one of the following: negative human chorionic gonadotropin test within 24 hours of treatment, documented hysterectomy, postmenopausal state (absence of menstrual bleeding for 2 years), or by premenarche. Providing that the patient remains sexually abstinent, exclusion of pregnancy can be done within 72 hours if allowed by local institutional policy. Caution is advised for patients who have had recent unprotected intercourse because pregnancy testing may remain negative for 7–10 days. The patient should be advised against planning future pregnancy for 6–12 months after treatment. The patient should have discontinued breastfeeding long enough to result in the cessation of lactation, which is generally 6-12 weeks before therapy, to reduce radiation dose to the breasts. Breastfeeding should not be resumed after but may be undertaken for subsequent pregnancies.

Education and prevention strategies for early complications, such as nausea and vomiting, sialadenitis, loss or alteration of taste, neck pain and swelling, and oral mucositis, should be discussed and provided to the patient.

4. Radiation precautions

Patients should be provided with a document stating the patient been given a radioactive substance, the date of administration, the name of the radiopharmaceutical, and the activity administered in the event that radioactivity is detected by monitoring devices in public facilities or during travel.

Radiation precautions and patient release criteria may be regulated federally by the Nuclear Regulatory Commission (NRC) in many states or by the state (with regulations that are closely patterned on the federal regulations and may be more restrictive). The radiation safety officer, medical physicist, or health physicist for the

local facility should provide information on the applicable regulations. Details on the federal regulations can be obtained at the NRC website, www.nrc.gov.

Regulatory requirements for hospitalization and other radiation protection vary among states and countries. Many of those guidelines are more stringent than those of the NRC. The NRC has three alternate criteria for allowing patient release from the hospital after I-131 sodium iodide therapy. They are

- i. When no individual member of the public is likely to receive more than 5 mSv (500 mrem) from that patient, assuming all other regulatory requirements for patient instructions and record keeping are met. NUREG-1556, volume 9, "Consolidated Guidance about Materials Licenses: Program-Specific Guidance about Medical Use Licenses," describes methods for calculating doses to other individuals and contains tables of activities not likely to cause doses exceeding 5 mSv (500 mrem). This guidance is not a regulation. Realistic and scientifically valid, less conservative calculations on patient release, based on the realities of patient life at home, have been published [10-13].
- ii. When the survey meter reading is <0.07 mSv/h (7.0 mrem/h) at 1 m. Some radiation meters measure exposure rates in milliroentgens per hour, but for low LET radiation (including β -particles and most x-rays and gamma rays), the authors of this document accept the approximation that 1 mR, 0.01 mSv, and 1 mrem are equivalent. Thus, the exposure rate at 7 mR/h will be equivalent to the dose rate at 0.07 mSv/h (7 mrem/h) [14].
- iii. When the administered activity is 1.22 GBq (33 mCi) or less.

If the total effective dose equivalent is likely to exceed 1 mSv (0.1 rem) to any member of the public and if the administered dosage is >0.26 GBq (7mCi), written instructions must be provided to the patient on actions to limit doses to others by using the "as low as reasonably achievable" (ALARA) principle. Individual Agreement States may have specific rules and regulations regarding the release of patients with significant residual activity. Details on the relevant federal regulations can be obtained at the NRC website (<https://www.nrc.gov>) or by telephone (301-415-7000).

The dose limits specified by the National Council on Radiation Protection and Measurements (NCRP) differ somewhat from the NRC regulations. Because the fetus and children are more sensitive to radiation injury than adults, the NCRP specifies that children and pregnant individuals, whether or not they are members of the patient's household, should be limited to 1 mSv (0.1 rem) exposure from a treated patient. If it is not feasible to limit contact between a treated patient and young children or a pregnant individual, it may be prudent to have the patient in a separate household for the first 3 days after therapy. Any individual who has no familial connection to the patient and for whom there is no emotional benefit of proximity to the patient should also be limited to 1 mSv (the NRC dose limit to a member of the public).

With simple precautions, the radiation dose to family members is low (considerably less than the NRC upper limit of 5 mSv [500 mrem]) even when patients are not admitted to a hospital [15]. In a study in which patients were instructed to sleep alone and avoid prolonged personal contact for 2 days after therapy, 65 household members received a mean dose of 0.24 mSv (24 mrem) (range 0.01–1.09 mSv [1–109 mrem]) [16].

Guidance provided to patients (and family members if applicable) on specific precautions to limit exposure to others may be locally defined and may vary based on the administered activity and specifics of the living situation. Patient calculations of radiation exposure to others can be performed using several assumptions and recommendations given to each patient about the time and distance to stay away from others. In general, precautions should seek to prevent transmission of bodily fluids to other individuals and to limit periods of time in close proximity to others. An example of a common precaution is allowing the treated patient sole use of a bathroom. Other less well-studied precautions include, but are not limited to, coaching patients to void while sitting, flushing the toilet twice after use, and not sharing eating or drinking utensils. Patients should also be provided with guidance as to when it is safe to return to work or school, again with an aim of limiting exposure to the public.

Bioassays of the thyroid gland of personnel administering I-131 sodium iodide should be performed periodically, depending on local regulations and institutional policy.

V. SPECIFICATIONS OF THE EXAMINATION AND TREATMENT

B. Unique Situations

Inpatient therapy or hospitalization after therapy

Inability to comply with all radiation safety precautions and instructions might require hospital admission, as determined by the authorized user.

If confinement in a health care facility is needed, the patient must stay in the room except in a medical or nonmedical (eg, fire) emergency, and access by personnel and visitors must be limited. If the admitting physician is different from the treating physician, there must be a mechanism to prevent premature discharge or release of the patient from confinement. Any significant medical conditions should be noted, and contingency plans made in case radiation precautions must be breached for a medical emergency, because concern about radiation exposure should not interfere with prompt, appropriate medical treatment of the patient. Hospital caregivers should be instructed in all relevant radiation safety procedures. Selected personnel providing direct patient care should be provided with appropriate radiation monitors (TLD, direct-reading dosimeters, etc). Caregivers who are or may be pregnant should be excluded from direct patient care.

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 of radioactivity. Food trays and linens should be stored in the patient's room until monitored and cleared by radiation safety staff. 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 reside there 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 this survey is performed.

Urinary incontinence, if present, might require catheterization for I-131 therapy to prevent radiation contamination. Peritoneal and hemodialysis are not contraindications for therapy but may impact the administered activity of I-131 given the prolonged residence time within the patient.

All routine blood work and laboratory specimens pending for a patient should be obtained prior to therapy with I-131 if possible.

V. SPECIFICATIONS OF THE EXAMINATION AND TREATMENT

C. Treatment of Benign Thyroid Disease

1. Therapy for Hyperthyroidism

a. Background

Hyperthyroidism can be a manifestation of multiple different diseases, not all of which are appropriately treated with I-131 sodium iodide. Specifically, subacute thyroiditis and factitious hyperthyroidism should not be treated with I-131. Thyroid diseases causing thyrotoxicosis from hyperthyroidism, which are amenable to I-131 therapy include Graves disease, toxic multinodular goiter, and solitary toxic nodule (in an adult). Solitary toxic nodules in children should generally be treated surgically. Other treatment options for hyperthyroidism, including thioamides medications (eg, propylthiouracil or methimazole) and surgical excision are available, and selection of appropriate therapy should be guided by a shared decision-making process between the patient and treating practitioner. Patients in thyroid storm are not candidates for I-131 therapy as the effects of I-131 will not occur rapidly enough to affect patient management and instead may exacerbate thyroid hormone release from the thyroid and complicate patient care. When applied, the goal of I-131 therapy is to achieve ablation of the hyperfunctioning thyroid tissue, rendering the patient hypothyroid or euthyroid. As much as possible, the goal should be to achieve remission with a single dose of I-131 sodium iodide.

b. Summary of selected data

- i. A total of 50%–90% of hyperthyroid patients reach a euthyroid or hypothyroid state within 1 year of treatment with I-131 sodium iodide [13].
- ii. In a study of 1,278 patients over an approximate 20-year period, hyperthyroid patients were rendered euthyroid or hypothyroid after a single dose of 600 MBq (16.2 mCi), 370 MBq (10 mCi), or 185 MBq (5 mCi) in 84.1%, 74.9%, and 63% of cases, respectively [14].
- iii. Failure of I-131 Sodium Iodide therapy for Graves disease is more common in patients with large thyroid volumes, high iodine uptake, and high iodine turnover [17].

c. Therapy recommendations

Optimally, the patient should be free of iodide-containing medications, iodinated contrast, exogenous thyroid hormone, and antithyroid medications. The patient should avoid foods containing very large amounts of iodine for the week prior to therapy; however, a strict low-iodine diet is usually unnecessary. Ideally, patients should not receive thioamide medications (eg, propylthiouracil or methimazole) for at least 2–7 days before therapy.

A recent radioiodine thyroid uptake measurement should be available (See the [ACR–SPR Practice Parameter for the Performance of Scintigraphy and Uptake Measurements for Benign and Malignant Thyroid Disease](#) [8].) The size of the thyroid gland and the percent uptake should be noted. Measurement of radioiodine uptake before therapy is necessary to (1) establish that a hyperthyroid state is causing thyrotoxicosis to avoid the inappropriate administration of I-131 radioiodine in the setting of subacute thyroiditis or, thyrotoxicosis factitia and (2) to guide selection of administered activity of I-131. Ultrasound may be contributory to estimate thyroid size and can identify unsuspected thyroid nodules that may have clinical relevance.

d. Administered activities

i. Diffuse hyperfunctioning thyroid/Graves disease

For adults, an initial activity of 3.0–7.4 MBq (80–250 μ Ci) per gram of thyroid (after adjusting for 24-hour radioiodine uptake) may be administered. Alternatively, an empiric administered activity of 185–555 MBq (5–15 mCi) may be given. Rarely, it may be necessary to administer an activity >1.22 GBq (33.0 mCi). Formal dosimetry is rarely, if ever, necessary to determine a safe and effective administered activity of I-131 for hyperthyroidism. For pediatric patients, the administered activity should be based on thyroid size and uptake [20]. Administered activities of 250 μ Ci/g [18,19] may be required to achieve a high frequency of successful ablation. If possible, I-131 therapy should be avoided in children <5 years of age [20].

ii. Toxic nodular goiter and solitary toxic nodule

These conditions tend to be more resistant to radioiodine therapy. In adults, the administered activity should be 7.4–14.8 GBq/g (200–400 μ Ci/g) of tissue. Activity of up to 1.22 GBq (33 mCi) or more may be administered. In children, surgical therapy is favored for these entities due to the radiation exposure of normal thyroid tissue from radiation emitted from the target nodule.

e. Side effects/complications

Side effects of I-131 therapy for hyperthyroidism are usually minor. Patients may occasionally experience neck tenderness and/orodynophagia from radiation thyroiditis that can be managed with oral anti-inflammatory medications. Sialadenitis may occur with higher administered activities and may be managed by the oral administration of sialagogues and/or anti-inflammatory medications. Serious complications are rare. However, on occasion, patients with severe hyperthyroidism may experience exacerbation of symptoms within the first 2 weeks following I-131 sodium iodide therapy. These symptoms usually respond to short-term beta blocker therapy but rarely may progress to frank thyroid storm. Patients considered to be at high risk of thyroid storm based on clinical assessment should be prophylactically started on beta blocker therapy or not treated with I-131 sodium iodide. Lower risk patients should be instructed to contact their referring physician or seek immediate medical care should symptoms of storm occur.

Hypothyroidism is a likely or even desired outcome of successful therapy of Graves disease or toxic nodular goiter and can occur within the first few months following therapy or even decades later, with a small, ongoing annual incidence. Hypothyroidism is treated with carefully monitored and titrated hormone-replacement therapy. Based on multicenter trials and one meta-analysis, there is no clear evidence of increased risk of thyroid carcinoma or other malignancy, infertility, or increased incidence of birth defects following I-131 therapy for hyperthyroidism [21].

f. Therapy failures and subsequent therapies

Factors associated with failed I-131 therapy of hyperthyroidism include thyroid size, thyroid uptake, and administered activity [22,23]. Larger thyroid glands, particularly those above 60 g, are more likely to be inadequately treated with a single dose of I-131 sodium iodide. Patients with larger thyroids should be considered for up-front surgical management or may require multiple I-131 treatments to achieve remission [24]. Lower radioiodine uptake and lower initial administered activities are more likely to result in persistent/inadequately treated hyperthyroidism and theoretically may increase the risk of secondary thyroid malignancy.

In patients who have not adequately responded to prior I-131 sodium iodide therapy, subsequent I-131 therapy may be given. An equal or higher treatment dosage is generally used for retreatment. To achieve the maximal therapeutic effect, repeat therapy is usually not recommended until at least 6 months after the most recent I-131 therapy.

V. SPECIFICATIONS OF THE EXAMINATION AND TREATMENT

D. Treatment of Malignant Thyroid Disease

1. Clinical Evaluation

Findings on thyroid ultrasound, abnormalities on Tc-99m pertechnetate, Tc99m sestamibi, or radioiodine thyroid scan, or F-18 fluorodeoxyglucose (FDG)-positron emission tomography (PET), can all increase the suspicion for the presence of thyroid carcinoma.

In one study of 285 patients with incidental thyroid hypermetabolism on F-18 FDG PET, the overall cancer risk for thyroid malignancy was 23% [26] with focal thyroid hypermetabolism associated with a risk of 31% [27][28].

Nodular thyroid abnormalities demonstrated on diagnostic computed tomography (CT) imaging of the thorax or neck may also prompt workup for thyroid carcinoma. Suspicion for locally advanced thyroid carcinoma may also be suggested by lymphadenopathy in the neck on soft-tissue neck ultrasound imaging, CT, or magnetic resonance imaging (MRI) or as detected by physical examination.

When there is suspicion for primary thyroid carcinoma by any imaging modality or by physical examination, fine-needle aspiration or surgical excision should be considered to achieve pathologic confirmation.

V. SPECIFICATIONS OF THE EXAMINATION AND TREATMENT

D. Treatment of Malignant Thyroid Disease

2.

Radiation precautions, and considerations unique to therapy of malignant thyroid disease

Radiation safety issues for pregnancy, breastfeeding, and lactation are discussed under section V.A.3-4.

Discussion of fertility should be considered, particularly in young patients who may need multiple therapies and in patients undergoing serial I-131 therapy.

Most experts recommend that patients wait 6–12 months after I-131 sodium iodide therapy before trying to conceive a child, although there are no reliable data on the validity of this suggested interval. A 12-month interval allows for follow-up imaging to evaluate the effectiveness of the treatment and for retreatment if deemed appropriate [39].

V. SPECIFICATIONS OF THE EXAMINATION AND TREATMENT

D. Treatment of Malignant Thyroid Disease

3. Therapy

a. Background

Iodine-avid differentiated thyroid cancers frequently take up radioiodine in the absence of significant amounts of residual normal thyroid tissue. In selected patients following near-total thyroidectomy, the thyroid remnant may be ablated with I-131 sodium iodide (remnant ablation). . A large thyroid remnant (eg, following a hemithyroidectomy) generally requires a completion thyroidectomy prior to radioiodine ablation. To facilitate follow-up and to optimize radioiodine therapy for locoregional or distant disease, the remnant normal thyroid must be eliminated Details regarding risk stratification of patients with thyroid cancer, appropriateness of radioiodine therapy in various clinical situations, and the overall management of patients with thyroid cancer are covered extensively elsewhere.

b. Summary of selected data

- i. A study evaluating thyroid cancer over a 40-year period reported that, for patients with cancers greater than or equal to 1.5 cm in diameter post thyroidectomy and without distant metastases, the addition of I-131 sodium iodide therapy alone for remnant thyroid ablation reduced the frequency of recurrence and cancer death by at least one-half and reduced the risk of recurrence by more than two-thirds [23].
- ii. In two phase III trials comparing results of I-131 sodium iodide therapy in patients with low-risk thyroid cancer post thyroidectomy using thyroid hormone withdrawal versus use of recombinant human thyrotropin, the frequency of successful ablation was found to be equivalent between I-131 sodium iodide activities of 1.1 GBq (30 mCi) and 3.7 GBq (100 mCi) [42,43]. There was also no difference in the frequency of successful ablation between patients withdrawn from thyroid hormone versus those who received recombinant human thyrotropin. A retrospective study raised some concerns about the effectiveness of activities lower than 2 GBq (54 mCi) in patients older than 45 years [44].

c. Treatment Therapy recommendations

I-131 sodium iodide has a physical half-life of 8.02 days. It emits beta radiation as well as gamma radiation, which is suitable for imaging. Because of increased sensitivity afforded by the therapeutic dosage of I-131 sodium iodide, posttherapy imaging is useful and usually recommended to identify sites of disease not detected on pretherapy iodine imaging. The typical interval for posttherapy imaging is between 2 and 10 days after administration of I-131 with evidence suggesting that both early (eg, day 3 or 4) and late (eg, day 6 or 7) imaging may provide greater sensitivity for metastatic differentiated disease.

d. Patient preparation

The serum thyroid-stimulating hormone (TSH) must be elevated, usually to a level in excess of 30 μ U/mL. This TSH elevation can be achieved either by not administering thyroid hormone following thyroidectomy for 2–4 weeks or by withholding thyroid hormone from a patient at a more remote time after surgery Administering recombinant human TSH may also be used to raise the patient's blood TSH. . Documentation of an elevated TSH level as well as adherence to a low-iodine diet for 1 to 2 weeks prior to treatment is recommended. Optimally, the patient's system should be free of iodide-containing medications, iodinated contrast material, and exogenous thyroid hormone (for withdrawal therapy). For further information, please refer to the Compounds That May Decrease Thyroid Iodine Uptake table in the [ACR–SPR Practice Parameter for the Performance of Scintigraphy and Uptake Measurements for Benign and Malignant Thyroid Disease](#) [8]. The patient should be fasting and abstain from eating 2–4 hours before and 1–2 hours

after therapy.

A pretherapy diagnostic whole-body radioiodine scan aids in assessing the volume of remnant thyroid (based on size and percent uptake) and the extent of locoregional or distant disease. Addition of SPECT/CT to the pretherapy whole-body radioiodine scan has been shown to increase sensitivity for, and better characterize, disease. Patient dosimetry based on serial whole-body radioiodine residence measurements and blood samples should be considered to safely maximize administered activity for patients with diffuse pulmonary metastases, patients with impaired renal function, patients with a large volume of metastatic disease, and patients likely to require, or undergoing, repeated therapies.

e. Administered activities

I-131 sodium iodide may be administered to patients of all ages for the management of thyroid cancer, but pediatric dosages should be weight adjusted [30,31].

The patient may need to be placed on radiation precautions.

- i. Remnant ablation Activities of 1.11.85 GBq (30–50 mCi) of I-131 Sodium Iodide administered orally are most often used.
- ii. Adjuvant therapy of suspected (but not known) residual disease without evidence of distant metastasis Activities of 3.7–5.55 GBq (100–150 mCi) of I-131 sodium iodide are usually administered.
- iii. Therapy of known metastases Activities equal to or greater than 5.55–7.4 GBq (150–200 mCi) of I-131 sodium iodide are usually administered. Patient dosimetry should be strongly considered in this patient subgroup.

f. Residual or recurrent disease

After successful remnant ablation, a measurable serum thyroglobulin level suggests functioning thyroid tissue and the possibility of recurrent disease and may be an indication for additional treatment. However, thyroglobulin levels are unreliable in the presence of antithyroglobulin antibodies. Falsely low thyroglobulin levels may occur in antibody-positive patients; therefore, antibody assays should accompany all thyroglobulin measurements. Even when a diagnostic whole-body scan is negative, if the stimulated thyroglobulin level is >10 ng/mL or there is other evidence of disease in a patient with a high risk of recurrence, empiric therapy with 3.7–7.4 MBq (100–200 mCi) can be considered. In the setting of a negative whole-body scan and suspected metastatic disease, an FDG-PET/CT scan may be helpful to identify and localize non-iodine-avid disease. (See the [ACR–SPR Practice Parameter for the Performance of Scintigraphy and Uptake Measurements for Benign and Malignant Thyroid Disease](#) [8].)

V. SPECIFICATIONS OF THE EXAMINATION AND TREATMENT

D. Treatment of Malignant Thyroid Disease

4. Complications

1. Side effects/complications

Following I-131 therapy for differentiated thyroid cancer, hydration is recommended; however, the use of sialagogues is debated. Acute sialadenitis is often transient with lower administered activities. With higher administered activities, permanent xerostomia has been reported in 2%–4% of affected patients and is generally associated with a history of single or multiple high administered activities of radioiodine.

Reports of pulmonary fibrosis and/or pneumonitis have been described in patients with diffuse pulmonary metastatic disease. A whole-body retention threshold of 2.96 GBq (80 mCi) at 48 hours is commonly used to avoid lung injury. ie, the upper limit of the administered activity should be 200 mCi unless dosimetry is performed). Pulmonary function studies should also be considered prior to treatment if there are widespread pulmonary metastases.

The potential for the development of secondary primary malignancies is low following high administered

activities of I-131 sodium iodide and is debated . No increased risk of secondary primary solid tumors has been identified. A large European study of 6,871 patients reported an increase in solid tumors and leukemia after I-131 therapy. A subsequent literature review, however, reassessed the data and reported a nonlinear dose effect. Review of the Surveillance, Epidemiology, and End Results program with a database of 18,882 patients and a mean follow-up of 61.8 months concluded that I-131 therapy slightly increased the risk of secondary primary malignancies . However, a significantly greater risk of leukemia or other secondary primary malignancies was reported for patients treated with cumulative activities of 22 GBq (600 mCi) of I-131 , particularly if combined with external beam radiotherapy. Almost all cases of secondary primary malignancies have occurred in patients who received cumulative administered activities in excess of 29.6 GBq (800 mCi). Significant bone marrow depression is likely when cumulative administered activities exceed 29.6 GBq (800 mCi).

2. Interactions of I-131 sodium iodide with other forms of diagnosis or treatment (combinations and/or interactions with clinical external-beam radiation therapy)

Patients with advanced local disease or regional recurrent disease or distant metastases, such as those with involvement of the central nervous system or aerodigestive tract, may be treated with both I-131 sodium iodide and external-beam radiation after thyroidectomy. The toxicity, acute and late, is likely to be additive within the field of irradiation.

To avoid potential radiation-induced spinal cord damage in patients with spinal metastases when I-131 sodium iodide therapy and external-beam radiotherapy are to be used in combination, dosimetry calculations are particularly important. A treatment planning method for combination external-beam therapy with radiopharmaceutical therapy is described by Hobbs et al [45].

VI. DOCUMENTATION

Reporting should be in accordance with the [ACR–ARS Practice Parameter for Communication: Radiation Oncology](#) [9].

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

VII. ACR STATEMENT On THERAPEUTIC USE OF UNSEALED RADIOPHARMACEUTICAL SOURCES

Based on their education, training pathway(s), initial board certification(s), and maintenance of certification(s), NRC Authorized User (AU) status, and clinical work experience, diagnostic radiologists (DRs), nuclear radiologists (NRs), nuclear medicine physicians (NMs), and radiation oncologists (ROs) may have the 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 NM, NR, DR, , or RO but do not hold AU status: These physicians may participate in the practice of therapy with I-131 sodium iodide (oral and parenteral administration) under the supervision of an AU for the specific therapeutic radiopharmaceutical. Although they may not issue written directives for I-131 sodium iodide therapy, they may administer such a dosage as designated by an AU;
- Physicians who are board-certified in NM, NR, DR, , or RO and hold AU status based on that certification and site-specific credentialing: These physicians may practice I-131 sodium iodide radioisotope therapy consisting of oral radioiodine at all dosage levels under their own AU qualifications;
- Physicians who are board-certified in NM, NR, DR, , or RO and hold the appropriate AU statuses and site-specific credentialing: These physicians may practice parenteral I-131 sodium iodide radioisotope therapy(ies) as permitted by their own specific training leading to such AU statuses.

VIII. RADIATION SAFETY

Radiologists, medical physicists, non-physician radiology providers, 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 who work with ionizing radiation must understand the key principles of occupational and public radiation protection (justification, optimization of protection, application of dose constraints and limits) and the principles of proper management of radiation dose to patients (justification, optimization including the use of dose reference levels). https://www-pub.iaea.org/MTCD/Publications/PDF/PUB1775_web.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 in accordance with ALARA principles. 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 applicable state, local, or other relevant regulatory agencies and accrediting bodies, as appropriate. Quantities of radiopharmaceuticals should be tailored to the individual patient by prescription or protocol, using body habitus or other customized method when such guidance is available.

Nationally developed guidelines, such as the [ACR's Appropriateness Criteria](#)[®], should be used to help choose the most appropriate imaging procedures to prevent unnecessary radiation exposure.

Additional information regarding patient radiation safety in imaging is available from the following websites – Image Gently[®] for children (www.imagegently.org) and Image Wisely[®] for adults (www.imagewisely.org). 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 periodically measured by a Qualified Medical Physicist in accordance with the applicable ACR Technical Standards. Monitoring or regular review of dose indices from patient imaging should be performed by comparing the facility's dose information with national benchmarks, such as the ACR Dose Index Registry and relevant publications relying on its data, applicable ACR Practice Parameters, 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; 2006, 2009, amended 2013, revised 2023 (Res. 2d).

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 Medical Nuclear Physics Performance Monitoring of Gamma Cameras](#) [46].

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