

Procedure Guideline for Therapy of Thyroid Disease with ^{131}I

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PART I: PURPOSE

The purpose of this guideline is to assist nuclear medicine practitioners in evaluating patients for therapy with ^{131}I (sodium iodide) for benign or malignant conditions of the thyroid gland, performing this treatment, understanding and evaluating the sequelae of therapy, and reporting the results of therapy.

PART II: BACKGROUND INFORMATION AND DEFINITIONS

Oral administration of ^{131}I has been a commonly accepted procedure for treatment of benign and malignant conditions of the thyroid since the 1940s. Physicians responsible for treating such patients should have an understanding of the clinical pathophysiology and natural history of the disease processes, should be familiar with alternate forms of therapy, and should be able to collaborate closely with other physicians involved in the management of the patient's condition. The treating physician should either see patients in consultation with the physician assuming overall management of the patient's condition or be prepared to assume that role. In the United States, the treating physician should be board certified in Nuclear Medicine, Radiology, or Radiation Oncology, or be able to document equivalent training, competency, and experience in the safe use and administration of therapeutic amounts of ^{131}I . In Europe, the treating physician should be board certified in Nuclear Medicine or Radiation Oncology.

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Licensure to possess ^{131}I and regulations regarding the release of patients treated with radioiodine vary from jurisdiction to jurisdiction. Physicians engaged in therapy with ^{131}I must be knowledgeable about and in compliance with all applicable laws and regulations.

The facility in which treatment is performed must have appropriate personnel, radiation safety equipment, and procedures available for waste handling and disposal, monitoring personnel for accidental contamination, and controlling spread of volatilized ^{131}I .

Definitions

- ^{131}I is a β -emitting radionuclide with a physical half-life of 8.1 d, a principal γ -ray of 364 KeV, and a principal β -particle with a maximum energy of 0.61 MeV, an average energy of 0.192 MeV, and a range in tissue of 0.8 mm.
- *Therapy* means the oral administration of ^{131}I as sodium iodide.
- *Benign conditions* include Graves' disease (toxic diffuse goiter), toxic or nontoxic nodular goiter, and autonomously functioning toxic or nontoxic nodules.
- *Malignant conditions* include thyroid cancer that is sufficiently differentiated to be able to synthesize thyroglobulin and, in most cases, accumulate radioiodine.

PART III: COMMON INDICATIONS

A. Benign Conditions

- Hyperthyroidism. ^{131}I may be indicated for the treatment of Graves' disease, toxic multinodular goiter, or toxic autonomously functioning thyroid nodules.
- Nontoxic multinodular/diffuse goiter. ^{131}I therapy has been used successfully to diminish the size of nontoxic multinodular/diffuse goiter.

B. Thyroid Cancer

- ^{131}I therapy has been used for postoperative ablation of thyroid remnants after thyroidectomy.
- ^{131}I therapy has been used to treat residual thyroid

cancer and metastatic disease after partial or complete thyroidectomy.

PART IV: PROCEDURE

A. Patient Preparation

1. For All Patients

- a. All patients must discontinue use of iodide-containing preparations, iodine supplements, thyroid hormones, and other medications that could potentially affect the ability of thyroid tissue to accumulate iodide for a sufficient time before contemplated therapy (Table 1).
- b. The treating physician must explain the procedure, treatment, complications, side effects, therapeutic alternatives, and expected outcome to the patient. Written information should be provided to the patient.
- c. The treating physician must obtain written informed consent before therapy.

2. For Therapy of Hyperthyroidism and Nontoxic Multinodular Goiter

- a. The results from recent measurements of thyroid hormone levels (free T₄, free T₃) and thyroid stimulating hormone (TSH) should be available and reviewed. The avidity of the thyroid gland for iodide must be established. This can be accomplished quantitatively using a recent radioiodine uptake (RAIU), or qualitatively using a thyroid scan. These procedures will differentiate silent thyroiditis and thyrotoxicosis factitia from other forms of hyperthyroidism.
- b. Pretreatment of selected patients with anti-thyroid drugs (ATD) to deplete thyroid hormone stores may be helpful. ¹³¹I therapy can

cause radiation thyroiditis with release of stored thyroid hormone into the circulation, resulting in occasional worsening of hyperthyroidism and, rarely, precipitation of thyroid storm. This is more likely to occur in patients with large, iodine-avid multinodular glands who are given larger amounts of ¹³¹I. Accordingly, elderly patients and patients with significant preexisting heart disease, severe systemic illness, or debility may benefit from pretreatment with ATD. The ATD needs to be discontinued for at least 3 d before the radioiodine therapy is given. The ATD can be resumed 2–3 d after treatment with ¹³¹I. Some experts recommend administering a larger amount of ¹³¹I in patients who have been pretreated with ATD. Treatment with β-blockers can be helpful for symptomatic control. β-Blockers need not be discontinued before treatment with ¹³¹I.

- c. The consent form should include the following items specific for the therapy of hyperthyroidism:
 - More than one ¹³¹I treatment may be necessary.
 - The risk of eventual hypothyroidism is high, especially after treatment of Graves' disease, and lifelong daily ingestion of a thyroid hormone tablet would then be necessary.
 - Long-term follow-up will be necessary.
 - Ophthalmopathy may worsen or develop after ¹³¹I therapy.
 - Rarely, there can be transient neck soreness or exacerbation of hyperthyroid symptoms secondary to radiation thyroiditis.

TABLE 1
Drug Interactions

Type of medication	Recommended time of withdrawal
Antithyroid medication (e.g., propylthiouracil, methimazole, carbimazole) and multivitamins	3 d for antithyroid drugs 7 d for multivitamins*
Natural or synthetic thyroid hormone (e.g., thyroxine, triiodothyronine)	2 wk for triiodothyronine [†] 4–6 wk for thyroxine [†]
Expectorants, kelp, agar, carageen, Lugol's solution, potassium iodide solution ("SSKI")	2–3 wk, depending on iodide content*
Topical iodine (e.g., surgical skin preparation)	2–3 wk*
Radiographic contrast agents	
Intravenous (water soluble)	3–4 wk (assuming normal renal function)
Lipophilic agents (rarely used)	>1 mo
Amiodarone	3–6 months or longer

*These time intervals relate to hyperthyroid patients. For thyroid cancer patients, a 6-wk time interval is recommended.

[†]These times apply only to thyroid cancer patients.

3. For Therapy of Thyroid Cancer

- a. Thyroid hormone medications must be withheld for a time sufficient to permit an adequate rise in TSH ($>30 \mu\text{IU/ml}$). This is at least 2 wk for triiodothyronine (T3) and 4 to 6 wk for thyroxine (T4). TSH may not rise to this level if a large volume of functioning tissue remains. Recombinant human TSH is not currently approved in the United States for use in ^{131}I therapy, although there is FDA approval for use in diagnostic testing.
- b. For patients receiving an ablative dose or treatment dose of radioiodine following a partial or complete thyroidectomy for thyroid cancer, the results from a recent measurement of TSH and the operative and histology reports should be available and reviewed. A baseline serum thyroglobulin should be obtained in the hypothyroid state. A complete blood count before treatment may be useful. Other laboratory tests such as a serum calcium (to exclude hypoparathyroidism postthyroidectomy) may be helpful.
- c. Many experts recommend a low iodide diet for 7–10 d before administration of therapy to improve iodine uptake. Since iodized salt is a major dietary source of iodide, compliance with a low iodide diet may be difficult, especially if restaurant food is eaten. Table 2 lists major food groups and other common sources of iodine. Red dye is found in many processed red- or pink-colored foods and medications.
- d. The presence of iodine accumulating thyroid tissue is routinely documented by uptake measurement and imaging (see “Procedure Guideline for Extended Scintigraphy of Differentiated Thyroid Cancer,” Society of Nuclear Medicine Procedure Guidelines Manual, 1999, p. 15). In selected patients, an uptake measurement and/or imaging may not be necessary. In the absence of antithyroglobulin antibodies, an elevated or rising serum thyroglobulin may also be a useful indicator of residual or recur-

TABLE 2
Dietary Sources of Iodine

Iodized salt
Milk/dairy products
Eggs
Seafood
Seaweed and kelp products
Commercial bread made with iodide conditioners
Chocolate
Iodide-containing multivitamins
FDC red dye #3

- e. A written informed consent form must be obtained and could include the following items specific for the therapy of thyroid cancer:
 - The purpose of the treatment is to destroy normal and cancerous thyroid tissue. Other normal tissues may also be affected.
 - More than one ^{131}I treatment may be necessary.
 - Early side effects may include nausea, occasional vomiting, pain and tenderness in the salivary glands, loss of saliva or taste, neck pain and swelling if a sizeable thyroid remnant remains after surgery, and decreased white blood cells that may result in increased susceptibility for infection. Generally these side effects are temporary.
 - Late side effects may include temporary infertility (in men this can be permanent as dosages progressively exceed 11.1 GBq [300 mCi]); rarely, permanent damage to the salivary glands resulting in loss of saliva or stones; excessive dental caries; reduced taste; and the very rare development of other cancers, including those of the stomach, bladder, colon, and salivary glands, and leukemia (only with very high cumulative doses).
 - These late side effects are rarely seen and should not deter a patient from taking ^{131}I for treatment of thyroid cancer.

B. Information Pertinent to Performing the Procedure

1. For All Patients

- a. The treating physician must obtain the patient's thyroid-related medical history and perform a directed physical examination. The cumulative administered activity of ^{131}I should be reviewed and recorded in the patient's record.
- b. The treating physician must confirm that appropriate laboratory testing has been performed and must review the results of these tests.
- c. Female patients who have the potential to be pregnant should routinely be tested for pregnancy within a few days before administration of the ^{131}I treatment. Occasionally, when historical information clearly indicates pregnancy

is impossible, a pregnancy test may be omitted at the discretion of the treating physician.

- d. All potentially breastfeeding/lactating women should be asked if they are lactating. If so, they should be asked to stop breastfeeding and therapy delayed until lactation ceases in order to minimize the radiation dose to the breast. The patient may not resume breastfeeding for that child. Nursing may resume with the birth of another child.
- e. The treating physician should confirm that the patient is continent of urine or that arrangements are made to prevent contamination caused by incontinence.
- f. The patient's identity must be confirmed in accordance with institutional policy before administration of ^{131}I .

2. For Hyperthyroid Patients

Dose selection. A variety of methods have been used to select the amount of administered activity. A common method is to use the estimated thyroid gland size and the results of a 24-h RAIU test to calculate the amount of ^{131}I to administer in order to achieve a desired concentration of ^{131}I in the thyroid gland. Delivered activity of 2.96–7.4 MBq (80–200 μCi) per gram of thyroid tissue is generally appropriate. The thyroid radiation dose depends on the RAIU as well as the biological and effective half-life of the radioiodine in the thyroid gland. This biological half-life can vary widely. Thyroid concentrations toward the upper end of the range (i.e., 7.4 MBq/gm [200 $\mu\text{Ci}/\text{gm}$]) are especially suitable for patients with nodular goiters, very large toxic diffuse goiters, and repeat therapies. In much of Europe, empiric rather than calculated dosage strategies are often used.

3. For Thyroid Cancer Patients

- a. **Dose selection.** A variety of approaches have been used to select the amount of administered activity. General guidelines are listed below:
 - For postoperative ablation of thyroid bed remnants, activity in the range of 2.75–5.5 GBq (75–150 mCi) is typically administered, depending on the RAIU and amount of residual functioning tissue present.
 - For treatment of presumed thyroid cancer in the neck or mediastinal lymph nodes, activity in the range of 5.55–7.4 GBq (150–200 mCi) is typically administered.
 - For treatment of distant metastases, activity of >7.4 GBq (200 mCi) is often given. The radiation dose to the bone

marrow is typically the limiting factor. Most experts recommend that the estimated radiation dose to the bone marrow be less than 200 rad. Detailed dosimetry may be indicated in patients who are treated with large amounts of radioactive iodine to determine how much ^{131}I can be safely administered. Retention of radioiodine in the body at 48 h should be <4.44 GBq (120 mCi), or <2.96 GBq (80 mCi) if diffuse lung metastases are present, to reduce toxicity.

- b. Oral administration of lithium carbonate prolongs the biological half-life of administered ^{131}I and occasionally may be useful in patients who have a rapid turnover of radioactive iodine. A short effective ^{131}I half-life can be a source of failure of ^{131}I therapy in metastatic lesions.
- c. Side effects may occur and are generally dose related. These are listed above in the consent form outline found in Section IV.A.3.e. Hydration of the patient, with instructions urging frequent urination for several days and efforts to increase salivary flow may reduce radiation exposure to the bladder and salivary glands. Antiemetics may be helpful. The patient should have at least 1 bowel movement a day to reduce colon exposure. Laxatives may be necessary.
- d. Patients should have extended scintigraphy approximately 1 wk after treatment for staging purposes.

C. Precautions

1. The treating physician must instruct the patient on how to reduce unnecessary radiation exposure to family members and members of the public. Written instructions should be provided and may be required in some jurisdictions.
2. Following treatment, patients should not become pregnant until their medical condition has been optimized. Opinions vary widely as to how long to defer pregnancy, but some centers recommend 6 mo after ^{131}I therapy for patients with hyperthyroidism and 12 mo for patients with thyroid cancer. The 12-mo interval allows for follow-up imaging to evaluate the effectiveness of the cancer treatment dose. Radiation exposure before conception is a very small risk compared with the usual risks of pregnancy.
3. If the patient is to be treated as an inpatient, nursing personnel must be instructed on radiation safety. Selected nursing personnel may be pro-

vided appropriate radiation monitors (film badge, direct-reading dosimeters, etc.). Any significant medical conditions should be noted and contingency plans made in case radiation precautions must be breached for a medical emergency. Concern about radiation exposure should not interfere with the prompt, appropriate medical treatment of the patient should an acute medical problem develop.

- Radiation surveys of the thyroid gland should be performed periodically on personnel administering ¹³¹I.

D. Radiopharmaceutical

- See Sections IV.B.2 and IV.B.3 for guidance on selection of the amount of administered activity for the treatment of hyperthyroidism and thyroid cancer, respectively. Therapeutic ¹³¹I can be administered in liquid or capsule form, but the prescribed amount must be verified in a dose calibrator before administration. If a liquid form is used, strategies for minimizing volatilization during dosage preparation and administration should be used such as venting the dose into a filtering system such as a fume hood and administering the dose to the patient shortly thereafter.
- Radiation Dosimetry in Adults. See Tables 3 and 4.

E. Reporting

The report to the referring physician should include the justification for therapy, pertinent historical data, physical findings, and laboratory tests,

TABLE 3
Absorbed Radiation Dose

Organ	mGy/MBq	Rad/mCi
Assuming no thyroid uptake (athyrotic)*		
Bladder wall	0.610	2.3
Lower colon wall	0.043	0.16
Kidneys	0.065	0.24
Ovaries	0.042	0.16
Testes	0.037	0.14
Stomach	0.034	0.13
Assuming 55% thyroid uptake and 20-g gland (hyperthyroid)†		
Thyroid	790	2,933
Bladder wall	0.290	1.1
Breast	0.091	0.34
Upper colon wall	0.058	0.21
Ovaries	0.041	0.15
Testes	0.026	0.10

*From ICRP 53, page 275.

†From ICRP 53, page 278.

TABLE 4

Radiation Dose to Red Marrow for 74–7,400 MBq (2–200 mCi) ¹³¹I*

Thyroid uptake (%)	Adult mGy/MBq (rad/mCi)	Child (10 y) mGy/MBq (rad/mCi)
0	0.035 (0.13)	0.065 (0.25)
5	0.038 (0.14)	0.070 (0.26)
35	0.086 (0.32)	0.160 (0.59)
45	0.100 (0.37)	0.190 (0.70)
55	0.120 (0.45)	0.220 (0.81)

*Dose may vary depending on the whole-body effective half-life of ¹³¹I. From ICRP 53, pages 275–278.

and should indicate that informed consent was obtained and the patient was informed of possible side effects.

PART V: ISSUES REQUIRING FURTHER CLARIFICATION

- The use of ¹³¹I whole-body imaging before ¹³¹I therapy for thyroid cancer and whether “stunning” of the thyroid remnant occurs.
- The role of alternative imaging agents such as ¹²³I to avoid possible stunning.
- The necessity of treating small (<1.0 cm) papillary cancers with ¹³¹I.
- Treatment of ¹³¹I-scan-negative, thyroglobulin-positive patients.
- The role of recombinant human TSH in therapy.

PART VI: CONCISE BIBLIOGRAPHY

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PART VII: DISCLAIMER

The Society of Nuclear Medicine has written and approved guidelines to promote the cost-effective use of high-quality nuclear medicine procedures. These generic recommendations cannot be applied to all patients in all practice settings. The guidelines should not be deemed inclusive of all proper procedures or exclusive of other procedures reasonably directed to obtaining the same results. The spectrum of patients seen in a specialized practice setting may be quite different from the spectrum of patients seen in a more general practice setting. The appropriateness of a procedure will depend in part on the prevalence of disease in the patient population. In addition, the resources available to care for patients may vary greatly from one medical facility to another. For these reasons, guidelines cannot be rigidly applied.

Advances in medicine occur at a rapid rate. The date of a guideline should always be considered in determining its current applicability.

