Radioactive Iodine for Differentiated Thyroid Carcinoma

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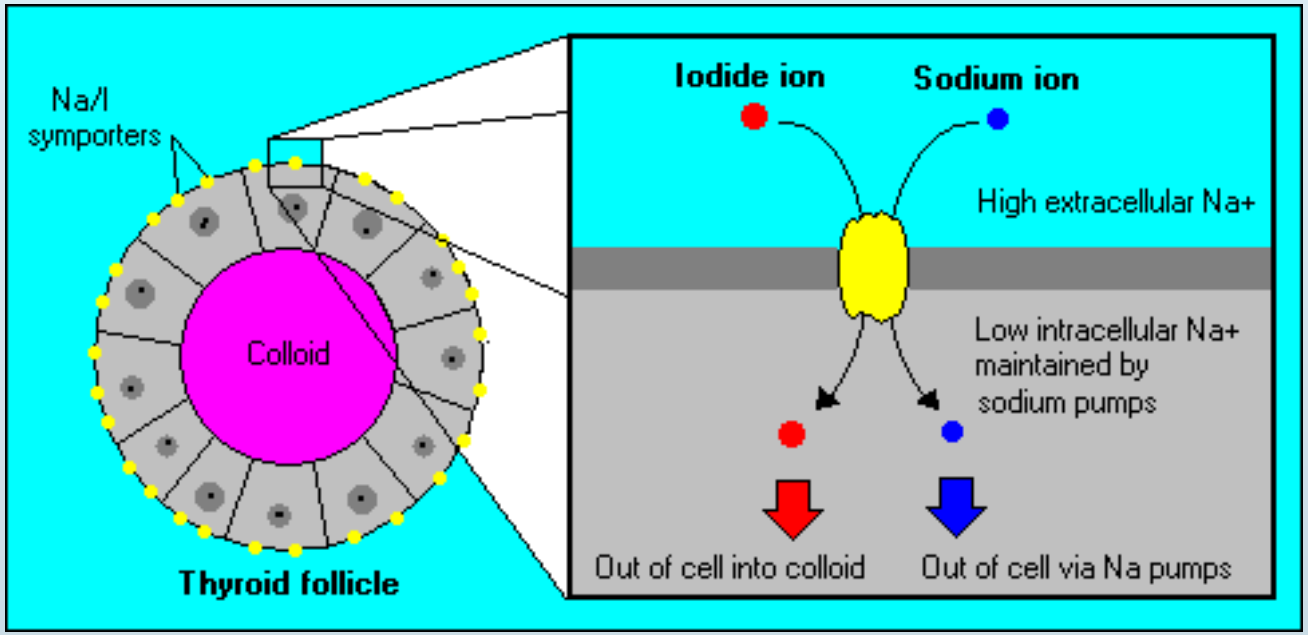
Case Question

- 48 y/o Male with T1N0Mx papillary thyroid carcinoma s/p total thyroidectomy. Pathology: Left lobe 1.5 cm in greatest dimension, Microscopic extrathyroidal extension(ETE) noted. Most likely post-surgical management?

A. Thyroid hormone replacement ASAP. No further management.
B. 100 mCi Na I-131 PO.
C. 30 mCi Na I-131 PO.
D. None of the above.

Radioiodine therapy

- Radioiodine therapy has been used in the management of patients with well-differentiated (papillary or follicular) thyroid cancer since the 1940s.
- Thyroid tissue has a unique ability to take up iodine from blood. Like iodine, radioiodine is taken up and concentrated in thyroid follicular cells because they have a membrane sodium-iodide transporter.



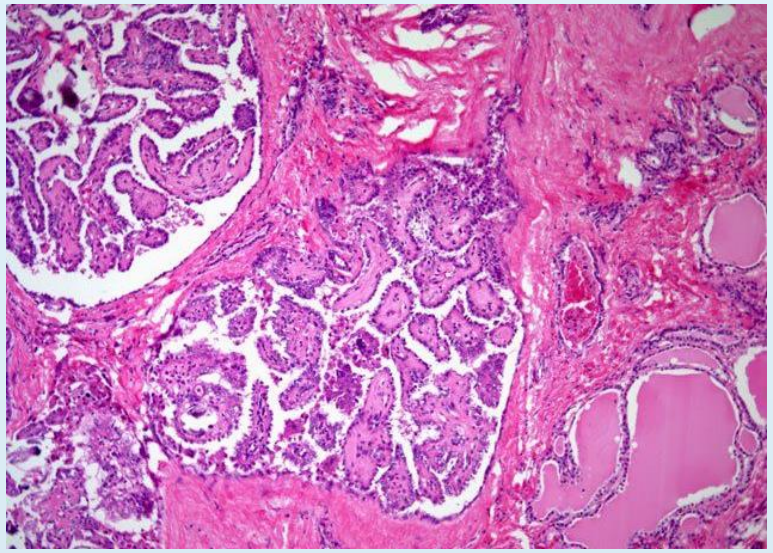
Radioiodine therapy

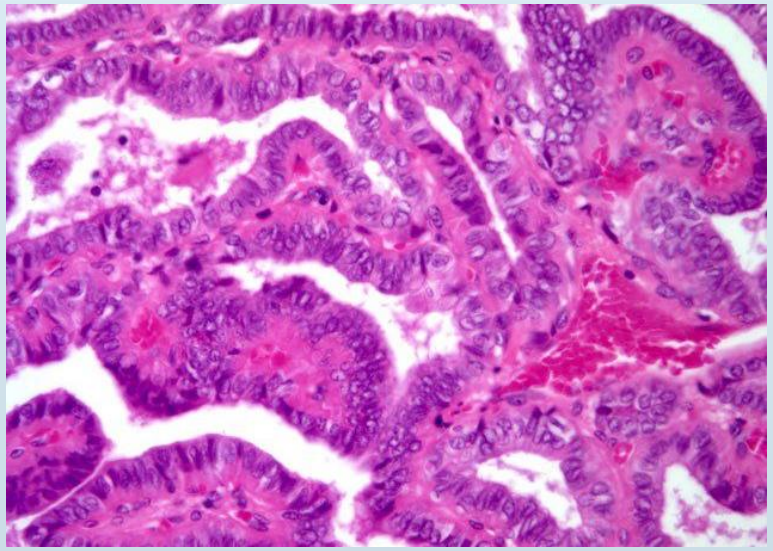
- I-131 causes acute thyroid cell death by emission of short path-length (1 to 2 mm) beta particles.
- Radioiodine must be taken up by thyroid tissue to be effective. As a result, it is of no value in patients whose thyroid cancers do not concentrate iodide (i.e., patients with medullary cancer, lymphoma, or anaplastic cancer).

Differentiated Thyroid Carcinoma

Thyroid epithelial-derived cancers are divided into three categories:

- Papillary cancer – 85 percent
- Follicular cancer – 12 percent
- Anaplastic (undifferentiated) cancer – <3 percent
- Papillary and follicular cancers are considered differentiated cancers
- Most anaplastic (undifferentiated) cancers appear to arise from differentiated cancers.

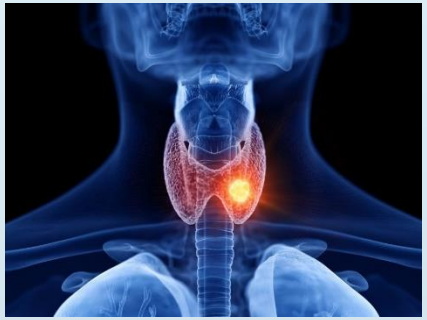




Differentiated Thyroid Carcinoma

Surgery is the primary therapy for patients with differentiated thyroid cancer.

- Preoperative ultrasound evaluation of the central and lateral neck lymph nodes is recommended for all patients with malignant cytological findings on the fine-needle aspiration (FNA). Other imaging modalities may also be used if needed.
- There are two potential surgical approaches to differentiated thyroid cancer: total (or near-total) thyroidectomy and unilateral lobectomy and isthmusectomy.
- Adequate preoperative staging will guide not only the surgical approach but also influence further management, such as radioiodine therapy dosing and follow up.



Risk Stratification

After surgery, the presence or absence of persistent disease and risk for recurrent disease should be assessed

- Serum TSH and serum thyroglobulin (Tg) should be obtained after surgery in order to better define the postoperative disease status
- Abnormal serum Tg values should prompt reevaluation of the completeness of the initial surgery (usually with neck ultrasonography) and consideration of the possibility of persistent metastatic disease.

TNM Classification

Differentiated and anaplastic thyroid carcinoma TNM staging AJCC UICC 8th edition

Primary tumor (T)	
Papillary, follicular, poorly differentiated, Hürthle cell and anaplastic thyroid carcinoma	
T category	**T criteria**
TX	Primary tumor cannot be assessed
T0	No evidence of primary tumor
T1	Tumor ≤2 cm in greatest dimension limited to the thyroid
T1a	Tumor ≤1 cm in greatest dimension limited to the thyroid
T1b	Tumor >1 cm but ≤2 cm in greatest dimension limited to the thyroid
T2	Tumor >2 cm but ≤4 cm in greatest dimension limited to the thyroid
T3	Tumor >4 cm limited to the thyroid, or gross extrathyroidal extension invading only strap muscles
T3a	Tumor >4 cm limited to the thyroid
T3b	Gross extrathyroidal extension invading only strap muscles (sternohyoid, sternothyroid, thyrohyoid, or omohyoid muscles) from a tumor of any size
T4	Includes gross extrathyroidal extension beyond the strap muscles
T4a	Gross extrathyroidal extension invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve from a tumor of any size
T4b	Gross extrathyroidal extension invading prevertebral fascia or encasing the carotid artery or mediastinal vessels from a tumor of any size
NOTE: All categories may be subdivided: (s) solitary tumor and (m) multifocal tumor (the largest tumor determines the classification).	
Regional lymph nodes (N)	
N category	**N criteria**
NX	Regional lymph nodes cannot be assessed
N0	No evidence of locoregional lymph node metastasis
N0a	One or more cytologically or histologically confirmed benign lymph nodes
N0b	No radiologic or clinical evidence of locoregional lymph node metastasis
N1	Metastasis to regional nodes
N1a	Metastasis to level VI or VII (pretracheal, paratracheal, or prelaryngeal/Delphian, or upper mediastinal) lymph nodes. This can be unilateral or bilateral disease.
N1b	Metastasis to unilateral, bilateral, or contralateral lateral neck lymph nodes (levels I, II, III, IV, or V) or retropharyngeal lymph nodes
Distant metastasis (M)	
M category	**M criteria**
M0	No distant metastasis
M1	Distant metastasis

TNM Classification

Prognostic stage groups				
Differentiated				
When age at diagnosis is...	**And T is...**	**And N is...**	**And M is...**	**Then the stage group is...**
<55 years	Any T	Any N	M0	I
<55 years	Any T	Any N	M1	II
≥55 years	T1	N0/NX	M0	I
≥55 years	T1	N1	M0	II
≥55 years	T2	N0/NX	M0	I
≥55 years	T2	N1	M0	II
≥55 years	T3a/T3b	Any N	M0	II
≥55 years	T4a	Any N	M0	III
≥55 years	T4b	Any N	M0	IVA
≥55 years	Any T	Any N	M1	IVB

Risk Stratification

ATA risk stratification system to estimate risk of persistent/recurrent disease

Low risk
Papillary thyroid cancer with all of the following present:
▪ No local or distant metastases
▪ All macroscopic tumor has been resected
▪ No invasion of locoregional tissues
▪ Tumor does not have aggressive histology (aggressive histologies include tall cell, insular, columnar cell carcinoma, Hürthle cell carcinoma, follicular thyroid cancer, hobnail variant)
▪ No vascular invasion
▪ No ^{131}I uptake outside the thyroid bed on the post-treatment scan, if done
▪ Clinical N0 or ≤5 pathologic N1 micrometastases (<0.2 cm in largest dimension)*
Intrathyroidal, encapsulated follicular variant of papillary thyroid cancer*
Intrathyroidal, well-differentiated follicular thyroid cancer with capsular invasion and no or minimal (<4 foci) vascular invasion*
Intrathyroidal, papillary microcarcinoma, unifocal or multifocal, including *BRAF* V600E mutated (if known)*

Intermediate risk
Any of the following present:
Microscopic invasion into the perithyroidal soft tissues
Cervical lymph node metastases or ^{131}I avid metastatic foci in the neck on the post-treatment scan done after thyroid remnant ablation
Tumor with aggressive histology or vascular invasion (aggressive histologies include tall cell, insular, columnar cell carcinoma, Hürthle cell carcinoma, follicular thyroid cancer, hobnail variant)
Clinical N1 or >5 pathologic N1 with all involved lymph nodes <3 cm in largest dimension*
Multifocal papillary thyroid microcarcinoma with extrathyroidal extension and *BRAF* V600E mutated (if known)*

High risk
Any of the following present:
Macroscopic tumor invasion
Incomplete tumor resection with gross residual disease
Distant metastases
Postoperative serum thyroglobulin suggestive of distant metastases
Pathologic N1 with any metastatic lymph node ≥3 cm in largest dimension*
Follicular thyroid cancer with extensive vascular invasion (>4 foci of vascular invasion)*

Radioactive Iodine?

Characteristics according to the ATA risk stratification system and AJCC/TNM staging system that may impact postoperative radioiodine decision-making

ATA risk staging (TNM)	Description	Body of evidence suggests RAI improves disease specific survival?	Body of evidence suggests RAI improves disease free survival?	Postsurgical RAI indicated?
▪ ATA low risk ▪ T1a ▪ N0, Nx ▪ M0, Mx	Tumor size ≤1 cm (uni- or multifocal)	No	No	No
▪ ATA low risk ▪ T1b, T2 ▪ N0, Nx ▪ M0, Mx	Tumor size >1 to 4 cm	No	Conflicting observational data	Not routine* — May be considered for patients with aggressive histology or vascular invasion (ATA intermediate risk).
▪ ATA low to intermediate risk ▪ T3 ▪ N0, Nx ▪ M0, Mx	Tumor size >4 cm	Conflicting data	Conflicting observational data	Consider* — Need to consider presence of other adverse features. Advancing age may favor RAI use in some cases, but specific age and tumor size cutoffs subject to some uncertainty.¶
▪ ATA low to intermediate risk ▪ T3 ▪ N0, Nx ▪ M0, Mx	Microscopic ETE, any tumor size	No	Conflicting observational data	Consider* — Generally favored based on risk of recurrent disease. Smaller tumors with microscopic ETE may not require RAI.
▪ ATA low to intermediate risk ▪ T1-3 ▪ N1a ▪ M0, Mx	Central compartment neck lymph node metastases	No, except possibly in subgroup of patients ≥45 years of age (NTCTCSG Stage III)	Conflicting observational data	Consider* — Generally favored, due to somewhat higher risk of persistent or recurrent disease, especially with increasing number of large (>2 to 3 cm) or clinically evident lymph nodes or presence of extranodal extension. Advancing age may also favor RAI use.¶ However, there is insufficient data to mandate RAI use in patients with few (<5) microscopic nodal metastases in central compartment in absence of other adverse features.
▪ ATA low to intermediate risk ▪ T1-3 ▪ N1b ▪ M0, Mx	Lateral neck or mediastinal lymph node metastases	No, except possibly in subgroup of patients ≥45 years of age	Conflicting observational data	Consider* — Generally favored, due to higher risk of persistent or recurrent disease, especially with increasing number of macroscopic or clinically evident lymph nodes or presence of extranodal extension. Advancing age may also favor RAI use.¶
▪ ATA high risk ▪ T4 ▪ Any N ▪ Any M	Any size, gross ETE	Yes, observational data	Yes, observational data	Yes
▪ ATA high risk ▪ M1 ▪ Any T ▪ Any N	Distant metastases	Yes, observational data	Yes, observational data	Yes

Radioactive Iodine?

We do not routinely administer radioiodine after lobectomy or total thyroidectomy to low-risk patients with differentiated thyroid cancer.

- Unifocal cancer <1 cm without other high-risk features (eg, without distant metastases, vascular invasion, gross extrathyroidal extension, worrisome histologic subtypes), even in the presence of small-volume regional lymph node metastases (less than five lymph nodes measuring less than 2 mm)
- Multifocal cancer when all foci are <1 cm and there are no other high-risk features
- Intrathyroidal cancer in the 1 to 4 cm range without other high-risk features
- Individual tumor- and patient-specific features may warrant radioiodine ablation in selected low-risk patients.

Goals of Radioiodine Therapy

Remnant ablation (Low to Intermediate risk) The primary goal of remnant ablation is destruction of presumably benign thyroid tissue after total thyroidectomy, to facilitate initial staging and follow-up studies.

- Improve the specificity of measurements of serum thyroglobulin (Tg) as a tumor marker
- Increase the specificity of I-131 scanning for detection of recurrent or metastatic disease by eliminating uptake by residual normal tissue

Low to Intermediate Risk

Remnant ablation

Characteristics according to the ATA risk stratification system and AJCC/TNM staging system that may impact postoperative radioiodine decision-making

ATA risk staging (TNM)	Description	Body of evidence suggests RAI improves disease specific survival?	Body of evidence suggests RAI improves disease free survival?	Postsurgical RAI indicated?
▪ ATA low risk ▪ T1a ▪ N0, Nx ▪ M0, Mx	Tumor size ≤1 cm (uni- or multifocal)	No	No	No
▪ ATA low to intermediate risk ▪ T3 ▪ N0, Nx ▪ M0, Mx	Tumor size >4 cm	Conflicting data	Conflicting observational data	Consider* — Need to consider presence of other adverse features. Advancing age may favor RAI use in some cases, but specific age and tumor size cutoffs subject to some uncertainty.¶
▪ ATA low to intermediate risk ▪ T3 ▪ N0, Nx ▪ M0, Mx	Microscopic ETE, any tumor size	No	Conflicting observational data	Consider* — Generally favored based on risk of recurrent disease. Smaller tumors with microscopic ETE may not require RAI.
▪ N1a ▪ M0, Mx		years of age (NTCTCSG Stage III)		extranodal extension. Advancing age may also favor RAI use.¶ However, there is insufficient data to mandate RAI use in patients with few (<5) microscopic nodal metastases in central compartment in absence of other adverse features.
▪ ATA low to intermediate risk ▪ T1-3 ▪ N1b ▪ M0, Mx	Lateral neck or mediastinal lymph node metastases	No, except possibly in subgroup of patients ≥45 years of age	Conflicting observational data	Consider* — Generally favored, due to higher risk of persistent or recurrent disease, especially with increasing number of macroscopic or clinically evident lymph nodes or presence of extranodal extension. Advancing age may also favor RAI use.¶
▪ ATA high risk ▪ T4 ▪ Any N ▪ Any M	Any size, gross ETE	Yes, observational data	Yes, observational data	Yes
▪ ATA high risk ▪ M1 ▪ Any T ▪ Any N	Distant metastases	Yes, observational data	Yes, observational data	Yes

Low to Intermediate Risk

Remnant ablation

Characteristics according to the ATA risk stratification system and AJCC/TNM staging system that may impact postoperative radioiodine decision-making

ATA risk staging (TNM)	Description	Body of evidence suggests RAI improves disease specific survival?	Body of evidence suggests RAI improves disease free survival?	Postsurgical RAI indicated?
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▪ ATA high risk ▪ T4 ▪ Any N ▪ Any M	Any size, gross ETE	Yes, observational data	Yes, observational data	Yes
▪ ATA high risk ▪ M1 ▪ Any T ▪ Any N	Distant metastases	Yes, observational data	Yes, observational data	Yes

Dose: 30 mCi

Radioactive Iodine

Clinical Trial > N Engl J Med. 2012 May 3;366(18):1663-73. doi: 10.1056/NEJMoa1108586.

Strategies of radioiodine ablation in patients with low-risk thyroid cancer

Martin Schlumberger [1], Bogdan Catargi, Isabelle Borget, Désirée Deandreis, Slimane Zerdoud, Boumédiène Bridji, Stéphane Bardet, Laurence Leenhardt, Delphine Bastie, Claire Schvartz, Pierre Vera, Olivier Morel, Danielle Benisvy, Claire Bournaud, Françoise Bonichon, Catherine Dejax, Marie-Elisabeth Toubert, Sophie Leboulleux, Marcel Ricard, Ellen Benhamou, Tumeurs de la Thyroïde Refractaires Network for the Essai Stimulation Ablation Equivalence Trial

Collaborators, Affiliations + expand

PMID: 22551127 DOI: 10.1056/NEJMoa1108586

Abstract

Background: It is not clear whether the administration of radioiodine provides any benefit to patients with low-risk thyroid cancer after a complete surgical resection. The administration of the smallest possible amount of radioiodine would improve care.

Methods: In our randomized, phase 3 trial, we compared two thyrotropin-stimulation methods (thyroid hormone withdrawal and use of recombinant human thyrotropin) and two radioiodine ((131)I) doses (i.e., administered activities) (1.1 GBq and 3.7 GBq) in a 2-by-2 design. Inclusion criteria were an age of 18 years or older; total thyroidectomy for differentiated thyroid carcinoma; tumor-node-metastasis (TNM) stage, ascertained on pathological examination (p) of a surgical specimen, of pT1 (with tumor diameter ≤1 cm) and N1 or Nx, pT1 (with tumor diameter >1 to 2 cm) and any N stage, or pT2N0; absence of distant metastasis; and no iodine contamination. Thyroid ablation was assessed 8 months after radioiodine administration by neck ultrasonography and measurement of recombinant human thyrotropin-stimulated thyroglobulin. Comparisons were based on an equivalence framework.

Results: There were 752 patients enrolled between 2007 and 2010; 92% had papillary cancer. There were no unexpected serious adverse events. In the 684 patients with data that could be evaluated, ultrasonography of the neck was normal in 652 (95%), and the stimulated thyroglobulin level was 1.0 ng per milliliter or less in 621 of the 652 patients (95%) without detectable thyroglobulin antibodies. Thyroid ablation was complete in 631 of the 684 patients (92%). The ablation rate was equivalent between the (131)I doses and between the thyrotropin-stimulation methods.

Conclusions: The use of recombinant human thyrotropin and low-dose (1.1 GBq) postoperative radioiodine ablation may be sufficient for the management of low-risk thyroid cancer. (Funded by the French National Cancer Institute [INCa] and the French Ministry of Health; ClinicalTrials.gov number, NCT00435851; INCa number, RECF0447.).

Goals of Radioiodine Therapy

Adjuvant treatment (Intermediate risk) Primary goal is destruction of subclinical tumor deposits that may or may not be present after surgical resection.

- Potential benefits of 131-I adjuvant treatment could include:
  - Destruction of subclinical, microscopic foci of disease remaining after surgery
  - Decreased risk of recurrence
  - Improved disease-specific survival
  - Improved progression-free survival

Intermediate Risk

Adjuvant treatment

Characteristics according to the ATA risk stratification system and AJCC/TNM staging system that may impact postoperative radioiodine decision-making

ATA risk staging (TNM)	Description	Body of evidence suggests RAI improves disease specific survival?	Body of evidence suggests RAI improves disease free survival?	Postsurgical RAI indicated?
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▪ ATA low risk ▪ T1b, T2 ▪ N0, Nx ▪ M0, Mx	Tumor size >1 to 4 cm	No	Conflicting observational data	Not routine* — May be considered for patients with aggressive histology or vascular invasion (ATA intermediate risk).
▪ ATA low to intermediate risk ▪ T3 ▪ N0, Nx ▪ M0, Mx	Tumor size >4 cm	Conflicting data	Conflicting observational data	Consider* — Need to consider presence of other adverse features. Advancing age may favor RAI use in some cases, but specific age and tumor size cutoffs subject to some uncertainty.¶
▪ ATA low to intermediate risk ▪ T1-3 ▪ N1a ▪ M0, Mx	Central compartment neck lymph node metastases	No, except possibly in subgroup of patients ≥45 years of age (NTCTCSG Stage III)	Conflicting observational data	Consider* — Generally favored, due to somewhat higher risk of persistent or recurrent disease, especially with increasing number of large (>2 to 3 cm) or clinically evident lymph nodes or presence of extranodal extension. Advancing age may also favor RAI use.¶ However, there is insufficient data to mandate RAI use in patients with few (<5) microscopic nodal metastases in central compartment in absence of other adverse features.
▪ ATA low to intermediate risk ▪ T1-3 ▪ N1b ▪ M0, Mx	Lateral neck or mediastinal lymph node metastases	No, except possibly in subgroup of patients ≥45 years of age	Conflicting observational data	Consider* — Generally favored, due to higher risk of persistent or recurrent disease, especially with increasing number of macroscopic or clinically evident lymph nodes or presence of extranodal extension. Advancing age may also favor RAI use.¶
▪ Any N ▪ Any M		data	data	
▪ ATA high risk ▪ M1 ▪ Any T ▪ Any N	Distant metastases	Yes, observational data	Yes, observational data	Yes

Intermediate Risk

Adjuvant treatment

Characteristics according to the ATA risk stratification system and AJCC/TNM staging system that may impact postoperative radioiodine decision-making

ATA risk staging (TNM)	Description	Body of evidence suggests RAI improves disease specific survival?	Body of evidence suggests RAI improves disease free survival?	Postsurgical RAI indicated?
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▪ Any N ▪ Any M		data	data	
▪ ATA high risk ▪ M1 ▪ Any T ▪ Any N	Distant metastases	Yes, observational data	Yes, observational data	Yes

Dose: 50-100 mCi

Goals of Radioiodine Therapy

Treatment of known disease (High Risk) The primary goal in the treatment of known disease is destruction of clinically apparent macroscopic disease (evidenced by either abnormal thyroglobulin values or structural findings) that is not amenable to surgical therapy.

- Radioiodine treatment of residual disease and metastatic disease may reduce the risk of recurrence and mortality, especially in small-volume disease that is radioiodine avid.

High Risk

Treatment of known disease

Characteristics according to the ATA risk stratification system and AJCC/TNM staging system that may impact postoperative radioiodine decision-making

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▪ ATA low to intermediate	Lateral neck or mediastinal lymph	No, except possibly in	Conflicting observational	Consider* — Generally favored, due to higher risk of persistent or recurrent disease, especially with
▪ ATA high risk ▪ T4 ▪ Any N ▪ Any M	Any size, gross ETE	Yes, observational data	Yes, observational data	Yes
▪ ATA high risk ▪ M1 ▪ Any T ▪ Any N	Distant metastases	Yes, observational data	Yes, observational data	Yes

High Risk

Treatment of known disease

Characteristics according to the ATA risk stratification system and AJCC/TNM staging system that may impact postoperative radioiodine decision-making

ATA risk staging (TNM)	Description	Body of evidence suggests RAI improves disease specific survival?	Body of evidence suggests RAI improves disease free survival?	Postsurgical RAI indicated?
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▪ ATA high risk ▪ T4 ▪ Any N ▪ Any M	Any size, gross ETE	Yes, observational data	Yes, observational data	Yes
▪ ATA high risk ▪ M1 ▪ Any T ▪ Any N	Distant metastases	Yes, observational data	Yes, observational data	Yes

Dose:100-200 mCi

Patient Preparation

Radioiodine uptake by thyroid tissue is stimulated by TSH.

- There are two methods for increasing TSH, thyroid hormone withdrawal(30 uiU/ml) or administration of recombinant human TSH (rhTSH [thyrotropin alfa]).

Radioiodine uptake is reduced by the presence of excess stable iodide.

- Patient is instructed to avoid all iodine-containing medications and to limit dietary intake of iodine for at least one week.

Contraindications

Pregnancy and breastfeeding are absolute contraindications to radioiodine therapy.

- Fetal thyroid tissue is functional by 10 to 12 weeks and could be destroyed by the radioiodine, resulting in cretinism.
- Negative pregnancy test 24 hours (or less) before treatment or history of surgical sterilization.
- Breastfeeding should be stopped at least six to eight weeks prior to radioiodine therapy to reduce uptake of radioiodine by breast tissue.

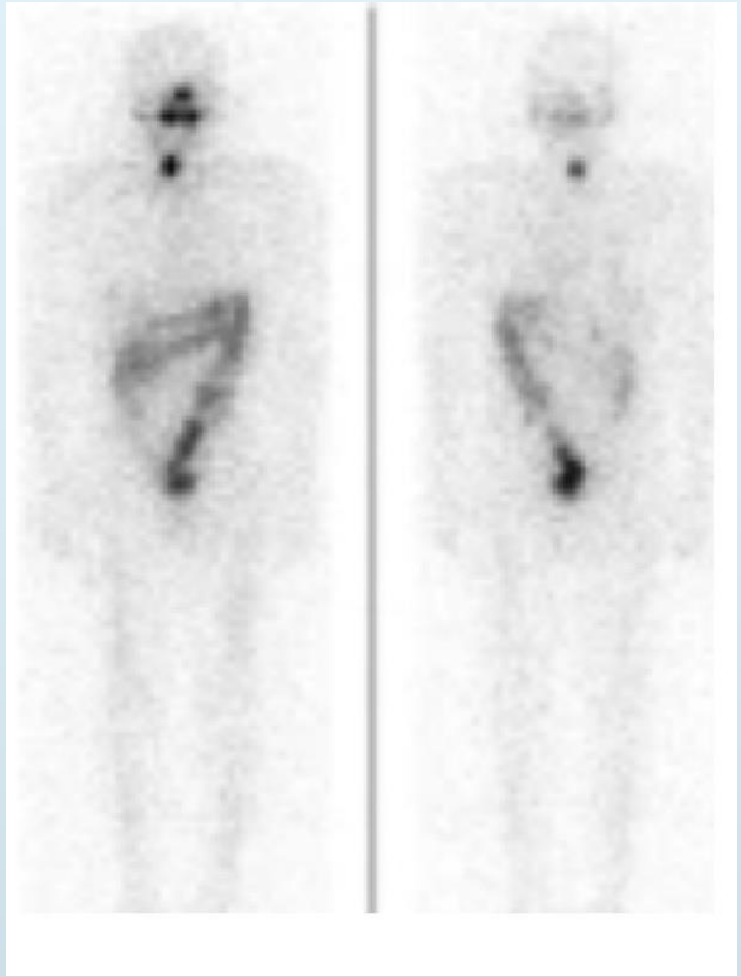
Radiation Safety

Patients who receive radioiodine have the potential to expose their household contacts to very low levels of radiation via body fluids or radiation emitting from their body.

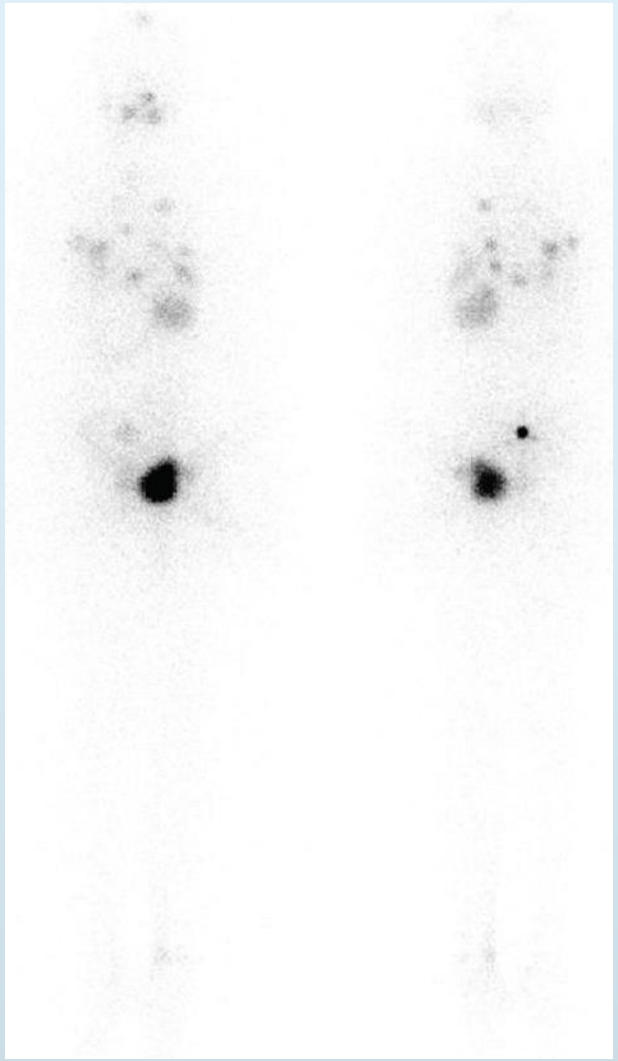
- Treated patients are given patient-specific advice on the necessary precautions to reduce radiation exposure to family members, caregivers, and the general public.
- Pregnancy should generally be delayed for at least six months after radioiodine therapy
- Men should delay attempts to produce pregnancy for a period of three to four months
- Travel — Low levels of I-131 activity can be picked up by radiation detection systems at airports. Treated patients may trigger alarms for as long as 95 days posttherapy.

Post Therapy Scan

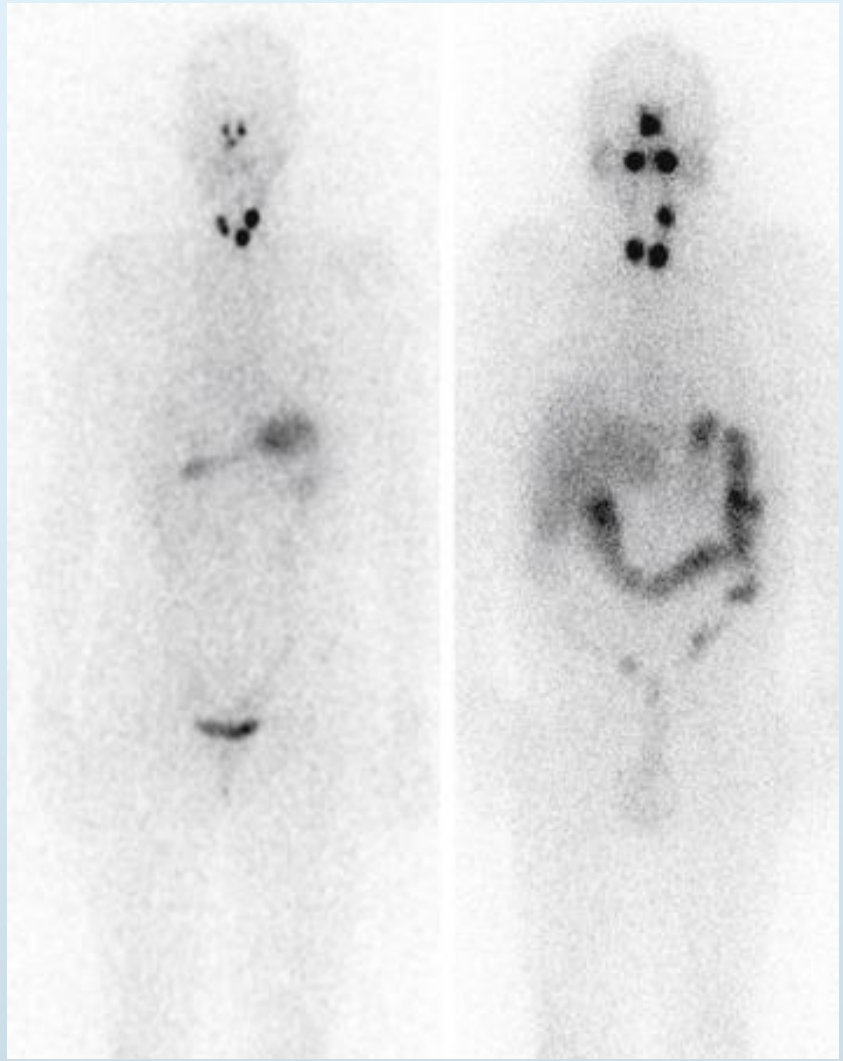
- Tumor uptake and biodistribution of radioiodine is confirmed by performing a whole-body scan 7 to 14 days after radioiodine treatment.
- Anterior and posterior whole body images are assessed for residual tissue and evidence of metastatic disease.
- SPECT-CT may be performed for anatomical correlation, if needed.



Post Therapy Scan



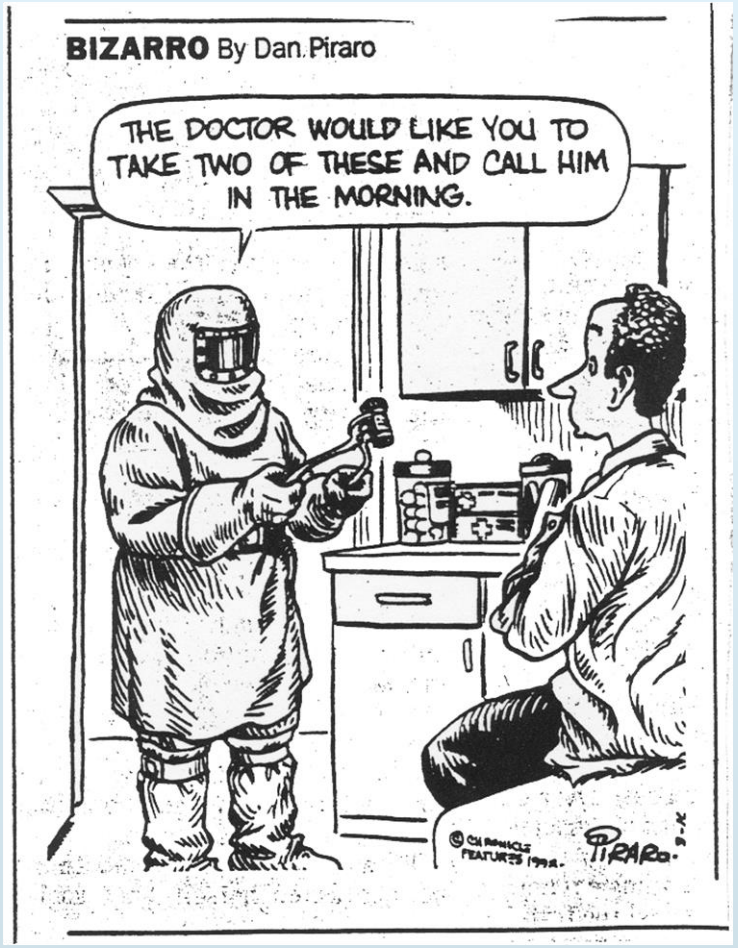
Lung and bone metastases



Neck lymph node metastases

Complications

- Sialadenitis — Most treated patients experience dose-related reductions in salivary flow, and some experience transient decreased or altered sense of taste.
- Nausea/Vomiting-*
- Neck swelling
- Gonadal function and fertility -Transient oligospermia and decreases in ovarian function may occur.
- Transient amenorrhea for one to four months occurs in roughly 10 to 25 percent of women.
- Nasolacrimal duct obstruction - presenting as epiphora (excessive tearing), reported to occur after as low an administered activity as 100 mCi.



Follow Up

Without evidence for possible or proven persistent disease (rising serum thyroglobulin, antithyroglobulin antibodies, indeterminate/suspicious structural findings), follow-up whole-body radioactive iodine scans are not used for routine surveillance.

- A negative whole body I-131 scan with above mentioned findings should be followed by PET-CT.
- rhTSH is recommended all patients who require radioiodine scanning, unless they are thought to be likely in need of subsequent radioiodine therapy that is preferably done using thyroid hormone withdrawal.
- Imaging is usually done at 48 hours using the rhTSH approach or at 48 to 72 hours following thyroid hormone withdrawal.

Case Question

- 48 y/o Male with T1N0Mx papillary thyroid carcinoma s/p total thyroidectomy. Pathology: Left lobe 1.5 cm in greatest dimension, Microscopic extrathyroidal extension(ETE) noted. Most likely post-surgical management?

A. Thyroid hormone replacement ASAP. No further management.
B. 100 mCi Na I-131 PO.
C. 30 mCi Na I-131 PO.
D. None of the above.

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A wise man once said…

The end is merely the start.

Thank You!