

Radioiodine (I-131) Therapy: Why, When & How Much? In 20 minutes



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Radioiodine (I-131) Therapy: Why, When & How Much?

Why is this so controversial? So many guidelines

Organization	Guideline
ATA	"RAI ablation is not recommended for patients with unifocal cancer < 1 cm without other higher risk features [such as clear margins, no vascular invasion, no lymph node involvement, no aggressive histological features, no distant metastases]."
EC*	Very low-risk group, which are patients with complete surgery, favorable histology, unifocal microcarcinoma (< 1 cm) with no extension beyond the thyroid capsule and without lymph node or distant metastases: "No benefit of post-operative ¹³¹ I." High-risk group, which are patients with documented distant metastases, persistent disease, incomplete tumor resection.
BTA	"They designate 'Postsurgical re (thyroid ablation)' ¹³¹ I ablative or tumoricidal [adjuvant] treatment of DTC with radioiodine should be considered in the postsurgical management of patients with a maximum tumor diameter less than 1.0 cm in the presence of high-risk features such as aggressive histology, incomplete resection, or distant metastases."
SNM	" ¹³¹ I ablative or tumoricidal [adjuvant] treatment of DTC with radioiodine should be considered in the postsurgical management of patients with a maximum tumor diameter greater than 1.0 cm or a maximum tumor diameter less than 1.0 cm in the presence of high-risk features such as aggressive histology, incomplete resection, or distant metastases."
NCCN *	No ¹³¹ I therapy when all of the following are met: negative margins, no contralateral lesions, no suspicious nodes, no distant metastases, thyroglobulin < 1 ng/ml with negative anti-thyroglobulin antibody, and radioiodine imaging negative. Suspected or proven thyroid bed uptake: consider adjuvant radioiodine ablation to destroy residual disease.
CSE	From a combination of algorithms from the ATA and SNM. No ¹³¹ I therapy when all of the following are met: negative margins, no suspicious nodes, no distant metastases, thyroglobulin < 1 ng/ml with negative anti-thyroglobulin antibody and radioiodine imaging negative. Suspected or proven thyroid bed uptake: consider adjuvant radioiodine ablation to destroy residual disease. Tumor 1-4 cm in diameter or aggressive variant

**Radioiodine (I-131) Therapy:
Why, When & How Much?**

Why is this so controversial?

- One term with different definitions and/or objectives,
- Different terms with identical definitions and/or objectives,
- So many different opinions regarding risk stratification,

**Radioiodine (I-131) Therapy:
Why, When & How Much?**

Why is this so controversial?

- So many different practice situations,
- Inadequate evidence based medicine,
- And many more factors.

Overview

- **Definitions of ^{131}I therapy**
 - *Remnant ablation,*
 - *Adjuvant treatment, and*
 - *Treatment of known locoregional and/or distant metastases.*
- **Amount of prescribed activity of ^{131}I**
- **Staging and Risk Stratification**
 - *Low,*
 - *Intermediate, and*
 - *High risk*
- **Indications for the various therapies**

Overview

- For this presentation, risk stratification, definitions, and recommendations are predominantly from the 2015 *draft* ATA guidelines.
- This does not necessarily mean that I agree with any or all of them.
- I will give my personal comments after each recommendation.

Overview

- *I don't care if you turn off your cell phones or not,*
- *But please withhold throwing all tomatoes and rotten eggs until the end of the presentation.*

Definitions

If your facility is like our facility, everybody is frequently using:

- **The same terms with different definitions and objectives, or**
- **The same definitions and objectives for different terms.**

Definitions

The following are definitions from the ATA guidelines of 2009 as well as the *draft 2015 guidelines.*

Definitions

“Remnant Ablation . . . is the use of ^{131}I to destroy residual functioning thyroid tissue after thyroidectomy. It’s objectives are to:

- (1) Facilitate the interpretation of subsequent serum thyroglobulin levels,
- (2) Increase the sensitivity of detection of loco-regional disease and/or metastatic disease on any subsequent follow-up radioiodine whole body scan,
- (3) Maximize the therapeutic effect of any subsequent ^{131}I therapies, and
- (4) Allow a post-therapy scan that may identify additional sites of metastases that were not identified on the pre-therapy scan or when a pre-therapy scan had not been performed.”

Definitions

“Remnant Ablation . . . is the use of ^{131}I to destroy residual functioning thyroid tissue after thyroidectomy. It’s objectives are to:

- There is nothing in the definition or objectives for remnant ablation regarding increasing progression free survival, increasing disease-free survival, or decreasing recurrence rates.

Definitions

“Adjuvant treatment “. . . is the use of ^{131}I to destroy unknown microscopic thyroid cancer and/or suspected but unproven remaining thyroid cancer with the objective of:

- (1) Potentially increasing disease-specific survival, progression free survival, decreasing recurrence and/or mortality from thyroid cancer.

Definitions

Treatment “. . . is the use of ^{131}I to destroy known loco-regional and/or distant metastasis with the objectives of potential cure, increase progression free survival, reduced recurrence, reduced mortality, and/or palliation.”

The use of the adjectives *loco-regional* or *distant metastatic* is used to modify the term **treatment**.

Definitions

Therapy “. . . is any generic use of ^{131}I including ^{131}I remnant ablation, ^{131}I adjuvant treatment, or ^{131}I loco regional or distant metastatic treatment.

Prescribed Activity	“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines	
Type of ¹³¹ I Therapy	Recommended	
Remnant Ablation	1.1 GBq (30 mCi) is generally favored.	

Prescribed Activity	“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines	
Type of ¹³¹ I Therapy	Recommended	
Adjuvant Treatment	Two different recommendations in two different sections.	
	1.1 GBq (30 mCi) to 5.55 GBq (150 mCi).	
	3.7 GBq (100 mCi) to 5.55 GBq (150 mCi).	

Prescribed Activity	Personal Comments	
Type of ¹³¹ I Therapy	Recommendations	
Adjuvant Treatment	Until further studies, recommend 3.7 GBq (100 mCi) to 5.55 GBq (150 mCi).	

Prescribed Activity	“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines	
Type of ¹³¹ I Therapy	Recommendation 77	
Treatment of Distant Mets Lung	Will discuss prescribed activity of ¹³¹ I for distant metastases after discussion of low and intermediate risk disease	

Risk Stratification

Low Risk

- (1) No local or distant mets.
 - (2) All macroscopic tumor has been resected.
 - (3) No tumor invasion of locoregional tissues or structures.
 - (4) No aggressive histology.
 - (5) No vascular invasion.
 - (6) Clinical N0 or ≤ 5 pathological N1 micrometastases (< 0.2 cm).
#6 is the most controversial.
7. If I-131 is given, no avid mets outside of thyroid bed on first post-treatment whole body scan.
 8. Intrathyroidal
 - a. Encapsulated FVPC
 - b. Well-differentiated follicular with only capsular invasion or minor vascular invasion.
 - c. Papillary microcarcinoma unifocal or multi-focal including V600E BRAF

Risk Stratification

Intermediate Risk

- (1) Clinical N1 or > 5 pathological N1 with all lymph nodes < 3 cm in largest dimension.
 - (2) RAI avid metastatic foci in neck on first post-tx whole body scan
 - (3) Aggressive histology
 - (4) Papillary thyroid cancer with vascular invasion
 - (5) Intrathyroid, papillary 1-4 cm, V600E BRAF muted
6. Multifocal papillary microcarcinoma with extrathyroidal extension and V600E BRAF muted.

Risk Stratification

High Risk

- (1) Macroscopic invasion into perithyroidal soft tissues (gross extrathyroidal extension)
- (2) Incomplete tumor resection
- (3) Distant metastases.

Low Risk

“Take-Home-Message” from the 2015 *draft* ATA Guidelines

Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?
<ul style="list-style-type: none"> *Tumor \leq 1 cm *Uni or multi-focal *No invasion / extension *No known positive nodes *No known metastases 	No	No	No

Low Risk		Personal Comments	
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?
*Tumor \leq 1 cm *Uni or multi-focal *No invasion / extension *No known positive nodes *No known metastases	No	No	Agree.

Low Risk		“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines	
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?
*Tumor 1 - 4 cm *No invasion / extension *No known nodes *No known metastases	No	*Conflicting data	*Not routine. *May be considered for patients with aggressive histology. *Does not say whether remnant ablation or adjuvant treatment.

Low Risk		Personal Comments	
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?
*Tumor 1 - 4 cm *No invasion / extension *No known nodes *No known metastases	No	*Conflicting data	*Consider remnant ablation with 30 mCi.

Low to Intermediate Risk		“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines	
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?
*Tumor > 4 cm *No invasion / extension *No known nodes *No known metastases	*Conflicting data	*Conflicting data	*Need to consider other adverse features such as age, aggressive histology *Does not say whether remnant ablation or adjuvant treatment.

Low to Intermediate Risk		Personal Comments		
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?	
*Tumor > 4 cm *No invasion / extension *No known nodes *No known metastases	*Conflicting data	*Conflicting data	*Remnant ablation with 30 mCi. *Consider adjuvant treatment with 100 - 150 mCi.	

Low to Intermediate Risk		“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines		
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?	
*Microscopic extrathyroidal extension (ETE) *Any tumor size *No nodes *No metastases	No	*Conflicting Data	*Consider. *Generally favored. *Smaller tumors with microscopic ETE may not require I-131. *Does not say if remnant ablation or adjuvant treatment.	

Low to Intermediate Risk		Personal Comments	
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?
*Microscopic extrathyroidal extension *Any tumor size *No nodes *No metastases	No	*Conflicting Data	*Remnant ablation with 30 mCi. *Consider adjuvant treatment with 100 to 150 mCi.

Low to Intermediate Risk		“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines	
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?
*Positive nodes in central compartment *No metastases	No, except possibly in pts \geq 45 y.o.	*Conflicting data	*Consider. *Generally favored due to higher risk of persistent or recurrent diseases especially with increasing number of macroscopic or clinically evident lymph nodes or presence of extra-nodal extension. *Does not say if remnant ablation or adjuvant treatment.

Low to Intermediate Risk		“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines		
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?	
*Positive nodes in central compartment *No metastases	No, except possibly in pts \geq 45 y.o.	*Conflicting data	*But if <5 microscopic nodal metastases in central compartment, insufficient data to mandate I-131.	

Low to Intermediate Risk		Personal Comments		
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?	
*Positive nodes in central compartment *No metastases	No, except possibly in pts \geq 45 y.o.	*Conflicting data	*Adjuvant treatment with 100-150 mCi.	

Low to Intermediate Risk		“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines	
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?
<p>*Positive nodes in lateral or mediastinum</p> <p>*No metastases</p>	No, except possibly in pts \geq 45 y.o.	*Conflicting data	<p>*Consider.</p> <p>*Generally favored due to higher risk of persistent or recurrent diseases especially with increasing number of macroscopic or clinically evident lymph nodes or presence of extra-nodal extension.</p> <p>*Does not say if remnant ablation or adjuvant treatment.</p>

Low to Intermediate Risk		Personal Comments	
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?
<p>*Positive nodes in lateral or mediastinum</p> <p>*No metastases</p>	No, except possibly in pts \geq 45 y.o.	*Conflicting data	<p>*Adjuvant treatment with 100-150 mCi.</p> <p>*Consider full or simplified dosimetry.</p>

High Risk		“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines		
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?	
*Any gross extrathyroidal extension (T4)	Yes	Yes	*Yes. *Does not say if remnant ablation or adjuvant treatment.	

High Risk		Personal Comments		
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?	
*Any gross extrathyroidal extension (T4)	Yes	Yes	*Adjuvant treatment with 100 to 150 mCi. *Consider full or simplified dosimetry.	

High Risk		“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines		
Risk Stratification	Improves disease-specific survival?	Improves disease-free survival?	¹³¹ I therapy?	
Distant metastases	Yes	Yes	Yes	

Prescribed Activity		“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines	
Type of ¹³¹ I Therapy	Recommendation 77		
Treatment of Distant Mets Lung	Pulmonary micrometastases should be treated with RAI therapy, and repeated every 6–12 months as long as disease continues to concentrate RAI and respond clinically, because the highest rates of complete remission are reported in these subgroups. (Strong recommendation, Moderate-quality evidence)		
	The selection of RAI activity to administer for pulmonary micrometastases can be empiric (100–200 mCi, or 100-150 mCi for patients >70 yo) or estimated by dosimetry to limit whole-body retention to 80 mCi at 48 hours and 200 cGy to the red bone marrow. (Strong recommendation, Moderate-quality evidence)		

Prescribed Activity	Personal Comments	
Type of ¹³¹ I Therapy	Recommendation 78	
Treatment of Distant Mets Lung	Radioiodine-avid macronodular metastases may be treated with RAI and treatment may be repeated when objective benefit is demonstrated (decrease in the size of the lesions, decreasing Tg), but complete remission is not common and survival remains poor.	
	The selection of RAI activity to administer can be made empirically (100–200 mCi) or by lesional dosimetry or whole-body dosimetry if available in order to limit whole-body retention to 80 mCi at 48 hours and 200 cGy to the red bone marrow. (Weak Recommendation, Low quality evidence)	

Prescribed Activity	Personal Comments	
Type of ¹³¹ I Therapy	Recommendations	
Treatment of Distant Mets Lung	1. With the nature of guidelines and variability of patients with pulmonary metastases, it is difficult to present very specific guidelines.	
	2. Too many factors that must be considered and/or presented in a consensus guidelines.	
	3. Must individualize!!!!!!	

**Prescribed
Activity**

Personal Comments

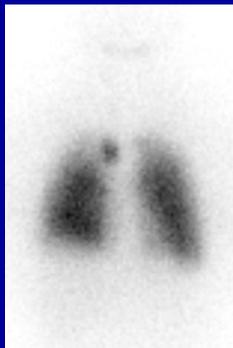
Individualize

- Age.
- Histology.
- Number of metastases.
- Potential for surgical excision.
- Size and pattern of metastasis(s).

**Prescribed
Activity**

Personal Comments

¹³¹I scan

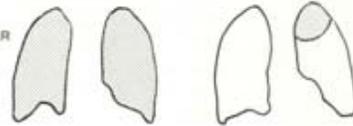


Diffuse micronodular
pattern with one
macronodular area

DIFFUSE

REGIONAL

MICRONODULAR



1. Micronodular disease can be diffuse or regional.
2. Better prognosis.
3. More responsive to ¹³¹I.

Prescribed Activity

Personal Comments

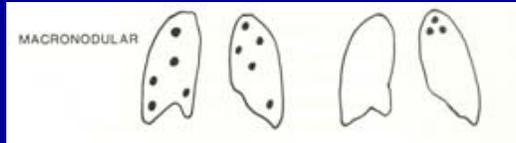
¹³¹I scan



Multiple macronodular pattern (arrowheads)

DIFFUSE

REGIONAL

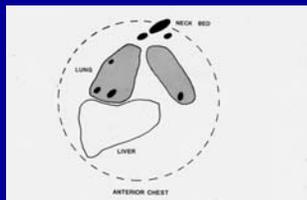
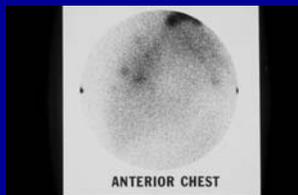


1. Macronodular disease can be both diffuse or regional.
2. Frequently reduced prognosis.
3. Often less responsive to ¹³¹I.

Prescribed Activity

Personal Comments

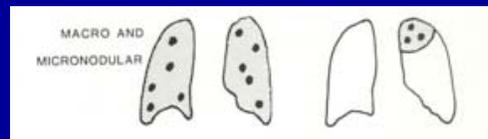
¹³¹I scan



Mixed macronodular and diffuse micronodular pattern.

DIFFUSE

REGIONAL



1. Mixed prognosis and response to ¹³¹I

Prescribed Activity	Personal Comments
<ul style="list-style-type: none"> •Age. •Histology. •Number of metastases. •Potential for surgical excision. •Size and pattern of metastasis(es). •Uptake of radioiodine. •Radiological evidence of disease •Other organs involved. •Signs and symptoms secondary to metastasis. •Response of metastases to any previous ¹³¹I treatment (e.g., indicated by physical exam, radioiodine scan, chest X-ray, US, CT, MRI, and serum Tg levels). 	<ul style="list-style-type: none"> •Response of CBC and absolute neutrophil count during the 3–6 wk period after any previous treatment. •Change in baseline CBC and differential after any previous treatment. •Pulmonary function tests pretreatment. •Change in pulmonary function tests after treatment. •Concomitant disease(s). •Facilities available. •Patient desire(s).

Prescribed Activity	Personal Comments															
<table border="1"> <thead> <tr> <th data-bbox="345 1239 557 1344">Type of ¹³¹I Therapy</th> <th data-bbox="557 1239 1289 1344">Recommendations</th> </tr> </thead> <tbody> <tr> <td data-bbox="345 1344 557 1480">Treatment of Distant Lung Mets</td> <td data-bbox="557 1344 1289 1480">1. Too many factors that must be considered and/or presented in a consensus guidelines.</td> </tr> <tr> <td data-bbox="345 1480 557 1533"></td> <td data-bbox="557 1480 1289 1533">2. Must individualize!!!!!!</td> </tr> <tr> <td data-bbox="345 1533 557 1606"></td> <td data-bbox="557 1533 1289 1606">3. Single pulmonary met; consider surgery.</td> </tr> <tr> <td data-bbox="345 1606 557 1680"></td> <td data-bbox="557 1606 1289 1680">4. Risk stratify (e.g. age, macronodular vs microdular, CT positive or negative, etc.</td> </tr> <tr> <td data-bbox="345 1680 557 1732"></td> <td data-bbox="557 1680 1289 1732">5. Consider full or simplified dosimetry.</td> </tr> <tr> <td data-bbox="345 1732 557 1785"></td> <td data-bbox="557 1732 1289 1785">6. Consider referring the patient</td> </tr> </tbody> </table>	Type of ¹³¹ I Therapy	Recommendations	Treatment of Distant Lung Mets	1. Too many factors that must be considered and/or presented in a consensus guidelines.		2. Must individualize!!!!!!		3. Single pulmonary met; consider surgery.		4. Risk stratify (e.g. age, macronodular vs microdular, CT positive or negative, etc.		5. Consider full or simplified dosimetry.		6. Consider referring the patient		
Type of ¹³¹ I Therapy	Recommendations															
Treatment of Distant Lung Mets	1. Too many factors that must be considered and/or presented in a consensus guidelines.															
	2. Must individualize!!!!!!															
	3. Single pulmonary met; consider surgery.															
	4. Risk stratify (e.g. age, macronodular vs microdular, CT positive or negative, etc.															
	5. Consider full or simplified dosimetry.															
	6. Consider referring the patient															

Prescribed Activity	“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines	
Type of ¹³¹ I Therapy	Recommendation 79	
Treatment of Distant Bone Mets	RAI therapy of iodine-avid bone metastases has been associated with improved survival and should be employed, although RAI is rarely curative. (Strong recommendation, Moderate-quality evidence)	
	The RAI activity administered can be given empirically (100–200 mCi) or determined by dosimetry. (Weak recommendation, Low-quality evidence)	

Prescribed Activity	Personal Comments	
Type of ¹³¹ I Therapy	Recommendations	
Treatment of Distant Bone Mets	If one or two focal bone metastases are amenable to local treatment such as surgery, then consider local treatment first if there is no other evidence of metastases.	
	Recommend dosimetry because one is trying to maximize the likelihood of delivering a radiation absorbed dose that is therapeutic.	
	Because full dosimetry is typically not available and is time consuming, consider adopting one of the two simplified methods of dosimetry, which may be performed in almost any nuclear medicine lab.	

Prescribed Activity	“Take-Home-Message” from the 2015 <i>draft</i> ATA Guidelines	
Type of ¹³¹ I Therapy	Recommendation 94	
Treatment of Distant Brain Mets	<p>While surgical resection and stereotactic external beam radiotherapy are the mainstays of therapy for CNS metastases, RAI can be considered if CNS metastases concentrate RAI. If RAI is being considered, stereotactic external beam radiotherapy and concomitant glucocorticoid therapy are recommended prior to RAI therapy to minimize the effects of a potential TSH induced increase in tumor size and RAI-induced inflammatory response. (Weak recommendation, Low-quality evidence)</p>	

Prescribed Activity	Personal Comments	
Type of ¹³¹ I Therapy	Recommendation	
Treatment of Distant Brain Mets	Recommend surgery first.	
	Recommend radiation therapy second.	
	<p>Even if there is radioiodine uptake in a brain metastases, recommend one of the above two interventions first, and then consider ¹³¹I therapy for other sites of distant metastases.</p>	

One Final Thought

**regarding ^{131}I prescribed activity
for locoregional and distant
metastases:**

**A small change in ^{131}I prescribed
activity may make a big difference
in outcomes.**

**A small change can make a big
difference in outcomes.**



A small change can make a big difference in outcomes.



A small change can make a big difference in outcomes.



One Final Thought

A small change in ^{131}I prescribed activity may make a big difference in outcomes.

Because 30 mCi may work as well as 100 mCi, may mean they are equally INEFFECTIVE.

*Special Thanks to the Staff of the
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