131-I Therapy Planning in Thyroid Cancer:
The role of diagnostic radioiodine scans

Anca M. Avram, M.D.
Associate Professor of Radiology

Department of Nuclear Medicine
University of Michigan
Ann Arbor, USA
Disclosures

Nothing to disclose
Objectives: define the role of pre-ablation scans with SPECT/CT for:

1. post-operative staging in thyroid cancer
2. post-operative risk stratification in thyroid cancer
3. post-operative management
4. Identification of regional and distant metastases
5. 131-I therapy planning: ablation, adjuvant treatment, targeted treatment for metastatic disease, dosimetry-guided 131-I therapy
Differentiated Thyroid Cancer (DTC)

- Most common forms of thyroid cancer are:
  - Papillary carcinoma (~80% of cases)
  - Follicular carcinoma (~10% of cases)
- In DTC, tumor cells retain the characteristics of normal differentiated thyroid cells.
  - Preferential ability to take up and store iodine
  - Secrete thyroglobulin (Tg)
Context

- 2.6 x increased incidence of Thy CA, 1973 – 2006
- This trend continues for the past 30 years
- 87% of new cases are T1 tumors (≤ 2 cm)
Differentiated Thyroid Cancer

• Generally a slow-growing tumor
  
  ≥98% 5-year survival rate with less advanced stages
  
  – ~50% 5-year survival in advanced cases (distant mets)

• Risk of recurrence, despite improvements in disease management

• Life-long monitoring used to detect persistent and recurrent disease at the earliest possible stage
DTC: At A Glance

- DTC is The 8th in the top 10 common cancers:

- Estimated New Cases in 2015: 62,450
- Estimated Deaths in 2015: 1,950 (3%)
- Large population of DTC survivors that need surveillance

2015 ATA Guidelines

- published in Jan, 2016 issue of *THYROID*
- monumental effort (16 authors; exhaustive literature review)
- Eval. of quality of evidence (good, moderate, weak)
- ACP grading system of Rec. (strong, weak, no rec)
- 133 pages
- 1078 references
- 101 recommendations
2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer

The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer

2015 ATA Guidelines

There is a broad range of new or modified recommendations in 2015 as compared to 2009 ATA Guidelines:

- 8 New Clinical Questions
- 21 New Recommendations
- 21 significantly changed Recommendations
The Result: a seismic shift in thyroid cancer management

- **Initial treatment**: dramatic pendulum swing away from prior standard of care for thyroid cancer treatment (i.e. total thyroidectomy, central neck dissection, post-op RAI Rx) to:
  - Less than total thyroidectomy for PTC < 4 cm
  - Not using RAI in the majority of patients (~ 85%) of thyroid cancer pts.

- **Surveillance strategy**: shift away from Dx and/or PostRx Scans to US surveillance and serial Tg testing
Initial Treatment Strategy is predicated on Risk Stratification (which is based on an estimation of the risk for recurrence)

The Risk of Recurrence Estimation is based on retrospective studies from 3 continents which have reported on the proportion of pts. with NO Evidence of Disease in each 2009 ATA category AFTER total thyroidectomy + RAI Remnant Ablation.

NED is defined as: stim. Tg < 1 ng/mL +
- no clinical or radiological evidence of ds.
(the length of follow-up is critical – usually 2 years)
### NED after Total Thyroidectomy + RAI Rx:

<table>
<thead>
<tr>
<th>ATA Risk Level</th>
<th>NED Rate</th>
<th>Persistent Ds Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low Risk</strong></td>
<td>78 – 91%</td>
<td>9 – 22%</td>
</tr>
<tr>
<td><strong>Intermediate Risk</strong></td>
<td>52 – 64%</td>
<td>36 – 48%</td>
</tr>
<tr>
<td><strong>High Risk</strong></td>
<td>30 – 32%</td>
<td>68 – 70%</td>
</tr>
</tbody>
</table>
Post-operative management

- Total thyroidectomy ± neck dissection
- Risk stratification (Histopathology)
  - Management without Ablation (Low-risk)
  - Hypothyroid/rh-TSH stimulated Fixed Dose 131-I Ablation (Intermediate and High-Risk)
    - 30 -100 mCi 131-I for ablation
    - >100 mCi 131-I for therapy
- Post therapy 131-I scan at 5 – 7 days

ATA Guidelines for Thyroid Cancer
<table>
<thead>
<tr>
<th>Factors</th>
<th>Description</th>
<th>Expected benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Decreased risk of death</td>
</tr>
<tr>
<td>T1</td>
<td>1 cm or less, intrathyroidal or microscopic multifocal</td>
<td>No</td>
</tr>
<tr>
<td>T2</td>
<td>&gt;2–4 cm, intrathyroidal</td>
<td>No</td>
</tr>
<tr>
<td>T3</td>
<td>&gt;4 cm</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>&lt;45 years old</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>≥45 years old</td>
<td>Yes</td>
</tr>
<tr>
<td></td>
<td>Any size, any age, minimal extrathyroidal extension</td>
<td>No</td>
</tr>
<tr>
<td>T4</td>
<td>Any size with gross extrathyroidal extension</td>
<td>Yes</td>
</tr>
<tr>
<td>Nx,N0</td>
<td>No metastatic nodes documented</td>
<td>No</td>
</tr>
<tr>
<td>N1</td>
<td>&lt;45 years old</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>&gt;45 years old</td>
<td>Conflicting data</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis present</td>
<td>Yes</td>
</tr>
</tbody>
</table>

**ATA**:
- **A**: Strongly recommends (good evidence); **B**: Recommends (fair evidence); **C**: Recommends (expert opinion); **D**: Recommends against (expert opinion); **E**: Recommends against (fair evidence); **F**: Strongly recommends against (good evidence); **I**: Recommends neither for nor against
What is the contribution of diagnostic Radio-iodine scans to management?

Individualized 131-I therapy

What Dose of 131-I therapy? Versus What Target for 131-I therapy?
Accurate Staging is Important

- knowing the extent of disease makes a difference

- Staging predicts survival

- Staging determines the strategy for initial treatment and for long-term surveillance

- AJCC TNM 7th Ed. was used for staging patients after total thyroidectomy
Prognosis

- Patients with stage I-II disease have favorable prognosis (mortality < 1% at 20 years) (low risk group)

- Mortality increases to 25-40% among patients at stages III and IV (high risk group)

*Jonklaas J et. al. Thyroid. 2006 (12):1229-42*
## DTC Staging – AJCC 7th Ed

<table>
<thead>
<tr>
<th>Stage</th>
<th>Age &lt; 45</th>
<th>Age ≥ 45</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>any T, any N, M0</td>
<td>T1, N0, M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>any T, any N, M1</td>
<td>T2, N0, M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>n/a</td>
<td>T3, N0, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1-T2-T3, N1a, M0</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>n/a</td>
<td>T4a, N0-N1a, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T1-T4a, N1b, M0</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>n/a</td>
<td>T4b, any N, M0</td>
</tr>
<tr>
<td>Stage IVC</td>
<td>n/a</td>
<td>any T, any N, M1</td>
</tr>
</tbody>
</table>
2009 ATA Risk Stratification

• **ATA Low Risk:**
  – no regional or distant metastases
  – complete tumor resection, no evidence of invasion
  – non-aggressive histology

• **ATA Intermediate Risk:**
  – microscopic invasion in peri-thyroidal tissues
  – cervical nodal metastases (or 131-I uptake outside of thyroid bed on PostRx Scan)
  – aggressive histology or vascular invasion

• **ATA High Risk:**
  – macroscopic invasion, incomplete resection
  – distant metastases
  – Tg. “out of proportion” of PostRx. findings
2015 ATA Pediatric Risk Stratification

• **Low-risk patients:**
  – Disease grossly confined to the thyroid
  – N0 or Nx or Incidental N1a (microscopic metastasis to a small number of central neck nodes)

• **Intermediate-risk patients:**
  – microscopic invasion in peri-thyroidal tissues
  – cervical nodal metastases: Extensive N1a, or minimal N1b
  – aggressive histology or vascular invasion

• **High-risk patients:**
  – macroscopic invasion, incomplete resection; extensive N1b
  – distant metastases

2015 – ATA Pediatric Thyroid Cancer Guidelines
2015 ATA RECURRENCE RISK

Risk of Structural Disease Recurrence
(In patients without structurally identifiable disease after initial therapy)

High Risk
- Gross extrathyroidal extension
- Incomplete tumor resection
- Distant metastases
- or lymph node >3 cm

Intermediate Risk
- Aggressive histology
- Minor extrathyroidal extension
- Vascular invasion
- or > 5 involved lymph nodes (0.2-3 cm)

Low Risk
- Intrathyroidal DTC
- ≤ 5 LN micrometastases (< 0.2 cm)

- FTC, extensive vascular invasion (∼30-55%)
- pT4a gross ETE (∼30-40%)
- pN1 with extranodal extension, >3 LN involved (∼40%)
- PTC, > 1 cm, TERT mutated ± BRAF mutated* (∼40%)
- pN1, any LN > 3 cm (∼30%)
- PTC, extrathyroidal, BRAF mutated* (∼10-40%)
- PTC, vascular invasion (∼15-30%)
- Clinical N1 (∼20%)
- pN1, > 5 LN involved (∼20%)
- Intrathyroidal PTC, < 4 cm, BRAF mutated* (∼10%)
- pT3 minor ETE (∼3-8%)
- pN1, all LN < 0.2 cm (∼5%)
- pN1, ≤ 5 LN involved (∼5%)
- Intrathyroidal PTC, 2-4 cm (∼5%)
- Multifocal PTMC (∼4-6%)
- pN1 without extranodal extension, ≤ 3 LN involved (2%)
- Minimally invasive FTC (∼2-3%)
- Intrathyroidal, < 4 cm, BRAF wild type* (∼1-2%)
- Intrathyroidal unifocal PTMC, BRAF mutated*, (∼1-2%)
- Intrathyroidal, encapsulated, FV-PTC (∼1-2%)
- Unifocal PTMC (∼1-2%)
ATA Guidelines: Selective use of 131-I therapy

- Low risk, and selected medium-risk patients are no longer recommended ablation after total thyroidectomy.

- Management decisions are predicated by histopathology-based risk stratification.

A post-therapy scan may not exist in all patients.

Without a diagnostic scan to complete staging after total thyroidectomy, regional or distant metastases may not be recognized and addressed at an early stage.
Individualized 131-I Treatment

Patient-specific 131-I therapy prescription:

- Clinical data (patient’s age and clinical presentation: with/without palpable lymphadenopathy)
- Surgical pathology report: defining T and N – depending on the extent of surgical dissection
- Post-operative Tg levels (suppressed/stimulated; Thyrogen vs. hypothyroid stimulation)
- Diagnostic imaging findings: neck US and DxWBS (123-I vs. 131-I scans, planar ± SPECT/CT imaging)
Progress: Hybrid SPECT/CT camera

- Co-registration of functional and anatomic data
- Superior image quality:
  - Improved spatial resolution
  - Improved contrast resolution
  - Application of scatter rejection algorithms
  - Iterative Reconstruction SPECT
  - CT-based Attenuation Correction

High quality images can be achieved with tracer doses of 131-I.
Improved I-131 SPECT imaging

- SPECT/CT
  - Facilitates activity localization, attenuation & partial volume correction
- High energy collimator
  - Sensitivity higher for ME, but desired geometric events higher for HE
- Thicker NaI crystal
  - Efficiency for 364 keV photons 2 times higher for 15.9 mm vs. 9.5 mm
- Dead time correction for post-therapy imaging
  - Count-rates should be < 50 kcps. Earliest imaging at 1 – 4 days
- Scatter correction
  - Triple Energy Window correction.
- Iterative reconstruction with accurate system model
  - Commercial software only models geometric component of CDR

*Dewaraja et al. MIRD 24. JNM 2013*
Concordance: Diagnostic vs. Post-therapy scans

McDougall IR et al. Nucl Med Comm, 1997:

(2 mCi) 131-I pre-ablation and post-Rx (8d) planar scans were concordant in 274 of 280 patients (98%);
in 2% pts. a relative decreased uptake in the previously detected foci was seen on the post-Rx.

Avram AM et al. JCEM, 2013:

(1 mCi) 131-I pre-ablation and post-Rx (2d) planar scans were concordant in 280 of 303 patients (92%):
- in only 4 of 303 pts. (1.3%) a relative decreased uptake in the previously detected foci was seen on the post-Rx.
- in 6% pts. additional foci were detected on post-Rx scan
  (in only 1.4% pts. the findings upstaged the patient)
UM Experience: individualized 131-I therapy

Focus:

To assess the contribution of diagnostic $^{131}$I scans with SPECT-CT for:

Differentiated Thyroid Cancer (DTC)

1. Staging
2. Risk Stratification
3. Management
Why is this important?

Define instances where initial staging based on clinical & surgical pathology (pTNM) changes after diagnostic $^{131}$I imaging

- Complete patients’ risk-stratification
- Define if the patient will / (will not) benefit from therapeutic $^{131}$I administration
- Define the target of $^{131}$I therapy
Study Design

- All patients were initially staged and risk stratified by Endocrinologist based on clinical and surgical pathology (pTNM)

- All $^{131}$I scans were interpreted to assess for thyroid remnant, nodal or distant metastases (2 independent readers)

- All patients were re-staged and re-stratified after incorporating the information from diagnostic $^{131}$I SPECT-CT to arrive at final TNM and final Risk Stratification
Study Design

The impact of findings on DxWBS + SPECT/CT were assessed regarding changes in management:

- the decision of treat or withhold 131-I therapy based on risk stratification
- the decision to refer to surgery for resection of bulky residual metastatic disease
- the prescribed 131-I activity defined as:
  - Low-activity (30-50 mCi)
  - Medium activity (100-150 mCi)
  - High activity (≥200 mCi)
• **Diagnostic $^{131}$I scans** (37 MBq, 1 mCi) are performed in all pts. at 4 weeks after total thyroidectomy

• 24 h whole body (WB) and static planar images of the neck and chest

• 24 h SPECT-CT imaging for:
  • characterization of central neck activity: thyroid remnant vs. nodal metastasis
  • anatomic localization of distant disease
  • evaluation of suspected physiologic mimics
Methods

320 consecutive pts. (47 ± 16 yrs, range 10 – 90)

Female 68%; Male 32%

<table>
<thead>
<tr>
<th>Tumor subtypes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Papillary</td>
<td>289 (90)</td>
</tr>
<tr>
<td>Follicular</td>
<td>22 (7)</td>
</tr>
<tr>
<td>Hurthle cell variant</td>
<td>9 (3)</td>
</tr>
<tr>
<td>High-risk features</td>
<td></td>
</tr>
<tr>
<td>Classic PTC</td>
<td>190 (59)</td>
</tr>
<tr>
<td>Follicular variant of PTC</td>
<td>51 (16)</td>
</tr>
<tr>
<td>Tall cell</td>
<td>26 (8)</td>
</tr>
<tr>
<td>Columnar</td>
<td>2 (1)</td>
</tr>
<tr>
<td>Cystic</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Sclerosing</td>
<td>1 (&lt;1)</td>
</tr>
<tr>
<td>Squamoid</td>
<td>6 (2)</td>
</tr>
<tr>
<td>Insular</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Anaplastic component</td>
<td>2 (1)</td>
</tr>
</tbody>
</table>

Avram AM et al. J Clin Endocrinol Metab 2013; 98(3):1163-71
Methods: Tumor Characteristics

Size: $2.4 \pm 1.8$ cm; range: 0.1-12 cm

Multifocality: 144 (45%)

Vascular invasion, present: 96 (30%)

Capsular invasion, present: 202 (63%)

Extrathyroidal extension, yes: 116 (36%)

Surgical margins:

Positive 26%; Negative 72%; Unknown 2%

Neck nodal metastases, pN1*** 149 (47%)

*** before diagnostic imaging
## Methods: Laboratory results

### TSH

- $< 30$ mIU/L: 15 (5%)
- $\geq 30$ mIU/L: 305 (95%)

### Thyroglobulin

- $< 0.5$ ng/mL: 74 (23%)
- 0.5 ng/mL to $< 10$ ng/mL: 149 (47%)
- 10 ng/mL to $< 100$ ng/mL: 66 (21%)
- 100 ng/mL to $< 1,000$ ng/mL: 22 (7%)
- $\geq 1,000$ ng/mL: 9 (3%)

### Anti-Tg. Ab., present

- Present: 50 (16%)
Results in Younger patients (n= 138)

$^{131}$I Fused Imaging revealed:

Nodal Mets. in 61 (44%) Young pts.

- Unsuspected Nodal Mets in 24 of 63 (38%) initially assigned pN0 or pNx $\rightarrow$ N1

- Residual post-surgery Nodal Mets in 37 of 75 (49%) pN1pts.

Distant Mets. in 5 (4%) Young pts.
(upstaged to Stage II disease)
<table>
<thead>
<tr>
<th>Cervical nodal metastases</th>
<th>pTNcM</th>
<th>TNM*</th>
<th>M0</th>
<th>M1</th>
<th>No Nodes on SPECT/CT</th>
<th>Nodes on SPECT/CT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>pN0</td>
<td>12</td>
<td></td>
<td>8</td>
<td></td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pN1a</td>
<td>24</td>
<td></td>
<td>16</td>
<td></td>
<td>40</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pN1b</td>
<td>14</td>
<td></td>
<td>21</td>
<td></td>
<td>35</td>
<td></td>
<td></td>
</tr>
<tr>
<td>pNx</td>
<td>27</td>
<td></td>
<td>16</td>
<td></td>
<td>43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>77</td>
<td></td>
<td>61</td>
<td></td>
<td>138</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distant metastases</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>cM0</td>
<td>133</td>
<td>5</td>
<td></td>
<td></td>
<td>138</td>
<td></td>
<td></td>
</tr>
<tr>
<td>cM1</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>AJCC TNM staging</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>138 (100%)</td>
<td>133 (96%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage II</td>
<td>0</td>
<td>5 (4%)</td>
<td></td>
<td></td>
<td>0</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
14 year old girl with bulky cervical nodal mets. T3, N1b, M0; Stage I
23 year old woman with mPTC
3.5 cm tumor with +ETE; 23+/30 bilateral neck
pT4a, N1b, M0; stage I
Restaging: T4a, N1b, M1; Stage II
Results in Older patients (n=182)

$^{131}$I Fused Imaging Upstaged 46 (25%) pts.

Nodal Mets. in 46 (25%) Older pts.

- Unsuspected Nodal Mets in 26 of 108 (24%) initially assigned pN0 or pNx $\rightarrow$ N1

- Residual post-surgery Nodal Mets in 25 of 74 (34%) pN1pts.

Distant Mets. in 18 (10%) Older pts.
## Table 4. Impact of Dx Scans in Older Patients

<table>
<thead>
<tr>
<th></th>
<th>pTNcM</th>
<th>TNM*</th>
<th>M0</th>
<th>M1</th>
<th>No Nodes on SPECT/CT</th>
<th>Nodes on SPECT/CT</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cervical nodal metastases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>pN0</td>
<td>38</td>
<td></td>
<td></td>
<td></td>
<td>7</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>pN1a</td>
<td>31</td>
<td></td>
<td></td>
<td></td>
<td>16</td>
<td>47</td>
<td>47</td>
</tr>
<tr>
<td>pN1b</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td>9</td>
<td>27</td>
<td>27</td>
</tr>
<tr>
<td>pNx</td>
<td>44</td>
<td></td>
<td></td>
<td></td>
<td>19</td>
<td>63</td>
<td>63</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>131</td>
<td></td>
<td></td>
<td></td>
<td>51</td>
<td>182</td>
<td></td>
</tr>
<tr>
<td><strong>Distant metastases</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>cM0</td>
<td>163</td>
<td>18</td>
<td></td>
<td></td>
<td></td>
<td>181</td>
<td></td>
</tr>
<tr>
<td>cM1</td>
<td>0</td>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>163</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
<td>182</td>
<td></td>
</tr>
<tr>
<td><strong>AJCC TNM staging</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage I</td>
<td>47 (26%)</td>
<td>29 (16%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage II</td>
<td>23 (13%)</td>
<td>18 (10%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage III</td>
<td>66 (36%)</td>
<td>49 (27%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IV A/B</td>
<td>45 (25%)</td>
<td>67 (37%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stage IV C</td>
<td>1 (0.6%)</td>
<td>19 (10%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
65 yo woman, mPTC
1.2 cm and 0.5 cm tumors
0/3 nodes central neck
pT1b, N0, M0; Stage I
Restaging
T1b, N1b, M0;
Stage IV A
56 year old woman
1.2 cm PTC, no ETE
0/3 central nodes
pT1b, N0, M0; Stage I
Restaging
T1b, N0, M1;
Stage IV C

SPECT/CT: right thyroid remnant; liver metastasis
Diagnostic (1 mCi) 131-I scan at 6 Mos. after 200 mCi RAI Rx:

interval resolution of liver metastasis and of thyroid remnant tissue
## Sub-analysis of T1 Tumors  \( n = 116 \) \( (36\%) \)

<table>
<thead>
<tr>
<th>Tumor Size</th>
<th>Number ( (%) )</th>
<th>Dx. Scans detected:</th>
</tr>
</thead>
</table>
| T1a (≤ 1.0 cm) | 49 (15\%) | - Nodal Mets in 22\%  
- Distant Mets in 4\% |
| T1b (≤ 2.0 cm) | 67 (21\%) | - Nodal Mets in 52\%  
- Distant Mets in 4.5\% |

Risk for distant metastases increased in Multifocal tumors

**Avram AM et al. J Clin Endocrinol Metab 2013; 98(3):1163-71**
Pre-ablation Scans Complete Staging

Characterization of N status and M status

- Detected regional mets. in 35% pts.
- Detected distant mets. in 8% pts.

Changes TNM staging:

- 4% of young pts.
- 25% of older pts.

Avram AM et al. J Clin Endocrinol Metab 2013; 98(3):1163-71
Pre-ablation Scans Complete Risk Stratification

Univ. of Michigan experience in 320 patients

Risk Stratification performed by Endocrinologist before and after information from pre-ablation scans was made available:

15% pts. (48/320) changed risk stratification after imaging information on nodal and distant metastatic status

- 28 pts. were changed to Intermediate Risk from Low Risk
- 20 pts. were changed to High Risk (3 from LR and 17 IR)

Avram AM et al. J Clin Endocrinol Metab 2015 May;100(5):1895-902
### Postoperative Patients (n=320)

#### Cervical Nodal Metastases

<table>
<thead>
<tr>
<th></th>
<th>No Nodes on SPECT/CT</th>
<th>Nodes on SPECT/CT</th>
<th>Total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pN0</td>
<td>50</td>
<td>15</td>
<td>65 (20%)</td>
</tr>
<tr>
<td>pN1a</td>
<td>55</td>
<td>32</td>
<td>87 (27%)</td>
</tr>
<tr>
<td>pN1b</td>
<td>32</td>
<td>30</td>
<td>62 (20%)</td>
</tr>
<tr>
<td>pNx</td>
<td>71</td>
<td>35</td>
<td>106 (33%)</td>
</tr>
<tr>
<td>Total</td>
<td>208</td>
<td>112</td>
<td>320</td>
</tr>
</tbody>
</table>

#### Distant Metastases

<table>
<thead>
<tr>
<th></th>
<th>M0</th>
<th>M1</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>cM0</td>
<td>296</td>
<td>23</td>
<td>319</td>
</tr>
<tr>
<td>cM1</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>296</td>
<td>24</td>
<td>320</td>
</tr>
</tbody>
</table>

#### ATA Risk Stratification

<table>
<thead>
<tr>
<th></th>
<th>Initial (pTN)</th>
<th>Final (after imaging)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Risk</td>
<td>97 (30%)</td>
<td>66 (20%)</td>
</tr>
<tr>
<td>Med. Risk</td>
<td>190 (60%)</td>
<td>201 (63%)</td>
</tr>
<tr>
<td>High Risk</td>
<td>33 (10%)</td>
<td>53 (17%)</td>
</tr>
</tbody>
</table>

Avram AM et al. J Clin Endocrinol Metab 2015 May;100(5):1895-902
Pre-ablation Scans contribute to Management

Univ. of Michigan experience in 320 patients

Management changed in 31% pts. (99/320) due to:

- Both Imaging and Tg information (n = 87)
- Imaging information (n = 7)
- Tg. level, being out of proportion to DxWBS findings (n = 5)

Avram AM et al. J Clin Endocrinol Metab 2015 May;100(5):1895-902
Decisions to treat or withhold RAI based on Risk Stratification

<table>
<thead>
<tr>
<th></th>
<th>RAI</th>
<th>Withhold</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial risk stratification</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>37</td>
<td>60</td>
<td>97</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>190</td>
<td>0</td>
<td>190</td>
</tr>
<tr>
<td>High risk</td>
<td>33</td>
<td>0</td>
<td>33</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>260</td>
<td>60</td>
<td>320</td>
</tr>
<tr>
<td><strong>Final risk stratification</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low risk</td>
<td>22</td>
<td>44</td>
<td>66</td>
</tr>
<tr>
<td>Intermediate risk</td>
<td>198</td>
<td>3</td>
<td>201</td>
</tr>
<tr>
<td>High risk</td>
<td>48</td>
<td>5</td>
<td>53</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>268</td>
<td>52</td>
<td>320</td>
</tr>
</tbody>
</table>

Avram AM et al. J Clin Endocrinol Metab 2015 May;100(5):1895-902
### Impact of initial and final Risk Stratification on 131-I Therapy

<table>
<thead>
<tr>
<th>Recommended Dose (mCi) of RAI I-131 to Be Given</th>
<th>None</th>
<th>Low (30–50)</th>
<th>Medium (100–150)</th>
<th>High (200+)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Initial risk stratification</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>60</td>
<td>34</td>
<td>3</td>
<td>0</td>
<td>97</td>
</tr>
<tr>
<td>Intermediate</td>
<td>0</td>
<td>5</td>
<td>185</td>
<td>0</td>
<td>190</td>
</tr>
<tr>
<td>High</td>
<td>0</td>
<td>0</td>
<td>32</td>
<td>1</td>
<td>33</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>60</td>
<td>39</td>
<td>220</td>
<td>1</td>
<td>320</td>
</tr>
<tr>
<td><strong>Final risk stratification</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>44</td>
<td>22</td>
<td>0</td>
<td>0</td>
<td>66</td>
</tr>
<tr>
<td>Intermediate</td>
<td>3</td>
<td>33</td>
<td>165</td>
<td>0</td>
<td>201</td>
</tr>
<tr>
<td>High</td>
<td>5</td>
<td>0</td>
<td>24</td>
<td>24</td>
<td>53</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>52</td>
<td>55</td>
<td>189</td>
<td>24</td>
<td>320</td>
</tr>
</tbody>
</table>
Identification of Distant Metastases led to dosimetrically guided RAI Rx.

32 year old woman
1.8 cm follicular-variant PTC
left lobe; + margins
- 15+/27 nodes central neck
- 6+/46 nodes left neck
- TSH 118 mU/L
- Tg 862 ng/mL
Dosimetry Calculations

- Whole Body Dosimetry: 0.56 cGy/mCi adm. activity
- Blood Dosimetry: 0.62 cGy/mCi adm. activity

RAI Rx. 320 mCi 131-I therapy
Blood (as surrogate for bone marrow).
Samples at 6, 24, 48, 72, 96 h,
Calculate radiation dose absorbed to blood
Goal: <200 cGy (rads)

Circulating T4 increases absorbed dose
in bone marrow over that in body.
131I Whole Body Dosimetry

Method using uptake probe or camera:
- count 2 h after oral dose $^{131}$I = 100%;
- count 2 days = % or residual fraction.

Calculation of administered dose,
- goal at 2 days <80 mCi; calculate
- 80 mCi/residual fraction
  = upper limit.
Well-differentiated Thyroid Carcinoma Guidelines Prevent Toxicity* from $^{131}$-I

1. Body retention of $^{131}$-I at 48 h**:
   \[ \leq 120 \text{ mCi, but} \]
   \[ \leq 80 \text{ mCi if diffuse lung metastases} \]

2. Absorbed radiation to blood:
   \[ \leq 200 \text{ cGy} \]

*prevent marrow depress & pneumonitis.
**dominates unless tumor makes T4.

Benua et al. AJR 1962;87:171.
Identification of large residual metastases led to surgical referral

45 year old man with 3.5 cm PTC
• 30+/58 bilateral metastatic lymph nodes:
  – central neck (17+/17)
  – right neck (9+/26)
  – left neck (4+/15)
3 large residual metastatic lymph nodes (~1 x 1.2 cm) at the sternal notch and in the left supraclavicular area.
Surgical referral prior to 131-I therapy
Diagnostic radioiodine scans provide information which can alter clinical strategy

Proposed changes in management based on information provided by radioiodine scans include:

- deciding whether to give or withhold 131-I treatment,
- indicating and guiding the extent of surgery when large metastatic deposits are present
- adjusting the prescribed 131-I activity for remnant ablation, adjuvant therapy or targeted treatment
- Indicating the need for alternative imaging strategies such as 18F-FDG PET when negative 131-I scans and elevated THYG levels

Individualized approach in patient management
Question 1

What is the MOST common type of thyroid cancer?
Q1: Most common thyroid cancer type is:

a) Follicular Thyroid Cancer
b) Hurthle Cell Thyroid Cancer
c) Medullary Thyroid Cancer
d) Papillary Thyroid Cancer
Q1: Most common thyroid cancer type is:

a) Follicular Thyroid Cancer
b) Hurthle Cell Thyroid Cancer
c) Medullary Thyroid Cancer
d) Papillary Thyroid Cancer
Q1: Answers

D is the correct answer:

Papillary Thyroid Cancer (PTC) represents 80% of all cases of DTC
Question 2

Regarding therapeutic approach, what is the most important feature of DTC?
Q2: Regarding therapy approach, the most important feature of DTC is:

a) The histologic subtype

b) Surgical resection margins

c) Ability to concentrate iodine (NIS expression and function)

d) The extent of local-regional spread
Q2: Regarding therapy approach, the most important feature of DTC is:

a) The histologic subtype

b) Surgical resection margins

c) Ability to concentrate iodine (NIS expression and function)

d) The extent of local-regional spread
Q2 Answers

C is the correct answer

Well Differentiated thyroid cancer cells maintain the ability to uptake and concentrate 131-I due to constitutive NIS expression. TSH stimulation increases the expression and function of NIS in thyroid cancer cell, resulting in increased 131-I uptake and retention within the tumor cell (i.e. radiation absorbed dose to tumor)

Adequate patient preparation (low-iodine diet, TSH stimulation) is important for optimizing 131-I therapy
Question 3

Pre-ablation radioiodine scans with SPECT/CT are **MOST** useful for which of the following?
Q3: Pre-ablation Scan is MOST useful for:

a) To complete post-operative thyroid cancer staging prior to 131-I therapy

b) To determine the dose of 131-I therapy

c) To alter the pre-operative management

d) To perform whole body dosimetry calculations
Q3: Pre-ablation Scan is MOST useful for:

a) To complete post-operative thyroid cancer staging prior to 131-I therapy

b) To determine the dose of 131-I therapy

c) To alter the pre-operative management

d) To perform whole body dosimetry calculations
Q3: Answers

A is the correct answer:

Preablation radio-iodine scans with SPECT/CT complete initial staging before management decisions regarding 131-I therapy are made.

- detected regional metastases in 35% patients and distant metastases in 8% patients

- change in staging in 4% of younger patients (age < 45 years) and 25% of older patients (age ≥ 45 years)

Avram AM et al. J Clin Endocrinol Metab 2013; 98(3):1163-71
Question 4

Which one of the following is the **MOST** important advantage of SPECT/CT when applied to radioiodine scintigraphy?
Q4: SPECT/CT is MOST useful for:

a) Improved characterization of primary tumor (T) status

b) Detection of regional metastases by improved characterization of nodal metastasis versus thyroid remnant

c) Detection of distant metastasis (M)

d) Improved characterization of oral radioiodine uptake as salivary secretions versus metastatic lesions
Q4: SPECT/CT is MOST useful for:

a) Improved characterization of primary tumor (T) status

b) Detection of regional metastases by improved characterization of nodal metastasis versus thyroid remnant

c) Detection of distant metastasis (M)

d) Improved characterization of oral radioiodine uptake as salivary secretions versus metastatic lesions
B is the correct answer:

SPECT/CT localizes focal activity to cervical lymph nodes and/or paratracheal activity in the surgical bed.

Review the surgical pathology report for tumor invasiveness into local structures and completion of surgical resection; these elements are of critical importance when interpreting the significance of paratracheal central neck activity as benign thyroid remnant versus residual disease.

Incorporating SPECT/CT into the protocol of pre-ablation radio-iodine scans is MOST useful for which of the following?
Q5: SPECT/CT is MOST useful for:

a) Reduces equivocal interpretations on planar radioiodine scintigraphy

b) Identifies physiologic radioiodine biodistribution patterns

c) Increases the specificity for disease detection as compared to planar radioiodine imaging

d) Improves the outcome of 131-I therapy
Q5: SPECT/CT is MOST useful for:

a) Reduces equivocal interpretations on planar radioiodine scintigraphy

b) Identifies physiologic radioiodine biodistribution patterns

c) increases the specificity for disease detection as compared to planar radioiodine imaging

d) Improves the outcome of 131-I therapy
Q5: Answers

C is the correct answer:

SPECT/CT increase diagnostic test performance mainly by an increase in **Specificity**:

- Planar studies demonstrated a sensitivity of 41%, specificity of 68%
- SPECT-CT demonstrated a sensitivity of 50%, specificity of 100%

*Barwick T et al. Eur J Endocrinol 2010;162(6):1131-9*