(Not so) New Guidelines for Management of Thyroid Nodules and Differentiated Thyroid Cancer

Minnesota/Midwest Chapter of AACE

Bryan R. Haugen, MD
University of Colorado, School of Medicine
Outline

• Some statistics
• New guidelines grading system

• New/changed guidelines
• Summary review of the guidelines

Disclosures
Research support/honoraria from Genzyme
Consultant for Eisai
Figure. Annual Incidence and 5-Year Survival Rates for Different Types of Cancer

Davis MM, JAMA 305:2343, 2011
Trends in Thyroid Cancer Incidence and Mortality in the United States, 1974-2013

Hyeyeun Lim, PhD; Susan S. Devesa, PhD; Julie A. Sosa, MD; David Check, BS; Cari M. Kitahara, PhD, MHS

<table>
<thead>
<tr>
<th>Thyroid Cancer</th>
<th>Annual increase (incidence)</th>
<th>Annual increase (mortality)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>3.6%</td>
<td>1.1%</td>
</tr>
<tr>
<td>Distant Mets</td>
<td>2.4%</td>
<td>2.9%</td>
</tr>
</tbody>
</table>

Papillary thyroid cancer incidence
## Adapted ACP system

<table>
<thead>
<tr>
<th>Recommendation and Evidence Quality</th>
<th>Description of supporting evidence*</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Strong Recommendation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-quality evidence</td>
<td>RCT without important limitations or overwhelming evidence from observational studies</td>
<td>Can apply to most patients in most circumstances without reservation</td>
</tr>
<tr>
<td>Moderate-quality evidence</td>
<td>RCT with important limitations or strong evidence from observational studies</td>
<td>Can apply to most patients in most circumstances without reservation</td>
</tr>
<tr>
<td>Low-quality evidence</td>
<td>Observational studies/case studies</td>
<td>May change when higher-quality evidence available</td>
</tr>
<tr>
<td><strong>Weak Recommendation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High-quality evidence</td>
<td>RCT without important limitations or overwhelming evidence from observational studies</td>
<td>Best action may differ based on circumstances or patients’ values</td>
</tr>
<tr>
<td>Moderate-quality evidence</td>
<td>RCT with important limitations or strong evidence from observational studies</td>
<td>Best action may differ based on circumstances or patients’ values</td>
</tr>
<tr>
<td>Low-quality evidence</td>
<td>Observational studies/case studies</td>
<td>Other alternatives may be equally reasonable</td>
</tr>
<tr>
<td><strong>Insufficient</strong></td>
<td>Evidence is conflicting, poor quality or lacking</td>
<td>Insufficient evidence to recommend for or against</td>
</tr>
</tbody>
</table>
Are the new guidelines different from the 2009 guidelines?

Goal: To be evidence-based and helpful

<table>
<thead>
<tr>
<th></th>
<th>2009</th>
<th>2015</th>
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</thead>
<tbody>
<tr>
<td>Recommendations</td>
<td>80</td>
<td>101</td>
</tr>
<tr>
<td>Sub-recommendations</td>
<td>103</td>
<td>175</td>
</tr>
<tr>
<td>References</td>
<td>437</td>
<td>1078</td>
</tr>
<tr>
<td>Tables</td>
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<td>17</td>
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<tr>
<td>Figures</td>
<td>5</td>
<td>8</td>
</tr>
</tbody>
</table>

New questions – 8
New recommendations – 21
Significantly changed recommendations – 21
Example of Strong Recommendations Based on Low-quality Evidence

Recommendation 33A: Preoperative use of cross-sectional imaging studies (CT, MRI) with intravenous (IV) contrast is recommended as an adjunct to US for patients with clinical suspicion for advanced disease.
Patient #1
48 yo male incidental 8 mm thyroid nodule
High suspicion sonographic pattern, no abnormal LN

Thyroidectomy, calcitonin, FNA, monitor

Risk of PTC?
Risk of bad outcome?
Sonographic patterns

- **High suspicion [malignancy risk 70-90%]:** Solid hypoechoic nodule or solid hypoechoic component of a partially cystic nodule with one or more of the following features: irregular margins, microcalcifications, taller than wide shape.

- **Intermediate suspicion [malignancy risk 10-20%]:** Hypoechoic solid nodule without high suspicion features

- **Low suspicion [malignancy risk 5-10%]:** Isoechoic or hyperechoic solid nodule, or partially (> 50%) cystic nodule, with eccentric solid area without high suspicion features

- **Very low suspicion [<3%]:** Spongiform or partially cystic nodules without high or intermediate suspicion features

- **Benign [<1%]:** Purely cystic nodules
Microcalcifications, hypoechoic nodule

irregular margins

irregular margins, extrathyroidal extension

nodule with irregular margins, suspicious left lateral lymph node

Microcalcifications, hypoechoic nodule

irregular margins

irregular margins, extrathyroidal extension

nodule with irregular margins, suspicious left lateral lymph node

Intermediate
10-20%

> 1 cm

hypoechoic solid regular margin

hypoechoic solid regular margin

hypoechoic solid regular margin

hypoechoic solid regular margin

Partially cystic with eccentric solid area

Partially cystic with eccentric solid areas

Spongiform

Partially cystic with eccentric solid area

Partially cystic with eccentric solid areas

Partially cystic with eccentric solid area

Partially cystic with eccentric solid areas

Benign

<1%

Biopsy not needed to r/o malignancy

Risk of malignancy

High
70-90%

> 1 cm

Low
5-10%

> 1.5 cm

Very low
<3%

> 2 cm

If at all

Figure 2
ACR Thyroid Imaging, Reporting and Data System (TI-RADS): White Paper of the ACR TI-RADS Committee

Franklin N. Tesler, MD, CM*, William D. Middleton, MD†, Edward G. Grant, MD*, Jenny K. Hoang, MBBS†, Lincoln L. Berland, MD*, Sharlene A. Trefey, MD†, John F. Cronan, MD*, Michael D. Beland, MD†, Terry S. Desser, MD†, Mary C. Frates, MD*, Lynwood W. Hammers, DO†, Ulrike M. Hamper, MD†, Jill E. Langer, MD*, Carl C. Reading, MD†, Leslie M. Scoutt, MD†*, A. Thomas Stavros, MD†*

ACR TI-RADS

COMPOSITION

(Choose 1)

- Cystic or almost completely cystic: 0 points
- Spongiform: 0 points
- Mixed cystic and solid: 1 point
- Solid or almost completely solid: 2 points

ECHOGENICITY

(Choose 1)

- Anechoic: 0 points
- Hyperechoic or isoechoic: 1 point
- Hypoechoic: 2 points
- Very hypoechoic: 3 points

SHAPE

(Choose 1)

- Wider-than-tall: 0 points
- Taller-than-wide: 3 points

MARGIN

(Choose 1)

- Smooth: 0 points
- Ill-defined: 0 points
- Lobulated or irregular: 2 points
- Extra-thyroidal extension: 3 points

ECHOGENIC FOCI

(Choose All That Apply)

- None or large comet-tail artifacts: 0 points
- Macrocalcifications: 1 point
- Peripheral (rim) calcifications: 2 points
- Punctate echogenic foci: 3 points

Add Points From All Categories to Determine TI-RADS Level

0 Points
TR1
Benign
No FNA

2 Points
TR2
Not Suspicious
No FNA

3 Points
TR3
Mildly Suspicious
FNA if ≥ 2.5 cm
Follow if ≥ 1.5 cm

4 to 6 Points
TR4
Moderately Suspicious
FNA if ≥ 1.5 cm
Follow if ≥ 1 cm

7 Points or More
TR5
Highly Suspicious
FNA if ≥ 1 cm
Follow if ≥ 0.5 cm*

*Follow if ≥ 0.5 cm if FNA is negative
Patient #1
48 yo male incidental 8 mm thyroid nodule
High suspicion sonographic pattern, no abnormal LN

Active surveillance (monitor)
(FNA is not required...
Follow-up for nodules that do not meet FNA criteria

RECOMMENDATION 24 (NEW)

A) Nodules with high suspicion US pattern: repeat US 6-12 months (Weak recommendation, Low-quality evidence)


C) Nodules with very low suspicion US pattern (including spongiform nodules) and pure cyst: the utility and time interval of surveillance US for risk of malignancy is not known. If US is repeated, it should be at > 24 months (No recommendation, Insufficient evidence)

D) Nodules < 1 cm without high suspicion US pattern do not require routine sonographic FU and if repeated, the US should be performed at 24 months or later (Weak recommendation, Low-quality evidence)
Patient #2
38 yo female 2.7 cm high suspicion sonographic pattern
No abnormal neck LN
FNA - PTC

Thyroidectomy with central neck dissection
Thyroidectomy
Thyroidectomy or lobectomy
Lobectomy
Observation
FNA - PTC
2.7 cm

Thyroidectomy or lobectomy?

2009 Recommendation: Thyroidectomy

Adam M, Ann Surg 2014
Barney BM, Head Neck 2011
Nixon IJ, Surgery 2011
Mendelsohn AH, Arch Otolaryn 2010
Haigh PI, Ann Surg Onc 2005

RECOMMENDATION 35
PTC >1 cm and <4 cm
No extrathyroidal extension, cNO (preoperative assessment)
NTT/TT or lobectomy
(Strong Recommendation, Moderate-quality evidence)
Patient #3
56 yo male FNA - PTC
US - no abnormal LN
Thyroidectomy and central neck dissection

Path report - 3.8 cm FVPTC, involved LN

Helpful pathology report?
Recommendation 46 (NEW)

Pathology reports should include:
AJCC/TNM criteria
Vascular invasion and number of vessels
Number of LN examined and involved
Size of the largest metastatic LN focus
Extranodal extension

(Strong recommendation, Moderate-quality evidence)

Variants with more favorable and unfavorable outcomes

(Strong recommendation, Low-quality evidence)

Variants associated with familial syndromes

(Weak recommendation, Low-quality evidence)

Randolph GW, Thyroid 2012
Yamashita H, Cancer 1997
Lango M, Thyroid 2013
Collini P, Histopath 2004

Cetta F, JCEM 2000
Laury AR, Thyroid 2011
Volante M, Cancer 2004
Patient #3
56 yo male FNA – PTC
US – no abnormal LN
Thyroidectomy and central neck dissection

Path report: 3.8 cm FVPTC
- Extrathyroid extension, negative margins
- No vascular invasion
- 11/12 LN involved, largest 1.2 cm, no ENE

T3N1aMX, Stage III, ATA intermediate risk

Post-op TSH 0.2, Tg 1.8, Ab <2
- No radioiodine
- Diagnostic WBS
  - 30-150 mCi 131I, consider rhTSH
  - 30-150 mCi 131I only after THW
  - 150-200 mCi 131I after THW
System for Estimating Risk of Persistent or Recurrent Disease
ATA Guidelines 2009

**Low Risk**
- Classic PTC
- No local or distant mets
- Complete resection
- No ETE
- No vascular invasion
- If given, no RAI uptake outside TB

78-91% NED
2-7% Structural Incomplete

Cooper et al, Thyroid 2009
Tuttle et al, Thyroid 2010
Vaisman et al, Clin Endo 2012
Pitoia et al, Thyroid 2013

**Intermediate Risk**
- Microscopic ETE
- Cervical LN mets
- Aggressive Histology
- Vascular invasion

52-63% NED
21-34% Structural Incomplete

**High Risk**
- Macroscopic gross ETE
- Incomplete tumor resection
- Distant Mets
- Tg elevation

14-31% NED
56-72% Structural Incomplete
<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Disease Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>High Risk</strong></td>
<td>Gross extrathyroidal extension, incomplete tumor resection, distant metastases, or lymph node &gt; 3 cm</td>
</tr>
<tr>
<td><strong>Intermediate Risk</strong></td>
<td>Aggressive histology, minor extrathyroidal extension, vascular invasion, or &gt; 5 involved lymph nodes (0.2-3 cm)</td>
</tr>
<tr>
<td><strong>Low Risk</strong></td>
<td>Intrathyroidal DTC ≤ 5 LN micrometastases (&lt; 0.2 cm)</td>
</tr>
</tbody>
</table>

- 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 PMC (~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 PMC, BRAF mutated*, (~1-2%)
- Intrathyroidal, encapsulated, FV-PTC (~1-2%)
- Unifocal PMC (~1-2%)

*BRCA-mutated breast cancer
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%)
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Unifocal PMC (∼1-2%)
Radioiodine – the success story of Nuclear Medicine

75th Anniversary of the first use of Iodine-131 in humans

V. Ralph McCready

RADIOACTIVE IODINE IN THE STUDY OF THYROID PHYSIOLOGY

VII. The Use of Radioactive Iodine Therapy in Hyperthyroidism

SAUL HERTZ, M.D.
Boston
and
ARTHUR ROBERTS, PH.D.
Cambridge, Mass.

In previously published experiments of this series, radioactive iodine was used as an indicator in the study of animal and human thyroid physiology and iodine metabolism. Much of this preliminary work was done with a view to the discovery of the conditions under which radioactive iodine might be administered with maximum radiational effect in the pathologic thyroid of patients ill with hyperthyroidism. The present paper is a progress report on our early experiences (1941-1946) with such “internal irradiation” in the treatment of 29 cases of hyperthyroidism. It is, indeed, a three to five year follow-up report on these cases.

Dr Saul Hertz treating a hyperthyroid patient
January 1941
Low-Risk Differentiated Thyroid Cancer and Radioiodine Remnant Ablation: A Systematic Review of the Literature

Livia Lamartina, Cosimo Durante, Sebastiano Filetti, and David S. Cooper

Department of Internal Medicine and Medical Specialties (L.L., C.D., S.F.), University of Rome “Sapienza,” 00185 Rome, Italy; and Division of Endocrinology, Diabetes, and Metabolism (D.S.C.), The Johns Hopkins University School of Medicine, Baltimore, Maryland 21287

Conclusions: Neck ultrasonography and serum thyroglobulin measurement are equivalent or superior in detecting and localizing residual disease compared to post-therapy whole-body scan. There is no evidence of RRA benefit in recurrence prevention for LR patients. There are conflicting data on IR patients and only a few studies with homogenous and properly stratified populations. A careful evaluation of tumor pathological features and patient characteristics and preferences should guide RRA decision making. (J Clin Endocrinol Metab 100: 1748–1761, 2015)
# Radioiodine Remnant Ablation/Adjuvant Therapy/Therapy

**Recommendation 51 (Table 14)**

<table>
<thead>
<tr>
<th>ATA recurrence risk TNM Staging</th>
<th>Description</th>
<th>Post-surgical RAI indicated?</th>
</tr>
</thead>
<tbody>
<tr>
<td>ATA Low Risk T1a/N0,NX/M0,MX</td>
<td>T ( \leq 1 \text{cm} ) (unifocal or multifocal)</td>
<td>No (Strong, Mod)</td>
</tr>
<tr>
<td>ATA Low Risk T1b, T2/N0,NX/M0,MX</td>
<td>T 1-4 cm</td>
<td>Not routine (W,L)</td>
</tr>
</tbody>
</table>

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**Hippocratic Oath (modern version)**

“I will apply, for the benefit of the sick, all measures [that] are required, avoiding those twin traps of overtreatment and therapeutic nihilism.”
### ATA recurrence risk

#### TNM Staging

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<td>No (S,M)</td>
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<td>T ≤ 1 cm (unifocal or multifocal)</td>
<td></td>
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<tr>
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<td>T 1-4 cm</td>
<td></td>
</tr>
<tr>
<td><strong>ATA High risk</strong></td>
<td>T4/any N/any M</td>
<td>Yes (S,M)</td>
</tr>
<tr>
<td>T4/any N/any M</td>
<td>Gross extrathyroidal extension</td>
<td></td>
</tr>
<tr>
<td><strong>ATA High risk</strong></td>
<td>M1 (any T, any N)</td>
<td>Yes (S,M)</td>
</tr>
<tr>
<td>M1 (any T, any N)</td>
<td>Distant metastases</td>
<td></td>
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</table>
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<td>T ≤ 1cm (unifocal or multifocal)</td>
<td>No (S,M)</td>
</tr>
<tr>
<td>ATA Low Risk T1b, T2/N0,NX/M0,MX</td>
<td>T 1-4 cm</td>
<td>Not routine (W,L)</td>
</tr>
<tr>
<td>ATA Low to intermediate risk T3/N0,NX/M0,MX</td>
<td>T &gt; 4cm or microscopic invasion</td>
<td>Consider (W,L)</td>
</tr>
<tr>
<td>ATA Low to intermediate risk T1-3/N1a/M0,MX</td>
<td>Central compartment LN metastases</td>
<td>Consider (W,L) (size and number)</td>
</tr>
<tr>
<td>ATA Low to intermediate risk Any T1-3/N1b/M0,MX</td>
<td>Lateral compartment LN metastases</td>
<td>Consider (W,L) (size, number, age)</td>
</tr>
<tr>
<td>ATA High risk T4/any N/any M</td>
<td>Gross extrathyroidal extension</td>
<td>Yes (S,M)</td>
</tr>
<tr>
<td>ATA High risk M1 (any T, any N)</td>
<td>Distant metastases</td>
<td>Yes (S,M)</td>
</tr>
</tbody>
</table>
Low- or High-Dose Radioiodine Remnant Ablation for Differentiated Thyroid Carcinoma: A Meta-Analysis

JCEM 98:1353-60, 2013

Weiwei Cheng,* Chao Ma,* Hongliang Fu, Jianing Li, Suyun Chen, Shuqi Wu, and Hui Wang

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Events</th>
<th>Total</th>
<th>Events</th>
<th>Total</th>
<th>Weight</th>
<th>Risk Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bal 1996</td>
<td>17</td>
<td>27</td>
<td>28</td>
<td>38</td>
<td>9.6%</td>
<td>0.85 [0.60, 1.21]</td>
</tr>
<tr>
<td>Caglar 2011</td>
<td>38</td>
<td>47</td>
<td>35</td>
<td>48</td>
<td>15.1%</td>
<td>1.11 [0.89, 1.38]</td>
</tr>
<tr>
<td>Fallahi 2011</td>
<td>71</td>
<td>171</td>
<td>117</td>
<td>170</td>
<td>16.0%</td>
<td>0.60 [0.49, 0.74]</td>
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<tr>
<td>Mallick 2012</td>
<td>182</td>
<td>214</td>
<td>184</td>
<td>207</td>
<td>23.4%</td>
<td>0.96 [0.89, 1.03]</td>
</tr>
<tr>
<td>Mäenpää 2008</td>
<td>42</td>
<td>81</td>
<td>43</td>
<td>77</td>
<td>11.8%</td>
<td>0.93 [0.70, 1.24]</td>
</tr>
<tr>
<td>Schlumberger 2012</td>
<td>325</td>
<td>365</td>
<td>324</td>
<td>364</td>
<td>24.2%</td>
<td>1.00 [0.95, 1.05]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>905</strong></td>
<td></td>
<td><strong>904</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>0.91 [0.79, 1.04]</strong></td>
</tr>
</tbody>
</table>

Total events: 675 vs. 731

Heterogeneity: Tau² = 0.02; Chi² = 30.25, df = 5 (P < 0.0001); I² = 83%
Test for overall effect: Z = 1.43 (P = 0.15)

2015 Recommendations
ATA low risk disease
ATA intermediate risk (lower risk features)
30 mCi ¹³¹I generally favored over higher doses

Strong recommendation, High-quality evidence
Radioiodine Remnant Ablation
LT4 withdrawal vs rhTSH

RECOMMENDATION 54A
ATA low and intermediate risk disease
Can use rhTSH (Thyrogen)
Noninferiority to WD, short-term QOL
Long-term outcomes (observations)
Strong recommendation, Moderate-quality evidence

Pacini F, JCEM, 2006
Lee J, Thyroid, 2010
Mallick U, NEJM 2012
Schlumberger M, NEJM 2012
Molinaro E, JCEM 2013
Tu J, Radiother Oncol 2014
Patient #3
56 yo male FNA - PTC
US - no abnormal LN
Thyroidectomy and central neck dissection

Path report: 3.8 cm FVPTC
  Extrathyroid extension, negative margins
  No vascular invasion
  11/12 LN involved, largest 1.2 cm, no ENE
T3N1aMX, Stage III, ATA intermediate risk

Post-op TSH 0.2, Tg 1.8, Ab <2

Above ablation dose - 150 mCi 131I, consider rhTSH
Patient #4
41 yo female PTC
Thyroidectomy

Path report: 3.5 cm PTC
  - Microscopic extrathyroid extension, negative margins
  - No vascular invasion
  - No LN removed

T3N0MX, Stage I, ATA low to intermediate risk
30 mCi 131I (rhTSH), WBS - TB only, Tg 2.6
6 month FU: TSH 0.4, Tg 0.2, neck US negative
1 year FU: TSH 0.3, Tg 0.1, neck US negative

Risk of structural recurrence:
  <5%, 10-20%, 50%, >75%
Assessing Response to Therapy

<table>
<thead>
<tr>
<th>Suppressed Tg</th>
<th>Stimulated Tg</th>
<th>Tg Trend</th>
<th>Tg antibodies</th>
<th>Neck exam</th>
<th>Imaging</th>
<th>Excellent Response</th>
<th>Indeterminate (good) Response</th>
<th>Incomplete Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 0.2 ng/ml</td>
<td>&lt; 1 ng/ml</td>
<td>Low</td>
<td>Absent</td>
<td>Normal</td>
<td>Negative</td>
<td>Detectable, but &lt; 1 ng/mL</td>
<td>Detectable, but &lt; 1 ng/mL</td>
<td>&gt; 1 ng/mL</td>
</tr>
<tr>
<td>&lt; 10 ng/mL</td>
<td>&lt; 10 ng/mL</td>
<td>Declining</td>
<td>Absent or declining</td>
<td>Normal</td>
<td>Negative</td>
<td>&lt; 1 ng/mL</td>
<td>&gt; 10 ng/mL Stable or rising</td>
<td>&gt; 10 ng/mL</td>
</tr>
<tr>
<td></td>
<td></td>
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<td>Persistent or rising</td>
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<td></td>
<td></td>
<td></td>
<td>Insignificant</td>
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</table>

Lower Risk Estimate
Stable Risk Estimate
Raise Risk Estimate

Courtesy of RM Tuttle
Application of Dynamic Risk Classification

Risk of Persistent/Recurrent Structural Disease

Tuttle RM, Thyroid 2010
Management Approaches Based on Response to Therapy
Low to intermediate risk patients

<table>
<thead>
<tr>
<th></th>
<th>Excellent</th>
<th>Indeterminate</th>
<th>Biochemical Incomplete</th>
<th>Structural Incomplete</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH target</td>
<td>0.5-2</td>
<td>0.1-0.5</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
</tr>
<tr>
<td>Serum Tg</td>
<td>yearly</td>
<td>yearly</td>
<td>6-12 months</td>
<td>3-6 months</td>
</tr>
<tr>
<td>Neck US</td>
<td>5 years</td>
<td>1-3 years</td>
<td>6-12 months</td>
<td>3-6 months</td>
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<tr>
<td>Stim Tg</td>
<td>No</td>
<td>maybe</td>
<td>consider</td>
<td>consider</td>
</tr>
<tr>
<td>WBS</td>
<td>No</td>
<td>maybe</td>
<td>consider</td>
<td>consider</td>
</tr>
<tr>
<td>Cross-sectional imaging</td>
<td>No</td>
<td>No</td>
<td>consider</td>
<td>yes</td>
</tr>
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</table>

More aggressive monitoring for high risk patients
# TSH targets based on benefits vs risks

**Table 17**

<table>
<thead>
<tr>
<th>Increasing Risk of TSH Suppression</th>
<th>Excellent</th>
<th>Indeterminate</th>
<th>Biochemical Incomplete **</th>
<th>Structural Incomplete</th>
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</thead>
<tbody>
<tr>
<td>No Known Risk</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Menopause</td>
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<tr>
<td>Tachycardia</td>
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<tr>
<td>Osteopenia</td>
<td></td>
<td></td>
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<tr>
<td>Age &gt; 60</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Osteoporosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Atrial Fibrillation</td>
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<td></td>
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<td></td>
</tr>
</tbody>
</table>

- **Excellent**: No suppression. TSH target 0.5–2.0 mU/L
- **Indeterminate**: Mild suppression. TSH target 0.1–0.5* mU/L
- **Biochemical Incomplete**: Moderate or Complete Suppression. TSH target < 0.1 mU/L
- **Structural Incomplete**: TSH target < 0.1 mU/L

*Note: *TSH targets based on benefits vs risks.*
Patient #5
68 yo female presented with back pain, no neuro Sx
2.6 cm L2 lesion, Bx - FTC
PET/CT - 5-6 bone mets, multiple pulm nodules (<1.5 cm)
Thyroidectomy - 2.3 cm FTC with vascular invasion
Post-op Tg 1200 (TSH 0.06)

THW diagnostic WBS
THW 100-200 mCi 131I
EBRT or thermal ablation to L2 prior to RAI
Start TKI (lenvatinib, sorafenib)
Entry into clinical trial

Phone a friend
bryan.haugen@ucdenver.edu
Patient #5
68 yo female metastatic FTC
2.6 cm L2 lesion

[C38] What is the role for directed therapy in advanced thyroid cancer?

RECOMMENDATION 93
B) Thermal ablation or stereotactic radiation should be considered prior to initiation of systemic treatment when the individual distant metastases are symptomatic or at high risk of local complications. (Strong recommendation, Moderate-quality evidence)

Consider EBRT or thermal ablation to L2 prior to RAI
Radioidine-refractory DTC

How is radioiodine refractory DTC defined? (new question)

RECOMMENDATION 91 (NEW)

Radioiodine-refractory structurally-evident DTC is defined in patients with appropriate TSH stimulation and iodine preparation in four basic ways:

1) the malignant/metastatic tissue does not ever concentrate radioiodine
2) the tumor tissue loses the ability to concentrate radioiodine
3) radioiodine is concentrated in some lesions but not in others
4) metastatic disease progresses despite significant concentration of radioiodine.

When a patient with DTC is classified as refractory to radioiodine, there is no indication for further radioiodine treatment. (Strong recommendation, Moderate-quality evidence)
What to do with patients who have RAI-refractory DTC?

- **Monitor** *(New recommendation 92)*
- **Directed Therapy** *(New recommendation 93)*
  - Surgery, EBRT, thermal ablation
- **Clinical trials** *(New recommendation 95)*
  -Clinicaltrials.gov
- **Systemic therapy** *(New recommendations 96-99)*
  - Kinase inhibitors, Bone-directed therapy
Management Algorithm for Patients with RAIR DTC (structural disease)

RAIR DTC patient

Progressive (<12 months) or symptomatic disease?

- Yes
  - Progressive (<12 months) or symptomatic disease?
    - Yes
      - Active surveillance TSH suppression
    - No
      - Failure of approved therapy
        - Clinical trial not available or appropriate
          - Consider off-label therapy
        - Consider entry into a clinical trial
  - No
    - Active surveillance TSH suppression

- No
  - Few lesions
    - Active surveillance TSH suppression
  - Many lesions
    - Consider directed therapy
      - Consider systemic therapy
        - FDA-approved therapy
          - Consider adding bone-directed therapy for bone metastases
    - Consider systemic therapy
      - FDA-approved therapy
        - Consider adding bone-directed therapy for bone metastases
Summary

• US sonographic risk patterns
• Don’t need to biopsy every nodule > 1 cm
• Don’t have to biopsy any nodule < 1 cm
• Lobectomy may be reasonable approach
• More detailed pathology reports
• Use of selective radioiodine, lower doses
• Cross-sectional imaging for higher risk disease
• Stage (AJCC/TNM), ATA recurrence risk, response to therapy
• Individualize TH therapy and TSH targets
• Radioiodine refractory DTC
  - Definition, monitoring, directed-therapy, clinical trials and systemic therapy
Acknowledgements

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