Thyroid Cancer Update

What's new in 2018?

R Michael Tuttle, MD
Clinical Director, Endocrinology Service
Memorial Sloan Kettering Cancer Center
Professor of Medicine
Weill Medical College of Cornell University
Overview

Describe the new 8th edition AJCC staging system

Describe a rational approach to active surveillance in low risk thyroid cancer

Describe a rational approach to selection of thyroid cancer patients for lobectomy
AJCC 8th Edition Update
Differentiated Thyroid Cancer:

What changed and why?
October 2016, AJCC published the 8th edition staging manual
Effective: 1 Jan 2018
Replaces the 7th edition used since 2009

8th Edition

Major Re-write

- Evidenced based medicine principles
- 18 expert panels: 420 contributors, 181 institutions, and 22 countries
- Expanded multispecialty editorial board supported by six core committees: content harmonization, precision medicine, evidence based medicine/statistics, imaging, data collection, professional organization/corporate relationships, and administration

Amin et al, CA Cancer J Clin 2017

www.cancerstaging.org
AJCC Staging Philosophy Has Evolved

8th Edition

Beyond Anatomic Staging

• Continues strong emphasis on anatomic staging
  • T, N, and M
• Endorses integration of non-anatomical prognostic variables in an effort to create a more contemporary personalized approach to risk stratification
• Genetic alterations, tumor markers, response to therapy
• Evolving philosophy reflected stage groups names (I-IV)
  • Anatomic stage groups (1st six editions)
  • Anatomic stage and prognostic groups (7th)
  • Prognostic stage groups (8th edition)

Amin et al, CA Cancer J Clin 2017

www.cancerstaging.org
Thyroid – Differentiated and Anaplastic Carcinoma

R. Michael Tuttle, Lilah F. Morris, Bryan R. Haugen, Jatin P. Shah, Julie A. Sosa, Eric Rohren, Rathan M. Subramaniam, Jennifer L. Hunt, and Nancy D. Perrier

Thyroid – Medullary

What were the major changes?

- Age at diagnosis cut off raised
  - Was 45 years, now is 55 years old
- In older patients
  - Minor extrathyroidal extension no longer mandates stage III
  - Lymph node metastases no longer mandates stages III/IV
- Many patients will be re-classified into lower prognostic stages
- Better separation between the prognostic stage groups

Tuttle, Haugen, Perrier. Thyroid 2017.
Perrier, Brierley, Tuttle. CA: A Cancer Journal for Clinicians, 2017
Increasing the age cut off to 55 yrs

Moves many patients to lower prognostic stage groups without worsening the prognosis in the lower stages

Establishment of an Intraoperative Staging System (iStage) by Improving UICC TNM Classification System for Papillary Thyroid Carcinoma


The age factor in survival of a population cohort of well-differentiated thyroid cancer

An International Multi-Institutional Validation of Age 55 Years as a Cutoff for Risk Stratification in the AJCC/UICC Staging System for Well-Differentiated Thyroid Cancer

Optimal Cutoff Age for Predicting Mortality Associated with Differentiated Thyroid Cancer
Age as a continuous variable

Ten year disease specific survival at different age cutoffs from age 30 to age 70 yrs

Survival from differentiated thyroid cancer: What has age got to do with it? Ganly et al, Thyroid 2015.
Increasing the age cut off to 55 yrs

9,484 WDTC Patients, 10 institutions, median follow up 5 yrs

<table>
<thead>
<tr>
<th>Younger</th>
<th>≥ 45 yrs</th>
<th>Older</th>
</tr>
</thead>
<tbody>
<tr>
<td>4,546 patients (48%)</td>
<td></td>
<td>4,938 patients (52%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>≥ 55 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>6,648 patients (70%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>≥ 45 yrs</th>
<th>≥ 55 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>4,546 patients (48%)</td>
<td>2,102 pts (22%)</td>
</tr>
</tbody>
</table>

Nixon et al, Thyroid 2016
Increasing the age cut off to 55 yrs

<table>
<thead>
<tr>
<th>Prognostic Stage</th>
<th>Age Cut Off</th>
<th>N (%)</th>
<th>10 yr DSS (Median 5 yrs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>45 yrs</td>
<td>6,600 (70%)</td>
<td>99.7%</td>
</tr>
<tr>
<td></td>
<td>55 yrs</td>
<td>7,736 (82%)</td>
<td>99.5%</td>
</tr>
<tr>
<td>II</td>
<td>45 yrs</td>
<td>741 (8%)</td>
<td>97.3%</td>
</tr>
<tr>
<td></td>
<td>55 yrs</td>
<td>441 (5%)</td>
<td>94.7%</td>
</tr>
<tr>
<td>III</td>
<td>45 yrs</td>
<td>1230 (13%)</td>
<td>96.6%</td>
</tr>
<tr>
<td></td>
<td>55 yrs</td>
<td>707 (8%)</td>
<td>94.1%</td>
</tr>
<tr>
<td>IV</td>
<td>45 yrs</td>
<td>913 (10%)</td>
<td>76.3%</td>
</tr>
<tr>
<td></td>
<td>55 yrs</td>
<td>600 (6%)</td>
<td>67.6%</td>
</tr>
</tbody>
</table>

Nixon et al, Thyroid 2016
Prognosis & LN metastasis

The challenges of LN risk stratification

LN mets are present in 60-80% of papillary microcarcinoma patients implying that small volume disease has little impact on DSS.

Clinically apparent LN mets have an impact on overall survival that is more apparent in older patients than young patients.

Prognosis probably related to lymph node size, number involved, lymph node ratio, extranodal extension, location (N1a vs. N1b), histology, molecular profile and concurrent gross ETE.

Young patients N1a/N1b → Stage I
Older patients N1a/N1b → Stage II

Microscopic Extrathyroidal Extension

7th Edition
Classified as T3
Stage III (> 45 yrs old)
Regardless of tumor size

T1 and T2
“Limited to the thyroid”
With or Without Microscopic ETE

Issues
Not a major risk factor

Defining ETE
“problematic and subjective”
(American College of Pathologists)

Incomplete tumor capsule

Gross Extrathyroidal Extension

Consistently shown to be risk factor for mortality

T3a
Intrathyroidal tumors > 4 cm (Stage II, >55 yrs)

T3b
Gross extrathyroidal extension invading only strap muscles from a tumor of any size (Stage II, >55 yrs)

Gross Extrathyroidal Extension

Invasion of Major Structures in the Neck
Significant Impact on Survival

T4a
Gross ETE subcutaneous soft tissues, larynx, trachea, esophagus, or RLN from any size tumor (Stage III, > 55 yrs)

T4b
Gross extrathyroidal extension invading pre-vertebral fascia or encasing the carotid or mediastinal vessels from any size tumor (Stage IVA, > 55 yrs)

**Molecular Markers and Prognosis**

**Multicenter study, 1,849 patients with PTC**
**56 PTC related deaths, median 3 yr follow-up**

<table>
<thead>
<tr>
<th>AJCC 7th Edition</th>
<th>BRAF V600E Mutate (45 deaths)</th>
<th>BRAF V600E Wild Type (11 deaths)</th>
<th>p value Survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1/443</td>
<td>1/664</td>
<td>0.02</td>
</tr>
<tr>
<td>II</td>
<td>1/77</td>
<td>0/127</td>
<td>NS</td>
</tr>
<tr>
<td>III</td>
<td>4/180</td>
<td>0/102</td>
<td>NS</td>
</tr>
<tr>
<td>IV</td>
<td>38/121 (31.4% mortality)</td>
<td>10/77 (13% mortality)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

(deaths/total number of patients)

Xing, JAMA 2013
# Practical Application

> Identification of metastatic disease (by any modality) within the first 4 months of thyroid surgery should be used to refine the N and M status.

<table>
<thead>
<tr>
<th>Distant Mets</th>
<th>Gross ETE present?</th>
<th>Tumor Size</th>
<th>LN status</th>
<th>Stage</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>&lt; 55 yrs old</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>I</td>
</tr>
<tr>
<td>Yes</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>II</td>
</tr>
<tr>
<td><strong>≥ 55 yrs old</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>No</td>
<td>≤4 cm (T1-2) ± Micro ETE</td>
<td>N0/Nx</td>
<td>I</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>N1a/N1b</td>
<td>II</td>
</tr>
<tr>
<td>Only strap muscles (T3b)</td>
<td>Any</td>
<td>Any</td>
<td></td>
<td>II</td>
</tr>
<tr>
<td>Subq, larynx, trachea, esophagus, RLN (T4a)</td>
<td>Any</td>
<td>Any</td>
<td></td>
<td>III</td>
</tr>
<tr>
<td>Prevertebral fascia, encasing major vessels (T4b)</td>
<td>Any</td>
<td>Any</td>
<td></td>
<td>IVA</td>
</tr>
<tr>
<td>Yes</td>
<td>Any</td>
<td>Any</td>
<td>Any</td>
<td>IVB</td>
</tr>
</tbody>
</table>

Tuttle, Haugen, Perrier. Thyroid 2017.
Validation of 8th Edition AJCC/TNM

3,176 patients, Samsung Medical Center, Seoul, Korea

Kim et al, Oral Oncology, 2017

AJCC 7th Edition

AJCC 8th Edition

10 yr DSS

99%

94%

80%

67%

65%
Projecting Survival in Papillary Thyroid Cancer: A Comparison of the 7th and 8th Editions of the AJCC/UICC Staging Systems in Two Contemporary National Patient Cohorts

SEER
64,342 patients

Pontius et al, Thyroid 2017
## Integrating AJCC and ATA Risk Categories

<table>
<thead>
<tr>
<th>Age at Diagnosis</th>
<th>AJCC 8th Edition Stage</th>
<th>ATA Low</th>
<th>ATA Intermediate</th>
<th>ATA High</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 55 yrs old</td>
<td>I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 55 yrs old</td>
<td>I</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>II</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>III</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The transition from a population based to a more “personalized” approach

David Byrd and Frederick Greene, Ann Surg Oncol 2017

<table>
<thead>
<tr>
<th>AJCC/UICC TNM Stage (Basic Classification)</th>
<th>TNM</th>
</tr>
</thead>
<tbody>
<tr>
<td>AJCC Prognostic Stage Groups (Advanced clinical relevance)</td>
<td>TNM Plus Prognostic Factors</td>
</tr>
<tr>
<td>AJCC “Personalized” (Advanced clinical and personal relevance)</td>
<td>TNM Plus Prognostic Factors Plus Risk Assessment Models Plus Clinical Trial Stratification</td>
</tr>
</tbody>
</table>

Population Outcomes | Personalized Outcomes
Risk Stratification in Thyroid Cancer

Dynamic, iterative, active process

Risk of Death from Thyroid Cancer
8th Edition TNM/AJCC, MACIS

Response to Therapy

Excellent
Biochemical Incomplete
Structural Incomplete
Indeterminate

Risk Stratification System
ATA, LATS, ETA

Haugen et al, ATA thyroid cancer guidelines, Thyroid 2016
Active Surveillance for Low Risk Papillary Thyroid Cancer
Diagnosis and Treatment of Thyroid Cancer

Usual presentation before the era of neck ultrasound/CT/MRI

Thyroid nodule or metastatic lymph nodes were found on physical examination

A few weeks later

Surgical resection of the thyroid and abnormal lymph nodes
Subclinical Thyroid Cancer is Present in > 10% of healthy adults.

Imaging tools are detecting many very small, subclinical thyroid cancers.

Ultrasound

US Guided FNA

Clinically significant disease

Iceberg

Subclinical, usually not significant

United States

62,000 new cases/yr
≈ 600,000 survivors

Subclinical reservoir
USA alone
32 million cases
Critical Questions

Is there a benefit to early detection and immediate treatment of thyroid cancer?

Is there a potential for harm in the early detection and immediate treatment of thyroid cancer?

Is a delayed treatment approach viable?
Abnormal ultrasound findings do not always require immediate cytological diagnosis and treatment

ATA Thyroid Cancer Guidelines
Balancing Potential Risks and Benefits

• Persistent/recurrent disease setting
  • Abnormal cervical lymph nodes < 8–10mm (2009 text; 2015 R65, R71)
  • “probably best managed with active surveillance (observation)...
    reserving FNA and subsequent intervention for documented
    structural disease progression.”

• Abnormal high suspicion thyroid nodules (70–90% malignant)
  • < 5 mm (2009 R5)
  • < 10 mm (2015 R8, R24)

• Active Surveillance “can be considered” for FNA + “very low risk tumors”
  (2015 p16 text, R12)
  • “e.g., no clinical or radiological evidence of invasion or metastases”
  • “e.g., papillary microcarcinomas without clinically evident metastases
    or local invasion, and no convincing cytologic evidence of aggressive
disease”

Cooper et al. Thyroid 2009 Haugen et al. Thyroid 2016
Observational Management Approach to Papillary Microcarcinoma

2,153 Low Risk Papillary Microcarcinoma Patients

Active Surveillance 1,179 (55%)
Immediate Surgery 974 (45%)

Median Follow-up 4 yrs (range 1-10 yrs)

Continued Observation 1,085 (92%)
Surgery, Stable Disease 61 (5.2%)
Increase Size Primary Tumor 27 (2.3%)
Novel LN Metastasis 6 (0.5%)

Salvage therapy is very effective

Oda et al, Thyroid 2016; 26(1): 150-155
Ito et al. Thyroid. 2013.
Patient Age Is Significantly Related to the Progression of Papillary Microcarcinoma of the Thyroid Under Observation

Outcomes after 10 years of observation

- Young (< 40 yrs)
- Middle Age (40 - 59 yrs)
- Older (≥60 yrs)

- Increase in size ≥ 3 mm (0.3 cm)
  - Young: 5.9%
  - Middle Age: 5.7%
  - Older: 2.2%

- Novel LN mets
  - Young: 5.3%
  - Middle Age: 1.4%
  - Older: 0.4%

- Progression
  - Young: 8.9%
  - Middle Age: 3.5%
  - Older: 1.6%
Active Surveillance for Patients With Papillary Thyroid Microcarcinoma: A Single Center’s Experience in Korea

Hyemi Kwon,1,2 Hye-Seon Oh,1 Mijin Kim,1 Suyeon Park,1 Min Ji Jeon,1 Won Gu Kim,1 Won Bae Kim,1 Young Kee Shong,1 Dong Eun Song,3 Jung Hwan Baek,4 Ki-Wook Chung,5* and Tae Yong Kim1*

192 PMC Patients
Followed for ≥ 1 year (Median 2.5 yrs)

<table>
<thead>
<tr>
<th>Decrease volume</th>
<th>Stable Volume</th>
<th>Increase 3mm &amp; Increase volume</th>
<th>Increase volume without 3 mm increase</th>
<th>Novel LN metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>(33/192) 17%</td>
<td>(132/192) 69%</td>
<td>(4/192) 2%</td>
<td>(27/192) 14%</td>
<td>(1/192) 0.5%</td>
</tr>
</tbody>
</table>

Asan Medical Center, Seoul, Korea
JCEM June 2017
Natural History and Tumor Volume Kinetics of Papillary Thyroid Cancers During Active Surveillance

R. Michael Tuttle, MD; James A. Fagin, MD; Gerald Minkowitz, MD; Richard J. Wong, MD; Benjamin Roman, MD, MSHP; Snehal Patel, MD; Brian Untch, MD; Ian Ganly, MD, PhD; Ashok R. Shaha, MD; Jatin P. Shah, MD; Mark Pace, MBBS, FRACP; Duan Li, MD; Ariadne Bach, MD; Oscar Lin, MD; Adrian Whiting, BS; Ronald Ghossein, MD; Inigo Landa, PhD; Mona Sabra, MD; Laura Boucai, MD; Stephanie Fish, MD; Luc G. T. Morris, MD, MSc

Published online August 31, 2017.
Table 1: Cohort characteristics of 291 low risk papillary thyroid cancer patients followed with active surveillance for more than 6 months

<table>
<thead>
<tr>
<th>Age at diagnosis (yrs)</th>
<th>Median Mean ± SD Range</th>
<th>51 52 ± 15 (20–86)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Female</td>
<td>25% (72)</td>
</tr>
<tr>
<td></td>
<td>Male</td>
<td></td>
</tr>
<tr>
<td>Cytology</td>
<td>Bethesda VI</td>
<td>84% (243)</td>
</tr>
<tr>
<td></td>
<td>Bethesda V</td>
<td></td>
</tr>
<tr>
<td>Distribution of Tumor Sizes</td>
<td>≤ 1 cm</td>
<td>78% (230)</td>
</tr>
<tr>
<td></td>
<td>1.1-1.5 cm</td>
<td></td>
</tr>
<tr>
<td>Appropriateness for active surveillance</td>
<td>Ideal</td>
<td>4% (13)</td>
</tr>
<tr>
<td></td>
<td>Appropriate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Inappropriate</td>
<td>2% (5)</td>
</tr>
<tr>
<td>Duration of active surveillance</td>
<td>Median Mean ± SD Range</td>
<td>25 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>29 ± 19 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td>6–166</td>
</tr>
<tr>
<td>Status at final follow-up</td>
<td>Continue on active surveillance</td>
<td>96% (279)</td>
</tr>
<tr>
<td></td>
<td>Surgery for increase in tumor size</td>
<td>1.7% (5)</td>
</tr>
<tr>
<td></td>
<td>Surgery despite stable tumor size</td>
<td>1.7% (5)</td>
</tr>
<tr>
<td></td>
<td>Lost to follow up</td>
<td>0.6% (2)</td>
</tr>
</tbody>
</table>
Active Surveillance of Low Risk Papillary Thyroid Cancer

291 MSKCC patients
< 1.5 cm PTC/Suspicious PTC
Median 2 yr follow up, Median age 51 yrs (20-86)

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Diameter increase of 3mm</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2.5%</td>
</tr>
<tr>
<td>12</td>
<td>12.1%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time (months)</th>
<th>Volume increase of 50%</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>11.5%</td>
</tr>
<tr>
<td>12</td>
<td>24.8%</td>
</tr>
</tbody>
</table>

Tuttle et al, JAMA Otolaryngology–Head & Neck Surgery, 2017
Percent Change in Tumor Volume
(n=291)

- Decreased > 50%
  (n=19)
  7%

- Stable (± 50%)
  (n=228)
  79%

- Increased > 50%
  (n=36)
  12%

Tuttle et al, JAMA Otolaryngology-Head & Neck Surgery, 2017
Active Surveillance of Low Risk Papillary Thyroid Cancer

Demonstrate remarkably consistent classic exponential growth curves

Tuttle et al, JAMA Otolaryngology-Head & Neck Surgery, 2017
Proper Patient Selection

Requires concurrent evaluation of three inter-related domains

- Tumor/US Characteristics
- Medical Team Characteristics
- Patient Characteristics

A clinical framework to facilitate risk stratification when considering an active surveillance alternative to immediate biopsy and surgery in papillary microcarcinoma. JP Brito, Y Ito, A Miyauchi, RM Tuttle. Thyroid 2015
Active Surveillance in Clinical Practice

Our standard approach

- **Tumor Volume**
- **Tumor Location**
- **Rate of Change (Doubling Time)**
- **Follow-up Strategy**
- **Intervention Indications**

**Neck Ultrasound**
- Baseline
- Every 6 months for 2 years
- Then less frequently
Proper selection of patients for lobectomy vs. total thyroidectomy and follow-up of patients treated with lobectomy
### Clinical Outcomes

#### Total thyroidectomy vs. Lobectomy

<table>
<thead>
<tr>
<th>Study</th>
<th>n (source)</th>
<th>Survival Benefit for Total Thyroidectomy (&lt; 4 cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bilimoria, et al</td>
<td>52,173 (NCDB)</td>
<td>Yes</td>
</tr>
<tr>
<td>Adam, et al</td>
<td>61,775 (NCDB)</td>
<td>No</td>
</tr>
<tr>
<td>Haigh, et al</td>
<td>5,432 (SEER)</td>
<td>No</td>
</tr>
<tr>
<td>Barney, et al</td>
<td>23,605 (SEER)</td>
<td>No</td>
</tr>
<tr>
<td>Mendelsohn, et al</td>
<td>22,724 (SEER)</td>
<td>No</td>
</tr>
<tr>
<td>Nixon, et al</td>
<td>889 (Single Center)</td>
<td>No</td>
</tr>
<tr>
<td>Matsuzua, et al</td>
<td>1,088 (Single Center)</td>
<td>No</td>
</tr>
</tbody>
</table>

Re-Opened the Door to Lobectomy

Bilimoria 2007

10 yr survival

98.4% for total vs. 97.1% for lobectomy (p<0.05)

Utility of US and serial TG in follow-up without total thyroidectomy/RAI

RECOMMENDATION 35

(A) For patients with thyroid cancer $>4 \text{ cm}.$ or with gross extrathyroidal extension (clinical T4), or clinically apparent metastatic disease to nodes (clinical N1) or distant sites (clinical M1), the initial surgical procedure should include a near-total or total thyroidectomy and gross removal of all primary tumor unless there are contraindications to this procedure.

(Strong recommendation, Moderate-quality evidence)

Haugen et al, Thyroid 2016
Operative Approach for Biopsy Proven Follicular Cell-Derived Malignancy

Oncologic Outcomes (Survival, Recurrence)
Adjuvant Therapy
Enhance Follow-up
Patient Preference

(B) For patients with thyroid cancer >1 cm and <4 cm without extrathyroidal extension and without clinical evidence of any lymph node metastases (cN0), the initial surgical procedure can be either a bilateral procedure (near-total or total thyroidectomy) or a unilateral procedure (lobectomy). Thyroid lobectomy alone may be sufficient initial treatment for low-risk papillary and follicular carcinomas; however, the treatment team may choose total thyroidectomy to enable RAI therapy or to enhance follow-up based upon disease features and/or patient preferences.

(Strong recommendation, Moderate-quality evidence)
Operative Approach for Biopsy Proven Follicular Cell-Derived Malignancy

2015 ATA Thyroid Cancer Guidelines

(C) If surgery is chosen for patients with thyroid cancer <1 cm without extrathyroidal extension and cN0, the initial surgical procedure **should be a thyroid lobectomy** unless there are clear indications to remove the contralateral lobe. Thyroid lobectomy alone is sufficient treatment for small, unifocal, intrathyroidal carcinomas in the absence of prior head and neck radiation, familial thyroid carcinoma, or clinically detectable cervical nodal metastases.

*(Strong recommendation, Moderate-quality evidence)*
The Prognostic Value of Primary Tumor Size in Papillary and Follicular Thyroid Carcinoma

A Comparative Analysis

Andreas Machens, M.D.
Hans-Jürgen Holzhauen, M.D.
Henning Drale, M.D.

1 Department of General, Visceral, and Vascular Surgery, Martin-Luther-University Halle-Wittenberg, Halle/Saale, Germany.
2 Department of Pathology, Martin-Luther-University Halle-Wittenberg, Halle/Saale, Germany.

2-4 cm PTC
Not classical PTC

Encapsulated FV-PTC

NIFT-P

Minimally invasive FTC

Possibly small volume, low risk, residual disease in LNs and contralateral lobe

FIGURE 1. Cumulative risks of extrathyroidal growth and lymph node metastasis. PTC: papillary thyroid carcinoma; FTC: follicular thyroid carcinoma.
A clinical framework to facilitate risk stratification when considering an active surveillance alternative to immediate biopsy and surgery in papillary microcarcinoma. JP Brito, Y Ito, A Miyauchi, RM Tuttle. Thyroid 2015
# A Clinical Framework for Decision Making with Regard to Extent of Initial Surgery

## Pre-operative Decision Making

<table>
<thead>
<tr>
<th>Ideal</th>
<th>Tumor/Imaging characteristics</th>
<th>Patient characteristics</th>
<th>Medical Team Characteristics</th>
</tr>
</thead>
</table>
| • < 1cm  
• Intrathyroidal  
• US, encapsulated  
• US, non-infiltrative  
• Thyroid o/w normal  
• Clinical N0 neck | • Minimalist mentality  
• Motivated patient  
• Willingness to accept possibility of small volume disease in contralateral lobe  
• Desire to preserve thyroid function (TSH < 2, Tg Ab neg)  
• Desire to minimize surgical complications  
• Open to intra-operative decision making | • Experienced MDT  
• Experienced US  
• Shared treatment philosophy  
• Uses RAI very selectively for ablation/adjuvant therapy and follow up  
• Frozen section available |
# A Clinical Framework for Decision Making with Regard to Extent of Initial Surgery

## Pre-operative Decision Making

<table>
<thead>
<tr>
<th>Tumor/Imaging characteristics</th>
<th>Patient characteristics</th>
<th>Medical Team Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Appropriate</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• 1–4 cm</td>
<td>• Minimalist/Maximalist</td>
<td>• Surgeon and endocrinologist agree on post-op management plan</td>
</tr>
<tr>
<td>• Benign appearing changes on US (Hashimoto’s, benign nodules)</td>
<td>• Desire to keep normal thyroid (or avoidance of surgical complications) outweighs concern for disease in the contralateral lobe or the desire for RAI</td>
<td>• Unlikely to include need for RAI</td>
</tr>
<tr>
<td>• Benign appearing LN’s</td>
<td>• TSH &gt; 2</td>
<td>• Comfortable that follow-up US is adequate for low risk patient</td>
</tr>
<tr>
<td>• US, infiltrative pattern</td>
<td>• Tg Ab positive</td>
<td></td>
</tr>
<tr>
<td>• Clinical N0 neck</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
A Clinical Framework for Decision Making with Regard to Extent of Initial Surgery

**Pre-operative Decision Making**

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<thead>
<tr>
<th>Tumor/Imaging characteristics</th>
<th>Patient characteristics</th>
<th>Medical Team Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inappropriate</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• &gt;4 cm</td>
<td>• Maximalist mentality</td>
<td>• Treatment team desires RAI for scanning/therapy or optimized serum Tg for staging and follow-up</td>
</tr>
<tr>
<td>• Extrathyroidal extension</td>
<td>• Patient desires total thyroidectomy and/or RAI</td>
<td></td>
</tr>
<tr>
<td>• Clinical N1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Distant metastases</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• High risk molecular profile</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Operative Approach for Biopsy Proven Follicular Cell-Derived Malignancy

[B9] Completion thyroidectomy

RECOMMENDATION 38

(A) Completion thyroidectomy should be offered to patients for whom a bilateral thyroidectomy would have been recommended had the diagnosis been available before the initial surgery. Therapeutic central neck lymph node dissection should be included if the lymph nodes are clinically involved. Thyroid lobectomy alone may be sufficient treatment for low-risk papillary and follicular carcinomas.

(Strong recommendation, Moderate-quality evidence)
A Clinical Framework for Decision Making in Thyroid Cancer

Post-operative Decision Making (My personal philosophy)

<table>
<thead>
<tr>
<th>Histological characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Ideal</strong></td>
</tr>
<tr>
<td>• Intrathyroidal classical PTC</td>
</tr>
<tr>
<td>• FV-PTC without vascular invasion</td>
</tr>
<tr>
<td>• NIFT-P</td>
</tr>
<tr>
<td>• Minimally invasive FTC (capsular invasion only)</td>
</tr>
<tr>
<td>• Clinical N0 and Pathology N0/Nx neck</td>
</tr>
<tr>
<td><strong>Appropriate</strong></td>
</tr>
<tr>
<td>• 1-4 cm</td>
</tr>
<tr>
<td>• Minor extrathyroidal extension</td>
</tr>
<tr>
<td>• Clinical N0 but Pathology N1 with &lt; 5 met LN all &lt; 0.5 cm in max size</td>
</tr>
<tr>
<td>• Minor vascular invasion</td>
</tr>
<tr>
<td>• 1-2 cm tumors with aggressive histology</td>
</tr>
<tr>
<td><strong>Inappropriate</strong></td>
</tr>
<tr>
<td>• Extensive vascular invasion</td>
</tr>
<tr>
<td>• &gt; 2 cm aggressive histology</td>
</tr>
<tr>
<td>• Clinical N1</td>
</tr>
<tr>
<td>• Gross extrathyroidal extension</td>
</tr>
</tbody>
</table>
A Clinical Framework for Decision Making in Thyroid Cancer

**Post-operative Decision Making**

<table>
<thead>
<tr>
<th>Serum Thyroglobulin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ideal</td>
</tr>
<tr>
<td>Non-stimulated Tg &lt; 10 ng/mL</td>
</tr>
<tr>
<td>Appropriate</td>
</tr>
<tr>
<td>Non-stimulated Tg 10-30 ng/mL</td>
</tr>
<tr>
<td>Inappropriate</td>
</tr>
<tr>
<td>Non-stimulated Tg &gt; 30 ng/mL (without other nodules)</td>
</tr>
</tbody>
</table>
A Clinical Framework for Decision Making with Regard to Extent of Initial Surgery

Decision making at 2 discrete time points: pre-op and post-op

A clinical framework to facilitate risk stratification when considering an active surveillance alternative to immediate biopsy and surgery in papillary microcarcinoma. JP Brito, Y Ito, A Miyauchi, RM Tuttle. Thyroid 2015
# A Practical Approach to Follow-up After Lobectomy

## Excellent disease specific survival

Highly sensitive disease detection techniques are not necessary

<table>
<thead>
<tr>
<th>Tumor/Imaging characteristics</th>
<th></th>
</tr>
</thead>
</table>
| **TSH goal**                 | • 0.5-2.5 mIU/mL  
• With or without levothyroxine |
| **Clinic visits**            | • Post-op (to review path, check TSH, Tg)  
• Then 6-12 month follow-up  
• Yearly for 2-3 years with exam  
• TSH, Free T4, Tg, TgAb with each clinic visit |
| **Imaging**                  | • Neck US 6-12 months, 3 yrs, and 5 yrs  
• Then very rarely |
| **Late completion thyroidectomy** | • Physical exam findings  
• Neck US findings  
• Need for RAI  
• Sustained, serial rise in Tg over time |