Head and Neck Cancer Staging: Purpose, Process and Progress

Jatin Shah
Head and Neck Cancer Staging

Purpose

➢ To measure the volume / extent of disease
➢ To plan selection of treatment
➢ To assess prognosis
➢ To compare outcomes of therapy
   - Across geographic regions
   - Among Institutions
➢ Among treatment modalities
Sir William Stewart Halstead

- William Stewart Halsted, the father of surgical oncology, theorized that cancer progression follows an orderly step-wise process beginning from primary tumor formation to distant metastasis, passing through regional lymph nodes, using Breast cancer as an example.

Early Attempts at Staging

In 1905, Steinthal in Germany first attempted to clinically stage breast cancer based on Halstead’s theory.
Tumor, Node, Metastases (TNM) in Staging Cancer

Pierre Denoix (1944)

- Introduced TNM Staging system
- UICC adapts TNM staging system 1954
- AJCC adopts TNM system
- AJCC / UICC collaborate - 1980s
UICC & AJCC

- UICC TNM Committee. 1954
- First organized a meeting on Jan. 9, 1959
- American joint Committee for Cancer Staging and End Results Reporting 1959
- National Cancer Conference on Classification
- and Staging. 1976
- American Joint Committee on Cancer. 1980
- 2nd Edition. 1983 (Added more sites)
- Increasing collaboration with UICC since 1980s
- Seven Editions published in the past
Head and Neck Cancer

AJCC / UICC

Now have a uniform globally applicable staging system
AJCC / UICC
8th Edition Revisions

In devising and revising any staging system the following points must be borne in mind.

Complexity
Discrimination
Compliance
The 5% rule
Complexity

A very detailed and complex system will very accurately predict outcome.

- The more the details and the more factors we add to the staging system, the more accurate and precise it will be in predicting outcome.
- However, the more complex the system gets it’s user friendliness diminishes and compliance declines.
- Thus any revision has to be a “compromise”, between the Ideal (most accurate and detailed) and the Practical (acceptable compliance).
Discrimination

The data collected should be analyzed to be able to discriminate different groups consistently in predicting outcomes and the groups should be equally distributed

- Hazard consistency
- Hazard discrimination
- Outcome prediction
- Balance

Compliance

High compliance in the utility of the staging system is required to make it meaningful and collect "large data".

Any staging system must be detailed and accurate enough (complex) to predict the impact of various anatomic and non-anatomic factors to make it relevant.

However, it should be such (simple) that it would be used widely, throughout the world, and thus user friendly to improve compliance.

Therefore, it is a compromise between the "Ideal and the Practical".
The 5 % Rule

Rare and exceptional observations and issues should be avoided.

Any disease, factor, issue, or observation which has an incidence of less than 5 %, is generally not considered for entering into the criteria for staging systems.
A comparison of published head and neck stage groupings in carcinomas of the oral cavity

Patti A Groome, Karleen Schulze, Morten Boysen, et al. (2001)

- Tested UICC/AJCC and seven other staging systems for estimation of prognosis and comparison of therapies in oral cancer
- Compared hazard consistency, hazard discrimination, outcome prediction, and balanced distribution
- Suggested TNM staging could be improved using empirically derived schemes
Frequency of Revisions

- Too frequent revisions to the staging system should be avoided, otherwise we will not be able to generate comparative data, to show outcomes of disease and therapy.
- On the other hand new discoveries and new knowledge must be incorporated in the revisions to the staging system, to continually improve it and make it more accurate and meaningful.
- Again a “Compromise between the Ideal and the Practical.”
Progression of T N M Staging

Pierre Denoix -1944 - TNM classification. 1953

American Joint Committee on Cancer Staging and End results reporting established . 1959

1st Edition – 1977  
2nd Edition - 1983

3rd Edition – 1988  

6th Edition -2002 - (AJCC / UICC)

7th Edition – 2009  
8th Edition - 2016
Evolution of the staging system

- TNM staging
- Non Anatomic prognostic factors
- Parallel recording of other Prognostic factors and new info.
- Testing - Validation - Introduction
- Nomograms
Inclusion of comorbidity in a staging system for head and neck cancer

Jay F Piccirillo (1995)

• Used conjunctive consolidation to incorporate comorbidity into staging system
• Accounted for performance status, symptom severity, comorbidity
• Adding co-morbidity improved prognostication over TNM staging alone
Is the current TNM System adequate?

- No
- Is it workable? Yes.
- Problems: It does not include functional status of the larynx, such as aspiration, incompetent larynx, status of airway and dysphagia
- The TNM system takes into consideration only anatomic factors of the tumor, and not patient related factors, such as smoking, alcohol, pulmonary status, general medical condition (Life style and Co Morbidities)
- The TNM system is “Static” and stages patients only at the time of initial diagnosis
- The TNM system does not include “Response to Therapy”, and thus is not dynamic.
AJCC – Head and Neck Task Force

- 28 Members
- Surgeons
- Radiation Oncologists
- Medical Oncologists
- Pathologists
- Radiologists
- Epidemiologists
- Basic research scientists
- Biostatistics, Registrars, Data Managers, Support staff
AJCC – Head and Neck Task Force

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- Randal Scott Weber, MD
- Bruce M. Wenig, MD
8th Edition Revisions

- **Goals**: Global applicability, incremental improvement and Harmony between AJCC and UICC
- A **Compromise** between a highly accurate but complex system, with low compliance, and a simpler, high compliance system, with somewhat diminished predictive capacity
cTNM and pTNM

- Sites that are predominantly treated non surgically such as the Nasopharynx, do not have detailed pathological information available, and are therefore staged by cTNM.
- Sites that are predominantly treated surgically, such as the oral cavity, have detailed pathological information available, and therefore have both cTNM and pTNM staging systems available.
8th Edition

Published October 2016 – Implement January 2018
Major Changes in 8th Edition
Head and Neck Cancer

- Addition of pathologic features of primary tumors in T staging, e.g. Tumor thickness
- Addition of the extent of disease in nodal metastases in N staging, e.g. Extra nodal extension (ENE)
- Separate staging system for HPV + Oropharynx cancer, compared to conventional Oropharynx staging
Changes in TNM Staging 8th Edition

- Skin (SCC)
- Nasopharynx
- Oropharynx
- Oral Cavity
- Thyroid
T staging for Skin Cancer

• Tis  Carcinoma in situ
• T1  < 2 cms in diameter
• T2  2 - 4 cms in diameter
• T3  => 4 cms in diameter, or minor bone erosion or, perineural invasion or deep invasion > 6 mms.
• T4  Tumor with gross cortical bone / marrow, skull base invasion and or skull base foramen invasion
T staging for Nasopharynx Cancer

- **T0** No primary tumor but EBV + neck nodes
- **T1** Tumor confined to Nasopharynx or extends to oropharynx, nasal cavity without parapharyngeal space invasion
- **T2** Tumor with extension to parapharyngeal space and/or adjacent soft tissue involvement (Pterygoids, prevertebral musc)
- **T3** Tumor with infiltration of bony skull base, cervical vertebrae, pterygoid plates, or paranasal sinuses
- **T4** Tumor with intracranial extension, invasion of cranial nerves, hypopharynx, orbit, parotid, or extensive soft tissue disease lateral to lateral pterygoid muscle
N Staging for Nasopharynx Cancer

- **N0** No metastases
- **N1** Unilateral nodes < 6 cms above the lower border of cricoid or uni or bilateral retropharyngeal nodes
- **N2** Bilateral neck nodes < 6 cms above lower border of cricoid
- **N3** Unilateral or bilateral nodes > 6 cms or extension of nodes caudal to lower border of cricoid.
Oropharynx Cancer

Incidence of Overall, HPV + & HPV - Oropharyngeal Cancers

Chaturvedi A K et al
JCO 2011 29:4294 - 4301
HPV + (p 16 +) Oropharynx Cancer

- A distinct clinical entity
- Younger patients
- Healthier patients
- Non Smokers
- Very responsive to treatment
- Excellent outcomes with even advanced disease
- Natural history is unlike tobacco induced Oropharynx cancer
HPV + Oropharynx Cancer

T Staging

- T categories remain the same as HPV –ve tumors, except there is no Tis and T4b

N Staging

- N0  No regional lymph node metastasis
- N1  One or more ipsilateral lymph node < 6 cms.
- N2  Contralateral or bilateral nodes, all < 6 cms.
- N3  Any lymph node /s > 6 cms.
# Oropharynx Cancer – Stage Groupings

**HPV +ve**

<table>
<thead>
<tr>
<th>When T is...</th>
<th>And N is...</th>
<th>And M is...</th>
<th>Then the stage group is...</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0, T1 or T2</td>
<td>N0 or N1</td>
<td>M0</td>
<td>I</td>
</tr>
<tr>
<td>T0, T1 or T2</td>
<td>N2</td>
<td>M0</td>
<td>II</td>
</tr>
<tr>
<td>T3</td>
<td>N0, N1 or N2</td>
<td>M0</td>
<td>II</td>
</tr>
<tr>
<td>T0, T1, T2, T3 or T4</td>
<td>N3</td>
<td>M0</td>
<td>III</td>
</tr>
<tr>
<td>T4</td>
<td>N0, N1, N2 or N3</td>
<td>M0</td>
<td>III</td>
</tr>
</tbody>
</table>

**HPV -ve**

<table>
<thead>
<tr>
<th>When T is...</th>
<th>And N is...</th>
<th>And M is...</th>
<th>Then the stage group is...</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis</td>
<td>N0</td>
<td>M0</td>
<td>0</td>
</tr>
<tr>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>I</td>
</tr>
<tr>
<td>T2</td>
<td>N0</td>
<td>M0</td>
<td>II</td>
</tr>
<tr>
<td>T3</td>
<td>N0</td>
<td>M0</td>
<td>III</td>
</tr>
<tr>
<td>T1, T2, T3, T4a</td>
<td>N1</td>
<td>M0</td>
<td>III</td>
</tr>
<tr>
<td>T4a</td>
<td>N0,1</td>
<td>M0</td>
<td>IVA</td>
</tr>
<tr>
<td>T1, T2, T3, T4a</td>
<td>N2</td>
<td>M0</td>
<td>IVA</td>
</tr>
<tr>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
<td>IVB</td>
</tr>
<tr>
<td>T4b</td>
<td>Any N</td>
<td>M0</td>
<td>IVB</td>
</tr>
<tr>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
<td>IVC</td>
</tr>
</tbody>
</table>
Up until now only surface dimension of the tumor was required for T staging. “Maximum diameter”
## Depth of Invasion (DOI) in Oral Cancer

<table>
<thead>
<tr>
<th>Tumor Thickness</th>
<th>Risk of occult nodal metastasis</th>
<th>Overall incidence of nodal metastasis</th>
<th>% Patients died with disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 2 mm</td>
<td>7 %</td>
<td>13 %</td>
<td>3 %</td>
</tr>
<tr>
<td>2.1 – 8 mm</td>
<td>26 %</td>
<td>46 %</td>
<td>17 %</td>
</tr>
<tr>
<td>&gt; 8 mm</td>
<td>41 %</td>
<td>65 %</td>
<td>35%</td>
</tr>
</tbody>
</table>

**Mucosa**

**Sub-mucosa**

Oral Cancer – 8th Edition T staging

Depth of Invasion (DOI) is added to the primary tumor staging (T)
0 - 5, 5 – 10 and > 10 mms
Depth of Invasion in 5 mm increments

- **T1** = < 2 cm
- **T2** = 2-4 cm
- **T3** = > 4 cm

- **T1** = < 5 mm
- **T2** = 5-10 mm
- **T3** = > 10 mm
Estimate of Depth of Invasion - DOI

Clinicians are expected to palpate the lesion and estimate the DOI as:

- **Thin** - < 5 mms
- **Thick** - 5 - 10 mms
- **Very thick** - >10 mms
Depth of Invasion (DOI) for T staging of Primary Tumors of the Oral cavity

T1 - Tumor ≤ 2 cms, DOI ≤ 5 mm

T2 - Tumor > 2 cm but ≤ 4 cm, and DOI ≤ 10 mm or
    Tumor ≤ 2 cm, DOI > 5 mm ≤ 10 mm

T3 - Tumor > 4 cm or tumor of any size and
    DOI > 10 mm

T4 - T4a : Locally advanced tumor
    T4b : Very advanced tumor
T Stage Migration due to DOI

22.8% Upstaged

Worse DFS (51.1% vs 80.4%) and OS (31.5% vs 58.6%) in upstaged patients

DFS and OS were similar for pT1 and pT2, but were worse for pT3 according to the 8th edition staging.

External validation of the AJCC Cancer Staging Manual, 8th edition, in an independent cohort of oral cancer patients

Leandro Luongo Matos a,⇑, Rogerio Aparecido Dedivitis b, Marco Aurélia Vamondes Kulcsar c, Evandro Sobroza de Mello d, Venâncio Avancini F. Alves e, Claudio Roberto Cernea

Oral Oncology 71 (2017) 47–53
N Staging – 7th Edition

- **N₀**: No nodes
- **N₁**: Ipsilateral <3 cm
- **N₂a**: Ipsilateral >3 cm <6 cm
- **N₂b**: Ipsilateral multiple <6 cm
- **N₂c**: Bilateral/contralateral <6 cm
- **N₃**: >6 cm
N Staging – 8th Edition

Extra Nodal Extension (ENE) of metastatic disease, is now added for N Staging of Mucosal Squamous Cell Carcinomas of the Upper Aero Digestive Tract.
N Staging for Oral cavity, Pharynx, Larynx

- **N0**  No regional lymph node metastasis
- **N1**  Metastasis in a single ipsilateral node < 3 cm and ENE –
- **N2**  Metastasis in a single ipsilateral node 3-6 cm and ENE – or multiple ipsilateral nodes < 6 cm and ENE -
- **N2a** Metastasis in a single ipsilateral or contralateral node 3-6 cm and ENE –
- **N2b** Metastasis in multiple ipsilateral nodes <6cm and ENE –
- **N2c** Metastasis in contralateral or bilateral nodes <6 cm and ENE –
- **N3a** Metastasis in a single node >6cm and ENE –
- **N3b** Metastasis in a single ipsilateral, multiple ipsilateral, contralateral or bilateral nodes of any size and ENE +
N Staging – 8th Edition

- N0: No evidence of nodal disease
- N1: Metastasis to ipsilateral lymph nodes
- N2A: Metastasis to ipsilateral deep cervical lymph nodes
- N2B: Metastasis to bilateral deep cervical lymph nodes
- N2C: Metastasis to contralateral deep cervical lymph nodes
- N3A: Metastasis to ipsilateral supraclavicular lymph nodes
- N3B: Metastasis to bilateral supraclavicular lymph nodes

Legend:
- Red circle: < 3cms ENE-
- Dark brown circle: 3 - 6 cms ENE-
- Black circle: > 6 cms ENE-
- Light brown circle: Any size ENE+
N stage migration due to ENE

29.2% Upstaged

Worse DFS (17.1% vs 61.2%) and OS (8.5% vs 37.9%) in upstaged patients

DFS and OS for pN1, pN2, a,b,c, and pN3b.
Worse outcomes were seen in patients with pN3b

External validation of the AJCC Cancer Staging Manual, 8th edition, in an independent cohort of oral cancer patients
Leandro Luongo Matos a,⇑, Rogerio Aparecido Dedivitis b, Marco Aurélio Vamondes Kulcsar c, Evandro Sobroza de Mello d, Venâncio Avancini F. Alves e, Claudio Roberto Cernea
Oral Oncology 71 (2017) 47–53
Differentiated Thyroid Cancer
Thyroid Cancer Staging – 8th Edition
Changes

- Age
- T staging
- N Staging
Age Cut Off at 55 - Validation

An International Multi-Institutional Validation of Age 55 Years as a Cut off In the AJCC Staging System for Well Differentiated Thyroid Cancer
Disease Specific Survival

Age cut off at 45 years

- Stage I: 100%
- Stage II: 97%
- Stage III: 97%
- Stage IV: 80%

Age cut off at 55 years

- Stage I: 100%
- Stage II: 94%
- Stage III: 94%
- Stage IV: 72%
Age cut off – 8th Edition

• Age at diagnosis cut off used for staging is increased from 45 to 55 years
Thyroid Cancer - T Staging - 8th Edition

- Minor extrathyroid extension is removed from the definition of T3, and does not affect T category
- **T3a. New category.** Tumors > 4cm limited to Thyroid gland
- **T3b. New category.** Tumor of any size with gross ETE involving strap muscles
- **T4a. Gross ETE involving nx, trachea, esophagus, recurrent nerve & soft tissues**
- **T4b. Gross ETE encasing carotid artery, mediastinal vessels or prevertebral faslarycia**
Thyroid Cancer - N Staging - 8\textsuperscript{th} Edition

- pN0. One or more cytologically or histologically confirmed benign lymph nodes
- N1a. Metastases to level VI or VII lymph nodes. (Pre tracheal, para tracheal, prelaryngeal / Delphian or upper mediastinal)
- N1b. Metastases to unilateral, bilateral or contralateral lateral neck lymph nodes, (Levels I,II,III,IV or V) or retropharyngeal lymph nodes
Alluvial flow diagram representing the restaging of patient cohorts from the seventh to the eighth edition of the American Joint Commission on Cancer/Union for International Cancer Control (AJCC/UICC) tumor, node, metastasis (TNM) staging system in (A) the Surveillance, Epidemiology, and End Results (SEER) program and (B) the National Cancer Database (NCDB). Numbers represent the absolute number of patients within each stage, with flow line width proportional to the number of patients moving to a new stage classification.

Unadjusted disease-specific survival (DSS) curves for patients with papillary thyroid cancer (PTC) in the SEER program using the AJCC/UICC TNM staging (A) seventh and (B) eighth edition models.

Unadjusted overall survival (OS) curves for patients with PTC in the SEER database using (C) the seventh and (D) the eighth edition models.

Similarly, unadjusted OS curves for patients with PTC in the NCDB database using (E) the seventh and (F) the eighth edition models.

Future Directions

- Incorporation of T N M and other tumor parameters such as histological morphological features, molecular markers, non-anatomical prognostic factors, SES, lifestyle and comorbidities, as well as response to therapy, into dynamic personalized prognostic nomograms.
Patient A has a 3cm tumor (red line), clinically positive nodes (purple line), tongue disease (yellow line), and no bone invasion (green line). The total sum of points, 138 (blue line) indicates that patient A has a 32.5% probability of dying of disease by 5 years post surgery.
A. Tongue Cancer. T2N1, Stage III. Survival probability - 34%

60-year-old white male who was a 20 pack-year smoker. He has diabetes and coronary artery disease and a maximum tumor dimension of 3.5 centimeters. His tongue tumor does not invade deep muscle, but has positive margins, and also has vascular invasion, perineural invasion and positive level II lymph node.

Post-operative prognostic nomogram for patient A. The 5-year predicted overall survival is 10%.
30-year-old white female non-smoker. She has a 2.5 centimeter tongue cancer but is otherwise healthy. Her tumor does not invade deep muscle and has negative margins. She does not have vascular invasion or perineural invasion, but she has positive level I lymph node.

Post-operative prognostic nomogram for patient B. The 5-year predicted overall survival is 80%.
## TNM Staging vs Nomogram

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patient A</th>
<th>Patient B</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>60 years old</td>
<td>30 years old</td>
</tr>
<tr>
<td>Tobacco User</td>
<td>20 pack-year smoker</td>
<td>Non-smoker</td>
</tr>
<tr>
<td>WUHNCI</td>
<td>1 – DM-2 and CAD</td>
<td>No Comorbidities</td>
</tr>
<tr>
<td>Site</td>
<td>Lateral Tongue</td>
<td>Ventral Tongue</td>
</tr>
<tr>
<td>Deep Muscle invasion</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Margin</td>
<td>Positive</td>
<td>Negative</td>
</tr>
<tr>
<td>Vascular Invasion</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Perineural Invasion</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Lymph Node Status</td>
<td>Positive Level II LN</td>
<td>Positive Level I LN</td>
</tr>
<tr>
<td>TNM Stage</td>
<td>III</td>
<td>III</td>
</tr>
<tr>
<td>Staging (5-Year OS)</td>
<td>34.1%</td>
<td>34.1%</td>
</tr>
<tr>
<td>Nomogram (5-year OS)</td>
<td><strong>10%</strong></td>
<td><strong>80%</strong></td>
</tr>
</tbody>
</table>
Head and Neck Cancer Staging

It is a continuously evolving and dynamic process incorporating new and valid information to improve accuracy and predictive power.
Head and Neck Cancer Staging

Thank You
Intra Thyroidal Tumors (up to 4 cms)

Disease Specific Survival 100%
Recurrence Free Survival 98%
<table>
<thead>
<tr>
<th>Characteristics (n=884)</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;45y</td>
<td>421 (48%)</td>
</tr>
<tr>
<td>&gt;45y</td>
<td>463 (52%)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>185 (21%)</td>
</tr>
<tr>
<td>Female</td>
<td>699 (79%)</td>
</tr>
<tr>
<td><strong>pT Stage</strong></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>634 (72%)</td>
</tr>
<tr>
<td>T2</td>
<td>250 (28%)</td>
</tr>
<tr>
<td><strong>Pathology</strong></td>
<td></td>
</tr>
<tr>
<td>Papillary</td>
<td>798 (90%)</td>
</tr>
<tr>
<td>Follicular</td>
<td>50 (6%)</td>
</tr>
<tr>
<td>Hurthle Cell</td>
<td>36 (4%)</td>
</tr>
<tr>
<td><strong>Risk Group</strong></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>370 (42%)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>449 (51%)</td>
</tr>
<tr>
<td>High</td>
<td>65 (7%)</td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
</tr>
<tr>
<td>Lobectomy</td>
<td>362 (41%)</td>
</tr>
<tr>
<td>Total Thyroidectomy</td>
<td>522 (59%)</td>
</tr>
</tbody>
</table>

- 884 consecutive pts
- All Intrathyroidal tumors
- All N 0 patients
- All M 0 patients
- All Differentiated
## 10 Year Survival

### Intra Thyroidal Tumors

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Lobectomy</th>
<th>Total Thyroidectomy</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local Recurrence Free Survival</td>
<td>100%</td>
<td>100%</td>
<td>NS</td>
</tr>
<tr>
<td>Neck Recurrence Free Survival</td>
<td>99.7%</td>
<td>99.2%</td>
<td>NS</td>
</tr>
<tr>
<td>Distant Recurrence Free Survival</td>
<td>99.7%</td>
<td>99.4%</td>
<td>NS</td>
</tr>
<tr>
<td>Disease Specific Survival</td>
<td>100%</td>
<td>100%</td>
<td>NS</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>91%</td>
<td>94%</td>
<td>NS</td>
</tr>
</tbody>
</table>
Extent of Surgery for Papillary Thyroid Cancer Is Not Associated With Survival

An Analysis of 61,775 Patients (ACS, NCDB 1998 – 2006)

Over all Survival: Tumors 1-4 cms.
Extent of Surgery for Papillary Thyroid Cancer Is Not Associated With Survival

An Analysis of 61,775 Patients (ACS, NCDB 1998 – 2006)

Overall Survival: PTC Tumors: 1-2 cms and 2.1-4 cm.
Differentiated Cancer of the Thyroid

Role of Elective Node Dissection

- Elective node dissection not recommended in young and low risk patients
- Elective node dissection may be considered in older or high risk patients

Survival – p N Stage – Age < 45

\[ P = 0.8 \]

Survival – p N Stage – Age >

\[ P < 0.001 \]
Challenging Established Paradigms in the Management of Thyroid Cancer

Age 45 is an accurate cut off for Risk Groups

Age is a recognized prognostic risk factor

- EORTC
- AJCC (45)
- MSKCC (45y)
- AGES (40y)
- AMES (40/50y)
- MACIS
<table>
<thead>
<tr>
<th>Stages</th>
<th>Patient age &lt;45 years</th>
<th>Patient age 45 years or older</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>T3, N0, M0</td>
<td>T1, N1&lt;sub&gt;a&lt;/sub&gt;, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2, N1&lt;sub&gt;a&lt;/sub&gt;, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3, N1&lt;sub&gt;a&lt;/sub&gt;, M0</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>T4&lt;sub&gt;a&lt;/sub&gt;, N0, M0</td>
<td>T1, N1&lt;sub&gt;b&lt;/sub&gt;, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T2, N1&lt;sub&gt;b&lt;/sub&gt;, M0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T3, N1&lt;sub&gt;b&lt;/sub&gt;, N0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>T4&lt;sub&gt;a&lt;/sub&gt;, N1&lt;sub&gt;b&lt;/sub&gt;, M0</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>T4&lt;sub&gt;b&lt;/sub&gt;, Any N, M0</td>
<td>Any T, Any N, M1</td>
</tr>
<tr>
<td>Stage IVC</td>
<td>Any T, Any N, M1</td>
<td>Any T, Any N, M1</td>
</tr>
</tbody>
</table>
Age Cut Off at 55 - Validation

Current Concepts in Head and Neck Surgery and Oncology 2017

An International Multi-Institutional Validation of Age 55 Years as a Cut off In the AJCC Staging System for Well Differentiated Thyroid Cancer
Disease Specific Survival

Age 45 years cut off

Stag I 10y DSS
I  100%
II 97%
III 97%
IV 80%

Age 55 years cut off

Stag I 10y DSS
I  100%
II 94%
III 94%
IV 72%
Impact of Age cut off at 55

- A change in age cut off affects 13% of patients
  - >8000 annually in the USA
- Results in wider distribution of outcomes
  - I-IV 45 – 100 → 81%
  - I-IV 55 – 100 → 72%

AJCC / UICC will adapt 55 year age cut off in the 7th Edition of Staging manual, starting 2017
Challenging Established Paradigms in the Management of Thyroid Cancer

Staging of T1a and T1b tumors is valid

AJCC TNM classification for differentiated thyroid cancer (DTC) subdivides T1 into

- T1a ($\leq 1\text{cm}$)
- T1b (1-2cm)

- The ATA guidelines recommend
  - Total Thyroidectomy for all tumors $>1\text{cm}$
  - Possibility of Lobectomy for tumors $\leq 1\text{cm}$
Do AJCC T1b tumors have poorer
1. overall survival
2. disease specific survival
3. recurrence free survival
compared to T1a tumors?
Comparison Study between T1a and T1b

3664 patients
MSKCC
1986-2010

Inclusion
(pT1pN0/XM0)
n = 1522

Exclusion
n = 2142
Tumor size >2cm
ETE
pN1 nodal disease
M1 disease

T1a
(≤1cm)
n = 899

T1b
(1-2cm)
n = 623
## Patient and Treatment Characteristics

### Comparison of T1a and T1b patient, tumor and treatment variables

<table>
<thead>
<tr>
<th></th>
<th>T1a</th>
<th></th>
<th>T1b</th>
<th></th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>&lt;45 yrs</td>
<td>335</td>
<td>37.3</td>
<td>293</td>
<td>47.0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥45 yrs</td>
<td>564</td>
<td>62.7</td>
<td>330</td>
<td>53.0</td>
<td></td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>726</td>
<td>80.8</td>
<td>491</td>
<td>78.8</td>
<td>0.351</td>
</tr>
<tr>
<td>Male</td>
<td>173</td>
<td>19.2</td>
<td>132</td>
<td>21.2</td>
<td></td>
</tr>
<tr>
<td><strong>Previous RT exposure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>843</td>
<td>93.8</td>
<td>598</td>
<td>96.0</td>
<td>0.058</td>
</tr>
<tr>
<td>Yes</td>
<td>56</td>
<td>6.2</td>
<td>25</td>
<td>4.0</td>
<td></td>
</tr>
<tr>
<td><strong>Thyroid Surgery</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; total thyroid</td>
<td>236</td>
<td>27.1</td>
<td>182</td>
<td>29.5</td>
<td>0.307</td>
</tr>
<tr>
<td>Total thyroid</td>
<td>634</td>
<td>72.9</td>
<td>434</td>
<td>70.5</td>
<td></td>
</tr>
<tr>
<td><strong>RAI therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No RAI</td>
<td>845</td>
<td>94.0</td>
<td>472</td>
<td>75.8</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
T1a and T1b - Outcomes

Disease specific Deaths, “0” in both groups

Over all Survival

Recurrence free Survival

2015 ATA Guidelines now accept Lobectomy for intrathyroidal tumors up to 4 cms
Challenging Established Paradigms in the Management of Thyroid Cancer

All patients with Differentiated Carcinoma need Total Thyroidectomy

Not necessarily.....

The complications following Total Thyroidectomy, and the quality of life after Total Thyroidectomy are issues that must be factored in the decision regarding “Unindicated Total Thyroidectomy practice”
# Lobectomy vs Total Thyroidectomy

<table>
<thead>
<tr>
<th>Characteristics (n=884)</th>
<th>Number (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td></td>
</tr>
<tr>
<td>&lt;45y</td>
<td>421 (48%)</td>
</tr>
<tr>
<td>&gt;45y</td>
<td>463 (52%)</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>185 (21%)</td>
</tr>
<tr>
<td>Female</td>
<td>699 (79%)</td>
</tr>
<tr>
<td><strong>pT Stage</strong></td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>634 (72%)</td>
</tr>
<tr>
<td>T2</td>
<td>250 (28%)</td>
</tr>
<tr>
<td><strong>Pathology</strong></td>
<td></td>
</tr>
<tr>
<td>Papillary</td>
<td>798 (90%)</td>
</tr>
<tr>
<td>Follicular</td>
<td>50 (6%)</td>
</tr>
<tr>
<td>Hurthle Cell</td>
<td>36 (4%)</td>
</tr>
<tr>
<td><strong>Risk Group</strong></td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>370 (42%)</td>
</tr>
<tr>
<td>Intermediate</td>
<td>449 (51%)</td>
</tr>
<tr>
<td>High</td>
<td>65 (7%)</td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td></td>
</tr>
<tr>
<td>Lobectomy</td>
<td>362 (41%)</td>
</tr>
<tr>
<td>Total Thyroidectomy</td>
<td>522 (59%)</td>
</tr>
</tbody>
</table>

- 884 consecutive pts
- All Intrathyroidal tumors
- All N 0 patients
- All M 0 patients
- All Differentiated
## Lobectomy vs Total Thyroidectomy

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Lobectomy</th>
<th>Total Thyroidectomy</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local Recurrence Free Survival</td>
<td>100%</td>
<td>100%</td>
<td>NS</td>
</tr>
<tr>
<td>Neck Recurrence Free Survival</td>
<td>99.7%</td>
<td>99.2%</td>
<td>NS</td>
</tr>
<tr>
<td>Distant Recurrence Free Survival</td>
<td>99.7%</td>
<td>99.4%</td>
<td>NS</td>
</tr>
<tr>
<td>Disease Specific Survival</td>
<td>100%</td>
<td>100%</td>
<td>NS</td>
</tr>
<tr>
<td>Overall Survival</td>
<td>91%</td>
<td>94%</td>
<td>NS</td>
</tr>
</tbody>
</table>
Larynx Cancer Staging – 5\textsuperscript{th} Edition

The International Federation of Head and Neck Oncologic Societies

Current Concepts in Head and Neck Surgery and Oncology 2017

- Supraglottis
- Glottis
- Subglottis
- T1 – T4
<table>
<thead>
<tr>
<th>T</th>
<th>5th Ed</th>
<th>6th Ed</th>
<th>7th Ed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tumor limited to one subsite of supraglottis with normal vocal cord mobility</td>
<td>Tumor limited to one subsite of supraglottis with normal vocal cord mobility</td>
<td>Tumor limited to one subsite of supraglottis with normal vocal cord mobility</td>
</tr>
<tr>
<td>2</td>
<td>Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside of the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx</td>
<td>Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside of the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx</td>
<td>Tumor invades mucosa of more than one adjacent subsite of supraglottis or glottis or region outside of the supraglottis (e.g., mucosa of base of tongue, vallecula, medial wall of pyriform sinus) without fixation of the larynx</td>
</tr>
<tr>
<td>3</td>
<td>Tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic tissues</td>
<td>Tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic tissues, paraglottic space, and/or minor thyroid cartilage erosion (e.g., inner cortex)</td>
<td>Tumor limited to larynx with vocal cord fixation and/or invades any of the following: postcricoid area, pre-epiglottic space, paraglottic space, and/or inner cortex of thyroid cartilage</td>
</tr>
<tr>
<td>4</td>
<td>Tumor invades through the thyroid cartilage, and/or extends into soft tissues of the neck</td>
<td><strong>T4a</strong> Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, etc.)</td>
<td><strong>T4a</strong> Moderately advanced local disease Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, etc.)</td>
</tr>
</tbody>
</table>
Supraglottis

The International Federation of Head and Neck Oncologic Societies

Current Concepts in Head and Neck Surgery and Oncology 2017

Changes from 5th

Addition of invasion of paraglottic space and minor cartilage invasion to T3

Division of T4 to T4a and T4b (Resectable & Unresectable)

Change of terminology for T4a and T4b to (Moderately advanced and Very advanced)
<table>
<thead>
<tr>
<th>T</th>
<th>5th Ed</th>
<th>6th Ed</th>
<th>7th Ed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tumor limited to vocal cord(s) (may involve anterior or posterior commissure) with normal mobility</td>
<td>Tumor limited to vocal cord(s) (may involve anterior or posterior commissure) with normal mobility</td>
<td>Tumor limited to vocal cord(s) (may involve anterior or posterior commissure) with normal mobility</td>
</tr>
<tr>
<td></td>
<td><strong>T1a</strong> Tumor limited to one vocal cord</td>
<td><strong>T1a</strong> Tumor limited to one vocal cord</td>
<td><strong>T1a</strong> Tumor limited to one vocal cord</td>
</tr>
<tr>
<td></td>
<td><strong>T1b</strong> Tumor involves both vocal cords</td>
<td><strong>T1b</strong> Tumor involves both vocal cords</td>
<td><strong>T1b</strong> Tumor involves both vocal cords</td>
</tr>
<tr>
<td>2</td>
<td>Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility</td>
<td>Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility</td>
<td>Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility</td>
</tr>
<tr>
<td>3</td>
<td>Tumor limited to the larynx with vocal cord fixation</td>
<td>Tumor limited to the larynx with vocal cord fixation and/or invades paraglottic space, and/or minor thyroid cartilage erosion (e.g., inner cortex)</td>
<td>Tumor limited to larynx with vocal cord fixation and/or invasion of paraglottic space, and/or inner cortex of thyroid cartilage</td>
</tr>
<tr>
<td>4</td>
<td>Tumor invades through the thyroid cartilage and/or to other tissues beyond the larynx (e.g., trachea, soft tissues of neck, extrinsic muscles of tongue and/or thyroid, or esophagus)</td>
<td><strong>T4a</strong> Tumor invades through the thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscle of the tongue, strap muscles, thyroid, or esophagus)</td>
<td><strong>T4a</strong> Moderately advanced local disease</td>
</tr>
<tr>
<td></td>
<td>Tumor invades prevertebral space, and/or outer cortex of thyroid cartilage</td>
<td>Tumor invades prevertebral space, and/or outer cortex of thyroid cartilage</td>
<td>Tumor invades prevertebral space, and/or outer cortex of thyroid cartilage</td>
</tr>
</tbody>
</table>
The International Federation of Head and Neck Oncologic Societies

Current Concepts in Head and Neck Surgery and Oncology 2017

Gottis

Changes from 5th to 6th to 7th to 8th Edition

- Addition of invasion of paraglottic space and minor cartilage invasion to T3
- Division of T4 to T4a and T4b (Resectable & Unresectable)
- Change of terminology for T4a and T4b to (Moderately advanced and Very advanced)
<table>
<thead>
<tr>
<th>T</th>
<th>5&lt;sup&gt;th&lt;/sup&gt; Ed</th>
<th>6&lt;sup&gt;th&lt;/sup&gt; Ed</th>
<th>7&lt;sup&gt;th&lt;/sup&gt; Ed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Tumor limited to subglottis</td>
<td>Tumor limited to subglottis</td>
<td>Tumor limited to subglottis</td>
</tr>
<tr>
<td>2</td>
<td>Tumor extends to vocal cord(s) with normal or impaired mobility</td>
<td>Tumor extends to vocal cord(s) with normal or impaired mobility</td>
<td>Tumor extends to vocal cord(s) with normal or impaired mobility</td>
</tr>
<tr>
<td>3</td>
<td>Tumor limited to larynx with vocal cord fixation</td>
<td>Tumor limited to larynx with vocal cord fixation</td>
<td>Tumor limited to larynx with vocal cord fixation</td>
</tr>
<tr>
<td>4</td>
<td>Tumor invades through cricoid or thyroid cartilage and/or extends to other tissues beyond the larynx (e.g., trachea, soft tissues of neck, including thyroid, esophagus)</td>
<td><strong>T4a</strong> Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid or esophagus)</td>
<td><strong>T4a</strong> Moderately advanced local disease Tumor invades cricoid or thyroid cartilage and/or invades tissues beyond the larynx (e.g., trachea, soft tissues of neck including deep extrinsic muscles of the tongue, strap muscles, thyroid or esophagus)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>T4b</strong> Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures.</td>
<td><strong>T4b</strong> Very advanced local disease Tumor invades prevertebral space, encases carotid artery, or invades mediastinal structures.</td>
</tr>
</tbody>
</table>
Subglottis

The International Federation of Head and Neck Oncologic Societies

Current Concepts in Head and Neck Surgery and Oncology 2017

Changes from 5th

- (Resectable & Unresectable)
- Change of terminology for T4a and T4b to
  (Moderately advanced and Very advanced)
<table>
<thead>
<tr>
<th>Stage</th>
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<tr>
<td>1</td>
<td>T1N0M0</td>
<td>T1N0M0</td>
<td>T1N0M0</td>
</tr>
<tr>
<td>2</td>
<td>T2N0M0</td>
<td>T2N0M0</td>
<td>T2N0M0</td>
</tr>
<tr>
<td>3</td>
<td>T3N0, T1,2,3, N1</td>
<td>T3N0, T1,2,3, N1</td>
<td>T3N0, T1,2,3, N1</td>
</tr>
<tr>
<td>4</td>
<td>IV A-T4N0,N1, Any TN2</td>
<td>IV A-T4a, N0,N1,N2 T1,2,3, N2</td>
<td>IV A-T4a, N0,N1, T1,2,3,4aN2</td>
</tr>
<tr>
<td></td>
<td>IV B- Any T N3</td>
<td>IV B- T4bAnyN,AnyTN3</td>
<td>IV B- BT4bAnyN,AnyTN3</td>
</tr>
<tr>
<td></td>
<td>IV C – Any T, Any N,M1</td>
<td>IV C – Any T, Any N,M1</td>
<td>IV C – Any T, Any N,M1</td>
</tr>
</tbody>
</table>
No major changes planned for T staging

Nodal staging will incorporate ENE in N staging

Non Anatomic factors will be recorded, such as: Socio economic status, BMI, P53, Comorbidity, Tobacco, alcohol abuse, EGFR, Immune status, etc.
Changes in Stage Groupings

The International Federation of Head and Neck Oncologic Societies

Current Concepts in Head and Neck Surgery and Oncology 2017

- No change for Stage 1, 2 and 3

- Stage 4, divided into three groups
  - 4a – Moderately advanced Locoregional Disease
  - 4b – Very advanced Locoregional Disease
  - 4c – Distant Metastatic Disease
## Differentiated Thyroid Cancer

### Prognostic Factors

<table>
<thead>
<tr>
<th>Mayo</th>
<th>Lahey</th>
<th>Mayo</th>
<th>Karolinska</th>
<th>MSKCC</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGES</td>
<td>AMES</td>
<td>MACIS</td>
<td>DAMES</td>
<td>GAMES</td>
</tr>
<tr>
<td>Age</td>
<td>Age</td>
<td>Metastases</td>
<td>DNA</td>
<td>Grade</td>
</tr>
<tr>
<td>Grade</td>
<td>Metastases</td>
<td>Age</td>
<td>Age</td>
<td>Age</td>
</tr>
<tr>
<td>Extension</td>
<td>Extension</td>
<td>Completeness Of resection</td>
<td>Metastases</td>
<td>Metastases</td>
</tr>
<tr>
<td>Size</td>
<td>Size</td>
<td>Invasion</td>
<td>Size</td>
<td>Size</td>
</tr>
</tbody>
</table>

### Risk Group Stratification
Differentiated Cancer of the Thyroid

Prognostic Factors
- Age
- Gender
- Size
- Extent
- Grade
- Dist. Mets.

Risk Groups (GAMES)
- Low
  - Age: <45
  - Gender: Female
  - Size: < 4 cms.
  - Extent: Intraglandular
  - Grade: Low
  - Dist. Mets.: Absent
- Intermediate
  - Age: >45
  - Gender: Female
  - Size: < 4 cms.
  - Extent: Intraglandular
  - Grade: Low
  - Dist. Mets.: Absent
- High
  - Age: >45
  - Gender: Male
  - Size: > 4 cms.
  - Extent: Extraglandular
  - Grade: High
  - Dist. Mets.: Present
Differentiated Thyroid Cancer

Risk Group Stratification

- Risk Group Stratification is the most important clinical parameter for selection of the extent of initial surgery, the need for adjuvant therapy, the degree of rigorous follow up, and for the assessment of overall prognosis, for local, regional, or distant failure and Survival.