OVERVIEW AND PRINCIPLES FOR CONTEMPORARY AJCC TNM STAGING

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EDITOR IN CHIEF, EIGHT EDITION AJCC TNM STAGING MANUAL

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Historical Perspective

• Staging based on the TNM concept was first championed by Dr. Pierre Denoix a surgical oncologist from Institut Gustave-Roussy, Paris (1943-52)

**Historical Perspective**

• Early efforts – Radiology community.
  - *International Commission on Stage Grouping and Presentation of Results (ICPR) of the International Congress of Radiology (1953)*

• International Union against Cancer (UICC) adopts TNM staging (1954)

**Historical Perspective**

• North American effort first organized as the American Joint Committee for Cancer Staging and End Results Reporting (AJC) (1959)
  • *American College of Surgeons, American College of Radiology, College of American Pathologists, College of Physicians, American Cancer Society & the National Cancer Institute*

  • AJC (1970) – adopted “objectives, rules & regulations of the AJC” – resulted in formulation and publication of systems of classification of cancer

  • First Edition of AJC staging manual published just 40 years ago, in 1977
Manual for Staging of Cancer (1977), American Joint Committee for Cancer Staging & End Result Reporting, 1st Edition

"Philosophy of staging by the TNM system":

• "It is intended to provide a way by which designation for the state of a cancer at various points in time can be readily communicated to others to assist in decisions regarding treatment and to be a factor in judgment as to prognosis. Ultimately, it provides a mechanism for comparing like or unlike groups of cases, particularly in regard to the results of different therapeutic procedures."

Historical Perspective

• 2nd Edition, 1983 – Additional sites added. It was conceded that “several recommendations are preliminary”. Agreement for consistency with TNM UICC staging system

• 1990’s – importance heightened by the mandatory requirement by Commission on Cancer – approved hospital use of AJCC-TNM system as the major language of cancer reporting – stimulated education of physicians & registrars with widespread use

• 6th Edition, 2002 – judicious, but minimal transition to include non anatomic factors that modified stage groups, e.g. serum markers in testis tumors


• Expansion of “relevant markers to make clear treatment decisions”
  • Mitotic rate in GI stromal tumors
  • PSA & Gleason Score in Prostate Cancer


Widely used by
• Clinicians
• Surveillance community & tumor registrars
• Researchers
• Patient advocates
• Patients

Roles:
• Communication
• Standardized nomenclature of cancer
• Clinical practice
  • Prognosis
  • Treatment recommendations
• Clinical trials
• Eligibility
• Stratification
• Research at all levels
• Reporting – population science
  • Longitudinal cancer instance
  • Changing spectrum of disease
  • Efficacy of treatment
  • Quality of care

Persistent Challenges to TNM Staging

• TNM largely limited to anatomic information
  – Lacks biologic data and impact of response
  – Creates ‘bins’ of like patients

• TNM does not meet needs of clinicians and patients
  – Individualized prognosis
  – Predict value of therapy
  – TNM risks marginalization

• TNM must maintain anatomic base
  – Population incidence and impact
  – Longitudinal changes
  – World wide use
AJCC Cancer Staging Manual Editions

<table>
<thead>
<tr>
<th>Edition</th>
<th>Publication</th>
<th>Effective dates for cancer diagnoses</th>
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</thead>
<tbody>
<tr>
<td>1st</td>
<td>1977</td>
<td>1978 – 1983 (6 years)</td>
</tr>
<tr>
<td>2nd</td>
<td>1983</td>
<td>1984 – 1988 (5 years)</td>
</tr>
<tr>
<td>4th</td>
<td>1992</td>
<td>1993 – 1997 (5 years)</td>
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<td>5th</td>
<td>1997</td>
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</tr>
<tr>
<td>6th</td>
<td>2002</td>
<td>2003 – 2009 (7 years)</td>
</tr>
<tr>
<td>7th</td>
<td>2009</td>
<td>2010 – 2016 (7 years)</td>
</tr>
<tr>
<td>8th</td>
<td>2016</td>
<td>2018 -</td>
</tr>
</tbody>
</table>

Average 5.6 years

Nomenclature

Classification
- A lower case prefix describes the time point in a patient's cancer continuum when stage is assigned, including:
  - c: clinical
  - p: pathological
  - yc/yp: post neoadjuvant (radiation or systemic) therapy – clinically/pathologically
  - a: autopsy

Category
- T, N, and M-specific data are used to assign a cancer site-specific T, N, and M category for a patient at a given classification

Subcategory
- Some diseases will have subcategories designed to facilitate reporting of more detailed information and often more specific prognostic information. Examples:
  - Breast cancer: T1a, T1b, T1c
  - Breast cancer: N2a, N2b
  - Prostate cancer: M1a, M1b, M1c

AJCC Prognostic Stage Groups (Stage Groups)
- Prognostic stage groups are assigned based on disease site-specific T, N, and M categories and relevant prognostic factors to group patients with similar prognosis and/or treatment approach.

Color Coding

<table>
<thead>
<tr>
<th>T Category</th>
<th>T Classification</th>
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<tbody>
<tr>
<td>T0</td>
<td>Primary tumor cannot be assessed</td>
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<tr>
<td>T1</td>
<td>Any primary tumor</td>
</tr>
<tr>
<td>T2</td>
<td>Any primary tumor with sentinel lymph node involvement</td>
</tr>
<tr>
<td>T3</td>
<td>Any primary tumor with regional lymph node involvement</td>
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<tr>
<td>T4</td>
<td>Any primary tumor with distant metastases</td>
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</table>

<table>
<thead>
<tr>
<th>N Category</th>
<th>N Classification</th>
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<tbody>
<tr>
<td>N0</td>
<td>No regional lymph node involvement</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node involvement</td>
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<tr>
<td>N2</td>
<td>Regional lymph node involvement with distant metastases</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>M Category</th>
<th>M Classification</th>
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<tbody>
<tr>
<td>M0</td>
<td>No distant metastases</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastases present</td>
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</table>

Evidence Based Approach

- Levels of evidence defined by EBM & Statistics core for key information ensure transparency
- Changes to stage definitions based on data - no changes to stage definition based on level 4 evidence

Overview of 8E Changes

- Revised Organizational Structure
- 13 New Chapters; new Staging Systems
- Updated Content
- New Paradigms
- New Features
- Split Chapters
- Merged Chapters
- Online Content
- Chapter on “General Staging Rules”
- Imaging section in all chapters
- Risk Assessment Model Chapter

8th Edition – What’s New?

MISSION AND VISION: TO BUILD A BRIDGE FROM A POPULATION BASED TO A MORE PERSONALIZED APPROACH

- Formally incorporate molecular biomarkers for accurate disease stratification and “personalize” staging of cancer while retaining anatomic stage paradigm through the Precision Medicine Core
Direction of Cancer Staging

- Cancer Stage
- Comprehensive Cancer Profile
  - Definitions of TNM
  - Prognostic Factors
  - Population-based
  - Personalized level

Prognostic Factors

- **Prognostic Factors Required for Staging** – included in stage groupings
- **Prognostic Factors Recommended for Clinical Care**
  - The 8th Edition distinctly identifies those factors that will be required for collection by standard setters
- **Other Factors for Clinical Care**
  - Web only

Risk Assessment Models

- Precision Medicine Core developed endorsement criteria for risk assessment modules in face-to-face meeting (Jan 23, 2015)
  - published in CA J Clin
- Members reviewed the literature for models - colon, lung, breast, prostate, melanoma, H&N, soft tissue
- Review additional models from other diseases in an ongoing manner and information will be posted on the website

New Paradigms

- Human papillomavirus (HPV): oropharyngeal carcinoma staging systems based on HPV status
- Separate staging systems for patients with neoadjuvant therapy (esophagus and stomach)
- Bone and soft tissue sarcoma (separate staging systems based on anatomic sites)
- Introduction of H category (TNMH) for heritable cancer trait in AJCC prognostic stage grouping of retinoblastoma
- Based on non-anatomic factors organ confined disease may be Stage III in Prognostic Stage Groups (e.g. prostate)
The 8th Edition

AJCC Cancer Staging Manual

Implementation of 8th Edition

• Cancer Staging Manual released October 1, 2016
• 8th Edition effective with cases diagnosed January 1, 2018
• One year to assimilate content into key stakeholder users: NCCN, CAP, Registrar community, EHR and LIS vendors

TAKE HOME MESSAGES – CURRENT STATUS

• Cancer Staging is becoming increasingly rigorous, evidence based, and moving from a "population-based" to a more "individualized" approach
• AJCC is transitioning to more comprehensive cancer profiling with inclusion of prognostic and predictive markers and risk assessment profiles
• ISUP consensus conferences have made important contributions to 8E Genitourinary chapters

Supplementary Online Resources:
• Risk Assessment Models
• Emerging Factors for Clinical Care
• Recommendations for Clinical Trial Stratification
• Illustrations
• References
TAKE HOME MESSAGES: FUTURE

• Refining cancer staging is a never ending process. AJCC plans to be more nimble and future staging revisions are likely to be more iterative, real time and web based.

• Staging is increasingly becoming a multidisciplinary team exercise. Although staging efforts were lead by surgical oncology (1940s) and radiology (1950s); surgical and molecular pathology and medical oncology have become, and will be key drivers of future refinements of staging in the team approach to cancer and precision medicine era… the work continues.

What's Changing Since the Last Edition - The Evolving Landscape (2008 - 2013 .....)

• Advances in molecular underpinnings of cancer - TCGA etc. - oncogenesis, progression, resistance – molecular classification of cancer
• Increasing availability of high throughput testing, mutational analysis (sequencing), microarrays (RNA, mi RNAs, SNPs, etc)
• Advances in informatics & computational biology; increased adoption of EHRs, data interoperability, real time risk calculating strategy apps (nomograms, tables, etc)
• Cancer care is increasingly coordinated through well defined clinical multidisciplinary teams
• Meaningful data is gradually becoming available on prognostic and predictive factors that may allow evidence-based decision making
• Surgical, medical (targeted) and radiation oncology therapies that continue to become more sophisticated, as are diagnostic modalities (imaging and pathology)
• Globalization of cancer – universal applicability of treatment & molecular advances


• Expanded Multidisciplinary Editorial Board: 6 members in 7E vs. 19 members in 8E
• Proactively created balanced Multidisciplinary Expert Panels
  – Surgical Oncologists
  – Medical Oncologists
  – Radiation Oncologists
  – Radiologists
  – Pathologists – Anatomic And Molecular
  – UICC TNM Committee Representative
  – CAP Cancer Committee Representative