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

- 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”
Subsequent Staging Manuals

- June 1980, the new name American Joint Committee on Cancer – AJCC – was selected and the decision for uniformity with identical definitions with the UICC was adopted
- 2nd Edition, 1983 – Additional sites added, conceded that “several recommendations are preliminary”, 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 transition of non anatomic factors that modified stage groups


- Roles:
  - Communication
    - Standardized nomenclature of cancer (doctor to patient, doctor to doctor)
  - Clinical practice
    - Staging & 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

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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 always meet needs of clinicians and patients – is it still relevant
  - Individualized prognosis
  - Predict value of therapy
  - TNM risks marginalization

- Should TNM maintain anatomic base
  - Population incidence and impact
  - Longitudinal changes
  - World wide use

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
- Maturing 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
AJCC Cancer Staging Manual Editions

<table>
<thead>
<tr>
<th>Edition</th>
<th>Publication</th>
<th>Effective dates for cancer diagnoses</th>
</tr>
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<tbody>
<tr>
<td>1\textsuperscript{st}</td>
<td>1977</td>
<td>1978 – 1983 (6 years)</td>
</tr>
<tr>
<td>2\textsuperscript{nd}</td>
<td>1983</td>
<td>1984 – 1988 (5 years)</td>
</tr>
<tr>
<td>3\textsuperscript{rd}</td>
<td>1988</td>
<td>1989 – 1992 (4 years)</td>
</tr>
<tr>
<td>4\textsuperscript{th}</td>
<td>1992</td>
<td>1993 – 1997 (5 years)</td>
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<tr>
<td>5\textsuperscript{th}</td>
<td>1997</td>
<td>1998 – 2002 (5 years)</td>
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<tr>
<td>6\textsuperscript{th}</td>
<td>2002</td>
<td>2003 – 2009 (7 years)</td>
</tr>
<tr>
<td>7\textsuperscript{th}</td>
<td>2009</td>
<td>2010 – 2017 (8 years)</td>
</tr>
</tbody>
</table>

The 8\textsuperscript{th} Edition

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The 8th Edition

Online Content: Set for Rolling Updates

- Staging forms
- Supplementary Online Resources:
  - Application Programming Interface (API) for software and app developers
- Risk Assessment Models
- Emerging Factors for Clinical Care
- Recommendations for Clinical Trial Stratification
- Illustrations
- References
- www.cancerstaging.org

AJCC Cancer Staging Manual Editions

- 3-Year Project
- 57 Chapters
- 16 Task Forces
- 266 individuals from
  - 5 continents
  - 11 countries

- 3-Year Project
- 83 Chapters
- 18 Expert Panels + 7 Cores
- 434 individuals from
  - 6 continents
  - 23 countries
  - 188 institutions

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## Release of 8th Edition

- Cancer Staging Manual released on October 6th, 2016
- 8th Edition effective with cases diagnosed January 1, 2018
- Print copies can be ordered through Springer.com

## Updates

- Updated staging systems in several chapters
- Updated content in each chapter
- Updated and more illustrations (manual and atlas in one)
- Updated histologic classifications and grading systems
- Updated WHO/IARC histology codes
Assigning Stage: The Role of the Managing Physician

• Staging requires the collaborative effort of many professionals, including the managing physician, pathologist, radiologist, cancer registrar and others

• While the pathologist and the radiologist provide important staging information, and may provide important T-, N-, and/or M-related information, stage is defined ultimately from the synthesis of an array of patient history and physical examination findings supplemented by imaging and pathology data

• Only the managing physician can assign the patient’s stage, since only (s) he routinely has access to all of the pertinent information from the physical exam, imaging studies, biopsies, diagnostic procedures, surgical findings, and pathology reports

New Feature: 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

• Data sources for stage definition changes and 8E content
  – NCDB
  – SEER
  – Multi-institutional databases
  – International databases (Lung, Melanoma, Esophagus…)
  – Publications
New Feature: Imaging Core & Section in each chapter

- Consistent and broad overview of applications of imaging in staging in each chapter
- Provides guidance to physicians when ordering tests
- Several imaging section chapters describe
  - what imaging tests are most appropriate for assessing tumor stage information
  - the temporal order in which the appropriate imaging tests are typically performed
  - the specific T, N, and M information that can be extracted from imaging tests for the cancer
- Several chapters - information for radiologists on reporting results
  - Structured reporting is promoted
  - Links or references to disease- or specialty-specific society guidelines

New Features: Precision Medicine Vision

- Prognostic factors
  - Required for prognostic stage grouping
  - Recommended for clinical care
  - Emerging factors (online only)

- Risk Assessment Models for select cancer sites

- Recommendations for Clinical Trial Stratification
Color Coding

<table>
<thead>
<tr>
<th>T Category</th>
<th>T Criteria</th>
<th>G</th>
<th>G Definition</th>
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<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
<td>GX</td>
<td>Grade cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
<td>G1</td>
<td>Well differentiated</td>
</tr>
<tr>
<td>Tis</td>
<td>High-grade dysplasia/carcinoma in situ</td>
<td>G2</td>
<td>Moderately differentiated</td>
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<tr>
<td>T1</td>
<td>Tumor invades the lamina propria</td>
<td>G3</td>
<td>Poorly differentiated</td>
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<tr>
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<td>Tumor invades the lamina propria</td>
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</tr>
<tr>
<td>T1b</td>
<td>Tumor invades the submucosa</td>
<td></td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>Tumor invades the muscularis propria</td>
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<td></td>
</tr>
<tr>
<td>T3</td>
<td>Tumor invades through the muscularis propria into the submucosa, or extends into nonperitoneal perimucosal tissue (mesentery or retroperitoneum) without serosal penetration*</td>
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<table>
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<th>N Criteria</th>
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<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Metastasis in one or two regional lymph nodes</td>
</tr>
<tr>
<td>N2</td>
<td>Metastasis in three or more regional lymph nodes</td>
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</table>

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

AJCC & FIGO

- First rules of female genital tract cancer staging was published in 1929 by the League of Nations.
- This rules evolved into the staging system developed and regularly updated by FIGO.
- In 1976, AJCC accepted the FIGO stage grouping for gynecologic cancers.
- Gynecologic cancer staging in all editions of the AJCC staging manual have been closely aligned with FIGO staging.

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FIGO Staging publication timelines

• **1988**: FIGO staging for all gynecologic cancers updated

• **2009**: FIGO staging for carcinoma of the vulva, cervix and endometrium.

• **2009**: FIGO staging for uterine sarcoma.

• **2014**: FIGO’s staging classification for cancer of the ovary, fallopian tube, and peritoneum: abridged republication.


Updates in Gynecologic Cancers: pN0(i+)

• Metastatic cancer to lymph node(s) fall into one of 3 categories based on the size of metastasis;
  – (1) Individual Tumor Cells (ITC) -- <0.2mm
  – (2) Micrometastasis – 0.2mm – 2mm
  – (3) Macrometastasis -- > 2mm

• ITC & Micrometastasis are jointly referred to as low volume metastasis (LVM).

• Micro & macrometastasis are both classified as N1

• The 8th Edition encourages documentation of pN0(i+), which will not currently change the stage grouping or FIGO stage but will be a helpful data to analyze in future.
Updates in Gynecologic Cancers: Vulva

- Melanoma has been removed from this chapter
- Melanoma should be staged according to the classification of skin melanoma (chapter 47) (I)
- Classification of p16 status should be collected if obtained (III)
- Full length of histologic subtypes according to the WHO classification of tumors is included
- A chapter on imaging is embedded with suggestions on how to document image findings

Updates in Gynecologic Cancers: Vulva

- Illustrations of the T, N and M categories are included therefore an owner of the 8th edition staging manual doesn’t need a separate atlas.
- Perineal lesions can be challenging to classify and the 8th edition offers the following recommendations;
  - Lesions clearly arising from the vulvar and spreads to the perineum/anus should be classified as vulvar.
  - Lesions clearly arising from the anus but extends to the perineum should be classified as perianal.
  - Perineal lesions that do not clearly arise from the anus or vulvar, clinician should denote exact location and favored impression regarding classification e.g. “perineum favor vulva” or perineum favor anus.
Updates in Gynecologic Cancers: Vulva

- There are only 4 categories of grading (Gx, G1, G2, and G3). Grade 4 has been removed.

Updates in Gynecologic Cancers: Vagina

- Mucosal melanoma of the vagina is not included in this edition of AJCC staging system.
- T1a (≤ 2cm) and T1b (>2cm) subcategories were added. Both are FIGO stage I.
- Similarly, T2a (≤ 2cm) and T2b (>2cm) subcategories were added. Both are FIGO stage II.
- These additions were made to distinguish a tumor size cut-off of 2 cm for prospective data collection for studying prognostic significance. (III)
Updates in Gynecologic Cancers: Vagina

- Full length of histologic subtypes according to the WHO classification of tumors is included.
- A chapter on imaging is embedded with suggestions on how to document image findings.
- There are only 4 categories of grading (Gx, G1, G2, and G3). Grade 4 has been removed.
- Kaplan-Meier curves by stage and tumor size (OS) from a large SEER data analysis are included.
- Illustrations of the T and N categories are included therefore an owner of the 8th edition staging manual doesn’t need a separate atlas.

Updates in Gynecologic Cancers: Cervix

- N1 has been removed from FIGO stage IIIB
- Involvement of para-aortic lymph nodes removed from the definition of M1

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Updates in Gynecologic Cancers: Cervix

- Full length of histologic subtypes according to the WHO classification of tumors is included.
- ***A chapter on imaging is embedded with suggestions on how to document image findings. Cervix was the strongest motivation for this chapter***
- There are only 4 categories of grading (Gx, G1, G2, and G3). Grade 4 has been removed.
- Illustrations of the T and N categories are included therefore an owner of the 8th edition staging manual doesn’t need a separate atlas.

Updates in Gynecologic Cancers: Corpus

- Leiomyosarcomas, endometrial stromal sarcomas and adenosarcomas now have a separate chapter called corpus uteri-sarcoma (chapter 54).
- Stage 0 and Tis have been removed.
- Endometrial intraepithelial carcinoma (EIC) should be considered a T1 cancer.
- Histologic Grade 4 has been removed, should be considered Grade 3.
- Lymph node micrometastasis (<2mm) to be reported as N1mi (pelvis) and N2mi (para-aortic).
Updates in Gynecologic Cancers: Corpus

- Full length of histologic subtypes according to the WHO classification of tumors is included.
- A chapter on imaging is embedded with suggestions on how to document image findings.
- There are only 4 categories of grading (Gx, G1, G2, and G3). Grade 4 has been removed.
- Illustrations of the T and N categories are included therefore an owner of the 8th edition staging manual doesn’t need a separate atlas.

Updates in Gynecologic Cancers: Corpus uteri-sarcoma

- This is a new chapter
- Full length of histologic subtypes according to the WHO classification of tumors is included.
- Uterine carcinosarcoma has been removed from sarcoma and now staged with the other corpus epithelial cancers.
- There are only 4 categories of grading (Gx, G1, G2, and G3). Grade 4 has been removed.
- Illustrations of the T and N categories are included therefore an owner of the 8th edition staging manual doesn’t need a separate atlas.
Updates in Gynecologic Cancers: Corpus uteri-sarcoma

- In alignment with FIGO, leiomyosarcoma and endometrial stromal sarcoma are similarly staged.
- Adenosarcoma is separately staged
- Grade is not a collected element in leiomyosarcoma, as all are high grade tumors.

Updates in Gynecologic Cancers: Corpus uteri-sarcoma

- Sarcomas and related tumors involving peritoneum or visceral organs represent an area of overlap between the soft tissue sarcoma chapters and gynecology chapters. The affected histologies include:
  - 8810 Adult fibrosarcoma
  - 8815 Solitary fibrous tumor
  - 8825 Inflammatory myofibroblastic sarcoma
  - 8890 Leiomyosarcoma - named leiomyomatosis peritonealis disseminate in GYN chapter with borderline behavior
  - 8936 Gastrointestinal stromal tumor – also called extra-gastrointestinal stromal tumor in GYN chapter
- Such staging should be deferred to the relevant soft tissue sarcoma chapter, A link is provided in the gyn. chapters
Updates in Gynecologic Cancers: Ovary, Fallopian tube & Primary Peritoneal Carcinoma

- Fallopian tube now shares the same staging and chapter as ovary and primary peritoneal carcinoma
- T1C has been split into 3 sub-categories; 1C1= intraoperative tumor rupture, 1C2= tumor rupture before surgery, 1C3= positive peritoneal washing.
- Former T2C has been eliminated.
- New N1: retroperitoneal (pelvic or para-aortic) LN spread without extra-pelvic peritoneal involvement.
- New N1a1(FIGO IIIA1i): LN metastasis up to 5 mm
- New N1b (FIGO IIIA1ii): LN metastasis > 5 mm

Updates in Gynecologic Cancers: Ovary, Fallopian tube & Primary Peritoneal Carcinoma

- New TIIIA2: Microscopic extra-pelvic peritoneal involvement
- TIIIB & TIIIC have been modified and both are now based on peritoneal metastasis only regardless of LN status.
- New: Parenchymal involvement of both liver and spleen is now M1b (FIGO stage IVB).
- New: Transmural involvement of intestine is now M1b (FIGO stage IVB).
Updates in Gynecologic Cancers: Ovary, Fallopian tube & Primary Peritoneal Carcinoma

- Full length of histologic subtypes according to the WHO classification of tumors is included.
- A chapter on imaging is embedded with suggestions on how to document image findings.
- There are only 5 categories of grading (Gx, GB, G1, G2, and G3). Grade 4 has been removed.
- Illustrations of the T, N and M categories are included therefore an owner of the 8th edition staging manual doesn’t need a separate atlas.

Updates in Gynecologic Cancers: Gestational Trophoblastic Neoplasms

- Complete and partial hydatidiform moles have been removed from this chapter.
- Full length of histologic subtypes according to the WHO classification of tumors is included.
- A chapter on imaging is embedded with suggestions on how to document image findings.
- Illustrations of the T and M categories are included therefore an owner of the 8th edition staging manual doesn’t need a separate atlas.
Thank you!

Questions