A Re-Introduction to Summary Staging and TNM Staging 7th Ed.

Summary Staging
- Most basic staging
- In widespread use since 1970s
  - Only one update (2000)
  - 2016 update being considered
- Applies to solid tumors
- Uses all information in record
- Five main categories
  - In situ
  - Localized
  - Regionalized
  - Distant
  - Unstageable

Timing Rule
- Information gathered through completion of surgeries OR 4 months, whichever is longer.
- Staging can be determined after treatment with radiation or systemic therapy if 4-month rule is followed and there is no disease progression
- Same as TNM 7th edition pathologic staging

Summary Stage Principles
- Uses both clinical and pathologic information
- Pathologic information takes precedence over clinical information
- When all malignant tissue is not removed, include information from gross observation
- Surgery observation takes precedence over clinical information if surgery observation or pathology disproves clinical
Summary Stage Principles
- First section (pp. 1-15) is a coding manual
- A few cancer types are histology specific
  - Most chapters based on primary site
  - Relatively few site-specific rules
- Ambiguous terminology listed
  - May be used to determine extent of disease
- If lymph nodes are not listed under ‘regional’ or a synonym of a regional node, assume they are distant
- List of synonymous terms in Summary Stage manual

In Situ (Code 0)
- Earliest stage
- “In place”
- No stromal invasion; no penetration of basement membrane
  - No sarcomas, lymphomas or hematopoietic diseases
- Guidelines
  - Epithelial tissues only (carcinoma and melanoma)
  - Must be diagnosed pathologically
  - If any evidence of invasion, no longer in situ

The Basement Membrane

Examples of Words Meaning In Situ
- Adenocarcinoma in adenomatous polyp with no stalk invasion
- Bowen’s disease
- Confined to epithelium
- Intracystic non-infiltrating
- Intraductal
- Intra-epidermal
- Intra-epithelial
- Intrasquamous
- Involvement up to but not including the basement membrane
- Non-infiltrating
- Non-invasive
- No stromal invasion
- Preinvasive
- Stage 0 (TNM stage group for many sites)
- Other site-specific terms
**Localized (Code 1)**

- Confined to organ of origin
- Can be widely invasive within organ of origin
  - Example: Multifocal breast tumors
- Names of anatomic substructures important
  - Examples: muscularis mucosae, muscularis propria, skeletal muscle

**Localized – Guidelines**

- May require surgical removal of organ
- Review all imaging reports and operative report for evidence of further spread
- Rule out in situ tumor and nodal involvement
- ‘Localized’ terminology
  - Microinvasion
  - Lymphatic invasion
  - Vascular invasion
  - Metastases within organ of origin
  - Multifocal
  - Multiple tumors of same cell type

**Invasive Cancer**

A Localized Tumor with Vascular Invasion

**Regionalized**

- Difficult to categorize properly
- Tumor beyond limits of organ of origin
- Potential for spread by more than one vascular or lymphatic route
- Subcategories
  - Regional direct extension
  - Regional to lymph nodes
  - Regional to lymph nodes and direct extension
  - Regional, NOS
Regional Categories

- Direct extension (Code 2)
  - Invasion through wall or capsule of organ into adjacent organs or tissues
  - Knowledge of regional anatomy important
- Regional to lymph nodes (Code 3)
  - Tumor cells in lymphatic channels filter out and grow in lymph nodes
  - Nodes may be some distance from primary and still be first level lymph drainage
- Regional nodes AND extension (Code 4)
  - Both continuous tumor extension and regional lymph node involvement
- Regional, NOS (Code 5)
  - Likely a clinical diagnosis; limited workup

Regional – Words to Watch

- Involvement of local lymph nodes
- Lymph node metastases
- Different names for lymph node chains

- Terminology
  - Disregard ‘palpable’, ‘shotty’, ‘swollen’, ‘visible’
  - Disregard ‘enlarged’, ‘lymphadenopathy’ EXCEPT for lung
  - ‘Mass in [body cavity]’ is staged as involvement of nodes
  - For lymphoma, any mention of nodes is staged as involvement

Distant (Code 7)

- Tumor spread to remote area of body
- Four methods of spread
  - Distant direct extension
  - Distant lymph nodes
  - Hematogenous metastases
  - Implantation metastases (seeding in body cavity)
- Systemic disease is always distant/disseminated
  - Leukemia, multiple myeloma

A Distant Metastasis

1. Tumor cell from primary site enters a remote organ through blood vessel
2. Tumor adheres to wall of capillary
3. Tumor cell penetrates capillary wall
4. Secondary tumor grows

Hematogenous spread
Usually WITHIN organ

### Distant Metastases – Guidelines

- Common sites of spread for solid tumors
  - Liver, Lung, Bones, Brain – not listed
- Rule out distant disease first
- Not all distant organs are listed
- Vascular invasion may not be distant
- Liver involvement may not be distant
- Unknown primary site is always unknown stage

### Not Applicable (Code 8)

- Used for
  - Benign CNS tumors
  - Borderline CNS tumors
  - Reportable by Agreement /0 or /1
- Never used for malignant tumors

### Unknown Stage (Code 9)

- Use sparingly
- Check all information sources including MDs
- Document reason for unknown stage in text
- Reasons
  - Patient expired
  - Patient refused workup
  - Contraindications to workup or treatment
  - Insufficient workup
  - Equivocal workup

### Direct Coding of Summary Stage

1. Determine primary site and histology
   - Ask ‘Where did it start?’ (primary site)
   - Ask ‘Where did it go?’ (spread to adjacent organs or distant sites)
   - Rule out in situ
   - Rule out distant disease
   - Rule out nodal involvement
   - Ask ‘How did it get there?’
     - Direct extension
     - Lymphatics
     - Discontinuous metastasis
       - Blood
       - Seeding/Nodules
Direct Coding of Summary Stage

2. Review site chapter
3. Match words with listings of structures and adjacent organs to identify correct stage and code

The Future – Summary Stage

- NPCR states
  - Direct coding of Summary Stage required as of 01/01/2015
- SEER areas
  - Summary Stage derived from direct coding of TNM as of 01/01/2016
  - Trying to avoid direct assignment of both TNM and Summary Stage
- COC
  - May again require Summary Stage depending on other standards setters' decisions

TNM
Tumor-Node-Metastasis Staging System

UICC-TNM Staging

- Developed by international committees
- Adopted more by clinicians than surveillance community
- Issues
  - Does not describe biology of cancer
  - Does not predict response to therapy
  - Changes frequently
  - Seven US editions since 1978
  - More complicated rules
  - Not all sites available
  - Brain, hematopoietic diseases
  - Staging of some sites may not be possible due to uncommon histology
  - Limited information in record
  - May be inaccurate even if completed by physician
The TNM System

AJCC and UICC definitions are almost identical

Other Resources

UICC-TNM Staging Issues
- Developed by international committees
- Requires compromise among experts
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UICC-TNM Staging Issues
- More complicated rules
- More complicated notation of stage
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    - Uncommon histology
    - Limited information in record
- May be inaccurate even if completed by physician
IMPORTANT!

- TNM was written by clinicians for clinicians
  - Some terms and situations not defined
  - No ambiguous terminology list
  - Some things are assumed
  - Includes chapters for diagnoses that are not reportable to population-based cancer registries

- TNM is academically/scientifically oriented
  - No “best stage”
    - “Pure” clinical and “pure” pathologic staging groupings are not real life
  - TNM groups individual cases with similar survival rates into categories
    - “Lumping” vs. “splitting”

CS vs TNM

- CS is the registrars’ coding system
  - Not a staging system
  - Handling of blanks, unknowns
  - Allows “mixed” staging

- CS coding instructions allow some assumptions
  - Inaccessible nodes rule
  - For some SSFs, if not reported, assume it’s not there

- TNM has broader definitions
  - No list of ambiguous terms
  - Ambiguous terms must be evaluated in context, not based on a list
  - Little guidance for registrars

TNM Staging Premise

- Cancer has a finite length and certain measurable events along time continuum
  - Mutation of single cell
  - Local growth (increase in size)
  - Invasion of organ’s parenchyma
  - Invasion of lymphatics within organ

- Cancer timeline, continued
  - Spread to regional lymph nodes
  - Direct invasion of adjacent tissues
  - Invasion of blood vessels and spread to distant organs
  - Time continuum varies by cancer type
    - Marker points defined for each type of cancer
General Rules for Staging

1. MICROSCOPIC CONFIRMATION
   - All cases should be confirmed microscopically.
   - Clinically diagnosed cases should be reported separately.
   - Cancers are classified by their ICD-O-3 primary site code.

2. TIMING - Clinical Staging (cTNM)
   - All information obtained prior to initiation of any treatment or within 4 months of diagnosis, whichever is shorter, with no disease progression.
   - Treatment decision includes watchful waiting
   - May be only common factor for some sites
   - Information used
     - Symptoms
     - Physical exam
     - Endoscopies
     - Biopsy for diagnosis
     - Imaging (tumor, lymph nodes, or distant sites)
     - Surgical exploration w/o resection
     - Other relevant examinations
   - Applications
     - Define initial treatment choice
     - International population comparison

3. CASES WITH NEOADJUVANT TREATMENT
   - Cases treated with neoadjuvant therapy (pre-operative systemic or radiation therapy) may have a second staging after treatment.
   - Should have clinical staging as baseline
   - Post-treatment staging labeled yc or yp
General Rules for Staging

4. PROGRESSION OF DISEASE
   - Only information obtained prior to documented progression of disease is used for staging.

5. UNCERTAINTY ABOUT CATEGORY (“Downstaging”)
   - If in doubt about correct T, N, or M value, use the lower (less advanced) category.
   - If in doubt about stage grouping, choose the lower stage.
   - If in doubt about prognostic factor, assign the lower category.

6. MISSING PROGNOSTIC FACTOR
   - If required non-anatomic factor is not available, stage group case assuming lowest value for factor.
   - Example: T2a N0 M0 prostate cancer but Gleason score and PSA unknown.
     Assign Stage Group I (PSA X, Gleason X).

Optional Descriptors

- Lymphatic Invasion
  - LX Lymphatic invasion cannot be assessed
  - L0 No lymphatic invasion
  - L1 Lymphatic invasion

- Venous Invasion
  - VX Venous invasion cannot be assessed
  - V0 No venous invasion
  - V1 Microscopic venous invasion
  - V2 Macroscopic venous invasion

- Perineural Invasion
  - PnX Perineural invasion cannot be assessed
  - Pn0 No perineural invasion
  - Pn1 Perineural invasion

- Residual Tumor
  - RX Presence of residual tumor cannot be assessed
  - R0 No residual tumor
  - R1 Microscopic residual tumor
  - R2 Macroscopic residual tumor

Additional Notes from Chapter 1

- Carcinoma in situ
  - Must be pathologically determined (pTis)
  - Mixed stage pTis cN0 cM0
  - Should be reported as both clinical and pathologic stage

- Subsequent primaries
  - Stage as new cancer
  - Do not stage with ‘y’ prefix unless neoadjuvant therapy to new primary

- Unknown primary site
  - No evidence of primary tumor (T0)
  - Stage according to site suspected by clinician
Additional Notes from Chapter 1

- **Multiple Primary Tumors**
  - Simultaneous tumors of same histology in one organ
  - Classify by highest T category
  - Add suffix of m for multiplicity or number of tumors, as in T2(m) or T2(3)
  - Example: Mastectomy specimen: 1 cm duct carcinoma UOQ and 2.3 cm duct carcinoma LOQ. Use greater sized tumor (2.3 cm) for staging. Assign pT2(m) or pT2(2).
  - Thyroid, ovary, fallopian tube, liver: Multiplicity part of T definitions
  - Lung: Multiple tumors may be classified in T or M depending on location

TNM Components

- **Descriptors** – 3 anatomic dimensions of spread
  - **T** = Tumor (extension and/or size)
  - **N** = Nodes (regional lymph nodes)
  - **M** = Metastasis
  - Other attributes
  - **Staging basis** (timing)
    - **Clinical** – all information prior to start of treatment
    - **Pathologic** – information from resected specimen
    - Other – autopsy, retreatment
  - **Stage Grouping** (aggregation)
    - Stage 0 (in situ) – Stage IV (distant)

**T – Tumor Locoregional Spread**

- Assessment of the primary cancer and any organs involved by contiguous extension
  - Local growth
  - Invasion of blood vessels or lymphatics within organ of origin
  - Within a body cavity, tumor seeding of organ tissues via body fluid
  - Direct invasion of adjacent tissues

**T Classification: Different Criteria for Different Cancers**

- **Tumor size**
  - Breast, parotid gland, oral cavity
  - Depth of invasion through wall of organ
  - Colon, bladder, melanoma
  - **Location and extension**
    - Lung, larynx, pancreas
  - **Other factors**
    - Tumor multiplicity (thyroid, liver)
    - Grade (sarcomas)
    - Prognostic factors (prostate, testis)
T Values 1–4 – Size

- **Example: Breast**
  - T1: Less than or equal to 2 cm
  - T2: > 2 cm to 5 cm
  - T3: > 5 cm
  - T4: Involving chest wall or skin

\[\text{Source: UICC TNM-interactive, Wiley-Liss, 1998}\]

T Values 1–4 – Invasion

- **Example: Bladder**
  - T0: No evidence of primary tumor
  - Ta: Noninvasive papillary carcinoma
  - Tis: Carcinoma in situ
  - T1: Subepithelial connective tissue
  - T2: Muscularis propria
    - T2a: Superficial muscularis
    - T2b: Deep muscularis
  - T3: Perivesical tissue
    - T3a: Microscopic
    - T3b: Macroscopic
  - T4: Beyond bladder
    - T4a: Prostatic stroma, uterus, vagina
    - T4b: Pelvic wall, abdominal wall

\[\text{Source: UICC TNM-interactive, Wiley-Liss, 1998}\]

T Values 1–4 – Extension

- **Example: Vocal cord (glottic larynx)**
  - T1: Limited to cords (normal mobility)
    - T1a: One cord
    - T1b: Both cords
  - T2: Extends to supra- or subglottis or impaired cord mobility
  - T3: Confined to larynx with vocal cord fixation; or extending to paraglottic space or inner cortex of thyroid cartilage
    - T3a: Microscopic
    - T3b: Macroscopic
  - T4: Through thyroid cartilage; trachea, soft tissues of neck, deep extrinsic muscles of tongue
    - T4a: Through thyroid cartilage; trachea, soft tissues of neck, deep extrinsic muscles of tongue
    - T4b: Prevertebral space, encasing carotid artery, invading mediastinal structures

\[\text{Source: UICC TNM-interactive, Wiley-Liss, 1998}\]

Bladder: Depth of Invasion

\[\text{Source: Re-introduction to TNM Staging, Wiley-Liss, 1998}\]
Tis – Carcinoma In Situ
- Primary tumor must be removed and microscopically proven to be non-invasive (pTis)
- Never a cT classification
- May be part of clinical or pathologic Stage Group 0

T0 – No evidence of primary tumor
- Tumor in primary site cannot be found

N – Regional Lymph Nodes
Lymph Node Involvement
- Absence or presence of metastases in primary lymph node drainage area of cancer

N0
- Regional lymph nodes have been clinically or pathologically proven to be free of metastatic disease

N1 – N3
- Increasing involvement of regional lymph nodes by number, location or size
  - N1 Regional lymph node metastasis
  - N2 3-6 regional nodes involved
  - N3a 7-15 regional nodes involved
  - N3b 16 or more regional nodes involved

Source: UICC TNMinteractive, Wiley-Liss, 1998
N1–3 – Location

- Example: Lung
  - N1 Peribronchial and perihilar nodes
  - N2 Ipsilateral mediastinal and/or subcarinal nodes
  - N3 Contralateral mediastinal or hilar nodes; scalene or supraclavicular node metastases

Lymph Nodes
- N1 Same side Peribronchial; Hilar
- N2 Same side Subcarinal; Mediastinal
- N3 Contralateral mediastinal; Contralateral hilar
  - Any scalene
  - Any supraclavicular

Adapted from R.S. Snell, Clinical Anatomy for Medical Students, 5th ed., 1995.

N1–3 – Size and Number

- Example: Renal Pelvis and Ureter
  - N1 Single node, 2 cm or less
  - N2 Single node > 2 to 5 cm or multiple nodes, all ≤ 5 cm
  - N3 Any metastasis > 5 cm

Using X (Unknown)

- TX Primary tumor cannot be assessed
- NX Regional nodes cannot be assessed
- X used when information is unknown
- TX or NX cannot be assigned to a stage group
  - Unless Any T or Any N M1
- Use TX or NX only when absolutely necessary

M – Distant Metastases

Systemic Involvement

- Absence or presence of distant metastases
  - Blood-borne metastases
    - Discontinuous from primary site
    - Direct distant extension
  - Progressive lymph node involvement
  - Seeding

Brain
Cervical Nodes
Liver
Adrenal
Bone
Distant sites
M – Distant Metastasis

**Categories**
- M0 Absence of metastatic disease
- M1 Presence of at least one area of distant metastases

**M1 subcategory example: prostate**
- M1a Non-regional lymph nodes
- M1b Bone(s)
- M1c Other site(s)

**Notes**
- MX not available in M category
- Minimal physical examination results in cM0
- pM0 not possible except at autopsy
- Classification choices: cM0, cM1, pM1

Stage Grouping

**A.k.a. anatomic stage/prognostic groups**
- Easily communicated summary of extent of disease and prognosis
- Used for prognostic estimates, tabulations and analysis
- Gathers cases based on anatomic extent of disease (T, N, M) plus relevant non-anatomic factors into categories to facilitate analysis
- 5 T x 3 N x 2 M categories = at least 30 combinations
- TNM classification and stage groups, once established, must remain unchanged in the medical records

Stage Grouping

**Generally “pure clinical” and “pure pathologic” stage groups defined**
- Commission on Cancer allows elements to be combined into “working stage” while treatment decisions are being made or when only partial information is available for either – not an AJCC TNM rule

**General concepts**
- Stage 0 Carcinoma in situ
- Stage I Confined to primary site
- Stage II Limited local extension and/or limited regional lymph node involvement
- Stage III More advanced local extension or regional lymph node involvement
- Stage IV Involvement of distant sites

Staging Basis

**c – Clinical stage:** Essential to select and evaluate therapy options
**p – Pathologic stage:** Provides most precise data to estimate prognosis, plan subsequent therapy, and calculate end results
**r – Recurrence/Retreatment stage:** Assessment of extent of tumor after recurrence after disease-free interval when further treatment is planned
**a – Autopsy stage:** Classification first determined at autopsy (no previous diagnosis of cancer)
Clinical Stage
- Assigned prior to cancer-directed treatment
- Derived from clinical observations
  - Specified in each chapter
- Ends when first cancer-directed treatment starts or decision is made not to treat
- Should not be changed based on subsequent information from treatment
- Clinicians will use when
  - No surgical treatment
  - Adjuvant treatment prior to surgery
  - Insufficient information to stage pathologically
- Clinical stage must be reported in COC-accredited facilities

Pathologic Staging
- Most precise estimate of prognosis
- Based on
  - Clinical information acquired before treatment PLUS
  - Pathologic examination of surgical specimen
  - … a combination of all findings
- If primary tumor can’t be removed
  - Case can be pathologically staged if highest T and N categories or M1 has been microscopically confirmed
- Specific requirements for pT, pN, pM
  - Presence of a pathology report is not automatically pathologic staging

Pathologic Staging – T
- Minimal requirement for assigning pT
  - Gross resection of primary
  - Margins may be microscopically involved
  - Must be able to evaluate highest pT category (size, invasion)
- If biopsy documents highest T category, can be classified as pathologic
- Some sites have specific rules
  - Prostate: Radical prostatectomy required
  - Bladder: Radical cystectomy required
  - Breast: At least a lumpectomy
Pathologic Staging – N

- Minimum requirement for assigning pN
  - Resection of minimum number of nodes to assure sufficient sampling
  - Number varies by primary site
  - Exception: sentinel node procedures
  - If recommended number of nodes not removed, can still classify pN
  - Pathologic examination of enough nodes to validate absence of regional lymph node metastases (pN0)
  - Evaluate highest pN category

Pathologic Staging – N

- pN assigned in conjunction with pT
  - If removal of primary tumor meets criteria for pathologic T, then not necessary to have microscopic confirmation of highest N category
  - If highest N category microscopically proven, then case is pN regardless of status of primary
  - Example: Lumpectomy for breast cancer with sentinel node biopsy of only Level I nodes = pT_ pN_ (sn)
  - If no removal of primary tumor, then lymph node biopsy or sentinel node procedure is cN

Pathologic Staging – N

- Isolated tumor cells (ITCs)
  - Identified by immunohistochemistry or molecular techniques, flow cytometry or DNA analysis
  - Definition
    - Single tumor cells or small clusters of cells 0.2 mm in diameter
    - Classified as pN0 except for melanoma and Merkel cell carcinoma

Pathologic Staging - M

- pM1 requires microscopic confirmation of metastatic site
- No pM0
- Assessment of metastases for pathologic TNM can be either clinical (cM0 or cM1) or pathologic (pM1) when pT and pN criteria are met
- CTCs (circulating) and DTCs (disseminated) or bone marrow micrometastases are cM0 (i+)
Post-Therapy Classification

- Also called intercurrent staging ('y' classification)
- Measures response to neoadjuvant treatment
  - Patient had systemic and/or radiation treatment before surgery
  - Case staged at conclusion of therapy
  - Clinical if no further treatment (ypTNM)
  - Pathologic if resection (ypTNM)
  - Stage group notation for no residual cancer:
    - ypT0  ypN0  cM0
  - Should have clinical staging as baseline
  - Allows assessment of response to therapy
  - Surgery must meet criteria for pathologic staging
  - Provides prognostic information and helps determine subsequent non-surgical treatment

Non-Anatomic Factors

- Supplementary data for some sites
- Also called prognostic factors
- Necessary for staging of some sites
  - Grade of tumor
    - Bone, sarcoma, prostate
  - Number of tumors
    - Thyroid, ovary
  - Age of patient
    - Thyroid
  - Prognostic factors
    - Testis, prostate
  - Cell type
    - Esophagus, thyroid
  - Location of tumor
    - Gallbladder, esophagus
  - Depth of invasion
    - Melanoma
  - Risk factors
    - Gestational trophoblastic tumor
  - Vascular invasion
    - Testis

Direct Coding of T, N, M, and Stage

1. Determine primary site and histology
   - Ask ‘Where did it start?’ (primary site)
   - Ask ‘Where did it go?’ (spread to adjacent organs or distant sites)
   - Ask ‘How did it get there?’
     - Direct extension (T)
     - Lymphatics (N)
     - Discontinuous metastasis (M)
       - Blood
       - Seeding/Nodules
2. Look up site chapter
3. Is histology included in this chapter?
TNM Wrap-Up

- General rules apply to all chapters
  - Site-specific rules provide additional information and may override general rules
- Four staging classifications
- T, N, M categories define anatomic extent of disease
- Prognostic (nonanatomic) factors provide additional information
- Staging bases defined by timing of treatment
- Cases grouped for staging
  - Comparison and analysis

The Future – TNM Stage Fields

- NPCR states
  - Directly assigned AJCC TNM (clinical and pathologic) as of 01/01/2015 required from COC-accredited hospitals, as available from non-COC facilities
- SEER areas
  - Directly assigned AJCC TNM (clinical and pathologic) as of 01/01/2015 required from COC-accredited hospitals when available
- COC-accredited hospitals
  - Directly assigned AJCC TNM (clinical and pathologic) as of 01/01/2015, “Staged by” and “Descriptor” fields

A Final Reminder

- Do not mix apples and oranges
  - CS rules do not apply to TNM
  - CS assumptions do not apply to TNM
- On January 1, 2016, with the apoptosis of CS,
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