Overview

- The extent or stage of tumor at the time of diagnosis is critical for:
  - Defining prognosis
  - Determining treatment
  - Inclusion and stratification for randomized clinical trials (RCT)
  - Evaluating the results of treatment and clinical trials
  - Facilitating comparison of care across cancer treatment centers
  - Population health and surveillance
  - Basis for translational research

Overview

- Anatomic staging is still mainstay of cancer staging
- Evolving role of non-anatomic factors
  - Provide critical information for stage grouping
  - Predict benefit of target-specific therapies
  - Enhancing clinical decision making
- Assigning stage is the role of the managing physician

Overview

- Several different staging systems based on anatomic factors
  - TNM staging classification system most widely used
  - American Joint Committee on Cancer (AJCC) and Union for International Cancer Control (UICC)
  - Other staging systems

Understanding Terminology

- Stage vs. stage group vs category vs classification
- ‘Stage’ should be reserved for aggregate information from TNM categorization
- Stage groups or prognostic stage groups:
  - Aggregate information from T, N and M and
  - Specified nonanatomic factor (“Prognostic Factors for Stage Grouping”) for specific cancer
Understanding Terminology

• Classification: lower case prefix used to describe point in time of Cancer Care continuum:
  - Clinical (c)
  - Pathologic (p)
  - Post-neoadjuvant therapy (yc or yp)
  - Recurrent or Retreatment (rc or rp)
  - Autopsy (a)

• Categorization: T, N, M and Prognostic Factors
  - T, N, or M data used to assign site-specific T, N, and/or M for a patient at a given point in time
  - E.g. T1 or N1c
  - Prognostic Factors for Stage Grouping
    - Non-anatomic factors that have strong correlation with prognosis
    - Site and tumor-specific
    - Used to determine stage group

• Subcategorization:
  - Specific cancers have subcategories to facilitate reporting of more detailed information
    - E.g. Breast: T1mi, T1a, T1b, T1c
  - Unknown designation X:
    - Used if information on T or N is unknown
    - Usually not able to assign stage group
    - TX or NX should only be used if absolutely necessary
    - There is no MX category

General Staging Rules

• Time Frame for staging cancers:
  - Clinical: From date of diagnosis before initiation of primary treatment or watchful waiting/supportive care to one of the following:
    - Four (4) months after diagnosis or
    - Date of cancer progression if progression occurs within the four month window

• Pathological: Information from clinical staging and data from resected specimen may be used if:
  - Surgical resection occurs within four months of date of diagnosis
  - To the date of cancer progression if progression occurs within the four month window
  - Can use information about extent of cancer up to the point of definitive resection if resection occurs outside of four month window and cancer has not clearly progressed
General Staging Rules

• Time Frame for staging cancers:
  - Neoadjuvant Therapy (yp): Time frame should be such that surgery and staging occur within time frame appropriate for disease specific circumstances

Synchronous vs metachronous tumors:
- Multiple tumors of the same histology in an organ:
  - Tumor of the highest T category is classified and staged
  - Use the (m) designation: e.g. pT3(m)N0
  - If number of tumors is important, then replace m with number e.g. pT3(4)N0
- Synchronous primaries in paired organs:
  - Classify and stage as separate tumors
- Site specific exceptions: thyroid, ovary, lung and liver

Pathological Classification (pTNM)
- Time Frame: from date of diagnosis to surgical resection in the absence of tumor progression
- Criteria: surgery is first therapy
- Based on:
  - Pathologic evaluation of resected specimen and
  - Clinical stage information prior to definitive surgery including:
    - Imaging studies
    - Clinical exam
    - Any biopsy or cytology information

Pathologic T Categorization (pT)
- Optimal based on resection of single specimen
- If fragmented or resected at several different procedures:
  - Reasonable estimate of tumor size should be made through pathologic assessment with the aid of imaging studies, if necessary
  - Direct extension of tumor into a node is classified as nodal involvement (pN)
  - Direct extension into an adjacent organ is not considered metastatic involvement (pM)

Pathologic Nodal Categorization (pN)
- pN only applied to regional lymph nodes
- Distant nodal involvement categorized as a metastasis (M)
- Only one node needs to be documented in resection specimen to assign pN
  - Chapters often have minimum number of nodes defined for optimal resection
  - Fine needle aspiration is sufficient to assign pN
- Direct extension of tumor into a regional lymph node:
  - Assigned as pN and not as part of pT categorization
Pathologic Nodal Categorization (pN)

- Evolving Concepts:
  - Isolated Tumor Cells and the use of the (i+) designator
  - Micrometases and use of the (mi) designator
  - Molecular techniques for identifying isolated tumor cells (mol+)

Pathologic M Categorization (pM)

- pM0 and pMX are not valid categories
- pM1 with subcategorization, as appropriate, is only valid category
- If biopsy of clinically suspicious lesion is negative for tumor, then no pM should be assigned
- Fine needle aspiration is sufficient for pM categorization

Understanding the Rules for Reporting after Neoadjuvant Therapy

- Represents the post-neoadjuvant therapy assessment
  - Use the ‘yp’ designator for definitive resection specimen
  - ypT and ypN represent pathologic response to neoadjuvant therapy
  - Complete pathologic response: ypT0N0
  - Partial pathologic response: assigned irrespective of original clinical categorization (e.g. cT3N1 may end up as ypT1N0 on resection)
  - M category is not changed in post-neoadjuvant therapy assessment

Understanding the Rules for Reporting after Neoadjuvant Therapy

- Histologic confirmation of residual cancer requires presence of non-necrotic tumor cells
  - Pools of acellular mucin or necrosis is not residual cancer
- Not all treatment prior to definitive resection is considered ‘neoadjuvant’

Putting It All Together for the Pathologist

- For accreditation purposes:
  - pTNM or ypTNM classification should be assigned on definitive resection specimens of primary tumor
  - For most accurate classification, should include information from prior biopsies, imaging, etc., as appropriate
  - Note any assumptions or equivocal findings in comment
  - Pathologist should not provide stage grouping

Putting It All Together for the Pathologist

- For optimal clinical care:
  - Biopsies:
    - In general, shouldn’t provide pTNM classification on biopsy specimens
    - Provide information necessary for appropriate clinical or pathologic classification in report, when possible
  - Resection of recurrent tumors
    - There is an rp designator, so pathologist should provide adequate information for staging, when possible
Putting It All Together for the Pathologist

For optimal clinical care:
- Understand the rules for pTNM classification!
  - A wealth of information in Chapter 1 of the AJCC Staging Manual
  - Understand the general rules for determining pT, N or M categories
  - There are differences between tumor sites so use the Staging Manual for clarification

For optimal clinical care:
- We are part of the multidisciplinary team involved in Cancer Care
  - Our responsibility does not end with issuing of report
  - Involvement and ongoing communication