1 Purposes and Principles of Cancer Staging

INTRODUCTION AND OVERVIEW

The extent or *stage* of cancer at the time of diagnosis is a key factor that defines prognosis and is a critical element in determining appropriate treatment based on the experience and outcomes of groups of prior patients with similar stage. In addition, accurate staging is necessary to evaluate the results of treatments and clinical trials, to facilitate the exchange and comparison of information among treatment centers, and to serve as a basis for clinical and translational cancer research. At a national and international level, the agreement on classifications of cancer cases provides a method of clearly conveying clinical experience to others without ambiguity.

Several cancer staging systems are used worldwide. Differences among these systems stem from the needs and objectives of users in clinical medicine and in population surveillance. The most clinically useful staging system is the tumor node metastasis (TNM) system maintained collaboratively by the American Joint Committee on Cancer (AJCC) and the International Union for Cancer Control (UICC). The TNM system classifies cancers by the size and extent of the primary tumor (T), involvement of regional lymph node (N), and the presence or absence of distant metastases (M), supplemented in recent years by carefully selected nonanatomic prognostic factors. There is a TNM staging algorithm for cancers of virtually every anatomic site and histology, with the primary exception in this manual being staging of pediatric cancers.

Philosophy of TNM Revision. The AJCC and UICC periodically modify the TNM system in response to newly acquired clinical data and improved understanding of cancer biology and factors affecting prognosis. Revision is one factor that makes the TNM system the most clinically useful staging system and accounts for its use worldwide. However, changes in staging systems may make it difficult to compare outcomes of current and past groups of patients. Because of this, the organizations only make these changes carefully and based on the best possible evidence.

The revision cycle for TNM staging is 6–8 years. This provides sufficient time for implementation of changes in clinical and cancer registry operations and for relevant examination and discussion of data supporting changes in staging. Table 1.1 shows the publication years for each of the versions of the TNM system up through this current seventh edition of the TNM system. The prior sixth edition was used for cases diagnosed on or after January 1, 2003. The seventh edition published in this manual is effective for cancer cases diagnosed on or after January 1, 2010.

Anatomic Staging and Use of Nonanatomic Information. Cancer staging is historically based solely on the anatomic extent of cancer and remains primarily anatomic. However, an increasing number of nonanatomic factors about a cancer and its host provide critical prognostic information and may predict the value of specific therapies. Among those factors known to affect patient outcomes and/or response to therapy are the clinical and pathologic anatomic extent of disease, the reported duration of signs or symptoms, gender, age and health status of the patient, the type and grade of the cancer, and the specific biological properties of the cancer. Clinicians use the pure anatomic extent of disease in defining treatment, but in many cases must supplement TNM with other factors in order to counsel patients and make specific treatment recommendations. As more of these factors are fully validated, it will be necessary to develop strategies to incorporate them into prognostic systems for patient management while maintaining the core anatomic structure of staging. The restriction of TNM to anatomic information has led clinicians to develop other prognostic systems and even led some to conclude that TNM is "obsolete" or "anachronistic."

As outlined in this chapter and throughout the *Manual* in many of the revised AJCC staging algorithms, nonanatomic factors are incorporated into stage grouping where needed. This practice started in a limited fashion in prior editions. However, anatomic extent of disease remains central to defining cancer prognosis. Most proposed nonanatomic prognostic factors in use have been validated only for patients with specific types of disease grouped largely on the anatomic stage (e.g., Gleason's score in early stage prostate cancer and genomic profiles that are validated only in women with node-negative breast cancer). Further, it is critical to maintain the ability to report purely anatomic information to allow comparability of patients treated using new prognostic schemas with patients treated in the past using prior anatomic schemas or with current patients for whom new prognostic factors are not obtained because of cost, available expertise, reporting systems, or other logistical issues.

Defining T, N, M and Timing of Staging Data. Stage is determined from information on the tumor T, regional nodes N, and metastases M and by grouping cases with similar prognosis. The criteria for defining anatomic extent of disease are specific for tumors at different anatomic sites and of different

TABLE 1.1. *AJCC Cancer Staging Manual* editions

Edition	*Publication*	*Dates effective for cancer diagnosed*
1	1977	1978–1983
2	1983	1984–1988
3	1988	1989–1992
4	1992	1993–1997
5	1997	1998–2002
6	2002	2003–2009
7	2009	2010–

histologic types. For example, the size of the tumor is a key factor in breast cancer but has no impact on prognosis in colorectal cancer, where the depth of invasion or extent of the cancer is the primary prognostic feature. Therefore, the criteria for T, N, and M are defined separately for each tumor and histologic type. With certain types of tumors, such as Hodgkin and other lymphomas, a different system for designating the extent of disease and prognosis, and for classifying its groupings, is necessary. In these circumstances, other symbols or descriptive criteria are used in place of T, N, and M, and in the case of lymphoma only the *stage group* is defined. The general rules for defining elements of staging are presented later, and the specifics for each type of disease are in the respective chapters.

Beginning with the sixth edition of the *AJCC Cancer Staging Manual*, TNM adopted a change in the rules for timing of staging data collection to coordinate data collection among the major cancer registry organizations in the USA including the North American Central Registry programs [e.g., the NCI Surveillance Epidemiology and End Results Program (SEER) and the National Program of Cancer Registries (NPCR) of the Center for Disease Control and Prevention], and the National Cancer Data Base, and to accommodate changing practice patterns with increased use of sensitive imaging studies that often were applied during the initial diagnostic phase of care, but occurred after surgery. The timing rules state that:

- *Clinical staging* includes any information obtained about the extent of cancer before initiation of definitive treatment (surgery, systemic or radiation therapy, active surveillance, or palliative care) or within 4 months after the date of diagnosis, whichever is *shorter*, as long as the cancer has not clearly progressed during that time frame.
- *Pathologic staging* includes any information obtained about the extent of cancer through completion of definitive surgery as part of first course treatment or identified within 4 months after the date of diagnosis, whichever is *longer*, as long as there is no systemic or radiation therapy initiated or the cancer has not clearly progressed during that time frame.

TNM Staging Classification: Clinical, Pathologic, Recurrent, Posttreatment, and Autopsy. Stage may be defined at a number of points in the care of the cancer patient. These include "pretreatment stage" or "clinical stage," and postsurgical or "pathologic stage." In addition, stage may be determined (a) after therapy for those receiving systemic or radiation therapy before surgery (termed neoadjuvant therapy) or as primary treatment without surgery, (b) at the time of recurrence, and (c) for cancers identified at autopsy.

Clinical stage (*pretreatment stage*) is the extent of disease defined by diagnostic study before information is available from surgical resection or initiation of neoadjuvant therapy, within the required time frame (see previous discussion). The nomenclature for clinical staging is cT, cN, and cM, and the anatomic stage/prognostic groups based on cTNM are termed the clinical stage groups. Clinical staging incorporates information obtained from symptoms; physical examination; endoscopic examinations; imaging studies of the tumor, regional lymph nodes, and metastases; biopsies of the primary tumor; and surgical exploration without resection. When T is classified only clinically (cT), information from biopsy of single or sentinel lymph nodes may be included in clinical node staging (cN). On occasion, information obtained at the time of surgery may be classified as clinical such as when liver metastases that are identified clinically but not biopsied during a surgical resection of an abdominal tumor.

Pathologic stage is defined by the same diagnostic studies used for clinical staging supplemented by findings from surgical resection and histologic examination of the surgically removed tissues. This adds significant additional prognostic information that is more precise than what can be discerned clinically before therapy. This pathologic extent of disease or pathologic stage is expressed as pT, pN, and pM.

Posttherapy stage (*yTNM*) documents the extent of the disease for patients whose first course of therapy includes systemic or radiation treatment prior to surgical resection or when systemic therapy or radiation is the primary treatment with no surgical resection. The use of so-called *neoadjuvant* therapy is increasingly common in solid tumors including breast, lung, gastrointestinal, head and neck, and other cancers. Posttherapy stage may be recorded as clinical or pathologic depending on the source of posttreatment information. The extent of disease is classified using the same T, N, and M definitions and identified as posttreatment with a "yc" or "yp" prefix (ycT, ycN, ycTNM; ypT, ypN, ypTNM). Note that American registry systems do not have a data element to record "yc" elements, but these may be recorded in the medical record. The measured response to therapy and/or the extent of cancer after therapy may be prognostic. It is also used to guide subsequent surgery or other therapy.

When a patient receives presurgical treatment and has a posttherapy yc- or yp-TNM stage, the *stage* used for surveillance analysis and for comparison purposes is the clinical stage before the start of therapy. Care should be taken not to record the postneoadjuvant therapy stage as the primary stage for comparison of populations or for clinical trials. This could lead to erroneous reports. For example, a patient with a clinical Stage III breast cancer after chemotherapy could have only residual carcinoma in situ. If the final y stage was used as the original stage, the cancer would be erroneously staged as Stage 0. This would be grossly misleading for a case that in fact presented as a locally advanced Stage III cancer.

Two other staging classifications are defined, though there are no data fields reserved for these stages in most cancer registry systems. The first of these is "*Retreatment*" *classification* (*rTNM*). This is used because information gleaned from therapeutic procedures and from extent of disease defined clinically may be prognostic for patients with recurrent cancer after a disease-free interval. Clearly the extent of recurrent disease guides therapy, and this should be recorded in the medical record using the TNM classification. It is important to understand that the rTNM classification does not change the original clinical or pathologic staging of the case. The second of these is the "*Autopsy*" *classification* (*aTNM*) used to stage cases of cancer not identified during life and only identified postmortem.

TNM Groupings. For the purposes of tabulation and analysis of the care of patients with a similar prognosis, T, N, and M are grouped into so-called *anatomic stage/prognostic groups*, commonly referred to as stage groups. Groups are classified by Roman numerals from I to IV with increasing severity of disease. Stage I generally denotes cancers that are smaller or less deeply invasive with negative nodes; Stage II and III define cases with increasing tumor or nodal extent, and Stage IV identifies those who present with distant metastases (M1) at diagnosis. In addition, the term Stage 0 is used to denote carcinoma in situ with no metastatic potential. Stage 0 is almost always determined by pathologic examination.

The primary TNM groupings are purely clinical or pathologic. However, in clinical medicine, it is often expedient to combine clinical and pathologic T, N, and M information to define a mixed stage group for treatment planning. An example of a clinical situation where such "mixed staging" is used clinically is a woman with breast cancer who has had the primary tumor resected providing pathologic T, but for whom there was no lymph node surgery, requiring use of the clinical N. The mixed stage combining clinical and pathologic information is sometimes referred to as *working stage*. However, pure clinical and pathologic stage is still defined for comparative purposes. In addition, clinical M status (M0 or M1) may be mixed with pathologic T and N information to define pathologic stage, and the classification pTis cN0 cM0 may be used to define both clinical and pathologic stage for in situ carcinoma. If there is pathologic evidence of metastases (pM1), it may be used with clinical T and N information to define clinical Stage IV and pathologic Stage IV.

The grouping recommendations in this manual are based primarily on anatomic information. Anatomic extent of disease is supplemented by selected nonanatomic prognostic factors in some disease sites. To denote the significance of this selective use of nonanatomic factors and to underscore the importance of anatomic information, the title of the groupings in the *AJCC Cancer Staging Manual* has been changed to "*Anatomic Stage/Prognostic Groups*."

Recording Cancer Stage in the Medical Record. All staging classifications, and most importantly clinical and pathologic T, N, and M and stage grouping, should be recorded in the medical record. Clinical stage is used in defining primary therapy (including surgery if surgery is performed), and when surgery is the initial treatment, subsequent systemic or radiation treatment is based on the pathologic stage. Recording clinical stage is also important because it may be the only common denominator among all cancers of a certain anatomic site and histology. Examples include lung cancer, advanced GI tumors, and head and neck cancers where surgery may not be performed, as well as cancers such as prostate cancer and others where surgical resection for limited disease may be omitted. In such scenarios, it may be impossible to compare cases where information is only obtained by clinical means with those where surgical resection is performed. For this reason, clinical stage remains an important component of application of the TNM staging system. This was reinforced in 2008 by the American College of Surgeons Commission on Cancer in its cancer program standards with the requirement that clinical stage be recorded in all cases.

There are many options for recording staging data in the medical record. These include documenting in the initial clinical evaluations, operative reports, discharge summaries, and follow-up reports. Physicians are encouraged to enter the stage of cancer in every record of clinical encounters with the cancer patient. In addition, a paper or electronic staging form may be useful to record stage in the medical record as well as to facilitate communication of staging data to a cancer registry. A simple form for collecting staging data is included for each disease site in this manual.

The Cancer Registry and the Collaborative Stage Data Collection System. Recording stage information in a cancer registry allows analysis of treatment effects and longitudinal population studies. Traditionally registries recorded the staging data provided in the medical record or on a staging form by the physician. With the increasing complexity of staging, the potential to incorporate various nonanatomic factors into staging algorithms, and the need to coordinate staging data collection for hospital- and population-based central registries, there was a need for a more standardized data collection tool for staging data. Such a system, termed the Collaborative Stage Data Collection System (CS), was developed by the AJCC and its cancer surveillance and staging partner organizations and implemented in cancer registries in the USA in 2004. It has also been implemented in parts of Canada with the expectation to implement throughout Canada by 2012.

In the CS system, T, N, and M data plus selected nonanatomic factors are recorded and a computer-based algorithm derives TNM stage as defined in the *AJCC Cancer Staging Manual*. The stage derivation uses the nonanatomic factors if they are available and derives a pure anatomic stage if they are not. In addition, the CS algorithm derives Summary Stage 1977 and 2000. In the CS system, the primary data defining T, N, and M are collected and stored in local registries and transmitted to central registries. T is derived from the size and local extension of disease, N from data elements that describe node status and the number of examined and positive nodes,

and M from an element that records the presence or absence of metastases. In addition, the CS system includes "site-specific factors" used to record information beyond the anatomic extent of disease. There are two types of site-specific factors: those that are required for deriving the "Anatomic Stage/Prognostic Group" (e.g., Gleason's Score in prostate cancer) and those that are key prognostic or predictive factors for a given disease (e.g., estrogen receptor and HER2/neu status in breast cancer). Anatomic stage/prognostic groups are calculated from the T, N, and M and relevant site-specific factors. Collaborative stage does not assign a "c" or "p" to the stage grouping but only to the TNM elements. The CS system-derived groups are not necessarily purely clinical or pathologic TNM groups, but represent the best stage that combines clinical and pathologic data.

Importantly, the CS system stores the primary data in an interoperable tagged format that may be exported for other purposes including application in prognostic models and nomograms and for research into new prognostic models. The data elements that are collected in the Collaborative Stage Data Collection System are shown in Table 1.2.

The Collaborative Stage Data Collection System has been revised to accommodate this seventh edition of the *AJCC Cancer Staging Manual.* Key revisions are expansion of the site-specific factors to accommodate added prognostic factors and additional data elements necessary to record the clinical stage used for all cases, and the yp stage after neoadjuvant therapy. This will collect information on pretreatment clinical stage prior to the initiation of therapy and the posttreatment pathologic stage (yp) after completion of neoadjuvant therapy in patients who have resection. Detailed information on the CS system and current CS data element standards is available at http://www.cancerstaging.org.

TABLE 1.2. Collaborative stage data collection system data elements

Tumor	CS tumor size (primary tumor size in mm)
	CS extension (direct extension of the primary tumor)
	CS tumor size/extension eval (method of evaluating T)[a]
Nodes	CS lymph nodes (regional lymph node involvement)
	CS lymph nodes eval (method of evaluating N)[a]
	Regional nodes positive (number nodes positive)
	Regional nodes examined (number nodes examined)
Metastases	CS Mets at Dx (distant metastases present at time of diagnosis
	CS Mets Eval (method of evaluating M)[a]
Site-specific factors	CHS site-specific factors (specific number defined by disease)[b]

[a] Method of evaluation fields: Define source of data – clinical (c) or pathologic (p); response to neoadjuvant therapy utilizing pathologic information (yp).

[b] Site-specific factors: Additional items necessary for (a) defining cancer stage group or (b) key prognostic factors including anatomic disease modifiers and nonanatomic factors (e.g., grade and tumor markers). Most disease sites use only a few of the available site-specific factor fields.

These tumor, node, and metastases fields for best stage are duplicated as needed for pretreatment and posttreatment stages.

For full description of Collaborative Stage Data Collection System, see http://www.cancerstaging.org/cstage/index.html.

NOMENCLATURE OF THE MORPHOLOGY OF CANCER

Cancer treatment requires assessment of the extent and behavior of the tumor and the status of the patient. The most widely used is TNM based on documentation of the anatomic extent of the cancer and selected related nonanatomic factors. The description of the anatomic factors is specific for each disease site. These descriptors and the nomenclature for TNM have been developed and refined over many editions of the *AJCC Cancer Staging Manual* by experts in each disease and cancer registrars who collect the information, taking into consideration the behavior and natural history of each type of cancer.

An *accurate microscopic diagnosis* is essential to the evaluation and treatment of cancer. The histologic and morphologic characteristics of tumors are generally reported by expert pathologists. This is best accomplished using standardized nomenclature in a structured report such as the synoptic reports or cancer protocols defined by the College of American Pathologists (CAP). In addition, for some cancers measurements of other factors including biochemical, molecular, genetic, immunologic, or functional characteristics of the tumor or normal tissues have become important or essential elements in classifying tumors precisely. Techniques that supplement standard histological evaluation including immunohistochemistry, cytogenetics, and genetic characterization are used to characterize tumors and their potential behavior and response to treatment.

Related Classifications. In the interest of promoting international collaboration in cancer research and to facilitate comparison of data among different clinical studies, use of the *WHO International Classification of Tumours* for classification and definition of tumor types, the *International Classifications of Diseases for Oncology* (*ICD-0*) codes for storage and retrieval of data, CAP protocols for pathology reporting of cancer pathology specimens, and the Collaborative Stage Data Collection System for collecting staging data is recommended. Given here is a summary of relevant related classification and coding systems with source citations.

- *World Health Organization Classification of Tumours, Pathology and Genetics.* Since 1958, the World Health Organization (WHO) has had a program aimed at providing internationally accepted criteria for the histological classification of tumors. The most recent edition is a ten-volume series that contains definitions, descriptions, and illustrations of tumor types and related nomenclature (WHO: World Health Organization Classification of Tumours. Various editions. Lyon, France: IARC Press, 2000–2008).
- *WHO International Classification of Diseases for Oncology* (*ICD-0*), *3rd edition.* ICD-0 is a numerical classification and coding system by topography and morphology (WHO: ICD-O-3 International Classification of Diseases for Oncology. 3rd ed. Geneva: WHO, 2000).

- *Systematized Nomenclature of Medicine* (*SNOMED*). Published by the CAP, SNOMED provides tumor classification systems compatible with the ICD-O system (http://snomed.org).
- *Collaborative Stage Data Collection System*. This system for collecting cancer staging data was developed through a collaboration of the AJCC and other standard setting organizations. Primary data are recorded on the size and extension of the primary tumor, the status of lymph nodes, and presence of distant metastases and certain "site-specific factors." These data are used to derive TNM stage and Summary Stage (http://www.cancerstaging.org/cstage/index.html).
- *CAP Cancer Protocols*. The CAP publishes standards for pathology reporting of cancer specimens for all cancer types and cancer resection types. These specify the elements necessary for the pathologist to report the extent and characteristics of cancer specimens. These elements are being coordinated with the *Collaborative Stage Data Collection System* to allow direct reporting of pathology elements to cancer registries (http://www.cap.org).
- *caBIG*. The National Cancer Institute of the USA has developed the Cancer Bioinformatics Grid (caBIG) to standardize data elements and integration of these elements for the reporting of information for clinical trials and to annotate biological specimens (http://cabig.cancer.gov).
- *Atlas of Tumor Pathology*. A comprehensive and well-known English language compendium of the macroscopic and microscopic characteristics of tumors and their behavior is the *Atlas of Tumor Pathology* series, published in many volumes by the Armed Forces Institute of Pathology in Washington, DC. These are revised periodically and are used as a basic reference by pathologists throughout the world (*Atlas of Tumor Pathology*, 3rd edition series. Washington, DC: Armed Forces Institute of Pathology, 1991–2002).
- *American College of Radiology Appropriateness Criteria*. The American College of Radiology maintains guidelines and criteria for use of imaging and interventional radiology procedures for many aspects of cancer care. This includes the extent of imaging testing that is recommended for the diagnostic evaluation of the extent of disease of the primary tumor, nodes, and distant metastases in a number of cancer types. The ACR appropriateness criteria are updated regularly (http://www.acr.org/ac).
- *Practice Guidelines of the National Comprehensive Cancer Network* (*NCCN*). The NCCN provides practice guidelines for most types of cancers. These guidelines are updated at least annually. They include recommendations for diagnostic evaluation and imaging for the primary tumor and screening for metastases for each cancer type that may be useful to guide staging (http://www.nccn.org).

GENERAL RULES FOR TNM STAGING

The TNM system classifies and groups cancers primarily by the anatomic extent of the primary tumor, the status of regional draining lymph nodes, and the presence or absence of distant metastases. The system is in essence a shorthand notation for describing the clinical and pathologic anatomic extent of a tumor. In addition, the AJCC recommends collection of key prognostic factors that either are used to define groupings or are critical to prognosis or defining patient care.

T The T component is defined by the size or contiguous extension of the primary tumor. The roles of the size component and the extent of contiguous spread in defining T are specifically defined for each cancer site.

N The N component is defined by the absence, or presence and extent of cancer in the regional draining lymph nodes. Nodal involvement is categorized by the number of positive nodes and for certain cancer sites by the involvement of specific regional nodal groups.

M The M component is defined by the absence or presence of distant spread or metastases, generally in locations to which the cancer spread by vascular channels, or by lymphatics beyond the nodes defined as "regional."

For each of T, N, and M the use of increasing values denotes progressively greater extent of the cancer as shown later. For some disease sites, subdivisions of the main designators are used to provide more specific prognostic information (e.g., T1mi, T1a, T1b, T1c or N2a, N2b in breast cancer or M1a, M1b, M1c for prostate cancer). Specific definitions for each cancer type are provided in the respective chapters. General designators for T, N, and M are shown later and general rules for applying these designators are shown in the tables. For each designator, the prefix of c, p, yc, yp, r, or a may be applied to denote the classification of stage (see later):

Primary Tumor (T)	
T0	No evidence of primary tumor
Tis	Carcinoma in situ
T1, T2, T3, T4	Increasing size and/or local extension of the primary tumor
TX	Primary tumor cannot be assessed (use of TX should be minimized)

Regional Lymph Nodes (N)	
N0	No regional lymph node metastases
N1, N2, N3	Increasing number or extent of regional lymph node involvement
NX	Regional lymph nodes cannot be assessed (use of NX should be minimized)

Distant Metastasis (M)

M0	No distant metastases
M1	Distant metastases present

Note: The MX designation has been eliminated from the AJCC/UICC TNM system.

The M1 category may be further specified according to the following notation signifying the location of metastases:

Pulmonary	PUL
Osseous	OSS
Hepatic	HEP
Brain	BRA
Lymph nodes	LYM
Bone marrow	MAR
Pleura	PLE
Peritoneum	PER
Adrenal	ADR
Skin	SKI
Other	OTH

Nonanatomic Prognostic Factors Required for Staging. In some cancer types, nonanatomic factors are required for assigning the anatomic stage/prognostic group. These are clearly defined in each chapter. These factors are collected separately from T, N, and M, which remain purely anatomic, and are used to assign stage groups. Where nonanatomic factors are used in groupings, there is a definition of the groupings provided for cases where the nonanatomic factor is not available (X) or where it is desired to assign a group ignoring the nonanatomic factor.

Use of the Unknown X Designation. The X category is used when information on a specific component is unknown. Cases where T or N is classified as X cannot be assigned a stage (an exception is *Any T* or *Any N M1*, which includes TX or NX, classified as Stage IV – e.g., TX NX M1 or TX N3 M1 are Stage IV). Therefore, the X category for T and N should be used only when absolutely necessary.

The category MX has been eliminated from the AJCC/UICC TNM system. Unless there is clinical or pathologic evidence of distant metastases, the case is classified as clinical M0 (cM0). Because of the requirement for pathologists to assign TNM on cancer pathology reports, and because the pathologist often does not have information to assign M, the CAP has dropped the M component from pathology templates to further discourage use of MX. The elimination of the code MX is a change in the seventh edition of the *AJCC Cancer Staging Manual* and *UICC TNM Cancer Staging Manual*. See later for rules for M classification.

The following general rules apply to application of T, N, and M for all sites and classifications (Table 1.3):

1. Microscopic confirmation: All cases should be confirmed microscopically for classification by TNM (including clinical classification). Rare cases that do not have any biopsy or cytology of the tumor can be staged, but survival should be analyzed separately. These cases should not be included in overall disease survival analyses.

TABLE 1.3. General rules for TNM staging

General rules for staging	
Microscopic confirmation	Microscopic confirmation required for TNM classification
	Rare cases without microscopic confirmation should be analyzed separately
	Cancers classified by ICD-O-3
	Recommend pathology reporting using CAP cancer protocols
Timing of data eligible for clinical staging	Data obtained before definitive treatment as part of primary treatment or within 4 months of diagnosis, whichever is shorter
	The time frame for collecting clinical stage data also ends when a decision is made for active surveillance ("watchful waiting") without therapy
Timing data eligible for pathologic staging	Data obtained through definitive surgery as part of primary treatment or within 4 months of diagnosis, whichever is longer
Timing of data eligible for staging with neoadjuvant therapy	Stage in cases with neoadjuvant therapy is (a) clinical as defined earlier before initiation of therapy and (b) clinical or pathologic using data obtained after completion of neoadjuvant therapy (ycTNM or ypTNM)
Staging in cases with uncertainty among T, N, or M categories	Assign the lower (less advanced) category of T, N, or M, prognostic factor, or stage group
Absence of staging-required nonanatomic prognostic factor	Assign stage grouping by the group defined by the lower (less advanced) designation for that factor
Multiple synchronous primary tumors in single organ	Stage T by most advanced tumor; use "m" suffix or the number of tumors in parentheses, e.g., pT3(m)N0M0 or pT3(4)N0M0
Synchronous primary tumors in paired organs	Stage and report independently
Metachronous primary tumors in single organ (not recurrence)	Stage and report independently
T0 staging – unknown primary	Stage based on clinical suspicion of primary tumor (e.g., T0 N1 M0 Group IIA breast cancer)

2. Eligible time period for determination of staging:
   a. *Clinical staging* includes any information obtained about the extent of cancer before initiation of definitive treatment (surgery, systemic or radiation therapy, active surveillance, or palliative care) or within 4 months after the date of diagnosis, whichever is *shorter*, as long as the cancer has not clearly progressed during that time frame.
   b. *Pathologic staging* includes any information obtained about the extent of cancer up through completion of definitive surgery as part of first course treatment or identified within 4 months after the date of diagnosis, whichever is *longer*, as long as there is no systemic or radiation therapy initiated or the cancer has not clearly progressed during that time frame.
3. Staging with neoadjuvant or primary systemic or radiation therapy: Cases with neoadjuvant, or primary systemic or radiation, therapy may have a second stage defined from information obtained after therapy that is recorded using a yc or yp prefix (ycTNM or ypTNM; y must always be modified as yc or yp). However, these patients should also have clinical stage recorded as this is the stage used for comparative purposes. Clinical stage includes only information collected prior to the start of treatment.
4. Progression of disease: In cases where there is documented progression of cancer prior to the initiation of therapy or surgery, only information obtained prior to documented progression is used for staging.
5. If uncertain, classify or stage using the lower category: If there is uncertainty in assigning a T, N, or M classification, a stage modifying factor (i.e., in clinical situations where it is unclear if the lymph nodes are N2 or N1), or anatomic stage/prognostic group, default to the lower (lesser) of the two categories in the uncertain range.
6. Nonanatomic factor not available: If a nonanatomic factor required for grouping is not available, the case is assigned to the group assuming that factor was the lowest or least advanced (e.g., lower Gleason's score in prostate cancer).

Stage Classifications. Five stage classifications may be described for each site (Table 1.4):

- Clinical stage/pretreatment stage, designated as cTNM or TNM
- Pathologic stage, designated as pTNM
- Post therapy or postneoadjuvant therapy stage, designated as ycTNM or ypTNM
- Retreatment or recurrence classification, designated as rTNM
- Autopsy classification, designated as a TNM

Clinical Classification. Clinical classification is based on evidence acquired before the initiation of primary treatment (definitive surgery, or neoadjuvant radiation or systemic therapy). The clinical stage (pretreatment stage) is essential to selecting primary therapy. In addition, the clinical stage is critical for comparison of groups of cases because differences in the use of primary therapy may make such comparisons based on pathologic assessment impossible, such as in situations where some patients are treated with primary surgery and others are treated with neoadjuvant chemotherapy or with no therapy.

Clinical assessment uses information available from clinical history, physical examination, imaging, endoscopy, biopsy of the primary site, surgical exploration, or other relevant examinations. Observations made at surgical exploration where a biopsy of the primary site is performed without resection or where pathologic material is not obtained are classified as clinical, unless the biopsy provides pathologic material on the highest possible T category in which case it is classified at pT (see pathologic staging later). Pathologic examination of a single node in the absence of pathologic evaluation of the primary tumor is classified as clinical (cN) (e.g., if sentinel node biopsy is performed prior to neoadjuvant therapy in breast cancer). Extensive imaging is not necessary to assign clinical classifications. Guides to the generally accepted standards for diagnostic evaluations of individual cancer types include the American College of Radiology Appropriateness Standards (http://www.acr.org/ac) and the NCCN Practice Guidelines (http://www.nccn.org).

TABLE 1.4. Staging classifications

Classification	*Data source*	*Usage*
Clinical (pretreatment) (cTNM)	Diagnostic data including symptoms, physical examination, imaging, endoscopy; biopsy of primary site; resection of single node/sentinel node(s) with clinical T; surgical exploration without resection; other relevant examinations	Define prognosis and initial therapy Population comparisons
Pathologic (pTNM)	Diagnostic data and data from surgical resection and pathology	Most precise prognosis estimates Define subsequent therapy
Post therapy (ycTNM or ypTNM)	Clinical and pathologic data after systemic or radiation before surgery or as primary therapy denoted with a yc (clinical) or yp (pathologic) prefix	Determine subsequent therapy Identify response to therapy
Retreatment (rTNM)	Clinical and pathologic data at time of retreatment for recurrence or progression	Define treatment
Autopsy (aTNM)	Clinical and pathologic data as determined at autopsy	Define cancer stage on previously undiagnosed cancer identified at autopsy

The clinical (pretreatment) stage assigned on the basis of information obtained prior to cancer-directed treatment is not changed on the basis of subsequent information obtained from the pathologic examination of resected tissue or from information obtained after initiation of definitive therapy. In the case of treatment with palliative care or active surveillance (watchful waiting), the information for staging is that defined prior to making the decision for no active treatment or that which occurs within 4 months of diagnosis, whichever is shorter. Any information obtained after the decision for active surveillance or palliative care may not used in clinical staging. Classification of T, N, and M by clinical means is denoted by use of a lower case c prefix (cT, cN, cM).

Clinical staging of metastases warrants special consideration. A case where there are no symptoms or signs of metastases is classified as clinically M0. There is no MX classification. The only evaluation necessary to classify a case as clinically M0 is history and physical examination. It is not necessary to do extensive imaging studies to classify a case as clinically M0. The optimal extent of testing required in many cancer types is provided in guidelines of the American College of Radiology Appropriateness Criteria (http://www.acr.org/ac) and in the National Comprehensive Cancer Network practice guidelines (http://www.nccn.org). The classification pM0 does not exist and may not be assigned on the basis of a negative biopsy of a suspected metastatic site. Cases with clinical evidence of metastases by examination, invasive procedures including exploratory surgery, and imaging, but without a tissue biopsy confirming metastases are classified as cM1. If there is a positive biopsy of a metastatic site (pM1) and T and N are staged only clinically, then the case may be staged as clinical and pathologic Stage IV.

Pathologic Classification. The pathologic classification of a cancer is based on information acquired before treatment supplemented and modified by the additional evidence acquired during and from surgery, particularly from pathologic examination of resected tissues. The pathologic classification provides additional precise and objective data. Classification of T, N, and M by pathologic means is denoted by use of a lower case p prefix (pT, pN, pM).

Pathologic T. The pathologic assessment of the *primary tumor* (*pT*) generally is based on resection of the primary tumor generally from a single specimen (Table 1.5). Resection of the tumor with several partial removals at the same or separate operations necessitates an effort at reasonable estimates of the size and extension of the tumor to assign the correct or highest pT category. Tumor size should be recorded in whole millimeters. If the size is reported in smaller units such as a tenth or hundredth of a millimeter, it should be rounded to the nearest whole millimeter for reporting stage. Rounding is performed as follows: one through four are rounded down, and five through nine are rounded up. For example, a breast tumor reported as 1.2 mm in size should be recorded for staging as a 1-mm tumor, and a 1.7-mm tumor should be recorded as a 2-mm tumor. If the tumor is not resected, but a biopsy of the primary tumor is performed that is adequate to evaluate the highest pT category, the pT classification is assigned. Some disease sites have specific rules to guide assignment of pT category in such cases.

TABLE 1.5. T classification rules

T determined by site-specific rules based on size and/or local extension
Clinical assessment of T (cT) based on physical examination, imaging, endoscopy, and biopsy and surgical exploration without resection
Pathologic assessment of T (pT) entails a resection of the tumor or may be assigned with biopsy only if it assigns the highest T category
pT generally based on resection in single specimen. If resected in >1 specimen, make reasonable estimate of size/extension. Disease-specific rules may apply
Tumor size should be recorded in whole millimeters. If the size is reported in smaller units such as a tenth or hundredth of a millimeter, it should be rounded to the nearest whole millimeter for reporting stage. Rounding is performed as follows: one through four are rounded down, and five through nine are rounded up
If not resected, and highest T and N category can be confirmed microscopically; case may be classified by pT or pN without resection

Pathologic N. The pathologic assessment of *regional lymph nodes* (*pN*) ideally requires resection of a minimum number of lymph nodes to assure that there is sufficient sampling to identify positive nodes if present (Table 1.6). This number varies among diseases sites, and the expected number of lymph nodes is defined in each chapter. The recommended number generally does not apply in cases where sentinel node has been accepted as accurate for defining regional node involvement and a sentinel node procedure has been performed. However, in cases where lymph node surgery results

TABLE 1.6. N classification rules

Categorize N by disease-specific rules based on number and location of positive regional nodes
Minimum expected number and location of nodes to examine for staging defined by disease type
If lymph node surgery is performed, classify N category as pathologic even if minimum number is not examined
Pathologic assessment of the primary tumor (pT) is necessary to assign pathologic assessment of nodes (pN) except with unknown primary (T0). If pathologic T (pT) is available, then any microscopic evaluation of nodes is pN
In cases with only clinical T in the absence of pT excision of a single node or sentinel node(s) is classified as clinical nodal status (cN)
Microscopic examination of a single node or nodes in the highest N category is classified as pN even in the absence of pathologic information on other nodes
Sentinel lymph node biopsy is denoted with (sn), e.g., pN0(sn); pN1(sn)
Lymph nodes with ITC only generally staged as pN0; disease-specific rules may apply (e.g., melanoma)
Direct extension of primary tumor into regional node classified as node positive
Tumor nodule with smooth contour in regional node area classified as positive node
When size is the criterion for N category, stage by size of metastasis, not size of node when reported (unless specified in disease-specific rules)

in examination of fewer than the ideal minimum number, the N category is still generally classified as pathologic N according to the number of positive nodes and/or location of the most advanced pathologic node resected. At least one node with presence or absence of cancer documented by pathologic examination is required for pathologic staging N. The impact of use of pathologic N classification with fewer than the minimum resected nodes may be subsequently defined by review of the number of resected nodes as recorded in a cancer registry.

Pathologic assessment of T (pT) is generally necessary to assign pathologic assessment of lymph nodes. In conjunction with pT, it is not necessary to have pathologic confirmation of the status of the highest N category to assign pN. However, if N is based on microscopic confirmation of the highest N category, it is pN regardless of whether T is pT or cT. For example, in the case of breast cancer with pT defined by resection, pN may be assigned solely on the basis of resected level I or II nodes, or a level I sentinel node without biopsy of level III or supraclavicular nodes. However, if there is microscopic confirmation of supraclavicular node involvement, the case may also be classified as pN3.

Specialized pathologic techniques such as immunohistochemistry or molecular techniques may identify limited metastases in lymph nodes that may not have been identified without the use of the special diagnostic techniques. Single tumor cells or small clusters of cells are classified as *isolated tumor cells* (ITC). The standard definition for ITC is a cluster of cells not more than 0.2 mm in greatest diameter. The appropriate N classification for cases with nodes only involved by ITC's is defined in the disease site chapters for those cancers where this commonly occurs. In most of such chapters, these cases with ITC only in lymph nodes or distant sites are classified as pN0 or cM0. This rule also generally applies to cases with findings of tumor cells or their components by nonmorphologic techniques such as flow cytometry or DNA analysis. There are specific designators to identify such cases by disease site [e.g., N0 (i+) in breast cancer to denote nodes with ITC only].

Pathologic M. The pathologic assignment of the presence of *metastases* (*pM1*) requires a biopsy positive for cancer at the metastatic site (Table 1.7). Pathologic M0 is an undefined concept and the category pM0 may not be used. Pathologic classification of the absence of distant metastases can only be made at autopsy. However, the assessment of metastases to group a patient by pathologic TNM groupings may be either clinical (cM0 or cM1) or pathologic (pM1) (e.g., pTNM = pT; pN; cM or pM). Cases with a biopsy of a possible metastatic site that shows ITC such as circulating tumor cells (CTCs) or disseminated tumor cells (DTCs), or bone marrow micrometastases detected by IHC or molecular techniques are classified as cM0(i+) to denote the uncertain prognostic significance of these findings and to classify the stage group according to the T and N and M0.

Pathologic staging depends on the proven anatomic extent of disease, whether or not the primary lesion has been completely removed. If a primary tumor cannot be technically removed, or when it is unreasonable to remove it, and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary tumor. Note that microscopic confirmation of the highest T and N does not necessarily require removal of that structure and may entail biopsy only.

TABLE 1.7. M classification rules

Clinical M classification only requires history and examination
Imaging of distant organ sites not required to assign cM0
Infer status as clinical M0 status unless known clinical M1
"MX" is not a valid category and may not be assigned
Elimination of "MX" is new with AJCC/UICC, 7th edition
Pathologic M classification requires a positive biopsy of the metastatic site (pM1)
Pathologic M0 ("pM0") is not a valid category and may not be assigned
Stage a case with a negative biopsy of suspected metastatic site as cM0
Case with pathologic T and N may be grouped as pathologic TNM using clinical M designator (cM0 or cM1) (e.g., pT1 pN0 cM0 = pathologic stage I)
Case with pathologic M1 (pM1) may be grouped as clinical and pathologic Stage IV regardless of "c' or "p" status of T and N (e.g., cT1 cN1 pM1 = clinical or pathologic stage IV)
ITC in metastatic sites (e.g., bone marrow)
Or circulating or DTCs classified as cM0(i+)
Disease-specific rules may apply

Posttherapy or Postneoadjuvant Therapy Classification (yTNM). Cases where systemic and/or radiation therapy are given before surgery (*neoadjuvant*) or where no surgery is performed may have the extent of disease assessed at the conclusion of the therapy by clinical or pathologic means (if resection performed). This classification is useful to clinicians because the extent of response to therapy may provide important prognostic information to patients and help direct the extent of surgery or subsequent systemic and/or radiation therapy. T and N are classified using the same categories as for clinical or pathologic staging for the disease type, and the findings are recorded using the prefix designator y (e.g., ycT; ycN; ypT; ypN). The yc prefix is used for the clinical stage after therapy, and the yp prefix is used for the pathologic stage for those cases that have surgical resection after neoadjuvant therapy. Both the ycTNM and ypTNM may be recorded in the medical record, though cancer registries will in general only record the ypTNM in cases where surgery is performed. The M component should be classified by the M status defined clinically or pathologically prior to therapy. If a biopsy of a metastatic site is positive, the case is classified as clinical and pathologic Stage IV. The estimate of disease prior to therapy is recorded using the clinical designator as described earlier (cTNM). The stage used for case comparisons and population purposes in these cases should be the clinical (cTNM) one.

Retreatment Classification. The retreatment classification (rTNM) is assigned when further treatment is planned for a cancer that recurs after a disease-free interval. The original stage assigned at the time of initial diagnosis and treatment does not change when the cancer recurs or progresses. The use of this staging for retreatment or recurrence is denoted using the r prefix (rTNM). All information available at the time of retreatment should be used in determining the rTNM stage. Biopsy confirmation of recurrent cancer is important if clinically feasible. However, this may not be appropriate for each component, so clinical evidence for the T, N, or M component by clinical, endoscopic, radiologic, or related methods may be used.

Autopsy Classification. TNM classification of a cancer may be performed by postmortem examination for a patient where cancer was not evident prior to death. This autopsy classification (aTNM) is denoted using the a prefix (aTNM) and should include all clinical and pathologic information obtained at the time of death and autopsy.

Stage Groupings. Cases of cancers with similar prognosis are grouped based on the assigned cT, cN, and cM and/or pT, pN and c/pM categories, and disease-specific groups of T, N, and M are defined. In select disease sites nonanatomic factors are required to supplement T, N, and M to define these groups. Termed *anatomic stage/prognostic groups*, and commonly referred to as stage groups, these form a reproducible and easily communicated summary of staging information (Table 1.8).

Groups are assigned increasing values that correlate with worsening prognosis. Stage I is usually assigned to tumors confined to the primary site with a better prognosis, stages II and III for tumors with increasing local and regional nodal involvement, and stage IV to cases with distant metastatic disease. In addition, a group termed stage 0 is assigned to cases of carcinoma in situ (CIS). Groupings may be expanded into subsets (e.g., stage II can become stage IIA, stage IIB) for more refined prognostic information.

TABLE 1.8. Anatomic stage/prognostic grouping rules

Define separate clinical and pathologic group for each case
May combine clinical and pathologic information as a "working stage" in either the pathologic or clinical classification when only partial information is available – this may be necessary for clinical care
Minimize use of TX and NX
Use of "X" for any component makes case unstageable
Case will not be usable in comparison analyses (exception: any combination of T and N including TX or NX with M1 is stage IV)
For groupings that require a nonanatomic factor, if factor is missing, stage using lowest category for that factor
Case with pT and pN and cM0 or cM1 staged as pathologic stage group
Case with cT and cN and pM1 staged as clinical and pathologic stage group
Carcinoma in situ, stage pTis cN0 cM0 as both clinical and pathologic stage 0

Generally, a pure clinical group and pure pathologic group are defined for each case, using the classifications discussed earlier. In the clinical setting, it is appropriate to combine clinical and pathologic data when only partial information is available in either the pathologic or clinical classification, and this may be referred to as the *working* stage.

Carcinoma in situ (CIS) is an exception to the stage grouping guidelines. By definition, CIS has not involved any structures in the primary organ that would allow tumor cells to spread to regional nodes or distant sites. Therefore, pTis cN0 cM0 should be reported as both clinical and pathologic stage 0.

The clinical, pathologic, and if applicable, posttherapy and retreatment, groups are recorded in the medical record. Once assigned according to the appropriate rules and timing, the stage group recorded in the medical record does not change. The rule applied to T, N, or M that in cases with uncertainty about the classification the cases are assigned the lower (less advanced) category also applies to grouping. One specific circumstance requires special comment. When there has been a complete pathologic response and the ypTNM is ypT0 ypN0 cM0, this is not a "stage 0" case as this would denote in situ disease, and as in every case, the stage for comparison of cases is the pretreatment clinical stage.

Multiple Tumors. When there are multiple simultaneous tumors of the same histology in one organ, the tumor with the highest T category is the one selected for classification and staging, and the multiplicity or the number of tumors is indicated in parentheses: for example, T2(m) or T2(5). For simultaneous bilateral cancers in paired organs, the tumors are classified separately as independent tumors in different organs. For tumors of the thyroid, liver, and ovary, multiplicity is a criterion of the T classification. Most registry software systems have a mechanism to record the m descriptor.

Metachronous Primaries. Second or subsequent primary cancers occurring in the same organ or in different organs are staged as a new cancer using the TNM system described in this manual. Second cancers are not staged using the y prefix unless the treatment of the second cancer warrants this use.

Unknown Primary. In cases where there is no evidence of a primary tumor or the site of the primary tumor is unknown, staging may be based on the clinical suspicion of the primary tumor with the T category classified as T0. For example, a case with metastatic adenocarcinoma in axillary lymph nodes that is pathologically consistent with breast cancer, but in which there is no apparent primary breast tumor may be classified as breast cancer – T0 N1 M0 (Table 1.9).

HISTOPATHOLOGIC TYPE, GRADE, AND OTHER DESCRIPTORS

Histopathologic Type. The histopathologic type is a *qualitative* assessment whereby a tumor is categorized according to the normal tissue type or cell type it most closely resembles

TABLE 1.9. Special classification/designator rules

ycTNM or ypTNM	Posttherapy classification: "y" prefix to utilize with "c" or "p" for denoting extent of cancer after neoadjuvant or primary systemic and/or radiation therapy	Assess clinical stage prior to initiation of therapy (cTNM)
		Use cTNM for comparison of cases and population surveillance
		Denote posttherapy T and N stage using "y" prefix – ycT; ycN; ypT; ypN
		yc is used for clinical information postprimary therapy systemic or radiation therapy, or postneoadjuvant therapy before surgery
		yp is used for pathologic postneoadjuvant systemic or radiation therapy followed by surgical resection
		Use clinical/pretreatment M status
r TNM	Retreatment classification	The original stage assigned at initial diagnosis and treatment should not be changed at the time of recurrence or progression
		Assign for cases where treatment is planned for cancer that recurs after a disease-free interval
		Use all information available at time of retreatment or recurrence (c or p)
		Biopsy confirmation desirable if feasible, but not required
a TNM	Autopsy classification	Applied for cases where cancer is not evident prior to death
		Use all clinical and pathologic information obtained at the time of death and at postmortem examination
m suffix	Multiple primary tumors	Multiple simultaneous tumors in one organ: Assign T by the tumor with the highest T category. Indicate multiplicity by "(m)" or "(number)" in parentheses – e.g., T2(m) or T2(5)

(e.g., hepatocellular or cholangiocarcinoma, osteosarcoma, squamous cell carcinoma). The *World Health Organization Classification of Tumours* published in numerous anatomic site-specific editions may be used for histopathologic typing. Each chapter in the *AJCC Cancer Staging Manual* includes the applicable ICD-O-3 histopathologic codes expressed as individual codes or ranges of codes. If a specific histology is not listed, the case should not be staged using the AJCC classification in that chapter.

Grade. The grade of a cancer is a qualitative assessment of the degree of differentiation of the tumor. Grade may reflect the extent to which a tumor resembles the normal tissue at that site. Historically, histologic stratification of solid tumors has been dominated by the description of differentiation with grade expressed as the overall histologic differentiation of the cancer in numerical grades from the most or well differentiated (grade 1) to the least differentiated (grade 3 or 4). This system is still used in some cancer types. For many cancer types, more precise and reproducible grading systems have been developed. These incorporate more specific and objective criteria based on single or multiple characteristics of the cancers. These factors include such characteristics as nuclear grade, the number of mitoses identified microscopically (mitotic count), measures of histologic differentiation (e.g., tubule formation in breast cancer), and others. For some cancer types these systems have been fully validated and largely implemented worldwide. Examples include the Gleason's scoring system for prostate cancer and the Scarff–Bloom–Richardson (Nottingham) grading system for breast cancer.

The recommended grading system for each cancer type is specified in the site-specific chapters. In general, when there is no specific grading system for a cancer type, it should be noted if a two-grade, three-grade, or four-grade system was used. For some anatomic sites, grade 3 and grade 4 are combined into a single grade – for example, poorly differentiated to undifferentiated (G3–4). The use of grade 4 is reserved for those tumors that show no specific differentiation that would identify the cancer as arising from its site of origin. In some sites, the WHO histologic classification includes undifferentiated carcinomas. For these, the tumor is graded as undifferentiated – grade 4. Some histologic tumor types are by definition listed as grade 4 for staging purposes but are not to be assigned a grade of undifferentiated in ICD-O-3 coding for cancer registry purposes. These include the following:

- Small cell carcinoma, any site
- Large cell carcinoma of lung
- Ewing's sarcoma of bone and soft tissue
- Rhabdomyosarcoma of soft tissue

The grade should be recorded for each cancer. Two data elements should be recorded: the grade and whether a two, three, or four-grade system was used for grading. If there is evidence of more than one grade of level or differentiation of the tumor, the least differentiated (highest grade) is recorded.

Residual Tumor and Surgical Margins. The absence or presence of residual tumor after treatment is described by the symbol R. cTNM and pTNM describe the extent of cancer in general without consideration of treatment. cTNM and pTNM can be supplemented by the R classification, which deals with the tumor status after treatment. In some cases treated with surgery and/or with neoadjuvant therapy there will be residual tumor at the primary site after treatment because of incomplete resection or local and regional disease that extends beyond the limit or ability of resection. The presence of residual tumor may indicate the effect of therapy, influence further therapy, and be

a strong predictor of prognosis. In addition, the presence or absence of disease at the margin of resection may be a predictor of the risk of recurrent cancer. The presence of residual disease or positive margins may be more likely with more advanced T or N category tumors. The R category is not incorporated into TMM staging itself. However, the absence or presence of residual tumor and status of the margins may be recorded in the medical record and cancer registry.

The absence or presence of residual tumor at the primary tumor site after treatment is denoted by the symbol R. The R categories for the primary tumor site are as follows:

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

The margin status may be recorded using the following categories:

- Negative margins (tumor not present at the surgical margin)
- Microscopic positive margin (tumor not identified grossly at the margin, but present microscopically at the margin)
- Macroscopic positive margin (tumor identified grossly at the margin)
- Margin not assessed

Lymph-Vascular Invasion. Indicates whether microscopic lymph-vascular invasion (LVI) is identified in the pathology report. This term includes lymphatic invasion, vascular invasion, or lymph-vascular invasion (synonymous with "lymphovascular").

ORGANIZATION OF THE *AJCC CANCER STAGING MANUAL* AND ANATOMIC SITES AND REGIONS

In general, the anatomic sites for cancer in this manual are listed by primary site code number according to the International Classification of Diseases for Oncology (ICD-O, third edition, WHO, 2000). Each disease site or region is discussed and the staging classification is defined in a separate chapter. There are a number of new chapters and disease sites in this seventh edition of the *AJCC Cancer Staging Manual.*

Each chapter includes a discussion of information relevant to staging that cancer type, the data supporting the staging, and the specific rationale for changes in staging. In addition, it includes definition of key prognostic factors including those required for staging and those recommended for collection in cancer registries. Each chapter ends with the specific definitions of T, N, M, site-specific factors, and anatomic stage/prognostic groups (Table 1.10).

TABLE 1.10. Chapter outline for the seventh edition of the *AJCC Cancer Staging Manual*

Staging at a Glance	Summary of anatomic stage/prognostic grouping and major changes
Changes in Staging	Table summarizing changes in staging from the 6th edition
Introduction	Overview of factors affecting staging and outcome for the disease
Anatomic Considerations	Primary tumor Regional lymph nodes Metastatic sites
Rules for Classification	Clinical Pathologic
Prognostic Features	Identification and discussion of nonanatomic prognostic factors important in each disease
Definitions of TNM	T: Primary tumor N: Regional lymph nodes M: Distant metastases
Anatomic Stage/ Prognostic Groups	
Prognostic Factors (Site-Specific Factors)	(a) Required for staging (b) Clinically significant
Grade	
Histopathologic Type	
Bibliography	
Staging Form	

Cancer Staging Data Form. Each site chapter includes a staging data form that may be used by providers and registrars to record the TNM classifications and the stage of the cancer. The form provides for entry of data on T, N, M, site-specific prognostic factors, cancer grade, and anatomic stage/prognostic groups. This form may be useful for recording information in the medical record and for communication of information from providers to the cancer registrar.

The staging form may be used to document cancer stage at different points in the course of therapy, including before the initiation of therapy, after surgery and completion of all staging evaluations, or at the time of recurrence. It is best to use a separate form at each point. If all time points are recorded on a single form, the staging basis for each element should be clearly identified.

The cancer staging form is a specific additional document in the patient records. It is not a substitute for documentation of history, physical examination, and staging evaluation, nor for documenting treatment plans or follow-up. The data forms in this manual may be duplicated for individual or institutional use without permission from the AJCC or the publisher. Incorporation of these forms into electronic record systems requires appropriate permission from the AJCC and the publisher.