Chapter 7: Staging and Classification

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History

The League of Nations Health Organization began the initial work on clinical classification of cancer in 1929. In 1943 Pierre Denoix of France initiated the TNM (tumor, node, metastases) system for classifying and staging malignant tumors. In 1950 the International Union Against Cancer (Union Internationale Contre le Cancer, UICC) appointed a Committee on Tumour Nomenclatures and Statistics and adopted as a basis for its work on clinical stage classification the general definitions of local extension of malignant tumors suggested by the World Health Organization (WHO) Subcommittee on the Registration of Cases of Cancer as well as Their Statistical Presentation. Meeting with the Committee on Stage-Grouping in Cancer and Presentation of the Results of Treatment of Cancer of the International Congress of Radiology in Copenhagen in 1953, the UICC reached agreement on a general technique for staging. In 1954 the Research Commission of the UICC set up a special Committee on Clinical Stage Classification and Applied Statistics under Dr Denoix to extend the general technique of classification to cover all site. Between 1954 and 1967 this committee published nine brochures describing classification, and in several cases clinical stage grouping, of 23 sites, including a separate paper outlining the rules of the TNM system (Union Internationale Contre le Cancer (UICC)), 1968). The committee recommended that for each site an initial 5-year trial period be undertaken.

In 1966 the UICC reorganized its committee structure, and the classification committee was renamed the Committee on TNM Classification. National committees on TNM classification were established in many countries. The most active of these was the American Joint Committee for Cancer Staging and End Result Reporting (COMBED), which was organized in 1959. This committee was formed for the purpose of developing a system of clinical staging of cancer by site that would be acceptable to the American medical profession (American Joint Committee (COMBED), 1977). The organizations sponsoring the committee (now called the American Joint Committee on Cancer - AJCC) including the American College of Surgeons, the American College of Radiology, the College of American Pathologists, the American College of Physicians, the American Cancer Society, and the National Cancer Institute. Each of the sponsoring organizations designates three members to the committee. The American College of Surgeons serves as the administrative sponsor. Subcommittees or task forces have been appointed to consider malignant neoplasms of selected anatomic sites to develop classifications.

In 1968 the UICC brochures were combined in a booklet, the *Livre de Poche*, which was published a year later, detailing recommendations for field trials, presentation of end results, and the determination and expression of cancer survival rates (UICC, 1968). The *Livre de Poche* was subsequently translated into 11 languages. The third edition, published in 1978 and revised in 1982, classifies and stages each of 31 cancer sites (Harmer, 1982).

The TNM committee of the UICC and the AJCC have been working along similar lines and with similar objectives, although their points of view and methods sometimes have differed. Cooperation between the two groups was necessary if internationally used

classification systems were to be agreed upon. Toward this goal, joint meetings of the UICC and AJCC were held regarding the classification for specific cancer sites, and the two groups agreed on a classification scheme (Baker, 1984). The recommendations of the AJCC in their revised Manual and the publications of the UICC in 1987 are identical (Beahrs et al, 1988). For the first time an international system for staging cancer is available.

Purpose of Classification and Staging

The practice of dividing cancer cases into groups according to stages arose because recovery or survival rates were higher for cases in which the disease was localized than for those in which the disease had extended beyond the site of origin. The stage of disease at the time of diagnosis is often a reflection of the rate of growth and extension of the neoplasm, the type of tumor, the tumor-host relationships, and the interval of time between the first symptom or sign noted by the patient and the time of diagnosis and treatment.

Staging of cancer is a traditional method of gathering groups of classified patients for the purpose of analysis. Recording accurate information on the extent of disease for each site serves a number of related objectives, including planning treatment, suggesting the prognosis, evaluating treatment results, facilitating the exchange of information between individuals and treatment centers, and assisting in the continuing investigation of human cancer. The principal purpose of international agreement on classification of cancer cases by extent of disease is to provide a method of conveying clinical experience without ambiguity (UICC, 1968).

General Rules of Classification

The UICC and AJCC have used the TNM system to describe the anatomic extent of cancer at the time of diagnosis before the application of definitive treatment, and from this has developed classification into stages, which can be useful as a guide to treatment and prognosis and in comparing the end results of treatment.

The TNM system is based on the assessment of:

T Extent of primary tumor.
N Condition of regional lymph nodes.
M Presence or absence of distant metastases.

All cases are identified by T, N, and M categories, which must be determined and recorded before any treatment is started. Confirmation of malignancy by histologic examination is obligatory. Traditional clinical-diagnostic staging demands that certain required patient assessments be performed. The UICC and the AJCC have suggested that for each site the specific methods of investigation available for TNM classification should be listed. These include (1) obligatory methods that should always be used for establishing extent, (2) additional methods that may be used in a particular site, and (3) special methods that may be available only in a minority of centers that are written into a TNM classification only when they are generally available. After being assigned T, N, and M categories including degrees of extension (T_1, T_2, and so on), patients are grouped into a number of clinical stages.

Certain tumors of the head and neck particularly lend themselves to clinical assessment more easily than others. Many of these tumors can be assessed by direct vision, palpation, and measurement of the primary tumor and its regional lymph nodes. Certain deep-seated tumors of the hypopharynx, esophagus, and sinuses are less satisfactory for easy classification.

Similarly, in many sites several types of cancer can occur, differing not only in their histologic patterns, but also in their clinical behavior. Because of this, it is necessary for all accessible sites to have histologic verification of the disease and to classify each tumor separately (Harmer, 1982).

Primary tumor

Numbers (eg, T_1, or T_2) indicate degrees of increasing extent of the primary tumor, and the number of these T categories may vary for each particular site. In general, the UICC has recommended that there be four. For each site the ideal is a limited number of qualities of each tumor assessed on clinical examination, such as directly measured size or a yes-or-no distinction, mobility or nonmobility, or fixation or nonfixation in relation to specific instances. Tumors easiest to classify are those arising in a single organ in which the tumor can be described in exact anatomic extent. A second group of tumors occurs in which the size and extent of the tumor are not so easily ascertained. These tumors can be described as to the extent of invasion or involvement of the neighboring sites in the region. A third type of tumor is more difficult to diagnose at all unless operative findings are taken into account.

Several degrees of T are used to describe the local extent of a primary tumor. T_0 means no primary tumor has been detected locally and is especially useful in patients with regional or distal cancer where the primary neoplasm remains occult even after thorough clinical examination. T_s indicates superficial carcinoma in sites where the cancer in the primary site is not believed to have penetrated the basement membrane. T_x indicates that the minimum requirements to appraise the primary tumor cannot be met.

Multiple tumors are considered under several headings. Those tumors occurring simultaneously should be classified independently. Those occurring simultaneously on the skin should have the actual number recorded. In those cases the highest T category is used, and the number of tumors is indicated in parentheses, such as (5) T_2.

Regional lymph nodes

Clinical findings regarding the regional cervical lymph nodes are defined for each site independently of the primary tumor. N_0 indicates no palpable lymph nodes. A designation such as N_1 or N_2 describes the clinical state of the nodes that are palpable. Cervical lymph nodes are described as mobile or fixed, as ipsilateral, bilateral, contralateral, or midline; as single or multiple; and by measured size, exact number, and anatomic extent. In the past the UICC has employed the category *a* where lymph nodes are palpable but not expected to contain metastatic growth and *b* if they are considered to contain growth: for example, N_{1a} or N_{1b}.

In certain sites (eg, the retropharyngeal or retroesophageal areas) the regional nodes are inaccessible to palpation and can be diagnosed only by means of conventional radiology, computed tomography (CT) scan, or magnetic resonance imaging (MRI).

Distant metastases

The absence or presence of distant metastatic disease is indicated by the letter *M*. M_0 indicates that no metastasis can be detected clinically, and M_1 indicates that metastasis other than regional lymph nodes is present. M_1 can be specified to include the anatomic area involves such as pulmonary (PUL), osseous (OSS), hepatic (HEP), brain (BRA), bone marrow (MAR), skin (SKI), and other (OTH).

Stage grouping

Combining cases classified by T, N, and M categories into groups based on criteria that are statistically predictive has been done. With four possible degrees of T, four degrees of N, and two degrees of M, the number of groups extending $T_1N_0M_0$ at one end of the scale to $T_4N_3M_1$ at the other is 32. For ease in reporting, stage grouping of TNM categories has been suggested. For example, stage grouping for the larynx is shown in Table 7-1.

Table 7-1. Stage grouping for cancer of the larynx

Clinical stage	TNM groups		
0	T_{is}	N_0	M_0
I	T_1	N_0	M_0
II	T_2	N_0	M_0
III	T_3	N_0	M_0
	T_1	N_1	M_0
	T_2	N_1	M_0
	T_3	N_1	M_0
IV	T_4	N_0	M_0
	T_4	N_1	M_0
	Any T	N_2	M_0
	Any T	N_3	M_0
	Any T	Any N	M_1.

Relationship of classification and staging to time

cTNM	Clinical diagnostic staging: extent of cancer determined before definitive treatment.
sTNM	Surgical evaluative staging: known extent of disease after surgical exploration or biopsy, or both.
pTNM	Postsurgical treatment pathologic staging: extent of disease following complete examination of therapeutically resected specimen.
rTNM	Retreatment staging: extent of disease in patient where treatment has failed and further treatment is being considered.
aTNM	Autopsy staging: extent of disease at time of autopsy.

The revised Manual recommends that four classifications be used. The include clinical (cTNM), pathologic (pTNM), retreatment (rTNM), and autopsy (aTNM) (Beahrs et al, 1988).

The UICC includes several additional descriptive terms for greater classification. The symbol *y* is used for cases in which definitive surgery is used after treatment by other methods. The UICC employs a system for indicating the type of examination on which the TNM categories are based. This system, called the *level of certainty* or *C factor*, is shown below (Harmer, 1982). Categories C_1, C_2, and C_3 are equivalent to clinical diagnostic staging, whereas C_4 is equivalent to postsurgical histopathologic classification.

C factor category definitions

C_1 Evidence from clinical examination only.
C_2 Evidence from special diagnostic means.
C_3 Evidence from surgical exploration only.
C_4 Evidence after definitive surgery and including complete examination of resected specimen.
C_5 Evidence from autopsy.

The AJCC (COMBED, 1977) has recognized that for cancer of certain sites the information made available by observation at the time of a surgical procedure (sTNM), as well as information from the pathologic examination of the operatively removed cancer (pTNM), could form the basis for useful classifications. This information is often useful as a supplement to the clinical-diagnostic staging.

It is evident that the biologic potentiality of different histologic types of cancer is such that different tumor types cannot be mixed together in a meaningful classification. Cases must be analyzed separately by histologic type (Messner, 1978). In some kinds of cancer, such as soft tissue sarcoma, histologic grading is of such significance that it becomes a necessary component of the classification system (Beahrs and Myers, 1983).

Histologically, tumors are named according to the resemblance of the tumor cells to corresponding normal cells, so that histogenetic classification of tumors roughly parallels the classification of normal tissue. Standardization of tumor nomenclature has been available in publications on tumor disease from the Armed Forces Institute of Pathology and in publications on nomenclature and classification from the WHO, which produced the International Classification of Diseases for Oncology (ICD-O) in 1976. The AJCC has recommended that the ICD-O (WHO, 1976) be used for coding neoplasms by typography and histology (morphology) and for describing tumor behavior (malignant, benign, in situ, or metastatic). This coded nomenclature is based on the *Manual of Tumor Nomenclature and Coding*, published by the American Cancer Society in 1968.

Information from the biopsy or examination of the specimen regarding tumor behavior and grading is of definite value in terms of classification and staging and has obvious treatment implications. Parameters available for study include descriptive indications of the number of mitoses, differentiation, circumscription or encapsulation of adjacent tissue, and invasion of nerves, lymphatics, and blood vessels. The microscopic depth of invasion can be measured exactly and, as in classification of skin or mucosal malignant melanoma, may be

of primary importance. Two factors are considered in microscopic grading of tumors: (1) differentiation or the amount of resemblance of the tumor cells to normal cells and tissue prototype and (2) an estimate of the growth rate based on the relative number of mitoses per unit of tumor cells (per a number of high-power microscopic fields) and an increase in nuclear chromatin (Meissner, 1978).

The revised Manual (Beahrs et al, 1988) recommends the following histopathologic grading system:

Histopathologic grade (G)

GX Grade cannot be assessed.
G1 Well differentiated.
G2 Moderately well differentiated.
G3 Poorly differentiated.
G4 Undifferentiated.

Several other optional classification descriptors are available for use (Beahrs et al, 1988). These include:

(m) indicates the presence of multiple tumors
y prefix to be used if classification is performed during or after multimodality therapy
r prefix used for staging recurrent tumor after a disease-free interval
L lymphatic invasion (LX-L2)
V venous invasion (VX-V2)
R presence or absence of residual tumor after treatment (RX-R2).

Clinical Trial of Classification Proposals

The basic objectives of any clinical trial of a classification system are to assess the practicability of the system and to see how far the system satisfies clinical requirements. Assessing practicability includes assessing the ability of physicians to determine the extent of disease, the consistency between physicians, and the ability to record the data in a usable reproducible.

If classification is to be valuable for prognosis, it should meet the following conditions (UICC, 1969):

1. Survival rates or behavior (recurrence rate or site response to a given method of treatment) should differ significantly from one category to another. (*Category* refers to the various degrees of extension defined by T, N, or M.)

2. Within each category survival and behavior should be reasonably consistent from one subcategory to another.

3. In different series where there is no difference in selection of patients, treatment method, or other factors influencing survival, corresponding categories of patients should have similar survival rates.

4. Survival rates should differ significantly in categories (T_1 from T_2, and so on) and from one stage to another.

Presentation of Results

Description of case material

The AJCC has noted that thorough and complete description of case material provides a necessary context for reporting end results and survival data. The following suggestions have been made regarding case material (Beahrs and Myers, 1983). All known cases of diagnosed cancer should be included. Any patients excluded from a report should be described as to number and characteristics. Exact dates of study must be noted. Knowing who did the work, as well as the nature of the place where the work was done, is essential. Each patient must have a specific histopathologic diagnosis. In the event of two separate primary tumors (whether simultaneous, synchronous, or metachronous), each should be considered independently; thus, in reports each would be treated without regard to the existence of the other. The specific clinical-diagnostic classification by site (cTNM) should be reported up to the date of initiation of tumor-directed therapy and thereafter not changed. The AJCC (COMBED, 1977) has also noted the importance of separating previously treated patients from those not previously treated, with the former staged as retreatment patients (rTNM).

Survival intervals

In the reporting of survival results, defining the starting time of the study is essential. This may be the date of diagnosis and staging of the tumor or the date of onset of therapy. Survival intervals should be selected with regard to the natural history of the disease studied. In the reporting of results, all the patients entering a survival interval should be included. Important time intervals include the crude survival time, length of response time, and time to recurrence. All patients should be followed at regular intervals.

Classification of patient condition

The condition of the patient at the end of each 12-month period can be recorded as alive (A), dead (D), or unknown or lost to follow-up (U). The following indicates the subdivision of patient status suggested by the AJCC (Beahrs and Myers, 1983). For purposes of uniformity, all patients lost to follow-up after each 12-month interval should be assumed to have died.

Alive, tumor free - no recurrence.
Alive, tumor free - after recurrence.
Alive with persistent, recurrent, or metastatic disease.
Alive with primary tumor.
Dead, tumor free.
Dead with cancer (primary, recurrent, or metastatic disease).

Dead, postoperative.
Unknown - lost to follow-up.

Survival rates

Direct and actuarial survival

The revised Manual suggests that calculated survival rates is the best single statistical index for measuring comparable efficacies of cancer therapies. Calculation of survival rates can be done either by direct or actuarial methods. The direct method indicates the percentage of patients alive at the end of a specified period using patients at risk for dying for that time period. The actuarial or life table method is a more complicated calculation that allows for the utilization of all follow-up data accumulated before the end of the closing date of the study. Using this method both annual and cumulative survival rates can be produced. These observed survival rates include all deaths regardless of cause. In studying cancer in specific sites it is also important to describe death due to cancer. The adjusted survival rate is the proportion of the initial patient group surviving if all other causes of death were not operating. Most important is that the specific method used in calculating survival rates must be indicated and that rates comparing the survival of different patient groups be computed by the same method (Beahrs et al, 1988).

Kaplan-Meier survival method

The Kaplan-Meier method of survival analysis is similar to the life table and also calculates the proportion surviving to each point in time that a death occurs (Kaplan and Meier, 1958). The life table and Kaplan-Meier methods are similar except that the Kaplan-Meier method addresses the problem of patients either lost or withdrawn during an interval. A relative survival rate can be calculated by using the observed rate from the Kaplan-Meier method and dividing it by the expected rate from the life table method (Beahrs et al, 1988).

Performance status of patient

The AJCC and the UICC have suggested recording information regarding the performance status of the patient. Three different performance scales have been used to measure the condition of the patient (Beahrs and Meyers, 1983). The revised Manual recommends the simplified AJCC scale (Beahrs et al, 1988):

Host (AJCC)

H	Physical state (performance scale) of patient, considering all cofactors determined at time of stage classification and subsequent follow-up examinations.
H_0	Normal activity.
H_1	Symptomatic and ambulatory; cares for self.
H_2	Ambulatory more than 50% of time; occasionally needs assistance.
H_3	Ambulatory 50% or less of time; nursing care needed.
H_4	Bedridden; may need hospitalization.

Karnofsky scale: criteria of performance status (PS)

100	Normal; no complaints; no evidence of disease.
90	Able to carry on normal activity; minor signs or symptoms of disease.
80	Normal activity with effort; some signs or symptoms of disease.
70	Cares for self; unable to carry on normal activity or do active work.
60	Requires occasional assistance but is able to care for most of own needs.
50	Requires considerable assistance and frequent medical care.
40	Disabled; requires special care and assistance.
30	Severely disabled; hospitalization indicated although death not imminent.
20	Very sick; hospitalization necessary; active supportive treatment necessary.
10	Moribund, fatal processes progressing rapidly.
0	Dead.
100-80	Able to carry normal activity; no special care needed.
70-50	Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.
40-0	Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.

Eastern Cooperative Oncology Group (ECOG) scale (grade)

Grade

0	Fully active; able to carry on all predisease activity without restrictions (Karnofsky 90 to 100).
1	Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature; for example, light housework, office work (Karnofsky 70 to 80).
2	Ambulatory and capable of all self-care but unable to carry out any work activities; up and about more than 50% of waking hours (Karnofsky 50 to 60).
3	Capable of only limited self-care; confined to bed or chair 50% or more of waking hours (Karnofsky 30 to 40).
4	Completely disabled; cannot carry on any self-care; totally confined to bed or chair (Karnofsky 10 to 20).

Conversion rate

The conversion rate (Rubin, 1974) is an attempt to describe the difference between the clinical-diagnostic stage, based on complete pretreatment evaluation, and the true pathologic stage:

Conversion rate = pTNM / cTNM

The conversion rate factor may determine how aggressive the treatment should be. For instance, skin cancer has a very low conversion rate, whereas cancer of the lung has a very high conversion rate.

Data-collecting forms

The importance of a data-collecting form for use in a classification system of each site has been recognized for some years. Such forms ensure the recording of the data necessary for category and stage classification. Recent emphasis has been on development of a checklist for each cancer site for which there is a stage classification (Beahrs and Myers, 1983).

Prediction of prognosis

One major objective of staging systems is the accurate prediction of prognosis, which thereafter provides guidelines for treatment selection. Study of the best prognosis of patients would include the study of those patients cured or with long-term nonrecurrence of cancer. Modern statistical methods can be used to identify which of the multiple patient variables from a specific and detailed tumor registry would be strongly predictive of nonrecurrence of cancer. Using logistic regression analysis of such data from a large head-and-neck tumor registry, Jacobs et al (1985) have identified the following variables as strongly predictive of nonrecurrence of cancer:

Absence of cervical lymph node metastasis (C_1).
Pathologic characteristics of the resected specimen (C_4).
Supraglottic primary site (C_2).
Glottic primary site (C_2).
Patient age (C_1).

The logistic regression model has the capability of predicting specifically the prognosis for each individual patient. For example, the probability of nonrecurrence of cancer for more than 3 years or until death, would be 72% in a 60-year-old patient with supraglottic cancer with no cervical nodal involvement and whose pathologic resection revealed tumor in the specimen with resection margins clear. The probability of nonrecurrence for the above patient with a single positive lymph node in the neck would be 59%. If the patient had been found to have tumor involving the margins of the resected specimen, the probability of nonrecurrence would be 47%.

The overall success rate employing logistic regression analysis in a large series of patients with head and neck cancer was 71& for correct classification. Applying the data to the variables of the present TNM system, a correct classification of 65% was achieved. The logistic regression analysis was a statistically significant improvement in the accurate prediction of prognosis over the correct predictive classification according to the presently used TNM system.

Success in Classification and Staging

The AJCC and UICC have taken the initial step in the creation of a successful classification system by agreeing on the importance of having one identical classification

system. Classification and staging systems will work only if the oncologic physician uses the system and reports the results in terms of the system. Although it is important not to change systems very often, it is obvious that new parameters for study will constantly be created, and tumor data forms must be designed with the capability to add this information. Only when it is required (by agreement) to report the data using the terms of the system (both at national and international meetings and in the world literature) will it be possible to assess the value of the system.

Site-specific Classification of Head and Neck Cancer

The staging recommendations of the revised Manual (Beahrs et al, 1988) for specific head and neck cancer sites follow the TNM staging recommendations, using the parameter of anatomic extent of disease. In several specific instances grade (soft tissue sarcoma of the head and neck) and age (thyroid cancer) are factors that have been added to the classification).

The revised Manual (Beahrs et al, 1988) has suggested a variety of procedures and special studies to be used in the process of staging a given tumor. Both clinical usefulness and cost effectiveness are areas of consideration. These suggestions are included in each specific head and neck site.

Table 7-2. Regional cervical lymph nodes (N): present classification

N_x	Regional lymph nodes cannot be assessed.
N_0	No regional lymph node metastasis.
N_1	Metastasis in a single ipsilateral lymph node, 3 cm or less in greatest dimension.
N_2	Metastasis in a single ipsilateral lymph node, more than 3 cm but not more than 6 cm in greatest dimension, or in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension, or in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.
N_{2a}	Metastasis in a single ipsilateral lymph node more than 3 cm but not more than 6 cm in greatest dimension.
N_{2b}	Metastasis in multiple ipsilateral lymph nodes, none more than 6 cm in greatest dimension.
N_{2c}	Metastasis in bilateral or contralateral lymph nodes, none more than 6 cm in greatest dimension.
N_3	Metastasis in a lymph node more than 6 cm in greatest dimension.

Table 7-2a. Classification of distant metastasis (M):

Distant metastases (M)

M_x	Presence of distant metastasis cannot be assessed.
M_0	No distant metastasis.
M_1	Distant metastasis.

The recommendations for the T categories are site specific and are detailed in terms of the anatomic extent of disease. The recommendation for classification of cervical node

involvement is applicable to all squamous cell carcinoma of the head and neck area. Table 7-2 shows the present cervical node classification.

In clinical evaluation the actual size of the nodal mass should be measured and allowance made for intervening soft tissues. It is recognized that most masses over 3 cm in diameter are not single nodes but are confluent nodes or tumor in soft tissues of the neck. The three stages of clinically positive nodes are N_1, N_2, and N_3. The use of subgroups for N_2 is recommended. Midline nodes are considered ipsilateral nodes (Beahrs and Myers, 1983).

Similarly, the revised Manual's recommendations for classification of distant metastases (see Table 7-2a) and stage grouping (Table 7-3) are applicable to all specific head and neck cancers.

Table 7-1. Stage grouping for head and cancer

Clinical stage	**TNM groups**		
0	T_{is}	N_0	M_0
I	T_1	N_0	M_0
II	T_2	N_0	M_0
III	T_3	N_0	M_0
	T_1	N_1	M_0
	T_2	N_1	M_0
	T_3	N_1	M_0
IV	T_4	N_0	M_0
	T_4	N_1	M_0
	Any T	N_2	M_0
	Any T	N_3	M_0
	Any T	Any N	M_1

For each specific site the AJCC (Beahrs and Myers, 1983) has recommended descriptions of tumor extension to neighboring areas, as well as description of specific tumor qualities, including, for example, whether the tumor is exophytic, superficial, infiltrating, ulcerated, or extending to, over, or into bone, and whether there is radiographic destruction of bone. The ICD-O numbers are given as specified by the WHO (1976).

Histopathologic type

The predominant cancer from all head and neck sites except the salivary gland, thyroid, and cervical esophagus primaries is squamous cell carcinoma. Histologic confirmation is necessary for valid classification. The revised Manual (Beahrs et al, 1988) refers to squamous cell carcinoma only for all head and neck sites except the salivary gland, thyroid, and cervical esophagus. Nonsquamous cell cancers of the oral cavity, pharynx, larynx, and nose and paranasal sinuses should be kept distinct and must be identified specifically.

Specific sites

Lip

Anatomy (ICD-0 140). The lip begins at the junction of the vermilion border with the skin and includes only the vermilion surface or that portion of the lip that comes into contact with the opposing lip. It is well defined into an upper (ICD-O 140.0) and lower lip (ICD-O 140-1) joined at the commissure (ICD-O 140.60) of the mouth. The mucosal surfaces of the lips are included with the oral cavity.

Clinical classification. The revised Manual places classification for the lips within the oral cavity. Previously the UICC (Harmer, 1982) used a specific classification for carcinoma of the vermilion surface of the lips. This classification is essentially unchanged in the revised Manual.

The tumor should be measured with a centimeter rule. Films of the mandible and CT scan of the oral cavity and neck are important. Histologic verification is required.

Classification

Primary tumor (T) (AJCC; Beahrs et al, 1988)

T_x	Primary tumor cannot be assessed.
T_0	No evidence of primary tumor.
T_{is}	Carcinoma *in site*.
T_1	Tumor 2 cm or less in greatest dimension.
T_2	Tumor more than 2 cm but not more than 4 cm in greatest dimension.
T_3	Tumor more than 4 cm in greatest dimension.
T_4	Tumor invades adjacent structures (eg, through cortical bone, tongue, and skin of neck).

Oral cavity

Anatomy (ICD-O 140-145).

Primary site. The oral cavity extends from the skin-vermilion junction of the lips to the junction of the hard and soft palate above and to the line of circumvallate papillae below and is divided into the following specific areas.

Buccal mucosa (ICD-O 140). This includes all the membrane lining of the inner surface of the cheeks (ICD-O 145) and lips (upper (ICD-O 140.3) and lower (ICD-O 140.4)), from the line of contact of the opposing lips to the line of attachment of mucosa of the alveolar ridge (upper and lower (ICD-O 145.1)) and pterygomandibular raphe.

Lower alveolar ridge (ICD-O 143.1). This ridge includes the alveolar process of the mandible and its covering mucosa, which extends from the line of attachment of mucosa in the buccal gutter to the line of free mucosa of the floor of the mouth. Posteriorly it extends to the ascending ramus of the mandible.

Upper alveolar ridge (ICD-O 143). The ridge includes the alveolar process of the maxilla and its covering mucosa, which extends from the line of attachment of mucosa in the upper gingival buccal gutter to the junction of the hard palate. Its posterior margin is the upper end of the pterygopalatine arch.

Retromolar gingiva (retromolar trigone) (ICD-O 145.6). This is the attached mucosa overlying the ascending ramus of the mandible from the level of the posterior surface of the last molar tooth to the apex superiorly, adjacent to the tuberosity of the maxilla.

Floor of the mouth (ICD-O 144). This is a semilunar space over the mylohyoid and hyoglossus muscles, extending from the inner surface of the lower alveolar ridge to the undersurface of the tongue. Its posterior boundary is the base of the anterior pillar of the tonsil. It is divided into two sides by the frenulum of the tongue and contains the ostia of the submaxillary and sublingual salivary glands.

Hard palate (ICD-O 145-2). This is the semilunar area between the upper alveolar ridge and the mucous membrane covering the palatine process of the maxillary palatine bones. It extends from the inner surface of the superior alveolar ridge to the posterior edge of the palatine bone.

Anterior two thirds of the tongue (oral tongue) (ICD-O 141). This is a freely mobile portion of the tongue that extends anteriorly from the line of the circumvallate papillae to the undersurface of the tongue at the junction of the floor of the mouth. It is composed of four areas: the tip, the lateral borders (ICD-O 141.2), the dorsum (ICD-O 141.1), and the undersurface (nonvillous surface of the tongue). The undersurface of the tongue is considered a separate category by the WHO (ICD-O 141.3).

Clinical staging. Assessment of the primary site includes a complete physical examination of the head and neck including palpation of the floor of the mouth and the base of the tongue, fiberoptic exam of the nasopharynx, hypopharynx, and larynx, and palpation of the neck.

Primary tumors and lymph nodes are carefully measured with a centimeter rule. Radiologic assessment includes plain and contrast films, panorex of the mandible, and CT scans and MRI examinations looking specifically for tumor size, extent of involvement, and bone invasion. Chest film is used to detect distant metastasis. Staining the surface mucosa with toluidine blue, panendoscopy, and studies of immune competence may be important. All clinical and pathologic data available before initial definitive treatment is instituted may be used for clinical staging.

In comparison with the previous Staging Manual (Beahrs and Myers, 1983), the revised Manual (Beahrs et al, 1988) includes a more specific definition for T_4 tumors. Also, the definitions of N_2 and N_3 are modified (see Table 7-2).

Classification

Primary tumor (T) (AJCC; Beahrs et al, 1988)

T_x Primary tumor cannot be assessed.
T_0 No evidence of primary tumor.
T_{is} Carcinoma *in situ*.
T_1 Tumor 2 cm or less in greatest dimension.
T_2 Tumor more than 2 cm but not more than 4 cm in greatest dimension.
T_3 Tumor more than 4 cm in greatest dimension.
T_4 Tumor invades adjacent structures (eg, through cortical bone, into deep (extrinsic) muscle of tongue, maxillary sinus, skin).

Pharynx

Anatomy

Primary site. The pharynx (including base of tongue, soft palate, and uvula) is divided into three regions: the oropharynx, the nasopharynx, and the hypopharynx).

Oropharynx (ICD-O 146). The oropharynx extends from the plane of the hard palate superiorly to the plane of the hyoid bone inferiorly and is continuous with the oral cavity. The faucial arch includes both the surfaces of the entire soft palate (ICD-o 145.3) and the uvula (ICD-O 145.4), the anterior border and base of the anterior tonsillar pillar, and the line of the circumvallate papillae. The base of the tongue (ICD-O 141.0) extends from the line of the circumvallate papillae to the junction with the base of the epiglottis (the vallecula (ICD-O 146.3)) and includes the pharyngoepiglottic and glossoepiglottic folds. The lateral wall (ICD-O 146.6) of the oropharynx is made up largely of the tonsil (ICD-O 146.0) and tonsillar fossae (ICD-O 146.1). The posterior tonsillar pillar (ICD-O 146.2), the narrow lateral wall, and the posterior wall (ICD-O 146.1) make up the pharyngeal wall.

Nasopharynx (ICD-O 147). The anterior limit of the nasopharynx is the choana, through which it is continuous with the nasal cavity. Its roof is attached to the base of the skull and slopes downward to become continuous with the posterior pharyngeal wall. The lateral wall is composed of the torus tubarius, the eustachian tube orifice, and that portion of the mucosa of the fossa of Rosenmüller (ICD-O 147.2) extending up to its apex and junction with the roof. The inferior limit of the nasopharynx is level with the plane of the hard palate.

Hypopharynx (ICD-O 148). The hypopharynx extends from the plane of the hyoid bone superiorly to the plane of the lower border of the cricoid cartilage inferiorly. It is made up of three distinct regions: the piriform sinus, the posterior surface of the larynx (the postcricoid area), and the lower posterior pharyngeal wall.

Each region is subdivided into sites that are summarized as follows:

I. Oropharynx (ICD-O 146)
   - A. Anterior wall (glossoepiglottic area) - tongue posterior to vallate papillae; base of tongue or posterior third (ICD-O 141.0)
   - B. Lateral wall
     1. Tonsil (ICD-O 146.0)
     2. Tonsillar fossa (ICD-O 146.1) and faucial pillars (ICD-0 146.2)
     3. Glossotonsillar sulci (ICD-O 146.2)
   - C. Posterior wall (ICD-O 146.7)
   - D. Superior wall
     1. Inferior surface of soft palate (ICD-O 156.3)
     2. Uvula (ICD-O 145.4)

II. Nasopharynx (ICD-O 147)*
   - A. Posterosuperior wall - extends from level of junction of hard and soft palates to base of skull (ICD-0 147.0, 147.1)
   - B. Lateral wall - includes fossa of Rosenmüller (147.2)
   - C. Inferior wall - consists of superior surface of soft palate (ICD-O 147.3)

III. Hypopharynx (ICD-O 148)
   - A. Pharyngoesophageal junction (postcricoid area) - extends from level of arytenoid cartilages and connecting folds to inferior border of cricoid cartilage (ICD-O 148.0)
   - B. Piriform sinus - extends from pharyngoepiglottic fold to upper end of esophagus (ICD-O 148.1); bounded laterally by thyroid cartilage and medially by surface of arytenoepiglottic fold (ICD-O 148.2) and arytenoid and cricoid cartilages
   - C. Posterior pharyngeal wall - extends from level of floor of vallecula to level of cricoarytenoid joints (ICD-O 148.3).

* The margin of the choanal orifices, including the posterior margin of the nasal septum, is included with the nasal fossa.

Clinical staging. The assessment of the primary site includes a complete examination of the head and neck including palpation of the base of tongue and fiberoptic examination of the nose, nasopharynx, hypopharynx, and larynx, and palpation of the neck. Neurologic examination of the cranial nerves is required. Imaging procedures, including plain films, CT, MRI contrast studies, and bone scans, are useful to evaluate the size of the tumor and the extent of disease. Histologic confirmation is required. Panendoscopy, assay of antibodies to the Epstein-Barr viral capsid antigen, and studies of immune competence are useful. Chest film is used to examine for distant metastasis. All data concerning clinical findings and pathology available before initial definitive treatment may be used for clinical staging.

In comparison to the previous Staging Manual (Beahrs and Myers, 1983), the revised Manual (Beahrs et al, 1988) maintains the definitions of the primary tumor (T) unchanged. The definitions for N_2 and N_3 have been modified (see Table 7-2).

Classification

Primary tumor (T) (AJCC; Beahrs et al, 1988)

T_x Primary tumor cannot be assessed
T_0 No evidence of primary tumor
T_{is} Carcinoma *in situ*

Oropharynx

T_1 Tumor 2 cm or less in greatest dimension
T_2 Tumor more than 2 cm but not more than 4 cm in greatest dimension
T_3 Tumor more than 4 cm in greatest dimension
T_4 Tumor invades adjacent structures (eg, through cortical bone, soft tissues of neck, deep (extrinsic) muscle of tongue)

Nasopharynx

T_1 Tumor limited to one subsite of nasopharynx
T_2 Tumor invades more than one subsite of nasopharynx
T_3 Tumor invades nasal cavity and/or oropharynx
T_4 Tumor invades skull and/or cranial nerve(s)

Hypopharynx

T_1 Tumor limited to one subsite of hypopharynx
T_2 Tumor invades more than one subsite of hypopharynx or an adjacent site, *without* fixation of hemilarynx
T_3 Tumor invades more than one subsite of hypopharynx or an adjacent site, *with* fixation of hemilarynx
T_4 Tumor invades adjacent structures (eg, cartilage or soft tissues of neck).

Larynx

Anatomy (ICD-O 161)

Primary site. The following anatomic definition of the larynx allows classification of carcinomas arising in the encompassed mucous membranes but excludes cancers arising on the lateral or posterior pharyngeal wall, the piriform fossa, the postcricoid area, the base of tongue, and the vallecula.

The anterior limit of the larynx is composed of the anterior or lingual surface of the suprahyoid epiglottis, the thyrohyoid membrane, the anterior commissure, and the anterior wall of the subglottic region, which is composed of the thyroid cartilage, the cricothyroid membrane, and the anterior arch of the cricoid cartilage.

The posterior and lateral limits include the arytenoepiglottic folds, the arytenoid region, the interarytenoid space, and the posterior surface of the subglottic space, represented by the mucous membrane covering the cricoid cartilage.

The superolateral limits are composed of the tip and the lateral borders of the epiglottis.

The inferior limits are made up of the plane passing through the inferior edge of the cricoid cartilage.

For purposes of this clinical stage classification, the larynx is divided into three regions: the supraglottis, the glottis, and the subglottis. The supraglottis (ICD-O 161.1) is composed of the epiglottis (both its lingual and laryngeal aspects), the arytenoepiglottic folds, the arytenoids, and the ventricular bands (false cords). The inferior boundary of the supraglottis is a horizontal plane passing through the apex of the ventricle. The glottis (ICD-O 161.0) is composed of the true vocal cords, including the anterior and posterior commissures. The lower boundary is the horizontal plane 1 cm below the apex of the ventricle. The subglottis (ICD-O 161.2) is the region extending from the lower margin of the cricoid cartilage. Representatives of the UICC have agreed to include the lingual surface of the epiglottis as part of the larynx.

The division of the larynx is summarized as follows:

Region	**Site**
Supraglottis	Ventricular bands (false cords) Arytenoids Epiglottis (both lingual and laryngeal aspects) Suprahyoid epiglottis Infrahyoid epiglottis Arytenoepiglottic folds
Glottis	True vocal cords including anterior and posterior commissure
Subglottis	Subglottis.

Clinical staging. Complete physical examination of the head and neck is performed. The physician examines the larynx using the indirect laryngeal mirror and flexible fiberoptic laryngoscope for inspection, and direct rigid laryngoscopy for inspection, palpation, and biopsy. Palpation of the neck for abnormal neck nodes and of the larynx to elicit fremitus indicates further extent of disease. Precise clinical descriptors including the status of vocal cord mobility are important (see Table 7-3a).

Table 7-3a. Description of tumor characteristics (larynx)

Superficial
Exophytic
Moderate infiltration
Deep infiltration
Impaired cord mobility
Cord fixation
Cartilage destruction
Tumor confined to larynx
Tumor extension to the following:
- Base of tongue
- Piriform sinus
- Postcricoid region
- Preepiglottic space
- Trachea
- Soft tissue or skin of neck.

Useful imaging techniques include CT and MRI scans to evaluate the size of the tumor and the extent of disease. Histologic confirmation is required. Panendoscopy and studies of immune competence are useful. Chest films are used to examine for distant metastasis. All clinical and pathologic data available before initial definitive treatment may be used for clinical staging.

In comparison to the previous Staging Manual (Beahrs and Myers, 1983), in the revised manual (Beahrs et al, 1988) the primary tumor (T) definitions are essentially unchanged. The definitions of N_2 and N_3 have been modified (see Table 7-2).

Zamora et al (1991) compared the 1983 and the 1988 AJCC staging systems for patients with primary supraglottic cancer. Cox (1972) regression analyses showed that the 1983 and the 1988 T-stage definition (T_1-T_4) successfully prognosticate for survival when patients had no positive neck nodes (N_0). In contrast, when positive neck nodes were present, the N-stage (N_0 to N_3) of the patient was more successful in prognosticating survival than the T-stage. Further analyses showed that the 1988 N-stage definition provided a clearer distinction between N_2 and N_3 lesions compared to the 1983 version. Combined-modality treatment significantly improved survival compared to single-modality treatment when patients progressed from N_0 to N_3 neck disease but not when patients advanced from T_1 to T_4. The authors concluded that the 1988 AJCC tumor (T) and nodal (N) staging system definitions for supraglottic cancer successfully prognosticate for T-stage (T_1-T_4) and N-stage (N_0-N_3) with better separation of N_2 and N_3 lesions as compared to the 1983 version.

Classification

Primary tumor (T) (AJCC; Beahrs et al, 1988)

Supraglottis

T_1 Tumor limited to one subsite of supraglottis with normal vocal cord mobility.
T_2 Tumor invades more than one subsite of supraglottis or glottis, with normal vocal cord mobility.
T_3 Tumor limited to larynx with vocal cord fixation and/or invades postcricoid area, medial wall of pyriform sinus, or preepiglottic tissues.
T_4 Tumor invades through thyroid cartilage, and/or extends to other tissues beyond the larynx (eg, to oropharynx, soft tissues of neck).

Glottis

T_1 Tumor limited to vocal cord(s) (may involve anterior or posterior commissures) with normal mobility.
  T_{1a} Tumor limited to one vocal cord.
  T_{1b} Tumor involves both vocal cords.
T_2 Tumor extends to supraglottis and/or subglottis, and/or with impaired vocal cord mobility.
T_3 Tumor limited to the larynx with vocal cord fixation.
T_4 Tumor invades through thyroid cartilage and/or extends to other tissues beyond the larynx (eg, oropharynx, soft tissues of neck).

Subglottis

T_1 Tumor limited to the subglottis.
T_2 Tumor extends to vocal cord(s) with normal or impaired mobility.
T_3 Tumor limited to larynx with vocal cord fixation.
T_4 Tumor invades through cricoid or thyroid cartilage and/or extends to other tissues beyond the larynx (eg, oropharynx, soft tissues of neck).

Paranasal sinuses

Anatomy (ICD-O 160.2)

Primary site. Cancer of the maxillary sinus is the most common of the paranasal sinus cancers; it is the only site to which the following classification applies. The ethmoid sinuses and nasal cavity may ultimately be defined similarly with further study. Tumors of the sphenoid and frontal sinuses are so rare as not to warrant staging.

Ohngren's line, a theoretic plane joining the medial canthus of the eye with the angle of the mandible, may be used to divide the maxillary antrum into the anteroinferior portion (the infrastructure) and superoposterior portion (the suprastructure).

Clinical classification. The assessment of the primary site requires a complete physical examination of the head and neck including inspection and palpation of the nose and nasopharynx, the oral cavity, and the orbit and its contents. Neurologic evaluation of the cranial nerves is required. Nasal and nasopharyngeal endoscopy is helpful. Palpation of the nodal stations of the neck with measurement of abnormal neck masses is required. Description of certain tumor characteristics is important (see Table 7-3b).

Table 7-3b. Description of tumor characteristics (paranasal sinuses)

Radiographic destruction of bone
Invasion of adjacent areas
- Skin
- Palate
- Nasopharynx
- Cribriform plate
- Orbit
- Base of skull
- Pterygoid muscles
- Pterygoid bone.

Imaging procedures including CT and/or MRI scans are required for assessment of tumor size and extent of disease, including the evaluation of possible bone destruction and involvement of the base of skull or intracranial extension. Panendoscopy may be useful. Chest film is used to examine for distant metastasis. Transnasal biopsy of the tumor is required for histologic confirmation.

In comparison to the previous Staging Manual (Beahrs and Myers, 1983), the revised Manual (Beahrs et al, 1988) has revised the primary tumor (T) definitions. The lymph node categories (N) have been changed so that they are the same as for other head and neck sites.

Zamora et al (1990) compared the 1983 and 1988 AJCC clinical classification for primary malignancies of the maxillary antrum. Cox regression analyses of survival curves showed increasingly worse prognoses for advanced tumors in both T-staging systems. Further analyses showed a significant difference in survival between T_3 and T_4 in the 1988, but not in the 1983 system. There were no significant differences in survival according to treatment modality or histologic type of malignancy. The authors concluded that the 1988 system prognosticates successfully for T-stage (1 to 4) and demonstrates significant improvement in detecting T_3 versus T_4 differences compared to the 1983 system ($p < .0010$.

Classification

Primary tumor (T) (AJCC; Beahrs et al, 1988)

T_x Primary tumor cannot be assessed.
T_0 No evidence of primary tumor.
T_{is} Carcinoma *in situ.*
T_1 Tumor limited to the antral mucosa with no erosion or destruction of bone.
T_2 Tumor with erosion or destruction of the infrastructure (see anatomic division, above), including the hard palate and/or middle nasal meatus.
T_3 Tumor invades any of the following: skin of cheek, posterior wall of maxillary sinus, floor or medial wall of orbit, anterior ethmoid sinus.
T_4 Tumor invades orbital contents and/or any of the following: cribriform plate, posterior ethmoid or sphenoid sinuses, nasopharynx, soft palate, pterygomaxillary or temporal fossae or base of skull.

Salivary glands

Anatomy (ICD-O 142)

Primary site. The major salivary glands include the parotid (ICD-O 142.0), submaxillary (submandibular) (ICD-O 142.1), and sublingual (ICD-O 142.2) glands. Tumors arising in minor salivary glands (mucus-secreting glands in the lining membrane of the upper aerodigestive tract) are not included in this staging system.

Clinical classification. The staging system used in the revised Manual (Beahrs et al, 1988) is based on a retrospective study from 11 institutions in the USA and Canada. Factors found to affect survival include histologic diagnosis, cellular differentiation of the tumor, tumor site, size, degree of fixation or local extension, and nerve involvement. The status of regional lymph nodes and of distant metastasis was significant. Four clinical variables are used in the present classification: tumor size, local extension of the tumor, palpability and suspicion of lymph nodes, and the status of distant metastasis.

Assessment of the primary site includes a complete examination of the head and neck including bimanual palpation of the floor of the mouth and rigorous examination of the nodal stations of the neck. Exact measurement of the primary site with a centimeter rule and of abnormal lymph nodes in the neck is required. Cranial nerve examination is mandatory. Specific clinical descriptors are useful (see Table 7-3c).

Table 7-3c. Description of tumor characteristics (salivary glands)

Mobile
Limited mobility
Fixed
Hard
Soft
Cystic
Adjacent tissue involved
Specify _____
Nerve involvement
- None
- Facial
- Hypoglossal
- Lingual
- Vagus
- Other _____
- Partial paralysis
- Complete paralysis.

Imaging studies include sialography, technetium scan, mandibular panorex, and CT and/r MRI scans with or without gadolinium. To date the most useful have been either CT scans with contrast or CT scans combined with sialography to evaluate the size of the tumor and the extent of disease. Biopsy of the tumor with histologic confirmation is mandatory. Chest film is used to examine for distant metastasis. All clinical and pathologic data available before initial definitive treatment may be used for clinical staging.

The revised Manual (Beahrs et al, 1988) reflects the recent UICC and AJCC agreement regarding the prognostic implication of "significant local extension". Review of survival data indicated that local extension is less ominous in smaller tumors than in larger ones (Beahrs et al, 1988). In the revised system, the presence or absence of local extension is indicated as a suffix to each separate T category representing the size of the primary tumor. The authors claim that the revised system correlates more closely with observed 5-year survivals than the previous system.

Histopathologic type. Salivary gland malignancies include a variety of specifically different tumors. Confirmation and reporting of the exact type of tumor is mandatory:

Acinic cell carcinoma
Adenoid cystic carcinoma (cylindroma)
Adenocarcinoma
Squamous cell carcinoma
Carcinoma in pleomorphic adenoma (malignant mixed tumor)
Mucoepidermoid carcinoma
- Well-differentiated (low-grade)
- Poorly differentiated (high-grade)

Other

Classification

Primary tumor (T) (AJCC; Beahrs et al, 1988)

T_x Primary tumor cannot be assessed.
T_0 No evidence of primary tumor.
T_1 Tumor 2 cm or less in greatest dimension.
T_2 Tumor more than 2 cm but not more than 4 cm in greatest dimension.
T_3 Tumor more than 4 cm but not more than 6 cm in greatest dimension.
T_4 Tumor more than 6 cm in greatest dimension.

Note: All categories are subdivided: (1) no local extension, (2) local extension. Local extension is clinical or macroscopic evidence of invasion of skin, soft tissues, bone, or nerve. Microscopic evidence alone is not local extension for classification purposes.

Thyroid gland

Although staging for cancers in other head and neck sites is based entirely on the anatomic extent of disease, it is not possible to follow this pattern for the unique group of malignant tumors that arise in the thyroid. Both the histologic diagnosis and the age of the patient are of such importance in the behavior and prognosis of thyroid cancer that these factors have to be accounted for in any staging system.

Anatomy (ICD-O 193).

Primary site. The thyroid gland ordinarily is composed of a right and a left lobe lying adjacent and lateral to the upper trachea and esophagus. An isthmus connects the two lobes, and in some cases a pyramidal lobe is present, extending upward anterior to the thyroid cartilage.

Clinical classification. Assessment of the primary site involves complete physical examination of the head and neck including inspection and palpation of the thyroid and the nodal stations of the neck. Indirect mirror and/or fiberoptic examination of the larynx to ascertain vocal cord mobility is required. Blood tests to evaluate thyroid function and serum calcitonin levels are necessary. Imaging examinations including ultrasound, technetium scan, and either CT or MRI scans as well as previous historical information and specific indicators are useful (see Table 7-3d).

Table 7-3d. Thyroid history

History of previous irradiation to head and neck area
Yes _____ No _____
Other endocrine disease present
Yes _____ No _____
Family history of thyroid cancer
Yes _____ No _____
Family history of endocrine tumors
Yes _____ No _____
Primary tumor
Location:
Right _____ Left _____ Midline _____
Size:
Largest diameter _____ cm
Characteristics:
Single _____ Multiple _____ Bilateral _____
Fixation (extension through thyroid capsule)
Yes _____ Massive _____ No _____
Neurologic involvement
Yes _____ No _____
Blood vessel invasion
Yes _____ No _____
Radioactive scan done
Yes _____ (Type) _____ No _____
Cold _____ Hot _____ Neither _____
Histologic type of cancer
___ Papillary (with or without follicular foci)
___ Follicular
___ Medullary
___ Undifferentiated
___ Unclassified.

Diagnosis of thyroid cancer must be confirmed by needle biopsy or open biopsy of the tumor. The revised Manual (Beahrs et al, 1988) states that information for clinical staging may be obtained by biopsy of lymph nodes or other areas of suspected local or distant spread.

Both clinical-diagnostic staging (cTNM) and surgical-evaluative staging (sTNM) may be used as a basis for staging thyroid cancer. Postsurgical resection-pathologic staging (pTNM) has furnished the greatest amount of evaluative evidence and proves most useful. It is essential that the system used for staging be identified clearly.

In comparison to the previous Staging Manual (Beahrs and Meyers, 1983) the revised Manual (Beahrs et al, 1988) uses 4 cm as a dividing measurement in the definitions of T_2 and T_3. Also in the current (1988) system, age is not considered in classifying medullary and undifferentiated cancers.

Histologic type. The present classification (Beahrs et al, 1988) of thyroid cancer uses the WHO classification:

Papillary carcinoma (with or without foci).
Follicular carcinoma (extent of invasion of tumor capsule should be noted).
Medullary carcinoma.
Undifferentiated (anaplastic) carcinoma.
Unclassified malignant tumor.

Classification

Primary tumor (T) (AJCC; Beahrs et al, 1988)

Note: All categories may be subdivided: (1) solitary tumor, (2) multifocal tumor (the largest determines the classification).

T_x Primary tumor cannot be assessed.
T_0 No evidence of primary tumor.
T_1 Tumor 1 cm or less in greatest dimension limited to the thyroid.
T_2 Tumor more than 1 cm but not more than 4 cm in greatest dimension limited to the thyroid.
T_3 Tumor more than 4 cm in greatest dimension limited to the thyroid.
T_4 Tumor of any size extending beyond the thyroid capsule.

Regional lymph nodes (N)

Regional lymph nodes are the cervical and upper mediastinal lymph nodes.

N_x Regional lymph nodes cannot be assessed.
N_0 No regional lymph node metastasis.
N_1 Regional lymph node metastasis.
- N_1 Metastasis in ipsilateral cervical lymph node(s).
- N_2 Metastasis in bilateral, midline, or contralateral cervical or mediastinal lymph node(s).

Stage grouping

Separate stage groups are recommended for papillary and follicular, medullary, and undifferentiated.

Papillary or follicular

	Under 45 years	45 years and older
Stage I	Any T, Any N, M_0	T_1, N_0, M_0
Stage II	Any T, Any N, M_1	T_2, N_0, M_0
		T_3, N_0, M_0
Stage III		T_4, N_0, M_0
		Any T, N_1, M_0
Stage IV		Any T, Any N, M_1.

Medullary

Stage I	T_1	N_0	M_0
Stage II	T_2	N_0	M_0
	T_3	N_0	M_0
	T_4	N_0	M_0
Stage III	Any T	N_1	M_0
Stage IV	Any T	Any N	M_1.

Undifferentiated

All cases are stage IV.

Stage IV	Any T	Any N	Any M.

Cervical esophagus (ICD-O 150.0)

Anatomy

Primary site. The cervical esophagus begins at the cricopharyngeal sphincter, which forms a bridge between the hypopharynx and the cervical esophagus. The upper margin of the cervical esophagus is at the level of the lower border of the cricoid cartilage and lies posterior and partially to the left of the trachea in the neck. Inferiorly it ends at the thoracic inlet (the suprasternal notch), about 18 cm from the upper incisor teeth. The location of the esophageal cancer is often measured from the upper central incisor teeth.

Histologically, the esophagus has four layers - mucosa, submucosa or lamina propria, muscle coat or muscularis propria, and adventitia. There is no serosal layer.

Regional lymph nodes. The lymph nodes of the cervical esophagus include the superior mediastinal, internal jugular, upper cervical, cervical, periesophageal, and supraclavicular nodes. Any lymph node involvement other than of the cervical or supraclavicular lymph nodes is considered distant metastasis.

Clinical staging. Assessment of the primary site requires inspection of the tumor with an endoscope, imaging with a contrast swallow test, and CT scan with intravenous contrast to evaluate the size and extent of the tumor. Chest CT is used to evaluate the inferior and

thoracic extent of the tumor as well as to check for distant metastasis. Biopsy for histologic confirmation is required.

Both clinical staging (cTNM) and postsurgical resection-pathologic staging (pTNM) are merged and a single classification is used for all regions of the esophagus. Involvement of the adjacent structures depends on the extent and location of the primary tumor. Structures involved with tumor should be specified.

The previous AJCC system (Beahrs and Meyers, 1983) has been modified so that invasion of adjacent structures is presently classified as T_4 (Beahrs et al, 1988). In the new system, stage II is subdivided into stage IIA and stage IIB for finer discrimination. This subdivision is based on lymph node involvement. The number of lymph node categories has been reduced from five to three.

Classification

Primary tumor (T) (AJCC; Beahrs et al, 1988)

T_x	Primary tumor cannot be assessed.
T_0	No evidence of primary tumor.
T_{is}	Carcinoma *in situ.*
T_1	Tumor invades lamina propria or submucosa.
T_2	Tumor invades muscularis propria.
T_3	Tumor invades adventitia.
T_4	Tumor invades adjacent structures.

Regional lymph nodes (N)

N_x	Regional lymph nodes cannot be assessed.
N_0	No regional lymph node metastasis.
N_1	Regional lymph node metastasis.

Stage grouping

Stage 0	T_{is}	N_0	M_0
Stage I	T_1	N_0	M_0
Stage IIA	T_2	N_0	M_0
	T_3	N_0	M_0
Stage IIB	T_1	N_1	M_0
	T_2	N_1	M_0
Stage III	T_3	N_1	M_0
	T_4	Any N	M_0
Stage IV	Any T	Any N	M_1.