PART I—SECTION 2: LAB TESTS, TUMOR MARKERS, AND SITE-SPECIFIC FACTOR NOTES

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INTEGRATING UPDATES THROUGH JANUARY 1, 2010
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LAB TESTS AND TUMOR MARKERS

RECORDING LAB TESTS AND TUMOR MARKERS IN SITE-SPECIFIC FACTORS

IMPORTANT NOTES

The following information is intended as a guide to help the registrar locate the test in the medical record and to identify which lab test results should be coded in the CS site-specific factors.

1. The results of many tumor markers and laboratory tests vary according to the laboratory conducting the test. The normal reference range and notes are included in the tumor marker comments as background information only.
   a. Whenever possible, code the clinician’s/pathologist’s interpretation of the lab test.
   b. In the absence of a doctor’s interpretation of the test, if the reference range for the lab is listed on the test report, the registrar can use that information to assign the appropriate code.
   c. Only when there is no clinician/pathologist interpretation of the lab test and no description of the reference range in the medical record should the registrar use the background information listed in these tumor marker notes to code the SSF.

2. In the coding instructions, only the codes pertaining to coding the test are listed. Refer to the Collaborative Staging Manual for additional code choices when the test results are not in the medical record.

3. What does SI mean? SI is the French abbreviation for International System, standard units of measure (meter, kilogram, second). Most SI values are based on the kilogram and the liter. A nanogram (ng) is one-thousandth of a microgram (μg). A milliliter (ml) is one-thousandth of a liter. So a lab value expressed in μg/L is equivalent to the same value expressed in ng/ml. Some lab values, such as hormone levels, are recorded in International Units per Liter (IU/L). This is equivalent to mIU/mL. The equivalence of mIU to ng varies according to what is measured.

   SI Conversion: 1 μg/L = 1 ng/ml. For example, 1 ng of AFP is approximately equal to 1 mIU.
   Note: Micrograms (μg) per liter may be printed as ug/L.

4. Prefixes and abbreviations. Units of measure can be described and written in various ways in the medical record. In some circumstances, the unit of measure may be dependent on the printer used for the report. For example, the prefix “micron” (one millionth of a unit) is represented in scientific notation by the Greek letter μ (μ), but not all printers have the capability to print Greek symbols. As a result, micro- may be printed as a lower case μ or as the abbreviation mc. Do not confuse the abbreviation for micro- (μ) with the abbreviation for Unit (an international system measurement, U). The tables below show abbreviations for units of measurement and the abbreviations for fractions or multiples of those units.
Common Codes in Site-Specific Factors

- In a numeric site-specific factor, such as a lab value for CEA, Chromogranin, CA-125, code 000 means a zero value on the test itself.
- The upper range of true values is usually 97.9 or 979 (depending on the type of test), with code 980 indicating that the true value was higher.
- If it is known that the test was ordered but there is no report in the record, code 997. This code is useful as a quality control flag to indicate cases where information may be available at a later date.
- If there is a statement that the test was not performed, use code 988. Do not assume that the test was not done if the report is missing from the medical record.
- If there is no information in the medical record about the lab value, use code 999.

Note: In CS version 1, the ‘not applicable code’ was 888, which limited the code range for lab

<table>
<thead>
<tr>
<th>Number</th>
<th>Prefix</th>
<th>Written</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,000,000</td>
<td>Mega-</td>
<td>M</td>
</tr>
<tr>
<td>1000</td>
<td>Kilo-</td>
<td>k</td>
</tr>
<tr>
<td>10</td>
<td>Deka-</td>
<td>da</td>
</tr>
<tr>
<td>1 (baseline)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1/10</td>
<td>Deci-</td>
<td>d</td>
</tr>
<tr>
<td>1/100</td>
<td>Centi-</td>
<td>c</td>
</tr>
<tr>
<td>1/1000</td>
<td>Milli-</td>
<td>m</td>
</tr>
<tr>
<td>One millionth</td>
<td>Micro-</td>
<td>m, u, or mc</td>
</tr>
<tr>
<td>One billionth</td>
<td>Nano-</td>
<td>n</td>
</tr>
<tr>
<td>One trillionth</td>
<td>Pico-</td>
<td>p</td>
</tr>
<tr>
<td>One quadrillionth</td>
<td>Femto</td>
<td>f</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Unit</th>
<th>Abbrev.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Liter</td>
<td>L, l</td>
</tr>
<tr>
<td>Unit</td>
<td>U</td>
</tr>
<tr>
<td>Meter</td>
<td>M</td>
</tr>
<tr>
<td>Unit-of- substance</td>
<td>Mole, mol</td>
</tr>
<tr>
<td>Gram</td>
<td>gr</td>
</tr>
<tr>
<td>milli-Equivalent</td>
<td>mEq</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femtomole</td>
</tr>
<tr>
<td>Microgram</td>
</tr>
<tr>
<td>Milliliter</td>
</tr>
</tbody>
</table>
test values. In CSv2, the code 888 was converted to 988. Code 988 appears as ‘obsolete data converted and retained’ if the site-specific factor was not used in version 1 and the field is used in version 2.

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>0 ng/ml</td>
</tr>
<tr>
<td>001</td>
<td>0.1 or less ng/ml</td>
</tr>
<tr>
<td>002-979</td>
<td>0.2-97.9 ng/ml</td>
</tr>
<tr>
<td>980</td>
<td>98.0 or greater ng/ml</td>
</tr>
<tr>
<td>988</td>
<td>OBSOLETE DATA CONVERTED AND RETAINED V0200</td>
</tr>
<tr>
<td></td>
<td>Code 888 was used in version 1 and was converted to 988 for version 2.</td>
</tr>
<tr>
<td>997</td>
<td>Test ordered, results not in chart</td>
</tr>
<tr>
<td>998</td>
<td>Test not done (test was not ordered and was not performed)</td>
</tr>
<tr>
<td>999</td>
<td>Unknown or no information</td>
</tr>
<tr>
<td></td>
<td>Not documented in patient record</td>
</tr>
</tbody>
</table>
The following tumor markers are common to several site or histology-specific schemas. The Tumor Marker Notes are in alphabetical order by the name of the test.

CA 19-9
*Appears in Schemas:* Stomach; Appendix carcinoma; Ampulla of Vater; Intrahepatic bile ducts; Perihilar bile duct; Distal bile duct; all subsites of Pancreas
*Source documents:* clinical laboratory report (blood serum), history and physical
*Other names:* Carbohydrate antigen 19-9; GICA; Gastrointestinal Cancer Antigen; CA-GI; Cancer Antigen-GI
*Normal reference range:* < 37 U/mL

Serum Carbohydrate Antigen 19-9 is an important tumor marker in the management of gastrointestinal and hepatobiliary malignancies. CA 19-9 is produced in excess by adenocarcinomas and released into the blood. It is elevated in pancreatic (70-80%), hepatobiliary (60%), and gastric (50-60%) malignancies. Levels above 1000 U/mL indicate the presence of metastases and probably unresectable tumor. CA 19-9 is also elevated in acute pancreatitis, cholangitis, cirrhosis and other conditions, so it is not useful as a screening test but has value in monitoring for possible recurrence of known cancer.

This site-specific factor is a three digit field with an implied decimal point between the second and third digits. Record in Units/milliliter (U/mL) the highest pre-treatment CA 19-9 lab value documented in the medical record. In Canada, the unit of measurement is KiloU/Liter (KU/L). To convert, multiply KU/L by 1000.

For example: A pretreatment CA 19-9 of 60 (60.0) U/mL would be recorded as 600.

CEA (CARCINOEMBRYONIC ANTIGEN) LAB VALUE AND INTERPRETATION
*Used in schemas:* Stomach; Small intestine; Appendix carcinoma; Colon; Rectum; Ampulla of Vater; Perihilar bile ducts; Distal bile ducts; Ampulla of Vater
*Source documents:* clinical laboratory report, sometimes pathology or cytology report; H&P, operative report; consultant report; discharge summary
*Other names:* Carcinoembryonic antigen
*Normal reference range*

Non-smoker: < 2.5 ng/ml (SI: < 2.5 μg/L)  
Smoker: < 5 ng/ml (SI: < 5 μg/L)

SI Conversion: 1 μg/L = 1 ng/ml.  
1 μg/mL = 1 mg/L

CEA is a protein molecule found in many different cells of the body but associated with certain tumors and with the developing fetus. CEA is used as a tumor marker especially for gastrointestinal cancers with colorectal cancer as the most frequent cause for an increased/elevated CEA. CEA is also elevated by biliary obstruction, alcoholic hepatitis and heavy smoking. CEA level is most frequently tested on blood serum, but it may be tested in body fluids and or biopsy tissue.

An abnormally high CEA level prior to tumor resection is expected to fall following successful removal of the cancer. An increasing value indicates possible recurrence.

CEA Lab Value is a three digit field with an implied decimal point between the second and third digits. The field CEA is the clinician’s interpretation of the lab value.
Record both the reported value and the clinician’s interpretation of the highest value prior to treatment. Code in nanograms per milliliter (ng/ml) the highest preoperative CEA lab value documented. If multiple CEA tests were performed prior to treatment, record the highest value.

**CEA Interpretation**
Code the corresponding interpretation of the CEA lab value as stated by the clinician. Use code 000 if there is a statement in the record that If there is no statement that the CEA is positive/elevated, negative/normal or the like, code the interpretation as 999.

010  Positive/elevated  
020  Negative/normal  
030  Borderline; undetermined whether positive or negative

**Notes:** CEA is not a screening test and is not specific to colorectal cancer. Unlikely to be benign if > 10 ng/ml. Distant metastasis most likely if >100 ng/ml.

**CHROMOGRAININ A (CGA)**

*Appears in Schemas:* Pancreas (endocrine, all subsites); Neuroendocrine tumors – Stomach; Small intestine; Appendix; Colon; Rectum; Ampulla of Vater

*Source documents:* pathology report (immunohistochemistry stain) or clinical lab report (blood serum)

*Other names:* Serum chromogranin A, CGA, chromogranin

*Normal reference range*
Path report: Positive/negative  
Lab: 6.0 – 40.0 ng/mL Results vary by laboratory

Chromogranin is a protein released from neuroendocrine cells found throughout the neuroendocrine system. As such, the presence of chromogranin in blood or tissue is a marker for neuroendocrine tumors. Although a positive test can indicate a neuroendocrine tumor, it cannot identify which organ is the source. Chromogranin A is positive more often for well-differentiated NET (carcinoid) than poorly-differentiated

This site-specific factor is a three digit field with an implied decimal point between the second and third digits. Record the highest CgA lab value recorded in the medical record prior to treatment. For example, pretreatment CgA of 400 nanograms per milliliter (ng/ml), record as 400.

**HPV (HUMAN PAPILLOMA VIRUS) STATUS**

*Appears in Schemas:* All head and neck sites (carcinoma and melanoma) except major salivary glands and “Other Pharynx”; Anus; Penis

*Source documents:* pathology report (immunohistochemical staining), molecular analysis

*Other names:* human papillomavirus, HPV, HPV DNA test, human papillomavirus in situ hybridization, HPV hybrid capture test; high risk types: hr-HPV, HRHPV

Human papilloma virus (HPV) has been identified as a factor in the development of a defined subset of head and neck cancers, particularly those of the oropharynx, and this is an active area of research interest. HPV is also associated with anal, penile, and cervical cancers. Clinical implications include HPV detection as a means of assessing cancer risk, detecting early cancers, suggesting the site of tumor origin for patients with clinically occult primary cancer, monitoring disease recurrence and progression, predicting clinical outcomes, and identifying patients who may benefit from immunology-based therapies. The association with HPV infections has been linked with an improved prognosis. HPV testing may be performed for prognostic purposes; testing may also be performed on metastatic sites to aid in the determination of the primary site.
Human papilloma viruses have been divided into high-risk and low-risk types. The table notes identify the high and low risk types. The codes are structured to collect specific information about two high-risk types, 16 and 18. Other high risk types are 31, 33, 35, 36, 45, 51, 52, 56, 58, 59, 68, 26, 53, 66, 67, 69, 70, 73, 82, 85. Low risk types are 6, 11, 32, 34, 40, 42, 44, 54, 61, 62, 64, 71, 72, 74, 81, 83, 84, 87, 89. The HPV vaccine is designed to protect against types 16 and 18 (associated with cervical cancer) and types 6 and 11 (associated with genital warts).

Note 5: Some tests for HPV, such as a hybrid capture test, only report negative or positive for high risk HPV without identifying types; use codes 025 and 050, respectively to report those test results.

Record the results of any HPV testing performed on pathologic specimens from the primary tumor or a metastatic site, including regional nodes. Read the codes carefully to make the correct selection.

- Code 000 means negative for any HPV; if the test results specify negative for high risk HPV with no mention of low risk HPV, use code 000.
- Code 010 is positive for any type of low risk HPV.
- Codes 020 through 060 indicate positive test results for high risk HPV. Codes 020 through 060 can be used with or without positive results for low risk types of HPV. Codes 030 through 050 can be used with or without positive results for other types of high risk HPV.
  - Use code 020 for types other than 16 or 18
  - Use code 030 for 16 and not 18
  - Use code 040 for 18 and not 16
  - Use code 050 for both 16 and 18
  - Use code 060 for types not specified.
- Use code 070 if the only information is that HPV results are positive, but risk and type of HPV not specified.
- Code 997 is a standard code in site-specific factor tables for test ordered but results not in chart.
- Code 998 is a standard code for test not done; the code description also shows that this code should be used if there is no pathologic specimen available for testing. If it is known that no specimen was taken, code 998 is the appropriate code to use, rather than code 999.
- Code 999 is a standard code for no information whatsoever available regarding this data item.

**LDH, LDH VALUE, LDH UPPER LIMIT OF NORMAL**

**Appears in Schemas:** MelanomaSkin, Testis, LymphomaOcularAdnexa

**Source documents:** clinical laboratory report; may be included in a liver or hepatic panel/profile, a cardiac panel, or a general metabolic panel of tests

**Other names:** LD, Lactate dehydrogenase, lactase dehydrogenase, lactic acid dehydrogenase.

**Normal reference range** varies widely by laboratory, patient age, and the units of measurement.

Examples of reference range lab values:

- Lab A Total LDH  71 – 207 U/L
- Lab B Total LDH  300 – 600 U/L
- Lab C Total LDH  45 – 90 U/L
- Lab D Total LDH  150 – 250 U/L

Elevated lactate dehydrogenase (LDH) is an indirect indication of possible tumor burden or damage to an organ, such as metastatic involvement of liver or lung, or a myocardial infarction. The total LDH should be the test value that is coded, but there are five fractions of LDH that measure tissue specific cellular damage: LD1 and LD2: heart, red blood cells and kidneys; LD3: lung; LD4 and LD5: liver, skin and
skeletal muscles. LDH is elevated in 60% of patients with nonseminomatous germ cell tumors of the testis. LDH is not a screening test, nor is it diagnostic of melanoma, ocular adnexal lymphoma, or testicular cancer.

**LDH (MelanomaSkin); LDH Interpretation (LymphomaOcularAdnexa); Preorchiectomy LDH Interpretation (Testis)**

Record the code describing the range of the highest LDH value prior to treatment, based on the reference range used by the lab. The codes vary slightly for each schema, but the concepts are the same.

<table>
<thead>
<tr>
<th>Ocular Adnexal</th>
<th>Melanoma</th>
<th>Testis</th>
<th>Lymphoma</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>998</td>
<td>998</td>
<td>Test not done; test not ordered and not performed</td>
<td></td>
</tr>
<tr>
<td>002</td>
<td>000</td>
<td>000</td>
<td>Within normal limits</td>
<td></td>
</tr>
<tr>
<td>004</td>
<td>010</td>
<td>010</td>
<td>Range 1: less than 1.5 times the upper limit of normal for that lab; <em>for melanoma only</em>: Stated as elevated, NOS</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>020</td>
<td><em>For ocular adnexal lymphoma only</em>: 1.5 to 5 times upper limit of normal</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>025</td>
<td><em>For ocular adnexal lymphoma only</em>: 5.1 to 10 times upper limit of normal</td>
<td></td>
</tr>
<tr>
<td>005</td>
<td>020</td>
<td></td>
<td>Range 2: 1.5 to 10 times the upper limit of normal for that lab</td>
<td></td>
</tr>
<tr>
<td>006</td>
<td>030</td>
<td>030</td>
<td>Range 3: more than 10 times the upper limit of normal for that lab</td>
<td></td>
</tr>
<tr>
<td>008</td>
<td>997</td>
<td>997</td>
<td>Test ordered, but results not in chart</td>
<td></td>
</tr>
</tbody>
</table>

To calculate whether the lab result is in a particular range, multiply the lab’s upper limit of normal (usually stated on the report) times 1.5. If the test result is within normal limits, code as 002. If the test result is elevated, determine whether it is less than 1.5 times the upper limit of normal (code 004), between 1.5 and 10 times the upper limit of normal (code 005) or more than 10 times the upper limit of normal (code 006).

*Example*  
Test result is 155.  
For Labs A and D (above), that result is within the normal range (code 000 for testis).  
For Lab C, the test result is elevated. Calculate 1.5 times the upper limit of normal for Lab C (1.5 x 90 = 135). For Lab C, this test result would be coded as 020 for testis, between 1.5 and 10 times the upper limit of normal.

For melanoma, an abnormal value (SSF4 codes 004-006) must be documented by at least two separate tests obtained more than 24 hours apart, according to the *AJCC Cancer Staging Manual*.  
**Note:** LDH may not be done for early stage melanomas. If so, code as 000.

**LDH Value (MelanomaSkin)**

Record the actual value of the LDH prior to treatment or within 6 weeks of diagnosis. The earlier test has priority. Code the actual value if between 001 and 800. Above 800, code the appropriate range. Read the range choices carefully as they differ as the values increase. A value over 10,000 is coded as 922. If test is not performed, code as 998.

**LDH Upper Limit of Normal (MelanomaSkin)**

This site-specific factor corresponds to LDH Value and can be used to calculate the range in the LDH [Interpretation] field. Code the upper limit of normal as stated on the clinical laboratory report

<table>
<thead>
<tr>
<th>Upper limit of normal</th>
</tr>
</thead>
<tbody>
<tr>
<td>001-979</td>
</tr>
<tr>
<td>997</td>
</tr>
<tr>
<td>998</td>
</tr>
<tr>
<td>Test not done</td>
</tr>
</tbody>
</table>
MICROSATELLITE INSTABILITY

*Appears in Schemas:* SmallIntestine, Colon, Rectum, Appendix [carcinoma]

- Code microsatellite instability (MSI), which is a molecular marker.
- MSI is a genetic test performed on tumor tissue to identify differences in length of sections of nonfunctioning DNA. The differences in length may be caused by problems with the genes that normally repair DNA.
- Highly positive MSI test may indicate that the gene repair problem is related to the development of cancer and that the patient may have hereditary nonpolyposis colorectal cancer (HNPCC or Lynch Syndrome). Low-positive or stable MSI result means it is unlikely that the cancer is genetic.
  - HNPCC is hereditary autosomal dominant cancer characterized by discrete adenomas of colon & rectum WITHOUT polyposis.
- MSI may also be a predictive marker of a patient’s response to chemotherapy as well as an indicator of the patient’s prognosis.
- Info about molecular marker MSI should be in pathology report.

MITOTIC COUNT

*Appears in Schemas:* GISTEsophagus, GISTStomach, NETStomach, GISTSmallIntestine, NETSmallIntestine, GISTColon, NETColon, GISTAppendix, GISTRectum, NETRectum, NETAmpulla, PancreasHead, PancreasBodyTail, PancreasOther, MelanomaSkin, GISTPeritoneum, MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris

*Source documents:* pathology report

*Other names:* Mitotic rate, mitotic index (a ratio—do not record this measurement), mitotic activity

Record the number of cells actively dividing as determined by the pathologist. The count will vary according to the type of tumor. Follow the instructions in the SSF notes.

- NET (ampulla, colon, rectum, small intestine, stomach): count per 10 high power fields (HPF*) or 2 square millimeters.
- GIST (appendix, colon, esophagus, peritoneum, rectum, small intestine, stomach): count per 50 HPF* or 5 square millimeters
- Melanoma of skin: count per square millimeter
- Ocular melanoma (choroids, ciliary body, iris): count per 40 HPF* or 4 square millimeters
  * The usual high power is 40x magnification.

This site-specific factor is a three digit field with an implied decimal point between the second and third digits. For example, if the mitotic count is reported as .5 mitoses per 10 HPF for a neuroendocrine tumor, record as 005. If the mitotic rate is reported as 12 mitoses per 50 HPF for a gastrointestinal stromal tumor, record as 120.
SITE-SPECIFIC NOTES
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SITE SPECIFIC FACTORS BY BODY SYSTEM
Note: Grayed-out items are included in this version.

Head and Neck – Carcinoma and melanoma
Lymph nodes
- Lymph Nodes Levels
- Upper/Lower Cervical
- Extracapsular Extension
HPV status
Thickness/depth
Schema discriminator

Upper GI
- Clinical assessment of Regional LN
- Specific location of tumor (esoph, stomach)
  - Number of reg LN with extracaps tumor
  - Distance to prox edge from incisors
  - Distance to distal edge from incisors
  - Crohn’s disease (sm intest)
  - Microsatellite instability (sm intest)
  - Schema discriminator
- CEA
- CA 19-9

GIST
- Mitotic count
- KIT IHC and mutation
- PDGFRA
- Multiplicity

NET
- Mitotic count
- Chromogranin A
- Urine 5-HIAA

Lower GI
- CEA
- Clinical assessment of Regional LN
- Tumor deposits
- Tumor regression grade
- Circumferential resection margin
- Microsatellite instability
- Perineural invasion
- KRAS
- 18q loss of heterozygosity
- HPV status (anus)

Biliary and Pancreas
- AFP
- Fibrosis score
- Creatinine
- Total bilirubin
- INR
- Tumor growth pattern
- Primary sclerosing cholangitis
- CA 19-9
- CEA
- Extent of liver resection
- Primary tumor location (gallbladder)
- Chromogranin A (pancreas)
- Mitotic count (pancreas)
- Schema discriminator

Lung and pleura
- Separate tumor nodules ipsilateral lung
- Visceral pleural invasion/elastic layer
- Pleural effusion (pleura)
- Mesothelioma subtype (pleura)
- History of asbestos exposure (pleura)
- Presence of chest pain (pleura)
- PET SUV (pleura)

Bone
- Tumor size 2nd largest dimension
- Tumor size 3rd largest dimension
- Percent necrosis post neoadjuvant chemo
- Resected pulmonary mets

Skin
- Measured thickness/depth
- Clark’s level
- Perineural invasion
- High risk features
- Size of LN
- Clinical status LN
- Tumor base transection status
- TIL
- Growth pattern prim tum
- Profound immune suppression
- Size mets in LN
- Extracaps Ext Reg LN
- ITCs Reg LN
- Ulceration
- LDH
- LDH value
LDH upper limits
Primary tumor mitotic rate
Primary tumor regression
Vertical growth phase
Peripheral blood involvement
Regional Lymph Node – Laterality

Soft Tissue
Grade for sarcomas
Neurovascular invasion
Bone involvement
Path P1: source pathology metastases specimen
Schema discriminator (peritoneum)

Breast
ERA/PRA
Number positive axillary LN
IHC LN
Molec studies LN
Tumor size invasive
Nottingham/Bloom Richardson score/grade
HER
IHC lab and interpretation
FISH lab and interpretation
CISH lab and interpretation
Result other/unknown test
Summary result of testing
Combination ER-PR-HER2
CTC and method of detection
DTC and method of detection
Assessment of ipsilateral axillary LN
Response to neoadjuvant treatment
Multigene signature method
Result/score multigene signature
Paget disease

GYN sites
FIGO stage Vu10, Va1, Ce1, CoCa1, CoAd1, CoSa1, Ov2, FT1, PI2, Pe2
Regional LN laterality (vulva) Vu11
Pelvic node status and assessment
Vu12-13, Va2-3, Ce2-3
Para-aortic node status and assessment
Va4-5, Ce4-5
Femoral inguinal node status and assessment Vu14-15
Distant (mediastinal, scalene) node status and assessment Va6-7
Mediastinal node status and assessment Ce6-7
Scalene node status and assessment Ce8-9
Number positive/examined pelvic nodes CoCa3-4, CoAd3-4, CoSa3-4, FT4-5

Number positive/examined para-aortic nodes CoCa5-6, CoAd5-6, CoSa5-6, FT6-7
Peritoneal cytology CoCa2, CoAd2, CoSa2
Percent non-endometrioid cell type in mixed histology tumors CoCa7, CoAd7, CoSa7
Omentectomy CoCa8, CoAd8, CoSa8
CA-125 Ov1, Pe1
Residual tumor status after cytoreductive surgery Ov3, Pe3
Tumor location after primary cytoreduction (debulking) surgery Ov4, Pe4
Malignant ascites Ov5
Biopsy metastatic site FT2
Primary tumor location FT3
Prognostic scoring index PI1
Schema discriminator Pe25

Male Genital
Involvement of corpus spongiosum/cavernosum
Percent poorly-differentiated tumor
Size LN metastases
Extranodal extension in regional LN
HPV status
PSA lab and interpretation
Extension-pathologic Gleason primary/secondary and score on core biopsy or TURP
Gleason primary/secondary and score on prostatectomy or autopsy
Gleason tertiary pattern
Number of cores positive/examined
Core biopsy findings
Clinical staging procedures
Radical orchietomy performed
Size of mets in LN
Preorchietomy AFP and interpretation
Preorchietomy HCG and interpretation
Preorchietomy LDH
Persistent elevation of tumor markers
Measured thickness
Clark’s level
Perineural invasion
High risk features
Size of LN

Kidney
Invasion beyond capsule
Vein involvement
Ipsilateral adrenal gland involvement
Collaborative Stage Data Collection System Coding Manual and Instructions
Part I Section 2: Site-Specific Notes

Sarcomatoid features
Tumor necrosis
Fuhrman grade
Size of metastasis in LN
Extranodal extension

Associated with HIV/AIDS

Lymphoma and Heme-Retic
Associated with HIV/AIDS
Systemic symptoms at diagnosis
IPI score
FLIPI score
IPS
JAK-2 (heme-retic)

Urinary Tract
WHO/ISUP grade
Depth renal parenchyma invasion
Size of metastasis in LN
Extranodal extension

CNS
WHO grade
KI-67/MIB-1
Karnofsky score
MGMT methylation
Chromosome 1p: Loss of Heterozygosity (LOH) Br, OthCNS 5
Chromosome 19q: Loss of Heterozygosity (LOH) Br, OthCNS 6
Surgical resection
Focus primary tumor
Intracranial Proliferative Fraction- Ki-67/MIB-1

Endocrine
Solitary vs. multifocal (thyroid)
Tumor weight (adrenal)
Vascular invasion (adrenal)
WHO grade (other endocrine)

Kaposi Sarcoma
TO BE COMPLETED IN NEXT VERSION (61 SSFs, 43 to finish)

Skin of Eyelid
- Measured thickness for SCC
- Clark’s level
- Perineural invasion
- Size of LN
- Sentinel LN biopsy
- Clinical status LN
- Tumor necrosis
- Pagetoid spread
- Mohs layers
- Prior radiation
- HIV status
- Solid organ transplant
- Leukemia
- Multiple carcinomas
- Muir-Torre Syndrome
- Xeroderma Pigmentosa

Clinic extension 2nd eye
- Clinical extension
- Ocular lymphoma
- Associated with HIV/AIDS
- Systemic symptoms
- IPI score
- FLIPI score
- Ki-67
- LDH
- Rheumatoid arthritis
- Sjogren syndrome
- Other Connective tissue disease
- Sicca syndrome
- Other viral infection
- Bacterial infection
- Other infection

Eye
- Tumor size
- Ki-67 lab value
- Tumor thickness
- Quadrants
- Grade – melanoma origin
- Measured basal diameter
- Size largest metastasis
- Chromosome 3 status
- Chromosome 6p status
- Chromosome 8q status
- Gene expression profile

(SEE 11-30-09 Email from Jennifer Seiffert)
- Mitotic count
- Mean diameter nucleoli
- Extravascular matrix patterns – loops
- Extravascular matrix patterns – networks
- Microvascular density
- PET SUV
- Schema discriminator (2 different)
- NM23
- Clinical node evaluation
- Perineural involvement
- Carcinoma ex pleomorphic adenoma
- Invasion beyond capsule
- Adenoid cystic carcinoma basaloid
- Pattern
- Mucoepidermoid carcinoma grade
- Orbital bone
- Extension evaluation at enucleation
- Retinoblastoma gene mutation
- Family history of retinoblastoma
- Globe sparing treatment failure
- Linear choroid involvement
Note: Source documents are suggested for some site-specific factors as the most likely source of information. If no source document is suggested, use any information provided in the medical record. If a pathology report is suggested, that document includes any addenda or revisions to the report, as well as any synoptic report, CAP protocol, cancer checklist information provided by the pathologist.

HEAD AND NECK SITES

The following site-specific factors apply as indicated in the table below (Table I-2-1) to the site-histology combination schemas listed.

SSF1 Size of Lymph Nodes
SSF2 OBSOLETE - Extracapsular Extension, Lymph Nodes for Head and Neck
SSF3 Levels I-III, Lymph Nodes for Head and Neck
SSF4 Levels IV-V and Retropharyngeal Lymph Nodes for Head and Neck
SSF5 Levels VI-VII and Facial Lymph Nodes for Head and Neck
SSF6 Parapharyngeal, Parotid, and Suboccipital/Retroauricular Lymph Nodes, Lymph Nodes for Head and Neck
SSF7 Upper and Lower Cervical Node Levels
SSF8 Extracapsular Extension Clinically, Lymph Nodes for Head and Neck
SSF9 Extracapsular Extension Pathologically, Lymph Nodes for Head and Neck
SSF10 HPV (Human Papilloma Virus) Status
SSF11 Measured Thickness (Depth)

Table I-2-1. Head and Neck Schema Site-Specific Factors

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Version date: 25 January 2010 I-2-17 Version 02.00.01
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<tr>
<td>C32.0</td>
<td>Melanoma LarynxGlottic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C32.1</td>
<td>Larynx Supraglottic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C32.1</td>
<td>Melanoma Larynx Supraglottic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C32.2</td>
<td>LarynxSubglottic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C32.2</td>
<td>Melanoma LarynxSubglottic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C32.3, C32.8-C32.9</td>
<td>LarynxOther</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C32.3, C32.8-C32.9</td>
<td>Melanoma LarynxOther</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**CODING REGIONAL LYMPH NODES**

For head and neck sites, regional lymph node information is coded in several fields (Table I-2-2).

Table I-2-2. Regional Lymph Nodes Data Fields
FIELD                        DESCRIPTION
CS Lymph Nodes              Regional lymph nodes: number, laterality
CS Reg Nodes Eval           Clinical or pathologic evaluation
CS LN Pos                   Number of lymph nodes microscopically positive
CS LN Exam                  Number of lymph nodes microscopically examined
SSF1                        Size of lymph node
SSF2                        OBSOLETE
SSF3                        Node Levels I – III
SSF4                        Node Levels IV – V, Retropharyngeal
SSF5                        Node Levels VI – VII, Facial
SSF6                        Other regional nodes: parapharyngeal, parotid, suboccipital
SSF7                        Upper/Lower Neck
SSF8                        Extracapsular Extension – Clinical
SSF9                        Extracapsular Extension – Pathologic

The CS Lymph Nodes field contains information about the nodes involved, their number and laterality. Site-Specific Factor (SSF) 1 is used to code the size of involved lymph nodes. Site-Specific Factor 2 was used in version 1 to code the presence of extracapsular extension. SSF2 is marked as obsolete in version 2; clinical and pathologic extracapsular extensions have been split out as SSFs 8 and 9. Site-Specific Factors 3 through 6 are used to code the presence or absence of lymph node involvement in each of 7 different lymph node levels and other nodal groups defined by AJCC. The definitions of the levels are the same for all applicable head and neck sites (see Figure I-2-1). Site-Specific Factor 7 is a prognostic indicator that further defines the involved lymph nodes as upper or lower cervical.

Figure I-2-1. Lymph Node Levels of Head and Neck

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Submental, submandibular</td>
</tr>
<tr>
<td>II</td>
<td>Upper deep cervical</td>
</tr>
<tr>
<td>III</td>
<td>Middle deep cervical</td>
</tr>
<tr>
<td>IV</td>
<td>Lower deep cervical</td>
</tr>
<tr>
<td>V</td>
<td>Posterior triangle</td>
</tr>
<tr>
<td>VI</td>
<td>Anterior compartment</td>
</tr>
<tr>
<td>VII</td>
<td>Superior mediastinal</td>
</tr>
</tbody>
</table>

NOTE: See further information on lymph node levels below.

In each of the three-digit site-specific factors 3 – 6, an individual digit represents lymph nodes of a single level. For example, the three digits of Site-Specific Factor 3 represent lymph nodes of Levels I, II and III, respectively. The digits of Site-Specific Factor 4 represent lymph nodes of Levels IV and V and the retropharyngeal nodes. The digits of Site-Specific Factor 5 represent lymph nodes of Levels VI and VII and the facial nodes. The digits of Site-Specific Factor 6 representing the remaining other groups as defined by AJCC. In each digit, code 1 means Yes, the nodes are involved or code 0 means No, the lymph nodes are not involved. See Figure 2a for the layout of Site-Specific Factors 3 through 6 and Figure 2b for the interpretation of a coded example.

Coding Unknown in SSF 3 – 6
In Site-Specific Factors 3 – 6 for lymph node levels, use code 9 only when it is unknown if lymph nodes
are involved. Within each of the Site-Specific Factors 3 – 6, do not code 9 in some positions and 0 or 1 in other positions. If specific information is available about the positive or negative status of some but not all nodes in any one level or group, assume that the rest of the nodes in the same Site-Specific Factor are negative and code accordingly.

**Figure I-2-2a. Layout of Site-Specific Factors for Head and Neck Sites**

<table>
<thead>
<tr>
<th>Site-Specific Factor</th>
<th>Description</th>
<th>1st digit</th>
<th>2nd digit</th>
<th>3rd digit</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSF3</td>
<td>Levels I – III</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Level I</td>
<td>Level II</td>
<td>Level III</td>
</tr>
<tr>
<td>SSF4</td>
<td>Levels IV – V, Retroph.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Level IV</td>
<td>Level V</td>
<td>Retropharyngeal</td>
</tr>
<tr>
<td>SSF5</td>
<td>Levels VI – VII, Facial</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Level VI</td>
<td>Level VII</td>
<td>Facial</td>
</tr>
<tr>
<td>SSF6</td>
<td>Other Groups</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parapharyngeal</td>
<td>Parotid</td>
<td>Suboccipital</td>
</tr>
</tbody>
</table>

**Figure I-2-2b. Example and Interpretation of Site-Specific Factors for Head and Neck Sites**

Example: Left radical neck dissection: 2 positive parotid nodes (<3 cm with extracapsular extension), 1 positive buccal (facial) node (2 cm), and 1 positive 2 cm submandibular node.

<table>
<thead>
<tr>
<th>Site-Specific Factor</th>
<th>Description</th>
<th>1st digit</th>
<th>2nd digit</th>
<th>3rd digit</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSF3</td>
<td>Levels I – III</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Level I</td>
<td>Level II</td>
<td>Level III</td>
</tr>
<tr>
<td>SSF4</td>
<td>Levels IV – V, Retroph.</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Level IV</td>
<td>Level V</td>
<td>Retropharyngeal</td>
</tr>
<tr>
<td>SSF5</td>
<td>Levels VI – VII, Facial</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Level VI</td>
<td>Level VII</td>
<td>Facial</td>
</tr>
<tr>
<td>SSF6</td>
<td>Other Groups</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Parapharyngeal</td>
<td>Parotid</td>
<td>Suboccipital</td>
</tr>
</tbody>
</table>

Stored in database as

<table>
<thead>
<tr>
<th>Site-Specific Factor</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSF 3</td>
<td>Level 1 only</td>
</tr>
<tr>
<td>SSF 4</td>
<td>All nodes neg</td>
</tr>
<tr>
<td>SSF 5</td>
<td>Facial nodes only</td>
</tr>
<tr>
<td>SSF 6</td>
<td>Parotid nodes only</td>
</tr>
</tbody>
</table>
Coding NOS

Note: When the only information available is “Regional nodes, NOS” or “Cervical nodes, NOS” or “Internal jugular lymph nodes, NOS” or “Lymph nodes, NOS,” code 0 in all digits of Site-Specific Factors 3 – 6.

Example 1  A carcinoma of the base of tongue involves bilateral submandibular nodes and left upper, mid-, and lower jugular nodes, the largest measuring 4 cm. There is no extracapsular extension. These are level I, II, III, and IV lymph nodes according to AJCC definitions. CS Lymph Nodes is coded 400 (bilateral or contralateral nodes). Site-Specific Factor 1 is coded 040 indicating the largest size. Site-Specific Factor 2 is coded 000 for no extracapsular extension. Site-Specific Factor 3 is coded 111, to show that levels I, II, and III are involved. Site-Specific Factor 4 is coded 100 to show that level IV is involved. Site-Specific Factors 5 and 6 are each coded 000, since no other nodes are involved.

Example 2  Laryngeal biopsy with squamous cell carcinoma, no other information available. CS Lymph Nodes is coded 99. Site-Specific factors 1 – 6 are each coded 999, since no information is available regarding lymph node involvement.

Example 3  Patient diagnosed elsewhere with carcinoma of oropharynx with cervical lymph node involvement. No other information available. CS Lymph Nodes is coded 500 (regional nodes, NOS, not stated if ipsilateral, bilateral, or contralateral, or if single or multiple). Site-specific Factors 1 and 2 are each coded 999. Site-Specific Factors 3-6 are each coded 000.

Definitions of Levels for Head and Neck Sites

The definitions of the levels and the lymph node chains included in each level are as follows:

Level I (First digit of SSF 3) contains the submental and submandibular triangles bounded by the anterior and posterior bellies of the digastric muscle, and the hyoid bone inferiorly, and the body of the mandible superiorly. Lymph node chains at this level:

- Submandibular
- Submaxillary
- Submental

Level II (Middle digit of SSF3) contains the upper jugular lymph nodes and extends from the level of the skull base superiorly to the hyoid bone inferiorly. Lymph node chains at this level:

- Jugulodigastric (subdigastric
- Upper deep cervical
- Upper jugular

Level III (Last digit of SSF3) contains the middle jugular lymph nodes from the hyoid bone superiorly to the level of the lower border of the cricoid cartilage inferiorly. Lymph node chains at this level:

- Middle deep cervical
- Mid-jugular

Level IV (First digit of SSF4) contains the lower jugular lymph nodes from the level of the cricoid cartilage superiorly to the clavicle inferiorly. Lymph node chains at this level:

- Jugulo-omohyoid (supraomohyoid)
- Lower deep cervical
- Lower jugular

Level V (Middle digit of SSF4) contains the lymph nodes in the posterior triangle bounded by the anterior border of the trapezius muscle posteriorly, the posterior border of the sternocleidomastoid muscle anteriorly, and the clavicle inferiorly. For descriptive purposes, Level V may be further subdivided into
upper, middle, and lower levels corresponding to the superior and inferior planes that define Levels II, III, and IV. Lymph node chains at this level:

Posterior cervical
Posterior triangle (spinal accessory and transverse cervical) (upper, middle, and lower, corresponding to the levels that define upper, middle, and lower jugular nodes)

**Level VI** (First digit of SSF5) contains the lymph nodes of the anterior central compartment from the hyoid bone superiorly to the suprasternal notch inferiorly. On each side, the lateral boundary is formed by the medial border of the carotid sheath. Lymph node chains at this level:

<table>
<thead>
<tr>
<th>Anterior deep cervical</th>
<th>Paratracheal</th>
<th>Pretracheal</th>
</tr>
</thead>
<tbody>
<tr>
<td>Laterotracheal</td>
<td>Prelaryngeal (Delphian)</td>
<td>Recurrent laryngeal</td>
</tr>
<tr>
<td>Paralaryngeal</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Level VII** (Middle digit of SSF5) contains the lymph nodes inferior to the suprasternal notch in the superior mediastinum. Lymph node chains at this level:

Upper mediastinal

**Other groups and their positions in site-specific factors**

<table>
<thead>
<tr>
<th>Buccinator (facial)</th>
<th>Last digit of SSF5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nasolabial</td>
<td>Last digit of SSF5</td>
</tr>
<tr>
<td>Parapharyngeal</td>
<td>First digit of SSF6</td>
</tr>
<tr>
<td>Periparotid and intraparotid</td>
<td>Middle digit of SSF6</td>
</tr>
<tr>
<td>Preauricular</td>
<td>Middle digit of SSF6</td>
</tr>
<tr>
<td>Retropharyngeal</td>
<td>Middle digit of SSF6</td>
</tr>
<tr>
<td>Sub-occipital</td>
<td>Last digit of SSF6</td>
</tr>
</tbody>
</table>

**SSF7: UPPER AND LOWER CERVICAL LYMPH NODES**

Site-Specific Factor 7 describes whether the involved lymph nodes are in the upper or lower part of the neck. Where SSFs 3 – 6 are more surgically oriented, SSF 7 is prognostic: for most sites in the head, the lower the involved nodes are in the neck, the worse the patient’s prognosis. The boundary between upper cervical and lower cervical is defined as the lower border of the cricoid cartilage, which is just below the larynx at the top of the trachea. This location is illustrated on Figure I-2-1. The location of various lymph node chains is listed in Table I-2-3.
Table I-2-3. Lymph Nodes of the Head and Neck Showing Level and Site-Specific Factor Positions

<table>
<thead>
<tr>
<th>Name</th>
<th>Level</th>
<th>SSF Code</th>
<th>SSF 3-6</th>
<th>Position</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior compartment</td>
<td>VI</td>
<td>Note 1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Anterior deep cervical</td>
<td>VI</td>
<td>Note 1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Buccinator (buccal)</td>
<td>F</td>
<td>10</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Central compartment</td>
<td>VI</td>
<td>Note 1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Cervical, NOS</td>
<td>--</td>
<td>40</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Deep cervical, NOS</td>
<td>--</td>
<td>40</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Delphian</td>
<td>VI</td>
<td>20</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Facial (NOS)</td>
<td>F</td>
<td>10</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Infra-auricular</td>
<td>PA</td>
<td>10</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Internal jugular, NOS</td>
<td>--</td>
<td>40</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Intraparotid</td>
<td>PA</td>
<td>10</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Jugulodigastric</td>
<td>II</td>
<td>10</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Jugulo-omohyoid</td>
<td>IV</td>
<td>20</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Laterotracheal</td>
<td>VI</td>
<td>20</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Level I node (NOS)</td>
<td>I</td>
<td>10</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Level II node (NOS)</td>
<td>II</td>
<td>10</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Level III node (NOS)</td>
<td>III</td>
<td>10</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Level IV node (NOS)</td>
<td>IV</td>
<td>20</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Level V node (NOS)</td>
<td>V</td>
<td>Note 1</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Level VA (NOS)</td>
<td>V</td>
<td>10</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Level VB (NOS)</td>
<td>V</td>
<td>20</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Level VI node (NOS)</td>
<td>VI</td>
<td>Note 1</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Level VII node (NOS)</td>
<td>VII</td>
<td>20</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Lower deep cervical</td>
<td>IV</td>
<td>20</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Lower jugular</td>
<td>IV</td>
<td>20</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Mandibular, NOS</td>
<td>--</td>
<td>20</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Mastoid</td>
<td>S?</td>
<td>10</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Mid jugular</td>
<td>III</td>
<td>10</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Mid neck</td>
<td>--</td>
<td>40</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Middle deep cervical</td>
<td>III</td>
<td>10</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Nasolabial</td>
<td>F</td>
<td>10</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Paralaryngeal</td>
<td>VI</td>
<td>10</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Parapharyngeal</td>
<td>PP</td>
<td>10</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>Paratracheal</td>
<td>VI</td>
<td>20</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Parotid</td>
<td>PA</td>
<td>10</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Periparotid</td>
<td>PA</td>
<td>10</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Postauricular</td>
<td>S?</td>
<td>10</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Posterior cervical</td>
<td>V</td>
<td>Note 1</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Posterior triangle</td>
<td>V</td>
<td>Note 1</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Preauricular</td>
<td>PA</td>
<td>10</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Prelaryngeal</td>
<td>VI</td>
<td>10</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Pretracheal</td>
<td>VI</td>
<td>20</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Recurrent laryngeal</td>
<td>VI</td>
<td>10</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Regional lymph node, NOS</td>
<td>--</td>
<td>40</td>
<td>--</td>
<td>--</td>
</tr>
<tr>
<td>Retropharyngeal</td>
<td>RP</td>
<td>10</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Spinal accessory</td>
<td>V</td>
<td>10</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Subdigastic</td>
<td>II</td>
<td>10</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Sublingual</td>
<td>I</td>
<td>10</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>
Table I-2-4. Site-Specific Factors 8 and 9 Coding Examples
### Example SSF 8 Clinical  SSF 9 Pathologic

<table>
<thead>
<tr>
<th>Note Description</th>
<th>Code 8</th>
<th>Code 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regional nodes negative</td>
<td>000</td>
<td>000</td>
</tr>
<tr>
<td>Regional nodes involved, no extracapsular extension</td>
<td>010</td>
<td>010</td>
</tr>
<tr>
<td>Regional nodes involved, statement of extracapsular extension</td>
<td>020</td>
<td>020, 030, 040</td>
</tr>
<tr>
<td>Nodes involved pathologically, seen only microscopically</td>
<td></td>
<td>020</td>
</tr>
<tr>
<td>Nodes involved pathologically, seen on gross dissection</td>
<td></td>
<td>030</td>
</tr>
<tr>
<td>Nodes involved pathologically, unknown if micro- or macroscopic</td>
<td></td>
<td>040*</td>
</tr>
</tbody>
</table>

### Regional nodes involved, unknown if extracapsular extension or extracapsular extension not stated

<table>
<thead>
<tr>
<th>Code 8</th>
<th>Code 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>030</td>
<td>050*</td>
</tr>
</tbody>
</table>

### Unknown if regional nodes involved; not assessed; not documented

<table>
<thead>
<tr>
<th>Code 8</th>
<th>Code 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>999</td>
<td>999</td>
</tr>
</tbody>
</table>

*No pathology report available*

---

### Site-Specific Factor 10 – HPV (Human Papilloma Virus) Status

*See [HPV Status](#) in LAB TESTS AND TUMOR MARKERS*

### Site-Specific Factor 11 – Measured Thickness (Depth)

**Appears in Schemas:** All head and neck sites (melanoma); carcinoma of oral cavity sites; Merkel cell carcinoma (Site-Specific Factor 1)

**Source documents:** pathology report

This site-specific factor measures tumor thickness or depth (vertical dimension), rather than size (lateral dimension). The depth of invasion of the primary tumor is recognized as an important predictor for risk of nodal metastases in some tumors. The depth of invasion or tumor thickness measurement for head and neck sites and Merkel cell carcinoma (all sites) is collected in tenths of millimeters as stated in the pathology report for the resected specimen. (This is similar to, but not the same as, Breslow depth of invasion, which is measured in hundredths of millimeters.) The thickness measurement should only be taken from a pathology specimen, not from a radiology report or other clinical measurement. Code a measurement specifically labeled as “thickness” or “depth” in the pathology. In the absence of this label, a measurement described as taken from the cut surface of the specimen can be coded. And in the absence of either of these labels, the third dimension in a statement of tumor size can be used by the registrar to code this field.

If the tumor is excised post-neoadjuvant treatment, tumor measurements cannot be compared before and after treatment to determine which would indicate the greater involvement. The same code is used for cases with no surgical procedure of the primary site, and cases with surgical procedure of the primary site after neoadjuvant treatment.

Code the actual tumor thickness or tumor depth in tenths of millimeters as stated in the pathology report, in the code range 001 to 979. Because the thickness table is similar to many other tables that collect a measurement, it is important to identify the correct unit of measurement. This is a three digit field with an implied decimal point between the second and third digits.

**Examples**

<table>
<thead>
<tr>
<th>Code 8</th>
<th>Code 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor thickness 0.1 mm – coded as 001</td>
<td></td>
</tr>
<tr>
<td>Breslow depth 0.74 mm – code as 007</td>
<td></td>
</tr>
<tr>
<td>Lesion 1 mm thick – code as 010</td>
<td></td>
</tr>
<tr>
<td>Thickness 2.7 mm – code as 027</td>
<td></td>
</tr>
<tr>
<td>Depth 10.6 mm – code as 106</td>
<td></td>
</tr>
</tbody>
</table>

The 900 codes are used to document specific case situations.

- Use code 988 for *Merkel cell carcinoma only* when tumor thickness or tumor thickness is not collected for the case
• Use code 990 when
  o the tumor is described as microinvasive
  o no size is given for a microscopic focus or foci
• Use code 997 for cases of in situ carcinoma in head and neck sites only
• Use code 998 when
  o no surgical resection of the primary site is performed
  o surgical resection takes places after neoadjuvant treatment
• Use code 999 when
  o the information is unknown, including cases in which the primary tumor is removed but the measurement of thickness cannot be determined from the pathology report
  o for Merkel cell carcinoma only: tumor is described as in situ (CS Extension code 000)

Site-Specific Factor 25 – Schema Discriminator
Source documents: pathology report, imaging report, endoscopy report

ICD-O topography code C11.1, posterior wall of nasopharynx, includes both the mucosal surface of the posterior wall and the adenoid or pharyngeal tonsil. Two CS version 2 schemas use C11.1, but the schemas map to different seventh edition TNM chapters. The posterior wall of nasopharynx (mucosal surface) is staged with nasopharynx, and the lymphoid tissues of the pharyngeal tonsil are staged with the oropharynx. In order to determine which schema should be presented to the abstractor for topography code C11.1, a schema discriminator has been included as Site-Specific Factor 25 for both Nasopharynx and PharyngealTonsil. This schema discriminator applies only to C11.1. For other nasopharyngeal sites (C11.0, C11.2, C11.3, C11.8, C11.9), this site-specific factor is blank.

Code the description of the true primary site as stated in the medical record.
• Use code 010 when the primary site is stated as posterior wall of nasopharynx (NOS); this will use the Nasopharynx schema to map to TNM.
• Use code 020 when the primary site is stated as adenoid, pharyngeal tonsil or nasopharyngeal tonsil; this will use the PharyngealTonsil schema to map to TNM.
• See schema for additional code choices.
UPPER GASTROINTESTINAL (UGI) TRACT
Esophagus, Stomach, Small Intestine
(See also sections on gastrointestinal stromal tumors (GISTs) and neuroendocrine tumors (NETs)

ANATOMY

Site-Specific Factor 2 – Specific Location of Tumor (Esophagus, Stomach)

Site-Specific Factor 4 – Distance to Proximal Edge of Tumor from Incisors (Esophagus, Esophagus-GE Junction)

Site-Specific Factor 5 – Distance to Distal Edge of Tumor from Incisors (Esophagus, Esophagus-GE Junction)

Site-Specific Factor 25 – Schema Discriminator: Involvement of Cardia and Distance from Esophagogastric Junction (EGJ) (Esophagus-GE Junction, Stomach)

The esophagus extends from the base of the hypopharynx to the cardiac opening of the stomach (Figure I-2-3). It is divided into the cervical esophagus above the clavicles and the thoracic esophagus below. The thoracic esophagus is divided into upper, middle, and lower sections. In ICD-O-3, there are two separate and incompatible sets of codes describing the anatomic subsites of the esophagus. Codes C15.0-C15.2 are based on radiographic landmarks (cervical-thoracic-abdominal). Codes C15.3-C15.5 are thirds of the esophagus, based on esophagoscopy measurements. Esophagus Site-Specific Factor 2 codes the specific location of the tumor within the esophagus.

The site of an esophageal primary is defined by its uppermost point; in other words, by the distance from the incisors (front teeth) to the proximal edge measured during esophagoscopy. For the Esophagus and Esophagus-GE Junction schemas, site-specific factor 4 codes the distance of the proximal edge of the tumor from the incisors, and site-specific factor 5 codes the distance to the distal edge of the tumor from the incisors.

The esophagus chapter of the AJCC Cancer Staging Manual seventh edition includes the esophagogastric junction (also called the cardia or gastroesophageal junction) and the proximal 5 cm of the stomach. The cardia is defined as the opening or junction between the esophagus and the stomach, and it is between 0.1 and 0.4 cm in length. In CSv2, there is a separate schema for Esophagus-GE Junction, which includes all of the cardia (C16.0) and is mapped to the seventh edition esophagus staging. Two additional stomach topography codes are included in the proximal 5 cm of the stomach, the fundus (C16.1) and body (C16.2) (Figure I-2-4). This 5 cm boundary measurement is based on the Siewert classification of gastroesophageal cancers, which defines an area 5 cm above and 5 cm below the cardia or esophagogastric junction. To determine whether a cancer in the fundus or body of the stomach
should be coded according to the esophagus schema or the stomach schema, it is necessary to identify the midpoint or epicenter of the tumor. If the midpoint is at or above the cardia, the tumor is definitely esophageal. If the midpoint of the tumor is within 5 cm below the cardia and the lesion extends to or across the cardia, the case should be coded with the Esophagus-GE Junction schema. If the midpoint of the tumor is within 5 cm below the cardia and the lesion does not extend to the cardia, the case should be coded with the stomach schema. Any tumor with a midpoint more distal than 5 cm from the cardia is coded with the stomach schema.

In order to determine which schema should be used for gastric tumors within 5 cm of the GE junction, a schema discriminator has been included as Site-Specific Factor 25. Select the code that best describes the location and extent of the tumor, and the computer algorithm will bring the correct schema to the screen.

In the stomach, specific subsites include the fundus (C16.1) and body (C16.2) mentioned above and the antrum (C16.3). Since the stomach is a relatively large organ, tumors in these subsites can be further described as being on the anterior or posterior wall, or along the lesser curvature (medial edge) or greater curvature (lateral or distal edge). Stomach Site-Specific Factor 2 codes the specific location of the tumor within the stomach for research purposes.

**Histologic Terminology**

1. The terminology preferred by pathologists for carcinoma in situ of the esophagus is *high grade dysplasia*. This terminology is not reportable to most cancer registries. Therefore, it may be a future issue that early/very low stage esophageal cancer is under-reported as a result of registry reporting terminology. If high grade dysplasia of the esophagus is a reportable cancer, it should be coded as 00 in CS Extension.

2. The seventh edition of the AJCC Cancer Staging Manual stage groups esophageal cancers differently by cell type. The computer algorithm that derives the stage group will look at the histology code to determine whether the case will map to either the adenocarcinoma stage grouping or the squamous cell carcinoma stage grouping. Squamous cell carcinomas generally have a worse prognosis than adenocarcinomas. If the diagnosis is a cancer of mixed histology or something other than adenocarcinoma or squamous cell carcinoma, the computer algorithm will group the case with the squamous cell carcinomas.
Clinical Assessment of Regional Lymph Nodes
Site-Specific Factor 1 (Esophagus, EsophagusGEJunction, Stomach)
Site-Specific Factor 2 (Small Intestine, Colon, Appendix [carcinoma], Rectum)

Source documents: imaging report, possibly physical exam; does not include surgical observation or lymph node biopsies

The purpose of this field is to document a diagnostic work-up to assess regional lymph nodes before surgery or neoadjuvant therapy. This data field handles correct mapping to the clinical N category when multiple involved regional lymph nodes are identified on imaging of the chest, abdomen or pelvis. Diagnostic procedures include CT, MRI, plain radiographs and endorectal ultrasound (EUS). It is possible, but unlikely, that a physical exam would show involved regional nodes for the gastrointestinal tract. Endoscopic procedures are excluded; they can only view the inside of the gastrointestinal tract and cannot assess regional lymph nodes.

Coding guidelines:

- Use code 000 when there is imaging or ultrasound and lymph nodes are not mentioned or stated to be uninvolved. A statement of “no adenopathy” of regional lymph nodes is sufficient to code 000.
- Use a code in the 100 – 399 range (varies by site) when imaging or ultrasound was done and there is a statement of a clinical N (N1, N2, N3 according to primary site).
- Use code 400 when imaging or ultrasound mentions clinically positive nodes but does not indicate how many or give a clinical N value.
- Codes 888 and 988 should not be used for cases diagnosed after January 1, 2010.
- Use code 999 when there is no imaging or ultrasound reported or it is unknown whether imaging or ultrasound was done.
- In addition, site-specific notes before the table indicate how to code this field when the number of clinically positive nodes is stated but a clinical N category is not stated.
- Gastrointestinal tract sites are included in the “inaccessible nodes rule,” but only in unusual cases are gastrointestinal tract sites staged clinically. Do not apply the “inaccessible nodes rule” to code this field. There must be an attempt to assess regional lymph nodes clinically prior to the start of treatment in order to code 000. If there is no diagnostic work-up to assess regional lymph nodes, use code 999.
- If a scan or ultrasound states adenopathy is present without a definitive statement that the nodes are clinically positive (such as fixed, matted, or metastatic terminology), code as 999. The terms adenopathy, enlargement, suspicious, and so forth are not sufficient to code as involvement.

Site-Specific Factor 3 – Number of Lymph Nodes with Extracapsular Extension (Esophagus, Esophagus GE Junction)

Source document: pathology report

Extracapsular extension is tumor involvement of the lymph node that spills beyond the wall of the node into the surrounding fat. Extracapsular extension is an unfavorable prognostic indicator. The source document is the pathology report. Pathologic extracapsular extension assessment includes both gross dissection (macroscopic) and microscopic examination. The code structure for this field is very similar to other data fields where lymph nodes are numbered.

- Code only the number of lymph nodes stated by the pathologist to have extracapsular extension.
- Use code 000 if there is no extracapsular extension
- Use code 097 if lymph nodes are positive but there is no statement that extracapsular extension is present.
- Use code 098 if no lymph nodes were removed.
• Use code 999 if there is no documentation whether lymph nodes are involved or whether extracapsular extension is present.

Site-Specific Factors 1 and 3 – CEA Value and Interpretation (Small Intestine)
See CEA in LAB TESTS AND TUMOR MARKERS

Site-Specific Factor 4 – Crohn Disease (Small Intestine)
Source documents: patient history, consultant reports, discharge summary

Crohn disease or Crohn’s disease is a chronic inflammation of the gastrointestinal disease, most commonly affecting the ileum. It is also called ileitis or enteritis and is part of a category of conditions called inflammatory bowel diseases. Crohn’s disease is not the same as irritable bowel syndrome (IBS) or ulcerative colitis. Crohn’s disease is believed to be an abnormal immune response to bacteria, foods, or other substances, producing chronic inflammation and even ulceration of the small bowel wall. It is associated with an increased risk of carcinoma in the small intestine. The presence of Crohn’s disease is an adverse prognostic factor. This site-specific factor codes the presence or absence of Crohn’s disease. If there is no statement in the record about Crohn’s disease, enteritis or ileitis, use code 999.

Site-Specific Factor 5 – Microsatellite Instability (Small Intestine)
See Microsatellite Instability in LAB TESTS AND TUMOR MARKERS
COLON, APPENDIX, RECTUM, ANUS
(See also sections on gastrointestinal stromal tumors (GISTs) and neuroendocrine tumors (NETs))

Site-Specific Factor 1 and Site-Specific Factor 3 – CEA Interpretation and CEA Lab Value (Colon, Appendix, Rectum)
See CEA Interpretation and Lab Value in LAB TESTS AND TUMOR MARKERS

Site-Specific Factor 2 – Clinical Assessment of Regional Lymph Nodes (Colon, Appendix, Rectum)
See Clinical Assessment of Regional Lymph Nodes in UPPER GI section.

Site-Specific Factor 4 – Tumor Deposits (Colon, Appendix, Rectum)
Source document: pathology report

Tumor deposits are separate nodules or deposits of malignant cells in perirectal or pericolic fat without evidence of residual lymph node tissue. These tumor deposits—also described as discontinuous extramural extension—have been defined in various ways in previous editions of the AJCC Cancer Staging Manual, including the terms malignant tumor foci, malignant peritumoral deposits and ‘satellite nodule.’ Tumor deposits are an adverse prognostic factor.

If present, tumor deposits may be found within the primary lymphatic drainage area of the tumor. They are different from direct extension from the primary tumor and may be the result of lymphovascular invasion with extravascular extension, a totally replaced lymph node, or discontinuous spread. Nodules of tumor outside the primary lymphatic drainage area of the tumor are coded as distant metastases in CS Mets at Dx. In CSv2, tumor deposits are coded in a site-specific factor that is used to map to the N category. Tumor deposits without positive regional lymph nodes will map to pN1c. Do not add the number of tumor deposits to positive regional lymph nodes when coding Lymph Nodes Positive.

- Code the number of tumor deposits reported in the pathology report. Do not count involved lymph nodes in this field, only tumor deposits.
- Use code 000 if the pathology report from a surgical resection does not mention tumor deposits.
- Use code 998 if tumor deposits are mentioned but a number is not reported.
- Use code 999 if tumor deposits are not mentioned in the record or if no surgical resection is performed.

Site-Specific Factor 5 – Tumor Regression Grade (Colon, Rectum)
Source document: pathology report

Tumor regression grade is a standardized code that indicates the patient’s response to neoadjuvant (preoperative) treatment. A low value (code 000 or 010) is associated with better prognosis. The information may also be given in descriptive terms rather than a code and may be called ‘treatment effect.’ Code the description of tumor regression only from the primary tumor specimen.

- Code the grade or descriptive term reported by the pathologist.
- Use code 000 if the pathologist describes complete response, “no viable tumor cells,” or “acellular pools of mucin” and no residual tumor.
- Use code 990 if the pathology report mentions treatment response is not more specific in terms of complete, moderate, minimal or poor response.
- Use code 998 if the patient had no preoperative (neoadjuvant) treatment or had no surgical resection.
Site-Specific Factor 6 – Circumferential Resection Margin (CRM) (Colon, Rectum)

Source document: pathology report

The CRM is also referred to as the radial margin or the mesenteric resection margin. This is the measurement of the distance from the deepest invasion of the tumor to the closest soft tissue margin of the specimen (see Figure I-2-5). In other words, the CRM is the width of the surgical margin at the deepest part of the tumor in an area of the large intestine or rectum without serosa (non-peritonealized rectum below the peritoneal reflection) or only partly covered by serosa (upper rectum, posterior aspects of ascending and descending colon). The CRM is not the same as the distance to the proximal and distal margins of the colon specimen. For rectal cancers, the circumferential resection margin is the most important predictor of local recurrence. This is a three digit field with an implied decimal point between the second and third digits.

- Record the CRM distance in millimeters as stated by the pathologist. For example, if the CRM is given as 1.8 millimeters, code as 018.
- Use code 000 if the margin is involved (positive) or if the tumor is less than 1 mm from the non-peritonealized surface.
- Use code 991 if the margin is negative and the distance is not stated.
- Use special codes 992 – 995 for situations where the CRM is stated non-specifically.
- Use code 997 if there is no residual tumor in the specimen.
- Use code 998 if no surgery was performed.
- Use code 999 if the CRM is not stated or is unknown.

Figure I-2-5. Circumferential Resection Margin.

Site-Specific Factor 7 – Microsatellite Instability (Colon, Appendix, Rectum)
See Microsatellite Instability in LAB TESTS AND TUMOR MARKERS

Site-Specific Factor 8 – Perineural Invasion (Colon, Rectum)

Source documents: pathology report

Other names: PNI, neurotropism

Perineural invasion is infiltration of nerves in the area of the lesion by tumor cells or spread of tumor along the nerve pathway. The presence of perineural invasion has been shown in several studies to be an indicator of poor patient prognosis.
Code whether perineural invasion is present based on the description in the pathology report. If perineural invasion is not mentioned in the pathology report, use code 000. If there is no pathology report, use code 998.

- **000** Perineural invasion not present/not identified
- **010** Perineural invasion present/identified
- **998** No histologic examination of primary site

See schema for additional code choices.

**Site-Specific Factor 9 – KRAS (Colon, Rectum)**

*Source document:* pathology report or clinical laboratory report  
*Other names:* K-Ras, K-ras, Ki-Ras

KRAS is an oncogene (a gene that, when mutated or overexpressed, helps turn a normal cell into a cancer cell). Mutations of KRAS indicate that a patient may not respond to the anti-EGFR drugs cetuximab (Erbitux) or panitumumab (Vectibix). ASCO recommends that Stage IV colorectal patients be tested for KRAS if anti-EGFR therapy is being considered. There are two types of KRAS genes: normal and mutated. The normal KRAS gene is also called the wild type allele; the mutated gene may be described as abnormal or having an abnormal codon (abnormal DNA sequence). Follow CS timing rules when completing this data item. If KRAS test was only performed on tissue from a recurrence of colorectal cancer, do not code the results in SSF9.

- Use code **010** if the pathologist describes KRAS as mutated or abnormal.
- Use code **020** if the pathologist indicates that KRAS is normal or “wild type.”
- Use code **988** when the central registry or the facility has determined that this item is not collectable.
- Use code **997** when there is a statement in the record that the test was ordered but the results are not available.
- Use code **998** when there is a statement in the record that the test was not ordered or not done.
- Use code **999** when there is no documentation in the record that the test was done or what the results were. This will usually be the code used when the patient has low state (Stage I or II) colorectal cancer.

**Site-Specific Factor 10 – Chromosome 18q: Loss of Heterozygosity (LOH) (Colon, Appendix, Rectum)**

*Source documents:* pathology report or clinical lab report  
*Other names:* allelic loss, gene deletion

Loss of heterozygosity (LOH) in a chromosome means that genetic material normally found in a specific area of a chromosome is missing. In other words, this is damage to the chromosome that results in failure of tumor suppression, which in turn may cause the development or progression of a malignancy. The specific chromosomal defect is on the long arm (q) of chromosome 18. Normal cells have two complete copies of each chromosome, a state called heterozygosity. The presence of 18q LOH is an adverse prognostic factor and may predict resistance to fluorouracil-based chemotherapy. Special molecular diagnostic tests look for missing genetic material.

- Use code **010** if the pathologist states the assay is positive for loss of heterozygosity.
- Use code **020** if the pathologist states the assay is negative for loss of heterozygosity.
- Use code **988** when the central registry or the facility has determined that this item is not collectable.
Collaborative Stage Data Collection System Coding Manual and Instructions
Part I Section 2: Site-Specific Notes

- Use code 997 when there is a statement in the record that the test was ordered but the results are not available.
- Use code 998 when there is a statement in the record that the test was not ordered or not done.
- Use code 999 when there is no documentation in the record that the test was done or what the results were.

Site-Specific Factor 11 – Histopathologic Grade (Appendix)
Source document: pathology report

The histopathologic grading of mucinous adenocarcinomas (morphology codes 8480, 8481 and 8490) appears to have prognostic value for appendiceal carcinomas. Mucinous adenocarcinomas have a better prognosis and are graded differently from intestinal-type adenocarcinomas—a two grade system, low or high. Adenocarcinomas of the appendix use a standard four-grade system. Grading is used in deriving AJCC stage groups IVA (low grade mucinous adenocarcinoma or well-differentiated adenocarcinoma with intraperitoneal metastasis) and IVB (high grade mucinous adenocarcinoma or moderately and poorly differentiated adenocarcinoma with non-peritoneal metastasis).

- Code histopathologic grade for all appendix carcinomas as described in the pathology report.
- Mucinous adenocarcinoma: Use code 001 for low grade. Use code 002 for high grade.
- Non-mucinous adenocarcinomas (codes other than 8480, 8481, and 8490):
  - Use code 001 for Grade 1 or well differentiated.
  - Use code 002 for Grade 2 or moderately differentiated.
  - Use code 003 for Grade 3 or poorly differentiated.
  - Use code 004 for Grade 4 or undifferentiated.
- Use code 998 if there was no histologic confirmation or the patient did not have surgery.
- Use code 999 if there is no information in the record about histopathologic grade.

Site-Specific Factor 12 – CA 19-9 (Appendix)
See CA 19-9 in Lab Tests and Tumor Markers

Site-Specific Factor 1 – HPV Status (Anus)
See HPV Status in Lab Tests and Tumor Markers
GASTROINTESTINAL STROMAL TUMORS (GIST)
(Esophagus, Stomach, Small intestine, Appendix, Colon, Rectum, and Peritoneum—omentum and mesentery)

Gastrointestinal stromal tumors (GISTs) are a rare type of soft tissue sarcoma (mesenchymal tumor). They are different from carcinomas of the gastrointestinal tract because they develop in the muscle layer and grow outward. These tumors were first described as a distinct entity in 1998 and codes were added to ICD-O-3 in 2000. GIST is an umbrella term covering most mesenchymal tumors of the stomach and intestine. Most tumors diagnosed as leiomyosarcomas a decade ago are now referred to as GISTs.

GISTs are believed to develop from the interstitial cells of Cajal that regulate peristalsis. Because the staging of GISTs is based on the size of the primary tumor and the mitotic count, a new chapter was added to the seventh edition of the AJCC Cancer Staging Manual, and new schemas were added to CS version 2. There are separate GIST schemas for esophagus, stomach, small intestine, appendix, colon, rectum and peritoneum (omentum and mesentery).

About 55% of GISTs occur in the stomach, followed by 30% in the small intestine. Other sites are much less frequent. Even in the stomach, GISTs are only 1-3% of all gastric malignancies. In the small intestine, GISTS are about 20% of all malignancies. About 35-50% of gastrointestinal stromal tumors are malignant. Both the GIST chapter of the AJCC Cancer Staging Manual and the schemas in CS version 2 can be used to code benign, borderline, and malignant GISTs, but only malignant GISTs should be reported to population-based cancer registries. Benign and borderline GISTS may be reportable-by-agreement in facility-based registries.

All GISTS use the same five site-specific factors, but to maintain site-specific factor formatting similar to carcinomas of the gastrointestinal sites, the numbering of the site-specific factors differs among the upper GI, lower GI, and peritoneum sites, as shown in Table I-2-5. Because carcinoembryonic antigen (CEA) is not pertinent to GIST, when new schemas were created for GIST of stomach, small intestine, colon, appendix and rectum, the site-specific factor for CEA was made obsolete. The same holds true for clinical assessment of regional lymph nodes for stomach, appendix, colon and rectum, because lymph node involvement by GIST is rare.

Table I-2-5. Site-specific Factor Locations for GIST Prognostic Factors

<table>
<thead>
<tr>
<th>SSF</th>
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<td>Esophagus</td>
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<td>Mitot count</td>
<td>KIT</td>
<td>IHC</td>
<td>KIT</td>
<td>gene</td>
<td>mut</td>
<td>PDG</td>
<td>gene</td>
<td>mut</td>
<td>Tumor</td>
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<td>Obs</td>
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<td>KIT</td>
<td>IHC</td>
<td>KIT</td>
<td>gene</td>
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<td>mut</td>
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<td>KIT</td>
<td>IHC</td>
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<td>gene</td>
<td>Tumor</td>
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Collaborative Stage Data Collection System Coding Manual and Instructions

Part I Section 2: Site-Specific Notes

Appendix

<table>
<thead>
<tr>
<th>Site</th>
<th>Obs</th>
<th>Obs</th>
<th>Mitotic count</th>
<th>KIT gene</th>
<th>PDF gene</th>
<th>Tumor mut</th>
<th>multipl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colon</td>
<td>Obs</td>
<td>Obs</td>
<td>Mitotic count</td>
<td>KIT gene</td>
<td>PDF gene</td>
<td>Tumor mut</td>
<td>multipl</td>
</tr>
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<td>Peritoneum</td>
<td>Mitotic count</td>
<td>KIT gene</td>
<td>PDF gene</td>
<td>Tumor mut</td>
<td>multipl</td>
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</tr>
</tbody>
</table>

Obs = obsolete; Mitot = mitotic; mut = mutation; multipl = multiplicity; PDG = PDGFRA

In the discussions below, the site-specific factors will be described by name rather than SSF number.

Mitotic Count
See Mitotic Count in Lab Tests and Tumor Markers
Mitotic count is a site-specific factor for a number of primary sites. For GIST, the standard measurement is the total number of mitoses per 50 high power fields (HPF at 40 times magnification) or per 5 square millimeters.

KIT Immunohistochemistry (IHC)
Source document: pathology report (special stain)
Other names: CD117, c-kit receptor, KIT receptor tyrosine kinase, or SCFR (stem cell factor receptor)

KIT is a gene that regulates cell growth and differentiation. Mutations of this gene become oncogenes and cause a gastrointestinal stromal tumor to ignore cellular control signals. About 85-90% of GIST tumors contain oncogenic mutations of the KIT receptor gene. KIT immunohistochemistry is a special immunofluorescent stain that turns mutated cells brown and confirms a diagnosis of GIST.

This tumor marker uses the standard code structure and definitions for a lab test evaluation—positive/elevated, normal/negative, and so forth. Code the result stated by the pathologist.

KIT Gene Mutation
Source document: specialty/reference lab report

This site-specific factor documents an even more precise test than KIT IHC. Only a few labs in the country can perform tests to look for specific mutations of the KIT gene, primarily of exon 11 and 9, and rarely of exons 13 and 17, so the source document is likely to be a report from a reference lab or an addendum to a pathology report. (An exon is a segment of a gene that contains instructions for making a protein.) Mutation of any of these specific exons, particularly 11 and 9, may indicate a better response to the targeted therapy drug imatinib mesylate (Gleevec) or sunitinib malate (Sutent) than tumors without the specific gene mutation. (See also PDGFR).

The code structure for this site-specific factor is more detailed than most SSFs, so read the choices carefully.
- Use code 000 if a KIT gene mutation test was performed and no mutations were found (test is negative or gene is stated to be normal or “wild type”).
- Use a code in the 010 – 040 range if the test was done and a specific exon mutation was found.
- Use code 800 if test was done and another specific mutation was identified.
• Use code 810 if test was done and more than one mutation was identified.
• Use code 850 if test was done and a mutation was found but was not specified.
• Use code 988 when the central registry or the facility has determined that this item is not collectable.
• Use code 997 when there is a statement in the record that the test was ordered but the results are not available.
• Use code 998 when there is a statement in the record that the test was not ordered or not done.
• Use code 999 when there is no documentation in the record that the test was done or what the results were.

PDGFR Gene Mutation
Source document: specialty/reference lab report

PDGFR stands for Platelet-Derived Growth Factor Receptor, a gene that encodes a cell surface tyrosine kinase receptor found in mesenchymal cells that regulates cell proliferation, cellular differentiation cell growth and development. PDGFR is also known as CD140A; MGC74795; PDGFR2; Rhe-PDGFR. PDGFR is mutually exclusive with KIT; in other words, about 81% of GISTS have a KIT mutation and 7.1% have PDGFR mutations, but no tumors have both mutations. The rest are normal genes, also called “wild type”. Results of this test will likely appear on a reference lab report or in an addendum to a pathology report.

Code the result stated by the pathologist.
• Use code 010 if the PDGFR gene mutation test was performed and mutations were found (test is positive).
• Use code 020 if the PDGFR gene mutation test was performed and no mutations were found (test is negative or gene is stated to be normal or “wild type”).
• Use code 988 when the central registry or the facility has determined that this item is not collectable.
• Use code 997 when there is a statement in the record that the test was ordered but the results are not available.
• Use code 998 when there is a statement in the record that the test was not ordered or not done.
• Use code 999 when there is no documentation in the record that the test was done or what the results were.

Tumor Multiplicity
Source document: pathology report

The number of anatomically separate GISTs has prognostic significance. Multiple separate tumors are rare, but do occur in patients with GIST and neurofibromatosis type 1 or familial GIST syndrome. It is important to understand that multiple separate GISTs in the specimen—including solitary omental tumors—should not be interpreted as widespread abdominal metastases. The AJCC Cancer Staging Manual describes the criteria for defining disseminated disease versus lower stage “tumor multiplicity.” The absence or presence of multiple GISTs is coded in a site-specific factor but not used to derive TNM stage.
• Use code 000 if there is only one GIST primary in the surgical specimen.
• Use code 010 if there is more than one GIST primary in the surgical specimen.
• Use code 999 if it is unknown whether multiple separate GIST primaries are present.
NEUROENDOCRINE TUMORS
(Stomach, Small intestine, Appendix, Colon, Rectum and Ampulla of Vater)

Neuroendocrine tumors (NET) originate in the diffuse neuroendocrine system from cells that produce small amounts of hormones in response to signals from the nervous system. There are neuroendocrine cells in many body systems, including respiratory tract, lung, skin (Merkel cell carcinoma), gastrointestinal tract, and endocrine glands. Neuroendocrine cells regulate neighboring cells. NETs are also called carcinoids, but the preferred terminology is well-differentiated neuroendocrine tumor. In the gastrointestinal system, abnormal production of hormones can cause unusual symptoms, such as flushing, fatty diarrhea (steatorrhea), and dumping syndrome.

Neuroendocrine tumors in general are rare, so they are not well understood and there may be difficulty in diagnosing them. Gastrointestinal NETs can grow slowly for many years before producing symptoms leading to diagnosis. Malignant NETs tend to be more aggressive than carcinomas and metastasize earlier. When they metastasize, the most common site is liver, but NETs will also metastasize to lymph nodes and bone. Small NETs less than 1 cm in size are unlikely to spread, but a tumor larger than 2 cm has a 95% chance of developing metastases. The principle criteria for staging NETs are size of tumor and depth of invasion, which are part of CS Tumor Size and CS Extension, respectively.

Well-differentiated neuroendocrine carcinoma (ICD-O-3 morphology code 8240; also called carcinoid, NOS) is most common in the appendix and rectum, and uncommon in the colon. Enterochromaffin (EC) cell carcinoid (8241) is most common in the appendix. Entero-Chromaffin-Like (ECL) cell tumor (8242) is most common in the gastric fundus or body. Neuroendocrine tumor (8246) is a broad term covering carcinoids and some adenocarcinomas. Atypical carcinoid (8249) is also included among the codes that are mapped to the TNM system, but is uncommon in the gastrointestinal tract. The NET schemas for stomach, small intestine, appendix, colon, rectum, and ampulla of Vater include malignant gastrinomas, which are found in the duodenum and ileum as well as the stomach. These morphology codes were not staged in the sixth edition of the AJCC Cancer Staging Manual. The CSv2 computer algorithm will not derive sixth edition T, N, M, or stage group when run.

All NETs schemas except appendix use the same three site-specific factors, but to maintain site-specific factor formatting similar to carcinomas of these gastrointestinal sites, the numbering of the site-specific factors differs among the upper GI and lower GI, as shown in Table I-2-6. Appendix uses only the Chromogranin A lab value. Because carcinoembryonic antigen (CEA) is not pertinent to NET, when new schemas were created for NET of stomach, small intestine, colon, appendix and rectum, the site-specific factor for CEA was made obsolete. The same holds true for clinical assessment of regional lymph nodes for stomach, appendix, colon and rectum, because lymph node involvement by NET is rare.

Table I-2-6. Site-specific Factor Locations for NET Prognostic Factors

<table>
<thead>
<tr>
<th>Site</th>
<th>SSF 1</th>
<th>SSF 2</th>
<th>SSF 4</th>
<th>SSF 5</th>
<th>SSF 6</th>
<th>SSF 11</th>
<th>SSF 12</th>
<th>SSF 13</th>
<th>SSF 16</th>
<th>SSF 17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stomach</td>
<td>Obs</td>
<td></td>
<td></td>
<td></td>
<td>Mitotic count</td>
<td>Chromogranin A</td>
<td>5-HIAA lab value</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Small Intestine</td>
<td>Obs</td>
<td></td>
<td></td>
<td></td>
<td>Mitotic count</td>
<td>Chromogranin A</td>
<td>5-HIAA lab value</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carcinoid Appendix</td>
<td>Obs</td>
<td>Obs</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Serum chromogranin A (CgA) lab value</td>
</tr>
<tr>
<td>Colon</td>
<td>Obs</td>
<td>Obs</td>
<td></td>
<td></td>
<td>Mitotic count</td>
<td>Chromogranin A</td>
<td>5-HIAA lab value</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
### Rectum

<table>
<thead>
<tr>
<th>Site</th>
<th>Mitotic count</th>
<th>Chromogranin A</th>
<th>5-HIAA lab val</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obs</td>
<td>Obs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Ampulla of Vater

<table>
<thead>
<tr>
<th>Site</th>
<th>Mitotic count</th>
<th>Chromogranin A</th>
<th>5-HIAA lab val</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obs</td>
<td>Obs</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Mitotic Count

*See Mitotic Count in Lab Tests and Tumor Markers*

Mitotic count is a site-specific factor for a number of primary sites. For NET, the standard measurement is the total number of mitoses per 10 high power fields (HPF at 40 times magnification) or per 2 square millimeters.

## Chromogranin A

*See Chromogranin A in Lab Tests and Tumor Markers*

Chromogranin A is a site-specific factor for a number of primary sites.

## 5-HIAA Lab Value

*Source documents:* clinical laboratory report (urine test)

*Other names:* 5-hydroxyindoleacetic acid (5-HIAA); quantitative 5-HIAA urine; 24 hour 5-HIAA; serotonin metabolite

*Normal reference range*

Qualitative: negative.

Quantitative: 1 – 10 mg/24 hours (5.2 – 52 micromol/24 hours SI units). Result above 25 mg/24 hours indicates carcinoid. Certain drugs and foods may also cause increased levels.

Carcinoids release excessive serotonin (a vasoconstrictor), which is metabolized to 5-HIAA and excreted in urine. The most common test requires the patient to save urine in a collection container for 24 hours and submit the specimen to the clinical laboratory for analysis. The test may also be performed on blood serum.

Record the highest urinary 5-HIAA lab value in milligrams per 24 hours as reported in the medical record prior to treatment.
A number of changes in CSv2 schemas resulted from revisions to chapters in the seventh edition of the AJCC Cancer Staging Manual, particularly in the liver and biliary sites. Intrahepatic bile ducts (C22.1) were separated from liver (C22.0). These schemas are now histology-specific. Primary liver cancers include morphology codes 8170-8175, hepatocellular carcinoma and its subtypes. Intrahepatic bile duct histologies include 8160, cholangiocarcinoma, 8161, bile duct cystadenocarcinoma, and 8180, combined hepatocellular and cholangiocarcinoma. Only these cell types will generate derived T, N, M and Stage Group for seventh edition mapping.

The extrahepatic bile ducts were split into three chapters: perihilar bile ducts (proximal to the origin of the cystic duct), the cystic duct, and distal bile duct (between the junction of the cystic duct and the ampulla of Vater). Perihilar bile ducts include the right, left, and common hepatic duct. Distal bile duct is essentially the common bile duct below the point where the cystic duct and common hepatic duct join. The separate stagings for the extrahepatic bile ducts caused an issue in CSv2 because all of the extrahepatic bile ducts are coded to C24.0 in ICD-O-3. Without extra information about the precise location of the tumor, the computer does not know which schema to present to the abstractor. Consequently, a “schema discriminator” is required to determine which CS schema is to be used for a case. Figure I-2-6 shows the ducts coded to C24.0.

Schema Discriminator (Site-Specific Factor 25 for Perihilar Bile Ducts, Cystic Duct, and Distal Bile Duct)

Code the location of the tumor, such as hepatic duct or Klatskin tumor. The computer algorithm will then bring up the schema based on the code entered in the schema discriminator. Code 030 will display the cystic duct schema; codes 040 and 070 will display the distal bile duct schema. All other codes will display the perihilar bile ducts schema because 70-80% of all extrahepatic bile duct malignancies arise in the hepatic ducts.

- 010 Perihilar bile duct(s)
  - Proximal extrahepatic bile duct(s)
  - Hepatic duct(s)
- 020 Stated as Klatskin tumor

Site-Specific Factor 1 – Alpha Fetoprotein (AFP) Interpretation (Liver, Intrahepatic Bile Ducts)
Site-Specific Factor 3 – Alpha Fetoprotein (AFP) Lab Value (Liver, Intrahepatic Bile Ducts)

Source documents: clinical laboratory report (blood serum radioimmunoassay or enzyme assay (EIA)); sometimes in history and physical or clinical statement in pathology report

Other names: αFP, aFP, Alpha Fetoprotein, Alpha-fetoprotein, α–fetoprotein; fetal alpha globulin

Alpha-fetoprotein (AFP) is a protein normally made by immature liver cells in the fetus. In adults, high AFP levels (> 500 ng/ml) in the blood occur only in hepatocellular carcinoma (>1000), liver metastases (from a primary elsewhere), and germ cell tumors of the testes and ovaries. Levels may be elevated in liver disease but are unlikely to be benign if > 500 ng/ml.

AFP Interpretation

Record the clinician’s interpretation of the highest value prior to treatment, based on the reference range used by the lab.

- 000 Test not done
- 010 Positive/elevated
- 020 Negative/normal
- 030 Borderline; undetermined whether positive or negative
- 080 Test ordered, results not in record

AFP Lab Value

Normal Reference Range: Adult men and non-pregnant women: 0-15 ng/ml (SI: 0-15 μg/L)

Record the highest value prior to treatment. The lab value and interpretation should be from the same test.

- 000 0 ng/ml
- 001-190 Actual value coded in ranges of ng/ml
- 200 10,000 ng/ml or greater
- 988 Not applicable for this schema (registry does not collect this SSF)
- 997 Test ordered, results not in chart
- 998 Test not done (test not ordered or not performed)
- 999 Unknown or no information

Site-Specific Factor 2 – Fibrosis Score (Liver, Intrahepatic Bile Ducts)

Hepatic fibrosis is common to many chronic liver diseases and can lead to cirrhosis and its related complications. Fifty to eighty percent of patients with primary liver cancer have cirrhosis. The fibrosis score, also called the Ishak score, is an indicator of underlying liver disease with prognostic significance. AJCC classifies fibrosis scores 0-4 (none to moderate fibrosis) as F0, and fibrosis scores 5-6 (severe...
Collaborative Stage Data Collection System Coding Manual and Instructions
Part I Section 2: Site-Specific Notes

fibrosis or cirrhosis) as F1.

000 F0: Fibrosis score 0-4 (none to moderate fibrosis)
001 F1: Fibrosis score 5-6 (severe fibrosis or cirrhosis) Code any mention of cirrhosis here.
999 Fibrosis score not recorded; Insufficient information; Not documented in patient record

The following SSFs are part of the Model for End-stage Liver Disease (MELD) score. The MELD score is used to assess the severity of chronic liver disease, and its original purpose was to help prioritize the patient’s risk of dying while waiting for a liver transplant. Because there are several variations of the MELD score calculation, CSv2 captures the three elements comprising it: serum creatinine, serum bilirubin, and the international normalized ratio (INR) for prothrombin time.

Site-Specific Factor 4 and Site-Specific Factor 5 – Creatinine Value and Unit of Measure (Liver)
Source documents: clinical laboratory report (blood serum or urine); value may be part of a metabolic panel
Other names: Serum creatinine, plasma creatinine (PCr), blood creatinine, Creat, Cre, urine creatinine (UCr). Do not confuse with creatinine clearance or creatine; these are unrelated tests.
Normal reference range
Women: 0.5-1.0 mg/dL (45-90 μmol/L)
Men: 0.7-1.2 mg/dL (60-110 μmol/L). Male values are usually higher due to greater muscle mass.
Normal value ranges may vary slightly among different laboratories.

Creatinine is actually an assessment of renal function and can be measured either in blood serum or urine. Creatinine value is a three digit field with an implied decimal point between the second and third digits. Record the highest blood serum value prior to treatment; do not code urine creatinine or creatinine clearance. A creatinine value of 0.7 milligrams per deciliter (mg/dL) would be recorded as 007; a value of 25.4 micromols per liter (μmol/L) would be recorded as 254. Any value over 98.0, such as value of 131 μmol/L would be recorded as 980. Record the unit of measurement in the next site-specific factor.

Creatinine Unit of Measure
There are two methods of describing creatinine concentrations in the blood, weight in grams (milligrams per deciliter), usually used in the US, and molecular count in moles (micromoles per liter) in Canada. Conversion: 1 mg/dL = 88.4 μmol/L. Code the unit of measure used by the facility laboratory.

000 Not done
010 Milligrams per deciliter (mg/dL)
020 Micromols per liter (μmol/L)
See schema for additional code choices.

Site-Specific Factor 6 and Site-Specific Factor 7 – Total Bilirubin Lab Value and Unit of Measure (Liver)
Source documents: clinical laboratory report (blood serum); value may be part of a metabolic or liver function panel
Other names: TBIL. Total bilirubin is a combination of direct (conjugated), indirect (unconjugated), and delta (conjugated bilirubin bound to albumin) bilirubin levels
Normal reference range 0.3-1.5 mg/dL (5-20.5 μmol/L). The normal range may vary slightly from lab to lab.

Bilirubin is produced from the breakdown of hemoglobin (the protein that binds oxygen) in red blood cells. The liver processes bilirubin by excreting it through bile into the intestine. If the liver is damaged, there will be too much bilirubin in the blood, and this can produce jaundice. Elevated bilirubin levels can
be indicative of liver or blood disorders or blockage of bile ducts.

Total bilirubin value is a three digit field with an implied decimal point between the second and third digits. Record the highest Total Bilirubin value in the blood prior to treatment; do not code individual conjugated, direct, unconjugated, indirect, or delta values or bilirubin in urine. A total bilirubin value of 0.4 milligrams per deciliter (mg/dL) would be recorded as 004; a value of 17.2 micromols per liter (μmol/L) would be coded as 172. Any value over 98.0, such as value of 105 μmol/L would be recorded as 980. Record the unit of measurement in the next site-specific factor.

**Bilirubin Unit of Measure**

There are two methods of describing bilirubin levels in the blood, weight in grams (milligrams per deciliter), usually used in the US, and molecular count in moles (micromoles per liter) in Canada. Conversion: 1 mg/dL = 17.1 μmol/L. Code the unit of measure used by the facility laboratory.

- 000 Not done
- 010 Milligrams per deciliter (mg/dL)
- 020 Micromols per liter (μmol/L)

See schema for additional code choices.

**Site-Specific Factor 8– International Normalized Ratio for Prothrombin Time (Liver)**

*Source documents: * clinical laboratory report (blood serum); value may be part of a metabolic or liver function panel; outpatient or ambulatory blood test (finger stick) reported in patient history

*Other names:* INR

*Normal reference range* Healthy person (normal clotting and not on anticoagulants): 0.9-1.3

The prothrombin time is a measure of how quickly the blood clots, which may also indicate liver disease. The international normalized ratio (INR) is a calculation of the patient’s prothrombin time divided by the normal mean prothrombin time for the particular thromboplastin reagent used and is expressed as a decimal number.

INR is a three digit field with an implied decimal point between the second and third digits. Record the highest INR value in the blood prior to treatment. An elevated level indicates the blood is too “thin” and does not clot properly, increasing the risk of bleeding. A value under 1.0 increases the risk of blood clots.

- 000 Not done
- 001-060 Actual value  
  *Example:* INR 3.3 – code as 033

See schema for additional code choices.

*Note:* For intrahepatic bile ducts, SSFs 4-9 are blank (coded as 988 Not applicable) to align SSFs with similar content for easier analysis.
Site-Specific Factor 10 – Tumor Growth Pattern (Intrahepatic Bile Ducts, Perihilar Bile Ducts)

Source document: pathology report

This site-specific factor documents the absence or presence of a periductal growth pattern by the cholangiocarcinoma. There are two types of growth patterns for intrahepatic bile duct carcinomas: mass-forming (60% of intrahepatic bile duct cases) and periductal infiltrating (20%), as well as a mixed type having characteristics of both (20%). The mass-forming type as the name implies, grow outward (radially) from the duct and invades the liver parenchyma in a well-defined mass. The periductal infiltrating type spreads longitudinally along the duct (see Figure I-2-7) in a diffuse manner that may be associated with poorer prognosis. Collection of this information on a national scale may help further define this association.

Record whether a periductal tumor growth pattern is absent or present. If a tumor growth pattern is not mentioned, code as 000. If the information is not collected by the facility, code as 988. If there is no pathology report, code as 999.

000 Absence of periductal component
010 Presence of periductal component
988 Not applicable: Information not collected for this case
999 Unknown or no information; Not documented in patient record

Site-Specific Factor 11 – Primary Sclerosing Cholangitis (Intrahepatic Bile Ducts, Perihilar Bile Ducts)

Source documents: patient history, pathology report, imaging reports

Other names: PSC, fibrosing cholangitis, chronic obliteratorive cholangitis, sclerosing cholangitis

Primary sclerosing cholangitis (PSC) is a progressive disease of the bile ducts (intra- and extrahepatic) resulting from chronic inflammation that hardens (scleroses) and narrows the ducts. As the ducts become blocked, bile builds up in the liver and damages liver cells. Ultimately, the scarring can become widespread in the liver, causing cirrhosis and liver failure.

Record whether PSC is absent or present. If PSC is not mentioned, code as 000. If the information is not collected by the facility, code as 988. If there is no documentation in the record or the record is not available, code as 999.

000 Absence of primary sclerosing cholangitis
010 Presence of primary sclerosing cholangitis
988 Not applicable: Information not collected for this case
999 Unknown or no information; Not documented in patient record

Site-Specific Factor 12 – CA 19-9 (Intrahepatic Bile Ducts, Perihilar Bile Ducts, Distal Bile Ducts)

Site-Specific Factor 1 – CA 19-9 (Ampulla, Pancreas {Head, Body and Tail, Other})
See CA 19-9 in Lab Tests and Tumor Markers

Site-Specific Factor 13 and Site-Specific Factor 14 – CEA Interpretation and CEA Lab Value (Perihilar Bile Ducts, Distal Bile Duct, Ampulla)  
See CEA Interpretation and Lab Value in Lab Tests and Tumor Markers

Site-Specific Factor 15 – Extent of Liver Resection (Gallbladder)  
Source documents: operative report or pathology report

The gallbladder is immediately adjacent to the underside of the liver and there is no serosa between the two organs. If an otherwise localized gallbladder primary is discovered during simple cholecystectomy, residual tumor may be left behind because the part of gallbladder edge more densely adherent to the liver may not be resected. The patient may be offered a second operation for radical excision of any residual tumor. This site-specific factor records the extent of liver tissue removed as part of the gallbladder resection. The liver is divided anatomically into eight segments. Segments IVB (lower portion) and V are the segments considered the gallbladder bed.

Record the type of liver resection as described in the operative report.

- 010 Partial hepatectomy (one or more liver segments)
- 020 Wedge resection
- 030 Right or left hepatectomy (formal lobectomy)
- 040 Extended hepatectomy (right or left trisectionectomy or trisegmentectomy)
- 050 Liver resection NOS
- 988 Not applicable: Information not collected for this case
- 998 No resection of liver
- 999 Unknown or no information; Not documented in patient record

Site-Specific Factor 16 – Primary Tumor Location within Gallbladder (Gallbladder)  
Source documents: operative report or pathology report

As noted in SSF 15, there is no serosa between the gallbladder and the liver. For staging purposes, it is important to know whether the primary tumor is close to the non-serosal side or the serosal side of the gallbladder. The side without serosa is called the hepatic side; the side with serosa is called the free peritoneal side. See Figure I-2-8.

Record the primary tumor location within the gallbladder at the time of cholecystectomy.

- 010 Tumor located on free peritoneal side of gallbladder
- 020 Tumor located on hepatic side of gallbladder
- 988 Not applicable: Information not collected for this case
- 998 No cholecystectomy performed; No primary tumor resected
- 999 Unknown specific location within gallbladder or no information; Not documented in patient record

Figure I-2-8. Primary Tumor Location within Gallbladder.
Site-Specific Factor 2 – Mitotic Count (Pancreas, all subsites)
See Mitotic Count in Lab Tests and Tumor Markers
Mitotic count is a site-specific factor for a number of primary sites. For the three pancreas schemas, the standard measurement is the total number of mitoses per 10 high power fields (HPF at 40 times magnification) or per 2 square millimeters.

Site-specific Factor 3 – Chromogranin A (Pancreas, all subsites)
See Chromogranin A in Lab Tests and Tumor Markers
Chromogranin A is a site-specific factor for a number of primary sites.
LUNG AND PLEURA

Major changes occurred in the staging of lung cancers in the seventh edition of the *AJCC Cancer Staging Manual*. For example, pleural effusion was moved from T4 to M1, and separate tumor nodules in the same lobe of the lung were moved from T4 to T3 while separate tumor nodules in a different lobe of the same lung were moved from M1 to T4. Two site-specific factors were added in CSv2.

For pleura, four additional site-specific factors were added to pleural effusion, which was a factor in CS version 1.

**Site-Specific Factor 1 – Separate Tumor Nodules in Ipsilateral Lung (Lung)**

*Source documents:* imaging reports and pathology reports

Beginning with cases diagnosed on or after January 1, 2010, separate tumor nodules in the same lung are recorded separately from CS Extension codes. This site-specific factor is used in “extra tables” along with Tumor Size, Extension, and Mets at Dx to determine the output values for T and M in seventh edition.

Record the presence or absence of separate tumor nodules in the lobes of the same lung (ipsilateral) as the primary site. Do not code separate tumor nodules in the opposite (contralateral) lung in this field; code them in CS Mets at Dx. Information about separate tumor nodules can be clinical (imaging) or pathological (pathology reports). If separate tumor nodules are not mentioned, code as 000.

- 000 No separate tumor nodules noted
- 010 Separate tumor nodules in ipsilateral lung, same lobe
- 020 Separate tumor nodules in ipsilateral lung, different lobe
- 030 (020 + 010) Separate tumor nodules, ipsilateral lung, same and different lobe
- 040 Separate tumor nodules, ipsilateral lung, unknown if same or different lobe

See schema for other code choices.

**Site-Specific Factor 2 – Visceral Pleural Invasion (VPI)/Elastic Layer (Lung)**

*Source documents:* pathology report

*Other names:* VPI, PL (number)

The seventh edition of the *AJCC Cancer Staging Manual* includes a newly standardized and precise definition of visceral pleural invasion (VPI). VPI is invasion of the surface of the outside of the visceral pleura (the pleura covering the lung) or invasion beyond the elastic layer of the pleura. The elastic layer may be identified on hematoxylin and eosin (H&E) stains or by special stains looking for the elastic fibers. An elastic stain is not needed in most cases to assess the pleura for invasion, only in cases where the distinction between PL0 and PL1 is unclear on H&E sections. Elastic stains may also be helpful in cases where the visceral and parietal pleura are adherent, making it difficult to know where is the visceral pleural surface and the parietal pleura.

VPI is relevant for peripheral lung tumors. The presence of visceral pleural invasion by tumors smaller than 3 cm changes the T category from pT1 to pT2 and increases the stage from IA to IB in patients with no nodal disease or stage IIA to IIB in patients with peribronchial or hilar nodes. Studies have shown that tumors smaller than 3 cm that penetrate beyond the elastic layer of the visceral pleura behave similarly to similar-size tumors that extend to the visceral pleural surface. Visceral pleural invasion should therefore be considered present not only in tumors that extend to the visceral pleural surface, but also in tumors that...
penetrate beyond the elastic layer of the visceral pleura. Four to six layers of visceral pleural may be described by the pathologist (see Figure I-2-9).

Four categories are defined for visceral pleural invasion:

PL0 Tumor surrounded by lung parenchyma or invades superficially into pleural connective tissue beneath elastic layer but does not completely traverse elastic layer of pleura (not classified as pleural invasion for staging purposes)

PL1 Tumor invades beyond elastic layer (classified as T2)

PL2 Tumor extends to surface of the visceral pleura (classified as T2)

PL3 Invasion of parietal pleura (classified as T3)

Record results of visceral pleural invasion as stated on pathology report. Code 988 if no pathologic examination of pleura is done. Do not code separate pleural tumor foci or nodules in this field (discontinuous pleural metastasis); see code 24 in Mets at Dx.

000 No evidence of visceral pleural invasion; Tumor does not completely traverse the elastic layer (PL0)

010 Invasion beyond the visceral elastic pleura, but limited to the pulmonary pleura; Tumor extends through the elastic layer (PL1)

020 Invasion to the surface of the pulmonary (visceral) pleura; Tumor extends to the surface of the visceral pleura (PL2)

030 Tumor extends to the parietal pleura (PL3)

040 Invasion of Pleura, NOS (use this code if uncertain whether elastic stain has been performed to identify visceral pleura invasion)

998 No histologic examination of pleura

999 Unknown if visceral pleural invasion is present; Not documented in patient record; Cannot be assessed

See schema for additional code choices.

**Site-Specific Factor 1 – Pleural Effusion (Pleura)**

*Source documents:* imaging, pathology and cytology reports  
*Other terms:* pleural fluid, thoracentesis

Pleural effusion is the accumulation of fluid between the two layers of pleura, visceral (covering the lungs) and parietal (lining the chest wall and covering the diaphragm). Pleural effusion is a symptom of mesothelioma that increases the summary stage from local to regional direct extension or from regional direct extension to distant depending on other factors about the case.

Record the absence or presence of pleural effusion. If pleural effusion is present and examined microscopically, record whether the pleural effusion is non-malignant, malignant, or not specified.

000 No pleural effusion

010 Pleural effusion, non-malignant (negative); includes pleural effusion seen on imaging but pleural fluid cytology is negative for malignant cells

020 Pleural effusion, malignant; includes pleural fluid cytology described as suspicious or suspicious for mesothelioma

030 Pleural effusion, NOS; includes pleural fluid cytology described as atypical or atypical mesothelial cells (not specifically non-malignant or malignant)

999 Unknown if pleural effusion
Site-Specific Factor 2 – Histologic Subtype (Pleura)

Source documents: pathology report, electron microscopy report, cytology report

The histologic types staged in the pleura chapter of the TNM seventh edition are:
- 9050 Malignant mesothelioma, NOS
- 9051 Fibrous mesothelioma; spindled mesothelioma; sarcomatoid mesothelioma; desmoplastic mesothelioma
- 9052 Epithelioid mesothelioma
- 9053 Biphasic mesothelioma

These histologic subtypes have prognostic significance, with epithelioid mesothelioma having a better prognosis than the other subtypes and desmoplastic mesothelioma having the worst prognosis. This site-specific factor captures more specific information about mesothelioma subtypes for research purposes than the ICD-O-3 morphology code.

Code the specific histology reported in the pathology report or cytology report.

- 000 No histologic subtype stated
- 010 Epithelioid (9052)
- 020 Biphasic (at least 10% of both epithelioid and sarcomatoid components) (9053)
- 030 Sarcomatoid (9051)
- 040 Desmoplastic (9051)
- 050 Other histologic subtype
- 998 No histologic examination of primary site

See schema for other code choices.

Site-Specific Factor 3 – History of Asbestos Exposure (Pleura)

Source documents: patient history, consultation notes, any mention in the medical record

A previous history of asbestos exposure (even more than 20 years prior to diagnosis) is the most common risk factor associated with mesothelioma.

Record any history of asbestos exposure stated in the medical record. If there is no mention of asbestos exposure in the record, code as 999.

- 000 No history of asbestos exposure/negative
- 010 History of asbestos exposure/positive

See schema for other code choices.

Site-Specific Factor 4 – Presence of Chest Pain (Pleura)

Source documents: patient history, consultation notes, any mention in the medical record

Chest pain may be the presenting symptom for a patient who is found to have pleural mesothelioma. Chest pain is usually the result of advanced mesothelioma invading the chest wall and is an adverse prognostic factor for the disease.

Record any statement of chest pain mentioned in the medical record. If the chest pain resulted in finding the diagnosis, use code 010. If the record is nonspecific about whether the chest pain resulted in finding the diagnosis, use code 020. If there is no mention of chest pain as a presenting symptom, code as 999.

- 000 No history of chest pain/negative
- 010 History of chest pain which resulted in work up or diagnosis
- 020 History of chest pain positive, NOS

See schema for other code choices.
Site-Specific Factor 5 – PET Standardized Uptake Values (SUV) (Pleura)

Source documents: imaging reports, specifically positron emission tomography

Other names: PET/CT scan, FDG-PET; 18-fluoro-2-deoxyglucose (FDG) scan, dual modality imaging

Combined positron emission scanning (PET) and computerized tomography (CT) is the most sensitive and accurate way to determine the extent of cancer spread. PET scanning assesses the metabolic function of a tumor—the higher the metabolic rate, the more rapidly cancer cells are growing, which is a sign of tumor aggressiveness. The metabolic activity is reported as a standardized uptake value (SUV), a measurement of the amount of radioactivity left in the cell after the glucose has been used. SUV is a calculation of tissue radioactivity, amount of injected dose, and body weight. A level of more than 3 indicates metabolic activity, but there is no definite “positive/elevated” or “negative/normal” value.

This site-specific factor is a three digit field with an implied decimal point between the second and third digits. Record the value for the SUV as reported in the medical record to one decimal place. For example, code a SUV of 4.8 as 048; code a SUV of 10.0 as 100.

001-500 PET Standardized uptake value to one decimal place
997 Test performed, unknown results
998 Test not done, not ordered and not performed

See schema for other code choices.
BONE

Site-Specific Factor 1 – CS Tumor Size – Second Largest Dimension (Bone)
Site-Specific Factor 2 – CS Tumor Size – Third Largest Dimension (Bone)

Source document: pathology report

Tumor size (clinical or pathologic) and grade of tumor are two of the most important predictors of outcome for bone malignancies, especially osteosarcoma and Ewing’s sarcoma. The three-dimensional description of pathologic tumor size is also an important prognostic factor. The largest tumor dimension is reported in CS Tumor Size. The other two dimensions are reported in SSF1 and SSF2. The structure of these two fields is the same as the three digit CS Tumor Size, where size is expressed in millimeters.

From the pathology report, record the second largest dimension of tumor size in SSF1 and the smallest dimension of tumor size in SSF2. Do not code clinical imaging sizes in the site-specific factors; use code 998 in SSF1 and SSF2 if the tumor is not resected. If there is no resection, a clinical or imaging measurement may be recorded in CS Tumor Size, but SSF1 and SSF2 are coded as 998. If there is no third dimension, code SSF2 as 999 Not documented.

Example 1  Tumor size is recorded in the pathology report as 3.7 cm x 5.2 cm x 2.7 cm. Code CS Tumor Size 052; code Site-specific Factor 1 Tumor Size Second Dimension as 037; code Site-specific Factor 2 Tumor Size Third Dimension as 027.

Example 2  Tumor size is recorded in the pathology report as 4.6 x 3.3 cm. Code CS Tumor Size as 046; code SSF1 as 033; code SSF2 as 998.

Example 3  X-ray of femur shows 7 cm tumor in mid-shaft confirmed by biopsy. Patient undergoes radiation therapy but no resection. Code CS Tumor Size as 070 (and code CS Tumor Size/Extension as 0); code SSF1 as 998; code SSF2 as 998.

Site-Specific Factor 3 – Percent Necrosis Post Neoadjuvant Chemotherapy (Bone)

Source document: pathology report

Other names: Histologic treatment response, therapy response, chemotherapy effect

For osteosarcoma and Ewing’s sarcoma/PNET, response to neoadjuvant chemotherapy is a prognostic factor. Patients with more than 90% tumor necrosis have a more favorable prognosis than those with less response. The CAP protocol for bone tumor resection gives the pathologist specific instructions for determining the percentage of tumor necrosis. A separate method (system of Picci) may describe response to treatment in grades: grade I (macroscopic viable tumor), grade II (microscopic viable tumor), or grade III (no viable tumor). Do not code the Picci grade system in this site-specific factor.

Record the exact percentage value of the tumor necrosis post neo-adjuvant chemotherapy as stated by the pathologist in the pathology report. This site-specific factor is a three digit field with an implied decimal point between the second and third digits. If the patient has no resection or was not treated with pre-operative chemotherapy, use code 998. Rounding instructions: 0.1 to 0.9% round up to 001.

Examples 10.4% therapy response: code as 014
25% tumor necrosis: code as 025
95% chemotherapy effect: code as 095

000 No tumor necrosis
001-100 Percent tumor necrosis
990 Tumor necrosis present, percent not stated
998 No histologic examination of primary site AND/OR No neoadjuvant chemotherapy
See schema for other code choices.

Site-Specific Factor 4 – Resected Pulmonary Metastasis (Bone)

Source documents: pathology report, history, other statements in medical record

Other names: lung metastasis at diagnosis

Primary bone cancers with lung metastases have a more favorable prognosis than bone cancers with liver or bony metastases, and solitary lung metastasis has more favorable prognosis than multiple lung metastasis. This field codes the number of lung metastases at the time of diagnosis and whether they were resected.

Record the number of pulmonary metastasis found at initial diagnosis that were resected, as documented in the pathology report. If lung metastases are present at diagnosis but not resected, code as 988

000  No lung metastasis resected
001-050 Record number of pulmonary metastasis that are resected
099  Lung metastasis resected, number unknown
988  Not applicable for this site (includes lung metastases present at diagnosis but not resected

See schema for other code choices.
SKIN
Skin, MelanomaSkin, MerkelCell (Skin, Penis, Scrotum, Vulva),
KaposiSarcoma, MycosisFungoides
(MelanomaEyelid is discussed with Eye sites)

Site-Specific Factor 1 – Measured Thickness/Depth (Skin, MelanomaSkin, Scrotum)

Source document: pathology report
Other names: maximum tumor thickness, Breslow depth of invasion, Breslow thickness, Breslow measurement

This site-specific factor measures tumor thickness or tumor depth (vertical dimension), not the size (lateral dimension). The depth of invasion of the primary tumor is recognized as an important predictor for risk of nodal metastases in some tumors. The depth of invasion or tumor thickness measurement for skin, scrotum, and melanoma of skin is collected in hundredths of millimeters as stated in the pathology report for the resected specimen. The measurement of tumor thickness (Breslow’s depth) is precisely defined in the melanoma protocol of the College of American Pathologists (CAP checklist) as a vertical measurement from the granular layer of the epidermis (or base of ulceration) to the deepest point of invasion, as measured on a calibrated ocular micrometer.

Code a measurement specifically labeled as “thickness” or “depth” or “Breslow depth of invasion” in the pathology report. In the absence of this label, a measurement described as taken from the cut surface of the specimen may be coded. And in the absence of either of these labels, the third dimension in a statement of tumor size can be used by the registrar to code this field.

If the tumor is excised post-neoadjuvant treatment, tumor measurements cannot be compared before and after treatment to determine which would indicate the greater involvement. The same code is used for cases with no surgical procedure of the primary site and cases with surgical procedure of the primary site after neoadjuvant treatment.

Because the thickness table is similar to many other tables that collect a measurement, it is important to identify the correct unit of measurement. The value collected for skin, scrotum and melanoma of skin is measured in hundredths of millimeters. This site-specific factor actually has two names: Measured Thickness (Depth), Breslow’s Measurement for melanoma of the skin and Measured Thickness (Depth) for skin and scrotum. Several codes from CS version 1 have been made obsolete and the data has been converted to a new code in CS version 2.

Code the actual tumor thickness, tumor depth, or Breslow’s measurement in hundredths of millimeters as stated in the pathology report, in the code range 001 to 979. This is a three digit field with an implied decimal point between the first and second digits.

Examples:
- Tumor described as 0.15 mm in depth – code as 015
- Lesion 1 mm thick – code as 100
- Breslow 2.5 mm – code as 250
- Thickness of 10 mm (1 cm) – code as 980 (9.80 millimeters or larger)

The 900 codes are used to document specific case situations.
- Use code 988 when tumor thickness, Breslow’s measurement or tumor thickness is not collected for the case
- Use code 990 for skin and scrotum only when
Collaborative Stage Data Collection System Coding Manual and Instructions
Part I Section 2: Site-Specific Notes

- there is a statement of microinvasion but no depth is given
- there is a description of a microscopic focus or foci but no depth is given
  - Use code 990 for skin and scrotum only when there is no histologic examination of the primary site
  - Use code 999 when
    - tumor depth or thickness information is unknown, including cases in which the primary tumor is removed but the measurement of thickness cannot be determined from the pathology report
    - tumor thickness or depth is not documented in the medical record
    - for melanoma of skin only: there is a statement of microinvasion but no depth is given
    - for melanoma of skin only: there is a description of a microscopic focus or foci but no depth is given

Site-Specific Factor 2 – Ulceration (MelanomaSkin)
Source documents: pathology report, physical exam, consultant notes, other statement in medical record

Ulceration of the epidermis over a cutaneous melanoma is an important adverse prognostic factor. The presence of ulceration upstages the tumor to the next higher category, for example from T1a to T1b. Ulcerated melanomas typically show invasion through the epidermis, whereas nonulcerated melanomas tend to lift the overlying epidermis. The determination of ulceration is based on several pathologic criteria and must be microscopically confirmed.

Code whether ulceration of the melanoma is present, based on information in the pathology report. If there is no mention of ulceration in the pathology report, assume ulceration is not present and code 000.

- 000 No ulceration present
- 001 Ulceration present
- 999 Unknown; Not stated; Not documented in patient record

Site-Specific Factor 3 – Clinical Status of Lymph nodes (MelanomaSkin, MerkelCell {Skin, Penis, Scrotum, Vulva})
Source documents: physical exam, consultant notes, other statement in record
Other names: micrometastasis, macrometastasis, occult nodal metastases

The tumor burden (microscopic versus macroscopic metastases) in regional lymph nodes is an important prognostic factor for cutaneous melanoma. According to the AJCC Melanoma Task Force, the majority of stage III patients have clinically occult rather than clinically apparent nodal metastases. Involvement of regional lymph nodes is based on both physical examination (palpation) and imaging, as well as microscopic confirmation resulting from diagnostic sentinel lymph node biopsy. This site-specific factor records whether microscopic lymph node metastases are present. This site-specific factor applies to tumor in regional lymph nodes only; do not code the status of in-transit metastases or satellite nodules in this field even though this information is collected in CS Lymph Nodes.

- Use code 000 when
  - there is no regional involvement (CS Lymph Nodes is 000)
  - in-transit metastases or satellite nodules are present (CS Lymph Nodes codes 130, 140, 150) but no lymph nodes are involved
  - lymph node metastases are clinically apparent but pathologically negative
- Use code 001 when
  - there are microscopic lymph node metastases or “micrometastases”
  - lymph nodes are negative on palpation or imaging but contain metastases on pathology
  - lymph node metastases are confirmed microscopically but there is no statement of the
clinical status in the medical record

- Use code 002 when
  - lymph node metastases are clinically apparent whether or not they are confirmed microscopically

000 No lymph node metastases
001 Clinically occult (microscopic) lymph node metastases only
002 Clinically apparent (macroscopic) lymph node metastases
999 Unknown if nodes are involved; Unknown or no information; Not documented in patient record

MELANOMA OF SKIN

Site-Specific Factor 4 – LDH (MelanomaSkin)
Site-Specific Factor 5 – LDH Value (MelanomaSkin)
Site-Specific Factor 6 – LDH Upper Limits of Normal (MelanomaSkin)
See LDH in Lab Tests and Tumor Markers
LDH is a site-specific factor for several primary sites.

Site-Specific Factor 7 Primary Tumor Mitotic Rate (MelanomaSkin)
See Mitotic Count in Lab Tests and Tumor Markers
Mitotic count or mitotic rate is a site-specific factor for a number of primary sites. For cutaneous melanoma, the standard measurement is the total number of mitoses per 1 square millimeter. For melanoma of skin, a mitotic rate of 1 or more mitotic figure per square millimeter is a powerful adverse prognostic factor, according to the College of American Pathologists.

Site-Specific Factor 8 – Primary Tumor Regression (MelanomaSkin)
Source documents: pathology report
Tumor regression is the patient’s immune response to a melanoma. It may be observed clinically as a scar or depigmentation in a previously pigmented mole or melanoma. Histologically, the melanoma has radial growth phase areas replaced by a scar or lymphocytic inflammation or other pathologic criteria. Regression involving more than 75% of the lesion—especially complete regression of the melanoma—is associated with an adverse prognosis. Vertical growth phase (see site-specific factor 9) regression is less common but also shows replacement of tumor cells by lymphocytes and/or fibrosis.

Code the status of primary tumor regression described in the pathology report. If no tumor regression is identified, code as 000.
  000 No regression present; Regression not identified; Regression absent
  001 Regression present
  998 No histologic exam of primary site
See schema for additional code choices.

Site-Specific Factor 9 – Vertical Growth Phase (MelanomaSkin)
Source documents: pathology report
Other names: VGP, vertical growth pattern
Melanomas develop in the basal layer of the epidermis and normally spread horizontally (radial growth) and upward toward the skin surface. When a melanoma begins to grow into the dermis it can access
lymphatic channels and blood vessels and spread to other parts of the body. This growth into the deeper layer of skin is called the vertical growth phase or VGP. VGP is an adverse prognostic factor for cutaneous melanoma. Nodular melanomas are more aggressive than superficial spreading melanomas because they are, by definition, vertical growth phase tumors. The pathologist has specific criteria for identifying VGP in different types of melanoma. VGP is independent of radial growth phase.

Record the absence or presence of vertical growth phase VGP as identified in the pathology report. If not vertical growth phase is identified, code as 000.

000 No vertical growth phase present; Vertical growth phase not identified; Vertical growth phase absent
001 Vertical growth phase present
998 No histologic exam of primary site
See schema for additional code choices.

Site-Specific Factor 10 – Clark’s Level (Skin, Scrotum)
Source documents: pathology report
Other names: anatomic level

There are two ways to measure the maximum tumor thickness of a skin cancer: in millimeters with a micrometer (Breslow’s depth of invasion, also called tumor thickness, measured in site-specific factor 1 for skin, melanoma of skin, and the Merkel cell schemas) and by assessing the deepest point of invasion in the layers of the skin. This site-specific factor codes the latter, which is called Clark’s level after its developer, Dr. Wallace Clark. The codes correspond to the five Clark levels. Because the thickness of the skin layers varies in different parts of the body (for example, the palm of the hand compared to the skin of the face), Clark levels are not as reliable a prognostic measure as measured depth of invasion, but are part of the “high risk features” coded in site-specific factor 12 for non-melanoma skin cancers other than Merkel cell.

Code the Clark level as described in the pathology report. If Clark level is not mentioned, use code 999.

010 Clark’s level I; In situ: noninvasive; intraepidermal; Basement membrane of epidermis is intact
020 Clark's level II; Papillary dermis invaded
030 Clark's level III; Papillary-reticular dermal interface invaded
040 Clark's level IV; Reticular dermis invaded
050 Clark's level V; Subcutaneous tissue invaded (through entire dermis)
998 No histologic examination of primary site
999 Unknown Clark's level; Cannot be assessed; Not documented in patient record
See schema for additional code choices.

Site-Specific Factor 11 – Perineural Invasion (Skin, Scrotum)
Source documents: pathology report
Other names: PNI, neurotropism

Perineural invasion is infiltration of nerves in the area of the lesion by tumor cells or spread of tumor along the nerve pathway. The presence of perineural invasion has been shown in several studies to be an indicator of poor patient prognosis. Perineural invasion is one of the “high risk features” coded in site-specific factor 12 for non-melanoma skin cancers other than Merkel cell.

Code whether perineural invasion is present based on the description in the pathology report. If perineural invasion is not mentioned in the pathology report, use code 000. If there is no pathology report, use code 998.
000 Perineural invasion not present/not identified
010 Perineural invasion present/identified
998 No histologic examination of primary site
See schema for additional code choices.

Site-Specific Factor 12 – High Risk Features (Skin, Scrotum)
Source documents: pathology report, consultation report, other statements in the medical record
Other names: high risk histologic features, high risk tumor features

In addition to the tumor size (diameter, not depth), the presence of certain specific “high risk” features is of prognostic significance for non-melanoma skin cancers other than Merkel cell. The presence of two or more of the high risk features listed below upstages a lesion 2 cm or less in greatest dimension from T1 to T2.

This site-specific factor is to be calculated and coded by the registrar. Information can be taken from any part of the medical record. Disregard any unknown or negative features; count only those that meet the criteria below (each positive feature equals one risk factor). Tally the number of high risk features present, and assign the code representing that number.

- **Histologic grade or differentiation:** Poorly differentiated/Undifferentiated (grade 3 or 4)—review pathology report and 6th digit of ICD-O morphology code elsewhere on the cancer registry abstract
- **Depth of tumor:** 4 mm or more in depth—review pathology report and site-specific factor 1, Depth of invasion (tumor thickness)
- **Clark's level IV or V:** review pathology report and site-specific factor 10, Clark level
- **Perineural invasion:**—review pathology report and site-specific factor 11, Perineural invasion
- **Lymphovascular invasion:**—review pathology report for mention of lymphatic, vascular, or lymph-vascular invasion, and the Lymph-Vascular Invasion data field elsewhere on the cancer registry abstract
- **Primary site:** skin of external ear (C44.2) OR skin of lip (hair-bearing, also called non-glabrous lip) (C44.0)—review physical exam, pathology report and other parts of the medical record, as well as ICD-O-3 primary site code elsewhere on the cancer registry abstract

000 No high risk features
001-006 1 to 6 high risk features (code exact number)
999 Unknown if any high risk features present
See schema for additional code choices.

Note: Site-specific Factors 13-15 are not used for skin or scrotum.

Site-Specific Factor 16 – Size of Lymph Nodes (Skin, Scrotum)
Source documents: pathology report, imaging report, physical exam, other statement in medical record

The size and number of involved lymph nodes are prognostic factors for non-melanoma skin cancer other than Merkel cell. This site-specific factor supplements the information in CS Lymph Nodes to enable mapping to the N category. The code structure and definitions are the same as for site-specific factor 1 in the head and neck sites. This site-specific factor captures information about the size of the entire involved lymph node, not just the size of the metastasis within the lymph node.
Code the largest dimension (diameter) in millimeters of the involved regional lymph node(s). The measurement may be clinical or pathologic (pathologic takes priority if there has been no neoadjuvant therapy). Do not code information about distant lymph nodes in this field.

- Use code 000 in this field if there are no regional lymph nodes involved (CS Lymph Nodes is coded 000).
- Use the appropriate code in the 991 to 997 range if the largest size of an involved regional node is described imprecisely (for example ‘less than 2 cm’ or ‘greater than 4 cm.’)
- If the only information given is a statement of N value by the clinician, code the corresponding size description in the 992 to 997 range.

**MERKEL CELL CARCINOMA**

**Site-Specific Factor 1 – Measured Thickness/Depth (MerkelCell (Skin, Penis, Scrotum, Vulva)**

*See Measured Thickness/Depth in the HEAD AND NECK section.*

For Merkel cell carcinoma, thickness is measured in tenths of millimeters, not hundredths as in the Breslow measurement for melanoma. For example, a Merkel cell carcinoma thickness of 7.4 mm is coded as 074 in this field and a 10.5 mm lesion is coded as 105. According to the author of the Merkel cell carcinoma chapter in the AJCC seventh edition, Merkel cell tumors are generally thicker than melanoma lesions, so the thickness scale was altered.

**Note:** If the tumor is reported by pathology as transected (in other words, the deep margin is involved) and the depth was reported, record the measurement in this field, and code Site-Specific Factor 19 Tumor Base Transection Status as 010.

If the tumor is in situ (CS extension code 000), code the measured depth as 999. 999 also means unknown or no information, not documented in chart, depth not stated.

**Note:** The Merkel cell carcinoma schemas use only site-specific factors 1, 3, 11 (MerkelCellVulva only) and 16-22.

**Site-Specific Factor 11 – Regional Lymph Node – Laterality (MerkelCellVulva)**

*Source documents:* pathology report, imaging, physical exam, other statement in record

The MerkelCellVulva schema is a combination of Merkel cell carcinoma and the standard schema for vulva as a gynecologic cancer. This site-specific factor is included in the MerkelCellVulva schema to retain compatibility with AJCC sixth edition for mapping of the N category.

Code the appropriate description of involved regional lymph nodes.

- 000 All regional lymph nodes are negative
- 010 Unilateral - all positive regional nodes are ipsilateral
- 020 Bilateral or contralateral – at least one positive regional lymph node is bilateral or contralateral
- 030 Regional lymph node(s) positive – laterality unknown
- 998 Lymph nodes not examined

See schema for additional code choices.

**Site-Specific Factor 16 – Size of Metastasis in Lymph Nodes (MerkelCell {Skin, Penis, Scrotum, Vulva})**

*Source documents:* pathology report
In the seventh edition of the *AJCC Cancer Staging Manual*, regional lymph node metastases (N1) for Merkel cell carcinoma are subcategorized as micrometastases (N1a) and macrometastases (N1b), but the size ranges for these subcategories are not defined. Micrometastases are diagnosed after removal and microscopic examination of the lymph nodes (sentinel node biopsy or lymphadenectomy). Macrometastases are identified by imaging and/or palpation and confirmed microscopically. This site-specific factor records the size of the metastasis within the lymph node in hundredths of millimeters so that a researcher can establish cut-off points for analysis.

Code the size of the largest metastasis or tumor nest in regional lymph nodes in *hundredths* of millimeters as stated in the pathology report. Do not code the size of the entire lymph node; use code 999 if the only stated size is for the entire lymph node. Do not code information about distant lymph nodes in this field. If size of metastasis is not stated, use code 999.

**Examples**
- Tumor nest 0.20 mm in size – code as 020
- 1 mm solitary metastasis – code as 100
- Macrometastasis 0.5 cm (50 mm) – code as 980
- Positive inguinal lymph node – code as 990

**Note:** the scale for this factor for Merkel cell carcinoma of the penis is different from the code scale for carcinoma of penis.

- 000 No regional lymph node involvement
- 001-979 0.01 - 9.79 millimeters
- 980 9.80 millimeters or larger
- 990 Metastasis or tumor nests in regional lymph nodes, size cannot be assessed, NOS
- 998 No histologic exam of regional lymph nodes

See schema for additional code choices.

**Site-Specific Factor 17 – Extracapsular Extension Regional Lymph Nodes (MerkelCell {Skin, Penis, Scrotum, Vulva})**

**Source documents:** pathology report

**Other names:** Extracapsular spread, ECS, extranodal extension, EE

Extracapsular extension is growth of tumor cells within a regional lymph node outward through the capsule of the lymph node and into surrounding connective tissue. This is not the same as direct tumor extension from the primary tumor into a lymph node. Extracapsular extension is an adverse prognostic factor not only for Merkel cell carcinomas, but for any primary site where lymph nodes are involved. Clinical extracapsular extension may be described as lymph nodes that are “fixed” or “matted”. This site-specific factor combines clinical and pathologic information into a single data item.

Code whether extracapsular extension is present clinically and/or pathologically of any involved regional lymph node(s). Do not code information about distant lymph nodes in this field. Read the code choices carefully—the case must meet both criteria listed in the code. Use code 000 in this field if there are no regional lymph nodes involved (CS Lymph Nodes is coded 000).

- 000 No lymph nodes involved
- 010 No extracapsular extension clinically AND extracapsular extension present on pathology
- 020 No extracapsular extension clinically AND extracapsular extension not present or not stated on pathology
- 030 No extracapsular extension clinically AND nodes not assessed pathologically
- 040 Extracapsular extension clinically AND extracapsular extension present on pathology
- 050 Extracapsular extension clinically AND extracapsular extension not present or not stated on pathology
- 060 Extracapsular extension clinically AND nodes not assessed pathologically
- 070 Extracapsular extension clinically unknown AND extracapsular extension present on pathology
Collaborative Stage Data Collection System Coding Manual and Instructions
Part I Section 2: Site-Specific Notes

080 Extracapsular extension clinically unknown AND extracapsular extension not present or not stated on pathology
90 Extracapsular extension clinically unknown AND nodes not assessed pathologically
See schema for additional code choices.

Site-Specific Factor 18) – Isolated Tumor Cells (ITCs) in Regional Lymph Nodes (MerkelCell {Skin, Penis, Scrotum, Vulva})
Source documents: pathology report

Isolated tumor cells (ITCs) for Merkel cell carcinoma are defined similar to ITCs for breast: single tumor cells or small clusters of tumor cells not more than 0.2 mm in greatest dimension. ITCs are usually detected by immunohistochemistry on sentinel lymph node biopsies. Examples of immunohistochemical staining methods are Cytokeratin 20 (CK20), CAM 5.2, pancytokeratin, and AE1/3. ITCs may be detected by routine H&E stains. However, in contrast to breast, ITCs for Merkel cell carcinoma are defined as positive lymph nodes (N1).

Record the status of isolated tumor cells as recorded by the pathologist. If metastases larger than 0.2 mm are identified, use code 300.
Use code 000 when
• lymph nodes were negative on microscopic examination and there is no mention of isolated tumor cells
• lymph nodes are negative on routine H&E stands and no immunohistochemical studies were done or it is unknown whether immunohistochemical studies were done
• lymph nodes are clinically negative, but no lymph nodes were removed for microscopic examination

000 Regional lymph nodes negative on routine H&E, no IHC studies for ITCs done or unknown if IHC studies done; Nodes clinically negative, not examined pathologically
010 Regional lymph nodes negative on routine H&E, IHC studies done and ITCs not present
020 Regional lymph nodes negative on routine H&E, IHC studies done and ITCs present
090 Regional lymph nodes negative on routine H&E, positive for tumor detected by IHC, size of tumor cell clusters or metastases not stated
100 Regional lymph nodes positive with ITCs on routine H&E
200 Regional lymph nodes positive with ITCs, NOS, method of detection not stated
300 Regional lymph nodes positive other than ITCs
See schema for additional code choices.

Site-Specific Factor 19 – Tumor Base Transection Status (MerkelCell {Skin, Penis, Scrotum, Vulva})
Source documents: pathology report
Other names: deep margin involvement

Tumor base transection means that the deep surgical margin of the tumor contains tumor cells. In other words, the surgeon cut through the deepest part of the tumor and left malignant cells behind which have the potential to recur at the primary site or spread elsewhere. A shave biopsy or curettage may transect the tumor base.

Record whether the tumor base was transected, based on statements in the pathology report. Use code 010 if the deep margin is involved. Use code 020 if the deep margin is free of tumor cells (not involved). If there is no pathology report, use code 998.
Site-Specific Factor 20 – Tumor Infiltrating Lymphocytes (TIL) (MerkelCell {Skin, Penis, Scrotum, Vulva})

Source documents: pathology report

Other names: TIL, lymphocytic infiltration, lymphocytic infiltrates, CD8+ T-cell infiltration

Tumor infiltrating lymphocytes (TIL) are specialized cancer-fighting cells of the immune system believed to represent the immune reaction/response to Merkel cells. TILs surround and disrupt tumor cells at the base of the vertical growth phase. The presence of TILs at the growth edges of a tumor is associated with a more favorable prognosis. The pathologist takes a semi-quantitative measurement of the number of TILs present and categorizes the response as brisk, non-brisk, or absent.

Assign the code that best describes the status of tumor infiltrating lymphocytes based on statements in the pathology report.

- 000 Absent, no tumor infiltrating lymphocytes – TILs not identified; no lymphocytes present, or lymphocytes present but do not infiltrate tumor
- 010 Tumor infiltrating lymphocytes present, non-brisk – lymphocytes infiltrate melanoma only focally or not along the entire base of the vertical growth phase
- 020 Tumor infiltrating lymphocytes present, brisk – lymphocytes diffusely infiltrate the entire base of the vertical growth phase or the entire invasive component of the melanoma
- 030 Tumor infiltrating lymphocytes present, NOS
- 998 No histologic examination of primary site

See schema for additional code choices.

Site-Specific Factor 21 – Growth Pattern Primary Tumor (MerkelCell {Skin, Penis, Scrotum, Vulva})

Source documents: pathology report

Merkel cell carcinomas derive from the Merkel cells associated with nerve endings. In most cases the tumor is centered in the dermis or sometimes in the subcutaneous tissue and usually does not involve the epidermis as cutaneous melanoma does. There are two types of Merkel cell carcinoma growth patterns, circumscribed (nodular) and diffusely infiltrative. Circumscribed Merkel cell carcinomas have a more favorable prognosis.

Code the growth pattern of the primary tumor as documented by the pathologist.

- 010 Circumscribed/nodular
- 020 Diffusely infiltrative
- 030 Sample inadequate to evaluate as stated in pathology report
- 998 No histologic examination of primary site

See schema for additional code choices.

Site-Specific Factor 22 – Profound Immune Suppression (MerkelCell {Skin, Penis, Scrotum, Vulva})

Source documents: patient history, consultation notes, other statement in medical record
Other names: immunosuppression

A patient who is immune suppressed due to any number of conditions is at much higher risk of developing Merkel cell carcinoma than a person with a normal immune system. Immune suppression means that the patient’s own immune system is weakened and cannot fight infections and other diseases. HIV patients, for example, have a 13.4 times increased risk of developing a Merkel cell carcinoma. Immune suppression is due to a lack of T lymphocytes (key cells of the immune system) and patients who have this defect have 10-30 times higher risk of Merkel cell carcinoma. According to AJCC, immunosuppressed patients tend to present with more advanced disease as well.

Code the clinician’s statement of a condition causing immune suppression as documented in the medical record. If more than one condition is described, use code 050.

- 000 No immune suppression condition(s)
- 010 HIV/AIDS
- 020 Solid organ transplant recipient – includes patients on anti-rejection drugs for transplants
- 030 Chronic lymphocytic leukemia
- 040 Non-Hodgkin lymphoma
- 050 More than one of the above conditions
- 060 Other specified diagnosis resulting in profound immune suppression – includes patients on chemotherapy drugs that cause bone marrow suppression and patients preparing for bone marrow transplants
- 070 Profound immune suppression present, diagnosis not recorded

See schema for additional code choices.

Site-Specific Factor 1 – Peripheral Blood Involvement (Mycosis Fungoides)

Source documents: pathology report, clinical laboratory reports of blood analysis (tissue and blood samples)

Other names: Peripheral blood involvement: circulating Sezary cells
T-cell clonality: T-cell receptor (TCR) gene rearrangement
Monoclonal: clone+, clone positive
Polyclonal: clone-, clone negative

Mycosis fungoides is the most common type of primary cutaneous T-cell lymphoma. Sezary syndrome is a more aggressive type of primary cutaneous T-cell lymphoma in which a specific type of malignant T lymphocytes (Sezary cells) is present in the circulating blood. Staging of mycosis fungoides includes analysis of the circulating blood for Sezary cells. This analysis can be done by microscopy or flow cytometry. Results of microscopy are reported as counts of Sezary cells per cubic millimeter or the percentage of Sezary cells as a proportion of total lymphocytes. Flow cytometry looks for specific cell surface markers such as CD26.

Information about peripheral blood involvement and T-cell clonality identified by polymerase chain reaction (PCR) or Southern blot analysis is combined in a “B” category unique to mycosis fungoides staging in the TNM system. The basic categories are B0 (no significant blood involvement); B1 (low blood tumor burden); and B2 (high blood tumor burden). Any mention of B2 puts the case into Stage IV. B0 and B1 are subcategorized by clonality. In the sixth edition of TNM and CS version 1, mycosis fungoides site-specific factor 1 described only the presence or absence of Sezary cells in circulating blood. In the seventh edition and CS version 2, the structure of SSF1 is more complex. Codes 001 to 003 have been made obsolete and new codes and definitions have been created to account for peripheral blood involvement and clonality. The lack of monoclonality (clone negative) generally indicates a better prognosis.
Code a statement of peripheral blood involvement and clonality (if given) as reported by the clinician from tissue and/or blood samples. If the physician does not provide a B rating but counts or percentages of neoplastic cells, flow cytometry test results, and/or clonality test results are performed, use the appropriate code for the amount of blood involvement with “clone unknown”.

000  No peripheral blood involvement; Less than 1000 Sezary cells

Codes 010 – 030: Presence of significant blood involvement

010  Clone negative; Stated as B0a
020  Clone positive; Stated as B0b
030  Clone unknown; Stated as B0 [NOS]

Codes 040 – 060: Low blood tumor burden: more than 5% of peripheral blood lymphocytes are atypical (Sezary) cells but does not meet the criteria of B2

040  Clone negative; Stated as B1a
050  Clone positive; Stated as B1b
060  Clone unknown; Stated as B1 [NOS]

070  High blood tumor burden: 1000/uL Sezary cells or more with positive clone; Stated as B2
080  Percent of atypical peripheral blood lymphocytes not stated and B rating not stated
090  Sezary cell counts, blood flow cytometry, and/or clonality results in chart, B rating not stated
100  Sezary cell counts, blood flow cytometry, and/or clonality tests ordered, test results not in chart, B rating not known

See schema for additional code choices.
SOFT TISSUE
Soft Tissue, Retroperitoneum, Peritoneum
(PeritoneumFemaleGen is discussed with GYN sites.)

The histologies for the soft tissue schema include a wide range of sarcomas and mixed tumors (non-carcinoma and non-hematopoietic) in the ICD-O-3 morphology code range 8800 to 9582, except 9140 Kaposi sarcoma, which has its own schema. The primary sites included in the soft tissue schema include the peripheral nerves and autonomic nervous system and the connective, subcutaneous, and other soft tissues throughout the body. The peritoneum schema includes omentum and mesentery primary sites and all sarcomas in the range 8800 to 9852 except gastrointestinal and endometrial stromal sarcomas (8935-8936) and Kaposi sarcoma (9140). The retroperitoneum schema includes the same histologies as peritoneum.

Site-Specific Factor 1 – Grade for sarcomas (SoftTissue, Retroperitoneum, Peritoneum)

Source documents: pathology report
Other names:FNCLCC grade, NCI grade

For soft tissue sarcomas, the grade of the tumor is the predominant prognostic indicator, and grade has been included as a category in TNM stage grouping for sarcomas since the first edition of the TNM system in 1978. Through the sixth edition, a four-grade system was used. There are a number of grading systems for adolescent and adult soft tissue tumors, the most widely used of which are the National Cancer Institute (NCI) system and the system of the French Federation of Cancer Centers Sarcoma Group (FNCLCC). Both are three-grade systems using criteria for mitotic activity, necrosis, and differentiation, and both are highly correlated with prognosis. The NCI system also quantifies cellularity and pleomorphism for certain types of sarcomas, making it somewhat more difficult to use. The seventh edition of the *AJCC Cancer Staging Manual* adopted the FNCLCC grading system as the preferred grading system. This site-specific factor allows any three grade system for sarcomas to be coded. It should be noted that stage grouping uses essentially a two tier system, where grade 1 is categorized as low grade and grades 2 and 3 are categorized as high grade. Grading should be attempted for all sarcomas, although a fine needle or core needle biopsy may not yield enough tissue to classify the tumor in a three-grade system.

Code the grade stated in the pathology report. Do not code “well differentiated” or “poorly differentiated” or similar terminology in this field. If the only information available is “low grade” or “high grade”, use code 100 or 200 as appropriate. Codes 010-030 take priority over codes 100 and 200. If there is no biopsy/resection or there is no microscopic examination of tissue from the primary site, use code 998.

010 Specified as Grade 1 [of 3]
020 Specified as Grade 2 [of 3]
030 Specified as Grade 3 [of 3]
100 Grade stated as “low grade” [NOS]
200 Grade stated as “high grade” [NOS]
998 No histologic examination of primary site
See schema for additional code choices.
Collaborative Stage Data Collection System Coding Manual and Instructions
Part I Section 2: Site-Specific Notes

Site-Specific Factor 2 – Neurovascular Invasion (SoftTissue, Retroperitoneum, Peritoneum)
Source documents: pathology report
Other names: blood vessel invasion/involvement, vascular invasion/involvement, involvement/invasion of nerve

Neurovascular invasion is tumor involvement of the nerves and blood vessels adjacent to the primary site. This is not the same as perineural invasion, which is a site-specific factor for skin cancers and other schemas. Tumor involvement of nerves and/or blood vessels is determined microscopically. (Vascular invasion may be included in the Lymph-Vascular Invasion field.)

Code the presence of neurovascular invasion as stated in the pathology report.
Use code 000 when
  • there is a statement in the pathology report that no neurovascular, vascular or nerve invasion is present
  • there is no mention of neurovascular, nerve, or vascular invasion in the pathology report
Use code 010 when the pathology report indicates that there is neurovascular invasion or that a nerve or blood vessel is involved by tumor.
Use code 998 when there is no microscopic examination of tissue from the primary site.
See schema for additional code choices.

Site-Specific Factor 3 – Bone Involvement (SoftTissue, Retroperitoneum, Peritoneum)
Source documents: imaging reports

Bone involvement is direct tumor extension from the primary sarcoma into adjacent bone. This field does not include distant or discontinuous metastases to the skeletal system. Information in this field is based on radiology and other imaging techniques. Pathologic confirmation of metastatic bone involvement is coded in site-specific factor 4.

Code the presence of bone involvement as stated in any imaging report.
Use code 000 when
  • there is a statement in the imaging report that there is no bony involvement present
  • there is no mention of bone involvement in the imaging report
Use code 010 when the imaging report indicates that there is bone involvement or that a bone is involved directly by tumor.
Use code 998 when there is no imaging done to look for bone involvement.
See schema for additional code choices.

Site-Specific Factor 4 – Pathologic M1: Source of Pathology Metastatic Specimen (SoftTissue, Retroperitoneum, Peritoneum)
Source documents: pathology report, other statement in medical record

This site-specific factor documents the type of distant metastasis identified at diagnosis and confirmed pathologically. Do not code progression of disease or distant recurrence in this field.

Code the type of distant metastasis that was microscopically confirmed. Do not include distant metastatic sites identified only by imaging or other clinical means. If more than one distant metastasis was confirmed microscopically, use code 060.
  000 No pathological mets at diagnosis identified
  010 Liver mets present/identified
020 Lung mets present/identified
030 Brain mets present/identified
040 Bone mets present/identified
050 Other mets present/identified
060 Combination of codes 010-050
998 No microscopic examination of metastatic site
See schema for additional code choices.

Site-Specific Factor 25 – Schema Discriminator (Peritoneum)

Source documents: face sheet, other statement of patient gender in medical record

Both sarcomas and carcinomas of the peritoneum can be staged. For peritoneum, a schema discriminator is necessary to identify the gender of the patient so that the correct schema can be presented to the abstractor. Carcinomas in the morphology code range 8000-8576, specialized gonadal neoplasms, and mixed complex and stromal neoplasms (except gastrointestinal stromal tumors) are coded with the same staging criteria for female patients as ovarian cancer in the PeritoneumFemaleGen schema.

Code 002, Female, presents the PeritoneumFemaleGen schema to the abstractor. All other categories of gender (codes 001, 003, 004, 009 and 100) present the Peritoneum schema to the abstractor. For males, a carcinoma of the peritoneum will output T NA  N NA  M NA  Stage NA.
BREAST

CODING REGIONAL LYMPH NODES
For breast, regional lymph node information is coded in several fields (Table I-2-7). These SSFs will be discussed as a group.

Table I-2-7. Regional Lymph Nodes Data Fields

<table>
<thead>
<tr>
<th>FIELD</th>
<th>DESCRIPTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>CS Lymph Nodes</td>
<td>Regional lymph nodes: number, laterality</td>
</tr>
<tr>
<td>CS Reg Nodes Eval</td>
<td>Clinical or pathologic evaluation</td>
</tr>
<tr>
<td>CS LN Pos</td>
<td>Number of lymph nodes microscopically positive</td>
</tr>
<tr>
<td>CS LN Exam</td>
<td>Number of lymph nodes microscopically examined</td>
</tr>
<tr>
<td>SSF3</td>
<td>Number of positive ipsilateral Level I-II Axillary Lymph Nodes</td>
</tr>
<tr>
<td>SSF4</td>
<td>Immunohistochemistry of Regional Lymph Nodes</td>
</tr>
<tr>
<td>SSF5</td>
<td>Molecular Markers of Regional Lymph Nodes</td>
</tr>
<tr>
<td>SSF19</td>
<td>Assessment of Ipsilateral Axillary Lymph Nodes</td>
</tr>
</tbody>
</table>

Coding regional lymph node involvement for breast cancers is more complex than for many other sites, especially when dealing with isolated tumor cells (ITCs) and micrometastases. The following definitions may help clarify the code choices in CS Lymph Nodes and Site-Specific Factors 3 – 5. For a more detailed explanation, see the section in the breast chapter of the AJCC Cancer Staging Manual, seventh edition, called “Specific Considerations for Evidence-Based Changes to the AJCC Cancer Staging Manual, seventh edition,” beginning on page 362.

Isolated Tumor Cells (ITCs). Pathologists can detect isolated tumor cells (ITCs) spread from a breast cancer into regional lymph nodes. These are very small deposits of tumor cells, no larger than 0.2 mm or no more than 200 cells—so small that they are not considered significant for assigning stage. They usually do not show evidence of malignant activity in the nodes, such as proliferation or stromal reaction. To be identified as ITCs, they must be single tumor cells or small clusters not more than 0.2 mm. As more data are collected about these ITCs, their prognostic significance may be better understood. In both the sixth and seventh editions, nodes containing only ITCs are not considered positive nodes and are classified as pN0 in TNM. ITCs are most often found using immunohistochemistry tests on sentinel lymph node specimens. The ITCs may sometimes also be seen on routine H&E stained sections.

Hematoxylin and Eosin (H & E). (from “Hematoxylin & Eosin: (The Routine Stain)”), by H. Skip Brown, BA, HT(ASCP), from: http://www.sigmaaldrich.com/img/assets/7361/Primer-H&Emay04.pdf. In histology, the standard or routine stain is the hematoxylin and eosin stain, better known as the “H&E” stain. With rare exceptions, every specimen being examined will first receive an H&E stain to give the laboratorian a visible look at the nucleus of the cells and their present state of activity. With most disease states there is abnormal growth and/or division in the nucleus of the cells. The hematoxylin and eosin stain uses two separate dyes, one staining the nucleus and the other staining the cytoplasm and connective tissue. Hematoxylin is a dark purplish dye that will stain the chromatin (nuclear material) within the nucleus, leaving it a deep purplish-blue color. Eosin is an orangish-pink to red dye that stains the cytoplasmic material including connective tissue and collagen, and leaves an orange-pink counterstain. This counterstain acts as a sharp contrast to the purplish-blue nuclear stain of the nucleus, and helps identify other entities in the tissues such as cell membrane (border), red blood cells, and fluid.
Immunohistochemistry (IHC). Immunohistochemistry (IHC) tests use antibodies to stain for proteins of interest in tissue specimens. The IHC test for metastatic breast cancer in lymph nodes uses antibodies to cytokeratin, so the test may be called cytokeratin (HC) staining, pankeratin (IHC) staining, immunocytochemistry, or immunochemistry. Specific stains include AE1, AE3, AE1/3, MNF116 and CAM5.2 Other IHC tests are used on the primary breast tumor, rather than the lymph nodes, to assess estrogen and progesterone receptors and HER-2 neu (human epidermal growth factor receptor). In Site-Specific Factor 4, code only IHC results for ITCs in lymph nodes.

Immunohistochemistry is an additional test performed by the pathologist on lymph nodes that are pathologically negative on standard H&E stains. If IHC is done, it will be noted as an addendum to the pathology report of the specimen or reported on a separate form. If there is no mention of IHC in the medical record, breast Site-Specific Factor 4 may be coded as 000 Not done.

Molecular Studies: Reverse Transcriptase/Polymerase Chain Reaction (RT-PCR). An even more sensitive test used to detect ITCs in lymph nodes is RT-PCR, a molecular test looking for expression of the genes of interest. This test is rarely done. If this test is done, record the information about ITCs in Site-Specific Factor 5.

Micrometastasis. When the tumor deposits in the lymph nodes are larger than 0.2 mm but not larger than 2.0 mm, they are defined as micrometastasis. Nodes with micrometastasis are defined as positive for staging.

In coding CS Lymph Nodes and Site-Specific Factors 3-5, the important things to abstract are the size of the tumor detected in the lymph nodes and the methods of detection. Table I-2-8 below may help in coding this information. Note that the table includes codes for axillary nodes only, not internal mammary nodes. The table is followed by examples to illustrate likely coding situations.

To use the table, identify the group (numbered I-VI) of applicable rows based on the information in column 2 that best represents the information in the case. Within that group, find the row or rows that represent the information in the case, and read right to the last four columns to find the codes to use. The group numbers are for convenience in using this chart only, and do not correlate with any anatomic groups of nodes.

Site-Specific Factor 3 – Number of Positive Ipsilateral Level I-II Axillary Lymph Nodes

Source documents: pathology report
In CS version 1, this field was called Number of Positive Ipsilateral Axillary Lymph Nodes. In CS version 2, the content has been modified slightly to limit the count of axillary lymph nodes to levels I and II on the same side of the body as the primary site. These nodes are the low axillary (level I and intramammary) and mid-axillary (level II, also called interpectoralt or Rotter’s nodes). Thus the count of axillary lymph nodes now excludes level III (high axillary, also called apical or infraclavicular; N3a), internal mammary (N3b) and supraclavicular (N3c) lymph nodes. The number of positive Ipsilateral Level I-II axillary lymph nodes determines the N category and the pathologic stage group.
## Table I-2-8. Examples of Lymph Node, IHC and Mol Coding Scenarios

<table>
<thead>
<tr>
<th>Case Information Categories with Examples</th>
<th>IHC and/or Mol Studies Done, or Method of Detection/Verification</th>
<th>CS Lymph Nodes</th>
<th>SSF3 (Number pos axillary nodes)</th>
<th>SSF4 (IHC)</th>
<th>SSF5 (Mol)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I. Clinical information only; no pathological information used to code CS Lymph Nodes; no nodes examined pathologically, nodes clinically NEGATIVE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 Nodes clinically negative, patient refused further workup.</td>
<td>None; does not apply</td>
<td>000</td>
<td>098</td>
<td>000</td>
<td>000</td>
</tr>
<tr>
<td>II. Clinical information only; no pathological information used to code CS Lymph Nodes; no nodes examined pathologically, nodes clinically POSITIVE</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2A. Fixed and matted ipsilateral axillary nodes clinically, patient had pre-op chemotherapy. Subsequent modified radical mastectomy showed negative axillary nodes. (CS Reg Nodes Eval = 5 in this case.)</td>
<td>None; does not apply</td>
<td>510</td>
<td>098</td>
<td>987</td>
<td>987</td>
</tr>
<tr>
<td>2B. Axillary nodes clinically positive, patient refused further workup.</td>
<td>None; does not apply</td>
<td>600</td>
<td>098</td>
<td>987</td>
<td>987</td>
</tr>
<tr>
<td>III. Nodes examined pathologically, nodes negative; no Isolated Tumor Cells (ITCs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOTE: SSF 4 and 5 are coded independently of each other.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3A. Modified radical mastectomy, path report with 12 lymph nodes neg for tumor, no special stains, cytokeratin, IHC, or molecular studies performed on lymph nodes.</td>
<td>Immunohistochemistry (IHC) (cytokeratin staining) not done, OR unknown if done</td>
<td>000</td>
<td>000</td>
<td>000</td>
<td>000</td>
</tr>
<tr>
<td>3B. Sentinel nodes neg on H&amp;E. Unknown if IHC done. RT-PCR done, negative for ITCs.</td>
<td>IHC done, neg for tumor</td>
<td>000</td>
<td>000</td>
<td>001</td>
<td>000</td>
</tr>
<tr>
<td>4. Sentinel nodes neg on H&amp;E. IHC (cytokeratin stain) performed, negative for ITCs. Molecular studies not done.</td>
<td>Molecular studies not done, OR unknown if done</td>
<td>000</td>
<td>000</td>
<td>001</td>
<td>000</td>
</tr>
<tr>
<td>5A. Sentinel nodes neg on H&amp;E. IHC (cytokeratin stain) performed, negative for ITCs. Molecular studies not done.</td>
<td>Molecular studies not done, neg for tumor</td>
<td>000</td>
<td>000</td>
<td>000</td>
<td>001</td>
</tr>
<tr>
<td>5B. Modified radical mastectomy, path report with 12 lymph nodes neg for tumor, no special stains, cytokeratin, IHC, or molecular studies performed on lymph nodes.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. Sentinel nodes neg on H&amp;E. Unknown if IHC done. RT-PCR done, negative for ITCs.</td>
<td>Molecular studies done, neg for tumor</td>
<td>000</td>
<td>000</td>
<td>000</td>
<td>001</td>
</tr>
<tr>
<td>IV. Nodes examined pathologically, Isolated Tumor Cells (ITCs) ONLY; Single tumor cells, or clusters &lt; 0.2mm OR Immunohistochemistry (IHC) pos, NOS</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NOTE: SSF 4 and 5 are coded independently of each other.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. Sentinel nodes initially neg on H&amp;E. IHC performed, positive for ITCs. No molecular studies done. ITCs then verified on H&amp;E slides of the sentinel nodes.</td>
<td>H&amp;E (routine stained slides)</td>
<td>050</td>
<td>000</td>
<td>002</td>
<td>000</td>
</tr>
<tr>
<td>8. Sentinel nodes neg on H&amp;E. Unknown if IHC performed. RT-PCR study done, neg for ITCs.</td>
<td>H&amp;E neg, immunohistochemistry (IHC)</td>
<td>000</td>
<td>000</td>
<td>000</td>
<td>001</td>
</tr>
</tbody>
</table>

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Version 02.00.01

10. Sentinel nodes neg on H&E. IHC (cytokeratin stain) performed, positive for ITCs. Unknown if molecular studies done.

11. Class 3 case abstracted from clinical history. Sentinel nodes neg on H&E. IHC on sentinel nodes was positive, NOS. Molecular studies not mentioned.

12A. Sentinel nodes neg on H&E. IHC (cytokeratin stain) performed, positive for ITCs. Unknown if molecular studies done.
12B. Class 3 case abstracted from clinical history. Sentinel nodes neg on H&E. IHC on sentinel nodes was positive, NOS. Molecular studies not mentioned.

13A. Sentinel nodes neg on H&E. Unknown if IHC performed. RT-PCR done, neg for ITCs.
13B. Sentinel nodes neg on H&E. IHC and RT-PCR negative for tumor.

14. Sentinel nodes neg on H&E. Cytokeratin stain showed clusters of tumor cells in the node up to 0.15 mm. RT-PCR was pos for ITCs.

V. Nodes examined pathologically
Tumor > 0.2mm and < 2.0mm (Micrometastasis)

15. Path report, final diagnosis: “Lymph Nodes: two of three sentinel lymph nodes positive for capsular micrometastases.” Microscopic description: “Sections of the first submitted sentinel lymph node demonstrate normal nodal architecture, however, on cytokeratin stain, micrometastases are noted in the capsule.”

<table>
<thead>
<tr>
<th></th>
<th>H&amp;E neg, micromets on IHC (cytokeratin staining) ONLY</th>
<th>130</th>
<th>001-097 (for this example, 002)</th>
<th>987</th>
<th>987</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H&amp;E pos for micromets</td>
<td>150</td>
<td>001-097 (for this example, 001)</td>
<td>987</td>
<td>987</td>
</tr>
</tbody>
</table>

VI. Nodes examined pathologically
Tumor > 2.0mm; positive lymph nodes

17. Axilla neg on palpation. Modified radical mastectomy, 2/14 nodes positive. Largest metastasis 0.8 cm.

|   | Does not apply | 250 or higher | 001-097 (for this example, 002) | 987 | 987 |
Site-Specific Factor 1 – Estrogen Receptor Assay

Other names: ER, Estrogen Receptor Assay, Estrogen Receptor Status, Estradiol Receptor, Estrogen Binding Protein, hormone receptor status (with PRA).

Site-Specific Factor 2 – Progesterone Receptor Assay

Other names: PR, PgR, Progesterone Receptor Assay, Progesterone Receptor Status, hormone receptor status (with ERA).

The following information applies to both Estrogen Receptor Assay and Progesterone Receptor Assay.

Source documents: pathology report (usually as an addendum), separate clinical laboratory report

Estrogen receptor (ER) positivity and progesterone receptor (PR) positivity are favorable prognostic factors in breast cancer, as well as endometrial carcinoma and meningioma. Positive results indicate a favorable response to endocrine (hormonal) therapy. Combined ER and progesterone receptor (PR) positivity is associated with increased response to antiestrogen therapies.

There are a variety of ways to report information on ER and PR results, but there is almost always a summary statement that the result is positive or negative.

Example 1

<table>
<thead>
<tr>
<th>Test Name</th>
<th>Assay Type</th>
<th>Staining</th>
<th>Percent Positive</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Estrogen Receptor</td>
<td>3+</td>
<td>72</td>
<td>Positive</td>
<td></td>
</tr>
<tr>
<td>Progesterone Receptor</td>
<td>3+</td>
<td>57</td>
<td>Positive</td>
<td></td>
</tr>
</tbody>
</table>

Example 2

The neoplastic cells show mild (1+/4+) cytoplasmic staining with the estrogen receptor marker. The neoplastic cells exhibit abundant (3+/4+) nuclear staining with progesterone receptor marker.

Example 3

ER positive (72%); PR positive (68%)

Record the pathologist’s interpretation of the assay value from the tumor specimen. If assays are performed on more than one specimen and any result is interpreted as positive, code as 010 Positive/elevated.

010 Positive/elevated
020 Negative/normal
030 Borderline; undetermined whether positive or negative

See schema for additional code choices.

Note: New guidelines for interpreting test results do not provide for a borderline result. Therefore, the code for borderline will rarely, if ever, be used for diagnoses 2010 forward. The new guidelines state that any test which results in 1% of the cells staining positive is a positive test. If <1% of cells stain, the test is considered negative.

The two most common ways to report ER and PR results are the proportion score (PS) (Table I-2-9) and the intensity score (IS) (Table I-2-10). Both the PS and IS are based on immunohistochemical staining of tumor cells.

The PS reports the percentage of tumor cells with positive nuclear staining. The IS is the degree of nuclear positivity; in other words, the average intensity
of all positive tumor cells on a scale from pale to dark. In some reports, these two scores are combined for a total score (TS, the sum of the PS and the IS). The Allred score, “H” score, or Quick score may be reported. Each of these is a total score for proportion and intensity. For each of these, results of 0 (None + None) or 2 (<1% + 1 Weak) are considered negative and any sum from 3 to 8 is considered positive.

Older ER and PR reports may have different cut-offs for negative and positive results.

*Immunoperoxidase (immunohistochemical) staining of tumor cell nuclei:*

- < 5% negative
- 5 – 19% borderline; also expressed as 1+ or +
- ≥ 20% positive; 20 – 80% also expressed as 2+ or ++
- > 80% also expressed as 3+ or +++

Another less frequently used assay is the amount of cytosol protein in the tumor sample. This is reported in femtomoles per milligram.

*Femtomoles (fmol/mg) of cytosol protein per milligram*

- < 6 negative
- 6-10 borderline
- > 10 positive
- > 100 highly positive


**Site-Specific Factor 6 – Size of Tumor-Invasive Component**

*Source document: pathology report*

This site-specific factor documents whether only the size of the invasive breast tumor was reported or whether the tumor size was a mix of invasive and in situ carcinoma. AJCC rules stated that the size of the invasive tumor should be used to determine the T category, but sometimes information on the invasive tumor size is not available. This field does not affect stage grouping, but can be used if needed by a researcher to analyze differences in outcomes within a T category.

Code the description that explains the CS Tumor Size code. In the descriptions, “pure” means either entirely invasive (code 000) or entirely in situ (code 010). “Mixed” means a combination of invasive and in situ is present in the tumor, not the entire specimen. The following descriptions are adapted from the wording in the SSF6 table.

- 000 Entirely invasive (no in situ) – purely invasive (can be mixed histologies no in situ is present)
- 010 Entirely in situ (no invasive component) – purely in situ; DCIS, LCIS
- 020 Mixed invasive and in situ, invasive size coded in CS Tumor Size
- 030 Mixed invasive and in situ, entire tumor size coded; invasive size stated AND in situ described as minimal (less than 25%) – EIC negative; extensive intraductal component not present
- 040 Mixed invasive and in situ, entire tumor size coded; invasive size not stated AND in situ described as extensive (25% or more) – extensive intraductal component present; EIC positive
- 050 Mixed invasive and in situ, entire tumors coded in CS Tumor Size because size of invasive component not stated AND proportions of in situ and invasive not known
- 060 Mixed invasive and in situ components present, unknown size of tumor (CS Tumor Size coded 999)
- 987 Unknown if invasive and in situ, unknown if tumor size represents mixed tumor or a “pure” tumor. Clinical tumor size coded.
Site-Specific Factor 7 - Nottingham or Bloom-Richardson (BR) Score/Grade

**Source document:** pathology report

**Other names for score:** Nottingham combined histologic grade, Elston-Ellis modification of Scarff-Bloom-Richardson grading system, Modified Bloom-Richardson, Scarff-Bloom-Richardson, SBR, Elston-Ellis (EE) modification, Nottingham modification

**Other names for grade:** BR grade, Nottingham grade, or Nottingham-Tenovus grade

The AJCC and College of American Pathologists recommend the Nottingham or Bloom-Richardson score and/or grade as the preferred method for reporting histologic grade for breast cancers. The score based on three factors: degree of tubule formation (histologic grade), mitotic activity, and nuclear pleomorphism (nuclear grade). Each of the factors receives a score of 1, 2, or 3, based on specific pathologic criteria.

Code the total score if given, as a priority. If the report describes any of the factors with words (low, intermediate, high) rather than numbers, do NOT attempt to translate these words into a number. The appropriate score will be reflected in the second digit of the code.

**Examples**

- 030 Score of 3 (1 + 1 + 1)
- 050 Score of 5
- 090 Score of 9 (3 + 3 + 3)

If the BR score is not given, look for a stated grade, which is a verbal summary of the score. Grades are based on the scores as shown above, but only the grade itself may appear in the chart or in the CAP Protocol. Grades are expressed as:

- Low grade (scores 3-5), also called BR Grade 1
- Intermediate grade (scores 6, 7), also called BR Grade 2
- High grade (scores 8, 9), also called BR Grade 3

If only the grade is stated and not a score, record the appropriate code for that grade. The first digit of 1 indicates that this is a grade rather than a score while the second digit reflects the actual numeric grade. Clinical-only diagnoses should be coded as 998 reflecting the fact that there is no histologic specimen to score.

- 110 Low Grade, score not given
- 120 Medium Grade, score not given
- 130 High Grade, score not given
- 998 No histologic examination of primary site
- 999 Neither BR grade nor BR score given; Unknown or no information; Not documented in patient record

**Note:** The Bloom-Richardson Score/Grade can be converted into the ICD-O grade/differentiation (6th digit) code. Refer to FORDS 2010 for the conversion table. Do not use the Bloom-Richardson Score/Grade to code the fields Grade Path System and Grade Path Value.
RECORDING HER2 INFORMATION

Nine of the 24 site-specific factors for breast collect information about HER2.

Site-Specific Factor 8 – HER2: IHC Test Lab Value
Site-Specific Factor 9 – HER2: IHC Test Interpretation
Site-Specific Factor 10 – HER2: FISH Test Lab Value
Site-Specific Factor 11 – HER2: FISH Test Interpretation
Site-Specific Factor 12 – HER2: CISH Test Lab Value
Site-Specific Factor 13 – HER2: CISH Test Interpretation
Site-Specific Factor 14 – HER2: Result of Other or Unknown Test
Site-Specific Factor 15 – HER2: Summary Result of Testing
Site-Specific Factor 16 – Combinations of ER, PR, and HER2

Source documents: pathology report (usually in an addendum to the report), specialized lab tests, reference laboratory report
Other names: HER2, HER2neu, erbB2, c-neu

HER2 is Human Epidermal growth factor Receptor 2, a protein on the surface of cancer cells that accepts growth signals. There are actually four HER categories; only HER2 is of interest for breast cancer. The presence of too many HER2 receptors (“overexpression”) indicates that the tumor may grow more aggressively. About 20% of breast cancers overexpress Her2. Overexpression is both a prognostic and predictive factor for breast cancer. A lack of overexpression indicates patient may not respond to certain therapies such as Herceptin, which is designed to “turn off” or deregulate the overexpression of HER2. There are several ways to measure HER2: immunohistochemistry (IHC), Fluorescence In Situ Hybridization (FISH), and Chromogenic In Situ Hybridization (CISH, pronounced ‘kish’). The information obtained from these tests plays a critical role in treatment planning, because HER2-positive patients tend to respond favorably to the expensive drug Herceptin (trastuzumab) or Tykerb (lapatinib), which work by blocking these receptors and preventing growth signals from getting through to the cancer cell. HER2-positive patients also may have a greater benefit from anthracycline-based adjuvant therapy, such as idarubicin. Usually only one test is performed, but if result of that single test is equivocal, American Society of Clinical Oncology (ASCO) guidelines recommend that a second test be performed.

Immunohistochemistry (IHC) Test and Interpretation
Site-specific factor 8 codes the IHC score in a range of 000 to 003, with additional codes for test not done and other explanations for missing information. Site-specific factor 9 codes the interpretation of the IHC score.

Immunohistochemistry or IHC is the most commonly used test for HER2 and is usually the initial HER2 test done. IHC is a special staining process performed on fresh or frozen breast cancer tissue removed during biopsy. IHC is used to show whether or not the cancer cells have HER2 receptors and/or hormone receptors on their surface. The IHC test gives a score of 0 to 3+ that indicates the amount of HER2 receptor protein on the cells in a sample of breast cancer tissue. If the tissue scores 0 to 1+, it is called “HER2 negative,” and Herceptin is not considered effective for tumors with IHC scores of 0 or 1+. When the result is 2+, the HER2 status of the tumor is not clear. This often leads to testing the tumor with FISH (see below). If the tissue score is 3+, it is called “HER2 positive,” and the patient is likely to receive Herceptin as part of first course therapy. (The symbols 1+, 2+, and so forth should be read as “1 plus” or “2 plus” rather than “1 positive” or “2 positive.”) It is important to note that results on the IHC test may vary from lab to lab and that some labs are more experienced with testing for HER2 than others. The IHC test results are most reliable for fresh or frozen tissue samples. IHC tends to be an unreliable way to test tissue that's preserved in wax or other chemicals.

Definitions of “positive” and “negative” interpretations for the test vary from one lab to another. Each
may have a different range for normal values. Look for the interpretation of the test by patient’s clinician or the facility pathologist as first priority. In the absence of the local doctor’s interpretation, look on the actual lab report for that particular lab’s reference values and use that information to assign the appropriate interpretation code. The codes for interpretation are similar to other site-specific factors that are evaluated as positive/elevated, negative/normal, borderline, and so forth. If neither a physician interpretation nor a lab reference range can be found, do not attempt to interpret the results; code as 999 unknown.

**Fluorescence In Situ Hybridization (FISH) and Interpretation**

FISH results are reported in SSFs 10 (ratio) and 11 (interpretation). The FISH test is another method of testing for overexpression of the HER2 gene that uses fluorescent pieces of DNA that attach only to the HER2 gene copies in cells, which can then be counted under a special microscope. The FISH technique is more expensive than IHC and takes longer to get the results, but it is also thought to be more accurate. The result is expressed as a ratio of the number of copies of the HER2 receptors to the control rather than as a score.

In SSF 10, code the exact ratio to two decimal places in the range 100 (1.00) to 986 (9.86), as stated in the report. For example, a FISH result of 5.5 would be reported as 550; a result of 11.85 would be reported as 987 (ratio of 9.87 or greater).

In SSF11, code the local doctor’s interpretation of the FISH test, if available; otherwise, look at the results on the lab report. For FISH, the definition of positive, negative or borderline varies from lab to lab. The code structure for this field is similar to other lab tests requiring an interpretation. If a FISH test was performed and the results are interpreted in the chart, record as positive, negative or borderline. If the test results are in the chart but there is no interpretation and no laboratory guideline given, use the guidelines in the following slide. If a FISH test was not done, code as 998.

**Chromogenic In Situ Hybridization (CISH) and Interpretation**

CISH results are reported in SSFs 12 (mean number) and 13 (interpretation). CISH is the most recent technique for determining HER2 status. It has only been approved in the United States since the spring of 2009. CISH works in a manner similar to FISH, by using small DNA probes to count the number of HER2 genes in breast cancer cells. But this test looks for color changes (not fluorescence) and doesn't require a special microscope, which makes it less expensive. In addition, unlike other tests, it can be used on tissue samples that have been stored in the lab. CISH is already in widespread use in Canada, and because of its advantages, CISH is likely to replace FISH testing in the US.

CISH results are expressed as the mean (average) number of HER-2/neu gene copies per cell. In other words, CISH is the ratio of the number of gene copies detected, divided by the number of tumor cell nuclei counted, for example, 253 gene copies divided by 60 nuclei counted = 4.22. In SSF 12, record the exact mean to two decimal places in the range 100 (1.00) to 986 (9.86), as stated in the report. For example, a CISH result of 4.22 would be reported as 422; a result of 11.85 would be reported as 987 (ratio of 9.87 or greater).

Record the interpretation of the CISH test in SSF13, which has a similar code structure to the HER2 IHC and HER2 FISH interpretation fields. For CISH, the definition of positive, negative or borderline varies from lab to lab. If a CISH test was performed and the results are interpreted in the chart, code as positive, negative or borderline. Usually, the results will be either positive or negative, because if the result of counting the mean number of gene copies per cell from 30 cells is between 4.0 and 6.0, another 30 cells are counted and the mean from those 60 cells is interpreted according to the following scoring guideline:

- **Non-amplification:** 1–5 signals/nucleus in tumor cells. Result: negative.
- **Amplification:** >5 signals/nucleus, or cluster of amplified signals/nucleus in >50% of tumor cells.
Result: positive.

**Result of Other or Unknown Test**

Site-specific factor 14 documents other types of HER2 testing, in other words, not IHC, FISH, or CISH. The most likely scenario will be a statement in the CAP Protocol or elsewhere in the chart that the patient is HER2 positive or HER2 negative, with no indication of how this information was determined and no test results in the chart. This may be particularly true for class of case 2 or cases being reported by freestanding radiation therapy or ambulatory surgery centers. Another possibility is the SISH (silver in-situ hybridization) test, which is still experimental. The code structure is the same as the IHC, FISH and CISH test interpretation fields. Code a statement of HER2 status (positive, negative, borderline) by the clinician/pathologist in this field when there is no information about the specific HER2 test is given in the chart.

**Summary of HER2 Testing**

Site-specific factor 15 can be derived from SS Factors 9, 11, 13, and 14. When there is only one test done (IHC, FISH, or CISH), repeat the result of that test in this field. When more than one Her2 test is done, code the final result in this field. To determine which result to code in this field, use the following guidelines:

- Gene-amplification tests are considered to be a more reliable test of the over-expression of the HER2 gene. Thus, if both an IHC and a gene-amplification test (FISH, CISH, etc.) were given, record the result of the gene-amplification test in this field.
- If the gene-amplification test is given first and the result is borderline/equivocal and an IHC is done to clarify these equivocal results, take the result of the IHC.

**Site-Specific Factor 16 – Combinations of ER, PR, and HER2**

This is another summary field that allows researchers to rapidly identify those women who are “triple negative”—ER negative, PR negative and HER2 negative—a group comprising approximately 15% of all breast cancer cases. Younger women, African American women, and Hispanic women are more likely to be triple negative than older women and Caucasians, meaning that they are unlikely to respond to hormone therapy or Herceptin as part of their breast cancer treatment.

SSF 16 uses information from site-specific factors 1, 2, and 15. The first digit reflects the result of ER testing, the second of PR testing, and the third HER2 testing. The values in each digit are simply 0 for a negative test result and 1 for a positive test result. Thus triple negative patients are coded 000 in this field. In contrast, code 111 identifies women who are triple positive. If the result of any of the three tests is borderline/equivocal, unknown, or not performed, code as 999.

**Site-Specific Factor 17 – Circulating Tumor Cells (CTC) and Method of Detection**

*Source documents:* pathology report, special laboratory report, reference laboratory report

Metastasis, the major cause of mortality in patients with cancer, is caused by tumor cells that escape from the primary tumor into the bloodstream and travel through the circulation to distant sites where they develop into secondary tumors. The number of circulating tumor cells before treatment is an independent predictor of progression-free survival and overall survival in patients with metastatic breast cancer. Although these circulating tumor cells (CTCs) provide a link between the primary tumor and metastatic sites, the factors involved in circulating tumor cell survival in the blood circulation and eventual metastases are not well understood. Highly sensitive and specific immunocytochemical and molecular assays now enable the detection and characterization of circulating tumor cells (CTCs) and disseminated tumor cells (DTCs—see site specific factor 18) at the single cell level in peripheral blood and bone.
marrow, providing insights into the first crucial steps of the metastatic process. CTCs and DTCs are defined as deposits of molecularly or microscopically detected tumor cells in circulating blood, bone marrow or other nonregional nodal tissue no larger than 0.2 mm identified in a patient without symptoms or signs of metastases.

While CTCs can be detected in the peripheral blood of cancer patients in low concentrations, isolating and identifying them is a difficult task. This site-specific factor collects two pieces of information about CTCs in the blood: whether they are present and what test was used to detect them. In this three-digit field, the first digit codes whether the test was negative (0), positive (1), or borderline (2). The second digit codes the type of test. A 0 in the second digit represents reverse transcriptase-polymerase chain reaction (RT-PCR), a gene-amplification test used for a number of other purposes including FISH and CISH tests for HER2 and sometimes for detection of isolated tumor cells in sentinel nodes. A 1 represents immunomagnetic separation (IMS), which should not be confused with immunohistochemical (IHC) stains. A 3 represents “other” test types, and a 4 represents unknown test type.

Immunomagnetic separation (IMS) is a laboratory tool that can efficiently isolate cells from body fluid or cultured cells. DNA analysis has supported the combined use of both this technique and RT-PCR. During IMS, antibodies coating paramagnetic beads bind to antigens present on the surface of cells thus capturing the cells and facilitating the concentration of these bead-attached cells. The concentration process is created by a magnet placed on the side of the test tube bringing the beads to it. IMS is a more precise test that takes precedence over RT-PCR.

This field collects information about circulating tumor cells in the blood only. Read the descriptions carefully to select the proper code to describe both the positivity and the type of test. If the information is not collected in the facility, use code 988. If the test was not done, use code 998.

Site-Specific Factor 18 – Disseminated Tumor Cells (DTC) and Method of Detection

Source documents: pathology report, special laboratory report, reference laboratory report

Despite the progress resulting from early detection and improved adjuvant therapy, the prognosis of breast cancer patients is still limited by the occurrence of distant metastases largely due to clinically occult micrometastases that remain undetected at primary diagnosis even by high-resolution imaging approaches. Recent research efforts have concentrated on the identification of additional parameters allowing individual risk assessment and stratification of patients for targeted therapies, since traditional prognostic factors are not sufficient to predict metastatic relapse and treatment decisions are still mainly based on statistical risk parameters. A large number of studies showed that the presence of DTCs in bone marrow has prognostic impact for primary breast cancer patients. DTCs are likely to escape from chemotherapy by maintaining a dormant nonproliferating state. However, isolated cells or small clusters of DTCs continue to be staged as no distant metastasis, M0(i+) in the seventh edition of TNM.

Similar to SSF 17, this site-specific factor collects two pieces of information about DTCs in the bone marrow: whether they are present and what test was used to detect them. In this three-digit field, the first digit codes whether the test was negative (0), positive (1), or borderline (2). The second digit codes the type of test. A 0 in the second digit represents reverse transcriptase-polymerase chain reaction (RT-PCR), a gene-amplification test used for a number of other purposes including FISH and CISH tests for HER2 and sometimes for detection of isolated tumor cells in sentinel nodes. A 1 represents immunohistochemistry (IHC). A 3 represents “other” test types, and a 4 represents unknown test type.

This field collects information about disseminated tumor cells in the bone marrow only. Read the descriptions carefully to select the proper code to describe both the positivity and the type of test. If the information is not collected in the facility, use code 988. If the test was not done, use code 998.
Site-Specific Factor 19 – Assessment of Positive Ipsilateral Axillary Lymph Nodes

This site-specific factor provides supplemental information on how the number of positive level I and II (and intramammary) lymph nodes was determined for site-specific factor 3, the N category and the stage group.

Codes with a “0” in the first digit represent single procedures only.
010 Clinical assessment only
020 Positive fine needle aspiration (FNA) only
030 Positive core biopsy: incisional
040 Positive core biopsy: excisional
050 Positive core biopsy: type not specified

For codes 110-140, the first digit is based on the sentinel node biopsy and the second digit is based on the lymph node dissection.
100 Positive sentinel node biopsy(ies) and no lymph node dissection
110 Positive sentinel node biopsy(ies) and negative lymph node dissection
120 Positive sentinel node biopsy(ies) and positive lymph node dissection
130 Negative sentinel node biopsy(ies) and positive lymph node dissection
140 No sentinel node biopsy and positive lymph node dissection
See schema for additional code choices.

Site-Specific Factor 20 – Assessment of Positive Distant Metastases

This site-specific factor evaluates how the information about positive metastasis in CS Mets at Dx and the four specific mets fields (bone, lung, liver, and brain) was determined. If multiple diagnostic methods were used, use the numerically highest code. If distant metastasis is coded as 000 (no positive metastasis), this field must also be coded to 000. For example, if the patient has a negative bone scan or a negative chest x-ray, do not code 020.

Code the source of positive metastatic findings only.
000 No positive metastases were identified
010 Clinical assessment
020 Radiography; Imaging (US, CT, MRI, PET)
030 Incisional biopsy; FNA
040 Excisional biopsy or resection with microscopic confirmation other than by biopsy
See schema for additional code choices.

Site-Specific Factor 21 – Response to Neoadjuvant Therapy

Neoadjuvant therapy is defined as systemic or radiation treatment administered prior to surgery in an attempt to shrink the tumor or destroy regional metastases. This site-specific factor documents whether that neoadjuvant therapy was successful.

Code the clinician’s statement regarding response to neoadjuvant therapy. Do not try to interpret or infer a response based on the medical record. As a guide for the clinician, the definitions below are from the AJCC Cancer Staging Manual, seventh edition. The registrar should not use these definitions to code this field.
010 Complete Response (CR) – absence of invasive carcinoma in breast and lymph nodes; must be determined by microscopic evaluation of tissues

020 Partial Response (PR) – a decrease in T and/or N category compared to pretreatment value and no increase, using same method of evaluation as baseline value; residual in situ cancer at primary site; residual tumor in lymph nodes of any size

030 No Response (NR) – no apparent change in the T or N category compared to pretreatment value, or an increase in T or N value at time of pathologic examination

998 No neoadjuvant therapy

See schema for additional code choices.

Site-Specific Factor 22 – Multigene Signature Method

Source documents: specialty reference laboratories (private companies with proprietary testing methods); the actual report may be included in the medical record or may be referenced by the clinician.

Other names: genomic profiling, Oncotype Dx, MammaPrint, multigene testing, multigene assay, microarray assay, molecular diagnostics for treatment planning

Multigene testing is usually done for node-negative patients to predict risk of recurrence within a specified time period or to predict the likelihood that the patient will respond to specific types of chemotherapy. Multigene testing helps tailor treatment for the woman’s specific cancer characteristics. Recent studies indicate that these tests may also be helpful in planning treatment and predicting recurrence in node positive women with small tumors. Some types of tests may be specific to ER positive or negative patients or women in a certain age range. Many different types of genetic testing are available, including IHC-based, FISH-based, RT-PCR-based, and genomic microarray-based multigene predictors.

The most common and best known multigene test method is the Oncotype DX Breast Cancer Assay (code 010). This test is for women with Stage I or II node negative and ER positive breast cancer. It is an RT-PCR based assay for 21 genes (16 cancer related genes and 5 control genes), including ER, PR, and HER2/neu. A recurrence score is generated that predicts the risk of recurrence at 10 years for women treated with tamoxifen. Women who have carcinomas with high recurrence scores may benefit most from the addition of CMF (cyclophosphamide, methotrexate, and 5-fluorouracil) chemotherapy, whereas women with low recurrence scores may be less likely to have a benefit.

MammaPrint (code 020) is a microarray assay performed only on fresh tissue containing at least 30% tumor cells and using a 70-gene RNA profile to identify a poor prognosis signature and a good prognosis signature. This test is for node-negative women under the age of 61 with ER positive or ER negative carcinomas. This tissue must be collected in a kit and received by the company within 5 days from excision.

Other (code 030) includes the various IHC-based, FISH-based, and other types of tests, including the Breast Cancer Gene Expression Ratio Assay (BCGERA), also called the H:I Ratio Test, and the Rotterdam Signature test. BCGERA is an RT-PCR assay of 6 genes intended for patients with ER positive, lymph node negative carcinomas, and separates carcinomas into high-risk and low-risk groups. The Rotterdam Signature is a 76-gene microarray assay for women with lymph node negative carcinomas that are either ER negative or ER positive. It does not overlap with the Oncotype DX or MammaPrint assays.

Site-Specific Factor 23 – Result/Score of Multigene Signature

This site-specific factor reports the outcome of the multigene signature test coded in SSF 22. Oncotype
Collaborative Stage Data Collection System Coding Manual and Instructions
Part I Section 2: Site-Specific Notes

Dx reports provide a score ranging from 1 to 100 on the front page of the report. This gives an “average rate of distant recurrence at 10 years.” Results of the MammaPrint and Breast Cancer Gene Expression Ratio Assay tests are reported as either Low Risk or High Risk (meaning the likelihood of developing distant recurrence) but may also be stated as good prognosis or poor prognosis.

Record the actual multigene signature score if given. If any tests results in a score of 100 or higher, code as 100.

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>001-099</td>
<td>Actual score</td>
</tr>
<tr>
<td>100</td>
<td>100 or more</td>
</tr>
<tr>
<td>200</td>
<td>Low risk of recurrence (good prognosis)</td>
</tr>
<tr>
<td>205</td>
<td>High risk of recurrence (poor prognosis)</td>
</tr>
</tbody>
</table>

See schema for additional code choices.

Site-Specific Factor 24 – Paget Disease

Source document: pathology report
Other names: DCIS involving nipple epidermis/skin

The final breast cancer site-specific factor documents the absence (code 000) or presence (code 010) of Paget disease. Paget disease is a scaly, crusting lesion of the nipple resembling eczema. ICD-O includes morphology codes for Paget disease by itself and combined with ductal or intraductal carcinoma. It is commonly associated with an underlying cancer in the breast, in which case the presence of Paget disease is disregarded and staging is based on the underlying tumor. Code any statement of Paget disease, clinical or pathologic, giving priority to the pathologic assessment. If physical or pathologic examination of the breast and nipple is negative or if Paget disease is not mentioned, code as 000. Use code 999 unknown when there is no clinical or pathologic examination of the nipple described in the medical record.
FEMALE GENITAL ORGANS
Vulva, Vagina, Cervix, CorpusCarcinoma, CorpusAdenosarcoma, CorpusSarcoma, Ovary, Fallopian Tube, Placenta, PeritoneumFemaleGen

This section covers 10 schemas of the gynecologic organs. The new PeritoneumFemaleGen schema includes a schema discriminator to separate soft tissue sarcomas of the peritoneum from carcinomas of the female peritoneum, which are staged in the TNM system with the ovary schema. In the seventh edition of TNM and therefore in CS version 2, corpus uteri has three histology-specific staging systems: endometrium and carcinomas (CorpusCarcinoma), ICD-O morphology codes 8000-8790, 8980-8981, 9700-9701; leiomyosarcomas and endometrial stromal sarcomas (ESS) (CorpusSarcoma), 8890-8898, 8930-8931; and adenosarcomas (CorpusAdenosarcoma), 8933 only.

Many of the site-specific factors are the same for multiple primary sites, but the numbering of the site-specific factors differs, as shown in Table I-2-11. These site-specific factors will be discussed generically (without reference to SSF numbers) below.

Table I-2-11. Site-specific Factor Locations for Gynecologic Organ Prognostic Factors

<table>
<thead>
<tr>
<th>FIGO Stage</th>
<th>Vulva</th>
<th>Vagina</th>
<th>Cervix</th>
<th>Corpus Carci- noma</th>
<th>Corpus Adeno- sarcoma</th>
<th>Corpus Sarcoma</th>
<th>Ovary</th>
<th>Fallopian Tube</th>
<th>Placenta</th>
<th>Peritoneum FemaleGen</th>
</tr>
</thead>
<tbody>
<tr>
<td>CA-125</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Peritoneal cytology</td>
<td></td>
<td>2</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Pelvic Node status/assess</td>
<td>12-13</td>
<td>2-3</td>
<td>2-3</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
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<tr>
<td>Resid tumor status/size after cytoreductive surgery</td>
<td></td>
<td>3</td>
<td>3</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Number pos/exam pelvic nodes</td>
<td></td>
<td>3-4</td>
<td>3-4</td>
<td>3-4</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Tumor location after prim cytoreductive surgery</td>
<td></td>
<td>4</td>
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<td>4</td>
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</tr>
<tr>
<td>Para-aortic node status/assess</td>
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<td>4-5</td>
<td>4-5</td>
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<td></td>
</tr>
<tr>
<td>Number pos/exam para-aortic nodes</td>
<td></td>
<td>5-6</td>
<td>5-6</td>
<td>5-6</td>
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<tr>
<td>Distant (mediastinal, scalene) node status/assess</td>
<td></td>
<td>6-7</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mediastinal node status/assess</td>
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<td>6-7</td>
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</tr>
</tbody>
</table>
FIGO STAGE

Source documents: clinician’s notes, consultant notes, pathology report, radiation therapy notes

FIGO Stage is collected for all gynecologic sites, although the position in the site-specific factors varies. FIGO is the French acronym for the Federation Internationale de Gynecologie et d’Obstetrique, the worldwide organization of obstetricians and gynecologists who maintain the international staging systems for female genital organs. In English, the organization is the International Federation of Gynecology and Obstetrics. The FIGO staging system has been adapted into the AJCC staging manual. FIGO uses Roman numerals and subscripts to define a stage. There is no T, N, or M descriptor with FIGO stage, only a stage group. For example, FIGO Stage IA is equivalent to T1a, FIGO Stage III can be either T3_ or N1, and FIGO Stage IV is M1. FIGO stages are included in the descriptions of codes in CS Extension, CS Lymph Nodes and CS Mets at Dx tables.

Definitions of the various FIGO stages vary from primary to primary, but the structure is similar throughout. In the most recent version (2008) of the FIGO staging systems for the various organs, and therefore carried over into the seventh edition of TNM and CS version 2, FIGO no longer includes an in situ stage (Tis, Stage 0) for vulva, vagina, cervix, corpus (all histologies), ovary, Fallopian tube, placenta, or peritoneum. In CS version 2, a diagnosis of carcinoma in any of these sites is coded as 987 in CS Extension and the FIGO stage site-specific factor is coded as 999.

Changes to FIGO Staging of Corpus Uteri

Extensive changes occurred in FIGO staging of corpus uteri between the sixth and seventh editions of TNM.

- FIGO staging of corpus cancers is surgical (based on surgery observation and pathology), rather than clinical. It is important to read operative notes when coding GYN cases.
- Positive peritoneal cytology does not affect FIGO stage for carcinomas of the corpus but should be reported separately (see CorpusCarcinoma site-specific factor 2).
- For adenosarcomas and sarcomas of the corpus, classify simultaneous tumors of the corpus and ovary or pelvis associated with endometriosis of the ovaries or pelvis as independent primary
• Read the description of corpus stage in the record carefully because references to Stage IC (invasion of more than half of myometrium) and IIA (involving endocervical glands only) are not used in seventh edition. Stage IC is now merged with Stage IB, and Stage II is no longer subcategorized. Stage IIIC is now subcategorized into Stage IIIC1 and IIIC2 for different involved regional lymph node chains. Consult the attending physician or a pathologist if a 2010 and forward diagnosis is staged using previous edition designations of IC, IIA, or IIIC.

Structure of Codes
For all sites, the structure of the FIGO site specific factor is the same, although not every schema uses every possible FIGO code. The first digit of the code is the FIGO Roman numeral stage; the second digit is an Arabic number representing the alphabetic subcategory; and the third digit is an Arabic number representing the sub-subcategory of the FIGO stage.

Examples
100 FIGO Stage I
112 FIGO Stage IA2 (cervix)
220 FIGO Stage IIB
330 FIGO Stage IIIC
331 FIGO Stage IIIC1 (corpus)
410 FIGO Stage IVA

Code the FIGO stage stated in the medical record by the clinician or pathologist. If no FIGO stage is mentioned, do not assign a FIGO stage from information in the record (do not attempt to stage the case), and do not complete this field by back-converting a statement of T, N, or M or the CS Extension code. If no FIGO stage is mentioned, code as 999.

STATUS, NUMBER AND ASSESSMENT OF LYMPH NODES

This section applies to the following site-specific factors, which have different positions in the site-specific factors:

Pelvic Node Status, Assessment Method Pelvic Node Status
Number of Positive Pelvic Nodes, Number of Examined Pelvic Nodes
Para-aortic Node Status, Assessment Method Para-aortic Node Status
Number of Positive Para-aortic Nodes, Number of Examined Para-aortic Nodes
Distant (Mediastinal, Scalene) Node Status, Assessment Method Distant (Mediastinal, Scalene) Node Status
Mediastinal Node Status, Assessment Method Mediastinal Node Status
Scalene Node Status, Assessment Method Mediastinal Node Status
Reg LN Laterality
Femoral Inguinal Node Status, Assessment Method Femoral Inguinal Node Status

Source documents: pathology report, imaging reports, physical exam, other statements in medical record

Involvement of regional and distant lymph nodes is an important prognostic factor for the gynecologic organs. Figure I-2-10 shows the regional and common distant lymph nodes for GYN cancers. Regional nodes vary among the female genital sites. Refer to the individual schemas for lists of regional and distant lymph nodes. The iliac nodes, the nodes adjacent to the organs (paracervical, parametrial and so forth), and other lymph nodes within the shadow of the pelvis are referred to collectively as pelvic lymph nodes, NOS. The scalene and mediastinal nodes are distant for every GYN site.

Information on lymph nodes is collected in two ways for the female genital cancers:
• Number of [specific named] nodes positive and examined
• Status of [specific named] nodes and method of assessment

When number of nodes positive and examined is requested (all histologies of corpus and also fallopian tube), the structure and rules for the site-specific factor are the same as for the CS fields Regional Lymph Nodes Positive and Regional Lymph Nodes Examined, except that the site-specific factor is a three-digit field with a leading zero. For example, three positive nodes would be coded in Regional Lymph Nodes Positive as 03 and in the site-specific factor as 003. Nodes Positive and Nodes Examined are coded from the pathology report.

When status and assessment of lymph nodes is requested (cervix, vulva and vagina), status refers to positive or negative, and assessment is the method by which the positive nodes were determined. These fields can be coded from the pathology report, imaging or other information in the record. For the status fields, the basic codes are 000 Negative, 010 Positive, and 998 Lymph nodes not examined. (See schemas for additional code choices.)

For the assessment fields, the basic codes are shown below. Higher codes take priority over lower codes if multiple assessment methods were used.

000 Lymph nodes were not assessed
010 Clinical assessment
020 Radiography; Imaging (US, CT, MRI, PET)
030 Incisional biopsy; FNA
040 Lymphadenectomy; Excisional biopsy or resection with microscopic confirmation other than by biopsy

See schema for additional code choices.

For all lymph node fields, code statements by the clinician or pathologist as appropriate.

Site-Specific Factor 11 – Regional Lymph Node Laterality (Vulva)

Source documents: pathology report, imaging, physical exam, other statement in record

This site-specific factor is included in the CSv2 vulva schema to retain compatibility with AJCC sixth edition for mapping of the N category.

Code the appropriate description of involved regional lymph nodes.
000 All regional lymph nodes are negative
010 Unilateral - all positive regional nodes are ipsilateral
020 Bilateral or contralateral – at least one positive regional lymph node is bilateral or contralateral
030 Regional lymph node(s) positive – laterality unknown
998 Lymph nodes not examined

See schema for additional code choices.
Site-Specific Factor 1 – CA-125 (Ovary; PeritoneumFemaleGen)

**Source documents:** clinical laboratory report (blood or serum test); may be reported in history, clinician or consultant notes or pathology report

**Other names:** Cancer Antigen 125, CA 125, CA125, Carbohydrate Antigen 125, mucin 16, MUC16

**Normal reference range** < 35 units per milliliter (U/ml); SI: < 35 kiloUnits/Liter (KU/L). May also be reported as micrograms/milliliter (μg/mL or ug/mL). Normal reference range may vary depending on the laboratory running the test.

CA-125 is a tumor marker that is not specific to ovarian or primary peritoneal cancer but is useful to monitor for success of treatment and recurrence. Because it can be elevated in many diseases affecting the peritoneal lining of the abdominal and pelvic cavity, it is not a screening test for women who have no history of cancer. Any value over 35 is highly correlated with cancer and about 80% of ovarian cancers show an elevated CA-125. However, a result in the normal range does not rule out cancer. Values up to 65 U/ml may be considered borderline, and values over 200 are unlikely to be due to a benign condition. CA-125 monitors for success of treatment and recurrence. After obtaining a baseline value prior to treatment, a lower result on a subsequent test indicates a response to treatment, and an increasing value indicates possible recurrence.

Record the clinician’s interpretation of the highest value prior to treatment from a blood or serum test, based on the reference range used by the lab. Do not code the result from thoracentesis or paracentesis fluid.

- 010 Positive/elevated
- 020 Negative/normal
- 030 Borderline; undetermined whether positive or negative

Site-Specific Factor 2 – Peritoneal Cytology (Corpus – all histologies)

**Source documents:** cytology reports (look for multiple reports), pathology report

**Other names:** peritoneal washings, peritoneal lavage, possibly paracentesis (if no surgery)

Peritoneal cytology looks for malignant cells in the fluid in the pelvic and peritoneal cavities. Excess natural fluid accumulation is called ascites. If at laparotomy an analyzable amount of ascites is not present, the surgeon may flood the pelvis and abdomen with saline solution then suction it out and send the fluid for cytology. Prior to the seventh edition of TNM, positive peritoneal cytology was coded in CS extension. In CS version 2 peritoneal cytology is reported separately but does not change the FIGO or TNM stage. The basic codes are 000 Negative and 010 Malignant cells positive. (See schema for additional code choices.) If there is no pathological specimen available for testing, use code 998.

Site-Specific Factor 7 – Percent Non-Endometrioid Cell Type In Mixed Histology Tumors (Corpus – all histologies)

**Source documents:** pathology report (cell type(s) and percentage of each type)

This site-specific factor corresponds to the FIGO grade of the endometrial cancer. It records the degree of tumor cell differentiation—the higher the grade, the more aggressive the tumor—and the grade of the tumor is a factor in deciding further treatment after surgery.

Endometrioid carcinoma is a hormonally dependent gland-forming carcinoma (adenocarcinoma). The most common non-endometrioid histology is papillary serous (10%), followed by clear cell (2% to 4%), mucinous (0.6% to 5%), and squamous cell (0.1% to 0.5%). According to the CAP 2010 endometrial carcinoma protocol, the term “mixed carcinoma” should only be used when two or more distinctive
subtypes of endometrial carcinoma are identified, each representing more than 10% of the tumor. A mixed cell carcinoma may be coded as 8323 in ICD-O. Some non-endometrioid endometrial carcinomas behave more aggressively than the endometrioid cancers, and even women with clinical stage I disease often have extrauterine metastasis at the time of surgical evaluation. Therefore, when technically and medically feasible, comprehensive surgical staging is helpful for women with non-endometrioid endometrial cancer histology. Comprehensive surgical staging includes hysterectomy, bilateral salpingo-oophorectomy, pelvic and para-aortic lymphadenectomy, and cytological evaluation of the abdominal cavity.

There are specific pathologic criteria for determining the degree of differentiation, as indicated in the corpus uteri chapter of TNM and the notes for this site-specific factor and are not repeated here. Morules are nodular structures found in endometrial-type glands formed by a peculiar metaplastic non-keratinizing squamoid epithelium. They are associated with both benign and malignant squamous differentiation in endometrial cancers. The term non-morular in the codes below means that the nodular structures are not present.

Assign the code for grade or percentage of non-endometrioid cell type from the pathology report. Do not translate a verbal grade (well, moderately, or poorly differentiated) to code this field.
- 001 Recorded as Grade I or 1; 5% or less of non squamous or non-morular solid growth pattern
- 002 Recorded as Grade II or 2; 6% - 50% of a non-squamous or non-morular solid growth pattern
- 003 Recorded as Grade III or 3; more than 50% of a non-squamous or non-morular solid growth pattern
- 999 No 2, 3 or 4 grade system available; unknown

See schema for additional code choices.

Site-Specific Factor 8 – Omentectomy (Corpus – all histologies)
Source documents: operative report, pathology report

The role of omentectomy (removal of the fatty apron in the front of the abdomen called the omentum) has not been established with certainty for corpus cancers, although it is a standard for ovarian cancer. This site-specific factor captures prospectively whether omentectomy was performed (code 010) or not performed (code 000) during hysterectomy. See schema for other code choices.

Site-Specific Factor 3 – Residual Tumor Status and Size after Cytoreductive Surgery (Ovary and PeritoneumFemaleGen)
Source documents: operative report, pathology report; discharge summary, chemotherapy records (inpatient and outpatient)
Other names: debulking, cytoreduction, residual tumor volume

The amount of ovarian tumor and the location of tumor (see Site-Specific Factor 4) remaining in the patient after initial ovarian or peritoneal cancer surgery are the most important prognostic factors for advanced disease. The intent of cytoreductive or debulking surgery—particularly for Stage III cancer—is to remove as much of the cancer in the pelvis and abdomen as possible so that chemotherapy will be more effective. The less left behind, the more likely the patient will respond well to adjuvant chemotherapy. This site-specific factor captures two pieces of information about residual tumor: residual tumor volume (amount) and whether the patient had chemotherapy. Information about residual tumor volume will be in the operative report; information about postoperative chemotherapy will be elsewhere in the medical record or physician notes. Residual tumor less than or greater than 2 cm differentiates T3b/Stage IIIB and T3c/Stage IIC tumors; this site-specific factor has a cut point of 1 centimeter.
Code the size of the largest residual tumor nodule remaining after the primary cytoreduction surgery from the operative report and if chemotherapy was administered post-operatively, increment the code to include that information.

- **000** None; No gross residual tumor
- **010** Residual tumor 1 centimeter or less
- **020** 010 and received chemotherapy
- **030** Residual tumor greater than 1 centimeter
- **040** 030 and received chemotherapy
- **990** Macroscopic residual tumor, size not stated
- **991** 990 and received chemotherapy
- **998** Patient did not have surgery; No histologic confirmation
- **999** Unknown; Not documented in patient record

**Site-Specific Factor 4 – Tumor Location After Primary Cytoreductive Surgery (Ovary and PeritoneumFemaleGen)**

*Source documents:* operative report, pathology report; discharge summary, chemotherapy records (inpatient and outpatient)

This site-specific factor is the companion to SSF 3 for Ovary and PeritoneumFemaleGen and identifies the organs or structures where the residual tumor was left. As with SSF3, the less residual tumor, the better the patient’s prognosis with postoperative chemotherapy. Two pieces of information are captured about residual tumor: the location of the residual tumor and whether the patient had chemotherapy. Information about the location of residual tumor will be in the operative report; information about postoperative chemotherapy will be elsewhere in the medical record or physician notes.

Record the code for the residual tumor farthest away from the ovary according to the operative report. Higher numbers take priority as they are higher in the peritoneal cavity. A number in a code repeats the description in that code number. For example, code 030 is ovary (code 010) plus fallopian tube and/or uterus (code 020). Then the next code in the list includes all organs mentioned in the previous description and the patient received chemotherapy. Code 180 means that there was residual tumor on the diaphragm and one or more of the previously listed organs. Code 190 means that there was residual tumor on the diaphragm and one or more of the previously listed organs and the patient received postoperative chemotherapy. In a code where multiple organs are described, such as 020 or 050, it is not necessary that all listed organs be involved with residual tumor.

- **010** Ovary
- **020** Fallopian tube; Uterus
- **030** 010 + 020
- **040** 010 + 020 and received chemotherapy
- **050** Pelvic peritoneum; retroperitoneum
- **060** 050 + (010 or 020)
- **070** 060 and received chemotherapy
- **080** Omentum
- **090** 080 + (010 or 020 or 050)
- **100** 090 and received chemotherapy
- **110** Abdominal peritoneum; retroperitoneum
- **120** 110 + (010 or 020 or 050 or 080)
- **130** 120 and received chemotherapy
- **140** Intestines
- **150** 140 + (010 or 020 or 050 or 080 or 110)
Site-Specific Factor 5 – Malignant Ascites (Ovary and PeritoneumFemaleGen)

*Source documents:* operative report, cytology reports (look for multiple reports), pathology report

*Other names:* ascitic fluid drainage, possibly paracentesis (if no surgery)

According to the AJCC, the presence of ascites does not affect staging unless malignant cells are present. Code the amount (how much) of malignant ascites (natural fluid) removed from the patient. Do not code the amount saline solution added and removed as part of a peritoneal washing or peritoneal lavage.

Ascites is usually described in the operative report in milliliters or liters. Record the amount of fluid in milliliters in the range 001-979. Three-quarters of a liter would be recorded as 750. A full liter or more would be coded as 980. If the clinician has estimated the amount of ascites, code that. If the amount is stated as “less than” code the amount; for example, code less than 500 ml as 500. If no malignant ascites are present, use code 000. If the volume is not stated, use code 990. See schema for other code choices.

Site-Specific Factor 2 – Biopsy of Metastatic Site (Fallopian Tube)

Although fallopian tube cancers are staged similar to ovarian cancers, some of the prognostic factors for this rare type of cancer are different. Site-specific factor 2 collects information about sites that were actually biopsied.

Code the organ that was biopsied, whether the result was negative or positive. In the range 100-130, the higher code takes priority.

- **100** Pathologic examination of metastatic tissue performed, NOS – Use this code if the site of biopsy is unknown or not stated.
- **110** Biopsy of the omentum was performed – A positive biopsy would also be coded in CS Extension
- **120** Biopsy of the small intestine was performed – A positive biopsy would also be coded in CS Extension
- **130** Biopsy of the liver parenchymal was performed – A positive biopsy would also be coded in Mets at Dx.
- **200** No pathologic examination of metastatic tissue performed – Use this code when no biopsy is performed.

See schema for additional code choices.

Site-Specific Factor 3 – Primary Tumor Location (Fallopian Tube)

*Source documents:* operative report, pathology report

Cancers that arise at the fimbrial end of the fallopian tube are believed to have a worse prognosis than other locations in the fallopian tube because the tumor cells are exposed directly to the peritoneal cavity even though they do not invade the tubal wall. The location of the tumor within the fallopian tube is collected prospectively to help researchers study this issue. The 10 centimeter long fallopian tube is
divided into five segments based on their anatomic location relative to the ovary and uterus (and some difference in physiology and functions). Figure I-2-11 shows the various segments of the fallopian tube. All segments are coded to primary site C57.0.

Code the location of the primary tumor within the fallopian tube if stated in the medical record. The segments and their site-specific factor codes are:

100 Fimbrial segment – “fingers” at lateral end of tube facing the ovary
110 Interstitial segment – passes through the uterine muscle into the uterine cavity
120 Isthmic segment – narrow muscular segment near the uterus
130 Ampullary segment – wide middle segment
140 Infundibular segment – funnel shaped segment inside the fimbria
200 Tumor in tubal location other than the fimbrial segment, NOS

See schema for additional code choices.

Site-Specific Factor 1 – Prognostic Scoring Index (Placenta)

The Prognostic Index is a non-anatomic risk factor scoring system that adds a fourth dimension to the stage grouping of gestational trophoblastic tumors (GTT) of the placenta. The score subcategorizes GTTs into low risk or high risk based on a point system. The eight risk factors and their point scores are shown in Table I-2-12, which lays out in table format the wording in the note for this site-specific factor.

Record the total point value for the Prognostic Index as stated by the clinician and code 010 if the point value is between 1 and 7 or code 110 if the point value is 8 or more. If there is no statement of point value, look for a statement of low risk (code 010) or high risk (code 110), or a statement of Substage A (code 050) or Substage B (code 150). If none of these clinician statements is available, the registrar may attempt to determine the point value and risk. If any one of the factors is unknown, stop trying to assign score, unless the risk category—low or high—has already been determined with the known factors. Use code 999 if risk factors are not assessed.

<table>
<thead>
<tr>
<th>RISK FACTOR</th>
<th>SCORE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>&lt;40</td>
</tr>
<tr>
<td>Antecedent pregnancy</td>
<td>Hydatidiform mole</td>
</tr>
<tr>
<td>Months from index pregnancy</td>
<td>&lt;4</td>
</tr>
<tr>
<td>Pretreatment HCG (IU/ml)</td>
<td>&lt;1,000</td>
</tr>
<tr>
<td>Largest tumor size incl. uterus</td>
<td>&lt;3 cm</td>
</tr>
<tr>
<td>Sites of mets</td>
<td>Lung only</td>
</tr>
<tr>
<td>Number of mets</td>
<td>0</td>
</tr>
<tr>
<td>Previous failed chemotherapy</td>
<td>Single drug</td>
</tr>
</tbody>
</table>

Table I-2-12. Prognostic Scoring Index
SCHEMA DISCRIMINATOR  (PeritoneumFemaleGen, Site-Specific Factor 25)

Source documents: face sheet, other statement of patient gender in medical record

Both sarcomas and carcinomas of the peritoneum can be staged. For Peritoneum and PeritoneumFemaleGen, a schema discriminator is necessary to identify the gender of the patient so that the correct schema can be presented to the abstractor. Carcinomas in the morphology code range 8000-8576, specialized gonadal neoplasms, and mixed complex and stromal neoplasms (except gastrointestinal stromal tumors) are coded with the same staging criteria for female patients as ovarian cancer in the PeritoneumFemaleGen schema.

In this field, code 002, Female, presents the PeritoneumFemaleGen schema to the abstractor. All other categories of gender (codes 001, 003, 004, 009 and 100) present the Peritoneum schema to the abstractor. For males, a carcinoma of the peritoneum will output T NA  N NA  M NA  Stage NA.
MALE GENITAL ORGANS
Prostate, Testis, Penis, Scrotum

The schemas for the male genital system have no site-specific factors in common. These sites will be discussed in order of their frequency of occurrence: prostate first, then testis, penis and scrotum.

PROSTATE

In CS version 1, prostate used all six site-specific factors. Of these, three have been made obsolete in CS version 2.

OBSOLETE Site-Specific Factor 4 – Prostate Apex Involvement
Effective with prostate cancer cases diagnosed on or after January 1, 2010, this field will no longer be collected. For 2010 diagnoses and forward, code this field as 988. For cases diagnosed prior to 2010 and coded in CS version 2, this field is to be coded as indicated in the notes before the table if the information is clearly documented in the medical record. The notes and code definitions have been improved in CSv2 and will not be repeated here.

OBSOLETE Site-Specific Factor 5 – Gleason Primary Pattern and Secondary Pattern Value and Site-Specific Factor 6 – Gleason Score
These two site-specific factors have been made obsolete because information on Gleason patterns and score from different procedures is needed for clinical stage group mapping and pathologic stage group mapping in the seventh edition of TNM. The data in this field is retained in the CS data record, but these two factors have been split into clinical information (SSFs 7 and 8) and pathologic information (SSFs 9 and 10)—see below.

Site-Specific Factor 1 – Prostate Specific Antigen (PSA) Lab Value and Site-Specific Factor 2 – Prostate Specific Antigen (PSA) Interpretation

PSA Value
Source documents: clinical laboratory report (blood or serum test), history, clinician note, pathology report
Other names: Prostate specific antigen, serum PSA, total PSA
Normal reference range: varies by age and race of patient. The reference range should be shown on the clinical laboratory report. In general, normal findings are 0 – 4.0 nanograms per milliliter (ng/ml). Optimal normal range is 0 – 2.6 ng/ml. Nanograms per milliliter may be reported as micrograms per liter (μg/L or ug/L). The number to be recorded in SSF1 is the same for both measurements.

Serum PSA is the most sensitive tumor marker for monitoring individuals with prostate cancer, including progression of disease and response to therapy. Although originally not intended to be a screening test, this relatively simple blood test has become a very common method of detecting new prostate cancer in its earliest stages. PSA can be totally negative when prostate cancer is found on digital rectal exam. In such cases, PSA will not be helpful in monitoring for recurrence. Serum PSA is not the same as free PSA or precursor PSA—do not record values from either of these tests in this field.

Record the highest PSA value prior to, and closest to, the initiation of treatment. This site-specific factor is a 3 digit field with an implied decimal point between the second and third digits.

Examples 12.4 – code as 124
4.2 – code as 042
94 – code as 940

If the actual value of the test exceeds 98.0, record as 980. Results for SSF1 and SSF2 should be from the same test.

Note: If more than one PSA is given in the three months prior to treatment, record the highest value even if it is not the closest to initiation of treatment. For example, a PSA on January 5, 2010 is 5.8. PSA on January 29, 2010 is 5.2. Biopsy February 22, 2010 is positive for adenocarcinoma. Code the highest PSA (from January 5) as 058.

PSA Interpretation  See also information for PSA above.
Source documents: history, clinician notes, consultation notes, other statements in medical record

Because the PSA value varies by the patient’s age, race, and other factors, as well as the test method, interpretation of the value is a clinical judgment on the part of the physician. If there is no interpretation of the PSA value in the record, use code 999. Do not infer a code for this field based on the normal values listed for PSA Value.

Record the clinician’s interpretation of the PSA value documented in SSF1.
  010 Positive/elevated
  020 Negative/normal
  030 Borderline; undetermined whether positive or negative
  See schema for other code choices.

Site-Specific Factor 3 – CS Extension-Pathologic
Source documents: pathology report

This site-specific factor records information about primary tumor extension based on the prostatectomy or autopsy specimen only. Information from core needle biopsies is coded in site-specific factor 14. Codes used in CS version 1 in the range 020 to 099 have been converted to three digits in CS version 2 to be more comparable with CS Extension-Clinical. The definitions for the same code may not be the same between CS Extension-Clinical and SSF3 CS Extension-Pathologic. New codes have been added as a result of revisions in AJCC seventh edition. There are also codes and descriptions in SSF3 that can only be determined microscopically from the prostate specimen. Read the code definitions carefully. Do not rely on memory from CS version 1 or codes from CS Extension-Pathologic to code SSF3.

Site-Specific Factor 7 – Gleason’s Primary Pattern and Secondary Pattern Value from Core Needle Biopsy/TURP
Site-Specific Factor 8 – Gleason’s Score from Core Needle Biopsy/TURP
Source documents: pathology reports from needle biopsies or transurethral resection of prostate

The Gleason system for grading prostate cancer is the one recommended by the AJCC and College of American Pathologists. Site-specific factors 7 and 8 code information on Gleason pattern and score from core needle biopsy or transurethral resection of the prostate (TURP) only. This information is used for clinical stage grouping in AJCC seventh edition and in predictive nomograms, such as the Kattan nomograms and the Partin tables, which guide individual treatment decisions. (Information on Gleason pattern and score from prostatectomy or autopsy is collected in SSFs 9 and 10—see below.) The pathologist determines the Gleason patterns and score by looking at prostate tissue under the microscope. He assigns a grade to the most predominant pattern (largest surface area of involvement—more than 50% of the tissue) and a grade for the secondary pattern (second most predominant) based on published
Gleason criteria. Gleason grades range from 1 (small, uniform glands) to 5 (lack of glands, sheets of cells). The cancer protocol for prostate published by the College of American Pathologists (CAP checklist or synoptic report) provides specific instructions to the pathologist for describing patterns and score from diagnostic procedures and prostatectomy specimens.

**Gleason Patterns**

Code the Gleason primary and secondary pattern values in SSF7. There is a long list of codes and definitions in the table, but it may be easier to assign a value if you understand the structure of the code. This is a three digit field. The first digit is always a 0. The second digit is the Gleason primary pattern value. The third digit is the Gleason secondary pattern value.

**Examples**

- Gleason 3 + 3 Code SSF7 as 033
- Gl 4 + 3 Code SSF7 as 043
- Gleason 4 Code SSF7 as 049 (assume a number in the range 2 to 5 is a primary pattern and code 9 unknown in third digit)
- Gleason 7 Code SSF7 as 099 (assume a number in the range 6 to 10 is a score and code SSF7 patterns as unknown)
- Gleason 10/10 Code SSF7 as 055 (only combination of values that equals 10)
- No needle biopsy or TURP performed: code as 998.
- No Gleason information on needle biopsy or TURP: code as 999.

**Note:** If there are multiple needle core biopsies or if both needle core biopsy and TURP are performed, code the specimen with the highest score or most aggressive pattern.

**Gleason Score**

The Gleason score is the sum of the values for the primary and secondary patterns coded in SSF7. The score ranges from 2 (1 + 1) to 10 (5 + 5). The SSF8 code is three digits, with the Gleason score in the right-most digit(s) and leading zeros.

**Examples**

- Gleason 3 + 3 – code SSF8 as 006
- Gl 4 + 3 – code SSF8 as 007
- Gleason 4 – code SSF8 as 004 (assume a number in the range 2 to 5 is a primary pattern and that as the score)
- Gleason 7 – code SSF8 as 007
- Gleason 10/10 – code SSF7 as 0510
- No needle biopsy or TURP performed – code as 998.
- No Gleason information on needle biopsy or TURP – code as 999.

**Site-Specific Factor 9 – Gleason’s Primary Pattern and Secondary Pattern Value from Prostatectomy/Autopsy**

**Site-Specific Factor 10 – Gleason’s Score from Prostatectomy/Autopsy**

**Source documents:** pathology report from prostatectomy or autopsy report

These two site-specific factors code information on Gleason pattern and score from prostatectomy or autopsy only. This information is used for pathologic stage grouping in AJCC seventh edition. (Information on Gleason pattern and score from core needle biopsy or TURP is collected in SSFs 7 and 8—see above.) The pathologist’s process for determining the Gleason primary and secondary patterns and Gleason score and examples of the codes are described in SSFs 7 and 8. The same format is used for prostatectomy or autopsy information.

**Examples**

- No prostatectomy performed – code as 998 in SSFs 9 and 10.
- Diagnosed at autopsy but no Gleason information – code as 999 in SSFs 9 and 10.

**Note:** If a tertiary pattern is documented in the prostatectomy pathology report, do not add it to either
SSF9 or SSF10. Gleason tertiary pattern in coded in SSF11—see below.

Site-Specific Factor 11 – Gleason Tertiary Pattern Value on Prostatectomy/Autopsy

*Source documents:* pathology report from prostatectomy or autopsy report

When a patient undergoes a radical prostatectomy, the pathologist will commonly look for a third or tertiary pattern in the specimen. When Gleason pattern 5 is present as a tertiary pattern, its presence should be recognized in the pathology report, as a high Gleason pattern appears to be an indicator for worse outcome. Studies indicate that a Gleason score 7, with tertiary pattern 5, is associated with a worse prognosis than without tertiary pattern 5, and is similar to the prognosis for Gleason score 8 – 10. For example, in a specimen where the primary Gleason pattern is 3, the secondary is 4 and there is less than 5% Gleason 5, the report should indicate a Gleason score of 7 (3+4) with tertiary Gleason pattern 5.

Record the tertiary pattern documented on prostatectomy or autopsy only. If a tertiary pattern is documented on needle core biopsy or TURP, it should be ignored. In this three digit field, the tertiary pattern value is coded in the middle digit in the range 010 to 050. If a tertiary pattern is not mentioned use code 999. If no prostatectomy or autopsy is performed, use code 998.

Site-Specific Factor 12 – Number of Cores Positive
Site-Specific Factor 13 – Number of Cores Examined

*Source documents:* pathology reports from core needle biopsies

*Other names for procedure:* needle core biopsy, needle biopsy, core biopsy, prostate biopsy, sextant biopsy, transrectal biopsy, ultrasound-guided biopsy, transperineal prostate biopsy, triggered-needle biopsy. Note: the procedure coded in these SSFs yield tissue for histologic examination, not just cells for cytology.

A diagnostic procedure can take as many as 20 or more core biopsies to determine the extent of the cancer within the prostate. Site-specific factor 12 captures the number of cores that contained cancer, and site-specific factor 13 captures the number of cores that were examined. Together these SSFs can provide researchers with a surrogate estimate of the percentage of the prostate involved by tumor, if that figure is not stated in the pathology report.

Code the exact number of positive core biopsies in SSF12 from information in the pathology report in the range 001 to 024. If 25 or more cores taken, use code 025. If the number of cores positive or cores examined is not documented in the record, code 991. If the percentage of tissue involved with cancer is stated but not the number of cores positive, do not calculate the number of positive cores; code as 991. See schema for additional code choices.

Code the total number of core biopsies microscopically examined by the pathologist in SSF13 from information in the pathology report following the same guidelines as for SSF12.

**Note:** Make no assumptions about the number of cores positive or examined based on the number of areas biopsied within the prostate (laterality, lobes, apex, base, or mid-prostate), because several cores may be taken from each area.

**Note:** If multiple biopsy procedures are performed during the diagnostic workup and within the CS timing rule, code only from the procedure that yielded the highest number of positive cores. Do not add together the cores positive or examined from the separate procedures.

Site-Specific Factor 14 – Core Biopsy Findings
Source documents: pathology report

The AJCC specifically excludes core biopsy findings from altering the clinical T value, which is based only on digital rectal exam and imaging. However, core biopsy findings help determine the extent of tumor and assist in treatment planning. In other words, for a clinically inapparent tumor biopsied as a result of an elevated PSA (cT1c), the finding of cancer in both lobes during core needle biopsy does not upstage the case to cT2c. Site-specific factor 14 documents the location of tumor discovered on core biopsy.

Code the pathologist’s statement of the presence of cancer on core biopsies. If more than one description applies, use the highest code. Note that the codes do not correspond with T values.

- 000 Negative needle core biopsy findings
- 010 Positive needle core biopsy findings in one lobe/side
- 020 Positive needle core biopsy findings in both lobes/sides – stated as bilateral
- 030 Positive needle core biopsy findings, location (lobes/sides) not stated
- 050 Positive needle core biopsy findings beyond prostate – also called extraprostatic extension (EPE) or extracapsular extension; includes involvement of seminal vesicles or periprostatic fat found in core biopsy specimen

See schema for additional code choices.

Site-Specific Factor 15 – Clinical Staging Procedures
Source documents: physical exam, clinician notes, imaging reports including ultrasonography, pathology report, other statements in medical record

This site-specific factor documents the type(s) of clinical staging procedure(s) performed. In particular, researchers need to know whether clinically inapparent tumor detected as a result of elevated PSA (T1c) was based on digital rectal exam (DRE) only or DRE plus imaging. Imaging includes transrectal ultrasound (TRUS) and endorectal coil magnetic resonance imaging (erMRI). Other imaging techniques that may be found in the record in a clinical trial or research setting, but which have not been shown to improve staging accuracy, include Doppler and color Doppler ultrasound, T2-weighted MRI, MR spectroscopic imaging (MRSI), and dynamic contrast-enhanced MRI (DCE-MRI).

Code the procedure(s) documented in the medical record that were used for clinical staging, whether the findings were positive or negative. This applies to all Extension codes, not just code 150 (T1c). Disregard any clinical procedures performed after needle biopsy or prostate surgery.

- 000 No digital rectal exam (DRE) and no imaging performed
- 010 Digital rectal exam (DRE) only, imaging not performed or unknown if performed
- 020 Imaging only, DRE not performed or unknown if performed
- 030 020 + 010: Imaging and digital rectal exam (DRE) performed

See schema for additional code choices.
TESTIS

In CS version 1, testis used five site-specific factors. Of these, three have been made obsolete and replaced by other site-specific factors in CS version 2. The data in the original site-specific factors 1 through 3 will be retained in the CS data record, but these SSFs are not to be used in CS version 2. The reason for the revised SSFs is that AJCC clarified that the tumor marker values should be captured prior to orchiectomy. This was not clear in CS version 1, so the data in SSFs 1 to 3 are a mix of pre- and post-orchiectomy information. In addition to revising the tumor markers into separate data fields for the lab value and the clinician’s interpretation of that lab value, an additional element has been added—persistence of elevated tumor markers—that documents the post-orchiectomy status of the markers for assigning the stage group IS.

The data elements and codes have been modified in CS version 2 to calculate the S value correctly. Any analysis of testis staging over time relying on the tumor marker data collected in CS version 1 might require review of medical records to verify the appropriate preoperative tumor marker values and the presence of persistent tumor markers post-orchiectomy.

**OBSOLETE Site-Specific Factor 1 – Alpha Fetoprotein (AFP)**

*REPLACED BY* Site-Specific Factor 6 – Preorchiectomy Alpha Fetoprotein (AFP) Lab Value and Site-Specific Factor 7 – Preorchiectomy Alpha Fetoprotein (AFP) Interpretation

**OBSOLETE Site-Specific Factor 2 – Human Chorionic Gonadotropin (hCG)**

*REPLACED BY* Site-Specific Factor 8 – Preorchiectomy Human Chorionic Gonadotropin (hCG) Lab Value and Site-Specific Factor 9 – Preorchiectomy Human Chorionic Gonadotropin (hCG) Interpretation

**OBSOLETE Site-Specific Factor 3 – LDH**

*REPLACED BY* Site-Specific Factor 10 – Preorchiectomy LDH Interpretation

**Site-Specific Factor 4 – Radical Orchiectomy Performed**

*Source documents:* operative report, pathology report

*Other names:* transinguinal orchiectomy

This site-specific factor documents whether radical orchiectomy was performed (code 001), not performed (code 000) or unknown (code 999). The information is used to map the T value in AJCC sixth edition.

A radical orchiectomy is defined as complete removal of the testicle, epididymis, and spermatic cord to the level of the internal inguinal ring, either as a diagnostic procedure or as treatment. The spermatic cord is usually excised with the testicle although the cord may not be mentioned in the pathology report. Unless the operative report says that the cord was not removed, assume that the procedure was a radical orchiectomy.
Site-Specific Factor 5 – Size of Metastasis in Lymph Nodes

Source documents: pathology report

In CS version 2, site-specific factor 5 codes incorporate not only size ranges for the metastasis in a lymph node mass, but also the absence or presence of extranodal extension and clinician statements of the N category. CS version 1 codes 001 to 003 have been made obsolete and the data converted to codes in the 010 to 030 range. The AJCC definitions for the N category describe “metastasis with a lymph node mass” of a stated size, rather than the size of the metastasis in the lymph node. Extranodal extension is defined as metastatic tumor growing from within the lymph node outward through the lymph node capsule and into surrounding connective tissues.

- Use code 010 when
  - the lymph node mass containing metastasis is up to 2 cm in size and there is no pathologic evidence of extranodal extension
  - the clinician stages the case as N1 without any further information about lymph nodes
- Use code 020 when
  - the lymph node mass containing metastasis is between 2 and 5 cm in size
  - there is a statement of extranodal extension regardless of the size of the lymph node mass
  - the clinician stages the case as N2 without any further information about lymph nodes
- Use code 030 when
  - the lymph node mass containing metastasis is more than 5 cm in size
  - the clinician stages the case as N3 without any further information about lymph nodes
- See schema for additional code choices.

Serum Tumor Markers for Testis

Tumor markers for testicular cancer serve several purposes: pre-orchiectomy to help determine the histologic cell type, post-orchiectomy to assist in treatment management for patients with germ cell tumors, and to provide an extra prognostic dimension (S) to AJCC stage grouping. For the pathologist, elevated levels of the markers alpha fetoprotein (AFP) or beta subunit of human chorionic gonadotropin (beta-hCG) may indicate the need for additional microscopic analysis of resected tissue. The serum lactate dehydrogenase (LDH) helps the clinician assess the patient’s metastatic tumor burden. APF, hCG, and LDH information is combined into the S (serum tumor marker) category in the TNM system, although each may be given an individual S value. The value used for stage group IS is calculated on the serum marker values measured post-orchiectomy (this is a change in AJCC seventh edition). In CS version 2, the computer algorithm compares the values coded in SSFs 7, 9 and 10 to derive an S value. To manually calculate the S category for other stage groups, lab values for the three markers must be within the ranges below.

- S0 All three markers are within normal limits
- S1 All three markers are done and all three are no more than minimally elevated
  - AFP <1000 ng/ml AND hCG <5,000 mIU/ml AND LDH <1.5 times N* or unknown
- S2 ANY marker is moderately elevated (not all three have to be done)
  - AFP 1000-10,000 ng/ml OR hCG 5,000-50,000 mIU/ml OR LDH 1.5-10 times N*
- S3 ANY marker is highly elevated (not all three have to be done)
  - AFP > 10,000 ng/ml OR hCG >50,000 mIU/ml OR LDH >10 times N*

* N = upper limit of normal

Note: According to AJCC, the S category can be determined for both AJCC sixth and seventh editions even if the LDH value is unknown.
Site-Specific Factor 7 – Preorchiectomy Alpha Fetoprotein (AFP) Interpretation

**Source documents:** clinical laboratory report (blood serum radioimmunoassay or enzyme assay (EIA)); sometimes in history and physical or clinical statement in pathology report

**Other names:** αFP, αFP, Alpha Fetoprotein, α-fetoprotein, α-fetoprotein; fetal alpha globulin

**Normal Reference Range** Adult men and non-pregnant women: 0-15 ng/ml (SI: 0-15 μg/L)

Alpha-fetoprotein (AFP) is a protein normally made by immature liver cells in the fetus. In adults, high AFP levels (> 500 ng/ml) in the blood occur only in hepatocellular carcinoma (>1000), liver metastases (from a primary elsewhere), and germ cell tumors of the testes and ovaries. Elevated AFP values are found in non-seminomatous malignancies and mixed tumors of the testis. AFP is used with HCG (SSFs 8 and 9) to identify the specific cell type of testicular cancer. AFP is not secreted by pure seminoma or teratoma. If AFP > 500 ng/ml, the underlying condition is unlikely to be benign. If AFP > 10,000 ng/ml at diagnosis, the patient is likely to have a poor prognosis. AFP is more useful in monitoring response to therapy than making a diagnosis. After orchiectomy, the AFP should fall to < 25 ng/ml in 25-35 days. If elevated AFP persists, this is an indication of residual tumor. Code persistence of elevated tumor markers in site-specific factor 11.

**AFP Lab Value**

Code the range that includes the highest AFP value prior to orchiectomy (this is a change from CS version 1). The lab value (SSF6) and interpretation (SSF7) should be from the same test. Read the descriptions carefully, as the ranges change substantially in the upper categories.

**Examples**
- AFP 35 ng/ml – code as 003 (30-39 ng/ml)
- AFP 270 ng/L – code as 030 (200-299 ng/ml; ng/ml = ug/L)
- AFP 5500 ng/ml – code as 150 (5000-5999 ng/ml)
- AFP 12,500 – code as 200 (> 10,000 ng/ml)
- AFP not done – code as 998

See schema for additional code choices.

**AFP Interpretation**

The AFP Interpretation is actually a category used to map the S (serum tumor marker) element for stage grouping testicular cancer in the TNM system.

Record the range of the highest value before orchiectomy (this is a change from CS version 1), based on the reference range used by the lab. The lab value (SSF6) and interpretation (SSF7) should be from the same test. If the clinician states an S value rather than an AFP test value, use the appropriate code.

000  Within normal limits (S0) – SSF6 code 000 or 001
010  Range 1: above normal but less than 1000 ng/ml (S1) – SSF6 codes 002 to 090
020  Range 2: 1000 – 10,000 ng/ml (S2) – SSF6 codes 100 to 190
030  Range 3: > 10,000 ng/ml (S3) – SSF6 code 200

See schema for additional code choices.

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Site-Specific Factor 8 – Preorchiectomy Human Chorionic Gonadotropin (hCG) Lab Value

Site-Specific Factor 9 – Preorchiectomy Human Chorionic Gonadotropin (hCG) Interpretation

**Source documents:** clinical laboratory report (blood or serum test), sometimes in history and physical or clinical statement in pathology report

**Other names:** Human chorionic gonadotropin, b-hCG, beta subunit HCG, beta hCG, β-hCG

**Normal reference range**
- < 2 ng/ml (SI: < 2 μg/L or < 2 ug/L) 1 ng/ml of HCG is approximately 5 mIU/ml.
- < 5 mIU/mL (< 5 IU/L) To record mIU/mL in ng/ml, divide the test result by 5.
Human chorionic gonadotropin is a hormone produced by the placenta and some germ cell tumors. Two subunits, alpha and beta, can be measured in blood or serum. The alpha subunit is a non-specific marker for pancreatic and pituitary tumors. Beta-hCG levels are never found in normal healthy men. When the presence of beta-hCG is detected in serum, it always indicates a malignancy. Beta-hCG is secreted by some non-seminomatous germ cell tumors and mixed tumors and is used with AFP to identify the specific cell type of testicular cancer. Beta-hCG is also useful in monitoring response to therapy. After orchiectomy, the hCG should be undetectable within 5 to 8 days. If elevated hCG persists, this is an indication of residual tumor. Code persistence of elevated tumor markers in site-specific factor 11.

**hCG Lab Value**

**Code** the range that includes the highest hCG value prior to orchiectomy (this is a change from CS version 1). The lab value (SSF8) and interpretation (SSF9) should be from the same test. Read the descriptions carefully, as the ranges change substantially in the upper categories. The code ranges are the same as for AFP up to code 190, but this site-specific factor includes higher ranges as well.

**Examples**
- hCG 47 ng/ml – code as 004 (40-49 ng/ml)
- hCG 520 ug/L – code as 050 (500-599 ng/ml; ng/ml = ug/L)
- hCG 5500 mIU/mL – code as 100 (1000-1999 ng/ml; 5500 mIU/mL = 1100 ng/ml)
- hCG 22,500 – code as 220 (20,000-29,999 ng/ml)
- hCG 60,000 ng/ml – code as 250 (> 50,000 ng/ml)
- hCG not done – code as 998

See schema for additional code choices.

**hCG Interpretation**

The hCG Interpretation is actually a category used to map the S (serum tumor marker) element for stage grouping testicular cancer in the TNM system.

Record the range of the highest value before orchiectomy (this is a change from CS version 1), based on the reference range used by the lab. The lab value (SSF8) and interpretation (SSF9) should be from the same test. If the clinician states an S value rather than an hCG test value, use the appropriate code.

000 Within normal limits (S0) – SSF8 code 000
010 Range 1: above normal but less than 5000 mIU/ml (S1) – SSF8 codes 001 to 140
020 Range 2: 5000 – 50,000 mIU/ml (S2) – SSF8 codes 150 to 240
030 Range 3: > 50,000 mIU/ml (S3) – SSF8 code 250

See schema for additional code choices.

**Site-Specific Factor 10 – Preorchiectomy LDH Interpretation**

See [LDH Lab Value](#), [LDH Interpretation](#), and [LDH Upper Limit of Normal in Tumor Markers Section](#). For testis, only the LDH Interpretation is coded. The test that is coded must be done prior to orchiectomy. LDH is non-specific for testicular cancer. Although part of the criteria for the S category in the TNM system, LDH is not routinely performed unless the patient has evidence of bulky or distant disease.

**Site-Specific Factor 11 – Persistent Elevation of Tumor Markers**

The testicular cancer tumor markers alpha fetoprotein (AFP), beta subunit of human chorionic gonadotropin (beta hCG), and lactate dehydrogenase (LDH) are measured prior to orchiectomy to assign the S category for TNM stage grouping. Stage group IS (Stage I with elevated serum markers, not “in situ”) must be determined by the clinician after orchiectomy, when the AFP and hCG markers should return to normal levels if the tumor has been completely removed. This requires serial tumor markers that
are usually done in an outpatient or medical office setting. Persistence of elevated tumor markers implies residual disease that needs additional treatment.

Code a statement by the clinician of whether elevated tumor markers persist after orchiectomy. If there is no physician statement, code as 999; do not code from lab results. The only exception is if the serum tumor markers were normal prior to orchiectomy; if so, code as 000.

- Use code 000 when
  - tumor markers returned to normal after orchiectomy
  - tumor markers were normal prior to orchiectomy
  - there is no persistence of elevated tumor markers
- Use code 010 when
  - there is a physician statement that tumor markers are still elevated
  - there is a physician statement of Stage IS
- See schema for additional code choices.

**PENIS**

**Site-Specific Factor 10 – Involvement of Corpus Spongiosum/Corpus Cavernosum**

*Source documents:* pathology report

*Other names:* Corpus cavernosum: corpora cavernosa (plural form); corpus cavernosum penis; Corpus spongiosum: corpus cavernosum urethrae; corpus spongiosum penis

Most tumors of the penis begin on the outer surface. Tumor involving the subepithelial connective tissue is T1. As tumor invades more deeply it may involve the major internal structures of the penis, which are the median corpus spongiosum surrounding the urethra and the two lateral corpora cavernosa (Figure I-2-12). T2 in the TNM system, CS Extension, and ICD-O topography codes do not distinguish between the corpus cavernosum and the corpus spongiosum, but involvement of these structures has prognostic implications because of the increased likelihood of nodal and distant metastases when there is invasion of the cavernosum or spongiosum. This site-specific factor allows researchers to do more detailed analysis in the future.

Code the pathologist’s statement of involvement of the corpus spongiosum or corpus cavernosum as documented in the pathology report.

- Use code 000 when there is
  - a statement in the pathology report that there is no involvement of the corpus spongiosum or corpus cavernosum
  - surgical resection of the penis and the pathology report is reviewed but does not mention corpus spongiosum/cavernosum involvement
- Use code 010 when only the corpus spongiosum (corpus cavernosum urethrae) is involved
- Use code 020 when only the corpus cavernosum is involved (or both corpora cavernosa)
- Use code 030 when both the corpus spongiosum and one or both corpora cavernosa are involved
- Use code 998 when
  - the surgical resection of the penis does not include the corpus spongiosum/cavernosum
  - there is no surgical resection of the penis
- See schema for other code choices.
Site-Specific Factor 11 – Percent Poorly-Differentiated Tumor

*Source documents:* pathology report

Penile cancer may be graded on a three-grade or four-grade system. (This information is coded in the fields Grade Path Value and Grade Path System.) The proportion of poorly differentiated tumor in the specimen is of prognostic importance. Deeper tumors tend to be more poorly differentiated. The presence of poorly differentiated cancer in more than 50% of the penectomy specimen is an independent predictor of lymph node metastases. The pathologist should report the percentage of poorly differentiated tumor, even if the majority of the tumor is well or moderately differentiated.

Code the pathologist’s statement of the percentage of poorly differentiated tumor in the specimen in the code range 001 (1%) to 100 (100%). Use code 000 if there is a statement that poorly differentiated tumor is not present or that no poorly differentiated tumor is identified. If the pathology report mentions poorly differentiated tumor but does not give a percentage, use code 990. See schema for additional code choices.

Site-Specific Factor 12 – HPV (Human Papilloma Virus) Status

See HPV Status in Tumor Markers.

Site-Specific Factor 16 – Size of Metastasis in Lymph Nodes

See Size of Metastasis in Lymph Nodes under BLADDER below.

*Note:* the code scale for this factor for carcinoma of the penis is different from the code scale for Merkel cell carcinoma of penis.

Site-Specific Factor 17 – Extranodal Extension of Regional Lymph Nodes

See Extranodal Extension of Regional Lymph Nodes under BLADDER below.

SCROTUM

The site-specific factors for scrotum are the same as those for non-melanoma skin other than Merkel cell.

Site-Specific Factor 1 – Measured Thickness/Depth

See Measured Thickness/Depth in the SKIN section.

Site-Specific Factor 10 – Clark’s Level

See Clark’s Level in the SKIN section.

Site-Specific Factor 11 – Perineural Invasion

See Perineural Invasion in the SKIN section.

Site-Specific Factor 12 – High Risk Features

See High Risk Features in the SKIN section.
Site-Specific Factor 16 – Size of Lymph Nodes
See Size of Lymph Nodes in the SKIN section.
URINARY TRACT

Kidney Parenchyma, Kidney Renal Pelvis [includes Ureter], Bladder, Urethra

The kidney (renal parenchyma) as a glandular, filtering organ has different site-specific factors than the lower urinary organs, which are more for collecting and storing urine.

KIDNEY

The kidney parenchyma is the area of the urinary tract that filters the blood to form urine that is collected, stored, and excreted by the lower urinary tract. Nearly all primary tumors of the kidney are glandular in origin—adenocarcinomas and particularly renal cell carcinomas.

Site-Specific Factor 1 – Invasion Beyond Capsule

Source documents: pathology report, imaging reports, surgery observation, other statements in medical record

The kidney is surrounded by a capsule, and the T element in the TNM system categorizes all extension beyond the renal capsule into T3 and T4. Perirenal fat involvement is an adverse prognostic indicator. This site-specific factor allows more specificity in the direction of tumor extension by listing specific structures outside the kidney, as outcomes may be different depending on the location of involved extracapsular structures.

Definitions for SSF1 Codes (See Figure I-2-13.)

- Lateral invasion – tumor extension toward the sides of the body, away from the renal pelvis and major blood vessels
- Medial invasion – tumor extension toward the center of the body
- Perinephric fat – the layer of fat (adipose tissue) outside the renal capsule but inside Gerota’s fascia
- Perisinus fat – the layer of fat adjacent to the renal sinus and medial to the kidney
- Renal sinus – the elongated oval indentation in the renal parenchyma occupied by the renal pelvis, renal calyces, blood vessels, nerves and fat

Code the description of tumor spread (invasion beyond capsule) as documented in the medical record. If a nephrectomy or partial nephrectomy is performed and the pathology report is available for review but there is no mention of invasion beyond the capsule, use code 000.

- 000 Invasion beyond capsule not present/not identified
- 010 Lateral invasion; Perinephric fat
- 020 Medial invasion; Renal sinus; Perisinus fat
- 030 020 + 010; Medial invasion plus lateral invasion; Renal sinus/perisinus fat invasion plus perinephric fat invasion

See schema for additional code choices

Figure I-2-13. Structures Adjacent to Kidney

Site-Specific Factor 2 – Vein Involvement

Involvement of veins from a renal cancer has prognostic implications because tumor cells can more easily disseminate through the bloodstream. This site-specific factor records information about the presence and level of involvement of specific major blood vessels included in the T3 category of TNM. Do not code microscopically identified involvement of small unnamed blood vessels within the kidney; this information is coded in the field Lymph-Vascular Invasion. The tumor may be described as a thrombus, a cluster of tumor cells present in the center of the vein but not attached to the wall of the vein. Direct tumor invasion of the wall of the inferior vena cava is not coded in this field but is Extension code 620 and T3c.

Record the code that best describes involvement of the renal vein and/or inferior vena cava (IVC) as described in the pathology report. If a nephrectomy or partial nephrectomy is performed and the pathology report is available for review but there is no mention of venous involvement, use code 000.

- 000 Vein involvement not present/not identified
- 010 Renal vein only – Extension code 601; T3a
- 020 IVC below the diaphragm only – Extension code 610; T3b
- 030 IVC above the diaphragm only – Extension code 620; T3c
- 040 IVC NOS only – Extension code 625; T3 (NOS)
- 050 020 + 010; IVC below the diaphragm plus renal vein – maps to T3b
- 060 030 + 010; IVC above the diaphragm plus renal vein – maps to T3c
- 070 040 + 010; IVC, NOS plus renal vein – maps to T3 NOS
- 080 030 + 020; IVC above the diaphragm plus IVC below the diaphragm – maps to T3c
- 090 030 + 020 + 010; IVC above the diaphragm plus IVC below the diaphragm plus renal vein – maps to T3c
- 998 No surgical resection of primary site

See schema for additional code choices.

Site-Specific Factor 3 – Ipsilateral Adrenal Gland Involvement

Source documents: pathology report

Other terms: suprarenal gland; same side (ipsilateral)

The adrenal gland is contained within Gerota’s fascia and is contiguous with the kidney, but it has its own lymphatic and vascular drainage systems. Involvement of the ipsilateral (same side) adrenal gland by kidney tumor—an adverse prognostic indicator—may be by direct extension (contiguous) or hematogenous (through the bloodstream; noncontiguous). Contiguous tumor spread is coded in CS Extension codes 630 to 645, all of which map to T4 in the AJCC seventh edition. Noncontiguous involvement is coded in CS Mets at Dx code 40. This site-specific factor gives researchers a complete picture specifically of adrenal gland involvement.

Code the description of ipsilateral adrenal gland involvement as stated in the pathology report.

- 000 Ipsilateral adrenal gland involvement not present/not identified
- 010 Contiguous involvement of ipsilateral adrenal gland – maps to T4 and Stage Group IV
- 020 Noncontiguous involvement of ipsilateral adrenal gland – maps to M1 and Stage Group IV
- 030 020 + 010; Noncontiguous plus contiguous involvement of ipsilateral adrenal gland – maps to T4, M1, Stage Group IV
- 040 Involvement of ipsilateral adrenal gland, not stated whether contiguous or noncontiguous – maps to Stage Group IV

See schema for additional code choices.
Site-Specific Factor 4 – Sarcomatoid Features

Source documents: pathology report
Other names: spindle cell features

The presence of sarcomatoid or spindle cell features in a kidney tumor is a strong adverse prognostic factor. There is a specific ICD-O morphology code for renal cell carcinoma, sarcomatoid or spindle cell (8318/3), but this site-specific factor documents any sarcomatoid or spindle cell features in any renal cell cancer. This site-specific factor applies to carcinomas only; rare sarcomas of the kidney should not be coded in this field.

Code the absence or presence of sarcomatoid features documented anywhere in the pathology report.
- Use code 000 when
  - there is a statement in the pathology report that sarcomatoid features are not present or not identified
  - a nephrectomy or partial nephrectomy is performed and the pathology report is available for review but there is no mention of sarcomatoid features
- Use code 010 when there is a statement in the pathology report that sarcomatoid features are present or are identified in the specimen.
- See schema for additional code choices.

Site-Specific Factor 5 – Histologic Tumor Necrosis

Source documents: pathology report

Necrosis in a tumor specimen is an indication that the malignancy is aggressive and has outgrown its blood supply. The presence of tumor necrosis is an adverse prognostic indicator for renal cell carcinomas.

Code the absence or presence of tumor necrosis documented anywhere in the pathology report.
- Use code 000 when
  - there is a statement in the pathology report that tumor necrosis is not present or not identified
  - a nephrectomy or partial nephrectomy is performed and the pathology report is available for review but there is no mention of tumor necrosis
- Use code 010 when there is a statement in the pathology report that tumor necrosis is present or is identified in the specimen.
- See schema for additional code choices.

Site-Specific Factor 6 – Fuhrman Nuclear Grade

Source documents: pathology report

Nuclear grade of the tumor is the most important prognostic factor after size of the primary tumor and overall anatomic stage. The Fuhrman grade originally published in 1992 is unique to renal cell carcinomas. It is a nuclear, not histologic, grade and is based on nuclear size and shape and the prominence of nucleoli in the tumor cells. The criteria for grades 1 to 4 are described in the kidney cancer protocol of the College of American Pathologists (CAP checklist).

Code the Fuhrman nuclear grade as stated in the pathology report in the range 010 (Fuhrman grade 1) to 040 (Fuhrman grade 4). This site-specific factor applies to renal cell carcinomas only. If another histologic type is diagnosed, code this field as 987. If the Fuhrman grade is not mentioned, use code 999.
If there was no histologic examination of the kidney tumor, use code 998. See schema for additional code choices.

Note: The Fuhrman nuclear grade can be converted into the ICD-O grade/differentiation (6th digit) code. Refer to FORDS 2010 for the conversion table. Do not use the Fuhrman nuclear grade to code the fields Grade Path System and Grade Path Value.

Site-Specific Factor 7 – Size of Metastasis in Lymph Nodes
See Size of Metastasis in Lymph Nodes under BLADDER below.

Site-Specific Factor 8 – Extranodal Extension of Regional Lymph Nodes
See Extranodal Extension of Regional Lymph Nodes under BLADDER below.

Site-Specific Factor 1 (Bladder, KidneyRenalPelvis, Urethra) – WHO/ISUP Grade
Source documents: pathology report
Other names: World Health Organization (WHO) Consensus grade, International Society of Urologic Pathology (ISUP) grade; urothelial carcinoma was formerly called transitional cell carcinoma

Histologic grade of tumor is an important independent prognostic factor for cancers of the lower urinary tract. In 2004, the World Health Organization (WHO) adopted the terminology and recommended grading system of the International Society of Urologic Pathology (ISUP) for urothelial carcinomas of the renal pelvis, ureter, bladder, and urethra, thereby standardizing a number of highly variable grading systems into a consensus classification. There are some differences between the WHO/ISUP system and previous systems, particularly in the number of grade categories. The 2004 consensus allows only “low grade” and “high grade” as categories for urothelial carcinomas. For flat urothelial lesions, this terminology distinguishes dysplasia (low grade intraurothelial neoplasia), which is not reportable to population-based cancer registries, from urothelial carcinoma in situ (formerly called transitional cell carcinoma in situ), which is reportable. For papillary lesions, both low grade and high grade papillary urothelial carcinoma are reportable.

Code the WHO/ISUP tumor grade as stated in the pathology report. This site-specific factor applies to urothelial (transitional cell) carcinomas only. If the diagnosis uses the term “low grade” or “high grade,” assume it is a WHO/ISUP grade and code appropriately. Use code 987 if the cell type is not urothelial (transitional cell) carcinoma. Use code 999 if the grade system uses numeric grades (grade ii, grade III, and so forth) or words (well, moderately, poorly differentiated).

010 Low grade urothelial carcinoma
020 High grade urothelial carcinoma
987 Not applicable; morphology is not urothelial (with or without a stated grade)
998 No histologic examination of primary site
999 Unknown WHO/ISUP grade; Not documented in patient record
See schema for additional code choices.

Note: The WHO/ISUP grade can be converted into the ICD-O grade/differentiation (6th digit) code. Refer to FORDS 2010 for the conversion table. This two-grade system can also be used to code the fields Grade Path System and Grade Path Value.

BLADDER

Version date: 25 January 2010
Site-Specific Factor 2 – Size of Metastasis in Lymph Nodes

**Source documents:** pathology report

In AJCC sixth and seventh editions, the N category describes the number and location of involved lymph nodes. This site-specific factor adds prognostic information by coding the size of the metastasis within the lymph node.

Code the size in whole millimeters of the largest metastasis in regional lymph nodes as stated in the pathology report. To convert metastasis sizes reported in centimeters to millimeters, multiply by 10. Round up to 1 (code 001) a metastasis reported as less than 1 mm in size. Do not code the size of the entire lymph node; use code 999 if the only stated size is for the entire lymph node. Do not code information about distant lymph nodes in this field. If size of metastasis is not stated, use code 999.

**Examples**
- Tumor nest 0.20 mm in size – code as 001 (round up to 1 mm)
- 1 mm solitary metastasis – code as 001
- Macrometastasis 0.5 cm (5 mm) – code as 005
- Metastasis 2.3 cm in node – code as 023
- Lymph node metastasis < 2 cm – code as 992
- Positive inguinal lymph node – code as 990

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>000</td>
<td>No regional lymph node involvement</td>
</tr>
<tr>
<td>001-979</td>
<td>1 - 979 millimeters</td>
</tr>
<tr>
<td>980</td>
<td>980 millimeters or larger (98 cm)</td>
</tr>
<tr>
<td>990</td>
<td>Microscopic focus or foci only, no size stated</td>
</tr>
</tbody>
</table>

See schema for additional code choices.

Site-Specific Factor 3 – Extranodal Extension of Regional Lymph Nodes

**Source documents:** pathology report, imaging reports, physical exam

**Other names:** ENE, extracapsular extension, ECE

The presence of extranodal extension (ENE) from regional lymph nodes is an important prognostic factor in genitourinary cancers because these patients are rarely cured without some type of systemic chemotherapy or radiation. Extranodal extension is defined as metastatic tumor growing from within the lymph node outward through the lymph node capsule and into surrounding connective tissues. ENE can be detected clinically, on gross examination of dissected lymph nodes, or microscopically.

Code clinical or pathologic statements regarding extranodal extension in involved regional lymph node(s). Pathologic findings indicating absence or presence of ENE take priority over clinical statements. Do not code extranodal extension found in distant lymph nodes.

- Use code 000 when no nodes are involved.
- Use code 010 when
  - there is a statement that ENE is not present
  - there is a documentation on imaging or pathology that the nodes are involved but there is no mention of ENE; in other words, there is no ENE documented on available reports
  - the involved lymph nodes are described clinically as mobile
- Use code 020 when
  - there is a clinical or pathologic statement of ENE
  - the involved lymph nodes are described clinically as fixed or matted
- Use code 030 when
  - there is a reference to involved nodes in the medical record, such as in the patient history, but no mention of ENE; in other words, there are no imaging or pathology reports available to review
  - there is a statement that nodes are involved but it is unknown whether ENE is present
RENAL PELVIS AND URETER

Site-Specific Factor 2 – Depth of Renal Parenchyma Invasion

Source documents: pathology report

Invasion of the renal parenchyma by a tumor of the renal pelvis is coded as 600 in CS Extension and classified as T3 in the TNM system. The extent or depth of invasion into the renal parenchyma, which may have prognostic implications, is coded in this site-specific factor.

Code the depth of invasion into the renal parenchyma in whole millimeters in the code range 001 (1 millimeter) to 979, as stated in the pathology report.

- Use code 000 when
  - there is a statement in the pathology report that renal parenchymal invasion is not identified or not present
  - there is a nephrectomy or partial nephrectomy and the pathology report is available for review, but invasion of the renal parenchyma is not mentioned or is not measured.
- Use code 991 if renal parenchyma invasion is present but the depth is not measured.
- See schema for additional code choices.
Central nervous system sites include all parts of the brain, meninges, spinal cord, and the pituitary and pineal glands and craniopharyngeal duct. There is no TNM staging for any of these primary sites, but there is a chapter for brain and spinal cord in the seventh edition of the \textit{AJCC Cancer Staging Manual}.

**Site-Specific Factor 1 – WHO Grade Classification (Brain, CNSOther, IntracranialGland)**

\textit{Source documents:} pathology report

The World Health Organization (WHO) has promoted a histological grading classification for central nervous system tumors since 1979. The most recent version was published in 2007 as part of the WHO classification of central nervous system tumors. Tumor grade is the most important prognostic indicator for response to therapy and outcomes for brain and spinal cord tumors. According to WHO, the classification is more of a “malignancy scale” than a strict histologic grading system. Therefore, the WHO grade is different from the ICD-O grade/differentiation value that is stored with the morphology code—do not use WHO grade to code the sixth digit of the ICD-O morphology code. WHO grade ranges from I (low proliferative potential and possibly surgically curable—essentially benign behavior) through IV (cytologically malignant, mitotically active neoplasms that are rapidly fatal). Most CNS tumors are assigned a WHO grade, so there is usually a one-for-one correspondence between the ICD-O morphology code and the WHO grade.

Code the WHO grade as documented in the pathology report. If no WHO grade is stated, use code 999. Do not code terminology such as well-, moderately-, or poorly differentiated in this field. Do not use WHO grade information to code the fields Grade Path Value and Grade Path System.

**Site-Specific Factor 2 – Proliferative Fraction – Ki-67/MIB-1 (Brain, CNSOther, IntracranialGland)**

\textit{Source documents:} pathology report, specialty or reference laboratory report

\textit{Other names:} Ki-67 proliferation marker, Ki-67 labeling index, KI-67 antigen expressing fraction, Ki-67 growth fraction, MIB 1-3, MIB-1, MIB-1 labeling index, labeling index fraction, labeling index (LI) percentage, MKI67 antigen

Ki-67 is a monoclonal antibody that reacts with an antigen expressed only by proliferating human cells. In other words, Ki-67 detects cells that are actively growing and dividing. High growth rate (high proliferative index) is associated with response to chemotherapy as well as decreased survival. Ki-67 is non-specific to neural tumors or lymphomas and can be used on any type of malignant tumor. The Ki-67 labeling index is the proportion of cells that react to the monoclonal antibody. The MIB-1 antibody measures Ki-67 expression. Its advantage is that MIB-1 can be used on formalin-fixed paraffin embedded tissue, whereas Ki-67 must be used on fresh tissue.

Code the numeric percentage (labeling index) stated in the pathology report as a whole number in the range 001 to 100. Round fractions of a percent to the closest whole number. If the Ki-67 is not reported as a percentage, code the appropriate terminology.

\textit{Examples} 
- Labeling index stated as 43% – code as 043
- Ki-67 proliferation marker 13.2% – code as 013
Collaborative Stage Data Collection System Coding Manual and Instructions

Part I Section 2: Site-Specific Notes

MIB-1 fraction 27.6% – code as 028
Ki-67 labeling index slightly elevated – code as 300

001-100 1-100% (code exact Labeling Index percentage)
200 Labeling Index normal
300 Labeling Index stated as slightly elevated and no percentage provided
400 Labeling Index stated as elevated and no percentage provided
998 Test not done (test was not ordered and was not performed)

See schema for additional code choices.

Site-Specific Factor 3 – Functional Neurological Status-The Karnofsky Performance Score/Scale (Brain, CNSOther)

Source documents: history and physical exam, consultant notes, other statements in medical record
Other names: KPS, Karnofsky performance status, Karnofsky scale, KS

The Karnofsky performance score (KPS) is a clinical assessment tool that measures a patient's ability to carry out activities of daily living (ADL). Uses include assessing the patient’s performance status to make treatment decisions and estimating prognosis. The KPS is a scale from 0 (dead) to 100 (normal, no complaints, no evidence of disease). The Karnofsky score is used for central nervous system tumors to assess the patient’s functional neurologic status.

The definitions of the scores are listed in the site-specific factor. Briefly, the general categories are:

Karnofsky Score
80 – 100 Able to carry on normal activity and to work; no special care needed.
50 – 70 Unable to work; able to live at home and care for most personal needs; varying amount of assistance needed.
0 – 40 Unable to care for self; requires equivalent of institutional or hospital care; disease may be progressing rapidly.

Code the Karnofsky performance status as stated by the clinician at the time of diagnosis. Use codes in the range 000 to 100. For example, a KPS stated as 80 is coded 080. Because determination of the KPS requires observation and assessment of patient’s activities, it may not be possible for the registrar to assign the KPS based on information in the medical record. If no KPS is given, use code 999. See schema for additional code choices.

Site-Specific Factor 4 – MGMT Methylation (Brain, CNSOther)

Source documents: pathology report, specialty or reference laboratory report

MGMT (O\(^\text{6}\)-methylguanine- methyltransferase) is a DNA repair enzyme. Methylation is a chemical process that changes the composition of an enzyme or protein. Methylation of MGMT “shuts down” DNA repair, which allows the damage done to DNA by chemotherapy to continue cytotoxicity and apoptosis. Thus a patient with an increased MGMT methylation is more likely to respond to alkylating agents such as temozolomide (Temodar) and the nitrosoureas, some of the few drugs effective for brain tumors. MGMT methylation is a special (not routine) test done on tumor tissue. It is used primarily for anaplastic oligodendroglioma, anaplastic astrocytoma and glioblastoma multiforme.

Code the description of methylation as stated in the pathology or reference laboratory report.

• Use code 010 if the description of the test result is “methylated,” “hypermethylated,” “high,” or “positive.”
• Use code 020 if the description of the test result is “unmethylated,” “low,” or “negative.”
• Use code 988 if the histology is other than oligodendroglioma, anaplastic astrocytoma, or
Collaborative Stage Data Collection System Coding Manual and Instructions
Part I Section 2: Site-Specific Notes

glioblastoma multiforme.

- Use code 998 if the tumor diagnosis is clinical and there is no examination of tissue.
- Use code 999 if there is no information in the medical record about MGMT methylation.

Site-Specific Factor 5 – Chromosome 1p: Loss of Heterozygosity (LOH) (Brain, CNSOther)
Site-Specific Factor 6 – Chromosome 19q: Loss of Heterozygosity (LOH) (Brain, CNSOther)

Source documents: pathology report or clinical lab report (specialized gene testing)

Other names: allelic loss, gene deletion

These two genetic tests are frequently done at the same time and reported together. Loss of heterozygosity (LOH) in a chromosome means that genetic material normally found in a specific area of a chromosome is missing. In other words, this is damage to the chromosome that results in failure of tumor suppression, which in turn may cause the development or progression of a malignancy. For 1p LOH (site-specific factor 5), the specific chromosomal defect is on the short arm (p) of chromosome 1. For 19q LOH (site-specific factor 6), the specific chromosomal defect is on the long arm (q) of chromosome 19. Normal cells have two complete copies of each chromosome, a state called heterozygosity. The loss of this section of the chromosome is associated with improved outcome. It can be used to aid diagnosis and to make treatment decisions because sensitivity to chemotherapy agents, such as lomustine, procarbazine, and vincristine, is increased with either 1p or 19q LOH. Special molecular diagnostic (polymerase chain reaction or gene amplification) tests look for missing genetic material. LOH for chromosome 1p and 19q is tested primarily for oligodendroglioma, anaplastic oligodendroglioma, oligoastrocytoma, and anaplastic oligoastrocytoma. It is infrequently tested for other gliomas, such as glioblastoma multiforme.

- Use code 010 if the pathologist states the assay is positive for loss of heterozygosity.
- Use code 020 if the pathologist states the assay is negative for loss of heterozygosity.
- Use code 988 when
  - the central registry or the facility has determined that this item is not applicable.
  - the histology is something other than glioma, oligodendroglioma or oligoastrocytoma.
- Use code 997 when there is a statement in the record that the test was ordered but the results are not available.
- Use code 998 when there is a statement in the record that the test was not ordered or not done.
- Use code 999 when there is no documentation in the record that the test was done or what the results were.

Site-Specific Factor 7 – Surgical Resection (Brain, CNSOther)

Source documents: operative report, pathology report

The extent of the surgical resection of a central nervous system tumor is correlated to the patient’s outcome and is also a determining factor in whether the patient receives adjuvant therapy. The more tumor that can be removed, the better the patient’s survival. This site-specific factor captures information on the type of surgery the patient received. The code structure is very similar to the FORDS 2010 surgery of primary site codes for site codes C70 – C72 (brain, spinal cord, cranial nerves, meninges, and other parts of central nervous system). Note, however, that the wording of codes 030 – 050 is not identical to the FORDS 2010 surgery codes. The notes above the SSF table contain similar exceptions as the FORDS 2010 surgery codes, such as not to code laminectomies for spinal cord primaries or stereotactic radiosurgery in this field.

Code the extent of surgical resection as described in the operative report and pathology report in this field as well as in the surgery of primary site field. Use code 000 if there was no surgical resection of the
primary site. Codes 040 and 055 are not used for spinal cord or nerve primaries.

000 None; no surgery of primary site; autopsy ONLY
010 Tumor destruction, NOS (no tissue)
020 Local excision (biopsy) of tumor, lesion or mass (tissue specimen sent to lab)
021 Subtotal resection of tumor, lesion or mass of brain (tissue specimen sent to lab)
022 Resection of tumor of spinal cord or nerve (less than half a lobe involved with tumor; tissue specimen sent to lab)
030 Radical, total of tumor, lesion or mass of brain (less than half a lobe involved with tumor)
040 Partial resection of lobe of brain (more than half of lobe involved with tumor)
055 Gross total resection of lobe of brain (lobectomy; more than half of lobe involved with tumor)
090 Surgery, NOS

See schema for additional code choices.

Site-Specific Factor 8 – Focus of Primary Tumor (Brain, CNSOther)

Source documents: pathology report, operative report (for resectable cases); imaging or other statements in medical record (for unresectable cases)

Other terms: multicentric (similar to multifocal)

Multifocal brain tumors, particularly for glioblastoma multiforme, have an even worse prognosis than solitary lesions of the same histology. Frequently, multifocal lesions cannot be seen with specialized imaging or by the surgeon at the time of resection. When they are not visualized and resected, they continue to grow and manifest later as recurrence. When they are identified during workup, they affect how the patient is treated. Therefore, whether the tumor is solitary or multifocal is an important supplemental prognostic factor with the histology and grade.

Code the status of tumor foci at diagnosis as described in the medical record. For resectable tumors, give priority to statements in the pathology report and operative report. For unresectable tumors, use information from imaging studies such as magnetic resonance imaging as well as clinician statements. Clinical information has priority over code 998.

- Use code 001 when the tumor is described as solitary, single, a single focus, or unifocal (developing in a single location).
- Use code 002
  - when the tumor is described as multifocal or multicentric (arising in multiple locations) – do not code tumors identified as intracranial metastases in this field
  - when the Multiplicity Counter field of the Multiple Primary and Histology coding rules is greater than 1 but not 99.
- See schema for additional code choices.
ENDOCRINE GLANDS
Thyroid, AdrenalGland, EndocrineOther

In the seventh edition of the *AJCC Cancer Staging Manual* and CS Version 2, adrenal gland was separated from “Other Endocrine” and is now staged in TNM. Also in CS Version 2, the pituitary and pineal glands and the craniopharyngeal duct were separated from “Other Endocrine” and placed in a separate schema, IntracranialGland. The “Other Endocrine” schema now includes the remaining sites: thymus, parathyroid gland, carotid body, aortic body and other paraganglia, as well as overlapping lesion of endocrine glands and endocrine gland, NOS.

**Site-Specific Factor 1 – Solitary vs. Multifocal Tumor (Thyroid)**

*Source documents:* pathology report, nuclear or other imaging

In the sixth edition of TNM, T1 through T3 could be subcategorized as T_a (solitary tumor) and T_b (multifocal tumor). In the seventh edition, information about the number of tumors is indicated as a subscript in parentheses: solitary tumor is represented as T_(s), multifocal tumor is represented as T_(m). This site-specific factor is used for mapping to AJCC sixth edition but is not used for seventh edition mapping.

Code the number of tumor foci as described in the medical record. Information from the pathology report takes priority over clinical information and imaging.

- Use code 000 when
  - there is no evidence of primary thyroid cancer – CS Extension is coded 950
  - the primary tumor is in ectopic thyroid tissue.
  - the clinician uses a T category suffix or descriptor of (s) for the case.
- Use code 001 when the tumor is described as solitary, single, a single focus, or unifocal (developing in a single location).
- Use code 002 when
  - the tumor is described as multifocal or multicentric (arising in multiple locations within thyroid) – do not code tumors identified metastases in this field.
  - the clinician uses a T category suffix or descriptor of (m) for the case.
- See schema for additional code choices.

**Note:** The rules for counting multifocal tumors for the purposes of AJCC staging are different from the definitions for the Multiplicity Counter in the Multiple Primary and Histology coding rules. For this site-specific factor count all multiple foci even if they are not measured and code 002 in this field.

**Site-Specific Factor 1 – OBSOLETE WHO Grade Classification (AdrenalGland, EndocrineOther)**

When the intracranial glands (pineal, pituitary and craniopharyngeal duct) and the adrenal gland were separated from the Other Endocrine schema in CS Version 2, the WHO Grade Classification was made obsolete because it applies only to the intracranial glands. The data coded in CS Version 1 has been retained but 2010 and forward cases do not use this field.

For cases diagnosed after January 1, 2010, code this field as 988 Not Applicable.
Site-Specific Factor 2 – Tumor Gland Weight (AdrenalGland)

**Source documents:** pathology report

All carcinomas of the adrenal gland are coded with the AdrenalGland schema. However, TNM staging of adrenal gland cancers applies only to carcinomas of the adrenal cortex or adrenal cortical carcinoma (ICD-O morphology 8370) of the adrenal gland, NOS. This site-specific factor provides additional prognostic information for adrenal cortical carcinomas, because not all small tumors (under 50 grams) are benign and not all tumors larger than 50 grams are malignant. A normal adrenal gland weighs 4-6 grams.

Code the weight of the gland (including tumor)—not just the weight of the tumor—in whole grams in the range 001 (1 gram) to 979 (979 grams—almost a kilogram) as documented in the pathology report. Code any weight more than 980 grams as 980. Use code 000 if no primary tumor or mass is found. See schema for additional code choices.

Site-Specific Factor 3 – Vascular Invasion (AdrenalGland)

**Source documents:** pathology report

**Other names:** venous invasion, large vessel invasion

The adrenal gland is highly vascular, and prognosis is worse for tumor invasion of large veins. A large vein is defined as having smooth muscle in its wall, in contrast to small vessels such as capillaries.

Record the code that best describes involvement of the adrenal vein, renal vein and/or inferior vena cava (IVC) as described in the pathology report. If there is a pathology report (in other words, if the adrenal gland is resected), and venous invasion is not mentioned, use code 000. Do not code references to lymphatic invasion in this field. Do not code microscopically identified involvement of small unnamed blood vessels; this information is coded in the field Lymph-Vascular Invasion. The tumor may be described as a thrombus, a cluster of tumor cells present in the center of the vein but not attached to the wall of the vein.

- 000  Vascular invasion not present/not identified
- 010  Invasion of adrenal vein only
- 020  Invasion of renal vein only
- 030  Invasion of inferior vena cava only
- 040  020 + 010; Invasion of renal vein and adrenal vein
- 050  030 + 010; Invasion of inferior vena cava and adrenal vein
- 060  030 + 020; Invasion of inferior vena cava and renal vein
- 070  030 + 020 + 010; Invasion of inferior vena cava, renal vein and adrenal vein
- 991  Large vessel venous invasion, vein not specified
- 998  No surgical resection of primary site

See schema for additional code choices.
KAPOSI SARCOMA

Site-Specific Factor 1 – Associated with HIV/AIDS

See Associated with HIV/AIDS under LYMPHOMA.

LYMPHOMA AND HEMATOPOIETIC
Lymphoma, HemeRetic

Site-Specific Factor 1 – Associated with HIV/AIDS (Lymphoma, Kaposi Sarcoma)

Source documents: clinical laboratory test, statement in medical record

Other names: HIV type 1, HIV type 2, ARC (AIDS related complex), PWA (person with AIDS), PWARC (person with ARC); older terms for HIV type 1: HTLV-3, LAV

Immune suppression is a common factor for lymphoma, Kaposi sarcoma, acquired immune deficiency syndrome (AIDS) and the presence of human immunodeficiency virus (HIV). Untreated, a person infected with HIV will eventually progress to AIDS. Certain types of cancer are associated with HIV and AIDS, including Hodgkin lymphoma, diffuse large B-cell lymphoma, and primary central nervous system lymphoma. This site-specific factor documents whether the patient has HIV infection or AIDS at the time of diagnosis.

Code whether the patient has HIV or AIDS, based on statements in the medical record. Do not assume that the patient is negative for HIV or AIDS unless there is a statement to that effect; use code 999 instead.

- Use code 001 when there is a statement in the record that
  - HIV or AIDS is present
  - the patient is positive for HIV or AIDS
  - the patient is infected with HIV or AIDS
  - the patient has a history of HIV or AIDS
  - an HIV or AIDS test has been done and is positive
- Use code 002 when there is a statement in the record that
  - HIV or AIDS is not present
  - the patient is negative for HIV or AIDS
  - the patient is not infected with HIV or AIDS
  - an HIV or AIDS test has been done and is negative
- Use code 999 when there is no mention of HIV or AIDS status in the medical record.

Site-Specific Factor 2 – Systemic Symptoms at Diagnosis (Lymphoma)

Source documents: patient history, progress notes, consultant notes, other statements in medical record

Other names: B symptoms; Fever: Pel-Ebstein fever, hyperpyrexia, febrile response

The stages of malignant lymphoma can be subclassified as A or B by whether certain specific constitutional symptoms are present at the time of diagnosis. The stage group suffix for a patient without these systemic symptoms is “A,” meaning absence of symptoms or asymptomatic; for example Stage IIA. The stage group suffix for a patient with any of the symptoms listed below is “B,” such as Stage IIIB.
The symptoms are carefully defined:

- Persistent, cyclic, unexplained fevers with a temperature over 38 degrees centigrade or 101.5 degrees Farenheit. Cyclic means elevated one week and normal or nearly normal the next week.
- Drenching night sweats requiring a change of bed clothes
- Weight loss greater than 10% of body weight in the six months prior to diagnosis, not accounted for by changes in diet or exercise.
- Minor symptoms include pruritus and generalized malaise, but these by themselves are insufficient to be classified as B symptoms. The same is true of alcohol intolerance (painful lymph nodes following consumption of alcohol), fatigue, or a short illness due to a suspected infection with associated fever.

The presence of these symptoms is more important prognostically for Hodgkin lymphoma than for non-Hodgkin lymphoma. Up to 30% of non-Hodgkin lymphoma patients and up to 33% of Hodgkin lymphoma patients will present with one or more of these adverse symptoms.

Code the description of the patient’s systemic symptoms based on statements in the medical record.

- Use code 000 when there is a statement in the record that
  - there are no B symptoms
  - the patient is asymptomatic
  - there is no mention of B symptoms in the history, physical exam, or other clinician notes
- Use code 010 when the medical record indicates that
  - any one or more of the following symptoms as defined above are present: fever, night sweats, weight loss
  - the patient has B symptoms
- Use code 020 when there is a statement that the patient has pruritus only. Pruritus (note: not spelled pruritis) is generalized, recurrent, unexplained itching, which is not a B symptom by itself.
- Use code 030 when pruritus and one or more of the symptoms listed in 010 are present.
- See schema for additional code choices.

SITE-SPECIFIC FACTORS 3 – 5: PROGNOSTIC SCORING SYSTEMS

CS version 2 and seventh edition of TNM include three non-anatomic indices or scoring systems: IPI (Site-Specific Factor 3) for primarily for B-cell non-Hodgkin lymphomas, FLIPI (Site-Specific Factor 4) for more indolent follicular lymphomas, and IPS (Site-Specific Factor 5) for Hodgkin lymphoma. Although each of these non-anatomic prognostic systems has specific application, physicians may use them interchangeably. For example, a clinician may describe the IPS for a non-Hodgkin lymphoma or may give a score without naming it or its criteria.

The following guidelines apply to site-specific factors 3, 4 and 5:

If the index or score is named (IPI, FLIPI, IPS) and the point value is given, code the score in the appropriate site-specific factor and code the other two SSFs as 999.

If the index or score is not named and a point value of 5 or less is documented, use code 999 in all three SSFs.

If the score is 6 or 7, assume that it is the International Prognostic Score. Code the score in site-specific factor 5 and code SSFs 3 and 4 as 999.

If the risk is stated as “low,” “intermediate,” or “high” but the index or score is not named, use code 999 in all three site-specific factors.

If a score is named and both the point value and risk category are documented, code the point value. Code only the statement/score/index documented by the clinician. Do not try to calculate the score or risk category based on information in the medical record.
Site-Specific Factor 3 – International Prognostic Index (Lymphoma)

**Source documents:** patient history, progress notes, consultant notes, other statements in medical record

The International Prognostic Index (IPI) was initially proposed in 1993, and is now recommended as a companion to the TNM system for making clinical decisions about lymphoma, because it can differentiate prognosis among patients in stages II, III and IV based on other clinical factors. The IPI was developed for aggressive non-Hodgkin lymphomas, but has practical application for other types of lymphomas as well. Recently, a revision of the IPI has been proposed for the more indolent follicular lymphomas (FLIPI—see site-specific factor 4)

The IPI tracks five independent prognostic variables for non-Hodgkin lymphoma, two of which are anatomically based. The variables are:

- Age of patient at diagnosis – age > 60 is worse
- Performance status of patient – ECOG score of 2 or more is worse. (ECOG is a scale from 0 to 4.)
- Lactate dehydrogenase (LDH) level – abnormal is worse
- Ann Arbor/AJCC stage – Stage III or IV (advanced) is worse
- Presence of extranodal involvement – more than one extranodal site is worse

Adverse characteristics for each of these factors are counted for a score of 0 to 5. For example, a 65 year old patient with AJCC Stage III lymphoma confined to lymph nodes and an elevated LDH would have a score of 3. Patients are then grouped into risk categories based on their scores. Low risk is a score of 0 or 1, low intermediate 2, high intermediate 3, and high risk 4 or 5. The risk categories help determine the patient’s chances of achieving remission, staying in remission, and overall survival.

Code the pretreatment point value for the IPI score as documented by the clinician in the range 000 (0 points) to 005 (5 points). If a risk category is described and points are not stated, use a code in the range 990 to 993. If there is no documentation of IPI score in the record, or if another scoring system is documented, use code 999 in this field. See also coding guidelines for SSFs 3-5 above, and see schema for additional code choices.

Site-Specific Factor 4 – Follicular Lymphoma Prognostic Index (FLIPI)

**Source documents:** patient history, progress notes, consultant notes, other statements in medical record

Because follicular lymphomas are more indolent than other types of non-Hodgkin lymphoma, the IPI (site-specific factor 3) is less useful as a predictor of outcome. A different set of variables known as the FLIPI was published for follicular lymphoma in 2004.

The FLIPI tracks five independent prognostic variables for follicular non-Hodgkin lymphoma, two of which are anatomically based. The variables are:

- Age of patient at diagnosis – age > 60 is worse
- Lactate dehydrogenase (LDH) level – abnormal is worse
- Ann Arbor/AJCC stage – Stage III or IV (advanced) is worse
- Number of nodal areas involved – more than four nodal areas is worse
- Serum hemoglobin (Hb, Hgb) concentration – less than 12 g/dL (grams per deciliter) is worse

Adverse characteristics for each of these factors are counted for a score of 0 to 5. For example, a 55 year old patient with stage II lymphoma, one extranodal site involved and a hemoglobin count of 9.0 would have a score of 1. Patients are then grouped into risk categories based on their scores. Low risk is a score of 0 or 1, low intermediate 2, high intermediate 3, and high risk 4 or 5. The risk categories help
determine the patient’s chances of achieving remission, staying in remission, and overall survival.

Code the pretreatment point value for the FLIPI score as documented by the clinician in the range 000 (0 points) to 005 (5 points). If a risk category is described and points are not stated, use a code in the range 990 to 992. If there is no documentation of FLIPI score in the record, or if another scoring system is documented, use code 999 in this field. See also coding guidelines for SSFs 3-5 above, and see schema for additional code choices.

Site-Specific Factor 5 – International Prognostic Score (IPS)

*Source documents:* patient history, progress notes, consultant notes, other statements in medical record

*Other names:* Hasenclever advanced Hodgkin’s disease prognostic score

The International Prognostic Score (IPS) was initially proposed in 1998 to address non-anatomic prognostic factors for Hodgkin lymphoma that could assist the clinician in making treatment decisions, either to possibly reduce treatment for patients with few risk factors (not over-treat) or to identify those patients who might not have a sustained response to standard treatment.

The IPS tracks seven independent prognostic variables for Hodgkin lymphoma, one of which is anatomically based. The variables are:

- Age of patient at diagnosis – age 45 or over is worse
- Gender – male is worse
- Ann Arbor/AJCC stage – Stage IV is worse
- Serum hemoglobin (Hb, Hgb) concentration – less than 10.5 g/dL (grams per deciliter) is worse
- Serum albumin (ALB) – < 4 g/dL is worse
- White blood cell count (WBC) – > 15,000/mm³ (cubic millimeter)
- Lymphocytopenia – < 600/mm³ (cubic millimeter)

Adverse characteristics for each of these factors are counted for a score of 0 to 7. For example, a 48 year old male with AJCC Stage III Hodgkin’s disease, elevated WBC at 20,000, and Hgb of 8.8 would have a score of 4. Hodgkin lymphoma patients are not grouped into risk categories based on their scores, but disease-free survival declines markedly when the point value is 5 or higher.

Code the pretreatment point value for the IPS score as documented by the clinician in the range 000 (0 points) to 007 (7 points). If there is no documentation of IPS score in the record, or if another scoring system is documented, use code 999 in this field. See also coding guidelines for SSFs 3-5 above, and see schema for additional code choices.

Site-Specific Factor 1 – JAK-2 (HemeRetic)

*Source documents:* clinical laboratory test (whole blood), reference laboratory test; anatomic pathology (polymerase chain reaction test on bone marrow)

*Other names:* Janus kinase 2 gene, JAK2 V617F, JAK2 exon 12, JAK2 exon13

JAK-2, a gene found in all humans, is involved in the development of blood cells. If JAK-2 has mutated, the person is more susceptible to develop a myeloproliferative disorder (MPD). The JAK-2 mutation, which is acquired rather than inherited, is found in as many as 90% of patients with polycythemia vera (PV), about half of patients with essential thrombocytopenia (ET), and slightly fewer patients with primary myelofibrosis (also known as agnogenic myeloid metaplasia and other terms). JAK-2 is used by clinicians to help classify MPDs. The most common histologies for which JAK-2 is tested are those listed above. Registrars can use JAK-2 information to help determine whether the MPD is reportable. JAK2 positivity indicates a malignant (clonal, irreversible) reportable disease, but is not diagnostic of a
specific MPD. Additional tests, such as a bone marrow biopsy, are necessary to determine the specific MPD histology. As the use of JAK-2 increases and is investigated for other hematopoietic histologies, it also has future potential for development of targeted therapeutics for the MPDs.

The principal JAK-2 test looks for a change (mutation) in an amino acid at a specific place on the JAK-2 gene called V617F. If the V617F test is negative, other JAK-2 mutation tests, such as those in exon 12 or 13 may be ordered to investigate a possible diagnosis of polycythemia vera. (An exon is a segment of a gene that contains instructions for making a protein.)

Code the result of the JAK-2 test as documented in a laboratory test or elsewhere in the medical record. Code this field for any hematopoietic, reticuloendothelial, immunoproliferative, myeloproliferative, or myelodysplastic disease for which JAK-2 is tested. For those diseases where JAK-2 is not mentioned in the record, or for a HemeRetic schema disease such as leukemia or multiple myeloma where JAK-2 is not normally tested, code as 999. If JAK-2 is positive but the specific mutation is not stated, code as 850.

000  JAK-2 test result stated as negative
010  JAK2 test performed, positive for mutation V617F in exon 14
020  JAK2 test performed, positive for mutation of exon 12
080  JAK2 test performed, positive for other specified mutation
081  JAK2 test performed, positive for more than one mutation
085  JAK2 test performed, positive NOS; specific mutation(s) not stated

See schema for additional code choices.
SKIN OF EYELID

Site-Specific Factor 1 – Measured Thickness (Depth) for Squamous Cell Carcinoma

Source document: pathology report

Other names: maximum tumor thickness, Breslow depth of invasion, Breslow thickness, Breslow measurement

This site-specific factor measures tumor thickness or tumor depth (vertical dimension), not the size (lateral dimension). The depth of invasion or tumor thickness measurement for squamous cell carcinoma of the skin of the eyelid is collected in hundredths of millimeters as stated in the pathology report for the resected specimen. The measurement of tumor thickness is precisely defined in the squamous cell carcinoma of the skin protocol of the College of American Pathologists (CAP checklist) as a vertical measurement from the granular layer of the epidermis (or base of ulceration) to the deepest point of invasion, as measured on a calibrated ocular micrometer. Tumor thickness may be described as Breslow depth of invasion, although the Breslow measurement is usually for cutaneous melanomas.

Code a measurement specifically labeled as “thickness” or “depth” in the pathology report. In the absence of this label, a measurement described as taken from the cut surface of the specimen may be coded. And in the absence of either of these labels, the third dimension in a statement of tumor size can be used by the registrar to code this field. Because the thickness table is similar to many other tables that collect a measurement, it is important to identify the correct unit of measurement. The value collected for cutaneous squamous cell carcinoma is measured in hundredths of millimeters.

Code the actual tumor thickness, tumor depth, (or Breslow’s measurement if so stated) in hundredths of millimeters as stated in the pathology report, in the code range 001 to 979. This is a three digit field with an implied decimal point between the first and second digits.

Examples
- Tumor described as 0.15 mm in depth – code as 015
- Lesion 1 mm thick – code as 100
- Breslow 2.5 mm – code as 250
- Thickness of 10 mm (1 cm) – code as 980 (9.80 millimeters or larger)

The 900 codes are used to document specific case situations.

- For skin of eyelid, code tumor thickness only for squamous cell carcinoma. Use code 987 for all other histologies.
- Use code 990 when
  - there is a statement of microinvasion but no depth is given
  - there is a description of a microscopic focus or foci but no depth is given
- Use code 998 when there is no histologic examination of the primary site.
- Use code 999 when
  - tumor depth or thickness information is unknown, including cases in which the primary tumor is removed but the measurement of thickness cannot be determined from the pathology report
Site-Specific Factor 2 – Clark’s Level
See Clark’s Level in the SKIN section.
For skin of eyelid, code Clark’s level only for squamous cell carcinoma. Use code 987 for all other histologies.

Site-Specific Factor 3 – Clinical Status of Lymph Nodes

Site-Specific Factor 4 – Size of Lymph Node
See Size of Lymph Nodes in the SKIN section.
For skin of eyelid, code size of lymph nodes only for squamous cell carcinoma. Use code 987 for all other histologies.

Site-Specific Factor 5 – Sentinel Lymph Node Biopsy

Site-Specific Factor 6 – Perineural Invasion
See Perineural Invasion in the SKIN section.

Site-Specific Factor 7 – Tumor Necrosis

Site-Specific Factor 8 – Pagetoid Spread

Site-Specific Factor 9 – Mohs Layers

Site-Specific Factor 10 – Prior Radiation

Site-Specific Factor 11 – HIV Status
See Associated with HIV/AIDS under LYMPHOMA for information about HIV status.
The code structure of this site-specific factor for skin of eyelid is different from that for lymphoma or ocular adnexal lymphoma.

Code whether the patient has HIV, based on statements in the medical record. Do not assume that the patient is negative for HIV unless there is a statement to that effect; use code 999 instead.

- Use code 000 when there is a statement in the record that
  - HIV is not present
  - the patient is negative for HIV
  - the patient is not infected with HIV
  - an HIV test has been done and is negative
- Use code 010 when there is a statement in the record that
  - HIV is present
  - the patient is positive for HIV
Site-Specific Factor 12 – Solid Organ Transplant

Site-Specific Factor 13 – Leukemia

Site-Specific Factor 14 – Multiple Carcinomas

Site-Specific Factor 15 – Muir-Torre Syndrome

Site-Specific Factor 16 – Xeroderma Pigmentosa
**EYE STRUCTURES**

The major structures of the eye (globe) are the retina, conjunctiva, and uvea, each of which has one or more schemas in CS version 2 (see Figure I-2-14). The uvea consists of the iris and ciliary body (C69.3, also called the anterior uvea) and choroid (C69.4, also known as the posterior uvea). The conjunctiva (C69.0) is a clear mucous membrane that covers the white part of the eye (sclera) and lines the inside of the eyelids. The retina (C69.2) is the innermost layer of the eye containing the neurons that result in vision. The orbit (C69.6) is the bony structure surrounding the soft tissues of the eye. The lacrimal gland (C69.5) is located in the orbit superior and lateral to the globe and produces the tears that keep the eye moist.

**SCHEMA DISCRIMINATORS FOR OPHTHALMIC SITES**

**Site-Specific Factor 25 – Schema discriminator: Melanoma Ciliary Body/Melanoma Iris**

Iris and ciliary body have the same ICD-O topography code (C69.3). However, for purposes of stage grouping in AJCC seventh edition, iris has its own T category definitions, which were carried over into CS version 2. Ciliary body is defined and staged with choroids. Consequently, a schema discriminator is necessary so that the CS computer algorithm knows whether the primary site is iris or ciliary body so that the appropriate tables will be presented to the coder.

**Site-Specific Factor 25 – Schema discriminator: Lacrimal Gland/Lacrimal Sac**

Lacrimal gland and lacrimal sac have the same ICD-O topography code (C69.5). However, AJCC seventh edition staging is limited to lacrimal gland. Consequently, a schema discriminator is necessary so that the CS computer algorithm knows whether the primary site is lacrimal gland versus the lacrimal sac and nasolacrimal duct so that the correct derived T values will be assigned by the mapping algorithm. No stage grouping is presently recommended for carcinoma of the lacrimal gland.

**Site-Specific Factor 1 – Tumor Size (Conjunctiva)**

**Site-Specific Factor 1 – Ki-67 Labeling Index Lab Value (Conjunctiva, LacrimalGland)**

*Source documents:* pathology report, specialty or reference laboratory report

*Other names:* Ki-67 proliferation marker, Ki-67 labeling index, KI-67 antigen expressing fraction, Ki-67 growth fraction, MIB 1-3, MIB-1, MIB-1 labeling index, labeling index fraction, labeling index (LI) percentage, MKI67 antigen
Ki-67 is a monoclonal antibody that reacts with an antigen expressed only by proliferating human cells. In other words, Ki-67 detects cells that are actively growing and dividing. High growth rate (high proliferative index) is associated with response to chemotherapy as well as decreased survival. Ki-67 is non-specific to ocular tumors, neural tumors or lymphomas and can be used on any type of malignant tumor. The Ki-67 labeling index is the proportion of cells that react to the monoclonal antibody by staining positive for the Ki-67 protein. The MIB-1 antibody also measures Ki-67 expression and may be used instead of Ki-67. Its advantage is that MIB-1 can be used on formalin-fixed paraffin embedded tissue, whereas Ki-67 must be used on fresh tissue.

Code the numeric percentage (growth fraction or labeling index) stated in the pathology report as a whole number in the range 001 to 100. Do not calculate the percentage or fraction from the report. Round fractions of a percent to the closest whole number. If the Ki-67 exact percentage is not given but the result is stated in a range, use the appropriate code in the 110–150 range. If the Ki-67 percentage is not reported as a percentage, code the appropriate proliferative rate terminology in the range 991–993.

*Examples*
- Labeling index stated as 43% – code as 043
- Ki-67 proliferation marker 13.2% – code as 013
- MIB-1 fraction 27.6% – code as 028
- Ki-67 growth fraction < 25% – code as 140
- Low proliferation rate – code as 992

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>001-100</td>
<td>1-100% (code exact labeling index or growth fraction percentage)</td>
</tr>
<tr>
<td>110</td>
<td>Stated as Ki-67 growth fraction (\leq 5%)</td>
</tr>
<tr>
<td>120</td>
<td>Stated as Ki-67 growth fraction (&gt; 5% – \leq 10%)</td>
</tr>
<tr>
<td>130</td>
<td>Stated as Ki-67 growth fraction (&gt; 10% – \leq 20%)</td>
</tr>
<tr>
<td>140</td>
<td>Stated as Ki-67 growth fraction (&gt; 20% – \leq 50%)</td>
</tr>
<tr>
<td>150</td>
<td>Stated as Ki-67 growth fraction (&gt; 50%)</td>
</tr>
<tr>
<td>991</td>
<td>Stated as low proliferation rate</td>
</tr>
<tr>
<td>992</td>
<td>Stated as increased proliferation rate</td>
</tr>
<tr>
<td>993</td>
<td>Stated as high proliferation rate</td>
</tr>
<tr>
<td>997</td>
<td>Ki-67 growth fraction study performed, results not available</td>
</tr>
</tbody>
</table>

See schema for additional code choices.

**Site-Specific Factor 1 – Measured Thickness (Depth) (MelanomaConjunctiva)**

*OB Solete for MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris – see Site-Specific Factor 3 Measured Thickness (Depth) below.*

See [Measured Thickness/Depth](#) in SKIN section.

The thickness of a lesion for melanoma of the conjunctiva is measured in *hundredths* of millimeters.

**Note:** In CS version 2, this site-specific factor was made obsolete for melanoma of the choroid, ciliary body, and iris because the scale of measurement changed. For these sites, thickness in *tenths* of a millimeter is recorded in Site-Specific Factor 3.

**Site-Specific Factor 2 – Quadrants (MelanomaConjunctiva)**

**Site-Specific Factor 2 – Measured Basal Diameter (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)**
Site-Specific Factor 3 – Grade – Melanoma Origin  (MelanomaConjunctiva)

Site-Specific Factor 3 – Measured Thickness (Depth)  (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)

Source document: pathology report
Other names: maximum tumor thickness, depth of invasion

This site-specific factor measures tumor thickness or depth (vertical dimension), rather than size (lateral dimension). The depth of invasion or tumor thickness measurement for melanomas of the choroid, ciliary body, and iris is collected in tenths of millimeters as stated in the pathology report for the resected specimen. (This is similar to, but not the same as, Breslow depth of invasion, which is measured in hundredths of millimeters.) The thickness measurement should only be taken from a pathology specimen, not from a radiology report or other clinical measurement. Code a measurement specifically labeled as “thickness” or “depth” in the pathology. In the absence of this label, a measurement described as taken from the cut surface of the specimen can be coded. And in the absence of either of these labels, the third dimension in a statement of tumor size can be used by the registrar to code this field.

Code the actual tumor thickness or tumor depth in tenths of millimeters as stated in the pathology report, in the code range 001 to 979. Because the thickness table is similar to many other tables that collect a measurement, it is important to identify the correct unit of measurement. This is a three digit field with an implied decimal point between the second and third digits.

Examples

- Tumor thickness 0.1 mm – code as 001
- Depth 0.74 mm – code as 007
- Lesion 1 mm thick – code as 010
- Thickness 2.7 mm – code as 027
- Depth 10.6 mm – code as 106

The 900 codes are used to document specific case situations. Use code 990 when the tumor is described as microinvasive or when no size is given for a microscopic focus or foci. Codes in the 991 to 996 range describe size ranges associated with the “tumor size categories” that comprise the T1 – T4 categories in the AJCC seventh edition.

- 991 Described as “≤ 3 mm”
- 992 Described as “> 3 mm” or “≤ 6 mm”
- 993 Described as “> 6 mm” or “≤ 9 mm”
- 994 Described as “> 9 mm” or “≤ 12 mm”
- 995 Described as “> 12 mm” or “≤ 15 mm”
- 996 Described as “> 15 mm”

See schema for additional code choices.

Site-Specific Factor 4 – Size of Largest Metastasis  (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)

* Site-Specific Factor 5 – Chromosome 3 Status  (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)
* Site-Specific Factor 6 – Chromosome 6p Status (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)

* Site-Specific Factor 7 – Chromosome 8q Status (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)

Site-Specific Factor 8 – Gene Expression Profile (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)
SEE 11-30-09 Email from Jennifer Seiffert

Site-Specific Factor 9 – Mitotic Count (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)
See Mitotic Count in Lab Tests and Tumor Markers
Mitotic count is a site-specific factor for a number of primary sites. For melanomas of the choroids, ciliary body and iris, the standard measurement is the total number of mitoses per 40 high power fields (HPF at 40 times magnification) or per 4 square millimeters.

Site-Specific Factor 10 – Mean Diameter Nucleoli (MLN) (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)

Site-Specific Factor 11 – Extravascular Matrix Patterns, Loops (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)

Site-Specific Factor 12 – Extravascular Matrix Patterns, Networks (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)

Site-Specific Factor 13 – Microvascular Density (MVD) (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)

Site-Specific Factor 14 – PET Standardized Uptake Values (SUV) (MelanomaChoroid, MelanomaCiliaryBody, MelanomaIris)
See PET Standardized Uptake Values (SUV) under LUNG AND PLEURA.

Site-Specific Factor 2 – Nuclear NM23 Staining (LacrimalGland)
Site-Specific Factor 3 – Clinical Evaluation of Lymph Nodes (LacrimalGland)

Site-Specific Factor 4 – Perineural Invasion (LacrimalGland)
See Perineural Invasion in the SKIN section.

Site-Specific Factor 5 – Carcinoma ex Pleomorphic Adenoma, Invasion Beyond Capsule (LacrimalGland)

Site-Specific Factor 6 – Adenoid Cystic Carcinoma-Presence of Basaloid Pattern (LacrimalGland)

Site-Specific Factor 7 – Mucoepidermoid Carcinoma-Grade (LacrimalGland)

Site-Specific Factor 8 – Orbital Bone (LacrimalGland)

Site-Specific Factor 1 – Extension Evaluated at Enucleation (Retinoblastoma)

Site-Specific Factor 2 – RB Gene Mutation (Retinoblastoma)

Site-Specific Factor 3 – Family History of Retinoblastoma (Retinoblastoma)

Site-Specific Factor 4 – Primary Globe-sparing Treatment Failure (Retinoblastoma)

Site-Specific Factor 5 – Linear Choroid Involvement (Retinoblastoma)

Site-Specific Factor 6 – Clinical Extension 2nd Eye (Retinoblastoma)
OCULAR ADNEXAL LYMPHOMA

Site-Specific Factor 1 – Associated with HIV/AIDS
See Associated with HIV/AIDS under LYMPHOMA AND HEMATOPOIETIC section.

Site-Specific Factor 2 – Systemic Symptoms at Diagnosis
See Systemic Symptoms at Diagnosis under LYMPHOMA AND HEMATOPOIETIC section.

Site-Specific Factor 3 – International Prognostic Index (IPI)
See International Prognostic Index (IPI) under LYMPHOMA AND HEMATOPOIETIC section.

Site-Specific Factor 4 – Follicular Lymphoma International Prognostic Index (FLIPI)
See Follicular Lymphoma International Prognostic Index (FLIPI) under LYMPHOMA AND HEMATOPOIETIC section.

Site-Specific Factor 5 – Ki-67 Labeling Index Lab Value
See Ki-67 Labeling Index Lab Value under EYE STRUCTURES.

Site-Specific Factor 6 – LDH Interpretation
See LDH, LDH Value, LDH Interpretation in LAB TESTS AND TUMOR MARKERS

Site-Specific Factor 7 – Rheumatoid Arthritis

Site-Specific Factor 8 – Sjogren’s Syndrome

Site-Specific Factor 9 – Other Connective Tissue Disease

Site-Specific Factor 10 – Sicca Syndrome

Site-Specific Factor 11 – Other Viral Infection

Site-Specific Factor 12 – Bacterial Infection

Site-Specific Factor 13 – Other Infection
1/25/2010: 42 ophthalmic SSFs to be completed