

British Columbia Association of Laboratory Physicians 2010 Minimum Diagnostic Guidelines for Cancer Diagnosis

Introduction

The 2010 BCALP Minimum Diagnostic Guidelines contain, to greater or lesser degree, changes and additions to every organ system protocol. This is because of significant changes to staging criteria in the 7th edition of the AJCC Cancer Staging Manual (which these guidelines incorporate), and because of advances in our knowledge of clinically important prognostic and treatment dependant variables in cancer diagnosis. The reader will notice significant alterations to the sections on laryngeal, lung, breast, melanoma and gynecologic tumours. The reader will also notice that the “M” component of the TNM staging system is to be reported only when distant metastasis is identified; “MX” is meaningless and “MO” can only be established at the time of autopsy. By necessity, previously grouped sections on pancreatic, biliary and small intestinal tumours have been divided into separate protocols, and new protocols have been provided for the appendix, anus, liver and squamous cancers of the skin. Thank you to Drs. Ken Berean, Richard Crawford, John English, Blake Gilks, Brian Skinnider and Torsten Neilson for their thoughtful contributions.

The clinical practice of anatomic pathology encompasses the activities of investigation, interpretation and communication. These diagnostic guidelines are intended as an aid to all of these activities. The goal has been to strike the correct balance between comprehensiveness, clarity, and brevity. The guiding principle has been to include only diagnostic criteria that are of prognostic or therapeutic significance to the patient, and that are reproducible between pathologists. The result is a framework, or skeleton, on which the pathologist can craft the pathology report. It does not constrain the communicative role of the pathologist to the filling in of mandatory software fields. The spirit of this document is one of respect for the requirements of our clinical colleagues and for us as diagnostic consultants.

Your critique of this document is always welcome.

Robert Wolber MD (Robert.wolber@vch.ca)
January 2010
Richmond, British Columbia

Index

<u>Ampulla of Vater Carcinoma</u>	3
<u>Anal Carcinoma</u>	4
<u>Appendix</u>	5
<u>Bladder Carcinoma</u>	9
<u>Breast Carcinoma</u>	10
<u>Cervical Carcinoma</u>	13
<u>Colon and Rectum</u>	15
<u>Endometrial Carcinoma</u>	17
<u>Esophageal Carcinoma</u>	19
<u>Extrahepatic Bile Duct Carcinoma</u>	7
<u>Gallbladder Carcinoma</u>	20
<u>Laryngeal Carcinoma</u>	21
<u>Lip/Oral Cavity/Pharynx</u>	22
<u>Liver- Hepatocellular Carcinoma</u>	23
<u>Lung Carcinoma</u>	24
<u>Melanoma</u>	38
<u>Ovarian Carcinoma</u>	27
<u>Pancreas (Exocrine and Endocrine) Carcinoma</u>	29
<u>Penis for Squamous Carcinoma</u>	30
<u>Prostate Needle Biopsies</u>	31
<u>Prostatectomy for Carcinoma</u>	32
<u>Renal Carcinoma</u>	34
<u>Skin- Melanoma</u>	38
<u>Skin- Squamous Cell Carcinoma</u>	40
<u>Small Intestine, Colon, Rectum</u>	41
<u>Soft Tissue Sarcoma</u>	36
<u>Stomach Carcinoma</u>	42
<u>Testis for Germ Cell Tumour</u>	43
<u>Thyroid Carcinoma</u>	44
<u>Vulva (non-melanoma)</u>	46

Ampulla of Vater Carcinoma

Microscopic diagnosis: Ampulla, ampullectomy/ pancreaticoduodenectomy-

- a) Positive for carcinoma, specify type: adenocarcinoma NOS, papillary type, intestinal type, mucinous, signet ring cell, squamous, other
- b) Tumour location: intra-ampullary, peri-ampullary, duodenal papilla
- c) Tumour grade: well, moderately, poorly differentiated
- d) Greatest linear tumour dimension
- e) Tumour extension: carcinoma in situ, limited to ampulla of Vater or sphincter of Oddi, invades duodenal wall, invades pancreas, invades peripancreatic soft tissues, invades extrapancreatic common bile duct, invades other adjacent organs or structures
- f) Margins: duodenal mucosal, pancreatic retroperitoneal (uncinate), bile duct, distal pancreatic (approach to closest margin in mm.)
- g) Lymph-vascular invasion (present/absent)
- h) pTNM tumour stage

Primary tumour (T)

- Tis- Carcinoma in situ
- T1- Tumour limited to ampulla of Vater or sphincter of Oddi
- T2- Tumour invades duodenal wall
- T3- Tumour invades pancreas
- T4- Tumour invades peripancreatic soft tissues or other adjacent organs or structures

Regional lymph nodes

- NX- Regional lymph nodes cannot be assessed
- NO- No regional lymph node metastasis
- N1- Regional lymph node metastasis

Distant metastasis

- M1- Distant metastasis

Anal Carcinoma

Microscopic diagnosis: Anus (canal, anorectal junction, perianal skin), polypectomy/ transanal disk resection/ abdominal-perineal resection-

a) Positive for (squamous cell carcinoma, adenocarcinoma, Paget disease, other)

b) Histologic grade (well, moderately, poorly differentiated)

c) Greatest linear tumour dimension

d) Tumour invasion (in-situ, lamina propria, muscularis mucosa, submucosa, sphincter muscle, perianal soft tissues, adjacent structures, perianal skin)

e) Resection margins (proximal mucosal, distal skin, radial; closest approach in mm.)

f) Lymph node status (perirectal, inguinal, iliac)

g) Pathologic staging (pTNM):

Primary tumour (T)

Tis- carcinoma in situ

T1- Tumour 2cm. Or less in greatest dimension

T2- Tumour more than 2cm. but not more than 5cm.

T3- Tumour more than 5cm. in greatest dimension

T4- Tumour of any size with invasion of adjacent organs (bladder, urethra, vagina).

Invasion of sphincter muscle alone is not classified as T4

Regional lymph nodes (N)

NX- Cannot be assessed

NO- No regional lymph node metastasis

N1- Metastasis in perirectal lymph node(s)

N2- Metastasis in unilateral inguinal or internal iliac lymph node(s)

N3- Metastases in perirectal and inguinal lymph nodes or bilateral inguinal or bilateral internal iliac lymph nodes

Distant metastasis (M)

M1- Distant metastasis

Appendix

Microscopic diagnosis: appendix, (resection, right hemicolectomy)-

a) Positive for: adenocarcinoma (well, moderately, poorly differentiated); mucinous (colloid) adenocarcinoma*; signet ring cell carcinoma*; goblet cell carcinoid**; pure carcinoid**

*greater than 50% mucinous or signet ring cell component

**goblet cell carcinoid tumours should be staged using TNM criteria for adenocarcinoma. For pure appendiceal carcinoids see specific protocol below

b) Greatest linear tumour dimension

c) Tumour invasion (intraepithelial, lamina propria, submucosa, muscularis mucosa, subserosa/mesoappendix, visceral peritoneum, adjacent structures).

If extra-appendiceal mucus is present, state if localized or diffuse (psuedomyxoma peritoneii) and if neoplastic epithelium is present in mucus.

d) Perforation (present/absent)

e) Lymph-vascular invasion or satellite peritumoural nodules (present/absent) (Irregular satellite peritumoural nodules are considered lymph-vascular tumour extension. Smooth contoured nodules are counted as lymph nodes.)

f) Resection margins: proximal (for appendectomy specimens), mesenteric margin (closest approach in mm.)

g) Lymph node status (x of y lymph nodes positive)

h) AJCC tumour stage (carcinoma)

Primary tumour (T)

Tis- Tumour limited to epithelium or lamina propria

T1- Tumour invades submucosa

T2- Tumour invades muscularis propria

T3- Tumour invades subserosa or mesoappendix

T4a- Tumour penetrates visceral peritoneum, including mucinous peritoneal tumour limited to right lower quadrant

T4b- Tumour directly invades other organs or structures

Regional lymph nodes (N)

NX- Regional lymph nodes cannot be assessed

NO- No regional lymph node metastasis

N1- Metastasis in 1 to 3 regional lymph nodes

N2- Metastases in 4 or more lymph nodes

Distant metastasis (M)

- M1a- Intraperitoneal metastasis beyond the right lower quadrant (including psuedomyxoma peritoneii)
- M1b- Non-peritoneal metastasis

AJCC tumour stage (carcinoid):

Primary tumour (T)*

- T1a- Tumour 1cm. or less in greatest dimension
- T1b- Tumour more than 1cm. but not more than 2cm.
- T2- Tumour more than 2cm. but not more than 4cm. or tumour with extension to the cecum
- T3- Tumour more than 4cm. or with extension to the ileum
- T4- Tumour directly invades other organs or structures

*Tumour size is the dominant local criterion for aggressive behavior, as opposed to depth of invasion. Perineural invasion by carcinoid is a common feature without prognostic significance

Regional lymph nodes (N)

- N0- No regional lymph node metastasis
- N1- Regional lymph node metastasis

Distant metastasis (M)

- M1- Distant metastasis

Extrahepatic Bile Duct Carcinoma

Microscopic diagnosis: Bile duct (common bile duct, right/left hepatic, common hepatic, cystic), segmental resection *or* pancreaticoduodenectomy specimen-

a) Positive for carcinoma, specify type (adenocarcinoma, papillary, mucinous, signet ring cell, squamous, small cell, biliary cystadenocarcinoma, other)

b) Histologic grade (well differentiated is >95% glandular pattern, moderately differentiated is 50% to 95% glandular pattern, poorly differentiated is <50% glandular pattern)

c) Tumour site (extra/intra-pancreatic common bile duct, right/left/common hepatic duct, cystic duct)

d) Greatest linear tumour dimension in cm.

e) Tumour extension (carcinoma in situ; confined to bile duct; invades beyond bile duct wall; invades duodenum, pancreas, gallbladder, or other adjacent organs or structures)

f) Margins: specify if involved by in situ or invasive tumour and distance to nearest margin in mm. (proximal bile duct, distal bile duct, gastric, duodenal, distal pancreatic, uncinate pancreatic/retroperitoneal)

g) Lymph-vascular invasion (present/absent). Perineural invasion adversely affects prognosis in univariate analysis, but may be present in both carcinoma and benign sclerosing cholangitis. Report when definitively present

h) Lymph node status (x of y positive)

i) Additional pathologic findings (sclerosing cholangitis, IBD, choledocal cyst, stones, Clonorchis sinensis infestation)

j) TNM Tumour stage

Primary tumour (T)

Tis- carcinoma in situ

T1- Tumour confined to bile duct

T2- Tumour invades beyond bile duct wall

T3- Tumour invades gallbladder, pancreas, duodenum, or other adjacent organs without involvement of celiac axis or superior mesenteric artery

T4- Tumour invades celiac axis or superior mesenteric artery

Regional lymph nodes (N)

NX- Regional lymph nodes cannot be assessed

NO- No regional lymph node metastasis

N1- Regional lymph node metastasis

Distant metastasis

M1- Distant metastasis

Bladder Carcinoma

Microscopic Diagnosis: Urinary Bladder, (transurethral resection/radical cystectomy or cystoprostatectomy)

- a) Positive for urothelial carcinoma (subtype, invasive/noninvasive)
- b) Tumour site(s) (single or multifocal)
- c) Greatest linear tumour dimension
- d) Tumour depth of invasion (lamina propria, submucosa, inner or outer half of muscularis propria, extravesical) * NOTE: Report should delineate, where possible, invasion into bladder lamina propria versus submucosa.
- e) Involvement of ureters, urethra, prostate or seminal vesicles
- f) Lymph-vascular invasion (present/absent)
- g) Histologic grade of invasive component (1,2,3)
- h) High grade flat carcinoma in situ (present/absent)
- i) Surgical margins: ureters, urethra, perivesical, periprostatic
- j) Lymph node status (if submitted)
- k) Prostate Gland (as per prostatectomy guidelines)

l) pTNM tumour stage

Primary Tumour (T)

- T1- tumour invades subepithelial connective tissue
- T2- tumour invades muscularis propria
- T3a- tumour invades perivesical tissue microscopically
- T3b- gross extravesical mass
- T4a- tumour invades prostate, uterus, vagina
- T4b- tumour invades pelvic wall

Regional Lymph Nodes

- NX- regional lymph nodes cannot be assessed
- NO- no regional lymph node metastasis
- N1- metastasis in single lymph node, 2cm. or less in greatest dimension
- N2- metastasis in single lymph node greater than 2cm. but less than 5cm. or multiple lymph nodes, none more than 5cm.
- N3- metastasis in one or more lymph node greater than 5cm.

Distant Metastasis (M)

- M1- distant metastasis

Breast Carcinoma

Microscopic Diagnosis: (Right/Left) Breast, (core biopsy, wire guided biopsy, segmental resection, mastectomy)

a) Invasive carcinoma, histologic type (see note below)

b) Greatest linear tumour dimension of invasive carcinoma (define gross or microscopic measurement: gross measurement is most accurate for multi-block tumour, microscopic for single-block tumour). Specify if multifocal

c) Extent of intraductal component (define: % of total tumour volume, type and nuclear grade (low, intermediate, high), with/without comedonecrosis). Note: AJCC only recognizes DCIS and LCIS (not DIN/LIN) for Tis classification

d) Nottingham Combined Histologic Grade of invasive carcinoma

Nuclear grade

- low = 1
- intermediate = 2
- high = 3

Mitotic rate

- <4/sq mm = 1 (low)
- 4-7/sq mm = 2 (intermediate)
- >7/sq mm = 3 (high)

Tubule formation

- >75% = 1 (high)
- 10-75% = 2 (intermediate)
- <10% = 3 (high)

Add points for each feature to obtain total score

- 3-5 points = well differentiated
- 6-7 points = moderately differentiated
- 8-9 points = poorly differentiated

e) Lymph-vascular invasion (identified/not identified); specify if dermal lymphatics are involved; specify if extensive

f) Surgical Margins (positive/negative/indeterminate); specify if in-situ or invasive carcinoma, orientation of positive margin, focal or extensive, and provide measurement of closest approach of nearest negative margins

g) Lymph node status (x of y lymph nodes positive for metastatic carcinoma, size of largest metastasis, with/without extranodal tumour spread) Note: Isolated Tumour Cell Cluster (ITC) is not greater than 0.2 mm; micrometastasis is 0.2-2.0 mm; metastasis is greater than 2.0 mm

h) Involvement of skin, nipple, or skeletal muscle by invasive carcinoma (present/absent)

i) Index microcalcifications (present/absent)

j) Status of background breast tissue (DIN, LIN, benign mass forming lesions)

k) Status of tissue biomarkers:

-Status of estrogen receptors (all invasive carcinomas and all resected in-situ carcinomas) and Allred score (0-8)

-Status of progesterone receptors (all invasive carcinomas)

-Status of Her2-neu expression (all invasive carcinomas)

Her2-neu expression is reported as negative (none, trace, or 1+), equivocal (2+ or 3+ in <30% of tumour cells), or positive (3+ in > 30% of tumour cells). All equivocal Her2-neu must be referred for FISH analysis.

-Ki-67 proliferative rate is reported as low (less than or equal to 10%) or high (greater than 10%, see note below)

l) pTNM tumour stage

Primary Tumour (T)

Tis- Carcinoma in situ (DCIS/LCIS)

T1mic- Microinvasion less than 1mm. in greatest dimension

T1a- Tumour more than 1mm. but not more than 5mm. in greatest dimension

T1b- Tumour more than 5mm. but not more than 1cm. in greatest dimension

T1c- Tumour more than 1cm. but not more than 2cm. in greatest dimension

T2- Tumour more than 2cm. but not more than 5cm. in greatest dimension

T3- Tumour more than 5cm. in greatest dimension

T4- Tumour of any size with direct extension in to chest wall or skin (note: pectoralis invasion is not considered chest wall invasion; simple dermal invasion without nodule formation or ulceration is not considered skin invasion)

T4a- Extension in to chest wall (intercostals or serratus muscles)

T4b- Edema or ulceration of breast skin or satellite skin nodules

T4c- Both T4a and T4b

T4d- Inflammatory carcinoma of breast

Regional Lymph Nodes (N)

NO- No regional lymph node metastasis

NO(i+)- ITCs detected by H&E or IHC, no deposit greater than 0.2 mm.

N1mi- Micrometastasis in ipsilateral axillary lymph node greater than 0.2 mm., none greater than 2 mm.

N1a- Metastasis in 1 to 3 axillary lymph nodes

N1b- Metastasis in internal mammary nodes detected by sentinel lymph node biopsy, not detected clinically

N1c- Metastasis in 1 to 3 axillary lymph nodes and internal mammary nodes, detected by sentinel lymph node biopsy, not detected clinically

N2a- Metastasis in 4 to 9 axillary lymph nodes

N2b- Metastasis in clinically apparent internal mammary lymph nodes with negative axillary lymph nodes

- N3a- Metastasis to 10 or more axillary lymph nodes or to any infraclavicular lymph nodes
- N3b- Metastasis in clinically apparent internal mammary lymph nodes and axillary lymph nodes
- N3c- Metastasis in supraclavicular lymph nodes

Distant Metastasis

- M1- Distant metastasis identified

*Note on tissue biomarkers and histologic classification:

The correlation of gene expression analysis and tissue biomarker studies by immunohistochemistry with the clinical course and response to therapy has modified our understanding of how breast carcinomas are most appropriately classified. While the traditional histologic divisions of ductal and lobular carcinoma are still of use, therapy is now predicated on tumour stage, grade, and categorization into one of four molecularly defined subtypes. These subtypes are well approximated by histologic and immunohistochemical means:

-Luminal A: grade low to intermediate; ER positive with high Allred score; Her2 negative; Ki-67 rate low (<10%); marginal benefit from systemic chemotherapy, high benefit from Tamoxifen/aromatase inhibitor therapy

-Luminal B: grade intermediate to high; ER positive with low Allred score; Her2 variable; Ki-67 rate high; responsive to systemic chemotherapy, variable response to Tamoxifen

-Her2 type: grade intermediate to high; ER negative; Her2 positive; Ki-67 rate high; responsive to trastuzumab and to systemic chemotherapy

-Basal type: grade high; ER/PR/Her2 negative; Ki-67 rate high; 75% are positive for either CK 5/6 or EGFR (other 25% tend to be of apocrine, squamous or metaplastic type); may be associated with a germline BRCA 1 mutation, responsive to systemic chemotherapy, no response to tamoxifen/aromatase inhibitors or trastuzumab

The Ki-67 proliferative rate aids in the distinction of these tumour types. It also is an independent, significant predictor of disease free survival. Many BC oncologists will consider information about the Ki-67 rate, along with tumour stage, grade, ER status and the patient's overall health, to help them define a group of patients who may reasonably choose to decline the adverse effects of systemic chemotherapy without adversely affecting outcome. Finally, recent surveys through the BCIPT program have demonstrated that the Ki-67 proliferative rate can be determined across BC laboratories with a high level of technical and interpretive reproducibility (87.4%). Therefore, the BCALP advocates the testing and reporting of Ki-67 proliferative rates, providing that laboratories monitor performance through the BCIPT program.

Cervical Carcinoma

Microscopic Diagnosis: Cervix, LEEP/cone excision; or cervix and parametrial tissues without uterus (radical trachelectomy); or Uterus, resection, with (radical hysterectomy) or without parametrial tissues; with or without pelvic lymph nodes:

- a) Cervical tumour cell type
- b) Grade of invasive carcinoma (typically assigned as G1, G2 or G3; there are no defined criteria for grading, it is not reproducible, and it isn't used to guide treatment)
- c) In situ component (present/absent)
- d) Depth and breadth of invasive component (see below for guidelines on measurement of depth of invasion). If possible, measure thickness of uninvolved cervical wall at point of deepest invasion.
- e) Lymph-vascular invasion (present/absent)
- f) Extension beyond cervix (parametrium, pelvic wall, vagina, bladder)
- g) Resection margins (**for cone biopsies specify**: ectocervical, endocervical or deep, with closest approach in mm; if mucosal margin is positive, state if it is positive for in situ or invasive disease)
- h) Lymph node status (number examined and number involved)
- i) pTNM tumour stage (note – FIGO stage, unlike TNM status, is assigned based on clinical criteria and cannot be assigned accurately by the pathologist)
Primary Tumor (T)
 - TX- Primary tumor cannot be assessed
 - To- No evidence of primary tumor
 - Tis- Carcinoma in situ
 - T1- Tumor confined to uterus
 - T1a- Invasive carcinoma diagnosed only by microscopy. All macroscopically visible lesions, even with superficial invasion, are T1b.
 - T1a1- Stromal invasion no greater than 3.0 mm in depth and 7.0 mm or less in horizontal spread
 - T1a2- Stromal invasion more than 3.0 mm and not more than 5.0 mm in depth, and 7.0 mm or less in horizontal spread (depth of invasion is measured from the stromal-epithelial junction, either glandular or surface, from which the tumor originates)
 - T1b- Macroscopically visible lesion confined to the cervix or microscopic lesion greater than pT1a2
 - T1b1- Tumor measures 4.0 cm or less in greatest dimension
 - T1b2- Tumor measures greater than 4.0 cm
 - T2- Tumor invades beyond uterus but not to pelvic wall or lower third of vagina
 - T2a- Without parametrial invasion

- T2a1- Tumour measures 4.0 cm or less in greatest dimension
- T2a2- Tumor measures greater than 4.0 cm
- T2b- With parametrial invasion
- T3- Tumor extends to pelvic wall and/or involves lower third of vagina and/or causes hydronephrosis or non-functioning kidney
- T3a- Tumor involves lower third of vagina, no extension to pelvic wall
- T3b- tumor extends to pelvic wall and/or causes hydronephrosis or non-functioning kidney
- T4- Tumor invades bladder or rectal mucosa and/or extends beyond true pelvis

Regional Lymph Nodes (N)

- NX- Regional lymph nodes cannot be assessed
- NO- No regional lymph node metastasis
- N1- Regional lymph node metastasis

Distant Metastasis (M)

- M1- Distant metastasis

Colon and Rectum

Microscopic Diagnosis: Colon, Rectum (specific site), resection (specify type)-

a) Positive for: adenocarcinoma (low grade or high grade); mucinous (colloid) carcinoma*; signet ring cell carcinoma*; “medullary” carcinoma**

*mucinous or signet ring cell components comprise >50% of tumour

**high grade tumours with a medullary growth pattern and numerous tumour infiltrating lymphocytes occurring in patients under 50 years of age are closely associated with hereditary non polyposis colon cancer syndromes and tumour cell microsatellite instability, with implications for family screening and chemotherapy response. These features should be noted if present

b) Tumour site (for rectal tumours, specify if above or below peritoneal reflection).

c) Greatest linear tumour dimension and fraction of bowel circumference involved by tumour

d) Tumour invasion (lamina propria, submucosa, muscularis propria, pericolic subserosal/perirectal adipose tissue, peritonealized serosa, adjacent organs or structures)

e) Surgical margins (proximal, distal, radial). Measure closest approach of tumour to radial margin in mm. (direct tumour extension within 1 mm or a positive lymph node at the radial margin are defined as positive).

f) Completeness of mesorectal excision specimen for rectal tumours (essentially complete with minimal defects/ incomplete with exposure of rectal muscularis propria).

g) Lymph-vascular invasion (present/absent, define if intramural or extramural)

h) Perineural invasion (present/absent)

i) Extramural tumour deposits (present/absent) - A tumor nodule in the pericolic/perirectal fat without evidence of residual lymph node tissue is classified as a tumor deposit and is not considered a positive lymph node. Such tumor deposits may represent discontinuous spread, lymph-vascular spread with extravascular extension, or totally replaced lymph nodes. In the absence of unequivocal lymph node metastases, tumor deposits are recorded as N1c

j) Lymph node status (x of y lymph nodes positive for metastatic carcinoma). See note*** below

k) Perforation (present/absent).

l) Status of noncarcinomatous mucosa (adenomas, CIBD, known hereditary polyposis syndromes).

m) K-RAS mutation status (if tested). Patients with advanced colorectal adenocarcinoma may be candidates for anti-EGFR therapy, if they have non-mutated codons 12 and 13 of K-RAS. If requested, a tumour tissue block should be referred for K-RAS genetic analysis and reported as “wild type” or “mutated”

n) pTNM tumour stage

Primary Tumour (T)

Tis- Tumour invades lamina propria

T1- Tumour invades submucosa

T2- Tumour invades muscularis propria

T3- Tumour invades colonic subserosa/ nonperitonealized perirectal tissues

T4a- Tumour penetrates visceral peritoneum (tumor present at the serosal surface with inflammatory reaction, mesothelial hyperplasia or erosion; or free tumor cells on the serosal surface with underlying erosion of the visceral peritoneum)

T4b- Tumour directly invades or is adherent to other organs or structures

Regional Lymph Nodes

NX- Regional lymph nodes cannot be assessed

No- No regional lymph node metastasis

N1a- Metastasis in 1 regional lymph node

N1b- Metastases in 2 or 3 regional lymph nodes

N1c- Tumour deposits in subserosa or pericolic/ perirectal soft tissues without regional lymph node metastasis

N2a- Metastases in 4 to 6 regional lymph nodes

N2b- Metastases in 7 or more regional lymph nodes

Distant Metastasis

M1a- Metastasis to a single organ or site

M1b- Metastases to more than one site or to the peritoneum

***A minimum of 12 lymph nodes are required to accurately predict pNO stage

Note Regarding Polypectomized Carcinomas: Within the colon and rectum, adenomas containing intramucosal carcinoma have no potential for metastasis but do require complete local resection. The risk of metastasis or local recurrence for invasive carcinoma in a malignant polyp treated by endoscopic removal alone is 10%-20%. Pathologic features associated with increased risk for an adverse outcome for a polypectomized carcinoma include: high tumour grade (poorly differentiated adenocarcinoma, signet ring cell carcinoma, small cell carcinoma); tumour less than 1mm. from the cauterized resection margin; small vessel invasion by tumour. These features should be reported.

Endometrial Carcinoma

Microscopic Diagnosis: Uterus (with or without tubes, ovaries), resection; with or without lymph nodes, peritoneal biopsies, or omentum

- a) Positive for (endometrioid, papillary serous, clear cell, etc.) adenocarcinoma
- b) FIGO tumour grade (for endometrioid or mucinous carcinomas)
 - 1 – 5% or less solid growth
 - 2 – 6-50% solid growth
 - 3 – more than 50% solid growth(Molecular growth excluded. High grade nuclei, defined as notable nuclear atypia or grade 3 atypia, appreciable at intermediate magnification, raises tumour grade by one. Serous and clear cell carcinomas are always grade 3.)
- c) Myometrial invasion: none, inner 1/2 of myometrium, outer 1/2 of myometrium (If possible, measure maximum depth of invasion and thickness of uninvolved myometrium at this site.)
- d) Lymph-vascular invasion (present/absent)
- e) Cervical involvement: absent, noninvasive i.e. mucosal involvement only, or invasive into cervical stroma
- f) Extrauterine spread, documenting site(s)
- g) Status of non-carcinomatous endometrium
- h) Lymph node status (if submitted), number examined and number involved
- i) pTNM tumour stage

Primary Tumor (T)

- T1- Tumor confined to corpus uteri
- T1a- Tumor limited to endometrium invades less than one-half of the myometrium
- T1b- Tumor invades one-half or more of the myometrium
- T2- Tumor invades cervix, with invasion of cervical stroma, but does not extend beyond uterus
- T3- Local and/or regional spread as specified in T3a and T3b
- T3a- Tumor involves serosa and/or adnexa (direct extension or metastasis)
- T3b- Involvement of vagina (direct extension or metastasis), parametrial tissues, rectal or bladder wall (without mucosal involvement), or pelvic wall(s) (frozen pelvis)
- T4- Tumor invades bladder mucosa and/or bowel mucosa

Regional Lymph Nodes (N)

- NX- Cannot be assessed
- NO- No regional lymph node metastasis
- N1- Regional lymph node metastasis to the pelvic lymph nodes

N2- Regional lymph node metastasis to para-aortic lymph nodes, with or without pelvic lymph node involvement

Distant Metastasis (M)

M1- Distant metastasis (includes metastasis to inguinal lymph nodes and/or abdominal lymph nodes other than para-aortic; excludes metastasis to vagina, pelvic serosa, or adnexa)

Esophageal Carcinoma

Microscopic Diagnosis: Esophagus, Resection:

- a) Positive for invasive (squamous, adeno, small cell) carcinoma (histologic grade)
- b) Primary tumour site- cervical esophagus, mid-esophagus, distal esophagus, esophago-gastric junction (EGJ). Adenocarcinoma arising at the EGJ or within the proximal 5cm of the stomach *and* involving the EGJ is staged as an esophageal tumour
- c) Longitudinal tumour dimension, semi-circumferential/ circumferential lesion
- d) Depth of invasion (lamina propria, muscularis mucosa, submucosa, muscularis propria, adventitia, adjacent structures)
- e) Lymph-vascular invasion (present/ absent)
- f) Surgical resection margin status (proximal, distal, radial; state if involved by dysplasia or invasive carcinoma; state closest approach of invasive carcinoma to margin in mm.)
- g) Treatment effect (post neo-adjuvant therapy, if applicable) (present/absent)
- h) Status of background mucosa (Barrett's mucosa, dysplasia)
- i) Lymph node status
- j) pTNM tumour stage

Primary Tumour (T)

- Tis- High grade dysplasia
- T1- Tumour invades lamina propria, muscularis mucosa (T1a) or submucosa (T1b)
- T2- Tumour invades muscularis propria
- T3- Tumour invades adventitia
- T4- Tumour invades adjacent structures

Regional lymph nodes (N)

- NO- No regional lymph node metastases
- N1- Regional lymph node metastasis in 1 or 2 nodes
- N2- Metastases in 3 to 6 node
- N3- Metastases in 7 or more nodes

Distant Metastasis (M)

- M1- Distant metastasis (specify site)

Gallbladder Carcinoma

Microscopic diagnosis: Gallbladder, resection (with hepatic duct, liver)-

- a) Positive for carcinoma, histologic type (adenocarcinoma, papillary carcinoma, intestinal, mucinous, signet ring cell, squamous, small cell, other)
 - b) Histologic grade (well, moderately, poorly differentiated)
 - c) Tumour site (body, neck, cystic duct)
 - d) Greatest linear tumour dimension in cm.
 - e) Tumour extension (invades: lamina propria, muscle layer, perimuscular connective tissue, penetrates visceral peritoneum, invades liver, invades extrahepatic bile ducts, invades adjacent organs and structures)
 - f) Lymph-vascular invasion (present/absent) Note: perineural invasion is common in gallbladder carcinoma and is associated with spread to the biliary tree, but may not have prognostic significance. Benign adenomyomatous hyperplasia may “invade” perineural spaces, reducing reproducibility.
 - g) Margins: cystic duct, perimuscular connective tissue, closest approach in mm.
 - h) Lymph node status (x of y lymph nodes positive)
 - i) TNM Tumour Stage
Primary tumour (T)
 - Tis- Carcinoma in situ
 - T1a- Tumour invades lamina propria
 - T1b- Tumour invades muscle layer
 - T2- Tumour invades perimuscular connective tissue, no extension beyond serosa or in to liver
 - T3- Tumour penetrates visceral peritoneum or invades liver and/or one more adjacent organ or structure
 - T4- Tumour invades portal vein, hepatic artery, or two or more extrahepatic organs or structures
- Regional lymph nodes (N)
- NX- Regional lymph nodes cannot be assessed
 - NO- No regional lymph node metastasis
 - N1- Metastasis to nodes along cystic duct, common bile duct, hepatic artery or portal vein
 - N2- Metastasis to periaortic, pericaval, celiac or mesenteric artery nodes
- Distant metastasis (M)
- M1- Distant metastasis (specify site)

Laryngeal Carcinoma

Microscopic Diagnosis: Larynx, radical laryngectomy

- a) Tumour type and grade (well, moderately, poorly differentiated)
- b) Tumour laterality (right, left, bilateral) and site (glottic, subglottic, supraglottic)*
- c) Tumour size (greatest dimension in cm.)
- d) Direct invasion of adjacent structures (supraglottis, subglottis, paraglottic space, pre-epiglottic space, vallecula, base of tongue, pyriform sinus): present/absent
- e) Invasion of laryngeal cartilage: present/absent/extent **
- f) Extralaryngeal spread: present/absent
- g) Lymph-Vascular invasion: present/absent
- h) Perineural invasion: present/absent
- i) Squamous cell carcinoma in-situ or squamous dysplasia: present/absent
- j) Surgical margin status and distance from margins in mm.
 1. Invasive carcinoma
 2. in-situ carcinoma, moderate/severe squamous dysplasia
- k) Lymph node status (site specific: submandibular; upper jugular; mid jugular; lower jugular; posterior cervical; juxtathyroid; paratracheal. Size of largest metastasis (<3 cm, 3-6 cm and >6 cm) and presence/absence of extranodal tumour spread should be mentioned.)

*Boundaries:

Supraglottis = tip of epiglottis and aryepiglottic folds to apex of ventricle

Glottis = apex of ventricle to 1 cm. below apex of ventricle

Subglottis= 1 cm below apex of ventricle to inferior rim of cricoid

**TNM stage:

Tumor stages T1 – T3 are dependent on the presence or absence of cord mobility (except for one definition of T3 is the presence of minor cartilage invasion, suggested to be less than 1/2 way through the cartilage). These parameters are clinically defined; hence pathological T staging is often not practical.

Lip/Oral Cavity/Pharynx

Microscopic Diagnosis: Lip/Oral Cavity/ Pharynx (specify site and laterality), excisional biopsy/ resection/ with lymph node dissection:

- a) Positive for squamous cell carcinoma (NOS, acantholytic, adenosquamous, basaloid squamous, papillary, spindle cell, verrucous, lymphoepithelial carcinoma). For nasopharynx, see below*
- b) Histologic grade (well, moderately, poorly differentiated)
- c) Greatest linear tumour dimension in cm.
- d) Tumor thickness: typically measured in mm. from the surface of the mucosa (without keratin layer in heavily keratinized tumors) or the surface of an ulcer to the deep margin (for oral/lip tumors less than 4 cm in greatest dimension)
- e) Surgical resection margin status (for invasive tumour and moderate/severe) squamous dysplasia: positive or negative (with distance to closest margin in mm.)
- f) Lymph-vascular invasion (present/absent)
- g) Perineural invasion (present/absent)
- h) Lymph node status: number of lymph nodes involved and their levels, size of largest lymph node (<3 cm, 3-6 cm, >6 cm**) and presence or absence of extranodal tumor spread
- i) For oropharyngeal carcinomas: HPV status (p16 immunohistochemistry or in situ hybridization for HPV DNA)

*Classification for nasopharyngeal carcinomas:

- i. Keratinizing squamous cell carcinoma (WHO-1)
- ii. Non-keratinizing carcinoma
 - Differentiated carcinoma (WHO-2)
 - Undifferentiated carcinoma (WHO-3)

**For the purposes of planning post-operative radiotherapy following neck dissection, lymph nodes greater than 3.0 cm are considered to have extranodal tumor spread, even if this is not demonstrated histologically. These patients are typically given adjuvant radiotherapy.

Liver- Hepatocellular Carcinoma

Microscopic diagnosis: Liver, (wedge, partial, total) resection-

a) Positive for (well, moderately, poorly differentiated; or fibrolamellar) hepatocellular carcinoma

b) Tumour focality (solitary or multiple)

c) Greatest linear tumour dimension in cm.

d) Tumour extension: confined to liver, invasion of portal vein, invasion of single or multiple branches of hepatic vein, penetrates visceral peritoneum, invades gallbladder, invades adjacent organs

e) Lymph-vascular invasion: macroscopic (large vessel) present/absent; microscopic (small vessel) present/absent

f) Resection margins: parenchymal margin positive or negative (closest approach in mm.); large vessel margin (if vessel invasion present)

g) Status of non-malignant liver: chronic hepatitis, cirrhosis, alcoholic liver disease, hemochromatosis

h) pTNM tumour stage:

Primary tumour (T)

T1- Solitary tumour without vascular invasion

T2- Solitary tumour with vascular invasion or multiple tumours none more than 5cm.

T3a- Multiple tumours more than 5cm.

T3b- Single or multiple tumours of any size involving a major branch of portal or hepatic veins

T4- Tumour with perforation of visceral peritoneum or with direct invasion of any adjacent organs other than the gallbladder

Regional lymph nodes (N)

NX- Cannot be assessed

NO- No regional lymph node metastasis

N1- Regional lymph node metastasis

Distant metastasis (M)

M1- Distant metastasis

Lung Carcinoma

Microscopic Diagnosis: Right/Left Lung, (wedge resection, segmentectomy, lobectomy, bilobectomy, pneumonectomy)-

- a) Positive for carcinoma, specify type (WHO Histologic Classification of Lung Tumours): See notes below*
- b) Tumour site: (upper, middle, lower lobe)
- c) Tumour focality: unifocal; separate tumour nodules, same lobe; separate tumour nodules, different lobes; multiple synchronous carcinomas**
- d) Greatest single tumour dimension in cm.
- e) Histologic grade: well (G1)/ moderately (G2)/ poorly (G3) differentiated, undifferentiated (G4). Note: by definition, squamous cell and adenocarcinomas are G1-G3, undifferentiated small cell and large cell carcinomas are G4
- f) Visceral pleural invasion: present/ absent. Note: visceral pleural invasion is present when tumour has penetrated the thicker of the two elastic laminae, typically the external layer
- g) Tumour extension: limited to bronchial wall; tumour invades main bronchus 2 cm. or more distal to carina; tumour invades main bronchus less than 2 cm. distal to carina; tumour invades carina; tumour invades parietal pleura, chest wall, diaphragm, mediastinal pleura, mediastinum, pericardium, heart, great vessels, trachea, esophagus, vertebral bodies or phrenic nerve
- h) Resection margins: bronchial (positive/negative for invasive/in situ carcinoma); vascular; parenchymal (staple margin of wedge, segmentectomy or lobectomy; peribronchial connective tissue margin of lobectomy or pneumonectomy); parietal pleural/chest wall; other attached tissue. If all margins negative give distance to nearest margin in mm.
- i) TNM tumour stage
Primary Tumour (T)
 - T1a- tumour 2cm or less in greatest dimension, surrounded by visceral pleura, not involving the main bronchus; or superficial spreading carcinoma of any size with invasive component limited to the bronchial wall, which may involve main bronchus
 - T1b- tumour greater than 2cm. but not more than 3cm. surrounded by visceral pleura, not involving the main bronchus
 - T2a- tumour more than 3 cm but not more than 5cm. not involving the main bronchus; or tumour 5cm. or less with involvement of the main bronchus 2cm. or more distal to the carina or with invasion of the visceral pleura or with obstructive pneumonitis involving the hilar region
 - T2b- tumour greater than 5cm. but not more than 7cm. in greatest dimension

- T3- tumour greater than 7cm. or tumour of any size that invades chest wall, diaphragm, phrenic nerve, mediastinal pleura or pericardium; or tumour of any size in the main bronchus within 2cm of the carina without involvement of the carina; or tumour associated with obstructive pneumonitis of the entire lung; or tumour of any size with a separate tumour nodule in the same lung
- T4- tumour of any size invading the mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve; esophagus, vertebral body, carina; or with separate tumour nodules in a different lobe of the ipsilateral lung

Regional Lymph Nodes (N)

- NX- regional lymph nodes cannot be assessed
- N0- no regional lymph node metastasis
- N1- metastasis in ipsilateral peribronchial or hilar lymph, and intrapulmonary nodes, including direct invasion by primary tumour
- N2- metastasis to ipsilateral mediastinal or subcarinal lymph nodes
- N3- Metastasis to contralateral mediastinal or hilar lymph nodes or to any scalene or supraclavicular lymph nodes

Distant Metastasis

- M1a- tumour nodule in contralateral lung; or tumour nodules within pleura; or malignant pleural or pericardial effusion
- M1b- distant metastasis outside of the lung or pleura

*Certain chemotherapeutic agents may be indicated for non-squamous cell lung carcinomas. Non-small cell carcinomas should be sub-classified as adenocarcinoma or squamous carcinoma whenever possible. Many adenocarcinomas are responsive to tyrosine kinase inhibitors. In cases where this distinction is not obvious by histology an immunohistochemical panel of TTF-1, p63 and CK5/6 has been recommended. A TTF-1 (+), p63 (-), CK5/6 (-) profile favours adenocarcinoma while a TTF-1 (-), p63 (+), CK5/6 (+) profile favours squamous carcinoma. It is recognized that a small percentage of non-small cell carcinomas will not be definitively segregated by this panel. Mucin stains are also recommended in this context.

Oncologists may request PCR-based EGFR mutational analysis (exons 19 and 21) to predict the responsiveness of an adenocarcinoma to tyrosine kinase inhibitors. These studies are currently available at the British Columbia Cancer Agency. The analysis is typically performed on formalin-fixed tissue; the entire block must be submitted as unstained slides or paraffin scrolls are insufficient.

Report papillary subtypes of adenocarcinoma – many of these have mutations of EGFR and are sensitive to tyrosine kinase inhibitors

Report micropapillary subtypes of adenocarcinoma – these have been identified as having worse outcomes compared to other adenocarcinomas of the same stage.

Report “mucinous bronchoalveolar cell” type of adenocarcinoma – these do not have EGFR mutations but harbor K-ras mutations; these tumours are not sensitive to tyrosine kinase inhibitors, which may be detrimental if administered.

**Histologic criteria for distinguishing separate synchronous primaries from multiple tumour nodules include: physically distinct tumours of different histologic types; or

histologically similar tumours arising from in situ lesions without evidence of common lymphatic spread and without extrapulmonary metastasis. Synchronous tumours are staged separately: report the highest T category followed by the number of tumours in parentheses

Ovarian Carcinoma

Microscopic Diagnosis: (right/left) Ovary, resection (or TAH-BSO)

a) Positive for (endometrioid, serous, mucinous, clear cell) carcinoma
(Borderline tumours, malignant germ cell tumors and malignant sex cord-stromal tumors are reported using the same guidelines.)

b) Tumour Grade: Grade assignment differs with different tumor cell types:

- Serous carcinomas – MD Anderson grading system
- Clear cell carcinomas – all are considered to be grade 3
- Mucinous carcinomas – Silverberg or WHO grading system
- Endometrioid carcinomas – Silverberg or WHO grading system, or FIGO endometrial carcinoma grading system

I. MD Anderson grading system (used for serous carcinomas only)

-Nuclear variation greater than 3:1 – high grade

-Nuclear variation less than or equal to three to one – low grade

*For problematic cases use mitotic activity to assign to low vs. high grade; if more than 12 mitoses per 10 HPF then high grade

II. Silverberg grading system

-Nuclear score - 1, 2, 3

-Mitotic score - <10 per 10 hpf = 1

- 10-24 per 10 hpf = 2

- 25 or more per 10 hpf = 3

-Architecture score - glandular = 1

- papillary = 2

- solid = 3

-Total score: 3-5 = Grade 1

-6-7 = Grade 2

-8-9 = Grade 3

III. WHO grading system

-G1 - well differentiated

-G2 - moderately differentiated

-G3 - poorly differentiated (tumors with minimal differentiation seen in very small foci)

c) Ovarian surface involvement (present/absent)

d) Tumour capsule intact/ruptured

e) Ovarian involvement unilateral/bilateral

f) Extraovarian spread (define sites of implants, for serous borderline tumors only, note whether the implants are invasive or non-invasive; size of implants)

g) Status of peritoneal washings (if known)

h) Lymph node status (if submitted); number examined and number involved

i) pTNM tumour stage

Primary Tumor (T)

TX- Cannot be assessed

T0- No evidence of primary tumor

T1- Tumor limited to ovaries (1 or both)

T1a- Tumor limited to 1 ovary; capsule intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings

T1b- Tumor limited to both ovaries; capsule intact, no tumor on ovarian surface. No malignant cells in ascites or peritoneal washings

T1c- Tumor limited to 1 or both ovaries with any of the following: capsule ruptured, tumor on ovarian surface, malignant cells in ascites or peritoneal washings

T2- Tumor involves 1 or both ovaries with pelvic extension and/or implants

T2a- Extension and/or implants on uterus and/or tube(s). No malignant cells in ascites or peritoneal washings

T2b- Extension to other pelvic tissues. No malignant cells in ascites or peritoneal washings

T2c- Pelvic extension and/or implants (T2a or T2b) with malignant cells in ascites or peritoneal washings

T3- Tumor involves 1 or both ovaries with microscopically confirmed peritoneal metastasis outside the pelvis (including liver capsule metastasis) and/or regional lymph node metastasis

T3a- Microscopic peritoneal metastasis beyond pelvis

T3b- Macroscopic peritoneal metastasis beyond pelvis 2 cm or less in greatest dimension

T3c- Peritoneal metastasis beyond pelvis more than 2 cm in greatest dimension and/or regional lymph node metastasis

Regional Lymph Nodes (N)

pNX- Cannot be assessed

pNo- No regional lymph node metastasis

pN1- Regional lymph node metastasis

Distant Metastasis (M)

pM1- Distant metastasis (including liver parenchymal metastasis and/or positive pleural fluid cytology)

Pancreas (Exocrine and Endocrine) Carcinoma

Microscopic Diagnosis:

Pancreas, (partial pancreatectomy/ pancreaticoduodenectomy)-

- a) Positive for carcinoma, specify type: ductal adenocarcinoma, mucinous adenocarcinoma (non-cystic), signet ring cell, anaplastic, osteoclastic giant cell, acinar cell, mucinous cystic neoplasm, intraductal papillary mucinous carcinoma, well differentiated endocrine tumour, poorly differentiated endocrine carcinoma
- b) Tumour site: head, body, tail, uncinate process (specify if multifocal)
- c) Greatest linear tumour dimension in cm.
- d) Tumour grade (well differentiated, poorly differentiated)
- e) Lymph-vascular invasion (present/absent)
- f) Perineural invasion (present/absent)
- g) Tumour extension: carcinoma in situ, confined to pancreas, invasion of ampulla or common bile duct, invasion of duodenal wall, invasion of peripancreatic soft tissues, invasion of adjacent organs or structures
- h) Surgical resection margins: common bile duct, uncinate process (retroperitoneal) margin, proximal and distal pancreas (partial pancreatectomy) with approach to closest margin in mm.
- h) Lymph node status
- i) Endocrine cell neoplasms only: tumour mitotic rate per 10hpf and spontaneous tumour necrosis (present/absent). These parameters correlate with malignant potential
- j) pTNM tumour stage
Primary Tumour (T)
 - T1- Tumour limited to pancreas, 2cm. or less in greatest dimension
 - T2- Tumour limited to pancreas more than 2 cm. in greatest dimension
 - T3- Tumour extends beyond pancreas but does not involve celiac axis or superior mesenteric artery
 - T4- Tumour invades celiac axis or superior mesenteric artery (unresectable)Regional Lymph Nodes (N)
 - N0- No regional lymph node metastasis
 - N1- Regional lymph node metastasisDistant Metastasis
 - M1- Distant metastasis

Penis for Squamous Carcinoma

Microscopic Diagnosis: Penis, resection

- a) Positive for invasive squamous cell carcinoma

- b) Tumour site (urethra, foreskin, glans, shaft)

- c) Tumour grade (well, moderately, poorly differentiated, or verrucous)

- d) Tumour extension: subepithelial connective tissue, tunica albuginea, corpus spongiosum, corpus cavernosum, urethra

- e) Lymph-vascular invasion (present/absent)

- f) In situ component (present/absent/extent, multifocal)

- g) Surgical margins: urethra, corpora, skin; define if positive for in situ or invasive disease

- h) Lymph node status

- i) Status of non-neoplastic epithelium (condyloma, inflammatory process)

- j) pTNM tumour stage

Primary Tumour (T)

- T1- tumour invades subepithelial connective tissue
- T2- tumour invades corpus spongiosum or cavernosum
- T3- tumour invades urethra or prostate
- T4- tumour invades other adjacent structures

Regional Lymph Nodes (N)

- NX- regional lymph nodes cannot be assessed
- NO- no regional lymph node metastases
- N1- metastasis to a single superficial inguinal lymph node
- N2- metastasis to multiple or bilateral superficial inguinal lymph nodes
- N3- metastasis to deep inguinal or pelvic lymph node(s)

Distant Metastasis (M)

- M1- distant metastasis

Prostate Needle Biopsies

Microscopic Diagnosis: Prostate, needle biopsy (or biopsies xN)*

- a) Positive for prostatic adenocarcinoma
- b) Gleason primary and secondary grade and score
- c) Number of and location of cores involved (if multiple at one site)
- d) Greatest single linear tumour dimension (confluent growth) or percentage involved
- e) Lymph-vascular space invasion (present/not identified)
- f) Extraprostatic fat involvement (present/not identified)
- g) High Grade PIN (report if present only)

*Use these same criteria for reporting TUPR specimens. Substitute number of chips involved (eg. 4 of 20 chips positive) for linear tumour dimension. Report prostatic urothelium and seminal vesicle status, if present.

Gleason Grading (omit if treatment effect evident)

- 1) Single, separate uniform glands closely packed, with definite edge.
- 2) Single, separate uniform glands loosely packed, with irregular edge.
- 3) Single, separate, scattered glands (very small or uniform) or smoothly circumscribed Papillary/cribriform masses.
- 4) Fused glands with ragged infiltration, with or without large pale cells (hypernephroid).
- 5) Solid masses with any necrosis (comedocarcinoma) or anaplastic raggedly infiltrating.

Gleason Score

Predominant pattern plus the worst of any additional patterns.

If only one pattern is seen, the grade is doubled to arrive at score.

Prostatectomy for Carcinoma

Microscopic Diagnosis: Prostate, radical resection

- a) Positive for prostatic adenocarcinoma
- b) Gleason primary and secondary grades and total score (omit if treatment effect evident)
- c) Sites involved (peripheral/transitional zone; single or both lobes; apex, mid or bladder base)
- d) Greatest single tumour dimension
- e) Estimated percent of gland involvement
- f) Tumour extension: limited to gland, extraprostatic extension (focal or established), seminal vesicles
- g) Lymph-vascular invasion or perineural invasion
- h) Surgical margins: peripheral, apex, bladder neck (define: mm. of involvement, type of tissue involved – capsule/soft tissue)
- i) Lymph node status (x of y positive, site specific)
- j) Status of non-malignant prostate (PIN)
- k) Status of prostatic urothelium (if abnormal)
- l) pTNM tumour stage

Primary Tumour (T)

- T1- There is no pathologic T1 classification
- T2a- unilateral, one-half of one lobe or less
- T2b- unilateral, more than one-half of lobe
- T2c- bilateral
- T3a- extraprostatic extension (focal or established*) or microscopic invasion of bladder neck
- T3b- invasion of seminal vesicle
- T4- invasion of rectum, levator muscles, and/or pelvic wall

Regional Lymph Nodes (N)

- NX- regional nodes not sampled
- NO- no positive regional nodes
- N1- metastases in regional nodes

Distant Metastasis (M)

M1a- metastasis in non-regional lymph node

M1b- bone metastasis

M1c- metastasis in another site

*Focal extraprostatic extension: involving less than 1 HPF in 1 or 2 sections

Established extraprostatic extension: more than focal

Renal Carcinoma

Microscopic Diagnosis: (Right/Left) Kidney, (segmental, simple, radical) resection-

- a) Positive for renal cell carcinoma, histologic subtype
- b) Tumour site(s) (pole, mid region, capsule, multiple)
- c) Greatest tumour dimension in cm.
- d) Nuclear grade (Fuhrman)
 - Grade 1- round nuclei: nucleoli visible only at x 400 magnification
 - Grade 2- slightly irregular nuclei; nucleoli visible at x 200 magnification
 - Grade 3- irregular nuclei; nucleoli visible at x 100 magnification
 - Grade 4- enlarged pleomorphic nuclei or giant cells
- e) Tumour extension (capsular perforation, renal sinus fat, adrenal, renal vein or segmental branches, IVC)
- f) Surgical margins (perinephric, hilar vascular, ureteric)
- g) Lymph- vascular invasion
- h) Lymph node status (if submitted)
- i) Status of non-malignant renal tissue
- j) pTNM tumour stage

Primary Tumour (T)

- T1a- tumour 4 cm or less in greatest dimension, limited to kidney
- T1b- tumour greater than 4cm but not more than 7cm, limited to kidney
- T2a- tumor more than 7cm but not more than 10cm, limited to kidney
- T2b- tumor more than 10cm, limited to kidney
- T3a- tumor grossly extends into renal vein or segmental branches; or tumor invades perirenal and/or renal sinus fat, but not beyond Gerota's fascia
- T3b- Tumor grossly extends into vena cava below the diaphragm
- T3c- tumour grossly extends into vena cava above diaphragm or invades wall of vena cava
- T4- tumour invades beyond Gerota's fascia (including contiguous extension into adrenal gland)

Regional Lymph Nodes (N)

- NX- regional lymph nodes cannot be assessed
- NO- no regional lymph node metastasis
- N1- metastasis in a single regional lymph node
- N2- metastasis in multiple regional lymph nodes

Distant Metastasis (M)
M1- distant metastasis

Soft Tissue Sarcoma

Microscopic Diagnosis: Soft tissue of (site), (resection/biopsy)-

- a) Sarcoma type
- b) Tumour grade (French system- see below*)
- c) Greatest linear tumour dimension in cm.
- d) Tumour depth: “superficial” if confined to skin and/or subcutis, “deep” if invades the fascia separating subcutis from deeper structures or if deep to this fascia, and “retroperitoneal” if in deep tissues of the retroperitoneal compartment
- e) Surgical resection margin: positive, microscopically positive, or negative
- f) Closest surgical margin and composition (fascia / periosteum, muscle, fibrofatty tissue)
- g) If closest margin is fascia / periosteum, provide second closest margin and composition
- h) Lymph-vascular invasion, if present; bone invasion, if present
- i) Approximate % of tumor that is viable vs. necrotic, along with a comment as to whether this is spontaneous or following neoadjuvant radiation and/or chemotherapy, if known
- j) TNM Tumour Stage
 - Primary tumour (T)
 - T1- Tumour 5cm. or less in greatest dimension
 - T1a- Superficial tumour
 - T1b- Deep tumour
 - T2- Tumour more than 5cm. in dimension
 - T2a- Superficial tumour
 - T2b- Deep tumour
 - Regional lymph nodes (N)
 - NX- Regional lymph nodes cannot be assessed
 - NO- No regional lymph node metastasis
 - N1- Regional lymph node metastasis
 - Distant Metastasis (M)
 - M1- Distant metastasis

*French grading system (Trojani or FNCLCC system): total of scores for differentiation, necrosis, and mitosis

-Differentiation score

-Close resemblance to adult tissue = 1

-Clearly malignant, but tumour type recognized by histology alone = 2

-Pleomorphic or undifferentiated sarcoma = 3 (small blue round cell tumors, as well as nonpleomorphic spindle cell tumors of uncertain histiogenesis such as synovial sarcoma, clear cell sarcoma, epithelioid sarcoma, and alveolar soft part sarcoma score as 3 by convention)

-Necrosis score

-None = 0

<50% = 1

≥50% = 2

-Mitotic score

0-9 per 10 hpf = 1

10-19 per 10 hpf = 2

20 or more per 10 hpf = 3

-Total score

2,3 = Grade 1 = low grade

4,5 = Grade 2 = high grade

6,7,8 = Grade 3 = high grade

Skin- Melanoma

Microscopic Diagnosis: Skin of (site), (biopsy/excision)

- a) Positive for invasive malignant melanoma, (histologic type)
- b) Breslow depth (mm, from top of granular layer)
- c) Ulceration (present/absent)
- d) Mitotic figures / square mm*
- e) Satellitosis (present/absent)
- f) Lymph-vascular or perineural space invasion (present/absent)
- g) Margins of excision (positive/negative, measurement of closest approach in special circumstances)
- h) Lymph node status (if applicable)
- i) pTNM Tumour stage

Primary Tumor (T)

- TX Primary tumor cannot be assessed (e.g., shave biopsy or regressed melanoma)
- To No evidence of primary tumor
- Tis Melanoma in situ
- T1a Melanoma ≤ 1.0 mm in thickness, no ulceration, <1 mitosis / mm²
- T1b Melanoma ≤ 1.0 mm in thickness with ulceration and/or 1 or more mitoses/mm²
- T2a Melanoma 1.01-2.0 mm in thickness, no ulceration
- T2b Melanoma 1.01-2.0 mm in thickness, with ulceration
- T3a Melanoma 2.01-4.0 mm in thickness, no ulceration
- T3b Melanoma 2.01-4.0 mm in thickness, with ulceration
- T4a Melanoma > 4.0 mm in thickness, no ulceration
- T4b Melanoma > 4.0 mm in thickness, with ulceration

Regional Lymph Nodes (N)

- NX Regional lymph nodes cannot be assessed
- No No regional lymph node metastasis
- N1 Metastasis in a single regional node
- N1a Clinically occult (microscopic) metastasis
- N1b Clinically apparent (macroscopic) metastasis
- N2 Metastasis in 2 – 3 regional nodes, or intralymphatic regional metastasis without nodal metastases
- N2a Clinically occult (microscopic) metastasis
- N2b Clinically apparent (macroscopic) metastasis
- N2c Satellite or in-transit metastasis without nodal metastasis

N3 Metastasis in 4 or more regional nodes, or matted metastatic nodes, or in-transit metastasis or satellite(s) with metastasis in regional node(s)

Distant Metastasis (M)

M1a Distant metastasis to skin, subcutaneous tissues or lymph nodes

M1b Metastasis to lung

M1c Metastasis to all other visceral sites or distant metastasis at any site associated with an elevated serum lactic dehydrogenase (LDH)

* For an Olympus BH2 microscope 1 square mm = 5hpf. In tumours where the invasive component is less than 1 mm² in area, an attempt should be made to extrapolate a rate per mm².

Skin- Squamous Cell Carcinoma

Microscopic Diagnosis: Skin of (site), (biopsy/excision)

- a) Tumour grade (well, moderately, poorly differentiated)
- b) Maximum tumour thickness (mm) measured from the granular layer of the overlying skin
- c) Invasion of subcutaneous tissues (present/absent)
- d) Vascular or perineural space invasion (present/absent)
- e) In-situ component, including actinic keratosis (present/absent)
- f) Surgical margins (peripheral, deep)
- g) Lymph node status
- h) pTNM tumour stage

Primary Tumor (T)

pTis- Carcinoma in situ

pT1- Tumour 2 cm or less in greatest dimension with less than two high risk features*

pT2- Tumour > 2 cm in greatest dimension, or any size with two or more high risk features*

pT3- Tumour with invasion of maxilla, mandible, orbit or temporal bone

pT4- Tumour with direct or perineural invasion of skull base or axial skeleton

Regional Lymph Nodes (N)

NX- Regional lymph nodes cannot be assessed

No- No regional lymph node metastasis

N1- Metastasis in a single ipsilateral node 3 cm or less in greatest dimension

N2- Metastasis in a single ipsilateral node, more than 3 cm but not more than 6 cm in greatest dimension (N2a); or in multiple ipsilateral nodes none more than 6 cm in greatest dimension (N2b); or in bilateral or contralateral nodes none more than 6 cm in greatest dimension (N2c)

N3- Metastasis in a node more than 6 cm in greatest dimension

Distant Metastasis (M)

M1- Distant metastasis

* High-risk features used in upstaging from T1 to T2 include site on the ear or mucosa of the lip, thickness of 4mm or more, invasion of subcutaneous tissues, poor differentiation, or vascular or perineural space invasion.

Small Intestine

Microscopic Diagnosis: Small Intestine (site)-

a) Positive for (well, moderately, poorly) differentiated adenocarcinoma (intestinal, mucinous, signet ring cell type)

b) Tumour site

c) Longitudinal tumour dimension and fraction of bowel circumference involved by tumour.

d) Depth of invasion (lamina propria, submucosa, muscularis propria, periintestinal soft tissues, peritonealized serosa, adjacent structures). Measure radial distance of tumour extension beyond muscularis propria in mm.

e) Surgical margins (proximal, distal, radial). Measure closest approach of tumour to radial margin in mm.

f) Lymph-vascular invasion (present/absent).

g) Lymph node status (x of y lymph nodes positive for metastatic carcinoma)

*Any mesenteric tumour deposit with a rounded contour counts as a replaced lymph node. Stellate deposits are defined as angiolymphatic tumour spread.

h) Perforation (present/absent).

i) Status of noncarcinomatous mucosa (adenomas, Crohn's disease, celiac disease, polyposis syndromes).

j) pTNM tumour stage

Primary Tumour (T)

T1a- Tumour invades lamina propria

T1b- Tumour invades submucosa

T2- Tumour invades muscularis propria

T3- Tumour invades subserosa or non-peritonealized perimuscular tissues with extension beyond muscularis of 2cm. or less

T4a- Tumour penetrates visceral peritoneum

T4b- Tumour directly invades other organs or structures

Regional Lymph Nodes

NX- Regional lymph nodes cannot be assessed

NO- No regional lymph node metastasis

N1- Metastasis in 1 to 3 regional lymph nodes

N2- Metastasis in 4 or more regional lymph nodes

Distant Metastasis

M1- Distant metastasis

Stomach Carcinoma

Microscopic Diagnosis: Stomach, (total/ distal/ proximal) resection:

a) Positive for (well, moderately, poorly) differentiated adenocarcinoma, histologic type: intestinal, diffuse, tubular, mucinous*, signet ring cell*
(*tumours that exhibit >50% mucinous or signet ring component)

b) Tumour location proximal (cardia** and body) or distal (antrum)
(**tumours occurring in the proximal 5cm of stomach and involving the esophago-gastric junction are staged as esophageal carcinomas)

c) Greatest longitudinal tumour dimension

d) Depth of invasion (lamina propria, muscularis mucosa, submucosa, muscularis propria, subserosal adipose tissue, visceral peritoneum, extension into adjacent organs)

e) Resection margins (proximal, distal, radial; distance to nearest margin in mm)

f) Lymph-vascular invasion (present/absent)

g) Lymph node status (x of y lymph nodes positive for metastatic carcinoma). Any mesenteric tumour deposit with a rounded contour counts as a replaced lymph node. Stellate deposits are defined as angiolymphatic tumour spread.

h) Status of non-carcinomatous mucosa (gastritis, intestinal metaplasia, dysplasia).

i) pTNM tumour stage

Primary Tumour (T)

T1- Tumour invades lamina propria or submucosa

T2a- Tumour invades muscularis propria

T2b- Tumour invades subserosa

T3- Tumour penetrates visceral peritoneum

T4- Tumour invades visceral peritoneum or adjacent structures

T4a- Tumour invades visceral peritoneum

T4b- Tumour invades adjacent structures (specify)

Regional Lymph Nodes (N)

N0- No regional lymph node metastasis

N1- Metastasis in 1 to 2 regional lymph nodes

N2- Metastasis in 3 to 6 regional lymph nodes

N3- Metastasis in 7 or more regional lymph nodes

Distant Metastasis (M)

M1- Distant metastasis

Testis for Germ Cell Tumour

Microscopic Diagnosis: (Right/Left) Testis, radical orchidectomy

- a) Positive for (germ cell tumour type)
- b) Tumour size
- c) Tumour extension (limited to testis, epididymis, or tunica albuginea; tumour invades tunica vaginalis; tumour invades spermatic cord; tumour invades scrotum)
- d) Lymph-vascular invasion (present/absent; non seminomatous GCT only)
- e) Estimated percent of different germ cell components (mixed GCT only)
- f) Surgical margins (peritesticular, adnexal structures, spermatic cord)
- g) Status of lymph nodes (if submitted)
- h) Status of non-neoplastic testis: spermatogenesis, intratubular germ cell neoplasm
- i) TNM tumour stage

Primary Tumour (T)

- T0- No evidence of primary tumour (histologic scar only)
- T1- tumour limited to testis, epididymis, or tunica albuginea without vascular invasion or invasion of tunica vaginalis
- T2- tumour limited to testis, epididymis with vascular invasion or invasion of tunica vaginalis
- T3- tumour invades spermatic cord, with or without vascular invasion
- T4- tumour invades scrotum

Regional Lymph Nodes (N)

- NX- regional lymph nodes cannot be assessed
- N0- no regional lymph node metastasis
- N1- lymph node metastasis, less than 2 cm, in 5 or fewer lymph nodes
- N2- lymph node metastasis greater than 2 cm but not more than 5 cm; or more than 5 positive lymph nodes, none greater than 5cm; or evidence of extranodal extension or tumor
- N3- lymph node metastasis greater than 5cm. in greatest dimension

Distant Metastasis (M)

- M1- distant metastasis

Thyroid Carcinoma

Microscopic Diagnosis: Thyroid, (right/left lobe or total) resection

- a) Positive for (papillary/follicular/medullary/other) carcinoma*
- b) Tumour location (or locations if multicentric)
- c) Greatest linear tumour dimension in cm.
- d) Encapsulation (complete/incomplete/absent); w/wo invasion
- e) Extrathyroidal extension (present/absent, include measurement)
- f) Lymph-vascular invasion**
- g) Surgical margins (if positive, include measurement)
- h) Lymph node status (ipsilateral, midline, bilateral, mediastinal)
- i) Status of non-neoplastic thyroid (thyroiditis, nodular hyperplasia)
- j) pTNM tumour stage

Primary Tumour (T)

TX- Primary tumor cannot be assessed

T0- No evidence of primary tumor

T1- Tumor 2 cm or less in greatest dimension, limited to the thyroid

T2 Tumor larger than 2 cm but 4 cm or smaller in greatest dimension, limited to the thyroid

T3- Tumor larger than 4 cm in greatest dimension limited to the thyroid or any tumor with minimal extrathyroid extension (e.g., extension to sternothyroid muscle or perithyroid soft tissues)

T4a- Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve

T4b- Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels

Note- all anaplastic carcinomas are considered T4 tumors.

T4a- Intrathyroidal anaplastic carcinoma—surgically resectable

T4b- Extrathyroidal anaplastic carcinoma—surgically unresectable

Regional lymph nodes (N)

Regional lymph nodes include the central compartment, lateral cervical, and upper mediastinal lymph nodes.

NX- Regional lymph nodes cannot be assessed

N0- No regional lymph node metastasis

N1- Regional lymph node metastasis

N1a- Metastasis to level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes)

N1b- Metastasis to unilateral or bilateral cervical or superior mediastinal lymph nodes

Distant metastases (M)

M1- Distant metastasis

***Tumor type**

Several variants of papillary carcinoma have been described with either better (encapsulated) or worse (tall cell, diffuse sclerosing, columnar) prognosis than conventional papillary carcinoma. However, the prognostic difference in some of these tumor types is related more to differences in size and extent of invasion.

****Lymph-vascular invasion**

Encapsulated follicular carcinomas are diagnosed based on capsular and/or vascular invasion. The vessels of interest are either in the capsule or outside of the tumor, and the presence of vascular invasion (including number of vessels) should always be recorded.

Vulva (non-melanoma)

Microscopic Diagnosis: Vulva, (partial, simple, radical) resection; with or without lymph nodes

a) Vulvar tumour cell type

b) Tumour grade for squamous cell carcinomas (well, moderately, poorly differentiated); invasive adenocarcinoma (Paget's disease) is not graded

c) Depth of invasion and greatest tumour dimension (gross measurement)
The depth of invasion is defined as the distance of the tumor from the epithelial-stromal junction of the most superficial dermal papilla to the deepest point of invasion, in mm.

d) Lymph-vascular space invasion (present/absent)

e) In-situ component (present/absent)

f) Extension to extra-vulvar sites (mention if present)

g) Surgical margins (peripheral, deep, vaginal; define whether positive for in situ or invasive disease)

h) Lymph node status; number examined, number involved. If two or fewer involved nodes, provide size of nodal metastases; indicate whether there is extracapsular extension by tumor.

i) Status of non-neoplastic mucosa (condyloma)

j) TNM tumour stage

Primary Tumor (T)

To- No evidence of primary tumor

Tis- Carcinoma in situ

T1- Tumor confined to vulva or vulva and perineum, is 2.0 cm or less in greatest dimension, and stromal invasion is present and measures less than or equal to 1.0 mm.

T2- Tumor confined to vulva or vulva and perineum and measures more than 2.0 cm or invades more than 1.0 cm

T3- Tumor invades any of the following: lower urethra, vagina, and anus

T4- Tumor invades any of the following: bladder mucosa, rectal mucosa, upper urethral mucosa; or is fixed to the pubic bone

Regional Lymph Nodes (N)

NX- Regional lymph nodes cannot be assessed

NO- No regional lymph node metastasis

- N1- 1 lymph node metastasis greater than or equal to 5 mm or 2 lymph node metastasis with both less than 5 mm
- N2- 2 or more lymph node metastases that are greater than or equal to 5 mm, or 3 or more lymph node metastases that are all less than 5mm
- N3- Lymph node metastasis with extra capsular spread
- N4- Fixed or ulcerated femoral-inguinal lymph nodes

Distant Metastasis (M)

- M1- Distant metastasis