COLLEGE of AMERICAN PATHOLOGISTS

Protocol for the Examination of Radical Orchiectomy Specimens From Patients With Malignant Germ Cell and Sex Cord-Stromal Tumors of the Testis

Version: Testis Radical Orchiectomy 4.0.1.2 **Protocol Posting Date:** August 2019

CAP Laboratory Accreditation Program Protocol Required Use Date: May 2020

Includes pTNM requirements from the 8th Edition, AJCC Staging Manual

For accreditation purposes, this protocol should be used for the following procedures AND tumor types:

Procedure	Description
Radical Orchiectomy	Includes specimens designated orchiectomy and orchidectomy
Tumor Type	**Description**
Germ cell tumors	Includes seminoma and variants, all non-seminomatous germ cell tumors, mixed germ cell tumors, Leydig cell tumors, Sertoli cell tumors, granulosa cell tumors, and placental site trophoblastic tumors
Sex cord-stromal tumors	Includes Leydig cell tumors, Sertoli cell tumors, granulosa cell tumors, and mixed sex cord tumors

This protocol is NOT required for accreditation purposes for the following:

Procedure
Retroperitoneal lymphadenectomy (consider Testis Retroperitoneal Lymphadenectomy protocol)
Primary resection specimen with no residual cancer (eg, following neoadjuvant therapy)
Cytologic specimens

The following tumor types should NOT be reported using this protocol:

Tumor Type
Paratesticular malignancies (consider Soft Tissue protocol)
Non-testis germ cell tumors (consider Extragonadal Germ Cell protocol)
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)
Sarcoma (consider the Soft Tissue protocol)

Authors
Gladell P. Paner, MD*; Satish K. Tickoo, MD*; Ming Zhou, MD, PhD*; Robert Allan, MD; Mahul B. Amin, MD; Sam S. Chang, MD; Peter A. Humphrey, MD, PhD; James McKiernan, MD; Jason Pettus, MD; Victor E. Reuter, MD; John R. Srigley, MD; Thomas M. Ulbright, MD
With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.
* *Denotes primary authors. All other contributing authors are listed alphabetically.*

Accreditation Requirements
This protocol can be utilized for a variety of procedures and tumor types for clinical care purposes. For accreditation purposes, only the definitive primary cancer resection specimen is required to have the core and conditional data elements reported in a synoptic format.

- Core data elements are required in reports to adequately describe appropriate malignancies. For accreditation purposes, essential data elements must be reported in all instances, even if the response is "not applicable" or "cannot be determined."
- Conditional data elements are only required to be reported if applicable as delineated in the protocol. For instance, the total number of lymph nodes examined must be reported, but only if nodes are present in the specimen.
- Optional data elements are identified with "+" and although not required for CAP accreditation purposes, may be considered for reporting as determined by local practice standards.

The use of this protocol is not required for recurrent tumors or for metastatic tumors that are resected at a different time than the primary tumor. Use of this protocol is also not required for pathology reviews performed at a second institution (ie, secondary consultation, second opinion, or review of outside case at second institution).

Synoptic Reporting
All core and conditionally required data elements outlined on the surgical case summary from this cancer protocol must be displayed in synoptic report format. Synoptic format is defined as:

- Data element: followed by its answer (response), outline format without the paired "Data element: Response" format is NOT considered synoptic.
- The data element should be represented in the report as it is listed in the case summary. The response for any data element may be modified from those listed in the case summary, including "Cannot be determined" if appropriate.
- Each diagnostic parameter pair (Data element: Response) is listed on a separate line or in a tabular format to achieve visual separation. The following exceptions are allowed to be listed on one line:
    - Anatomic site or specimen, laterality, and procedure
    - Pathologic Stage Classification (pTNM) elements
    - Negative margins, as long as all negative margins are specifically enumerated where applicable
- The synoptic portion of the report can appear in the diagnosis section of the pathology report, at the end of the report or in a separate section, but all Data element: Responses must be listed together in one location

Organizations and pathologists may choose to list the required elements in any order, use additional methods in order to enhance or achieve visual separation, or add optional items within the synoptic report. The report may have required elements in a summary format elsewhere in the report IN ADDITION TO but not as replacement for the synoptic report i.e. all required elements must be in the synoptic portion of the report in the format defined above.

Summary of Changes

Version 4.0.1.2
Updated Note G Serum Markers

Surgical Pathology Cancer Case Summary

Protocol posting date: August 2019

TESTIS: Radical Orchiectomy

Select a single response unless otherwise indicated.

Specimen Laterality
___ Right
___ Left
___ Not specified

Tumor Focality
___ Unifocal
___ Multifocal
___ Cannot be determined

Tumor Size
Greatest dimension of main tumor mass (centimeters): ___ cm
+ Additional dimensions: ___ x ___ cm

Greatest dimensions of additional tumor nodules (centimeters) (required only if applicable): ___ cm[#]
___ Cannot be determined (explain): _____

[#]*Note: Include additional greatest dimensions for additional nodules as necessary*

Histologic Type (Notes A, B, and C)

Intratubular Germ Cell Neoplasia
___ Germ cell neoplasia in situ (GCNIS)
___ Other intratubular germ cell tumor (specify): _____

Seminoma
___ Seminoma
___ Seminoma with syncytiotrophoblastic cells

Non-seminomatous types
___ Embryonal carcinoma
___ Yolk sac tumor, postpubertal type
___ Choriocarcinoma
___ Mixed germ cell tumor
- ___ Seminoma (specify percentage): _____%
- ___ Embryonal carcinoma (specify percentage): _____%
- ___ Yolk sac tumor, postpubertal type (specify percentage): _____%
- ___ Choriocarcinoma (specify percentage): _____%
- ___ Teratoma (specify percentage): _____%
- ___ Other (specify type and percentage): _____%

Non-Choriocarcinomatous Trophoblastic Tumor
___ Non-choriocarcinomatous trophoblastic tumor, NOS
___ Placental site trophoblastic tumor
___ Epithelioid trophoblastic tumor
___ Cystic trophoblastic tumor

Teratoma
___ Teratoma, postpubertal type
___ Teratoma with somatic-type malignancy (specify type): _____

Testicular Scar/Regressed Germ Cell Tumor
___ Scar diagnostic of regressed germ cell tumor
___ Scar suspicious for regressed germ cell tumor

Germ Cell Tumors Unrelated to Germ Cell Neoplasia in situ
___ Spermatocytic tumor
___ Spermatocytic tumor with a sarcomatous component
+ ___ Teratoma, prepubertal type
    + ___ Well-differentiated neuroendocrine tumor (monodermal teratoma)
    + ___ Other (specify): _____

Sex Cord-Stromal Tumor
___ Leydig cell tumor
___ Leydig cell tumor, malignant
___ Sertoli cell tumor, NOS
___ Sertoli cell tumor, malignant
___ Sertoli cell tumor, large cell calcifying
___ Sertoli cell tumor, intratubular large cell hyalinizing
___ Granulosa cell tumor, adult type
___ Granulosa cell tumor, juvenile type
___ Fibroma-thecoma
___ Sex cord-stromal tumor, mixed type (specify components and approximate percentages): _____
___ Sex cord-stromal tumor type, unclassified

Tumor Containing Both Germ Cell and Sex Cord-Stromal Elements
___ Mixed germ cell-sex cord stromal tumor, gonadoblastoma

___ Other histologic type not listed, (specify): _____

Tumor Extension (select all that apply) (Note D)
___ No evidence of primary tumor
___ Germ cell neoplasia in situ only
___ Tumor limited to testis
___ Tumor invades rete testis[#]
___ Tumor invades hilar soft tissue
___ Tumor invades epididymis
___ Tumor invades through tunica albuginea and perforates tunica vaginalis (mesothelial layer)
___ Tumor invades spermatic cord
___ Tumor invades scrotum
___ Tumor invades other structures (specify): _____
___ Cannot be assessed

[#] *See Note D for definition of rete testis invasion.*

Margins

Spermatic Cord Margin
___ Cannot be assessed
___ Uninvolved by tumor
___ Involved by tumor

Other Margin(s) (required only if applicable)
___ Cannot be assessed
___ Uninvolved by tumor (specify margin(s)): _____
___ Involved by tumor (specify margin(s)): _____

Lymphovascular Invasion (Note E)
___ Not identified
___ Present
___ Cannot be determined

Regional Lymph Nodes
___ No lymph nodes submitted or found

Lymph Node Examination (required only if lymph nodes are present in the specimen)

Number of Lymph Nodes Involved: _____
___ Number cannot be determined (explain): _____
Specify Site(s) (if applicable): _____
Note: Sites may include interaortocaval, paraaortic, paracaval, preaortic, precaval, retroaortic, retrocaval, or other lymph nodes.

Lymph Node Metastasis (required if any lymph nodes are involved)
Size of Largest Lymph Node (or Nodal Mass) Involved (centimeters): ___ cm

+ Size of Largest Metastatic Deposit (centimeters): ___ cm
+ Specify Site: _____

Extranodal Extension
___ Not identified
___ Present
___ Cannot be determined

Histologic subtype of germ cell tumor in involved lymph nodes (if applicable, specify): _____

Number of Lymph Nodes Examined: _____
___ Number cannot be determined (explain): _____

Pathologic Stage Classification (pTNM, AJCC 8th Edition) (Note F)
Note: Reporting of pT, pN, and (when applicable) pM categories is based on information available to the pathologist at the time the report is issued. Only the applicable T, N, or M category is required for reporting; their definitions need not be included in the report. The categories (with modifiers when applicable) can be listed on 1 line or more than 1 line.

TNM Descriptors (required only if applicable) (select all that apply)
___ m (multiple)
___ r (recurrent)
___ y (posttreatment)

Primary Tumor (pT)
___ pTX: Primary tumor cannot be assessed
___ pT0: No evidence of primary tumor
___ pTis: Germ cell neoplasia in situ
___ pT1: Tumor limited to testis (including rete testis invasion) without lymphovascular invasion
___ pT1a: Tumor smaller than 3 cm in size[#]
___ pT1b: Tumor 3 cm or larger in size[#]
___ pT2: Tumor limited to testis (including rete testis invasion) with lymphovascular invasion OR Tumor invading hilar soft tissue or epididymis or penetrating visceral mesothelial layer covering the external surface of tunica albuginea with or without lymphovascular invasion
___ pT3: Tumor directly invades spermatic cord soft tissue with or without lymphovascular invasion
___ pT4: Tumor invades scrotum with or without lymphovascular invasion

[#] *Subclassification of pT1 applies only to pure seminoma*

Regional Lymph Nodes (pN)
___ pNX: Regional lymph node cannot be assessed
___ pN0: No regional lymph node metastasis
___ pN1: Metastasis with a lymph node mass 2 cm or smaller in greatest dimension and less than or equal to five nodes positive, none larger than 2 cm in greatest dimension
___ pN2: Metastasis with a lymph node mass larger than 2 cm but not larger than 5 cm in greatest dimension; or more than five nodes positive, none larger than 5 cm; or evidence of extranodal extension of tumor
___ pN3: Metastasis with a lymph node mass larger than 5 cm in greatest dimension

Distant Metastasis (pM) (required only if confirmed pathologically in this case)
___ pM1: Distant metastasis
___ pM1a: Nonretroperitoneal nodal or pulmonary metastases
___ pM1b: Nonpulmonary visceral metastases

Specify site(s), if known: _____

+ Pre-Orchiectomy Serum Tumor Markers (select all that apply) (Notes F and G)
+ ___ Unknown
+ ___ Serum marker studies within normal limits
+ ___ Alpha-fetoprotein (AFP) elevation
+ ___ Beta subunit of human chorionic gonadotropin (b-hCG) elevation
+ ___ Lactate dehydrogenase (LDH) elevation

+ Post-Orchiectomy Serum Tumor Markers (select all that apply) (Notes F and G)
+ ___ Unknown
+ ___ Serum marker studies within normal limits
+ ___ Alpha-fetoprotein (AFP) elevation
+ ___ Beta subunit of human chorionic gonadotropin (b-hCG) elevation
+ ___ Lactate dehydrogenase (LDH) elevation

+ Serum Tumor Markers (S) (Note G)
+ ___ SX: Serum marker studies not available or performed
+ ___ S0: Serum marker study levels within normal limits

	LDH		HCG (mIU/mL)		AFP (ng/mL)
+ ___ S1:	<1.5 X N[#]	and	<5,000	and	<1,000
+ ___ S2:	1.5-10 X N	or	5,000-50,000	or	1,000-10,000
+ ___ S3:	>10 X N	or	>50,000	or	>10,000

[#] *N indicates the upper limit of normal for the LDH assay.*

+ Additional Pathologic Findings (select all that apply) (Note H)

+ ___ None identified
+ ___ Germ cell neoplasia in situ (GCNIS)
+ ___ Microlith
+ ___ Sertoli cell nodule (Pick's adenoma)
+ ___ Atrophy
+ ___ Other (specify): _____

+ Comment(s)

Explanatory Notes

A. Tissues Submitted for Microscopic Evaluation
The entire testicular tumor may be blocked if it requires 10 blocks or less (tissue may be retained for special studies); 10 blocks of larger tumors may be taken, unless the tumor is greater than 10 cm, in which case 1 block may be submitted for every 1 cm of maximum tumor dimension. Blocks must contain the interface with nontumorous testis, as well as the tunica albuginea, even away from the tumor, because lymphatic invasion is best appreciated in the peritumoral tissue, as well as in the vessels within and under/parallel to the tunica. When there are multifocal tumors (with greater than or equal to 2 separate tumor nodules), additional tumor nodule(s) should also be sampled. Tissues to be sampled include:

- Tumor, including interface with surrounding testis, and tunica albuginea
- All of the grossly different appearing areas in the tumor
- Testicular hilum/mediastinum testis
- Uninvolved testis, including tunica albuginea
- Epididymis
- Spermatic cord, including cord margin
- Other lesion(s)
- All identifiable lymph nodes[#]
- Other tissue(s) submitted with specimen

[#] *For large masses that have obliterated individual nodes, 1 section for every centimeter of maximum tumor dimension, including grossly different looking areas, is recommended.*

The margins in a specimen resected for a malignant tumor of the testis, depending on the extent of the surgery, include spermatic cord margin, the parietal layer of tunica vaginalis, and scrotal skin.

B. Histologic Type
The protocol mainly applies to malignant tumors of the testis, the vast majority of which are of germ cell origin. It may also be applied to other malignant or potentially malignant tumors of the testis included in the classification shown below.[1-12] For hematolymphoid neoplasms involving the testis, refer to the corresponding CAP protocols.

World Health Organization (WHO) Histologic Classification of Testicular Tumors (2016)[13]

Germ Cell Tumors Derived From Germ Cell Neoplasia In Situ
Noninvasive germ cell neoplasia
- Germ cell neoplasia in situ
- Specific forms of intratubular germ cell neoplasia

Tumors of a single histologic type (pure forms)
- Seminoma
- Seminoma with syncytiotrophoblastic cells

Nonseminomatous germ cell tumors
- Embryonal carcinoma
- Yolk sac tumor, postpubertal type
- Trophoblastic tumors
  - Choriocarcinoma
  - Nonchoriocarcinomatous trophoblastic tumors
  - Placental site trophoblastic tumor
  - Epidermoid trophoblastic tumor
  - Cystic trophoblastic tumor
- Teratoma, postpubertal type
- Teratoma with somatic-type malignancy

Nonseminomatous germ cell tumors of more than one histologic type
- Mixed germ cell tumor

Germ cell tumors of unknown type
- Regressed germ cell tumor

Germ Cell Tumors Unrelated to Germ Cell Neoplasia In Situ
Spermatocytic tumor
Teratoma, prepubertal type
- Dermoid cyst
- Epidermoid cyst
- Well-differentiated neuroendocrine tumor (monodermal teratoma)
- Yolk sac tumor, prepubertal type

Mixed teratoma and yolk sac tumor, prepubertal type
York sac tumor, prepubertal type

Sex Cord-Stromal Tumors
Pure tumors
Leydig cell tumor
- Malignant Leydig cell tumor

Sertoli cell tumor
- Malignant Sertoli cell tumor
- Large cell calcifying Sertoli cell tumor
- Intratubular large cell hyalinizing Sertoli cell neoplasia

Granulosa cell tumor
- Adult granulosa cell tumor
- Juvenile granulosa cell tumor

Tumors in the fibroma-thecoma group
Mixed and unclassified sex cord stromal tumor
- Mixed sex cord-stromal tumor
- Unclassified sex cord-stromal tumor

Tumor Containing Both Germ Cell and Sex Cord-Stromal Elements
Gonadoblastoma

Miscellaneous
Ovarian epithelial-type tumors
- Serous cystadenoma
- Serous tumor of borderline malignancy
- Serous cystadenocarcinoma
- Mucinous cystadenoma
- Mucinous borderline tumor
- Mucinous cystadenocarcinoma
- Endometrioid adenocarcinoma
- Clear cell adenocarcinoma
- Brenner tumor

Juvenile xanthogranuloma
Hemangioma

Hematolymphoid Tumors
Diffuse large B-cell lymphoma
Follicular lymphoma
Extranodal NI/T-cell lymphoma, nasal type
Plasmacytoma
Myeloid sarcoma
Rosai-Dorfman disease

Tumors of Collecting Duct and Rete Testis
Adenoma
Adenocarcinoma

Tumors of Paratesticular Structures
Adenomatoid tumor
Mesothelioma
    Well-differentiated papillary mesothelioma
Epididymal tumors
    Cystadenoma of the epididymis
    Papillary cystadenoma
    Adenocarcinoma of the epididymis
Squamous cell carcinoma
Melanotic neuroectodermal tumor
Nephroblastoma
Paraganglioma

Mesenchymal Tumors of the Spermatic Cord and Testicular Adnexa
Apipocytic tumors
    Lipoma
    Well-differentiated liposarcoma
    Dedifferentiated liposarcoma
    Myxoid liposarcoma
    Pleomorphic liposarcoma

References

1. Lawrence WD, Young RH, Scully RE. Sex cord-stromal tumors. In: Talerman A, Roth LM, eds. *Pathology of the Testis and Its Adnexa.* New York, NY: Churchill Livingstone; 1986:67-92.
2. Proppe KH, Scully RE. Large-cell calcifying Sertoli cell tumor of the testis*. Am J Clin Pathol*. 1980;74:607-619.
3. Young RH, Talerman A. Testicular tumors other than germ cell tumors*. Semin Diagn Pathol*. 1987;4:342-360.
4. Kim I, Young RH, Scully RE. Leydig cell tumors of the testis: a clinicopathological analysis of 40 cases and review of the literature*. Am J Surg Pathol*. 1985;9:177-192.
5. Mostofi FK, Price EBJ. *Tumors of the Male Genital System: Atlas of Tumor Pathology*. 2nd series. Fascicle 8. Washington DC: Armed Forces Institute of Pathology; 1973.
6. Eble JN, Sauter G, Epstein JI, Sesterhenn IA. *World Health Organization Classification of Tumours*: *Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs.* Lyon, France: IARC Press; 2004.
7. Mostofi FK, Spaander P, Grigor K, Parkinson CM, Skakkebaek NE, Oliver RT. Consensus on pathological classifications of testicular tumours*. Prog Clin Biol Res*. 1990;357:267-276.
8. Young RH, Scully RE. *Testicular Tumors.* Chicago, IL: ASCP Press; 1990.
9. Ulbright TM. Testicular and paratesticular tumors. In: Mills SE, ed. *Sternberg's Diagnostic Surgical Pathology.* 4th ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2004:2167-2232.
10. Ulbright TM, Amin MB, Young RH. *Tumors of the Testis, Adnexa, Spermatic Cord, and Scrotum.* Third Series. Fascicle 25. Washington, DC: Armed Forces Institute of Pathology; 1999.
11. Ro JY, Dexeus FH, El-Naggar A, Ayala AG. Testicular germ cell tumors: clinically relevant pathologic findings. *Pathol Annu*. 1991;26:59-87.
12. Ferry JA, Harris NL, Young RH, Coen J, Zietman A, Scully RE. Malignant lymphoma of the testis, epididymis, and spermatic cord: a clinicopathologic study of 69 cases with immunophenotypic analysis. *Am J Surg Pathol*. 1994;18:376-390.
13. Moch H, Humphrey PA, Ulbright TM, Reuter VE. *WHO Classification of Tumours of the Urinary System and Male Genital Organs.* Geneva, Switzerland: WHO Press; 2016.

C. Scar

Testicular scars, particularly in patients presenting with metastatic disease and clinically inapparent testicular primaries, may represent regressed, "burnt-out" testicular germ cell tumors. There are 2 established criteria to indicate a scar is diagnostic of a regressed germ cell tumor (GCT): a scar with associated germ cell neoplasia in situ (GCNIS) or a scar that contains coarse intratubular calcifications within expanded tubular profiles, which correspond to dystrophic calcifications that occurred in completely necrotic intratubular embryonal carcinoma.

Features that are suspicious for, although not diagnostic of, regressed germ cell tumors include testicular atrophy, microlithiasis, and, in the scar, lymphoplasmacytic infiltrates and prominent vascularity.[1] In otherwise pure seminoma, such partial regression may have clinically important implications, since it is possible that some of these scars may represent regression of a nonseminomatous germ cell tumor component of the tumor.

References

1. Balzer BL, Ulbright TM. Spontaneous regression of testicular germ cell tumors: an analysis of 42 cases. *Am J Surg Pathol.* 2006;30(7):858-865.

D. Invasion of the Rete Testis, Hilar/Mediastinal Soft Tissue, Epididymis or Tunica Vaginalis

Tumors invading the tunica vaginalis (perforating the mesothelial lining) (Figure 1, Tumor A) are considered category pT2 by the American Joint Committee on Cancer (AJCC) TNM staging system. Invasion of rete testis is not assigned a higher pT category than that for a tumor limited to the testis. Rete testis invasion has been reported by some to be associated with higher risk of relapse in clinical stage I seminoma.[1] Rete testis invasion is that the invasive tumor involves the rete testis stroma, with or without luminal involvement. Pagetoid extension of GCNIS into the rete testis should not be considered rete testis invasion. Hilar soft tissue invasion (Figure 1, Tumor B) is the predominant pathway of extratesticular extension for testicular tumors.[2,3] There is evidence beginning to accumulate that rete testis and hilar soft tissue invasion have predictive value for metastatic disease in patients with nonseminomatous GCTs.[3] *Invasion of epididymis and hilar soft tissue is staged as pT2 by the 8th edition of AJCC TNM.* [4]

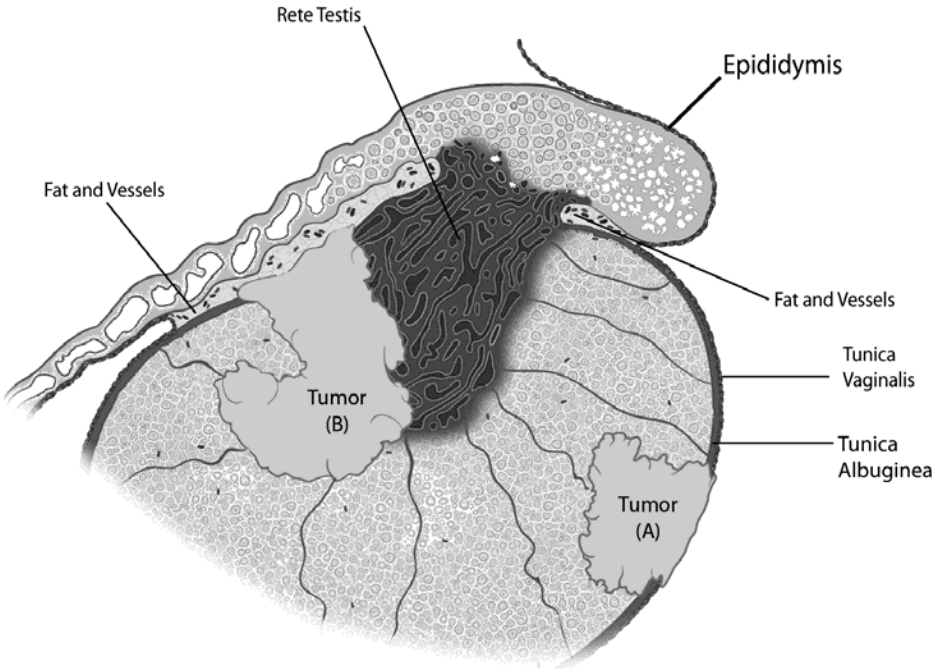

Figure 1. Diagrammatic representation of a tumor (Tumor A) invading tunica vaginalis, perforating through the mesothelium, and another tumor (Tumor B) partly involving the rete testis and invading the hilar soft tissue. Figure courtesy of Satish K. Tickoo, MD.

1. Warde P, Specht L, Horwich A, Oliver T, Panzarella T, Gospodarowicz M, von der Maase H. Prognostic factors for relapse in stage I seminoma managed by surveillance: a pooled analysis. *J Clin Oncol.* 2002;20:4448-4452.
2. Dry SM, Renshaw AA. Extratesticular extension of germ cell tumors preferentially occurs at the hilum. *Am J Clin Pathol.* 1999;111:534-538.
3. Yilmaz A, Cheng T, Zhang J, Trpkov K. Testicular hilum and vascular invasion predict advanced clinical stage in nonseminomatous germ cell tumors. *Mod Pathol.* 2013;26(4):579-586.

4. Amin MB, Edge SB, Greene FL, et al, eds. *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017.

E. Venous/Lymphatic Vessel Invasion

In several studies, the presence of vascular space invasion (usually lymphatic but possibly also capillary or venous invasion) has been correlated with a significantly elevated risk for distant metastasis.[1-7] This observation, therefore, is most pertinent for patients who have clinical stage I disease, ie, those who have no evidence of spread beyond the testis by clinical examination (including radiographic and serum marker studies). Some clinicians manage the patients with clinical stage I disease who lack evidence of lymphatic or vascular invasion in their orchiectomy specimens (with possibly other favorable prognostic features, such as relatively small amounts of embryonal carcinoma) by close follow-up examinations rather than intervention.

According to the 8th edition AJCC TNM staging system, discontinuous involvement of the spermatic cord soft tissue via a vascular thrombus is better regarded as a metastatic deposit (pM1). Presence of only an intravascular tumor in the spermatic cord in the absence of parenchymal invasion is considered pT2.[8]

References

1. Jacobsen GK, Rorth M, Osterlind K, et al. Histopathological features in stage I non-seminomatous testicular germ cell tumours correlated to relapse: Danish Testicular Cancer Study Group. *APMIS*. 1990;98:377-382.
2. Marks LB, Rutgers JL, Shipley WU, et al. Testicular seminoma: clinical and pathological features that may predict para-aortic lymph node metastasis*. J Urol*. 1990;143:524-527.
3. Hoeltl W, Pont J, Kosak D, Honetz N, Marberger M. Treatment decision for stage I non-seminomatous germ cell tumours based on the risk factor “vascular invasion.” *Br J Urol*. 1992;69:83-87.
4. Sesterhenn IA, Weiss RB, Mostofi FK, et al. Prognosis and other clinical correlates of pathologic review in stage I and II testicular carcinoma: a report from the Testicular Cancer Intergroup Study. *J Clin Oncol*. 1992;10:69-78.
5. Horwich A, Alsanjari N, A’Hern R, Nicholls J, Dearnaley DP, Fisher C. Surveillance following orchidectomy for stage I testicular seminoma*. Br J Cancer*. 1992;65:775-778.
6. Sturgeon JF, Jewett MA, Alison RE, et al. Surveillance after orchidectomy for patients with clinical stage I nonseminomatous testis tumors. *J Clin Oncol*. 1992;10:564-568.
7. Moul JW, McCarthy WF, Fernandez EB, Sesterhenn IA. Percentage of embryonal carcinoma and of vascular invasion predicts pathological stage in clinical stage I nonseminomatous testicular cancer. *Cancer Res*. 1994;54:362-364.
8. Amin MB, Edge SB, Greene FL, et al, eds. *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017.

F. Staging

The protocol recommends staging according to the AJCC TNM staging system.[1] Additional criteria for staging seminomas according to a modification of the Royal Marsden system are also recommended.[2] Some studies suggest that the staging of patients with seminoma by the TNM system is less meaningful therapeutically than staging by a modification of the Royal Marsden method. Also, the data from a large Danish study of seminomas clinically limited to the testis do not support the conclusion that local staging of the primary tumor, as performed in the TNM system, provides useful prognostic information; rather, the most valuable prognostic indicator was the size of the seminoma.[3] This protocol therefore encourages the use of the TNM system with optional use of the modified Royal Marsden staging system for patients with seminoma.

AJCC TNM and Stage Groupings

By AJCC convention, the designation “T” refers to a primary tumor that has not been previously treated. The symbol “p” refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

TNM Descriptors
For identification of special cases of TNM or pTNM classifications, the "m" suffix and "y," "r," and "a" prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The "m" suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The "y" prefix indicates those cases in which classification is performed during or following initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a "y" prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The "y" categorization is not an estimate of tumor prior to multimodality therapy (ie, before initiation of neoadjuvant therapy).

The "r" prefix indicates a recurrent tumor when staged after a documented disease-free interval and is identified by the "r" prefix: rTNM.

The "a" prefix designates the stage determined at autopsy: aTNM.

References
1. Amin MB, Edge SB, Greene FL, et al, eds. *AJCC Cancer Staging Manual.* 8th ed. New York, NY: Springer; 2017.
2. Thomas G, Jones W, VanOosterom A, Kawai T. Consensus statement on the investigation and management of testicular seminoma 1989*. Prog Clin Biol Res*. 1990;357:285-294.
3. von der Maase H, Specht L, Jacobsen GK, et al. Surveillance following orchidectomy for stage I seminoma of the testis. *Eur J Cancer*. 1993;29A:1931-1934.

G. Serum Markers
The protocol emphasizes the importance of relevant clinical information in the pathologic evaluation of specimens. Serum marker studies play a key role in the clinical management of patients with testicular germ cell tumors.[1-3] The occurrence of elevated serum levels of alpha-fetoprotein (AFP) or the beta subunit of human chorionic gonadotropin (b-hCG) may indicate the need for additional sections of certain specimens if the initial findings do not account for such elevations. Information regarding serum marker status (lactate dehydrogenase [LDH], AFP, and b-hCG) is also important in the "S" categorization of the tumor for stage groupings. Postorchiectomy serum markers are important for the assignment of stage IS.

The serum tumor markers (S) category comprises the following:
- Alpha fetoprotein (AFP) – half-life 5 to 7 days
- Human chorionic gonadotropin (hCG) – half-life 1 to 3 days
- Lactate dehydrogenase (LDH)

References
1. Chisolm GG. Tumour markers in testicular tumours. *Prog Clin Biol Res*. 1985;203:81-91.
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H. Additional Pathologic Findings
Important findings include Leydig cell hyperplasia, which may be correlated with b-hCG elevation; scarring, the presence of hemosiderin-laden macrophages, and coarse intratubular calcifications in expanded tubular profiles

(distinct from microlithiasis), which may indicate regression of a tumor; testicular atrophy; sertoli cell nodules (Pick's adenoma), which most often are associated with undescended testes, and abnormal testicular development (eg, dysgenesis or androgen-insensitivity syndrome).[1,2]

References
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I. Metastatic Tumor

Often the most important distinction in patients with metastatic testicular germ cell tumor following initial chemotherapy is the differentiation of metastatic residual teratoma from nonteratomatous types of germ cell tumor. Pure teratomatous metastasis is generally treated by surgical excision alone, whereas patients who have other residual germ cell tumor components are usually treated with additional chemotherapy.