# Neoplasia of the Testis - Orchidectomy Histopathology Reporting Guide

ICCR

Family/Last name _____

Given name(s) _____

Date of birth  DD – MM – YYYY

Patient identifiers _____

Date of request  DD – MM – YYYY

Accession/Laboratory number _____

Elements in **black text** are REQUIRED. Elements in grey text are RECOMMENDED.

## CLINICAL INFORMATION (Note 1)

○ Not provided

☐ Previous history of testicular cancer, *specify*
_____

☐ Previous therapy, *specify*
_____

☐ Other, *specify*
_____

## SERUM TUMOUR MARKERS (select all that apply) (Note 2)

○ Not provided
○ Provided

☐ Serum tumour markers within normal limits
OR
Specify serum tumour markers used, level and date markers were drawn

Date _____    ☐ AFP _____ ug/L

☐ LDH _____ IU/L    ☐ b-HcG _____ IU/L

## OPERATIVE PROCEDURE (Note 3)

○ Not specified
○ Orchidectomy, partial
  ○ Right    ○ Left    ○ Not specified
○ Orchidectomy, radical
  ○ Right    ○ Left    ○ Not specified
○ Other, *specify*
_____

## TUMOUR FOCALITY (Note 4)

○ Cannot be assessed
○ Indeterminate
○ Unifocal
○ Multifocal, *specify number of tumours in specimen*
_____

## MAXIMUM TUMOUR DIMENSION (select all that apply) (Note 5)

○ Cannot be assessed

☐ Dimensions (largest tumour)
_____ mm x _____ mm x _____ mm

☐ Dimensions of additional tumour nodules
_____ mm x _____ mm x _____ mm
_____ mm x _____ mm x _____ mm
_____ mm x _____ mm x _____ mm

## MACROSCOPIC EXTENT OF INVASION (select all that apply) (Note 6)

○ Cannot be assessed
☐ Confined to testis
☐ Invades epididymis
☐ Invades tunica vaginalis
☐ Invades hilar structures
☐ Invades spermatic cord
☐ Invades scrotum
☐ Other, *specify*
_____

## BLOCK IDENTIFICATION KEY (Note 7)
*(List overleaf or separately with an indication of the nature and origin of all tissue blocks)*

## HISTOLOGICAL TUMOUR TYPE (Note 8)
*(Value list from the World Health Organisation Classification of tumours. Pathology and genetics of urinary system and male genital organs (2016))*

☐ Germ cell tumour, *specify type and percentage*
_____  ⇒ _____ %
_____  ⇒ _____ %
_____  ⇒ _____ %
_____  ⇒ _____ %

☐ Other, *specify*
_____

## MICROSCOPIC EXTENT OF INVASION (Note 9)

**Rete testis of stromal/interstitial type**
- ( ) Not submitted
- ( ) Not involved
- ( ) Involved

**Epididymis**
- ( ) Not submitted
- ( ) Not involved
- ( ) Involved

**Hilar fat**
- ( ) Not submitted
- ( ) Not involved
- ( ) Involved

**Tunica albuginea** (white fibrous capsule around testicular parenchyma)
- ( ) Not submitted
- ( ) Not involved
- ( ) Involved

**Tunica vaginalis** (either mesothelial layer of the tunica vaginalis)
- ( ) Not submitted
- ( ) Not involved
- ( ) Involved

**Spermatic cord**
- ( ) Not submitted
- ( ) Not involved
- ( ) Involved

**Scrotal wall**
- ( ) Not submitted
- ( ) Not involved
- ( ) Involved

## LYMPHOVASCULAR INVASION (Note 10)
- ( ) Not identified    ( ) Present
  - ⬇ Specify type
  - [                    ]

## INTRATUBULAR LESIONS (Note 11)
**Germ cell neoplasia in situ**
- ( ) Not identified    ( ) Present

**Other intratubular lesions**
- ( ) Not identified    ( ) Present
  - ⬇ Specify type
  - [                    ]

## MARGIN STATUS (Note 12)
**Partial orchidectomy**
- ( ) Cannot be assessed
- ( ) Involved
- ( ) Not involved
  - ⬇ Distance of tumour from closest margin [        ] mm

## Radical orchidectomy
- ( ) Cannot be assessed
- ( ) Spermatic cord margin involved
- ( ) Spermatic cord margin not involved
- [ ] Other margin involved, *specify*
  - [                    ]

## COEXISTENT PATHOLOGY (Note 13)
- ( ) None identified
- [ ] Hemosiderin-laden macrophages
- [ ] Atrophy
- [ ] Other, *specify*
  - [                    ]

## ANCILLARY STUDIES (Note 14)
- ( ) Not performed
- ( ) Performed, *specify*
  - [                    ]

## RESPONSE TO NEOADJUVANT THERAPY (Note 15)
- ( ) Response present
- ( ) Response absent
- ( ) No prior treatment
- ( ) Response cannot be assessed (*explain reasons*)
  - [                    ]

## PATHOLOGIC STAGING (TNM 8th edition)## ^ (Note 16)
- [ ] m - multiple primary tumours
- [ ] r - recurrent
- [ ] y - post-therapy

**Primary tumour (pT)**
- ( ) TX    Primary tumour cannot be assessed
- ( ) T0    No evidence of primary tumour
- ( ) Tis    Germ cell neoplasia in situ
- ( ) T1    Tumour limited to testis without lymphovascular invasion
- ( ) T1a*    Tumour smaller than 3 cm in size
- ( ) T1b*    Tumour 3 cm or larger in size
- ( ) T2    Tumour limited to testis with lymphovascular invasion, or tumour invading hilar soft tissue or epididymis or penetrating visceral mesothelial layer covering the external surface of tunica albuginia with or without lymphovascular invasion
- ( ) T3    Tumour invades spermatic cord with or without lymphovascular invasion
- ( ) T4    Tumour invased scrotum with or without lymphovascular invasion

\* Subclassification of pT1 applies only to pure seminoma.

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^ Please note that implementation of AJCC TNM 8th edition has been deferred until January 2018 in some jurisdictions. UICC 7th edition or AJCC 7th edition may be useful in the interim.

# Scope

The dataset has been developed for the reporting of both partial and radical orchidectomy specimens from patients with neoplasia of the testis. The protocol applies to all germ cell and sex cord-stromal tumours of the testis. Paratesticular malignancies are excluded. This dataset does not include information on the excision of residual masses after chemotherapy. A separate dataset is available for the reporting of retroperitoneal lymphadenectomy specimens. For bilateral tumours, complete a separate dataset for each.

# Note 1 - Clinical information (Recommended)

**Reason/Evidentiary Support**

This is a recommended rather than a required item as it is the responsibility of the clinician requesting the pathological examination of a specimen to provide information that will have an impact on the diagnostic process or affect its interpretation. The use of a standard pathology requisition/request form including a checklist of important clinical information is strongly encouraged to help ensure that relevant clinical data is provided by the clinicians with the specimen.

Relevant past medical history and known risk factors associated with testicular tumours should be provided, including ethnicity, cryptorchidism (and location of testis; intrascrotal, inguinal, intra-abdominal), history of orchidopexy, prior testicular germ cell tumour, family history of testicular tumours and clinical syndromes associated with testicular tumours.

Any recent history of injury or torsion or of previous chemotherapy may cause extensive or complete tumour necrosis which will affect the morphology of the remaining viable tumour.

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# Note 2 - Serum tumour markers (Recommended)

**Reason/Evidentiary Support**

The serum tumour markers, alpha-fetoprotein (AFP), beta subunit of human chorionic gonadotropin (b-hCG), and lactate dehydrogenase (LDH), play an essential role in the management of men with testicular tumours and have been included in the staging system for testicular tumours as an "S" stage.[1] The "S" stage is usually based on the **post**-orchidectomy serum tumour marker values, which reflect the degree of marker production by the patient's metastatic disease and correlate best with prognosis. In advanced disease, the marker levels closest to the start of chemotherapy should be used to determine the final "S" stage and may significantly differ (higher or lower) than pre-orchidectomy markers. In select cases of advanced disease when orchidectomy is deferred until after chemotherapy, the markers used for staging are not obtained post-orchidectomy. It is important to recognize the half-life of b-hCG (1–3 days) and AFP (5–7 days) when assigning the "S"

stage to a patient with declining markers post-orchidectomy. Patients with AFP or b-hCG that decline at or more rapidly than the expected half-life following orchidectomy and have no evidence of metastatic disease on imaging should be followed until marker normalization or rise in order to differentiate between Stage IA/B and Stage IS disease. The latter implies metastatic disease is present even when not apparent on imaging.

Since the tumour markers obtained prior to orchidectomy are typically what is available to the pathologist, in most cases, the pathologist is not able to assign the "S" stage and notation of "SX" should be used, similar to when nodal and metastasis stages cannot be assigned. Nevertheless, the pre-orchidectomy marker levels are important and should be provided to the pathologist whenever possible. The occurrence of elevated serum levels of AFP or b-hCG may indicate the need for additional sections of certain specimens if the initial findings do not account for such elevations. For each marker, notation of the level and date it was drawn or the lack of availability should be noted in the pathology report. In addition, for LDH, the upper limit of normal for the assay should be provided when available. Ideally serum makers would be a 'required' data item, however there is often difficulty with obtaining these at the time of reporting. There are also occasional testes removed for trauma which have incidental germ cell tumours.

Anatomic Stage/Prognostic Groups

| Group | T | N | M | S |
|---|---|---|---|---|
| Stage 0 | pTis | N0 | M0 | S0 |
| Stage I | pT1-4 | N0 | M0 | SX |
| Stage IA | pT1 | N0 | M0 | S0 |
| Stage IB | pT2 | N0 | M0 | S0 |
| | pT3 | N0 | M0 | S0 |
| | pT4 | N0 | M0 | S0 |
| Stage IS | Any pT/TX | N0 | M0 | S1-3 |
| Stage II | Any pT/TX | N1,N2,N3 | M0 | SX |
| Stage IIA | Any pT/TX | N1 | M0 | S0 |
| | Any pT/TX | N1 | M0 | S1 |
| Stage IIB | Any pT/TX | N2 | M0 | S0 |
| | Any pT/TX | N2 | M0 | S1 |
| Stage IIC | Any pT/TX | N3 | M0 | S0 |
| | Any pT/TX | N3 | M0 | S1 |
| Stage III | Any pT/TX | Any N | M1 | SX |
| Stage IIIA | Any pT/TX | Any N | M1a | S0 |
| | Any pT/TX | Any N | M1a | S1 |
| Stage IIIB | Any pT/TX | N1,N2,N3 | M0 | S2 |
| | Any pT/TX | Any N | M1a | S2 |
| Stage IIIC | Any pT/TX | N1,N2,N3 | M0 | S3 |
| | Any pT/TX | Any N | M1a | S3 |
| | Any pT/TX | Any N | M1b | Any S |

Prognostic Factors

Serum Tumour Markers (S)

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.*

The Serum Tumour Markers (S) category comprises the following:

- AFP – half-life 5 to 7 days
- hCG – half-life 1 to 3 days
- LDH.

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# Note 3 - Operative procedure (Required)

**Reason/Evidentiary Support**

Whether the surgical procedure is a radical or partial orchidectomy must be stated, as this will influence the assessment of surgical margins. For bilateral tumours, complete a separate dataset for each testis.

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# Note 4 - Tumour focality (Required)

**Reason/Evidentiary Support**

There is no specific paper dealing with multifocality in germ cell tumours, however many show multifocal tumours which may coalesce together to form a complex multifocal nodule. The noting of multifocality is important, as the separate nodules may contain different tumour elements which may affect prognosis.[2] Secondly, the determination of maximum tumour diameter depends on whether the tumours are multifocal or unifocal. Rare testicular tumours may be associated with multifocality and suggest a variety of syndromes.[3]

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# Note 5 - Maximum tumour dimension (largest tumour) (Required)

**Reason/Evidentiary Support**

It has been shown in a number of studies that the maximum tumour dimension has prognostic significance, especially in seminomas.[4] In a pooled analysis of data from four large cohort studies (638 patients) of patients with stage I seminoma, size (tumour size> 4 cm) was independently predictive of recurrence at five years on multivariate analysis. If the tumour was >4 cm, there was a two-fold increased risk of recurrence. In another study on multivariable analysis, tumour size above median (cut-point of 3 cm) was a predictor for relapse, HR 1.87 (95% Confidence Interval (CI) 1.15–3.06)).[5] The 3-year relapse risk based on the primary tumour size alone increased from 9% for a 1 cm primary tumour to 26% for an 8 cm tumour.[5] This is supported by other studies, especially for seminoma.[6]

The evidence for the importance of size in non-seminomatous germ cell tumours is less well established, as other factors (vascular invasion) are more important. However, as it is often not apparent whether the tumour is a seminoma or non-seminoma on macroscopy, size measurement is required. We suggest that when there is multifocality, the longest diameter of the largest focus be recorded and that the maximum diameter of the additional nodules also be recorded. Where the nodules coalesce, this may be difficult to calculate. Evidence for the relevance of this is disputed but we suggest that tumours should be counted as separate if there is intervening parenchyma.

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## Note 6 - Macroscopic extent of invasion (Required)

**Reason/Evidentiary Support**

The macroscopic extent of the disease may be difficult to discern even on close inspection of the testis and hilar structures. The vast majority of radical orchidectomies will not include the scrotum unless the surgeon finds evidence of invasion at surgery. The testis parenchyma is bound by the tunica albuginea except in the region where the rete testis connects with the epididymis and vas deferens. Adjacent to the hilum in this area is a small amount of hilar fat. The tunica albuginea is bound by a double layer of mesothelium, termed the tunica vaginalis (Figure 1). Involvement of the hilar soft tissue epididymis or tunica vaginalis may be challenging to detect. Also diffusely infiltrative tumours such as intertubular seminoma which infiltrate between the tubules may not be easy to detect, meaning that the size of the tumour may in fact be larger than that suspected macroscopically. Therefore all suspected areas of invasion seen macroscopically should be conformed microscopically by appropriate sampling for confirmation (see below).
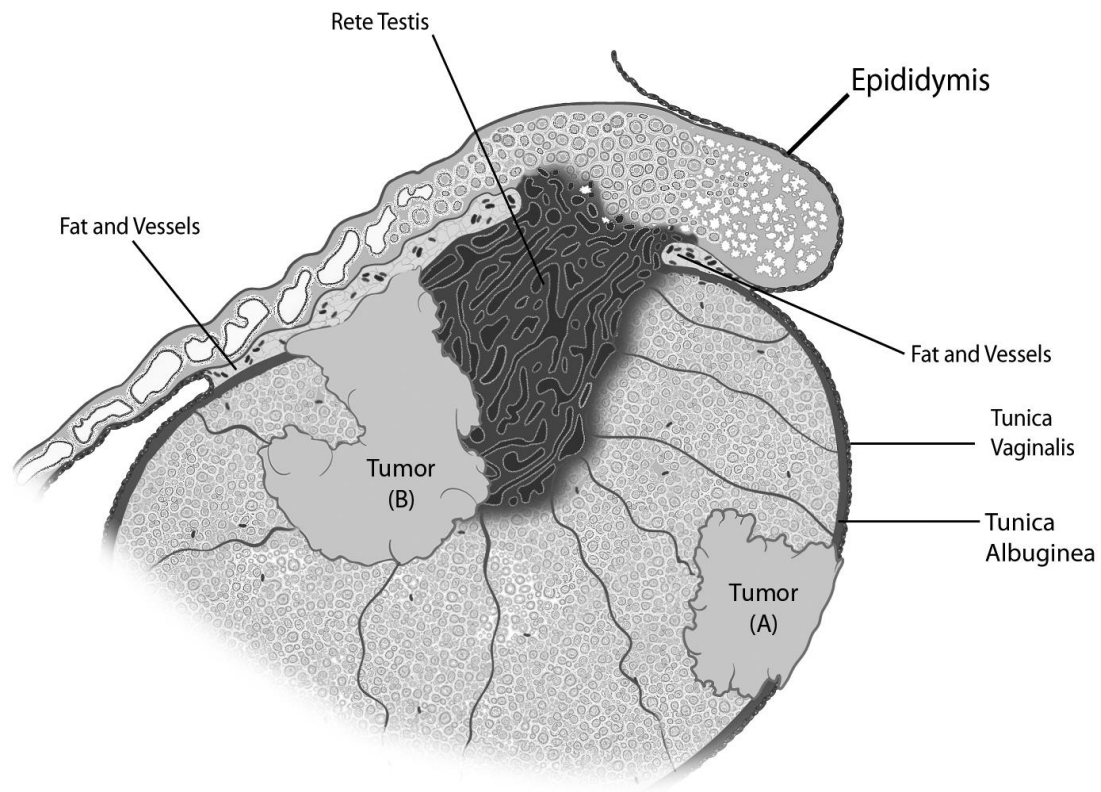
**Figure 1.** Diagrammatic representation of a tumor (Tumor A) invading the tunica vaginalis, perforating through the mesothelium, and another tumor (Tumor B) partly involving the rete testis and invading the hilar soft tissue. Figure courtesy of Satish K. Tickoo. MD. Source: College of American Pathologists (CAP) *Protocol for the examination of specimens from patients with malignant germ cell and sex cord-stromal tumors of the testis (October 2013).*

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## Note 7 - Block identification key (Recommended)

**Reason/Evidentiary Support**

The origin/designation of all tissue blocks should be recorded and it is preferable to document this information in the final pathology report. This is particularly important should the need for internal or external review arise. The reviewer needs to be clear about the origin of each block in order to provide an informed specialist opinion. If this information is not included in the final pathology report, it should be available on the laboratory computer system and relayed to the reviewing pathologist. Recording the origin/designation of tissue blocks also facilitates retrieval of blocks, for example for further immunohistochemical or molecular analysis, research studies or clinical trials.

Tumour sampling should be generous to ensure documentation of all tumour types present. Germ cell tumours should, as a minimum be sampled at 1 block per cm of tumour. However while this may be adequate for a non seminomatous germ cell tumour, to represent different elements, it has been

recommended that seminomas are more generously sampled than this, as small foci of non seminoma will change patient management; if the tumour is small (less than 2 cm) it can be completely sampled.[7] Pure seminomas should be sampled especially thoroughly to exclude small areas on non- seminomatous germ cell tumour. It is important that blocks include the adjacent testicular parenchyma to allow for the assessment of lymphovascular invasion (LVI) and germ cell neoplasia in situ (GCNIS).

Different areas of the tumour must be sampled, particularly including haemorrhagic and necrotic areas and solid/fleshy areas. All of the haemorrhagic tumour must be blocked, as choriocarcinoma is often haemorrhagic with little residual viable tumour.

Sections of tumour should include at least one section showing the relation of the tumour to the testicular hilum. If the tumour is well away from the hilum, there should be a separate section of the hilum clearly showing this region is free of tumour.

Sections of tumour should include the adjacent tunica albuginea and vaginalis and adjacent testicular parenchyma. Sections of uninvolved testicular parenchyma should be included. A block from the cord resection margin should be taken. This block should be taken prior to incision of the tumour to avoid contamination.[8]

**Orchidectomy specimens for clinically localised disease**

Blocks are selected to represent:
- the cord resection margin and base of cord (further cord blocks depending on macroscopy)
- the relationship of the tumour(s) to the rete testis, epididymis and cord
- the minimum distance of the tumour to the nearest inked resection margin for partial orchidectomies
- all areas of the tumour(s) with different macroscopic appearances (solid, cystic, pale or haemorrhagic)
- adjacent testis including the tunica albuginea (and vaginalis), a common site for vascular invasion
- uninvolved testis.

It is recommended that a record is kept of a good representative paraffin block of tumour and whether frozen tissue has been stored.

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# Note 8 - Histological tumour type (Required)

**Reason/Evidentiary Support**

The classification of testicular tumours is taken from the World Health Organisation (WHO) 2016 classification.[9]

## WHO classification of tumours of the testis and paratesticular tissue[a][9]

| Descriptor | ICD-O codes |
|---|---|
| **Germ cell tumours derived from germ cell neoplasia in situ (GCNIS)** | |
| *Non-invasive germ cell neoplasia* | |
| Germ cell neoplasia in situ | 9064/2 |
| Specific forms of intratubular germ cell neoplasia | |
| *Tumours of one histological type (pure tumours)* | |
| Seminoma | 9061/3 |
| Seminoma with syncytiotrophoblast cells | |
| Non-seminomatous germ cell tumours | |
| Embryonal carcinoma | 9070/3 |
| Yolk sac tumour, postpubertal-type | 9071/3 |
| Trophoblastic tumours | |
| Choriocarcinoma | 9100/3 |
| Non-choriocarcinomatous trophoblastic tumours | |
| Placental site trophoblastic tumour | 9104/3 |
| Epithelioid trophoblastic tumour | 9105/3 |
| Cystic trophoblastic tumour | |
| Teratoma, postpubertal-type | 9080/3 |
| Teratoma with somatic-type malignancies | 9084/3 |
| *Non-seminomatous germ cell tumours of more than one histological type* | |
| Mixed germ cell tumours | 9085/3 |
| *Germ cell tumours of unknown type* | |
| Regressed germ cell tumours | 9080/1 |
| **Germ cell tumours unrelated to germ cell neoplasia in situ** | |
| Spermatocytic tumour | 9063/3 |
| Teratoma, prepubertal type | 9084/0 |
| Dermoid cyst | |
| Epidermoid cyst | |
| Well-differentiated neuroendocrine tumour (monodermal teratoma) | 8240/3 |
| Mixed teratoma and yolk sac tumour, prepubertal-type | 9085/3 |
| Yolk sac tumour, prepubertal-type | 9071/3 |
| **Sex cord-stromal tumours** | |
| *Pure tumours* | |
| Leydig cell tumour | 8650/1 |
| Malignant Leydig cell tumour | 8650/3 |
| Sertoli cell tumour | 8640/1 |
| Malignant Sertoli cell tumour | 8640/3 |

| Descriptor | ICD-O codes |
|---|---|
| Large cell calcifying Sertoli cell tumour | 8642/1 |
| Intratubular large cell hyalinizing Sertoli cell tumour | 8643/1 |
| Granulosa cell tumour | |
| Adult granulosa cell tumour | 8620/1 |
| Juvenile granulosa cell tumour | 8622/0 |
| Tumours in the fibroma-thecoma group | 8600/0 |
| *Mixed and unclassified sex cord-stromal tumours* | |
| Mixed sex cord-stromal tumour | 8592/1 |
| Unclassified sex cord-stromal tumour | 8591/1 |
| **Tumour containing both germ cell and sex cord-stromal elements** | |
| Gonadoblastoma | 9073/1 |

a The morphology codes are from the International Classification of Diseases for Oncology (ICD-O). Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour; /2 for carcinoma in situ and grade III intraepithelial neoplasia; and /3 for malignant tumours.
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**Percentage of different tumour components in mixed germ cell tumours**

The percentage of the different tumour elements has been shown to be predictive of the relapse risk in non-seminomatous germ cell tumours (NSGCT), especially the percentage of embryonal carcinoma. As well as the percentage of embryonal carcinoma as a core data item, the approximate percentages of other tumour elements should also be given. The presence of LVI, embryonal carcinoma and yolk sac tumour were risk factors for relapse in a study of 132 patients.[10] A second study showed that 25/85 men who had predominantly embryonal carcinoma histology relapsed.[11] Of 93 men with stage I NSGCTs who were placed in a surveillance study following orchidectomy, 81 men had predominantly embryonal carcinoma component in their primary tumour and a third of these developed metastases, whereas none of the men lacking an embryonal carcinoma component developed metastases (p=0.05).[12] An older surveillance study in 373 men with stage I NSGCT suggested that 'undifferentiated cells' and the absence of yolk sac elements in the primary tumour were able to identify men with a high risk of relapse.[13]

Giving 'exact' percentages in a mixed non-seminomatous germ cell tumour may be challenging, as some elements may be extremely small, and it may occasionally be difficult to distinguish closely intermingled elements (such as yolk sac tumour and embryonal carcinoma). We suggest that only basic 'eyeball' style quantitation is required. For example, the difference between 10% embryonal carcinoma and 90% embryonal carcinoma may be important in determining the need to adjuvant therapy. However a difference of 5 or 10% is likely insignificant. For NSGCTs which are of pure type, then the percentage of the pure type should be listed as 100%.

Mention of areas of scarring is helpful, particularly in pure seminoma or teratoma cases as they may indicate areas of regression, which might have represented other tumour types. These findings can explain the occasional discordance between the orchidectomy tumour type and that seen in metastatic deposits.
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# Note 9 - Microscopic extent of invasion (Required and Recommended)

**Reason/Evidentiary Support**

**Rete testis**

Rete testis invasion is the direct invasion of tumour into the stroma of the rete testis and does not include pagetoid spread of GCNIS into the tubules of the rete.[4] In the pooled cohort surveillance study of pure seminomas, rete testis invasion was independently predictive of recurrence at five years on multivariate analysis, conferring an increased risk of recurrence by a factor of 1.7 (95% CI 1.1–2.6).[4] Other studies of pure seminoma show differing results. Two cohort analyses of 425 and 744 patients respectively confirmed this.[6,14] However, two other studies of 685 patients[5] and 1954 patients[15] showed that rete testis invasion was not a significant predictor for relapse when compared with tumour size.

For NSGCTs, there is less evidence that rete testis invasion is an important prognostic factor,[16] probably because other factors such as the percentage of embryonal carcinoma and vascular invasion are more important.

Rete testis invasion and tumour size are also interdependent. It should be noted that most of the studies listed above did not include formal prospective pathological review and were a retrospective assessment of pathological reports by clinicians. Data on rete testis involvement was missing in many cases, and there is doubt in some studies whether pagetoid invasion of the rete was assessed. A survey of recent practice in Europe showed many pathologists did not distinguish between pagetoid and interstitial invasion of the rete.[17] Rete testis and tumour size were not part of the TNM 7th edition[1,18] however tumour size using a cut off of 3 cm has now been incorporated into the American Joint Committee on Cancer (AJCC) 8th edition[19] for pure seminomas only, separating the pT1 stage into pT1a and pT1b. Both rete testis invasion and size are used by many clinicians to determine adjuvant chemotherapy and are part of existing European clinical guidelines.[20,21]

**Hilar soft tissue invasion**

Invasion of the hilar soft tissues is a common mode of extratesticular spread.[22] One study has shown that it predicts high stage at presentation,[16] but there has been previously no consensus on the correct way to stage hilar soft tissue invasion[17] Following a consultation conference by the International Society of Urological Pathologists (ISUP)[23] and adoption by the AJCC 8th edition[19] it has been decided to stage soft tissue invasion as pT2. Soft tissue invasion has been defined as 'invasion of the adipose tissue and soft fibrous connective tissue present…beyond the boundaries of the rete testis.[19]

**Epididymal  invasion**

There is no evidence on the prognostic significance of epididymal invasion. Although in previous editions of AJCC[18] and Union for International Cancer Control (UICC)[1] manuals (7th editions) it has been designated as pT1, the evidence and consensus for pT2 staging of soft tissue has necessitated a

redesignation of epididymal invasion as pT2 in the AJCC 8th edition[19] as it is normally secondary to this.

**Direct invasion of the cord**

This is regarded as a core data item as it is required for TNM staging but evidence on its prognostic significance in seminoma is lacking. In a large cohort study of stage I seminoma, spermatic cord invasion was not found to be independently prognostic for recurrence.[14] In contrast, it was identified as an adverse prognostic factor in another study.[24] In a review of 326 testicular germ cell tumours, of which 79 had tumour in the spermatic cord, most cases (72%) were thought to be due to contamination compared to 19% cases of true involvement and with 8.9% showing both contamination and true involvement.[8] Spermatic cord contamination was most frequently seen with seminomas. To differentiate cord invasion from hilar soft tissue invasion, it has been defined as 'tumour extending beyond the angle between the epididymis and spermatic cord proper or tumour surrounding the vas deferens'.[19]

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# Note 10 - Lymphovascular invasion (Required and Recommended)

**Reason/Evidentiary Support**

In several studies, the presence of vascular space has been correlated with a significantly elevated risk for distant metastasis, particularly in NSGCTS. Some clinicians manage the patients with clinical stage I disease that lack evidence of lymphatic or vascular invasion in their orchidectomy specimens by surveillance.

Most of the previous studies on LVI appear not to use immunochemistry routinely in its diagnosis. Although one recent paper suggests that the routine use of immunochemistry to identify LVI may be helpful, further studies are needed and at present we recommend that diagnosis should be made on H&E backed up by immunochemistry for lymphovascular vessels in challenging cases.[25]

We recommend that vascular invasion be called either present or 'not identified' as equivocation in the report is unhelpful to the clinician. We advise restricting the definition of vascular invasion so that those cases which are equivocal are assigned as 'not identified'. Vascular invasion is much more likely to be seen at the periphery of the tumour than within the centre of solid tumour masses. It is often seen in fibrous bands surrounding or intersecting the main tumour mass, as well as in the region of rete testis. LVI may be seen in the tunica albuginea, spermatic cord vessels or the parenchyma of the testis. All warrant a stage of pT2.

In seminoma, although vascular invasion is a statistically significant factor for predicting for relapse in occasional small historical cohort studies,[26] it has not proved independently statistically significant in stage I seminoma in large cohort pooled studies;[4,14] however, it was found significant in a recent cohort of 1954 patients.[15] This may be secondary to the frequent presence of tumour smearing artefact in seminoma, making identification of genuine LVI challenging.

For NSGCTs, LVI has been shown in multiple studies to be a powerful predictor of metastatic disease and recurrence.[10,12,27-32]

If LVI is present in a mixed or combined germ cell tumour, it is good practice to state which subtype of tumour is showing the LVI as this may alter clinical management if it was an embryonal carcinoma component showing LVI versus classical seminoma. Indicating that a case is 'uncertain' for vascular invasion is unhelpful for the treatment of patients with germ cell tumours.

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## Note 11 - Intratubular lesions (Required and Recommended)

**Reason/Evidentiary Support**

The term germ cell neoplasia in situ (GCNIS) has replaced the previous terms, carcinoma in situ (CIS), intratubular germ cell neoplasia, unclassified  (IGCNU) and testicular intraepithelial neoplasia (TIN). None of the previous terms was entirely correct and led to much confusion in the literature. GCNIS is not a 'carcinoma' nor is it 'intra-epithelial', and the term IGCNU, was confusing due to the use of the term 'unclassified' which many replaced by 'undifferentiated'.

In fact, the true in situ area for the development of germ cell tumours is in a specific intratubular location,  the 'spermatogonial niche' between the basement membrane and the tight junctions between adjacent Sertoli cells.

GCNIS is the precursor lesion for the most common variants of invasive germ cell tumours. Although not a prognostic factor, it should be a core item, as its absence may raise the suspicion of a non-GCNIS associated tumour, which have differing prognosis and treatments, as well as the possibility that the tumour is a non-germ cell tumour mimic of a germ cell tumour (notably some Sertoli cell tumours).

'Pagetoid' invasion of the rete testis occurs when GCNIS-like cells infiltrate the epithelial cells of the rete but do not invade the rete stroma. The significance of pagetoid type rete invasion is unknown but is generally accepted that these represent infiltration of GCNIS rather than invasive seminoma.

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## Note 12 - Margin status (Required)

**Reason/Evidentiary Support**

Whether the surgical procedure is a radical or partial orchidectomy must be stated, as this will influence the assessment of surgical margins. Specifically, in the case of partial orchidectomy specimens, it is important that the intratesticular surgical margin is carefully evaluated to ensure that no residual tumour is present in the remaining testis.

For radical orchidectomies there is little evidence that surgical margin status has been studied as an independent prognostic factor separately from stage and other known indicators. The only true surgical margin is the spermatic cord margin in a usual radical orchidectomy and involvement with stromal invasion is rare. Very rarely in a widely invasive tumour, scrotal skin may be included. This should be easily apparent in such cases, and it would be appropriate to state whether the scrotal skin margin was invaded by tumour.

Occasionally the spermatic cord margin may include vessels showing vascular invasion by tumour. This is vascular invasion, and does not represent a positive margin.

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## Note 13 - Coexistent pathology (Recommended)

**Reason/Evidentiary Support**

'Burnt out' germ cell tumours may present as scarring, with the presence of hemosiderin-laden macrophages, and intratubular calcification, with surrounding GCNIS and must be carefully evaluated. Signs of testicular dysgenesis, androgen insensitivity, Klinefelter's syndrome or other intersex conditions may be identified or suggested by close examination of the testicular parenchyma. These might include residual gonadoblastoma or ovarian type tissue for intersex conditions. Leydig cell hyperplasia which may be correlated with b-hCG elevation and testicular atrophy may also be seen in dysgenetic gonads (e.g. dysgenesis or androgen-insensitivity syndrome).[33,34]

It may be helpful to give the status of the surrounding parenchyma to the tumour: especially the amount of spermatogenesis present and degree of atrophy. The status of the parenchyma is of great importance in some types of testicular neoplasm (prepubertal type teratoma in particular) and also may indicate the functioning status of the contralateral testis.

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## Note 14 - Ancillary findings (Recommended)

**Reason/Evidentiary Support**

Most testicular tumours can be identified on histological examination, though some difficulties may be encountered in differentiating between some types. Immunohistochemistry may be extremely helpful in distinguishing between tumour types and may be helpful in some cases.[35]

Isochromosome i(12p) FISH testing which, although not entirely specific, may be a useful additional test in confirming a tumour as a germ cell tumour related to GCNIS as opposed to a type unrelated to GCNIS such as prepubertal type teratomas and prepubertal type yolk sac tumours.[36]

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## Note 15 - Response to neoadjuvant therapy (Recommended)

**Reason/Evidentiary Support**

Occasionally patients with advanced disease and raised tumour markers are treated with chemotherapy prior to orchidectomy. When the orchidectomy is performed it may show evidence of residual disease. The prefix y is used when staging cases after treatment.

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## Note 16 - Pathologic staging (Required)

**Reason/Evidentiary Support**

This dataset includes the AJCC TNM 8th edition definitions.[19] The implementation of AJCC TNM 8th edition has been deferred until January 2018 in some jurisdictions. AJCC 7th edition[18] or UICC 7th edition[1] may be useful in the interim. If TNM 7th edition is used the following points should be noted:

- Epididymal invasion is staged as T2 by AJCC 8th edition and T1 by UICC and AJCC 7th editions.
- Soft tissue invasion is staged as T2 by AJCC 8th edition and T3 by UICC and AJCC 7th editions.
- Pure seminomas may be substaged as pT1a if less than 3 cm and pT1b if more than 3 cm by AJCC 8th edition whereas there is no division in UICC and AJCC 7th editions.

The classification applies only to germ cell tumours of the testis. Although pathologists may not be aware of specific levels to allow stage grouping, the details are provided here for information. Primary testicular germ cell tumours are occasionally removed after therapy, especially when patients present with widespread metastases. In these cases, we suggest filling out both the Orchidectomy datasheet, adding y as a prefix to the TNM classification and adding in an open comment section, the percentage of necrosis seen.

The extent of primary tumour is usually classified after radical orchidectomy, and, for this reason a *pathologic* stage is assigned.

Note:  Except for pTis and pT4, extent of primary tumour is classified by radical orchidectomy. TX may be used for other categories in the absence of radical orchidectomy. The prefix y is used for post-chemotherapy orchidectomy specimens.

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