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Neoplasia of the Testis Histopathology Reporting Guide Retroperitoneal Lymphadenectomy

ICCR

Family/Last name | Date of birth DD – MM – YYYY

Given name(s)

Patient identifiers | Date of request DD – MM – YYYY | Accession/Laboratory number

Elements in **black text** are CORE. Elements in **grey text** are NON-CORE.

☐ indicates multi-select values ◯ indicates single select values

SCOPE OF THIS DATASET

CLINICAL INFORMATION (Note 1)

◯ Information not provided
◯ Information provided (select all that apply)
- ☐ Previous history of testicular cancer, *specify*
- ☐ Previous therapy, *specify*
- ☐ Other clinical information, *specify*

SERUM TUMOUR MARKERS (Note 2)

◯ Not provided
◯ Provided
- ◯ Serum tumour markers within normal limits

Specify serum tumour markers used, level and date markers were drawn (select all that apply)

Date | ☐ AFP ug/L | ☐ LDH | ☐ b-HcG IU/L

SPECIMEN(S) SUBMITTED (select all that apply) (Note 3)

◯ Not specified
☐ Retroperitoneal lymphadenectomy, *specify nodal site(s)*

For each nodal site: ◯ No disease ◯ Necrosis ◯ Viable tumour

SPECIMEN(S) SUBMITTED (Note 3) continued

☐ Brain
☐ Lung
☐ Liver
☐ Other, *specify*

SIZE OF LARGEST LYMPH NODE (Note 4)

◯ Cannot be assessed

Maximum dimension mm

Additional dimensions mm x mm

SIZE OF LARGEST NODAL METASTASIS (Note 5)

◯ Cannot be assessed

Maximum dimension mm

Additional dimensions mm x mm

BLOCK IDENTIFICATION KEY (Note 6)

(List overleaf or separately with an indication of the nature and origin of all tissue blocks)

HISTOLOGICAL TUMOUR TYPE (select all that apply) (Note 7)

(Value list based on the World Health Organization Classification of Urinary and Male Genital Tumours (2022))

☐ Viable tumour
- ◯ Absent
- ◯ Present
  - %

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HISTOLOGICAL TUMOUR TYPE (Note 7) **continued**

☐ Germ cell tumour, *specify type and percentage*

	%
	%
	%
	%

☐ Other, *specify*

MARGIN STATUS (Note 8)

◯ Cannot be assessed
◯ Not involved

Distance of tumour from closest margin ____ mm

Specify closest margin(s), if possible

◯ Involved

Specify margin(s), if possible

EXTRANODAL EXTENSION (Note 9)

◯ Indeterminate
◯ Not identified
◯ Present

PATHOLOGICAL STAGING (UICC TNM 8th edition)[a] (Note 10)

TNM Descriptor (only if applicable)

◯ y - post-therapy

Regional lymph nodes (pN)

◯ NX[b] Regional lymph nodes cannot be assessed
◯ N0 No regional lymph node metastasis
◯ N1 Metastasis with a lymph node mass 2 cm or less in greatest dimension and five or fewer positive nodes, none more than 2 cm in greatest dimension
◯ N2 Metastasis with a lymph node mass more than 2 cm but not more than 5 cm in greatest dimension; or more than five nodes positive, none more than 5 cm; or evidence of extranodal extension of tumour
◯ N3 Metastasis with a lymph node mass more than 5 cm in greatest dimension

Distant metastasis (pM) (if resected)

◯ No distant metastases
◯ M1 Distant metastasis
◯ M1a Non-regional lymph node(s) or lung
◯ M1b Other sites

[a] *Reproduced with permission. Source: UICC TNM Classification of Malignant Tumours, 8th Edition, eds by James D. Brierley, Mary K. Gospodarowicz, Christian Wittekind. 2016, Publisher Wiley (incorporating any errata published up until 12th July 2024).*

[b] *NX should be used only if absolutely necessary.*

Definitions

CORE elements

CORE elements are those which are essential for the clinical management, staging or prognosis of the cancer. These elements will either have evidentiary support at Level III-2 or above (based on prognostic factors in the National Health and Medical Research Council (NHMRC) levels of evidence[1]). In rare circumstances, where level III-2 evidence is not available an element may be made a CORE element where there is unanimous agreement by the Dataset Authoring Committee (DAC). An appropriate staging system e.g., Pathological TNM staging would normally be included as a CORE element.

Molecular and immunohistochemical testing is a growing feature of cancer reporting. However, in many parts of the world this type of testing is limited by the available resources. In order to encourage the global adoption of ancillary tests for patient benefit, International Collaboration on Cancer Reporting (ICCR) includes the most relevant ancillary testing in ICCR Datasets as CORE elements, especially when they are necessary for the diagnosis. Where the technical capability does not yet exist, laboratories may consider temporarily using these data elements as NON-CORE items.

The summation of all CORE elements is considered to be the minimum reporting standard for a specific cancer.

NON-CORE elements

NON-CORE elements are those which are unanimously agreed should be included in the dataset but are not supported by level III-2 evidence. These elements may be clinically important and recommended as good practice but are not yet validated or regularly used in patient management.

Key information other than that which is essential for clinical management, staging or prognosis of the cancer such as macroscopic observations and interpretation, which are fundamental to the histological diagnosis and conclusion e.g., macroscopic tumour details, may be included as either CORE or NON-CORE elements by consensus of the DAC.

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Scope

The dataset has been developed for the reporting of retroperitoneal and other lymphadenectomy specimens as well as visceral metastasis excision specimens from patients of any age with malignant tumours of the testis. The protocol applies to all malignant germ cell and sex cord-stromal tumours of the testis. Paratesticular malignancies are excluded. A separate ICCR dataset is available for the reporting of orchidectomy specimens.[2]

The second edition of this dataset includes changes to align the dataset with the World Health Organization (WHO) Classification of Tumours, Urinary and Male Genital Tumours, 5th edition, 2022.[3] The ICCR dataset includes 5th edition Corrigenda, July 2024.[4] In development of this dataset, the DAC considered evidence up until July 2024.

A list of changes in this dataset edition can be accessed here.

The authors of this dataset can be accessed here.

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Note 1 – Clinical information (Core and Non-core)

Retroperitoneal lymph node dissection (RPLND) may be performed at the time of diagnosis of a testicular tumour, or may be performed after chemotherapy, and this will affect the likely pathological changes seen. Although the majority of excisions will be for germ cell tumours,[5] primary prophylactic excisions for malignant sex cord- stromal tumours are also occasionally performed.[6]

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Note 2 – Serum tumour markers (Non-core)

Serum marker studies play a key role in the clinical management of patients with testicular germ cell tumours and in the monitoring of recurrent disease.[7-9] Novel markers such as mi-371a-3p may be used in the future but are not at present ready for routine use.[10,11] Most patients who undergo post chemotherapy RPLND will have negative markers following orchiectomy as those with positive markers will be treated with further chemotherapy or radiotherapy. 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. Serum markers may be used if available to define anatomic stage/prognostic groups in RPLND specimens, as shown below.[12,13]

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

A ‘y’ prefix indicates those cases in which classification is performed during or following initial multimodality therapy (i.e., chemotherapy, radiation therapy, or both chemotherapy and radiation therapy).

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

LDH - lactate dehydrogenase
hCG - human chorionic gonadotropin
mIU/mL - milli-international units per millilitre
AFP - alpha-fetoprotein
ng/mL - nanograms per millilitre
#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 – Specimen(s) submitted (Core)

The type of retroperitoneal surgery performed is dependent on which testis was affected by tumour and a number of different surgical approaches are possible. Although there are exceptions, right-sided tumours metastasise to the interaortocaval lymph nodes first followed by the precaval and paracaval lymph nodes. Left sided testicular tumours metastasise to the para- and preaortic areas. Contralateral involvement is more frequent in right sided tumours as well as in bulky disease. The practice of specimen submission differs greatly, but often surgeons will resect separate nodal sites in separate containers.

After chemotherapy, it is common practice to excise other remaining sites of disease, apart from RPLNDs and these should be identified.

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Note 4 – Size of largest lymph node (Core and Non-core)

There is a lack of clarity in the Union for International Cancer Control (UICC) and American Joint Committee on Cancer (AJCC) TNM8 as to whether to record the size of the 'largest lymph node' or 'largest nodal metastasis'.[12,13] In the vast majority of cases these will be identical, but this does not exclude the possibility that in selected cases these might differ. As in any other organ the largest lymph node diameter should be recorded as well as the largest lymph node metastasis. We recognise that these will be the same in the vast majority of resection cases.

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Note 5 – Size of largest nodal metastasis (Core and Non-core)

A number of studies have shown that the 'size of the retroperitoneal nodes' is associated with the presence of tumour (teratoma and also of viable malignant elements).[14,15] There is a lack of clarity whether this is a measurement of the lymph node or metastasis though in most cases these will be identical. Nodal metastasis size may be difficult to measure when nodes are confluent. The DAC suggest that where separate nodes are not readily identifiable then the largest diameter of the overall tumour be recorded.[16,17] The other two dimensions are non-core items.

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Note 6 – Block identification key (Non-core)

The origin/designation of all tissue blocks should be recorded. This information should ideally be documented in the final pathology report and 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. It may be useful to have a digital image of the specimen and record of the origin of the tumour blocks in some cases.

Recording the origin/designation of tissue blocks also facilitates retrieval of blocks for further immunohistochemical or molecular analysis, research studies or clinical trials.

Comprehensive sampling is essential for residual masses, as the identification of even a small area of a different subtype can alter patient management and impact on prognosis. Although the recommendation of one block per centimetre of tumour is usual, more may be required to adequately represent all the macroscopically different areas of tumour. The number of nodes harvested has been shown to impact on prognosis.[18,19]

Blocks are selected to represent:

- all areas of the positive node(s) with different macroscopic appearances (solid, cystic, pale or haemorrhagic)
- the minimum distance of the tumour to the nearest resection margin (which may be inked)
- all macroscopically negative nodes to search for micrometastatic disease.

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

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Note 7 – Histological tumour type (Core)

The classification of testicular tumours is taken from the WHO Classification of Tumours, Urinary and Male Genital Tumours, 5th edition, 2022 (Table 1).[3] The ICCR dataset includes 5th edition Corrigenda, July 2024.[4] Please note that some of these entities do not metastasize but the entire classification is given here for completeness.

Table 1: World Health Organization classification of tumours of the testis and paratesticular tissue.[3]

Descriptor	ICD-O codes[a]
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	
Gonadoblastoma	9073/1
The germinoma family of tumours	
Seminoma	9061/3
Non-seminomatous germ cell tumours	
Embryonal carcinoma	9070/3
Yolk sac tumour, postpubertal-type	9071/3
Choriocarcinoma	9100/3
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
Mixed germ cell tumours of the testis	
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
Yolk sac tumour, prepubertal-type	9071/3
Testicular neuroendocrine tumour, prepubertal-type	8240/3
Mixed teratoma and yolk sac tumour, prepubertal-type	9085/3

[a] The morphology codes are from the International Classification of Diseases for Oncology (ICD-O).[20] Behaviour is coded /0 for benign tumours; /1 for unspecified, borderline, or uncertain behaviour: /2 for carcinoma in situ and grade lll intraepithelial neoplasia; /3 for malignant tumours, primary site: and /6 for malignant tumours, metastatic site. Behaviour code /6 is not generally used by cancer registries. Subtype labels are indented. Incorporates all relevant changes from the 5th edition Corrigenda, July 2024.[4]

Note: Only a limited subset of these tumours are capable of spread to retroperitoneal nodes.

Retroperitoneal lymph node dissection (RPLND) before treatment

The type of tumour identified in an RPLND is crucial information to determine further treatment.
The tumour in prechemotherapy RPLNDs (also referred to as primary RPLNDs) generally (but not always) show similar findings to that in the orchidectomy specimen. In primary setting, pathologic N staging is more commonly used to determine the need for adjuvant chemotherapy with pN0 and pN1 leading to surveillance and pN2 and pN3 (rare) leading to adjuvant chemotherapy.

Retroperitoneal lymph node dissection (RPLND) after treatment

After chemotherapy, and especially in late relapses, the pathology may be substantially different from that seen in primary RPLND.[21] In general terms, after chemotherapy, 40-50% of germ cell tumour cases show pure necrosis with no viable tissue seen. A further 40% show teratoma, while the remaining 10% show a mixture of 'malignant' germ cell elements such as embryonal carcinoma, or yolk sac tumour, and a small number may show somatic transformation. Pure teratomatous metastasis is generally treated by surgical excision alone, whereas patients who have other residual germ cell tumour components are usually treated with additional chemotherapy. Metastatic sex cord-stromal tumours are also occasionally operated upon.[6] Even the type of tumour seen substantially affects the prognostic and therapeutic implications[22] with, for example, certain variants being associated with a good outcome[23] while others are associated with an intermediate,[24] or more aggressive course.[25] Diagnosis of these variants may be challenging and require expert consultation.

The percentage of 'viable malignant cells' has also shown to be a determinant of prognosis in a number of studies.[26-29] 10% is the most common cut-off used to determine the need for further treatment.[30]

For post-chemotherapy residual masses, particularly in the absence of a biopsy diagnosis prior to treatment, it is often useful to examine areas of necrosis, as ghost outlines of the tumour often remain and allow the distinction between seminoma and non-seminomatous germ cell tumour. The reporting of number and location of lymph nodes involved by necrosis, fibrosis, xanthomatous and fibroxanthomatous reaction is important to the treating physician to evaluate the extent and distribution of tumour in different lymph nodes. There is evidence that fibrosis often represents neoplastic stroma originating from teratoma or yolk sac tumour.[31] The spindle cells in the areas of fibrosis are often reactive to cytokeratin and display allelic loss (85%) and 12p anomalies (33%) characteristic of germ cell tumours. Xanthomatous and fibroxanthomatous reaction may sometimes pose a diagnostic challenge and immunohistochemical staining for evaluation of residual tumour is deemed necessary in occasional cases. It is important to recognise that residual viable malignancy (embryonal carcinoma, yolk sac tumour, classical seminoma or choriocarcinoma) may trigger further chemotherapy and therefore it is important to only report viable elements along with percentage of viable tumour and not semi-viable or non-viable tumour. Necrosis and post-chemotherapy teratoma would not usually trigger further therapy, unless the clinical situation dictates otherwise. In the case of cystic trophoblastic tumour (CTT), an explanatory note should be provided to caution the physicians against further chemotherapy. Data for CTT are limited but the largest study of 15 patients with follow-up showed that 11 did not recur, three showed late recurrences of possibly unrelated yolk sac tumour and the one patient who did recur with a rise in hCG had unresected residual masses.[23] For post-chemotherapy RPLND, it may be desirable to embed more of the specimen if it is found to contain necrosis or non-viable tumour to exclude small foci of viable tumour.

Secondary somatic malignancy is rare and challenging to diagnose. The tumour typically consists of an expansile and pure population of atypical mesenchymal or epithelial cells and occupies at least 5 millimetres (mm) in diameter often with invasion of other components or structures outside the lymph node.[3] Sarcomas are the most common type, though some post-chemotherapy sarcoma-like tumours may be sarcomatoid yolk sac tumours.[32] Embryonic neuroectodermal tumour (previously called primitive neuroectodermal tumour[33]) is another relatively common somatic-type malignancy which behaves aggressively.[34,35] Most carcinomas are adenocarcinomas, usually not otherwise specified (NOS) type. Occasionally, patients may develop nephroblastoma.[36]

A somatic malignancy in a metastasis increases likelihood of dying from the disease and if it is localised, surgical resection is the optimal treatment.[25] Patients usually respond poorly to the treatment for conventional germ cell malignancy.[37] Some somatic malignancies may respond to a specific chemotherapy that is effective for the specific subtype, so accurate subtyping of the somatic transformation is important.

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Note 8 – Margin status (Core and Non-core)

Complete resection of viable 'malignant' germ cell elements is an important prognostic factor in RPLND and therefore is a core element.[30] It is therefore important to liaise with the surgeon to ensure that all margins are true margins, especially when adjacent lymph nodes/tissue is removed individually. Use of marking sutures may be useful in these circumstances to indicate orientation.[28,29,38-40]

There is no evidence whether the distance to the margin is prognostic in these specimens and therefore this has been listed as non-core as it is standard practice in other pathological neoplastic diseases.

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Note 9 – Extranodal extension (Core)

The detection of extranodal extension of disease has been studied in a number of publications, and although some have shown it to be an indicator of poor prognosis, this may not be independently significant of other prognostic parameters such as tumour size, incomplete excision and type of tumour. However, in the TNM staging it upstages from pN1 to pN2 and is utilised as a cut off point for the decision on further chemotherapy.[41,42]

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Note 10 – Pathological staging (Core)

This dataset includes the updated UICC 8th edition definitions,[12] which now are optimally aligned with the AJCC 8th edition definitions.[13]

The staging will depend on the nature of the resected specimens. Although most post-chemotherapy resections are of lymph node groups, usually in the retroperitoneum, there are occasional resections of other post-chemotherapy specimens from the lung, brain, liver or other sites. Most, but not all, of these specimens will either be of teratoma or show necrosis. All non-lymphoid sites should be classified under M.

An alternative method of staging which may be used is the modified Royal Marsden staging system (see below).[43] This staging method has been suggested in some studies to be more prognostically significant and helpful in guiding further therapy than TNM and it is included below as it is requested by some oncological centres and still used in some large scale trials.[44,45]

TNM8 Descriptors for RPLNDs and other metastatic resections of primary testicular neoplasms[12,13]

Regional lymph nodes (pN)

The regional lymph nodes are the abdominal para-aortic (peri-aortic), pre-aortic, interaortocaval precaval, paracaval, retrocaval, and retro-aortic nodes. Nodes along the spermatic vein should be considered regional.

Laterality does not affect the N classification.

The intrapelvic and the inguinal nodes are considered regional after scrotal or inguinal surgery.

A ‘y’ prefix indicates those cases in which classification is performed during or following initial multimodality therapy (i.e., chemotherapy, radiation therapy, or both chemotherapy and radiation therapy).

Modified Royal Marsden Staging System

Stage I	Tumour confined to the testis	
Stage II	Infradiaphragmatic nodal involvement	
	IIA	Greatest dimension of involved nodes less than 2 centimetres (cm)
	IIB	Greatest dimension of involved nodes 2 cm or more but less than 5 cm
	IIC	Greatest dimension of involved nodes 5 cm or more but less than 10 cm
	IID	Greatest dimension of involved nodes 10 cm or more
Stage III	Supraclavicular or mediastinal involvement	
Stage IV	Extranodal metastases	

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