Belgian Cancer Registry

Paediatric cancer stage guidelines for the Belgian general cancer registration, incidence year 2020

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Abbreviations

BCR	Belgian Cancer Registry
CNS	Central nervous system
CSF	Cerebrospinal fluid
c	Clinical
FIGO	International Federation of Gynecology and Obstetrics
FNCLCC	French Federation of Cancer Centers Sarcoma Group
ICD-0 3	International Classification of Diseases for Oncology, 3th edition
IDRF	Imaging-defined risk factor
INRGSS	International Neuroblastoma Risk Group Staging System
IRSS	International Retinoblastoma Staging System
M	Distant metastasis
N	Regional lymph node metastasis
p	Pathological
RBC	Red blood cells
T	Extent of primary tumour
UICC	Union for International Cancer Control
WBC	White blood cells
WBCR	Web-based cancer registration
y	Classification after neoadjuvant treatment

1 Aim of the document

The Belgian Cancer Registry recommends to include the Tiered staging system described in the chapter "Paediatric Tumours" of the TNM booklet, 8th edition[1] into their general cancer registration. This staging system is based on the Toronto Paediatric Cancer Stage Guidelines, which were determined on the consensus meeting held in 2014[2] and actualised in the consensus meeting in October 2019 in Lyon[3]. This document indicates and explains all the guidelines used for this registration.

2 Scope of application

- Those guidelines have to be applied by all paediatric hemato-oncology centres of Belgium for the registration of all children **aged 0-14 years at diagnosis**.
- Only for the data of incidence year 2020 and later, so **starting from incidence date January 1st 2020**!

3 Indications

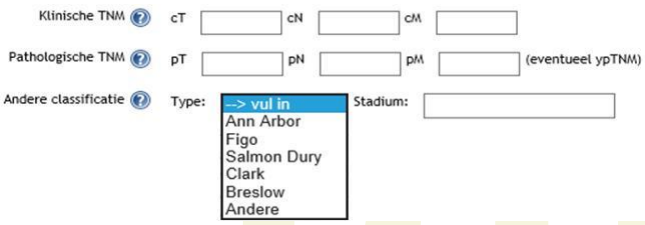
3.1 For the guidelines

- For the 14 types of tumours that are discussed in this manual:
  - We will notify in the beginning of each chapter if the TNM is applicable for the cancer group, and if so, the pages of the TNM 8th edition where you can find the information about this TNM.
  - You also have to fill out the paediatric cancer stage, whether or not the TNM is applicable.
  - Starting from the incidence year 2019, we will use the Tier 2 classification for every tumour type.

3.2 For the registration

- If applicable, **fill out the TNM classification** for all kind of tumours.
- Fill out the paediatric cancer stage in the **Other Classification variable** (Figure 1).
- For each cancer group, the stage overview is given for your information. It is also indicated in red which stage information should be registered by the Oncological Care Programs.

A



[1] TNM Classification of Malignant Tumours, Eighth Edition. Edited by Brierley JD, Gospodarowicz MK and Wittekind C, 2017 Union for International Cancer Control (UICC). Published by John Wiley & Sons, Ltd. p.247-53.
[2] Gupta S *et al.* Paediatric cancer stage in population-based cancer registries: the Toronto consensus principles and guidelines. Lancet Oncol. 2016 Apr;17(4):e163-72.
[3] Gupta S *et al.* Development of paediatric non-stage prognosticator guidelines for population-based cancer registries and updates to the 2014 Toronto Paediatric Cancer Stage Guidelines. Lancet Oncol. 2020 Sep;21(9):e444-51

B

Figure 1: Dutch (A) and French (B) version of the variables cTNM, pTNM and Other classification as they appear in the general web-based cancer registration (WBCR) of a new cancer diagnosis.

4 Paediatric cancer stage guidelines

4.1 Leukaemia

4.1.1 Acute lymphoblastic leukaemia (ICD-O 3: 9811→ 9818, 9835, 9837, 9727)

- ***TNM classification***: not applicable.
- ***Paediatric cancer stage***: use the Tier 2 which is determined according to the COG classification[4].

Stage	Explanation	Registration
CNS 1	No clinical sign* of CNS involvement and no blasts in the CSF	Other classification: Other → Stage: CNS1
CNS 2	No clinical sign* of CNS involvement but blasts in the CSF with either WBC < 5 µL CSF Or WBC ≥ 5 µL CSF, RBC ≥ 10 µL CSF and WBC/RBC in CSF ≤ 2x WBC/RBC in blood**	Other classification: Other → Stage: CNS2
CNS 3	Clinical signs* of CNS involvement or blasts in the CSF with WBC ≥ 5 µL CSF and either RBC < 10 µL CSF Or RBC ≥ 10 µL CSF and WBC/RBC in CSF > 2x WBC/RBC in blood**	Other classification: Other → Stage: CNS3

CSF: cerebrospinal fluid. WBC: white blood cells. RBC: red blood cells

* Clinical signs of central nervous system (CNS) involvement includes radiologic evidence of intracranial, intradural mass; cranial nerve palsy, eye/brain involvement or hypothalamic syndrome.
Extra-ocular orbital masses, severe headaches and eye swelling (in the absence of signs of cranial nerve involvement) are not sufficient to constitute CNS involvement.

** This comes from the Steinherz-Bleyer algorithm: a lumbar puncture will be considered as traumatic (i.e. blood introduced in the CSF) if the ratio of the White Blood Cells to the Red Blood Cells in the CSF divided by the same ratio in the blood equals more than 2. If the other conditions are met (WBC ≥ 5 µL CSF and RBC ≥ 10 µL CSF), a traumatic lumbar puncture, which could worsen the outcome, has to be classified as CNS 3, and a non-traumatic one as CNS 2.

[4] Winick N *et al.* Impact on initial CSF findings on outcome among patients with national cancer institute standard- and high-risk B-cell acute lymphoblastic leukemia: A report from the Children's Oncology Group. Journal of Clinical Oncology, 2017 Aug;35(22), 2527-2534.

4.2 Lymphoma

4.2.1 Hodgkin's Lymphoma (ICD-O 3: 9650→9653, 9659, 9663)

- ***TNM classification***: not applicable.
- ***Paediatric cancer stage***: use the Tier 2 classification which is determined according to the Lugano classification, an updated version of the Ann Arbor (see TNM 8th edition page 235 for more information)[1].

Stage	Explanation	Registration
Lugano stage I A/B	Involvement of a single lymph node region or localised involvement of a single extralymphatic organ or site	Other classification: Other → Stage: Lugano IA or Lugano IB *
Lugano stage II A/B	Involvement of two or more lymph node regions on the same side of the diaphragm, or localised involvement of a single extralymphatic organ or site and its regional lymph node(s) with or without involvement of other contiguous lymph node regions on the same side of the diaphragm	Other classification: Other → Stage: Lugano IIA or Lugano IIB *
Lugano Bulky stage II	Stage II disease with a single nodal mass greater than 10cm in maximum dimension or greater than a third of the thoracic diameter as assessed on CT.	Other classification: Other → Stage: Lugano Bulky IIA or Lugano Bulky IIB *
Lugano stage III A/B	Involvement of lymph node regions on both sides of the diaphragm, which may also be accompanied by involvement of the spleen	Other classification: Other → Stage: Lugano IIIA or Lugano IIIB *
Lugano stage IV A/B	Disseminated (multifocal) involvement of one or more extralymphatic organs, with or without associated lymph node involvement, or non-contiguous extralymphatic organ involvement with involvement of lymph node regions on the same or both sides of the diaphragm	Other classification: Other → Stage: Lugano IVA or Lugano IVB *

* A and B classification:

Each stage should be divided into A and B according to the absence (A) or presence (B) of defined general symptoms, which include:

- Unexplained weight loss of more than 10% of the usual body weight in the 6 months prior to first attendance
- Unexplained fever with temperature above 38°C
- Night sweats (e.g. those that require change of bedclothes)

4.2.2 Non-Hodgkin's Lymphoma (ICD-O 3: 9591, 967_→971_)

- ***TNM classification***: not applicable.
- ***Paediatric cancer stage***: use the Tier 2 which is determined according to the St Jude/Murphy classification[5].
- ***Burkitt*** : even if both Burkitt lymphoma and leukaemia have the same code 9687/3, only the Burkitt lymphoma has to be classified. There is no paediatric cancer stage for the leukaemic presentation of the Burkitt lymphoma.

Stage	Explanation	Registration
St Jude/Murphy I	Involvement of a single tumour mass or nodal area, excluding the abdomen and mediastinum	Other classification: Other → Stage: St Jude/Murphy I
St Jude/Murphy II	Single tumour (extranodal) with regional node involvement or Two or more nodal areas on the same side (either above or below) of the diaphragm or Two or more single (extranodal) tumours, with or without regional node involvement, on the same side (either above or below) of the diaphragm or A completely resected primary gastrointestinal tract tumour with or without involvement of associated mesenteric nodes only	Other classification: Other → Stage: St Jude/Murphy II
St Jude/Murphy III	Tumours (extranodal) or nodal areas on opposite sides (above and below) of the diaphragm or Any primary intrathoracic tumours (mediastinal, hilar, pulmonary, pleural or thymic) or Extensive* (unresectable) primary intra-abdominal disease or Any paraspinal or epidural tumours regardless of other tumour sites	Other classification: Other → Stage: St Jude/Murphy III
St Jude/Murphy IV	Initial CNS and/or bone marrow involvement	Other classification: Other → Stage: St Jude/Murphy IV

*Extensive disease typically exhibits spread to para-aortic and retro-peritoneal areas by implants and plaques in mesentery or peritoneum, or by direct infiltration of structures adjacent to the primary tumour. Ascites may be present, and complete resection of all gross tumour is not possible.

[5] Rosolen A. *et al*. Revised International Pediatric Non-Hodgkin Lymphoma Staging System. Journal of Clinical Oncology, 2015 Jun;33(18):2112-2118

4.3 Nervous system tumours

4.3.1 Ependymoma* & Medulloblastoma** (and other CNS embryonal tumours***) (ICD-O 3: * 9383,9391→9394; ** 9470→9472, 9474, 9490; *** 9473, 9500→9504, 9508)

- ***TNM classification***: not applicable.
- ***Paediatric cancer stage***: use the Tier 2 classification which is classified according to the M-stage[6]. This classification is only applicable to the tumour types that can be found above, and does not apply to the other CNS tumours.
  Do not mistake this M-stage with the M-category of the TNM classification !

Stage	Explanation	Registration
M0	Absence of visible disease beyond the primary tumour on imaging (MRI brain and spine) and absence of tumour cells in the cerebrospinal fluid	Other classification: Other → Stage: M0
M1	Tumour cells in the cerebrospinal fluid	Other classification: Other → Stage: M1
M2	Visible metastases in the brain	Other classification: Other → Stage: M2
M3	Visible metastases in the spine or cervicomedullary (junction)	Other classification: Other → Stage: M3
M4	Metastases outside of the central nervous system	Other classification: Other → Stage: M4

[6] Harisiadis L. and Chang C. H. Medulloblastoma in Children: A correlation between staging and results of treatment. International Journal of Radiation Oncology ° Biology ° Physics, 1977; 2, 833-841

4.3.2 Neuroblastoma (ICD-O 3: 9490, 9500)

- ***TNM classification***: not applicable.
- ***Paediatric cancer stage***: use the Tier 2 classification which is made according to the International Neuroblastoma Risk Groupe Staging System (INRGSS), a clinical classification system that is determined prior to any treatment, including surgery.

Stage	Explanation	Registration
INRGSS - localised L1	Localised tumour confined to one body compartment, neck, chest, abdomen or pelvis, and with the absence of imaging-defined risk factors (IDRFs)*. An isolated finding of intraspinal tumour extension that does not fulfil the criteria for an IDRF* is consistent with stage L1.	Other classification: Other → Stage: INRGSS L1
INRGSS - locoregional L2	Locoregional tumours with the presence of one or more IDRFs*. The tumour may be ipsilateral continuous within body compartments (ie, a left-sided abdominal tumour with left-sided chest involvement should be considered stage L2). However, a clearly left sided abdominal tumour with right-sided chest (or vice versa) involvement is defined as metastatic disease.	Other classification: Other → Stage: INRGSS L2
INRGSS - metastatic M	Distant metastatic disease (ie, not contiguous with the primary tumour) except as defined for stage MS. Non regional (distant) lymph node involvement is metastatic disease. However, an upper abdominal tumour with enlarged lower mediastinal nodes or a pelvic tumour with inguinal lymph node involvement is considered locoregional disease. Ascites and/or pleural effusion, even with malignant cells, do not constitute metastatic disease unless they are remote from the body compartment of the primary tumour.	Other classification: Other → Stage: INRGSS M
INRGSS - MS disease	Metastatic disease confined to skin, liver and/or bone marrow in children < 18 months of age (547 days). MIBG scintigraphy must be negative in bone and bone marrow.	Other classification: Other → Stage: INRGSS MS

* For more information regarding IDRFs, see Table 1.

Table 1: Imaging-defined risk factors (IDRFs) in neuroblastic tumours

Table 1. Image-Defined Risk Factors in Neuroblastic Tumors

Ipsilateral tumor extension within two body compartments
Neck-chest, chest-abdomen, abdomen-pelvis
Neck
Tumor encasing carotid and/or vertebral artery and/or internal jugular vein
Tumor extending to base of skull
Tumor compressing the trachea
Cervico-thoracic junction
Tumor encasing brachial plexus roots
Tumor encasing subclavian vessels and/or vertebral and/or carotid artery
Tumor compressing the trachea
Thorax
Tumor encasing the aorta and/or major branches
Tumor compressing the trachea and/or principal bronchi
Lower mediastinal tumor, infiltrating the costo-vertebral junction between T9 and T12
Thoraco-abdominal
Tumor encasing the aorta and/or vena cava
Abdomen/pelvis
Tumor infiltrating the porta hepatis and/or the hepatoduodenal ligament
Tumor encasing branches of the superior mesenteric artery at the mesenteric root
Tumor encasing the origin of the coeliac axis, and/or of the superior mesenteric artery
Tumor invading one or both renal pedicles
Tumor encasing the aorta and/or vena cava
Tumor encasing the iliac vessels
Pelvic tumor crossing the sciatic notch
Intraspinal tumor extension whatever the location provided that:
More than one third of the spinal canal in the axial plane is invaded and/or the perimedullary leptomeningeal spaces are not visible and/or the spinal cord signal is abnormal
Infiltration of adjacent organs/structures
Pericardium, diaphragm, kidney, liver, duodeno-pancreatic block, and mesentery
Conditions to be recorded, but *not* considered IDRFs
Multifocal primary tumors
Pleural effusion, with or without malignant cells
Ascites, with or without malignant cells

Abbreviation: IDRFs, image-defined risk factors.

Adopted from Monclair *et al.*, 2009.[7]

[7] Monclair T *et al.* The International Neuroblastoma Risk Group (INRG) staging system: an INRG Task Force report. Journal of Clinical Oncology, 2009; 27: 298–303.

4.4 Ophthalmic, renal and hepatic tumours

4.4.1 Retinoblastoma (ICD-O 3: 9510→9514)

- ***TNM classification***: has to be registered (for more information about this TNM, see TNM 8th edition, p.226-229)[1].
- ***Paediatric cancer stage***: use the Tier 2 classification which is made according to the International Retinoblastoma Staging System (IRSS), a pathological classification system determined after enucleation.
- In case of bilateral disease, two registrations should be performed.

Stage	Explanation	Registration
IRSS stage 0	The tumour is confined to the globe, enucleation has not been performed	Other classification: Other → Stage: IRSS 0
IRSS stage I	Enucleation with negative margins (R0)	Other classification: Other → Stage: IRSS I
IRSS stage II	Enucleation with microscopic residual disease (R1)	Other classification: Other → Stage: IRSS II
IRSS stage III	Involvement of the orbit and/or metastases to regional lymph nodes	Other classification: Other → Stage: IRSS III
IRSS stage IV	Metastatic disease	Other classification: Other → Stage: IRSS IV

R: residual tumour.

The staging subclassifications described in Table 2 can be further specified during registration (a-b, a1-2, b1-3), but are not required.

Table 2: International Retinoblastoma Staging System (IRSS)

Stage 0. Patients treated conservatively
Stage I. Eye enucleated, completely resected histologically
Stage II. Eye enucleated, microscopic residual tumour
Stage III. Regional extension
  a. Overt orbital disease
  b. Preauricular or cervical lymph node extension
Stage IV Metastatic disease
  a. Hematogenous metastasis (without CNS involvement)
    1. Single lesion
    2. Multiple lesions
  b. CNS extension (with or without any other site of regional or metastatic disease)
    1. Prechiasmatic lesion
    2. CNS mass
    3. Leptomeningeal and CSF disease

Adopted from Chantada *et al.*, 2006.[8]
CNS: central nervous system; CSF: cerebrospinal fluid.

[8] Chantada G *et al.* A proposal for an international retinoblastoma staging system. Pediatr Blood Cancer 2006; 47:801–05.

4.4.2 Renal tumours, except renal cell carcinomas (ICD-O 3: C64.9)

- ***TNM classification***: not applicable.
- ***Renal cell carcinomas are not included because they follow the TNM classification (which is applicable for them)***.
- ***Paediatric cancer stage***: Two staging systems exist for the Tier 2 classification :
  - Children's Oncology Group (COG) / National Wilms Tumour Study Group (NWTSG)
    - Utilised after surgical resection, no chemotherapy prior to surgery
  - International Society of Paediatric Oncology (SIOP)
    - Utilised after surgical resection, patient did receive chemotherapy prior to surgery
- In case of bilateral disease, two registrations should be performed.

Stage	Explanation	Registration
Stage I	See Table 3	Other classification: Other → Stage: COG I or SIOP I
Stage II		Other classification: Other → Stage: COG II or SIOP II
Stage III		Other classification: Other → Stage: COG III or SIOP III
Stage IV		Other classification: Other → Stage: COG IV or SIOP IV

Table 3: Staging system for renal tumours

COG/NWTSG (before chemotherapy)	*SIOP (after chemotherapy)*
Stage I Tumour is limited to the kidney and completely excised: • Renal capsule intact, not penetrated by tumour • No tumour invasion of veins or lymphatics of renal sinus • No nodal or haematogenous metastases • No prior biopsy • Negative margins	**Stage y-I** Tumour limited to kidney and completely resected: • Renal capsule may be infiltrated by tumour, but tumour does not reach the outer surface • Tumour may protrude or bulge into the pelvic system or ureter, but does not infiltrate • Vessels of renal sinus not involved
Stage II Tumour extends beyond kidney but completely resected: • Tumour penetrates renal capsule • Tumour in lymphatics or veins of renal sinus • Tumour in renal vein with margin not involved • No nodal or haematogenous metastases • Negative margins	**Stage y-II** Tumour extends beyond kidney but completely resected: • Tumour penetrates renal capsule into perirenal fat • Tumour infiltrates the renal sinus and/or invades blood and lymphatic vessels outside renal parenchyma but is completely resected • Tumour infiltrates adjacent organs or vena cava but is completely resected
Stage III Residual tumour or nonhaematogenous metastases confined to abdomen: • Involved abdominal nodes • Peritoneal contamination or tumour implant • Tumour spillage of any degree occurring before or during surgery • Gross residual tumour in abdomen • Biopsy of tumour (including fine-needle aspiration) prior to removal of kidney • Resection margins involved by tumour	**Stage y-III** Incomplete excision of the tumour (gross or microscopic extension beyond the resection margins): • Involved abdominal lymph nodes, including necrotic tumour or chemotherapy-induced changes • Tumour rupture before or intraoperatively • Tumour has penetrated the peritoneal surface • Tumour thrombi present at resection margins • Surgical biopsy prior to resection (does not include needle biopsy)
Stage IV Haematogenous metastases or spread beyond abdomen at diagnosis	**Stage IV** Haematogenous metastases or spread beyond abdomen at diagnosis.

Adopted from Aitken JF *et al.*, 2017.[9]

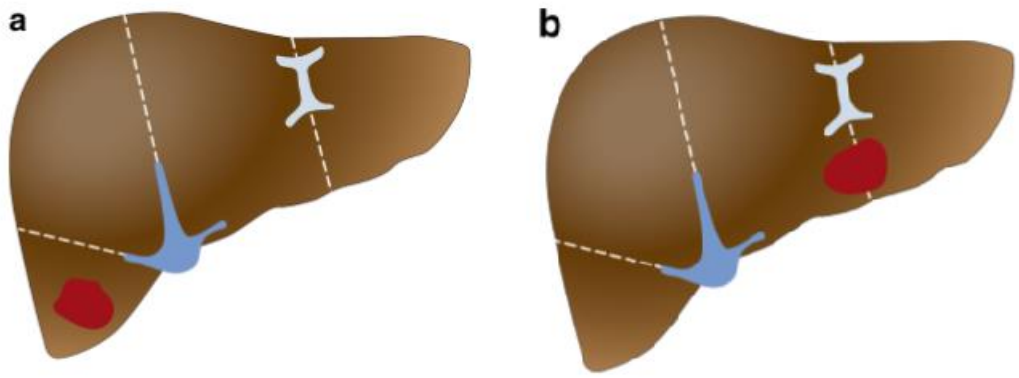
[9] Aitken JF et al., Childhood cancer staging for population registries according to the Toronto Childhood Cancer Stage Guidelines, Cancer Council Queensland and Cancer Australia: Brisbane, Australia; 2017.

4.4.3 Hepatoblastoma (ICD-O 3: 8970)

- ***TNM classification***: not applicable.
- ***Paediatric cancer stage***: use the Tier 2 which is made according to the PRETEXT classification, a system that uses the hepatic and portal veins to divide the liver into 5 sections (see Figure 2).

Stage	Explanation	Registration
Stage I	Only 1 liver section is involved, leaving 3 contiguous sections free of tumour	Other classification: Other → Stage: Pretext I
Stage II	1 or 2 liver sections are involved, but 2 contiguous sections are free of tumour. Tumours that only involve the caudate lobe (segment 1) are considered to be Stage II	Other classification: Other → Stage: Pretext II
Stage III	Tumour invades 3 liver sections and 1 liver section is free of tumour or tumour involves 2 liver sections and 2 non-contiguous liver sections are free of tumour	Other classification: Other → Stage: Pretext III
Stage IV	All 4 sections are involved. There is no liver section free of tumour	Other classification: Other → Stage: Pretext IV

Figure 2[10]: Example of a Stage I (a) and II (b) liver tumour according to the PRETEXT classification.



[10] Towbin AJ *et al.* 2017 PRETEXT: radiologic staging system for primary hepatic malignancies of childhood revised for the Paediatric Hepatic International Tumour Trial (PHITT), Pediatric Radiology, 2018;48:536-554.

4.5 Bone and soft tissue tumours

4.5.1 Osteosarcoma* & Ewing's Sarcoma** (considered together as Bone tumours) (ICD-O 3: * 9180→9187, 9191→9195,9200; ** 9364)

- ***TNM classification***: has to be registered, except for surface/juxtacortical osteosarcoma for which the TNM is not applicable (for more information about this TNM, see TNM 8th edition, p.120-123)[1].
- ***Paediatric cancer stage***: use the Tier 2 classification which indicates if the tumour is metastatic or not.

Stage	Explanation	Registration
Localised	Tumour confined to area of origin, including regional lymph nodes	Other classification: Other → Stage: Localised
Metastatic	Distant metastases present	Other classification: Other → Stage: Metastatic

Note that "skip lesions", "skip metastases" or "seeding" in the same bone as the primary tumour are considered localized and not metastatic; if in a different bone to the primary tumour these are considered metastatic.

4.5.2 Rhabdomyosarcoma (ICD-O 3: 8900→8905,8910,8912,8920,8921)

- ***TNM classification***: has to be registered. Be careful, the paediatric TNM options are different from the adult options (for more information about this TNM, see TNM 8th edition, p.248)[1].
- ***Paediatric cancer stage***: use the Tier 2 classification which incorporates this paediatric TNM classification with the anatomical site of the tumour.

Stage	Explanation	Registration
Stage I	Any T; Any N; M0; Favourable site*	Other classification: Other → Stage: Toronto I
Stage II	T1a, T2a; N0; M0; Unfavourable site**	Other classification: Other → Stage: Toronto II
Stage III	T1a, T2a; N1; M0; Unfavourable site** T1b, T2b; Any N; M0; Unfavourable site**	Other classification: Other → Stage: Toronto III
Stage IV	Any T; Any N; M1; Any site	Other classification: Other → Stage: Toronto IV

* Favourable anatomic sites: Orbit, head and neck (excluding parameningeal tumours) and genito-urinary sites (excluding bladder and prostate tumours).
** Unfavourable anatomic sites: Bladder, prostate, extremity, cranial, parameningeal, trunk, retro-peritoneum and all other sites not noted as favourable.

TNM clinical classification for Rhabdomyosarcoma:

T - Primary tumour

TX Primary tumour cannot be assessed
T0 No evidence of primary tumour
T1 Confined to a single anatomic site
T1a Tumour 5 cm or less in greatest dimension

T1b Tumour more than 5 cm in greatest dimension
T2 Extension beyond anatomic site
T2a Tumour 5 cm or less in greatest dimension
T2b Tumour more than 5 cm in greatest dimension

N - Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Regional lymph node metastasis

M - Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis

4.5.3 Soft Tissue Sarcoma other than Rhabdomyosarcoma

- ***TNM classification***: has to be registered if applicable. This will depend on the histological type and anatomical site of the tumour (for more information about this TNM, see TNM 8th edition, p.124-126)[1].
- ***Paediatric cancer stage***: use the Tier 2 classification which incorporates the TNM classification with the tumour grade.

Stage	Explanation	Registration
Stage I	Any T; N0; M0 ; G1 or GX (Low Grade)	Other classification: Other → Stage: Toronto I
Stage II	T1; N0; M0; G2 or G3 (High Grade)	Other classification: Other → Stage: Toronto II
Stage III	T2 or T3 or T4; N0; M0; G2 or G3 (High Grade) Any T; N1; M0; Any G	Other classification: Other → Stage: Toronto III
Stage IV	Any T; Any N; M1; Any G	Other classification: Other → Stage: Toronto IV

4.5.3.1 Histopathological grading

The French Federation of Cancer Centers Sarcoma Group (FNCLCC) grading system has some limitations. In some tumours, grading is less informative than the histological type. This system should not be used in tumours that rarely metastasise. Given their diversity, it is considered as unrealistic to develop a grading system for every specific histological type. However, it has been agreed that the FNCLCC system performs correctly for the most frequent sarcoma types. It is thus recommended to use the FNCLCC in general and, when not possible, to take the differentiation score as the grade. The FNCLCC system is based on three independent parameters that are the differentiation degree (1 to 3), the mitotic activity (1 to 3) and the extent of necrosis (1 to 2), according to the definitions in Table 4.

Table 4: Definition of histopathological parameters in the FNCLCC grading system.

FNCLCC parameter	Score	Definition
Differentiation score	1	Well-differentiated liposarcoma Well-differentiated leiomyosarcoma Malignant neurofibroma Well-differentiated fibrosarcoma
	2	Myxoid liposarcoma Conventional leiomyosarcoma Conventional MPNST Conventional fibrosarcoma Myxofibrosarcoma Myxoid chondrosarcoma Conventional angiosarcoma
	3	High grade myxoid (round cell) liposarcoma Pleomorphic liposarcoma Dedifferentiated liposarcoma Rhabdomyosarcoma Poorly differentiated/pleomorphic leiomyosarcoma Poorly differentiated/epithelioid angiosarcoma Poorly differentiated MPNST Malignant Triton tumour Synovial sarcoma Extraskeletal osteosarcoma Extraskeletal Ewing sarcoma Mesenchymal chondrosarcoma Clear cell sarcoma Epithelioid sarcoma Alveolar soft part sarcoma Malignant rhabdoid tumour Undifferentiated (spindle cell and pleomorphic) sarcoma
Mitotic count score (established on the basis of 10 HPF; 1 HPF = 0.1734 mm²)	1	0-9 mitoses per 10 HPF
	2	10-19 mitoses per 10 HPF
	3	≥20 mitoses per 10 HPF
Necrosis score	0	No necrosis
	1	<50% tumour necrosis
	2	≥50% tumour necrosis

Adopted from the WHO Classification of Tumours of Soft Tissue and Bone, 2013, p.17.[11]
FNCLCC: French Federation of Cancer Centers Sarcoma Group; HPF: high-power field.

These three parameter scores are summed (total sum 2-8) to determine the FNCLCC grade:

- FNCLCC grade 1: Total sum 2-3
- FNCLCC grade 2: Total sum 4-5
- FNCLCC grade 3: Total sum 6-8
- FNCLCC grade X: Grade cannot be assessed

Grades 1 and X are considered Low Grade, grades 2 and 3 are considered High Grade. This signifies that a tumour with differentiation score 3 is automatically High Grade since the minimal mitotic count score is 1 (= total sum ≥4).

[11] WHO Classification of Tumours of Soft Tissue and Bone, Fourth Edition. Edited by Fletcher *et al.*, 2013 WHO. Published by International Agency for Research on Cancer (IARC). p.17-18.

4.6 Reproductive system tumours

4.6.1 Ovarian tumour (ICD-O 3: C56.9)

- ***TNM classification***: has to be registered if applicable. This will depend on the histological type of the tumour (for more information about this TNM, see TNM 8th edition, p.179-183)[1].
- ***Paediatric cancer stage***: use the Tier 2 classification which corresponds to the International Federation of Gynecology and Obstetrics stage (FIGO).

Stage	Explanation	Registration
FIGO stage I	Tumour confined to the ovaries (one or both)	Other classification: Figo → Stage: I
FIGO stage II	Tumour extension to pelvis without extension to peritoneum outside the pelvis nor to retroperitoneal lymph nodes	Other classification: Figo → Stage: II
FIGO stage III	Tumour extension to peritoneum outside the pelvis and/or retroperitoneal lymph nodes	Other classification: Figo → Stage: III
FIGO stage IV	Distant metastases present (excludes peritoneal metastases)	Other classification: Figo → Stage: IV

The FIGO staging subclassifications described in the TNM 8th edition, p.179-183[1] can be further specified during registration (A-C, Ali, Alii), but are not required.

4.6.2 Testicular tumour (ICD-O 3: C62.0, C62.1, C62.9)

- ***TNM classification***: has to be registered (for more information about this TNM, see TNM 8th edition, p.195-198)[1].
- ***Paediatric cancer stage***: use the Tier 2 classification which is made according to the TNM classification.
- In case of bilateral disease, two registrations should be performed.

Stage	Explanation	Registration
Stage I	Any T; N0; M0	Other classification: Other → Stage: Toronto I
Stage II	Any T; N1, N2, N3; M0	Other classification: Other → Stage: Toronto II
Stage III	Any T; Any N; M1	Other classification: Other → Stage: Toronto III

TNM clinical classification for Testis Tumour:

T - Primary Tumour

Except for pTis and pT4, where radical orchiectomy is not always necessary for classification purposes, the extent of the primary tumour is classified after radical orchiectomy; see pT. In other circumstances, TX is used if no radical orchiectomy has been performed.

N - Regional Lymph Nodes

NX Regional lymph nodes cannot be assessed
N0 No regional lymph node metastasis
N1 Metastases to single or multiple lymph nodes, each ≤2 cm in greatest dimension
N2 Metastases to single or multiple lymph nodes, >2 cm but ≤5 cm in greatest dimension
N3 Metastases with a lymph node mass >5 cm in greatest dimension

M - Distant Metastasis

M0 No distant metastasis
M1 Distant metastasis
M1a Non-regional lymph node(s) or lung metastasis
M1b Distant metastasis other than to non-regional lymph nodes and lung

pTNM pathological classification for Testis Tumour:

pT - Primary tumour

pTX Primary tumour cannot be assessed (see T - Primary Tumour)
pT0 No evidence of primary tumour (e.g. histological scar in testis)
pTis Intratubular germ cell neoplasia (carcinoma *in situ*)
pT1 Tumour limited to testis and epididymis without vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis
pT2 Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginea with involvement of tunica vaginalis
pT3 Tumour invades spermatic cord with or without vascular/lymphatic invasion
pT4 Tumour invades scrotum with or without vascular/lymphatic invasion

pN - Regional Lymph Nodes

pNX Regional lymph nodes cannot be assessed
pN0 No regional lymph node metastasis
pN1 Metastases to single or maximum 5 lymph nodes, each ≤2 cm in greatest dimension
pN2 Metastases with a lymph node mass >2 cm but ≤5 cm in greatest dimension; or evidence of extranodal extension of tumour
pN3 Metastases with a lymph node mass >5 cm in greatest dimension

pM - Distant Metastasis

pM1 Distant metastasis microscopically confirmed
pM1a Non-regional lymph node(s) or lung metastasis
pM1b Distant metastasis other than to non-regional lymph nodes and lung

5 Paediatric cancer stage : Summary

- If applicable, fill out the TNM classification for all kind of tumours.
- In the table below, you can find a summary of the tiered paediatric cancer staging.
- Starting from the incidence year 2019, only the Tier 2 staging systems will be used.

	Tier 1 staging system	Tier 2 staging system
ALL	CNS neg/pos	CNS 1/2/3
Hodgkin's lymphoma	Lugano stage I/II/III/IV A/B	Lugano stage I/II/III/IV A/B
Non-Hodgkin lymphoma	Limited/Advanced	St Jude/Murphy stage I/II/III/IV
Ependymoma	M0/M+	M0/ 1/ 2/ 3/ 4
Medulloblastoma and other CNS embryonal tumours	M0 or localised/M+ or metastatic	M0/ 1/ 2/ 3/ 4
Neuroblastoma	Localised/Locoregional/Metastatic/ INRGSS – MS disease	INRGSS – Localised L1/ Locoregional L2/ Metastatic M/ MS disease
Retinoblastoma	Localised (intraocular)/ Regional (orbital or regional lymph nodes)/ Distant (extra-orbital)	IRSS stage 0/I/II/III/IV
Renal tumours, except renal cell carcinomas	Localised/Metastatic	NWTSG/COG or SIOP stage I/II/III/IV
Hepatoblastoma	Localised/Metastatic	PRETEXT stage I/II/III/IV
Osteosarcoma	Localised/Metastatic	Localised/Metastatic
Ewing's sarcoma	Localised/Metastatic	Localised/Metastatic
Rhabdomyosarcoma	Localised/Metastatic	TNM stage I/II/III/IV
Non-rhabdomyosarcoma soft-tissue sarcomas	Localised/Metastatic	TNM stage I/II/III/IV
Ovarian tumour	Localised/Regional/Metastatic	FIGO stage I/II/III/IV
Testicular tumour	Localised/Regional/Metastatic	TNM stage I/II/III