

## TNM Classification for Retinoblastoma

The TNM (Tumour, Node, Metastasis) classification is developed, monitored and enforced by the American Joint Commission on Cancer and the Union Internationale Contre le Cancer (AJCC/UICC). Many cancers have a unique TNM classification, but TNM has traditionally been used only for extension of retinoblastoma beyond the eye.

The TNM classification for retinoblastoma was redeveloped in 2010 to incorporate the International Intraocular Retinoblastoma Classification which has been favoured by physicians worldwide in staging tumour within the eye.

The system includes both clinical (cTNM) and pathological (pTNM) findings. Primary retinoblastoma (T) is divided into four groups, with several sub-groups in each, and many additional descriptors. The stages from cT1a – cT3b closely reflect the five stages of the International Intraocular Retinoblastoma Classification. Stage cT3 (IIRC Group E) indicates high risk for invasion of tissues surrounding the eye, and the need for urgent removal of the eye. Stage pT2 and pT3 confirm invasion of surrounding tissues. Stages cT4, pT4 N and M involve significant disease invasion of tissues beyond the eye.

From June 2010, researchers are required to state TNM classification alongside or in place of IIRC / REC in manuscripts submitted for journal publication or conference presentation.

When both eyes are affected, each eye is staged independently. When only one stage is stated in patient reports for a bilateral child, this refers to the stage of the worst eye, as an indicator of risk to the child's life.

### Clinical Classification (cTNM)

#### Primary Tumour (T)

cTX: Primary Tumour cannot be assessed.

cT0: No evidence of primary tumour.

**cT1: Tumours no more than 2/3 the volume of the eye, with no vitreous or subretinal seeding:**

cT1a: No tumour in either eye is greater than 3mm in largest dimension, or located closer than 1.5mm to the optic nerve or fovea.

cT1b: At least one tumour is greater than 3mm in largest dimension, or located closer than 1.5mm to the optic nerve or fovea. No retinal detachment or subretinal fluid beyond 5mm from the base of the tumour.

cT1c: At least one tumour is greater than 3mm in largest dimension, or located closer than 1.5mm to the optic nerve or fovea, with retinal detachment or subretinal fluid beyond 5mm from the base of the tumour.

**cT2: Tumours no more than 2/3 the volume of the eye with vitreous or subretinal seeding. Can have retinal detachment:**

cT2a: Focal vitreous and / or subretinal seeding of fine aggregates of tumour is present, but no large clumps or "snowballs" of tumour cells.

cT2b: Massive vitreous and / or subretinal seeding is present, defined as diffuse clumps or "snowballs" of tumour cells.

**cT3: Severe Intraocular Disease:**

cT3a: Tumour fills more than 2/3 of the eye.

cT3b: One or more complications present which may include tumour-associated neovascular or angle closure glaucoma, tumour extension into the anterior segment, hyphema, vitreous hemorrhage or orbital cellulitis.

**cT4: Extra-ocular disease detected by imaging studies:**

cT4a: Invasion of optic nerve.

cT4b: Invasion into the orbit.

cT4c: Intracranial extension not past the chiasm.

cT4d: Intracranial extension past chiasm.

Note: The following suffixes may be added to the appropriate T categories:

"m" indicates multiple tumours (eg, T2 [m2]).

"f" indicates cases with a known family history.

"d" indicates diffuse retinal involvement without the formation of discrete masses.

**Regional Lymph Nodes (N)**

cNX: Regional lymph nodes cannot be assessed.

cN0: No regional lymph node metastasis.

cN1: Regional lymph node metastasis involvement (preauricular, cervical, submandibular).

cN2: Distant lymph node involvement.

### **Distant Metastasis (M)**

cMX: Presence of distant metastasis cannot be assessed

cM0: No distant metastasis

#### **cM1: Systemic metastasis:**

cM1a: Single lesion to sites other than Central Nervous System.

cM1b: Multiple lesions to sites other than Central Nervous System.

cM1c: Prechiasmatic Central Nervous System lesion(s).

cM1d: Postchiasmatic Central Nervous System lesion(s).

cM1e: Leptomeningeal or CerebroSpinal Fluid involvement.

### **Pathologic Classification (pTNM)**

#### **Primary Tumour (pT)**

pTX: Primary Tumour cannot be assessed.

pT0: No evidence of primary tumour.

pT1: Tumour confined to the eye with no optic nerve or choroidal invasion.

#### **pT2: Tumour with minimal optic nerve and / or choroidal invasion:**

pT2a: Tumour superficially invades optic nerve head but does not extend past lamina cribrosa, **or** tumour exhibits focal choroidal invasion.

pT2b: Tumour superficially invades optic nerve head but does not extend past lamina cribrosa **and** tumour exhibits focal choroidal invasion.

#### **pT3: Tumour with significant optic nerve and / or choroidal invasion:**

pT3a: Tumour invades optic nerve past lamina cribrosa but not to surgical resection line, **or** tumour exhibits massive choroidal invasion.

pT3b: Tumour invades optic nerve past lamina cribrosa but not to surgical resection line **and** exhibits massive choroidal invasion.

**pT4: Tumour invades optic nerve to surgical resection line or exhibits extra-ocular extension elsewhere.**

pT4a: Tumour invades optic nerve to resection line, but no extra-ocular extension identified.

pT4b: Tumour invades optic nerve to resection line, and extra-ocular extension identified.

### **Regional Lymph Nodes (pN)**

pNX: Regional lymph nodes cannot be assessed.

pN0: No regional lymph node metastasis.

pN1: Regional lymph node involvement (preauricular, cervical).

N2: Distant lymph node involvement.

### **Metastasis (pM)**

pMX: Presence of metastasis cannot be assessed.

pM0: No distant metastasis.

### **pM1: Metastasis to sites other than Central Nervous System**

pM1a: Single lesion

pM1b: Multiple lesions

pM1c: CNS metastasis

pM1d: Discrete masses without leptomeningeal and / or CSF involvement

pM1e: Leptomeningeal and / or CSF involvement

### **TNM Descriptors**

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

- “m” (suffix) indicates the presence of multiple primary tumours in a single site and is recorded in parentheses: pT(m)NM.
- “y” (prefix) indicates those cases in which classification is performed during or following initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy).
- The cTNM (clinical) or pTNM (pathological) category is identified by a “y” prefix. The ycTNM or ypTNM categorizes the extent of tumour actually present at the time of that examination. The “y” categorization is not an estimate of tumour prior to multimodality therapy (ie, before initiation of neoadjuvant therapy).
- “r” (prefix) indicates a recurrent tumour when staged after a documented disease-free interval, and is identified by the “r” prefix: rTNM.
- “a” (prefix) designates the stage determined at autopsy: aTNM.

### **Additional Descriptors**

#### **Residual Tumour (R):**

Tumour remaining in a patient after therapy with curative intent (eg, surgical resection for cure) is categorized by a system known as R classification, shown below.

- RX: Presence of residual tumour cannot be assessed.  
 R0: No residual tumour.  
 R1: Microscopic residual tumour.  
 R2: Macroscopic residual tumour.

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R classification is relevant to the status of the margins of a surgical resection specimen. That is, tumour involving the resection margin on pathologic examination may be assumed to correspond to residual tumour in the patient, and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

#### **Vessel Invasion**

Vessel invasion (lymphatic or venous) does not affect the T: category indicating local extent of tumour, unless specifically included in the definition of a T category. In all other cases, lymphatic and venous invasion by tumour are coded separately as follows.

#### **Lymphatic Vessel Invasion (L)**

- LX: Lymphatic vessel invasion cannot be assessed.

- L0: No lymphatic vessel invasion.
- L1: Lymphatic vessel invasion.

**Venous Invasion (V)**

- VX: Venous invasion cannot be assessed.
- V0: No venous invasion.
- V1: Microscopic venous invasion.
- V2: Macroscopic venous invasion.