Tumor classification

In modern oncology tumors can not be diagnosed without assessing many aspects of the cancerous process. Some of the basic tumor classification strategies that come together to form a well-described tumor will be listed below. Only when a tumor is classified properly the doctor can lay a diagnosis, adequate therapy and prognosis.

When any tissue is suspected to be undergoing tumor transformation it needs to be examined by visual inspection (if possible) or other methods (X-ray, CT). When in doubt, suspicious tissue sample is removed from a patient's body (biopsy) and delivered to an institute or department of pathology (pathological anatomy) where it is properly evaluated by an experienced pathologist.

The pathologist uses various techniques to examine and determine as many aspects of the tissue as possible. He or she inspects the sample under microscope (morphology of the cells). Cytology of the tissue might not be enough to determine the type of tumor, so methods of imunohistochemistry (staining the sample with specific antibodies) or molecular-genetics (mostly looking for DNA changes, FISH) can be used as well. Examination with other clinical traits leads to determining the type, grade and stage of the tumor.

Typing

Typing the tumor means classifying it into a known category (blue books by WHO). Tumors emerging from the same tissue might be a different type even having similar clinical traits - this step is crucial for choosing the right therapy.

- In terms of the behavior of tumors there are two main categories:

1. **benign tumors**;
2. **malign tumors**.

A benign tumor is a mass of cells (tumor) that lacks the ability to either invade neighboring tissue or metastasize (spread throughout the body). When removed, benign tumors usually do not grow back, whereas malignant tumors sometimes do. [1] A malignant tumor contrasts with a non-cancerous benign tumor in that a malignancy is not self-limited in its growth, is capable of invading into adjacent tissues, and may be capable of spreading to distant tissues. A benign tumor has none of those properties.

Malignancy in cancers is characterized by anaplasia, invasiveness, and metastasis. [2]

This is a division by tumor properties, often unrelated to the prognosis as some malignancies can be fully cured; on the contrary, some benign tumors can be life-threatening.

Sometimes a third category is stated - **premalignant**: In these tumors, the cells are not yet cancerous, but they have the potential to become malignant.[3] Cervical dysplasia for example, sometimes it is described as carcinoma-in-situ.

- Looking at histogenesis of the tumor:

1. **Mesenchymal tissue tumors**: Mesenchymal tissue neoplasms are soft tissue tumors, also known as connective tissue tumors, which are relatively frequent in domestic animals and have a high incidence in some species.[4]. Benign tumors are distinguished by the suffix -oma, malignant by sarcoma.
2. **Hematopoietic cells**: Bone marrow-derived cells that normally mature in the bloodstream - leukemia x Bone marrow-derived cells that normally mature in the lymphatic system - lymphoma
3. **Epithelial tumors**: Originating from epithelial cells, subtypes of these are adenomas, adenocarcinomas and carcinomas (and carcinoma in situ).
4. **Neuroectodermal neoplasm** is a neoplasm or tumor of the neuroectoderm. [5] Neuroendocrine carcinomas (pituitary adenoma) or nonepithelial neuroectodermal neoplasms (malignant melanoma)
5. **Germ cell tumor** is a neoplasm derived from germ cells. Mostly localised in gonads, but can be found in other localizations as well (mediastinum). Two main classifications: germinomatous or seminomatous germ-cell tumors (seminoma, germinoma) and nongerminomatous or nonseminomatous germ-cell tumors (choriocarcinoma, teratoma, gonadoblastoma)
6. **Mezotelioma** Mesothelioma is a type of cancer that develops from the thin layer of tissue that covers many of the internal organs (known as the mesothelium).[6]

In determining the tumor the pathologist has to assess many aspects of the tissue and cell morphology, like N/C ratio (nucleus to cytoplasm), nuclei shape, whether the nuclei are looking alike and the chromatin density (nucleolus visibility). Shape and arrangement of cells is evaluated, fibrous stroma structure differs in many tumor types as well. These morphological traits lead the pathologist to which imunohistological antibody spectrum he or she should use to determine the type of tumor (using whole spectrum of antibodies would be extremely expensive).

Following the WHO classification, each tumor is assigned a numerical code. The morphology axis provides five-digit codes ranging from M-8000/0 to M-9989/3. The first four digits indicate the specific histological term. The fifth digit after the slash (/) is the behaviour code, which indicates whether a tumour is malignant, benign, in situ, or uncertain (whether benign or malignant).[7]

Grading

The neoplastic grading is a measure of cell anaplasia (reversion of differentiation) in the sampled tumor and is based on the resemblance of the tumor to the tissue of origin. [8] In other words, grading means determining the "degree of differentiation" (or de-differentiation) of a tumor.

It is indicated by the letter **G** . Grading has prognostic and predictive value. Usually, the less differentiated the tumor, the more "aggressive" it is, but it tends to be more sensitive to treatment. There are more grading systems as some tumors have their own specific.

GX Grade cannot be assessed
G1 Well differentiated (Low grade)
G2 Moderately differentiated (Intermediate grade)
G3 Poorly differentiated (High grade)
G4 Undifferentiated (High grade)

Staging

TMN

The TNM Classification of Malignant Tumors (TNM) is a globally recognised standard for classifying the extent of spread of cancer. It is a classification system of the anatomical extent of tumor cancers and is used in classifying malignant tumors mostly.

	TNM
T	describes the size of the original (primary) tumor and whether it has invaded nearby tissue
N	describes nearby (regional) lymph nodes that are involved
M	describes distant metastasis (spread of cancer from one part of the body to another)

Primary tumor (T)

TX: Main tumor cannot be measured.
T0: Main tumor cannot be found.
T1, T2, T3, T4: Refers to the size and/or extent of the main tumor. The higher the number after the T, the larger the tumor or the more it has grown into nearby tissues. T's may be further divided to provide more detail, such as T3a and T3b.

Regional lymph nodes (N)

NX: Cancer in nearby lymph nodes cannot be measured.
N0: There is no cancer in nearby lymph nodes.
N1, N2, N3: Refers to the number and location of lymph nodes that contain cancer. The higher the number after the N, the more lymph nodes that contain cancer.

Distant metastasis (M)

MX: Metastasis cannot be measured.
M0: Cancer has not spread to other parts of the body.
M1: Cancer has spread to other parts of the body. [9]

TMN classification can be extended by using prefixes as **cTMN** (before treatment), **pTMN** (stage assigned by histopathologic examination), **yTMN** (after chemotherapy and/or radiation therapy) and more. Other parameters stated are **G 1–4** for grade of differentiation, **S 0–3** describing serum tumor markers, **L 0–1** is invasion into lymphatic vessels and **V 0–2** invasion into vein (none, microscopic, macroscopic) according to wikipedia.[10]

Taking these in count TMN classification of a tumor may look like: pT1 pN0 M0 R0 G1 of a Stage I. cancerous process or pT4 pN2 M1 R1 G3 as an example of Stage IV. cancer.

Roman Numeral Staging

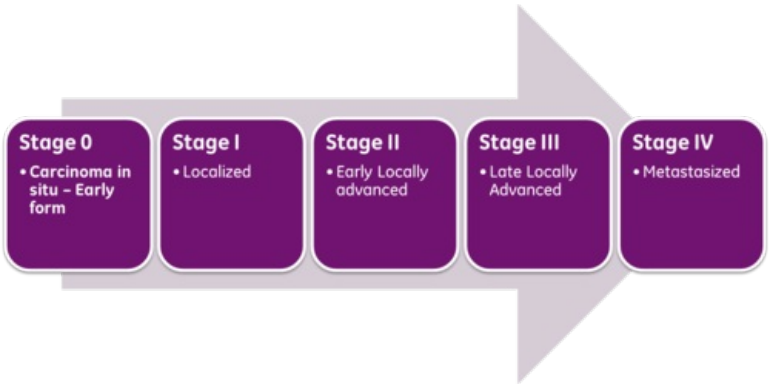
This staging system uses four roman numerals and describes the progress of cancerous process.

Stage 0 This stage describes cancer in situ, which means “in place.” Stage 0 cancers are still located in the place they started and have not spread to nearby tissues. This stage of cancer is often highly curable, usually by removing the entire tumor with surgery.

Stage I This stage is usually a small cancer or tumor that has not grown deeply into nearby tissues. It also has not spread to the lymph nodes or other parts of the body. It is often called early-stage cancer.

Stage II and Stage III In general, these 2 stages indicate larger cancers or tumors that have grown more deeply into nearby tissue. They may have also spread to lymph nodes but not to other parts of the body.

Stage IV This stage means that the cancer has spread to other organs or parts of the body. It may also be called advanced or metastatic cancer.



Cancer stages

Rating

Rating stands for determining the expression of important molecules and receptors in tumor cells. Some of the markers determined via immunohistochemical methods are:

- Harkers of cell proliferation and proliferation regulating molecules: **Ki-67**,**p53**
- **Hormone receptors** like estrogen and progesterone receptors in breast cancer or androgen receptors in prostate cancer
- Receptros with therapeutic potential: **HER-2/neu** in breast cancer

Links

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