PIP Digest

CCRA ACRC Canadian Cancer Research Alliance / Alliance canadienne pour la recherche sur le cancer

PIP PPP Patient Involvement in Cancer Research Program / Programme de Participation des Patients à la recherche sur le cancer

UNDERSTANDING CANCER: Cancer Staging and Tumour Grading

This PIP Digest provides information about cancer staging and tumour grading, methods that help health care providers assess cancers to determine prognosis and plan cancer treatments.

Key concepts

- Clinical approaches to systematically assessing tumours and prognosis

Related PIP Digests

- Understanding Cancer: What is Cancer and Types of Cancer

Cancer Staging[1]

Stage refers to the extent of the cancer, such as how large the tumour is, and if it has spread. Knowing the stage of your cancer helps your healthcare provider understand the extent to which your cancer has progressed and your chance of recovery as well as identify the best treatment plan, including clinical trials that may be appropriate.

How Stage Is Determined

Stage may be determined by imaging, lab tests or other tests and procedures. There are many staging systems.

Most staging systems include information about:

- The location of the tumour
- The size of the tumour and/or the depth of invasion
- Whether the cancer has spread to nearby lymph nodes or to a different part of the body

The TNM Staging System

The TNM system is the most widely used cancer staging system.

- **T** refers to the size and extent of the main or primary tumour.
- **N** refers to the number or location of nearby lymph nodes that have cancer.

[1]Adapted from https://www.cancer.gov/about-cancer/diagnosis-staging/staging

- M refers to whether the cancer has metastasized.

When your cancer is described by the TNM system, there will be numbers after each letter that give more details about the cancer—for example, T1N0MX or T3N1M0. The following explains what the letters and numbers mean:

Primary tumour (T)

- TX: Main tumour cannot be measured with the available information.
- T0: Main tumour cannot be found.
- T1, T2, T3, T4: Refers to the size and/or extent of the main tumour. The higher the number after the T, the larger the tumour 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 with the available information.
- N0: There is no cancer in nearby lymph nodes.
- N1, N2, N3: Refers to the number and/or location of lymph nodes that contain cancer. The higher the number after the N, the more lymph nodes that contain cancer.

Distant metastasis (M)

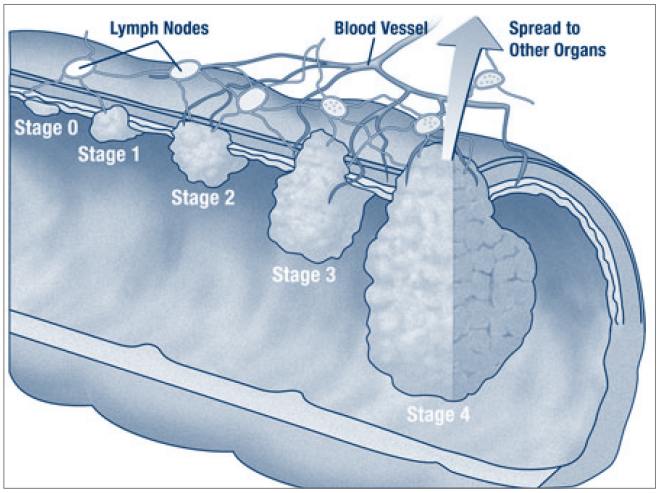
- MX: Metastasis cannot be measured with the available information.
- M0: Cancer has not spread to other parts of the body.
- M1: Cancer has spread to other parts of the body.

Stage Grouping

In clinical discussions with patients, physicians may describe stage as follows:

- Stage 0: Abnormal cells are present but have not invaded nearby tissue. Also called carcinoma in situ.
- Stage I: The tumour is malignant but small and has not grown outside the organ of origin.
- Stage II and III: The tumour is large and/or has started to invade surrounding tissues and lymph nodes.
- Stage IV: There is metastatic spread – the cancer has spread to distant organs.

The diagram below shows the five cancer stages in colorectal cancer.



Cancer Staging in Colorectal Cancer
From: https://www.co.ontario.ny.us/919/Tests-for-Colorectal-Cancer

Other Ways to Describe Stage

Another staging system that is used groups the cancer into one of five main categories. This staging system is more often used by cancer registries than by healthcare providers:

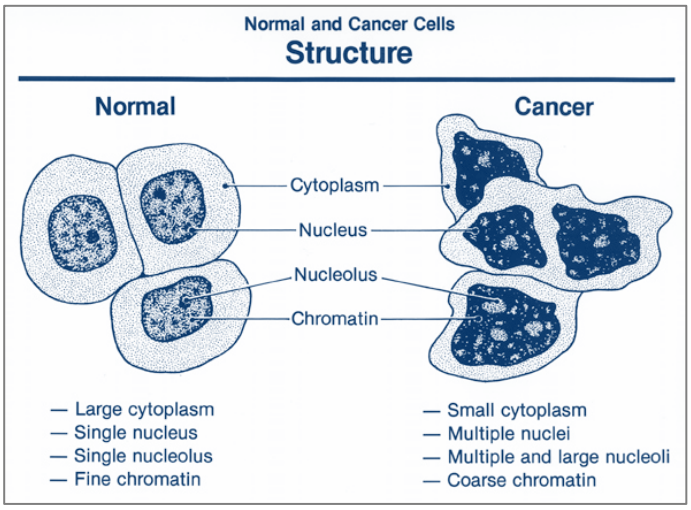
- In situ: abnormal cells are present but have not spread to nearby tissue.
- Localized: cancer is limited to the place where it started, with no sign that it has spread.
- Regional: cancer has spread to nearby lymph nodes, tissues, or organs.
- Distant: cancer has spread to distant parts of the body.
- Unknown: there is not enough information to stage the cancer.

Tumour Grade[2]

Tumour grade is the description of a tumour based on how abnormal the tumour cells and the tumour tissue look under a microscope. It is an indicator of how quickly a tumour is likely to grow and spread.

If the cells of the tumour and the organization of the tumour's tissue are close to those of normal cells and tissue, the tumour is called "well-differentiated." These tumours tend to grow and spread at a slower rate than tumours that are "undifferentiated" or "poorly differentiated," which have abnormal-looking cells and may lack normal tissue structures. Based on these and other differences in microscopic appearance, clinicians assign a numerical "grade" to most cancers. The factors used to determine tumour grade can vary between different types of cancer.

[2]Adapted from https://www.cancer.gov/about-cancer/diagnosis-staging/prognosis/tumour-grade-fact-sheet.



Source: https://visuals.nci.nih.gov/details.cfm?imageid=2512. Pat Kenney (Illustrator).

Tumour grade is not the same as the stage of a cancer. Cancer stage refers to the size and/or extent (reach) of the original (primary) tumour and whether cancer cells have spread in the body.

How is tumour grade determined?

If a tumour is suspected to be malignant, part or all of it will be removed during a procedure called a biopsy. A pathologist (a specialist in interpreting and diagnosing the changes caused by disease in tissues and body fluids) then examines the biopsied tissue to determine whether the tumour is benign (non-cancerous) or malignant (cancerous). The pathologist also determines the tumour's grade and identifies other characteristics of the tumour.

How are tumour grades classified?

Grading systems are highly dependent on the person's cancer. In general terms, however, tumours are graded as 1, 2, 3, or 4, depending on the amount of abnormality. In Grade 1 tumours, the tumour cells and the organization of the tumour tissue appear close to normal. These tumours tend to grow and spread slowly. In contrast, the cells and tissue of Grade 3 and Grade 4 tumours do not look like normal cells and tissue. Grade 3 and Grade 4 tumours tend to grow rapidly and spread faster than tumours with a lower grade.

If a grading system for a tumour type is not specified, the following system is generally used:[3]

- GX: Grade cannot be assessed (undetermined grade)
- G1: Well differentiated (low grade)
- G2: Moderately differentiated (intermediate grade)
- G3: Poorly differentiated (high grade)
- G4: Undifferentiated (high grade)

[3]American Joint Committee on Cancer. *AJCC Cancer Staging Manual.* 7th ed. New York, NY: Springer; 2010.

Some Cancer Type-specific Grading Systems

Breast and prostate cancers are common types of cancer that have their own grading systems.

For breast cancer, doctors most often use the Nottingham grading system (also called the Elston-Ellis modification of the Scarff-Bloom-Richardson grading system). This system grades breast tumours based on the following features:

- Tubule formation: how much of the tumour tissue has normal breast (milk) duct structures
- Nuclear grade: an evaluation of the size and shape of the nucleus in the tumour cells
- Mitotic rate: how many dividing cells are present, which is a measure of how fast the tumour cells are growing and dividing

Each of the categories gets a score between 1 and 3; a score of "1" means the cells and tumour tissue look almost like normal cells and tissue, and a score of "3" means the cells and tissue look mostly abnormal. The scores for the three categories are then added, yielding a total score of 3 to 9. Three grades are possible:

- Total score = 3–5: G1 (Low grade or well differentiated)
- Total score = 6–7: G2 (Intermediate grade or moderately differentiated)
- Total score = 8–9: G3 (High grade or poorly differentiated)

For prostate cancer, the Gleason scoring system is used to grade prostate cancer. The Gleason score is based on biopsy samples taken from the prostate. The pathologist checks the samples to see how similar the tumour tissue looks to normal prostate tissue. Both a primary and a secondary pattern of tissue organization are identified. The primary pattern represents the most common tissue pattern seen in the tumour, and the secondary pattern represents the next most common pattern. Each pattern is given a grade from 1 to 5, with 1 looking the most like normal prostate tissue and 5 looking the most abnormal. The two grades are then added to give a Gleason score. The American Joint Committee on Cancer*[4] recommends grouping Gleason scores into the following categories:

- Gleason X: Gleason score cannot be determined
- Gleason 2–6: The tumour tissue is well differentiated
- Gleason 7: The tumour tissue is moderately differentiated
- Gleason 8–10: The tumour tissue is poorly differentiated or undifferentiated

How does tumour grade affect a patient's treatment options?

Doctors use tumour grade and other factors, such as cancer stage and a patient's age and general health, to develop a treatment plan and to determine a patient's prognosis (the likely outcome or course of a disease; the chance of recovery or recurrence). Generally, a lower grade indicates a better prognosis. A higher-grade cancer may grow and spread more quickly and may require immediate or more aggressive treatment.

The importance of tumour grade in planning treatment and determining a patient's prognosis is greater for certain types of cancer, such as soft tissue sarcoma, primary brain tumours, and breast and prostate cancer.

[4] American Joint Committee on Cancer. *AJCC Cancer Staging Manual.* 7th ed. New York, NY: Springer; 2010.

Digital Pathology Will Mean Faster Cancer Diagnoses

Digital pathology is the virtual version of the conventional microscopy used in pathology. The tissue slices that are viewed under a microscope are scanned by a computer and information about their characteristics are appended to the image. In recent years, there has been increased uptake of digital pathology for the purposes of electronically transferring pathology images and assessments/interpretations to different locations (telepathology). Large databases of these digitized images have been created around the world. Artificial intelligence technologies are being applied to these large databases and validated by experts so that increasingly accurate interpretations can be made.

The Canadian government with industry partners has made significant investments through the "Industry Consortium for Image Guided Therapy (ICIGT)" led by the Sunnybrook Research Institute in Toronto. The Laboratory for Knowledge Inference in Medical Image Analysis (abbreviated as the Kimia Lab) at the University of Waterloo with partner, Huron Digital Pathology, is leading a major effort to apply machine learning techniques to digital images and this work will have a transformative impact on the diagnosis and treatment of cancer. For more information, see https://kimialab.uwaterloo.ca/kimia/index.php/research/.

View these videos to learn more:

- Learn Oncology. *The Staging and Grading of Cancer*. (YouTube) July 15, 2015 [4:01 minutes] https://www.youtube.com/watch?v=UCNx78zIrwU
- Sectra. *Digital pathology: Lessons learned and benefits of digitizing*. (YouTube) May 17, 2017 [4:36 minutes] https://www.youtube.com/watch?v=3P6knHMdSXs

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