Cancer diagnosis: staging and imaging

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Introduction

After diagnosis, the extent of tumour spread (tumour stage) must be determined as accurately as possible; it has implications on optimal management and allows for prognostication. A standardised system aids in communication, standardisation of treatment and allows for consistency in reporting of disease outcomes.

There are several staging systems used in oncology. The most frequently used one is the TNM (Tumour, Node, Metastasis) system maintained by the Union for International Cancer Control (UICC).

The TNM staging system

This divides the elements of tumour spread into three categories: extent of tumour invasion (T), involvement of regional lymph nodes (N), and distant haematogenous metastases (M).

The definition of T, N and M differs for each disease site. The principles are below:

T	x 0 is 1-4	cannot be assessed occult (no primary tumour evident) in situ (i.e. non invasive) increasing T stage implies increasing size and/or degree of invasion into the organ or surrounding tissues.
N	x 0 1-3	cannot be assessed node negative N stage increases with increasing number of nodes, presence of large or matted nodes, or nodes more distant from the primary tumour.
M	0 1	no metastases metastatic disease present (usually implying haematogenous spread)

Other modifiers

Prefixes are used to provide more detail of the TNM staging. Common ones are:

c: clinical stage, meaning the stage has been determined by clinical examination and imaging

p: pathologic stage, meaning the stage has been confirmed via histology or cytology.

y: indicates the TNM stage has been determined after completion of neoadjuvant therapy.

For example, ypT3N1M0 rectal cancer is one that has been resected after neoadjuvant therapy, with histology showing invasion through the full thickness of the rectal wall and involvement of 1-3 regional lymph nodes.

Each tumour type has a stage grouping, which is the categorisation of malignancies into stages from I to IV. A single stage grouping may have multiple TNM stages assigned within it, generally those with a similar prognosis. In lung cancer for example, T4N0M0, T3-4N1M0 and T1-3N2M0 all lie within Stage IIIA. Stage IV disease is almost universally when there has been haematogenous spread and in most cases indicates the disease is incurable.

Other staging systems

While the TNM system is most common, there are some malignancies (e.g. cervix, lymphoma) where it is not used at all and other systems are well established.

Female reproductive system cancers (cervix, uterus, ovary, vagina)

The FIGO (International Federation of Gynaecology and Obstetrics) system is used. The stage is determined by features such as degree of invasion, ureteric obstruction, lymphadenopathy and peritoneal seeding. It ranges from Stage I to IV.

Lymphoma

The Ann Arbor classification is used to describe how many lymph node regions are involved and whether the nodes are on one or both sides of the diaphragm. The presence or absence of “B symptoms” (night sweats, fevers, weight loss of >10%) is an important prognostic factor and this has been incorporated into the staging system as a suffix after the stage descriptor.

For example, Stage IIIB Hodgkin’s lymphoma indicates the presence of B symptoms and involvement of nodal stations on both sides of the diaphragm.

Colon cancer

This has a TNM system, however the Dukes Classification system is still widely used. In this, the stage is classified from A to D based on depth of invasion, nodal involvement and distant metastases.

Small cell lung cancer

This does utilise TNM staging, however more commonly it is simply divided into limited and extensive stage, based on whether the disease is intrathoracic and can be encompassed within a radiation portal. Extensive stage disease is generally considered incurable.

Other (non staging) parameters

It would be remiss to discuss staging and prognostication without mentioning other disease parameters which play a very important role in determining treatment and prognosis. The important variables differ depending on the tumour site but include:

- tumour grade
- hormone receptor status
- specific serum markers (eg PSA, LDH, hCG)
- chromosomal abnormalities (eg 1p19q co-deletion in oligodendroglioma)
- Clark level (melanoma).

Performance status and *weight loss* are independent prognostic factors, and a patient with apparent early stage disease but a poor performance status or significant, unexplained weight loss is unlikely to tolerate, or be cured by, aggressive treatment.

Imaging modalities

Imaging is one of the most important ways to determine the disease stage. These can be divided into structural and functional imaging.

Structural imaging

This includes plain X-ray, CT or MRI. These will demonstrate gross tumour due to the size and shape of the tumour, enlarged lymph nodes or destructive lesions. The sensitivity of such imaging may be improved by the use of contrast, including intravenous or intraluminal contrast. Tumours generally display contrast enhancement due to the leakiness of abnormal blood vessels within the tumour (neovascularisation). Intraluminal contrast can be used to demonstrate filling defects -- for example, a barium swallow may demonstrate a tumour in the oesophagus.

Functional imaging

These fall within the realm of nuclear medicine. A radioactive isotope is administered which localises to specific areas. The areas of tracer accumulation are collected by a special detector (e.g. gamma camera) and reconstructed to form a picture. These can quickly highlight abnormal areas which may be difficult to see on structural scans.

A bone scan (using technetium-99m) is used to identify bone metastases. It is taken up in areas of high bone turnover, so is not specific for metastases; “hot spots” may correlate to areas of bone healing (e.g. fracture) or infection (e.g. osteomyelitis). Similarly, predominantly lytic metastases may not be detected on bone scan.

Positron Emission Tomography (PET) scanning is the gold standard of staging for many cancers. A variety of different tracers may be used but by far the most common is 18-fluorodeoxyglucose (18-FDG). FDG is a glucose analog and concentrates in areas of high metabolic activity. There is physiological uptake in the brain, heart and urinary tract (it is excreted renally) and false positives may result from infection, inflammation or granulomatous diseases. Particularly when fused with a low dose CT, PET helps differentiate benign from malignant lymph nodes and identifies small metastatic deposits in bone and soft tissue that may be occult on conventional imaging. It is not useful in all cancers however, particularly those with low metabolic rate, e.g. prostate cancer.

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