Oncology

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1 Principles of cancer surgery

For most solid tumours, surgery remains the definitive treatment and the only realistic hope of cure. However, surgery has several roles in cancer treatment including **diagnosis**, **removal of primary disease**, **removal of metastatic disease**, **palliation**, **prevention and reconstruction**.

1.1 Diagnosis and staging

In most cases the **diagnosis** of cancer has been made **before** definitive **surgery** is carried out but occasionally a surgical procedure is required to make the diagnosis. This is particularly true of patients with **malignant ascites where laparoscopy has an important role in obtaining tissue for diagnosis**. **Laparoscopy** is also widely used for the staging of intra-abdominal malignancy, particularly **oesophageal and gastric cancer.** Recently, **sentinel node biopsy** in **melanoma and breast cancer** has attracted a great deal of interest. **Staging laparotomy** used to be an important aspect of the staging of lymphomas but with more accurate cross-sectional imaging and the more widespread use of chemotherapy this practice is now largely redundant.

1.2 Removal of primary disease

Radical surgery for cancer involves **removal of the primary tumour and as much of the surrounding tissue and lymph node drainage as possible** in order not only to ensure local control but also to prevent spread of tumour through the lymphatics. Although the principle of local control is still extremely important, it is now recognised that **ultra-radical surgery probably has little effect on the**

development of metastatic disease, as evidenced by the randomised trials of radical versus simple mastectomy for breast cancer. It is important, however, to appreciate that high quality, meticulous surgery taking care not to disrupt the primary tumour at the time of excision is of the utmost importance in obtaining a cure in localised disease and in preventing local recurrence.

1.3 Removal of metastatic disease

Under certain circumstances surgery for metastatic disease may be appropriate. This is particularly true for **liver metastases arising from colorectal cancer** where successful resection of all detectable diseases can lead to **long-term survival in about one third of patients**. With multiple liver metastases, it may still be possible to take a surgical approach by using **in situ ablation with cryotherapy** or **radiofrequency energy**. Another situation in which surgery may be of value is **pulmonary resection for isolated lung metastases, particularly from renal cell carcinoma.**

1.4 Palliation

In many cases surgery is not appropriate for cure but may be extremely valuable for palliation. A good example of this is the patient with a **symptomatic primary tumour who also has distant metastases**. In this case, **removal of the primary will increase the patient's quality of life but will have little effect on the ultimate outcome.** Other situations where surgical palliation is appropriate include **bypass** procedures such as an ileo-transverse anastomosis to alleviate symptoms of obstruction caused by an inoperable caecal cancer or bypassing an unresectable carcinoma at the head of the pancreas by cholecysto- or choledocho-jejunostomy to alleviate jaundice.

2 Radiotherapy

Surgery is complemented by the modality of radiation therapy as part of a multimodal approach for many types of cancer. Like surgery, radiotherapy is typically **focused on locoregional disease control**. For that reason, many of the same principles apply to surgery and radiation oncology, such as patient selection, recognition of the behavior or tumor biology for a particular patient and cancer, and assessment of both short-term and long-term toxicities of therapy.

2.1 Mechanisms of Radiation Delivery

Energy emitted from a source travelling through space is termed “radiation.” As the energy passes through materials it interacts with those substances in one of two forms: **photons or freely propagating particles**. Lower-energy photons make up the energy in visible light and only interact with the surfaces of objects. **Higher-energy photons are used in diagnostic and therapeutic radiology** and can pass through tissues to interact with deeper material and either reveal or impact underlying structures. **Freely propagating particles carrying kinetic energy can be protons, electrons, or alpha-particles**. These charged particles interact with other charged particles as they travel along their path. As photons or charged particles interact with biologic materials within the target area in the setting of therapeutic radiation, the interactions lead to ionization and subsequent biologic damage.

2.2 Tissue Response to Radiation

The **direct effect of ionizing radiation is ionization of DNA molecules** and the downstream effects of the damage to this critical cellular molecule. The **indirect** effect of ionizing radiation is best exemplified by the radiolysis of water molecules leading to the generation of **free radicals**. Free reactive species interact with DNA

molecules causing indirect damage. **The majority of total DNA damage is from this second**, indirect effect. The proportional relationship between oxygen tension within tissues and the resultant damage caused by ionizing radiation is termed the oxygen effect. The ***phenomenon is explained by the capacity to generate a greater concentration of free radicals in oxygen-rich tissues than in hypoxic environments.***

- The **delivery of radiation** is dependent on the tumor location and characteristics, **External beam radiation** therapy is the most commonly employed therapeutic radiation strategy.
- **Intensity modulated radiation therapy (IMRT)** is an enhanced version of external beam therapy. IMRT uses mechanical devices or multiple beam integration to adjust the intensity within each beam in order to account for irregular patient surfaces or sensitive structures near the treatment region.
- **Stereotactic body radiation therapy (SBRT)** is a more specialized delivery system used for patients with brain tumors, lung cancer, and liver tumors.
- The use of **radioactive implants, or brachytherapy**, is common in the treatment of prostate and gynecologic cancers.
- **Intraoperative radiation therapy**

Regarding **timing** of radiotherapy, it could be:

- **Perioperative** radiation therapy with or without chemotherapy sensitizers is commonly employed for tumors, such as rectal cancers, gastroesophageal cancers, and soft tissue sarcomas.
- When surgical therapy is combined with radiation and chemotherapy, this is often referred to as **trimodality** therapy.

- Chemotherapy is often combined with radiation as a definitive therapy for cancers that are either unresectable or exquisitely radiosensitive (**concurrent chemoradiation**).
- **Definitive radiation** therapy is not commonly employed for these locally advanced cancers

3 The Role of Chemotherapy in Cancer Management

Unlike surgical resection or radiation therapy, the goal of chemotherapy is not necessarily localized or locoregional but **systemic cancer treatment**. The setting in which chemotherapy is given can be defined **as neoadjuvant, conversion, adjuvant, or palliative**, dependent on the goals of the planned treatment course.

- **Neoadjuvant chemotherapy** is administered **prior to** a planned curative **surgical resection**. An example of neoadjuvant chemotherapy is in the treatment of advanced gastric cancer. The potential benefits: to **treat micrometastatic**, **improve** tumor-related **symptoms**, to allow for a period of time where **metastatic disease can present precluding** unwarranted surgical resection, and an in **vivo method of determining tumor chemosensitivity**.
- **Conversion chemotherapy** (**convert unresectable to respectable tumor**) is also administered prior to surgical resection but the baseline tumor is considered unresectable, typically due to technical reasons, unlike in the neoadjuvant setting. An **example**: **metastatic colorectal liver metastases** where upfront surgical resection is precluding by a sufficient future liver remnant. The goal of conversion chemotherapy is to **downsize** the baseline tumor allowing **a safe curative resection**.

- **Adjuvant chemotherapy** is administered in the postoperative setting **after the primary or metastatic tumor is surgically resected**. This is perhaps the most common setting of chemotherapy administration.
- **Palliative chemotherapy** is the setting defined as unr**esectable primary or metastatic cancer** where the goal of chemotherapy is **prolongation of life** and not necessarily conversion to a curative resection.

4 Biological therapy

The increasing knowledge of cancer genetics and biology has generated potential new targets for systemic therapeutic regimens ushering in potential individualized cancer treatments. The best example of a genetic abnormality with a systemic therapy specific for a molecular target is the **BCR-ABL chromosomal translocation seen in patients with chronic myelogenous leukemia (CML)**.

5 Principles of combined treatment

Cytotoxic drugs are rarely used as single agents; radiotherapy and chemotherapy are often given together. It is a strategy designed to combat drug resistance. **By the time of diagnosis many tumours will contain cancer cells that, through spontaneous mutation, have acquired resistance to cytotoxic drugs.** There are three main principles upon which the choice of drugs for combination therapy is based: (1) use drugs **active against the diseases** in question; (2) use drugs with **distinct modes of action**; (3) use drugs with **non-overlapping toxicities**.

6 Palliative therapy

The distinction between palliative and curative treatment is not always clear cut and will become increasingly blurred as professional and public attitudes to towards the management of cancer change. **Patients will live with their cancers**, perhaps for

years. They will **die <u>with</u> cancer**, but **not necessarily <u>of</u> cancer**. Palliative treatment has as its **goal the relief of symptoms**. Sometimes this will involve treating the underlying problem, as with palliative radiotherapy for bone metastases, sometimes it will not. Sometimes it may be inappropriate to treat the cancer itself, but that does not imply that there is nothing more to be done, it simply means that there may be better ways to assuage the distress and discomfort caused by the tumour.

7 End-of-life care

End-of-life care is distinct from palliative care. Patients treated palliatively may survive for many years; end-of-life care concerns the last few months of a patient's life. Many issues, such as symptom control, are common to both palliative care and to end-of-life care but there are also problems which are specific to the sense of approaching death. These include a heightened sense of spiritual need, profound fear and the specific needs of those who are facing bereavement. The concept of the 'good death' has been embedded in many cultures over many centuries. Healthcare professionals deal with many deaths and sometimes forget that the patient who hopes for a good death has only one chance to get it right. This is why end-of-life care is worth considering in its own right and not as a mere appendage to palliative care.