Head and neck cancer is the sixth most common cancer worldwide representing a wide range of malignancies. This issue of Cancer Forum focuses on mucosal (non-nasopharyngeal) head and neck squamous cell carcinoma (SCC). A small section is also devoted to non-melanomatous cutaneous skin cancer.

The cure of locally advanced mucosal head and neck SCC with surgery alone is commonly said to be in the order of 30%. Coutard in the 1920s demonstrated the ability of external beam radiotherapy alone to cure cancers of the pharynx and larynx. By 1957 MacComb and Fletcher recognised the benefit of a combined approach of surgery and post-operative radiotherapy in locally advanced mucosal head and neck SCC.

By the 1980s, following a randomised trial initiated by the Radiation Therapy Oncology Group (RTOG) in the 1970s, the superiority of post-operative radiation therapy compared with pre-operative treatment was established. Since that time, efforts have been made in identifying and refining the clinico-pathological risk factors warranting post-operative radiotherapy, determining the optimal radiotherapy dose and improving outcomes with the use of treatment intensification through altered fractionation and chemo-radiotherapy.

Peters et al on a prospective trial evaluated the optimal post-operative radiation dose for locally advanced mucosal head and neck SCC, based on clinical and pathological risk factors. The most significant high-risk feature identified was the presence of extracapsular nodal extension. This was one of the first studies to define high-risk features. The impact of these features were further validated in a subsequent study reported by KK Ang et al.

Early attempts at organ preservation using induction chemotherapy and radiotherapy were reported by the Department of Veteran Affairs and European Organisation for Research and Treatment of Cancer Larynx preservation studies. Both demonstrated that the use of induction chemotherapy followed by radiotherapy in responders for laryngeal and hypopharyngeal tumours, respectively, could result in preservation of the larynx, without a survival disadvantage compared with immediate surgery and post-operative radiotherapy.

Over the last two decades many centres have moved toward organ-preservation for locally advanced mucosal head and neck SCC through use of radiotherapy with or without chemotherapy. However, in the absence of high quality randomised evidence comparing surgery and post-operative radiotherapy with chemo-radiotherapy, the debate of which approach to use continues in many multidisciplinary clinics.

Altered fractionation

Disappointing outcomes with conventionally fractionated radiation therapy in locally advanced mucosal head and neck SCC led to the investigation of altered fractionated radiotherapy. Based on radiobiological principles, the use of accelerated, hyperfractionated or a combination of both schedules has been examined in randomised trials comparing outcomes with conventionally fractionated radiotherapy. Late radiation effects are partly dependent on the fraction size of the radiation dose, as discussed by Poulsen. Hyperfractionated radiotherapy aims to deliver a higher total dose, without an increase in late radiation effects, using radiation fraction sizes less than the conventional dose of 1.8-2.0Gy. Accelerated radiotherapy aims to reduce the overall treatment time by reducing the use of multiple daily fractions in an attempt to overcome the phenomenon of accelerated repopulation, which occurs around four weeks following insult to the tumour. A combination of hyperfractionation and accelerated radiotherapy can also be employed. The use of altered fractionation is often at the expense of increased acute radiation side-effects. Most randomised data has demonstrated superiority of altered fractionated radiotherapy with respect to loco-regional control, compared with conventionally fractionated radiotherapy.

Chemotherapy

The role of chemotherapy in the definitive, post-operative and recurrent/metastatic setting in locally advanced mucosal head and neck SCC, along with novel therapeutic agents, is discussed by Guminski. The benefit of combined chemotherapy and radiotherapy in the definitive treatment of locally advanced mucosal head and neck SCC, and post-operatively in high-risk disease, is well established. In both scenarios there is a 12% reduction in risk of cancer.
death and an absolute benefit of 4% in five-year survival. More recent data suggests that the absolute survival benefit is 8% five-year survival.\textsuperscript{13,14}

The benefit of definitive concurrent chemo-radiotherapy compared with radiotherapy has been reported in many randomised clinical trials, while the role of induction chemotherapy remains uncertain.\textsuperscript{14,17}

**Endoscopic laser**

The use of endoscopic laser resection of mucosal head and neck SCC has gained increased popularity over the past decade, particularly in the treatment of early laryngeal cancer. The benefit of the CO\textsubscript{2} laser is that it can haemostatically excise lesions with a high degree of accuracy.

The goals of treatment with early glottic SCC include curing the cancer with minimal toxicity and optimal voice quality. From a practical point of view a treatment that offers cure with one visit as opposed to six weeks of radiotherapy is appealing to both the patients and radiotherapy departments with long waiting lists. Despite the absence of randomised data it would appear that both provide similar local control. Which treatment provides superior functional outcome and is definitely more economical still remains controversial. Kleid and Iseli discuss laser surgery, techniques, advantages and risks, and functional outcome.

**Functional outcomes**

Regardless of whether surgery, radiotherapy, chemotherapy or a combination of these treatments is employed, each has its own short and long term effects on speech and swallowing. These effects often have a significant impact on overall quality of life (QoL). The speech pathologist is commonly the professional left to rehabilitate patients with the resulting functional deficits due to their malignancy and treatments received. Perry and Frowen have performed a comprehensive review of the speech and swallowing outcomes in patients treated with surgery and chemo-radiotherapy and conclude by providing a guide in the rehabilitation of speech and swallowing following treatment.

**Nutritional management**

Malnutrition is a well recognised and common problem in head and neck cancer patients. Lifestyle, along with tumour and treatment factors, all contribute to the problem.

Malnourishment often has a significant impact on complication rates, ability to complete and recover from treatment and overall QoL. When to intervene and what modalities to use, such as a nasogastric or percutaneous endoscopic gastrostomy tube (PEG), are common problems faced by clinicians and other health professionals. Careful screening and early intervention appear the key to correcting and maintaining adequate nutritional status pre and post treatment, including surgery, radiotherapy and chemotherapy. Davidson et al discuss this in greater detail.

**Future directions**

**Positron Emission Tomography (PET)**

Fluoro-deoxy-glucose PET scanning has emerged as a valuable diagnostic tool in the staging, therapeutic monitoring and restaging of head and neck cancers. It has a high positive and negative predictive value in the detection of disease and is valuable in the detection of unsuspecting metastatic disease not recognised by conventional structural imaging, such as CT. With the advent of CT-PET both structural and functional imaging can be obtained synchronously. PET scanning is also increasingly used to facilitate radiotherapy, as the images can be fused with the planning CT scans. PET can also be used in biological characterisation of tumours. The use of compounds such as fluorine-18 fluoromisonidazole can be used to detect the degree of hypoxia in tumours. Hicks and Shakhel provide insight into the use of PET in head and neck cancer and its potential future roles.

**Novel prognostic markers**

Great research efforts are being made in trying to predict the aggressiveness of certain tumours and responsiveness to the various treatment modalities. The ultimate aim is to better tailor the treatment to suit the profile of the tumour and therefore improve outcome with the least morbidity.

There are currently no reliable tumour markers for head and neck SCC. Coman et al examine the role of gene profiling, microarray technology and the current state of tumour markers in head and neck cancer.

**Advanced non-melanomatous skin cancer of the head and neck**

Non-melanomatous cutaneous malignancies of the head and neck are a common problem in Australia. While the majority are early basal cell carcinomas and SCC, there is a subset of patients with high-risk disease that have a high risk of loco-regional recurrence or risk of distant metastases. These include locally advanced SCCs and merkel cell carcinoma. Veness has provided a comprehensive overview of the management of high-risk non-melanomatous cutaneous malignancies.

**References**


