

## Radiation oncology

RADIOTHERAPY IS ONE of the cornerstones of cancer treatment, being a component of management in at least half of all cancer patients. Increasingly, radiotherapy is used in multimodal treatment protocols in combination with surgery and chemotherapy. The best outcomes are achieved when specialists in each of these disciplines work in a multidisciplinary way, understanding the benefits and limitations that each brings to the patient's management. The aim is to individualise treatment using the best evidence available while continually advancing our knowledge through clinical trials. The Trans-Tasman Radiation Oncology Group has taken a leadership role in this regard.

Advances in radiation oncology have historically been linked to developments in technology and biology. Never has this been more evident than in the present era.

**Technology.** The power of ionising radiation as a therapeutic tool lies in its ability to penetrate non-invasively to any part of the body. The challenge is to target tumour tissue and minimise normal tissue toxicity. This requires sophisticated techniques for disease localisation, treatment planning, delivery and verification. Excellence in oncological imaging is at the heart of modern radiation oncology. The advent of fast, multislice CT scanners, new MRI techniques, metabolic imaging with PET and the advent of machines producing fused CT and PET scans has revolutionised radiation oncology. Patients can now be more accurately staged, their disease can be precisely localised, and treatment can be planned accordingly.<sup>1</sup>

Modern planning for radical radiotherapy involves the delineation on cross-sectional scans of the target volumes to be irradiated and the normal tissues to be excluded from the high dose volume. The ability to achieve three-dimensional conformal dose distributions allows critical normal tissues to be spared from injury and tumour doses to be increased safely. In the case of prostate cancer this has been shown to translate into improved outcomes.<sup>2</sup> The ability to sculpt the high dose radiation volume to match tumour localisation is maximised by intensity-modulated radiation therapy. This technique uses a computer-controlled beam-shaping device in the head of the linear accelerator, which changes the beam shape continually during radiation exposure to produce any desired dose distribution. This is a far cry from the situation only a few years ago, when the only method of protecting normal tissues was to insert a lead block in the radiation beam, external to the treatment machine.

For treatment verification and quality assurance, electronic portal imaging systems that provide a real-time digital image of each treatment field are now available. These allow detection of variations from the intended treatment set-up.

Unfortunately, these technologies are available at only a few Australian centres, and use is severely restricted because of the under-resourcing of radiation oncology departments.

A balance has to be struck between offering sophisticated treatment to some patients and forcing longer waiting times for treatment on others. Our goal for the next five years must be to redress the shortfalls in infrastructure so the advantages of existing technology will become more widely available.<sup>3</sup>

**Biology.** In the past five years, many of the seeds of earlier research have come to fruition with proven clinical benefit in randomised trials. Perhaps the best example is the development of integrated protocols combining radiotherapy with chemotherapy<sup>4</sup> or hormonal therapy for many cancers, including lung, cervix, rectum, larynx/pharynx, breast and prostate cancer.

The explosion of knowledge in molecular biology and genetics has led to new understanding of how ionising radiation causes cell death and has provided the rationale for trials combining radiation with designer-made inhibitors of molecular pathways, such as those mediated by EGFR and Ras oncogenes. Intensive research into the molecular determinants of radiation-induced apoptosis has created the possibility of selectively manipulating these mechanisms to improve the therapeutic ratio. Another major research focus is to identify predictively patients who are genetically predisposed to radiation injury and who, if treated with radiotherapy, are at risk of severe complications. Excluding this small group of patients would allow dose escalation for others, resulting in increased local cure rates.

The next five years will see a revolution in the molecular phenotyping of tumour and normal tissues, using gene-array microchip technology. Within each anatomical/histological subtype, tumours will be characterised at the molecular level in a way that will permit rational application of the most effective treatment modalities, including radiation. The ultimate aim is to combine molecular characterisation with the technological sophistication of radiation treatment to use this powerful anti-cancer weapon to maximum benefit.<sup>5</sup>

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