



Radiotherapy

RADIOTHERAPY – MAINTAINING FOCUS THROUGHOUT THE CANCER JOURNEY

Gerard Adams¹ and Sandro V Porceddu^{1,2}

1. Department of Cancer Services, Princess Alexandra Hospital, Brisbane, Queensland.

2. University of Queensland, Faculty of Health Sciences, School of Medicine, Brisbane, Queensland.

Email: Gerard_Adams@health.qld.gov.au and Sandro_Porceddu@health.qld.gov.au

Unfortunately, one in two Australians is destined to suffer from cancer in their lifetime.¹ Fifty per cent of them should receive radiotherapy at some point during their treatment.² Any person without a personal experience of radiotherapy is, at some point in their life, likely to watch a family member or close friend undergo treatment, yet specific knowledge of radiotherapy and its application in modern practice is not well understood in either the lay or health professional communities.

In this edition of *Cancer Forum* we aim to give some insight into important issues, surrounding modern radiotherapy practice. While far from comprehensive, we will touch on many key issues including the development of technologies that allow better identification and delivery of radiation to the target with minimisation of dose to normal tissues, as well as novel applications of radiotherapy that can assist in tumour control while retaining organ function. We also discuss the challenges in dealing with the after effects of treatment in long-term survivors, along with the balancing act required to optimise treatment for those not destined to survive long term.

There have been major advances in our ability to deliver radiotherapy over the last few decades. Matthew Foote gives a summary of the technical developments that allow us to prescribe plans that are highly conformal to the target volume.³ The sharp drop-off in dose at very short distances from the target has the dual potential of allowing more dose to the tumour while sparing surrounding normal tissues. While evidence showing that adoption of these techniques has resulted in improved survival figures is lacking, the clear evidence of reduced toxicity in itself merits their use in modern practice. However, such highly conformal radiotherapy planning can be counterproductive unless it is coupled with confident and precise identification of the target at both the planning and delivery stages.

Mike Fay describes how the emergence of new functional imaging modalities – typically with ¹⁸F-deoxyglucose PET – has aided our ability to accurately define the target volume.⁴ In the past, when radiotherapy targets were delineated with the aid of anatomical imaging, initially x-ray and later CT scans, there was more uncertainty in differentiating tumour and normal tissues. Less conformal plans probably helped reduce the chances of a geographical miss. Although PET has its own limits of

resolution, under some circumstances it can be used to precisely identify the target more accurately, allowing the confident application of highly conformal plans with less chance of a geographical miss.

Throughout a course of treatment there may be changes to the tumour volume, organ shift and changes in body shape (eg. weight loss). This can create further uncertainty in the accuracy of radiotherapy delivery. Tomas Kron describes how a third aspect of radiotherapy – accurate and consistent delivery – has developed.⁵ The concept of image guided radiotherapy (IGRT) relates to the ability to identify the target volume at the time of treatment delivery, with the option to adapt the beam depending on findings. As discussed in this article there are many important aspects to take into account when choosing the appropriate method of IGRT. These include the indication for radiotherapy, financial cost, time and additional radiation dose.

It is clear that the developments described so far are dependent on each other and that the delivery of modern highly conformal radiotherapy techniques would be neither possible nor desirable unless coupled with improvements in target identification and IGRT.

Bryan Burmeister explores the complex process of radiotherapy,⁶ which relies on the work of a highly skilled team that includes radiation oncologists, radiation therapists and medical physicists. Safe and accurate delivery of treatment for patients relies on the skills of all individuals, with many potential sources for error. Coupled with this is the importance of consistency in delivery between departments. Good quality assurance methods are essential to ensure consistent high quality radiotherapy within a department, as well as between departments at a national and international level. Radiotherapy is perhaps unique in its complexity and this paper highlights how failure to provide high quality radiotherapy plans can result in significantly poorer outcomes for patients.

In an era where the availability of technology described in the first three papers appears to be expanding exponentially, some objective evaluation of the relative merits of the various options is necessary.³⁻⁵ Improvements in the delivery of radiotherapy over the last few decades have resulted in the ability to use it as the backbone of non-surgical cancer treatments aimed at curing cancer

while maintaining organ function. Organ preserving radiotherapy treatments with reasonable chances of cure are now possible for head and neck,⁷ oesophagus,⁸ lung,⁹ prostate,¹⁰ bladder,¹¹ anal,¹² cervix,¹³ and vulval cancers.¹⁴ Not all developments however, rely on expensive high end technology. Arthur Sun Myint and colleagues describe the use of fairly simple (and inexpensive) technology that can be applied to a selected population of early low rectal cancers.¹⁵ This technology relies on the direct application of very high doses – 110 Gy to the tumour using superficial x-rays. The properties of these x-rays mean that the dose falls off very rapidly over only a few millimetres, sparing surrounding tissues from significant dose. Clearly this technology is only suitable for use in a small, select group of patients. However, wider application of these techniques has the potential to not only save patients from the morbidity and mortality of aggressive surgery – but also to achieve significant cost savings for the health service as a whole.

Another aspect of this paper is discussion of a “wait and watch policy for complete responders.” While we classify various tumour types as “radiosensitive” or “radioresistant”, it is clear that within any tumour group there is a wide spectrum of responses in individual tumours. There is ongoing research trying to identify factors that predict response – but currently this is largely poorly understood. Nevertheless, modern treatment strategies are moving away from a one size fits all approach towards an individualised approach, whereby a predictable marker of good response (such as favourable response on post-treatment MRI scan) can be used to safely select patients who may avoid morbid surgery. Although currently only around 10% of patients undergoing chemoradiation for rectal cancer fulfil the wait and watch criteria,¹⁶ improvements in imaging and or therapy – eg. more potent chemoradiation - may mean that in the future even more patients with rectal cancer will be able to be spared surgery.

Such tailored, individualised treatments are not new to the world of radiotherapy. Susan Wiltshire and Andrew Potter discuss provisions for palliative radiotherapy in modern practice.¹⁷ A wide range of total dose and number of fractions are possible. The art of radiotherapy is selecting the “correct” schedule for individual patients. This takes into account symptoms, location of metastases, nature of primary lesion, time since diagnosis or progression, as well as other factors such as the workload of the department. It is encouraging to see that such a large body of high quality research has been undertaken in an area that some may consider is less important than potentially curative treatment. Also as shown in the article by Foote, the application of high intensity techniques involving stereotaxis has been readily incorporated into palliative treatment options.³ However, it is important that clear and realistic treatment goals are made at the outset and that radiation oncologists use the resources available to them wisely.

The final two articles in our series address radiotherapy issues from a different perspective, namely treatment related side-effects. Speech pathologists Ellen Mills and Robyn Burnett discuss the important role allied health professionals play in helping us minimise the unwanted effects of radiotherapy.¹⁸ Patients do suffer significant

short-term side-effects from radiation that need to be managed during treatment. But potentially more disabling are the long-term side-effects, with detrimental effects on long-term quality of life. It is interesting to think about the difficulties in carrying out research in this field. It appears that many patients are unwilling to take part in studies – possibly due to them (and perhaps their doctors) rating avoidance of long-term side-effects as a low priority at the time of treatment. However, the final article by Wheeler illustrates what a heavy burden the toxicity from treatment places on survivors as well as society as a whole.¹⁹

It is not really surprising that the perspective of both patients and health professionals changes depending on what point of the cancer journey they are at. However, if we learn lessons from the past, it is important that we as health professionals encourage current patients to actively take part in studies that help us evaluate both the short-term and long-term effects of treatments for their cancers. It is only by gaining this information now that we will be able to address the significant issues affecting the increasing proportion of patients who survive long term after cancer treatment.

Common abbreviations used in this forum

ACTH	adrenocorticotrophic hormone
ESCC	epidural spinal cord compression
CBCT	cone beam CT
IMRT	intensity modulated radiotherapy
IGRT	image guided radiotherapy
Linac	linear accelerator
SBRT	stereotactic body radiation therapy
SRS	stereotactic radiosurgery
SRT	stereotactic radiotherapy
TSH	thyroid stimulating hormone
WBRT	whole brain radiotherapy

References

1. Cancer Council Australia. Frequently Asked Questions (FAQ). [Internet] Sydney: Cancer Council Australia, September 2011. Available from www.cancer.org.au/aboutcancer/FAQ.htm#573. Accessed May 2012.
2. Cancer Council NSW. Improving Radiotherapy. Where to from Here? A report for the NSW Government. [Internet] Sydney: Cancer Council NSW, May 2009. Available from: http://www.cancercouncil.com.au/wp-content/uploads/2011/10/Improving-Radiotherapy_Roadmap_May-2009.pdf Accessed May 2012.
3. Foote M. The Development of Advanced Radiotherapy Treatment Techniques. *Cancer Forum*. 2012;36(2):73-76.
4. Fay M, Thomas P. Impact of Developments in Functional Imaging in Defining the Target for Radiotherapy. *Cancer Forum*. 2012;36(2):77-79.
5. Kron T. New Developments in Image Guidance for Radiotherapy. *Cancer Forum*. 2012;36(2):80-85.
6. Burmeister B. Quality assurance in radiation oncology. *Cancer Forum*. 2012;36(2):86-88.
7. Pignon JP, Le Maître A, Maillard E, Bourhis J. Meta-analysis of chemotherapy in head and neck cancer (MACH-NC): An update on 93 randomised trials and 17,346 patients. *Radiother Oncol*. 2009;92:4-14.
8. Cooper JS, Guo MD, Herskovic A, Macdonald JS, Martenson JA, Al-Sarraf M et al. Chemoradiotherapy of Locally Advanced Esophageal Cancer:

- Long-term Follow-up of a Prospective Randomized Trial (RTOG 85-01). *JAMA*. 1999;281:1623-1627.
9. Aupérin A, Le Péchoux C, Pignon JP, Koning C, Jeremic B, Clamon G et al. Concomitant radio-chemotherapy based on platin compounds in patients with locally advanced non-small cell lung cancer (NSCLC): A meta-analysis of individual data from 1764 patients. *Ann Oncol*. 2006;17:473-483.
 10. Denham JW, Steigler A, Lamb DS, Joseph D, Turner S, Matthews J et al. Short-term neoadjuvant androgen deprivation and radiotherapy for locally advanced prostate cancer: 10-year data from the TROG 96.01 randomised trial. *Lancet Oncol*. 2011;12:451-459.
 11. James ND, Hussain SA, Hall E, Jenkins P, Tremlett J, Rawlings C et al. Radiotherapy with or without Chemotherapy in Muscle-Invasive Bladder Cancer. *N Engl J Med*. 2012;366:1477-1488.
 12. Anal Cancer Trial Working Group. Epidermoid anal cancer: results from the UKCCCR randomised trial of radiotherapy alone versus radiotherapy, 5-fluorouracil and mitomycin. *Lancet*. 1996;348:1049-54.
 13. Green JA, Kirwan JM, Tierney JF, Symonds P, Fresco L, Collingwood M et al. Survival and recurrence after concomitant chemotherapy and radiotherapy for cancer of the uterine cervix: a systematic review and meta-analysis. *Lancet*. 2001;358:781-786.
 14. Wahlen SA, Slater JD, Wagner RJ, Wang WA, Keeney ED, Hocko JM et al. Concurrent radiation therapy and chemotherapy in the treatment of primary squamous cell carcinoma of the vulva. *Cancer*. 1995;75:2289-94.
 15. Sun Myint A, Ramani VS, Montazeri A, Perkins K, Myerson R, Gerard JP. Novel Radiation Techniques – A Personalised Approach for Patients with Rectal Cancer. *Cancer Forum*. 2012;36(2):89-92.
 16. Maas M, Beets-Tan RGH, Lambregts DMJ, Lammering G, Nelemans PJ, Engelen SME et al. Wait-and-See Policy for Clinical Complete Responders After Chemoradiation for Rectal Cancer. *J Clin Oncol*. 2011;4633-4640.
 17. Wiltshire S, Potter A. Palliative Radiotherapy in Modern Practice. *Cancer Forum*. 2012;36(2):93-97.
 18. Mills E, Burnett R. Functional outcomes after radiotherapy for early glottic cancer. *Cancer Forum*. 2012;36(2):97-99.
 19. Wheeler G. Surviving radiotherapy -what the future holds. *Cancer Forum*. 2012;36(2):100-105.