Innovations to Improve Radiation Treatments and the Training of Radiation Oncologists

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This Thesis is presented for the degree of Masters of Public Health of The University of Western Australia

School of Population Health
The University of Western Australia

In collaboration with
Centre for Population Health Research
Curtin University
STATUTORY DECLARATION

I certify that the work in this thesis is my own except where duly acknowledged. I also certify the contents of this thesis have not been included in any other work submitted by the author for another degree.

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SYNOPSIS

The purpose of this study was to develop and prospectively test a number of innovations that might simplify or improve various aspects of specialist Radiation Oncology training or radiation treatment. Opportunities for innovation in radiation therapy were systematically considered. Areas of particular need identified included the development and application of knowledge regarding radiotherapy and where treatments are difficult for patients. The particular areas of innovation most suitable to the circumstances included themes of the training of Radiation Oncologists, patient immobilisation and shortened courses of radiotherapy. A series of studies were developed utilising a range of different study designs and endpoints.

Methods

1. A workshop to help prepare candidates to sit their specialist examination was developed – including new methods to provide feedback to candidates, and to assess learning environments.
2. A scientific writing skills training workshop was developed based on a literature review. Participants were asked to complete questionnaires before and after the course.
3. A new method of producing patient immobilisation casts using lightweight hand-held laser surface scanners was developed. The feasibility of the process was examined and measures such as Radiation Therapists’ satisfaction with masks were assessed.
4. A new, inexpensive and simple, method to produce customised neck supports was developed. Set-up accuracy was assessed by comparing two consecutive cohorts of patients.
5. A randomised trial was performed using a single 9-MeV electron chest wall prophylactic treatment following invasive thoracic procedures in patients with malignant pleural mesothelioma, compared to no treatment in 58 procedure sites.
6. Twenty-eight patients with symptomatic liver metastases received targeted (partial or whole) liver irradiation consisting of 10 Gy in two fractions over 2 days.
7. Thirty-five patients undergoing breast-conserving surgery received targeted tumour bed irradiation consisting of 5 Gy (at 10 mm) in a single fraction (then completed external beam radiotherapy as usual).

Results

1. Assessment of a training course for advanced trainees showed strengths but a number of variations were identified that may be useful for future workshops. Three of 24 questions regarding the registrars learning environment had less than 80% favourable responses – two of these questions related to workload.
2. Following a short writing workshop, there was an improvement in participants’ perceptions of their own skills. Half the participants felt that the workshop made it more likely that they would publish.
3. The scanner-based method of mask production was found to be simple, accurate, and non-invasive. There was a reduction in Radiation Therapist labour required and the masks produced
were reported to result in improved mask fitting, daily reproducibility, patient immobilisation and patient comfort.

4. Statistically significant differences favouring the customized neck supports included a reduced total displacement error (mean 3.4 vs. 2.1 mm) and a reduced left–right setup error (mean 1.8 vs. 1.1 mm).

5. A single treatment to prevent chest wall tract metastasis was found to be ineffective with no statistically significant difference in tract metastasis over no treatment. A low relapse rate was found in both arms.

6. Palliative liver radiotherapy produced individual symptom response rates of 53–66% at 2 weeks. Partial or complete global symptomatic responses were noted in 15 patients (54%) overall. The treatment was well tolerated.

7. An intraoperative breast treatment using the Intrabeam device was found to be feasible and able to be delivered without difficulty. The treatment was well tolerated, with only one patient experiencing any grade 3/4 toxicities.

**Conclusion**

A number of innovations in radiation oncology training (to promote research publication and improve skills and knowledge as assessed by examination performance) and treatment (including technique and dose-schedule) were developed and found to be of benefit and/or to warrant further investigation. In one case, a single dose of radiotherapy to prevent chest wall metastasis was found ineffective, but the comparison control arm provided important information about the potential need for such treatments. In addition to the specific results, the types and extent of innovations in radiation oncology are considered. Issues such as appropriate study design and relevant endpoints are addressed. The value of a systematic approach to innovation is discussed. Organisational and individual requirements for innovation considered. The impact of the studies on practice is discussed.
ACKNOWLEDGEMENTS

I would like to acknowledge the contributions of my collaborators and co-authors.

I am grateful to all patients and health professionals who participated in the studies.

I would like to thank my supervisors Professor James Semmens and Professor David Preen at Curtin University and the University of Western Australia respectively.

I am particularly grateful to Clinical Professor David Joseph and Clinical Professor Nigel Spry at the Department of Radiation Oncology, Sir Charles Gairdner Hospital for their guidance.

I would like to thank Lynda, Charlie and Harry for their support.
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Overview of Radiation Oncology
Innovation & identifying suitable areas to explore innovations in Radiation Oncology
Radiation Oncologist training as a target for Innovation
Literature review for training clinical radiation oncologist skills
Literature review for training in Scientific Writing Skills
Reference to “Publication rates of abstracts presented at annual scientific meetings: how does the Royal Australian and New Zealand College of Radiologists compare?”
Patient immobilisation as a target for Innovation
Literature review for Customised Cast Production
Literature review for Customised Neck Support
Hypofractionated treatments as a target for Innovation
Literature review for Hypofractionated treatments in Malignant Pleural Mesothelioma
Literature review for Hypofractionated treatments in Liver Metastases
Literature review for Hypofractionated treatments in Breast cancer
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Chapter 5. A simple and inexpensive method to routinely produce customised neck supports for patient immobilisation during radiotherapy.

Chapter 6. A randomised trial of single-dose radiotherapy to prevent procedure tract metastasis by malignant mesothelioma

Chapter 7. A prospective trial of short-fractionation radiotherapy for the palliation of liver metastases
### Chapter 8. A Prospective trial of intraoperative radiation treatment for breast cancer

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<td>1-year</td>
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<td>2-y</td>
<td>2-year</td>
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<tr>
<td>4DCT</td>
<td>4-dimension Computed Tomography</td>
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<td>ANZ</td>
<td>Australia and New Zealand</td>
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<td>APR</td>
<td>Abstract to Publication Ratio</td>
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<td>ASM</td>
<td>Annual Scientific Meetings</td>
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<td>AUD</td>
<td>Australian Dollar</td>
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<td>CRC</td>
<td>Colorectal Cancer</td>
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<td>EBM</td>
<td>Evidence Based Medicine</td>
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<td>EBRT</td>
<td>External Beam Radiotherapy</td>
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<tr>
<td>EORTC</td>
<td>European Organization for Research and Treatment of Cancer</td>
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<td>FNA</td>
<td>Fine Needle Aspiration</td>
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<tr>
<td>FRANZCR</td>
<td>Fellow/Fellowship of the Royal Australian and New Zealand College of Radiologists</td>
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<td>G</td>
<td>Grade</td>
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<td>GI</td>
<td>Gastrointestinal</td>
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<td>Gy</td>
<td>Gray</td>
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<tr>
<td>H&amp;N</td>
<td>Head and Neck Region</td>
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<tr>
<td>HAI</td>
<td>Hepatic Artery Infusion</td>
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<td>HCC</td>
<td>Hepatocellular Carcinoma</td>
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<td>HDRPB</td>
<td>High Dose Rate Prostate Brachytherapy</td>
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<tr>
<td>IFRT</td>
<td>Involved Field Radiation Therapy</td>
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<td>IGRT</td>
<td>Image Guided Radiation Therapy</td>
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<td>IMRT</td>
<td>Intensity Modulated Radiation Therapy</td>
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<tr>
<td>IORT</td>
<td>Intraoperative Radiation Therapy</td>
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<tr>
<td>KMS</td>
<td>Kasabach-Merrit Syndrome</td>
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<tr>
<td>LC</td>
<td>Local Control</td>
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<td>LFTs</td>
<td>Liver Function Tests</td>
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<td>LM</td>
<td>Liver metastases</td>
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<tr>
<td>MDM</td>
<td>Multidisciplinary Meetings</td>
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<td>MeV</td>
<td>Megaelectron Volts</td>
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<td>Acronym</td>
<td>Full Form</td>
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<tr>
<td>Mo</td>
<td>Months</td>
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<td>MPM</td>
<td>Malignant Pleural Mesothelioma</td>
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<td>NCP</td>
<td>Non-Coplanar Radiation Therapy</td>
</tr>
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<td>NET</td>
<td>Neuro-Endocrine Tumours</td>
</tr>
<tr>
<td>NR</td>
<td>Not Reported</td>
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<tr>
<td>NSCLC</td>
<td>Non-Small Cell Lung Cancer</td>
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<td>OS</td>
<td>Overall Survival</td>
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<td>POP</td>
<td>Plaster of Paris</td>
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<td>Pt.</td>
<td>Patient</td>
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<td>QA</td>
<td>Quality Assurance</td>
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<td>RANZCR</td>
<td>Royal Australian and New Zealand College of Radiologists</td>
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<td>RCT</td>
<td>Randomized Controlled Trials</td>
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<td>RFA</td>
<td>Radiofrequency ablation</td>
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<td>RILD</td>
<td>Radiation-Induced Liver Disease</td>
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<td>RO</td>
<td>Radiation Oncologist</td>
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<tr>
<td>RT</td>
<td>Radiation Therapy/ Radiation Therapist</td>
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<td>RTOG</td>
<td>Radiation Therapy Oncology Group</td>
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<tr>
<td>SIRT</td>
<td>Selective internal RT</td>
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<td>SBRT</td>
<td>Stereotactic Body Radiotherapy</td>
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<tr>
<td>SOT</td>
<td>Supervisors of Training</td>
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<td>TROG</td>
<td>Trans-Tasman Radiation Oncology Group</td>
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<tr>
<td>WLRT</td>
<td>Whole-Liver Radiation Therapy</td>
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PUBLICATIONS ARISING FROM THIS THESIS*


*Corresponding author
* This thesis is presented as a series of peer-reviewed publications.

PUBLICATIONS APPENDED IN SUPPORT OF THIS THESIS


Chapter 1. Introduction

Ongoing innovation in Radiation Oncology is required to improve outcomes for patients. Useful innovations can include both new technologies and new ways of doing things. There is value in being an active participant in innovation, rather than simply being a recipient of others innovations, but this requires the development of skills and sustained effort.

RADIATION ONCOLOGY

Radiation Oncology plays a key treatment role in many cancers. Its effectiveness depends on available treatment methods and technologies, appropriately trained professionals and an adequate knowledge base.

INNOVATION AND THE IDENTIFICATION OF SUITABLE AREAS TO EXPLORE

INNOVATIONS IN RADIATION ONCOLOGY

This thesis describes and examines a number of innovations in radiotherapy (with an emphasis on making components of radiotherapy process easier on people or more effective). Radiotherapy is a complicated multi-step process, and each step is a potential area of innovation. Figure 1 shows a conceptualisation of the component steps in radiotherapy. This explicitly includes the evidence base that underpins decision-making.
The studies described in this thesis represent an attempt to gain practical experience in a range of innovations in Radiation Oncology (differing in target, type and degree). The author previously completed a Masters of Business Administration (MBA) with an explicit plan to develop the skills and knowledge required for innovation (e.g. by studying process management, project management and entrepreneurship). The areas selected for investigation in this thesis, were identified by the candidate systematically examining the processes outlined in Figure 1 for innovations that could be achieved in the single-institutional or multi-institutional setting of Australia and New Zealand.

Table 1 show examples of innovations, taken from the candidates own publications (grouped by the categories shown in Figure 1).

Figure 1. Radiotherapy – broad categories of process / decisions

- Pt assessment / management selection
- Radiotherapy (or not)
  - +/- chemotherapy
  - +/- surgery
- Dose-fractionation
- Volumes
- Technique
- Planning
- Fixation
- Verification

Evidence Base

- Applying Evidence
- Developing Evidence
Table 1. Examples of Innovations examined by the author in peer-reviewed publications

<table>
<thead>
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<th>RT Component</th>
<th>Cancer</th>
<th>Innovation</th>
<th>Reference</th>
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<td>+/- chemo</td>
<td>Pancreas</td>
<td>Chemo-RT</td>
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<td>+/- surgery</td>
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<td>Dose/fractionation</td>
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Abbreviations. Pt = patient; Path = pathology; CRC = Colorectal Cancer; KMS = Kasabach-Merrit Syndrome; RT = Radiation Therapy; MPM = Malignant Pleural Mesothelioma; NSCLC-IV = Non-Small Cell Lung Cancer, Stage 4; Hypo# = hypofractionated RT; HD-LP = Lymphocyte Predominant Hodgkins Disease; IFRT = Involved Field RT; IORT = Intraoperative RT; NCP = Non-Coplanar RT; sim & treat = RT Simulation and treatment; H&N= Head & Neck Cancers; HDR = High Dose Rate Prostate Brachytherapy; corr = correction; QA = Quality Assurance; RO = Radiation Oncologist; Part 2 = RANZCR Part 2 Fellowship Exam; EBM = Evidence Based Medicine; MDM = Multidisciplinary Meetings.
The particular areas of innovation most suitable to the circumstances included themes of the training of Radiation Oncologists, patient immobilisation and hypofractionation. This thesis describes a number of specific innovations that were developed and prospectively tested.

**RADIATION ONCOLOGIST TRAINING AS A TARGET FOR INNOVATION**

The first two studies look at how training and knowledge acquisition might be improved and simplified, with the same overall objective of improving the administration of appropriate treatments as all the studies.

**LITERATURE REVIEW RELATING TO PROPOSED INNOVATIONS IN THE TRAINING OF RADIATION ONCOLOGISTS CLINICAL SKILLS (including the value of a workshop including practice and feedback in preparing candidates to sit the RANZCR faculty of radiation oncology fellowship Part 2 examination)**

The Part 2 examination for fellowship of the Royal Australia and New Zealand College of Radiologists (RANZCR) Faculty of Radiation Oncology (FRO) assesses each candidate’s ability to practice independently as a specialist Radiation Oncologist. Since the early 1990s, there has been a course held annually to help prepare candidates to sit this examination. Such a course has a range of potential benefits for participants, for example, improving their exam technique, helping them decide whether they are ready to sit the examination and providing ideas to improve training within their own department. The organization of the course has rotated between local volunteers in Brisbane, Sydney and Melbourne. Although the RANZCR supports the principle of the course, it is not involved, other than providing for the attendance of the Chief Censor. There is no standing framework for the courses. Its aims, content and method are up to the local organizer. There is no information on the value of the courses or how they could be improved. Although such a course may be useful, most preparation for the Part 2 examination for fellowship depends on the registrars’ routine learning environment (i.e. within each registrars’ home department). There is little information about the learning
environment of radiation oncology registrars. Izard et al. surveyed all post-Part 1 examination radiation oncology registrars in 1992 and received 30 eligible replies from 42 registrars.\textsuperscript{28} Their most important finding was that there was a gap in terms of the registrars’ perceptions of their training needs and what was actually provided. However, in the 13 years since that survey, there have been improvements in registrar training. For example, there has been a greater focus on formal training programmes.\textsuperscript{29} This and other developments may have decreased the importance of such pre-Part 2 examination training courses. The aims of this study are to examine the perceived value of such a course and its component parts, to identify possible improvements and to assess attending registrars’ learning environments. We therefore collected detailed information from participants before and after the training workshop in 2005. The methods and results are described in Chapter 2.

LITERATURE REVIEW RELATING TO A PROPOSED INNOVATIONS IN THE TRAINING OF RADIATION ONCOLOGISTS RESEARCH SKILLS (specifically the use of a workshop to improve scientific writing skills)

Another important area of radiation oncologist skills and the development of effective treatments includes scholarship and the production of scientific knowledge. I previously examined the publication rate of abstracts presented at annual Royal Australian and New Zealand College of Radiologists (RANZCR) conferences and the publishing journals.\textsuperscript{30} This is not one of the papers forming the core of the thesis (but is attached as appendix 1). All free paper research abstracts (oral or poster) presented by RANZCR radiologists, radiation oncologists and trainees at the four consecutive meetings between 1996 and 1999 were identified retrospectively from conference programs. The PubMed database (http://www.ncbi.nlm.nih.gov/PubMed/) was searched to determine whether or not the abstract had been published as a full paper. Of the 480 free paper research abstracts, 168 (35\%) had been published as full articles. The overall abstract to publication ratio for radiology was 29\% and for radiation oncology was 41\%. Papers were published in a variety of journals but Australasian Radiology accounted for 27\%. 
The mean time between presentation and publication was 16.5 months (median 17 months). These overall abstract to publication ratios are lower than those reported for overseas-based meetings in each respective area. Guidelines to scientific committees could increase the APR by more rigorous selection of abstracts. Future research should look at barriers to the publication of research findings, and identify ways to assist the publication process.

Research is the basis for improvements in clinical practice, and all medical practitioners need to understand its principles. However, the study described above showed that only a minority of abstract presentations at Royal Australian and New Zealand College of Radiologists (RANZCR) Annual Scientific Meetings (ASM) had been subsequently published. The overall abstract : publication ratio for radiology was 29% and for radiation oncology, 41%. Unpublished research has significant implications for the medical community. Other studies have shown that most unpublished research is never actually submitted to a journal for review. The cited reasons for failure to publish, such as a lack of time, to a large extent reflect a lack of skills. Scientific writing skills are different from the skills required for designing and carrying out research. An improvement in scientific writing skills is likely to improve submission and success rates. There are a small number of studies examining scientific writing skills training for doctors. These report substantial benefits, but the interventions are intensive and have been based in academic departments. For example, Sommers et al. reported the benefit of a 2.5-day course, and Pololi et al. used monthly 75-min sessions over 7 months. My colleagues and I specifically wanted to address the problem of unpublished research from RANZCR ASM and felt that a training intervention would most appropriately be held in conjunction with the 2004 ASM. For practical reasons, our writing programme was limited to a 3-h workshop held concurrently with the final morning session of the conference. We believed that such a course would be useful, but as there are no reports defining the value of short courses of scientific writing skills training, we sought to assess this by asking participants to complete self-assessments before the workshop and 6–8 weeks afterwards. The methods and results are described
PATIENT IMMOBILISATION AS A TARGET FOR INNOVATION

The same objective of improving treatment might be achieved by addressing other components of the radiotherapy process. There have been significant technical improvements in the ability to accurately deliver radiotherapy. However, immobilization methods have yet to take full advantage of available technology. Possibilities for innovation include better immobilisation casts and neck supports.

LITERATURE REVIEW RELATING TO A PROPOSED INNOVATION IN THE IMMOBILISATION OF PATIENTS FOR RADIOTHERAPY (specifically Surface laser scanning to routinely produce casts for patient immobilisation)

Plastic casts are used to reduce patient movement during treatment of head, neck and brain malignancies with radiotherapy. Polyethylene-based casts are usually produced by first taking a Plaster of Paris (POP) ‘negative’ impression from the patient. A ‘positive’ is then made, which is used to vacuum form an immobilisation cast. Making the ‘negative’ can be messy, stressful for patients and labour intensive. Recent innovations have led to a variety of techniques for medical imaging. Laser surface scanning is a non-invasive method for acquiring 3-D surface images.\textsuperscript{40} Recently a light-weight, hand-held, laser surface scanner has become commercially available, the Polhemus FastSCAN (Polhemus). The FastSCAN device has found many medical applications, including the production of prostheses and orthoses and the documentation of injury.\textsuperscript{41-43} This technology was developed to routinely produce immobilization casts for radiotherapy and its value assessed. The methods and results are described in Chapter 4.

LITERATURE REVIEW RELATING TO A PROPOSED INNOVATION IN THE IMMOBILISATION OF PATIENTS FOR RADIOTHERAPY (specifically to routinely produce customised neck supports)
Having improved one part of head & neck immobilization, with benefits in comfort and accuracy, this led my colleagues and me to look at other complementary improvements. Accurate and reproducible patient positioning is fundamental to the success of fractionated radiotherapy. This is particularly so for conformal and intensity-modulated radiation therapy, where poor patient positioning could result in geographic misses or inadvertent overdosing of normal tissue. When patients are to receive radiation therapy for head and neck (H&N) or brain tumours, immobilization aids usually include a combination of patient face masks and neck supports. While most effort spent on improving immobilization has focused on face masks, the use of an appropriate neck support may also be critical. It is important that neck supports accurately fit individual patients’ neck contours. Until recently, our department, like most others, selected one of a small number of standard neck rests (examples are shown in Chapter 5 - Fig. 1, p.60). These not only might have been a poor match for a patient’s neck contour but also provided no support to prevent lateral movement. A better solution is customized neck support production; however, this has several drawbacks. For many years, two-part polyurethane pourable foam has been used to create personalized neck supports. However, the liquids require mixing (to the required consistency), which can be messy and time consuming. There are also significant occupational health and safety issues related to toxic fume production. My co-investigators and I reported on an improved method of customized face mask production using laser surface scanning. In this report, we have sought to identify and investigate improved technology to develop a method to routinely make customized neck supports for patients prescribed radiotherapy to the brain or H&N regions. The methods and results are described in Chapter 5.

**HYPOFRACTIONATED TREATMENT COURSES AS A TARGET FOR INNOVATION**

One method of making treatments easier on patients (and making more use of their limited time, particularly for patients receiving palliative radiotherapy) has been hypofractionation. This has been a successful approach for bone metastases, inoperable lung cancers and other sites. Any advantages from shorter courses have to be weighed against possible increases in side effects and/ or decreased benefits.
In recent years, the incidence of malignant pleural mesothelioma (MPM) has been increasing rapidly. Chest wall seeding following invasive procedures is a problem, and has been reported to occur in 19% of patients following thoracoscopy. These subcutaneous masses are often symptomatic and refractory to radiotherapy (RT). Two nonrandomised series and one randomised controlled trial have demonstrated that a prophylactic three-fraction course of RT reduces the procedure tract metastasis rate to 0%. Recent reviews and guidelines recommended prophylactic radiotherapy following thoracic procedures. My colleagues and I undertook a randomised trial to test a more convenient single radiation treatment. The methods and results are described in Chapter 6.

The same approach of shorter treatment courses has potential advantages for palliation at other sites, such as liver metastases. Liver metastases are common, and when they are advanced, they often cause pain, sweats, nausea and vomiting. The response rate to first-line systemic chemotherapy depends on the primary site, and although it can be as high as 60% for breast cancer, it is lower for most sites. Chemotherapy is associated with side-effects such as nausea, vomiting, alopecia and tiredness. Second-line chemotherapy is less likely to be effective. The palliative value of fractionated whole-liver radiotherapy (WLRT) has been demonstrated in a number of series, with low levels of acute toxicity. The largest series prospectively studied 183 patients and reported symptom response rates of 80%. Smaller series have also examined WLRT in combination with systemic or regional chemotherapy, and reported
symptomatic responses of 63–90%.\textsuperscript{63,64} The use of WLRT (with or without chemotherapy) is rare in clinical practice, possibly due to a belief that hepatic irradiation inevitably leads to radiation hepatitis. In fact, the liver tolerates high doses of radiation well providing that only part is irradiated\textsuperscript{65} or that whole-liver doses are kept below 30 Gy in two Gy fractions or 21 Gy in three Gy fractions.\textsuperscript{66,67} The published hepatic palliative radiation schedules require patient attendance for between seven and 22 fractions. Shorter courses of treatment would have less detrimental impact on patients’ remaining lives and might provide equal palliation. A retrospective review of a pilot experience with 21 patients receiving 10 Gy in two fractions described response rates (complete and partial) of 87.5% for hepatic pain and 50% for abdominal distension (N. Spry, pers. comm., 1998). This review formed the basis of a prospective multicentre trial to assess the effectiveness and tolerability of short-course radiation (10 Gy in two fractions separated by 6–24 h): Trans-Tasman Radiation Oncology Group trial TROG 98.04.14. The methods and results are described in Chapter 7.

LITERATURE REVIEW RELATING TO A PROPOSED INNOVATION IN THE RADIOTHERAPY OF BREAST CANCER (specifically intraoperative radiation treatment for breast cancer)

The same approach of shorter treatment courses can be applied in radical settings with new technologies. Breast conserving surgery with postoperative radiotherapy has been shown to be as effective as mastectomy in terms of overall survival, but with improved cosmesis.\textsuperscript{68–71} Adjuvant radiation treatment is usually given 5 days each week, over a 5–7 week period. This may be a significant inconvenience to women, particularly those who reside some distance from a treatment centre, have difficulties with transport, or a full-time career. In addition, adjuvant breast irradiation makes up to 30% of radiation oncology department workloads, at a time when radiation staff and machine time are scarce in both Australia and New Zealand. Unfortunately, trials attempting to omit radiotherapy in selected women after breast conserving surgery have shown unsatisfactory local recurrence rates.\textsuperscript{68,73–77} Even women with small mammographically
detected breast cancers should be offered adjuvant irradiation. An X-ray source small enough to be placed inside a tumour bed to deliver its treatment has been developed (Intrabeam, initially from Photoelectron Corporation, now produced by Carl Zeiss). In the USA, the device has received approval from the Food and Drug Administration for use at any body site. It has a number of potential applications, and although it has mainly been studied as a neuro-oncological treatment, it seems ideally suited for therapy of breast cancer. A series of applicators of varying diameters are available, which allows the correct size to be chosen for any surgical cavity after breast conservation surgery. Low energy 50 kV X-rays are produced that have limited penetration, and so deliver a dose that is relatively high at the surface of the applicator but which falls off rapidly with distance. We prescribe a 5 Gy dose at 10 mm depth from the applicator surface, given in a single treatment. The procedure lengthens theatre times but otherwise there are few logistical issues (e.g. no purpose built room shielding is required). The pilot experience with Intrabeam for breast cancer in the UK, has been reported recently. Such intraoperative radiation treatment (IORT) may be effective as the sole adjuvant radiotherapy for selected low risk patients. Prior to testing this in a randomized trial, we performed a prospective feasibility trial using the IORT as a method replacing the 1–2 week tumour bed ‘boost’ component of a standard external beam radiation treatment (EBRT) course. This allowed us to test whether this IORT treatment was possible in routine practice at an Australia centre, and whether acute toxicity was acceptable when EBRT was also used – as might be required if final pathology results were less favourable than expected. The methods and results are described in Chapter 8.

The resulting studies are reported in the following chapters 2-8. UWA allows presentation as a series of papers. Each is a reformatted (according to UWA’s regulations) version of a published, peer-reviewed paper.
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Chapter 2. Preparing to sit the Royal Australia and New Zealand College of Radiologists Faculty of Radiation Oncology Fellowship Part 2 examination: The value of a workshop including practice and feedback

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The candidate made substantial contributions to each of study conception, study design, literature search, data collection, data analysis, data interpretation, manuscript preparation, manuscript editing, and manuscript revision/review. In addition the candidate was the corresponding author.
SUMMARY

A workshop has been held annually to help prepare candidates to sit the Royal Australia and New Zealand College of Radiologists Part 2 Faculty of Radiation Oncology examination. This study examined the value of such a course and its component parts and assessed attendees’ learning environments. We collected detailed information from participants before and after the training workshop in 2005. A specific feature of this workshop included the use of an examination technique feedback form to facilitate the provision of systematic and comprehensive feedback to individual candidates after mock examination. Participants completed course evaluation forms and a learning environment survey. There were 22 candidate participants. The course and its components of this course were perceived very positively – including the examination technique feedback forms and written advice. Only three of the 24 questions regarding the registrars learning environment had less than 80% favourable responses – two of these questions related to workload. The course design described seems reasonably satisfactory in that it included the components ranked most highly by candidates. We also identified a number of variations that may be useful for future workshops. Although learning environments were generally good, we identified a perceived problem with workloads affecting a significant number of registrars.
INTRODUCTION

The Part 2 examination for fellowship of the Royal Australia and New Zealand College of Radiologists (RANZCR) Faculty of Radiation Oncology (FRO) assesses each candidate’s ability to practice independently as a specialist Radiation Oncologist. Since the early 1990s, there has been a course held annually to help prepare candidates to sit this examination. Such a course has a range of potential benefits for participants, for example, improving their exam technique, helping them decide whether they are ready to sit the examination and providing ideas to improve training within their own department. The organization of the course has rotated between local volunteers in Brisbane, Sydney and Melbourne. Although the RANZCR supports the principle of the course, it is not involved, other than providing for the attendance of the Chief Censor. There is no standing framework for the courses. Its aims, content and method are up to the local organizer. There is no information on the value of the courses or how they could be improved.

Although such a course may be useful, most preparation for the Part 2 examination for fellowship depends on the registrars’ routine learning environment (i.e. within each registrars’ home department). There is little information about the learning environment of radiation oncology registrars. Izard et al. surveyed all post-Part 1 examination radiation oncology registrars in 1992 and received 30 eligible replies from 42 registrars.1 Their most important finding was that there was a gap in terms of the registrars’ perceptions of their training needs and what was actually provided. However, in the 13 years since that survey, there have been improvements in registrar training. For example, there has been a greater focus on formal training programmes.2 This and other developments may have decreased the importance of such pre-Part 2 examination training courses.

The aims of this study are to examine the perceived value of such a course and its component parts, to identify possible improvements and to assess attending registrars’ learning environments. We therefore collected detailed information from participants before and after the training workshop in 2005.
MATERIALS AND METHODS

We designed a course to prepare candidates to sit the RANZCR FRO Part 2 exam that incorporated several specific features. The main aim of the course was to improve exam technique, in particular relating to verbal, rather than written, assessment. That is, the focus of the course was on techniques that allow candidates to show their skills and experience and to present themselves in the best possible light. The course was made open to those intending to sit the Part 2 exam within 12 months. The course was held over a weekend, 3.5 months before the earliest formal exams. The first day began with an introductory session with the Chief Censor. After this, there were five interactive sessions with tutors, who had been directed to ask participants questions as they would be questioned in a formal examination. Four sessions related to clinical exams and one to the pathology viva. Each of these sessions was 1 hour in duration. On the final day, candidates underwent mock examination, being questioned around a series of cases, each similar to those seen in recent actual examinations. Questions and outline answers were supplied to examiners and images for consideration were projected on computer screen. There were 10 examiners who worked in pairs, examining groups of two or three. The examination time was 2 h, but as candidates’ preparedness varied, the time and number of cases to be covered in the examination was left to the examiners’ discretion. Examiners did not examine candidates from their own department and were not current College examiners.

Before the course, a focus group of current or former Supervisors of Training (SOT) was asked to develop written advice to improve examination technique. This written material was sent to candidates before the course. The same group developed 10 criteria suitable to be used in an examination technique feedback form. The aim of this form was to facilitate the provision of systematic and comprehensive feedback to individual candidates after the mock examination. This form, together with a generic list of questions regarding clinical cases, is shown in Appendix I. This is not an attempt to replicate marking sheets that might be used by examiners, but rather is designed to be of use in identifying to candidates where their exam technique could be improved. The candidates were provided with examples of the feedback forms before the course. After
the mock examination each candidate was provided with feedback from the examiners including an individual marked examination technique feedback form. That is, each candidate’s performance in each case was reviewed and criteria felt in need of improvement were noted and feedback provided to the candidate. In addition to the mock examination outlined above, most candidates were videotaped performing for one case individually. This was either a clinical scenario or a short case involving the physical examination of a patient. The examiner for this section not only gave immediate feedback but also supplied each candidate with videotape of their performance for their own later personal review. Time did not allow all candidates to undergo videotaping.

**Assessment before the workshop**

Before the workshop, participants were asked to complete a learning environment survey regarding the learning environment provided by their own radiation oncology department. This survey was based on one designed for and used to survey resident medical officers. Each question addresses an aspect of learning for which there is evidence to support its importance. The construct validity of the modified version was checked by members of the RANZCR Curriculum Advisory Group, which led to the removal of questions considered to be ambiguous or repetitive. The resultant learning environment survey includes 24 questions, each with four choices of agreement with accompanying statements (strongly agree, agree, disagree and strongly disagree) on a Likert scale. The 24 questions address seven aspects of the learning environment: autonomy (two questions), opportunities for learning (six), participation in formal training programmes (three), role clarity (three), social support in the workplace (three), on-the-job supervision (four) and workload (three). The learning environment survey is provided in Appendix II.

**Assessment after the workshop**

Immediately following the workshop, participants were asked to complete a questionnaire regarding the value of the course and its components, how well the course met its goals and what components should be included in future courses.
Each examiner was asked three questions regarding the value of the exam technique feedback form. These are shown in Appendix III. In addition, the frequency that each of the 10 aspects of exam technique was assessed as requiring improvement was recorded.

RESULTS

The candidates

There were 22 candidate participants, from a number of states/countries: Western Australia (one), New South Wales (eight), Victoria (eight), New Zealand (one), South Australia (one) and Queensland (three).

Learning environment survey

All 21 registrar participants completed the learning environment survey. One participant who has an overseas fellowship and who is practising as a consultant was excluded from this survey. Only three of the 24 questions regarding the registrars learning environment had less than 80% positive responses (i.e. responses that favoured the learning environment). These were two of the three questions related to workload and one of three questions related to the formal training programme. Specifically – I have sufficient time to reflect on my learning experiences (71% agreed), I often feel swamped by work (24% agreed) and the formal education programmes give me access to valuable social support (71% agreed). The remaining responses favoured the learning environments in 81–100% (strongly in 0–67%). The number of registrars answering positively approximately 20 or more statements, of the total 24, was 19 (90%). The remaining two registrars, respectively, answered 18 and 19 statements positively.

Post-workshop assessments

Twenty-one candidates completed post-workshop assessments. One candidate was unable to attend the second day and was excluded from the post-workshop survey. The value of components of this course is shown in Figure 1.
Candidates agreed with statements between 90 and 100%, with strong agreement ranging between 38 and 80%. The extent to which each participant agreed the course had achieved its aims is shown in Figure 2.

Candidates agreed with statements between 90 and 100%, with strong agreement ranging between 24 and 67%. The participants' opinions on the preferred components of future sessions are shown in Figure 3.
There was almost universal agreement that future sessions should include each of component parts of the current course. All those who responded to the question regarding videotaping felt it should be included – the question, however, was only answered by 76% of candidates (not all course participants had undergone videotaping, with this response rate potentially including all those who had done so).

Regarding components that were not included in the current workshop, there was majority support for a session on evaluating radiotherapy plans (100%), a workshop (81%) or lecture (62%) on essay writing techniques and a psychologist speaking on stress management (57%). A minority supported the future inclusion of didactic lectures (19%).

**Exam technique feedback forms – use and opinion of examiners**

Examiners agreed the forms (i) were useful in providing feedback (80%); (ii) would be useful to candidates (80%); (iii) were easy to use; and (iv) were easy to apply (70%). One pair of examiners, whose responses are included above, did not use the forms. The results of the use of the exam technique feedback forms to emphasize specific aspect warranting improvement by candidates is shown in Figure 4.
On average, criteria for improvement were noted once per viva case assessed. All 10 criteria were used; most commonly, candidates were noted as having failed to show their experience adequately.

**DISCUSSION**

We have clearly showed that the Part 2 examination preparation course together with each of its individual components is perceived by participants as being very useful. A number of innovations were received positively; in particular, the written advice supplied to participants before the workshop and the use of the newly developed examination technique feedback forms. The course design we used above seems reasonably satisfactory in that it included the components ranked most highly by candidates. We also identified a number of variations that may be useful for future workshops. Although learning environments were generally good, we identified a problem with workloads affecting a significant number of registrars.

The major weakness of this study is that we are asking about the value of a preparation workshop before candidates have sat the examination. Although it might be useful to ask candidates about the benefit of the course after they have sat the examination, this would be confounded by a range of factors. Another weakness is that any course will have to cater to candidates with different learning needs. For example, the pathology

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*Fig. 4.* Use of specific criteria on the examination technique feedback form (i.e. characteristics that candidates needed to better show that they possess). ■ occasions; □ individuals.
viva session was probably to be of most benefit to those who do not have regular formal sessions with a pathologist. Similarly, the learning environment assessment applies only to registrars at this stage of their training and may not reflect perceptions of more junior trainees. The major strength of this paper is that we asked the candidates’ opinions directly. This group of registrars, that is, those in final preparation for their Part 2 examination, are both experienced and focused on learning environments. Therefore, their opinion on current learning environments needs to be respected. Also, the learning environment survey in particular, is a well-designed instrument and we obtained a good response rate.

With any assessment of performance, it is important that candidates understand its requirements. This makes realistic practice of critical importance.⁵,⁶ There is little information about the value of mock examinations for postgraduate fellowship examination preparation, although it has been showed to benefit both candidate radiologists and urologists.⁷,⁸ Our article is the only one of which we are aware, in the field of radiation oncology. Likewise, the results of the learning environment survey provide unique information. In 1992, Izard et al. surveyed trainees at a range of stages and identified a perceived deficiency in the amount of formal teaching.¹ In 2000, Veness et al. examined registrar access to Internet-based sources of evidence and found that only 39% of registrars accessed radiation oncology journals online, identifying this as a source of concern.⁹ In contrast, it appears that this group of registrars generally feel they have good learning environments; however, workload issues were identified as a problem for a significant number. Recently, all SOT were asked to describe the learning environment in their own department, using the same questions as our workshop participants. Twenty-one of 27 SOT responded. Only four questions received less than 80% of responses favouring the learning environment. Two of those four questions were the same as two of the three questions for which less than 80% of workshop participants’ responses favoured the learning environment. The shared questions addressed whether there was sufficient time to reflect on learning experiences and trainees being swamped by work. This suggests that workload issues need to be addressed for candidates preparing for the Part 2 examination. The two other questions
that received less than 80% of responses favouring the learning environment addressed autonomy and respect. Of particular concern, 10 of 21 SOT disagreed trainees at their centre had sufficient autonomy. An important difference was that the SOT responses involved all levels of trainees within each SOT department. It seems probable that more senior candidates are given the autonomy they require. Whether perceived heavy workloads negatively affect final exam preparation, where exposure to clinical material rather than textbooks alone is important, is not known.

The results regarding value of course and components are important for a number of reasons. The course not only requires some effort to organize but also may be a burden on registrars, for example, who may be funding their own interstate or trans-Tasman travel. The format we have described could be a model for development for future workshops. The perceived value of the written material and of the exam technique feedback forms is of particular interest because they can easily be made widely available. If the written notes can be further developed (including the input of examiners), then they might be usefully published in Australasian Radiology. The exam technique feedback form is included as an appendix to this article, with which we have included a list of generic questions that might prompt realistic examination questioning. They provide an easy way for a candidate to get comprehensive and systematic feedback. This is important because candidates are not good at judging their own performance.10 The potential issues of excessive workload might be addressed in a number of ways. Departments might need to look at providing, or increasing, protected time for registrars. The ratio of registrars to consultants may need to be decreased where logistically possible.

The correlation between the course and the College is unlikely to change. Efforts are, however, underway to improve the understanding of SOT and others, about what examiners are looking for. The Part 2 examination tests knowledge and skills that are used in day-to-day practice.3,11 However, a major issue regarding exam preparation is that, at present only examiners and perhaps recent candidates understand the process of assessment in detail.5,6 SOT are often selected because they are closest to the exam and those responding to a recent survey had a median of 5 years post fellowship.
experience. Although this means SOT often have recent examination experience, there needs to be better communication between examiners and SOT. The College is currently looking to improve this, and a recent meeting attended by both SOT and examiners was a useful first step. The College is working to make assessment criteria used by examiners more explicit.

Learning environments for registrars are currently under review. The learning environment questionnaire used here appears to be usefully adapted to radiation oncology. Here we have focused registrars at only one stage of training. Registrars at other earlier stages may have different requirements. It is planned to use the same questionnaire to survey all levels of trainees as part of the curriculum review process. The results of such surveys could then be used to assess the value of any changes to the content and delivery of training. Shakespeare et al. recently reviewed educational methods and their suitability to radiation oncology. They examined individually negotiated learning contracts; a mentor programme; task-based learning; tutorial programmes; protected time for self-directed learning and facilitation of research, education, administration and quality assurance roles. The requirements of SOT is probably to increase substantially. How this is to be addressed will require sensible planning.

CONCLUSIONS

The pre-Part 2 preparation course appears to be a valuable teaching exercise. The model we used seems to be satisfactory. This article provides a framework for future courses, avoiding the need for repeated reinvention. The information collected should facilitate the design and execution of future sessions. However, both the Part 2 examination and the preparation course require a process of continuous improvement. The learning environment of trainees requires monitoring. We have identified a potential problem with workloads that needs to be addressed.
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APPENDIX I

Evaluation form
Thorough Could demonstrate more thoroughness
Systematic Could appear more systematic
Clear communication Could be clearer
Confidence Could display more confidence
Experienced Could demonstrate experience better
Maturity and Perspective Could identify priorities better
Reasoned approach Could display rational approach better
Decisive Could be more decisive
Knowledgeable Could display knowledge better
Sensible (and safe) Could be more conventional

A generic question set – for clinical case discussion
What is your assessment?
What would you do?
Why would you do it?
How would you do it?
Is there anything else you would do?
What would you tell the patient?
What will the outcome be?
What options are there? Is there any other way of doing things?

APPENDIX II

The learning environment questionnaire
Please rate your agreement with following statements regarding the learning environment in your department (Strongly agree, agree, disagree, strongly disagree)
These questions relate to your level of autonomy
1. I have freedom to set my own work priorities
2. I have a level of autonomy appropriate to my level of training
These questions relate to opportunities for learning at work
3. I have access to up-to-date learning resources at work when I need them
4. I have access to a variety of patients and presenting problems appropriate to my level of training
5. I have opportunities to acquire the skills appropriate to my level of training
6. I receive on the job teaching in specialty areas targeted at my learning needs
7. Teaching and training are emphasized in this department
8. My work is routine and repetitious
These questions relate to participation in formal training programmes
9. I am given relief from duties to participate in formal education programmes
10. The formal educational programs are targeted at my learning needs
11. The formal educational programs give me access to valuable social support
These questions relate to role clarity
12. I am aware to whom I should report, in a variety of circumstances
13. I get mixed messages about duties and responsibilities
14. I am clear about my work relationships with staff in the department
These questions are about social support in the workplace
15. I do not feel part of the team
16. There is a sense of cooperation and mutual respect in the department
17. I have a good sense of rapport with senior people in the Department
These questions are about on-the-job supervision
18. Advice and back up from more experienced colleagues is readily available to me at all times
19. I receive direct supervision and feedback from an experienced colleague when doing a task for the first time
20. I receive direct supervision and feedback that is sufficient for my level of training
21. The supervision and feedback given to me is clear, specific and supportive
These questions are about your workload
22. My time at work is utilised productively
23. I have sufficient time to reflect on my learning experiences
24. I often feel swamped with work
APPENDIX III

The post workshop assessments
Please rate your agreement with following statements. (Strongly agree, agree, disagree, strongly disagree)
For candidates
Regarding the value of the course components
1. The course overall met my learning needs
2. The pre-course written materials were useful
3. The session with the Chief Censor was useful
4. The pathology viva session was useful
5. The clinical scenario sessions were useful
6. The mock viva exam was useful
7. The technique feedback forms were useful
How well did the course meet its goals?
8. It gave me useful information about exam technique
9. It has helped me decide when to sit the exam
10. It has helped me to identify my weaknesses
11. It provided useful discussion with my peers
12. It has given me useful ideas how I can improve training in my own department
Future courses should include:
13. A session with the Chief Censor
14. Interactive clinical scenario sessions
15. A pathology viva session
16. A mock viva exam
17. Short case(s)
18. The use of examiner feedback forms
19. Video taping of a short case/viva presentation
20. A psychologist speaking on dealing with stress
21. Didactic lectures
22. A session on evaluating radiotherapy plans
23. A lecture on essay writing technique
24. A workshop on essay writing
For examiners:
Regarding the examination feedback forms
1. The forms were useful to me in providing feedback
2. The forms will be useful to candidates
3. The forms were easy to use and to apply
Chapter 3. The value of a scientific writing training workshop for radiologists and radiation oncologists

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SUMMARY

A substantial amount of radiological and radiation oncological research carried out in Australasia is not published. Therefore, a scientific writing skills training workshop was held in conjunction with the 2004 Royal Australian and New Zealand College of Radiologists Annual Scientific Meeting. Registration for the 3-h-long workshop was open to all conference attendees but numbers were limited. The workshop was led by an experienced facilitator who used content based on a literature review. Participants were asked to complete questionnaires rating their agreement with statements regarding their writing abilities and resources before the workshop. Those who attended the workshop repeated the questionnaire 6–8 weeks afterwards. Comparison of the paired preworkshop and post-workshop responses showed increases in the median category of agreement with statements regarding having the required skills, having advice available and understanding the structure of scientific articles. In addition, all participants reported that they found the workshop useful, said that they would recommend attendance to others and felt that such workshops should be available at future Royal Australian and New Zealand College of Radiologists Annual Scientific Meetings. Half the participants felt that the workshop made it more likely that they would publish. We have shown that even short workshops appear to have benefits and should be encouraged.
INTRODUCTION

Research is the basis for improvements in clinical practice, and all medical practitioners need to understand its principles. However, a recent study showed that only a minority of abstract presentations at Royal Australian and New Zealand College of Radiologists (RANZCR) Annual Scientific Meetings (ASM) had been subsequently published. The overall abstract : publication ratio for radiology was 29% and for radiation oncology, 41%. Unpublished research has significant implications for the medical community. Other studies have shown that most unpublished research is never actually submitted to a journal for review. The cited reasons for failure to publish, such as a lack of time, to a large extent reflect a lack of skills.

Scientific writing skills are different from the skills required for designing and carrying out research. An improvement in scientific writing skills is likely to improve submission and success rates. There are a small number of studies examining scientific writing skills training for doctors. These report substantial benefits, but the interventions are intensive and have been based in academic departments. For example, Sommers et al. reported the benefit of a 2.5-day course, and Pololi et al. used monthly 75-min sessions over 7 months.

We specifically wanted to address the problem of unpublished research from RANZCR ASM and felt that a training intervention would most appropriately be held in conjunction with the 2004 ASM. For practical reasons, our writing programme was limited to a 3-h workshop held concurrently with the final morning session of the conference. We believed that such a course would be useful, but as there are no reports defining the value of short courses of scientific writing skills training, we sought to assess this by asking participants to complete self-assessments before the workshop and 6–8 weeks afterwards.

METHODS

A scientific writing workshop was held at the 2004 RANZCR ASM. All participants completed a preworkshop questionnaire, and 6 weeks following the workshop they completed a second questionnaire, which repeated a series of questions.
Demographics

For each participant, the number of previous publications was determined by a search of Medline, and the number of conference abstracts accepted at the 2004 ASM was determined from the conference programme. The date each registrant was awarded their basic medical degree was obtained from the Medical Directory of Australia. Participants were asked whether they had completed but not submitted a scientific article or had a scientific article rejected in the preceding 6 months.

Workshop content and method

The workshop was held concurrently with the final day of the RANZCR ASM. We adopted the specific aim of enabling participants to transform conference presentations into published papers. Following a review of published work, we felt content should include, in particular, the skills of clear writing, an understanding of the structure of scientific articles, selection of appropriate topics and selection of the right journals for individual articles. One of us (D. P.), who has led a number of workshops in Australia and Hong Kong concerning writing research papers in health care, facilitated the workshop. The workshop numbers were limited and registrants were charged a nominal fee ($A20). Participants were asked to bring an abstract or an uncompleted manuscript. The background of registrants and their baseline self-assessments, as described subsequently, were made available to the workshop facilitator before the workshop to allow further customization of content.

Questionnaires

Participants were asked to complete questionnaires before the workshop and 6–8 weeks afterwards. Ten questions were included in both questionnaires. These questions were related to the workshop content outlined above and addressed motivations together with both global and specific scientific writing skills. Participants were asked to rate their agreement with statements on a scale of 1–5 (corresponding to strong agreement, agree somewhat, neither agree nor disagree, disagree somewhat and strongly disagree, respectively).
Specifically, participants were asked how strongly they would agree that they (i) want to publish a scientific article; (ii) have the skills needed to write a scientific article; (iii) have persons from whom they can get advice about scientific writing; (iv) can choose a suitable journal to which to submit an article; (v) can choose a suitable topic for a scientific article; (vi) understand the structure of scientific articles; (vii) can write clearly; (viii) have the time needed to write a scientific article; (ix) have the support and resources needed to write a scientific article; and (x) believe the effort of writing a scientific article would be recognized.

The preworkshop and postworkshop responses were compared to see if there were any changes in the median answer in each category.

In addition, the first questionnaire contained questions (yes/no) regarding previous writing training and experience. These asked whether the participants had had any formal post-graduate scientific writing training, had had the chance to have formal postgraduate scientific writing training, had had a paper accepted (as first or second author), had completed but not submitted a manuscript in the past 6 months, or had had a manuscript rejected. The second questionnaire contained additional statements (to be rated for agreement as above) regarding participants’ perceived value of the workshop as follows: the workshop was useful, I would recommend the workshop to others, similar workshops should be offered at each RANZCR conference and I am now more likely to successfully publish.

RESULTS

The session participants completed and returned preworkshop and postworkshop questionnaires. The participants were four radiologists, three radiation oncologists and one radiation oncology advanced trainee. Another two individuals registered and completed baseline questionnaires but were unable to attend the workshop, so their data are not included. The participants had a median of 2.5 citations (0–19) on Medline, with five participants having at least one first or second author citation. Seven were authors of abstracts accepted for the 2004 ASM (four were first or second authors). Registrants had graduated with their primary medical degree 3–36 years earlier. All
participants reported that they had not had the opportunity to attend any postgraduate scientific writing courses. Two participants reported having had manuscripts rejected in the preceding 6 months.

Baseline self-assessments (agreement with statements) from the eight participants are shown in Table 1.

<table>
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<th>Statement</th>
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<td>Want to publish</td>
<td>88‡</td>
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<td>Have skills</td>
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<td>Can get advice</td>
<td>25</td>
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<td>Can choose journal</td>
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<td>Can choose topic</td>
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<td>Understand structure</td>
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<td>Can write clearly</td>
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<td>Have support</td>
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<td>Efforts recognized</td>
<td>38</td>
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Postworkshop responses are shown in bold. ‡Agreement (1–2); neither agree nor disagree (3); disagreement (4–5). †Category containing median response. §One baseline response not supplied. —, 0%

The majority agreed that they wanted to publish, could choose suitable journals, could choose suitable topics, did understand the structure of scientific articles, could write clearly, had support and believed their efforts would be recognized. However, strong agreement was uncommon, and at least two participants disagreed with statements in the categories of having the required skills, having advice available, understanding the structure of scientific manuscripts and being able to write clearly.

All eight of the participants attending the workshop completed a second questionnaire 6–8 weeks after the workshop. The median category of answer for postworkshop questionnaires was compared with baseline (Table 1). There were increases in the
median category of response, before and after the workshop, for questions concerning three factors – having the required skills, having advice available and understanding the structure of scientific article categories. There was also a decrease in the median category of response for the belief that respondents had sufficient time. There were no differences in the median category of response for the remaining skills. Participants also supplied an assessment of the value of the workshop to themselves and others. All participants found the workshop useful (three (38%) felt this strongly), said that they would recommend it to others (four (50%) felt this strongly) and felt that workshops should be available at future RANZCR ASM (three (38%) felt this strongly). Half the participants felt that attending the workshop made them more likely to publish.

DISCUSSION

We found some benefits from a short course addressing scientific writing skills available to attendees at the 2004 RANZCR ASM. Baseline self-assessment showed a perceived skills deficit, even in a group with significant clinical and publication experience. Following the workshop, there were positive differences in the median category for having the required skills, having advice available and understanding the structure of scientific articles. These results indicate that even short courses can raise skill levels. However, there was a negative change in assessments of having time to write. We suspect that although improved general writing skills can reduce the time required to write a paper, this effect was probably countered by a more realistic estimate by study participants of the time and effort involved. This category also does not directly reflect skills in the same way as the other categories do. Similarly, there was no effect noted on several target skills. Nevertheless, there was significant perceived benefit by participants who valued the workshop as entirely positive and half felt that they were now more likely to publish. Participants rated the workshop highly and felt that similar events should be more widely available and included in future RANZCR ASM.

One weakness of the study is that although the workshop was held to address the problem of unpublished research (by improving writing skills), assessment was in terms of self-perception, rather than objective measurement. Against this, it should be noted
that the postworkshop questionnaires were completed at an appropriate time, at least 6 weeks after the workshop. This allowed participants the time to have attempted further writing. The study included only a small number of participants, reflecting the nature of a workshop with limited numbers, but still provides evidence for the feasibility of such sessions and addresses a range of practical issues (e.g. content). Finally, the study may have underestimated the benefits available. Only one attendee was a registrar and many participants actually had significant writing experience, with most having been first or second authors of papers in the past. It was confirmed during the workshop that some were attending to gain skills to facilitate the work of junior staff. So in fact, the benefits of the workshop may be greater if those with the most need were targeted. To our knowledge, this is the first time that such a short course to improve scientific writing skills for doctors has been assessed. Others have investigated the benefits of much more intensive programmes based in academic departments. Sommers et al. presented the result of a 2.5-day workshop. Pre/post self-assessment data indicated significant increases in perceived knowledge and skills. Follow-up qualitative interviews showed that participants felt that the workshop motivated them to begin and sustain writing projects, gave them skills that made their writing more effective and demystified the submission and publication processes. Preworkshop and postworkshop rates of publication showed a significant increase. Pololi et al. described the effects of seven monthly 75-min sessions (in addition to the provision of protected writing time) as part of a faculty development programme, and found that participants completed at least one scholarly manuscript. Hekelman et al. described a faculty development instructional programme that included seminars, workshops and feedback from senior advisers, which resulted in publication by 13 of the 40 faculty participants. There is evidence, then, that intensive skills development programmes can improve skills and publication rates. Although we have shown benefits of a short scientific writing workshop, we would expect that a longer session might offer greater benefits. A longer session (e.g. an 8-h day) would allow the content to be greatly expanded. For example, we could have discussed topics such strategies for dealing with co-authors or how to manage rejection of manuscripts. Holding such a workshop in conjunction with the RANZCR ASM also
has a number of advantages. Participants may have prepared a piece of research for presentation and, if so, are keen to move to the publishing stage. Also, there is the potential opportunity to take advantage of the skilled attendees as tutors. However, this may restrict attendance. In this case, two registrants were unable to attend the workshop because the workshop was held concurrently with the RANZCR meeting. It might be best to hold such training on days immediately before or after the major conference. We hope that such workshops could become a standing feature of the ASM. It should be noted that all participants in this workshop indicated that they had not previously had the opportunity to attend a postgraduate writing course.

CONCLUSION

Research is an important part of clinical practice. To reflect this, many specialist training programmes, including, recently, the RANZCR’s Faculty of Radiation Oncology, require a piece of research to be conducted by advanced trainees. However, the results of much research are unpublished because of a lack of scientific writing skills. This study has shown that scientific writing instruction, even with brief interventions, provides benefits. We believe, and our participants agreed, that such workshops should be widely available, particularly at meetings such as the RANZCR ASM. Ideally, they would be longer and held adjacent to the meeting, not concurrently.
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Chapter 4. Surface laser scanning to routinely produce casts for patient immobilization during radiotherapy

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The candidate made substantial contributions to each of study conception, study design, literature search, data collection, data analysis, data interpretation, manuscript preparation, manuscript editing, and manuscript revision/review. In addition the candidate was the corresponding author.
SUMMARY

Immobilization casts are used to reduce patient movement during the radiotherapy of head and neck and brain malignancies. Polyethylene-based casts are produced by first taking a Plaster of Paris ‘negative’ impression of the patient. A ‘positive’ mould is then made, which is used to vacuum form an immobilization cast. Taking the ‘negative’ cast can be messy, stressful for patients and labour intensive. Recently, lightweight hand-held laser surface scanners have become available. These allow an accurate 3-D representation of objects to be generated non-invasively. This technology has now been applied to the production of casts for radiotherapy. Each patient’s face and head is digitized using the Polhemus FastSCAN (Polhemus, Colchester, VT, USA) scanner. The electronic data are transferred to a computer numerical controlled mill, where a positive impression is machined. The feasibility of the process was examined, the labour required and radiation therapists’ satisfaction with aspects of the produced masks assessed. The scanner-based method of mask production was found to be simple, accurate and non-invasive. There was a reduction in radiation therapist labour required. Masks produced with the scanner-based method were reported to result in improved mask fitting, daily reproducibility, patient immobilization and patient comfort.
INTRODUCTION

There have been significant improvements in the ability to accurately deliver radiotherapy. However, immobilization methods have yet to take full advantage of available technology. Plastic casts are used to reduce patient movement during treatment of head, neck and brain malignancies with radiotherapy. Polyethylene-based casts are produced by first taking a Plaster of Paris (POP) ‘negative’ impression from the patient. A ‘positive’ is then made, which is used to vacuum form an immobilization cast. Making the ‘negative’ can be messy, stressful for patients and labour intensive. Recent innovations have led to a variety of techniques for medical imaging. Laser surface scanning is a non-invasive method for acquiring 3-D surface images.\(^1\) Recently a lightweight, hand-held, laser surface scanner has become commercially available, the Polhemus FastSCAN (Polhemus). The FastSCAN device has found many medical applications, including the production of prostheses and orthoses and the documentation of injury.\(^1-4\) This technology was developed to routinely produce immobilization casts for radiotherapy and its value assessed.

MATERIALS AND METHODS

The production of casts using a hand-held laser scanner is carried out using a combination of a commercially available hand-held laser scanner, software and a computer numerical controlled (CNC) mill. This results in accurate 3-D positive models of the patient’s face. The steps are summarized in Figure 1.

Fig. 1. The steps involved in vacuum-formed mask production, for both scanner-based and Plaster of Paris methods of taking impressions. CNC, computer numerical controlled; POP, Plaster of Paris.
Patient scanning procedure

The FastSCAN hand-held laser scanner uses two miniature cameras arranged symmetrically at an offset angle on either side of a centrally mounted laser line generator and calculates the surface position using triangulation. An electromagnetic tracker measures the position and orientation of the scanner in space and removes the need for a rigid mechanical scanning gantry. The patient remains still while the radiation therapist, in a manner analogous to spray painting, manually sweeps the scanner over the patient as seen in Figure 2a.

Fig. 2. Patients undergoing mask impression procedure by two methods: (a) laser hand scanner, and (b) Plaster of Paris.
Overlapping sweeps of the face and neck are made with the scanner, with care taken to include the submental and submandibular regions, and the auricular helix. As the data are collected, an image appears simultaneously on the computer screen. The actual scanning typically takes 20 s.

Data processing
The scanner software ‘FastSCAN for Oncology’ is an integrated package able to detect patient movement during scanning (by use of a magnetic transmitter) and crop the digitized surface to the required dimensions. The ‘FastRBF Extensions’ plug-in module (FarField Technology, Christchurch, New Zealand) allows the 3-D computer model to be operated as a closed mesh, in a form suitable for sending directly to the CNC mill.5

CNC milling
A stereolithography file from the scanner software is emailed to the Medical Technology and Physics department within the hospital, where tool-paths for the CNC mill are calculated. A pre-prepared, machineable plaster block of Rayite 100 (US Gypsum Company, Chicago, IL, USA) of dimensions 300 mm x 200 mm x 150 mm is placed into the CNC mill and the result is an accurate 3-D model of the face (Fig. 3).
Vacuum forming

The steps in the process following this are identical to the department’s previous standard practice, that is, the model is used to form a plastic face-mask with a vacuum former.

Assessment of the scanner-based method

The feasibility of the process was assessed by noting any difficulties found. Estimates were made of the time and labour involved in the POP and scanner-based methods. In addition, radiation therapists (RT) working in the department were asked to give their opinion on their experience of the 6-month period following the introduction of the new method into routine practice. All RT were asked to complete an anonymous questionnaire regarding their opinions on how the final immobilization casts constructed using the FastSCAN method compared with the casts that were made using the Plaster of Paris (POP) method. The questionnaire had a scale of 1–5, where scores indicated the casts were substantially less satisfactory (1), slightly less satisfactory (2), equally
satisfactory (3), slightly more satisfactory (4), or substantially more satisfactory (5), respectively. Questions addressed cast fitting (in the region of the chin, nose and superior skull, respectively), daily reproducibility of the set-up, match to patient contours, patient immobilization and patient comfort. RT with experience in the actual production of casts by both POP and FastSCAN methods were asked to assess three additional aspects; namely ease of mask production, mask accuracy and patients ability to tolerate the mask production procedure.

RESULTS

Feasibility

After no problems being seen after an initial 2-week period (when both methods were used), the scanning-based method was adopted to produce all immobilization casts required in the department. This assessment reported here was undertaken after the process had been used to produce 120 casts. One cast was made using the POP method, when the CNC mill suffered a temporary mechanical problem.

Time and labour involved

Making a POP-based mask is estimated to take the following length of time: taking the negative impression using the POP method, which requires two RT, each taking 15 min; preparation of negative, 5 min; pouring of mould, 10 min; and then preparation of positive impression taking 30 min. So totally the process requires takes 75 min of RT labour. In comparison, the time from commencement to completion of a file ready for sending to the milling machine was on average 15 min (requiring only one RT throughout). There are also approximately 20 min of biomedical technician labour in preparing the CNC mill for machining, but once started, the CNC mill is fully automated. The actual milling takes approximately 60 min. In both cases the same vacuum forming procedure is used (which takes approximately 45 min).
Radiation therapist satisfaction

Nineteen of 25 (76%) RT returned questionnaires and results are shown in Table 1.

By far most RT felt that the mask fitting, reproducibility, accuracy, immobilization and patient comfort were improved over POP methods and this was rated as a substantial improvement by 5–13 (26–68%) respondents in each category. All seven RT involved in mask construction noted a substantial improvement in ease of mask production, mask accuracy and patients tolerance of the procedure.

**DISCUSSION**

The feasibility of a new method of creating immobilization masks has been clearly shown. Many advantages over the traditional method using POP impressions were identified. Using a laser scanner to produce masks has the advantages of being fast, accurate and requiring no invasive contact with the patient. This latter aspect results in improved patient tolerance of the process. The POP method involves applying strips of wet plaster bandage to a patient's face while manually smoothing these to avoid air gaps (Fig. 2b). The process is generally well tolerated, but can be distressing, in particular to children and patients with claustrophobia. It is also labour intensive, and in terms of time
saved, each mask produced with FastSCAN saves 60 min of RT time. There are other potential time savings, for example, the time waiting for POP to dry. Many roles have been proposed in radiotherapy for laser scanning.\textsuperscript{6-8} This is the first time it has been introduced into routine practice for immobilization cast production. A direct comparison of the two methods of cast production was not carried out, as it would have been unreasonable to make patients undergo both methods (once the method of production was found to function satisfactorily). However, the RT who assessed the benefits had extensive experience with masks produced by both methods. Some centres use thermoplastic rather than polyethylene-based casts.\textsuperscript{9,10} Vacuum-formed polyethylene casts are transparent (so RT can easily see the fit and change in contour) and are more rigid, which aids beam direction. The FastSCAN technique is more forgiving than the POP method; however, it is important that hair is covered (using a tubular retention bandage), as the cameras will not pick up the laser image as it passes over hair. Also, substantial metal objects must be kept at least 0.5 m away from the immediate scanning environment, as metal interferes with the tracking of the scanner. Additionally, the patient must still lie still for the 20 s that it takes to scan. Producing a good image requires the correct distance and speed of scanning – however, the quality is immediately apparent and the process retrievable, in contrast to the POP method, where quality may not become apparent until deficiencies are noted at the time of fitting the final mask. Although there are definite benefits, these improvements need to be weighed against costs; namely the variable costs involved in the production of individual masks and the fixed costs of the scanner and software ($A45 000) and CNC milling machine ($A45 000–$160 000). The CNC mill, however, has a variety of uses in the hospital, including milling aluminium compensators for radiotherapy treatment. A vacuum former is also required with either method of cast production. The machineable plaster used to produce the positive mould costs $A35 per block. There is an RT labour saving of approximately 60 min per cast (at the cost of an additional cost of approximately 20 min of biomedical technician time). The labour saving would be greater if the requirements for poorly fitting POP masks to be remade were considered.
CONCLUSION

The surface laser scanning system described is a practical alternative to traditional POP impressions. The main potential benefits are that there is a reduction in RT labour to produce a mask, the procedure is less objectionable to patients and masks are available more quickly when needed (e.g. if a patient already receiving treatment requires a new mask). It is now the standard method of mask production used in this department.
REFERENCES


Chapter 5. A simple and inexpensive method to routinely produce customized neck supports for patient immobilization during radiotherapy

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The candidate made substantial contributions to each of study conception, study design, literature search, data collection, data analysis, data interpretation, manuscript preparation, manuscript editing, and manuscript revision/review. In addition the candidate was the corresponding author.
SUMMARY

Accurate and reproducible patient positioning is fundamental to the success of fractionated radiotherapy. Poor patient positioning could result in geographic misses. We have recently reported on an improved method of customized face mask production using laser surface scanning. In this report, we sought to identify and develop a method to routinely make customized neck supports for patients prescribed radiotherapy to the brain or head and neck regions. We identified a potentially suitable product—sealed packs containing two liquids that produce expanding polyurethane foam when mixed—and developed a method for their use. The neck supports are inexpensive and simple to produce (taking less than 5 min of radiation therapist labour). We assessed the customized neck supports in several ways. The effect on setup accuracy was assessed by comparing two consecutive cohorts of patients. Statistically significant differences favouring the customized neck supports included a reduced total displacement error (mean 3.4 vs. 2.1 mm) and a reduced left–right setup error (mean 1.8 vs. 1.1 mm). This is consistent with the greater support provided by the customized neck supports. This method could easily be undertaken by other departments.
INTRODUCTION

Accurate and reproducible patient positioning is fundamental to the success of fractionated radiotherapy.\(^1\) This is particularly so for conformal and intensity-modulated radiation therapy, where poor patient positioning could result in geographic misses or inadvertent overdosing of normal tissue.\(^2-4\) When patients are to receive radiation therapy for head and neck (H&N) or brain tumours, immobilization aids usually include a combination of patient face masks and neck supports. While most effort spent on improving immobilization has focused on face masks, the use of an appropriate neck support may also be critical.\(^5\) It is important that neck supports accurately fit individual patients’ neck contours. Until recently, our department, like most others, selected one of a small number of standard neck rests (examples are shown in Fig. 1).

![Fig. 1. Two examples of non-customized neck supports.](image)

These not only might have been a poor match for a patient's neck contour but also provided no support to prevent lateral movement. A better solution is customized neck support production; however, this has several drawbacks. For many years, two-part polyurethane pourable foam has been used to create personalized neck supports.
However, the liquids require mixing (to the required consistency), which can be messy and time consuming. There are also significant occupational health and safety issues related to toxic fume production.

We have recently reported on an improved method of customized face mask production using laser surface scanning. In this report, we have sought to identify and investigate improved technology to develop a method to routinely make customized neck supports for patients prescribed radiotherapy to the brain or H&N regions.

METHODS

Several requirements for the production of customized neck supports were first identified. These criteria included that the end product needed to provide a better fit and greater comfort than current methods and ideally provide greater surface contact between patient and treatment couch. The neck supports needed to be suitable for all patients, that is, for different neck sizes and contours. At the same time, the production had to be cost-effective (in terms of the product and radiation therapist labour) and to avoid health and safety issues such as those associated with traditional two-part polyurethane pourable foam production. The final product also had to meet departmental requirements regarding attenuation of the radiation beam. We identified a potentially suitable product, specifically Instapak Quick_ RT (RT stands for room temperature) foam bags, manufactured by Sealed Air (www.sealedair.com). These are sealed packs containing two liquids, which activate into expanding polyurethane foam when mixed (Fig. 2).
The bags are available in various sizes (#10, #20, #40, #60 and #80). This product has been developed for, and is sold to, for the packaging industry, offering custom-fit protective foam cushions. A suitable method of production of customized neck supports for clinical use was developed. The Instapak Quick_ RT bag is placed into a freezer 30–40 min before use. This has the dual advantage of reducing the final expanded volume and slowing the exothermic reaction—allowing more time to work forming the support. The patient is positioned supine and correctly aligned with the sagittal laser and baseboard. The patient is then asked to sit up and the Instapak Quick_ RT bag is placed over the baseboard, making sure that the bag is positioned under the shoulders and head and is centred laterally. The Instapak package comprises a large polyethylene bag with a foil-sealed strip at one end. The foil strip encloses and protects two liquid sachets labelled ‘A’ and ‘B’. When both sachets are broken and the component liquids are mixed, polyurethane air-filled foam is produced. To mix the liquids together, the seal between part A and part B is broken with hand pressure and the radiation therapist ‘pats’ back and forth on the A and B ovals. As the foam begins to expand and ‘pops’ into the rest of the bag, the radiation therapist gently positions the patient back down, aligning midline with the sagittal laser. The foam, when mixed, expands directly into the polyethylene bag and moulds to the patient’s contour before it hardens. The combined liquid expands to fill all gaps under the patient’s shoulders, neck and behind the back of
the skull. Restraining sides attached to the baseboard are used to contain the foam a fixed width. Excess foam can be removed with a sharp blade once it has properly set. Figure 3 shows a completed example.

![Image](image.png)

**Fig. 3.** A completed customized neck support.

The product must be used in a well-ventilated room (as recommended by the manufacturer). There are small perforations at the top of the bag, which vent expanded air and these must be left unobstructed. Physics assessments were carried out to check both the transmission factor and any effect on surface dose. Dose measurements were made with 6-MV photons incident upon a 5-cm slab of foam (the average thickness used for support) enclosed in its polyethylene package. Dose measurements were also taken for 6-MV photons incident upon a 1-cm slab of foam enclosed by the foil liner that protects the component mixing pouches before use. Parallel plate ion chamber measurements were taken to determine surface doses for a 6-MV photon beam. The effect of the customized neck supports on setup accuracy was assessed by comparing two consecutive cohorts of patients, specifically the last 20 consecutive patients having
the ‘old’ method of neck support and the first 20 consecutive patients having the ‘new’ method of individually customized neck supports. Port films were used and were taken according to the department’s routine policy (i.e. typically weekly or more often if errors). All patients were undergoing H&N or brain irradiation. During planning CT and the actual treatment, patients were positioned supine on a flat couch, with a foam knee support to position the patients’ legs comfortably. All patients had customized face masks produced with surface laser scanning. We retrospectively recorded the deviation from initial setup in each direction and any moves ordered by the physician. Quantitative assessment of setup errors detected through portal imaging using the old and new neck support methods included examination of the mean, standard deviation and range of errors. Setup error components examined were the absolute value of errors in the superior–inferior (SI), left–right (LR) and anterior–posterior directions, and the total displacement error (TOT) obtained from the square root of (SI squared + AP squared + LR squared). Values were examined both including the influence of error corrections (‘shifts’) and with the corrections artificially removed to examine the population effect of correcting setups. Significance of differences in setup errors between groups was assessed using a two-tailed t-test.

RESULTS
The method of production was introduced into routine practice without problems. The Department of Radiation Oncology at Sir Charles Gairdner Hospital has been using these sealed polyurethane foam bags for more than a year for all patients undergoing radical radiotherapy to the brain and H&N regions (and currently also, all patients undergoing palliative treatment to the H&N region are also fitted with a customized neck support). Initially, Instapak Quick_ Tuff bags were used and the manufacturer has now replaced these with the Instapak Quick_ RT as of January 2007. The only difference noted in practice is increased heat generation once the foam is expanding. This is reduced by placing the bags in the freezer and by placing a thin towel (such as a tea towel) between the patient and the bag. This method offers obvious improvements over the previous method of neck supports. The new method eliminates the gap between
shoulders and the treatment couch, preventing the patient changing position as they relax during the treatment course. It also cradles the H&N in the lateral dimension, reducing rotation. Radiation therapists in the mould room report that patients appear more comfortable and are much more likely to be correctly centred on the couch at initial setup when they return to the mould room for mask fitting. Radiation therapists carrying out daily treatments report that patients appear more comfortable, that they are more able to determine whether the patient is positioned correctly, that setup on the machine is faster than before and that lateral rotation is reduced. We have found that different sizes appear suitable for different regions to be treated. Specifically, #10 is best suited to patients having treatment to their face and neck and #20 suitable for patients having their brain treated (when it is necessary for the base of skull to be vertical). In addition, options for patient positioning have been improved, for example, the support allows patients’ shoulders to be raised, which in turn allows for greater neck extension. The larger bag is extremely useful when presented with a patient who has severe kyphosis. Being able to provide comfortable support for these patients, who are unable to lie flat, has improved their treatment experience over what would otherwise be expected by experienced radiation therapists. Patients have commented on a ‘smell’ during neck support production but have not found this unpleasant. The routine production of a customized neck support takes less than 5 min of radiation therapist’s time (with placement of bags in freezer 30–40 min before). The cost of the product is approximately AUD $3.40 per unit. They are sold in a carton of 180 (#10) or 128 (#20). As all patients undergoing radiotherapy to the brain or H&N region attend the mould room before planning, to have an immobilization mask made, the manufacture of a customized neck support has not added any inconvenience—there is no need for additional trips. Physics measurements showed that a 5-cm-thick block of foam showed an attenuation of approximately 0.5% and a 1.7% increase in surface dose when used in a typical setup with the photon beam traversing both the couch and the foam block before entering the patient. A 1-cm-thick foil-lined block of the foam (which might also be in the treatment field for some patients) showed an attenuation of approximately 0.4% and a 4.6% increase in surface dose when used in the same setup. This was judged to
be satisfactory. The general distribution of setup errors determined by routine port films for each technique is shown graphically in Figure 4 and histograms of the data are presented in Figure 5.

**Fig. 4.** Box and whisker plots of the distribution of errors for (a) superior-inferior (SI), (b) anterior-posterior (AP), (c) left-right (LR) and (d) total (TOT) components. The sample size in each case is shown in each box. The centre of the box represents the mean error in each case, the box 2 represents standard deviations and the whiskers represent the minimum and maximum absolute errors.

**Fig. 5.** Histograms of distributions of setup errors for (a) Superior-Inferior (SI), (b) Anterior-Posterior (AP), (c) Left-Right (LR) and (d) Total (TOT) component.
Table 1 shows the P-values obtained for t-tests of significance in differences in the setup error data comparing (i) the old method with the new method; (ii) the old method including position shifts with the same data though with the effect of shifts removed and (iii) the new method including position shifts with the same data though with the effect of shifts removed.

<table>
<thead>
<tr>
<th></th>
<th>SI</th>
<th>AP</th>
<th>LR</th>
<th>TOT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Old method (including shifts) vs new method (including shifts)</td>
<td>0.295</td>
<td>0.303</td>
<td>0.047*</td>
<td>0.001*</td>
</tr>
<tr>
<td>Old method (excluding shifts) vs old method (excluding shifts)</td>
<td>0.046*</td>
<td>0.303</td>
<td>0.007</td>
<td>0.346</td>
</tr>
<tr>
<td>New method (excluding shifts) vs new method (excluding shifts)</td>
<td>0.251</td>
<td>0.274</td>
<td>0.284</td>
<td>0.841</td>
</tr>
</tbody>
</table>

*Values of P < 0.05. AP, anterior-posterior; LR, left-right; SI, superior-inferior; TOT, total.

Statistically significant differences were found for the TOT between the old (mean 3.4 mm) and new (mean 2.1 mm) setup methods; the LR setup error between the old (mean 1.8 mm) and new (mean 1.1 mm) setup methods and the SI setup error between the patient data for the old method including shifts (mean 1.3 mm) and the same data with the effect of shifts removed (mean 1.6 mm).

**DISCUSSION**

We have described a simple and inexpensive method to routinely produce customized neck supports for patient immobilization during radiotherapy that could easily be achieved by other departments. This method has not been previously reported. The process is relatively straightforward and the neck supports produced appear to be a substantial improvement on our previous method. Subjective advantages include an obvious greater ability to individualize H&N support. Objectively, setup errors were showed to be reduced, even in a small sample.

In particular, as might be expected from a neck support with greater lateral support, the LR setup errors were most significantly reduced. The entire costs are small and there are no significant physical issues. The process is more convenient than other methods such as traditional two-part foam neck support production. This is the first time this system has been described, but others have noted the value of greater customization.
Bentel et al. examined a customized H&N support system that included a head support made to conform to the posterior contour of the H&N and reported that the customized supports improved reproducibility. van Lin et al. compared two different H&N supports more quantitatively and found that a customized support reduced both systematic and random errors compared with their standard but flexible alternative. In that report, Orfit masks covering head and shoulders were used for all patients. They compared a single ('one size fits all' neck cushion) with a system using a soft bag filled with polystyrene beads, which hardened when moistened and were able to be moulded to the patient. This system resulted in good craniocaudal curvature (with improved craniocaudal and ventrodorsal errors) but they noted insufficient curvature and support of the moulded back in the LR direction (and no difference in LR setup errors).

If the procedure and product were complex and/or expensive, it may have been worthwhile to undertake a comprehensive randomized study with more patients and daily electronic portal imaging device images. However, our results from 40 non-selected patients, using port films taken according to the departmental treatment policy, provide a convincing assessment of the merits of this new inexpensive and simple method of patient immobilization. The combination of customized neck support with immobilization masks produced using surface laser scanning offers a highly individualized system. It is possible that the benefits in setup errors might be greater than other departments might see with less precisely individualized face masks (e.g. Orfit mask). However, others have reported no substantial difference in patients’ setup accuracy between Orfit and thermoplastic masks.

CONCLUSION
A method using Instapak Quick_ RT to manufacture a customized head and neck support for patients receiving radiotherapy to the brain or H&N has been developed and implemented into routine use at our centre. The method of neck support has advantages over competing methods. This is a simple and inexpensive method that could be easily implemented by other radiation departments. The neck supports produced appear to
offer improved reproducibility and offer better flexibility to address variability in patients’ shape and specific treatment requirements.

REFERENCES


Chapter 6. A randomised trial of single-dose radiotherapy to prevent procedure tract metastasis by malignant mesothelioma

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The candidate made substantial contributions to each of literature search, data collection, data analysis, data interpretation, manuscript preparation, manuscript editing, and manuscript revision/review. In addition the candidate was the corresponding author.
SUMMARY

A single 9-MeV electron treatment, following invasive thoracic procedures in patients with malignant pleural mesothelioma, was examined. In all, 58 sites were randomised to prophylactic radiotherapy or not. There was no statistically significant difference in tract metastasis. A single 10-Gy treatment with 9-MeV electrons appears ineffective.
INTRODUCTION
In recent years, the incidence of malignant pleural mesothelioma (MPM) has been increasing rapidly.\(^1\) Chest wall seeding following invasive procedures is a problem, and has been reported to occur in 19% of patients following thoracoscopy.\(^2\) These subcutaneous masses are often symptomatic and refractory to radiotherapy (RT).\(^3\) Two nonrandomised series and one randomised controlled trial have demonstrated that a prophylactic three-fraction course of RT reduces the procedure tract metastasis rate to 0%.\(^2,4,5\) Recent reviews and guidelines recommended prophylactic radiotherapy following thoracic procedures.\(^6,7\) We undertook a randomised trial to test a more convenient single radiation treatment.

METHODS

Patients
The eligibility criteria included: histological confirmation of MPM; age greater than 18 years; and, a clearly identifiable procedure site. Written informed consent was obtained from all trial patients. The study had received institutional ethics committee approval.

Prophylactic radiation treatment
Patients were randomised after stratification by procedure type, to receive either a single dose of electron beam chest wall radiotherapy or no prophylactic therapy. A dose of 10 Gy in a single fraction was delivered to the chest wall, using 9-MeV electrons. The dose was prescribed at 100%. No bolus was used. Radiotherapy was given within 15 days of thoracic procedures.

Data collection and follow-up
In all cases, the site of the procedure was recorded, tattooed and photographed, to allow accurate subsequent assessment. Physicians assessed patients clinically for masses in the region of the procedure, at 3 and 6 months, then 6-monthly until death. Acute and late radiation toxicities were assessed and graded according to the RTOG/EORTC criteria.\(^8\) Patients were assessed for early radiation toxicity at 1 week by the treating
radiation oncologists, and subsequently for late radiation effects by the respiratory physicians.

**Statistical methods**

The primary outcome measure of the trial was procedure tract metastasis. No effect on overall survival of the patients was expected. The trial was designed with 80% power to detect a 20% reduction in tract metastasis with prophylactic chest wall irradiation (i.e. from an expected 20 to 0%) at the 5% one-sided alpha significance level. The estimated number of tract metastases following prophylactic RT was based on three published studies, all reporting no failures. The calculated minimum sample size of 54 sites was increased to 58 to allow for patients who might be lost to follow-up. Tract metastasis-free survival was defined from the time of randomisation to the development of a clinically apparent metastasis in the immediate region of the procedure site or to the last follow-up information. Overall survival was defined as the interval from the date of randomisation to the date of death or the last follow-up information. The crude incidence of tract metastasis in the two trial arms was compared using Fisher’s exact test (this was one-tailed, as radiotherapy will not increase the rate of tract metastasis). Tract metastasis-free survival was compared by log rank testing. The crude tract failure rates for the three-procedure strata were compared using a two-sided Fisher’s exact test. All analyses were performed on an intent-to-treat basis, and were performed with the use of SPSS (Chicago, IL) statistical software.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>The characteristics of sites registered on study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>RT arm (n = 28)</td>
</tr>
<tr>
<td></td>
<td>Number (%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td></td>
</tr>
<tr>
<td>Mean</td>
<td>70.0</td>
</tr>
<tr>
<td>Range</td>
<td>53.7–85.1</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26 (93%)</td>
</tr>
<tr>
<td>Female</td>
<td>2 (7%)</td>
</tr>
<tr>
<td>Procedure</td>
<td></td>
</tr>
<tr>
<td>Thoracoscopic drain/thoracoscopy</td>
<td>11 (39%)</td>
</tr>
<tr>
<td>FNIA</td>
<td>13 (46%)</td>
</tr>
<tr>
<td>Abrams needle</td>
<td>4 (14%)</td>
</tr>
<tr>
<td>RT given</td>
<td>28 (100%)</td>
</tr>
</tbody>
</table>
RESULTS

Between December 1997 and July 2003, 58 procedure sites were registered into the trial, from 43 patients; 28 sites were randomised to the prophylactic chest wall RT arm and 30 sites to the control arm. In all, 10 patients had two, and one patient three, sites separately randomised. The clinical characteristics of the 58 sites are summarised in Table 1. Overall, 22 sites had undergone thoracic drainage or thoracoscopy, nine sites Abrams needle and 27 sites fine needle aspiration (FNA) prior to randomisation. One patient in the control arm was given prophylactic radiotherapy at his request. The radiotherapy fields used ranged from 4- to 8-cm diameter circles.

Both early and late toxicity following radiotherapy were mild with no RTOG/EORTC grade 2, 3 or 4 reactions noted. The overall median survival from randomisation was 8.7 months, with a 1-year survival of 35%. Only seven patients remain alive.

There was no statistically significant difference in tract metastasis between the two arms of the trial, with three (10%) metastases in the control arm and two (7%) in the prophylactic RT arm (p = 0.53). The freedom from tract metastasis survival for the two arms was not significantly different on log rank testing (p = 0.82). The crude rates of tract metastases overall were 22% for Abrams needles, 9% for thoracic drains and 4% for FNA, and these were not statistically significantly different (p = 0.23).

DISCUSSION

We performed a randomised controlled trial examining the effect of a single dose of prophylactic chest wall radiotherapy following invasive procedures in MPM. There was no statistically significant difference in procedure tract metastases. Our study was relatively large with precise follow-up, and included patients who had undergone a range of procedures.

Tract metastases in the control arm of the trial were low. The median rate in the literature following thoracoscopies is 19%. Similar tract metastasis rates are reported for Abrams and other large needles. Pleurectomy and extra-pleural pneumonectomy have high rates of chest wall failure without prophylactic RT. There is little information on tract metastasis following fine needle aspiration, but in our study this procedure
carried the lowest risk of malignant seeding (although this was not statistically significantly). The risk of seeding appears to be related to procedure and technique.

A dose of 10 Gy delivered in a single fraction using 9-MeV electrons does not appear to be effective in preventing procedure tract metastasis. The relative effective dose for different radiation schedules can be estimated using the linear-quadratic model. For cancers, 10 Gy in a single fraction is equivalent to delivering 12 Gy in six 2-Gy fractions. For comparison, 21 Gy in three fractions is equivalent to approximately 42 Gy in 21, 2-Gy fractions. That is, the dose we used was equivalent to approximately 40% of the reported three-fraction schedules. This lower dose could be expected to be less effective, but the actual difference in outcome depends on steepness of the tumour control probability curve. Our study suggests a clinically important dose–response over this dose range. Another possible explanation for the lack of effect is that 9 MeV electrons might be inadequately penetrating. The French non-randomised series and subsequent randomised trial used higher energy 12–15 MeV electrons while the British study employed 140- or 250-kV photons. These alternative radiations give a higher dose beyond approximately 3 cm depth in tissue. However, 9 (or less) MeV electrons successfully deliver post-mastectomy chest wall radiotherapy (e.g.,), and this seems a less likely explanation. We did not demonstrate a benefit from a single dose of prophylactic chest wall irradiation. We continue to recommend prophylactic treatment to be used following high-risk procedures, delivering 21 Gy in three fractions.

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4. Boutin C, Rey F. Thoracoscopy in pleural malignant mesothelioma: a prospective
study of 188 consecutive patients. *Cancer* 1993; **72**: 389–393


Chapter 7. A prospective trial of short-fractionation radiotherapy for the palliation of liver metastases

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The candidate made substantial contributions to each of literature search, data collection, data analysis, data interpretation, manuscript preparation, manuscript editing, and manuscript revision/review. In addition the candidate was the corresponding author. Dr Nigel Spry developed the concept and designed the study.
**SUMMARY**

The purpose of this study was to prospectively examine the effectiveness and tolerability of a simple radiotherapy technique for the palliation of symptomatic liver metastases. Twenty-eight patients with symptomatic liver metastases were enrolled from seven centres, and received targeted (partial or whole) liver irradiation consisting of 10 Gy in two fractions over 2 days. Symptoms at baseline were hepatic pain (27 patients), abdominal distension (19), night sweats (12), nausea (18) and vomiting (eight). Twenty-two patients (76%) had failed previous treatment with chemotherapy, hormonal therapy and/or high-dose steroids. Symptoms and potential toxicities were prospectively assessed at the time of treatment, then 2, 6 and 10 weeks later. Individual symptom response rates were 53–66% at 2 weeks. Partial or complete global symptomatic responses were noted in 15 patients (54%) overall. The treatment was well tolerated with two patients (7%) experiencing grade 3 toxicity (one vomiting and one diarrhoea); however, four patients reported temporary worsening of pain shortly after treatment. This simple and well-tolerated treatment achieves useful palliation.
INTRODUCTION

Liver metastases are common, and when they are advanced, they often cause pain, sweats, nausea and vomiting. The response rate to first-line systemic chemotherapy depends on the primary site, and although it can be as high as 60% for breast cancer, it is lower for most sites.\textsuperscript{1,2} Chemotherapy is associated with side-effects such as nausea, vomiting, alopecia and tiredness.\textsuperscript{3} Second-line chemotherapy is less likely to be effective. The palliative value of fractionated whole-liver radiotherapy (WLRT) has been demonstrated in a number of series, with low levels of acute toxicity.\textsuperscript{4-6} The largest series prospectively studied 183 patients and reported symptom response rates of 80%. Smaller series have also examined WLRT in combination with systemic or regional chemotherapy, and reported symptomatic responses of 63–90%.\textsuperscript{9,10} The use of WLRT (with or without chemotherapy) is rare in clinical practice, possibly due to a belief that hepatic irradiation inevitably leads to radiation hepatitis. In fact, the liver tolerates high doses of radiation well providing that only part is irradiated\textsuperscript{11} or that whole-liver doses are kept below 30 Gy in two Gy fractions or 21 Gy in three Gy fractions.\textsuperscript{12,13} The published hepatic palliative radiation schedules require patient attendance for between seven and 22 fractions. Shorter courses of treatment would have less detrimental impact on patients’ remaining lives and might provide equal palliation. A retrospective review of a pilot experience with 21 patients receiving 10 Gy in two fractions described response rates (complete and partial) of 87.5% for hepatic pain and 50% for abdominal distension (N. Spry, pers. comm., 1998). This review formed the basis of a prospective multicentre trial to assess the effectiveness and tolerability of short-course radiation (10 Gy in two fractions separated by 6–24 h): Trans-Tasman Radiation Oncology Group trial TROG 98.04.14

METHODS AND MATERIALS

Eligibility

Eligible patients were those with symptoms of hepatic pain, abdominal distension, night sweats, nausea and/or vomiting attributable to liver metastases, an Eastern Cooperative Oncology Group performance status of ≤ 3 and an expected survival time exceeding 1 month. Liver metastases had to be documented by ultrasound or CT scan. Any
radiosensitizing or myelosuppressive chemotherapy had to have been discontinued for 4 weeks, while the effects of any concurrent steroid or hormonal treatment had to have been observed to be stable for at least 2 or 4 weeks, respectively. Patients were excluded if there was major symptomatic disease outside the liver or if they had received prior radiotherapy to the liver. Each centre had approval for the study from its institutional ethics committee.

**Treatment**

**Volume**

The intention was to treat the entire symptomatic portion of the liver with a margin of at least 2 centimetres, which could include the whole liver. Treatment was given with anterior and posterior opposing fields using megavoltage photons. Shielding was recommended to be used where possible, and was required for one kidney if the field would otherwise cover both kidneys. In our series, the entire right kidney was included in all but two patients.

**Dose and fractionation**

A dose of 10 Gy was prescribed to the midplane in two fractions of 5 Gy to be separated by 6–24 h. All patients completed planned radiotherapy; however, three patients had interfraction intervals of >24 h (two of 48 h and one 72 h). Premedication with dexamethasone 12 mg and an antiemetic was recommended.

**Assessment of symptoms, toxicity and survival**

Symptoms and potential toxicities were prospectively scored by the attending physician at baseline, at the time of the second fraction and then at 2, 6 and 10 weeks post-therapy. Symptom grade was based on the worst level experienced over the preceding 3 days, with descriptions shown in Table 1.
<table>
<thead>
<tr>
<th>Severity grade</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hepatic pain severity</td>
<td>No pain</td>
<td>Mild pain</td>
<td>Moderate pain</td>
<td>Severe pain</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>None</td>
<td>Mild discomfort</td>
<td>Intermittent: least daily</td>
<td>Constant (most or all of the time)</td>
</tr>
<tr>
<td>Night sweats</td>
<td>None</td>
<td>Minor abnormal sweating</td>
<td>Intermittent night sweats &lt; 1 per week</td>
<td>Frequent drenching night sweats requiring change of bedclothes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Toxicity Grade</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>None</td>
<td>Able to eat</td>
<td>Intermittent significantly decreased</td>
<td>No significant intake, requiring IV fluids</td>
</tr>
<tr>
<td>Vomiting</td>
<td>None</td>
<td>1 episode in 24 h over pre-treatment</td>
<td>2–5 episodes in 24 h over pre-treatment</td>
<td>&gt; 5 episodes in 24 h over pre-treatment; or need for IV fluids requiring intensive care</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>None</td>
<td>Increase of &lt;4 stools/day over pre-treatment</td>
<td>Increase of 4–6 stools/day, or nocturnal stools</td>
<td>Increase of &gt;7 stools/day or Incontinence, or need for parenteral support for dehydration</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Physiological consequences requiring intensive care; hemodynamic collapse</td>
</tr>
</tbody>
</table>
The pain score was calculated as the product of pain severity and pain frequency scores. The use of analgesic and other medications was recorded at each assessment. Telephone assessment was allowed and was used for 32, 21 and 27% of the reviews at 2, 6 and 10 weeks, respectively. Additionally, a single categorical response question was asked of the final 17 patients: ‘Overall how do you believe that this treatment has been helpful to you; Not at all, a little bit, quite a bit or very much?’ Survival was measured from the date of treatment, and cause of death was noted.

**Analysis**

Response was analysed in two ways. First, individual symptoms at each assessment point were compared to baseline and classified as better, stable or worse (or new) irrespective of the development of new or progressive symptoms in other areas. For pain, the assessment of change was made independently of changes in analgesia. Second, a global response score (incorporating all patient symptoms) was defined as follows: (i) complete response: complete disappearance of all hepatic symptoms; no new hepatic symptoms; no antiemetic medication required; no regular analgesic medication for hepatic symptoms required; (ii) partial response: reduction of at least one grade in one hepatic symptom or a two-point reduction in pain score, and no increase in the grade of any hepatic symptom; (iii) stable disease: no change in hepatic symptoms, or with improvement considered to be less than a partial response, or deterioration considered to be less than an increase in severity of at least one grade; and (iv) progression: any increase in severity of at least one grade. Patients known to be alive, but for whom a symptom assessment at 2, 6 or 10 weeks was missing were scored as ‘no response’. Overall, 21% of 61 potential assessments were missed. Five patients failed to be assessed for symptom response on any occasions but had baseline symptom and initial toxicity assessment.
RESULTS

Twenty-eight patients were contributed from seven centres between May 1998 and December 2000. Their baseline characteristics are shown in Table 2.

<table>
<thead>
<tr>
<th>Table 2. Patient characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total number</td>
</tr>
<tr>
<td>Men</td>
</tr>
<tr>
<td>Women</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Range</td>
</tr>
<tr>
<td>Primary site and histology</td>
</tr>
<tr>
<td>Colorectal adenocarcinoma</td>
</tr>
<tr>
<td>Non-small cell lung cancer</td>
</tr>
<tr>
<td>Oesophageal adenocarcinoma</td>
</tr>
<tr>
<td>Small cell lung cancer</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>ECOG performance</td>
</tr>
<tr>
<td>0</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
</tbody>
</table>

ECOG, Eastern Cooperative Oncology Group

All patients gave written informed consent. Twenty-two of the patients (76%) had failed prior treatment for liver metastases with chemotherapy, hormonal therapy and/or high-dose steroids. The baseline symptom grades are shown in Table 3.

<table>
<thead>
<tr>
<th>Table 3. Baseline symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom/grade</td>
</tr>
<tr>
<td>Distention</td>
</tr>
<tr>
<td>Night sweats</td>
</tr>
<tr>
<td>Nausea</td>
</tr>
<tr>
<td>Vomiting</td>
</tr>
<tr>
<td>Pain score</td>
</tr>
<tr>
<td>Number</td>
</tr>
<tr>
<td>Percent</td>
</tr>
</tbody>
</table>

NA, not applicable.

Hepatic pain was the most-common symptom (experienced by all but one patient). All but one patient had symptoms in more than one category. The median survival was 10 weeks (range 12 days to 46.5 weeks). Death was due to progressive disease in all patients. Twenty-six (93%) patients were alive at the end of 2 weeks, 16 (57%) patients
at the end of 6 weeks and 12 (43%) patients at the end of 10 weeks. The responses of individual symptoms are shown in Table 4.

Table 4. Individual symptom responses (compared to baseline)

<table>
<thead>
<tr>
<th>Symptom</th>
<th>2 weeks</th>
<th>6 weeks</th>
<th>10 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Better</td>
<td>17 (65%)</td>
<td>10 (63%)</td>
<td>7 (59%)</td>
</tr>
<tr>
<td>Stable</td>
<td>1 (4%)</td>
<td>3 (19%)</td>
<td>0</td>
</tr>
<tr>
<td>Worse</td>
<td>3 (12%)</td>
<td>1 (6%)</td>
<td>0 (46%)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Better</td>
<td>11 (61%)</td>
<td>3 (30%)</td>
<td>3 (30%)</td>
</tr>
<tr>
<td>Stable</td>
<td>2 (11%)</td>
<td>4 (21%)</td>
<td>1 (11%)</td>
</tr>
<tr>
<td>Worse</td>
<td>1 (6%)</td>
<td>1 (10%)</td>
<td>3 (25%)</td>
</tr>
<tr>
<td>Night sweats</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Better</td>
<td>8 (66%)</td>
<td>5 (63%)</td>
<td>4 (57%)</td>
</tr>
<tr>
<td>Stable</td>
<td>2 (17%)</td>
<td>1 (13%)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>Worse</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Nausea</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Better</td>
<td>9 (53%)</td>
<td>4 (44%)</td>
<td>4 (57%)</td>
</tr>
<tr>
<td>Stable</td>
<td>3 (18%)</td>
<td>2 (22%)</td>
<td>2 (25%)</td>
</tr>
<tr>
<td>Worse</td>
<td>1 (7%)</td>
<td>1 (11%)</td>
<td>1 (14%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Better</td>
<td>5 (64%)</td>
<td>1 (100%)</td>
<td>1 (100%)</td>
</tr>
<tr>
<td>Stable</td>
<td>1 (13%)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Worse</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Denominator for percentages is the number of patients alive at time of assessment (having particular symptom at baseline).

At 2 weeks, between 53 and 66% of individual symptoms present at baseline improved. Although the majority of symptoms assessed at subsequent points show similar responses, these are based on fewer patients. The median pain score for patients with pain was four at baseline, two at 2 weeks and one at both 6 and 10 weeks. Review of the baseline pain scores of those patients assessed at 2, 6 and 10 weeks revealed a median score of four. Thus, the improvement reflects a true improvement in the median score rather than the preferential loss to follow up or death of patients with higher pain scores. Global symptomatic responses were noted at one or more assessments in 15 patients (54%). Only two patients achieved a complete global response.
Patient perception of benefit

Of the 17 patients asked, 12 patients (75%) reported a perceived overall benefit on at least one occasion. On half of occasions, this was described as ‘quite a bit’ or ‘very much’. During follow up, many patients were noted to have developed symptoms not present at baseline. At 2 weeks, there were eight (two distension, five night sweats, one nausea), at 6 weeks, there were seven (two distension, three nausea two vomiting), and at 10 weeks, there were six new symptoms (one distension, two nausea, three vomiting).

Toxicity

Treatment was well tolerated overall. The incidence of grade 3 toxicity was 7% (one episode of nausea and one of diarrhoea), both within 2 weeks of radiotherapy. However, in addition, four patients experienced a temporary increase in pain shortly after treatment. The pain began within hours for three patients, within days for the other patient. In three cases, the pain was mild, and in all cases, the 2-week pain scores were improved on baseline (or again absent in the one patient who didn't have pain at baseline).

DISCUSSION

Our prospective study shows that short-course hepatic irradiation achieves useful palliation in patients when symptoms have become refractory to other treatment options. It was well tolerated (with only 7% incidence of grade 3 toxicity), consistent with reports by others describing hepatic irradiation. However, few patients obtained either a long-lasting or complete benefit. The percentage of patients who benefit is similar to that seen with other palliative treatments such as radiotherapy for brain metastases, advanced lung cancer and bone metastases. In patients with few other options for treatment (most patients had already failed dexamethasone and/or chemotherapy), our results suggest that this treatment is worthwhile. Our response rate is lower than that reported with protracted fractionation schedules, and it is possible that our dose fractionation is less effective. Leibel et al studied 187 patients treated with WLRT to a dose of 21 Gy in
seven fractions (the patients were randomized to receive the radiosensitizer misonidazole as well, or not). Patients’ symptoms were assessed weekly for the first month, then at 2, 4 and 6 months and then every 3 months thereafter. Abdominal pain was scored on the same four-point scale of severity we have used, and 80% had an improvement following therapy, with complete resolution noted in 54% of cases. Reporting our results in this way, 41% of our patients had relief following treatment, and this was complete in 30%. However, in other palliative settings, equivalence is reported for short and longer fractionation schedules, for example, treating pain due to bone metastases and for the palliation of lung cancer.16–18

We suggest our poorer response rate might be attributed to less favourable disease in our patients. Our patients might have been referred later with a greater tumour burden, and many in our series were treated only after failing chemotherapy. Fewer patients in this report had colorectal primaries (which have a better prognosis). The median survival of patients treated in Leibel's series was 17 weeks compared to the 10 weeks in our series. A randomized phase III study would be required to address whether protracted fractionation might increase the response rate. However, the improvement would have to be large to justify additional treatment episodes in a setting where patient survival is measured in weeks only. Ideally, our study would have included formal quality-of-life measures rather than symptom responses and treatment toxicities alone. We initially attempted to collect health-related quality of life using a validated questionnaire. However, the level of missing data made this assessment unreliable and it is not reported.

This study demonstrates that a two-fraction course of hepatic radiotherapy offers useful palliation to half of patients with minor toxicity. Premedication and monitoring for temporary acute exacerbation of pain is required. A further prospective study is required to define the duration of benefit, and to clarify whether more protracted fractionation schedules offer better palliation. Earlier referral and treatment might provide greater benefits. The palliative benefits of radiotherapy need to be compared with the unproven but more widely used second- and third-line chemotherapy. Comparative studies should
include quality-of-life measures. The traditional reluctance to employ radiotherapy for palliation of liver metastases is not justified.

ACKNOWLEDGEMENTS

We thank Data Manager Joan Smurthwaite, Sir Charles Gairdner Hospital, Perth, for the collection and maintenance of the trial data.
REFERENCES


Chapter 8. A Prospective Trial of Intraoperative Radiation Treatment for Breast Cancer

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The candidate made substantial contributions to each of study conception, study design, literature search, data collection, data analysis, data interpretation, manuscript preparation, manuscript editing, and manuscript revision/revision. In addition the candidate was the corresponding author.
SUMMARY

Background: A new device, Intrabeam, is available for intraoperative radiotherapy. We have prospectively examined its feasibility and tolerability in delivering adjuvant breast cancer treatment.

Methods: Thirty-five patients undergoing breast-conserving surgery received targeted tumour bed irradiation consisting of 5 Gy (at 10 mm) in a single fraction. This single intraoperative treatment was used to replace the external beam radiotherapy ‘boost’ that would usually be given in 10 daily treatments following 5 weeks of whole breast irradiation. Patients later completed external beam radiotherapy as usual. Potential toxicities were prospectively assessed fortnightly prior to external beam radiotherapy, weekly during it, and 3 monthly subsequently.

Results: The intraoperative radiotherapy was able to be delivered without difficulty, either at time of initial cancer surgery or as a second procedure. When performed as a separate procedure the median operating time was 56 min. The treatment was well tolerated, with only one patient experiencing any grade 3 or 4 toxicities – this was acute grade three itch. There was an overall early breast infection rate of 17%. No unexpected toxicities were seen.

Conclusions: This simple and well-tolerated treatment delivers a useful radiation dose to the area of highest risk of tumour recurrence. The early infection rate is similar to that reported in the literature, for treatments without intraoperative radiotherapy. Whether such a treatment may adequately replace the entire adjuvant radiation therapy treatment for low-risk patients is now being studied in a randomized trial.
INTRODUCTION

Breast conserving surgery with postoperative radiotherapy has been shown to be as effective as mastectomy in terms of overall survival, but with improved cosmesis.\textsuperscript{1–5} Adjuvant radiation treatment is usually given 5 days each week, over a 5–7 week period. This may be a significant inconvenience to women, particularly those who reside some distance from a treatment centre, have difficulties with transport, or a full-time career. In addition, adjuvant breast irradiation makes up to 30% of radiation oncology department workloads, at a time when radiation staff and machine time are scarce in both Australia and New Zealand. Unfortunately, trials attempting to omit radiotherapy in selected women after breast conserving surgery have shown unsatisfactory local recurrence rates.\textsuperscript{1,6–10} Even women with small mammographically detected breast cancers should be offered adjuvant irradiation.

An X-ray source small enough to be placed inside a tumour bed to deliver its treatment has been developed (Intrabeam, initially from Photoelectron Corporation, now produced by Carl Zeiss). In the USA, the device has received approval from the Food and Drug Administration for use at any body site. It has a number of potential applications, and although it has mainly been studied as a neuro-oncological treatment, it seems ideally suited for therapy of breast cancer.\textsuperscript{11–17} A series of applicators of varying diameters are available, which allows the correct size to be chosen for any surgical cavity after breast conservation surgery. Low energy 50 kV X-rays are produced that have limited penetration, and so deliver a dose that is relatively high at the surface of the applicator but which falls off rapidly with distance. We prescribe a 5 Gy dose at 10 mm depth from the applicator surface, given in a single treatment. The procedure lengthens theatre times but otherwise there are few logistical issues (e.g. no purpose built room shielding is required). The pilot experience with Intrabeam for breast cancer in the UK, has been reported recently.\textsuperscript{18–20} Such intraoperative radiation treatment (IORT) may be effective as the sole adjuvant radiotherapy for selected low risk patients. Prior to testing this in a randomized trial, we performed a prospective feasibility trial using the IORT as a method replacing the 1–2 week tumour bed ‘boost’ component of a standard external beam radiation treatment (EBRT) course. This allowed us to test whether this IORT treatment
was possible in routine practice in Australia, and whether acute toxicity was acceptable when EBRT was also used – as might be required if final pathology results were less favourable than expected.

METHODS

Patients and surgical treatment

Between July 2001 and October 2003, patients planned to undergo breast-conserving surgery for breast cancer were offered participation in this phase II prospective trial. Here the radiation therapy boost that would have been delivered over a 2-week period was given instead by a single dose of IORT delivered by Intrabeam. Initially the study was open to all patients, but the eligibility criteria were later changed to allow only low risk patients who would meet the eligibility criteria for an upcoming randomized trial (this is described in more detail in the discussion). Institutional ethics approval was granted, and written informed consent obtained from each patient. Patients underwent whatever breast conservation and axillary surgery they would otherwise have received, in addition to the intrabeam treatment. The IORT could be performed either at time of other surgery or as separate procedure at a later date. The operating times and total duration of the procedures, were prospectively recorded.

Intraoperative radiation treatment

The Intrabeam device is fitted to a mobile stand, on an arm that is movable and in perfect balance when a button is depressed but otherwise stable. The device is calibrated prior to each treatment, and a range of sizes of sterilized spherical applicators is available. Once adequate wide local excision has been performed and haemostasis achieved, the appropriate size applicator is selected – that is, the size that fits comfortably without producing tension in the surrounding tissue. The device and its stand are wrapped in a sterile clear plastic cover, and the applicator attached. The applicator, now attached to the device, is positioned in the surgical cavity and a purse string suture is used to conform the target breast tissue to the surface of the applicator. The skin is gently everted and two stay sutures are used to prevent direct contact with
the applicator. Five Gray is prescribed at a depth of 10 mm, and the physicist calculates the appropriate treatment duration to deliver this. The treatment takes approximately 20 min, but varies with the size of the applicator selected. During treatment the anaesthetist, oncologist and physicist remain in theatre behind a mobile shielded screen, while other staff leave the room (Fig. 1).

![Fig. 1. The Intrabeam device sited in the surgical cavity prior to treatment.](image)

Treatment can be interrupted if, for example, the anaesthetist needs to attend to the patient. After completion of radiation, the temporary stitches are removed and the wound is closed in the usual manner. Prophylactic antibiotics (a single injection at the time of surgery) were used for none of the first 16 patients, but all of the remaining patients.

**Other adjuvant therapies**

Following the definitive surgical procedure and IORT, patients went on to receive appropriate systemic treatment and postoperative adjuvant radiotherapy. EBRT of 45 Gy in 25 fractions to the whole breast was usual.
Assessment of complications and radiation toxicity

Following surgery, patients were assessed fortnightly (until EBRT commenced) by a research nurse or radiation oncologist, for any complication of surgery or the Intrabeam treatment. In addition, patients were assessed for complications and acute radiation toxicity weekly during each of the 5 weeks of radiation therapy (RT), then at 1 month. Patients were then assessed for late radiation complications, at 3 monthly intervals, beginning 3 months after completing EBRT, by the radiation oncologist. Particular note was made of any breast haematoma, seroma or infection, or axillary infection or lymphocele requiring intervention. An infection was defined by the commencement of an antibiotic. Early breast infections were defined as those occurring within 30 days of IORT. Any acute radiation toxicity was graded according to the National Cancer Institutes’ Common Toxicity Criteria (version 2.0) for radiation dermatitis, breast pain or other radiation toxicity. Any late radiation toxicity was scored using the Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer (RTOG/EORTC) Late Radiation Morbidity Scoring Scheme. Patients also completed cosmesis, quality of life (EORTC QLQ C30 and BR23 breast cancer specific modules) and body image assessments, which will be reported with additional follow up.

RESULTS

Thirty-five patients, one with bilateral disease, were treated using the Intrabeam device. Patient and cancer details are shown in Table 1.
Fourteen of the patients usually reside more than a 1-h drive away, but seven relocated to Perth to receive their EBRT. Half of the cancers would be considered low-risk. Details of the surgical and postoperative adjuvant treatments are shown in Table 2.

<table>
<thead>
<tr>
<th>Table 1. Patient and cancer details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
</tr>
<tr>
<td>Number of breasts treated</td>
</tr>
<tr>
<td>Age (years)</td>
</tr>
<tr>
<td>Reside more than 1 h away</td>
</tr>
<tr>
<td>Screen detected</td>
</tr>
<tr>
<td>Prior hormone replacement therapy</td>
</tr>
<tr>
<td>Contraindications to EBRT</td>
</tr>
<tr>
<td>Cancer details</td>
</tr>
<tr>
<td>Size (mm)</td>
</tr>
<tr>
<td>Grade</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>Hormone receptor positive</td>
</tr>
<tr>
<td>Nodes</td>
</tr>
<tr>
<td>N0</td>
</tr>
<tr>
<td>N1</td>
</tr>
<tr>
<td>NX</td>
</tr>
<tr>
<td>Low risk†</td>
</tr>
</tbody>
</table>

†For the randomized trial this is defined as a postmenopausal patient with a unifocal tumour, <20 mm, grade 2, of ductal or special type, and N0. For the purposes of this study we have also included NX patients. EBRT, external beam radiation treatment.

Although breast-conserving surgery had been planned, three patients went on to mastectomy, due to findings on their pathology. Postoperative radiotherapy was planned
in all but four patients, including two of the patients treated with mastectomy. Two patients had relative contraindications to EBRT, so were planned to have IORT alone – one patient had previously undergone mantle irradiation for Hodgkin’s disease, and one patient had Systemic Lupus Erythematosus. Seven patients have yet to complete EBRT. Radiation treatment was to breast tangents alone (45 Gy in 25 fractions over 5 weeks) in most cases. One of the mastectomy patients had her chest wall treated. Three patients had four field radiotherapy (i.e. regional nodal treatment in addition to their breast/chest wall irradiation) because of extensive nodal involvement. The median time between IORT and commencement of EBRT was 93 days (range 37–221 days). Details of the IORT are shown in Table 3.

<table>
<thead>
<tr>
<th>Table 3. Intrabeam treatment – by concurrent breast surgery procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>IORT performed with:</td>
</tr>
<tr>
<td>Total number</td>
</tr>
<tr>
<td>Applicator size (mm)</td>
</tr>
<tr>
<td>20</td>
</tr>
<tr>
<td>25</td>
</tr>
<tr>
<td>30</td>
</tr>
<tr>
<td>35</td>
</tr>
<tr>
<td>40</td>
</tr>
<tr>
<td>45</td>
</tr>
<tr>
<td>50</td>
</tr>
<tr>
<td>Duration of IORT (min)</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Range</td>
</tr>
<tr>
<td>Ax. surgery at time of IORT</td>
</tr>
<tr>
<td>Operating time (min)</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Range</td>
</tr>
<tr>
<td>Total duration GA (min)</td>
</tr>
<tr>
<td>Median</td>
</tr>
<tr>
<td>Range</td>
</tr>
</tbody>
</table>

†Two patients had additional measurements (e.g. ultrasound) performed intraoperatively during WLE, and one patient underwent bilateral breast WLE and axillary dissections. IORT, intraoperative radiation treatment; WLE, wide local excision.

The procedures were performed by one of five surgeons, in conjunction with one of two radiation oncologists. IORT was performed at the time of definitive wide local excision in 24 cases, with a re-excision in three cases, or as separate procedure in nine cases. None of the patients undergoing re-excision had received prior IORT. In 22 cases, both breast and axillary surgery were performed at the same procedure as the Intrabeam treatment. The applicator sizes used were smaller when Intrabeam was performed as
separate procedure, as the cavity contracts following initial surgery. When performed as a separate procedure applicators 25 mm or less were usual, compared to 40 mm or more when Intrabeam was performed earlier. The median time to deliver the IORT, not including the time to set-up or take down the device (i.e. the ‘beam-on’ time) was 19 min. The median operating time and total duration of general anaesthesia, when IORT alone was performed, was 56 and 79 min, respectively. Table 4 shows the radiation toxicities of the IORT and/or EBRT.

<table>
<thead>
<tr>
<th>Table 4. Acute and late radiation toxicity grading</th>
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</thead>
<tbody>
<tr>
<td>Grade</td>
</tr>
<tr>
<td>Acute radiation toxicity – worst NCI CTC grade</td>
</tr>
<tr>
<td>RT dermatitis</td>
</tr>
<tr>
<td>Pain</td>
</tr>
<tr>
<td>Other</td>
</tr>
<tr>
<td>Late radiation toxicity – worst RTOG/EORTC grade</td>
</tr>
<tr>
<td>Skin</td>
</tr>
<tr>
<td>Lung</td>
</tr>
<tr>
<td>Subcutaneous</td>
</tr>
<tr>
<td>Other</td>
</tr>
</tbody>
</table>

NCI CTC, National Cancer Institute Common Toxicity Criteria; RTOG/EORTC, Radiation Therapy Oncology Group/European Organization for Research and Treatment of Cancer.

The median follow up is 8.9 months, with a range of 0.2–27.7 months. Twenty-seven patients have been followed up for at least 4 weeks following completion of EBRT (or 1 month post IORT if no EBRT was planned), while 11 patients have been followed up for over 1 year post IORT. The worst National Cancer Institute Common Toxicity Criteria (NCI CTC) grade of acute radiation toxicity experienced by each patient included only one grade 3 or 4 toxicity, this was grade 3 itch. No patients experienced RTOG/EORTC grade 3 or 4 late toxicity.

Six patients experienced either a breast haematoma or seroma requiring management (e.g. aspiration) following IORT but before EBRT. One patient required aspiration of an axillary lymphocele prior to IORT, and an additional 10 patients required such treatment between IORT and EBRT. A number of patients developed breast and/or axillary infections, which are shown in detail in Table 5.
Six patients (17%) developed a breast infection within 30 days of the IORT procedure. However, 17 patients in all (over the total duration of follow-up) experienced a breast or axillary infection requiring antibiotics. Two patients experienced both an axillary infection and a breast infection. Two patients required admission, and two patients required treatment with antibiotics on more than one occasion. The rate of early breast infections in those not given prophylactic antibiotics was 25% (four of 16 patients), while in those given prophylactic antibiotics it was 11% (two of 19 patients). Two patients had axilla infections prior to IORT and later also went on to have prophylactic antibiotics at the time of the IORT procedure. None of the cases in which Intrabeam alone was given as second procedure have developed an infection. No patients have had a local recurrence, although this is not an endpoint of the study because of the small numbers of patients involved.

### DISCUSSION

We have demonstrated that breast IORT delivered by the Intrabeam device is feasible in an Australian hospital. In this study, Intrabeam was used to replace only the 2-week boost in an otherwise conventional course of adjuvant radiation treatment. Such treatment may be able to be used as sole treatment for favourable tumours, but this needs to be assessed in a randomized trial. It was associated with some complications, and does require an investment in the cost of the machine and the time of the personnel using it. This typically included almost an hour of operating time per patient, at least during the learning stage. The cost of the Intrabeam device and floor stand is approximately $A590 000. This treatment is unlikely to be economical simply as a routine method of tumour bed boost delivery, but may be cost-effective if it were able to

<table>
<thead>
<tr>
<th></th>
<th>Early (≤30 days)</th>
<th>Late (&gt;30 days–1 year)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Breast</td>
<td>6</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>Axilla</td>
<td>5†</td>
<td>1</td>
<td>6†</td>
</tr>
<tr>
<td>Both</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

†Two additional patients developed axillary infection prior to IORT.
replace entire courses of EBRT. The benefits to patients, including reductions in time off work, transport and accommodation costs might be substantial, as in the case of the 14 women in our series who usually live over 1 h drive away from the nearest radiotherapy centre. In addition, freeing space on linear accelerators allows other patients to be treated with shorter waiting times. We plan to carry out a detailed cost–benefit analysis with a health economist. The actual treatments themselves went smoothly. We have now moved to performing the IORT as a separate procedure rather than at the time of other breast or axillary surgery. This appears easier to schedule, and allows the final pathology to be available prior to IORT – avoiding problems such as close margins at initial resection requiring further surgery.

We assessed patients closely for complications, and found minimal radiation reactions. There was, however, an acute breast infection rate of 17%. As we noted a possible increased risk of breast infections in the early part of this study, we moved to using prophylactic antibiotics given at the time of the procedure. This resulted in an apparent decrease in the rate of infections from 25% to 11%. This reduction may also be related to the use of a separate procedure list. The rate of early breast infection is similar to the 4–21% reported in the literature for these types of operation. Reid et al. recently reported a prospective audit of the first 30 postoperative days following clean general surgical wounds. Assessment included inpatient review by a research nurse, and subsequent outpatient follow up by patient telephone interview. With this method of assessment – similar to ours, they found the rate for acute breast infection was 16%. The investigators noted that the overall wound-infection rate was higher than previously described, and felt this was due to the finding that two-thirds of infections occur after discharge from hospital. In our study, there was a rate of late infections of 14%, but there is little comparative data available in the literature. The rate of severe late infections has recently been estimated at 3–5% for patients undergoing breast-conserving surgery and irradiation. The relatively high rate of infections we have noted, may be due to the inclusion of milder infections and closer follow up. In addition, as an infection was defined by the use of antibiotics, and as there may have been a low threshold for starting treatment, this may overestimate the true infection rate. Our follow
up is not long enough to demonstrate all potential late effects of radiation, but we will continue to monitor for them. Vaidya et al. have recently reported their experience on 25 patients where, like this study, they replaced the routine boost to the tumour bed with IORT using the Intrabeam device. They had no major complications and no patients had developed local recurrence at the time of the report. One minor complication was a problem with wound healing due to radio-necrosis caused by the applicator being positioned too close to the skin. This had been reported prior to our study, and we incorporated changes to our IORT technique to avoid this.

As mentioned, trials attempting to omit radiotherapy in selected women after breast conserving surgery, summarized in Table 6, have given unsatisfactory results.

<table>
<thead>
<tr>
<th>Trial</th>
<th>Max. tumour size (cm)</th>
<th>Local recurrence RT vs No RT</th>
<th>Reporting method</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSABP¹</td>
<td>4</td>
<td>10% 35%</td>
<td>12-year actuarial</td>
</tr>
<tr>
<td>Uppsala-Orebro⁶</td>
<td>2</td>
<td>9% 24%</td>
<td>10-year actuarial</td>
</tr>
<tr>
<td>Ontario⁷</td>
<td>4</td>
<td>11% 35%</td>
<td>8-year crude</td>
</tr>
<tr>
<td>Scottish⁸</td>
<td>4</td>
<td>6% 25%</td>
<td>68-month crude</td>
</tr>
<tr>
<td>British⁹</td>
<td>5</td>
<td>13% 35%</td>
<td>71-month crude</td>
</tr>
<tr>
<td>Milan¹⁰</td>
<td>2.5</td>
<td>6% 24%</td>
<td>10-year crude</td>
</tr>
</tbody>
</table>

RT, radiation therapy.

However, there has been interest in giving more limited radiotherapy (i.e. to the tumour bed rather than treating the entire breast). This has been tested in a randomized trial with patients receiving EBRT to either standard fields or EBRT to the involved quadrant only. Overall there was a higher local recurrence rate in patients treated with the limited field, but among the 504 cases of infiltrating duct carcinoma there was no significant difference. This suggests that in selected patients, EBRT could reasonably be limited to part of the breast; however, this treatment requires the same time and resources as standard EBRT. Other complicated approaches to limit treatment to the tumour bed, using brachytherapy or IORT with a mobile linear accelerator have been reported.

Curative EBRT is given in multiple fractions, as this relatively spares the normal tissues from late radiation effects. Single treatments to curative doses with EBRT are not tolerated, but with this form of IORT we make use of the fact that the radiation dose falls
off exponentially with the distance from the surface of the applicator. Using the linear-quadratic model and assuming an alpha–beta ratio of three, we can calculate the equivalent dose for normal tissue late effects. At 1 cm from the applicator, the dose is 5 Gy in a single fraction – in terms of late effects this is approximately equivalent to only 8 Gy in 2-Gy fractions. A small volume receives higher doses, but there is significant ‘volume effect’ for normal tissue reactions, so the effect will be less than would be expected if a large volume were irradiated to the same dose. Equivalent doses in terms of cancer treatment can also be estimated using the linear quadratic model, assuming an alpha–beta ratio of 10. For example, the dose at the surface of the applicator is nominally equivalent to 50 Gy in 2-Gy fractions (i.e. similar to an entire course of EBRT). Although the linear quadratic model accounts for fractionation effects, IORT as described may be more biologically effective than predicted due to advantages such as immediate treatment (which avoids tumour repopulation). The actual biological effectiveness of this treatment will depend on the 3-dimensional distribution of the tumour clonogens. Such treatment may be more effective for more favourable pathology tumours. We have recently commenced enrolment into an international randomized multicentre trial comparing targeted IORT delivered using the Intrabeam with conventional postoperative radiotherapy. All patients randomized will receive some adjuvant radiation therapy (either IORT or EBRT), and in addition any appropriate systemic therapies. It is possible the local recurrence rate with IORT alone may be slightly higher (than with a full course of EBRT), but lower than with no RT at all. This trade off may be acceptable to patients, and we are studying this in a separate ‘patient preference’ study. This randomized study is part of an international collaboration; however, we will be entering only lower risk patients (postmenopausal women, with unifocal tumours, <20 mm, Grade ≤2, of ductal or special type and node negative). Adjuvant breast IORT with the Intrabeam device is feasible and non-toxic when used to replace an EBRT boost. Care should be taken not to stretch skin over the applicator, and prophylactic antibiotics should probably be used. IORT may be better used to replace an entire 5–7 weeks of EBRT, in highly selected patients. This simple, effective technique is to be tested in a randomized trial, which has already started accrual.
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Chapter 9. Discussion and Conclusions

This thesis reports the prospective examination of a number of specific innovations in radiotherapy delivery and training (each attempting to simplify and improve the process for the individuals undergoing interventions). Some innovations were successful (i.e. the innovative new method tested delivered measurable improvements compared to historic or concurrent groups) while others were unsuccessful (i.e. the innovation was not more successful than its predecessor). All the studies however usefully added to the knowledge base. This chapter gives an opportunity to reflect on a number of aspects of trials of innovations in radiation oncology. For example, the different endpoints that might be of value in radiotherapy and appropriate study designs (and how this varies with the extent and nature of innovation). I also discuss potential weaknesses of the studies, as well as their clinical and training applications.

THE INNOVATIONS STUDIED AND THE EXTENT TO WHICH THEY WERE NOVEL

A number of areas for potential innovation were described in Chapter 1. Some of these were more suitable for development and testing in the Australia / New Zealand or single institutional (and low-resource) environments. The identified areas most suitable for potential innovation belonged to three themes – improvements in professional skills, improvements in RT delivery technique and (clinical studies of) hypofractionation. It is worth considering the extent of innovation each study included in this thesis represented. It is not always clear when a change in radiation therapy is an extension of an existing technology or in fact it is different enough to warrant the technology being considered “new”. The United States’ National Commission for the Protection of Human Subjects of Medical and Behavioral Research described innovative therapies as being characterized by being both novel and non-validated. This is true for at least aspects of each of the studies presented. Each of the studies looking at hypofractionation were relatively novel. For example, although mesothelioma procedure sites and liver metastases have been treated with palliative radiotherapy, one and two-fraction courses
had not been reported. Intrabeam had been trialled but in relatively few centres (and indeed some problems had been identified). In fact, Intrabeam treatment has remained novel enough that another Australian centre published essentially the same study over 6 years after ours. Although many roles have been proposed in radiotherapy for laser scanning, this was the first time it has been introduced into routine practice for RT immobilization cast production. Likewise, our method of producing customized neck supports for patient immobilization during radiotherapy had not been previously reported. The writing course was the first time that such a short course to improve scientific writing skills for doctors has been assessed. The fellowship training course had a number of innovative features including the first use of a validated tool for assessing the learning environment of radiation oncology registrars.

Another way of considering innovation is whether it represents a change in technology, or a change in a way of doing things. Figure 2 plots schematically the relative change in technology versus the relative change in method (i.e. ways of doing), for the studies included in the thesis (and, for the purposes of discussion, two other studies described later). It is of course noted that changes in technology and method often go together. For example, Intrabeam was a dramatic change in technology and also in the usual practice of breast irradiation. As noted, the IORT trial was carried out largely with a view to the treatment being tested as a sole treatment for selected women with breast cancer. Being able to omit the EBRT component of treatment might have dramatic benefits for patients. In contrast, a two-fraction course of radiotherapy (rather than say 10 fractions), involves only a small changes in method (and no change in technology) – but that is not to say that it is not of significant benefit for patients (e.g. 8 fewer treatment visits).
The innovations tested here, except for IORT, were necessarily less “significant innovations” than say Intensity-Modulated Radiation Therapy (IMRT), CyberKnife and proton therapy. Some experts, such as Halperin, believe the most important clinical question facing radiation oncology is whether randomized prospective trials are necessary to assess significant innovative technologies. Criteria have been proposed to identify when innovations should be considered “significant”. These include the need for physician retraining to perform the new procedure; the potential for harm; and where there are major (opportunity) costs to the health care system. The IORT method reported here meets these criteria for being significant, as it required physician retraining and (a relatively great risk of) potential harm. By contrast, the other innovations studies here were generally designed to be “easier” on patients (e.g. less toxic and/or less inconvenient) or radiation oncologists (e.g. by maximising learning opportunities), with low-risk and low-cost. This thesis describes a number of novel treatments that were developed to be suitable for testing in the available environment. They varied in the extent of change in technology and method, but all were notably different from the current management.
APPLICATIONS OF THE STUDIES RESULTS IN CONTEXT

Each of the studies described has had potential for impacts on practice. These investigations have been done in the setting of other independent developments elsewhere. The actual impact of the studies is discussed.

APPLICATIONS AND RECOMMENDATIONS ARISING FROM THE STUDIES OF INNOVATIVE APPROACHES TO PROFESSIONAL TRAINING IN RADIATION ONCOLOGY

The first major theme considered for innovation is Radiation Oncologist professional training and development, with a particular emphasis of workshops (and subsequent activities). In Chapter 2 we clearly showed that a number of innovations to the Part 2 examination preparation course were likely to be of benefit; in particular, the written advice supplied to participants before the workshop and the use of the newly developed examination technique feedback forms. The use of a newly developed tool to assess learning environments demonstrated these were generally satisfactory, we identified a problem with workloads affecting a significant number of registrars. Since then there have been significant changes to the radiation oncology specialist training. Some of these changes directly addressed some of the issues raised. Some of the identified strengths were retained. There remain significant opportunities for further improvement (including some of the innovations outlined here). Chapter 3 demonstrated that scientific writing instruction, even with brief interventions, provides benefits. Baseline self-assessment showed a perceived skills deficit, even in a group with significant clinical and publication experience. Following the workshop, there were positive differences in the median category for having the required skills, having advice available and understanding the structure of scientific articles. These results indicate that even short courses can raise skill levels. We believe, and our participants agreed, that such workshops should be widely available, particularly at meetings such as the RANZCR ASM. Ideally, they would be longer and held adjacent to the meeting, not concurrently.
Other resources subsequently available include publications such as from Veness, which provide specific advice for ANZ radiation oncologists who are inexperienced at seeing research through to publication. 21

Professional training and development is a relatively neglected area for study. Interventions and methods of study are not as well developed as they are for clinical studies. Yet, it is a potential high yield area – with likely benefits in patient outcomes (e.g. by best applying the clinical evidence already available). A significant barrier is the difficulty in assessing relevant outcomes. An attempt to do so in the area of multidisciplinary meetings is discussed below. Training requires a significant investment of resources. Again, attempts to make training more cost-effective may give useful results.

CLINICAL TRANSLATION AND RECOMMENDATIONS ARISING FROM THE STUDIES OF INNOVATIVE APPROACHES TO PATIENT IMMOBILISATION

The next “accessible” area for innovation was patient immobilisation. We found that the surface laser scanning system described is a practical alternative to traditional POP impressions. 4 The main potential benefits are that there is a reduction in RT labour to produce a mask, the procedure is less objectionable to patients and masks are available more quickly when needed (e.g. if a patient already receiving treatment requires a new mask). Subsequently a method using Instapak Quick RT to also manufacture a customized head and neck support for patients receiving radiotherapy to the brain or H&N was developed. 5 The process is relatively straightforward and the neck supports produced appear to be a substantial improvement on our previous method. Subjective advantages include an obvious greater ability to individualize H&N support. Objectively, setup errors were showed to be reduced, even in a small sample. In particular, as might be expected from a neck support with greater lateral support, the LR setup errors were most significantly reduced. The entire costs are small and there are no significant physical issues. The process is more convenient than other methods such as traditional
two-part foam neck support production. The combination of customized neck support with immobilization masks produced using surface laser scanning offers a highly individualized system. It is now the standard method used in our department. The area of patient immobilisation is managed differently by different departments, but here we have provided more possible solutions for others and/or a basis for further innovations.

**CLINICAL TRANSLATION AND RECOMMENDATIONS ARISING FROM THE STUDIES OF INNOVATIVE HYPOFRACTIONATION**

This thesis includes three studies looking at innovative treatments involving hypofraction. Each study was clinical with potential direct impact on treatment. We did not demonstrate a benefit from a single dose of prophylactic chest wall irradiation for MPM. We also noted the low recurrence rate in the control arm - the uncertain value of radiotherapy for chest wall prophylaxis, was highlighted by a later randomised study. This too showed a low chest-wall recurrence rate in the control arm and no benefit from prophylactic radiotherapy (this time using the traditional 21 Gy in 3 fractions). The combination of the results from these two studies, has led to most centres stopping the use of routine chest wall prophylaxis. This has meant many patients have been able to avoid unnecessary treatment.

We demonstrated that breast IORT delivered by the Intrabeam device is feasible in an Australian hospital. In this study, Intrabeam was used to replace only the 2-week boost in an otherwise conventional course of adjuvant radiation treatment. Such treatment may be able to be used as sole treatment for favourable tumours, but this needed to be assessed in a randomized trial. Intrabeam intraoperative radiation treatment as sole treatment for low risk patients has been shown to have a low recurrence rate (at this length of follow-up) in a large randomised trial.

The liver metastases study demonstrates that a two-fraction course of hepatic radiotherapy offers useful palliation to half of patients with minor toxicity. Premedication
and monitoring for temporary acute exacerbation of pain are required. The candidate is a co-author of a systematic review of evidence for radiation therapy in the treatment of liver metastases and sole author of a related textbook chapter: “Liver metastases. Radiation Therapy in Palliative Cancer Care” – attached as Appendix 2. Those reviews consider issues in detail but are briefly summarised. Short course WLRT, such as used in our study, is seldom utilised, but may have useful palliative benefits. Since our study, there has been the development of more aggressive treatment of liver (and other) metastases using newer methods of treatment such as Stereotactic Body Radiation Treatment (SBRT). The role of, and experience with, SBRT to treat liver metastases is also described in the appended textbook chapter.

Each of the clinical studies (including the “negative” mesothelioma study) has had a clinical impact in our department and effected evidence based practice elsewhere.

STUDY DESIGNS & METHODOLOGICAL ASPECTS

One particularly noteworthy feature of the investigations described in Chapters 2 to 8, is the broad range of study methods and designs. These serve to illustrate a range of issues that are discussed below. Some are unique to Radiation Oncology, while others are more broadly applicable.

THE VARIETY OF STUDY DESIGNS USED TO EVALUATE INNOVATIONS

Different study designs are suitable for different innovations. These need to be achievable and make the most of available opportunities. There are limited resources to carry out studies and careful consideration and planning is needed to best achieve what is required. It is useful to consider the study designs used here and their appropriateness to degree of innovation. This thesis intentionally used a range of study designs. These ranged from randomised trials addressing clinical treatments through to questionnaires regarding the training of radiation oncologists.
Controlled Trials (RCTs) are the most convincing studies for evidence (and rank second highest in the hierarchy of evidence, behind meta-analyses which themselves pool the results of multiple RCT), the ability to perform these is relatively limited by resources (i.e. they are relatively difficult and expensive to perform). Here we used a RCT design in Chapter 6 (A randomised trial of single-dose radiotherapy to prevent procedure tract metastasis by malignant mesothelioma). The randomised nature of the trial allowed comparison of the intervention to no treatment (both in terms of effectiveness and side effects). In Chapter 7 (A prospective trial of short-fractionation radiotherapy for the palliation of liver metastases) we used a multi-centre prospective design and Chapter 8 (A prospective trial of intraoperative radiation treatment for breast cancer) a single-centre prospective design. Prospective designs are much preferred (to the alternative of retrospective studies) because the likelihood is far greater that treatment and assessments are relatively uniform (i.e. retrospective studies often have a range of treatments and assessments, and also risk selection and other biases). Multicentre studies allow greater numbers of patients to be accrued, but protocols need to be clearly understood by a range of investigators. If multiple centres participate, this may show the results might be achieved at many centres (rather than one “expert” centre). Chapters 7 and 8 used mainly comparison with published results. While IORT definitely needed to be tested in a randomised trial (particularly if it was going to be the sole treatment) we performed a local study primarily to test feasibility. The next major theme is RT delivery through innovative approaches to immobilisation, in Chapter 4 (Surface laser scanning to routinely produce casts for patient immobilisation during radiotherapy) and Chapter 5 (A simple and inexpensive method to routinely produce customised neck supports for patient immobilisation during radiotherapy). Chapter 4 used comparison by RT judgements and various process measurements, while Chapter 5 used comparison by examining objective displacement measurements. Chapters 2 and 3 used various questionnaires; some were snapshots only, while others were repeated to allow comparison. This thesis incorporates a range of study designs, where different innovative treatments / methods were felt able to be best assessed in different ways.
THE CHOICE OF ENDPOINTS TO BE ASSESSED

The series of studies presented here illustrates the range of endpoints that might be used in radiation oncology studies. In the clinical studies this included objective cancer endpoints (such as the rate of procedure tract metastasis). Although these are often clearest, the mesothelioma study illustrates the attention to detail that may be required (e.g. tattoos to identify treated and untreated control areas, methods and timing of assessments). The studies also used treatment side effects endpoints (according to standardised scoring systems) and assessment of symptoms. In the immobilisation studies, endpoints included objective and subjective measures. In the studies of training there were both pragmatic scores and carefully validated questionnaires (specifically the learning environment questionnaire). Some of the study endpoints were not able to be easily quantified, but were none-the-less worthy of comment. For example, laser surface scanning clearly avoids distress associated with the previous POP method (which involves applying strips of wet plaster bandage to a patient’s face while manually smoothing these to avoid air gaps). Different endpoints were used for different innovations (and had to fit with the study designs used).

PARTICULAR ISSUES AND CHALLENGES INVOLVED IN ASSESSING NOVEL TREATMENTS

Testing novel treatments can raise a number of issues / challenges, such as avoiding new (and therefore unfamiliar) problems. There need to be mechanisms in place to identify unexpected problems (e.g. unexpected side effects). The Intrabeam method was relatively new when we investigated this. Vaidya et al. reported their experience on 25 patients where, like our study, they replaced the routine boost to the tumour bed with IORT using the Intrabeam device. 22-24 They identified a problem with wound healing due to radionecrosis caused by the applicator being positioned too close to the skin. This had been reported prior to our study, and we incorporated changes to our IORT technique to avoid this. One aspect of assessing an innovative treatment may include
the need to assess complications not normally seen with radiotherapy (e.g. breast infection rates). This was also illustrated by the IORT study. We assessed patients closely for complications, and found minimal radiation reactions, but an acute breast infection rate of 17%. As we noted a possible increased risk of breast infections in the early part of this study, we moved to using prophylactic antibiotics given at the time of the procedure. This resulted in an apparent decrease in the rate of infections from 25% to 11%. This reduction may also be related to the use of a separate procedure list. Our follow up was not long enough to demonstrate all potential late effects of radiation, but we will continue to monitor for them. Investigators examining novel treatments need think about the possible of introducing new problems.

**ASSESSING FEASIBILITY (AND THE DEVELOPMENT ONGOING IMPROVEMENTS)**

Innovation treatments or processes may not work as expected. While the studies tested possible benefits, another aspect of innovation is the need to assess feasibility, particularly in real world settings. This also incorporates the identification of areas for further adaption. Again using the IORT study as an example, the actual treatments themselves went smoothly without excessive use of theatre resources. We then moved to performing the IORT as a separate procedure rather than at the time of other breast or axillary surgery. This appears easier to schedule, and allows the final pathology to be available prior to IORT – avoiding problems such as close margins at initial resection requiring further surgery. Another example is the FastSCAN technique – while it is more forgiving than the POP method; it is important that hair is covered (using a tubular retention bandage), as the cameras will not pick up the laser image as it passes over hair. Also, substantial metal objects must be kept at least 0.5 m away from the immediate scanning environment, as metal interferes with the tracking of the scanner. Producing a good image requires the correct distance and speed of scanning – however, the quality is immediately apparent and the process retrievable, in contrast to the POP method, where quality may not become apparent until deficiencies are noted at the time of fitting the final mask. The examples above, illustrate the testing of the
feasibility of innovations in practice. They also highlight the importance of adaption or fine-tuning procedures.

THE IMPORTANCE OF COMPARATORS IN STUDY DESIGN

One of the important elements of study design is the choice of comparators. The benefits of having a comparison arm of a RCT are illustrated in Chapter 6. Tract metastases in the control arm of the trial were low (and lower than expected). This result raised the possibility that no intervention at all might be required. Similar results were later obtained by others (and are discussed in the section on clinical translation). While a RCT generally has an appropriate comparison group, this is much more difficult to assess in non-randomised studies (e.g. to determine whether a historical control group is appropriate). Without a randomised control arm, the mesothelioma study, would likely have been reported that the investigational treatment, had a significant benefit (a type I error or “false positive” result). This serves as a reminder that in non-randomised studies, the comparison group or benchmark result needs to be carefully considered. This point is also illustrated by consideration of the response rate of the liver metastases study (using a shorter than usual fraction schedule) – this was lower than that reported with protracted fractionation schedules. One important question to consider was to consider whether this was due to differences in the treatment or the patients (comparison group). Leibel et al studied 187 patients treated with WLRT to a dose of 21 Gy in seven fractions (the patients were randomized to receive the radiosensitizer misonidazole as well, or not). Patients’ symptoms were assessed weekly for the first month, then at 2, 4 and 6 months and then every 3 months thereafter. Abdominal pain was scored on the same four-point scale of severity we have used, and 80% had an improvement following therapy, with complete resolution noted in 54% of cases. Reporting our results in this way, 41% of our patients had relief following treatment, and this was complete in 30%. We felt our poorer response rate might be attributed to less favourable disease in our patients. Our patients might have been referred later with a greater tumour burden, and many in our series were treated only after failing chemotherapy. Fewer patients in this report had colorectal primaries (which have a
better prognosis). The median survival of patients treated in Leibel’s series was 17 weeks compared to the 10 weeks in our series. A randomized phase III study would be required to address whether protracted fractionation might increase the response rate. However, the improvement would have to be large to justify additional treatment episodes in a setting where patient survival is measured in weeks only. The choice of comparators for the results of innovative treatments is a major consideration.

**COMPARING RADIATION TREATMENTS USING DOSE-EQUIVALENTS (ESTIMATED BY THE LINEAR-QUADRATIC METHOD)**

It is sometimes difficult to compare treatments. One relatively unique aspect of the three hypofraction studies is the attempt to quantify the difference between the innovative and “standard treatments”. With each of the clinical studies attempts were made to look at radiation dose-equivalence (for comparison with other treatments), using the linear-quadratic model. For example, for cancers (such as malignant pleural mesothelioma), 10 Gy in a single fraction is equivalent to delivering 12Gy in six 2-Gy fractions. For comparison, 21 Gy in three fractions is equivalent to approximately 42Gy in 21, 2-Gy fractions. That is, the dose used was equivalent to approximately 40% of the reported three-fraction MPM schedules. This lower dose could be expected to be less effective, but the actual difference in outcome depends on steepness of the tumour control probability curve. The IORT study raises even more complex questions. Using the linear-quadratic model and assuming an alpha–beta ratio of three, we can calculate the equivalent dose for normal tissue late effects. At 1 cm from the applicator, the dose is 5 Gy in a single fraction – in terms of late effects this is approximately equivalent to only 8 Gy in 2-Gy fractions. A small volume receives higher doses, but there is significant ‘volume effect’ for normal tissue reactions, so the effect will be less than would be expected if a large volume were irradiated to the same dose. Equivalent doses in terms of cancer treatment can also be estimated using the linear quadratic model, assuming an alpha–beta ratio of 10. For example, the dose at the surface of the applicator is nominally equivalent to 50 Gy in 2-Gy fractions (i.e. similar to an entire
course of EBRT). Although the linear quadratic model accounts for fractionation effects, IORT as described may be more biologically effective than predicted due to advantages such as immediate treatment (which avoids tumour repopulation). The actual biological effectiveness of this treatment will depend on the 3-dimensional distribution of the tumour clonogens. Such treatment may be more effective for more favourable pathology tumours. The linear quadratic model was used to give a rough approximation of the difference in radiation dose-schedules. However it has weaknesses and some aspects of calculating dose-equivalence remain unclear. Another crucial aspect is the slope and position on the dose-response curve (i.e. there may not be a linear relationship between dose and response). In the situations described the dose-equivalent is given more as a rough illustration. It may be more useful where investigators are matching schedules for particular (acute or late) effects, making the dose-response curve less important.

THE DIFFICULTIES OF ASSESSING PATIENT BENEFIT FROM CLINICAL TREATMENTS

The benefits from some treatments are hard to assess and quantify, especially where there are multiple endpoints (and so the benefit of an innovative treatment is likewise, difficult to prove). This is particularly so for palliative treatments and this is illustrated by the liver metastases study. Although there were benefits of WLRT, few patients obtained either a long-lasting or complete benefit. The percentage of patients who benefit is similar to that seen with other palliative treatments such as radiotherapy for brain metastases, advanced lung cancer and bone metastases. The example discussed illustrates the difficulty of assessing some treatments with clinical endpoints. This especially applies to palliative treatments where patients continue to deteriorate (and treatments may only help some symptoms).
COST-EFFECTIVENESS ASSESSMENT FOR INNOVATIVE TREATMENTS

Costs and the related concept of Cost-effectiveness are of particular concern for innovations in treatment and training. While some innovations may decrease costs, many might increase costs. Any increased cost needs to be weighed against increased benefits. One difficulty in assessing the value of treatments is that costs and benefits may accrue to different stakeholders (e.g. increased costs of an innovation may largely benefit someone other than those funding the innovation). While most of the innovations here were designed to be low-cost (or lowering costs, compared to alternatives), cost-effectiveness had to be considered. In the clinical studies looking at fewer treatments than otherwise would have been used, there is obviously potential cost savings. In the trial of IORT there were potential cost savings, but also cost increases. This included the cost of the device but also its operation. We explicitly considered this. Intrabeam requires an investment in the cost of the machine and the time of the personnel using it. This typically included almost an hour of operating time per patient, at least during the learning stage. The cost of the Intrabeam device and floor stand is approximately $A590 000. This treatment is unlikely to be economical simply as a routine method of tumour bed boost delivery, but may be cost-effective if it were able to replace entire courses of EBRT. The benefits to patients, including reductions in time off work, transport and accommodation costs might be substantial, as in the case of the 14 women in our series who usually live over 1 h drive away from the nearest radiotherapy centre. In addition, freeing space on linear accelerators allows other patients to be treated with shorter waiting times. Other studies needed to consider costs such as labour and delays, in the patient immobilization studies. Our former method of cast production was labour intensive, and in terms of time saved, each mask produced with FastSCAN saves 60 min of RT time. There are other potential time savings, for example, the time waiting for POP to dry. Although there are definite benefits, these improvements need to be weighed against costs; namely the variable costs involved in the production of individual masks and the fixed costs of the scanner and software ($A45 000) and CNC milling machine ($A45 000–$160 000). The CNC mill, however, has a variety of uses in the hospital, including milling aluminium compensators for radiotherapy treatment. A
vacuum former is also required with either method of cast production. The machineable plaster used to produce the positive mould costs $A35 per block. There is an RT labour saving of approximately 60 min per cast (at the cost of an additional cost of approximately 20 min of biomedical technician time). The labour saving would be greater if the requirements for poorly fitting POP masks to be remade were considered. The examples above highlight some of the ways cost-effectiveness might be assessed. There are more involved and comprehensive methods, but again we have to apply the appropriate levels of study to the particular innovation.

POSSIBLE WEAKNESSES OF THE REPORTED STUDIES (INCLUDING STUDY DESIGNS)

This thesis used a range of study methods. One study used the “gold standard” RCT design. In other situation, other designs were more appropriate. In each case, potential weaknesses need to be considered. The mesothelioma study had relatively strong design, but as discussed the rate of chest wall procedure site recurrence was lower than expected in the control arm. Studying a higher risk group might better have shown possible benefits of radiotherapy. However it did address the question affecting the greatest number of such patients. The liver metastases study would potentially benefitted from formal quality-of-life measures rather than symptom responses and treatment toxicities alone. We initially attempted to collect health-related quality of life using a validated questionnaire. However, the level of missing data made this assessment unreliable. The IORT study was a feasibility study, done prior to participation in a planned RCT. However, as discussed, a RCT is indicated for a significant innovation (and indeed has since been undertaken). The Fastscan process might have been more convincing if a direct comparison of the two methods of cast production was carried out, but it would have been unreasonable to make patients undergo both methods (once the method of production was found to function satisfactorily). Likewise the neck support study might have been more convincing with a comprehensive randomized study with more patients and daily electronic portal imaging
device images. However, our results from 40 non-selected patients, using port films taken according to the departmental treatment policy, provide a convincing assessment of the merits of this new inexpensive and simple method of patient immobilization. One weakness of the writing skills study is that although the workshop was held to address the problem of unpublished research, assessment was in terms of self-perception, rather than objective measurement. Against this, it should be noted that the postworkshop questionnaires were completed at an appropriate time, at least 6 weeks after the workshop. This allowed participants the time to have attempted further writing. The study included only a small number of participants, reflecting the nature of a workshop with limited numbers, but still provides evidence for the feasibility of such sessions and addresses a range of practical issues (e.g. content). The study may also have underestimated the benefits available. Only one attendee was a registrar and many participants actually had significant writing experience, with most having been first or second authors of papers in the past. It was confirmed during the workshop that some were attending to gain skills to facilitate the work of junior staff. So in fact, the benefits of the workshop may be greater if those with the most need were targeted. The major weakness of fellowship preparation course study was that we are asking about the value of a preparation workshop before candidates have sat the examination. Although it might be useful to ask candidates about the benefit of the course after they have sat the examination, this would be confounded by a range of factors. Another weakness is that any course will have to cater to candidates with different learning needs. For example, the pathology viva session was probably to be of most benefit to those who do not have regular formal sessions with a pathologist. Similarly, the learning environment assessment applies only to registrars at this stage of their training and may not reflect perceptions of more junior trainees. The major strength of this paper is that we asked the candidates’ opinions directly. This group of registrars, that is, those in final preparation for their Part 2 examination, are both experienced and focused on learning environments. Therefore, their opinion on current learning environments needs to be respected. Also, the learning environment survey in particular, is a well-designed instrument and we obtained a good response rate. Each study had a number of
strengths and weaknesses. Most of the weaknesses might have been overcome by more detailed and comprehensive studies (that would increase confidence in the results). However in most cases, the studies were felt to be sufficient for the extent and type of innovation.

**FUTURE DIRECTIONS**

Innovation is capable of being presented as a discipline, capable of being learned, and capable of being practised. Real success is based on the ability to learn and repeat the required behaviours. Innovation can usefully be considered as a process which consists of scanning the internal and external environment for opportunities, selecting potential opportunities based on strategic criteria, providing resources, implementing projects, and then learning from the experience. Organisations that support innovation are ones whose structure and behavioural norms encourage and enable innovation.

As mentioned in the introduction the candidate continues to look for areas suitable for further innovation and thorough testing. Promising areas for relatively low-cost, highly cost-effective improvements include maximising the effectiveness of multi-disciplinary team meetings (both for direct patient care and also as educational opportunities). In one study, I examined the survival impact of multidisciplinary meetings. Patients with inoperable non-small cell lung cancer diagnosed and managed at a single institution over a one-year period were identified. Those whose case had been discussed at a multidisciplinary meeting (MDM) had better survival than those whose case was not discussed (mean survival: 280 days vs. 205 days, log-rank p=0.048). This led to another study examining the resources MDMs require to function. I am a co-investigator of a study looking at the value of peer-review in improving MDM function.

I have also been part of a team using new technological improvements to deliver better palliative treatments. Specifically we developed and tested the use of On-Board Imaging to plan and deliver palliative radiotherapy in a single cohesive patient appointment.
have also been involved in examining the potential of new methods of waiting list optimisation to improve outcomes for patients. 44

Innovations are not always better (e.g. in terms of results, side effects, and cost-effectiveness). This is illustrated by a meta-analysis of 57 RTOG randomised trials, all involving radiotherapy, which showed that newer treatments were only as likely as standard therapies to have better survival (but were more likely to have greater adverse effects).15 The candidates own review of the results for TROG trials show similar findings (manuscript in preparation). Innovations in radiotherapy are often more expensive (sometimes substantially). There is a real need to examine the cost-effectiveness of newer highly resource intensive methods.

CONCLUSIONS

A number of innovations in radiation oncology training (to promote research publication and improve skills and knowledge as assessed by examination performance) and treatment (including dose-schedule and technique) were developed then prospectively tested.1-7 The studies examined simple improvements in radiation oncologist training to improve learning for specialist exams and to develop scientific writing skills; a less unpleasant method of producing patient immobilisation casts and a complementary simple method to produce customised neck supports; the use of a shorter than usual course of radiotherapy for chest wall prophylactic treatment in malignant pleural mesothelioma; the use of shorter than usual treatment course for the palliation of liver metastases; the use of shorter than usual treatment as a boost in breast-cancer (with a view to sole treatment in later studies). In each case the focus was on innovations in radiotherapy (with an emphasis on making them easier or more effective in a simple manner). These innovations were studied and found to be of benefit and/ or to warrant further investigation. In one case, a short fractionation a single dose of radiotherapy to prevent chest wall metastasis was found ineffective, but the study provided useful additional information regarding the risk of procedure tract metastases. The studies
described in Chapters 2-8, and the other studies briefly mentioned above, demonstrate that innovations in radiotherapy (with an emphasis on making RT easier or more effective in a relatively simple manner) can be developed, even in the single institution or ANZ setting. There are different types and degrees of innovation. Different cases will present different opportunities and constraints. Innovations require testing, although different study designs may be more suitable for different innovations.
REFERENCES


Appendix 1. Publication referred to in the Introduction chapter


The candidate made substantial contributions to each of study conception, study design, literature search, data collection, data analysis, data interpretation, manuscript preparation, manuscript editing, and manuscript revision/review. In addition the candidate was the corresponding author.

The article itself is included in the hardcopy thesis only (for copyright reasons).
Appendix 2. Publication referred to in the Discussion Chapter


The candidate was sole author.

This publication was based in part on two other co-authored publications.


The candidate made substantial contributions to each of literature search, interpretation, manuscript preparation, manuscript editing, and manuscript revision/review for those two manuscripts.

The article itself is included in the hardcopy thesis only (for copyright reasons).