1182

Final Decision Analytic Protocol (DAP) to guide the assessment of intensity modulated radiation therapy for cancer treatment delivery

February 2013

Table of Contents

MSAC and PASC

The Medical Services Advisory Committee (MSAC) is an independent expert committee appointed by the Minister for Health and Ageing (the Minister) to strengthen the role of evidence in health financing decisions in Australia. MSAC advises the Minister on the evidence relating to the safety, effectiveness, and cost-effectiveness of new and existing medical technologies and procedures and under what circumstances public funding should be supported.

The Protocol Advisory Sub-Committee (PASC) is a standing sub-committee of MSAC. Its primary objective is the determination of protocols to guide clinical and economic assessments of medical interventions proposed for public funding.

Purpose of this document

This document will be used to guide the assessment of an intervention for a particular population of patients.

The protocol guiding the assessment of the health intervention has been developed using the widely accepted "PICO" approach. The PICO approach involves a clear articulation of the following aspects of the research question that the assessment is intended to answer:

Patients – specification of the characteristics of the patients in whom the intervention is to be considered for use

Intervention – specification of the proposed intervention and how it is delivered

Comparator – specification of the therapy most likely to be replaced by the proposed intervention

Outcomes – specification of the health outcomes and the healthcare resources likely to be affected by the introduction of the proposed intervention

Purpose of application

A proposal for an application requesting MBS listing of intensity modulated radiation therapy (IMRT) for cancer treatment delivery was received from the Trans Tasman Radiation Oncology Group (TROG) by the Department of Health and Ageing in August 2011. As a result of the completion of the Assessment of New Radiation Oncology Treatments and Technologies (ANROTAT) project being undertaken by TROG, the Faculty of Radiation Oncology of the Royal Australian and New Zealand College of Radiologists has now taken responsibility for sponsoring this application.

This application also subsumes application 1211 Volumetric Modulated Arc Therapy that was considered at the August and December PSAC meetings. Volumetric Modulated Arc Therapy is a form of IMRT and will be addressed in this application as part of the review of clinical and economic literature.

Intensity modulated radiation therapy is already being delivered in some centres around Australia and is funded through existing mechanisms for three dimensional conformal radiation therapy (3DCRT). As a result of the increased infrastructure costs, as well as complexity of treatment associated with IMRT over 3DCRT, the additional resource requirements associated with the delivery of IMRT are not adequately reimbursed through the current funding mechanism. In response to this situation this application is seeking to have IMRT listed separately from 3DCRT on the Medicare Benefits Schedule.

The NHMRC Clinical Trials Centre, as part of its contract with the Department of Health and Ageing, drafted this decision analytical protocol to guide the assessment of the safety, effectiveness and cost-effectiveness of IMRT in order to inform MSAC's decision-making regarding public funding of the intervention.

Background

Current arrangements for public reimbursement of radiotherapy

Funding for radiotherapy is provided through numerous avenues including:

- The Federal government.
    - The Federal government funds radiotherapy services for private patients (including non-admitted patients treated at public facilities under rights of private practice arrangements) across Australia through the Medicare Benefits Schedule (MBS). A co-payment may be required from the patient or private health insurance organisation (or both) as part of this service delivery funding model.
    - Radiation Oncology Health Program Grants (ROHPGs). ROHPGs cover the capital costs of approved radiotherapy equipment. Public and private institutions may be eligible for receipt of ROHPGs, however payments are only made for services that also attract a Medicare benefit.

    - MBS and ROHPG payments represent the vast majority of funding for radiotherapy services.
- State and territory governments.
    - This funding covers the provision of public outpatient and eligible inpatient radiotherapy services within each state or territory. Specific funding models vary between jurisdictions, however services are funded from state or territories budgets.

Radiotherapy delivered as either external beam radiotherapy (EBRT or brachytherapy is reimbursed through the MBS along with the simulation, dosimetry and verification steps involved in the planning and delivery of such treatment. IMRT and 3DCRT are both forms of EBRT. These are described further in later sections of this document.

MBS funding of IMRT is currently facilitated though the following MBS item numbers associated with 3DCRT:

Simulation: 15550 and 15553. New MBS item numbers associated with IMRT are <u>not</u> being sought for IMRT through this application.

Dosimetry: 15556, 15559 and 15562. New MBS item numbers associated with IMRT <u>are</u> being sought for IMRT through this application.

Treatment: 15215, 15230, 15245 and 15260 (lung)

15218, 15233, 15248 and 15263 (prostate)

15221, 15236, 15251 and 15266 (breast)

15224, 15239, 15254 and 15269 (other)

For each of the above indications new MBS item numbers associated with IMRT <u>are</u> being sought through this application.

Verification: MBS items numbers 15700, 15705, 15710.

Many of the MBS item descriptors associated with 3DCRT differ only in the description of the site of treatment. As an example MBS item descriptors associated with the treatment of lung cancer are given below.

Table 1: Current MBS item descriptor for 15550 (Simulation)

Category T2– Radiation Oncology
MBS 15550 SIMULATION FOR THREE DIMENSIONAL CONFORMAL RADIOTHERAPY without intravenous contrast medium, where: (a) treatment set up and technique specifications are in preparations for three dimensional conformal radiotherapy dose planning; and (b) patient set up and immobilisation techniques are suitable for reliable CT image volume data acquisition and three dimensional conformal radiotherapy treatment; and (c) a high-quality CT-image volume dataset must be acquired for the relevant region of interest to be planned and treated; and (d) the image set must be suitable for the generation of quality digitally reconstructed radiographic images (See para T2.3 of explanatory notes to this Category) Fee: $658.60 Benefit: 75% = $493.95 85% = $584.10

Table 2: Current MBS item descriptor for 15556 (Dosimetry)

Category T2– Radiation Oncology
MBS 15556 DOSIMETRY FOR THREE DIMENSIONAL CONFORMAL RADIOTHERAPY OF LEVEL 1 COMPLEXITY where: (a) dosimetry for a single phase three dimensional conformal treatment plan using CT image volume dataset and having a single treatment target volume and organ at risk; and (b) one gross tumour volume or clinical target volume, plus one planning target volume plus at least one relevant organ at risk as defined in the prescription must be rendered as volumes; and (c) the organ at risk must be nominated as a planning dose goal or constraint and the prescription must specify the organ at risk dose goal or constraint; and (d) dose volume histograms must be generated, approved and recorded with the plan; and (e) a CT image volume dataset must be used for the relevant region to be planned and treated; and (f) the CT images must be suitable for the generation of quality digitally reconstructed radiographic images (See para T2.3 of explanatory notes to this Category) Fee: $664.40 Benefit: 75% = $498.30 85% = $589.90

Table 3: Current MBS item descriptor for 15215, 15230, 15245 and 15260 (Treatment, lung)

Category T2– Radiation Oncology
MBS 15215 RADIATION ONCOLOGY TREATMENT, using a single photon energy linear accelerator with or without electron facilities - each attendance at which treatment is given - 1 field - treatment delivered to primary site (lung) Fee: $59.65 Benefit: 75% = $44.75 85% = $50.75
MBS 15230 RADIATION ONCOLOGY TREATMENT, using a single photon energy linear accelerator with or without electron facilities - each attendance at which treatment is given - 2 or more fields up to a maximum of 5 additional fields (rotational therapy being 3 fields) - treatment delivered to primary site (lung) Derived Fee: The fee for item 15215 plus for each field in excess of 1, an amount of $37.95
MBS 15245 RADIATION ONCOLOGY TREATMENT, using a dual photon energy linear accelerator with a minimum higher energy of at least 10MV photons, with electron facilities - each attendance at which treatment is given - 1 field - treatment delivered to primary site (lung) Fee: $59.65 Benefit: 75% = $44.75 85% = $50.75
MBS 15260 RADIATION ONCOLOGY TREATMENT, using a dual photon energy linear accelerator with a minimum higher energy of at least 10MV photons, with electron facilities - each attendance at which treatment is given - 2 or more fields up to a maximum of 5 additional fields (rotational therapy being 3 fields) - treatment delivered to primary site (lung) Derived Fee: The fee for item 15245 plus for each field in excess of 1, an amount of $37.95

Table 4: Current MBS item descriptor for 15705 (Verification, multiple projection)

Category T2– Radiation Oncology
MBS 15705 RADIATION ONCOLOGY TREATMENT VERIFICATION - multiple projection acquisition when prescribed and reviewed by a radiation oncologist and not associated with item 15700 or 15710 - each attendance at which treatment involving three or more fields is verified (ie maximum one per attendance). *(See para T2.4 of explanatory notes to this Category)* Fee: $76.60 Benefit: 75% = $57.45 85% = $65.15

Table 5: Number of claims for MBS item numbers associated simulation and dosimetry for 3DCRT and external beam radiotherapy generally from July 2011 to June 2012

	MBS Item	Total claims
Simulation	15550	28,243
	15553	2,408
Dosimetry	15556	5,239
	15559	6,483
	15562	17,600
Treatment (lung)	15215	81
	15230	3,808
	15245	233
	15260	41,004
Treatment (prostate)	15218	11
	15233	6,155
	15248	316
	15263	199,626
Treatment (breast)	15221	558
	15236	18,690
	15251	23,170
	15266	226,376
Treatment (other sites)	15224	725
	15239	20,044
	15254	31,094
	15269	298,702
Verification	15700	104,382
	15705	269,371
	15710	66,143

Source: Medicare Item Reports service accessed at https://www.medicareaustralia.gov.au/statistics/mbs_item.shtml on 6th February 2013.

Regulatory status

A list of medical devices associated with the planning and delivery of IMRT is given in Table 6.

Table 6: Australian register of therapeutic goods details of devices associated with the delivery of IMRT.

Product	ARTG Number	GMDN Description	Name of Manufacturer
Tomotherapy® Hi-Art System	124503	Unclassified	Accuray Inc
Linear accelerator	121112	Accelerator system, stereotactic radiosurgery	BrainLab AG
Collimator	196919/186855/165043/165042	Collimator, accelerator system, motorized, automatic aperture control	Elekta Ltd
Linear accelerator	111760	Accelerator system, linear	Elekta Ltd
Planning system	187299	Radiation therapy treatment planning system	Elekta Ltd
Planning system	118156	Radiation therapy treatment planning system	Philips Medical Systems Inc
Linear accelerator	165502	Accelerator system, linear	Siemens Ltd
Planning system	186322	Radiation therapy treatment planning system	Siemens Ltd
Collimator	119985[a]	Collimator, accelerator system, motorized, automatic aperture control	Varian Medical Systems Inc
Linear accelerator	121225	Accelerator system, stereotactic radiosurgery	Varian Medical Systems Inc
Linear accelerator	116839	Accelerator system, linear	Varian Medical Systems Inc
Planning system	119983	Radiation therapy treatment planning system	Varian Medical Systems Inc

Intervention

Description of the medical condition

Cancer is a range of diseases where abnormal cells grow rapidly and can spread uncontrolled throughout the body. These cancerous cells can invade and destroy surrounding tissue and spread (to distant parts of the body. An estimated 114, 000 new cases of cancer were diagnosed in Australia in 2010 and the Cancer Council Australia estimates that 1 in 2 Australians will be diagnosed with cancer by the age of 85. Cancer is now the leading cause of death in Australia, and although mainly affecting the older population, is a leading cause of premature death. Many patients live for a number of years with a diagnosis of cancer, potentially requiring ongoing intervention to support quality of life.

Other non-malignant lesions are also appropriately treated with radiation therapy, such as benign intracranial tumours and extra-cranial lesions.

Over 50% of patients with cancer will benefit from treatment programs that have radiation therapy as a component with or without other treatment modalities. The treatment can be part of a curative

program or to help ease the symptoms of more advanced disease. For curative treatments particularly, higher radiation doses are more likely to achieve control.

Description of the intervention

Like other forms of radiation therapy, IMRT delivers ionizing radiation to cancerous cells. Ionizing radiation damages the DNA of the cell which ultimately leads to cell death. Radiation beams must pass through normal tissues, such as the skin and organs surrounding the tumour before they reach the targeted tumourous cells. In order to minimise damage to normal tissues radiation beams are aimed from several angles with the aim of intersecting at the tumour and providing a much larger absorbed dose of radiation at that site than the surrounding healthy tissue.

Successive advances in radiation therapy delivery technologies have led to the ability to deliver ionizing radiation to the target tumour cells with increasing accuracy. The development of 3DCRT, in which the profile of radiation beams may be shaped to fit the profile of the target using a multi-leaf collimator (MLC) allows a higher dose of radiation to be delivered to the tumour than conventional techniques whilst reducing the damage caused to the surrounding normal tissue.

IMRT is a technological advance from 3DCRT. While both 3D and IMRT deliver beams that are geometrically shaped, IMRT adds the ability to modulate the intensity of constituent beams. Thus, IMRT results in the delivery of numerous intensity levels for a single beam direction. The highly customisable radiation dose able to be delivered using IMRT is able to maximise tumour dose whilst minimising radiation exposure to surrounding normal tissue. This may result in better tumour targeting, with reduced incidence and severity of side effects, and improved treatment outcomes than 3DCRT (Hummel 2010).

IMRT treatment may be delivered using instruments developed by various manufacturers. Whilst this range of instrumentation has differential features or configurations, the treatment delivered is of the same or very similar nature. The delivery of IMRT involves the use of some form of MLC, (already incorporated into modern linear accelerators) whose leaves can be individually partitioned creating beam apertures of various dimensions and dose intensity within each aperture (Mangar et al. 2005;RANZCR 2011):

Current systems for the delivery of IMRT delivery are:

- Static/Fixed gantry systems used to deliver 'Step and Shoot' or 'Dynamic MLC' treatment approaches.
    - 'Step and shoot' uses the MLC to construct a sequential series of different shaped conformal fields. Areas of intermediate dose are created if they are blocked out by the MLC for some of the fields.
    - 'Dynamic MLC' allows leaf pairs to be programmed to move independently of each other during the few minutes of each treatment whilst the beam is continuously switched on.
- Rotational (Dynamic) gantry systems referred to in this document as Intensity Modulated Arc Therapy (IMAT).
    - These systems allow for the position of the gantry, dose rate and leaf speed to be independently varied throughout delivery of treatment. This includes volumetric modulated arc therapy (VMAT), hybrid arc therapy and helical IMRT systems. It should be noted that in helical IMRT (tomotherapy) the gantry and the couch (dynamic treatment couch) both move during treatment

As outlined in the *Faculty of Radiation Oncology Position Paper: Techniques and Technologies in Radiation Oncology – 2011 Horizon Scan* (RANZCR 2011), 'each of these technologies deliver IMRT, although the technology involved is produced by different manufacturers and can be differently configured.'

Delivery of the intervention

Administration:

The administration of radiation therapy is carried out by a team including radiation oncologists, medical physicists, and radiation therapists. Depending on the site to be treated additional expertise involved in the treatment planning and delivery may include a diagnostic radiologist and / or surgeon.

The same patient referral procedure for existing radiation therapy delivery methods will apply to IMRT. Treatment with IMRT requires several stages:

1. Simulation
2. Planning
3. Physics Quality assurance
4. Target verification (via image guidance)
5. Treatment
6. Treatment verification

The exact procedures required in each stage varies depending on what type of cancer is being treated and individual patient circumstances.

Dose:

The total dose of radiation delivered will vary according to the type of cancer being treated and individual patient circumstances. As an example, a course of a treatment for lung cancer is recommended to be between 60-70 Gy delivered in 2 Gy fractions with the implementation of a dose escalation course of treatment delivering up to 74 Gy (NCCN 2011). Thus, a patient may be required to undergo up to 37 treatment sessions over a course of lung cancer treatment.

Frequency of administration:

Treatment sessions are typically given daily and on an outpatient basis.

Duration of treatment:

The duration of individual treatment sessions is dependent on the number of fields that are delivered. A time and motion study undertaken by Van de Werf et al. 2011 presented a mean treatment time of 13.6 minutes for the delivery of 5-7 fields using static IMRT, with treatment delivery using IMAT being approximately half that of static IMRT. While the time of delivery of radiation is shorter for IMAT than for static IMRT, other factors such as patient preparation and positioning are roughly equivalent, thus the overall treatment session time is only marginally decreased when IMAT is employed over static IMRT.

An entire course of treatment may last up to seven weeks depending on the number of individual treatment sessions required.

Facility requirements and geographic limitations:

Treatment will be given primarily in an outpatient setting and would be carried out in the same specially designed bunkers as other radiation therapy delivery technologies.

Similarly to other radiation therapy treatments, access to IMRT would most likely be limited to speciality facilities located in capital cities and major regional centres, however any Australian radiation oncology centre will be able to deliver IMRT with the appropriate facilities, equipment, qualified personnel and established quality assurance programs.

Prerequisites

The delivery of IMRT may require more capital investment compared to a standard 3DCRT linear accelerator and treatment planning system, specifically software and hardware enabled for IMRT treatment planning and delivery.

A multi-disciplinary range of radiation oncology professionals are required for the safe and effective utilisation of IMRT. These include radiation oncologists, radiation therapists, medical physicists and engineers (Potters et al. 2010). The application states that these health service staff would continue to work under the direction and supervision of the radiation oncologist who holds the relevant Medicare provider numbers and other professional accreditations.

Co-administered and associated interventions

The use of image-guidance throughout the delivery of IMRT:

The ability of IMRT to sculpt the dose around complex contours with very narrow margins is enhanced by the use of image-guidance during treatment. Although forms of image-guided radiation therapy (IGRT) are currently reimbursed through the MBS, these items do not accurately reflect the difference between verification imaging and the use of online image guidance throughout the delivery of IMRT that allows for high-quality images to be processed within the treatment room and while the patient is positioned for treatment. The applicants have submitted a separate application to the Department of Health and Ageing for the listing of online IGRT items (Application 1319).

Associated interventions:

Similar clinical examinations and tests are used in diagnosis and staging of cancers whether a patient is to receive treatment with IMRT or alternate radiation therapy delivery systems. Sometimes the resources required for patient simulation and dosimetry are greater when treatment is provided using IMRT over 3DCRT due to the increased complexity of treatment plans delivered with IMRT.

Table 7: MBS item numbers for 3DCRT radiotherapy treatment protocols requiring patient simulation and dosimetry.

MBS number	Procedure	Fee
15550	Simulation	$658.60
15556	Dosimetry – Level 1 complexity	$664.40
15559	Dosimetry – Level 2 complexity	$866.55
15562	Dosimetry – Level 3 complexity	$1,120.75

The insertion of fiducial markers may be required in some cases when using either 3DCRT or IMRT. For example, as the prostate gland is difficult to image and mobile, and the implantation of radio-opaque markers into the prostate provides fixed reference points during a course of radiotherapy. The aim of this is to facilitate identifying the precise location of the prostate using imaging which, in turn, leads to the ability to deliver radiotherapy more accurately. Fiducial marker implantation for this purpose is MBS interim funded (MBS item 37217). Fiducial marker implantation is performed under ultrasound guidance prior to the commencement of therapy, and this ultrasound procedure is claimed at the same time (MBS item 55603).

Table 8: MBS item numbers associated with the implantation of fiducial markers into the prostate.

MBS number	Procedure	Fee
55603	Transrectal ultrasound	$109.10
37217	Fiducial seed implantation	$138.30

Depending on individual patient circumstances surgery, neo-adjuvant/concurrent chemotherapy or other therapies may be co-administered with radiation therapy.

The same examinations performed during and following treatment, as well as any treatment required for the management of adverse events, are the same whether a patient receives treatment with IMRT or other radiation therapy approaches. Given that IMRT may be associated with fewer acute and long-term adverse events the treatment required for these may be reduced with the use of IMRT over existing systems.

Listing proposed and options for MSAC consideration

Proposed MBS listing

The proposed MBS items associated with IMRT would fall under Category 3 – Therapeutic Procedures. It is proposed that treatment with IMRT should be rebated in the same way as current procedures for radiotherapy. However in consideration of the increased complexity and labour requirements involved in the planning and delivery of IMRT it may be anticipated that the MBS fees sought will be greater than those associated with 3DCRT.

Separate MBS item descriptors have been proposed for the planning and treatment stages of delivering radiation therapy using IMRT. PSAC determined at its December 2012 meeting that this was appropriate. It was noted that the cost of the equipment and any additional software for planning, treatment and the image guidance would need to be considered under the ROHPG scheme.

The below tables outline the proposed MBS descriptions for the planning and treatment associated with IMRT. PSAC agreed that the items should enable treatment to be billed per fraction, as there may be more than one fraction given in a single day.

The applicant advised that fees would be derived from the costing information supplied from the TROG ANROTAT project. PSAC noted that the Radiation Oncology MBS Review may also lead to refinements in both the fees and the item descriptors.

Table 9: Proposed MBS item descriptor for computerised planning for IMRT

Category 3, Group T2 – Radiation Oncology Computerised Planning
MBS 155XX. Dosimetry for Intensity Modulated Radiotherapy treatment plan using CT image volumetric dataset. The planning process must include the following; 1. The IMRT planning process must maximize the differential between target dose and normal tissue dose based on the review and assessment by a Radiation Oncologist. 2. All gross tumour targets, clinical targets, planning targets and organs at risk as defined in the prescription must be rendered as volumes. 3. The organs at risk must be nominated as planning dose goals or constraints and the prescription must specify the organs at risk as dose goals or constraints. 4. Dose calculations and dose volume histograms must be generated in an inverse planned process using a specialized calculation algorithm with prescription and plan details approved and recorded with the plan. 5. A CT image volume dataset must be used for the relevant region to be planned and treated. 6. The CT images must be suitable for the generation of quality digitally reconstructed radiographic images. 7. The final dosimetry plan must be validated using robust quality assurance processes by both the Radiation Therapist and Medical Physicist and approved by the Radiation Oncologist prior to delivery. This may include; • The Determination of the accuracy of the dose fluence delivered by the MLC and Gantry position (static or dynamic) • Ensuring the plan is deliverable, data transfer is acceptable and validation checks are completed on a linear accelerator • Validating the accuracy of the derived IMRT treatment plan in a known dosimetric phantom • Determining the accuracy of planned doses in comparison to delivered dose to designated points within the phantom and/or dosimetry device. Fee: Under development

Table 10: Proposed MBS item descriptor for treatment delivery using IMRT

Category 3, Group T2 – Radiation Oncology – Megavoltage
MBS 152XX RADIATION ONCOLOGY TREATMENT with IGRT imaging facilities utilising an Intensity Modulated Treatment Delivery (Static Gantry or IMAT Mode) at each attendance at which treatment is given using a IMRT Plan (in association with MBS Item XXXX). Fee: Under development

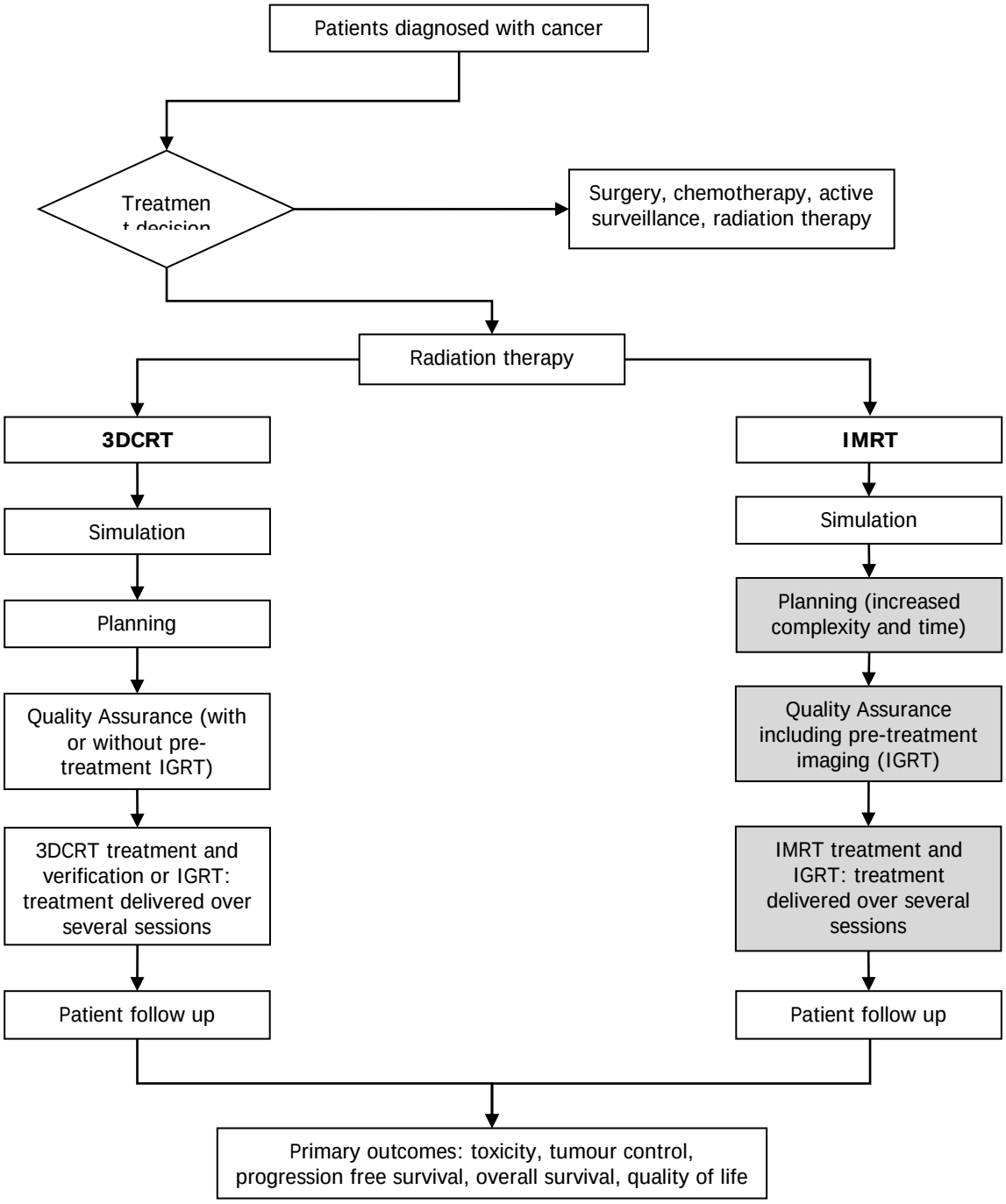
Clinical place for proposed intervention

IMRT is an alternate treatment delivery method to existing forms of radiation therapy. Whilst able to be used to deliver radiation to tumours that are currently treated with radiation therapy, the ability of IMRT to sculpt around complex shapes makes it especially suited for the treatment of tumours that are adjacent to vulnerable structures.. Thus, while not all patients will require IMRT there are circumstances where this treatment would be preferred over 3DCRT. The applicant outlines the use of IMRT reflect quality practice in the curative treatment of nasopharyngeal carcinoma, head and neck cancer, anal cancer, prostate cancer. Expert advice further outlines that IMRT is increasingly used in the treatment of gynaecological cancer and for tumours in the upper gastrointestinal tract and central nervous system.

The eligible patient populations for treatment with IMRT or other forms of radiation therapy are the same. The decision to pursue IMRT would be based on the treating physicians' consideration of individual patient circumstances and assessment of superiority of IMRT over 3DCRT as a treatment approach. When IMRT is pursued it would be a direct substitute for 3DCRT.

The clinical algorithm presented in Figure 1 is a generalised representation of radiation therapy with curative intent. IMRT may also be used to deliver radiation therapy in a palliative context, however the applicant has indicated that uptake of IMRT in a palliative context is relatively low and is estimated to represent less than 20% of the services delivered.

Figure 1. Generalised clinical management algorithm for cancer patients undergoing radiotherapy. Differences between 3DCRT and IMRT are highlighted grey.



Comparator

The majority of treatments with radiation therapy are currently delivered using 3DCRT. The technology to plan and deliver 3DCRT treatment is standard throughout Australian radiation therapy departments and the experience base using this approach is large.

The planning and delivery of 3DCRT is currently listed on the MBS (refer to Tables 2 and 3). For the purposes of this protocol, IMRT is considered a direct substitute for 3DCRT.

Clinical claim

The applicant describes that IMRT is associated with two main benefits in comparison with 3DCRT:

1. In disease sites where the use of IMRT allows a higher radiation dose to be delivered there is a higher probability of local control and cure of the cancer.
2. IMRT has an enhanced safety profile resulting from its ability to deliver radiation with increased precision. This may result in a reduction in early and late toxicity events.

Based on the clinical claims above, and the Departmental guidelines outlined in Table 11, it is expected that a cost-effectiveness or cost-utility analysis would be undertaken as part of the wider assessment of IMRT. This however will be dependent on the evidence that is available during the assessment. Any other approach adopted following the review of this evidence would need to be justified in the report.

Table 11:Classification of an intervention for determination of economic evaluation to be presented

<table>
<tr><td colspan="2" rowspan="2"></td><td colspan="4">Comparative effectiveness versus comparator</td></tr>
<tr><td colspan="2">Superior</td><td>Non-inferior</td><td colspan="2">Inferior</td></tr>
<tr><td rowspan="5">Comparative safety versus comparator</td><td rowspan="3">Superior</td><td colspan="2" rowspan="3">CEA/CUA</td><td rowspan="3">CEA/CUA</td><td>Net clinical benefit</td><td>CEA/CUA</td></tr>
<tr><td>Neutral benefit</td><td>CEA/CUA*</td></tr>
<tr><td>Net harms</td><td>None^</td></tr>
<tr><td>Non-inferior</td><td colspan="2">CEA/CUA</td><td>CEA/CUA*</td><td colspan="2">None^</td></tr>
<tr><td rowspan="3">Inferior</td><td>Net clinical benefit</td><td>CEA/CUA</td><td rowspan="3">None^</td><td colspan="2" rowspan="3">None^</td></tr>
<tr><td>Neutral benefit</td><td>CEA/CUA*</td></tr>
<tr><td>Net harms</td><td>None^</td></tr>
</table>

Abbreviations: CEA = cost-effectiveness analysis; CUA = cost-utility analysis

* May be reduced to cost-minimisation analysis. Cost-minimisation analysis should only be presented when the proposed service has been indisputably demonstrated to be no worse than its main comparator(s) in terms of both effectiveness and safety, so the difference between the service and the appropriate comparator can be reduced to a comparison of costs. In most cases, there will be some uncertainty around such a conclusion (i.e., the conclusion is often not indisputable). Therefore, when an assessment concludes that an intervention was no worse than a comparator, an assessment of the uncertainty around this conclusion should be provided by presentation of cost-effectiveness and/or cost-utility analyses.

^ No economic evaluation needs to be presented; MSAC is unlikely to recommend government subsidy of this intervention

Outcomes and health care resources affected by introduction of proposed intervention

Clinical outcomes

The outcome measures applicable to assessing the response to radiation therapy are:

Safety:

Rates and severity of acute and long-term toxicity events associated with IMRT treatment.

Effectiveness:

- Tumour response determined by the tumours physical reaction to treatment.
- Local control as determined by the cessation of tumour growth.
- Progression free survival rates
- Overall survival rates
- Quality of life.

Health care resources

As previously outlined the main difference in resource utilisation between radiation treatment delivered by IMRT and 3DCRT are the increased time and complexity of the treatment planning stage as well as the use of imaging (IGRT) at each treatment session. Although both 3DCRT and IMRT treatment plans will benefit from daily online IGRT imaging, it is more likely that treatment using IMRT would need online verification. Medical advice has been that daily IGRT imaging is not required in all currently used 3DCRT treatment plans.

A report published on the uptake of IMRT details that approximately 33% of patients receiving radiation treatment would benefit from IMRT (William et al., 2010). The use of IMRT would, in most cases, be as an alternative to treatment delivery using 3DCRT. As IMRT is currently being funded though the MBS item numbers covering 3DCRT the potential listing of IMRT on the MBS could result in a decrease in the number of claims for 3DCRT as those patients treated with IMRT would be billed though the appropriate IMRT item numbers. The use of IMRT in patients that would otherwise have been treated with 3DCRT would result in a corresponding increase in claims for MBS item numbers for IGRT, as well as IMRT planning.

Should treatment with IMRT result in changes in the rates of acute and long-term toxicities there would be corresponding change in the utilisation of the health care resources used to treat or manage these complications. IMRT may also result in improved rates of cancer control, thus avoiding or delaying health care resource use associated with tumour progression, as well as an increase in quality of life. The potentially reduced costs associated with the claimed superior safety and effectiveness profile of IMRT may offset the increased costs associated with treatment. This potential should be explored through the economic evaluation of IMRT.

Table 11:List of resources to be considered in the economic analysis (not exhaustive)

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS	Safety nets*	Other govt budget	Private health insurer	Patient	Total cost
Resources provided to identify eligible population										
Specialist Consultation	Specialist	Outpatient								
- Resource 2, etc										
Resources provided to deliver proposed intervention (IMRT)										
- Simulation	Radiation Oncologist	Outpatient								
- Dosimetry	Radiation Oncologist	Outpatient								
- Quality Assurance	Radiation Oncologist	Outpatient								
- Target Verification	Radiation Oncologist	Outpatient								
- Treatment	Radiation Oncologist	Outpatient								
- Verification	Radiation Oncologist	Outpatient								
Resources provided in association with proposed intervention (IMRT)										
- Additional imaging	Specialist	Outpatient								
- Implantation of fiducial seeds (where relevant)	Specialist	Outpatient								
- Specialist Consultation	Specialist	Outpatient								
Resources provided to deliver comparator (EBRT as above)										
- Resource 1	nil									
- Resource 2, etc										
Resources provided in association with comparator 1 (EBRT as above) (e.g., pre-treatments, co-administered interventions, resources used to monitor or in follow-up, resources used in management of adverse events, resources used for treatment of down-stream conditions)										
- Resource 1										
- Resource 2, etc										

* Include costs relating to both the standard and extended safety net.

Proposed structure of economic evaluation (decision-analytic)

Table 12: Summary of extended PICO to define research question that assessment will investigate

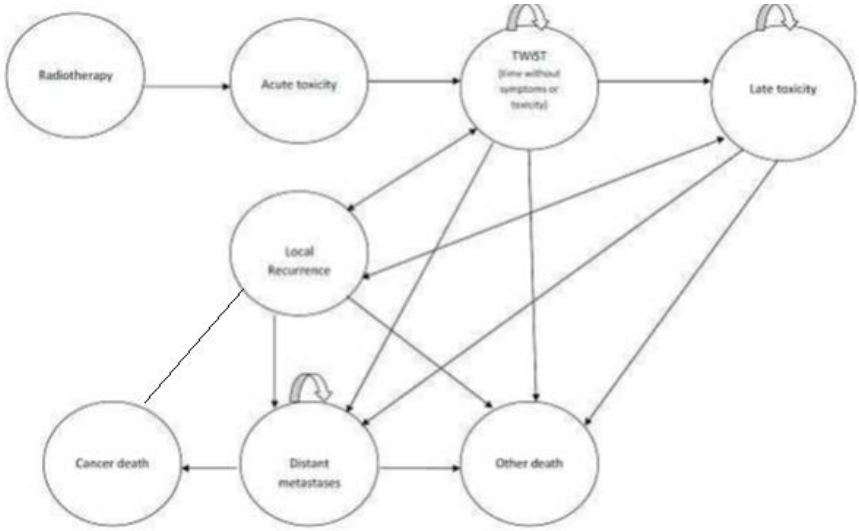
Patients	Intervention	Comparator	Outcomes to be assessed	Healthcare resources to be considered
Patients with a definitive diagnosis of cancer for whom treatment with radiation therapy is being considered.	Intensity modulated radiation therapy delivered by either: • Static Gantry IMRT • IMAT Treatment is to be conducted in conjunction with imaging studies at the time of each treatment session (IGRT)	3D Conformal radiation therapy	Safety: Acute and long-term toxicities associated with radiation therapy. Effectiveness: Response to treatment determined by: Local control (cessation of tumour growth) Progression free survival Overall survival Quality of life.	Resources associated with treatment: • Simulation • Dosimetry • Quality assurance • Target verification • Treatment • Verification • Patient follow up. Resources for ongoing patient monitoring post-treatment. Resources for treating acute and long-term toxicities of radiation treatment. Resources for treating the progression of cancer
Question for public funding: What is the safety, effectiveness and cost-effectiveness of radiation therapy delivered using IMRT in comparison with 3DCRT?				

The applicant has already outlined a proposal for an economic model that will be used in the assessment. This model describes several health states associated with the downstream consequences of radiation therapy will be incorporated into a Markov model. These health states will be the same irrespective of whether IMRT or 3DCRT is used to guide to deliver treatment. Different rates of transition between the states are expected, and these will inform relative cost-effectiveness of IMRT in comparison to 3DCRT. Health states listed for inclusion in the Markov model are:

- Radiotherapy
- Acute toxicity
- Late toxicity
- Time without symptoms or toxicity (TWIST)
- Local recurrence
- Distant metastases
- Cancer death
- Other death

The applicant has further supplied a generic framework relating to the Markov model which is provided at Figure 2.

Figure 2: Applicants proposed framework for the assessment of IMRT using Markov modelling.



Consideration of capital and labour costs:

Regardless of the economic structure the review will need to outline additional capital costs in respect to the proposed adoption of IMRT in the health system. This will include purchase of additional equipment for planning and delivery of IMRT as well as any additional staff required to undertake IMRT.

An estimation of the costs and resources associated with IMRT treatment of tumours in the anal canal, nasopharynx and prostate are available from a report of a clinical trial through the ANROTAT project. The costing data collected in this trial will be incorporated into the economic evaluation.

References

Hummel, S. 2010. *Intensity-modulated radiotherapy for the treatment of prostate cancer: a systematic review and economic evaluation* Prepress Projects.

Mangar, S.A., Huddart, R.A., Parker, C.C., Dearnaley, D.P., Khoo, V.S., & Horwich, A. 2005. Technological advances in radiotherapy for the treatment of localised prostate cancer., 41, 908-921 available from: http://www.sciencedirect.com/science/article/pii/S0959804905000511

NCCN 2011, *NCCN clinical practice guidelines in oncology (NCCN guidelines™) non-small cell lung cancer*, National Comprehensive Cancer Network, 1.2012.

Potters, L., Gaspar, L.E., Kavanagh, B., Galvin, J.M., Hartford, A.C., Hevezi, J.M., Kupelian, P.A., Mohiden, N., Samuels, M.A., & Timmerman, R. 2010. American Society for Therapeutic Radiology and Oncology (ASTRO) and American College of Radiology (ACR) practice guidelines for image-guided radiation therapy (IGRT)., 76, 319

RANZCR 2011, *Faculty of radiation oncology position paper: techniques and technologies in radiation oncology 2011 horizon scan*, Royal Australian and New Zealand College of Radiologists.

Van de Werf, E., Verstraete, J., & Lievens, Y. 2011. The cost of radiotherapy in a decade of technology evolution.

Williams, M.V., Cooper, T., Mackay, R., Staffurth, J., Routsis, D. & Burnet, N. 2010. The Implementation of Intensity-modulated Radiotherapy in the UK. Clinical Oncology, 22, 623-628.