Australian Government

Medical Services Advisory Committee

# Public Summary Document

## *Application 1182 – Intensity Modulated Radiation Therapy (IMRT) in the treatment of cancer*

| | |
|---|---|
| **Applicant:** | **Royal Australian and New Zealand College of Radiologists** |
| **Date of MSAC consideration:** | **63rd MSAC Meeting, 1-2 April 2015**<br>**62nd MSAC Meeting, 26-28 November 2014** |

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, see at www.msac.gov.au

### 1. Purpose of application and links to other applications

An application requesting MBS listing of intensity-modulated radiation therapy[1] (IMRT) for cancer treatment delivery was received from the Trans-Tasman Radiation Oncology Group (TROG) by the Department of Health 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 within the Royal Australian and New Zealand College of Radiologists (RANZCR) has now assumed responsibility for sponsoring this application.

### 2. MSAC's advice to the Minister – April 2015 consideration

After considering the available evidence presented in relation to safety, clinical effectiveness and cost-effectiveness of Intensity Modulated Radiation Therapy (IMRT) in the treatment of cancer, MSAC supported public funding of IMRT on a cost neutral basis relative to three dimensional conformal radiotherapy (3D-CRT).

[1] IMRT is an umbrella term for techniques used to deliver radiation therapy where the beam intensity can be modulated such as: Linac based fixed beam IMRT such as step and shoot; Linac based rotational IMRT such as volumetric modulated arc therapy and helical tomotherapy; Helical non C-arm based IMRT.

## Summary of consideration and rationale for MSAC's advice

MSAC considered this application alongside MSAC application 1319 for image guided radiation therapy (IGRT) prior to or alongside external beam radiation therapy (EBRT) including IMRT.

MSAC reaffirmed that, on balance, there is insufficient evidence of superior outcomes for IMRT compared to 3D-CRT. MSAC agreed that IMRT should be MBS listed, with separate items to support further data collection on utilisation and cost effectiveness. However, MSAC directed that this listing be cost neutral relative to 3D-CRT.

MSAC received advice from the Department about a cost neutral implementation package. This package was developed in discussion with the applicant and GenesisCare. MSAC was advised that the frequency of treatment verification for 3D-CRT and IMRT was similar, with MBS data indicating a median of 30 verification scans per course of curative treatment. Based on 2013-14 data, the package provides for a median course of curative IMRT being:

- Simulation session x 1
- Dosimetry session x 1
- Treatment session x 33
- IGRT x 30

MSAC noted advice that the average MBS expenditure for a course of treatment with 3DCRT or image-guided IMRT (IG-IMRT) was $12,359. MSAC agreed that the fee structure for the proposed IG-IMRT items to redistribute funds to better reflect clinical practice was appropriate. The proposed fee structure comprised:

- 40% of total for simulation and dosimetry
- 60% of total for treatment
- Separate fees for verification scans

The proposed expenditure will be offset from substitutions for existing MBS items 15553, 15562, 15710 and the 3D-CRT treatment items.

MSAC accepted that the calculations were as robust as could be achieved with the available data set. It was noted that the calculations rely on MBS data for number of fields per treatment session which is an approach that does not reflect current clinical practice. MSAC noted the reinvestment of expenditure into radiation oncology treatment in the public sector relative to the private sector. MSAC was advised that some of these issues are likely to be addressed during the Review of Radiation Oncology Health Program Grants Scheme which will commence shortly.

MSAC noted that subject to the passage of legislation from 1 January 2016 the new Medicare Safety Net will be capped at 150% of the Schedule Fee, which will limit the proportion of out-of-pocket costs that count towards the safety net threshold.

### *MSAC Review of November 2014 Discussion*

MSAC reviewed the discussion from the November 2014 consideration of this application including:

- IMRT is currently funded under existing MBS items for 3D-CRT.

- The applicant is seeking separate items and higher fees based on claims of superior outcomes, more complex planning and increased treatment time requirements compared to 3D-CRT.
- The capacity to target complex tumours with the radiation dose and avoid adjacent structures may provide an advantage in some patients, such as those with small volume tumours located near critical organs.
- IMRT has the potential to reduce the rate and severity of treatment side effects such as radiation toxicity compared with 3D-CRT but this needs to be supported by evidence.
- The delivery of IMRT is more complex and requires increased time during the planning stage.
- For comparative safety, MSAC agreed that most of the evidence indicated that IMRT is as safe as, but no safer than 3D-CRT. MSAC noted that some studies suggested reduced acute and late toxicity with IMRT compared with 3D-CRT. However, a number of the comparative studies reported more extended follow-up of patients treated with 3D-CRT than IMRT. Therefore, late events were more likely to have been captured for the 3D-CRT group.
- For comparative effectiveness,. MSAC noted the limited data for IMRT and inconsistent results for tumour response, local control, progression-free survival (PFS) and overall survival. MSAC observed that some of the effectiveness data suggested advantages with IMRT. However, MSAC agreed that there was inadequate evidence of superior health outcomes for IMRT.
- The economic evaluation referenced the 'Assessment of New Radiation Oncology Technology and Treatment' (ANROTAT) and estimates of the incremental cost of delivering IMRT for small and high volume disease. MSAC was concerned that ANROTAT relied heavily on expert opinion for derivation of utilities, quality of life (QoL) of various health states and costs and that at times these appeared unreasonable (e.g. assuming men with stable prostate cancer but no toxicity are in a perfect health state [a utility of 1.0]).
- MSAC did not support a higher fee for IMRT as there was insufficient evidence of superior effectiveness.
- MSAC was concerned about the additional economic impact of image-guided radiotherapy (IGRT) given this technique would be required at each treatment session. MSAC recommended that if IMRT were to be listed, there should not be any incremental cost arising from IGRT use.
- MSAC discussed concerns raised by the applicant regarding the interpretation of evidence and the validity of the assessment. However, MSAC agreed with ESC that the assessment report generally represented a fair analysis of a poor dataset.

## MSAC's November 2014 consideration

After considering the strength of the available evidence in relation to safety, clinical effectiveness and cost-effectiveness, MSAC deferred the application, noting the co-dependence of IMRT and IGRT, until the Department has provided the further information requested for IGRT.

MSAC concluded that there was insufficient evidence overall of improved health outcomes over the comparator of 3D-CRT, and so foreshadowed its intention to support funding of IMRT on the basis of an implementation strategy that would achieve budget neutrality, such as adopting the same MBS fees as apply to 3D-CRT.

## Summary of consideration and rationale for MSAC's advice

MSAC considered this application alongside MSAC application 1319 IGRT prior to or alongside EBRT including IMRT.

MSAC noted that IMRT for treatment of cancer (curative or palliative) is not specifically listed on the MBS but is currently being funded via existing MBS items for radiation therapy. The applicant is proposing new items and fees for this intervention. IMRT delivers ionising radiation to cancerous cells in a similar way to 3D-CRT. However, while both technologies deliver geometrically shaped beams, the intensity of the beams generated by IMRT is able to be modulated which results in a customisable radiation dose to target a tumour better while sparing surrounding non-tumour tissues therefore potentially improving treatment outcomes. MSAC noted the capacity to sculpt the radiation around complex tumour volumes to avoid adjacent structures may provide a treatment advantage in some patients, such as those with small volume tumours located near critical organs. MSAC observed that while IMRT had the potential to reduce the rate and severity of treatment side effects (i.e., radiation toxicity outcomes), compared with 3D-CRT, the delivery of this intervention would likely be associated with increased complexity and increased time requirements at the treatment planning stages.

Comparative clinical evaluation of IMRT against 3D-CRT was informed by a systematic review of 163 studies, which evaluated safety (acute and late toxicity) and clinical effectiveness (tumour response, local control of tumour, progression-free survival (PFS), overall survival, quality of life) outcomes across a range of cancer types.

MSAC considered that the data indicated there may be benefits for IMRT compared with 3D-CRT in terms of a reduction in acute and late toxicity; however, a large proportion of the literature suggested that IMRT is as safe as but no safer than 3D-CRT despite the increased dose of radiation in several of the studies. MSAC noted that a number of the observational studies reported extended periods of follow-up in patients treated with 3D-CRT compared with IMRT, suggesting a greater opportunity for late events to have been captured in the 3D-CRT group.

MSAC noted that the clinical effectiveness data for IMRT were limited and the results inconsistent for tumour response, local control, PFS and overall survival. MSAC observed that although the effectiveness data suggested some advantages of IMRT, there was inadequate evidence of superior health outcomes, and MSAC concluded that IMRT appears to be as effective as 3D-CRT.

The economic evaluation presented noted data from the 'Assessment of New Radiation Oncology Technology and Treatment' (ANROTAT) study. The results suggested that the cost of delivering IMRT is likely significantly lower than the MBS items which would be claimed currently. However, MSAC noted that the Applicant advised the cost associated with the delivery of IMRT is greater than that estimated in the ANTROTAT study. MSAC was concerned that the conclusions from the ANROTAT study, such as derivation of utilities, QoL of various health states and IMRT costs were heavily reliant on expert opinion rather than actual data and in some cases appeared to be unreasonable – such assuming men with stable cancer but no toxicity are in a perfect health state (a utility of 1.0).

The assessment report also contained data provided by Genesis Care regarding estimates of the incremental cost of delivering IMRT for small and high volume disease compared with

3D-CRT. In this analysis, higher costs were reported for IMRT compared with 3D-CRT for the treatment of both large volume and small volume disease.

MSAC noted the application requested a premium fee for IMRT compared with 3D-CRT, since IMRT is more resource intensive. Given the lack of evidence of superior effectiveness, MSAC considered an increased fee for IMRT was not justified. MSAC also noted that IGRT would be used every time a patient was treated with IMRT and this may also impact on overall costs. MSAC considered that there should not be any incremental cost to the MBS if IMRT was listed.

MSAC noted that the applicant was dissatisfied with the contracted assessment report because the applicant was of the opinion that the report continued to demonstrate a poor understanding of radiation therapy, the application and the data. However, MSAC agreed with ESC that the assessment report generally represented a fair analysis of a poor dataset.

## 3. Background

MSAC has not previously considered IMRT for use in cancer treatment.

This application was considered by ESC in June 2014. Following discussion with the applicant additional analysis was commissioned to revise the assessment report following publication of new evidence.

## 4. Prerequisites to implementation of any funding advice

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

Similar to 3D-CRT, a multi-disciplinary team of radiation oncologists, radiation therapists and medical physicists is required for IMRT.

## 5. Proposal for public funding

Tables 1 and 2 outline the proposed MBS descriptors for the planning and treatment associated with IMRT.

Table 1: Proposed MBS item descriptor for computerised planning for IMRT

| Category 3, Group T2 – Radiation Oncology Computerised Planning |
|---|
| MBS XXXXX<br><br>SIMULATION for Intensity Modulated Radiation Therapy, with or without intravenous contrast medium, where:<br>1. treatment set up and technique specifications are in preparations for IMRT dose planning; and<br>2. patient set up and immobilisation techniques are suitable for reliable CT image volume data acquisition IMRT; and<br>3. a high-quality CT-image volume dataset must be acquired for the relevant region of interest to be planned and treated; and<br>4. the image set must be suitable for the generation of quality digitally reconstructed radiographic images<br><br>DOSIMETRY for Intensity Modulated Radiotherapy treatment plan using CT image volume dataset(s). The planning process must include the following;<br>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.<br>2. All gross tumour targets, clinical targets, planning targets and organs at risk as defined in the prescription must be rendered as volumes<br>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<br>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<br>5. A CT image volume dataset must be used for the relevant region to be planned and treated<br>6. The CT images must be suitable for the generation of quality digitally reconstructed radiographic images.<br>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;<br>a. The determination of the accuracy of the dose fluence delivered by the MLC and Gantry position (static or dynamic).<br>b. Ensuring the plan is deliverable, data transfer is acceptable and validation checks are completed on a linear accelerator.<br>c. Validating the accuracy of the derived IMRT treatment plan in a known dosimetric phantom.<br>d. Determining the accuracy of planned doses in comparison to delivered dose to designated points within the phantom and/or dosimetry device.<br><br>Fee: Under development |

Table 2: Proposed MBS item descriptor for treatment delivery using IMRT

| Category 3, Group T2 – Radiation Oncology – Megavoltage |
|---|
| MBS XXXXX<br><br>Radiation Oncology Treatment with IGRT imaging facilities utilizing an intensity modulated treatment delivery (fixed or dynamic gantry linear accelerator or non linear accelerator) mode at each attendance at which treatment is given using a IMRT Plan (in association with MBS Item 15564).<br><br>Fee: Under development |

IMRT requires the same patient referral pathway as 3D-CRT. IMRT may be curative or to palliate. Radiation therapy requires a multidisciplinary team including radiation oncologists, medical physicists and radiation therapists. Some site-specific cancers may also involve a diagnostic radiologist and/or surgeon.

## 6. Summary of Public Consultation Feedback/Consumer Issues

Consumers expressed concern that IMRT may lead to higher costs for the community, specifically staffing and capital costs. It was noted that some consumers may assume that the latest treatments are the best treatments because of a lack of information about radiation exposure and side effect management. This can make it difficult to assess impact of some treatments on safety and wellbeing. This is particularly relevant to consumers with cancer who depend on their clinicians to provide evidence based advice on treatment when they are at their most vulnerable.

The Protocol Advisory Sub-Committee (PASC) received two responses to the public consultation request from professional bodies (the Australasian College of Physical Scientists and Engineering in Medicine and the Royal Australian and New Zealand College of Radiologists) and thirteen responses from the public.

Overall, public consultation feedback for the proposal was positive, although concern was expressed about the greater financial and resource investment required. It was noted that IMRT requires a robust and quality assurance framework to ensure safe, effective delivery.

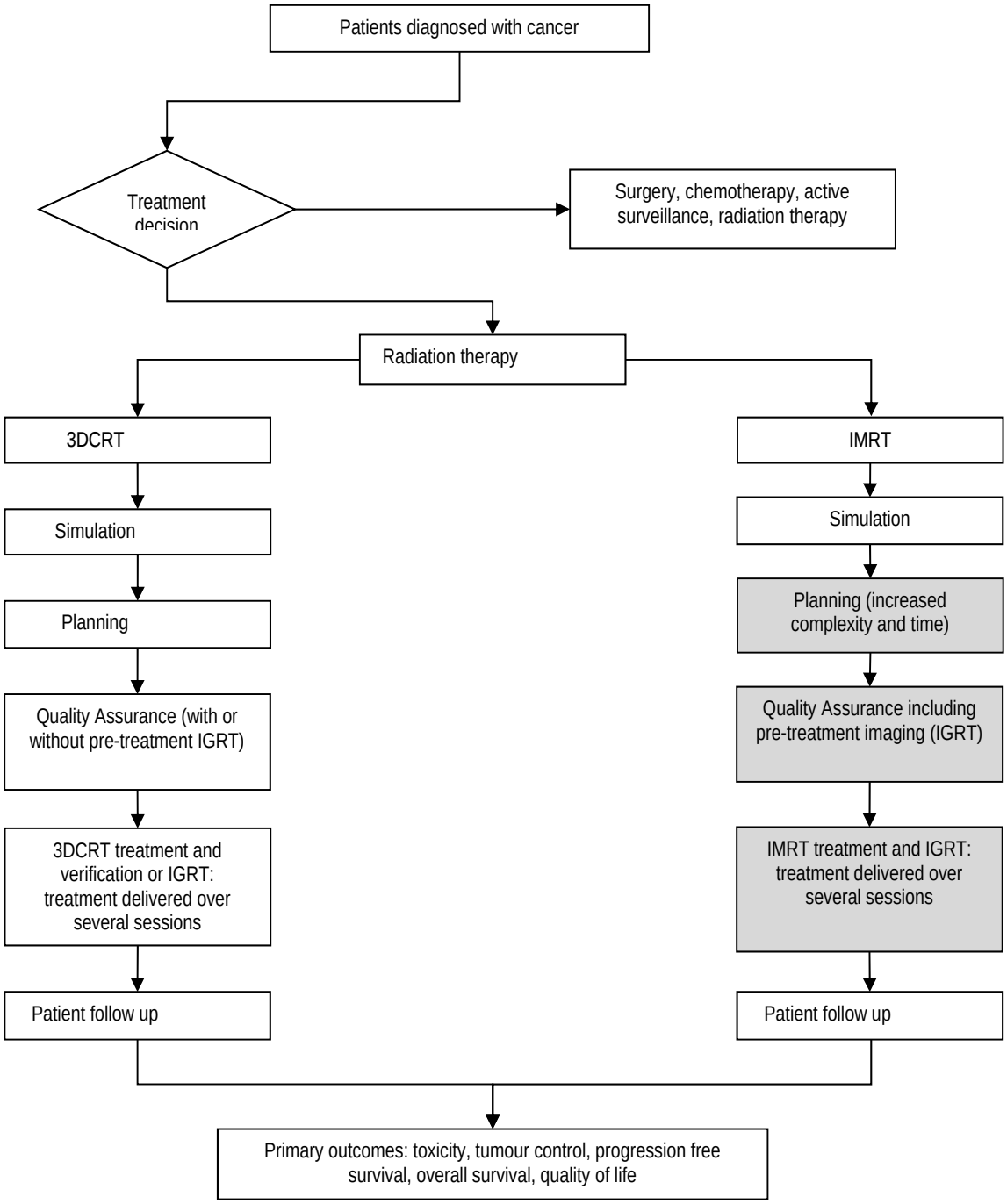
Public consultation supported IMRT based on the claimed advantages noting that it may lead to better patient outcomes as it is able to more accurately target tumours, reduce toxicities associated with radiation therapy and, by extension, increase survival and progression free survival.

It was noted that the fee for IMRT should take into account the increased complexity.

## 7. Proposed intervention's place in clinical management

IMRT is a form of external beam radiation therapy (EBRT) delivered with a linear accelerator ("linac"). Both 3D-CRT and IMRT deliver ionising radiation in geometrically shaped beams to cancer cells. However, with IMRT the intensity of each beam can be modulated. This means that the treatment can be customised to maximise the radiation dose delivered to the tumour. In addition, the radiation dose can be sculpted around complex tumour volumes making it attractive for the treatment of tumours that are adjacent to critical organs. It is claimed that this results in better outcomes compared with 3DCRT, including reduced incidence and severity of side effects such as acute and late toxicity (Hummel 2010). The application claims that IMRT is more complex, requires more planning time and is more resource intensive than 3D-CRT. It is proposed for treatment of generic cancers. While not all patients will require IMRT, that there are circumstances where this treatment would be preferred over 3D-CRT, such as with prostate, anal and head and neck cancers.

Figure 1 shows the generalised clinical management algorithm for cancer patients undergoing radiotherapy. Differences between 3D-CRT and IMRT are highlighted in grey.




## 8. Comparator

At present, the standard of care in radiation therapy is 3D-CRT. Treatment with 3D-CRT is delivered using a linear accelerator with a computerised planning system. The technology is widespread throughout Australian radiation therapy departments.

The proposed comparator, 3D-CRT, is reimbursed under existing MBS items, which are also being claimed for IMRT. The majority of these services are provided as non-admitted patient services.

For the purposes of this assessment, IMRT is considered a direct substitute for 3D-CRT (when applicable for the patient).

## 9. Comparative safety

The comparative acute and late/chronic safety of IMRT and 3D-CRT studies are categorised in tables 3 and 4.

Table 3 Overall summary of the comparative acute toxicity associated with IMRT versus 3D-CRT

| Cancer | RCT | | | Comparative studies | | |
|---|---|---|---|---|---|---|
| | Favours IMRT | No difference | Favours 3D-CRT | Favours IMRT | No difference | Favours 3D-CRT |
| Brain | - | - | - | - | N=1 (n=54) | - |
| Breast | N=2 (n=751) | N=1 (n=851) | - | N=5 (n=1568) | N=1 (n=233) | - |
| Connective tissue | - | - | - | N=1 (n=375) | - | - |
| Gastrointestinal | - | - | - | N=6 (844) | N=6 (300) | - |
| Gynaecological | N=1 (n=44) | - | - | N=5 (n=685) | N=2 (n=194) | N=1 (n=48) |
| Head & neck[c] | N=1 (n=60)[a]<br>N=4 (n=826)[b] | N=1 (n=94) | - | N=9 (n=1680) | N=6 (n=913) | - |
| Immunological | - | - | - | N=1 (n=90) | N=1 (n=94) | - |
| Lung[c] | - | - | - | - | N=3 (n=448) | N=1 (n=544) |
| Prostate[c] | - | - | - | N=13 (n=5582) | N=9 (2043) | N=1 (n=44) |
| Skin | - | - | - | - | - | - |

N=number of studies; (n=number of patients, based on number randomised or enrolled)

[a] includes Nutting 2011 and Gupta 2012

[b] includes Nutting 2011, Gupta 2012, Kam 2006 and Peng 2012

[c] excludes SEER data

Table 4 Overall summary of the comparative late/chronic toxicity associated with IMRT versus 3D-CRT

| Cancer | RCT | | | Comparative studies | | |
|---|---|---|---|---|---|---|
| | Favours IMRT | No difference | Favours 3D-CRT | Favours IMRT | No difference | Favours 3D-CRT |
| Brain | - | - | - | N=1 (n=26) | N=1 (n=54) | - |
| Breast | N=2 (n=1033) | N=1 (n=486) | - | N=1 (n=172) | N=2 (n=343) | - |
| Connective tissue | - | - | - | - | N=1 (n=375) | - |
| Gastrointestinal | - | - | - | N=2 (n=461) | N=5 (n=302) | - |
| Gynaecological | - | - | - | N=4 (n=802) | N=3 (n=326) | N=1 (n=33) |
| Head & neck | N=2 (n=182)[a]<br>N=4 (n=826)[b] | - | - | N=13 (2167) | N=8 (n=1604) | - |
| Immunological | - | - | - | - | N=1 (n=94) | - |
| Lung | - | - | - | N=2 (n=541) | N=2 (233) | - |
| Prostate[c] | - | - | - | N=11 (n=4429) | N=12 (n=4763) | - |
| Skin | - | - | - | - | - | - |

N=number of studies; (n=number of patients, based on number randomised or enrolled)

[a] includes Nutting 2011 and Gupta 2012

[b] includes Nutting 2011, Gupta 2012, Kam 2006 and Peng 2012

[c] excludes SEER data

While the data suggest there may be less late toxicity from IMRT compared with 3D-CRT, most of the literature indicates that there is no difference.

## 10. Comparative effectiveness

Tumour response

Two studies reported tumour response to IMRT or volumetric modulated arc therapy (VMAT) compared with 3D-CRT in the treatment of oesophageal and non-small cell lung cancer (NSCLC) cancer. Neither study reported any statistical analysis of the observed rates of progressive or stable disease, or partial or complete response. While the results reported for oesophageal cancer did not indicate any differences between treatments, those reported for NSCLC appeared to favour VMAT.

Local control

A number of included studies reported local control rates:

- One study reported that 24% and 72% of IMRT and 3D-CRT patients treated for brain cancer experienced local tumour progression (statistical analysis not reported).
- A study including patients with connective tissue sarcomas reported no statistically significant differences between treatments for loco-regional control at 5 years.
- Among the gastrointestinal cancer studies, local tumour progression was not statistically significantly different between treatments in the three studies reporting this outcome.

- Two gynaecological cancer studies reported no statistically significant differences between treatments for loco-regional control at 1 year or 3 years.
- Fourteen of the head & neck trials/studies reported loco-regional control. Whilst five studies reported statistically significant better loco-regional control in those treated with IMRT compared with 3D-CRT, no differences were reported in nine studies.
- Four-year local control was not statistically different in patients with lymphomas treated with IMRT or 3D-CRT.
- One study reported a significantly better 1-year local control in lung cancer patients treated with IMRT compared to 3D-CRT, whereas no significant difference was observed between the treatments in two others.

Progression-free survival (PFS)

A number of studies included in this review reported comparative progression-free survival:

- Of the studies reporting PFS amongst patients with brain cancer who were treated with IMRT or 3D-CRT, one reported that 71% and 64% of IMRT and 26% and 18% of 3D-CRT patients remained progression free at 1 and 2 years, respectively (statistical analysis not reported). Another study reported no statistically differences in PFS between treatments at one year.
- Statistically significantly improved 3-year PFS was observed in patients with anal cancer treated with IMRT in one study, however no differences were observed at 3 years or at 2 years in three other studies. Similarly, no differences were observed between treatments in a study including patients treated for gastric cancer at 2 years or in two other studies including patients with pancreatic or rectal cancer.
- Among the gynaecological cancer studies, significantly improved PFS was observed in one study, but no differences were observed for 2-year PFS or 5-year disease free survival in two other studies.
- Two-year disease free survival was statistically significantly improved among those treated with IMRT compared with 3D-CRT for head & neck cancers in one study, but no difference in this outcome was observed in three other head & neck cancer studies.

Overall survival

Thirty-five studies included in this review reported comparative overall survival. Of these:

- Seven studies – (one brain, one anal one gastric, two cervical and two head & neck cancer studies) reported statistically significantly improved overall survival amongst those treated with IMRT compared with 3D-CRT, whereas,
- Twenty-seven studies reported no differences: one brain, one breast, three anal, three gastric, two oesophageal, one rectal, two cervical, and 14 head & neck cancer studies; and
- One study reported statistically significantly improved overall survival in patients with prostate cancer treated with 3D-CRT compared with IMRT.

Quality of life

Quality of life (QoL) assessments were reported in head & neck (nine studies) and prostate cancer (four studies).

In the head & neck cancer studies, seven studies reported statistically significant differences between the treatment groups (although that the impact of IMRT was small on all QoL scales in one study), and two studies observed no significant differences.

In the prostate studies, no significant differences in QoL measures were observed in any of the studies.

## 11. Economic evaluation

The application sought an MBS fee based on costing information contained in the ANROTAT study.

The assessment report provided a cost-minimisation analysis. This was appropriate given the lack of evidence supporting superior safety and effectiveness outcomes for IMRT.

Costs were based on estimates from the ANROTAT study for the treatment of prostate, anal and nasopharyngeal cancer ($2,216, $3,111 and $3,197). The assessment report found that, depending on assumptions, the cost of delivering IMRT was likely significantly lower than the items which would be claimed currently.

However, the applicant advised that the cost associated with delivery of IMRT would be greater than that estimated in ANROTAT, because of greater planning and capital costs. GenesisCare (the largest private-sector provider of radiation therapy services in Australia) subsequently provided estimates of the *incremental* cost of delivering IMRT for small and high volume disease compared with 3D-CRT. In the table below, the assessment group used these figures to derive *total* costs for delivering IMRT compared to 3D-CRT. However, it should be noted that the Department is yet to fully verify the cost impacts of IMRT (compared to 3D-CRT).

Table 5 Total costs associated with delivering 3D-CRT and IMRT for small and high volume disease based on the data provided by Genesis Care

| Component | Small volume disease | | | High volume disease | | |
|---|---|---|---|---|---|---|
| | 3D-CRT | IMRT | Increment | 3D-CRT | IMRT | Increment |
| Delivery costs | | | | | | |
| Doctor time | *$573* | *$701* | $127 | *$892* | *$637* | $255 |
| RT time | *$1,389* | *$1,941* | $551 | *$1,759* | *$2,603* | $845 |
| Physics time | *$15* | *$91* | $76 | *$15* | *$91* | $76 |
| Total per course (delivery) | *$1,978* | *$2,733* | $755 | *$2,411* | *$3,586* | $1,176 |
| Associated costs | | | | | | |
| Payroll tax | *$99* | *$137* | $38 | *$121* | *$179* | $59 |
| Equip & maintenance[a] | *$906* | *$1,449* | $543 | *$906* | *$1,449* | $543 |
| Medial and Associated | - | - | $0 | - | - | $0 |
| Floor space/bunker | - | - | $0 | - | - | $0 |
| Rent | - | - | $0 | - | - | $0 |
| Outgoings | - | - | $0 | - | - | $0 |
| Utilities[b] | *NR* | *NR* | $28 | *NR* | *NR* | $36 |
| Communications[c] | *NR* | *NR* | $28 | *NR* | *NR* | $36 |
| Staff related[d] | *$59* | *$82* | $23 | *$73* | *$108* | $35 |
| Overheads[e] | *$99* | *$137* | $38 | *$121* | *$179* | $59 |
| Total per course[f] (delivery + associated) | *$3,141* | *$4,538* | $1,452 | *$3,632* | *$5,501* | $1,944 |
| Depreciation & interest costs | | | | | | |
| Depreciation[g] | *$1,468* | *$2,797* | $1,329 | *$1,468* | *$2,797* | $1,329 |
| Interest[h] | *$354* | *$720* | $366 | *$354* | *$720* | $366 |
| Total per course[f] (delivery + associated + depreciation & interest) | *$4,963* | *$8,055* | $3,147 | *$5,454* | *$9,018* | $3,638 |

[a] 3D-CRT linac=$375,000/414 courses ($906); IMRT linac=$442,500/414 courses ($1,068) = difference of $163. Paid for the capability to conduct IMRT, but only applied in 30% of cases, thus increment is $163/30% = $543. Total cost for IMRT = $906+$543 = $1,449

[b] additional $1.00/attendance for additional power

[c] additional $1.00/attendance for additional data

[d] 3.0% for staffing costs

[e] 5.0% for staffing costs

[f] total costs calculated for 3D-CRT and IMRT excluding utility and communications costs as these could not be elucidated from the available data. Incremental costs include these variables.

[g] 3D-CRT linac=$607,798/414 courses ($1,468); IMRT linac=$772,798/414 courses ($1,867) = difference of $399. Paid for the capability to conduct IMRT, but only applied in 30% of cases, thus increment is $399/30% = $1,329. Total depreciation for IMRT = $1,468+$1,329 = $2,797

[h] 3D-CRT linac=$3,857,500/414 courses *3.8% ($354); IMRT linac=$5,057,500/414 courses * 3.8% ($464) = difference of $110. Paid for the capability to conduct IMRT, but only applied in 30% of cases, thus increment is $110/30% = $366. Total interest for IMRT = $354+$366 = $720

## 12. Financial/budgetary impacts

MSAC agreed that based on a cost minimisation approach, the cost of a course of IMRT should not exceed that of 3D-CRT. This should not result in any incremental cost to the MBS.

## 13. Key issues from ESC for MSAC

ESC noted that the applicant was of the opinion that the report continued to demonstrate a poor understanding of radiation therapy, the application, and the data. While taking into account the applicant's concerns, ESC considered that the assessment generally represented a good analysis of a poor dataset.

In considering the ANROTAT study, ESC noted that the conclusions from the study were heavily reliant on expert opinion from TROG (such as in the determination of transition probabilities and quality of life of various health states). ESC supported the exclusion of the ANROTAT study from the evidence section of the assessment report, but considered its outcomes in reaching the views.

ESC noted the recent publication in peer-reviewed literature of the Beadle et al (2014) paper. ESC considered that the quality of the study was not low and represented a good use of observational data, noting that the authors tried to account for selection bias by using propensity score matching and an Instrumental Variables (IV) approach. ESC noted that, to be a valid instrument, clinician experience must affect patient outcome via the provision of IMRT, and not directly (i.e. not independently of the provision of IMRT). That is, to affect patient outcomes, clinician experience must be correlated with the decision by the clinician to offer IMRT as a treatment option and not directly correlated with patient outcomes. Based on this, ESC considered the chosen IV in Beadle et al (2014) to be a weak instrument because of the argument that it is plausible that a clinician's experience could affect patient outcomes independently of the choice of IMRT or 3D-CRT.

ESC also considered that the study did not inform a comparison of IMRT against the comparator that PASC recommended (and the applicant accepted) – 3D-CRT – as the study assumed individuals who did not have an IMRT planning code were treated with either 2D-CRT or 3D-CRT.

ESC noted that IGRT (image-guided radiation therapy) is likely to be used every time a patient is treated with IMRT and that the imaging requirements for IMRT are considerably greater than for 3DCRT.

ESC noted ARPANSA advice that they have not assessed the radiation safety of IMRT. However, ESC also noted advice from the Faculty of Radiation Oncology that TROG has performed three dosimetric studies and that 34 site visits have been performed in 25 radiation therapy centres in Australia and New Zealand. ESC considered that further data from these site visits would be useful.

ESC noted the cost minimisation approach against 3D-CRT was adopted due to inconsistent evidence of improved safety and clinical benefit of IMRT. ESC considered this was appropriate and noted that Australian cost data were used by the assessment group by applying a "bottom-up" costing approach (using Genesis Care incremental cost estimates) and a "top-down" costing approach (using MBS fees). ESC noted the applicant disagreed with the cost-minimisation analysis and its conclusions, and also noted the applicant's view that the costs proposed in the ANROTAT study were not indicative of the full cost, nor of costings available from Genesis Care.

ESC noted the detailed discussion of the utilities used in the ANROTAT study. While data enabling the computation of QALYs were collected from patients undergoing IMRT and 3D-CRT in the ANROTAT study, these were not reported. Rather the reported utilities were derived from a standard gamble exercise with eight radiation therapy professionals. ESC noted that some of the resulting utilities (e.g. a value of unity—indicating perfect health—for time without symptoms or toxicity [TWiST] among cancer survivors) were implausible. ESC noted additional uncertainties outlined in the Assessment Report in respect of the utilities used in the ANROTAT modelling for various grades of acute and late toxicity.

ESC noted that IGRT necessary for IMRT involves a much higher workload for medical physicists; and that there is an international shortage of medical physicists. This may have an impact on patient access if IMRT and IGRT are listed on the MBS.

ESC noted that, should MSAC agree that the evidence does not support higher MBS reimbursement, there appears to be no reason to create separate MBS items for IMRT (separate to 3D-CRT), unless it was thought to be useful to document future IMRT utilisation. However, should the same item numbers be used for IMRT as for 3D-CRT, the item descriptors would need to be revised.

## 14. Other significant factors

Nil

## 15. Applicant's comments on MSAC's Public Summary Document

The Faculty of Radiation Oncology (FRO) commends the MSAC for the development of an MBS item number for IMRT, which will enable the collection of good quality data on its utilisation. However, we still contend there is ample evidence for the efficacy and safety of IMRT – which is already the global standard of care for many cancer patients, such as those with head and neck, genitourinary and anal cancers. In fact, when assessing cases for the Australian government's Medical Treatment Overseas Program (MTOP), it has long been accepted by the Department of Health (DoH) that IMRT is the appropriate comparator to use in these complex cases, rather than 3DCRT. We also wish to reiterate our disappointment in the way Assessment of New Radiation Oncology Technology and Treatments (ANROTAT) data and framework have been dealt with/interpreted, given the significant investment, guidance and oversight received from the DoH in its development, as well as the fact that peer reviewed publications from ANROTAT are now appearing. In fact, the ANROTAT Markov model in assessing cost-benefit is gaining acceptance in the academic literature as a sound and reliable assessment model.

(See http://jop.ascopubs.org/content/8/3S/e31s.full and http://www.ncbi.nlm.nih.gov/pubmed/24929702).

The focus on randomised controlled trials (RCTs) to gain evidence regarding new or evolving technologies and techniques in radiation therapy has to change, because the developments in technology and techniques are incremental. Also, subjecting cancer patients to RCTs in this setting to gain evidence (including cost-benefit and cost utility) is difficult and presents ethical challenges. Radiation therapy uses similar principles across the board – delivering radiation to the cancer while minimising radiation to the surrounding healthy tissue. An RCT that would randomise some patients into an arm where they get less radiation to the cancer and/or more to normal organs cannot be ethically supported.

## 16. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website at: www.msac.gov.au.