Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1147 - Implantation of fiducial markers into the prostate gland or prostate surgical bed for external beam radiotherapy

Sponsor/Applicant/s: **Royal Australian and New Zealand College of Radiologists (RANZCR) and the Australia and New Zealand Association of Urological Surgeons (ANZAUS)**

Date of MSAC consideration: **1 August 2013**

1. Purpose of application

In April 2010, an application requesting the MBS listing of implantation of fiducial markers (FMs) into the prostate gland or prostate surgical bed for External Beam Radiotherapy (EBRT) was received from the Royal Australian and New Zealand College of Radiologists (RANZCR) and the Australian and New Zealand Association of Urological Surgeons (ANZAUS) by the Department of Health.

The proposed medical service involves the implantation of radio-opaque, sterile FMs into the prostate to serve as fiducial reference points during radiotherapy in patients with prostate cancer. Prior to radiotherapy treatment planning and delivery, FMs (usually 3-4) are implanted into the prostate using a trans-rectal or trans-perineal needle insertion approach under ultrasound guidance. Some form of anaesthesia (usually local) may also be used during the procedure. It may be provided in an ambulatory care setting or in a day surgery facility. Healthcare professionals involved in providing the service may include radiologists, urologists, radiation oncologists, or other appropriately skilled physicians who are skilled in the use of trans-rectal ultrasound, anaesthetists or theatre staff as required. The proposed service is not a therapeutic medical service on its own but rather is used as part of the delivery of EBRT.

The proposed medical service is currently covered under an interim funded MBS item 37217, introduced on 1 July 2011 to enable collection of data on usage to inform the current assessment. The service had previously been claimed under another MBS item (37218) which referred to 'PROSTATE, needle biopsy of, or injection into (Anaes.)' without specifying what was injected or for what purpose. Billing of item 37218 for this procedure was prohibited by the Department from 1 January 2010.

The proposed medical service is intended primarily for patients who undergo EBRT for the local control of prostate cancer. The current standard for EBRT in Australia is 3-dimensional conformal radiotherapy (3D-CRT) with intensity-modulated radiotherapy (IMRT) as an emerging technique. EBRT may be delivered alone or in combination with high-dose rate

brachytherapy (HDRBT) as a boost. The Final Decision Analytic Protocol (DAP) for the current assessment also includes a smaller, secondary target population: prostate cancer patients who undergo adjuvant or salvage EBRT after radical prostatectomy. The overall target population for the proposed medical service is therefore: patients with prostate cancer, scheduled for EBRT (definitive or post-prostatectomy, using 3D-CRT or IMRT, with or without dose escalation or boost).

2. Background

There have been no previous MSAC reviews for the implantation of fiducial markers into the prostate gland or prostate surgical bed for external beam radiotherapy. Comparable and related reviews are listed below in Table 1.

As described above, the proposed medical service had previously been claimed under another MBS item (37218) which referred to 'PROSTATE, needle biopsy of, or injection into (Anaes.)'. Billing of item 37218 for this procedure was prohibited by the Department from 1 January 2010, and was amended to specifically exclude the implantation of radio-opaque markers; a new, interim-funded item (37217) for implantation of FMs was introduced on 1 July 2011.

This is the first review of the interim item, with cessation or continuation of the item dependent on the MSAC outcome.

Applications 1319, 1182 and 1211 are most relevant to the current assessment, and are undergoing the MSAC assessment process. These items were considered by the Protocol Advisory Sub-Committee (PASC) in December 2012.

Table 1. Other applications/reviews relevant to the current assessment

No	Application title	Progress
1319	The use of Image Guided Radiation Therapy (IGRT) in the treatment of cancer	2nd PASC in December 2012, Final DAP released
1211	Volumetric Modulated Arc Therapy for Lung, Prostate, breast and other extra-cranial cancers such as spine, kidney, liver and pancreatic	2nd PASC in December 2012, Final DAP released
1182	The use of Intensity Modulated Radiation Therapy (IMRT)	2nd PASC in December 2012, Final DAP released
1158	Robotic image-guided stereotactic precise beam radiosurgery and radiotherapy for lung cancer and prostate cancer	Completed, MSAC appraisal in December 2012, MSAC minutes released
1089.1	Review of Interim Funded Service: Brachytherapy for the Treatment of Prostate Cancer	Completed, considered by the MSAC in December 2010, MBS item 15338 implemented

3. Prerequisites to implementation of any funding advice

The proposed service involves the use of a medical device that is not exempt from the regulatory requirements of the *Therapeutic Goods Act 1989* (Section 2.5, the Application). The medical device, 'Nucletron Pty Limited – Marker, lesion localization, implantable; Australian Register of Therapeutic Goods (ARTG) Entry 143069' mentioned in the Application (Section 2.5, the Application) has an identical product registered under Entry 141476. Both ARTG Entry 141476 and Entry 143069 were registered with the TGA, with 141476 registered in 2007. For unknown reasons, possibly due to a modification of product, Entry 143069 was cancelled in 2011.

A number of implantable medical devices under the same product name of 'marker, lesion localization, implantable' relevant to the current assessment are identified in the ARTG (Appendix D, Assessment Report). This list may not be exhaustive.

Some radiation oncology services also make up FMs "in-house", which are not subject to TGA approval.

4. Proposal for public funding

The proposed item descriptor (Table 2) is the same as the PASC approved item descriptor, which was presented within the Final DAP, with an exception that there has been a proposed addition of the following qualifying statement in the Assessment Report:

"The procedure must be performed by a urologist or a radiation oncologist at an approved site, and be associated with a service to which item 55603 applies."

The reasoning for the proposed addition is that the proposed procedure will be performed by a urologist or radiation oncologist skilled in the use of trans-rectal ultrasound (as stated on p.14 of the Application), and that other similar implantation procedures also have similar interim item description (e.g. implantation of radioactive seeds for brachytherapy for MBS item 37220).

Table 2 Proposed MBS item descriptor

Category 3 – THERAPEUTIC PROCEDURES
MBS [item number XXXXX] Prostate, implantation of radio-opaque fiducial markers into the prostate gland or prostate surgical bed to assist in the delivery of external-beam radiotherapy. The procedure must be performed by a urologist or a radiation oncologist at an approved site, and be associated with a service to which item 55603 applies. Multiple Services Rule (Anaes.) Fee: $138.30 Benefit: 75% = $103.75 85% = $117.60

ESC identified issues with the item descriptor regarding the clinicians specified to provide the service, the definition of an 'approved site' and the use of ultrasound with the proposed service. This is discussed later in this document (p.11).

The proposed schedule fee is the current schedule for the interim MBS item 37217, introduced on 1 July 2011 to cover the proposed medical service pending outcome for the current assessment. Current MBS explanatory notes on multiple services rule are presented in Appendix E of the Assessment Report.

5. Consumer Impact Statement

The use of implanted prostate FMs and planar kilovoltage (kV) or megavoltage (MV) imaging is the most frequently used IGRT technique in Australia (Hayden 2010). As the proposed service is not a new service and is already reimbursed under interim MBS item 37217, the proposed listing is not anticipated to have any major impact/change in public access to the service.

If a patient is ineligible for this service, or the service is not available, the alternative technique for prostate irradiation would continue to be the conventional method using bony landmarks. There would be no additional costs to the patient associated with this.

6. Proposed intervention's place in clinical management

Conventionally, bony landmarks are used as surrogates for prostate position. The disadvantage of this method is that the prostate is not imaged directly, so the planned

planning target volume (PTV) must be larger than the soft tissue target (clinical target volume [CTV]) to account for uncertainties in the position of the CTV. The consequences of this are that the surrounding normal tissue is at risk of receiving radiation dosages that are higher than desirable, elevating the risk of normal tissue toxicity and side effects. There is a consequent limit to the radiation dose that can safely be delivered to the CTV, possibly resulting in a lower probability of tumour control.

Pre-implanted radio-opaque FMs facilitate image-guided radiotherapy (IGRT) by allowing the position of these markers to be checked during the delivery of RT against reference images derived at the treatment planning process. This, in turn, creates the possibility of improving the treatment by decreasing the planning target volume (PTV) margin, the dose delivered to the adjacent critical structures (e.g. bladder and rectum) and thus may have the potential benefit of decreased RT-related toxicity. More accurate delivery of treatment may also allow escalated doses of RT to be delivered to the clinical target.

The proposed medical service is intended to be used as image guidance in daily RT treatment verification/correction, in patients scheduled for definitive EBRT for prostate cancer or in patients scheduled for adjuvant/salvage EBRT post-radical prostatectomy. It is expected that the proposed medical service will substitute directly for the use of bony landmark-based image guidance in radiotherapy treatment verification/correction. Prior to the listing of the interim funded MBS item 37217, clinicians had been performing the procedure and claiming a subsidy for it under item MBS 37218. MBS item 37218 was revised at the time of the introduction of MBS 37217 to prohibit that practice.

7. Other options for MSAC consideration

Nil

8. Comparator to the proposed intervention

The comparator is intermittent verification of the target using bony landmarks. This is accepted as appropriate in the Final DAP.

The comparator of intermittent target verification using bony landmarks is not listed within the MBS, as the comparator is built into the oncology treatment clinical pathway.

9. Comparative safety

The assessment of the procedural safety of the implantation of FMs is based on four large case series (Gill 2012; İğdem 2009; Langenhuijsen 2007; Escudero 2010) which specifically assessed adverse events (AEs)/complications following implantation of FMs for EBRT.

The majority of the AEs reported in the four case series were transitory in nature, with most resolving within two weeks of implantation. Minor AEs included haematuria lasting longer than three days, voiding complaints and obstructive symptoms. AEs reported across all four studies included rectal bleeding, pain and fever. For patients with pain, a proportion received analgesics; similarly, patients with fever were given antibiotics. In one study, three patients required hospitalisation as a result of fever, with one of those patients developing septicaemia (grade 4 infection) following insertion of FMs (Gill 2012). Two studies reported marker migration or misplacement that did not result in any clinical sequelae (Escudero 2010; Langenhuijsen 2007).

Overall, the majority of patients who undergo implantation of FM have no, or minor AEs. However, a small percentage of patients may experience moderate complications, potentially resulting in further medical intervention. None of the safety studies included patients receiving adjuvant/salvage post-prostatectomy.

10. Comparative effectiveness

Table 3 Summary of clinical evidence to inform comparative clinical effectiveness and safety

Clinical outcomes	Basis of evidence	Summary of evidence and interpretation
Survival	None	No comparative evidence identified
Local tumour control	One case series with historical controls (Zelefsky 2012)	• PSA relapse-free survival at 3 years was significantly better for high-risk patients in the high-dose IMRT (86.4 Gy) cohort with FM as image guidance (97%) versus the cohort without FM (77.7%). Note however that only 35 high-risk patients contributed to the survival data in the FM group. In addition, it is not clear about the applicability of study results to clinical practice in Australia as the ultra-high dose of 86.4 Gy used in the study is rare in Australia (see eviQ clinical guidelines in Appendix C, Assessment Report).
Health-related QoL	One case series with historical controls (Lips 2007)	• There was no significant difference in change in mean QoL scores between the FM group (IMRT) and non-FM group (3D-CRT) except for 6 QoL items at one month after completion of RT favouring FM for 5 of the 6 items. Between-group difference was not statistically significant for any of the QoL items at 6 months after completion of RT Validity of results of between-group comparison is highly uncertain as the comparison groups differed in more than one aspect apart from the use of FMs in one group (e.g. dose-escalated IMRT was used in the FM group versus 3D-CRT without dose-escalation in the non-FM group; clinical practice may differ as there was a big gap in study period between the 2 groups-2003/04 versus 1997/2001)
Treatment-related morbidity – GI or rectal AEs	4 case series with historical controls	• Risk of acute grade 1 GI AEs appears to be greater with FM-based EBRT than with bony landmark-based EBRT, while risk of acute grade 2 GI AEs appears to be lower with FM-based EBRT. • Self-assessed moderate to severe rectal AEs (diarrhoea, rectal pain, urgency) were significantly lower in the FM group compared with the non-FM group at 8-26 months after 3D-CRT. • 3-year ≥grade 2 rectal AEs was low and similar for both FM and non-FM groups, despite the use of ultra-high dose IMRT (86.4 Gy) (Zelefsky 2012)
Treatment-related morbidity – GU AEs	4 case series with historical controls	• Risk of acute grade 1 GU AEs was greater while grade 2 AEs was lower with the FM group than with the non-FM group in 2 studies (Zelefsky 2012; Chung 2009). • Gill (2011) reported the reverse direction of results at 6 months after RT; in addition, risk of grade 3 GU AEs was lower with the FM group. • Self-assessed moderate to severe urinary AEs were similar in the FM and non-FM groups at 8-26 months after 3D-CRT (Singh 2013) • 3-year ≥grade 2 GU AEs were significantly lower in the FM group than in the non-FM group, despite the use of ultra-high dose IMRT (86.4 Gy) (Zelefsky 2012).
Safety of the implantation of FMs	4 cohort studies/case series	Most complications were minor and were of a transitory nature, with few lasting longer than 2 weeks. The most serious complication occurred in a study of 234 men, where one patient developed a grade 4 infection (sepsis)

Overall, there is a lack of high level evidence to compare the clinical effectiveness of FM-based EBRT versus bony landmark-based EBRT in patients receiving definitive EBRT for prostate cancer. There is no evidence available to compare clinical effectiveness in patients receiving adjuvant/salvage EBRT post-prostatectomy.

11. Economic evaluation

Owing to the lack of high level evidence to compare clinical effectiveness and safety of FM-based versus bony landmark-based EBRT, a simple cost comparison analysis is presented within Assessment Report, under Table ES.5. The results are presented of the cost comparison analysis, based on the assumption of similar clinical effectiveness and safety of FM-based and bony landmark-based EBRT.

The Assessment group was asked to revise this cost comparison to take into account all known costs both to the Government and to the patient of the implantation procedure, noting differences between services performed in and out of hospital.

The Assessment group was asked to provide a cost comparison for EBRT for the following four scenarios.

1. Bony landmark-guided EBRT with 10 pre-treatment verifications;
2. Bony landmark-guided EBRT with 37 pre-treatment verifications;
3. FM-based EBRT with 37 pre-treatment verifications; and
4. FM-based EBRT with dose escalation (2 extra fractions) and 39 pre-treatment verifications.

12. Financial/budgetary impacts

The Assessment group was asked to revise the financial impacts taking into consideration all costs to the MBS, such as the EMSN flow on, accounting for inpatient and outpatient service volumes, and the four above case scenarios (11. Economic Evaluation Scenarios).

ESC was also concerned that the financial implications may have been grossly understated by the suggested level of uptake of only 30%, when the descriptor would mean that the maximum possible uptake could be as high as 99%.

A revised cost analysis based on Departmental 2011-12 utilisation data, estimated the weighted total cost to the MBS (including EMSN) to be $177.92 (including $4.72 average EMSN cost) per implantation procedure conducted out-of-hospital and $277.10 per implantation procedure undertaken in-hospital. Based on the percentage split of in-hospital and out-of-hospital procedures for 2011-12 (42.4% versus 57.6% respectively), the weighted average total cost to the MBS (including EMSN) was $219.97 (including $2.72 average EMSN cost) per implantation procedure. The overall weighted average out-of-pocket (OOP) cost was $414.91 per procedure.

For an updated cost comparison, MSAC accepted that the most relevant scenario to current Australian clinical practice consistent with the clinical advice provided by RANZCR and USANZ and with MBS utilisation data was a comparison of:

- FM-based EBRT – total dose 78 Gy, daily pre-treatment verification; against
- Bony landmark-based EBRT – total dose 74 Gy, daily pre-treatment verification.

Under this scenario, the average total cost (MBS incl. EMSN) was estimated to be $12,068.17 per patient for a course of FM-based EBRT versus $11,240.60 for bony landmark-based EBRT, resulting in an incremental cost of $827.57 per patient. The average

total OOP cost was estimated to be $933.22 per patient for a course of FM-based EBRT versus $491.73 for bony landmark-based EBRT, resulting in an incremental cost of $441.49 per patient.

MBS utilisation data, covering the period 1 September 2011 to 31 December 2012, for a cohort of 6,334 patients who received EBRT for prostate cancer within the 2012 calendar year indicated that 1,809 (29%) patients had previously received FMs and of these 1755 (97%) patients have verification items claimed. MSAC noted that the estimated incremental cost to the MBS of FM-based EBRT *vs* landmark-based EBRT was $6.5 million over 4 years.

13. Key issues for MSAC from ESC

Key uncertainties on comparative clinical effectiveness and safety

- There are no head-to-head randomised clinical trials that evaluated the comparative clinical effectiveness and safety of FM-based versus bony landmark-based EBRT.
- The best evidence available on comparative clinical effectiveness is based on a few single institution case series that used FM-based EBRT versus historical case series that used bony landmark-based EBRT in the same institution. Apart from one study (Zelefsky 2012), the differences in the interventions used in the intervention and comparison groups encompassed more than just the use of FM-based versus bony landmark-based image guidance (e.g. different RT techniques were used in Lips (2009)).
- There are no comparative studies (randomised or non-randomised) that evaluated the comparative clinical effectiveness in patients receiving adjuvant/salvage EBRT post-prostatectomy.

Overall, there is a lack of high level evidence to compare the clinical effectiveness and safety of FM-based EBRT versus bony landmark-based EBRT in patients receiving definitive EBRT for prostate cancer or in patients receiving adjuvant/salvage EBRT post-prostatectomy. However there was an indicative trend in the evidence that the intervention is as clinically effective as the comparator.

It was felt by ESC that the new Kok (May 2013) evidence should also contribute to the Assessment for MSAC consideration. Although the Kok study suggested a positive result, it did not provide conclusive evidence. It had a weak design (retrospective, non-randomised), with insufficient survival time horizons, and non-direct comparisons of radiation exposure levels and number of fractions. There was concern over the disparity in the number of patients in each treatment arm. ESC raised concern regarding the Zelefsky study (2012) which gathered evidence on the effectiveness of bony landmarks from 2006-2008 while the evidence on FM was gathered between 2008-2009. This raised the question of the extent to which differences in effectiveness may have been attributable to technological advances that also occurred during this period. For example, it was noted that there have been significant developments in the use of computed tomography (CT) in radiotherapy planning from 2006-2009 and that this may have contributed to the apparent benefit of FM-based over bony landmark-based EBRT guidance observed in this study. ESC therefore queried whether or not the use of CT in radiotherapy planning allowed for an increase in the effectiveness in the identification of bony landmarks, thereby potentially offering similar gains to those obtained with FM guidance.

ESC noted the concerns raised by the applicant that operator skill may affect the clinical effectiveness of the intervention and noted that none of the studies took that issue into account. ESC also noted the following statement from the Australian study by Bell *et al.* (2010, p.84) that "…the accuracy of defining the seed position is limited by a 1x1mm pixel resolution. Consequently, the accuracy of defining the position of objects as small as seed

markers is subjective and operator dependent when viewed at such a high magnification of the image…".

Key uncertainties on procedural safety

- Safety in terms of procedural complications in patients receiving adjuvant/salvage EBRT post-prostatectomy is not known. Local clinical guidelines (eviQ) recommend the use of online daily imaging matching to surgical clips or bony anatomy (Appendix C).

Evidence for the safety of the implantation of FMs is based on four large case series. Overall, FM implantation appears to be safe and well tolerated, with the majority of patients experiencing either no or minor AEs. A small percentage of patients may experience moderate complications; however, the extent of the burden of these complications for both the patient and the health system remains uncertain.

ESC raised the concern that the late and/or long-term AEs were of particular concern when considering the effectiveness of FM-based EBRT compared with standard EBRT. Due to the nature of FMs, it is noted that there are more considerable AEs due to the dose escalation (from 74 Gy, 37 fractions to 78 Gy, 39 fractions) which is available when FMs are used. The Assessment Report lacks sufficient high level evidence on late and long term AEs, and on survival, to reach a definitive conclusion regarding safety.

ESC also noted that the cost estimates fail to account for the physical cost of the FM, the cost of the ultrasound, and the consequential Extended Medicare Safety Net (EMSN) effects that are implied when the FMs are placed in the outpatient setting. The Assessment group was asked to revise the cost model to take account of these shortcomings.

14. Other significant factors

This was discussed by ESC and amendments were made which were:

1. Removal "urologist or a radiation oncologist";

ESC agreed that the MBS item descriptor should not limit the service to being performed only by a urologist or radiation oncologist as there may be other practitioners trained in trans-rectal ultrasound.

2. Removal of "at an approved site";

The descriptor should not be limited to 'approved sites' as the FMs for this item are not radioactive; an approved site is not required.

3. Removal of "associated with a service to which item 55063 applies".

ESC believes that as ultrasound is an integral component in the placement of the FMs, the item descriptor and Schedule fee should explicitly include ultrasound. This would mean that, rather than linking to a specific ultrasound item, the item would include ultrasound being delivered with the intervention. An example of the item descriptor is provided below. MSAC would need to consider the additional fee associated with including ultrasound within this item. The fee for the proposed item could remain the same as the interim item, or it could incorporate all, or part, of the current fee for ultrasound under item 55603.

ESC Suggested Item Descriptor

Category 3 – THERAPEUTIC PROCEDURES
MBS [item number XXXXX] Prostate, implantation of radio-opaque fiducial markers into the prostate gland or prostate surgical bed to assist in the delivery of external-beam radiotherapy under the guidance of trans-rectal ultrasound. Multiple Services Rule (Anaes.) Fee: $138.30 + Ultrasound Component Benefit: (75% = $103.75 85% = $117.60) + Ultrasound Component

ESC noted that there is limited information on the differences and the impact that in-house created FMs might have on the safety and/or effectiveness of the procedure and the savings that may be realised by hospital which may or may not flow on to the patient.
ESC felt that there were issues to be considered with regard to the regulatory and quality assurance aspects associated with the implementation of FM-based EBRT, particularly perhaps when FMs are manufactured by hospitals in-house.

15. Summary of consideration and rationale for MSAC's advice

The applicant proposes that the implantation of radiopaque fiducial markers (FMs) into the prostate gland or prostate surgical bed under transrectal ultrasound (TRUS) guidance in patients with prostate cancer prior to external-beam radiotherapy (EBRT) allows more accurate and reproducible pre-treatment verification of the target tumour volume than conventional verification using bony landmarks. The applicant claims this permits more precise and escalated dose delivery to the target and reduces radiotoxicity to adjacent structures (particularly rectum and bladder), or both. Pre-treatment verification using FMs is applicable to conventional three-dimensional conformal radiotherapy (3DCRT) and to the newer modalities of intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT).
MSAC noted that implantation of FMs into the prostate gland or prostate surgical bed for EBRT is currently funded via interim MBS item 37217, introduced on 1 July 2011. Previously, the service had been claimed under MBS item 37218. The Department became aware that the implantation of FMs into the prostate gland or prostate surgical bed for EBRT was being incorrectly billed under item 37218, which was intended for the "injection" of antibiotics or other medicines, and as such, created the interim listed item 37217 for this service. Billing of item 37218 for this procedure was prohibited by the Department from 1 January 2010.MSAC noted that, because FMs do not currently meet the criteria for listing on the Prosthesis List, patients will likely continue to pay the cost of the FMs if the service is listed on the MBS. The Committee considered this matter should be referred for further consideration by the Department.

MSAC agreed that the appropriate comparator to FM implantation followed by EBRT is EBRT supported by intermittent verification of the target volume relying on bony landmarks.

MSAC noted that the evidence of safety and comparative clinical effectiveness of implantation of FMs was limited and of low quality, and that none of the safety or comparative clinical effectiveness studies included patients receiving adjuvant/salvage EBRT post-prostatectomy.

Based on four large case-control series, the majority of the adverse events (AEs) reported after FM implantation were transitory in nature with most resolving within two weeks of implantation. Thus, the procedure appears to be safe and well tolerated.

The evidence of comparative clinical effectiveness of FM-based EBRT versus bony landmark-based EBRT in patients receiving definitive EBRT for prostate cancer was limited

to retrospective, historical non-randomised comparisons (four single-institution case series and one comparative study). Survival data from Zelefsky (2012) showed significant PSA relapse-free survival only for a small number of high-risk patients (n = 35) using a high radiotherapy dose (86.4Gy). MSAC noted this is not applicable to Australian practice. Health-related quality of life (QoL) data from Lips (2007) showed an initial statistically and clinically significant difference favouring the FM group (IMRT, 76Gy) over the non-FM group (3D-CRT, 70Gy) in four of the six QoL assessments conducted at one month. However, after six months there was no clinically or statistically significant difference for any of the QoL assessments after completion of radiotherapy. For treatment-related morbidity outcomes there were no differences in the frequency of moderate-severe early gastrointestinal (GI) or genitourinary (GU) AEs. Limited data suggested a reduction in the frequency of moderate-severe late GI AEs with FM use (not quantifiable), while data on the risk of moderate-severe late GU AEs were conflicting.

MSAC noted that any benefit of FM use could not be separated from the effects of radiotherapy dose escalation.

MSAC recognised that insufficient evidence of safety or comparative clinical effectiveness limited the economic evaluation to a simple cost comparison analysis. An initial analysis compared daily FM-based pre-treatment verification against the minimum "acceptable" standard of daily bony landmark-based verification for the first three fractions followed by weekly verification (10 verification episodes for a typical 74Gy course of 3DCRT [eviQ Cancer Treatment Online, Cancer Institute NSW]) However, this comparison was sensitive to the baseline frequency of landmark-based verification and, to a lesser extent, to the use of dose escalation (typically, from 74Gy in 37 fractions to 78Gy in 39 fractions). Clinical advice from the Royal Australian and New Zealand College of Radiologists (RANZCR) and the Urological Society of Australia and New Zealand (USANZ) was that standard clinical practice in Australia is daily treatment verification for both bony landmark-based EBRT and FM-based EBRT. MSAC noted this was consistent with MBS utilisation data for the average number of radiotherapy and treatment verification items claimed for both patient cohorts. In addition, the Evaluation Sub-Committee (ESC) was concerned that the full costs to both the patient and Government, including implications for the Extended Medicare Safety Net (EMSN), were not captured in the initial analysis.

A revised cost analysis based on Departmental 2011-12 utilisation data, estimated the weighted total cost to the MBS (including EMSN) to be $177.92 (including $4.72 average EMSN cost) per implantation procedure conducted out-of-hospital and $277.10 per implantation procedure undertaken in-hospital. MSAC noted that the main difference in costs between inpatients and outpatients was the cost of hospital accommodation and the cost of anaesthetic items. Based on the percentage split of in-hospital and out-of-hospital procedures for 2011-12 (42.4% *versus* 57.6% respectively), the weighted average total cost to the MBS (including EMSN) was $219.97 (including $2.72 average EMSN cost) per implantation procedure. The overall weighted average out-of-pocket (OOP) cost was $414.91 per procedure.

For an updated cost comparison, MSAC accepted that the most relevant scenario to current Australian clinical practice consistent with the clinical advice provided by RANZCR and USANZ and with MBS utilisation data was a comparison of:

- FM-based EBRT – total dose 78 Gy, daily pre-treatment verification; against
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Under this scenario, the average total cost (MBS incl. EMSN) was estimated to be $12,068.17 per patient for a course of FM-based EBRT versus $11,240.60 for bony landmark-based EBRT, resulting in an incremental cost of $827.57 per patient. The average total OOP cost was estimated to be $933.22 per patient for a course of FM-based EBRT versus $491.73 for bony landmark-based EBRT, resulting in an incremental cost of $441.49 per patient.

MBS utilisation data, covering the period 1 September 2011 to 31 December 2012, for a cohort of 6,334 patients who received EBRT for prostate cancer within the 2012 calendar year indicate that 1,809 (29%) patients had previously received FMs and of these 1755 (97%) patients have verification items claimed. Based on the above cost comparison and assuming the proportion of patients having FM-based verification remains constant. MSAC noted that the estimated incremental cost to the MBS of FM-based EBRT *vs* landmark-based EBRT was $6.5 million over 4 years.

MSAC recommended that the current MBS interim item descriptor remain unchanged, except from specifying "radiopaque" (rather than "gold") fiducial markers. MSAC also recommended that the following matters should be addressed in any future proposed descriptor:

- No restriction should be placed on the type of practitioner providing the service, as the service may be provided by radiologists, urologists, radiation oncologists, or other appropriately trained physicians who are skilled in the use of TRUS;
- There is no requirement for "approved sites". MSAC noted this term was related to radiation safety provisions associated with brachytherapy which is unnecessary as fiducial markers are not radioactive; and
- Consideration should be given to including TRUS as part of the item and associated fee instead of being listed as a separate service linked to the descriptor.

MSAC advised that the interim funding of the implantation of FMs into the prostate gland or prostate surgical bed for EBRT should explicitly be revisited by MSAC as part of the broader review of radiation oncology including IMRT and IGRT, which will be conducted by the Department.

16. MSAC's advice to the Minister

MSAC considered the strength of the available evidence in relation to the safety, clinical effectiveness and cost-effectiveness of implantation of fiducial markers into the prostate gland or prostate surgical bed for external beam radiotherapy. Based on this consideration, MSAC supports continuation of the current interim public funding arrangements pending completion of its review of Radiation Oncology, including intensity-modulated and image-guided radiation therapy.

17. Applicant's comments on MSAC's Public Summary Document

The Faculty of Radiation Oncology, RANZCR believes that radiologists must be included as a recognised specialist to provide the service, as they have the appropriate skills to do so. We acknowledge that MSAC has considered our expressed views that no restriction should be placed on the type of practitioner providing the service and recommended this should be addressed in any future proposed descriptor. We are fortunate to have been able to work successfully with MSAC and its subcommittees during an evolving period to produce an outcome that is beneficial to cancer patients who require the most modern techniques of delivery of radiation therapy, and look forward to on-going co-operative efforts in the current and future MSAC applications.

18. Context for decision

This advice was made under the MSAC Terms of Reference.

MSAC is to:

Advise the Minister for Health and Ageing on medical services that involve new or emerging technologies and procedures and, where relevant, amendment to existing MBS items, in relation to:

- the strength of evidence in relation to the comparative safety, effectiveness, cost-effectiveness and total cost of the medical service;
- whether public funding should be supported for the medical service and, if so, the circumstances under which public funding should be supported;
- the proposed Medicare Benefits Schedule (MBS) item descriptor and fee for the service where funding through the MBS is supported;
- the circumstances, where there is uncertainty in relation to the clinical or cost-effectiveness of a service, under which interim public funding of a service should be supported for a specified period, during which defined data collections under agreed clinical protocols would be collected to inform a re-assessment of the service by MSAC at the conclusion of that period;
- other matters related to the public funding of health services referred by the Minister.

Advise the Australian Health Ministers' Advisory Council (AHMAC) on health technology assessments referred under AHMAC arrangements.

MSAC may also establish sub-committees to assist MSAC to effectively undertake its role. MSAC may delegate some of its functions to its Executive sub-committee.

19. Linkages to other documents

MSAC's processes are detailed on the MSAC Website at: www.msac.gov.au.