Australian Government

Department of Health

Application Form

Magnetic Resonance Image Guided Radiation Therapy

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires to determine whether a proposed medical service is suitable.

Please use this template, along with the associated Application Form Guidelines to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted.

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the contact numbers and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

Email: hta@health.gov.au
Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant): Elekta Pty Ltd
Corporation name: Elekta Pty Ltd
ABN: REDACTED
Business trading name: Elekta Pty Ltd

Primary contact name: REDACTED

Primary contact numbers
Business: REDACTED
Mobile: REDACTED
Email: REDACTED

Alternative contact name: REDACTED

Alternative contact numbers
Business: REDACTED
Mobile: REDACTED
Email: REDACTED

2. (a) Are you a lobbyist acting on behalf of an Applicant?

☐ Yes
X No

(b) If yes, are you listed on the Register of Lobbyists?

☐ Yes
☐ No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

3. Application title

Magnetic Resonance Image Guided Radiation Therapy (MR-IGRT)

4. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

Radiation therapy is one of the main treatments for cancer and is an effective treatment for a very wide range of cancer types, stages and locations.
Radiation therapy uses a controlled dose of radiation to kill cancer cells or damage them so they cannot grow, multiply or spread. The radiation is usually in the form of focused x-ray beams, also known as photons. It is a localised treatment, which means it generally affects only the part of the body where the radiation is targeted.

5. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

Radiation therapy, an important therapeutic option for cancer patients, has two primary goals; to deliver sufficient dose to the treatment target to achieve local control and to maintain the dose to normal surrounding tissue (organs at risk, or OARs) at sufficiently low levels to achieve acceptable toxicity. These two goals are confounded by a number of uncertainties; the exact boundaries of the target, the target location at the time of treatment, and the boundaries and locations of the OARs. By diminishing these uncertainties through the use of Magnetic Resonance (MR) Image Guidance, reductions in the safety margins (and consequent Planned Treatment Volume or PTV) and better dose discrimination are permitted, resulting in improved tumour control and reduced toxicity. It may also allow clinicians to deliver a higher dose of radiation per fraction to the tumour, which may improve treatment outcomes or reduce the number of treatment sessions.

6. (a) Is this a request for MBS funding?

X Yes
☐ No

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

X Amendment to existing MBS item(s)
☐ New MBS item(s)

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service:

15275 RADIATION ONCOLOGY TREATMENT with IGRT imaging facilities undertaken

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

i. **X** An amendment to the way the service is clinically delivered under the existing item(s)
ii. ☐ An amendment to the patient population under the existing item(s)
iii. ☐ An amendment to the schedule fee of the existing item(s)
iv. ☐ An amendment to the time and complexity of an existing item(s)
v. ☐ Access to an existing item(s) by a different health practitioner group
vi. ☐ Minor amendments to the item descriptor that does not affect how the service is delivered
vii. ☐ An amendment to an existing specific single consultation item
viii. ☐ An amendment to an existing global consultation item(s)

ix. ☐ Other (please describe below):

Insert description of 'other' amendment here

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

i. ☐ A new item which also seeks to allow access to the MBS for a specific health practitioner group
ii. ☐ A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)
iii. ☐ A new item for a specific single consultation item
iv. ☐ A new item for a global consultation item(s)

(f) Is the proposed service seeking public funding other than the MBS?

X Yes
☐ No

If yes, please advise:

Radiation Oncology Health Program Grant funding for the Linac if likely to be applied for by the Clinical Sites

7. What is the type of service:

X Therapeutic medical service
☐ Investigative medical service
☐ Single consultation medical service
☐ Global consultation medical service
☐ Allied health service
☐ Co-dependent technology
☐ Hybrid health technology

8. For investigative services, advise the specific purpose of performing the service *(which could be one or more of the following)*:

i. ☐ To be used as a screening tool in asymptomatic populations
ii. ☐ Assists in establishing a diagnosis in symptomatic patients
iii. ☐ Provides information about prognosis
iv. ☐ Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy
v. ☐ Monitors a patient over time to assess treatment response and guide subsequent treatment decisions

9. Does your service rely on another medical product to achieve or to enhance its intended effect?

☐ Pharmaceutical / Biological
☐ Prosthesis or device
X No

10. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

☐ Yes
X No

(b) If yes, please list the relevant PBS item code(s):

Insert PBS item code(s) here

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

☐ Yes (please provide PBAC submission item number below)
X No

Insert PBAC submission item number here

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

Trade name: Insert trade name here
Generic name: Insert generic name here

11. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

☐ Yes
X No

(b) If yes, please provide the following information (where relevant):

Billing code(s): Insert billing code(s) here
Trade name of prostheses: Insert trade name here
Clinical name of prostheses: Insert clinical name here
Other device components delivered as part of the service: Insert description of device components here

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

☐ Yes
X No

(d) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

☐ Yes
X No - not currently in Australia

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

Device: REDACTED
Manufacturer: REDACTED

12. Please identify any single and / or multi-use consumables delivered as part of the service?

Single use consumables: Insert description of single use consumables here
Multi-use consumables: Insert description of multi use consumables here

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

13. (a) If the proposed medical service involves the use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer or any other type of therapeutic good, please provide the following details:

Type of therapeutic good: Medical Device Included Class IIb
Manufacturer's name: REDACTED
Sponsor's name: REDACTED

(b) Is the medical device classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?

☐ Class III
☐ AIMD
X N/A

14. (a) Is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

☐ Yes (If yes, please provide supporting documentation as an attachment to this application form)
X No

(b) If no, has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?

X Yes (if yes, please provide details below)
☐ No

ARTG listing, registration or inclusion number: 307588
TGA approved indication(s), if applicable: Malignant and benign diseases anywhere in the body as determined by a licensed medical practitioner
TGA approved purpose(s), if applicable: REDACTED.

15. If the therapeutic good has not been listed, registered or included in the ARTG, is the therapeutic good in the process of being considered for inclusion by the TGA?

☐ Yes (please provide details below)
☐ No

Date of submission to TGA: Insert date of submission here
Estimated date by which TGA approval can be expected: Insert estimated date here
TGA Application ID: Insert TGA Application ID here
TGA approved indication(s), if applicable: If applicable, insert description of TGA approved indication(s) here
TGA approved purpose(s), if applicable: If applicable, insert description of TGA approved purpose(s) here

16. If the therapeutic good is not in the process of being considered for listing, registration or inclusion by the TGA, is an application to the TGA being prepared?

☐ Yes (please provide details below)
☐ No

Estimated date of submission to TGA: Insert date of submission here
Proposed indication(s), if applicable: If applicable, insert description of proposed indication(s)
Proposed purpose(s), if applicable: If applicable, insert description of proposed purpose(s) here

PART 4 – SUMMARY OF EVIDENCE

17. **Provide an overview of all key journal articles or research published in the public domain related to the proposed service that is for your application (limiting these to the English language only).** ***Please do not attach full text articles, this is just intended to be a summary.***

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
1.	Clinical Introduction	**Biological responses of human solid tumor cells to X-ray irradiation within a 1.5-Tesla magnetic field generated by a magnetic resonance imaging-linear accelerator.** *Bioelectromagnetics. 2016 Oct;37(7):471-80. doi: 10.1002/bem.21991. Epub 2016 Jul 19.* *Authors: Wang L, Hoogcarspel SJ, Wen Z, van Vulpen M, Molkentine DP, Kok J, Lin SH, Broekhuizen R, Ang KK, Bovenschen N, Raaymakers BW, Frank SJ*	Devices that combine magnetic resonance imaging with linear accelerators (MRL) represent a novel tool for MR-guided radiotherapy. However, whether magnetic fields (MFs) generated by these devices affect the radiosensitivity of tumours is unknown. We investigated the influence of a 1.5-T MF on cell viability and radioresponse of human solid tumours.	https://onlinelibrary.wiley.com/doi/abs/10.1002/bem.21991	Epub 2016 Jul 19.

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
2.	Clinical Introduction	**The development of the MRI linac system for online MRI-guided radiotherapy: a clinical update.** *J Intern Med. 2016 Aug;280(2):203-8. doi: 10.1111/joim.12516. Epub 2016 May 19.* *Authors: Lagendijk JJ, van Vulpen M, Raaymakers BW*	In this clinical update, we describe the development and the expected clinical impact of the UMC Utrecht MRI linac (MRL) system. This combination of a radiotherapy accelerator with a diagnostic quality 1.5 T MRI scanner provides real-time imaging at the moment of treatment, thus providing unprecedented targeting accuracy.	https://onlinelibrary.wiley.com/doi/full/10.1111/joim.12516	*Epub 2016 May 19.*

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
3.	Clinical Introduction	**The MRI-Linear Accelerator Consortium: Evidence-Based Clinical Introduction of an Innovation in Radiation Oncology Connecting Researchers, Methodology, Data Collection, Quality Assurance, and Technical Development.** *Front Oncol. 2016 Oct 13;6:215. doi: 10.3389/fonc.2016.00215. eCollection 2016.* *Authors: Kerkmeijer LG, Fuller CD, Verkooijen HM, Verheij M, Choudhury A, Harrington KJ, Schultz C, Sahgal A, Frank SJ, Goldwein J, Brown KJ, Minsky BD, van Vulpen M*	An international research consortium has been formed to facilitate evidence-based introduction of MR-guided radiotherapy and address how the MR-linac could be used to achieve an optimized radiation treatment approach to improve patients' survival, local, and regional tumour control and quality of life.	http://dx.doi.org/10.3389/fonc.2016.00215	*2016 Oct 13*

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
4.	Dosimetry	**Dosimetry for the MRI accelerator: the impact of a magnetic field on the response of a Farmer NE2571 ionization chamber.** *Phys Med Biol. 2009 May 21;54(10):2993-3002. doi: 10.1088/0031-9155/54/10/002. Epub 2009 Apr 23.* *Authors: Meijsing I, Raaymakers BW, Raaijmakers AJ, Kok JG, Hogeweg L, Liu B, Lagendijk JJ*	Utrecht is constructing a 1.5 T MRI scanner integrated with a linac. The goal is to facilitate soft-tissue contrast based image-guided radiotherapy, to escalate the dose to the tumour while sparing surrounding normal tissues. Dosimetry for the MRI accelerator has to be performed in the presence of a magnetic field.	http://dx.doi.org/10.1088/0031-9155/54/10/002	*Epub 2009 Apr 23.*

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
5.	Dosimetry	**Installation of the 1.5 T MRI accelerator next to clinical accelerators: impact of the fringe field.** *Phys Med Biol. 2009 Sep 21;54(18):N409-15. doi: 10.1088/0031-9155/54/18/N02. Epub 2009 Aug 18.* *Authors: Kok JG, Raaymakers BW, Lagendijk JJ, Overweg J, de Graaff CH, Brown KJ*	In the UMC Utrecht a prototype MRI accelerator has been installed to investigate the feasibility of real-time, MRI guided radiotherapy. The system consists of a 6 MV Elekta (Crawley, UK) accelerator and a 1.5 T Philips (Best, The Netherlands) MRI system. The system is installed in a standard radiotherapy bunker.	http://dx.doi.org/10.1088/0031-9155/54/18/N02	*2009 Aug 18.*

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
6.	Workflow and Clinical Service	**Apres Mois, Le Deluge": Preparing for the Coming Data Flood in the MRI-Guided Radiotherapy Era.** Authors: Kiser KJ, Smith BD, Wang J, Fuller CD Front Oncol. 2019 Sep 30;9:983. doi: 10.3389/fonc.2019.00983. eCollection 2019. PMID: 31632914 Folder: AAA Online Library/Main Library	Magnetic resonance imaging provides a sea of quantitative and semi-quantitative data. While radiation oncologists already navigate a pool of clinical (semantic) and imaging data, the tide will swell with the advent of hybrid MRI/linear accelerator devices and increasing interest in MRI-guided radiotherapy (MRIgRT), including adaptive MRIgRT	https://www.frontiersin.org/articles/10.3389/fonc.2019.00983/full	2019 Sep 30

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
7.	Clinical Improvement	Magnetic resonance-guided radiation therapy: A review. Authors: Chin S, Eccles CL, McWilliam A, Chuter R, Walker E, Whitehurst P, Berresford J, Van Herk M, Hoskin PJ, Choudhury A J Med Imaging Radiat Oncol. 2019 Oct 23. doi: 10.1111/1754-9485.12968. PMID: 31646742 Folder: AAA Online Library/Main Library	Magnetic resonance-guided radiation therapy (MRgRT) is a promising approach to improving clinical outcomes. Image guidance, adaptive planning and MRI in radiation therapy have been increasing over the last two decades. MRgRT can potentially transform radiation oncology by improving tumour control, quality of life and increasing access of treatment by shortening treatment courses.	https://onlinelibrary.wiley.com/doi/abs/10.1111/1754-9485.12968?af=R	2019 Oct 23

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
8.	Workflow and Clinical Service	The transformation of radiation oncology using real-time magnetic resonance guidance: A review. Authors: Hall WA, Paulson ES, van der Heide UA, Fuller CD, Raaymakers BW, Lagendijk JJW, Li XA, Jaffray DA, Dawson LA, Erickson B, Verheij M, Harrington KJ, Sahgal A, Lee P, Parikh PJ, Bassetti MF, Robinson CG, Minsky BD, Choudhury A, Tersteeg RJHA, Schultz CJ Eur J Cancer. 2019 Oct 11;122:42-52. doi: 10.1016/j.ejca.2019.07.021. PMID: 31614288	Radiotherapy (RT) is an essential component of effective cancer care and is used across nearly all cancer types. The direct integration of MRI with linacs represents a development with the potential to dramatically impact cancer research/treatment. Real-time MRI-guided RT is transforming the workflows of virtually every aspect of RT.	https://www.ejcancer.com/article/S0959-8049(19)30429-0/fulltext	2019 Oct 11

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
9.	Workflow and Clinical Service	MR-guidance in clinical reality: current treatment challenges and future perspectives. Authors: Corradini S, Alongi F, Andratschke N, Belka C, Boldrini L, Cellini F, Debus J, Guckenberger M, Horner-Rieber J, Lagerwaard FJ, Mazzola R, Palacios MA, Philippens MEP, Raaijmakers CPJ, Terhaard CHJ, Valentini V, Niyazi M Radiat Oncol. 2019 Jun 3;14(1):92. doi: 10.1186/s13014-019-1308-y. PMID: 31167658 Publisher: Radiat Oncol	Magnetic Resonance-guided radiotherapy (MRgRT) marks the beginning of a new era. MR is a versatile and suitable imaging modality for radiotherapy, as it enables direct visualisation of the tumour and the surrounding organs at risk. Moreover, MRgRT provides real-time imaging to characterise and eventually track anatomical motion.	https://ro-journal.biomedcentral.com/articles/10.1186/s13014-019-1308-y	2019 Jun 3

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment, including providing the trial registration number to allow for tracking purposes.*

**** If the publication is a follow-up to an initial publication, please advise.*

18. Identify yet to be published research that may have results available in the near future that could be relevant in the consideration of your application by MSAC (limiting these to the English language only). *Please do not attach full text articles, this is just intended to be a summary.*

	Type of study design*	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)**	Website link to research (if available)	Date***
1.	Clinical Trial – Recruiting 200 Patients	Prospective Evaluation of Radiotherapy Using Magnetic Resonance Image Guided Treatment Royal Marsden NHSFT, London, United Kingdom	The purpose of PERMIT is to collect information on the treatment of radiotherapy patients using a MR linac to guide treatment. The aim is to use this information to support the introduction of MR Linac into clinical practice.	https://ClinicalTrials.gov/show/NCT03727698	November 2023
2.	Clinical Trial – Recruiting 30 Patients	Prospective Evaluation of Radiotherapy Using Magnetic Resonance Image Guided Treatment Royal Marsden NHSFT, London, United Kingdom	The aim of this study is to assess the technical feasibility of delivering radical radiotherapy for prostate cancer using the MR-Linac, including the feasibility of changing the radiotherapy plan on a daily basis to mirror internal anatomy changes.	https://clinicaltrials.gov/ct2/show/NCT03658525	August 2020

	Type of study design*	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)**	Website link to research (if available)	Date***
3.	Multi-institution Prospective Observational 6000 Patients	The MOMENTUM Study: The Multiple Outcome Evaluation of Radiation Therapy Using the MR-Linac Study UMC Utrecht The Netherlands Cancer Institute Sunnybrook Health Sciences Centre M.D. Anderson Cancer Center The Christie NHS Foundation Trust Royal Marsden NHS Foundation Trust Medical College of Wisconsin Elekta	Innovation in radiation therapy has resulted in the development of MR-guided radiation therapy (MRGRT) which allows high precision radiotherapy under real time MR visualization. High precision MRGRT has the potential of dose escalation and margin reduction and may potentially lead to higher cure rates and less toxicity.	https://clinicaltrials.gov/ct2/show/NCT04075305	February 1, 2024

	Type of study design*	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)**	Website link to research (if available)	Date***
4.	Prospective Observational 173 Patients	PRIMER: Development of Daily Online Magnetic Resonance Imaging for Magnetic Resonance Image Guided Radiotherapy The Royal Marsden NHS Foundation Trust, Sutton, Surrey, United Kingdom	The MR Linac integrates high quality MRI with a state-of-the-art radiotherapy machine. This revolutionary technology has the potential to change the way radiotherapy is delivered. Investigating improved precision and accuracy in targeted delivery will mean reductions in margins around tumours leading to higher cure rates with significantly fewer side effects.	https://clinicaltrials.gov/ct2/show/NCT02973828	June 2020

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment.*

****Date of when results will be made available (to the best of your knowledge).*

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

19. **List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the service (please attach a statement of clinical relevance from each group nominated):**

    Royal Australian and New Zealand College of Radiologists Faculty of Radiation Oncology (RANZCR FRO)

    Australian Society of Medical Imaging and Radiation Therapy (ASMIRT)

    Australasian College of Physical Scientists and Engineers in Medicine (ACPSEM)

20. **List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):**

    Same professional bodies as above, comparator service is IGRT on Cone Beam CT (CBCT) equipped Linacs.

21. **List the consumer organisations relevant to the proposed medical service (please attach a letter of support for each consumer organisation nominated):**

    REDACTED

22. **List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service:**

    Device: REDACTED

    Manufacturer: REDACTED

23. **Nominate two experts who could be approached about the proposed medical service and the current clinical management of the service(s):**

    REDACTED

    Please note that the Department may also consult with other referrers, proceduralists and disease specialists to obtain their insight.

PART 6 – POPULATION (AND PRIOR TESTS), INTERVENTION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

24. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease in terms of both morbidity and mortality:

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 (metastasise) 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 extracranial 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, but can only be safely delivered if the exact location of the target within the body can be determined.

External beam radiation therapy (EBRT) is the most widely used type of radiation therapy. The radiation is delivered by high-energy photons that come from a machine called a linear accelerator (or linac, for short). The radiation is usually given daily over several weeks and delivered as an outpatient in a radiotherapy department. Three-dimensional conformal radiation therapy (3DCRT) is a form of EBRT that uses tumour imaging scans and computers to very precisely map its location in three dimensions. The radiation beams are matched to the shape of the tumour and delivered from several directions. By aiming the radiation more precisely, it may be possible to reduce radiation damage to normal tissues and increase the radiation dose to the cancer. Intensity modulated radiation therapy (IMRT) is a newer more advanced form of EBRT. As with 3DCRT, computer programs are used to precisely map the tumour in three dimensions. In addition to delivering beams from several directions, the intensity (strength) of the beams can be adjusted. This gives even more control over the conformity and heterogeneity of the dose, decreasing the radiation reaching sensitive normal tissues while delivering higher doses to the tumour.

Radiation therapy is integral to the management of most cancers. IGRT is indicated for the treatment of a range of cancers, including (but not limited to) head and neck, prostate, bladder, breast, oesophagus, liver, pancreas, rectum and lung cancers.

Initial use of MR-linac will focus on cancers of the brain, breast, cervix, oesophagus, lung, oropharynx, pancreas, prostate, oligometastatic sites, liver, bladder and rectum through the MR-linac consortium activities. The below table represents the current utilisation breakdown of the MR-linac patient indications to date as well as 2015 statistics for the Australian population on Cancer Incidence and Deaths. (Sourced from Australia Government: Australian Institute of Health and Welfare – Cancer data in Australia website https://www.aihw.gov.au/reports/cancer/cancer-data-in-australia/acim-books)

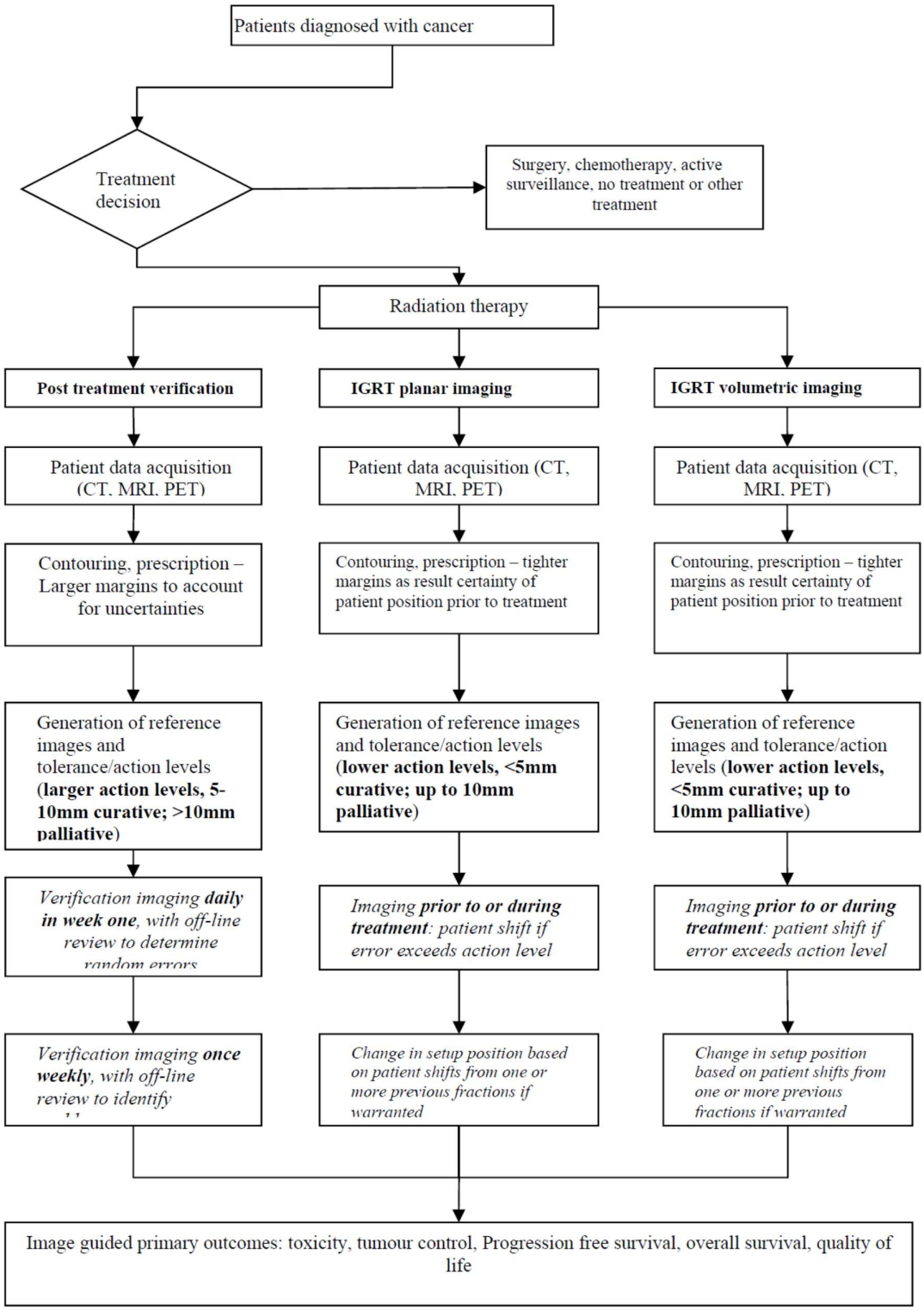
INDICATIONS (Consortium Tumour Site Groups)	**% of Global Patients treated to date on MR-linac**	**2015 Incidence Australia (potential patient cases)**	**2015 Number of Deaths Australia**
Brain/GBM	1%	1,787	1,365
Breast	6%	17,004	2,924
Oesophagus	1%	1,469	1,312
Head&Neck	2%	3,697	1,121
Liver	8%	2,079	1,785
Pancreas	3%	3,307	2,911
Prostate	29%	18,878	3,159
Rectum	17%	5,120	2,527
Oligometastatic	22%		
Bone	6%	255	101
Nodal boosts	1%		
Lung	1%	11,788	8,416
Larynx	2%	638	212

25. **Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed medical service, including any details of how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the service:**

    Same as for IGRT, seeking submission documents from RANZCR for Application 1319 – Image-guided radiation therapy for cancer treatment delivery and approval to reference for this response.

26. **Define and summarise the current clinical management pathway *before* patients would be eligible for the proposed medical service (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway up to this point):**

    Same as for IGRT, seeking submission documents from RANZCR for Application 1319 – Image-guided radiation therapy for cancer treatment delivery and approval to reference for this response.


Patients diagnosed with cancer
Treatment decision
Surgery, chemotherapy, active surveillance, no treatment or other treatment
Radiation therapy
Post treatment verification
IGRT planar imaging
IGRT volumetric imaging
Patient data acquisition (CT, MRI, PET)
Patient data acquisition (CT, MRI, PET)
Patient data acquisition (CT, MRI, PET)
Contouring, prescription – Larger margins to account for uncertainties
Contouring, prescription – tighter margins as result certainty of patient position prior to treatment
Contouring, prescription – tighter margins as result certainty of patient position prior to treatment
Generation of reference images and tolerance/action levels (larger action levels, 5-10mm curative; >10mm palliative)
Generation of reference images and tolerance/action levels (lower action levels, <5mm curative; up to 10mm palliative)
Generation of reference images and tolerance/action levels (lower action levels, <5mm curative; up to 10mm palliative)
Verification imaging daily in week one, with off-line review to determine random errors
Imaging prior to or during treatment: patient shift if error exceeds action level
Imaging prior to or during treatment: patient shift if error exceeds action level
Verification imaging once weekly, with off-line review to identify
Change in setup position based on patient shifts from one or more previous fractions if warranted
Change in setup position based on patient shifts from one or more previous fractions if warranted
Image guided primary outcomes: toxicity, tumour control, Progression free survival, overall survival, quality of life

PART 6b – INFORMATION ABOUT THE INTERVENTION

27. Describe the key components and clinical steps involved in delivering the proposed medical service:

The MR Image Guided Radiation Therapy processes proposed in this application involves volumetric data sets being obtained at the planning stages and again during treatment verification/delivery. Analysis, interpretation and treatment alignment can be adjusted and/or adapted during treatment and in accordance with narrower margins where appropriate. Review and assessment of the images enables trained staff (using specialised software) to make adjustments to the patient or machine positional parameters ensuring the radiation is precisely focussed on the target area (the tumour). This maximises the prescribed and delivered dose to the target and minimises the radiation to normal tissues close to the target and provides the opportunity to gain maximum tumour control and decrease possible side effects associated with the treatment. The procedure for every treatment fraction is similar to the standard procedure with conventional linacs: patient setup, imaging, adaptation, treatment. The MR-linac introduces a higher level of Imaging with MR and a capability for more sophisticated adaptive functionality, which enables the user to optimise the dose distribution of the treatment plan on every fraction in an online setting (i.e. while the patient is in the machine).

Different clinical cases have different objectives, depending on the dose being delivered and whether anatomy of interest is subject to deformations. Consequently, the MR-linac supports two adaptive workflows: Adapt to position, where the reference dose is shifted to the daily target position, is an efficient workflow in terms of time and expertise required in the online environment; adapt to shape, where the dose is adjusted to conform to the daily deformed anatomical structures, is more resource intense and will improve conformity when high doses per fraction are being delivered. During plan adaptation, advanced imaging protocols can be applied to collect real-time anatomical or biological information regarding treatment effects on the tumour and surrounding tissue.

28. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

N/A

29. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

N/A

30. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency):

Limitations are consistent with patient safety limitations for existing MRI and Linear Accelerator devices.

31. If applicable, identify any healthcare resources or other medical services that would need to be delivered <u>at the same time</u> as the proposed medical service:

N/A

32. If applicable, advise which health professionals will primarily deliver the proposed service:

Use of the MR-linac involves the same professionals as for IGRT utilising a Cone-Beam CT equipped Linac - Radiation Oncologists, Medical Physicists and Radiation Therapists.

The staffing levels are the same except for more complex workflows (adapt to shape) when the Radiation Oncologist and Physicist and Radiation Therapist staff may be required collectively at the treatment machine.

33. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

N/A

34. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

N/A

35. If applicable, advise what type of training or qualifications would be required to perform the proposed service, as well as any accreditation requirements to support service delivery:

Radiation Oncologist, Medical Physicist, Radiation Therapist – normal qualifications.

User and safety training are required to ensure the safe and effective use of MR-linac to treat patients, as well as support seamless adoption of the technology into the clinic.

REDACTED

36. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select <u>ALL</u> relevant settings):

- **X** Inpatient private hospital (admitted patient)
- **X** Inpatient public hospital (admitted patient)
- **X** Private outpatient clinic
- **X** Public outpatient clinic
- ☐ Emergency Department
- ☐ Private consulting rooms - GP
- ☐ Private consulting rooms – specialist
- ☐ Private consulting rooms – other health practitioner (nurse or allied health)
- ☐ Private day surgery clinic (admitted patient)
- ☐ Private day surgery clinic (non-admitted patient)
- ☐ Public day surgery clinic (admitted patient)
- ☐ Public day surgery clinic (non-admitted patient)
- ☐ Residential aged care facility
- ☐ Patient's home
- ☐ Laboratory
- ☐ Other – please specify below

Specify further details here

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

Aligns with all other current Radiation Oncology Services which are provided across these multiple settings

37. Is the proposed medical service intended to be entirely rendered in Australia?

- **X** Yes
- ☐ No – please specify below

Specify further details here

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

38. Nominate the appropriate comparator(s) for the proposed medical service, i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system (including identifying health care resources that are needed to be delivered at the same time as the comparator service):

The comparator is a Linac with image guidance by a Cone Beam CT imaging system. Similar the Cone Beam CT Imaging for IGRT, The major potential benefit of MR Imaging for IGRT is that the dose of radiation being delivered to the target tumour can be maximised while minimising the unintended dose that is delivered to the surrounding tissues. IGRT can assist in the detailed planning, dosimetric calculation, quality assurance of the plan and in optimising the delivery. The use of the process would provide superior tumour control and surrounding tissue protection. In addition to its effect on cancer control and cure rates, there are other benefits for the technology. In the acute or treatment phase, there would be a potential reduction in toxicity and side effects experienced by patients including a reduction in the number of cases requiring acute care and medical intervention during or immediately after treatment. In the 3-6 month period after treatment, there would be a potential reduction in such toxicities as strictures, fractures, scar tissue formation together with less reliance on medications such as pain control and steroids and improved quality of life.

Initially, treatment using MR-linac will compare dosimetric outcomes such as margin reduction and resultant decreased dose to organs at risk (decreased toxicity) with the standard of care on a cone-beam CT linac. The key difference is the MR-linac can Image without radiation dose, in addition to providing a higher quality Image for guidance.

Once this dosimetric advantage is demonstrated, subsequent studies will aim to demonstrate directly that there is a reduction in toxicity, or that the dose to the target can be escalated in an effort to improve local control of disease without additional toxicity.

Additionally or Alternatively, the dosimetric advantage may allow for treatments to be delivered using compressed fractionation schemes (hypofractionation, SBRT) that will afford greater convenience and quality of life to patients.

Increased frequency of imaging with MR has an additional benefit of not increasing radiation exposure as is the case when using Cone Beam CT for IGRT.

Future studies for some disease sites may aim to compare MR-IGRT with surgery or may aim to reduce the need for surgery or other adjuvant therapies based on response assessments over the course of MR-IGRT delivery.

39. Does the medical service (that has been nominated as the comparator) have an existing MBS item number(s)?

X Yes (please list all relevant MBS item numbers below)
☐ No

15275 RADIATION ONCOLOGY TREATMENT with IGRT imaging facilities undertaken to implement an IMRT dosimetry plan.

Required with item 15275 are items 15555 SIMULATION FOR INTENSITY-MODULATED RADIATION THERAPY (IMRT) and 15565 Preparation of an IMRT DOSIMETRY PLAN. The Simulation and Dosimetry workflows and processes will be consistent with current practice when implemented with a MR-linac.

40. Define and summarise the current clinical management pathway/s that patients may follow *after* they receive the medical service that has been nominated as the comparator (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway that patients may follow from the point of receiving the comparator onwards, including health care resources):

Same as for IGRT, seeking submission documents from RANZCR for Application 1319 – Image-guided radiation therapy for cancer treatment delivery and approval to reference for this response.

41. (a) Will the proposed medical service be used in addition to, or instead of, the nominated comparator(s)?

☐ In addition to (i.e. it is an add-on service)
X Instead of (i.e. it is a replacement or alternative)

(b) If instead of (i.e. alternative service), please outline the extent to which the current service/comparator is expected to be substituted:

The MR-linac will introduce the capability use MR Image Guidance for enhanced image quality at the time of pre-treatment verification with the aim to reduce target volume margins and organs at risk included in the target volume and reduce treatment toxicity as well as to provide the opportunity for shorter hypofractionated prescribed courses of treatment. The MR-linac will therefore introduce a clinical choice for Tumour Sites which demonstrate benefit of reduced target volume margins and hypofractionated courses.

42. Define and summarise how current clinical management pathways (from the point of service delivery onwards) are expected to change as a consequence of introducing the proposed medical service, including variation in health care resources (Refer to Question 39 as baseline):

The application for Magnetic Resonance Image Guided Radiation Therapy is only planning to include the use of MRI as the Image Guidance modality in the existing 15275 RADIATION ONCOLOGY TREATMENT with IGRT MBS item. The use of a MR-linac will substitute X-ray, Ultrasound or CT Imaging with MR Imaging with additional benefits of enhanced Image Quality and real-time, non-ionising imaging as the foundation for IGRT delivery of an IMRT dosimetry plan. All aspects of the clinical management pathway are aligned with current clinical practice to deliver IGRT services.

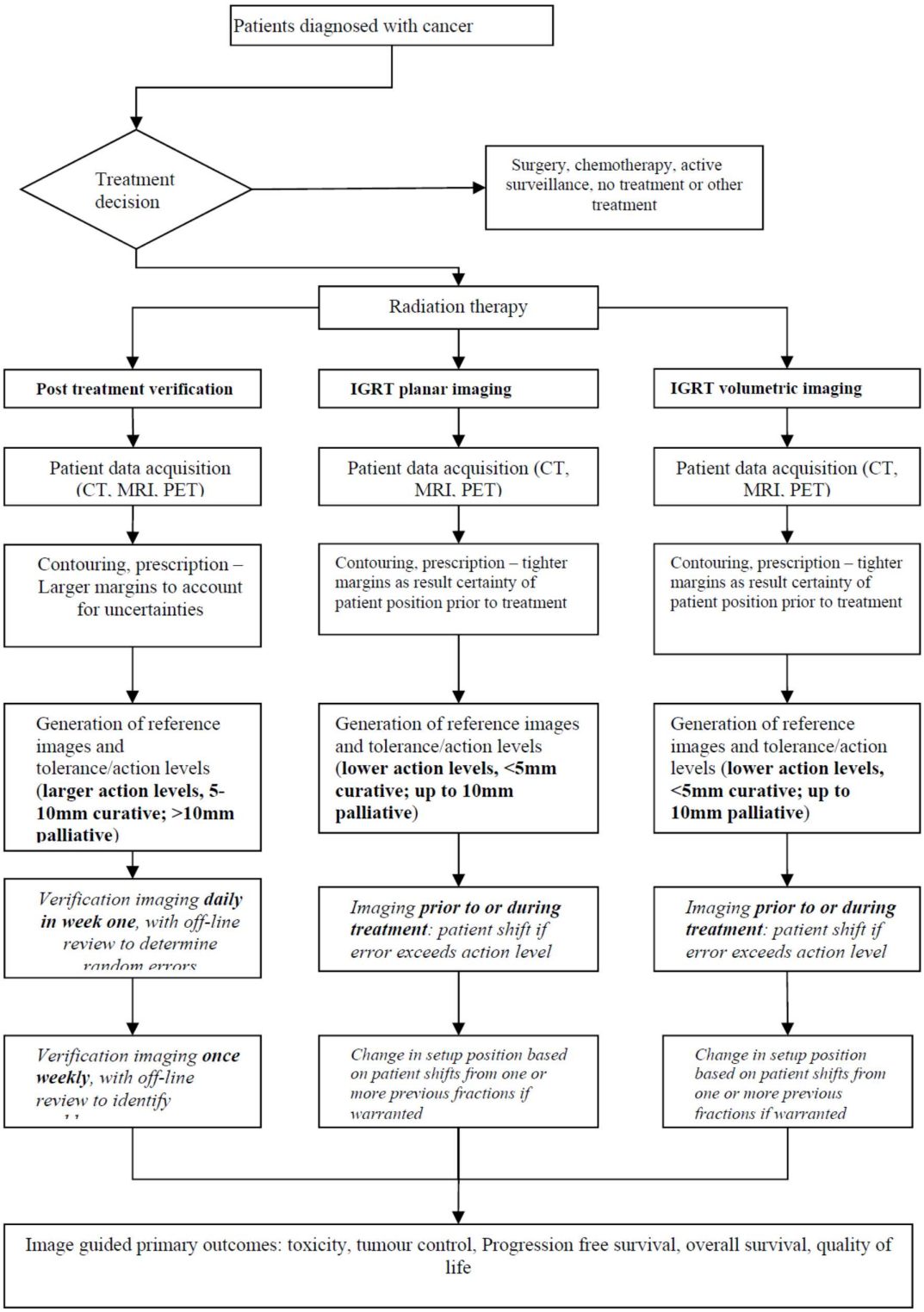
Below is the IGRT explanation and clinical management pathway from the existing 15275 RADIATION ONCOLOGY TREATMENT with IGRT imaging facilities undertaken to implement an IMRT dosimetry plan. This is referenced in the attached MSAC Public Summary Document Application 1319 – Image-guided radiation therapy for cancer treatment delivery (1319FinalPSD-IGRT-Accessible.pdf) where MR is identified as a further option for IGRT.

IGRT is the process of frequent two and three-dimensional imaging that is captured as close as possible to the time of treatment or concurrent with treatment delivery. The images enable the patient or beam position to be corrected before or during treatment delivery. IGRT is used when there is complex dosimetry and in situations where it may be difficult to reproduce the patient position.

IGRT may be delivered using a range of technology:

- two-dimensional imaging localises the target by matching planar kilovoltage (kV) radiographs, fluoroscopy or megavoltage (MV) images with digital reconstructed radiographs (DRRs) from the planning CT.
- three-dimensional imaging which localises the target by comparing a cone-beam computed tomography (CBCT) dataset with the planning computed tomography (CT) dataset from planning.
- ultrasound for image guidance which allows automated scanning from outside of the treatment room.

MRI guided IGRT which provides real-time image guidance is a further option.


Patients diagnosed with cancer
Treatment decision
Surgery, chemotherapy, active surveillance, no treatment or other treatment
Radiation therapy
Post treatment verification
IGRT planar imaging
IGRT volumetric imaging
Patient data acquisition (CT, MRI, PET)
Patient data acquisition (CT, MRI, PET)
Patient data acquisition (CT, MRI, PET)
Contouring, prescription – Larger margins to account for uncertainties
Contouring, prescription – tighter margins as result certainty of patient position prior to treatment
Contouring, prescription – tighter margins as result certainty of patient position prior to treatment
Generation of reference images and tolerance/action levels (larger action levels, 5-10mm curative; >10mm palliative)
Generation of reference images and tolerance/action levels (lower action levels, <5mm curative; up to 10mm palliative)
Generation of reference images and tolerance/action levels (lower action levels, <5mm curative; up to 10mm palliative)
Verification imaging daily in week one, with off-line review to determine random errors
Imaging prior to or during treatment: patient shift if error exceeds action level
Imaging prior to or during treatment: patient shift if error exceeds action level
Verification imaging once weekly, with off-line review to identify
Change in setup position based on patient shifts from one or more previous fractions if warranted
Change in setup position based on patient shifts from one or more previous fractions if warranted
Image guided primary outcomes: toxicity, tumour control, Progression free survival, overall survival, quality of life

PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

43. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):

MR Guided Radiation Therapy using MR-linac has the potential to improve outcomes, reduce patients' treatment burden and enable personalised cancer therapy.

Tumours change shape and size and their position relative to surrounding tissue over the course of treatment and during individual treatment sessions. This results in uncertainty about the location of tumour and normal tissue during treatment and necessitates increased planned treatment volume (PTV) margins in order to ensure complete dosing of the tumour. Larger PTV margins increase the amount of normal tissue that is dosed, which causes more widespread or more severe toxicity that can lead to acute and long-term side effects and reduced quality of treatment outcomes.

The ability to see and monitor radiation dosing in real time could substantially reduce uncertainty about where radiation is being delivered, allowing PTV margin reductions that could better spare healthy tissue. Smaller PTVs may enable delivery of higher doses to the tumour, which could improve efficacy, while minimizing toxicity. Real-time dose monitoring also allows calculation of the total amount of radiation accumulated in the tumour or surrounding tissue at any point over the course of therapy. Subsequent treatments can then be adjusted to ensure that the actual dose delivered is consistent with the planned dose, which is critical for optimising outcomes.

MR-linac using Magnetic Resonance Imaging represents an important evolution in Linear Accelerator technology. It builds upon a long and rich chronicle of closer and closer integration of advanced imaging with radiotherapy treatment delivery technologies. Historically, use of these combined technologies has led to clear improvements in treatment outcomes, and stretched the boundaries of innovation in delivery systems. Limitations of the current technologies, however, have impaired advances and limited clinicians' abilities to both target areas of disease, avoid critical structures and adapt therapy. These limitations are largely due to imaging constraints.

MR-linac directly addresses these limitations and constraints by equipping a state-of-the art radiotherapy delivery system with MR Image guidance capabilities that, for all intents and purposes, completely eliminates these constraints. The combined MR-linac system, based on two technologies that have a long-standing record of safety and effectiveness, represents a natural and important evolution in the field. Combined, they have many immediate and longer-term basis potentially providing safer and more effective performance than predicate devices which serve as their foundation.

There are a number of clinical challenges related to the combination of MR and ionizing radiation. First, there is the effect of the Magnetic field on physical dose distribution. The magnetic field affects the pathway of all secondary electrons generated by the interaction of the photon radiation beam and patient tissue. This effect is most pronounced at tissue density interfaces such as between air and bone or air and soft tissue. These manifestations have become known as the 'Electron Return Effect' (ERE) and the 'Electron Streaming Effect' (ESE). These effects are readily managed. In the case of the Electron Return Effect, the treatment planning system utilised with the MR-linac is capable of modelling the effect and optimizing the treatment plans provided all areas of the interest are identified and included within the plan. Studies have demonstrated that this generally reduces the effect to a point where it is non-significant. In instances where the plan is unacceptable, it will be clear to the treatment team prior to instituting any treatments on the device as in the case with conventional radiotherapy. Other mitigations such as use of bolus material on surface prone to electron streaming are also available to reduce this risk.

An additional concern exists over a speculative effect of the Magnetic field on the radiobiological effect in tissue (biological) resulting from the physical dose distribution. The clinical evaluation review concludes that, while there is interest in investigating a speculative combined MR + RT radiobiological effect, no clear mechanism for this effect has been elucidated. The literature, which is extensive on the issue, suggests that any such effect, if present, is miniscule. No such effect has ever been identified in patients imaged with MR or treated with radiotherapy in or near the presence of a weak or strong magnetic field. Furthermore, a clinical study intended to measure the magnitude of such an effect would be impractical. The benefit of using MR-based image guidance is believed to far outweigh the impact of this "speculative" concern.

MR-linac has the ability to greatly reduce target uncertainty, allowing the operator to focus on disease areas, in real time, without the use of ionizing radiation. This has the potential for reducing toxicity from radiation, allowing dose escalation and improving patient outcomes.

In conclusion, MR-linac has been reported as a medical device that is deemed as safe and effective, and that risks associated with its proper use are by far outweighed by its potential to benefit patients it will treat.

44. Please advise if the overall clinical claim is for:

☐ Superiority
X Non-inferiority

45. Below, list the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be specifically measured in assessing the clinical claim of the proposed medical service versus the comparator:

Safety Outcomes: MR Safety and Radiation Safety for clinical application of MR Guided Radiation Therapy

Clinical Effectiveness Outcomes: Tumour Control (Survival) and Normal Tissue Toxicity (Side Effect) comparison with Disease Free Survival and Quality of Life measures.

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

46. Estimate the prevalence and/or incidence of the proposed population:

Equivalent to incidence relative to existing Linacs. Cancer incidence 140,000 (2018) where 1 in 2 patients should then receive Radiation Therapy. Many of the clinical Tumour Sites would be appropriate for use with MR-linac, excluding patients with contraindications for MR and obese patients unable to fit into the device.

47. Estimate the number of times the proposed medical service(s) would be delivered to a patient per year:

Due to the hypofractionation expected with the MR-linac the opportunity to reduce the number of fractions per treatment course is expected to be closer to 5 over time following clinical introduction and protocol development, currently on Linacs the average number of fractions per treatment course is 20. Time required for Daily Imaging and Treatment on the MR-linac will be longer than with conventional Linacs, however 900-1000 Patient Courses per MR-linac year will be a possibility with 5 fraction courses compared with the current 414 Patient Courses per Linac year at present.

48. How many years would the proposed medical service(s) be required for the patient?

The MR-linac enables shorter (hypofractionated) treatment courses with potential to reduce current 40 fraction courses to 5 fractions, improving access to Radiation Therapy due to greater efficiency and less disruption to Patient lives due to daily treatment requirements.

49. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

Based on an introductory learning and development period and ramp up of workload the MR-linac in Australia would be expected to deliver 400-500 Patient Courses in Year 1.

50. Estimate the anticipated uptake of the proposed medical service over the next three years factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors) as well as provide commentary on risk of 'leakage' to populations not targeted by the service:

Over the next 3 years it is expected at least 10 MR-linacs will be in operation in Australia.

PART 8 – COST INFORMATION

51. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

The cost per treatment fraction of providing MR IGRT is expected to be higher than existing IGRT due to factors including the equipment cost, the imaging and treatment fraction times and the professional resources required. However the benefits of real-time imaging with no radiation dose and capability to adapt the treatment plan daily to the target and normal tissue volumes for optimal patient outcomes need to be acknowledged. The MR-linac cost is approximately 3x higher than a conventional CBCT Linac. Imaging and treatment fraction times are expected to be 2-3 times longer than on a CBCT Linac due to the MR Image acquisition and time to adapt the Treatment Plan to the daily patient anatomy, however total Treatment Courses may require fewer fractions than CBCT resulting in an increase in overall efficiency of Patient Treatment Courses per year. MR-linac workflows are still developing and the professional resources (Radiation Oncologist, Physicist and Radiation Therapist) involvement at the Treatment Delivery may be higher than with current conventional CBCT Linacs.

52. Specify how long the proposed medical service typically takes to perform:

Typically MR Guided Radiation Therapy will be delivered over multiple treatment fractions with each treatment taking approximately 30-45 minute. By implementing MR Guided Radiation Therapy, the potential of using a hypofractionated treatment course prescriptions is increased and the possibility of reducing the treatment courses to 5 fractions.

53. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and medical service usage characteristics that would define eligibility for MBS funding.

Category (insert proposed category number here) – (insert proposed category description here)
Proposed item descriptor: insert proposed item descriptor here Fee: $(insert proposed fee here)