Technology Guidance

Magnetic Resonance Image Guided Radiation Therapy

for patients with cancer

Technology Guidance from the MOH Medical Technology Advisory Committee

Guidance Recommendations

The Ministry of Health's Medical Technology Advisory Committee has not recommended subsidy for magnetic resonance image guided radiation therapy (MR-IGRT) for patients with cancer.

Funding status

MR-IGRT is not recommended for subsidy in patients with the abovementioned indications.

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Factors considered to inform the recommendations for funding

Technology evaluation

1.1. The MOH Medical Technology Advisory Committee ("the Committee") considered the evidence presented for the technology evaluation of MR-IGRT for treating cancer. The Agency for Care Effectiveness (ACE) conducted the evaluation in consultation with clinical experts from the public healthcare institutions. Published clinical and economic evidence for MR-IGRT were considered in line with its registered indications.

1.2. The evidence was used to inform the Committee's deliberations around five core decision-making criteria:

- Clinical need of patients and nature of the condition;
- Overall benefit of the technology for the patient and/or the system;
- Cost-effectiveness (value for money) – the incremental benefit and cost of the technology compared to existing alternatives;
- Estimated annual technology cost and the number of patients likely to benefit from the technology; and
- Organisational feasibility, which covers the potential impact of adopting technology, especially barriers for diffusion.

1.3. Additional factors, including social and value judgments, may also inform the Committee's deliberations.

Clinical need

2.1. Cancer is the leading cause of death in Singapore, accounting for approximately 28% of all deaths in 2021. Despite various treatment modalities, cancer may eventually spread to other parts of the body leading to significant morbidity and mortality. Radiation therapy is a treatment modality that uses high doses of radiation to kill cancer cells. External beam radiation therapy is the most common treatment option for patients with cancer. Precision in radiation therapy allows higher doses of radiation to be delivered to the tumours to improve chances of cure or control, while sparing normal tissues to reduce potential toxicities. In local clinical practice, cone-beam computed tomography image guided radiation therapy (CBCT-IGRT) is considered the current standard of care for patients requiring external beam radiation therapy.

2.2. CBCT-IGRT combines CBCT, an imaging technology, with linear accelerators to improve the precision of radiation delivery. In those with a moving cancer lesion (e.g., lung cancer) or cancer lesion surrounded by moving tissues and organs (e.g., prostate cancer), further adjustment of radiation dose during the radiation therapy session is required to minimise the exposure of adjacent healthy tissues to radiation. CBCT-IGRT lacks this ability.

2.3. MR-IGRT combines real-time magnetic resonance imaging with linear accelerator, which allows in-treatment adjustment of radiation doses which enables radiation

therapy to be delivered with higher level of precision while sparing surrounding normal tissue and reduce potential toxicities. The incorporation of MR technology also provides better soft tissue definition than CBCT technology.

Overall benefit of technology

3.1. The Committee acknowledged that CBCT-IGRT was the main comparator to MR-IGRT in patients with cancer requiring high precision radiation therapy. The Committee noted that evidence base comprised two health technology assessment (HTA) reports from the Australian Medical Services Advisory Committee and Canadian Agency for Drugs and Technologies in Health, and 16 additional primary studies. The evidence mostly included observational studies that were non-comparative.

3.2. The Committee noted that based on limited comparative evidence in lung cancer and cervical cancer, MR-IGRT appeared to have comparable safety profile to CBCT-IGRT. Single-arm studies found that toxicity associated with MR-IGRT was mostly mild to moderate (Common Terminology Criteria for Adverse Events [CTCAE] grade ≤2), and severe to very severe toxicity (CTCAE grade ≥3) was generally infrequent.

3.3. For clinical effectiveness, the Committee noted that non-comparative observational studies found that at two-year follow-up in mainly mixed cancer populations, MR-IGRT was associated with low to moderate overall survival and progression-free survival rates, and moderate to high local control rates. In patients with prostate cancer, improved biochemical response as shown by lower prostate-specific antigen levels from baseline to follow-up (1 month to 13 months) was observed. Change in quality of life (QoL) from baseline to follow-up (up to four months) was minimal.

3.4. The Committee further noted that key limitations in the clinical evidence included the low-level evidence and low methodological quality of most studies, small samples, short follow-up periods, and considerable heterogeneity in population, treatment plans, outcome measures, and reporting. These limitations made it difficult to make firm conclusions on the comparative safety or clinical effectiveness of MR-IGRT compared to CBCT-IGRT.

Cost effectiveness

4.1. The Committee noted that no in-house cost-effectiveness analysis was conducted. The cost-effectiveness of MRI-IGRT was based on three published economic evaluations on patients with prostate cancer, which included one cost-minimisation analysis from Australia based on non-inferiority claims, and two cost-effectiveness analyses from the Netherlands and the USA.

4.2. The Committee noted that MR-IGRT would likely cost more than CBCT-IGRT due to

higher capital and staff costs associated with MR-IGRT. Overall, the cost-effectiveness of MR-IGRT depended on the number of fractions required and degree of toxicities for MR-IGRT. Key limitations in the economic evidence were the lack of comparative evidence on MR-IGRT, potential variations in radiotherapy protocols, and applicability to cancer types beyond prostate cancer.

4.3. The Committee further noted that MR-IGRT for cancer treatment is currently reimbursed in Australia based on cost-neutrality from the Medicare Benefits Schedule (MBS) perspective as the same MBS fees applied for MR-IGRT and CBCT-IGRT. Additionally, no reimbursement recommendations were provided in Canada citing the need for additional evidence on clinical effectiveness and cost-effectiveness to determine the role of MR-IGRT in cancer treatment. Overall, the Committee considered that MR-IGRT is unlikely to be cost-effective in cancer treatment in the local context.

Estimated annual technology cost

5.1. Based on an annual estimate of about 1,809 eligible patients with cancer requiring radiation therapy in Singapore who would benefit from Government subsidy for MR-IGRT, the Committee noted that the annual cost impact to the public healthcare system was estimated to be ≥SG$10 million. The estimated cost impact was sensitive to the number of eligible patients.

Organisational feasibility

6.1. The Committee noted that MR-IGRT is currently not available in any PHI or private healthcare institution in Singapore. If MR-IGRT is introduced to local public healthcare institutions, major retrofitting of existing radiation therapy facilities or building of new facility would be needed to accommodate the MR-IGRT equipment. Radiation therapy technologists would also need to be trained to operate the equipment. New workflows and longer MR-IGRT treatment session could also limit the daily capacity of MR-IGRT service provision.

Additional considerations

7.1. The Committee noted that there were 17 ongoing studies on MR-IGRT expected to be completed between 2022 to 2030 – 13 single-arm trials, three trials comparing different MR-IGRT protocols (e.g., different number of MR-IGRT treatment sessions and radiation doses, and one large international registry (N=10,000).

Recommendations

8.1. Based on available evidence, the Committee recommended not subsidising MR-IGRT in cancer treatment in view of the insufficient evidence to demonstrate its additional clinical benefits when compared to CBCT-IGRT. The Committee considered that MR-IGRT is unlikely to be cost-effective given its substantial capital but comparable effectiveness with CBCT-IGRT. Additionally, MR-IGRT has high annual cost, organisational feasibility issues, and an evolving evidence base.