Use of linear accelerators with on-board magnetic resonance imaging (MRI) for real-time MRI-guided radiation therapy treatments

English Summary
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SUMMARY

Use of linear accelerators with on-board magnetic resonance imaging (MRI) for real-time MRI-guided radiation therapy treatments

Background

External radiotherapy is the treatment modality most commonly used in radiation oncology. Medical imaging is essential for planning and executing radiotherapy treatments in order to provide optimal target volume coverage and ensure that the adjacent healthy tissues and the organs at risk (OAR) are protected against radiation-induced complications. Computed tomography (CT) is the imaging modality used most often in radiation oncology. It sometimes requires implanting radio-opaque markers (fiducial markers) to indicate the location of the cancerous lesions, an invasive procedure with a risk of complications. Magnetic resonance imaging (MRI) is increasingly used to support CT, as it provides better contrast between the cancerous lesions and the surrounding soft tissues, which can obviate the need to use these markers in certain circumstances.

Curative radiotherapy treatments are administered using an imaging-guided approach (IGRT) in the treatment room in order to position the patient and assist the irradiation. The most common IGRT devices are linear accelerators (linacs) with on-board CT. Treatments administered with these devices are relatively well tolerated by most patients. However, various factors contribute to making certain cancers more difficult to treat with the usual IGRT approaches. The challenges associated with IGRT can be due to, for example, the difficulty visualizing the tumour by CT, its deformation over the treatment course, movement of internal structures during and between treatment sessions, or the proximity of OAR to the target volumes. Access to higher-performing imaging modalities when planning and executing RT could potentially improve clinical outcomes in certain patients (e.g., an improvement in the adverse effects profile, tumour control and overall survival).

Magnetic resonance-guided radiotherapy (MRgRT) is a novel IGRT modality. The latest generation of MRgRT machines combine on-board MRI with a linac (MR-linac). Two MR-linacs are commercially available: the MRIdian Linac (ViewRay Inc., Ohio, USA) and the Unity (Elekta Ltd, Stockholm, Sweden). These instruments were approved by Health Canada in 2017 and 2019, respectively.

in 2014, the Institut national d'excellence en santé et en services sociaux (INESSS) published an information brief on real-time magnetic resonance imaging (MRI)-guided radiation therapy. Because of the lack of scientific evidence, INESSS could not draw any conclusions regarding the efficacy of this technology.

Task

The Ministère de la Santé et des Services sociaux (MSSS) asked INESSS to produce a report 1) to assess the relevance of making MRgRT with MR-linacs available to patients with tumours that are difficult to treat with conventional IGRT, and 2) to determine the recommended conditions for introducing this technology in Quebec, given its maturity.
Methods

A rapid scientific literature review was conducted to document clinical experience with MR-linacs and the oncological outcomes obtained in patients treated with this technology. Furthermore, contextual and experiential data was gathered from experts through an advisory committee and ad hoc individual consultations. A narrative synthesis on the health need and on the clinical and organizational aspects of using this technology was conducted using data from this consultation process. Lastly, an economic analysis was performed using data from the consultation process and the MSSS's 2017-2018 annual financial and statistical reports.

Results

Clinical data

No study involving patients treated with an MR-linac was identified. The available evidence was obtained with the MR-60 Cobalt device (the ViewRay MRIdian system), which was the first MRgRT system on the market. This evidence was considered transposable to MR-linacs (expert opinion).

A description of the Siteman Cancer Center (SCC)'s clinical experience reported increasing use of MRgRT for the local treatment of abdominal cancers (pancreas and duodenum, hepatobiliary ducts, and oligometastases) in patients likely to derive benefit from an MRI-guided online adaptation approach. Apart from these cases and a small number of cases of thoracic and pelvic cancers, online adaptation was not a rationale for use of MRgRT. Partial and accelerated irradiation after primary resection of low-risk stage 0-1 breast cancer has also accounted for an increasingly large share of cases treated with this technology. For this clinical application, tumour bed intra-fraction motion management via cinematic MRI-assisted gating was the main rationale for use of MRgRT. MRgRT has been used infrequently for the local treatment of other types of cancer ($\leq 5\%$ of cases), or its use has decreased over time.

Prospective and retrospective studies without a control group have reported oncological outcomes for the use of MRgRT to treat abdominal, thoracic, and head and neck (H&N) cancers. Despite the heterogeneity of both the cancer histologies and the RT protocols described in these studies, their treatment reflects current practice with conventional linacs for these types of lesions (expert opinion). In the case of abdominal and H&N cancers, the local and systemic tumour control and overall survival outcomes appeared to be of the same order of magnitude as those with the linacs used in current practice. The same goes for adverse events and radiation-induced complications. However, in the case of abdominal lesions, opinions are divided over whether or not their frequency is lower than that with treatments using conventional linacs. In the case of thoracic cancers, the number of patients and the duration of follow-up were insufficient to rule on the efficacy and safety results. Patient quality of life during and after treatment could not be assessed from the available data. In short, the clinical data have shown the feasibility of MRgRT for administering conformal RT treatments using a conventional or hypofractionated fractionation regimen or in stereotactic conditions (SABR). However, because of the limitations identified in the studies, the accuracy of the estimate of the clinical efficacy of MRgRT and the extent of its adverse effects is uncertain. Furthermore, these limitations compromise the studies' external validity.
Assessment of therapeutic value

The clinical data from the studies that used MR-\textsuperscript{60}\textsuperscript{cobalt} are too immature to permit recognizing MRgRT as having therapeutic value (expert opinion). This technology is still at an experimental stage of its development. However, it does hold some promise for certain emerging clinical applications for abdomen cancers, in particular, hypofractionated and/or adaptive treatments for pancreatic and liver cancers. In the absence of evidence, this promise arose from expert opinions. Preliminary estimates seem to indicate that the unmet need regarding these types of cancer would potentially concern 50 to 150 patients a year in Québec. In short, it is too early to define the potential role of MR-linacs in radiation oncology’s therapeutic arsenal.

Organizational data

Introducing MR-linacs would require a major infrastructure investment. Depending on the system considered, the option of retrofitting an existing infrastructure at a reasonable cost or building a new infrastructure should be examined, taking into account the financial and logistical repercussions of the various possible scenarios.

Switching from CT-based IGRT to MRgRT would involve an additional layer of complexity that would have repercussions in terms of medical personnel training needs. A knowledge upgrade would be needed on the safety measures pertaining to MRI machines, image management and interpretation, and the logistics of implementing treatments (planning, validation, execution, cross-verification and quality assurance). The learning curve would differ according to the degree of familiarity with MRI at the facility concerned (depending on whether or not it has incorporated planning MRI).

Because of the complexity of MRgRT, treatment sessions with an MR-linac would be longer and involve more resources than conventional IGRT with a linac (radiation oncologists, radiologists, technologists and medical physicists). These issues are a concern for the organization of care in Québec, where there is both a shortage of qualified personnel and radiotherapy wait lists. Concerns regarding the compatibility of the information technology infrastructure and the quality assurance tools have also been raised. Given the absence of evidence showing a clinical benefit and the concerns regarding the organization of care, it would be counterproductive to use MR-linacs as substitutes for conventional linacs. In other countries, certain facilities that have implemented MR-linac have chosen to do so on an experimental basis, notably, by teaming up with the research consortiums created by the manufacturers.

Economic data

The results of the economic analysis are highly uncertain. The economic model used includes a probabilistic analysis to specifically take into account the uncertainty regarding the price of a linac, the maintenance costs of Elekta’s devices, and the time allotted to complete a treatment session. The costs associated with personnel training and paying physicians when MR-linacs are used are not included in the analysis, with the result that the costs in this model are underestimated.

Taking these uncertainties into account, the results of the probabilistic analysis indicate that there is, over a 10-year horizon, an 80 % probability that the incremental cost of an MR-linac device relative to a conventional linac would vary between $11.7 M and $20.1 M for Elekta’s Unity system and $12.7 M and $18.4 M for ViewRay’s MRIdian Linac system. The technology is not deemed efficient, as there are no data showing an incremental clinical benefit to justify the higher costs associated with introducing and using MRI-linacs.
Deliberation

After analyzing the best available data, and in the absence of evidence showing a clinical benefit, the members of INESSS’s Comité d’excellence clinique en santé (CEC – santé) believe that public funding of MR-linacs for clinical use would not be a fair and reasonable option. In short, it is the opinion of the CEC – santé’s members that, for now, if this emerging technology were introduced in Québec, limited implementation in an experimental context would be more appropriate.

INESSS’s RECOMMENDATIONS

In light of the CEC – santé’s deliberation, INESSS makes the following recommendations:

Because of the considerable uncertainty regarding the therapeutic value of MR-linac, INESSS feels that this treatment modality should be made available only in a clinical research context. In such case, if applicable, the purchase of these devices should:

- Be limited to a small number because of the low volume of patients for whom a potential benefit is anticipated at this time;
- Include a commitment on the part of the facilities concerned to participate in generating evidence to help define the role of MR-linac in radiation oncology’s therapeutic arsenal; and
- Involve an agreement with the manufacturer to limit the financial risk and share the burden of generating evidence.