Lattice radiotherapy in the curative or palliative treatment of deep, large tumours and metastatic or irresectable disease

Summarized from: Candal Pedreira C., Varela Lema L, Maceira Rozas MC, Faraldo Vallés MJ, Mejuto Martí T. Radioterapia lattice en el tratamiento curativo o paliativo de tumores profundos, de gran volumen y enfermedad metastásica o irresecable. Madrid: Ministerio de Sanidad. Santiago de Compostela: Agencia Gallega para la Gestión del Conocimiento en Salud, ACIS, Unidad de Asesoramiento Científico-técnico; Avalia-t; 2025

PDF at the following link: https://runa.sergas.gal/xmlui/handle/20.500.11940/22601

INTRODUCTION

Due to their characteristics, deep, large, metastatic, and/or unresectable tumors have a poorer prognosis and survival rate compared to tumors that do not present these characteristics, partly due to the inability to achieve effective treatment with conventional therapies. In this context, Lattice Radiotherapy (LRT), a type of spatially fractionated radiotherapy (SFRT), emerges as an alternative for treating these tumors. LRT is characterized by delivering a spatially heterogeneous radiation dose within the tumor, combining high-dose regions (peaks) with low-dose regions (valleys). Dose uniformity at the peaks is achieved through precise planning, which maximizes the therapeutic effect in selected areas of the tumor. The available scientific literature explains the effectiveness of LRT through a combination of factors, primarily the bystander and abscopal effects, as well as immunomodulation. Additionally, due to the administration of heterogeneous doses, radiation toxicity is reduced in areas adjacent to the tumor.

OBJECTIVES

The primary objective of this report is to evaluate the effectiveness and safety of Lattice Radiotherapy compared to conventional treatments for large solid tumors, deep tumors, and metastatic or unresectable diseases.

The specific objectives are: 1) To evaluate the effectiveness of LRT in terms of tumor control, symptom relief, survival, and quality of life; 2) To assess the safety of LRT in terms of toxicity; 3) To evaluate patient acceptability, satisfaction, and perspectives regarding LRT; and 4) To describe the most relevant economic and organizational considerations related to the implementation of this technique.

METHODS

We performed a systematic review of health literature until November 2024. We conducted a search in relevant health databases:

- Specialized databases for systematic reviews and health technology assessment reports, such as Cochrane Library, Epistemonikos, and PROSPERO.
- General databases, including Medline, Embase, and Web of Science.

- Clinical trial registries, such as ClinicalTrials.gov and ICRTRP.

Two independent investigators selected and reviewed the articles according to previously established selection criteria. The information was synthesized following the GRADE system and presented in evidence tables.

RESULTS

From the bibliographic search, 8 articles met the predefined selection criteria. Of these, 7 were case series, and 1 was a cross-sectional study.

Regarding the case series, they included a total of 144 patients with a mean age of 68.5 years. Six of the case series included large tumors (with a size cutoff between 5 and 7 cm). Three studies focused on a single tumor location (lung, breast and cervix). The doses at the vertices and periphery, as well as fractionation schemes, varied widely across studies.

Regarding treatment safety, 169 adverse events were recorded, of which 65.8 % were grade 1, 28.9 % were grade 2, 2.6 % were grade 3, and 2.6 % were grade 4. Survival was measured from one month to two years after treatment. Among studies with a six-month follow-up, overall survival ranged from 50% to 86.4 %, while at 12 months or longer, it ranged from 46.7 % to 86.4 %. Median survival time ranged from 3.8 months to 16 months. The proportion of patients experiencing tumor reduction ranged from 80 % to 100 %. The percentage of tumor reduction varied widely between studies and across time points. Regarding tumor response, the partial response rate ranged from 13 % to 80 %, and the complete response rate varied between 17 % and 100 %.

Four studies assessed symptomatology, all concluding that the intervention had a beneficial effect. Two studies analyzed quality of life, both suggesting that LRT may improve it, primarily due to symptom relief. The certainty of the evidence according to the GRADE system was rated as low to very low for all reported outcomes.

Regarding the cross-sectional study, it was a survey involving professionals engaged in radiotherapy treatments. Most participants were from the United States. A total of 73 participants were included, 75 % of whom had not received specific training in spatially fractionated radiotherapy. About 45 % had used the LRT at least once, with the most commonly used techniques being intensity-modulated radiotherapy (IMRT) and volumetric modulated arc therapy (VMAT).

DISCUSSION

Eight of the nine included studies were case series, and the remaining study had a cross-sectional design. Therefore, no studies were identified that provided comparative data between the LRT and other treatments. Furthermore, the included studies were heterogeneous in terms of LRT characteristics and patient populations, limiting the generalizability of the results.

Nevertheless, the identified studies provide valuable insights. The recorded adverse events were mostly mild, suggesting that LRT has a favorable safety profile. Additionally, most patients experienced tumor volume reduction and partial or complete response to treatment. However, due to the limited follow-up time in these studies, it is not possible to draw medium- to long-term conclusions regarding safety, effectiveness in tumor volume reduction, and survival. Knowledge gaps persist, including whether the administered dose could lead to increased toxicity.

CONCLUSIONS

Currently, the evidence on LRT for deep, large, metastatic, and/or unresectable tumors is limited and based on non-comparative studies, which precludes drawing definitive conclusions. More robust studies are needed to assess its effectiveness, safety and medium- to long-term feasibility.

Safety

The safety of Lattice radiotherapy in deep, large, metastatic, and/or unresectable tumors is very uncertain, i.e., the available results are unreliable. In the published case series, adverse events were generally mild (grade 1 or 2), with respiratory events predominating in treatments for thoracic tumors. There are no results regarding the impact of tumor location and dose-response relationship on the occurrence of LRT-related toxicity.

Effectiveness

The effectiveness of Lattice radiotherapy in deep, large, metastatic, and/or unresectable tumors is very uncertain, i.e., the results are unreliable. It has not been possible to draw firm conclusions on tumor volume reduction, tumor response or survival, nor on how pre-, concomitant and/or subsequent treatments may affect clinical outcomes.

The lack of studies directly comparing Lattice radiotherapy with conventional radiotherapy or other types of fractionated radiotherapy limits the comparative evaluation of its benefits and disadvantages. This lack of controlled studies, the variability between studies and methodological limitations do not allow definitive conclusions to be drawn.

Implementation

The implementation of Lattice radiotherapy in clinical practice may require specific training of healthcare personnel in treatment planning and delivery. In addition, standardization of protocols is necessary to reduce variability in outcomes and ensure consistency in clinical application.

Research needs

There is a need to develop quality clinical studies with controlled and tumor-specific designs that evaluate both the safety and effectiveness of Lattice radiotherapy in comparison with other treatments