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Evaluation of results and costs of high precision radiotherapy (VMAT) compared with conventional radiotherapy (3D) in the treatment of cancer patients with spinal cord compression of metastatic origin

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Abstract

Background: The aim of this study was to evaluate the results and economic costs of using volumetric modulated arc therapy (VMAT) (5 fr x 5 Gy), compared with other conventional 3D radiotherapy schemes such as "5 x 4 Gy" and "10 x 3 Gy".

Materials and methods: The data about the direct costs for the public health system was obtained from the Economic Information "Management per Patient" System available at the Integrated Health Organization Ezkerraldea Enkarterri Cruces. It is a model of real costs per patient which uses a bottom-up methodology which connects all sources of information generated in clinical practice, integrating healthcare information with economic information. This system presents the real cost per individualized patient, and shows the traceability of all clinical care.

The costs of “typical patients” requiring hospital admission were identified for each of the three radiotherapy schemes based on the clinical activity and the material and human resources that were used.

Results: The 5 x 5 Gy scheme has a cost of EUR 4,801.48, which is 1.64% higher (EUR 77) than the “5 x 4 Gy” scheme (EUR 4,724.05). The “10 x 3 Gy” scheme has a cost of EUR 8,394.61, which is 74.8% higher (EUR 3,593) than the “5 x 5 Gy” scheme. The main cost factor in the “10 x 3 Gy” scheme is hospitalization, since patients are at hospital for 2 weeks compared with 1 week in the “5 x 5 Gy” scheme.

Conclusions: The cost per patient of the VMAT “5 x 5 Gy” radiotherapy scheme is notably lower than that of the “10 x 3 Gy” scheme (conventional 3D radiotherapy), with the advantage of being administered in half the time. In relation to the scheme with 5 Gy x 4 sessions, the cost is similar to that of the “5 x 5 Gy” scheme.

Key words: metastatic spinal cord compression; radiotherapy alone; costs; volumetric modulated arc therapy

Introduction

Patients diagnosed with cancer can present spinal cord compression with a 5–10% probability throughout the natural history of their disease. It is a debilitating condition, of an urgent nature, which can lead to irreversible motor deficit for the patient, with notable deterioration in quality of life. Although surgery may be an option for patients with good prognostic factors, radiation therapy is the most frequently administered treatment [1]. However, the optimal radiotherapy regimen for these patients is still under debate.

There are 3D radiotherapy treatment schemes of differing duration commonly used in daily clinical practice, such as the administration of 10 sessions of 3 Gy until a total dose of 30 Gy is reached over two weeks [2], 5 sessions of 4 Gy until 20 Gy [2, 3] is reached over a week or 8 Gy in a single session [4].

Against this background, the international phase II PREMODE study [5] has recently been published, comparing a high-precision radiotherapy scheme for a volumetric modulated arcotherapy (VMAT) technique (25 Gy in 5 sessions, “5 x 5 Gy”) with a control group undergoing conventional 3D radiotherapy scheme (20 Gy in 5 sessions, “5 x 4 Gy”). The phase 2 trial cohort and the control group were compared using propensity score methods to account for baseline differences, balance covariates, and remove selection biases that might arise from these potential confounders.

According to the PREMODE study, the “5 x 5 Gy” high-precision radiotherapy scheme presented 95% local progression-free survival at 6 months, which was significantly higher ($p = 0.026$) than the conventional “5 x 4 Gy” 3D radiotherapy scheme. It also presented low toxicity (2.5% grade 3 toxicity), and had no significant differences in overall survival ($p = 0.82$) or motor function ($p = 0.51$) [5].

Subsequently, results were published comparing patients treated in the PREMODE study and a cohort of 213 patients treated in a previous trial [3] who received a dose of 30 Gy in 10 fractions. The 5 x 5 Gy regimen obtained similar results in terms of progression-free survival, functional results, and overall survival compared to the 30 Gy regimen in 10 fractions.

Palliative radiation therapy treatments for spinal cord compression are generally performed using conventional 3D planning. High precision radiotherapy is normally preferred for radical intent treatments due to its greater planning complexity and lack of evidence demonstrating a benefit over conventional 3D therapy in the palliative setting. [6, 7].

The objective of this study is to evaluate the economic cost of using high-precision radiotherapy according to the PREMODE study (5 x 5 Gy), compared to the different conventional radiotherapy schemes, such as “5 x 4 Gy” and “10 x 3 Gy”, in particular taking into account the practical utility of this study, and the possibility of reducing the number of fractions necessary to obtain the same [8] or even greater [5] clinical benefit in frail and debilitated patients.

Materials and methods

The PREMODE study [5] is an international multicentre phase II trial that included patients with a diagnosis of spinal cord compression of metastatic origin, who were candidates for palliative radiotherapy using a high-precision technique.

The current study data about the direct costs for the public health system was obtained from the Economic Information “Management by Patient” System available at the Integrated Health Organization Ezkerraldea Enkarterri Cruces (OSI EEC). This Information System is based on a model of real costs per patient using a bottom-up methodology which connects all the sources of information generated in clinical practice, integrating healthcare information with economic information. This system presents, in detail, the real cost per individualized patient, and is able to show the traceability of all clinical care [Real World Data (RWD)], since it covers the whole range from primary care to specialized care.

Using this source of information, the cost of patients requiring hospital admission was identified for each of the three radiotherapy schemes, based on the clinical activity and the material and human resources that were used. To compare the available treatment alternatives, the incremental cost-effectiveness ratio was used. The incremental cost-effectiveness ratio is an informative measure generated from such an analysis and represents the ratio of the difference in cost between two medical interventions to the difference in outcomes between the two interventions [9].

The cost of the patients is broken down into three phases: phase 1 (diagnosis), phase 2 (preparation for radiotherapy treatment) and phase 3: treatment.

It should be noted that not all patients with spinal cord compression require hospital admission, but hospitalisation is for those who need it, either due to pain or motor deficit. Furthermore, admission may occur in some phase of the treatment and not during the entire treatment. Due to the clinical variability in the study of these patients, to calculate the entire cost, patients in need of hospital admission were monitored to quantify the resources necessary throughout the treatment. The supplementary material (Tab. 2–4) gives a detailed description of the cost attributable to each of the activities, and the cost that was used as a model for calculating the costs of each of the radiotherapy schemes (including a detailed description of the cost following the radiotherapy planning and execution workflow).

Results

Using the aforementioned methodology, the resources needed to address the three treatment phases were analysed and the costs for performing the following radiotherapy schemes are described below (see Tab. 1):

- “5 x 5 Gy” — five 5 Gy sessions in one week (high precision radiotherapy scheme with VMAT from the PREMODE study);
- “5 x 4 Gy” — five 4 Gy sessions in a week (conventional 3D radiotherapy);
- “10 x 3 Gy” — Ten 3Gy sessions in two weeks (conventional 3D radiotherapy).

The 5 Gy x 5 sessions scheme has a cost that is 1.64% higher (EUR 77) than the “5 x 4” scheme, but it has a local progression-free survival at 6 months of 95%, which is significantly higher than 75.98% of the “5 x 4 Gy” scheme (25% higher). This assumes an incremental cost-effectiveness ratio of 4.05 euros for each percentage point increase in disease-free survival at 6 months (EUR 77/19%).

The “10 x 3 Gy” scheme has a cost that is 74.8% higher (EUR 3,593) than the “5 x 5” scheme, with a 6-month local progression-free survival and overall survival rate of 7% ($p = 0.36$) and 8% ($p = 0.74$) lower, respectively. Therefore, the 10 x 3 scheme is considered a dominating alternative. The main cost factor in the “10 x 3 Gy” scheme is hospitalisation, since it lasts for 2 weeks instead of 1 week (as in the “5 x 5 Gy” scheme).

Discussion

The results obtained in relation to the costs attributable to each of the radiotherapy schemes support the use of the “5 x 5” scheme with VMAT from the perspective of health system resource consumption.

The objective of the PREMODE study was to contrast a scheme that was short (increasing the dose in each session), effective and well tolerated. Five sessions of 5Gy (administered in one week) with a high precision technique using VMAT are equivalent to 31.3 Gy of equivalent biological dose (EQD2) for tumour cell death (considering an alpha/beta of 10), in a similar way to a 30 Gy scheme administered over 2 weeks (32.5 Gy). Moreover, 5 x 4 Gy sessions administered with a conventional 3D technique are equivalent to a 23.3Gy dose (EQD2) for an alpha/beta of 10.

Furthermore, we must consider that the dose that can be administered with VMAT using the “5 x 5 Gy” scheme is similar to a classic 30 Gy scheme in 2 weeks, but administered in half the time (one week instead of two), with the consequent benefit for patients [10] and a shorter hospital stay (in the case of patients who require it because of motor deficit).

One of the limitations of this study is that its results cannot be directly extrapolated, from an international point of view, although we consider it applicable in general terms to the public health system hospitals in our country (Spain).

The instrument to be used to assess value for money is the Quality Adjusted Life Year (QALY). Currently, there are countless requirements for resources to pay for health. The QALY is a measure of disease burden, including both the quality and the quantity of life lived (establishing the cost of a new drug, technology or a health care intervention). The QALY can be used to provide a value for these treatments or interventions that can be used for comparison between new and previously established treatments [11].
Therefore, the QALY allows us to turn the lock of a cost-benefit-analysis of medical interventions. Unfortunately, we also acknowledge this limitation in the present study. We calculated the economic cost of three different radiation schedules in order to justify the use of VMAT in palliative patients. However, data regarding QALY is not included. The strength of the study is that the calculations were carried out with a real cost system, prospectively, during the admission and treatment of the patients.
The appropriate use of health resources [12] with different radiotherapy treatment techniques [13] is increasingly being emphasized, although the publications are in general scarce, especially in the case of palliative radiotherapy [14–16].
To our knowledge, this is the first economic study that justifies the use of a VMAT technique for palliative radiotherapy of patients with spinal cord compression. We consider that the results of the PREMODE study [5] support the use of a VMAT technique as a good alternative for palliative treatment for patients with spinal cord compression, combining a rational use of healthcare resources, with the maximum possible clinical benefit for patients [7].

Conclusion

The cost per patient of the “5 x 5” high-precision radiotherapy scheme is notably lower than the “10 x 3” scheme, of 30 Gy in two weeks (conventional 3D radiotherapy), with the advantage of being administered in half the time. In relation to the 5 Gy x 4 sessions scheme, the cost is similar to the “5 x 5” scheme, but with the observed clinical advantage in the improvement of local progression-free survival in favour of the “5 x 5” scheme.
As a final conclusion, the evaluation of procedures and the introduction of organizational improvements have a significant impact on healthcare organisations. This organisational change meant a more efficient use of resources, as well as an improvement in the health outcomes of patients.

Conflict of interest

Authors declare no competing interest.

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References

1. Patchell RA, Tibbs PA, Regine WF, et al. Direct decompressive surgical resection in the treatment of spinal cord compression caused by metastatic cancer: a randomised trial. Lancet. 2005; 366(9486): 643–648, doi: 10.1016/S0140-6736(05)66954-1, indexed in Pubmed: 16112300.

2. Rades D, Lange M, Veninga T, et al. Preliminary results of spinal cord compression recurrence evaluation (score-1) study comparing short-course versus long-course radiotherapy for local control of malignant epidural spinal cord compression. Int J Radiat Oncol Biol Phys. 2009; 73(1): 228–234, doi: 10.1016/j.ijrobp.2008.04.044, indexed in Pubmed: 18539406.

3. Rades D, Šegedin B, Conde-Moreno AJ, et al. Radiotherapy With 4 Gy × 5 Versus 3 Gy × 10 for Metastatic Epidural Spinal Cord Compression: Final Results of the SCORE-2 Trial (ARO 2009/01). J Clin Oncol. 2016; 34(6): 597–602, doi: 10.1200/JCO.2015.64.0862, indexed in Pubmed: 26729431.

4. Hoskin PJ, Hopkins K, Misra V, et al. Effect of Single-Fraction vs Multifraction Radiotherapy on Ambulatory Status Among Patients With Spinal Canal Compression From Metastatic Cancer: The SCORAD Randomized Clinical Trial. JAMA. 2019; 322(21): 2084–2094, doi: 10.1001/jama.2019.17913, indexed in Pubmed: 31794625.

5. Rades D, Cacicedo J, Conde-Moreno AJ, et al. Precision Radiation Therapy for Metastatic Spinal Cord Compression: Final Results of the PRE-MODE Trial. Int J Radiat Oncol Biol Phys. 2020; 106(4): 780–789, doi: 10.1016/j.ijrobp.2019.11.401, indexed in Pubmed: 31812719.

6. Olson R, Schlijper R, Chng N, et al. SUPR-3D: A randomized phase iii trial comparing simple unplanned palliative radiotherapy versus 3d conformal radiotherapy for patients with bone metastases: study protocol. BMC Cancer. 2019; 19(1): 1011, doi: 10.1186/s12885-019-6259-z, indexed in Pubmed: 31660894.

7. Barton M, Batumalai V, Spencer K. Health Economic and Health Service Issues of Palliative Radiotherapy. Clin Oncol (R Coll Radiol). 2020; 32(11): 775–780, doi: 10.1016/j.clon.2020.06.013, indexed in Pubmed: 32646615.

8. Rades D, Cacicedo J, Conde-Moreno AJ, et al. Comparison of 5 × 5 Gy and 10 × 3 Gy for metastatic spinal cord compression using data from three prospective trials. Radiat Oncol. 2021; 16(1): 7, doi: 10.1186/s13014-020-01737-7, indexed in Pubmed: 33413492.

9. Bambha K, Kim WR. Cost-effectiveness analysis and incremental cost-effectiveness ratios: uses and pitfalls. Eur J Gastroenterol Hepatol. 2004; 16(6): 519–526, doi: 10.1097/00042737-200406000-00003, indexed in Pubmed: 15167152.

10. Butala AA, Williams GR, Fontanilla HP, et al. Making the Most of a Crisis: A Proposal for Network-Based Palliative Radiation Therapy to Reduce Travel Toxicity. Adv Radiat Oncol. 2020; 5(6): 1104–1105, doi: 10.1016/j.adro.2020.07.013, indexed in Pubmed: 32838072.

11. Kim YE, Jung YS, Ock M, et al. A Review of the Types and Characteristics of Healthy Life Expectancy and Methodological Issues. J Prev Med Public Health. 2022; 55(1): 1–9, doi: 10.3961/jpmph.21.580, indexed in Pubmed: 35135043.

12. Rossi R, Danesi V, Massa I, et al. The challenge of sustainability in healthcare systems: cost of radiotherapy in the last month of life in an Italian cancer center. Support Care Cancer. 2021; 29(5): 2735–2742, doi: 10.1007/s00520-020-05718-0, indexed in Pubmed: 32989523.

13. Xie Y, Guo B, Zhang R. Cost-effectiveness analysis of radiotherapy techniques for whole breast irradiation. PLoS One. 2021; 16(3): e0248220, doi: 10.1371/journal.pone.0248220, indexed in Pubmed: 33684139.

14. Qu XM, Chen Y, Zaric GS, et al. Is SABR Cost-Effective in Oligometastatic Cancer? An Economic Analysis of the SABR-COMET Randomized Trial. Int J Radiat Oncol Biol Phys. 2021; 109(5): 1176–1184, doi: 10.1016/j.ijrobp.2020.12.001, indexed in Pubmed: 33309977.

15. Fèvre CLe, Menoux I, Pin Y, et al. Coût de la radiothérapie des métastases osseuses en France : étude rétrospective monocentrique. Cancer/Radiothérapie. 2019; 23(1): 1–9, doi: 10.1016/j.canrad.2018.01.009.

16. Duran I, Fink MG, Bahl A, et al. Health resource utilisation associated with skeletal-related events in patients with bone metastases secondary to solid tumours: regional comparisons in an observational study. Eur J Cancer Care (Engl). 2017; 26(6), doi: 10.1111/ecc.12452, indexed in Pubmed: 26865392.

Figure 1. Example of a treatment plan with volumetric modulated arc therapy (VMAT)

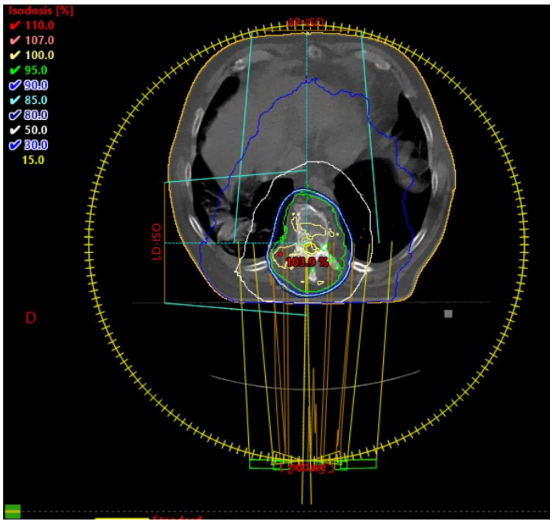

Figure 2. Example of a treatment plan with 3D (three fields)

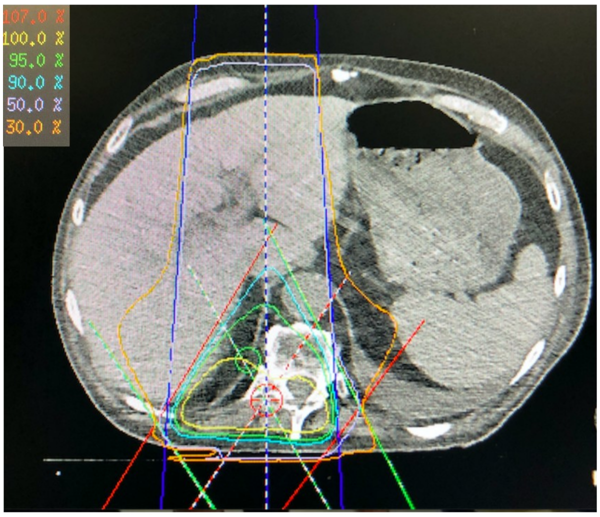

Table 1. Treatment scheme costs

Phases	**Scheme cost [EUR]**		
	5 x 5 Gy	**5 x 4 Gy**	**10 x 3Gy**
Phase 1: Diagnosis	915.27	915.27	915.27
Phase 2: Treatment Preparation	218.85	138.22	138.22
Phase 3: Treatment	3,667.36	3,670.56	7,341.12
Total cost of process	**4,801.48**	**4,724.05**	**8,394.61**

Table 2. Cost per typical patient in 5 x 5 Gy scheme in PREMODE clinical trial

Activity	Quantity	Cost [EUR]	
Emergency admission	1	554.84	**PHASE 1 Diagnosis**
Oncological radiotherapy consultation (first visit)	1	106.96	
Oncological radiotherapy nursing consultation	1	99.62	
MRI whole spinal cord	1	145.03	
Lab test and tumour marker	1	8.82	
		915.27	
CT planning without contrast	1	99.62	**PHASE 2 Treatment Preparation**
MRI and CT fusion + contouring (20 mins RTT)	1	119.23	
Treatment volume contouring (30 mins doctor)	1		
Dosimetry calculation (40 mins physicist)	1		
Quality control (25 mins physicist)	1		
Quality control (15 mins machine time)	1		
Dosimetry approval (5 mins doctor)	1		
		218.85	
Hospital admission 7 days	7	2,992.15	**PHASE 3 Treatment**
BeamView CBCT (daily) (10 mins machine time)	5	522.11	
Radiotherapy sessions (5 mins machine time)	5		
Radiotherapy treatment	5		
Weekly follow-up radiotherapy consultation (doctor)	1	53.48	
Weekly follow-up nursing consultation	1	99.62	
		3,667.36	
		4,801.48	**Total cost**

MRI — magnetic resonance imaging; CT — computed tomography; RTT — trained radiation therapist; CBCT — cone-beam computed tomography

Table 3. Cost per typical patient in 5 x 4 Gy (3D) scheme following routine clinical practice

Activity	Quantity	Cost [EUR]	

Emergency admission	1	554.84	**Phase 1: diagnosis**
Oncological radiotherapy consultation (first visit)	1	106.96	
Oncological radiotherapy nursing consultation	1	99.62	
MRI whole spinal cord	1	145.03	
Lab test and tumour marker	1	8.82	
		915.27	
CT planning without contrast	1	99.62	**Phase 2: treatment preparation**
MRI and CT fusion + contouring (20 mins RTT)	1	38.60	
Treatment volume contouring (15 mins doctor)	1		
Dosimetry calculation (15 mins physicist)	1		
Dosimetry approval (5 mins doctor)	1		
		138.22	
Hospital admission 7 days	7	2,992.15	**Phase 3: treatment**
BeamView CBCT (initially) (2 mins machine time)	1	3.20	
Radiotherapy sessions (15 mins machine time)	5	24.01	
Radiotherapy treatment	5	498.10	
Weekly follow-up radiotherapy consultation (doctor)	1	53.48	
Weekly follow-up nursing consultation	1	99.62	
		3,670.56	
		4,724.05	**Total cost**

MRI — magnetic resonance imaging; CT — computed tomography; RTT — trained radiation therapist; CBCT — cone-beam computed tomography

Table 4. Cost per typical patient in 10 x 3 Gy (3D) scheme following routine clinical practice

Activity	Quantity	Cost [EUR]	
Emergency admission	1	554.84	**Phase 1: diagnosis**
Oncological radiotherapy consultation (first visit)	1	106.96	
Oncological radiotherapy nursing consultation	1	99.62	
MRI whole spinal cord	1	145.03	
Lab test and tumour marker	1	8.82	
		915.27	

CT planning without contrast	1	99.62	**Phase 2: treatment preparation**
MRI and CT fusion + contouring (20 mins RTT)	1	38.60	
Treatment volume contouring (15 mins Doctor)	1		
Dosimetry calculation (15 mins Physicist)	1		
Dosimetry approval (5 mins Doctor)	1		
		138.22	
Hospital admission 14 days	14	5,984.30	**Phase 3: treatment**
BeamView CBCT (1 weekly) (4 mins machine time)	2	1,050.62	
Radiotherapy sessions (30 mins machine time)	10		
Radiotherapy treatment	10		
Weekly follow-up radiotherapy consultation (doctor)	2	106.96	
Weekly follow-up nursing consultation	2	199.24	
		7,341.12	
		8,394.61	**Total cost**

MRI — magnetic resonance imaging; CT — computed tomography; RTT — trained radiation therapist; CBCT — cone-beam computed tomography