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Review Article

# Survival outcomes after using charged particle radiotherapy as a treatment modality for gliomas: A systematic review and meta-analysis

Bareq S. Al-Lami [a], Baqer S. Al-Lami [a], Yasir S. Al-Lami [a]

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## Abstract

### Introduction

Charged particle therapy is an emerging radiation treatment for a number of tumors; however, more research is needed to determine its safety and efficacy when treating intra-axial brain tumors (commonly known as gliomas). The overall survival of patients treated with charged particle radiation versus those receiving photon therapy were compared in this systematic review and meta-analysis.

### Methods

The databases used as part of the search strategy were the following: MEDLINE (PubMed), Google Scholar, Scopus, and Cochrane. The search was conducted in order to find pertinent clinical studies. A random-effect meta-analysis was used to generate pooled estimates of overall survival at 1,3, and 5 years.

### Results

Nineteen studies with a total of 1140 patients were included in this meta-analysis. Following treatment, the patient's follow-up period lasted 44.4 months (range: 14.3 - 91.2 months). At one year (relative risk 1.17, 95% CI 1.07 - 1.28; $p = 0.049$), three years (relative risk 1.73, 95% CI 1.41 - 2.12; $p = 0.001$), and five years (relative risk 2.00, 95% CI 1.52 - 2.63; $p = 0.005$), charged particle radiotherapy had a significantly higher pooled overall survival than photon therapy.

### Conclusion

Charged particle therapy could be associated with better clinical outcomes for patients with gliomas compared to photon therapy. More prospective randomized trials and comparative studies are strongly encouraged to enable accurate meta-analysis and a better exploration of prognosis.

## Résumè

### Introduction

La protonthérapie est un nouveau traitement par rayonnement pour un certain nombre de tumeurs; cependant, des recherches supplémentaires sont nécessaires pour déterminer sa sécurité et son efficacité dans le traitement des tumeurs cérébrales intra-axiales (communément appelées gliomes). Cette revue systématique et cette méta-analyse ont comparé la survie globale des patients traités par protonthérapie à celle des patients traités par photothérapie.

### Méthodologie

Nous avons consulté PubMed, Google Scholar, Embase, Scopus et Cochrane pour trouver des études cliniques pertinentes. Une méta-analyse à effets aléatoires a été réalisée pour générer des estimations groupées de la survie globale à 1, 3 et 5 ans, ainsi que de l'incidence des événements indésirables pour chaque modalité de traitement.

### Résultats

Dix-neuf études portant sur un total de 1 140 patients ont été incluses dans cette méta-analyse. Après le traitement, la période de suivi des patients a duré 44,4 mois (intervalle: 14,3 - 91,2 mois). À un an (risque relatif 1,17, IC 95% 1,07 - 1,28; $p$ = 0,049), trois ans (risque relatif 1,73, IC 95% 1,41 - 2,12; $p$ = 0,001) et cinq ans (risque relatif 2,00, IC 95% 1,52 - 2,63; $p$ = 0,005), la protonthérapie a eu une survie globale groupée significativement plus élevée que la photonthérapie.

### Conclusion

La protonthérapie pourrait être associée à de meilleurs résultats cliniques pour les patients atteints de gliomes que la photonthérapie. Il est vivement recommandé de réaliser davantage d'essais randomisés prospectifs et d'études comparatives pour permettre une méta-analyse précise et une meilleure exploration du pronostic.


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## Introduction

Intra-axial brain tumors, commonly known as gliomas, are common primary brain tumors that account for 32% of all brain tumors and 80% of tumors within the malignant subset [1]. Based on the recent World Health Organization classification (2007), gliomas are histologically separated into four grades, ranging from relatively symptomless Grade I pilocytic astrocytoma to almost universally fatal Grade IV glioblastoma [2]. Due to their biological aggressiveness or location in close proximity to critical structures, gliomas continue to cause high morbidity and mortality [3] the 5-year overall survival rate of patients treated with standard surgical intervention is 9.8% [4]. Therefore, the urge to find a more effective and safe treatment for patients with gliomas is strong.

In order to treat gliomas, recent developments highlight a multimodality approach that includes postoperative radiation therapy to improve local control of advanced disease with positive surgical margins and extend the period until recurrence following surgical resection [5]. Due to their benefits in enhancing dose conformity and sparing vital normal tissue, photon-based radiotherapies, such as intensity-modulated radiotherapy (IMRT) and conventional three-dimensional conformal photon therapy (3D-CRT), are now widely used in almost all treatment sites. Another development in the strategy of increasing the radiation dose to the tumor target volume while decreasing the radiation dose to the nearby healthy structures is charged particle radiotherapy. Charged particle radiation is different from photon-based therapy in that it minimizes unwanted exit dosage and delivers the majority of beam energy to the target, independent of its depth [6], according to

the Bragg peak phenomenon. Additionally, charged particle radiation provides higher biological efficacy, resulting in an even greater degree of pathologic tissue cell destruction [7]. From a clinical standpoint, these benefits provide a chance to enhance the therapeutic ratio of radiation for gliomas and quality of life outcomes such as weariness, neurocognitive impairment, and hormone imbalances.

Although charged particle radiation has been shown to be dosimetrically superior to other forms of radiation therapy for the treatment of gliomas [8], [9], [10], [11], it is unclear if this advantage translates into a clinically significant survival benefit. Charged particle radiation is less accessible than photon-based therapy, necessitates an expensive infrastructure, is more expensive, and has inconsistent insurance company coverage because of unknown treatment outcomes [12]. The overall amount of research comparing charged particle radiotherapy directly to photon-based therapy is restricted due to the relative rarity of gliomas, the length of time required to complete a clinical trial, and the high cost of charged particle radiotherapy treatment facilities. In order to compare the overall survival results between charged particle radiation and photon-based therapy in the treatment of gliomas, a systematic review and meta-analysis of the published studies were conducted.

## Section snippets

## Methods

PRISMA criteria were followed in conducting this systematic review. The population for the literature search was defined as the published studies looking at the role of charged particle radiotherapy in glioma patients; the intervention was defined as patients treated with charged particle radiotherapy; the comparison was defined as the outcome of patients receiving charged particle radiotherapy compared to those receiving photon therapy; and the outcomes were defined as treatment-related…

## Results

A thorough review of the literature yielded 3745 potential papers, of which 254 were obtained for analysis in full. Nineteen studies, comprising six studies utilizing photon treatment and thirteen using charged particle radiation, ultimately satisfied the inclusion criteria and were included in this study. Three studies on carbon-ion treatment (CIRT) and ten studies on proton beam therapy (PBT) were included in the review of charged particle radiotherapy [15], [16], [17], [18], [19], [20], [21]…

## Discussion

Up to this day, this meta-analysis was the first to investigate the benefits of photon therapy and charged particle therapy for treating glioma patients on this scale. Nineteen studies, including 1140 patients, fulfilled the inclusion criteria and were incorporated into the meta-analysis. This review adds to the existing literature by providing a comprehensive analysis of a large group of patients, specifically focusing on gliomas. This systematic review and meta-analysis, due to the larger…

## Conclusion

In conclusion, the systematic review and meta-analysis have provided valuable insights into the comparative effectiveness of charged particle radiotherapy versus photon therapy for intra-axial brain tumors, particularly gliomas. By synthesizing data from nineteen studies involving 1140 patients, this analysis underscores the potential superiority of charged particle radiotherapy, including proton and carbon-ion therapy, in improving

overall survival rates at 1, 3, and 5 years compared to…

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