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## Abstract

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## Proton Therapy in Cancer Treatment: A Systematic Review of Randomized Controlled Trials

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### Abstract

**Objectives:**

The evidence on proton therapy in cancer treatment is emerging, but there are limited randomized trials published to date. This study aimed to summarize the randomized studies evaluating the proton therapy in the treatment of malignancies.

**Methods:**

A search was conducted through scientific databases to identify randomized controlled trials (RCTs) comparing proton therapy with standard treatment in any malignancy. We assessed the risk of bias of each trial using the revised Cochrane tool (RoB 2.0). The outcomes of interest were efficacy and toxicity. We employed Synthesis Without Meta-analysis (SWiM) approach to summarize the data qualitatively.

**Results:**

Five low-risk-of-bias trials with 591 patients were identified. These trials evaluated a variety of malignancies, including esophageal cancer, non-small cell lung cancer, glioblastoma, hepatocellular carcinoma and solid tumor leptomeningeal metastasis. Four trials compared proton therapy with photon therapy; one trial (hepatocellular carcinoma) compared with radiofrequency ablation. A study (leptomeningeal metastases) showed that proton craniospinal irradiation significantly improved overall survival (OS) and progression-free survival (PFS), compared to photon in-field radiation therapy. Whereas the other four studies demonstrated no differences in OS and PFS. Two studies (esophageal cancer and glioblastoma) demonstrated a reduction in toxicity burden.

**Conclusion(s):**

Proton therapy is a promising novel radiotherapy modality with potentials in improving survival outcomes and minimizing toxicity in cancer treatment of both curative and palliative intents. Further studies on other tumor subsites are underway.