# INPLASY PROTOCOL

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## Proton beam therapy versus current standard radiation therapy in the treatment of rhabdomyosarcoma in children: A systematic review

Noonan, L[1]; O'Donovan, T[2]; Devine, A-M[3]; Barry, A; England, A[4]; McEntee, MF[5].

**Review question / Objective:** How does the use of proton beam therapy in the treatment of localised rhabdomyosarcoma in children impact their survival outcomes compared to standard external beam radiation therapy using photons?

**Condition being studied:** Clinical effectiveness of radiation therapy treatment for rhabdomyosarcoma tumours in children.

**Study designs to be included:** Original/primary peer reviewed research including randomised control trials, clinical trials, comparative studies. Narrative literature reviews, dosimetric studies, planning and simulation studies, case studies, and short communications will be excluded.

## INTRODUCTION

**Review question / Objective:** How does the use of proton beam therapy in the treatment of localised rhabdomyosarcoma in children impact their survival outcomes compared to standard external beam radiation therapy using photons?

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## METHODS

**Search strategy:** The following databases will be systematically searched electronically to identify published literature relating to radiation therapy treatment in paediatric rhabdomyosarcoma patients: PUBMED/MEDLINE, EMBASE, the

Cochrane Library, CINAHL and Scopus. The search will be conducted using Medical Subject Heading (MeSH) terms if available and free text terms and will include combinations of the following key words: 'rhabdomyosarcoma', 'paediatrics/ pediatrics/children/childhood cancer', 'proton therapy/proton beam therapy', 'external beam radiation therapy/ radiotherapy'. A comprehensive search of grey literature will also be carried out. The search will be restricted to primary research literature published in English between January 2011 and December 2021. Only studies on localised disease will be included, and those concerning metastatic disease only will be excluded. Mixed studies including both localised and metastatic disease may be included if results of clinical outcomes for each group are reported separately. Due to the expected paucity of eligible studies, there will be no search restrictions on tumour subtype or primary tumour site. Studies which include the use of other treatment modalities in addition to radiation therapy may be included.

**Participant or population:** Children <18 years with histologically and pathologically confirmed localised rhabdomyosarcoma.

**Intervention:** Proton Beam Therapy.

**Comparator:** Standard photon external beam therapy (EBRT) techniques including 3D conformal, IMRT and VMAT.

**Study designs to be included:** Original/ primary peer reviewed research including randomised control trials, clinical trials, comparative studies. Narrative literature reviews, dosimetric studies, planning and simulation studies, case studies, and short communications will be excluded.

**Eligibility criteria:** NA.

**Information sources:** PUBMED/MEDLINE, EMBASE, the Cochrane Library, CINAHL and Scopus.

**Main outcome(s):** Measures of clinical effectiveness including event free survival, overall survival, progression free survival, local control.

**Additional outcome(s):** Measures of toxicity (acute and late).

**Data management:** Each database will be searched individually, and their results combined. Two researchers will independently review titles, abstracts and full texts of records found during initial search and screening process to assess whether the studies selected are eligible for inclusion in this systematic review as per the selection criteria. In the case of discrepancy surrounding inclusion eligibility, all reviewers will discuss the matter until a clear conclusion is reached. Data extraction will be carried out using a modified data collection form such as the Cochrane data collection form for interventional studies including RCTs and non-RCTs, specifically adapted for this review. Depending on the types of studies selected, several versions of the data collection forms may be required. Extracted data will be exported to and managed by an open access data system such as Covidence. Duplicates will be identified and removed. All decisions regarding data extracted will be discussed and decided by consensus. In the case of discrepancies, investigators will be contacted for further clarification of data and results. Data collection forms and data systems will be piloted prior to review.

**Quality assessment / Risk of bias analysis:** Comparative qualitative studies will be assessed for quality of results using the Cochrane Collaboration tool for assessing risk of bias (RoB) (Sterne et al., 2019). This tool will be applied to each individual study eligible for review following data extraction, and each study will be assessed by six domains of bias including: selection bias (randomisation and allocation concealment), performance bias (blinding of patients and personnel), detection bias (blinding of assessment of outcomes), attrition bias (incomplete data), reporting bias (selective reporting) and other sources of potential bias.

**Strategy of data synthesis:** A detailed narrative synthesis will be carried out. This will include a description of how the intervention of proton therapy works and for whom this applies, description of the preliminary findings of the included studies, investigation of relationships that exist between included studies, and assessment of the robustness of results. Statistical meta-analysis may also be included in the review however the possibility of this analysis will only become apparent following extraction of the data.

**Subgroup analysis:** NA.

**Sensitivity analysis:** NA.

**Language restriction:** English.

**Country(ies) involved:** Ireland.

**Other relevant information:** NA.

**Keywords:** Rhabdomyosarcoma, paediatrics/pediatrics, proton beam therapy, radiation therapy/radiotherapy, external beam.

**Dissemination plans:** Conference presentations (ESTRO) and peer-reviewed journal article (JMIRS).

**Contributions of each author:**
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