



Contribution ID: 376

Type: **Invited Presentation**

## Recent Advances in Hadron Therapy

Recent advances in hadron therapy, particularly proton and carbon ion therapy, are reshaping the landscape of cancer treatment by offering increased precision, reduced toxicity, and expanded clinical indications. Technological innovations in beam delivery systems, adaptive treatment planning, and real-time imaging have significantly enhanced dose conformality while minimizing exposure to surrounding healthy tissue. These developments are particularly impactful for treating tumours in complex anatomical regions or radioresistant cancers, where conventional X-ray therapy often falls short. The emergence of compact and cost-effective facility designs is addressing long-standing concerns about infrastructure complexity and expense, making hadron therapy more accessible. Furthermore, accelerator-driven Boron Neutron Capture Therapy (BNCT) is re-emerging as a promising modality, benefiting from advancements in accelerator technology and boron compound development.

Another innovative frontier is FLASH therapy, an experimental but highly promising technique in hadron therapy involving ultra-high dose rate irradiation, which has shown potential to reduce normal tissue toxicity while maintaining tumour control in preclinical settings. High-intensity particle beams, essential for translating FLASH into clinical hadron therapy, are driving the next generation of facility designs. Looking further ahead, the promising results of preclinical research in radioactive ion beams, mini-beam therapy, and alternative ion species (beyond protons and carbon) is opening new avenues for optimizing the precision and biological effectiveness of hadron therapy.

Beyond physics and engineering, biology is poised to drive the next leap in hadron therapy. The generation of complex DNA damage by high linear energy transfer (LET) particles is linked to the accumulation of cytosolic DNA, which in turn activates innate immune responses. This raises the prospect of synergistic effects between hadron therapy and immunotherapy. In parallel, insights into DNA repair pathway choice are revealing promising biomarkers for treatment selection and novel targets for radiosensitization. As these multidisciplinary advances converge, hadron therapy is transitioning from a niche modality to a cornerstone of precision oncology.

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**Track Classification:** Nuclear Physics Applications