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## Pre-Clinical Studies on Heavy Ion Minibeam Therapy

Charged particles, characterized by superior relative biological effectiveness (RBE) and more targeted depth dose deposition as compared with photons, have the potential to significantly enhance the therapeutic index of minibeam radiation therapy (MBRT). Proton minibeam radiation therapy has emerged as a compelling technique, showcasing remarkable normal tissue sparing for both skin and brain coupled with superior tumor control effectiveness compared to standard therapy [1]. The high therapeutic index of MBRT could be further enhanced by combining MBRT with heavy ions, leveraging their reduced multiple Coulomb scattering and higher RBE compared to protons. Notably, carbon exhibits indications of enhancing the immune response more effectively than photons or proton beams [2], suggesting potential synergies with immune priming in MBRT.

Motivated by these findings, our team undertook a series of preclinical studies to elucidate the impact of heavy ion minibeam therapy (MBT) on both normal tissues and different types of tumors.

Preclinical studies with carbon minibeam on osteosarcoma-bearing mice, conducted at GSI in Germany, indicate tumor growth delay comparable to standard carbon therapy.

We also explored very heavy ions, such as neon and argon, which show promise for treating hypoxic tumors due to their beneficial oxygen enhancement ratio. Neon MBT, implemented at HIMAC in Japan, significantly reduces normal tissue toxicity [3] and delays tumor growth in carcinoma-bearing mice.

This talk presents an overview of preclinical studies on (charged) particle minibeam therapy (PMBT), focusing on heavy ion MBT. Despite the promising results, further preclinical investigations are crucial to assess the efficacy of heavy ion MBT across diverse tumors. Investigating the impact of heavy ion MBT on complex tissues such as lung, liver, heart, muscles, and nervous tissues is essential to fully comprehend its potential benefits and limits and pave the way for its clinical translation.

### References

- [1] Prezado Y, Jouvion G et al., Int Radiat Onc Biol Phys (2019)
- [2] Tinganelli W, Durante M. Cancers (2020)
- [3] Prezado Y, Hirayama R et al., Cancers (2021)

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