Proton Radiation Therapy (PRT) has emerged as a powerful anticancer modality, demonstrating rapid growth in hadrontherapy over recent decades. Due to its inverse dose deposition profile, the modality has a unique inverse dose deposition profile that allows precise delivery of high doses to targeted deep tissues while minimizing exposure to surrounding healthy tissue [1]. Recently, innovative approaches have been developed to enhance its relative biological effectiveness (RBE), adding boron in low concentrations to the body which, upon proton activation, releases three high-energy alpha particles [2].

Beyond oncology, low-dose Radiation Therapy (RT) exhibits hormetic effects, producing non-toxic biological responses that have therapeutic potential beyond killing cancer cells. For instance, RT has been effective in treating peripheral amyloidosis, a disease characterized by protein aggregation which resembles widespread neurodegenerative disorders such as Alzheimer's (AD), Parkinson's (PD), or Huntington diseases (HD) [3].

Hence, we aim to develop advanced PRT techniques, combined with boron-based compounds, to target toxic amyloids associated with neurodegenerative disorders. We hypothesize that this approach, particularly in combination with low-dose PRT, will reduce amyloid aggregation and toxicity while significantly enhancing RBE.

With the intent to simulate the impact of PRT on amyloid structures, Topas nBio, a Monte Carlo simulation tool that models particle interactions and radiobiological effects at the subcellular level was utilized. The "pdb4dna" extension of Topas nBio enables the integration of biomolecules from the Protein Database Bank (PDB) and simulates radiation-induced strand breaks. We modified this extension to study amyloid breakage specifically. Additionally, preliminary simulations of proton-boron capture therapy (PBCT) are being conducted to validate its occurrence in the simulation. Future work will focus on applying boron to amyloid structures to enhance breakage compared to standard PRT, laying the groundwork for innovative therapeutic approaches and irradiate in vitro cell samples contained the identified compounds and verify via microscopy techniques the impact of proton irradiation in the systems.

References

[1] Paganetti, H., ed. 2012. Proton therapy physics (Milton: Chapman and Hall/CRC).

[2] Cirrone, G. A. P., et al. 2018. "First experimental proof of Proton Boron Capture Therapy (PBCT) to enhance proton therapy effectiveness." Scientific Reports 8, 1141.

[3] Coelho, C. M., et al. 2022. "Radiation as a Tool against Neurodegeneration—A Potential Treatment for Amyloidosis in the Central Nervous System." International Journal of Molecular Sciences 23, 12265