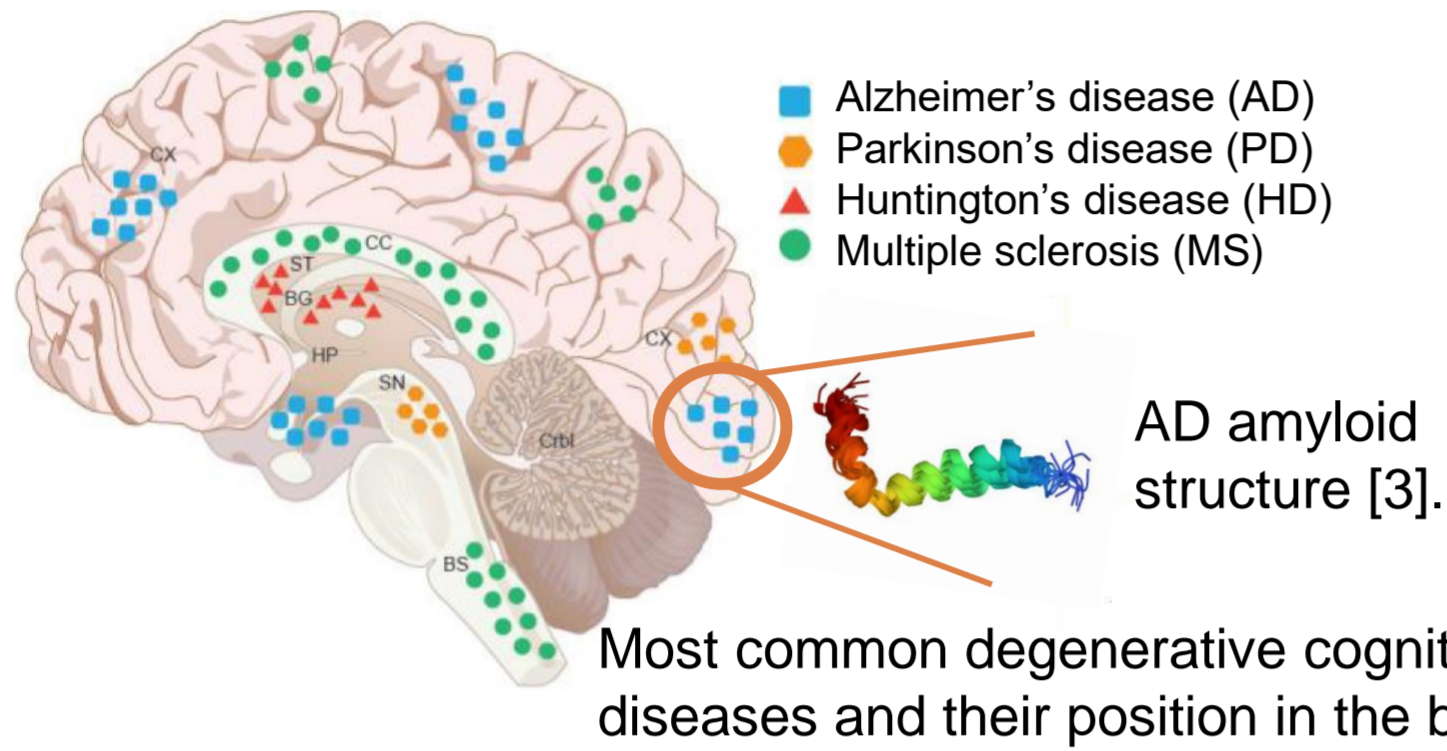


## Introduction

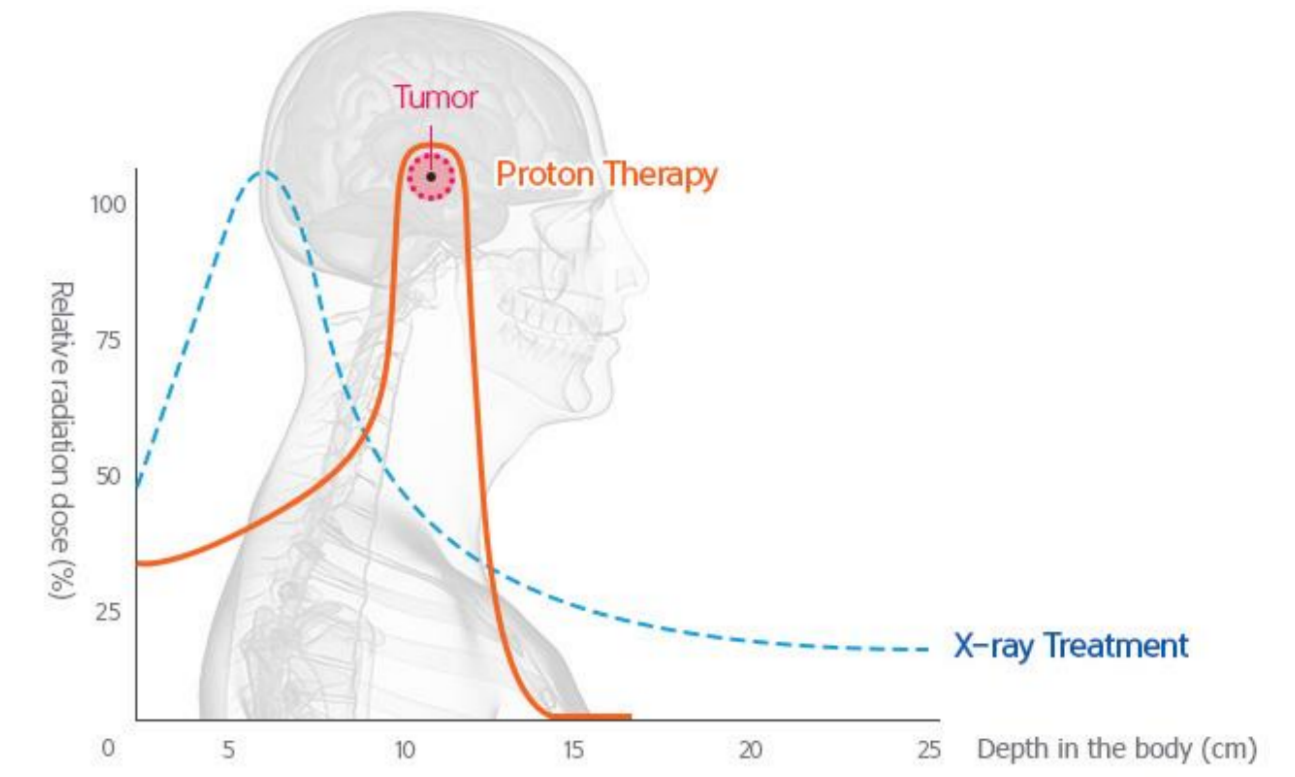
**Neurodegenerative diseases** are characterized by the accumulation of misfolded proteins, known as amyloid, which resist degradation and disrupt normal cellular functioning [1,2].



**Low-dose photon radiotherapy**, has shown positive results on AD and PD [5,6].

Some clinical trials are ongoing.

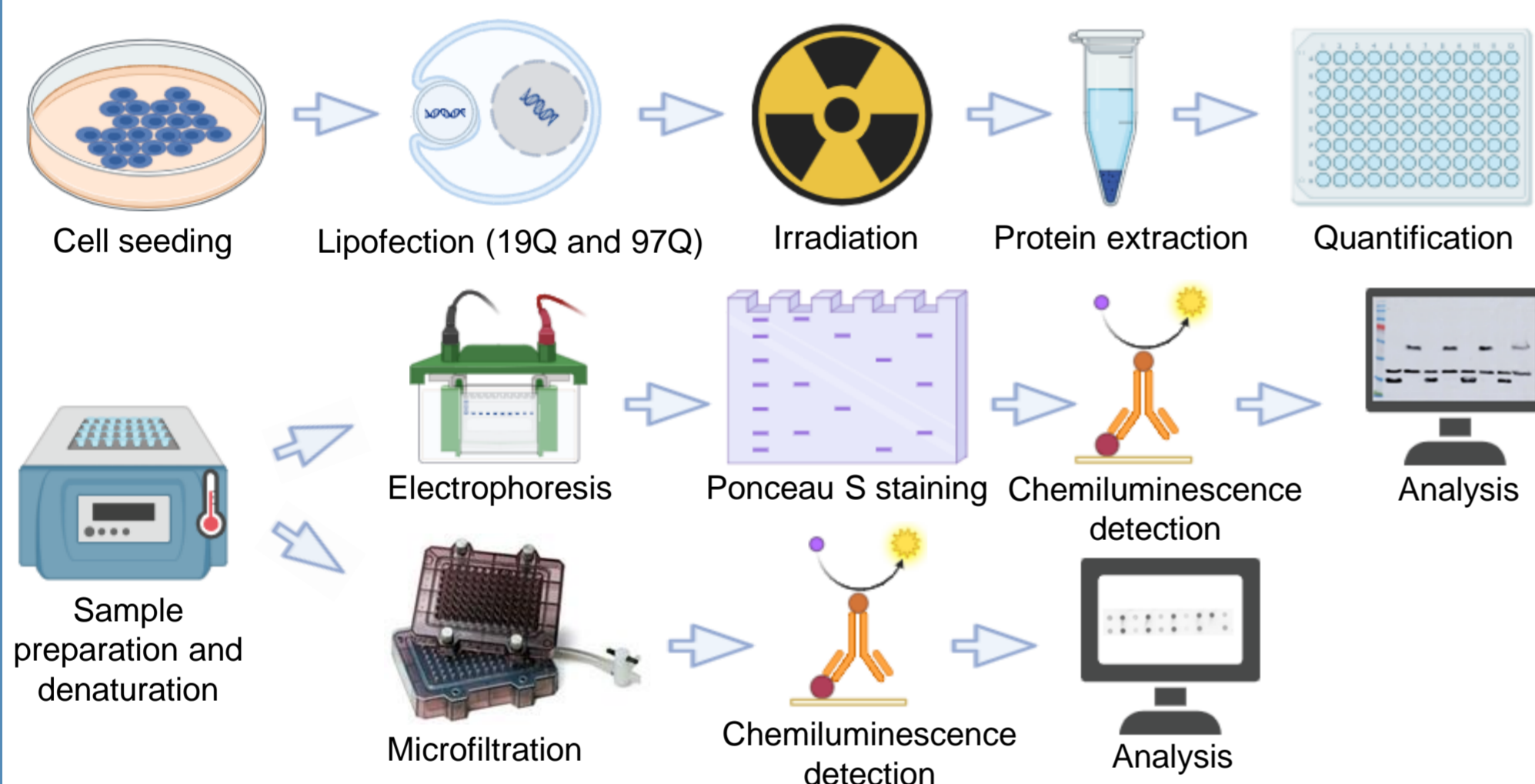
**Proton therapy** presents several **advantages** over conventional radiotherapy and is already clinically applied to noncancerous brain tumours [7].



Proton therapy (PT) dose deposition profile [8]. While protons penetrate the tissue, they gradually slow down and transfer energy to the tissue. Near the end of the beam range, there is a sharp increase in energy transfer, after which the beam stops, and the energy transfer drops to zero.

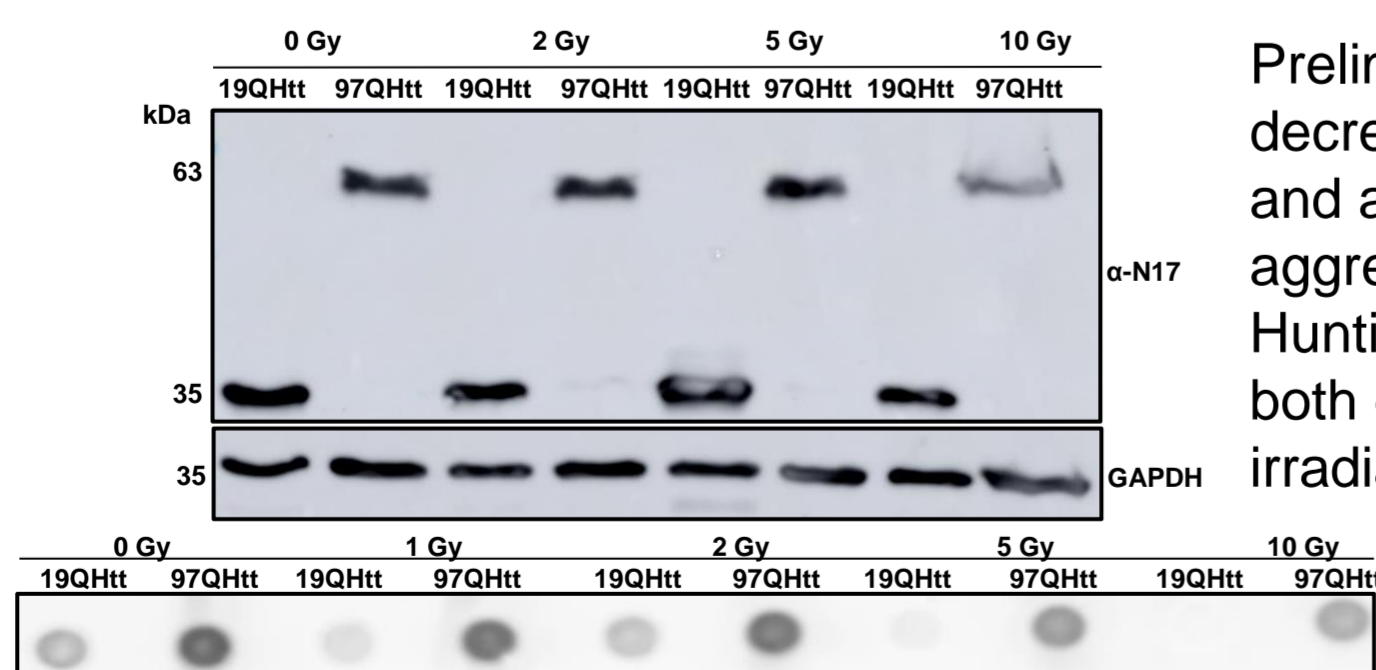
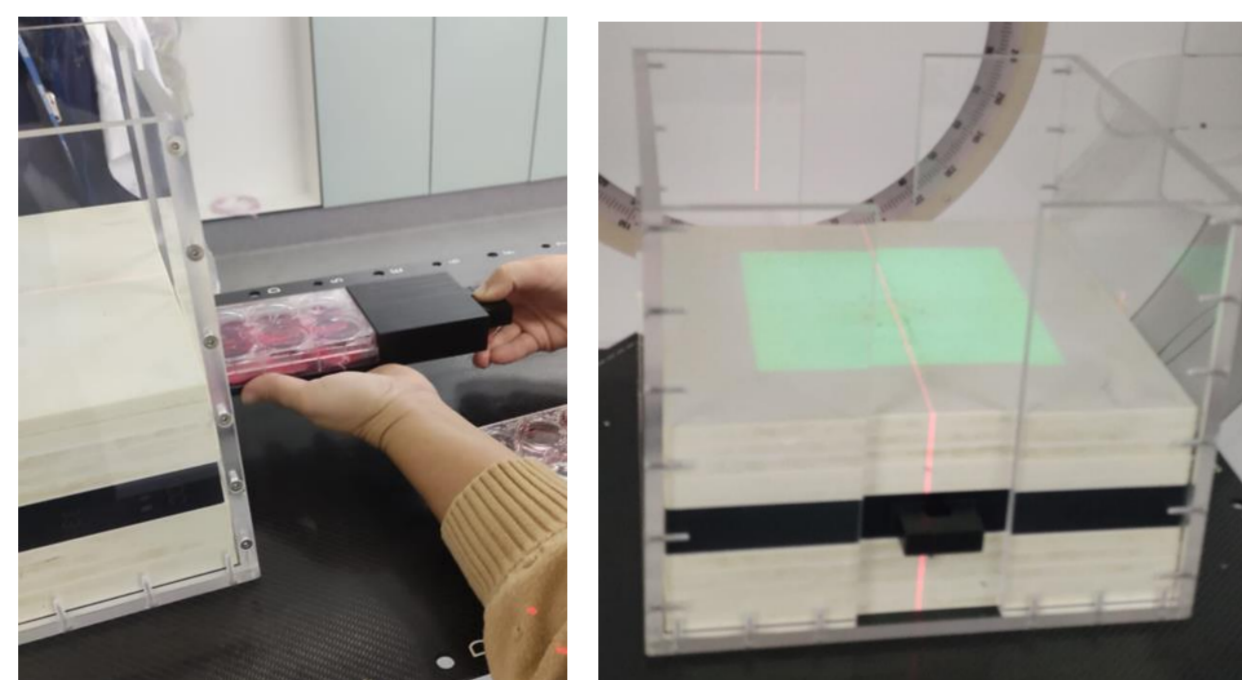
## Multidisciplinary Approach: Biochemistry and Nuclear Physics join forces

### Study the radiation effects on the brain using established cell lines



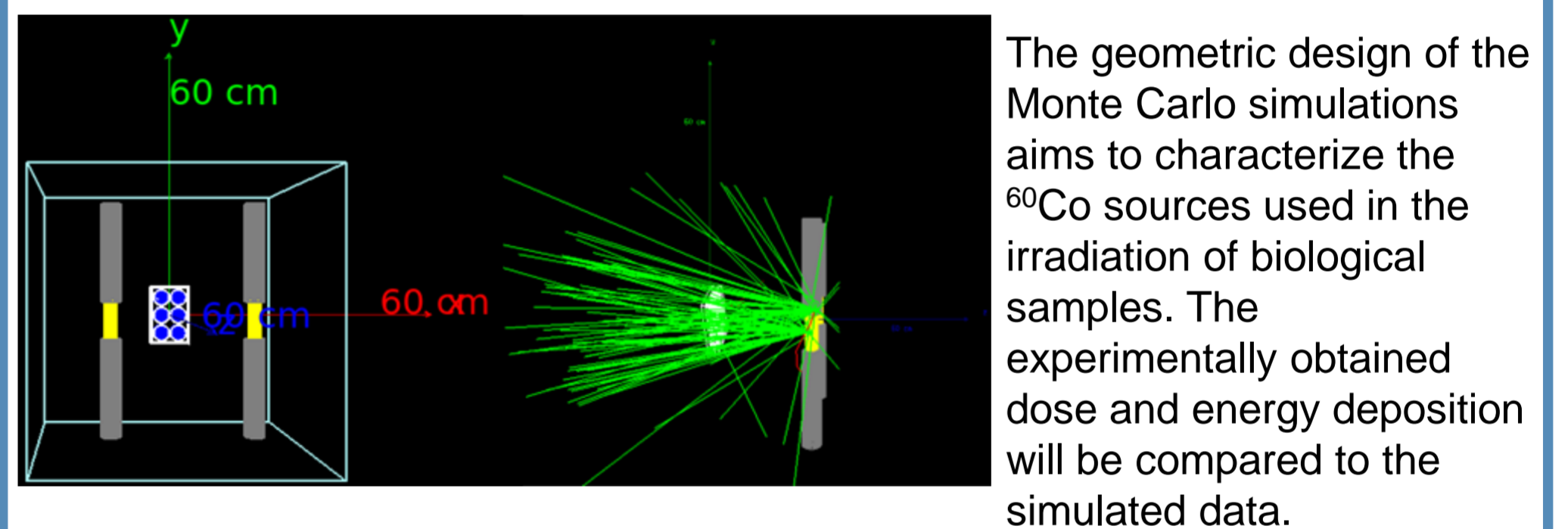
Schematic representation of the experimental procedure to study the expression and aggregation of proteins associated with neurodegeneration in HeLa cells expressing the wild type (19Q) or the mutant (97Q) Huntingtin protein after irradiation.

Placement of the biological samples in the radiobiological phantom and confirmation of the alignment at a clinical linear accelerator facility.

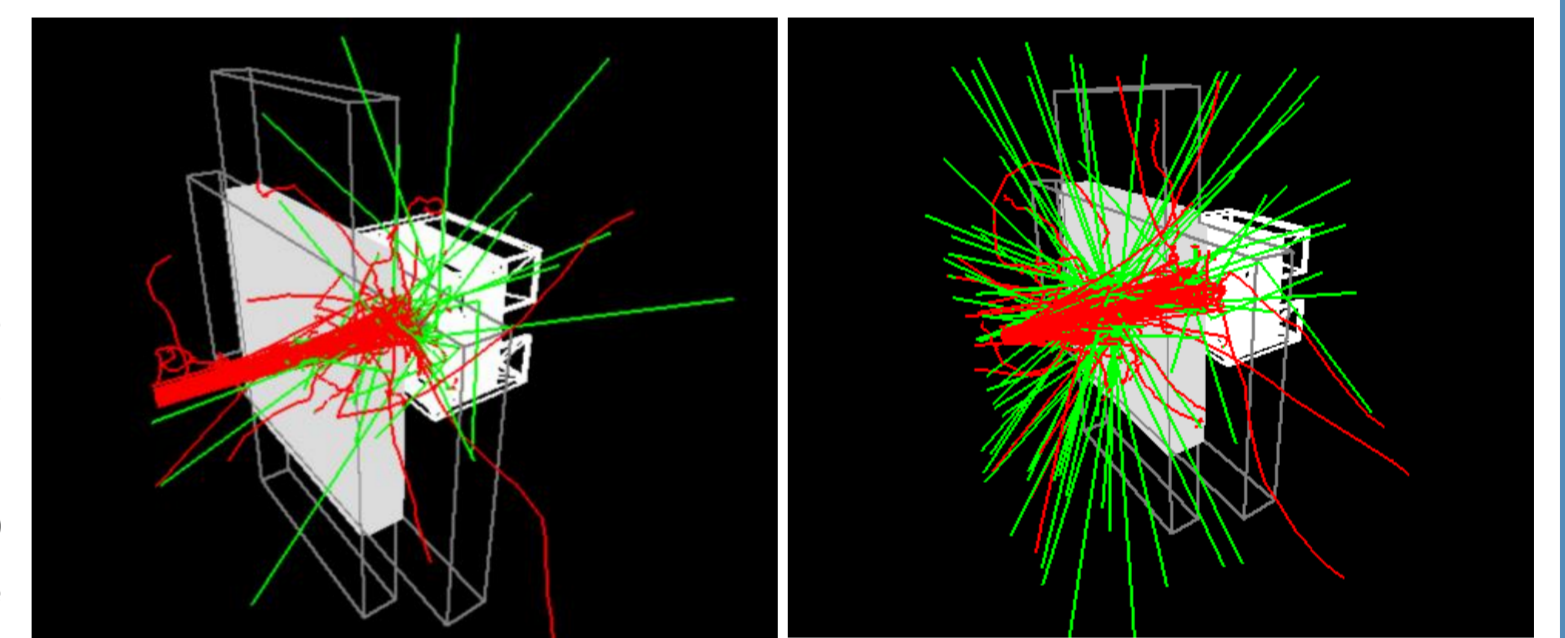


Preliminary results show a decrease in the expression and a reduction in the aggregation of mutant Huntingtin (Htt) induced by both gamma and photon irradiations.

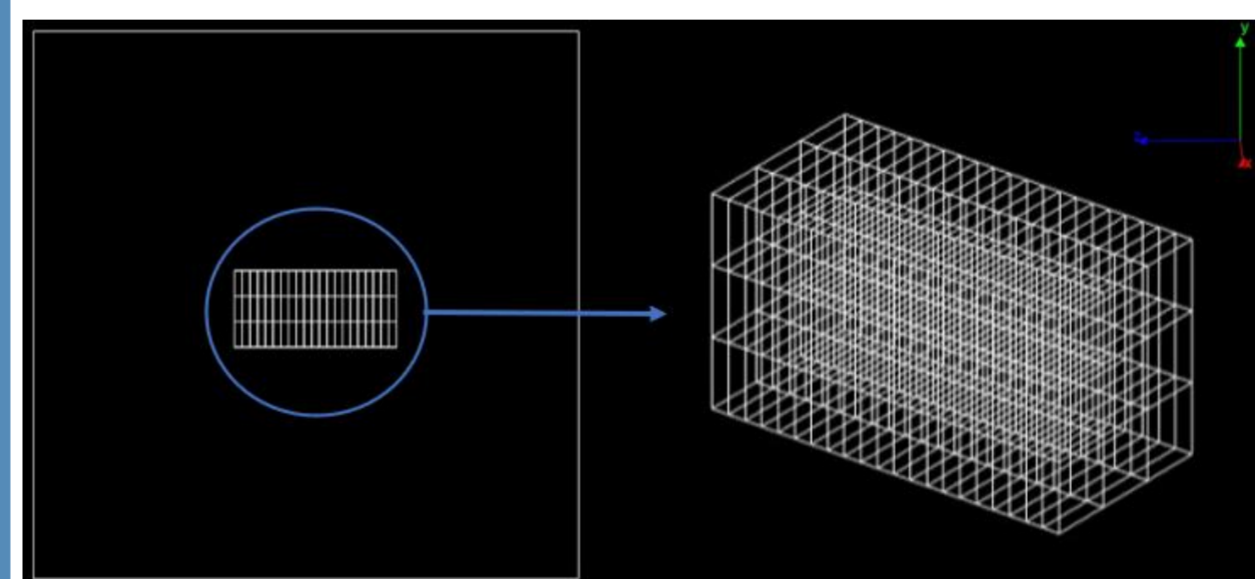
### TOPAS Monte Carlo simulations



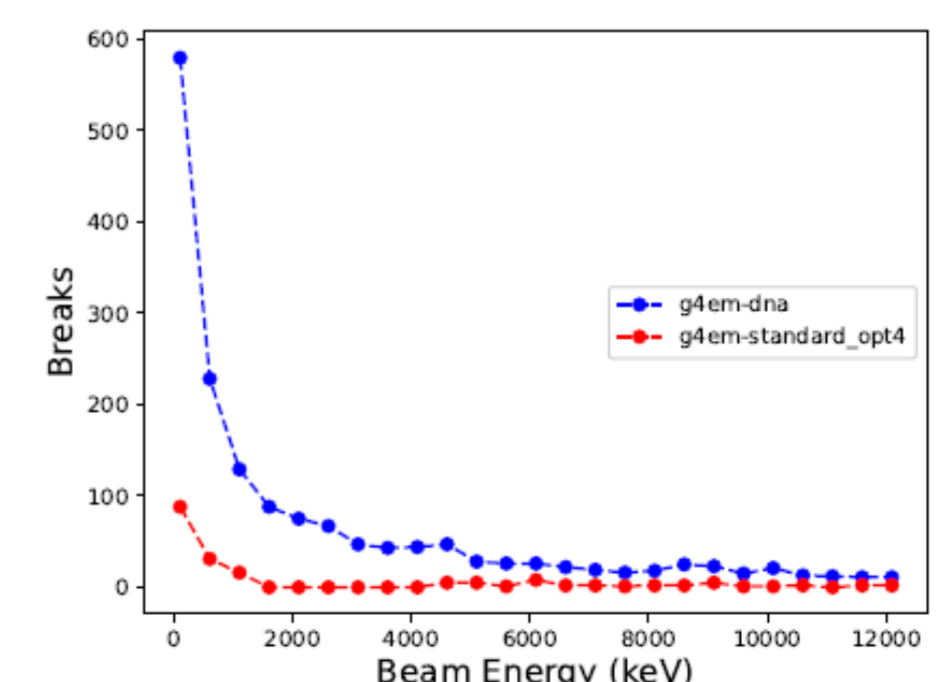
Simulation of 2 x-ray beam profiles: a pencil beam with a cylindrical shape and a cone beam that shoots particles at an angle relative to the z axis of the phantom [9].



The geometry defined for the amyloid structure, retrieved from the Protein Data Bank, was replicated along the x, y and z axes to increase the probability of energy deposition occurring near an atom of the amyloid [10].



Total number of strand breaks on the amyloid induced by a proton beam ranging from 100 keV to 12.5 MeV, using two different physics lists [10].



## References

- Kumar V., Sami N, Kashav T, Islam A, Ahmad F, Hassan MI. Protein aggregation and neurodegenerative diseases: From theory to therapy. *European Journal of Medicinal Chemistry*. 2016; 124:1105-20.
- Gandhi J, Antonelli AC, Afridi A, Vatsia S, Joshi G, Romanov V, Murray IV, Khan SA. Protein misfolding and aggregation in neurodegenerative diseases: a review of pathogenesis, novel detection strategies, and potential therapeutics. *Rev Neurosci*. 2019; 30(4):339-58.
- Crescenzi O, Tomaselli S, Guerrini R, Salvadori S, D'Ursi AM, Temussi PA, Picone D. 11YT - Solution structure of the Alzheimer's disease amyloid beta-peptide (1-42). 2002 [last accessed 06/06/2022]. Available from: <https://www.rcsb.org/structure/11yt> [last accessed 06/06/2022].
- Hussain R, Zubair H, Pursell S, Shahab M. Neurodegenerative Diseases: Regenerative Mechanisms and Novel Therapeutic Approaches. *Brain Sci*. 2018; 8(177).
- Marples B, et al. Cranial irradiation significantly reduces beta amyloid plaques in the brain and improves cognition in a murine model of Alzheimer's Disease (AD). *Radiother Oncol*. 2016; 118(1):43-51.
- Ceyzériat K, Tournier BB, Millet P, Frisoni GB, Garibotto V, Zilli T. Low-Dose Radiation Therapy: A New Treatment Strategy for Alzheimer's Disease? *J Alzheimers Dis*. 2020; 74(2):411-9.
- Paganetti H, Beltran C, Both S, Dong L, Flanz J, Furutani K *et al*. Roadmap: proton therapy physics and biology. *Phys Med Biol*. 2021; 66(5).
- Samsung Medical Center. Principles of Proton Therapy. Available from: How it works - What is Proton Therapy? - SAMSUNG PROTON THERAPY CENTER ([samsunghospital.com](http://samsunghospital.com)) [last accessed 25/11/2022].
- Vaz JP, Coelho CM, Teubig T. Radiobiological Phantom Characterization. *LIP Student Publications*. LIP-STUDENTS-23-3.
- Scharff H, Rebouta MT, Pereira L, Coelho C, Teubig P. Radiation "bombs" in amyloids. *LIP Student Publications*. LIP-STUDENTS-22-23.

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