The potential benefits of proton therapy for neurodegenerative disorders

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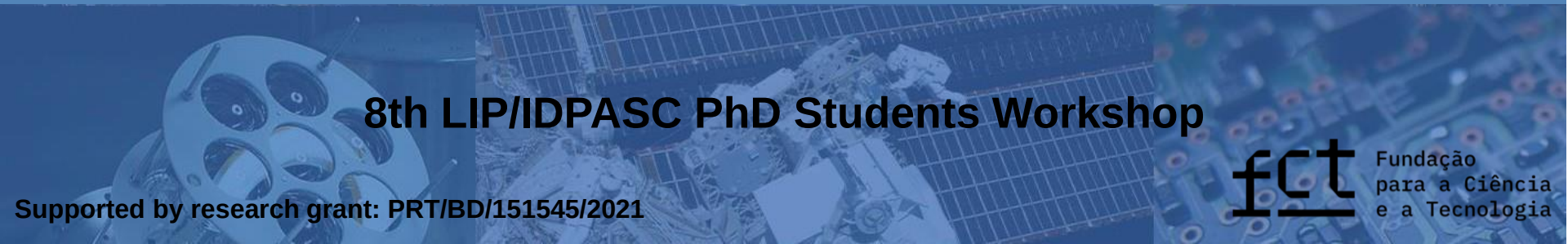

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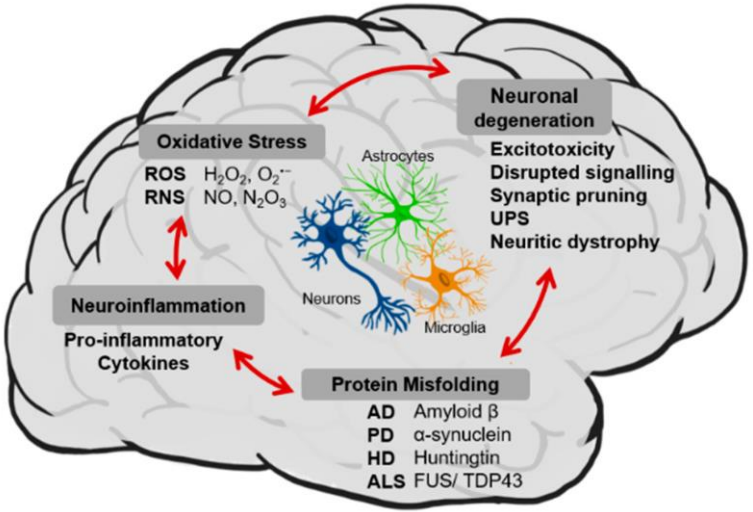
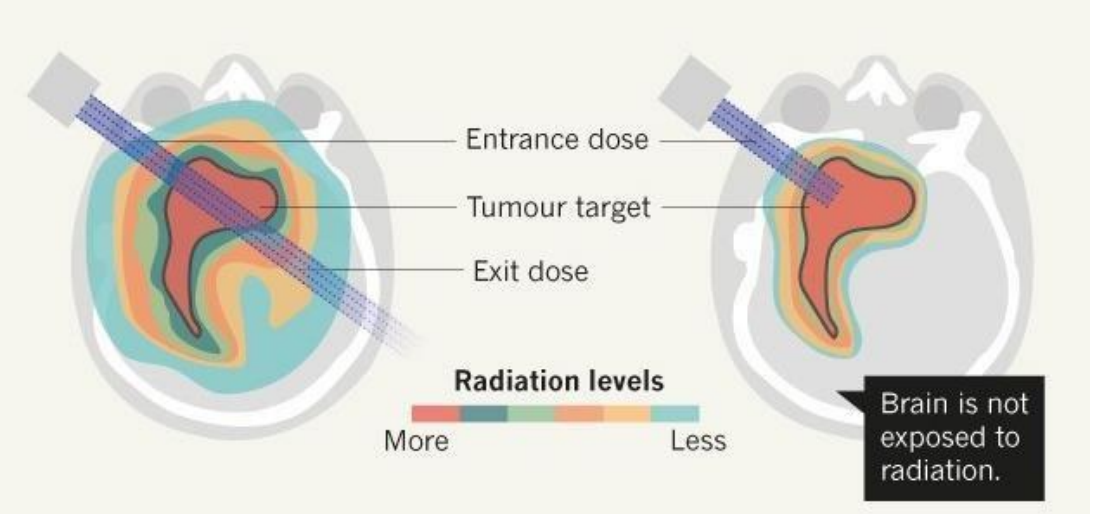
INTRODUCTION



Main distinctive features of **neurodegeneration** and neurodegenerative disorders (Carregosa, D. *et al*. *Nutrients* (2021). DOI:10.3390/nu13092940)



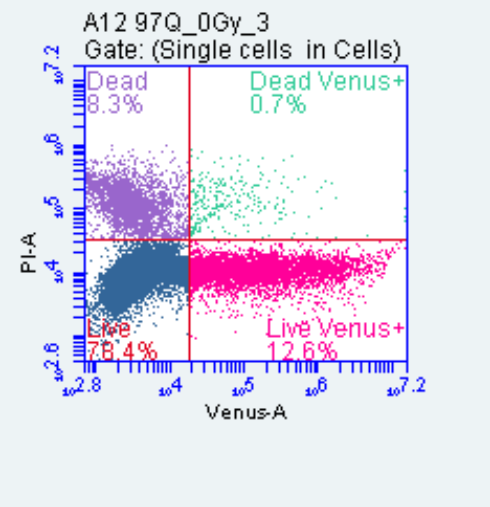
Comparison of **radiation dose levels** between conventional **Radiation Therapy** and **Proton Therapy** (Bortfeld, T.R., Loeffler, J.S. *Nature* (2017). DOI:10.1038/549451a)

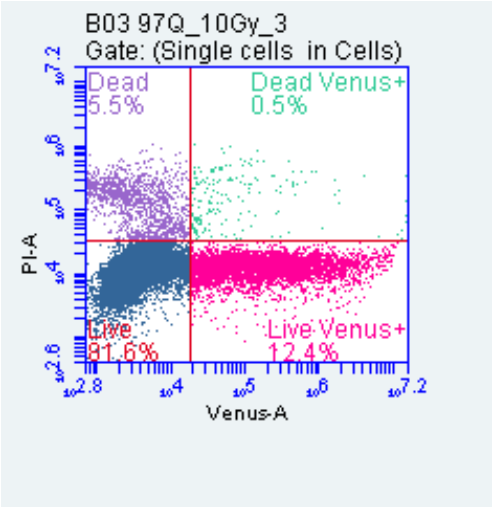
OBJECTIVES

Can we unravel the **protein aggregates** with **PT**, without killing the cells?

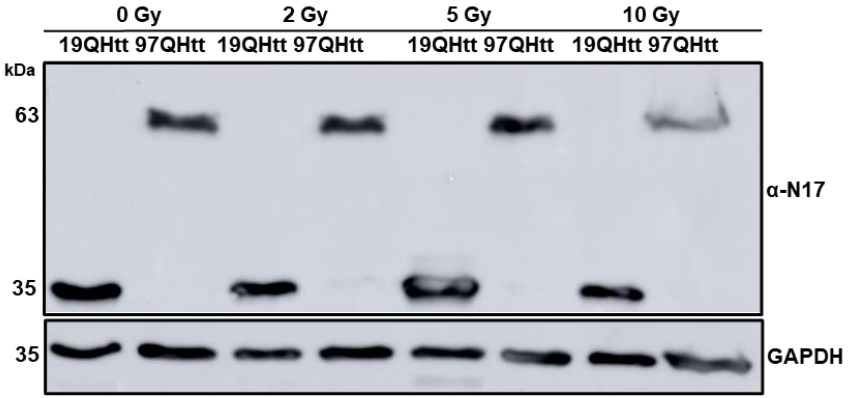
- Assess the potential of **PT** to **disrupt or mitigate** the formation of **toxic protein amyloids** linked to neurodegenerative disorders
- Investigate the effects of different **radiation** modalities on the structural integrity and conformational changes of **toxic protein amyloids**
- Investigate the **biochemical** and **biophysical** mechanisms underlying the optimal **PT** conditions to **disrupt amyloid deposits**

GAMMA-RAYS EXPERIMENTS





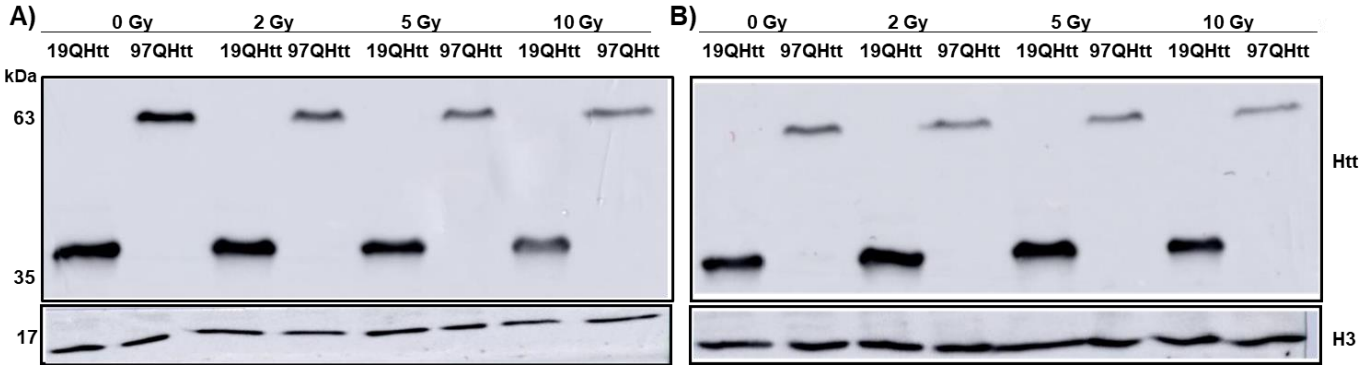
Analysis of **cell death** and **transfection efficiency** in **irradiated and non-irradiated HeLa cells**, immediately after the irradiation



Representative **Western blot** of samples extracted from transfected HeLa cells **24 h after the irradiation**, demonstrating a **reduction** in the **expression** of **Htt**

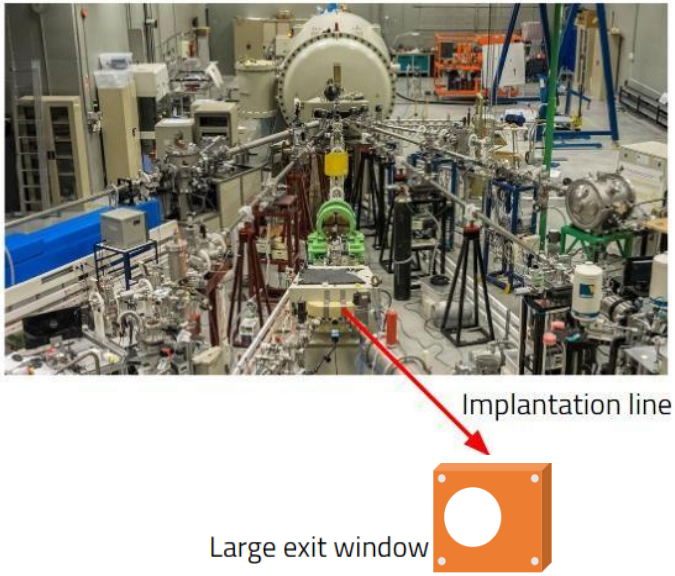
ELECTRONS AND PHOTONS EXPERIMENTS

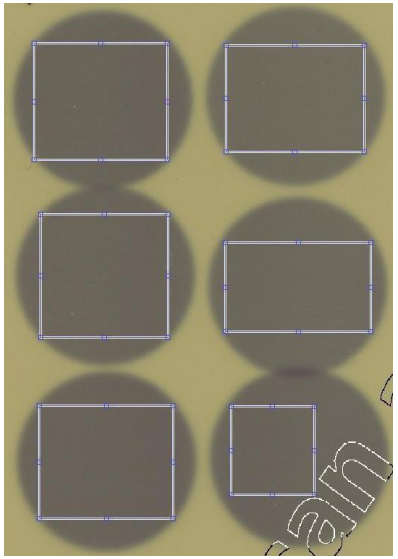
Positioning of the **biological samples** in the phantom for the **irradiation** with a clinical **photon beam**

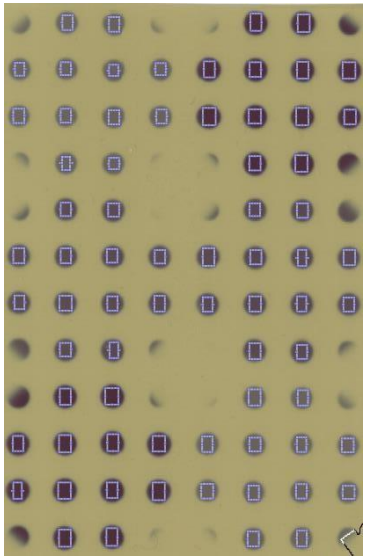


Expression of Htt in cells **24 h post-radiation** with a clinical **electron beam (A)** and with a **clinical photon beam (B)**, both demonstrating a **reduction** in the **expression** of **Htt**

PROTON EXPERIMENTS







The basis for an **external proton beam line** at CMAM has been **set** and is **ready** for **biological sample irradiation** - Coelho C. et al (In preparation)

FUTURE WORK

- Establish an ***in vitro* model** for assessing the **impact of radiation** on **aggregate formation** – On going
- Conduct **Monte Carlo simulations** to elucidate **radiation effects** on **protein aggregates**
- Employ **proton irradiation** on **biological samples** followed by comprehensive **biochemical analysis**

THANKS!

Cell Structure and Dynamics

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ProtoTera Grant - PRT/BD/151545/2021, Centre grants to LIP UIDB/50007/2020, UIDP/50007/2020 and LA/P/0016/2020 and UID/Multi/04349/2019 Centre grant to C2TN. Work supported by UIDB/04046/2020 (DOI: 10.54499/UIDB/04046/2020) and UIDP/04046/2020 (DOI: 10.54499/UIDP/04046/2020) Centre grants from FCT, Portugal (to BioISI) and the TWIN2PIPSA twinning grant from the European Research Council (ID: 101079147).