

# Updates on radiobiology research in Birmingham

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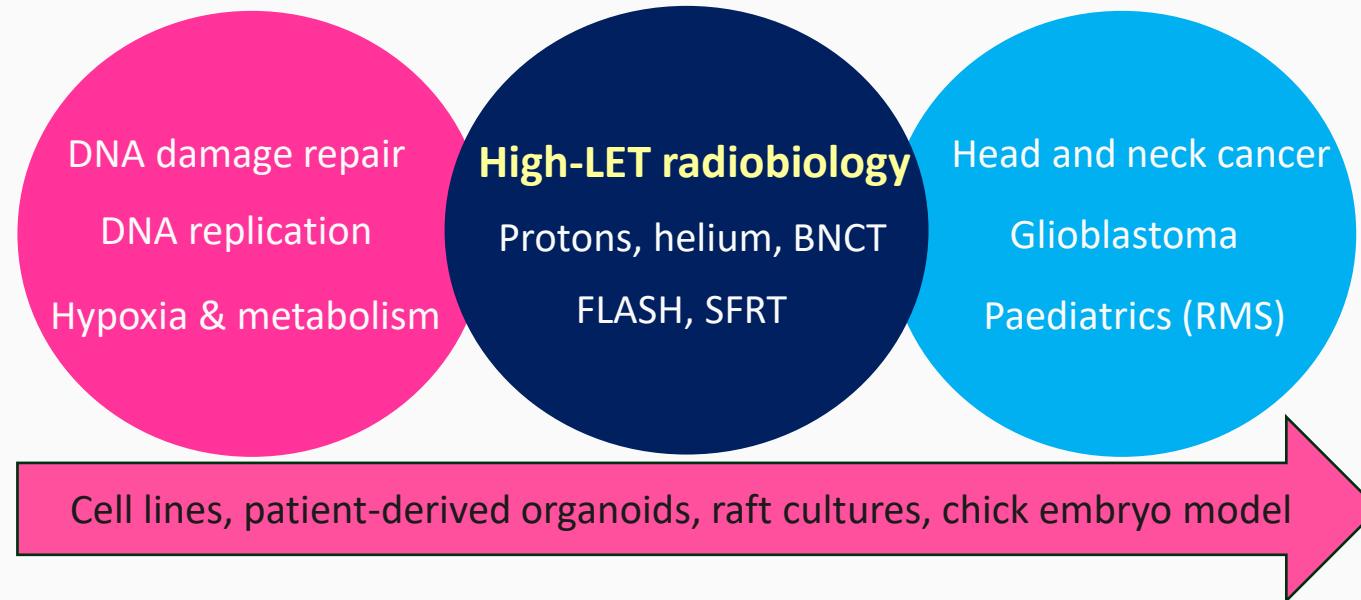
CANCER  
RESEARCH  
UK

RadNet  
Birmingham



# Mission Statement of RadNet Birmingham

- To explore the **radiobiological impact of protons and high-LET radiation** at the molecular and cellular level, which can be exploited for optimising the treatment of specific cancers

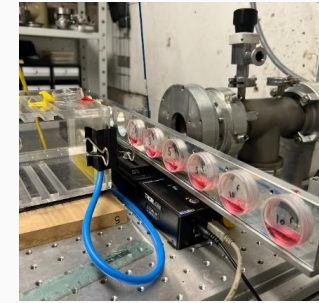
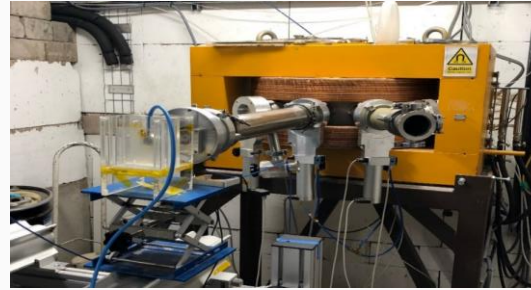


# Biophysics Research Infrastructure

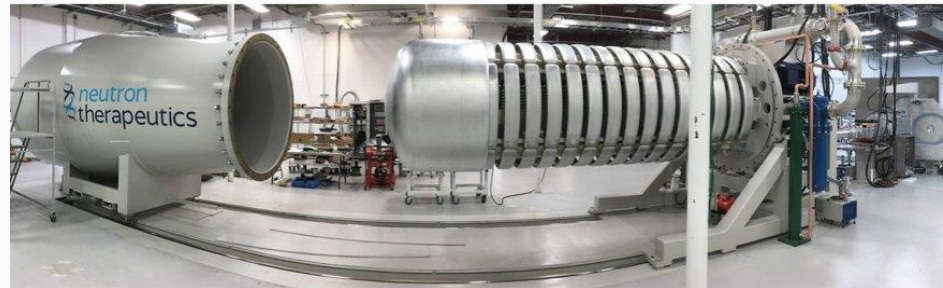
- Research dedicated (no clinical userbase).
- Optimised for flexibility and precision.
- Responsive, multipurpose co-located biology facilities.
- Unique in UK/Europe, attracting external collaborators.

MC-40 cyclotron

*Protons and particle ions in different spatial (SFRT) / temporal (FLASH) configurations*



*High flux accelerator-driven neutron source - Boron neutron capture therapy (BNCT)*



*Radiobiology facilities - 150 kV X-ray irradiator, 2x hypoxia workstations*



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# Identification of targets for radiosensitisation in response to proton beam therapy

*Relatively high-LET protons (~10 keV/um)*

- The strand break binding protein poly(ADP-ribose) polymerase-1, PARP-1 (Carter *et al.*, 2019, *IJROBP*).
- Poly(ADP-ribose) glycohydrolase, PARG (Fabbrizi *et al.*, 2024, *Cell Death Dis*).
- 8-oxoguanine DNA glycosylase, OGG1 (Fabbrizi *et al.*, 2024, *Cell Death Dis*).

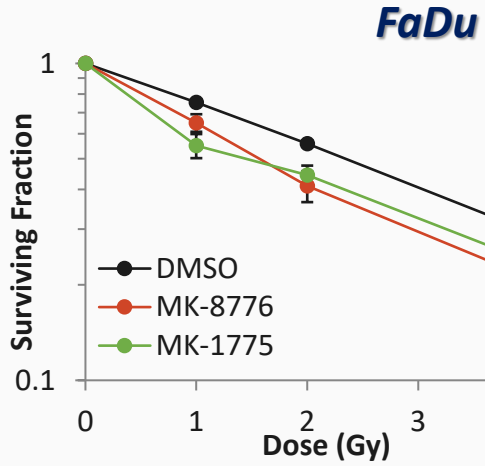
*Low-LET protons (~1 keV/um)*

- The DNA double strand break repair protein kinases, ATM, ATR and DNA-PKcs (Fabbrizi *et al.*, 2024, *Cell Death Discov*).

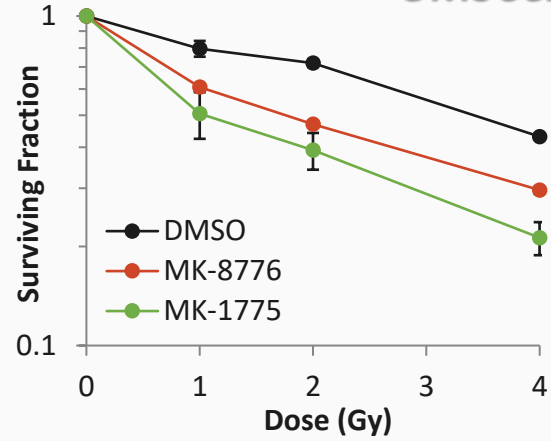


# Targeting Chk1 and Wee1 sensitises cells to low and high-LET protons

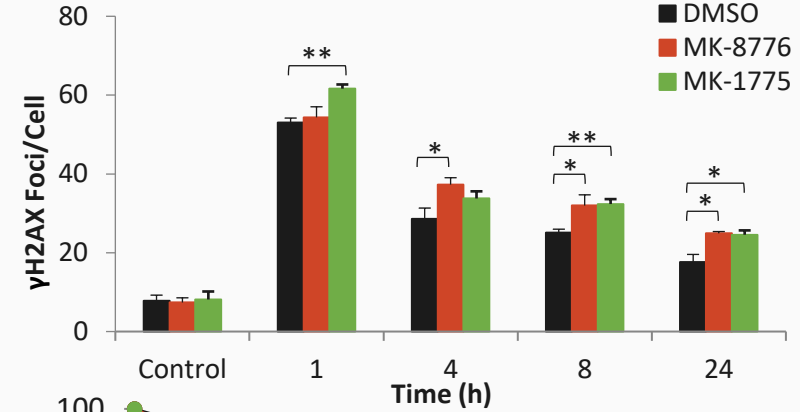
**X-rays**



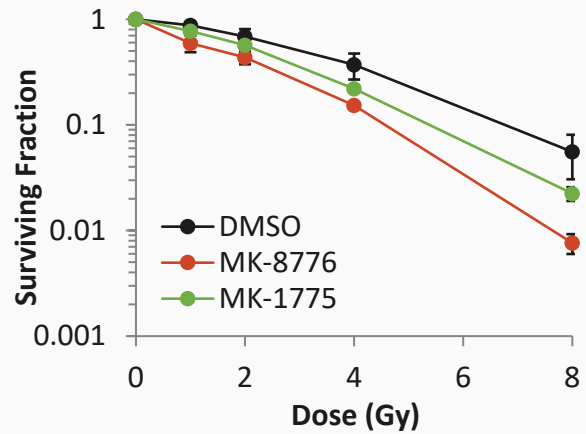
**UMSCC12**



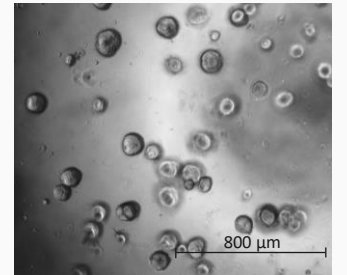
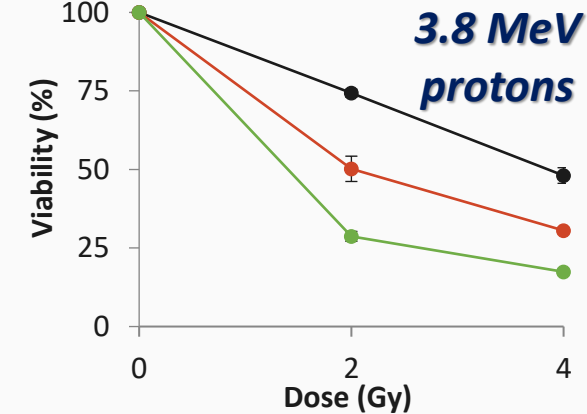
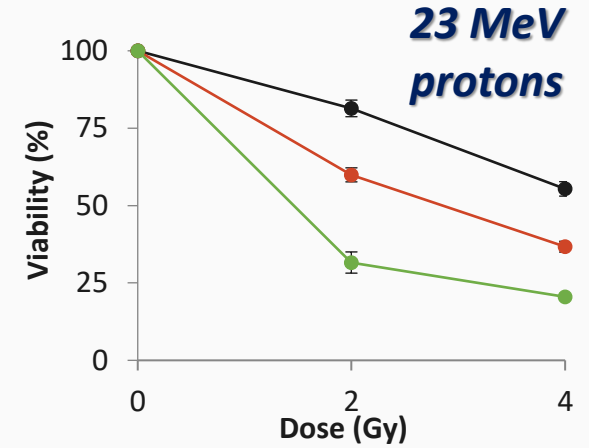
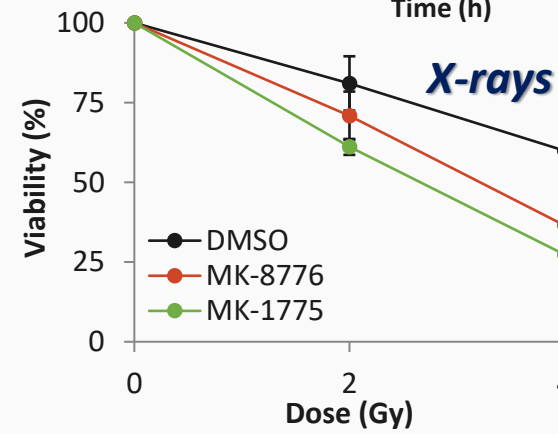
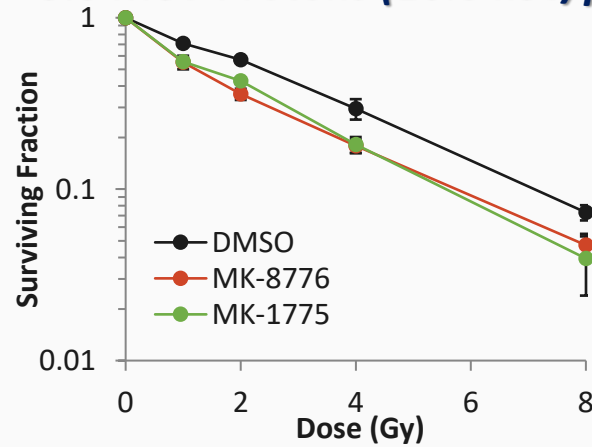
**UMSCC12**



**23 MeV Protons (2.7 keV/μm)**



**3.8 MeV Protons (10.8 keV/μm)**



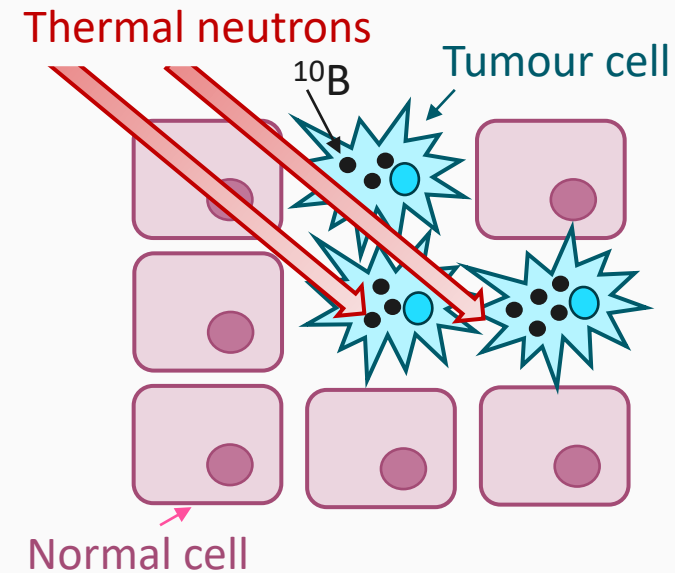
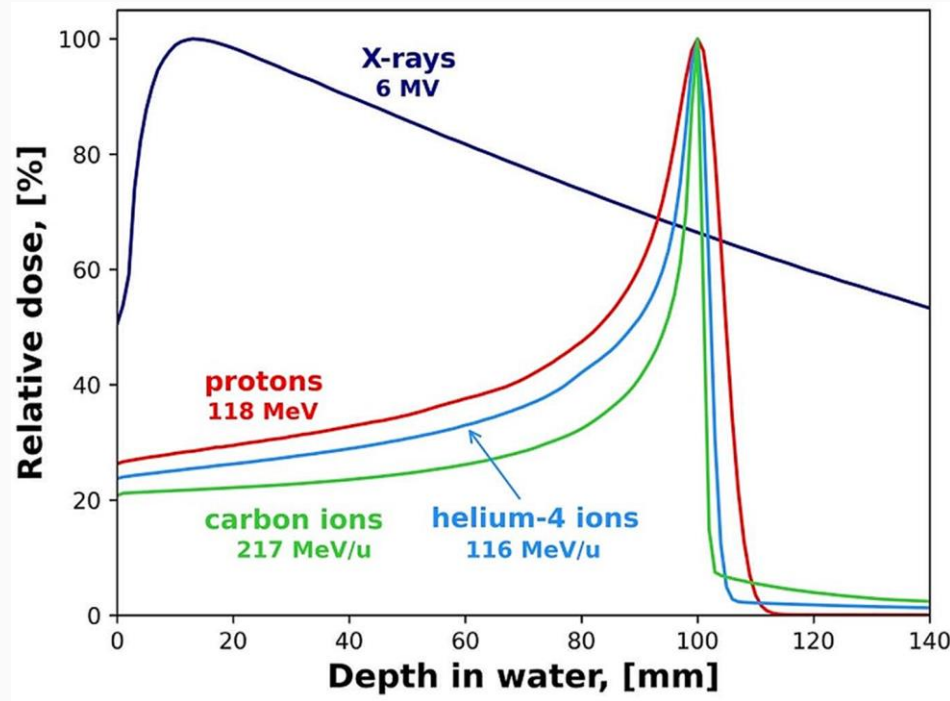
**HN041**



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Melia et al., (2025) Cell Death Dis

# Benefits of helium ion therapy and boron neutron capture therapy (BNCT)



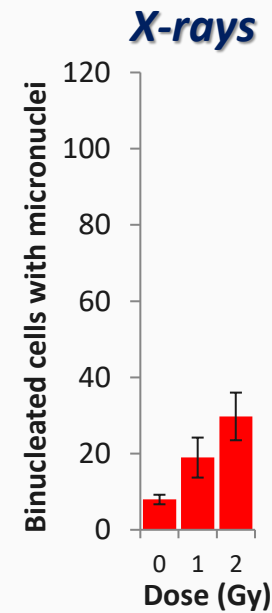
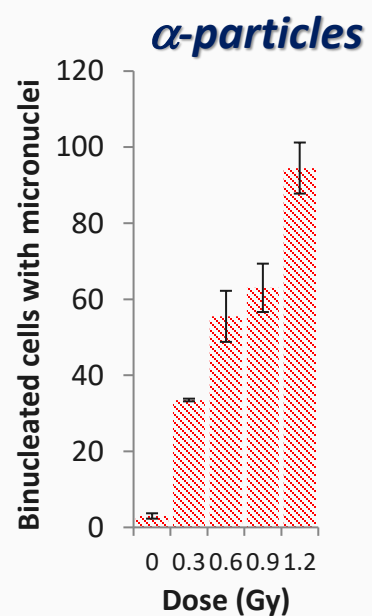
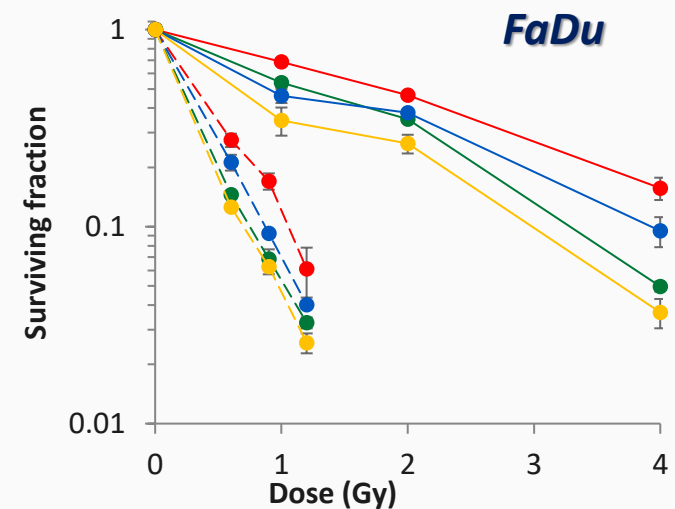
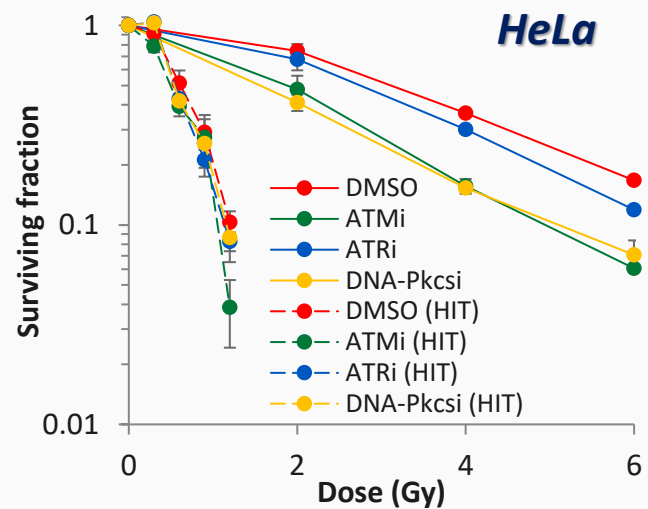
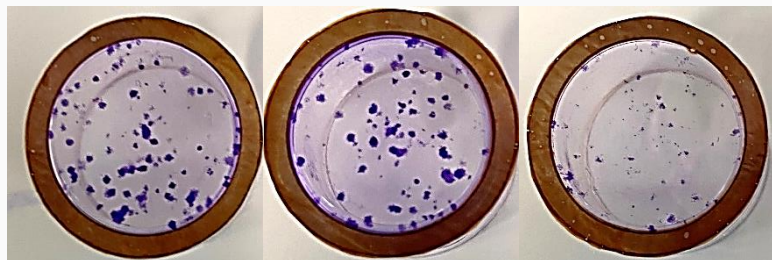
- More precise tumour targeting (sharper Bragg peak with helium than protons; specific boron uptake with BNCT).
- Enhanced biological effectiveness ( $\sim 30\text{-}100\text{ keV}/\mu\text{m}$  helium;  $>100\text{ keV}/\mu\text{m}$  BNCT).



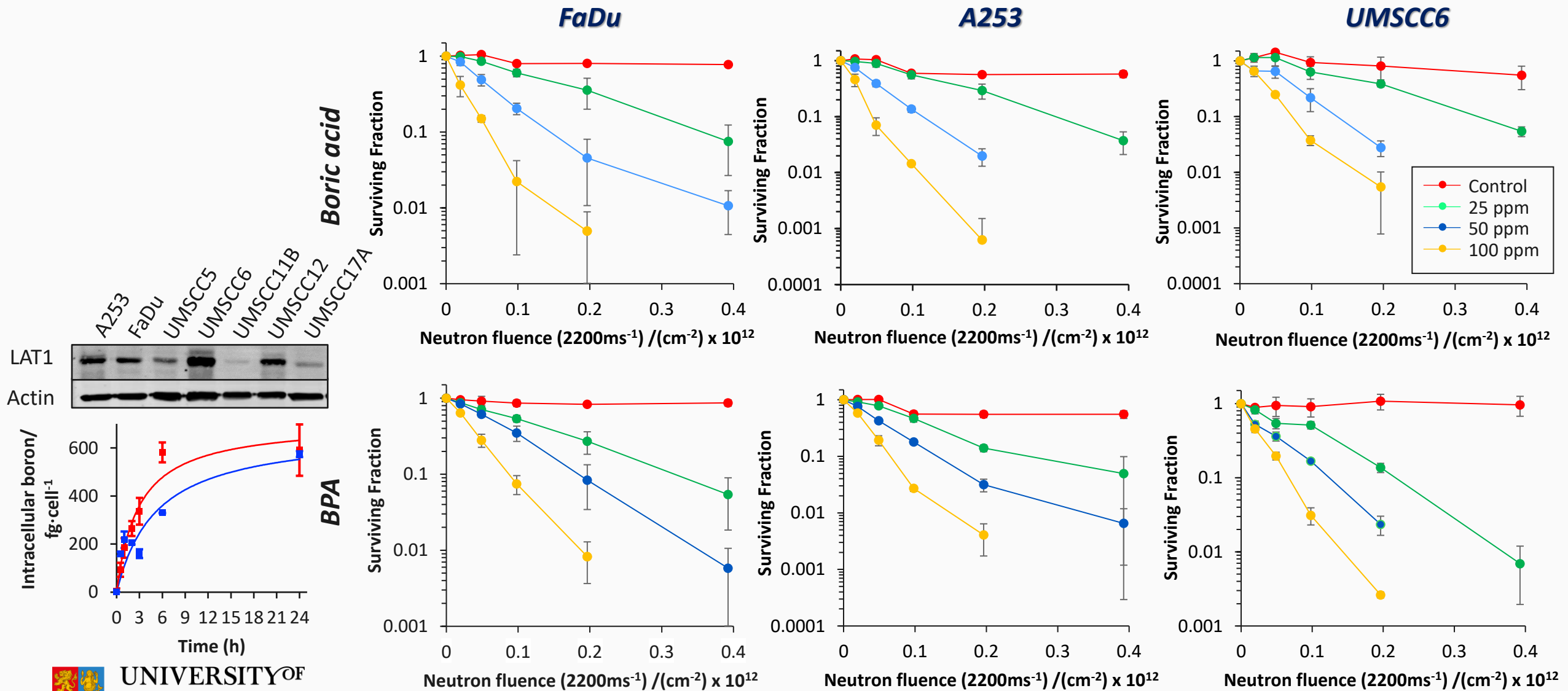
# The radiobiology of helium ions



X-ray dose



# The radiobiology of BNCT



(collaborations with Cancer Research UK, Neutron Therapeutics and TAE Life Sciences)



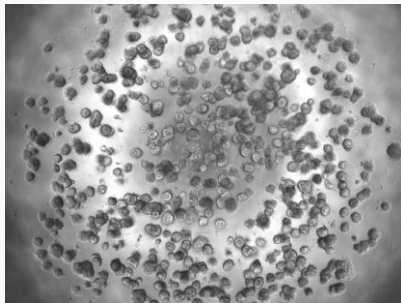
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# Development of tumour models via RadNet Birmingham

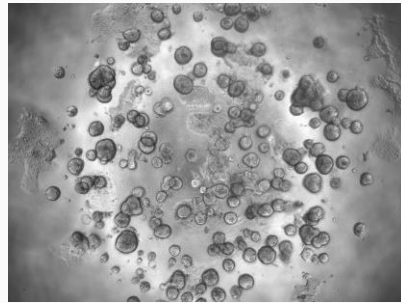
- Define the **therapeutic potential** of protons and high-LET radiation, focussing on head and neck, glioblastoma and paediatrics (rhabdomyosarcoma)

## *Patient-derived organoids*

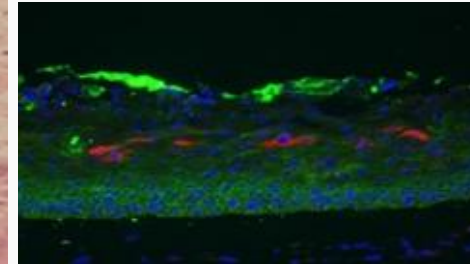
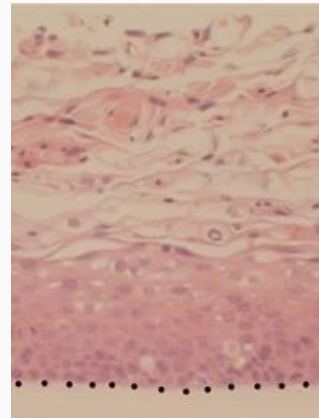
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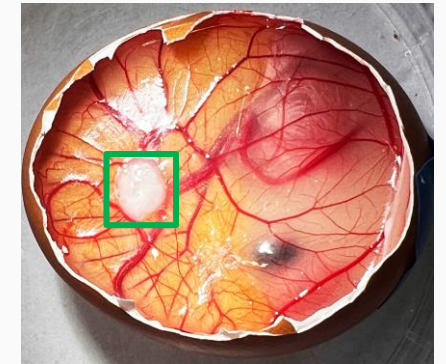
HNC-2

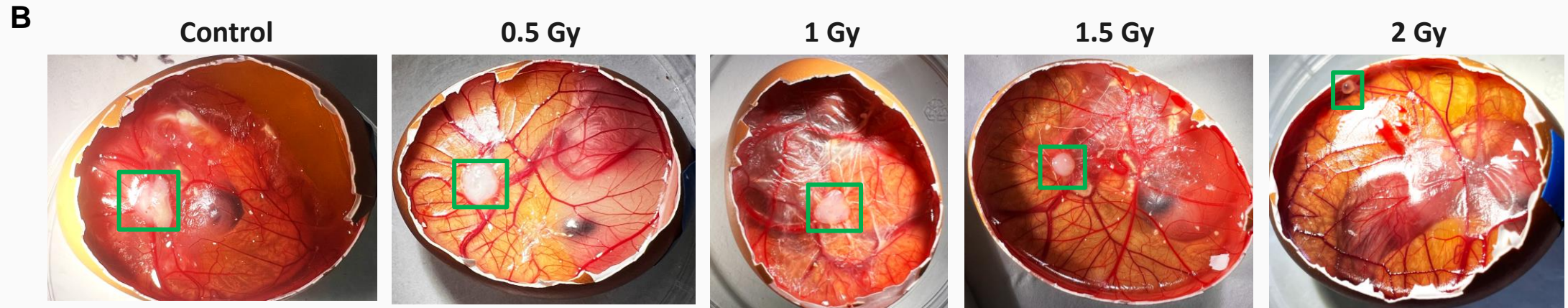
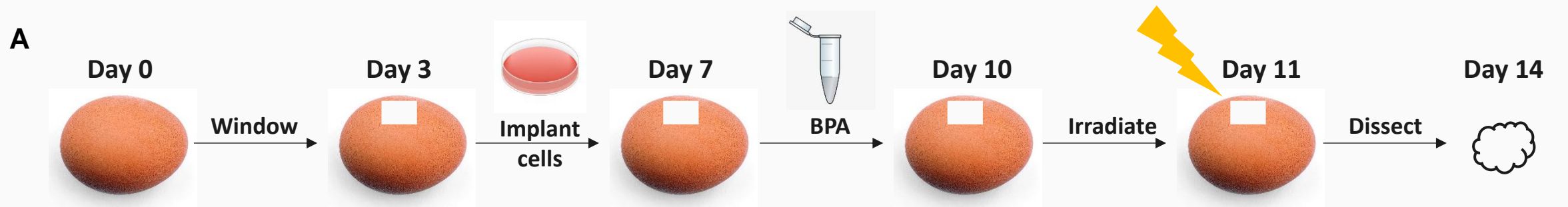


## *Raft cultures*



## *Chick embryo (CAM) model*





# Acknowledgements

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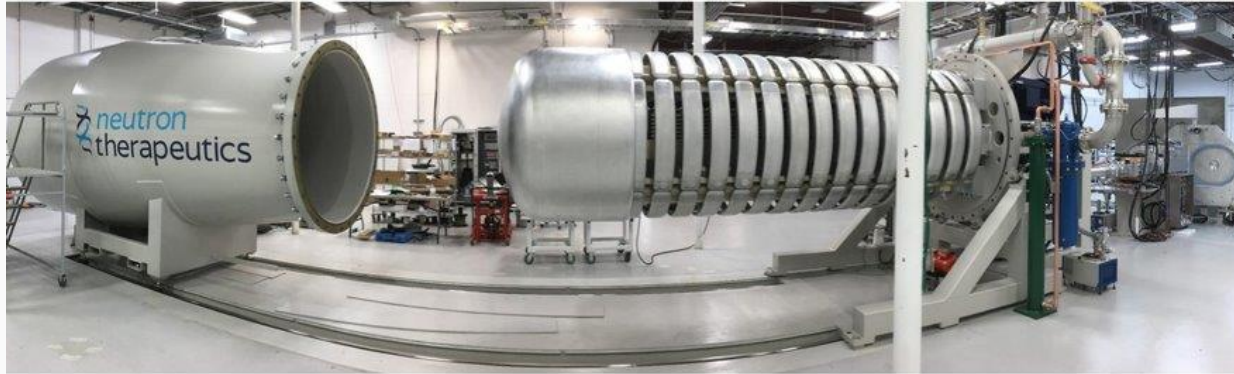
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