Pillar 1;
A systematic approach to radiobiology

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21.05.26

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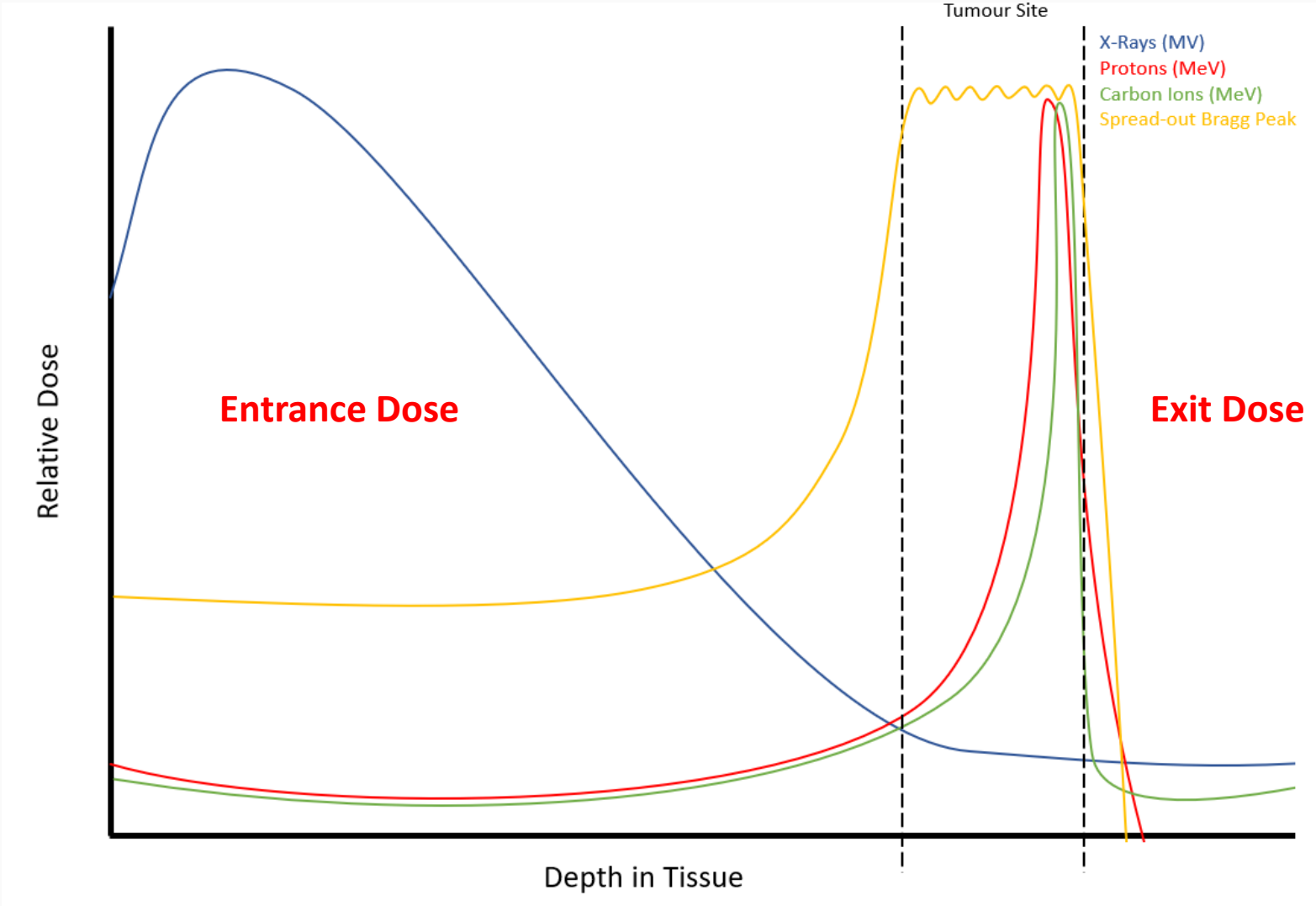
CANCER RESEARCH UK | RadNet Birmingham

Particle Therapy

- Different particle types
- Spread-out Bragg Peak
- Variation in modality characteristics – energy, LET



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Melia and Parsons (2023)

Current facilities for investigating radiobiology

- Conventional sources – linac/cyclotron/synchrotron

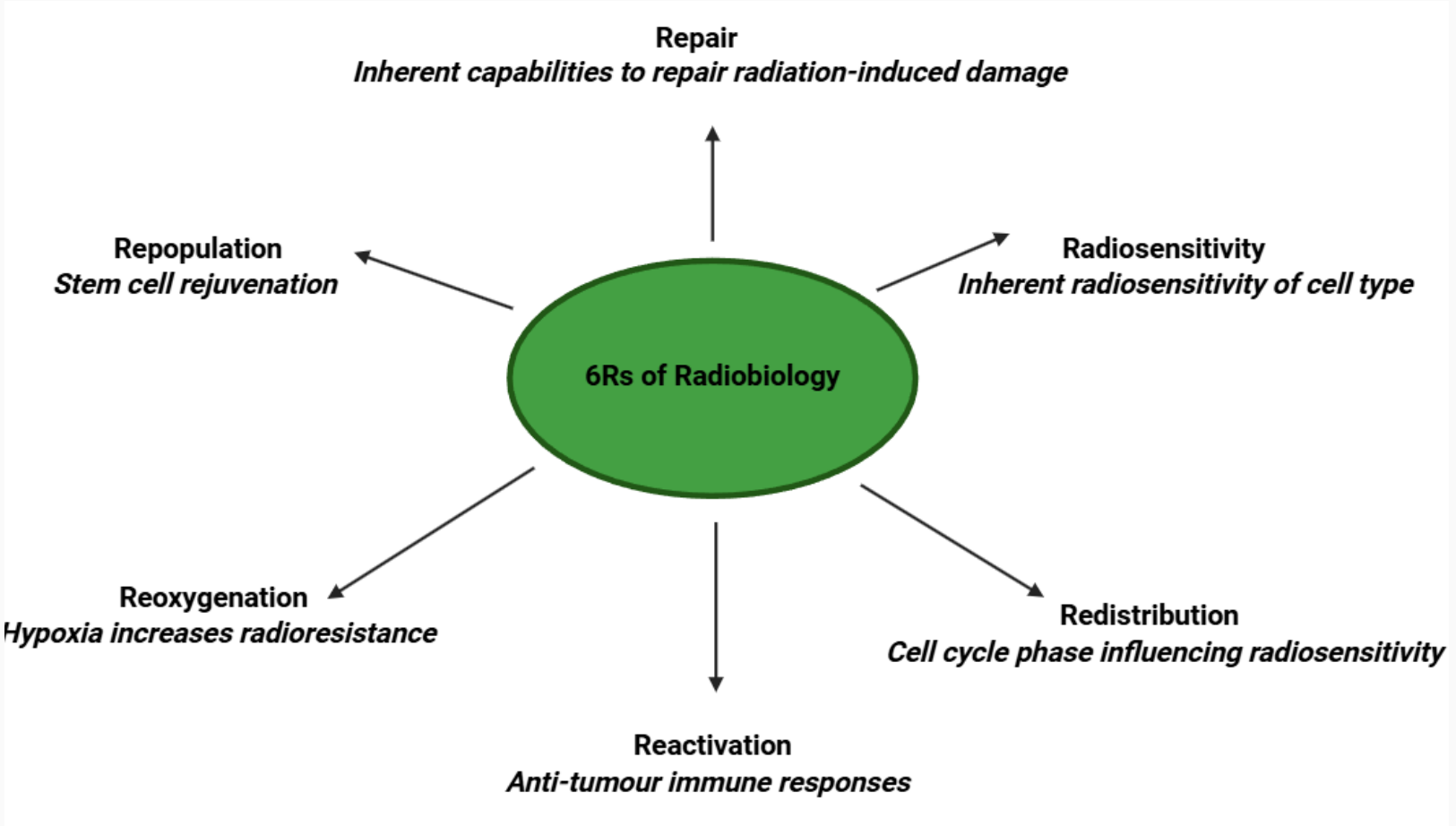
Fabbrizi, et al. (2025)

- Laser-driven sources

- Struggles for full radiobiology end points:
  - Irradiation spot sizes
  - Uniformity in dose
  - Proton energy variation
  - Shot-to-shot variation
  - Available ion species

Radiobiology

- DNA damage and repair
- Tumour microenvironment
- Immune responses



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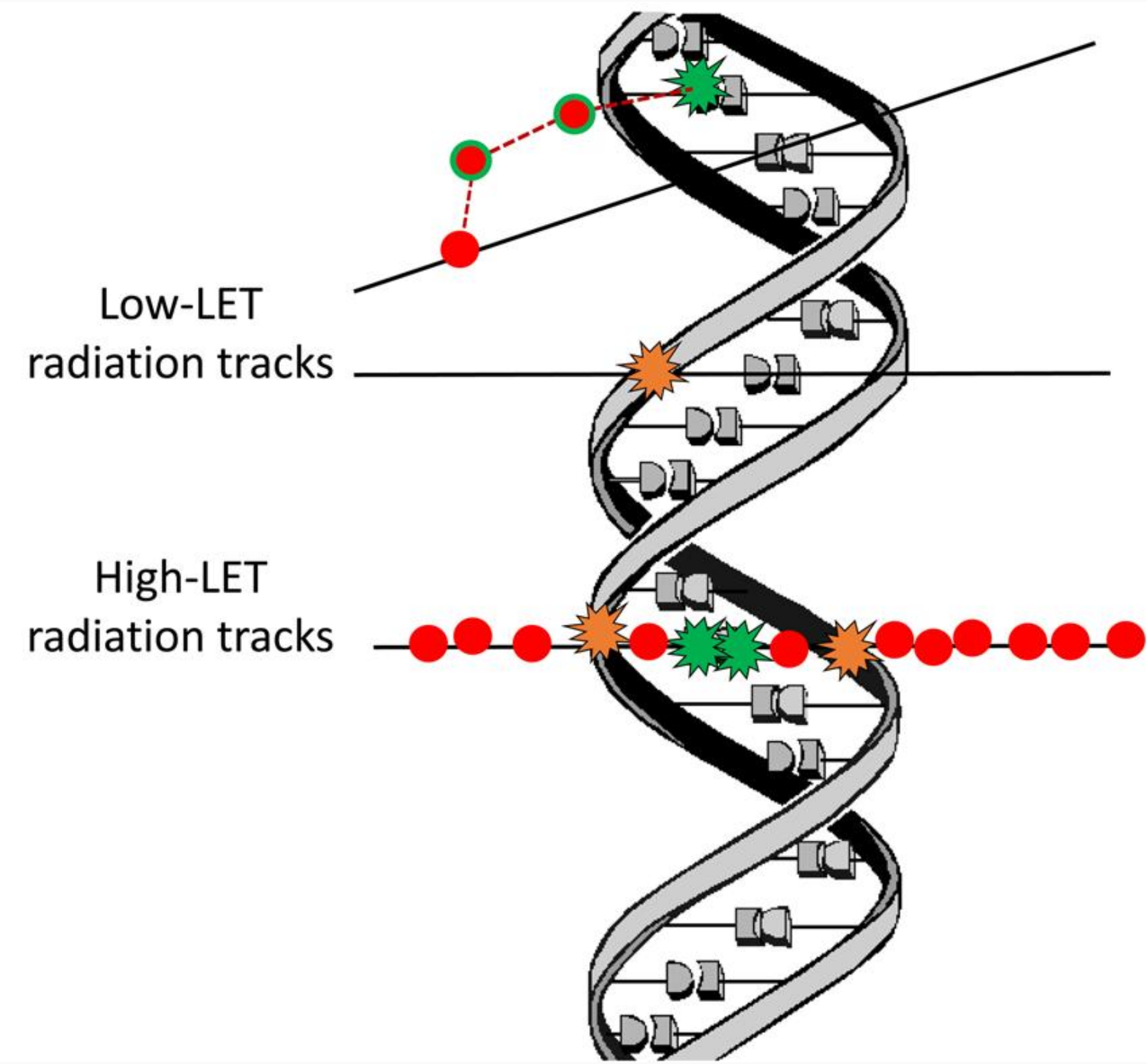
DNA Damage and Repair

- Type of damage depends on the radiation modality and LET;

  - Base damage
  - Single-strand breaks
  - Double-strand breaks
  - Complex/clustered DNA damage

- Various repair mechanisms determined by;

  - Cell cycle stage
  - Mutational profile
  - Protein expression or activation
  - Hypoxia (low oxygen concentrations)



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Fabbrizi and Parsons (2022)

Tumour Microenvironment

- Vasculature
- Stromal cells (Cancer-associated fibroblasts)
- Extracellular matrix
- Signalling molecules
- Hypoxia (low oxygen concentrations)
- Immune infiltration

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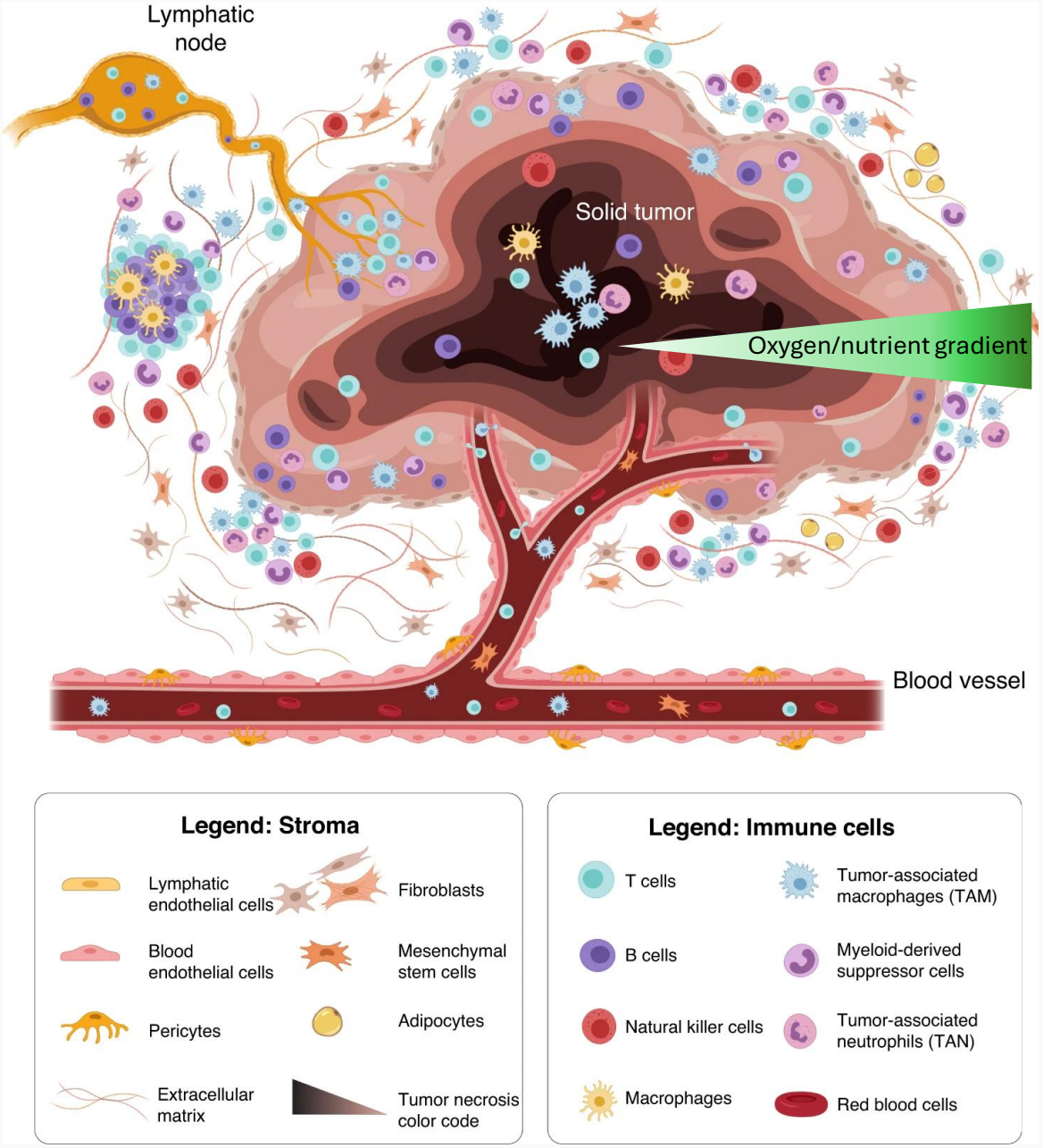


Abizanda-Campo, et al. (2023)

Immunological responses

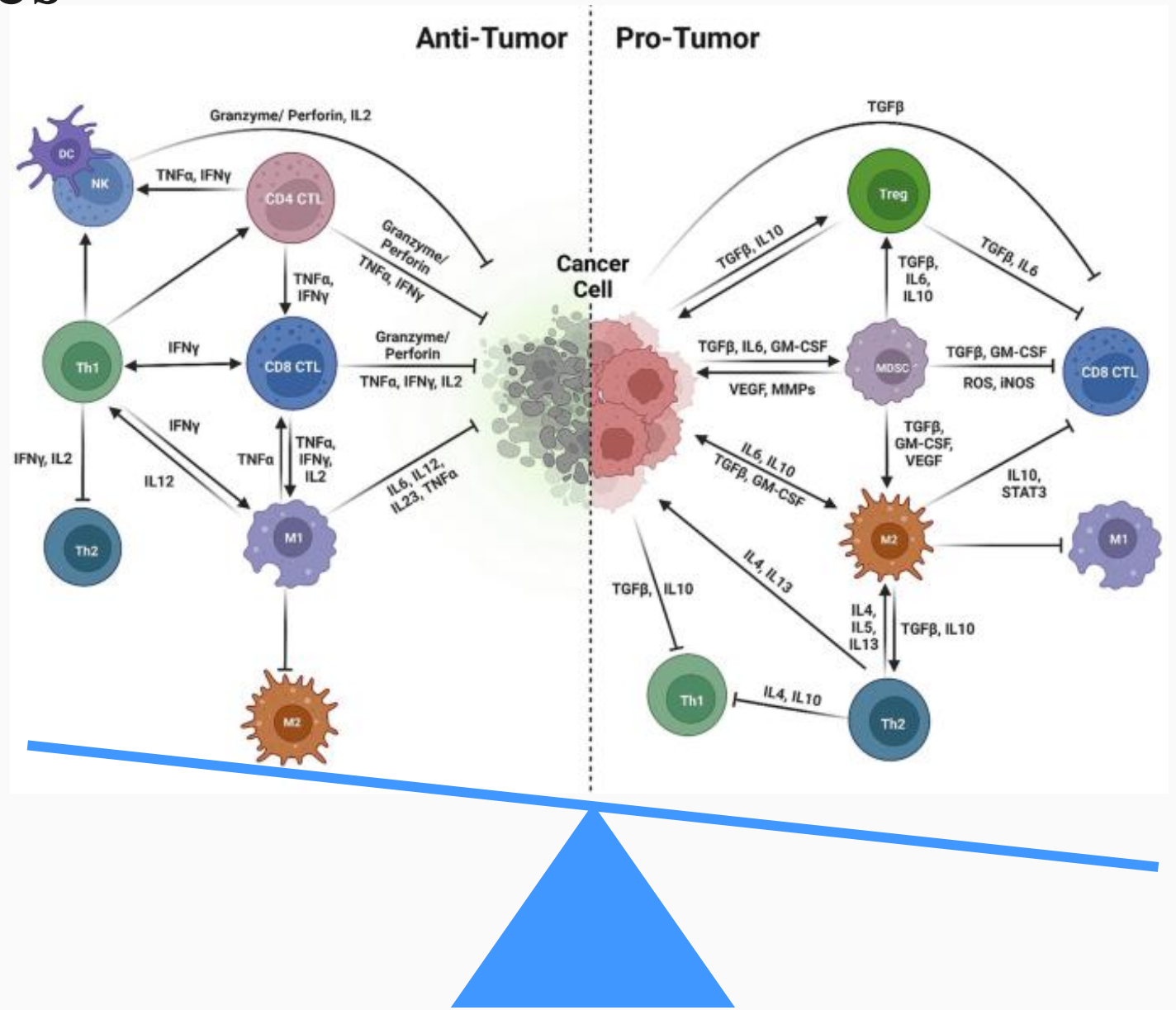
- Immune infiltration – local or systemic response?

- Uncertainties:
  - Does the radiation modality matter?

  - Does LET influence immune activation?

  - How does dose-rate or spatially fractionated beams alter immune responses?

  - Can these approaches synergise with existing immunotherapies?



Chong, Walsh and Ho. (2024)

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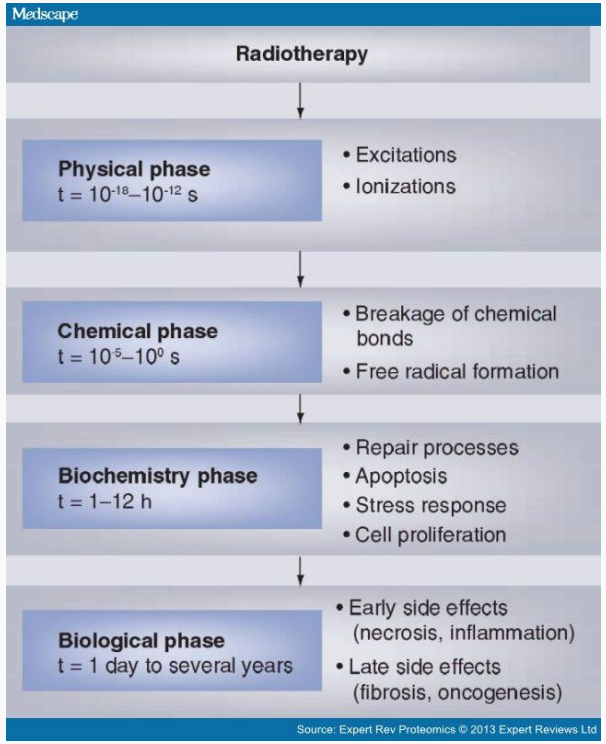
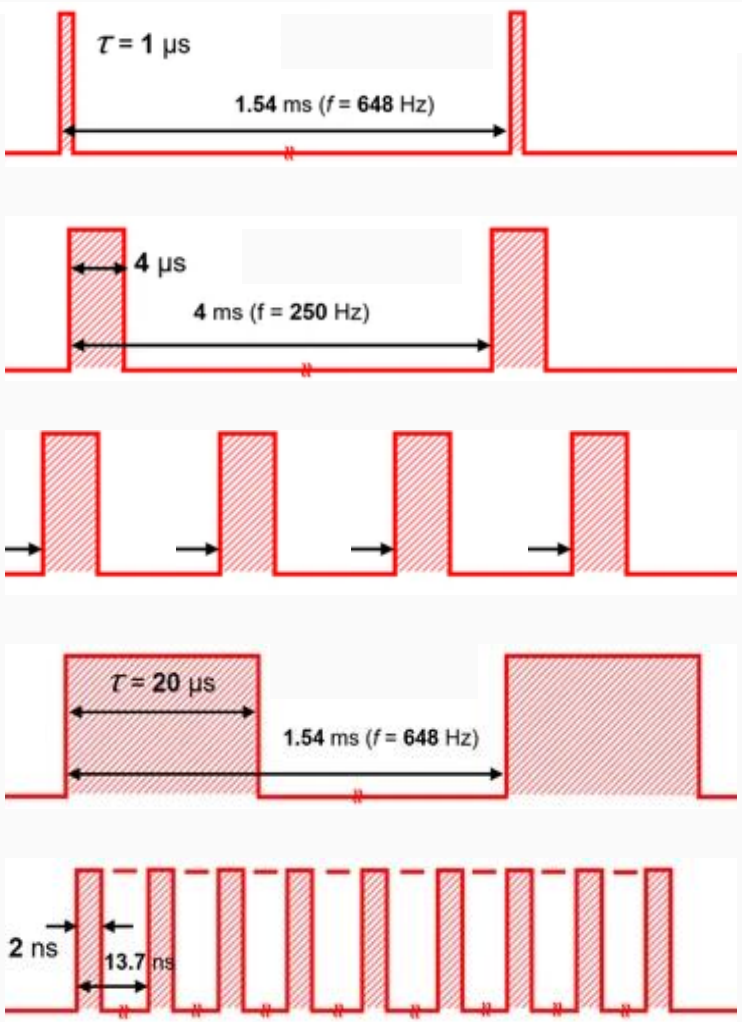
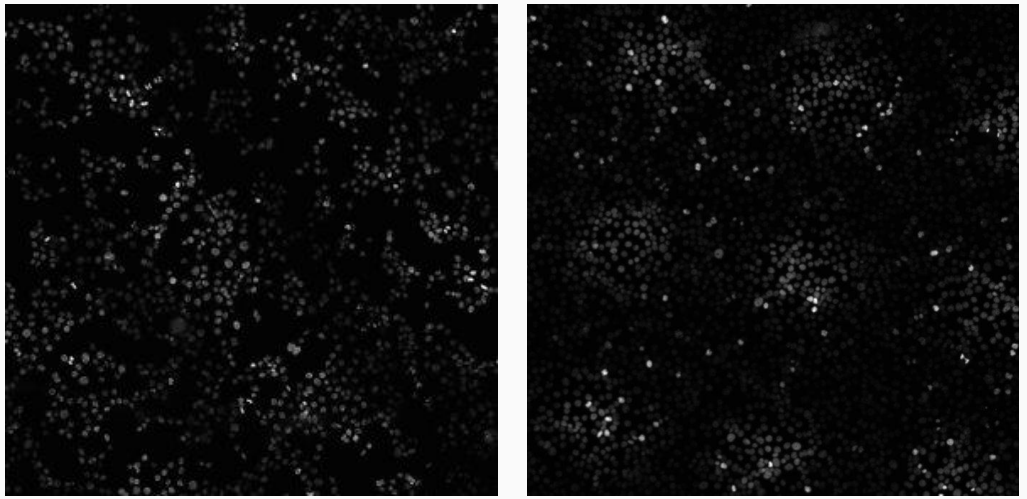
Beam factors that could alter tumour response

- Dose
- Dose-rate
- Pulse structure
- Spatial fractionation
- Particle type, energy and LET



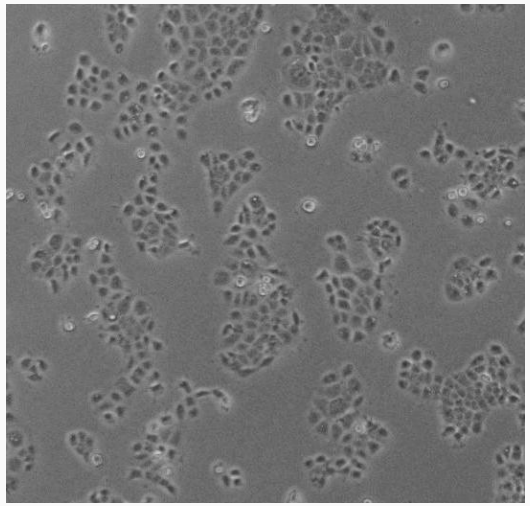


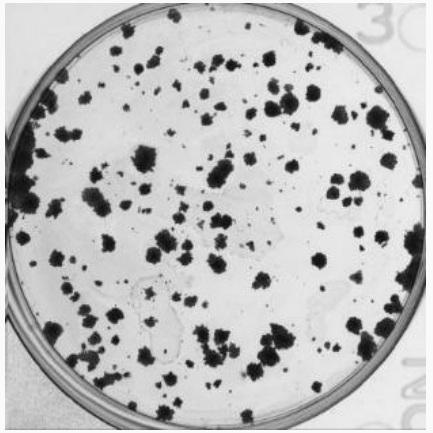


Diffenderfer et al. (2021)

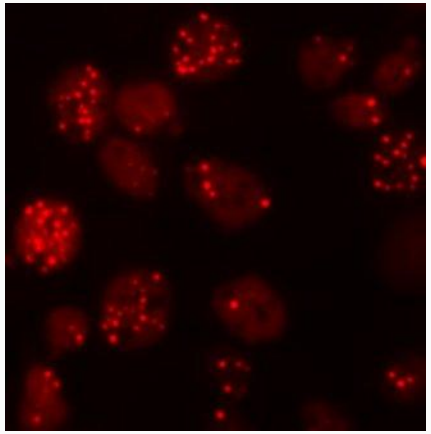
How do we get there? From cells to patients

- **2D –** fundamental responses, critical for first understandings and insight into tumour cell responses

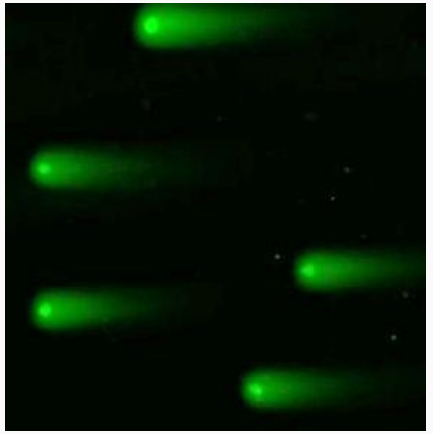




- 3D – more complex, clinically relevant models



- In vivo;
- Chick embryos
- Zebra fish
- Mice



Essential for translational studies and development of clinical trials

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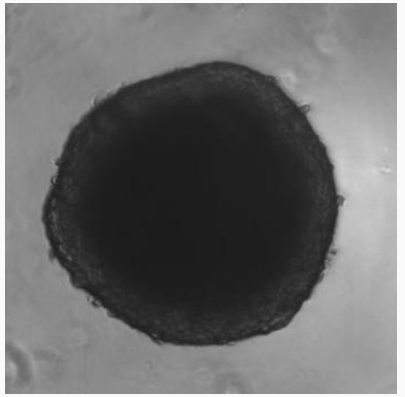

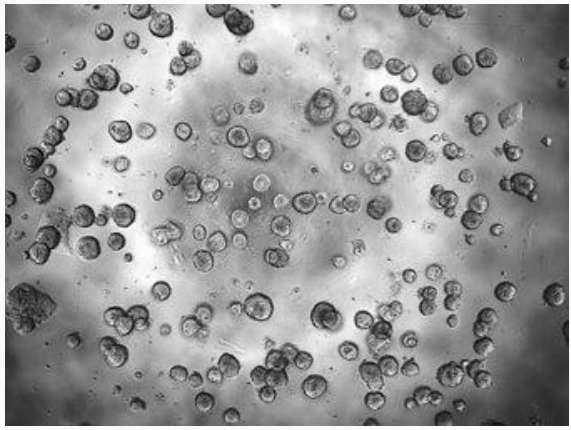

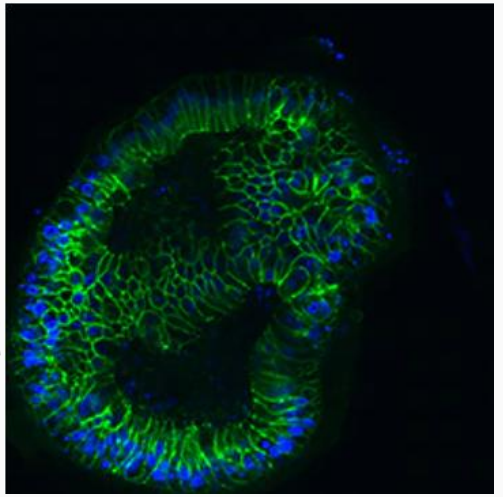

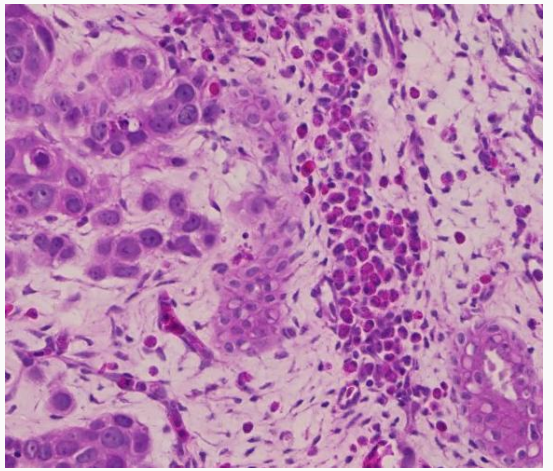

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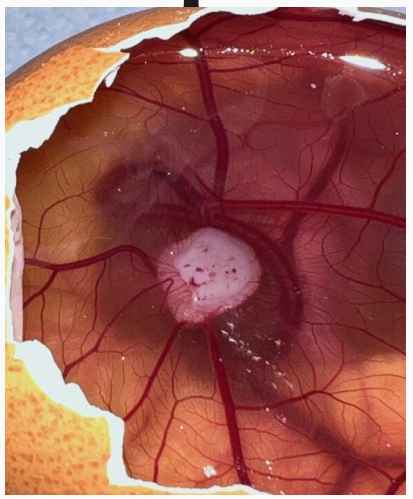

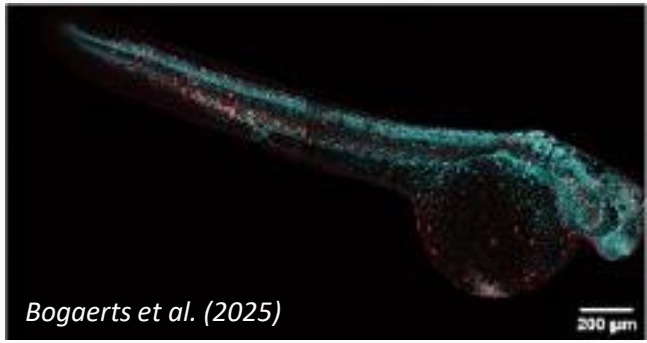

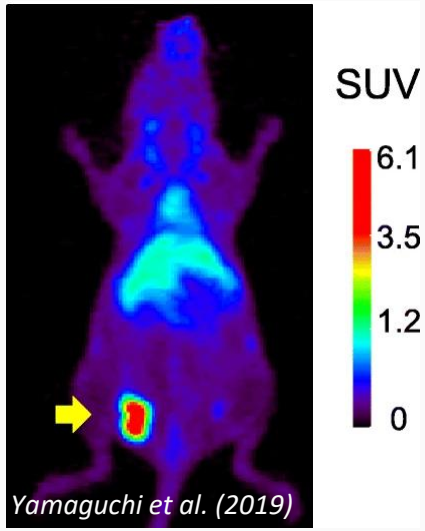

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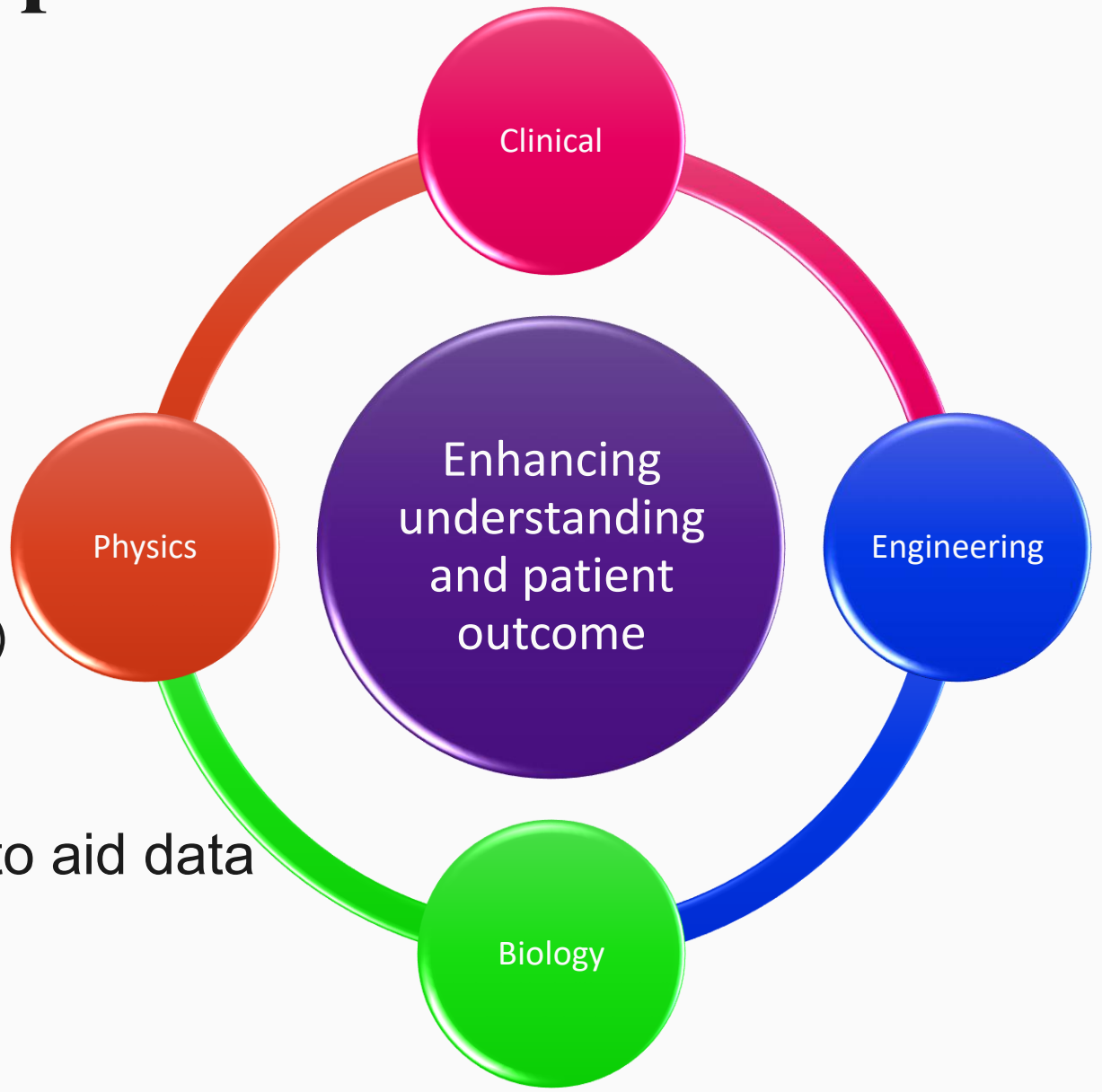
Why is LhARA critical to help us achieve this…

- Flexible beam facility that can manipulate;
  - Ion species
  - Energy
  - In time and space

- Beam facility designed for radiobiology;
  - Beam characteristics and manipulation
  - High throughput biological end stations
  - Animal facilities
  - Radiobiology lab with state-of-the-art facilities
  - Customisable endstations (hypoxia, RT microscopy)

- Development of novel in beam diagnostics
- Generation of machine learning techniques to aid data interpretation



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The LhARA Collaboration

Thank you!