

First VHEE-FLASH Dosimetry and Radiobiology Studies at CLARA

Dr Kristina Small



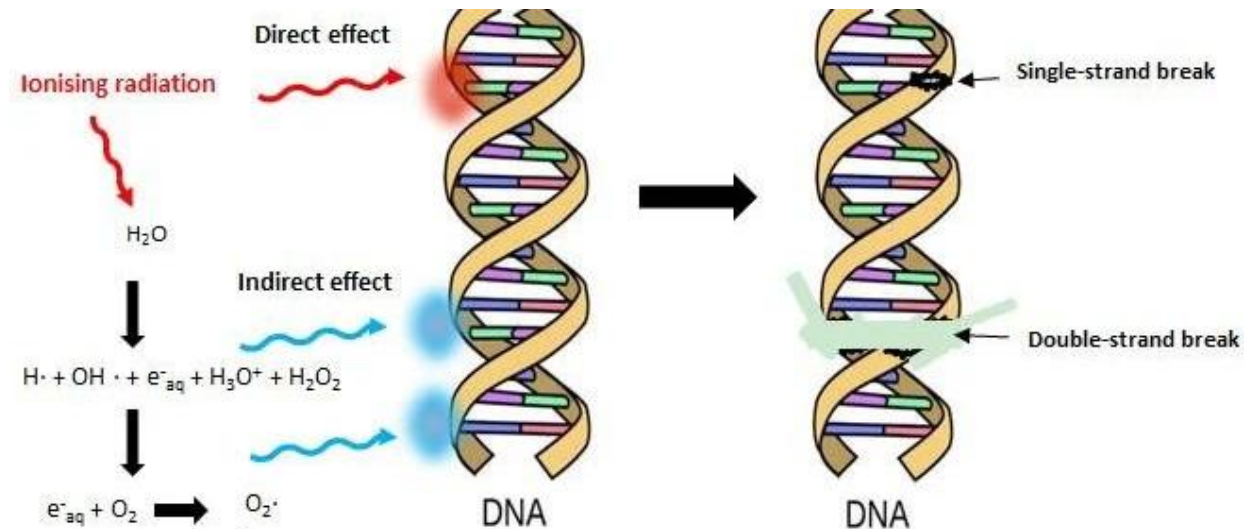
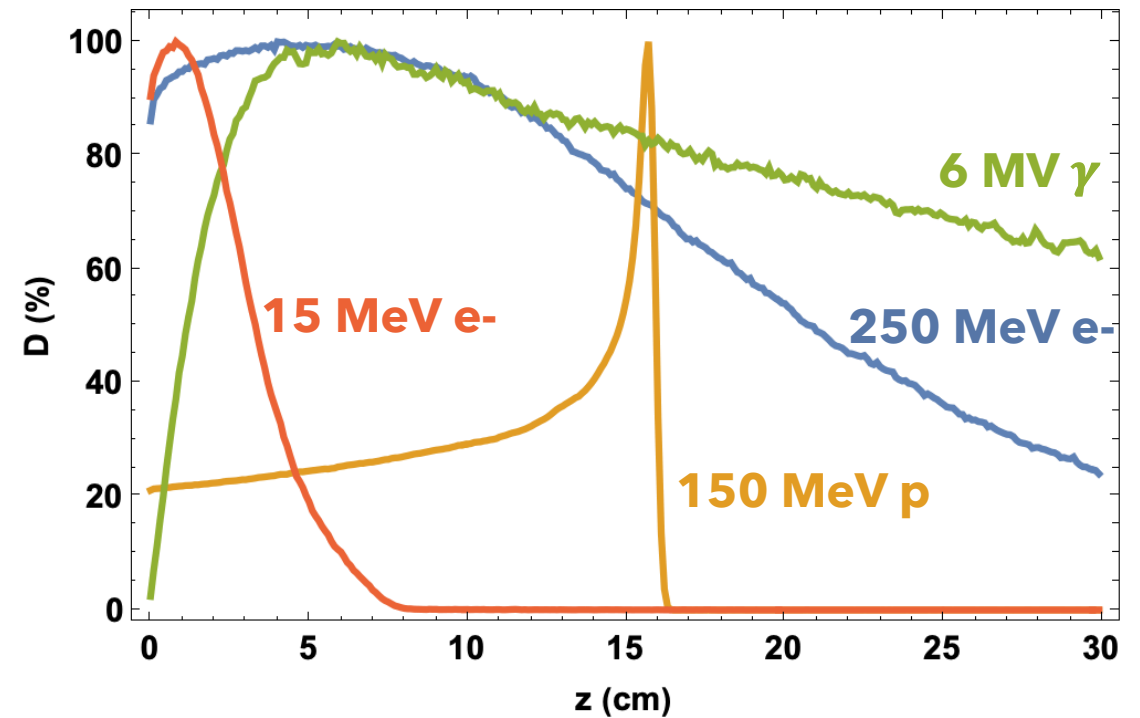
The University of Manchester



Novel Radiotherapy - VHEE

Very High Energy Electron radiotherapy will use 100-250 MeV electrons to treat cancer. Key advantages:

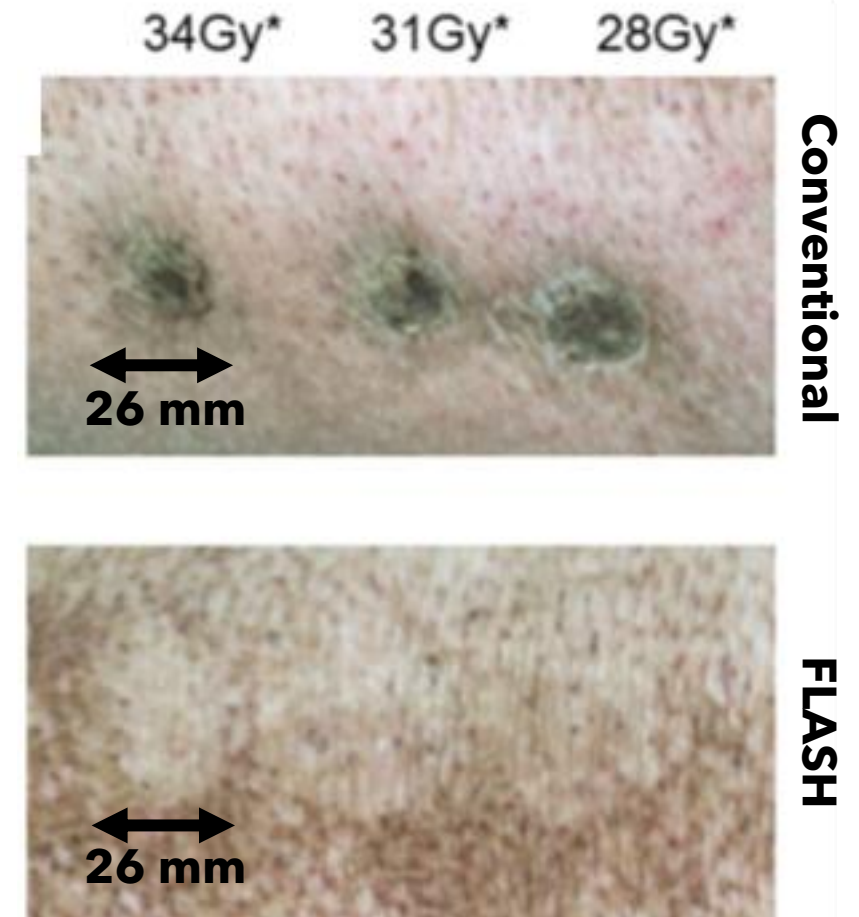
- Increased range in tissue - can treat deep-seated tumours
- Reduced lateral beam spread - lower dose delivered to healthy tissue surrounding a tumour
- Insensitivity to inhomogeneities - changes in tissue density do not affect dose delivery as for other charged particles
- **Similar DNA damage rates compared with established radiotherapy modalities**



Novel Radiotherapy - FLASH



- Radiotherapy dose delivered in ms/us/ns timescales, rather than minute timescales for conventional radiotherapy
- Consistently shown to significantly reduce radiation-induced side effects in healthy tissue
- Also maintains similar tumour control compared with conventional radiotherapy
- Precise mechanisms underpinning FLASH are still not fully understood...



Novel Radiotherapy – VHEE-FLASH



Limitations

Low energy electrons can't reach deep tumours

Rapid beam spread – increased normal tissue dose

Heavy ions require large magnetic fields

Solutions

VHEEs penetrate further into tissue

Reduced lateral beam spread

VHEEs can be rapidly scanned using quadrupole magnets

VHEE-FLASH in Europe



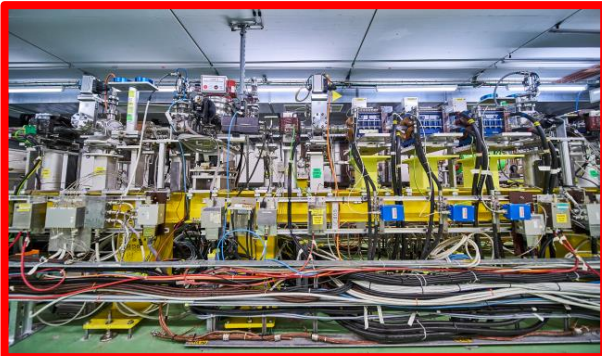
CLARA - 100-250 MeV



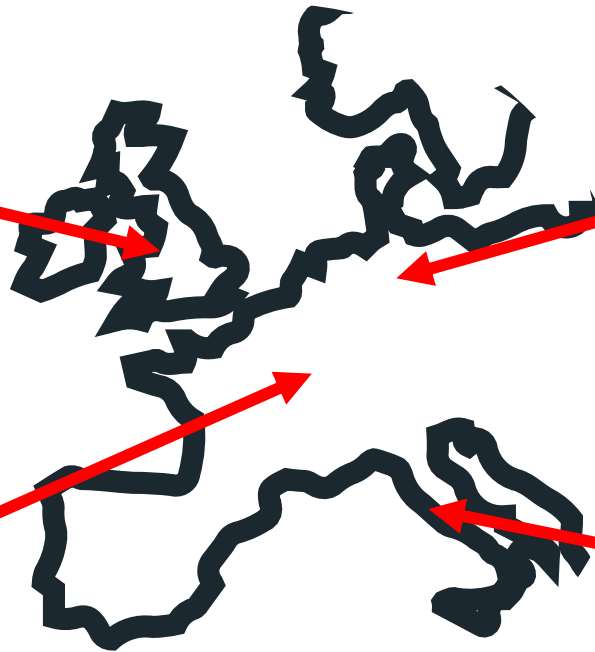
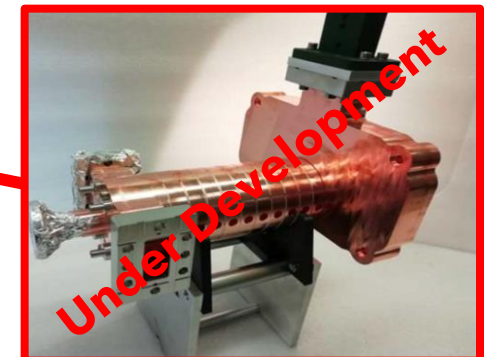
ARES - 100-155 MeV



CLEAR - 60-220 MeV



SAFEST - 80-100 MeV



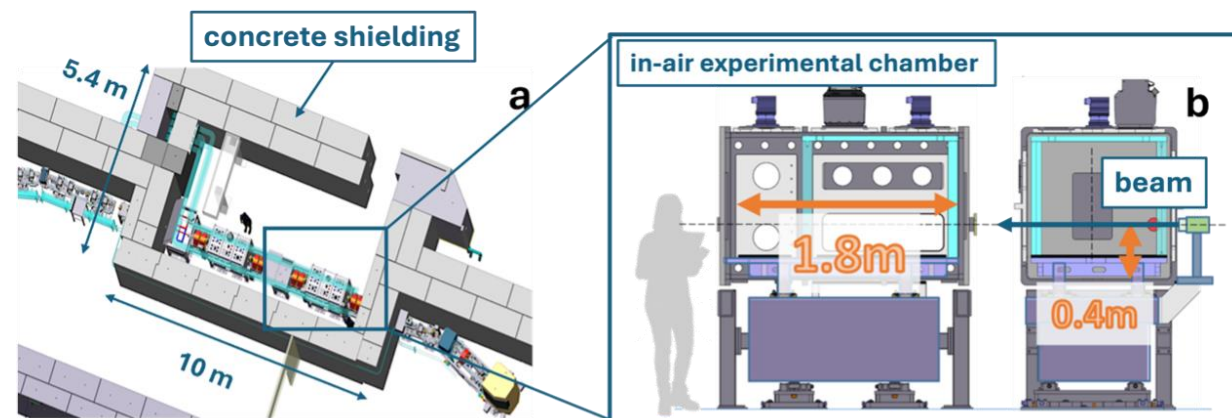
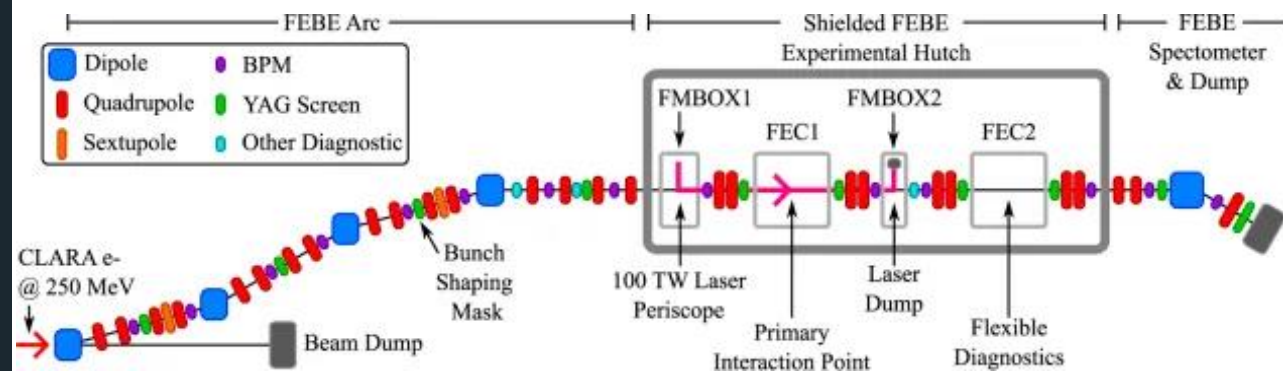
VHEE-FLASH at CLARA

CLARA Phase 1: 20-50 MeV, 250 pC, 10 Hz

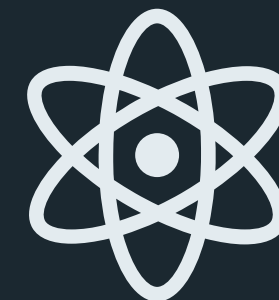


CLARA Phase 2: 100-250 MeV, 5-250 pC, 10-100 Hz

- Designed for novel accelerator techniques and applications
- Full Energy Beam Exploitation (FEBE) area allows for flexible in-air and in-vacuum experiments



VHEE-FLASH at CLARA



Beam Parameter	CLARA
Energy Range	100-250 MeV
Bunch Charge	5-250 pC
Repetition Rate	10-100 Hz
Relative Energy Spread	0.01% (low charge) 0.1% (high charge)
Beam Exit Window	250 μm Be

Covers full clinical VHEE energy range

Can irradiate at both conventional and FLASH dose rates (> 40 Gy/s)

Low energy spread = reliable and repeatable beam - key for clinical VHEE machine design

Easy access to FEBE experimental chambers - rapid sample setup and throughput

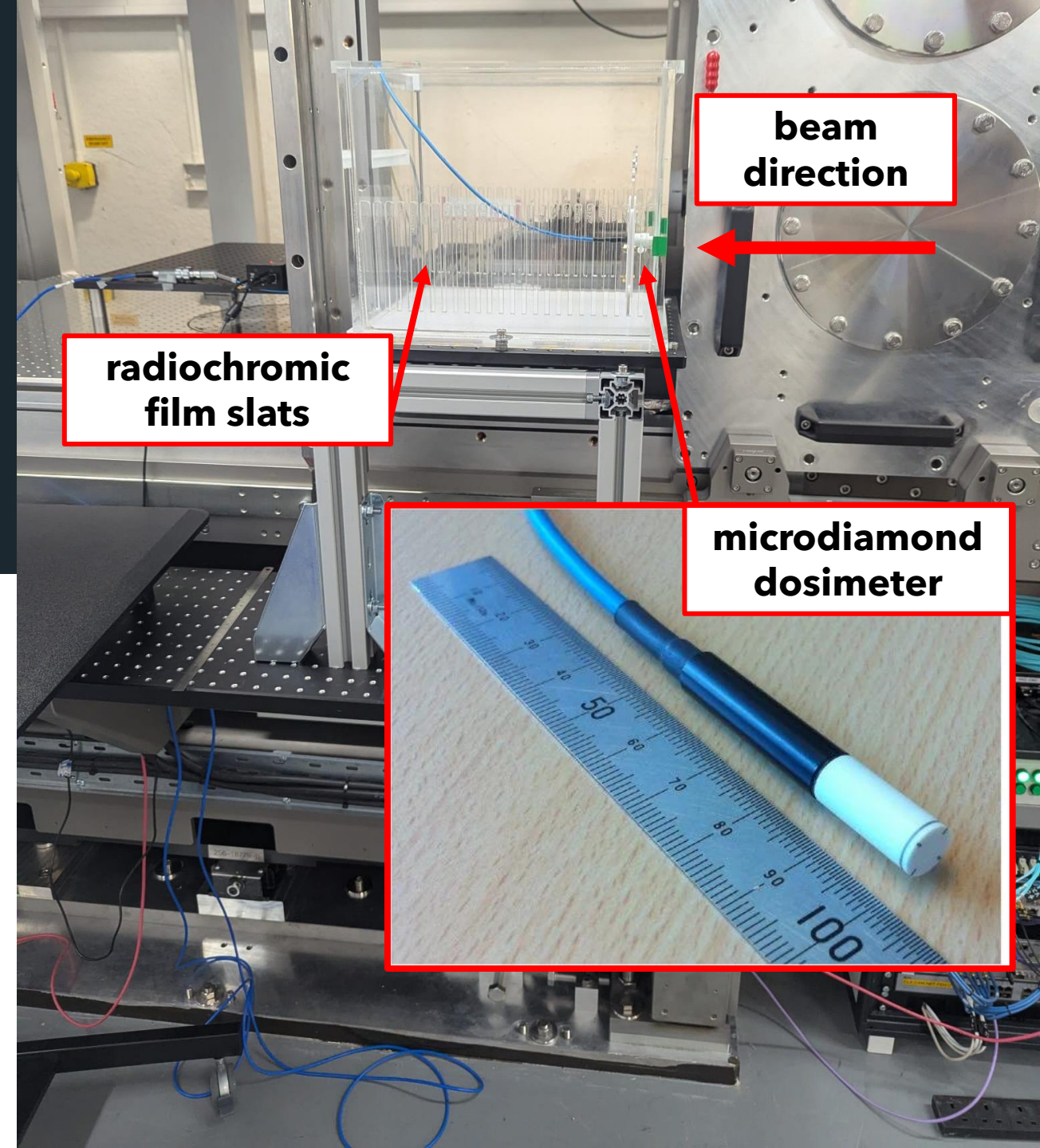
First Studies - Beam Characterisation

Aim - establish beamline parameters required for reliable, repeatable VHEE conv and FLASH irradiation

First studies in Feb/Mar 2026

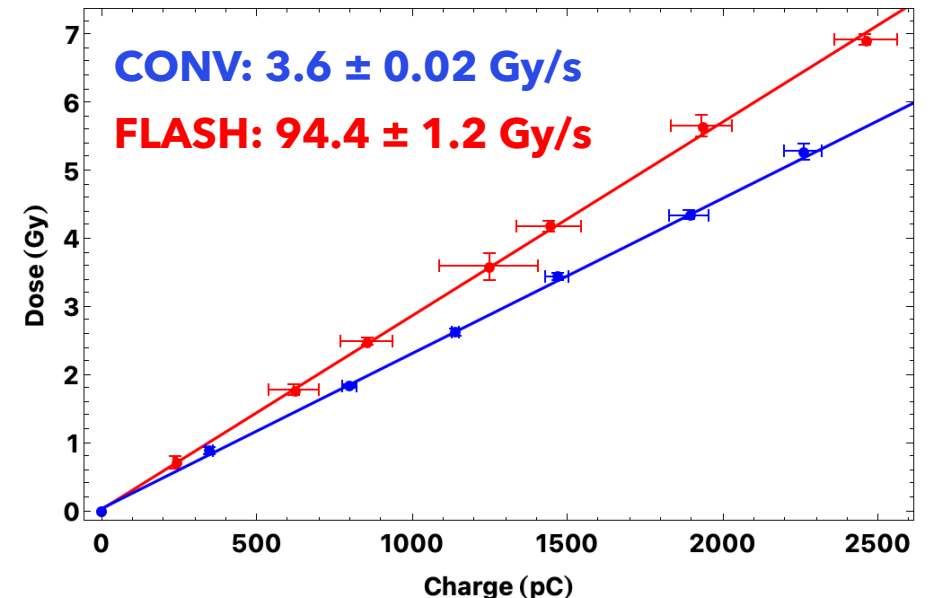
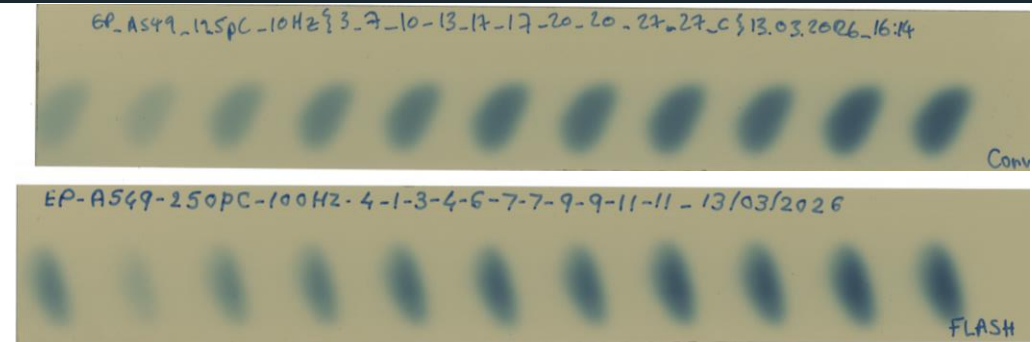
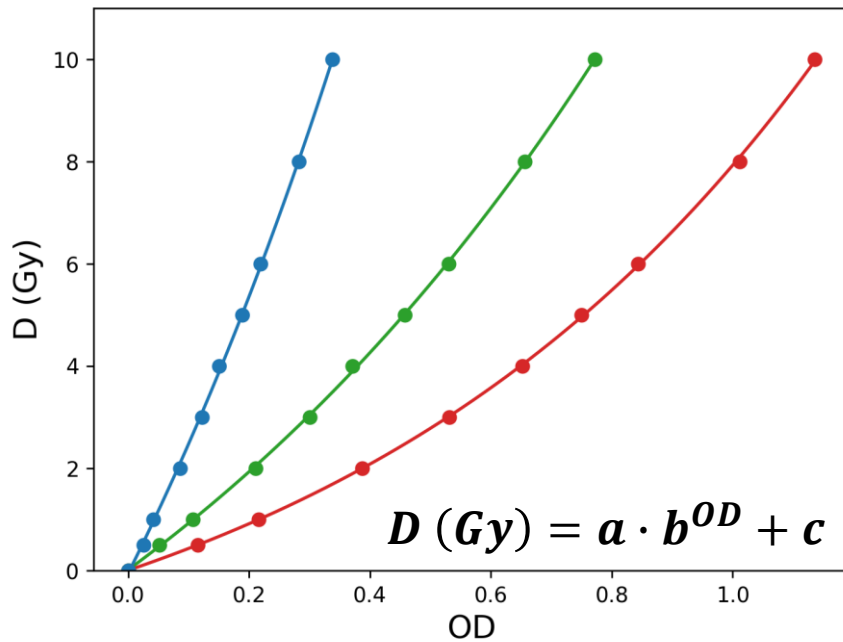
Delayed and real-time dosimetry performed with EBT4 film and microdiamond dosimeter

Dose vs. charge relationship analysis for Conv and FLASH irradiation



First Studies – Beam Characterisation

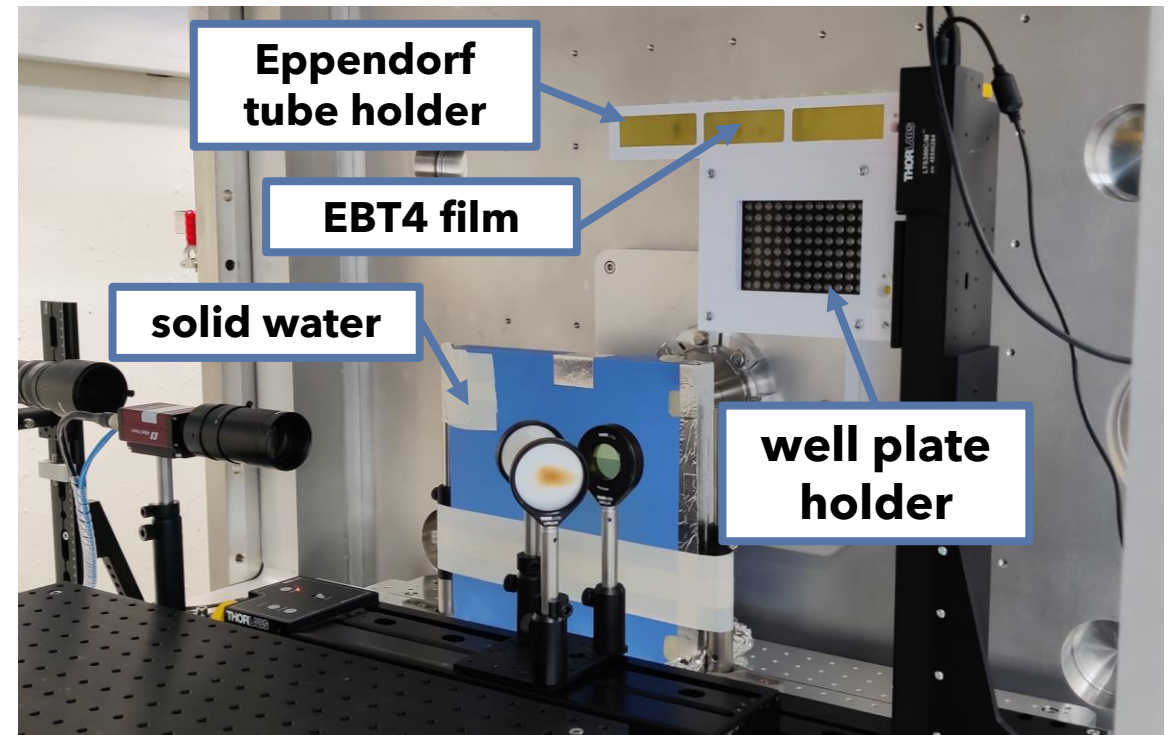
X-Ray EBT4 film calibration



First Studies – Cell Survival



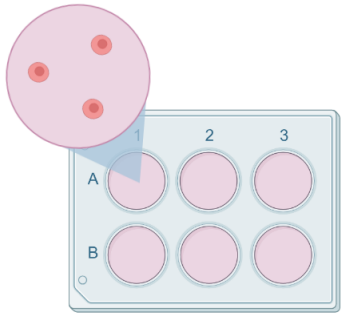
- First VHEE cell irradiations in UK performed at CLARA in March 2026
- Human lung adenocarcinoma (A549) cell samples irradiated over 0-8 Gy
- Cell survival analysed through clonogenic assay and survival curves plotted
- Cell survival results compared with results from 300 kVp X-rays (OCRB) and 154 MeV electrons (ARES)



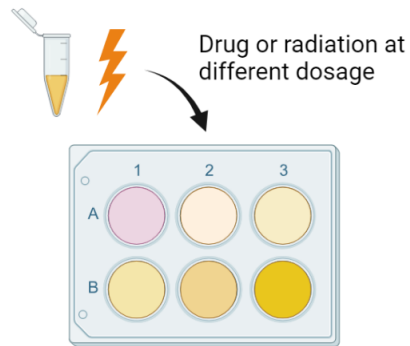
First Studies – Cell Survival



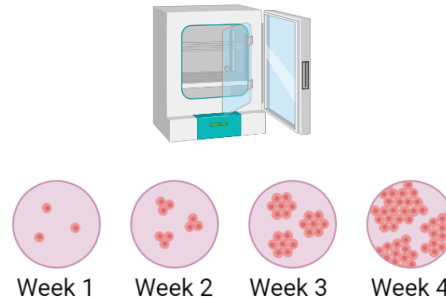
- ① Seed cells at low density in well plate



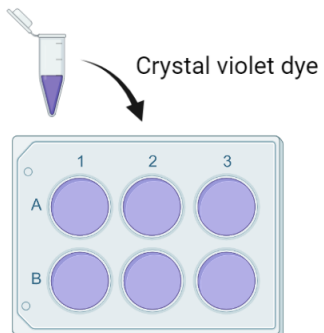
- ② Treat cells



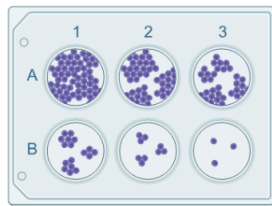
- ③ Incubate cells and monitor colony growth



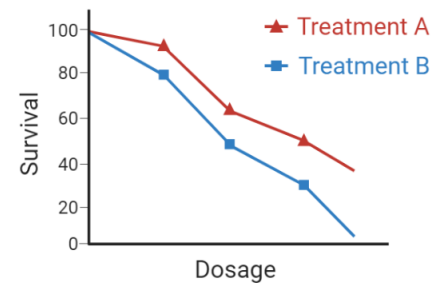
- ④ Wash, fix and stain colonies



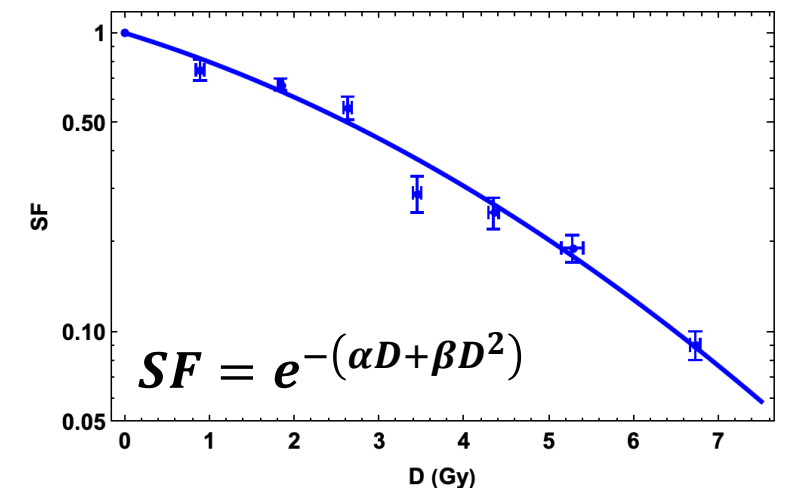
- ⑤ Count stained colonies



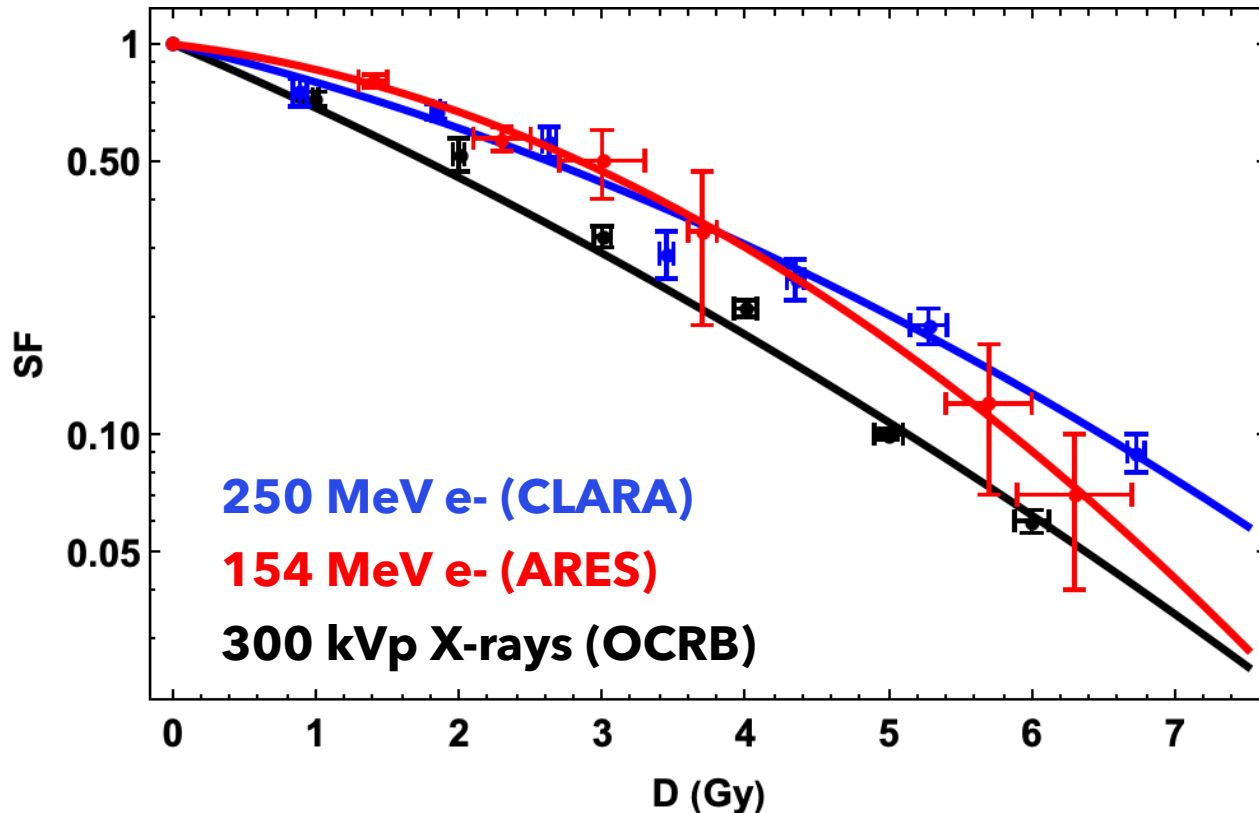
- ⑥ Survival analysis



$$SF = \frac{\text{colonies counted}}{\text{cells seeded}}$$



First Studies – Cell Survival

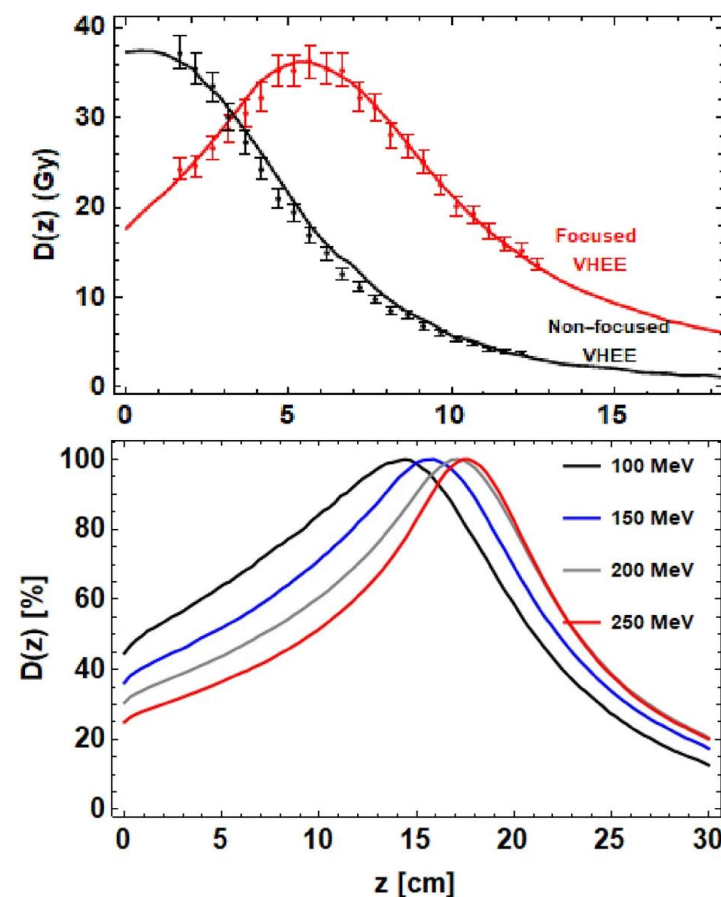


Parameter	250 MeV e- e-	154 MeV e- e-	300 kVp X-rays X-rays
α	0.20 ± 0.03	0.10 ± 0.07	0.06 ± 0.08
β	0.024 ± 0.007	0.05 ± 0.03	0.07 ± 0.03
R^2	0.988	0.966	0.971
D_{50}	2.63 ± 0.32	2.85 ± 0.23	2.82 ± 0.23
D_{10}	6.49 ± 0.60	5.87 ± 0.23	5.45 ± 0.23

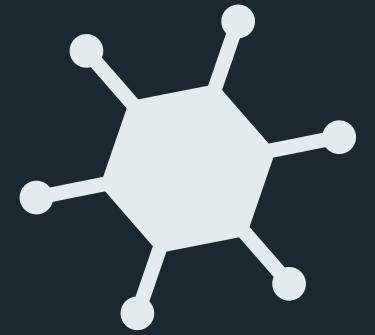
Moving Forward – Beam Characterisation and Focusing



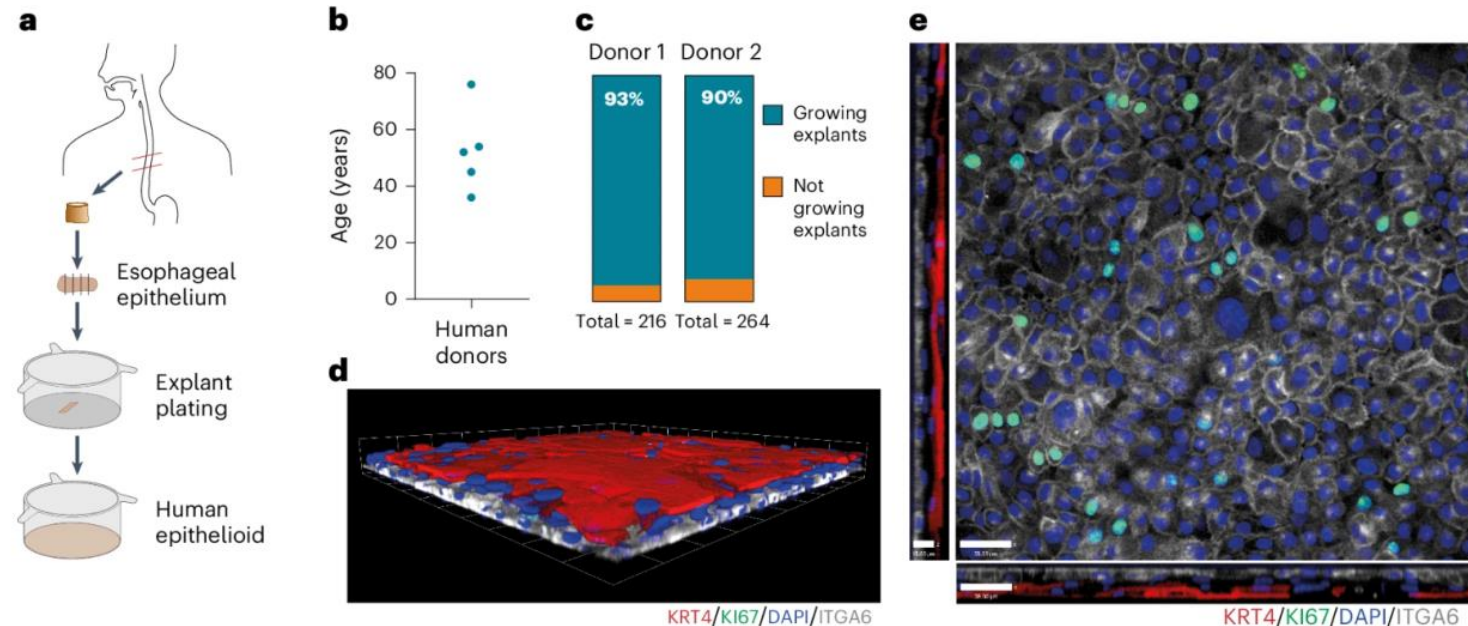
- How do we treat the correct region in a patient?
- Successful focusing has been achieved at depths up to 5 cm (Whitmore et al.) – not far enough for most patients!
- Aim – beam focusing using quadrupole magnets at patient-relevant depths (10-20 cm)
- Initial simulation work underway – translating quadrupole optimisation in vacuum to dose profile in water phantoms



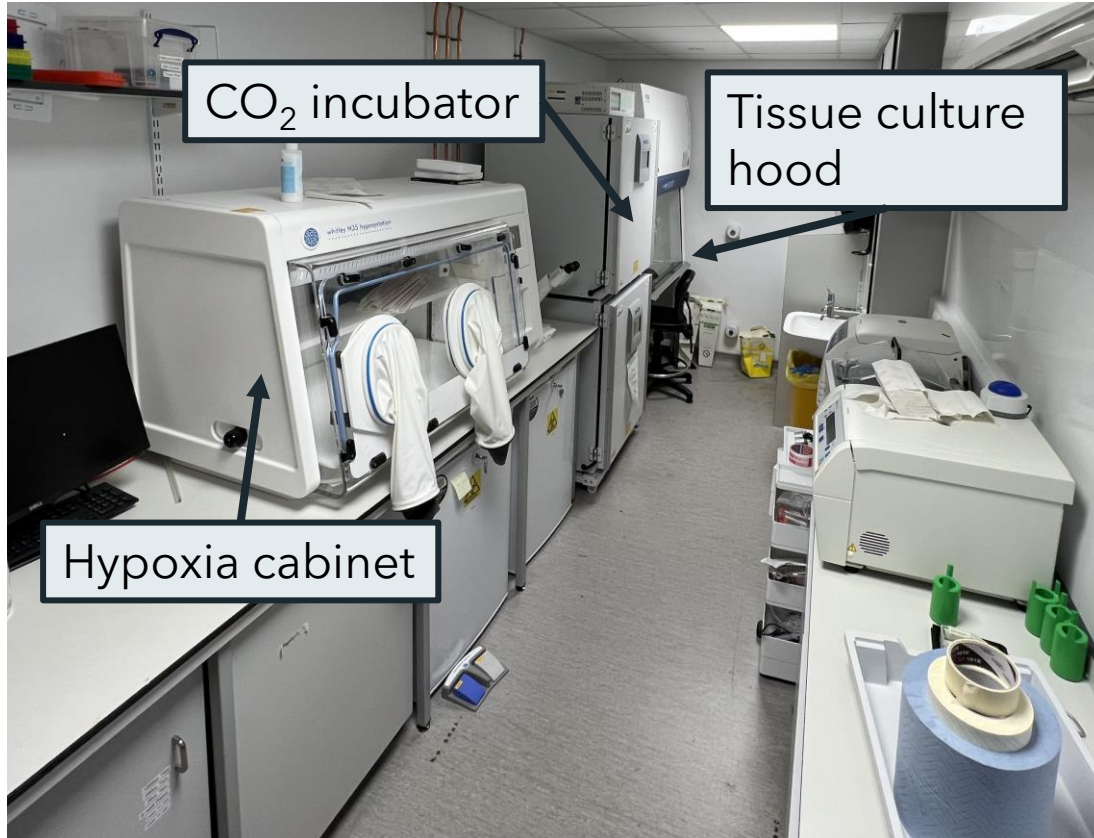
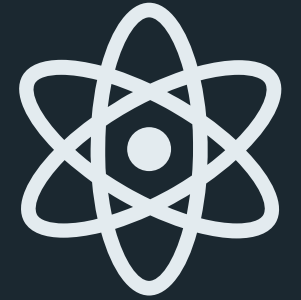
Moving Forward – Healthy Tissue and Tumour Response



- Tissues and tumours are much more complex than simple cells in a flask – how do their responses differ to Conv and FLASH irradiation?
- Multi-dimensional cell models more closely approximate the *in vivo* environment
- Novel model – human-derived epithelioids. Allows study of long-term radiation effects



Radiobiology at CLARA



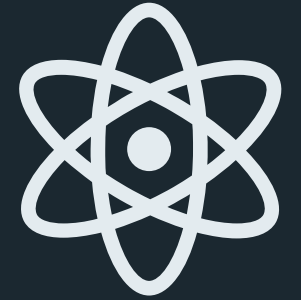
Multidisciplinary approach:

- Expertise in accelerator physics will inform research into machine design
- Collaboration with PRECISE will inform patient-focused research – dosimetry, treatment planning, radiobiology

Short-term aim – set up a biological lab workspace for cell work. Will allow increasingly complex radiobiology

Long-term aim – establish CLARA as a European/global centre for VHEE-FLASH radiotherapy research

Conclusions



- VHEE and FLASH radiotherapy have the potential to revolutionise cancer treatment, particularly lung cancers
- The CLARA beamline is ideal for research into VHEE-FLASH radiotherapy
- Early studies have shown viability of CLARA beamline for VHEE-FLASH dosimetry and radiobiology
- Expansion of biological laboratory facilities will allow for increasingly complex VHEE-FLASH experiments

Acknowledgements



Roger M Jones

Deepa Angal-Kalinin

James Jones

Stewart Boogert

CLARA Operations Team

Michael Taylor

Nicholas Henthorn

Amy Chadwick

Emma Baglin

Adam Aitkenhead