First VHEE-FLASH Dosimetry and Radiobiology Studies at CLARA

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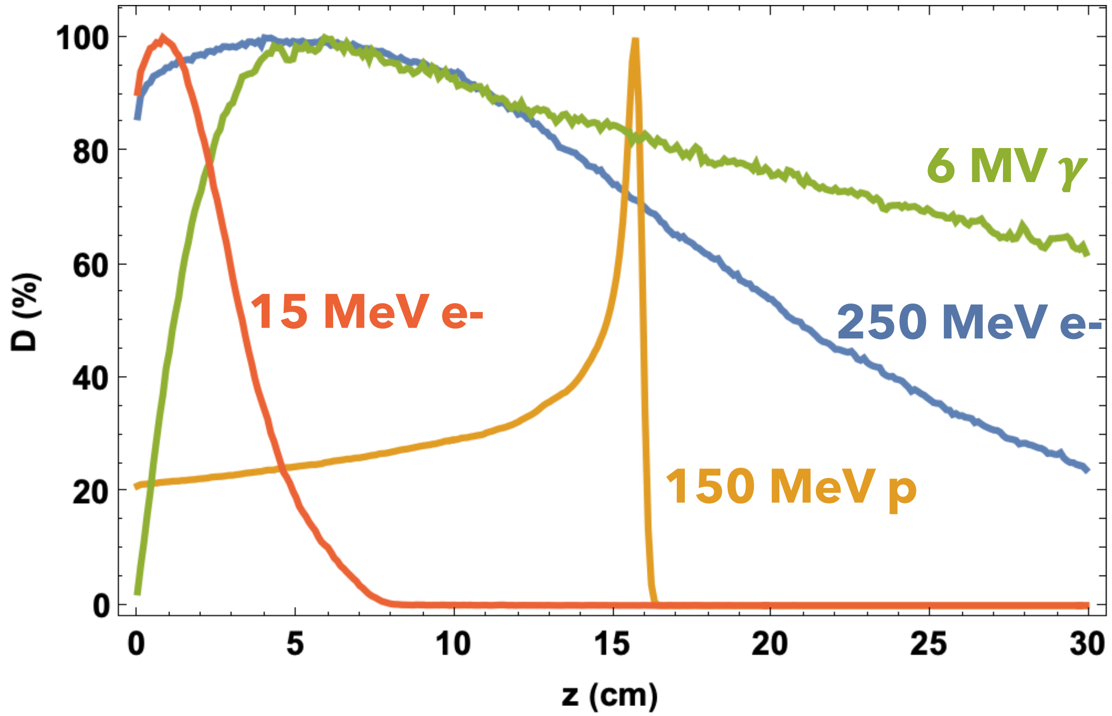
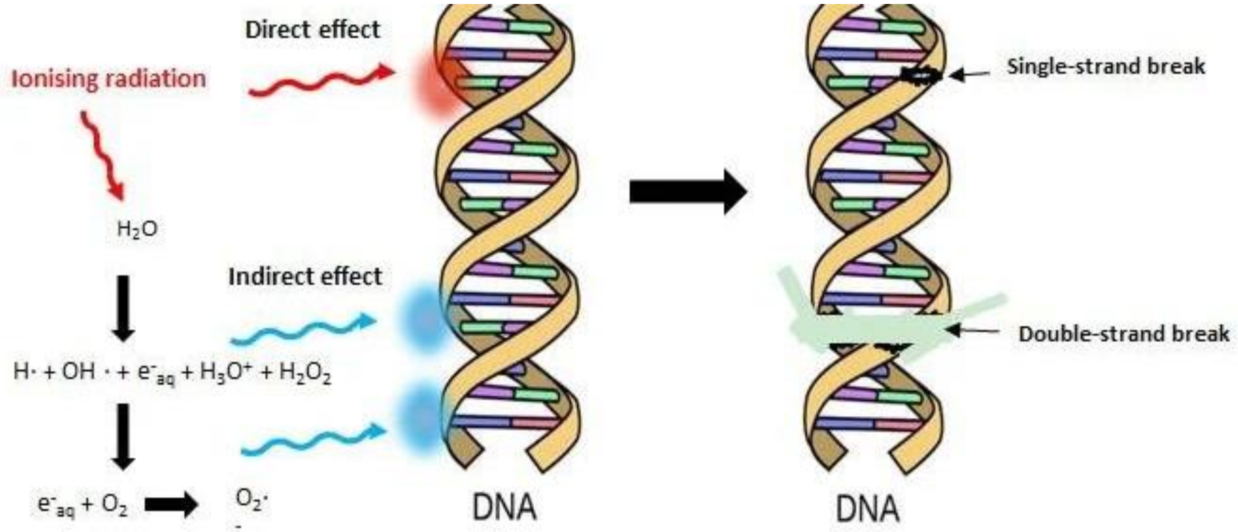
Novel Radiotherapy – VHEE



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

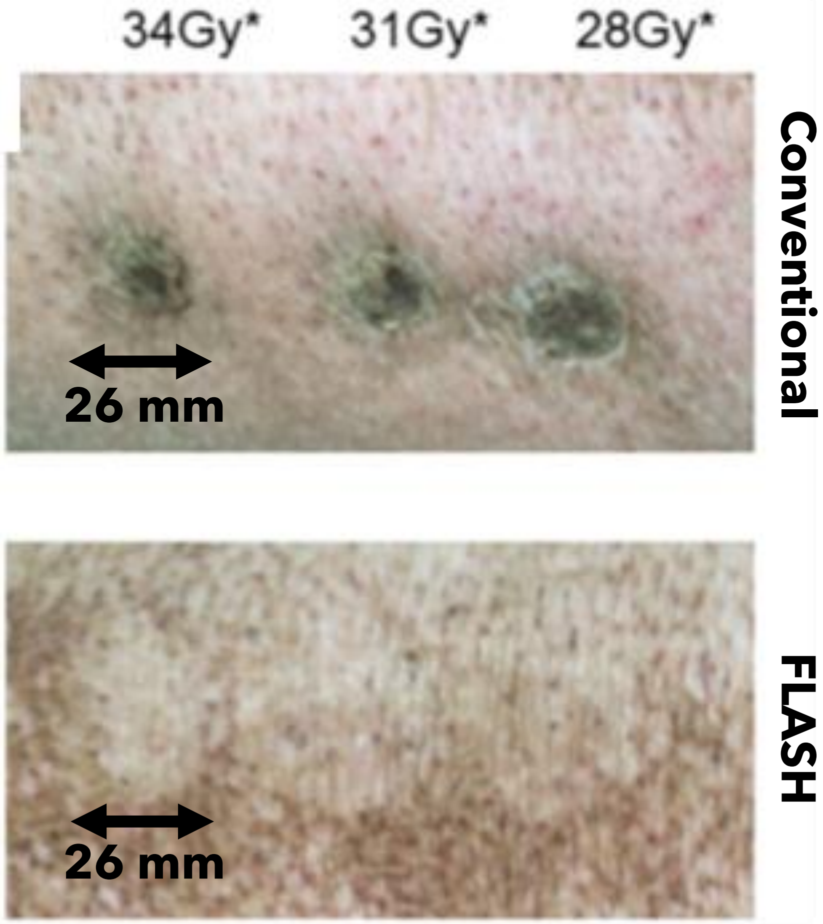
- Increased range in tissue – can treat deep-seated tumours
- Reduced lateral beam spread – lower dose delivered to healthy tissue surrounding a tumour
- Insensitivity to inhomogeneities – changes in tissue density do not affect dose delivery as for other charged particles
- **Similar DNA damage rates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



Small, K. et al. *Sci. Rep.* 11 (2021)

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…



Vozenin, M. C. *et al.*. *Clin. Cancer Res.* **25**, 35–42 (2019)

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

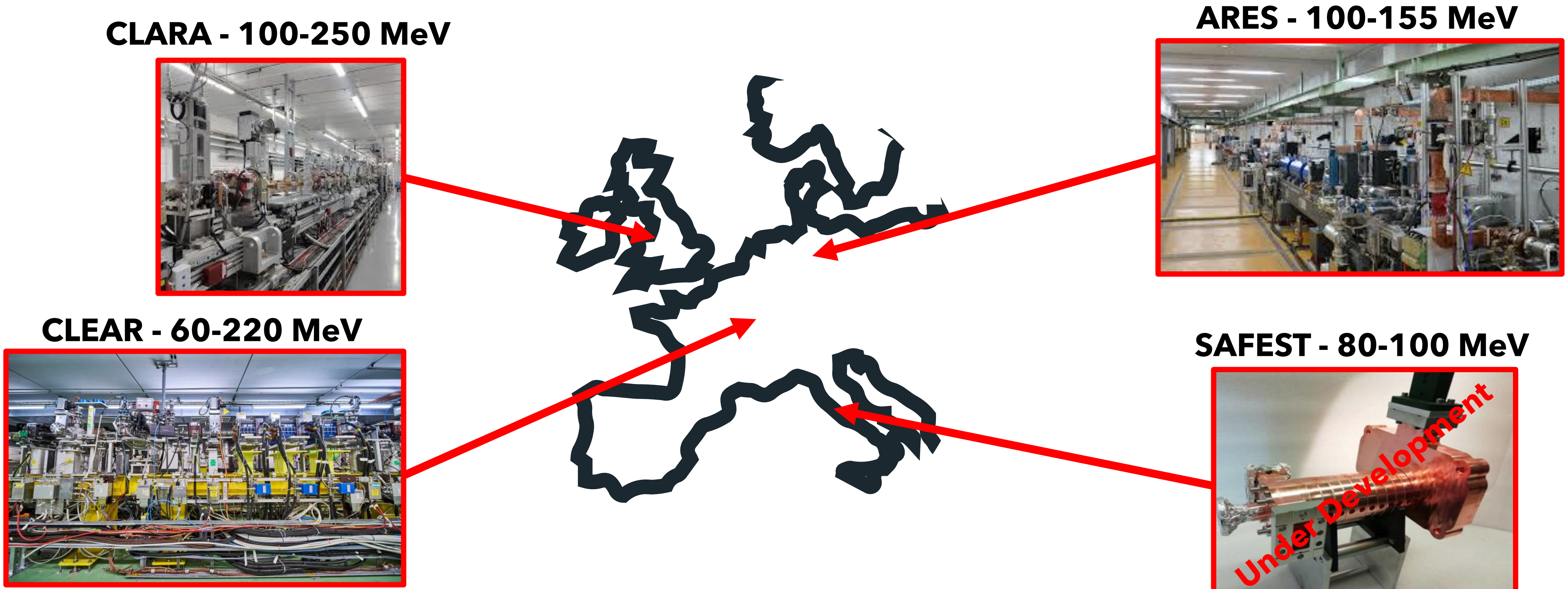
VHEEs penetrate further into tissue

Reduced lateral beam spread

VHEEs can be rapidly scanned using quadrupole magnets

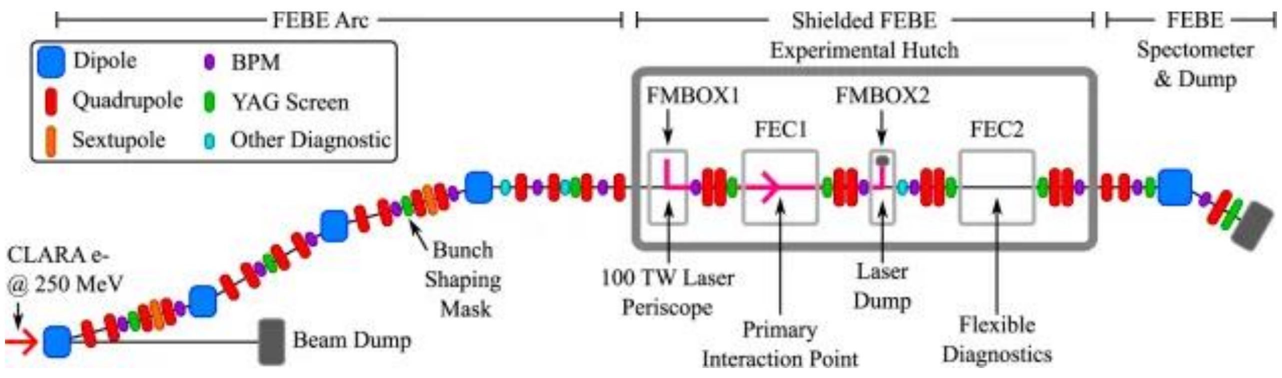
Vozenin, M. C. *et al.*. *Clin. Cancer Res.* **25**, 35–42 (2018).

VHEE-FLASH in Europe



K. Small *et al.* Nuclear Inst. And Methods in Physics Research, B **565** 165752 (2025)

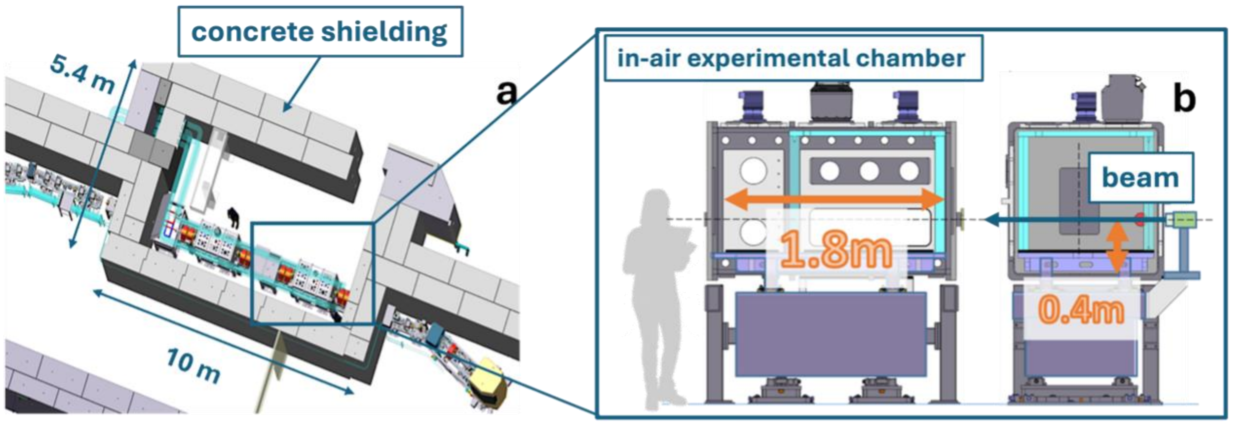
VHEE-FLASH at CLARA



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

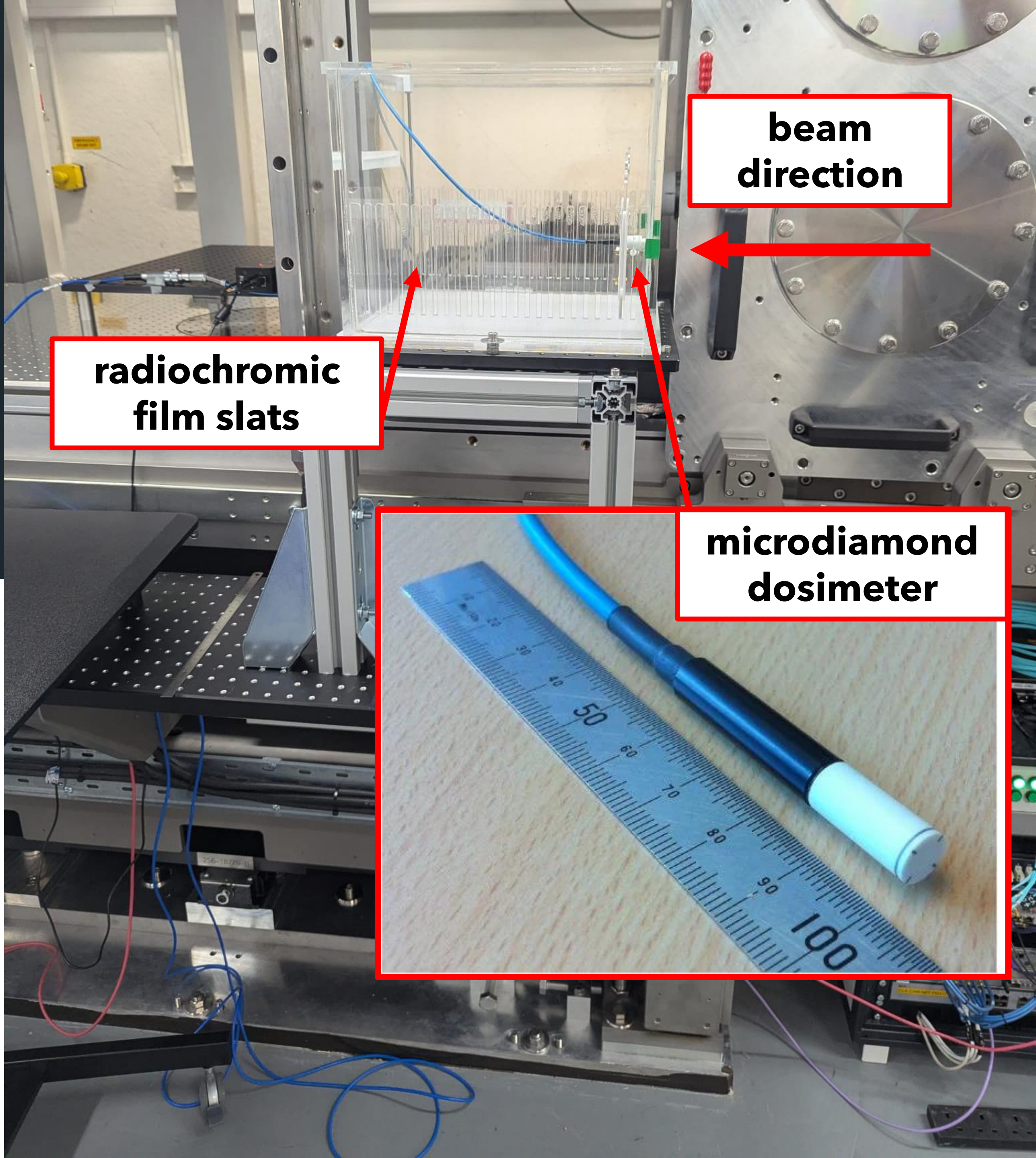
First Studies – Beam Characterisation

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

First studies in Feb/Mar 2026

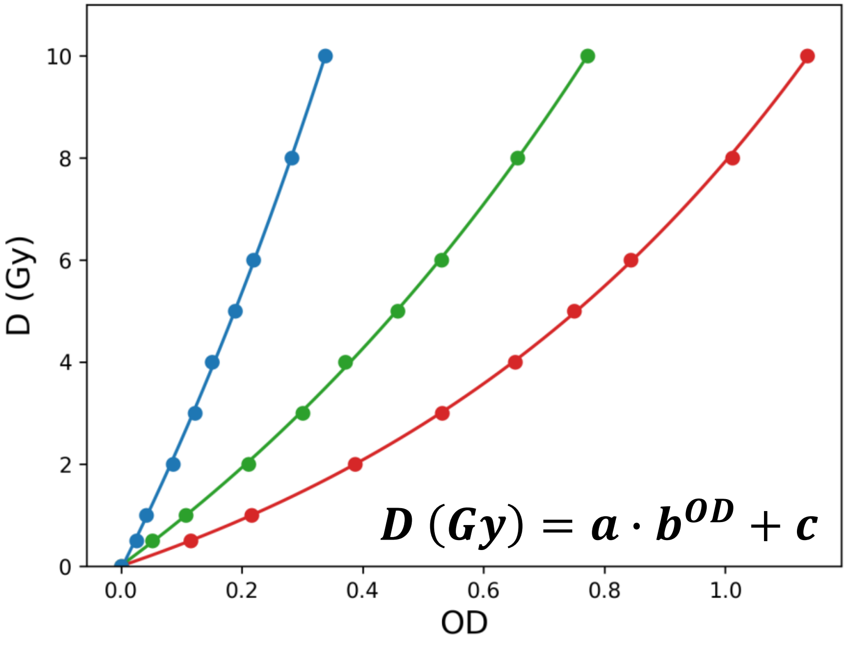
Delayed and real-time dosimetry performed with EBT4 film and microdiamond dosimeter

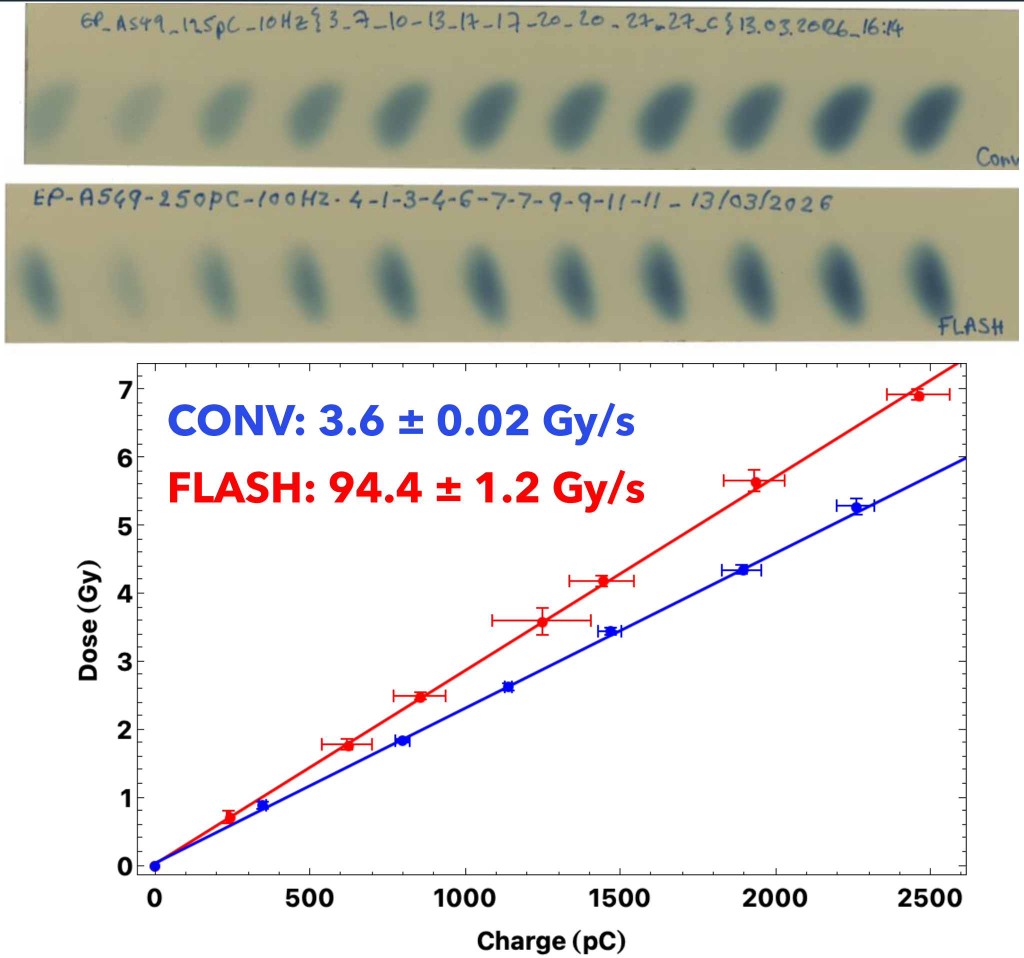
Dose vs. charge relationship analysis for Conv and FLASH irradiation



First Studies – Beam Characterisation

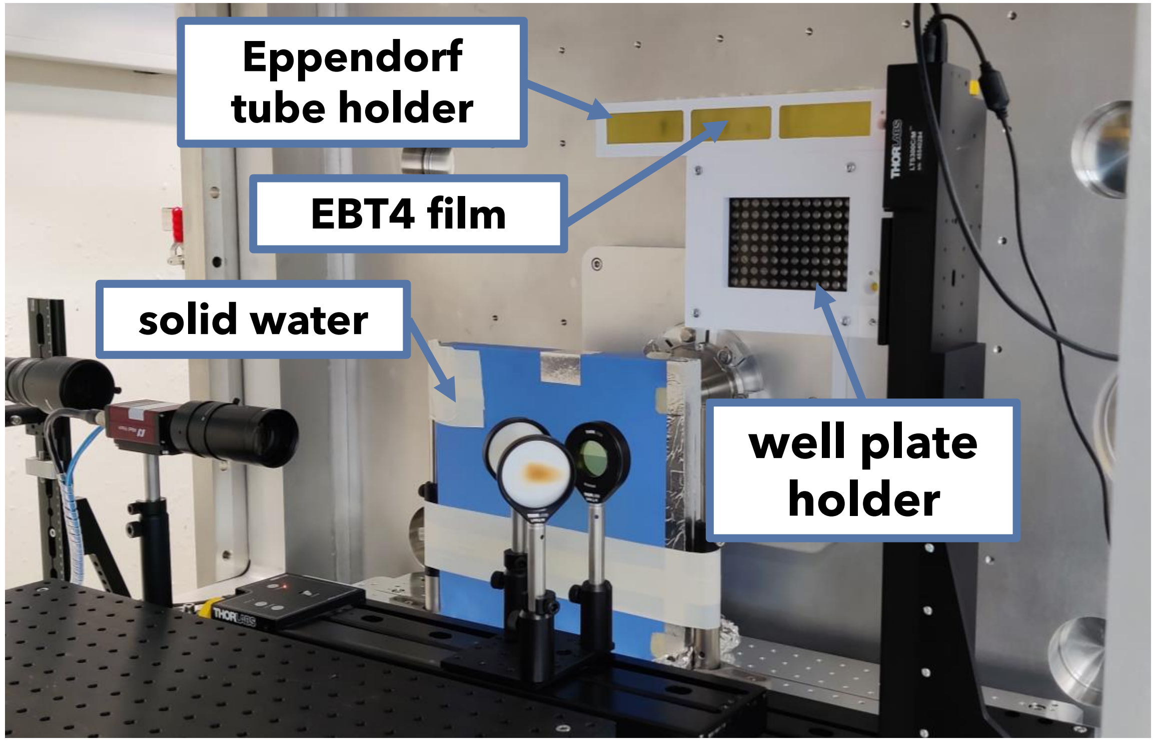
X-Ray EBT4 film calibration



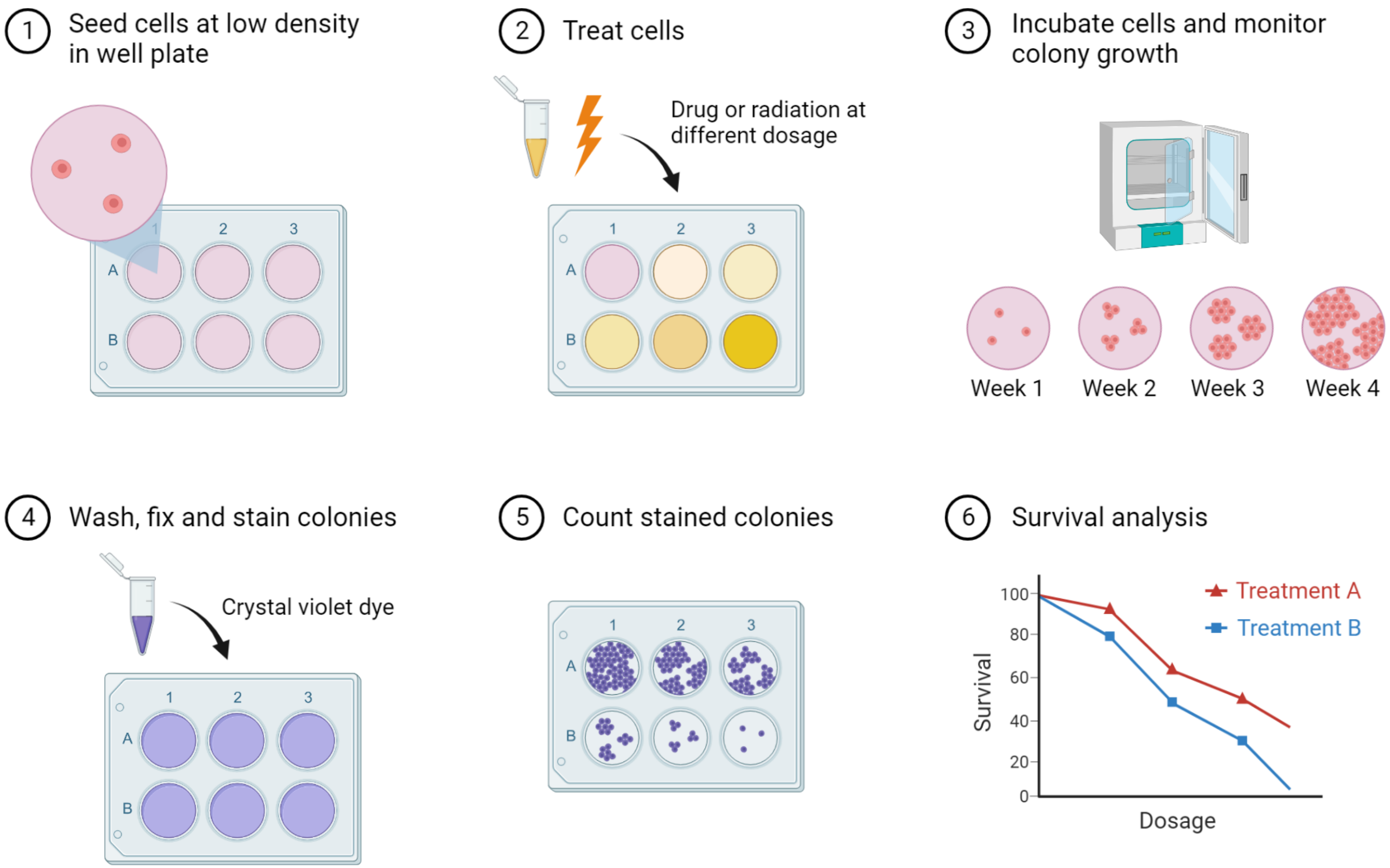


First Studies – Cell Survival

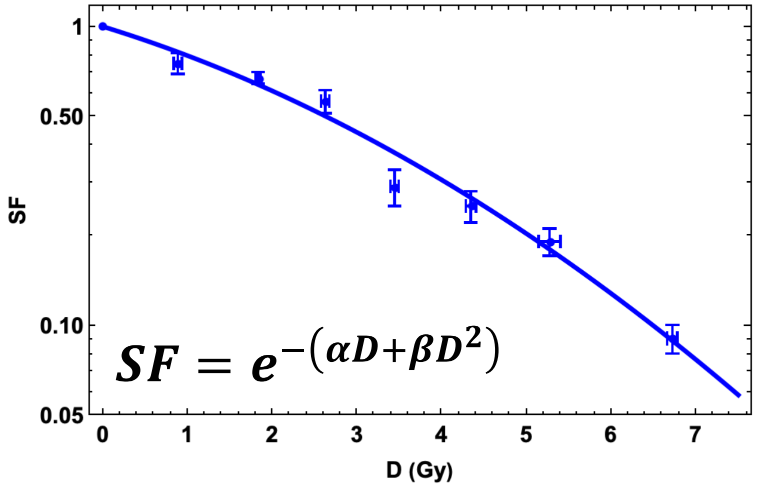
- First VHEE cell irradiations in UK performed at CLARA in March 2026
- Human lung adenocarcinoma (A549) cell samples irradiated over 0-8 Gy
- Cell survival analysed through clonogenic assay and survival curves plotted
- Cell survival results compared with results from 300 kVp X-rays (OCRB) and 154 MeV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



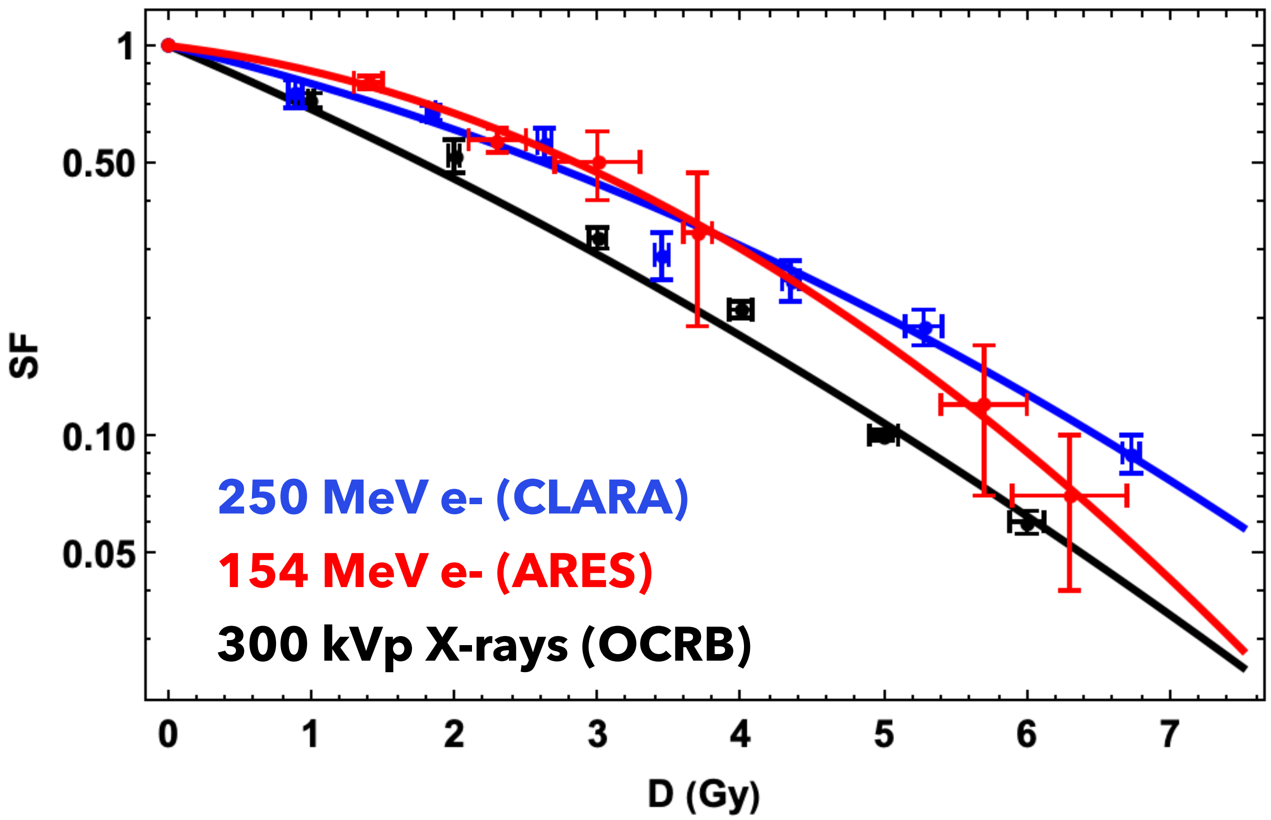
First Studies – Cell Survival



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



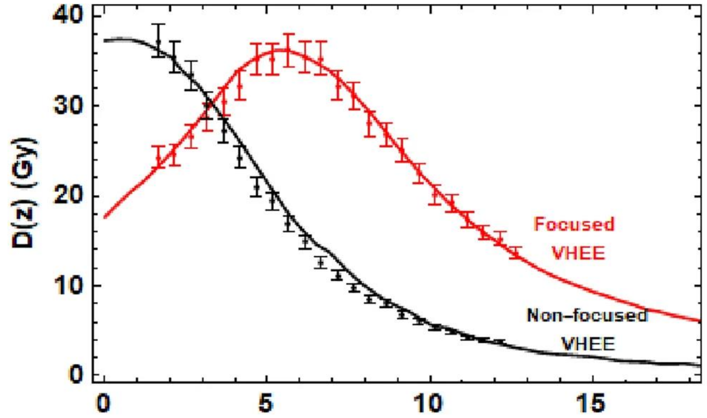
First Studies – Cell Survival

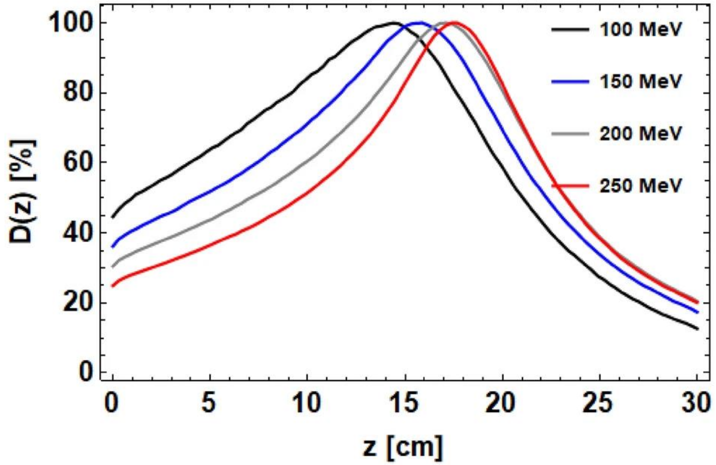


Parameter	250 MeV e-	154 MeV e-	300 kVp X-rays
α	0.20 ± 0.03	0.10 ± 0.07	0.06 ± 0.08
β	0.024 ± 0.007	0.05 ± 0.03	0.07 ± 0.03
R^2	0.988	0.966	0.971
D_{50}	2.63 ± 0.32	2.85 ± 0.23	2.82 ± 0.23
D_{10}	6.49 ± 0.60	5.87 ± 0.23	5.45 ± 0.23

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



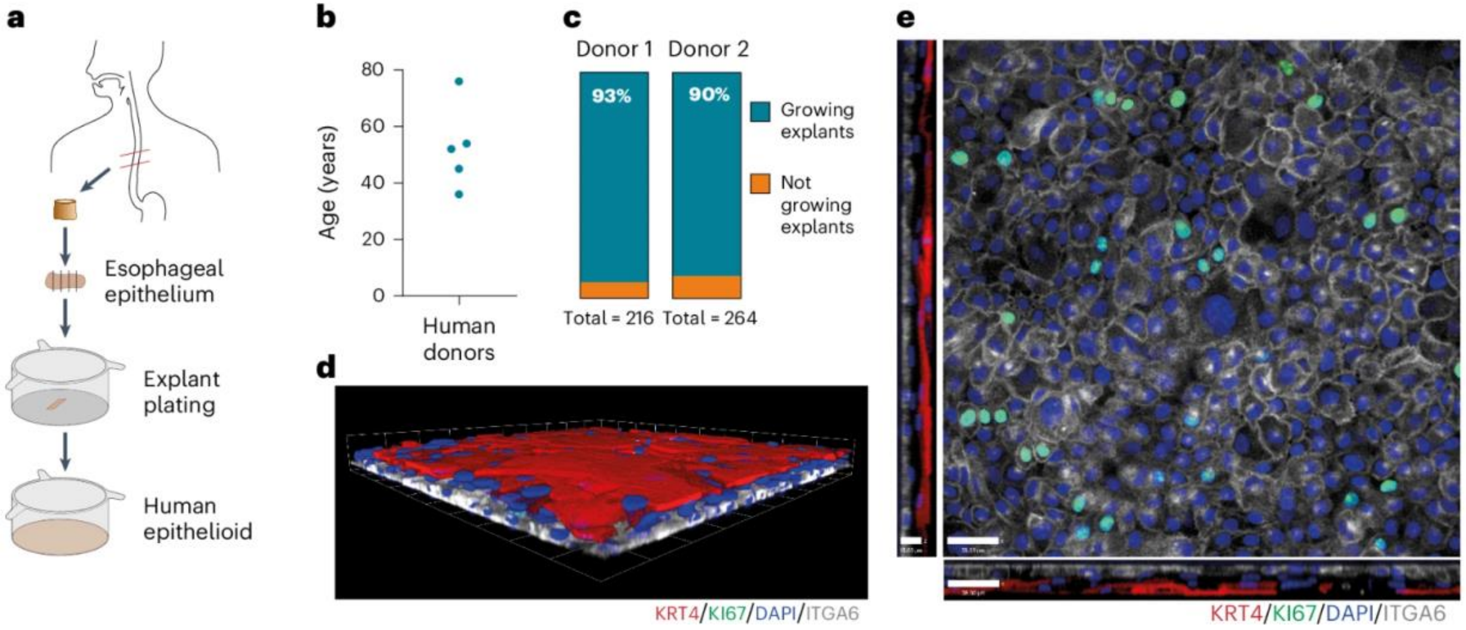


Whitmore, L. *et al. Sci. Rep.* **14** (2024)

Whitmore, L. *et al. Sci. Rep.* **11** (2021)

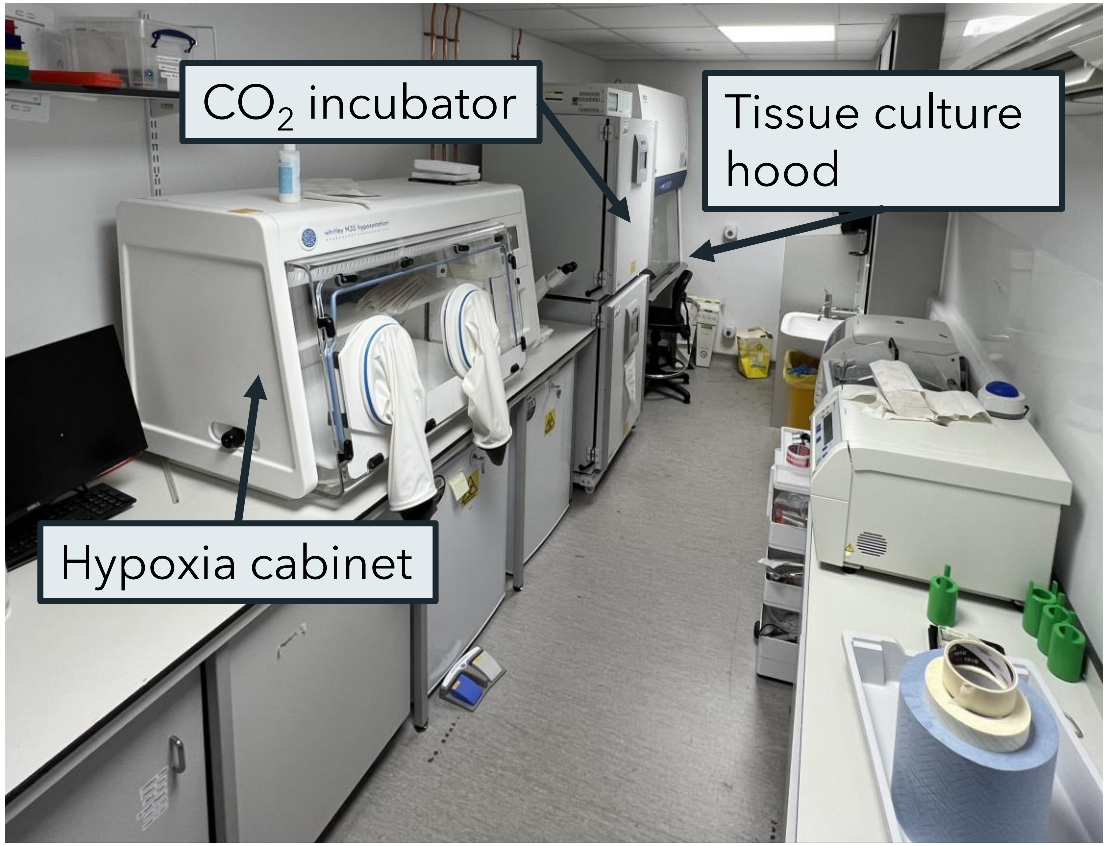
Moving Forward – Healthy Tissue and Tumour Response

- 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



Herms, A. *et al. Nature Genetics* **56**, 2158-2173 (2024)

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

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