Laser-Driven Very High Energy Electrons for Femtosecond-Scale Irradiation of In Vitro Cell Lines

H. Maguire[1], C. McAnespie[1], P. Chaudhary[2], S.W.Botchway[3], O. Finlay[3], E. Gerstmayr[1], G. Nersisyan[1], C. McDonnell[4], K. M. Prise[4], G. Schettino[2], G. Sarri[1]

[1] School of Mathematics and Physics, Queen's University Belfast , BT7 1NN, Belfast, UK
[2] Radiotherapy and Dosimetry Group, National Physical Laboratory, Middlesex, TW11 0LW, UK
[3] Central Laser Facility, Rutherford Appleton Laboratory, Harwell Campus, Didcot, OX11 0QX, Oxford, UK
[4] Patrick G. Johnston Centre for Cancer Research, Queen's University Belfast , BT7 1NN, Belfast, UK

QUEEN'S UNIVERSITY BELFAST — THE PATRICK G JOHNSTON CENTRE FOR CANCER RESEARCH — central laser facility — NPL

Introduction

Laser-driven plasma accelerators (LPAs) achieve accelerating gradients >10s of GV/m offering a compact and cost-effective alternative to conventional RF accelerators for VHEE generation.

Very high energy electrons (VHEEs) can:

- achieve excellent dose conformity and **deep penetration depths** [1]
- **enhance the sparing of critical structures** while providing similar/superior target coverage than photons
- show **reduced susceptibility to tissue inhomogeneities** [2].

*Proof-of-principle experiments, using laser-driven electron sources capable of **single-shot, Gy-scale irradiation** at unprecedented dose rates in the range of **10^{10} - 10^{13} Gy/s**, demonstrated:*

- ***significant increases in RBE following femtosecond VHEE irradiation [3]**, and*
- ***no significant differences in RBE following picosecond electron beam irradiation [4],***

when compared with conventional sources.

We present the characterisation of **two laser-driven, ultra-short electron sources** and the radiation response of **seven in vitro cell lines.**

Two normal (AGO1522D, RPE-1) and five cancerous cell lines (E2, MCF7, DU145, HeLa S3, H460) are presented.

Results were compared to a conventional x-ray source **(2.4Gy/min)** at the PGJCCR, QUB.

LWFA VHEE Beams

Laser parameters:

- E_L = 10 J
- τ_{FWHM} = 45 fs
- a_0 = 1.4 ± 0.1
- n_e ~ 3 x 10^{18} cm^3

e^- beam characteristics:

- VHEE beams (100-800 MeV)
- τ_b = ~150 fs
- $\bar{Q}$ = 1.8 ± 0.4 nC
- Low divergence (1.4 ± 0.4 mrad)
- >3 Gy per shot over cm^2 areas
- Dose rates >10^{13} Gy/s

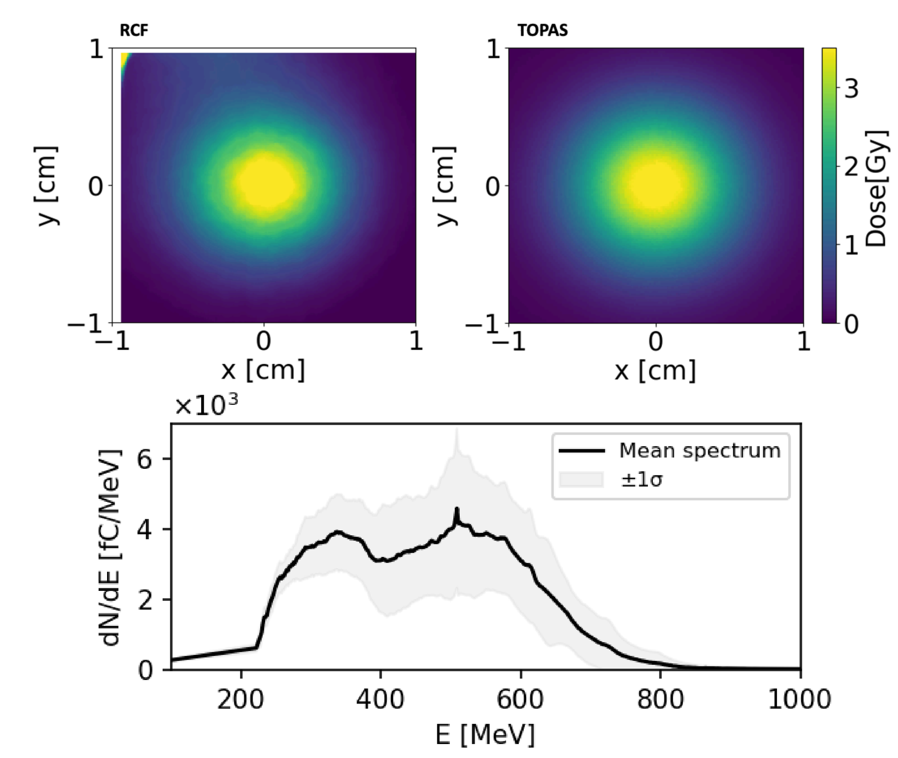


Figure 1. Dose profiles from RCF measurements and corresponding TOPAS simulations. Angularly integrated energy spectra of 10 consecutive shots.

Laser-Solid E Beams

Laser parameters:

- E_L = 8-10 J
- τ_{FWHM} = 0.8 ps
- a_0 = 4.1 ± 0.2
- 25μm Au

e^- beam characteristics:

- 1-8MeV (T = 1.6 MeV)
- τ_b = ~10-20ps
- N_e = ~2.9 x10^{11}
- Large divergence (0.56 rad)
- >8 Gy per shot over cm^2 areas
- Dose rates >10^{10} Gy/s

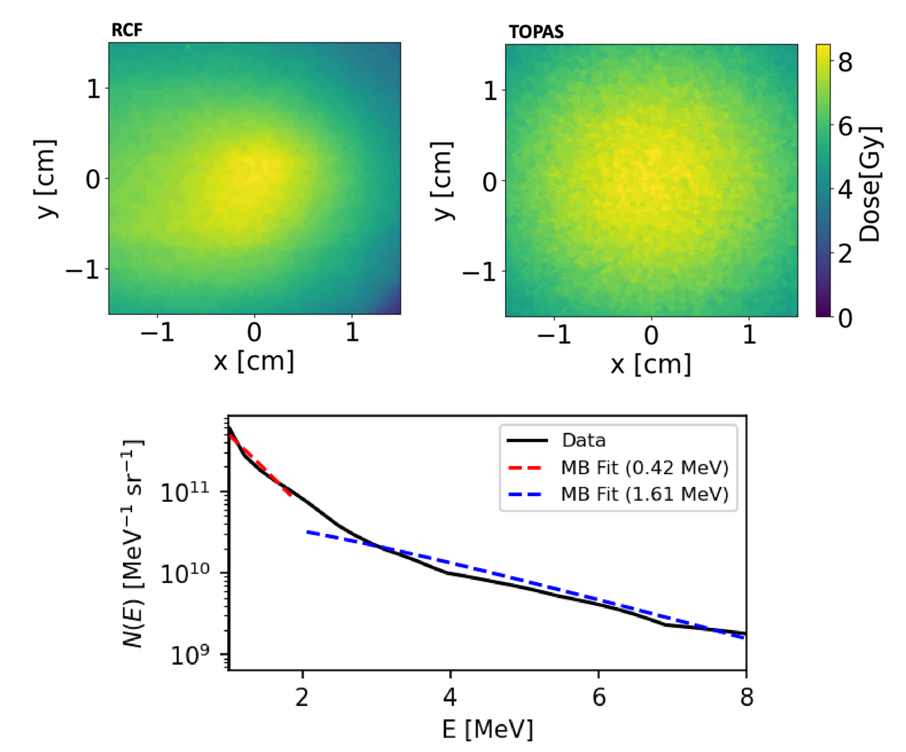


Figure 2. Dose profiles from RCF measurements and corresponding TOPAS simulations. Angularly integrated energy spectra with Maxwell-Boltzmann fits.

Clonogenic Assays

Clonogenic assays measured the cell **survival fraction** following irradiation, with results modelled using the linear-quadratic (LQ) equation:

$$SF = \exp - (\alpha D + \beta D^2)$$

Relative biological effectiveness (RBE) at 50% survival was calculated relative to a conventional x-ray (CONV) source:

$$\text{RBE}(50) = \frac{D_{50}\ of\ CONV}{D_{50}\ of\ Electron\ Source}$$

LQ model parameters and RBE calculations were obtained using **MCMC sampling** with emcee. Statistical analysis was performed using Wilcoxon Rank-Sum test;

ns, not significant, *p < 0.05, **p < 0.01.

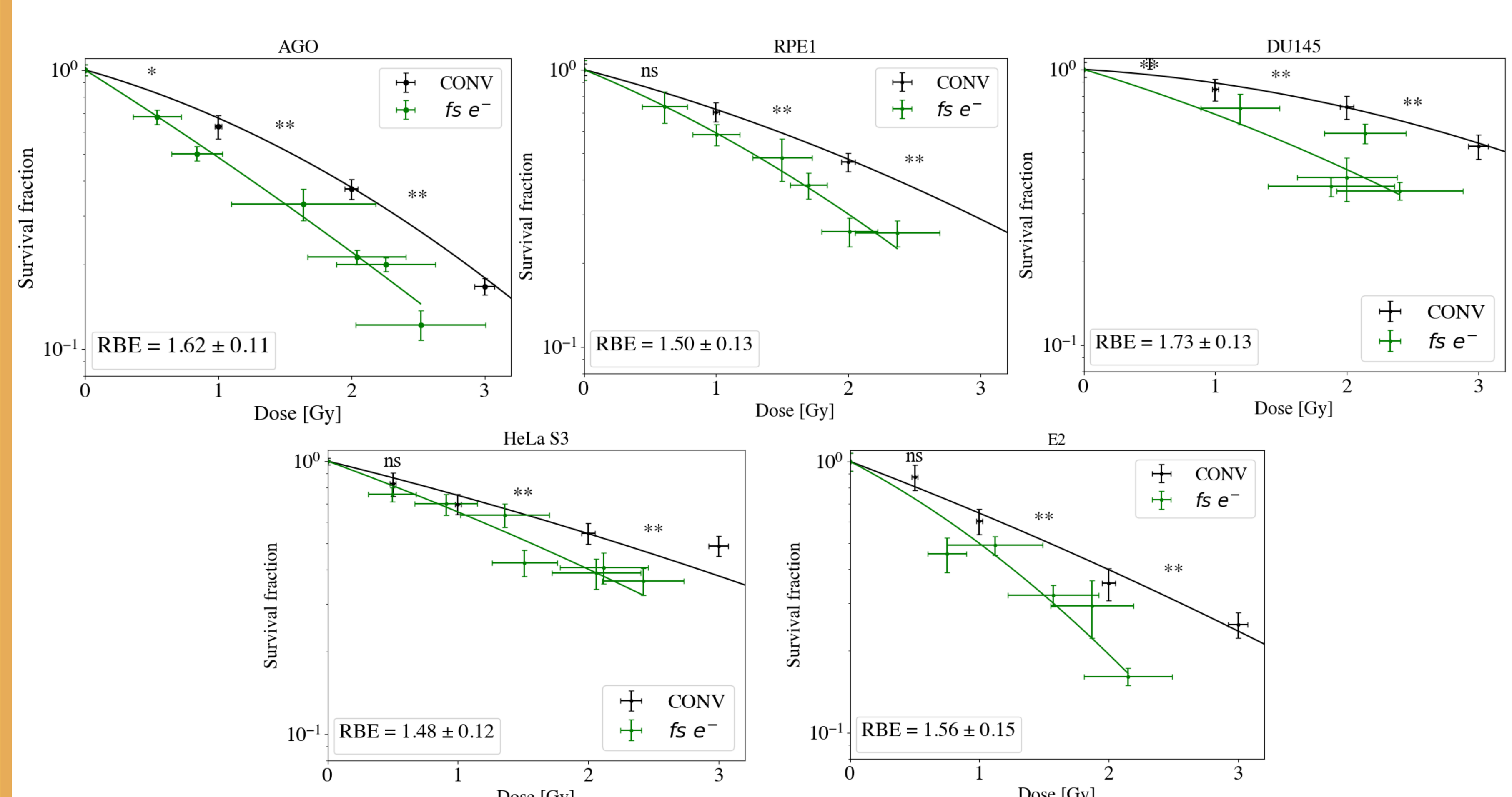


Figure 3. Clonogenic assays. Survival curves fitted with the LQ model are shown for AGO1522D, RPE-1, DU145, HeLa S3 and E2.

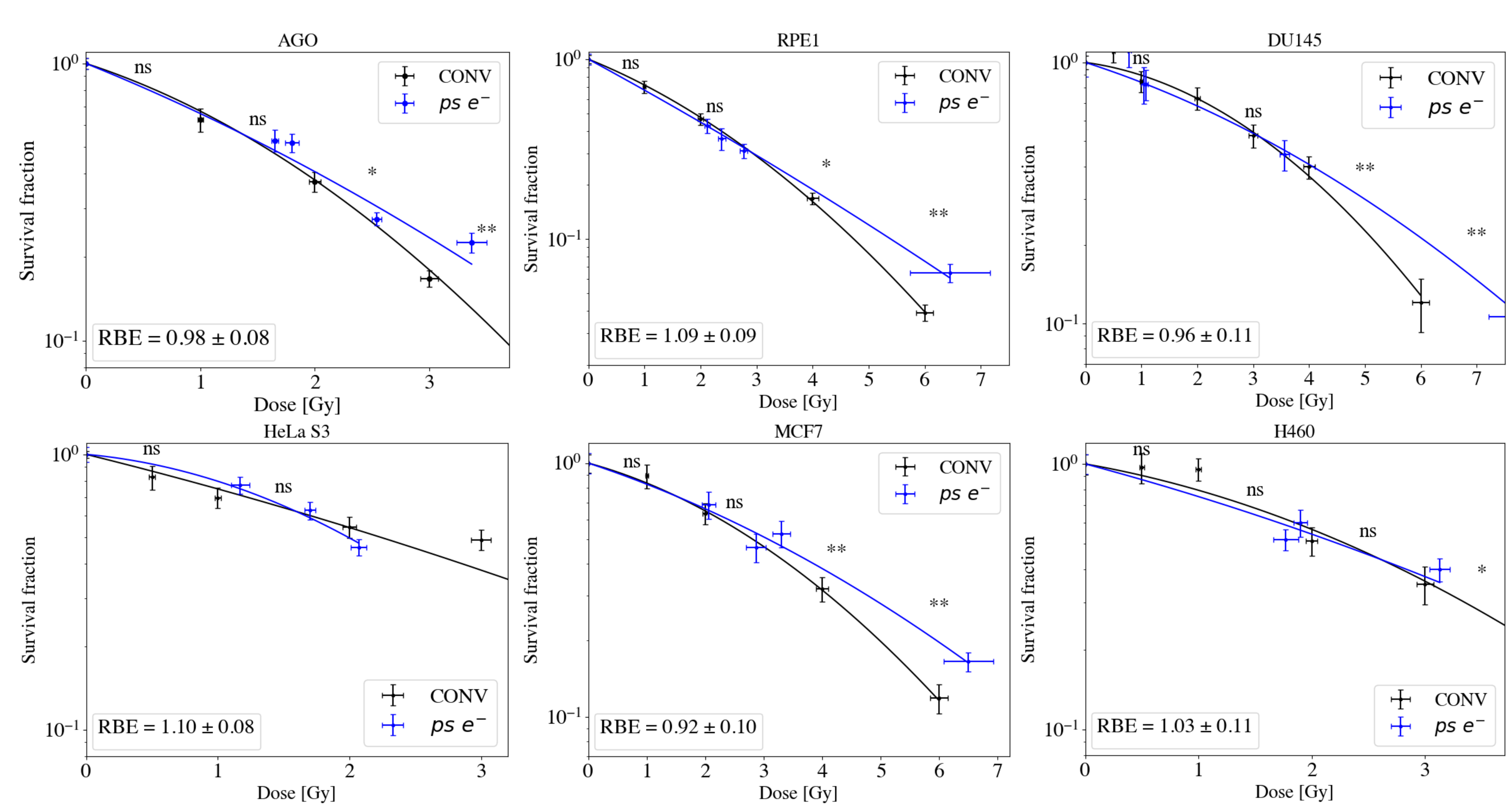


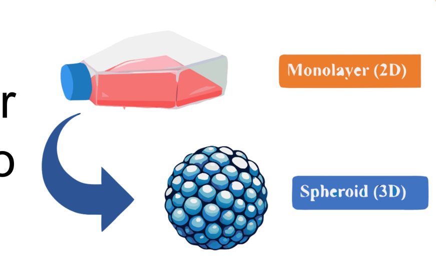
Figure 4. Clonogenic assays. Survival curves fitted with the LQ model are shown for AGO1522D, RPE-1, DU145, HeLa S3, MCF7, H460.

Conclusions

- A **significant increase in RBE** was observed for all cell lines following irradiation with fs VHEE beams
- **No difference** in RBE was observed following irradiation with ps electron beams at low dose
  - At higher doses, a **FLASH-like sparing effect** was shown for 4/6 cell lines, indicated as significant increases in SF
  - First demonstration of FLASH-like effects at dose-rates >10^{10} Gy/s
- Dose profiles from RCFs and TOPAS (Geant4) simulations demonstrated good transverse and longitudinal dose uniformity across the cell regions

Next Steps

- **3D Spheroid Models**
  - Spheroids mimic the 3D structure and cellular environment of tumors advancing towards future in vivo applications



- **Dosimetry** of ultra-short electron beams is not trivial:
  - Plane-parallel ionisation chambers experience charge collection inefficiency at high dose-rates [5]
  - RCFs are suitable for high dose-rate VHEE dosimetry but fail to provide dose measurements in real-time [6]

References

[1] A. Hart et al. (2024). doi: 10.1109/JSEN.2024.3353190
[2] B. Palma et al. (2015). doi: 10.1118/1.4925419
[3] C. A. McAnespie et al. (2024) doi: 10.1088/1361-6560/adec36
[4] C. A. McAnespie et al. (2025) doi: 10.1103/PhysRevE.110.035204
[5] M. McManus et al. (2020). doi: 10.1038/s41598-020-65819-y
[6] A. Subiel et al. (2017). doi: 10.1016/j.ejmp.2017.04.029

***ACKNOWLEDGEMENT* - This poster presentation has received support from the European Union's Horizon 2020 Research and Innovation programme under Grant Agreement No 101004730.**

QUEEN'S UNIVERSITY BELFAST — SCHOOL OF MATHEMATICS AND PHYSICS

Email: hmaguire11@qub.ac.uk

EAAC2025 — EUROPEAN NETWORK FOR NOVEL ACCELERATORS EuroNNAc — iFAST