IMPERIAL

LhARA

# Global trends in laser-driven radiobiology

An evaluation of field trends, beam capability and requirements for radiobiology

Josie McGarrigle
17 November 2026

# Data collection & analysis

# Analysis aims

| | | |
|---|---|---|
| 1 | **Collect data** | Compile database of all laser driven radiobiology experiments |
| 2 | **Find trends** | Explore how beam and sample parameters might be correlated |
| 3 | **Evaluate biology** | Compile survival and foci data to look for global trends |
| 4 | **PoPLaR** | Explore how PoPLaR fits with the current global experiments |
| 5 | **LhARA** | Explore gaps in the field, how LhARA can fill these gaps & what would requirements be |

# Data selection

Summary of data selection using PICO analysis and PRISMA flow

**32**
Candidate publications

**10**
Excluded after full-text review

**22**
Included in the analysis

**21 PROTON / 1 CARBON**
Nearly all included studies are proton-only

**4 IN VIVO**
3 zebrafish embryo studies + 1 mouse-ear study

# Search criteria

## What information was stored?

### Information was stored about:

**Laser–target**

Short, intense proton/ion bunch

›

**Transport**

Focusing + energy spread

›

**Beam shaping**

Scatterers, apertures

›

**Diagnostics**

Energy, dose and timing

›

**Biology**

Survival, γH2AX.

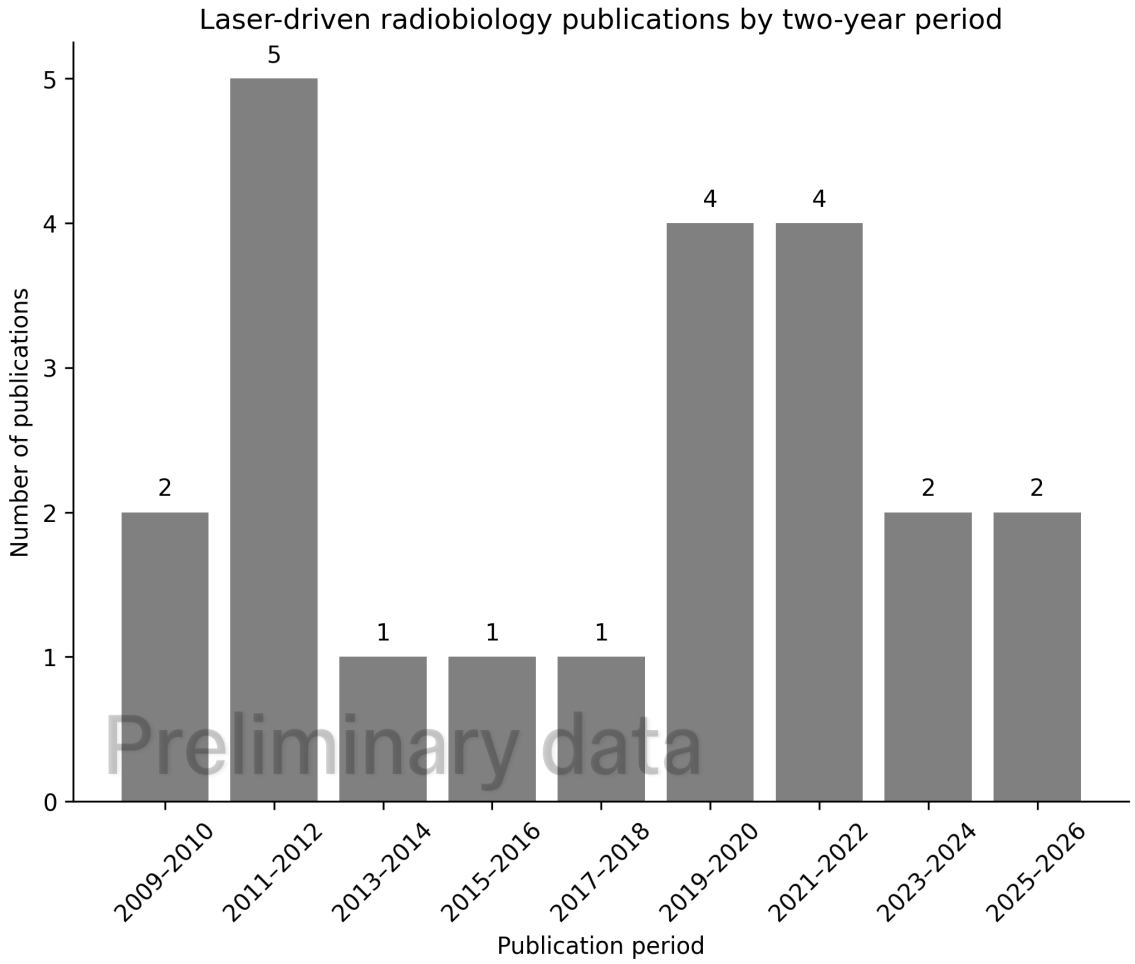
### Limits:

- Not all papers stored individual energies, doses etc. Some gave ranges- max and mins were stored in this case.
- Not all parameters had results from multiple papers- these were excluded from analysis
- Repeated use of same beamlines may produce repeated parameter values across different papers

# Field-wide trends

# Publication activity

## Publication frequency from 2019-present in 2 year increments

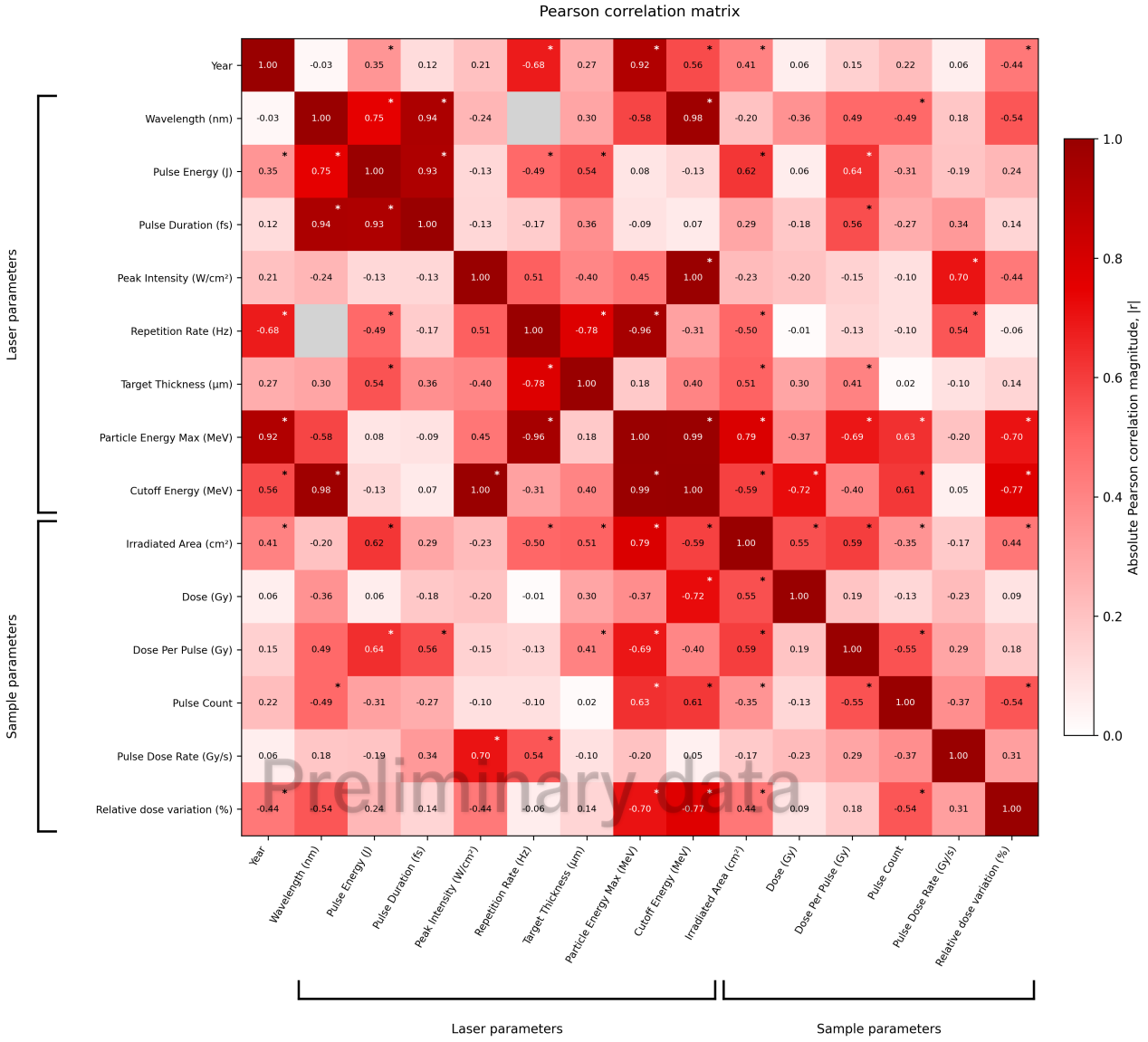



### Reading the trend

- Peak of 5 papers in 2011–12
- 8 across 2019–22
- 4 across 2023–25
- 0 papers in 2026 (at time of collection)

# Parameter correlation analysis

## Pearson correlation scores




## Top relations:

### Beam parameters with beam parameters

**R = +0.99**

Peak laser intensity vs cutoff energy (n=13)

### Beam parameters with sample parameters

**R = −0.77**

Cutoff energy vs relative dose variation (n=19)

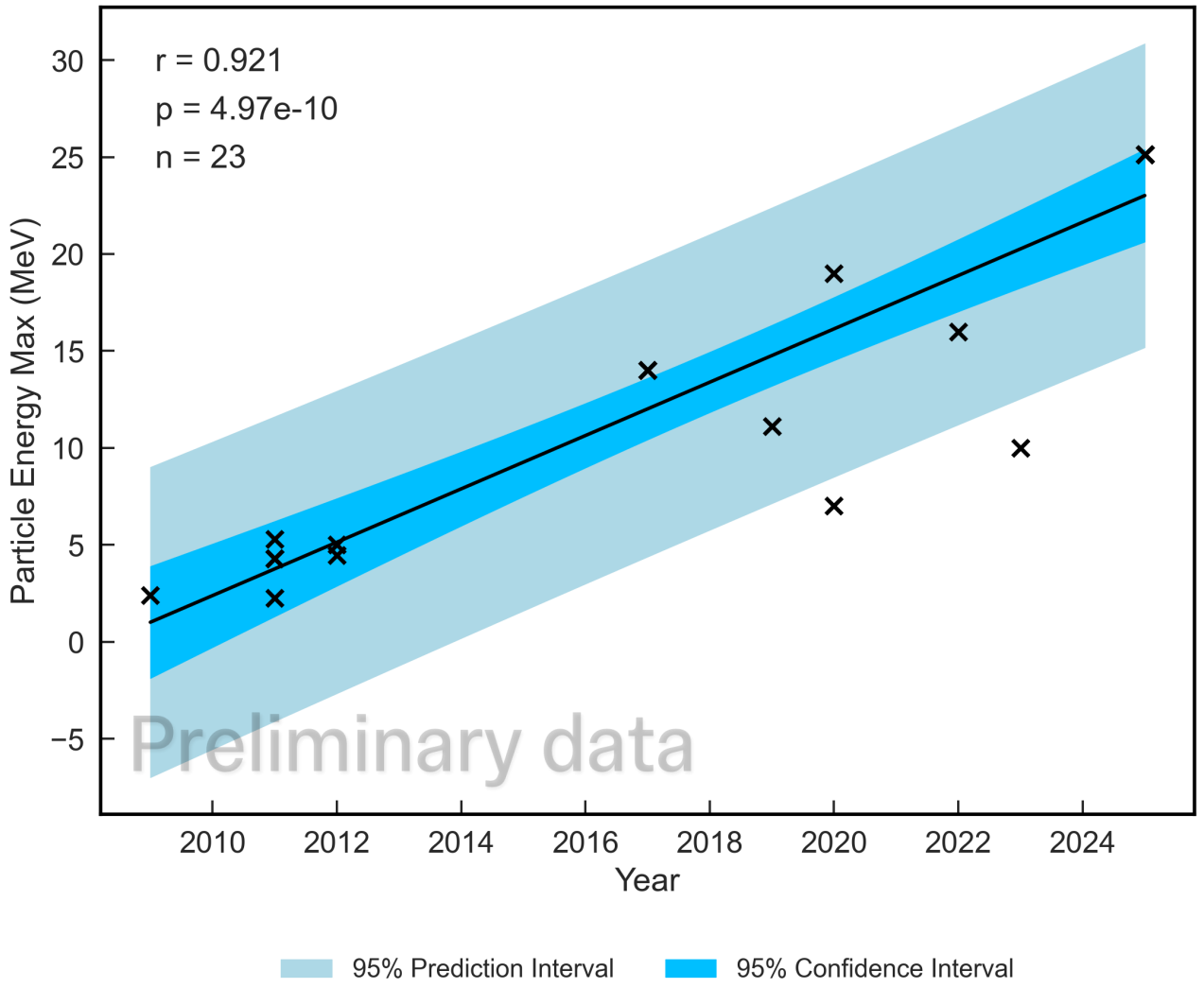
### Correlations with year

**R = +0.92**

Year vs maximum particle energy (n=23)

# Maximum particle energy has increased over time

Maximum energy of particles at the sample vs year of publication




**R = 0.921**

Maximum energy vs publication year

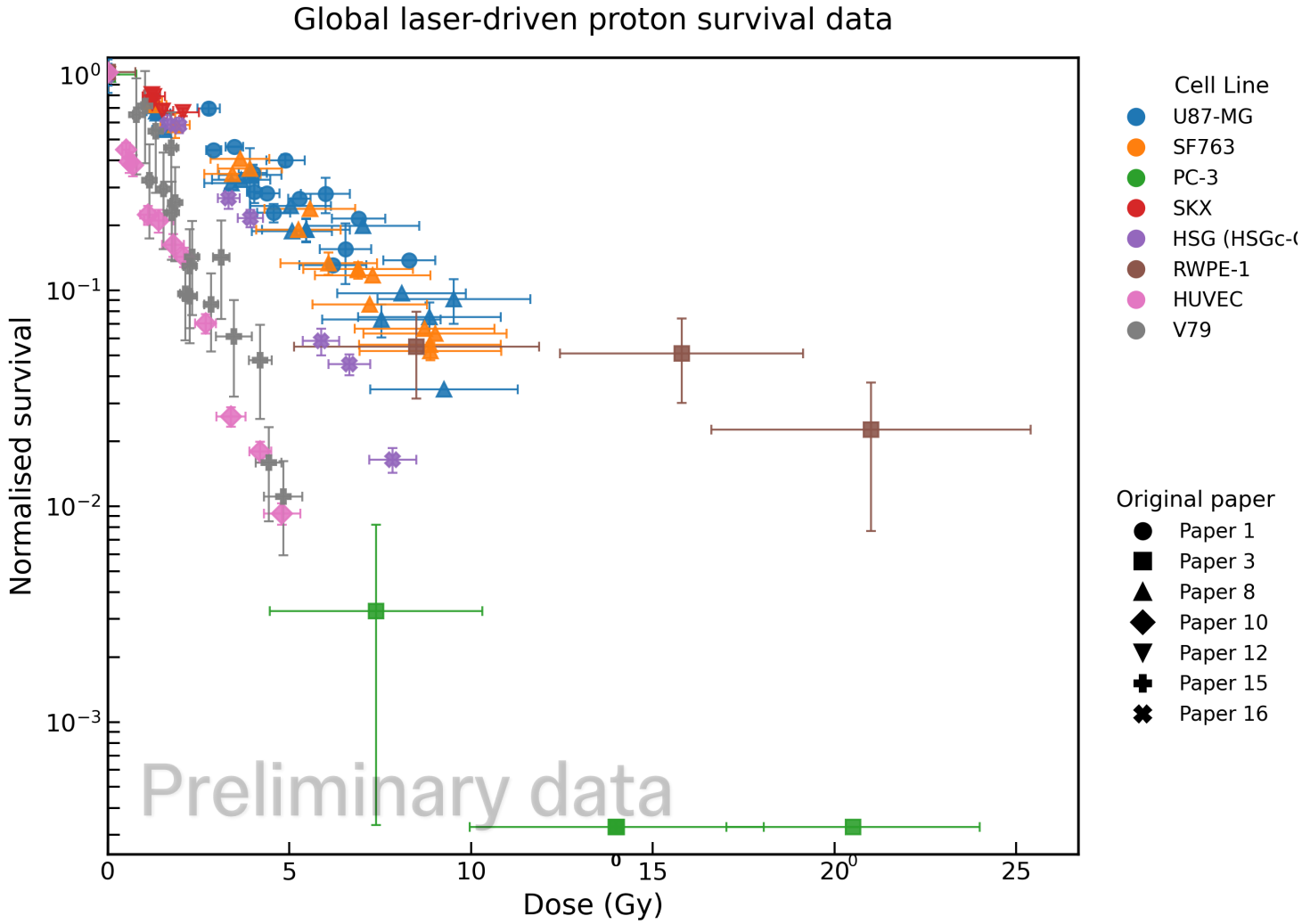
**N = 23**

Conditions used in reported correlation

# Biological data

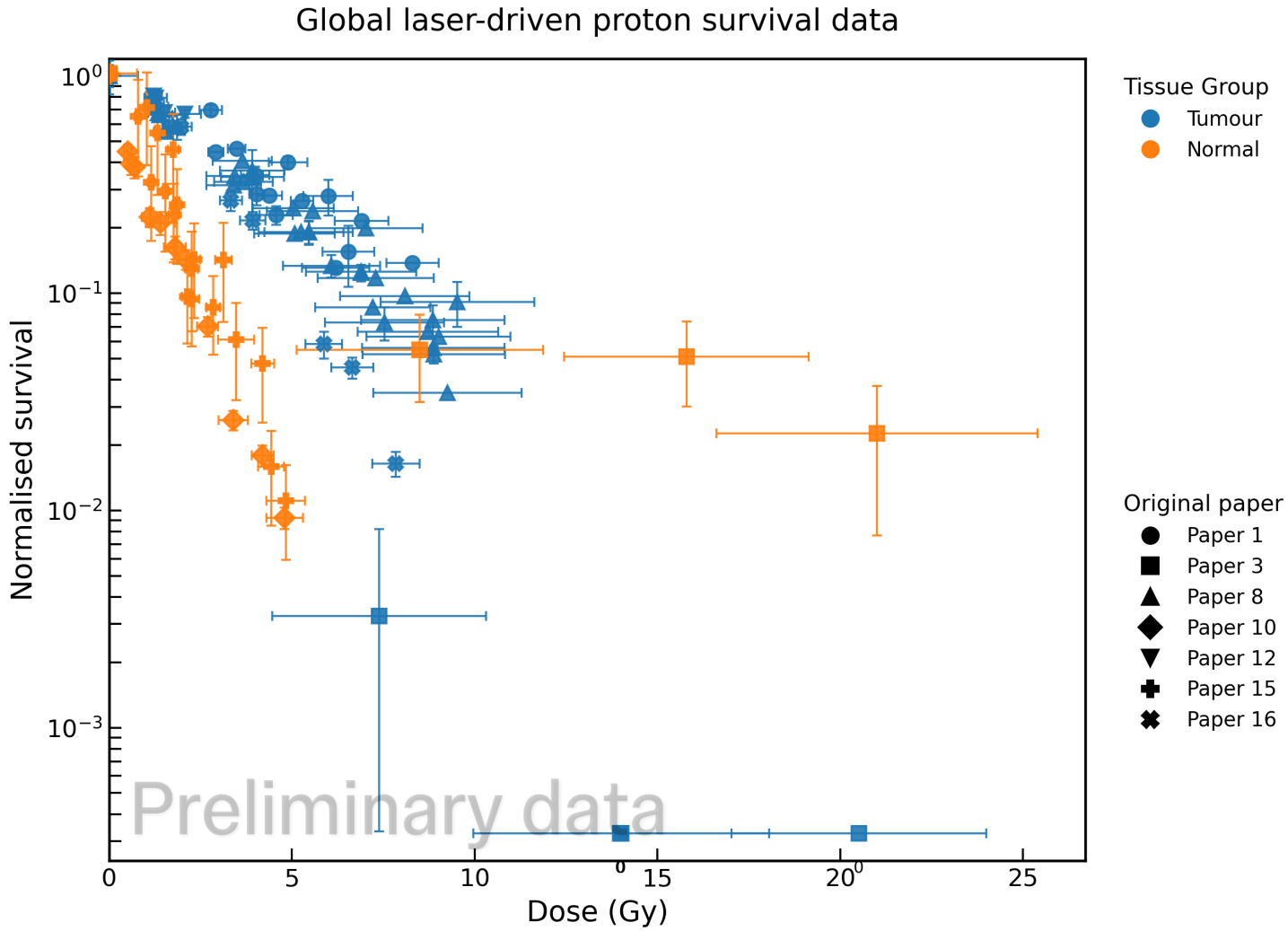
# Clonogenic survival: separated by cell line & paper

Survival curves colour coded by cell line, marker shape defines paper.



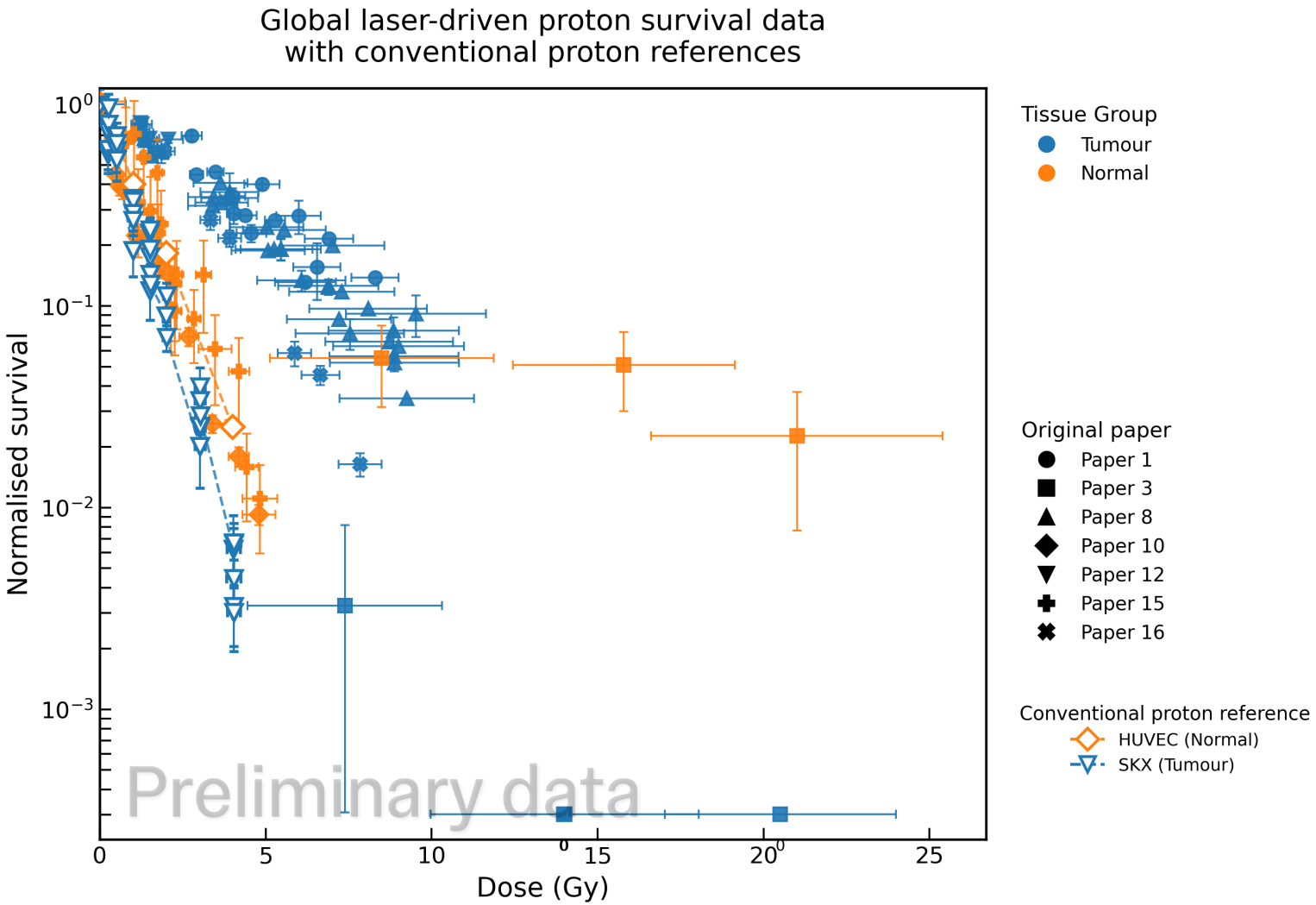
# Clonogenic survival: separated by tissue type & paper

Survival curves colour coded by tissue type, marker shape defines paper.



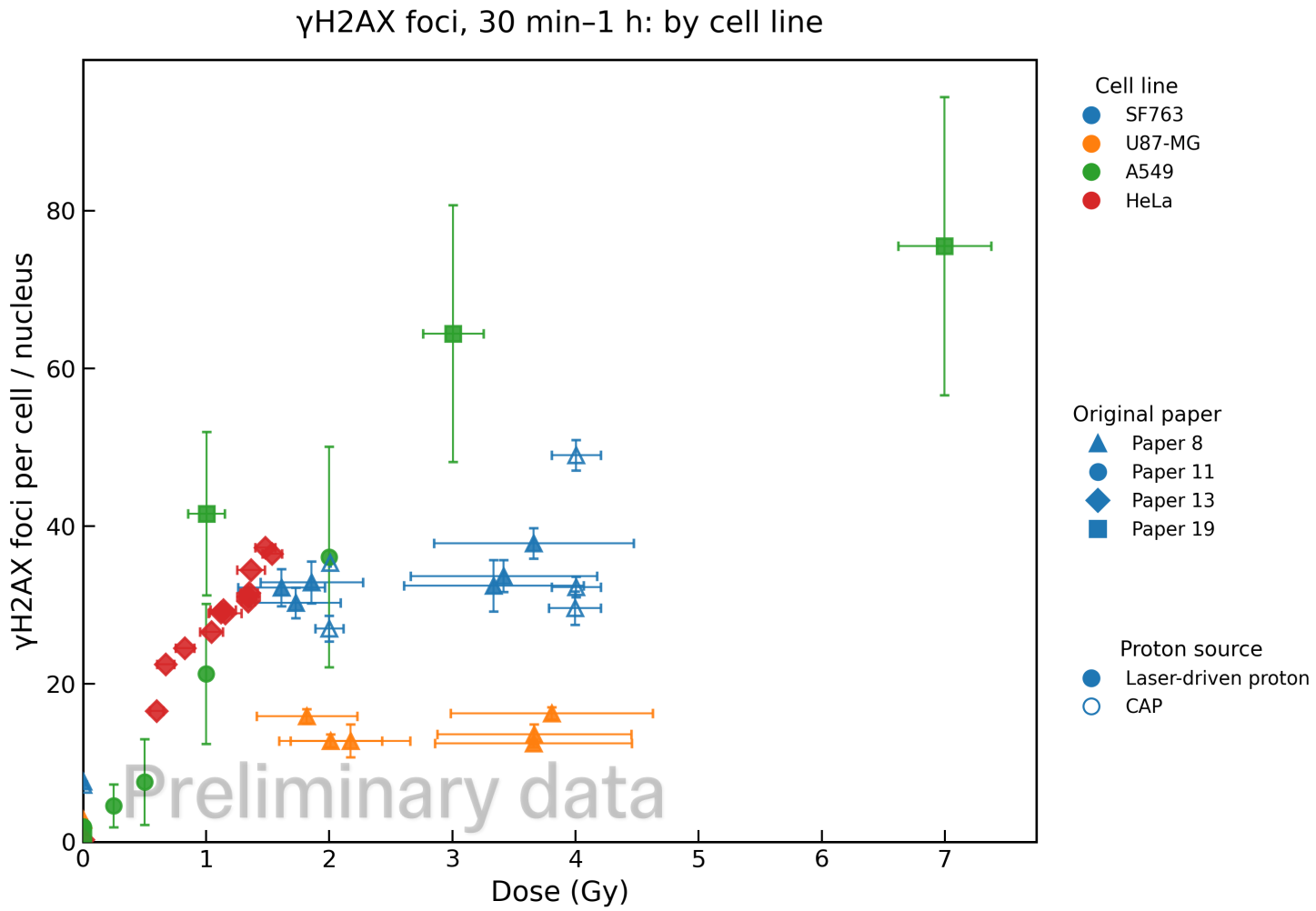
# Clonogenic survival: comparing to reference radiation

Survival curves colour coded by tissue type, marker shape defines paper, hollow markers represent CAP.



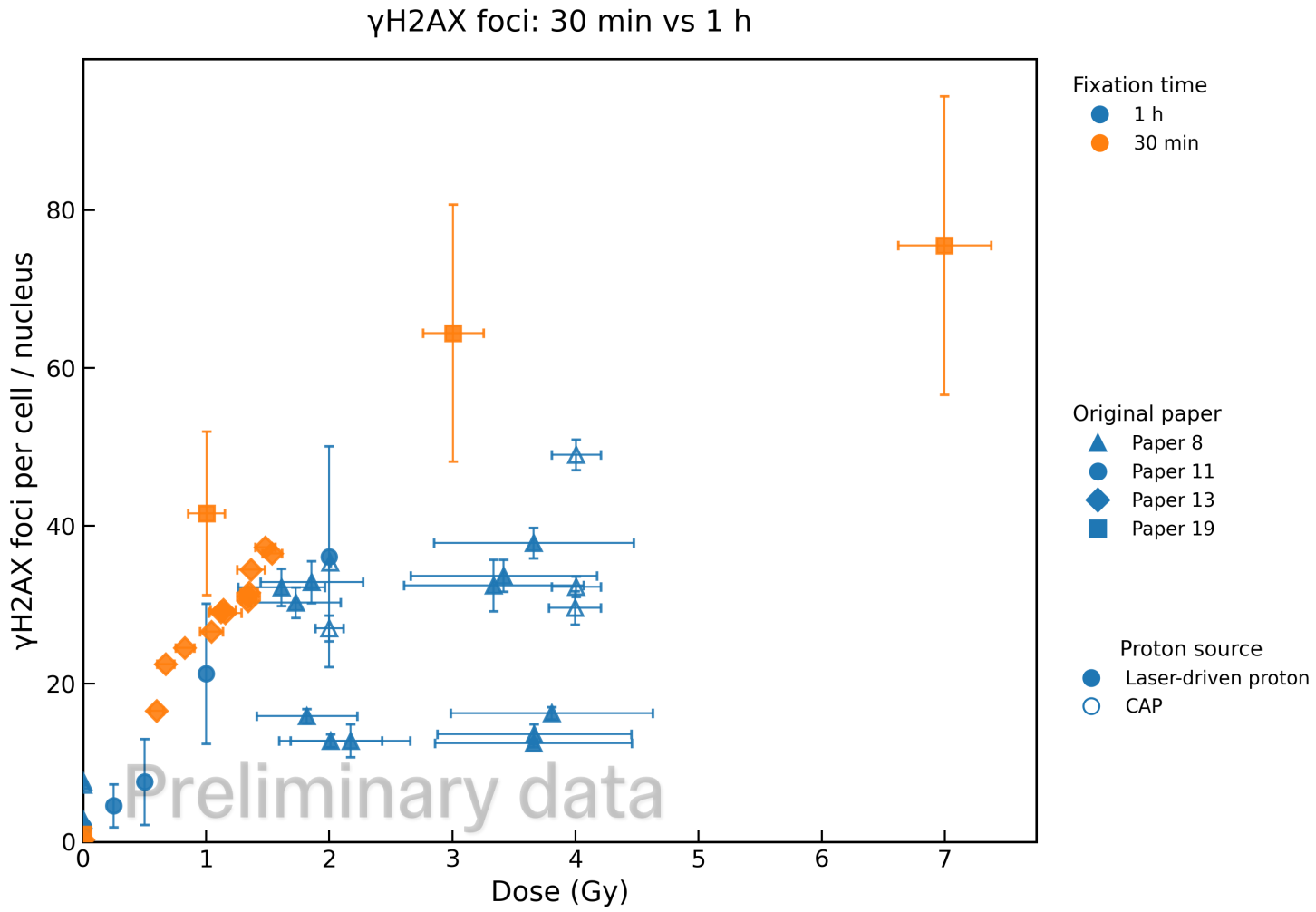
# Early γH2AX signals

γH2AX foci per cell over dose, colour coded by cell line, marker shape defines paper, hollow markers represent CAP.



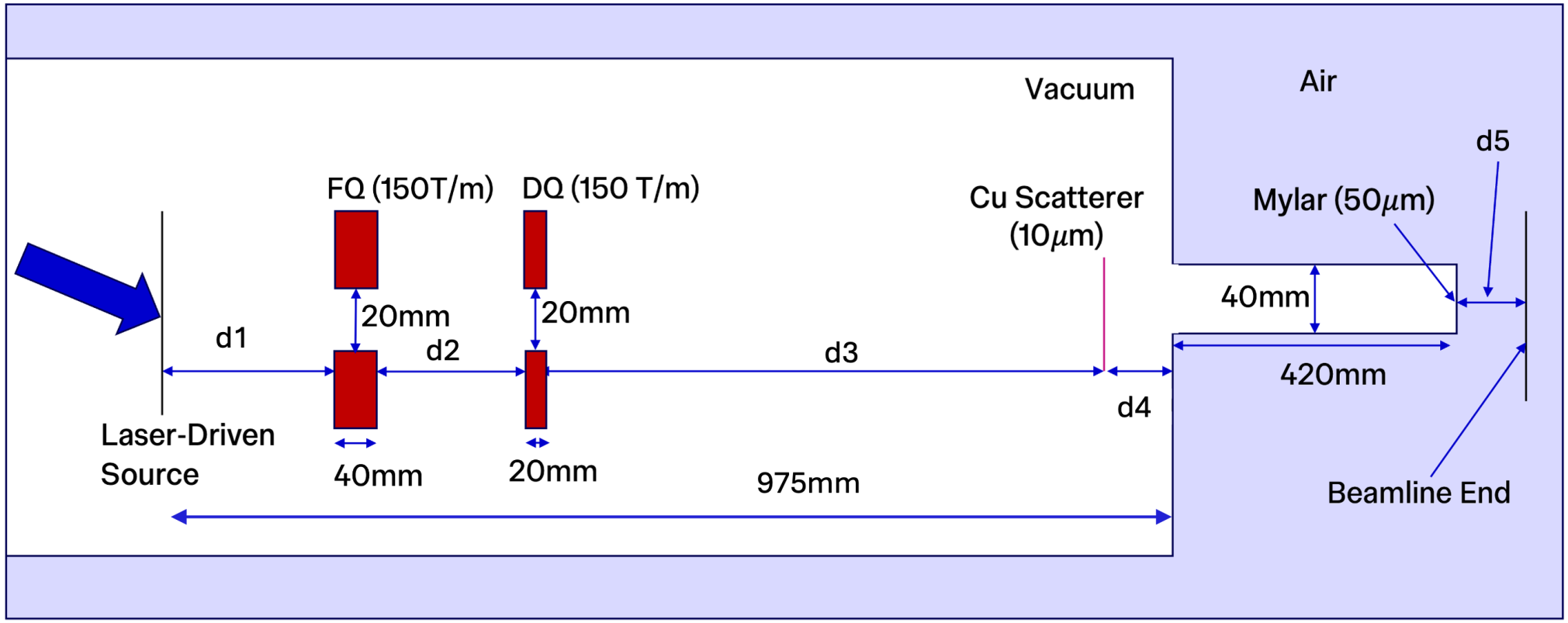
# Early γH2AX signals

γH2AX foci per cell over dose, colour coded by time point, marker shape defines paper , hollow markers represent CAP.



# PoPLaR

# PoPLaR




C. Dyson Phase 2 Technical Note

**SOURCE**

SCAPA laser-driven protons

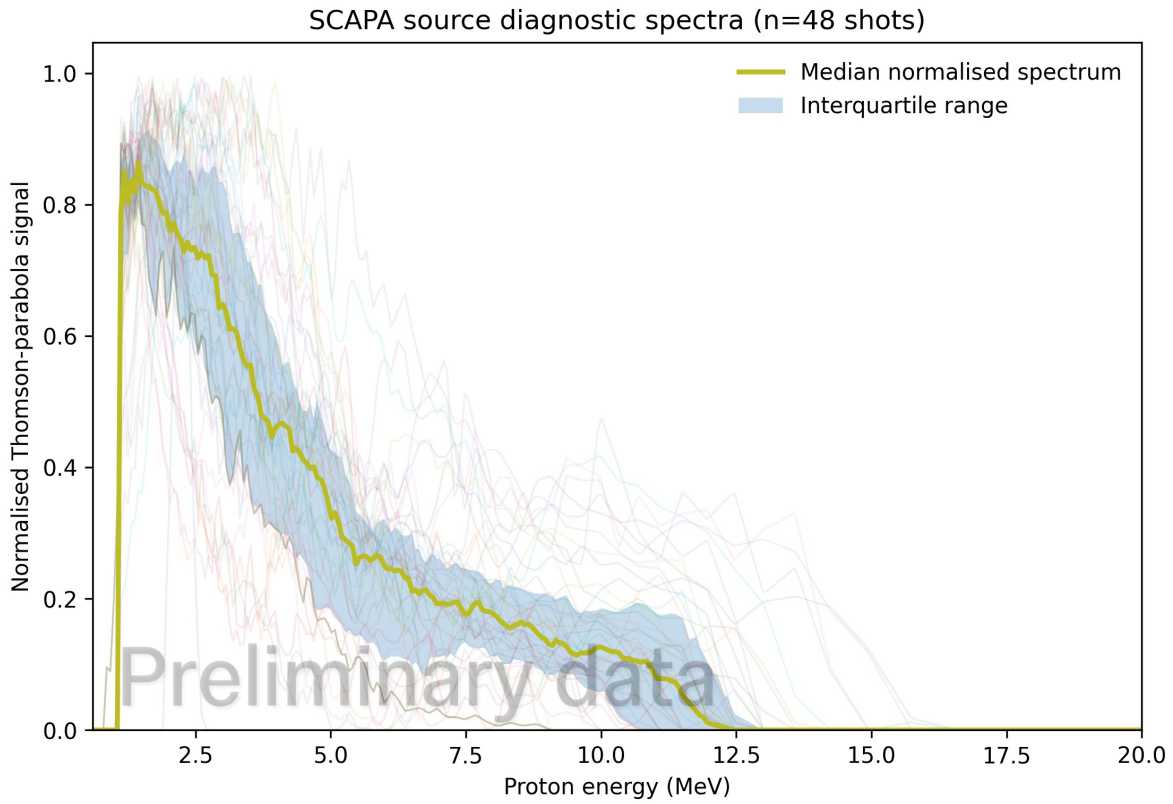
**TRANSPORT**

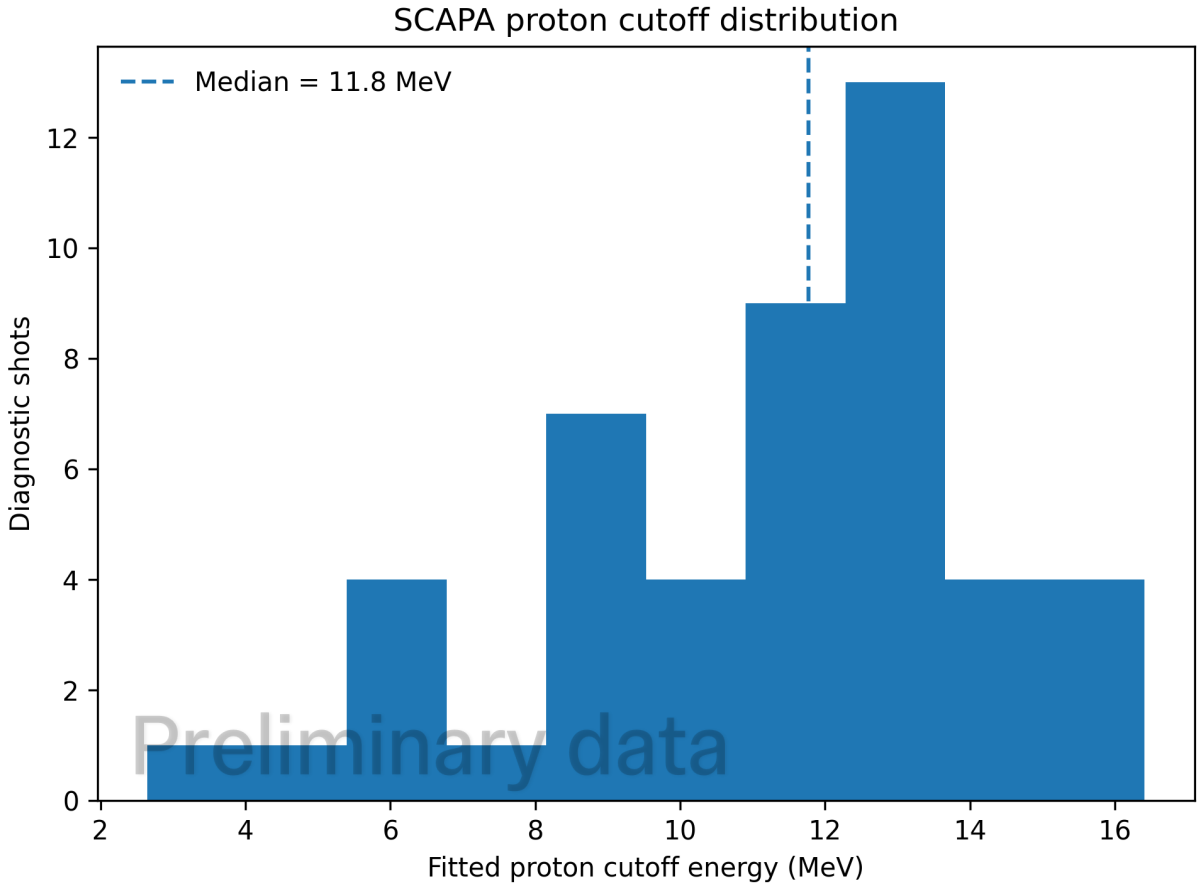
150 T/m PMQ doublet, Cu scatterer

**SAMPLE**

Cell carousel

# PoPLaR energy spectrum




## AT SOURCE

Cutoff ~12–16 MeV, centered near 14 MeV

## AT CELLS

Proton median 11.8 MeV

# Comparing PoPLaR to the global data

| Sample type | Dose (Gy) | Dose per shot (Gy) | Max spatial variation (%) | Shot-to-shot dose variation (%) |
|---|---|---|---|---|
| **Cell** | 0.433–37.1 (n=33) | 0.0022–3.35 (n=31) | 9 (n=10) | 9.37–40 (n=28) |
| **Zebrafish embryo** | 10.37 (n=1) | 10.37 (n=1) | 10 (n=1) | 13.69 (n=1) |
| **Mouse ear** | 4 (n=1) | 0.66 (n=1) | 5 (n=1) | 10 (n=1) |
| | | | | |
| **PoPLaR** | ~2.28–7.97 | ~0.57 | ~13.93 | ~23.84–37.72 |

Preliminary data

PoPLaR currently meets the general dose requirements in-vitro remit and in-vivo mouse ear;
Limitations-- beam reproducibility, dose variability and live sample dosimetry.

# PoPLaR spatial uniformity

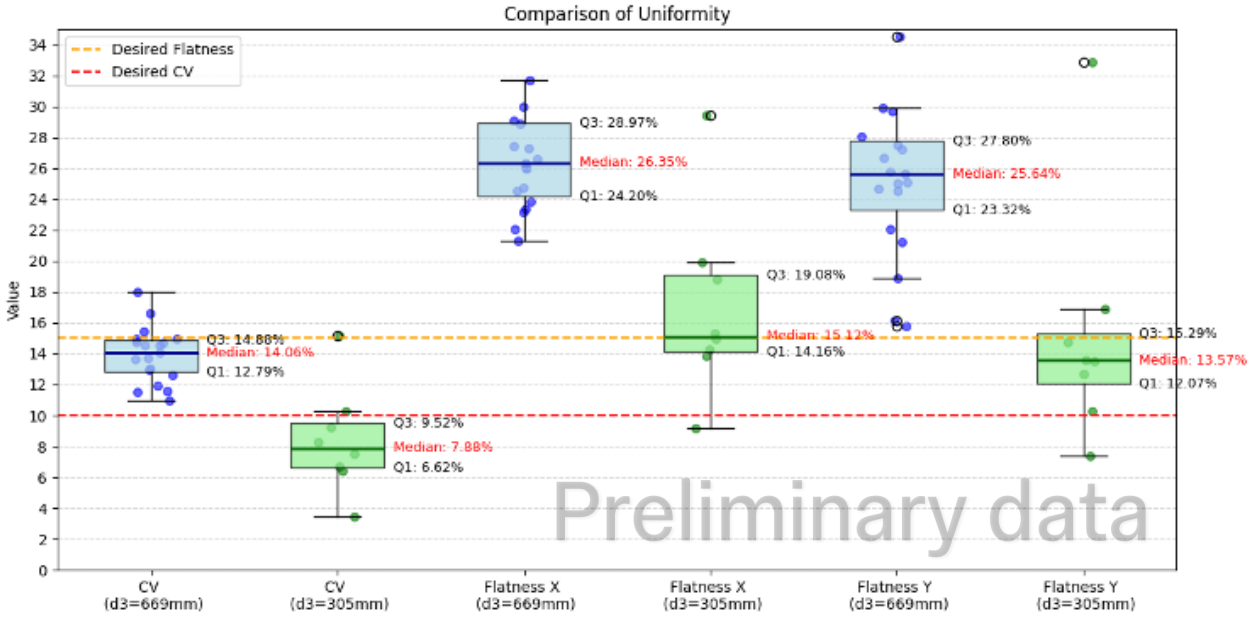
**CV = 13.93%**
**Original scatterer position (669 mm)**

→

**CV = 8.38%**
**Scatterer moved to 305 mm**

## Spatial non-uniformity can be improved

- Moving the 10 μm Cu scatterer from 669 mm to 305 mm downstream of PMQ2 reduced CV from 13.93% to 8.38%
- Improved uniformity came with a reduction in mean dose per shot: 0.57 Gy → 0.27 Gy (more shots required)
- CV of ~8% places improved PoPLaR within the range achieved by several published laser-driven radiobiology systems
- Dose per shot being 0.27 Gy/shot still sits within the existing field range (0.0022–3.35 Gy/shot)




*Preliminary data. C. Dyson Phase 2 Technical Note.*

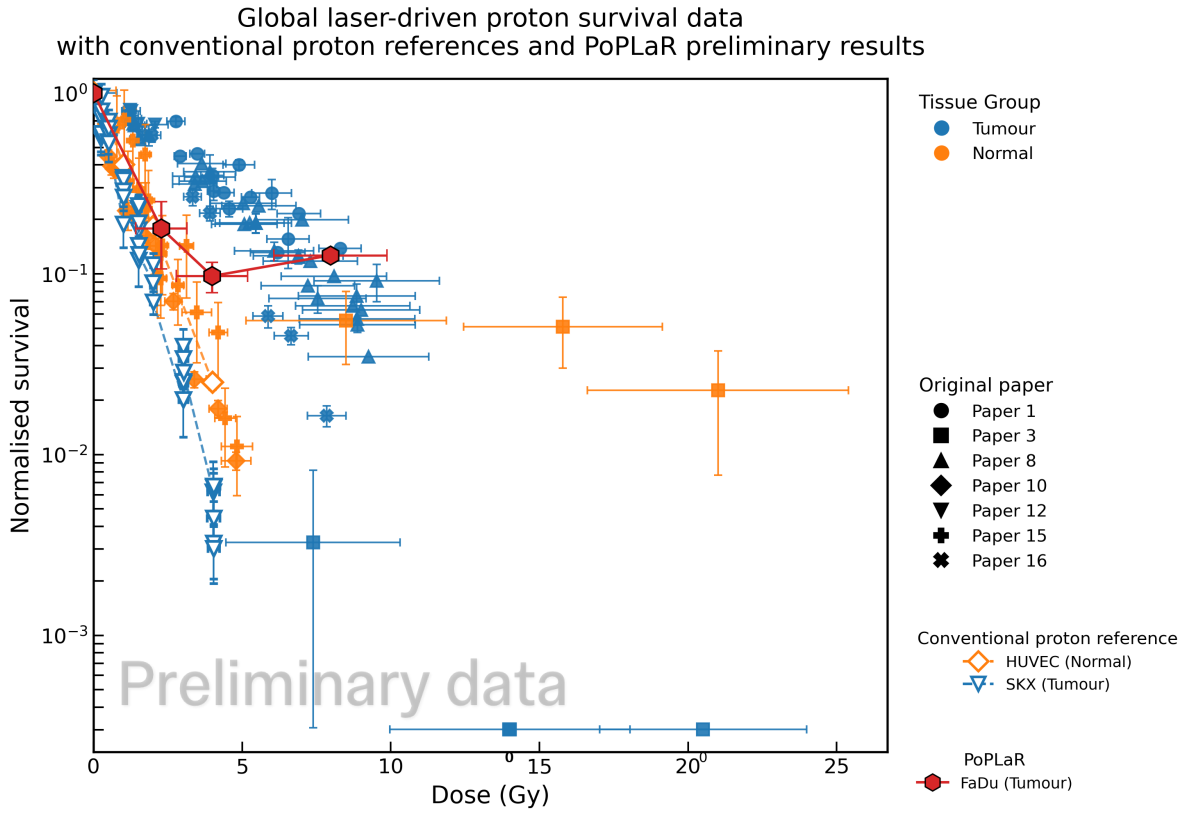
# PoPLaR: Experiment 1

## FaDu clonogenic survival: preliminary results

| Shots | Dose (Gy) | Surviving Fraction (SF) | n (dishes) |
|---|---|---|---|
| 4 | 2.28 ± 0.86 | 0.178 ± 0.072 | 8 |
| 7 | 3.99 ± 1.20 | 0.097 ± 0.019 | 6 |
| 14 | 7.97 ± 1.90 | 0.127 | 1 |

Preliminary data

- Results are of a similar order of magnitude to previously reported global laser-driven proton survival data
- SF at 2.28 and 3.99 Gy align more closely with published normal tissue trend; 7.97 Gy shows greater agreement with tumour trend
- Limitations:
  - 3 experimental repeats not achieved at all dose points
  - Doses are approximate & not recorded for the cell dish itself



# PoPLaR: Experiment 2

## Shot-to-shot reproducibility: preliminary results

- Three independent 4-shot (~2.28 ± 0.86 Gy) irradiations of FaDu cells

**12% shot-to-shot survival repeatability**

| Repeat | Surviving Fraction (SF) | n (dishes) |
|---|---|---|
| 1 | 0.111 | 4 |
| 2 | 0.116 | 2 |
| 3 | 0.138 | 4 |
| **Mean ± SD** | **0.122 ± 0.014** | **3 repeats** |

Preliminary data

- Shot-to-shot fluctuations did NOT produce large differences in clonogenic survival at this dose level
- **However**: dose was recorded only on RCF irradiated after cell dishes so the dose delivered to each dish remains uncertain
- Agreement between repeats could simply reflect low shot-to-shot variation during **these** specific three irradiations
- On-shot per-dish dosimetry is required!

# New modalities

# New modalities

Time and spatial beam modulations

## FLASH- Ultra high dose rate irradiation

**CONVENTIONAL FLASH CRITERION**

Mean dose rate generally >40 Gy/s

## MBRT- Minibeam Radiation Therapy

**MINIBEAM SCALE**

Narrow beam segments ~1 mm or smaller

# FLASH literature

## Reported successful proton FLASH conditions

| Environment | Biological model | Particle energy (MeV) | Total dose (Gy) | Mean dose rate (Gy/s) |
|---|---|---|---|---|
| **In vitro** | Cells | 4.5–20 | 0.5–20 | 10–1000 |
| **In vivo** | Zebrafish | 68–228 | 9–43 | 100–9000 |
| **In vivo** | Mouse | 20–250 | 10–60 | 57–930 |
| **In vivo** | Rat | 226–250 | 5–25 | 60–257 |

Preliminary data

PoPLaR overlaps the cell energy and dose; advanced in-vivo FLASH requires higher energy for in-vivo and controlled delivery.

# MBRT literature

## Reported successful proton minibeam conditions

| Environment | Biological model | Particle energy (MeV) | Total dose (Gy) |
|---|---|---|---|
| **In vitro** | Cells | 100 | 2–20 |
| **In vivo** | Mouse | 100 | 20–30 |
| **In vivo** | Rat | 100 | 10–30 |

Preliminary data

PoPLaR dose range adequate for in-vitro and some of the mouse studies, lower energy.

# PoPLaR: assessment and development priorities

1

## Shot-resolved, per-dish dosimetry

Implement on-shot dose measurement for every dish simultaneously using scintillating fibres and Monte Carlo calibration. Real-time dose feedback removes the main current limitation on data quality.

2

## Beam reproducibility & shot-to-shot variability

Reduce shot-to-shot dose variation.

3

## Spatial uniformity at higher dose

Maintain improved 8% CV at higher cumulative doses.

Addressing dosimetry and variability will unlock systematic, repeated biological studies and direct integration into the broader LhARA programme.

# Conclusions

| | | |
|---|---|---|
| 1 | **Field progression** | Reported maximum energy has grown, but the literature remains small, limited particle type and in-vivo experiments. |
| 2 | **Biology** | Survival and DNA damage have been successfully explored at 6 and 4 different beamlines, respectively. |
| 3 | **PoPLaR fit** | Current SCAPA-to-cell energy and total dose lie within established in-vitro ranges. Improved dose and variability would allow PoPLaR to experiment with complex biological endpoints. |
| 4 | **Development priority** | Shot-resolved dosimetry, reproducibility and spatial control. |

IMPERIAL

LhARA

# Thank you