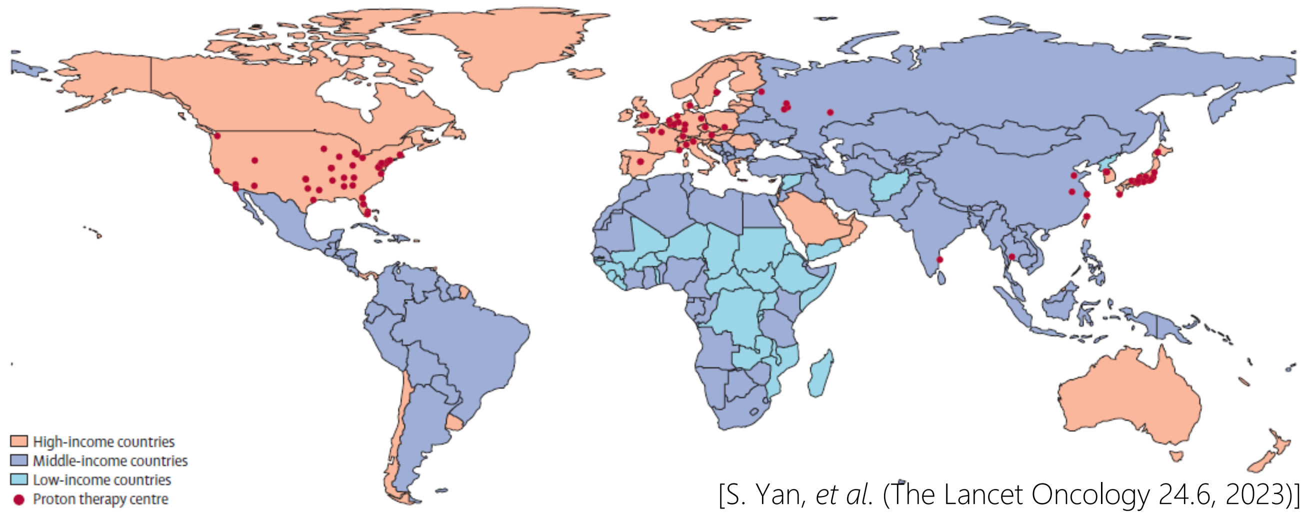
Recent progress on laser-driven ion acceleration and its application to proton therapy

Aarón Alejo

Workshop on Technologies & applied research at the future Valencian proton-therapy facility

Why a laser-accelerator alternative?



[S. Yan, *et al.* (The Lancet Oncology 24.6, 2023)]

→ Significant increase in facilities capable of performing proton-therapy, but mostly limited to high-income countries

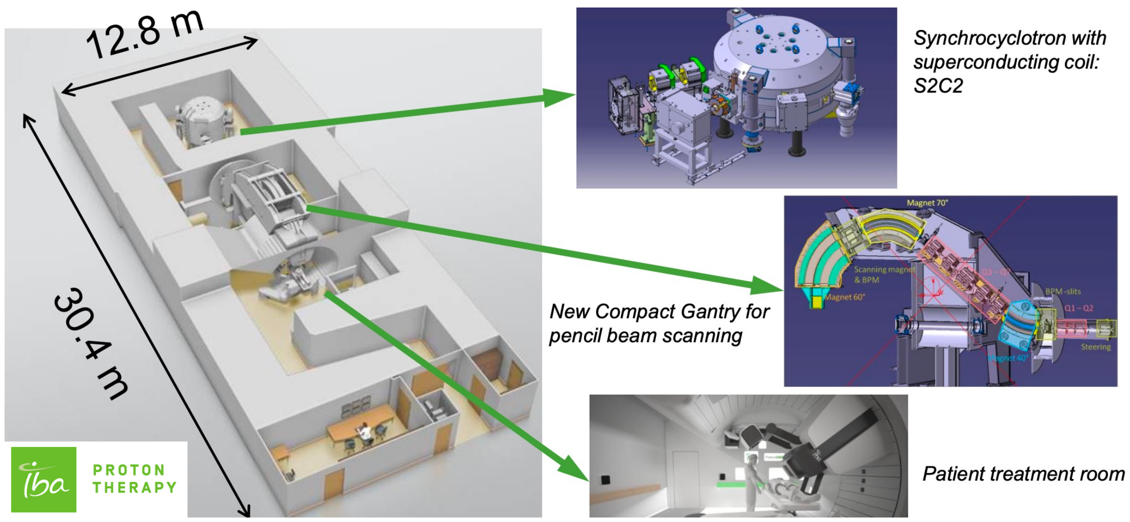
⇒ **Need for democratisation of the technology**

→ A major fraction of the budget is devoted to radio-protection of the large facility.

→ Also, manipulation of high-energy proton beams results in bulky and costly gantries.

→ Appeal for irradiation with different sources and energies

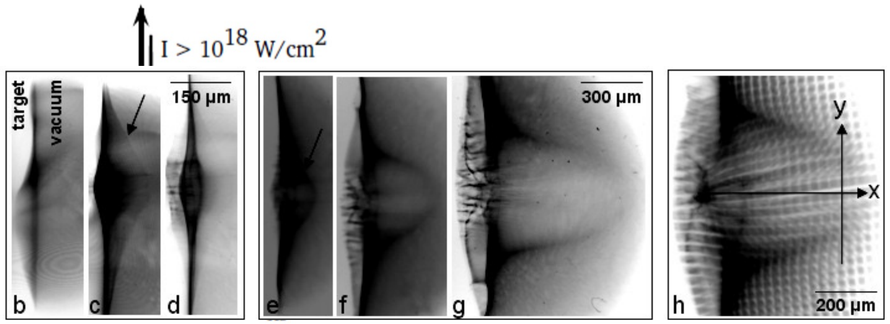
⇒ **Scope for a compact, laser-based alternative?**

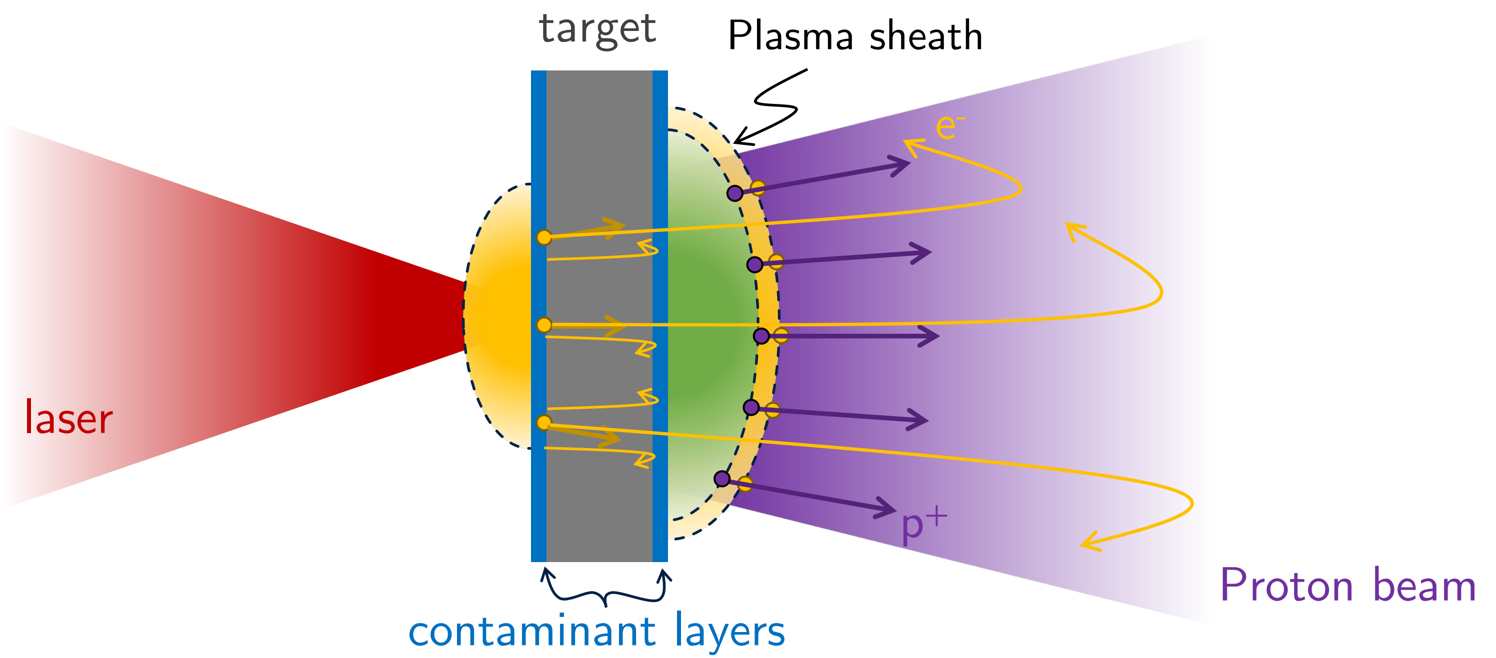


Laser-driven ion acceleration

Ion acceleration in a nutshell (TNSA)

1. Target ionization – Plasma generation
2. Plasma heating
3. Ion acceleration





Properties of TNSA proton beams

IGFAE Instituto Galego de Física de Altas Enerxías | USC Universidade de Santiago de Compostela | XUNTA DE GALICIA

→ Maxwell-like energy spectrum up to multi-MeV energies

→ Divergence of up to tens of degrees divergence

→ Cut-off energy scales with laser intensity as $\propto I_L^{1/2\text{-}1}$

→ The ion beam is multi-species, dominated by the lightest species (protons)

→ Other appealing properties,

	Laser-driven
Emittance (mm mrad)	0.002
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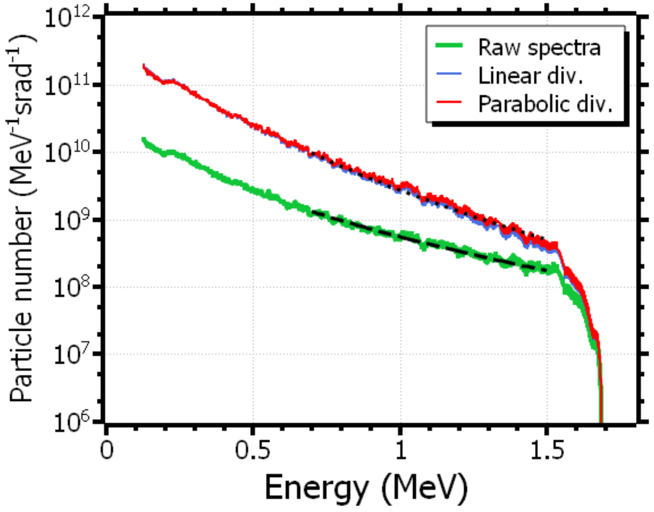
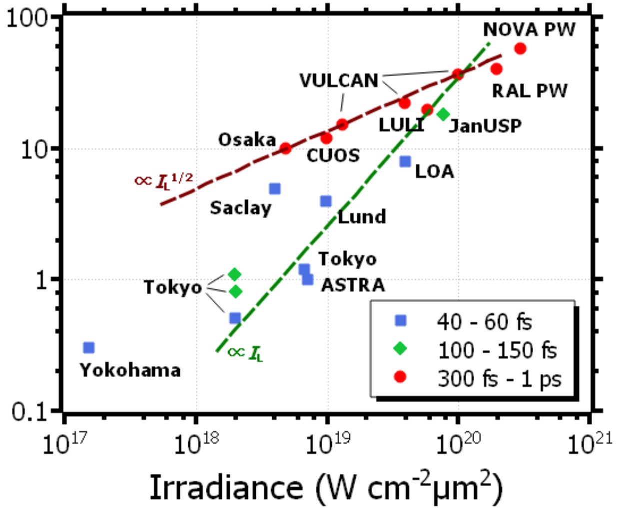
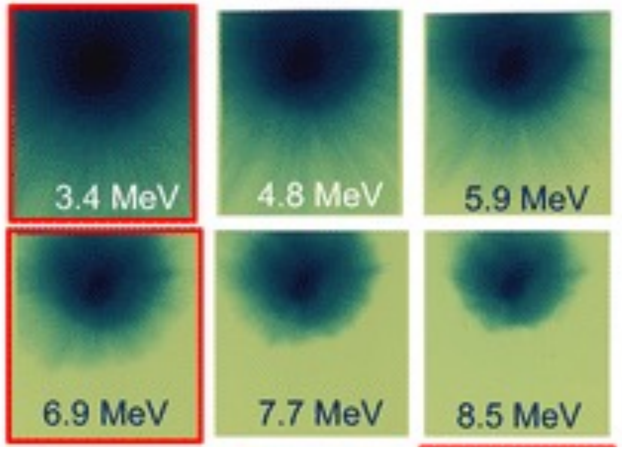
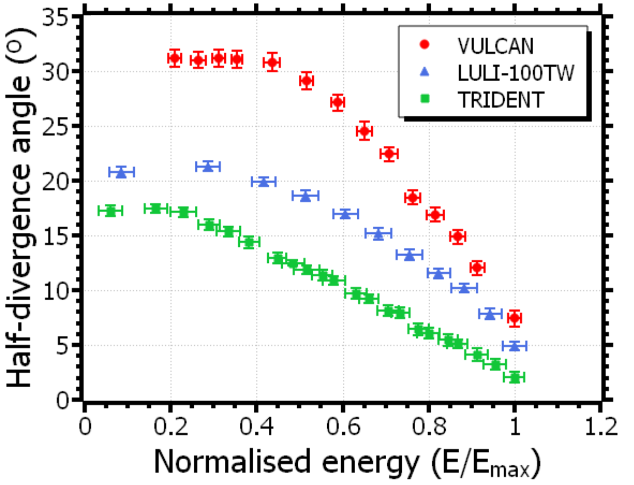
Beam energy (MeV)	≤100
Beam charge (pC)	10^3









[S. Heronting, *et al.* (Cyclotrons-16., 2016)]

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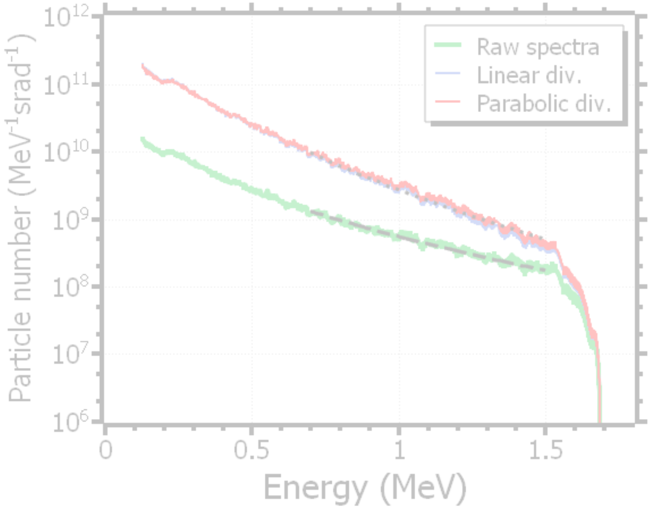

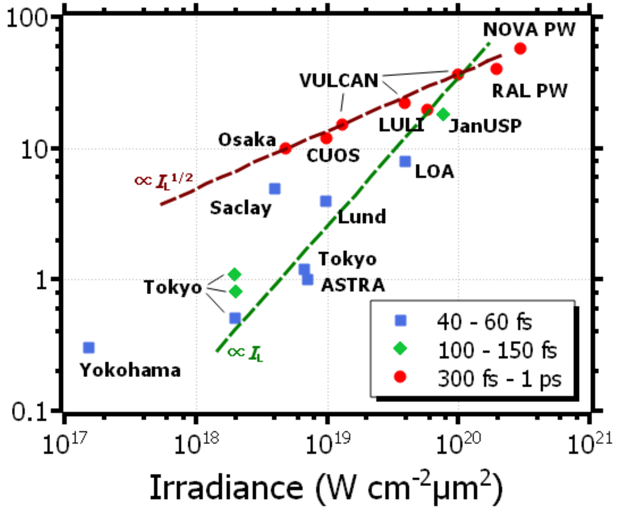

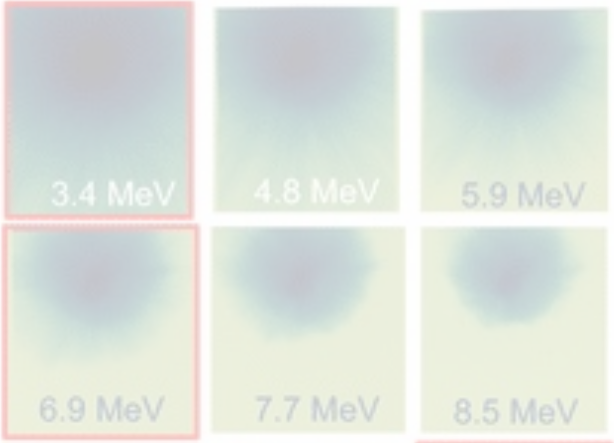

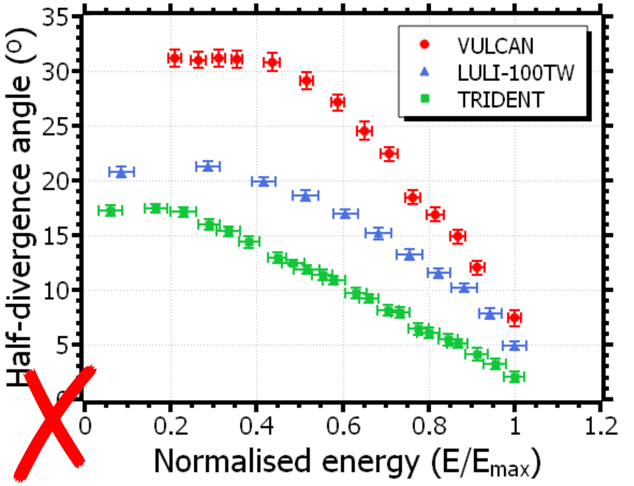

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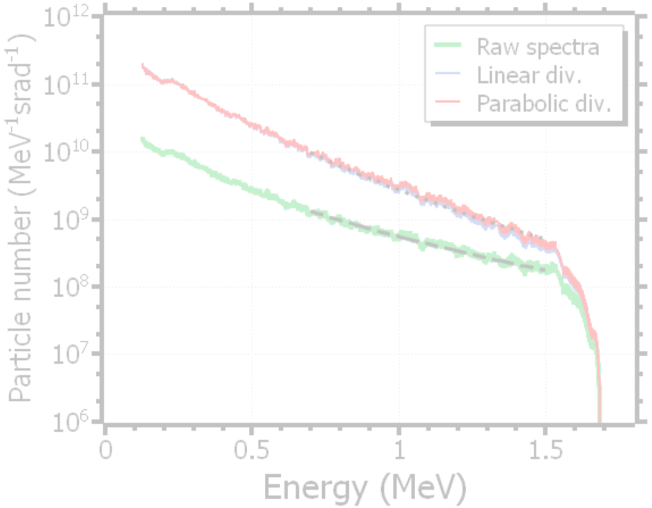

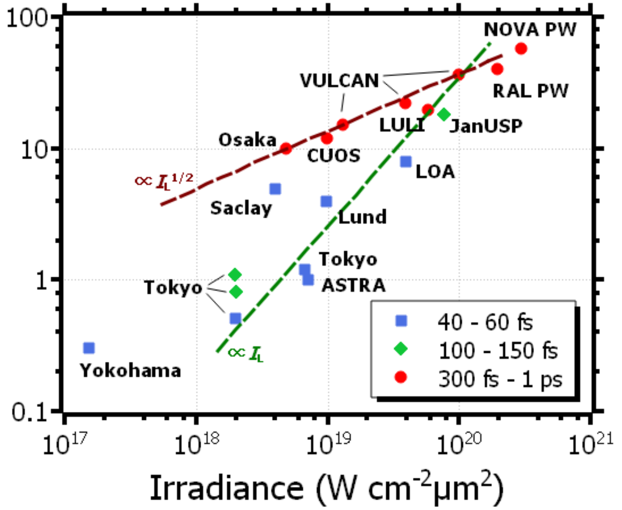

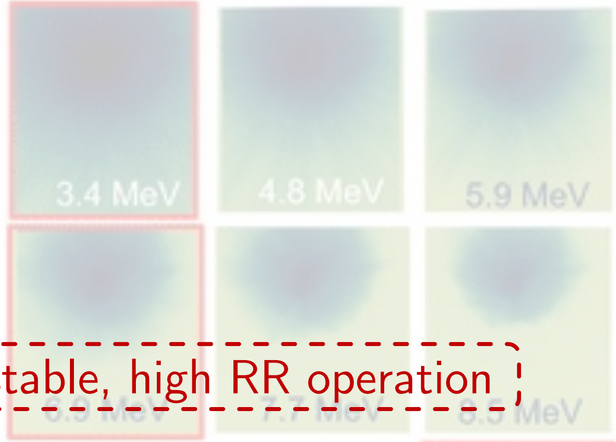

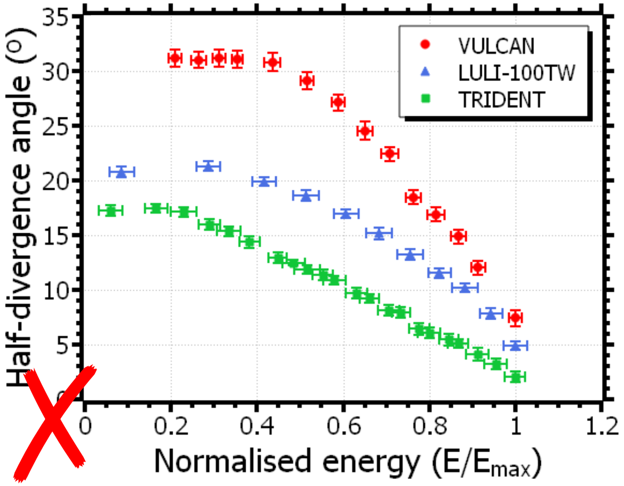

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Need stable, high RR operation

[S. Heronting, *et al.* (Cyclotrons-16., 2016)]

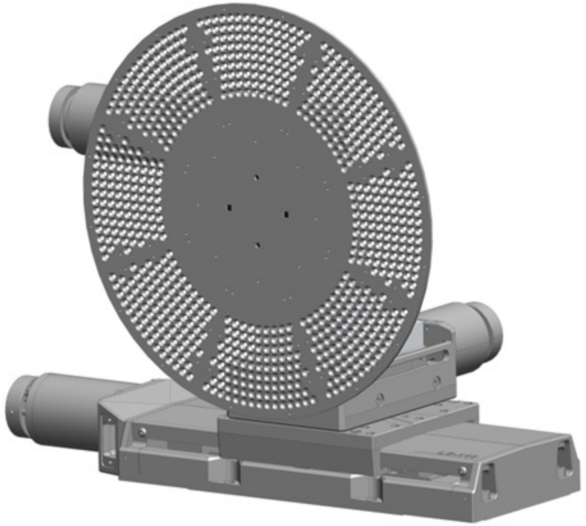
Stability & HRR Operation

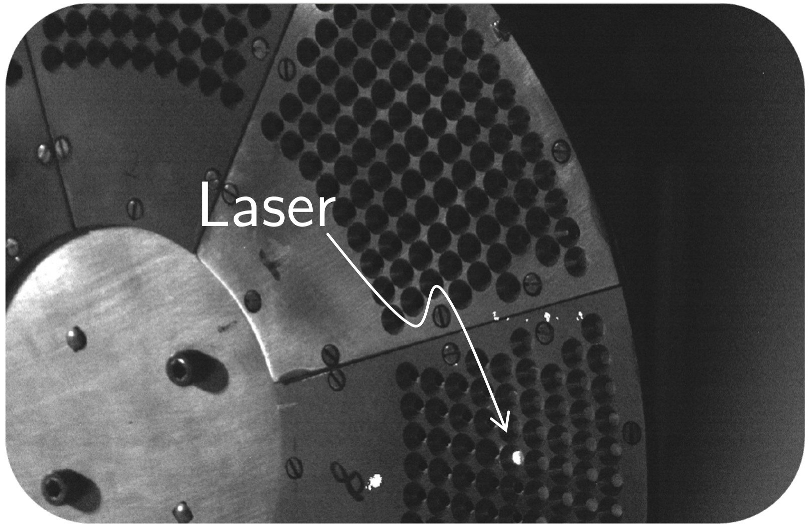
→ Applications require the proton source to be stable and capable of operating at high repetition rates

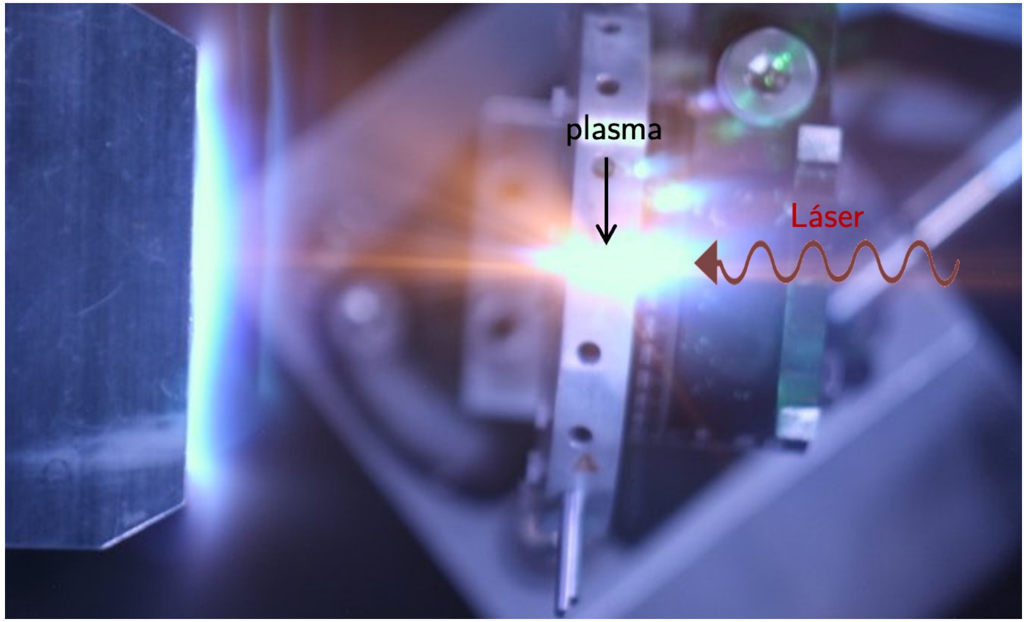
⇒ Laser and target must be stable and accurately aligned

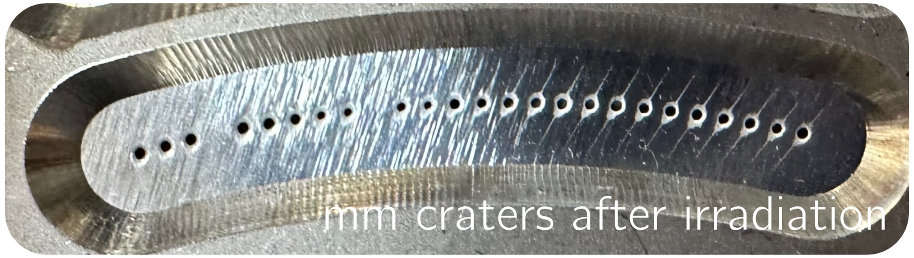
→ Targets are destroyed following each irradiation

→ We developed a novel target system capable of μm-precision alignment and multi-Hertz acceleration









[J. Peñas, A. Alejo, *et al.* (Accepted HPLSE, 2024)]

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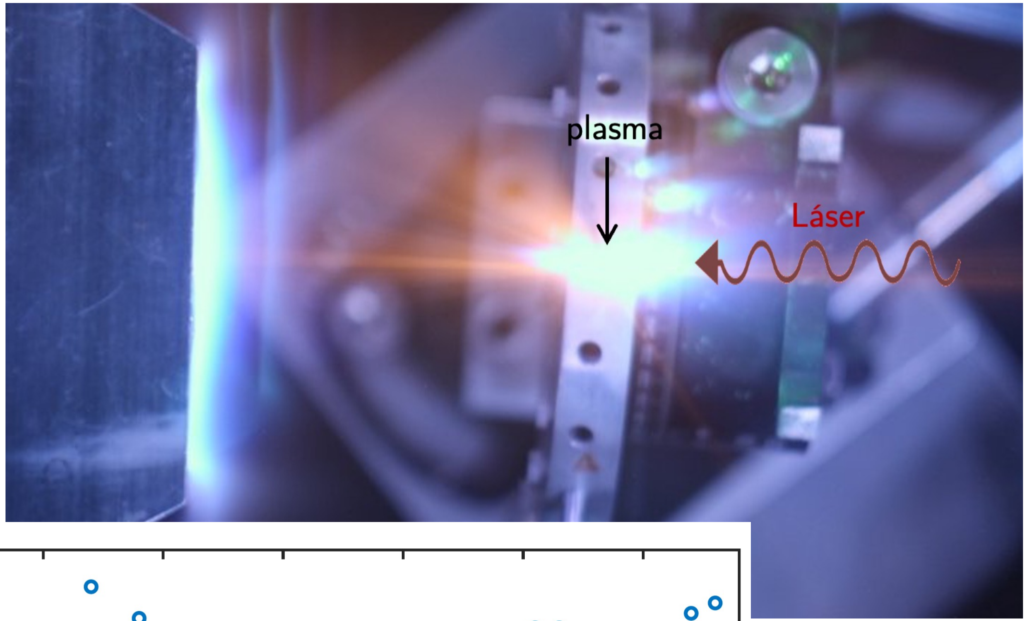

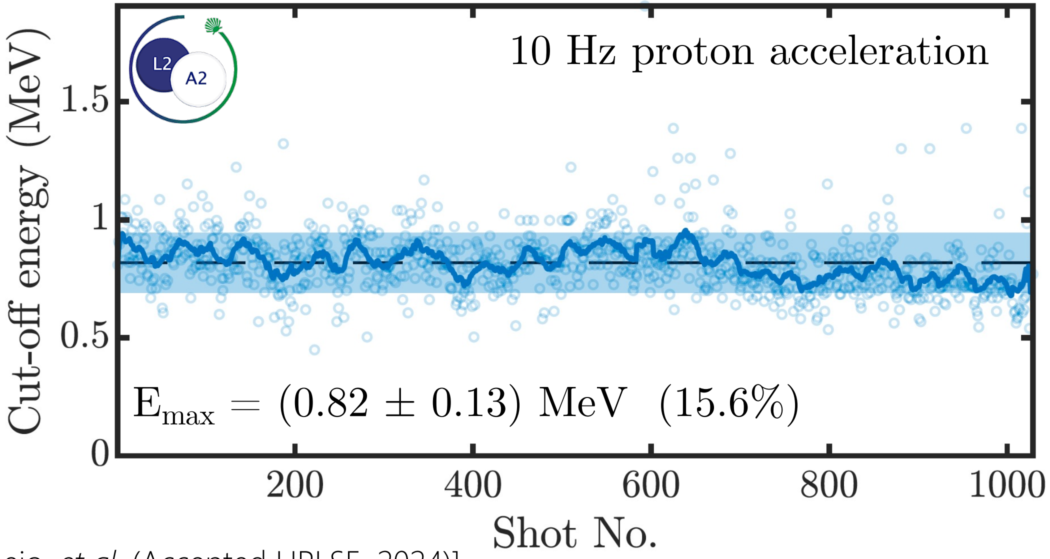

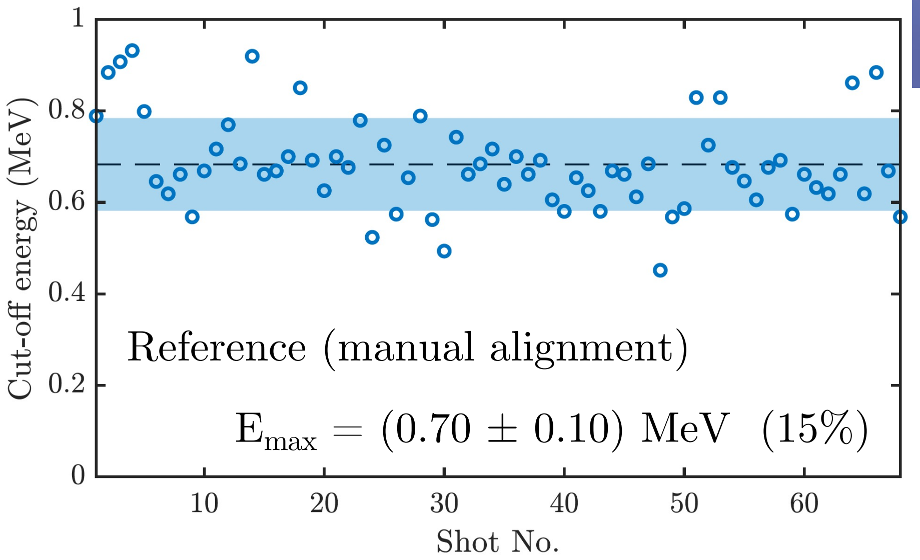

[J. Peñas, A. Alejo, *et al.* (Accepted HPLSE, 2024)]

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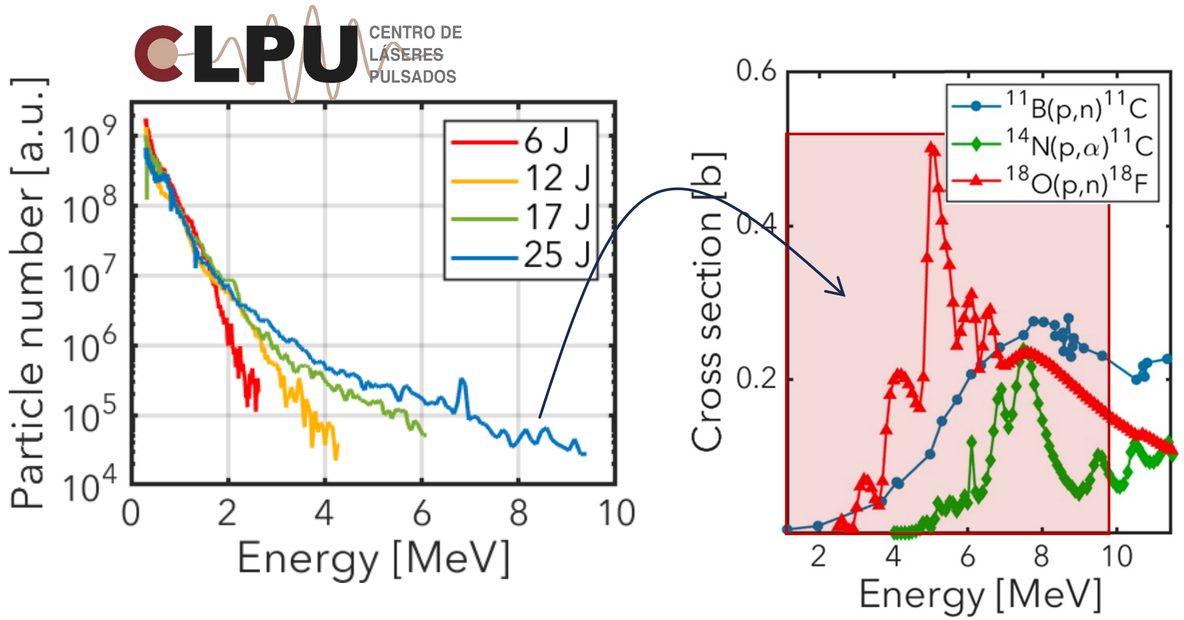
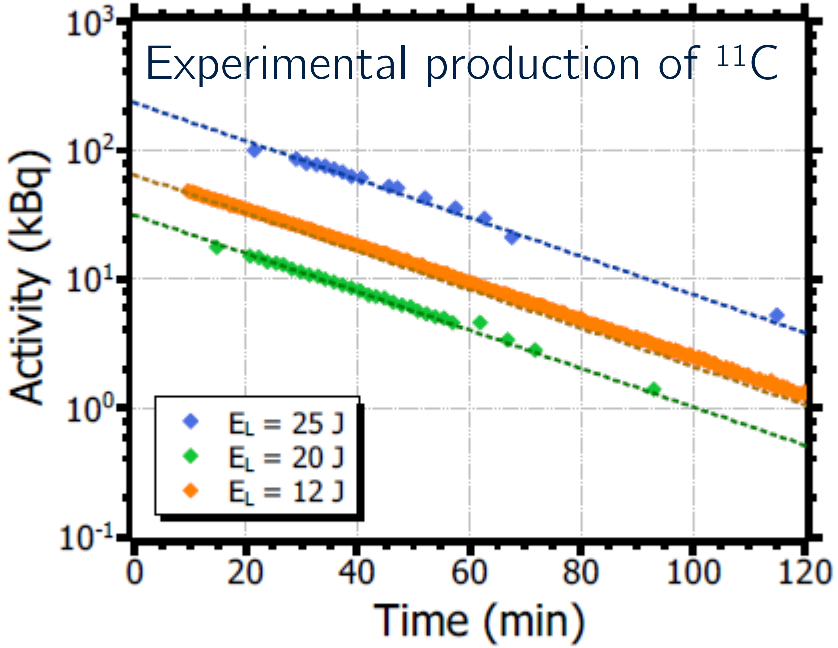
Already good enough for certain applications:

Radio-Isotope generation for medical imaging





E_{laser} (J)	# Shots	A/shot [kBq]	Total Activity[kBq]
12	40	1.8	68.6
20	10	3,2	31.5
25	20	12.4	233.8

On the path to generate pre-clinical activity levels from LD sources

[J. Peñas, A. Alejo, *et al.* (Submitted Sci. Rep., 2024)]

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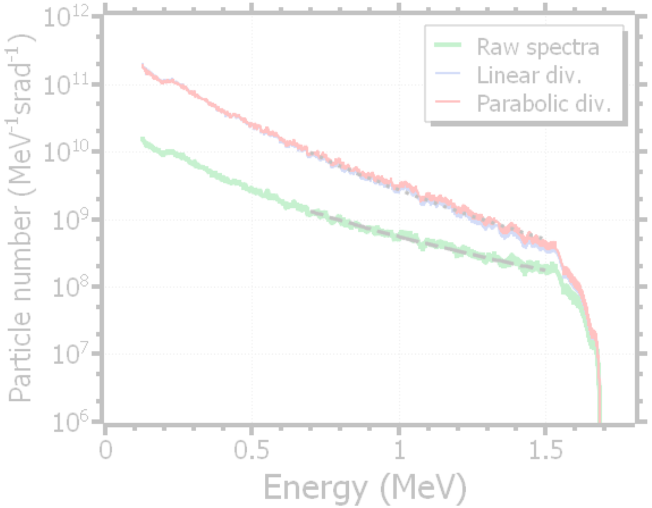

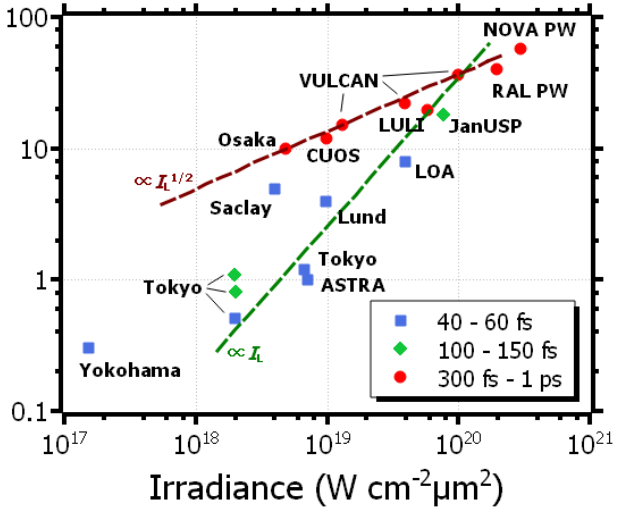

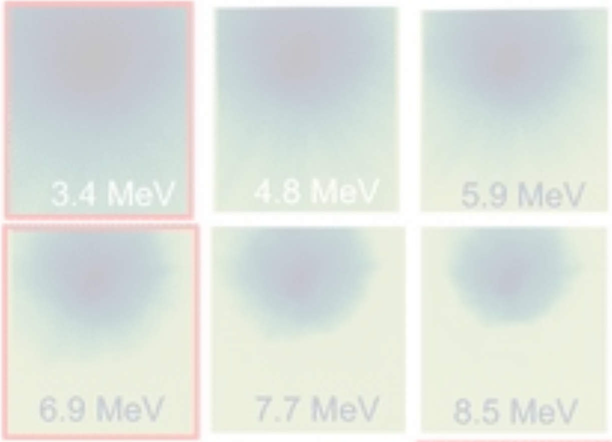

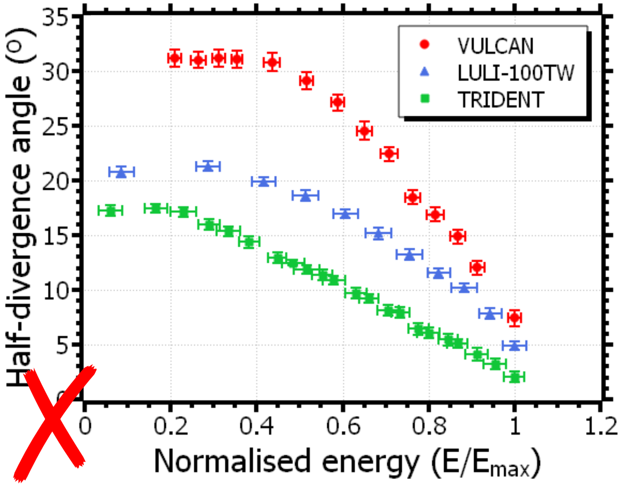

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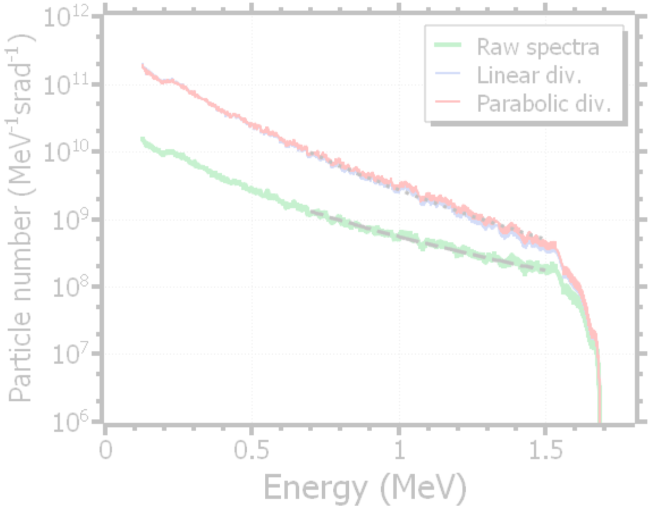
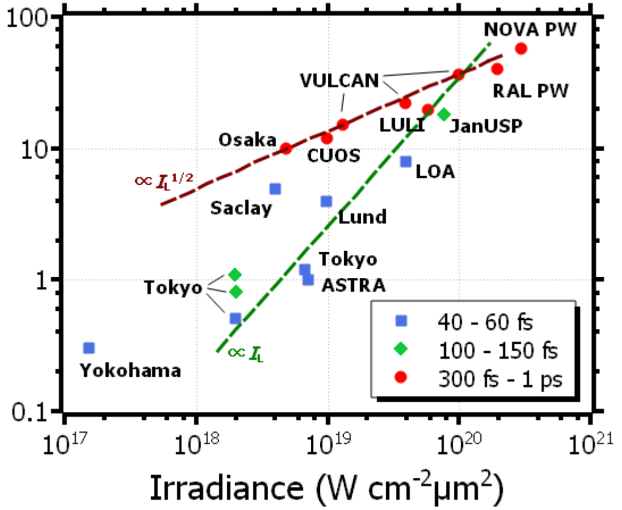
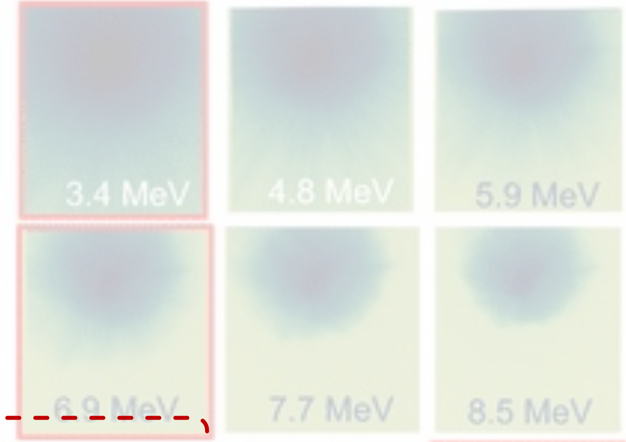
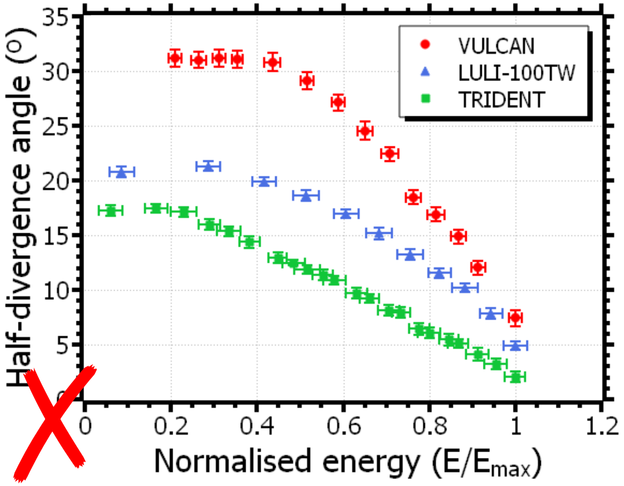
Increase energy

[S. Heronting, *et al.* (Cyclotrons-16., 2016)]







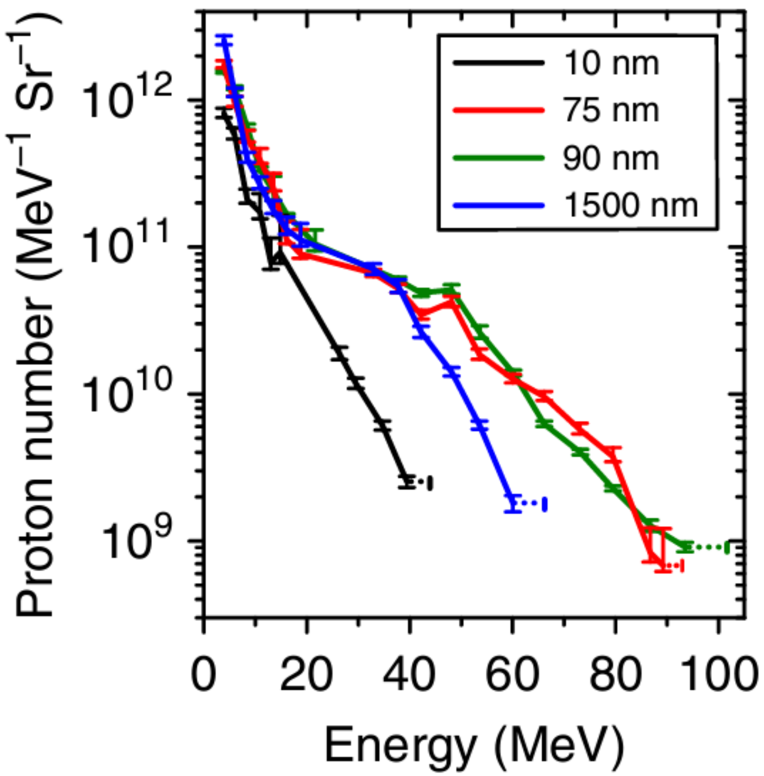


Energy increase and heavier species

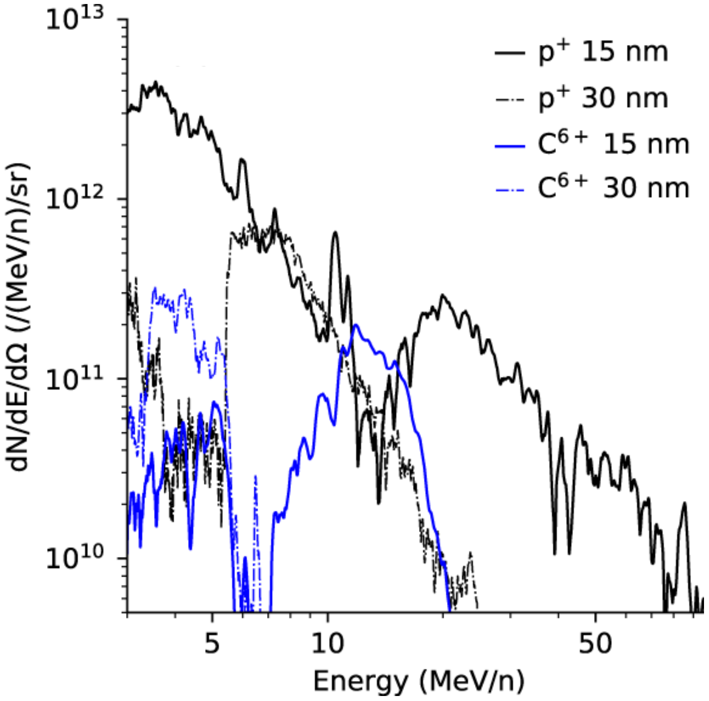
→ Energies in excess of 100 MeV are required for applications, including PT, not achieved **so far** from TNSA

→ Hybrid acceleration schemes are being studied. Current *published* record proton energy is 100 MeV

→ In addition to a mixed proton-electron-gamma source, heavier species can be accelerated using lasers

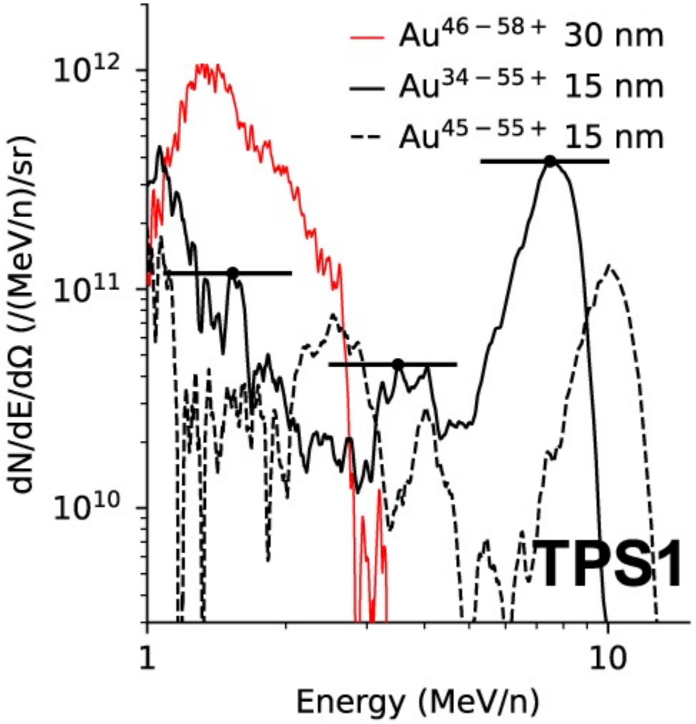


[A. Higginson, *et al.* (Nature communications 9.1, 2018)]



Narrow-band C ions

[P. Chaudhary, *et al.*,Phys. Med. & Bio. 68.2, 2023)]



>2 GeV Au ions

[P. Martin, *et al.* (Communications Physics 7.1, 2024)]

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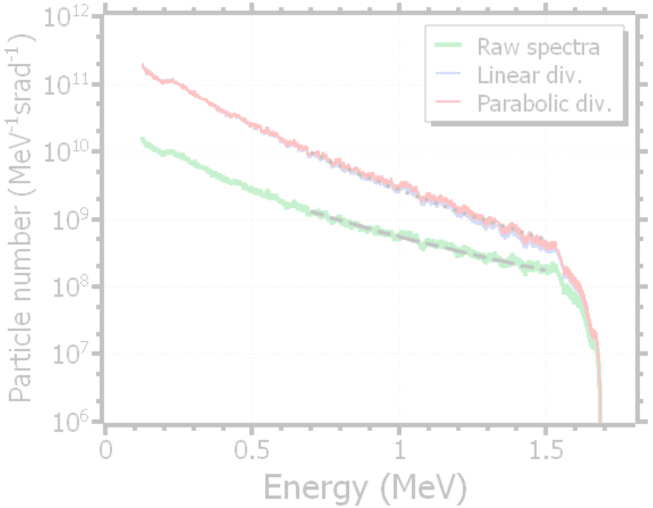
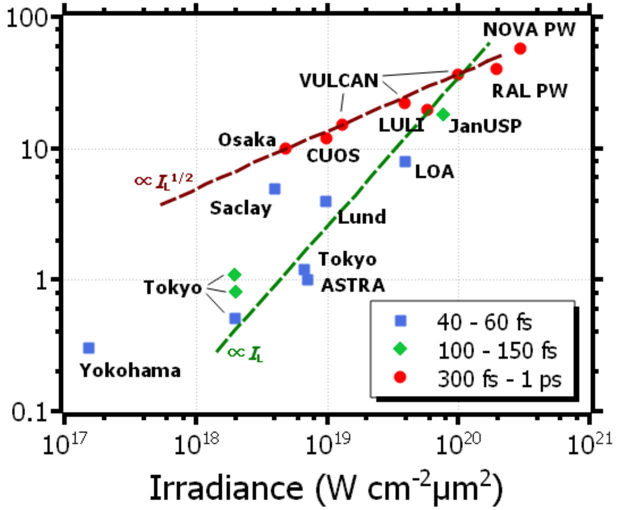
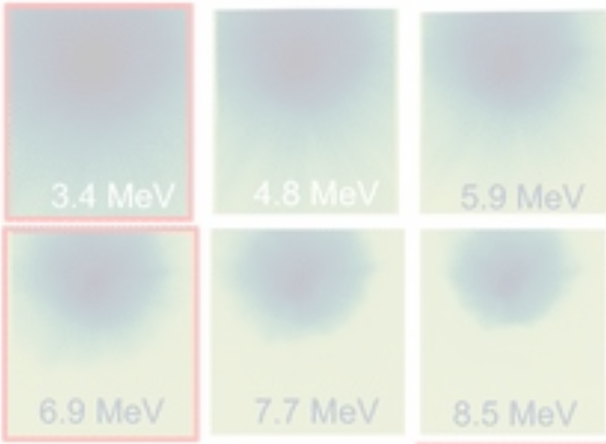
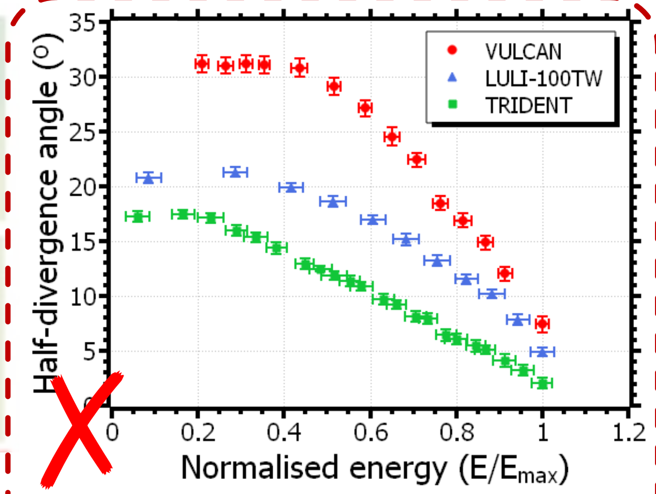




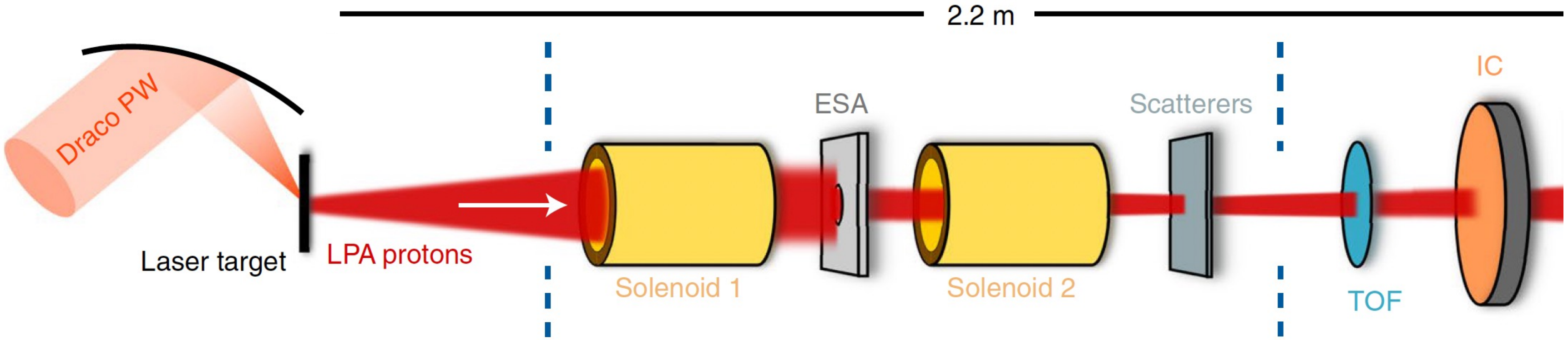




Flux enhancement

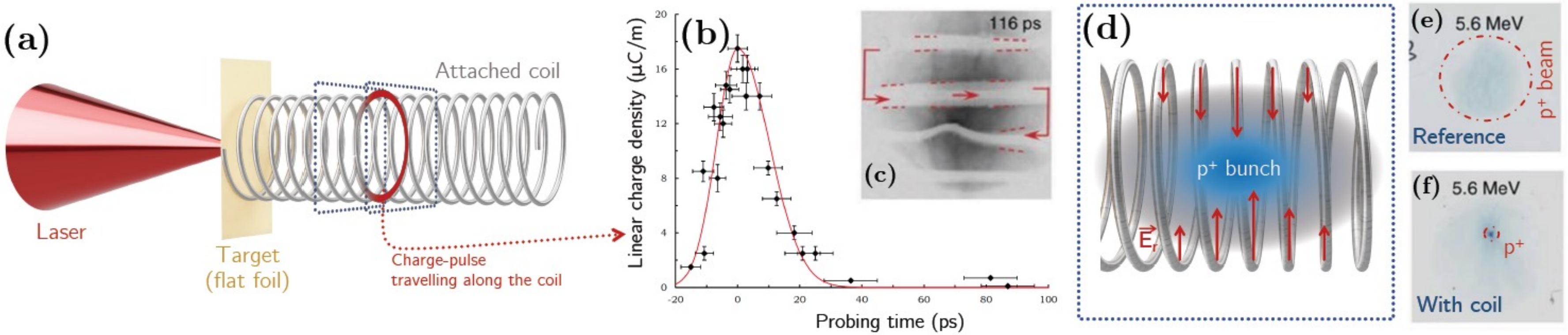
→ In order to ensure the high fluxes required for a sample at a distance from source, beam manipulation is required.

→ Conventional manipulation based on magnetic quadrupoles can be used ⇒ **bulky solution**



[F. Kroll, *et al.* (Nature Physics 18.3, 2022)]

→ On-going research to develop all-optical, compact solutions for ion beam collimation



[S. Kar, *et al.*, (Nature communications 7.1, 2016)]

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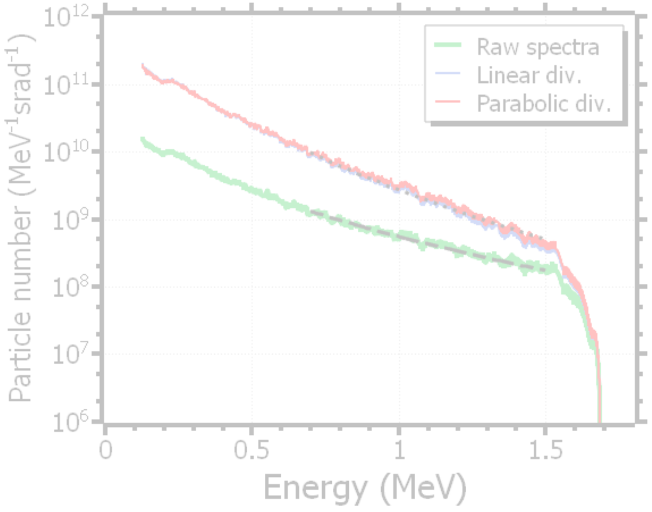
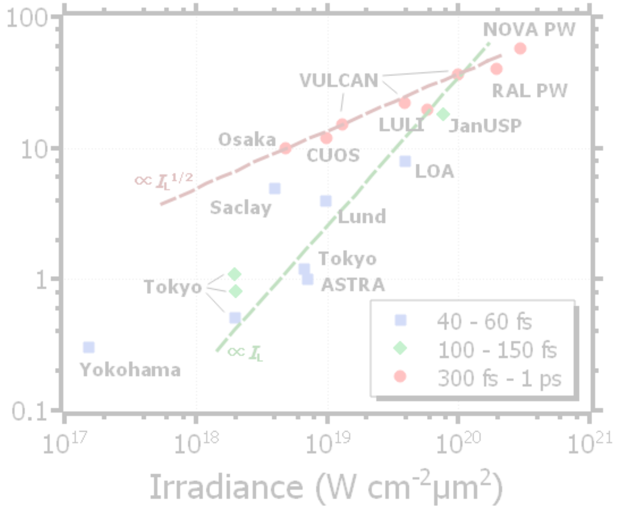
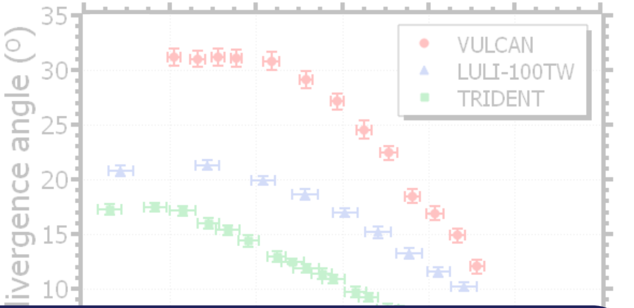




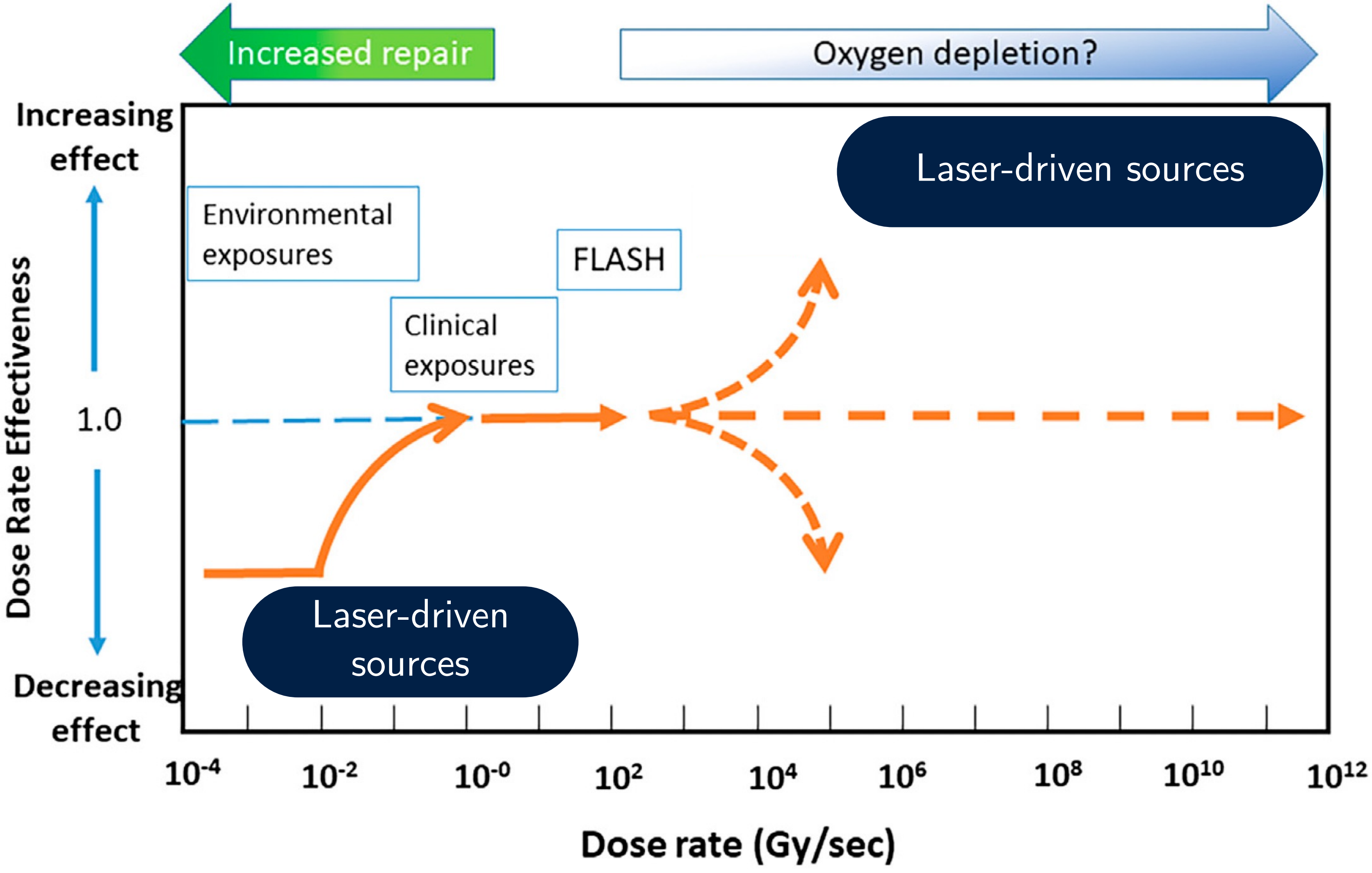
Work in progress...



Parallel work in radio-biology?

Radiobiology experiments using LD protons

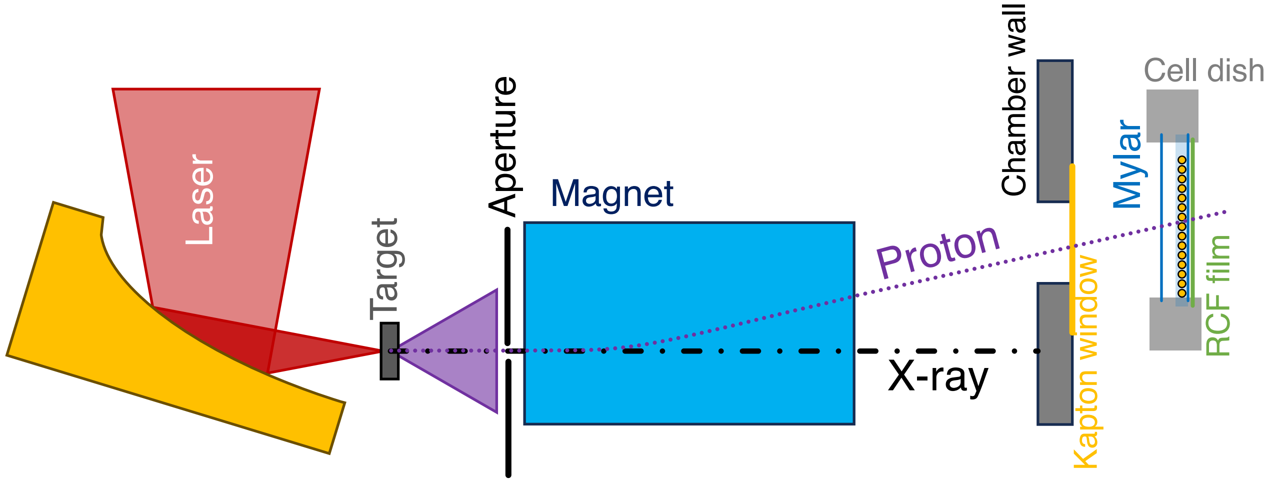
The regime



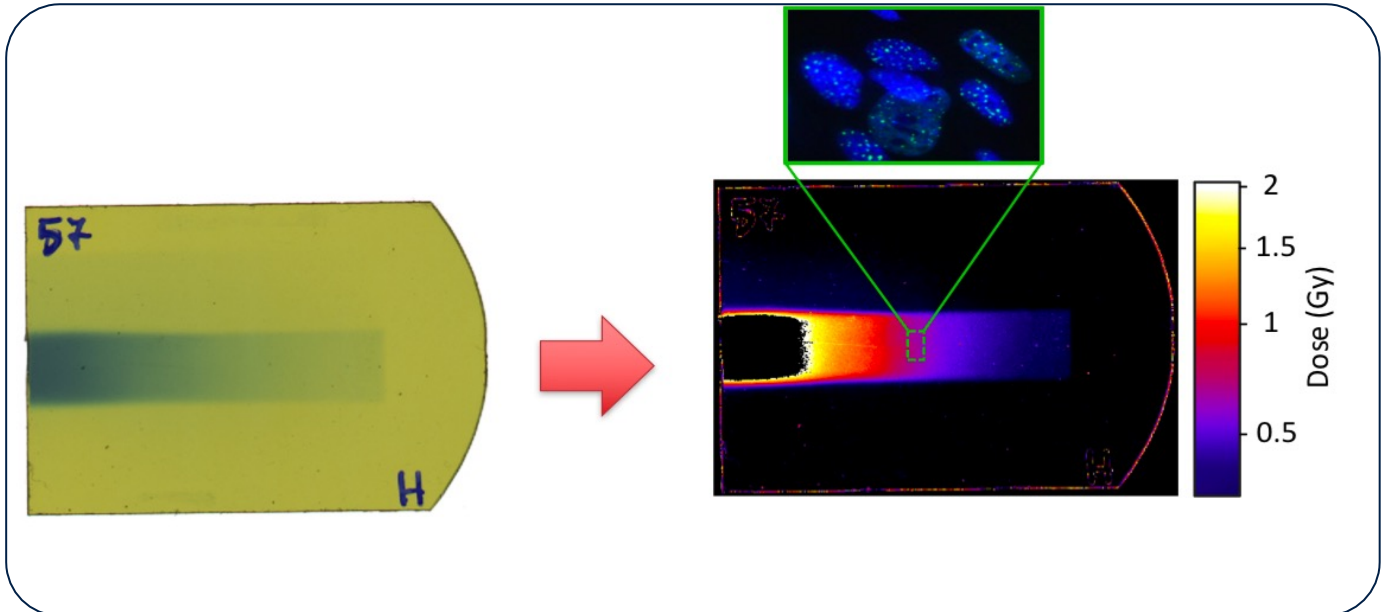
[P. Chaudhary, *et al*. (Frontiers in Physics 9, 2021)]

Experiments and diagnostics

→ Several critical aspects need to be considered when designing proof-of-principle experimental setups.



1. The basic, easy setup can be used as starting point
2. Laser-plasma interaction must take place in vacuum
3. The ion beam is intrinsically multi-modal & divergent
4. Crucial to measure on-shot dose
   - Using ionization chambers is complicated due to an increase in ion recombination → Reliable?
   - Faraday cups are being studied, but struggle due to harsh conditions of interaction.
   - Passive detectors, such as radiochromic films, most commonly used in experiments



In-vitro Cell irradiation

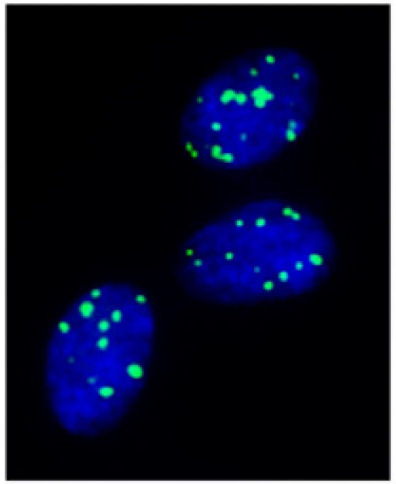
In-vitro Cell irradiation

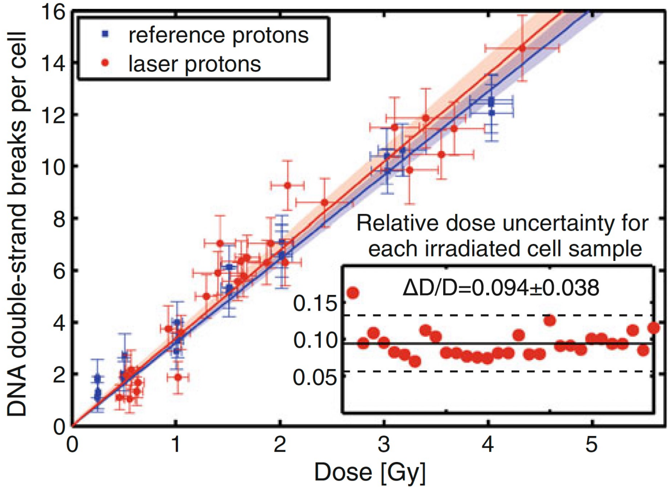
Double-strand break

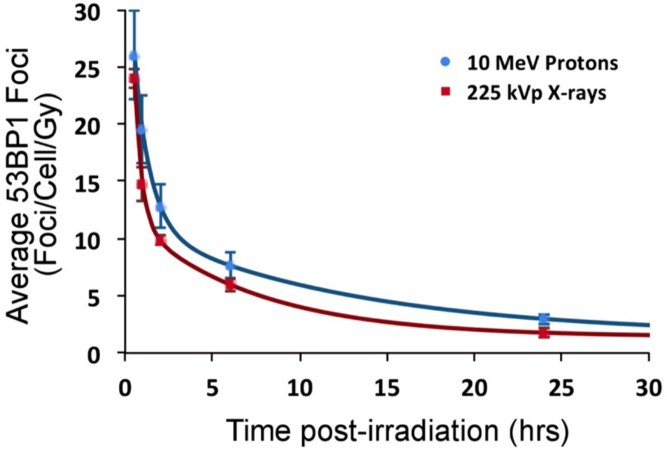
→ Most studies of DNA damage by laser-driven protons have been based on double-strand break analysis using the foci formation assay.

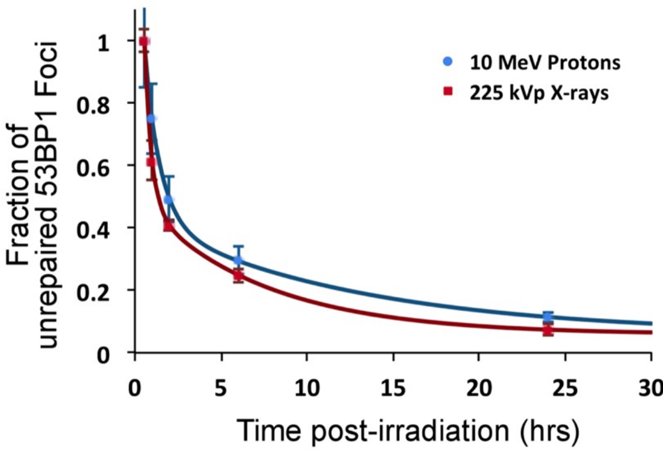
→ No significant differences found between DSB damage induced by accumulation of modest average-dose irradiation of laser-driven protons with respect to those cyclotron accelerated.

→ More recently, single-shot irradiation of human skin fibroblast cells (AG01522B) with dose rate 10^9Gy/s have been show to yield analogous results to irradiation with protons at a dose ratio of 0.06Gy/s.









[D. Doria, *et al.* (AIP Advances, 2012); K. Zeil, *et al.* (Appl. Phys. B, 2013)]

In-vitro Cell irradiation

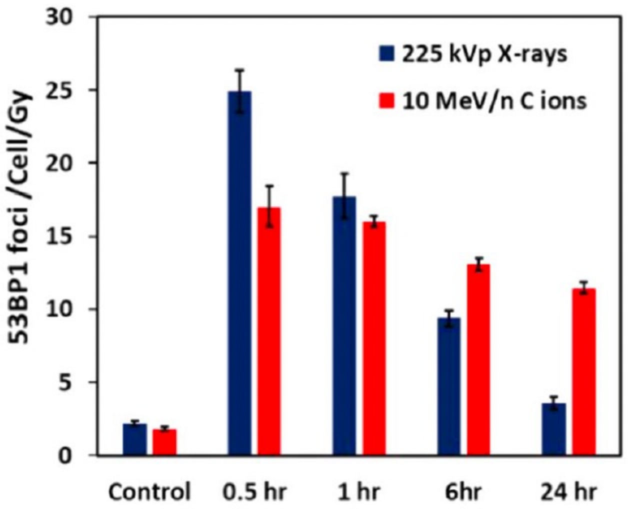
Double-strand break

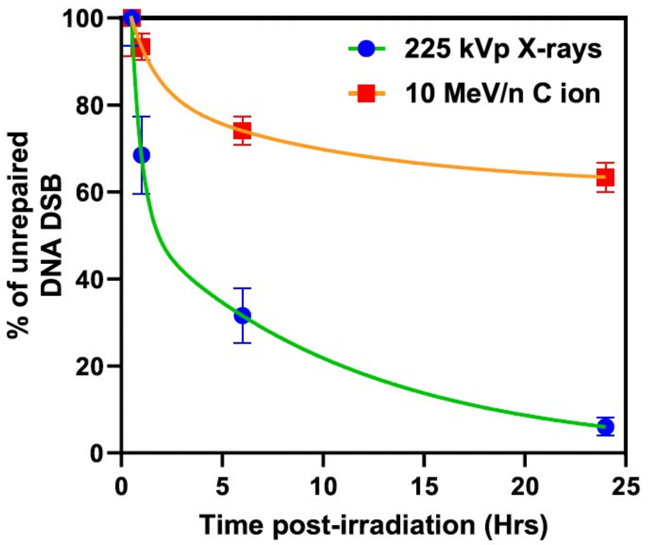
→ Most studies of DNA damage by laser-driven protons have been based on double-strand break analysis using the foci formation assay.

→ No significant differences found between DSB damage induced by accumulation of modest average-dose irradiation of laser-driven protons with respect to those cyclotron accelerated.

→ More recently, single-shot irradiation of human skin fibroblast cells (AG01522B) with dose rate 10^9Gy/s have been show to yield analogous results to irradiation with protons at a dose ratio of 0.06Gy/s.

*** Damage using laser-driven carbons also being studied! Enhanced RBE, but cannot compare with low dose rate.**





[D. Doria, *et al.* (AIP Advances, 2012); K. Zeil, *et al.* (Appl. Phys. B, 2013); P. Chaudhary, *et al.* (Phys. Med. Biol. , 2023)]

In-vitro Cell irradiation

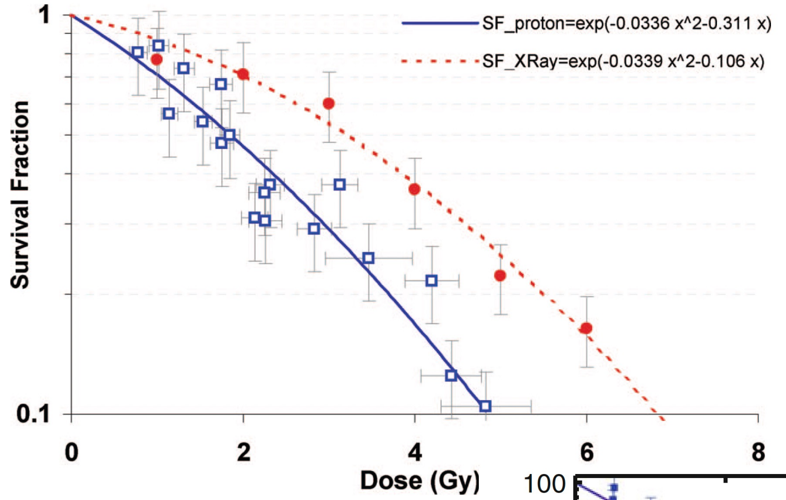
DSB

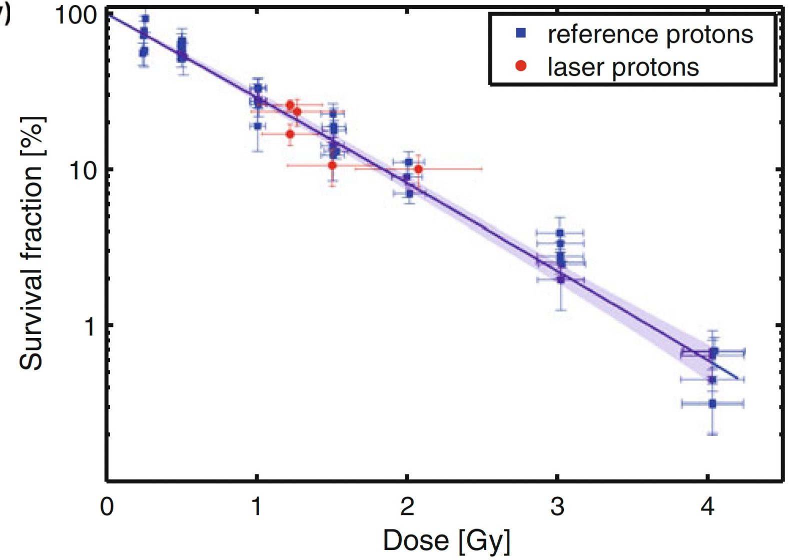
Clonogenic cell survival

→ Clonogenic assays are a useful tool to study radiation survival dose-response.

→ Single-shot survival of Chinese Hamster fibroblast cells (V79) with dose rates exceeding 10^9Gy/s has been studies, reporting a RBEs of 1.4.

→ Furthermore, the difference in survival of squamous cell carcinoma cell line (SKX) when irradiated with laser-driven and continuous proton sources has been studied, with indications that similar RBE are achieved in both cases.





[D. Doria, *et al.* (AIP Advances, 2012); K. Zeil, *et al.* (Appl. Phys. B, 2013)]

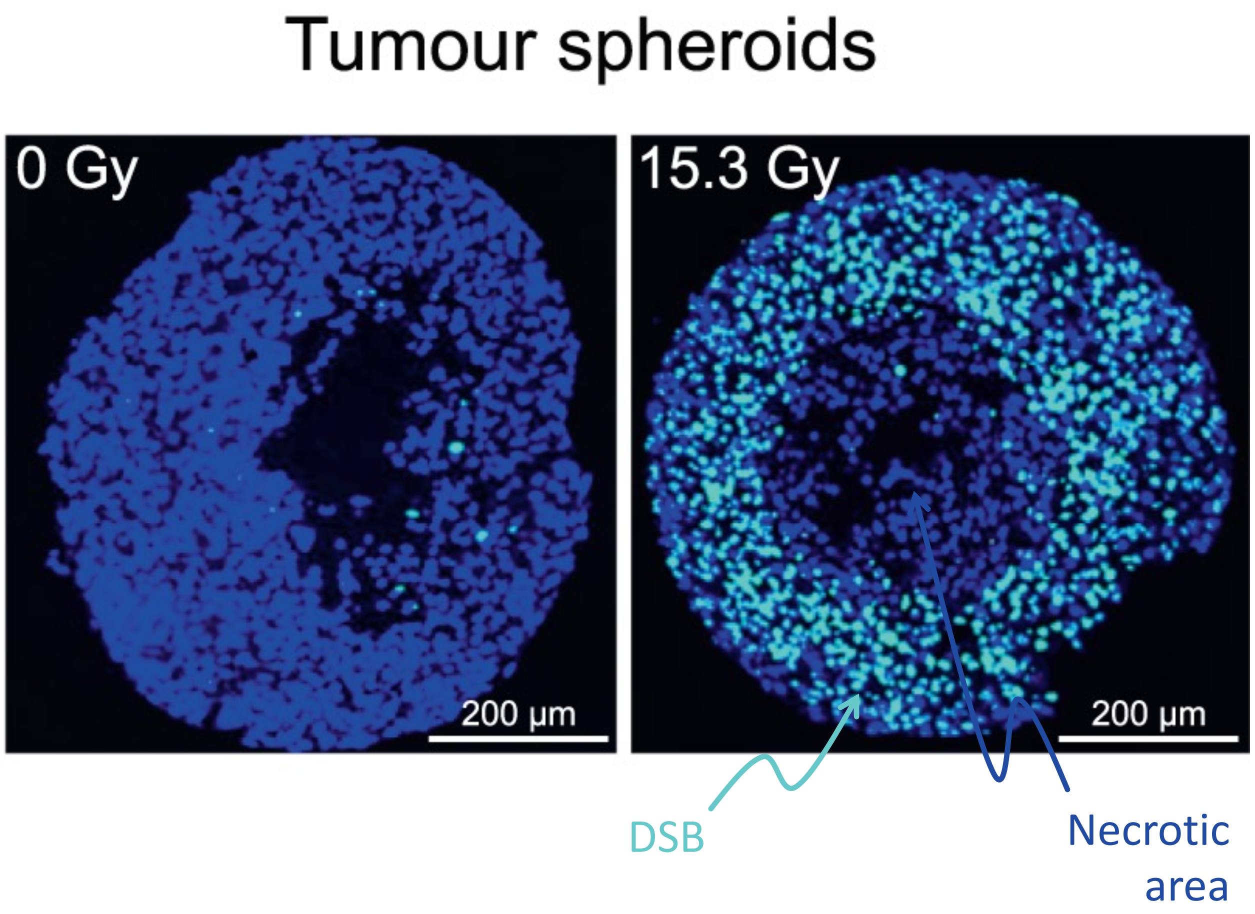
In-vitro Cell irradiation

DSB | Clonogenic cell survival | 3D cell culture models

→ 3D Spherical or organoid model systems have been suggested as a link between cellular in-vitro models and in-vivo animal tumours

→ Neurosphere models are particularly relevant for laser-driven ion studies: uniform irradiation can be achieved given the smaller sizes

→ Recent demonstration of the uniform irradiation with a multi-shot 15.3 Gy dose of 3D spheroids of human tongue cancer cells with a solenoid focused laser-driven proton beam.

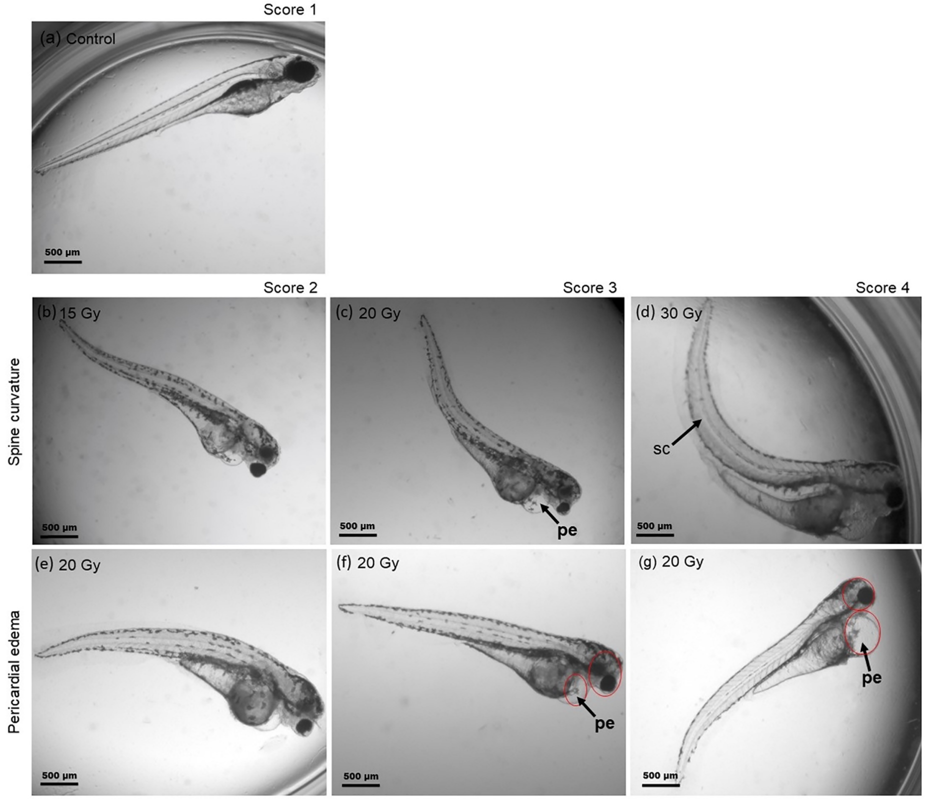


[F.E. Brack. *et al.* (Sci. Rep. (2020)]

In-vivo experiments

Zebrafish embryos

- → Zebrafish embryos are a suitable in-vivo model, thanks to the matching between the body size and the laser-driven proton beam spot size.
- → Different radiobiological endpoints can be used: size, shape of spine, pericardial swelling.
- → Recent demonstration of irradiation validates this approach, obtaining RBE values comparable to previous findings in animal trials.



	mid-SOBP	plateau
RBE_{30Gy} ± se	1.60 ± 0.32	1.41 ± 0.08
RBE_{20Gy} ± se	1.20 ± 0.04	1.13 ± 0.08

[E.R. Szabó, *et al.* (PLoS One, 2018)]

In-vivo experiments

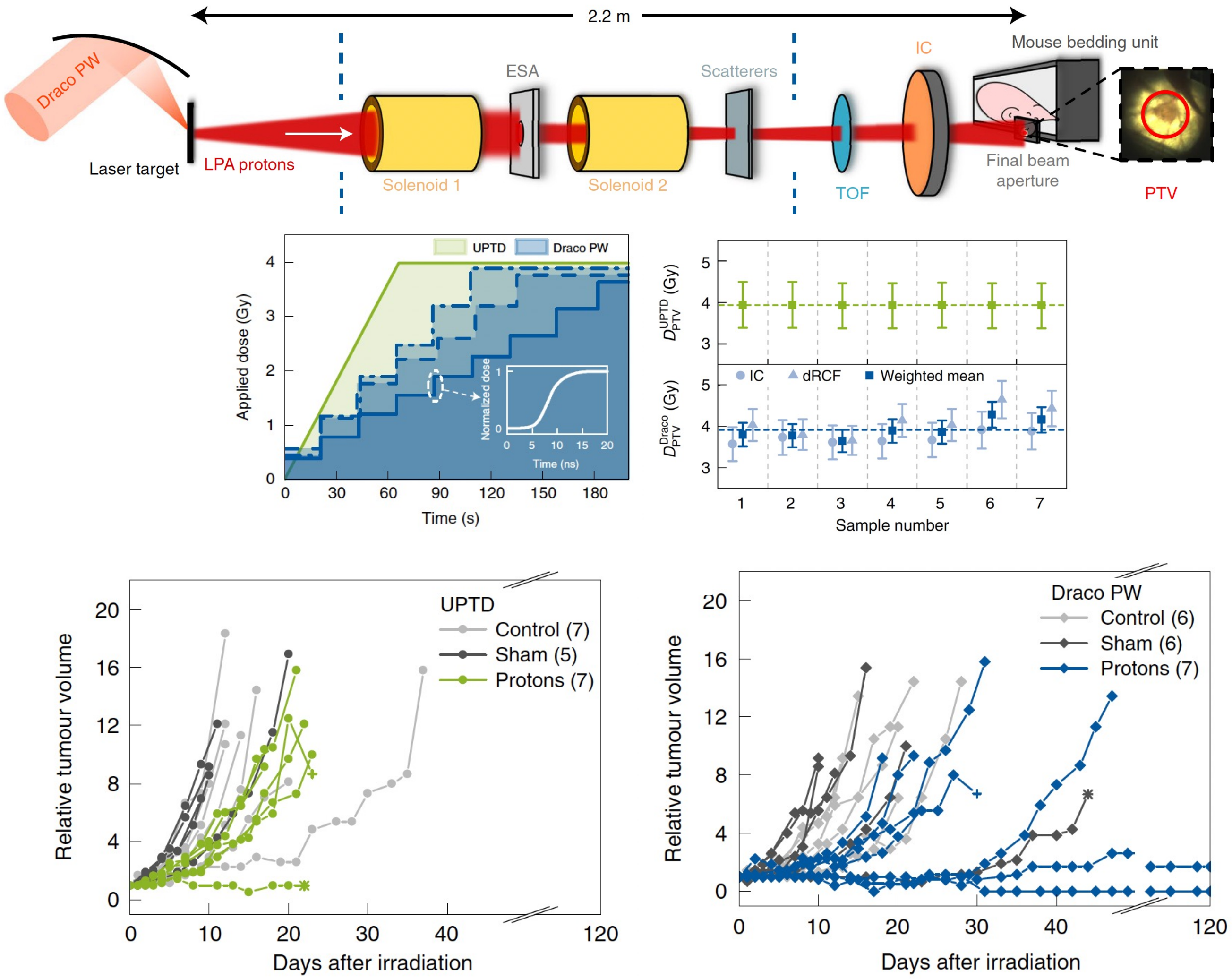
Zebrafish embryos

In-vivo mouse ear

→ A mouse ear tumour model proposed in 2014 as potential suitable testbed for in-vivo studies using laser-driven ion beams.

→ A stable, compact laser-driven proton source with energies greater than 60 MeV has been recently employed to homogeneously deliver a prescribed dose of 4 Gy.

→ The platform is demonstrated to be able to deliver tunable, single-shot doses up to 20 Gy of mm-scale volumes on ns-timescales.

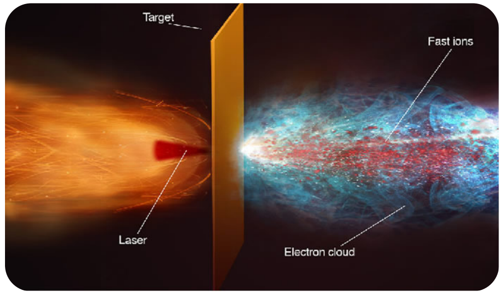


[F. Kroll, *et al.* (Nature Physics, 2023)]

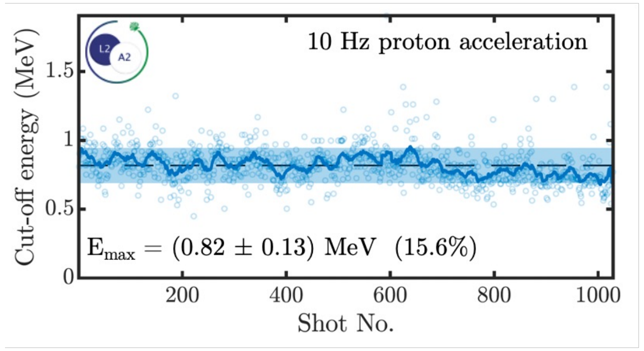
Conclusions

Conclusions

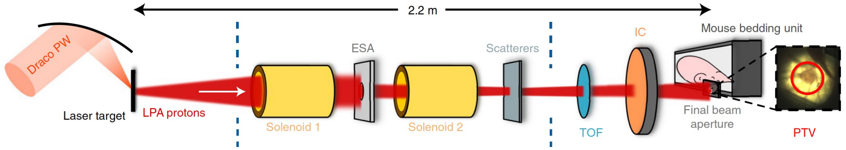
- Significant scope for cost-effective, compact accelerators, where laser-based systems appear as a potential future alternative.



- On-going efforts to improve the ion beam properties, particularly stability, energy and divergence.



- Enabling technology to study radiobiological effects of ultra-high ($>10^9$ Gy/s) dose rate irradiation.
  →Access to conventional facilities critical to compare!



Thank you!