



Laser-Plasma Applications I: Radioisotope production for medical applications

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Radioisotopes in medicine



Pre-clinical research tracers

Pharmacokinetic assays and in vivo molecular screening

Main radionuclides

^{11}C , ^{18}F , ^{32}P , ^{35}S

Medical imaging: PET + SPECT

Functional mapping with Positron Emission Tomography (PET) and Single Photon Emission CT (SPECT)

SPECT / PET

$^{99\text{m}}\text{Tc}$, ^{201}Tl , ^{123}I | ^{18}F , ^{11}C , ^{13}N , ^{15}O

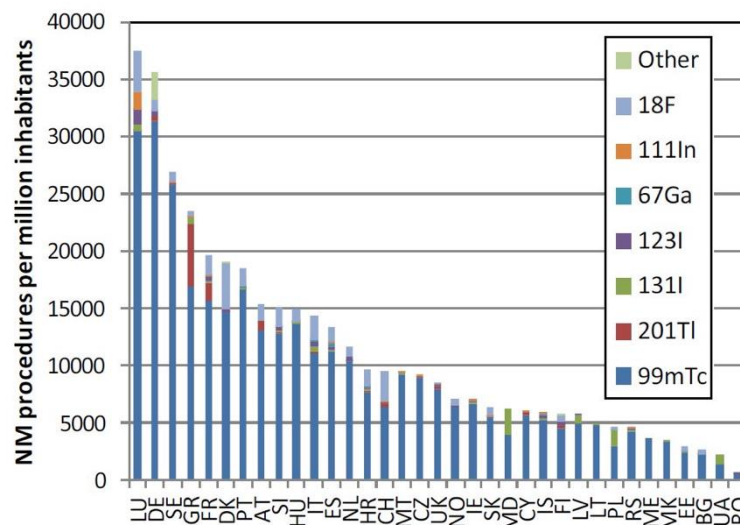
Therapy

Cytotoxic dose delivery to tumoural tissues

Brachytherapy + Targeted therapy

^{103}Pd , ^{125}I | ^{225}Ac , ^{177}Lu , ^{211}At

50+ million nuclear medicine procedures are performed each year and the demand for radioisotopes is increasing at up to 5% annually (770 M\$ in 2025, expected 1560 M\$ in 2034).



Positron Emission Tomography

PET Imaging

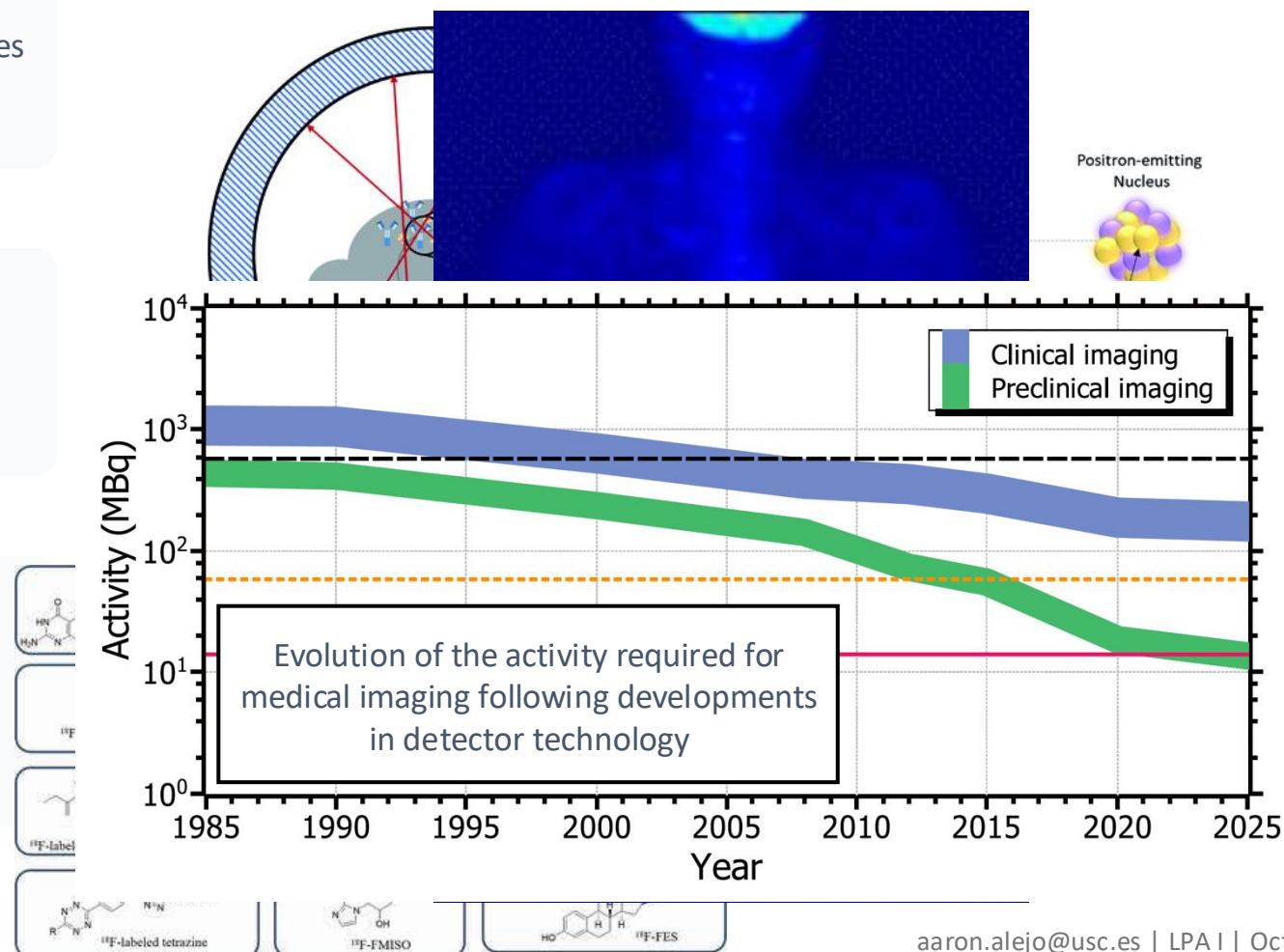
Positron emission tomography is one of the most accurate techniques for producing 3D images for medical diagnosis

Physical Mechanism

The patient is injected with a β^+ -emitting radioisotope. After decay, the electron-positron annihilation results in the emission of two 511 keV photons in coincidence (180°).

Isotope requirements

The typical activity required for pre-clinical and clinical imaging is in the range of **tens and hundreds of MBq**, respectively.



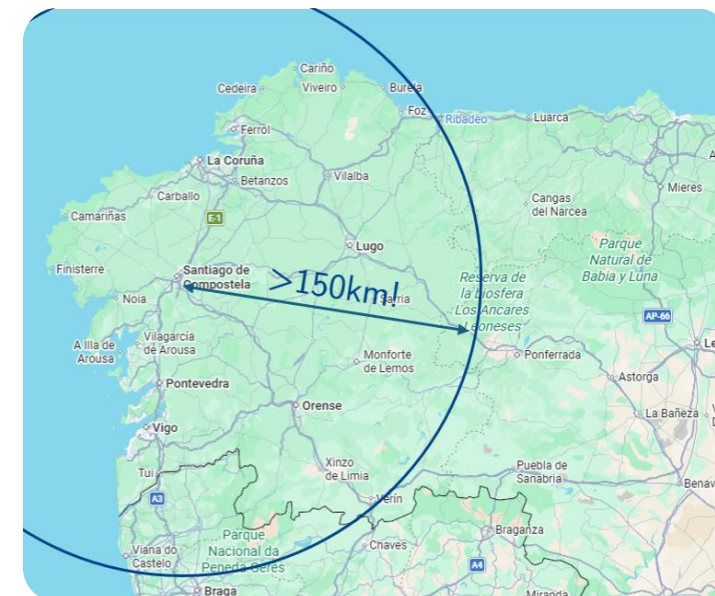
Producing PET isotopes

The production of β^+ radioisotopes for PET imaging is based on cyclotron technology.

- Cyclotrons have a high installation cost and require extensive shielding.
- Sustainable production relies on centralised production centres and regional distribution to large areas.
- This limits the potential radionuclides to those with longer lifetimes.

Radioisotope production in dedicated cyclotrons:

- **IBA Cyclone KIUBE:** 18 MeV – 300 μ A, (^{18}F , ^{68}Ga , ^{89}Zr , ^{11}C),
e.g. 1100 GBq ^{18}F in 120 min., 290 GBq ^{11}C in 40 min.
- **IBA Cyclone KEY:** 9 MeV – 60 μ A, (^{18}F , ^{11}C), e.g. 110 GBq ^{18}F in 120 min., 700 MBq ^{11}C in 40 min.



Radioisotope	Half-life (mins)
^{11}C	20
^{13}N	10
^{15}O	2
^{18}F	110
$^{99\text{m}}\text{Tc}$	360

- Proton acceleration: Target Normal Sheath Acceleration
- Continuous acceleration at High repetition rate
- Production of preclinical levels of ^{11}C
- Towards clinical production



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Proton acceleration

Proton Acceleration. TNSA

1. Target ionisation

Early in the interaction ($I > 10^{18}$ W/cm²), the laser impinging onto the target causes ionisation of the material and formation of a plasma

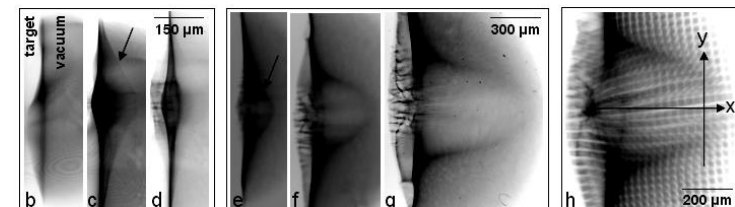
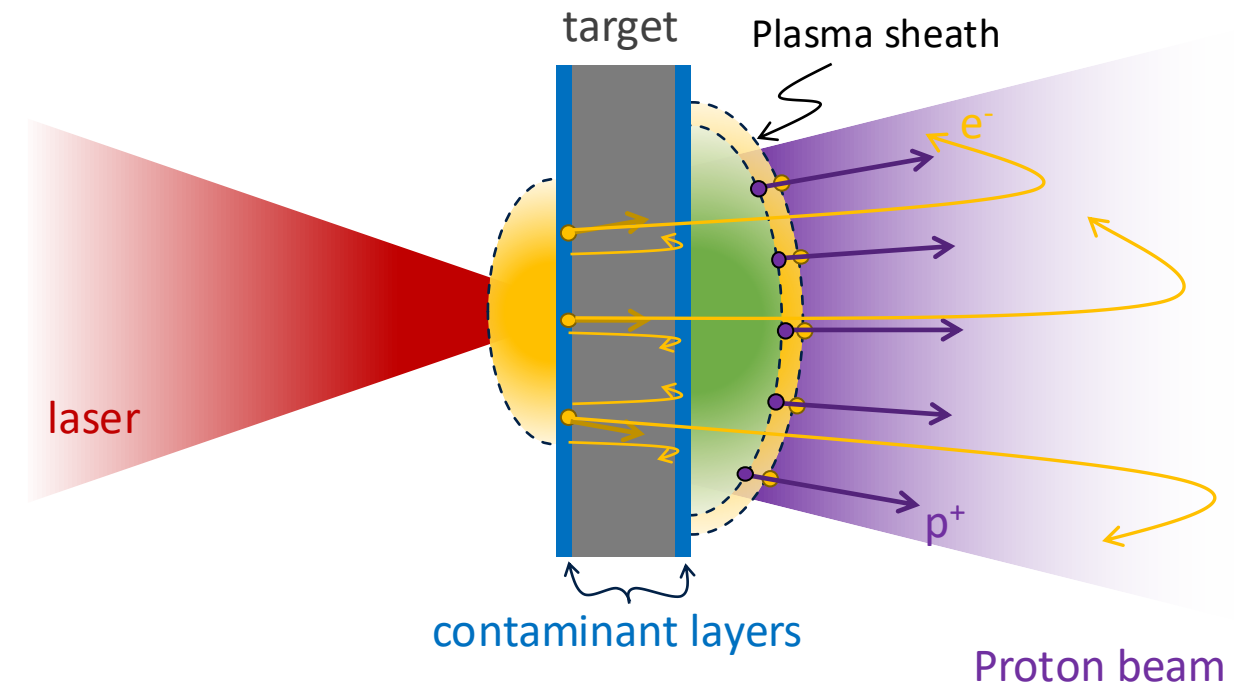
2. Plasma heating & Electron Transport

At ultra-high intensities ($I > 10^{18}$ W/cm²), the laser drives hot electrons via $\mathbf{J} \times \mathbf{B}$ ponderomotive heating at front surface.

$$E_B \sim \frac{1}{c} \frac{d\psi}{dt} \sim \frac{1}{c} \frac{d}{dt} \left(\frac{1}{2} \frac{E_0^2}{\omega_p^2} \right) \sim \frac{E_0^2}{\omega_p^2} \frac{d\omega_p}{dt}$$

3. Field Ionization & Ion Acceleration

TV/m electrostatic sheath field ionizes contaminant layer (H₂O, hydrocarbons) and accelerates protons normal to target.



Characteristics of LD beams

Thermal-like Broad Energy Spectrum

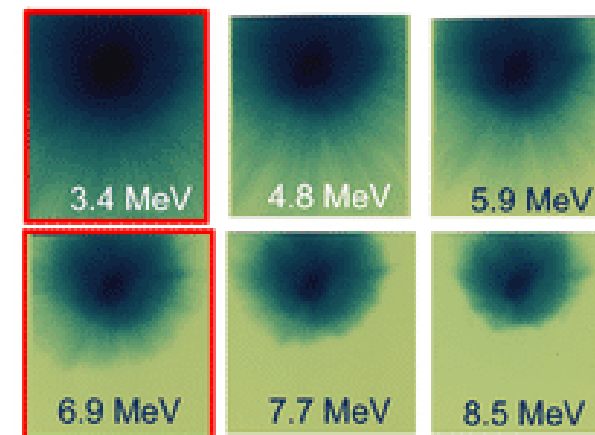
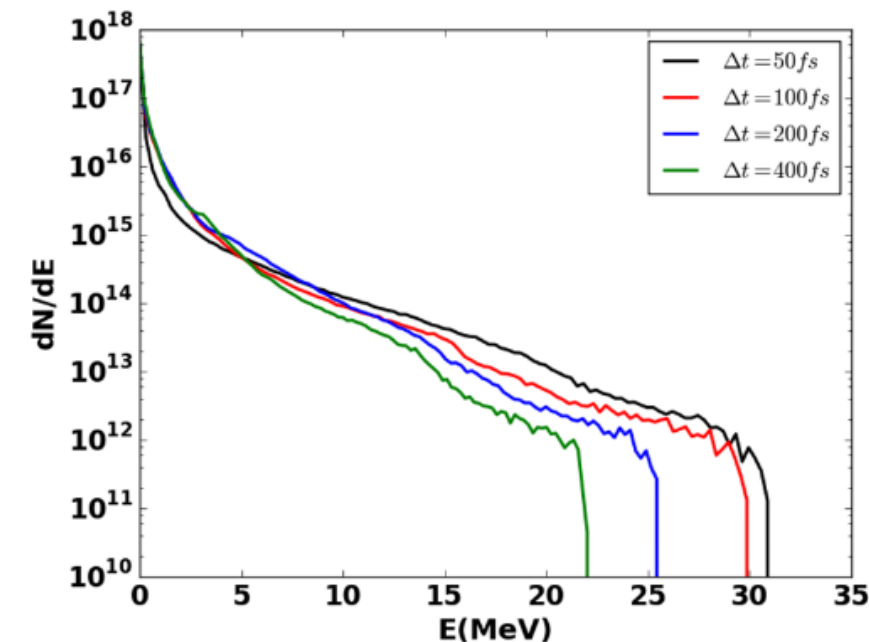
Exponential energy distribution with a sharp maximum cut-off energy $E_{\max}$ (up to ~ 85 – 100 MeV in modern PW facilities).

Divergence & Energy Correlation

Half-angle divergence decreases with higher energy (higher energy protons emitted along central axis).

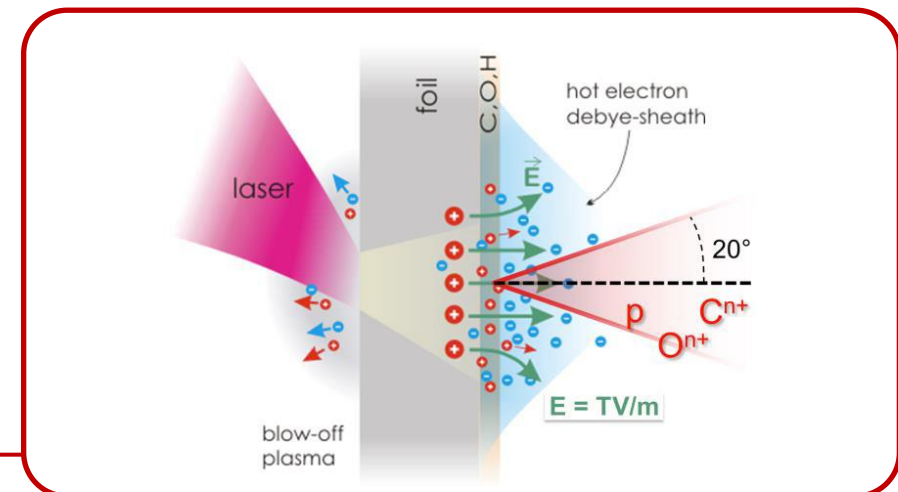
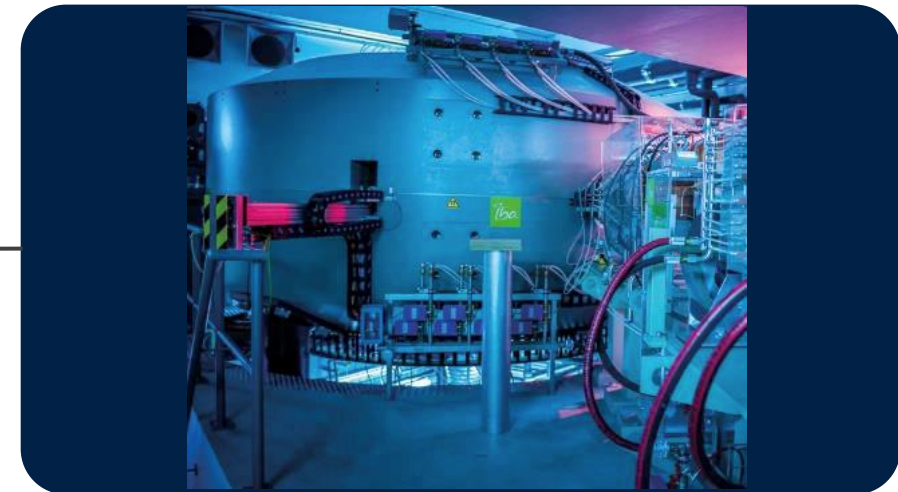
Laminar Emission & High Directionality

Low transverse emittance (< 0.01 mm·mrad) with virtual point-source origin inside solid foil.



Comparison with conventional acc.

	Laser-driven	Conventional
Acceleration length (m)	~ 1	$\sim 10^{-6}$
Energy distribution	Continuous (MB)	Quasi-Monoenergetic
Beam divergence	10s	0.1 – 1
Emittance (mm mrad)	0.002	0.5
Brightness (p^+ /pulse)	$10^9 - 10^{13}$	$10^7 - 10^9$
Duration (ps)	< 1	10^3
Source size (μm)	10 - 200	1000
Rep. Rate (Hz)	1 - 1000	10^7



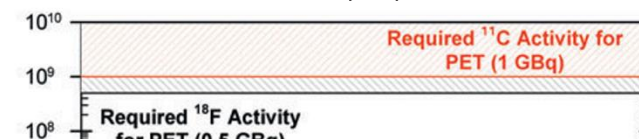
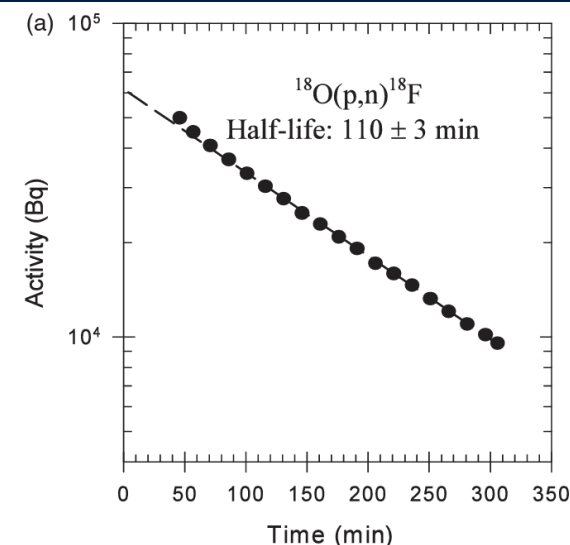
Producing ^{11}C from TNSA protons

First experiments on ^{11}C production

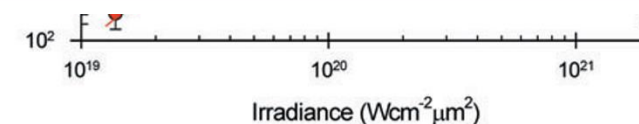
The idea of using laser-driven ions to generate radio-isotopes was proposed soon after acceleration was achieved (2001)

up to ~ 2 MBq / shot

- Pioneering studies by Ledingham et al. using the Vulcan laser (300J, 750fs)
- The activation achieved was 100 kBq/shot (^{18}F), and 2 MBq/shot (^{11}C), but the repetition rate was 1 shot/20 minutes, limiting the maximum achievable activation below the required levels.
- It was acknowledged that with the advent of **HRR systems**, activation levels useful for medical imaging could be achieved



References	E_L [J]	Rep. rate	^{11}C activity [kBq]
Spencer <i>et al.</i>	120	Single shot	200
Ledingham <i>et al.</i>	300	Single shot	3000
Fritzler <i>et al.</i>	1	Single shot	1.2
Tayyab <i>et al.</i>	2.4	Single shot	5.2



[KWD Ledingham et al., J. Phys. D., 37, (2004)]



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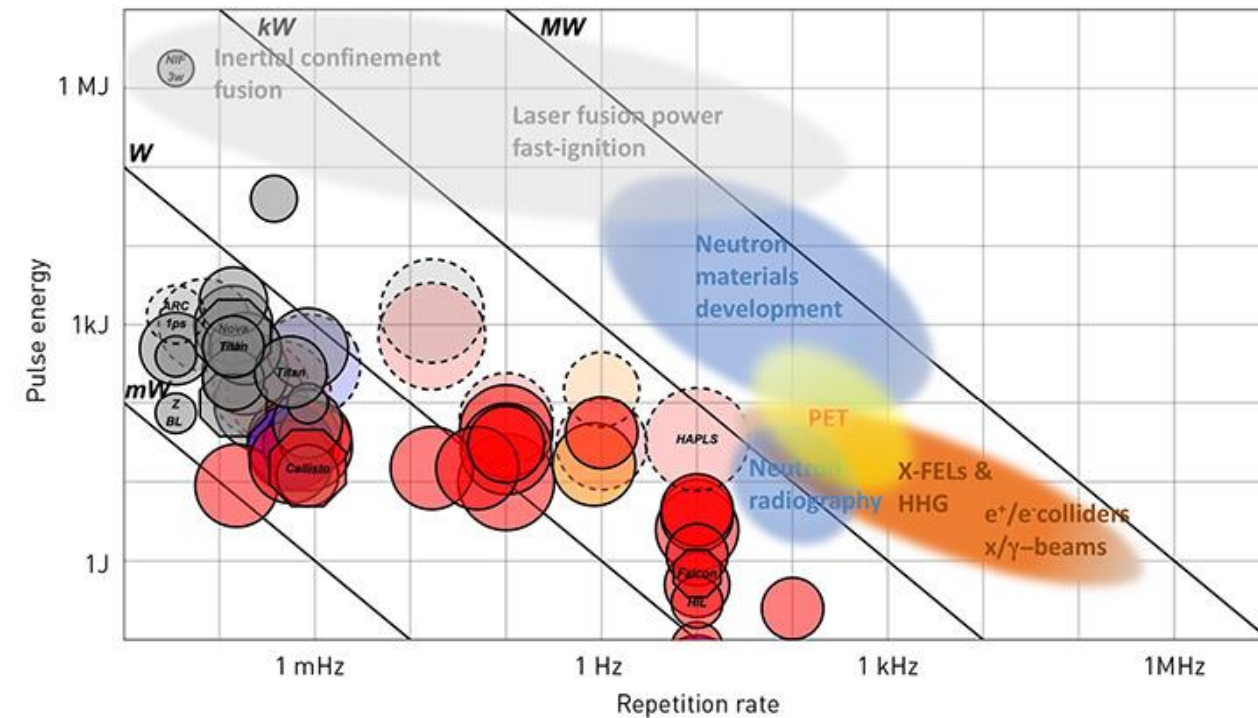
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Towards HRR accelerators

Accelerators @ Multi-Hz rates



- Historically, the repetition rate was limited by the laser operation to a shot every few minutes (Nd:glass)
- Introduction of Titanium:Sapphire lasers allowed to increase the repetition rate, starting with PW lasers capable of firing every 20 seconds.
- Laser technology has evolved to allow for continuous operation at 10s of TW at >10 Hz, and PW lasers operating at multi-Hz rates.
- **The bottleneck is now on the target operation.**



Accelerators @ Multi-Hz rates



Tape drives

Raster targets

Different groups are developing targets
compatible with high repetition rate operation

Liquid jets

Liquid crystals

Cryogenic ribbons

Near-critical
gas jets

Tape drive Systems



MECHANISM & OPERATION

Motorised spool-to.spool transport system advancing a thin ribbon between shots. Foil thickness typically on the scale of micrometers.

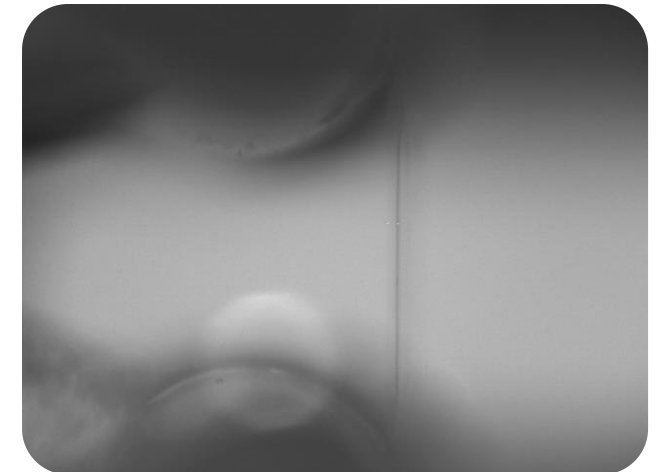
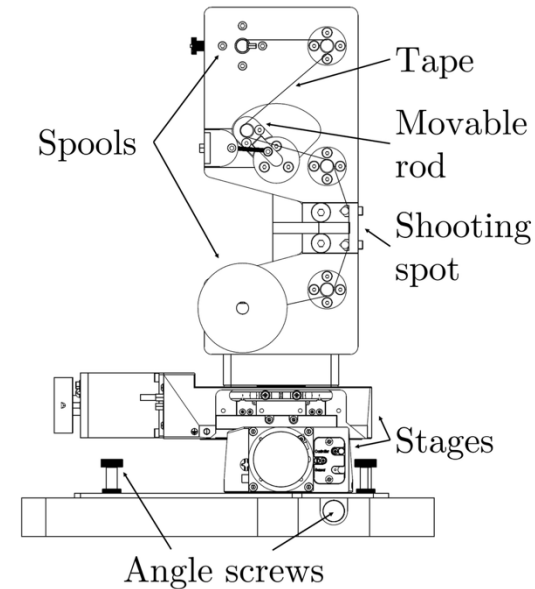
- Different tape materials can be used (Aluminium, Copper, Mylar, ...)
- Repetition rate limited by tape and motors
 - X-ray generation by Joule-class lasers up to 3Hz has been demonstrated
 - For ion acceleration, it has been shown up to 0.2Hz

✓ Key Advantages

- High solid density ($n_e \sim 10^{23} \text{ cm}^{-3}$)
- Proven high-energy proton yields (TNSA)
- Robust & Mechanically simple

⚠ Technical challenges

- Tape vibration affects focal position.
- Debris damages focusing optics
- Tape tensioning under vacuum



Target wheels



MECHANISM & OPERATION

A high-precision motorised disk featuring hundreds of micro-engineered thin foils or structured targets. Combines high-speed rotation with radial translation to irradiate fresh targets for each laser shot

- Capable of hosting 1000s of shots @ up to 10Hz operation
- Flexibility in terms of target material and thickness
- Manufacturing precision introduces significant deformation between regions, beyond the Rayleigh range of focusing optics

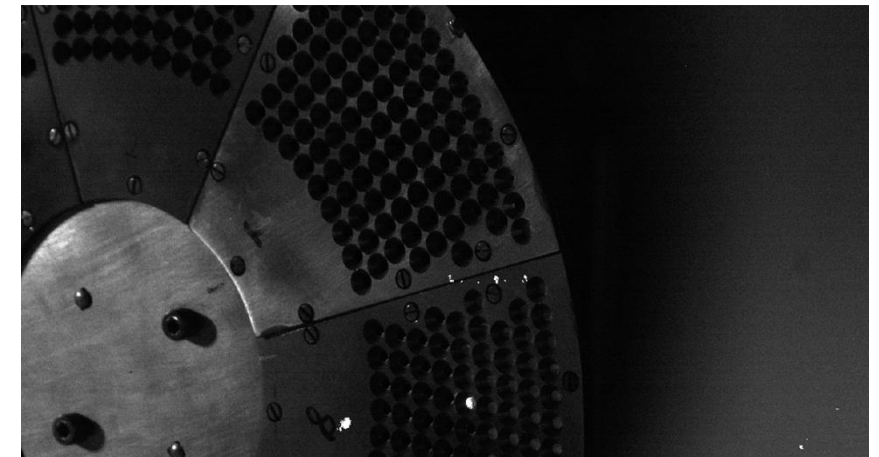
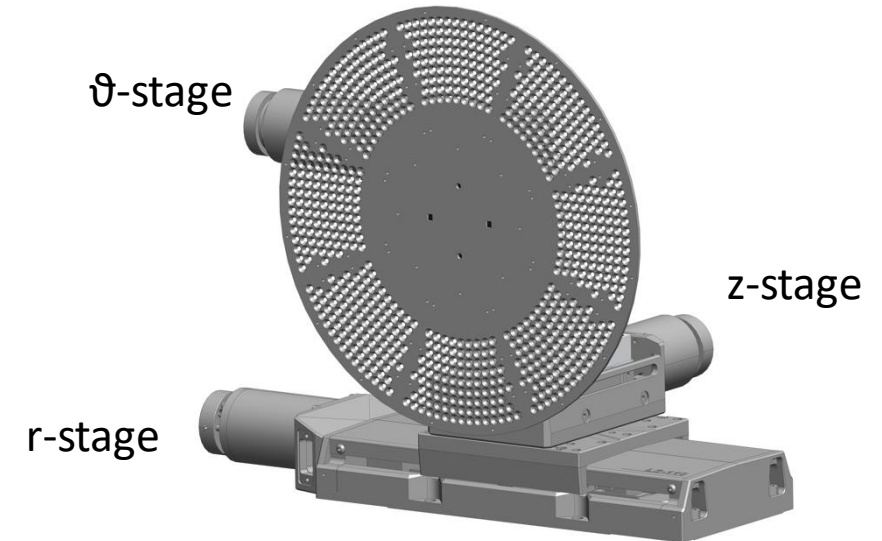
⇒ Individual target alignment is required

✓ Key Advantages

- High positioning accuracy (<5 μm)
- Supports complex structured μ -targets.
- Demonstrated operation @10Hz

⚠ Technical challenges

- Finite shot capacity per loading.
- Significant debris on nearby optics.
- Complex alignment encoding needed.



Liquid jets



MECHANISM & OPERATION

High-pressure liquid jets, colliding cylindrical fluid streams. (forming flat liquid sheets), or high-frequency micro-droplets.

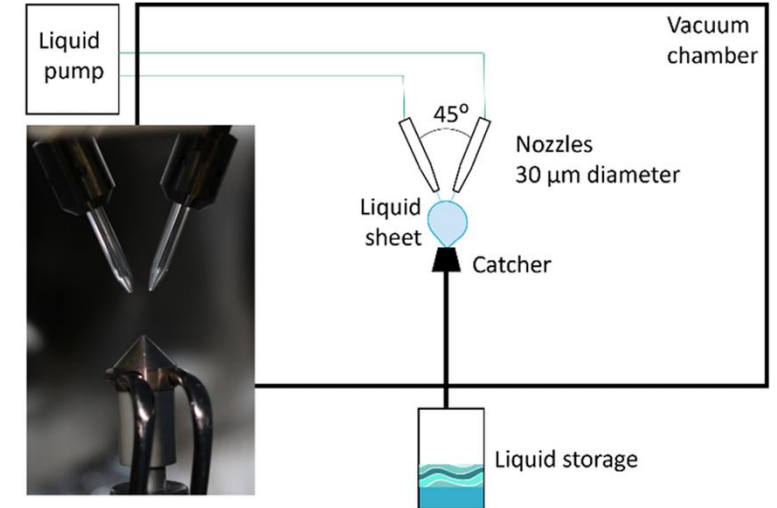
- 10s of μm jets are preferred to avoid nozzle clogging.
- Heated (70°C) catcher is required to collect water and prevent vacuum degradation.
- Thin sheets can be generated in a stable manner, surviving to irradiation.

✓ Key Advantages

- Potential for kHz-scale operation.
- Debris-free, extending optics' lifetime
- Self-healing liquid target interface

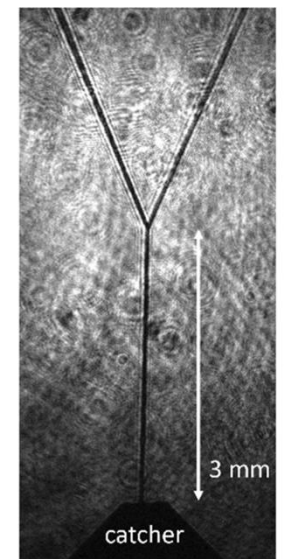
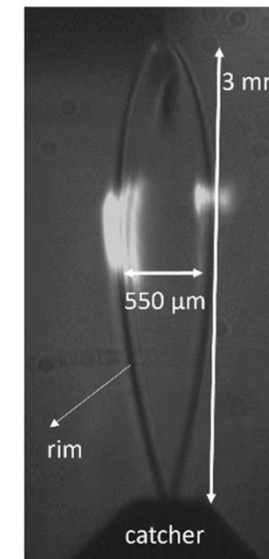
⚠ Technical challenges

- Vacuum degradation (vapour pressure)
- Requires differential vacuum pumping
- Sheet thickness control ($>1\mu\text{m}$)



a) 15° shadowgraphy

b) 90° shadowgraphy



Near-critical gas jets



MECHANISM & OPERATION

High-pressure Supersonic nozzles firing dense pulses of gas (typically H_2 or He), ionised to near-critical density ($\sim 10^{21}\text{cm}^{-3}$). Triggers volumetric Acceleration mechanisms (Shock Wave Acceleration, ...)

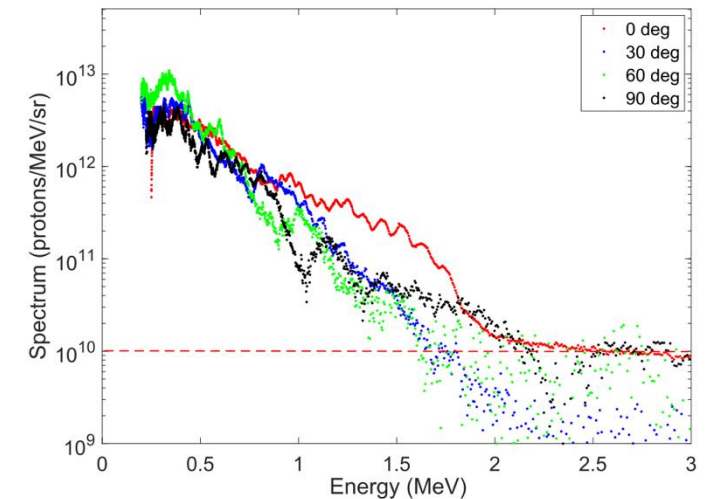
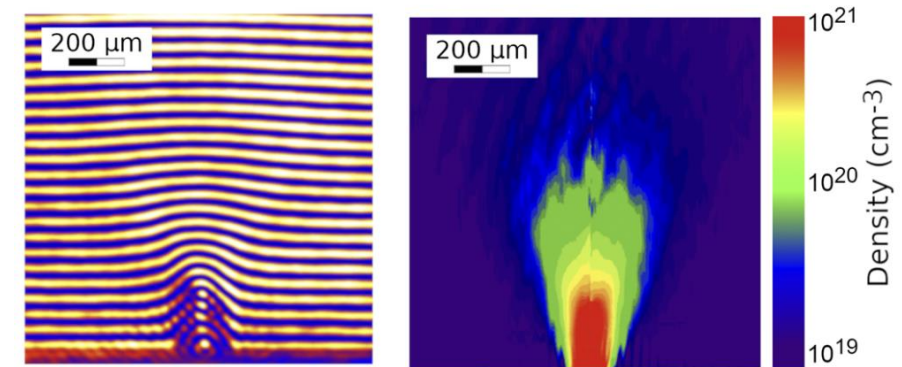
- Great interest in designing gas jets with backing pressures as high as 1000bar
- Experimental demonstration of required densities (close to the nozzle!)
- First experiments show ion acceleration from these gases to MeV energies

✓ Key Advantages

- 100% Debris-free
- Scalable to kHz rate operation
- Potential for narrow energy spread

⚠ Technical challenges

- Lower density limits cutoff
- High gas load on vacuum pumps
- Sharpening density gradients required



Cryogenic ribbons



MECHANISM & OPERATION

Continuous *in-situ* cryogenic extrusión of solid hydrogen or deuterium ribbons at 10–20 K. Delivers solid density while ensuring zero heavy element contamination (pure proton source)

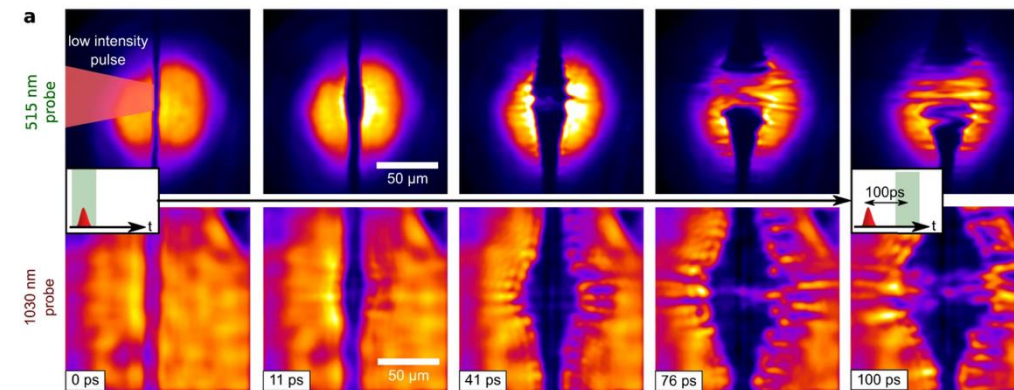
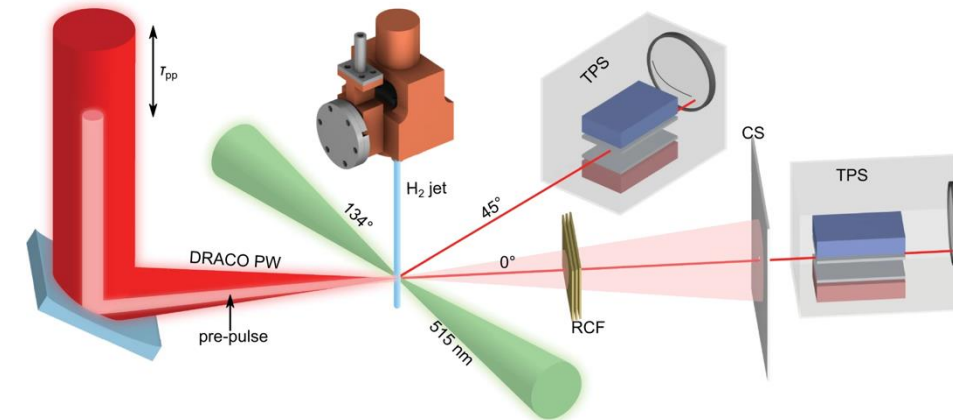
- Solution particularly interesting due to the production of high purity ion sources, instead of multi-species.
- Extremely complex system, mainly explored by groups with long-standing experience in cryogenic systems.

✓ Key Advantages

- Pure H⁺/D⁺ source.
- Real solid density ($n_e \sim 10^{22} \text{ cm}^{-3}$)
- Negligible debris (evaporation)

⚠ Technical challenges

- Complex cryogenic UHV engineering
- Thermal load & ribbon mechanical drift
- Extrusion speed limitations



Comparison of targets



Target type	$n_e(\text{cm}^{-3})$	Debris risk	Max rep rate (Hz)	Primary challenge
 Tape drive	$\sim 10^{23}$	High	1 – 10	Tape vibration, z-alignment
 Target wheel	$\sim 10^{23}$	High	1 – 10	Shots per loading
 Liquid jets	$\sim 10^{22} - 10^{23}$	Low	10 – 1000	Vapour pressure
 Gas jets	$\sim 10^{21}$	Zero	10 – 1000	Lower cutoff energies
 Cryo ribbons	$\sim 10^{22} - 10^{23}$	Negligible	<1	Cryo-UHV complexity



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Preclinical ^{11}C production

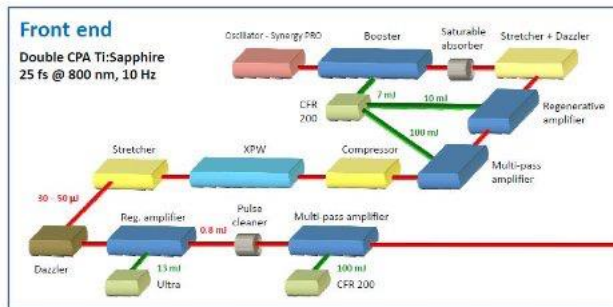
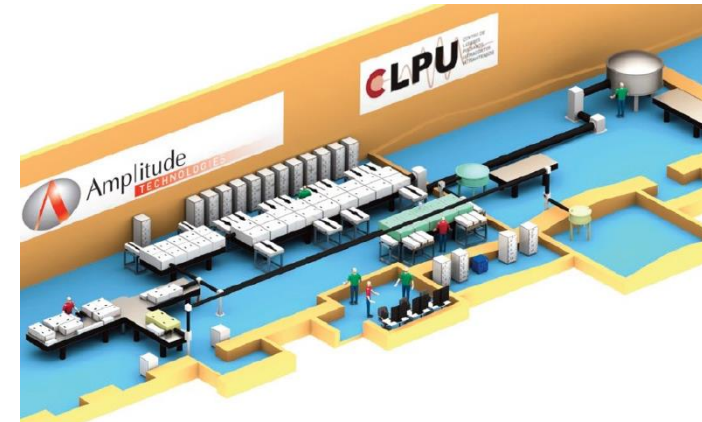
Recent results @ CLPU



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VEGA-1 (20TW)

VEGA-2 (200TW)

VEGA-3 (1PW)

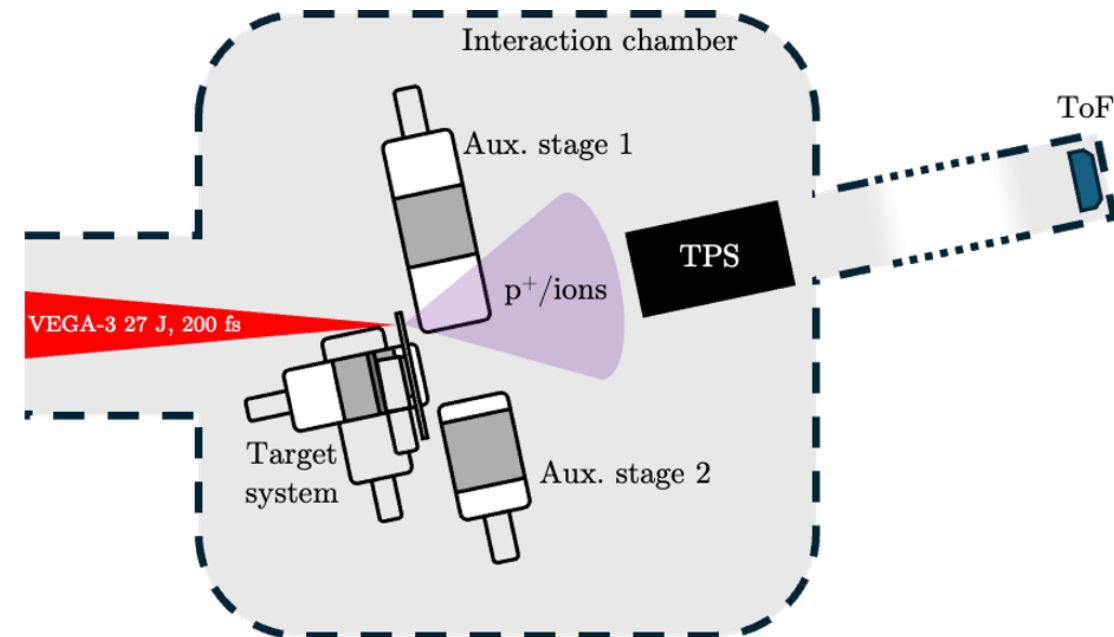
The experiment



EXPERIMENTAL CAMPAIGN

Demonstration of continuous proton acceleration at rates up to 1 Hz, and its application to production of Carbon-11

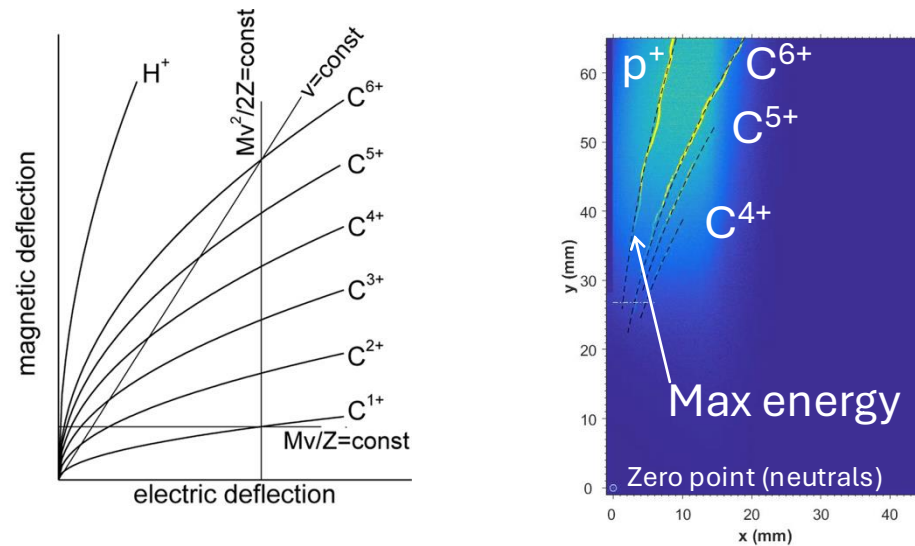
- Focused laser energies up to 25 J, using pulse durations between 30 fs and 200 fs, focussed onto the target using an f/11 OAP.
- Ion beams characterised using RCF stacks, TPS, and ToF.
- Due to the extreme EPM, all stages were physically disconnected from the controller during the laser irradiation.
- Stable target operation shown at up to 1 Hz (also demonstrated at up to 10 Hz at L2A2 (50 TW – Santiago de Compostela, Spain))



Main ion diagnostic: TPS

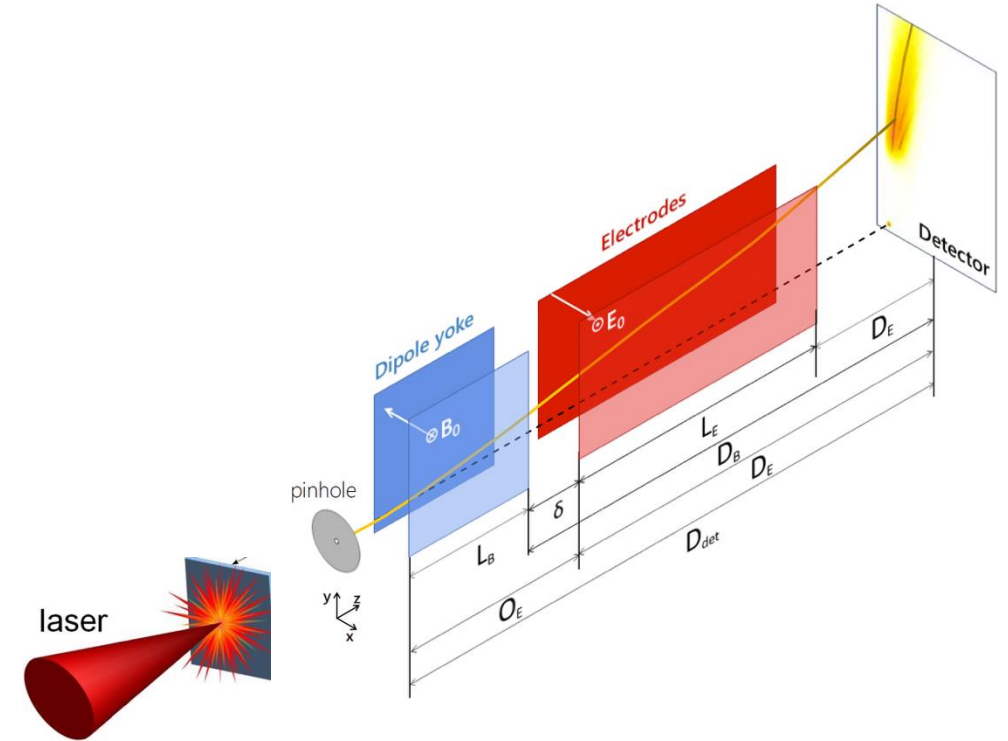
Thomson Parabola Spectrometer

Diagnostic for ion beams using parallel electric and magnetic fields, separating ion species depending on their charge-to-mass ratio



$$x = \frac{\gamma}{\gamma^2 - 1} \frac{qE_0 L_E}{mc^2} (D_E + L_E/2) ,$$

$$y = \frac{qB_0 L_B}{mc\sqrt{\gamma^2 - 1}} (L_B/2 + D_B) ,$$



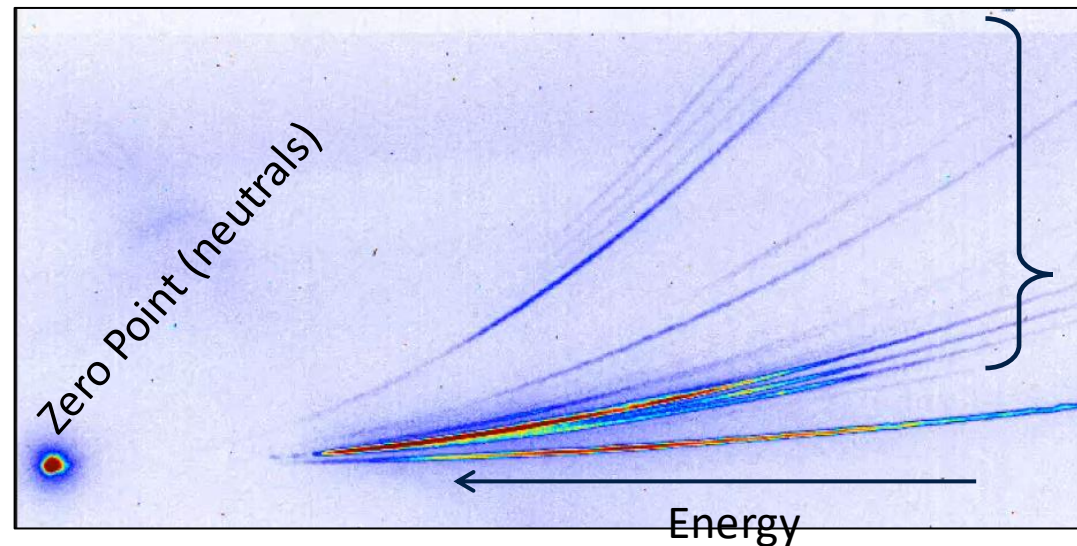
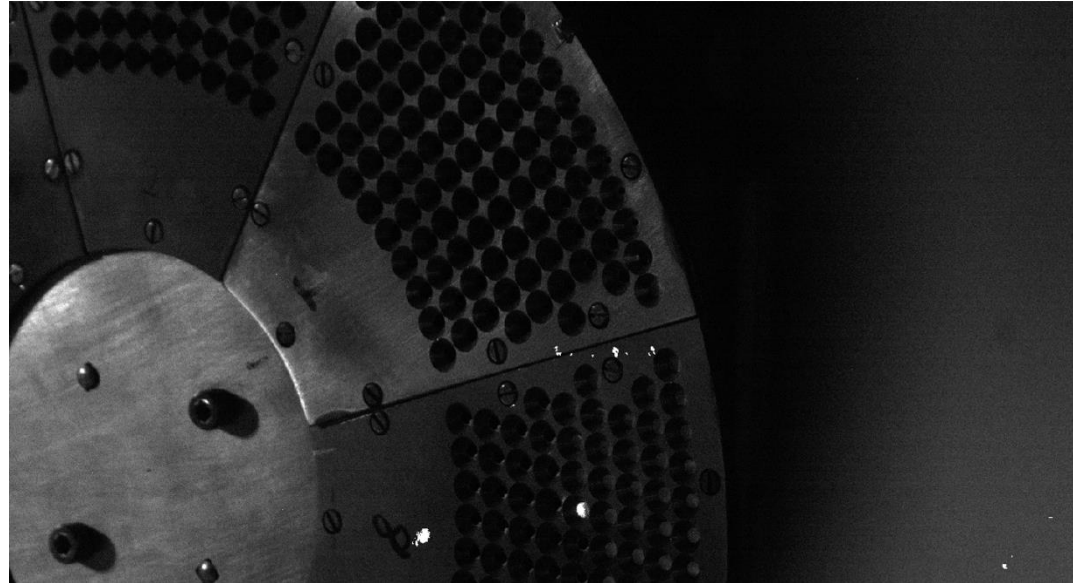
Ion acceleration @ 0.1Hz



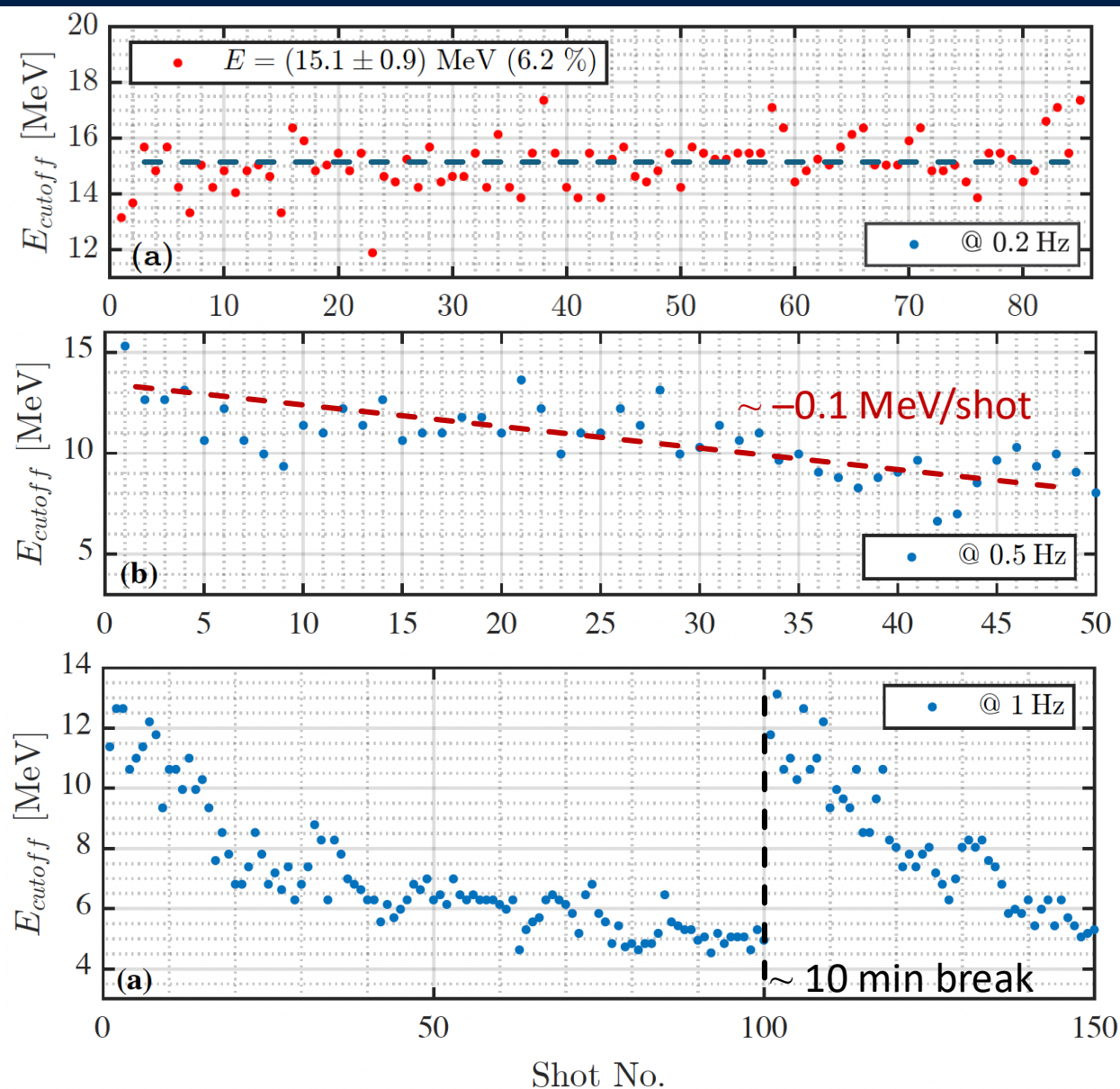
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Stability of the acceleration



0.2 Hz – Stable

Stable proton acceleration for hundreds of shots, with a cut-off energy of $15.1 \pm 0.9 \text{ MeV} (6.2\%)$.

0.5 Hz – Slow degradation

As the shooting rate increases, the cut-off energies degrade, reaching lower values as the number of shots increases.

1 Hz – Rapid degradation

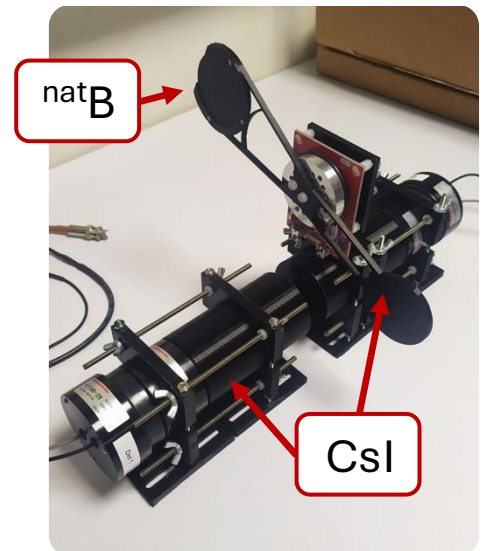
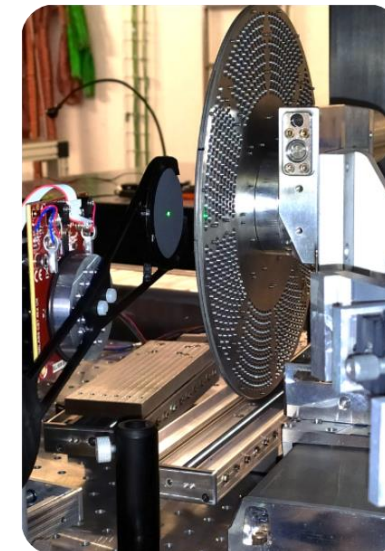
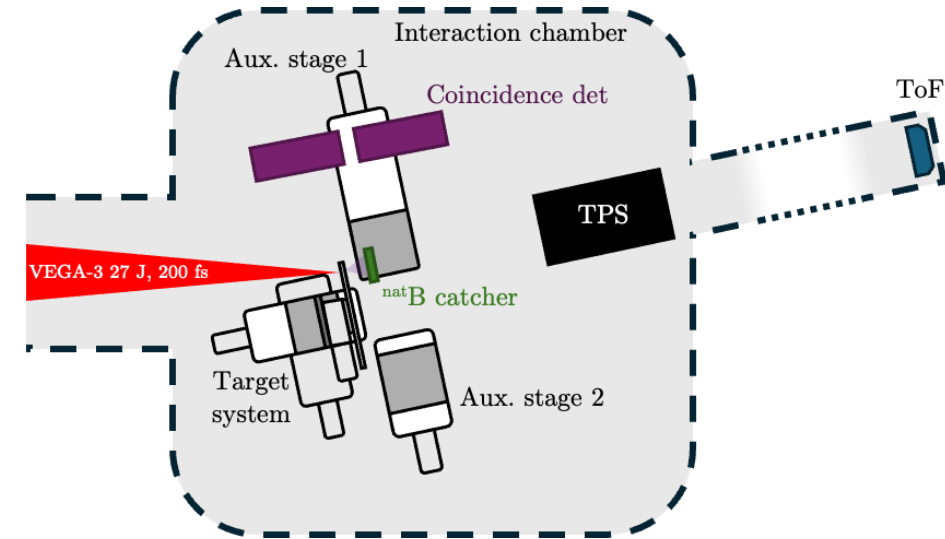
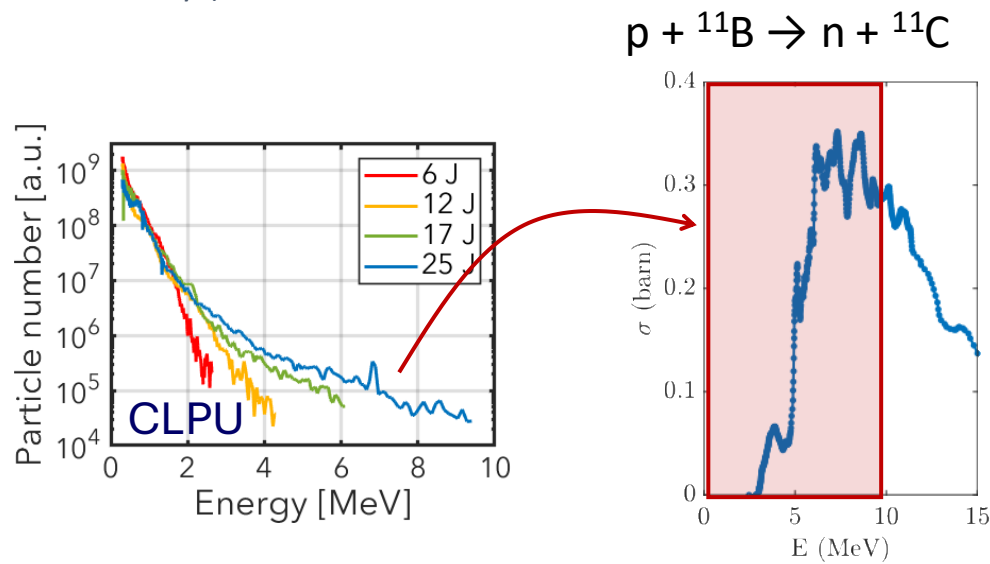
For irradiations at the maximum available rate (1 Hz), the worsening of the acceleration becomes more apparent. Following investigations, this is caused by **degradation of laser operation rather than target operation**

Comparison with conventional acc.

EXPERIMENTAL CAMPAIGN

Demonstration of continuous proton acceleration at rates up to 1 Hz, and its application to production of Carbon-11

- Natural boron was irradiated to produce ^{11}C .
- Developed a compact setup to enable irradiation of an activation sample and measure its activity in vacuum conditions (no need for let-up).
- Measurements based on coincidence detection (only measurements of β^+ decays)



Preliminary test

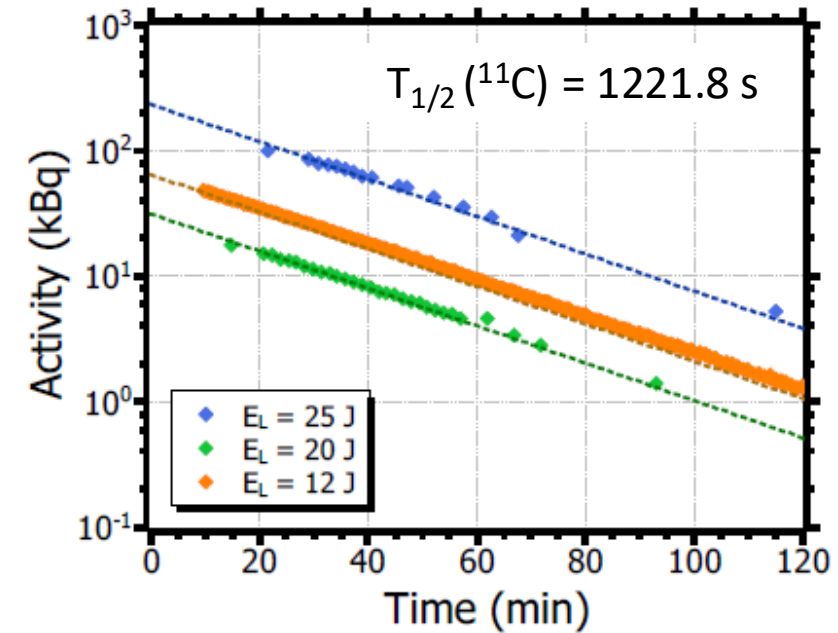
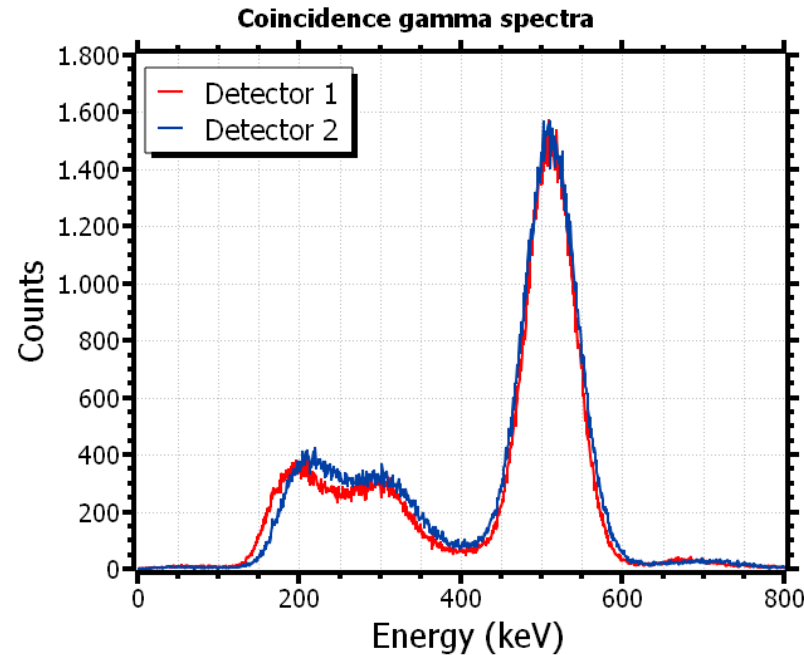


PoP Demonstration

→ Demonstrated continuous ^{11}C production in multi-shot operation (20 shots at 0,1 Hz).

→ Reproduced the half-life of ^{11}C .

→ Achieved activities above 10 kBq per shot.



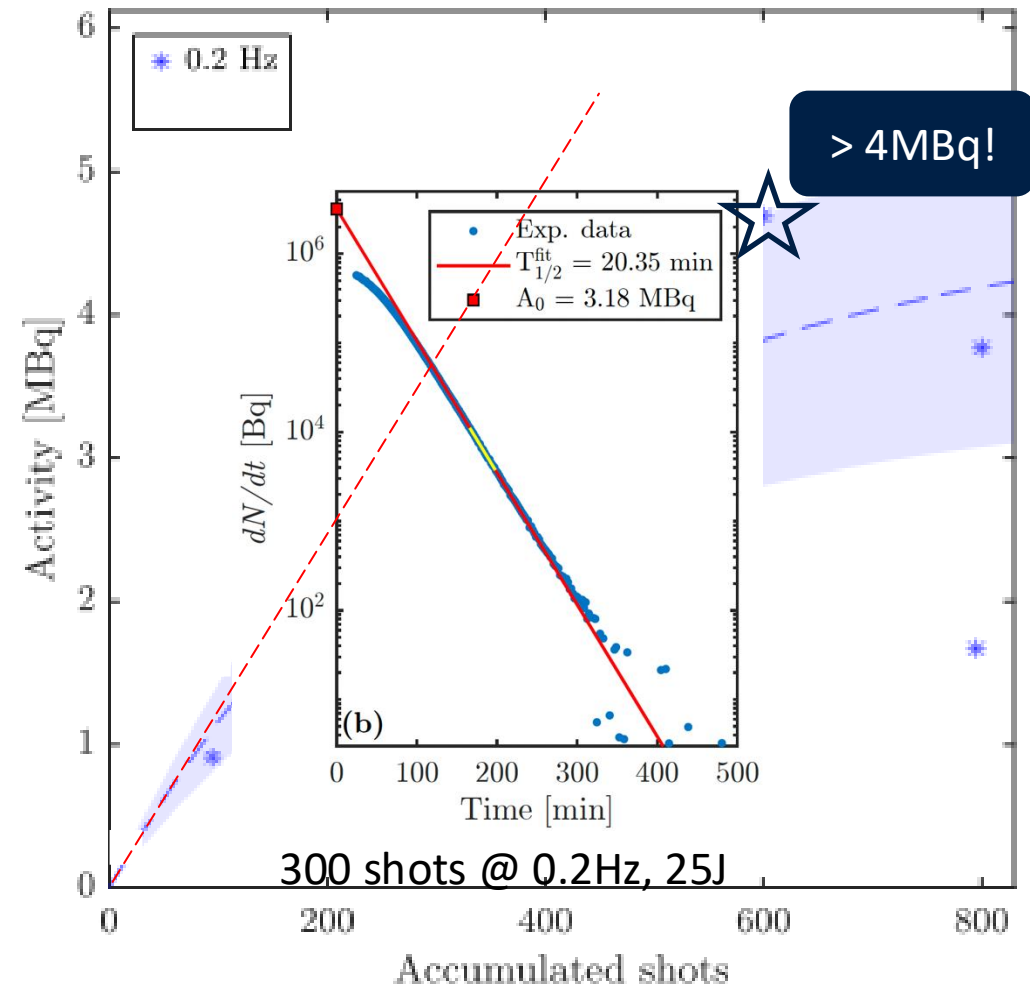
Laser energy [J]	Repetition Rate [Hz]	# shots	Activity per shot [kBq]	Total activity [kBq]
12	0,2	40	1.8	68.6
20	0,1	10	3.2	31.5
25	0,1	20	12.4	233.8

Pre-clinical activities of ^{11}C



Demonstration of production of preclinical activities of ^{11}C using a HRR laser system

- Demonstrated > 4 MBq production from accumulation of 600 shots.
- At 0.2 Hz, the trend follows the expected dependence of the activity produced on the number of shots.
- Although 1 Hz operation should have generated higher activities, the drop in laser performance resulted in a saturation of the maximum activity produced.



The problem with debris



MECHANISM & OPERATION

A high-precision motorised disk featuring hundreds of micro-engineered thin foils or structured targets. Combines high-speed rotation with radial translation to irradiate fresh targets for each laser shot

- Capable of hosting 1000s of shots @ up to 10Hz operation
- Flexibility in terms of target material and thickness
- Manufacturing precision introduces significant deformation between regions, beyond the Rayleigh range of focusing optics

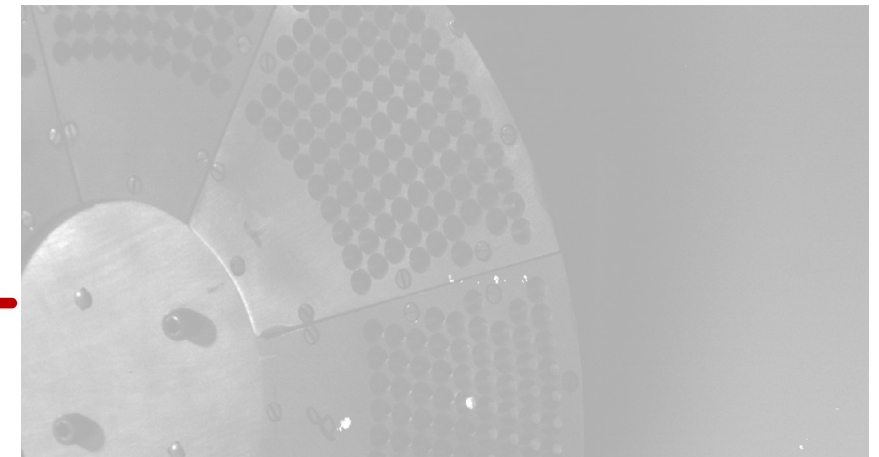
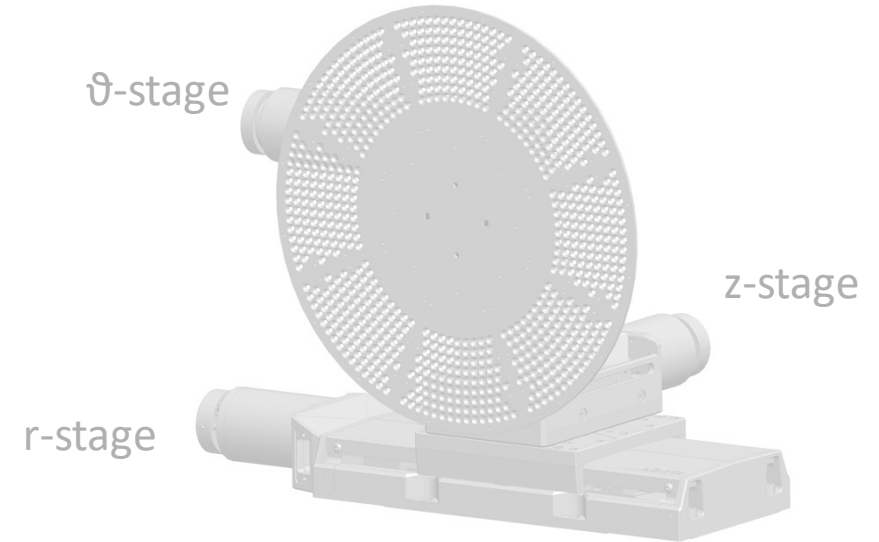
⇒ Individual target alignment is required

✓ Key Advantages

- High positioning accuracy ($<5 \mu\text{m}$)
- Supports complex structured μ -targets.
- Demonstrated operation @10Hz

⚠ Technical challenges

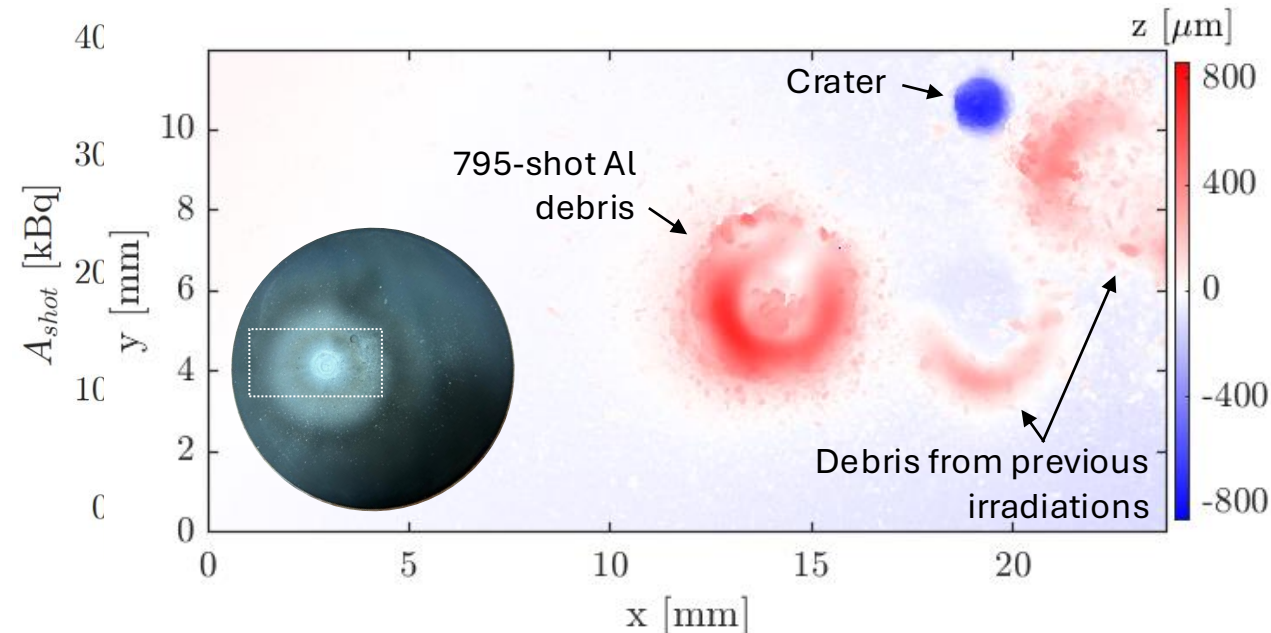
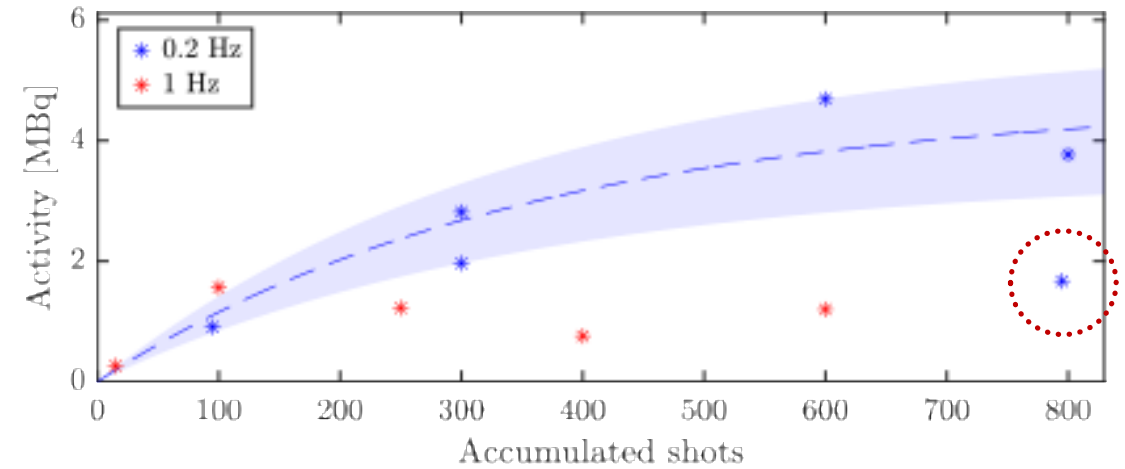
- Finite shot capacity per loading.
- Significant debris on nearby optics.
- Complex alignment encoding needed.



The problem with debris



- We struggled to reproduce numerically the trend we observe for the activity, especially some points.
- Post analysis of the boron catcher surface using a confocal microscope shows debris deposition up to $>800\mu\text{m}$! Estimated $0.8\mu\text{m}/\text{shot}$.
- Protons are slowed down (even stopped) within this layer, modifying the spectrum reaching the catcher.
- Numerical calculations of activity produced considering the initial spectrum and its evolution due to debris match the observations.
- Activity per shot was actually **30-50 kBq/shot** initially!





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Clinical production

A clinically relevant accelerator



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10 Hz

Optimum repetition rate

100 TW

Compact, commercial system

N₂

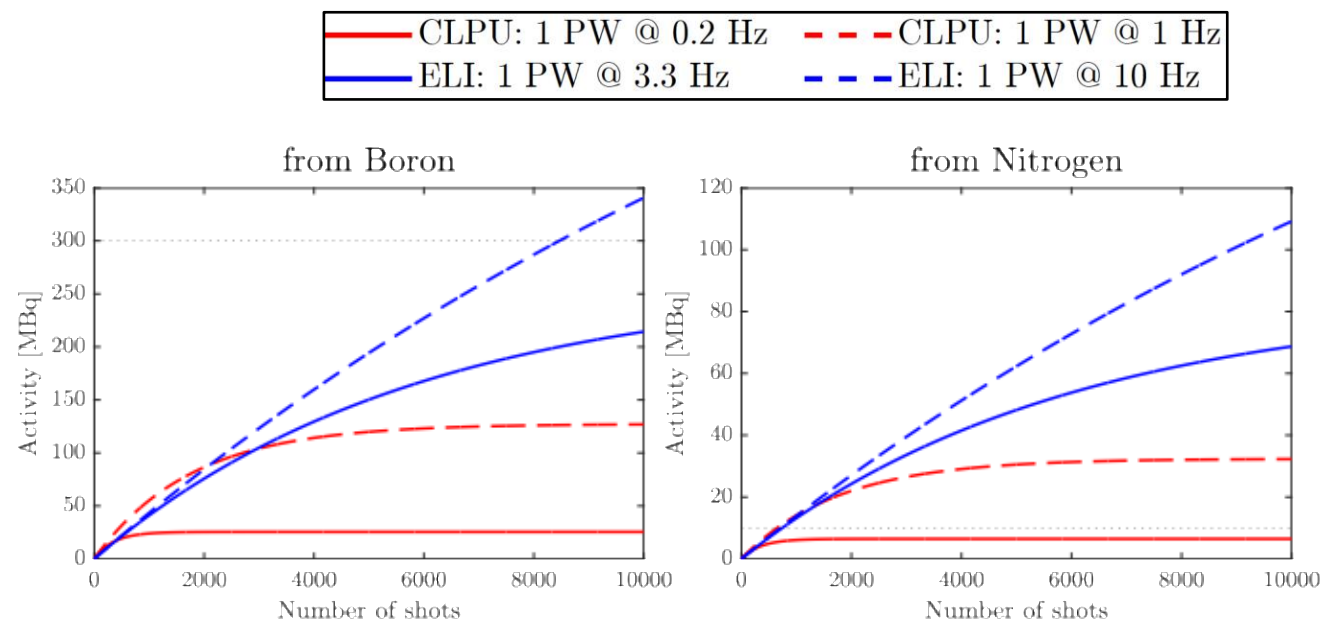
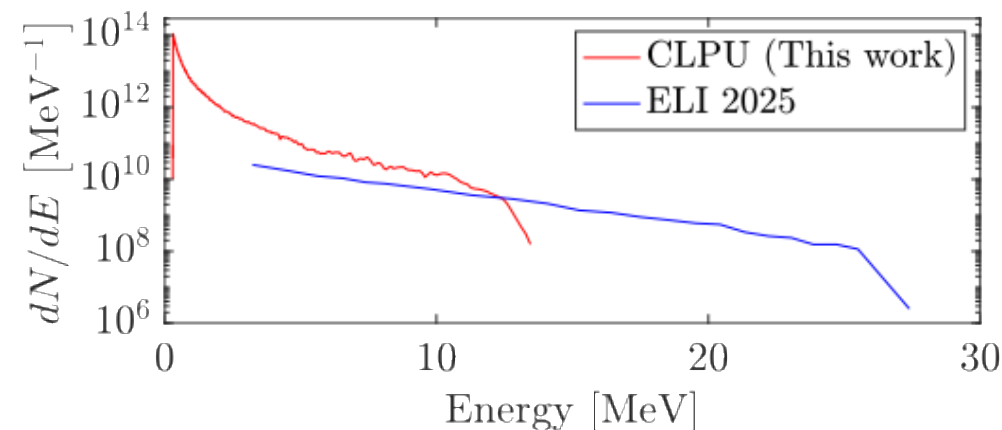
Nitrogen activation sample

Near-future perspective

Feasibility of clinical activities using real-life targets?

- Clinical imaging requires activities on the order of 100s of MBq
- Using a boron solid sample is simple, but real-life production is based on the use of nitrogen

- Now that the simulations can reproduce the experimental results, we can simulate activities achieved under ideal conditions: higher repetition rates and debris mitigation.
- Focus here: CLPU up to 1 Hz, ELIMAIA up to 10 Hz.
- Levels corresponding to clinical studies of ^{11}C can be achieved at ELI @ 3.3Hz irradiating boron
- On the path to clinical production using N_2 as catcher, the preferred route to extract the isotopes, but with higher energy threshold.

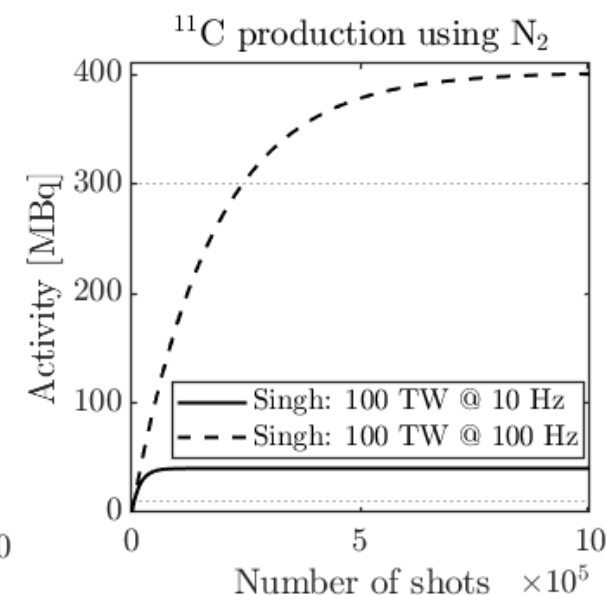
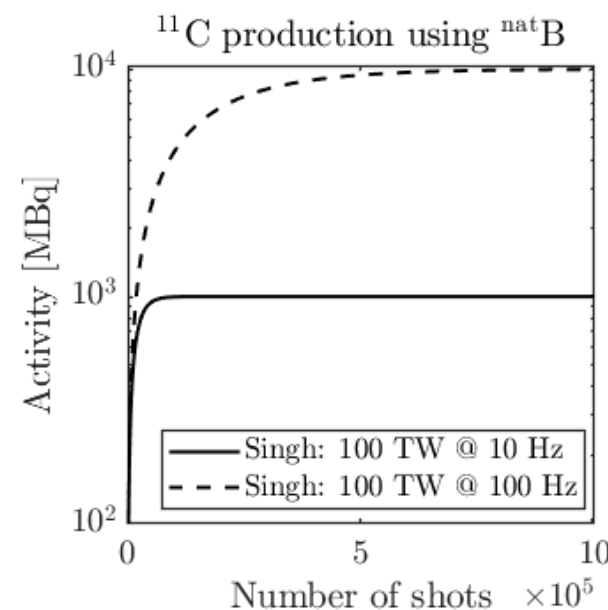
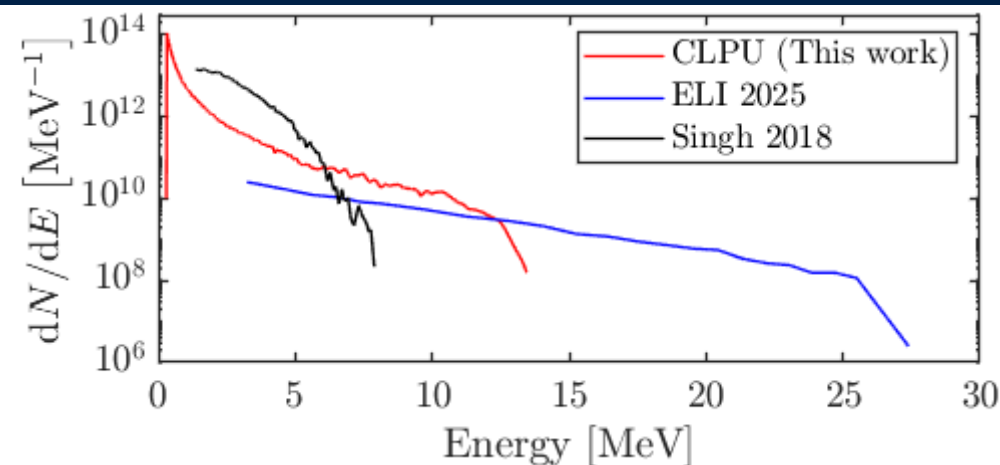
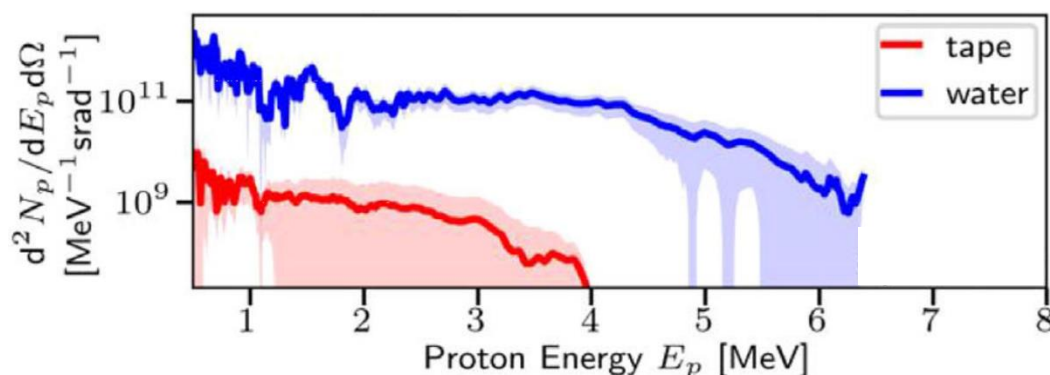


Compact systems

Can we use compact (<100TW) systems?

Not realistic to deploy PW-class lasers in hospitals, instead compact comercial systems should demonstrate their viability.

- High-flux proton beam reported using a 100 TW system by improving the laser contrast (Singh at al. Physics of Plasmas 25.11 (2018)).
- Clinical activity achievable through accumulation of thousands of shots at HRR.
- Strong increase on beam charge reported using a water jet target with 200 mJ pulses (Streeter et al. Nat Comms 16.1 (2025)).





IGFAE

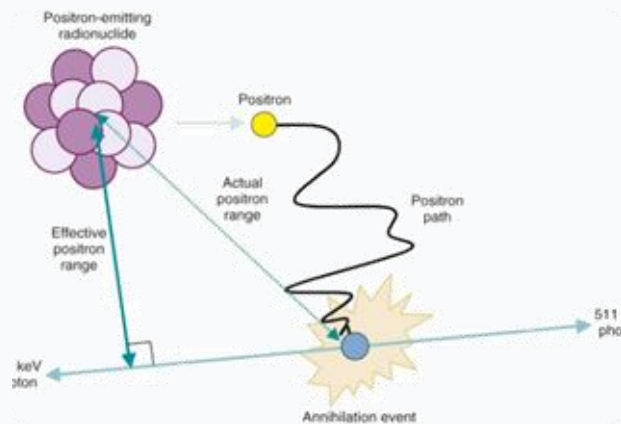
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Summary

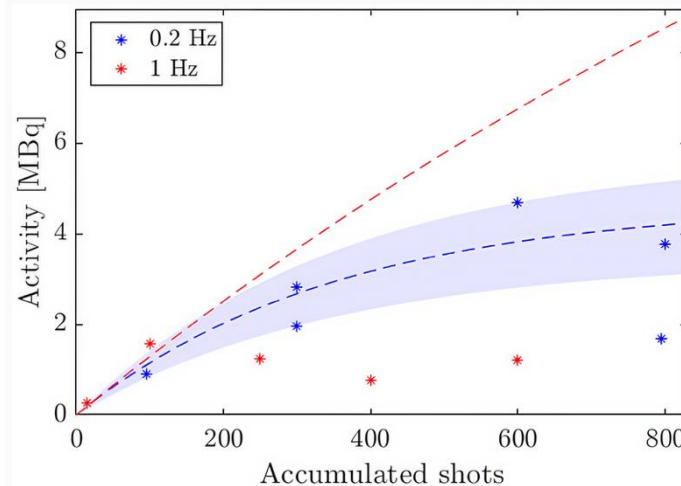
^{11}C & PET

PET is a powerful medical imaging technique, and compact laser-based accelerators can be an enabling technology.



Preclinical

Thanks to developments in laser technology and target systems compatible with multi-Hertz operation, production of preclinical activities has been demonstrated.



Clinical

Clinical activities are within reach using systems already available, and even potential for more compact systems.

