Plasma accelerator applications II: photon science, medical

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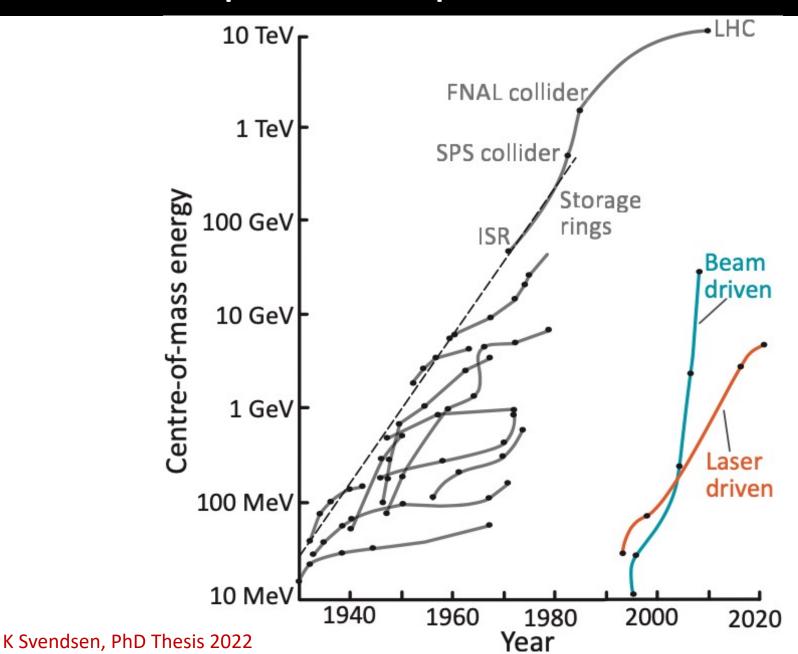
Bad Honnef Physics School on Plasma Acceleration 5-10 February 2023







Development of particle acceleration



Why particle accelerators matter



Discovery Science

Particle accelerators are essential tools of discovery for particle and nuclear physics and for sciences that use x-rays and neutrons.



Medicine

Tens of millions of patients receive accelerator-based diagnoses and therapy each year in hospitals and clinics around the world.



Industry

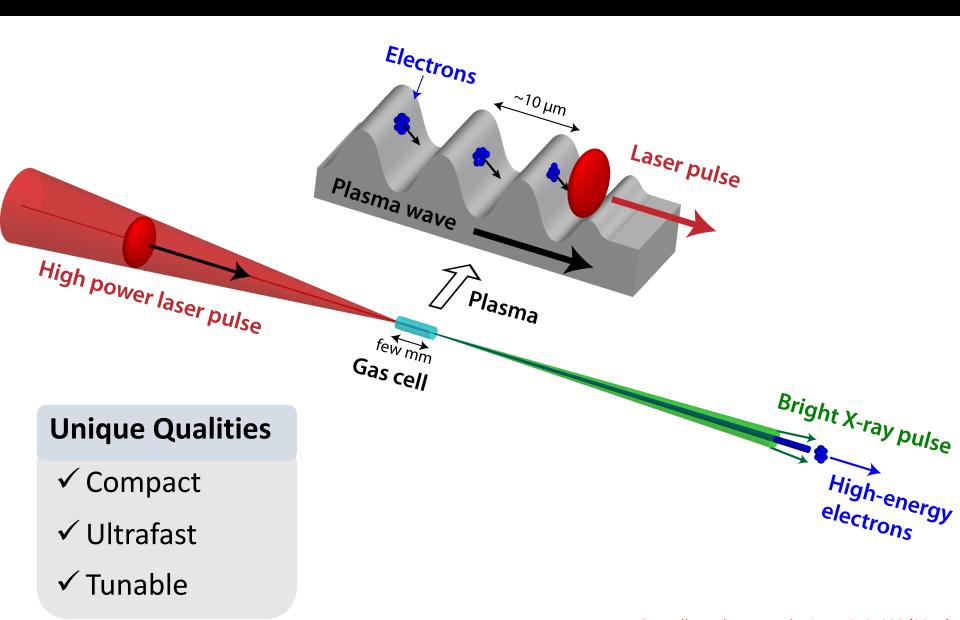
Worldwide, hundreds of industrial processes use particle accelerators – from the manufacturing of computer chips to the cross-linking of plastic for shrink wrap and beyond.



Security

Particle accelerators play an important role in ensuring security, including cargo inspection and materials characterization.

Laser-plasma acceleration and X-ray generation



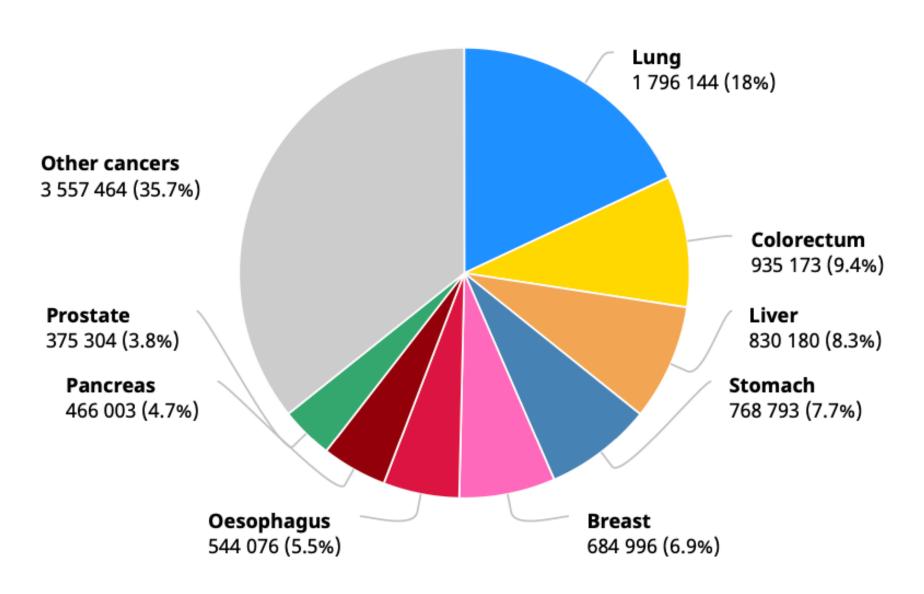
Outline

Laser-accelerated electron beams for radiotherapy

Betatron X-rays for imaging and spectroscopy

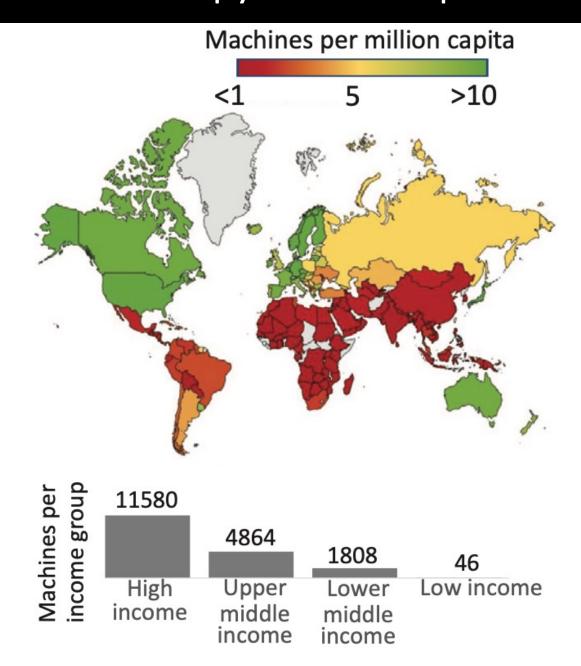
Other light sources based on plasma accelerators

Number of deaths in 2020, both sexes, all ages



Total: 9 958 133 deaths

Number of radiotherapy machines per million citizens



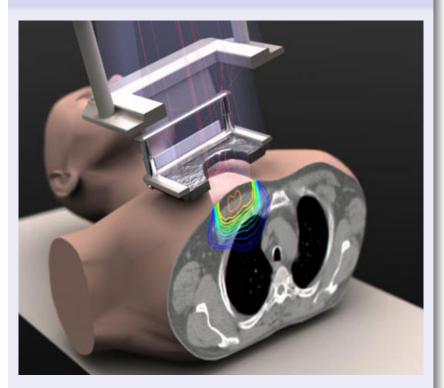
External beam radiotherapy

Clinical oncology machine



- 5-20 MeV electron beam
- X-rays by bremsstrahlung

Direct electron irradiation



- Electrons have limited range
- Underlying structures spared

Stopping power and dose

Low energy electrons primarily lose energy through **collisions** which leads to **ionization** and **excitation**. Contributes to the dose **near the track**.

High-energy electrons primarily lose energy by **radiation** (**bremsstrahlung**). Energy spent is **carried away** from the track by photons.

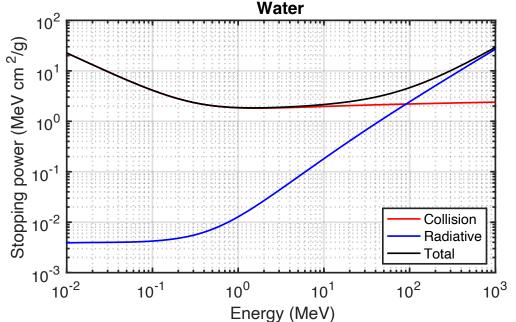
The stopping power is the mean rate of energy loss

$$S(x) = -\frac{dE}{dx}$$

The locally deposited dose is

$$D(x) = \Phi \frac{S_{col}(x)}{\rho}$$

where $\boldsymbol{\Phi}$ is the particle flux density



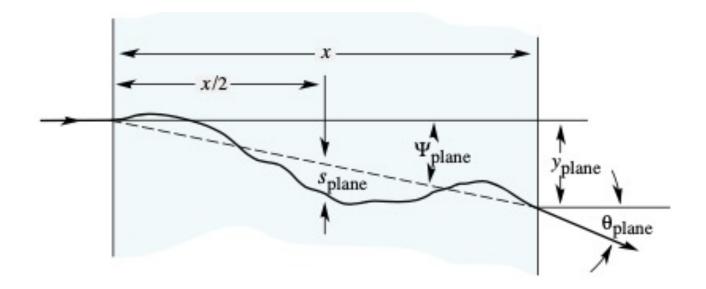
The databases ESTAR, PSTAR, and ASTAR calculate stopping-power and range tables for electrons, protons, or helium ions for many different materials: https://www.nist.gov/pml/stopping-power-range-tables-electrons-protons-and-helium-ions

Multiple scattering

Multiple collisions and radiative interactions lead to

- 1. Secondary low-energy particles
- 2. Multiple scattering

of the primary particles. Multiple scattering leads to an increased beam divergence and a wider dose distribution



Monte-Carlo simulations

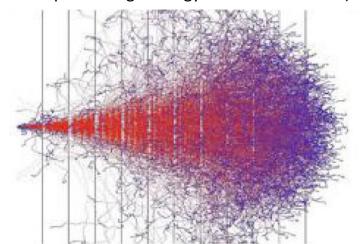
Simulates the passage of particles through matter invoking relevant physics

Particles and interaction physics are modelled using probability distributions

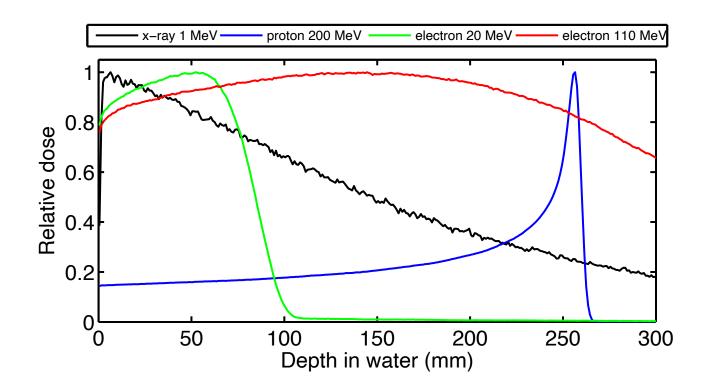
Used in radiotherapy and dosimetry to model the interactions between radiation and human tissue, and to predict the distribution of radiation dose within the patient's body.

Examples of codes

- PENELOPE (Physically-Based Simulation of Electron and Photon Transport)
- GEANT4 (Simulation toolkit for particle physics)
- MCNP (Monte Carlo N-Particle)
- FLUKA (Fluctuation and Transport of High Energy Particles in Matter).



Dose deposition for different particles

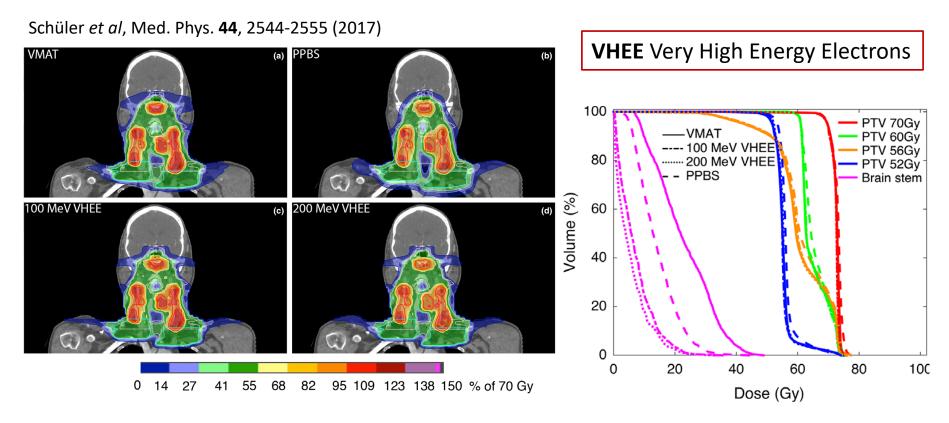


Low energy electrons < 20 MeV widely used for superficial tumours

High energy electrons > 100 MeV not yet available in hospitals

Can high-energy electrons be useful for radiotherapy?

Potential advantage of high energy electrons



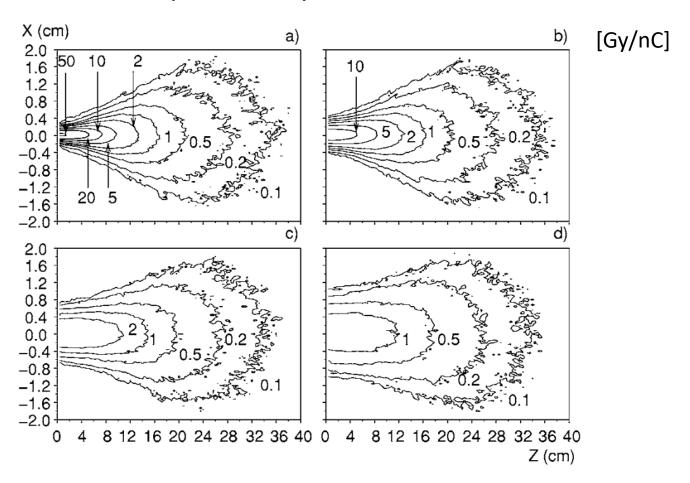
Compared to X rays (IMRT, VMAT), high-energy electrons (100-200 MeV) can give

- Similar coverage of the target volume
- Better sparing of critical structures and organs at risk

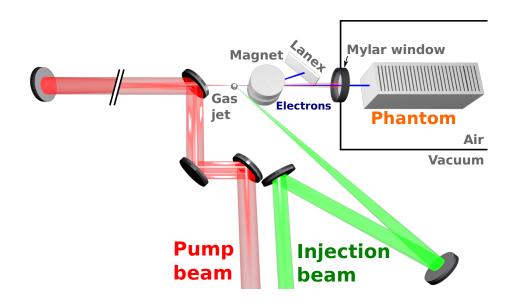
Can plasma accelerators provide such beams?

Isodose curves for laser-accelerated electrons

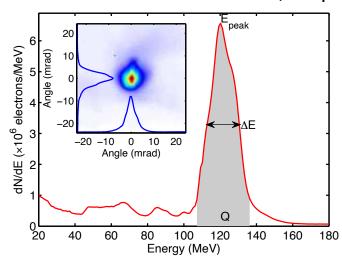
Monte-Carlo simulation study in GEANT4 Dose deposition by 170 MeV electrons



Experimental setup



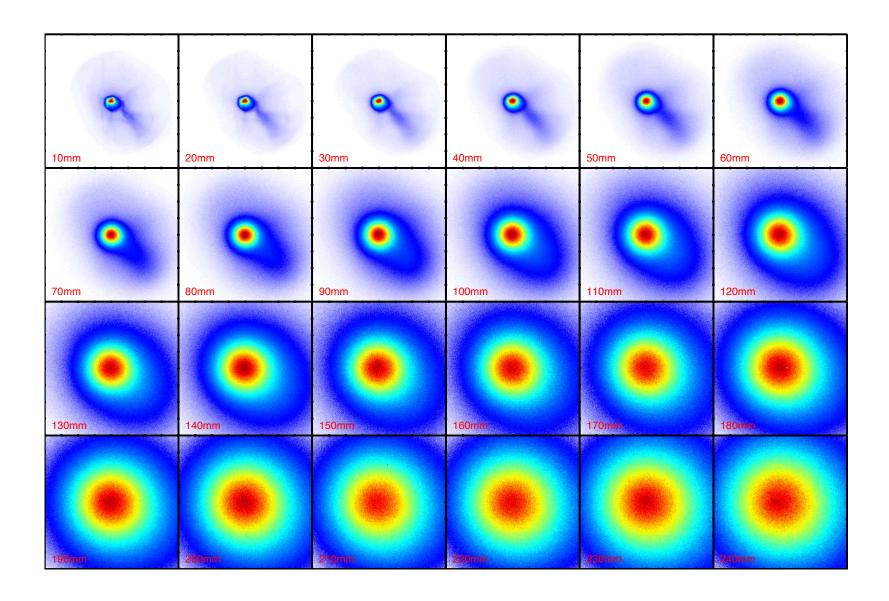
Electron beam: 120 MeV; 30 pC



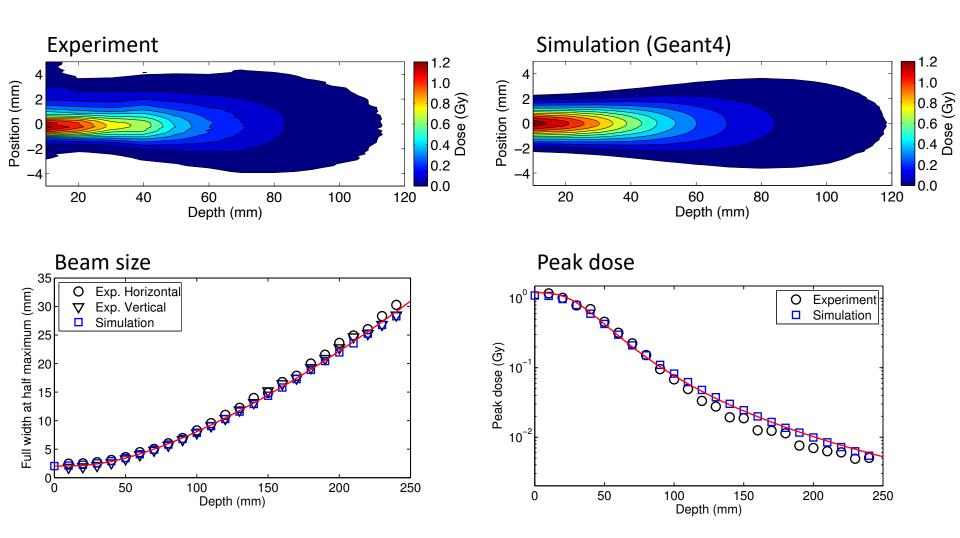


Blocks of polystyrene (10 mm) + Fuji film detectors (40x40 mm²)

Measured dose profiles

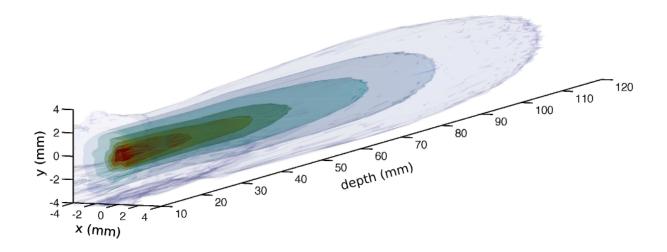


Comparison to simulation



Lundh et al, Medical Phys. 39, 3501-3508 (2012)

Laser-accelerated VHEE's for radiotherapy?



Treatment plan

Total treatment dosage: 20-80 Gy

Fractional daily dosage: 2 Gy/day

Laser-plasma beam

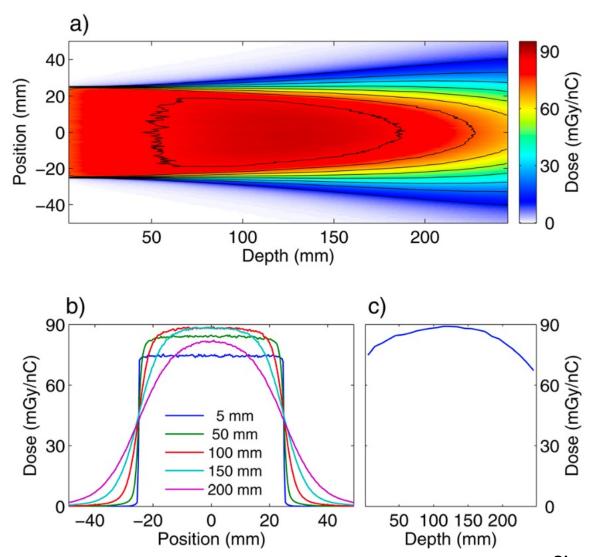
1 Gy/shot over 2x2 mm²

200 shots (20 s): 2 Gy over 20x20 mm²

Reasonable numbers

Broad irradiation field

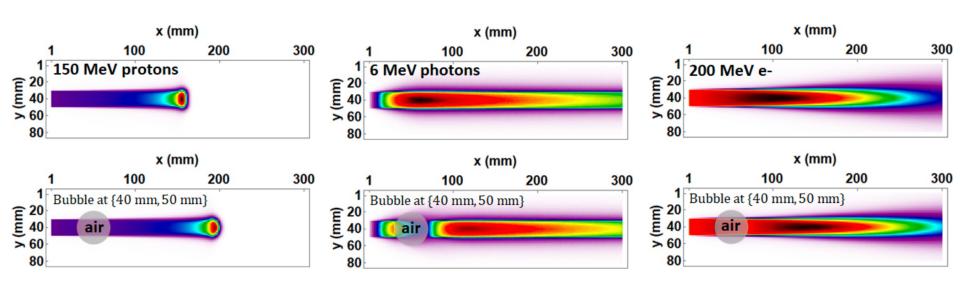
Lateral scattering is mitigated when using a broad irradiation field



Simulation in GEANT4

Impact of inhomogeneities

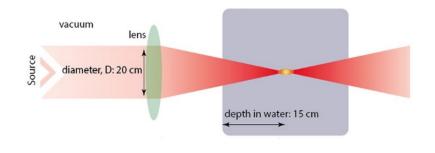
- Inhomogeneities (air bubbles, bone, etc.) can negatively impact the dose delivered compared to the dose plan.
- This simulation study shows that the dose deposition by high-energy electrons is less sensitive to inhomogeneities when compared to protons and x-rays. This effect is also confirmed by dose measurements.

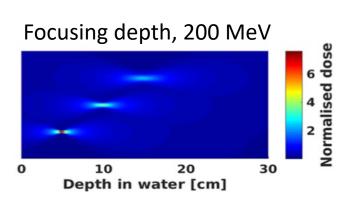


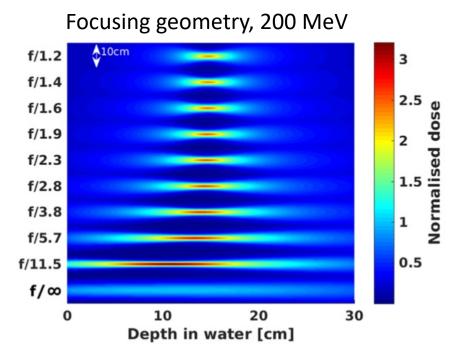
Focused electron beams

Contrary to X-rays, electrons can be magnetically focused to increase the dose at depth.

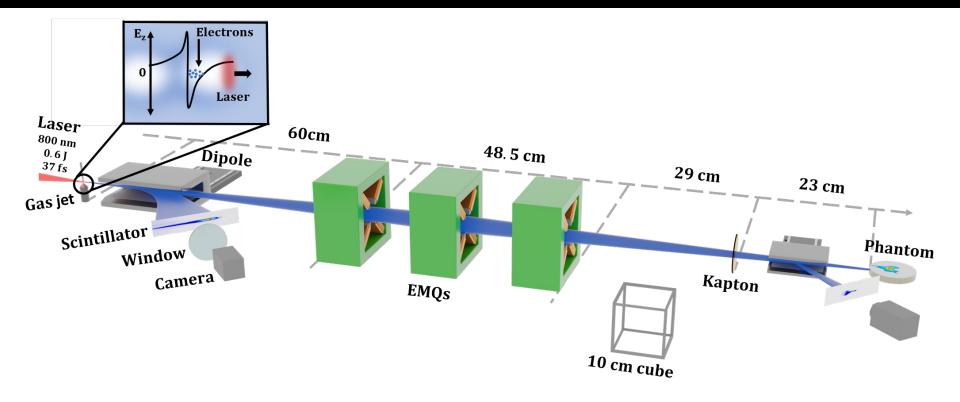
In this simulation study, the influence of the focusing geometry and focusing depth is explored.







Beam shaping using EMQ magnets



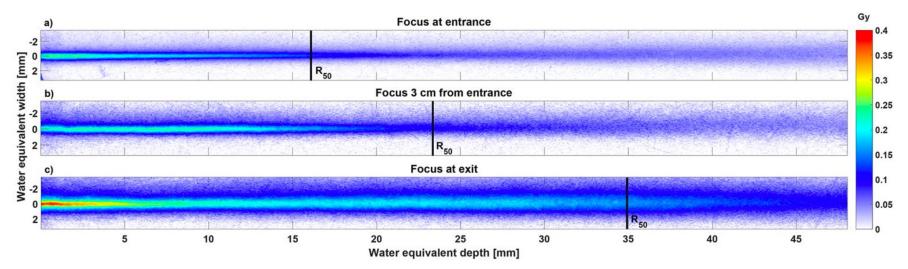
Focusing the beam at depth

- ✓ Mitigates lateral spread
- ✓ Gives more uniform dose



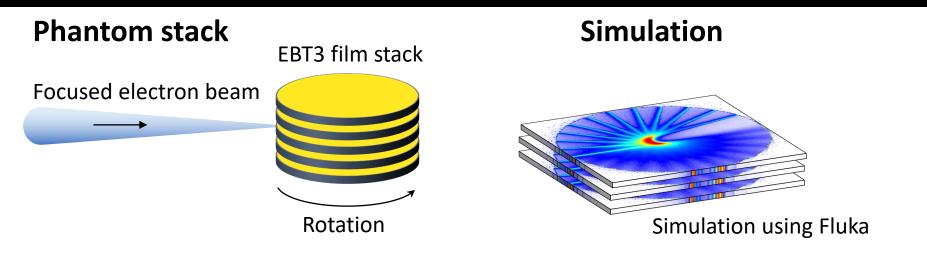
Dose deposition by focused beams

Changing focal plane changes the dose depth distribution



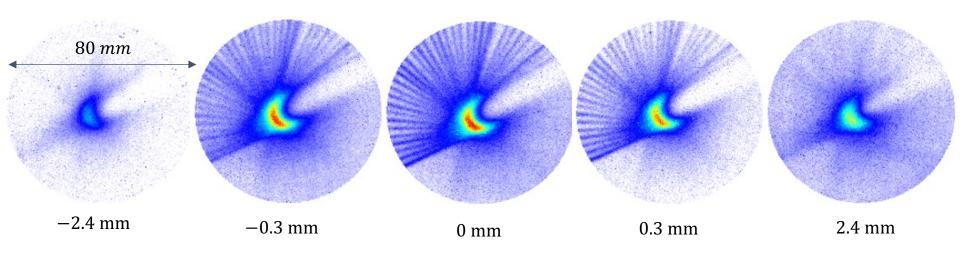


Multiple irradiation angles



Measurement – concave volume

36 angles, 10 pulses/angle

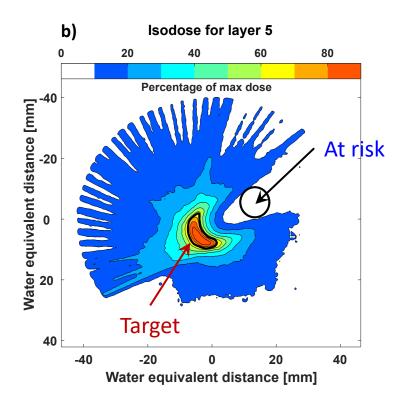


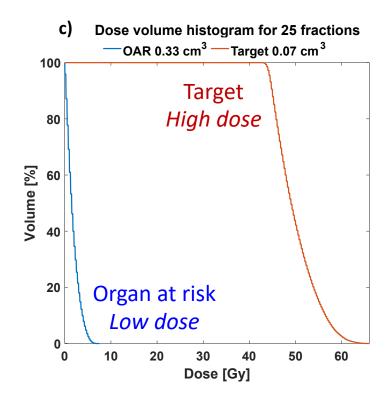
Layers at different heights from beam center

K. Svendsen *et al*, Sci Reports **11**, 5844 (2021)

Towards stereotactic radiotherapy

Purpose of stereotactic radiotherapy is very precise delivery of the dose to the target volume







Multi-field irradiation and intensity modulation

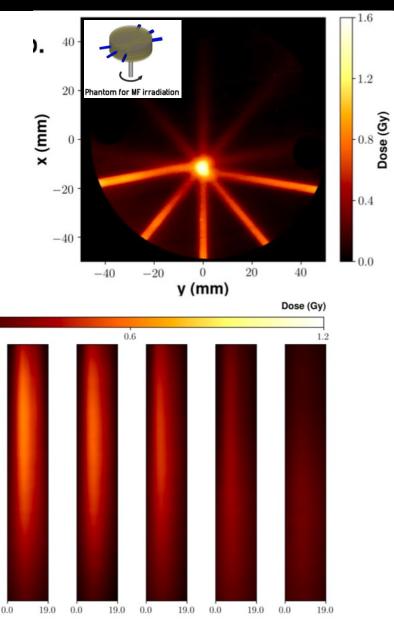
29.5

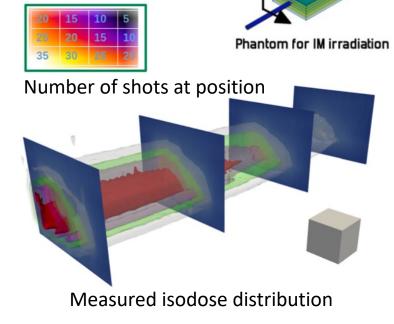
88.5

y (mm)

 Multi-field irradiation provides precise dose delivery in the target volume

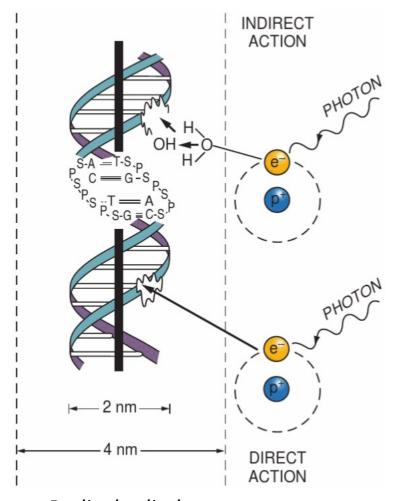
 Intensity-modulated radiation field by controlled exposure at different locations





L. Labate et al., Sci Rep 10, 17307 (2020)

Direct and indirect action of radiation



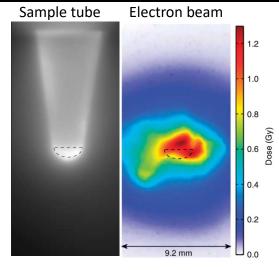
Radical cylinder

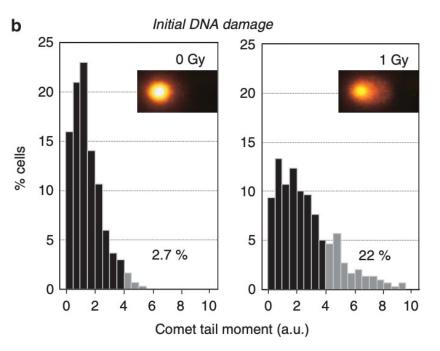
Direct action: a secondary electron resulting from absorption of an x-ray photon interacts with the DNA to produce an effect.

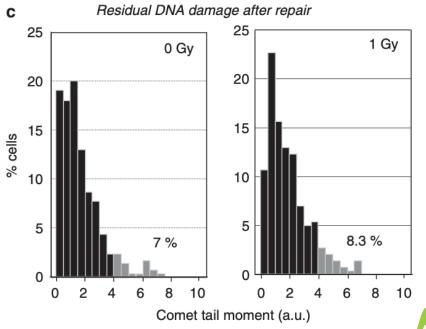
Indirect action: a secondary electron interacts with, for example, a water molecule to produce a hydroxyl radical (OH-), which in turn produces the damage to the DNA.

Towards ultrafast radiation biology

- Evaluation of DNA damage by comet assay
- 5×10^5 human skin cancer cells (A431) exposed to 1 Gy in a single shot (duration few fs)
- Measurable assessment of immediate and reversible DNA damage in carcinoma cells can be explored at the single-cell level.





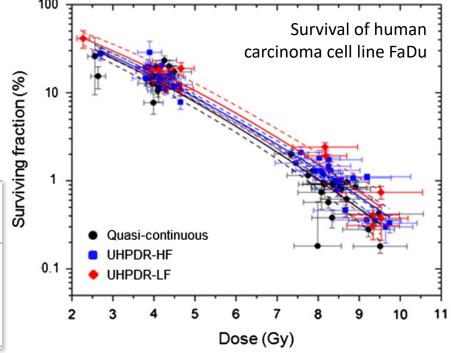


Radiobiological response to pulsed radiation

Results reveal that ultra-high pulse dose rates of 10¹⁰ Gy/min and the low repetition rate of laser accelerated electrons have **no statistically significant influence** (within the 95% confidence intervals) on the radiobiological effectiveness of megavoltage electrons.

Radiation quality	$\alpha \pm \text{SE/Gy}^{-1}$	$\beta \pm SE/Gy^{-2}$	R^2	$RBE_{0.1} \pm SE$
200 kVp X-ray	0.394 ± 0.041	$\boldsymbol{0.030 \pm 0.007}$	0.951	
ELBE: Quasi- continuous	$\textbf{0.405} \pm \textbf{0.038}$	$\boldsymbol{0.021 \pm 0.005}$	0.831	0.95 ± 0.11
ELBE: UHPDR-HF	$\boldsymbol{0.397 \pm 0.021}$	$\boldsymbol{0.018 \pm 0.003}$	0.943	0.92 ± 0.09
ELBE: UHPDR-LF	$\textbf{0.334} \pm \textbf{0.046}$	$\boldsymbol{0.023 \pm 0.006}$	0.913	0.86 ± 0.12

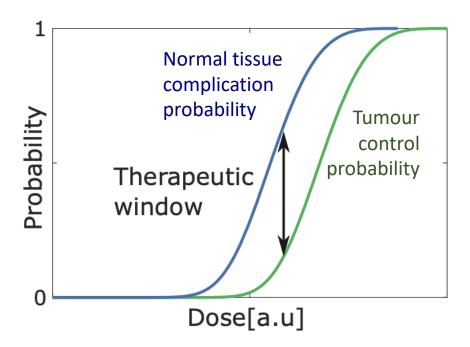
	20 MeV ELBE electron beam			
		Ultra-high pulse dose rate		
Beam Parameter	Quasi-continuous	High frequency	Low frequency	
Pulse frequency	13 MHz	13 MHz	$2.5\mathrm{Hz}$	
Pulse length	~ 5 ps	~ 5 ps	~ 5 ps	
Dose per pulse	~ nGy	~ mGy	~ mGy	
Irradiation time	~ min	$\leq 1 \text{ms}$	≤30 min	
Mean dose rate/Gy min ⁻¹	4.1 ± 0.2	$(0.54 \pm 0.05) \times 10^6$	$\boldsymbol{0.38 \pm 0.03}$	
Pulse dose rate/Gy min ⁻¹	$\sim 10^{4}$	$\sim 10^{10}$	$\sim 10^{10}$	



The therapeutic window

The therapeutic window in radiotherapy refers to the delicate **balance** between the **dose required to effectively treat** a cancerous tumor and the **dose that can cause harm** to normal, healthy cells in the surrounding tissue.

Increasing the therapeutic window improves the treatment



Perspectives for FLASH therapy

FLASH therapy is the delivery of very high dose rates (>40 Gy/s)

FLASH effect provides better sparing of healthy tissue

not yet completely understood

Femtosecond electron bunches from LWFA

- Allow radiobiological studies at ultra-high dose rates
- \succ High repetition rate (>10 Hz) is also needed for delivering the high total dose (\sim 1-10 Gy) in very short time (\sim 100 ms)

Seminal paper

V Favaudon et al., "Ultrahigh dose-rate FLASH irradiation increases the differential response between normal and tumor tissue in mice", Science Transl. Med. **6** (2014)

Review articles

M Kim *et al*, IEEE Transactions on Radiation and Plasma Medical Sciences **6** (2021) Hughes and Parsons, Int. J. Molecular Sciences **5** (2020)

Conclusions

VHEE-RT is attracting more and more interest from medical community

VHEE-RT could be the next important societal application

LPAs are offering several advantages over conventional accelerators

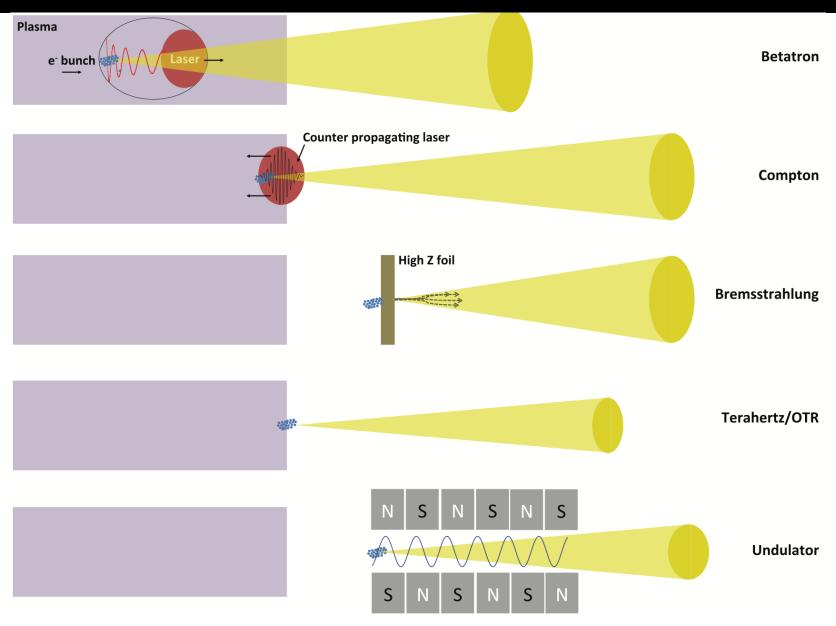
Outline

Laser-accelerated electron beams for radiotherapy

Betatron X-rays for imaging and spectroscopy

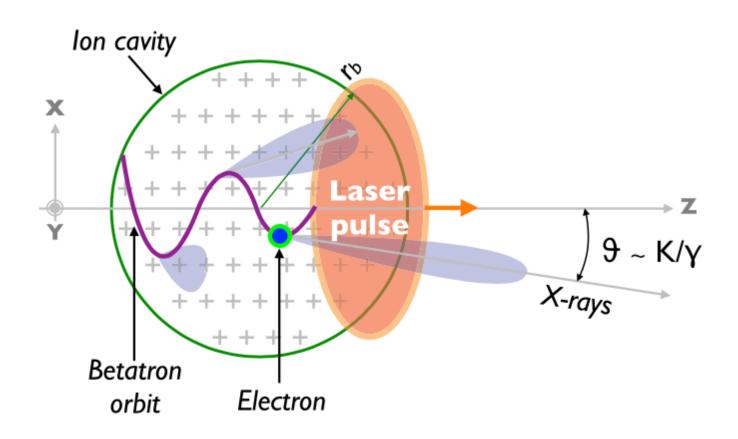
Other light sources based on plasma accelerators

Light sources based on LWFA



F Albert and AGR Thomas, Plasma Phys. Control. Fusion **58**, 103001 (2016)

Betatron oscillations in an ion cavity



Review article

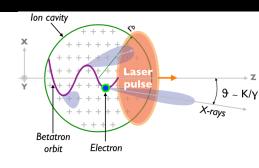
S Corde et al, "Femtosecond x rays from laser-plasma accelerators", Rev Mod Phys **85**, (2013)

Betatron oscillation in an ion channel

Gauss's law and assuming cylindrical symmetry

$$\nabla \cdot \mathbf{E} = \frac{\rho}{\epsilon_0}$$

$$\Rightarrow \frac{1}{r} \frac{d}{dr} (rE_r) = \frac{q_e n_e}{\epsilon_0} \Rightarrow E_r = \frac{q_e n_e}{\epsilon_0} \frac{r}{2}$$



Assuming transverse motion is small and does not change the total energy of the particle ($p_{\perp} \ll p_z$ and $\gamma \simeq \gamma_{z0} \simeq const$)

$$\frac{dp_{\perp}}{dt} = -q_e E_r \Rightarrow \frac{d}{dt} (\gamma m_e v) = -\frac{m_e \omega_p^2}{2} r \Rightarrow \frac{d^2 r}{dt^2} = -\frac{\omega_p^2}{2\gamma} r$$

Which is the equation of motion of a harmonic oscillator with frequency

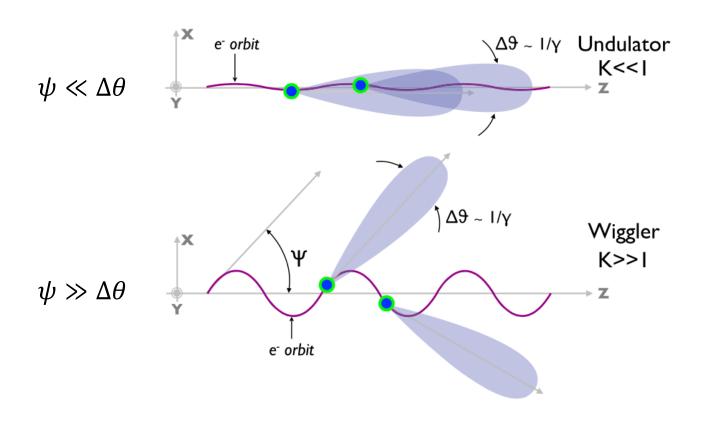
$$\omega_{\beta} = \frac{\omega_p}{\sqrt{2\gamma}}$$

The transverse motion is sinusoidal: $r = r_{\beta} \cos \omega_{\beta} t$

Maximum angle of the trajectory

$$\psi = \left(\frac{dr}{cdt}\right)_{\text{max}} = \frac{r_{\beta}\omega_{\beta}}{c} = \frac{K}{\gamma} \Rightarrow \left[K = \gamma r_{\beta}\omega_{\beta}/c\right]$$

Undulator and wiggler regimes



 ψ Maximum angle of the electron velocity vector

 $\Delta\theta = 1/\gamma$ Opening angle of the radiation cone

 $K=\gamma\psi$ Dimensionless parameter separating the regimes

Radiation from a relativistic electron

Energy radiated within a spectral band $d\omega$ centered on the frequency ω and within a solid angle $d\Omega$:

$$\frac{d^2I}{d\omega d\Omega} = \frac{q_e^2}{16\pi\epsilon_0 c} \left| \int_{-\infty}^{\infty} e^{i\omega[t-\vec{n}\cdot\vec{r}(t)/c]} \frac{n\times\left[(\vec{n}-\vec{\beta})\times\dot{\vec{\beta}}\right]}{\left(1-\vec{\beta}\cdot\vec{n}\right)^2} dt \right|$$

 $\vec{r}(t)$ is electron position at time t

 $ec{eta}$ is electron velocity normalized to c

 $\vec{\dot{\beta}} = d\vec{\beta}/dt$ is electron acceleration normalized to c

 \vec{n} is the observation direction

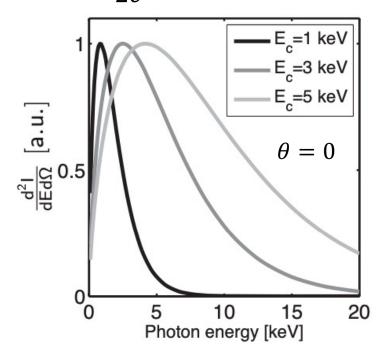
Synchrotron radiation

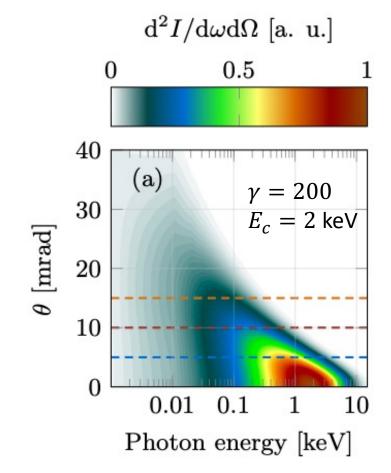
The radiation emitted over N_{β} betatron periods

$$\frac{d^{2}I}{d\omega d\Omega} = N_{\beta} \frac{3hq_{e}^{2}}{\pi^{3}c} \frac{\gamma^{2}\zeta^{2}}{1 + \gamma^{2}\theta^{2}} \left[\frac{\gamma^{2}\theta^{2}}{1 + \gamma^{2}\theta^{2}} \mathcal{K}_{1/3}^{2}(\zeta) + \mathcal{K}_{2/3}^{2}(\zeta) \right]$$

$$\zeta = \frac{E}{2E_c} (1 + \gamma^2 \theta^2)^{3/2}$$

$$E_c = \frac{3\hbar}{2c} \gamma^3 \omega_{\beta}^2 r_{\beta}$$





First measurements of betatron X-rays

Beam-driven

Laser-driven

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PHYSICAL REVIEW LETTERS

1 April 2002

VOLUME 93. NUMBER 13

PHYSICAL REVIEW LETTERS

week ending

X-Ray Emission from Betatron Motion in a Plasma Wiggler

Shuoqin Wang, ¹ C. E. Clayton, ¹ B. E. Blue, ¹ E. S. Dodd, ¹ K. A. Marsh, ¹ W. B. Mori, ¹ C. Joshi, ¹ S. Lee, ² P. Muggli, ² T. Katsouleas, ² F. J. Decker, ³ M. J. Hogan, ³ R. H. Iverson, ³ P. Raimondi, ³ D. Walz, ³ R. Siemann, ³ and R. Assmann ⁴ University of California, Los Angeles, California 90095

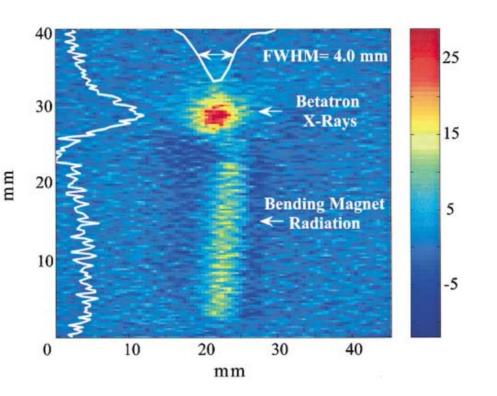
⁴University of California, Los Angeles, California 90099 ³Stanford Linear Accelerator Center, Stanford, California 94309 ⁴CERN, Switzerland

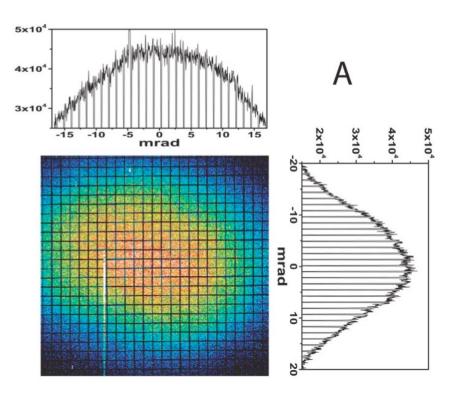
(Received 8 October 2001; published 19 March 2002)

Production of a keV X-Ray Beam from Synchrotron Radiation in Relativistic Laser-Plasma Interaction

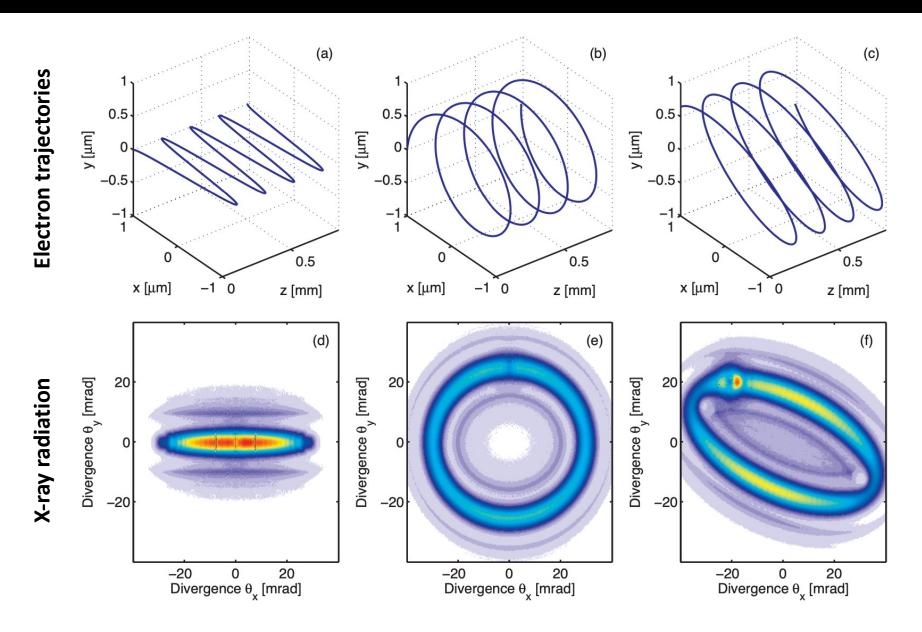
Antoine Rousse, ¹ Kim Ta Phuoc, ^{1,2,*} Rahul Shah, ² Alexander Pukhov, ³ Eric Lefebvre, ⁴ Victor Malka, ¹ Sergey Kiselev, ³ Fréderic Burgy, ¹ Jean-Philippe Rousseau, ¹ Donald Umstadter, ² and Daniéle Hulin ¹ Laboratoire d'Optique Appliquée, ENSTA, CNRS UMR7639, Ecole Polytechnique, Chemin de la Hunière, 91761 Palaiseau, France. ² Center for Ultrafast Optical Science, University of Michigan, 2200 Bonisteel Blvd, Ann Arbor, Michigan, 48109, USA. ³ Institut fuer Theoretische Physik I, Heinrich-Heine-Universitaet, Duesseldorf, 40225 Duesseldorf, Germany.

⁴Département de Physique Théorique et Appliquée, CEA/DAM Ile- de-France, BP 12, 91680 Bruyéres-le-Châtel, France (Received 22 January 2004; published 23 September 2004)

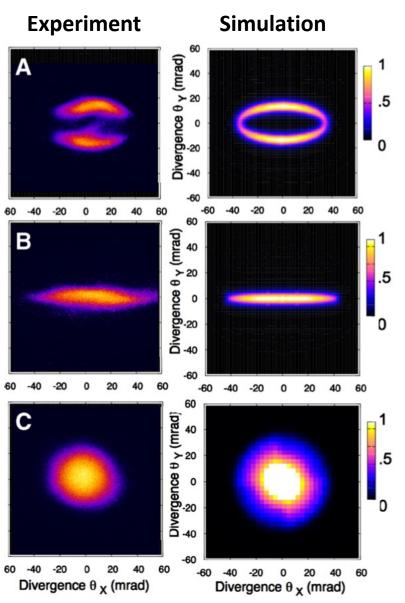




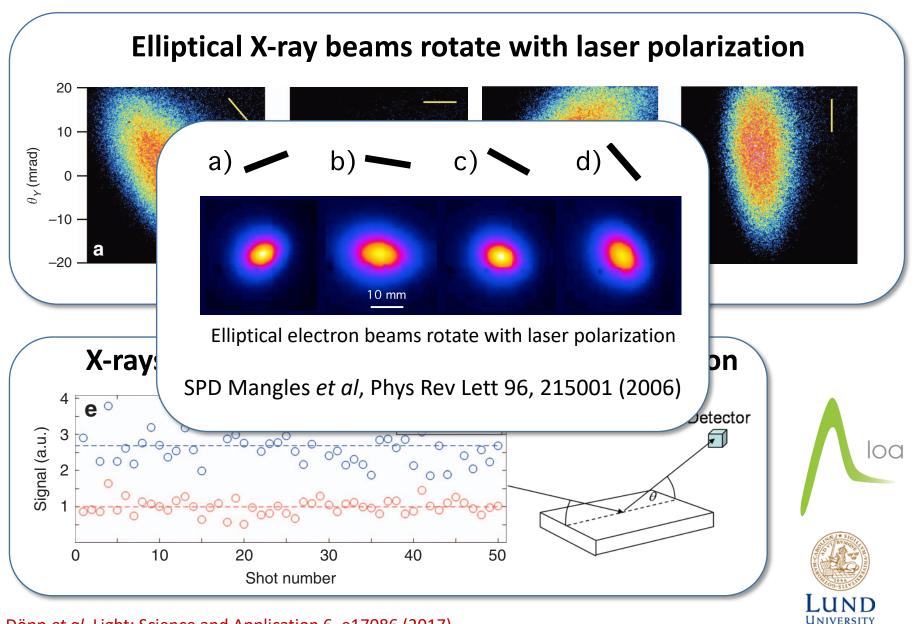
Electron trajectories shapes radiation



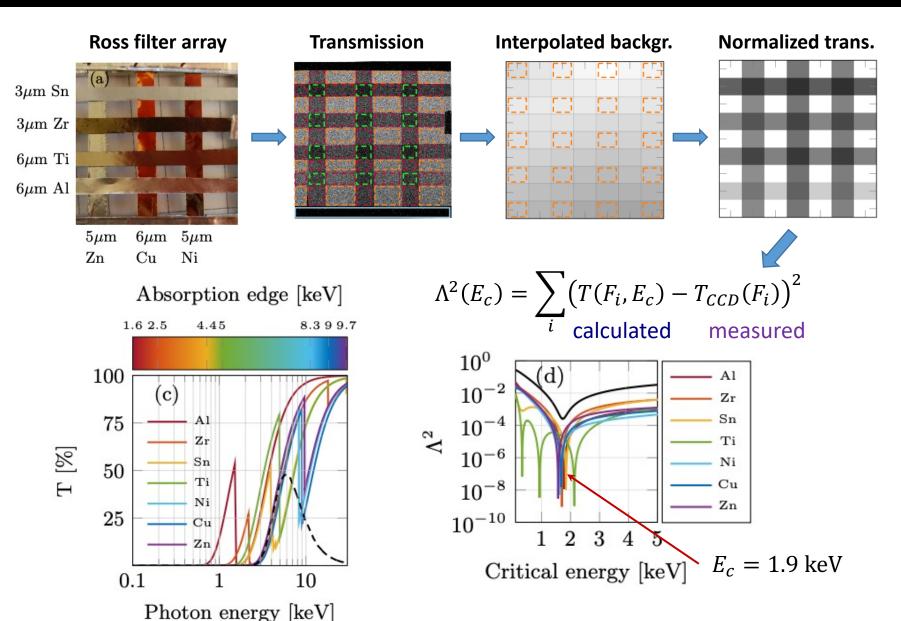
Electron trajectories shapes radiation



Tunable X-ray polarization



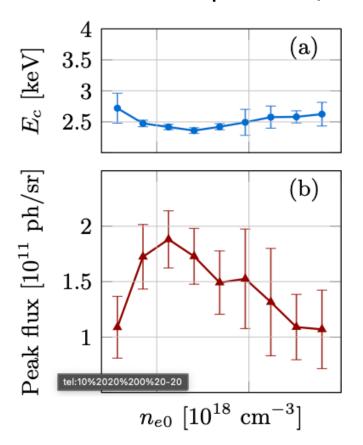
Spectral characterization using Ross filters



Source characterization using Ross filters

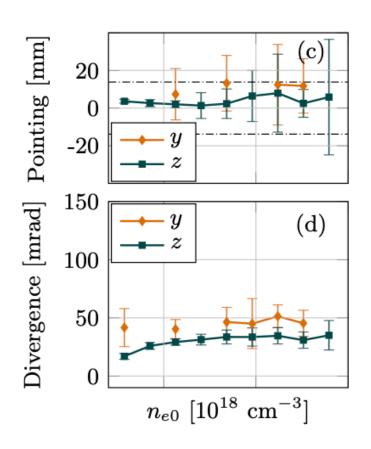
Critical energy: 2-3 keV

Flux: 1-2 • 10¹¹ photons/sr



Divergence: 30 × 40 mrad

4·10⁹ photons

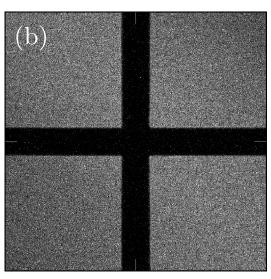


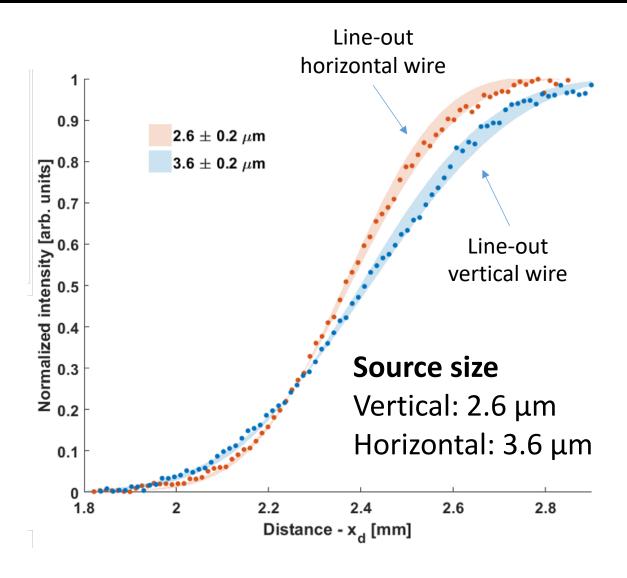
Betatron as a diagnostic for LWFA electrons

25 μm tungsten wires



Wire shadow on CCD





Betatron as diagnostic of LWFA

$$E_c = \frac{3\hbar}{2c} \gamma^3 \omega_{\beta}^2 r_{\beta} \qquad \omega_{\beta} = \frac{\omega_p}{\sqrt{2\gamma}}$$

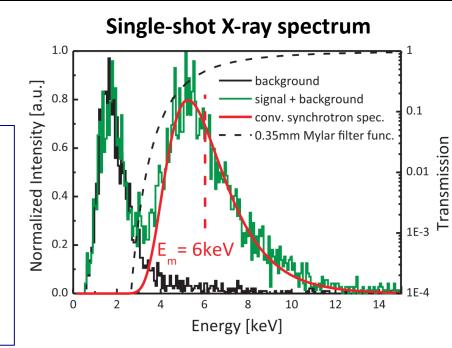
- X-ray spectrum measured by single photon counting technique
- Simultaneous measurements of electron- and X-ray spectrum
- Allows measurement of the electron beam size (oscillation amplitude)

Source size measurements

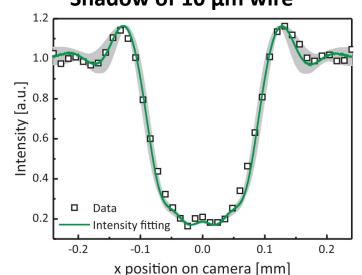
X-ray spectrum: $r_{\beta} = 0.9 \pm 0.3 \; \mu m$

Fresnel diffraction: $r_{\beta}=1.8\pm0.3~\mu m$

PIC simulation: $r_{\beta} = 1.5 \pm 0.2 \; \mu m$

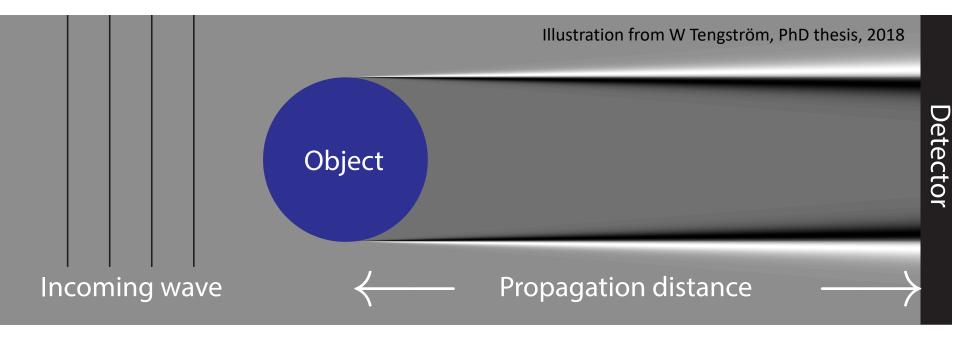


Shadow of 10 µm wire



Phase-contrast imaging

Propagation-based phase-contrast imaging



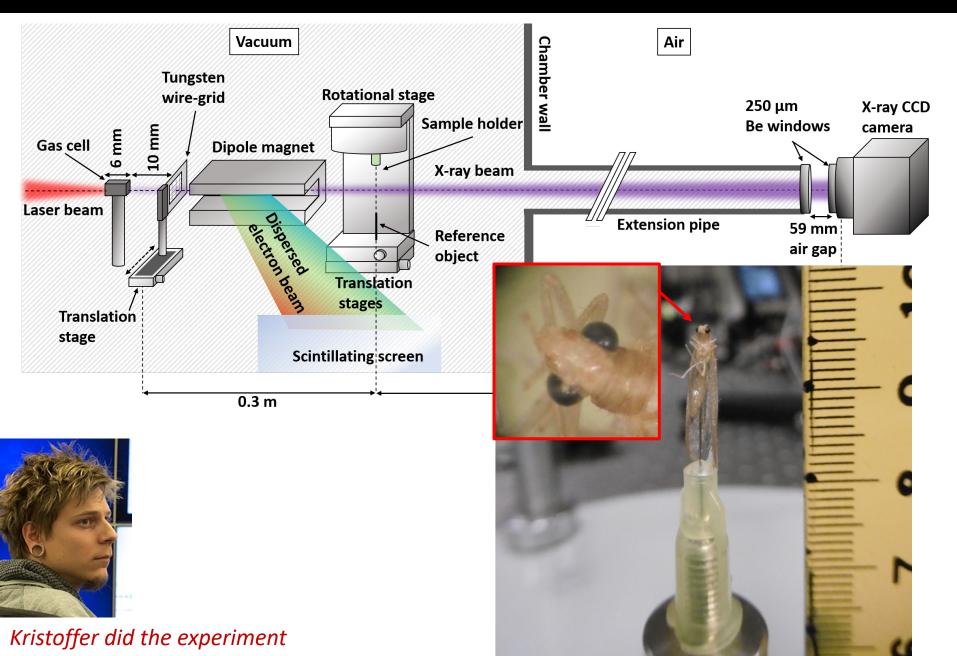
Relies on changes in the refractive index

Ideal for low-absorbing samples

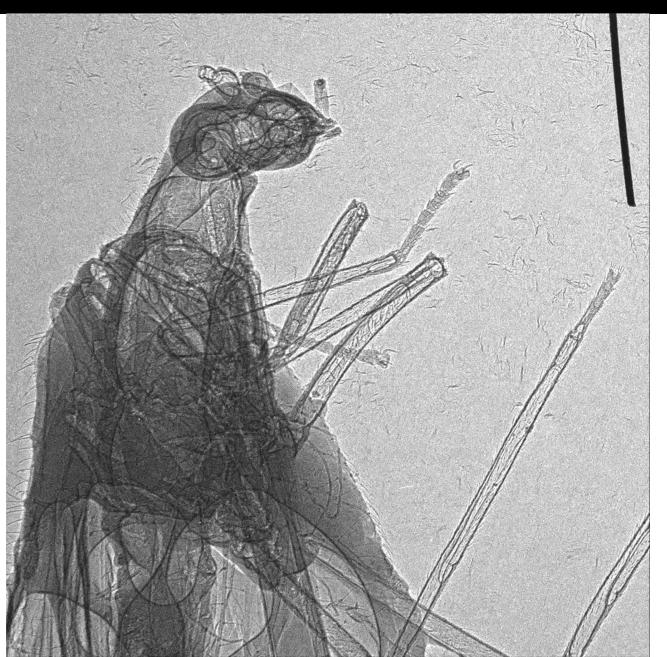
Projected thickness is obtained using algorithms

Requires high spatial coherence -> small source size

Setup for phase-contrast imaging

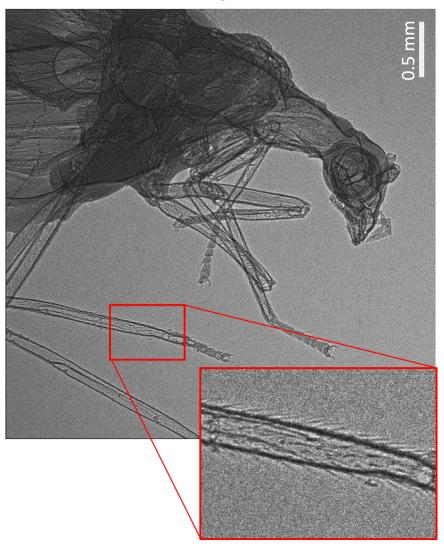


Phase-contrast tomography

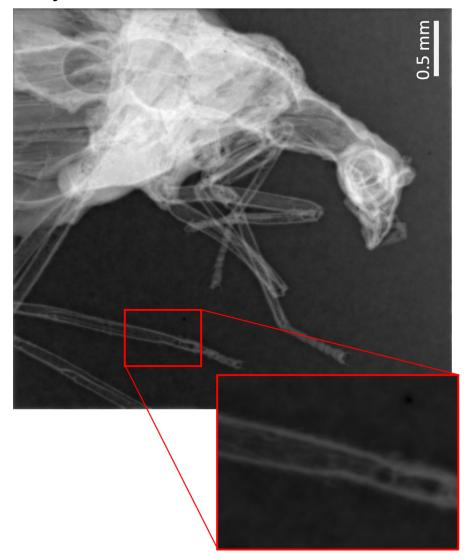


Phase-contrast image

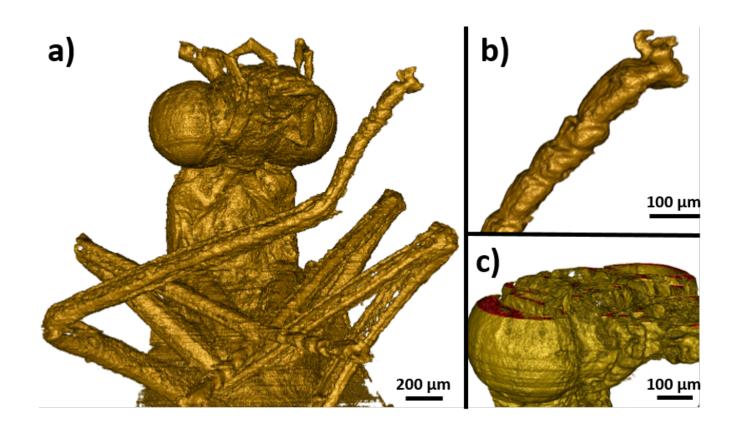
Phase-contrast image



Projected thickness

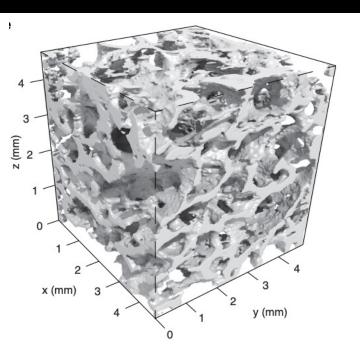


3D rendering



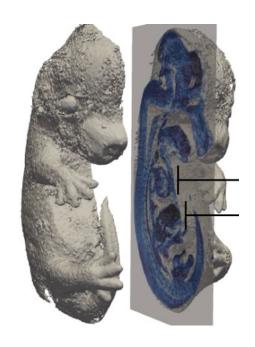
10 µm structures can be resolved in tomogram

Tomography for medical purposes

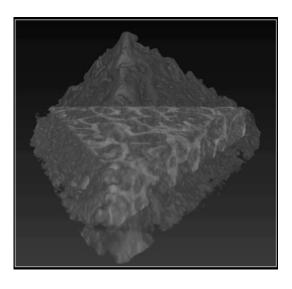


Tomographic reconstruction of trabecular bone sample

J M Cole *et al*, Sci Rep **5** (2015)



High-resolution μ CT of a mouse embryo J M Cole et~al, PNAS **115** (2018)



Quick micro-tomography A Döpp *et al*, Optica **5** (2018)

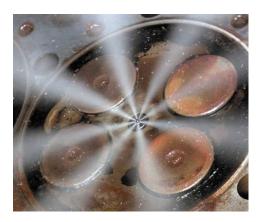
Spray applications

Internal Combustion Engines Applications: Diesel and GDI sprays

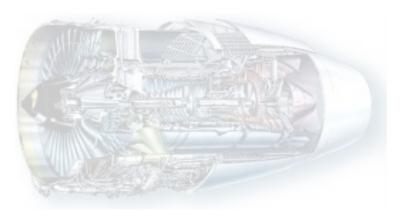








Gas Turbines Applications: Aero Engines







Spray imaging with laser plasma accelerator

Understanding breakup and atomization of sprays is essential for improving e.g. engine efficiencies.

Challenges Fast dynamics (ns to μs)

Highly scattering media

Multiple jets in the same spray

Approach Mass flow: X-ray imaging

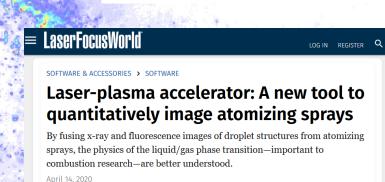
Atomization: 2-photon LIF

Scientist

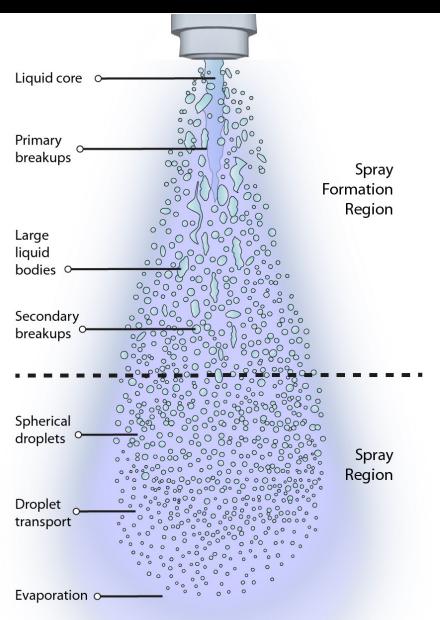
A Clear View of Cloudy Sprays

BY CHARLES O. CHOL

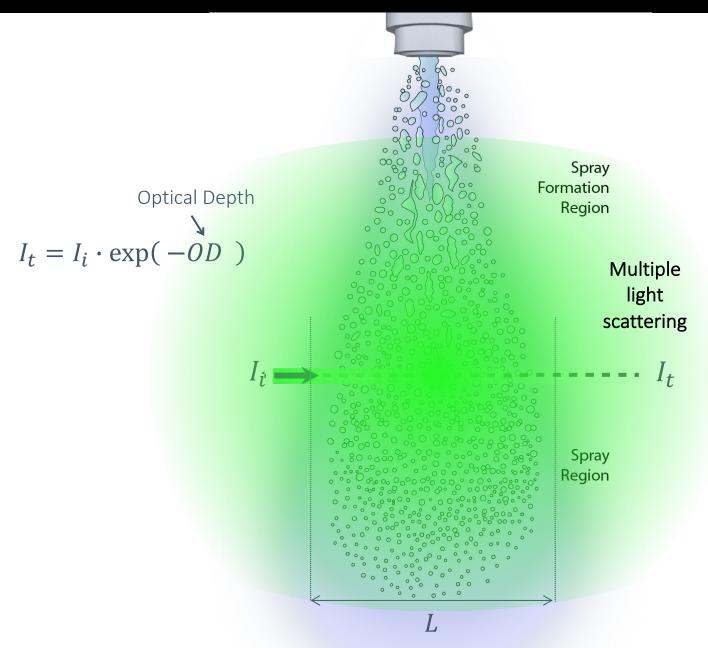
Lasers and x-rays combined can capture quick-changing droplets as they break apart and evaporate.

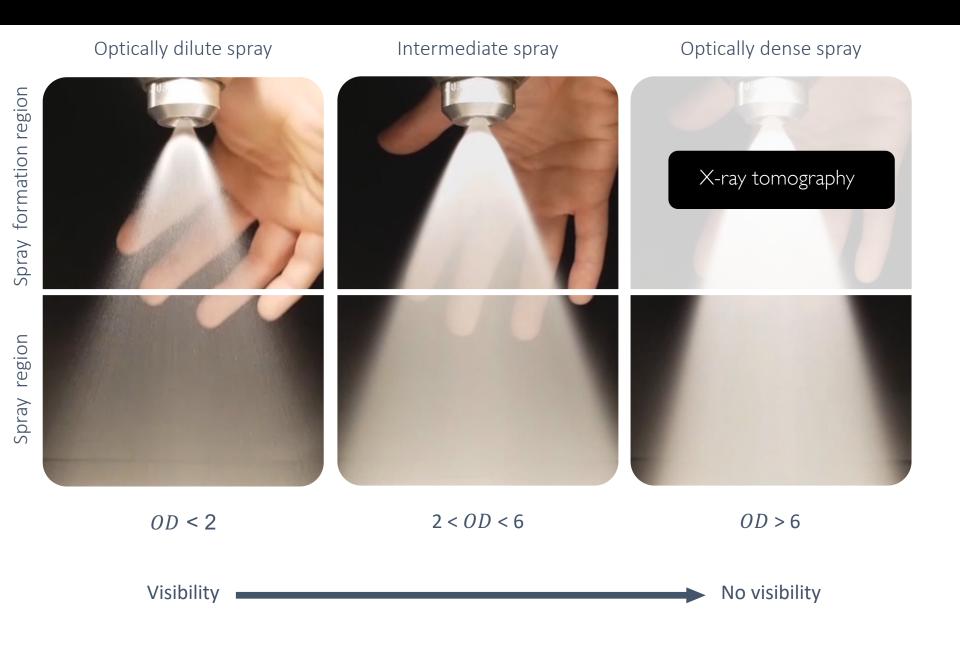


Atomizing sprays

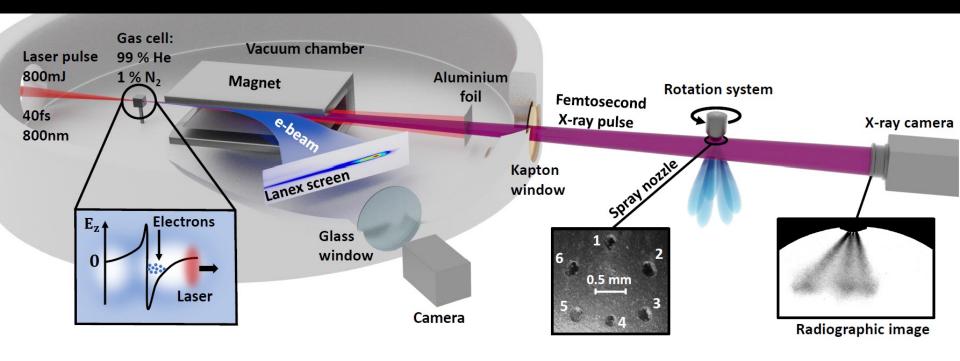


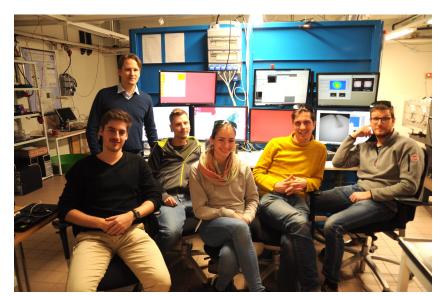
Atomizing sprays





Experimental setup

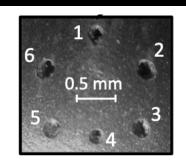


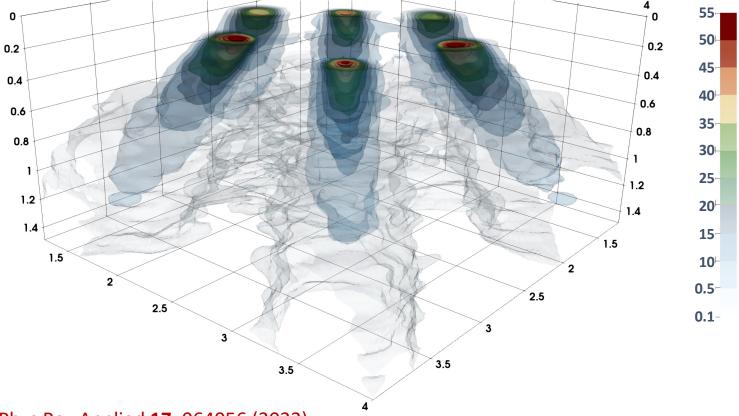


X-ray absorption



Transient spray tomography



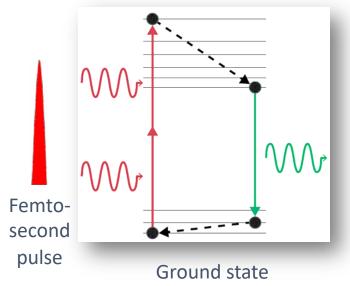


D. Guenot et al, Phys Rev Applied 17, 064056 (2022)

H. Ulrich et al, Phys of Fluids **34**, 083305 (2022)

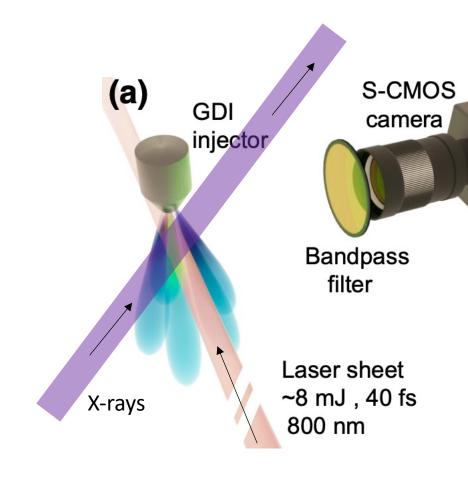
Combining X-rays and flourescence

2-photon laserinduced flourescence

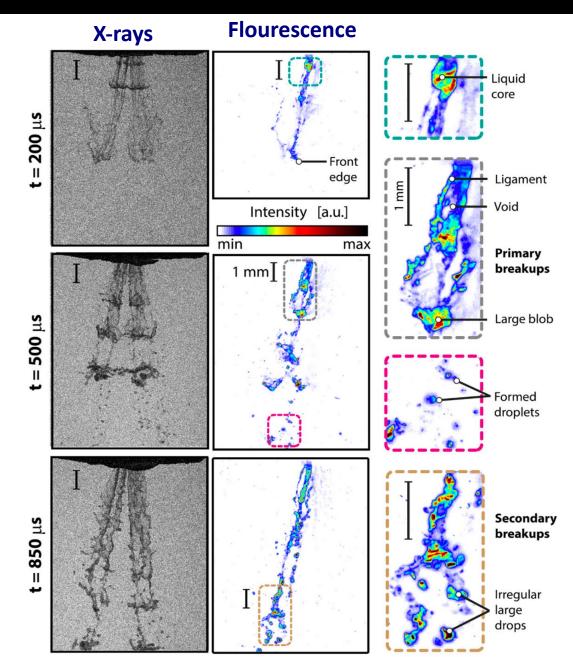




Technique developed by Edouard Berrocal (Lund University)



Simultaneous recordings





Diego Guenot *et al,* Optica **7**, 131-134 (2020)

Outline

Laser-accelerated electron beams for radiotherapy

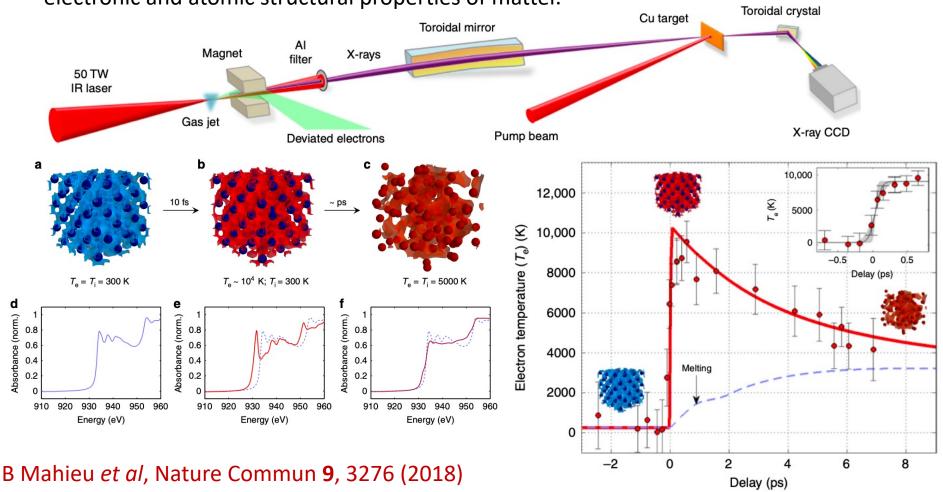
Betatron X-rays for imaging and spectroscopy

Other light sources based on plasma accelerators

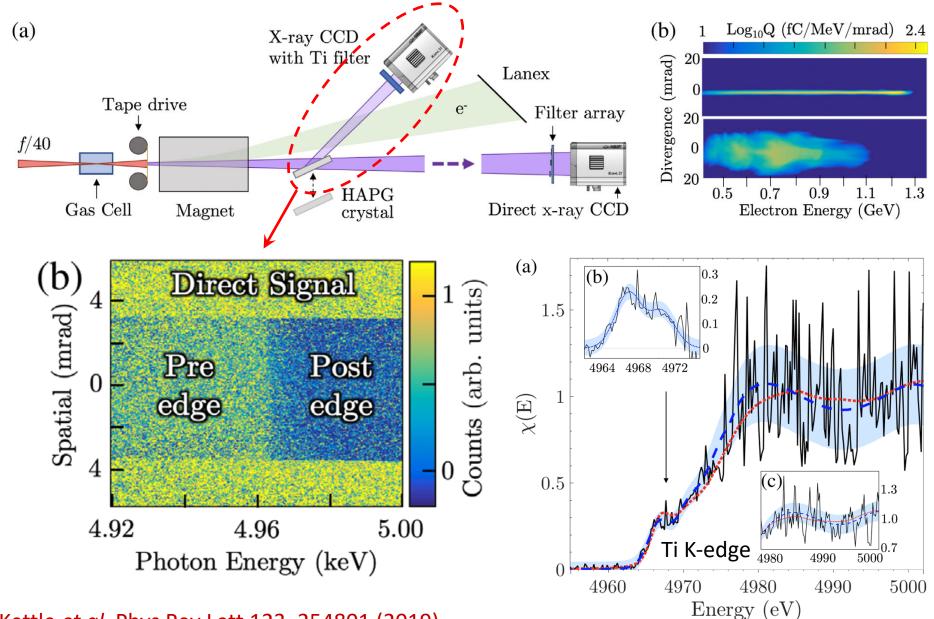
Probing warm dense matter using XANES

WDM (Warm dense matter) lies between solid and plasma with a temperature of a few 10⁴ K. It is a subject of increased interest due to its importance for planetary physics, inertial confinement fusion research, and material science.

XANES (X-ray absorption near-edge structure) is an essential tool to study the electronic and atomic structural properties of matter.



Towards Ultrafast X-ray Spectroscopy



Kettle et al, Phys Rev Lett 123, 254801 (2019)

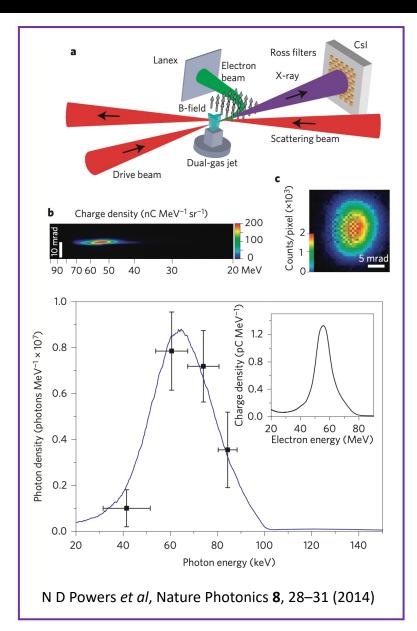
Outline

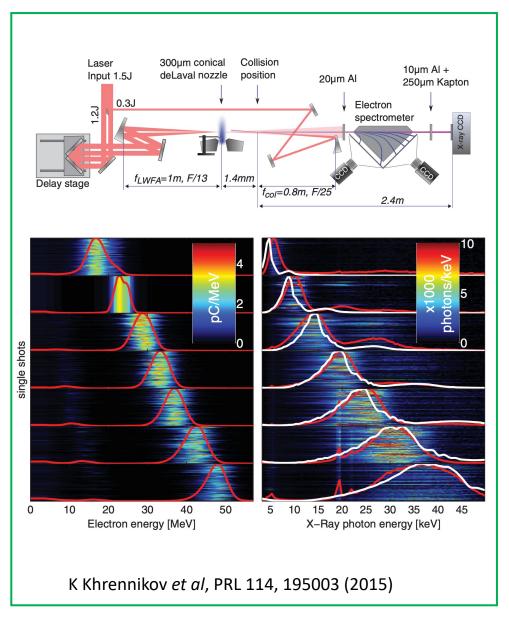
Laser-accelerated electron beams for radiotherapy

Betatron X-rays for imaging and spectroscopy

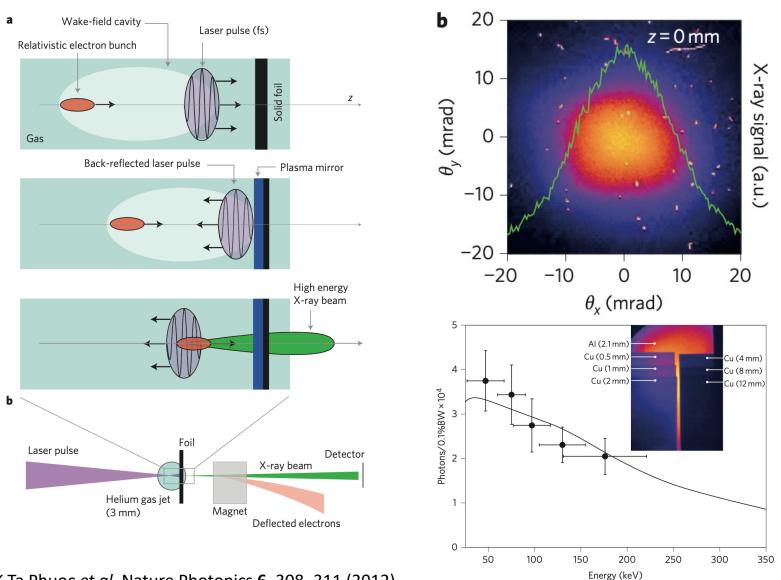
Other light sources based on plasma accelerators

Hard X-rays from Compton scattering



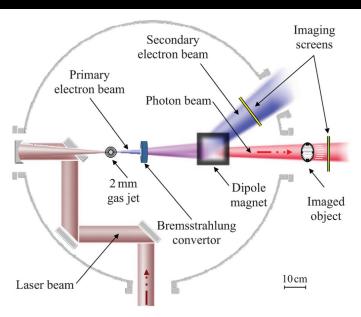


Compton scattering using only one laser beam

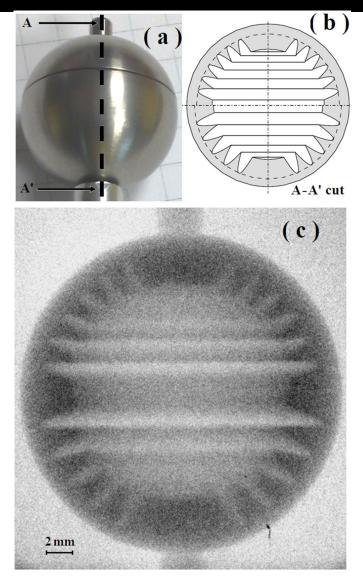


K Ta Phuoc et al, Nature Photonics 6, 308–311 (2012)

Gamma-ray source for radiography

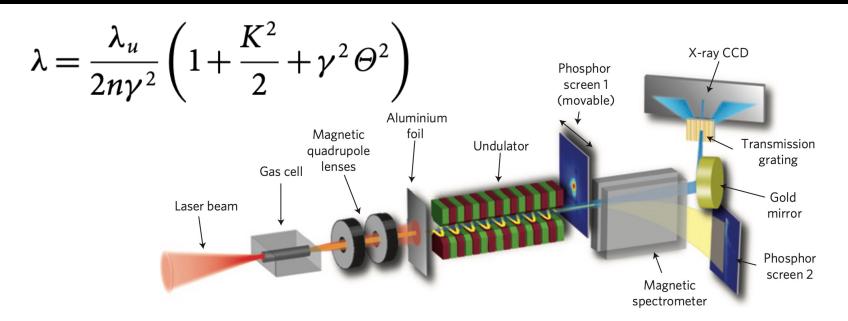


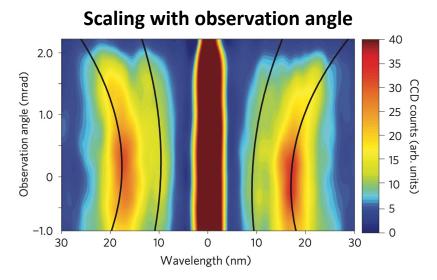
- Laser: 30 TW, 30 fs laser
- Electrons: 100 MeV, 70 pC
- 1 mm tantalum Bremsstrahlung converter
- Image plate detector
- Copper foil enhances gamma detection (converts gamma-rays to low-E electrons)

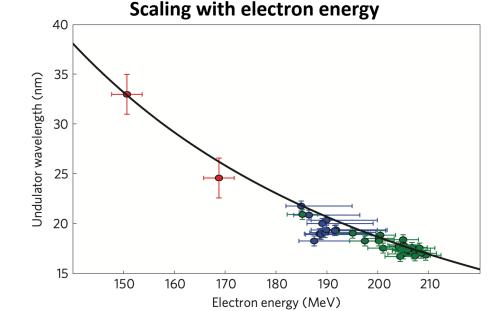


Radiograph of a dense hollow sphere (20 mm diameter tungsten)

Laser-driven soft-X-ray undulator source



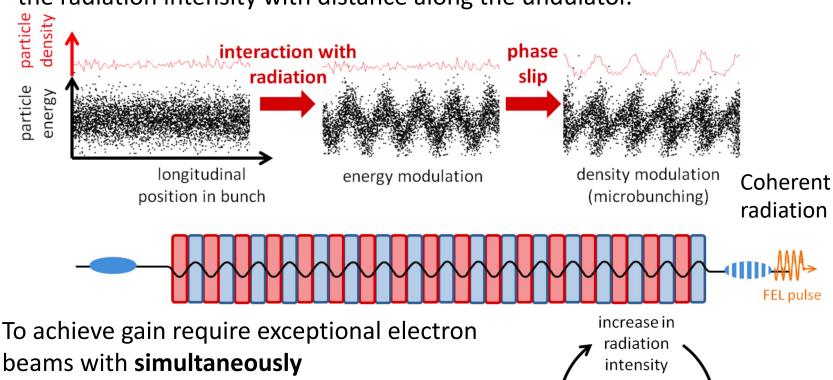




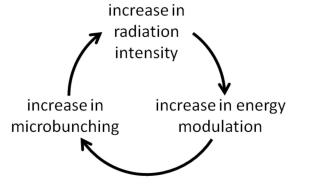
M Fuchs et al, Nature Physics 5, 826–829 (2009)

Coherent radiation from an undulator

Electrons in a bunch passing through an undulator can interact with the radiation produced by other electrons within the bunch so that "microbunches" start to develop, which gives an exponential increase in the radiation intensity with distance along the undulator.

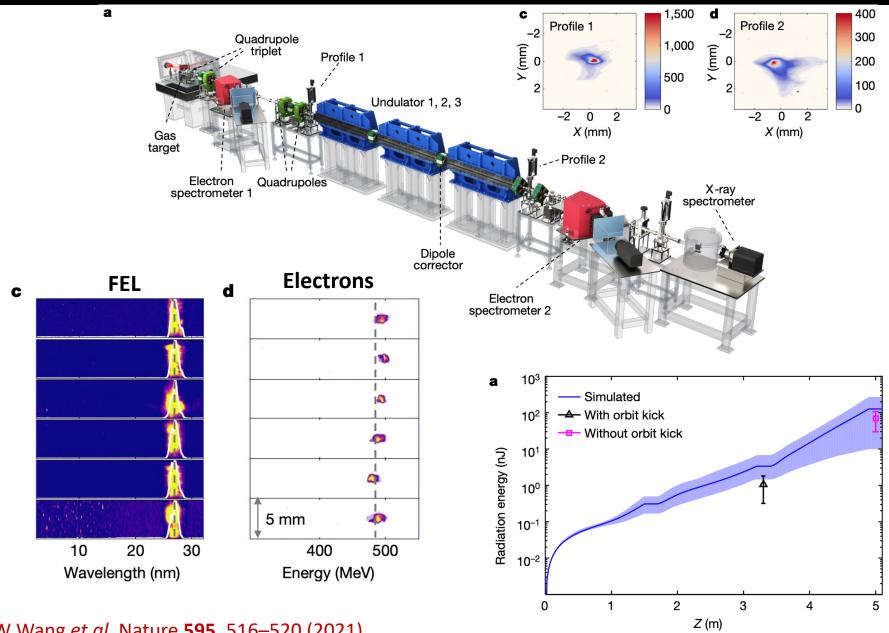


- High peak current (kA)
- Low normalized emittance (<1 mm mrad)</p>
- Low energy spread (<1%)</p>



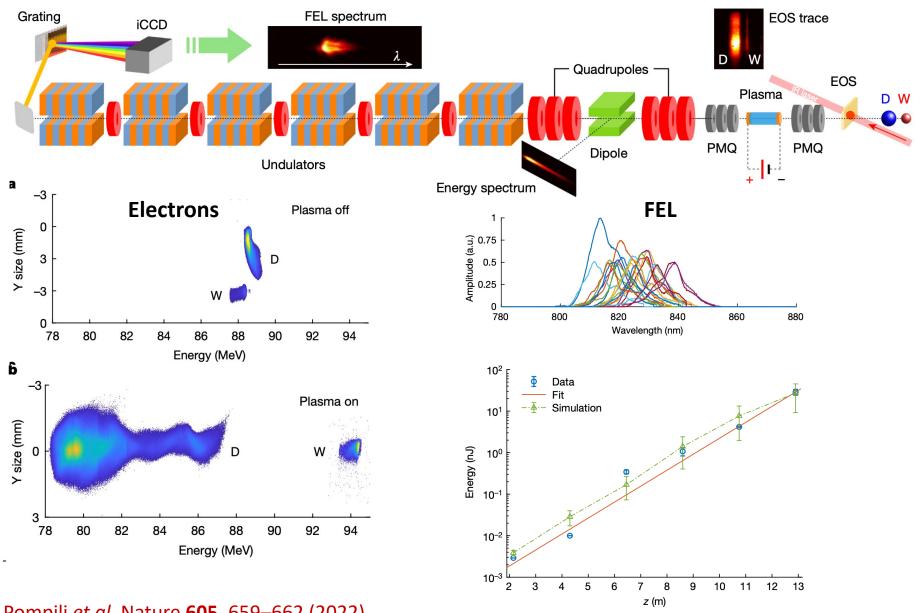
Slide: A Wolski, CAS 2012

Laser-driven FEL



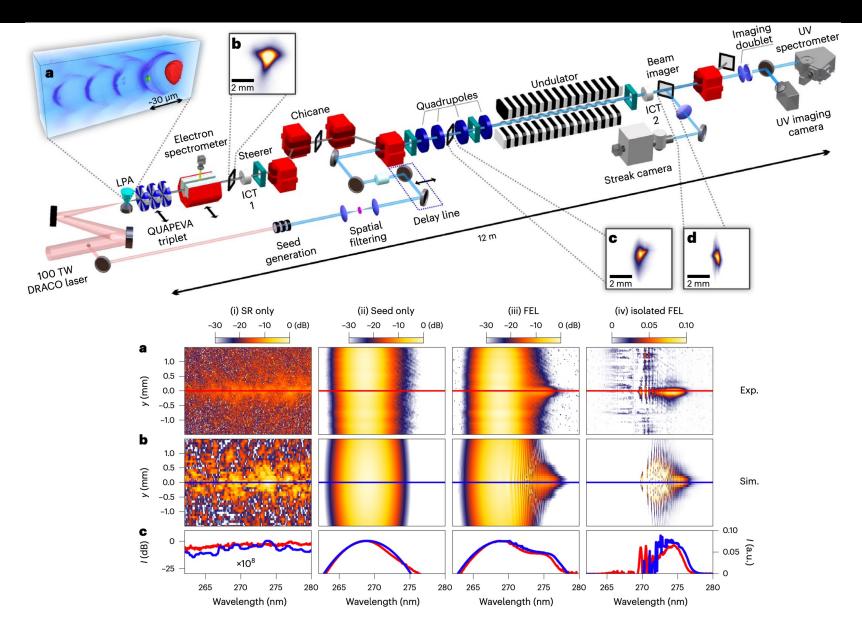
W Wang *et al*, Nature **595**, 516–520 (2021)

Beam-driven FEL



R Pompili et al, Nature **605**, 659–662 (2022)

Seeded FEL



Conclusion

High-power lasers needed for plasma acceleration are already available as commercial products, and in compact setups suitable for space-limited environments in industrial or hospital settings.

This is the **perfect time** to identify key areas where compact laser-plasma accelerators can have a **deep** societal impact.

Congratulations for joining at this perfect time!