Laser-driven ion acceleration: emerging mechanisms and progress towards biomedical applications

M.Borghesi,

Centre for Plasma Physics
The Queen's University of Belfast

QUEEN'S UNIVERSITY BELFAST

A-SAIL

ADVANCED STRATEGIES FOR ACCELERATING IONS WITH LASERS

EPSRC
Pioneering research and skills

CCAP seminar series
Imperial College London
26 May 2021

Outline

- Ultra-intense lasers and particle acceleration

- Ion beams: TNSA, RPA

- Current research:
    carbon acceleration from ultrathin foils
    target-based beam transport

- Perspectives for biomedical use /motivation

- Radiobiology investigations
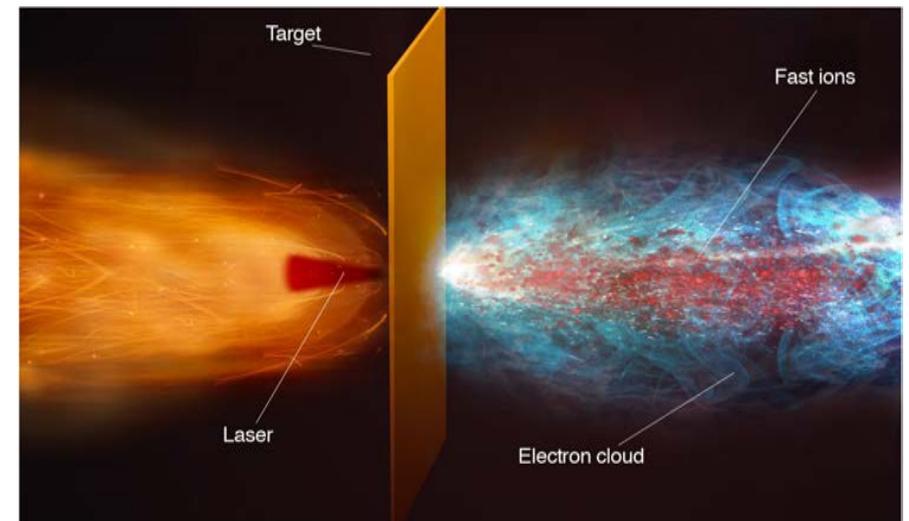
State-of-the-art lasers achieve high power in ultrashort pulses

CPA - chirped pulse amplification

1 Short light pulse from a laser.

2 The pulse is stretched, which reduces its peak power.

3 The stretched pulse is amplified.

4 The pulse is compressed and its intensity increases dramatically.

Grating pair, pulse stretcher

Amplifier

Grating pair, pulse compressor
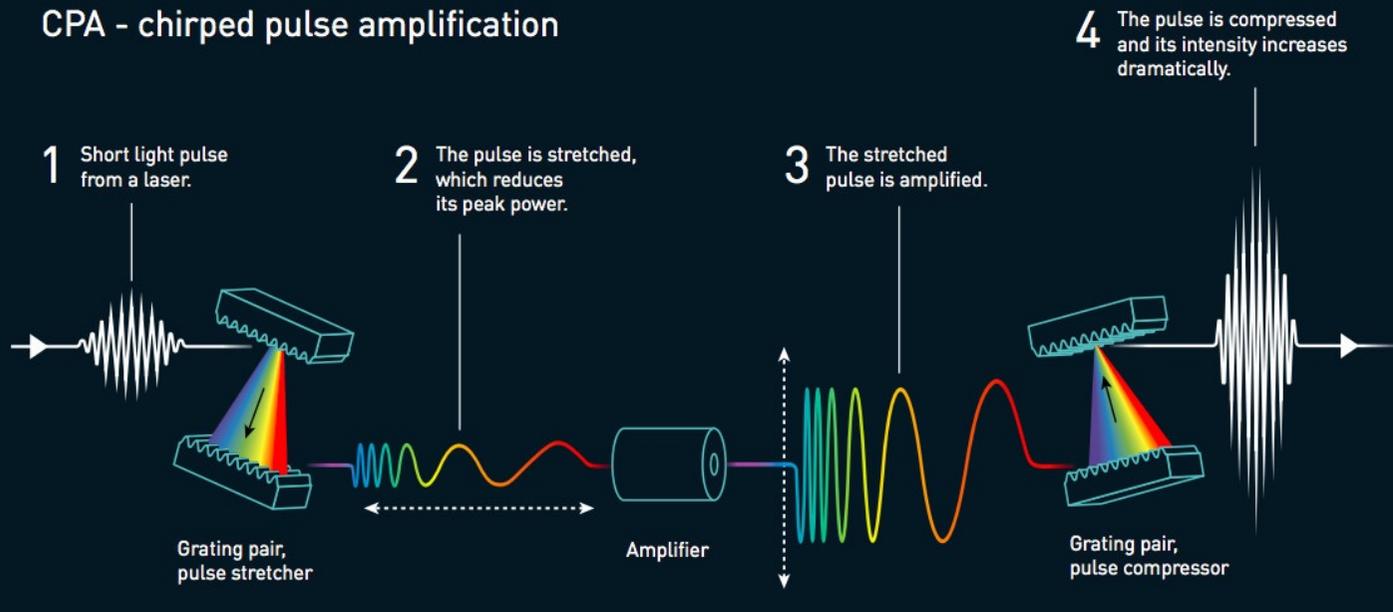
CPA invented in 1980s

100s TW- PW systems developed in 90s/00s (RAL, UK/LLNL, US)

Nobel prize 2018

Example: VULCAN laser (RAL,UK) 500 J of energy concentrated in a pulse of 500 fs duration

Power = 1 PetaWatt = 10^{15} W

If focused to a small spot

$r_0 \sim$ *few micrometer*
Intensity up to 10^{21} W/cm^2

THE NOBEL PRIZE IN PHYSICS 2018

Arthur Ashkin   Gérard Mourou   Donna Strickland

"for groundbreaking inventions in the field of laser physics"

THE ROYAL SWEDISH ACADEMY OF SCIENCES
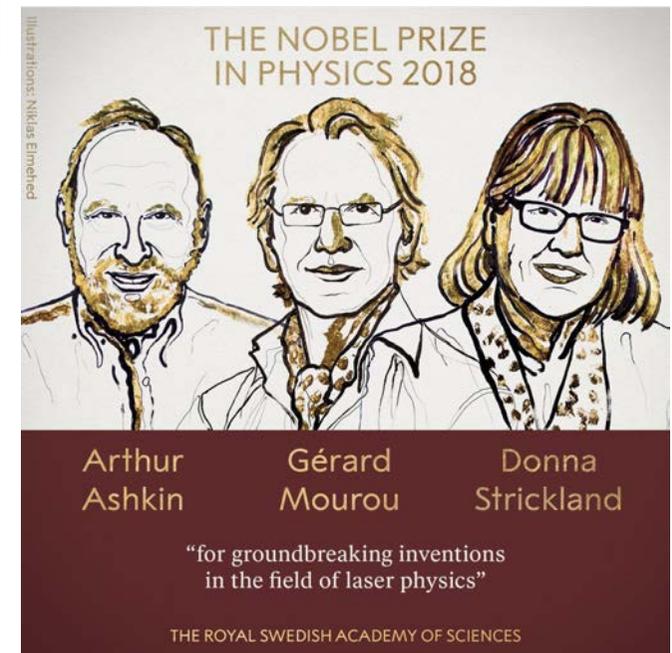
Two main classes of CPA lasers

High energy CPA systems

- Nd: Glass technology

- 100s J energy, up to PW power

- Low repetition rate

- 100s fs duration

- $I_{max} \sim 10^{21}$ Wcm^2

VULCAN, RAL (UK)
Phelix, GSI (De)
Trident, LANL (US)
Texas PW, Austin (US)

…..

Ultrashort CPA systems

- Ti:Sa technology

- 10s J energy, up to PW power

- 1-10 Hz repetition

- 10s fs duration

- $I_{max} \sim 10^{21}$ Wcm^2

GEMINI, RAL (UK)
Draco, HZDR (De)
Pulser I, APRI (Kr)
J-Karen, JAEA (J)

…..

Extreme energy confinement in space and time leads to extreme conditions

$I \sim 5\ 10^{20}\ W/cm^2$

Electric field

$$E = \sqrt{4\pi \frac{I}{c}} = 3 \cdot 10^{13}\,V/m \sim 50 \frac{e}{r_b^2}$$

Ultrafast ionization and plasma production

Electron momentum

$$p_{osc} = \frac{eE}{\omega} = 8.5\,m_e c$$

Heating of electrons to relativistic energies

Radiation Pressure

$$P_{rad} = \frac{I}{c} \sim 30\,Gbar$$
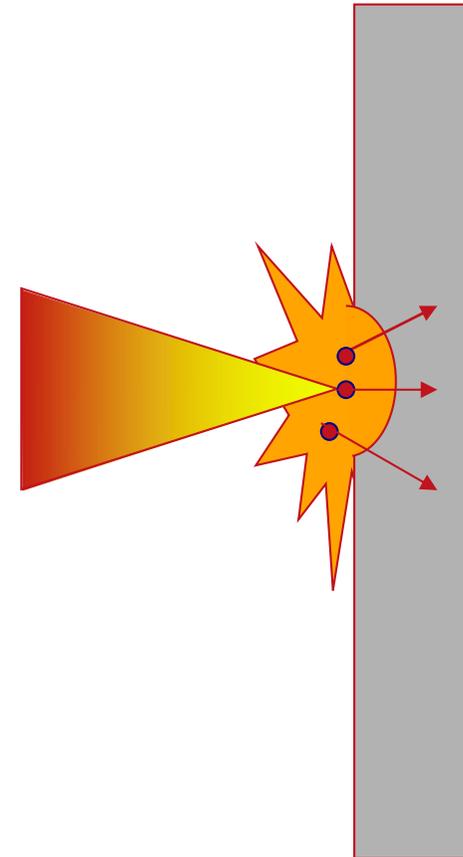
Ultrastrong pressure applied to the target surface

Laser-acceleration of particles

Plasma can support very large E-fields
(up to 10^{12} V/m = TV/m) via local charge separation
initiated by the laser pulse

Cf: in RF accelerators
(cyclotron/LINAC)

$E_{max} \sim 50$ MV/m

Very short acceleration distances:
compact accelerators

Ultrashort particle sources:
femtosecond/picosecond duration

Very bright sources:
Significant dose delivery

Electron accelerator

Ion accelerator

Proton accelerators

Thin layers of contaminants
Ponderomotive electron acceleration
Target Normal Sheath Acceleration

Preplasma
Plasma expansion
Electron sheath
E~TV/m
Ions
μm
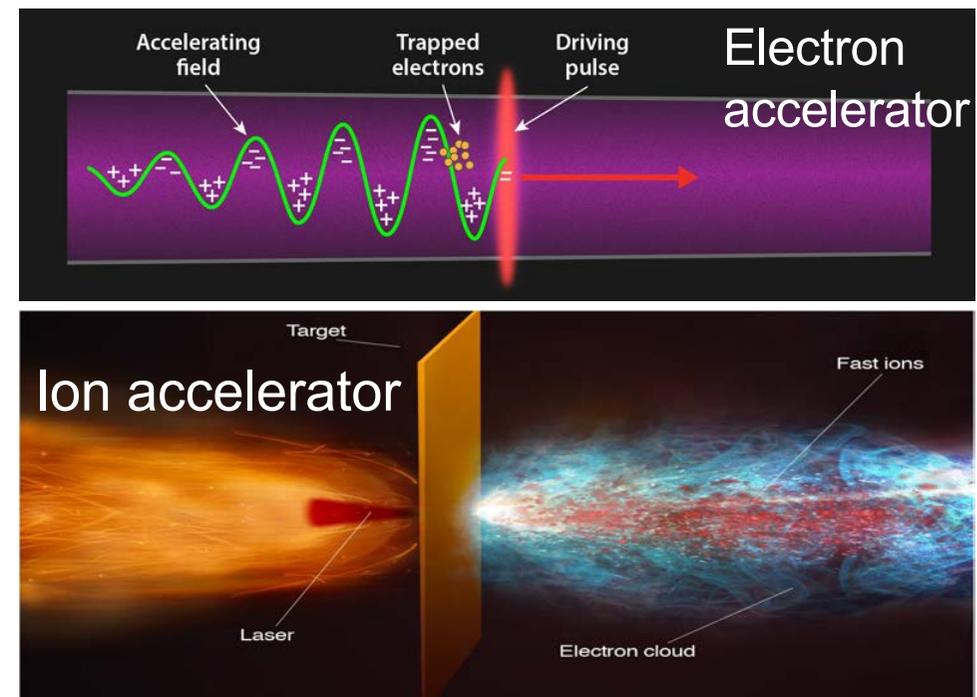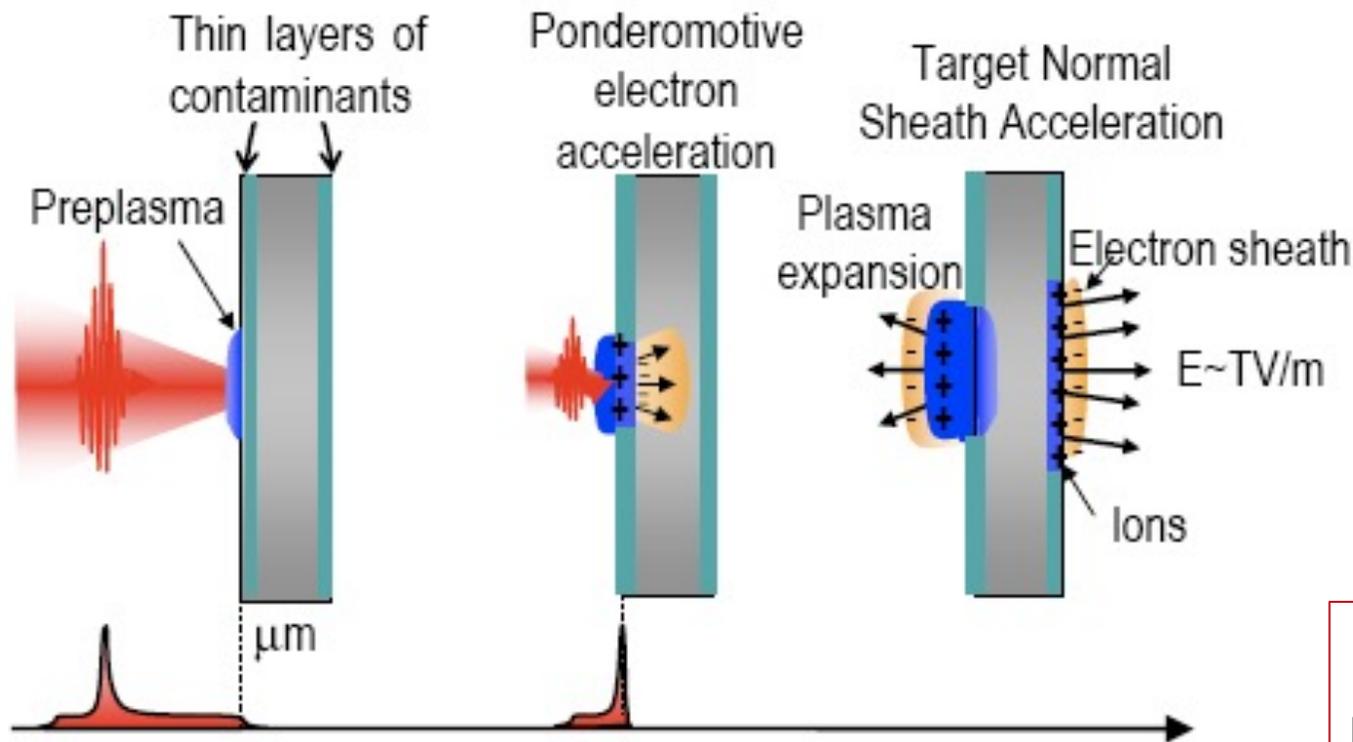
TNSA (Target Normal Sheath Acceleration)

$$E_{acc} = \sqrt{\frac{n_h K T_h}{\varepsilon_0}}$$

scales with laser intensity/energy

$E_{ions} \sim I^{0.5-1}$

Initial observations:

Clark *et al*, PRL, 84 ,670 (2000)

Maksimchuk *et al*, PRL, 84, 4108 (2000)

Snavely *et al*, PRL, 85,2945 (2000)

Reviews:

Macchi, Borghesi, Passoni, Rev. Mod. Physics, 85, 751 (2013)

M. Borghesi, in L. A. Gizzi *et al.* (eds.), Springer Proceedings in Physics 231, 143-164 (2019)

Properties of TNSA proton beams

Short duration at source:

bursts with duration ~ ps

Broad spectrum:

continuum up to 10s of MeV
in a divergent beam
E_{max} ~ 85 -100 MeV

F.Wagner *et al*, Phys. Rev. Lett., 116, 205002 (2016)
A.Higginson et al, Nature Comm., 9, 724 (2018)

High laminarity:

rms emittance < 0.01 π mm-mrad

High brightness:

10^{11} –10^{13} protons/ions per shot

High intensity pulse

relativistic electron cloud   proton beam

aluminum foil   5MeV   15MeV   25MeV

Typical spectrum from VULCAN PW

Number of protons per MeV

Proton energy (MeV)
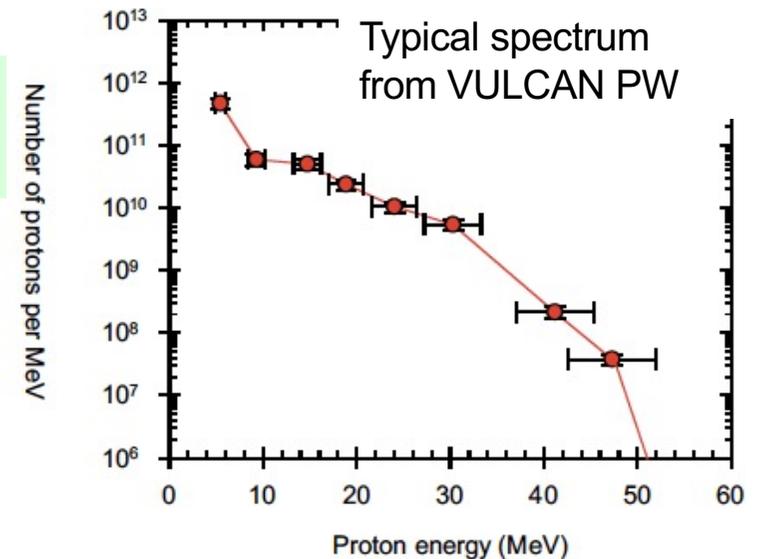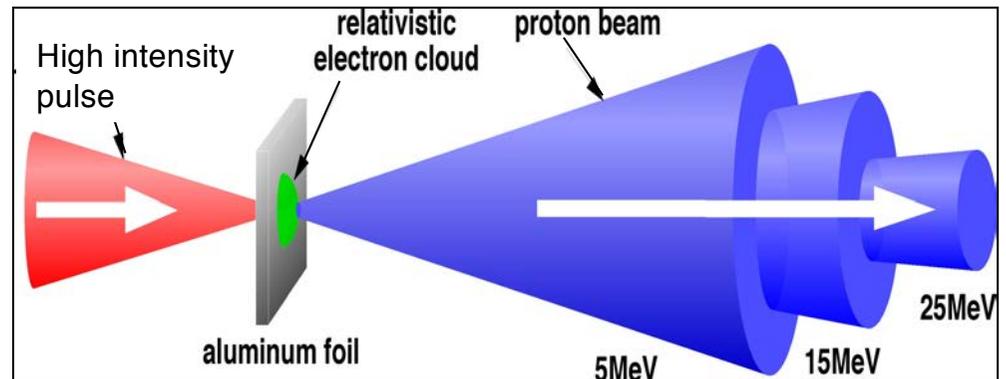
Alternative mechanisms investigated for different ions

Laser pulse

Ions
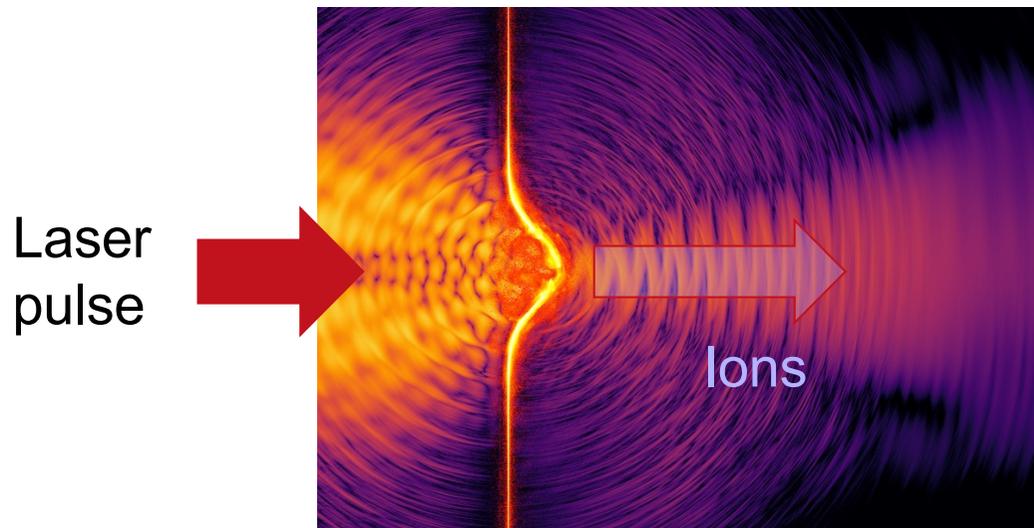
Radiation pressure acceleration of ultrathin foils (~ 10 nm)

Particularly effective on bulk species within the target (e.g. **carbon**)

Acceleration by radiation pressure

Radiation pressure upon light reflection from a mirror surface:

$$p_R = \frac{2I_L}{c}$$
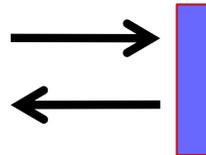
P_L=60 Gbar @ 10^{20}Wcm^{-2}

In a plasma the effect is felt by the electrons via the **ponderomotive force**

$$f_p = -\frac{m}{4}\frac{\partial}{\partial x}v_{os}^2(x)(1-\cos 2\omega_0 t)$$

Normally, the electron heating effect masks any steady pressure effect

Non-oscillating term   Oscillating term

Steady pressure,
transferred to ions via space-charge

JXB heating,
hot electrons

Laser 2ω

0ω

E

Laser-polarization can be used to control the balance between the two terms

A.Macchi *et al*, PRL **94**, 165003 (2005)
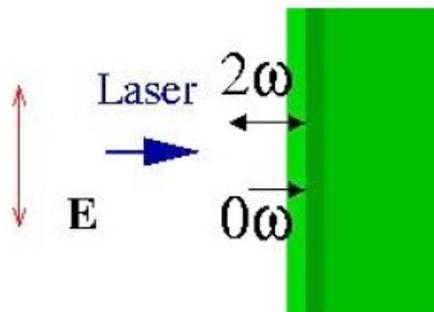
Linear polarization

Laser 2ω

E

0ω
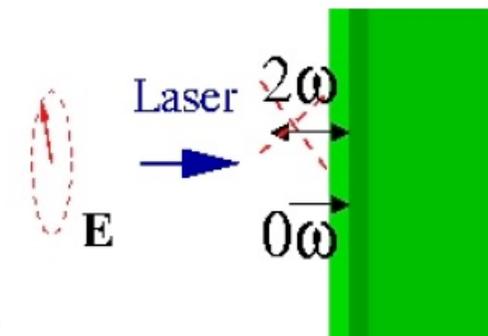
Circular polarization

Interaction with ultrathin foils : Light Sail

T.Esirkepov, et al. Phys. Rev. Lett., **92**, 175003 (2004)
APL Robinson et al, NJP, **10**, 013021 (2009)

- Bulk acceleration: equally efficient on different species

- Fast scaling with intensity $E_{ions} \sim (I\tau/\eta)^2$
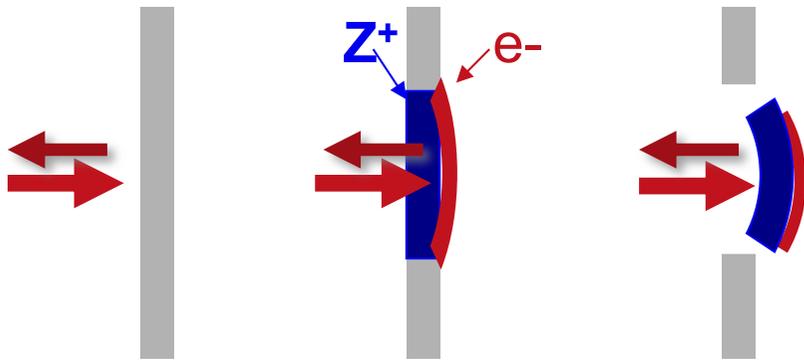
Target must stay opaque:

Ideal conditions realized for ultrahigh contrast, CP pulses (minimized electron heating)

Similar concept used for solar sails – space travel

Nanosail D2, (US)
Jan 2011

Transparency onset terminates the action of radiation pressure

Experiments with ultrathin foils – efficient Carbon acceleration

Radiation Pressure Acceleration (Bulk acceleration)

<u>ASTRA GEMINI results</u>
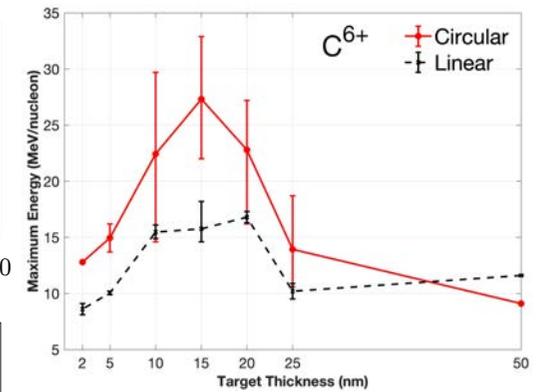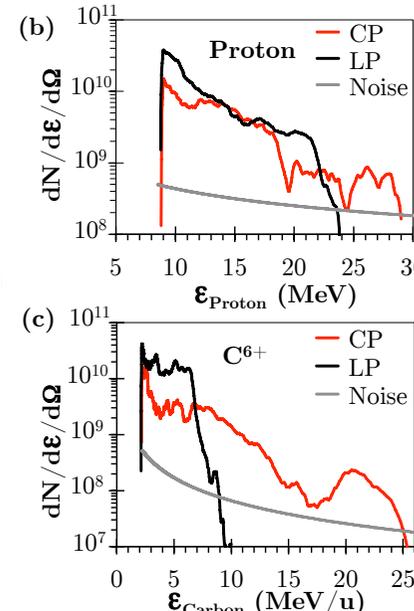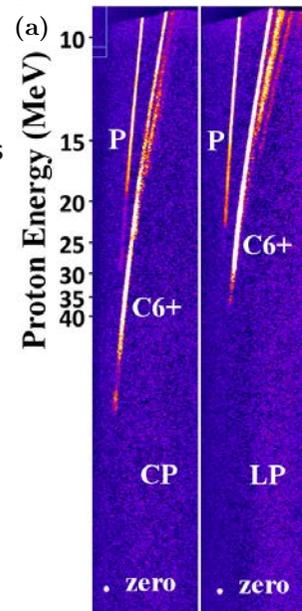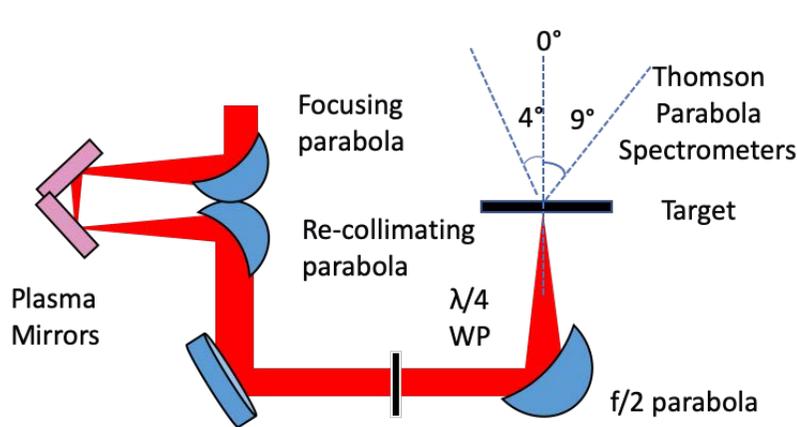
GEMINI: 40 fs, 6 J, ~ 5 10^{20} W/cm^2, plasma mirror for contrast enhancement, polarization control

Optimum thickness for RPA:

$$\eta \approx \pi \frac{n_0}{n_c} \frac{\ell}{\lambda} \sim a_0$$

- **Strong dependence on polarization, onset of Light Sail acceleration**
- **Particularly interesting for bulk Carbon acceleration**
- **Existence of an intensity dependence, optimum target thickness**

3D PIC simulations clarify the acceleration scenario

C.Scullion *et al,* Phys. Rev. Lett., **119**, 054801 (2017)
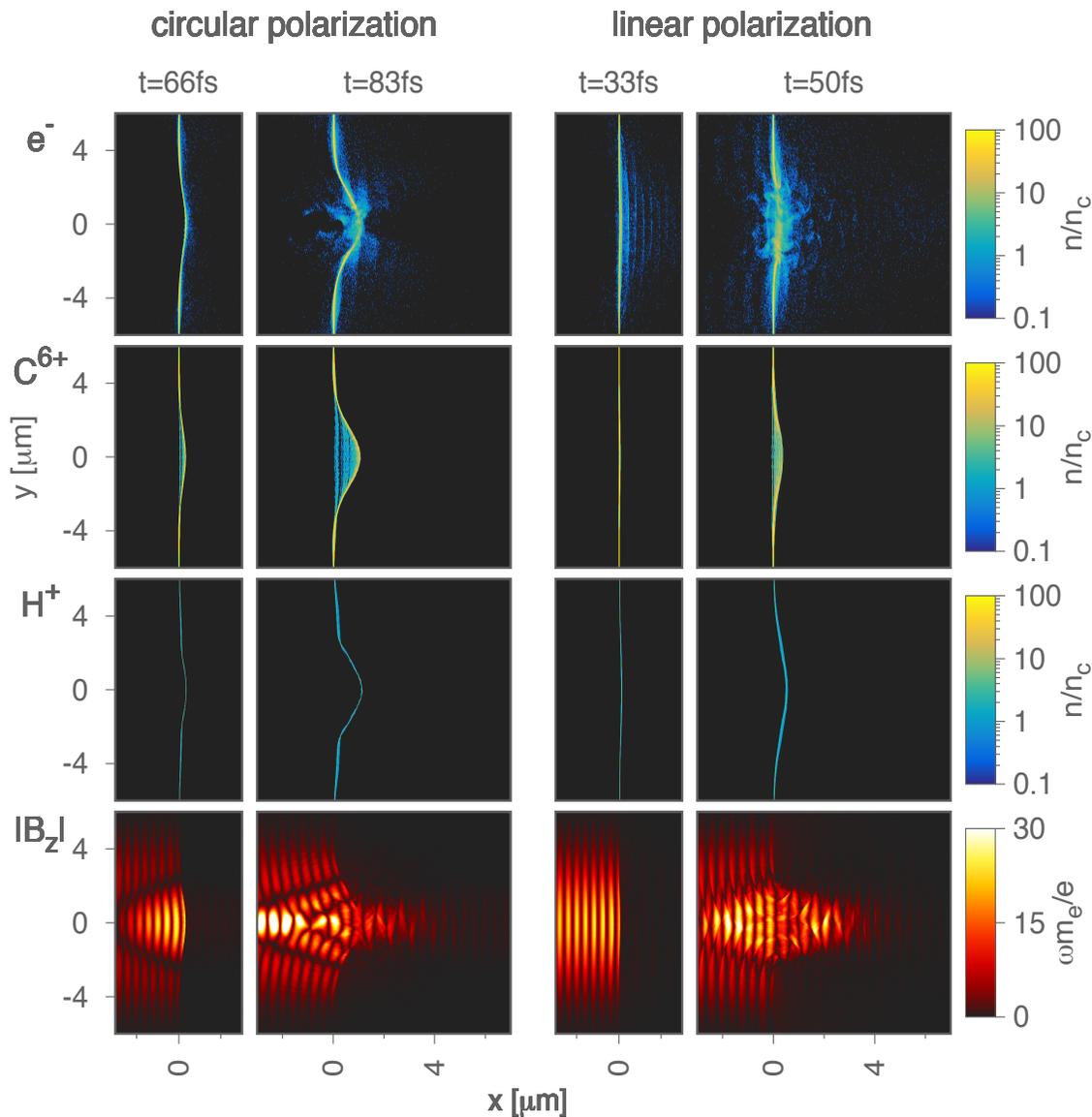

Linear polarization:
strong heating,
early transparency,
target decompression

Circular polarization:
Opacity maintained for longer
Radiation pressure applied more
efficiently
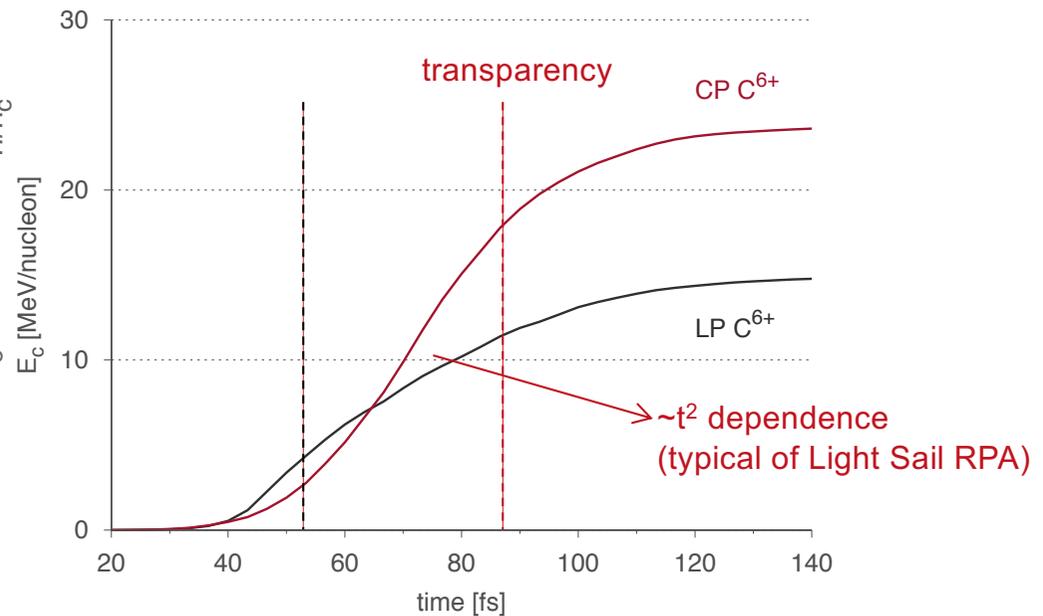
Scaling of Carbon energies to higher intensities
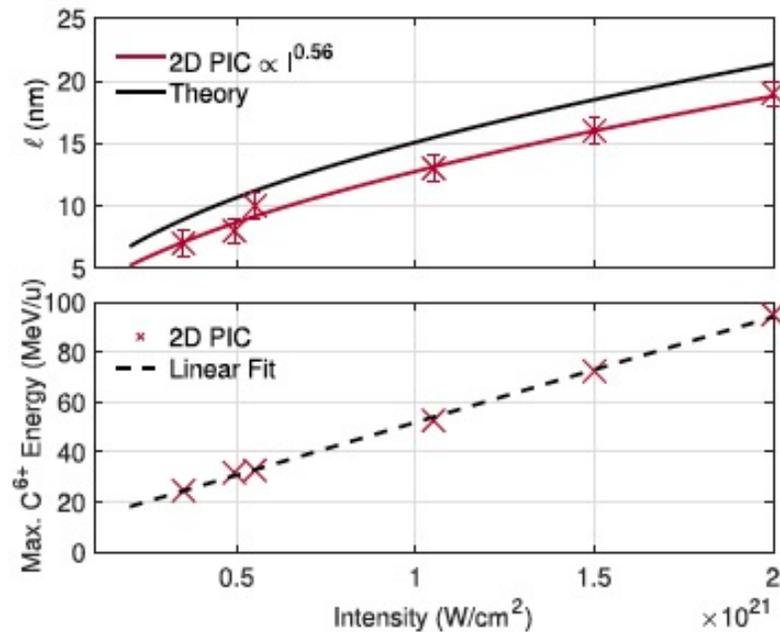

f/2 focusing , 40 fs,
(GEMINI conditions)

$$E_{ions} \sim \left(I\tau/\eta\right)^2 \implies E_{opt} \sim \left(\frac{I}{\sqrt{I}}\right)^2 \sim I$$
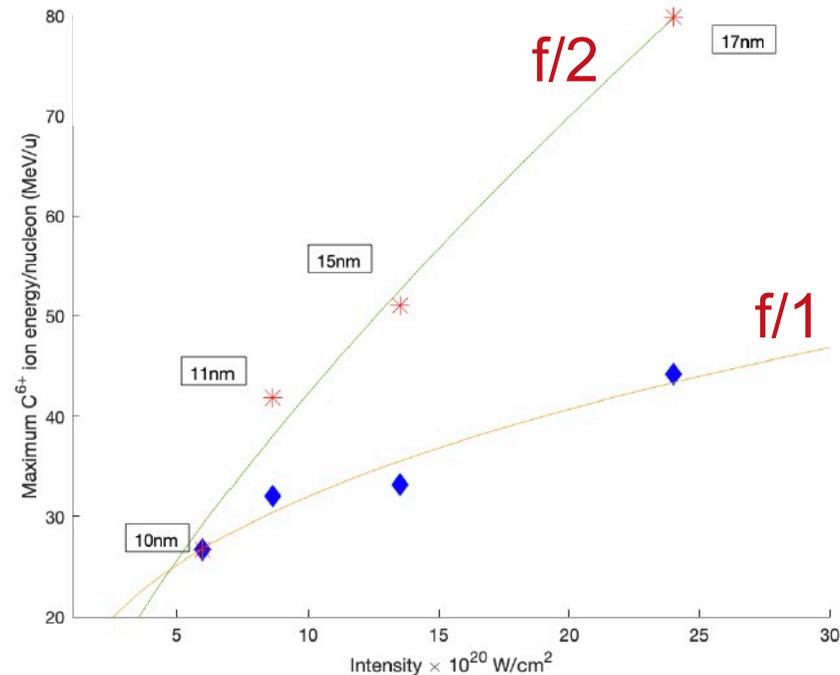
$$\eta_{optimum} \sim a_0 \sim \sqrt{I}$$

Increasing intensity by tighter focusing has some limitations

A.McIlvenny et al, PPCF, **62**, 054001 (2020)

Role of secondary factors (pulse's rising edge)

A. McIlvenny *et al*, submitted (2021)
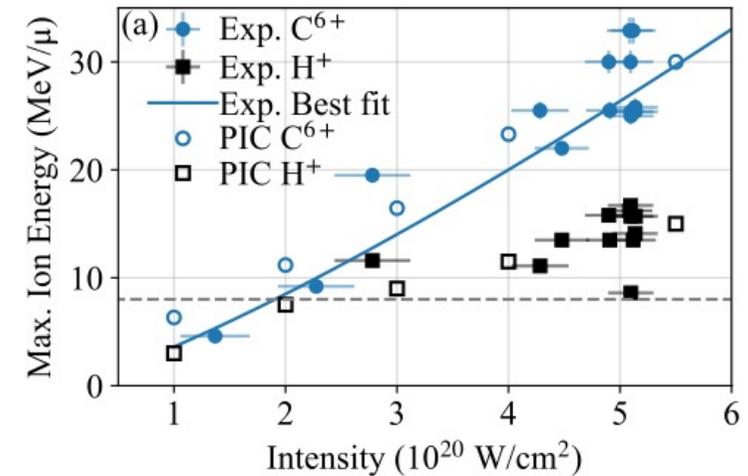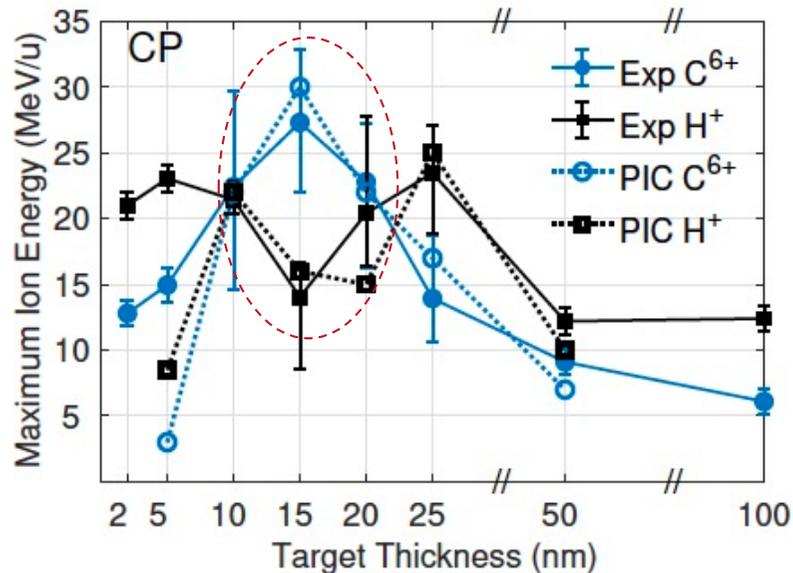
At the optimum thickness, precursor energy leads to pre-expansion of protons, which are not accelerated efficiently.
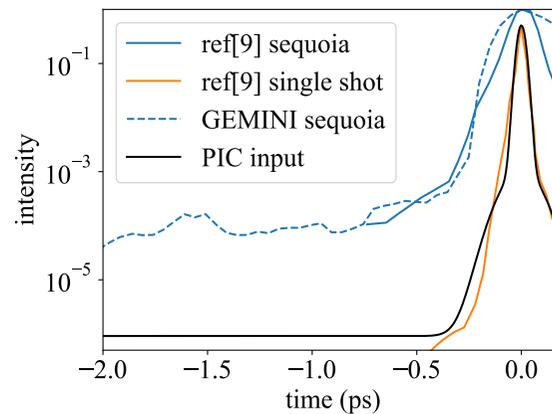
Modelling the laser rising edge on ps time scales is key to understanding the different species dynamics

Possibility of **pure Carbon** acceleration at high energy

Radiotherapy proposed early on as a target application

Reduced cost/shielding:

- Laser transport rather than ion transport

  (vast reduction in radiation shielding)

- Possibility to reduce size of gantry

Vision **first proposed in** :

S.V. Bulanov *et al*, Phys. Lett. A, **299**, 240 (2002)
E. Fourkal et al, Med Phys., **30**, 1660 (2003)
V. Malka, *et al*, Med. Phys., **31**, 1587 (2004)

Flexibility:

- Possibility of controlling output energy and spectrum

- Possibility of varying accelerated species

- Spectral shaping for direct "painting" of tumour region

Novel therapeutic/diagnostic options

- Mixed fields: x-ray + ions

- In-situ diagnosis

- Proton radiography/PET…
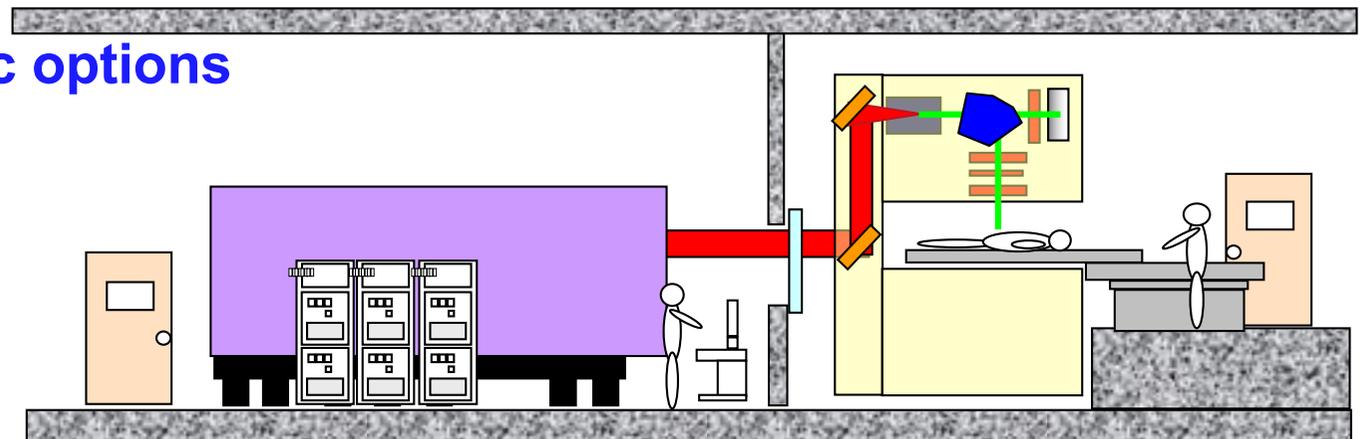
Growing interest in highly pulsed delivery (FLASH)

Tumor control (TC)

Normal tissue complication (NTC)

TC without NTC

Conventional
FLASH

Therapeutic window

Probability in %

Dose →

Relative radiosensitivity

Oxygen tension

Normal tissue (physoxic) → Radiation resistance increases → Normal tissue protection

Tumour (hypoxic) → Radiation resistance unchanged → No change in tumour damage
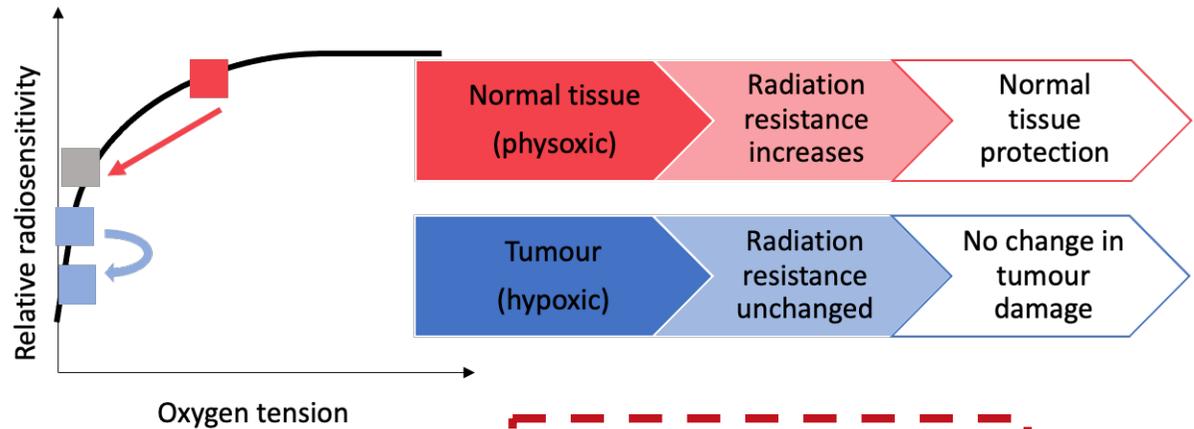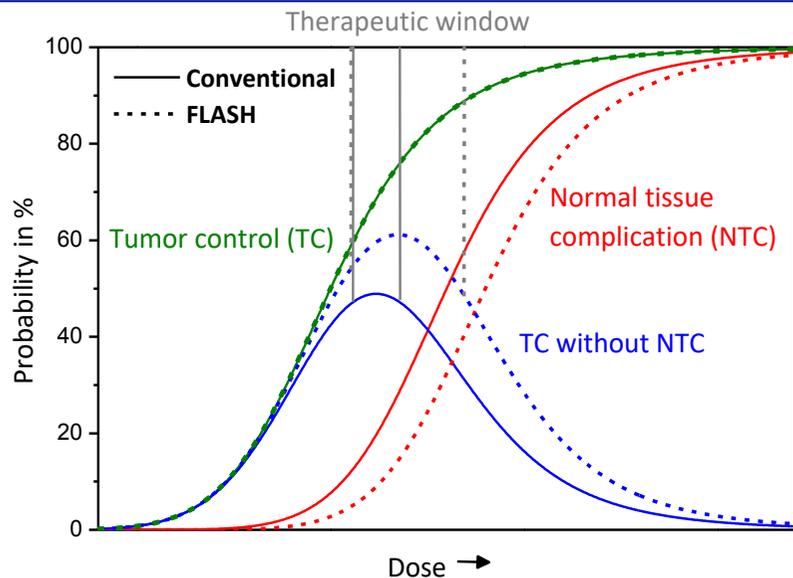
FLASH parameters
- 1 – 10 Gy per pulse
- 10^6 Gy/s per pulse
- 40 – 1000 Gy/s mean dose rates
- 100 ms dose delivery

Compared to conventional treatment, FLASH radiotherapy is
- as effective in destroying tumours
- less damaging to healthy tissues

Examples:
mice lung and brain irradiations
(prevention of lung fibrosis , protection of blood vessels, bronchi, sparing of spatial memory)

Fauvadon, Sc Transl med (2014)
Gruel, Radiotherapy Oncology (2016)

Laser – driven particles are naturally ultrashort, and can reach dose rates many order of magnitude higher than used in FLASH

Can this be beneficial to radiotherapy?

conventional radiotherapy   FLASH radiotherapy   VHEE radiotherapy (RF-driven)   laser-driven electron beams   laser-driven proton beams   proton therapy with synchrocyclotron   FLASH proton beam

Challenges of current research

- **Demonstrate feasibility of ion beam production**
  - High energy
  - Natively narrow energy distribution
  - High repetition, stability

- **Develop methods of beam transport/ delivery**
  - magnetic based or target based

- Assess the **biological effectiveness** of ultrashort ion bunches

- **Development of appropriate dosimetry**

Several activities in Europe to advance these issues:

OncoRay (HZDR, Dresden)

LIGHT (GSI Darmstadt)

CALA (Munich)

ELIMAIA/ELIMED @ ELI Beamlines (IoP, Cz)

UHDPULSE (EU Network on dosimetry)

LHARA (UK consortium, IC/STFC)

A-SAIL (UK consortium, EPSRC)

Several approaches pursued for beam delivery for pre-clinical studies
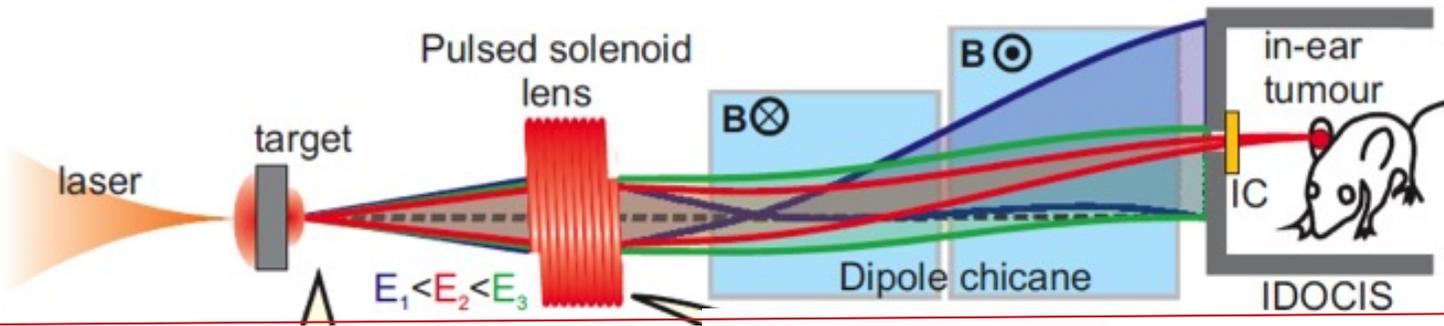
Zeil et al. Appl. Phys. B 110, 437 (2013)

ELIMAIA
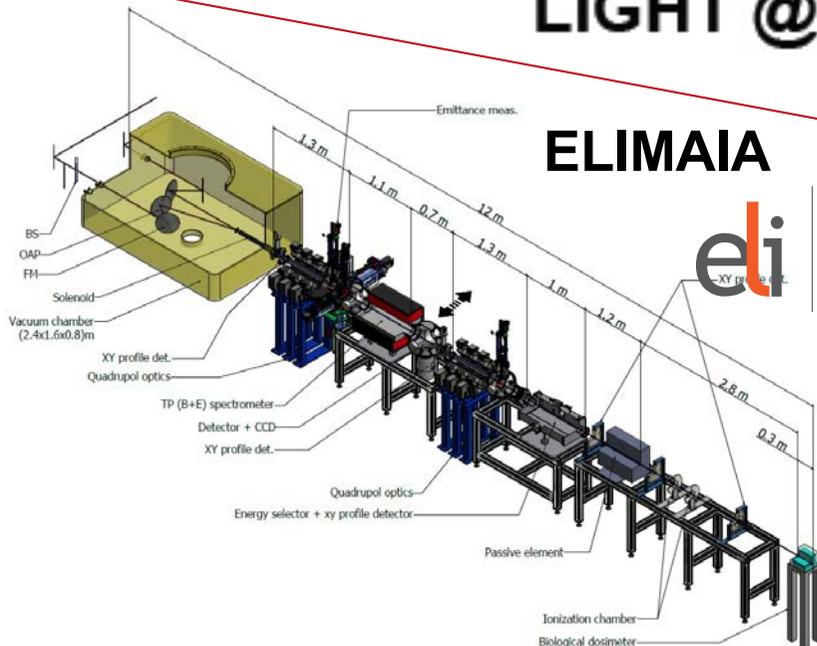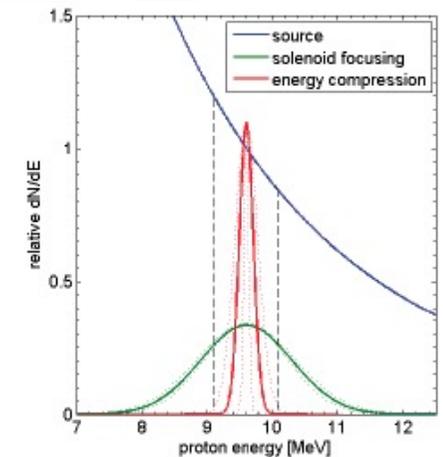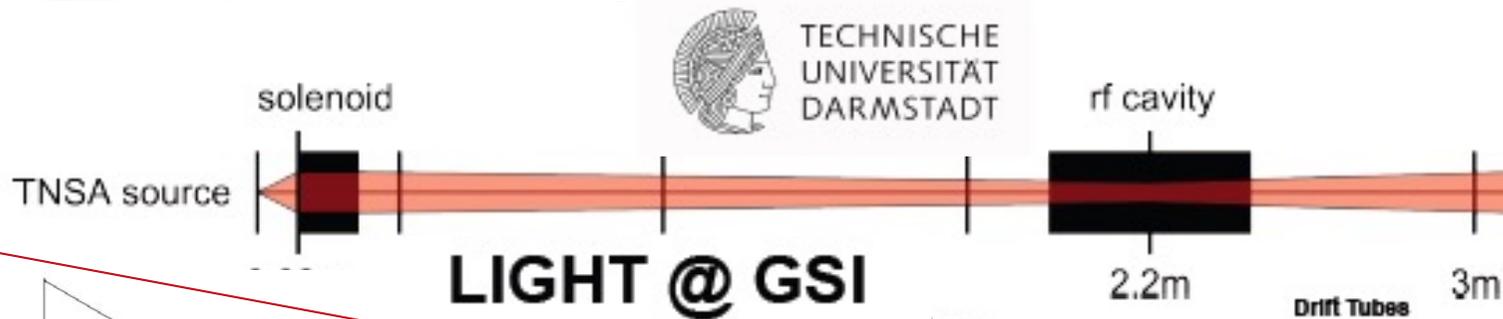
INFN (It)

1 PW, 10 Hz laser source
Targeting 60 MeV delivery
Conventional elements for controlling beam properties
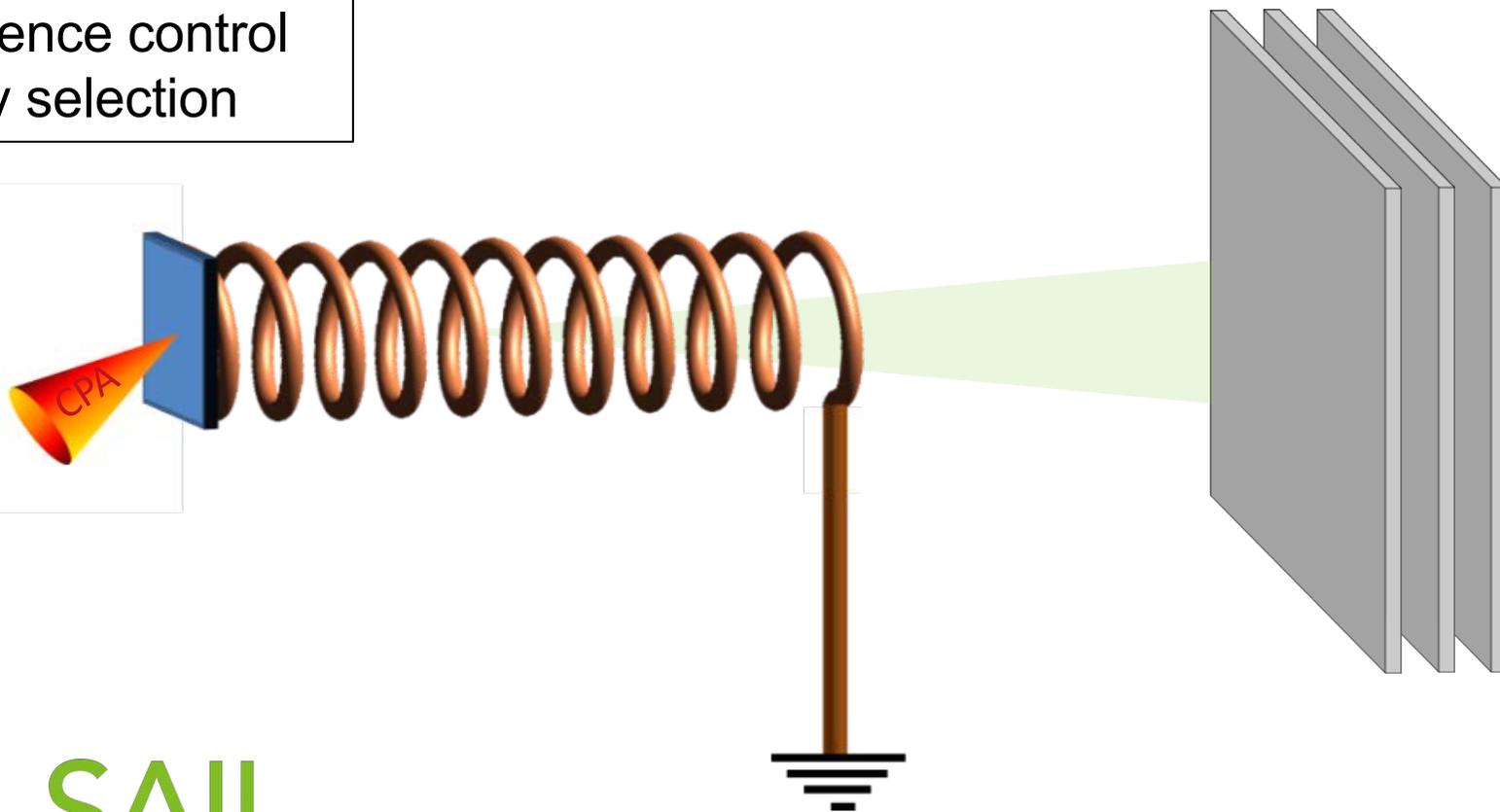
High amplitude EM pulses from intense interactions

Ejected charge

Wire

Laser
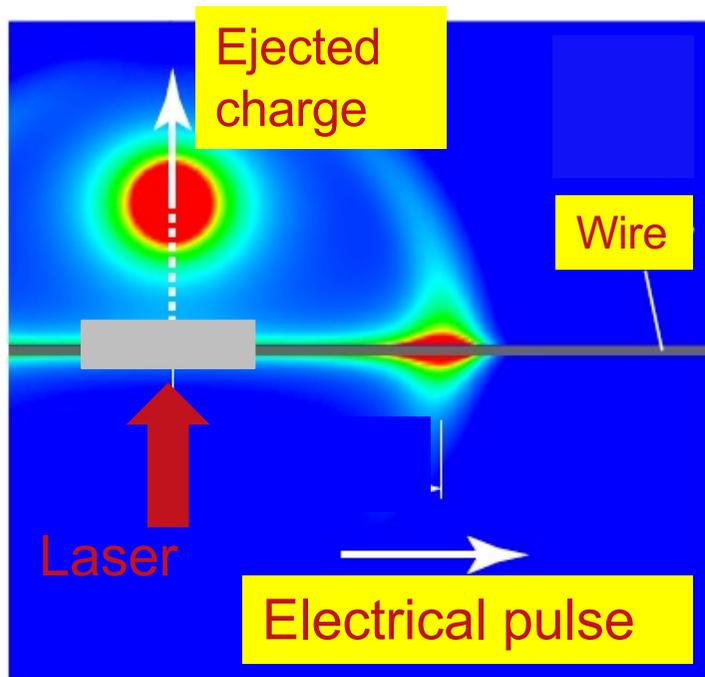
Electrical pulse

Large amplitude, ultrashort unipolar electrical pulses propagating at v ~ c are launched by high intensity interactions

The pulse carries positive charge away from the interaction region contributing to the target neutralization

K. Quinn *et al*, Phys. Rev. Lett., 102, 194801 (2009)
S. Tokita *et al*, Sci. Rep.,5, 8268 (2015)
A. Poye et al, PRE, 91, 43106 (2015)
H. Ahmed, NIMA, 829, 172 (2016)

61ps

Q~ 60 nC

15-20 ps

Linear charge density [µC/m]

Difference betrween probing time and charge arrival time (ps)
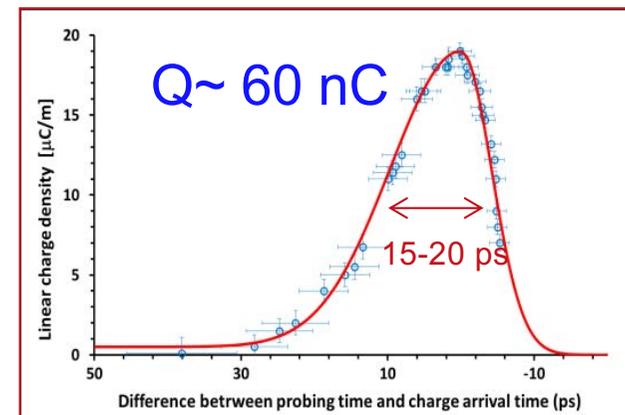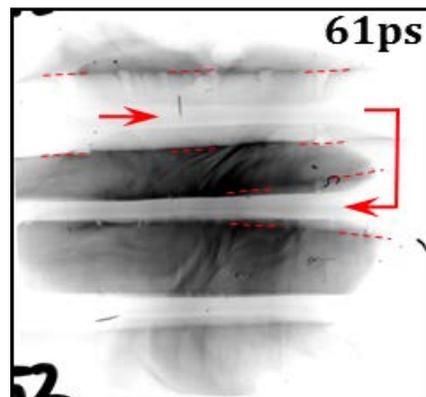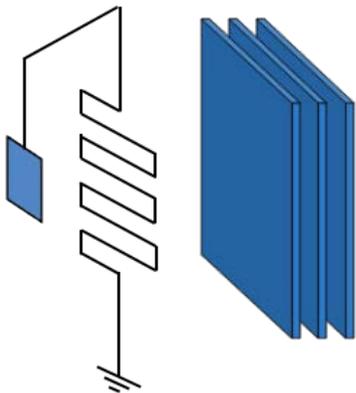
Coil targets for proton beam optimization
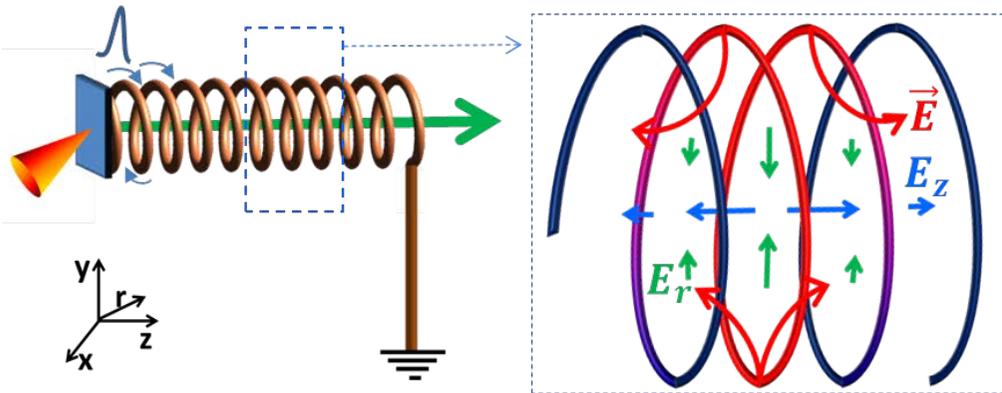
EM pulse propagating along coiled wire at v ~ c
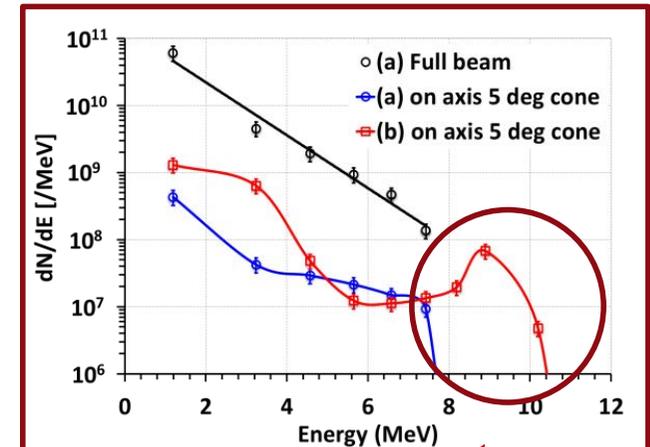
The field structure is essentially equivalent to the field of a **charged ring**
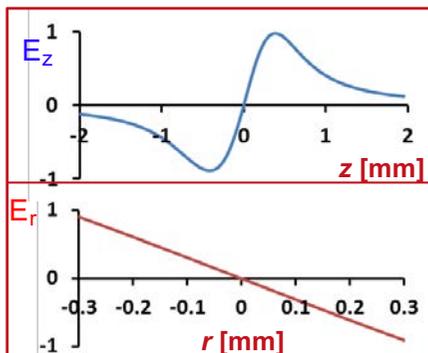
Choice of geometry(coil diameter, pitch) allows "longitudinal" synchronization with a group of protons
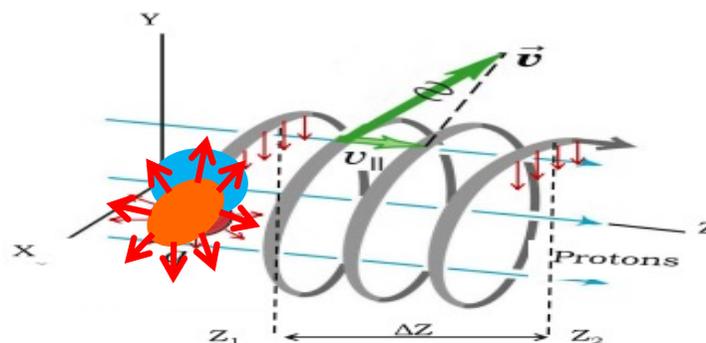
Re-accelerated bunch

mm
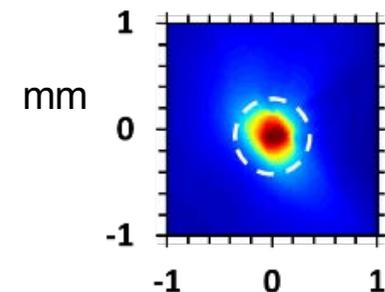
⇒ Divergence < 1°
measured at 35 mm
from the target

ARCTURUS laser, Dusseldorf (De)

High energy implementation

Data obtained using Titan Laser, LLNL: ~ 120 J in ~ 0.6 ps, f/3 focusing, Intensity ~2×10^{20} W/cm^2

RCF stack at 6 cm from foil

Coil diameter and pitch~ 700 μm, L~ 8 mm
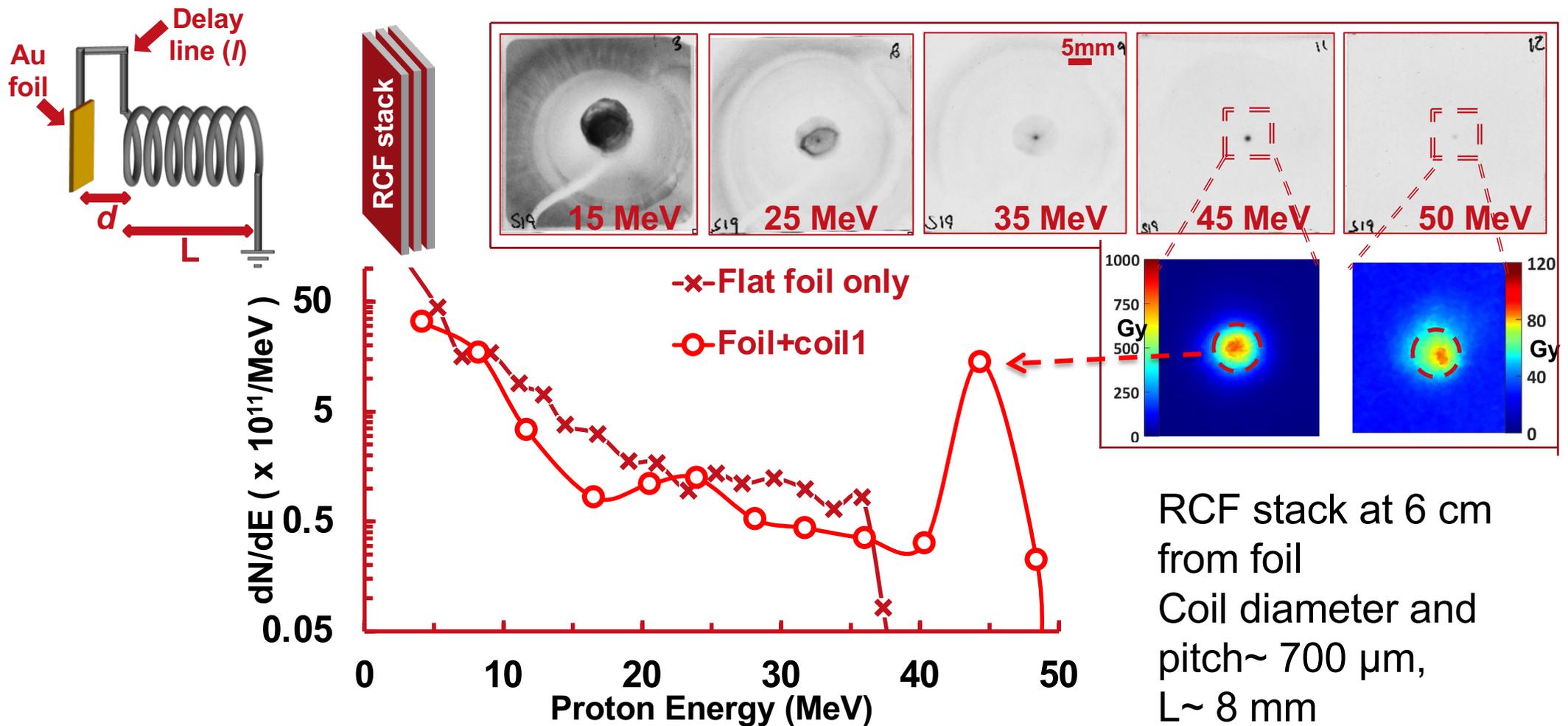
Dephasing saturates the post-acceleration process

Data from VULCAN PW

Legend:
- Simulations-constant pitch
- Experimental data
- Simulations-varying pitch
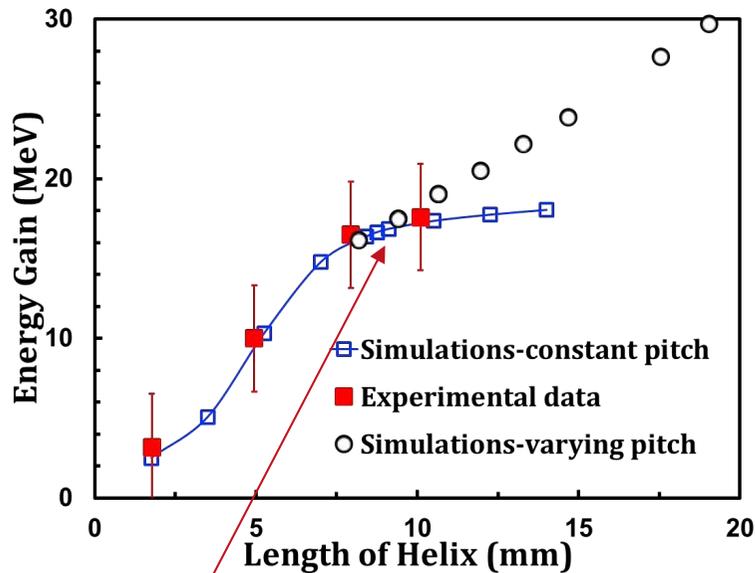
Dephasing: protons overtake the accelerating structure

Two solutions:

1) Variable coils

$$p(z) = 2\pi r \sqrt{\frac{\gamma_p^2 - 1}{(\beta_{EM}^2 - 1)\gamma_p^2 + 1}}$$

2) Multi-staging


Simulation for 30 MeV protons

Constant pitch   Variable pitch
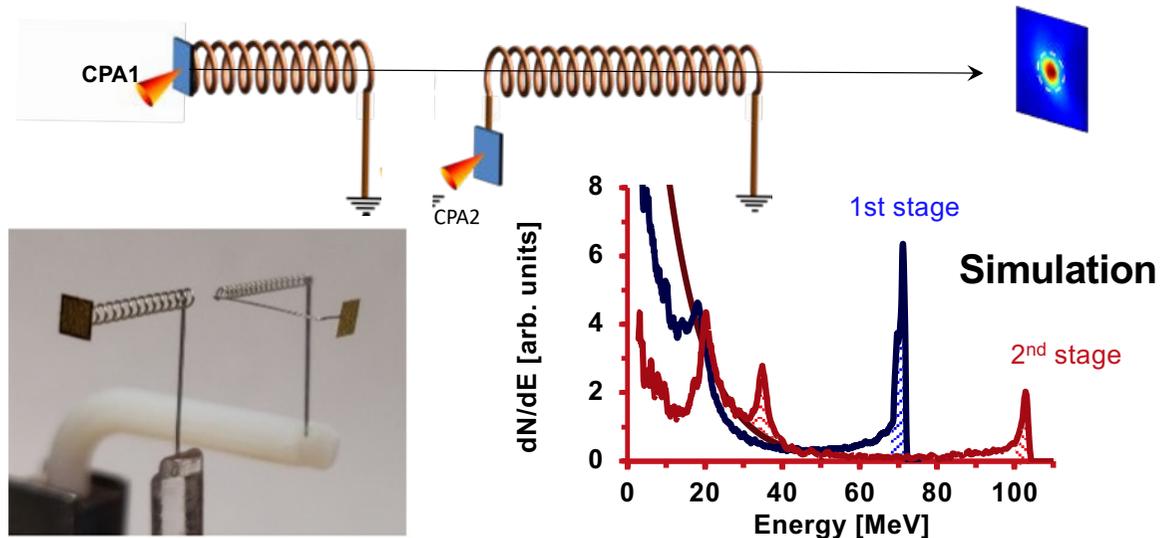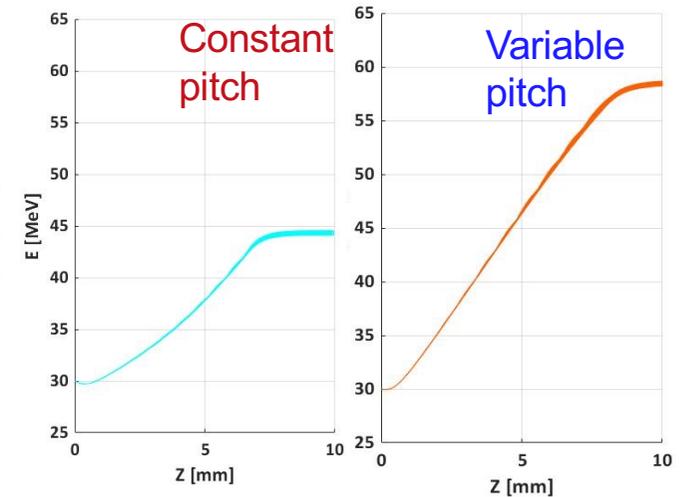
Opportunities for compact beamline development

Coil coupled to magnetic selector
(quadrupole or dipole system)

Challenges:
Pointing stability
Repeatability
Repetition rate
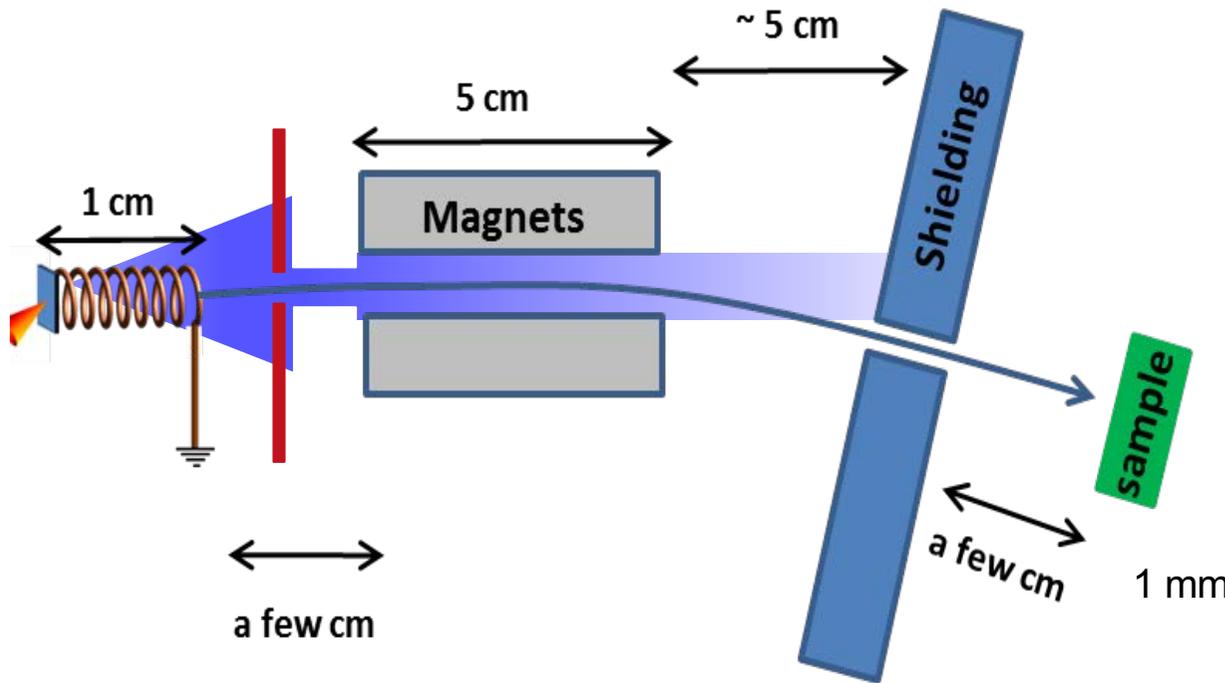
Collimated emission from
helicoidal targets :
Higher dose and dose rate
Higher spectral quality

Gy-doses on a single shot
basis at much higher energies
Opportunities for very localized
delivery
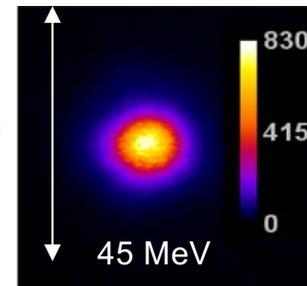
Dose profile on VULCAN
PW at 5 cm from target
(expanding beam)
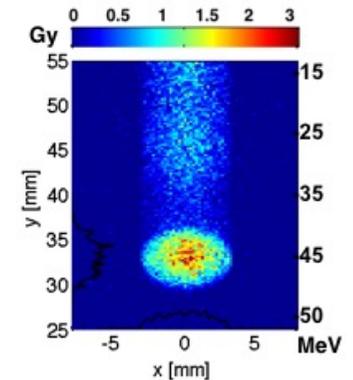
Beam at cell
plane

Radiobiology at ultra-high dose rate
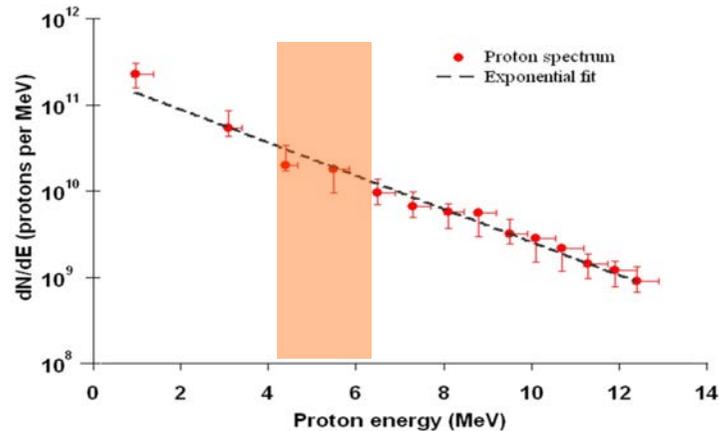
Laser-driven ions (TNSA) within a range ΔE are emitted at the source within a time $\Delta T <$ ps.

Time of flight dispersion @ ~ 10s of cm results in dose deposition in 100s ps - ns pulses

**Dose rates > 10^9 Gy/s** can be achieved: compare with ~Gy/s (~100Gy/s) used in standard (FLASH) radiotherapy

Largely unexplored regime of radiobiology:

Local depletion of oxygen affecting cell radiosensitivity

Collective effects from track overlap

Potential commonalities with **FLASH effects** (sparing effects for sublethal irradiations)

DNA DSB damage 53BP1 foci, γH2AX | 6-well plate Clonogenic Assay | SIPS Assay | 3D Spheroids From Brack et al [70]
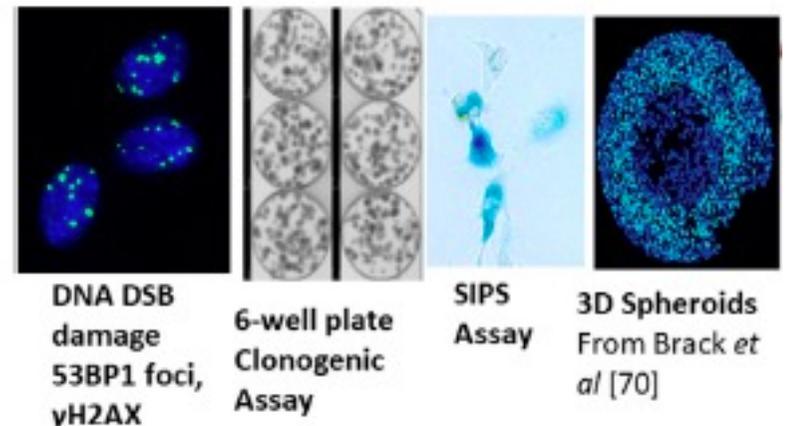
Dose-rate effects : unknown for UHDR pulses
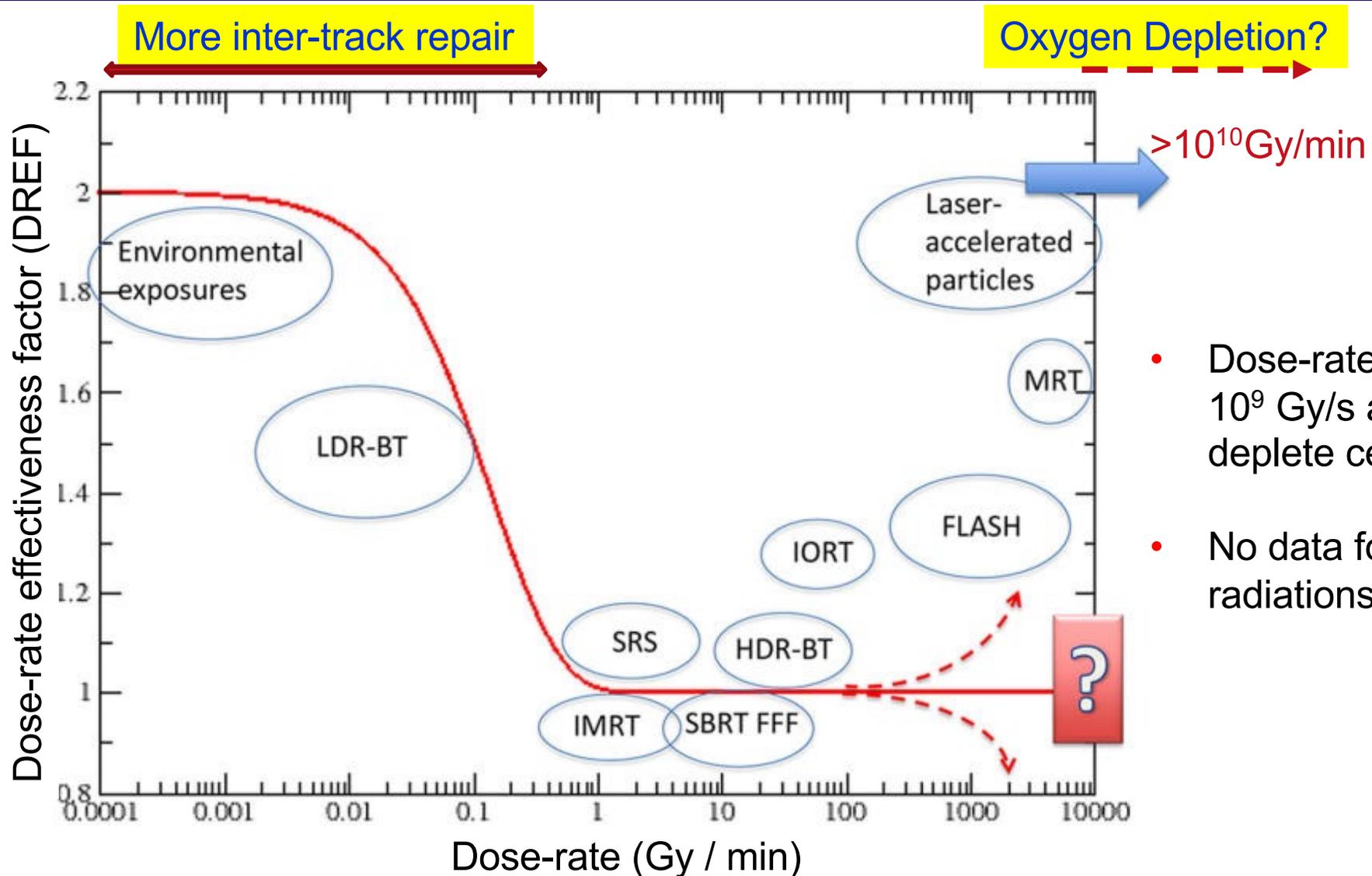
Durante *et al.,* BJR 2018, **91**: 20170628

Pre-clinical studies: biological effects of laser-driven ions

Several groups have been active in using laser-driven ions for cell irradiation studies

At QUB, we carry out this work in collaboration with the **Centre for Cancer Research** (Prof. K. Prise)

- **APRC, JAEA (Japan)**
- **HZDR (Germany)**
- **LMU/MPQ (Germany)**
- **LOA (France)….**

Key Questions:

➤ What is the biological response of cells to ultrashort ion bursts ?

➤ How does oxygen presence affect ultra-high dose rate radiobiology?

➤ Do FLASH sparing effects extend to ultrahigh dose rate laser-driven pulses?

Review paper:
P. Chaudary *et al*,
Front. Phys,**10**, 3389 (2021)

In our experiments we aim to deliver
 ~ **Gy-level doses** in **single** ultrashort (100 ps- ns) pulses

Typical set-up for laser-driven radiobiology

F. Hanton et al, Sci. Report, **9**, 4471 (2019)
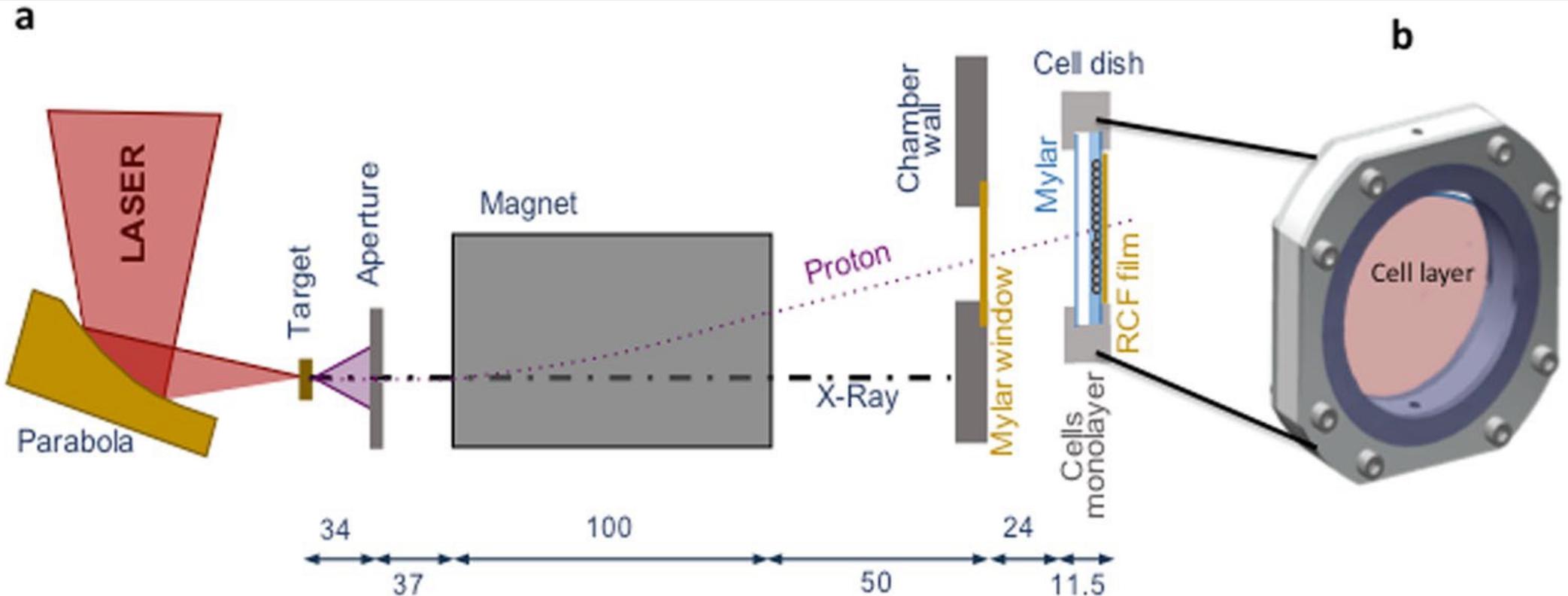
- Linearly polarised beam with intensity ~**3 x 10^{20}Wcm^{-2}**
- Dipole magnet (1T) implemented to disperse ions with respect to energy.
- Compact system to maximize dose and dose rate to cells (~ 1-10 Gy, > 10^9 Gy/s)
- System can be tailored for Carbon ion irradiations

Irradiation set-up - VULCAN laser


Cell dish containing 1ml of media and 400,000 cells
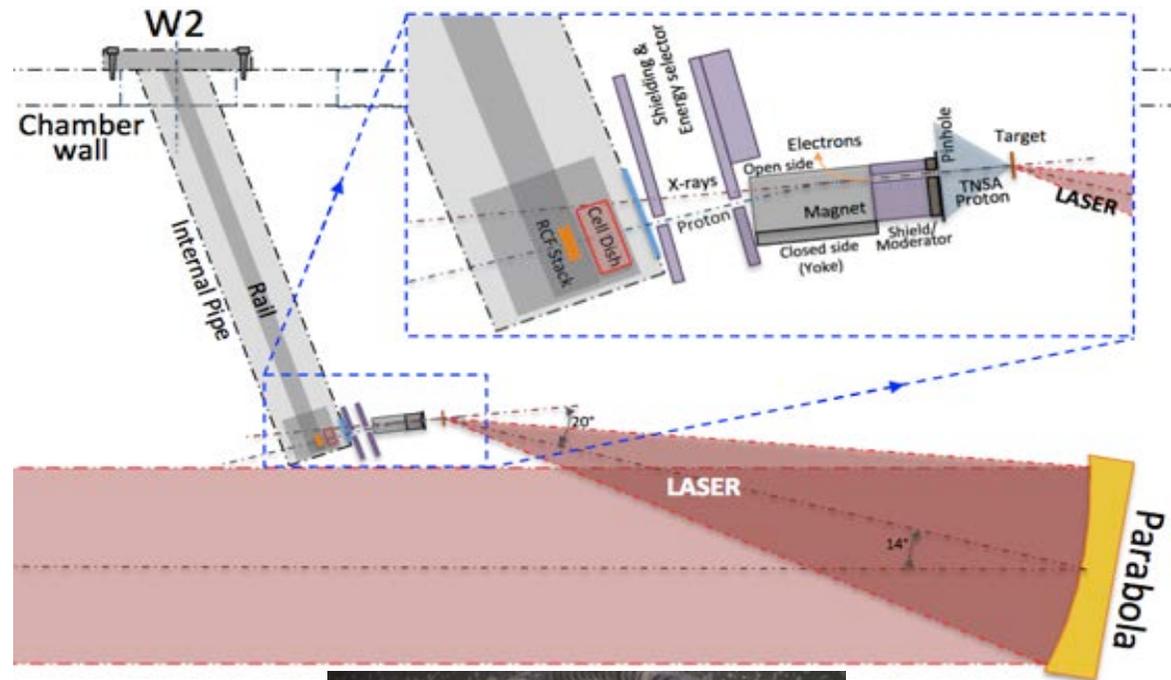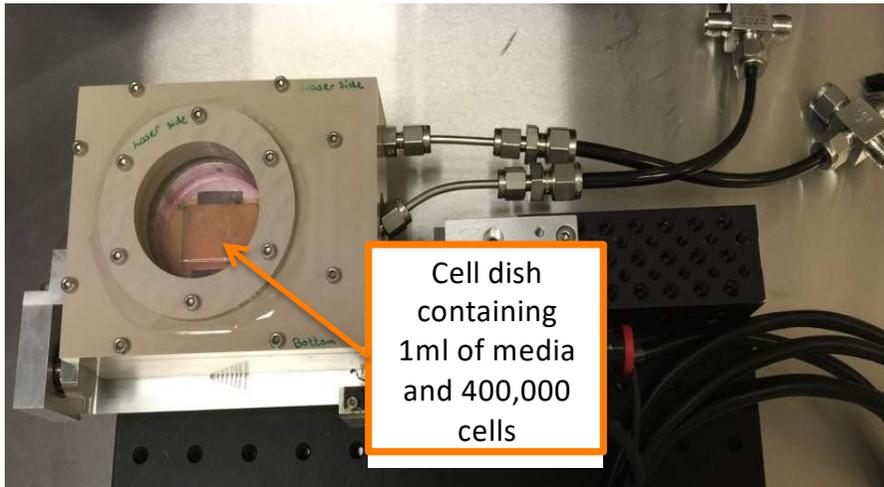
Example: DNA damage studies
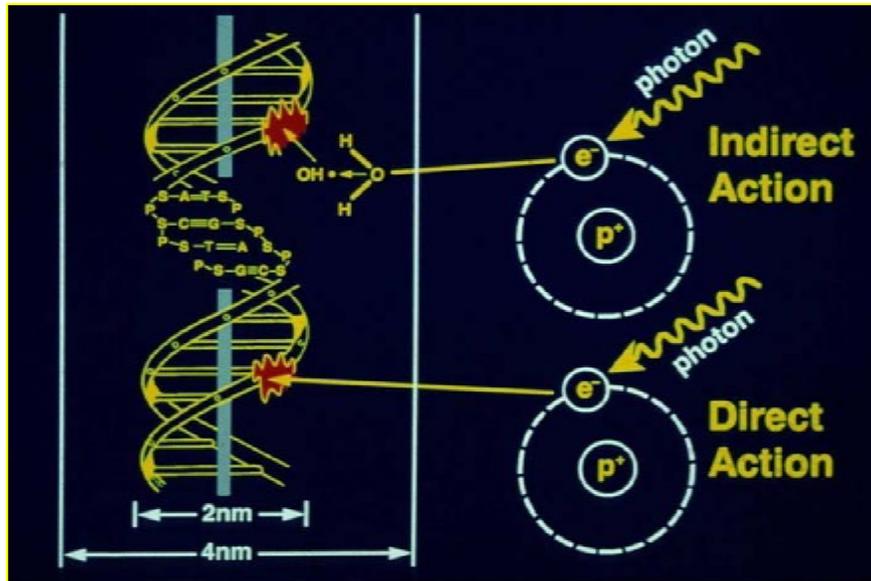
Radiation damages cellular DNA through direct and indirect effects

- Most important DNA damage is **double strand break (DSB,** two breaks close to each other on opposite strands) .

- DSB difficult to repair, mis-repair can lead to mutations and even cell death.

53BP1 foci

DNA damage and repair (53BP1 immunofluorescence):
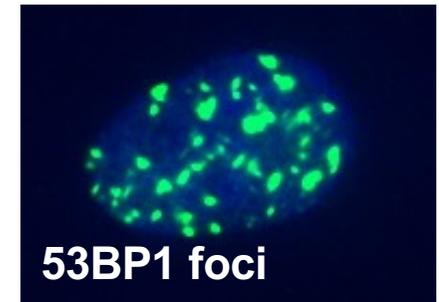
| Cell irradiation | → | Cell fixing | → | Cell staining | → | Counting of foci |

0.5- 24 hr

Process involving an agent which binds to DSBs

Foci (regions of accumulation of the agent) are highlighted , e.g. by fluorescence

DNA repair dynamics investigated up to 24 hours

F. Hanton *et al*, Sci. Report, **9**, 4471 (2019)
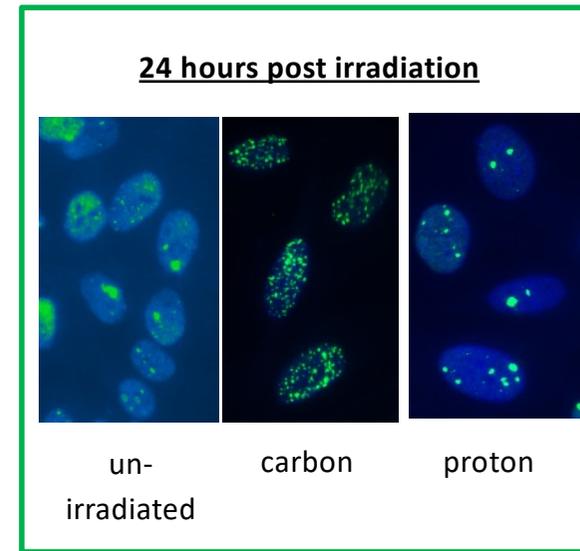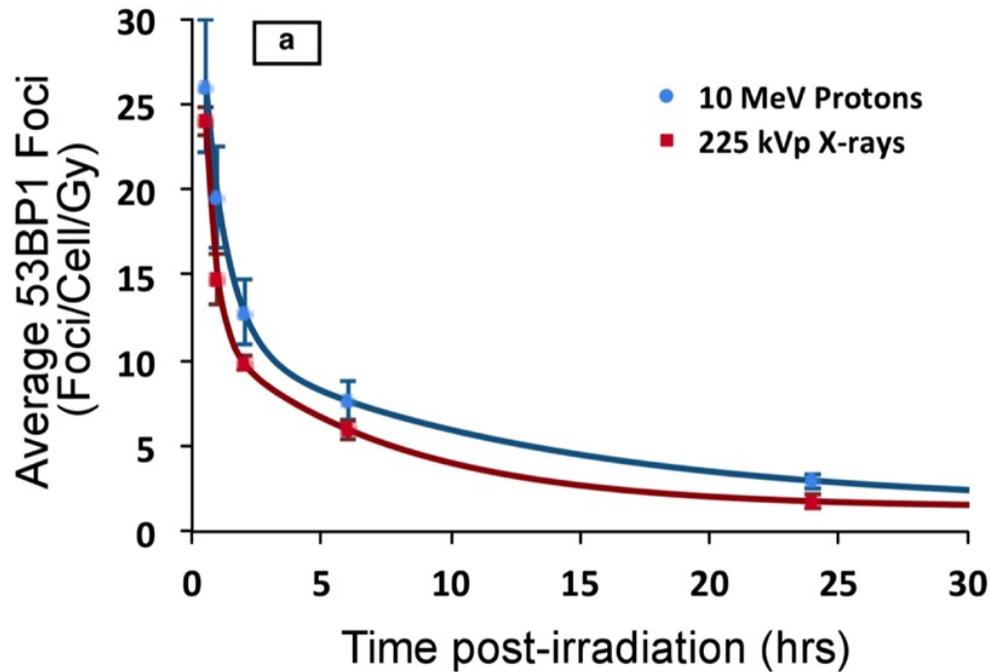
Cell line:
AG01522
Human
fibroblast
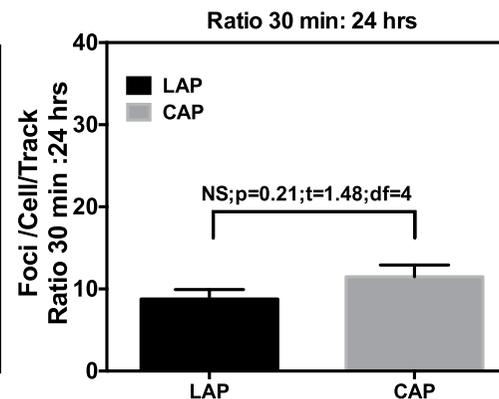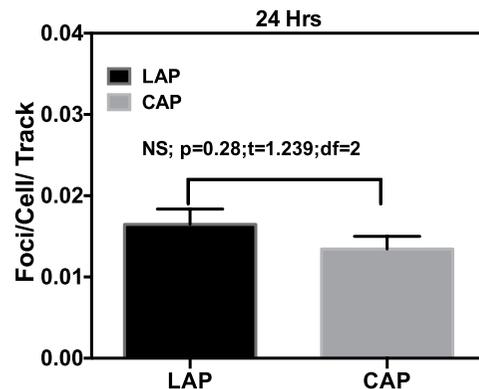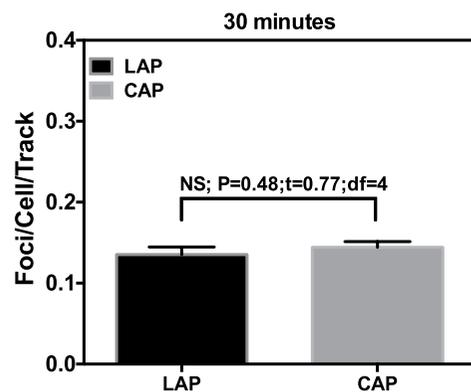
Results in line with
expectations
from conventional
irradiations

Conclusions

- **Laser-driven ion acceleration** is a technology **radically different** from established acceleration methods, with several aspects potentially attractive as a future driver for particle delivery in radiotherapy:
  e.g. optical transport , variable species (H, C,….), multi-beam opportunities

- The ultrashort time structure of the ion pulses can be exploited for **dose deposition at ultra high dose rates**, and is of particular relevance in the context of the growing interest in FLASH radiotherapy

- We have discussed opportunities for acceleration and delivery of carbon ions (**RPA on ultrathin foils**), conditioning and reacceleration of TNSA protons (coil targets), as well the use of laser-driven protons in **radiobiology experiments**.

- Ongoing technological developments promise significant progress in performance of laser-ion accelerators within next 3-5 years (energy ranges, repetition rate, etc.) which will increase further their application range

Contributors

P. Chaudhary, S.Kar, F.Hanton, D. Gwynne, C. Majorino, A. McIlvenny, B Odlizilik, C. Scullion, A.McMurray, K. Polin, K.Prise, *Queen's University Belfast*

H. Padda, S. Williamson, P. McKenna, *University of Strathclyde*

H. Ahmed, C. Spindloe, R. Pattathil, D. Neely, Central Laser Facility, RAL

E.J. Ditter, O. Ettlinger, G. Hicks, Z. Najmudin, *Imperial College London*

L Romagnani, *LULI, Ecole Polytechnique (France)*

D. Doria, ELI Nuclear Physics (Romania)

G.Milluzzo, F. Romano, G.A.P.Cirrone
Laboratori Nazionali del Sud, INFN (Italy)

A. Macchi, Istituto Nazionale di Ottica, CNR (Italy)