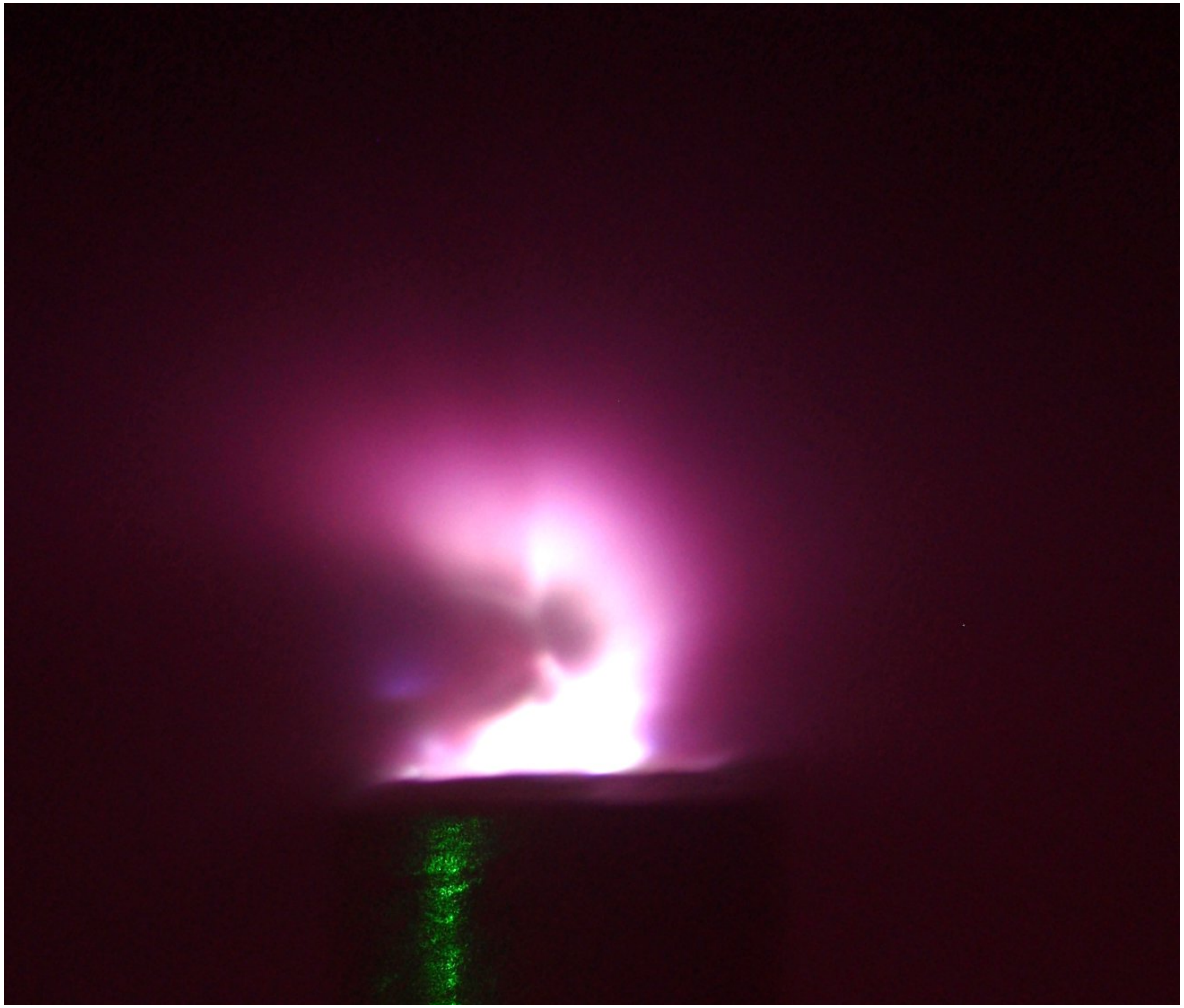


“Review of Laser Driven Ion Beams for Medical Applications”
CCAP Plenary Meeting
06/11/2018

Oliver Ettlinger

This may not be a complete list!

Who is interested in this work?*

Queens University, Belfast

GSI, Darmstadt

HZDR, Dresden

LULI, Paris

Munich

Catania, Sicily / Naples

ELIMAIA-ELIMED

J-KAREN, Japan

Requirements for laser-driven ion beams

i. Fundamental ion acceleration

ii. Beam capture and transport systems

iii. Effect of unique ion source properties

Requirements for laser-driven ion beams

i. **Fundamental ion acceleration**

ii. Beam capture and transport systems

iii. Effect of unique ion source properties

Fundamental Ion Acceleration

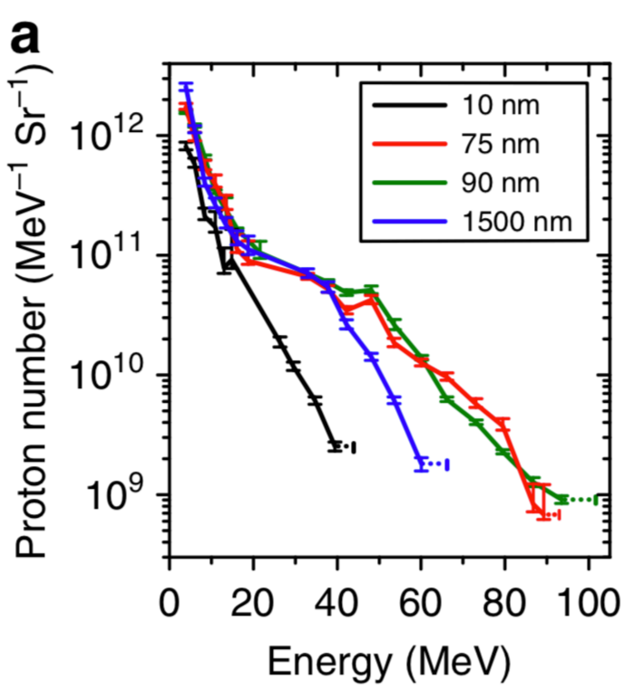
Current status:

(a) Peak Energy - “nearly” 100MeV…

DOI: 10.1038/s41467-018-03063-9 OPEN

Near-100 MeV protons via a laser-driven transparency-enhanced hybrid acceleration scheme

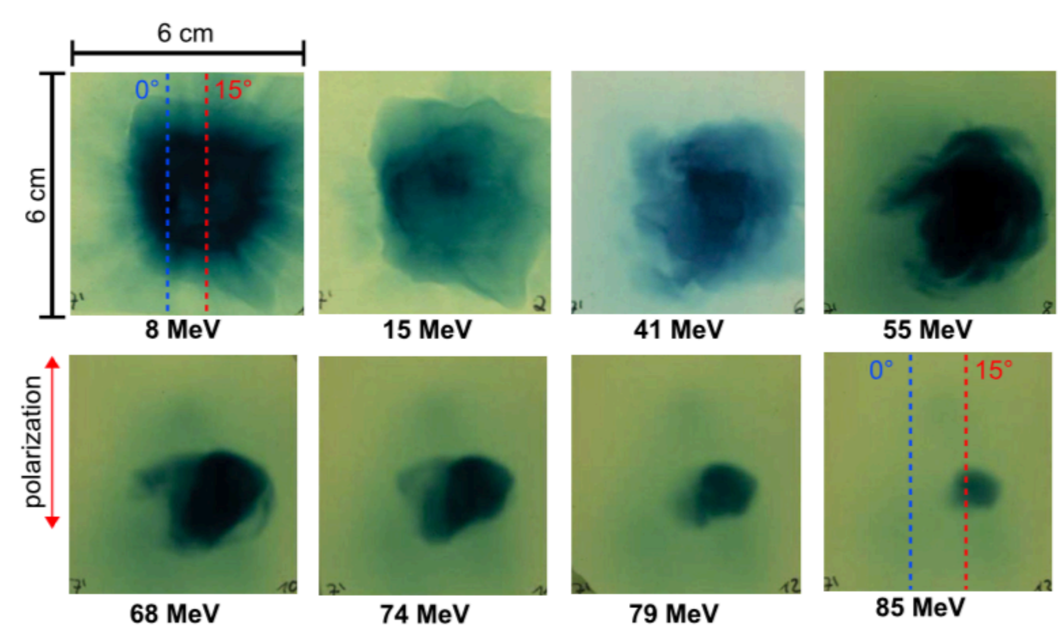
A. Higginson[1], R.J. Gray[1], M. King[1], R.J. Dance[1], S.D.R. Williamson[1], N.M.H. Butler[1], R. Wilson[1], R. Capdessus[1], C. Armstrong[1,2], J.S. Green[2], S.J. Hawkes[1,2], P. Martin[3], W.Q. Wei[4], S.R. Mirfayzi[3], X.H. Yuan[4], S. Kar[2,3], M. Borghesi[3], R.J. Clarke[2], D. Neely[1,2] & P. McKenna[1]



PRL 116, 205002 (2016) PHYSICAL REVIEW LETTERS week ending 20 MAY 2016

Maximum Proton Energy above 85 MeV from the Relativistic Interaction of Laser Pulses with Micrometer Thick CH_2 Targets

F. Wagner,[1,2,*] O. Deppert,[3] C. Brabetz,[1] P. Fiala,[3] A. Kleinschmidt,[3] P. Poth,[3] V. A. Schanz,[3] A. Tebartz,[3] B. Zielbauer,[1] M. Roth,[3] T. Stöhlker,[1,2] and V. Bagnoud[1,2]



Fundamental Ion Acceleration

Current status:

(b) Energy spread - lots of work using different acceleration schemes and structured targets

Vol 439|26 January 2006|doi:10.1038/nature04492 nature

LETTERS

Laser-plasma acceleration of quasi-monoenergetic protons from microstructured targets

H. Schwoerer[1], S. Pfotenhauer[1], O. Jäckel[1], K.-U. Amthor[1], B. Liesfeld[1], W. Ziegler[1], R. Sauerbrey[1], K. W. D. Ledingham[1,2,3] & T. Esirkepov[4,5]

Vol 439|26 January 2006|doi:10.1038/nature04400 nature

LETTERS

Laser acceleration of quasi-monoenergetic MeV ion beams

B. M. Hegelich[1], B. J. Albright[1], J. Cobble[1], K. Flippo[1], S. Letzring[1], M. Paffett[1], H. Ruhl[2], J. Schreiber[3,4], R. K. Schulze[1] & J. C. Fernández[1]

PRL **106,** 014801 (2011) PHYSICAL REVIEW LETTERS week ending 7 JANUARY 2011

Monoenergetic Proton Beams Accelerated by a Radiation Pressure Driven Shock

Charlotte A. J. Palmer,[1] N. P. Dover,[1] I. Pogorelsky,[2] M. Babzien,[2] G. I. Dudnikova,[3] M. Ispiriyan,[4] M. N. Polyanskiy,[2] J. Schreiber,[1,5,6] P. Shkolnikov,[4] V. Yakimenko,[2] and Z. Najmudin[1]

nature physics ARTICLES

PUBLISHED ONLINE: 13 NOVEMBER 2011 | DOI: 10.1038/NPHYS2130

Collisionless shocks in laser-produced plasma generate monoenergetic high-energy proton beams

Dan Haberberger[1], Sergei Tochitsky[1], Frederico Fiuza[2], Chao Gong[1], Ricardo A. Fonseca[2,3], Luis O. Silva[2], Warren B. Mori[1] and Chan Joshi[1]*

Fundamental Ion Acceleration

Current status:

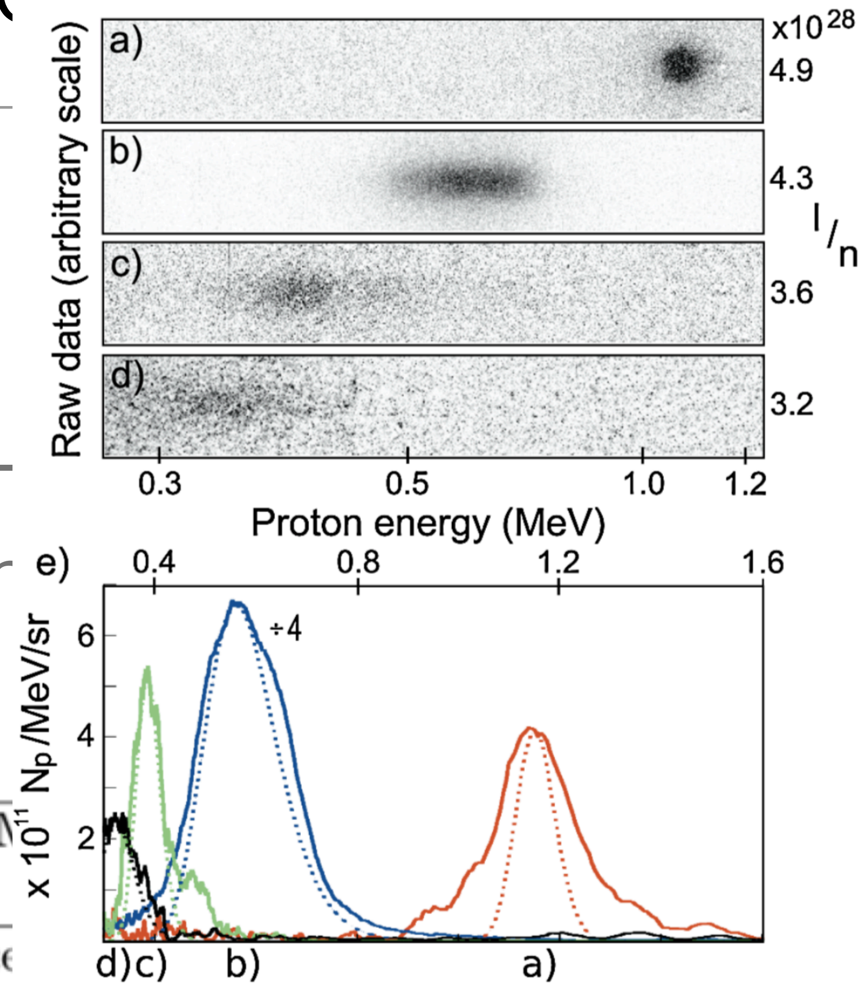
(b) Energy spread - lots of work using different acceleration schemes and structured targets

Author	Acceleration Mechanism	Species	Peak Energy [MeV/u]	Energy Spread [%]	Peak Signal [particles/MeV/sr]
Schwoerer et al. [129]	Sheath Acceleration	protons	1.2	40	5×10^{12}
Hegelich et al. [132]	Sheath Acceleration	protons	3	17	5×10^{9}
Henig et al. [251]	LS-RPA	C^{6+}	2.9	35	5×10^{9}
Palmer et al. [141]	HB-RPA	protons	1.1	4	3.5×10^{12}
Haberberger et al. [167]	CSA	protons	20	1	1×10^{7}
This work - lowest spread	HB-RPA	protons	0.55	5.3	5.9×10^{11}
This work - highest energy	HB-RPA	protons	1.85	12.2	3.6×10^{11}

Fundamental Ion Acceleration

Current status:

(b) Energy spread - fferent acceleration schem



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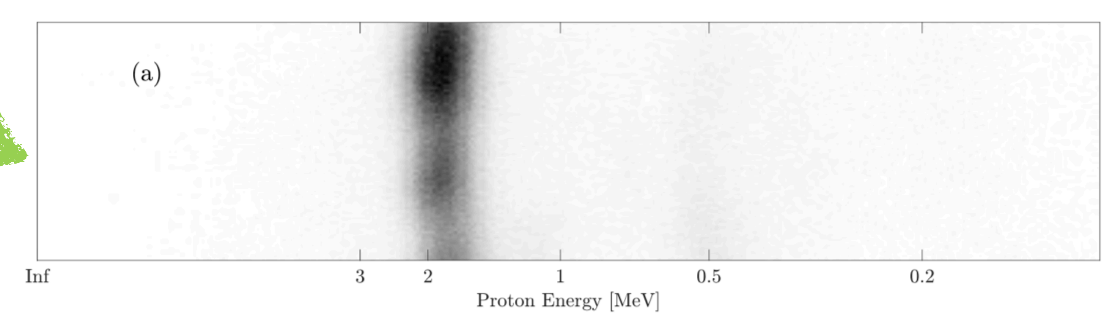

Fundamental Ion Acceleration

Current status:

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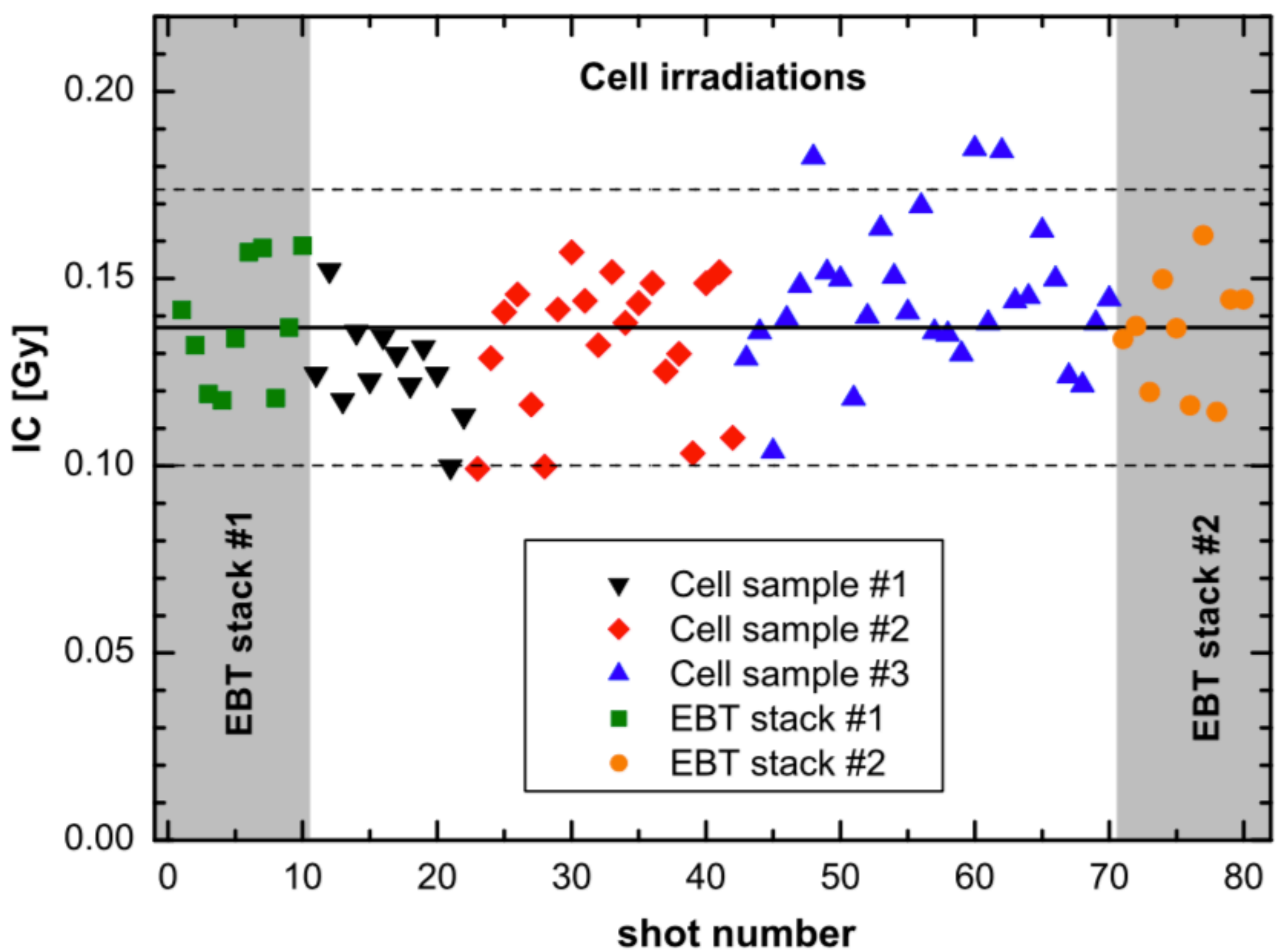
Fundamental Ion Acceleration

Current status:

(c) Proton energy stability



Kraft et al. New J. Phys. (2010)

±28% dose stability

±5% dose uniformity required for any given voxel*

*Linz & Alonso PRAB (2007)

Requirements for laser-driven ion beams

i. **Fundamental ion acceleration**

- Energies steadily increasing - nearly achieving the 100MeV milestone
- Already demonstrated few % energy spreads
- Stability is improving, but needs significant

ii. Beam capture and transport systems

iii. Effect of unique ion source properties

Requirements for laser-driven ion beams

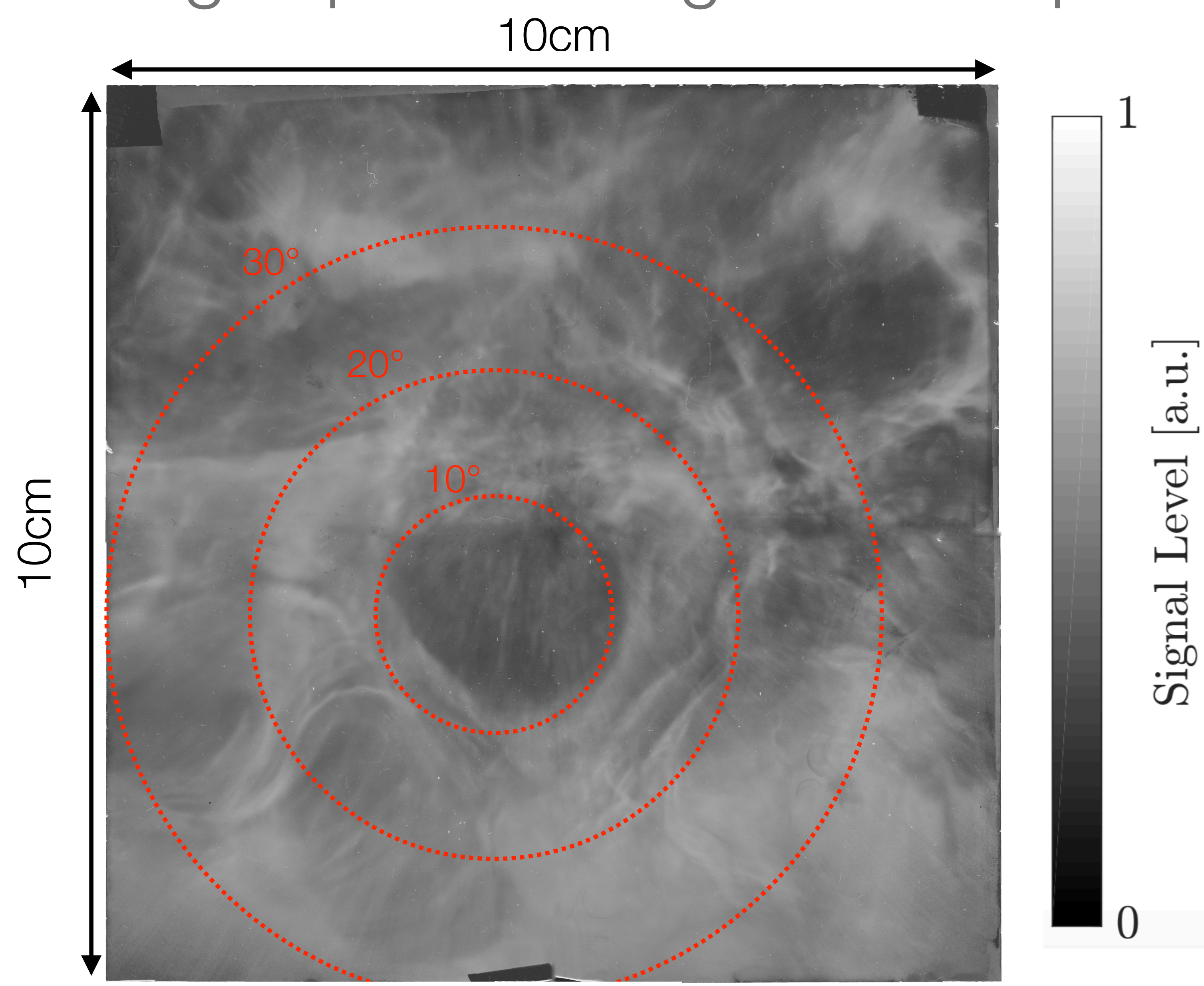
i. Fundamental ion acceleration

ii. **Beam capture and transport systems**

iii. Effect of unique ion source properties

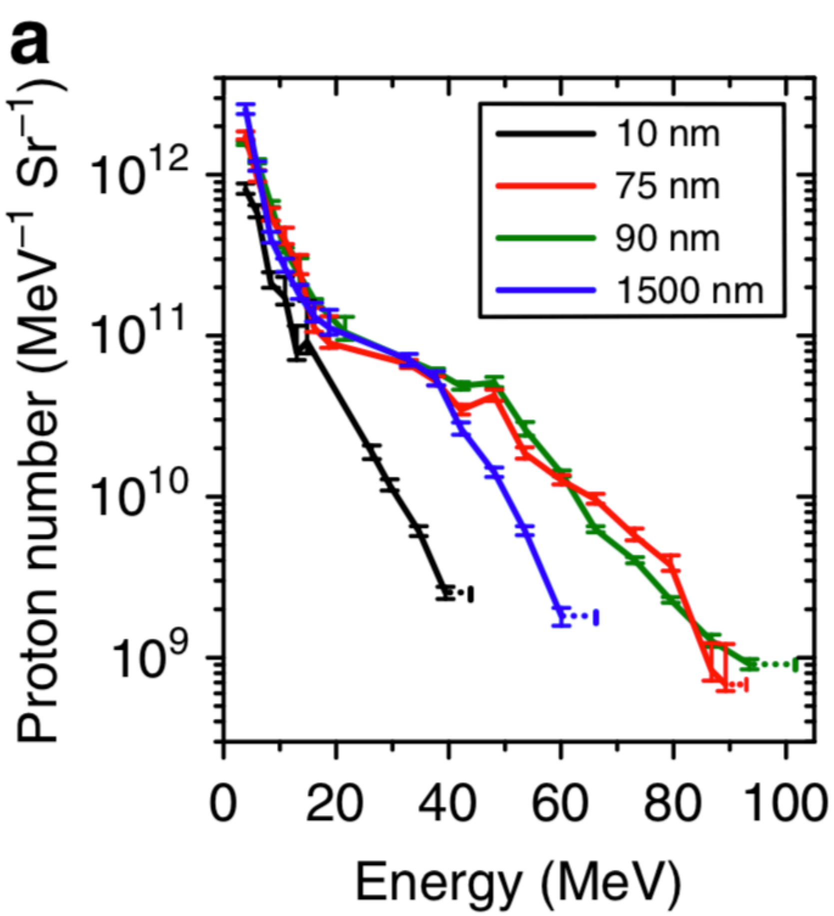
Beam Capture and Transport

- Challenging because:
  - ion beams can have high spatial divergence and poor spatial uniformity



Beam Capture and Transport

- Challenging because:
  - ion beams can have high spatial divergence
  - energy distribution is broad



DOI: 10.1038/s41467-018-03063-9 OPEN

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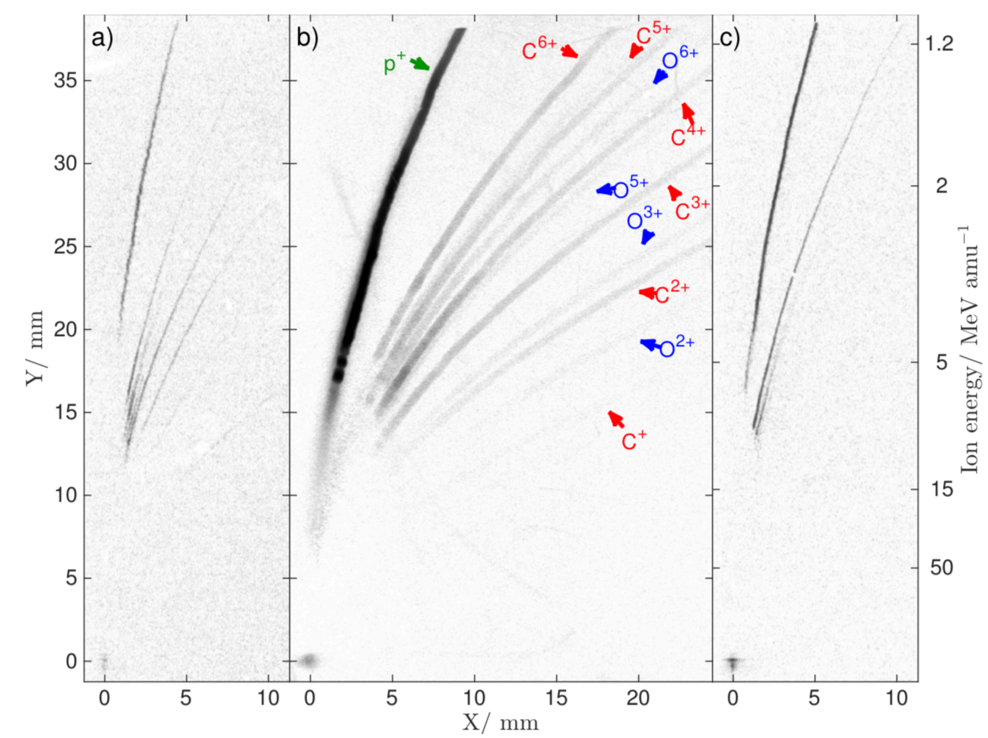
Beam Capture and Transport

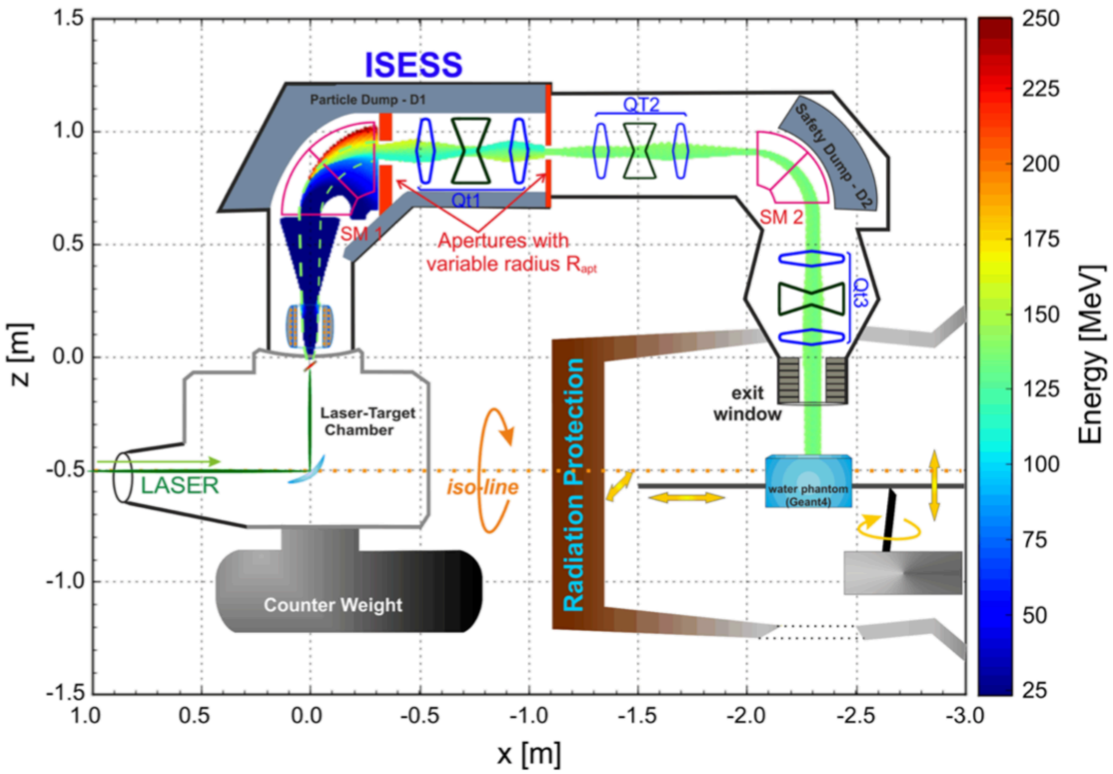
- Challenging because:
  - ion beams can have high spatial divergence
  - energy distribution is broad
  - often multi-species (protons, carbon, oxygen etc.)



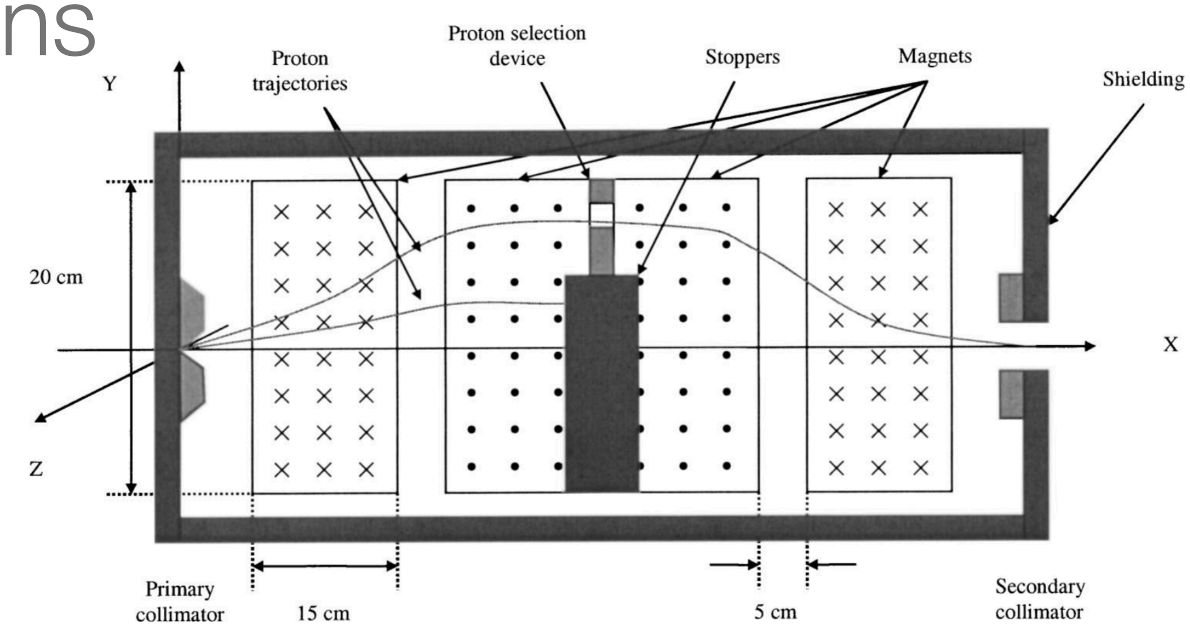
G. Hicks Thesis (2015)

Beam Capture and Transport

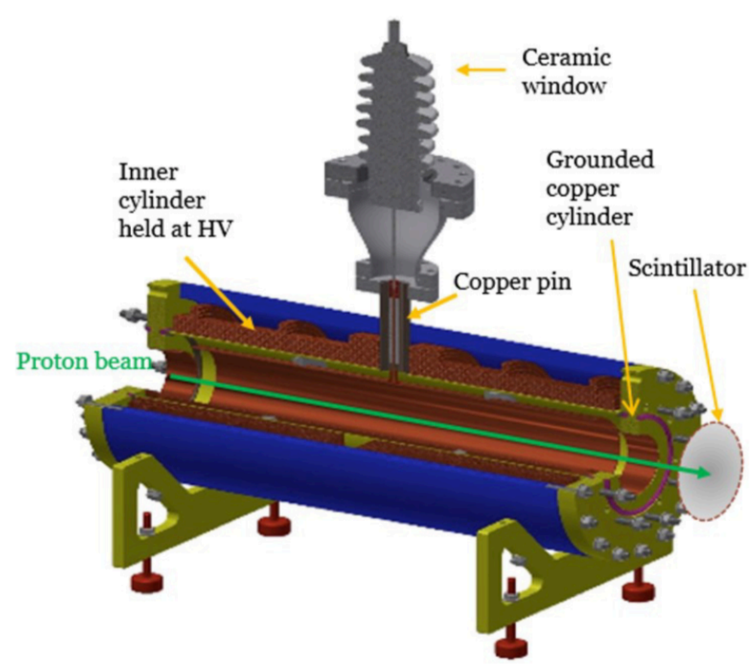
- A number of proposed solutions



Masood et al. Appl. Phys. B (2014)



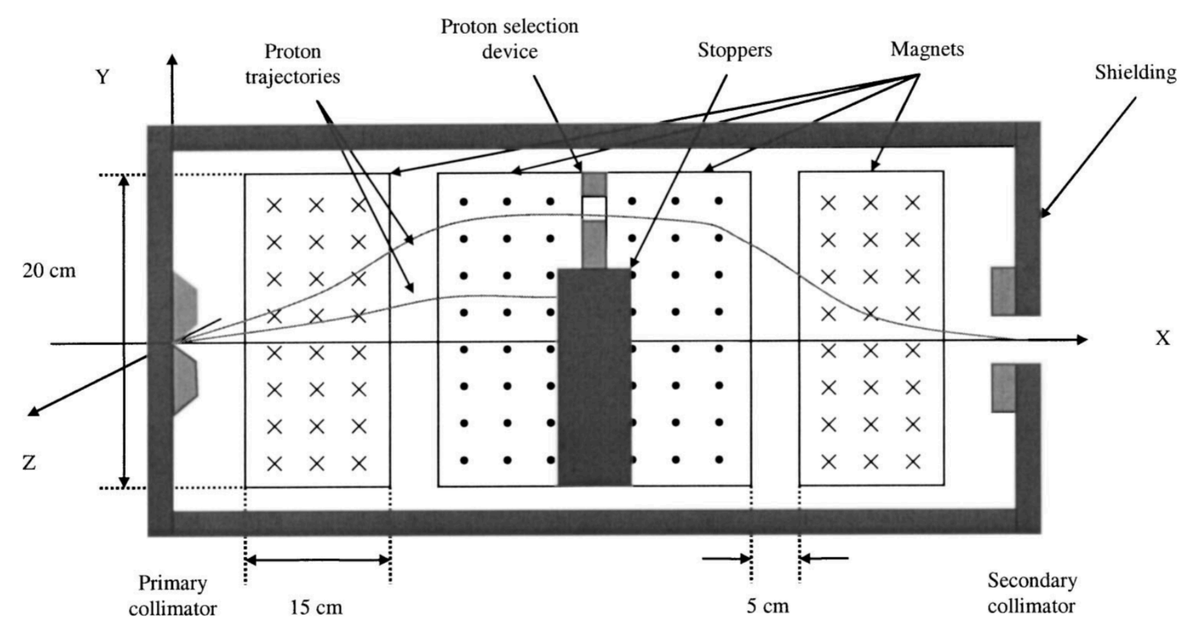
Luo et al. Med Phys. 32 (2005)



Pozimski et al. Laser and Particle Beams (2013), Posocco et al. Proc. IPAC (2016)

Beam Capture and Transport

- A number of proposed solutions
  - Luo et al. propose using 4 superconducting magnetic dipoles with a moveable aperture
    - mono-energetic pencil beam
    - <0.1% of beam used
    - high secondary radiation



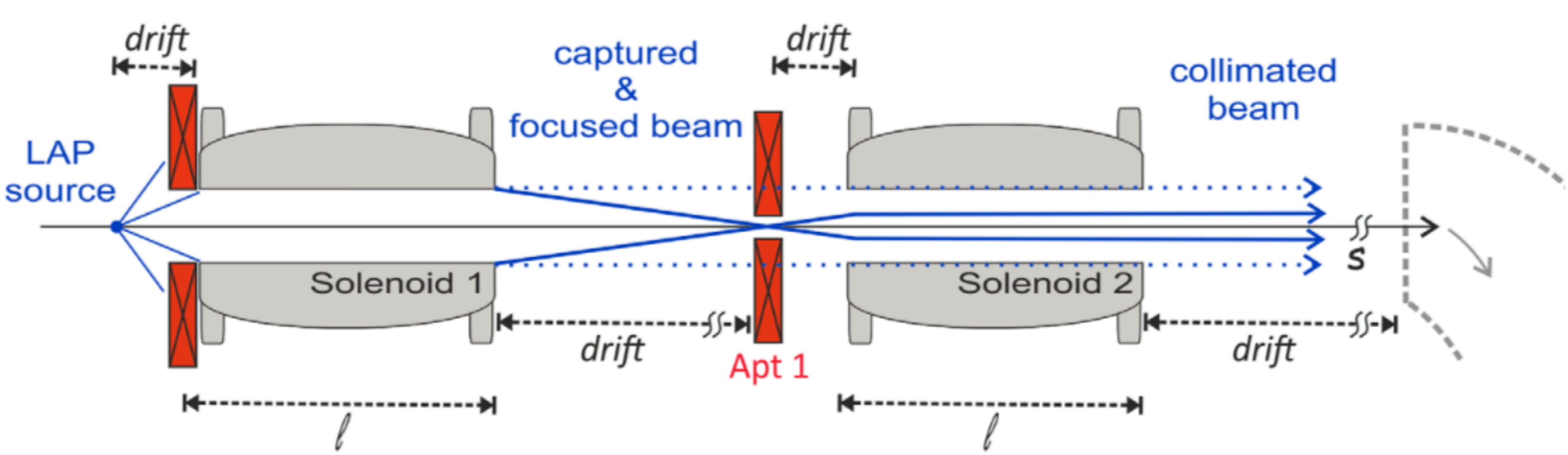
Luo et al. Med Phys. 32 (2005)

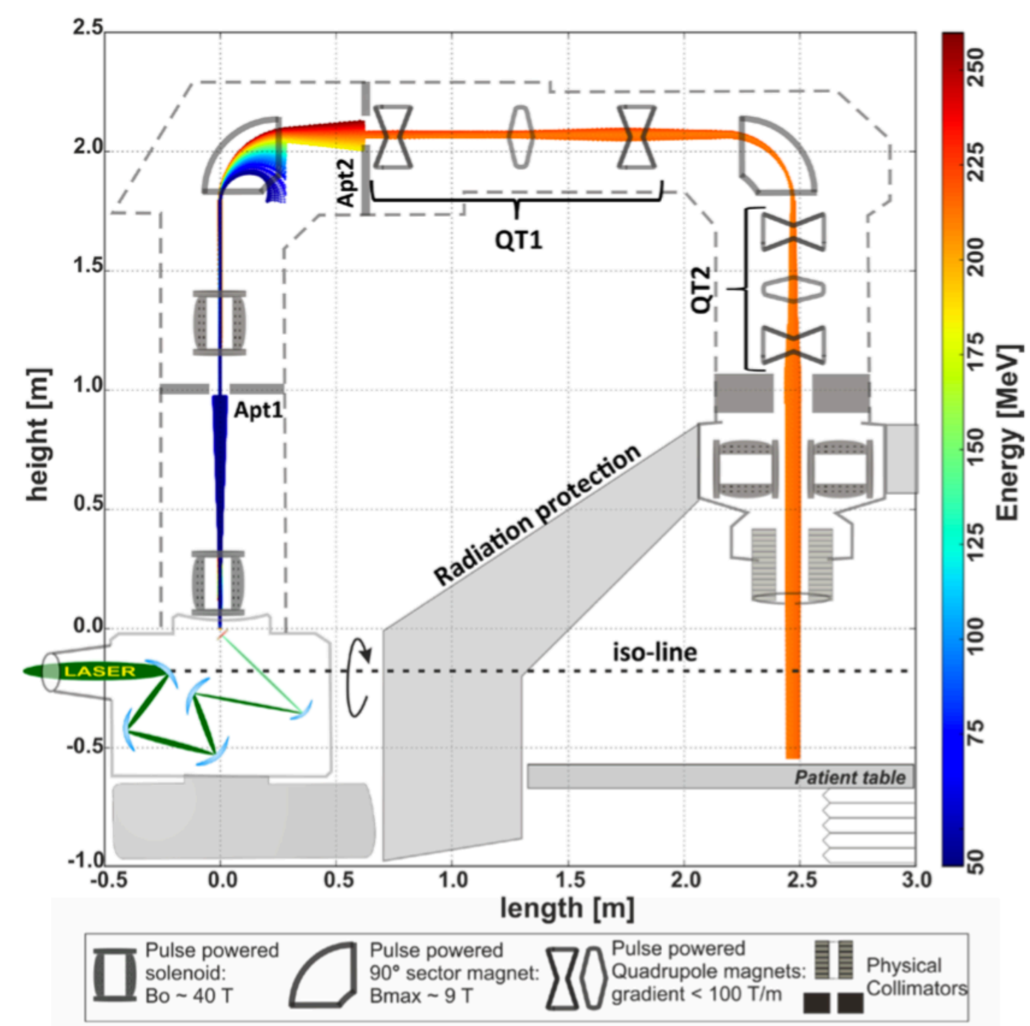
Beam Capture and Transport

- A number of proposed solutions
  - Masood et al. (Appl. Phys. B (2014), Phys. Med. Biol. (2017)) have proposed a number of designs based on pulsed solenoids
    - exploits the broadband nature of laser accelerated beams to generate beams with variable mean energy, and ~20% energy spread

Beam Capture and Transport

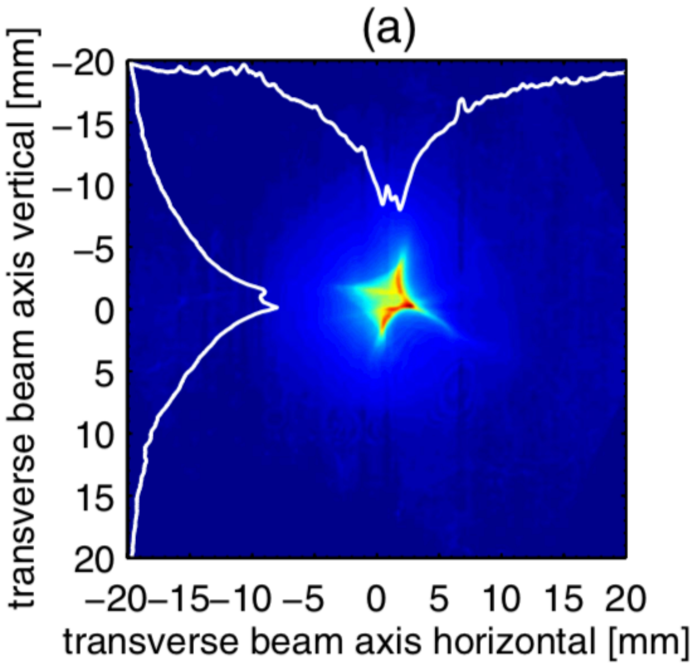
- A number of proposed solutions
  - Masood et al. (Appl. Phys. B (2014), Phys. Med. Biol. (2017)) have proposed a number of designs based on pulsed solenoids

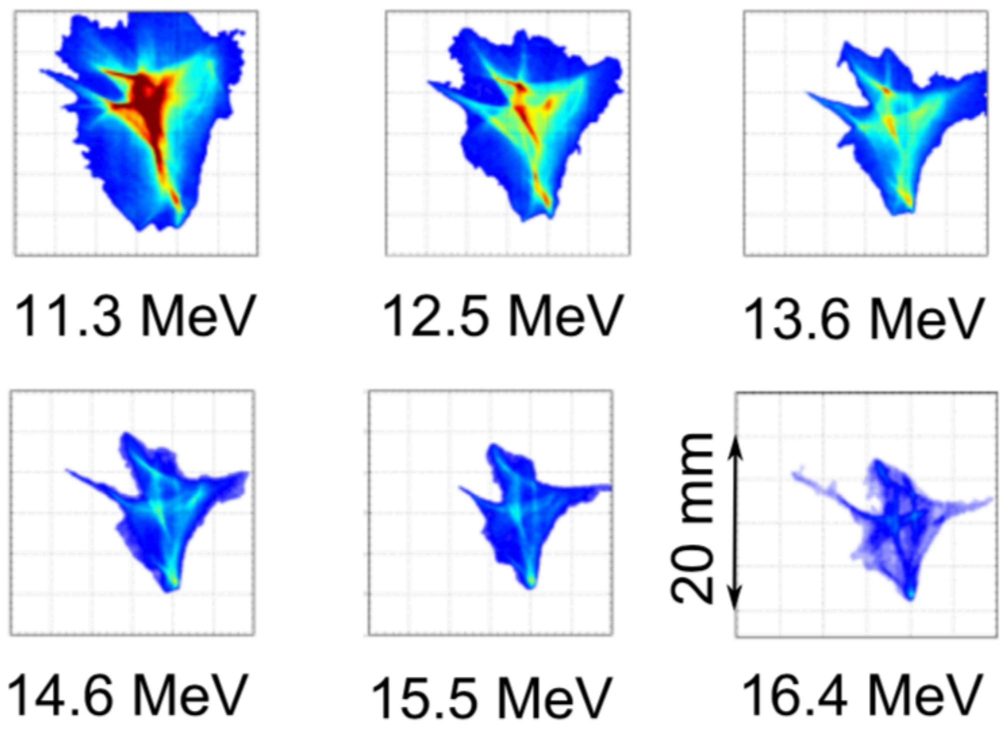




Beam Capture and Transport

- A number of proposed solutions
  - Other authors have already experimentally exploited pulsed solenoids





Busold et al. PRSTAB (2013)
Busold et al. Nuclear Instr. and Methods A (2014)

Requirements for laser-driven ion beams

i. Fundamental ion acceleration

ii. **Beam capture and transport systems**

- a range of possible solutions, with a number already having been demonstrated in some capacity

iii. Effect of unique ion source properties

Requirements for laser-driven ion beams

i. Fundamental ion acceleration

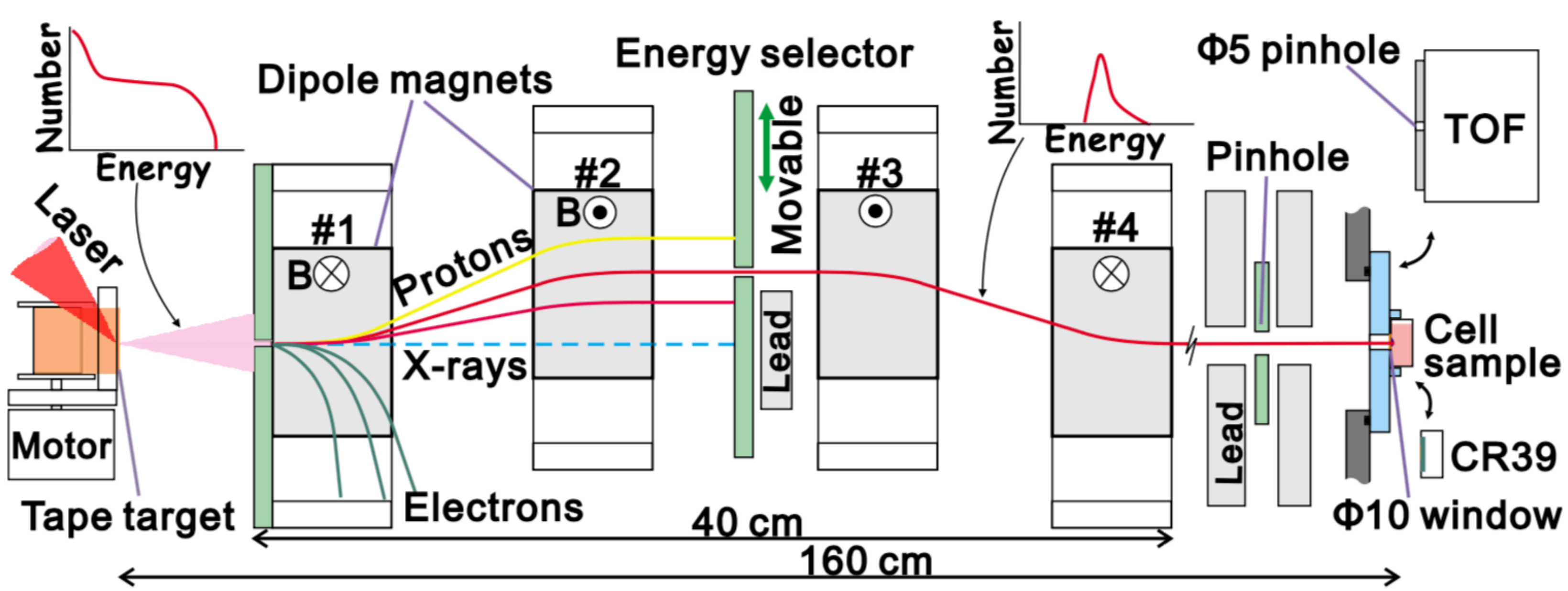
ii. Beam capture and transport systems

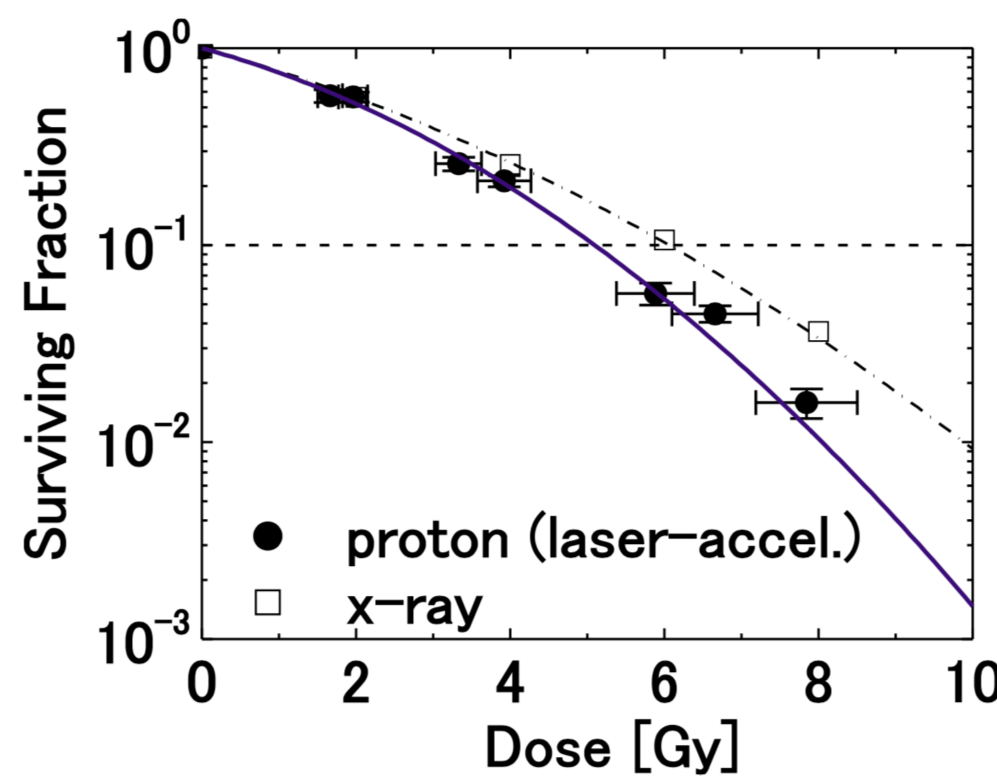
iii. **Effect of unique ion source properties**

- What effect do these potential ultra-high dose rates have on the biology?
    - Do doses of ~10^9Gy/s have biological benefits (compared to 10^0 - 10^3Gy/s conventionally)?
    - Are laser sources at least “as-good” as conventional sources?

RBE and Laser Sources

- Some of the earliest work by Yogo et al. at J-KAREN laser system in Japan
    - in vivo studies with a 2.25MeV proton beam and energy width ΔE/E ~ 30% (4MV reference x-rays)





Yogo et al. Appl. Phys. Lett. (2011)

RBE and Laser Sources

- A large amount of subsequent interest from various groups

Bin et al. Appl. Phys. Lett. (2012)

>10^9Gy/s over single ns fractionation for protons
equivalent dose given with 200kV x-rays

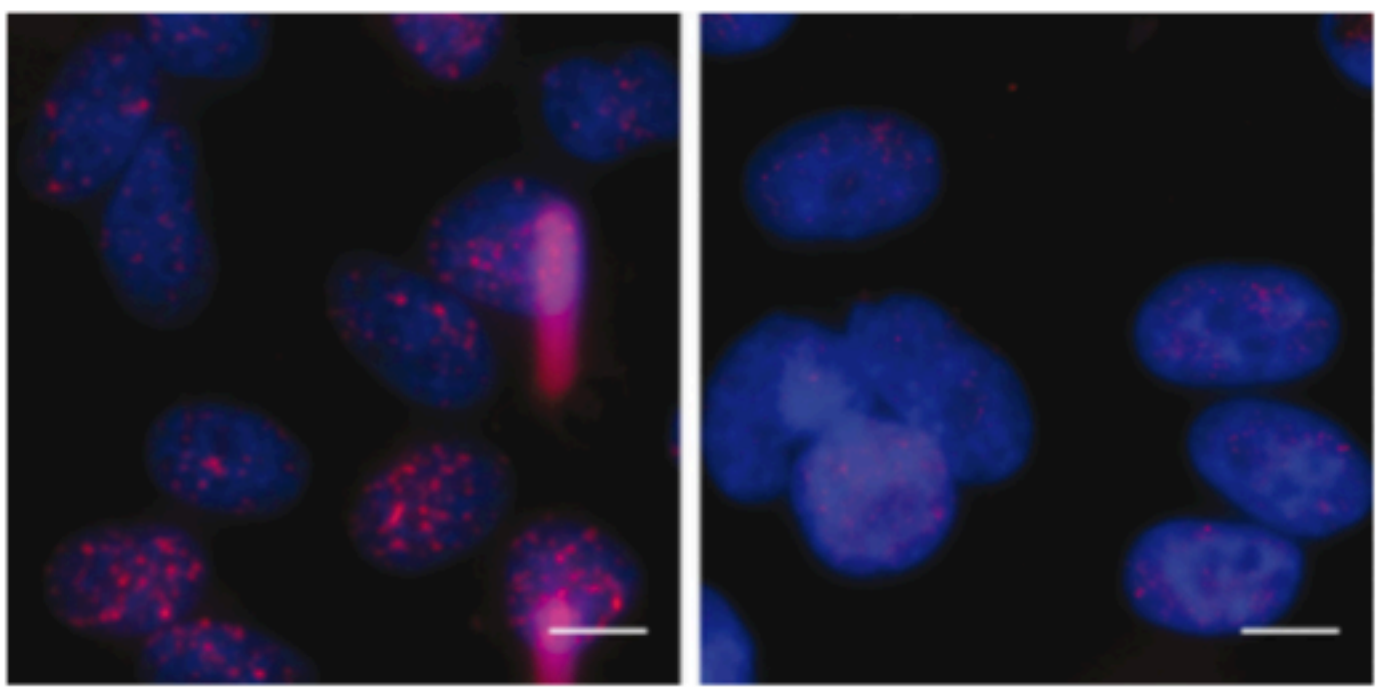


FIG. 5. Initial DNA damage in HeLa cells. (a) Sample exposed to a mean dose of 1.0 Gy and (b) corresponding unirradiated control. Foci of γ-H2AX (red) and cell nuclei (blue) are shown (3D microscopy, maximum intensity projections, background correction, contrast enhanced). The red vertical bars in (a) are part of the grid used for spatial registration (Fig. 4). Horizontal scale bars, 10 μm.

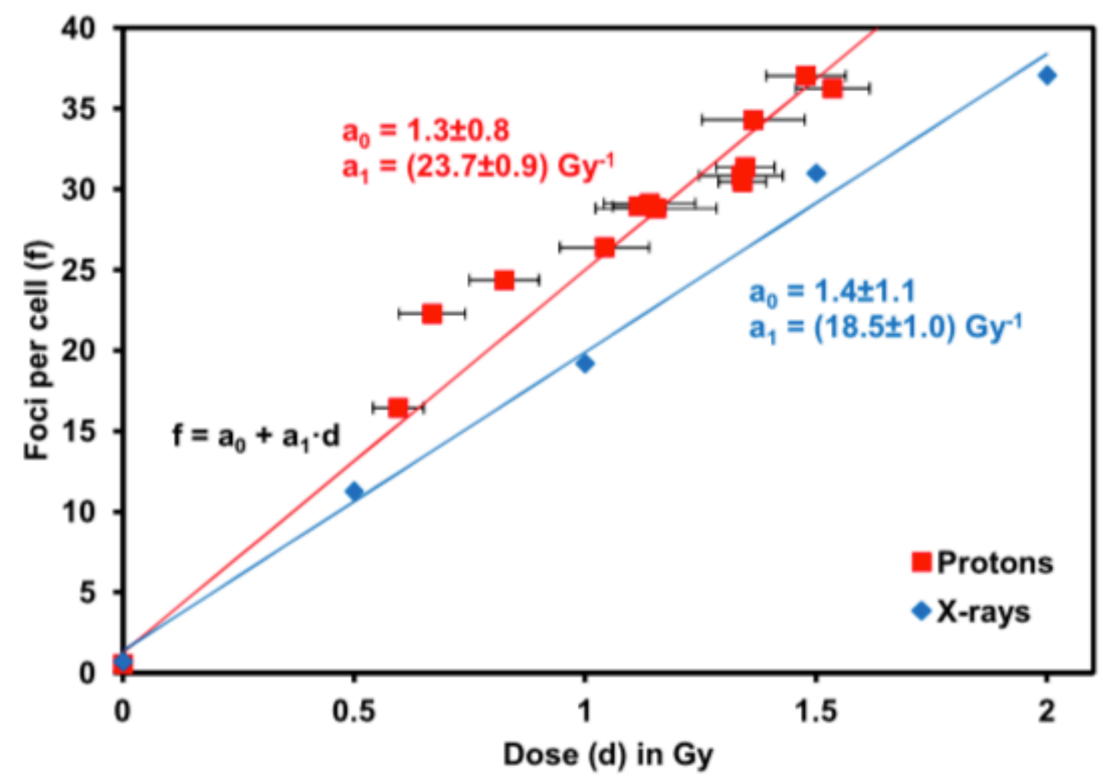


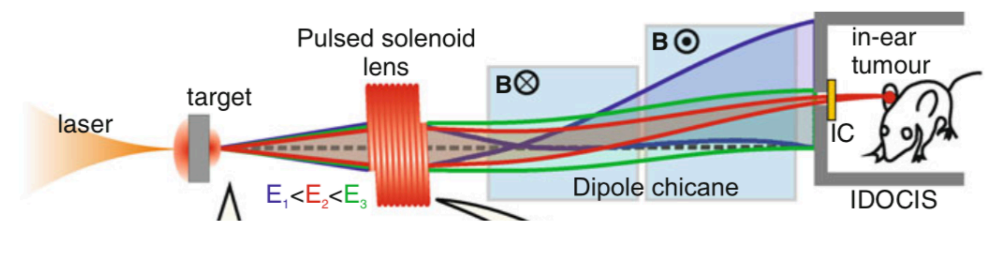
FIG. 6. Mean number of γ-H2AX foci per cell as a function of dose for laser-driven protons and 200 kV X-rays. Each data point for protons contains ~20 cells. Error bars in dose show the dose inhomogeneity (standard deviation) across the regions of interest used for evaluation.

RBE and Laser Sources

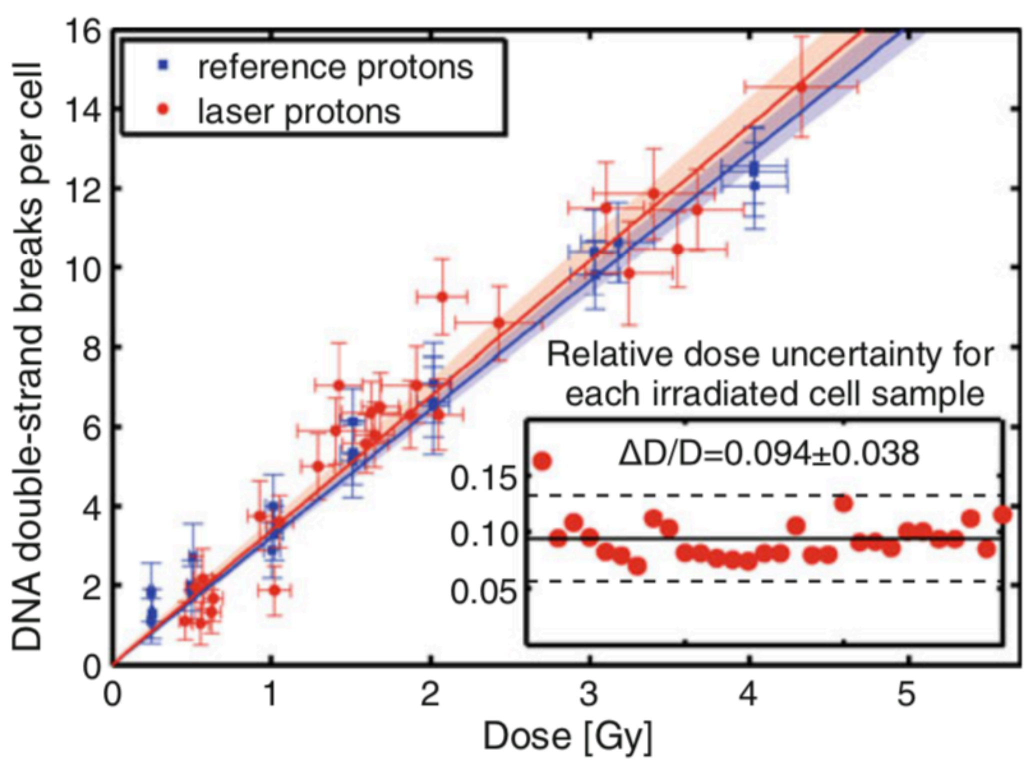
- A large amount of subsequent interest from various groups

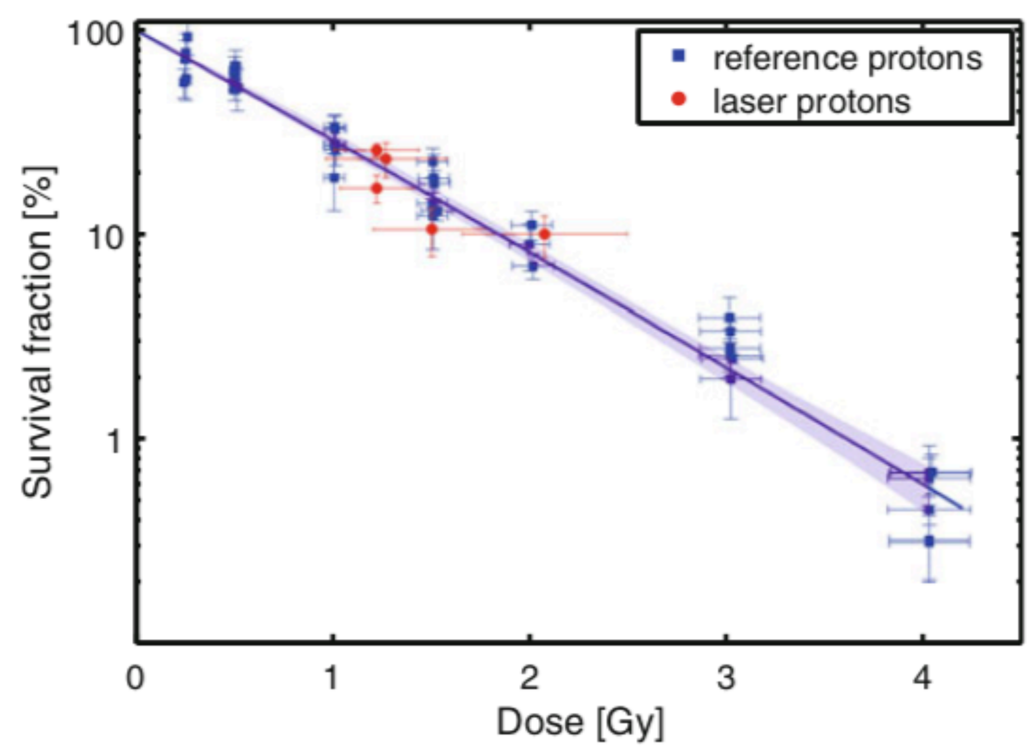
Kraft et al. New J. Phys. (2010)
Zeil et al. Appl. Phys. B (2013)

HZDR HELMHOLTZ ZENTRUM DRESDEN ROSSENDORF



>10^7Gy/s over multiple fractionations (for beam homogeneity) compared with 1.1Gy/min for conventional source

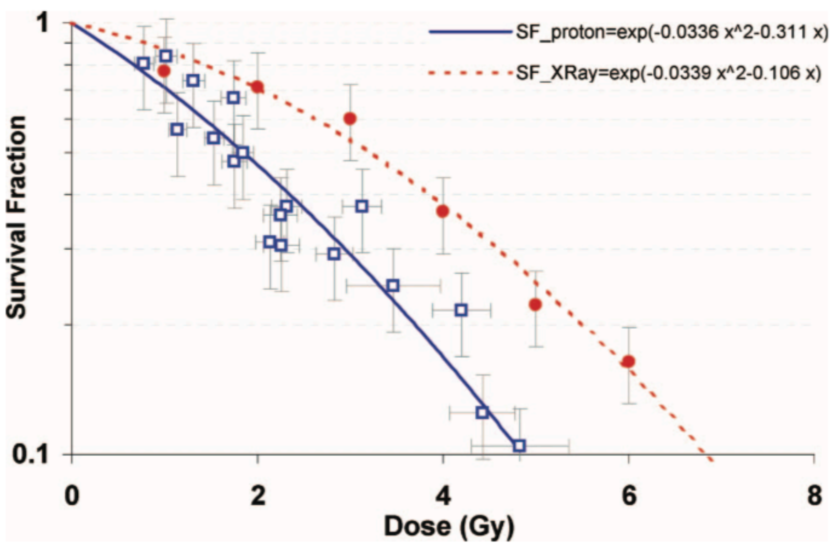




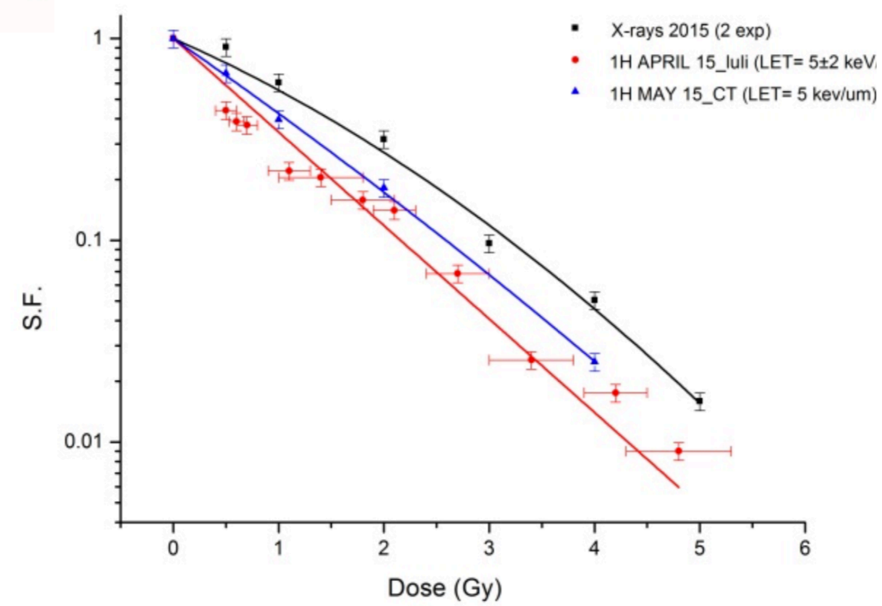
RBE and Laser Sources

- A large amount of subsequent interest from various groups

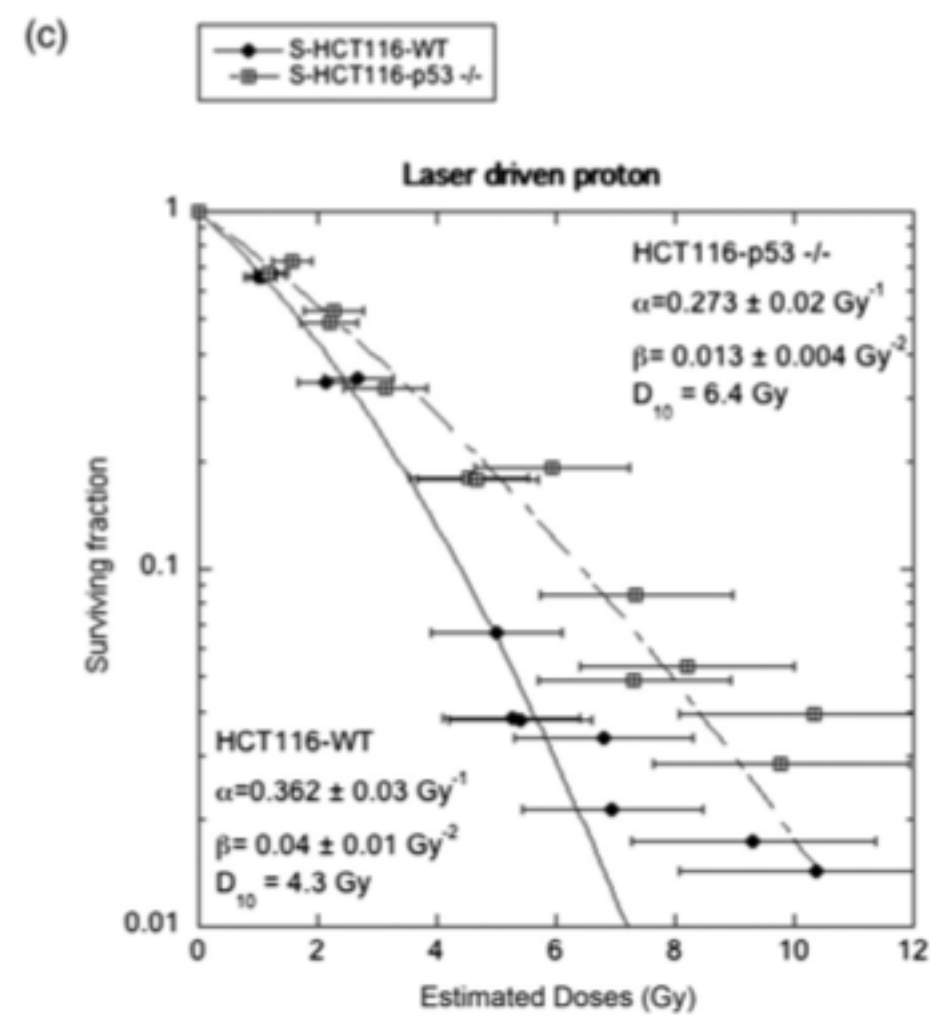
Doria et al. AIP Advances (2012)



Manti et al. JINST (2017)



Pommarel et al. PRAB (2017)



RBE and Laser Sources

- A large amount of subsequent interest from various groups
    - Studies using research accelerators which can mimic these high dose rates have also been conducted

Auer *et al. Radiation Oncology* 2011, **6**:139
http://www.ro-journal.com/content/6/1/139

RADIATION ONCOLOGY

RESEARCH **Open Access**

Survival of tumor cells after proton irradiation with ultra-high dose rates

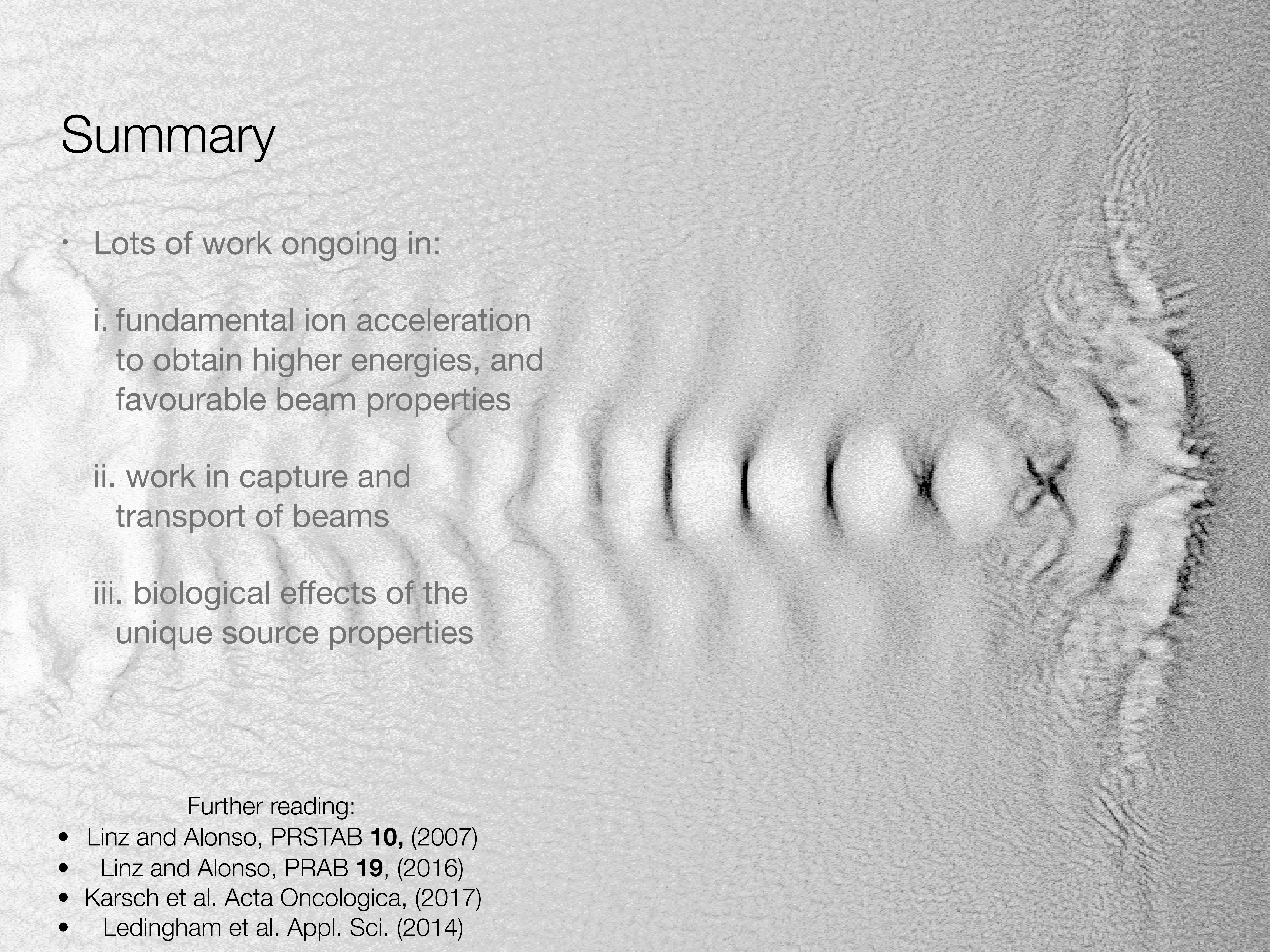
Susanne Auer[1], Volker Hable[2], Christoph Greubel[2], Guido A Drexler[1], Thomas E Schmid[3], Claus Belka[1], Günther Dollinger[2] and Anna A Friedl[1*]

The Effects of Ultra-High Dose Rate Proton Irradiation on Growth Delay in the Treatment of Human Tumor Xenografts in Nude Mice

Author(s): O. Zlobinskaya, C. Siebenwirth, C. Greubel, V. Hable, R. Hertenberger, N. Humble, S. Reinhardt, D. Michalski, B. Röper, G. Multhoff, G. Dollinger, J. J. Wilkens and T. E. Schmid
Source: Radiation Research, 181(2):177-183.
Published By: Radiation Research Society
https://doi.org/10.1667/RR13464.1

RBE and Laser Sources

- A large amount of subsequent interest from various groups
    - Studies using research accelerators which can mimic these high dose rates have also been conducted
- Lots of ongoing research to better understand the effect of these ion sources



Summary

- Lots of work ongoing in:

  i. fundamental ion acceleration to obtain higher energies, and favourable beam properties

  ii. work in capture and transport of beams

  iii. biological effects of the unique source properties

Further reading:

- Linz and Alonso, PRSTAB **10,** (2007)
- Linz and Alonso, PRAB **19**, (2016)
- Karsch et al. Acta Oncologica, (2017)
- Ledingham et al. Appl. Sci. (2014)