Harnessing Physical Forces for Medical Applications Symposium
UCLA
Nov. 16, 2018

Laser-driven Medicine: A prelude

Toshiki Tajima
Norman Rostoker Chair Professor
Department of Physics and Astronomy
UCI

In memory of and dedication to
the late Profs. +**J. M. Dawson** and +**N. Rostoker**

abstract

1. History of laser accelerator, which drove the laser technology and vice versa
2. Elements of laser acceleration: a novel path toward tiny radiobeams (electrons, ions, X-rays (gamma-rays), neutrons, and radio-isotopic beams)
3. Convergence with **nanotechnology**, **biotechnology**
4. Potentiality: portability, intra-operative, endoscopic, theranostics, ….

History of laser accelerator: Elements of innovation

Advent of collective acceleration (1956)

CERN Symposium
ON HIGH ENERGY ACCELERATORS
AND PION PHYSICS

Geneva, 11th - 23rd June 1956

Proceedings

COHERENT PRINCIPLE OF ACCELERATION OF CHARGED PARTICLES

V. I. VEKSLER

Electrophysical Laboratory, Academy of Sciences, Moscow

This paper will include a very brief description of a new principle regarding the acceleration of charged particles.

In all existing accelerators of charged particles, the constant and varying electric field accelerating them is created by a powerful external source, and hence the strength of the field is independent, in the first approximation, of the number of particles which are being accelerated.

In resonance accelerators, the electromagnetic field has to be synchronized with the movement of the particles (this is of particular importance in linear accelerators). Finally, none of the existing methods permits the acceleration of neutral bunches of particles.

A new principle of particle acceleration is set forth below. Its distinctive feature lies in the fact that the particle-accelerating electric field is produced by the interaction of a geometrically small group of accelerated particles with another group of charges, plasma or an electromagnetic wave. This method has a number of important features. It appears, in the first place, that the magnitude of the accelerating field produced by this interaction and acting on each particle depends on the numbe-

Theoretical studies of various aspects of the coherent acceleration method have been made by M. S. Rabinovich, A. A. Kolomenski, B. M. Bolotovski, L. V. Kovrizhnikh and I. V. Iankov, as well as by A. I. Akhiezer, Ia. Fainberg and their collaborators. The calculations made by these theoretical workers shed light on a number of complicated problems connected with the development of the different variants of this new acceleration principle, and it therefore seems appropriate to describe the new method despite the fact that a great many problems involved still await solution.

1. *Acceleration of charged bunches by means of the medium*

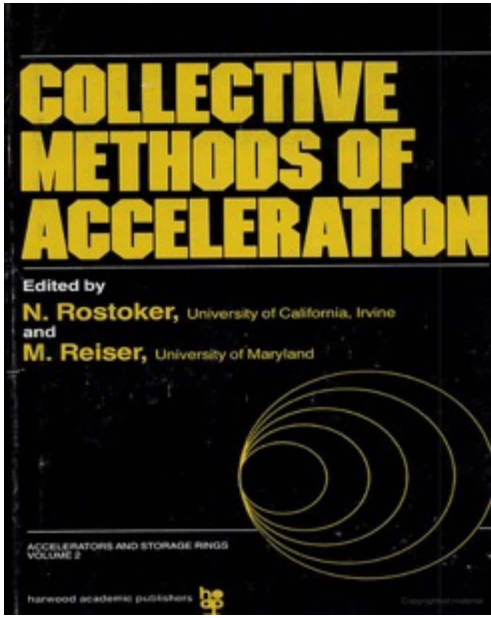
It was pointed out in a paper by Tamm that the loss of energy by particles due to Čerenkov radiation could be reversed, i.e. the medium travelling at a great velocity past charged particles should be able to convey energy to the latter. Up to now, however, no attention has been paid to the possibility of developing an acceleration process of this kind by using a high density electron beam (plasma) as the moving medium. Of course, if a single charge e is

Prehistoric activities (1973-75, 78)

Professor N. Rostoker

Collective acceleration suggested:
Veksler (1956)
(**ion** energy)~ (M/m)(electron energy)

Many experimental attempts (~'70s):
led to **no** such amplification
(ion energy)~ (**several**)x(electron)
Mako-Tajima found its reason (1978)



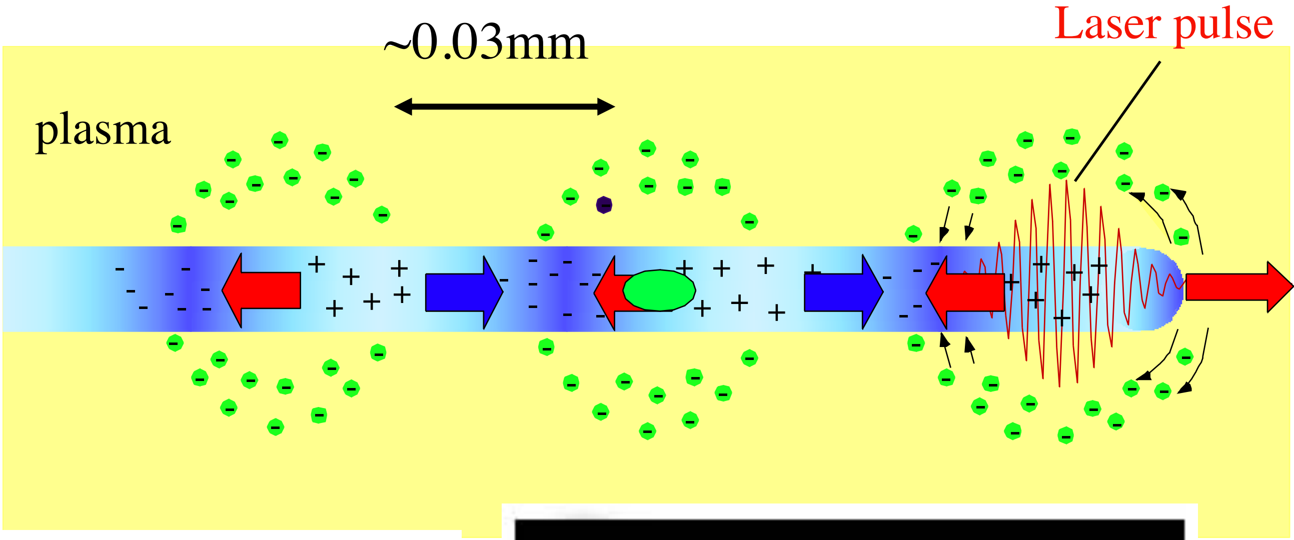
Professor J. Dawson

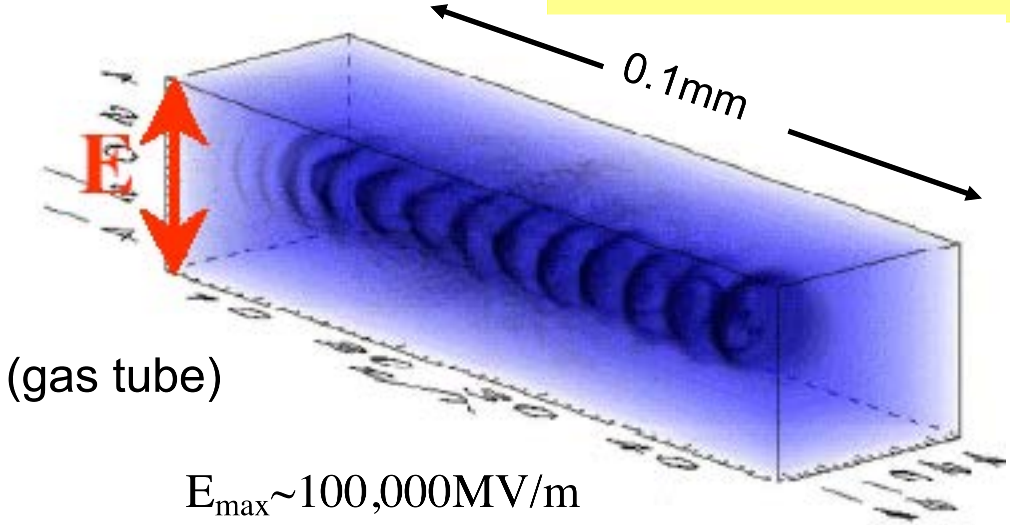
Introduction of wakefields (Tajima-Dawson, 1979)
→ **electron acceleration** possible
with **trapping (with Tajima-Dawson field. 1979)**, more tolerant for sudden process

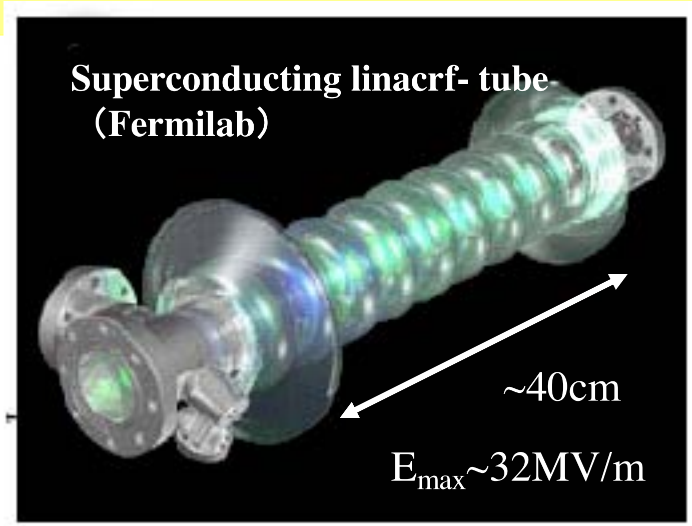
However, requires relativistically strong laser (see next development)

Laser wakefield (Tajima-Dawson, 1979 @UCLA)

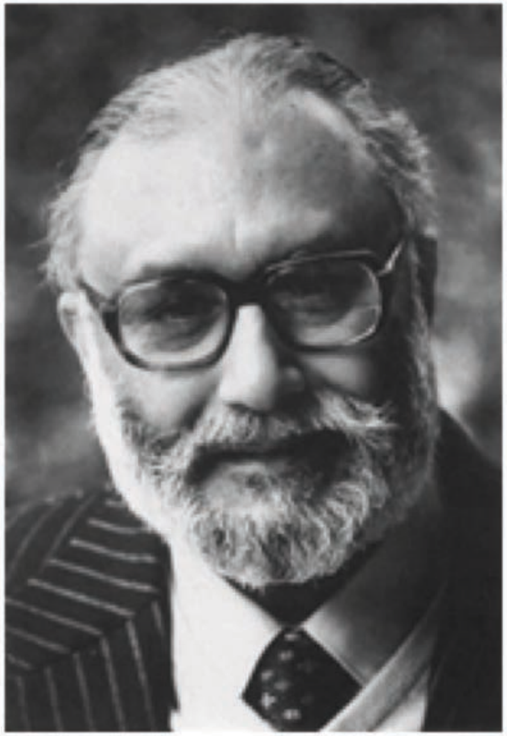
Thousand-fold Compactification over conventional accelerators







The late Prof. Abdus Salam*



At ICTP Summer School (1981),
Prof. Salam summoned me and discussed
about laser wakefield acceleration.

Salam: *'Scientists like me began feeling that we had less means to test our theory. However, with your laser acceleration, I am encouraged'.* (1981)

He organized the Oxford Workshop
on laser wakefield accelerator in 1982.

Effort: many scientists over many years to realize his vision / dream
High field science: spawned. (* 1979 Nobel Prize in physics)

The superconducting RF proton linac at the SNS at Oak Ridge National Laboratory is providing valuable experience for a future ADS accelerator.
Image credit: ORNL.

Laser technology invented (1985)

Professor Gerard Mourou*

* 2018 Nobel in Physics

Chirped pulse amplification (CPA) invented:
to overcome the gain medium nonlinearities
in spatially expanded amplification to
temporal expansion:
smaller, shorter pulse, more intense,
higher reprate,
all simultaneous.
→ relativistically strong laser realized (1990's)

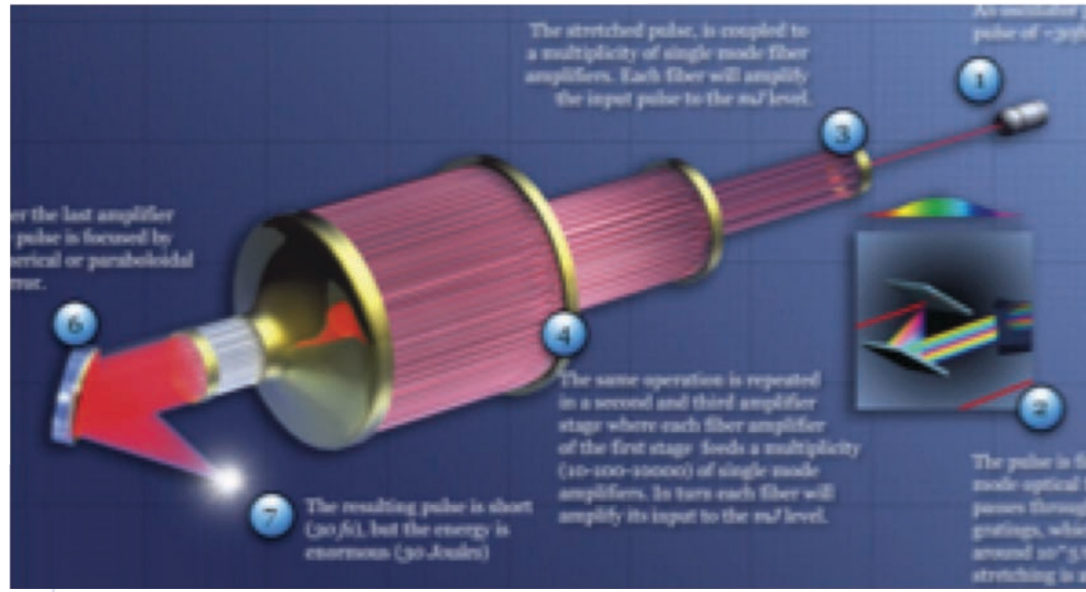
→ many table-top TW and PW lasers world-wide
first Chair, ICUIL (International Committee for
Ultra Intense Lasers)
toward EW laser (*Extreme Light Infrastructure)*

→ First LWFA experiments
(Nakajima,..., Tajima, Phys. Scrip. 1994; Modena et al, 1995)
→ drives High Field Science

Laser accelerators demanded more laser inventions

CAN fiber laser (2013)

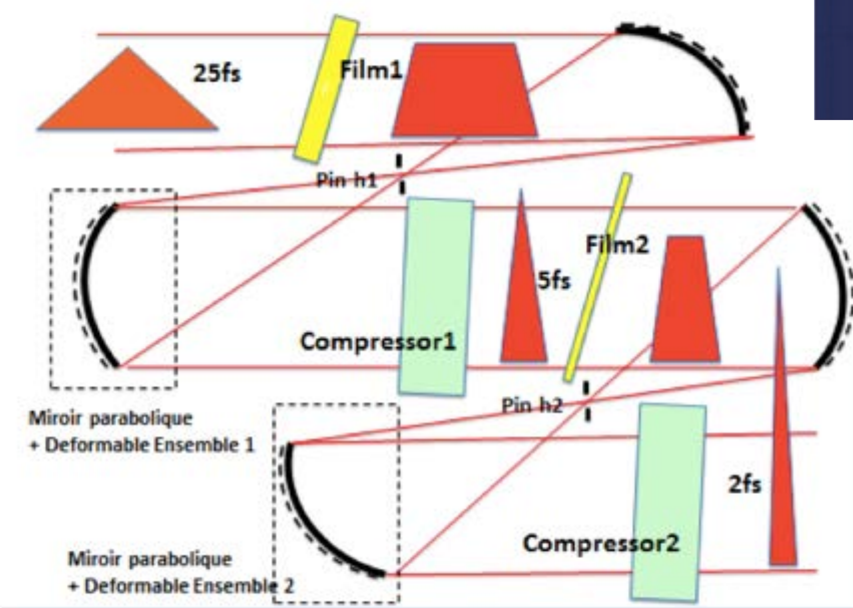
← tiny laser (like a hair μm individually),efficiency, large rep-rate,
yet, large average power (by bundles)



Mourou*, Brockelesby, Tajima, Limpert (2013)

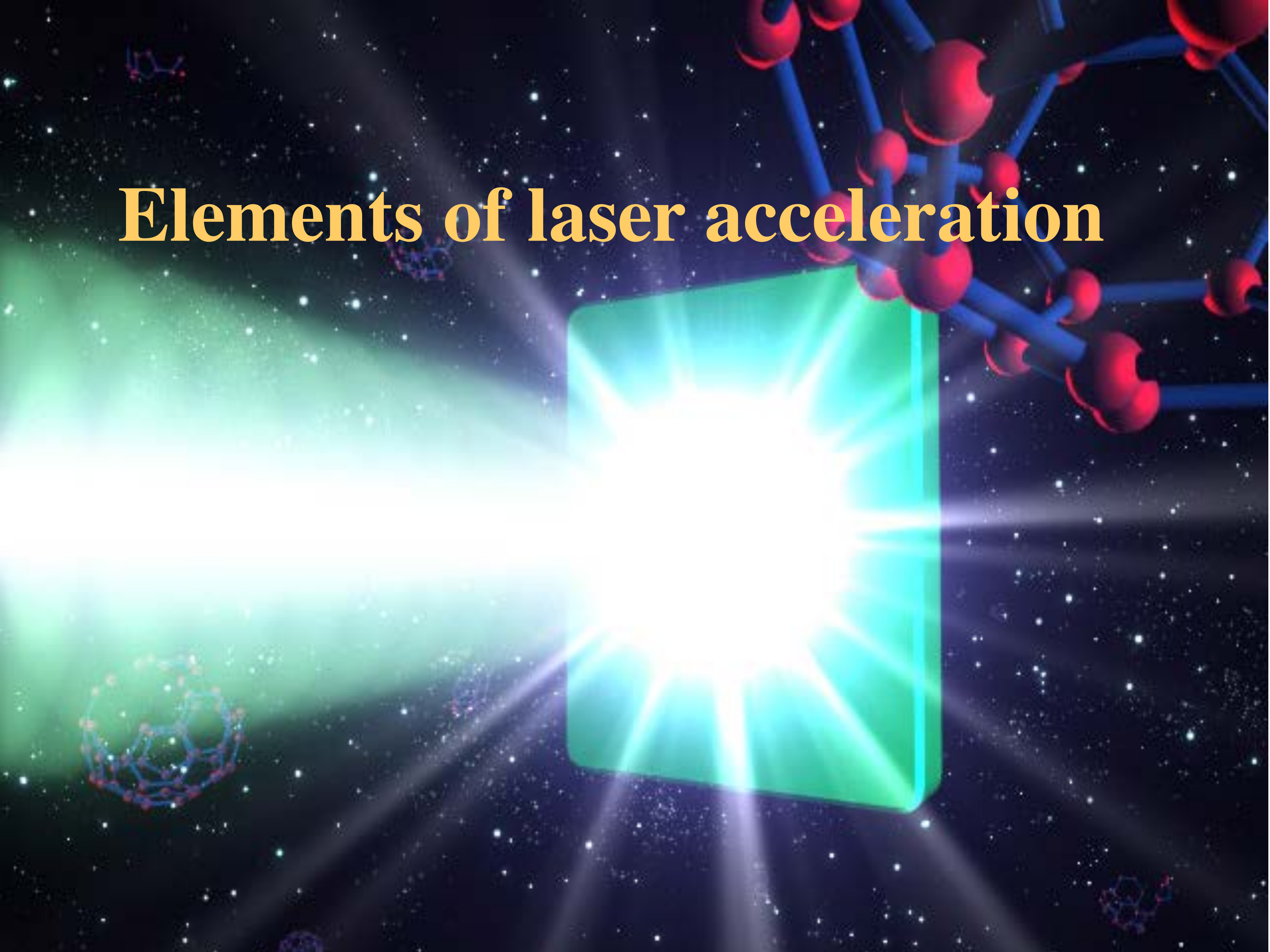
Thin Film Compression (2014)

← even shorter pulse (*fs*)



Mourou* et al, (2014)

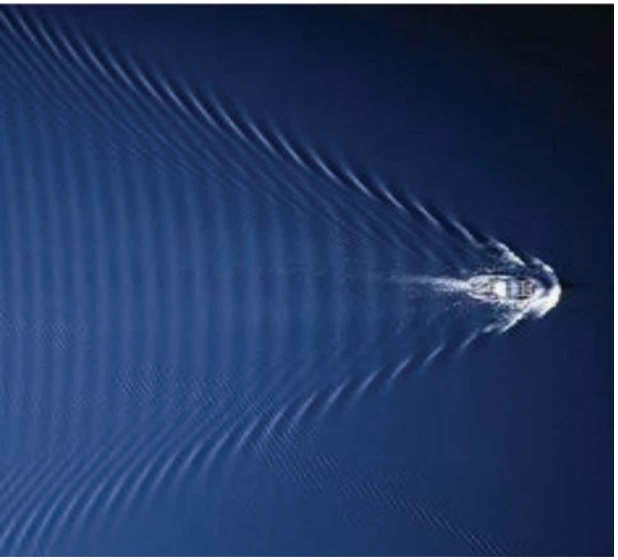
Elements of laser acceleration



Laser Wakefield (LWFA):

Wake phase velocity >> thermal speed ($v_{ph} >> v_{th}$) maintains **coherent** and **smooth** structure

Tsunami phase velocity becomes ~0, causes **wavebreak** and **turbulence**

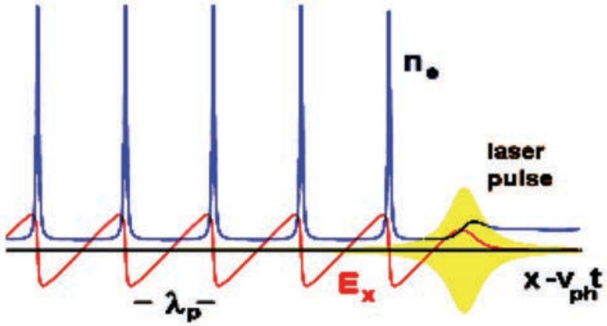


vs

"Onigokko (hide 'n seek)" state

Strong beam (of laser / particles) drives plasma waves to saturation amplitude: $E = m\omega v_{ph} /e$

No wave breaks and wake **peaks** at v≈c



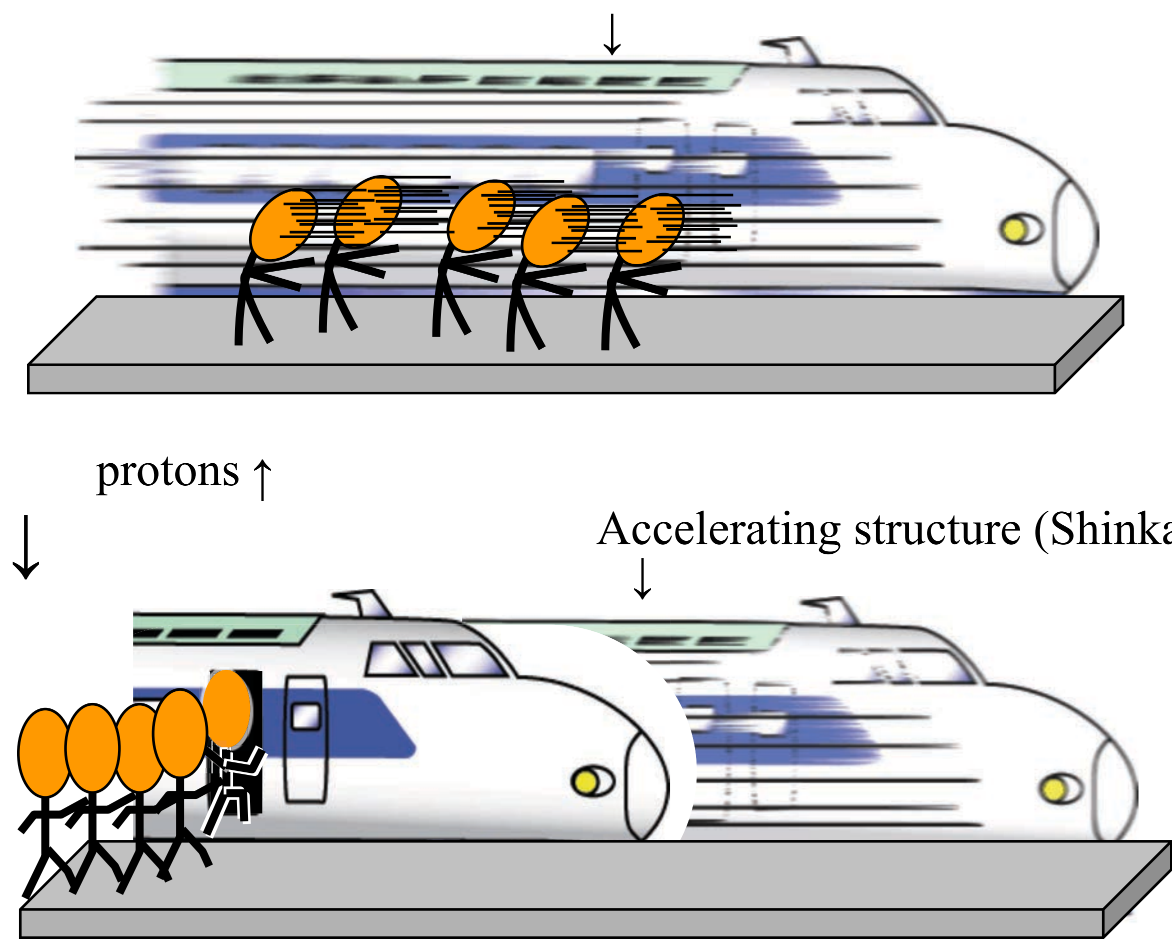
← relativity regularizes (*relativistic coherence*)

Wave **breaks** at v<c

Relativistic coherence enhances beyond the **Tajima-Dawson field** $E = m\omega_p c /e$ (~ GeV/cm)

Adiabatic (Gradual) Acceleration of Ions

from #1 lesson of Mako-Tajima problem

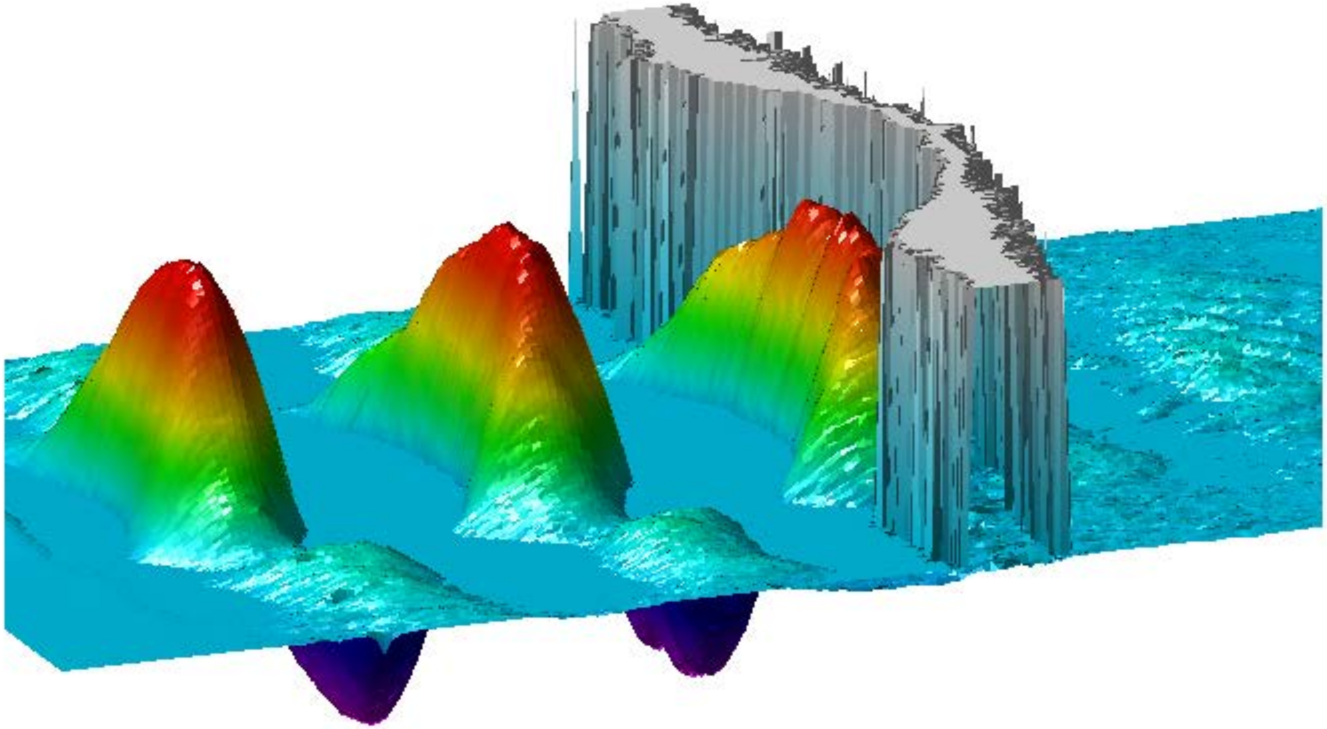


Inefficient if <u>suddenly</u> accelerated

Efficient when <u>gradually</u> accelerated

Lesson #1: gradual acceleration → Relevant for ions

Laser -Thin Foil Interaction

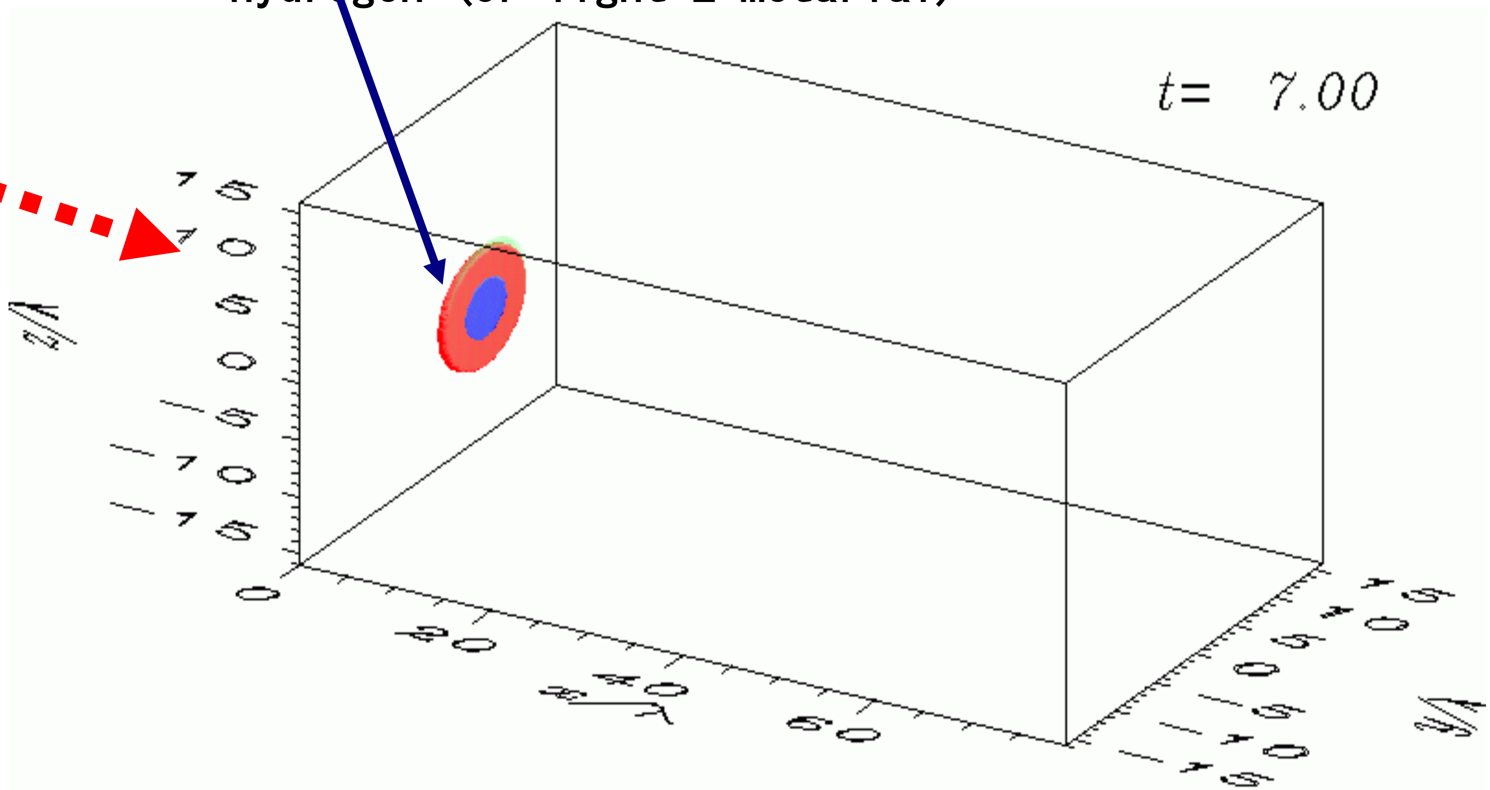


X. Yan et al., 2009

Radiation (Laser) Pressure Acceleration

Double layer target (metal layer with smaller hydrogen (or light Z metarial)

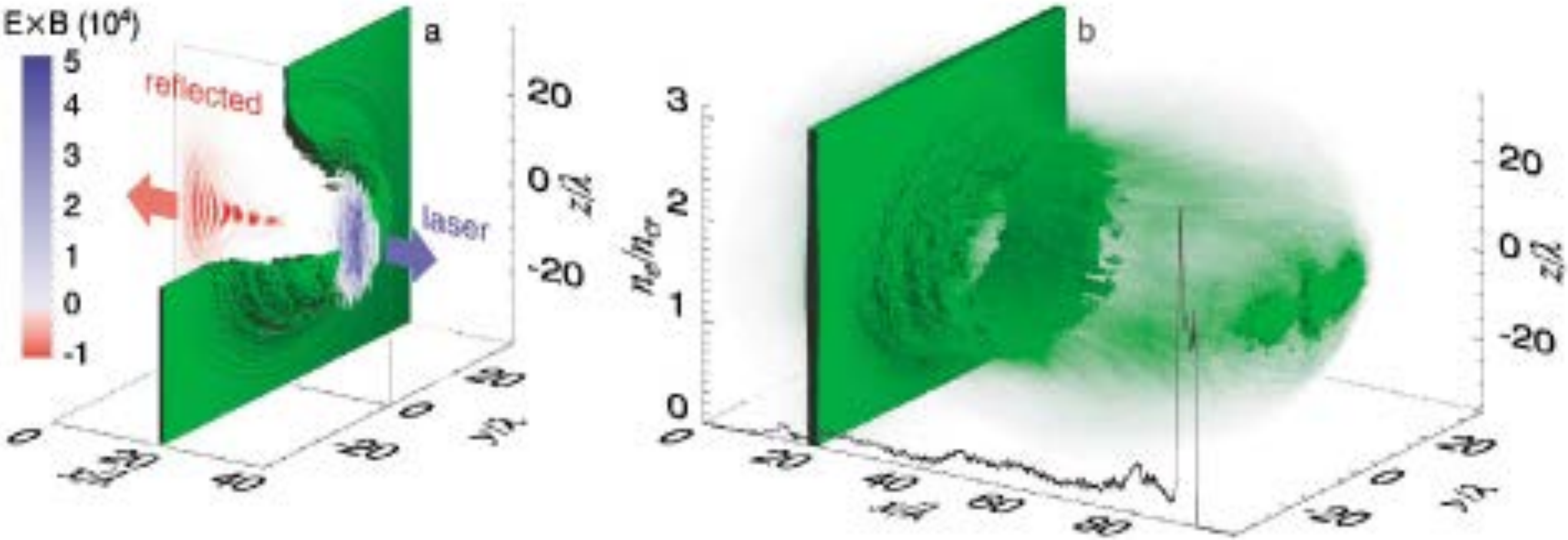
laser



code REMP

Esirkepov et al.(2002)

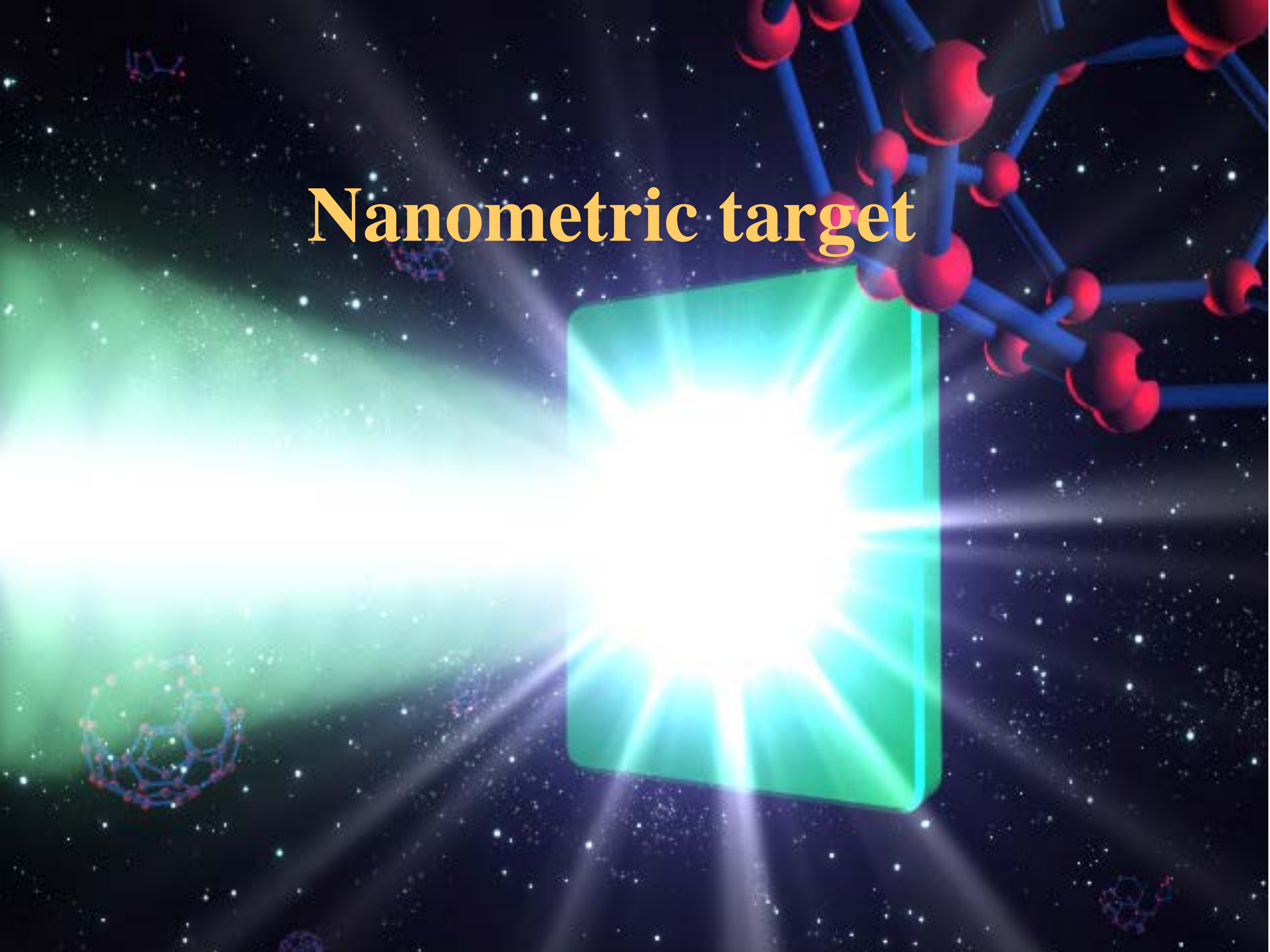
Radiation (Laser) Pressure Acceleration



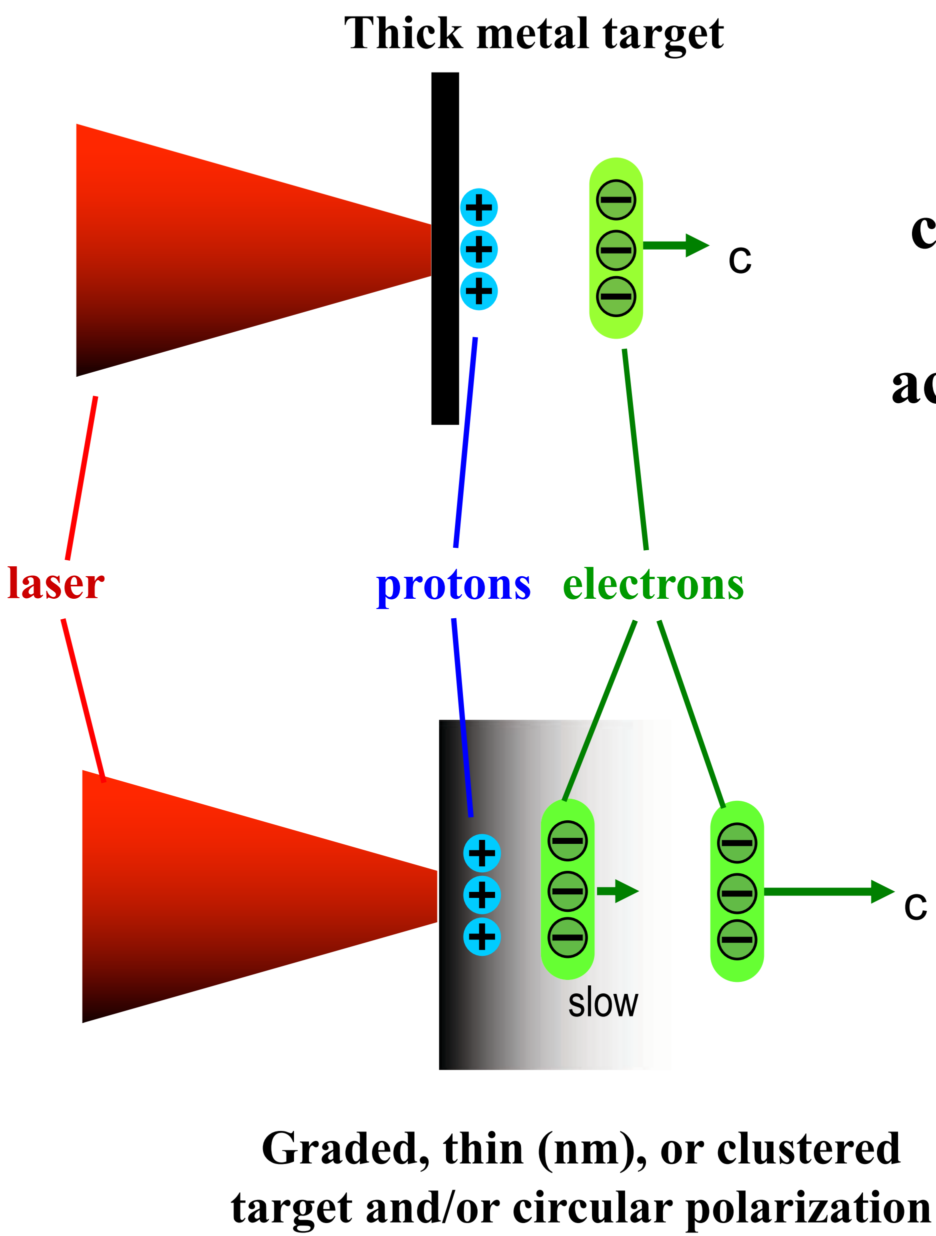
Radiation dominant regime

Esirkepov et al. (2004)

Nanometric target



Adiabatic acceleration (2)



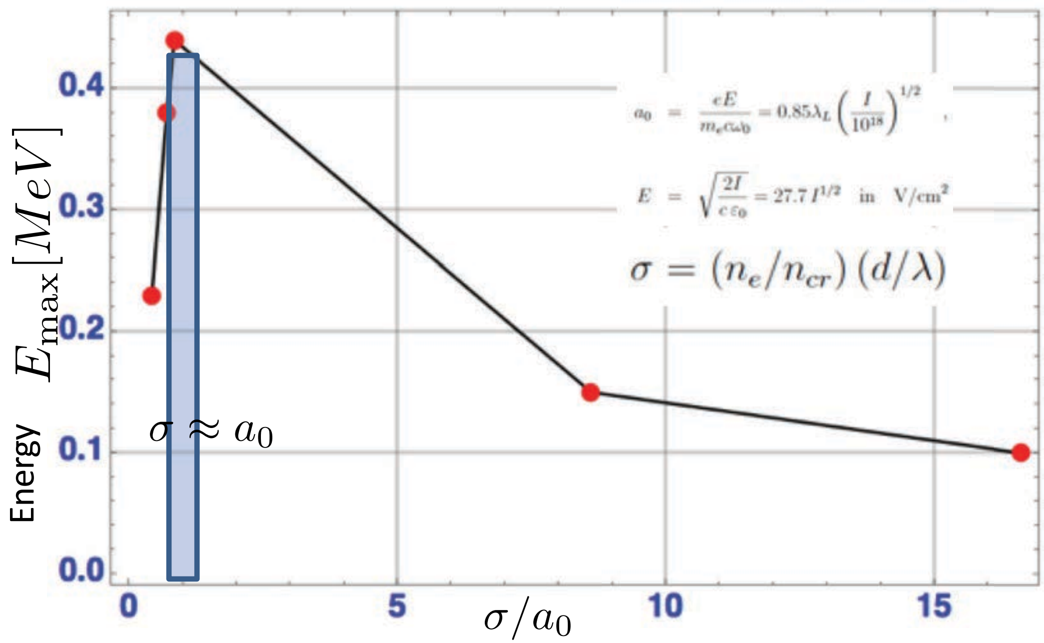
Most experimental configurations of laser proton acceleration(2000-2009)

Innovation ("Adiabatic Acceleration") by laser (2009-)

= Method to make the electrons within ion trapping width

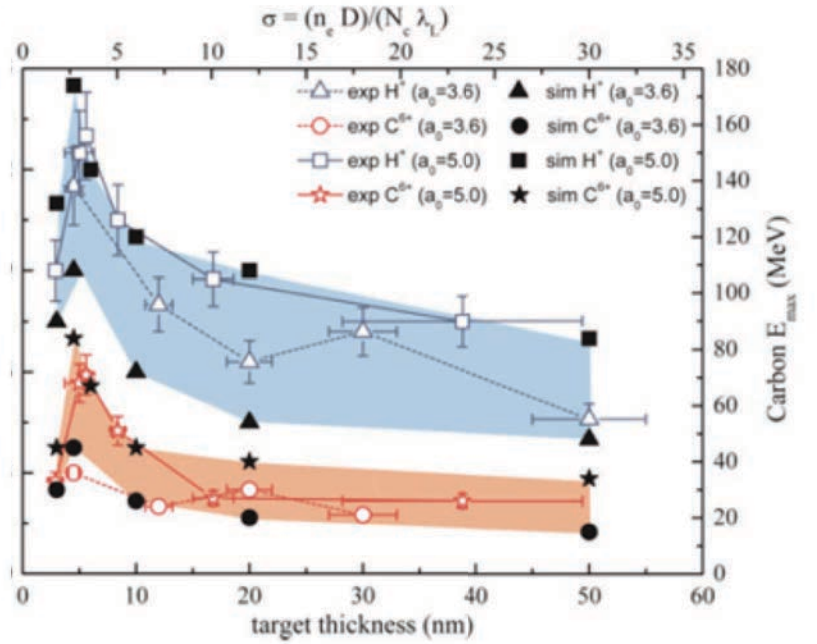
Target thickness scales with a_0
Coherent Acceleration of Ions by Laser (CAIL)

Deuteron energy vs. thickness of foil



target thickness [normalized to laser intensity]

Our simulation

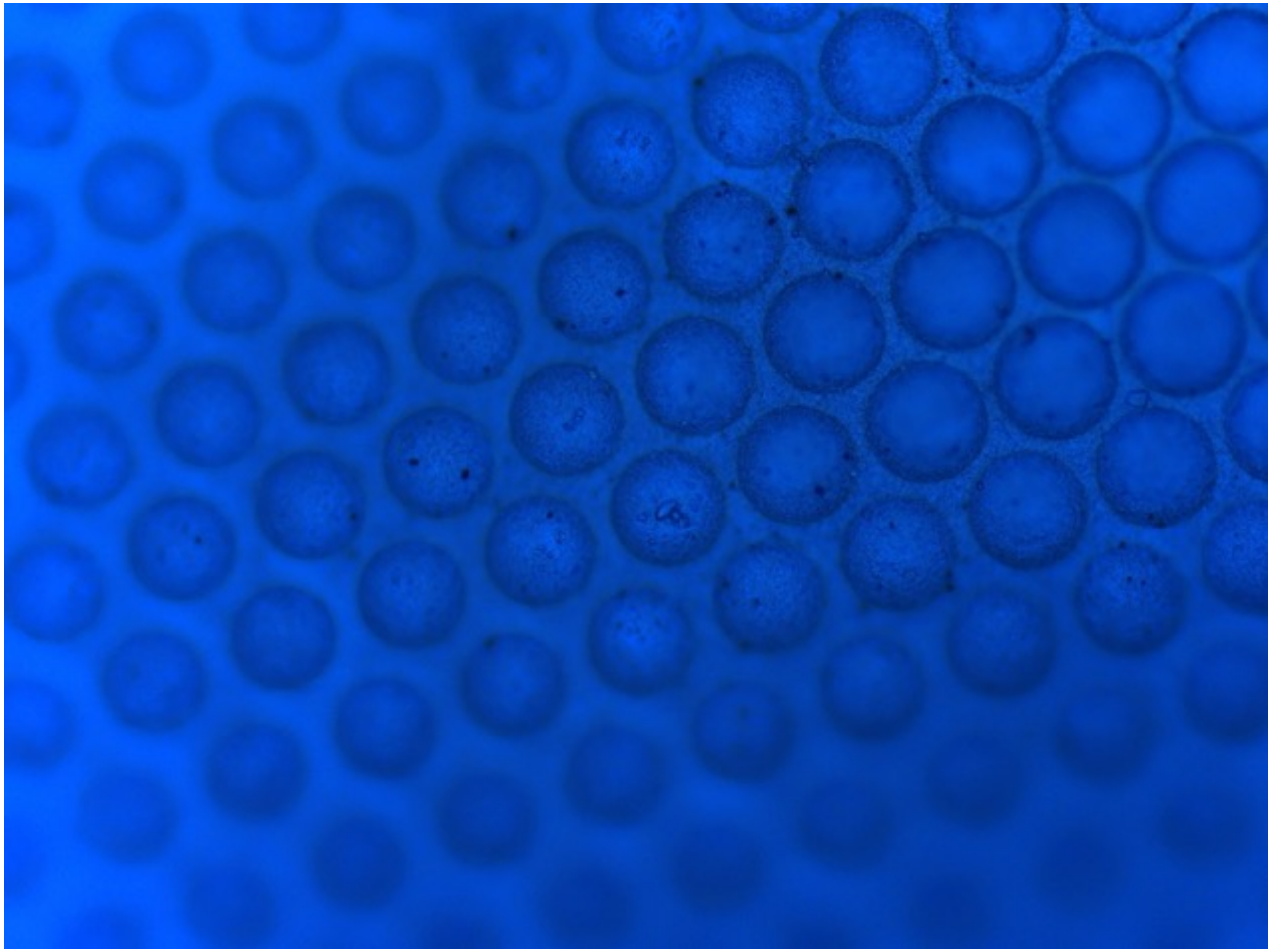


Experiment: Steinke,..Tajima (2010)

Optimum parameters (sweet-spot) for ion acceleration at $\sigma \approx a_0$

Necas, Tajima (2018)

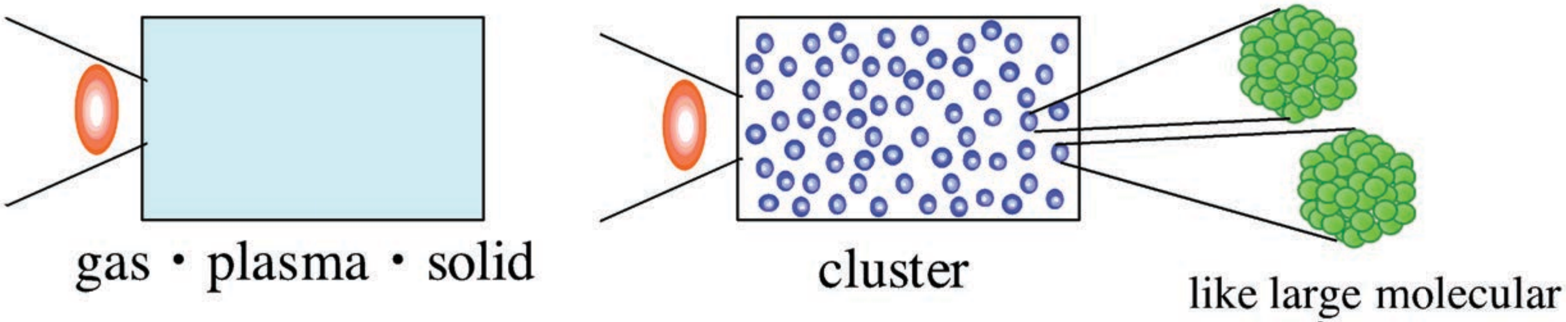
Nanostructured target



(Habs, 2009)

Why is Laser-Cluster Interaction Strong?

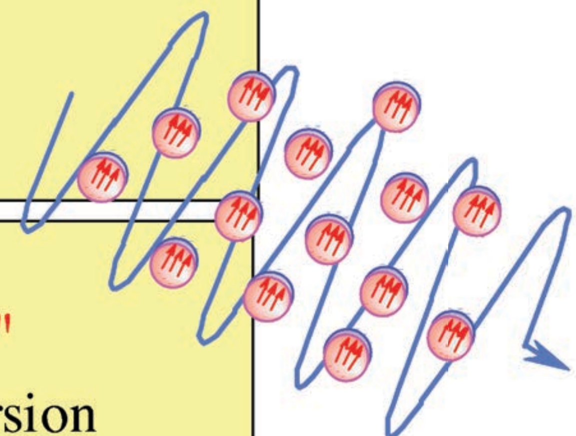
"clusterd phase" vs. "gas", "plasma", "solid phase"



Transverse polarization manifest

- "Small particle system" and enhanced fluctuation
  - free energy originated from the surface is NOT neglected.
  - energy and structual deformation/fluctuation

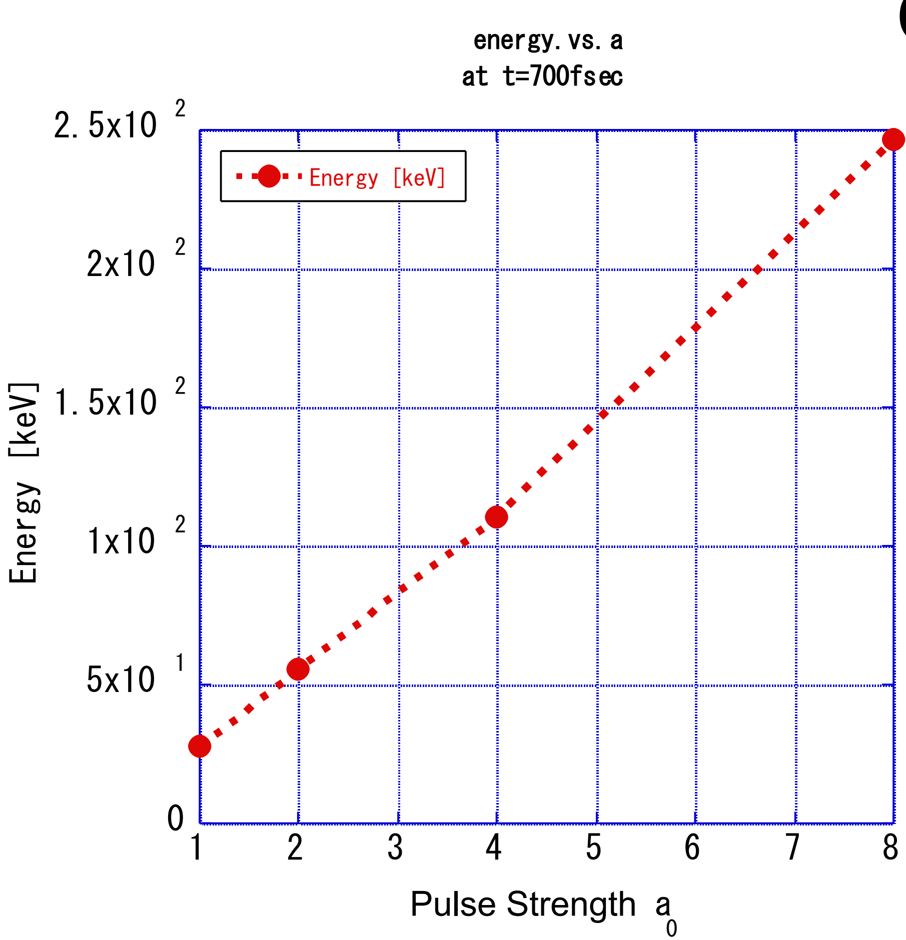
- Freedom of tansverse polarization through "surface"
  - different nature in linear and non-linear dispersion



(Y.Kishimoto)

R. H. Doremus, J. Chem. Phys. 40, 2389 (1964)
A. Kawabata and R. Kubo, J. Phys. 40, 1765 (1966)

Maximum energy vs. laser intensity

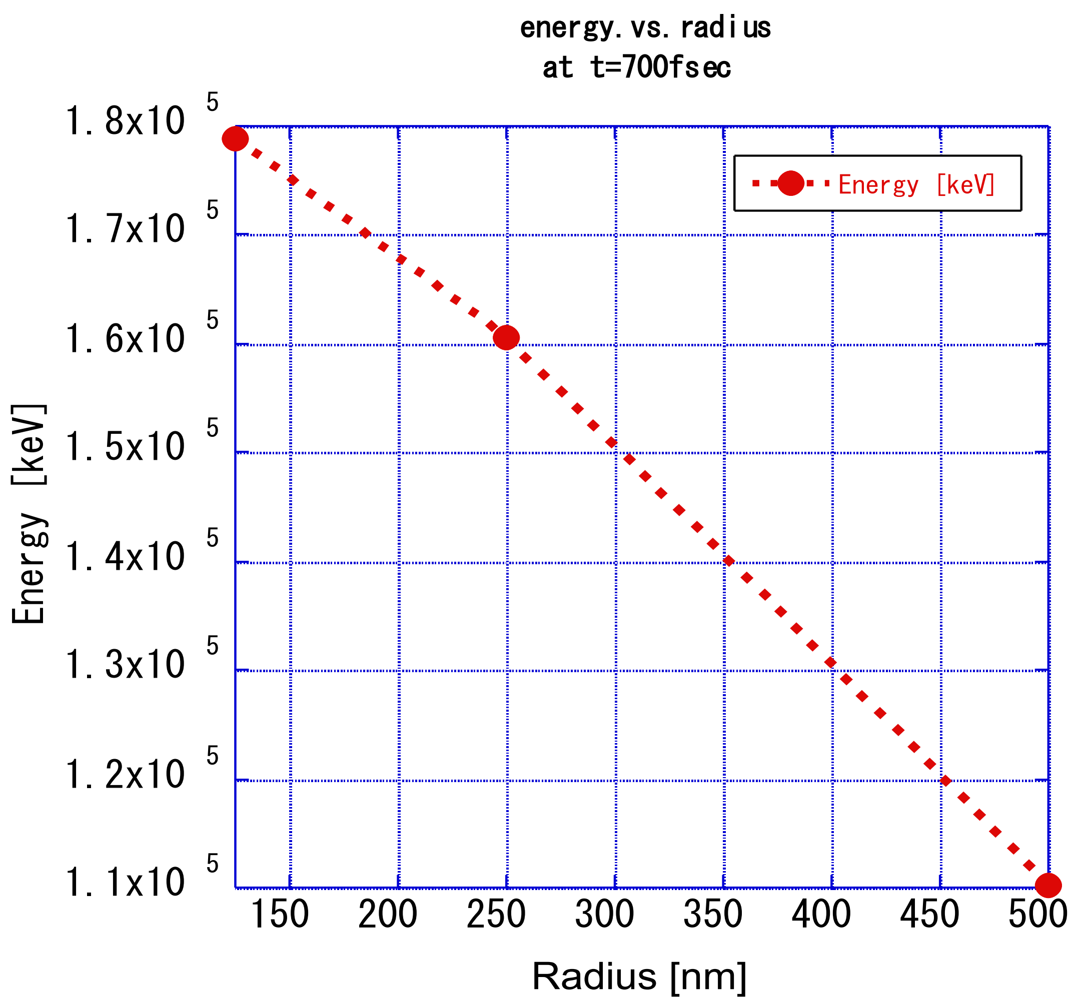


Cluster target scaling

Consistent to the Theory by Yan et al. (2009), though it is based on thin film case

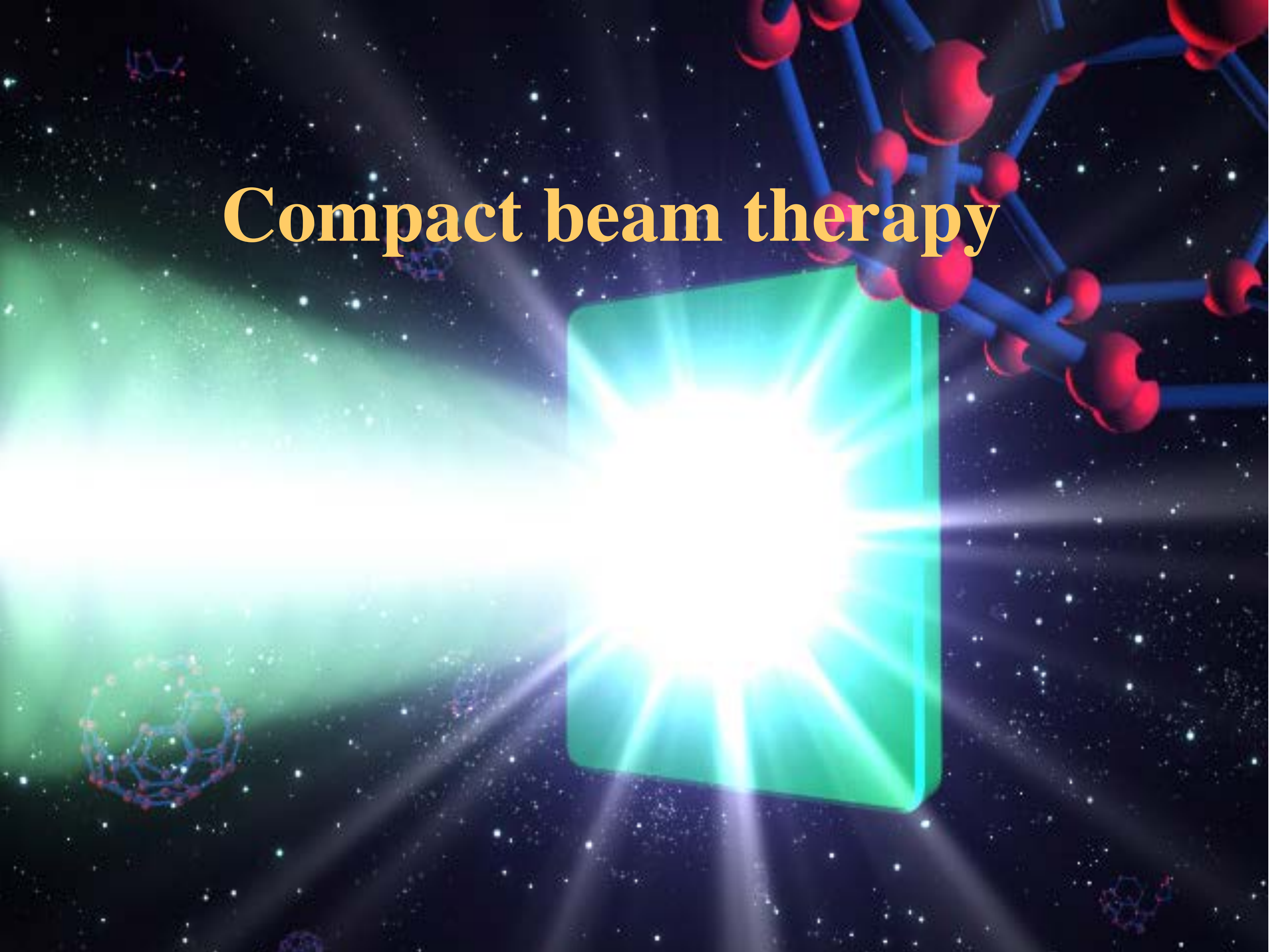
Ion Energy vs. Cluster Radius

Cluster target scaling: ion energy ~ 1/(cluster radius)



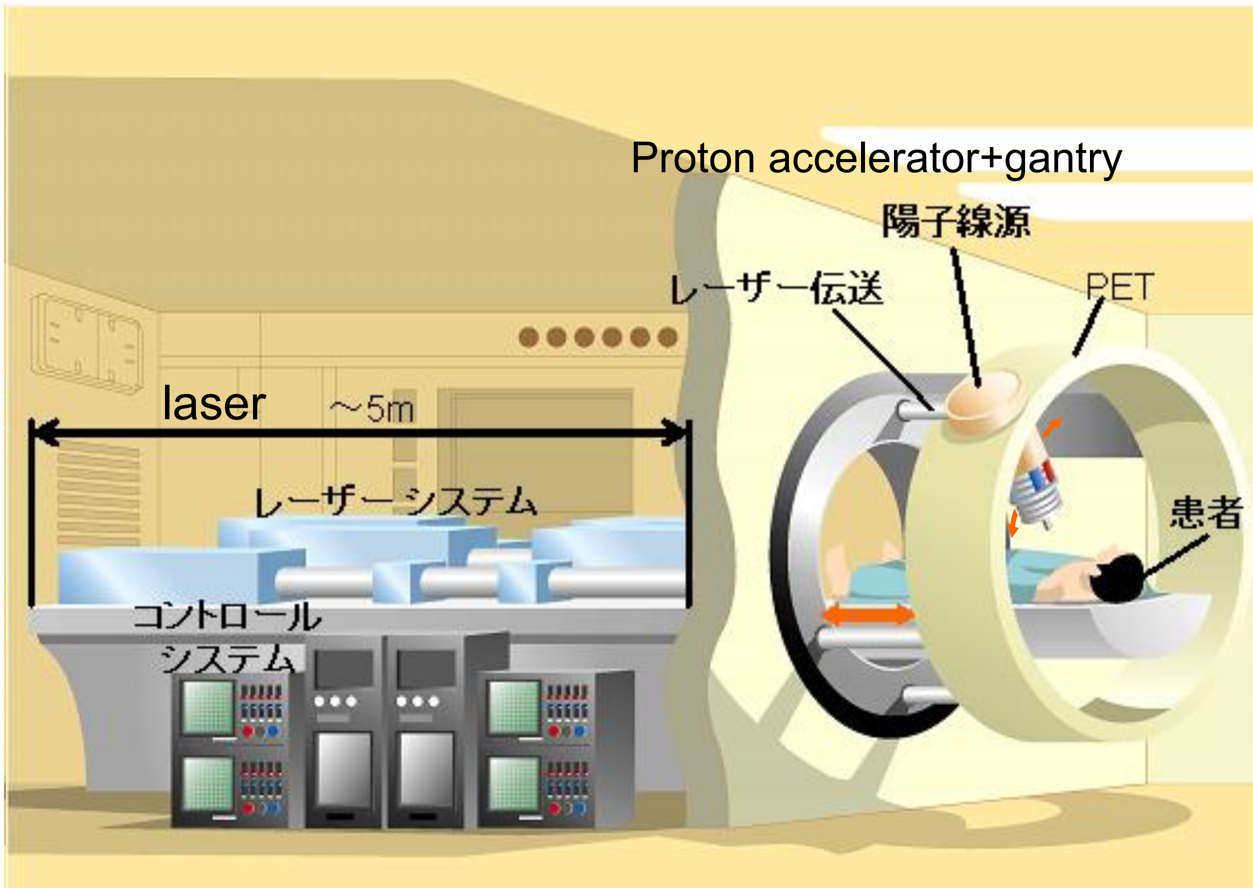
Kishimoto, Tajima (2009)

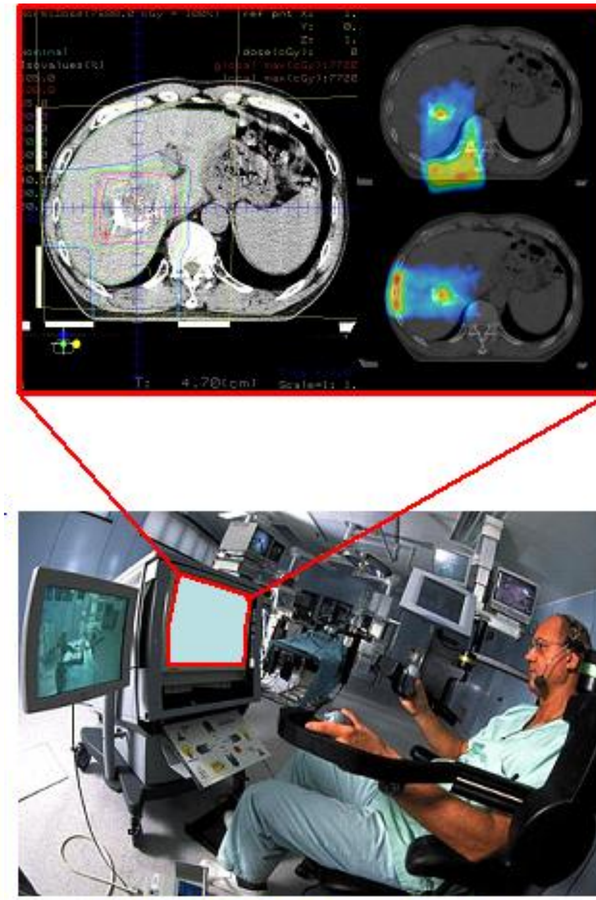
Compact beam therapy



Toward Compact Laser-Driven Ion Therapy

PET or γray image of autoradioactivation

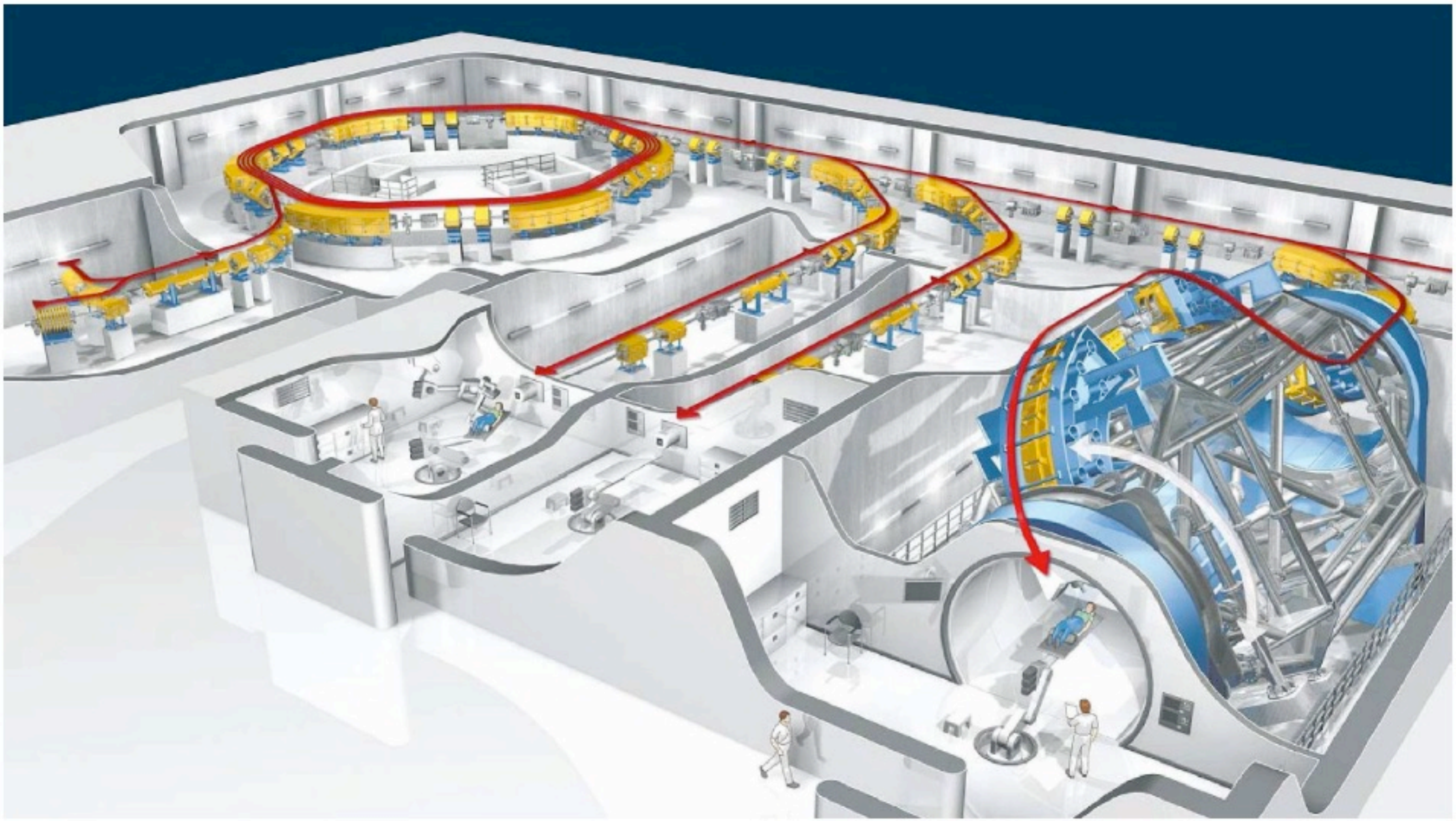




治療計画（診断と照射）

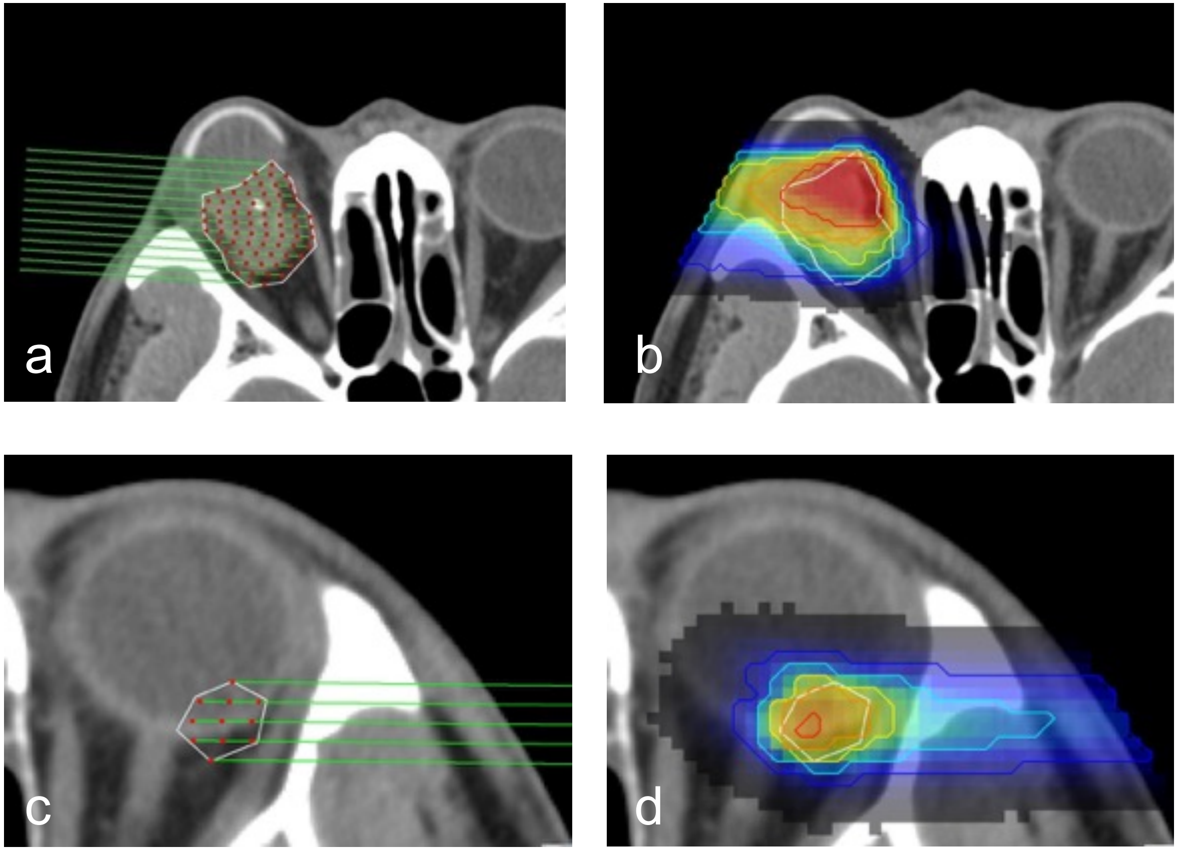
Laser particle therapy (image-guided diagnosis→irradiation→dose verification) targeting at smaller pre-metastasis tumors with more accuracy

Artist's view of the Heavy Ion Therapy Center (HIT) in Heidelberg



Spot-Scanning Simulation of Laser Proton Radiotherapy

(Simulation of dose distribution)



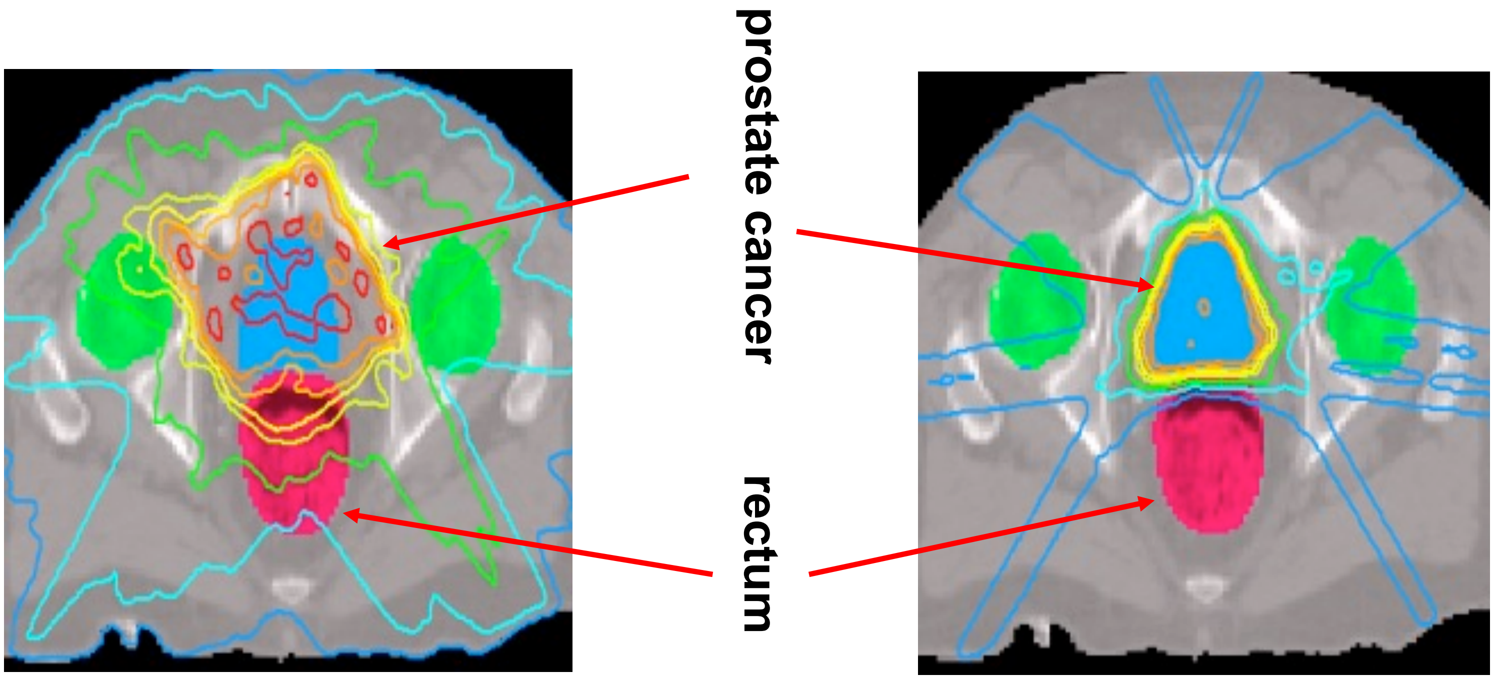
Spot-scanning simulation of laser proton radiotherapy for eye melanoma (a,b) and ARMD (c,d).

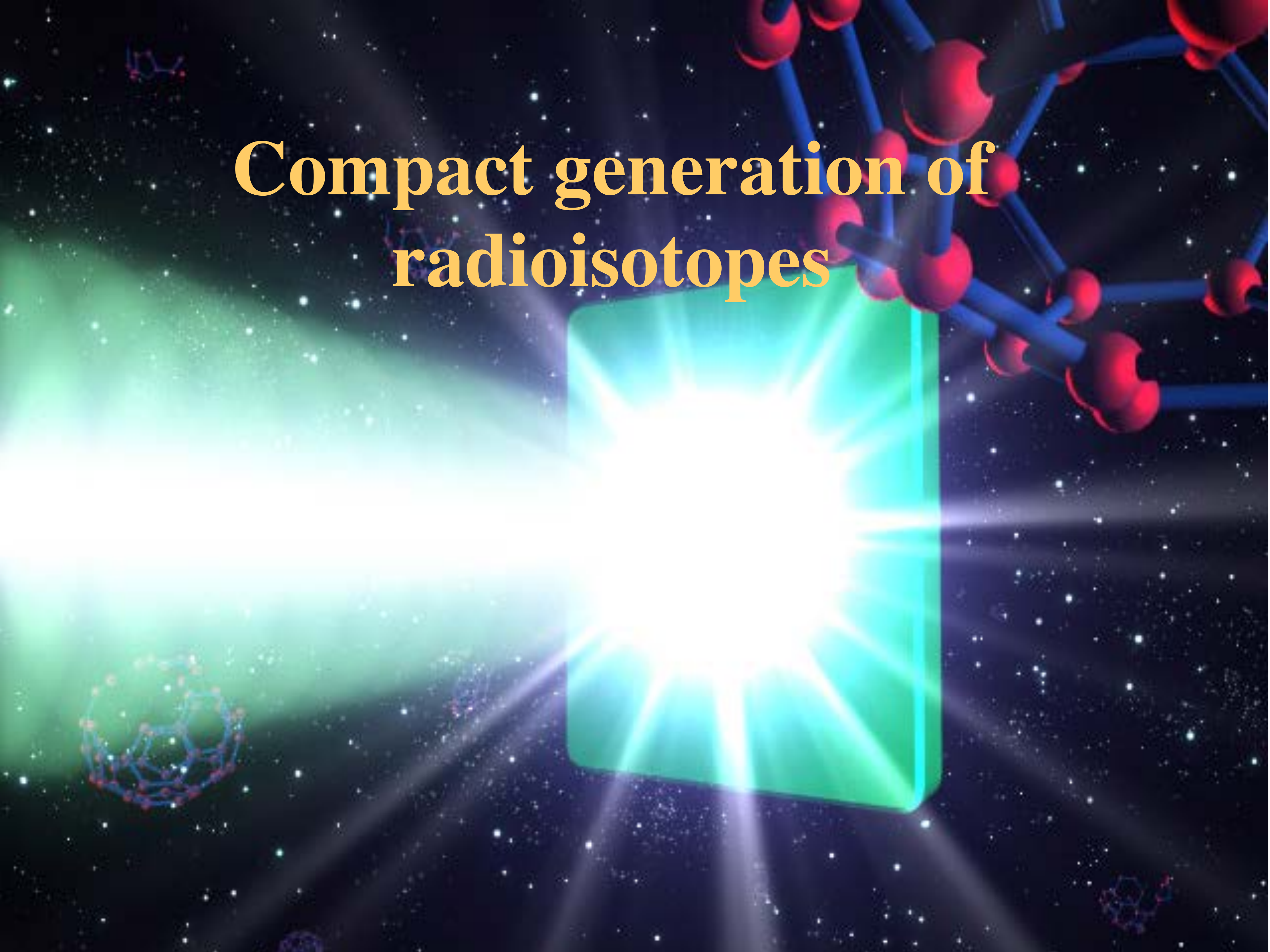
Particle-in-cell simulation (PIC) software which calculates the properties of laser-accelerated protons, Monte-Carlo simulation software, and visualization tools for the dose evaluation were used. Iso-dose curve:Blue: 25%, Sky blue: 50%, Yellow: 75%, Orange: 90%, Red: 110%.

Miyajima(JAEA)2005

Comparison of radiotherapy with the Bragg peak: Intensity Modulated Radio Therapy

X-ray IMRT | Proton IMRT




Compact generation of radioisotopes

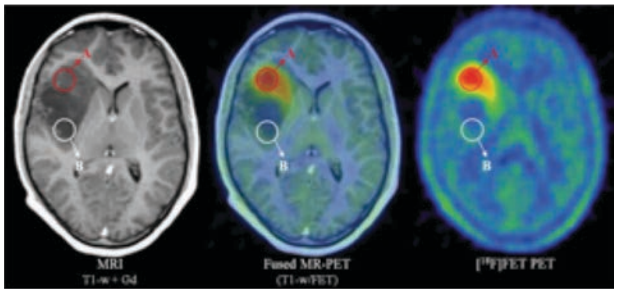
Compact laser-driven isotope generation

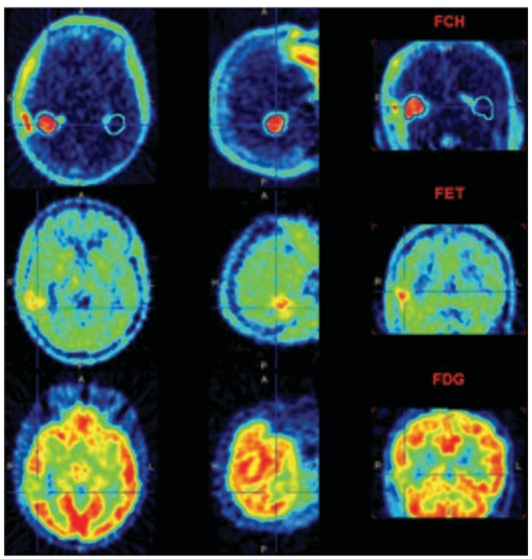
Some isotopes: so short life times that next door generation necessary

Compact sources for energy-specific electrons, ions, radio-isotopic ions, neutrons,
monoenergetic energy-sepctfic X-ray (and gamma) photons

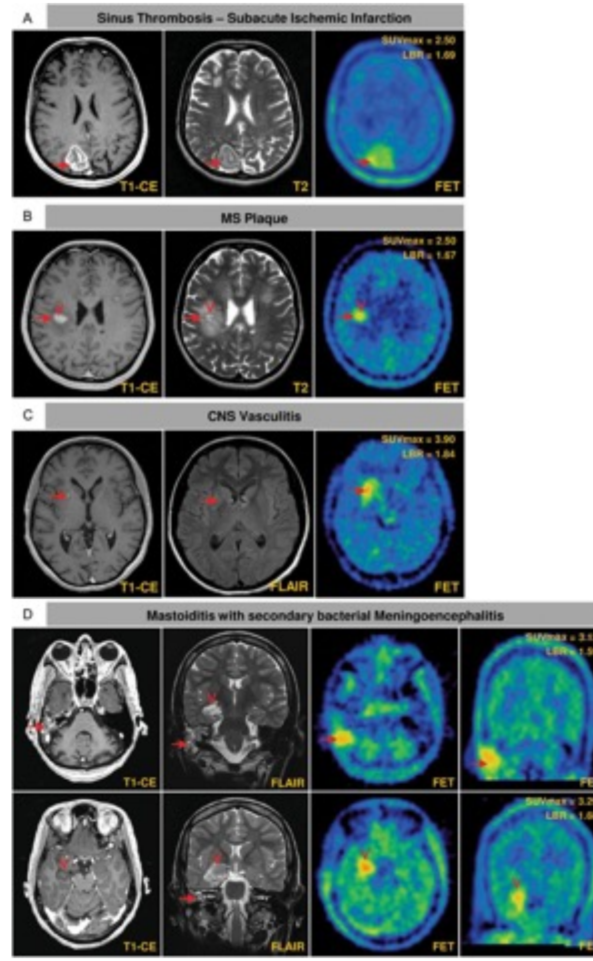
Technologies: *CPA lasers, CAN fiber lasers, TFC (Thin film Compression),
CAIL acceleration of ions, wakefield acceleration

F-18-FET



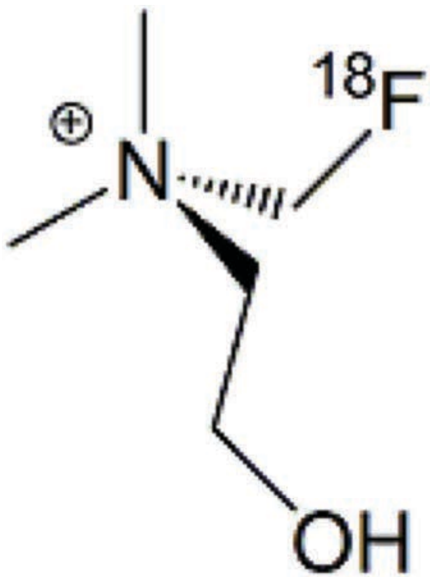


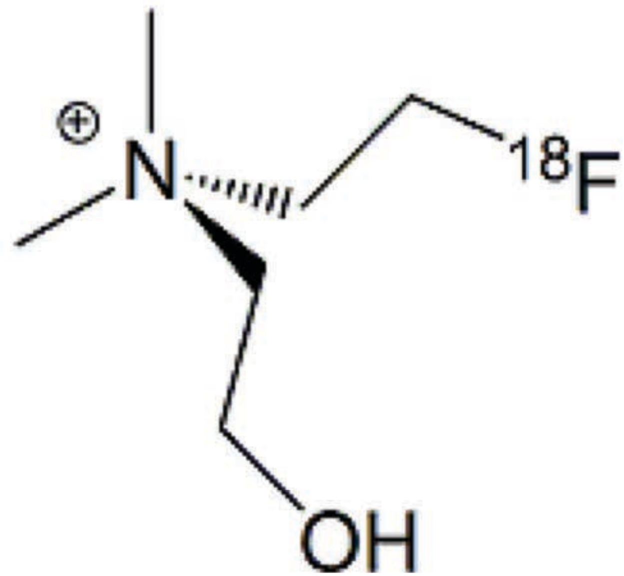
Brain tumor



Neuroinflammation

[^{18}F]CHOLINE

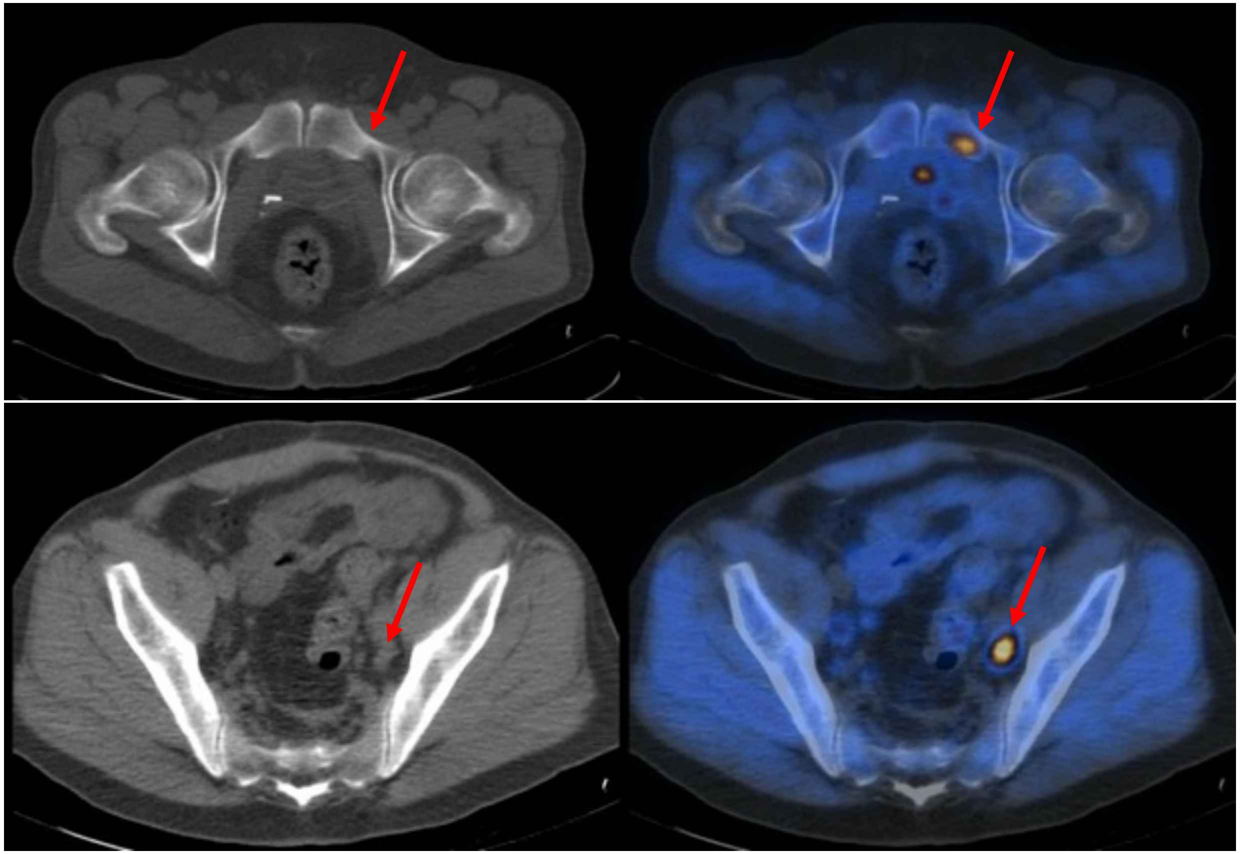




[^{18}F]Fluoromethylcholine

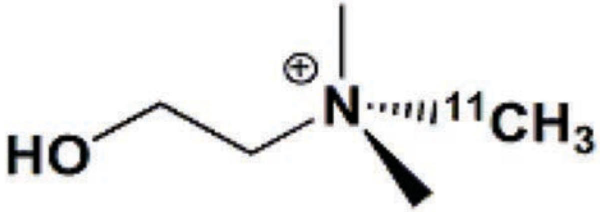
[^{18}F]Fluoroethylcholine

[^{18}F]CHOLINE



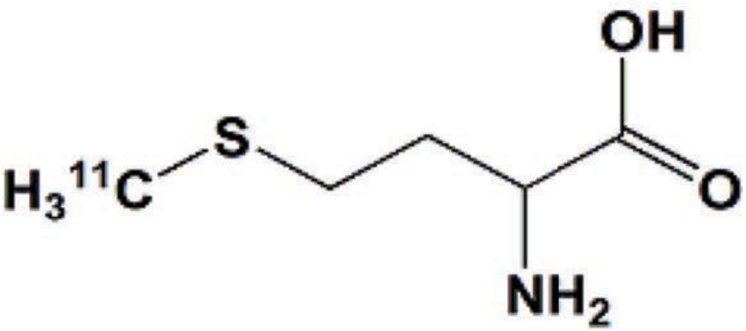
Prostate cancer

[^{11}C]Tracers



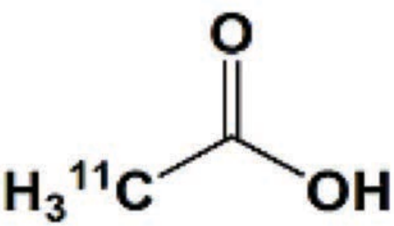
[^{11}C]Choline

Synthesis of cell membrane phospholipids



[^{11}C]Methionine

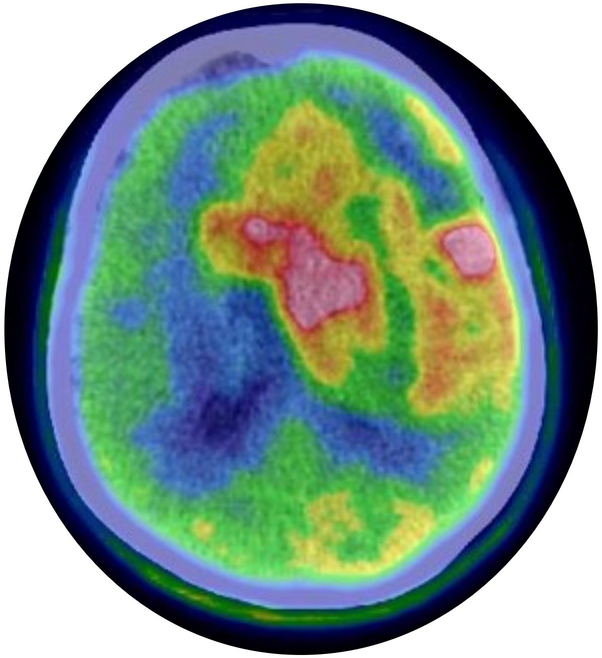
Protein synthesis



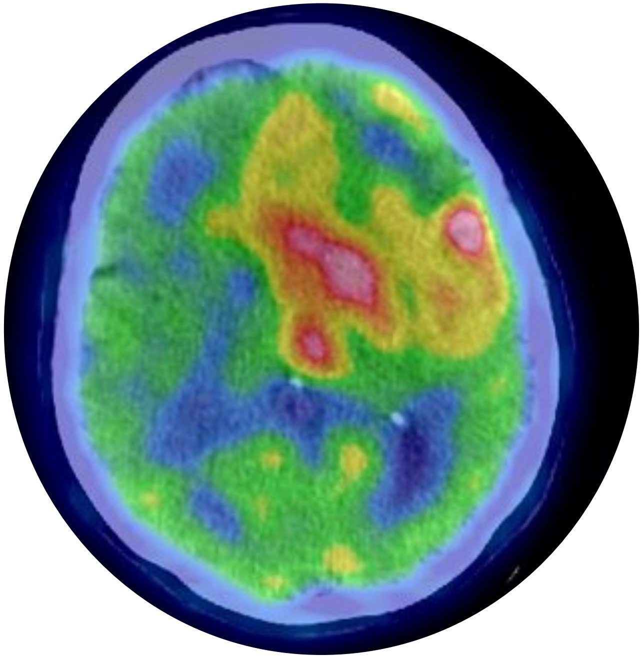
[^{11}C]Acetate

Fatty-acid metabolism

[^{11}C]Methionine



Before therapy



After therapy

Astrocytoma (no response)
(courtesy by PET Centre St. Orsola Hospital, Bologna)

Emerging radioisotopes and (alternative) production routes

All medical radioisotopes now produced in reactors **can be produced alternatively** or **can be replaced** by isotopes which can be produced other than in a nuclear reactor

Particle Accelerators

Linear

- Ge-68/Ga-68, and Sr-82/Rb-82, Zn-65, Mg-28, Fe-52, Rb-83 (200 MeV proton beam, 150 uA)

Cyclotrons (10-100 MeV, up to 2 mA)

- F-18, Sr-82, Cu-64,O-15, C-11, Br-77, I-124, Y-86, Ga-66/68, Cu-60/61, Zr-89, Tc-99m

New routes

Compact systems (Bench-scale electronic devices for achieving various high-energy nuclear reactions):

proton accelerator: production of F-18, In-111, I-123, C-11, N-13, O-15

alpha linac: Sn-117m, Ac-225, As-73, Fe-55, At-211, Cd-109, Y-88, Se-75, Po-210

neutron sources

Electron-beam accelerator

- Bremsstrahlung 10-25 MeV electrons proposed for isotope production through:
- ❑ Photo-fission of heavy elements
- ❑ (γ ,n) reactions
- ❑ Photo-neutron activation and (n,2n) reactions

Emerging radioisotopes and (alternative) production routes

Emerging medical radioisotopes: β-emitters and theragnostic agents – *in preclinical and clinical research*: Lu-177, Ho-166, Re-186/188, Cu-67, Pm-149, Au-199, Y-90

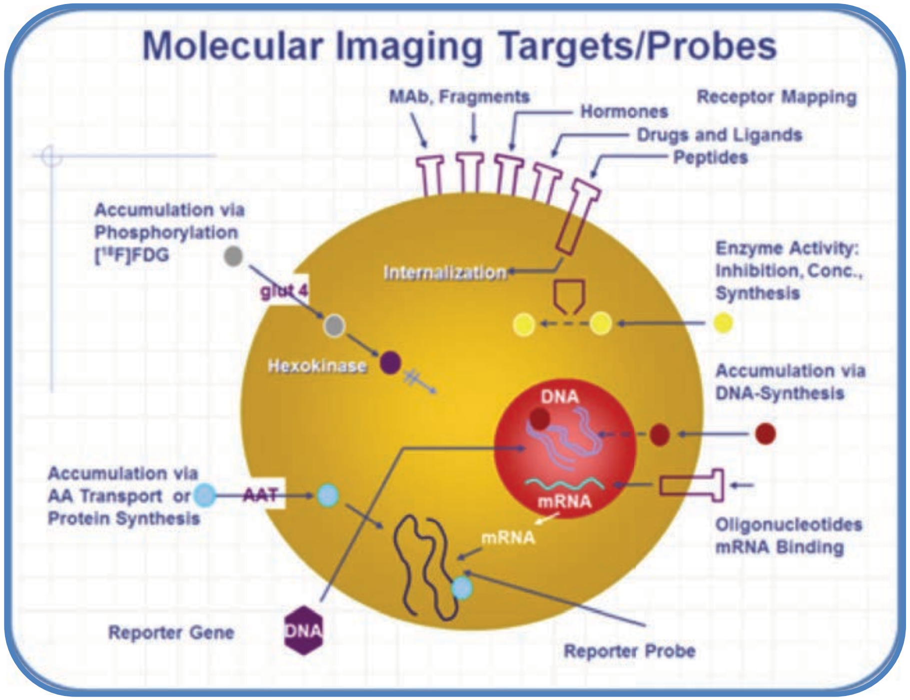
Radio nuclide	Emission	Half-life (hrs)	Production Mechanism	Particle/gamma Energy (MeV)
^{67}Cu	β (0.14 MeV) γ (0.18 MeV)	62	$^{68}Zn(p, 2p)$ $^{70}Zn(p,\alpha)$ $^{67}Zn(n,p)$ $^{68}Zn(\gamma,p)$	Ep (>> 30) Ep (>> 30) Reactor Eγ (>19) σ = 0.03 barn
^{47}Sc	β (0.16 MeV) γ (0.16 MeV)	3.35 d	$^{48}Ti(\gamma,p)$	Eγ (>27) σ = 0.01 barn
^{186}Re	β (0.35 MeV) γ (0.14 MeV)	3.7 d	$^{187}Re(\gamma,n)$	Eγ (>15) σ = 0.6 barn
^{149}Pm	β (1.072 MeV)	53.08	$^{150}Nd(\gamma,n)^{149}Nd$	Eγ (>12.5) σ =0.22 barn
$^{152/155/161}Tb$	β^+ (1.08 MeV) EC (0.86, 0.10 MeV) β^- (0.154 MeV), Auger	17.5/ 127,2 165.3	$^{152}Tb/^{155}Tb$ proton-induced spallation $^{160}Gd(n,\gamma)^{161}Gd$	Neutron source Reactor

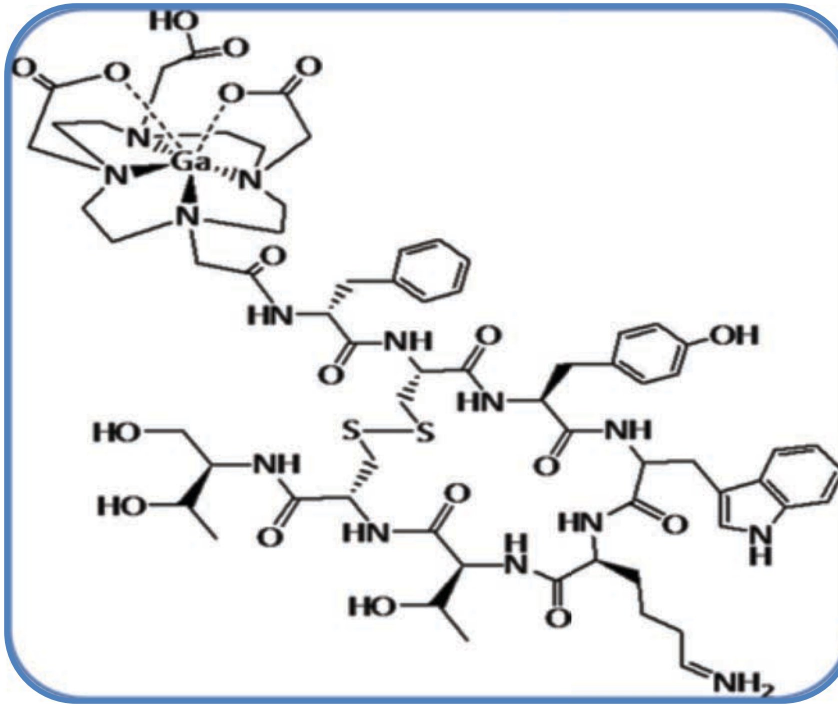
Emerging radioisotopes and (alternative) production routes

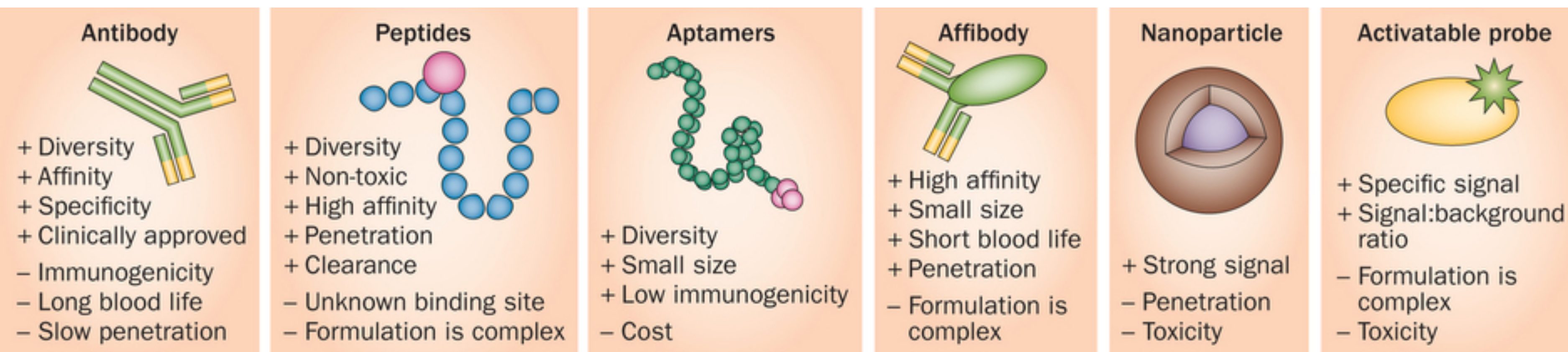
Emerging medical radioisotopes: α-emitters and Auger-electrons emitters

Radio nuclide	Emission	Half-life (hrs)	Production Mechanism	Particle Energy (MeV)
^{211}At	α	7.2	$^{210}Bi(\alpha,2n)$	Eα (30)
^{225}Ac	α (5.8 MeV) β (0.1 MeV)	240	^{229}Thorium generator Ion exchange from ^{225}Ra $^{226}Ra(p,2n)$ $^{226}Ra(\gamma,p)$	 Reactor Ep (25–8) Eγ (>19) σ = 0.02 barn
^{224}Ra/ ^{212}Pb/ ^{212}Bi	α (5.7 MeV)/ β^- (0.1 MeV)/ α (6.0 MeV), *β* (0.77 MeV)	3.7/ 10.64 h /60 .6 m	$^{226}Ra(\gamma,2n)$	Eγ (>16) σ = 0.1 barn
^{165}Er	A (0.038 MeV) γ (0.05 MeV)	10.3	$^{166}Er(\gamma,n)$	Eγ (>13) σ = 0.3 barn
^{149}Tb	α (3.967 MeV) β (0.7MeV)	4.12	$^{152}Gd(p,4n)^{149}Tb$, $Ta(p, X)^{149}Tb$	

MOLECULAR IMAGING / SYSTEMIC RADIOTHERAPY RADIOPHARMACEUTICALS

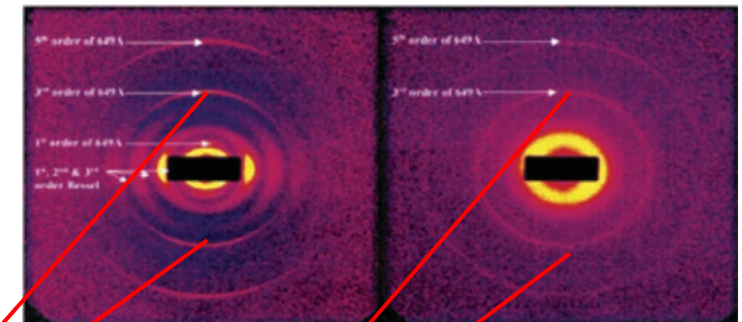






Compact monoenergtic X-rays

Small-angle X-ray scattering (SAXS)



normal tissue contains collagen fibrils in regular, hexagonal-like arrangement

healthy

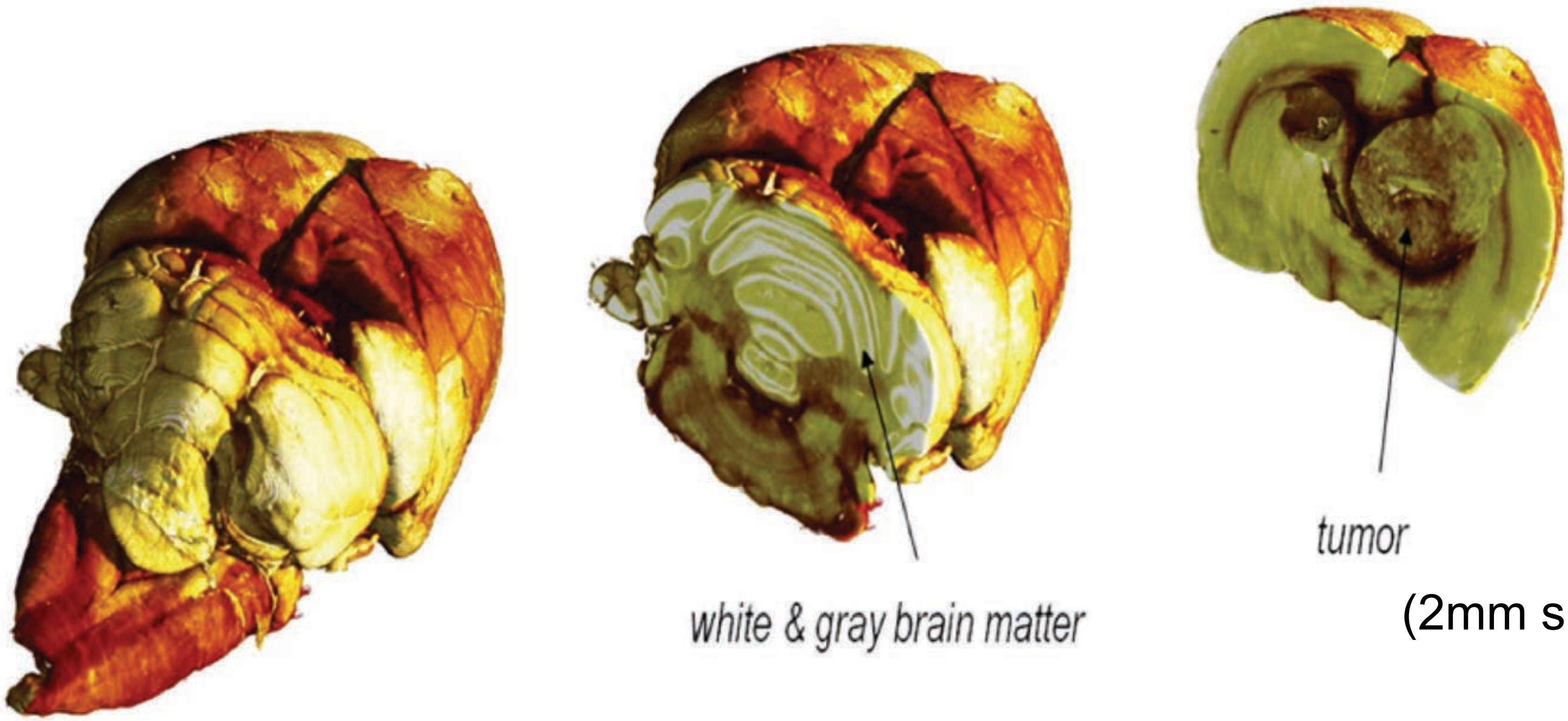
cancerous

micro-x-ray beam

cancer cells degrade regular structure of collagen fibrils, making them thinner and their axial period longer

vision: direct cancer diagnosis without biopsy

State-of-the-art 3D phase-contrast tomography at highly brilliant synchrotron radiation sources (@ESRF Grenoble/ France)



(2mm size)

contact:
franz.pfeiffer@psi.ch &
www:
http://people.epfl.ch/franz.pfeiffer

F. Pfeiffer et al., Phys. Med. Biol. 52, 6923 (2007)

Small tumor detection and therapy

(by such method as Phase Contrast Imaging)

Early tumor detection:

- Less chance of metastasis
- Higher Quality-of-Life (QoL)
- Fit for laser acceleration approach

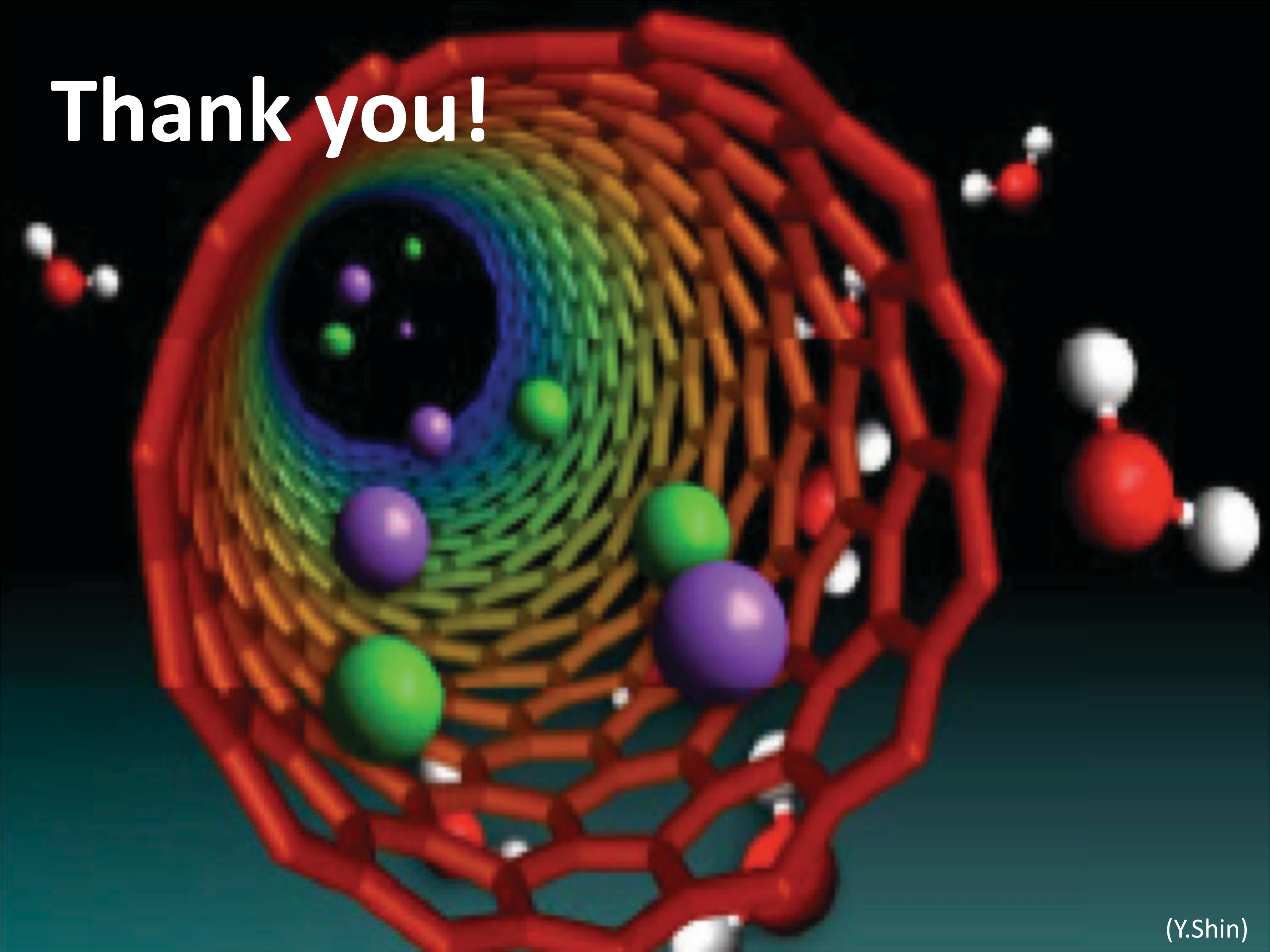
(compact laser accelerator:

not good for large dose)

Conclusions

1. Laser acceleration introduced: compact, innovative, broad radio-sources (electrons, ions, neutrons, gamma/X-rays)
2. Wakefield: plasma's unique robust high energy state
3. Convergence of laser and **nanotechnology** (and biotechnology): matches well to produce new innovative radio-sources (s.a. ions, neutrons, X-rays)
4. Modes of compact radio-sources: intra-operative, fiber, portable, ultrafast, endoscopic, short-lived isotopes, theranostics

Thank you!



(Y.Shin)