Application of Microbeams of Ionization Radiation

K. Koyama, KEK
M. Uesaka, University of Tokyo

Outline

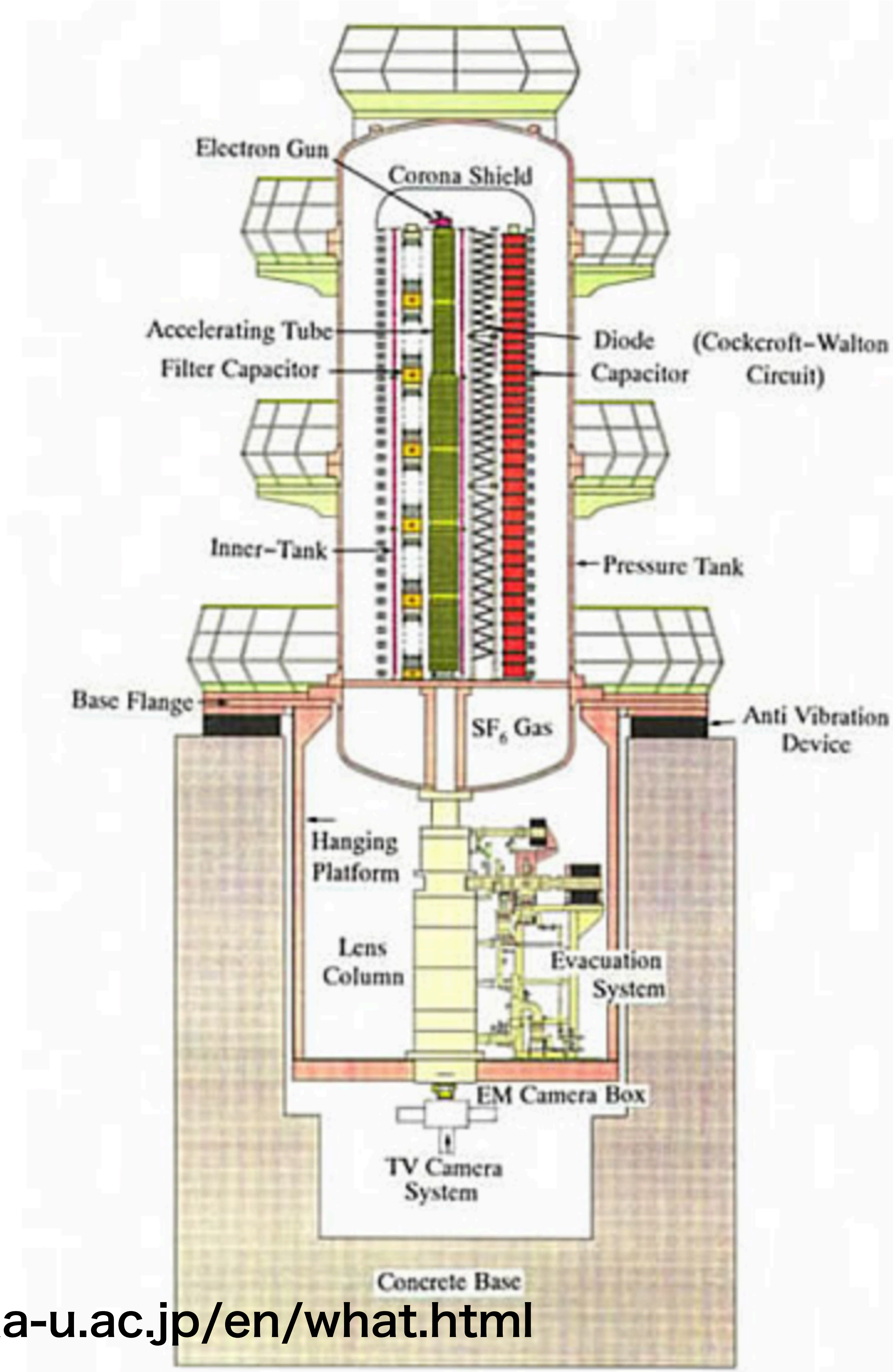
- Summary of microbeams
- Cancer therapy
  - Accelerator on a robotic arm
  - Therapy by electron beams
- Radiobiology research
  - Required conditions
  - Estimation of the energy gain
  - Estimation of the electron current
  - Experimental setup
- Summary

Application of Microbeams of Ionization Radiation

	Energy	Spot size (Equipment)	Sources	Applications
Ion	2-3 MeVu	≤ 1 μm (Micro capillary / Pinholes / Focusing) Focusing	Van de Graaf, etc Cyclotron	Non-destructive analysis (NDA) PIXSE, RBS, SIMS Micro fabrication
X-Ray	20 -50 keV	≈ 1 μm (Grazing incidence mirrors)	X-ray tube Synchrotron	NDA XRF (Z ≤ 20) Micro fabrication
	100 - 150 keV		Synchrotron	Deep-NDA HE-XRF (all Z)
	> MeV	≈ 1 mm	Linac	Radiation therapy
Electron	20 -30 keV	≤ 1 μm (Magnetic lens)	Scanning electron microscope	NDA (<<1 μm) EMP, EPMA, EMPA Micro fabrication
	> 1 MeV		MeV electron microscope	Deep-NDA EMP, EPMA, EMPA

PIXE : Particle Induced X-ray Emission
RBS : Rutherford Backscattering Spectrometry
SIMS : Secondary Ion-microprobe Mass Spectrometry

XRF : X-Ray Fluorescence
EMP: Electron microprobe
EPMA: Electron probe microanalyzer
EMPA: Electron micro probe analyze



http://www.uhvem.osaka-u.ac.jp/en/what.html

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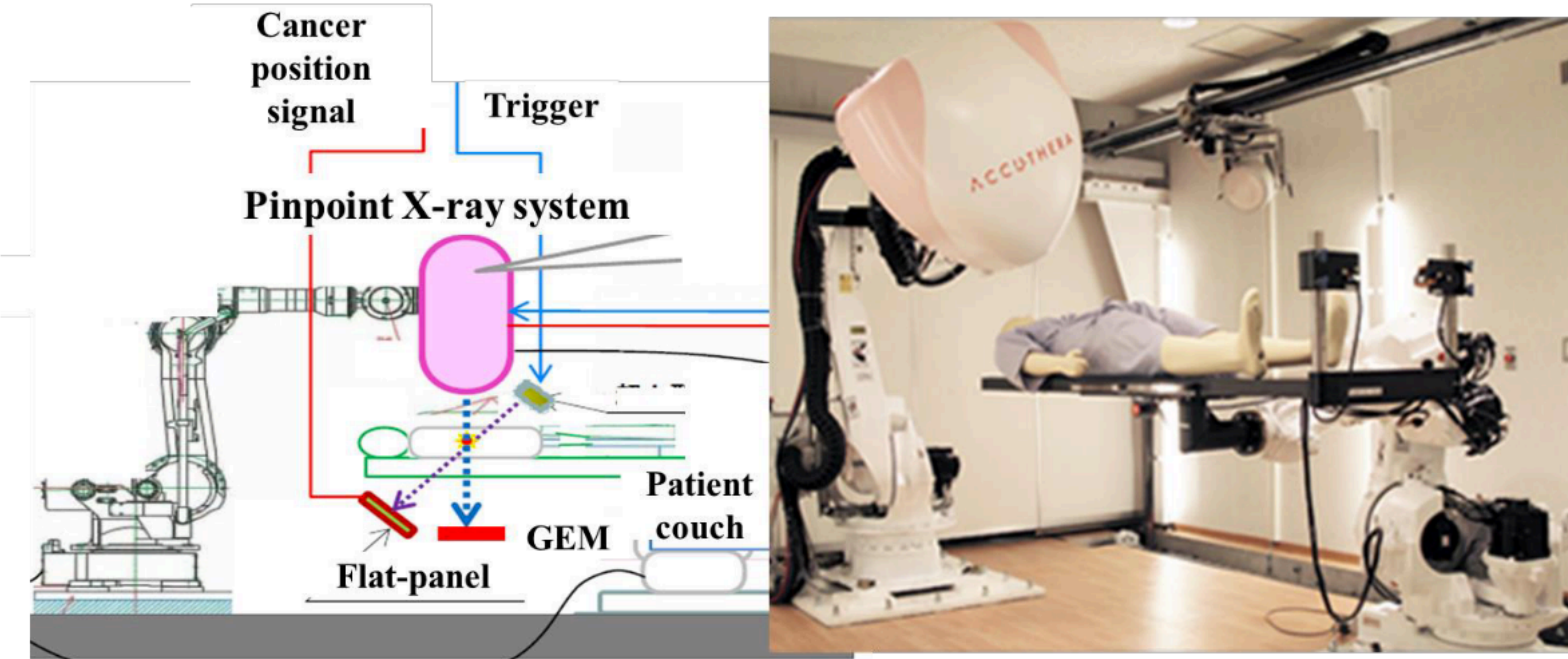
X-band Linac for Cancer treatment

The dynamic tracking aiming at moving lung cancer becomes possible in order to reduce the irradiation dose for surrounding normal organs.

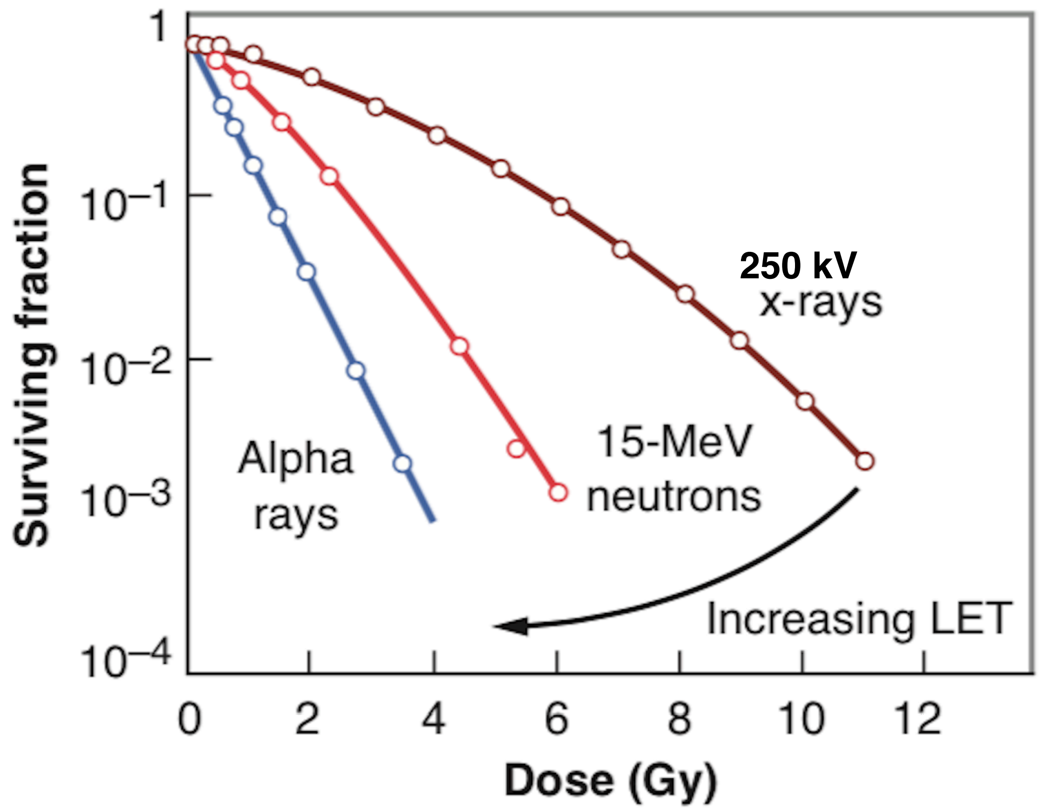


https://accuthera.com

Figure 3 6 MeV pinpoint X-ray dynamic tracking therapy system

max. 2Gy/min, max 250 pps, τ=3 μs,
Beam diameter 1.2mmΦ,
Field area 410mmx410mm@1m

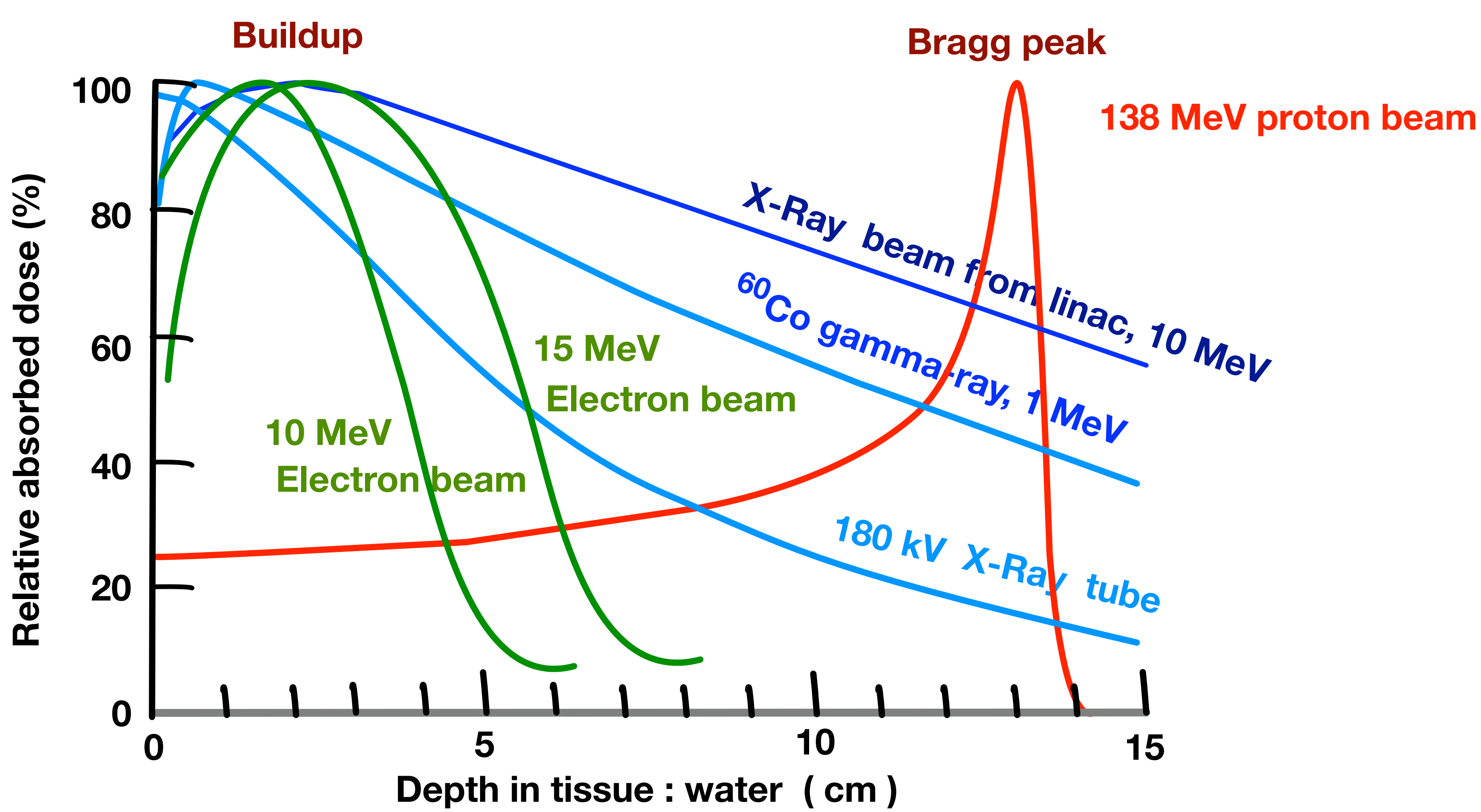
The Cancer treatment by the Electron/X-ray beams



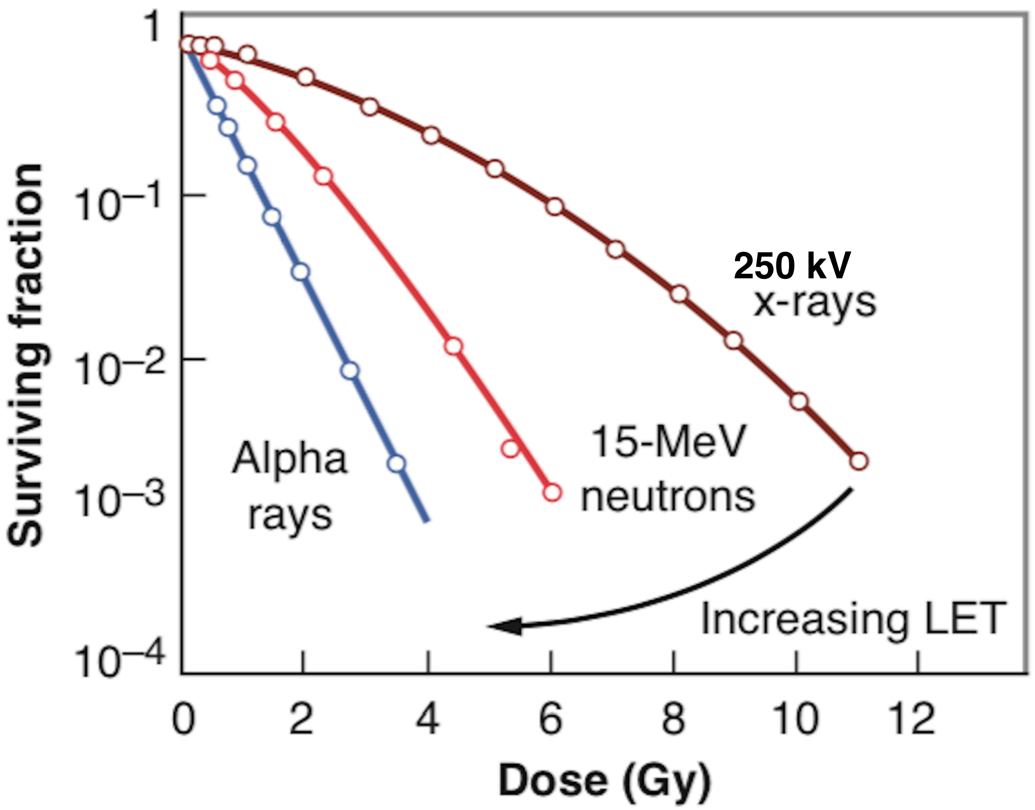
0.5 ~ 1 Gy/min

Solid Tumor (squamous cell carcinoma, Adenocarcinoma, etc.) **50 ~ 60 Gy**

Fractionated Irradiation **5 ~ 6 Gy/exposure (10 min)**
4 ~ 5 exposure/week



The Cancer treatment by the Electron/X-ray beams



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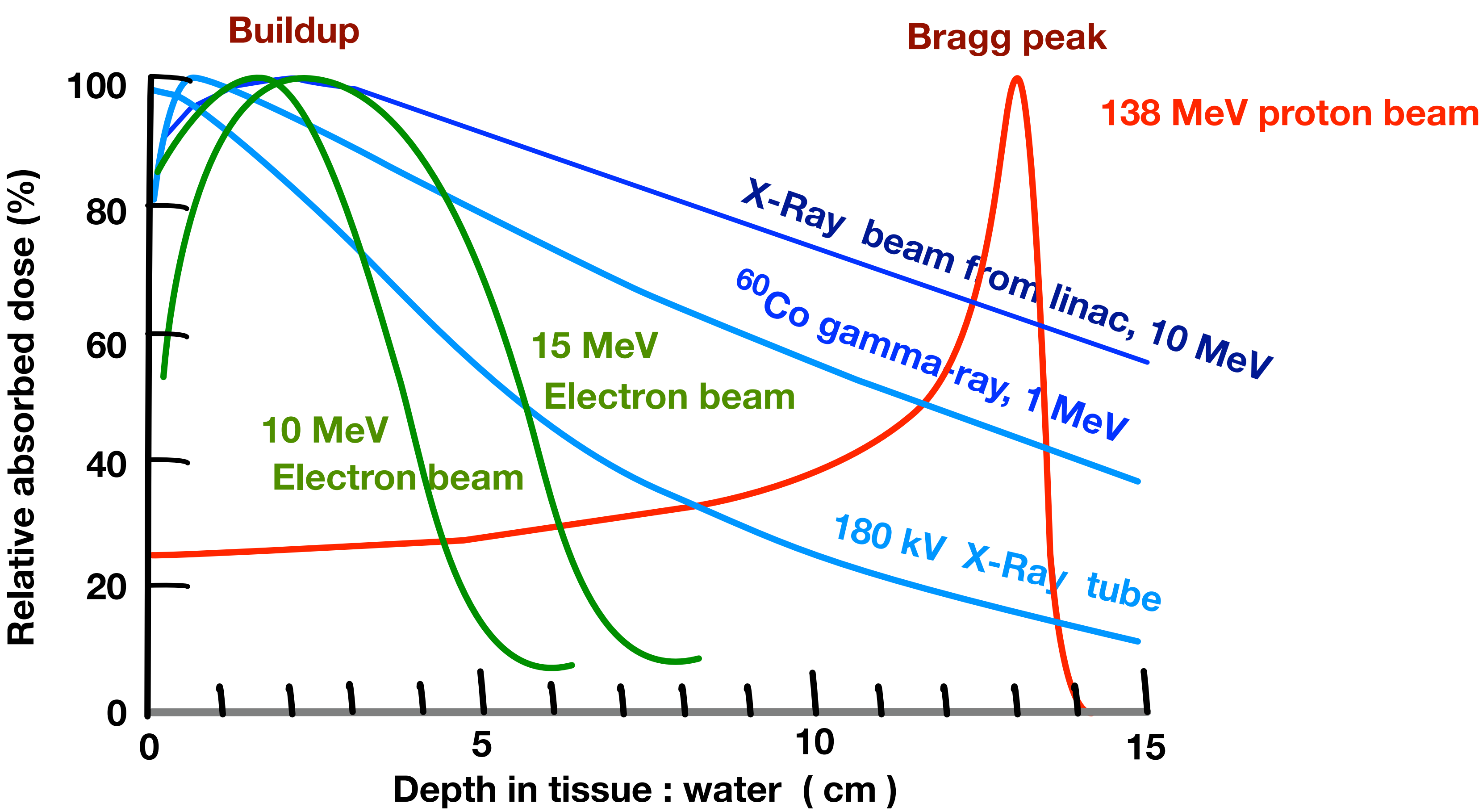

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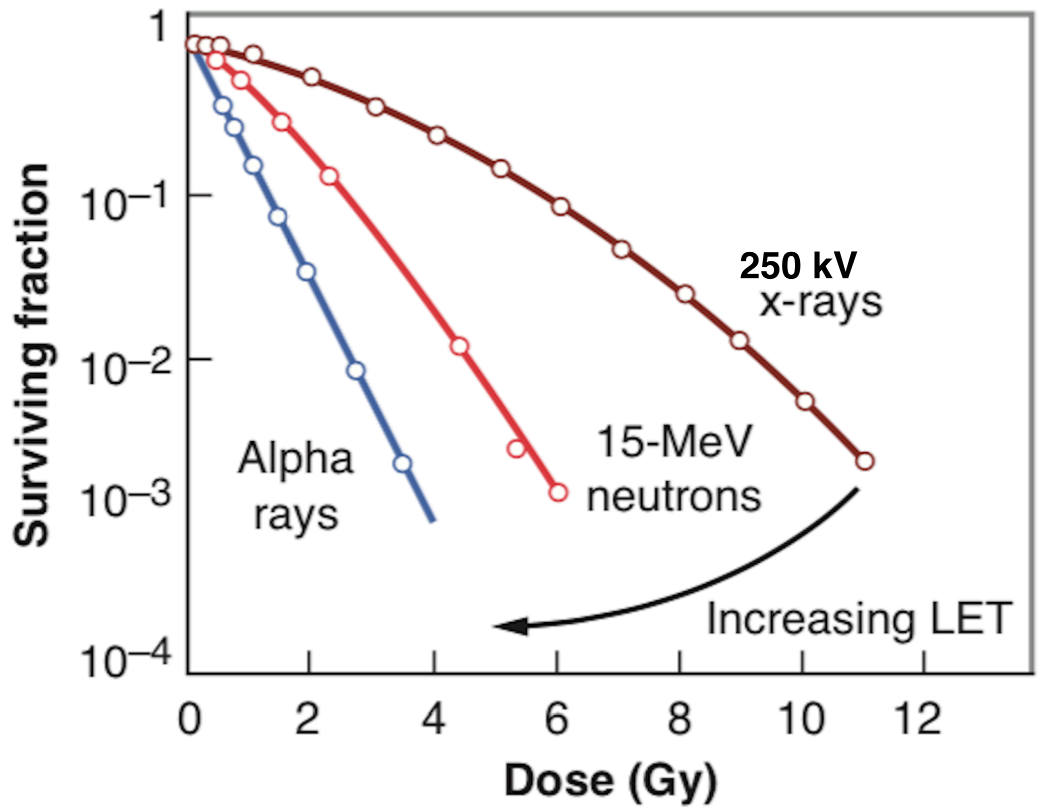

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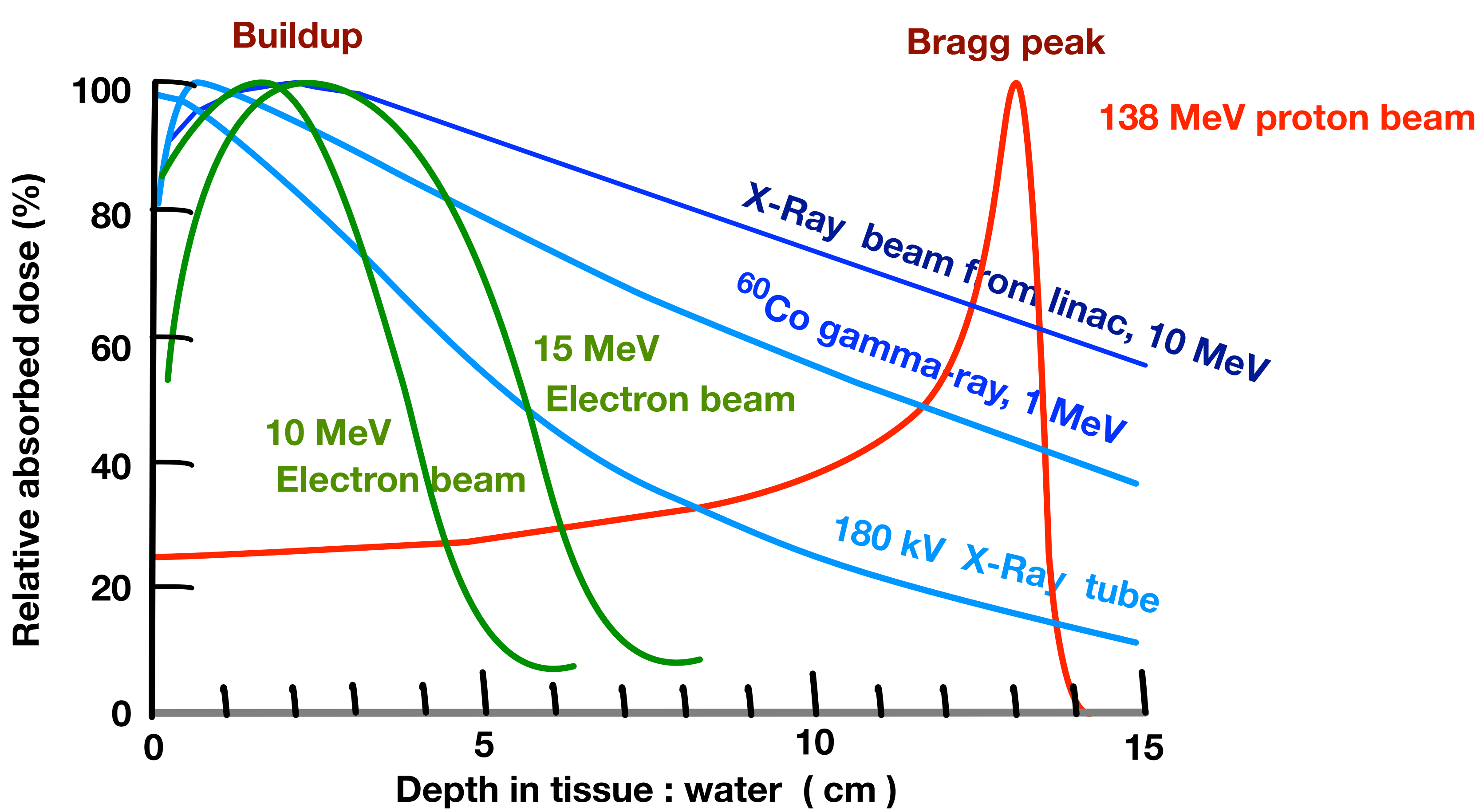
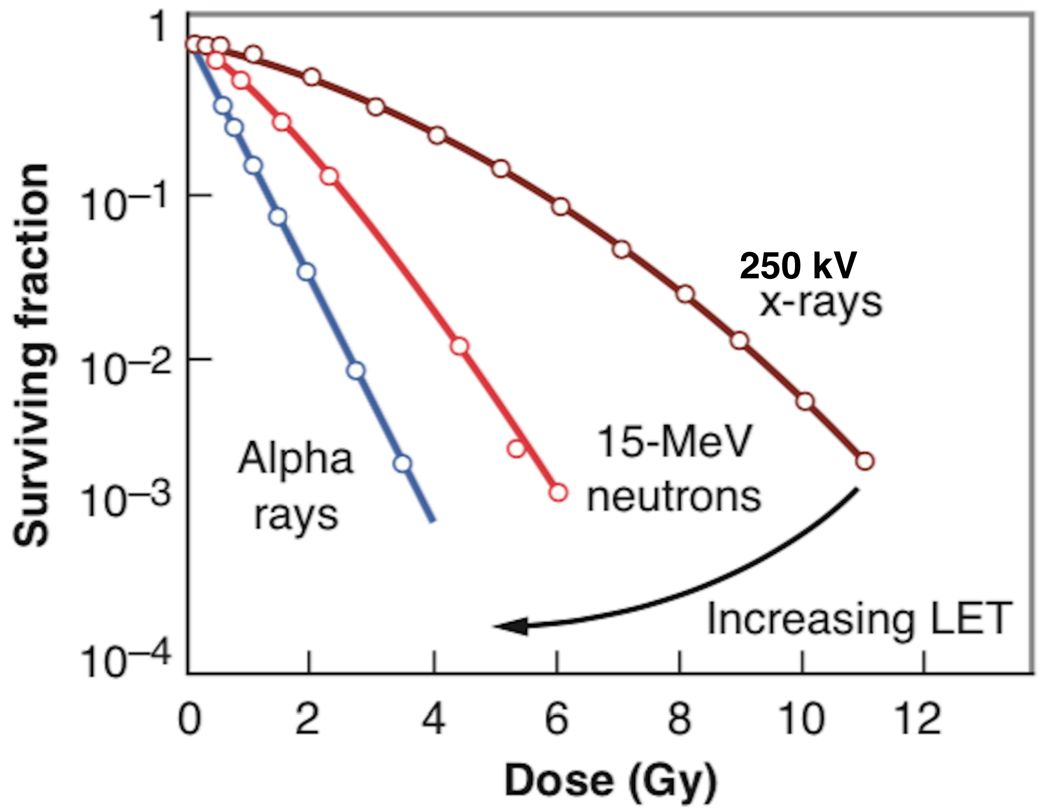


Hadron beam is the most suitable.

The Cancer treatment by the Electron/X-ray beams



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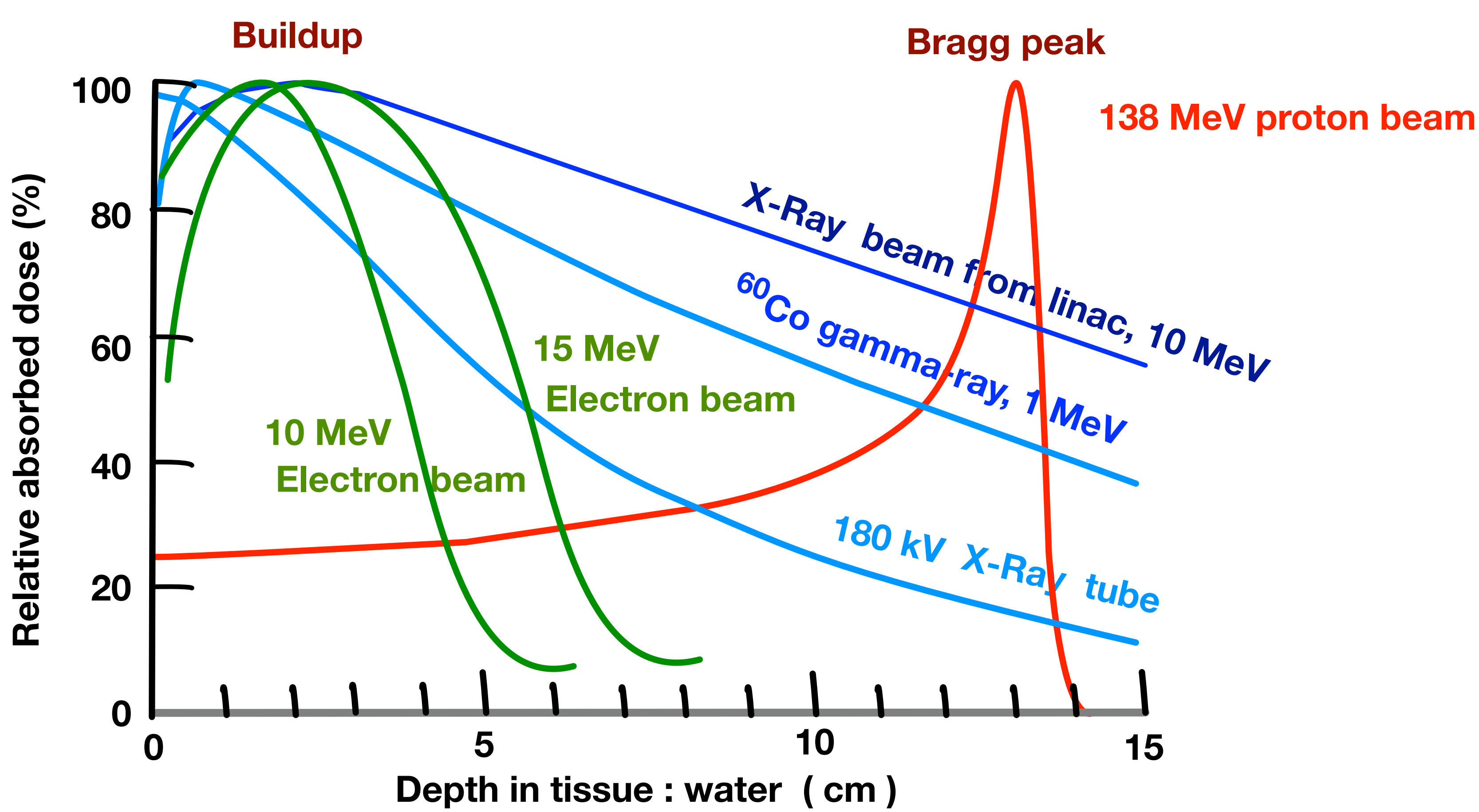

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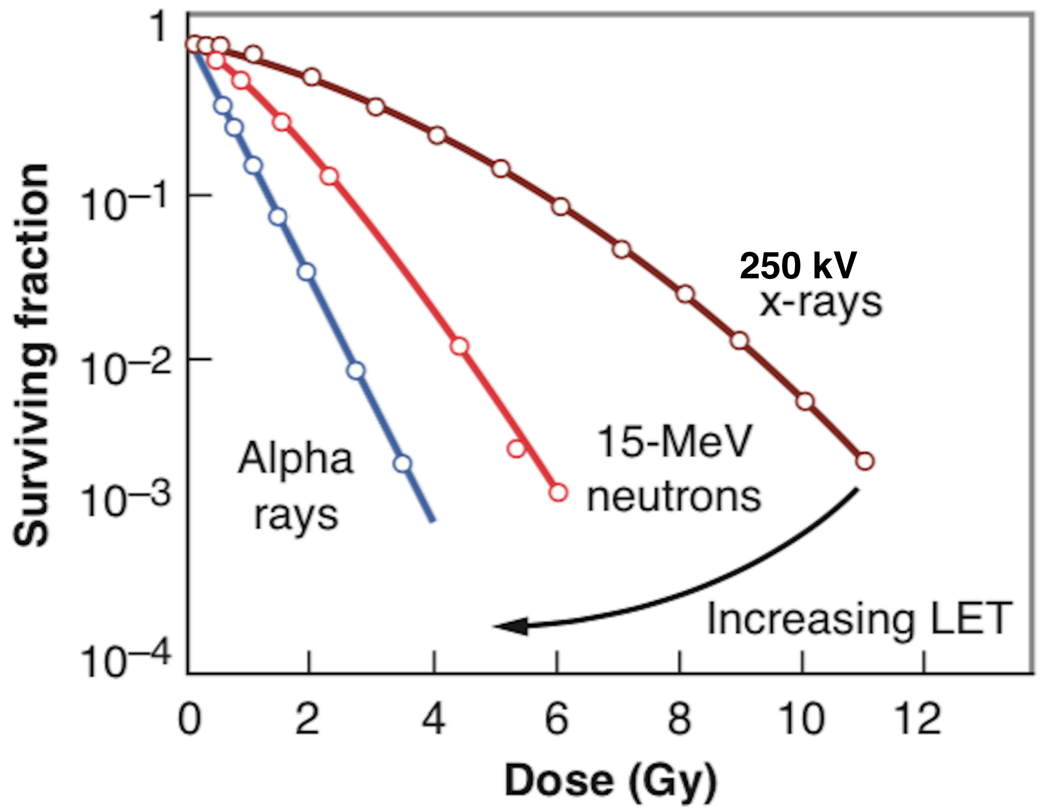
Low energy electron (< 100 MeV) beam is applicable to shallow tumors.

The Cancer treatment by the Electron/X-ray beams



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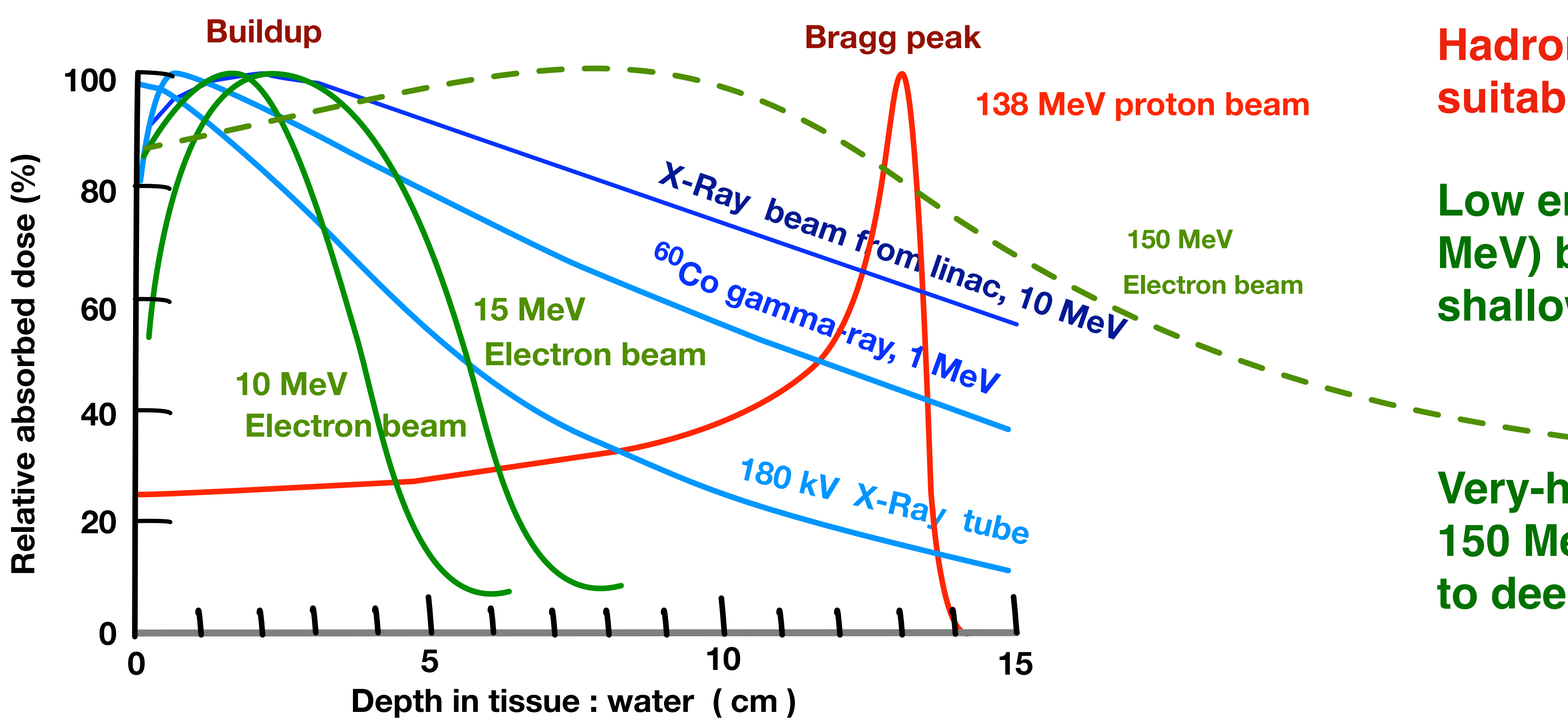


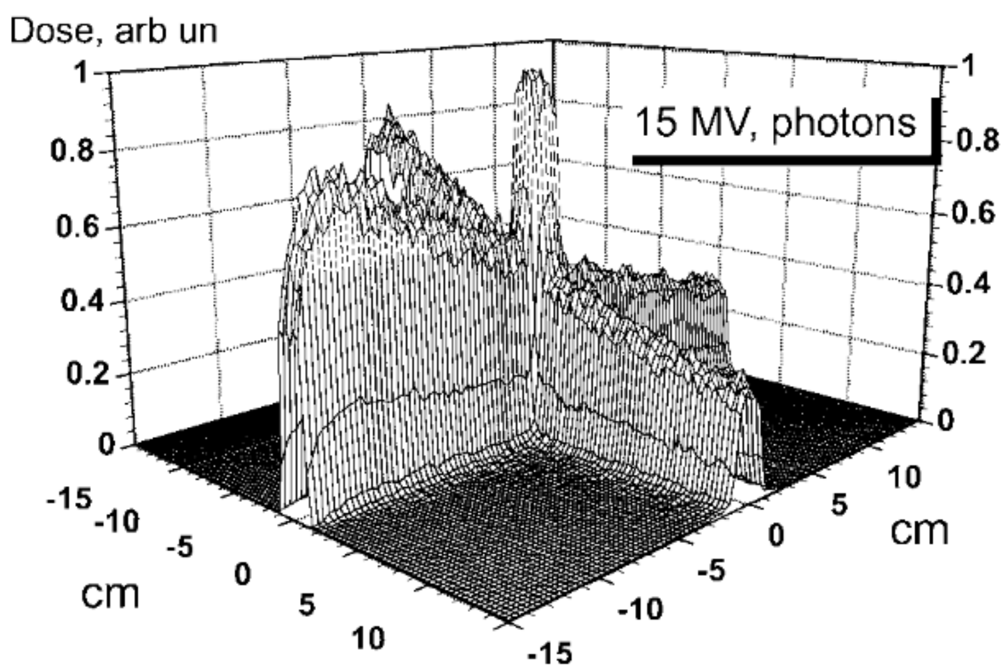
Hadron beam is the most suitable.

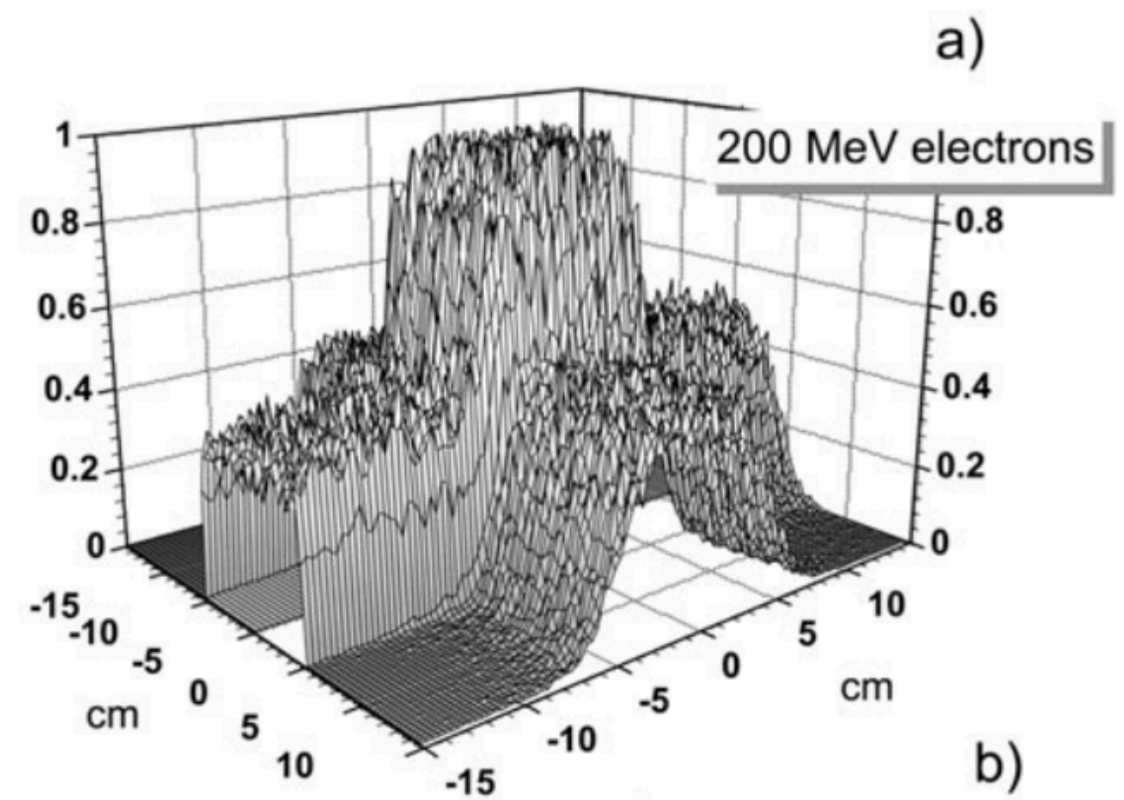
Low energy electron (< 100 MeV) beam is applicable to shallow tumors.

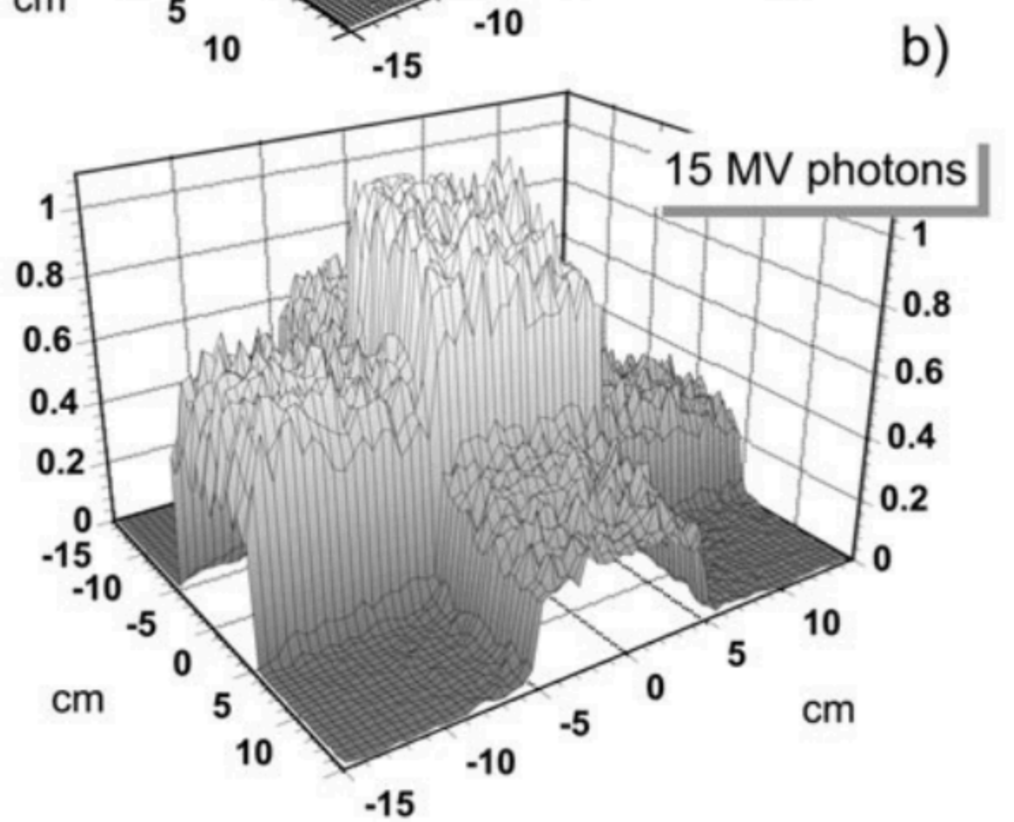
Very-high energy electron (> 150 MeV) beam is applicable to deep tumors.

Very High Energy Electron Therapy (VHEET) > 100 MeV,

C Yeboah, et al., "Optimization of intensity-modulated very high energy (50–250 MeV) electron therapy" Phys. Med. Biol. **47,** 1285–1301 (2002)
C DesRosiers , et al., "150–250 MeV electron beams in radiation therapy" Phys. Med. Biol. **45,** 1781–1805 (2000).







VHEE forms a concentrated dose-area.

Problem might be a beam dump of the transmitted electron.

The beam direction moves.

; Gamma ray emission in treatment room.

Summary: Radiation treatment

E-beam surgery of deep cancer from outside the body is hard because of the gamma-ray from the beam dump.

Cancer on a body surface (skin cancer, laryngeal cancer , etc) might be therapeutic objective.

An accelerator on an endoscope for alimentary canal. (Seems to be suitable for DLA. Required dose rate would be satisfied by operating DLA at a few MHz)

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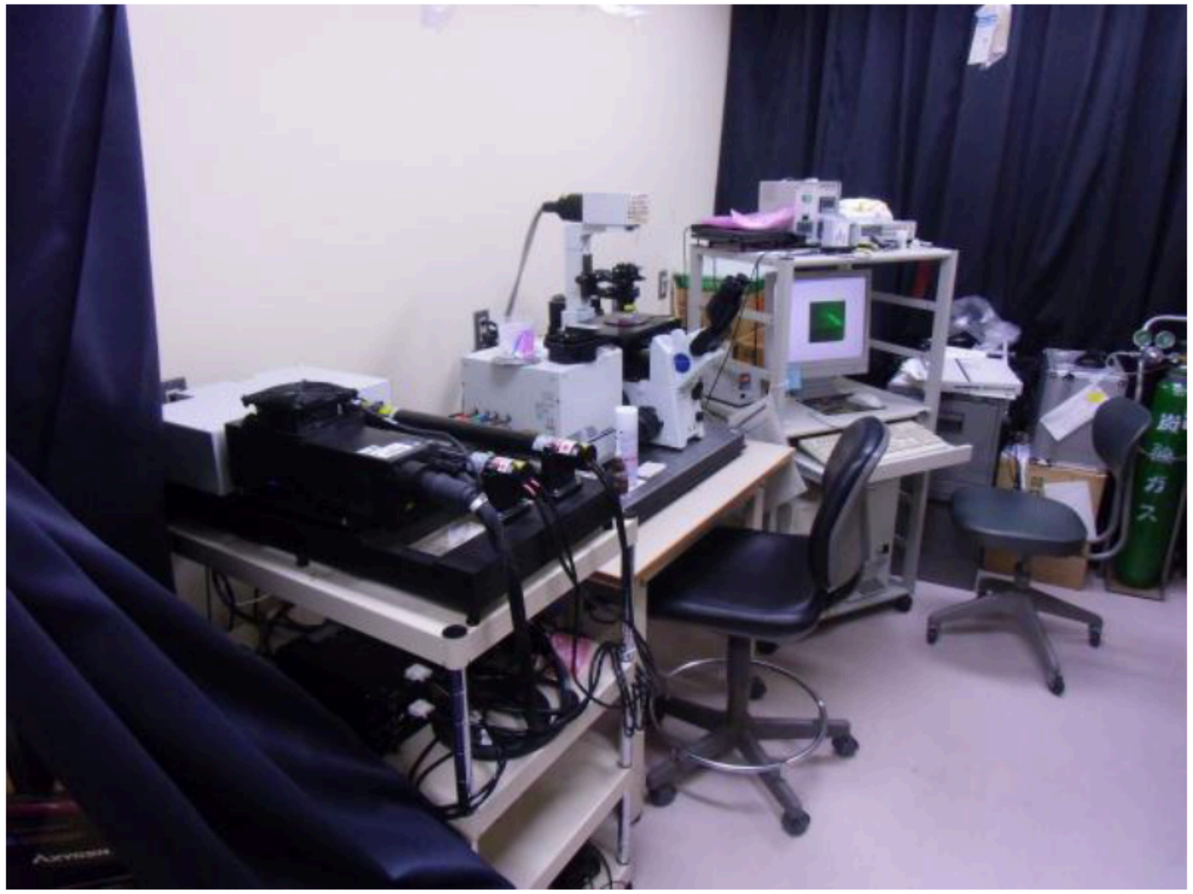
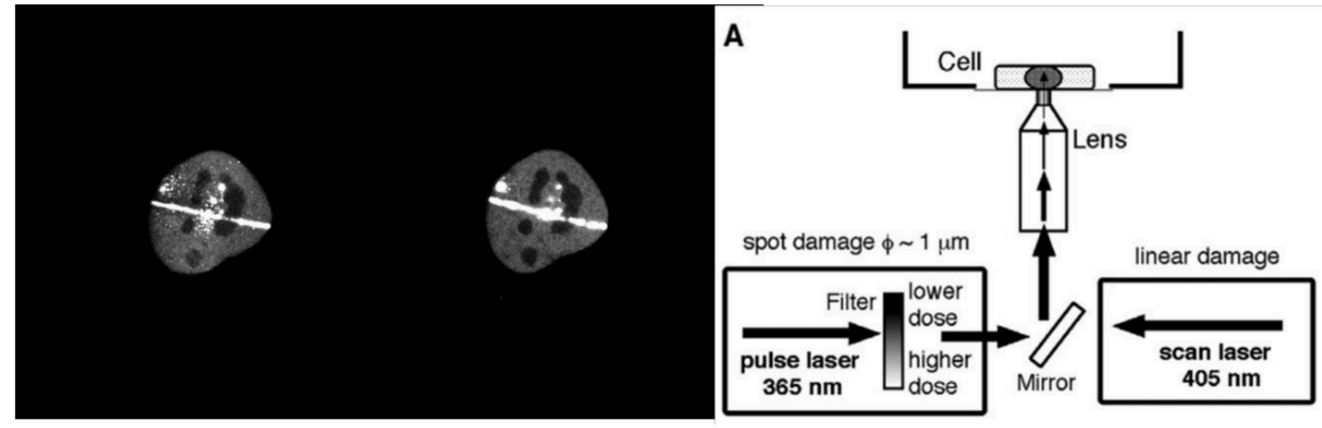
Observation of the DNA damage/repair by using laser and microscopy





(a) 20 sec after irradiation (b) 200 sec (c) Irradiation and scanning system

Figure 9 On-line observation of DNA damage/repair by UV laser. Irradiation is done by 405nm laser 30 scans with photosensitizer, and the scanning is done by 488nm laser, by 20sec interval x10 times, and U2OS (human osteosarcoma) cells transfected by GFP-XRCC1 (Single strand break marker) are used.

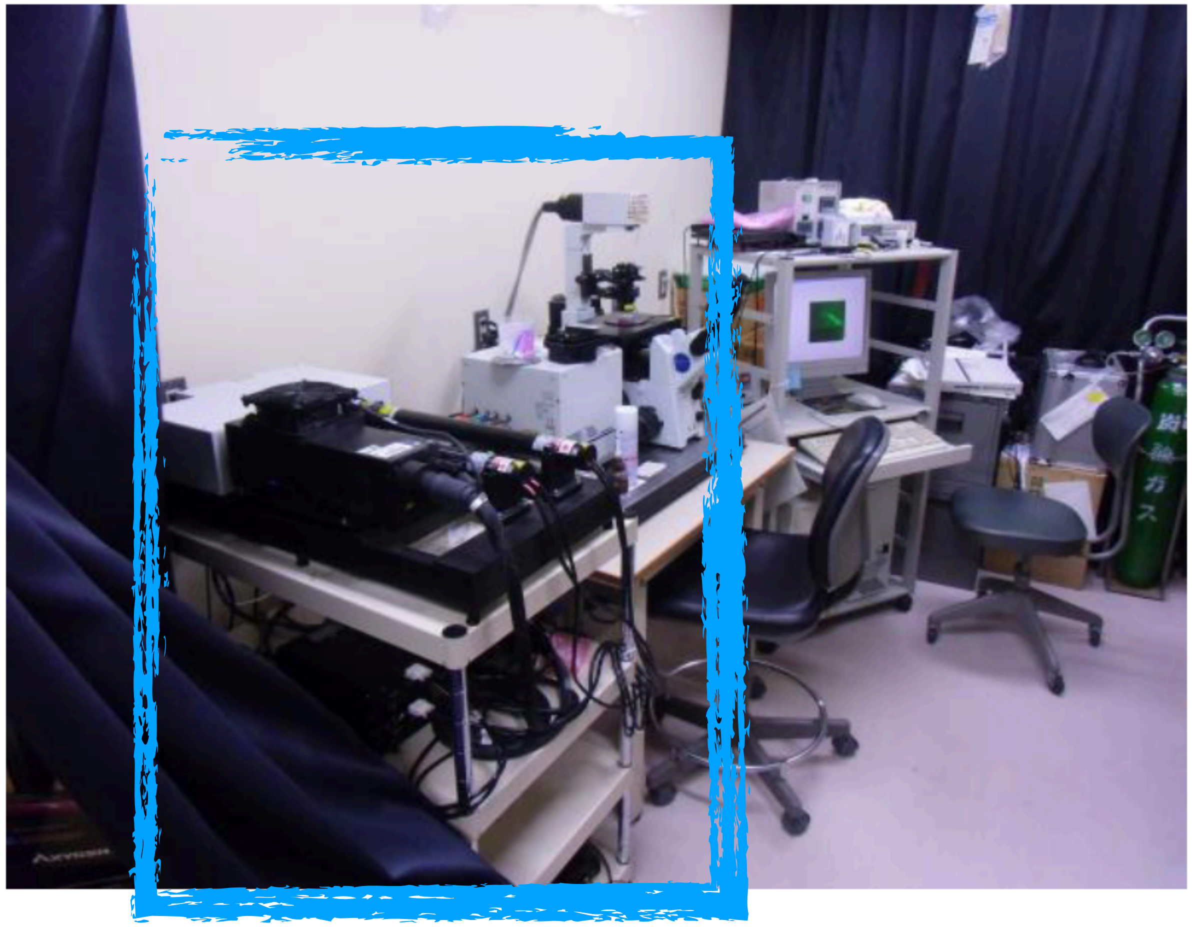
Figure 8 On-line observation system of DNA damage/repair by UV laser and optical microscopy (Prof.Akira Yasui, Tohoku University)

Uesaka, et al., IOP Conf. Series: Materials Science and Engineering **79** (2015) 012015.

Photosensitized regent is used to induce free radical-induced damage to DNA .

Different from the actual process of the DNA damage.

Observation of the DNA damage/repair by using laser and microscopy



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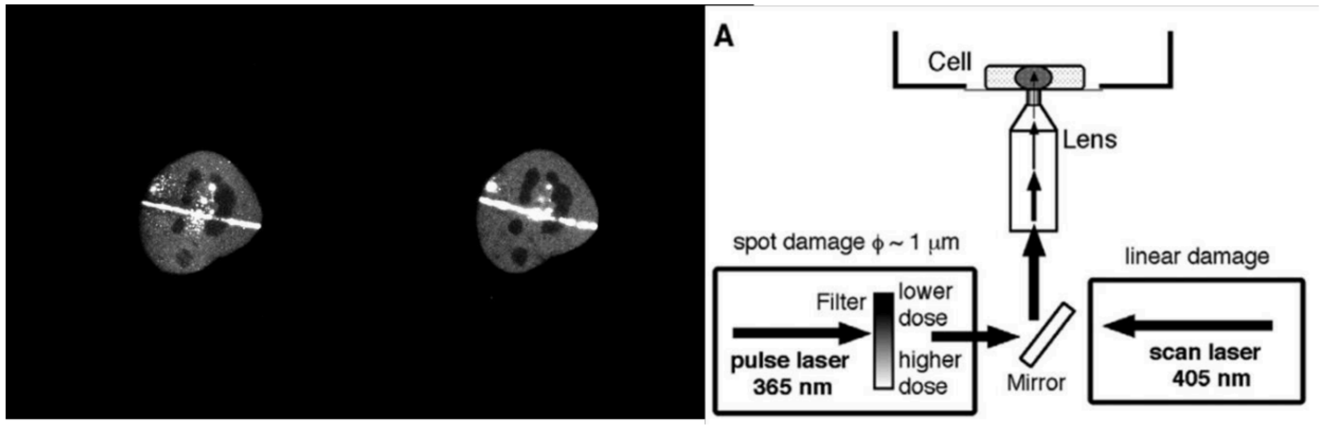

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Different from the actual process of the DNA damage.

Is it possible to apply DLA to the radiobiology research?

The DLA is one of the promising device to deliver the microbeam in a small scale lab.

Required beam parameters

K.Koyama, et al., J. Phys. B: At. Mol. Opt. Phys, **47,** 234005 (2014) .

Beam energy;

Lower limit ; **Blurring due to the multiple scattering**
$\leq$ Spatial resolution

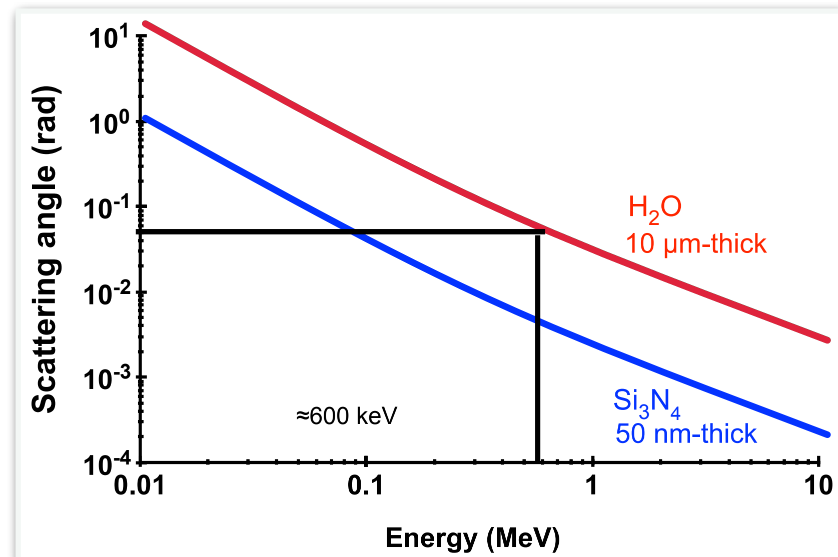
Scattering angle $\theta_0 \leq$ **0.05 rad**

>0.5 MeV higher energy is better

$$\theta_0 = \frac{13.6\,[\mathrm{MeV}]}{\beta c p}\sqrt{x/X_0}\,[1 + 0.038\ln(x/X_0)]\,,$$

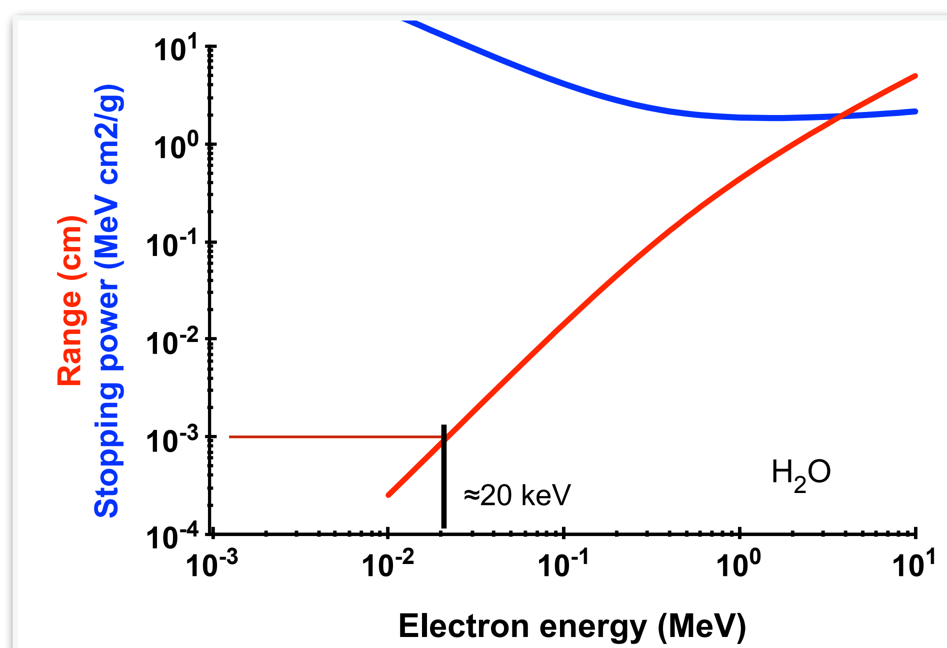
$$X_0 = \frac{716.4\,[\mathrm{g\ cm^{-2}}]\,A}{Z\,(Z+1)\ln\left(287/\sqrt{Z}\right)}.$$

G. R. Lynch and O. I. Dahl, Nucl. Instrum. Methods B **58**, 6 (1991).
Eidelman S et al.(Particle Data Group), Phys. Lett. B **592** 1 (2004).



Precise analysis with EGS5 is ongoing to estimate the spatial resolution.

Upper limit ; **Regulation (Radiation safety)**
< 1 MeV

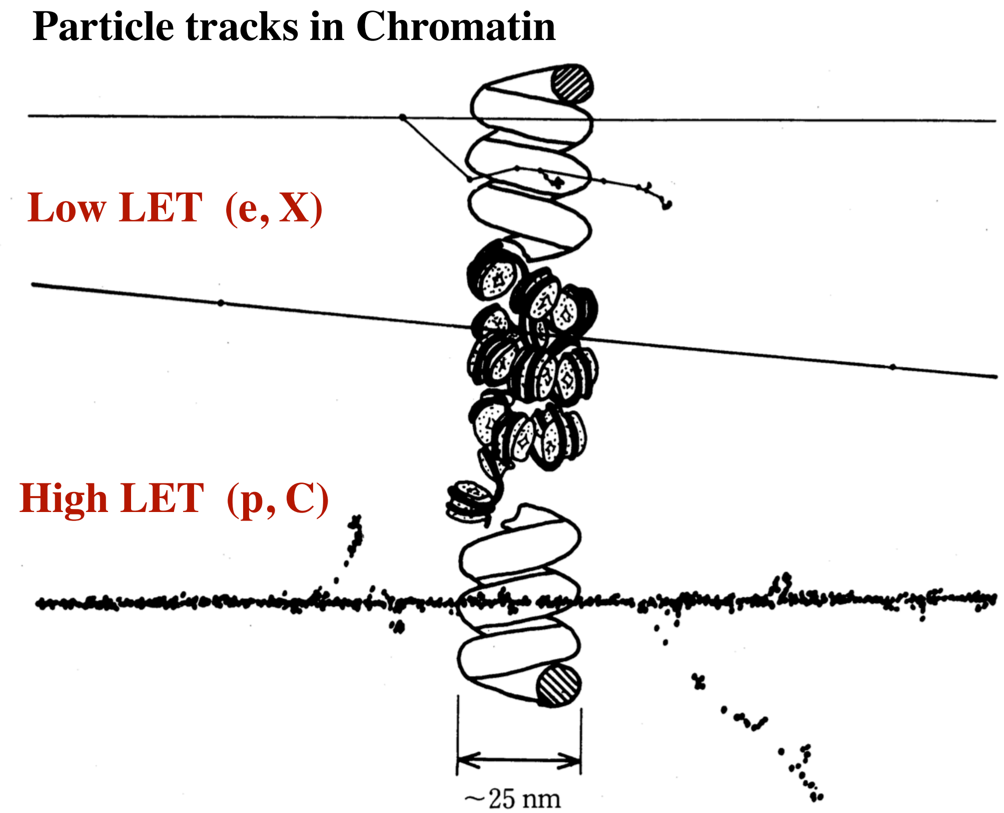


Beam size;

Beam size < 1 μm ≈ Spatial resolution

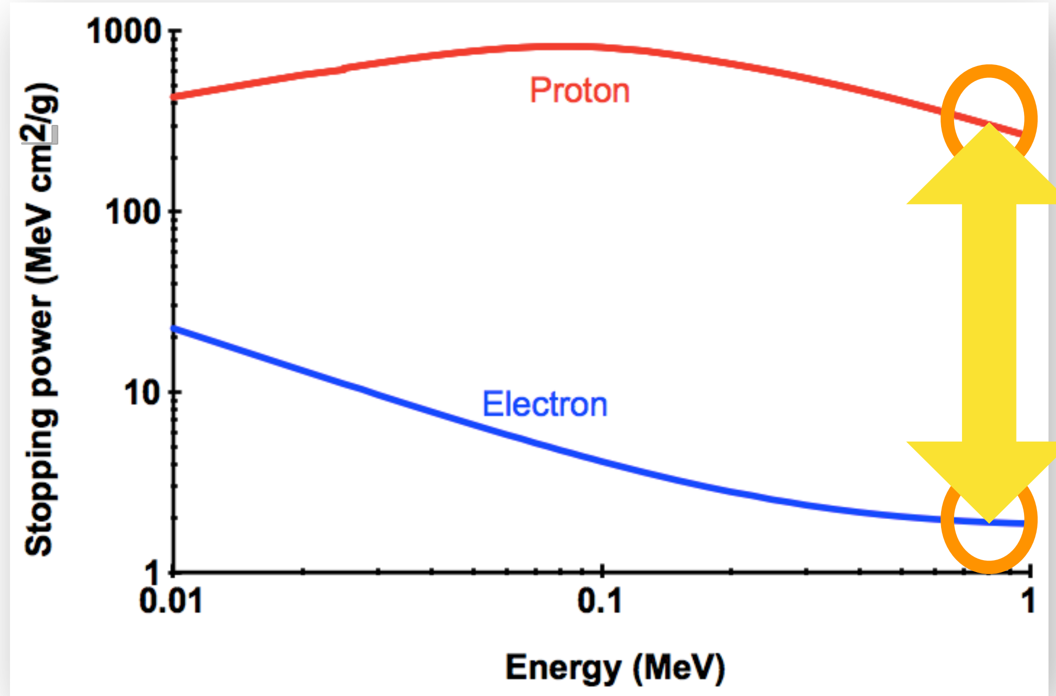
What is the required number of electrons?

Single proton can cause the DNA double-strand break (DSB) by the dense ionization localized within about 5 nm from the proton track.
It is hard to make the double strand break by the electron.



In order to make the DSB, the radiation dose of 25 mGy - 150 mGy is required.

At least, 10^2 electrons/(μm^2 min) are required for the experiment.

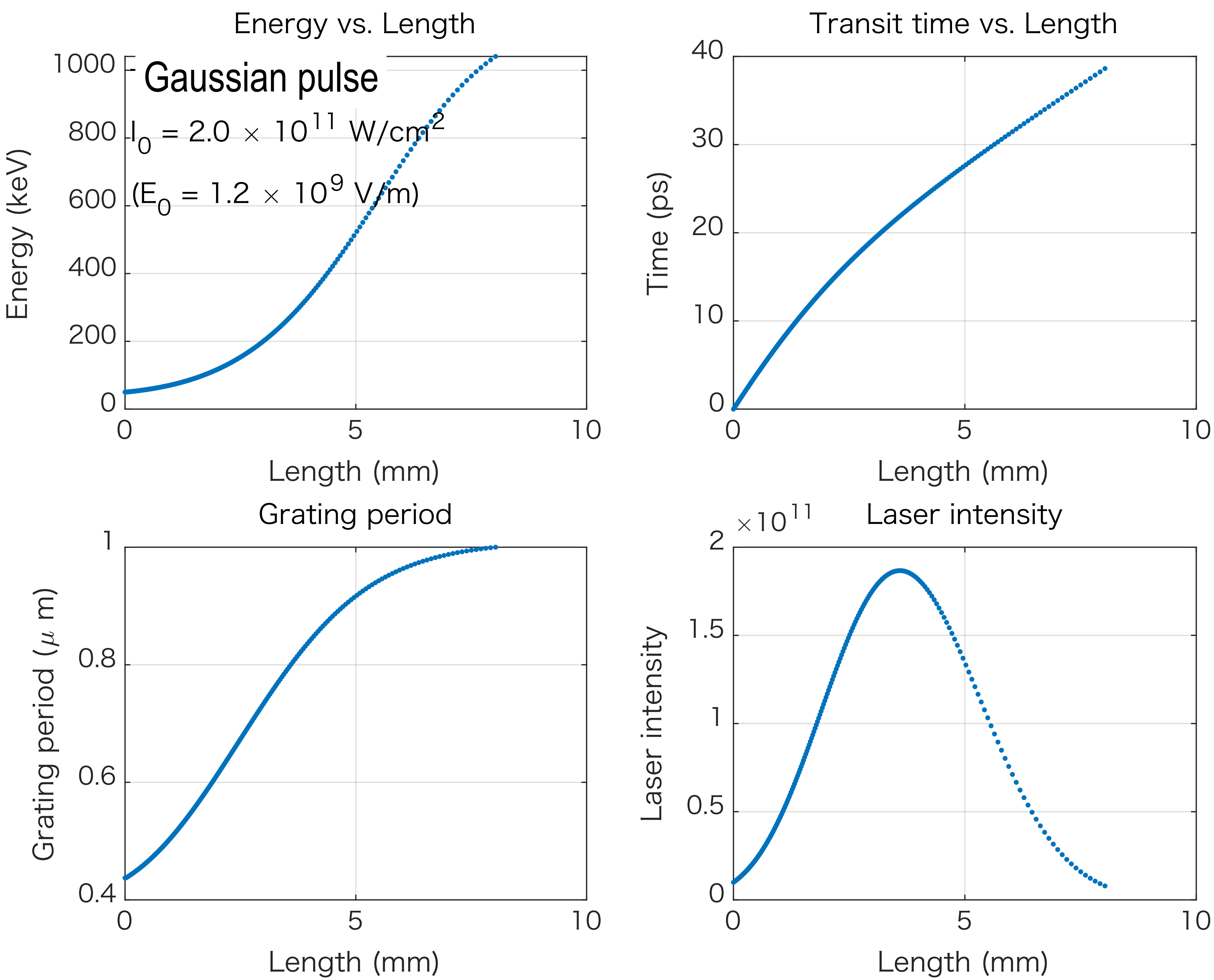


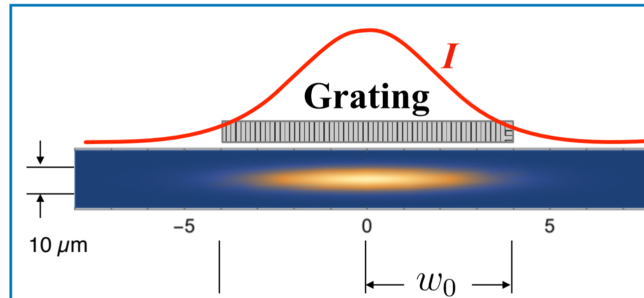
SINGLE PULSE

Acceleration by Gaussian pulse laser

$$I = I_0 \exp\left(-2\frac{x^2}{w_0^2} - \frac{t^2}{t_0^2}\right),$$
$$E = E_0 \exp\left(-\frac{x^2}{w_0^2} - \frac{t^2}{t_0^2}\right)$$

$w_0 = 4$ mm,
$t_0 = 18$ ps
injected at $-w_0, -t_0$





LASER

FWHM of focus
4.7 mm x 0.006 mm

FWHM of pulse duration
30 ps

Laser power
60 MW

Laser energy
1.8mJ/pulse

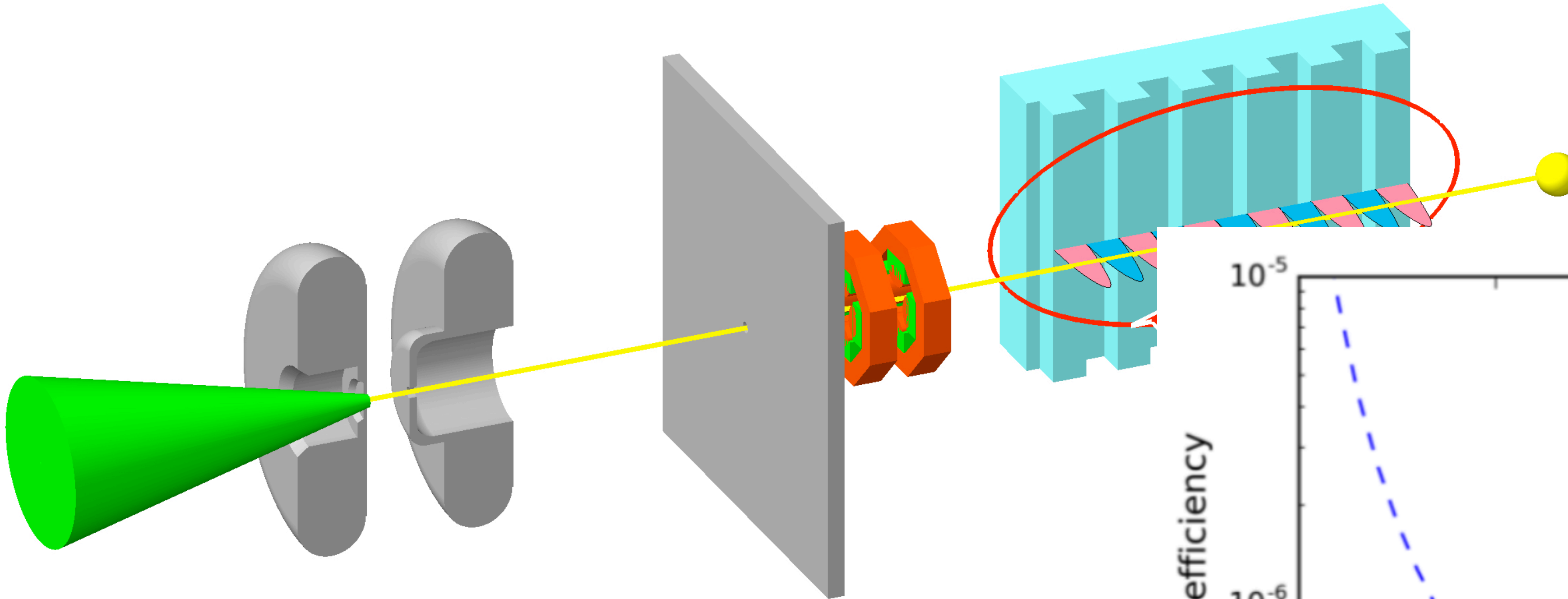
107 steps of different periods

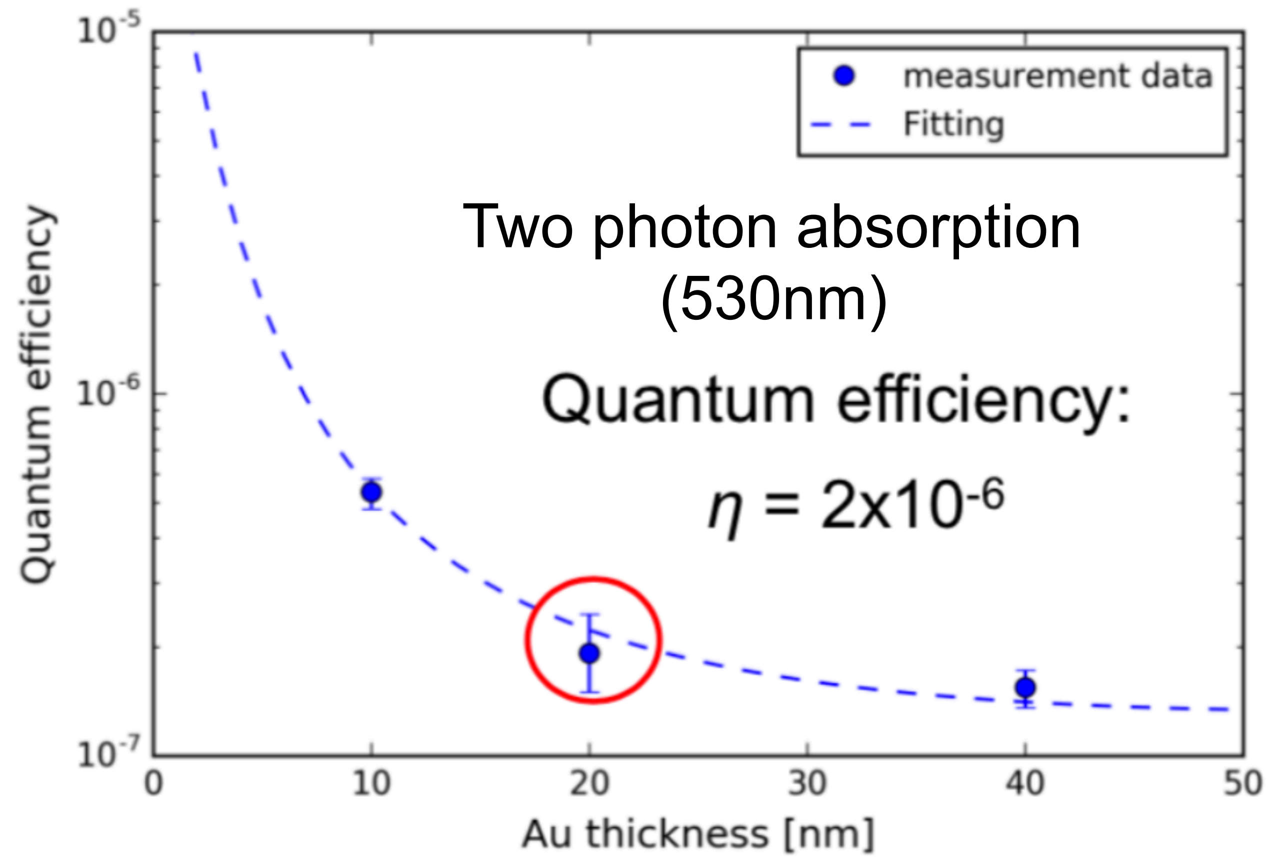
Output energy 1.01 MeV

Acceleration length 7.7mm

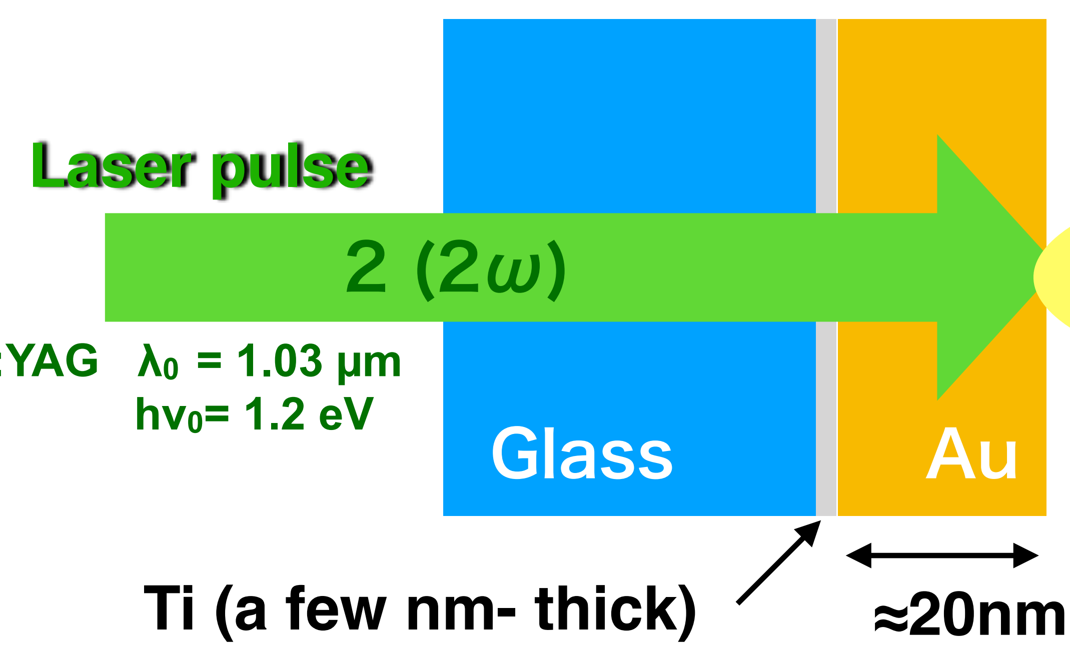
Acceleration time 37.5 ps

Electron current estimation





Courtesy of T. Shibuya



Yb:YAG λ_0 = 1.03 µm
$h\nu_0$= 1.2 eV

$$Q = e\frac{\eta_{qe}E_L}{h\nu}$$

$e = 1.6 \times 10^{-19}$ C

η_{qe} : **Quantum efficiency**

E_L : **Laser energy**

$h\nu$: **Photon energy**

Electron current estimation

Child-Langmuir limit

$$J_{CL} = \frac{4\varepsilon_0}{9}\sqrt{\frac{2e}{m_e}}\frac{V^{3/2}}{d^2}$$

$$= 180\ \mathrm{A/cm^2} \quad @\ d = 3.8\mathrm{mm},\ V = 50\mathrm{kV}$$

$$Q_{CL} = 1.4\ \mathrm{fC} \quad @\ \tau = 10\mathrm{ps},\ 2r_s = 10\mu\mathrm{m}$$

Charge of photoelectron

$$Q\,[\mathrm{C}] = 9 \times 10^{-7} E_L\,[\mathrm{J}] \quad @\ h\nu = 2.34\ \mathrm{eV}$$

$$\eta_{qe} = 2 \times 10^{-6}$$

Laser pulse

$$E_L = 1.6\ \mathrm{nJ}$$

$$P_L = 160\ \mathrm{W}$$

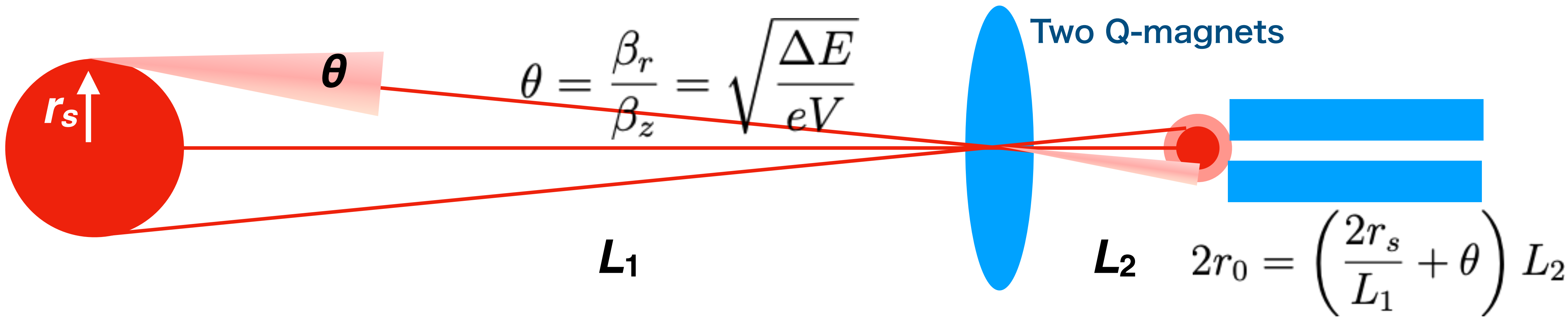
$$I_L = 2 \times 10^8\ \mathrm{W/cm^2}$$

Normalized emittance

$$\epsilon_n = \pi\beta\gamma r_s\theta \approx \pi r_s\sqrt{2\Delta E/m_e c^2}$$

$$\Delta E = (h\nu - \Phi_w)/3,\ \theta \approx \sqrt{\Delta E/eV}$$

Number of electrons and Beam size of injected beam



The cross section of the e-beam at the DLA entrance is a function of the source size r_s and the beam divergence angle θ.

$$2r_0 = \left(\frac{2r_s}{L_1} + \theta\right) L_2$$

$$\begin{aligned} \Delta E &= 0.2 \text{ eV} \sim 0.7 \text{ eV} \\ \theta &= 4\ \mu\text{rad} \sim 14\ \mu\text{rad} \\ \epsilon_n &\approx (1.4 \sim 2.6) \times 10^{-2} \text{ mm} - \text{mrad} \end{aligned}$$

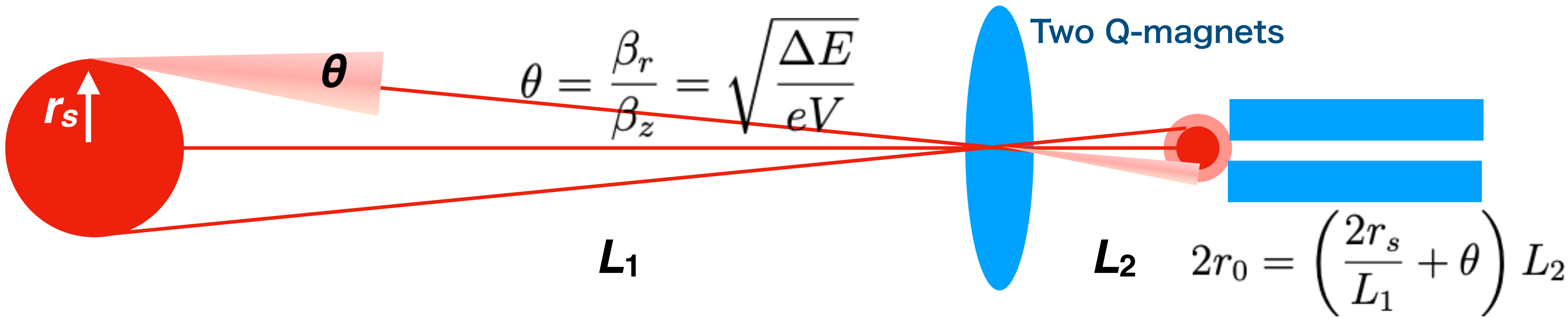
$$2r_0 \approx \boxed{0.3\ \mu\text{m} \sim 0.8\ \mu\text{m}} \ @\ L_1 = 500\text{mm},\ \ L_2 = 50\text{mm}$$

Aberrations

Due to the geometrical loss of electrons (aperture ratio, nonparallel), the passing ratio of electron is 40 % ~ 15%.

$$Q \approx 0.56 \text{ fC} \sim 0.21 \text{ fC} \quad (3500\ e \sim 1300\ e)$$

Number of electrons and Beam size of injected beam



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Supposing the usable ratio of electrons is 1% for the does experiment, **the required number of 10^2 el/(μm^2 min) might be achieved by 3 to 8 shots.**

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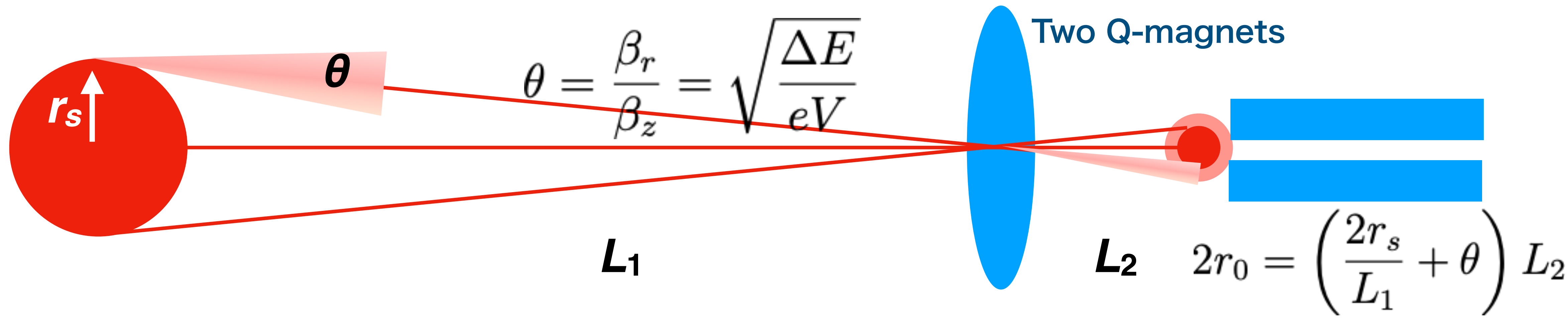

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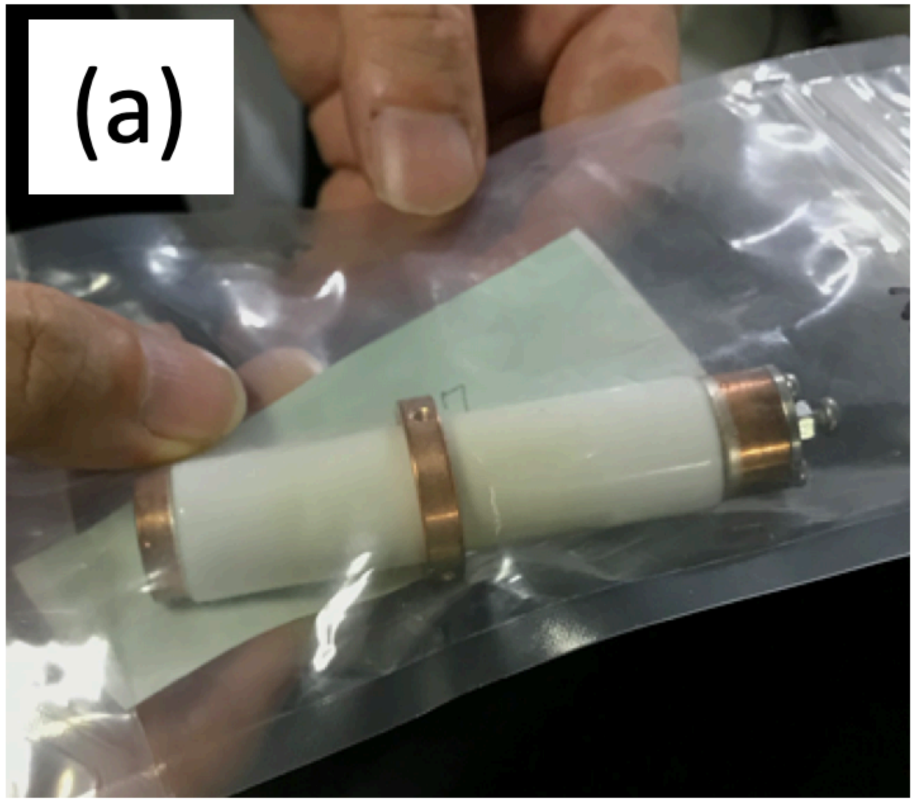
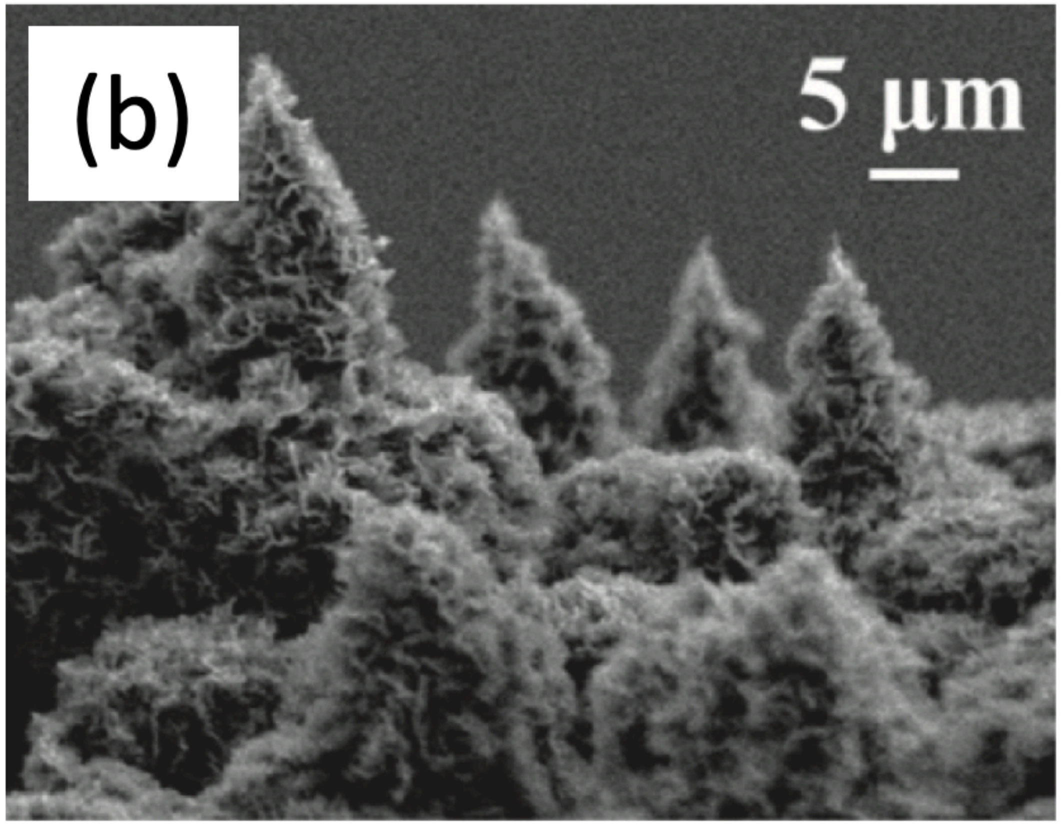
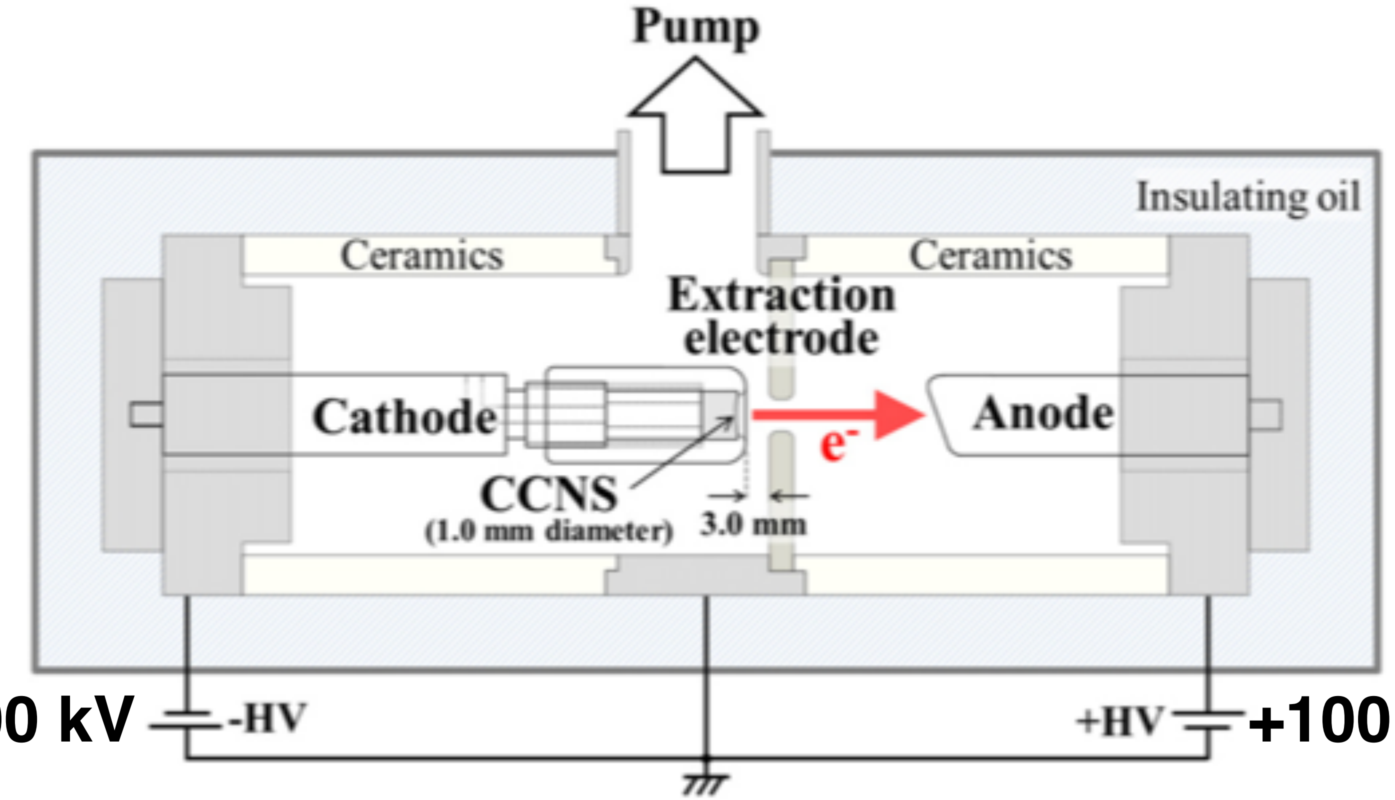
To downsize the electron gun



200kV X-Ray tube



Coniferous Carbon-Nano Structure (CCNS)



-100 kV

+100 kV

Courtesy of R. Suzuki @AIST

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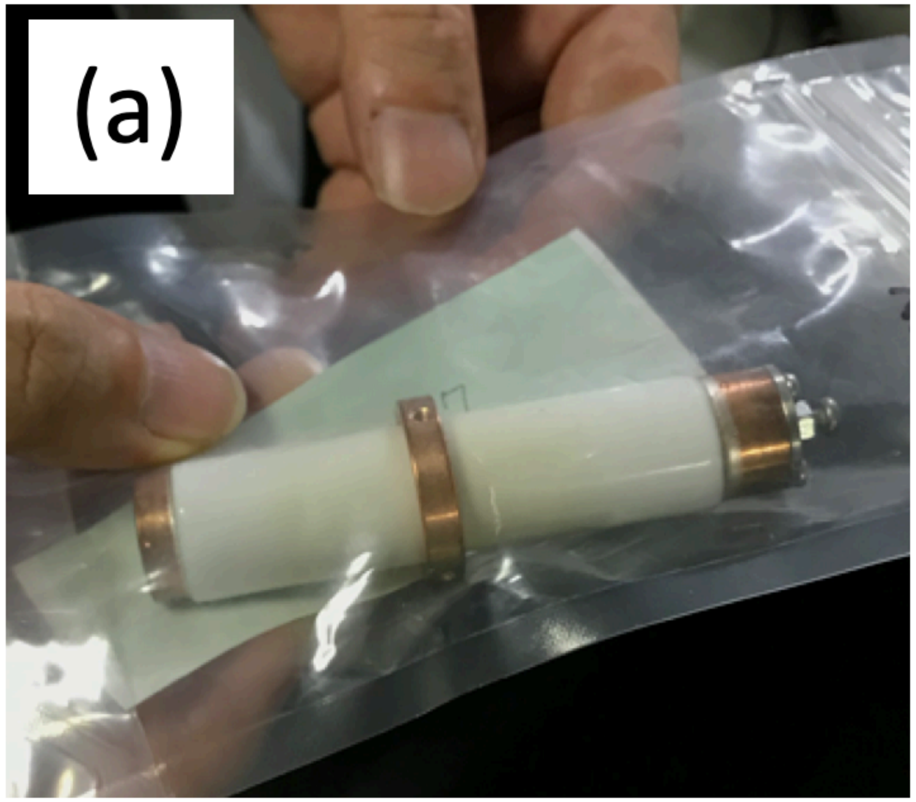

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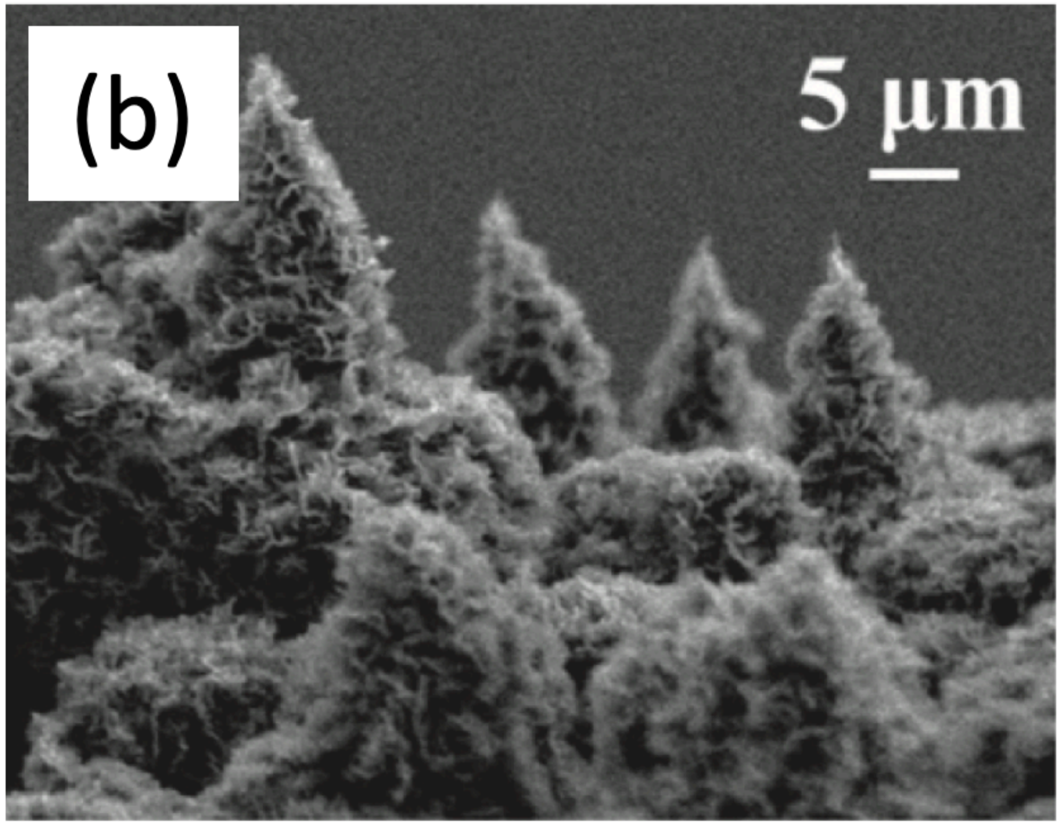
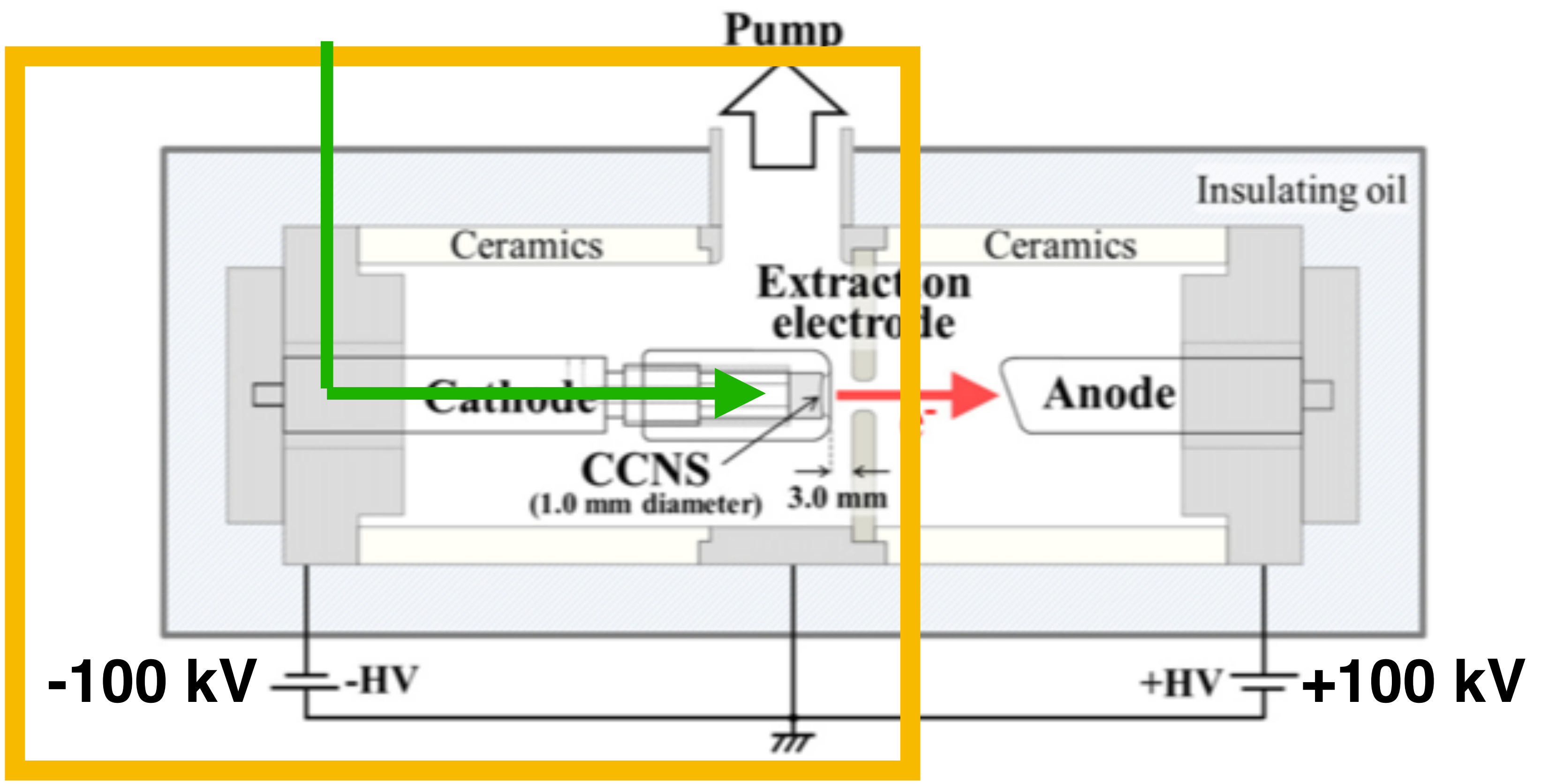


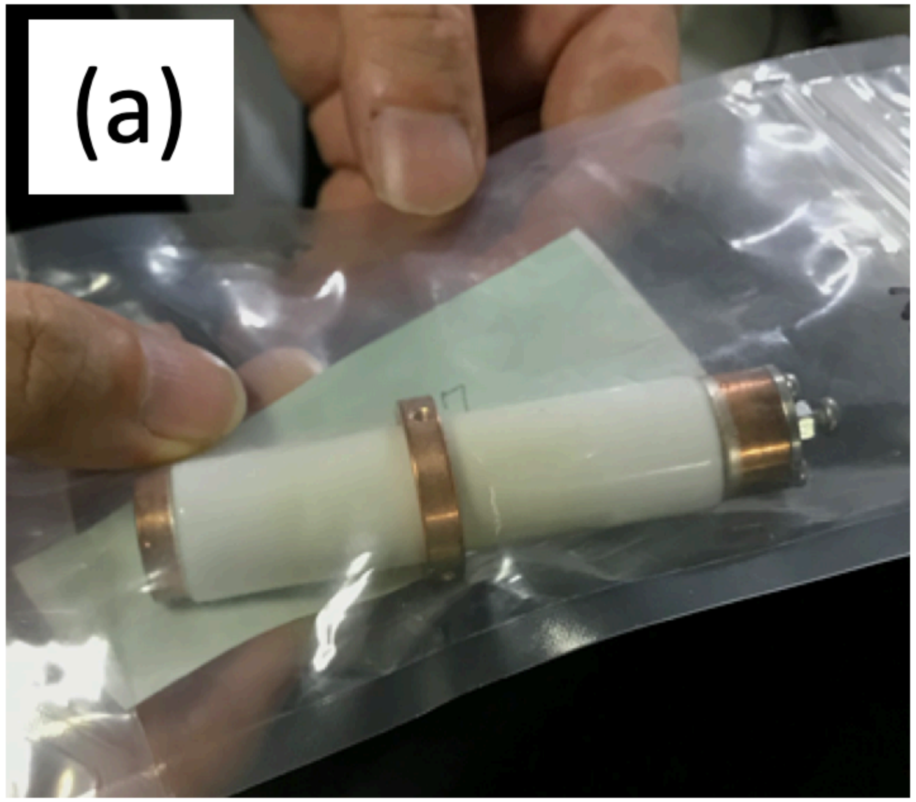
Coniferous Carbon-Nano Structure (CCNS)

An extraction voltage of 100 kV is possible in a 5-cm long e-gun.

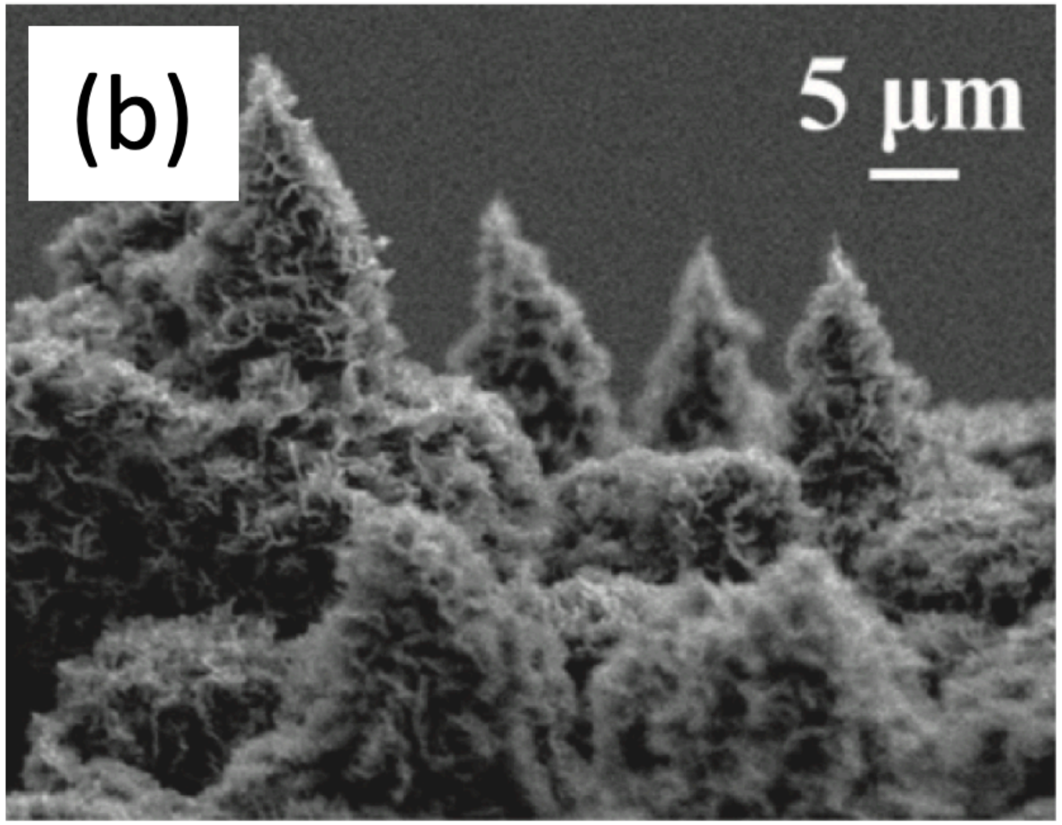


Courtesy of R. Suzuki @AIST

To downsize the electron gun



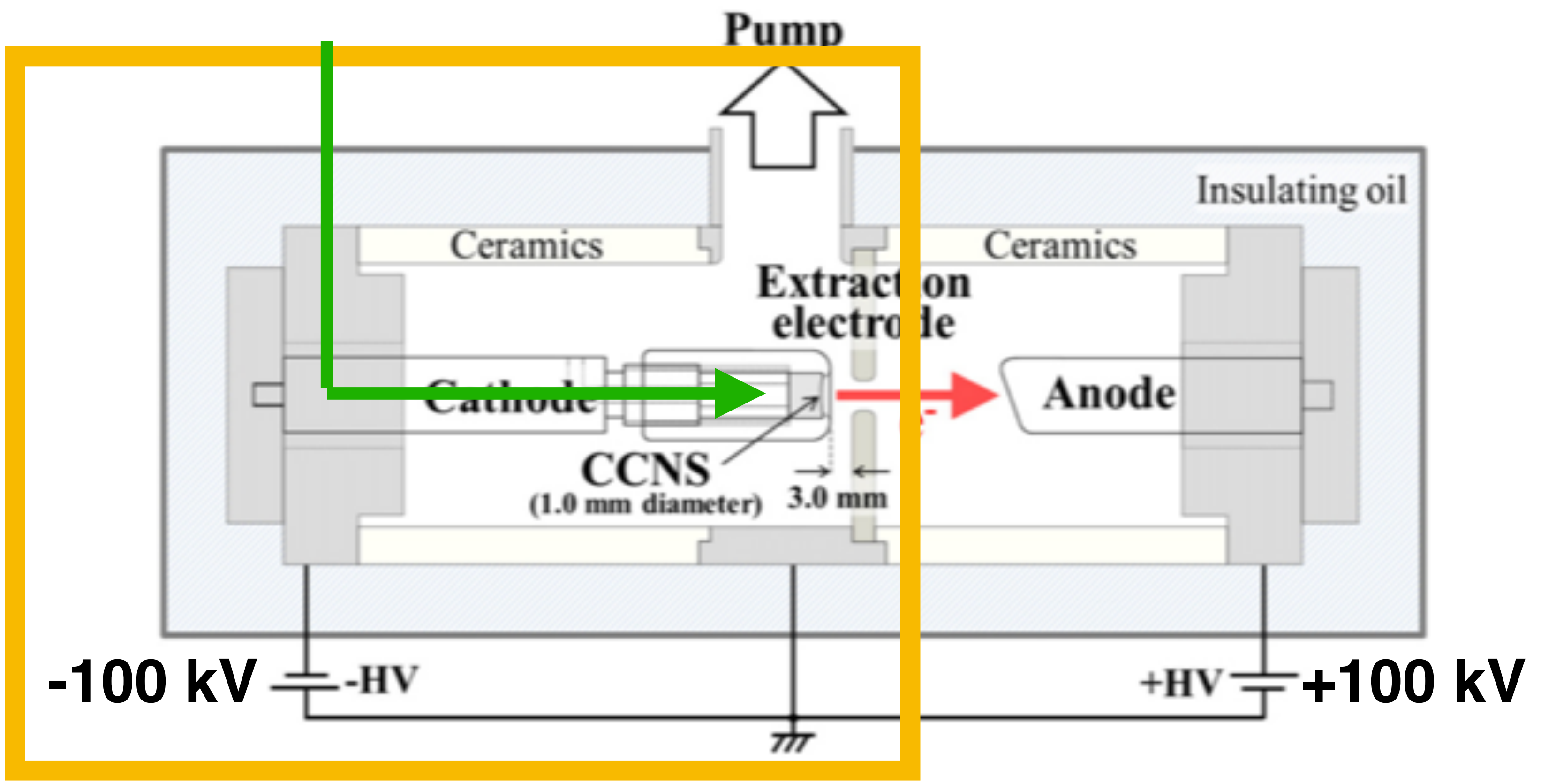
200kV X-Ray tube



Coniferous Carbon-Nano Structure (CCNS)

An extraction voltage of 100 kV is possible in a 5-cm long e-gun.

Photoelectric gun might be better to control an emission area.

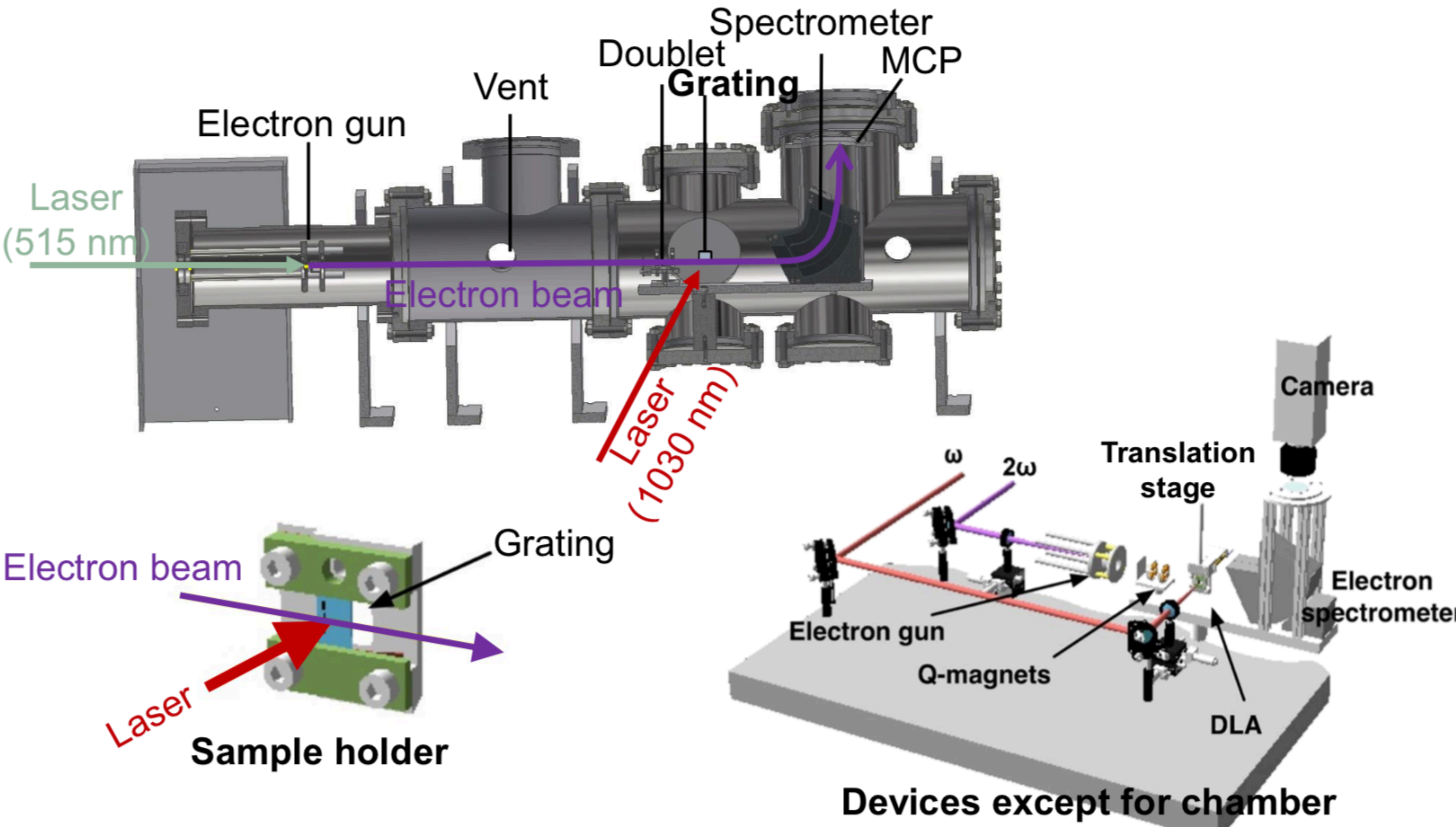


Courtesy of R. Suzuki @AIST

Courtesy of Z. Chen

DLA structures

- For accommodating those devices for the experiment.



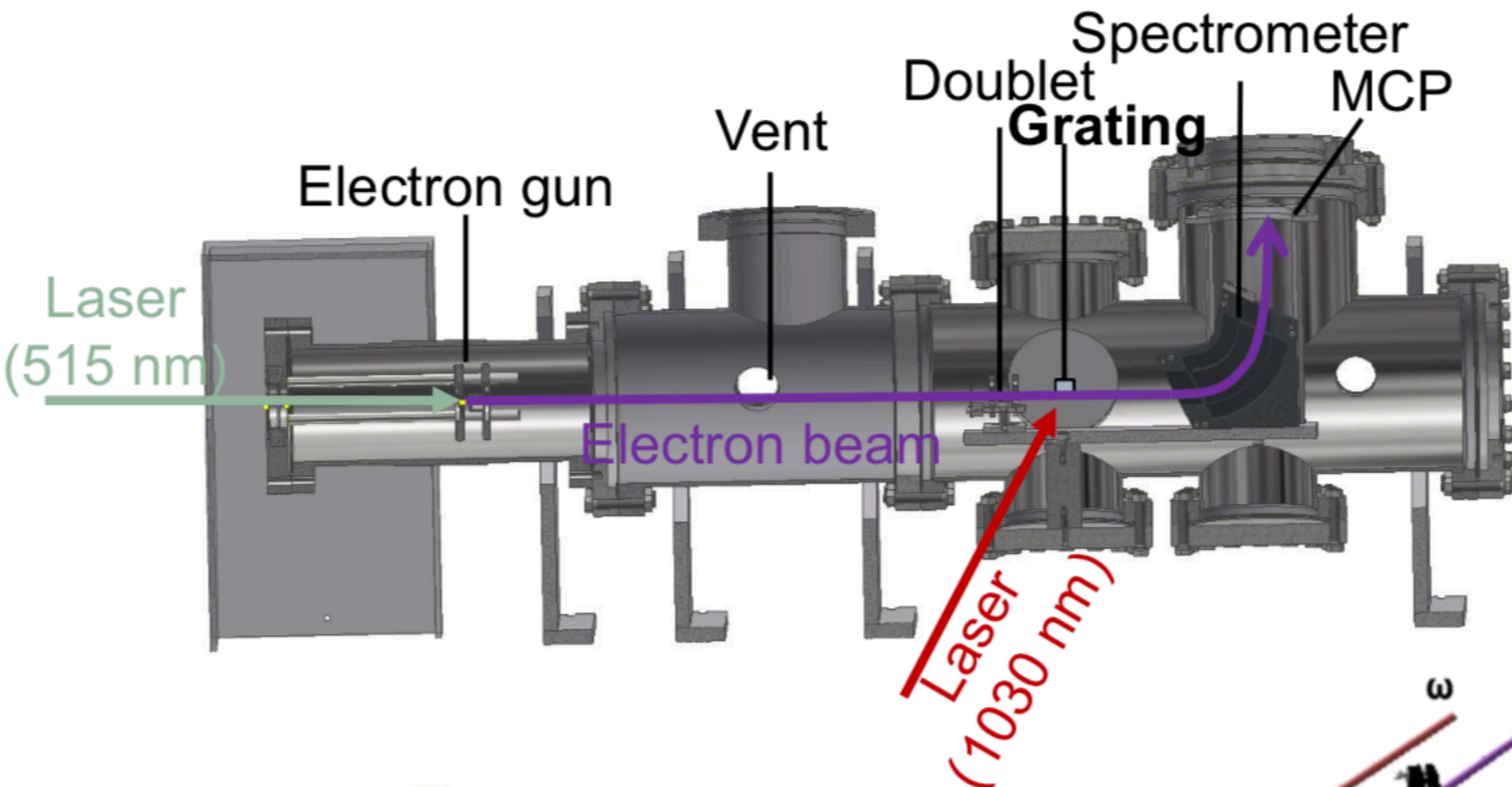
Sample holder

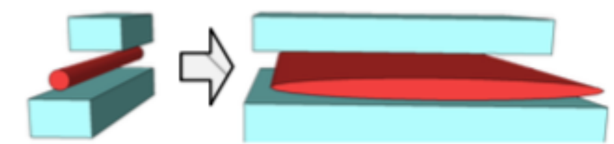
Devices except for chamber

Courtesy of Z. Chen

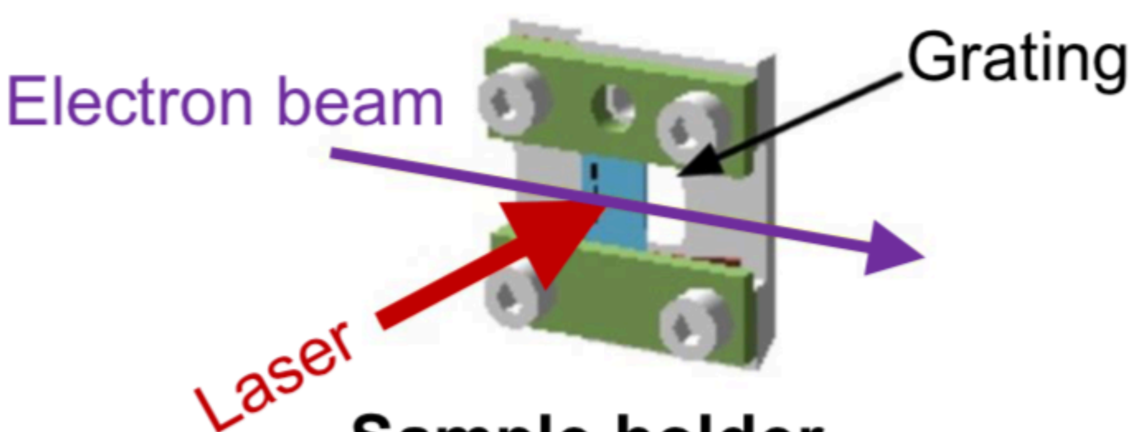
DLA structures

- For accommodating those devices for the experiment.

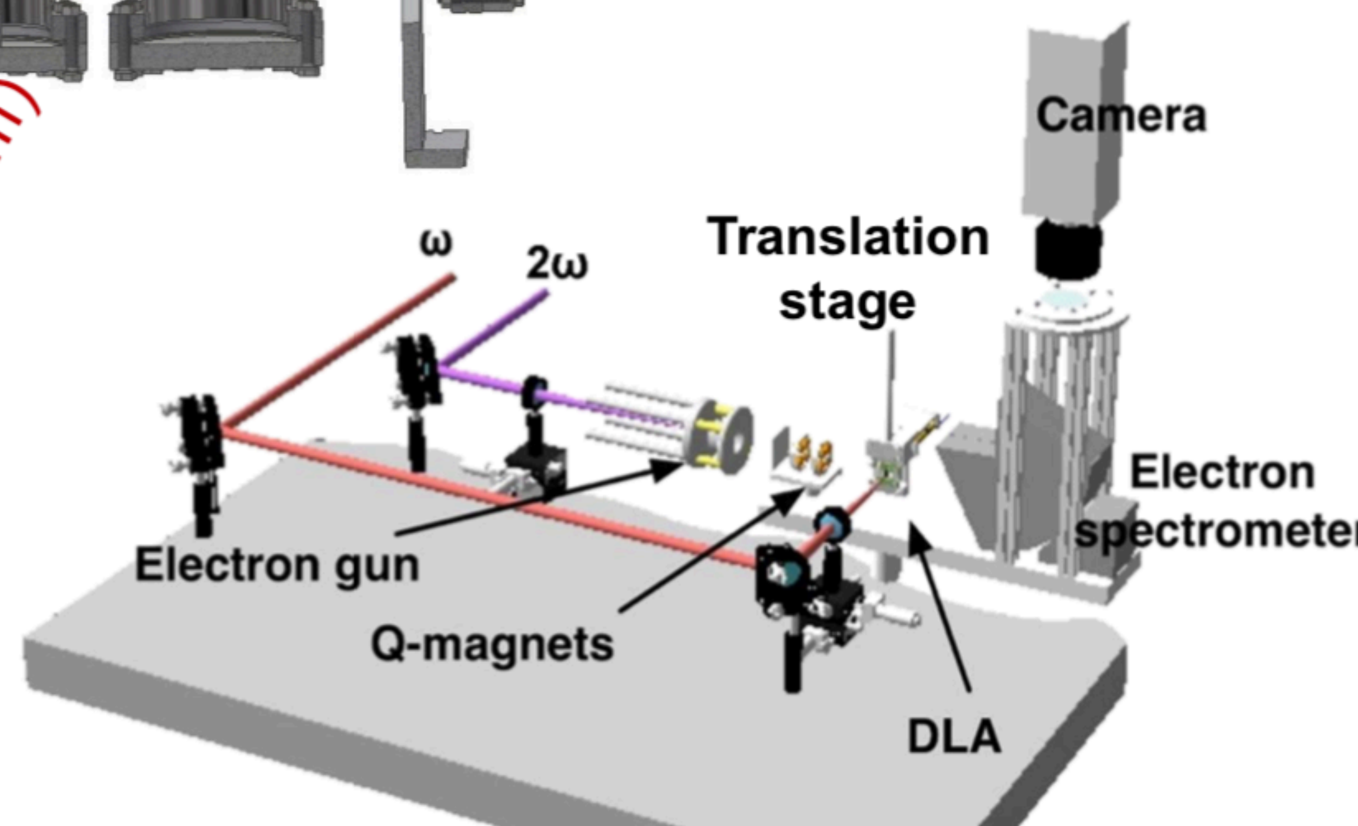




Q-magnet will be used for making a laminar beam



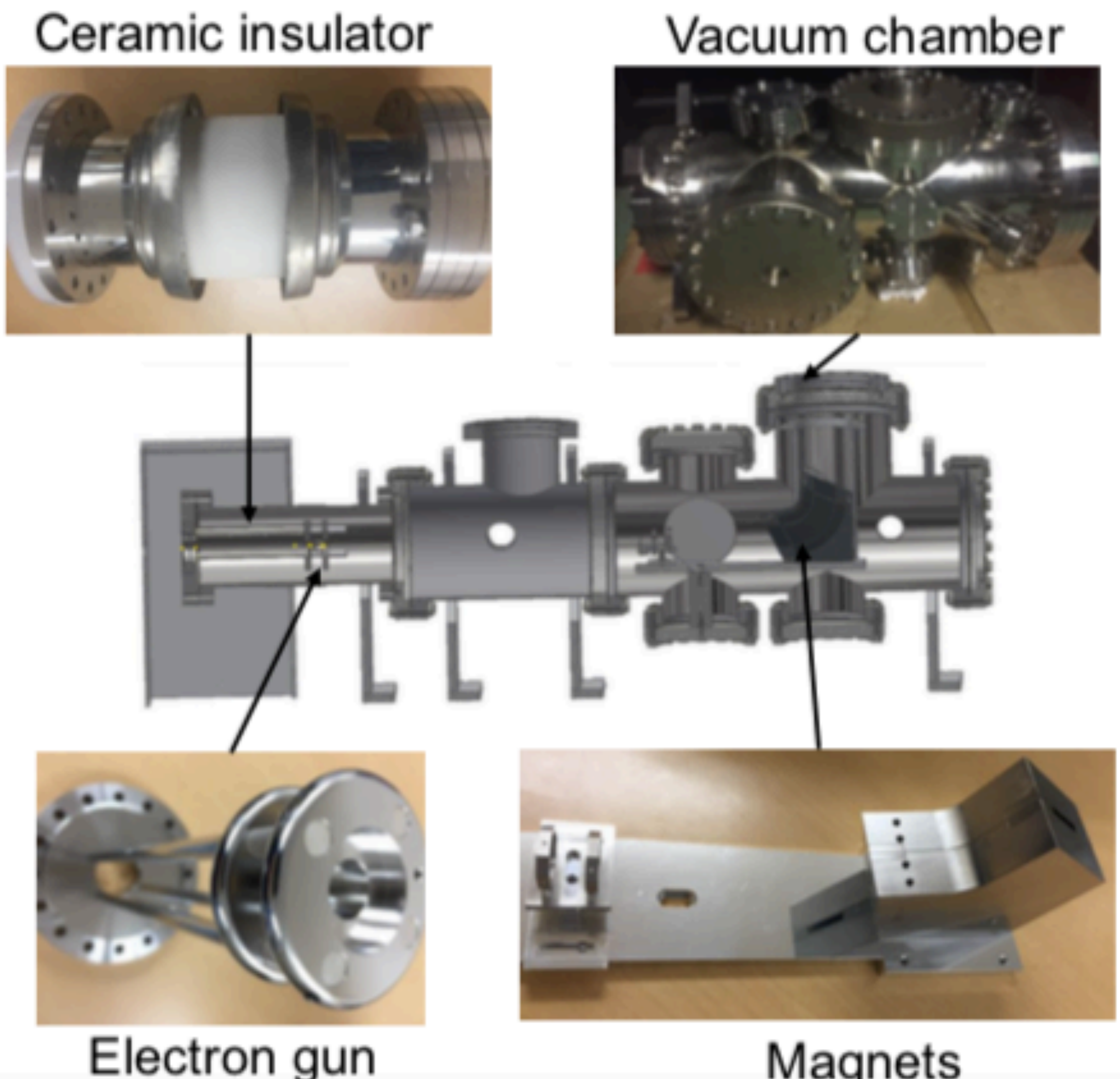
Sample holder



Devices except for chamber

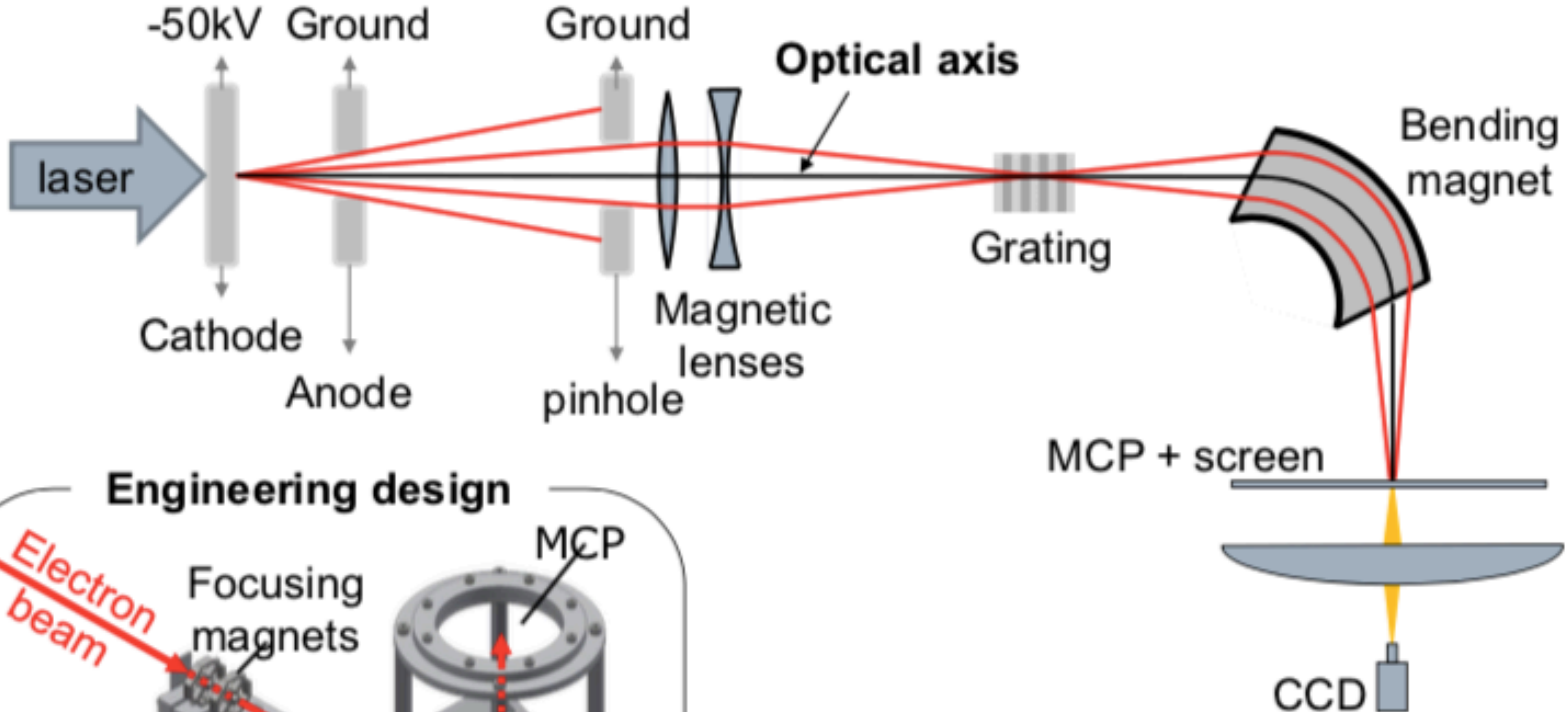
Fabrication of the designed devices

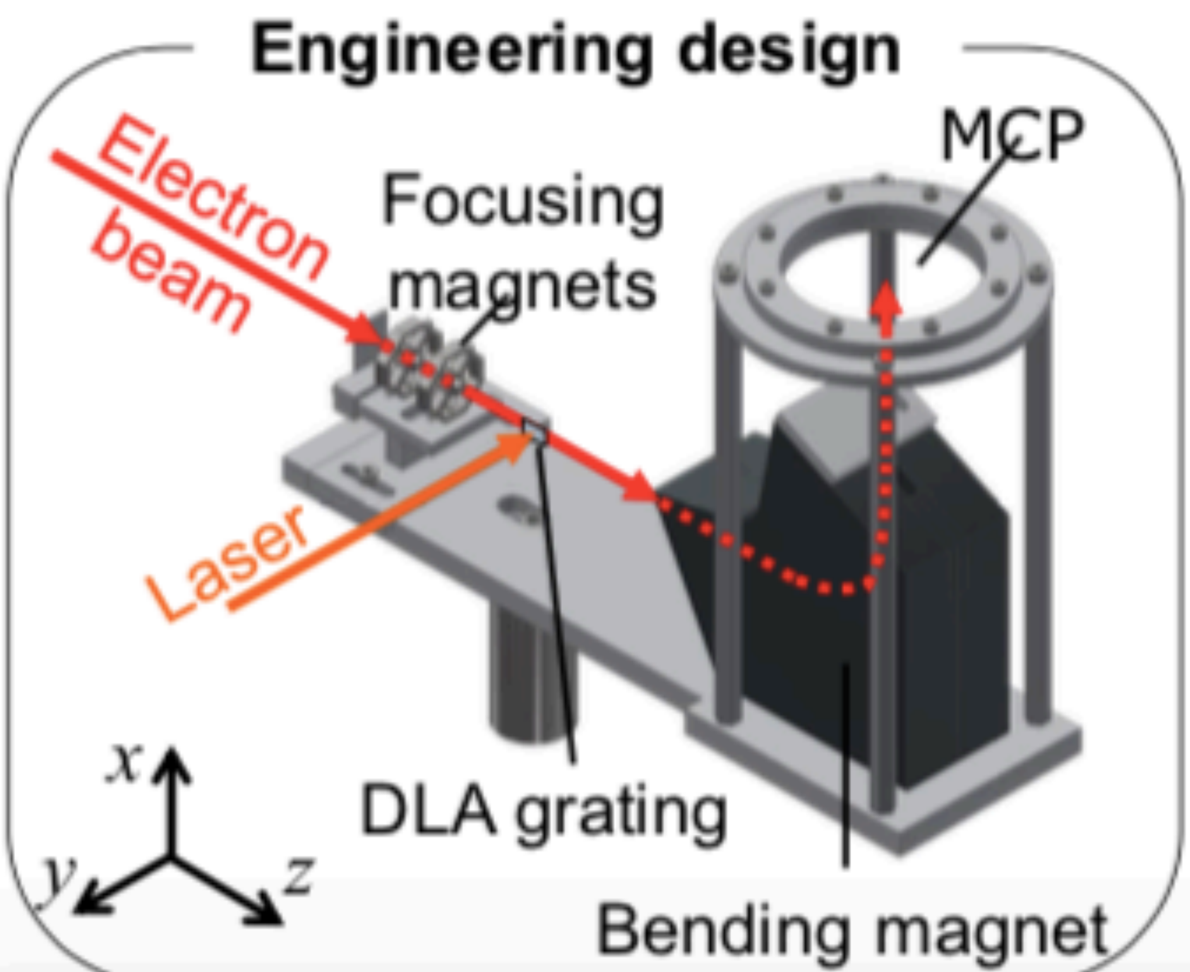
- All the devices for the experiment have been fabricated.



Courtesy of Z. Chen

Magnets design

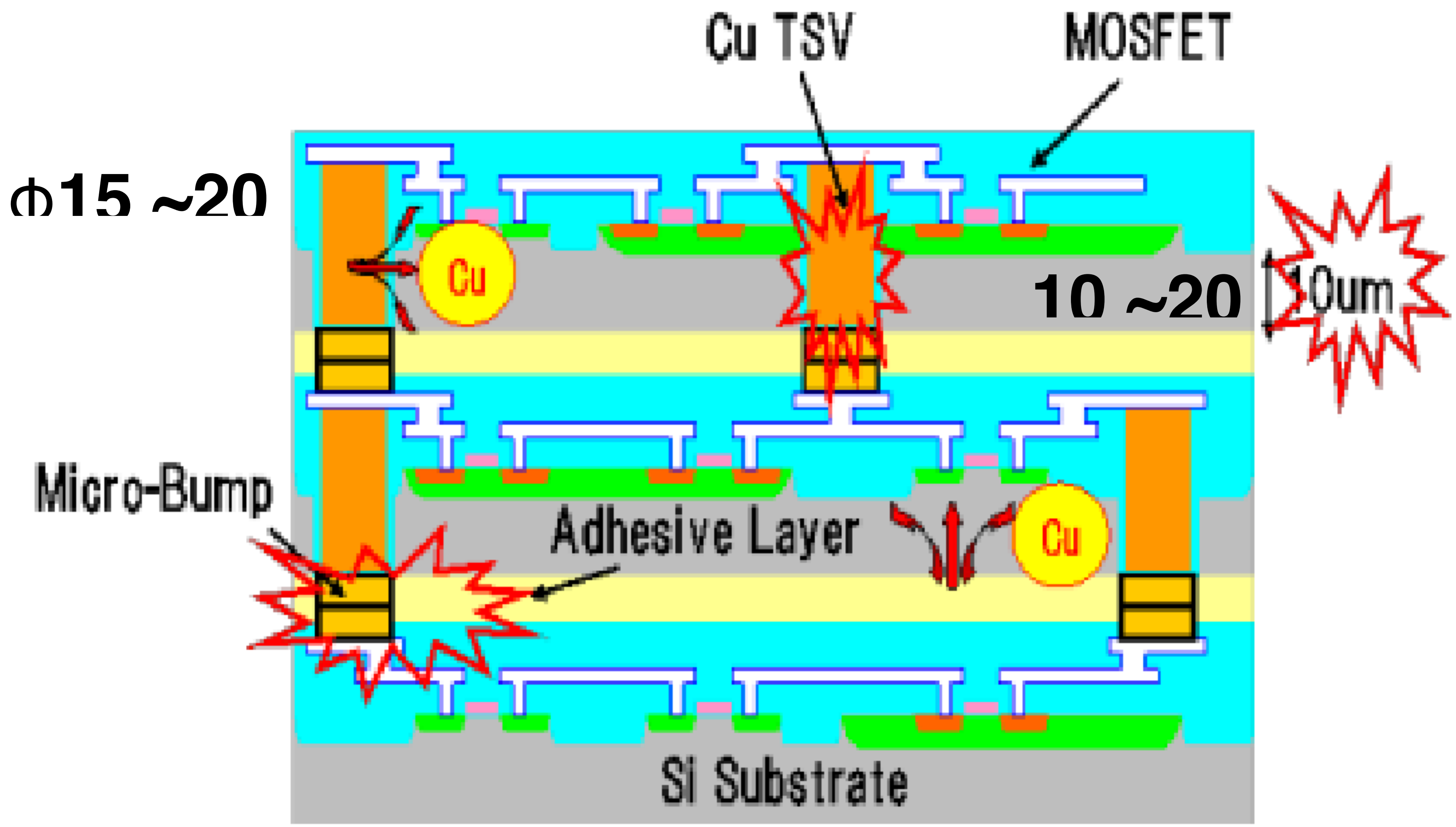




- Double focusing of electrons (in the bending plane and the transverse plane) is required.

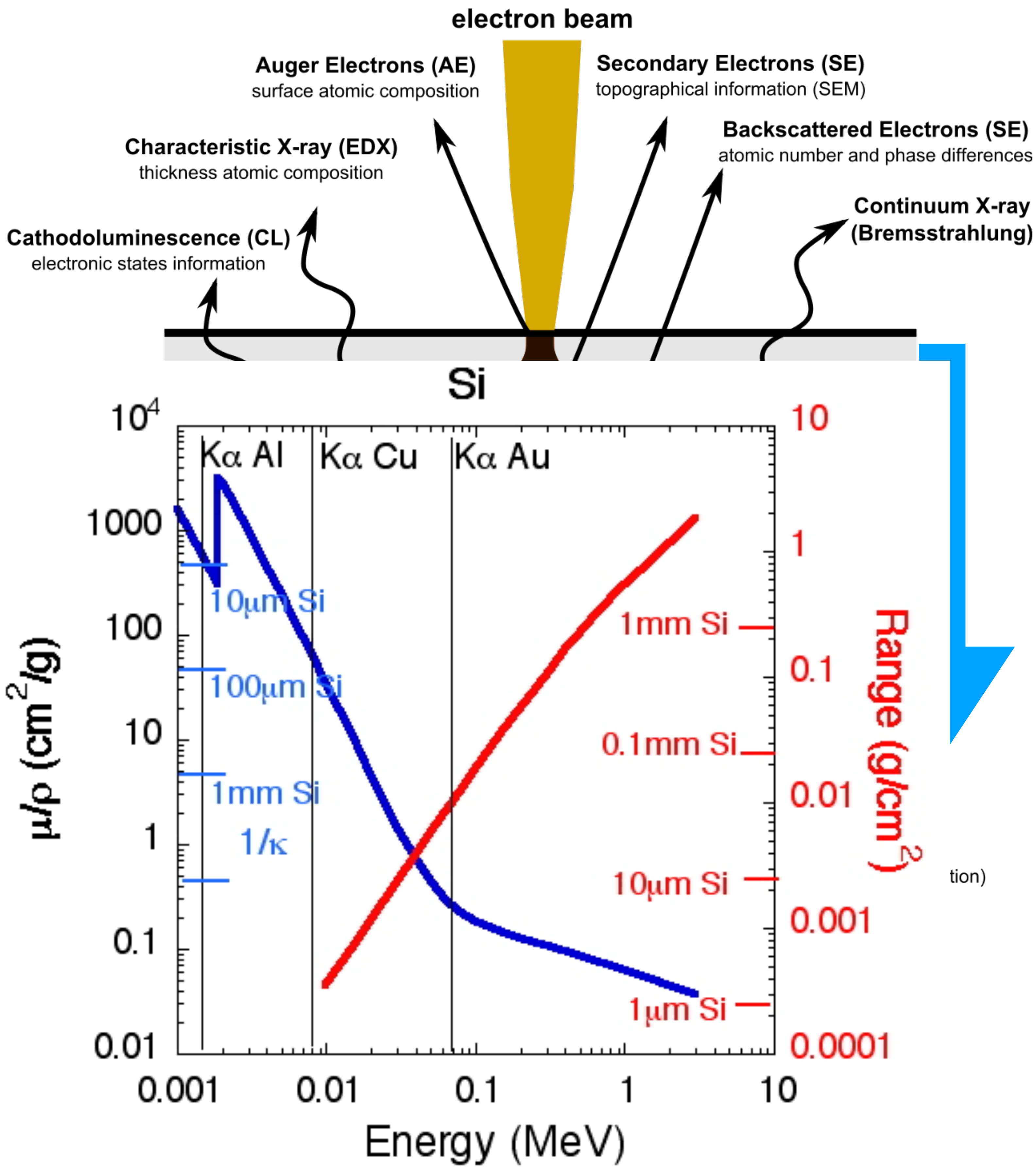
Industrial Application

Present LSI has a two dimensional structure.
SEM is used for the inspection.



Courtesy of Prof. Koyanagi, Tohiku University

Electron Beam Interaction with Matter

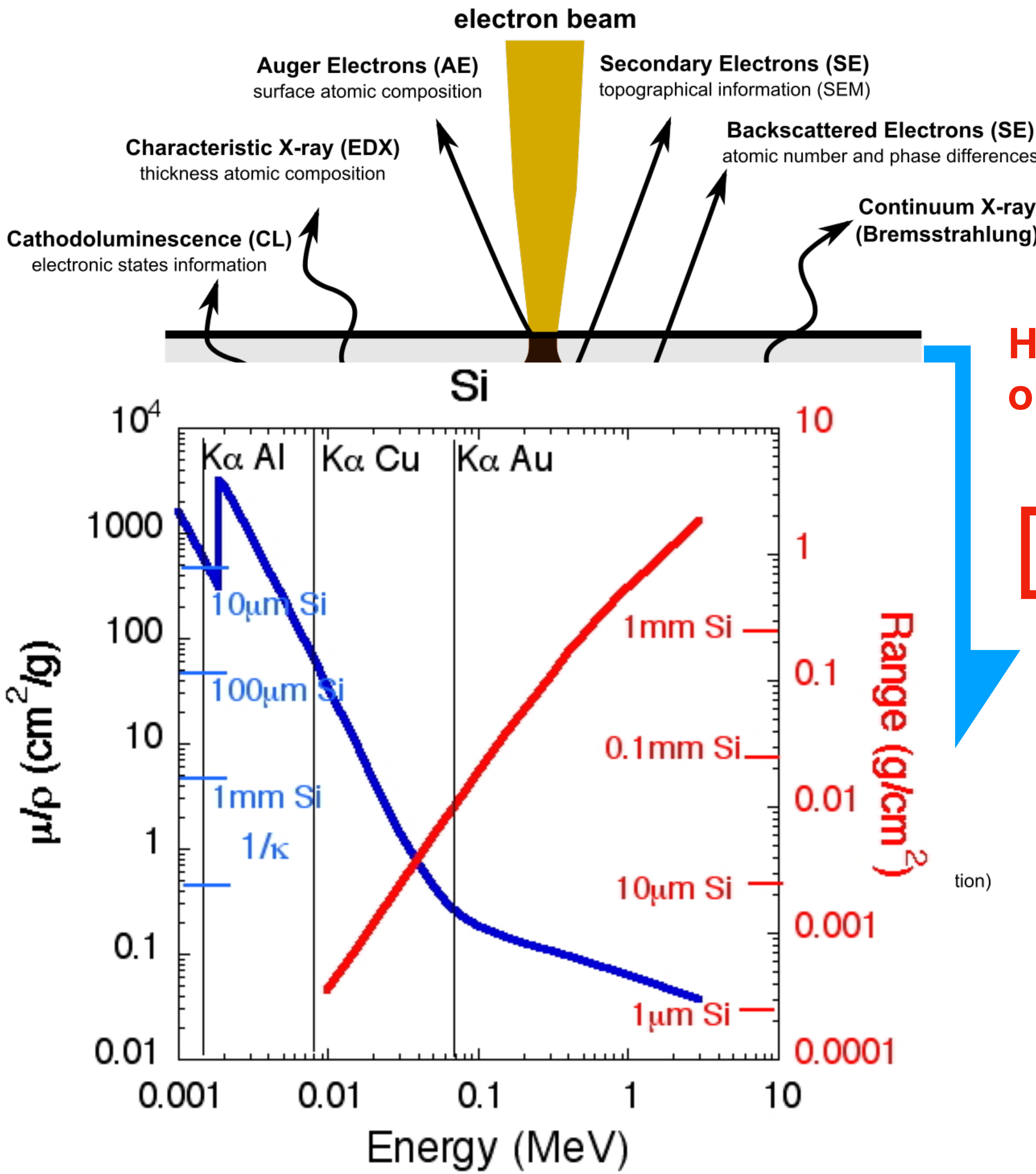


≈ 100 nm . ≈ 10 keV

≈ 100 *um* . ≈ 500 keV

≈ 1 cm . ≈ 10 MeV

Electron Beam Interaction with Matter



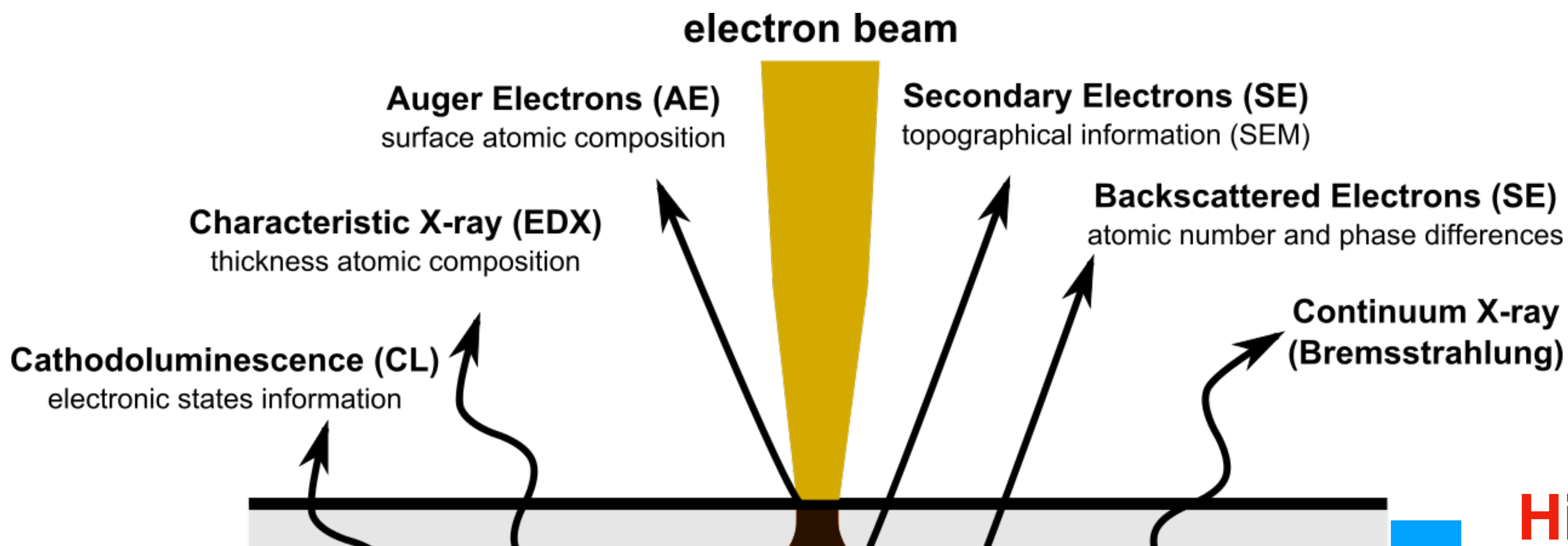
High-energy electron enables to observe the depth of 3D LSI.

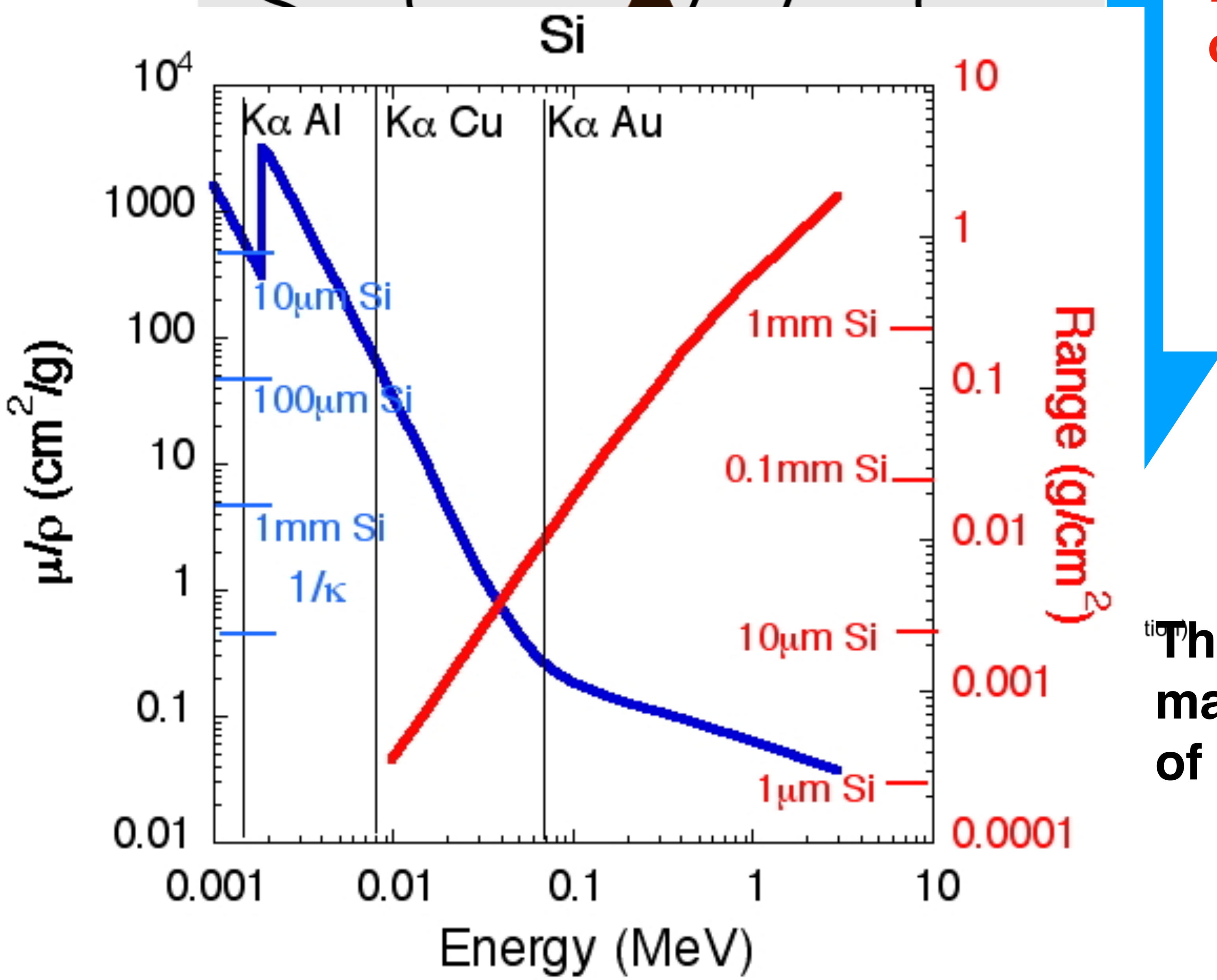
≈ 100 nm . ≈ 10 keV

≈ 100 *u*m . ≈ 500 keV

≈ 1 cm . ≈ 10 MeV

Electron Beam Interaction with Matter





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The X-ray fluorescence of low-Z materials (Z<20) from the depth of Si is hard to detect.

Summary

- **Cancer therapy**
  - **High dose rate of ≈ 1Gy/min is required.**
- **Radiobiology research**
  - **0.5~ 1 MeV, > 100 el/min μm^2**
  - **1 MeV, by the 5 mm-long DLA**
  - **100 el/min in 0.5~1MeV range is possible**
  - **Experimental setup will be installed and begin the experiment by …..**
- **Industry**
  - **Inspection of the depth of material.**
    (50 ~ 100 μm)