October 10, 2005
ICFA Workshop on
The Physics and Applications of High Brightness Beams

"Medical Application of Multi-beams Compton Scattering Monochromatic Tunable Hard X-ray Sources"

Nuclear Professional School
University of Tokyo

Mitsuru Uesaka

Staged Development of Compact Accelerator at University of Tokyo

S-band Linear Accelerators

RF 2.856 GHz

Gradient 10 MV/m

User Facility

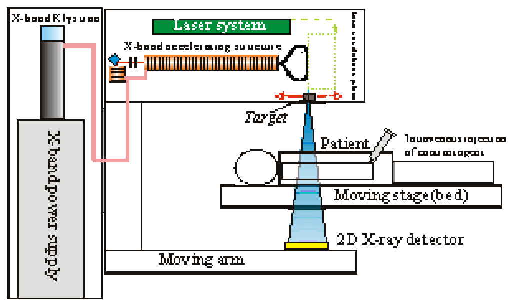
Application:Radiation Chemistry/Physics, Beam Physics

Size: Building

X-band Linear Accelerator

RF 11.424 GHz

Gradient 40 V/m



Proto-type Development

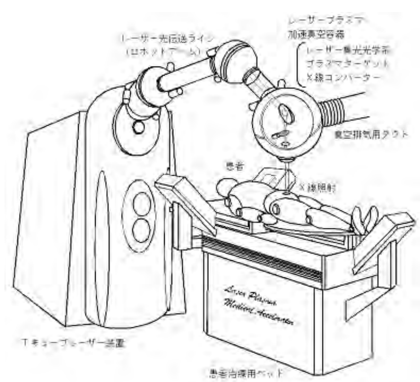
Application:Dual-Energy/Subtraction X-ray CT for Medical Use

Size: Room

Laser Plasma Accelerator

RF 10～100 THz

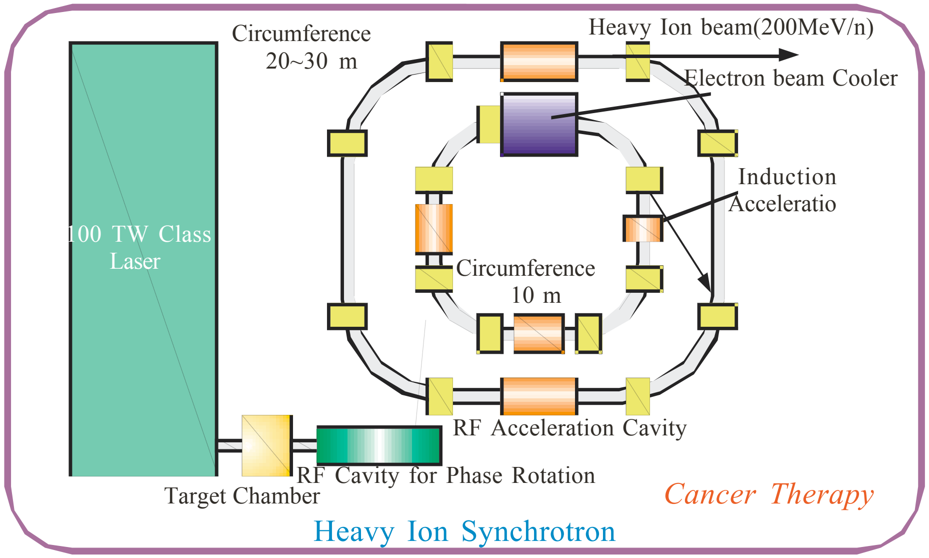
Gradient ～100GV/m

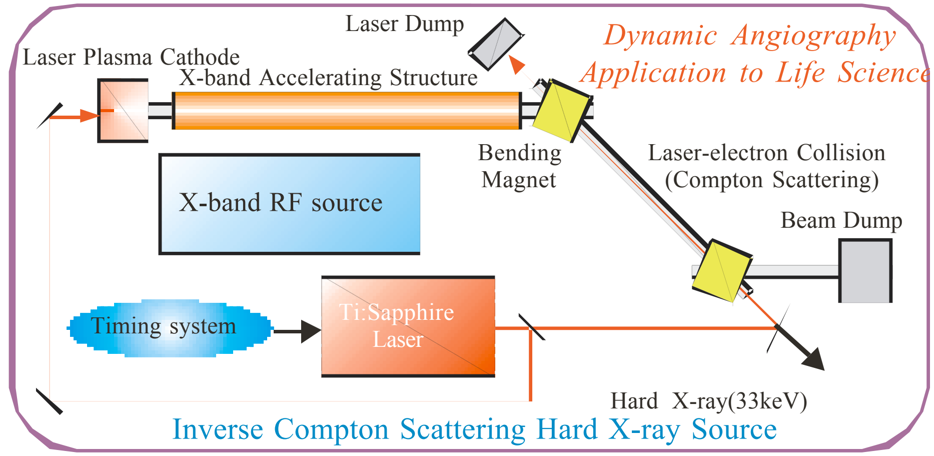


Beam Physics

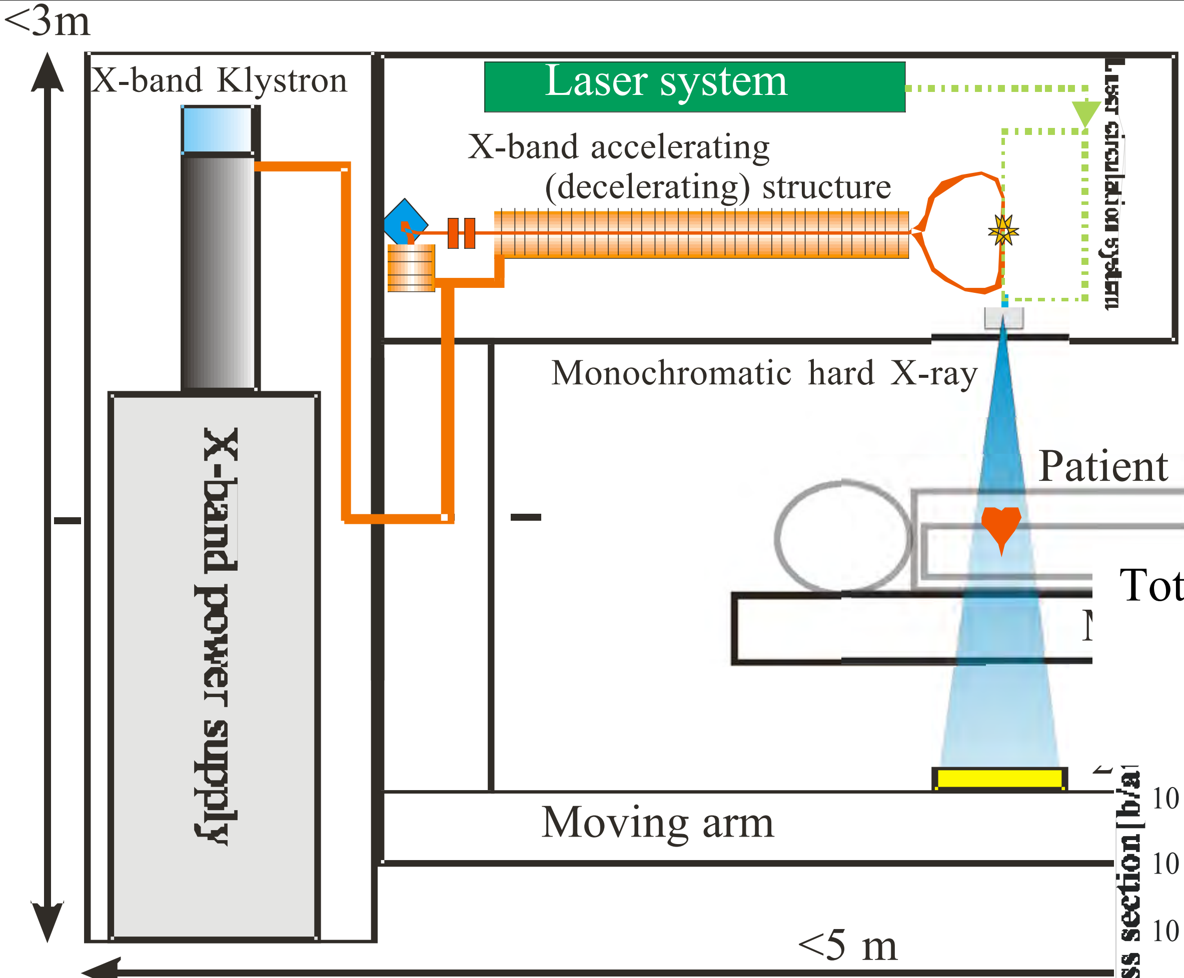
Size: Table-top

Development of Advanced Compact Accelerators

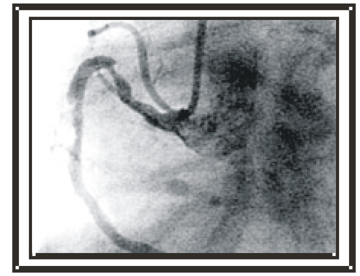




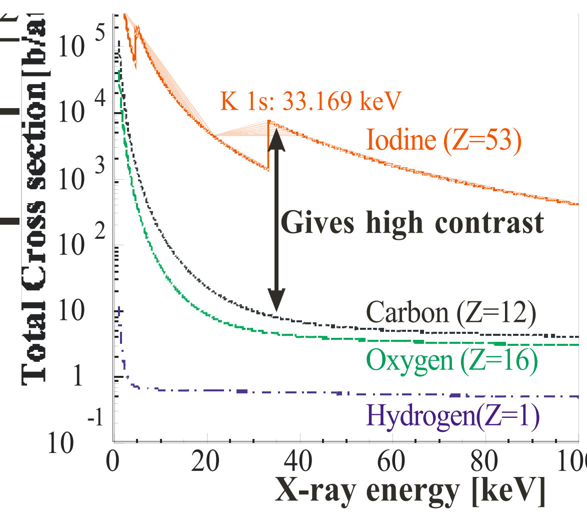
Monochromatic Tunable Hard X-ray Source by X-band-linac/YAG-laser Compton Scattering



Dynamic image of coronary artery



Total Cross Section of X-ray attenuation for various elements



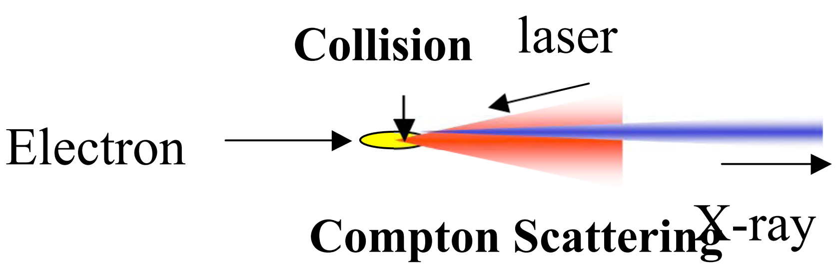
Scale of system: less than 5m x 5m(with the power supply)

Price: ~4 million dollars

X-ray energy(max.): 10~50 keV

X-ray intensity: >10^9photons/s(total)

Monochromatic Hard X-ray by Compton Scattering



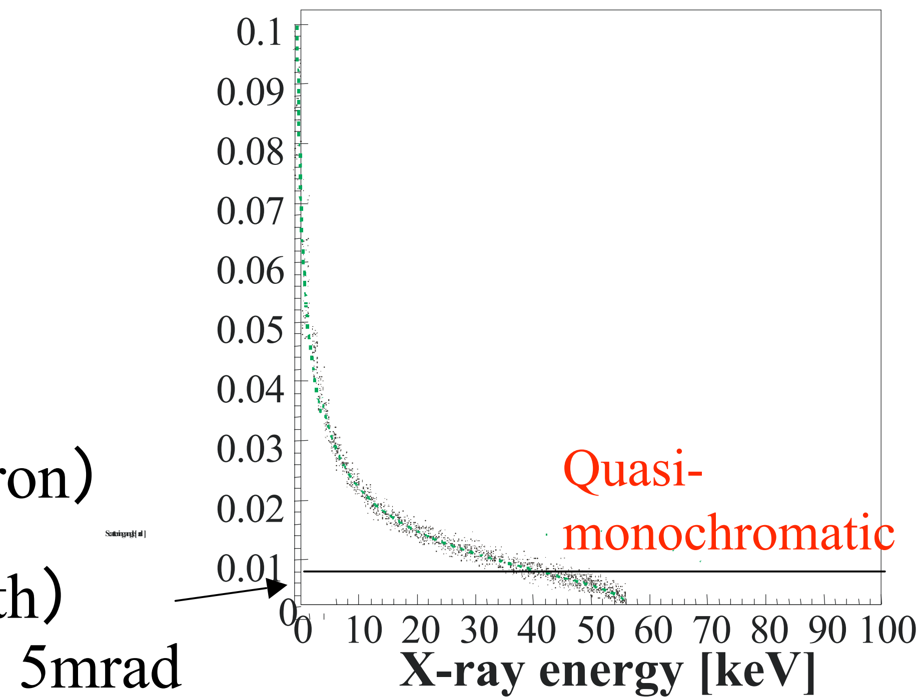
$$\lambda_r = \frac{\lambda_L}{2\gamma^2}\left(1 + \frac{1}{2}K^2\right)$$

(K: Wiggling angle of electron)

$\lambda_L \approx 1\mu m$ (laser wavelength)

$\gamma \leq 10^2 \quad (50MeV)$

$\lambda_\gamma \leq 1\mathring{A}$ (X-ray)



X-ray energy vs Angle

First and Second Generation Inverse Compton Scattering X-ray Sources

First Generation

MXI Sys/Vandervilt, PLEADES, U.Tokyo/KEK/JAERI, Sumitomo etc.

-Single-electron-single-laser Compton scattering
-First demonstration and application
-Intensity up to only 10^6 photons/s
-Rather large fluctuation due to the time-jitter
between electron and laser pulses

Second Generation

U.Tokyo, Lyncean Tech.(R.Ruth), Sumitomo/AIST, etc.

-Multi-scattering of electron- and laser-pulses
-Intensity of more than 10^8 photons/s
-A variety of applications for medicine, protein structural analysis,
security and nuclear engineering

Performance of Linac/Laser Inverse Compton X-ray Source

Laboratory	Electron Energy	Charge	Wavelength & Power of Laser	X-ray Energy & Intensity	Uncertainty of X-ray Intensity
SHI[1]	14 MeV (S-band)	400 pC Single Bunch	800nm, 300 mJ, (Ti:Sapphire, 300 ps)	3.5 keV < 1.0E+4 photons/shot	50%
MXI Systems Inc[2]	25 MeV (S-band)	500 pC Single Bunch	1 μm, 20 J (Nd:Glass)	12～50 keV 1.0E+8 photons/sec	50%
LLNL[3]	57 MeV (S-band)	250 pC Single Bunch	780 nm, 400 mJ (Ti:Sapphire, fs)	40～80 keV 1.0E+7 photon/ssec	50%
SLAC	60 MeV (S-band)	500 pC Single Bunch	800 nm, 300 mJ (Ti:Sapphire, fs)	20～85 keV 1.0E+8 photons/s	80%
Univ. of Tokyo /NIRS/KEK[4]	35 MeV (X-band)	20 pC×10000 Multi Bunches	1 μm, 2 J, (Nd:YAG, 10 nsec)	33 keV 1.0E+8 photons/s	<10%

[1] :M.Yorozu *et al.* Jpn.J.Appl.Phys., Vol.40 (2001) pp. 4228-4232
[2] :F.E.Carroll *et al.* Am.J.Rentgenol. 181 (2003) 1197
[3] :W.J.Brown *et al.* Phys.Rev.Lett.Vol.7 060702 (2004)
[4] :K.Dobashi *et al.* Jpn.J.Appl.Phys., Vol.44 (2005) pp. 1999-2005

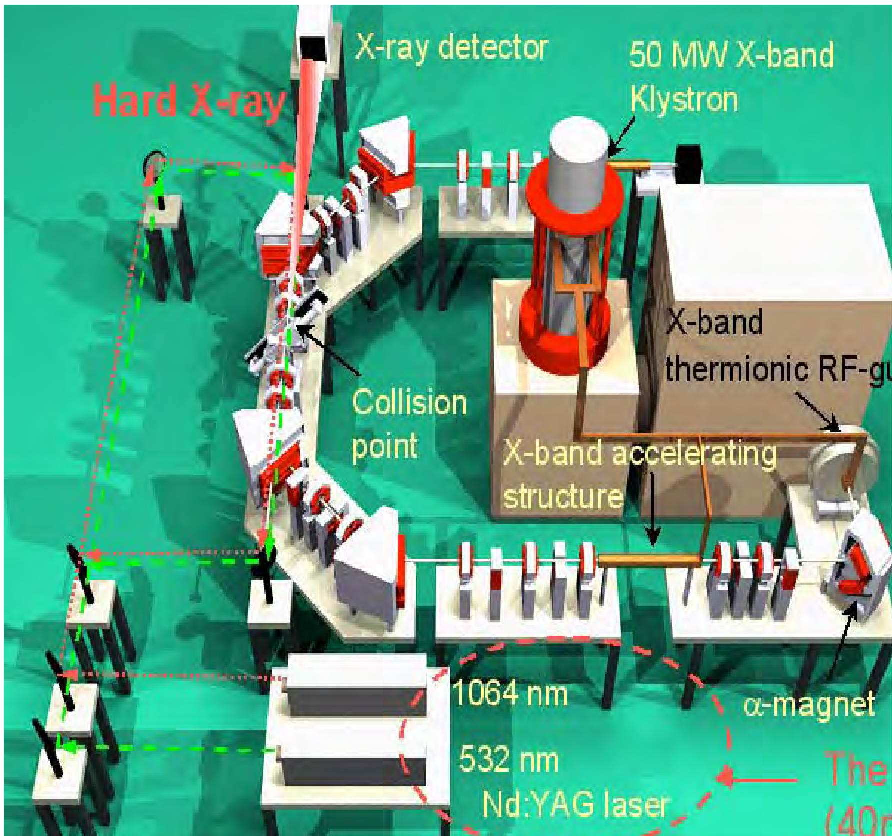
Performance of Typical Monochromatic Tunable Hard X-ray Source

Laboratory	Source of X-ray	Changing method of X-ray Energy	X-ray Intensity	Changing time	Intensity Fluctuation
KEK, SPring-8, etc	SR	Diffraction grating	10^{11} photons/sec	~ 10 min.	< 10 %
Iwate Med. Univ ,etc[5]	Discharged Plasma	Electrode	~ 10^{6} photons/sec	~ hours	? (Unknown)
Univ. of Tokyo /NIRS/KEK	Compton Scattering	Wavelength of Laser	10^{8} photons/sec	~ 40 msec (@ 25 Hz)	< 10 %

[5] :M. Sagae *et al.* Jpn.J.Appl.Phys., Vol.44 (2005) pp. 446-449

Compton scattering hard X-ray source

Compact hard X-ray source based on Compton Scattering



The X-ray energy can be changed quickly (40ms) by introducing two lasers

Properties of the generated X-ray

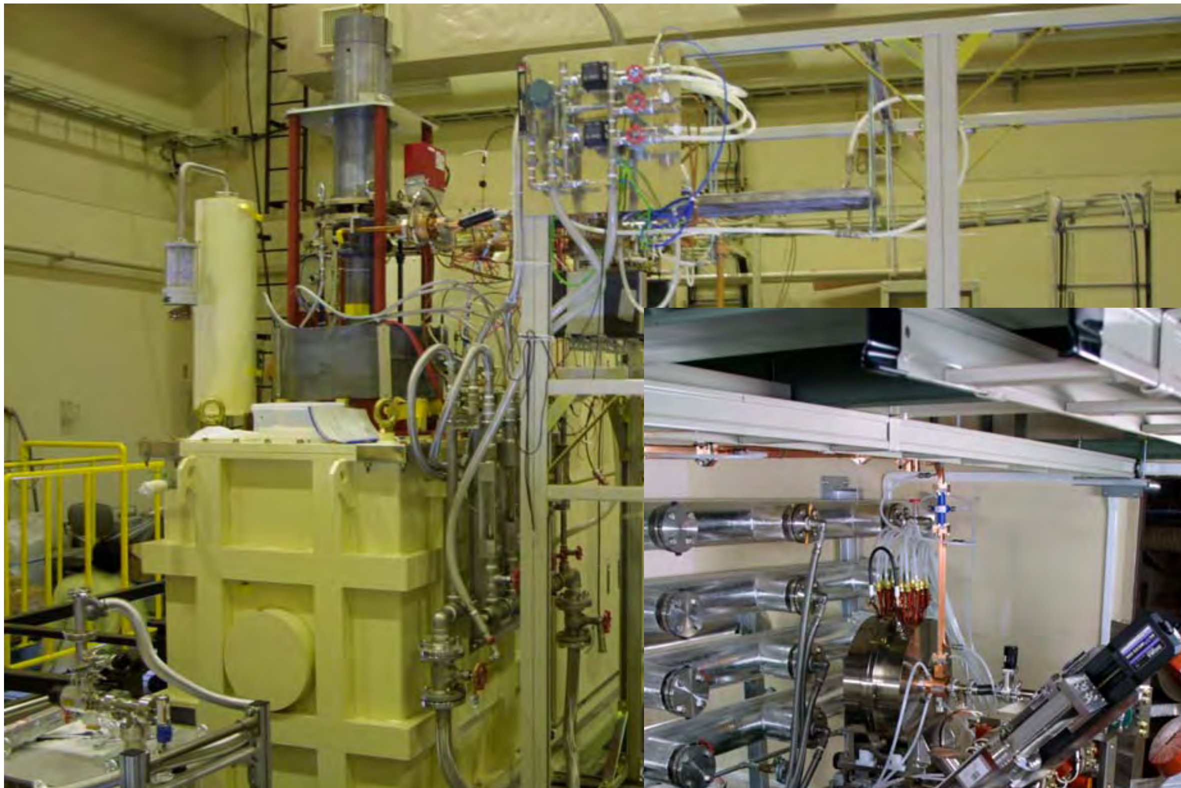
Electron beam energy : 35 MeV, Charge : 20 pC/bunch

Laser wavelenght (nm)	1064	532
Pulse energy (J/pulse)	2.5	1.4
X-ray yield (photons/pulse)	9.9×10^{6} (10^{8})	4.4×10^{6} (10^{8})
Maximum X-ray energy (keV)	21.9	43.8
Energy spread (%) rms	1-10	

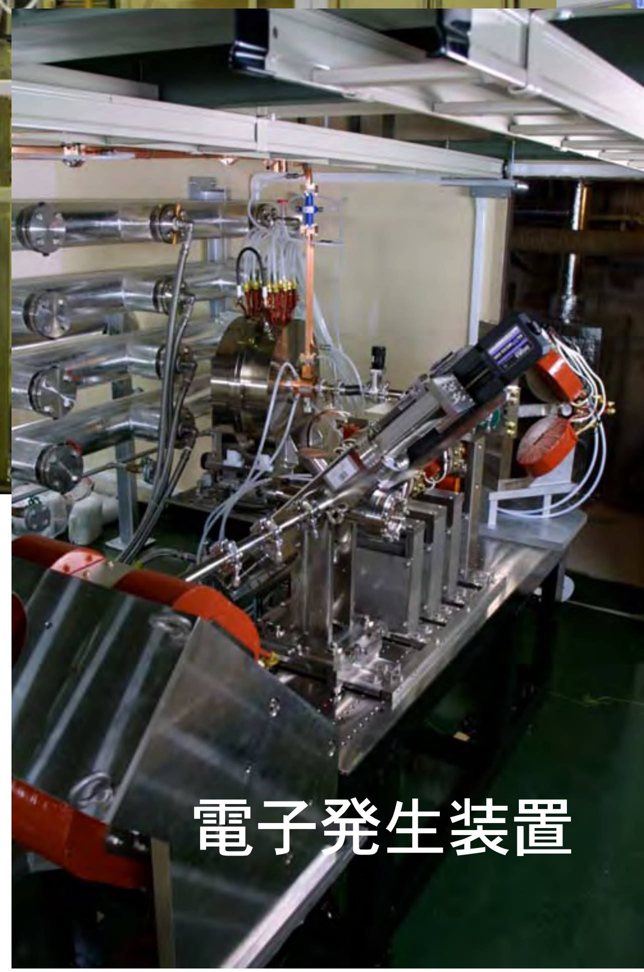
10 pps with laser circulation

Details are in RPAP006 and WPAP019

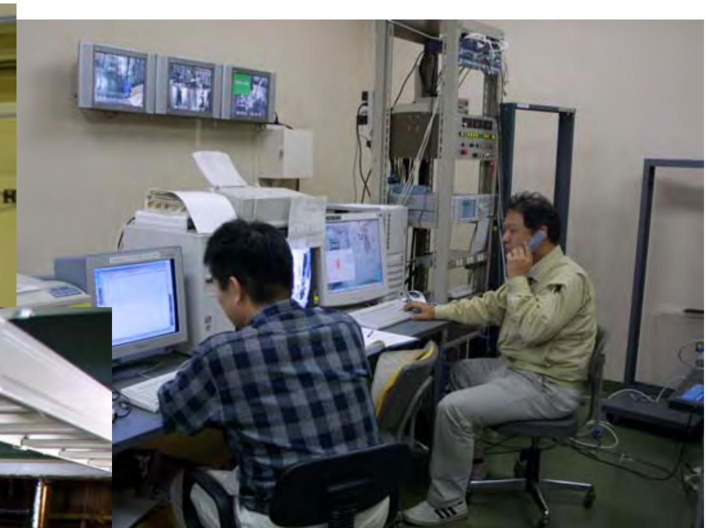
医療用小型ライナック室



電波発生装置

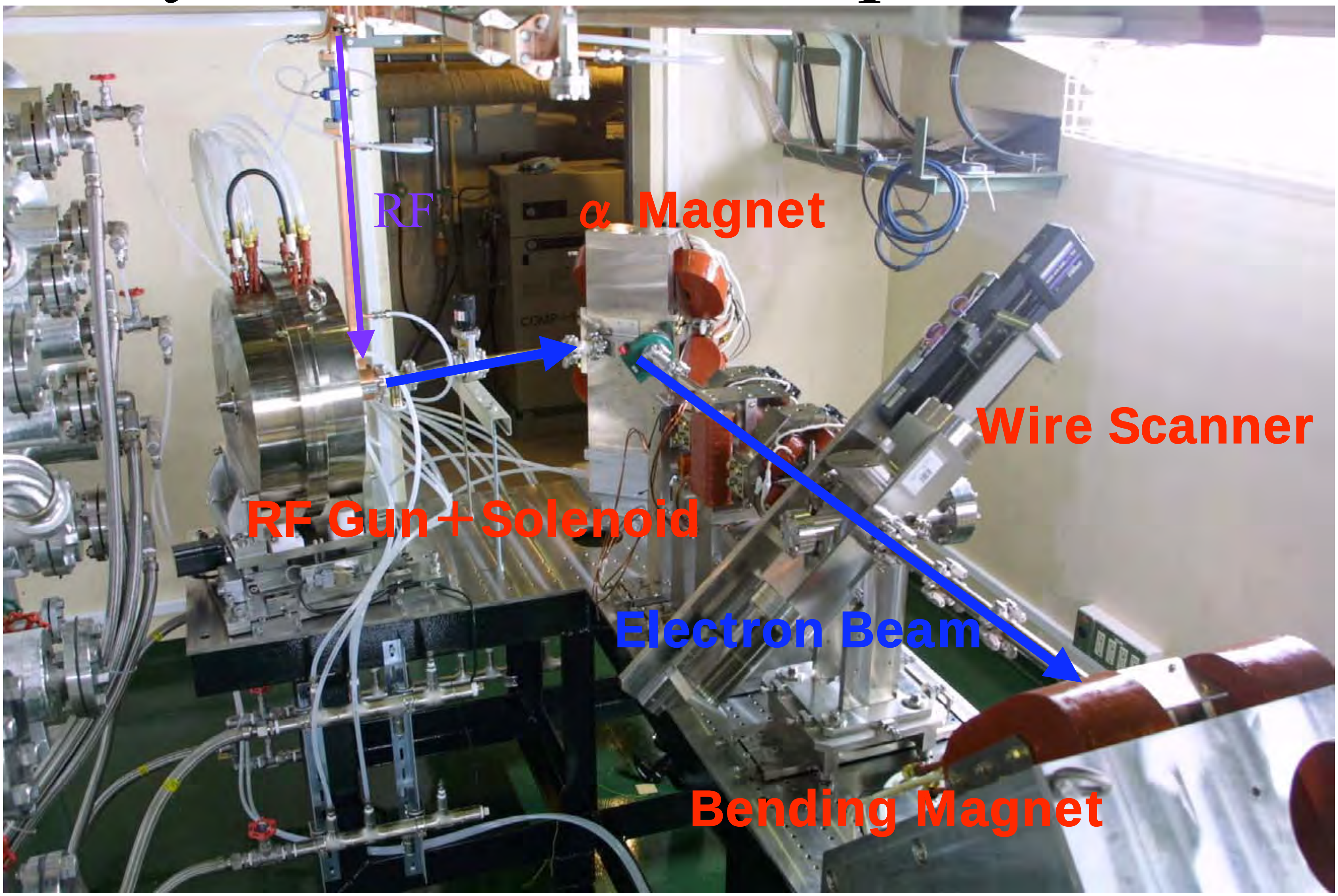


電子発生装置



コントロール
ルーム

System of Beam-Experiment



Laser circulation system

RF pulse length: ζ 10000 bunches

Laser pulse length: 10 ns(FWHM)

ζ collide with 110 bunches

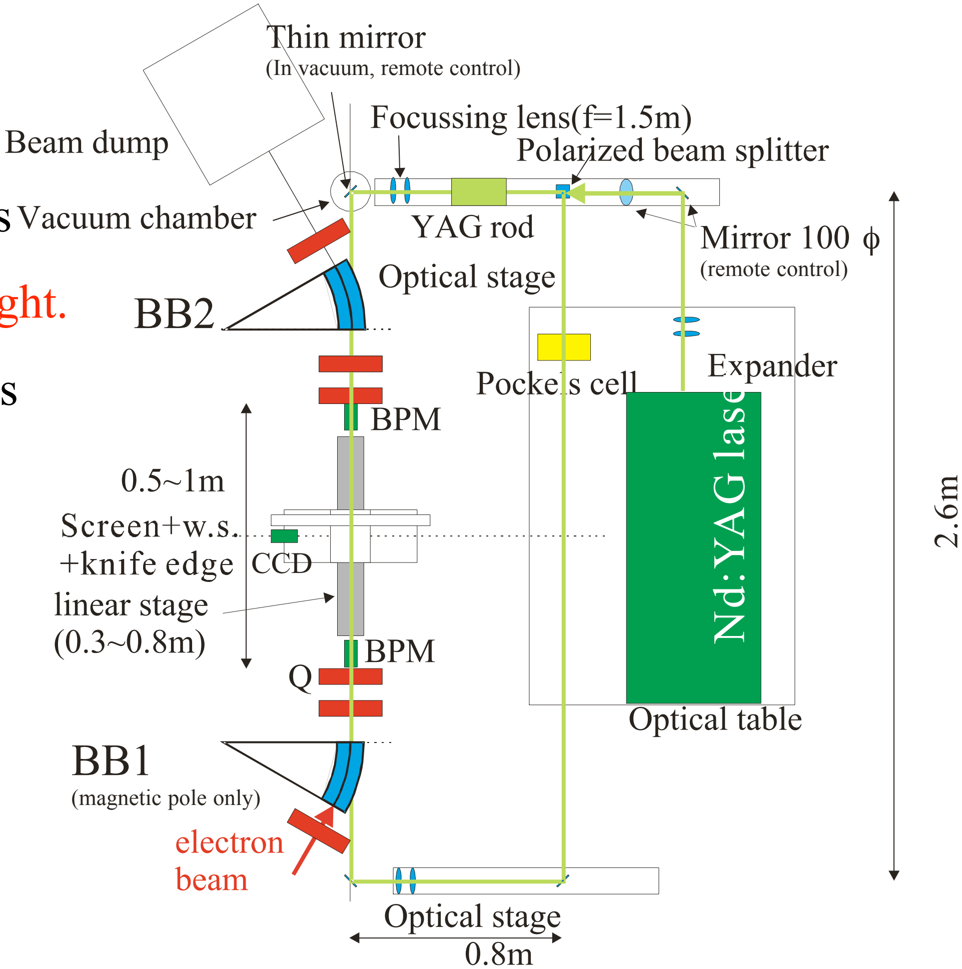
Increase X-ray yield by re-incident the laser light.

21 ns per a revolution ζ 47 revolutions per 1ms

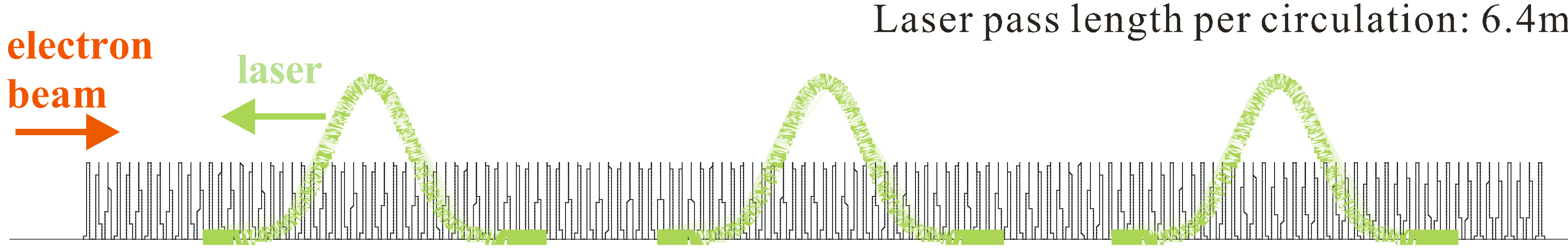
Enhancement:

- 10 times(max.) with 90% transmission per revolution: 10^9photons/s

- 100 times with 5J pulse and laser power compensation by Nd:YAG rod: 10^{10}photons/s



Laser pass length per circulation: 6.4m(21ns)

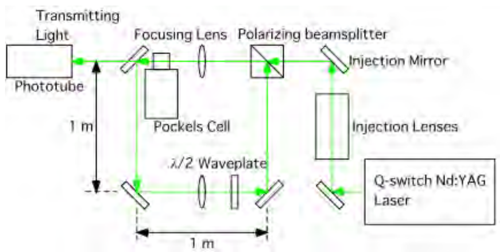


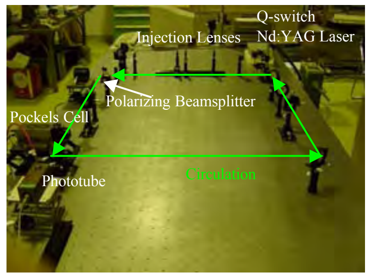
Experiment

We are doing a proof-of-principle experiment for the laser pulse circulation system.
Purposes of the experiment are
-Proving enhancement of the laser intensity in the circulation system.
-Measurement of the revolving laser, the transmission efficiency and the enhancement amount.
-Establishment of a technique to control the laser beam profile at the collision point in order to apply the system into the hard X-ray source.

Property of the Laser

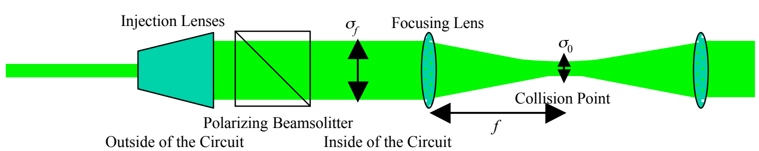
Wavelength	$\lambda = 532$ nm Q-switch Nd:YAG Laser (2nd harmonic)
Pulse Energy	25 mJ/pulse @532nm
Pulse Width	3-5 ns (FWHM)





Experimental Setups

Control of the Beam size at the Collision Point



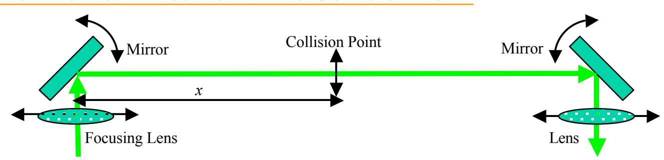
The beam size at the collision point σ_0 (rms) is

$$\sigma_0 = M^2 \frac{\lambda}{4\pi} \frac{f}{\sigma_f}$$

σ_f: Beam size at the focusing lens
f: Focal length of the focusing lens

The beam size at the collision point is controlled outside of the circuit.

Control of the Beam Position at the Collision Point



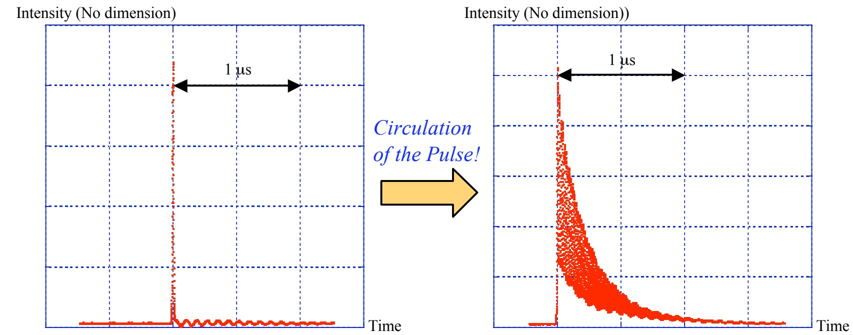
The beam position at the collision point is $r = x\theta + l$

θ: Angle of the mirror before the collision point (0.02° accuracy). ⇐ Rough Control
l:Position of the focusing lens (5µm accuracy). ⇐ Precise Control

To avoid an error due to circulation, we move the lens and mirror after the collision point equally to the focusing lens and the mirror before the collision point.

Results

Intensity of the Laser Pulse



Incident Laser Pulse

Laser Pulse in the Circulation System

The laser pulse revolves more than 50 times (650 ns).
Attenuation of the laser pulse energy at 400 ns (the 30th revolution) is approximately 80%.

-The transmission efficiency is lager than 90 % (A>0.9).
-Using the circulation system, the X-ray yield will become more than 10 times .

⇐ $I_0 A^{30} = 0.2 I_0$

$I_0 = 94.7\%$

Therefore,
the monochromatic hard X-ray source will generate at least 10^9 photons/sec with the laser pulse circulation system!

Summary

-We develop the laser pulse circulation system for the compact monochromatic hard X-ray source.
-Using this system, the X-ray yield will become 10 times lager.
-In the experiment, the transmission efficiency was lager than 90% and the laser intensity became more than 10 times.
-We do further experiments for laser profile control at the collision point.

REFERENCES
[1] M. Uesaka et al., "X-band RF Gun/Linac for inverse Compton Scattering", 21th Int. LINAC Conf., Gyeongju, Korea, 2004.
[2] K. Dobashi et al., AAC 2004, inpress.
[3] A. Fukasawa et al., presented at APAC , Beijing, China, 2001.
[4] F. Ebina et al., "Laser circulation system for compact monochromatic hard X-ray generator", Proc. 1st Particle Accelerator meeting, Japan 2004.
[5] F. E. Carroll, American Journal of Roentgenology 179 583 (2002).
[6] A. E. Vieks et al., "Development of an X-band Photoinjector at SLAC", 21th Int. LINAC Conf., Gyeongju, Korea, 2004.

Applications

- **Static/dynamic imaging by 100 μm spatial resolusion**

- **Dual energy X-ray CT to get 3D distributions of atomic-number- and electron-densities for light atoms up to ^{43}Tc**

- **Subtraction CT across the K-edge to get 3D distribution of specified atoms**

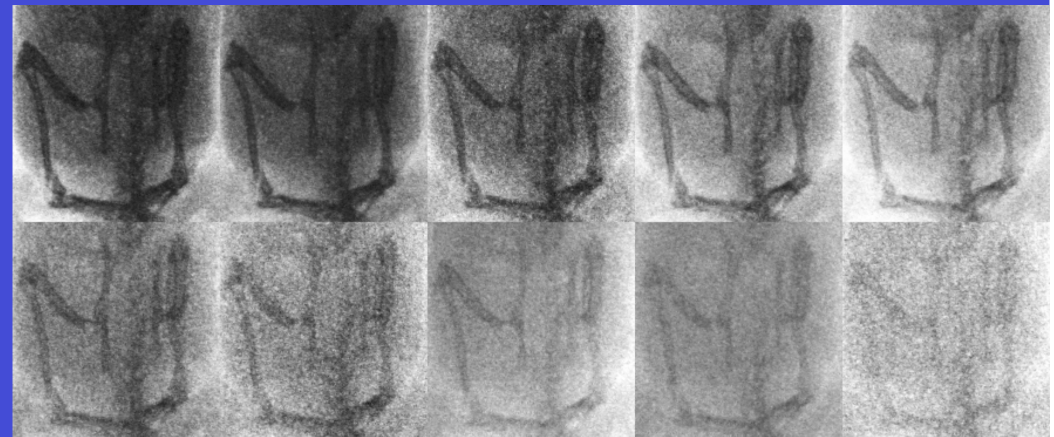
- **Protein structural analysis**

Energy differences in a finger

19 keV

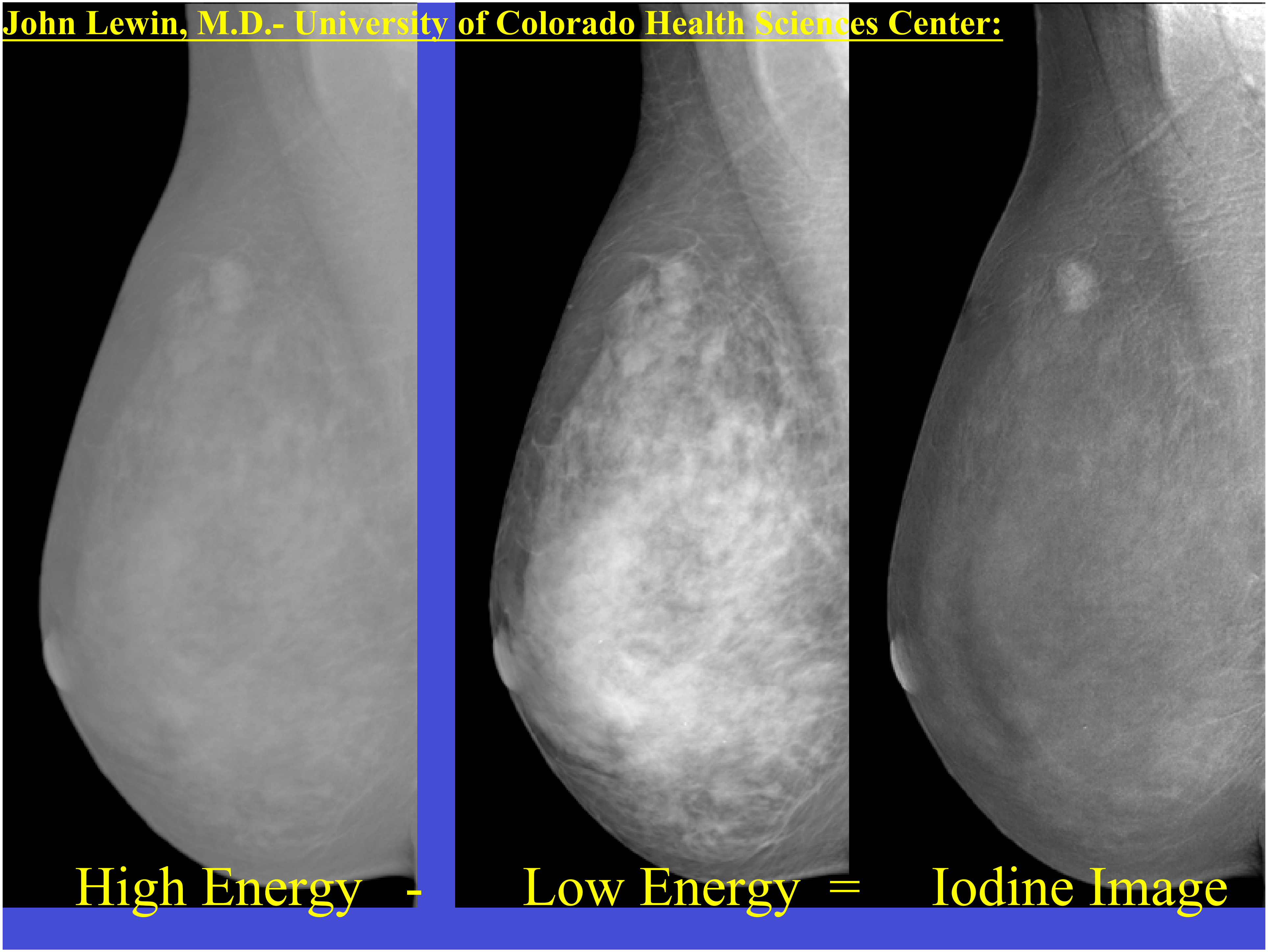
29 keV

or in a body, such as a mouse

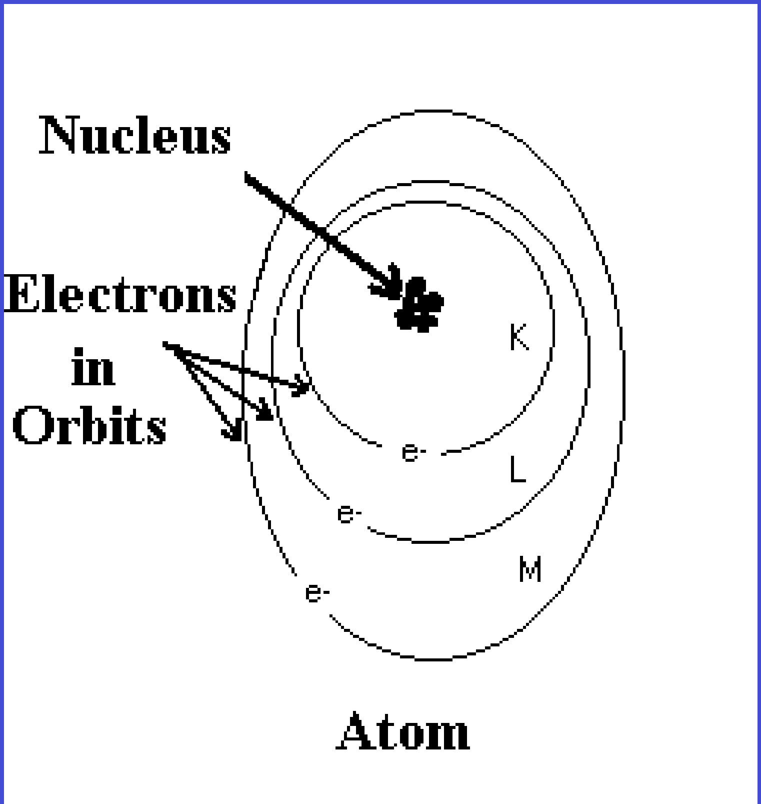


Energy movie from 15 keV to 33 keV

We have the ability to specifically tune the X-rays to the imaging task at hand.

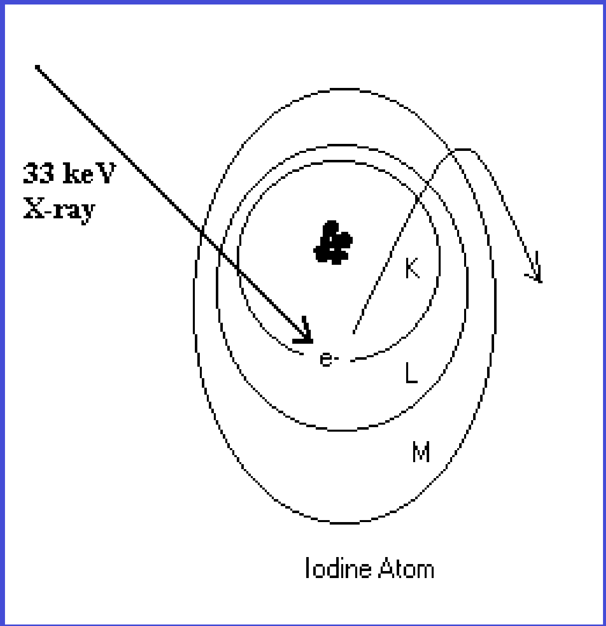

John Lewin, M.D.- University of Colorado Health Sciences Center:
High Energy -
Low Energy =
Iodine Image

Stylized diagram of an atom:



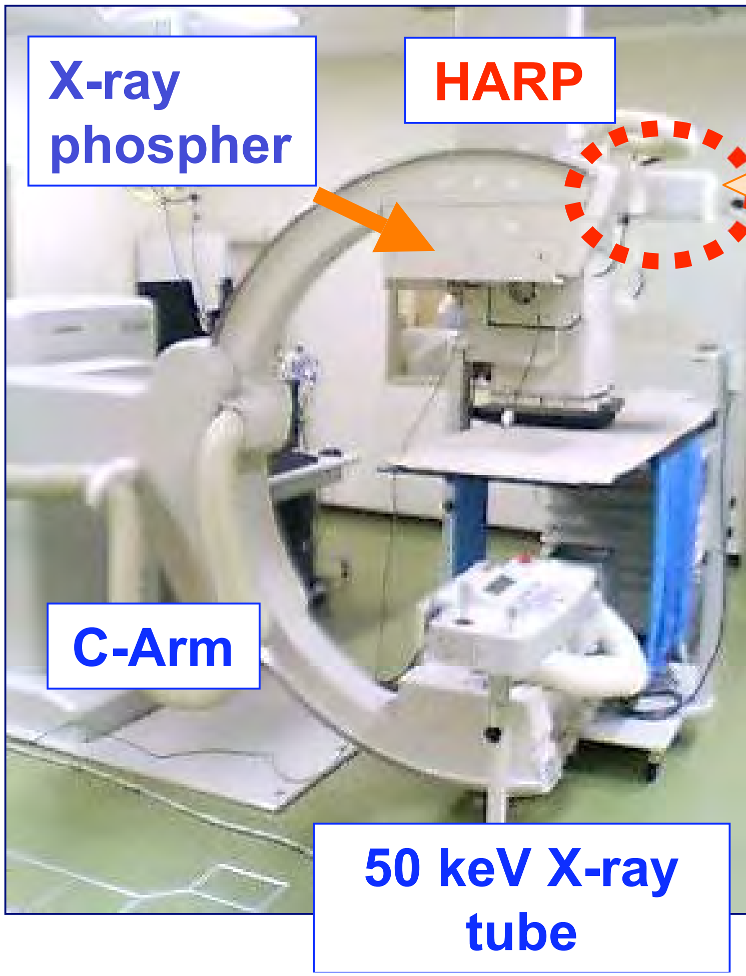
Each electron is bound in its orbit by a characteristic energy for that particular atom/orbit. This is called its binding energy. The binding energy is different for each atom in the periodic chart.

Our beam can be tuned to just the right energy to knock the k-shell electron out of its orbit. For the Iodine atom that energy is 33.2 keV.

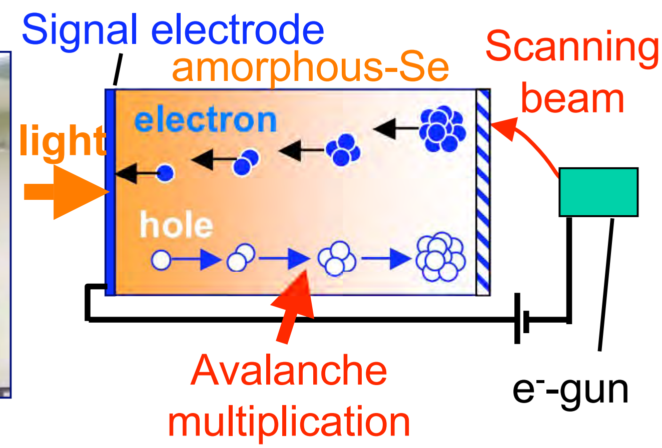


Ultra Micro-vessel Angiography for Diabetic Femur and Thrombus @ NCVC (National CardioVascular Center)

X-ray tube (50kVp) with high-sensitivity HARP camera



HARP (High-gain Avalanche Rushing amorphous Photoconductor) camera



Micro-vessels visualized by contrast agent

Imaging area:
20cm × 20cm

Space resolution:
25 μm

Ultra Micro-vessel Angiography by Compact Monochromatic Hard X-ray Source

Ultra Mico-vessel angiography by monochromatic hard X-ray

- 30 images/s
- Space resolution: 25 μm

Required photon intensity

4.8×10^{10} photons/mm^2/s @33-35keV 4.8×10^{9} photons/mm^2/s @51-54keV

Compact hard X-ray source based on electron-laser collision

- 10 times circulated laser colliding with electron

Expected photon intensity

2×10^{7} photons/mm^2/s @33-35keV 1×10^{7} photons/mm^2/s @51-54keV

Angiography by the compact hard X-ray source

- High-sensitivity HARP camera
- 10 images/s
- Pixel size (100 μm ×100μm)

Photon intensity is reduced

Angiography can be performed!
(Space resolution: 100 μm)

Future plan to perform ultra micro-vessel angiograpphy

High power laser (7J/pulse), 40 times circulated laser, Wide length of electron macro pulse and Small light spot (25 μm diameter) etc… → Space resolution: 25 μm

3D Evaluation of Atomic Number Distribution

1. Light Atoms up to ^{43}Tc
- Interpolation of the X-ray attenuation constant between charateristic edges is available.
- 3D distributions of the atomic number density and electron density can be obtained
- Their spatial resolution is determined by the X-ray source size.

2. Heavy Atoms
- The interpolation does not work.
- Subtraction CT gives 3D distribution of specified atoms.

Linear attenuation coefficient is approximately written as a function of Z and E

$$\mu \cong \rho \frac{N_A}{A} Z \left(4\sqrt{2} Z^4 \alpha^4 \left(\frac{mc^2}{E} \right) \phi_0 \sum_{nll'} f_{nll'} + \sigma_{KN} + \frac{Z(1 - Z^{b-1})}{Z'^2} \sigma_{SC}^{coh}(Z', E') \right)$$
$$= \rho_e \left(Z^4 F(Z, E) + G(Z, E) \right)$$

ρ : mass density
N_A: Avogadro's number
σ_{KN}: Klein-Nishina cross section
σ_{SC}: Coherent scattering cross section of standard element Z'
Z'=8 (Oxgen) and $E'=(Z'/Z)^{1/3}E$

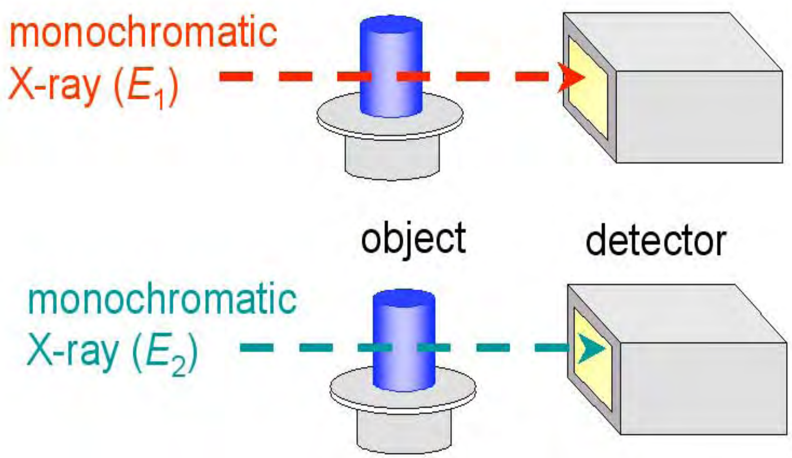
Effective atomic number and electron density are derived from linear attenuation coefficients for two energies

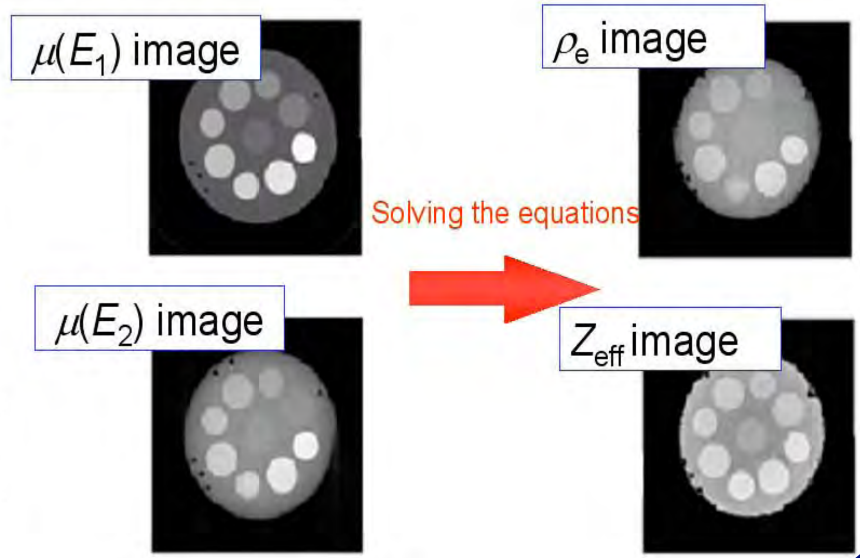
$$\mu(E_1) = \rho_e \left(Z^4 F(Z, E_1) + G(Z, E_1) \right)$$
$$\mu(E_2) = \rho_e \left(Z^4 F(Z, E_2) + G(Z, E_2) \right)$$

Effective atomic number
$$Z^4 = \frac{\mu(E_2) G(Z, E_1) - \mu(E_1) G(Z, E_2)}{\mu(E_1) F(Z, E_2) - \mu(E_2) F(Z, E_1)}$$

Electron density
$$\rho_e = \frac{\mu(E_1) F(Z, E_2) - \mu(E_2) F(Z, E_1)}{F(Z, E_2) G(Z, E_1) - F(Z, E_1) G(Z, E_2)}$$

Dual-energy X-ray CT experiment



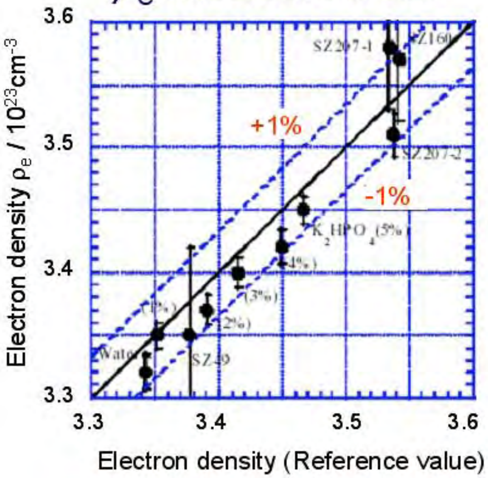


Torikoshi(NIRS), et al.

Dual-energy X-ray CT by SR light sources

Electron density and atomic number have been measured for biological materials consist of light elements (Z≤20) [1,2]

ρ_e measurement



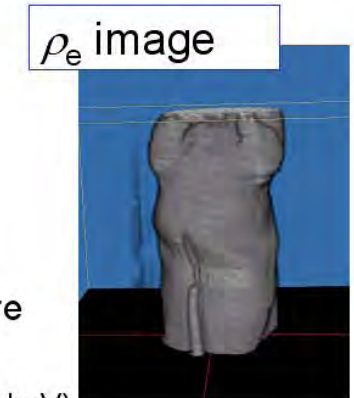
Precise electron density can be measured in agreement with 1 % of the theoretical values

(X-ray energy : 40 keV, 70 keV)

Volume data of a rat are constructed

(X-ray energy : 40 keV, 70 keV)

Volume rendering of a rat



Torikoshi(NIRS) et al.

Dual-energy CT for atomic number identification in a material

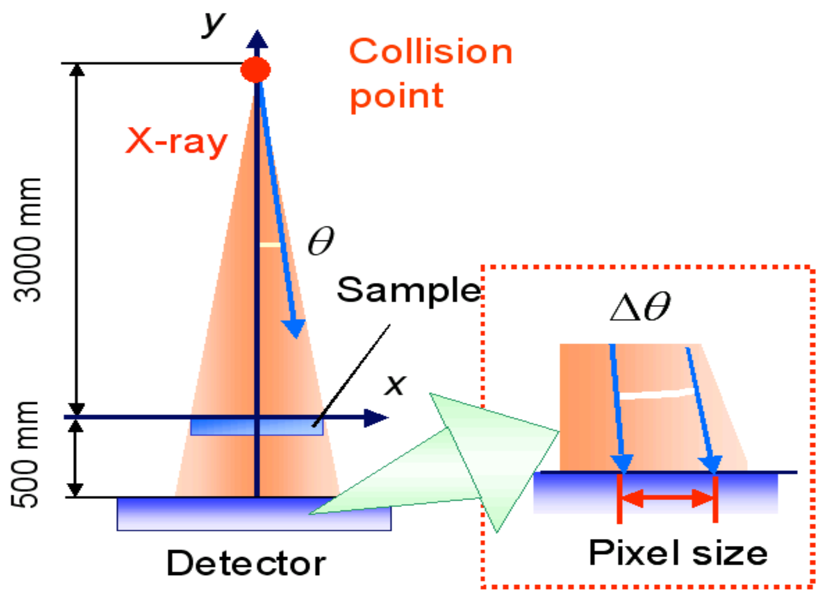
Can we apply the method to medium *Z* elements?

- The dual-energy analysis cannot be used below K-edge energy of a atom
- When maximum X-ray energies are 21.9 keV and 43.8 keV, elements up to Z = 38 should be identified
- Energy spread $\Delta E/E$ of the monochromatic X-ray

SR light :10^{-1} – 10^{-2} % (negligible), Compact X-ray source : 1 to 10%

Numerical simulation to examine applicability

Applicability of the dual-energy analysis



Assuming a point light source
Pixel size : 0.1 to 1.0 mm
Electron beam energy : 35MeV
Laser wavelength: 1064nm, 532nm
Maximum X-ray energy: 21.9keV, 43.8keV

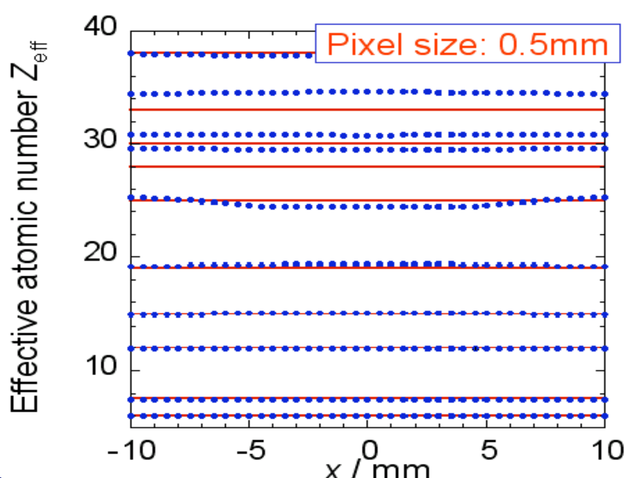
Energy spread $\Delta E/E$: 1 to 10%

X-ray energy depends on the position on the detector

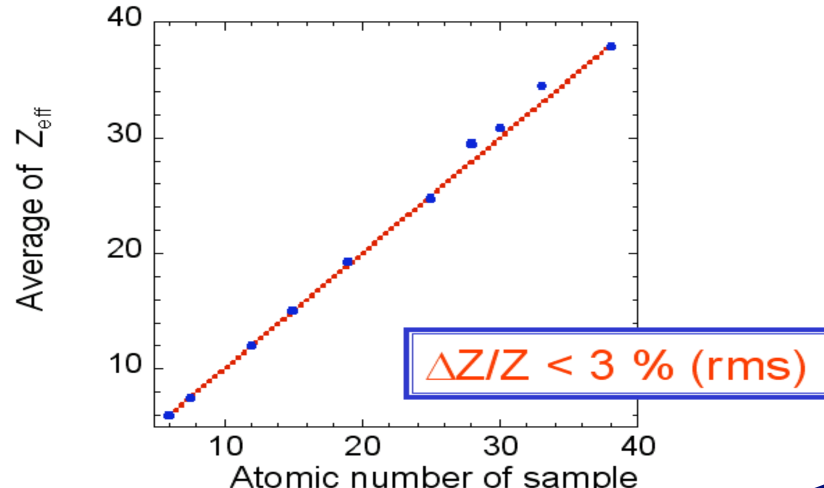
Pixel size : 0.5mm
$\Delta\theta$: less than 0.2 mrad
$\Delta E/E$ in a pixel: 0.1 %

Effective atomic number simulated by considering the X-ray energy profile

Effective atomic number calculated at each pixel

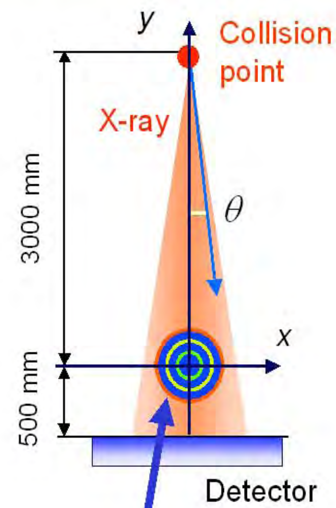


Average of the effective atomic numbers

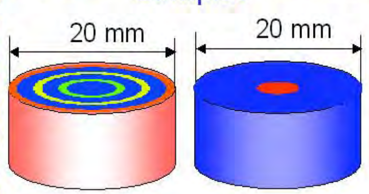


CT simulation for low to medium Z elements

Geometry of the CT system

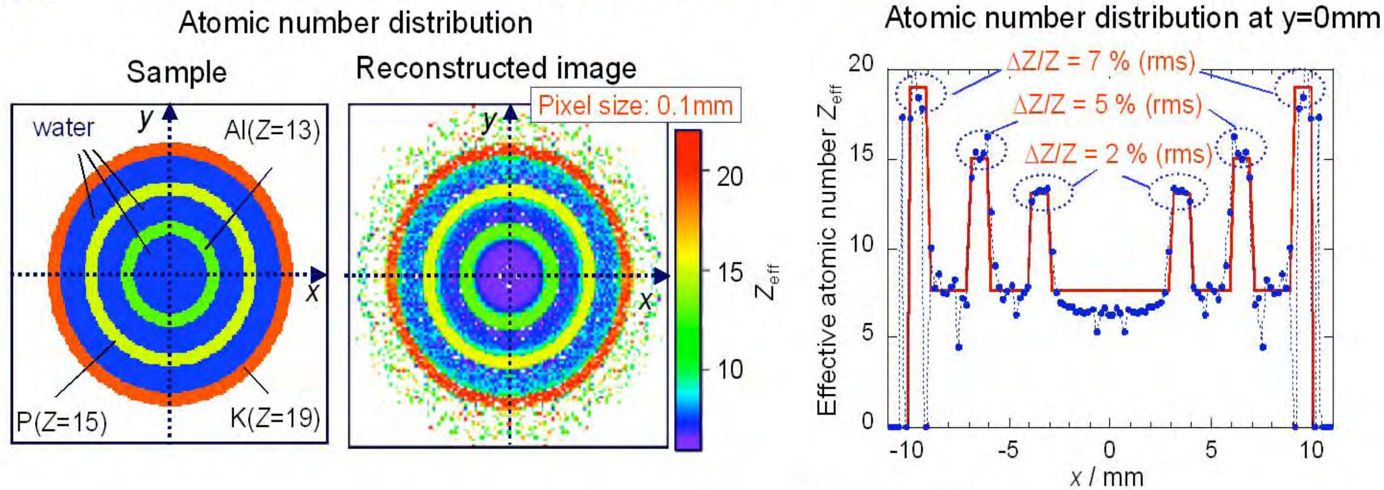


Samples

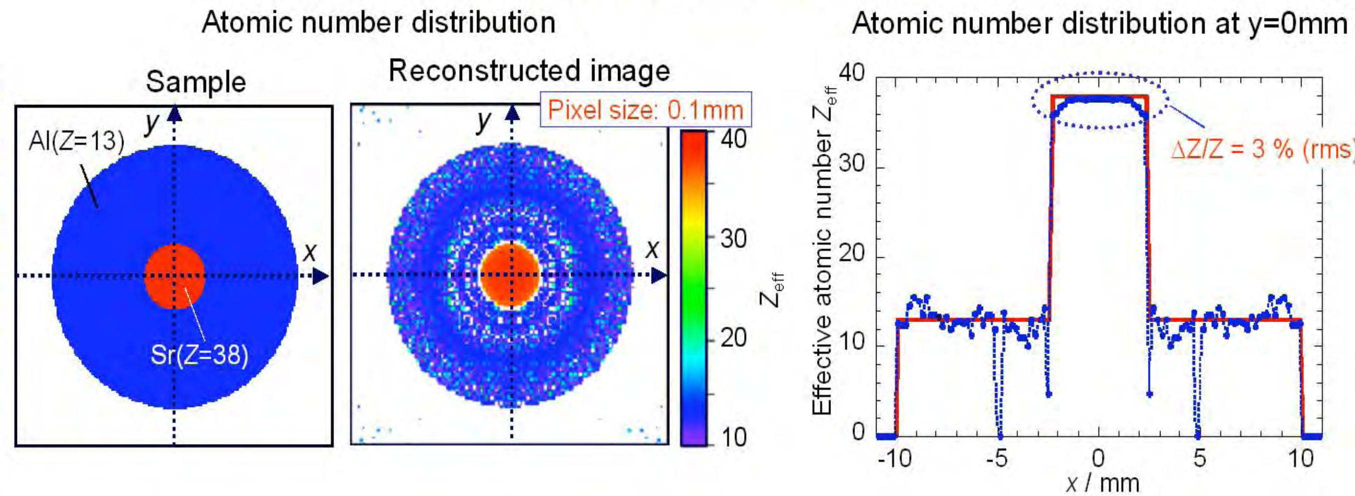


Cylindrical sample contains low to medium Z elements is simulated

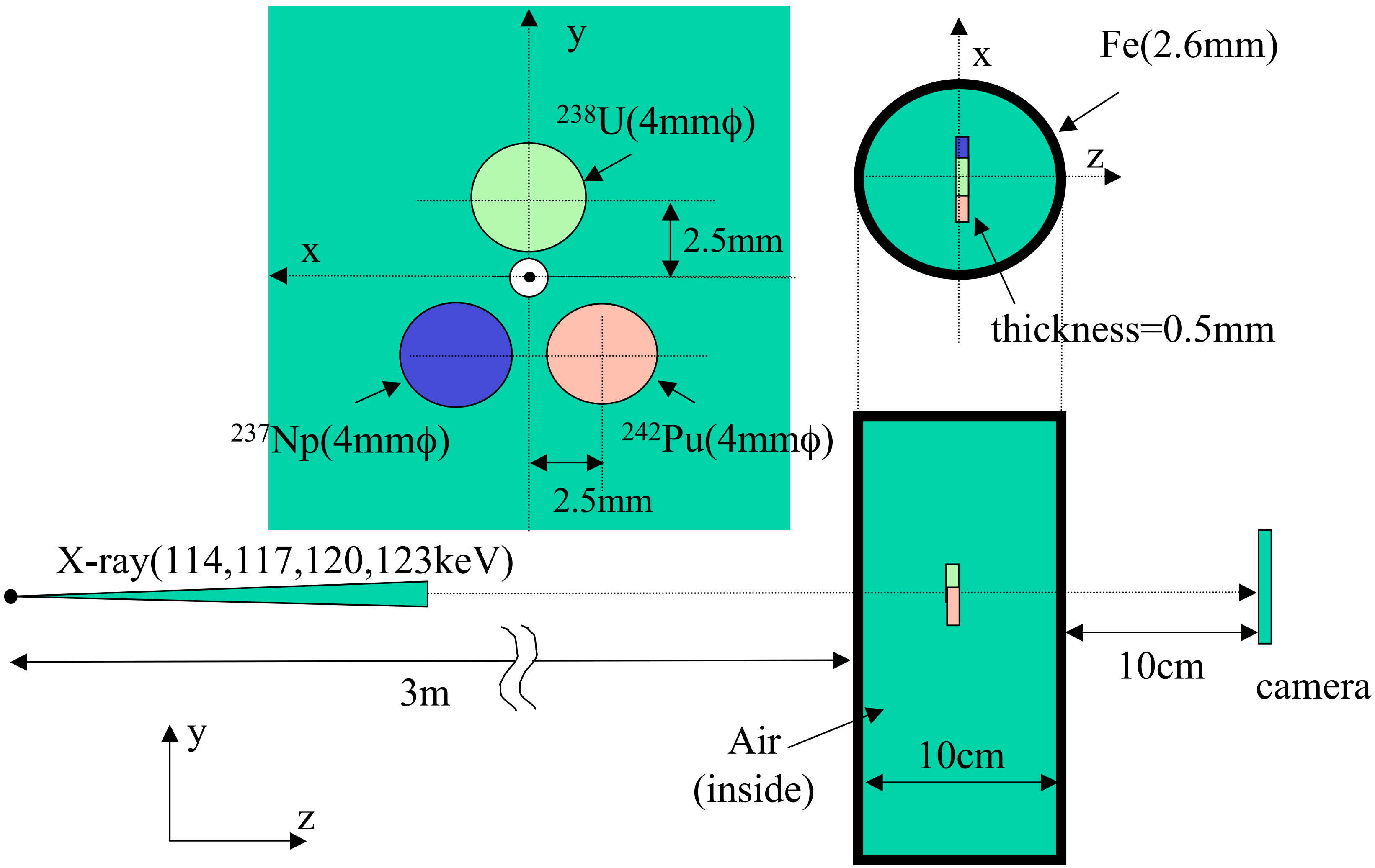
Sample 1 (low Z elements)



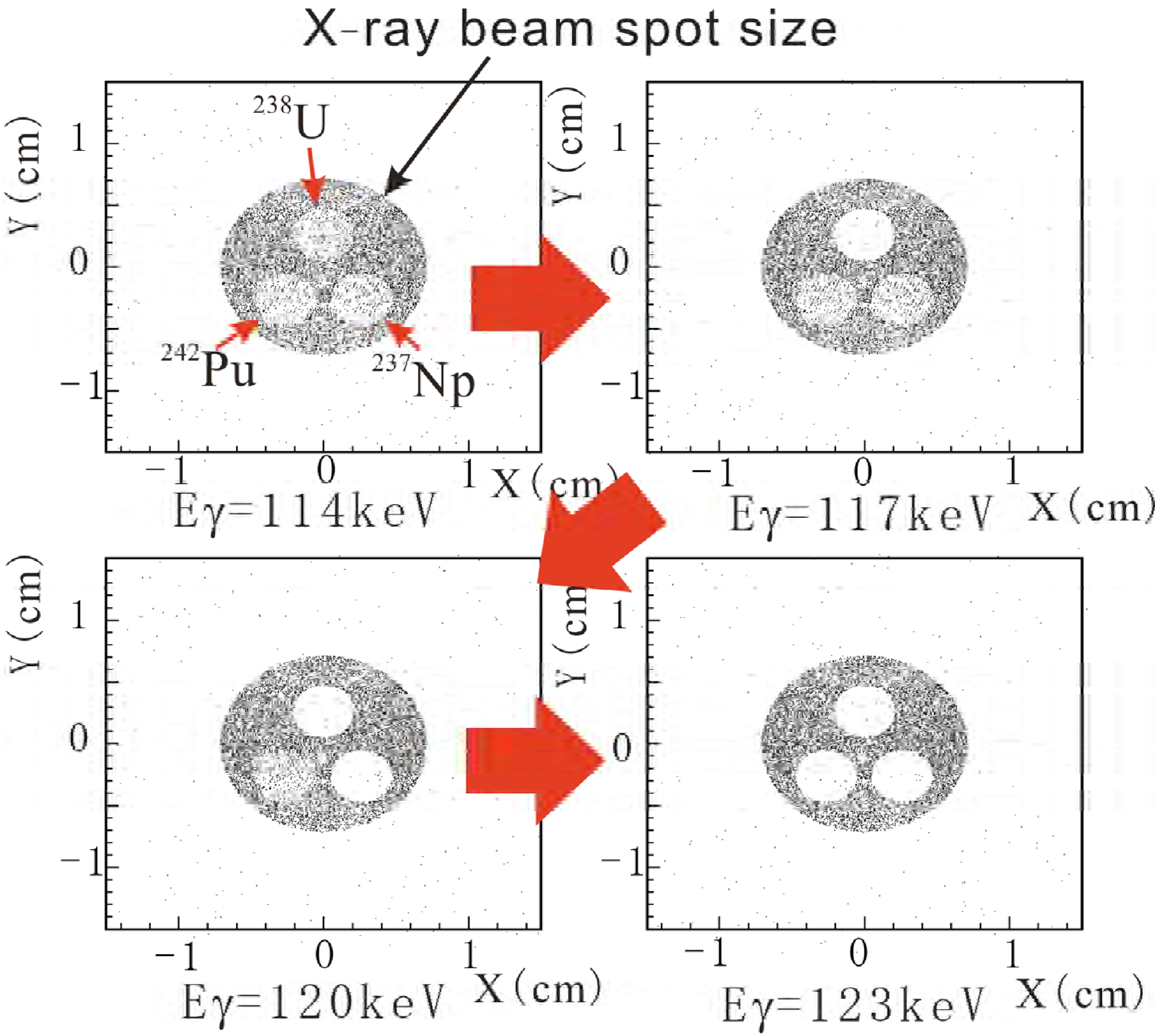
Sample 2 (medium Z elements)



Atomic number identification for material inside iron can
(EGS4 test geometry) (**** **Radiography** ****)



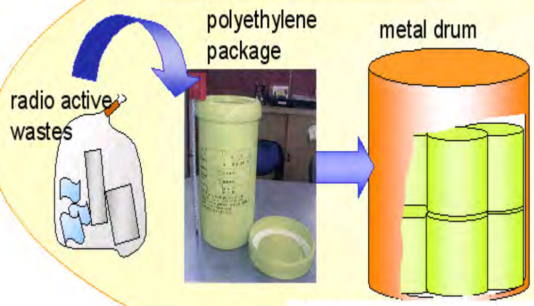
X-ray distribution at CCD camera (just a plot. Pixel size is not considered)



Application plans of the compact hard X-ray source

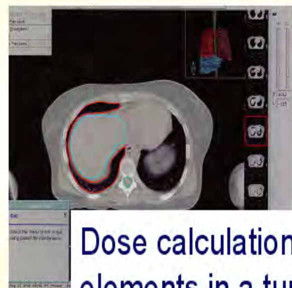
Atomic number identification by dual-energy X-ray CT

Nondestructive test



Element analysis inside a package

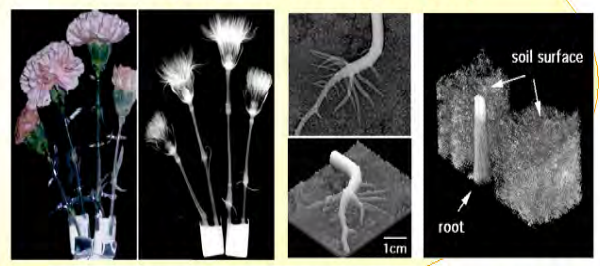
Radiation Treatment Planning



Dose calculation by considering elements in a tumor for advanced radiation therapy

Neutron radiography with X-ray CT

Imaging of water in a plant [3,4]

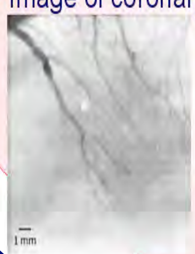


Movement of a element in a living plant

Compact monochromatic hard X-ray source

Micro vessel angiography

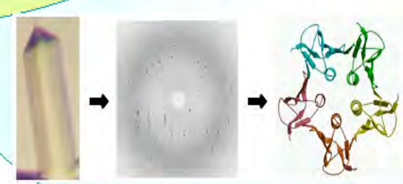
Image of coronary [5]



Diameter of micro vessel is less than 100μm

Micro vessel angiography will be tested with spatial resolution of 100μm

Protein structural analysis



Structure analysis in a small laboratory

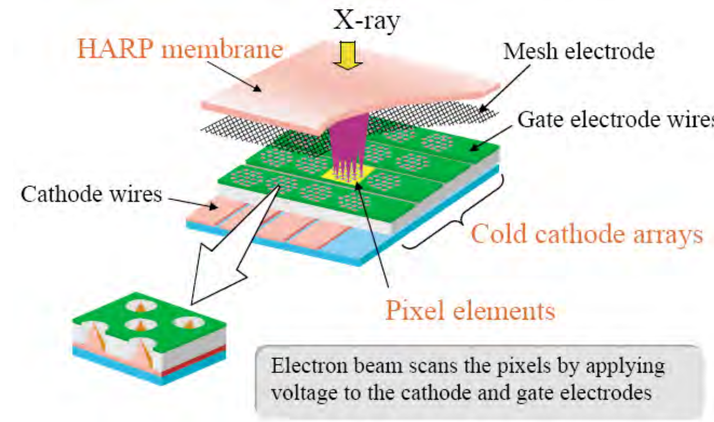
Scheme of CCB X-Ray Testing System

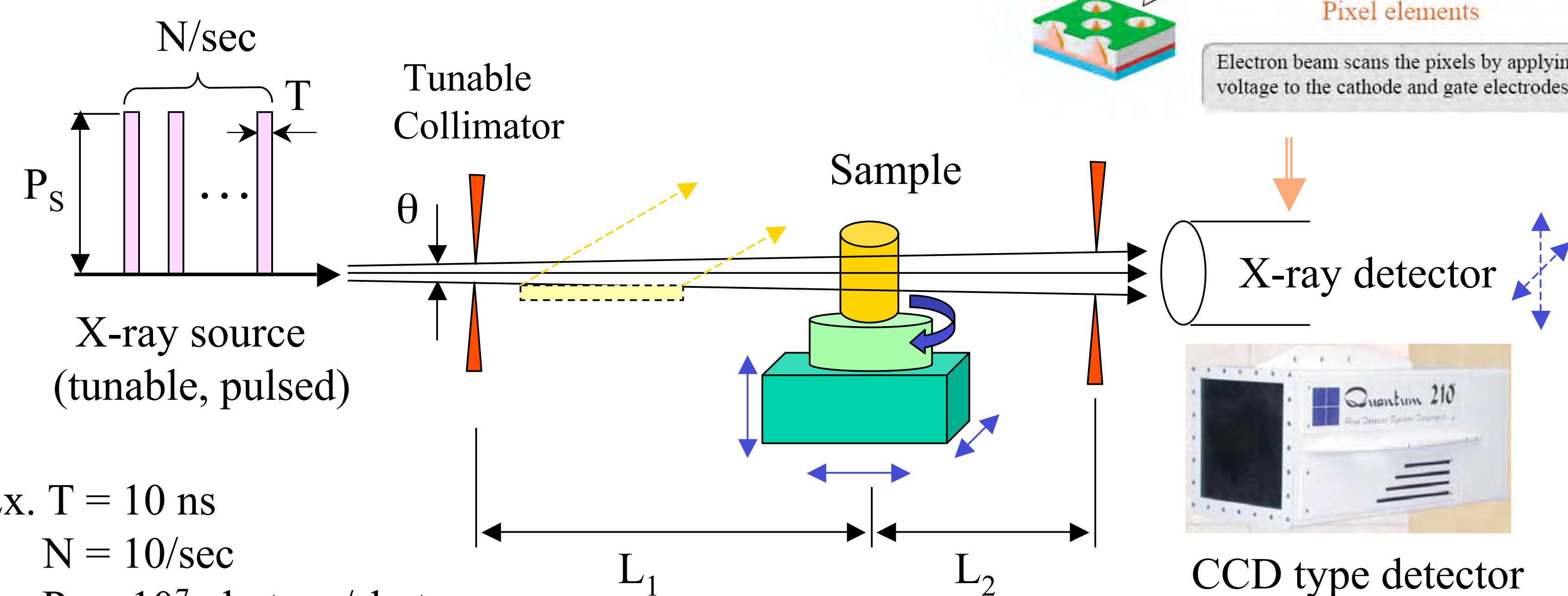
Compact Compton Backscattering

Hard X-ray Source (UTNL)

Photon energy:
10 ~ 50 keV

HARP-based detector (NHK)





Ex. T = 10 ns

N = 10/sec

$P_S = 10^7$ photons/shot

$P_F = 10^8$ photons/s

~ 10^9 photons/s; laser circulation

Periodic Motion of Sample (< 200 Hz)

CCD type detector

Active area: 21cm x 21cm

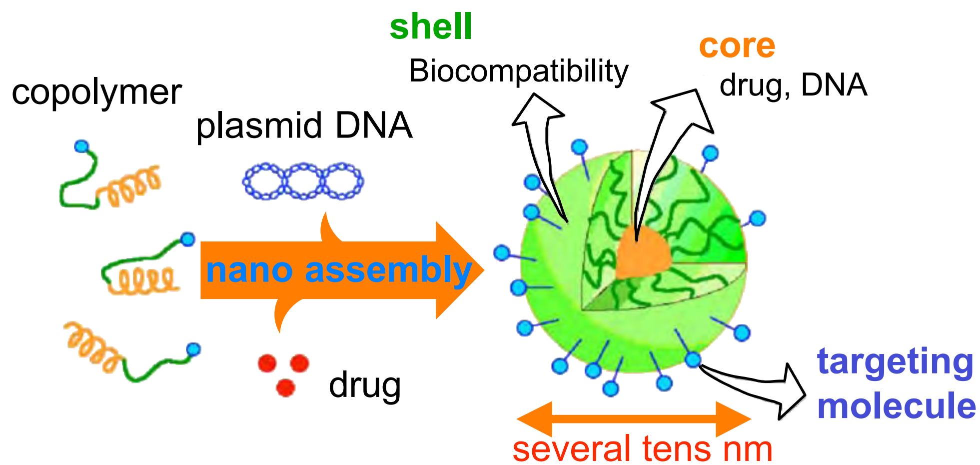
Spatial resolution: 90 μm

(~ 0.5 MUSD)

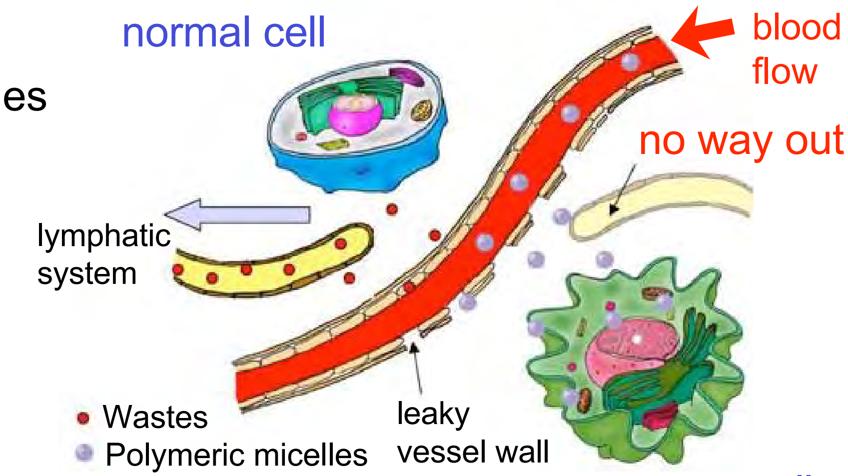
Applications of Hard X-ray and Nano Particles for Cancer Therapy and Diagnosis

Polymeric micelles for drug delivery

- Application for cancer therapy
- Site-specific targeting and accumulation by micelles



Tumor targeting



Ref.
K. Kataoka *et. al.* Adv. Drug Del. Rev. **47** (2001) 113.
K. Kataoka lab. http://bmw.mm.t.u-tokyo.ac.jp

X-ray application for cancer therapy and diagnosis with micelles

Diagnosis

- X-ray imaging of tumors
- Contrast agent including Iodine delivered and accumulated by micelles

Therapy

- Enhanced radiation damage to cancer cells targeted and stimulated by micelles with specific agents
- X-ray irradiation to micelles for nuclei acid and protein delivery to cancer cells

4D(space and time) control of Chemo-radiology

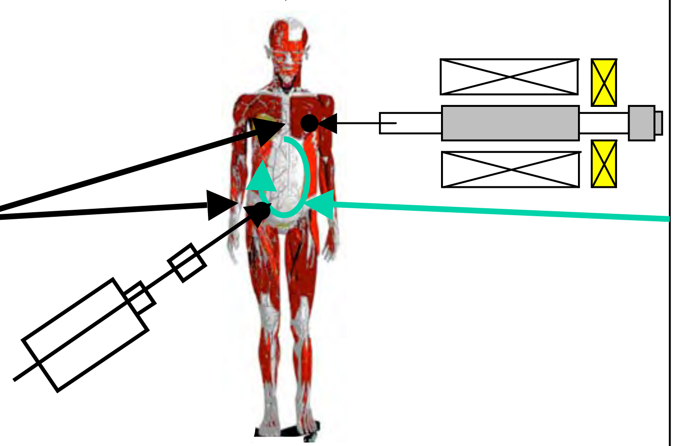
M.Uesaka(Nuclear Engineering Research Laboratory, Univ.Tokyo)
K.Nakagawa(Department of radiology, Univ.Tokyo Hospital)

1. Advanced compact accelerators available at hospital
- **higher RF(C,X,Ka,Ku,W-bands)**
- **Compton scattering hard X-rays**
- **compact ion accelerator**
- **Table-top TW laser**

2. Spatial control
(i)X-ray and electron
- **IMRT**

(ii)Compton scattering hard X-rays
- **Intravenous angiography**
- **Auger electron therapy**

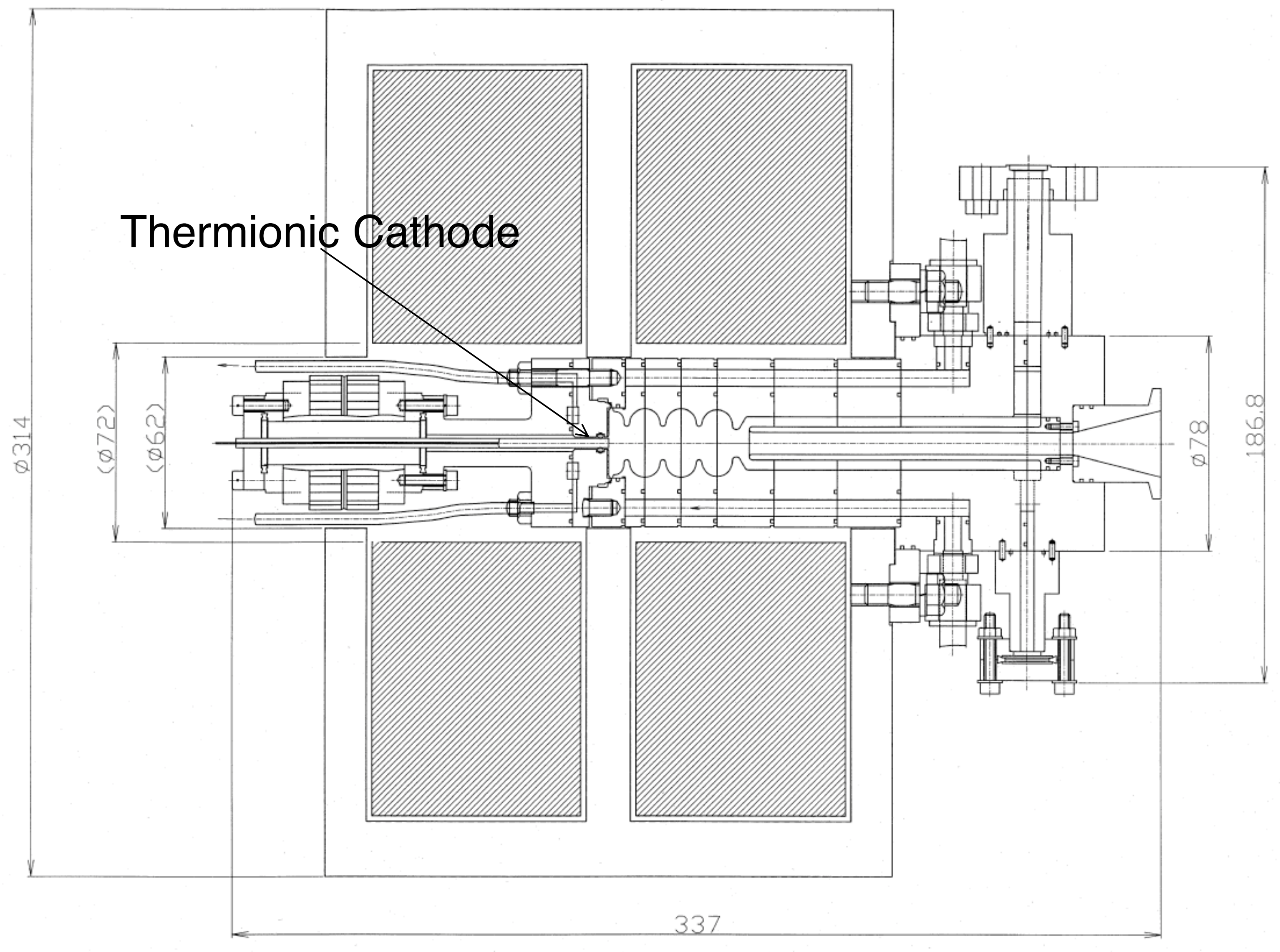
(iii)Precise spatial dosimetry
- **new material and phantom**



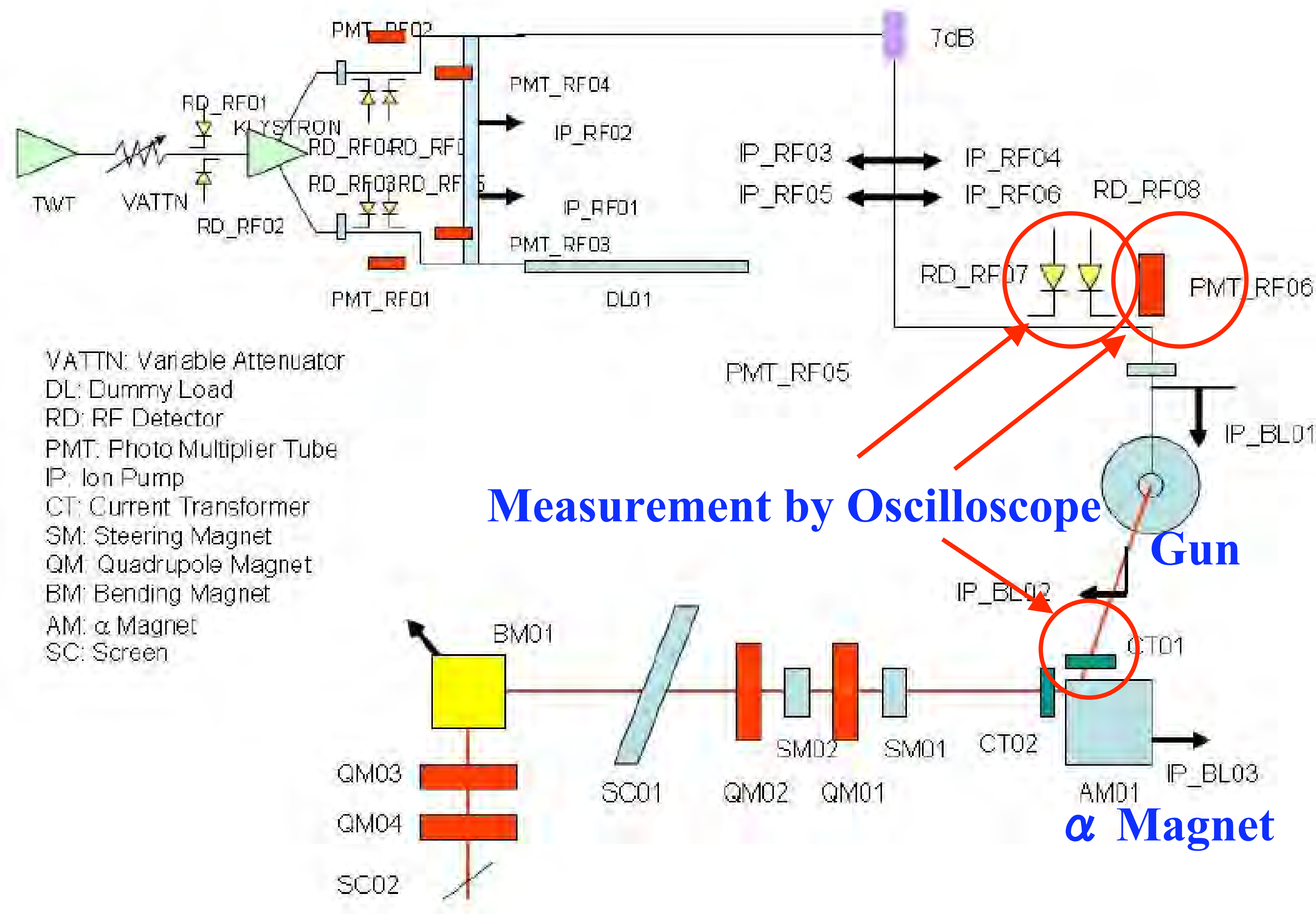
3.Temporal control
- **simulation and diagnosis for circulatory system(medicine, contrast agent, Au powder)**
- **Timing control of irradiation**
- **detection and control of oxygen content**
- **radiation chemistry of bio-water and control of OH radical content**
- **simulation and diagnosis of blood flow in capillary**
- **PET analysis**

4. Upgrading and optimization by integrated treatment program

Structure of RF Gun

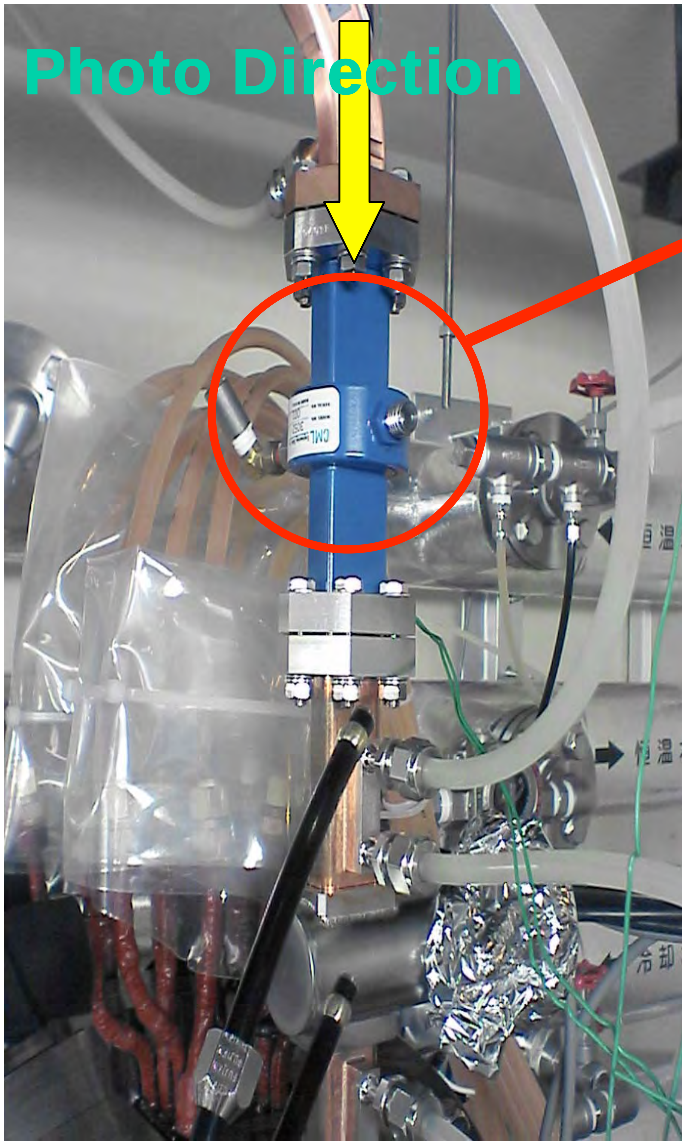


System of RF Gun Aging

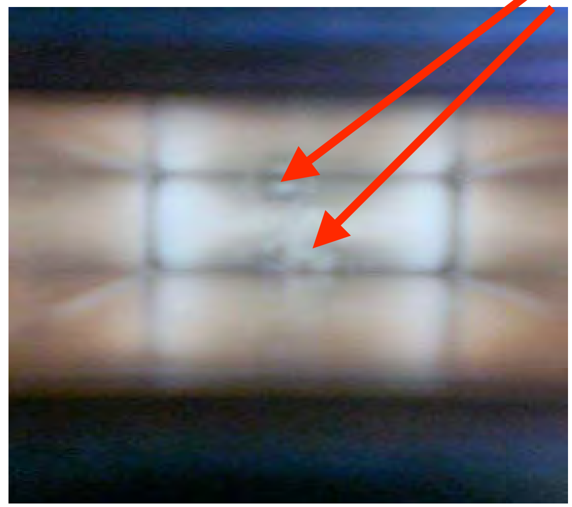


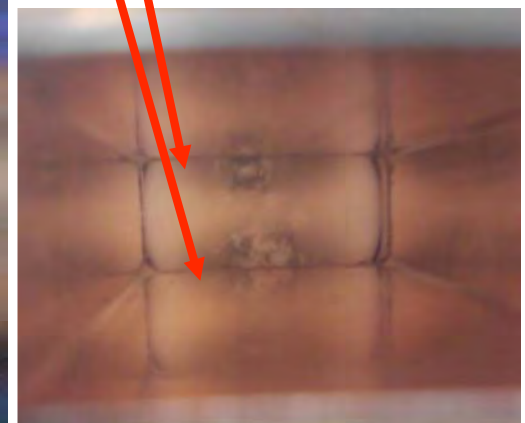
Trouble Point

Discharge @ RF Window（12MW）



Discharged Signatures





・Discharge of multi-pactaring

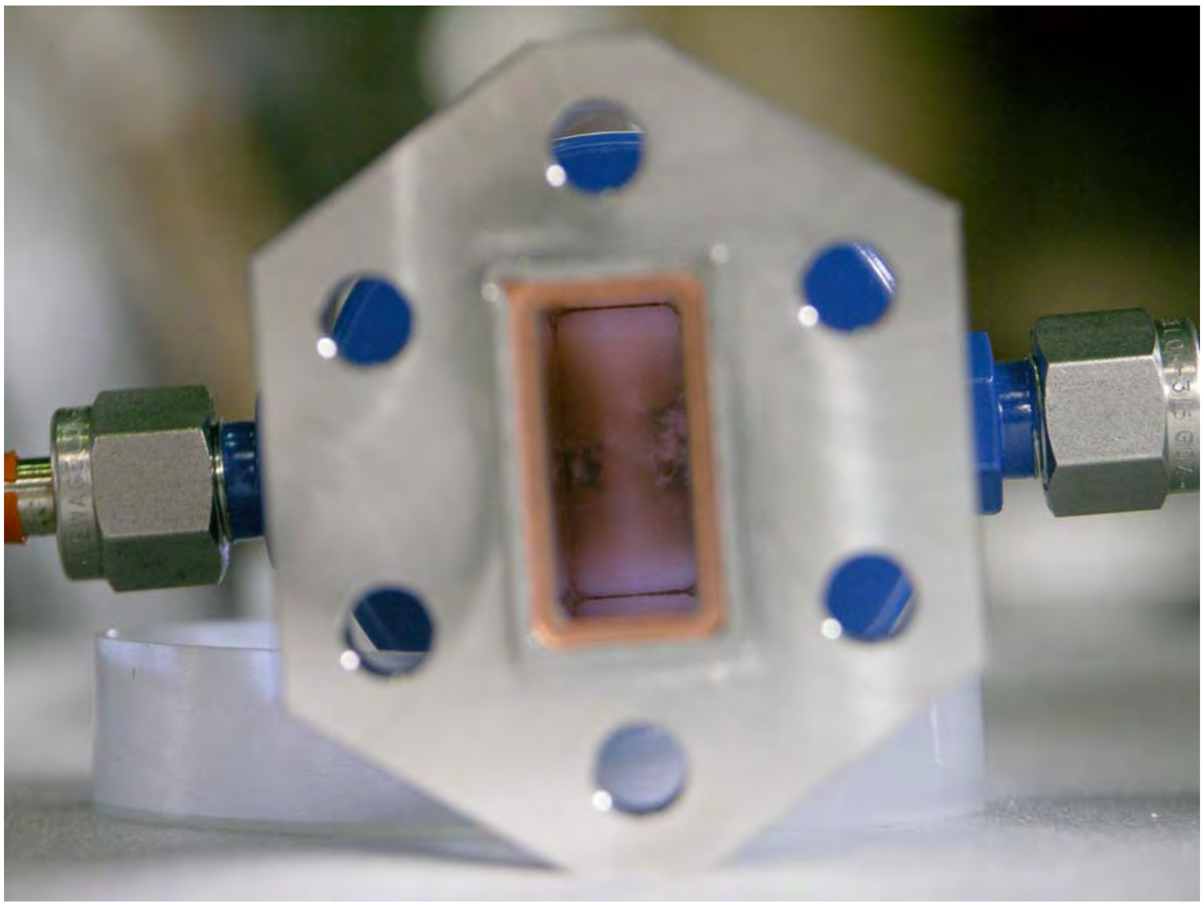
In addition, We could not see discharged signature at Gun side.

↓

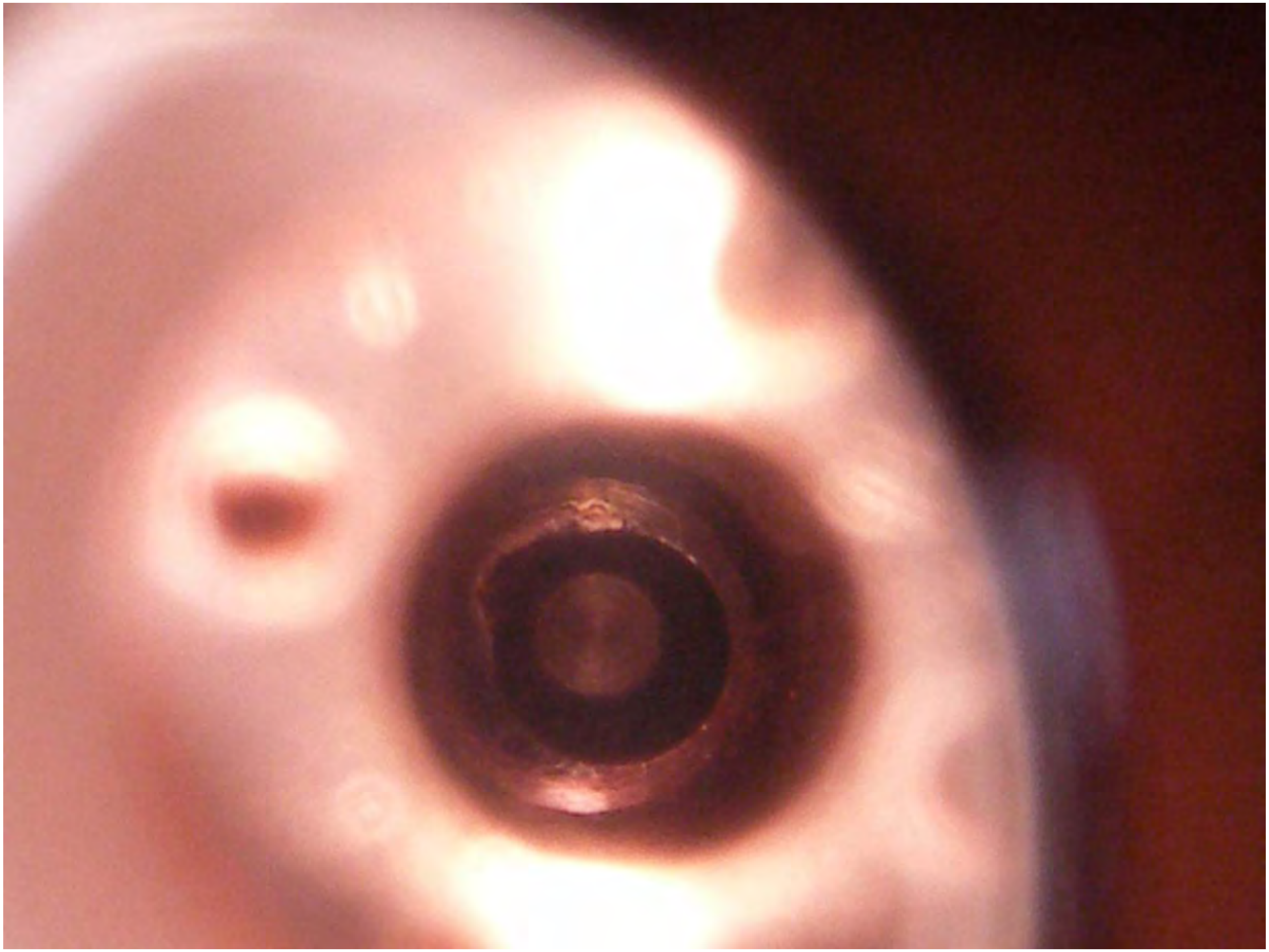
Worse vacuum at upstream

Amplified discharge

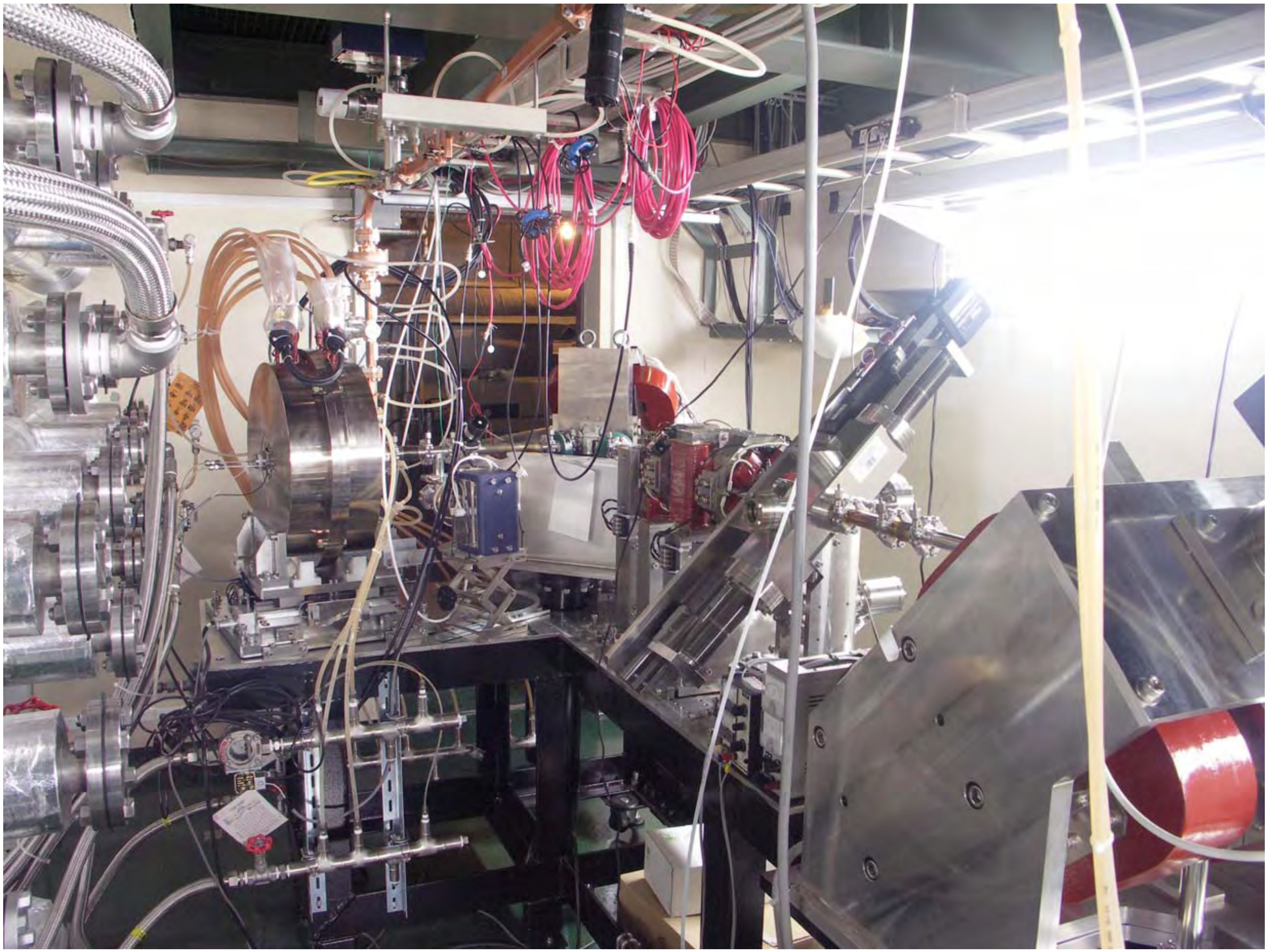
Discharged Signatures



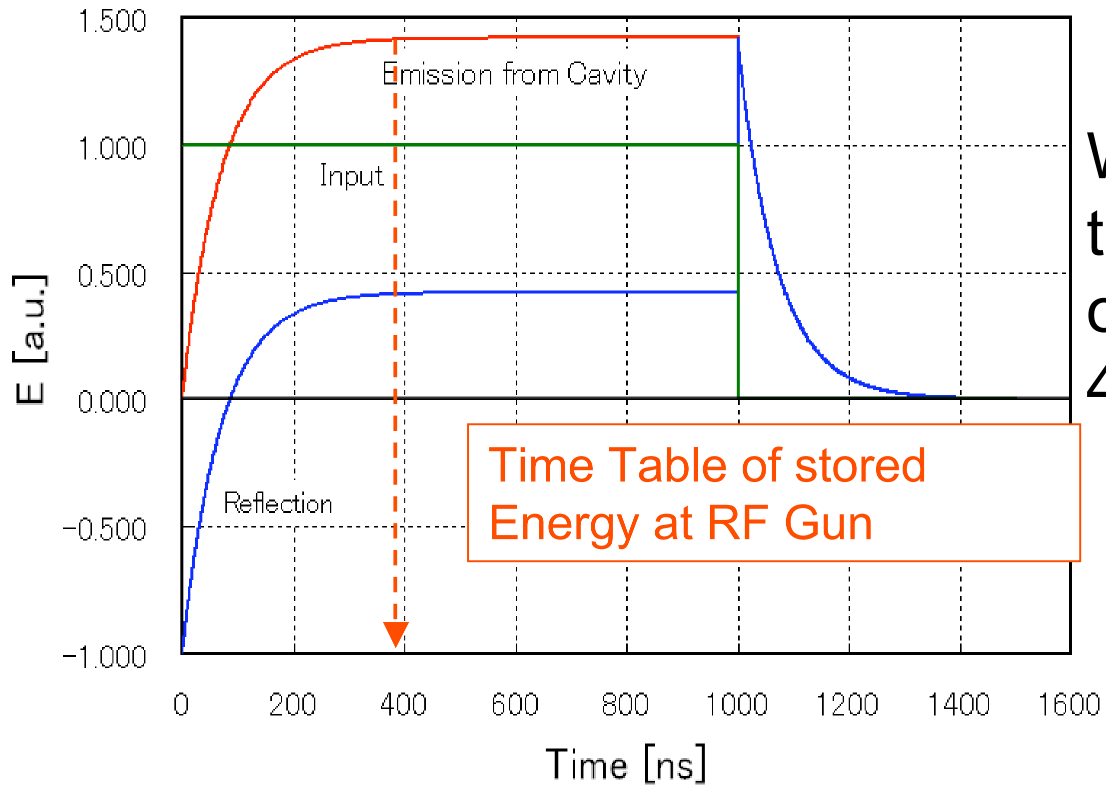
Cathode



New Beam Line



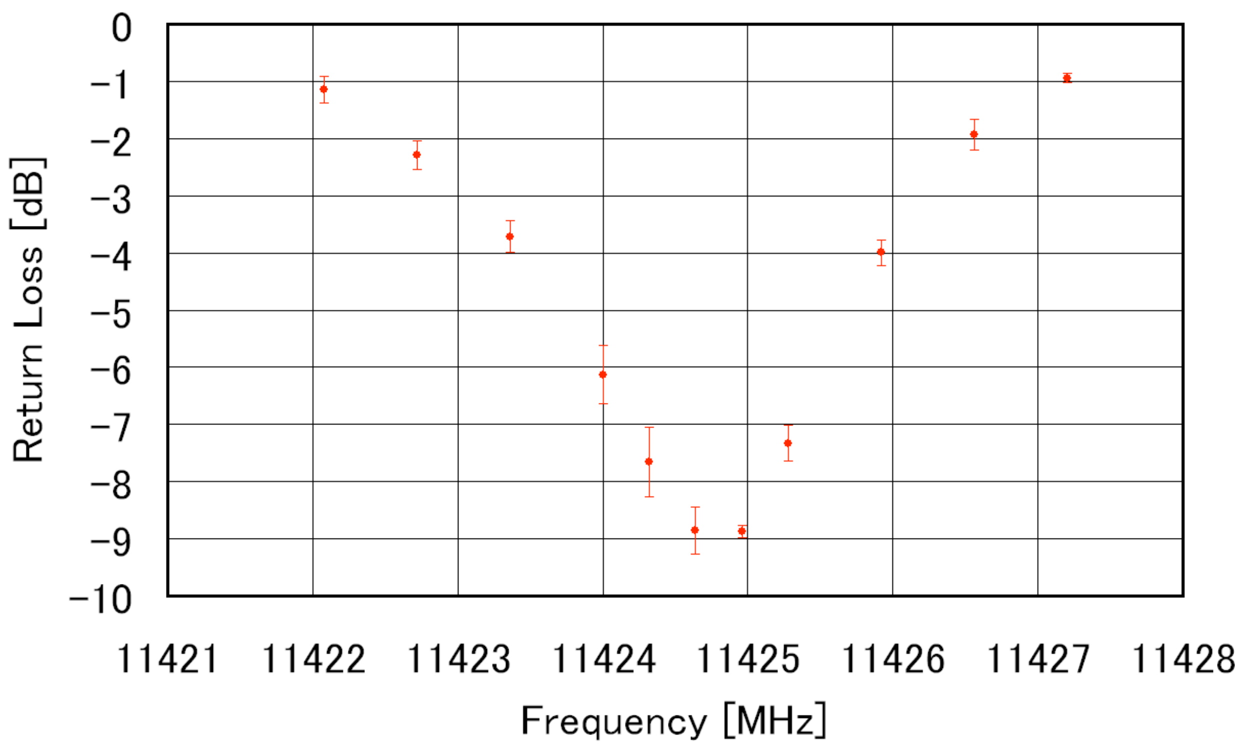
Stored Energy & Reflection



We can evaluate the characteristics of the gun with 400ns pulse.

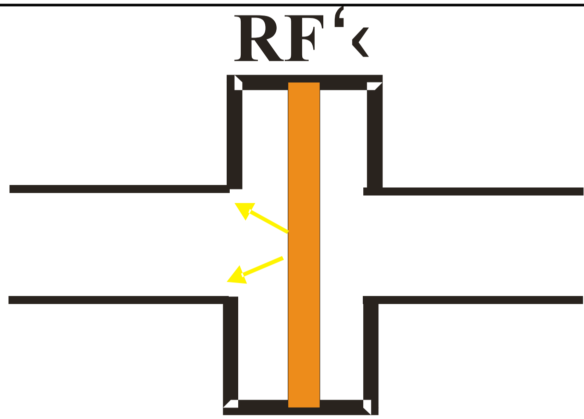
Flat → Cavity has been filled

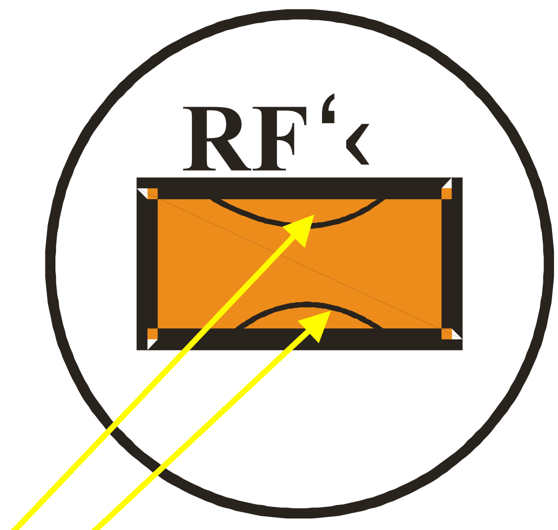
Return loss at the gun



Discharged signatures remain like shape of 8.

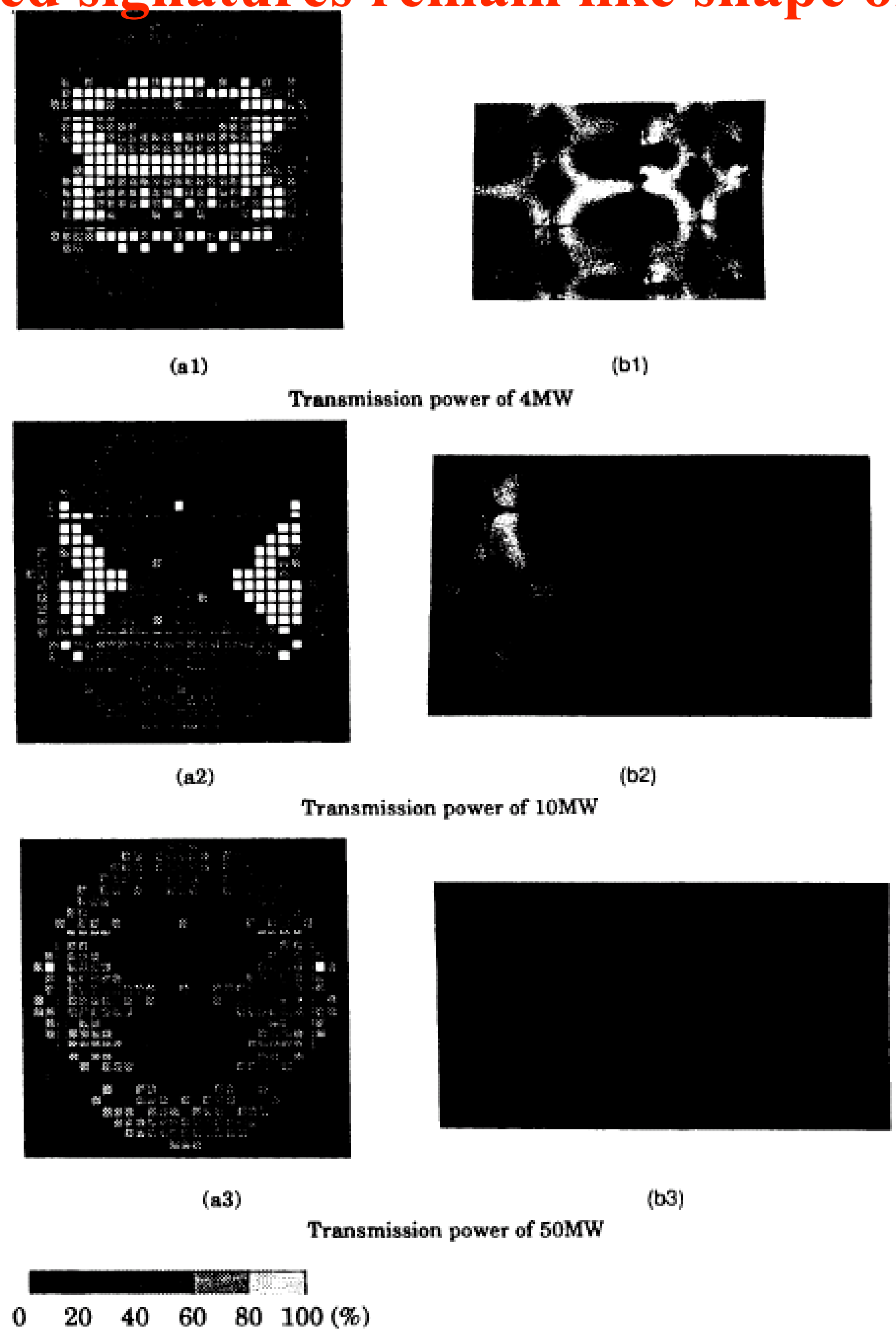
Discharge of multi-pactaring



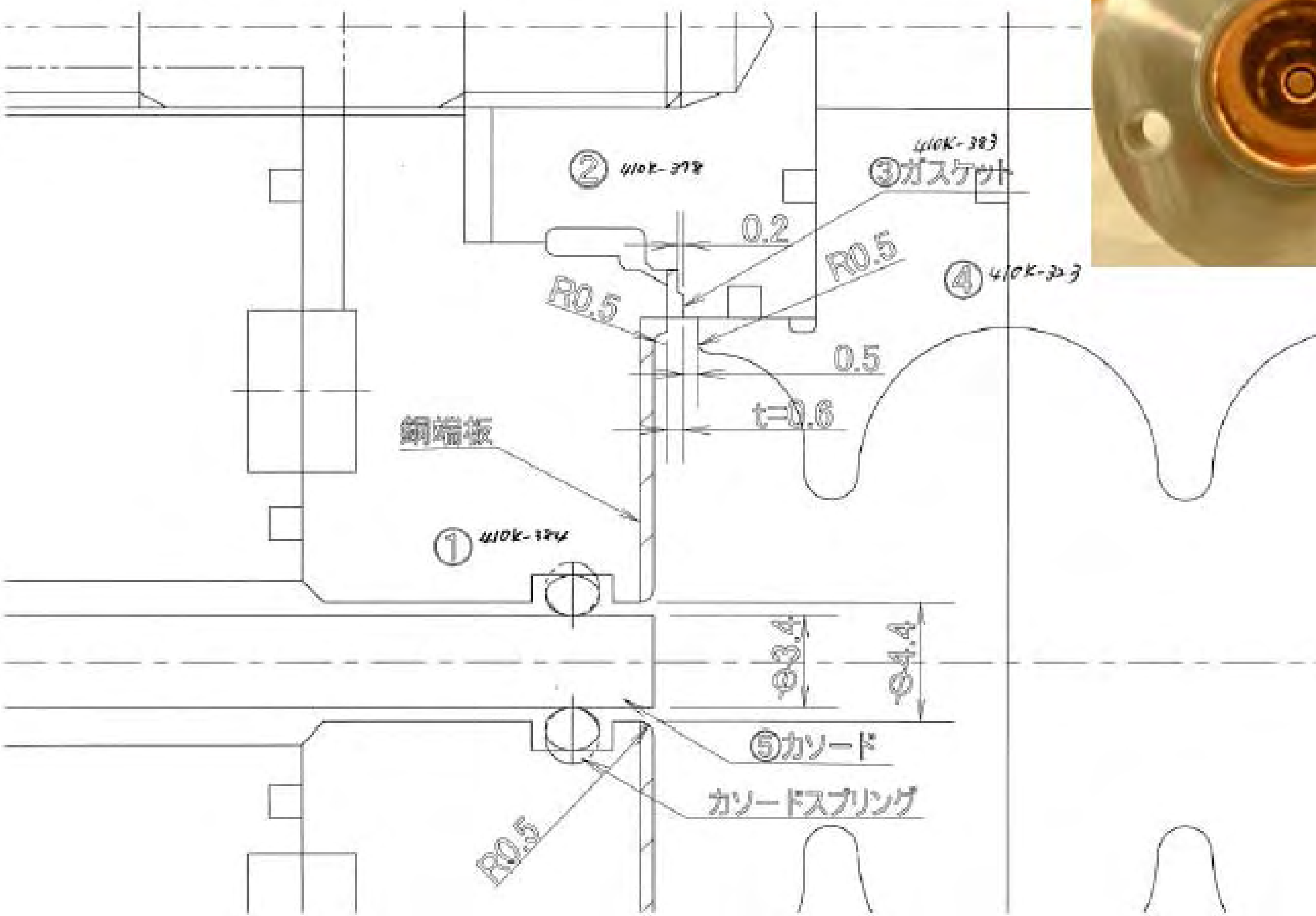


Discharged Signatures

Development of an S-band RF Window
for Linear Colliders
A.MIURA and H.MATSUMOTO
KEK Preprint 92-215 March 1993 A



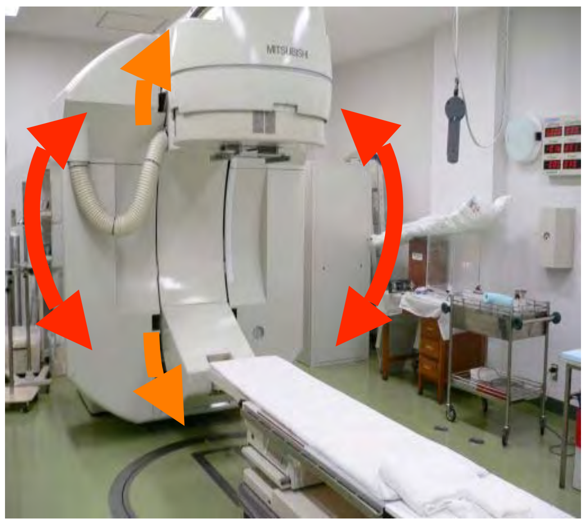
付録 B　ガスケット・カソード周辺詳細図および写真



Design of New Compact Stereotactic X-band Therapy Machine

Stable and high-current commercial S-band machine, but large

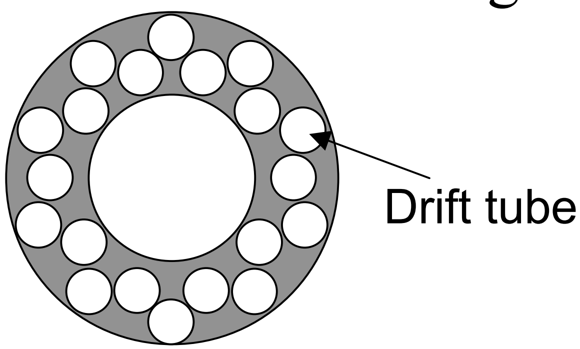
Compact X-band(9.3GHz) machine, but unstable and low-current



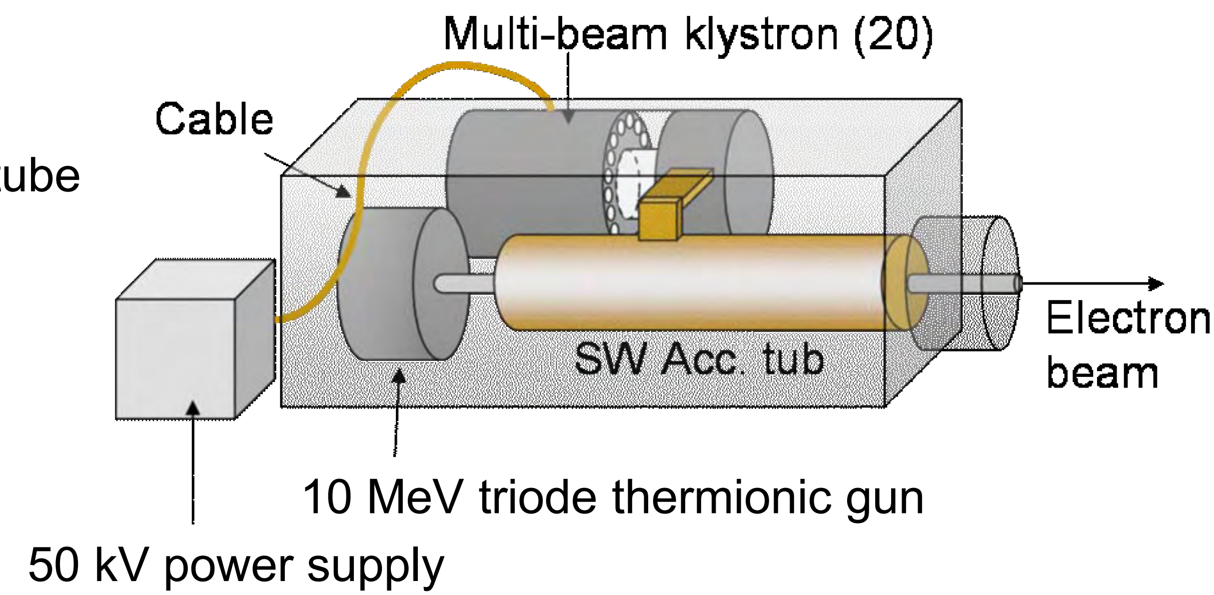
This stability and high-currents

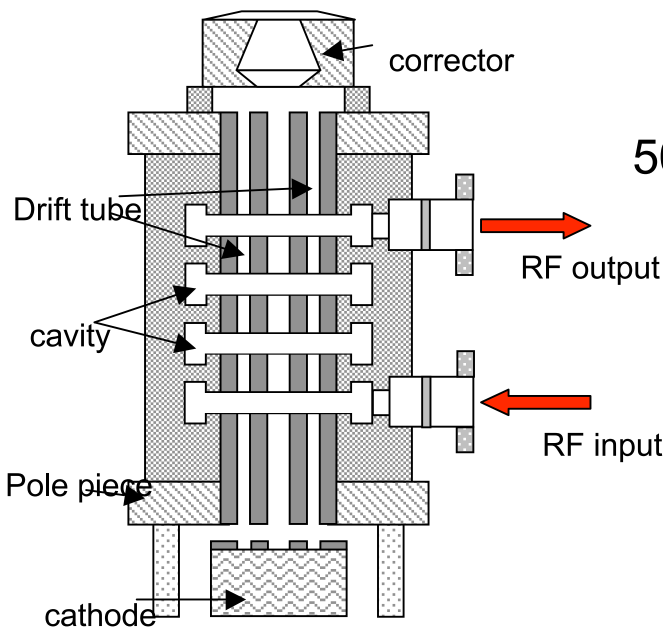
This size

Schematic layout of compact accelerator using multi-beam klystron (Type 1)

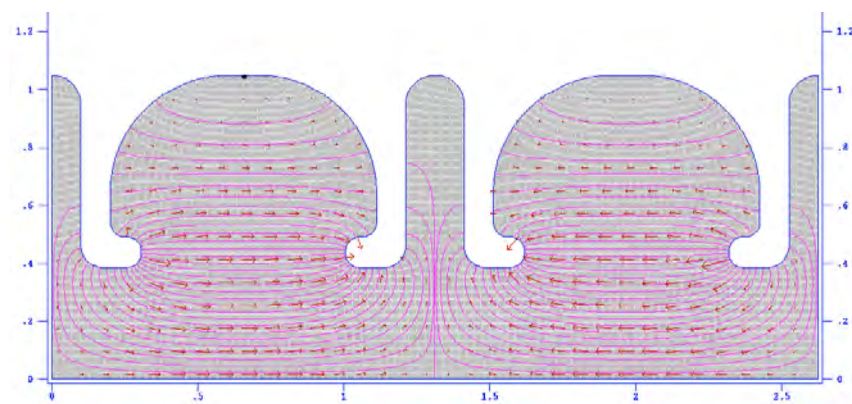


Top view



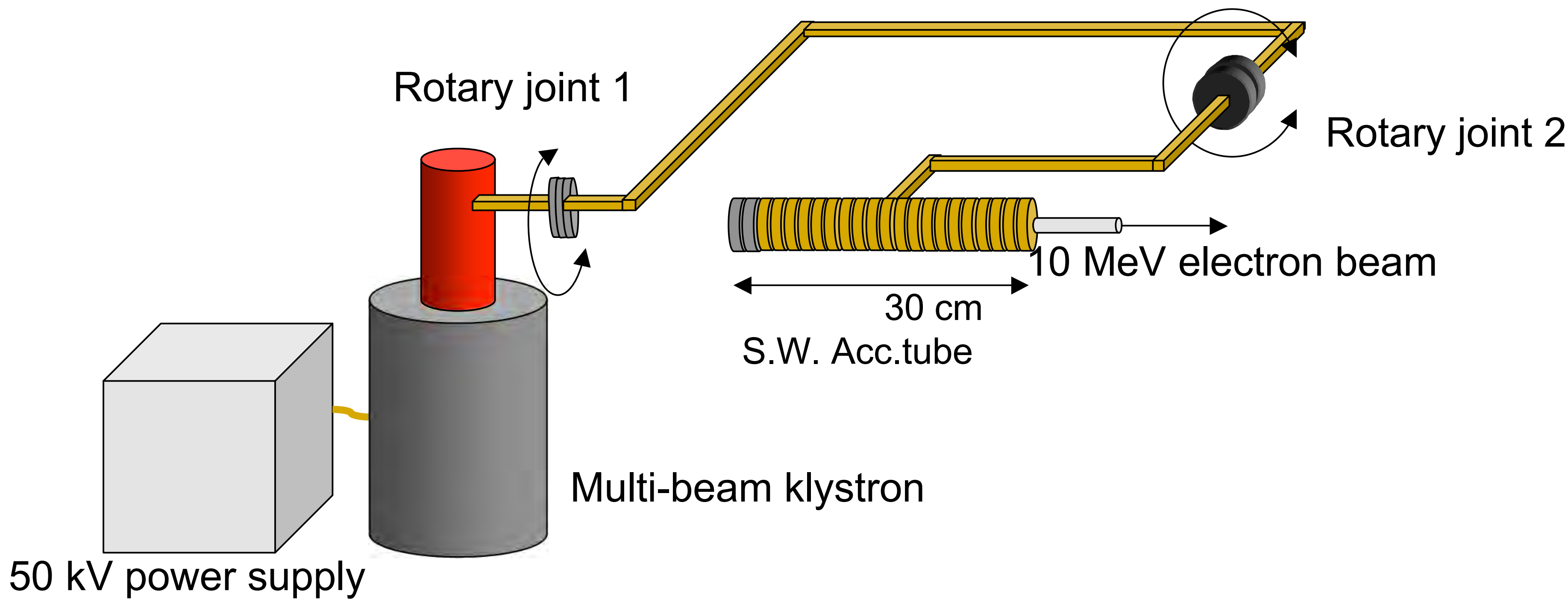


Side view



Structure of standing wave acc. tube

Schematic layout of compact accelerator using multi-beam klystron (Type 2)



Hard X-ray Sources by Thomson Scattering

Nuclear Engineering Research Laboratory
Graduate School of Engineering
University of Tokyo

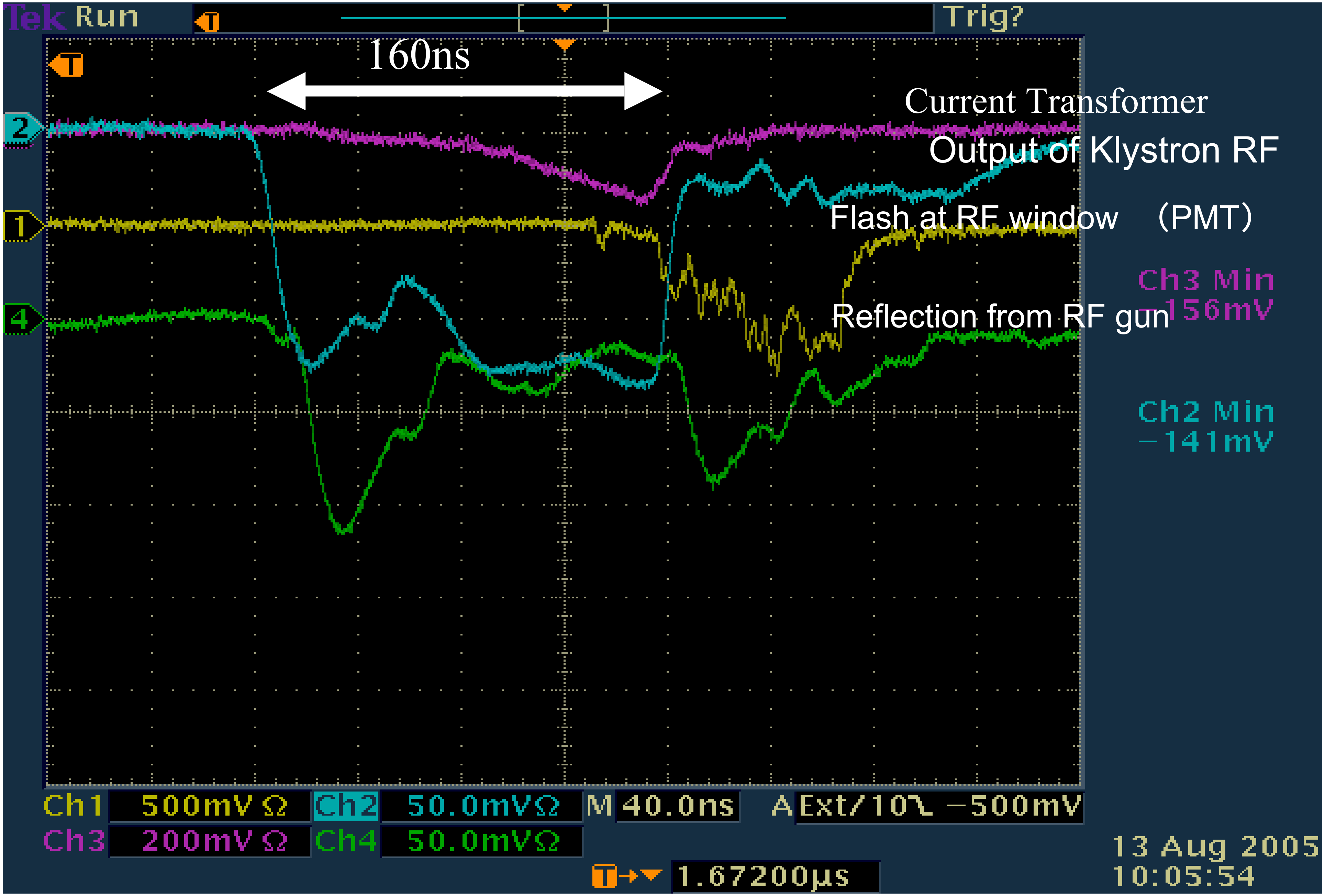
	Electron energy	Electron Charge	Laser wave length Laser Power	X-ray energy Photon number
Sumitomo [1] Heavy Industry	14 MeV (S-band)	400pC Single bunch	800nm, 300mJ (Ti:Sapphire, 300ps)	3.5keV <1.0E+4 photon/shot
MXI Systems Inc [2]	25MeV (S-band)	500pC Single bunch	1μm, 20J (Nd:Glass)	12, 50keV <1.0E+8 photon/sec
Univ.Tokyo/NIRS / KEK [3]	**35MeV (X-band)**	**20pCx10000 Multi bunch**	**1μm, 2J (Nd:YAG, 10ns)**	**33keV <1.0E+8 photon/sec**
Univ.Tokyo /NIRS	**~10MeV (Laser Plasma Acc.)**	**>10pC Single bunch**	**800nm, 300mJ (Ti:Sapphire, 40fs)**	**10-20keV ~2.0E+7photon/sec**

[1] :M.Yorozu *et al.* Jpn.J.Appl.Phys., Vol.40 (2001) pp. 4228-4232
[2] :F.E.Carroll *et al.* Am.J Rentgenol. 181 (2003) 1197
[3] :K.Dobashi *et al.* Jpn Appl.Phys., Vol.44 (2005) pp. 1999-2005

Therapy Accelerator

	Average Current	Peak Current	Repetition rate
Present Medical Linac Acc.	~30mA	~500 mA (3μs)	300Hz
Laser Plasma Acc.	~100 pA	~200 A (~50fs)	10Hz

Waveform of Oscilloscope



History of RF aging of RF-gun