3rd ILSF Advanced School on Synchrotron Radiation and Its Applications

September 14-16, 2013

Synchrotron Radiation in Medical Sciences

Ehsan Salimi
Science Group
Iranian Light Source Facility

Synchrotron Radiation in Medical Sciences

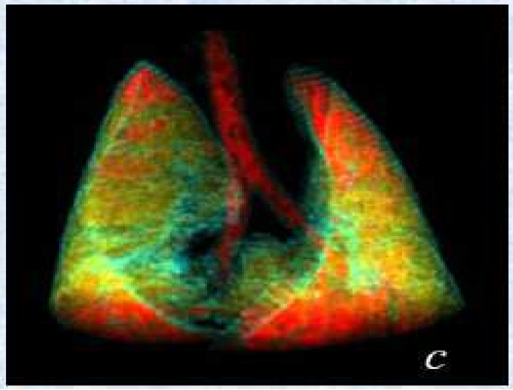
Growth and Outlook for an Emerging Field of Science

Wilhelm Roentgen's Laboratory
University of Wurtzburg 1895

115 Years
Later

European Synchrotron Radiation Facility
Grenoble France, 2010

Frau Roentgen's Hand



3D monochromatic high-resolution
dynamic digital imaging

Outline

- **Accelerators For Medical Applications**

- **Advantages of using SR for medical applications**

- **SR X-rays imaging techniques**
  - Absorption, K-edge and L-edge imaging
  - PHase Contrast Radiography (PHC)
  - Diffraction Enhanced Imaging (DEI)

- **Radiotherapy techniques with SR X-rays**
  - Microbeam Radiation Therapy (MRT)
  - Stereotactic Synchrotron Radiation Therapy (SSRT)

- **Medical Beamlines in Other Facilities**

ACCELERATORS FOR MEDICAL APPLICATIONS

- More than half of particle accelerators at present running in the world are devoted to medical applications.
- The main areas of use are: (i) radioisotope production, (ii) radiotherapy, (iii) biomedical research.

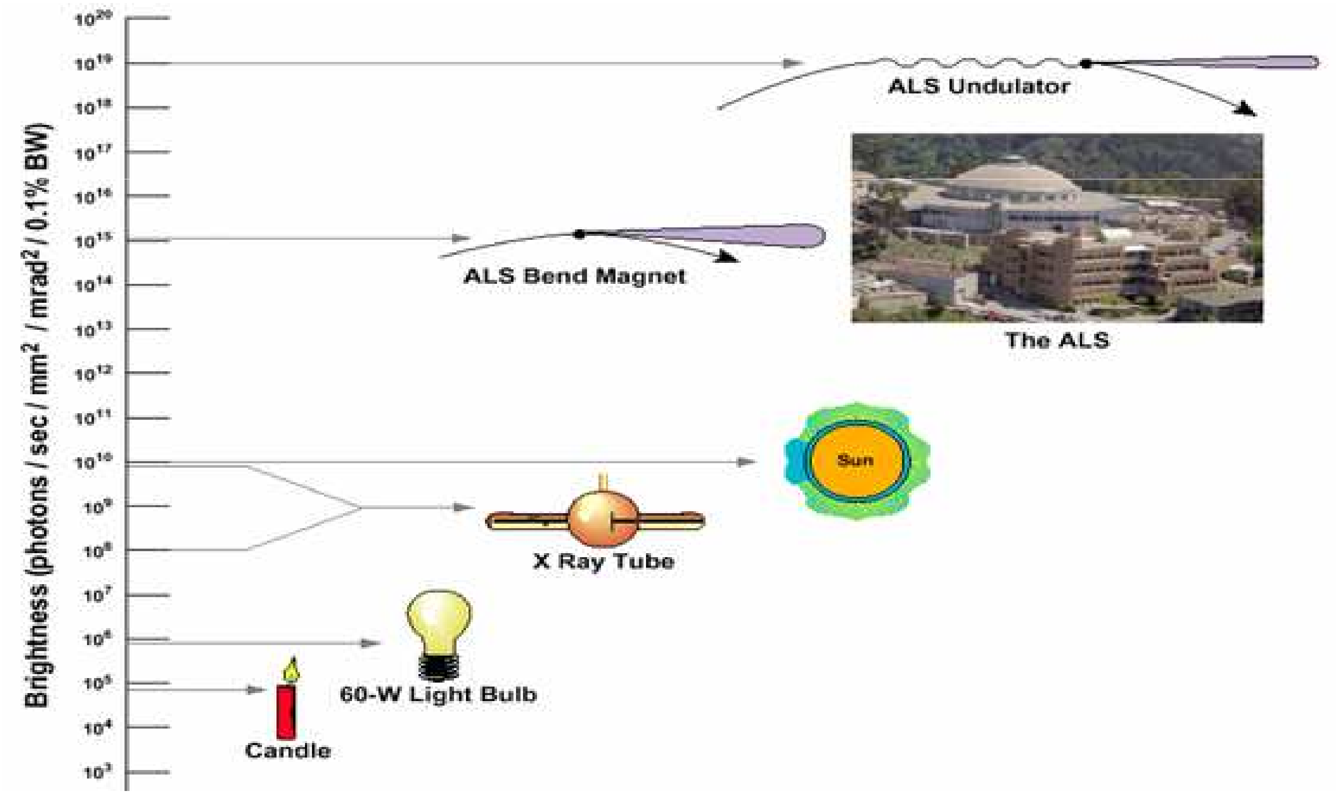
- 80% of all the biomedical accelerators are devoted to radiotherapy with either X-rays or hadron beams.

Cancer

- Worldwide the estimated number of new cancer cases each year is expected to rise from 10 millions in 2000 to 15 millions by 2020.
- Cancer is second cause of death in High-income countries and third in Iran
- Therefore combating cancer is a major societal and economical issue in the world

Advantages of using SR for medical applications

1. Brilliant quick experiments on small samples, high dose-rates, reduction of exposure time



Advantages of using SR for medical applications

2. Collimated – the beam can be focused down to less than a micron, reduced scatter on images

3. Continuous spectrum - from infrared to hard x-rays, optical devices select and scan

4. Polarised – this minimises background scattering, improves sensitivity and enables measurement of circular dichroism

5. Pulsed – the electron bunches produce nanosecond light pulses, enabling process kinetics to be followed and 'movies' of reactions to be made.

Medical imaging with synchrotron radiation

- SR Medical imaging techniques are based on absorption and refraction of X-rays.
- Phase effects techniques require a high degree of spatial coherence of the radiation and it seems possible only at SR facilities.
- Excellent results is due to the small opening angle in the vertical direction and the possibility to place the detector at a large distance.
- Beam hardening due to the sample absorption of the low energy photons is also avoided.

Phase detection imaging

- Conventional radiologic studies are based on only absorption effects.
- The effects on propagation of the X-ray wave can be described by the refraction index n: $n = 1 - \delta + i\beta$
- imaginary component β related to the absorption and by a real component α related to phase-shift due to scattering of the waves.
- Phase contrast may also prove useful in biological and medical studies because it falls off less quickly at higher energies than absorption contrast: δ αE-2 , whereas β αE-4.
- By increasing the energy, phase contrast imaging could allow a significant dose reduction with little deterioration of the diagnostic information.

phase contrast imaging

- Beyond the detail, the waves refracted (phase shifted) by the detail itself strongly interfere with the unrefracted waves.

- This interference effect takes place along the border of the detail inside a narrow angular region and it results in strong interference patterns inside this region that could be detected

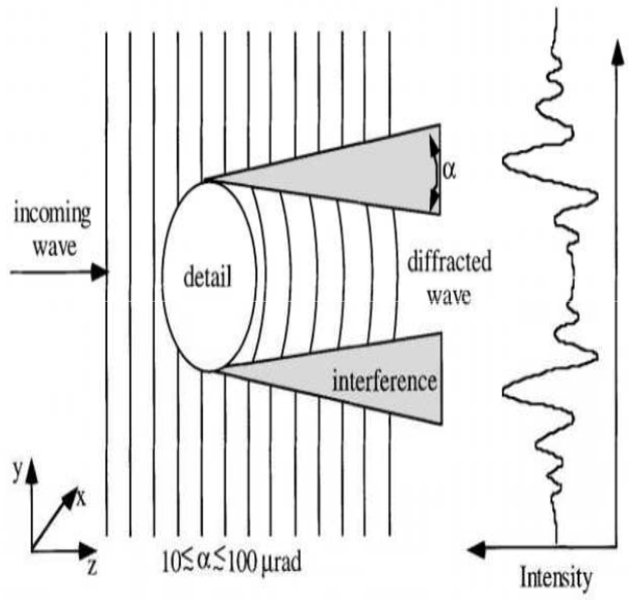
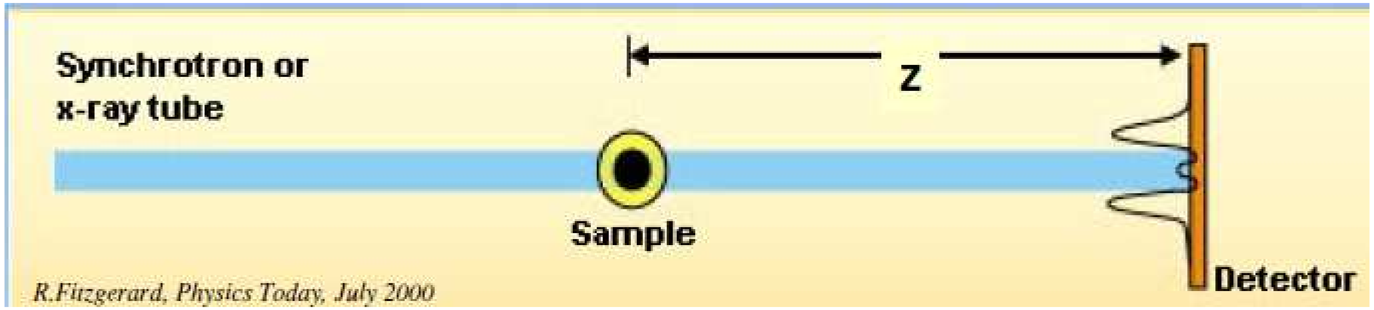
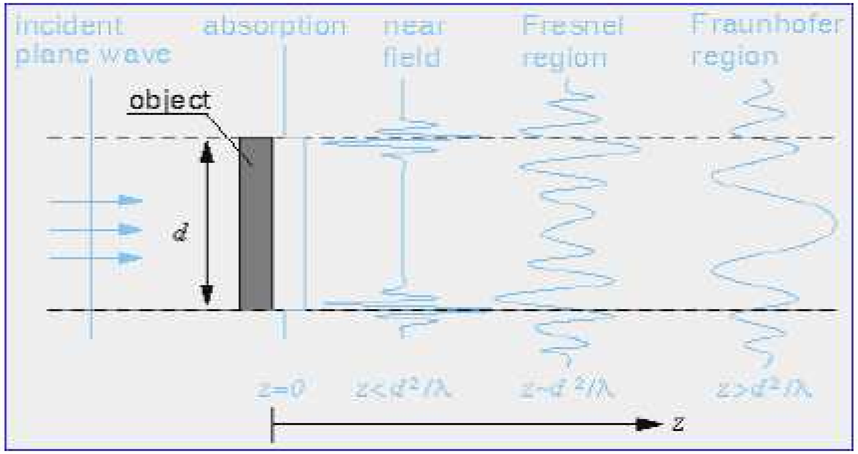


Figure 1.4: Scheme of the process that governs the in-line phase contrast technique.

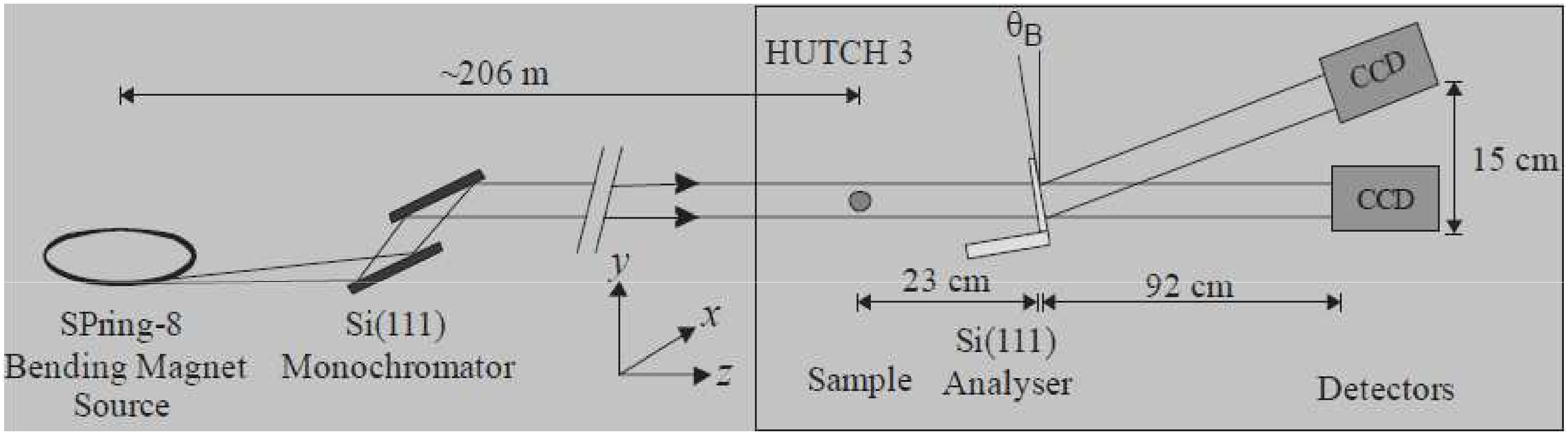
PHase-Contrast radiography (PHC)



- The technique exploits the high spatial coherence of the X-ray source.
- z =0 -> absorption image
- For z > 0 -> interference between diffracted and un diffracted wave produces edge and contrast enhancement. A variation of δ is detected

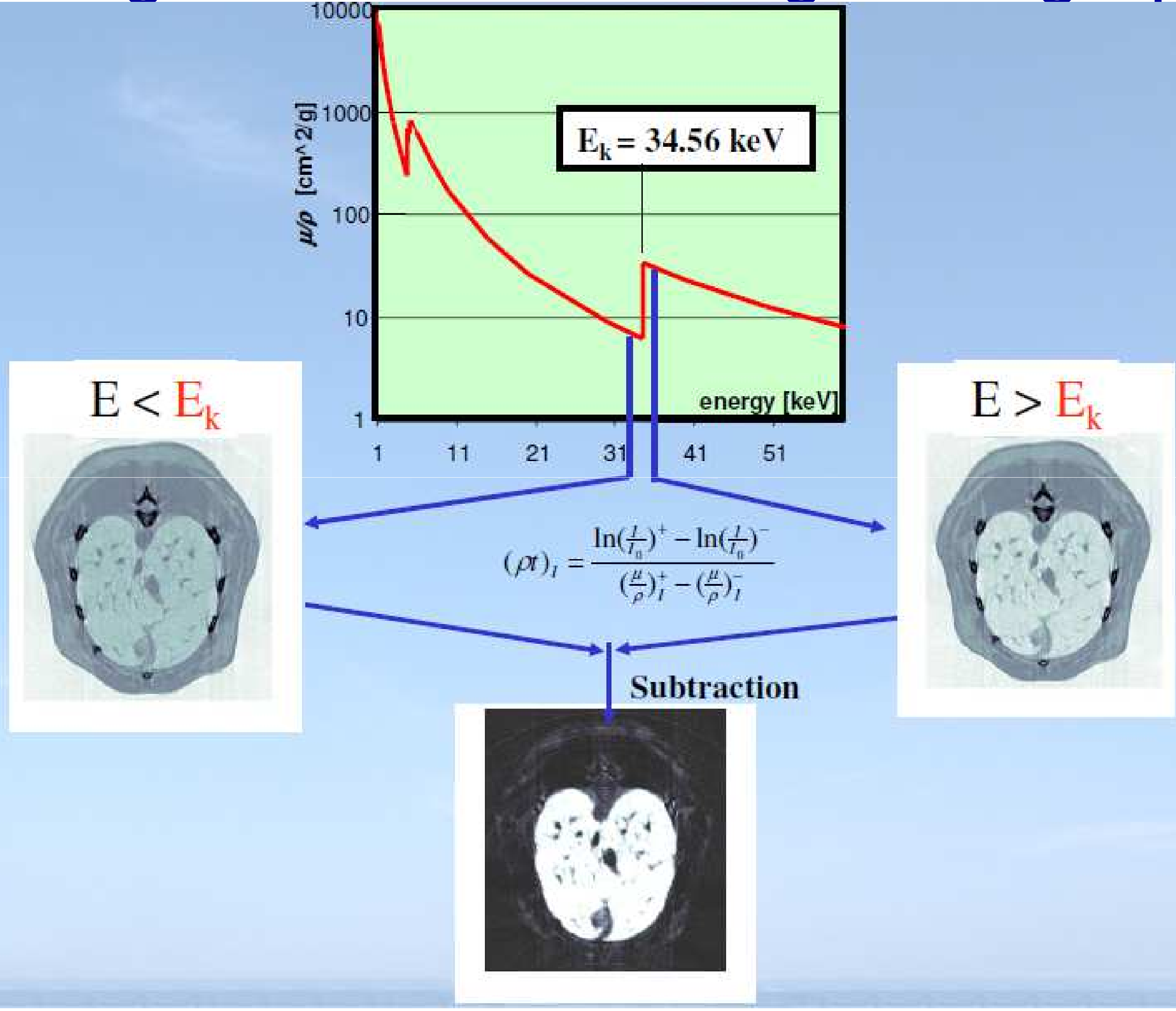


Imaging Setup



- **Beamline 20B2, Spring-8, Japan. 25 keV beam of highly coherent radiation.**

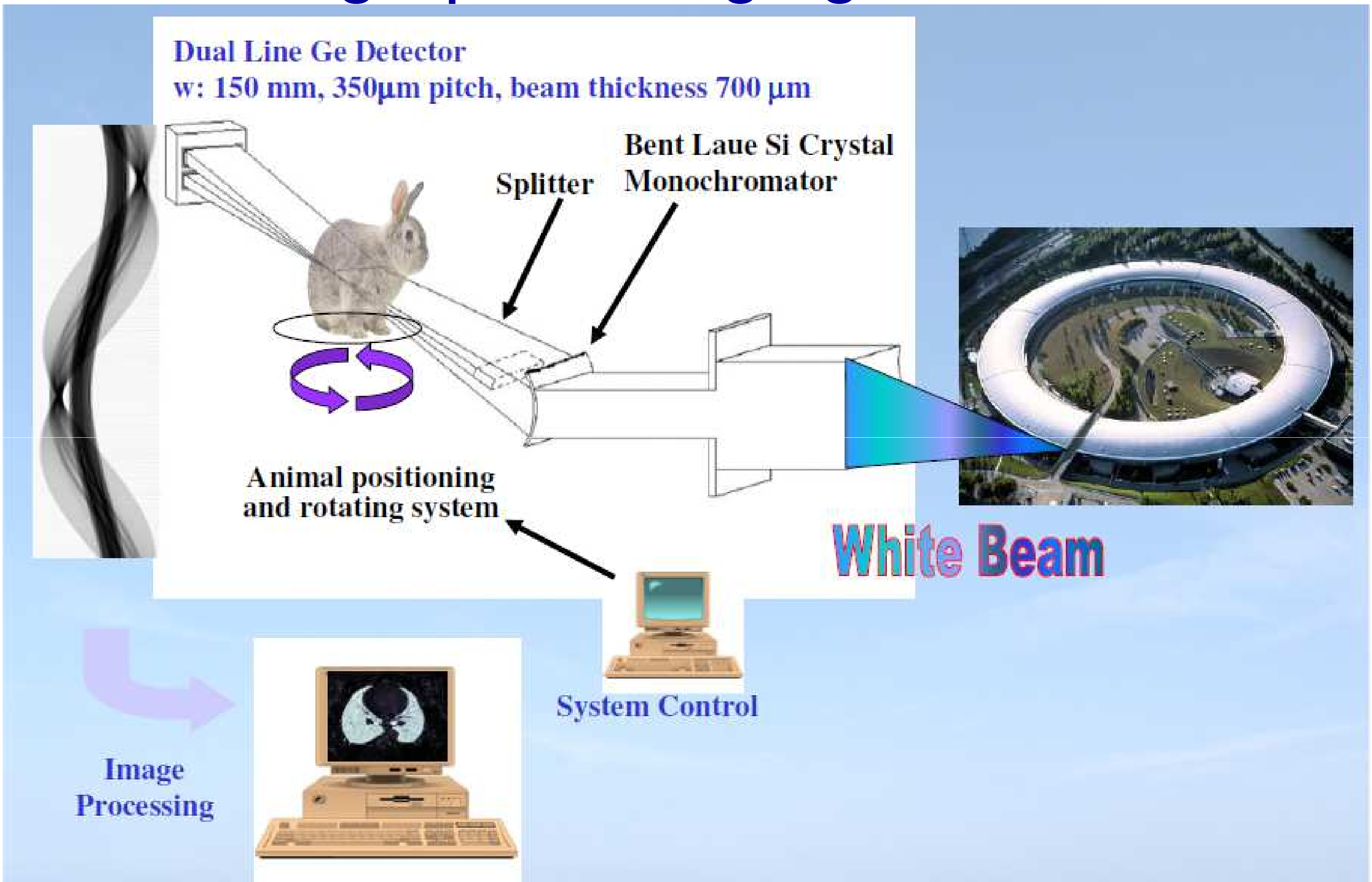
K-edge Subtraction Lung Tomography



$$(\rho t)_I = \frac{\ln(\frac{I}{I_0})^+ - \ln(\frac{I}{I_0})^-}{(\frac{\mu}{\rho})_I^+ - (\frac{\mu}{\rho})_I^-}$$

Courtesy of A.Bravin (ESRF)

Tomographic imaging at ESRF

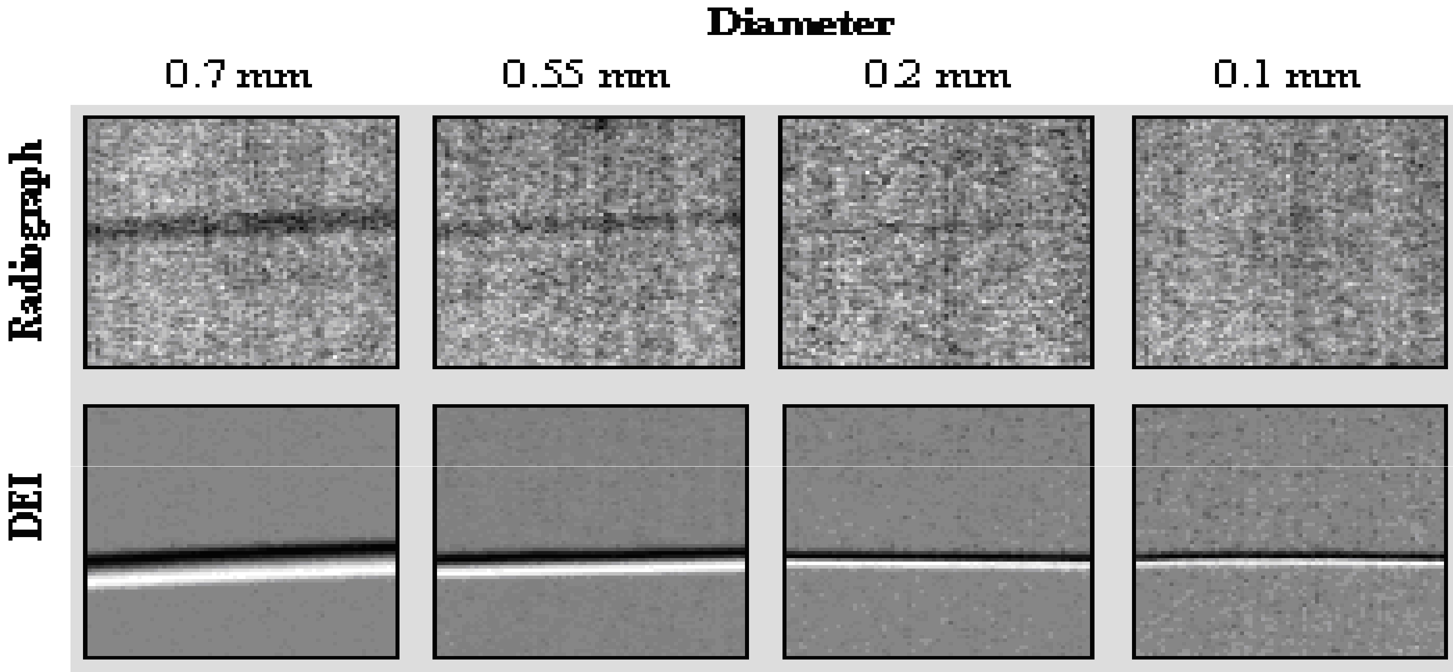


Courtesy of A.Bravin (ESRF)

Applications

- Mammography
- Bronchography
- Musculoskeletal imaging
- Coronary angiography
- Micro-angiography
- Computed tomography
- Micro-tomography
- Cartilage and bone imaging

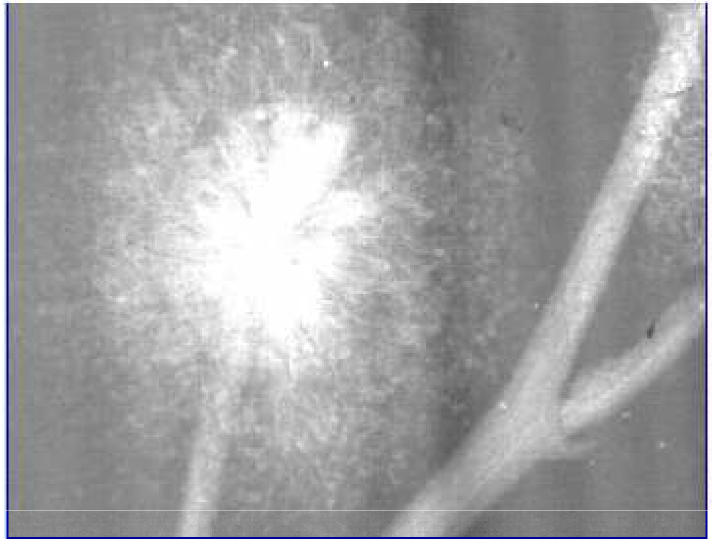
Comparison

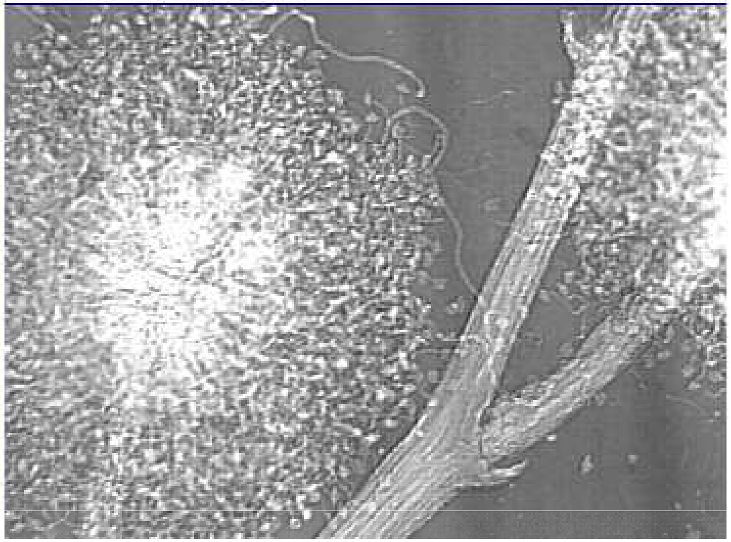


Conventional radiograph vs. DEI image of a nylon fiber. With conventional radiography, smaller objects show little contrast, a drawback that is not seen in the DEI images.

Images of a Mimosa flower

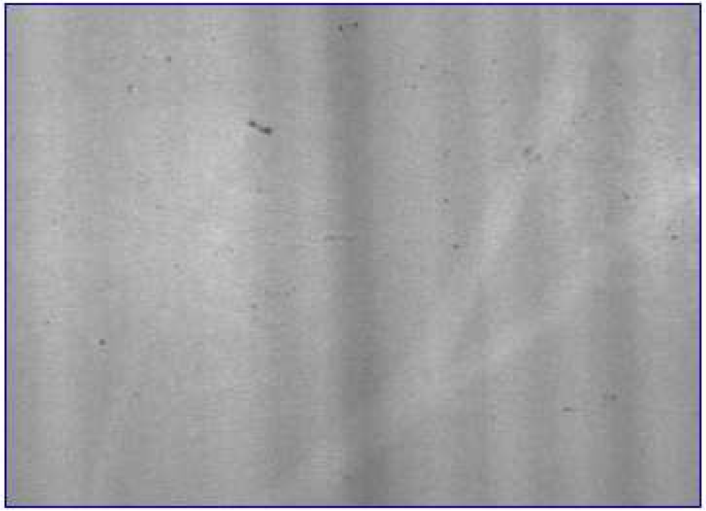
25 keV

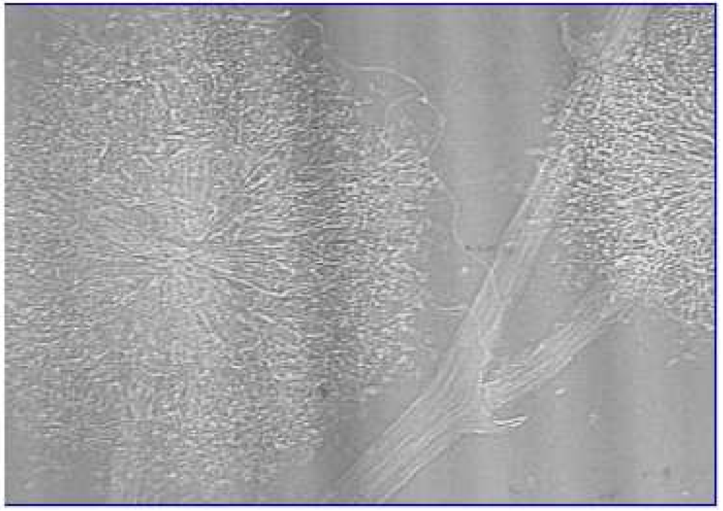




Absorption | Phase-contrast

10 keV





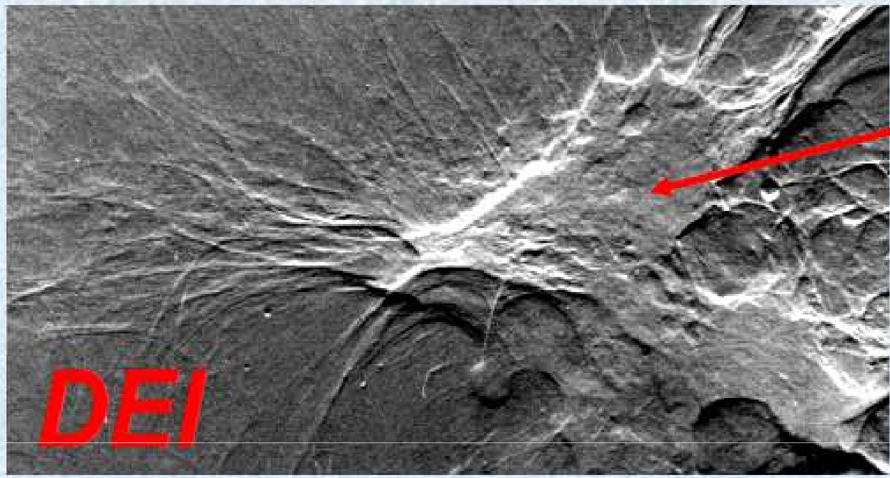
X-ray imaging of the lung

Absorption Contrast

Phase Contrast, 25 keV, z=2 m

Courtesy of Marcus Kitchen, School of Physics

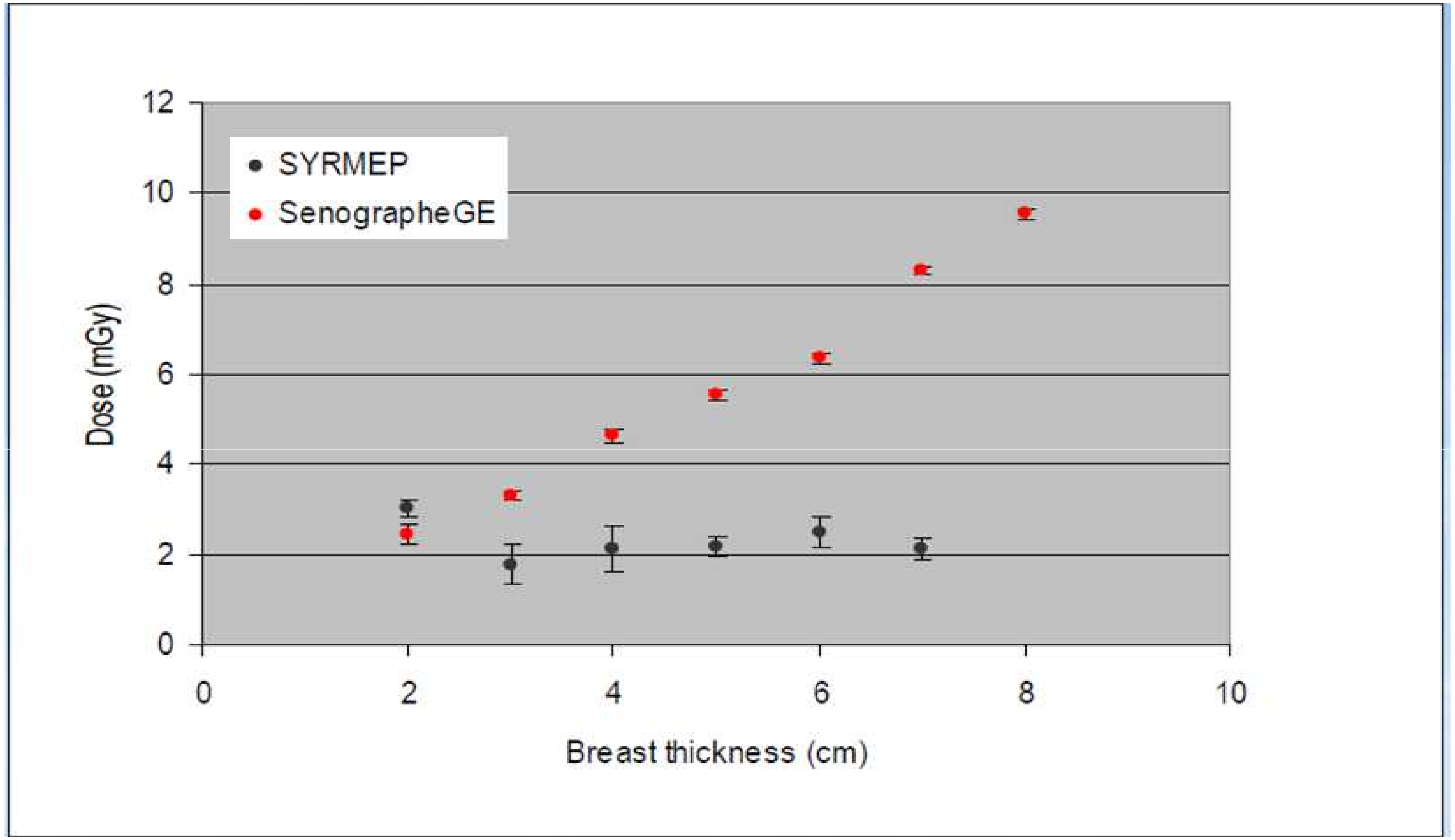
Lower dose in DEI



~0.020mGy exposure
25 times less exposure
than conventional

~5mGy exposure

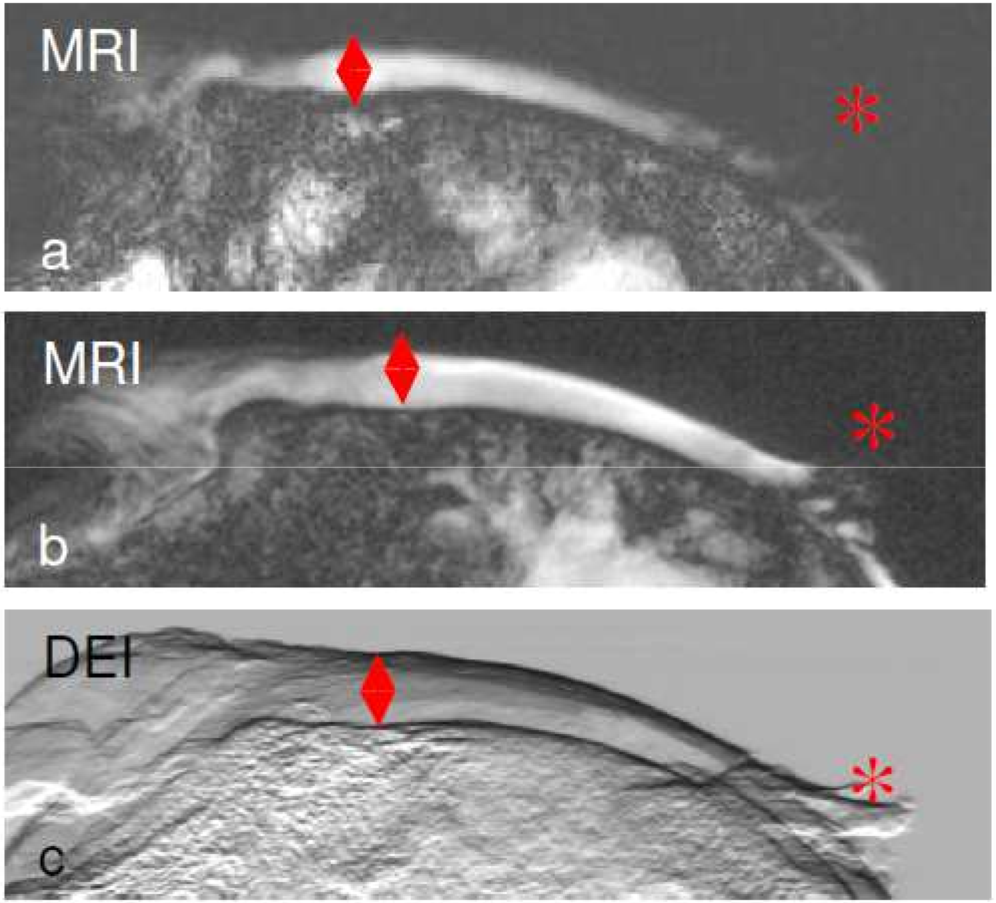
Dose Comparison



Average Entrance Skin Doses delivered to patients at SYRMEP and at the conventional mammographic unit (Senographe GE)

Vertical bars indicate the data distribution of each thickness class

Femur head core cuts: comparison with MRI

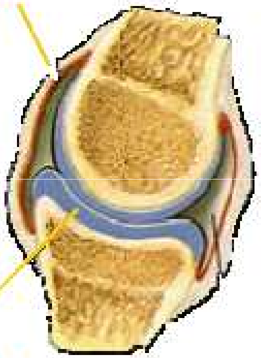


5 sec

150 sec

A Wagner, M Aurich, N Sieber, M Stoessel, WD Wetzel, K Schmuck , M Lohmann, B Reime, J Metge, P Coan, A Bravin, F Arfelli, L Rigon, RH Menk, G Heitner, T Irving, Z Zhong, C Muehleman, J A Mollenhauer sumbitted to NIM A

DEI studies of the finger joint

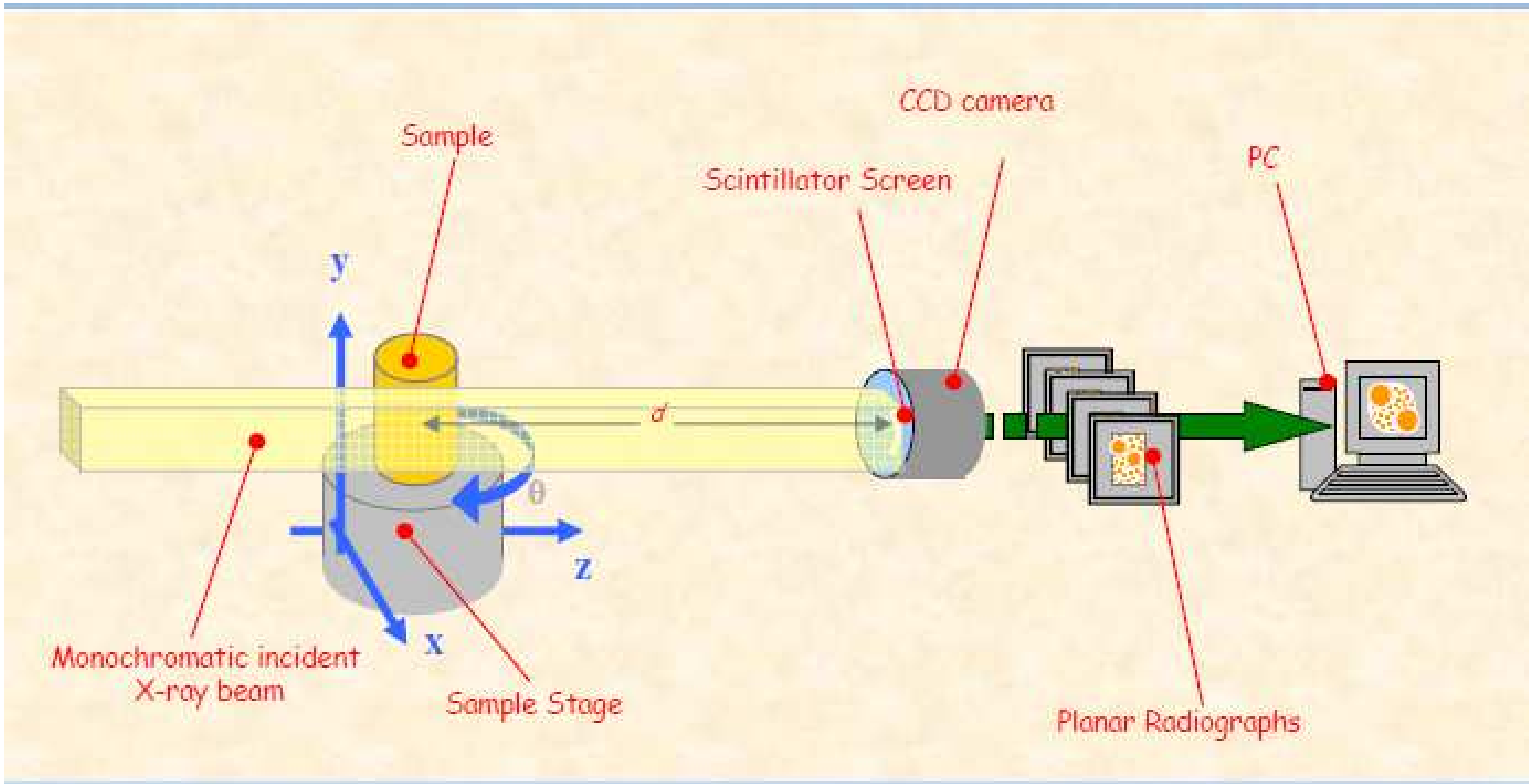


Conventional radiograph

Apparent absorption image @ 20keV at ELETTRA

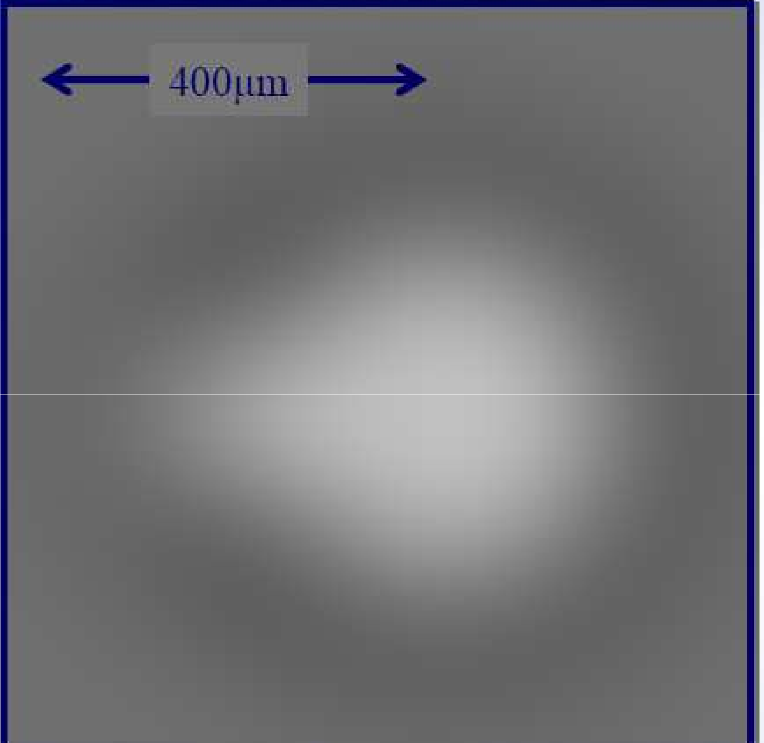
Daresbury, Elettra, University of Trieste Collaboration within PHASY project: R. Lewis et al.

Computed μ-Tomography (μ -CT)



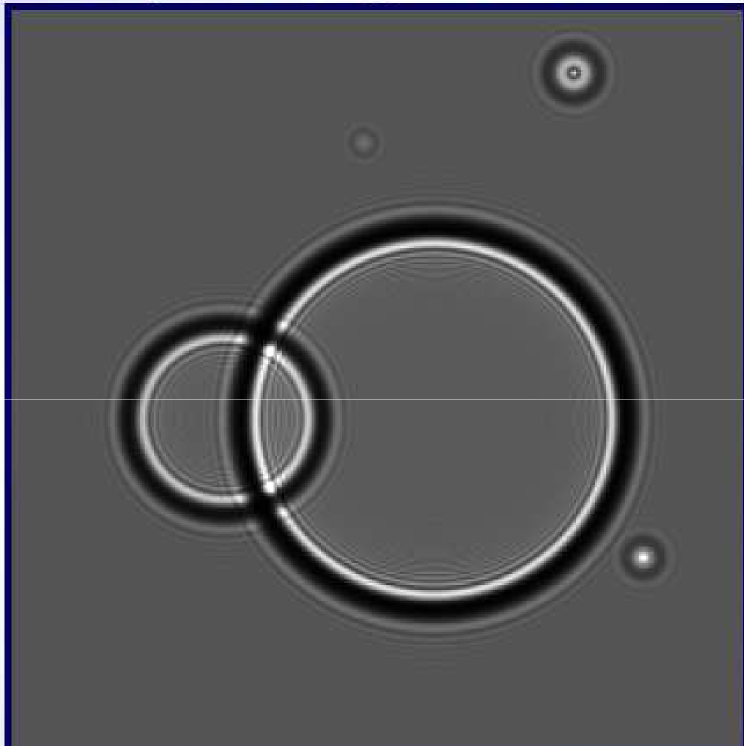
Phase Contrast Imaging

- Air bubbles in water. Pixel Size = 2.8 µm, Energy=25 keV



X-ray set: R_1=1.0 m

Source fwhm: 100×100µm



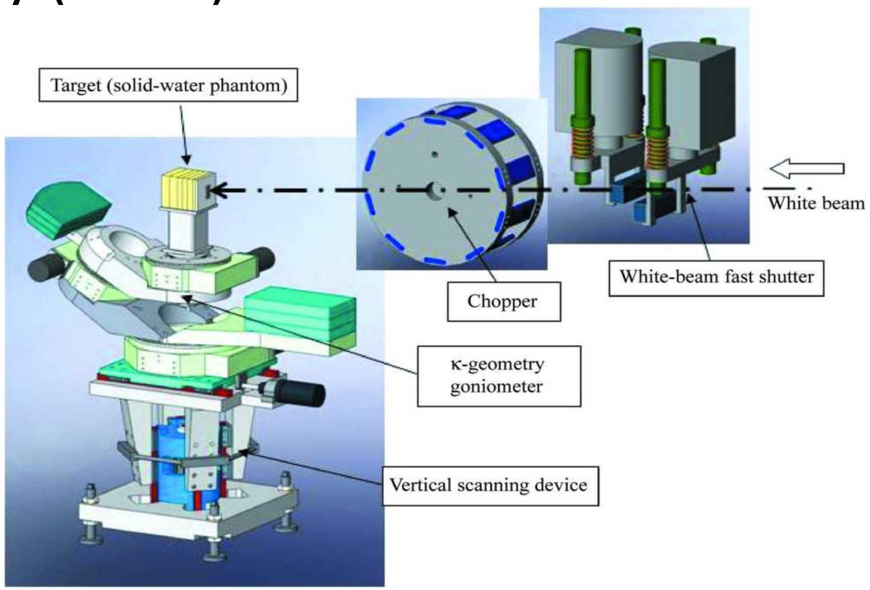
SP8 BL20B2: R_1=210.0 m

Source fwhm: 150×10µm

Synchrotron Radiation Therapy

Modern technological radiotherapy techniques:

- 3-Dimensional Conformal Radiotherapy
- Intensity-Modulated Radiation Therapy (IMRT)
- Image-guided radiation therapy (IGRT)
- Boron Neutron Capture Therapy (BNCT)
- Ion Therapy
- Stereotactic Radiosurgery

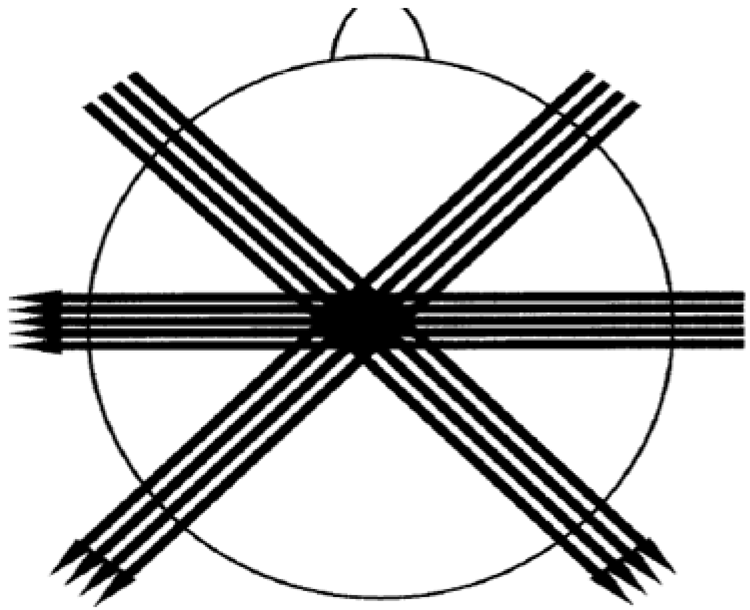


Synchrotron Radiation Therapy

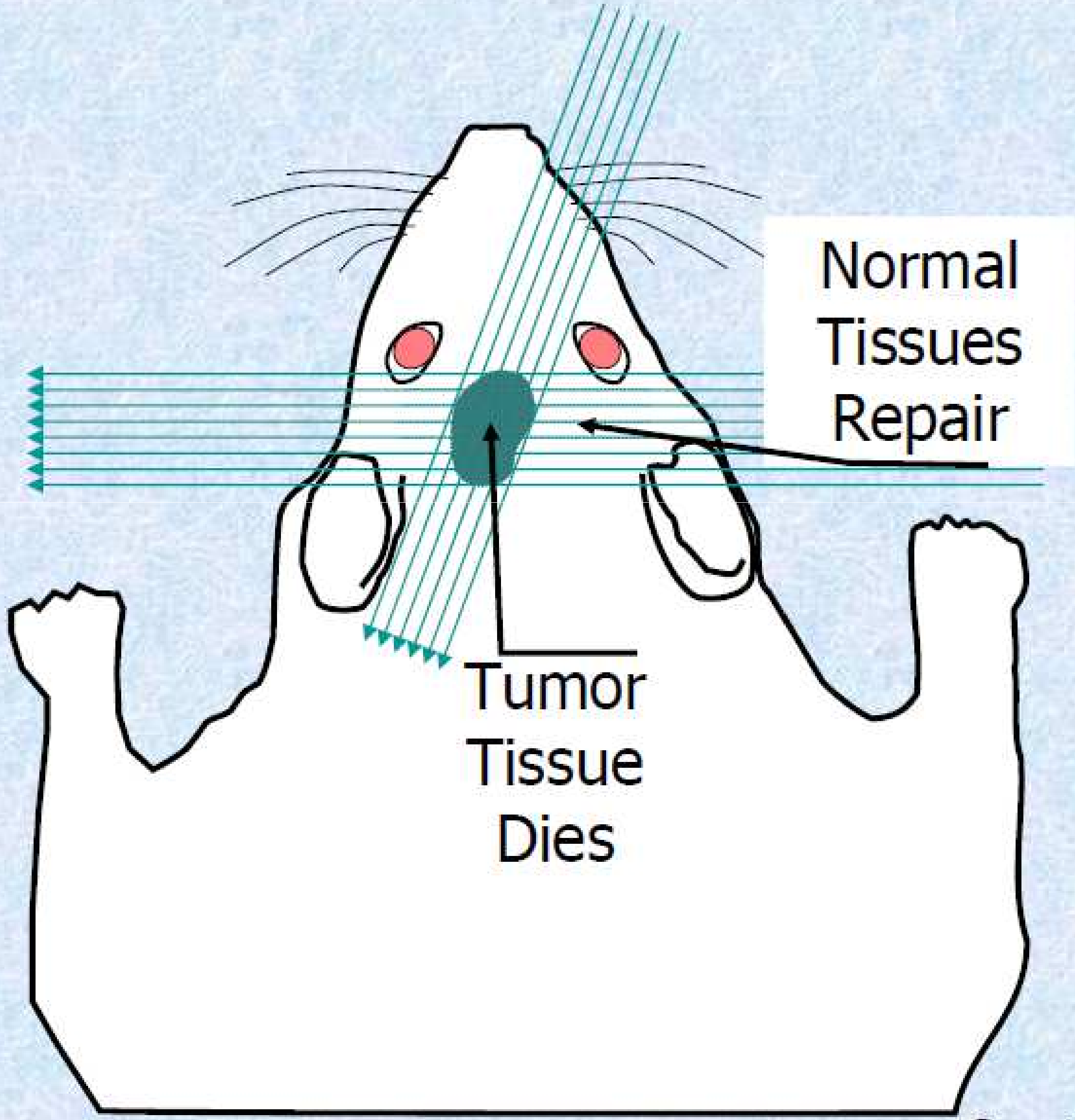
- It was Larsson (1983) who first pointed out the properties of synchrotron radiation that were desirable for radiotherapy.

- The inherent high collimation means that it can be targeted with great accuracy onto small tumours whilst the ability to tune the energy of a monochromatic beam means that the beam energy can be optimized for a particular depth.

In order to achieve this the beam is split by collimators into many smaller beams (microbeams), which are spatially separated but parallel. The typical thickness of each microbeam is 20–50 µm with a separation of 100–200 m



Bidirectional Irradiation (MRT)



Courtesy of Avraham Dilmanian
BNL Medical Dept

Microbeam Therapy

- High doses (>100 Gy) are delivered in one fraction by using arrays of parallel thin beams. In MRT beam widths range from 25 to 100 mm, whereas in MBRT the beam width employed at the ESRF is 600 mm.

- MBRT might be a promising technique to treat brain tumors and some illness like epilepsy with no significant secondary effects.

Microbeam Therapy

The main attributes of microbeams are:

(a) Their sparing effect on normal tissues, including the central nervous system (CNS).

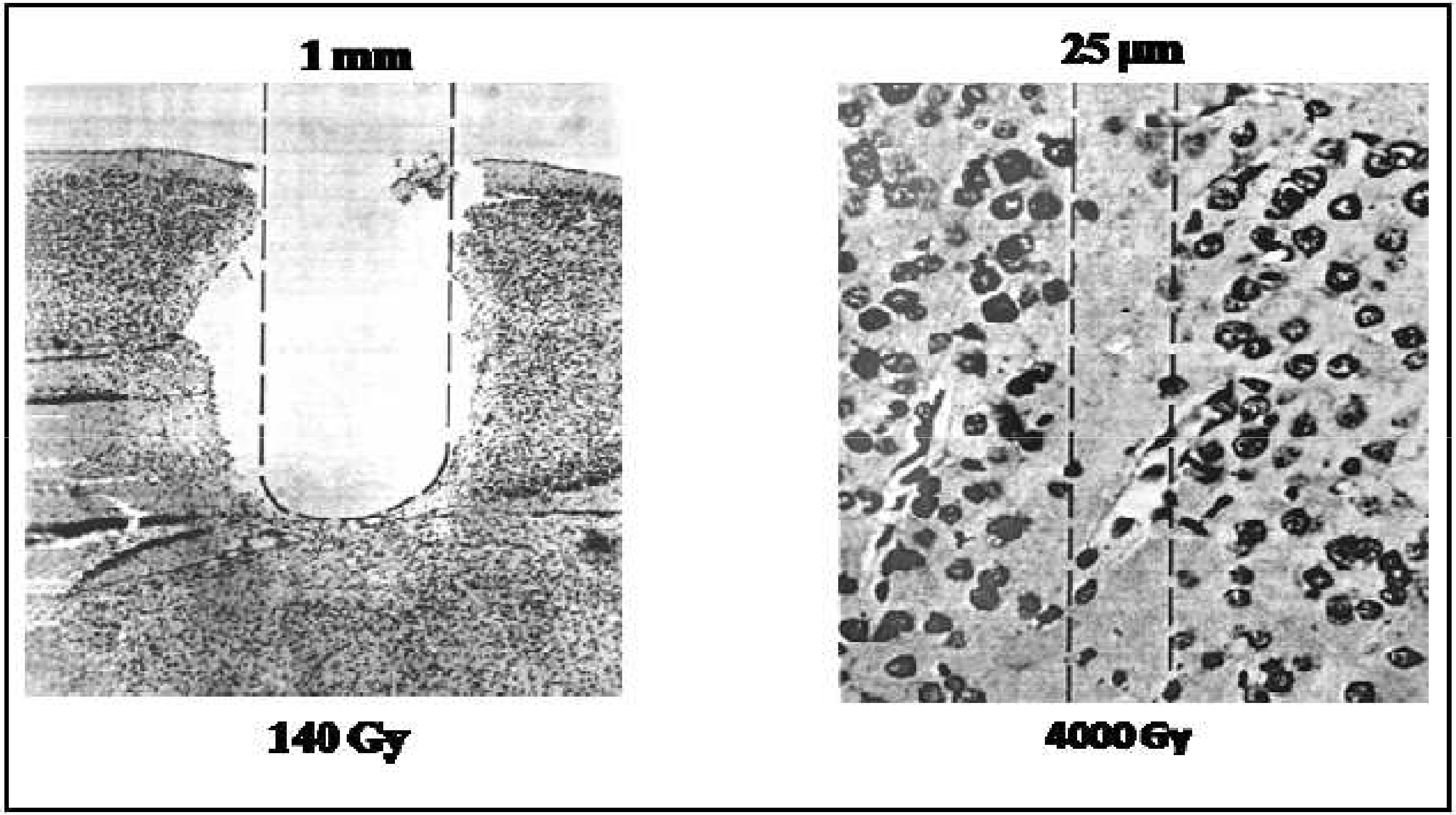
(b) Their preferential damage to tumors.

Microbeam Therapy

Microbeam radiation therapy is aimed at clinical applications of:

- Pediatric brain tumors
- Tumors in the radio-sensitive organs such as those of the lower brain and spinal cord.

Dose comparison



Histological images after irradiation using a millimetric beam (left) or a microbeam (right).

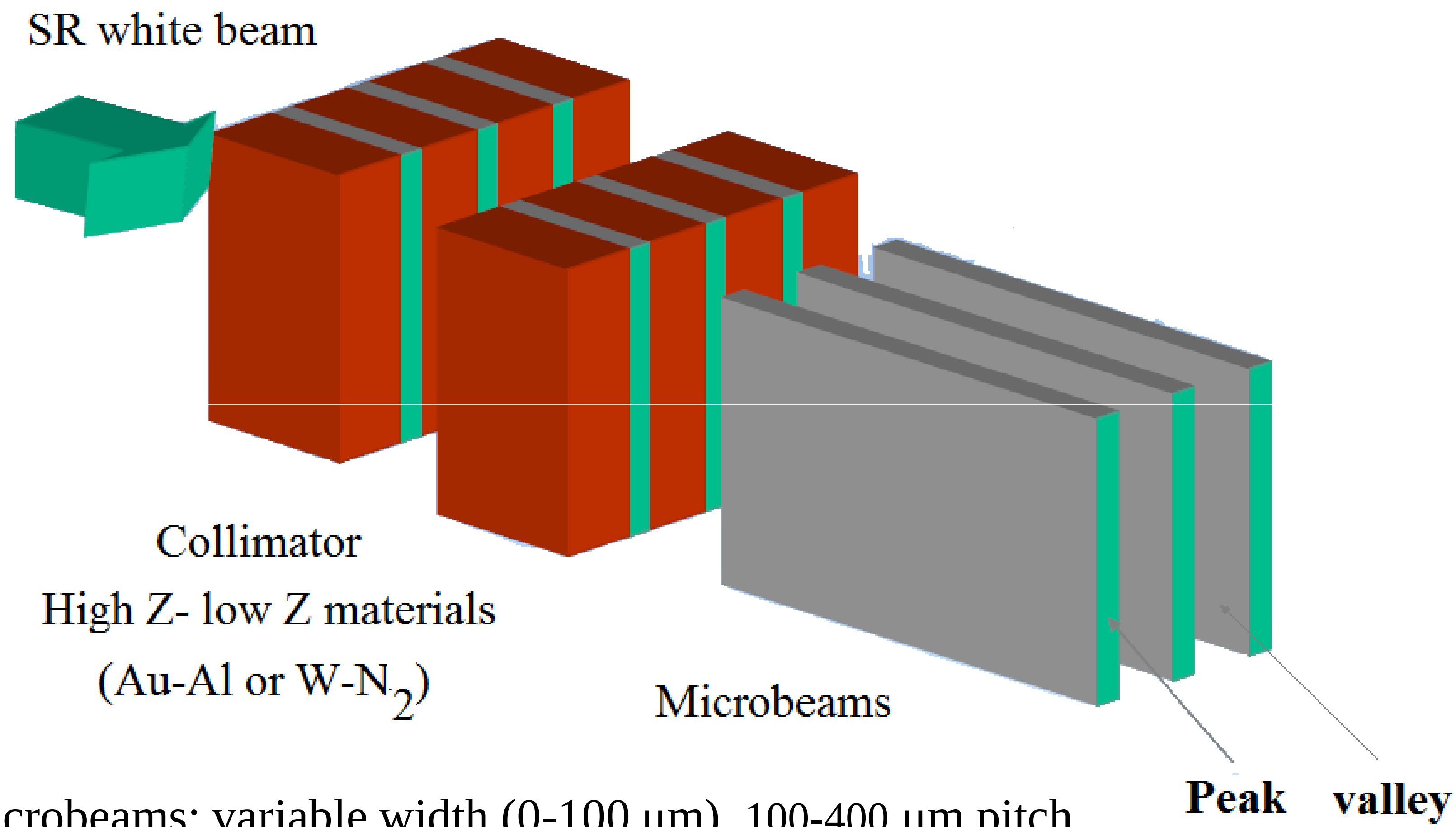
Zeman et al., Radiat. Res. 15, 496,1961

Dose volume-effect

Beam diameter (µm)		Threshold dose (Gy)
25	CELLS	4000
75		500
250		360
1000	Tissues	140

(Fike & Gobbel, 2001)

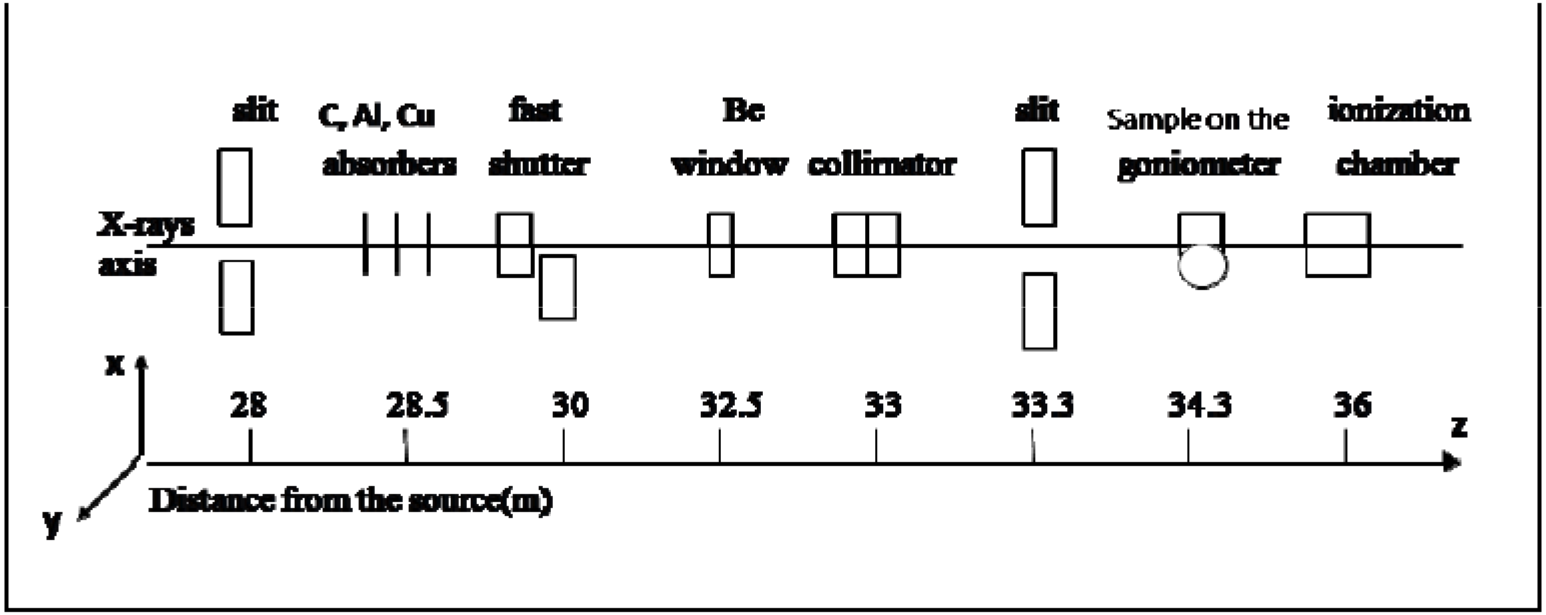
Microbeams production



Microbeams: variable width (0-100 μm), 100-400 μm pitch
50-125 microbeam array to cover up to 5x5 cm2

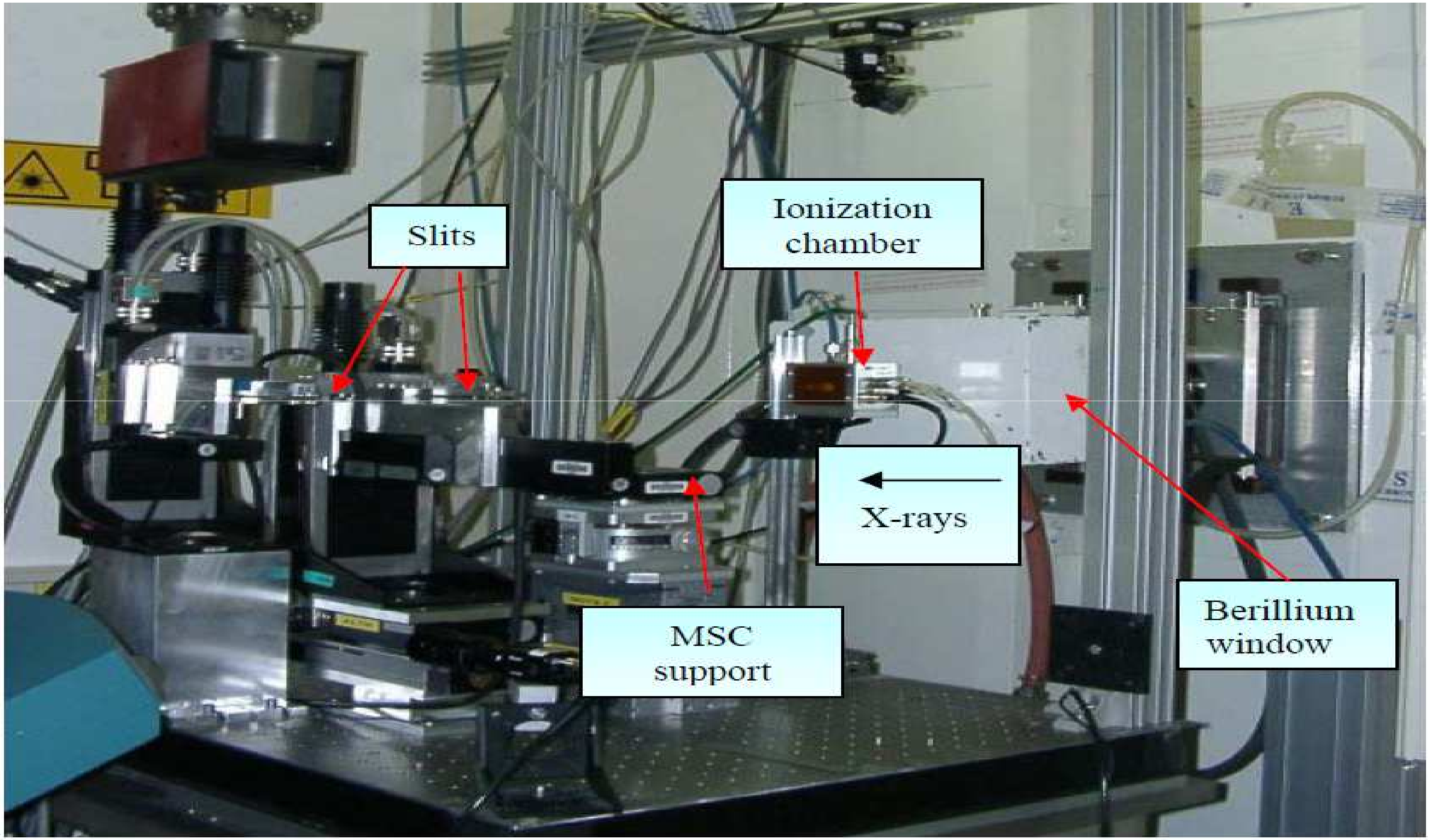
Brauer et al. Rev.Sci.Instr.76, 064303, 2005

The experimental station for MRT



Schematic representation of the beamline setup for MRT, indicating the distance of each element from the light source.

System setup

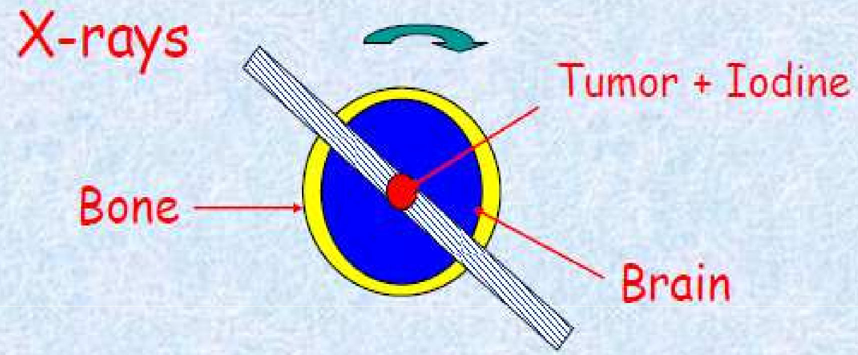


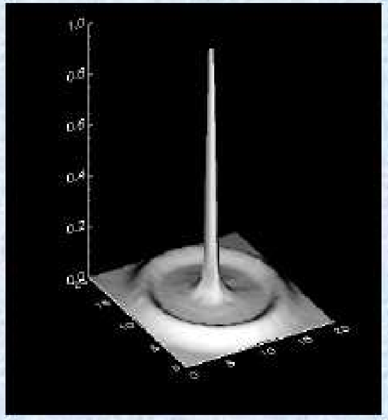
Setup of the MRT experimental hutch (multislit collimator).

Photon Activation Therapy (PAT)

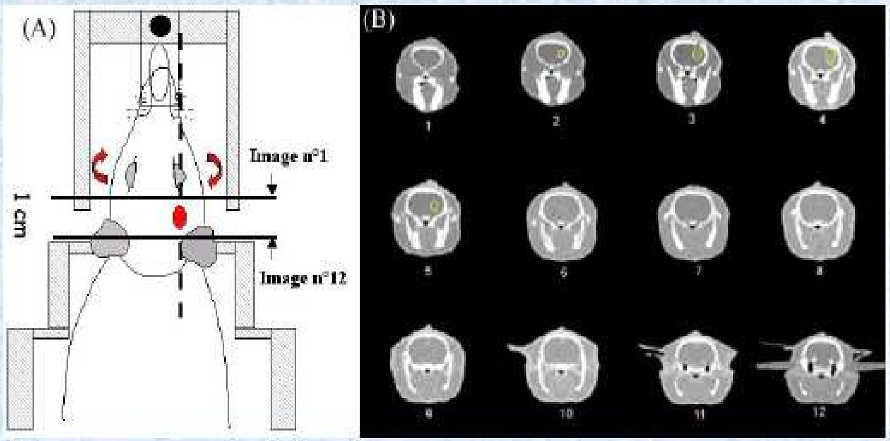
- PAT is an analogous method where a cascade of Auger and photoelectrons is created in the tumour during irradiation by a monochromatic SR beam.
- PAT is a two-step therapy, where a sufficient concentration of a high-*Z containing compound is* physiologically directed to the tumour.
- SR with an energy slightly above the K-absorption edge is targeted on the tumour, and the Auger electrons deposit their energy near the atom where photoabsorption takes place.
- Consequently, the heavy absorbing atoms should be incorporated as close to the DNA of the tumor cell as possible.

Contrast Enhanced Stereotactic Radiotherapy





Radiation Dose



Contrast Agent

Components

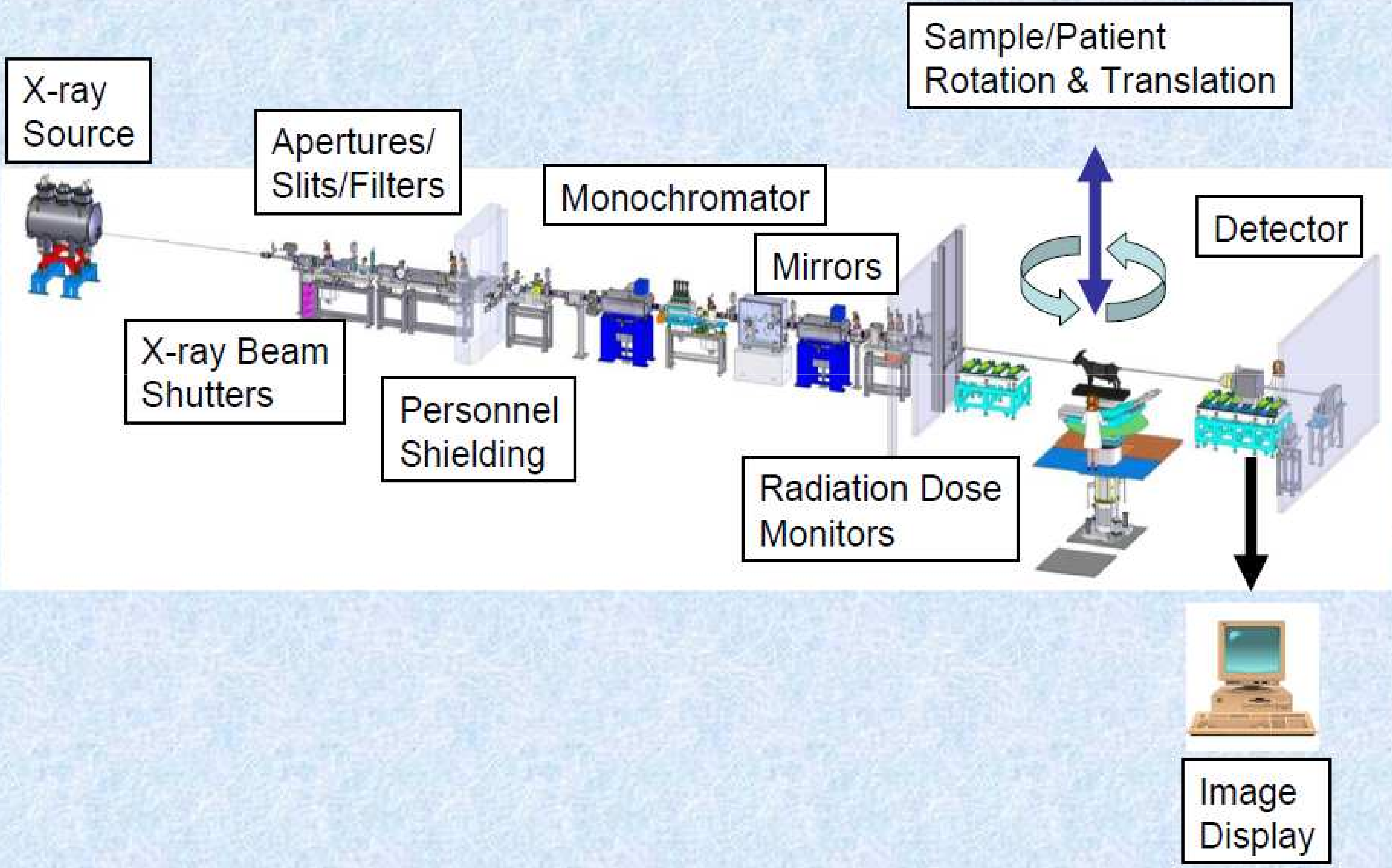
- Insertion device (bending magnet, wiggler, undulator)
- Front end (shieldings, filters, shutters, filters)
- Different hutches (imaging and therapy)
- Control room(s)
- Sample preparation laboratories
- Animal preparation room
- Cell laboratory
- Chemical laboratory

Advantages vs Disadvantages

- Higher Quality of Images, Lower dose to patient, Higher contrast, Faster, Higher resolution, Capable of treatment of resistant tumors, Higher sensitivity (submicron)

- Preclinical (research) stage, Higher costs, Unknown, Not ease of access

Typical Biomedical Beamline



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Thanks

for

your attention