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Pt. 1

Cours/Lecture Series



1994- 1995 ACADEMIC TRAINING PROGRAMME

LECTURE SERIES

SPEAKER : Alberto DEL GUERRA / University of Ferrara, Italy
TITLE : Detector applications in medicine and biology
TIME : 9, 10, 11, 12 & 13 January from 11.00 to 12.00 hrs
PLACE : Auditorium

ABSTRACT

In recent years new diagnostic and therapeutic methods have been attracting more and more dedicated attention by the scientific community. The goal is a better understanding of the anatomy, physiology and pathology of the human being in an effort to find more appropriate medical prevention, diagnosis and therapy. Many of the achievements obtained so far derive from the use and the optimisation of detectors and techniques, which originated in the other fields of physics. The spin-off of High Energy Physics to Medical Physics has been particularly relevant in the field of detectors for medical imaging and especially for medical imaging with ionizing radiation. In this series of lectures, starting from the requests of each technique and/or application I will attempt to present a survey of the detectors for medicine and biology. Various fields of medical imaging will be touched : radiology, digital radiography, mammography, Single Photon Emission Computed Tomography, Positron Emission Tomography and radiotherapy. The capabilities of the major types of detectors (1-D and 2-D position sensitive, and pixel type) will be correspondingly analyzed : scintillation, gaseous and solid state detectors. Finally some specific applications as in synchrotron radiation and in the biological field will be addressed.

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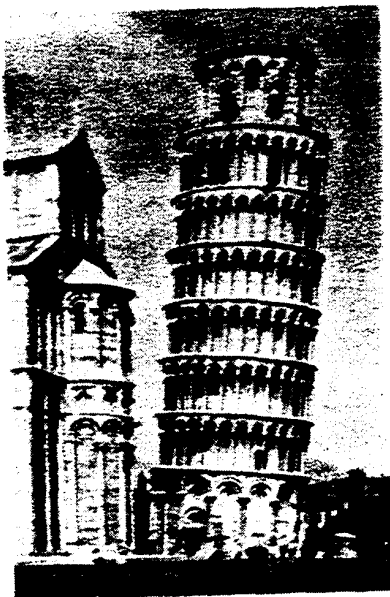
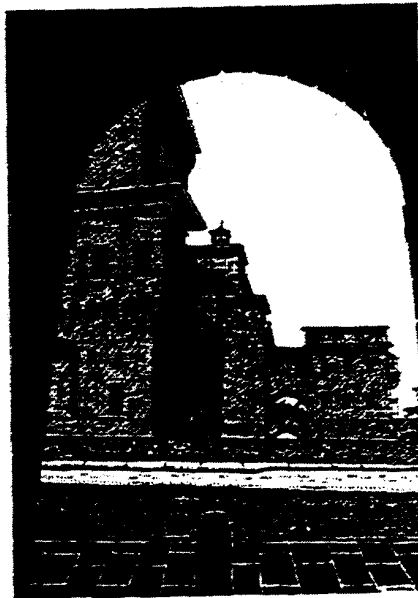
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Detectors for Medicine and Biology

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(CERN - Academic training - 9,10,11,12 &13 January 1995)



Contents

LECTURE # 1 (Monday 9 January)

- 1. - Introduction**
- 2. - Radiology (X-rays)**
 - 2.1 - Historical background
 - 2.2 - Principles : the film and its properties
 - 2.3 - How to overcome film limitations
 - 2.4 - Dose considerations
 - 2.5 - Digital applications with gaseous detectors

LECTURE # 2 (Tuesday 10 January)

- 2.6 - Digital applications with solid state detectors
- 2.7 - Special applications with Synchrotron Radiation

LECTURE # 3 (Wednesday 11 January)

- 3. Nuclear Medicine**
 - 3.1 - Historical background
 - 3.2 - Principles -the tracer - the radioisotopes
 - 3.3 - The Anger camera and its properties
 - 3.4 - SPECT (principles)
 - 3.5 - Clinical examples
 - 3.6 - How to improve SPECT

LECTURE # 4 (Thursday 12 January)

- 3.7 - PET
- 3.8 - How to improve PET

LECTURE # 5 (Friday 13 January)

- 4. Biology applications**
 - 4.1 - Autoradiography and radiocromatography
 - 4.2 - Cristallography
- 5. Monte Carlo as an aid to detector design in Medical Physics**
- 6. Radiotherapy**
 - 6.1 - 3-D treatment planning
 - 6.2 - Portal imaging
 - 6.3 - Hadron therapy
- 7. Conclusions**

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RADIN and MEDIM collaborations (INFN group V)
Cagliari - Pisa - Ferrara - Napoli



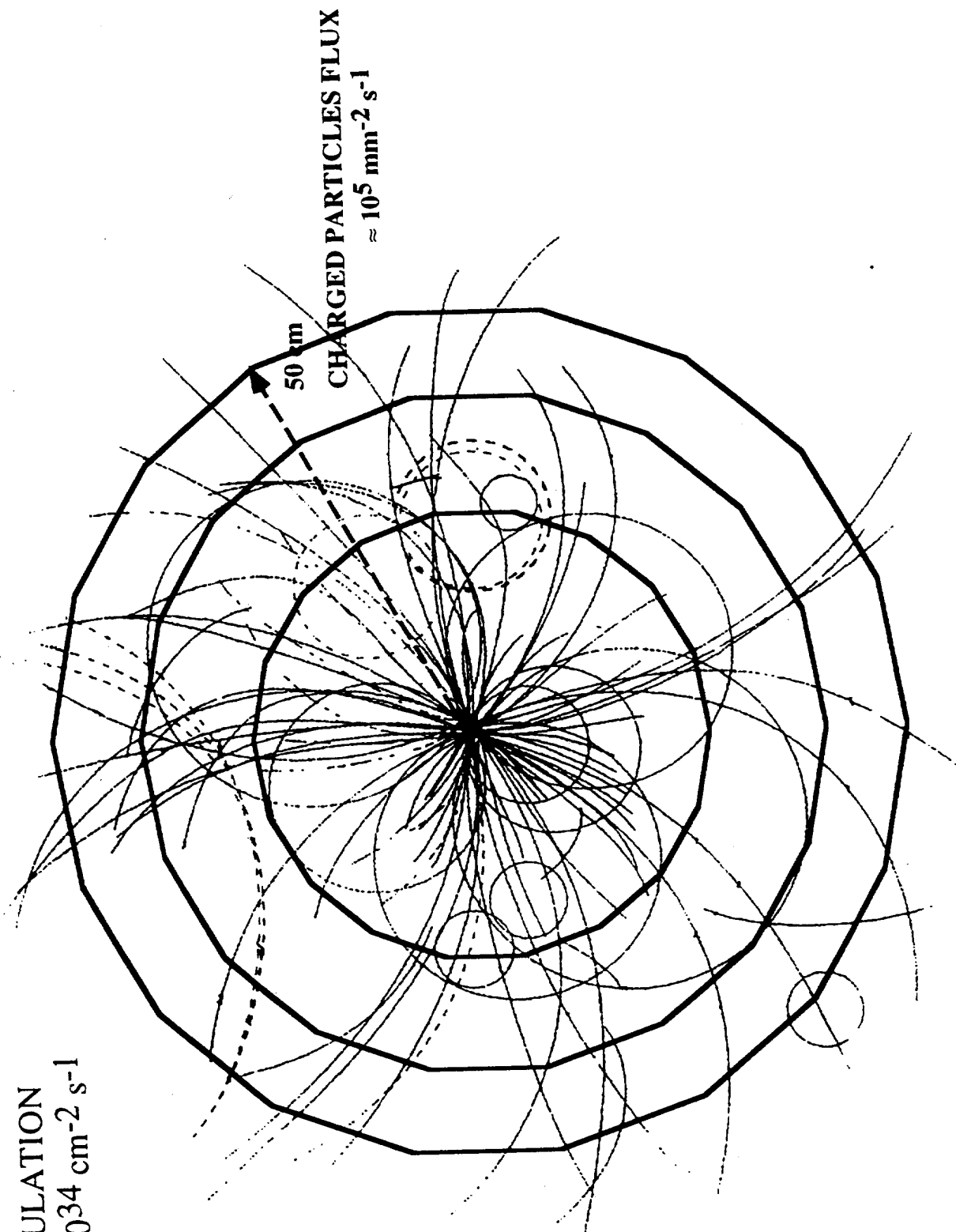
Figure 4A

The first medical radiograph This radiograph of Mrs. Roentgen's hand was made by Roentgen before he announced his discovery of x rays. On January 1, 1896, Roentgen sent a copy of a separate printing of his first paper on x rays and examples of his x-ray photographs to several colleagues. Photographic positive prints made from the x-ray plate of his wife's hand and eight other plates formed the collection from which he selected the examples forwarded to his colleagues with his paper.

LARGE HADRON COLLIDER: ONE CROSSING (MINIMUM BIAS BACKGROUND)

CMS SIMULATION

$L = 1.8 \times 10^{34} \text{ cm}^{-2} \text{ s}^{-1}$



Example:

Problems solved for HEP experiments:

1. μ -strip silicon detector for charged particle tracking
2. Dimension: 4x (5x5 cm²) ; thickness \leq 500 μ m
3. Electronics for m.i.p. (in 300 μ m \approx 70 keV energy loss)
low noise : 200 e⁻
reasonably fast : 50 -100 ns
integration on VLSI (see Viking)
4. Trigger
5. DAQ for collider
low multiplicity
sparse readout via multiplexer (in between two pulses)
6. n. of channels: 10⁶-10⁷
7. event size: 10⁶ bytes (level 1 trigger)
8. n. of sellable apparatus: 1 (may be two!!)
But the apparatus is made of thousands of modules!

Problems to be tackled for Imaging with X-rays (10-100 keV):DR

1. μ -strip silicon detector for X-rays
2. Dimension: $20 \times 20 \text{ cm}^2$; thickness ($300 \mu\text{m} - 3 \text{ mm}$)
3. Electronics for X-rays (down to 10 keV)
low noise : 200 e⁻
fast : 10 ns
integration on VLSI
4. *Self-Triggering*
5. DAQ for DR
 $5 \times 10^4 \text{ Hz/mm}^2$ (on a $20 \times 20 \text{ cm}^2$ $2 \times 10^9 \text{ Hz}$)
1 s acquisition time (duty cycle 100%)
6. n. of channels: $10^3 - 10^4$
7. event size: 1 bit - 10 bytes
8. n. of sellable apparatus: $10^3 - 10^6$

Experiment in HEP

Exp in Medical Physics

Group size:	$10^2 - 10^3$ people	1 or 2
Preparation:	5 - 10 years	5' - 10'
Data collection:	1 - 5 years	1' - 5'
Data analysis:	1 - 5 years	1' - 5'
Run by:	physicists	technician
Analyzed by:	physicists w/ hardware & software	physician "mostly by experience"

However in both cases the right approach is the same:

- *I have the best detector for .. what??*
- *I have this experiment to do w/ these requirements.
Which is the best detector?*



Industriele Illustration
Lecteur d'essai, l'industriel en mesure de l'électro-
lignes d'essai et des générateurs en 1880 à 1890
A certain-oid example of physics devices to mechanics

1880-1890
5

Detectors for Bio-Medical Imaging w/ ionising (mostly X and γ) radiations

1. DIAGNOSIS

(Discipline)

(Parameters measured)

(Medical application)

- **X-RAY RADIOLOGY**

2-D Film

X-ray absorption

Anatomy; mineral content

X-ray TCT

Density and average Z

movement of contrast

DSA

Contrast distribution

material

ULTRASOUND

Acoustic impedance mismatch;
sound velocity and attenuation

Anatomy; tissue structural
characteristics; blood velocity

- **NUCLEAR MEDICINE**

Planar scintigraphy

Concentration of

Metabolism; receptor site

ECT

radionuclides

concentration and flow

NUCLEAR MAGNETIC RESONANCE

MRI Concentration of nuclides (^1H ,...);
relaxation parameters T1 and T2

Anatomy of tissues; free water
content; flow concentration of

MRS Frequency shifts due to
chemical forms

some molecular species and
contrast agents

OTHER Techniques

Biomagnetism, BioImpedance, ...

- **SOME BIOLOGICAL APPLICATIONS**

Autoradiography

Cristallography

2. THERAPY

- **only RADIOTHERAPY**

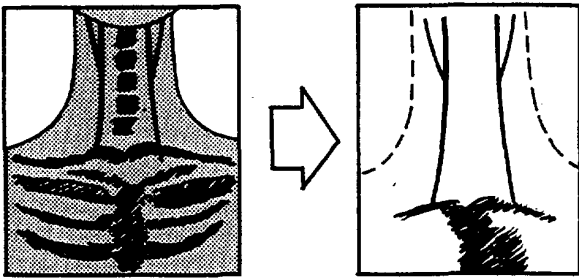


Figure 1. Contrast filled vessels are extracted from the background using DSA.

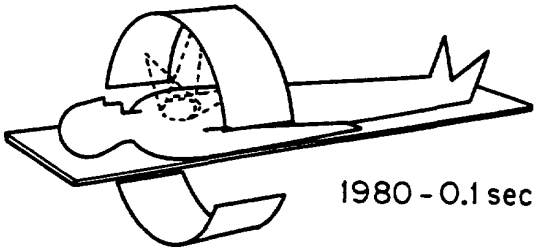


Figure 2. X-ray computed tomography measures photon attenuation coefficients.

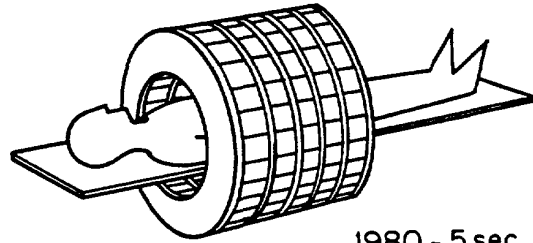
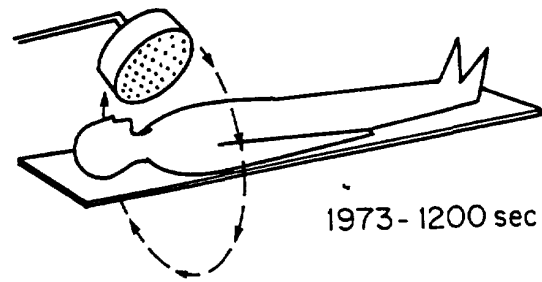


Figure 5. Emission tomography has evolved from the Anger camera to multilayer positron tomographs.

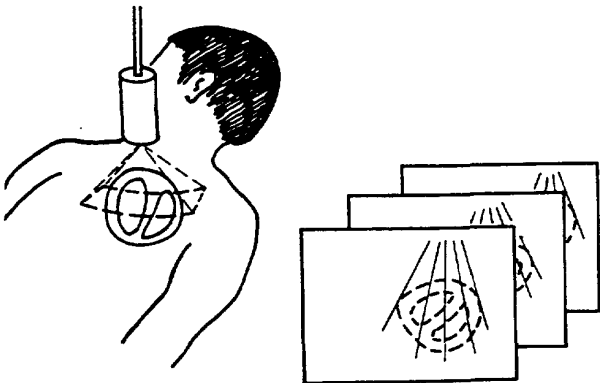


Figure 3. Ultrasound measures surface movement and blood velocity.

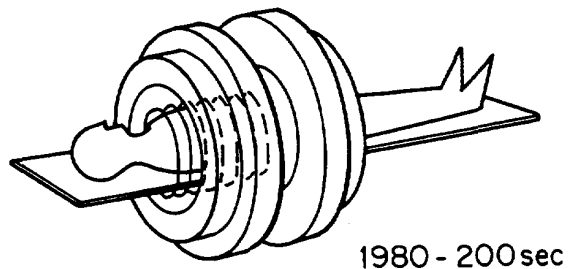
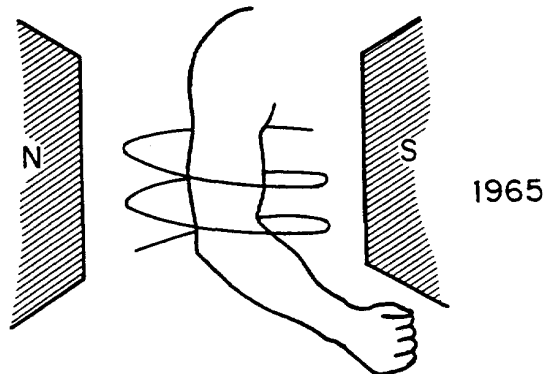


Figure 6. Nuclear magnetic resonance measures the chemical state and abundance of some nuclei (e.g., ^1H , ^{23}Na , ^{32}P).

Name Theodore Roosevelt Attending Physician and Surgeon Monmouth
 Race W Age 53 Nativity U.S.A. Occupation Ex. President. U.S.
 Where and by whom employed _____
 Diagnosis _____
 Admitted Oct 14, 1912 Hour 10:30 P.M. Discharged D. & L. Results Taken on regular basis

Color	Odor	Reaction	Sp. Gr.	Sugar	Albumen	Remarks
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Urinanalysis:

Examination made by Dr. Ray showed location of bullet about 1 in below nipple on right side and about 4 1/2 in to right of mid line lodges against 4th rib.

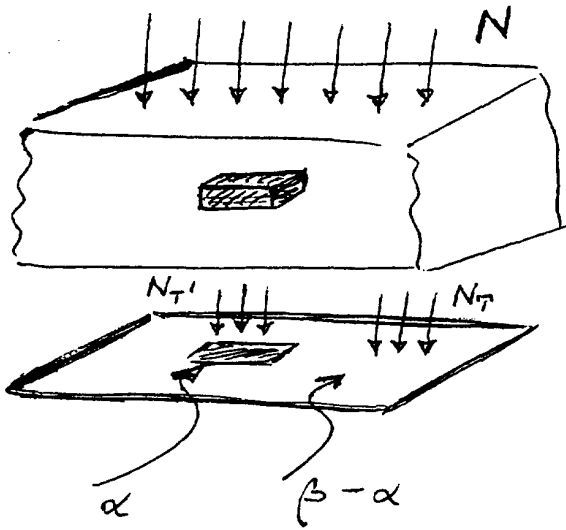
J. B. Jansen

Treatment:

Shaved the area around the wound. Washed the area around the wound with 50% of alcohol. Painted inside and outside of the wound with 10% tincture iodine. Applied dry steril gauze dressing.

from: Nancy Knight "75 years of the RSVA. Approaching a century of Radiology. Museum & Information Resources. In: RADIOGRAPHIES Stephen Balter, Guest Ed., November 1989, vol 9(6) - p. 1109

Radiological Imaging



fluences exposure
 $N \text{ [ph/mm}^2] \propto X \left(= \frac{\Delta Q}{\Delta m} \right)$

N_T transmitted fluence

$$\text{Signal} = |n - n'| \quad \begin{aligned} n &= N_T (\beta - \alpha) \\ n' &= N_T' \alpha \end{aligned}$$

$$\text{Noise} = \sqrt{n + n'} \text{ (from Poisson statistic)}$$

$$\text{SNR} = \frac{|n - n'|}{\sqrt{n + n'}}$$

Signal to Noise Ratio

$$\text{SCR} = \frac{|n - n'|}{(n + n') / 2} = \frac{2 * \text{SNR}}{\sqrt{n + n'}}$$

Signal to Contrast ratio

for $n \gg n'$ $\text{SNR} = \frac{|n - n'|}{\sqrt{n}}$

$$\text{SCR} = \frac{2 * \text{SNR}}{\sqrt{n}}$$

for $n \approx n'$ $\text{SNR} = \frac{|n - n'|}{\sqrt{2} \sqrt{n}}$

$$\text{SCR} = \frac{2 * \text{SNR}}{\sqrt{2} \sqrt{n}}$$

For $\beta = 2\alpha$, $\sqrt{\alpha} = d$ and $N_T \approx N_T'$

$$\text{SCR} = \frac{2 * \text{SNR}}{d \sqrt{N_T} \sqrt{2}} = \frac{\sqrt{2} * \text{SNR}}{d \sqrt{N_T}}$$

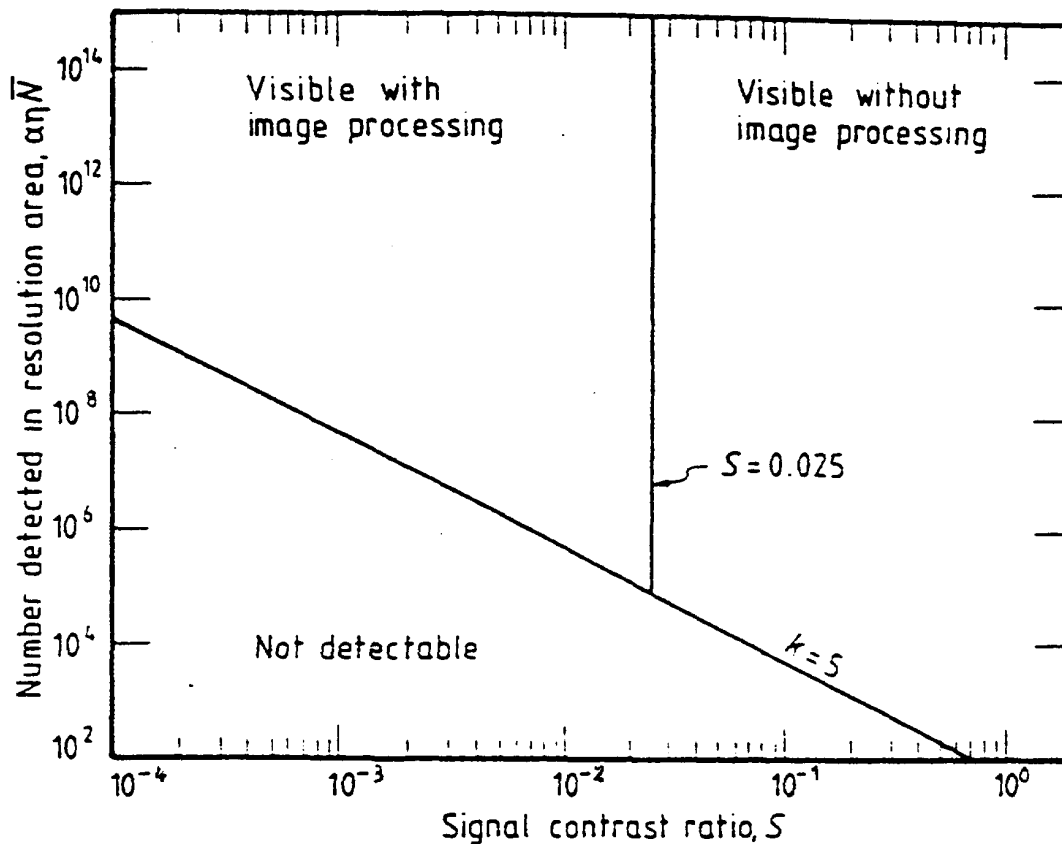
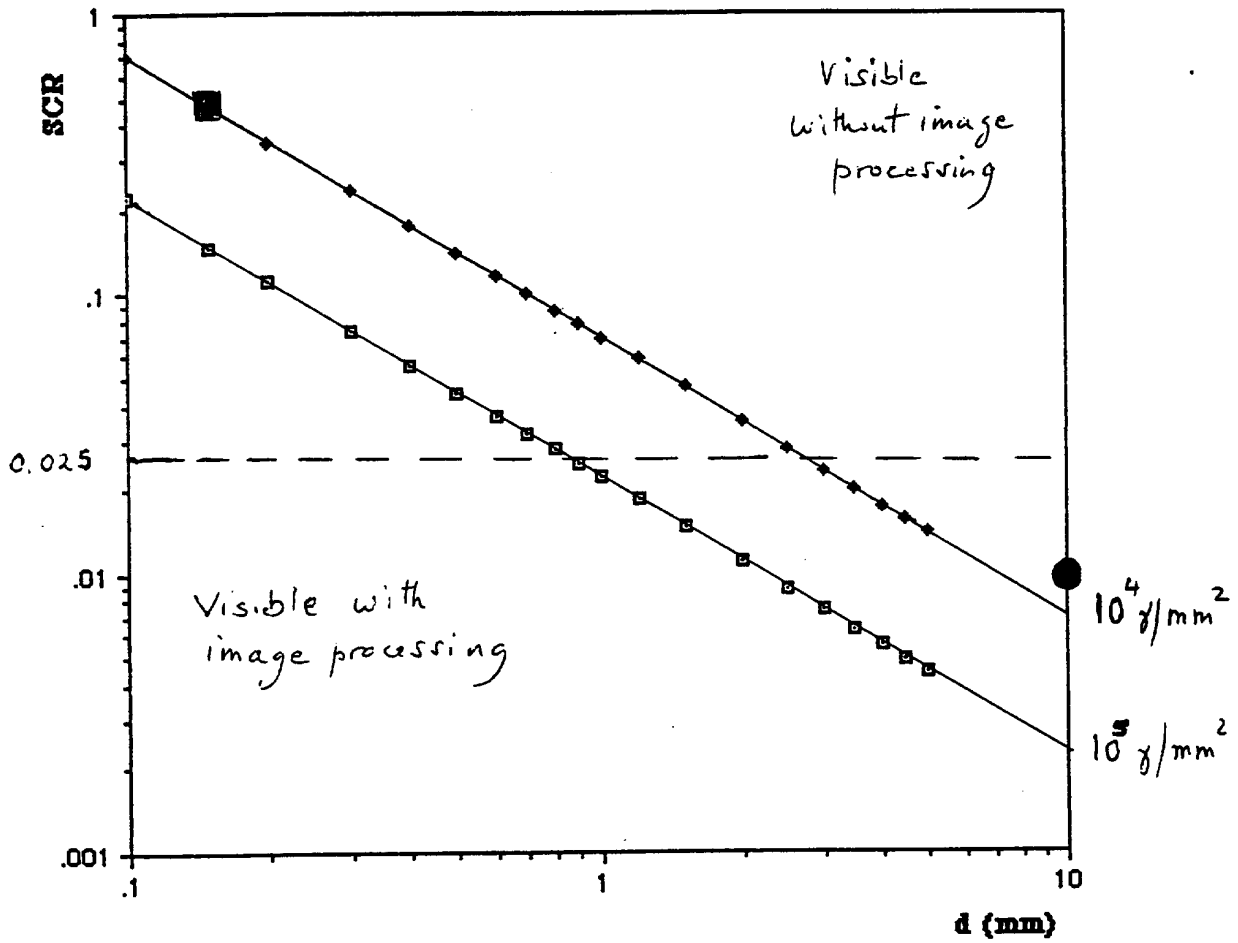


Fig. 2. Number of photons detected in a given resolution area as a function of signal contrast ratio. Threshold signal-to-noise ratio is taken as 5 in this example, with the visibility threshold of 2.5% (η is the area of the spatial resolution element, α is the X-ray detection efficiency of the imaging system and \bar{N} is the average transmitted X-ray fluence. [Courtesy Dr. J.W. Motz and Med. Phys. 5 (1978) 8.]

$$SCR = \frac{\sqrt{2} * SNR}{\sqrt{n}} \quad (\text{for equal area})$$

$$SNR \geq k = 5$$

$k=5$



● → nodule (1cm ϕ , 10% SCR)

▣ → μ -calcification (150 μm ϕ , 50% SCR)
(100-200 μm)

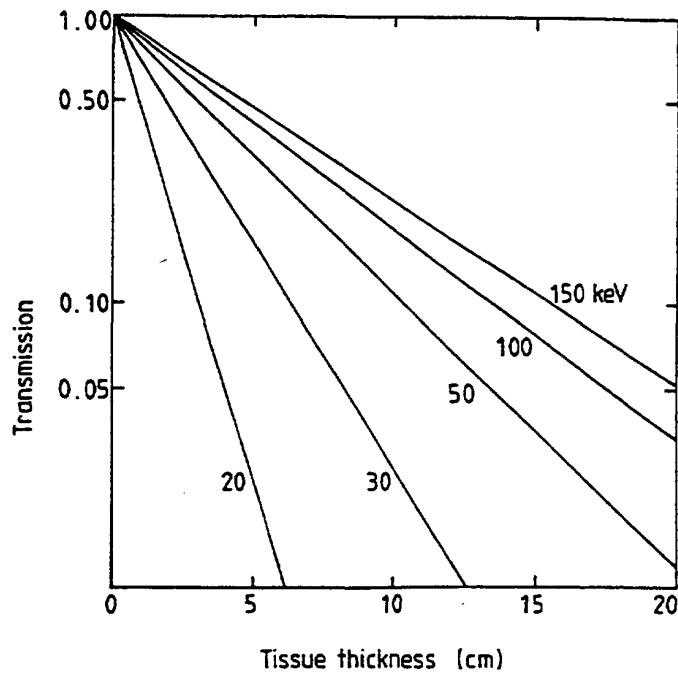


Figure 2.3 Transmission of monoenergetic photons through soft tissue. Curves are shown for photon beams with energies 20, 30, 50, 100 and 150 keV.

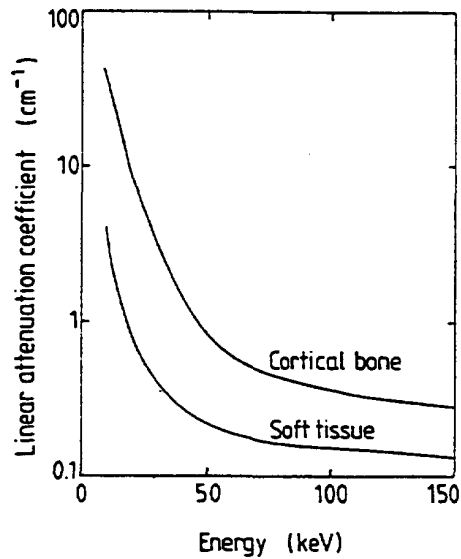


Figure 2.5 Variation with energy of the linear attenuation coefficients for soft tissue and cortical bone.

Diagnostic radiology with x-rays

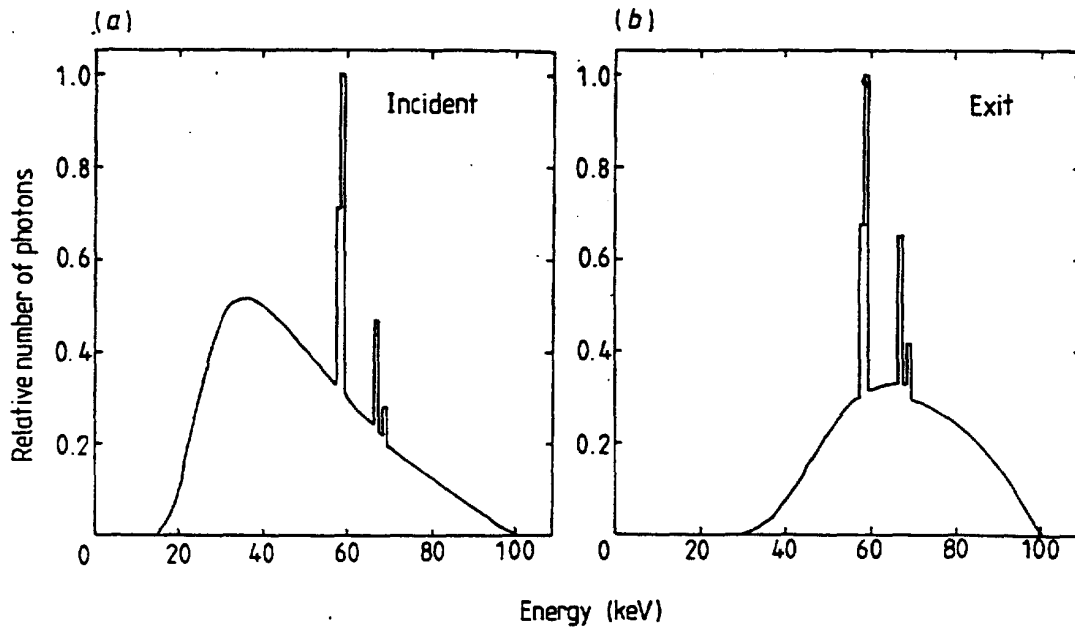


Figure 2.11 X-ray spectra for an x-ray tube with a tungsten target; 100 kV constant potential with 2.5 mm aluminium added. The spectra are shown both before and after attenuation by 18.5 cm soft tissue plus 1.5 cm bone. (The spectra are based on the work of Birch *et al* (1979).)

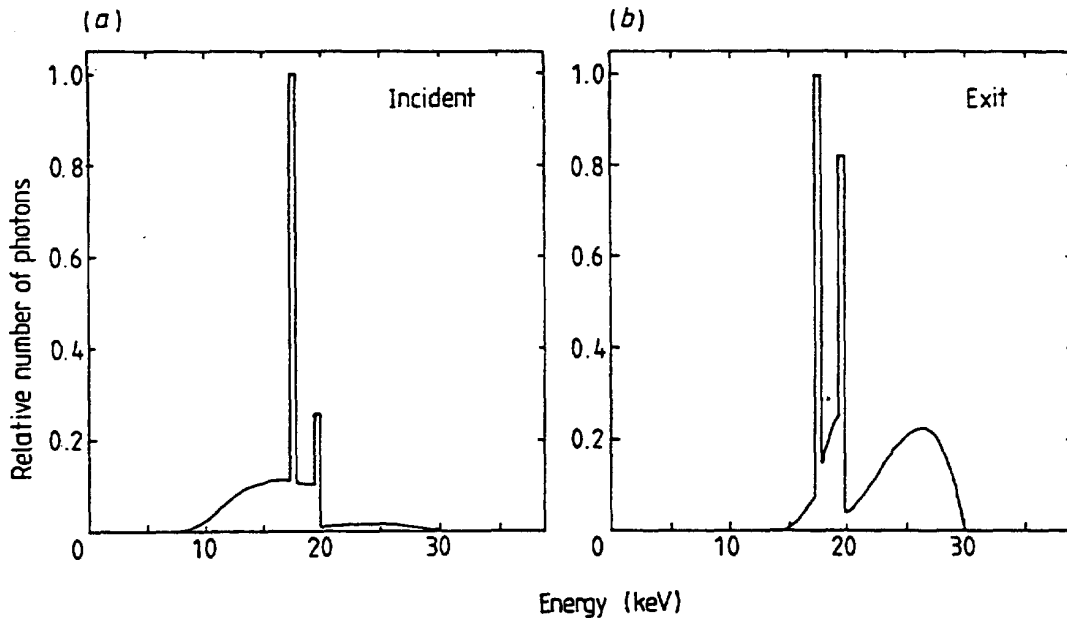


Figure 2.12 X-ray spectra for an x-ray tube with a molybdenum target; 30 kV constant potential with 0.03 mm molybdenum filter. The spectra are shown both before and after attenuation by 5 cm tissue. (The spectra are based on the work of Birch *et al* (1979).)

from: D. Dance "Diagnostic radiology with x-rays", In: "The Physics of Medical Imaging" S. Webb (Ed)

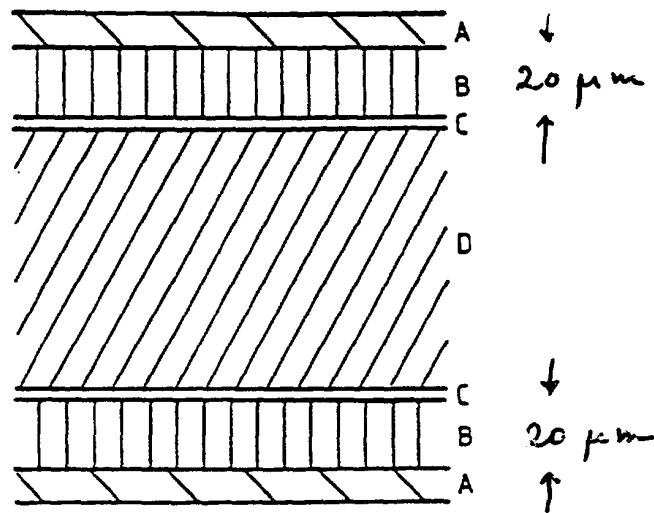


Figure 2.16 Construction of direct-exposure x-ray film: A, protective coating; B, film emulsion ($20\ \mu\text{m}$) of silver halide grains in gelatin; C, subbing layer; D, film base ($200\ \mu\text{m}$). (After Barrett and Swindell (1981) p196.)

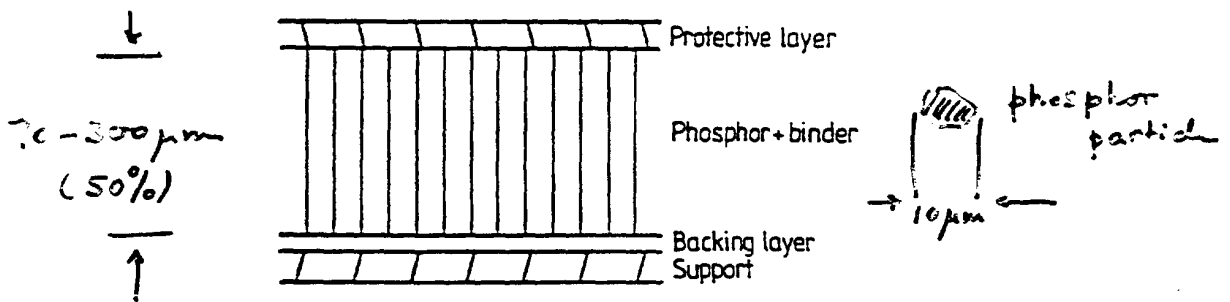


Figure 2.19 Construction of a fluorescent screen.

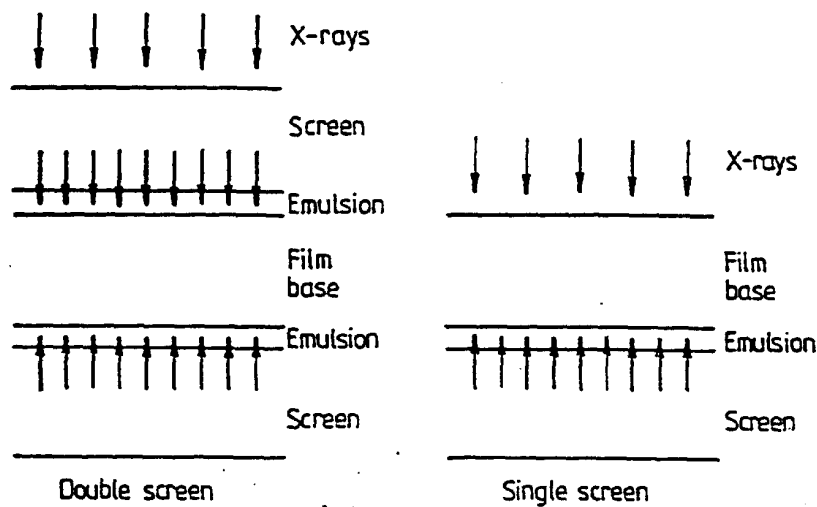


Figure 2.20 The use of double and single screens. The arrows at the top of each figure represent the incident x-rays, which interact in the screens, and the arrows originating in the screens represent the light fluorescent photons, which expose the film emulsion.

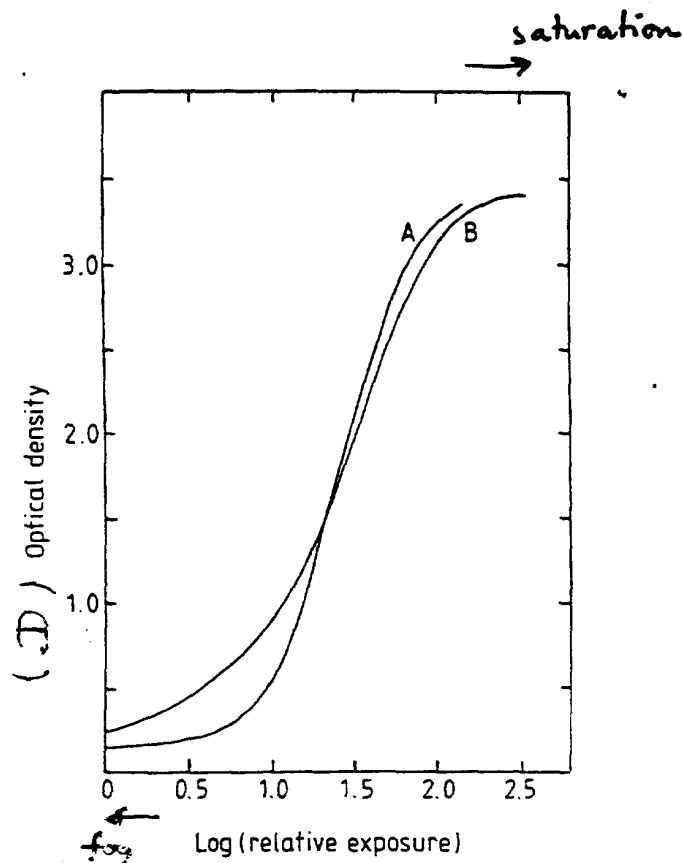


Figure 2.17 Film characteristics for a direct-exposure x-ray film (curve A, equation (2.31)) and for a screen film (curve B). The speed of the direct exposure film has been increased so that the shapes of the two curves can be compared. The two films have the same fog level and maximum density.

from: D. Dance "Diagnostic Radiology with X-rays",
 In: The Physics of Medical Imaging, S. Webb (Ed.)

- $D = \log_{10} \left(\frac{I_0}{I} \right)$
- $D = D_{MAX} [1 - \exp(-K X_n)]$
- film latitude Γ (film gamma) $n=2-3$
 $D \sim \Gamma \log_{10} \frac{X}{X_0}$

X-ray radiology **diagnostic range**: 10 -100 keV

- film:
- high spatial resolution (few μm)
 - high contrast (curve A, high Γ , narrow latitude)
 - low efficiency (20 μm)

film+screen

calcium tungstate

terbium activated rare-earth oxysulphide (X_2O_2S) phosphors

$X =$ *gadolinium*
lanthanum
or *yttrium*

- moderate high spatial resolution (10-20 μm)
- good contrast (curveB, low Γ , wide latitude)
- high efficiency

typical values: 100% at 10 keV

45% at 40 keV

10% at 70 keV

noise

- quantum mottle
- variation in energy absorbed per interacting photon
- inhomogeneities in phosphor coating (structure mottle)
- fluctuations in light fluorescent photons yield
- fluctuations in the number of silver halide grains in the emulsion (film granularity)

$$\text{DQE} = \text{Detective quantum efficiency} = \left[\frac{\text{SNR (out)}}{\text{SNR (in)}} \right]^2 \quad (\leq 1)$$

$$\text{DQE}_{\text{tot}} = \text{DQE}_1 * \text{DQE}_2 \dots * \text{DQE}_N$$

Main film limitations:

- Limited dynamic range (narrow latitude)
- Lack of digital processing

Transducers for digital imaging:

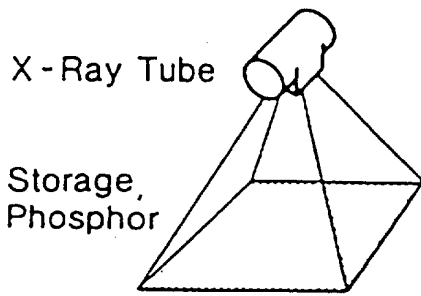
AREA EXPOSURE

- Digital screen-film system
Illumination of the film w/ light followed by a visual assessment of variation in transmittance (viewing box)
- TV camera
Standard viewing box and digitising by TV frame
 - cheap and easy
 - bandwidth and dynamic range limitations
- Laser scanner
Raster scanner of the X-ray film by small focussed spot (10 μm minimum, 100-200 μm standard)
- Image Intensifier + Television system
CsI phosphor
- Photostimulable luminescence

DIRECT DIGITAL IMAGING

(2-D, 1-D and point scanning)

Exposure



Scanning

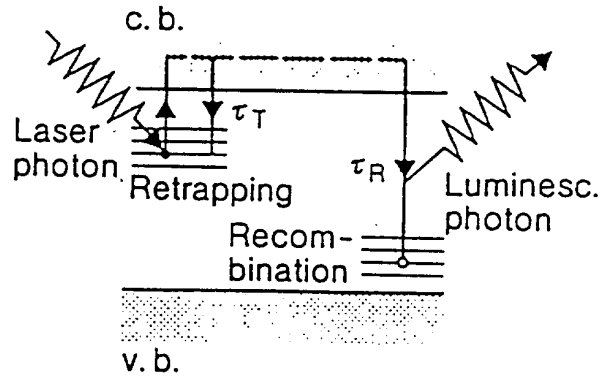
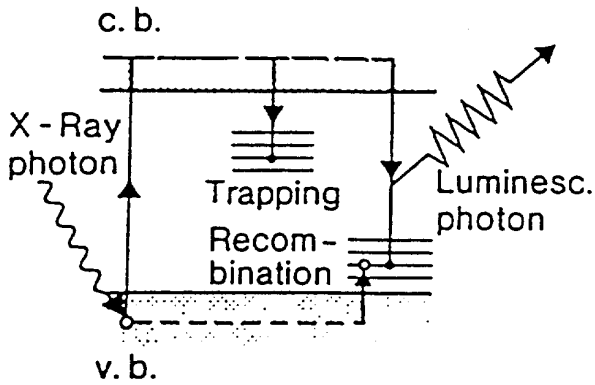
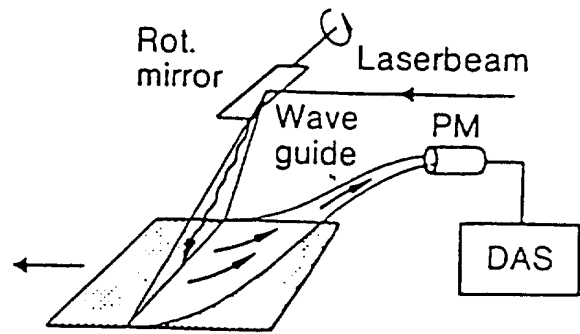


Fig. 1 - X-ray imaging via storage phosphors. Upper half: Scheme of apparatus. Lower half: Physical principle.

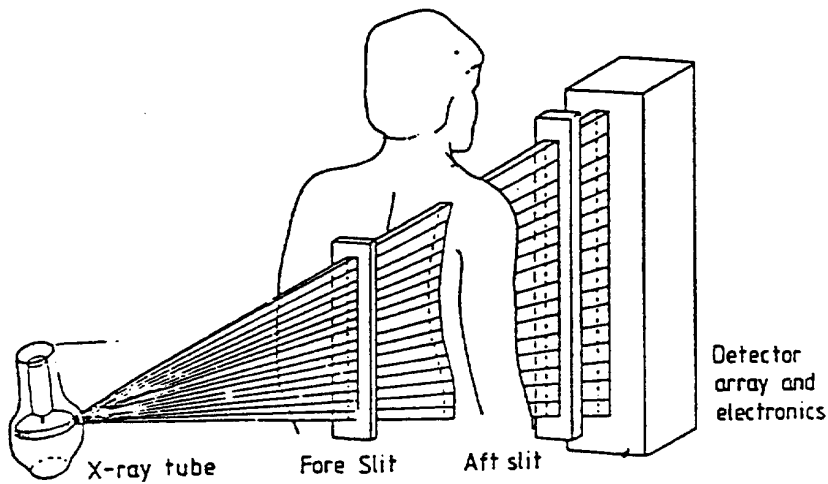


Fig. 4. A prototype digital radiography system for examination of the chest. The X-ray beam is collimated to a narrow fan beam by two mechanically connected vertical slits. [Courtesy Picker International Ltd and Radiology 148 (1983) 259.]

Gaseous and Semiconductor Detectors for Digital Medical Imaging

Single photon counting

Gaseous	MultiWire Proportional Chamber MicroStrip Gas Chamber
Semiconductor	Microstrip solid state crystal (Si, Ge, HgI ₂) Pixel solid state crystal (Si, GaAs, CdTe)

Integrating

Semiconductor	CCD matrices Photosensitive diode arrays Amorphous silicon
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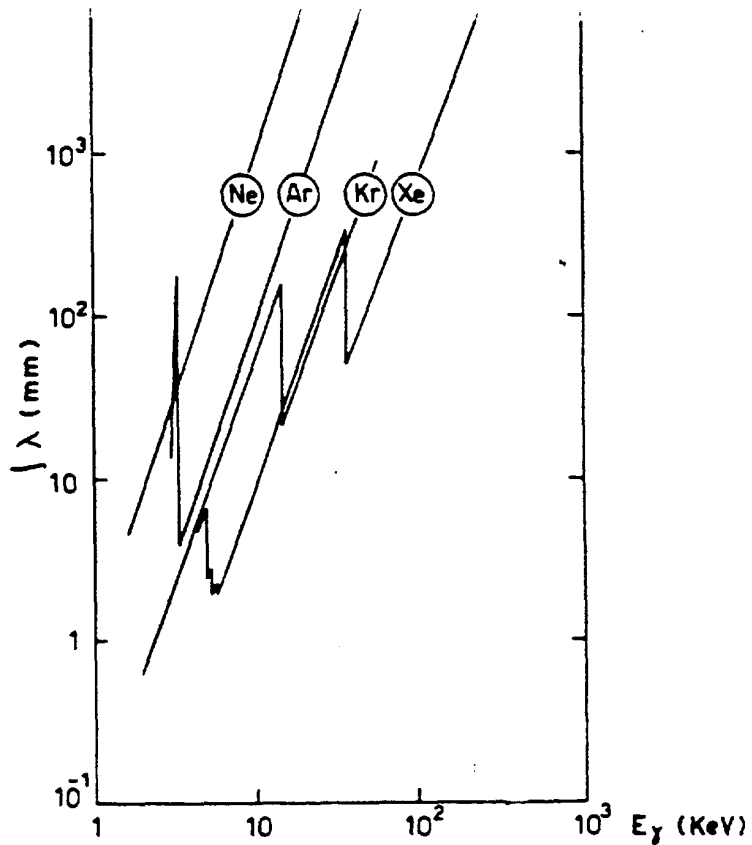


Fig. 2 - Cammino libero medio della radiazione in alcuni gas nobili, alla pressione di 1 atmosfera (2).

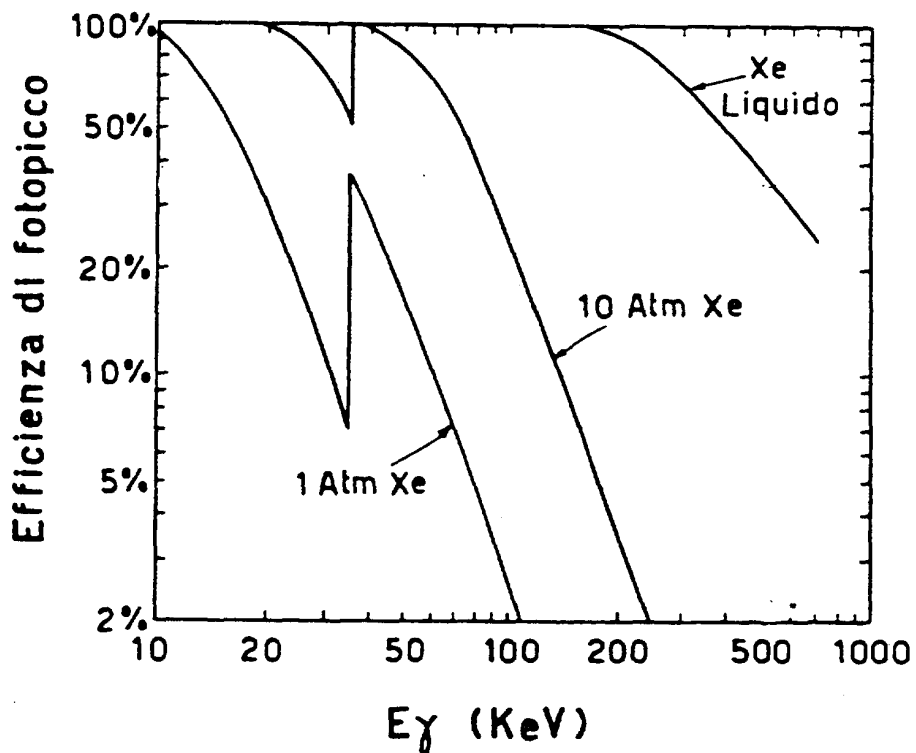


Fig. 3 - Efficienza di fotopicco in funzione dell'energia per una MWPC di spessore 2.5 cm con riempimento: a Xenon gassoso (a 1 atm e a 10 atm) e a Xenon liquido (10).

Table 1
Physical characteristics of the semiconductors

Semi-conductor	ρ [g/cm ³]	Z	E_{gap} [eV]	ϵ [eV]	T_{working} [K]	K-edge [keV]	ρ_c [Ω cm]	$\mu_{e,h}, \tau_{e,h}$ [cm ² /V]
Si	2.33	14	1.12	3.6 [1]	300	1.8	$\approx 10^3$	0.42, 0.22
Ge	5.33	32	0.67	2.9 [3]	77	11.1	$\approx 10^2$	0.72, 0.84
GaSe	4.55	31, 34	2.03	4.5 [4]	300	10.3, 12.6		$10^{-7}, 10^{-7}$ $1.5 \times 10^{-6}, 2.5 \times 10^{-6}$
InP	4.78	49, 15	1.30	4.2 [6]	300	27.9, 2.1	$\approx 10^7$	$4.8 \times 10^{-6}, \leq 10^{-7}$
CdS	4.84	48, 16	2.60	7.3 [15]	300	26.7, 2.4		$8.6 \times 10^{-6}, 4.0 \times 10^{-7}$
GaAs	5.32	31, 33	1.43	4.3 [3]	300	10.3, 11.8	$\approx 10^7$	$8.6 \times 10^{-5}, 4.0 \times 10^{-6}$
InSb	5.77	49, 51	0.20	0.6 [15]	4	27.9, 30.4		$10^{-5}, 7.5 \times 10^{-6}$
CdSe	5.80	48, 34	1.73	5.5 ^a	300	26.7, 12.6		$2.0 \times 10^{-5}, 1.5 \times 10^{-6}$
CdTe	6.20	48, 52	1.44	4.7 [3]	300	26.7, 31.8	$\approx 10^9$	$2.0 \times 10^{-3}, 4.0 \times 10^{-4}$
PbI ₂	6.20	82, 53	2.55	7.7 ^a	300	88.0, 33.2	$> 10^{13}$	$8.0 \times 10^{-6}, 2.0 \times 10^{-7}$
HgI ₂	6.40	80, 53	2.13	4.2 [7]	300	83.1, 33.2	10^{13}	$10^{-4}, 10^{-5}$
TlBr	7.56	81, 35	2.68	6.5 [18]	300	85.5, 13.5	$\approx 10^{12}$	$1.6 \times 10^{-5}, 1.5 \times 10^{-6}$

^a Calculated from Klein's empirical formula [4].

from: W. Bencivelli et al
Nucl. Instr. Meth. A 310 (1991) 210

Table 2.2 Doses for some common radiological examinations.

Examination ^a	Dose (mGy)
CC breast	1.2
AP chest	0.3
AP lumbar spine	9.2
AP pelvis	6.6
AP skull	4.4

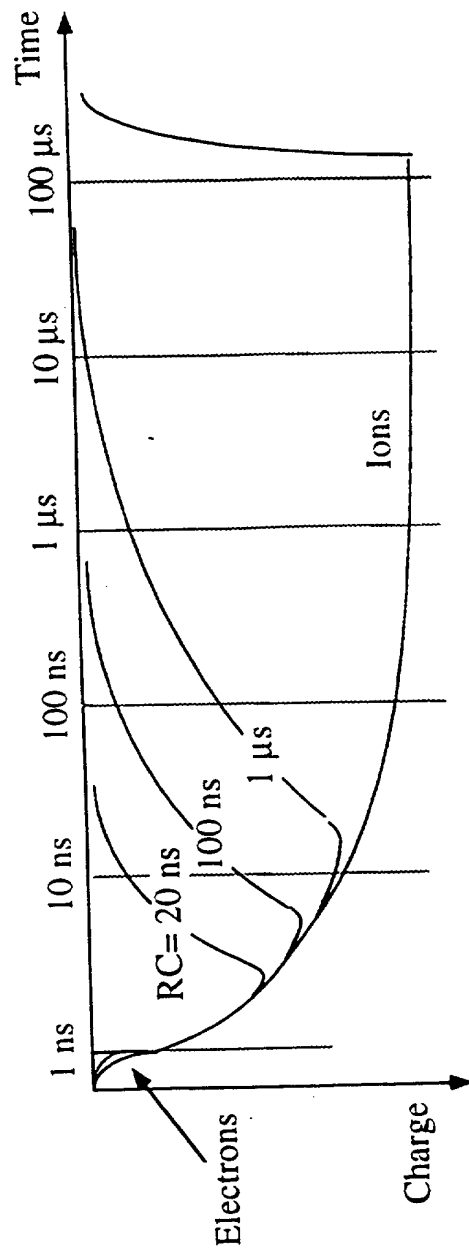
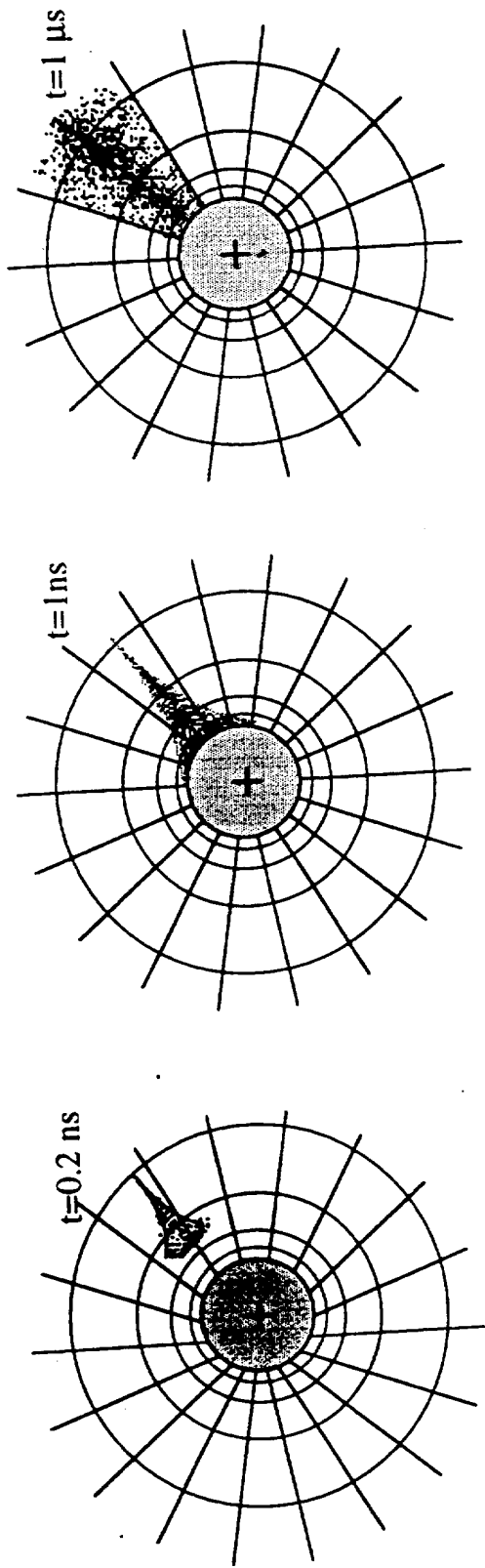
^a CC = cranio-caudad view or projection.
AP = antero-posterior view or projection.

Table 2.3 Effective dose equivalent (mSv) and organ doses (mGy) (breast, red bone marrow, lung, thyroid, skin, ovaries and testes) for selected radiological examinations.

Examination	Doses per examination							
	Eff. dose equiv.	Breast	RBM	Lung	Thyroid	Skin	Ovary	Testes
Barium meal	3.8	2.2	2.6	8.7	1.1	2.1	3.6	0.3
Barium enema	7.7	0.7	8.2	3.2	0.2	5.1	16.0	3.4
IVU ^a	4.4	0.7	1.9	7.0	0.2	1.9	0.8	0.1
Cholecystography	1.0	0.4	0.8	1.6	0.1	0.8	0.4	0.0

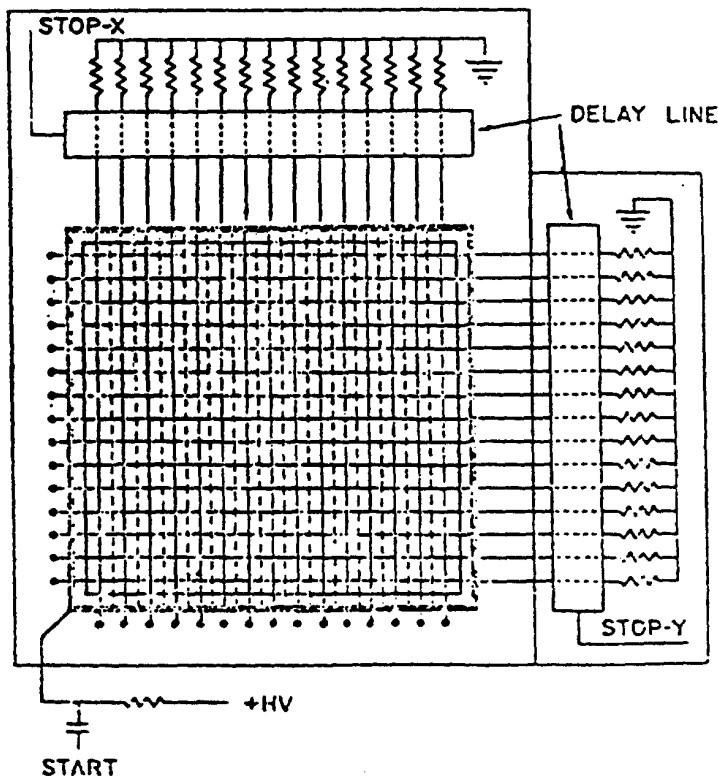
^a Intravenous urography.

AVALANCHE GROWTH AND SIGNAL FORMATION



METHODS OF POSITION READOUT

- (A) AMPLIFIER-ENCODER/WIRE ON ANODE WIRES OR CATHODE STRIPS REQUIRES MUCH ELECTRONICS. NEED CENTER OF GRAVITY SENSING.
- (B) CHARGE DIVISION. INTERCONNECT CATHODE STRIPS BY CAPACITORS OR RESISTORS. MEASURE CHARGE AT BOTH ENDS OF CHAMBER. MODERATE POSITION ACCURACY. LIMITATION: ONLY ONE IONIZING TRACK CAN BE READ ON EACH EVENT. TWO OR MORE TRACKS ARE READOUT AS AN AVERAGE POSITION.
- (C) DELAY LINE READOUT. CONNECT DELAY LINE CAPACITATIVELY TO ORTHOGONAL PLANES OF CATHODE WIRES OR TO ANODE WIRES AS WELL. BY TIMING ARRIVAL OF SIGNALS TO BOTH ENDS CAN DETERMINE POSITION TO ACCURACY OF 0.1 MM. MAIN LIMITATION X,Y AMBIGUITY WHEN MULTIPLE TRACKS OCCUR.



2.3 - Bone densitometry: Rationale

Passive (film) detection has an unparalleled resolution in densitometry studies. However, the radiographic film suffers from the intrinsic chemical fog which diminishes the sensitivity and the density resolution of this technique.

⇒ a MWPC with

1. good detection efficiency ⇒ Xenon (4 atm)
2. good spatial resolution ⇒ monochromatic source just above the Xe K-edge (34.6 keV)
3. high rate capability ⇒ fast TDC's and histogramming memories

Parameters*:

Active area	<u>128 mm x 128 mm</u>
Anode wire pitch	1 mm
Anode-cathode gap	3 mm
Cathode strips with fast delay line read-out	50 ns/cm
Xenon (80%)-CO ₂ (20%)	4 atm
Entrance window	300 μm - 0.07 g/cm ³ - 300 μm G-10 - Rohacell 71 - G-10
Read out system	Charge sensitive preamplifier Fast shaping amplifier Constant Fraction Discriminator 2-TDC's (500 ns conversion time) 1 dedicated two-D 128x128 pixels histogramming CAMAC memory

* R.Bellazzini, A.Brez, A.Del Guerra , et al. Nucl Instr Meth Phys Res1984, 228, 193-200

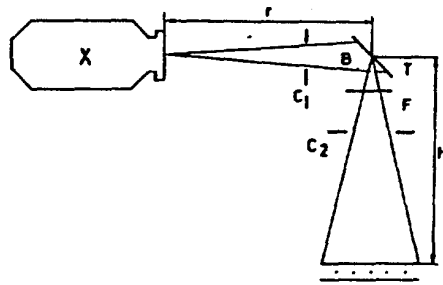
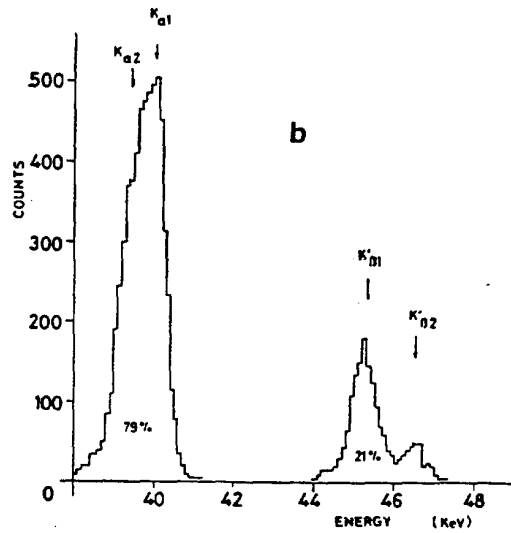


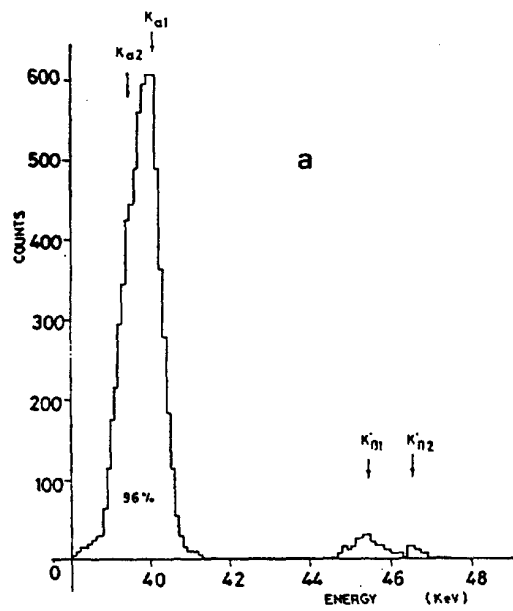
Fig. 1. A scheme of the fluorescent X-ray source: C1: entrance collimator, C2: exit collimator, T: target, F: filter.

Table 1
X-ray energy selection.

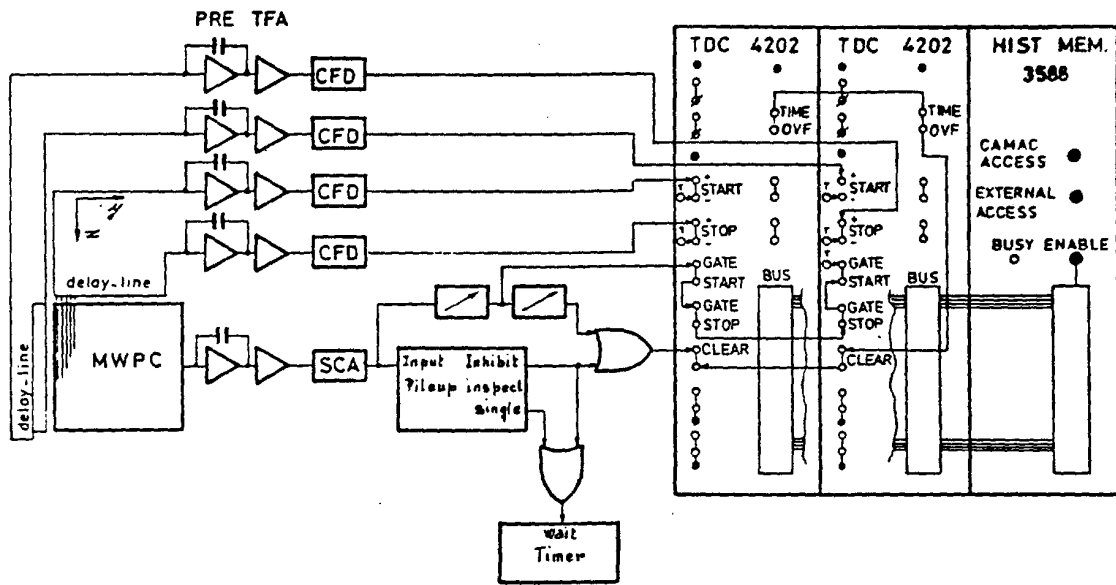
Target	samarium	gadolinium	dysprosium
Filter	neodymium	samarium	gadolinium
Energy	40 keV	42 keV	45 keV



SAMARIUM
TARGET



SAMARIUM
TARGET
+
NEODYMIUM FILTER



Block diagram of the position read-out system.

read write \rightarrow 1.2 μ s
800 kHz

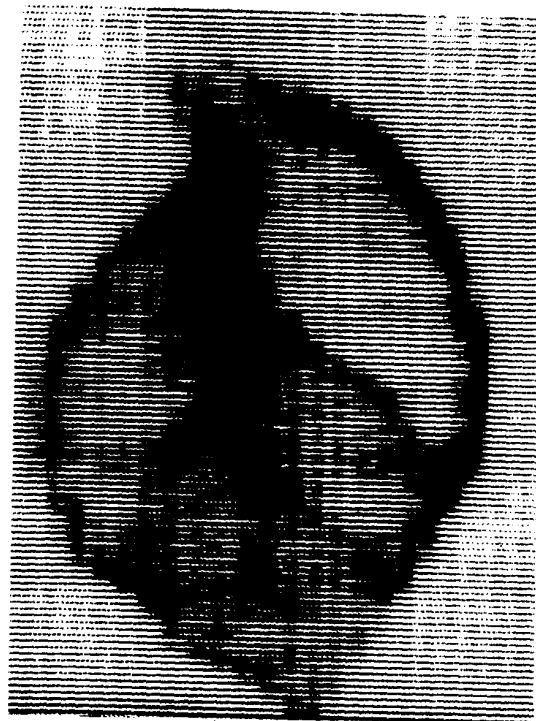


Fig. 13. A MWPC shell radiography.

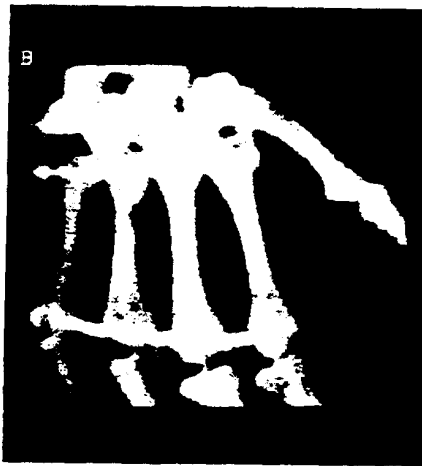


Fig. 6. The two dimensional bone mass distribution of a wrist of a human skeleton.

The system is now under clinical trial, as single photon absorptiometer at the energies of both I-125 (27.4 keV) and Gd-153 (42 and 100 keV) or as dual photon absorptiometer using one of the two pairs of isotopes (I-125, Gd-153) or (I-125, Am-241). Compared to standard DPA the MWPC system has a much lower repositioning error \Rightarrow this allows its use in regions with a large gradient of bone mineral density, such as the calcaneus or the very distal site of the forearm (both can be imaged in a few minutes), which seem superior in identifying early osteoporosis.

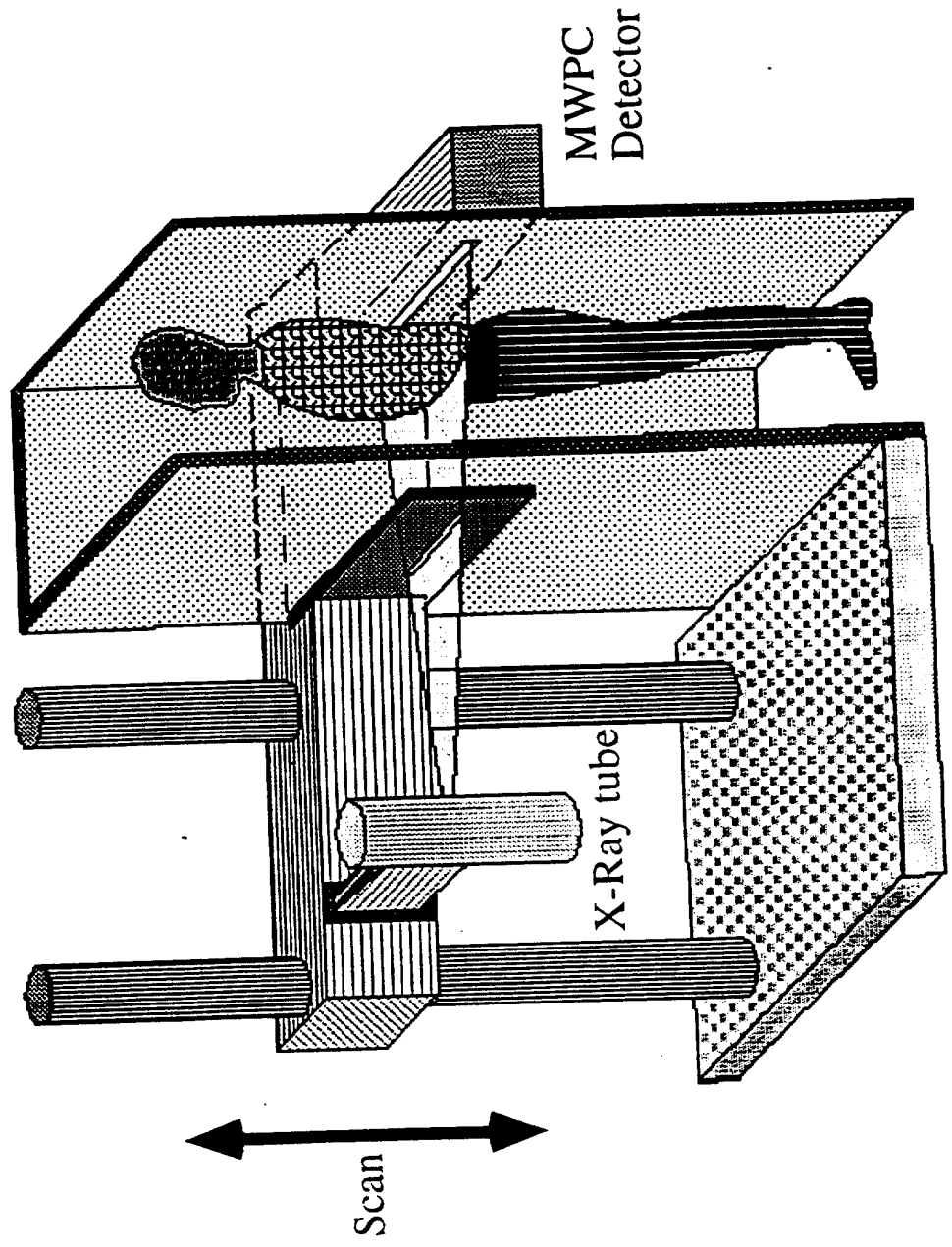
* F. Angelini, R. Bellazzini, A. Brez et al. Bone densitometry of the Peripheral Skeleton with a new photon counting and imaging device. Investigative Radiology, 1989, 24(9), 684-691.

DIGITAL RADIOGRAPHY WITH MWPC:

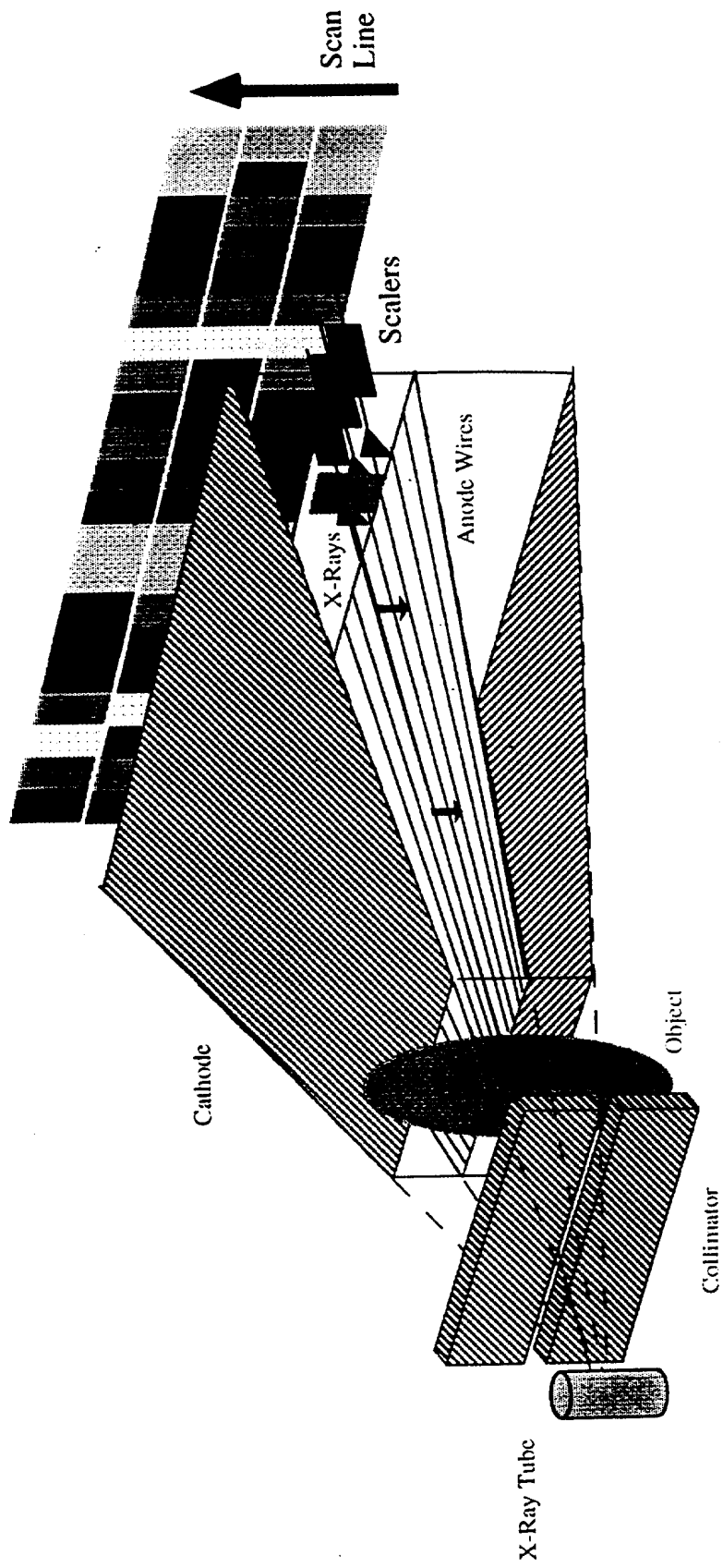
Budker Institute for Nuclear Physics, Novosibirsk (Russia)

S. Baru et al, Nucl. Instr. Methods A283 (1989) 431

E. Babichev et al, Nucl. Instr. Methods A323 (1992) 49



DIGITAL X-RAY MWPC DETECTOR:



C940612D

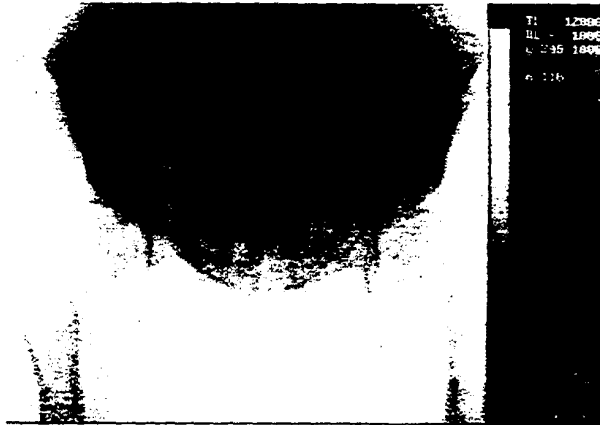


Fig. 5 - Image of the pelvis of a pregnant woman (photo from a TV monitor).



Fig. 6 - Image of the chest (photo from a TV monitor).

SIBERIAN DIGITAL RADIOGRAPHY DEVICE (SDRD)

MWPC: 1 mm wire spacing
 50 mm absorption
 Xe-CO₂ at 3 Atmospheres
 Efficiency 30% at 60 keV

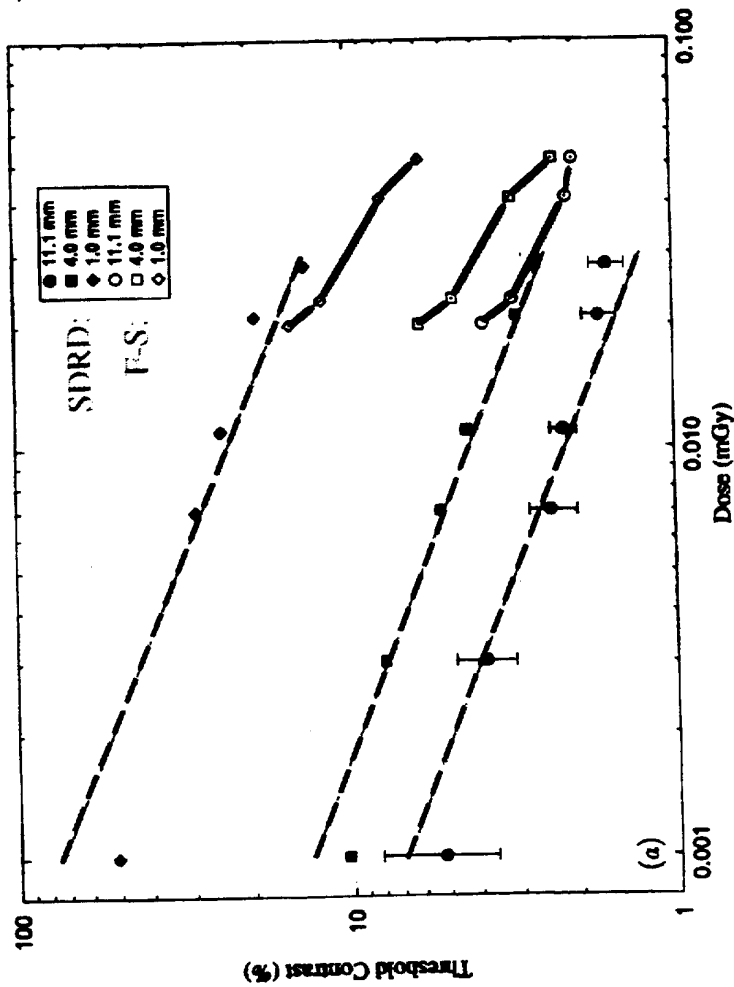
Max Data Rate: 600 kHz per channel
 Image Size: 320 x 256 pixels, 1mm²

Typical exposure times: 30 ms per line
 10 s per image

EXPOSURES FOR CLINICAL EXAMINATIONS (ENTRANCE SKIN DOSES IN mGy)

	SDRD	F-S (NRPB)
Chest	0.015	0.23
Abdomen	0.03	8.43
Lumbar Spine	0.292	22.80

THRESHOLD CONTRAST COMPARISON AS A FUNCTION OF DOSE:

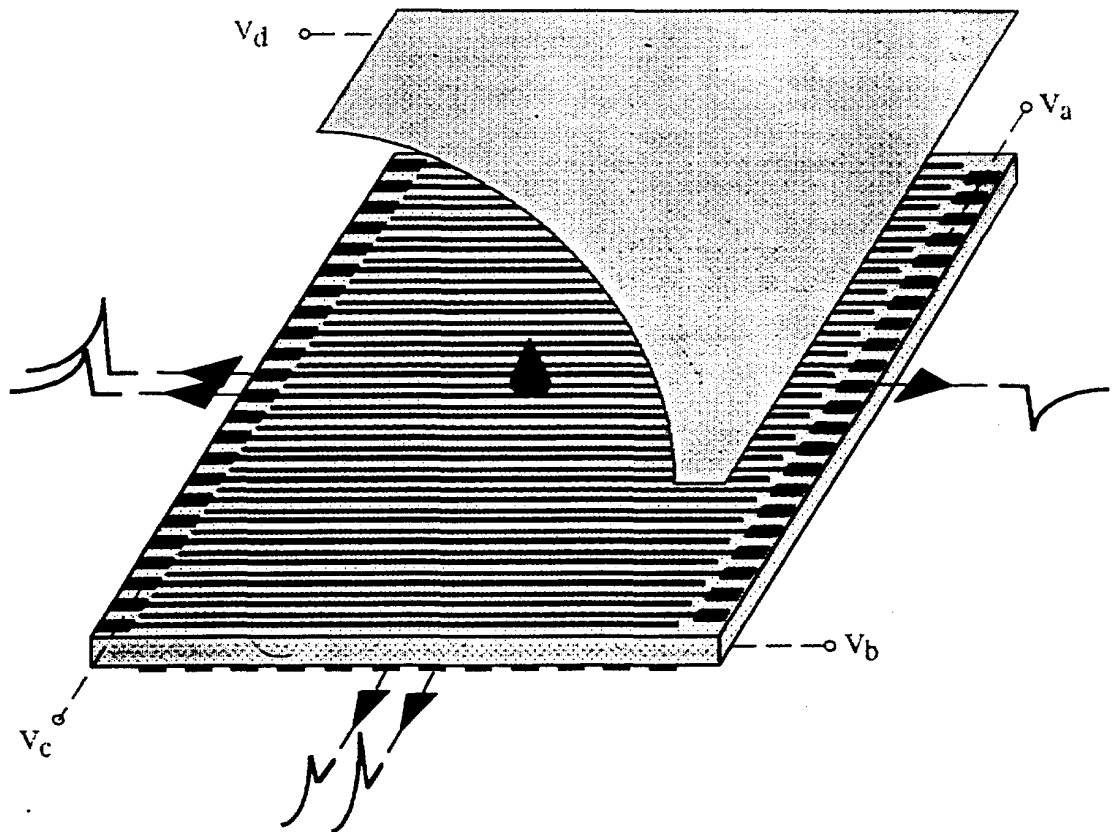
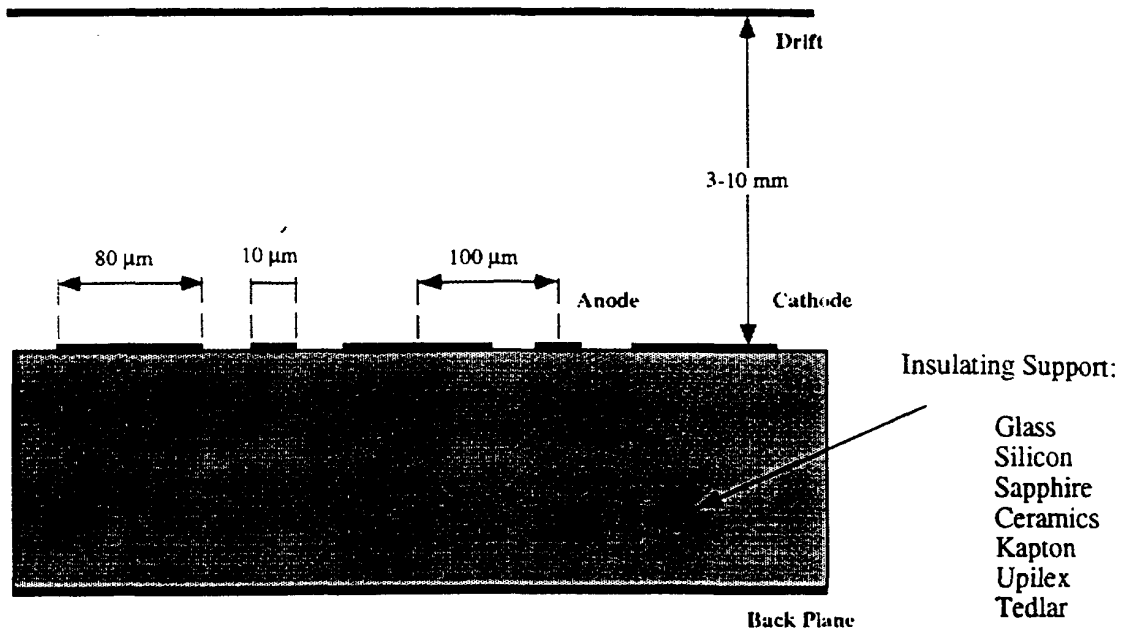


SDRD: SIBERIAN DIGITAL RADIOGRAPHY DEVICE
 F-S: UK FILM-SCREEN SYSTEM

A. Martinez-Davalos, R.D. Speller, J.A. Horrocks, D.J. Miller, S.E. Baru, A.G. Khabakhpashev, O.A. Ponomarev, L.I. Shekhtman
 Phys. Med. Biol. 38 (1993) 1419

MICRO-STRIP GAS CHAMBER

A. Oed, 1988

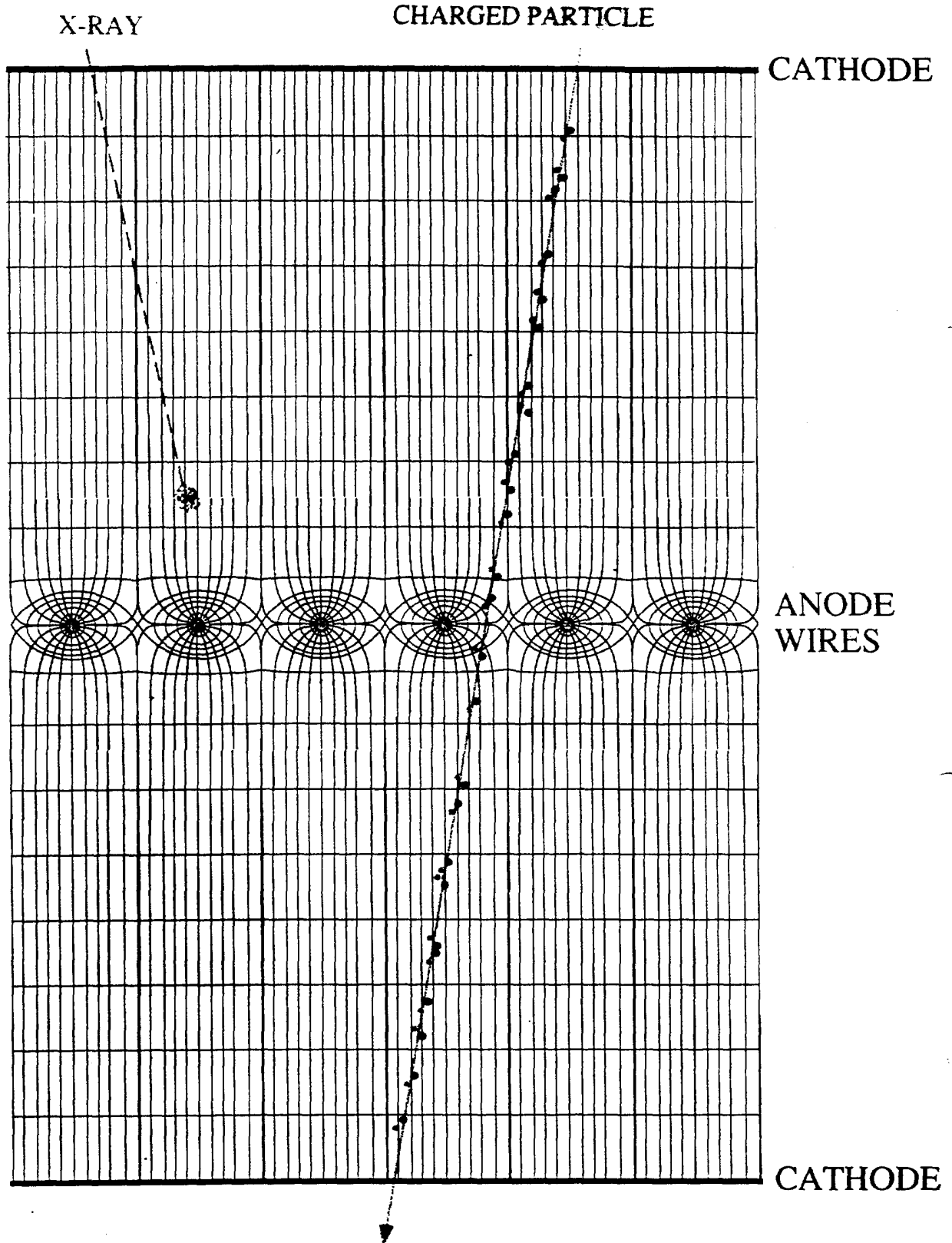


2-D and 3-D MSGC

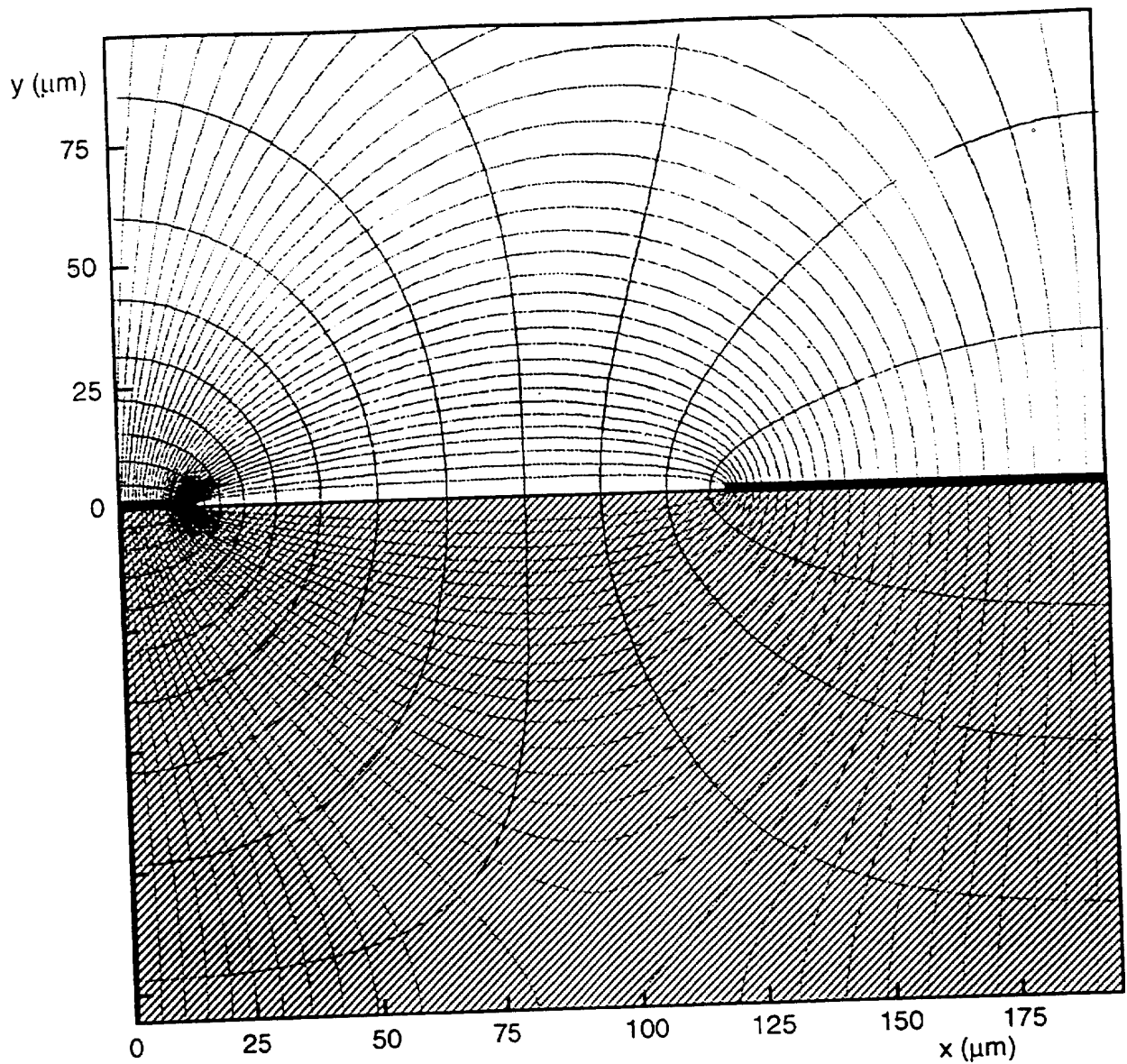
A. Oed, Nucl. Instrum. Methods A263 (1988) 35

MULTIWIRE PROPORTIONAL CHAMBER

George Charpak (1968)



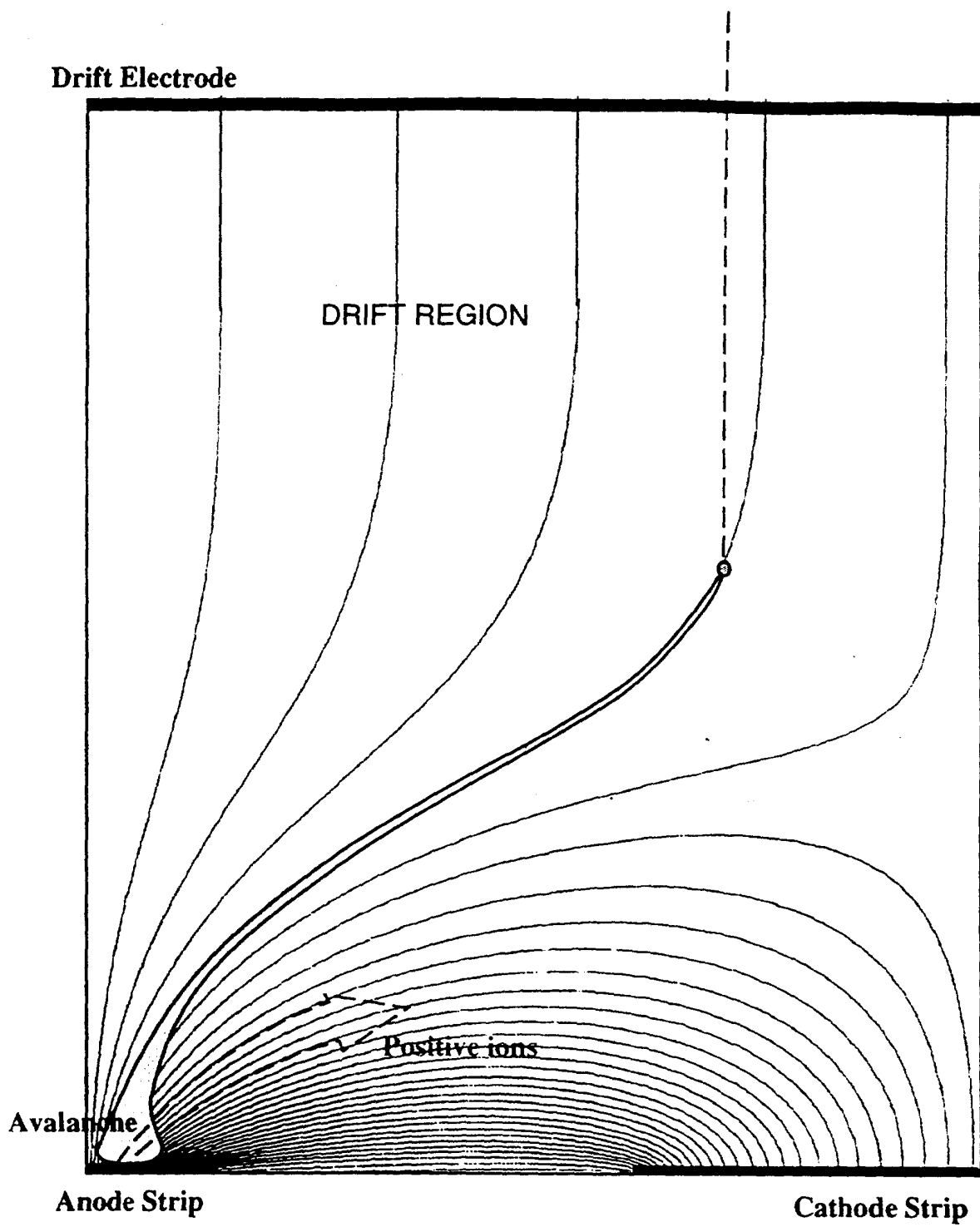
FIELD LINES AND EQUIPOTENTIALS IN THE MSGC:



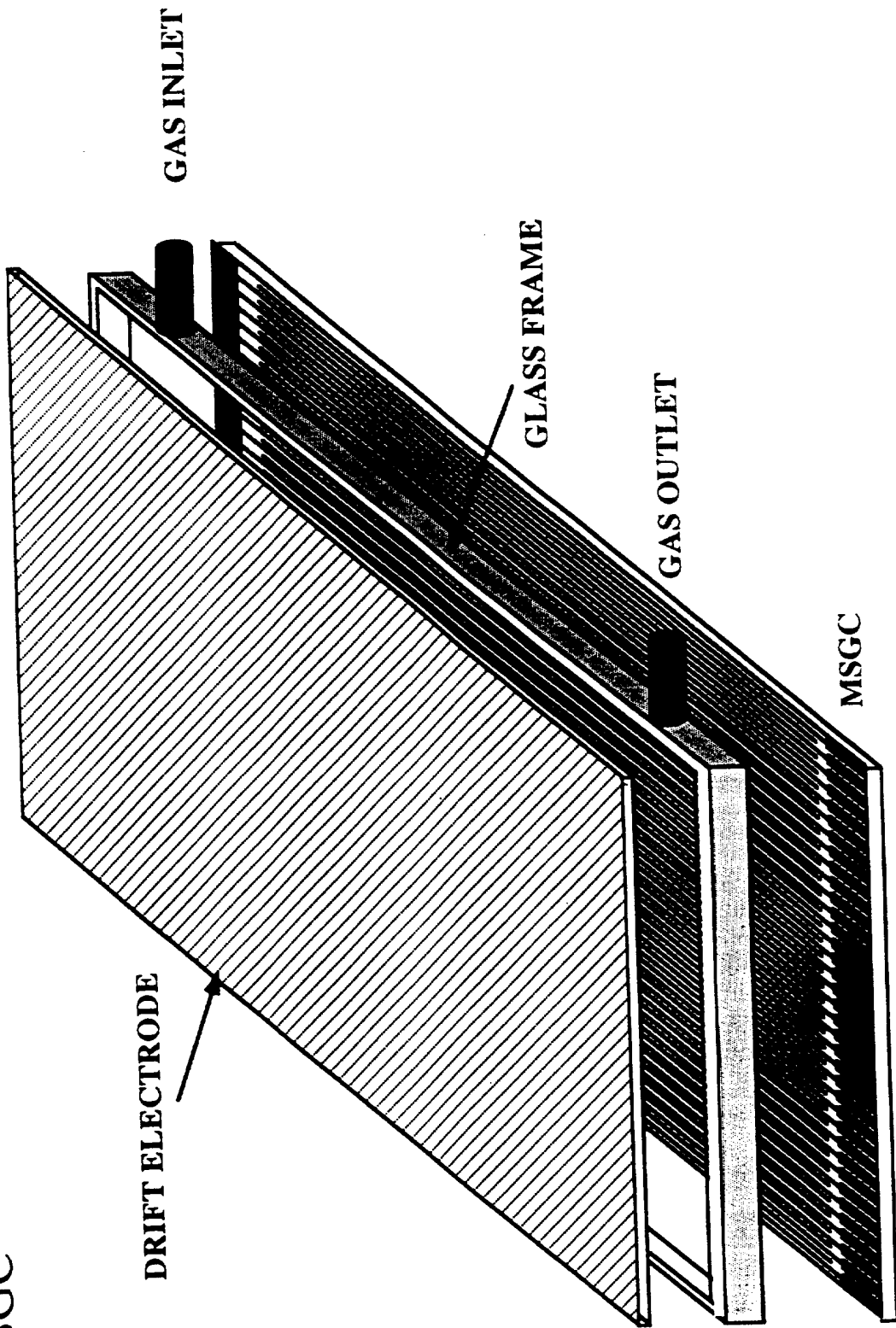
J.J. Florent, J. Gaudaen, L. Ropelewski and F. Sauli, Nucl. Instrum. Methods **A329** (1993) 125.

C940621B

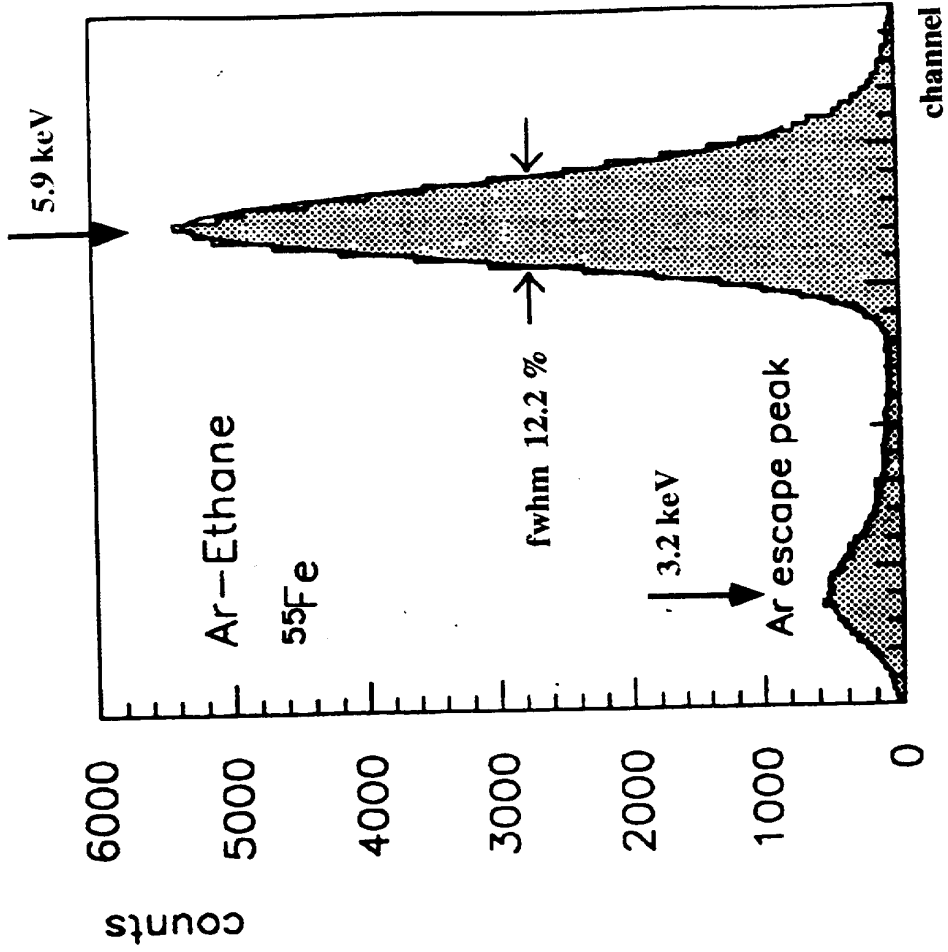
ELECTRIC FIELD LINES IN MSGC:



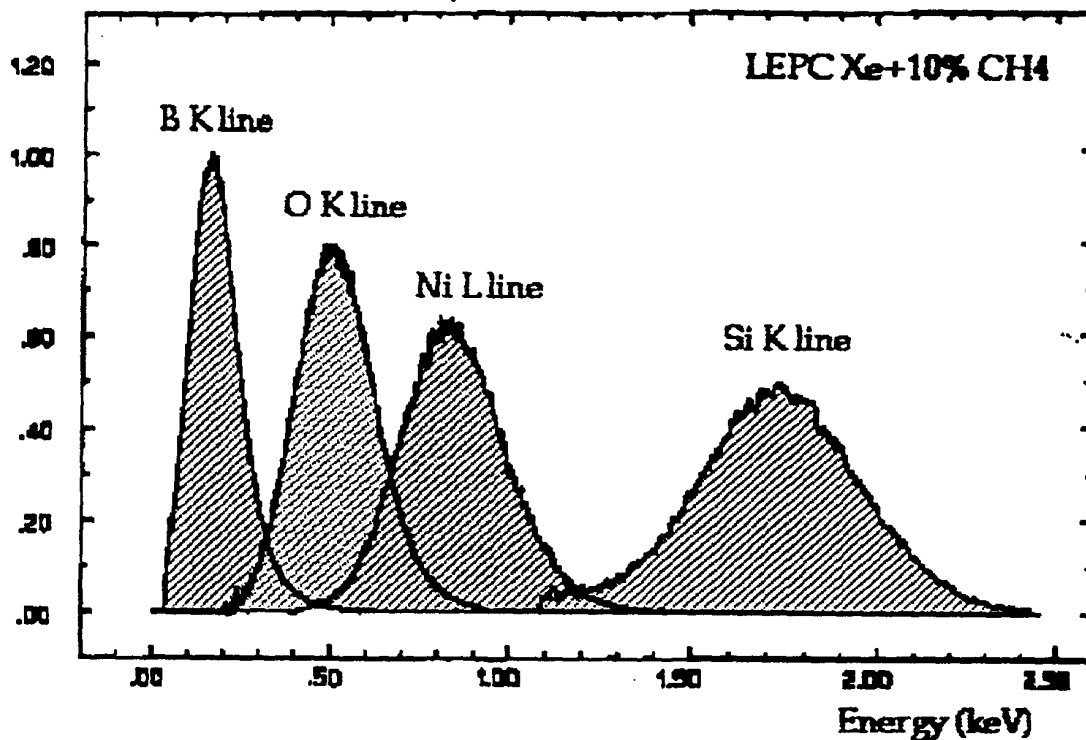
GLASS MSGC



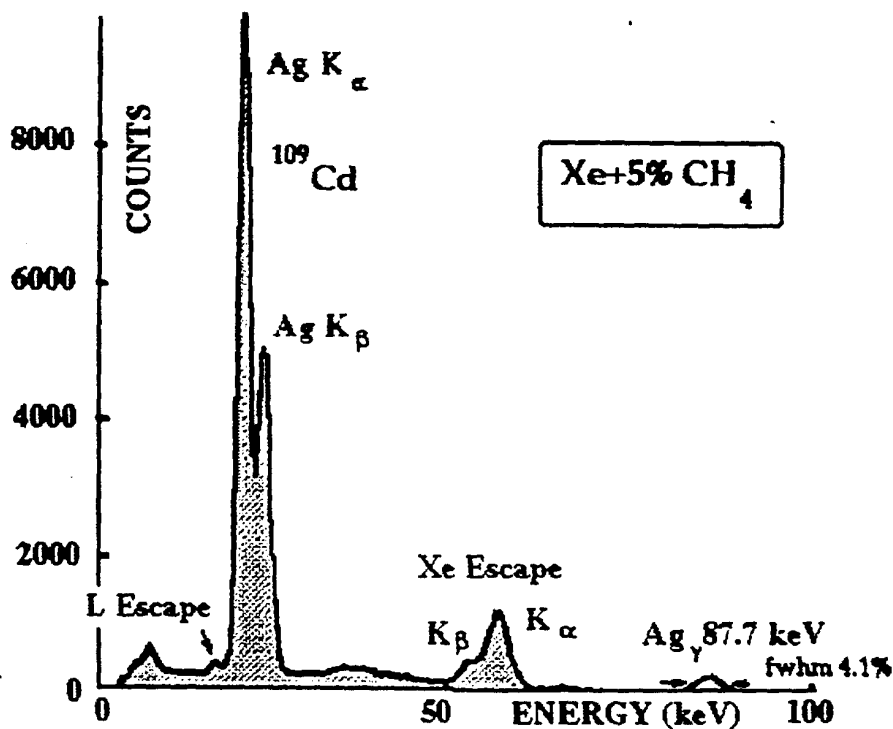
MSGC: VERY GOOD ENERGY RESOLUTION



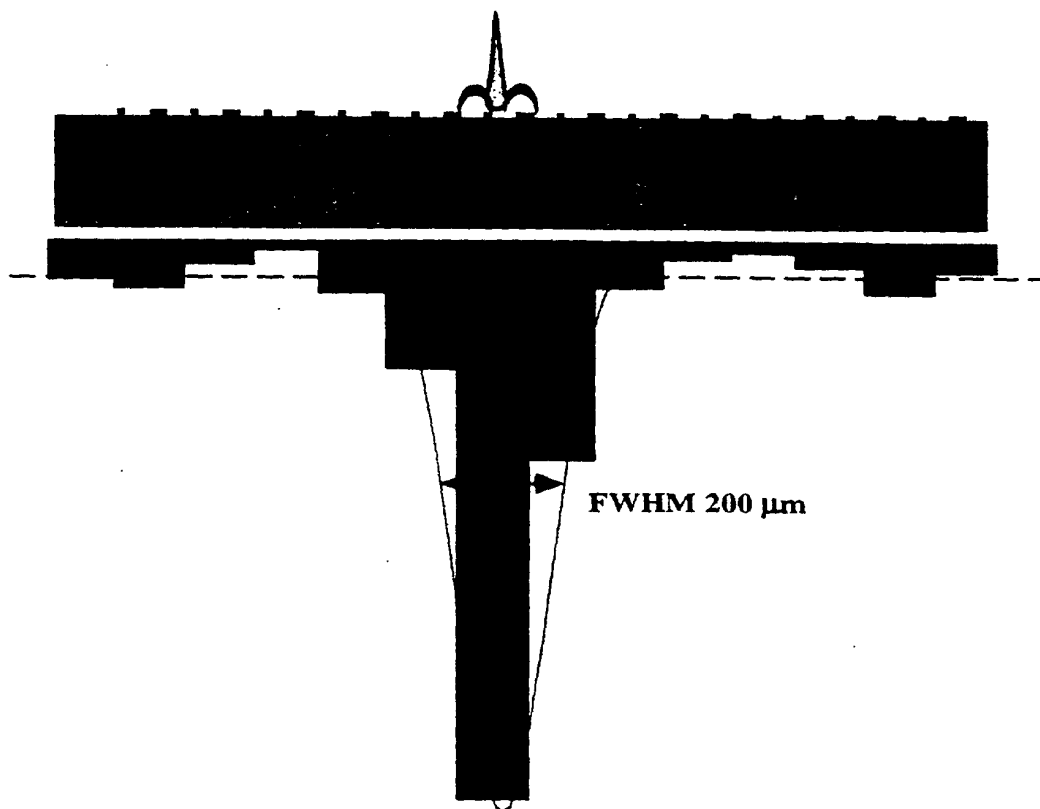
Energy resolution (low energy region):



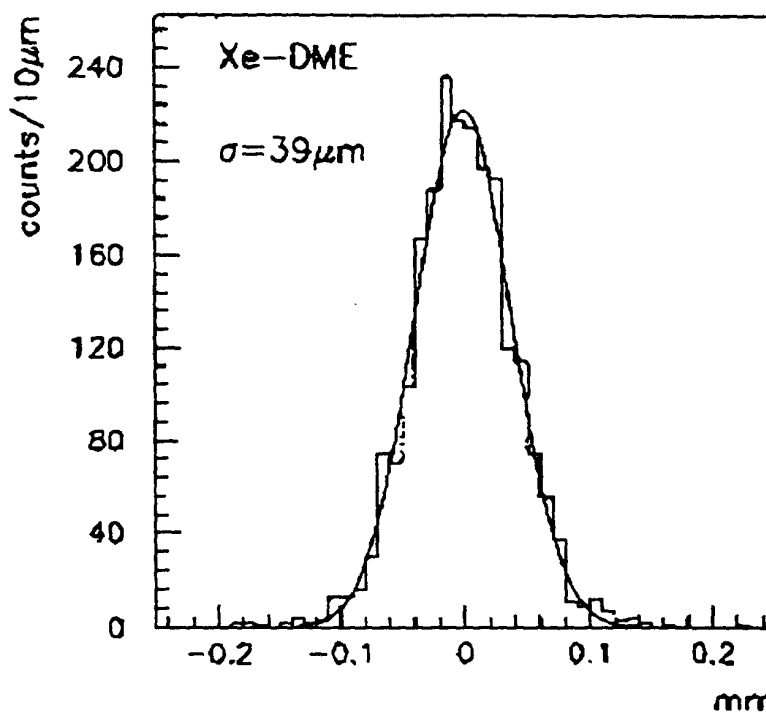
Energy resolution (high energy region):

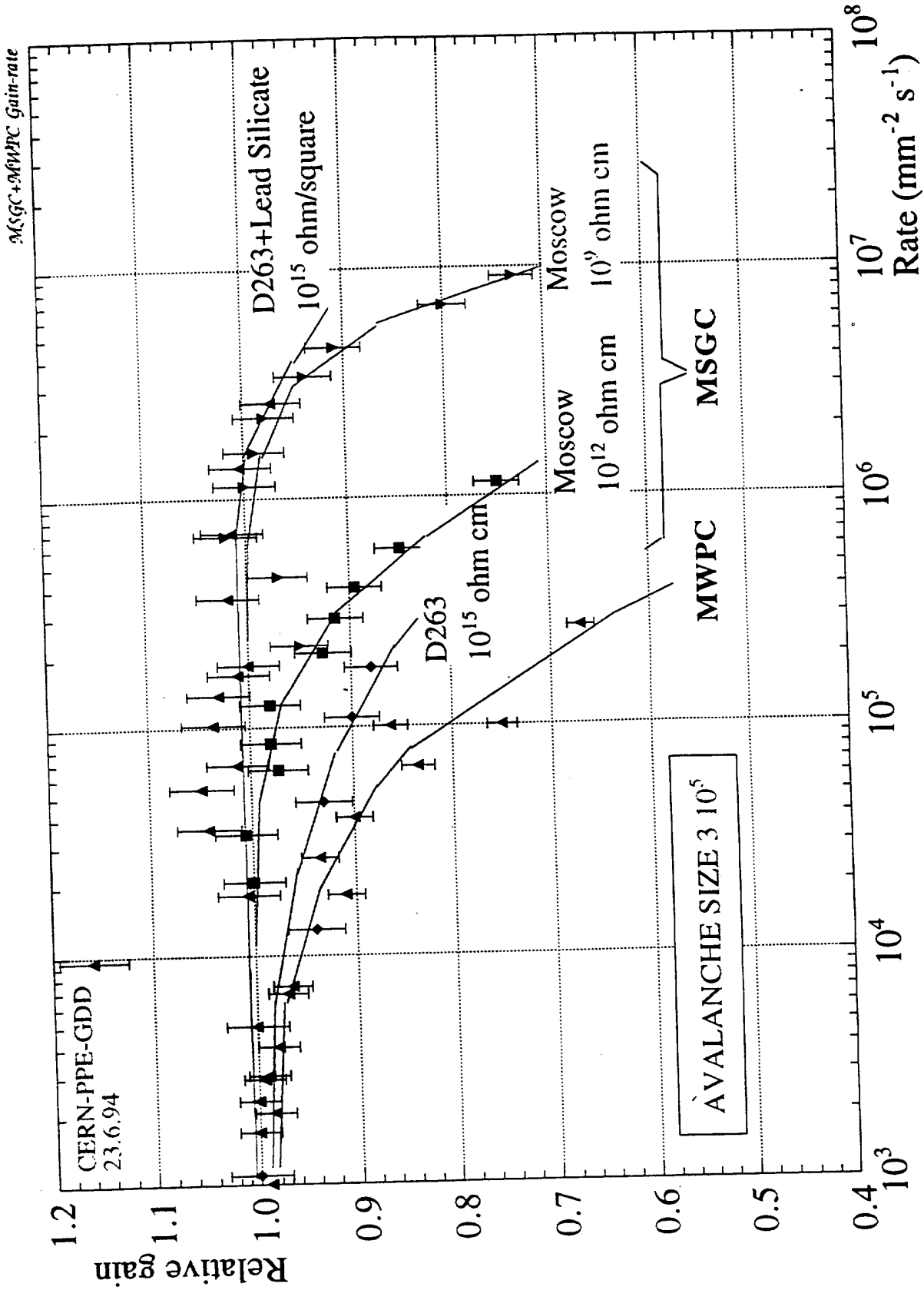


MICRO-STRIP GAS CHAMBER STRIP RESPONSE FUNCTION

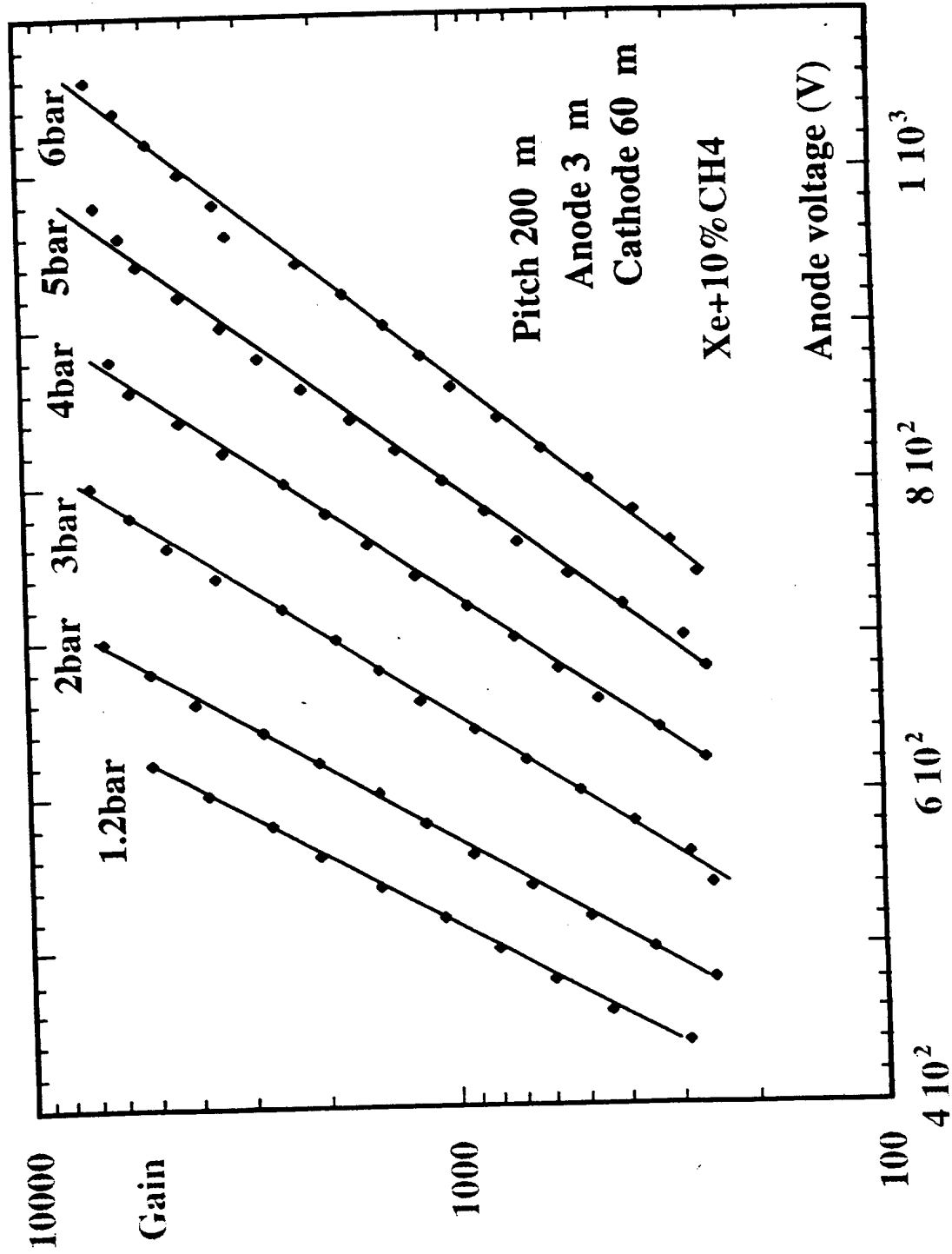


LOCALIZATION ACCURACY (MINIMUM IONIZING TRACKS):

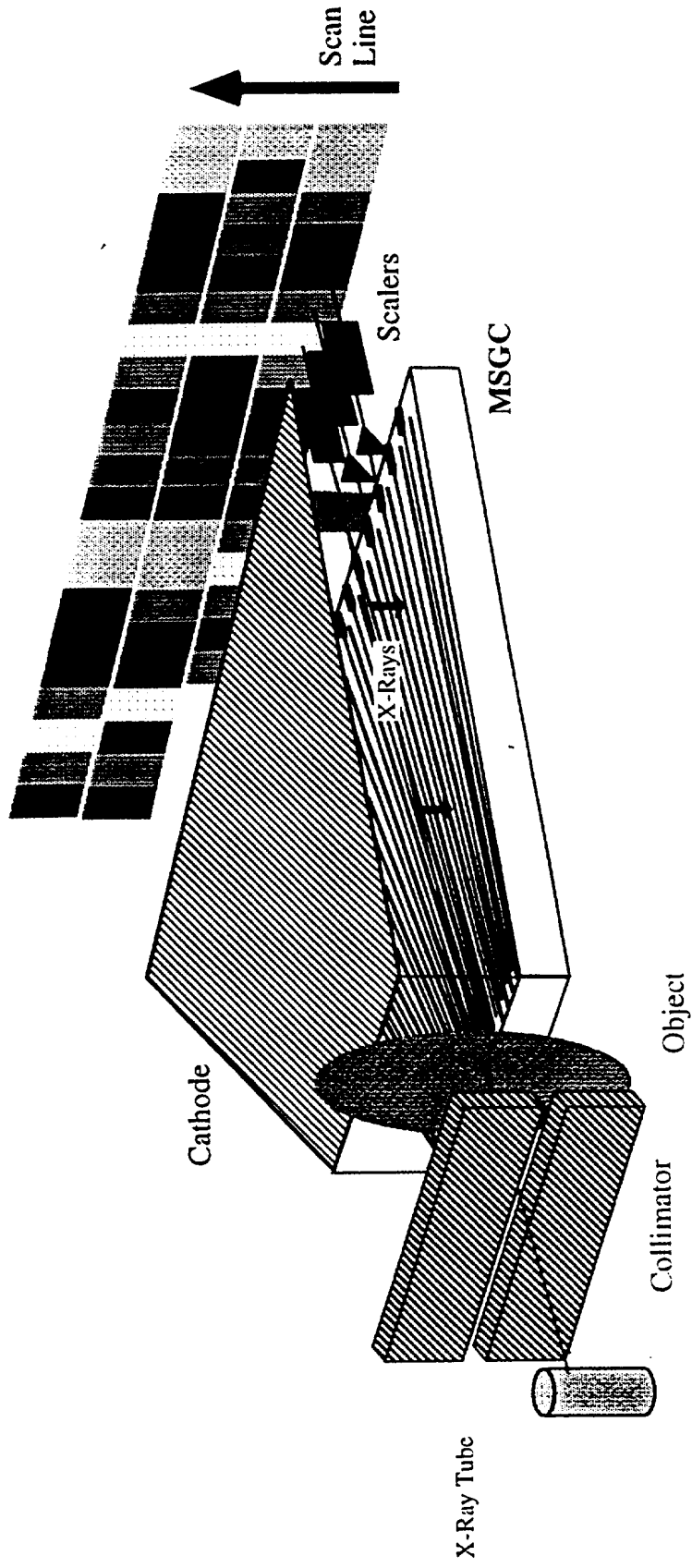


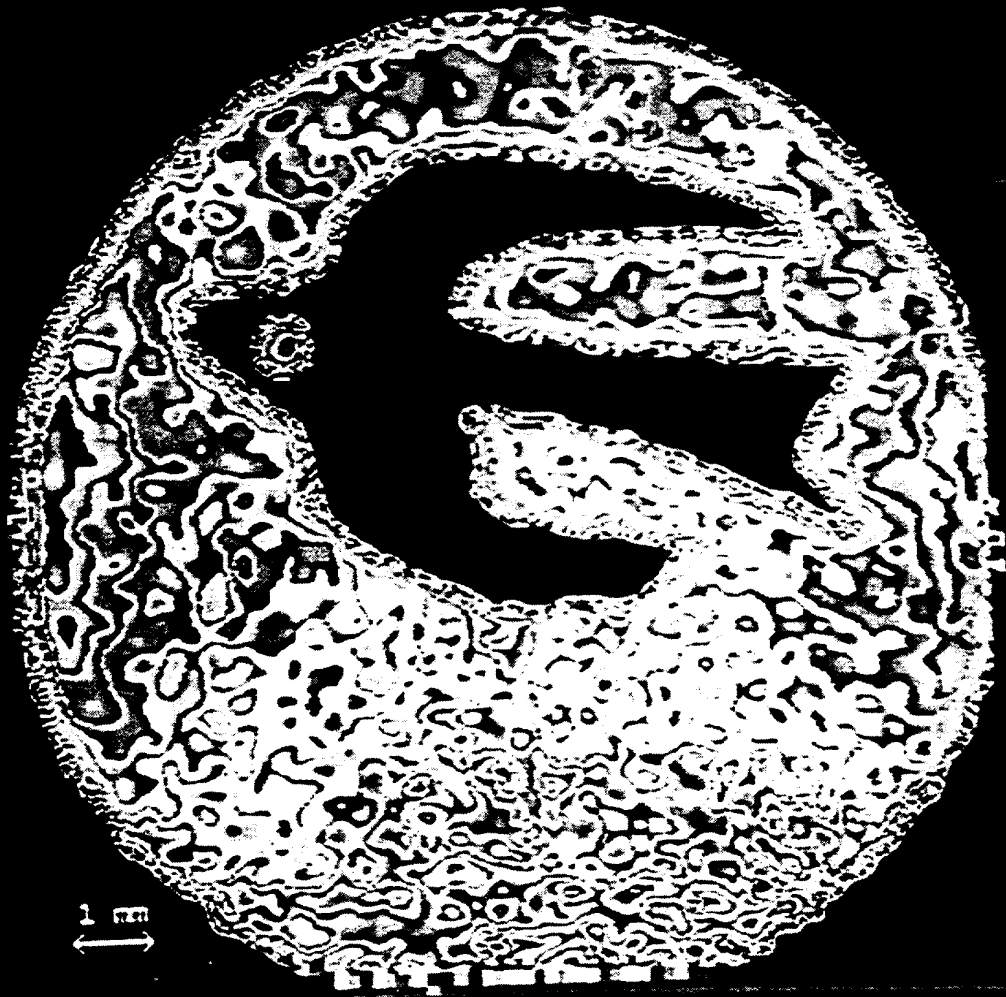


OPERATION OF MSGC AT HIGH PRESSURES:



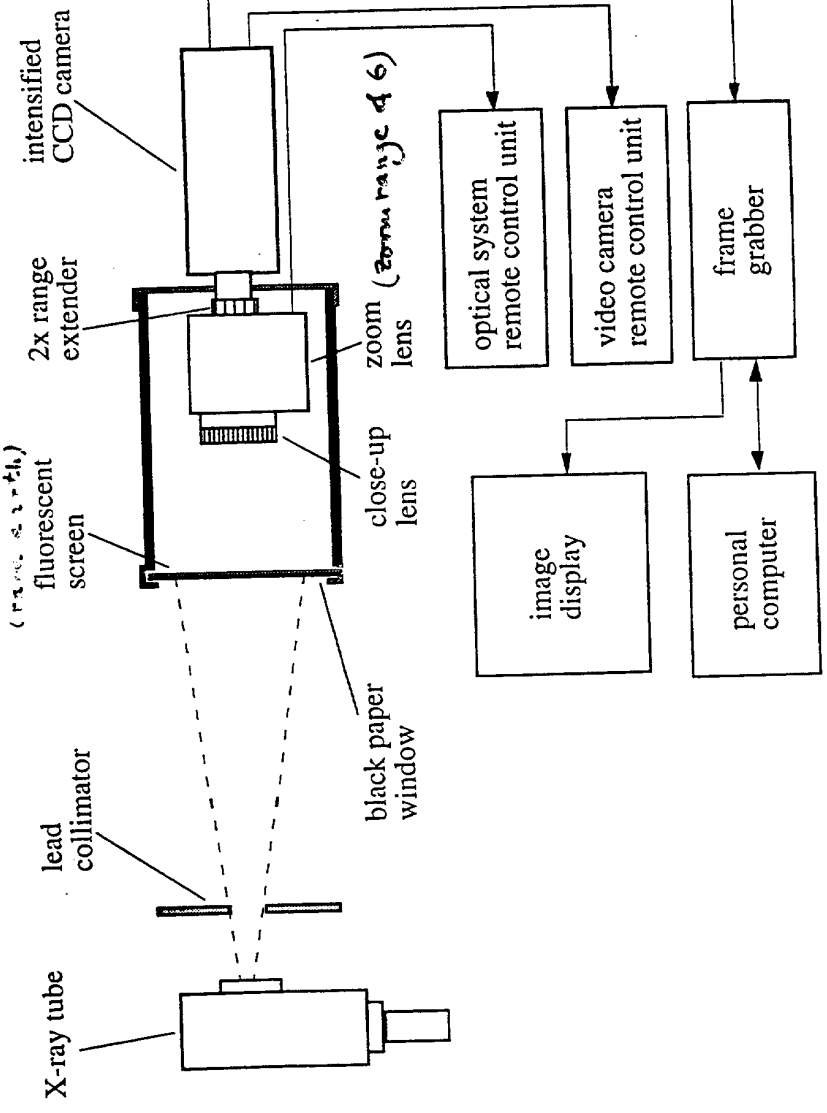
DIGITAL X-RAY MSGC DETECTOR:





(High resolution (1.75 μm) (25 lp/mm) (1.75 μm II+ 600 x 575 pixel CCD array) [25 lp/mm])

intensified CCD camera (1.75 μm II+ 600 x 575 pixel CCD array) [25 lp/mm]



Gambaccini et al. 1994 SPIE proceedings 2132, 295-300.
 from Gambaccini et al. 1994, Physica Medica, X(2)(1994)47

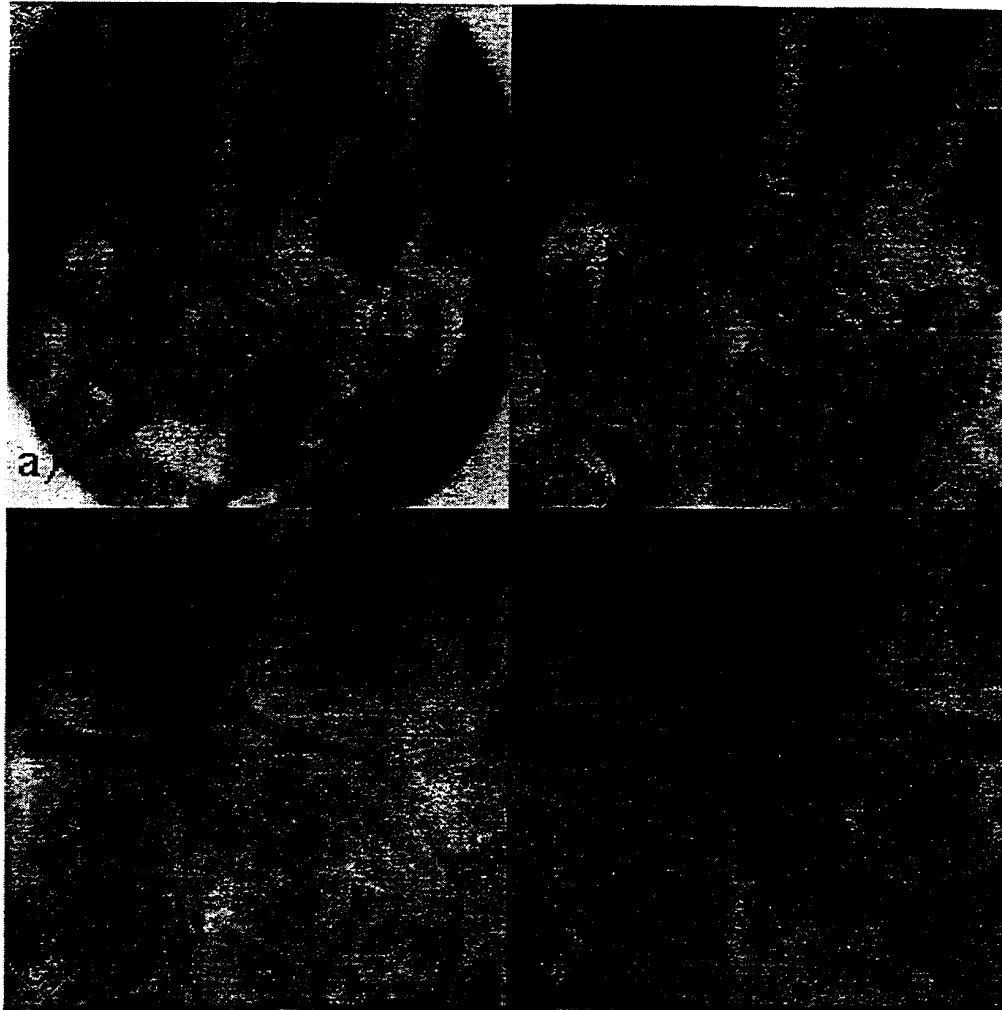
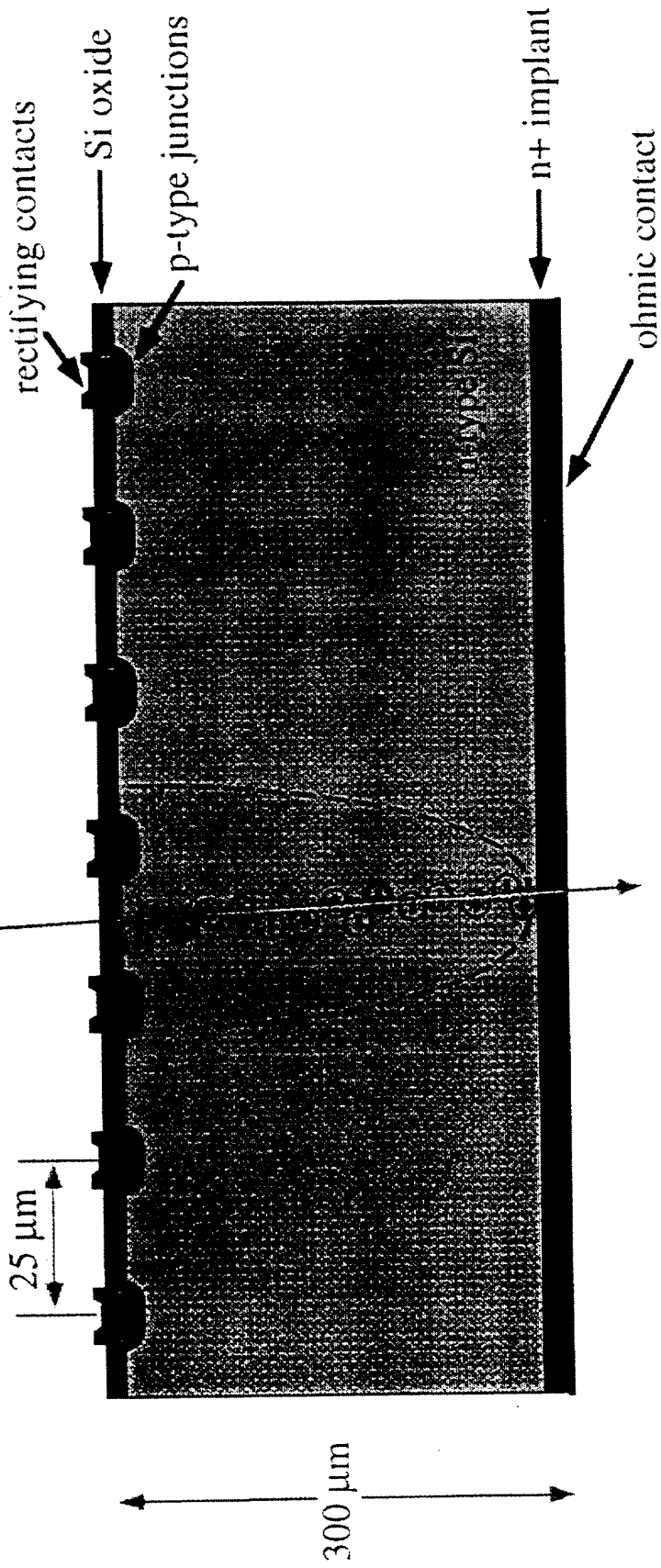


Fig. 3. Radiographic images of the phantom of a hand. Zoom factors: a) 1 x; b) 1.7 x; c) 2.8 x; d) 4.6 x.

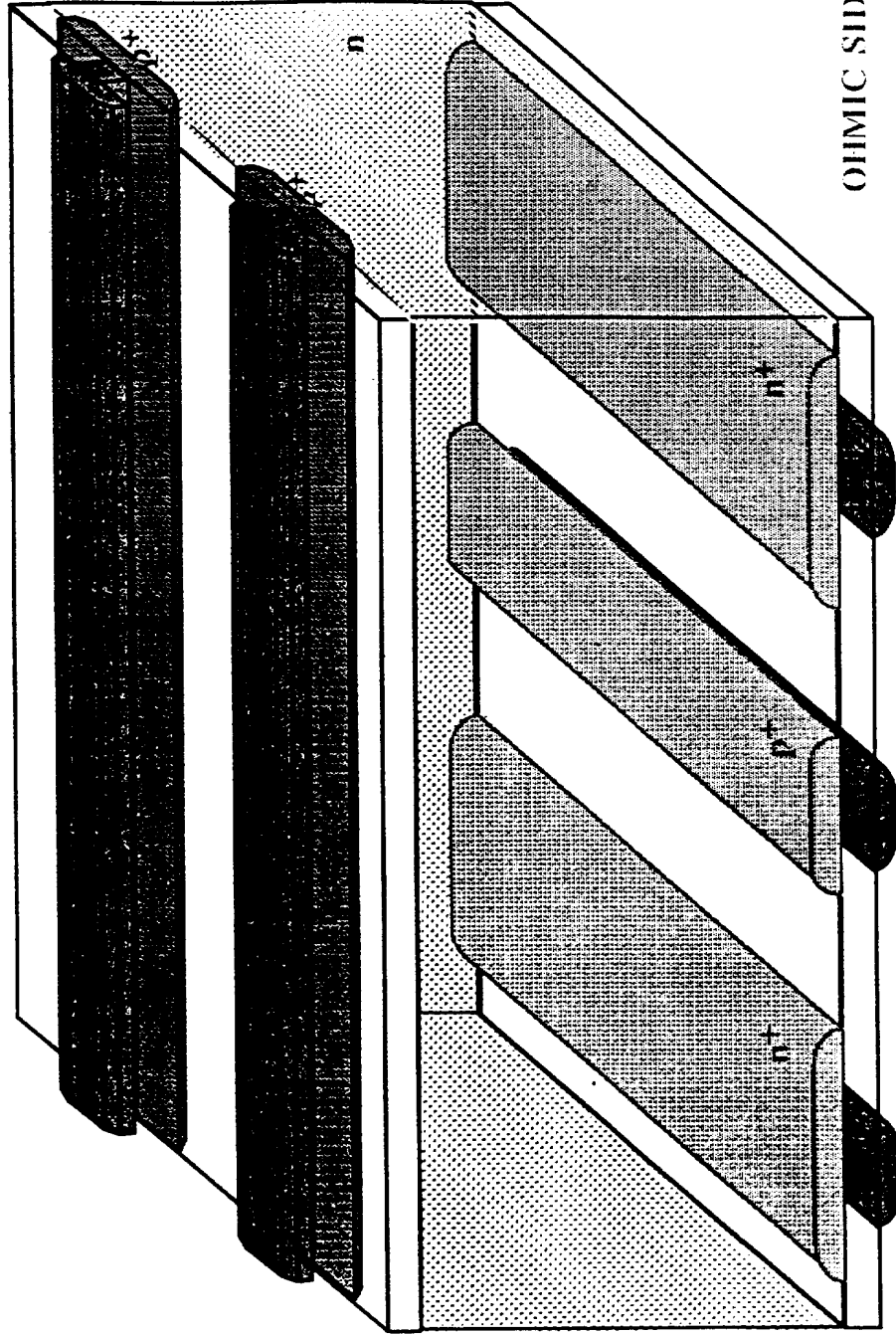
SILICON MICRO-STRIP DETECTOR:



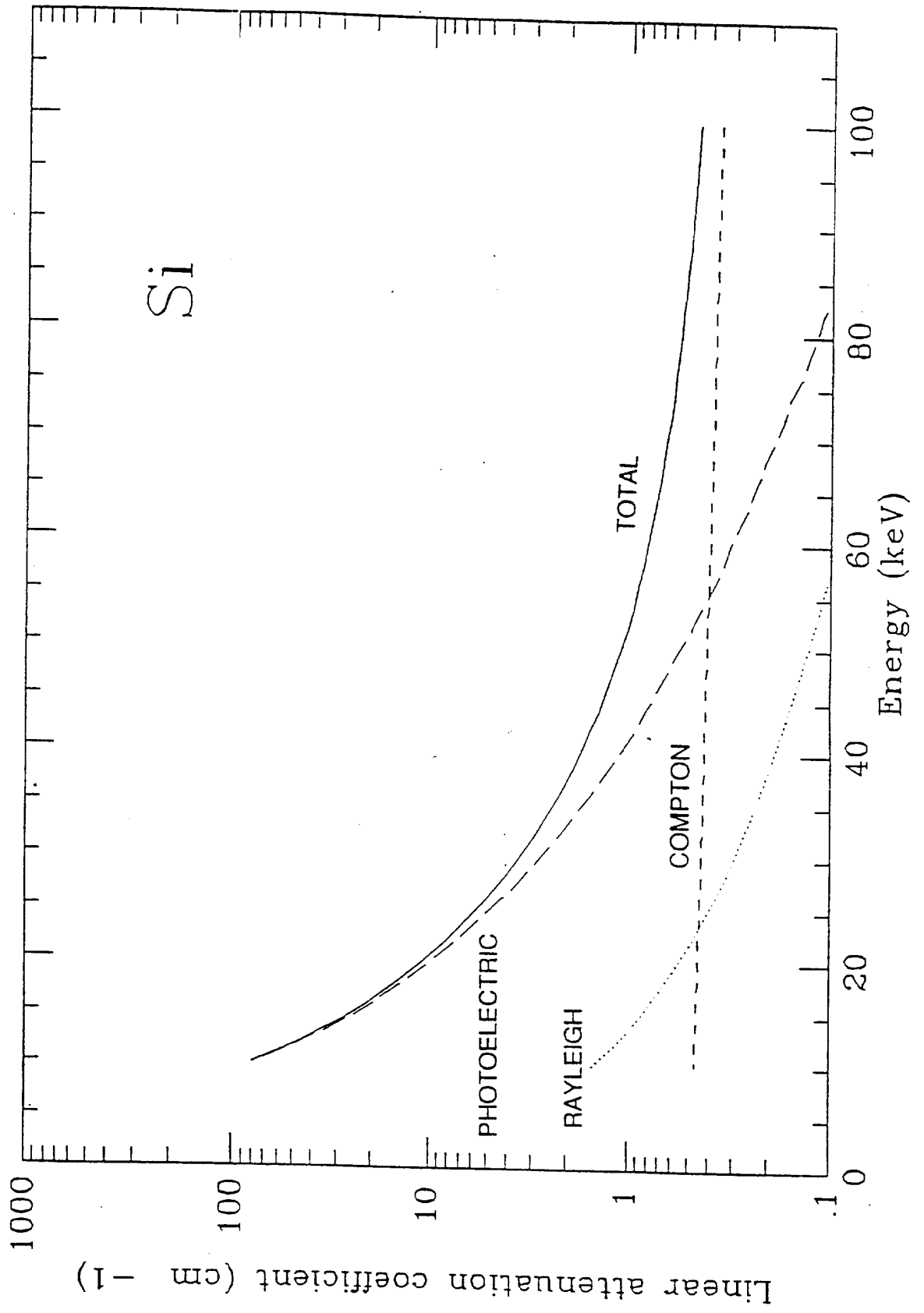
J. Kemmer, Nucl. Instrum. Methods 169 (1980) 499

TWO-DIMENSIONAL SILICON MICROSTRIP

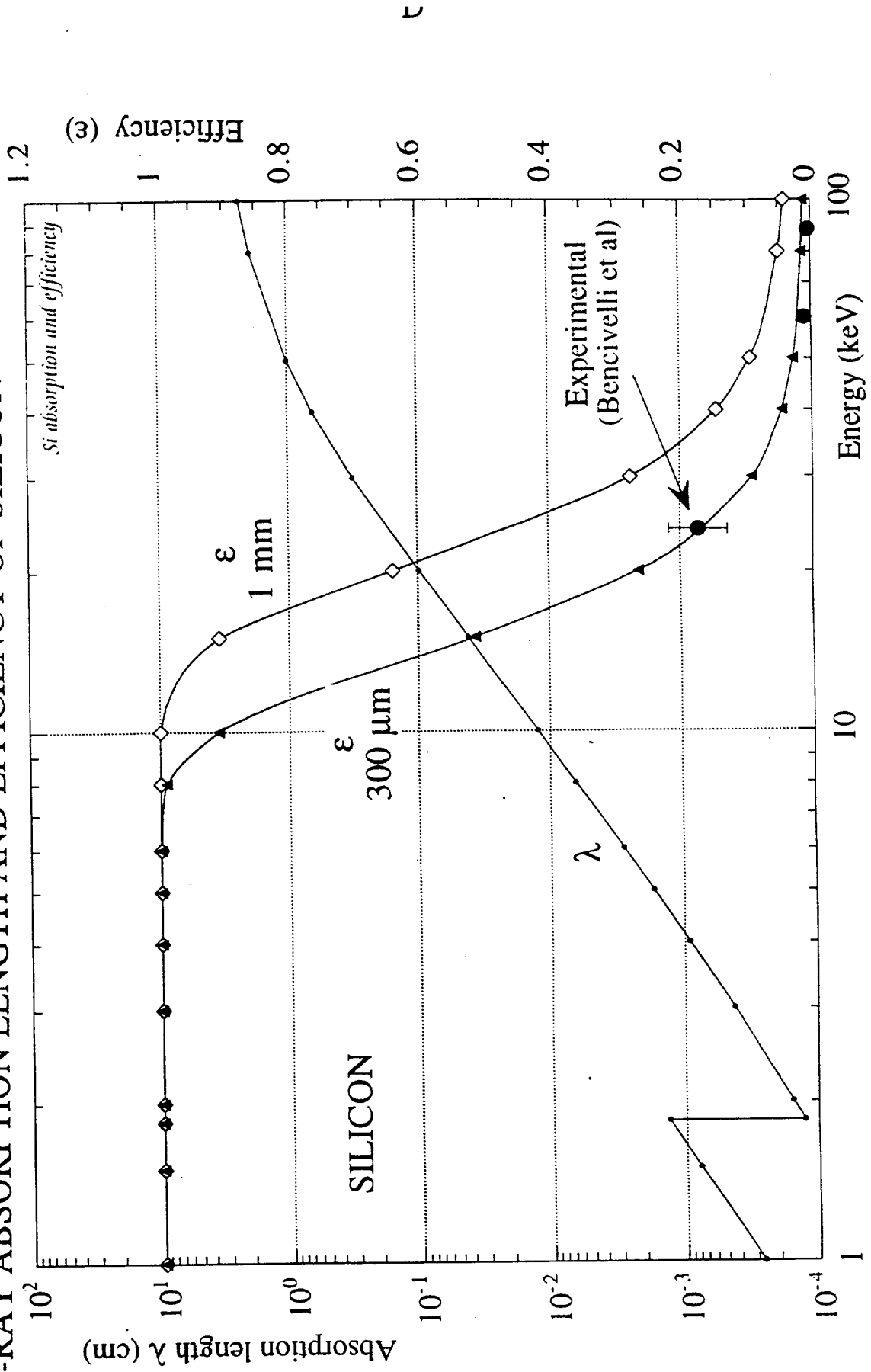
JUNCTION SIDE



OHMIC SIDE



X-RAY ABSORPTION LENGTH AND EFFICIENCY OF SILICON



00
4/10

SUMMARY OF EGS4 CAPABILITIES AND FEATURES

- * The radiation transport of electrons (+ or -) or photons can be simulated in any element, compound or mixture.
- * The dynamic range of charged particles goes from 10 keV to a few thousand GeV, while the dynamic range of photon energies lies between 1 keV and several thousand GeV.
- * The following physical processes are taken into account by the EGS4 Code System:
 - Bremsstrahlung production
 - Positron annihilation in flight and at rest
 - Molière multiple scattering
 - Møller ($e^- e^-$) and Bhabha ($e^- e^+$) scattering
 - Continuous energy loss applied to charged particle tracks
 - Pair production
 - Compton scattering
 - Coherent (Rayleigh) scattering
 - Photoelectric effect

146
KMT

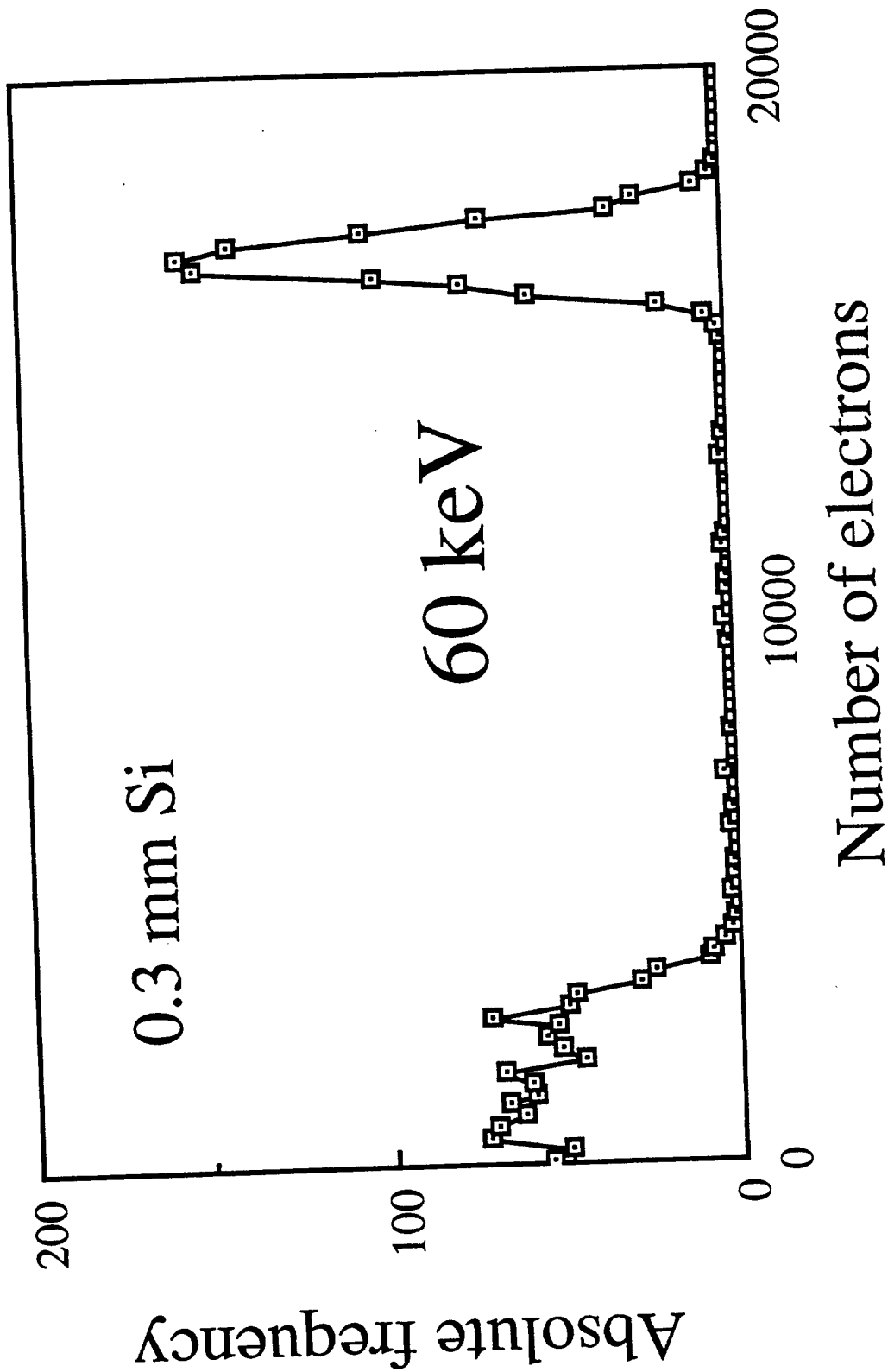


Fig. 6a: Charge deposit for 60 keV incident photons

($^{241}\text{Am} \rightarrow 60 \text{ keV}$)

($^{109}\text{Cd} \rightarrow \approx 22 \text{ keV}$
 $\approx 80 \text{ keV}$)

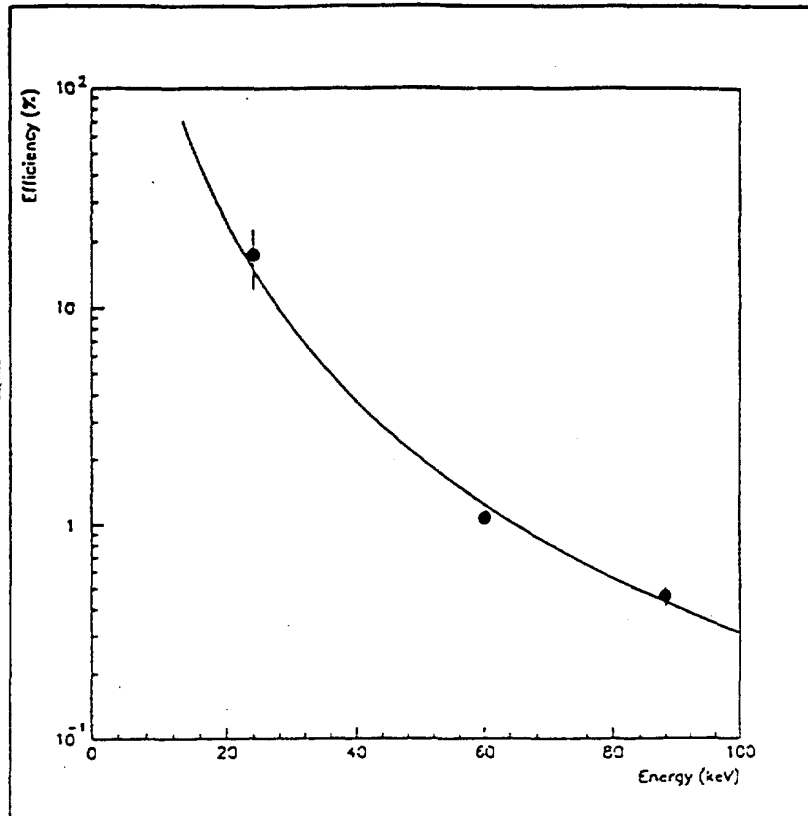


Figure 6: Experimental efficiency (%) for 24, 60 and 88 keV photons. The solid line represents the MonteCarlo simulation.

• Energy resolution $\sigma/E \sim 13\%$

H. Bucci et al., IEEE Trans. Med. Phys. NS40(1993)983

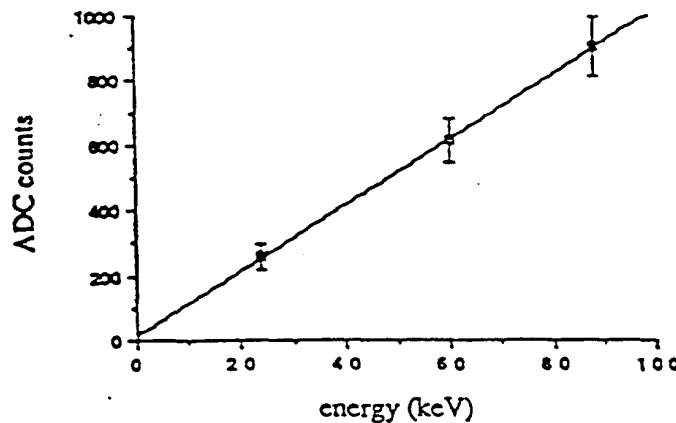


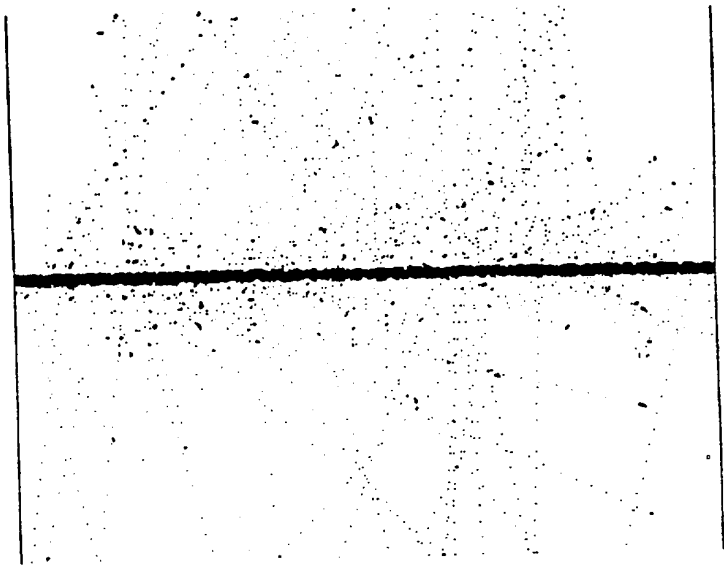
Figure 1. Charge released in the crystal (ADC counts) versus photon energy. The vertical bars are the standard deviations as calculated by a Gaussian fit to the charge distribution.

• Spatial resolution

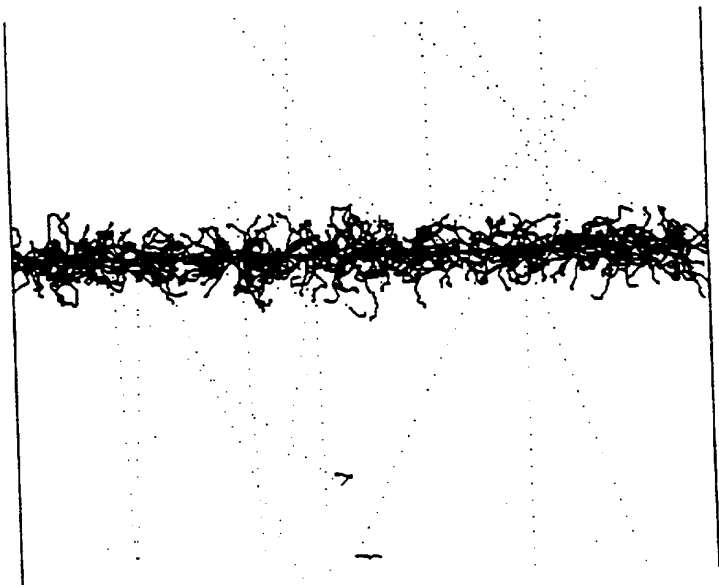
$$\sigma = 8 \mu\text{m} - 22 \mu\text{m}$$

B. Allread et al., Phys. Med. Biol. 37(1992)1167

20 keV



60 keV



0.3 mm Si

Fig. 7: Plot (side view) of 20000 tracks of photons (dotted) and electrons inside a 0.3 mm thick Si crystal.

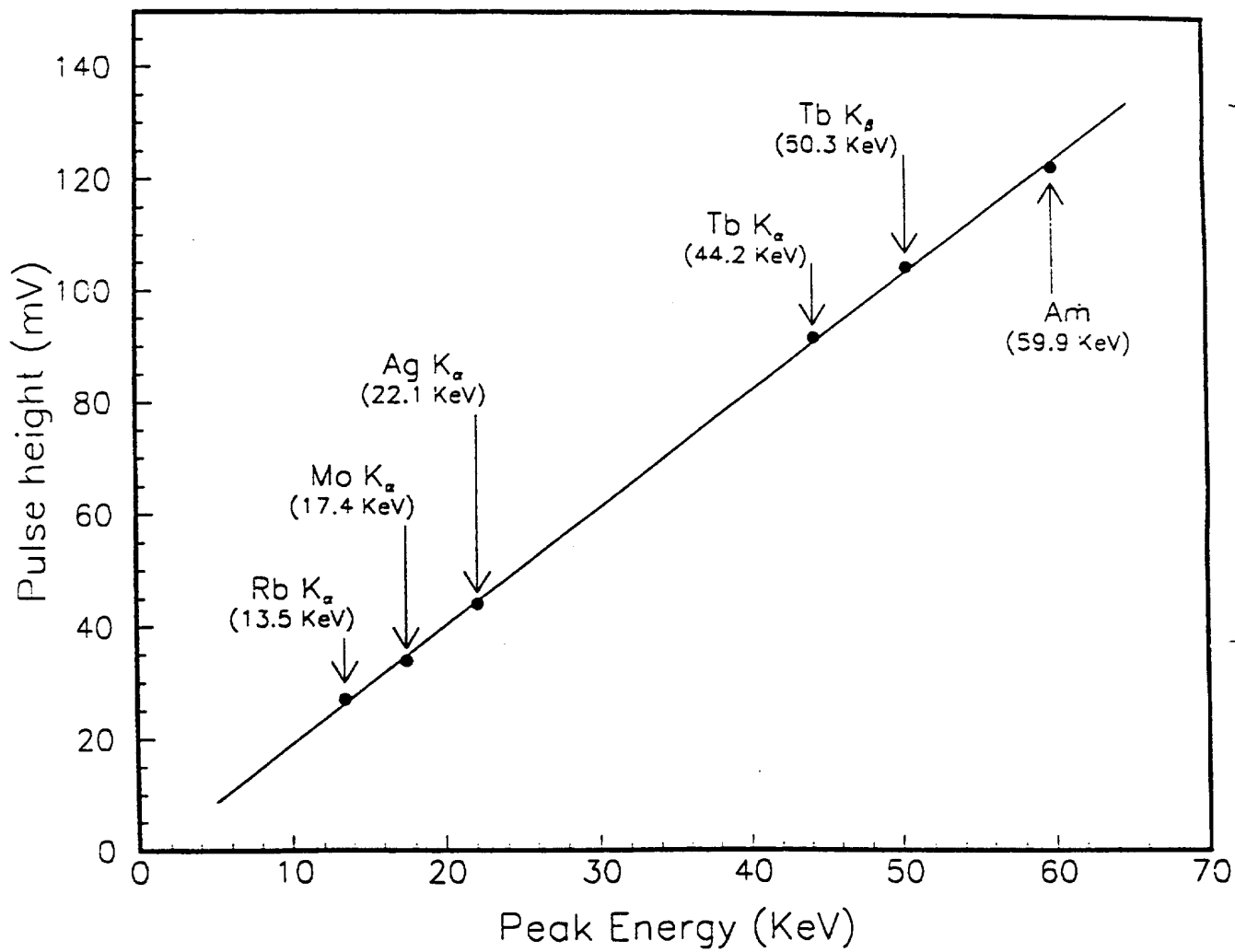
A new 2-Dimensional High Resolution Si Detector for β - and γ -Radiography

A. Czermak¹, P. Jalocha¹, A. Kjensmo², G. Malamud³, E. Nygård⁴, C. Rönnqvist⁵,
F. Santos⁶, J. Straver² and P. Weilhammer³

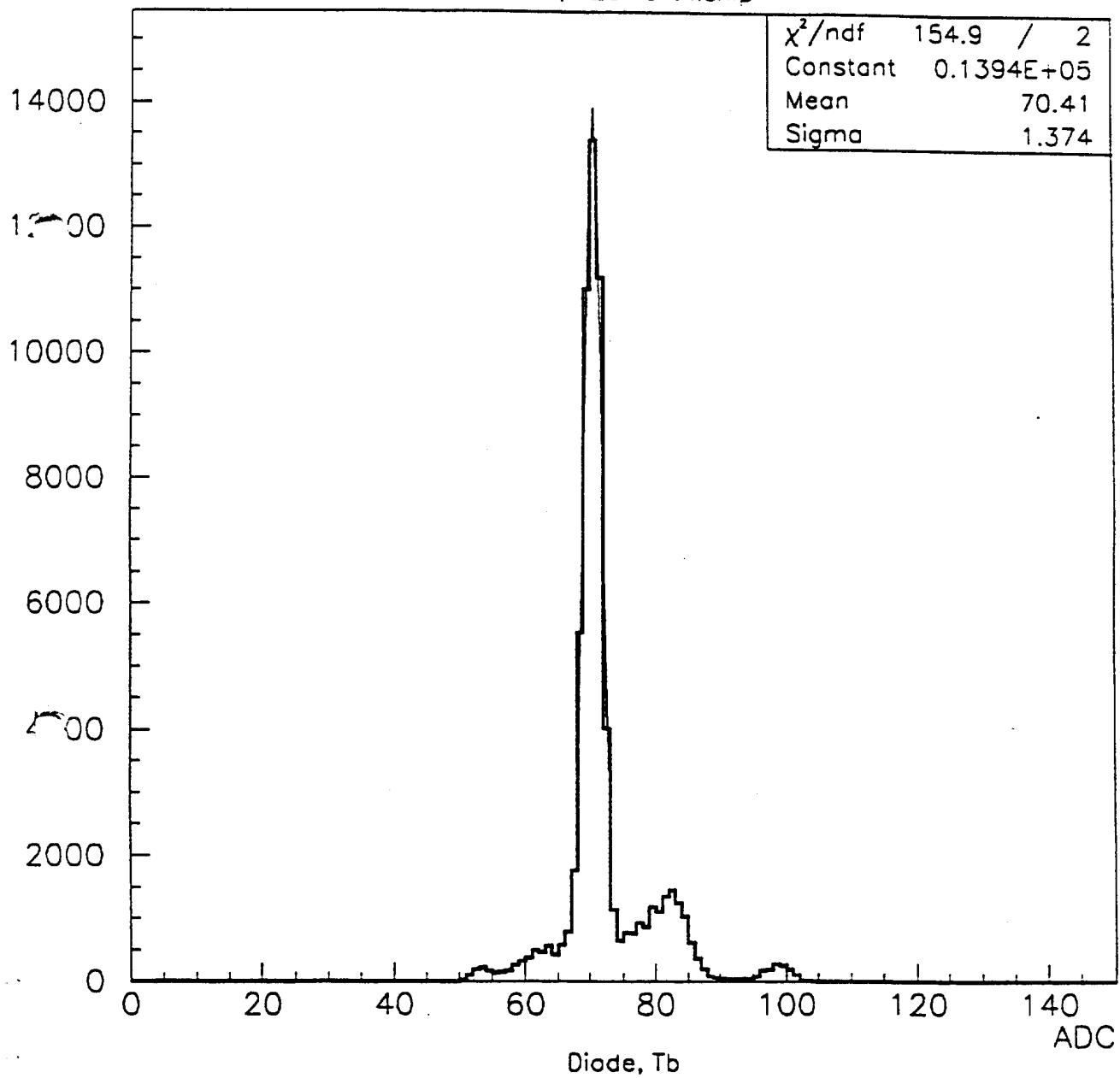
1. IFJ, Cracow, Poland
2. IDE AS, Oslo, Norway
3. CERN, Geneva, Switzerland
4. University of Oslo, Norway
5. SEFT, Helsinki, Finland
6. Federal Univ. of Rio de Janeiro, Rio de Janeiro, Brazil

A double-sided silicon microstrip detector read out by a CMOS low noise self-triggering 128-channel chip has successfully been tested with low energy γ - and X-rays and β -emitting sources for imaging of simple patterns. The readout chip is described in detail, as well as the detector, the ancillary electronics and the data acquisition. Images of the size of $6.4 \times 6.4 \text{ mm}^2$ are presented. The readout pitch is $50 \mu\text{m}$ in both the x - and the y -direction. The energy resolution for the $44.23 \text{ keV K}_{\alpha}$ -line from Tb is measured to 0.86 keV ($240 e^- \text{ rms}$). For β -patterns with ^{35}S , the spatial spread is in good correlation with the range of the particles ($130 \mu\text{m}$).

Contribution to 6th Pisa
Meeting on Advanced Detectors
22-28 May 1994, La Biodola
Isola d'Elba



Diode, 128-ch. xchip

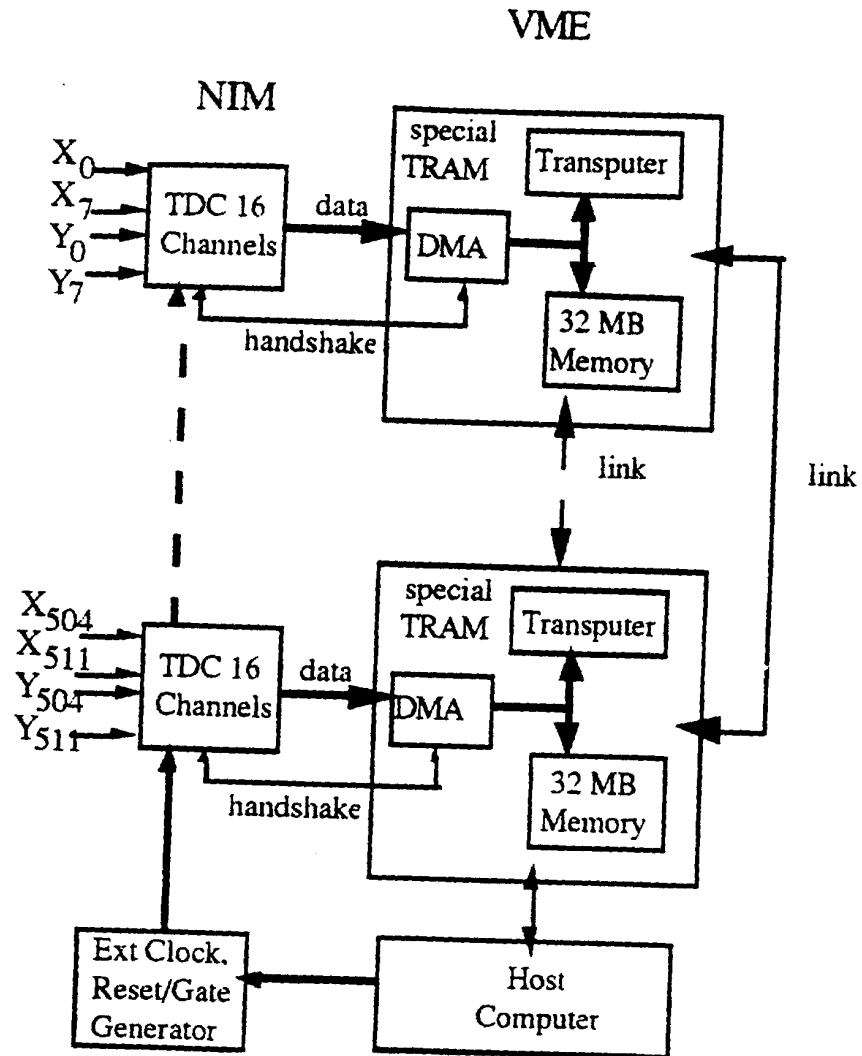




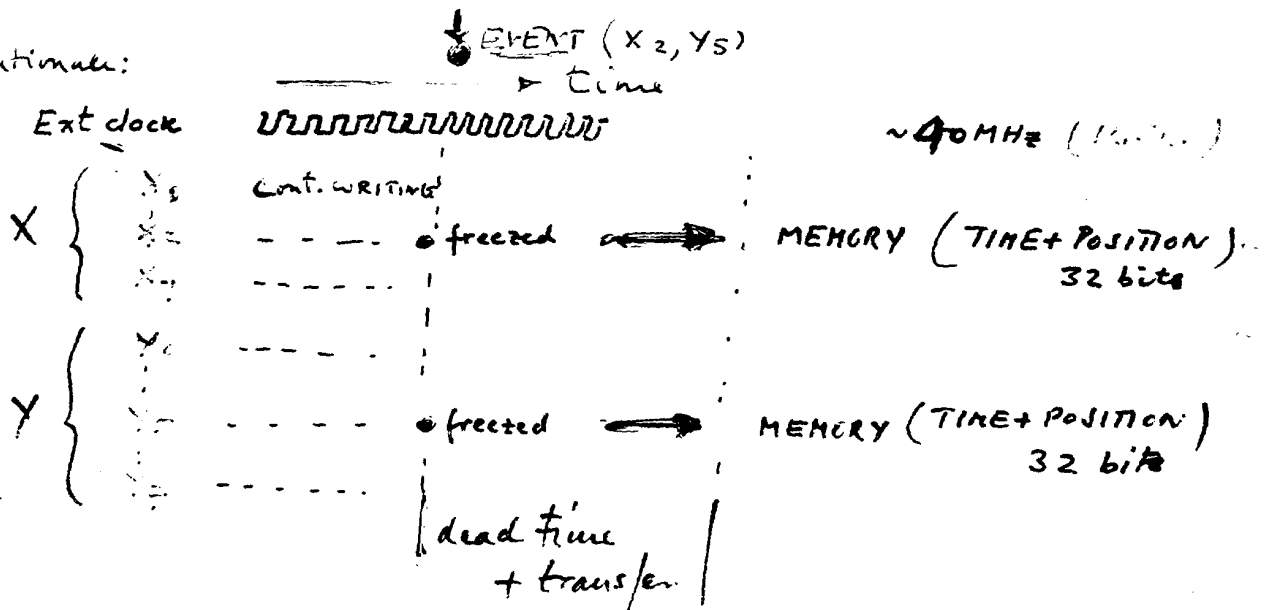
Imaging Test with an X-ray Tube

- X-ray tube operated at 30 kV and 15 mA with a molybdenum target and molybdenum filtration
- Energy spectrum: 10-30 keV,
K peaks: 17.4, 19.6 keV
- Photon flux: $6.4 \cdot 10^5 \text{ s}^{-1} \text{ mm}^{-2}$
- Net acquisition time \approx 100 ms ($1/10 \text{ s}$)
- Strip read-out pitch 100 μm , 20x20 pixels
- Phantoms:
 - steel sphere (700 μm)
 - hole (500 μm) in lead slab
 - square wave test pattern (50 μm thick Pb)

SLIDE



Rationale:



CU

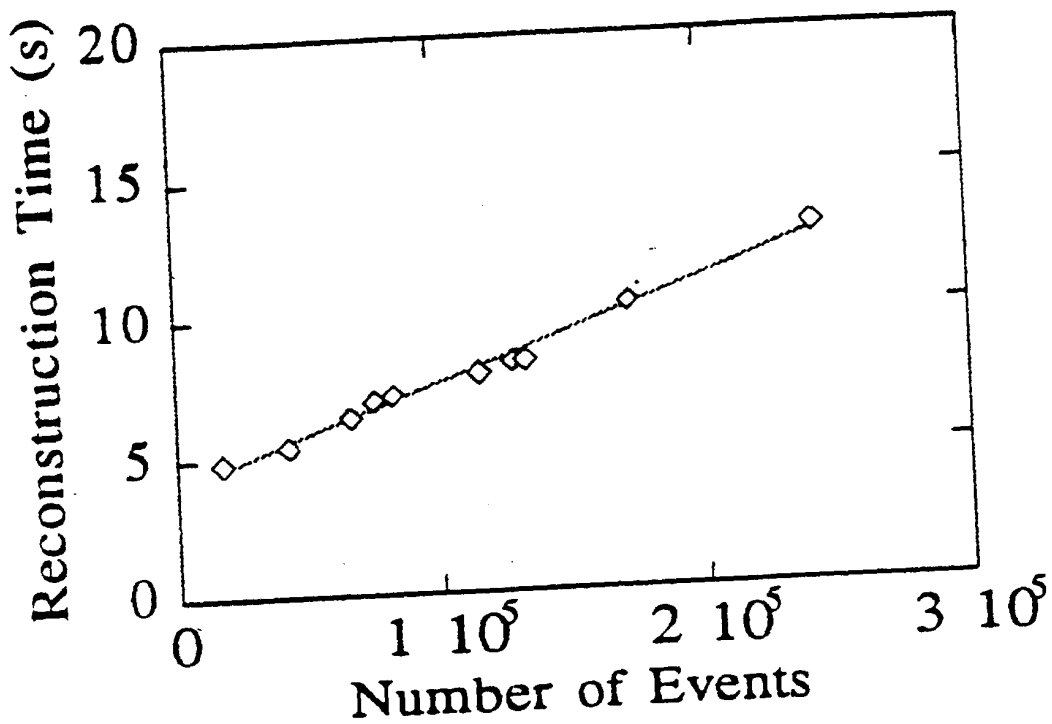


Figure 2: Reconstruction time versus number of events stored in the memory of each transputer

5s for images presented

~ 45' for 5x5 cm² goal

⇒ T9000

x 1/10

i860

x

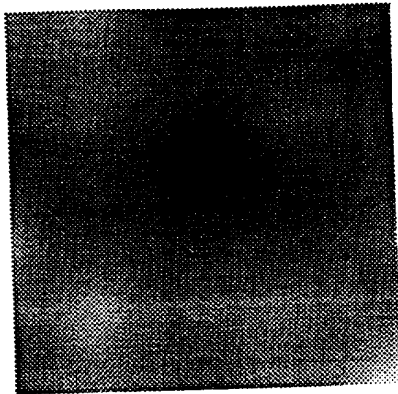
software

x

} Real Time
< 5'

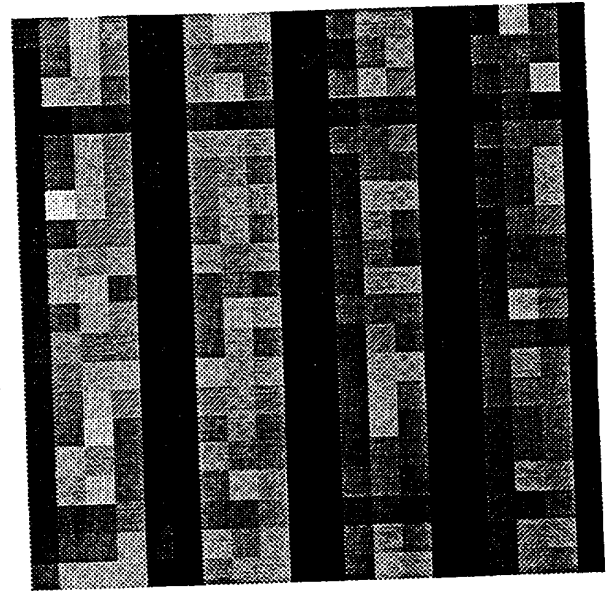
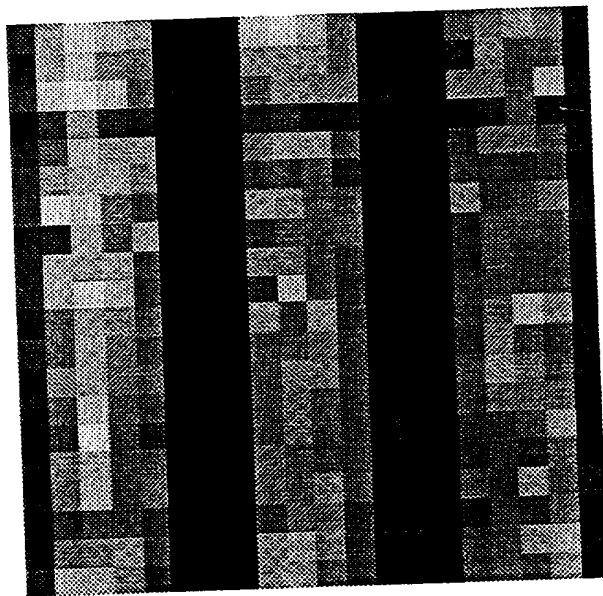
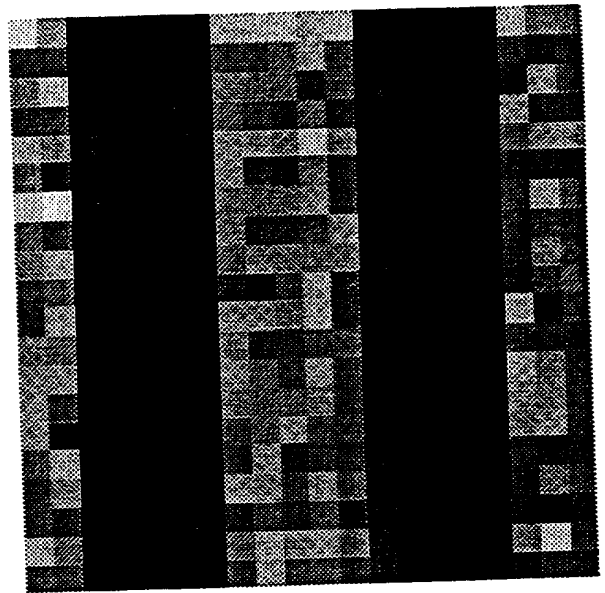
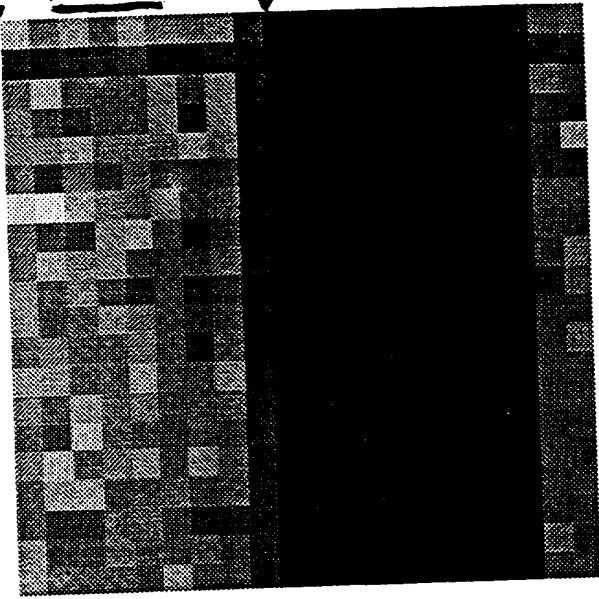
M. Conti et al., IEEE Trans. Nucl. Sci. NS-37 (1990) 1522

(The very first image
June 1992)

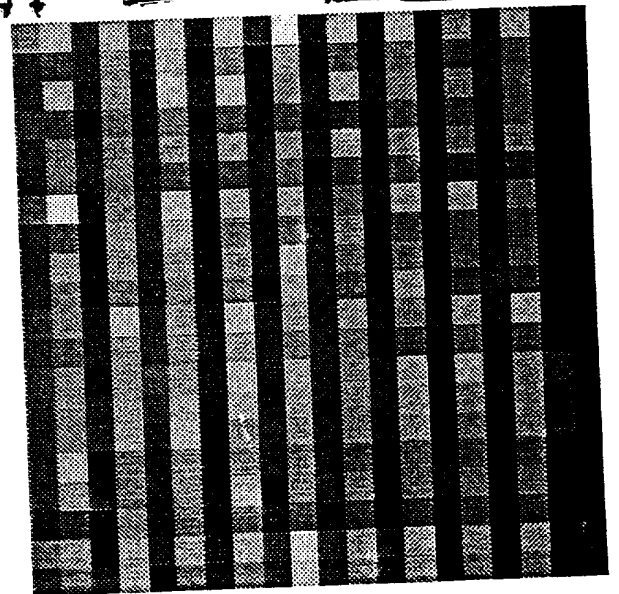
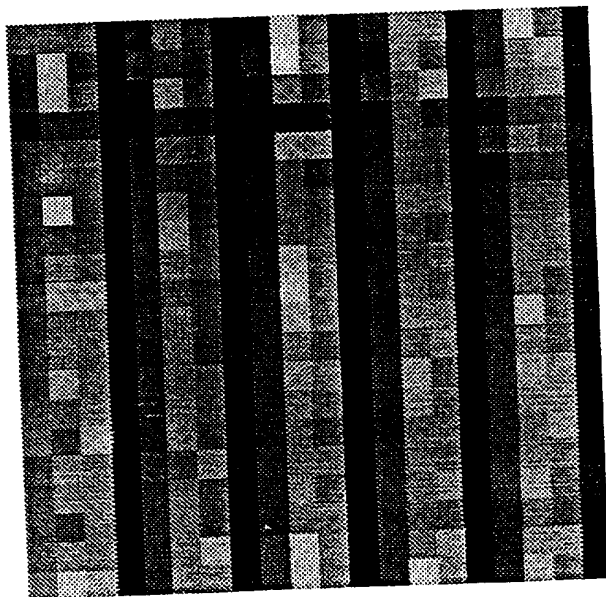


500 μ m hole in lead

→ ↓ 1 mm ↓ ←



→ ↓ ← 100 μm ≡ 5 ft/mm



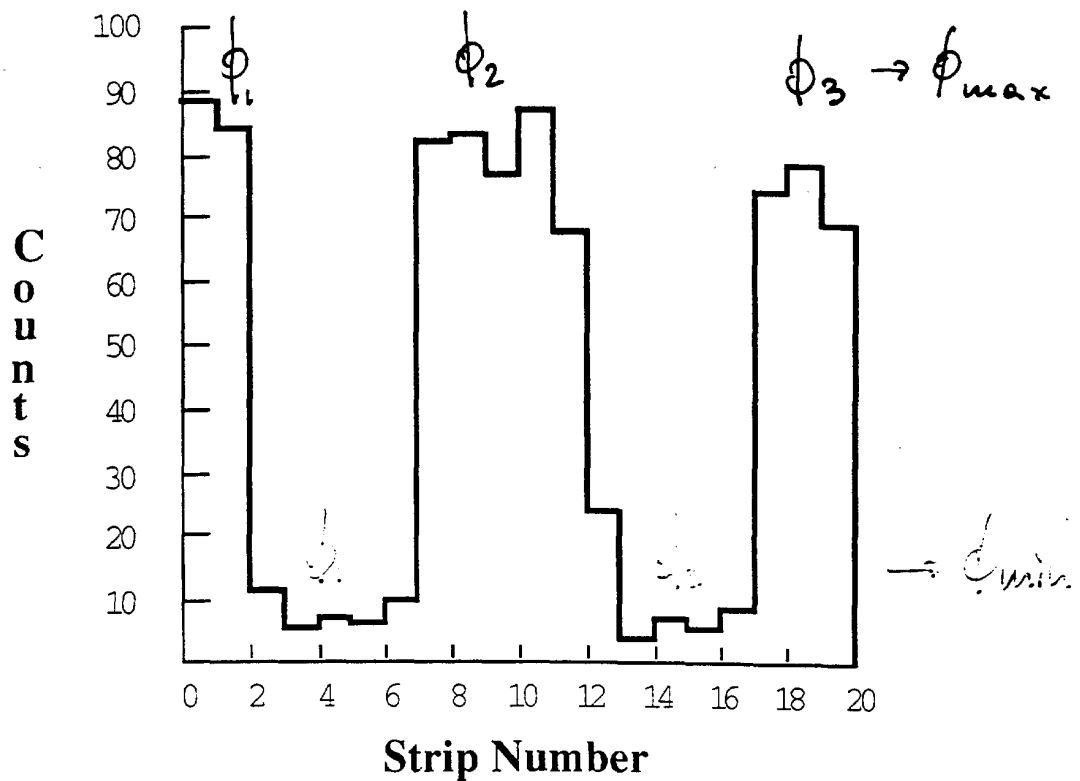


Image profile along the J direction obtained with an 1 line pair per mm square wave test pattern. The vertical axis shows the average pixel content for an 100 ms acquisition time.

From profiles we obtain Contrast:

$$C_{\text{output}} = (\Phi_{\text{max}} - \Phi_{\text{min}}) / (\Phi_{\text{max}} + \Phi_{\text{min}})$$

Φ_{max} is the average number of counts at the maxima
 Φ_{min} the corresponding average at the minima for each frequency

Contrast Transfer Function

$$\text{CTF}(\nu) = \frac{C_{\text{output}}(\nu)}{C_{\text{input}}}$$

C_{output} is defined as $(\Phi_{\text{max}} - \Phi_{\text{min}})/(\Phi_{\text{max}} + \Phi_{\text{min}})$,
 Φ_{max} is the average number of counts at the maxima,
 Φ_{min} the corresponding average at the minima for
each frequency,

C_{input} is defined as $(\Phi_{\text{air}} - \Phi_{\text{Pb}})/(\Phi_{\text{air}} + \Phi_{\text{Pb}})$,
 Φ_{air} is the average number of counts obtained with
no test pattern,

Φ_{Pb} the average number of counts obtained with a
Pb slab as thick as the test pattern (50 μm) in
front of the detector,

We measured for C_{input} a value of 0.94.

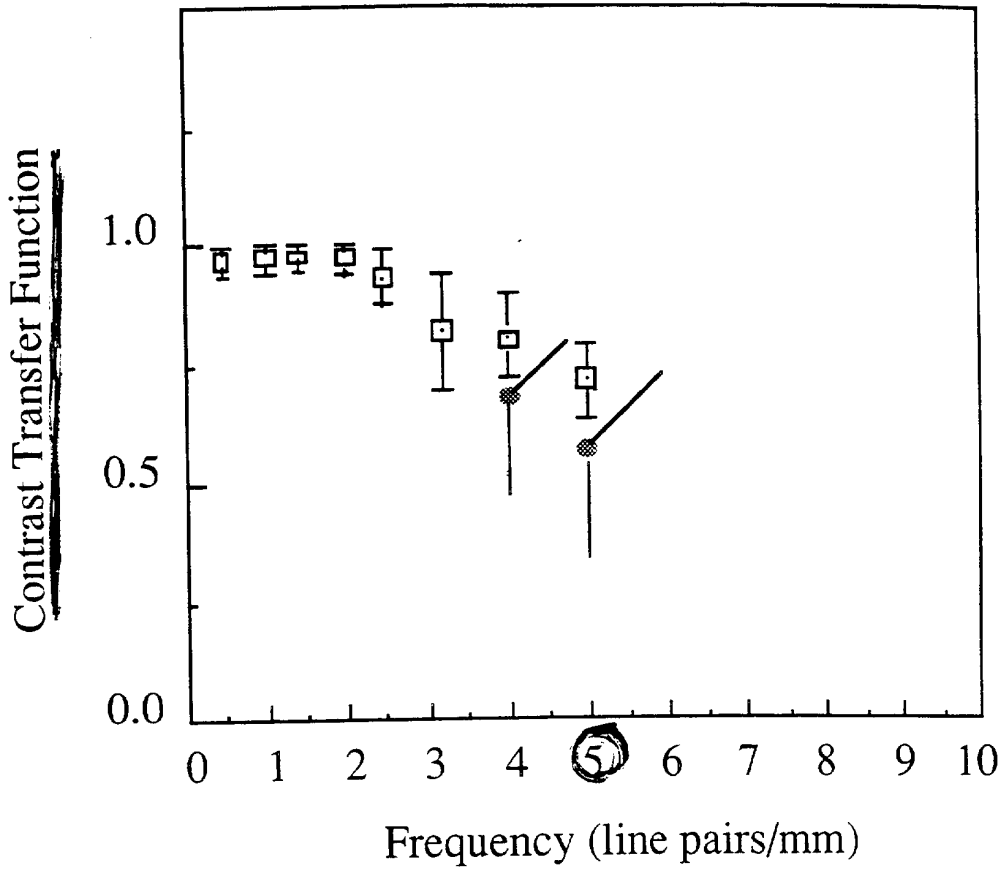
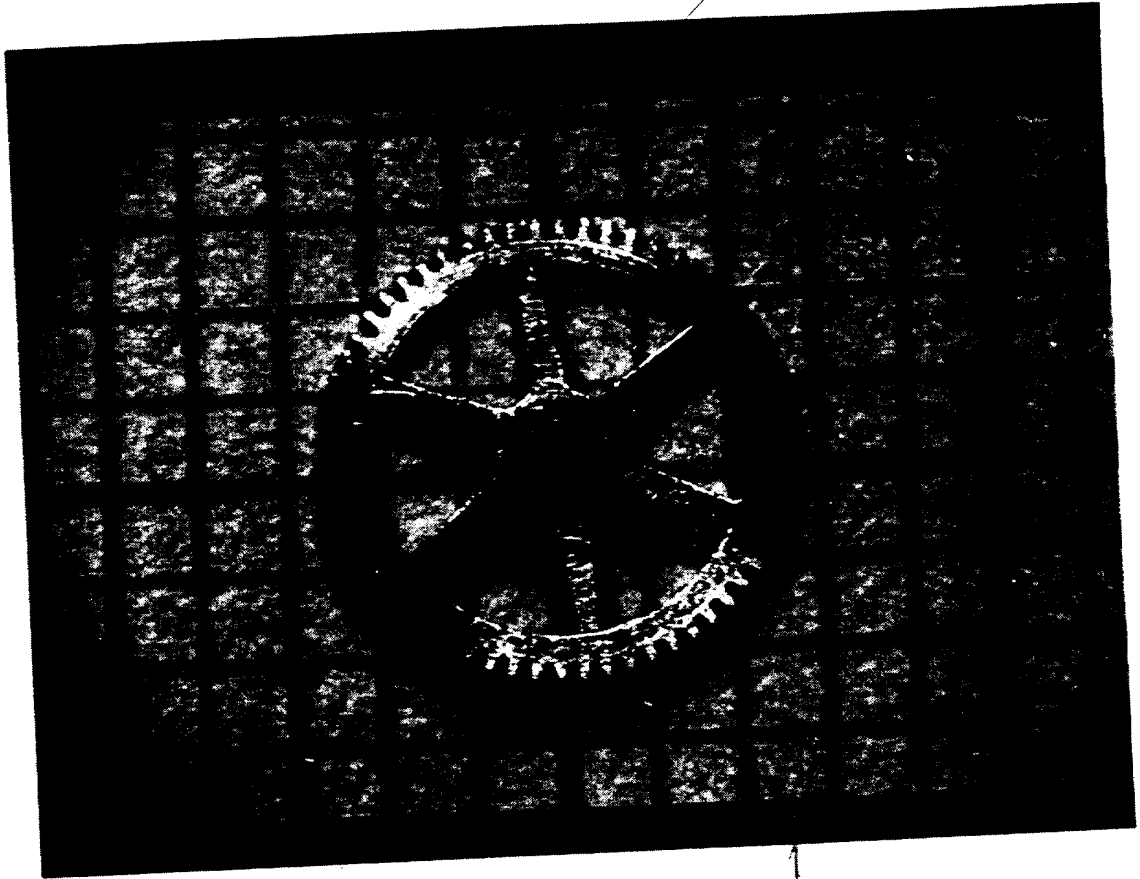


Figure 6 : Contrast Transfer Function

Frequency (lp/mm)	Contrast
Measurements in phase	
0.5	0.96 ± 0.03
1.0	0.97 ± 0.03
1.4	0.97 ± 0.03
2.0	0.97 ± 0.03
2.5	0.93 ± 0.05
3.2	0.82 ± 0.12
4.0	0.80 ± 0.09
5.0	0.71 ± 0.08
Measurements out of phase	
4.0	0.68 ± 0.18
5.0	0.57 ± 0.16

(100 μm)

tooth pitch 270 μ m



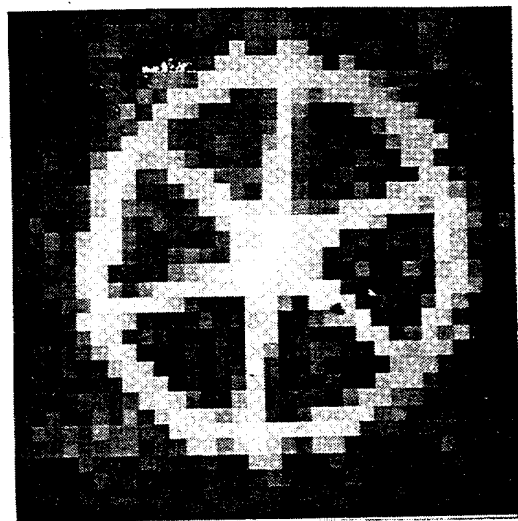
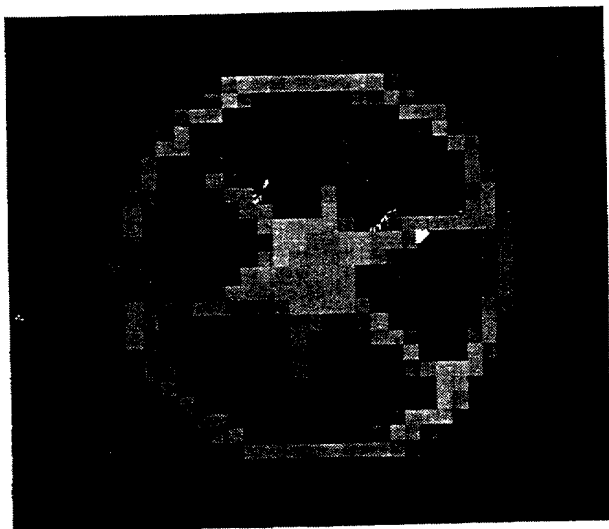
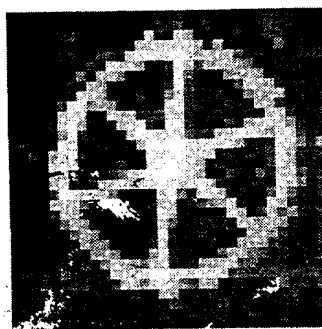
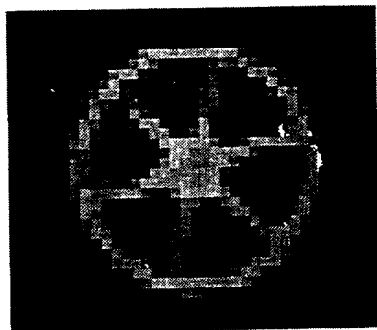
5.36 mm

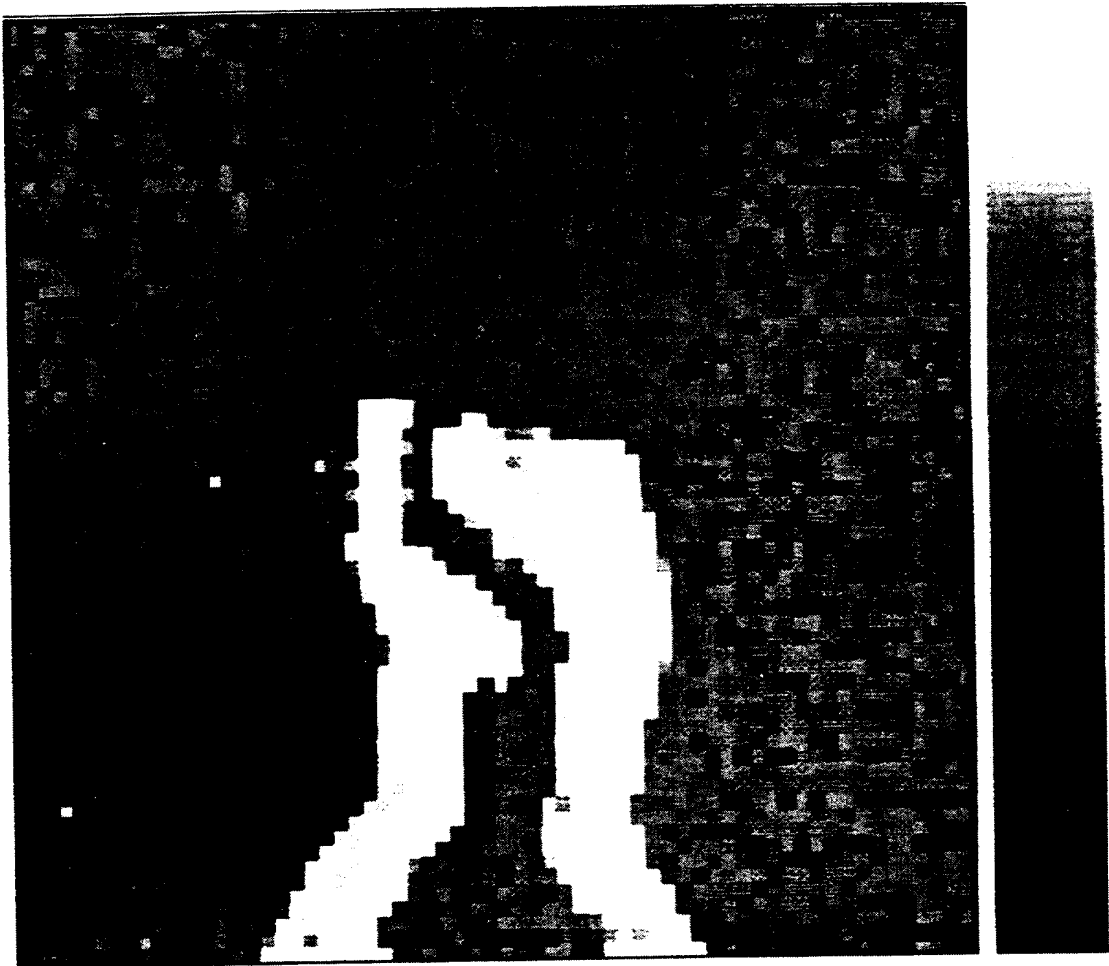
ACQUISIZIONE IN LISA

FILM
DIGITIZER



DUAL STRIP
DETECTOR

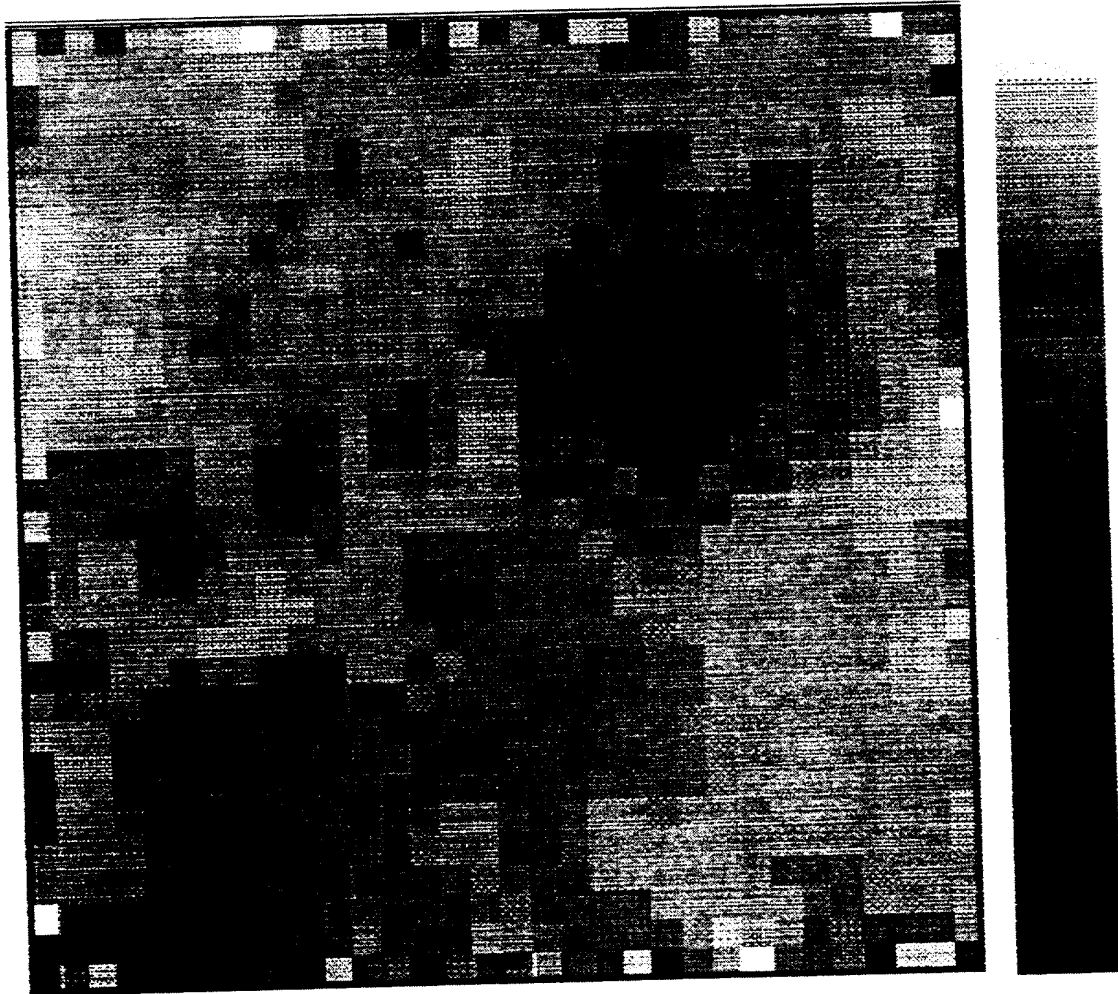




Holes in aluminium slab

diameters 1 mm

depth 1 mm, 0.5 mm

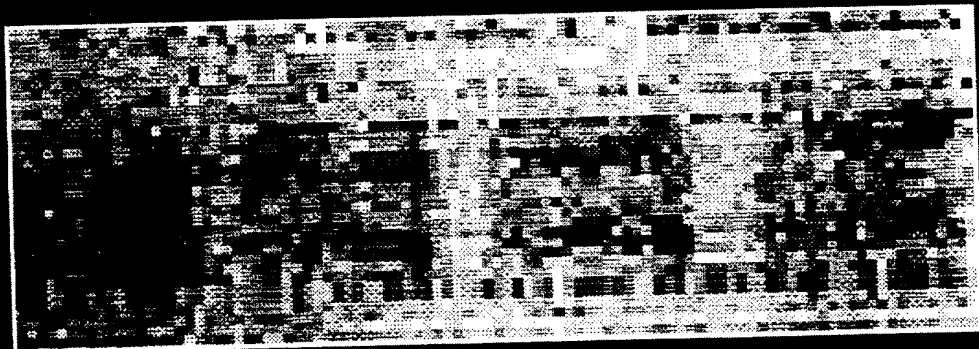


SCR = $(34 \pm 2) \%$

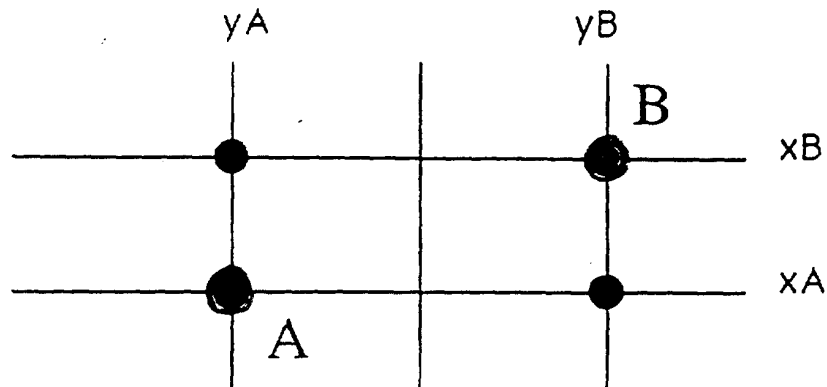
SNR = 10.1 ± 0.5

SCR = $(13 \pm 2) \%$

SNR = 3.8 ± 0.5



ONE PROBLEM OF THE MICROSTRIPS GEOMETRY: DOUBLE OR MULTIPLE HITS



- $(X_A, Y_A), (X_B, Y_B)$ RIGHT COMBINATION
- $(X_B, Y_A), (X_A, Y_B)$ WRONG COMBINATION (GHOSTS)

THE EFFECTS ARE ARTIFACTS ON THE IMAGES.

REMEDIES:

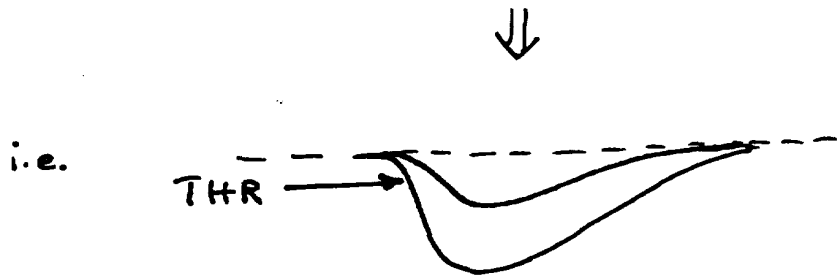
- SOFTWARE FILTERS (NN),
- VERY FAST ELECTRONICS TO MAKE THE RIGHT COINCIDENCES IN A VERY SHORT TIME.

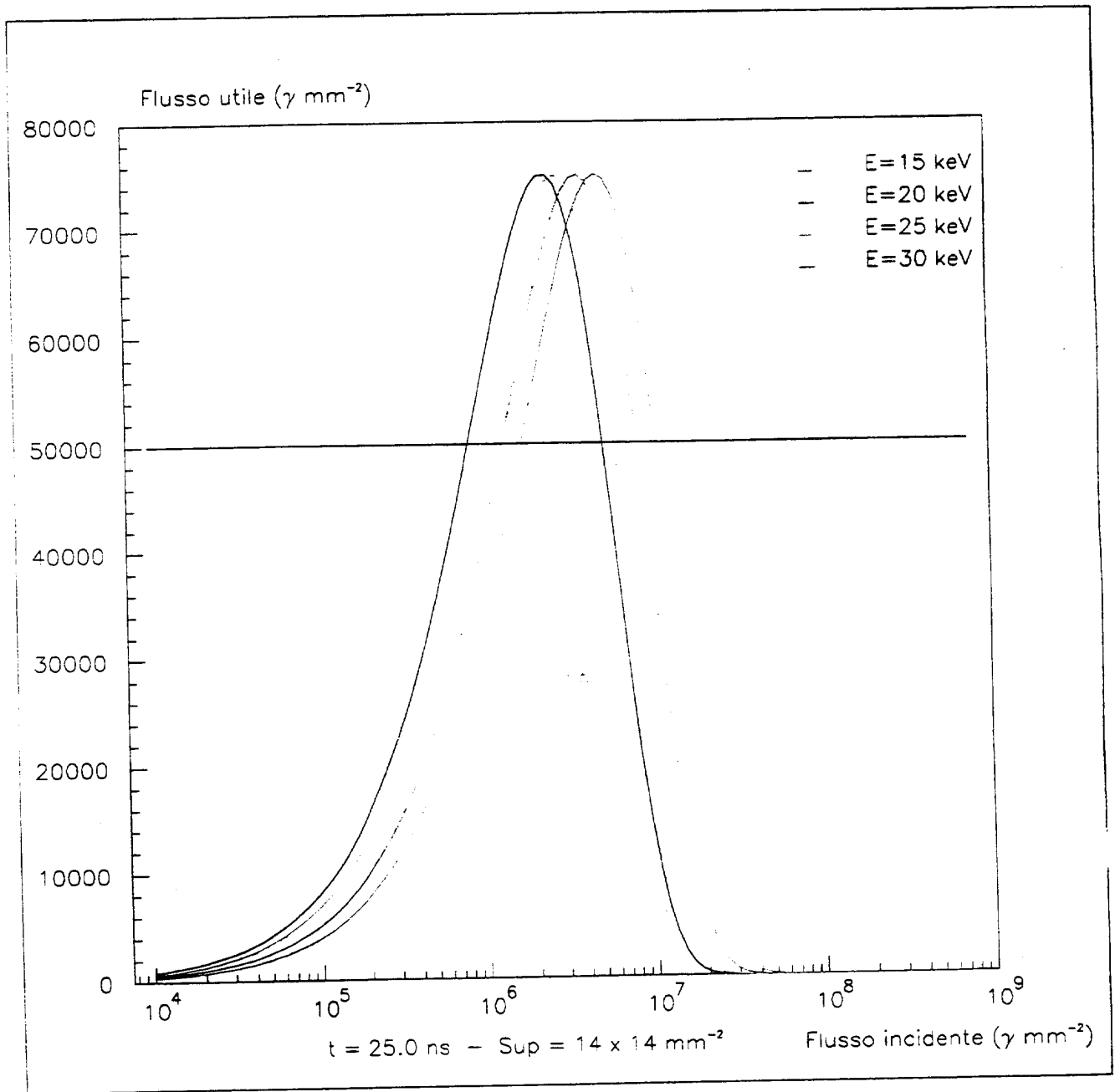
We studied the effect of these double counting as applied to mammography examination for a 300 μm silicon crystal

$$N_T = 5 * 10^4 \text{ photons/mm}^2 \quad T_{\text{exposure}} = 1 \text{ s}$$
$$E_\gamma \approx 20 \text{ keV} \quad T_{\text{sampling}} = 10 \text{ ns (coincidence resolution)}$$

To be taken into account:

- Poisson statistic
- Efficiency of the detector
- Effects due to $|T_\Omega - T_J|$ and to the time slew

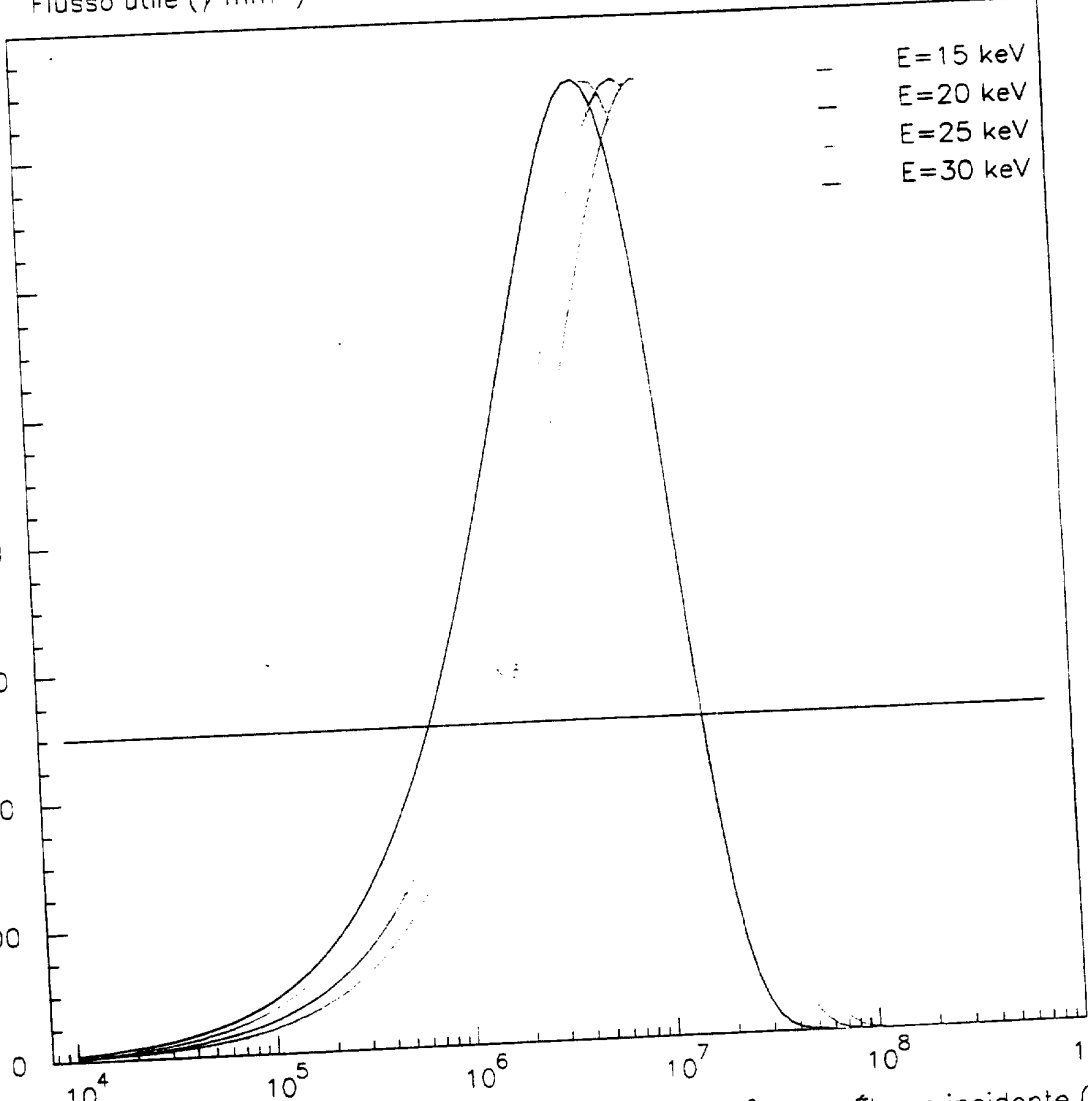




$\times 10^2$
Flusso utile ($\gamma \text{ mm}^{-2}$)

1600
1400
1200
1000
800
600
400
200
0

- - E=15 keV
- - E=20 keV
- - E=25 keV
- - E=30 keV



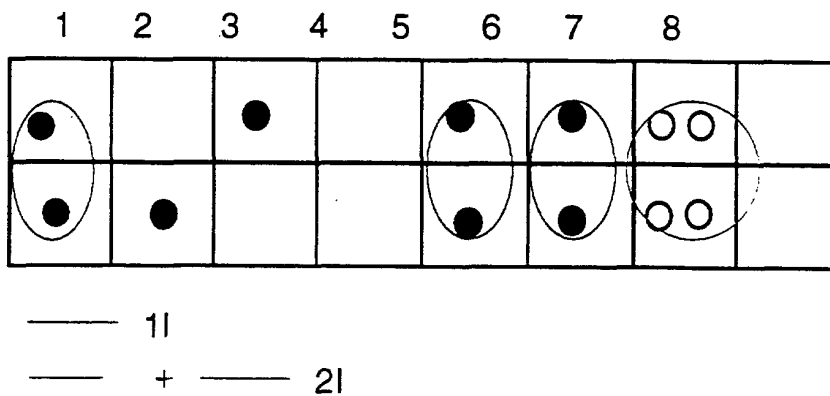
$t = 12.5 \text{ ns}$ - Sup = $14 \times 14 \text{ mm}^{-2}$

Flusso incidente ($\gamma \text{ mm}^{-2}$)

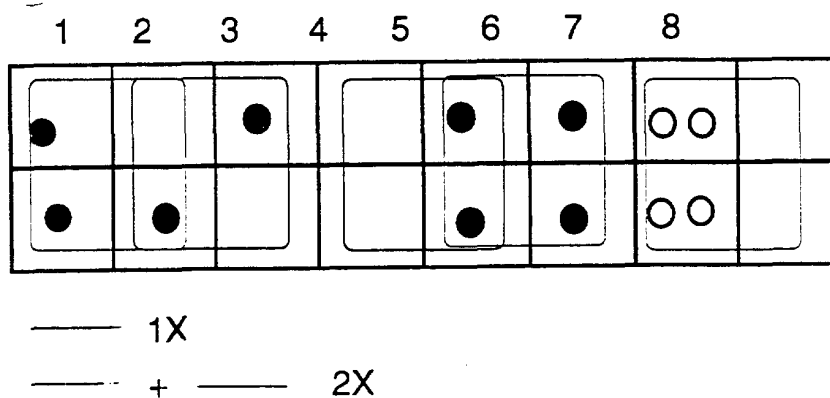
RECONSTRUCTION ALGORITHMS

- Singles: one event per time slot (type 1)
- Doubles: two (maximum) events per time slot (type 2)

ALGORITHM I (examines only one time slot)



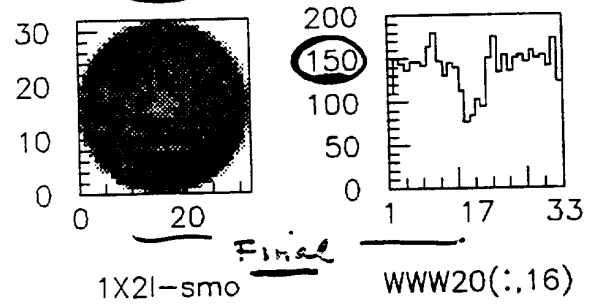
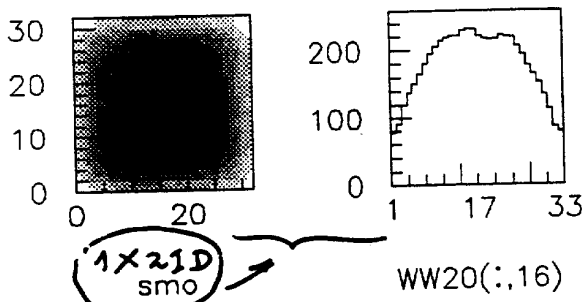
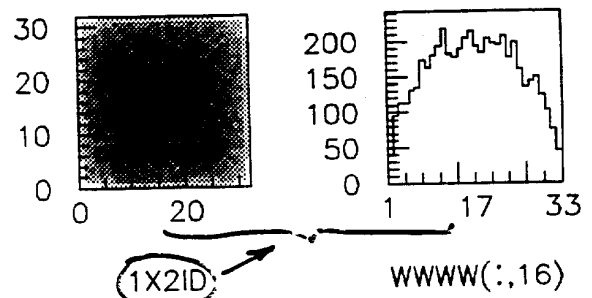
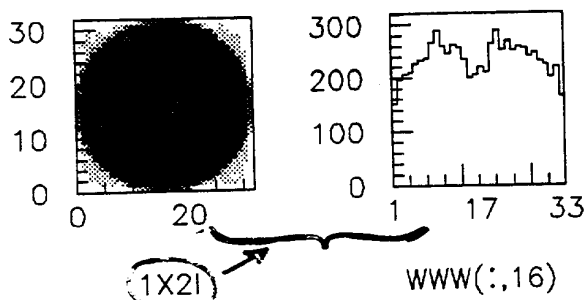
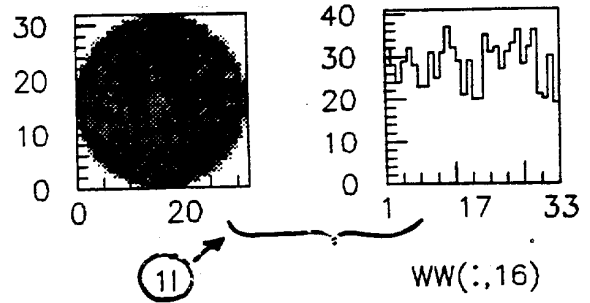
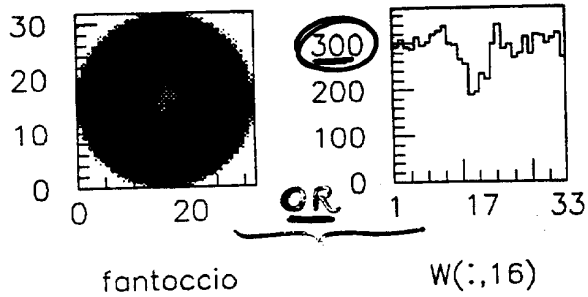
ALGORITHM X (examines two adjacent time slots)



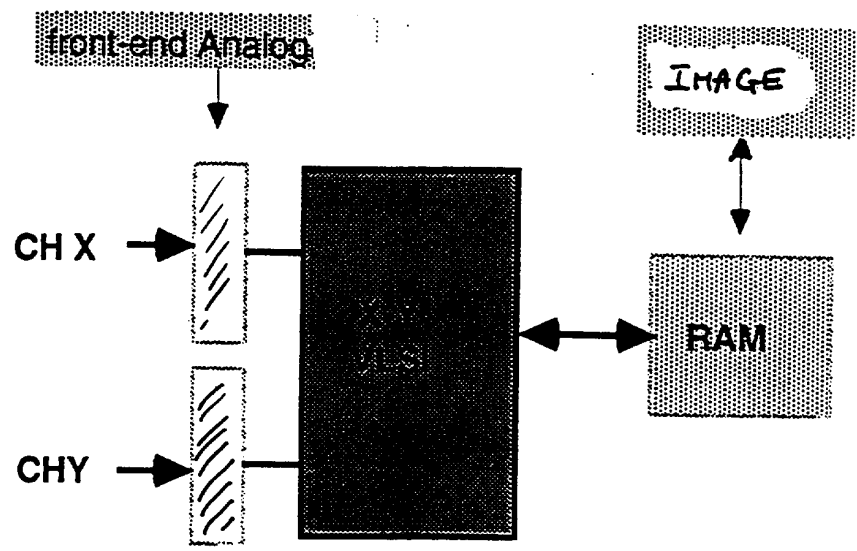
Combination of X with I (1X1I, 1X2I, 2X2I...)

Software simulation

Hardware implementation (VLSI)

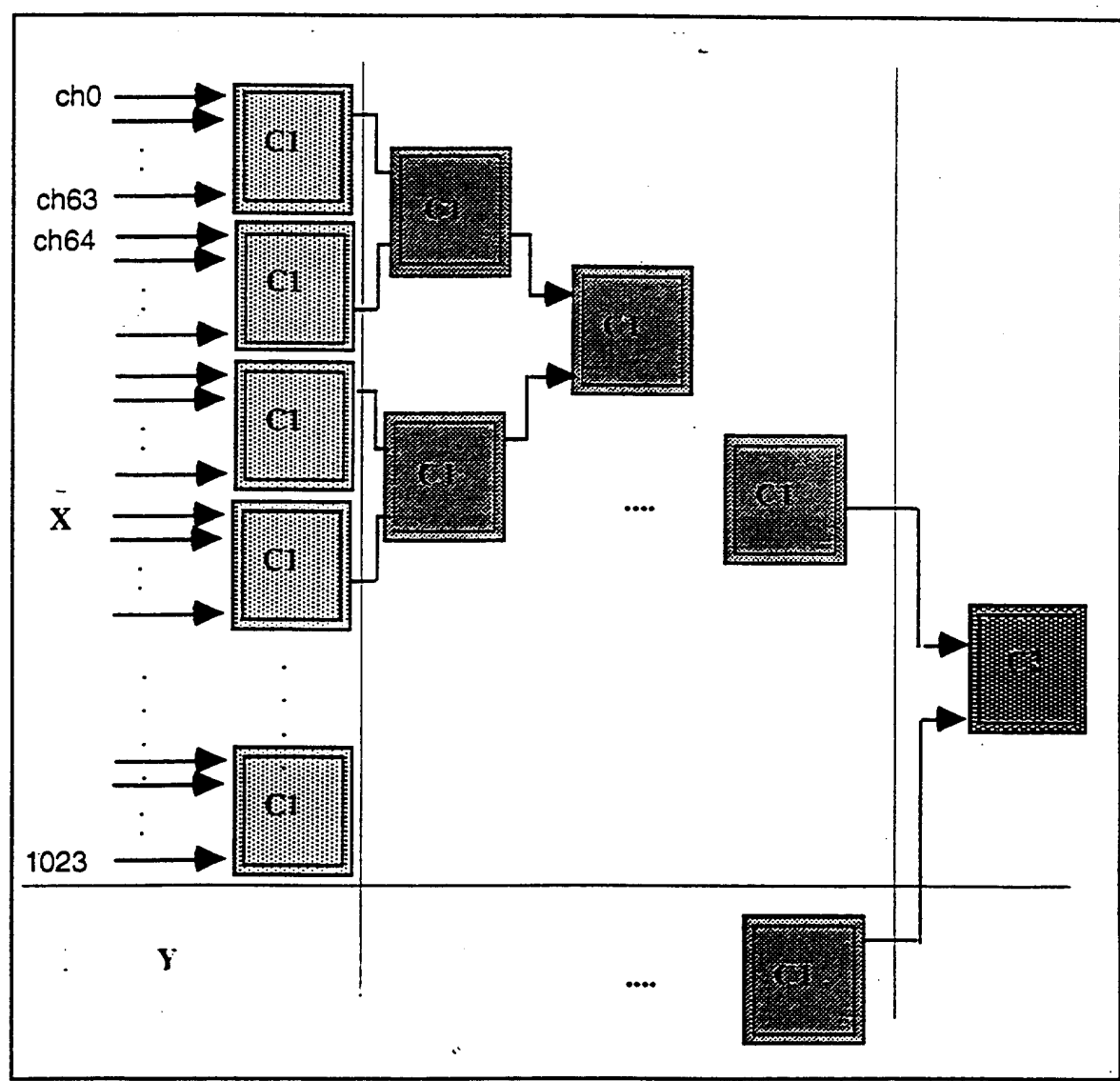


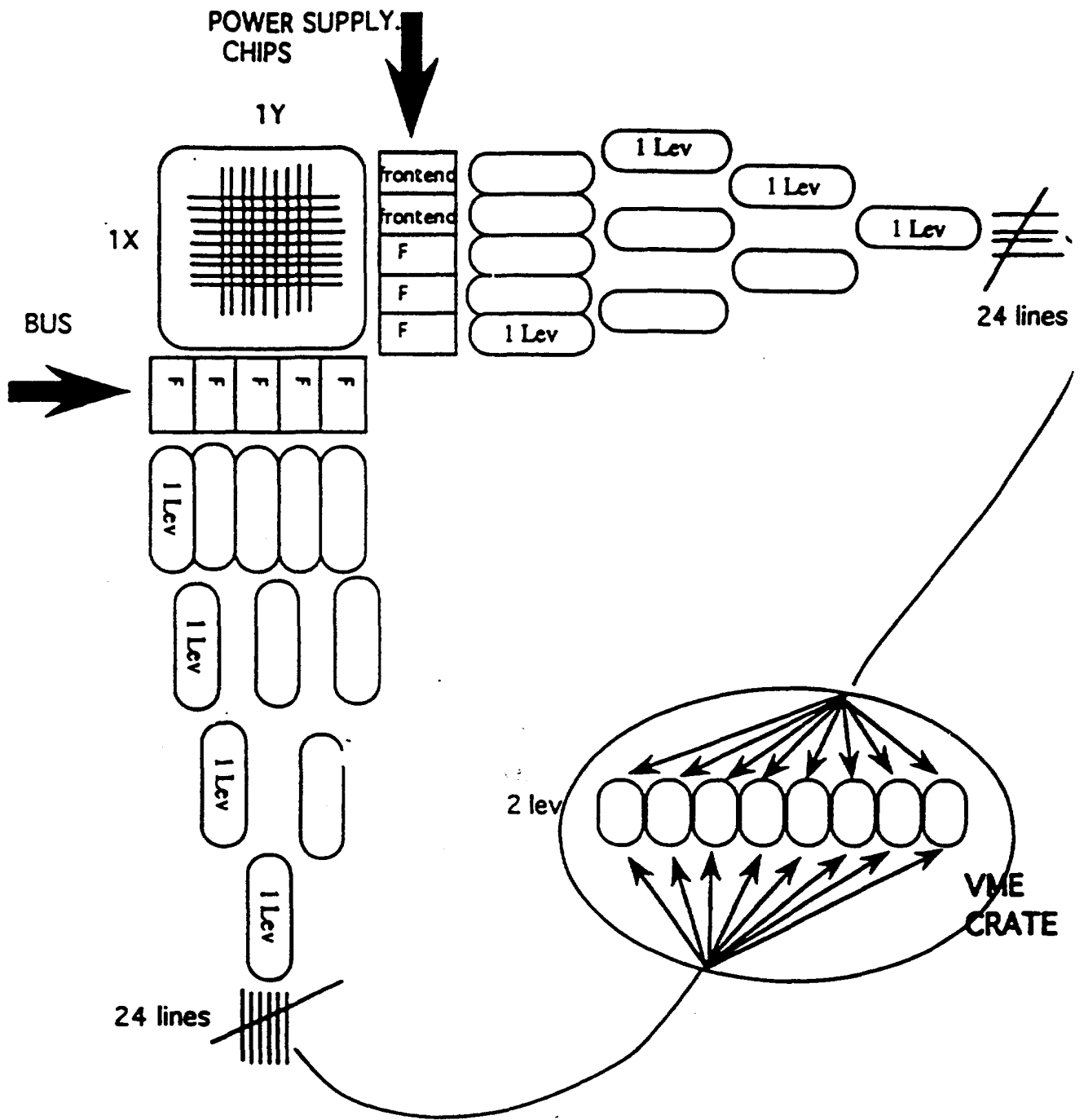
● DAQ in frame



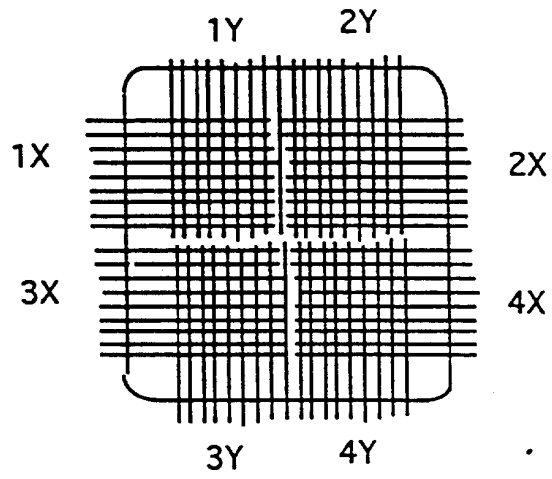
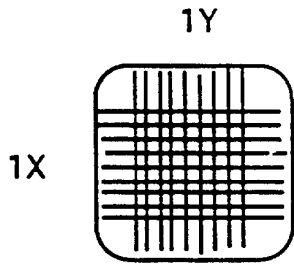
● Pipeline Architecture

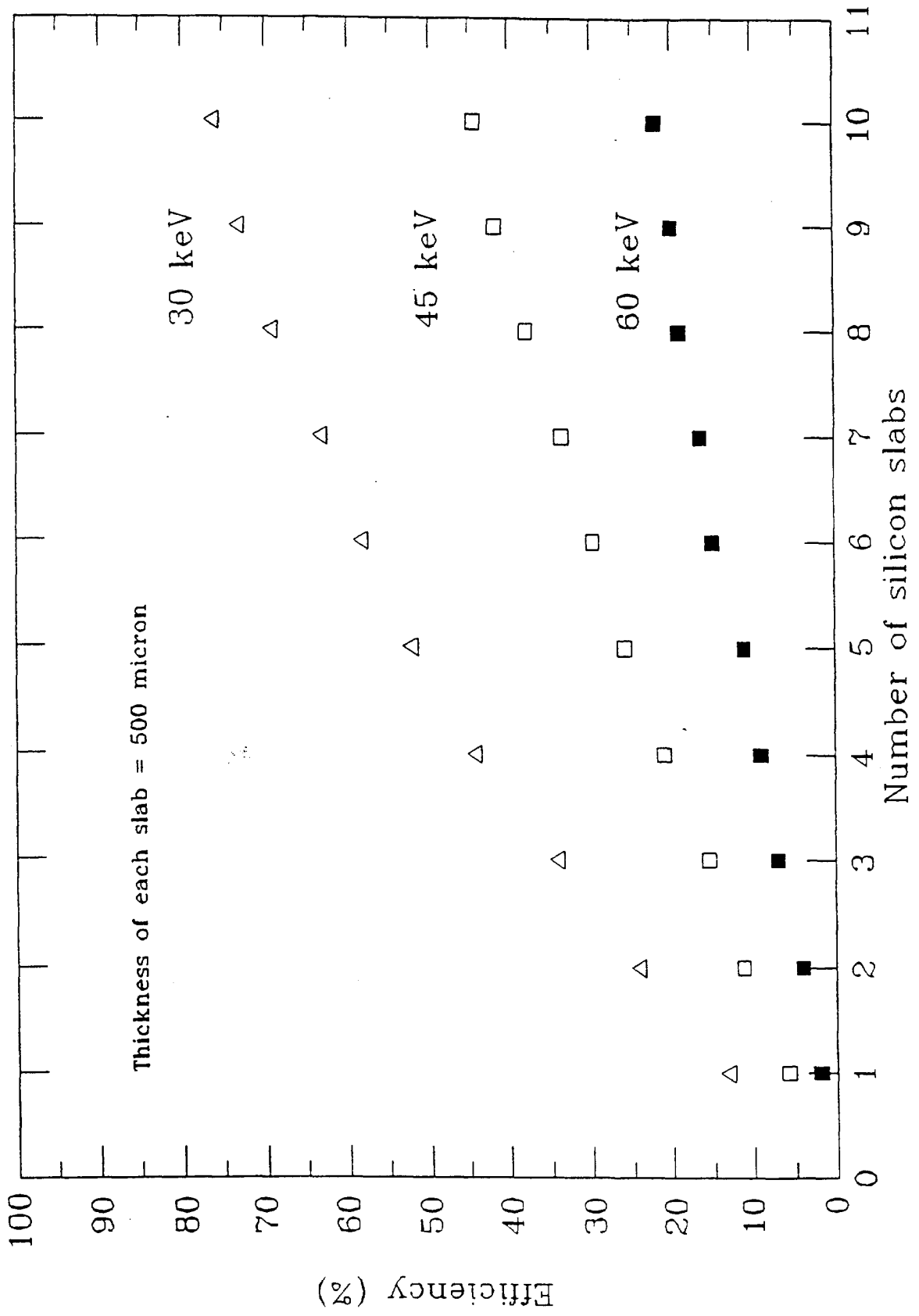
(Synchronous clock at 100 MHz) $\Rightarrow t_{\text{sampling}} = 10 \text{ ns}$



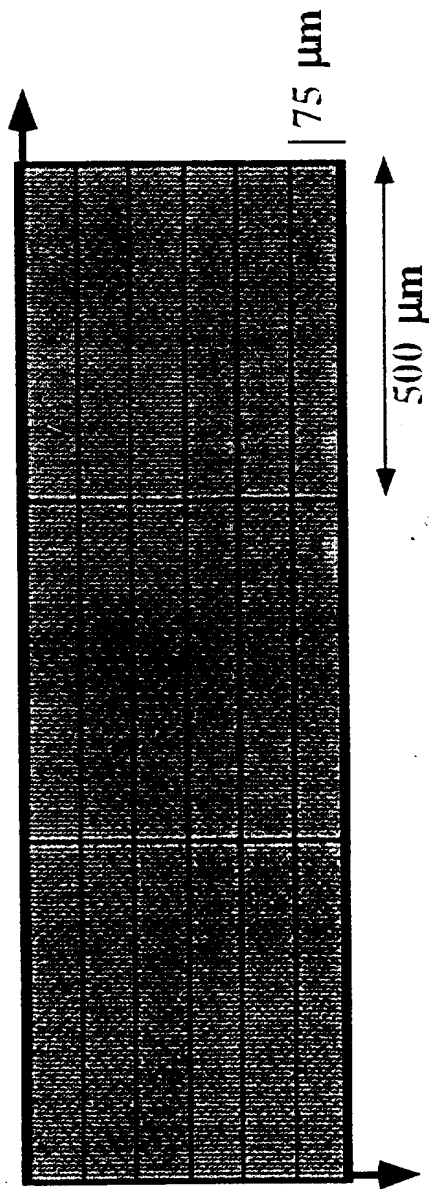


64 STRIPS PER CHIP

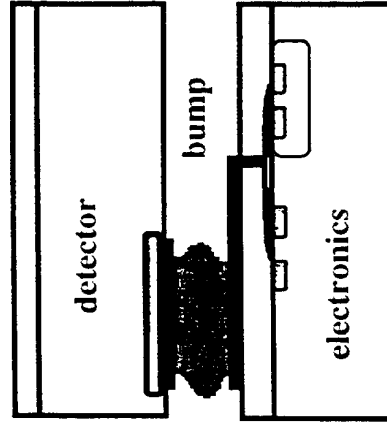




SILICON PIXEL DETECTOR



The detector is bump-bonded to the read-out chips:



CERN RD-19 (E. Heijne) and WA-97

M. Campbell et al. Nucl. Instrum. Methods A.342 (1994) 52

E. Heijne, Physica Medica 9 (1993) 109

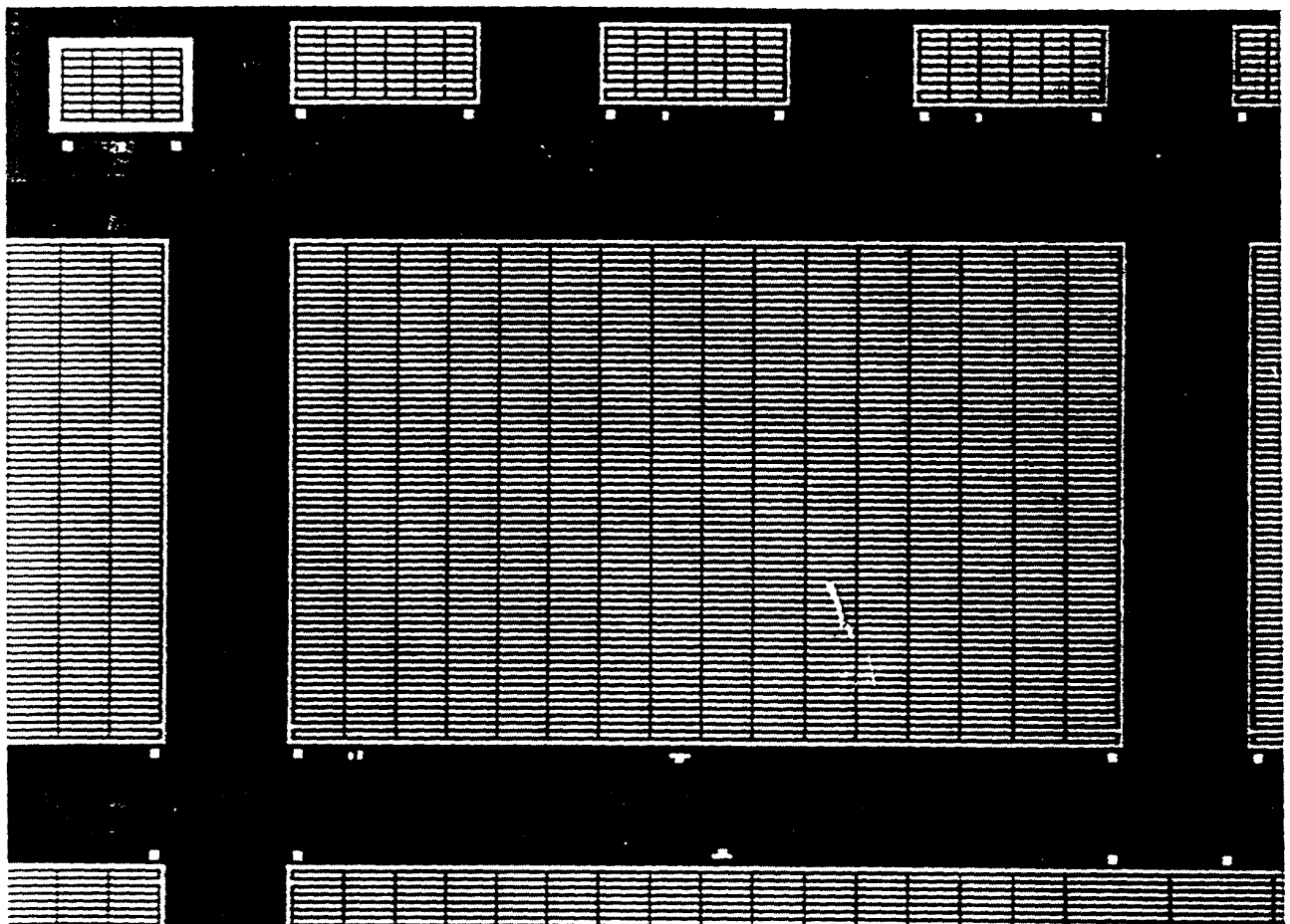
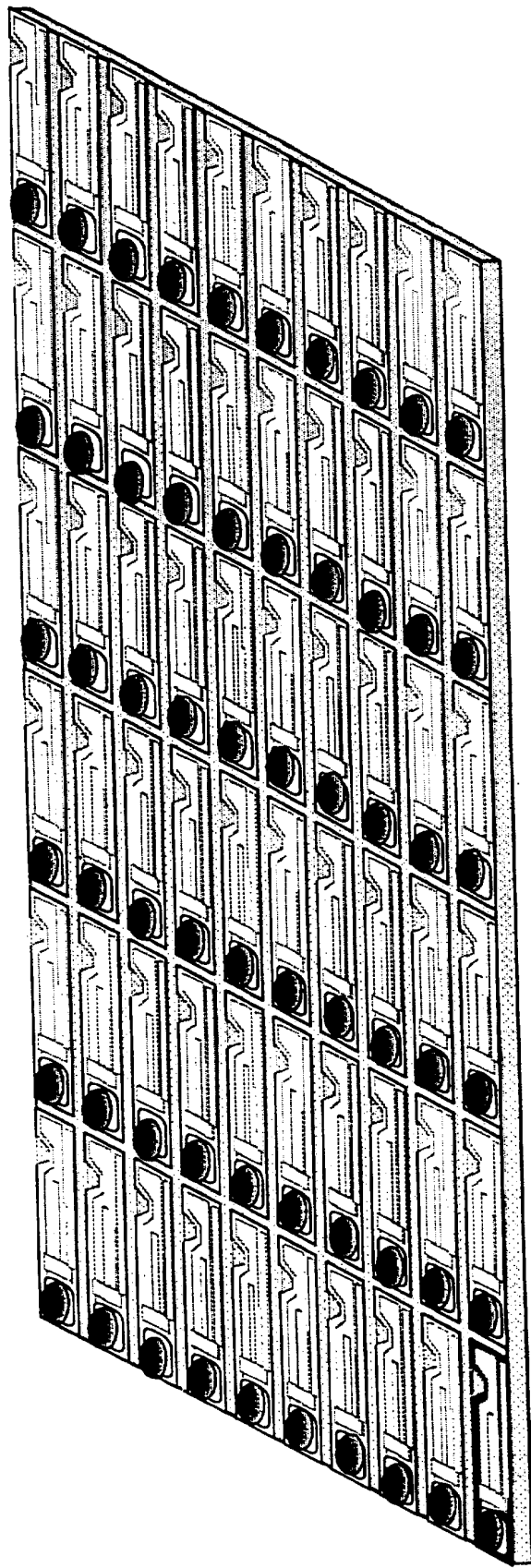
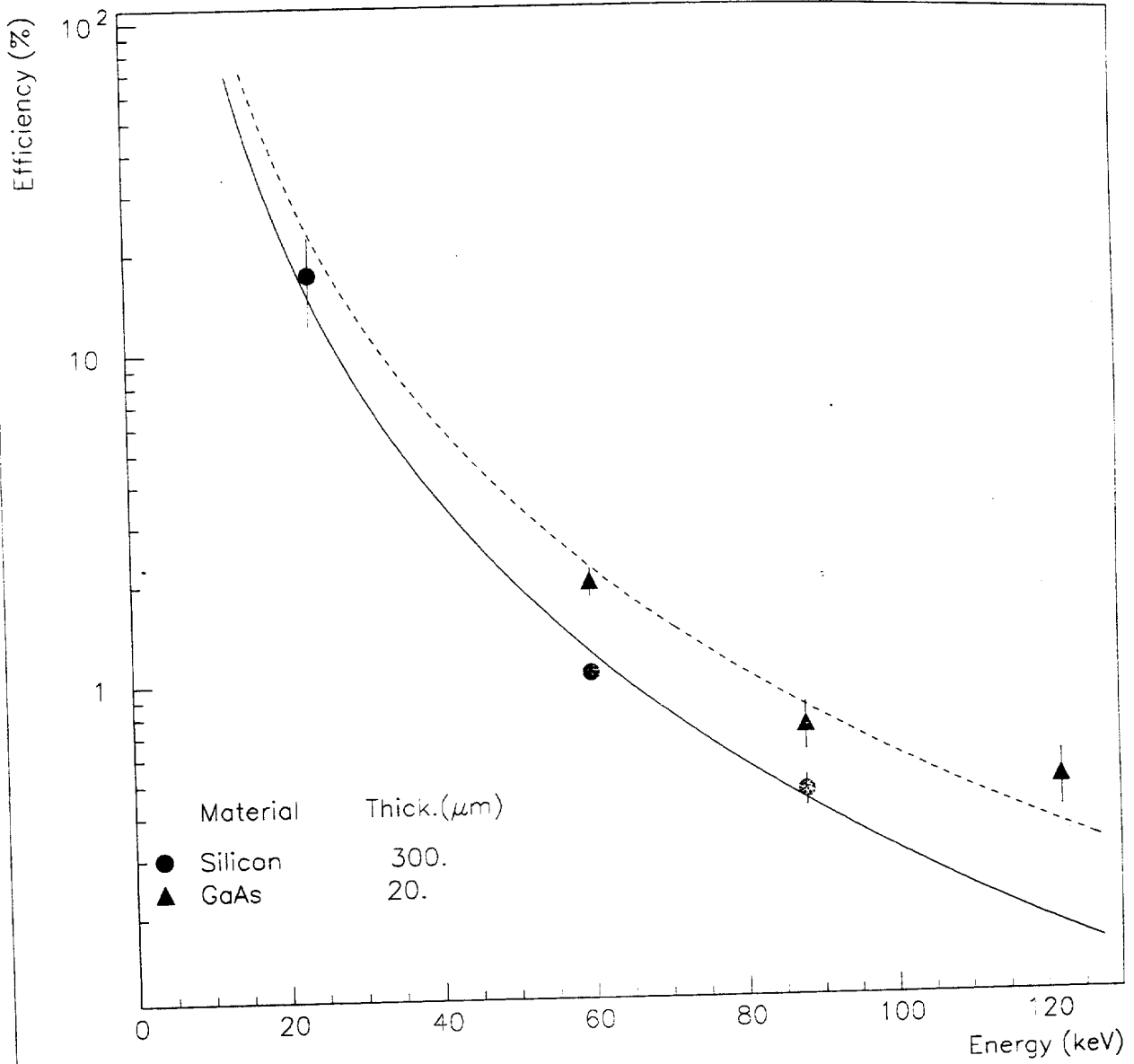


Fig. 1 - Photograph of a part of a processed detector wafer. In the middle is shown a large silicon detector (8.3 mm x 6.6 mm) with 2-dimensional segmentation. Each segment (pixel) has dimension $75 \mu\text{m} \times 500 \mu\text{m}$ and is an individual diode element. The separation between segments is achieved by an oxide layer. Under total depletion condition 100% efficiency is obtained without any insensitive region between the segments. The various smaller structures seen around the main detector are test detectors to be cut off.

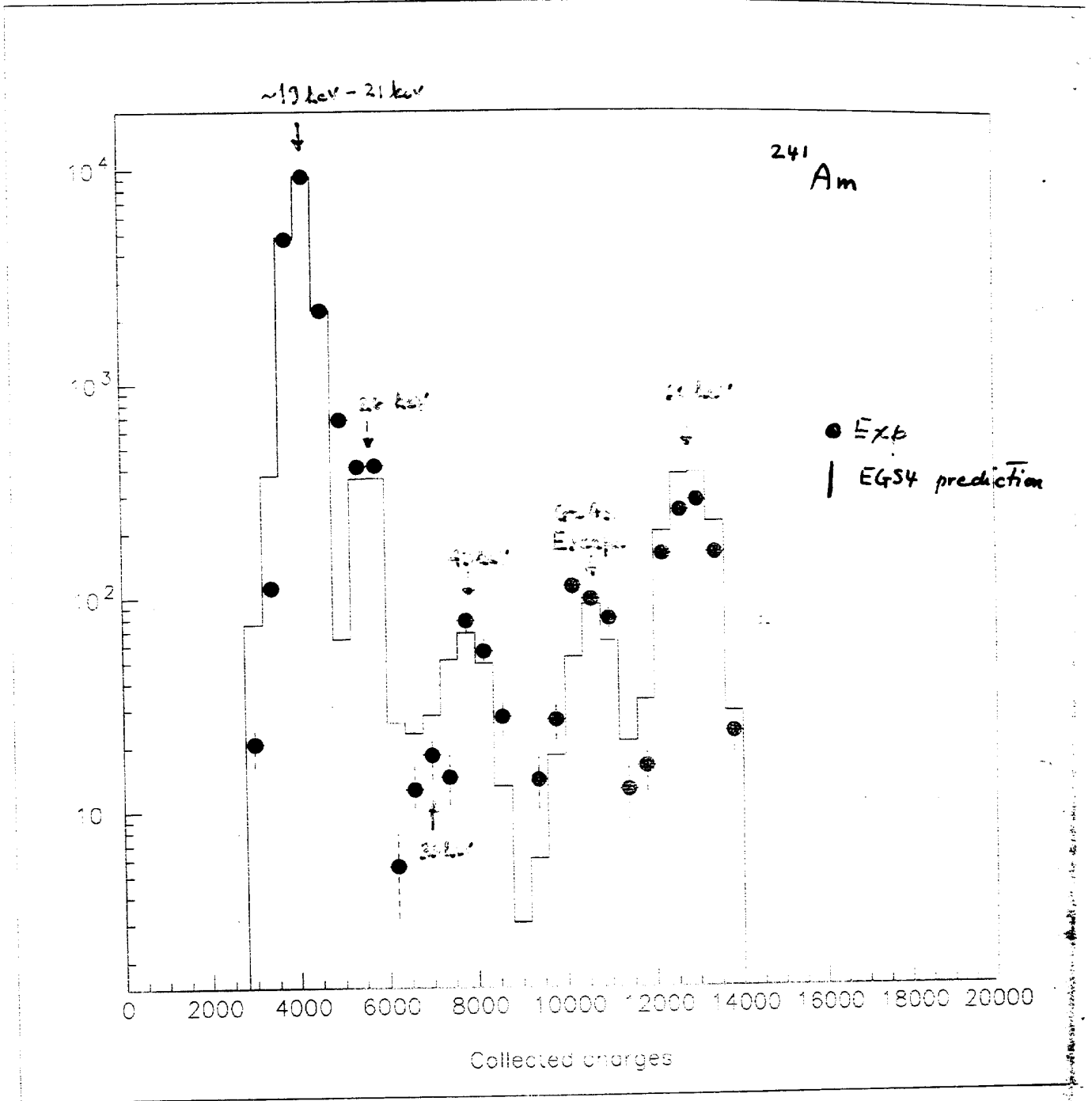
PIXEL AMPLIFIERS WITH BUMP BONDS





▲ W. Benoit-Lévy, et al., *J. Appl. Phys.*, **61**, 4358 (1987) 547

from Beccivelli et al, *Nucl. Instr. Meth. A* 346 (1994) 372.



ANSTO detector (as described in the paper)

↓
(Liquid Phase Epitaxy)

LPE (Liquid Phase Epitaxy)

Detector #	Material firm	Contacts firm	Thickness (μm)	Pixel diameter (mm)
1	AXT	ALENIA	350	2
②	MCP	Un. Glasgow	⑧0	①
3	MCP	Un. Glasgow	630	2
4	SUMITOMO	ALENIA+	200	3
5	SUMITOMO	ALENIA	200	3
6	NIPPON M.	Un. Lecce	400	1
⑦	NIPPON M.	Un. Lecce	⑦0	→ 0.2++ ←

Fabrication and geometrical characteristics of the LEC detectors.

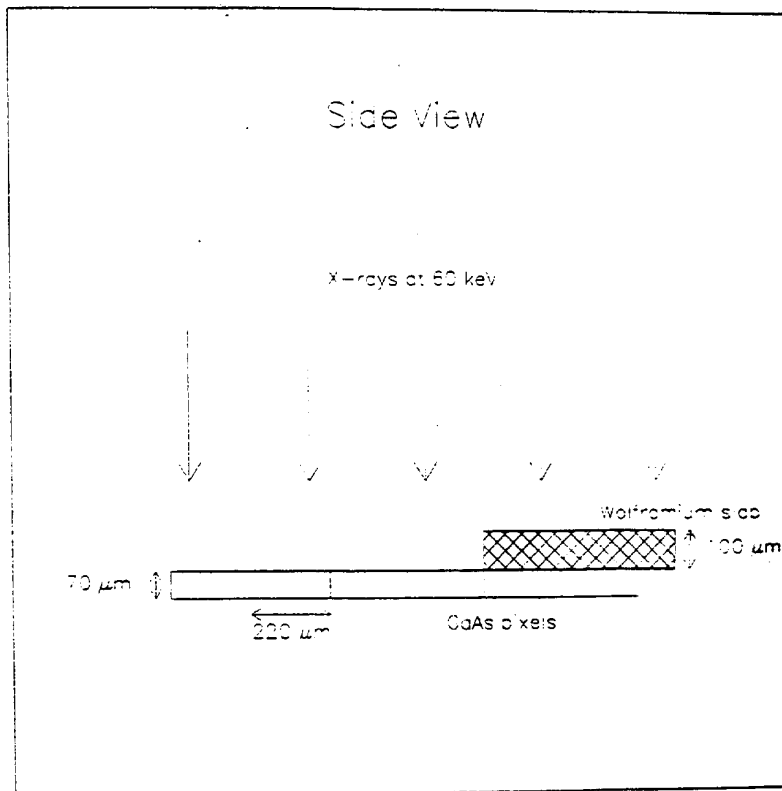
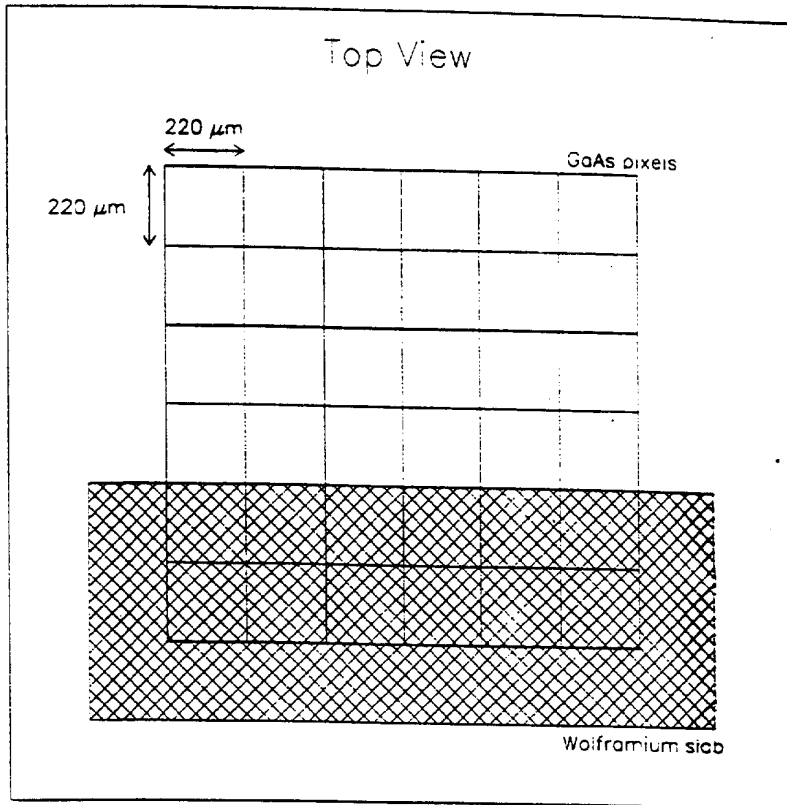
+ The rear surface has been polished.

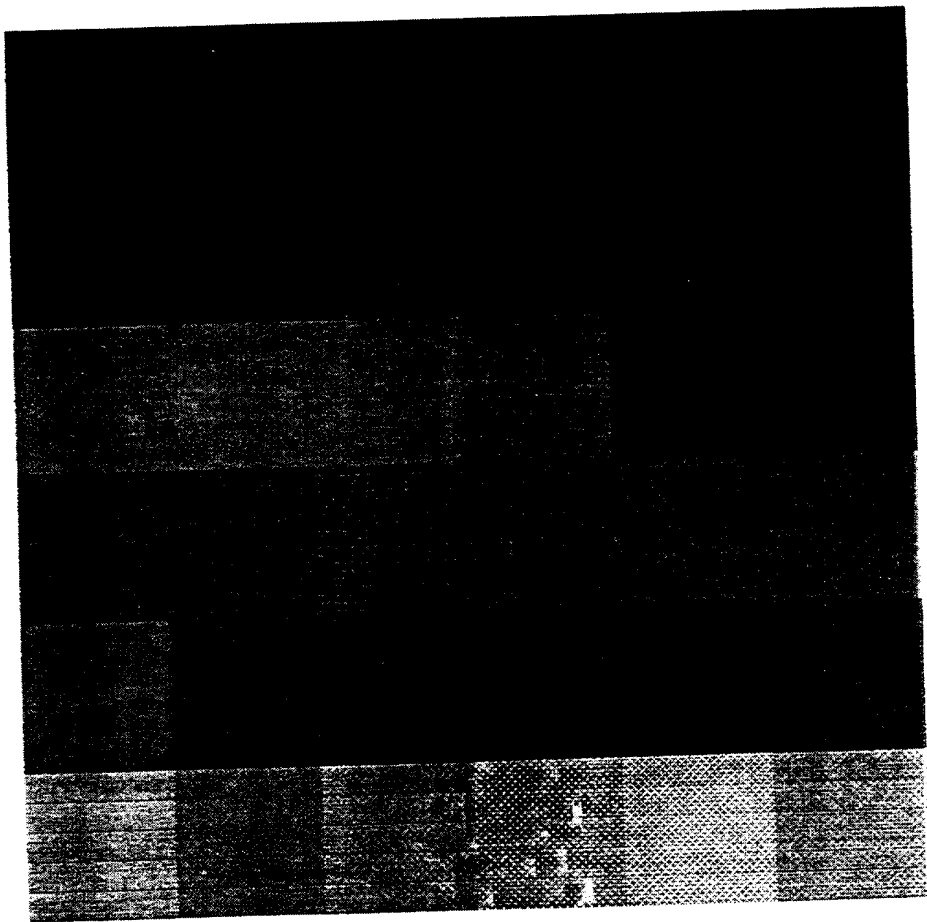
++ Side length of the square pixel.

#	V _{bias} (V)	cce (%)	σ/E (%)	J (Acm ⁻²)	C (Fcm ⁻²)	C _g (Fcm ⁻²)
1	350	43.7±8.8	20.2±4.1	(1.9±0.2)10 ⁻⁶	(8.0±0.8)10 ⁻¹⁰	3.3 10 ⁻¹¹
②	80	⑧1.9±6.1	⑦5.5±0.6	(2.2±0.2)10 ⁻⁶	(1.5±0.2)10 ⁻¹⁰	1.4 10 ⁻¹⁰
3	450	36.4±11.5	32.7±10.7	(1.1±0.1)10 ⁻⁶	(1.6±0.2)10 ⁻¹¹	1.9 10 ⁻¹¹
4	160	60.5±15.0	24.8±6.1	(2.8±0.3)10 ⁻⁶	(6.2±0.6)10 ⁻¹¹	5.7 10 ⁻¹¹
5	160	63.1±14.7	23.4±5.4	(3.0±0.3)10 ⁻⁶	(6.4±0.6)10 ⁻¹¹	5.7 10 ⁻¹¹
6	700	39.1±14.9	38.0±10.9	(3.6±0.4)10 ⁻⁶	(1.3±0.1)10 ⁻¹¹	2.9 10 ⁻¹¹
⑦	80	⑧7.6±4.8	⑤5.5±0.3	(7.9±0.8)10 ⁻⁶	(a)	1.6 10 ⁻¹⁰

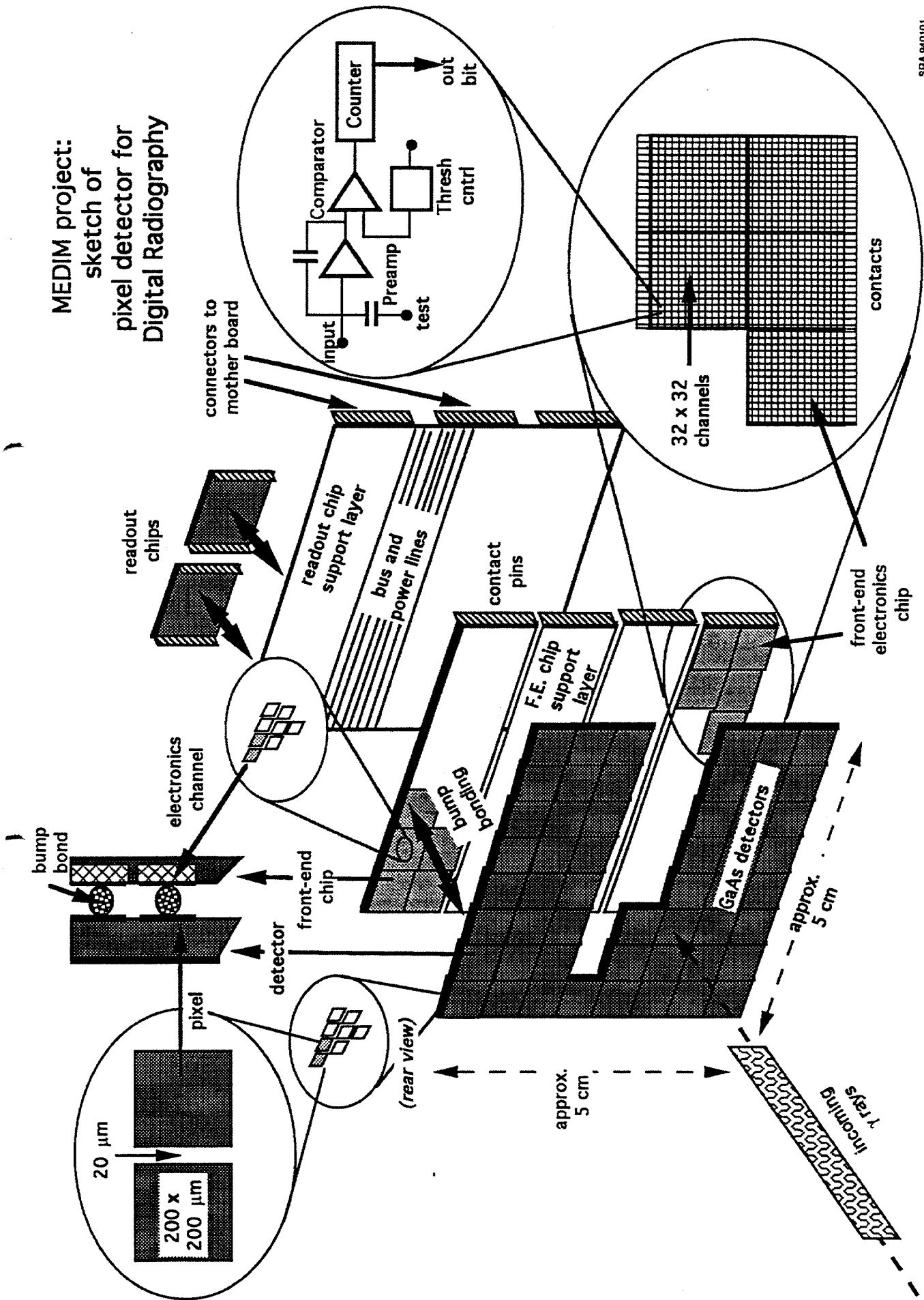
Charge collection efficiency (cce) and energy resolution (σ/E) at 60 keV photon energy, measured density current (J), measured density capacitance (C) and geometrical density capacitance (C_g) for all detectors at the maximum bias voltage. (a): The value of the capacitance (F) is lower than the sensitivity of the capacitance meter, due to the pixel dimensions.

M

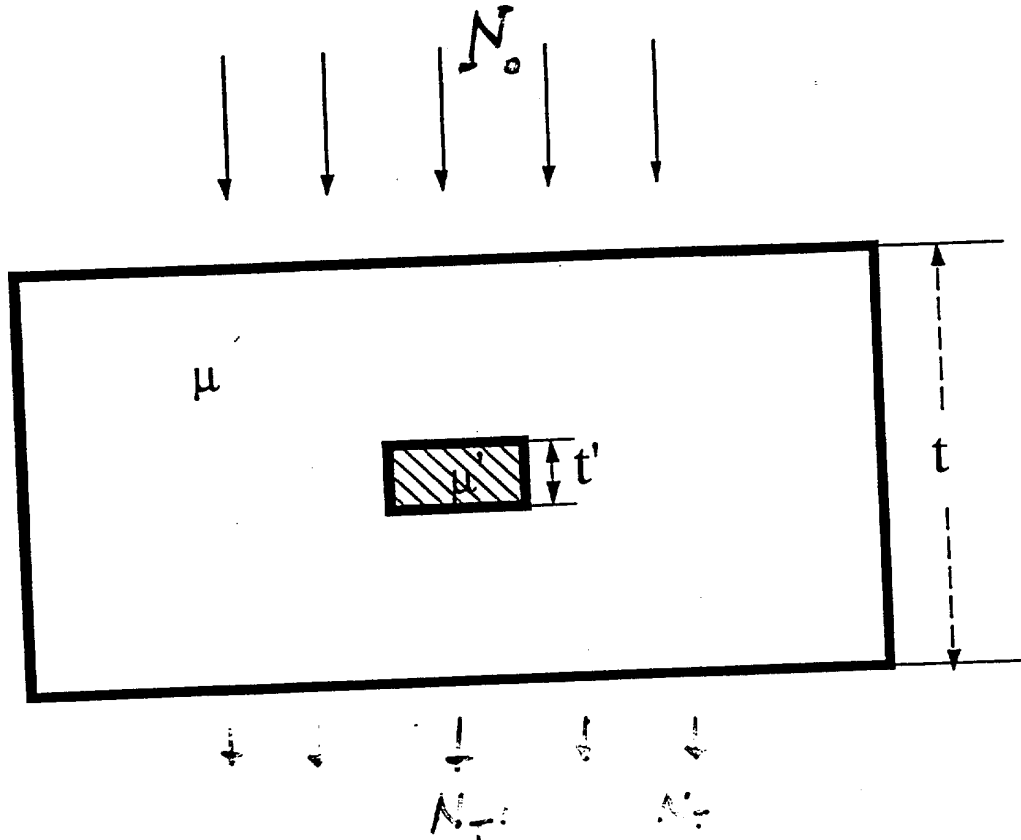




**MEDIM project:
sketch of
pixel detector for
Digital Radiography**



from Jennings et al. Medical Physics 8 (1981) 629



$$n = N_T A = N_0 A e^{-\mu t}$$

$$n' = N_T' A = N_0 e^{-\mu(t-t')} e^{-\mu t'}$$

$$C = \frac{|n - n'|}{n + n'} = \frac{|N_0 A e^{-\mu t} - N_0 A e^{-\mu(t-t')} e^{-\mu t'}|}{N_0 A e^{-\mu t} + N_0 A e^{-\mu(t-t')} e^{-\mu t'}}$$

for $n \approx n' \Rightarrow (\mu - \mu') t' \ll 1$

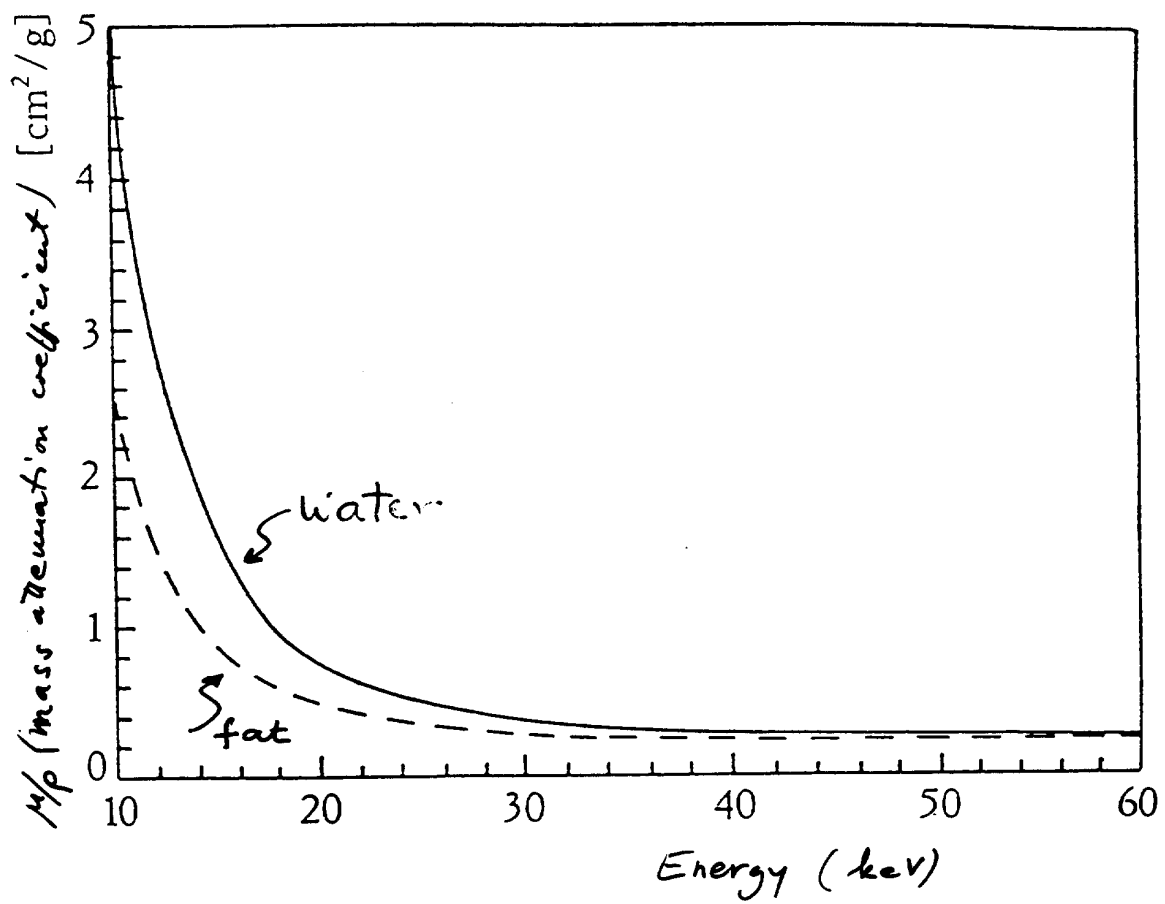
$$\approx \frac{|\mu' - \mu| t'}{2}$$

$$G_{\text{noise}} = \frac{\delta / |n - n'|}{\frac{n + n'}{2}} \quad \text{for } n \approx n' = \frac{\sqrt{n}}{n} = \frac{1}{\sqrt{n}} \quad \text{assuming } \eta \ll 1$$

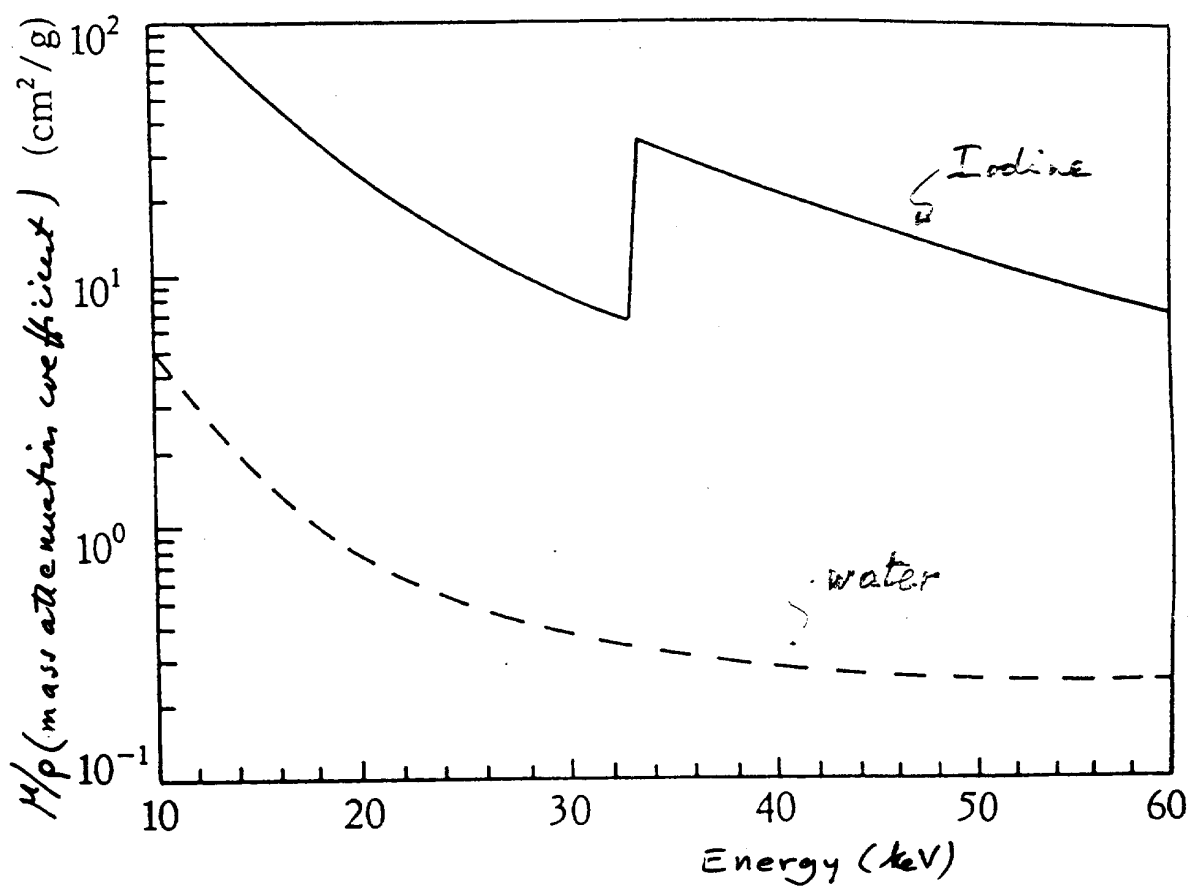
$$= \frac{1}{\sqrt{\eta n}} = (\eta N_0 A e^{-\mu t})^{-1/2}$$

$$\text{SNR} = \frac{|n - n'|}{\sqrt{n + n'}} \quad \text{for } n \approx n' = C \times \sqrt{2} \times \sqrt{n} = \sqrt{2} C / G_{\text{noise}}$$

$$\boxed{\text{SNR}^2 = 2 \left[\frac{C}{G_{\text{noise}}} \right]^2 = \frac{1}{2} (\mu' - \mu)^2 t'^2 = \eta N_0 A e^{-\mu t}}$$



Breast tissue : 80% water + 20% fat
 Tumor : 100% water



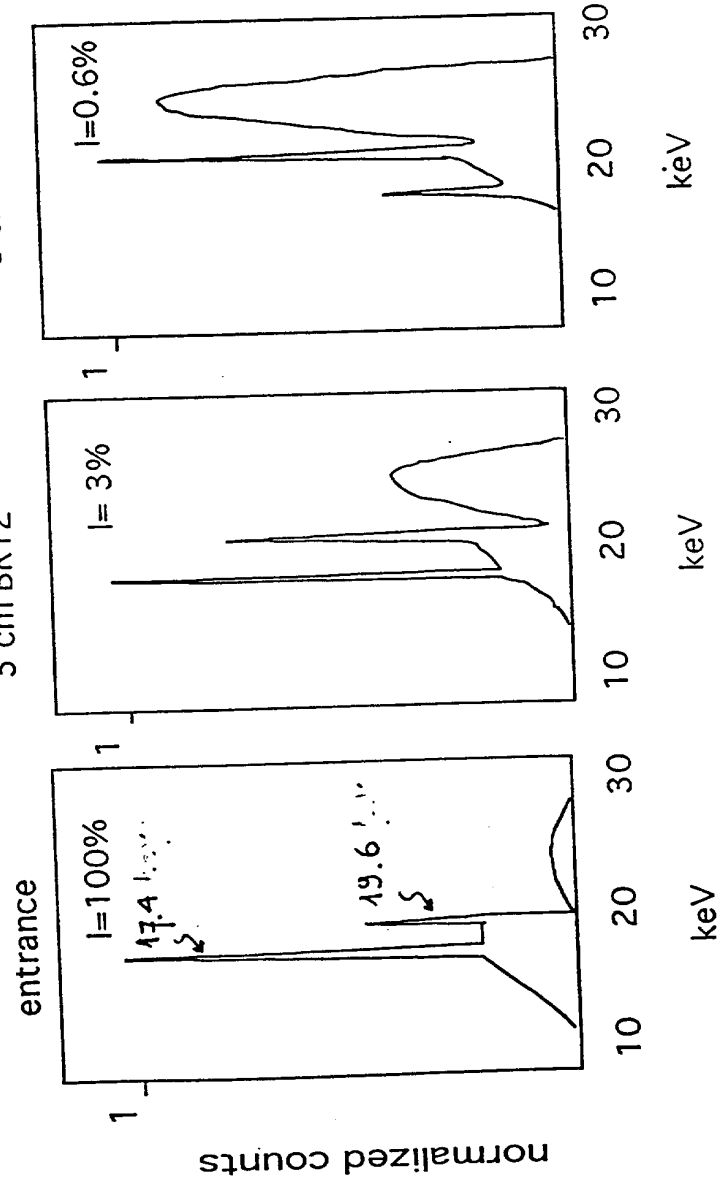
CONVENTIONAL MAMMOGRAPHY

X-ray tube generally used in mammography:

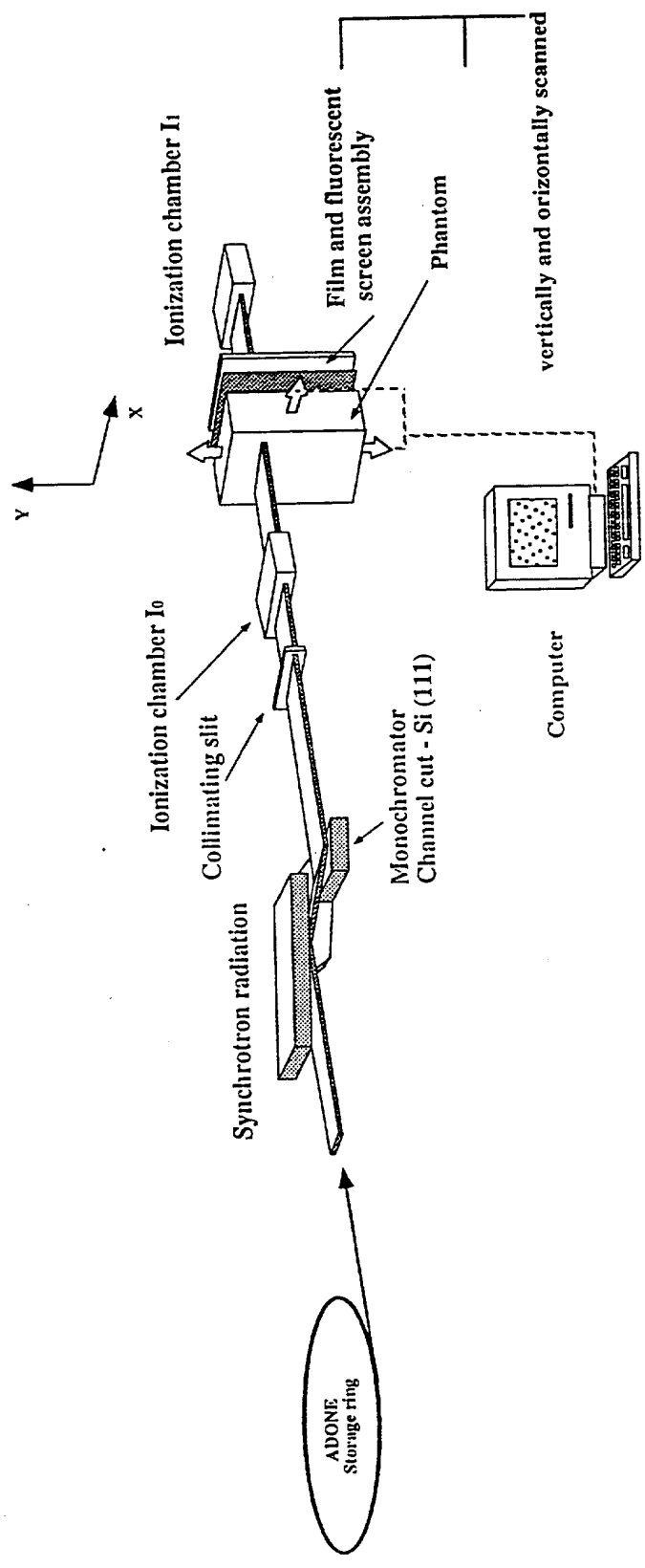
anode molybdenum
 window beryllium
 added filtration molybdenum 0.030 mm

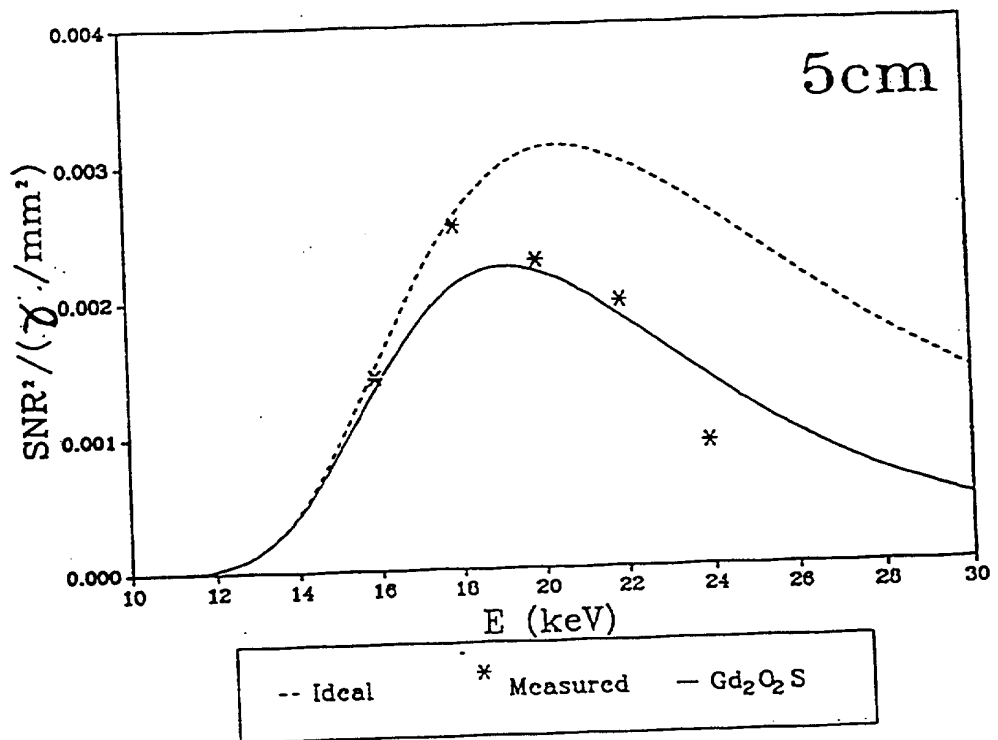
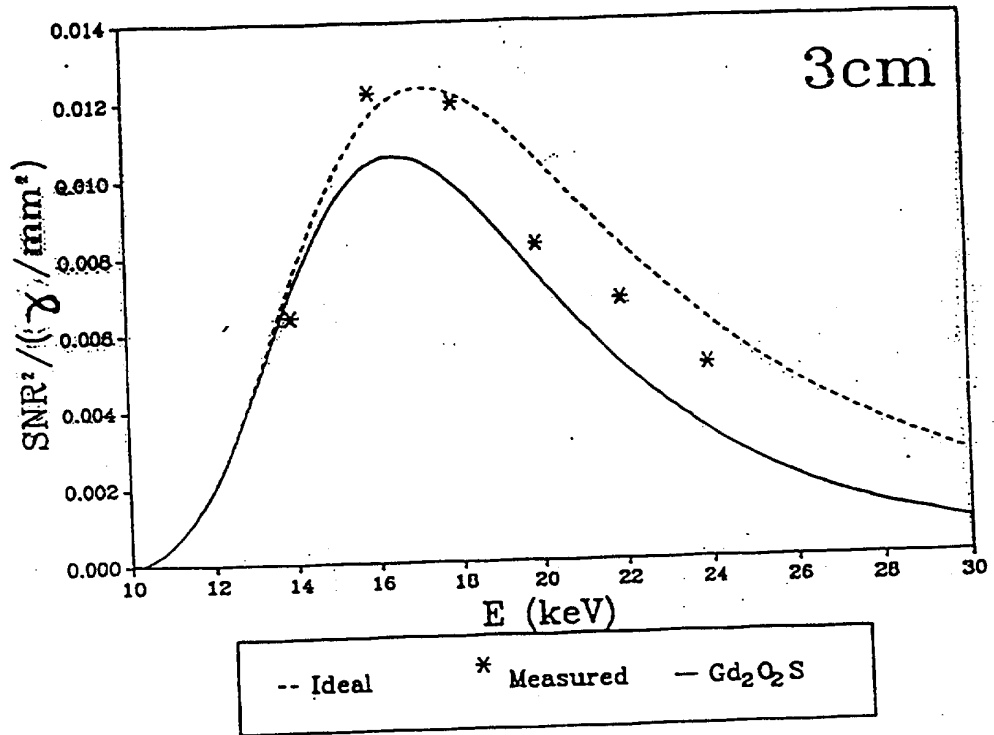
transmitted by
 8 cm BR12

transmitted by
 5 cm BR12



SYNCHROTRON RADIATION MAMMOGRAPHY





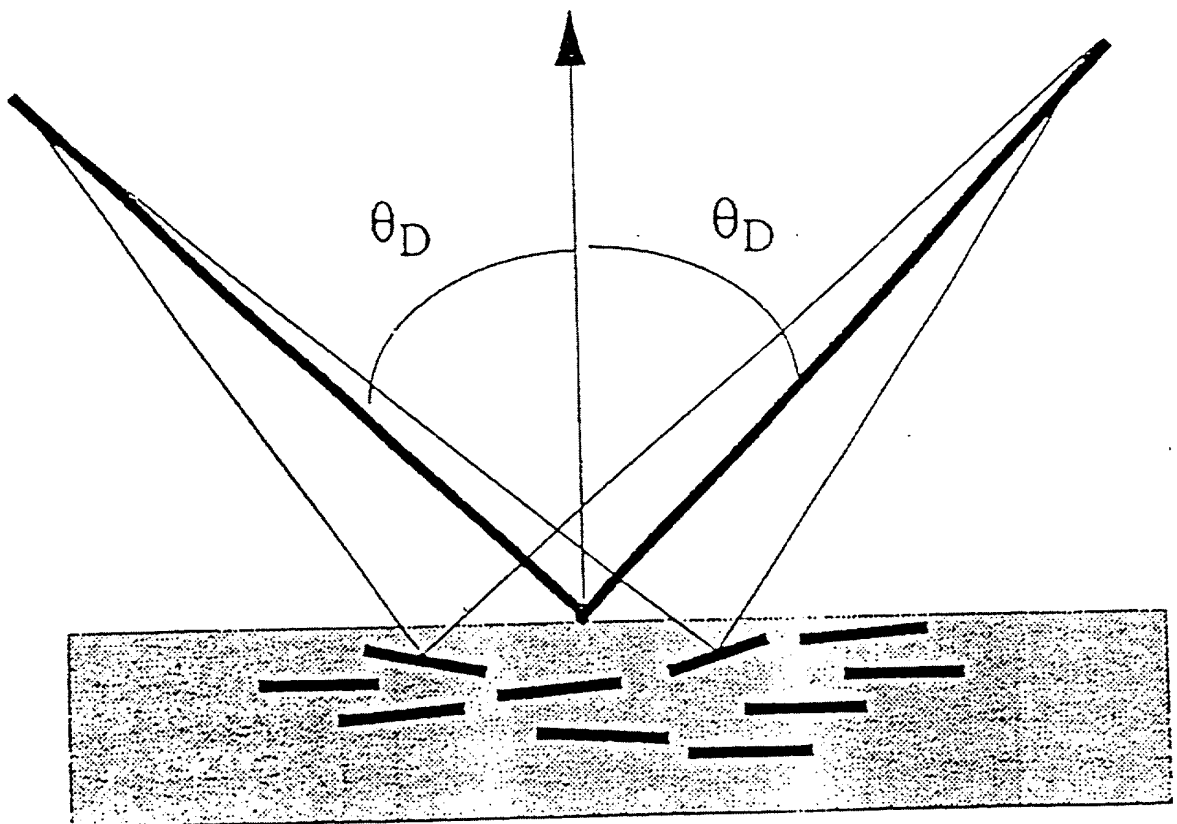
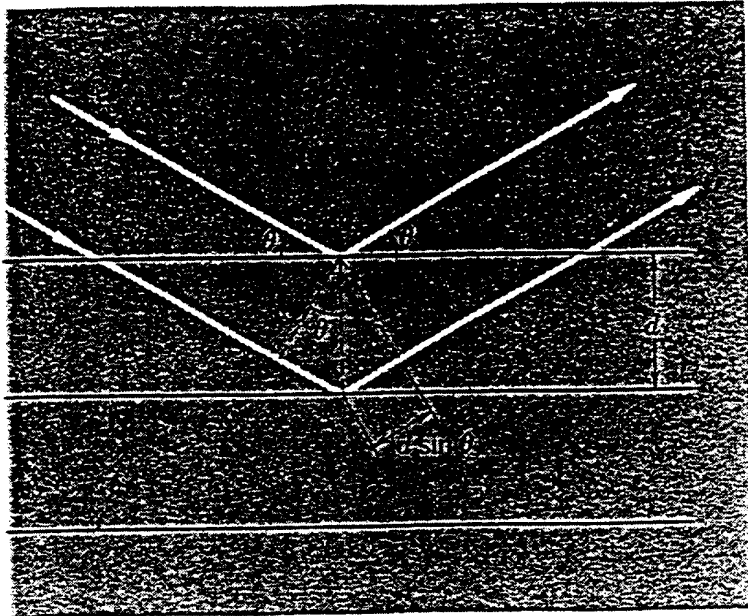
from Burattini et al, *Physics Medicine*, VI (1990) 299

Table. 3. Entrance exposure (with backscatter), BR12 entrance dose and mean dose to a BR12 phantom 5 cm thick delivered by synchrotron radiation and conventional mammography.

IMAGING SOURCE	entrance exposure X_e	entrance dose D_e	mean dose D
Synchrotron radiation 17 keV	887 mR 2.29 10^{-4} C/kg	585 mrad 5.85 mGy	155 mrad 1.55 mGy
Synchrotron radiation 18 keV	406 mR 1.05 10^{-4} C/kg	268 mrad 2.68 mGy	80.2 mrad 0.802 mGy
Conventional 26 kV no grid	508 mR 1.31 10^{-4} C/kg	335 mrad 3.35 mGy	<u>74.2 mrad</u> <u>0.742 mGy</u>
Conventional 28 kV grid	1055 mR 2.72 10^{-4} C/kg	696 mrad 6.96 mGy	<u>151 mrad</u> <u>1.51 mGy</u>

E. Berattini et al., Eur. J. Radiol. 4 (1994) 464

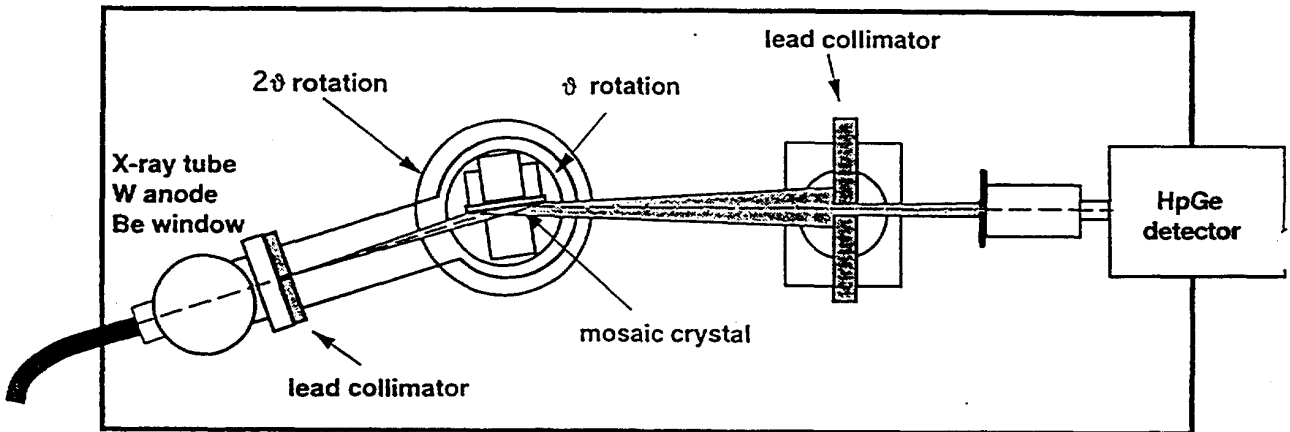
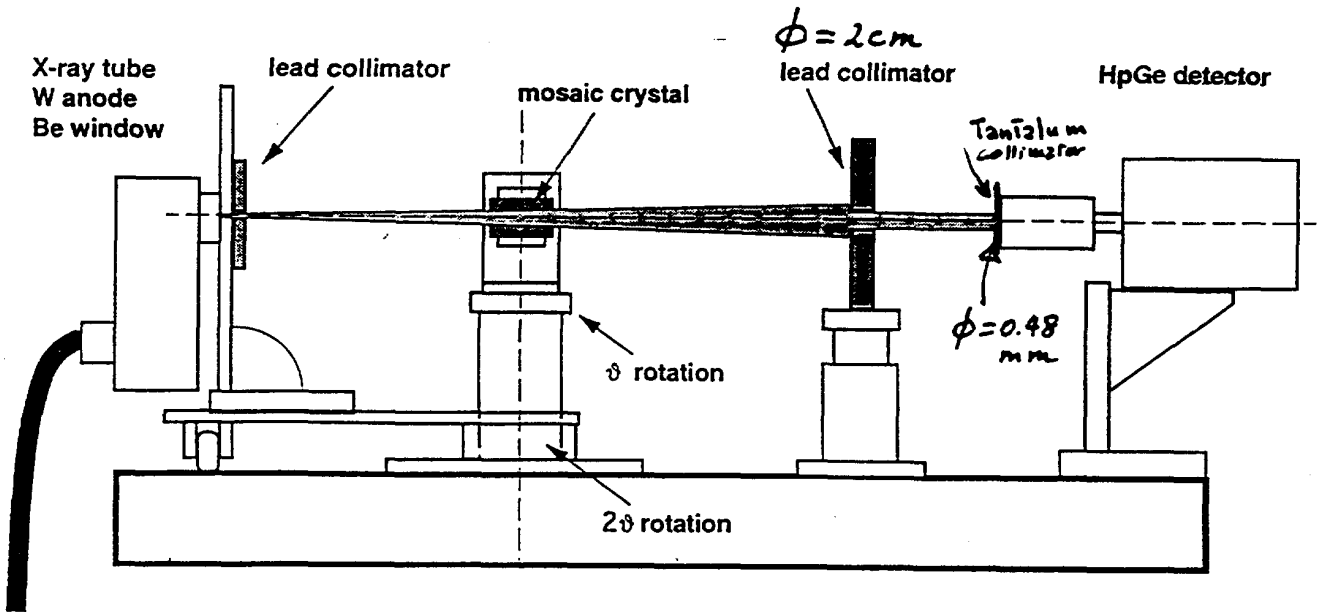
Bragg law $\Rightarrow 2d \sin \theta = \lambda$

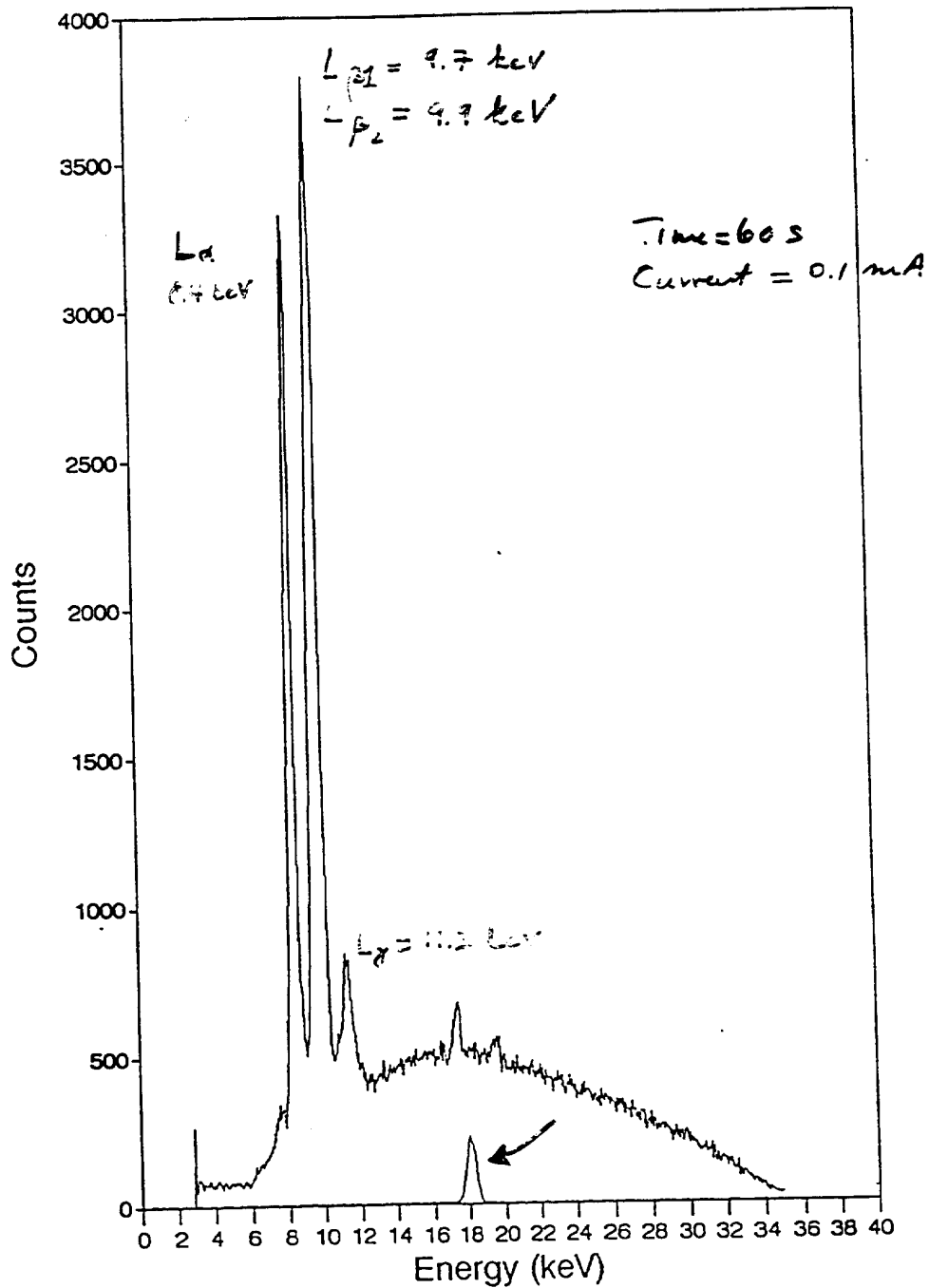


Mosaic spread $\sim 0.2^\circ$ (Frost)

from: F. Frontera et al, SPIE vol. 1549 "X-ray, and gamma-ray..."
 pg 113 (103)

spectrometric assembly



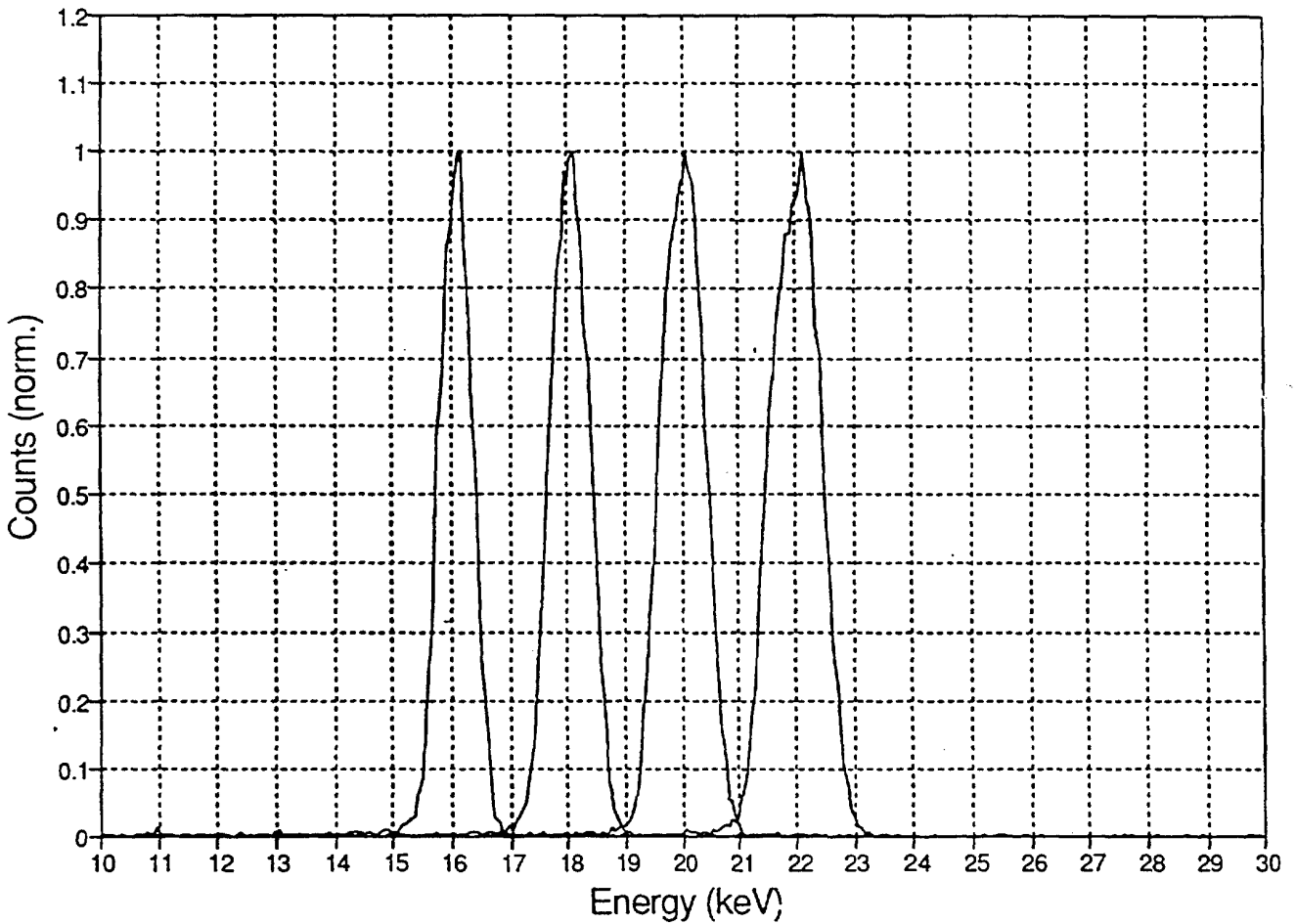


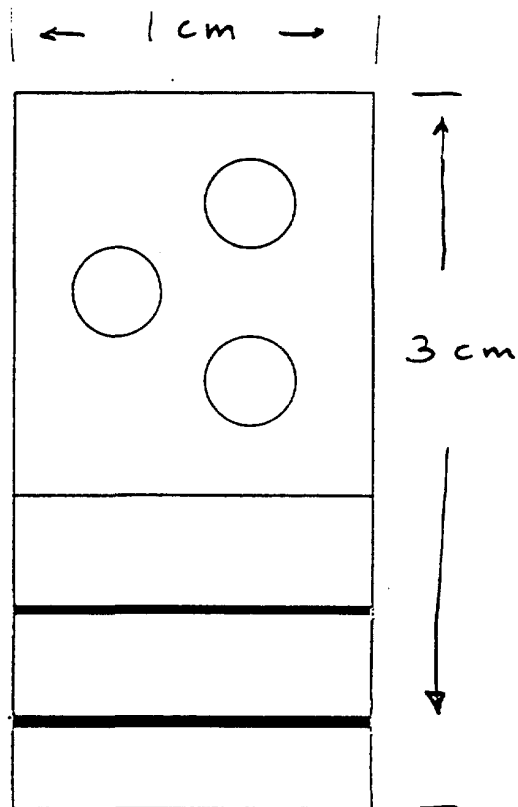
$$E_p = 30 \text{ keV}$$

Energy (keV)	photon flux (photons mA ⁻¹ s ⁻¹ mm ⁻²)	FWHM (keV)	Energy Resolution (%)
16	1.16 x 10 ⁴	0.67	4.1
18	1.60 x 10 ⁴	0.83	4.5
20	1.90 x 10 ⁴	0.94	4.7
22	2.14 x 10 ⁴	1.06	4.8

16 - 22 keV

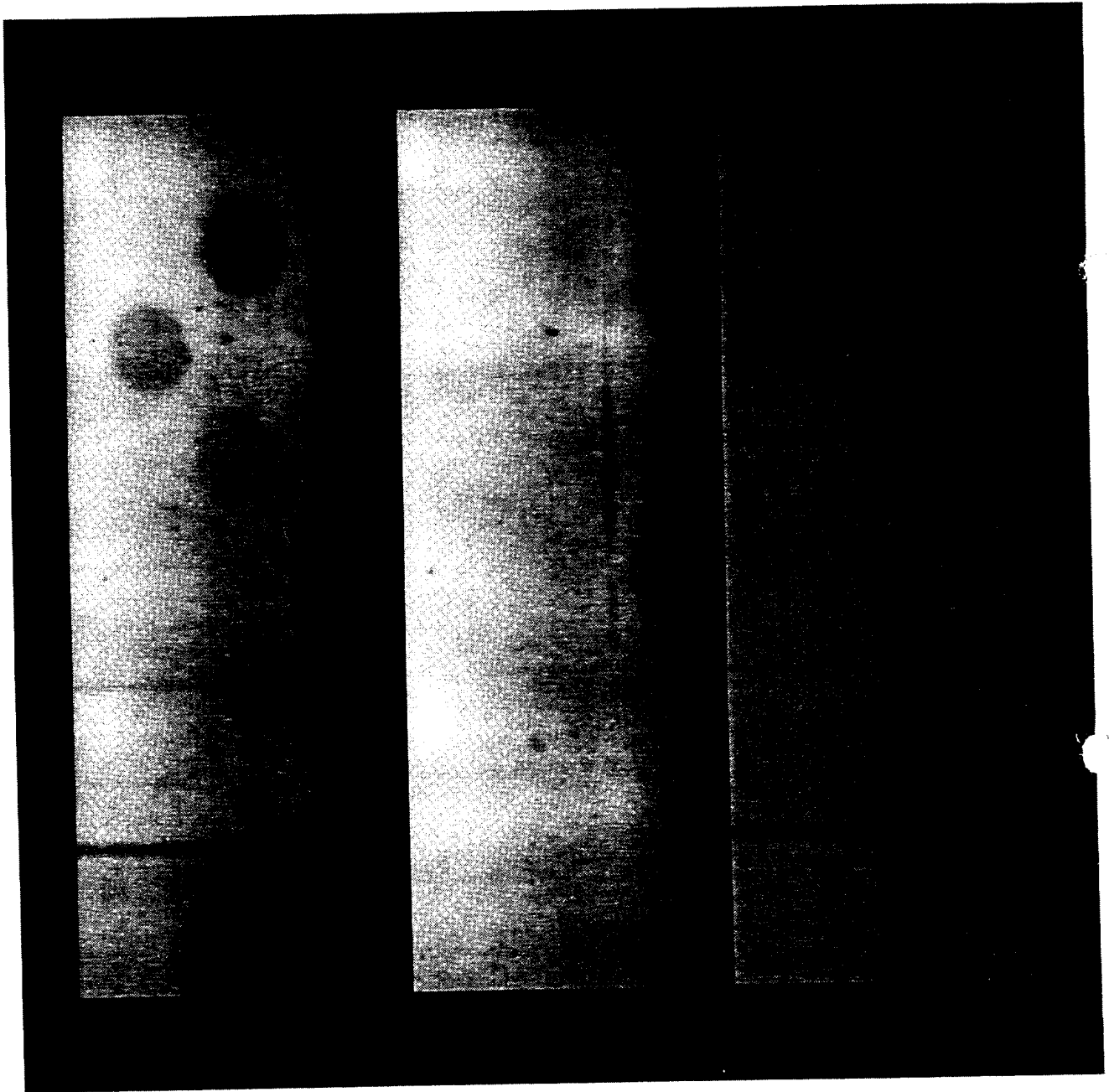
(4-5%)





Thickness (mm)

	0.5	0.25	0.125
Aluminium disks ($\varnothing=3$ mm)	0.5	0.25	0.125
Aluminium wires	0.5	0.25	0.125
<i>Contrast</i>	<i>0.6</i>	<i>0.3</i>	<i>0.15</i>



ORIGINAL

Background
(flood field)

CORRECTED



A Position Sensitive Multi Channel Ion Chamber (MCIC) for Non Invasive Coronary Angiography with Synchrotron Radiation

H. J. Besch¹, W. R. Dix², U. Großmann¹, J. Heuer², R. Langer¹, M. Lohmann², R. H. Menk²,
H. W. Schenk¹, U. Tafelmeier², M. Wagener¹, A. H. Walenta¹, H. C. Xu¹

1. Universität-Gesamthochschule-Siegen, Fachbereich Physik, Siegen (Germany)
2. Hasylab at DESY, Hamburg (Germany)

Abstract

A position sensitive 1-dimensional x-ray detector with high dynamic range ($> 20000:1$) for a high photon flux ($> 10^9$ photons/mm²·s) with fast image recording sequence (in principle up to 1 MHz) has been developed for medical applications. A detective quantum efficiency DQE of at least 55% could be achieved for 33 keV photons. The position resolution is $450 \mu\text{m}$ (fwhm) for this energy.

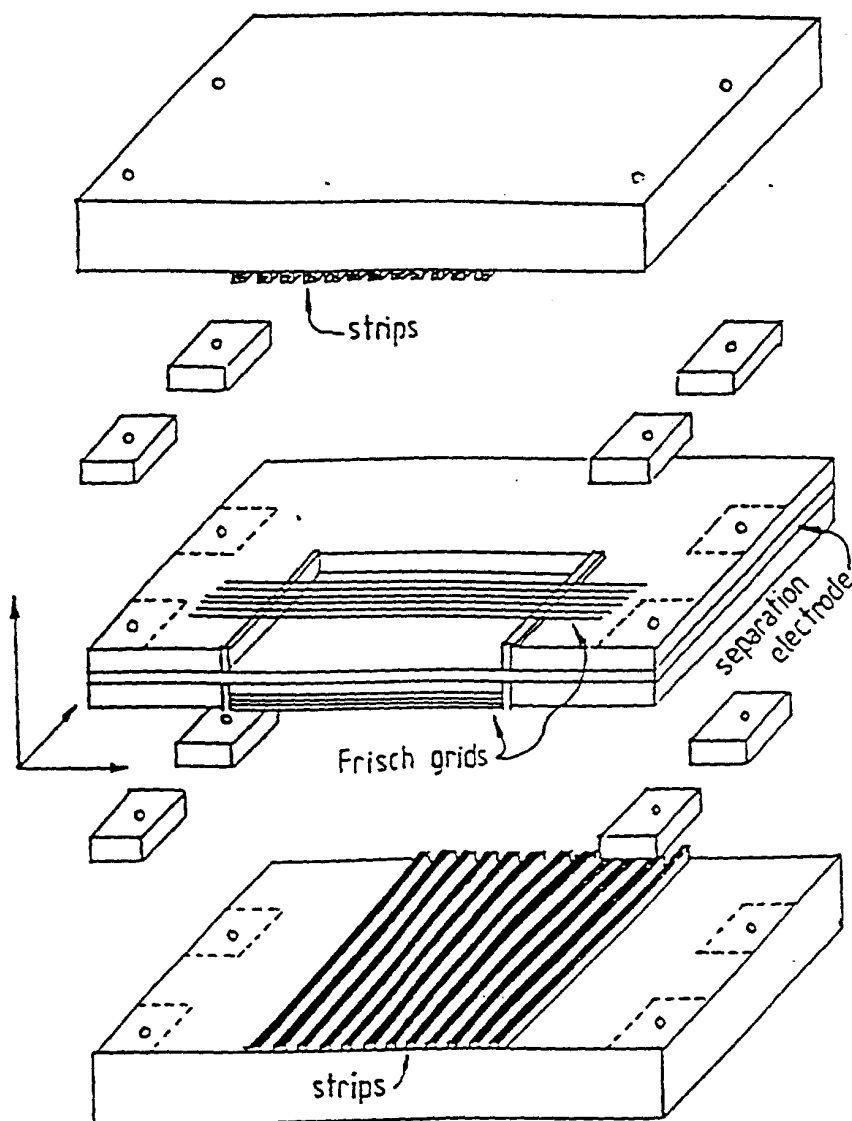
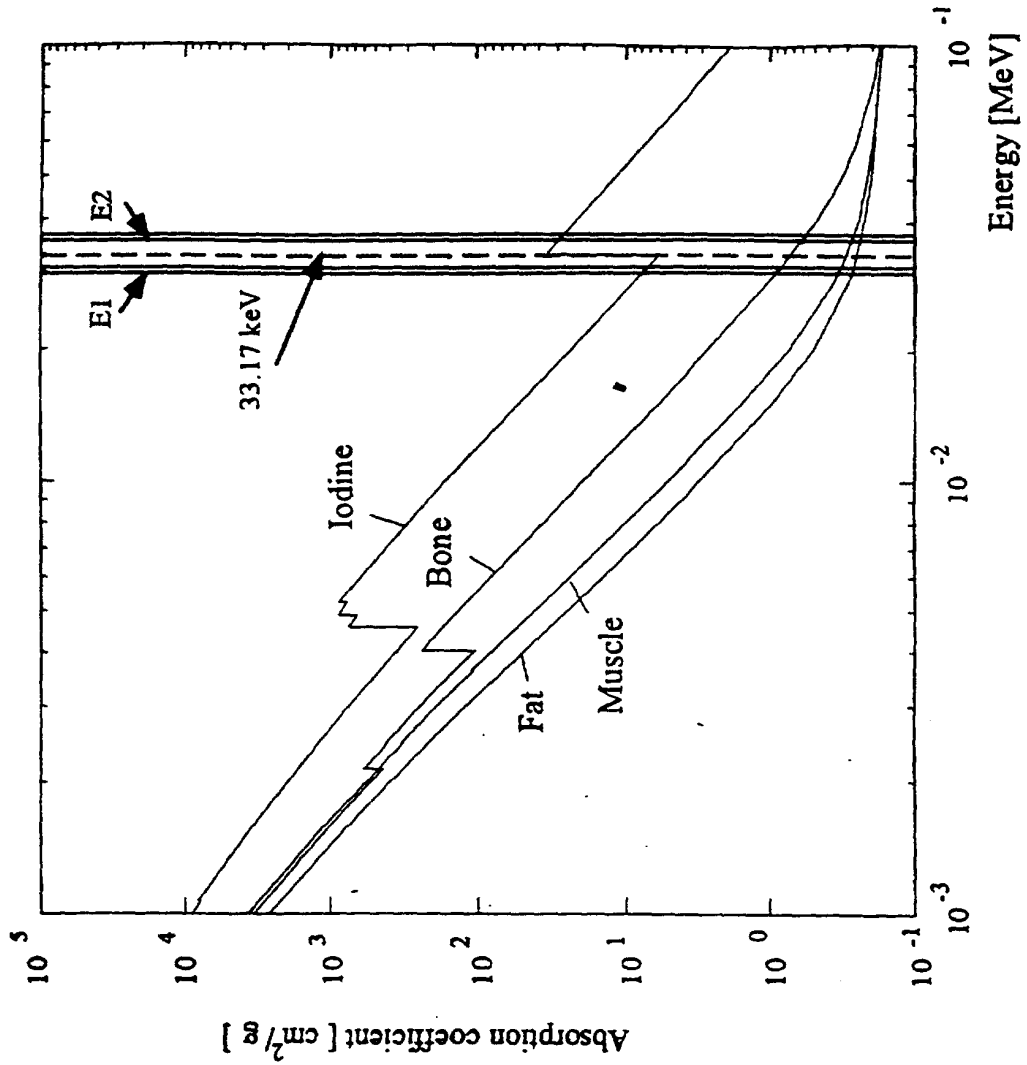


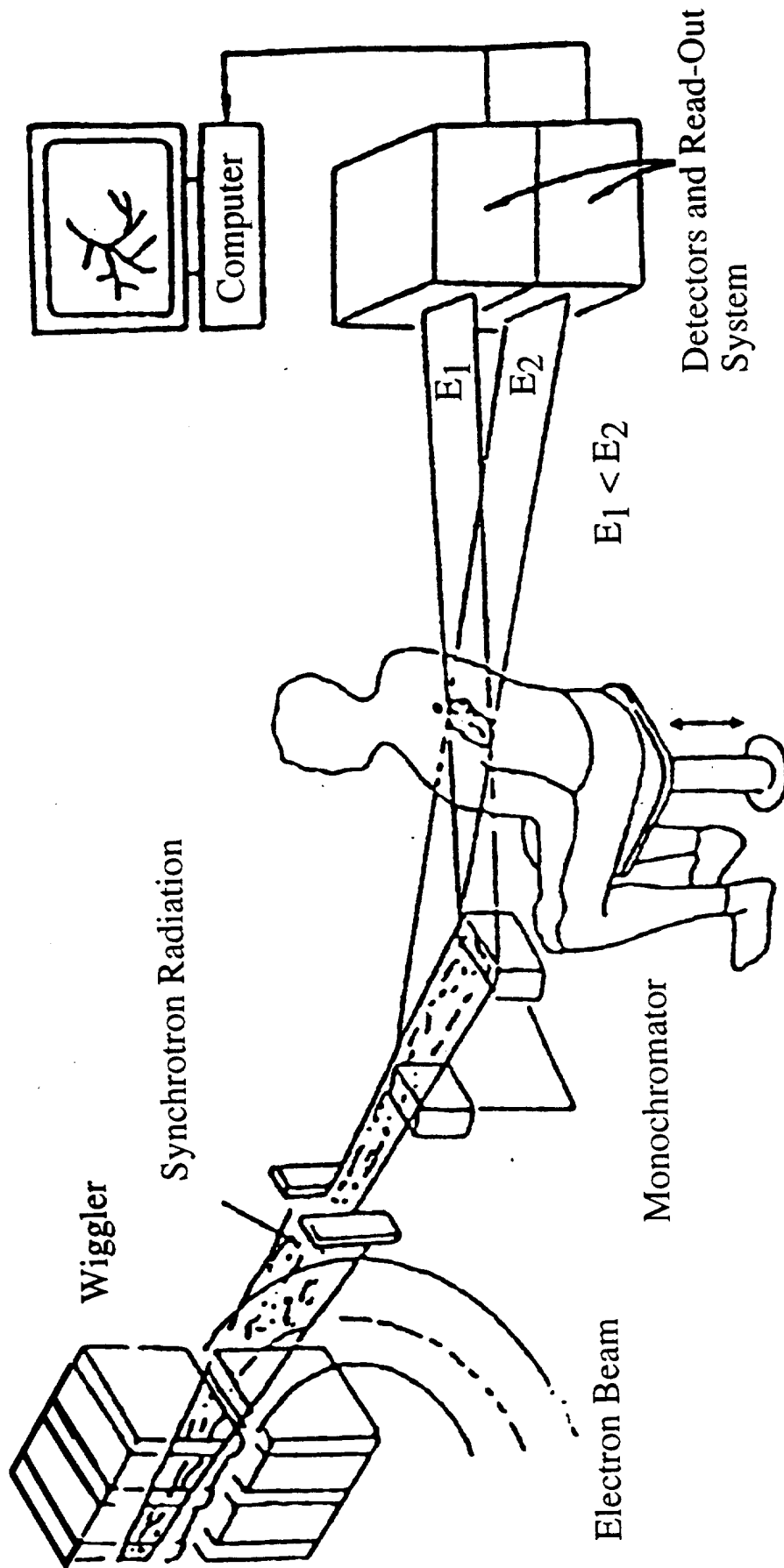
Fig. 3 - Exploded view of the multi-channel ion chamber pair.

DIGITAL SUBTRACTION CORONARY ANGIOGRAPHY



NON-INVASIVE CORONARY ANGIOGRAPHY WITH SYNCHROTRON RADIATION

DESY (Hamburg)



H.J. Besh et al, Phys. Medica IX (1993) 171
W.-R. Dix et al, DESY SR 94-01

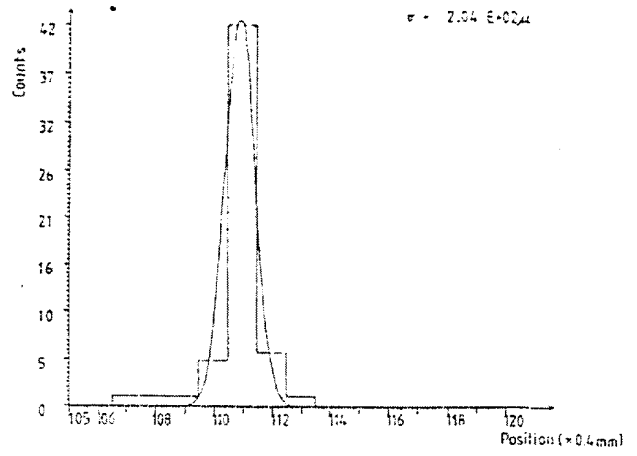


Fig. 5 - Resolution Curve of the Detector.



Fig. 6 - Radiography of the Heart of a Pig.

112

A. Thompson et al
"A 1200 Element Si(Li) Detector for Synchrotron-Based
Coronary Angiography", *Physica Medica* 1X(1993) 165-

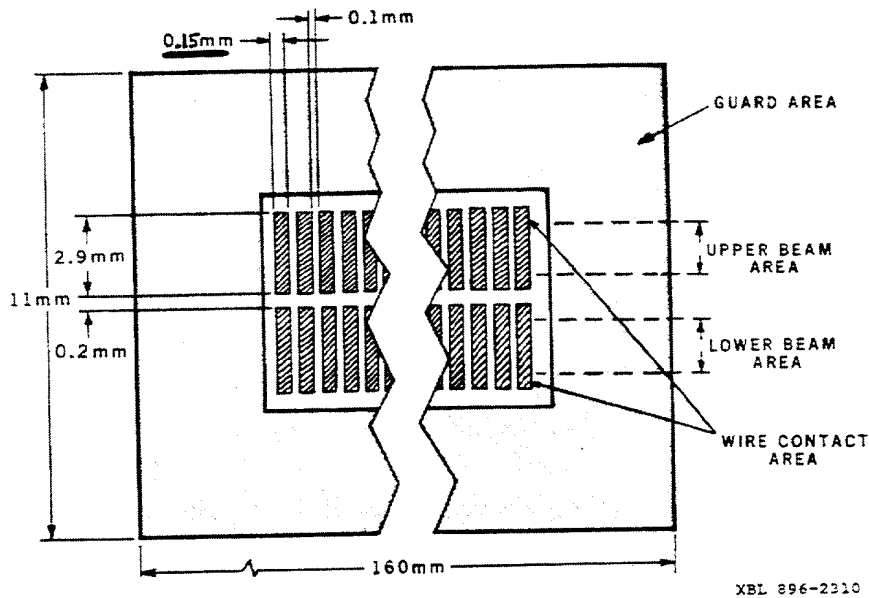


Fig. 2 - Geometry of multi-element detector.

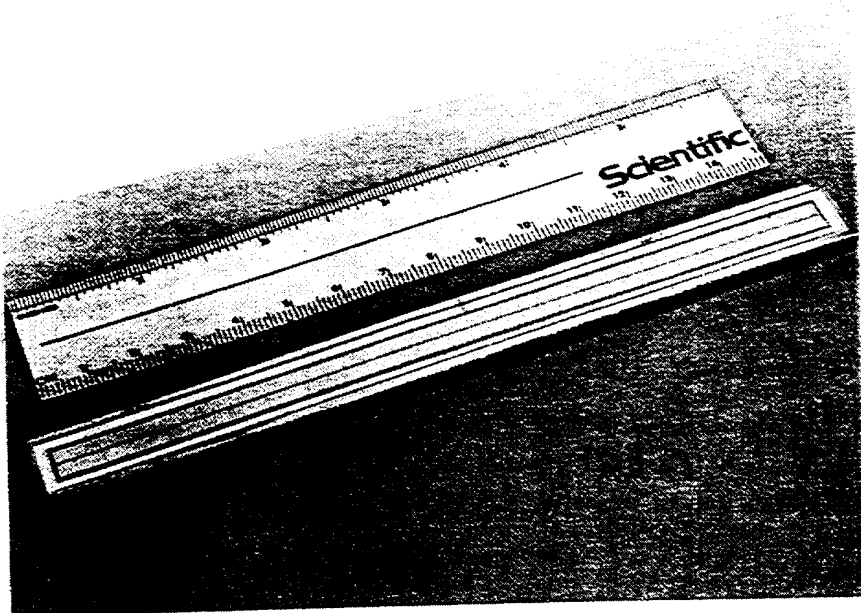
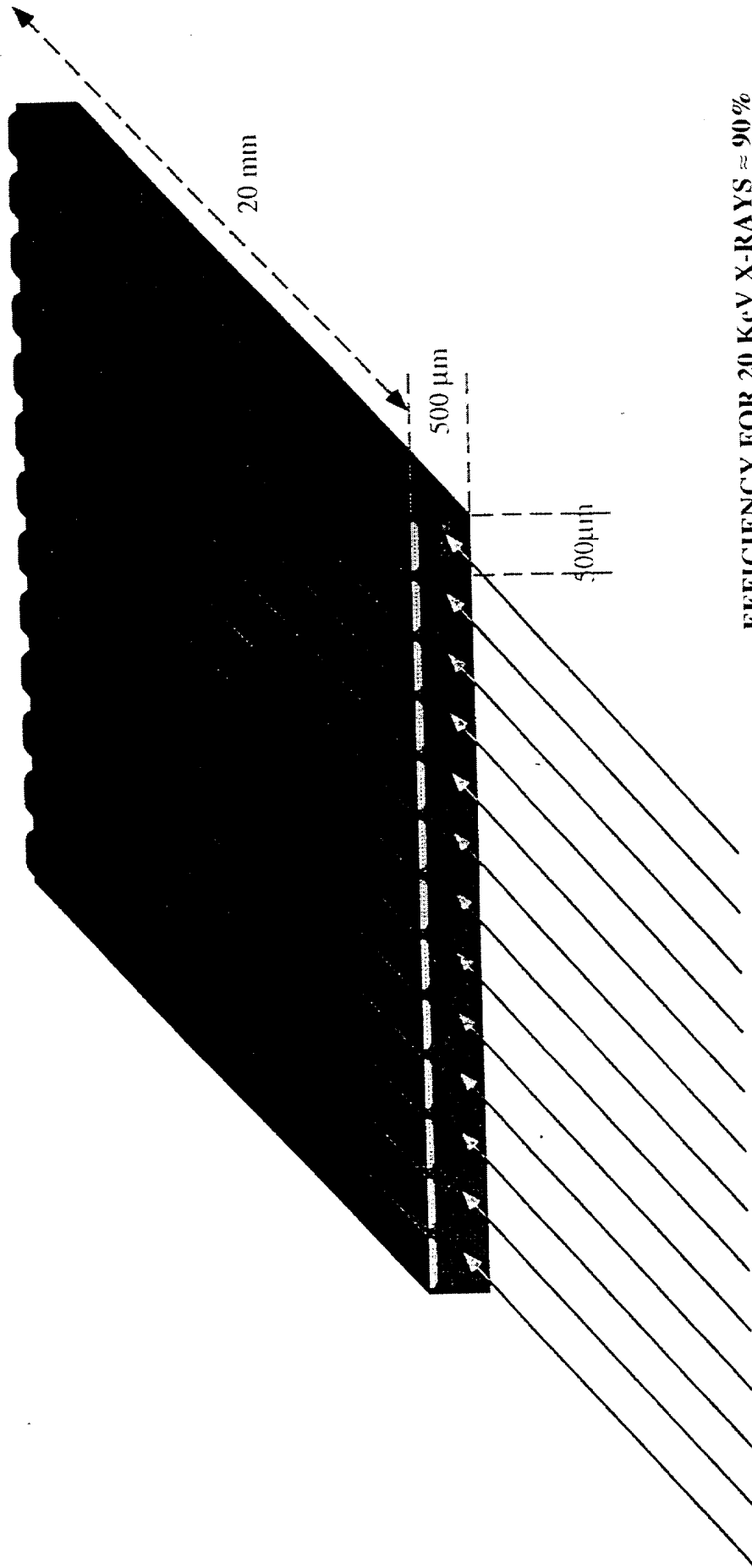


Fig. 3 - Photograph of 1200 element detector before installation in the cryostat.



Fig. 7 – Image of patient taken with the 600 element detector system.

SILICON X-RAY DETECTOR FOR DIGITAL RADIOGRAPHY:
SYRMEP



EFFICIENCY FOR 20 KeV X-RAYS \approx 90%

X-RAYS

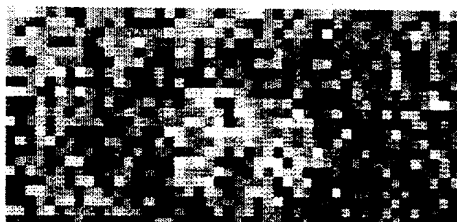
F. Arfelli et al, INFN/IC-94/09
Synchrotron Radiation Facility (ELETRA), Trieste, Italy

DIGITAL RADIOGRAPHY OF STANDARD MAMMOGRAPHY PHANTOM

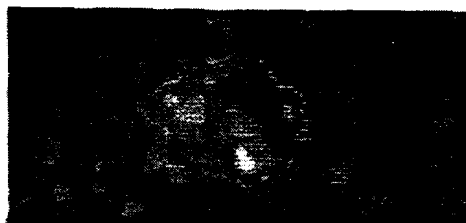
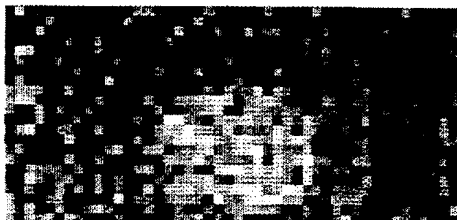
6 mm Ø. 75 µm thick aluminum disk emedded in 16 mm thick plastic

Fluence
(photons/mm²)

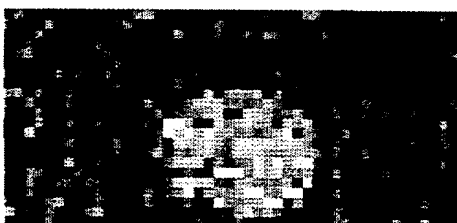
6.9 x 10³



2.2 x 10⁴



3.8 x 10⁴



7.5 x 10⁴

