FORSCHUNGSZENTRUM ROSSENDORF

WISSENSCHAFTLICH-TECHNISCHE BERICHTE

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Workshop on

X-rays from electron beams

Editor: Harald Prade

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FORSCHUNGSZENTRUM ROSSENDORF



WISSENSCHAFTLICH-TECHNISCHE BERICHTE

FZR-287

Februar 2000

Workshop on X-rays from electron beams

with special emphasis on possible developments at ELBE Transparencies of the Workshop Forschungszentrum Rossendorf, February 24 - 26, 2000

Editor: Harald Prade

Workshop on X-rays from electron beams

with special emphasis on possible developments at ELBE

Presently, at the Forschungszentrum Rossendorf (FZR) the ELBE facility - a superconducting Electron accelerator of high Brilliance and low Emittance (ELBE) with a maximum electron energy of 40 MeV and a beam current of up to 1 mA - is under construction. The electron beam of ELBE is intented to drive different facilities for producing secondary radiation of various modalities as infrared photons, quasimonochromatic X-rays, polarized bremsstrahlung and photoneutrons. One of the main research objectives at ELBE will be dealing with the development of novel non-conventional X-ray sources for radiobiological applications.

Therefore, in the first part of the workshop latest investigations in the field of X-ray sources based on the electron-solid interaction like channeling, parametric X-ray and transition radiation, the influence of acoustic waves on the X-ray production and aspects of X-ray optics as well as the possibility of Compton backscattering off the ELBE electron beam have been discussed. The second part of the workshop has mainly been devoted to radiobiological investigations with monochromatic X-rays, but also the actual status of medical imaging with monochromatic X-rays has been presented.

Responsible for the scientific program and the local organization were W. Enghardt, E. Grosse, U. Lehnert, J. Pawelke, H. Prade and W. Wagner. The work in the Workshop Office including culinary service was done by Mrs. D. Hachenberger, J. Kerber and H. Römer.

The organizers have to thank their sponsors, the German Research Community (DFG), the Saxon State Ministry for Science and Art (SMWK) as well as the Executive Board of the Forschungszentrum Rossendorf for its essential financial support, which was very important for the success of the workshop.

On behalf of the Organizing Committee,

Harald Frack



Workshop on X-rays from electron beams

Forschungszentrum Rossendorf (FZR) Institute of Nuclear and Hadron Physics

February 24 - 26, 2000 Auditorium, Building 120, FZR

Programme

Thursday, February 24

11:30 Registration and visits to ELBE (under construction)

(Chairman: H. Prade)

13:30	F. Pobell (FZR)	Welcome
14:00	N. F. Shulga (Kharkov)	Mechanism of coherent radiation by relativistic electrons
14:50	W. Wagner (FZR)	Quasi-monochromtic X-rays from ELBE
15:40	Coffee break	
16:10	H. Backe (Mainz)	X-ray research with the 855 MeV electron beam at MAMI
17:00	P. Rullhusen (Geel)	Radiation produced by electrons interacting with flat and modulated surfaces
17:50	I. G. Grigorieva (Moscow)	Highly oriented pyrolytic graphite for X-ray bending and focusing
Friday	y, February 25	(Chairman: A P Potulitsin)
		(Chanman, 1X, 1, 1 Otymosh)
09:00	A. R. Mkrtchyan (Yerevan)	Investigation of channeling radiation under the influence of acoustic waves
09:25	A. H. Mkrtchyan (Yerevan)	Investigation of PXR under the influence of acoustic waves
09:50	H. W. Barz (FZR)	Compton backscattering of laser light off the ELBE electron beam
10:40	Coffee break	
11:10	M. A. Piestrup (Stanford)	Compound refractive lenses for X-ray sources

12:00	H. Genz (Darmstadt)	Channeling radiation as a probe in the solid state plasma accelerator regime
13:00	Lunch	
Friday	y, February 25	(Chairman: W. Enghardt)
14:00	D. Frankenberg (Göttingen)	Relative biological effectiveness of X-rays for mammography
14:50	D. Harder (Göttingen)	Chromosome aberrations by soft and ultrasoft X-rays: Microdosimetric and radiobiological aspects
15:40	Coffee break	
16:10	M. Hill (Oxfordshire)	Radiobiological investigations with mono- chromatic soft X-rays
17:00	B. D. Michael (Middlesex)	A focused soft X-ray microbeam for investigating the radiation responses of individual cells
17:50	W. Mondelaers (Gent)	Application of X-rays for medical purposes
18:45	Buffet	
Saturd	lay, February 26	(Chairman: E. Grosse)
09:00	K. Kobayashi (Ibaraki)	Radiation biology at the KEK Photon Factory
09:45	W. Thomlinson (Grenoble)	Synchrotron medical imaging: From amplitude to phase
10:30	Coffee break	-
10:50	S. Fiedler (Grenoble)	Current status of the coronary angiography project at ESRF
11:20	D. Hermsdorf (Dresden)	Biological experiments with low energy charged particles
11:50	A. Panteleeva (FZR)	Cell survival studies with X-rays
12:10	J. Pawelke (FZR)	A device for cell irradiation with low energy quasi-monochromatic photons at ELBE
12:30	H. Backe/D. Harder/ W. Thomlinson/W. Enghardt	Closing remarks

Lunch

Production of Quasi-Monochromatic X-Rays from Electron Beams

N. F. Shulga:

Mechanism of coherent radiation by relavistic electrons in crystals

Zey 2 256' >> Sey Rr-F. $d\mathcal{E} \sim \left(\sum_{\mathbf{g}} \frac{dq_{ii}}{q_{i}^{4}} \right) \left(\int_{\mathbf{g}} d^{2}q_{i} \quad \vec{q}_{i} \quad |\mathcal{U}_{q}|^{2} \right)$ tor high energy (E - 20) 8/1~1 - Coherent length 2881 M²W $q_{ii} \ge \delta = \frac{\omega m^2}{2 \varepsilon \varepsilon'}$ 19 et ~ ~ ~ (c Set & RT-F (Ter-Mikaelian 1952) Coherent length 1338 m2w $u(r) = \frac{2e^{2}}{r}e^{-r/R}$ mc > q1 ert > t/k Sey 4. er ~! Inthilly . Haz ~~ ~~ R 9" ett ~ 5 2 abore-barrier) radiation (Aphiezer etal, Chenneling) (Kiemakher, 1946) 1970 Akhierer, P. Fomin, N. Shul ya (322) Const. Field approx Tickhomirovi 1982 (synchrotron approx) Shulya, 1980. Buier etal, 1983. I'm ball, Cue, 1983 off. Ter-Miraelian (look) & discort Ferretti cb at regular and chaptic Morokhouskii etal (1922) Bermann etal (1970, 1922) dyna mical cheers (1986,) 1933 Bethen Heitler (d 6 AH) 5 --- } } 6261 - 5861 motion (1992,) experiments überall 0961 19.33 10561 505533080 szozska หา e+ e-Pemeranchuk (1953) experiment 1994. 1928 Migdal D 3 SOV amon ph ous 47 Ş Landay media SLAC



Akhiezer, Shurrya. Sov. Phys. Usp. 30 (1983) 192







Fig.3.7. Bremsstrahlung intensity spectrum in a diamond crystal measured by the Frascati group (f_{0} = 1 GeV, 0 = 4.6 ±0.1 mrad, a = 0⁰). The *solid* arrow is the calculated spectrum



et, e - dependence of CB (1969 - 1972)Theory · A. Akhiezer, P. Fomin, N. Shuliga (JETP Lett. 1970) $d\mathcal{G}_{coh} = d\mathcal{G}_{coh}^{(Born)} \cdot \left(1 + \frac{e}{1e!} \ge \frac{R}{\alpha} \frac{2e^2}{\varepsilon \alpha \theta^2} + \cdots\right)$ $2\frac{1}{2}\frac{R}{\alpha}\frac{2e^{2}}{\epsilon\alpha\beta^{2}}\sim\frac{--9c_{h}}{R^{2}}$ 111

. R. Walker, B. Bermann et al. (PRL. 1970; Phys. Rev. A 11, 1972)

. V.L. Morokharski, G. Kovalenka et al. (JETP Lett. 1972) CHANNELING OF POSITRONS OF 1 GeV ENERGY

V.L. Morokhovskii, G.D. Kovalenko, I.A. Grishaev, A.N. Fisun, V.I. Kasilov, B.I. Shramenko, and A.N. Krinitsyn
Physico-technical Institute of the Ukrainian Academy of Sciences
Submitted 30 June 1972
ZhETF Pis. Red. <u>16</u>, No. 3, 162 - 164 (5 August 1972)



Fig. 1. Bremsstrahlung energy flux vs. angle between the direction of the beam and the silicon [110] crystal axis: a - positrons, b - electrons.

2

CHANNELING AND COMERENT BREMSSTRAHLUNG EFFECTS FOR RELATIVISTIC POSITRONS AND ELECTRONS

R. L. Waiker Department of Applied Science, University of California, Davis, California \$5516

and

B. L. Berman, R. C. Der, T. M. Kavanagh, and J. M. Khaa Lawrence Radiation Laboratory, University of California, Livermore, California 94550 (Received 10 Decomber 1989; revised manuscript received 27 April 1970)



FIG. 2. (a) Foward (s0.1 deg) bremsstrahlung detected by the fonizzion chamber, for 28-MeV positrons facidant on 8.2 -min allicon erystal. J et at magin between the barm axis and the (100 crystallographic direction. 8) Similar dita, bit with a j-is. Med absorber between the crystal and the detector. Ourses absorber between the crystal and the detector. Ourses

FIG. 3. (a) Forward (a0.1 dag) bremastrahlung detexted by the fontaxion-chamber, for 28-MeV electrons incident on a 50-mm allicon crystal. J fis the-angle between the barm axis and the (13) crystallographic direction, (b) Similar disk both with a j-in. Sec.inbacobar between the crystal and the descior. Curves are normalized to equal dir-kinami values:



FIG. 1. Somethering of 20-MeV (a) positroom and (b) electrone into an angular range 0, to 1,0 deg with respect to the beam. Duta ar into the start sition crystal, and 0 is the angle between the (11) crystallotraphic direction and the beam tait. Qurves are mormalized to equal off-channel values. Our best scatiering dats, for the (11) direction of a 19-m a fillion crystal, aboved a channeling minimum that was $\sim \frac{1}{2}$



the Burn theory of Coherent radiation. But the prediction of the Born theory CB were in [[] good agreement with experiments when



 $U(\vec{r}) \rightarrow U(x_1y) = \frac{1}{L_2} \int_{-\infty}^{\infty} u(\vec{r} - \vec{r}_n)$ B =- - PU(xy) Fig. 4. Motion of a fast positively charged particle (a) in the field of a single atom string and (b) in the periodic field of atom strings of a diamond I P P = would P2 -> P1 J. Lindhurd (1965) $\frac{d\vec{p}}{dt} = -\vec{v} U(\vec{r})$ $\frac{d\vec{p}}{dt} = -p U(x,y)$ ŝ 0 0 14 5 0 0 0 ional to the (100) axis. 0 0 0 0 <u>9</u> crystal in 1 426 10-2 rail 4-01 trajectory is close to rectilinear N. Shulga JETP 1:24. 1980, v:32, Euronal, quasi-classical, classical approximation $\approx dG_{coh} \cdot \left(1 + O\left(\frac{\psi^2}{\psi^2}, r.9\right)\right)$ abore - Barrier (intinite) motion particles in the tield 0.166. clipole approximation. channeling (finite) or velocity changes in jump apprexim. of atomic strings. Synchretron approximation Π Λ Λ $l_c \gg \frac{R}{\psi}$ $l_c \ll R$ 44040 RZez 2. 89 221 dG (WKB) 1. 4 >> 4c チベチ。 89->1

. Random string approx decon -... Z) dq dq ... Fandom Überall (1956) Phys. Rev. 1. 103. Akhierer et al. Sov. Phys. Usp. (1982); Phys. Rep. 1921 ge=0 . Dynamical chaos Vamer E=1Gev, S'; , (100> , 4= 2.10-3 rad. Semiclassical and classical CB 9/,00 00 M. Ter-Mikaelian (1952) SETPUSS. dGcoh { rtt)} H. UBErall (1960) Z. Naturforth. A 19. 02 to , , pariodic .Regular motion . Вогп арргохіт. $d\mathcal{E}_{abh} \rightarrow \cdots \geq \cdots$ 8 °9/,90 for 4 << 1 only $g_{z} = 0$ l give the major contribution in doc м. Тст - Мікиєвуни (1469) 4. I in merini (1968) 20 11 20 CON Phase USA 30/1982/192 A. Akhieser, N. Shuliya U. Timm (1921) Continuous string potential in the theory $\beta_{\parallel} \approx \beta_{z} + \psi(\beta_{x} \cos \alpha + \beta_{y} \sin \alpha).$ $d\overline{b_c} \sim \frac{dw}{w} \left(\sum_{a=a}^{\infty} \left| \frac{g_1^a}{g_1^a} \right| w_g \right|^2 \left(1 + \cdots \right)$ string potential. ! of coherent radiation. Reviews : $U(x,y) = \frac{1}{2} \int d^2 \sum u(r-r_n)$ Continuous σ

V (X,Y) - two-dimentional periodic field. Character of the particle motion in crystal. The character of motion is determined by Let us consider the motion in continuous $P_{z} >> P_{L}$. The motion can be regular and chartic. a number of integrals of motion. A.E. Akhiezer, N.F. Shuliya, V.E. Truten' . Dynamical chaos phenomenon Dynamicul chaos phenomenon ... Regular motion $\frac{i}{\delta} = -\frac{1}{E} \frac{\partial}{\partial g} U(\bar{g})$ string potential. × 4= 104° -10 チョンプ チョナ

oh 010 1990 V. 203. A.209 - 343.







Results :

character of motion (regular or chaotic) Being appreciably clependent on a) initial conditions, b) charge sign, c) relation between 4 and 4c (E_L and U_b)

Measurement of the linear polarization of channeling radiation

in silicon and diamond

M. Rzepka, G. Buschhorn, E. Diedrich, R. Kotthaus, W. Kufner, W. Rößl, K. H. Schmidt Maz-Planck-Institut für Physik (Werner-Heisenberg-Institut), 80805 München, Germany

P. Hoffmann-Stascheck, H. Genz, U. Nething, A. Richter Institut für Kernphysik, Technische Hochschule Darmetadt, 61289 Darmstadt, Germany

J. P. F. Sellschop

University of the Witwatersrand, 2050 Johannesburg, South Africa



FIG. 9. a) Azimuthal distributions of the mitagent yield of $\Theta = 80^\circ$ Compton scattered axial channeling radiation produced with the mixon (100) axis exactly algoned (drichs) and for two different tilt angles (0.05° and 0.18°) in the (119) plane. The curve theorek for of cor? 9° distributions to the data. b) Energy dependence of the Ranar pointhation of axial channeling radiation for tha (100) axis exactly aligned (drichs) and tilted by 0.05° and 0.18°.



Si Ψ =2.42 Ψ c to <100> aligned to (100) E=32MeV







 $\frac{diE}{diu} = 2\pi e^{i} \omega \left\{ \frac{dq}{5} \left[1 - 2\frac{\delta}{4} \left(1 - \frac{\delta}{4} \right) \right] \left(|W_k|^2 + |W_y|^2 \right),$ 1 2 Tier 5 91 52 (|Wx| 2 - |Wy| 2). dE/dw 8 92 92 (|Wx| 2 - |Wy| 2). • all ω $\left(\frac{2R}{\sqrt{c}} + \frac{3d^{4}}{\omega}\right)$ • polarization and spectrum · averaged on different trajectories • test

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 $\widetilde{W}_{x,y}(q) = \int_{-\infty}^{\infty} dt \quad \widetilde{V}_{L,x,y} \quad e^{iqt}.$ Ali ~ led = 2 2 20 Kall= vatit 1

+ Zath Čine igth



Fig. 1. Coherent radiation spectrum of 150 GeV electrons in a diamond crystal at $\psi = 10^{-3}$ rad and sin $\alpha = 0.21$ (a), sin $\alpha = 0.2$ (b), sin $\alpha = 0.195$ (c), sin $\alpha = 0.185$ (d), $(\sigma_0 = Z^2 e^{\delta}/m^2)$.

I've egges ag . B.

 $\beta_{ll} = \beta_{z} + \psi(\beta_{y} \cos \alpha + \beta_{x} \sin \alpha) = \delta_{z} = \frac{\omega m^{2}}{2 \varepsilon(\varepsilon - \alpha)}.$

1. $3_{z}=0$. 2. $3_{z}=0$, $3_{y} \neq 0$. 3. $3_{z}=3_{y}=0$, $3_{x}\neq 0$, $d \leq 1$. 4. large varbue of the 131. $3_{z}=0$, $3_{y}=-\frac{27}{6}$, $3_{x}=5,\frac{25}{6}$, $d \leq \frac{1}{2} + \beta$.

λo ų) ~ (4/3 gx $\left(\frac{1}{5}+\beta\right)\cdot 5\frac{2\hat{n}}{\alpha}$ <u>30</u> ॥ उच्च 의 비원 기원

(022) (011) × P1= P4





Fig. 1. Coherent radiation spectrum of 150 GeV electrons in a diamond crystal at $\psi = 2 \times 10^{-3}$ rad and $\alpha = 0.199$. Solid line – simulations results; dashed line – calculations by Eq. (1); $\sigma_0 = 2^2 e^{0} m^{-2}$.



Fig. 2. Polarization of coherent radiation of 150 GeV electrons in a diamond crystal at $\psi = 2 \times 10^{-3}$ rad and $\alpha = 0.199$.



Fig. 3. Trajectory of 150 GeV electrons in a diamond crystal in the plane orthogonal to the < 001 > axis.









Si Ψ =80 Ψ c to <100> α =199mrad to (110) E=1GeV without thermal vibrations



























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 $\int -\frac{d}{g} + \frac{d}{h}, \quad g \leq k$ S> k 0 $U(\hat{s}) = \langle U(\hat{s}) \rangle$ (ያ)ታ



 $\frac{close}{d\varphi} = L\varphi \left| \frac{d\varphi}{d\theta} \right|$

 $\xi_{1}^{(WKB)} = \xi_{1}^{MS} \frac{\rho_{2}^{2} - 2\epsilon U(s) - e^{2}}{2s} - \xi_{1}^{NS} \frac{\rho_{2}^{2} - e^{2}}{2s}$ $\frac{d\mathcal{E}_{q}}{d\varphi} = \frac{L4}{2\pi\rho_{L}} \left| \sum_{\ell=1}^{\infty} e^{i\ell\varphi} \left(e^{2i\xi_{\ell-1}} \right) \right|$ Quantum theory

414 S 41126. " " "

&= 3x=0, gy to ocd <<1 two g important for CB · splitting of CB maxima gz=0, gx≠0, d=0 $\beta_{ll} = \beta_{2} + \psi \left(g_{x} \cos_{3} \alpha + \beta_{y} \sin_{n} \alpha \right) \ge \delta = \frac{\omega_{1} m^{2}}{2 \varepsilon (\xi - \omega)}$ · simulation of CB · dynamical chaos gz≠0 different E. 67 Mechanismas of CB · quantum effects at low E. · CB and channeling road. CB for real traject. · fine structure of cb CB type B row effect point effect C 90 120 150 4 = 0,8 4 80 E = 10 mer, Si, <100> 0.2 0.3 0.4 0.5 4/4 8 90 120 150 000 0.0 2LR4 201 0.8 0.4 0.6 0.2 4= 0,24c 30 Let de = F

. Ch and parametric tad

. CB and synchrotron rad

. LPM - effect for CB

W. Wagner:

Quasi-monochromatic X-rays from ELBE

Quasi- monochromatic X-Rays from the ELBE Radiation Source

W. Wagner

W. Enghardt A. Panteleeva U. Lehnert J. Pawelke B. Naumann H. Prade W. Neubert

Collaboration partners

Technical University Darmstadt Johannes-Gutenberg-University Mainz ROBL ESRF Grenoble, France Institute of Applied Problems of Physics, Yerevan, Armenia Yerevan Physics Institute, Armenia

"Workshop on X-rays from electron beams" Rossendorf, February 24 - 26, 2000





A new set the ray we say lighting that the fight [14] and it the water, at the 17/19

ELBE

is a new superconducting El estror asselerator of high Brillance and low Emitiance developed and presently under construction in Possendorf near Oresden

This facility will deliver secondary hears, of different kinds

High-brilliant witeleed radiation coming from different free-electron liasors កើត្តិនិទ

- Intensive bremsstrahlung × rays for nuclear spectroscopy
- Cuasi-monochromatic X-rays
- $\widetilde{\mathbb{C}}$. Neutrons via ($_{3,n}$) in the 0-1 \star 10 MeV range (106 (s cm-
- Positrons via e*-e-pair production (10* /s cm/)

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Floorplan of the new building for ELBE

RSCHUNGSZENTRUM ROSSENDORF



institut für Kein- und Hadronenphysik

Superconducting Acceleration Structure



The acceleration structure consists of two nine-cell RFcavities made of Nb.

The cavities have been developed at DESY in Hamburg for the TESLA (Tera Electron Volt Superconducting Linear Accelerator) test facility.

First successful tests at DESY showed that acceleration gradients up to about 20 $\ensuremath{\mathsf{MV/m}}$ can be achieved.

The ELBE design is based on the rather conservative value of 10 MV/m.

Technical parameters

Operation temperature	
Operation frequency	
Resonator quality	

1.8 K 1.3 GHz 10¹⁰

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First electron injector for ELBE

- FEL high bunch charge short bunchlength (ps) lower micropulse repetition rate due to HF power two bunchers for injection (260 MHz and 1.3 GHz)
- X-ray source low-emittance beam small beam divergence moderate bunch charge large micropulse repetition rate (cw - beam)

In the first stage of ELBE (20 MeV) an injector based on a thermionic triode gun, as used for the FEL at HEPL Stanford, will be available.

This injector was optimized for the formation of a low -emittance beam with a maximum average current of 0.1 mA for radiation physics.

Furthermore, design work has been initiated for a laser-driven superconducting RF-gun of high brilliance as needed to perform Compton backscattering studies.

้วินก	thermion	ic triode gun	s.c. RF gun
Values	design	measured	design
Micropulse repetition rate	11.8	(13) MHz	1.3 GHz / 650 MHz
Maximum bunch charge / pC	85 (77) / 8	3.5	85 (1) / 1000
Maximum average current / mA	1/ 0.1		100 / 650
Transverse emittance (rms) / a mm mrad	7/1.2	9.4 / 5.4	0.77 (0.06) / 1.25
Norm. trans. emittance (rms) ~ mm mrad (20 MeV)	4 / 0.75	10.9	
Bunch lenght (90 %) / ps	5.1	2.9	
Energy width (rms) / keV	33	64	
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FORSCHUNGSZENTRUM ROS Institut für Kern- und Hadronenohvsik Non-conventional sources of quasi-monochromatic X-rays

Channeling radiation



Characteristics of X-ray sources

Photon number

[MeV / s]	[bh / s]	[ph / s 0.1% BW]	[ph / s sr]	[ph / s mm²]	[ph / mm²]	
$I = P_R = dE / dt = dN_x \cdot h(0) / dt$	$\phi = dN_x / dt$	∳ _s = d²N _× / dt (Δ hω/ hω)	$d\phi / d\Omega = d^2 N_x / dt d\Omega$	$R = d^2 N_x / dt dA$	$F = dN_{*}/dA$	
intensity	flux	spectral flux	flux density	radiance	fluence	

Source quality

- divergence (focussing)- spatial resolution

s mrad ² 0.1% BW]	ε _x ε _y = φ _s / 2π σ _r σ _n
_۷ . [ph /	_σ , σ _γ , = φ _s / 4π [±] ι
S = φ _s / 2πα, σ	B = φ _s / 4π' σ, ο
brightness	brilliance

[ph / s mm² mrad² 0.1% BW] $\mathbf{B} = \phi_{\mathrm{s}} / 2\pi \varepsilon_{\mathrm{t}}$

Ř

Radiation _I	production efficiency	
yield	$Y = d^2 N_x / dN_e d\Omega$	[ph / sr per e [.]]
efficiency	n1 = P _R / P _{beam}	(W _R / W _{beam}) [%]
spec. brillianc	ce B _s = B e / i E _s = B e / mc² iγ roc /	
Chromatic	ity Ibn / H	
Tunability		

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X-ray sources with a continuous spectrum

Bremsstrahlung (BS) and characteristic X-rays (CX) (medium : X-ray tubes)

 $B_{\tau} = 10^{6-9}$ ph / s mm² mrad² 0.1%BW i = (10⁻² - 1) A; 10-100 kV

Synchrotron radiation (SR, WR, UR) (dipol magnets, wiggler, undulator ; electron or positron beams)

 $E_c = 3 \text{ ch } \gamma^3 / 4\pi \text{ R} = 10 \text{ keV}$ $\gamma = (7-9) 10^3 \text{ E}_e = 4-5 \text{ GeV}$

 $B_s = 10^{13-15} \text{ ph/s mm}^2 \text{ mrad}^2 \text{ 0.1\%BW}$ i = 100 mA

Transition radiation (TR)

(medium boundary, foil stacks-RTR ; electron beams)

 $E_{cut} = \gamma h \omega_p / 2\pi = 10 \text{ keV}$ $\gamma = 350$ $E_e = 150-170 \text{ MeV}$

 $B_{5 \text{ keV}} = 10^{13} \text{ ph/s mm}^2 \text{ mrad}^2 \text{ } 0.1\% \text{BW}$ i = 100 μ A; 855 MeV

Quasi-monochromatic X-ray sources

Channeling radiation (CR) (crystalline medium : electron beams)

$$E_{v} = 30 \text{ keV}$$
 $\gamma = 40 \quad E_{e} = 20 \text{ MeV}$ $i = 100 \text{ }\mu\text{A}$

 $B_{CR} = 3 \ 10^{6} \text{ ph/s mm}^2 \text{ mrad}^2 \ 0.1\% \text{BW} \quad (B_{CR}^{5\% \text{BW}} = 10^{8})$

Parametric X-rays (PXR)

(crystalline medium : electron beams)

 $B_{CR} = 10^{5} \text{ ph/s mm}^2 \text{ mrad}^2 0.1\% BW$ low background

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(-) (90%) = 0.24 mrad

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-0.020 0.000 × [cm]

-0.5

രം = 0.12 mrad

emittance : B 20 MeV

 $\varepsilon_{\rm f}$ = 1.4 π mm mrad

σ, = 1mm

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Lorentz - transformed dipol pattern

Photon frequency







Diamond **Properties** cubic surface-centered <u>ः</u> lattice with base = 2dense package atomic distance = 1.54 Å **Z** = 6 (bremsstrahlung) 6 • density $\rho = 3.51 \text{ g/cm}^2$ • $T_s = 3540$ °C at norm. cond. S. $\bullet_{\rm D} = 1860 \ {}^{\circ}{\rm K}$ metastable ¹²C configuration high heat conductivity









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Occupation probability





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Basic conditions

CR data estimated

- ⊔ E_e = 20 MeV
- ⊔ ΔΕ/Ε < 5 · 10 ⁻³ ⊔ i_e = 100 μΑ
- ⊔ ε_n ≈ 1 π mm mrad
- u diamond d = 80 µm
 - planes {110}
- $\Psi_{\rm cr} = 1.8 \text{ mrad}$ transition 1 - 0 -7
- $\Box \quad d\Phi/d\Omega = 3.8 \cdot 10^{14} \text{ ph/sr s}$ = 0.61 ph / sr e⁻ = 29.36 keV = 10 % Υ₁₋₀ ے 1-0 ل BW
- $_$ N $_{\rm 1/3V}\text{=}$ 8.2 \cdot 10 10 ph/s



Angiographie mit Channelingstrahlung

Estimation with respect to DSA

Parameter	for $E_k(I)$	for $E_k(Gd)$
E _x / keV Electron energy E _e / MeV	33.17 21.5	50.24 27.7
Yield Y / ph / e [.] sr	0.73	1.3
Flux density $d\phi/d\Omega$ / ph/srs	4.55 x 10 ¹⁴	8.2 x 10 ¹⁴
θ _{5%} / mrad ΔΩ _{5%} / sr	5.3 8.9 x 10 ⁻⁵	4.15 5.4 x 10 ⁻⁵
Flux 🖕 _{5%} / ph / s	4.0 x 10 ¹⁰	4.4 x 10 ¹⁰
Distance d / m Area A / mm ² (D / mm)	2 355 (21.3)	2.5 338 (20.8)
Radiance / ph / mm ² s	1.1 x 10 ⁸	1.3 x 10 ⁸
Fluence / ph / pixel (200 ms)	5.7 x 10 ⁷	6.6 x 10 ⁶
Required fluence / ph / pixel	1.8 x 10 ⁷	6.0 x 10 ⁶
Heart A = 3850 mm ² at d / m	6.7	8.4
Fluence / ph / pixel (200 ms)	5.1 x 10 ⁶	5.8 x 10 ⁵
factors: current (2), thickness (2) monochromator (0.5)	(4)	(10)
W Wagner <i>u</i> fz-rossendorf.de	and the second	Postfach 51 01 19 D - 01314 Dresden

Comparison with DSA at NIKOS

(e⁺ storage ring DORIS III at DESY Hamburg)

Parameter	for E _k (I)			
E _x / keV Electron energy E _e / GeV	33.17 4.5			
Heart at NIKOS: (simultaneous scanning Radiance / ph / mm ² s	at two energies) 2.7 x 10 ¹¹			
Fluence / ph / pixel	6.8 x 10 ⁷	(3.8)		
Required fluence / ph / pixel	1.8 x 10 ⁷			
Heart at ELBE: (200 ms shot at one ene Fluence / ph / pixel (200 ms) factors: current 1 mA ???	ergy) 5.1 x 10 ⁶ 10	(13)		
What agent concentration and what minimum irradiation area are acceptable for medics ???				
What current can principally be operated ???				
What image processing can provide ???				

W Wagner a Iz-rossendorf.de





Theory predicts: Deflected intensity up to nearly 100 % !











Quasi-monochromatic X-ray beams

Reduction of bremsstrahlung background

Bragg reflection :





thick mosaic crystal

Intensity loss about 50 %

Dynamical Laue diffraction :

temperature (T) gradient
 acoustic field





10

Simulation of bremsstrahlung (W. Neubert)



Photons per 3* 10⁶ electrons

10,







<u>Summary</u>

1. Intense tunable non-conventional X-ray sources can be obtained at the electron beam of ELBE using

	E _x / keV	
·	0 50	100
(transition radiation)	1. za za za za za za za zamena go	• • •
	•	
PXR	: 	
channeling radiation		

- **2.** Bremsstrahlung background can be reduced by BRAGG reflection or dynamical Laue diffraction applying ultrasound.
- **3.** Application of DSA would need maximum beam current (1 mA), but not continuously (makropulses), and image processing.
- 4. First application of CR: cell irradiation (J. Pawelke).
- 5. New method of structure analysis with PXR (A.H. Mkrtchyan).
- 6. Stimulation of CR by ultrasound (A.R. Mkrtchyan).

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H. Backe:

Selected topics of X-ray research at MAMI

Selected Topics of X-Ray Research at MAMI

(H. Backe, Workshop on X rays from electron beams, February 24-26, 2000)

- 1. Introduction
- 2. Novel Interferometer with two Spatially Separated, Phase Correlated X-Ray Sources
- 3. Investigation of Parametric X Radiation
- 4. Transition Radiation as a Hard X-Ray Source
- 5. Conclusion



Processes



ALL STREET, ST

The Complex Index of Refraction



 $\frac{1}{c} = \frac{1}{c} = \frac{1}$



Motivation - Interferometer



Novel Interferometer with two Spatially Separated, Phase Correlated X-Ray Sources



Soft X-Ray Interferometer with Undulator Radiation

Martin Contraction of the local division of



Basic Principle of the Interferometer



Oscillations





Development of a Hard X-Ray Interferometer with Transition Radiation

Transition Radiation



single interface intensity:

$$I_0 = \frac{d^2 N_0}{(d\hbar\omega/\hbar\omega) d\Omega} = \frac{\alpha \theta^2 \omega^2}{16 \pi^2 v^2} (Z_1 - Z_2)^2$$

formation length:

$$Z_{i} = \frac{4c}{\omega} (\gamma^{-2} + \theta^{2} + \omega_{p}^{2}/\omega^{2})^{-1}$$

plasma frequency $\Theta_p^2 = 4\pi t_e c^2 n_e Z$

atomic density n_a

classical electron radius $r_e = 2.818 \text{ fm}$



Transition Rackation

from single foil:







 $\Delta'(\theta,d) = 1/2 (\gamma^{-2} + \theta^2) (d - t_2) \implies d = 0.01 \text{ mm} ..10 \text{ mm}$

absolute measurement of foil distance d necessary

Experimental Set-up

. :



CALCULATION OF THE OWNER OWNER OF THE OWNER OWNER



 $n(\omega) = 1 - \delta(\omega) - i\beta(\omega)$ dispersion \Rightarrow phase shift absorption => attenuation

nickel K-edge





Fit of two dimensional TR Distribution 10 μ m Be, 2 μ m Ni, $d = 668 \mu$ m, $\hbar\omega = 9925 \text{ eV}$ Measurement



fits of simulations at fixed θ and fixed $\hbar\omega\text{=}9975~\text{eV}$



Parametric X-Ray Radiation



Feranchuk-Ivashin Model



Theoretical Angular Distribution

(I.D Feranchuk & A.V. Ivashin: J.Physique, 46 (1985)1981)

Si (111),
$$\theta_B = 22.5^{\circ}$$

 $\theta_{ph} = (1/\gamma^2 + |\chi_0|)^{1/2}$, $|\chi_0| \simeq \left(\frac{\omega_p}{\omega}\right)^2$, $\hbar\omega_p = 31\text{eV}$
 $\gamma = 1673$



Investigation of the Production Mechanism of Parametric X-ray Radiation

K.-H. Brenzinger et al., Z. Phys. A 358 (1997) 107



How Narrow is the Line Width of Parametric X-ray Radiation

K.-H. Brenzinger et al., Phys. Rev. Lett. 79 (1997) 2462





 $\frac{\text{Line Width of Backward PXR}}{\text{for Diamond and Silicon at E = 855 MeV}}$ $fr = \sqrt{\frac{1}{2} + (\frac{9}{16})^2}$ PXR $h_{12p} = 3 \text{ dev} (Si)$ $e^{-\frac{1}{2} + \frac{1}{2} - \frac{1}{2} + \frac{1}{2} - \frac{1}{2} + \frac{1}{2$

<u>Multiple Scattering (σ_{θ} space angular divergence)</u>



Backward PXR





F Ko F Ky E E



Principle of the Fast Tunable Monochromator for Digital Subtraction Imaging





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Contrast Generation



d≡(2.4 ± 0.2)µm



Contrast Generation





H. Backe, N. Clawiter, N. Elbai, H. Euteneuer, F. Hagenbuck,H. Jacobs, K.-H. Kaiser, O. Kettig, G. Kube, W. Lauth,H. Mannweiler, D. Schroff, Th. Walcher

X1-Collaboration, Institut für Kernphysik, Johannes Gutenberg – Universität Mainz

Th. Kerschner, H. Koch, H. Matthäy, M. Schütrumpf, A. Wilms, M. Zemter

> Institut für Experimentalphysik, Lehrstuhl I, Ruhr-Universität Bochum

> > L. Strüder MPI-Halbleiterlabor München

P. Holl, J. Kemmer, R. Stötter, C.v. Zanthier KETEK GmbH, Oberschleißheim
P. Rullhusen:

Radiation produced by relativistic electrons interacting with flat and modulated surfaces

Radiation produced by relativistic electrons interacting with flat and modulated surfaces

P.Rullhusen

Rossendorf, 24.2.2000

Motivation:

Transition radiation: advantage: intense (P∝i)

continuous spectrum ($\omega_c \Rightarrow \gamma \omega_p$) for single foil interference (stack of foils) \Rightarrow absorption losses

Smith-Purcell effect:

advantage:

 $\frac{\Delta\lambda}{\lambda} = \frac{\sin\theta}{(\beta^{-1} - \cos\theta)} \Delta\theta$ monochromatic

intensity $\propto \exp(-z/h_{int})$, $h_{int} = \frac{1}{2}\beta\gamma\lambda$ ($\zeta = 0$)

but:

but:











Solutions of the grating problem Shallow sinusoidal gratings (h/D < 0.14): Rayleigh method $\sum_{n=-\infty}^{\infty} E_{y_n} e^{i(xt_{x,n}+xt_{x,n})} = -E_y(x, z)$ Integral method: calculate $E_{y_n}(x, z), H_{y_n}(x, z)$ inside the grooves from $E_{y_n}(x, z), H_{y_n}(x, z_n)$ on the grating surface using Greens theorem -> system of coupled integral equations of 2nd kind : $n \cdot \nabla E_y(r_p) = \frac{1}{2}n \cdot \nabla E_y'(r_p) - P_{L}(n \cdot \nabla E_y')(n \cdot \nabla G) ds$ $H_y'(r_p) = \frac{1}{2}H_y'(r_p) - P_{L}H_y'(n \cdot \nabla G) ds$















-











I. G. Grigorieva:

Highly oriented pyrolytic graphite for X-ray bending and focusing





Structure



Block structure of commercially produced HOPG. Acoustic microscope "Elzam", f=100 MHz Scale 1000x800 microns, 125 microns under the surface (in collaboration with V.M.Levin, Institute of Chemical Phisics of RAS)

Peculiarities of HOPG monochromators

1. High integral reflectivity

002 reflection 004 reflection

 $R_i \approx 1 \ 10^{-2} rad$ $R_i \approx 1.5 \ 10^{-3} rad$

2. Wide mosaic spread

Short focus HOPG

Standard crystals	1.0 (+/-0.2) degree			
Best commercially available crystals	0.4 degree			
Best crystals available in scientific research	0.3 degree			

- Carbon 99.99% with thermoconductivity 1400 Wm/K Good thermo- and radiactive stability as the result
 - Arbitrary shape
 Large solid angle of detection (about90%)
 Wide transmission band

7. Thickness variable with a step of 20 microns









FIG.4. Parabolic HOPG crystal and the intensity distribution in the focal spot.

FIG.2. Mosaic spread of the HOPG crystal deposited on a flat mould as a function of thickness



B.Beckhott, B.Kanngiesser Physics: Department, University of Bremen D-28334 Bremen, Germany



B.Beckhoff, B.Kannglesser

FIG.5A. Shape and schematical layer orientation of the 'pure focusing HOPG-' and the Johansson type toroid



FIG.5B. Schematical sketch of experimental set-up for the measurements spatial intensity and energy distribution in focal spot.



FIG. 6 Spatial intensity distribution in the focal spot in two different intensity scales. The four squares have side lengths of respectively 2mm, 4mm, 6mm and 8mm

and Ba are achived within 300s in helium atmosphere. *Detection limits of between 1 and 7 mg/g for the elements P,S,CL,Ca,Cu,Zn *Simultaneous analysis of the elements Na- U.

st Low powered X-ray tubes with a power of 50 W as the radiation source

- a benchtop X-ray fluorescence spectrometer SPECTRO XEPOS

used in



Spherical HOPG as a polarization target

2



D-28334 Bremen, Germany b. beckhoff, p. r. annaliesser Rhysics, Department University of Bremer

M

J.Heckel

Departments of Rhysics Pr.0.330440(D-28634 Birgmen, Germany

P. Chevailiter, LPAN, Universite Pierre, et Man Curie, Paris et LURE, Universi Paris Sud, Orsay

3

Imox (Si(Li))

10⁶+

Diffusá

pics sommes (Fe,Cr,Ni)

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104-

cr Fe



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Inox (Graphite cylindrique)

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10 IteV FIG.15. The spectra of statifiess steel obtained without (a) and with the help of the dispersion filter. Filter made from a graphite cylinder of 16,2 mm of inner diameter

5. 5

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leev?

iu, r. ivijijogo, ov Institute of Geology SDIRAS, 630090 Novosibirsk, Russia

8.Beckhoff, B.Kanngiesse: Department of Physics, P.O.330440, D-28334 Bremen, Germany





FIG. 9. The view of broad-band filter made from seven stepped toroidal segments and energy dependence of its focusing gain.





FIG. 11, The scheme included primary and secondary monochromatisation by two HOPG cylinder of 10mm inner diameter (45 kV, 30 mA Molybdenum and Silver anode X-ray (ube). Yu.P.Kolmogorov Institute of Geology, 630090 Novosibirsk, Russia

Table3. The element content of ecological standards, analysed with the 'two cylinders' scheme.

Thie set-up includes:

45kV, 30 mA Molybdenum and Silver anode X-ray tube

25mm² 165 eV resolution Si(Li) detector with analogue electronics

Multichannel amplitude analyser (IBM-286 + 300 MHz Wilkinson type ADC)

Graphite-optical device consists of primary monochromator and energy band filter from pyrolitic graphite.

A set of medico-biological standards has been examined. The results are represented in Table.3.

	IAET reference samples				NIES		SU reference samples			
	A11 Milk Powder	A13 Animal Blood	H-9 Mixed Human Diet	SOIL-7 Soil	VEP-8 Vehicle Exhaust Pamiculates	PS-2 Soit	Human Hair	CBMT-01 Grass Mixture	CBMT-02 Ash of Grass Mixture	
к	17200	2500	8300	12100	11:50	6800				
Ca	12900	286	2310	163	5300	81:00			•	
TÌ	48			3000		6400	70		122	
V	0.1*			66	. 17	250			-5	
Cr	0.257*		0.15*	60	25.5	, 75	2		10	
Mn	0.377*		11.8	631		770	0.5	108	1317	
Fe	3.65	2400	33.5	25700		65300	50	200	2440	ľ
Ni	0.93	1	0.27	<u>;</u> 26	18.5	40	8.0		8	.
Cu	0.838	4.3	2.9	11	67	210	11	2.3	28	
Zn	38.9	13	27.5	104	1040	343	150	34	415	
Ga				: 10	ļ					
As	0.048*		0.088*	13.4	2.6	12	2.6	0.18	2.2	
Se	0.034*	0.24	0.11	0.4	1:3		0.15	•		
Br	14	22	7.5	7	56	17	4.1	8	98.	1
Rb	30.8	2.3	8	51	4.6	42	0.14	65	79	ļ.
Sr	5.4		3	108	89	110	9.2	25	305	
Y				21					5	
Zr	ł			185	1					
Nb				12].			
Mo	1.3		0,24	2.5	6.4				· •	
Ag					0.2		1			- -
Cď	0,526			1.3	1.1	0.82				1
Sb	1			1.7	6	2				
Ha							0.06		5	
Ph	0.27	0.18	0.16	60	219	105	1:9	13	16	
1.2		-//-]			1		

Elements with amount marked * were obtained in ash residuum.

The energy band filler from pyrolitic graphite was not used for elements with amount > 1 ppm.





FIG. 7 Spectra of Fe samples on ellipsoidal HOPG as crystalanalyser: (a)Screw of 4mm diameter energy resolution 123 eV



EXPERIMENT

X-ray source: Ti laser-produced plasmas (0.53 m/ 2.5 J/ 2.ns/ 10¹⁵ W/cm²) Hamos spectrograph, R=20 mm, orientation, detector — RAR 2492 photoilim. Dispertion D=0.02324 A/mm Spectra

spocta

Mice(III order of reflection)

Graphite (200 microns)



RESULTS

Maximum intensity: I max/I max = Graphile/ Mice = 4 - 6 Integral intensity I max Δx Δy : Graphile/ Mice = 60 Integral reflectivity: Graphile/ Mice = [120, -:300] 10⁻⁸ rad. (Gilfrich - 120; good agreement) Spectral resolution (observed): Mice $\frac{1}{2}/\Delta \lambda = 1080$ 'Graphite $\frac{1}{2}/\Delta \lambda = 400$ (line broadening) $\frac{1}{2}/\Delta \lambda = 1080$ 'Graphite $\frac{1}{2}/\Delta \lambda = 400$ (line broadening) $\frac{1}{2}/\Delta \lambda = 764$. (Land k-satellites) mosaic tg 0/50 = 50 for $50 = 0.5^{-5}$ Δy broadening $\rightarrow 0.24^{-5}$

CONCLUSIONS

1. Maximum intensity - 4-6 times

2: Mosaic focusing (observed spectral resolution/ mosaic = 480 - 764/50 = 10 - 15 hmes) :

3. Integral intensity - almost 2 orders (60 times); very perspective for fluorescence analysis!

Log Spiral HOPG Monochromator for Fluorescence XAFS

Fluorescence emitted from Cr50V50 Sample Exitation due to tuning the incident beam energy just above the Cr edge



Direct fluorescence (detected by energy dispersive detector)



The spectrum is monochromatizated with the log spiral (energy dispersive detector detecs monochromatized fluorescence)

D.M.Pease Physics Department, University of Connecticut Storrs, Connecticut

CONCLUSIONS

Short focus HOPG crystals is a X-rays optic elements of a high intensity based on unique brightness of the material and large solid angle of the accepted radiation.

They are an efficient device at a reasonable price for

- modification of the excitation beam

- filtration of characteristic radiation

- analysis of characteristic radiation in detection systems

It opens the possibility to use HOPG:

- in microprobing;

- in trace element XFA of objects with small mass or with heavy or radioactive matrix;

- in analysis of ultra thin films and coatings;

- in medical applications including irradiation of small pathological seat in human body without deterioration of the adjacent tissues.

The high efficiency of HOPG optics gives a chance to decrease the intensity and, hence, the radioactive hazard of the X-ray sources used for scientific and medical purposes.

A. R. Mkrtchyan:

Investigation of channeling radiation under the influence of acoustic waves







HF resonator.





20MeV channeled electron radiation for X-cut single quartz crystall under the influence of hypersonic waves ($\theta_g = 2500, \theta_y = 5300, \omega = 10024$ KHz, $P = 10W, M = 5 \times 10^{-5}$.)

20MeV channeled electron radiation for X-cut single quartz crystall under the influence of hypersonic waves ($\theta_g = 2500, \theta_r = 5300, \omega = 0 \text{kHz}, P = 0 \text{W}, M = 5 \times 10^5$)



Energy, Ke

)

t

20MeV channeled electron radiation for X-cut single quartz crystall under the influence of hypersonic waves ($\theta_g=2400, \theta_r=5300, \omega=0$ KHz, $P=0W, M=5 \times 10^5$)



20MeV channeled electron radiation for X-cut single quartz crystall under the influence of hypersonic waves ($\theta_g = 2500, \theta_y = 5300, \omega = 10024$ KHz, $P = 15W_{,,}M = 5 \times 10^{-5}$.)





20MeV channeled electron radiation for X-cut single quartz crystall under the influence of hypersonic waves ($\theta_g=2400, \theta_q=5300, \omega=10024$ KHz, $P=15W, M=5*10^5$)

20MeV channeled electron radiation for X-cut single quartz crystall under the influence of hypersonic waves ($\theta_g=2400, \theta_r=5300, \omega=10024$ KHz, P=10W $M=5 \times 10^5$)



A. H. Mkrtchyan:

Investigation of PXR under the influence of acoustic waves









1

C.1.



Rocking Curve For X-Cut SiO₂ Crystal, d=0.795mm Working Plane 1011



Rocking Curve For X-Cut SiO₂ Crystal, d=0.795mm Working Plane 2022











O_{Bragg} (Degree)





Contract Contract







Alpikogramma For X-Cut SiO₂ Crystall, d=810m

0



150



Alpikogramma For Z-Cut LiNbO, Crystall, d=650m

30



180

с,








H. W. Barz:

Compton backscattering of laser light off the ELBE electron beam

Compton backscattering of laser light off the ELBE electron beam

H.W. Barz

Institut für Kern- und Hadronen-Forschungszentrum Rossendorf physik

- 1. Electrons in laser fields
- 2. Differential cross section and polarization
- 3. Effective cross sections, production rates

1. Election in Laser field

-|

25-Feb-00

X-rays-2000



$$\begin{aligned} \mathcal{L} = \mathcal{L}$$

pourson cross lection



E &	60 keV	220 MeV	1.8 GeV	29 GeV
تە ت	ちょう	2.6 (ml	8 600	46 Gev
	÷186	LEGS	PRING8	SLAC





Polari zation

linear polanited e-

(d) × + 1 ~ 2

••

compton polairimeter





$$Effective Cross section.$$

$$\frac{d^{2}\varepsilon}{d\xi^{2}} \sim \int de e^{-\frac{(k+h)^{2}}{2k\epsilon^{2}}} \int dS e^{-\frac{e^{\frac{k}{2}}{2k\epsilon^{2}}} \times dS} \frac{d^{2}\varepsilon}{dR} \times \int dS e^{-\frac{e^{\frac{k}{2}}{2k\epsilon^{2}}} \times dS} = \frac{d^{2}\varepsilon}{dR} \times \int dS e^{-\frac{1}{2}k\epsilon^{\frac{k}{2}}} \times \int dS e^{-\frac{1}{2}k\epsilon^{\frac{k}{2}}} \times \int dS e^{-\frac{1}{2}k\epsilon^{\frac{k}{2}}} \times \int dS e^{-\frac{1}{2}k\epsilon^{\frac{k}{2}}} \times \int dS e^{\frac{1}{2}k\epsilon^{\frac{k}{2}}} \times \int dS e^{\frac{1}{2}k\epsilon^{2$$





higher intensity

• narrow focus $A = \pi (0.1 \text{ um})^{L}$ $A = \Delta 0 = 0.7 \text{ und}$

 $\Delta \sigma_{e} = 0.1 \text{ mmod}$ $\dot{N}_{e} = 10^{5}/5$

. internal IR laserfield in the optical resonator







Summary

- 200 - -

ŧř

$$\frac{5 \times peched}{100} \frac{10^{3} \text{ c}^{-1}}{100} \frac{10^{3} \text{ c}^{-1}}{100} \frac{10^{3} \text{ c}^{-1}}{100} \frac{1000}{100} \frac{1000}{10$$

M. A. Piestrup:

Compound refractive lenses for novel X-ray sources

Compound Refractive Lenses for Novel X-ray Sources

Melvin A. Piestrup, H. Raul Beguiristain, Charles K. Gary, Richard H. Pantell*, J. Theodore Cremer, Roman Tatchyn* *

> Adelphi Technology, Inc. 2181 Park Blvd. Palo Alto, California, 94306

*Stanford University ** Stanford Synchrotron Radiation Laboratory

Adelphi Technology, Inc.

D Publications and Patents

- Toshihisa Tomie, US Patent #5,594,773 "X-ray Lens" (Jan. 14, 1997) filed Jan. 1994.
- A. Snigivrev, V. Kohn, I. Snigireva and B. Lengeler, "A compound refractive lens for focusing high-energy X-rays, Nature 384, 49 (1996).
- J. T. Cremer, M. A. Piestrup, H. R. Beguiristain, C. K. Gary, R. H. Pantell, R. Tatchyn "Refractive X-ray Lenses using Low Density Plastics," Rev. of Scientific Instruments 70, (Sept. 1999)

Focusing: Papers and Patents

- M. A. Piestrup, R. H. Pantell, J. T. Cremer and H. R. Beguiristain, "Refractive X-ray Lenses," US Patent submission (filed May 1999).
- B. Lengeler, C. G. Schroer, M. Richwin, J. Tommeler, M. Drakopolulos, A. Snigirev and I. Snigireva, "Appl. Phys. Lett. 74, 3924 (1999).
- H. R. Beguiristain, M. A. Piestrup, R. H. Pantell, C. K. Gary and J. T. Cremer "Development of compound refractive lenses for xrays," Conference proceedings, 11th US National Synchrotron Radiation Instrumentation Conference (Oct. 1999).
- M. A. Piestrup H. R. Beguiristain, R. H. Pantell, C. K. Gary, J. T. Cremer and R. Tatchyn, "Compound Refractive Lenses for Novel X-ray Sources," Conference proceedings, RREPS(99) submitted to Nucl. Instrum. Methods A. (1999)





Adelphi Technology, Inc.





fraction at x-ray photon energies

 $n = 1 - \delta + i\beta$

 δ is between $10^{\text{-5}} \, \text{and} \, 10^{\text{-7}}$

n is less than 1

 $f = \frac{R}{2\delta} \quad \text{single lens, if } R = 0.3 \text{ mm, } d = 3 \times 10^{-6},$ then f = 50 meters $f = \frac{R}{2N\delta} \quad \text{N lenses, if } N = 100 \text{ then } f = 50 \text{ cm!}$

Adelphi Technology, Inc.

 X roys
 F=R/28

 X roys
 F=R/2N8

 X roys
 F=R/2N8



Apertures of Lenses





Adelphi Technology, Inc.

B. Aperture

1. Physical aperture = 2R

2. Spherical aberration aperture, A_s

This occurs for a circular lens and not a parabolic lens. The aperture is defined as twice the radius at which there is π phase shift error due to the non-parabolic curvature.

$$\frac{A_s}{2} = \left[4R^2\lambda r_i\right]^{.25}$$

where $r_i = \text{distance}$ between lens and image

3. Absorption aperture, A_a

 $A_a/2 =$ radius at which the power through the lens is reduced by the factor Exp[-2]

$$A_a = 4\sqrt{\frac{f\delta}{\mu}}$$



Adelphi Technology, Inc.





Adelphi Technology, Inc.



C. Gain

Gain = ratio of the on-axis intensity with and without the less in place

1-d Gain for an incoherent source = $\frac{Ar_0}{\sigma_0 f}$

where r_0 = distance from source to lens

$$\sigma_0$$
 = source size

For a symmetrical source, 2-d Gain = $[1-d \text{ Gain}]^2$

Including base absorption:



Gain (with base) = $Exp(-\mu Nd)$ X Gain (without base)

Typical parameters: $\sigma_0 = .4$ mm, $r_0 = 17$ m, f = 1m, d = .01mm,

N =100 With Be at 8keV: $\mu = .17 \text{mm}^{-1}$, $A_a = .71 \text{mm}$ This gives: 1-d Gain = 25 2-d Gain = 760

NORMALIZED GAIN VE WAVELENGTH



Source: synchrotron radiation (SSRL) distance from source to lens = 16.8msource size = .44 X 1.7mm 2.4 to 30 keV energy tuning 5×10^{-4} energy resolution



The intensity profile of the radiation is measured by the

translatable slit on the left.





1-D Lens Parameters

Lens Number Designation	1.2	3.1
Material	Acrylic	polyethylene
	(Lucite)	
Chemical Formula	C ₅ H ₈ O ₂	CH ₂
ρ , Density (gm/cm ³)	1.2	0.96
δ	2.87 x 10 ⁻ ⁰	4.34 x 10 ⁻⁷
$\mu(1/m)$	498	18
N, Numbers of holes	50	200
R, Hole Radius (µm)	250	160
f, Calculated Focal Length (cm)	87.1	93 .
Δ, Min. Wall thickness (μm)	50	75
S_d , Vertical Source size ⁶ (μ m)	445	445
Source-to-lens distance (m)	16.8	16.8
Photon Energy (keV)	9.0	19.5
F_d , Calculated Focal Line Width (μ m)	24.3	26.0
Measured Focal Line Width (µm)	70 (Fig. 3)	32.1 (Fig. 4)
Id, Calculated Image Distance (cm)	92	98
Measured Image Distance (cm)	68.6	84
G, Calculated Gain	1.5	3
Calc. Ave. Transmission through Lens	24%	75%
R_p , Calc. parabolic radius, (μ m)	75	50
R_a , Calc. absorption radius, (μ m)	142	298

Adelphi Technology, Inc.



Focal Length as a Function of Photon Energy





Measure Image Distance and Image Spot Size for Lens

Photon Energy (keV)	Calculated Focal length [m]	Calculated Image Distance[m]	Measured Image Distance[m]	Measured Image Line Width [µm]	Source Width from Image line width [µm]
12	0.35	0.35	0.33	21	1070
15	0.55	0.56	0.58	25	720
18	0.79	0.82	0.79	30	640
19.5	0.92	0.97	0.84	32	644

Adelphi Technology, Inc.





Unit Lens

- * 0.4 mm diameter
- Absorption
 aperture 180 μm
- * 23 μ m thick
- $*5 \ \mu m \ minimum$





Waist as a Function of Distance



Source Size: Vertical: 0.45 mm Horiz.: 1.7 mm







2-d Gain for mylar lens







What Adelphi CRLs can give you!

- Focal lengths below 1 meter
 - 20 cm has been done with 1-D
 - 60 cm has been done with 2-D
- Good transmission and gain at moderate photon energies!
- Expected apertures of 1 mm or larger!



Adelphi Technology, Inc.

Y-ray Lenses with Novel Sources (PXR, TR, CR, Combinations)

- Only done experimental work with synchrotron radiation
- * Should work well with novel sources
 - Source size can be small (size of electron beam)
 - Sources are collimated like synchrotron radiators
 - Near Field of TR source looks Guassian

Cost : \$2000 - 4000

GKeV to 16 KeV 2.D. lenses.



Benefits!

*"In-line Optic"
*Works at Hard X-rays
*Works with Novel X-ray Sources
*Inexpensive
*Imaging Possible (Unlike Capillary Optic)

D Compound Refractive Lens

- *Number of lenses 200
- R = 1.6 mm
- *Mechanical Aperture = 0.4 mm
- *Absorption Aperture = 0.31 mm at 8 keV
- *Minimum Thickness = 5 microns
- *Focal Length = 97 cm

H. Genz:

Channeling radiation as a probe in the solidstate plasma accelerator regime



Channeling Radiation as a probe in the solid state plasma accelerator regime

Harald Genz Institut für Kernphysik Technische Universität Darmstadt

- Motivation
- Channeling
- Experiment and first result

Rossendorf, February 24 - 26 2000; Workshop on X-rays from electron beams



Progress in Energy

High energy physics: 12 orders of magnitude

•Limit of electromagnetic acceleration: 35 MeV/m •Large dimensions TESLA

R. Hofstadter (1968):

"To anyone who has carried out experiments with a large modern accelerator there always comes a moment when he wishes that a powerful spatial compression of his equipment could take place. If only the very large and massive pieces could fit in a small room"



Importance of plasma acceleration

• Considerably larger gradients in plasma

 $eE_{max} = 0.97 (n_0)^{1/2} eV/cm$

Gaseous plasma: 1 GeV/cm Solid state plasma: 100 GeV/cm

- <u>Cash</u>

S-DALINAC

Gaseous plasma

- Acceleration of electrons
- Laser induced plasma wave
- **`95:** proof of principle
- **`99:** short distances moderate acceleration

Solid state plasma acceleration

Chen, Noble:

- Make use of plasma in solid state
- Plasma electron beam induced
- Channeling to guide the particles through the crystal
- Channeling process as cooler



Open questions:

• Can the electron couple to the field? • Do the crystals stand the field? S-DALINAC lab. system U • _ e-ΔE =ħῶ ~~~ У $U^{R} = \gamma \cdot U$ rest system Y


A Statement of the second s





- 10 nC/puls x 500 pulses/macrobunch x 1/500 µs = 10 mA average
- photon flux 3.1 10⁹ photons/s sr
- peak photon flux 4.3 10²⁰ photons/sr (in 10 ps)
- photon energy

15 - 25 keV

photon flux 10⁵ higher than at S-DALINAC





Block Diagram of Laser System



A0 photo injector



Strahleigenschaften

• normalized transverse RMS emittance :

 $\epsilon_{n,y} = \beta \gamma (\langle y^2 \rangle \langle (y^2)^2 \rangle - \langle yy^2 \rangle^2)^{1/2} = 5.5 \pm 0.8 \text{ mm mrad}$

• bunch length :

 $\sigma_t = 7.1 \pm 0.2 \text{ ps}$

• charge :

به مقدَّمة المحالية المحالية في

 $\underline{\mathbf{q}} = 1 \, \underline{\mathbf{n}} \mathbf{C} - 18 \, \underline{\mathbf{n}} \mathbf{C}$

• charge density :

 $\rho_{\text{bunch}} = \frac{3 \times 10^{15} \text{ electrons / cc}}{1 \text{ nC}} \quad (1 \text{ nC})$

Darmstadt-Fermilab experiment

.















A channeling radiation experiment



The Darmstadt-Fermilab-A0-team

Fermilab

R.A. Carrigan, Jr., J.-P. Carneiro, P.L. Colestock, H.T. Edwards, W.H. Hartung and K.P. Koepke

Rochester M. J. Fitch

UCLA N. Barov

Darmstadt

J. Freudenberger, S. Fritzler, H.G., A. Richter and A. Zilges

Johannesburg J.P.F. Sellschop



S-DALINAC

Biomedical Applications of Quasi-Monochromatic X-Rays

D. Frankenberg:

Relative biological effectiveness of X-rays for mammography







interstitial deletion d.1 \mathcal{A}_2



deletion

 $^{\circ}$

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 $\gamma = \alpha \cdot D + \beta D^2$

Yield of exchange aberrations:

 $y = \alpha \times D + \beta \times D^2$

Values of α for ⁶⁰Co gamma rays (reference) (12 values in the literature)

> $\overline{\alpha}$ = (2.26 ± 1.6)10⁻²Gy⁻¹ Range: (0.33 - 5.5)10⁻²Gy⁻¹

Values of α for x-rays (180 - 250 kVp) (16 values in the literature)

> $\overline{\alpha} = (5.07 \pm 1.93)10^{-2} \text{Gy}^{-1}$ Range: (2.38 - 9.50)10^{-2} \text{Gy}^{-1}

 $RBE_{60Co} = 2.26 \pm 2.5$

Radiation	Dose Range (Gy) (Rate)	$\alpha \pm S.E.$ (× 10 ⁻² Gy ⁻¹)	$\begin{array}{c} \text{Limiting RBE} \\ (\alpha_x / \alpha_\gamma) \end{array}$	Reference
220 kVp X rays	0.5-4 (0.5 Gy min ⁻¹)	4.04 ± 0.3		Bauchinger (1984)
⁶⁰ Co γ rays	0.5-4 (0.5 Gy min ⁻¹)	1.07 ± 0.41	3.8	
250 kVp X rays	0.05-2 (1.0 Gy min ⁻¹)	4.37 ± 0.99		Fabry <i>et al.</i> (1985)
⁶⁰ Co γ rays	0.05-2 (acute)	2.97 ± 0.80	1.5	
250 kVp X rays	0.056 (1.0 Gy min ⁻¹)	3.64 ± 0.53		Lloyd (1986a)
⁶⁰ Co γ rays	0.056 (0.5 Gy min ⁻¹)	1.42 ± 0.44	2.6	
220 kVp X rays	0.25-3.75 (0.5 Gy min ⁻¹)	4.34 ± 0.81		Littlefield <i>et al</i> . (1989)
⁶⁰ Co γ rays	0.25-4 (0.5 Gy min ⁻¹)	1.57 ± 0.66	2.8	

 TABLE 2.8—Low Dose RBE_M for x rays versus gamma rays for dicentrics in human lymphocytes^a

*Data from scoring first division metaphases.

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 $\overline{\mathsf{RBE}} = 2.7 \pm 0.9$

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KINZLER L. VOGELSTEIN

<u>Cell systems available to investigate</u> radiation -induced neoplastic transformation

SHE	(embryonic Syrian hamster cells)
BALB/3T3	(embryonic mouse cells)
C3H10T1/2	(embryonic mouse cells)

CGL1 (hybrid HeLa x human skin fibroblast)



t the shakes sumbor



Figure 3. Molyhdenum-filtered and rhodium-filtered x-ray spectra produced with a tungsten anode at 25 kV and 30 kV, respectively.





Fig.11 Probability to find a certain number of ionizations within a certain distance in e⁻-tracks

PARETZKE et al. 1981



1060 k 350





Genomic frequencies of radiation-induced translocations in Go-lymphocytes using FISH



absorbed dose/Gy

The most important characteristics of the CGL system



- Very stable cell lines with 90 100 chromosomes.
- On chromsomes 11 and 14 are loci of tumor suppressor genes.
- Tumorigenicity is induced when one **tumor** suppressor gene of each of the fibroblast chromosomes 11 and 14 is lost.
- Tumorigenicity is associated with the expression of the intestinal alkaline phosphatase (IAP). (IAP is expressed by the HeLa cells.) Thus, neoplastically transformed cells (or clones) can be identified by the expression of IAP.
- Expression of IAP can be detected simply and rapidly by a substrate of IAP, i. e.
 "Western Blue (WB)". This compound is cleaved by IAP leading to a blue insoluble precipitate.

References

Stanbridge et al., Somatic Cell Genet. Z. 699-712, 1981

Redpath et al., Radiat. Res. 110, 468-472, 1987

Mendonca et al., Radiat. Res. 131, 345-350, 1992 und Radiat. Res. 149, 246-255, 1998







Summary

- Current radiation risk estimates are based on the efficiency of 2-5 MeV gamma rays.
- It is assumed that the efficiency of gamma- and x-rays as well as electrons with LETs up to $11 \text{ keV}/\mu m$ are all equally effective.
- Data in the literature suggest that this assumption is not valid.
- Therefore, there is a need to determine the LET-dependence of the RBE up to 11 keV/ μ m (2 5 MeV gamma-rays up to mammography x-rays, i. e. 29 kVp x-rays) for the relevant end points.
- Using a human hybrid cell line the RBE of mammography x-rays relative to 200 kVp x-rays for neoplastic cell transformation amounts to 3.3.
- Considering the RBE of 300 kVp x-rays relative to ⁶⁰Co gamma-rays an RBE of at least 7 can be expected for mammography x-rays relative to ⁶⁰Co gamma-rays.
- This means an underestimation of mammography x-rays by a factor of at least 7.

Project

"Mammography x-rays"

- P. Virsik-Peuckert
- K. Konstantin
- K. Kelnhofer
- K. Bär

100

- M. Frankenberg-Schwager
- D. Frankenberg

D. Harder:

Chromosome aberrations by soft and ultrasoft X-rays: Microdosimetric and radiobiological aspects

Proposed mechanisms of radiation-induced chromosome exchange:

B component

Pairwise interaction between doublestrand breaks of DNA via NHEJ (non-homologous end joining)

& component

- a) Deletion of DNA segments + single strand invasion
- b) Denaturation of micleosome by thermal spike + single strand invasion.

Proposed experiments: 1) Aconstic pulse by 10 ps electron bunch 2) Ultrasoft X-rays: Search for DNA segments 3) Tunable ultrasoft X-rays: energy requirement 4) Brdlerd experiments



Proposed thermal dissociation of hydrogen and Van der Waals bonds in nucleosomal DNA



Time resolved properties of acoustic pulses generated in water and in soft tissue by pulsed proton beam irradiation—A possibility of doses distribution monitoring in proton radiation therapy



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ACOUSTIC PRESSURE (Pa)

Acoustic pulses generated in water by pulsed proton beam irradiation at three different temperatures.

Pulse duration: 50 ns; proton energy: 100 MeV; absorbed dose (Bragg peak): 5 cGy/pulse.

Pressure wave generated by the passage of a heavy charged particle in water

Y. Y. Sun and Ravinder Nath Department of Therapeutic Radiology. Yale University School of Medicine. 333 Cedar Street. New Howen, Cannecicu. 06510



Attuation of EM-Waves in Water



Attenuation Coefficient [m⁻¹]









SINGLE-STRANDED DNA CONTAINING THE GENE FOR THE PROTEIN OVALBUMIN WAS ALLOWED TO HYBRIDIZE WITH OVALBUMIN MESSENGER RNA. THE EIGHT EXONS (L, 1-7) OF THE GENE ANNEAL TO THE COMPLEMENTARY REGIONS OF RNA, AND THE SEVEN INTRONS (A-G) LOOP OUT FROM THE HYBRID. THE 5' AND 3' ENDS OF THE MESSENGER ARE INDICATED, AS IS THE POLY-A TAIL.











Chromosome aberration yields in 100 cells without (a-d) and with gold foil (e-h)







Electron spectrum at the gold surface: Photo- and Auger electrons





Chromatinfaser und Elektronenreichweite: Doppeltreffer bei niedriger Energie unmöglich





Mutation Research, 149 (1985) 67~72 Elsevier

MTR 03983

Direct analysis of radiation-induced chromosome fragments and rings in unstimulated human peripheral blood lymphocytes by means of the premature chromosome condensation technique

Gabriel E. Pantelias^{1,2} and H. David Maillie¹



Fig. 2. Yield of ring chromosomes per cell in human peripheral blood lymphocytes exposed in vitro to varying X-ray doses up to 805 rad. Rings were analyzed immediately after exposure (\bullet) or 1 h (\times), 2 h (\blacktriangle), of 24 h (\bullet) after exposure. Bars indicate standard deviations calculated from 2–3 independent Expts.

Direct analysis of radiation-induced chromosome fragments and rings in unstimulated human peripheral blood lymphocytes by means of the premature chromosome condensation technique

Gabriel E. Pantelias^{1,2} and H. David Maille¹ Pertment of Radiants Biology and Biologica, University of Rechter, School of Medices and Dentstry, Rechester, NY 1442, and ⁷Laboratory of Radiobiology and Biological Constraints, Graduates and American (A 94142 (U.S.A)



Fig. 3. Yield of chromosome fragments (\blacksquare) and ring chromosomes (\bullet) per cell in human peripheral blood lymphocytes exposed in vitro to 645 rad of X-rays and analyzed at various times after exposure.


 $Y_{exch} = \propto D$ dsb N Г 2 dsb/ 30 nm





K= 70/80 50 Gy



Binding of Ku heterodimer to dsb ends, recruitment and activity of DNA-PK_{CS}



C. Featherstone and S. P. Jackson,

Mut. Res. 434 (1999) 3 - 15

Model for nonhomologous end joining (NHEJ) by annealing broken strands at sites of microhomology



Topologie der paarweisen Läsions-Interaktion zwischen Chromosomen-Domänen



M. N. Cornforth, On the nature of interactions leading to radiation-induced chromosomal exchange. Int. J. Radiat. Biol. 56, 635 - 643 (1989)



FIG. 3. Total frequency of intergenomic exchange events resulting from the four different fusion protocols described in the legend to Fig. 1. Total events include symmetrical exchanges (reciprocal translocations) as well as asymmetrical exchanges (dicentrics).





Characteristic K, L ... line spectra of the elements of atomic number Z as a function of wavelength λ .



 $= \left(\frac{dE}{dx}\right)$ Linear energy L_{Δ} transfer



Consistent chromosomal changes in leukemias and lymphomas (examples)

Neoplasm	chromosome aberration		
Acute lymphocytic leukemia	t(9;22)(q13;q32) t(4;11)(q21;q23)		
Chronic lymphocytic leukemia	t(11;14)(q13;32) Trisomy 12		
Chronic myeloid leukemia	t(9;22)(q34;q11)		

Cline, M.J.: The molecular basis of leukemia, New Engl. J. Med. **330** (1994)328-336 Luzzatto, L., and Pandolfi, P.P.:Leukemia, a genetic disorder of hemopoetic cells Brit. Med. J. **307** (1993)579-580

Mitelman, F., Heim, S.: Quantitative acute leukemia cytogenetics. Genes, Chromosomes and Cancer 5 (1992)57-66

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Carlos and a second second

M. Hill:

Radiobiological investigations with monochromatic soft X-rays

Radiobiological investigations with 'monochromatic' soft X-rays

Mark A. Hill

MRC, Radiation & Genome Stability Unit, Harwell, Oxfordshire, OX11 0RD, U.K.

Overview

- Biological effects of radiation
- Why use ultrasoft X-rays?
- Practicalities of irradiating biological samples
- A few examples of biological experiments
 - Mammalian cell survival
 - Induction and repair of DNA double-strand breaks
 - Chromosome aberrations
 - Plasmid DNA studies radiation chemistry
- Summary

Biological effects of radiation

	Molecular -	damage to macromolecules such as
Radiation		DNA, RNA, enzymes
Cell	Cellular -	chromosome aberrations apoptosis reproductive cell death gene mutations transformation
		genomic instability
	Organism -	death (high dose) cancer (low dose)
	Population -	Genetic modification

Radiation induced DNA strand breaks



A small clustered damage (simple DSB) resulting from a local cluster of ionisations within a single track

Radical diffusion distances in cells are very small (<4nm)

Damage to DNA

Simple damage

Base damage



Single strand break (SSB)

Т	7	Т	T	Т	Т
1_					L

Double strand breaks (DSB)



Complex damage

Complex SSB



Complex DSB



Very complex DSB



Relevance of ultrasoft X-rays

Why use ultrasoft X-rays?

- Provide a unique tool for investigating energy and spatial requirements of radiation damage
 - produce isolated tracks of electrons
 - small, well defined energies
 - very short tracks comparable to critical structures of the cell, such as DNA, nucleosomes and chromatin fibre

X-ray	energy (keV)	dominant electron energy (keV)		combined csda range	attenuation length in tissue
		photo-	auger-	(nm)	(μm^{-1})
CK	0.28	0.25	-	7	0.56
\mathbf{Cu}_{L}	0.96	0.42	0.52	38	0.47
Al_K	1.49	0.96	0.52	68	0.14
Tiĸ	4.55	4.02	0.52	500	0.007

Energies available at the MRC:

Sample ultrasoft X ray tracks



Schematic of radiation tracks in chromatin fibre



Relevance of ultrasoft X-rays

• These low energy electrons are similar to the numerous secondary electrons produced by most irradiations



(~30% of absorbed dose produced by low energy electrons 0.1-5keV for 60 Co γ -rays) Nikjoo and Goodhead

Nikjoo and Goodhead (1991) Phys. Med. Biol., 36, 229

Irradiation of biological samples with ultrasoft X-rays



MRC ultrasoft irradiation rig



MRC Low Dose Rate Irradiation Rig



Biological sample irradiation



X-ray attenuation and Cell Morphology



V79 Cell thickness distribution measured by confocal microscopy



Variation in nuclear area with height through central section of flattened V79 cell



Hill et al. (1998) Phys. Med. Biol., 43, 351.

Importance of cell morphology



Tailing is a well know phenomenon for low-penetration radiations

Tight control of the cell growth conditions is essential to minimise the effect of the tail.

Specifically, optimising growth conditions conditions to reproducibly obtain:

- a good cell monolayer
- well attached and well flattened cells

Examples of radiobiological experiments







Chromosome aberrations viewed using FISH





Aberrations induced in chromosome 1





Carbon K aberration data

- Provides further support for the hypothesis that damaged DNA may be able to interact with undamaged DNA
- Data suggest that a simple chromosome exchange can be induced by the passage of a <u>single</u> electron track.
- Suggests that even for the lowest dose of low-LET radiation there is a finite probability of producing DNA rearrangement.

Radiation induced DNA strand breaks



Low scavenging capacities

'Indirect' strand break break

High scavenging capacities

Diffusion distance of OH radicals very small (<4nm in cells) significantly reducing OH induced strand breaks to a level similar to that produced directly by radiation in DNA.

Plasmid DNA studies



•Relative proportions can be determined by gel electrophoresis

• Scavenging capacity determined by concentration of Tris.

Low scavenging capacity

- Probe of yield of OH radicals escaping radiation track.

High scavenging capacity

- Model system for DNA damage in cell



Hill and Smith (1994) Radiat. Phys. Chem., 43, 265.



Dose dependence for loss of supercoiled plasmid DNA (pUC18)



Yield of OH radicals escaping radiation tracks vs photon energy



Ultrasoft X-ray Summary

- Ultrasoft X-rays can be used to investigate the energy and spatial requirements of radiation damage.
- Low energy electrons are similar to the numerous secondary electrons produced by most radiation.
- Due to the significant attenuation through the cell. It is essential to have a tight control on the growth conditions to reproducibly obtain:
 - a good cell monolayer.
 - well attached and well flattened cells.

Experimental Summary

- Ultrasoft X-rays are generally more effective at producing biological damage than γ-rays for a given dose, due to the increasing clustering of ionisations on the nanometer scale.
- Low energy, secondary electrons (100eV 5000eV) are believed to be the critical component of low LET radiation tracks rather than the more numerous isolated events.
- C_K X-ray aberration data provides further support for the hypothesis that damaged DNA may be able to interact with, undamaged DNA.
- Ultrasoft X-ray experiments can provide invaluable bench mark data for theoretical simulations. For example:
 - DSB yield with photon energy
 - OH yield with photon energy

Acknowledgements

MRC Radiation and Genome Stability Unit

Biophsics group Dudley Goodhead David Stevens Hoo shang Nikjoo DNA damage group Peter O'Neill Cathy deLara Stan Botchway <u>Cytogenetics</u> Carol Griffin Paul Simpson John Savage

<u>Microscopy</u> Stuart Townsend

B. D. Michael:

A focused soft X-ray microbeam for investigating the radiation responses of individual cells

A FOCUSED SOFT X-RAY MICROBEAM FOR INVESTIGATING THE RADIATION RESPONSES OF INDIVIDUAL CELLS

G Schettino¹, M Folkard¹, AG Michette², KM Prise¹, B Vojnovic¹ and BD Michael¹

¹Gray Laboratory Cancer Research Trust, Mount Vernon Hospital, Northwood, Middlesex, U.K.

²Department of Physics, King's College London, U.K.

Work supported by:

- Cancer Research Campaign, U.K.
- Biotechnology and Biological Sciences Research Council, U.K.
- European Union
- U.S. Department of Energy

Two main experimental approaches to radiation biology of cells

Conventional or "broad-field"



- In general, cells are randomly traversed by radiation tracks
- Results are generally scored as an average throughout the exposed population

Microbeam



- · Cells are targeted individually with counted tracks under automated control
- Results are generally scored in individual cells, or their progeny

Early work on ionising radiation microbeams with cells

Zirkle and co-workers in the 1950's

New generation of radiobiology microbeams developed since ~1990

a) Charged-particle microbeams

- Texas A&M University (formerly at Battelle Pacific Northwest Labs.)
- Columbia University, New York

JAERI, Takasaki, Japan

- Gray Laboratory, U.K.
- Others under development in Japan, U.S.A. and Europe

b) X-ray/electron microbeams

- Gray Laboratory, U.K.
- Others under development in Japan and U.S.A.

Uncertainties in extrapolation of radiation risk



Applications of microbeams in radiation biology

Spatial resolution

• To resolve the targets and pathways involved in cellular effects of radiation

Dose resolution

• To determine cellular radiation effects down to the ultimate low-dose limit - traversal by a single track

Overall objective

Information to develop improved models of radiation effects

- for radiotherapy
- for estimation of radiation risks







Particles Available

Particle	Energy at cell surface (MeV)	LET at cell surface (keV/µm)
Protons	< 4.0	> 10
Helium-3	< 5.6	> 65
Helium-4	< 4.0	> 100

Microbeam irradiation





10 ions per cluster

Target every cell nucleus within a population -1

- V79 cells
- 3.2 MeV protons
- Micronuclei scored 24 hours later
- One proton deposits 0.02 Gy/nucleus



Prise et al., 1999





723

Figure 1. Survival of V79 cells irradiated with 250 kVp X-rays solid) or neutrons (open). Symbols represent mean ± SEM. Survival was measured using the DMIPS survival assay, see text. The lines represent the fit of the Induced Repair model to the X-ray data solid line), the LQ fit to the X-ray data dashed lines and exponential fit to the neutron data (dotted lines).



Evidence for bystander effects

- Increased levels of SCE in CHO cells irradiated with low doses of $\alpha\mathchar`-$ particles
 - Nagasawa and Little, 1994. 1992
- Increased p53 expression in lung epithelial cells exposed to low doses of $\alpha\text{-}$ particles
 - Hickman et al., 1994
- Extracellular factors involved in SCE following α-particle exposure
 - Lehnert and Goodwin, 1997
- Medium from irradiated cells reduces the survival of unirradiated cells
 - Mothersill and Seymour, 1997
- Target for chromosomal damage larger than the nucleus
 - Manti et al., 1997
- · Bystander effects and genomic instability
 - Lorimore et al., 1998
- Bystander effects and cell-cell communication
 - Azzam et al., 1998
- Bystander effect after single cell irradiated
 - Prise et al., 1998

Using microbeams to study the role of extranuclear targets and bystander effects









Dish scored 1 - 3 days later for micronucleated and apoptotic cells




Gray Laboratory Focused Soft X-ray facility



(Failed and a





Microprobe Source



Schematic of the Gray Laboratory Microfocus X-ray source





Beam Characteristics



Ultrasoft X-ray Microprobe





Dosimetry

87% of absorbed energy deposited in 1.6 μm³



LE ZENER DELLA





Radiation-induced bystander effects



Summary

- 1) The modern generation of microbeams provides an important tool to investigate new aspects of how cells respond to radiation:
 - a) Identification of targets and pathways
 - b) Determination of extreme low-dose responses
- 2) At present, the development of light-ion microbeams is more advanced than that of X-ray, electron and heavy-ion microbeams
- 3) Data obtained so far demonstrate the power of microbeam methods to study:
 - a) Radiation bystander effects
 - b) Effects related to the distribution of energy deposition within the cell
 - c) Low-dose adaptive responses
 - d) Single-track effects

41

W. Mondelaers:

Application of X-rays for biomedical purposes





Overview

- Accelerator facility
- High-power white photon beams
 - high-dose radiotherapy
 - medical standard dosimetry
 - human grafts and implants
 - novel biomaterials

- Tunable monochromatic photon beams
 - biomedical applications

APPLICATION of X-RAYS for **BIOMEDICAL PURPOSES**

at the

GENT UNIVERSITY

15 MeV LINEAR ELECTRON ACCELERATOR FACILITY

W.Mondelaers

Workshop on X-rays from electron beams with special emphasis on possible developments at ELBE

15 MeV 2% duty factor LINEAR ELECTRON ACCELERATOR FACILITY

- intense electron beams up to 2 mA
- high beam power density up to 140 kW/cm²
- good energy resolution $\Delta E/E < 1\%$ (50 80%)
- high pulse repetition frequency up to 5000 Hz
- intense X-ray beams
 polarised and unpolarised



ACCELERATOR

BEAM TRANSPORT SYSTEM



- radiation physics
- biomaterials research \Leftarrow
- polymer chemistry
- atomic and solid-state physics
- medicine

₩

- food technology
- space research
- agriculture
- high-dose dosimetry





Biomedical applications of intense broad photon fields

- High-dose radiotherapy
 - extracorporeal bone tumours therapy
- Medical dosimetry

- primary standard dosimetry
- in vivo dosimetry
- Irradiation of implants
 - human grafts
 - artificial implants
 - graft-versus-host disease
- Synthesis of biomaterials
 - hydrogels
 - surface modification

Intraoperative extracorporeal irradiation in primary bone tumours therapy

Radical ablative surgery

- \Rightarrow limb saving techniques
 - endoprosthesis
 - allograft
 - bridging techniques

Disadvantages:

- loosening or breakage
- well-fitting allograft
- immunological rejection
- bone bank

₽

extracorporeal irradiation of endograft

One operative session:

- excission of bone
- extracorporeal irradiation 300 Gy
- reimplantation
 - Slow revitalisation of matrix
 - neovascularization
 - resorption of graft bone
 - depsoition of new host bone

Homogeneous photon irradiation field - homogeneity ± 2% - diameter 20 cm - dose rate 3 Gy/s

?? Conventional radiotherapy machines ??



- Dynamic electron beam scanning
- Static photon beam flattening
 Classical solution: high-Z target and filter

⇒ systematic theoretical and experimental study Monte Carlo: EPCOT EGS4, BEAM, DOSXYZ

3D dose mapping



energy spectrum of non-filtered 5 MV photon beam

1.00

0.90















2

2

radial distance (cm)









- mechanical scanning with multileat collimator
- scanning of photon beam -- ^i

Karolinska Irstitute (Söderstrom 1000): surerlicisl and deep-seated tumours 6 - 15 MeV

Intraoperative extracorporeal irradiation in primary bone tumours therapy

~ 100 patients treated

proximal and distal femur	46 %
pelvic rim	22 %
proximal tibia	11 %
humerus	8 %
fibula	5 %
radius, ulna, scapula	

 \downarrow

78 % 10 years actuarial survival rate

 \leftrightarrow 60 - 80 % other techniques

Heidelberg, Tubingen, Osaka

Bremsstrahlung configuartion for intensity-modulated therapy

theoretical and experimental or	f
broad beams	
<u>narrow</u> beams	

- FWHM 30 40 mm at 1 m
- energy range 6 15 mV
- high electron photon conversion yield
- full stopping low-Z target
- full stopping sandwich target
- optimised mono- or multilayer target
 + purging magnet

Primary standard dosimetry

Primary standard dosimetry

Belgian Primary Standard Laboratory



ionisation chambers <> primary standard

 \leftrightarrow TPR²⁰₁₀ = dose at 20 cm / dose at 10 cm

%dd(10) = % depth dose at 10 cm

calibration factor N_{DwQ}

0.2% uncertainty

Beam quality dependence factor k_a:

spectral characteristics of X-ray field

Beam quality specifiers:

Calibration standard

depth-dose distributions



 heat chemical defect correction factors

- hydrogen saturation oxygen content
- Chemical heat defect by radiation-induced species:

 $N_{DwO(0)}$

- dose dependence

Radiation treatment of human grafts and artificial implants

the human eye sclerae of



imflammation rejection 1 prosthesis

⇒ 'packed' in human sclerae

- less reactions
- synchronous movement

lyophylization \rightarrow sterilization 25 kGy \rightarrow tissue bank

- maxillo-facial reconstruction bone fragments:
- hydrogels for burn wounds cardiological stents polymeric implants human implants:

10 0% graft-versus-host disease lymphocytes

• blood:

Radiation treatment of biomaterials

RADIATION-INDUCED POLYMERISATION:

for synthesis of new biomaterials:

- biodegradable polymers
- hydrogels for burn wound treatment
- porous polymeric hydrogels for

advanced drug delivery systems

- → constant release
- → signal-responsive
- RADIATION-INDUCED SURFACE GRAFTING: to immobilise bioactive agents to improve biocompatibility

→ fixation of HD cell cultures on PE

→ heparine filter

RADIATION-INDUCED STERILISATION: mechanical properties biodegradability

swelling and permeability of hydrogels



Signal-responsive hydrogels

macromolecular networks swollen in water

PVME 60 kGy at 100 kGy/h temperature controlled



- \rightarrow discontinuous swelling behaviour
- Grafting of biofunctional groups on PVC beads ٠ Hemodyalisis of uremic patients: blood + artificial surfaces \rightarrow coagulation



heparine absorbing filter • X-ray induced grafting of HEMA on PVC beads (2-hydroxyethyl methacrylate)

- hydroxyl groups couple chemically with functional polyamidoamines
 - \rightarrow heparine absorber

Other research applications

- TREATMENT of FOOD PRODUCTS and PACKAGING MATERIALS
 - chemical, physical, sensorial, microbial and nutritional characteristics
 - identification and dose assesment
 - interaction food packaging materials
- HIGH-DOSE DOSIMETRY
 - EPR spectra of alanine and other systems
- RADIATION-INDUCED PLANT MUTATION .
- DETECTOR CALIBRATION (SOHO project) ٠
- **RADIATION DAMAGE STUDIES**
- e⁻ IRRADIATION-INDUCED DEFECTS in Si
- **BIODEGRADABILITY OF PLASTICS**
- STERILISATION OF WOOD AND SOIL PRODUCTS

Tunable monochromatic X-ray source



Tunable monochromatic X-ray source

PHOTON





L.

K. Kobayashi:

Radiation biology at the KEK Photon Factory

Radiobiology at the KEK Photon Factory

Katsumi Kobayashi Photon Factory National Accelerator Research Organization Japan

University of Tokyo <u>Takashi ITO</u> Atsushi ITO

Rikkyo University Kotaro HIEDA Yoshihiko HAYAKAWA Akira AZAMI Taisuke HIRONO Mikio SAITO Hiroyuki YAMADA

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National Cancer Research Institute Nobuo MUNAKATA

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Yokohama City University Masami WATANABE Masao SUZUKI

Japan Atomic Energy Research Institute Akinari YOKOYA

National Institute of Radiological Sciences Takeshi YAMADA

Photon Factory Noriko USAMI Katsumi KOBAYASHI

Radiobiology at the KEK Photon Factory

1. Introduction

Rationale to use synchrotron radiation for radiobiology

- 2. Facility and apparatuses
 - Beam line, irradiaition apparatus and supporting facilities for biology
- 3. Some of the results
 - 3a. Energetics of strand break induction in DNA using dry plasmid
 - 3b. Molecular fragmentation dependent upon the photoabsorption site
 - 3c. Energy dependence of chemical reactions in aqueous systems

Fricke solution, strand breaks in plasmid DNA in solution

3d. Research on cell lethality and mutagenesis

Radiobiological processes

Ionization/excitation

Photoabsorption Energy deposition

Thermalization (deactivation)

Spatial distribution

Radicals (water)

┛

Biomolecule radicals

Stable molecular changes (damage)

Repair

Biological effects





Fig. 4. Alternative microscopic descriptions of radiation quality. The diagram shows the individual atomic interactions along a random 120-nm-long segment of the path of an 8-MeV α particle and various microdosimetric descriptions which can be applied to it. Delta rays with ranges as great as ~0.4 μ m are possible from such an α particle. Shown for comparison is a DNA double helix (diameter 2 nm) on the same scale.

Energy deposition by high energy particles



Amount of energy per deposition event has wide variety.

Energy deposition by monochromatic photons





6 total the King of

Characteristics of synchrotron radiation (SR)















- 1. Gate monitor/controller
- 2. Shower room for decontamination
- 3. Waste storage room
- 4. Image process room
- Fluorescence microscopy, Cooled CCD camera, Image data analyzer (Mac quadra 950)
- 5. Radioisotope handling room
- Autoclaves(2) 6. Mammalian cell laboratory
- - CO2 incubators(3), Clean benches(3), Microscopes(2), Coulter counter, Low-temp centrifuge, Shakers(2), Refrigerator
- 7. Storage room for radioisotopes
- 8. Micro-organism laboratory
- Micro-organism facoratory Incubators(4), Shakers(3), Microscope, Centrifuge, Balances(2), Refrigerators(2)
 Biochemistry laboratory Ultracentrifuge, HPLC system, Electrophoresis apparatuses(4), Ice-maker, Deep freezer, Drying sterilizer, Spectrophotometer
- 10. Radioisotope measurement room
- Liquid scintillation counter, Gas flow counter
- 11. Experimental station for irradiation
- 12. Sewer tanks



$$f_{\rm sc}(D) = e^{-(b_{\rm ssb} + b_{\rm dsb})D}$$
$$f_{\rm lin}(D) = b_{\rm dsb} D e^{-b_{\rm dsb}D}$$





Molecules tested



Cystathionine

Methionine



Product	Cystathionine		Methionine	
	2472 eV	2466 eV	2472 eV	2466 eV
a-Aminobutyric acid	38	13	41	11
Glycine	1.2	1.0	1.9	0.77
Alanine	75	28	n.d.	n.d.

Production efficiencies (pmol/MR) of a-aminobutyric acid and glycine from cystathionine and methionine irradiated at the X-ray energies of 2472 eV and 2466 eV. Efficiencies for alanine was calculated by assuming the peak of alanine and/or ethylcysteine contains alanine only.

n.d. : not detected

X-ray photon

$$X$$
-ray photon
 H_2O
 H_2O
 $Photo electric effect$
 $E_{el} = E_{h\nu} - I$

Oxygen Kishell I~0.5KeV

LET along the electron tracks of different energies

Photoelectron by 2 keV photon

₩₩₩₩

Photoelectron by 7 keV photon



Photoelectron by 10 keV photon

High

LET

Low

<u>Fricke Dosimeter</u> 1 mM Fe^{2+} 0.8 N H_2SO_4 pH 0.4

 $G(Fe^{3+}) = g(OH) + 3g(e_{aq}) + 3g(H) + 2g(H_2O_2)$

Oxidation yield of Fe²⁺ to Fe³⁺: (Y-ray) 15.6 ions per absorbed energy of 100 eV

Increase of Fe³⁺ : Detected with absorption at 304 nm


Oxidation yield of Fe(2+) ion

- 0
- Δ
- Hoshi et al. (1992) Freyer et al. (1989) Yamaguchi (1989) ICRU report, recommended values (1970)
 - Present study •
- · · · Magee and Chaterjee (1987)



Energy (keV)



(Tomita et al, 1997)



"Hot field" and "Cold field". "Hot field" is produced transiently along the trajectory of charged particles. In highly concentrated solution, solute molecules exist in "Hot field", and can participate into the reactions between radicals.

W* or R : water radicals, Fe²⁺: ferrous ion in Fricke solution, A: ATP molecule

LET along the electron tracks of different energies



Absorption spectrum of DNA film around the K-shell absorption edge of Phosphorus. (Kobayashi et al., 1991)



State of the second sec

Biological effects of phosphorus photoabsorption on yeast cells.



Induction of excess fragments of chromosome by monochromatic soft X-rays around K-shell absorption edge of phosphorus. -Lesions irreparable by post-irradiation incubation-



W. Thomlinson:

Synchrotron medical imaging: From amplitude to phase



Synchrotron Medical Imaging: From Amplitude to Phase

W. Thomlinson ESRF Grenoble, France



10²²

10

1018

10¹⁶

10¹⁴

10¹²

10¹⁰

108

10

3rd

generation source Diffraction limit

ESRF futur

ESRF (1996)

ESRF (1994)

peneration

sources

¹generation

sources

X-ray tubes

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1900 1920 1940 1960 1980 2000

Year

SYNCHROTRON BRILLIANCE AND ESRF FLUX

- ESRF ID 17 @ 200mA - Wiggler: 1.4T - 1.6m - 150mm



Photon Energy (KeV)



DUAL-ENERGY K-EDGE SUBTRACTION



TWO EQUATIONS - TWO UNKNOWNS



Solution:

$$(\rho t)_{I} = \frac{\ln(\frac{I}{I_{0}})^{+} - \ln(\frac{I}{I_{0}})^{-}}{(\frac{\mu}{\rho})_{I}^{+} - (\frac{\mu}{\rho})_{I}^{-}}$$

With a similar equation for the soft tissue.

AMPLITUDE AND PHASE

Complex Index of Refraction n in a medium:

$$n = 1 - \delta + i\beta$$
Plane wave: $e^{inkz} = e^{i(1-\delta)kz} \times e^{-\beta kz}$

$$k = \frac{2\pi}{\lambda}$$

Phase shift related to δ : $(1 - \delta)$

Absorption related to β : $\mu = \frac{4\pi}{\lambda}\beta$

Energy Dependences:

$$\beta(E) = (hc / 4\pi E)\mu(E) \sim O(E^{-4})$$

$$\delta = (r_0 h^2 c^2 / 2\pi E^2) N_0 f_R \sim O(E^{-2})$$

$$\delta \approx 1.3 x 10^{-6} \rho \lambda^2 \sim 10^{-6}$$

Refraction Angles:

and the second

$$\alpha = \int_{0}^{t(y,z)} \frac{1}{n(x,y,z)} \frac{\partial n(x,y,z)}{\partial z} dx \sim \mu radians$$



PHASE/AMPLITUDE RATIO FOR LIGHT ELEMENTS







Basic Configuration for Computed Tomography



Iodine and Gadolinium K-Absorption Edges









Above





Subtraction





SRCT images obtained on rats bearing glioma







Gadolinium

lodine



SRCT images after gadolinium injection



Kinetic study on a rat brain bearing a glioma





Iodine SRCT images





mg/cm³ (SD/mean %)

periphery center contralateral

1.35 (15%)0.6 (30%)0.17 (36%)

iodine

@ 4 mH/kg (NA) @ 23.3 mgHnt









Histology



Skull, 2. Brain
 Tumor contrast enhancement

THE LUNGS





Mass Attenuation Coefficient of Xe













Phantom120_scan4 image "tissue"













(Carrier and a second



- Spanne *et al*

MULTICRYSTAL:

"SCHLIEREN" - Goetz et al "REFRACTION" - Shilstein & Podurets "DISPERSION" - Ingal & Beliaevskaya "PHASE CONTRAST" - Wilkins et al

"DIFFRACTION ENHANCED IMAGING" - Chapman et al



MONOCHROMATOR $\lambda/\Delta\lambda = 10^4$



Intensity Distribution: $I = |1 + P_r * (1 - A)|^2$

A = absorption function

$$P_r(x, y) = \frac{1}{\sqrt{i\lambda r}} \exp\left(i\pi \frac{x^2 + y^2}{\lambda r}\right)$$

If $r \ll \Delta^2 / \lambda$ \implies Contrast = Absorption If $\sqrt{\lambda r} \sim \Delta$ \implies Contrast = Edge Enhanced

Optimal Distance for Spatial Frequency f is: $r_{opt} \approx \frac{1}{2} \lambda f^2 \sim r$



P. Spanne et al





CALLST PERSONNEL





$$I_{B}^{\pm} = I_{R}R\left(\theta_{B} \pm \frac{\theta_{D}}{2} + \delta_{Z}\right)$$

$$\approx I_{R}\left[R\left(\theta_{B} + \frac{\theta_{D}}{2}\right) + \frac{dR}{d\theta}\left(\theta_{B} + \frac{\theta_{D}}{2}\right) \pm \delta_{Z}\right]$$

2 equations - 2 unknown: I_R and δz

Absorption:
$$I_R = \frac{I_B^+ + I_B^-}{2R}$$

Refraction Angle: $\delta z = \frac{R}{\left(\frac{dR}{d\theta}\right)} \left(\frac{I_B^+ - I_B^-}{I_B^+ + I_B^-}\right)$









Discovery of DEI

Mammography Quality Assurance Object

- American College of Radiology Mammography Phantom
- This phantom contains objects which simulate features presented by lesions in breast tissue (masses, fibrils and specks). Images are scored according to the number of targets detected in a category (i.e. masses, fibrils and specks).
- Manufactured by Gammex RMI: Model 156.
- Sketch at right shows objects imbedded in pharatom
- Phantom is approximately 3 in x 3 in x 2 in

Region Materia k 1.154 mmgdonfib 2.112 mm. donfilez 3.089mmn&milian 4.075 mmn.do nailan 5.0 54 mm yéb nellen 6.040 mm nån miller 7.054 mm indiction a - akification Editioni amo invitated an-alcification 9.032 mmsimulated a-alcification 10.024 mms invitated p-alcification 11.016 mms included a - alaticatio 17.200 mm tum zhin : 13.1 00 mm ture rhis mas 14.075 mm tuno elile mes 15.0 50 mm tomo r hile mass 15.025 mm tomo z bile mass



DEI Group



Comparison - Conventional and DEI



Мар

Conventional

DEI





Physics of DEI



DEI Group

DEI Group



Refraction - Absorption Analysis





Where did excess contrast come from?



x-ray beam fixed on on turn or simulation s - then analyzer is rotated in angle

DEI Graup

Human Breast Tissue DEI Image

DEI Group NSLS Feb. 1998



Apparent Absorption



Refraction

At Peak of Rocking Curve

PROPERTY AND INC.

30keV DEI Mouse Images





DEI Sources of Contrast

- DEI
 - Normal Absorption
 - Refraction
 - Extinction -or- Scatter Rejection
- Compare with Radiography...
 - Normal Absorption





(FILMER A

ESRF

SCIENTISTS: S. Fiedler, G. Le Duc, C. Nemoz, P. Spanne, A. Snigirev, W. Thomlinson
POST-DOCS: A. Bravin, I. Troprès
ENGINEERING: M. Renier, E. Brauer-Krisch
TECHNICIAN: T. Brochard
COMPUTING: G. Berruyer
SAFETY: P. Berkvens
STUDENT: C. Johannessen

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DIFFRACTION ENHANCED IMAGING GROUP

MEDICAL PERSONNEL: E. Pisano SCIENTISTS: D. Chapman, E. Johnston, D. Sayers, Z. Zhong

S. Fiedler:

Current status of the coronary angiography project at the ESRF

Current status of the coronary angiography project at the ESRF

by Stefan Fiedler



Collaborators



ESRF

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University Helsinki

P. Suortti





- Medical Motivation
- K-edge subtraction angiography
- instrumentation and procedures
- comparison of contrast agents (I versus Gd)
- first human patient at the ESRF
- conclusions & perspectives

History of Synchrotron coronary angiography patient programs



- Stanford / SSRL (Rubenstein et al.; '86)
- Brookhaven / NSLS(Thomlinson et al.; '90)
- Hamburg / Hasylab (Dix et al.; '90)

- Tsukuba / Photon Factory (Ando et al.; '96)



Epidemiology (industrialized countries)

Cardiovascular diseases is 1st cause of adult mortality. 30% of all deaths. 300.000 deaths/year (USA). In half of the cases the first sign of the disease is death !

Infarct

Stenosis of the coronary arteries. Ischemia of the heart muscle. Death.





aim:

imaging of coronary arteries down to 1mm diameter to detect narrowing of the aterial lumen due to atherosclerosis

difficulty:

small and moving structure

conventional method:

intra-arterial (femoral artery) catherterization

injection of iodine contrast agent to obtain image with filtered radiation from X-ray tube

wide spread method (e.g. 300 000 examinations per year in France)

Coronary Angiography lechniques

Conventional method.

advantages (+) excellent image quality 'cinematographic' imaging => combination with angioplasty disadvantages (invasive. i.e. & 1.5% complications (20.5% serious) EO. 1% mortality, 0.3% myocardial infarches, 20.1% cerebral vascular accidants allergic reaction to contrast agait MR! Fast CT Dichromography with SR

minimal invasive techniques :

Assume

ncludes

Bone





K-edge Digital Subtraction Angiography



principle :

- intravenous injection of contrast agent (I,Gd)
- simultaneous recording of two images with two energies above and below the K-edge of the contrast agent

• subtraction of the images (suppression of tissue and bone contrast) requirement for radiation source :

- two monochromatic beams wide enough to cover human heart
- intense enough to image arteries with a contrast agent diluted

(by factor of ~40) faster than one heartbeat i.e. ~10Gy/s

-> synchrotron

The aim is not to replace conventional angiography but to provide minimal invasive diagnostic tool particularly for follow up examinations after angioplasty (danger of re-stenosis: 30%).



Angiography Setup



Double line Ge-detector



Angiography Monochromator





Bent Laue monochromator

- Asymmetrically ct Si(111) crystal
- •water cooled (gravity flow); in He atmosphere
- Energy range:17 51 keV
- Focal spot: 0.75 * 150 mm²
- Focal distance: 7m (bending radius 12m)
- Energy bandwidth: 450eV
- •flux (angiography conditions) : 2.5 *1012 ph/s
- Harmonic content (60mm gap for 33keV) : 0.3%

Patient Positioning System / Imaging huch





Design for angiography & CT (6 degrees of freedom) Z-axis: • pneumatically assisted DC motor

- max. speed: 500mm/s
- •max. acceleration: 1m/s²
- 600 mm stroke
- Moving mass: 2.6T

Detector System



Germanium Detector

- Monolithic P-type Ge crystal
- Thickness: 2mm
- LN cooled
- Two lines with 432 pixels
- Spatial resolution: 350µm
- Active zone: 20 * 150 mm²
- Leakage current < 5pA/pixel

Electronics

- Charge integration mode (1ms 100ms)
- Dynamic range: 16bit (8 gain settings corresponding to 1.5pA – 16µA)
- 1 integrator and 1 ADC / pixel

PAtientSafetySystem



Simplified PASS diagram (if condition is ok, the contact is closed)



Dosimetry



- Doserate used for patient studies : approx.10Gy/s

(depending on wiggler gap, ring current, slit settings, filters)

- Dose per scan: 5 - 35mGy

(depending on chair speed and dose rate)

- Dose for entire examen: 200mGy

(comparable to conventional angiography)

- Dose is monitored during scan and inhibits exposure when exceeded



Doserate/Gap for 200mA ring current

wiggler gap [mm]







Right coronary artery

Left anterior descending artery

physical properties of lodine and Gadolinium



- for in vivo studies radiation dose is main limitation

large tissue attenuation at 33.17keV

->

choice of higher Z material as contrast agent

e.g. Gadolinium (50.2keV)

problem: available concentrations

Contrast medium	Iodine	Gadolinium
Atomic number	53	64
Atomic weight	126.9	157.25
Density [g/cm3]	4.92	7.88
Energy K-edge [keV]	33.169	50.239
$\frac{\mu}{\rho} [cm^2/g] \text{ contrast agent (E < Ek)}$	6.55	3.8
$\frac{\mu}{\rho} [cm^2/g] \text{ contrast agent } (E > Ek)$	35.93	18.53
$\frac{\Delta \mu}{\rho} [cm^2/g]_{\text{contrast agent}}$	29.38	14.73
$\frac{\mu_{ax}}{\rho} [cm^2/g]$ tissue	0.330	0.232
$\frac{\mu_{\rm shi}}{\rho} [cm^2/g]_{\rm tissue}$	0.116	0.041
$\frac{\mu_{ac}}{\rho} [cm^2/g]$ bone	0.630	0.230







Gadolinium

Cochon de 70 kg

Séquence temporelle (1.3 sec entre 2 images)

Agent de contraste : Gadobutrol (84 ml @ 157 mg/ml)

Injecté en veine cave supérieure

Dose de rayonnement X 24 mGy/Image

H. Elleaume INSERM 2000



Angiography Protocol

ESRF

26

- STEP 1: Conventional angiogram followed by angioplasty
- STEP 2: Follow-up medical examination 3 4 months later

If new anglogram is required :

- STEP 3: ESRF Transvenous Angiography within 1 week (target vessel: RCA)
- STEP 4: Conventional angiogram within 1 day


t = 16.834 t = 18

t = 18.095



LAO 30⁰ IODINE CONTRAST AGENT ESRF JAN. 27, 2000







LAO 30⁰ 10DINE CONTRAST AGENT ESRF JAN. 27, 2000





T=12.981 sec



T = 15.429 sec

Experimental challenges



Source & X-ray Optics:

- presence of higher harmonic energies (0.5% at 60mm wiggler gap) in monochromatic radiation reduces image contrast
- strong heat-load on crystal optics deforms horizontal beam profile
- •filters & windows can produce phase contrast
- Procedures and others
- superposition of arteries due to non-stereoscopic projection complicates diagnosis
- exact determination of transit times of contrast agent to coronary arteries needed to achieve optimum contrast
- synchronization of chair movement with ECG at high cardiac frequency in series of scans difficult (one scan within every heartbeat is desirable)

Summary



- Beamline for in-vivo k-edge subtraction technique commissoned
- Intravenous coronary angiography on pigs
- Comparison of I and Gd contrast agents higher concentrations of Gd needed
- First human patients examined
- Images of clinical relevance obtained (diagnosis confirmed by conventional angiograms)

In future :

- Extension of Medical protocol to other target vessels
- Improvement of optics (harmonics, heat-load)
- Faster Imaging
- Stereoscopic imaging?

D. Hermsdorf:

Biological experiments with low energetic charged particles

Motivation

- a lot of experiments with high energetic charged particles stimulated by research projects in astronautics and heavy ion therapy (GSI and HMI)
- rare experiments with low energetic charged particles (E< 10 MeV) with partially contradictory results
- further need for scientific research in:
 - ⇒ biological effect of Radon and Radon daughters (α -particles with $E_{\alpha} < 7.7$ MeV) (environmental exposition of human population)
 - ⇒ biological effect of neutrons (charged secondary particles, mainly recoilprotons with $E_p < E_n$) (safeguards and personal dosimetry)
 - \Rightarrow test of models for description of the biological effect of ionising radiation in dependence on
 - \rightarrow type of particle,
 - \rightarrow LET,
 - \rightarrow distribution structure of the deposited energy and others

Biological Experiments with Low Energetic Charged Particles

B. Dörschel, D. Hermsdorf und H. Kühne

Dresden University of Technology, Institute for radiation Protection Physics D- 01062 Dresden

Contents

- 1. Motivation
- 2. Problems for irradiation facilities
- 3. Problems for biological experiments
- 4. First results and outlook

State of Art

Demands for accelerator technique

- beam line with extraction (irradiation in air)
- acceleration of different particles (low and medium masses)
- acceleration in the energy range of interest (E< 10 MeV)
- operability of the accelerator in the nA current regime
- homogeneous radiation field in the order of 10 cm^2

Facilities with extracted particle beam in Germany:

Institution	Type of Accelerator	Particles and Energy/MeV	External beam	Remarks
HMI	· Cyclotron	р ~ 70	horizontal	essentially for therapy
1.MU (Garehing)	Tandem	p/d/α 24/24/36	vertical upwards	Test phase
PTB	Cyclotron van de Graff	p/α 20/28	vertixal down	under construction
FZR	Cyclotron	p/d/α 13/14/28	horizontal	put out of operation 12/1999
FZR/TUD	Tandem	p/d/α/C/O 9/9/14/24/32	horizontal	project for 2000

First Experiments

Cyclotron U-120 at Rossendorf Research Centre

Particles and nominal energies (at the exit window):

- \Rightarrow protons 7 and 13 MeV
- \Rightarrow deuterons 14 MeV
- $\Rightarrow \alpha$ -particles 28 MeV

Particle flux reduction :

- \Rightarrow scattering foil and beam collimation
- \Rightarrow Rutherford scattering



Ranges of particle flux: \Rightarrow direct beam up to 10^8 cm⁻² s⁻¹ \Rightarrow scattered beam < 100 cm⁻² s⁻¹

Homogeneous radiation field

Beam softening by scttering targets and air distance

Example: 8.2 MeV protons



Homogeneity of \pm 10% in a distance of \pm 1 cm from the beam axis

Determination of the Dose

Example: 8.2 MeV protons

- $d \approx 5 10 \, \mu m$ Thickness of the cell layer :
- $\Delta E \approx 30 60 \text{ keV}$ Energy loss within the layer:
- LET roughly constant in the layer ſî

 $LET = 5.5 \text{keV}/\mu\text{m}$

\Rightarrow Dose D can be approximated by:

$D = \varphi - \frac{1}{\rho} LETt$	3	particle flux density	density of the cell	linear energy transfer
	with	:. ტ	: d	LET:

irradiation time

Important: ſſ

using the spectral flux density resulting in a twofold in the case of a stronger energy loss within the cell depth in the layer has to be taken into account by layer the dependence of LET on the penetration integration procedure

Biological Test Experiments

(Institute for Zoology, TUD) (measurement of the enzymatic activity of the culture) R1 fish liver cells 8.2 MeV protons cell survival 1 to 100 Gy MTT-Test Biological end point: Method of Analysis: Range of Doses: Cell culture: **Particles:**

(background enhancement at higher Doses) detection of survived but non $S = \exp(-\alpha D - \beta D^2)$ Determination of simple photometry fertile cells Method of Evaluation: Disadvantage: Advantage: ᡗ Î



 \Rightarrow curvature β (shoulder)



DFG-Project

"Correlation of physical parameters with the cellulare effect of soft photons and low energetic charged particles"

Participants:

- \Rightarrow Institute for Zoology (Prof. Gutzeit)
- ⇒ Clinic for Radiation Therapy (Dr. Dörr)
- \Rightarrow Institute for Radiation Protection Physics

• Biological experiments

- \Rightarrow cell survival studies (improved analysis)
- \Rightarrow DNA- damage studies (Comet assay)
- \Rightarrow cytogenetic studies (FISH)
- \Rightarrow specific cell cycle studies (ELISA)
- \Rightarrow stress response studies (hsp70 expression)
- \Rightarrow genetic expressions (cDNA arras)

• Theoretical activities

- $\Rightarrow Description of the biological effect in dependence$ $on the energy deposited by <math>\delta$ -electrons in the vicinity of the track of a charged particle within a cell
- \Rightarrow Comparison with experimental results obtained by irradiations with soft photons from the

ELBE source

Future Activities

- beam extraction and set-up of a new irradiation facility at the Tandem of the Rosendorf research Centre
- improvement of the experimental conditions
- \Rightarrow Homogeneity of the radiation field
- \Rightarrow Management of the biological samples
- \Rightarrow other cell cultures (conventional cell types)
- Experiments with cells seeded and cultivated on radiation sensitive detectors
- \Rightarrow solid state nuclear track detectors (SSNTD, CR-39)
- \Rightarrow best properties for simultaneous
 - \Rightarrow particle identification
 - \Rightarrow localisation of hitted cells by image analysing system
 - \Rightarrow energy loss measurement
 - \Rightarrow cell layer thickness determination
- \Rightarrow position resolved dosimetry (Micro-Dosimetry)

A. Panteleeva:

Cell survival studies after X-ray irradiation

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Cell Survival Studies after X-ray Irradiation

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W. Dörr, B. Dörschel

TU Dresden

Workshop on X-rays from electron beams February 24 - 26, 2000

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Introduction

The **ELBE** Radiation Source for radiobiological studies

- Superconducting electron accelerator, producing an Electron beam of high quality (high Brilliance and low Emittance)
- In comparison to the synchrotron facilities, ELBE radiation source is cheaper
- in comparison to the sources of characteristic X-rays, ELBE produces X-rays of tuneable energy

Measurement of RBE of X-rays in the energy range 10-50 keV is the first research project

First stage of the project (performed at the Medical Science Dept. of TU Dresden)

- Acquiring experience with cell culture, and determination of growth conditions of the particular cell line
- Obtaining a reference cell-survival curve at a conventional X-ray source
- Determination of the special requirements to soft X-ray irradiation

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Determination of cell culture conditions

Cell line: NIH/3T3 mouse embryo ... wide - spread use for various studies

- well-established cell line
- contact-inhibited

Growth conditions :

- 37º incubator
- humidified atmosphere with 5% CO₂

Tested NIH/3T3 sources:

- ATCC collection
- DKFZ collection

Tested media: Medium1:

Dulbecco's MEM

- 10 % Fetal Calf Serum
- 20mM HEPES buffer
- 100U /100µg /ml penicillin / streptomycin
- 1mM Sodium pyruvate
- 1% (v/v) non-essential aminoacids

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Medium2:

Dulbecco's MEM

- 10 % Fetal Calf Serum
- 20mM HEPES buffer
- 100U /100µg /ml penicillin / streptomycin

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Irradiation with a conventional X-ray source:

- Cells are seeded in 25 cm² polystyrene culture flasks. allowed to reach confluence
- Irradiated as monolayer
- X-ray generator, operated at 200 kV / 20 mA, yielding a dose rate of 1.2 Gy/min

Survival assay:

- · Cells are trypsinized immediately after irradiaiton
- · Appropriate numbers of cells for each dose are seeded in 5mm Petri dishes
- · Cultures are fixed and stained after 10-11 days
- Colonies with more than 50 cells are scored as survivors

Plating efficiency of NIH/3T3 cells from DKFZ source in different media



Survival of NIH/3T3 cells (DKFZ source)



Survival of NIH/3T3 cells (ATCC source)



Different passages investigated



Data for NIH/3T3 survival from the literature

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Linear-quadratic Model fit of the X-ray irradiation survival

Each point represents the mean value of several experiments

Dose, Gy

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Multitarget Model fit of the X-ray irradiation survival



Literature Source	Plating Efficiency, %	D ₀ , Gy	n
Hetzel, 1976	not reported	1.30	6.5 ± 0.4
FitzGerald, 1985	4.3	1.45	9.10
Sklar, 1988	not reported	1.41 ± 0.12	3.4 ± 0.2
Kasid, 1989	not reported	2.02 ± 0.11	3.1 ± 0.8
Gorgojo, 1989	70 -100	1.18	6.5
Harris, 1990	not reported	1.35 ± 0.09	40 ± 5
Nagasawa, 1990	not reported	1.7	2.5
Samid, 1990	not reported	1.27 ± 0.09	3
present experiment	10.5	1.8 ± 0.1	2.7 ± 0.5

Literature data for NIH/3T3 cell line

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Experimental design for irradiation at ELBE

Requirements for irradiation with low-energy X-rays:

- Minimal thickness of material between cells and irradiation source
- Suitable membrane material, providing cell attachment and growth
- Sufficient amount of medium covering the cell monolayer

Beamline design requirements:

- Vertical position of cells during irradiation
- Comparatively long irradiation procedure (up to 40 min)



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Possibilities of cell survival without medium:

By the dye exclusion assay: Cells can survive only when covered with liquid

Membrane material	Pore size, μm	Growth of cells as monolayer	PE, %
Anopore 1)	0.02	good	8.1
Anopore ¹⁾	0.2	very good	8.4
polycarbonate 1)	3	very good	to be checked
polycarbonate 1)	0.4	very good	to be checked
PTFE ²⁾	0.4	bad	to be checked
polycarbonate ²⁾	0.4	excellent	to be checked

Determination of membrane properties:

Producer: ¹⁾ NUNC GmbH ²⁾ IWAKI corp

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Conclusions

Achieved results:

- Obtaining experience in cell survival studies and determination of the special requirements to soft Xray irradiation
- Obtaining a reference cell-survival curve at a conventional X-ray source, in a good agreement with literature data

Current stage of our research:

- Establishment of a cell laboratory at ELBE
- Design of the dose delivery system

Future plans:

- Extending the photon energy to the ultra-soft range
- Investigations with other radiation sources

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510

J. Pawelke:

A device for cell irradiation with low energy quasi-monochromatic photons at ELBE

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A Device for Cell Irradiation with Low Energy Quasi-Monochromatic Photons at ELBE

Workshop on X-rays from electron beams Rossendorf, February 24-26, 2000

J. Pawelke, W. Enghardt, U. Lehnert, B. Naumann, W. Neubert, A. Panteleeva, H. Prade, W. Wagner

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Introduction

Radiobiological Studies with Quasi-Monochromatic X-Rays at ELBE

Generation of secondary X-rays by:

Channeling radiation (10 keV $\leq E_{\gamma} \leq 100$ keV) Parametric X-rays (2 keV $\leq E_{\gamma} \leq 40$ keV)

- Transition radiation ($E_v \leq 0.5 \text{ keV}$)
- Compton backscattering

First research project:

Measurement of RBE of X-rays in the energy range 10-50 keV Cell survival studies after irradiation with channeling X-rays

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ELBE Facility



Beamline layout



•• magnet gap: 60 mm

RBE determination by cell survival

Requirements:

- Dose rate of ≥1Gy/min
- Homogeneous dose delivery to the irradiated field
- Sufficient low background radiation level
- Absolute dosimetry with high accuracy
- A cell laboratory available

Desirable:

Calculation of spatial and spectral dose distribution for channeling as well as background radiation



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Dose rate dependence on channeling photon energy

Calculations based on the experimental data

 of photon yield for channeling in diamond (110) plane, 1→ 0 transition, 10% BW [TU Darmstadt, H. Genz et al., Phys. Rev. B53 (1996) 8922]

and assuming:

- 100 μA electron beam (12 40 MeV)
- a 100 μm thick crystal
- 0.5 mm water equivalent absorbing material in front of the cell monolayer
- 20 µm cell monolayer



Angular distribution of channeling radiation



Distance dependence of dose rate and dose rate spread



Dose rate in the target centre

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Maximal dose rate difference in the target in percentage of the maximum dose rate

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Calculations are for 12 MeV and 20 MeV electron beams.

Background radiation

by

• other channeling transitions

e.g. 20 MeV electron energy $1 \rightarrow 0$ transition: photon energy: 30 keV dose rate: 1.5 Gy/min $2 \rightarrow 1$ transition: photon energy: 17 keV dose rate: 1.7 Gy/min

- bremsstrahlung
- neutrons generated by (γ,n) reaction

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Monte Carlo simulation by GEANT (CERN Program

Calculation of dose contribution by bremsstrahlung





742

target chamber

(Distance between channeling crystal and cell monolayer: 150 cm)

Sources of bremsstrahlung generation are: crystal, beam tube, magnet section

Calculation of dose contribution by bremsstrahlung



Calculation of dose contribution by neutrons

- <u>GEANT</u>: calculation of photon flux φ(r, E,)
- <u>Consider</u>: realistic beam line geometry
- <u>Assume:</u> all components are made from iron
- <u>S. Costa et al., Nuovo Cimento 51B (1967) 199:</u> photo-neutron reaction cross section σ_m(E,)
- <u>Calculate</u>: neutron production rate N_n
- <u>M. Barbier, Induced radioactivity, North Holland</u> <u>Publ. Co., Amsterdam, 1969:</u> neutron energy spectrum dN_n/dE_n for iron (E_n ≤ 6.5 MeV)
- J. Broerse, Monograph on basic physical data for neutron dosimetry: kerma factors for water
- <u>Consider</u>: target geometry ($\Delta x = 20 \ \mu m$, $\emptyset = 2 \ cm$)
- <u>Calculate</u>: dD/dt integrated over neutron spectrum

dD/dt = 0.8 cGy/min(quality factor: ~ 10)

Conclusion

- Modification of electron optical elements of the radiation physics beamline to
 - reduce background radiation
 - be more flexible about target positioning

Current stage of our research:

- More sophisticated calculation of dose contribution by neutrons (FLUKA, MCNP)
- Monte Carlo simulation for modified beamline
- Photon background suppression by Bragg reflection (HOPG)
- Design of dose delivery and dose monitoring system

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Modified beamline layout



- decreased distance between channeling crystal and dipole magnet section: 80 cm
- increased magnet gap: 110 mm

Reduction of bremsstrahlung (neutron) background by about a factor of 5



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9