Norman Kleiman, Ph.D.

Director, Eye Radiation and
Environmental Research Laboratory,
Columbia University Mailman
School of Public Health

Radiation Cataract

Recent insights and findings regarding risk of radiation cataract following occupational and environmental exposures



GILBERT W. BEEBE SYMPOSIUM ON 30 YEARS AFTER THE CHERNOBYL ACCIDENT

The National Academies of Sciences, Engineering and Medicine



INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION

ICRP ref 4825-3093-1464

Statement on Tissue Reactions

Approved by the Commission on April 21, 2011

(1) The Commission issued new recommendations on radiological protection in 2007 (ICRP, 2007), which formally replaced the Commission's 1990 Recommendations (ICRP, 1991a). The revised recommendations included consideration of the detriment arising from non-cancer effects of radiation on health. These effects, previously called deterministic effects, are now referred to as tissue reactions because it is increasingly recognised that some of these effects are not determined solely at the time of irradiation but can be modified after radiation exposure.







INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION

ICRP ref 4825-3093-1464

- (2) The Commission has now reviewed recent epidemiological evidence suggesting that there are some tissue reaction effects, particularly those with very late manifestation, where threshold doses are or might be lower than previously considered. For the lens of the eye, the threshold in absorbed dose is now considered to be **0.5 Gy**.
- (3) For occupational exposure in planned exposure situations the Commission now recommends an equivalent dose limit for the lens of the eye of **20 mSv** in a year, averaged over defined periods of 5 years, with no single year exceeding **50 mSv**.





Interventional cardiologists



Residents of contaminated buildings



Infants treated for facial hemangiomas



Chernobyl "Liquidators"

A-bomb survivors



Radiological technologists





Astronauts



Report of Task Group on the Implications of the Implementation of the ICRP Recommendations for a Revised Dose Limit to the Lens of the Eye Summary

This report was commissioned by the IRPA President to provide an assessment of the impact on members of IRPA Associate Societies of the introduction of ICRP recommendations for a reduced dose limit for the lens of the eye.

The report summarises current practice and considers possible changes that may be required.

Recommendations for further collaboration, clarification and changes to working practices are suggested.

May 2013







Immediate Release February 14, 2011

NCRP Releases Report No. 168, Radiation Dose Management for Fluoroscopically-Guided Interventional Medical Procedures

NCRP Report No. 168, Radiation Dose Management for Fluoroscopically-Guided Interventional Medical Procedures, provides recommendations and supporting information on radiation dose management for patients and medical staff during the use of fluoroscopic systems for guiding diagnostic and therapeutic medical procedures.





Radiation Exposure of the Anesthesiologist in the Neurointerventional Suite

Zirka H. Anastasian, M.D.,* Dorothea Strozyk, M.D.,† Philip M. Meyers, M.D.,‡ Shuang Wang, Ph.D.,§ Mitchell F. Berman, M.D., M.P.H.||

Anesthesiology 114, 512-520, 2011

Core Curriculum

A Summary of Recommendations for Occupational Radiation Protection in Interventional Cardiology

Ariel Durán, ¹ MD, FACC, Sim Kui Hian, ² MBBS, FRACP, Donald L. Miller, ³ MD, John Le Heron, ^{4*} BSc(Hons), FACPSEM, Renato Padovani, ⁵ PhD, and Eliseo Vano, ⁶ PhD

Journal of Radiation Research, 2013, 54, 315–321 doi: 10.1093/jrr/rrs104 Advance Access Publication 9 November 2012

Quantitative evaluation of light scattering intensities of the crystalline lens for radiation related minimal change in interventional radiologists: a cross-sectional pilot study

Toshi ABE^{1,*}, Shigeru FURUI², Hiroshi SASAKI³, Yasuo SAKAMOTO³, Shigeru SUZUKI⁴, Tatsuya ISHITAKE⁵, Kinuyo TERASAKI¹, Hiroshi KOHTAKE², Alexander M. NORBASH⁶, Richard H. BEHRMAN⁷ and Naofumi HAYABUCHI¹

Radiation-associated Lens Opacities in Catheterization Personnel: Results of a Survey and Direct Assessments

Eliseo Vano, PhD, Norman J. Kleiman, PhD, Ariel Duran, MD, Mariana Romano-Miller, MD, and Madan M. Rehani, PhD

J Vasc Interv Radiol 2013; 24:197-204

Radiation Protection Dosimetry (2011), pp. 1-5

doi:10.1093/rpd/ncr010

PRINCIPLES FOR THE DESIGN AND CALIBRATION OF RADIATION PROTECTION DOSEMETERS FOR OPERATIONAL AND PROTECTION QUANTITIES FOR EYE LENS DOSIMETRY

J. M. Bordy^{1,*}, G. Gualdrini², J. Daures¹ and F. Mariotti²

¹CEA, LIST, Laboratoire National Henri Becquerel (LNE LNHB), F91191 Gif sur Yvette Cedex, France ²ENEA-BAS-ION IRP Radiation Protection Institute, Via dei Colli 16, 40136 Bologna (BO), Italy

Radiation Protection Dosimetry (2011), pp. 1-5

doi:10.1093/rpd/ncr299

Catheterization and Cardiovascular Interventions 78:770–776 (2011)

RADIATION AND CATARACT

Madan M. Rehani^{1,*}, Eliseo Vano², Olivera Ciraj-Bjelac³ and Norman J. Kleiman⁴

¹International Atomic Energy Agency, Vienna, Austria

²Radiology Department, Complutense University, Madrid, Spain

³Vinca Institute of Nuclear Sciences, Belgrade, Serbia

Original Studies

Occupational Radiation Dose During Transcatheter
Aortic Valve Implantation

VALVULAR AND STRUCTURAL HEART DISEASES

Loes D. Sauren, 1* PhD, Leen van Garsse, 2 MD, Vincent van Ommen, 3 MD, PhD, and Gerrit J. Kemerink, 4 PhD





CATARACT

A change in transparency of the lens





Why study the lens?

Why do we still care about cataract?





Cataract and World Blindness

- 25 million blind people globally due to cataract
- 119 million individuals visually impaired by lens opacification
- Cataract is still the leading cause of blindness in the 3rd world
- Lens opacities can be found in 96% of all individuals older than 60 yrs
- With an increasingly healthy, aging population, the societal and economic burden of cataract surgery is expected to greatly increase
 - Cataract surgery represents 12% of the U.S. Medicare budget and 60% of all Medicare visual costs

WHO, 2002, Eye Diseases Research Prevalance Group, 2004









Hans Bethke



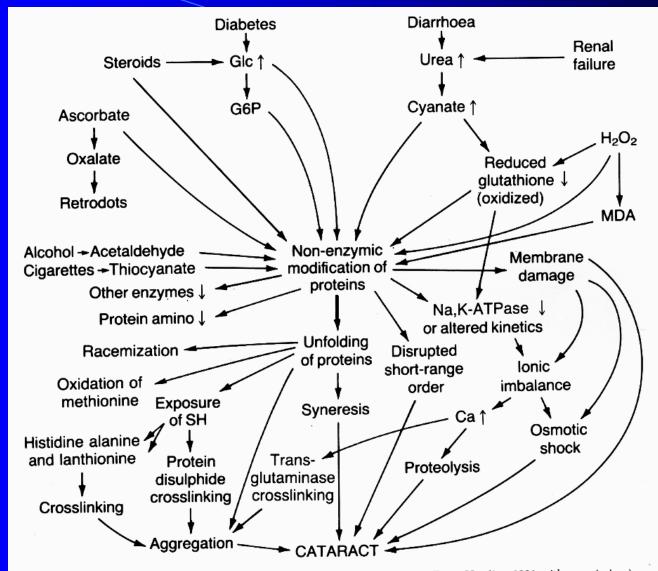


Figure 9.22 The pathways leading to lens protein degradation and cataract. (From Harding 1991 with permission.)



Major Cataract Subtypes

- Cortical
- Nuclear
- Posterior SubCapsular (psc)
- Mixed





RADIATION CATARACT

a specific subset of lens opacities





Posterior SubCapsular (PSC)



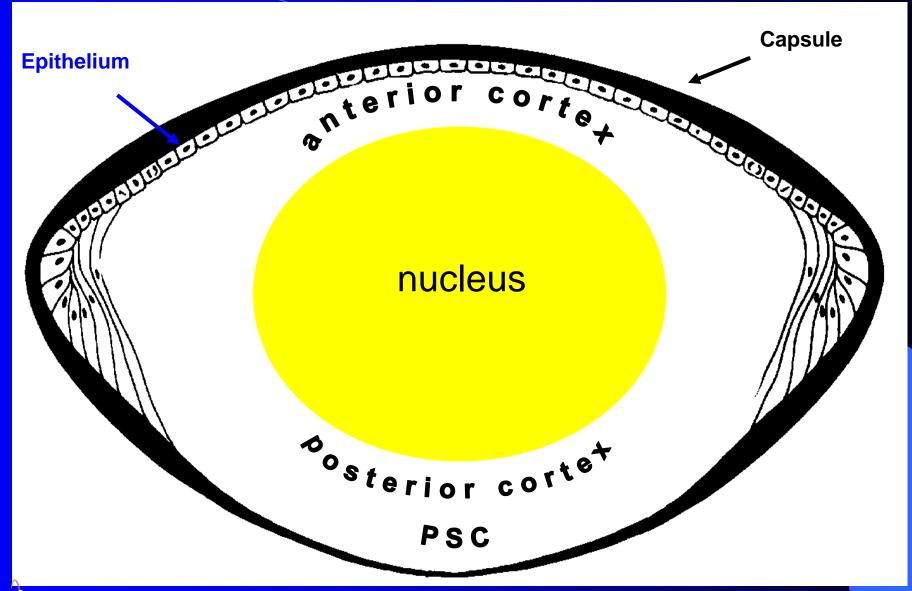


Classical Radiation Cataract

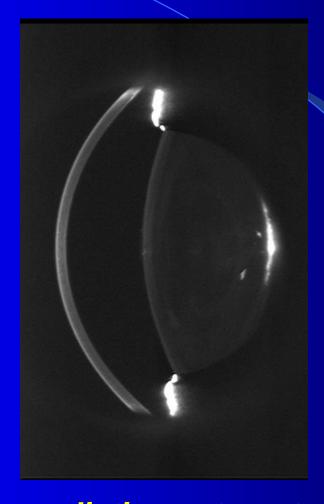
A lens opacity most often originating near the visual axis, first appearing in the posterior subcapsular region of the lens











radiation cataract (Scheimpflug image)





Why study radiation cataract?





Why do we care about radiation cataract?

- Impact on workers
- May be preventable
- Model for low-dose exposure
- Canary in a coal mine?



Before picking up a date, Doug always tested his breath on a canary that he kept in the car.







REVIEW Open Access

Cancer and non-cancer brain and eye effects of chronic low-dose ionizing radiation exposure

Eugenio Picano^{1*}, Eliseo Vano², Luciano Domenici³, Matteo Bottai⁴ and Isabelle Thierry-Chef⁵

Abstract

Background: According to a fundamental law of radiobiology ("Law of Bergonié and Tribondeau", 1906), the brain is a paradigm of a highly differentiated organ with low mitotic activity, and is thus radio-resistant. This assumption has been challenged by recent evidence discussed in the present review.

Results: lonizing radiation is an established environmental cause of brain cancer. Although direct evidence is lacking in contemporary fluoroscopy due to obvious sample size limitation, limited follow-up time and lack of focused research, anecdotal reports of clusters have appeared in the literature, raising the suspicion that brain cancer may be a professional disease of interventional cardiologists. In addition, although terminally differentiated neurons have reduced or mild proliferative capacity, and are therefore not regarded as critical radiation targets, adult neurogenesis occurs in the dentate gyrus of the hippocampus and the olfactory bulb, and is important for mood, learning/memory and normal olfactory function, whose impairment is a recognized early biomarker of neurodegenerative diseases. The head doses involved in radiotherapy are high, usually above 2 Sv, whereas the low-dose range of professional exposure typically involves lifetime cumulative whole-body exposure in the low-dose range of < 200 mSv, but with head exposure which may (in absence of protection) arrive at a head equivalent dose of 1 to 3 Sv after a professional lifetime (corresponding to a brain equivalent dose around 500 mSv).

Conclusions: At this point, a systematic assessment of brain (cancer and non-cancer) effects of chronic low-dose radiation exposure in interventional cardiologists and staff is needed.

Keywords: Brain cancer, Cognitive effects, Interventional cardiologist, Radiation exposure, Risk





- Terrestrial ionizing radiation and cataract
 - risk(s) to the general population
 - risk(s) to occupational workers
- Galactic cosmic radiation and cataract
 - risk(s) to space travelers
- Appropriateness of current dose limits
 - relevance of low dose radiation exposure and cataract to overall human health





Potential Low-Dose Radiation Exposures

- Accidental
 - Chernobyl, Fukushima, future??
 - contaminated buildings (e.g. Taiwan)
 - Goiânia
- Terrorism
 - dirty bomb
- Occupational
 - interventional physicians
 - associated nurses and technicians
 - nuclear medicine personnel
 - nuclear plant workers
 - industrial workers
 - astronauts
 - uranium miners
- Medical
 - Diagnostic procedures
 - Therapeutic treatments
- Environmental
 - geography (Denver, USA; Kerala, India; Ramsar, Iran)





The lens is one of the most radiosensitive of all tissues





The accessibility of the lens to repeated, non-invasive measurement facilitates long-term studies of low-dose radiation exposures.





Potential visual disability and morbidity resulting from radiation cataract and/or its treatment is greatly underappreciated.





Potential surgical/post-surgical complications of cataract extraction

- Endophthalmitis
- Uveitis
- Hyphema
- Corneal edema
- Choroidal hemmorrhage
- Cystoid macular edema
- Lens dislocation
- Rupture of the posterior capsule
- Retinal detachment
- Glaucoma
- Posterior subcapsular opacification
- Pain and discomfort





Cataract surgery risk estimates

- Posterior Sub-Capsular Opacification
 - 10%
- Cystoid Macular Edema
 - 1-10%
- Retinal Detachment
 - 0.5%
- Permanent Vision Loss
 - 0.1%
- Death
 - 0.01%





HEALTH PHYSICS SOCIETY
Comments on ANPR, 10 CFR 20
November 10, 2014
Docket ID No. NRC-2009-0279

Issue 2: Occupational Dose Limit for the Lens of the Eye

Q2–2: How should the impact of a radiation-induced cataract be viewed in comparison with other potential radiation effects?

Response: The Society wishes to bring the following information to the attention of the Commission:

"...available data suggests mortality following cataract surgery is on the order of 0.1% and that morbidity, defined both from an ophthalmological as well as medical standpoint, is consider-ably higher. Of equal import, prior to a documented clinical need for cataract surgery, there may be accompanying progressive decreases in visual acuity, contrast sensitivity and visual function that may negatively impact worker performance"

"In conclusion, the combined morbidity and mortality risks of surgical correction of radiation-induced cataracts (1% or more) and the, as yet unquantified, risk of a physician misdiagnosing or mistreating a patient because of loss of visual acuity due to the presence of an undiagnosed cataract, greatly outweighs the risk of cancer in affected individuals."



Radiation cataract provides a model for studying long-term biological effects following lowdose ionizing radiation exposures in environmental or occupational settings.





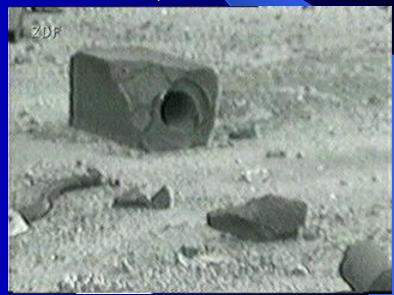
Chernobyl, USSR 1986



Chernobyl Nuclear Power Station Reactor 4



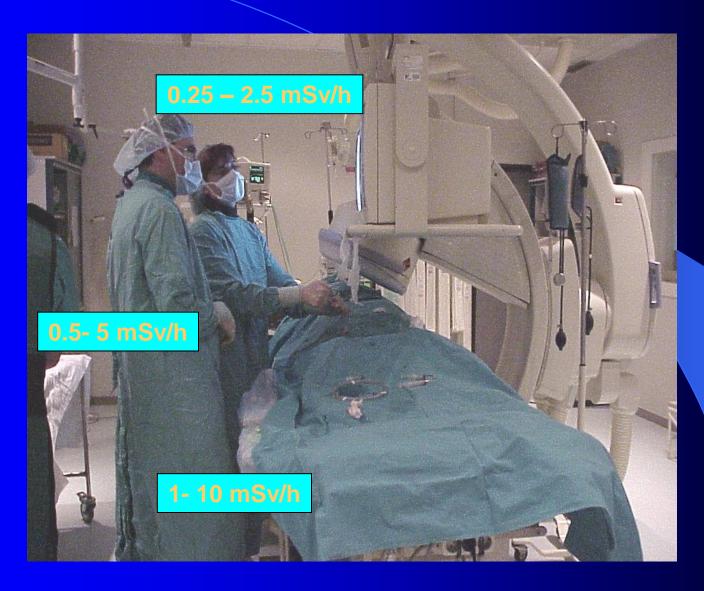
"Liquidators"



Radioactive graphite core ejected from the reactor



Interventional Medicine







Risk for Radiation-Induced Cataract for Staff in Interventional Cardiology: Is There Reason for Concern?

Olivera Ciraj-Bjelac, 1 PhD, Madan M. Rehani, 2* PhD, Kui Hian Sim, 3 MBBS, FRACP, Houng Bang Liew, 3 MBBS, FRCP, Eliseo Vano, 4 PhD, and Norman J. Kleiman, 5 PhD

Objectives: To examine the prevalence of radiation-associated lens opacities among interventional cardiologists and nurses and correlate with occupational radiation exposure. Background: Interventional cardiology personnel are exposed to relatively high levels of X-rays and based on recent findings of radiation-associated lens opacities in other cohorts, they may be at risk for cataract without use of ocular radiation protection. Methods: Eves of interventional cardiologists, nurses, and age- and sex-matched unexposed controls were screened by dilated slit lamp examination and posterior lens changes graded using a modified Merriam-Focht technique. Individual cumulative lens X-ray exposure was calculated from responses to a questionnaire and personal interview. Results: The prevalence of radiation-associated posterior lens opacities was 52% (29/56, 95% CI: 35-73) for interventional cardiologists, 45% (5/11, 95% CI: 15-100) for nurses, and 9% (2/22, 95% CI: 1-33) for controls. Relative risks of lens opacity was 5.7 (95% CI: 1.5-22) for interventional cardiologists and 5.0 (95% CI: 1.2-21) for nurses, Estimated cumulative ocular doses ranged from 0.01 to 43 Gv with mean and median values of 3.4 and 1.0 Gy, respectively. A strong dose-response relationship was found between occupational exposure and the prevalence of radiation-associated posterior lens changes. Conclusions: These findings demonstrate a dose dependent increased risk of posterior lens opacities for interventional cardiologists and nurses when radiation protection tools are not used. While study of a larger cohort is needed to confirm these findings, the results suggest ocular radio-protection should be utilized. © 2010

Key words: cardiac catheterization; fluoroscopy; occupational exposure; posterior subcapsular cataract (psc); lens op^ain.

RADIATION RESEARCH 174, 490-495 (2010) 0033-7587/10 \$15.00 © 2010 by Radiation Research Society. All rights of reproduction in any form reserved. DOI: 10.1667/RR2207.1

Radiation Cataract Risk in Interventional Cardiology Personnel

Eliseo Vano, al Norman J, Kleiman, bl. Ariel Duran, al Madan M, Rehani, al Dario Echeverrie and Mariana Cabrera

Radiology Department, Complutense University, Madrid, Spain; bepartment of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, New York; Invasive Cardiology, University Hospital, Montevideo, Uruguny; International Atomic Energy Agency, Vienna, Austria; Fundación Cardio Infantil, Bogota, Colombia; and Flundación Offalmologica Nacional, Bogota, Colombia

Vano, E., Kleiman, N. J., Duran, A., Rehani, M. M., Echeverri, D. and Cabrera, M. Radiation Cataract Risk in Interventional Cardiology Personnel. *Radiat. Res.* 174, 490–495 (2010). of such changes increases progressively with dose until vision is impaired and cataract extraction surgery is required (5, 6, 8). The latency of such changes is inversely related to dose. During typical fluoroscopy working conditions, and if radiation protection tools are

routinely used, X-ray exposure to the eyes of rventional cardiologists, other physicians and/or medical personnel working in catheterization labories can be high (9–14). These individuals often ain close to patients and may therefore be within a 1-scatter X-radiation field for several hours a day ng cardiac interventional procedures.

International Commission on Radiological P

Radiation-associated Lens Opacities in Catheterization Personnel: Results of a Survey and Direct Assessments

Eliseo Vano, PhD, Norman J. Kleiman, PhD, Ariel Duran, MD, Mariana Romano-Miller, MD, and Madan M. Rehani, PhD

ABSTRACT

Purpose: To estimate ocular radiation doses and prevalence of lens opacities in a group of interventional catheterization professionals and offer practical recommendations based on these findings to avoid future lens damage.

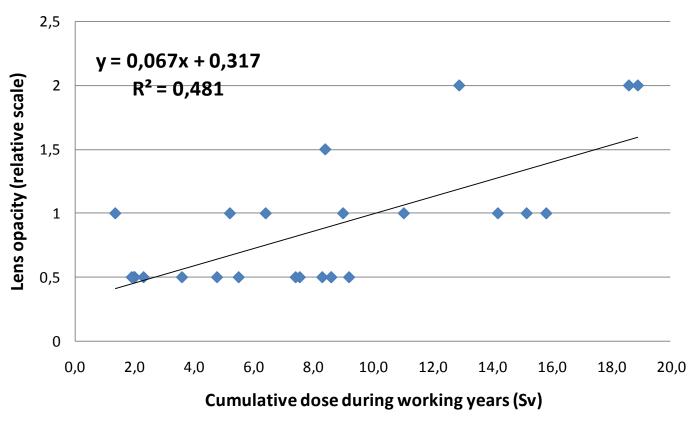
Materials and Methods: Subjects included 58 physicians and 69 nurses and technicians attending an interventional cardiology congress and appropriate unexposed age-matched controls. Lens dose estimates were derived from combining experimental measurements in catheterization laboratories with questionnaire responses regarding workload, types of procedures, and use of eye protection. Lens opacities were observed by dilated slit lamp examination using indirect illumination and retroillumination. The frequency and severity of posterior lens changes were compared between the exposed and unexposed groups. The severity of posterior lens changes was correlated with cumulative eye dose.

Results: Posterior subcapsular lens changes characteristic of ionizing radiation exposure were found in 50% of interventional cardiologists and 41% of nurses and technicians compared with findings of similar lens changes in < 10% of controls. Estimated cumulative eye doses ranged from 0.1–18.9 Sv. Most lens injuries result after several years of work without eye protection.

Conclusions: A high prevalence of lens changes likely induced by radiation exposure in the study population suggests an urgent need for improved radiation safety and training, use of eye protection during catheterization procedures, and improved occupational dosimetry.



Lens injury severity versus dose (cardiologists)



Vano, Kleiman, et al JVIR 2013





- Is there new data on human radiation cataract risk? Are proposed new eye dose limits appropriate?
- What is the relevance of radiation cataract in animal models to human radiobiology?
 - -Can we utilize radiation cataract as a "biomarker" of radiation exposure?
 - -Can we model radiation sensitivity and /or population heterogeneity effects using this approach
 -i.e., can we identify specific genes that confer sensitivity or resistance to radiation cataract?
- Can we find alternative methodologies for quantitating lens opacities for that better estimate any visual disability caused by radiation exposure?





Additional data regarding the dose threshold, if any, for visual disability is essential for better risk assessment and further refinement of suggested exposure guidelines.





How did we derive the guidelines for lens exposure limits?





Prior to 2012, eye exposure guidelines were based on the view that radiation cataract is a "deterministic" event with a relatively high threshold radiation dose





Lens Exposure Limits

| | Old | New |
|-----------------------|--------------------------------|---|
| Annual exposure limit | 150 mSv | 20 mSv (5 yr avg) |
| Cataract "threshold" | 2 Sv (acute) 8 Sv (chronic) | 0.5 Sv (acute) 0.5 Sv (chronic) 0.5 Sv (protracted) |





Establishing an accurate dose threshold, if any, for radiation cataractogenesis is critical for risk assessment and exposure guidelines.





1897: Chalupecky reports cataract in x-rayed rabbits







Chalupecky, H., "Ober die Wirkung der Rontgenstrahlen auf das Auge und die Haut. Centralbl. Augenheilk. 21, 234, 267, 368, 1897.





Early Radiation Cataract Studies

Ophthalmological survey of atomic bomb survivors in Japan in 1949" Trans. Am. Ophthalmol. Soc. 48, 1950





"Cyclotron-induced radiation cataracts" Science 110, 1949

- Chalupecky, 1897
- Rohrschneider, 1932
- Hiroshima, Nagasaki, 1945
- Cyclotron , 1940's
- Poppe, Cogan, 1950's
- Merriam & Focht, 1957, 1962
- Merriam & Worgul, 1976





Early Radiation Cataract Studies

- Important historical studies that helped define the nature of radiation cataract and establish initial guidelines for safe exposures to the lens.
- Failed to take into account increasing latency period as dose decreases.
- Did not have sufficient sensitivity to detect early lens changes.
- Relatively few subjects with doses below a few Gy.





Historical Threshold Estimates (Sv)

| threshold dose | reference | # subjects |
|----------------|-------------------------|------------|
| 5 - 15 | anecdotal, pre-1950 | 100 |
| 2 - 5.5 | Merriam and Focht, 1957 | 276 |
| 0.7 - 1.4 | Otake, 1982 | 2,124 |
| 0.4 - 0.7 | Woroul 2007 | 8 600 |





Additional data regarding the dose threshold, if any, for visual disability is essential for better occupational and environmental risk assessment and further refinement of suggested exposure guidelines.





Fukushima, Japan 2011



- Total releases somewhat uncertain
- Primarily ¹³¹I and ¹³⁷Cs

Future health consequences? Susceptible sub-populations? Eye pathology?





HUMAN STUDIES

Recent studies of radiation cataract risk: Epidemiological findings



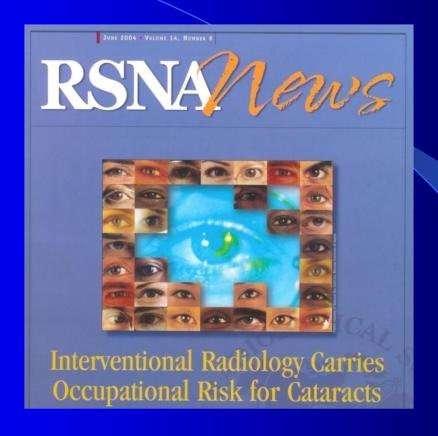


More recent studies are consistent with a very low or even zero threshold model for radiation cataract

| Diagnostic procedures | Klein, 1993 |
|------------------------|----------------------|
| Radiotherapy | Wilde, 1997 |
| | Hall, 1999 |
| Astronaut core | Cucinotta, 2001 |
| | Rastegar, 2002 |
| Atomic bomb survivors | Nakashima, 2006 |
| | Neriishi, 2007, 2012 |
| Contaminated buildings | Chen, 2001 |
| Chernobyl | Day, 1995 |
| | Worgul, 2007 |
| Occupational Risk | Worgul, 2004 |
| | Chodick, 2008 |







B.V. Worgul, Z.J. Haskal and A.K. Junk (2004) RSNA News 14, 5-6, 2004





Nakashima, Neriishi, et al. (2006) A reanalysis of atomic-bomb cataract data, 2000–2002: a threshold analysis. *Health Phys.* **90**, 154-160.

"exposure blind" evaluation of lens photographs

threshold dose estimate of 0.6 Gy and 0.7 Gy for cortical and psc opacities, respectively 95% confidence interval included 0 Gy

significant dose—response associations for posterior subcapsular opacities; OR@1Gy = 1.41

greater radiation risk for psc opacities among those exposed at younger ages





Neriishi, Nakashima, et al. (2007) Postoperative cataract cases among atomic bomb survivors: radiation dose response and threshold. *Rad Res* **168**:404-408.

Neriishi, Nakashima, et al. (2012) Radiation dose and cataract surgery incidence in atomic bomb survivors, 1986-2005. Radiology 265:167-174.

first documentation of <u>clinically relevant visual disability</u> (cataract extraction) following low dose exposure

threshold dose estimate of 0.45 Gy
95% confidence interval of 0.1-1.0Gy

At the time of the study (2005), the youngest survivors were only 57 years old, suggesting that additional cases may occur in future years.

Underestimates risk as some individuals may decline cataract extraction or be poor candidates for surgery.



Risk of Cataract after Exposure to Low Doses of Ionizing Radiation: A 20-Year Prospective Cohort Study among US Radiologic Technologists

G. Chodick, N. Bekiroglu, M. Hauptmann, B.H. Alexander, D.M. Freedman, M.M. Doody, L.C. Cheung, S.L. Simon, R.M. Weinstock, A. Bouville and A.J. Sigurdson

Am. J. Epidemiol. 168, 620-631 (2008)

- long term, prospective analysis of self-reported cataract diagnosis in 35,700 individuals 22-44 years old at study onset





Chernobyl





PREVALENCE OF LENS CHANGES IN UKRAINIAN CHILDREN RESIDING AROUND CHERNOBYL*

Richard Day, Michael B. Gorin, and Andrew W. Eller

Abstract-The objective of this study is to determine the prevalence and characteristics of lens changes in the eyes of a pediatric population, 5-17 y old, living in the permanent control zone around the Chernobyl nuclear reactor and to compare these findings with those from an unexposed control population. A total of 1,787 children are reported on (996 exposed and 791 unexposed). Over three-quarters of the subjects examined in this study show a form of minor change, termed focal lens defect, in the cortical and/or nuclear portions of the lens of the eye. The exposed group shows a small (3.6%), but statistically significant excess (p = 0.0005) of subclinical posterior subcapsular lens changes similar in form to changes identified in atomic bomb survivors. These posterior subcapsular changes tend to occur in boys 12-17 y old and in exposed children who report consuming locally grown mushrooms on a regular basis.

Health Phys. 68(5):632-642; 1995

Key words: Chernobyl; radiation effects; health effects; children

Lymphocytes, immature bone marrow cells, intestinal epithelium and germ cells are the most radiosensitive groups of cells in the human body. The lens of the eye, the lining of the stomach, esophagus, mouth, and skin are only slightly less sensitive to ionizing radiation (IAEA 1991). Radiation-induced lens opacities (cataracts) have been described after acute, high dose exposures in adults under clinical, occupational, wartime, and experimental conditions (Cogan 1950; Dodo 1962; Voelz 1967; Adams et al. 1983; CCMD 1981; Miller et al. 1967; Otake and Schull 1982, 1990; Mettler and Moseley 1985; Merriam and Focht 1957; Merriam and Worgul 1983; Worgul et al. 1991; Medvedovsky and Worgul 1991). The sensitivity of the lens of the eye in children, particularly under conditions of long-term exposure to low levels of ionizing radiation, has not been similarly assessed.

The BEIR V report (NAS 1990) concludes, on the

Health Phys, 1995

Table 3. Summary of posterior subcapsular lens changes in exposed and unexposed subjects.

| Posterior lens change's | Exposed $(n = 996)$ | Unexposed $(n = 791)$ | Total $(n = 1787)$ | Exact statistical significance (one-sided) |
|--|---------------------|-----------------------|--------------------|--|
| Heavy posterior subcapsular sheens | 8 (0.8%) | 1 (0.1%) | 9 (0.5%) | p=0.0439 ^a |
| Posterior subcapsular opacities (LOCSIII) | | | | |
| Level 1 | 23 (2.3%) | 8 (1.0%) | 31 (1.7%) | $p = 0.011^{b}$ |
| Level ≥2 | 5 (0.5%) | 0 (0.0%) | 5 (0.3%) | $p = 0.054^{\circ}$ |
| Total PSC opacities | 28 (2.8%) | 8 (1.0%) | 36 (2.0%) | $p = 0.0048^{d}$ |
| Any posterior lens change | 36 (3.6%) | 9 (1.1%) | 45 (2.5%) | $p = 0.0005^{\circ}$ |



Columbia University
MAILMAN SCHOOL
OF PUBLIC HEALTH

Radiation Protection Dosimetry Vol. 74, No. 4, pp. 235–238 (1997) Nuclear Technology Publishing

THE EVALUATION OF THE IRRADIATION LEVELS OF THE SKIN, EYE LENSES AND GONADS FOR CHERNOBYL LIQUIDATORS

D. P. OsanovState Research Centre of Russia, Institute of Biophysics123182 Zhivopisnaja 46, Moscow, Russia

Received March 25 1997, Amended September 1 1997, Accepted September 12 1997

Abstract — The γ as well as β radiation doses received by liquidators who performed clean-up works at the Chernobyl power plant in summer 1986 were measured. The measurements were conducted for the whole body, skin and eye lenses by using multilayer thermoluminescence dosemeters. In summer–autumn 1986 the absorbed doses of β radiation in the skin, eye lenses and gonads for liquidators working in the industrial area were more than the whole-body doses of γ radiation by factors of approximately 30, 4.5 and 3.0 respectively. Such levels of skin and eye lens irradiation are large enough for the induction of deterministic or stochastic effects.

Rad Prot Dosim, 1997

- Absorbed β-radiation doses to the eye lens are ~ 4.5x greater than whole body γ-radiation doses
- Mean γ whole body dose of 170 mGy (>1 Gy eye dose)
 Eye dose levels are consistent with development of
- radiation cataract in Liquidators

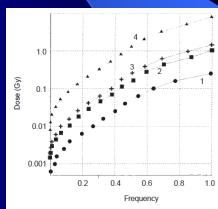


Figure 6. The integral frequency distributions of β radiation doses to the skin (4), to the eye lenses (3), to the gonads (2) and total body (1) γ -radiation for liquidator constructing the Chemobyl Sarcophagus in 1986.





The Ukrainian American Chernobyl Ocular Study (UACQS)

- A cohort epidemiological study of cataract onset and progression in Liquidators.
- Included longitudinal quantitative nonsubjective analyses of radiation cataract development and progression in a relatively low-dose exposed human population.
- Acquisition, archiving and molecular analyses of lens tissue removed during cataract surgery.

Ukrainian Ministry of Health Mailman School of Public Health Department of Energy National Cancer Institute





Cataracts among Chernobyl clean-up worker: Implications regarding permissible eye exposures

B.V. Worgul, Y.I. Kundiyev, N.M. Sergiyenko, V.V. Chumak, P.M. Vitte, C.P Medvedovsky, E.V. Bakhanova, A.K. Junk, O.Y. Kyrychenko, N.V. Musijachencko, S.A. Shylo, O.P. Vitte, S. Xu, X. Xue and R.E. Shore

Radiat. Res. 167, 233-243 (2007)

The Ukrainian American Chernobyl Ocular Study (UACOS)









Numbers of Subjects and Exclusions

| | | 0/ |
|--|--------|----------|
| Circumstance | Number | % |
| 1. Total Database received from SCRM | 32,826 | |
| 2. Examined cohort (Total) | 12,638 | |
| 3. Examined subjects who are not included in the total Database received from SCRM | 841 | |
| 4. Included subjects in cohort for analysis | 11,797 | 100.0 |
| 5. Excluded number with preliminary ophthalmological criteria | 507 | 4.3 |
| 6. Excluded number with preliminary epidemiological criteria | 1,337 | 11.3 |
| 7. Cohort subject to epidemiological analysis | 9,953 | 84.4 |
| 8. Excluded number with dosimetry criteria | 1,346 | 11.4 |
| 9. Cohort analyzed epidemiologically which have confirmed and reconstructed doses. | 8,607 | 73.0 |





Selected Variables* vs. Geometric-Mean Dose Group

| | Dose Groups (mSv) | | | | | |
|------------------------------|-------------------|----------------|---------------|-----------------|-----------------|----------------|
| Variable | 0-49 | 50-99 | 100-199 | 200-399 | 400-699 | 700+ |
| No. of Workers | 1,300 | 1,550 | 3,776 | 1,431 | 364 | 186 |
| Geometric Mean Dose | 26.1 ± 16.5 | 78.1 ± 15.0 | 136.6 ± 26.3 | 266.1 ± 47.7 | 534.3 ± 87.0 | 974.8 ± 307.4 |
| Arithmetic Mean Dose | 32.4 ± 21.0 | 99.1 ± 19.7 | 174.2 ± 33.5 | 340.3 ± 61.5 | 665.7 ± 126.2 | 1197.4 ± 349.5 |
| Age at Exposure | 34.2 ± 8.2 | 32.0 ± 6.8 | 31.8 ± 6.5 | 32.3 ± 7.4 | 37.8 ± 8.5 | 39.9 ± 7.2 |
| Age at 1 st Exam. | 46.4 ± 8.4 | 44.4 ± 6.8 | 43.9 ± 6.5 | 44.5 ± 7.5 | 50.4 ± 8.7 | 52.0 ± 7.4 |







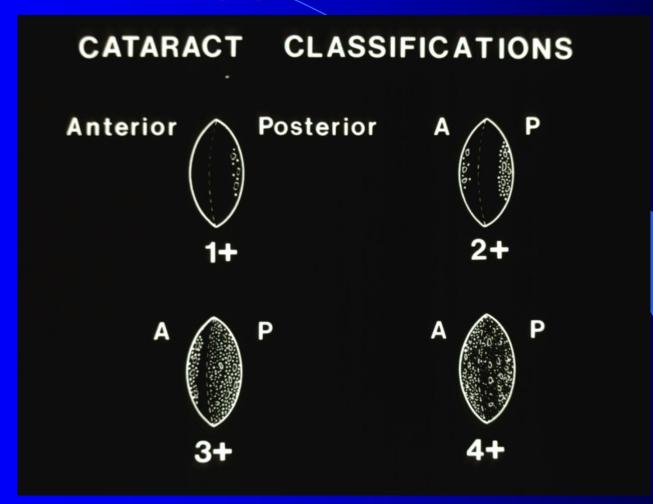
Cataract Staging

Focht & Merriam, 1957





Slit Lamp Imaging of Radiation Cataract Grades



Merriam-Focht Scoring





Outcomes at 1st Examination ("Prevalence" Data)

| Outcome | Either Eye | Left Eye | Right Eye | |
|--|--------------|--------------|--------------|--|
| | N (%) | N (%) | N (%) | |
| Polychromatic sheen | 1575 (25.6) | 1,516 (25.0) | 1,532 (25.2) | |
| Early pre-cataract changes | 2,211 (32.7) | 2128 (31.8) | 2149 (32.0) | |
| Stage 1-5 cataract | 1,944 (22.6) | 1,889 (22.0) | 1,862 (21.7) | |
| Stage 1 cataract | 1,870 (21.9) | 1811 (21.3) | 1780 (21.0) | |
| Stage 2 cataract | 97 (1.1) | 69 (0.8) | 76 (0.9) | |
| Stage 3-5 cataract | 15 (0.2) | 9 (0.1) | 6 (0.1) | |
| Stage 1-5 cataract, excluding nuclear | 1,757 (20.4) | 1,697 (19.7) | 1,672 (19.5) | |
| Stage 1 cataract, excluding nuclear | 1,693 (19.7) | 1634 (19.0) | 1604 (18.7) | |
| Stage 2-5 cataract, excluding nuclear | 90 (1.1) | 63 (0.7) | 68 (0.8) | |
| Early PSC changes | 1580 (18.4) | 1502 (17.5) | 1516 (17.6) | |
| Stage 1 PSC cataract | 1464 (17.2) | 1397 (16.5) | 1384 (16.3) | |
| Early Superficial Post. Cort. Changes | 1912 (28.2) | 1833 (27.3) | 1849 (27.5) | |
| Stage 1 Superficial Post. Cort Cataract | 1817 (21.2) | 1733 (20.3) | 1730 (20.3) | |





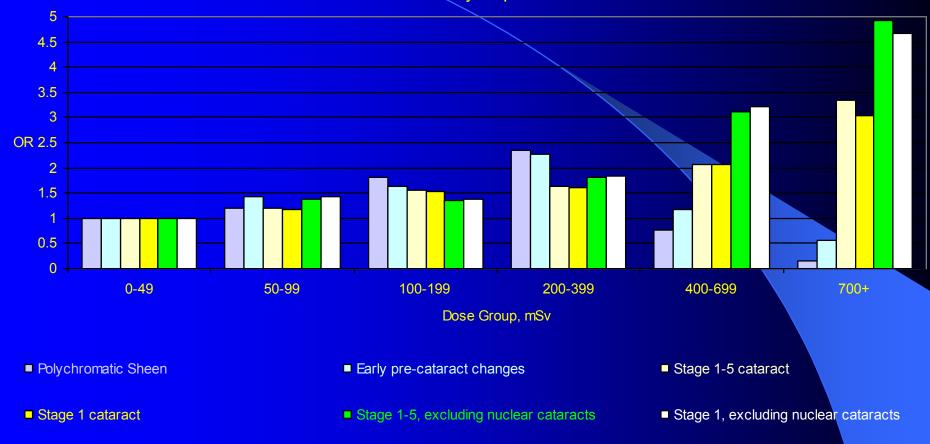
Outcomes at 2nd Examination (Incidence Data)

| Outcome | Either Eye N (%) | Left Eye N (%) | Right Eye N (%) |
|--|---------------------|-------------------|--------------------|
| Polychromatic sheen | 425 (9.6) | 417 (9.5) | 412 (9.4) |
| Early pre-cataract changes | 488 (11.0) | 465 (10.6) | 462 (10.5) |
| Stage 1-5 cataract | 387 (5.7) | 361 (5.4) | 366 (5.4) |
| Stage 1 cataract | 381 (5.6) | 354 (5.3) | 358 (5.4) |
| Stage 2 cataract | 20 (0.2) | 16 (0.2) | 16 (0.2) |
| Stage 3-5 cataract | 7 (0.1) | 4 (0.1) | 6 (0.1) |
| Opacity progression | | 828 (9.6) | 836 (9.7) |
| Stage 1-5 cataract, excluding nuclear | 274 (3.9) | 254 (3.7) | 256 (3.7) |
| Stage 1 cataract, excluding nuclear | 268 (3.8) | 248 (3.6) | 250 (3.6) |
| Stage 2-5 cataract, excluding nuclear | 16 (0.2) | 11 (0.1) | 12 (0.1) |
| Early PSC changes | 541 (17.6) | 517 (17.3) | 512 (7.2) |
| Stage 1 PSC cataract | 252 (3.5) | 230 (3.2) | 235 (3.3) |
| Early Superficial Changes | 297 (6.7) | 284 (6.5) | 280 (6.4) |
| Stage 1 Superficial Post. Cort. Cataract | 295 (4.4) | 267 (4.0) | 277 (4.1) |





Adjusted Odds Ratios for Cataract Outcome Variables (Incidence Data) Among the Chernobyl Liquidators

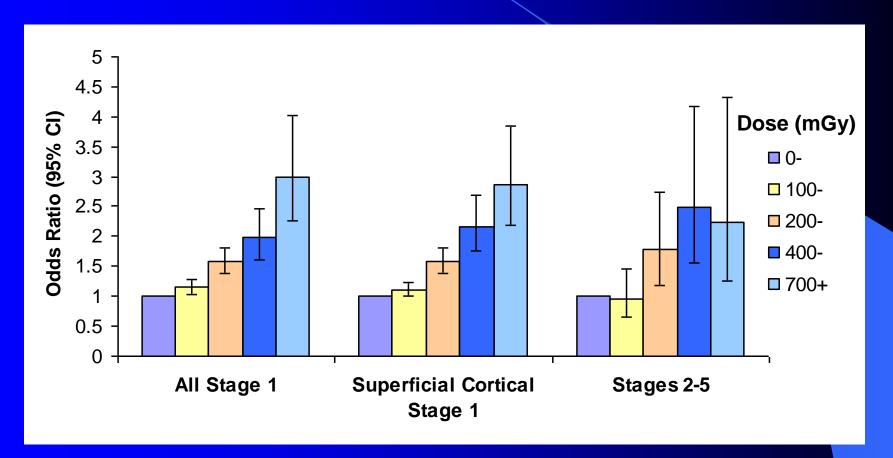


- 30% prevalence of pre-cataractous changes at first exam
- Median dose 123 mGy
- Dose threshold estimates of 350 mGy, CI not exceeding 700 mGy
- Dose response relationship for several endpoints
 - (e.g., stage 1 cataract; OR @ 1Gy = 1.42)





Cataracts According to Lens Radiation Dose in Chernobyl Cleanup Workers







These new studies provide additional support for the hypothesis that the threshold radiation cataract dose in human populations may be significantly lower than currently accepted.



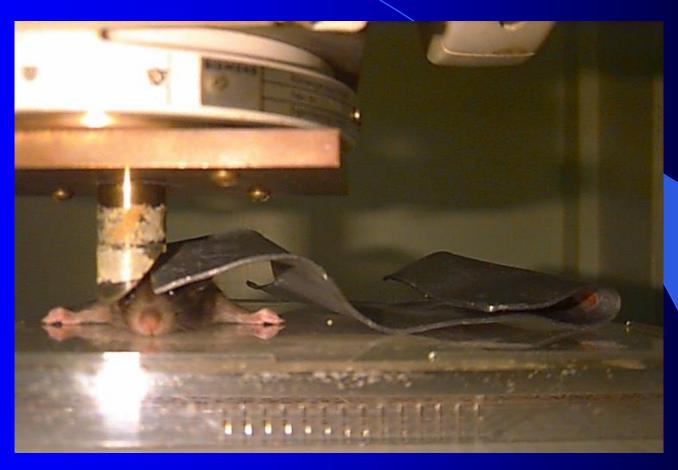


ANIMAL STUDIES





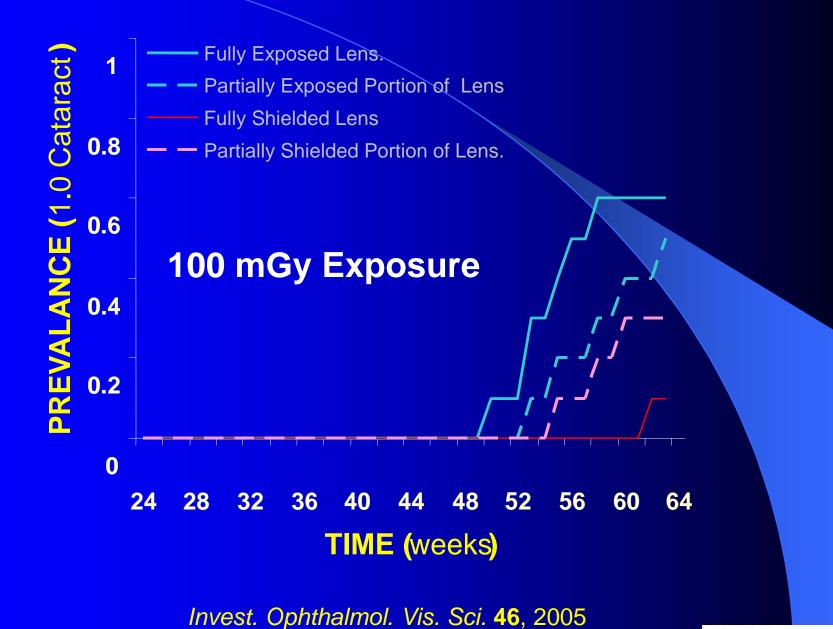
LABORATORY STUDIES

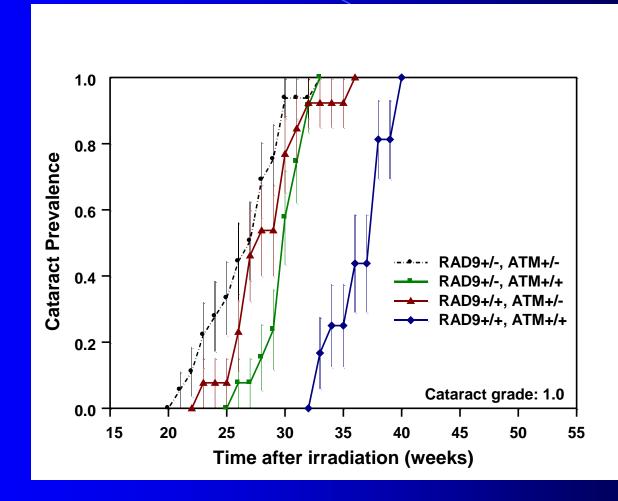


Irradiation of the mouse lens by 500 mGy X-ray (Contralateral eye shielded)





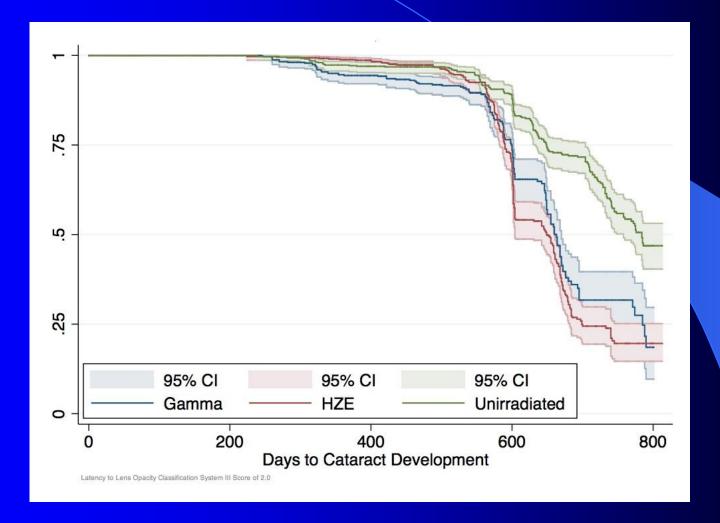








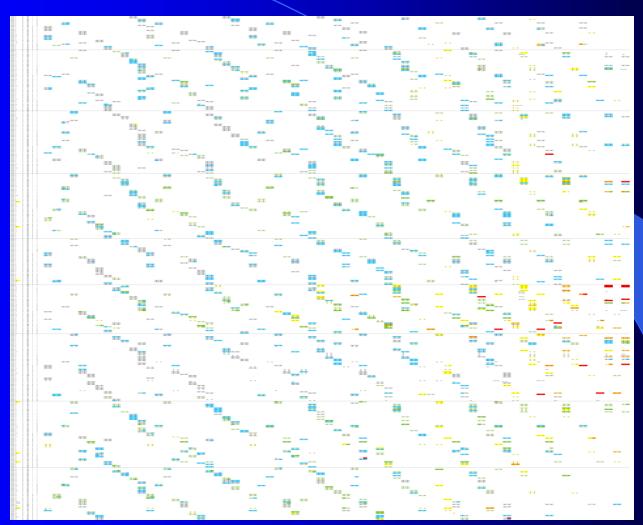
Cataract Prevalence among unexposed, gamma and HZE irradiated outbred mice







Familial Predisposition for Radiation Cataract in Outbred Mouse Populations



Family grouping



time



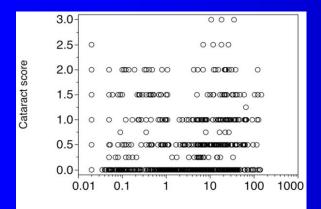
ECOLOGICAL STUDIES





Elevated Frequency of Cataracts in Birds from Chernobyl





Background radiation (μSv/h)

Mean cataracts in birds from Chernobyl in relation to background radiation level

Elevated Frequency of Cataracts in Birds from Chernobyl

Timothy Alexander Mousseau¹, Anders Pape Møller²*

1 Department of Biological Sciences, University of South Carolina, Columbia, South Carolina, United States of America, 2 Laboratoire d'Ecologie, Systématique et Evolution, CNRS UMR 8079, Université Paris-Sud, Orsay, France

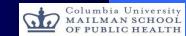
Abstract

Background: Radiation cataracts develop as a consequence of the effects of ionizing radiation on the development of the lens of the eye with an opaque lens reducing or eliminating the ability to see. Therefore, we would expect cataracts to be associated with reduced fitness in free-living animals.

Methodology/Principal Findings: We investigated the incidence of lens opacities typical of cataracts in more than 1100 free-living birds in the Chemobyl region in relation to background radiation. The incidence of cataracts increased with level of background radiation both in analyses based on a dichotomous score and in analyses of continuous scores of intensity of cataracts. The odds ratio per unit change in the regressor was 0.722 (95% CI 0.648, 0.804), which was less than odds ratios from investigations of radiation cataracts in humans. The relatively small odds ratio may be due to increased mortality in birds with cataracts. We found a stronger negative relationship between bird abundance and background radiation when the frequency of cataracts was higher, but also a direct effect of radiation on abundance, suggesting that radiation indirectly affects abundance negatively through an increase in the frequency of cataracts in bird populations, but also through direct effects of radiation on other diseases, food abundance and interactions with other species. There was no increase in incidence of cataracts with increasing age, suggesting that yearlings and older individuals were similarly affected as is typical of radiation cataract.

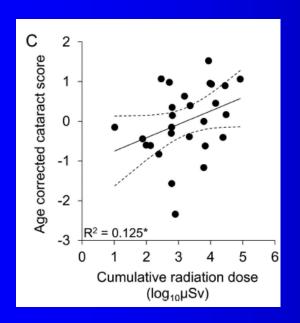
Conclusions/Significance: These findings suggest that cataracts are an under-estimated cause of morbidity in free-living birds and, by inference, other vertebrates in areas contaminated with radioactive materials.

PLoS ONE 8(7): e66939; 2013





Age-Adjusted Cataract Severity in Chernobyl Vole Populations



Fitness costs of increased cataract frequency and cumulative radiation dose in natural mammalian populations from Chernobyl

Philipp Lehmann^{1,2}, Zbyszek Boratyński³, Tapio Mappes¹, Timothy A. Mousseau⁴ & Anders P. Møller⁵

A cataract is a clouding of the lens that reduces light transmission to the retina, and it decreases the visual acuity of the bearer. The prevalence of cataracts in natural populations of mammals, and their potential ecological significance, is poorly known. Cataracts have been reported to arise from high levels of oxidative stress and a major cause of oxidative stress is ionizing radiation. We investigated whether elevated frequencies of cataracts are found in eyes of bank voles *Myodes glareolus* collected from natural populations in areas with varying levels of background radiation in Chernobyl. We found high frequencies of cataracts in voles collected from different areas in Chernobyl. The frequency of cataracts was positively correlated with age, and in females also with the accumulated radiation dose.

Sci Rep 6, 19974; 2016

| | Total N | Length (mm) | Weight (g) | Molar length (mm) | Cataracts (score*) | Radiation (μSv/hour) | Accumulated radiation (μSv) |
|---------|------------|----------------|--------------|-------------------------|-----------------------|-------------------------|-----------------------------|
| Females | 34 | 92.9 ± 1.2 | 22.5 ± 0.8 | 1.2 ± 0.2 | 2.0 ± 0.3 | 2.5 ± 0.8 | 8020 ± 2924 |
| Males | 54 | 90.8 ± 1.1 | 22.2 ± 0.6 | 0.9 ± 0.1 | 2.1 ± 0.2 | 1.4 ± 0.3 | 6909 ± 2317 |







Biol. Lett. (2007) 3, 483-486 doi:10.1098/rsbl.2007.0226 Published online 14 August 2007

Community ecology

Species richness and abundance of forest birds in relation to radiation at Chernobyl

A. P. Møller^{1,*} and T. A. Mousseau²

¹Laboratoire de Parasitologie Evolutive, CNRS UMR 7103, Université Pierre et Marie Curie, Bâtiment A, 7ème étage, 7 quai St Bernard, Case 237, 75252 Paris Cedex 05, France

²Department of Biological Sciences, University of South Carolina, Columbia, SC 29208, USA

*Author for correspondence (amoller@snv.jussieu.fr).

The effects of low-level radiation on the abundance of animals are poorly known, as are the effects on ecosystems and their functioning. Recent conclusions from the biology forum and reports in the popul cerning the effects of radiation filet on animals have left the impre Evolutionary biology Chernobyl exclusion zone is a tl tem, filled with an increasing n species. Surprisingly, there are n



Published online 27 November 2007

Biol. Lett. (2008) 4, 63-64

doi:10.1098/rsbl.2007.0430

Comment

Is Chernobyl radiation really causing negative individual and populationlevel effects on barn swallows?

Møller and co-workers (Møller et al. 2007) observe an 'elevated frequency of abnormalities in barn swallows (Hirundo rustica) at Chernobyl' and 'can think of no alternative explanations other than exposure to radiation that can have caused the observed patterns'. However, an obvious alternative hypothesis (e.g. Pikulik & Plenin 1994) is that apparent impacts on birds may be due to ecosystem changes resulting from the abandonment of contaminated land. In this and previous papers, Møller



Biol. Lett. (2007) 3, 414-417 doi:10.1098/rsbl.2007.0136 Published online 17 April 2007

Evolutionary biology

Elevated frequency of abnormalities in barn swallows from Chernobyl

A. P. Møller^{1,*}, T. A. Mousseau², F. de Lope³ and N. Saino4

Growing Up with Chernobyl

Working in a radioactive zone, two scientists learn tough lessons about politics, bias and the challenges of doing good science

Correspondence

Long-term census data reveal abundant wildlife populations at Chernobyl

T.G. Deryabina¹, S.V. Kuchmel¹, L.L. Nagorskaya², T.G. Hinton³, J.C. Beasley⁴, A. Lerebours⁵, and J.T. Smith5,*

Following the 1986 Chernobyl accident, 116,000 people were permanently evacuated from the 4,200 km² Chernobyl exclusion zone [1]. There is continuing scientific and public debate surrounding the fate of wildlife that remained in the abandoned area. Several previous studies of the Chernobyl exclusion zone (e.g. [2,3]) indicated major radiation effects and





Lens Changes in Wild Mice and Voles from Chernobyl





Rodent Species Trapped



Apodemus sylvaticus





Myodes glareolus







Trap Locations and Dose Rates

Physical Locations

- >60 different trap locations throughout the Exclusion Zone
- mean µSv/hr determined from 16 measurements in each trap location (4m x 4m grid)
- Range = 0.18 ("cold") to >130 μSv/hr ("hot")





"Red Forest"





730 μSv/hr









Pripyat



1.05 µSv/hr









Wooded Forest





NPP





Chornobyl Town







Mushrooms



17.26 μSv/hr



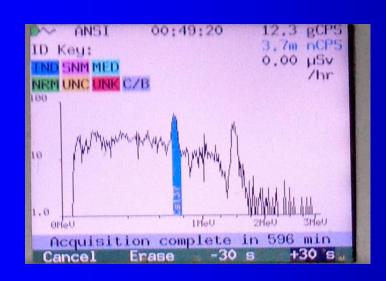
62.89 μSv/hr



Gamma Counts

Individual Whole Body Gamma Counts

- >180 voles and >120 mice
- Dose range = 10-20 cpm (background) to >5,000 cpm









The "Lab"

















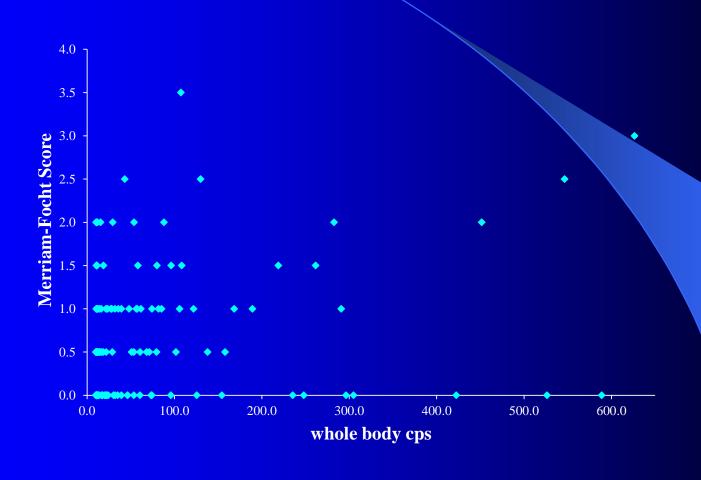
Physical Measurements

- Weight
- Length
- Gender
- Head diameter
- Physical examination
- Whole body gamma count
- Dilated slit lamp exam
- Intraocular pressure





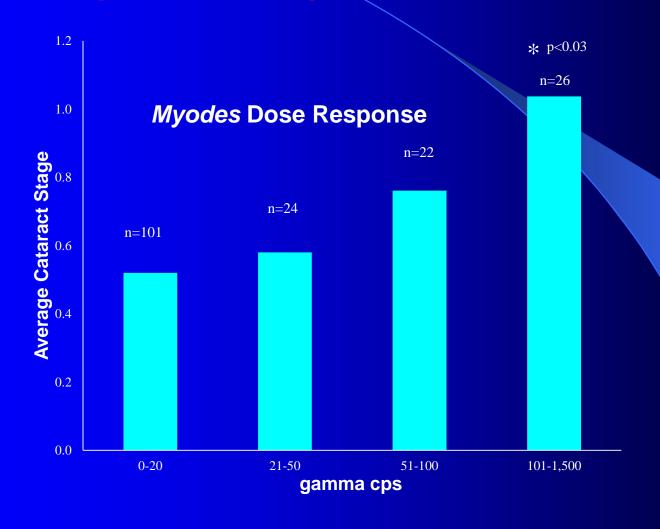
PSC severity in Chernobyl voles







Average M-F Stage in Chernobyl Voles







Findings

No overt, visually disabling cataract observed Merriam-Focht lens opacity scores relatively low PSC prevalence lower than expected

- Relatively young age of all animals
 - Very few older mice or voles
 AND
- suspected high mortality for visually impaired animals











Kiev University Voles

Radiation Cataract Prevalence in <u>captive</u> Myodes trapped in "cold" regions or "hot" regions at young ages and raised in captivity at Kiev University for 20+ months

- Captured in either Kiev or Chernobyl at ~ 2 months old
 - Old animals average age = 22 months
 - n=70









Cataract prevalence in "old" hot voles

| | Kiev captured-young | Kiev captured-old | "Hot" Chernobyl captured-old |
|--------------------------|------------------------|----------------------|---------------------------------|
| | | | |
| M-F Score 0.5 or greater | 0.19 | 0.11 | 0.76 * |
| M-F Score 1.0 or greater | 0 | 0 | 0.14* |
| | | | |

| | Kiev captured-female | Kiev captured-male | "Hot" Chernobyl captured-female | "Hot" Chernobyl captured-male |
|--------------------------|-------------------------|-----------------------|---------------------------------|-------------------------------|
| | | | | |
| M-F Score 0.5 or greater | 0.13 | 0.24 | 0.80* | 0.73* |
| M-F Score 1.0 or greater | 0 | 0 | 0.0 | 0.27* |
| | | | | |





Conclusions

Recent findings in both human and animal populations exposed to radiation as a result of the Chernobyl nuclear accident, as well as in other epidemiological cohorts, support radiation cataract development after relatively low environmental exposures.





Additional studies, including continuing follow-up of the Chernobyl Liquidator cohort, may help further refine appropriate risk guidelines and the radiation cataract "threshold" for environmental and/or occupational exposures





Radiation cataract provides a unique model for studying longterm human health effects following low-dose ionizing radiation exposures in environmental or occupational settings.





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Colorado State University

Mike Weil, PhD

National Council on Radiation Protection (NCRP)

Committee 2-3: Radiation Safety Issues for Image-Guided

Interventional Medical Procedures; Steve Balter, PhD

International Commission on Radiological Protection (ICRP)

Symposium Organizing Committee, Julian Preston, PhD

Committee 1; Tissue reactions and other non-cancer effects of radiation;

Fiona Stewart, PhD

IAEA

RELID: Madan Rehani, PhD, Eliseo Vano, PhD

U.S. Department of Energy (DOE)

Low-dose Radiation Research program

NASA

Space Radiation Health Program













LOW DOSE RADIATION RESEARCH PROGRAM

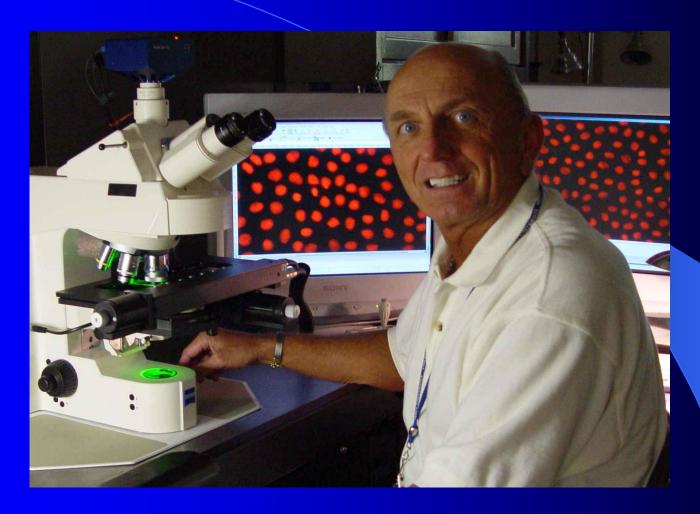












Basil V. Worgul, Ph.D., 1947-2006
Professor of Radiation Biology
Departments of Ophthalmology and Radiology
Columbia University



