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School of Public Health

Radiation-related Cataracts in Clean-up Workers

Radiation Epidemiology & Dosimetry Course

National Cancer Institute www.dceg.cancer.gov/RadEpiCourse

Scientific and epidemiological background for radiation risk to the lens of the eye

Norman J. Kleiman, Ph.D.

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Mailman School of Public Health
Columbia University, New York, NY

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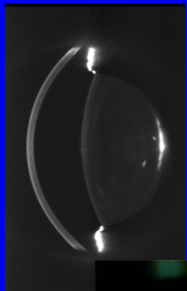

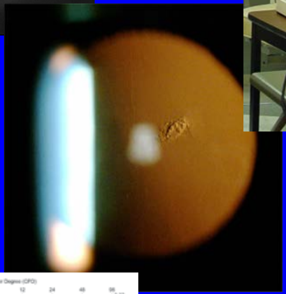

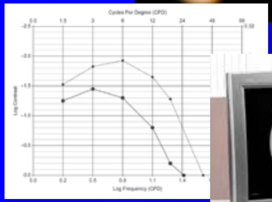

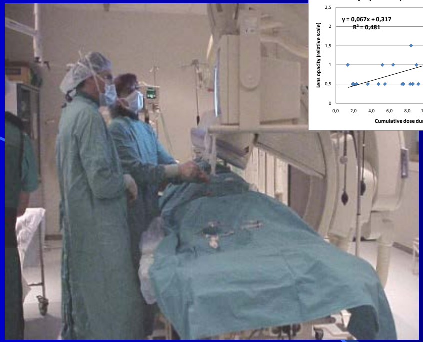

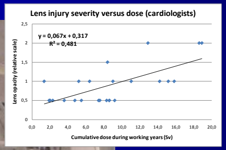

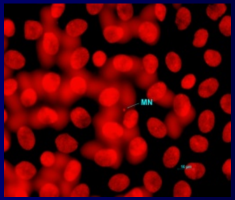

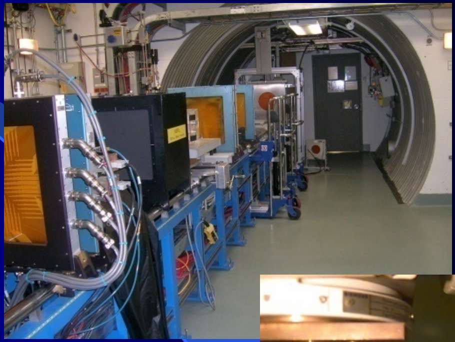

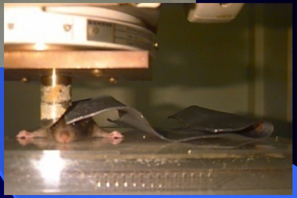

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INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION

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.

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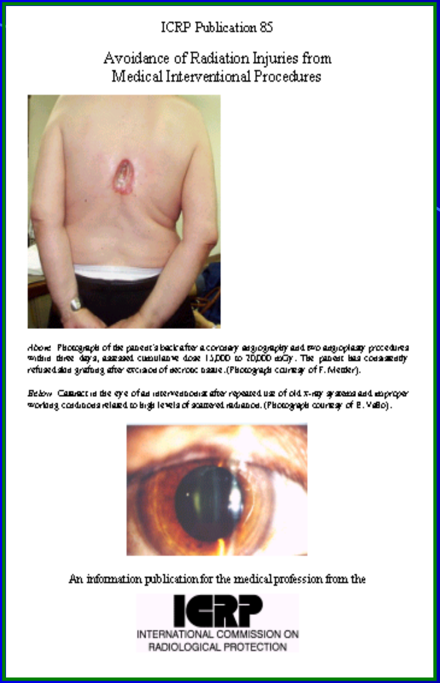
ICRP ref 4825-3093-1464

(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**.


ICRP Publication 85

Avoidance of Radiation Injuries from Medical Interventional Procedures

An information publication for the medical profession from the

ICRP
INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION

Retrospective Evaluation of Lens Injuries and Dose: "RELID"

The British Journal of Radiology, 71 (1998), 728–733 © 1998 The British Institute of Radiology

Lens injuries induced by occupational exposure in non-optimized interventional radiology laboratories

[1]E VAÑÓ, PhD, [1]L GONZÁLEZ, PhD, [2]F BENEYTEZ, MD and [3]F MORENO, MD

Chernobyl “Liquidators”

Interventional cardiologists

Residents of contaminated buildings

Infants treated for facial hemangiomas

Radiological technologists

A-bomb survivors

Astronauts

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IRPA

INTERNATIONAL RADIATION PROTECTION ASSOCIATION

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

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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

Catheterization and Cardiovascular Interventions 81:562–567 (2013)

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 FURUI[2], Hiroshi SASAKI[3], Yasuo SAKAMOTO[3], Shigeru SUZUKI[4],
Tatsuya ISHITAKE[5], Kinuyo TERASAKI[1], Hiroshi KOHTAKE[2], Alexander M. NORBASH[6],
Richard H. BEHRMAN[7] and Naofumi HAYABUCHI[1]

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. Gualdrini[2], J. Daures[1] and F. Mariotti[2]
[1]CEA, LIST, Laboratoire National Henri Becquerel (LNE LNHB), F91191 Gif sur Yvette Cedex, France
[2]ENEA-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

RADIATION AND CATARACT

Madan M. Rehani[1,*], Eliseo Vano[2], Olivera Ciraj-Bjelac[3] and Norman J. Kleiman[4]
[1]International Atomic Energy Agency, Vienna, Austria
[2]Radiology Department, Complutense University, Madrid, Spain
[3]Vinca Institute of Nuclear Sciences, Belgrade, Serbia
[4]Mailman School of Public Health, Columbia University, New York, NY, USA

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

VALVULAR AND STRUCTURAL HEART DISEASES

Original Studies

Occupational Radiation Dose During Transcatheter Aortic Valve Implantation

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

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CATARACT

A change in transparency of the lens

Why study the lens?

Why do we still care about cataract?

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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

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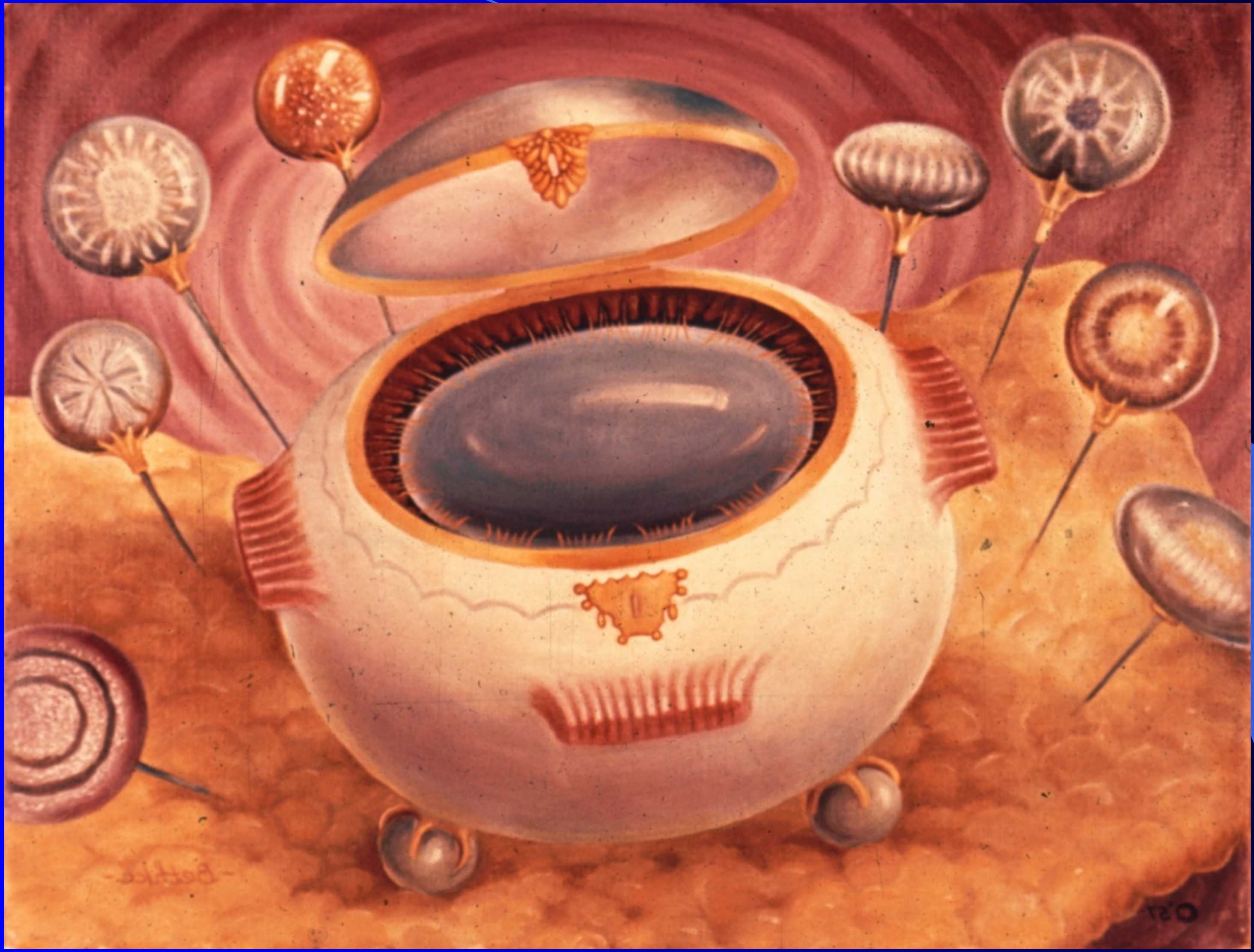

Hans Bethke

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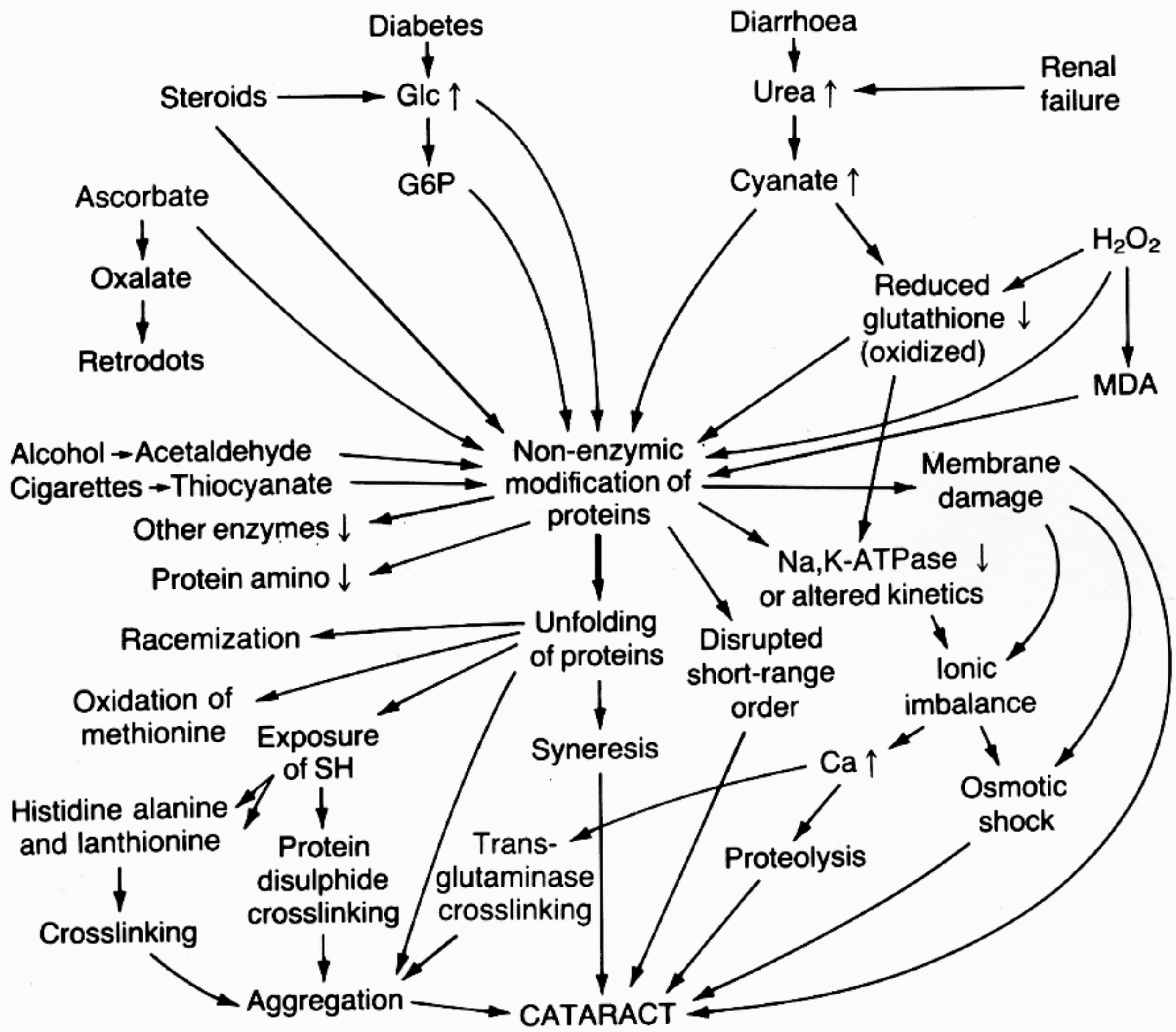
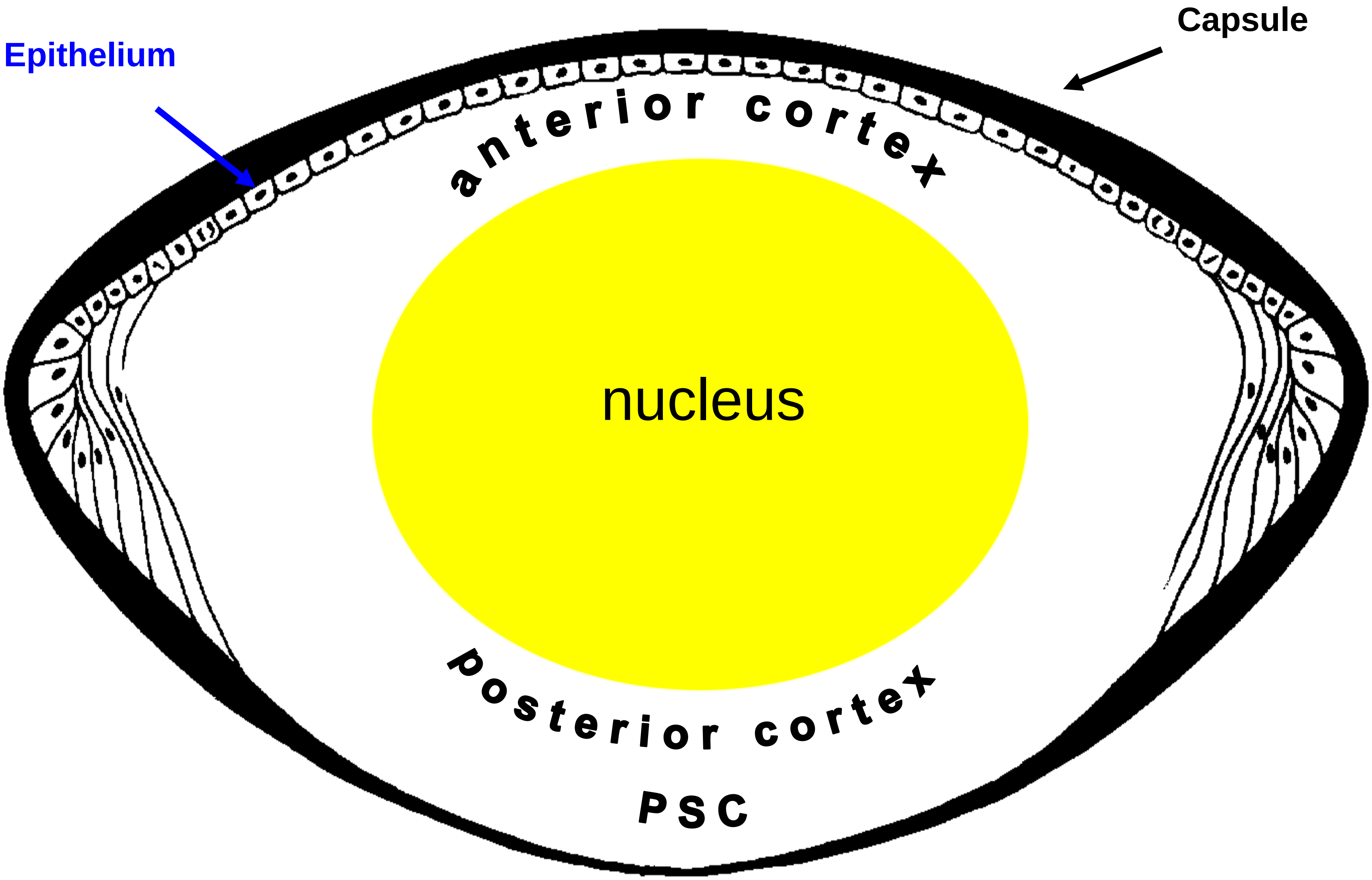


Figure 9.22 The pathways leading to lens protein degradation and cataract. (From Harding 1991 with permission.)

Major Cataract Subtypes

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



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Posterior SubCapsular (PSC)

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RADIATION CATARACT

a specific subset of lens opacities

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Classical Radiation Cataract

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

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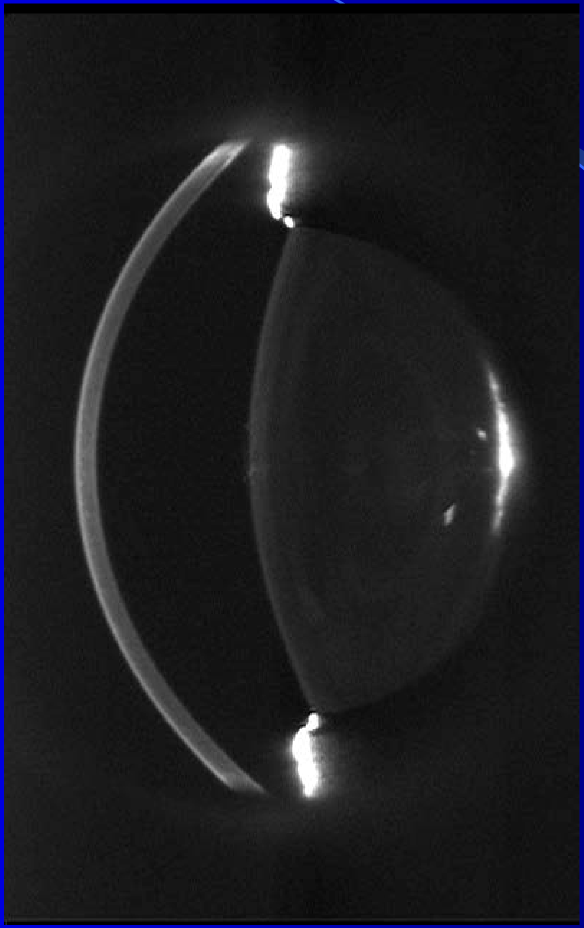

radiation cataract

(Scheimpflug image)

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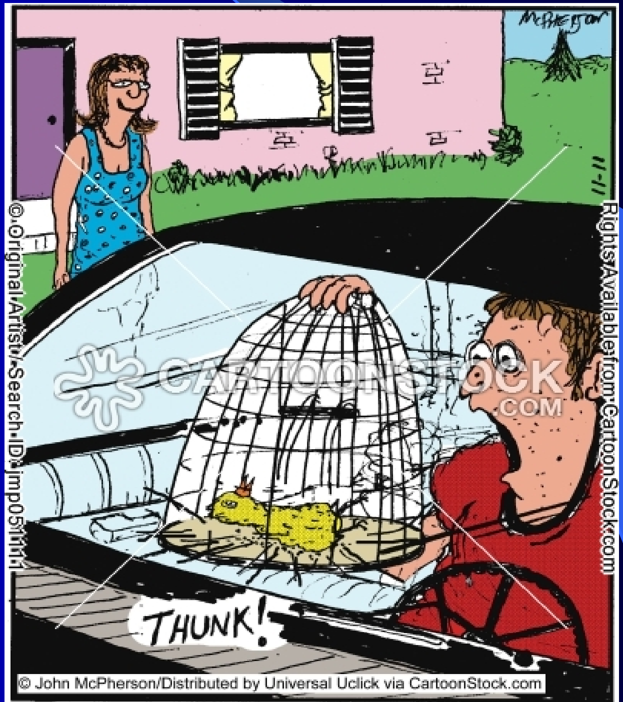
Why do we care about radiation cataract?

- 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.

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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.

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Ionizing radiation exposures that produce minimally detectable and/or clinically relevant eye effects

	DOSE (Gy)	
TISSUE	MINIMALLY DETECTABLE CHANGES	VISUALLY DEBILITATING CHANGES
Lids	6	40
Conjunctiva	5	35
Cornea	30	30
Sclera	15	200
Iris	16	16
Lens	0.05	0.5
Retina	25	25

NCRP Report No. 130, 1999; ICRP Pub 118, 2012

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

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. "

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

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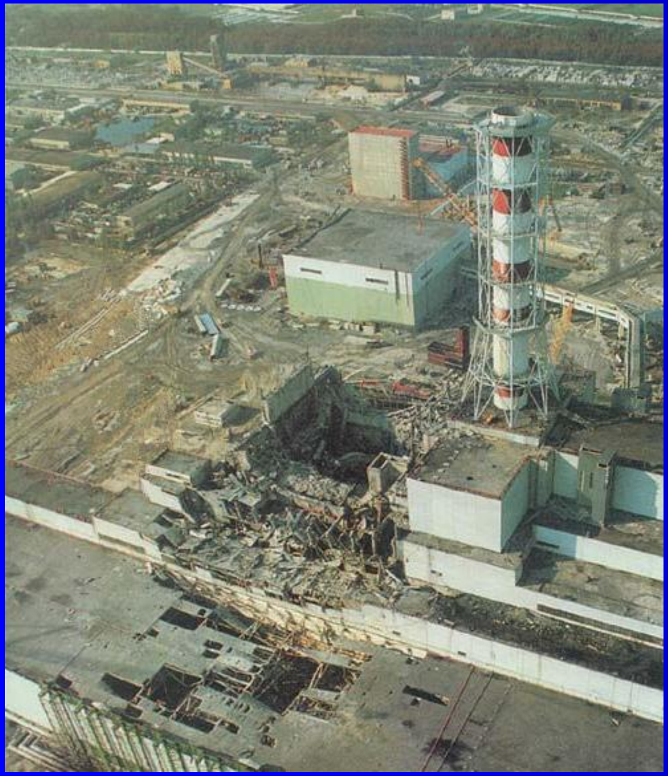
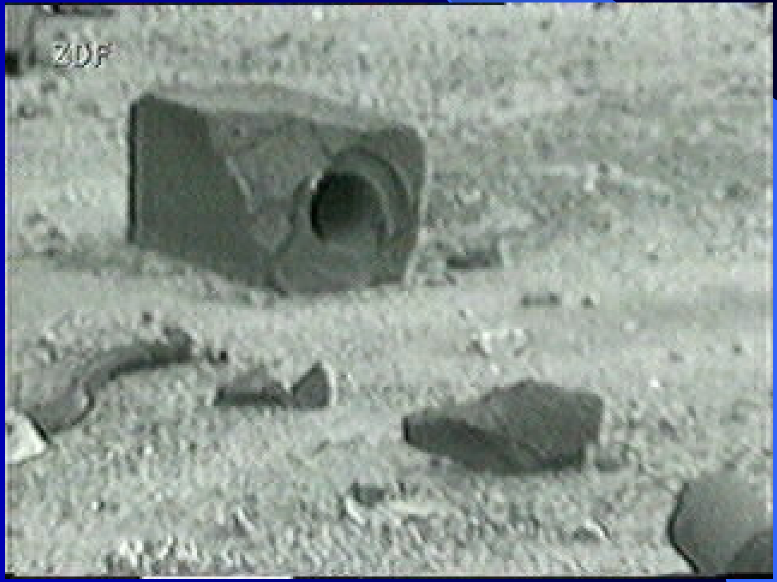
Chernobyl, USSR 1986



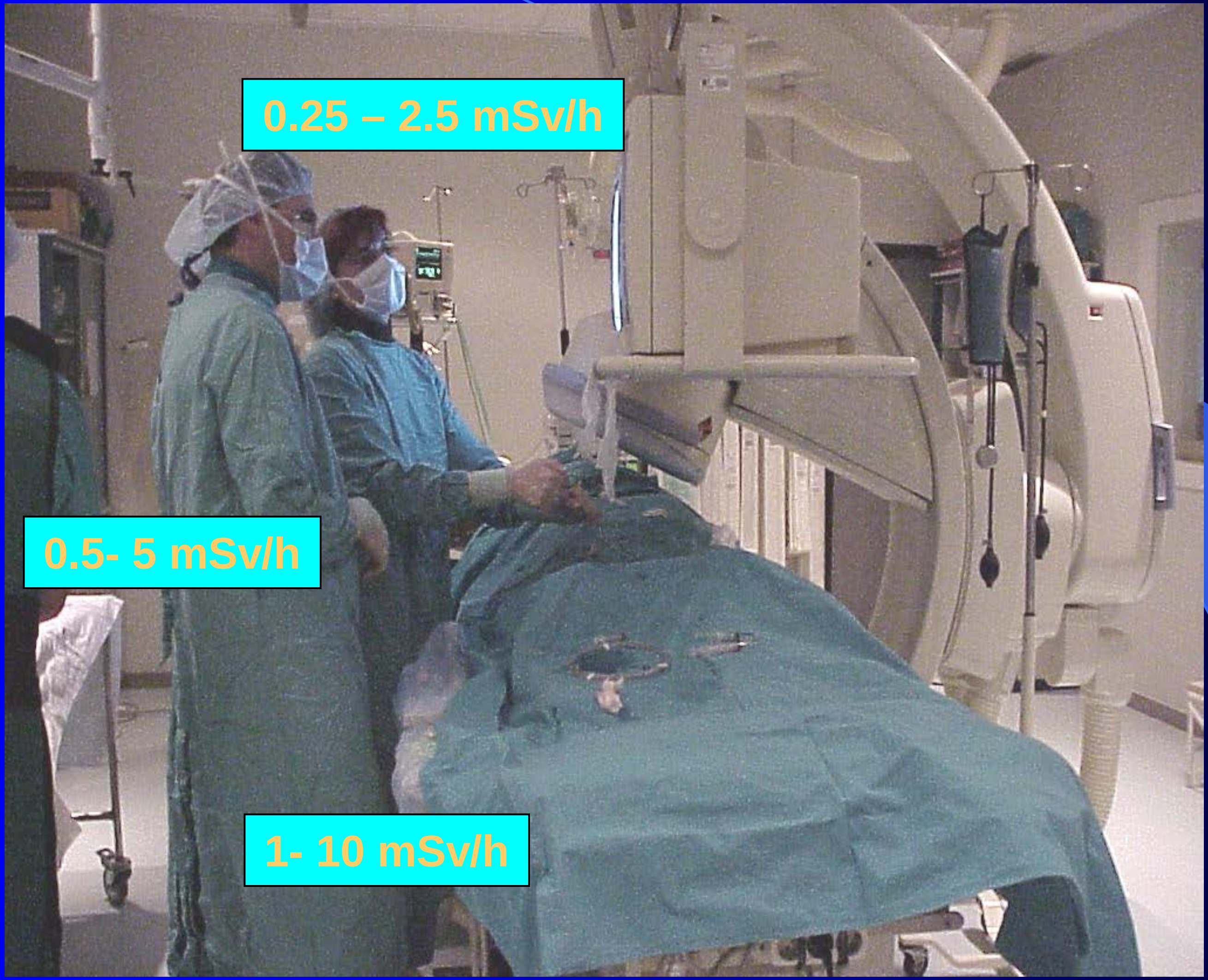
Chernobyl Nuclear Power Station Reactor 4

"Liquidators"



Radioactive graphite core ejected from the reactor

Interventional Medicine



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Potential Low-Dose Radiation Exposures

- Accidental
  - Chernobyl, Fukushima, future??
  - contaminated buildings (*e.g. Taiwan*)
- 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)

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Occupational exposure to the lens

increasing usage

Radiologists

Cardiologists

Gastroenterologists

Orthopedists

Urologists

Vascular medicine

Neurologists

Anesthesiologists

Nurses and technicians

Other workers

…limited study

Interventional Radiology Risks?

SIR TODAY • 39th ANNUAL SCIENTIFIC MEETING

Today's Featured Abstract Presentations

8:00 – 8:09 a.m., Room 5B

C-Arm Ct Of The Pulmonary Arteries: Does It Provide Additional Information For The Diagnostic Work-Up Of Patients With Chronic Thromboembolic Pulmonary Hypertension Prior To Surgical Or Interventional Treatment?

Jan Hinrichs, Institut für Diagnostische und Interventionelle Radiologie

- Presented during "Venous Malformations"

Walk-ins Needed for Cataract Study

A cataract screening research study initiated by the SIR Safety and Health Committee is taking place on-site at the SIR 2014 Annual Scientific Meeting.

SIR Safety and Health Committee member Stephen Balter, PhD, notes that the results of this project will be important as currently 90 percent of the data on this subject comes from the cardiology community. Data culled from the effort will address an important member safety issue.

This Safety and Health Committee project's resulting publication is intended to be submitted to the *Journal of Vascular and Interventional Radiology* for the first right of refusal.

The type and severity of characteristic radiation-induced posterior lens changes, including potential for posterior subcapsular cataract, will be examined in an IR cohort attending the SIR Annual Scientific Meeting. The findings will then be compared to various medical and nonmedical professional control groups, including non-interventional radiologists who are not normally exposed to X-rays.

Findings from this study may help in developing appropriate occupational guidelines for exposure to low levels of ionizing radiation and determining future risk of radiation cataract development.

No appointment is needed to participate in this important study—all walk-ins are welcome!

North Tower Marriott – Torrey Pines 1 & 2
(hotel next to San Diego Convention Center)
Monday to Wednesday, 7:00 a.m. – 6:00 p.m.

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How much exposure?

- 17 million interventional fluoroscopic procedures (USA) (NCRP-2009)
    - *4.6 million cardiac*
    - *3.4 million vascular*
    - *8.6 million non-vascular*
- 8.6% annual increases

Health Physics ***103****: 80-99, 2012*

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Number of Percutaneous Coronary Interventions (PCI) in the United States

An estimated 658,000 US patients receive inpatient PCI therapy each year. From 1987 to 2004, the number of procedures increased 326%.

scai.org

High demand for image-guided procedures strains interventional radiologists

The frequency of major and minor procedures was compared to the assignment of medical records numbers to normalize for changes in hospital-wide activity, and the results modeled by linear regression. The final analysis showed a 245% increase in total procedures over the past decade

auntminnie.org

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- *Is there new data on human radiation cataract risk? Are proposed new eye dose limits appropriate?*
- *What is the relevance of radiation cataract 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?*

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

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

(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**.

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)

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

*The purpose of radiation protection is to prevent **deterministic events** of clinical significance and limit **stochastic effects** to levels that are acceptable, given societal concerns.*

Biological Effects

- Deterministic Effects – Thresholds
  - *e.g*, cell killing. Occurs above a certain dose below which, the effect <u>does not</u> occur *e.g*. erythema (skin reddening), radiation burns.
- Stochastic Effects – Probability increases with dose
  - *e.g.,* cell transformation, carcinogenesis.
  - radiation cataract?

How did we derive the guidelines for lens exposure limits?

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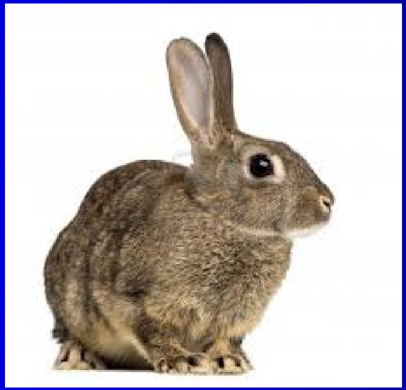
1897: Chalupecky reports cataract in x-rayed rabbits



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

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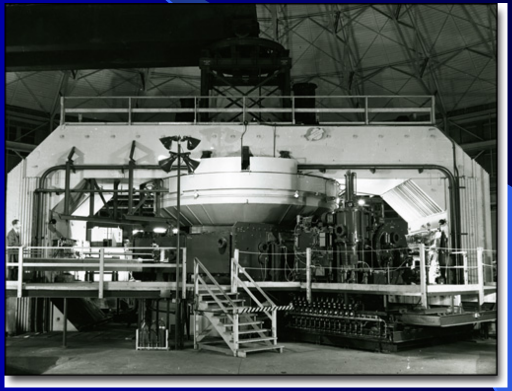
Early Radiation Cataract Studies

"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**

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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	*Worgul, 2007*	8,600

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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.

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Fukushima, Japan 2011

- Total releases somewhat uncertain
- Primarily ^{131}I and ^{137}Cs

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

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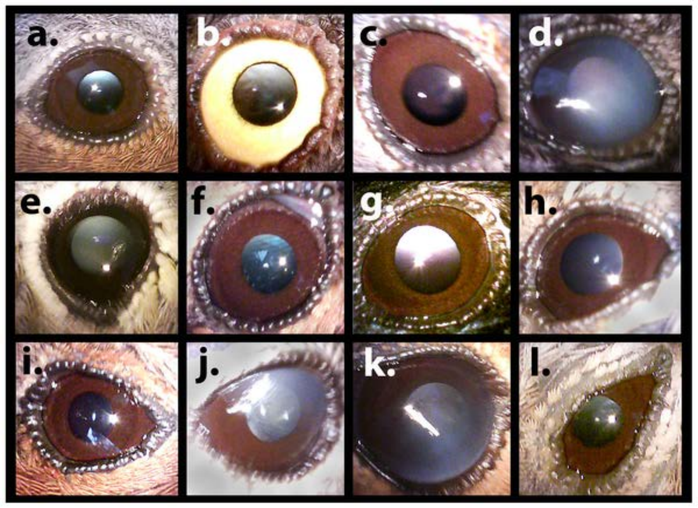
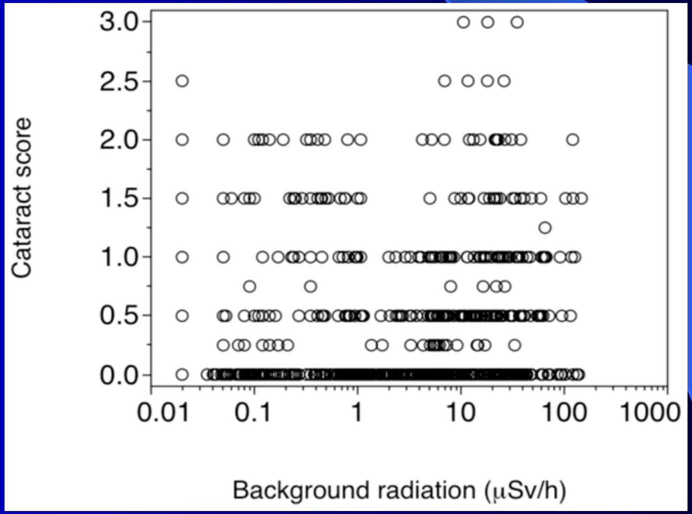
Photographs of selected eyes from Chernobyl birds



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



Mousseau, 2013 Elevated Frequency of Cataracts in Birds from Chernobyl. PLoS ONE 8: e66939

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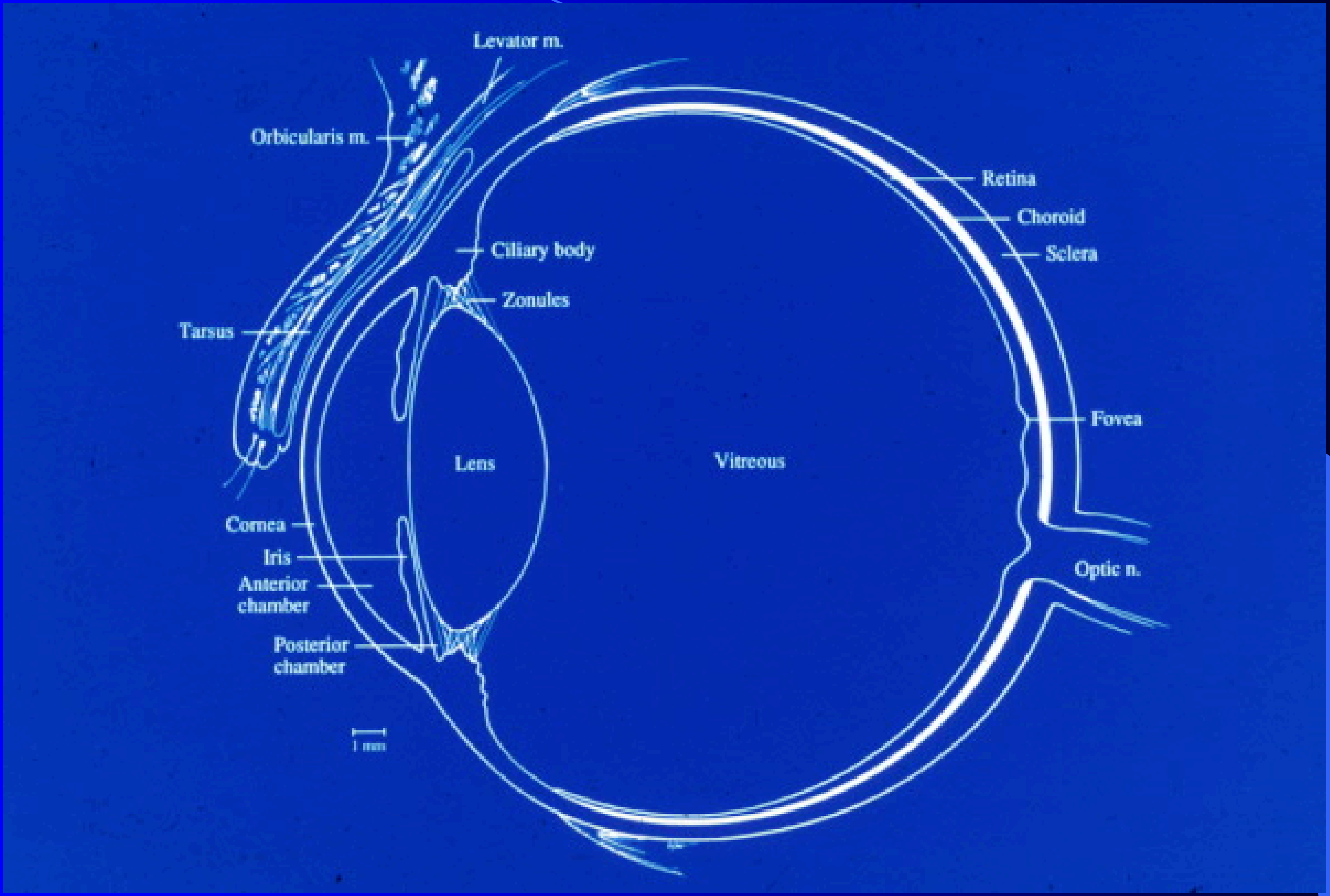
The lens



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Lens Features

- *An avascular, optically clear tissue*
- *The lens grows in size and cell number throughout life*
- *Almost all of the lens mass is composed of unique, elongated lens fiber cells*
- *Lens fiber cells have the highest protein concentration of any cell type; up to 99% in some species!*
- *Lens fiber cells have no nuclei or mitochondria yet these cells remains metabolically active for decades*
- *There is no cell loss or removal from the lens*
- *No naturally occurring primary lens cell tumors*
- *Primary lens pathology: lens opacification: “cataract”*

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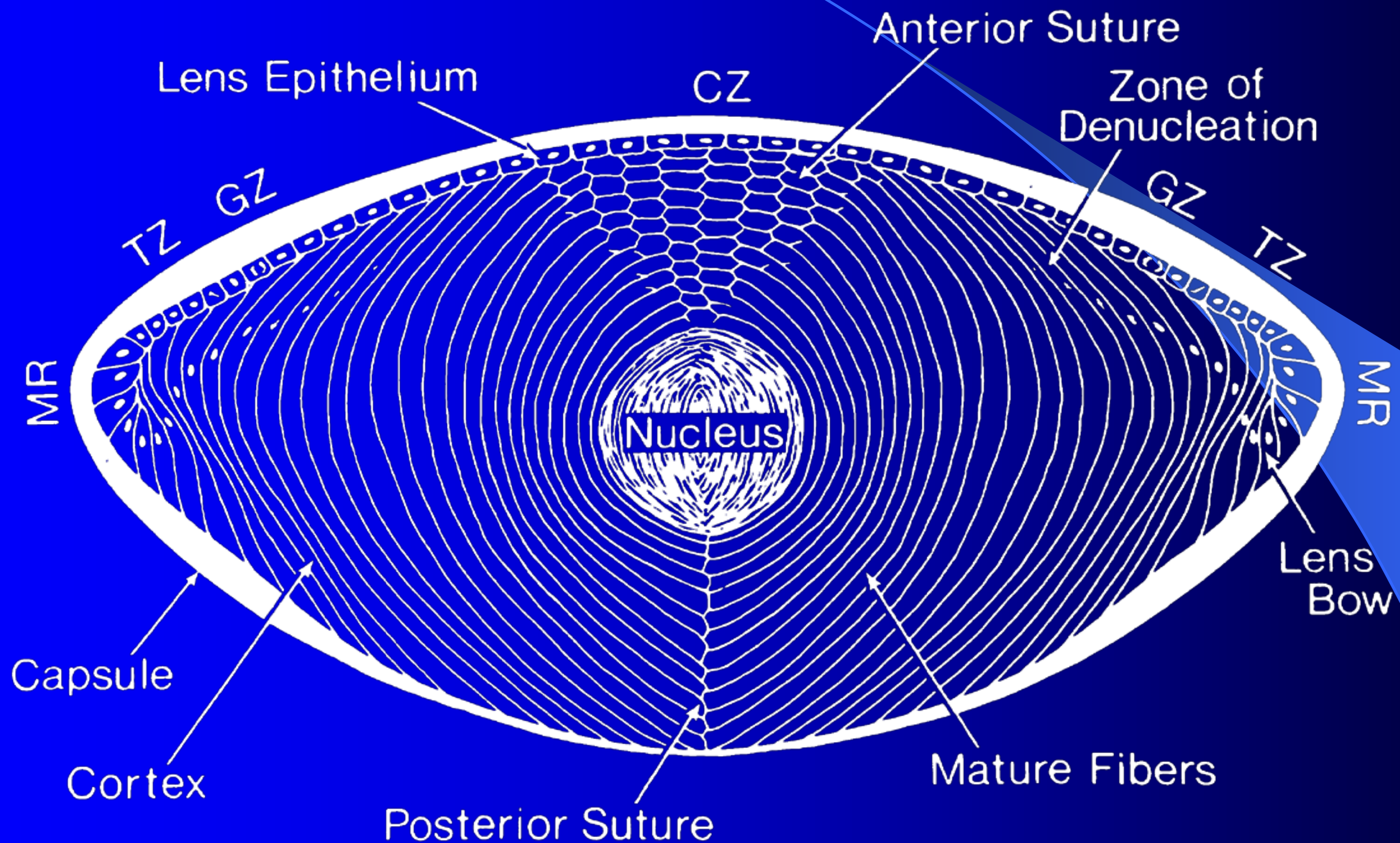
Anterior Suture
Lens Epithelium
CZ
Zone of
Denucleation
GZ
TZ
GZ
TZ
MR
MR
Nucleus
Lens
Bow
Capsule
Cortex
Posterior Suture
Mature Fibers

Three things to remember about the lens

The lens grows throughout life

The source of that growth is a proliferating subset of the anterior epithelial cell monolayer

Transparency is dependent on proper division and differentiation of the progeny of this proliferative population

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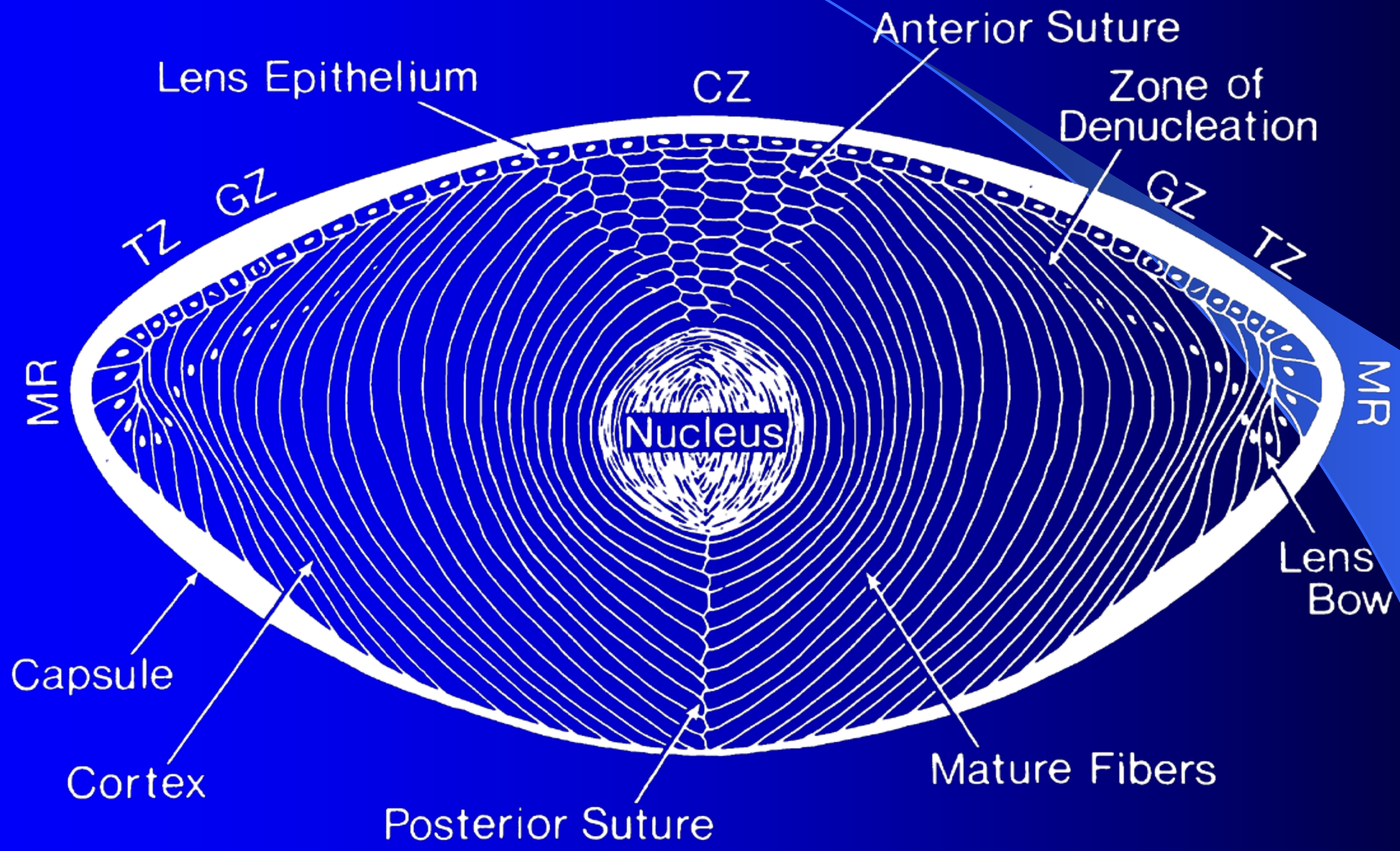

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Radiation Cataract Pathomechanism

Genotoxic damage to the lens epithelium

Lens shielding studies
Mitotic inhibition studies
Irradiation of posterior 2/3 lens

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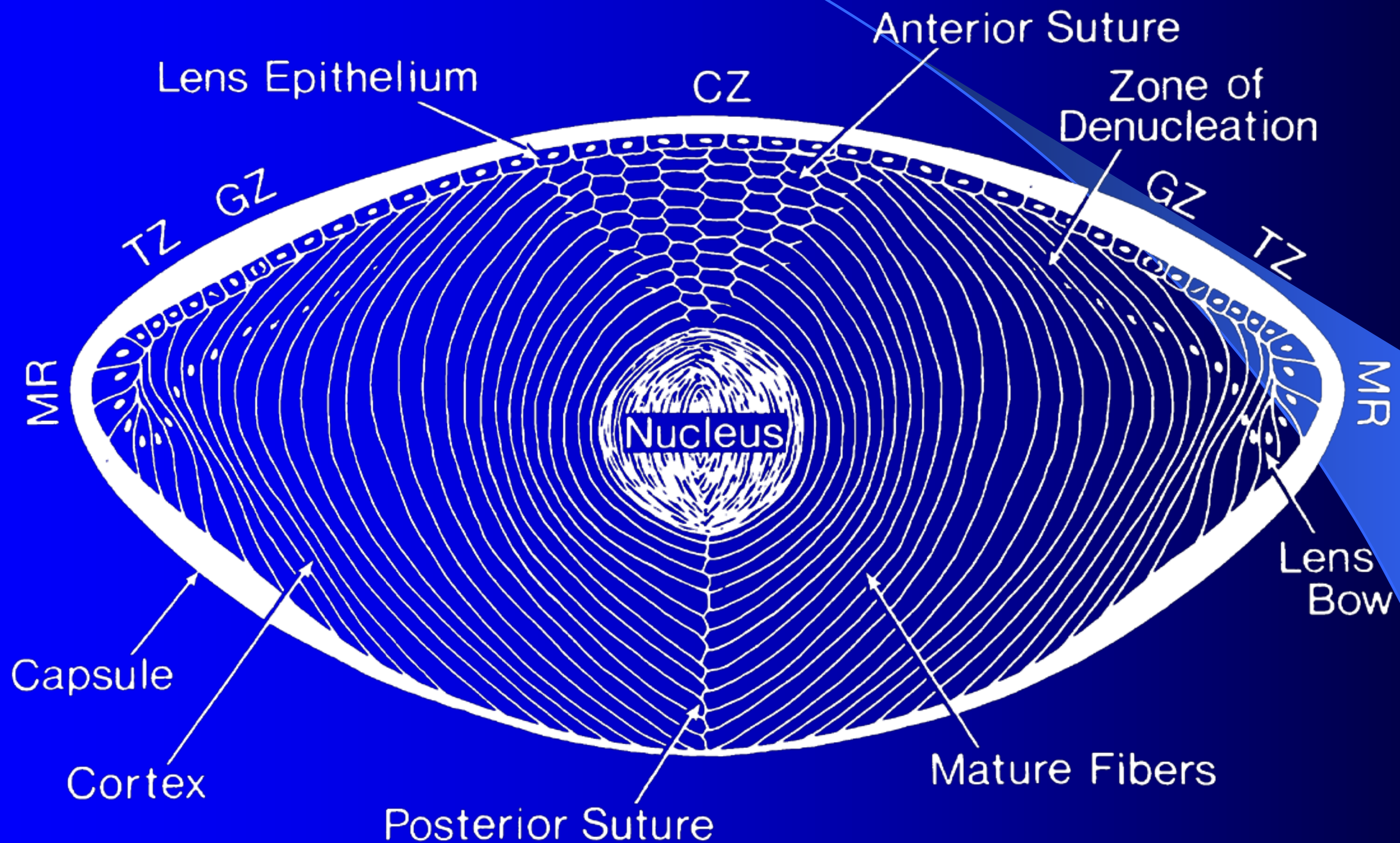
Anterior Suture
Lens Epithelium
CZ
Zone of
Denucleation
GZ
TZ
GZ
TZ
MR
MR
Nucleus
Lens
Bow
Capsule
Cortex
Posterior Suture
Mature Fibers

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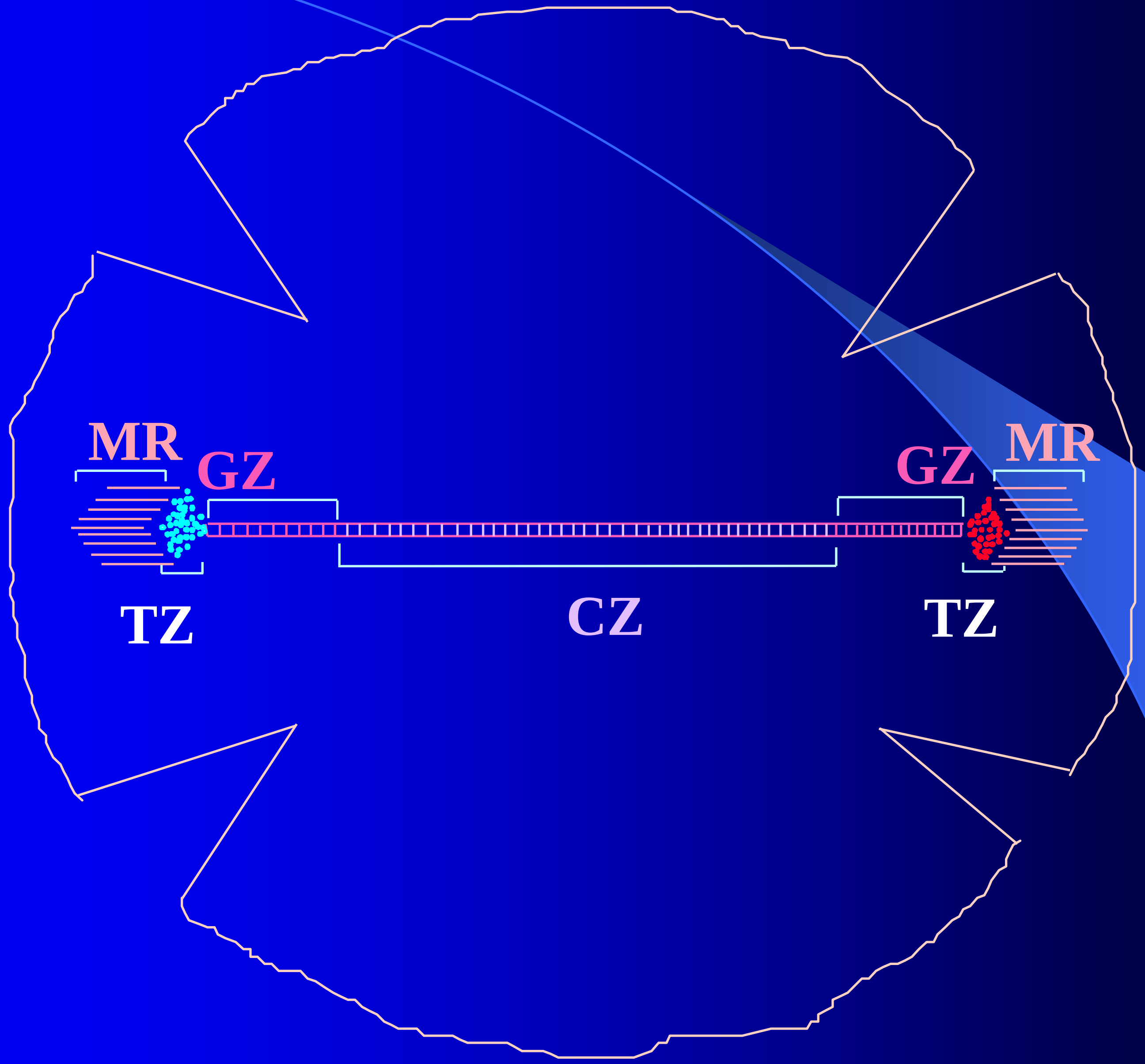
The radiation target is a small proliferating subset of the lens epithelial population



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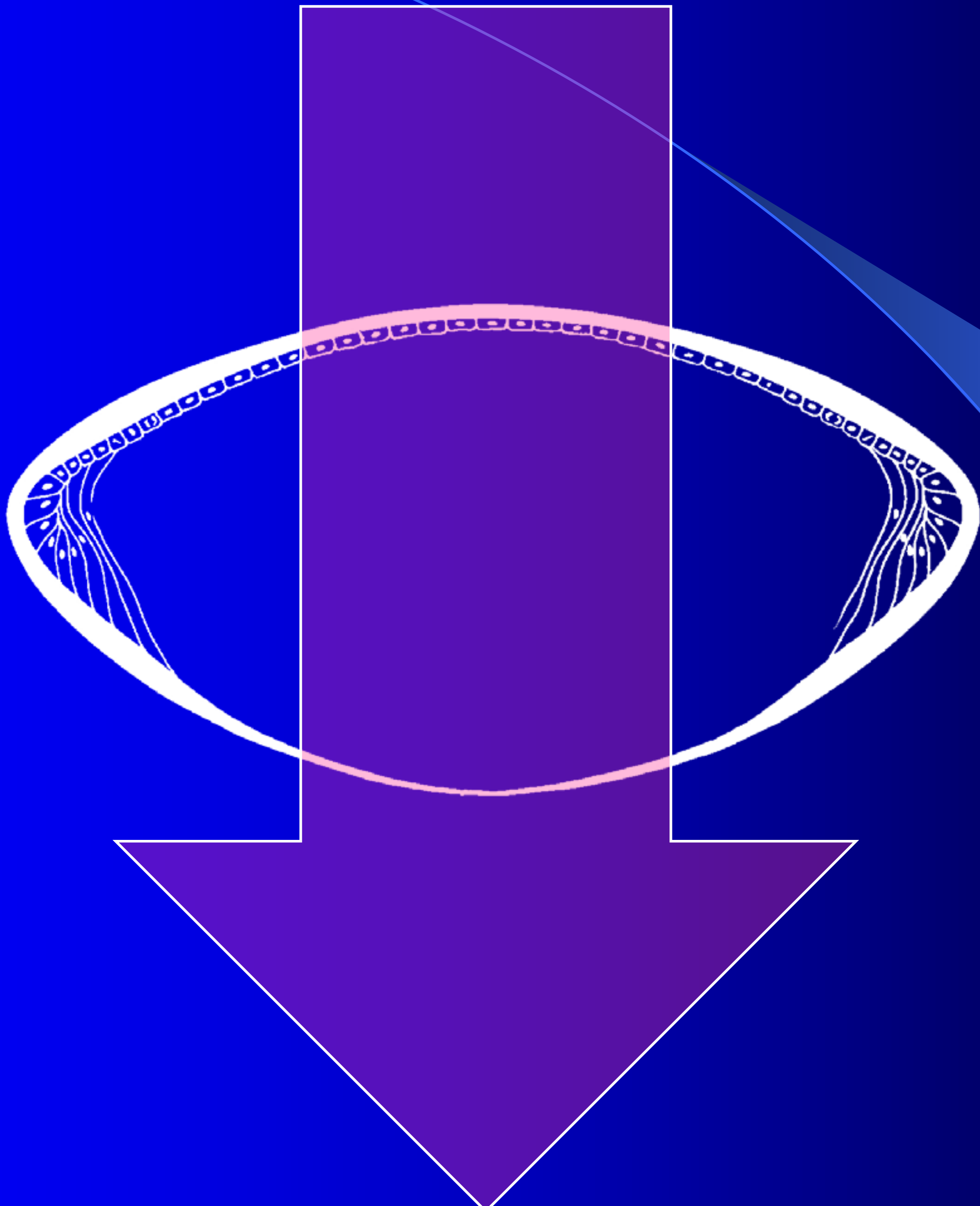
X-ray

X



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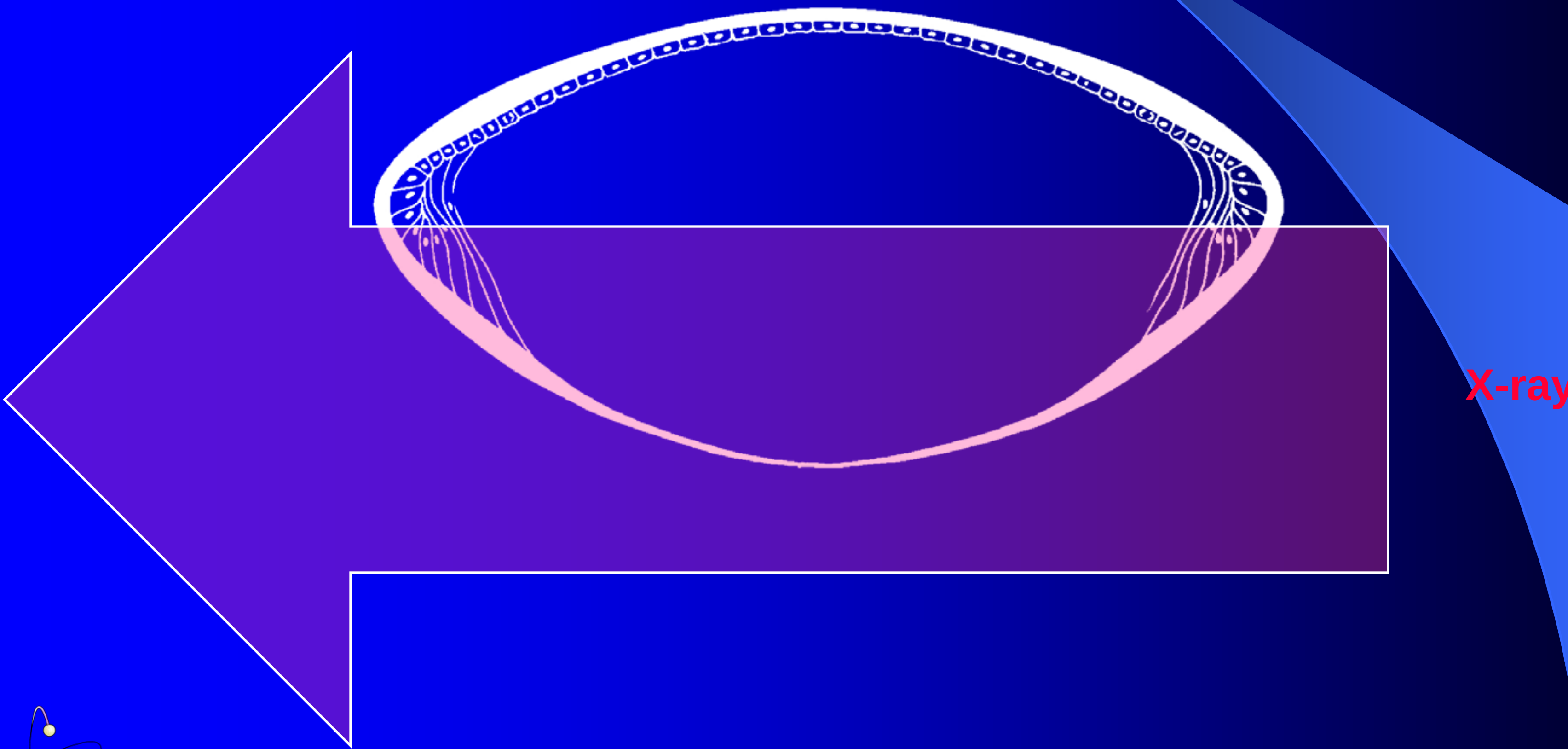
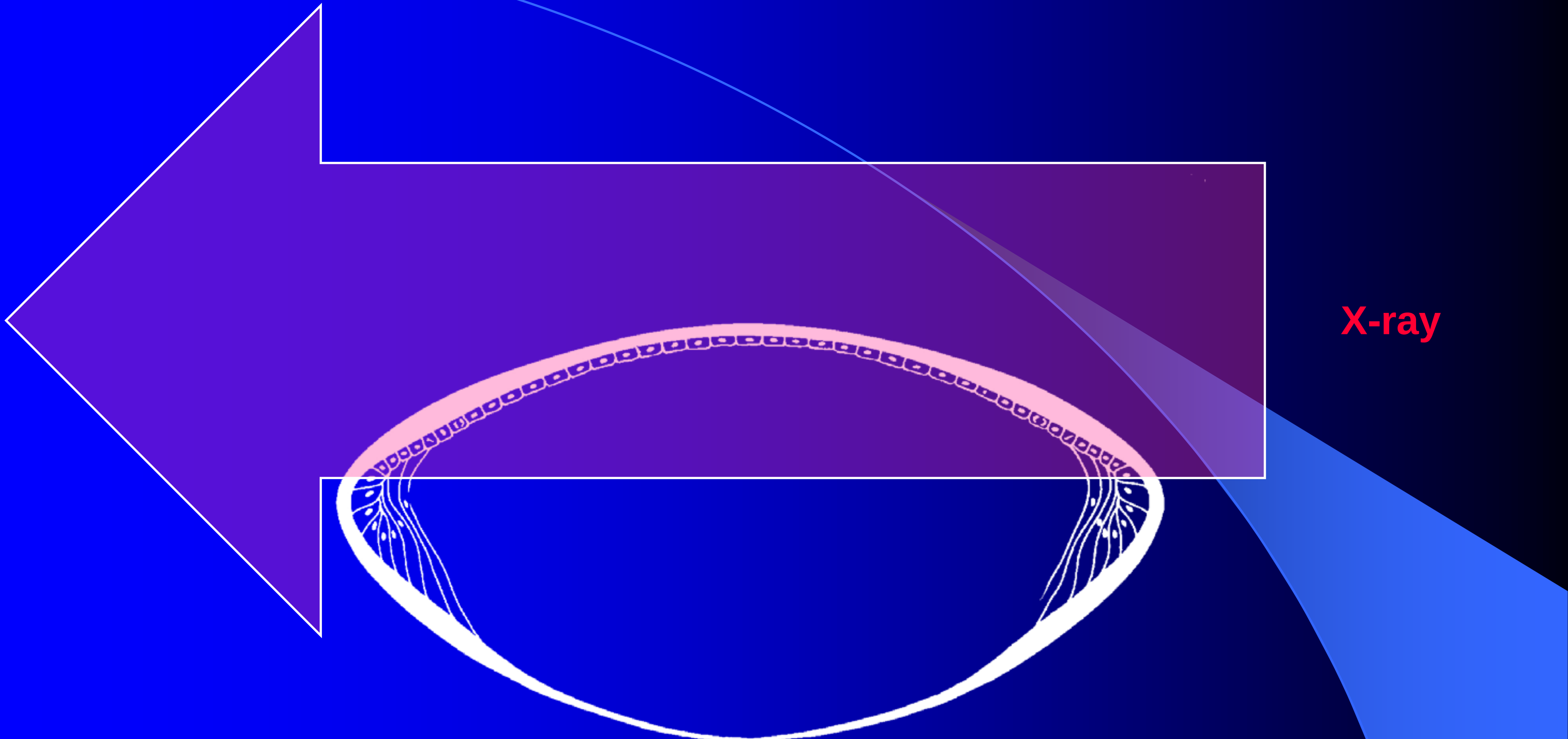
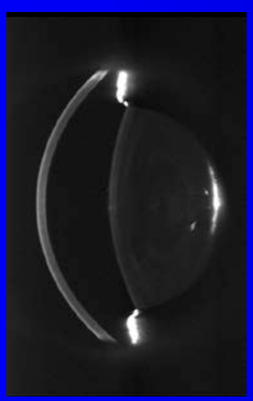
X







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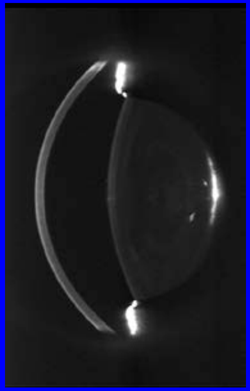
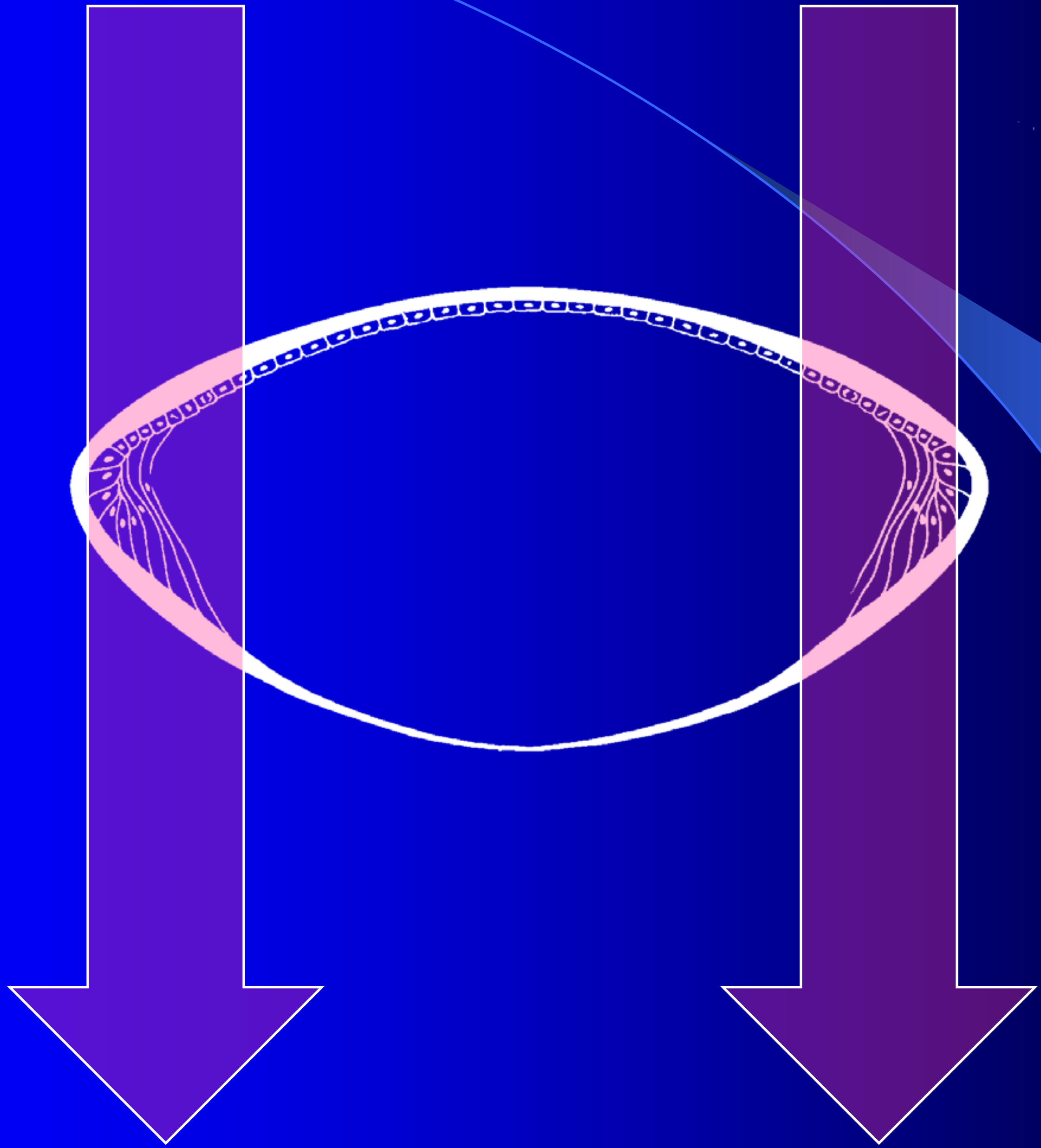
X-ray





IONIZING RADIATION

Damage to Lens Epithelial DNA

[*dividing cells*] → [*differentiating cells*]

Abnormal Lens Fibers

Loss of Transparancy

CATARACT

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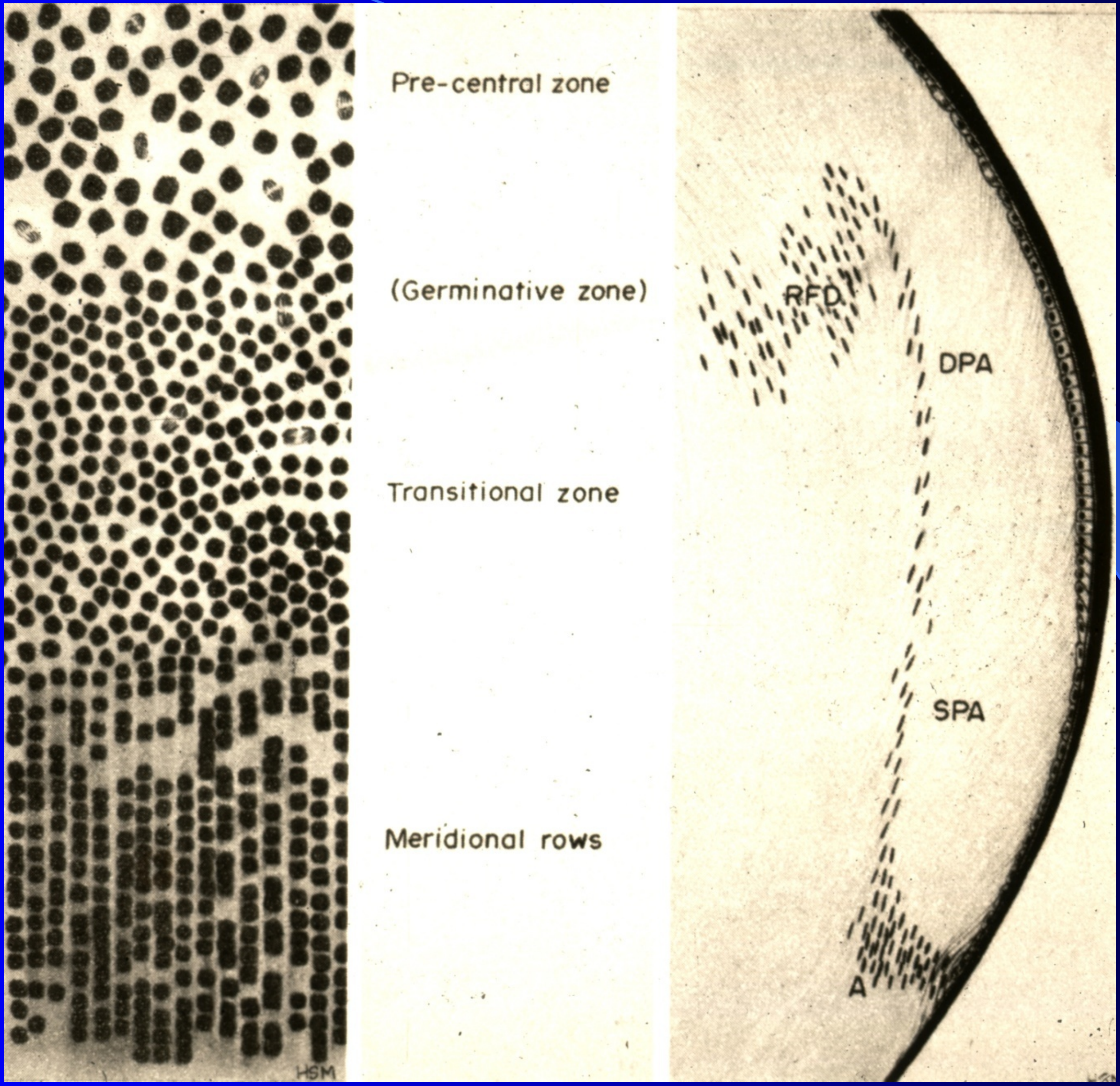

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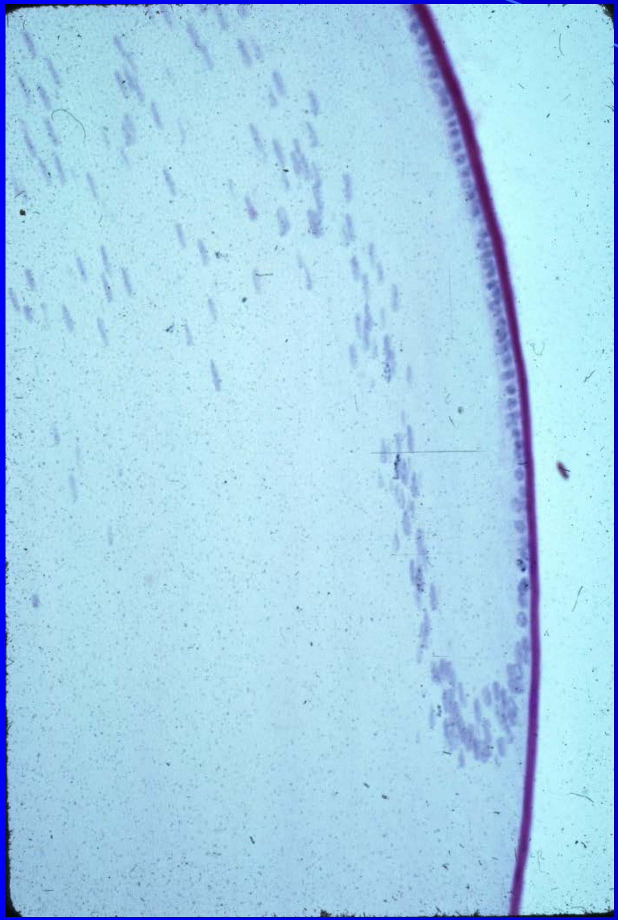
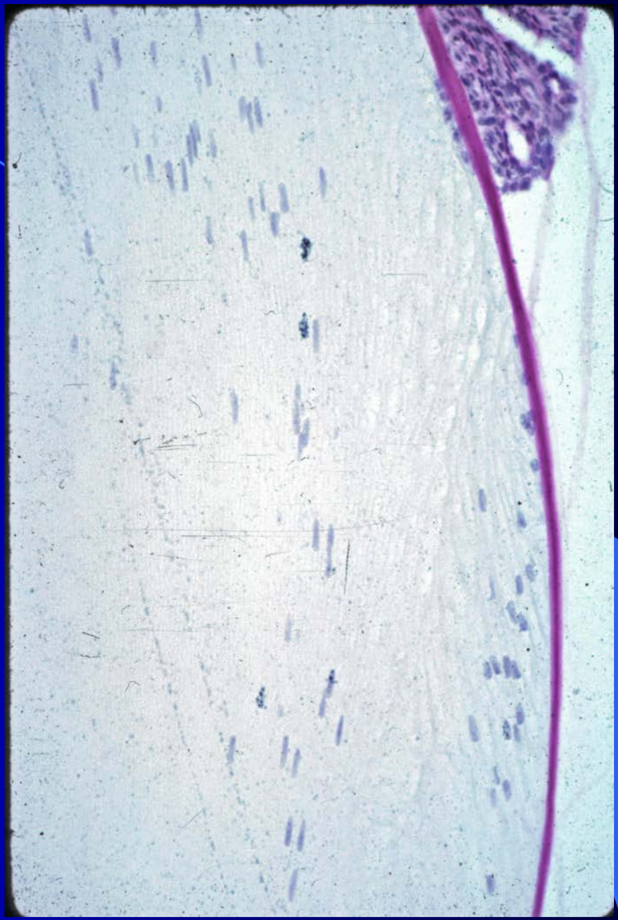


normal



irradiated

Transparency is dependent on proper differentiation of maturing lens fiber cells

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Visualizing Lens Opacities

- *Retroillumination*
- *Biomicroscopy (slit lamp)*
- *Scheimpflug Imaging*

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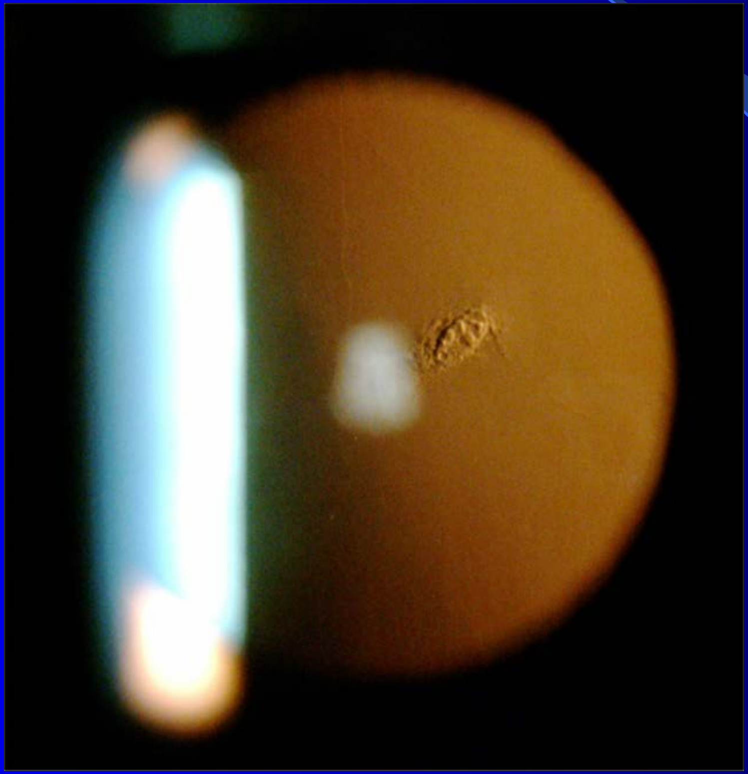

Retroillumination image

Nikon FS-3 Photo-Zoom Slit Lamp

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Nidek EAS-1000 Scheimpflug Camera

Quantifying radiation-induced lens changes “cataract staging”

Merriam-Focht scoring
LOCS II
LOCS III
Focal Lens Defects
Digital Scheimpflug

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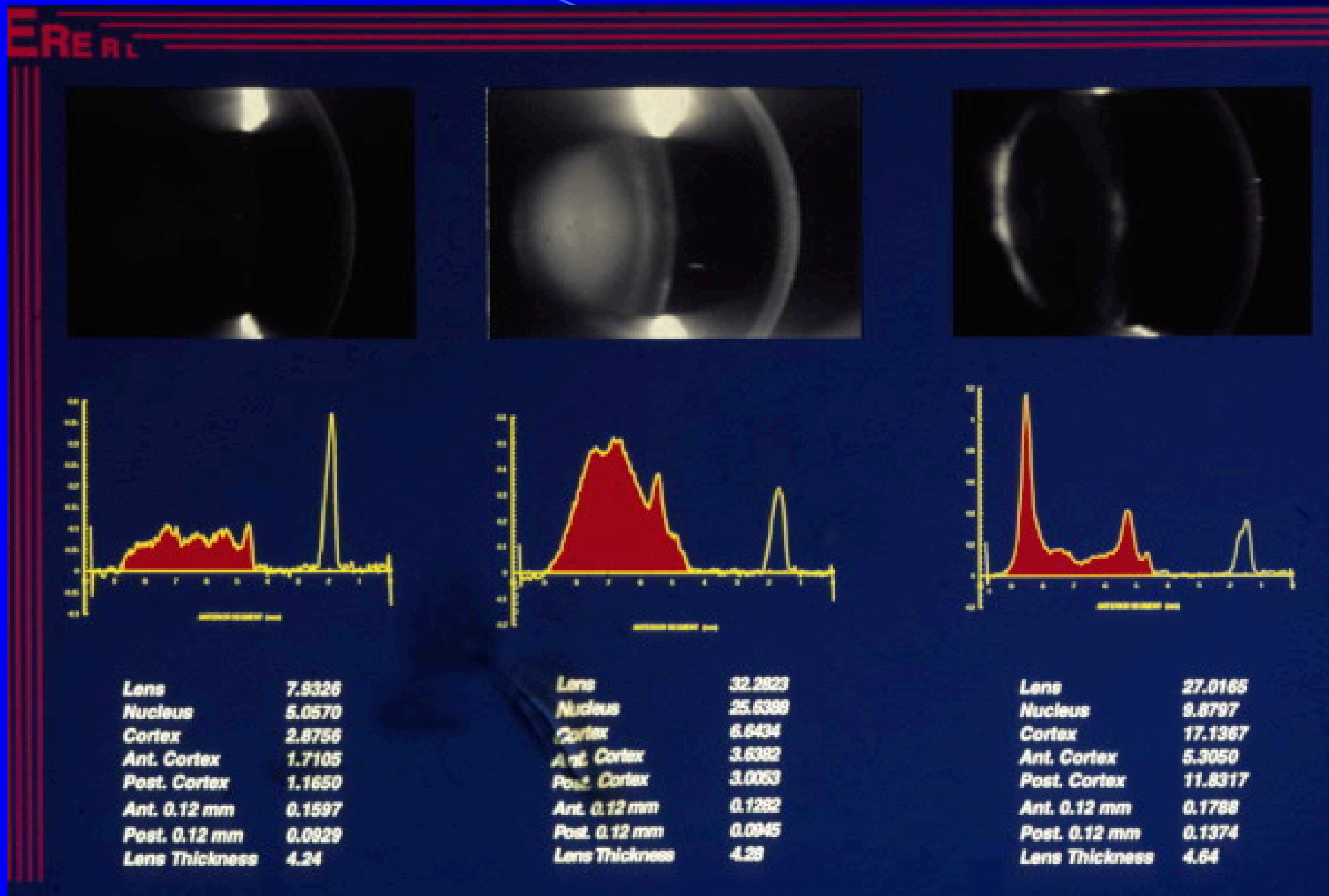
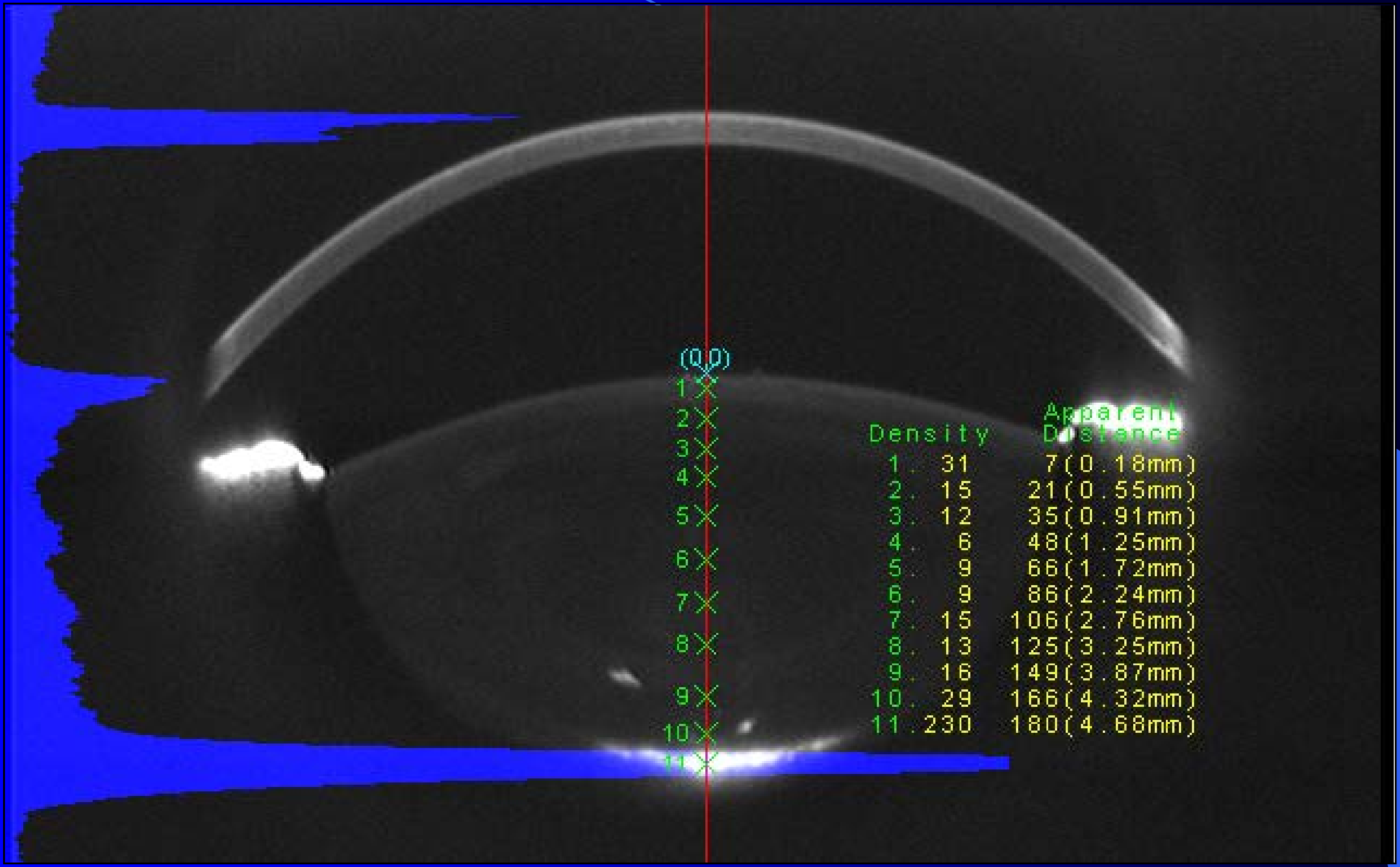

ERERL
Lens 7.9326
Nucleus 5.0570
Cortex 2.8756
Ant. Cortex 1.7105
Post. Cortex 1.1650
Ant. 0.12 mm 0.1597
Post. 0.12 mm 0.0929
Lens Thickness 4.24
Lens 32.2823
Nucleus 25.6388
Cortex 6.6434
Ant. Cortex 3.6382
Post. Cortex 3.0053
Ant. 0.12 mm 0.1282
Post. 0.12 mm 0.0945
Lens Thickness 4.28
Lens 27.0165
Nucleus 9.8797
Cortex 17.1367
Ant. Cortex 5.3050
Post. Cortex 11.8317
Ant. 0.12 mm 0.1788
Post. 0.12 mm 0.1374
Lens Thickness 4.64

Scheimpflug Imaging of Radiation Cataract



Quantitative analysis of lens changes

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Cataract Staging

Focht & Merriam, 1957

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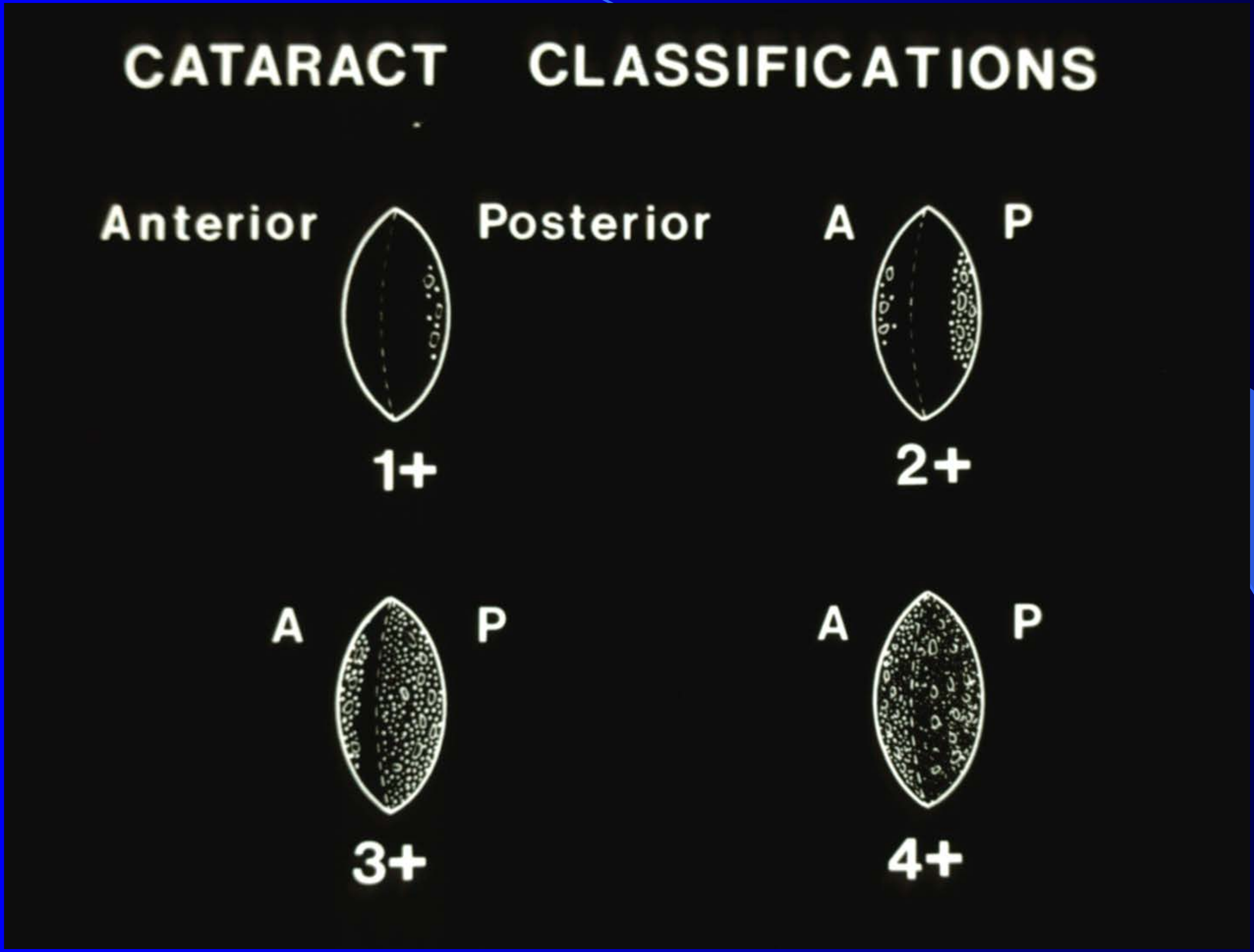
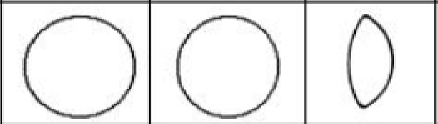
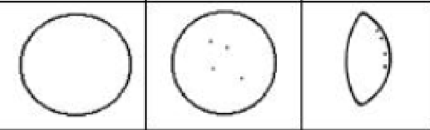
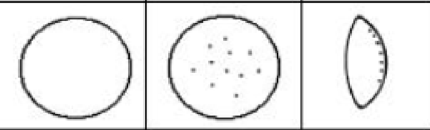
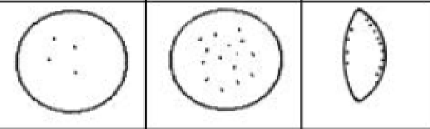
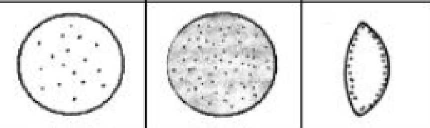
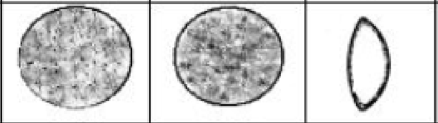
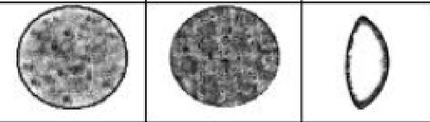
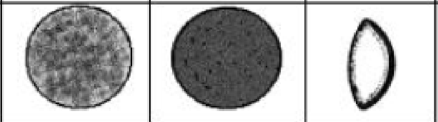
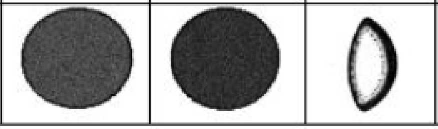
Slit Lamp Imaging of Radiation Cataract Grades



Merriam-Focht Scoring

SCORE	APPEARANCE			DESCRIPTION
	Anterior	Posterior	Sagittal	
0				Transparent Lens…**NO** opacities or dots discernible posteriorly **OR** anteriorly
0.5				Anterior **OR** posterior region* has <u><</u> **4** dots **AND** the other is transparent
1.0				Anterior **OR** posterior region has > **4** dots **AND** the other is transparent
1.5				One region has > **4 AND** the other <u><</u> **4** dots
2.0				Both anterior **AND** posterior have > **4** dots
2.5				"Cloudy Skies". Vitreous visible through scattered anterior opacification
3.0				Posterior viewable but not vitreous **AND** anterior has scattered opacification
3.5				Total posterior opacity AND anterior near totally opaque with only occasional breaks
4.0				Anterior cortex completely opaque preventing viewing beyond superficial layers

* *Posterior Region* is defined as the superficial cortex, which includes the Posterior Subcapsular (PSC) area.

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EARLY “PRECATARACTOUS” LENS CHANGES

- A polychromatic sheen associated with the posterior capsule
- Discrete (non-aggregated) dots which number < 10
- Individual vacuoles which number < 5

Stage 1 Cataract (Onset)

A discrete, superficial cortical opacity which can take the form of a small spot (visible on retro-illumination), aggregates of dots (>10) or vacuoles (>5), cortical spokes, waterclefts, or granulated opacities.

Stage 2 Cataract (Progression)

Extensive cortical changes collectively occupying approximately 25% of the area of the lens. Subjectively, if less or more than 25% is involved, a Stage 1.5+ or 2.5+, respectively, is noted.

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Visually Disabling Changes

Stage 3 Cataract

Advanced cortical changes . Slit beam does not reach vitreous.

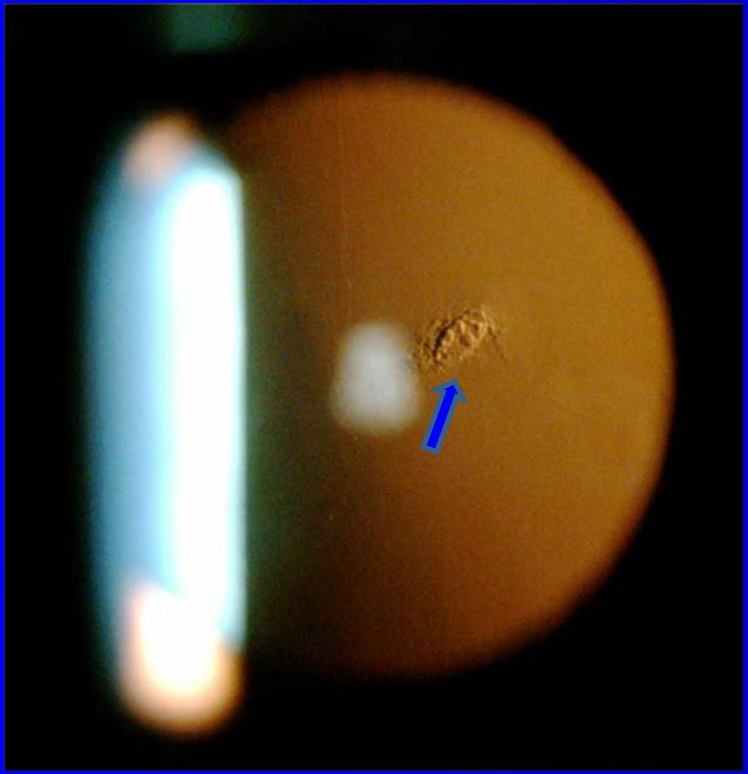
Stage 4 Cataract

Near-total lens opacification. In some areas it is possible to see the nucleus or posterior cortex of the lens.

Stage 5 Cataract

Mature cataract. Total lens opacification. Pearly white lens.

Radiation Induced Posterior Subcapsular Opacity

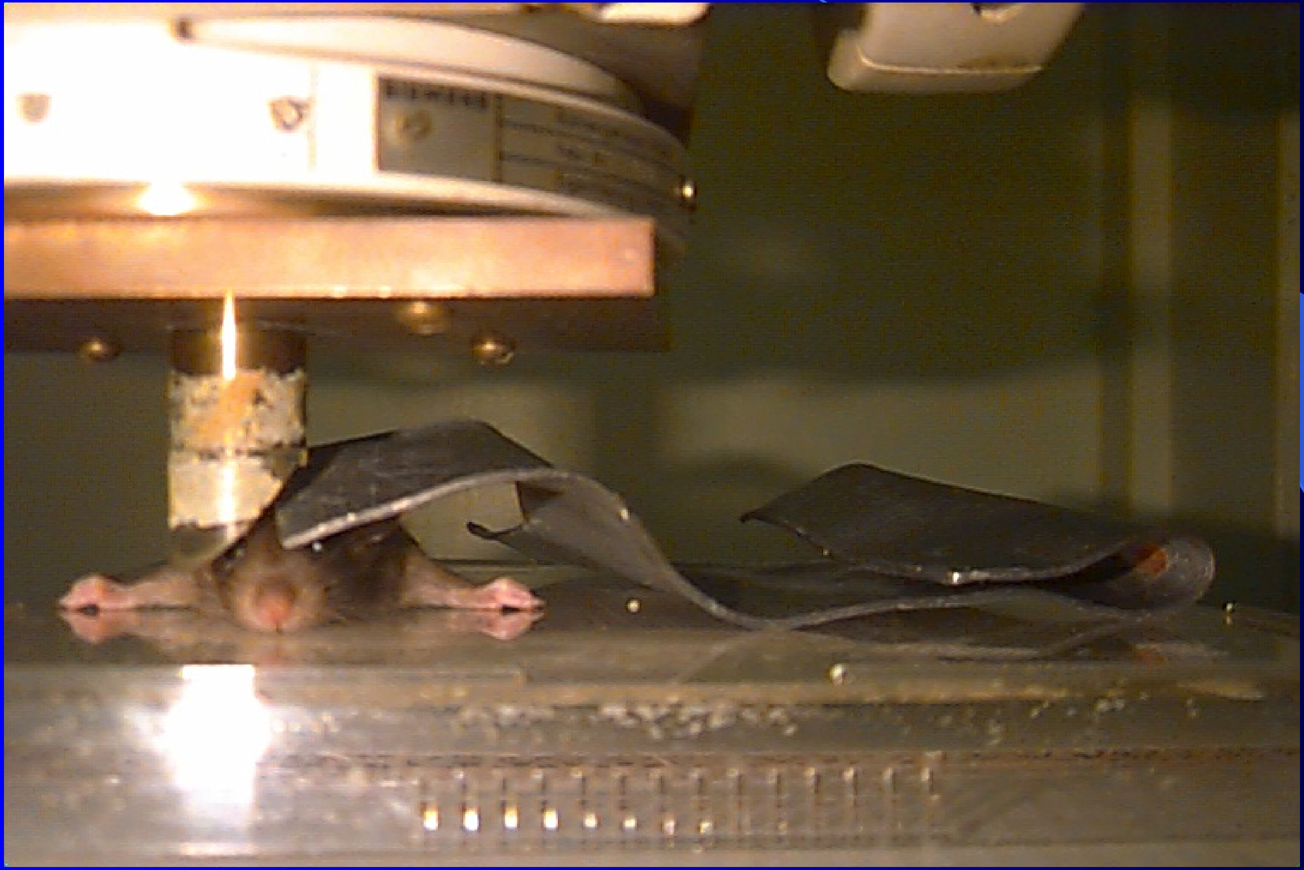


Retroillumination

Slit Lamp Exam

Interventional cardiologist with 22 years experience

ANIMAL STUDIES



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

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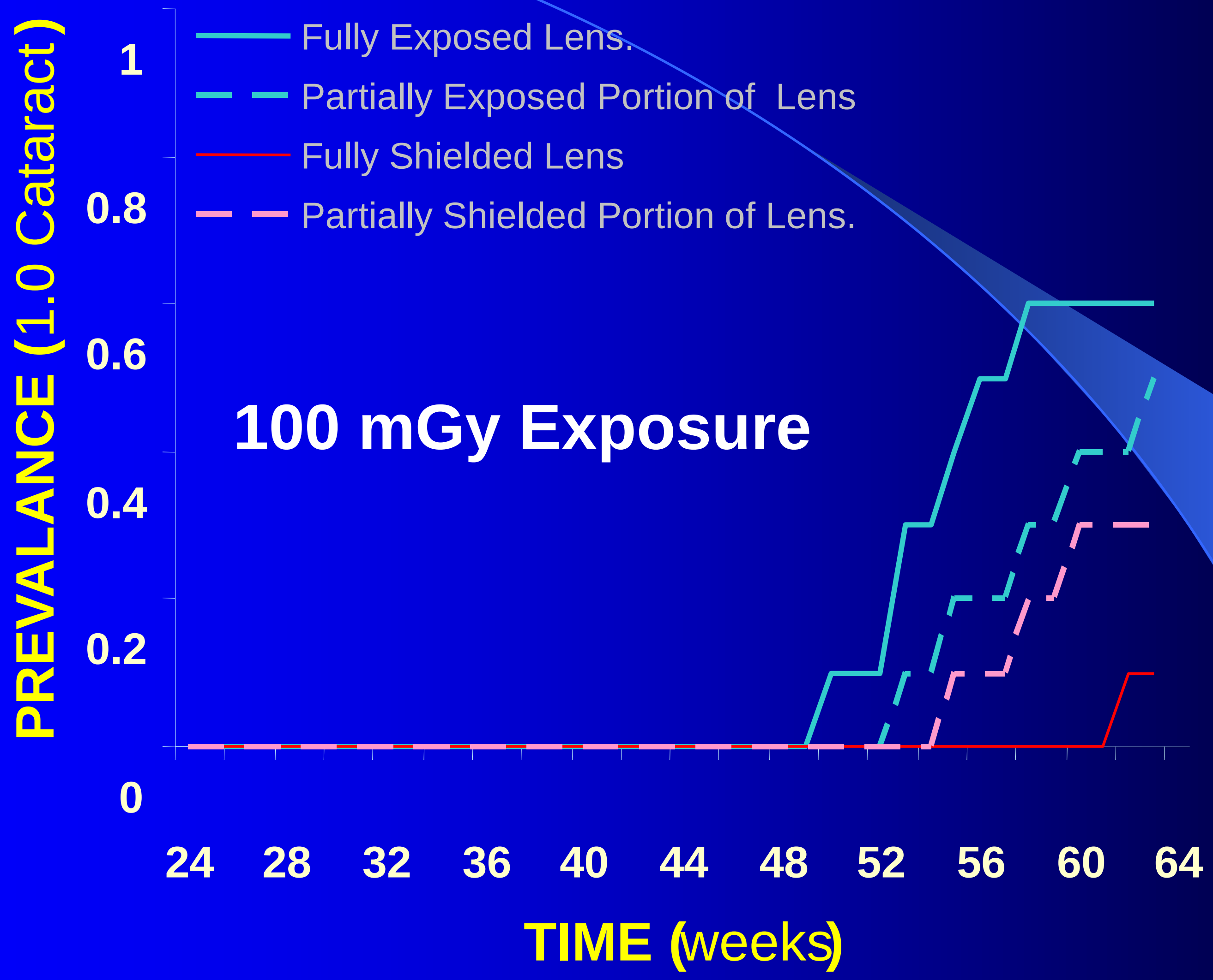

Invest. Ophthalmol. Vis. Sci. **46**, 2005

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Significance

Because rodents are highly predictable surrogates for radiation cataractogenesis in humans, the observation that 100 mGy is cataractogenic in rats is of concern. This animal study is supported by a human epidemiological study of ~12,000 Chernobyl clean-up workers which demonstrated that doses <250 mGy were cataractogenic, as well as studies of CAT-Scan patients (Klein, 1993), astronauts (Cucinotta, 2002) and re-examinations of A-bomb survivors (Nakashima, 2006, Neriishi, 2007).

Furthermore, the radiation cataract model may provide an alternative method for examining bystander effects in complex tissue.

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Experimental Rodent models for Genetic Susceptibility to Radiation Cataractogenesis

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Radiation Protection Philosophy

Most radiation risk estimates

assume

that the human population is

homogeneous in radiosensitivity

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Areas Where Uniform Radiosensitivity Is Assumed

- Radiation protection for the general public
- Occupational exposure limits
- Radiotherapy and radio-diagnostic protocols

Potential consequences of radiosensitive sub-populations

- Unethical to put radiosensitive individuals in situations where they might receive high exposures.
- Dose limits and therapeutic efficacy may be compromised (on both ends)
- Radiosensitive individuals may be at high risk for damage from occupational exposure (*e.g.* interventional physicans, astronauts).
- For patients, diagnostic or radiotherapeutic protocols need to be modified on an individual basis for maximum effect and minimum damage to normal tissue
- Inclusion of such individuals in studies distorts the shape of calculated dose-response relationships, especially at low doses.

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Radiosensitivity

- Variable treatment response in patients receiving radiation therapy
- Reaction of healthy tissue after radiation therapy
- Greater predisposition for radiation-induced tumors than the general population
- Inter-individual variability in repairing DNA lesions or eliminating damaged cells
- Intra-individual cell response variability according to dose and dose rate

Evidence in humans of a radiosensitive sub-population

- Severe reaction to radiotherapy in a few percent of patients.
- AT homozygotes are exquisitely radiosensitive.
- Early breast cancer in a subset of Japanese women who survived Hiroshoma or Nagasaki.
- Increased risk of breast cancer following chest X-ray in individuals carrying BRCA1 and 2 mutations.

Genetic predisposition for the development of radiation-associated meningioma: an epidemiological study

P. Flint-Richter and S. Sadetzki

The Lancet Oncology **8,** 403-410 (2007)

- clustering of multiple cases of radiation-associated meningioma in given families

for all children irradiated for tinea capitis risk of radiation-associated meningioma is 1/100. However, in some families the risk is 4/5.

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Multiple Diagnostic X-rays for Spine Deformities and Risk of Breast Cancer

C.M. Ronckers, M.M. Doody, J.E. Lonstein, M. Stovall and C.E. Land

Cancer Epidemiology Biomarkers & Prevention 17, 605-613 (2008)

- *Dose response was significantly greater (P = 0.03) for women who reported a family history of breast cancer in first- or second-degree relatives (excess relative risk/Gy = 8.37 v. 2.86)*

Phenotypically normal, potentially radiosensitive, sub-groups in the general population

- **1-3 % of the U.S. population are *Atm* heterozygotes**
- **1 in 250 women carry *Brca1* or *Brca2 mutations***
- **2% of people possess *Rad9* polymorphisms**
- **Unknown incidence of mutation and polymorphisms in other relevant genes and regulatory elements**

Radiation Cataract is a good model system for understanding genetic determinants of radiosensitivity

- The lens is one of the most radiosensitive tissues

- Onset and progression of radiation cataract can be studied non-invasively over a long period

- Genetically defined mouse models can be utilized to investigate the role of specific genes and gene combinations on the onset and progression of radiation-induced lens opacities.

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Mice

Wildtypes:

$Atm^{+/+}$, $Rad9^{+/+}$
$Atm^{+/+}$, $Brca1^{+/+}$

Single heterozygotes:

$Atm^{+/-}$, $Rad9^{+/+}$
$Atm^{+/-}$, $Brca1^{+/+}$
$Atm^{+/+}$, $Rad9^{+/-}$
$Atm^{+/+}$, $Brca1^{+/-}$

Double heterozygotes:

$Atm^{-/-}$, $Rad9^{-/-}$
$Atm^{-/-}$, $Brca1^{-/-}$

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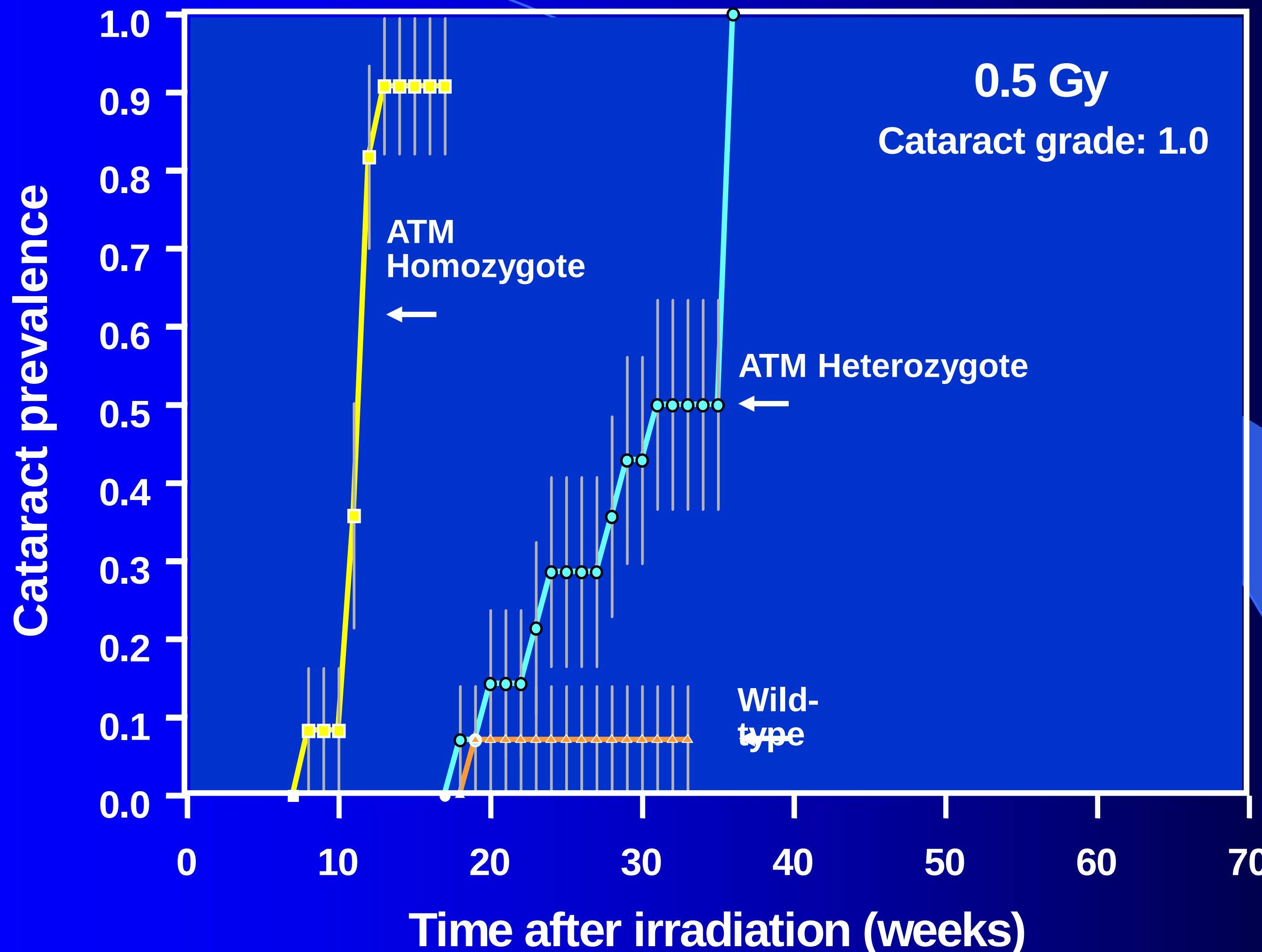
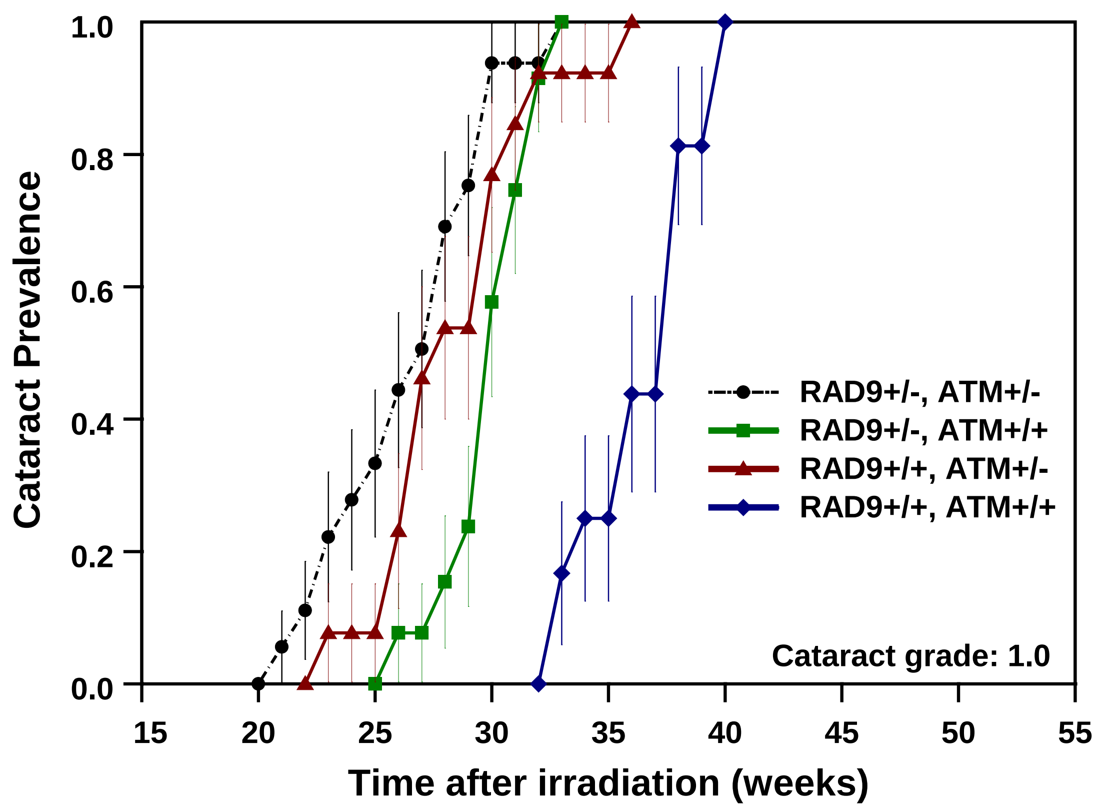


Rad Environ Biophys **45**, 2006



Radiat. Res **168**, 2007

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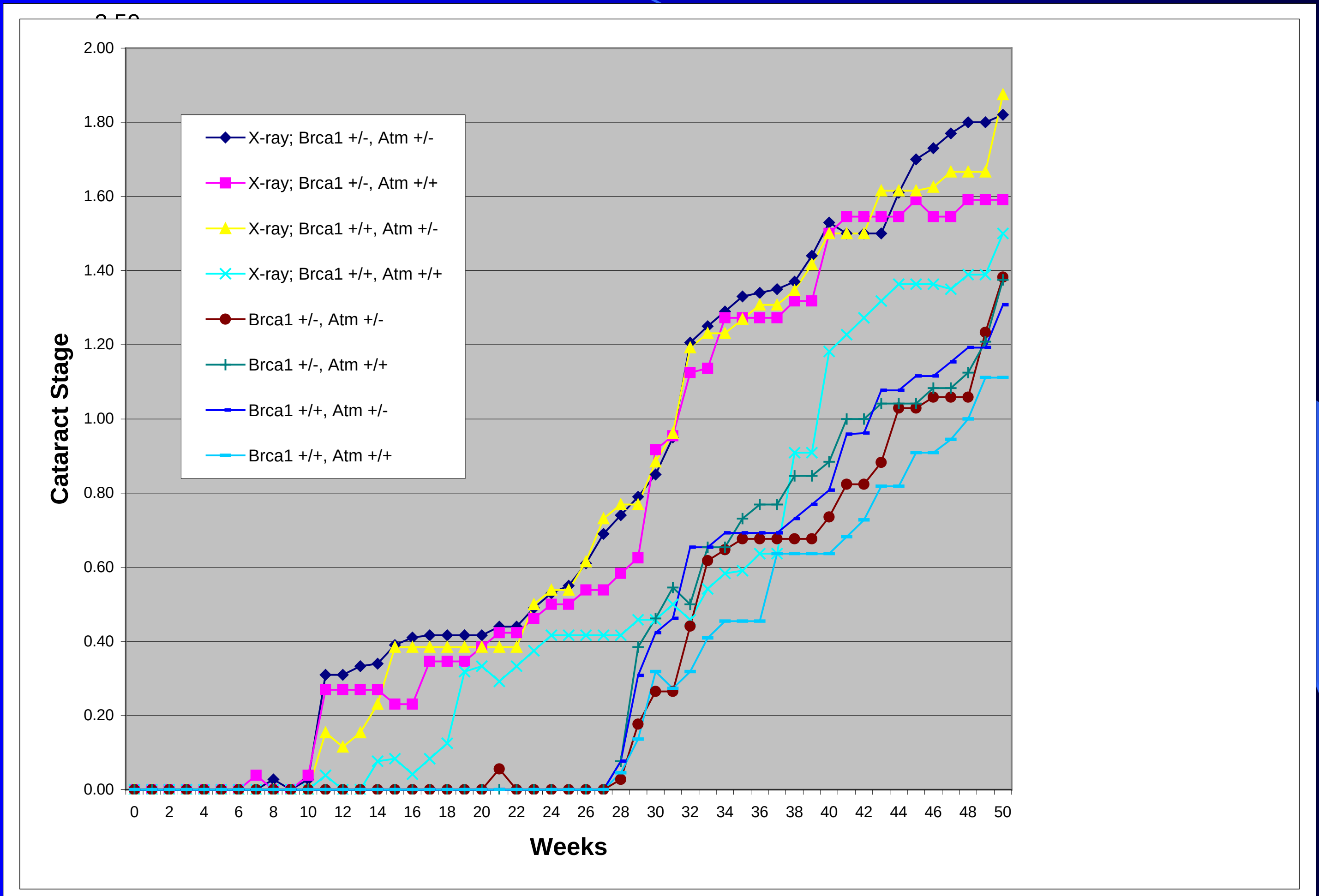
500 mGy X-ray



Invest. Ophthalmol. Vis. Sci. ***47***, 2006

The Response of Twenty-Seven Inbred Strains of Mice to Daily Doses of Whole-Body X-Irradiation[1]

THOMAS H. RODERICK

The Jackson Laboratory, Bar Harbor, Maine

INTRODUCTION

Studies of numerous inbred strains of mice have shown the importance of genetic factors in determining the variation of response to irradiation (references cited by Roderick, *1*). The present study of twenty-seven inbred strains was an attempt to ascertain the approximate limits of genetic variability of inbred strains, and in so doing to identify other strains of very high and very low resistance to whole-body X-irradiation. Heritability was found to vary significantly with season, and general fitness appeared to be an indicator of radioresistance.

Radiation Research ***20***, *631-639, 1963.*

Characterization of the Tumor Spectrum Arising in HZE Ion Irradiated Outbred Mice

-*Carcinogenesis data to date is from inbred mice or rats with limited genetic heterogeneity*

-*Tumor spectrum that might arise in an HZE ion exposed outbred population is unknown*

Specific Aims:

1. Characterize the tumor spectrum in a heterogeneous stock of mice irradiated with HZE nuclei and compare to similar populations of γ-ray irradiated or unirradiated mice.

2. Identify moderate and major effect quantitative trait loci (QTL) that underlie susceptibility to spontaneous, γ-ray-induced and HZE ion-induced tumors and determine overlap, if any, betweengroups.

Mike Weil, CSU

Heterogeneous Mouse Stock

- Robert Hitzemann, Oregon Health and Sciences University
- 8 progenitor strains:
A/J, AKR/J, BALB/cJ, C3H/HeJ, C57BL/6J, CBA/J, DBA/2J, LP/J
-mating schemes to breakdown linkage disequilibrium and to maximize genetic heterogeneity
- 48 mouse “families”

Irradiation

-Brookhaven National Laboratory
-0.4 Gy HZE or 3 Gy gamma irradiation

Genotyping

- Identify overlapping or unique loci that control susceptibility to spontaneous, γ-ray induced, and HZE ion-induced tumors
- analyze >7,800 SNP markers/genome
- Perform Quantitative trait locus (QTL) analysis

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Irradiation of the mouse by 1,000 MeV/amu high-LET ^{56}Fe in the *NASA Space Radiation Laboratory* (NSRL) at Brookhaven National Laboratory.

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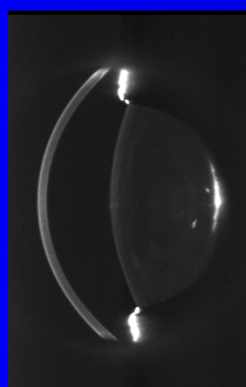
RADIATION RESEARCH **156**, 460–466 (2001)
0033-7587/01 $5.00

Space Radiation and Cataracts in Astronauts

F. A. Cucinotta,[a,1] F. K. Manuel,[b] J. Jones,[a] G. Iszard,[b] J. Murrey,[c] B. Djojonegro[c] and M. Wear[c]

[a] *NASA Johnson Space Center,* [b] *Kelsey-Seybold Clinic, and* [c] *Wyle Laboratories, Houston, Texas 77058*



What is the role of population diversity on the individual likelihood of developing radiation-induced cataracts and visual disability?

The <u>same mouse population</u> of 1800 individuals is being using to examine the effect of population diversity on

- **radiation cataract and visual disability**
- **the tumor spectrum**
- **cognitive outcomes**
- **urine metabolomic profiles**

This collaborative, multi-institutional approach should provide a very powerful method to examine four different biological outcomes of concern to NASA as well as permit comparison of the effects of HZE ion irradiation vs low-LET gamma irradiation on these endpoints.

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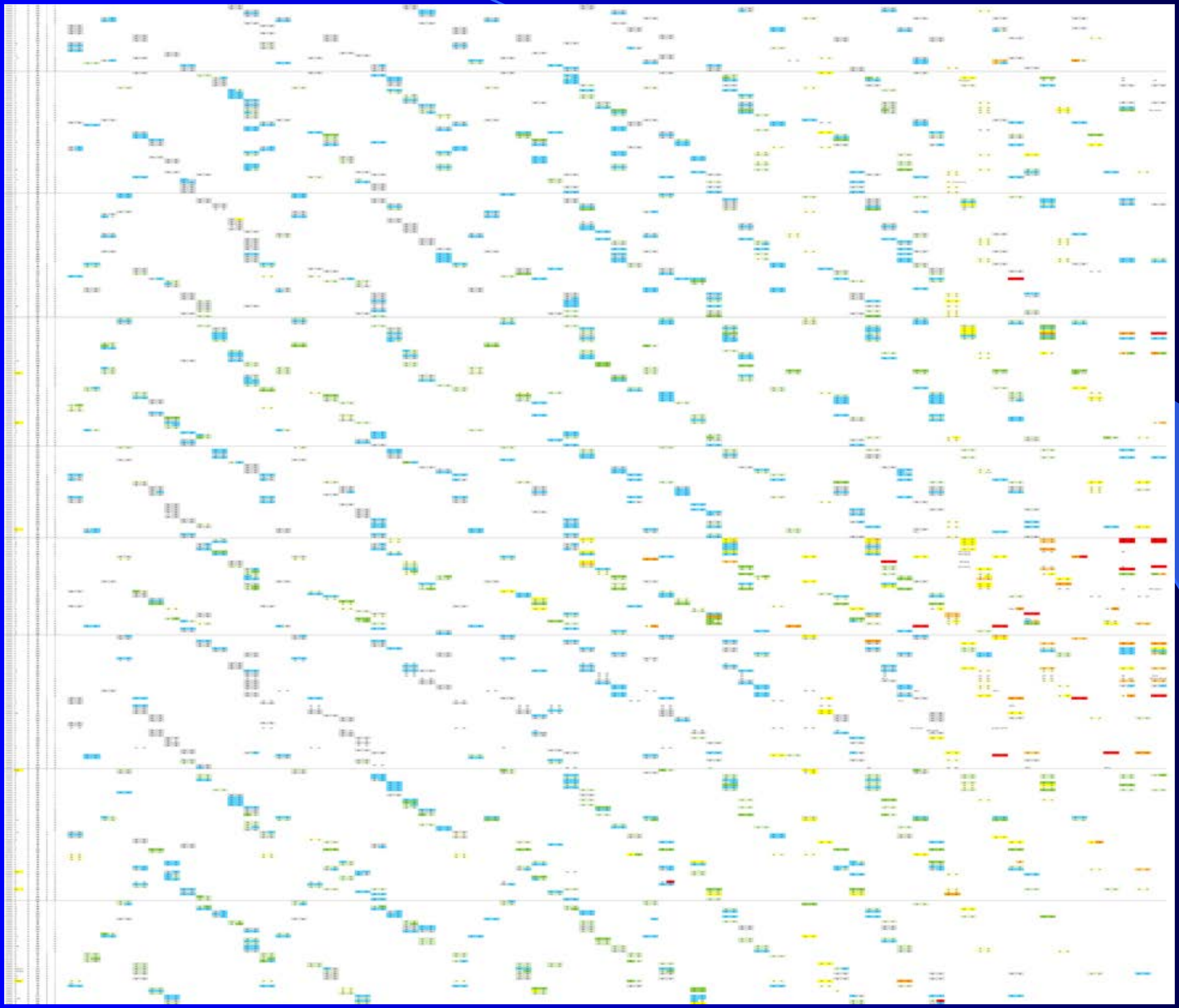
Family Predisposition for Radiation Cataract

Family grouping



time

increasing cataract severity shown from gray to blue to orange to red

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Not just subjective estimation of cataract stage but actual radiation-associated visual disability in mice.

Contrast Sensitivity Testing

Virtual Optomotor Testing (VOT)

- **Method for quantitatively determining what a mouse "sees"**
- **Independent of traditional measures of visual acuity**
  (*e.g.*, Eye Chart)
- **Quantifies changes in spatial frequency and contrast sensitivity**
- **Permits tracking of both onset and progression of change**

Prusky GT, Alam NM, Beekman,S, Douglas RM. Rapid quantification of adult and developing mouse spatial vision using a virtual optomotor system. *Invest Ophthalmol Vis Sci* 2004; **45**:4611.

Douglas RM, Alam NM, Silver BD, McGill TJ, Tschetter WW, Prusky GT. Individual differences in contrast sensitivity functions: the lowest spatial frequency channels. *Vis Neurosci* 2005; **22**: 677.

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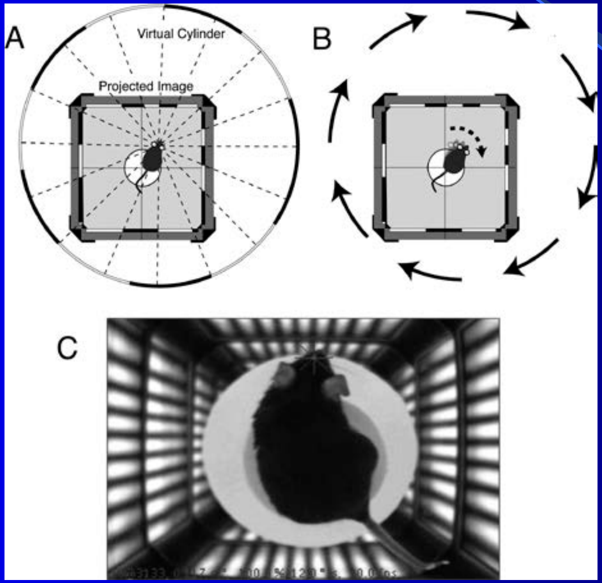
Four computer monitors arranged in a square with a platform in the middle containing the mouse



A vertical sine wave grating is projected onto the four monitors as the computer alters the frequency and/or contrast in stepwise fashion

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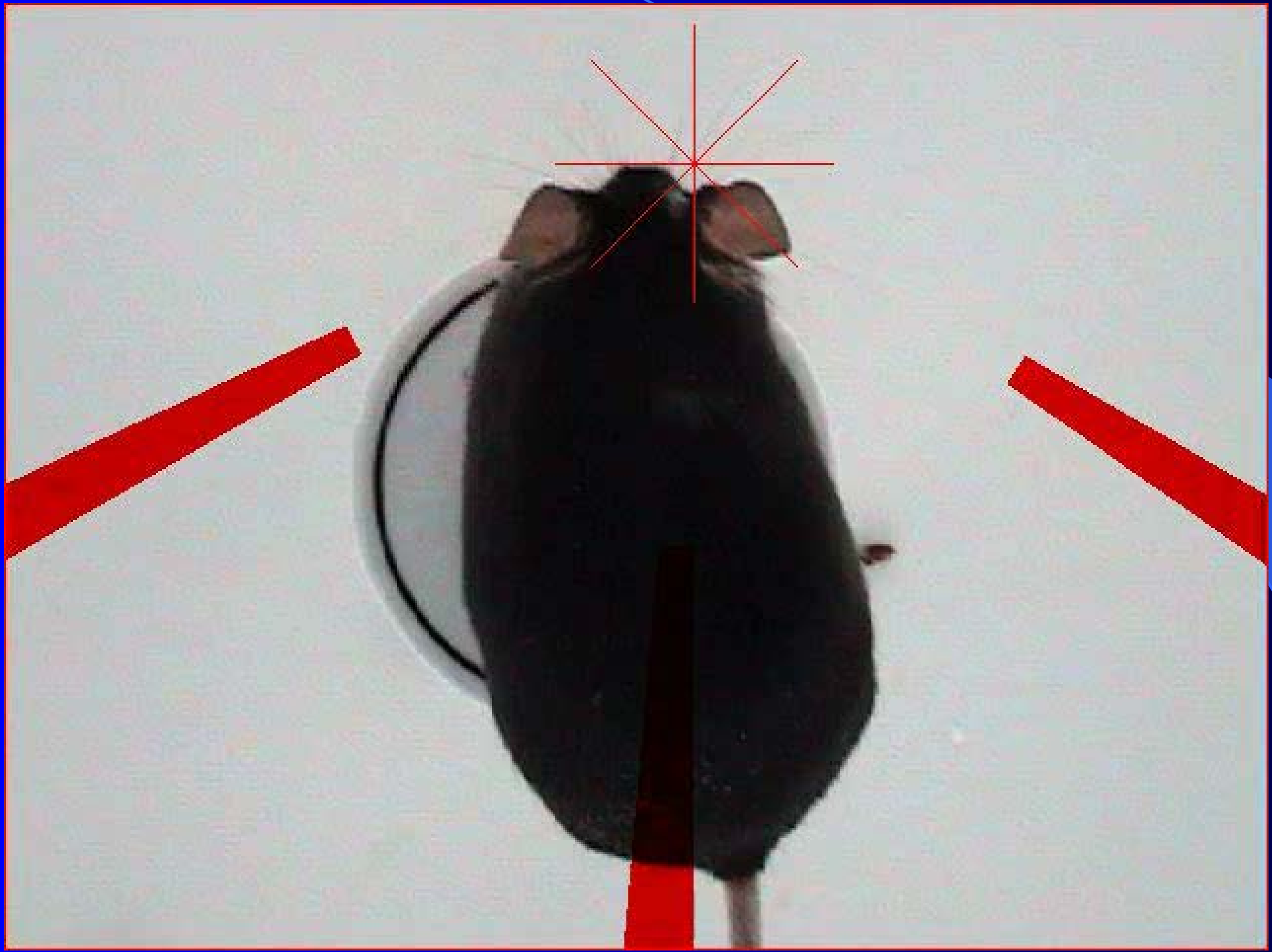

VOT contrast and frequency threshold measurements in a control, unirradiated mouse

Frequency threshold for 99.0% contrast:
CCW (left): 0.381 c/d
CW (right): 0.375 c/d
Combined: 0.378 c/d

Contrast threshold for 0.064 c/d
CCW (left): 6.3%
CW (right): 6.7%
Combined 6.5%

Time	Freq	Contrast	Direction	Correct
11:44:46 AM	0.064	100.0	1	1
11:44:51 AM	0.064	100.0	-1	1
11:45:03 AM	0.064	75.0	1	1
11:45:07 AM	0.064	50.0	1	1
11:45:23 AM	0.064	25.0	1	1
11:45:32 AM	0.064	75.0	-1	1
11:45:37 AM	0.064	50.0	-1	1
11:45:45 AM	0.064	25.0	-1	1
11:46:00 AM	0.064	12.5	1	1
11:46:11 AM	0.064	12.5	-1	1
11:46:31 AM	0.064	6.2	1	0
11:47:07 AM	0.064	6.2	-1	0
11:47:21 AM	0.064	9.4	1	1
11:47:33 AM	0.064	9.4	-1	1
11:47:50 AM	0.064	7.8	-1	1
11:47:58 AM	0.064	7.8	1	1
11:48:04 AM	0.064	6.2	-1	0
11:48:35 AM	0.064	6.2	1	0
11:48:43 AM	0.064	7.0	-1	1
11:48:50 AM	0.064	7.0	1	0
11:48:55 AM	0.064	7.8	1	1
11:49:07 AM	0.064	6.6	-1	1
11:49:18 AM	0.064	7.4	1	1
11:49:23 AM	0.064	6.2	-1	0
11:49:27 AM	0.064	6.4	-1	1
11:49:39 AM	0.064	6.3	-1	1
11:50:02 AM	0.064	7.0	1	1
11:50:34 AM	0.064	6.2	-1	0
11:50:41 AM	0.064	6.3	-1	1
11:51:00 AM	0.064	6.3	-1	1
11:51:04 AM	0.064	6.3	-1	1
11:51:14 AM	0.064	6.6	1	0
11:51:29 AM	0.064	6.8	1	1
11:51:34 AM	0.064	6.3	-1	1
11:51:39 AM	0.064	6.3	-1	1
11:52:26 AM	0.064	6.7	1	1
11:52:46 AM	0.064	6.6	1	0
11:52:56 AM	0.064	6.7	1	1

VOT contrast and frequency threshold measurements in irradiated mice: comparisons with Merriam-Focht scores

Irradiated mouse A: OD 0.0, OS 1.0

<u>Frequency threshold</u> for 99% contrast:
CCW (left): 0.292 c/d
CW (right): 0.383 c/d
Combined: 0.338 c/d

<u>Contrast threshold</u> for 0.064 c/d:
CCW (left): 29.5%
CW (right): 9.0%
Combined: 19.3%

Irradiated mouse B: OD 2.0, OS 2.0

<u>Frequency threshold</u> for 99% contrast:
CCW (left): 0.211 c/d
CW (right): 0.219 c/d
Combined: 0.215 c/d

<u>Contrast threshold</u> for 0.064 c/d:
CCW (left): 55.1%
CW (right): 53.1%
Combined: 54.1

Unirradiated mouse
Frequency threshold for 99.0% contrast: 0.378 c/d
Contrast threshold for 0.064 c/d: 6.5%

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HUMAN STUDIES

More recent studies of occupational risk: Epidemiological findings

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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

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

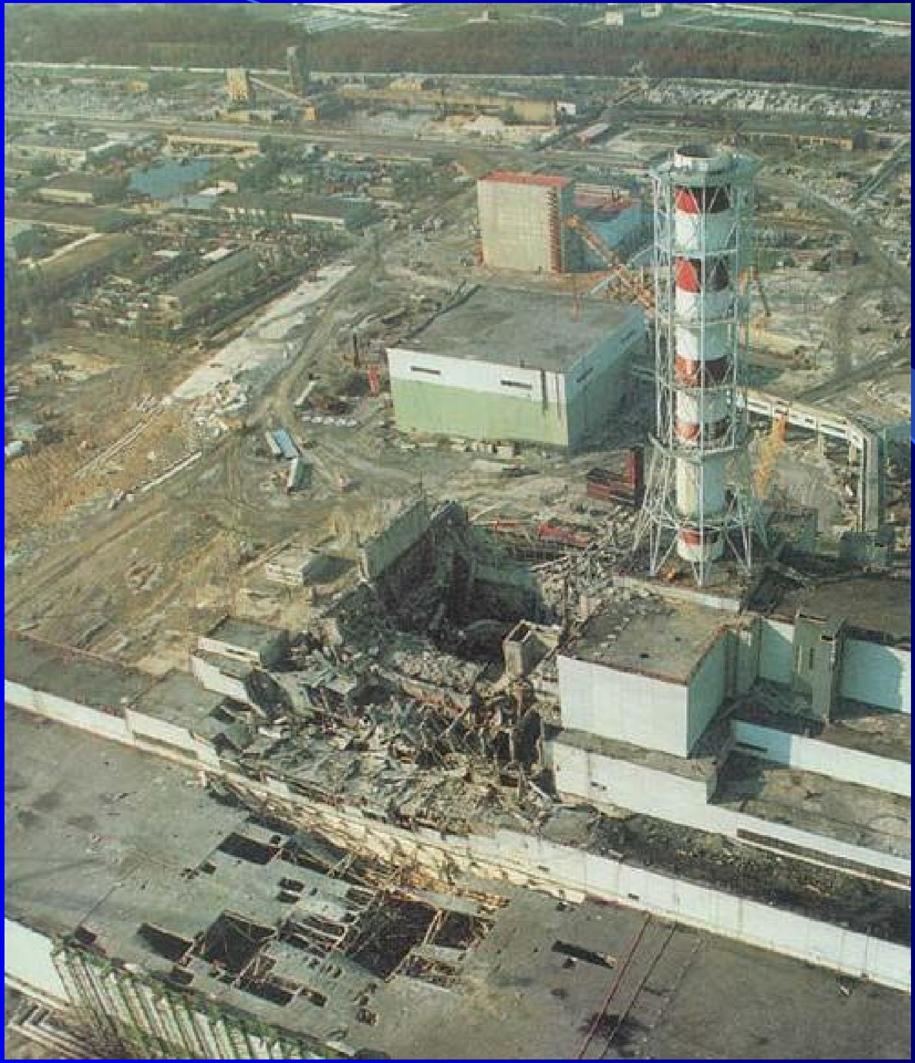
- Pilot study involving eye exams of 59 interventional radiologists 29-62 years old

- Frequency and severity of posterior subcapsular cataract increased with age and years in practice

- Nearly half of those examined had early lens changes associated with radiation cataract

- 5/59 had clinically significant posterior subcapsular cataracts (psc)

- 22/59 had posterior dots and vacuoles characteristic of early psc development



Chernobyl Nuclear Power Station Reactor 4

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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)

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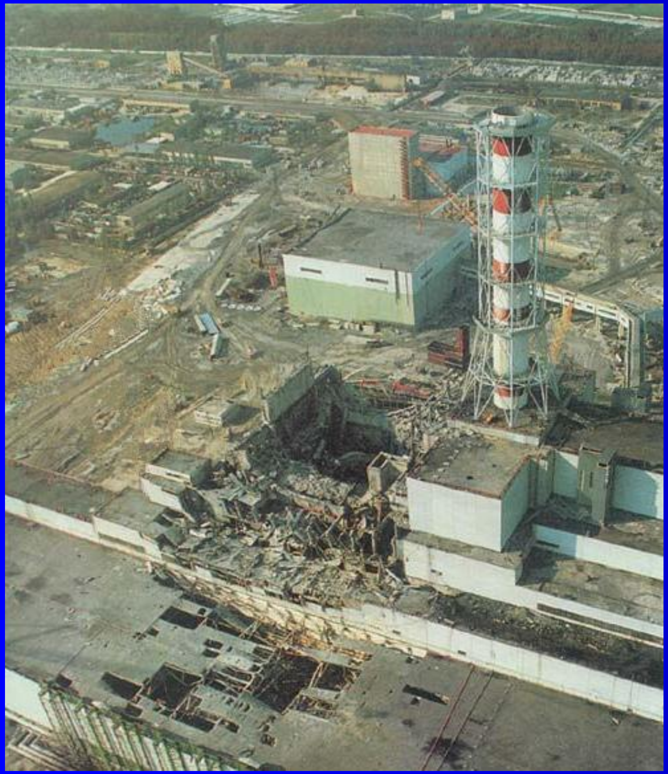
"Liquidators"



Chernobyl Nuclear Power Station Reactor 4

Radioactive graphite core ejected from the reactor

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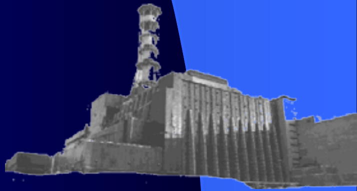
The Ukrainian American Chernobyl Ocular Study (UACOS)

GOALS

A cohort epidemiological study (with a nested case control subset) of cataract onset and progression using standardized subjective parameters.

The establishment of a program for the acquisition, archiving and analyses of lens epithelial tissue removed during routine cataract extraction procedures.

Quantitative analyses of radiation cataract development and progression in humans employing new technologies for a longitudinal non-subjective evaluation of lens transparency.



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Numbers of Subjects and Exclusions

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

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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 1st 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

*** Means ± S.D.**

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Outcomes at 1st Examination ("Prevalence" Data)

Outcome	Either Eye N (%)	Left Eye N (%)	Right Eye 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)

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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)

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Adjusted Odds Ratios & (95% Confidence Intervals) Prevalence Data

	Dose Groups (mSv)					
Variable	**0-49**	**50-99**	**100-199**	**200-399**	**400-699**	**700+**
Prevalence Data (Exam 1)						
No. of Subjects	1,300	1,550	3,776	1,431	364	186
Polychromatic Sheen	1.00	0.76 (0.60-0.96)	1.62 (1.34-1.95)	1.93 (1.55-2.40)	1.14 (0.79-1.66)	1.01 (0.60-1.70
Early pre-cataract changes	1.00	0.81 (0.66-0.98)	1.53 (1.30-1.81)	1.82 (1.49-2.21)	1.57 (1.13-2.18)	2.43 (1.52-3.89
Stage 1-5 cataract	1.00	0.60 (0.49-0.73)	0.81 (0.68-0.95)	1.21 (1.01-1.46)	1.59 (1.22-2.08)	1.90 (1.35-2.68
Stage 1 cataract	1.00	0.60 (0.49-0.73)	0.81 (0.69-0.96)	1.22 (1.01-1.47)	1.55 (1.18-2.04)	2.03 (1.44-2.86
Stage 2-5 cataract	1.00	0.65 (0.31-1.39)	0.80 (0.44-1.45)	1.48 (0.81-2.71)	2.13 (1.09-4.17)	1.13 (0.41-3.10
Stage 1-5, excl. nuclear cataracts	1.00	0.59 (0.48-0.72)	0.78 (0.66-0.92)	1.16 (0.96-1.41)	1.40 (1.07-1.83)	1.70 (1.21-2.39
Stage 1, excl. nuclear cataracts	1.00	0.59 (0.48-0.73)	0.77 (0.65-0.91)	1.15 (0.95-1.39)	1.33 (1.01-1.75)	1.71 (1.21-2.41
Early PSC changes	1.00	0.86 (0.70-1.07)	1.48 (1.24-1.77)	1.40 (1.14-1.72)	0.95 (0.67-1.34)	1.25 (0.83-1.89
Stage 1 PSC cataracts	1.00	0.67 (0.54-0.84)	0.99 (0.83-1.18)	1.22 (1.00-1.49)	0.99 (0.74-1.33)	1.03 (0.72-1.49
Early Superficial Post. Cort.Changes	1.00	0.77 (0.63-0.95)	1.38 (1.16-1.64)	1.59 (1.30-1.95)	1.15 (0.82-1.62)	1.54 (0.98-2.42
Stage 1 Superficial Post. Cort. Cataract	1.00	0.58 (0.47-0.71)	0.82 (0.69-0.96)	1.21 (1.00-1.46)	1.56 (1.19-2.06)	1.64 (1.16-2.31

Adjusted Odds Ratios & (95% Confidence Intervals) Incidence Data

	Dose Groups (mSv)					
Variable	**0-49**	**50-99**	**100-199**	**200-399**	**400-699**	**700+**
Incidence Data [B]						
Polychromatic Sheen	1.00	1.22 (0.82-1.83)	1.81 (1.28-2.56)	2.36 (1.60-3.49)	0.74 (0.30-1.82)	0.16 (0.02-1.23
Early pre-cataract changes	1.00	1.42 (0.98-2.05)	1.62 (1.16-2.24)	2.29 (1.58-3.31)	1.15 (0.54-2.46)	0.55 (0.12-2.52
Stage 1-5 cataract	1.00	1.15 (0.76-1.75)	1.53 (1.07-2.18)	1.64 (1.08-2.49)	1.91 (1.04-3.49)	3.31 (1.75-6.28
Stage 1 cataract	1.00	1.14 (0.75-1.73)	1.51 (1.06-2.16)	1.61 (1.06-2.45)	1.91 (1.04-3.49)	3.00 (1.56-5.79
Stage 1-5, excluding nuclear cataracts	1.00	1.40 (0.86-2.28)	1.37 (0.89-2.11)	1.87 (1.16-3.02)	3.03 (1.65-5.58)	4.81 (2.51-9.21
Stage 1, excluding nuclear cataracts	1.00	1.46 (0.89-2.38)	1.40 (0.90-2.17)	1.91 (1.17-3.11)	3.15 (1.70-5.81)	4.55 (2.33-8.88
Early PSC changes	1.00	1.31 (0.92-1.88)	1.79 (1.32-2.44)	2.09 (1.49-2.95)	0.68 (0.31-1.46)	0.55 (0.19-1.59
Stage 1 PSC cataracts	1.00	1.08 (0.65-1.78)	1.34 (0.88-2.04)	1.92 (1.21-3.05)	1.43 (0.72-2.83)	1.42 (0.63-3.19
Early Superficial Post. Cort Changes	1.00	1.17 (0.76-1.81)	2.10 (1.45-3.03)	2.88 (1.92-4.33)	0.57 (0.20-1.65)	1.67 (0.61-4.58
Stage 1 Superficial Post. Cort Cataract	1.00	1.00 (0.64-1.58)	1.19 (0.82-1.75)	1.51 (0.97-2.34)	2.25 (1.23-4.09)	3.58 (1.90-6.75

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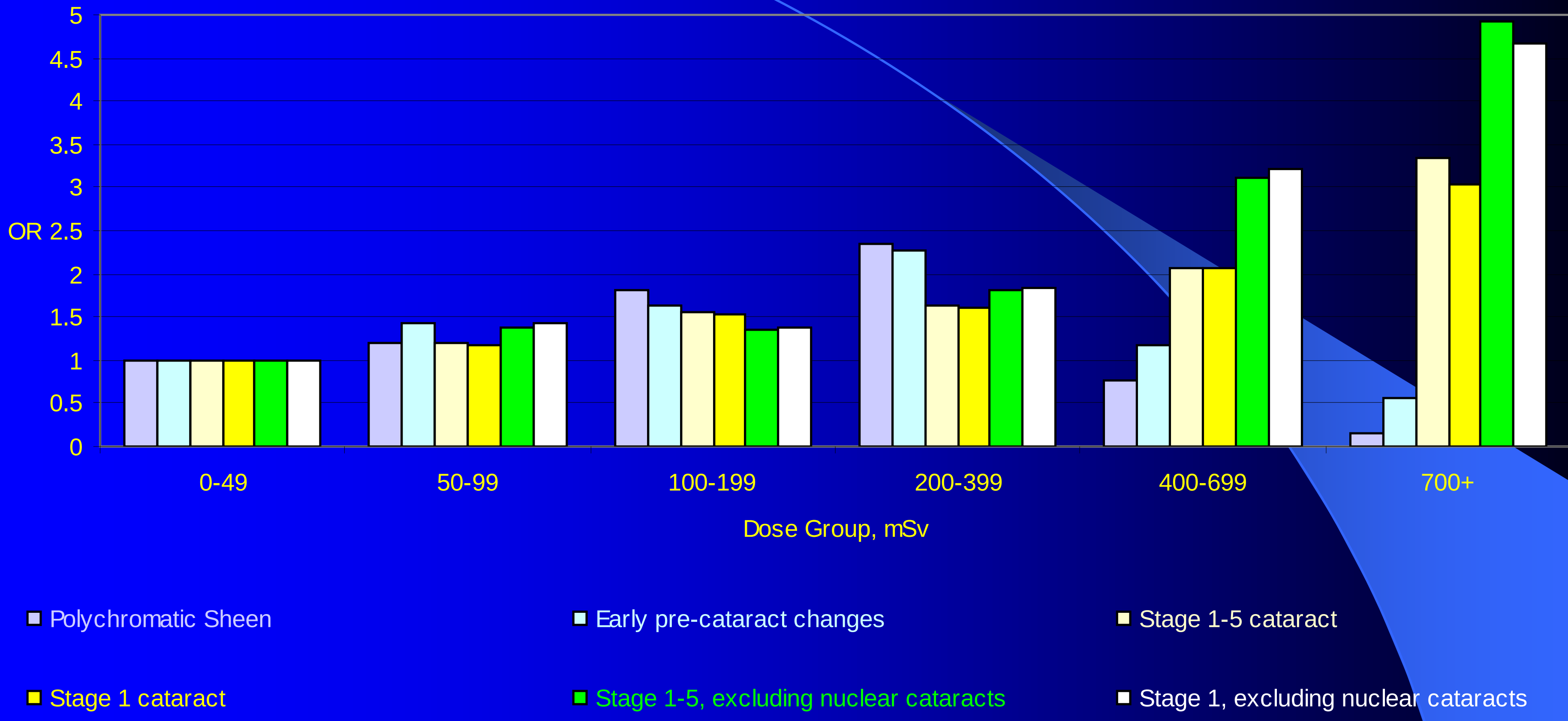
Adjusted Odds Ratios for Cataract Outcome Variables (Incidence Data) Among the Chernobyl Liquidators



- 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)

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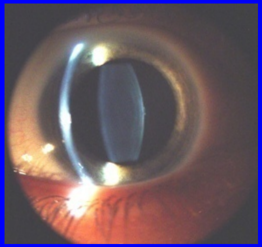
Nakashima, Neriishi, *et al.* (2006) A reanalysis of atomic-bomb cataract data, 2000–2002: a threshold analysis. *Health Phys.* **90**, 154-160.



"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 clinically relevant visual disability (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.

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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

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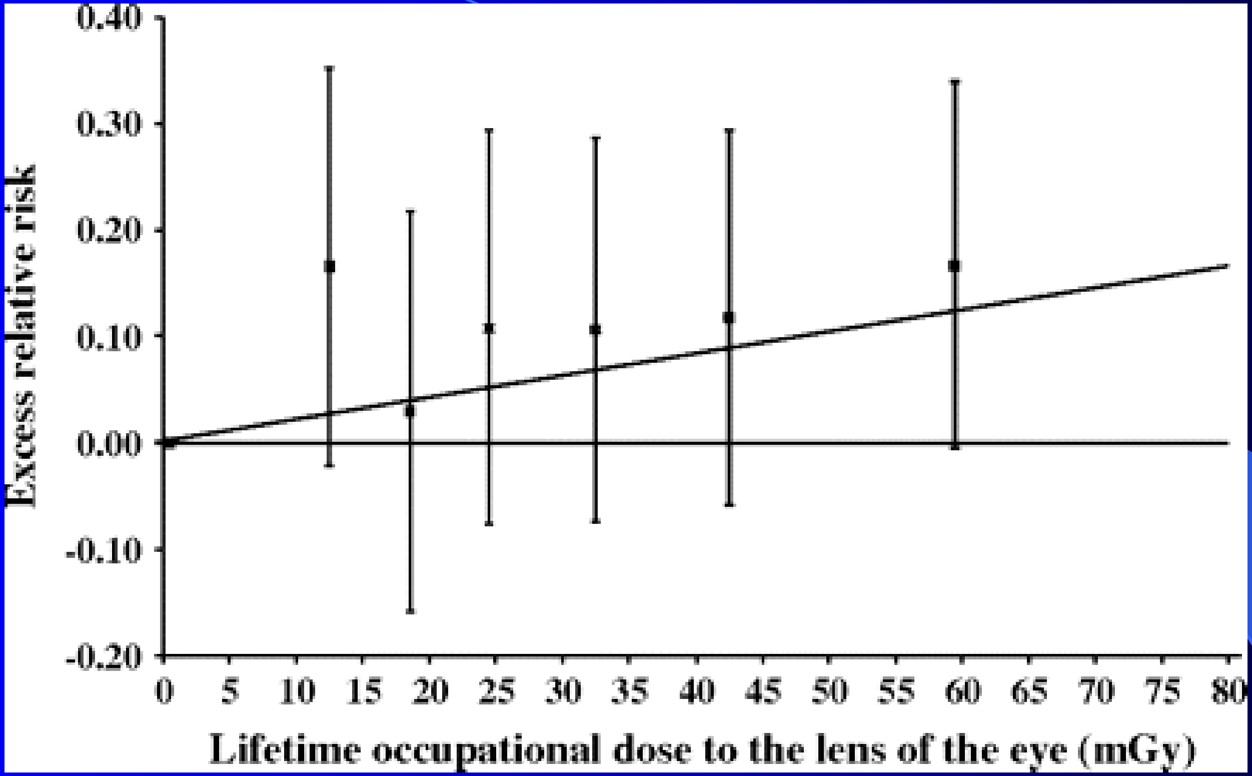
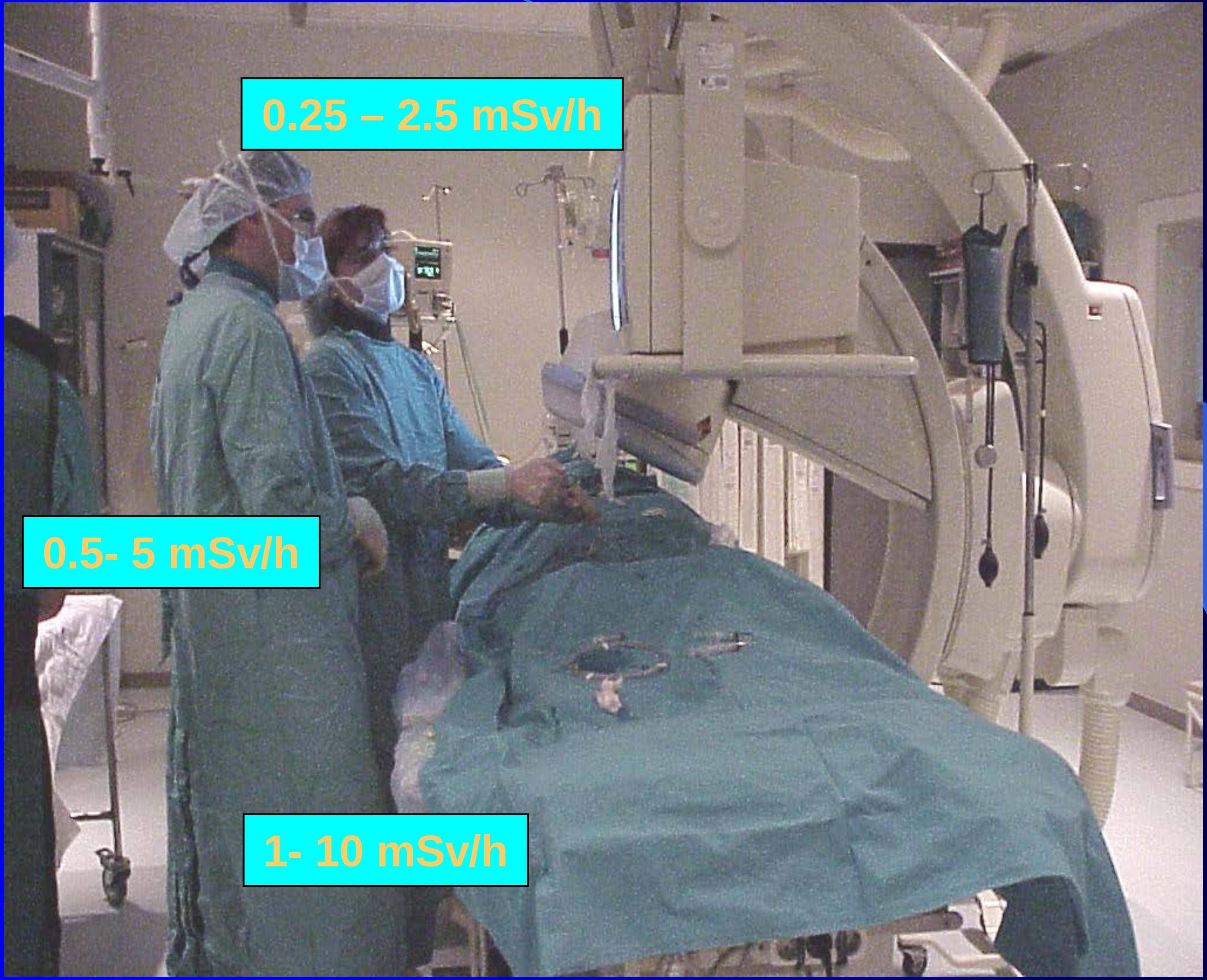


- adjusted cataract hazard ratio of 1.18 for those in the highest exposure range (60 mGy) as compared to those in the lowest (5 mGy)
- the median occupational ionizing radiation dose to the lens was estimated to be 28.1 mGy for the entire cohort

Interventional Medicine



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Kim, et al., *Health Physics* **103**:80, 2012
Koukorova et al., *Rad Prot Dosim*etry **144**:482, 2011
Domienik et al., Rad Prot Dosimetry 144:2011

A single procedure could expose the lens to as much as

0.5-1.0 mSv *(mean=0.075 µSv)*

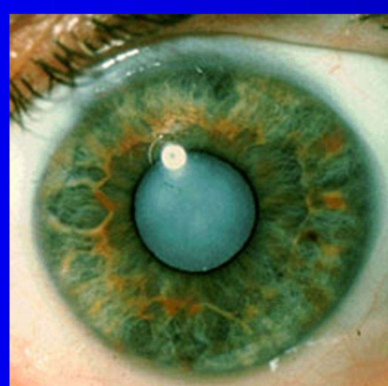
thus, IF

If a physician does three procedures/day, five days/wk, 40 wks/yr, it's possible to receive an annual dose >300 mSv!

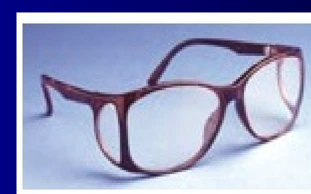
(mean =45 mSv)

AND

if there are no elements of protection! …



Radiation cataract



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IAEA.org
International Atomic Energy Agency

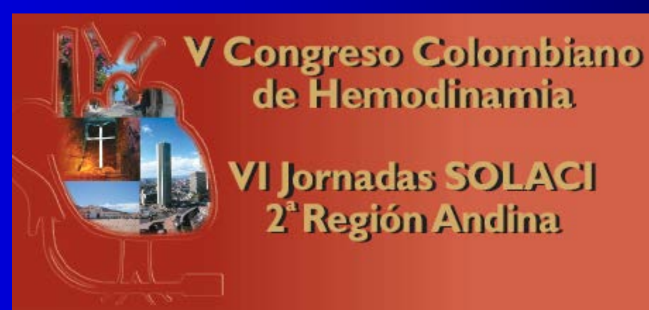
RELID

Retrospective Evaluation of Lens Injuries and Dose

- **Conducted at regional meetings of cardiologists and medical workers in Bogotá, Colombia, Montevideo, Uruguay, Bulgaria and Malaysia.**
- **Detailed questionnaire about medical, ocular and occupational history**
- **Dilated, comprehensive slit lamp of the lens**
- **Correlate occupational radiation exposure with radiation cataract risk**

SOLACI
SOCIEDAD LATINOAMERICANA DE CARDIOLOGIA INTERVENCIONISTA

NATIONAL HEART ASSOCIATION OF MALAYSIA



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Catheterization and Cardiovascular Interventions 76:826–834 (2010)

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: Eyes 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 Gy 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.

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

RADIATION RESEARCH 174, 490–495 (2010)
0033-7587/10 $15.00

DOI: 10.1667/RR2207.1

Radiation Cataract Risk in Interventional Cardiology Personnel

Eliseo Vano,[a,1] Norman J. Kleiman,[b,1,2] Ariel Duran,[c,1] Madan M. Rehani,[d,1] Dario Echeverri[e] and Mariana Cabrera[f]

[a] Radiology Department, Complutense University, Madrid, Spain; [b] Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University, New York, New York; [c] Invasive Cardiology, University Hospital, Montevideo, Uruguay; [d] International Atomic Energy Agency, Vienna, Austria; [e] Fundación Cardio Infantil, Bogota, Colombia; and [f] Fundación Oftalmologica 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 -scatter X-radiation field for several hours a day ng cardiac interventional procedures.

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.

J Vasc Interv Radiol ***24***:197-204, 2013

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Findings

- **Many IC's have early lens changes associated with radiation cataract, including posterior dots and vacuoles predictive of future psc development**
  - *Merriam Focht scores of 0.5-1.5*
- **Some cardiology suite nurses have similar early lens changes**
  - *Merriam Focht scores of 0.5 in one or both eyes*
- **Small numbers of cardiologists have clinically significant psc**

- **Very few non-medical professionals (<10%) without prior history of radiation exposure had lens changes of the sort noted after radiation exposure.**

- ***IAEA-RELID: Bogota, Montevideo, Bulgaria, Buenos Aires***

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Prevalence

Subjects (n)	Posterior subcapsular opacities in one or both eyes	*P* value
Interventional cardiologists (58)	22 (37.9%)	< 0.005
Nurses and technicians (58)	12 (20.7%)	0.13
Unexposed controls (93)	11 (11.8%)	

Subject characteristics and prevalence of posterior lens changes in interventional cardiologists, nurses and technicians (Bogotá/Montivideo cohort

Subjects	Mean age (yrs)	Range (yrs)	Mean working time (yrs)	Cumulative occupational lens dose (Sv)	Range (Sv)
Interventional Cardiologists	46 ± 8	30-69	14 ± 8	6.0 ± 6.6	0.1-27
Nurses and Technicians	38 ± 7	22-60	7 ± 5	1.5 ± 1.4	0.2-4.5
Controls	41±10	20-66	n/a	n/a	

*Vano, Rad Res **174**:490-495, 2010*

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Dose Response

Dose (Sv)	Number of subjects	Number of subjects with posterior lens changes*	OR	95% CI
0 (Control)	22	2 (9%)	1.0	n/a
0.5-1	8	2 (25%)	3.8	0.36-39
1-2	11	5 (45%)	8.2	1.4-47
2-3	9	5 (55%)	13	2.1-81
>3	16	12 (75%)	16	4.2-58
	Total: 67	34 (51%)	5.4	2.0-14

Grade 0.5 or higher in either eye

The number of interventional cardiology workers (cardiologists or nurses) with posterior lens changes characteristic of ionizing radiation exposure as a function of total cumulative ocular occupational exposure. (Malaysian cohort)

*Ciraj-Bjelac, Cathet Cardio Interv **76**:826-834,2010*

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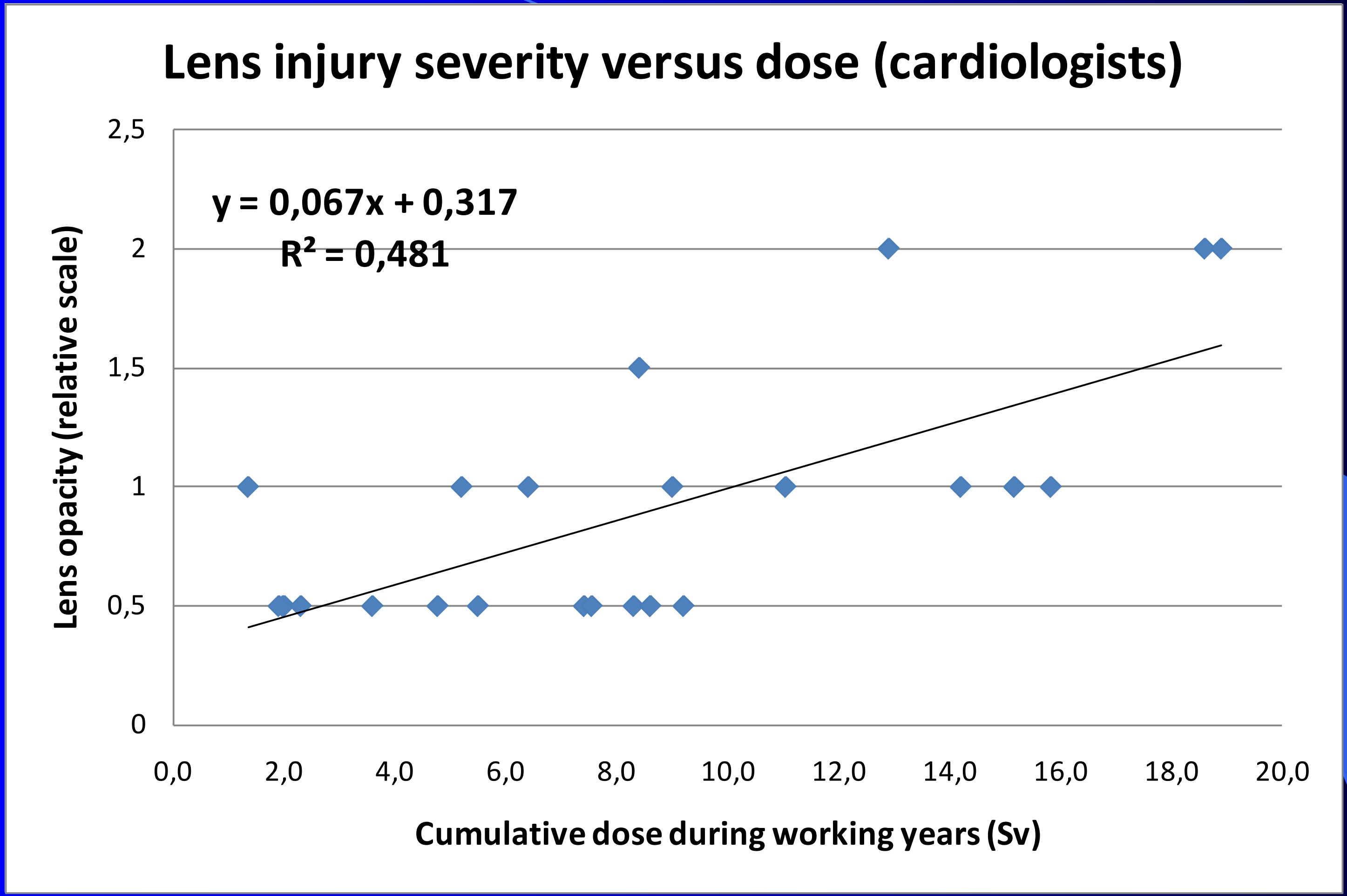

Vano, Kleiman, et al JVIR 2013

- **Most cardiologists with early lens changes reported never or infrequently utilizing eye protection**

- **Frequency and severity of posterior lens changes increase with age and years in practice**

Jacob *et al. BMC Public Health* 2010, **10**:537
http://www.biomedcentral.com/1471-2458/10/537

BMC Public Health

STUDY PROTOCOL — Open Access

Occupational cataracts and lens opacities in interventional cardiology (O'CLOC study): are X-Rays involved?

Sophie Jacob[1*], Morgane Michel[1], Christian Spaulding[2], Serge Boveda[3], Olivier Bar[4], Antoine P Brézin[5], Maté Streho[5], Carlo Maccia[6], Pascale Scanff[7], Dominique Laurier[1], Marie-Odile Bernier[1]

Lens opacities among physicians occupationally exposed to ionizing radiation – a pilot study in Finland

Mrena S, Kivelä T, Kurttio P, Auvinen, A.

***Scand J Work Environ Health* 2011;37(3):237-243**

Eye lens radiation exposure and repeated head CT scans: A problem to keep in mind

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Interventional cardiologists and risk of radiation-induced cataract: Results of a French multicenter observational study ☆

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ARTICLE INFO

Article history:
Received 29 March 2012
Accepted 22 April 2012
Available online 18 May 2012

Keywords:
Invasive procedure
X-rays
Ionizing radiation
Cardiologist
Eye exposure
Cataract

ABSTRACT

Background: Interventional cardiologists (ICs) are exposed to X-rays and may be at risk to develop cataract earlier than common senile cataract. Excess risk of posterior subcapsular cataract, known as radiation-induced, was previously observed in samples of ICs from Malaysia, and Latin America. The O'CLOC study (Occupational Cataracts and Lens Opacities in interventional Cardiology) was performed to quantify the risk at the scale of France.
Methods: This cross-sectional multicenter study included an exposed group of ICs from different French centers and an unexposed control group of non-medical workers. Individual information was collected about cataract risk factors and past and present workload in catheterization laboratory. All participants had a clinical eye examination to classify the lens opacities (nuclear, cortical, or posterior subcapsular) with the international standard classification LOCS III.
Results: The study included 106 ICs (mean age $= 51 \pm 7$ years) and 99 unexposed control subjects (mean age $= 50 \pm 7$ years). The groups did not differ significantly in the prevalence of either nuclear or cortical lens opacities (61% vs. 69% and 23% vs. 29%, respectively). However, posterior subcapsular lens opacities, were significantly more frequent among ICs (17% vs. 5%, $p = 0.006$), for an OR = 3.9 [1.3–11.4]. The risk increased with duration of activity but no clear relationship with workload was observed. However, the risk appeared lower for regular users of protective lead glasses (OR = 2.2 [0.4–12.8]).
Conclusions: ICs, in France as elsewhere, are at high risk of posterior subcapsular cataracts. Use of protective equipment against X-rays, in particular lead glasses, is strongly recommended to limit this risk.

Internat J Cardiol ***167***:*1843-1847, 2013*

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The rate of progression of such radiation associated lens changes is slow.

Nevertheless, eye protection is recommended to delay progression and limit future cumulative dose to the lens.

Radiation Protection Dosimetry (2011), pp. 1–5
doi:10.1093/rpd/ncr299

RADIATION AND CATARACT

Madan M. Rehani[1,*], Eliseo Vano[2], Olivera Ciraj-Bjelac[3] and Norman J. Kleiman[4]
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When this paper was about to go to press, the International Commission on Radiological Protection released a statement recommending a change in the threshold dose for the eye lens and dose limits for eye for occupationally exposed persons. It is clear that the earlier published threshold for radiation cataract is no longer valid. Epidemiological studies among Chernobyl clean-up workers, A bomb survivors, astronauts, residents of contaminated buildings, radiological technicians and recent surveys of staff in interventional rooms indicate that there is an increased incidence of lens opacities at doses below 1 Gy. Nevertheless, eye lens dosimetry is at a primitive stage and needs to be developed further. Despite uncertainties concerning dose threshold and dosimetry, it is possible to significantly reduce the risk of radiation cataract through the use of appropriate eye protection. By increasing awareness among those at risk and better adoption and increased usage of protective measures, radiation cataract can become preventable despite lowering of dose limits.

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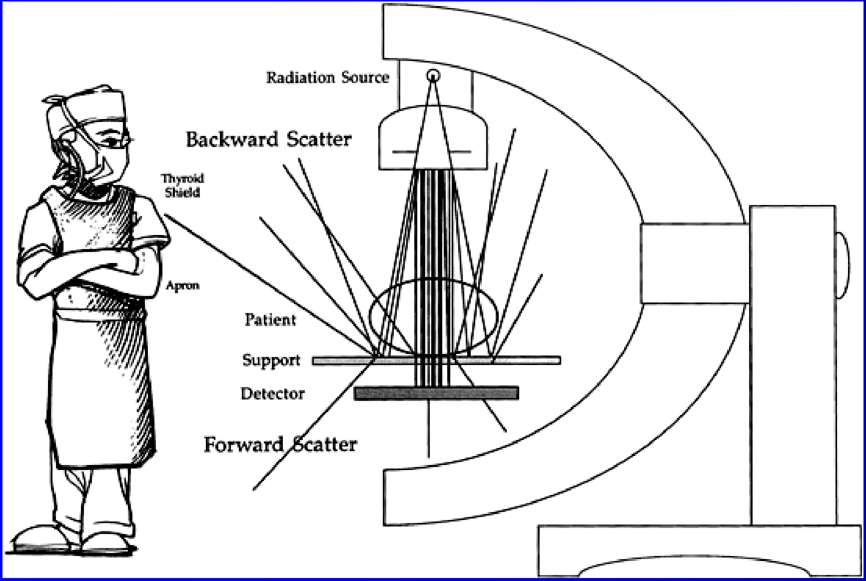
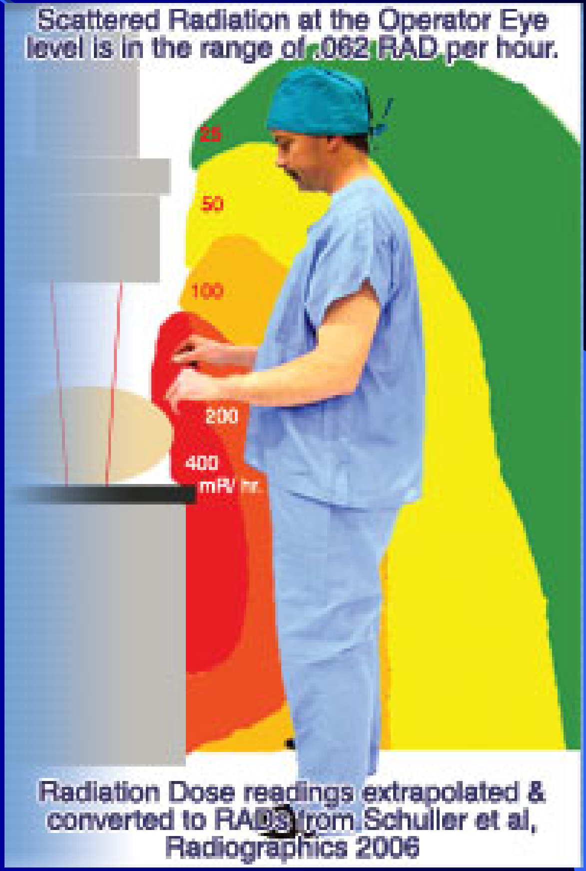
Eye Protection!!

Weight: 80 g
Equivalent to 0.75mm of lead
Front and lateral protection is essential

Scattered dose to the lens





mean operator radiation dose per case :

19-800 (median = 113) µSv at eye level

*Health Physics **103**: 80-99, 2012*

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~2-7X reduction

TABLE I Radiation Exposure with the Magnitude in Reduction Due to the Use of Leaded Glasses

Projection*	Unprotected Lens Dose (μrem)	Protected Lens Dose (μrem)	Magnitude Reduction†
Posteroanterior pelvic	13.3	0.9	14.8
Pelvic inlet (45°)	131.5	15.9	8.3
Pelvic inlet (25°)	27.1	5.5	4.9
Pelvic outlet (45°)	59.0	5.2	11.3
Pelvic outlet (50°)	27.5	3.0	9.2
Obturator oblique (30°)	0	0	NA
Iliac oblique (30°)	48.9	6.0	8.2
Pelvic obturator outlet (30° RAO, 30° caudal)	32.3	3.8	8.5
"Teepee" (modified obturator outlet), 33° RAO, 20° caudal	0	0	NA
Pelvic inlet iliac oblique (30° LAO, 30° cranial)	102.2	8.3	12.3
View down the iliac wing (modified obturator inlet)	8.9	1.0	8.9
Lateral view of sacrum with image intensifier opposite surgeon	256.8	23.9	10.7
Lateral view of sacrum with image intensifier next to surgeon	21.8	2.6	8.4
Posteroanterior hip	19.5	2.1	9.3
Cross-table lateral view of hip (hip bumped up on sheet roll)	21.6	1.0	21.6
Lateral view of hip with cephalad tilt (hip bumped on sheet roll)	26.0	3.0	8.7

*RAO = right anterior oblique, and LAO = left anterior oblique. †NA = not applicable.

*Burns, J Bone Joint Surg Am **95**:1307-1311, 2013*

Effect of leaded eyewear and additional shielding

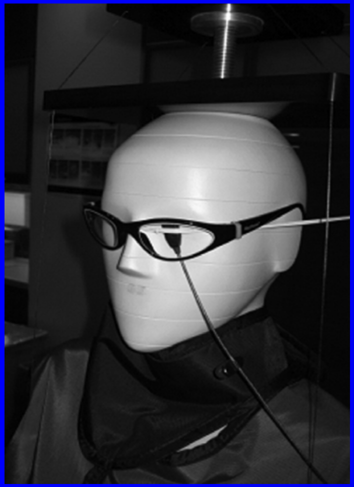

Table 1
Left Lens Exposure while Operating at Patient's Groin during Low-dose PA Fluoroscopy and In-room PA DSA of Upper Abdomen

	Low-dose PA Fluoroscopy			PA DSA		
	Lens Dose Rate		Lens Dose Reduction Factor	Lens Dose Rate		Lens Dose Reduction Factor
Shielding Strategy	mSv/h	mR/h		mSv/h	mR/h	
Image intensifier at 20 cm	1.18	135	—	—	—	—
Image intensifier at 3 cm (close)	0.54	62	—	—	—	—
Plus leaded table skirt	0.492	56.2	RM	4.3	500	RM
Plus unleaded eyeglasses	0.489	55.8	1.0	4.3	500	1.0
Plus leaded eyeglasses	0.052	5.9	9.5	0.64	74	6.8
Plus scatter-shielding drape	0.041	4.7	12.0	0.18	20.3	24.6
Plus leaded eyeglasses and scatter-shielding drape	LLD	LLD	> 1,000	0.032	3.5	143
Plus ceiling-suspended shield	LLD	LLD	> 1,000	0.028	3.2	132
Plus ceiling-suspended shield and scatter-shielding drape	LLD	LLD	> 1,000	LLD	LLD	> 1,000
Plus rolling shield	LLD	LLD	> 1,000	LLD	LLD	> 1,000

Note.—LLD = below the lower limit of detection (0.001 mSv/h); RM = reference measurement.

25X increased protect**ion**

*Thornton, J Vasc Interven Radiol **21**:1703-1707, 2010*

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Education Works!

Procedure	Protection	Use of protection (%)[a]		P value
		Before education	After education	
Complicated PICC	Leaded eyeglasses	13.2±6.5	45.8±17.4	<0.01
Non-PICC	Leaded eyeglasses	38.7±15.8	43.9±21.8	NS
	Hanging shield	27.9±6.5	43.5±6.4	<0.01
	Eyeglasses or shield or both	49.0±14.5	62.3±14.4	0.02

IR use of leaded eyewear and/or ceiling suspended shields

Sheyn, Pediatr Radiol 38:669-674, 2008

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.

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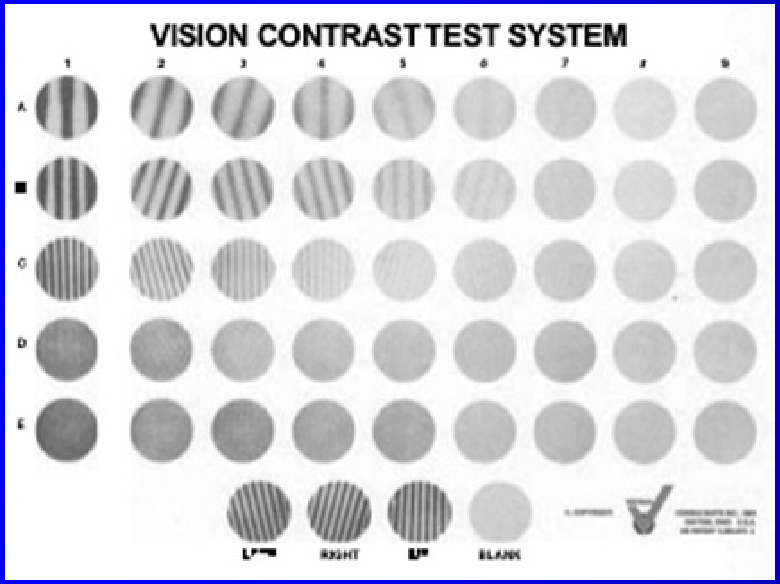
Additional studies, for example in other interventional physician cohorts and associated medical workers, may help further refine appropriate risk guidelines and the radiation cataract “threshold” for occupational exposure

Future Interventional Medicine Studies

- **Large cohort size**
- **Broad representation age, gender, procedure**
- **Well documented exposure history**
- **Appropriate controls (*eg*; SocioEconomicStatus)**
- **Real –time eye dose measurements**
- **Careful dilated slit lamp exam**
- **Contrast Sensitivity Testing**
- **Long-term follow-up to study rate of progression**

Human Contrast Sensitivity Testing

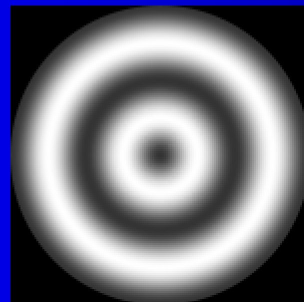
Traditional Testing of Contrast Sensitivity

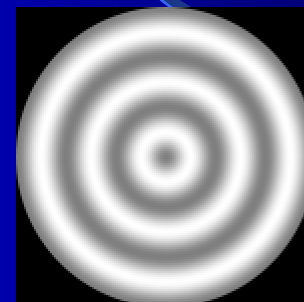


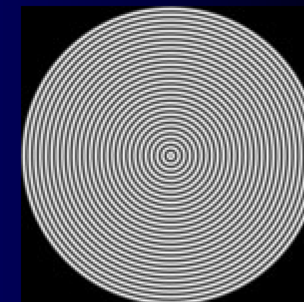
Visitech chart

Peli-Robson chart

Holladay Automated Contrast Testing







- Rotationally symmetric targets
- Randomly presented optotypes
- Test time < 5 min/eye
- Testing at 1.5, 3, 6, 12, 18 cycles/degree
- 1-100% contrast under mesopic or photopic luminence

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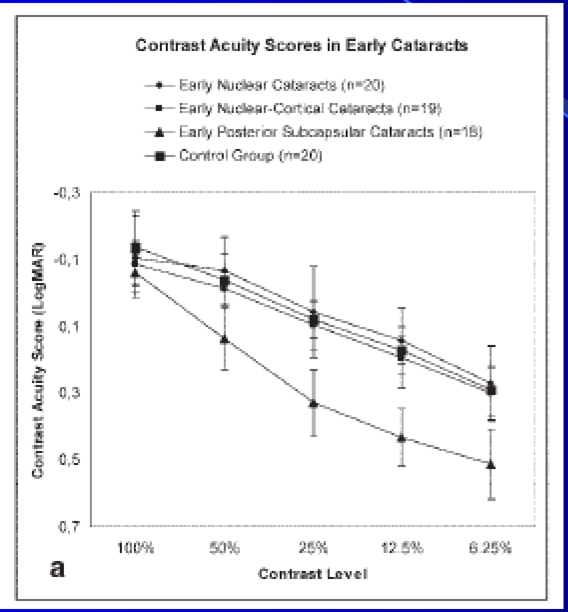
Stifter E, Sacu S, Thaler A, Weghaupt A. Contrast acuity in cataracts of different morphology and association to self-reported visual function. *Invest Ophthalmol Vis Sci* 2006; **47**:5412.



…analyses searching for statistically significant differences between the pairs of cataract groups, contrast acuity scores of the early nuclear and early nuclear-cortical cataract groups were comparable to those of the normal-sighted control group at all contrast levels (*P* > 0.05). <u>In contrast, patients with early PSC had significantly reduced contrast acuity scores at decreasing contrast level</u>.

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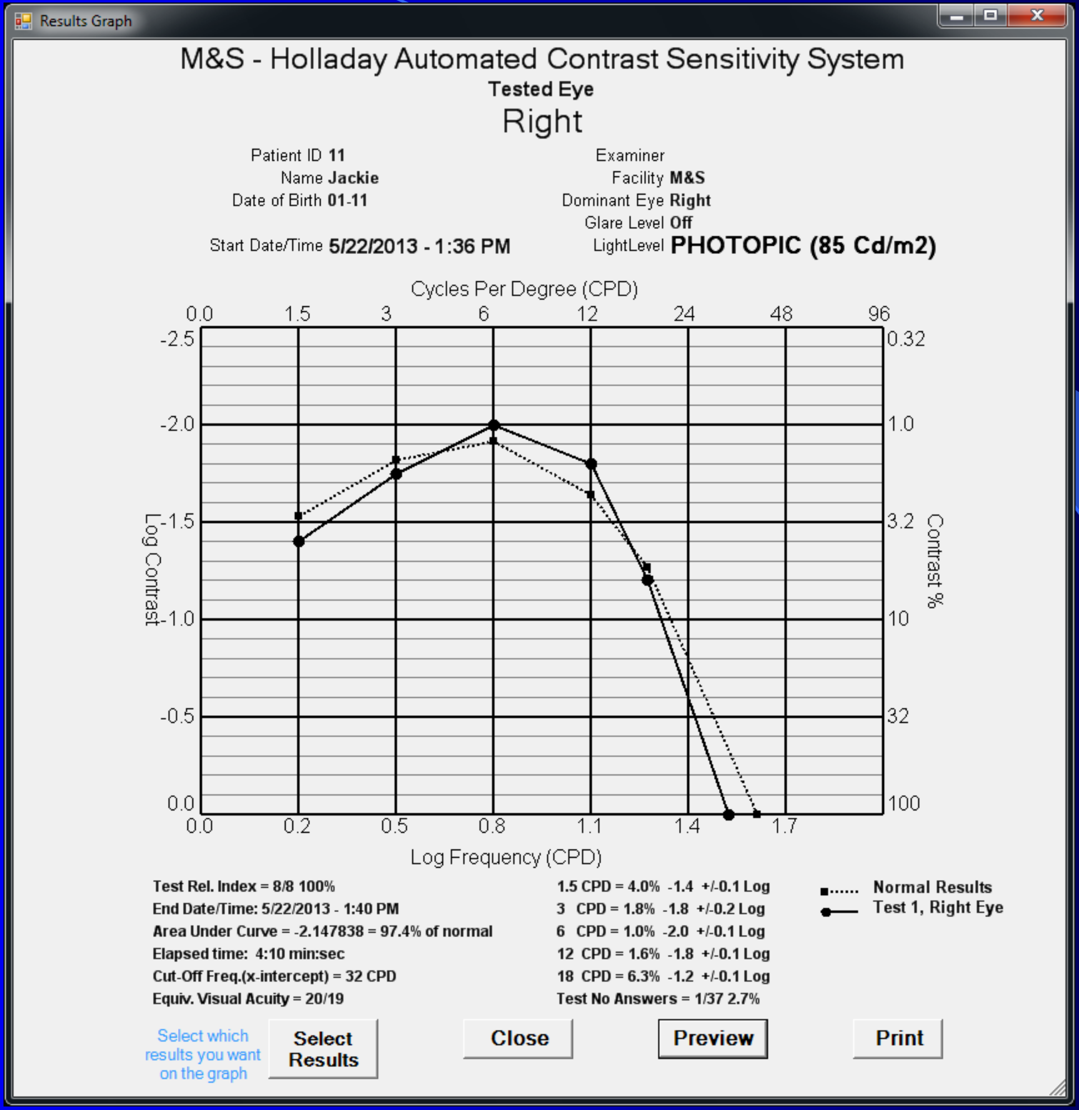

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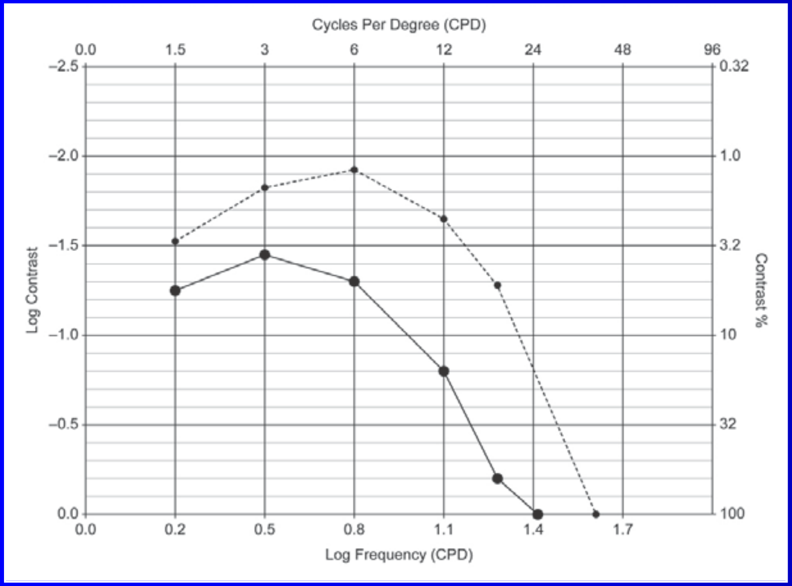
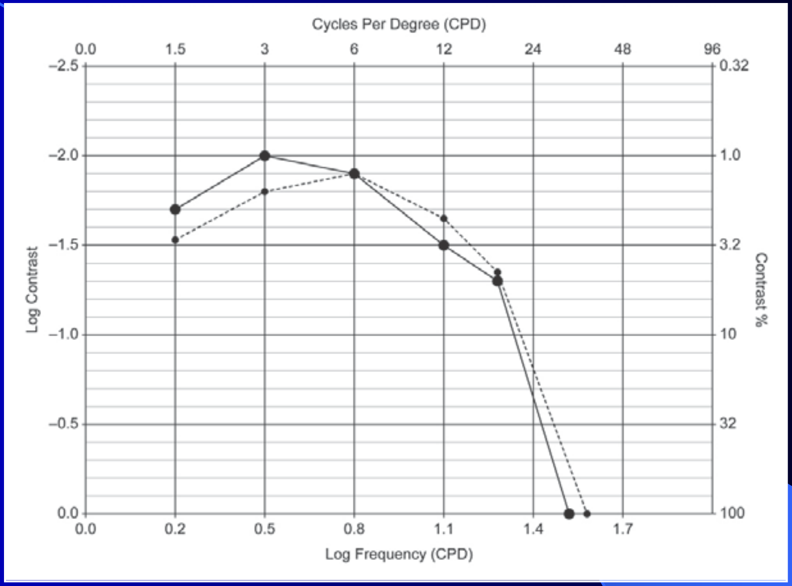
Contrast Sensitivity Testing in Interventional Cardiology



IC subject A

(abberrent)

M-F 1.5



IC subject B

(normal)

M-F 0.0

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Conclusions:

As compared to conventional slit lamp exam, in both human subjects and animal models, Contrast Sensitivity Testing may provide an alternative, complementary methodology for defining and quantifying visual disability due to radiation exposure.

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

Potential post-operative visual complications of cataract surgery

- Glare and flare
- Decreased acuity
- Decreased contrast sensitivity
- Photophobia
- Stereopsis

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%

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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. "

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Radiation cataract provides a <u>model</u> for studying long-term biological effects following low-dose ionizing radiation exposures in environmental or occupational settings.

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Picano *et al. BMC Cancer* 2012, **12**:157
http://www.biomedcentral.com/1471-2407/12/157

BMC Cancer

REVIEW **Open Access**

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

Eugenio Picano[1*], Eliseo Vano[2], Luciano Domenici[3], Matteo Bottai[4] and Isabelle Thierry-Chef[5]

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: Ionizing 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

Radiation Protection Dosimetry (2011), Vol. 147, No. 1–2, pp. 305–309
Advance Access publication 9 August 2011
doi:10.1093/rpd/ncr344

RISK ESTIMATES FOR MENINGIOMAS AND OTHER LATE EFFECTS AFTER DIAGNOSTIC X-RAY EXPOSURE OF THE SKULL

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[2]Immanuel Hospital, Berlin, Germany

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This study aims to investigate the contribution of diagnostic exposures to the rising rates of brain tumours and other neoplasms which are observed in several industrial nations. Included are benign tumours in the head and neck region and cataracts which are neglected in usual risk estimates by international and national radiation protection committees. Dose–effect relationships for tumours of the brain, skin, thyroid and other sites of the head region, leukaemia and cataracts are taken from the literature. Risk estimates are derived for paediatric head computed tomographies (CTs) as well as for brain tumours in adults. On the basis of estimates for Germany about the number of head scans, the annual rate of radiation-induced diseases is calculated. About 1000 annual paediatric CT investigations of the skull will lead to about three excess neoplasms in the head region, i.e. the probability of an induced late effect must be suspected in the range of some thousands. Additionally, a relevant increase of cataracts must be considered. The radiation-induced occurrence of meningiomas and other brain tumours most probably contributes to the continuously increasing incidence of these diseases which is observed in several industrial nations, as well as the exposure of the bone marrow by CT to the increase of childhood leukaemia.

About 1000 annual paediatric CT investigations of the skull will lead to about three excess neoplasms in the head region, i.e. the probability of an induced late effect must be suspected in the range of some thousands. Additionally, a relevant increase of cataracts must be considered.

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Brain tumours among interventional cardiologists: a cause for alarm? Report of four new cases from two cities and a review of the literature. A. Roguin, J. Goldstein and O. Bar.

EuroIntervention 2012 Jan;7(9):1081-6. doi: 10.4244/EIJV7I9A172.

Conclusions: In interventional cardiologists and radiologists, the left side of the head is known to be more exposed to radiation than the right. A connection to occupational radiation exposure is biologically plausible, but risk assessment is difficult due to the small population of interventional cardiologists and the low incidence of these tumours. This may be a chance occurrence, but the cause may also be radiation exposure. Scientific study further delineating occupational risks is essential. Since interventional cardiologists have the highest radiation exposure among health professionals, major awareness of radiation safety and training in radiological protection are essential and imperative, and should be used in every procedure.

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Brain and Neck Tumors Among Physicians Performing Interventional Procedures

Ariel Roguin, MD, PhD[a,*], Jacob Goldstein, MD[b], Olivier Bar, MD[c], and James A. Goldstein, MD[d]

Physicians performing interventional procedures are chronically exposed to ionizing radiation, which is known to pose increased cancer risks. We recently reported 9 cases of brain cancer in interventional cardiologists. Subsequently, we received 22 additional cases from around the world, comprising an expanded 31 case cohort. Data were transmitted to us during the past few months. For all cases, where possible, we endeavored to obtain the baseline data, including age, gender, tumor type, and side involved, specialty (cardiologist vs radiologist), and number of years in practice. These data were obtained from the medical records, interviews with patients, when possible, or with family members and/or colleagues. The present report documented brain and neck tumors occurring in 31 physicians: 23 interventional cardiologists, 2 electrophysiologists, and 6 interventional radiologists. All physicians had worked for prolonged periods (latency period 12 to 32 years, mean 23.5 ± 5.9) in active interventional practice with exposure to ionizing radiation in the catheterization laboratory. The tumors included 17 cases (55%) of glioblastoma multiforme (GBM), 2 astrocytomas (7%), and 5 meningiomas (16%). In 26 of 31 cases, data were available regarding the side of the brain involved. The malignancy was left sided in 22 (85%), midline in 1, and right sided in 3 operators. In conclusion, these results raise additional concerns regarding brain cancer developing in physicians performing interventional procedures. Given that the brain is relatively unprotected and the left side of the head is known to be more exposed to radiation than the right, these findings of disproportionate reports of left-sided tumors suggest the possibility of a causal relation to occupational radiation exposure. (Am J Cardiol 2013;111:1368−1372)

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Special Thanks

NCI Radiation Epidemiology Branch

Columbia University Center for Radiological Research

David Brenner, PhD

Eric Hall, PhD, DSci

Colorado State University

Mike Weil, PhD

National Council on Radiation Protection *(NCRP)*

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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

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RELID: Madan Rehani, PhD, Eliseo Vano, PhD

U.S. Department of Energy *(DOE)*

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Questions and Answers

U.S. Department of Health and Human Services
National Institutes of Health | National Cancer Institute
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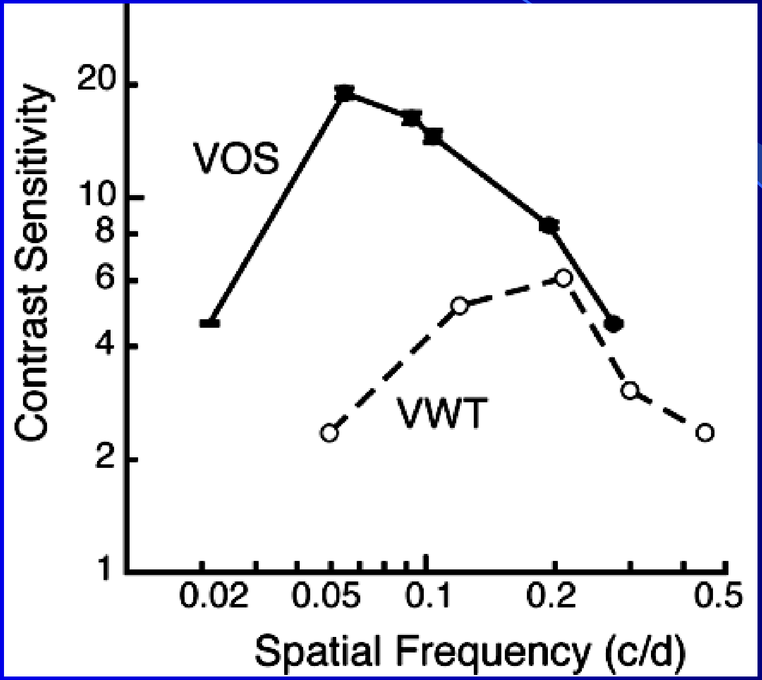

contrast sensitivity as a function of change in spatial frequency

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