Radiation Cataract

Norman J. Kleiman, Ph.D.
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Prior to 2011, eye exposure guidelines were based on the view that radiation cataract is a "deterministic" event with a relatively <u>high</u> threshold radiation dose

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Establishing an accurate dose threshold, if any, for potential eye damage is critical for radiation 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 does not occur *e.g*. erythema (skin reddening), radiation burns.
- Stochastic Effects – Probability increases with dose
  - *e.g.,* cell transformation, carcinogenesis.

Radiation cataract?

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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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INTERNATIONAL COMMISSION ON RADIOLOGICAL PROTECTION

ICRP ref 4825-3093-1464

Radiation Cataract

(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**.

Annals ICRP 2012; 41: 1-322

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History of ICRP Recommendations for Radiation Dose Limits to the Lens

	Annual exposure limit	Putative Cataract threshold
ICRP 1977	300 mSv	15 Sv
ICRP 2007	150 mSv	5 Sv acute/8 Sv protracted
ICRP 2012	20 mSv	500 mGy (acute/protracted/chronic)

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IAEA Safety Standards

for protecting people and the environment

Radiation Protection and Safety of Radiation Sources: International Basic Safety Standards

INTERNATIONAL ATOMIC ENERGY AGENCY
VIENNA, 2014

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THE MEDICAL PHYSICS CONSULT

CrossMark

MAHADEVAPPA MAHESH, MS, PhD, RICHARD L. MORIN, PhD

National Council on Radiation Protection and Measurements Commentary Number 26: Impact of Revised Guidance on Radiation Protection for the Lens of the Eye

Lawrence T. Dauer, PhD, Nobuyuki Hamada, PhD, Eleanor A. Blakely, PhD

NCRP Commentary No. 26. *Intern J Radiat Biol 2017; 93*:1015-23

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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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EPRI | ELECTRIC POWER RESEARCH INSTITUTE

2014 TECHNICAL REPORT

Epidemiology and Mechanistic Effects of Radiation on the Lens of the Eye

Review and Scientific Appraisal of the Literature

“In regards to thresholds, there is not currently enough available information to make any new specific conclusion with regard to chronic exposure threshold for cataracts”

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How did we derive the guidelines for lens exposure limits?

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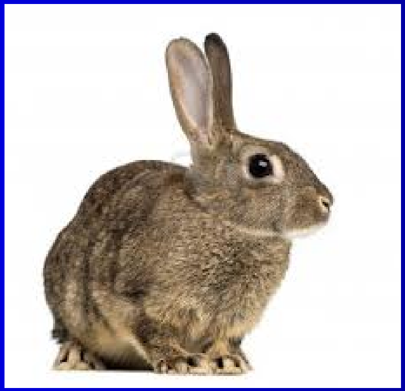
1897: Chalupecky reports cataract in x-rayed rabbits



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

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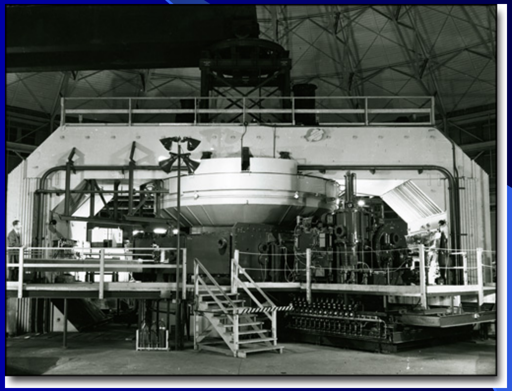
Early Radiation Cataract Studies

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



"Cyclotron-induced radiation cataracts" *Science* **110**, 1949

- **Few subjects with low doses**
- **Short follow-up**
- **Less sensitive techniques**

- **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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More recent studies are consistent with a much lower threshold model for radiation cataract

Chernobyl “Liquidators”

Interventional medicine workers

Residents of contaminated buildings

Infants treated for facial hemangiomas

Radiological technologists

A-bomb survivors

Astronauts

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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.‖

Anesthesiol 2011; 114:512-20.

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]

REVIEW ARTICLE

Radiation protection of the eye lens in medical workers—basis and impact of the ICRP recommendations

[1,2]STEPHEN GR BARNARD, BSc, [1]ELIZABETH A AINSBURY, PhD, [2]ROY A QUINLAN, PhD and [1]SIMON D BOUFFLER, PhD

[1]Public Health England, Centre for Radiation, Chemical and Environmental Hazards, Chilton, Didcot, UK
[2]Durham University, School of Biological and Biomedical Sciences, Durham, UK

Br J Radiol 2016; 89:20151034

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

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

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

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The accessibility of the lens to non-invasive measurement facilitates investigation designed to examine environmental, mechanistic and genetic influences on radiation cataract development

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Mutation Research 770 (2016) 238–261

Contents lists available at ScienceDirect

Mutation Research/Reviews in Mutation Research

journal homepage: www.elsevier.com/locate/reviewsmr
Community address: www.elsevier.com/locate/mutres

ELSEVIER

Ionizing radiation induced cataracts: Recent biological and mechanistic developments and perspectives for future research

CrossMark

Elizabeth A. Ainsbury[a,*], Stephen Barnard[a], Scott Bright[b], Claudia Dalke[d], Miguel Jarrin[e], Sarah Kunze[d], Rick Tanner[a,1], Joseph R. Dynlacht[c,1], Roy A. Quinlan[e,1], Jochen Graw[d,1], Munira Kadhim[b,1], Nobuyuki Hamada[f,**]

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[b] *Genomic Instability Group, Department of Biological and Medical Sciences, Oxford Brookes University, Gipsy Lane Campus, Headington, Oxford OX3 0BP, UK*
[c] *Indiana University School of Medicine, Department of Radiation Oncology, 535 Barnhill Drive, RT 041, Indianapolis, IN 46202-5289, USA*
[d] *Helmholtz Zentrum München GmbH, German Research Center for Environmental Health, Institute of Developmental Genetics, Ingolstädter Landstrasse 1, 85764 Neuherberg, Germany*
[e] *Biophysical Sciences Institute, University of Durham, Durham DH1 3LE, UK*
[f] *Radiation Safety Research Center, Nuclear Technology Research Laboratory, Central Research Institute of Electric Power Industry (CRIEPI), 2-11-1 Iwado-kita, Komae, Tokyo 201-8511, Japan*

A R T I C L E I N F O

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IR
Radiation cataract
Radiation lens effects
Lens biology

A B S T R A C T

The lens of the eye has long been considered as a radiosensitive tissue, but recent research has suggested that the radiosensitivity is even greater than previously thought. The 2012 recommendation of the International Commission on Radiological Protection (ICRP) to substantially reduce the annual occupational equivalent dose limit for the ocular lens has now been adopted in the European Union and is under consideration around the rest of the world. However, ICRP clearly states that the recommendations are chiefly based on epidemiological evidence because there are a very small number of studies that provide explicit biological, mechanistic evidence at doses <2 Gy. This paper aims to present a review of recently published information on the biological and mechanistic aspects of cataracts induced by exposure to ionizing radiation (IR). The data were compiled by assessing the pertinent

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Why the lens?

Why radiation cataract?

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The lens is one of the most radiosensitive of all tissues

BJO
British Journal of Ophthalmology

Editorials

The lens is more sensitive to radiation than we had believed

The lens of the eye has long been recognised to be one of the most radiosensitive regions of the body, but our knowl-

formation leading to the accumulation of debris in the subcapsular region at the posterior pole. Changes have also

Br J Ophthalmol 1997; 81:257-9

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	0.1	0.5
Retina	25	25

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

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CATARACT

A change in transparency of the lens

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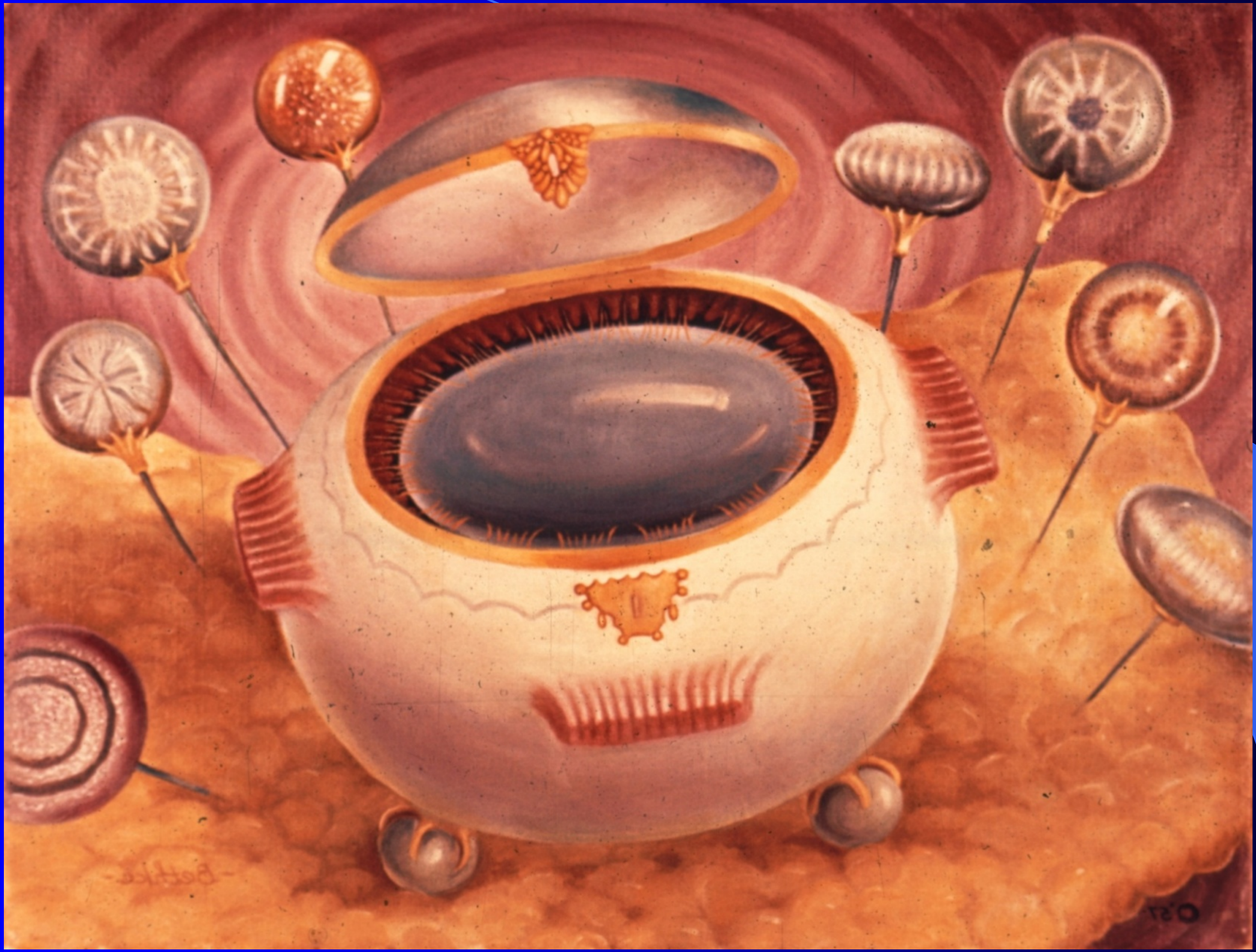

Hans Bethke

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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RADIATION CATARACT

a specific subset of lens opacities

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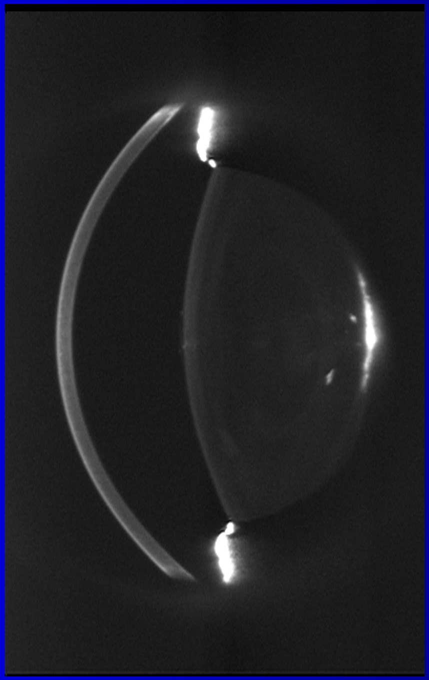
A lens opacity most often originating at our near the visual axis, first appearing in the posterior subcapsular region of the lens



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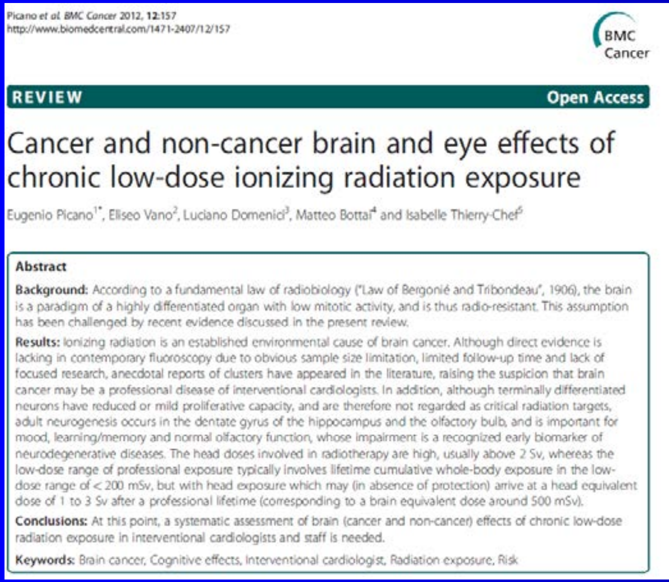
Why do we care?

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


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]

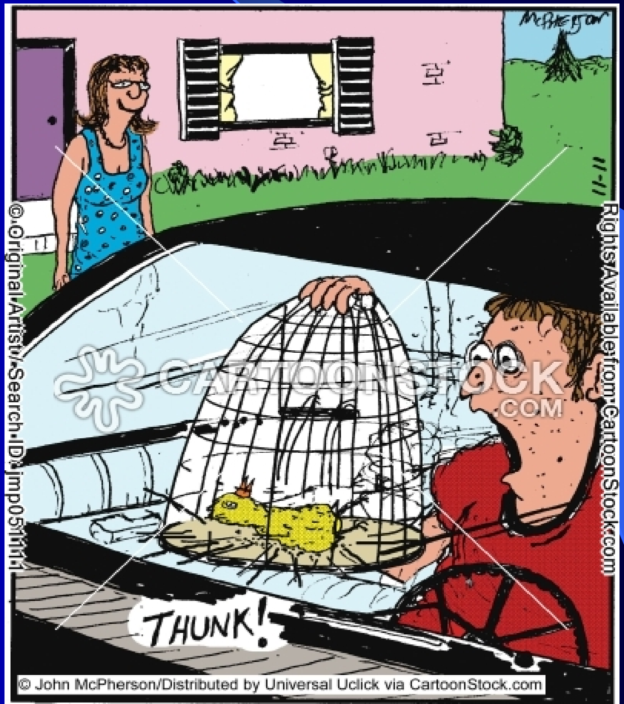
Abstract

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



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

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Radiation cataract provides a way to study potential human health risks following occupational low-dose ionizing radiation exposures.

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

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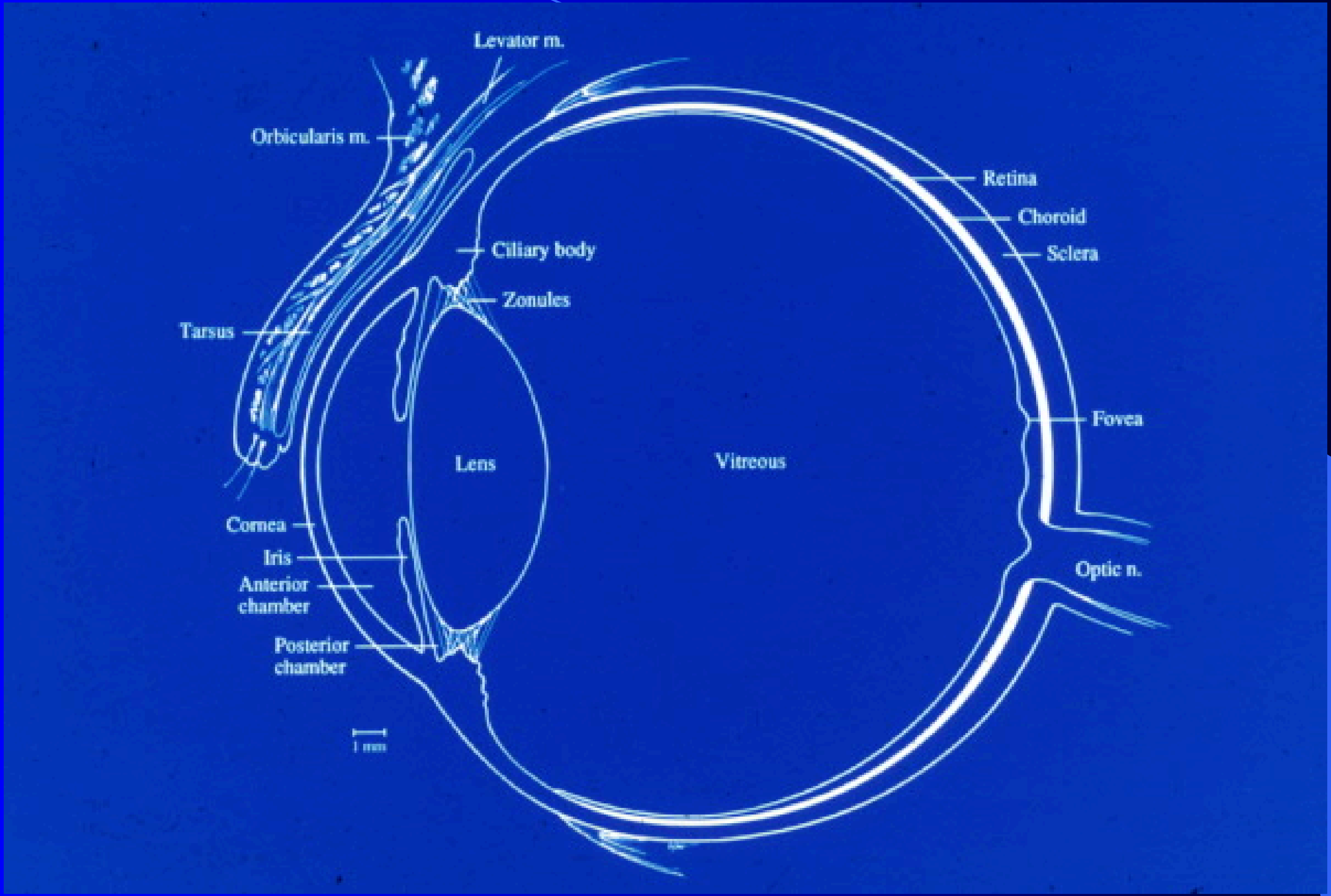
The lens



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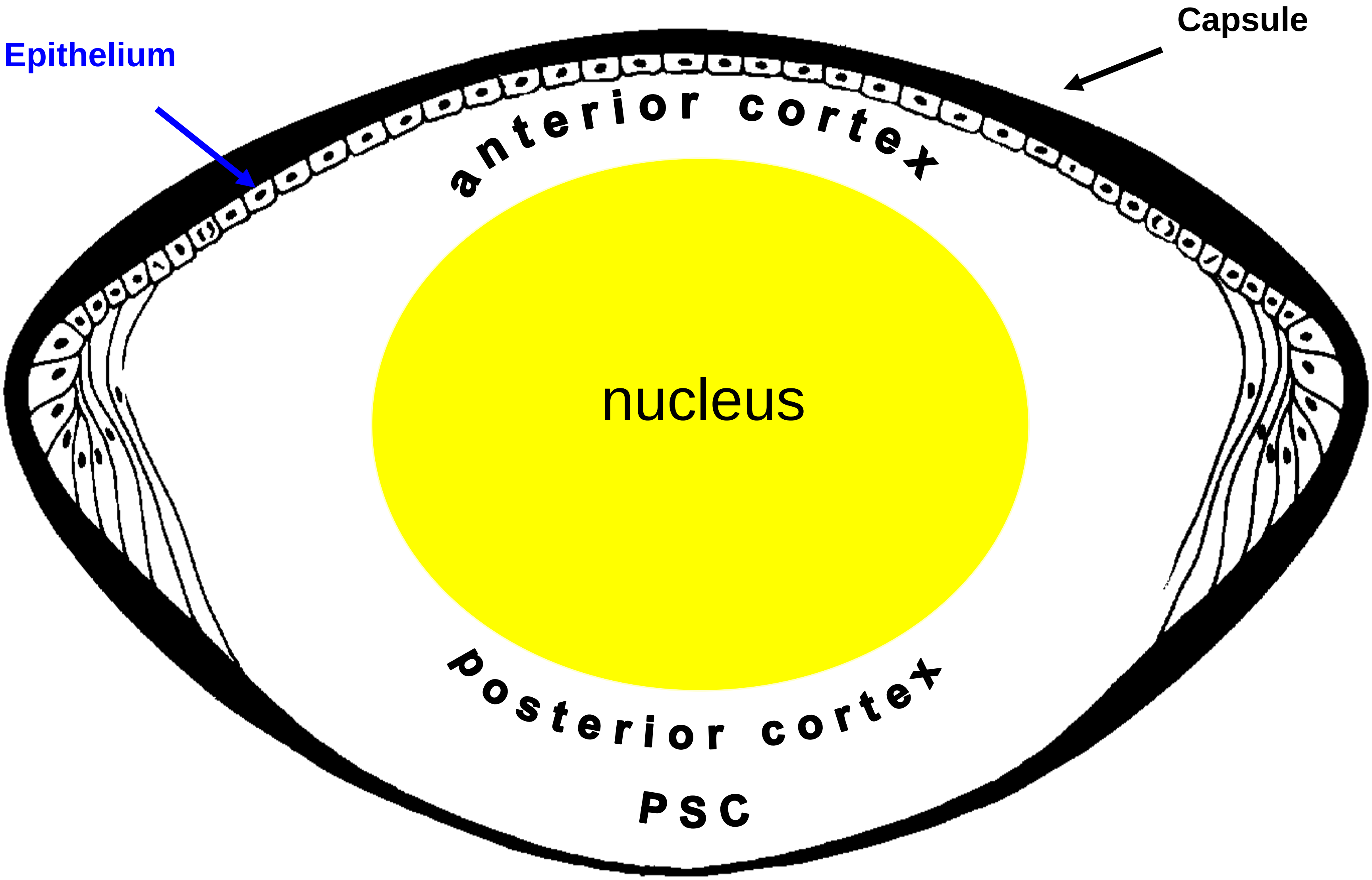
Capsule
Epithelium
anterior cortex
nucleus
posterior cortex
PSC

Major Cataract Subtypes

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

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Posterior SubCapsular (PSC)

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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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IONIZING RADIATION

Damage to Lens Epithelial DNA

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

Abnormal Lens Fibers

Loss of Transparancy

CATARACT

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Measuring Lens Damage

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

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Nikon FS-3 Photo-Zoom Slit Lamp

Nidek EAS-1000 Scheimpflug Camera

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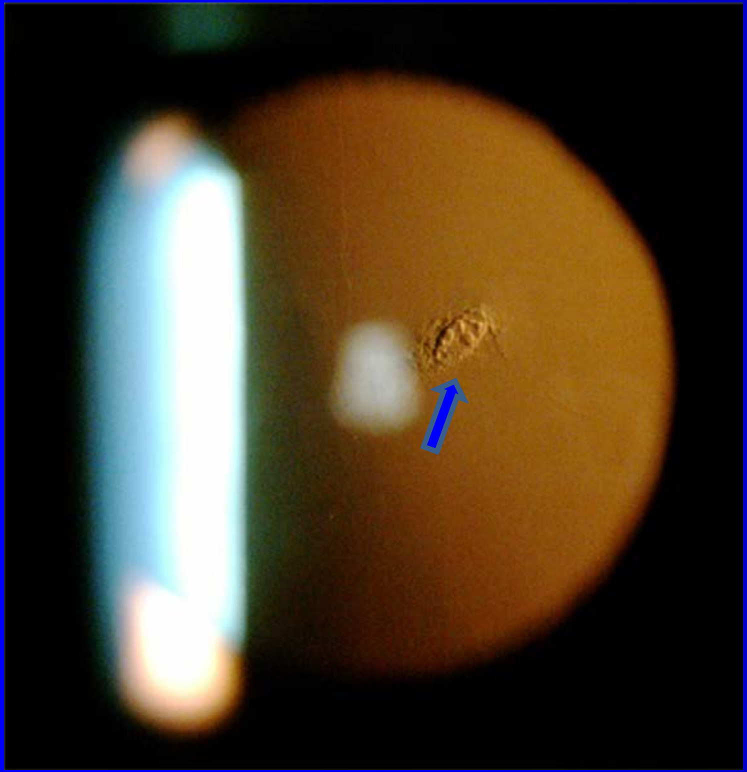
Radiation Induced Posterior Subcapsular Opacity



Retroillumination

Slit Lamp Exam

Interventional cardiologist with 22 years experience

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Quantifying radiation-induced lens changes “cataract staging”

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

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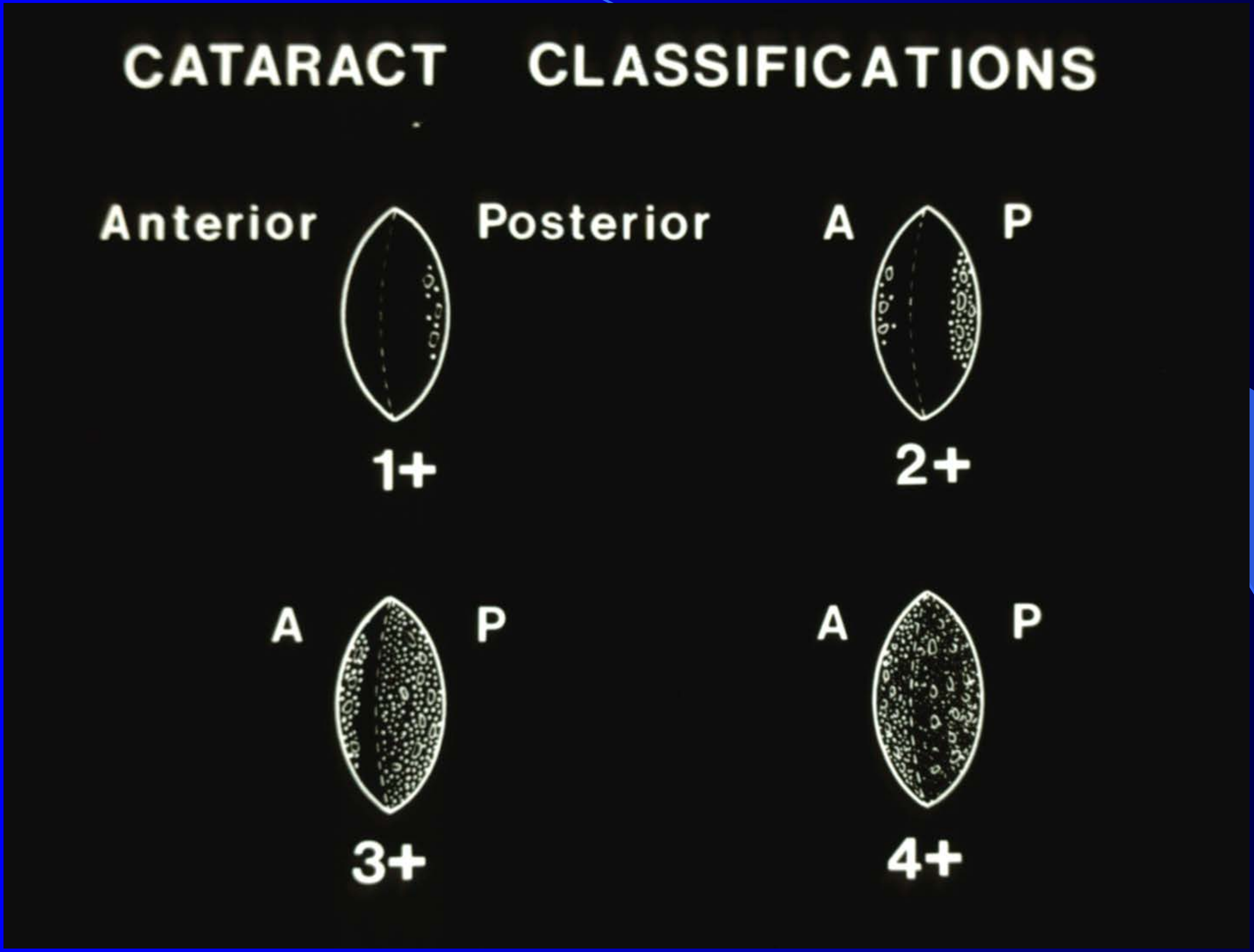
Slit Lamp Imaging of Radiation Cataract Grades



Merriam-Focht Scoring

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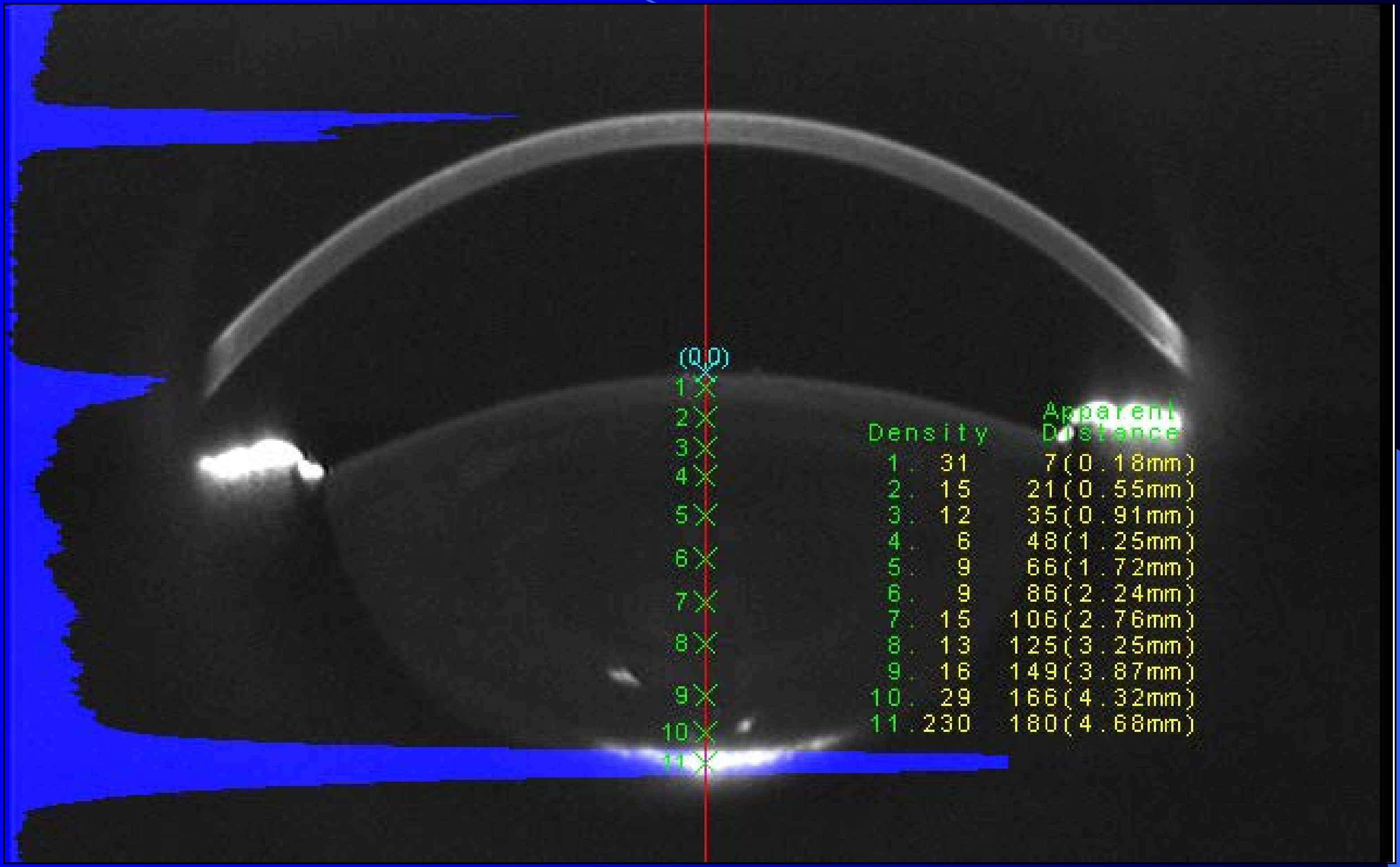
Scheimpflug Imaging of Radiation Cataract



Quantitative analysis of lens changes

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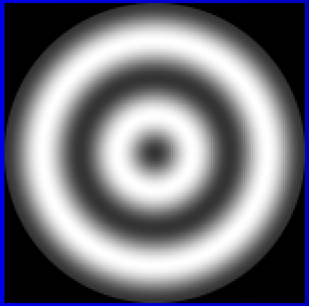
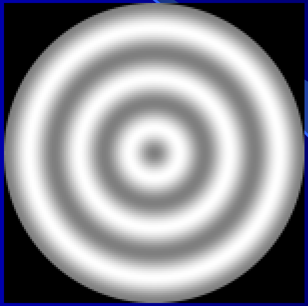
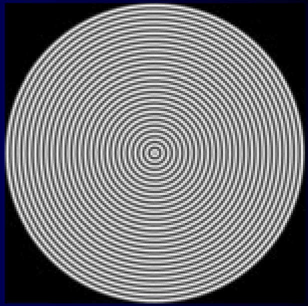
Holladay Automated Contrast Testing







- 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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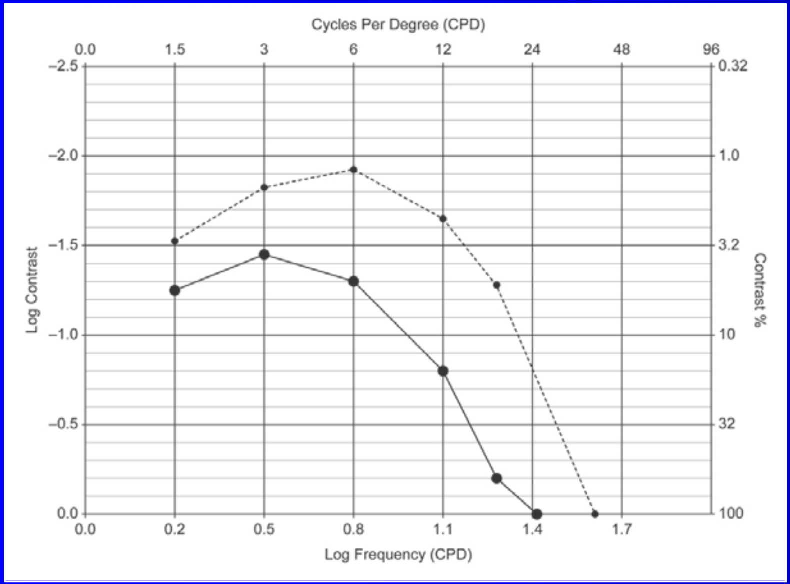
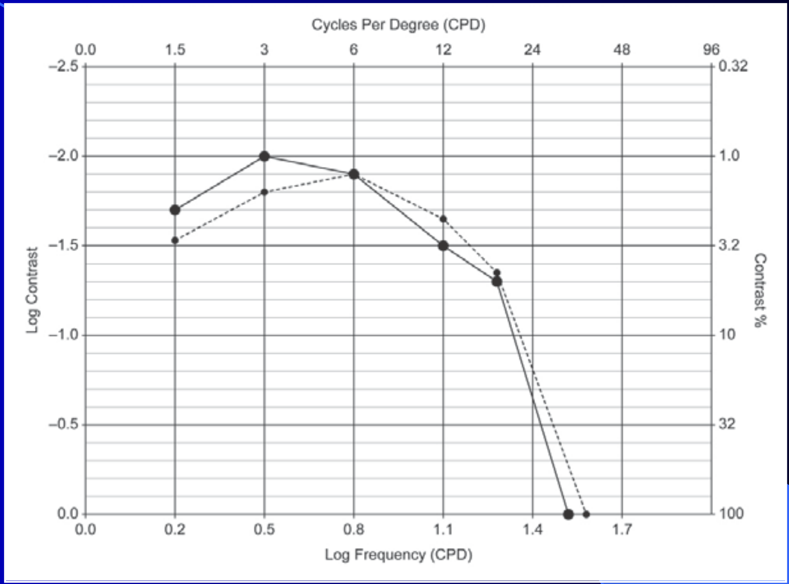
Contrast Sensitivity Testing in Interventional Cardiology



IC subject A

(abberrent)

M-F 1.5



IC subject B

(normal)

M-F 0.0

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How can we reduce or eliminate radiation exposure risks to the eye?

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Eye Protection!!

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

Effect of leaded eyewear and additional shielding

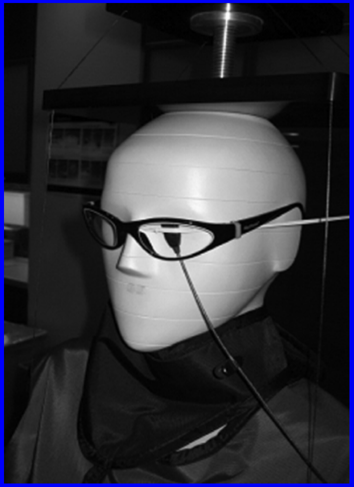

Table 1
Left Lens Exposure while Operating at Patient's Groin during Low-dose PA Fluoroscopy and In-room PA DSA of Upper Abdomen

	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 protection

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

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The treatment for cataract is surgical removal

- There are no therapeutic interventions to slow or reverse cataract formation
- Cataract surgery has a “success rate” of >90%
  (defined as an improvement in vision)

Nevertheless…..

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

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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

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Potential post-operative visual complications of cataract surgery

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

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Cataract surgery risk estimates

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

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

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

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

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

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

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

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Continued follow-up of various occupationally exposed human cohorts as well as additional experimental animal studies will likely help further refine the radiation cataract “threshold”, inform appropriate ocular risk guidelines, and lead to a better understanding of fundamental mechanistic principles underlying adverse ocular health outcomes in exposed populations.

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Special Thanks

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Low-dose Radiation Research program

NASA

Space Radiation Health Program

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U.S. DEPARTMENT OF ENERGY | Office of Science
LOW DOSE RADIATION RESEARCH PROGRAM

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