Guidance on Radiation Dose Limits for the Lens of the Eye

Status of NCRP SC 1-23, Commentary No. 26

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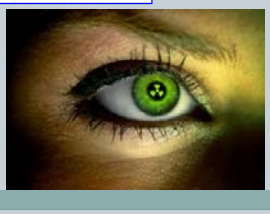

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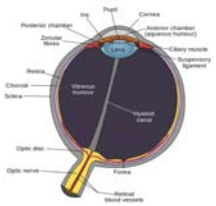
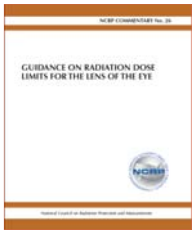
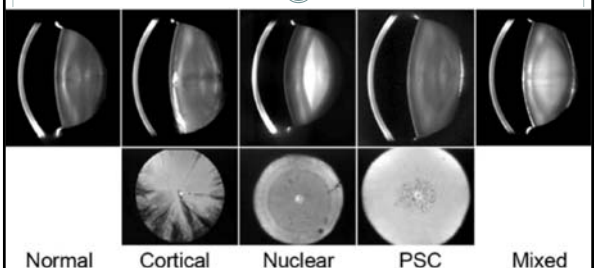




Cataract Types



NCRP Commentary 26

NCRP Commentary No. 26 - Core Questions

- Should radiation-induced cataracts be characterized as stochastic or tissue reactions?
- What effects do LET, dose rate, acute and/or protracted dose delivery have on radiation cataract induction and progression?
- How should detriment be measured and/or evaluated for radiation cataracts?
- Based on current evidence, should NCRP change the recommended annual occupational equivalent dose limit for the lens of the eye?

Objectives of Radiation Protection

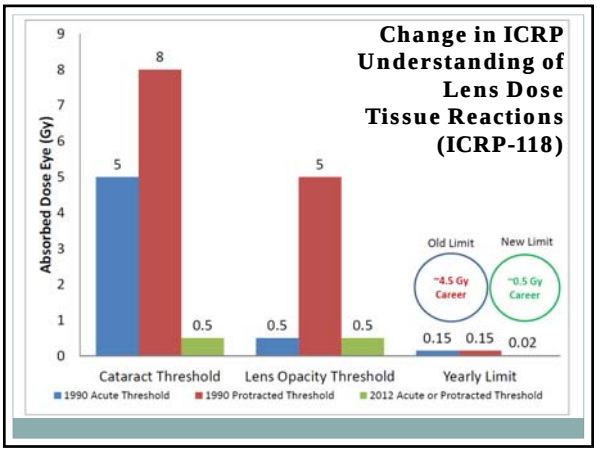
- To prevent the occurrence of clinically significant radiation induced **deterministic effects** by adhering to dose limits that are below the apparent threshold levels and...
- To limit the risk of **stochastic effects, cancer and genetic effects** to a reasonable level in relation to societal needs, values, benefits gained and economic factors.

NCRP-116 (1993)

Principles of Radiation Protection

- **Justification** – on the basis that the expected benefits to society exceed the overall societal cost.
- **Optimization** – to ensure that the total societal detriment from justifiable activities is maintained ALARA, economic and social factors being taken into account.
- **Limitation** – application of individual limits to ensure that procedures of justification and ALARA do not result in individuals or groups exceeding levels of acceptable risk.

NCRP-91 (1987) & NCRP-116 (1993)



Previous Occupational Dose Limits (mSv)

Limit	NCRP-116	ICRP-103/118
Effective Dose		
- Annual	50 /y	20 /y
- Cumulative	10 x Age	Avg of 5 y, no y > 50
Equivalent Dose		
- Lens	150 /y	20/y
		Avg of 5 y, no y > 50
- Skin, Hands, Feet	500 /y	500 /y

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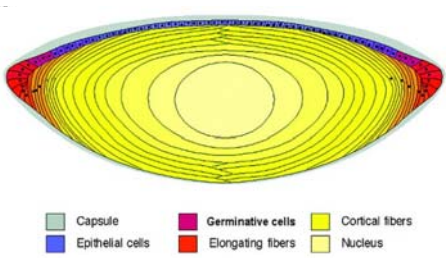
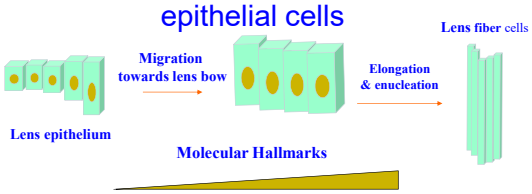
EYE BIOLOGY & LENS EFFECTS

Cross-section of Human Lens



Normal Differentiation of Lens epithelial cells



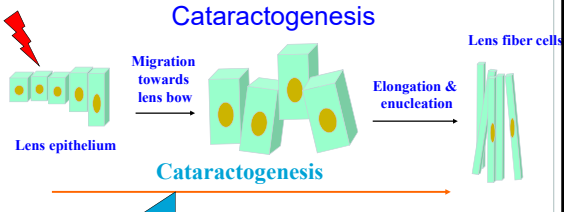
Molecular Hallmarks

Differentiation genes
Apoptosis sensitivity
Cyclin-dependent kinase inhibitors CDKIs

Cyclin-dependent kinases
E2F1/Rb

Blakely, 2014

Underlying Mechanism of Radiation-induced Cataractogenesis



Cataractogenesis

Etiology still not fully known – multifactorial.

Differentiation genes
Apoptosis sensitivity
Cyclin-dependent kinase inhibitor CDKI (p21)

Cyclin dependent kinases E2F1/Rb

Blakely, 2014

Review and Summary of Eye Biology & Lens Effects

- Lens Anatomy & Proliferative Organization
- Cataracts
  - Cataracts / Opacifications
  - Types / Severity
  - Causes / Mechanisms
  - Examination and Quantification of Lens Changes (scoring)
- Radiation Effects
  - Normal Tissue Complication Probability for Lens
- Radiation Cataractogenesis
  - Dose / Dose Rate
  - Fractionation / RBE
  - Age / Gender / Steroid
  - Latency
- Mechanisms
  - Cell Biology
  - Protein Accumulation
  - Molecular Biology
  - Oxidative Stress
  - DNA Damage
  - Genetic Susceptibility

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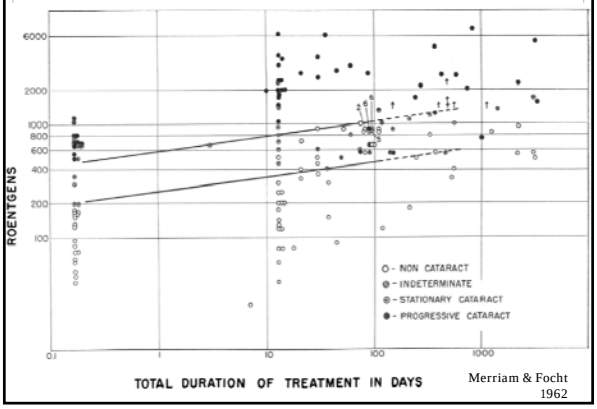
EPIDEMIOLOGY

Dose for Cataract / Non-Cataract Cases vs. Overall Treatment Time



Merriam & Focht 1962

Populations Evaluated (>60 publications)

- Atomic Bomb Survivors.
- Chernobyl Liquidators and Cleanup workers.
- Medical Patients.
- Health Care Personnel.
- Flight Personnel and Astronauts
- Other Occupational
- External Exposure
- Internal Exposure
- Single Person Results
- Population Studies and Residentially Exposed

- Large Variation in Studies:
  - Only a few investigate low dose effects.
  - Differ in:
    - Radiation source / type.
    - Exposure condition.
    - Study design / size.
    - Method (if any) of dose estimation.
    - Range of lens doses.
    - Lens detriment endpoint.
    - Method (and possible scoring) of endpoints.
    - Adjustments or assessment of potential other risk factors and/or confounders.

Quality of Epidemiological Studies (EPRI, 2014)

- Quality score according to methodology strengths and weakness
  - Typical approach when evaluating available epidemiologic evidence for outcomes due to exposures (as does the EPA, e.g., Wartenberg et al, 2010).
  - 0 for expected good design.
  - +1 for strengths.
  - -1 for evident shortcomings.
- 9 Tier I – most informative.
- 15 Tier II – important.
- 34 Tier III – unreliable.

Quality Evaluated On:

1. Study Design
2. Dosimetry
3. Age Adjustment
4. Confounding Causes
5. Numerical Risk Assess
6. Exposure-Response
7. Account for Latency
8. Reporting Bias
9. Selection Bias
10. Pathology Method
11. Blinded Path or Scoring
12. Cataract Scoring Method

Odds Ratio Meta-analysis

- Tier 1 and 2 Studies that provided Odds Ratio covered ~4 population groups:
  - Atomic Bomb Survivor Cohorts
    - Some difficulties – lack of standard photographic method, unclear focus of photographs difficult to judge, retro-illumination camera not used for examination of cortical and PSC cataracts.
    - In process of revising the studies (RERF 2014).
  - Chernobyl Liquidators and Clean-up Workers
  - Clinically Exposed Infants
  - Radiation Technologists
    - < 60 mGy questionnaire study with relatively high RR but not statistically significant.

Odds Ratio Meta-analysis

- Recognizing several limitations and questions, the meta-analysis results of these 4 study populations:
  - PSC OR=1.45 at 1 Gy (95%, 1.15-1.85).
  - Cortical OR=1.37 at 1 Gy (95%, 1.20-1.56).
  - Mixed OR=1.75 at 1 Gy (95%, 1.26-2.46).
  - Nuclear OR=1.07 at 1 Gy (95%, 0.5-2.0).
- Likelihood of an association between exposure to ionizing radiation at ~1 Gy and initiation or development of PSC, mixed, and/or cortical cataracts.

Threshold Evaluations ?

- Only two(2) Tier 1 or Tier 2 study populations evaluated threshold for cataractogenesis: A-Bomb (which may be re-evaluated), and Chernobyl.
- Considerable uncertainty in these estimates, which depend heavily upon the dose response function used and uncertainties in dose estimates.
- Too few data, not possible to perform meta-analysis.
- Currently not enough available information to make any new specific conclusions with regard to chronic or acute exposure thresholds for cataracts.

Populations / Protection

- Medical
  - Patients
  - Interventional Radiology and Cardiology
  - Radiopharmacy, Radiochemistry, Nuclear Medicine
  - Other workers
- Nuclear Facilities
  - Issues with EDEX?
  - High Beta Fields?
  - Protection Factors?
- Industrial Radiography
- Astronauts / Pilots

- Engineering, Safe Work Practices, Administrative Controls
- PPE
  - Screens, Goggles, Leaded Glasses
  - Face Shields
  - Respirator Face Shields
  - Bubble Suit Masks
- Monitoring Lens Dose

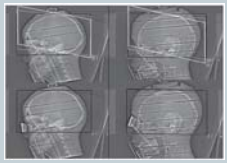
Patient Potential for >0.5 Gy to Lens of Eye

- Radiation Therapy
  - External Beam
  - Brachytherapy
- Neuroradiology Interventional Procedures
- Repeated Brain Perfusion CT
  - 81-348 mGy (Zhang2012)
  - 124 mGy (Perisinakis2013)
- Repeated Head CT
- Repeated Dental Cone Beam CT?

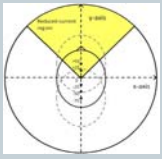
- Optimization strategies should attempt to minimize the possibility of exceeding 0.5 Gy for lens of eye in patients, both for individual high-dose exposures and multiple moderate dose exposures (repeated head CT or interventional procedures)

(Vano, Miller, Dauer 2015)

Lens Dose – CT Optimization Strategies



(Nikupaavo et al 2015, AJR)



(Kudomi et al 2014, ECR)

(Prins et al 2011, Oral Surg)

Measurable Unprotected LDE (mSv/y)

2011 Data MSKCC and Commercial Radiopharmaceuticals

(Dauer, HPJ, 2013)

Exposed Medical Staff	Avg	Min	25%	50%	75%	95%	99%	Max
IR/FGI MD no Pb glasses	11.1	0.1	0.5	7.0	19.3	32.5	35.7	36.5
Radiopharmacist	4.7	0.1	4.3	5.0	6.4	8.0	8.5	8.6
IR/ FGI Tech-Nurse no Pb	2.5	0.1	0.4	1.1	1.9	12.0	19.1	19.3
NM Tech-Nurse	2.4	0.1	0.3	0.9	2.8	9.8	15.5	19.0
Hospital Average **	2.1	0.1	0.2	0.5	2.0	8.5	19.6	36.5
NM MD	1.9	0.1	0.5	1.4	2.6	6.2	7.2	7.6
Research Radiochem	1.9	0.1	0.1	0.6	3.3	6.3	7.8	8.2
Commercial Radiopharm	1.6	0.1	0.1	0.3	1.3	7.1	23.5	**70.2**
Health Physics – Rad Safety	1.1	0.1	0.5	1.0	1.9	2.2	2.3	2.3
Inpatient Nurse	0.4	0.1	0.2	0.3	0.4	0.9	1.8	2.2

How to Monitor Lens Dose?

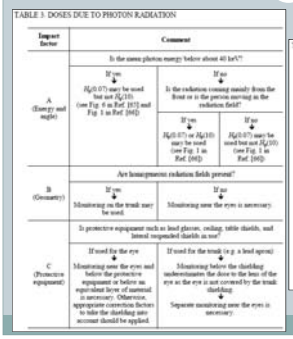


TABLE 3. DOSES DUE TO PHOTON RADIATION

Impact factor	Comment		
A (Energy and angle)	Is the mean photon energy below about 40 keV?		
	If yes → $H_p(0.07)$ may be used but not $H_p(10)$ (see Fig. 6 in Ref. [83] and Fig. 1 in Ref. [66]).	If no → Is the radiation coming mainly from the front or is the person moving in the radiation field?	
		If yes → $H_p(0.07)$ or $H_p(10)$ may be used (see Fig. 1 in Ref. [66]).	If no → $H_p(0.07)$ may be used but not $H_p(10)$ (see Fig. 1 in Ref. [66]).
B (Geometry)	Are homogeneous radiation fields present?		
	If yes → Monitoring on the trunk may be used.	If no → Monitoring near the eyes is necessary.	
C (Protective equipment)	Is protective equipment such as lead glasses, ceiling, table shields, and lateral suspended shields in use?		
	If used for the eye → Monitoring near the eyes and below the protective equipment or below an equivalent layer of material is necessary. Otherwise, appropriate correction factors to take the shielding into account should be applied.	If used for the trunk (e.g. a lead apron) → Monitoring below the shielding underestimates the dose to the lens of the eye as the eye is not covered by the trunk shielding → Separate monitoring near the eyes is necessary.	

IEAE TE-1731, 2013

TABLE 4. DOSES DUE TO BETA RADIATION

Impact factor	Comment	
A (Energy and angle)	Is the maximum beta energy above about 0.7 MeV?	
	If no → No monitoring due to beta radiation is necessary as it does not penetrate to the lens of the eye.	If yes → Monitoring is necessary as described in lines B and C.
B (Geometry)	As beta radiation fields are usually rather inhomogeneous, monitoring of the dose to the lens of the eye is necessary with the dosimeter placed near the eyes. However, it may not be needed if a thick enough shield is used, see impact factor C.	
C (Protective equipment)	Is protective equipment such as shields and glasses that are thick enough to absorb the beta radiation in use?	
	If used for the eye → Consider 'photon radiation' as the beta radiation is completely absorbed in the shielding; however, bremsstrahlung has to be taken into account — the contributions from both that produced outside and that produced inside the shielding.	If not used → $H_p(3)$ is the only appropriate quantity.

Monitoring in Medicine

Properly calibrated $H_p(3)$ with dosimeter worn close to eye – if impractical … consider the following:

Hp(0.07) or Hp(10)	Hp(0.07)	Hp(3)
At trunk	At Eyes behind glasses - *or* At neck and apply CF	If beta >0.7 MeV – *and* Not shielded
Radiochemistry	Interventional Radiology	Beta Brachytherapy
Radiopharmacy	Interventional Cardiology	Beta Radiochemistry
Nuclear Medicine Staff	Interventional Tech	Beta Radiopharmacy
Researchers (> 40 keV)	Interventional Nurse	Beta Researchers
Brachytherapy general	Interventional Anesthesia	
Floor Nurses	Implant Brachytherapy	
General Radiology Tech		
Health Physics		

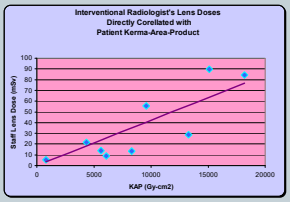
(Quinn B, Miodownik D, Dauer L, et al 2016)

Lens of Eye Monitoring - Some Challenges

- Absorbed dose to the lens in mGy.
  - Lens modeling
  - How best to monitor with available dosimeters?
- Shielding and PPE modeling
- Interventionalists (radiology/cardiology)
  - Badge location (generally outside the collar, nearer eye needed?, shield correction factor?)
- What if leaded glasses or ceiling shields are used?
  - Divide by 3+ if audited use can be verified/validated– likely a conservative estimate of actual lens dose.

ALARA / Optimization for IR Staff

- Training, Behavior Modification & PPE
  - ~45% reduction in LDE over 3 year period.
- Protect the Patient = Protect the staff

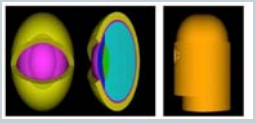


Dauer et al, 2010, JVIR

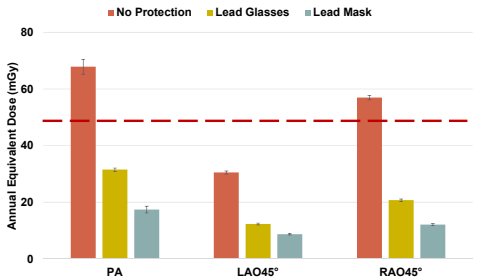
Lieto and Jackson 2000

ICRP External Dose Factors for Lens of Eye

- Stylized eye phantoms.
- New dose conversion coefficients.
- ICRP-116, Appendix F.



Monte Carlo Assessment of Dose to the Lens of the Eye IR (Xu, Dauer et al. 2016 [RPI/MSKCC]– AAPM meeting)



SC 1-23, Commentary No. 26 Conclusions

- Should radiation-induced cataracts be characterized as stochastic or tissue reactions?
  - Several authors indicate radiation-induced opacities may be stochastic in nature.
  - Mechanism and link between induction of minor opacities and occurrence of clinically-relevant, visual-impairing cataracts within a relevant timescale is still far from clear.
  - Best epidemiological evidence still indicates a threshold model.
  - Continue to use this model for radiation protection purposes.
  - Not possible to make a specific quantitative estimate of the threshold at this time.

SC 1-23, Commentary No. 26 Conclusions

- What effects do LET, dose rate, acute and/or protracted dose delivery have on cataract induction and progression?
  - Although different studies have looked at many of these factors independently, there is still very little evidence upon which to base an answer to this question.
  - Mechanistic evidence is perhaps stronger in some instance (e.g., differential effect of increased radiation ionization qualities enhancing the induction and progression of opacities).
  - More high-quality epidemiological and mechanistic studies are required. Need for better dosimetry and scoring methods.

SC 1-23, Commentary No. 26 Conclusions

- How should detriment be evaluated for cataracts?
  - Vision-impairing cataracts could be considered the endpoint of greatest concern. They certainly may affect individuals' ability to carry out their occupations or other daily tasks.
  - Mechanisms underlying transition of minor lens opacifications to clinically significant vision-impairing cataracts are still not well understood.
  - Commentary No. 26 encourages NCRP-168 recommendation to regard eye exposures in much the same way as whole-body exposures (*i.e., ensure exposures are consistent with ALARA principles*). This includes careful justification and optimization in exposure situations including radiation doses to the lens of the eye.

SC 1-23, Commentary No. 26 Conclusions

- Based on current evidence, should NCRP change the recommended limit for the lens of the eye at this time?
  - Current epidemiology and biology studies indicate an association between exposure to ionizing radiation and initiation or development of PSC, cortical and/or mixed visually-impairing cataracts for various exposure situations, perhaps even at lower doses than previously considered for lens dose limits.
  - As in prior NCRP Report No. 132, use absorbed dose when addressing specific tissue reactions (or deterministic effects).
  - Reduce Occupational Annual lens of eye limit to **50 mGy.**
  - Member of Public Annual lens of eye limit as **15 mGy.**