### Cataract Types

<table>
<thead>
<tr>
<th>Normal</th>
<th>Cortical</th>
<th>Nuclear</th>
<th>PSC</th>
<th>Mixed</th>
</tr>
</thead>
</table>

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.

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.
Change in ICRP Understanding of Lens Dose Tissue Reactions (ICRP-118)

Previous Occupational Dose Limits (mSv)

<table>
<thead>
<tr>
<th>Limit</th>
<th>NCRP-116</th>
<th>ICRP-103/118</th>
</tr>
</thead>
<tbody>
<tr>
<td>Effective Dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Annual</td>
<td>50 /y</td>
<td>20 /y</td>
</tr>
<tr>
<td>- Cumulative</td>
<td>10 x Age</td>
<td>Avg of 5 y, no y &gt; 50</td>
</tr>
<tr>
<td>Equivalent Dose</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Lens</td>
<td>150 /y</td>
<td>20 /y</td>
</tr>
<tr>
<td>- Skin, Hands, Feet</td>
<td>500 /y</td>
<td>500 /y</td>
</tr>
</tbody>
</table>

Guidance on Radiation Dose Limits for the Lens of the Eye
NCRP SC 1-23, Commentary No. 26

Eye Biology & Lens Effects
Cross-section of Human Lens

Normal Differentiation of Lens epithelial cells

Underlying Mechanism of Radiation-induced Cataractogenesis

Differentiation genes
Apoptosis sensitivity
Cyclin-dependent kinase inhibitor CDKI (p21)
Cyclin dependent kinases E2F1/Rb

Etiology still not fully known – multifactorial.

Elongation & enucleation

Blakely, 2014

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

## Guidance on Radiation Dose Limits for the Lens of the Eye

**NCRP SC 1-23, Commentary No. 26**

### EPIDEMIOLOGY

![Lens Opacities Classification System](image)

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

![Graph showing dose vs. treatment time](image)
Populations Evaluated (>60 publications)

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

(Nikapuro 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

<table>
<thead>
<tr>
<th>Occupied Medical Staff</th>
<th>Avg</th>
<th>Min</th>
<th>25%</th>
<th>50%</th>
<th>75%</th>
<th>95%</th>
<th>99%</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>IR/FGI MD with Pb glasses</td>
<td>11.1</td>
<td>0.1</td>
<td>0.5</td>
<td>7.0</td>
<td>19.3</td>
<td>32.5</td>
<td>35.7</td>
<td>36.5</td>
</tr>
<tr>
<td>Radiopharmacist</td>
<td>4.7</td>
<td>0.1</td>
<td>4.3</td>
<td>5.0</td>
<td>6.4</td>
<td>8.0</td>
<td>8.5</td>
<td>8.6</td>
</tr>
<tr>
<td>IR/FGI Tech-Nurse</td>
<td>2.5</td>
<td>0.1</td>
<td>0.4</td>
<td>1.1</td>
<td>1.9</td>
<td>12.0</td>
<td>19.1</td>
<td>19.3</td>
</tr>
<tr>
<td>Hospital Average</td>
<td>2.1</td>
<td>0.1</td>
<td>0.2</td>
<td>0.5</td>
<td>2.0</td>
<td>8.5</td>
<td>19.6</td>
<td>36.5</td>
</tr>
<tr>
<td>Radiology MD</td>
<td>1.9</td>
<td>0.1</td>
<td>0.5</td>
<td>1.4</td>
<td>2.6</td>
<td>6.2</td>
<td>7.2</td>
<td>7.6</td>
</tr>
<tr>
<td>Research Radiochem</td>
<td>1.9</td>
<td>0.1</td>
<td>0.1</td>
<td>0.6</td>
<td>3.3</td>
<td>6.3</td>
<td>7.8</td>
<td>8.2</td>
</tr>
<tr>
<td>Commercial Radiopharm</td>
<td>1.6</td>
<td>0.1</td>
<td>0.1</td>
<td>0.3</td>
<td>1.3</td>
<td>7.1</td>
<td>23.5</td>
<td>70.2</td>
</tr>
<tr>
<td>Health Physics – Rad Safety</td>
<td>1.1</td>
<td>0.1</td>
<td>0.5</td>
<td>1.0</td>
<td>1.9</td>
<td>2.2</td>
<td>2.3</td>
<td>2.3</td>
</tr>
<tr>
<td>Inpatient Nurse</td>
<td>0.4</td>
<td>0.1</td>
<td>0.2</td>
<td>0.3</td>
<td>0.4</td>
<td>0.9</td>
<td>1.8</td>
<td>2.2</td>
</tr>
</tbody>
</table>
**How to Monitor Lens Dose?**

IEAE TE-1731, 2013

**Monitoring in Medicine**

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

<table>
<thead>
<tr>
<th>$H_p(0.07)$ or $H_p(0.05)$</th>
<th>$H_p(0.07)$</th>
<th>$H_p(3)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>At trunk</td>
<td>At Eyes behind glasses - or at neck and apply CF</td>
<td>If beta &gt; 0.7 MeV – and Not shielded</td>
</tr>
</tbody>
</table>

- Radiochemistry
- Radiopharmacy
- Nuclear Medicine Staff
- Researchers (> 40 keV)
- Brachytherapy general
- Floor Nurses
- General Radiology Tech
- Health Physics


**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

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.

- 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.

- 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.
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.