EPRI Lens of the Eye R&D

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Together…Shaping the Future of Electricity

EPRI's Mission

Advancing ***safe***, ***reliable***, ***affordable*** and ***environmentally responsible*** electricity for society through global collaboration, thought leadership and science & technology innovation

Independent, Collaborative, Nonprofit

EPRI Initiatives Following ICRP Statement on Tissue Reactions (ICRP Publication 118)

Fundamental Science
- Evaluation of epidemiology and mechanistic effects (3002003162)
- Analysis of monitoring practices (3002000486)

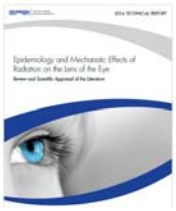
Plant Application
- Good practices and considerations for monitoring lens of the eye (current)
- Protection factors for lens of the eye (2017+)

Communication
- Support of NCRP Commentary
- 2016 EPRI Workshop (3002009112)
- Ongoing industry discussions

Epidemiology and Mechanistic Effects on the Lens of the Eye (3002003162)

Objectives:

- Perform an independent "state of the science" evaluation to understand the technical basis for the ICRP recommendations.
  - Include studies post-ICRP publication
  - Assess relative strength of scientific studies



Evaluate Previous and Current ICRP Basis and Criteria → Review Current Epidemiological and Mechanistic Study Results → Assess risk (probability) for cataracts → Publish EPRI Analysis and Communicate Findings

Approach

- Rigorous, systematic approach to assess the methodological strengths and weaknesses/limitations
- Applied transparent criteria and classified studies by quality tiers
- Meta-analyses of reliable studies
  - Cataract Risks (odds ratio at 1 Gy)
  - Threshold Effects
- Review of molecular, cellular, and animal studies on the basic types and biology of cataract development

Methodology

- **Literature Review:**
  - Evaluated > 300 studies, reviews, and other references
  - Larger number of studies than previous reviews
- **Evaluation Matrix:**
  - Established criteria based on EPA example*
  - Categorized human studies into 3 tiers:
    - Tier 1: Most informative
    - Tier 2: Less useful due to shortcomings
    - Tier 3: Unreliable for meta-analysis Mentioned for completeness and general trends
- **Epidemiology Review Criteria:**
  - Dosimetry
  - Pathology Method
  - Dose Response Analysis
  - Age Adjusted
  - Blinded Pathology
  - Cataract Scoring Type
  - Confounding
  - Latency
  - Numerical Risk Assessment
  - Selection Bias
  - Reporting Bias

*Wartenberg et al 2000

Cataract Epidemiology Study Evaluation

- 59 Epidemiology Studies Evaluated
  - 9 – Tier 1
  - 17 – Tier 2
  - 33 – Tier 3
- 4 of the Tier 1 or 2 studies provided risk ratios for a given dose.
  - A-Bomb (Nakashima)
  - US Radiology Techs (Chodick)
  - Infant Clinical Study (Hall)
  - Chernobyl Cleanup Workers (Worgul)

Limited, high quality, epidemiological studies

Key Conclusions – Associations with Various Types of Cataracts

- **There are limited, high quality, epidemiological studies available.**
- **Meta-analysis suggests an association exists between radiation and the initiation/development of posterior subcapsular, cortical, and mixed cataracts.**
- **Effects are being seen at exposure levels that are somewhat less than earlier estimates.**

Table 1
Results of Odds Ratio Meta-analysis at 1 Gy by Cataract Type

Cataract Type	Odds Ratio at 1 Gy	95% Confidence Interval	Relevant Studies with the Specific Cataract Type
Posterior subcapsular	1.45 *1.45	1.25-1.68 *1.15-1.85	Worgul 2007, Hall 1999 and Nakashima 2006
Cortical	1.37 *1.50	1.20-1.56 *1.21-1.87	Worgul 2007, Hall 1999 and Nakashima 2006
Nuclear	1.07 *1.07	0.89-1.28 *0.9-2.0	Worgul 2007, Nakashima 2006 (nuclear opacity)
Mixed	1.75	1.26-2.46	Worgul 2007, Chodick 2008

*Nakashima 2006 excluded

Cortical Cataract

Posterior Subcapsular Cataract

Key Conclusions – Dose Thresholds

- **Quantitative estimate of a specific dose threshold (adverse effect dose) is not yet possible**
  - Limited available studies that evaluated thresholds (A-Bomb and Chernobyl)
  - Uncertainties exist with the studies
    - Dose estimate uncertainties
    - Lens opacity/cataract detection not standardized

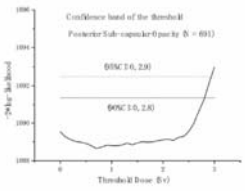


Figure 3-3
Estimation of Threshold Dose in A-bomb survivor study
(reproduced from Nakashima et al., 2006, Figure 2)

Presence or value of a dose threshold still unknown

Key Conclusions – Other Observations

- Shift in protection criteria by ICRP
  - Belief that minor lens opacifications may progress to cataracts
  - Previous recommendations were based on visually-impairing cataracts but new criteria places more emphasis on minor lens opacifications
- Biological studies are helpful but difficult to extrapolate to human exposures.

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