Radiation Cataract

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The lens of the eye is one of the most radiosensitive tissues in the body. Ocular ionizing radiation exposure results in characteristic, dose related, progressive lens changes leading to cataract formation. While initial, early stages of such opacification may not cause visual disability, the severity of such changes progressively increases with dose until vision is impaired and cataract extraction surgery may be required. The latency of such changes is inversely related to dose.

Considerable uncertainties surround the relationship between cataract development and threshold dose. Current national and international ocular-radiation protection guidelines are predicated on the view that cataractogenesis is a deterministic event and requires a threshold radiation dose before lens opacities will develop. The ICRP and the NCRP have reported threshold values for visually disabling cataracts of 2-10 Sv for single brief exposures and >8 Sv for chronic exposures. Recently, however, the ICRP reported "*studies have suggested that the lens of the eye may be more radiosensitive than previously considered*" and noted there is considerable uncertainty concerning radiation risk to the lens. These more recent findings suggest there may be significant risk for radiation cataract in a variety of populations exposed to low doses of ionizing radiation including patients undergoing diagnostic CT scans or radiotherapy, atomic bomb survivors, residents of radioactively contaminated buildings, victims of the Chernobyl accident, astronauts and occupationally exposed medical personnel. These observations raise important concerns and have significant implications for medical and occupational exposures. The concept and validity of a radiation cataract dose threshold is critical not only to risk assessment but also to theories regarding pathomechanism(s) of its development.

In our laboratory, we utilize radiation cataract as a model to study the effects of low-dose ionizing radiation exposure in a complex, highly differentiated tissue. Work includes use of cell and organ culture, animal radiation cataract models for both low-dose exposure and genetic components of radiosensitivity, and human occupational exposure studies. Animal studies are well suited to examine the relationship between radiation, dose, genetics and cataractogenesis at both tissue and cellular levels and have great relevance to human radiation exposure and health outcomes. For example our laboratory has demonstrated dose-related significant lens opacification to as little as 100 mGy X-rays or 5 cGy ^{56}Fe and preliminary data suggests that there may be an even lower threshold dose, if any, for cataractogenesis. Extension of the presumed radiation cataract threshold in animal models to even lower doses is likely to be important to the development of appropriate guidelines for human radiation risk.
Our animal studies have also examined the combined effects on cataractogenesis of irradiation with both low and high-LET radiation, with great relevance to human exposure to cosmic radiation.

Other recent animal experimental work suggests that individual genetic differences in radiosensitivity might help explain the wide variation in reported time of cataract onset, degree of opacification and subsequent progression to visual disability among various exposed individuals. For example, examination of the effect(s) of single or multiple haploinsufficiency for *Atm*, *Brca1, Rad9*, *p53, p21* or *PTEN* suggests expression of these genes, which have important roles in recognizing and repairing radiation induced DNA damage, inducing cell cycle arrest and initiating apoptosis, are related to onset, latency and progression of radiation cataract.

At the same time, immunohistochemical studies of the lens epithelium from animals sacrificed at various time points following irradiation have identified the time course of various markers of cell death, clastogenic damage and DNA damage and repair.

Lastly, recent data from our laboratory, involving examination of posterior lens opacities in interventional physicians and associated medical workers, finds a significantly elevated incidence of radiation associated lens changes in these individuals indicating significant risk of radiation cataract following occupational exposure in this cohort.

Thus, new data from animal models and exposed human populations suggests that lens opacities occur at doses far lower than those generally assumed to be cataractogenic and that genetic determinants of radiosensitivity may influence risk. These findings have important implications for both radiotherapy and occupational exposure in radiosensitive subsets of the human population. Lastly, given that all national and international risk standards for ocular exposure are predicated on a relatively high threshold, current guidelines for ocular radiation safety require reassessment. This work may aid in determining future national terrestrial and space radiation risk policies.

Technical assistance from Ms. Janice David and support from Drs. Adam Rusek and Peter Guida (BNL; NSRL & Medical Department) is gratefully acknowledged. This research is supported by the Department of Energy, Office of Science, Low Dose Radiation Research Program, DE-FG02-07ER64334 (NJK) and NASA grant, NNJ05HI38G (EJH).