Investigation of the Biological Effects and Mechanisms of Low Dose Radiation on Cataracts

Technical Lead: Richard Richardson

CNL

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OBJECTIVE

Perform research to help support Canadian radiation protection regulations and guidance to better understand radiation's biological effects regarding promotion of cataracts to the public and workers. This work has the potential to influence recommendations or regulations of the International Committee on Radiation Protection (ICRP), Health Canada and the CNSC applicable to nuclear workers, clinical procedures, and in space.

TASKS PERFORMED IN THE FIRST 6 MONTHS OF THE FISCAL YEAR

TASK 1: *In Vitro* Experiments

Order materials for *in vitro* experiments

- Considered human lens epithelial cells (**LECs**) transformed with an adenovirus 12-SV40 virus hybrid (Ad12-SV40). These immortalised LECs from supplier ATCC require biosafety level 2.
- Working on upgrade of laboratory in Biological Research Facility to level 2.
- Purchased frozen LECs from ScienCell. These 'mortal' cells were isolated from human lens.
- Purchased hypoxia chamber (**Fig. 1**) by Baker Ruskin. The InVivo O_2 500 cost ~$65,000 and was delivered in August.

Carry out preliminary *in vitro* experiments

- Studied LECs slowing down after X5-6 doublings.
- Showed that the seeding number of cells alters growth.
- Studied effect of gamma irradiation on LECs in normoxic conditions (**Fig. 2**) and with a hypoxia mimic.

TASK 2: Model the Irradiation of the Eye

Monte Carlo simulations / modeling

- Built human eye model in Monte Carlo simulation environments and conduct simulations for selected radiations.
- Implemented a geometrical model of 1 eye and 2 eyes embedded inside a head phantom from from Behrens et al. 2009 (**Fig. 3**) & 2011.

Benchmarking against published models

- Calculation of photon & neutron kerma per unit fluence to radiosensitive, insensitive, and overall lens and comparison to data published by Behrens et al. 2011 & Manger et al. 2012.

Review of biology of radiation-induced cataracts (Deliverable #2)

- Identified issues important to radiation-induced cataracts in the feasibility study including the hypoxic eye lens and the role of the oxygen effect (**Fig. 4**).
- Worked on an article with Elizabeth Ainsbury of Public Health England and Christina Prescott, Wilmer Eye Institute, John Hopkins University.

FEDERAL STAKEHOLDERS

Health Canada, Canadian Nuclear Safety Commission, Canadian Space Agency

COLLABORATORS

McGill University (Medical Physics Unit)

EXPECTED OUTCOMES

- *Acquire human eye cells for experimentation*, is on target (Deliverable #1, due 2019 Sep 30).
- *Completion of benchmark tests of dosimetric eye model,* is on target (Milestone #1, due 2020 Jan 31).
- *Submit review of biology of radiation-induce cataracts for a peer-reviewed journal* (Deliverable #1, due 2020 Feb 28).

ACHIEVEMENTS AND SUCCESSES

- Purchased LECs and hypoxia chamber
- Working on upgrade of laboratory in Biological Research Facility to level 2, so can experiment with 'immortalized' LECs.
- Carried out experiments on LECs testing for cell growth and senescence, optimal seeding density, effects of hypoxia mimic and the effect of gamma radiation on cell growth.
- Implemented an eye model and begun the benchmarking of doses against published data.
- Prepared draft paper with external coauthors of a review of biology of radiation-induced (and other risks factors) cataracts

FUTURE WORK

2019-20 FY:

- Utilize the hypoxia chamber in further pilot tests on LECs.
- Upgrade a laboratory and its documentation to level 2.
- Carry out further benchmarking of eye model for neutrons and add new target components in addition to the traditional lens.
- Prepared draft paper with external coauthors of a review of biology of radiation-induced cataracts.

2020-21 FY:

- Examine the effects of low-LET gamma radiation exposures on LECs and the oxygen-dependence of biological endpoints, such as cell death and unrepaired nuclear DNA damage.
- Other biological end points will also be considered such as mitochondrial DNA deletions and cellular metabolomics.
- A report will be drafted on the Monte Carlo simulation results with regard to the oxygen effect on lens and non-lens target volumes in the eye.
- Disseminate findings of review on cataracts risks to scientific meetings.

2021-22 FY:

- Complete the experimental observations and draft journal paper the *in vivo* experimentation and the oxygen effect of LECs
- Complete a peer-reviewed journal paper on both the theoretical analyses of eye target dosimetry accounting for the oxygen effect.

Fig. 1: Hypoxia chamber

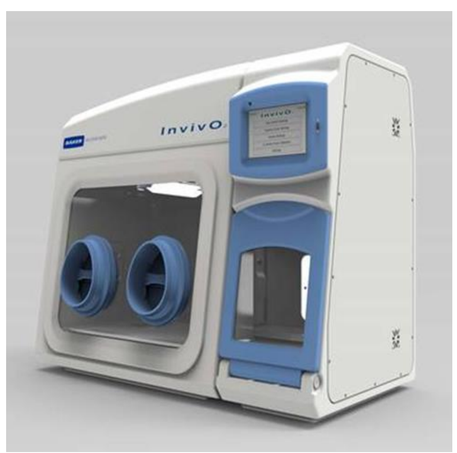


Fig. 2: Effect of gamma irradiation on LEC growth

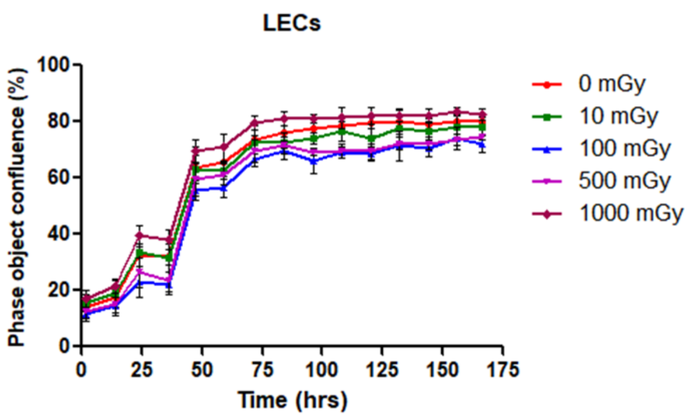


Fig. 3: Electron dose calculated to various target tissues using single eye model by Behrens *et al.* 2009.

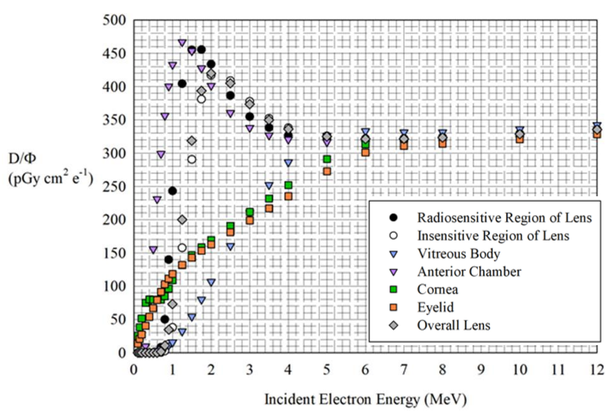
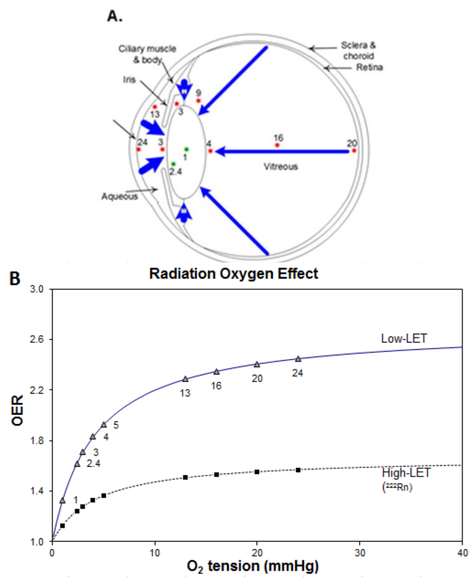


Fig. 4: A) Oxygen levels, mmHg in the eye, and B) the 'oxygen effect' and oxygen enhancement ratio (OER)



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