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Temperature-controlled *in vivo* ocular exposure to 1090-nm radiation suggests that near-infrared radiation cataract is thermally induced

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Abstract. The damage mechanism for near-infrared radiation (IRR) induced cataract is unclear. Both a photochemical and a thermal mechanism were suggested. The current paper aims to elucidate a photochemical effect based on investigation of irradiance-exposure time reciprocity. Groups of 20 rats were unilaterally exposed to 96-W/cm^2 IRR at 1090 nm within the dilated pupil accumulating 57, 103, 198, and 344 kJ/cm^2, respectively. Temperature was recorded at the limbus of the exposed eye. Seven days after exposure, the lenses were macroscopically imaged and light scattering was quantitatively measured. The average maximum temperature increases for exposure times of 10, 18, 33, and 60 min were expressed as 7.0 ± 1.1, 6.8 ± 1.1, 7.6 ± 1.3, and 7.4 ± 1.1°C [CI (0.95)] at the limbus of the exposed eye. The difference of light scattering in the lenses between exposed and contralateral not-exposed eyes was 0.00 ± 0.02, 0.01 ± 0.03, -0.01 ± 0.02, and -0.01 ± 0.03 transformed equivalent diazepam concentration (tEDC), respectively, and no apparent morphological changes in the lens were observed. An exposure to 96-W/cm^2 1090-nm IRR projected on the cornea within the dilated pupil accumulating radiant exposures up to 344 kJ/cm^2 does not induce cataract if the temperature rise at the limbus is <8°C. This is consistent with a thermal damage mechanism for IRR-induced cataract. [DOI: 10.1117/1.JBO.20.1.015003]

Keywords: infrared radiation; temperature; forward light scattering; lens.

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1 Introduction

Since the late 1800s, surveys of glass and steel workers have implied an association between infrared radiation (IRR) and cataract induction.[1–3] Vogt[4] suggested that IRR cataract results from direct absorption of IRR in the crystalline lens. Goldmann[5] hypothesized that IRR cataract is due to temperature rise induced by IRR in the iris and heat transfer into the lens from the iris. This was supported by Verheoff et al.[6] Wolbarsht advocated that near-infrared radiation cataract can be photochemically induced.[7]

Presently, it is believed that IRR damage in the lens is wavelength independent.[8] Based on Goldmann's[9] and Wolbarsht's[10] findings and Scott's heat transport model,[11] Vos and Van Norren[12] calculated a threshold temperature rise of 5°C in the lens and stated that an irradiance of 1 kW/m^2 would not increase the temperature of the anterior segment of the eye more than 5°C. The current safety guideline for IRR exposure in the crystalline lens is consistent with thermal damage as it is set as a constant irradiance level of 10 mW/cm^2.[13]

However, two previous findings implied reciprocity between irradiance and exposure duration, which is characteristic of a photochemical effect. Wolbarsht[7,14,15] stated cataract formation after *in vivo* exposures of rabbits to ~1.4 kJ/cm^2 on the lens only with a CW Nd:YAG (1064 nm) laser using irradiances ranging between 1.4 and 28 W/cm^2. Pitts et al.[16,17] claimed a threshold dose for *in vivo* exposure to low irradiance IRR of 3.5 kJ/cm^2. This was based on *in vivo* exposure of rabbits to wide-band IRR derived from a Xenon arc source, 715 to 1400 nm (mainly <1100 nm), using irradiances ranging between 2 and 4 W/cm^2.

Previously, we found that 197 W/cm^2 1090-nm IRR exposure on the cornea within the dilated pupil for a minimum of 8 s induces cataract with a temperature increase of 10°C in the anterior segment of the eye.[18,19]

The purpose of the present study was to investigate if the previously suggested photochemical threshold for near-IRR induced cataract, 1.4 kJ/cm^2,[7,14,15] is consistent with irradiance—exposure duration reciprocity, indicating a photochemical nature of cataract formation.

2 Materials and Methods

2.1 *Animals*

Six-week-old albino Sprague–Dawley female rats were used. Animals were kept and treated according to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. Ethical approval was obtained by Uppsala Djurförsöksetiska Nämnd (C 29/10).

2.2 *Temperature Measurement*

Temperature was measured with thermocouples (HYP0, OMEGA, USA) connected to an integrated analogue-digital

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converter (TC-08, OMEGA, USA). During recording, the digital data were collected by LabVIEW (National Instruments, USA).

2.3 *Radiation Source*

Eyes were exposed to IRR at 1090 nm emitted from a single-mode CW fiber laser (Model SP-120C, SPI Lasers, UK). The radiation beam was divergent on the cornea with a 2 mm spot size projected within the dilated pupil diameter (Fig. 1). The details of the exposure setup were described elsewhere.[19]

2.4 *Experimental Procedure*

The animals were anesthetized with ketamine 95 mg/kg plus xylazine 14 mg/kg intraperitoneally, 10 min before exposure. The pupils of both eyes were dilated with tropicamide instilled in both eyes. Immediately before exposure to IRR, both eyes were checked for pre-existing opacity in the lens with slit-lamp microscopy. No pre-existing opacity was found in any of the animals. Five minutes after pupillary dilation, the animals were unilaterally exposed to 1090-nm IRR. During exposure, temperature was measured with one thermocouple placed at the limbus of the exposed eye. The cornea was humidified during exposure to minimize thermal increase and concomitantly preserve the optical properties of the cornea to allow constant IRR exposure into the lens. The animals were sacrificed seven days after the exposure and both lenses were extracted by a posterior route for light scattering measurements and macroscopic photographing. The intensity of forward light scattering was measured as described elsewhere.[20]

2.5 *Experimental Design*

Altogether, 80 animals were randomly divided into four radiant exposure groups of 10, 18, 33, and 60 min, resulting in a total dose of 57, 103, 198, and 344 kJ/cm^2, respectively. All animals were unilaterally exposed to 96 W/cm^2 coherent IRR at 1090 nm within the dilated pupil while temperature was recorded at the limbus of the exposed eye. One week after exposure, light scattering was measured three times on each eye and the lens was photographed in dark-field illumination.

2.6 *Statistical Parameters*

The significance limit and the confidence level were set to 0.05 and 0.95, respectively, considering the sample size.

3 Results

3.1 *Temperature Evolution*

For each animal, the measured temperature increase, ΔT (°C), at increasing time, t (s), after exposure was fitted with an exponential model[19] [Eq. (1)], rendering the asymptote maximum temperature increase, ΔT_{Max} (°C), and the rate constant, k (s^{-1}), for each animal:

$$\Delta T = \Delta T_{\mathrm{Max}}(1 - e^{-k \cdot t}) + \varepsilon. \quad (1)$$

Then, maximum temperature increase and the rate constant were estimated as a 95% confidence interval for the mean for each radiant exposure group (Table 1).

In all the four radiant exposure groups, the *in vivo* exposure to 96 W/cm^2 1090-nm IRR was found to result in a temperature elevation of 7°C at the limbus of the exposed eye.

The average temperature rise as a function of time, applying Eq. (1) and using the parameters estimated in Table 1, was calculated (Fig. 2).

It is seen that the temperature evolution was independent of radiant exposure when the peak temperature rise was kept <8°C.

Table 1 Parameters for evolution of temperature at the limbus of the exposed eye as a function of time with exposure to 96 W/cm^2 infrared radiation induced at 1090 nm.

Radiant exposure (kJ · cm^{-2})	Maximum temperature rise (°C)	Rate constant $(s^{-1}) \times 10^{-2}$	Increase time (s)
	95% confidence interval for the mean in the exposed eyes (d.f. = 19)		
57	7.0 ± 1.1	8 ± 5	12
103	6.8 ± 1.1	7 ± 3	14
198	7.6 ± 1.3	5 ± 2	21
344	7.4 ± 1.1	5 ± 3	20

3.2 *Lens Appearance Seven Days After Exposure*

All rats were examined to exclude cataract before exposure.

One week after *in vivo* exposure to IRR, no cataract was observed in any of the four radiant exposure groups and no apparent difference of macroscopic appearance of the lenses between exposed and contralateral nonexposed eyes was found (Fig. 3).

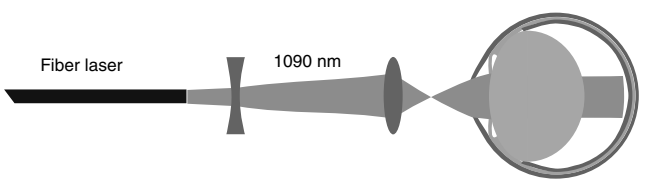

Fig. 1 Optical configuration used for exposures.

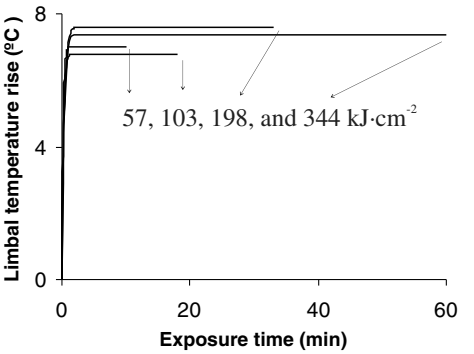

Fig. 2 Predicted temperature evolution at the limbus of the exposed eye as a function of exposure time.

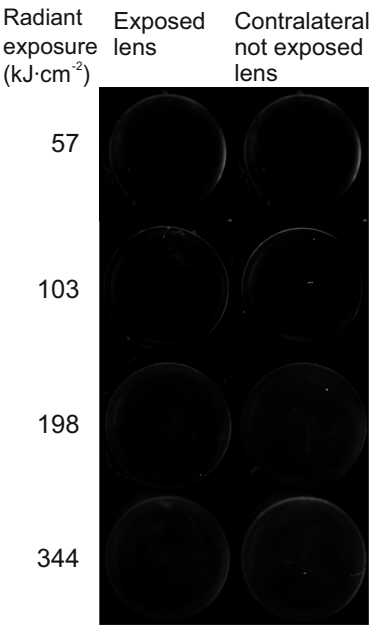

Fig. 3 Macroscopic appearance of the lens in dark-field illumination one week after *in vivo* exposure to 96 W/cm^2 infrared radiation. Both lenses shown originate from the same animal.

3.3 *Light Scattering Measurements*

One week after exposure to IRR, for all radiant exposure groups, the difference of light scattering between exposed eye and contralateral eye was not different from 0 (Fig. 4).

An analysis of variance according to the model in the Appendix showed that there was no significant difference among the exposure time groups (F-statistic = 0.67, $F_{0.95;3;76}$ = 2.72).

4 Discussion

The current study investigated if cataract is induced after *in vivo* exposure to 96 W/cm^2 1090-nm IRR when the radiant exposure is high enough (extended exposure time). Further, the temperature evolution was measured.

In the current paper, rats were chosen because they are available at an reasonable price in sufficient numbers to allow statistical inference. Wolbarsht proposed a photochemical effect based on a rabbit model.[7,14,15] Generally, experimental data based on animal experiments require caution in direct interpretation to consequences for humans. However, it is implausible that the photochemical properties of the lens are species dependent.

The irradiance used for the exposures in the current experiment was selected to be half of that inducing cataract at an exposure time of 8 s[18,19] but using exposure times leading to a [36;216] times higher radiant exposure. The highest radiant exposure used was limited by the duration of anesthesia. Renewal of the injection anesthesia would have hampered the positioning of the beam in the pupil.

Previously, we recorded temperature with thermocouples at the limbus, in the vitreous behind the lens, and on the sclera close to the optic nerve, respectively.[19] In the current experiment, we chose to record temperature at the limbus only to allow for high accuracy without any risk for mechanical cataract induction.

The finding that an exposure to 1090-nm IRR of 96 W/cm^2 induced ~7°C temperature rise at the limbus of the exposed eye

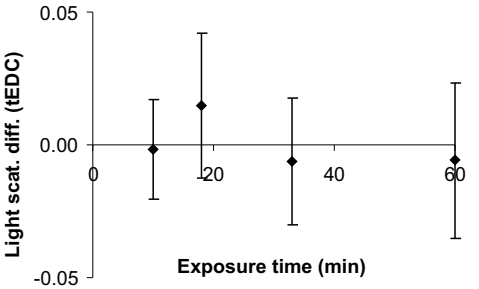

Fig. 4 Lens light scattering difference between exposed eye and contralateral not-exposed eye after 57, 103, 198, and 344 kJ · cm^{-2}. Bars are 95% confidence interval for the mean difference, d.f. = 19.

in all the radiant exposure groups (Fig. 2, Table 1) indicates that ocular temperature rise during IRR exposure probably depends on irradiance rather than exposure time. In fact, with the currently used irradiances, temperature elevation could exceed 7°C without corneal cooling with the humidifying agent.

Our observation that there was no light scattering evolution in the lens and no light scattering difference among the four groups at one week after exposure to 96-W/cm^2 IRR with an exposure time up to 1 h (Fig. 4) illustrates that for an irradiance of 96 W/cm^2, no significant light scattering (Figs. 3 and 4) was induced for exposure times within an exposure time interval of [10;60] min corresponding to radiant exposures in the interval [57; 344] kJ/cm^2, on the condition that the temperature rise at the limbus is <8°C.

The highest radiant exposure used in the current experiment when keeping the temperature rise at the limbus <8°C was 246 times higher than that claimed for photochemical cataract induction in rabbits by Wolbarsht et al.[7,14,15] and 98 times higher than that reported for photochemical cataract induction by Pitts et al.[16,17] The important difference between our observations and those previously published[7,14–17] is that we reported a temperature rise <8°C, while no temperatures were stated by Wolbarsht and Pitts. The plausible explanation to the fact that despite using a considerably higher radiant exposure than Wolbarsht and Pitts, we did not observe any cataract development, suggests there was a temperature rise in the previous experiments.[7,14–17] Thus, our observations strongly suggest that below 350 kJ/cm^2, 1090-nm IRR does not cause photochemical damage in the lens.

We previously showed that exposure on the cornea within the dilated pupil to 197 W/cm^2 of 1090-nm IRR requires at least 8 s to induce cataract, and the 8-s exposure induced a temperature increase of 10°C in the anterior segment.[18,19] The current findings that 96-W/cm^2 1090-nm IRR with 1-h exposure does not result in direct damage in the lens if the temperature rise is <8°C implicates that IRR-induced cataract is caused by indirect heat absorption in tissues surrounding the lens or, alternatively, possibly by a local inflammatory reaction induced by temperature rise in tissues surrounding the lens, or both.

5 Conclusion

An exposure to 96-W/cm^2 1090-nm IRR projected on the cornea within the dilated pupil accumulating radiant exposures up to 344 kJ/cm^2 does not induce cataract if the temperature rise at the limbus is <8°C. This is inconsistent with a photochemical effect as suggested by Wolbarsht[7] and consistent with the hypothesis that IRR causes cataract thermally.[5,6]

Appendix: Model for Analysis of Variance

An experimental measurement, x_{ij}, is the sum of the population mean, μ, a term for the variation among experiment groups, α_i ($i = 1, 2, 3, 4$), and a term for the variation among animals, including measurement error, $\varepsilon_{j(i)}$. ($j = 1, 2, \ldots 20$) [Eq. (2)]:

$$x_{ij} = \mu + \alpha_i + \varepsilon_{j(i)}. \tag{2}$$

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Zhaohua Yu is a PhD candidate, and his interest concentrates on the damage mechanism of near-IRR cataracts.

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Martin Kronschläger is a PhD. His interest includes studies on prevention of experimental cataract induced by ultraviolet radiation.

Per Söderberg is a professor and chair of ophthalmology in Uppsala University. His interest focuses on the interaction of optical radiation and the eye, cataract measurement, contrast sensitivity, virtual reality cataract surgery, corneal endothelium biometry, and digital visual acuity charts.