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Influence of Anesthesia on Ocular Effects and Temperature in Rabbit Eyes Exposed to Microwaves

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To investigate the effect of systemic anesthesia on ocular effects and temperature in rabbit eyes exposed to microwaves, one eye each of 43 male pigmented rabbits (Dutch, 1.8–2.2 kg) was exposed at 2.45 GHz for 60–20 min (300 mW/cm^2; 108 W/kg), either under anesthesia (ketamine hydrochloride (5 mg/kg) + xylazine (0.23 mg/kg)) or without anesthesia. Changes in the anterior segment were evaluated by image analysis utilizing a Scheimpflug camera, specular microscopy, and a laser flare cell meter. Temperatures within the eye were measured during microwave exposure by a Fluoroptic thermometer. The exposed eyes showed miosis, conjunctival congestion, corneal edema, and an increase in the light scattering of the anterior shallow cortex in the pupillary area of the lens. The group under systemic anesthesia showed much stronger symptoms than those treated without anesthesia. All of the anterior ocular changes disappeared within a week. The highest temperature during exposure was in the vitreous, followed by the anterior chamber, and the retrobulbar cavity of the orbit. The ocular temperatures of the rabbits under systemic anesthesia were 2–9 °C higher than those without anesthesia. Body temperature showed an increase of 1 °C during the exposure. Acute high intensity microwave exposure temporarily induced anterior segments inflammation and lens changes. The more pronounced ocular effects in the anesthetized rabbits were associated with the significantly higher ocular temperatures in the anesthetized animals. The influence of systemic anesthesia on ocular changes should be considered. Bioelectromagnetics 25:228–233, 2004.

Key words: lens light scatter; ocular inflammation; cataract; microwave

INTRODUCTION

Now that mobile phones have become part of daily life in industrialized countries, there is concern over the health hazards that they may present due to exposure to microwaves. Safety guidelines for limiting exposures to electromagnetic fields [e.g., ICNIRP, 1998 and IEEE Std. C95.1, 1999] have already been developed to protect humans from possible health hazards. Those guidelines are relevant to the exposures by mobile phones, as there is no scientific evidence indicating hazards below those exposure limits. Only a limited part of the body is exposed during the use of mobile phones. Safety guidelines limit local specific absorption rate (SAR) in such exposures. The exposure limit is 1.6 W/kg for the general public and 8 W/kg for occupational exposure in the US, and 2 and 10 W/kg, respectively, in European countries and in Japan.

Those values have their rationale based on the research database of the past and on thermal considerations. However, there is not much experimental evidence that directly indicates an established hazard

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of localized exposure to form a rationale for the exposure limit. Further evidence is necessary to establish the validity of guidelines for limiting the local SAR in localized exposures.

Ocular effects, including cataracts of high intensity exposure, are among those effects of microwave exposure [Daily et al., 1948; Richardson et al., 1948]. Recently, Elder [2003] published a comprehensive review of the literature on ocular effects induced by radio frequency exposure.

Guy et al. [1975] investigated the effect of microwave exposure to the lens in albino rabbits under systemic anesthesia and determined the microwave level threshold for inducing lens opacification (cataract) [150 mW/cm^2 incidence (138 W/kg maximum absorbed power density in the vitreous) for 100 min]. Saito et al. [1998] performed an experiment using white rabbits under nonanesthesia conditions with 26.5 W/kg SAR for 160–240 min and found no cataractous change. Kues et al. [1985] found corneal endothelial abnormalities in systemic anesthesia conditions with 20–30 mW/cm^2 (2.45 GHz continuous waves (CW)) exposure. In contrast, Kamimura et al. [1994] reported that no abnormality was found on corneal endothelial cells in the same kind of study without anesthesia. To help clarify the effect of anesthesia, an investigation was made on the influence of systemic anesthesia or no anesthesia on ocular effects induced by microwave exposure under the same experimental conditions.

MATERIALS AND METHODS

The rabbits used in this study were cared for and handled in accordance with the Guidelines for Animal Experiments at Kanazawa Medical University. Forty-three young adult male pigmented rabbits (Dutch, 1.8–2.2 kg, 13–16 weeks old) were kept in a specific pathogen free animal room. They were given a sterilized commercial diet and sterilized water ad libium. These rabbits were used only once in an experiment.

A schematic view of the exposure system is shown in Figure 1. A dielectric-loaded small waveguide antenna (aperture size: 12.6×28.5 mm) was used to expose the rabbits to microwave radiation (Fig. 2). The relative permittivity of the dielectric material ''macerite'' was about 6. The aperture of the antenna was covered by a polyvinyl chloride slab. The distance between the antenna aperture (without polyvinyl chloride) and surface of the rabbit cornea was 40 mm. The eyes of the rabbits were exposed unilaterally to 2.45 GHz for 60–120 min with 300 mW/cm^2 incident power density at the corneal surface, either under anesthesia (ketamine hydrochloride (5 mg/kg) + xylazine (0.23 mg/kg) injected intramuscularly) or

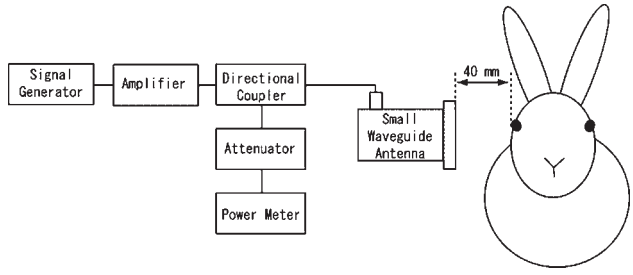

Fig. 1. Diagrammatic representation of the animal exposure system.

without anesthesia. The rabbits were fixed in a rabbit holder (made of polycarbonate) when exposed to microwaves, and two rabbits (anesthetized and nonanesthetized) were exposed simultaneously as one pair (Fig. 3).

SAR inside a numerical rabbit model was analyzed by the finite difference time domain (FDTD) method [Wake et al., 2002]. Average SAR in the exposed eye was about 108 W/kg with the exposure of 300 mW/cm^2 incident power density. The rabbit model has a 1 mm resolution and the eye was modeled with five kinds of ocular tissues. The average SAR over the exposed whole eye, cornea, anterior chamber, lens, vitreous, and sclera were 108, 105, 141, 138, 105, and 75 W/kg, respectively with the exposure of 300 mW/cm^2 incident power densities. The maximum SAR for the 1 mm^3 region in the vitreous was above 200 W/kg for the same condition.

The control group consisted of three pairs of sham exposed rabbits. The sham exposure group was treated the same as the MW exposure group, but without MW exposure. A pair of rabbits was set at the front of a MW antenna. All equipment switches were turned on except the switch on the microwave generator.

Changes in the anterior segment were observed before exposure and 1, 3, 7, and 14 days after. Changes

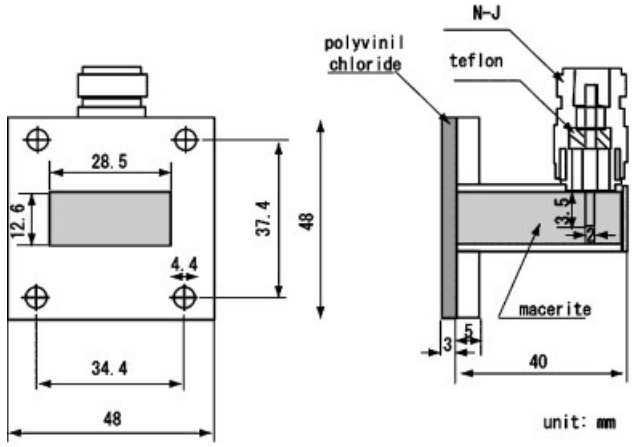

Fig. 2. A schema of a dielectric-loaded small waveguide antenna.

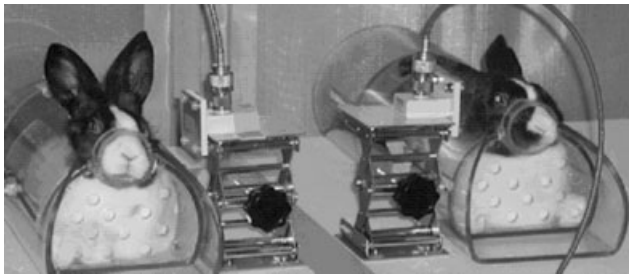

Fig. 3. Experimental setup for microwave exposure.

in the corneal surface and parenchymal layer and crystalline lens layers were objectively evaluated with a Scheimpflug camera [Kojima and Sasaki, 1992]. Damage to the corneal endothelial cells was observed through a specular microscope (CSP-580, Konan, Osaka, Japan). Inflammation in the aqueous humor (anterior uveitis) was observed by a slit lamp microscope, and the degree of inflammation was objectively evaluated through a laser flare cell meter (FC-2000, Kowa).

During microwave exposure, temperatures of the eye segments were measured by a Fluoroptic thermometer (Luxtron 790, Luxtron, Santa Clara, CA) according to the following procedures: the rabbit eyes were anesthetized with 0.4% oxybuprocaine hydrochloride ophthalmic solution (eye drop application); then, thermometer probes (0.5 mm in diameter) were inserted into the anterior chamber, vitreous, and retrobulbar cavity of the orbit. The tip of the thermal probes for the anterior chamber and vitreous was set at the center of the pupil area in the eye (Fig. 4). Body (rectal) temperature was measured by a Fluoroptic thermometer (FL-2000, Anritsu, Tokyo, Japan). A flexible thermal probe (1.6 mm in diameter) was inserted 15 cm into the rectum. Two Fluoroptic thermometers were compared to a standard thermometer. Room temperature and humidity were also measured with a psychrometer.

Fifteen minutes after the temperature probes were inserted into the eye (after the anesthesia of the eye had worn off), the eyes were exposed to 300 mW/cm^2 for 1 h, after which there was a cooling time of 1 h. Fifteen minutes after administration of systemic anesthesia, the rabbits were again exposed to 300 mW/cm^2 for 1 h. To observe the accumulated effect of both exposure times on the rise in temperature, the eye temperatures were monitored during the 300 mW/cm^2 exposures, including the cooling time of 1 h in the nonanesthetized rabbits.

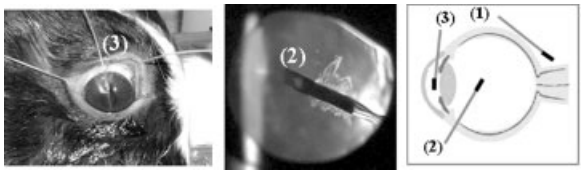

Fig. 4. Site of ocular temperature measurements. (**1**) Retrobulber cavity in the orbit (**right image**), (**2**) vitreous (retroillumination image indicate the tip of thermal probe in the vitreous, **middle image**), (**3**) anterior chamber (**left image**).

Eyes of the exposed and nonexposed sides (MW exposure group and sham exposure group) were evaluated for comparisons.

All data indicate mean $\pm$ SD. Experimental data was evaluated using a Student's two-tailed *t*-test. $P < .05$ was considered significant.

RESULTS

The exposed rabbit eyes showed miosis, conjunctival congestion, and corneal edema. All of these changes disappeared within a week. An increase in the light scattering in the anterior shallow cortex of the exposed lens was noticed at 1 day after exposure (Fig. 5). In the anesthetized rabbits, the effect reached a peak 3 days after exposure and, at 7 and 14 days, decreased to a level below that seen 1 day after exposure (Fig. 6). As shown in Figure 6, the changes were much more pronounced in the systemic anesthesia group. This observation is also demonstrated in the photographs of rabbit eyes at 3 days after exposure (Fig. 5). Anterior uveitis (iritis and/or iridocyclitis) in the exposed eyes of the anesthetized rabbits showed a significantly higher degree ($P < .05$) of inflammation (634 ± 166 photon count/millisecond (pc/ms)) compared to the nonexposed eyes (9.8 ± 8.3 pc/ms) immediately after exposure (Fig. 7). In contrast, the nonanesthetized rabbits showed a lower degree of inflammation (215 ± 316 pc/ms (exposed eye); 6.9 ± 4.5 pc/ms (nonexposed eye)). The exposed eye inflammation of the nonanesthetized group recovered to a level equivalent to that of the nonexposed eye after 3 days, while in the anesthetized group, the exposed eyes showed photon counts that were around five times stronger than those of the nonanesthetized group (Fig. 7).

The highest temperature during exposure was seen in the vitreous, followed by the anterior chamber, and the retrobulbar cavity of the orbit. The temperatures in these three locations in rabbits under systemic anesthesia were 2–9 °C higher than those without anesthesia (Fig. 8). In the nonanesthetized group, there was no significant temperature difference between the first and second exposure to the eye segments, except for the temperature of the anterior chamber, which was higher during the second exposure than the first. Within 1 h, the anterior chamber temperature did not return to a normal temperature after the first exposure. The rectal temperature showed an increase of 1 °C during the

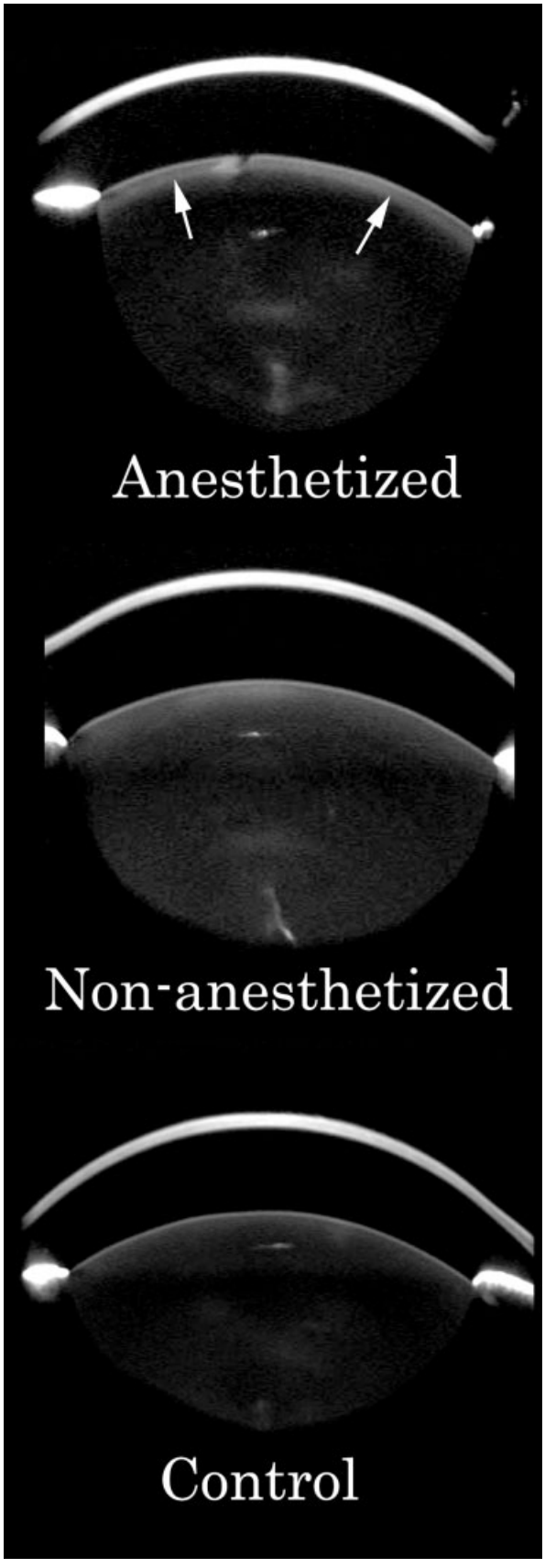

Fig. 5. Lens images 3 days after microwave exposure. Anesthetized rabbits showed anterior shallow cortical lens change (arrows).

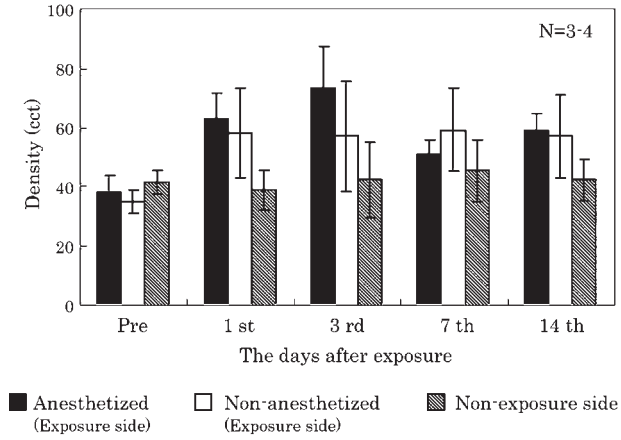

Fig. 6. Time course of lens scattering changes. N = 3–4 rabbit's data in each point.

exposure. Figure 8 indicates the comparison of temperature rising pattern during MW exposure with and without anesthesia.

DISCUSSION

Although investigations related to the ocular effects of microwave exposure have been performed by several authors, there are differences in the experimental conditions of ocular studies in living eyes, especially those concerning the use of anesthesia during microwave exposure. Some authors [Kamimura et al., 1994] concluded that ocular effects reported by others [e.g., Kues et al., 1985] were due to the use of anesthetics. These results suggest that the effect of anesthesia on microwave-induced ocular effects needs to be clarified. In addition, progress has been made in the experimental methodology applied to ocular research since the late 1990s. For these reasons, we investigated the same kind of studies that had been performed by previous authors, but used both anesthetized and nonanesthetized animals and with several technologies that have been developed recently.

The threshold microwave exposure conditions that induced lens opacification in anesthetized rabbits was 150 mW/cm^2 for 100 min (maximum SAR in the vitreous: 138 W/kg), and the effect was described as ''a milky band in the posterior cortex, and this was often reversible'' [Guy et al., 1975]. We confirmed lens changes with 300 mW/cm^2 exposure for 120 min

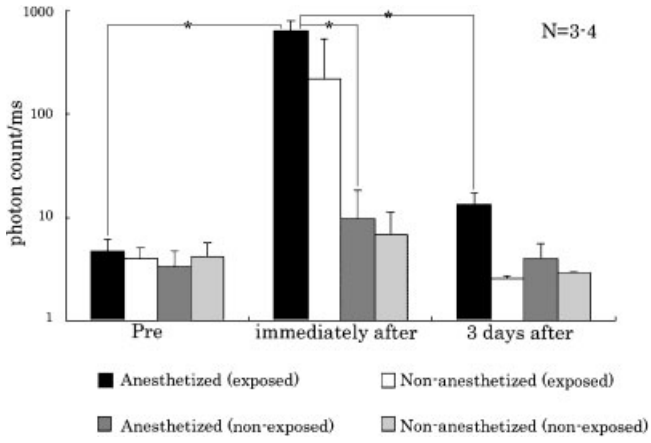

Fig. 7. Time course of flare value changes. N = 3–4 rabbit's data in each point. *$P < .05$

(maximum SAR in the vitreous: above 200 W/kg). However, the lens change was only seen in anesthetized rabbits and did not occur in the nonanesthetized rabbits' eyes. In addition to our use of nonanesthetized animals, there were other differences in the experimental methods in this study and the one performed by Guy et al. [1975]. These differences are (1) difference in the antennae type, (2) distance between the antennae and the surface of the rabbit cornea. In the previous study, a dipole antenna with corner reflector was used, but in this study the open aperture waveguide antenna was used. The near field of each radiation source is quite different, resulting in different SAR distribution, even if the incident power density around eye is at same level. (3) Albino versus pigmented animals. In the previous study albino rabbits were used, but in this study only pigmented rabbits were used. It is well recognized in the ocular toxicological study field that pigmented animals are appropriate subjects. (4) With and without anesthesia.

The authors consider that among the above differences, general anesthesia had the main influence on the appearance of cataractous changes. Fraunfelder and Burns [1970] reported that acute reversible lens opacity (superficial anterior subcapsular lens opacity) is caused by drugs (narcotics, phenothiazines, epinephrine), cold, anoxia, asphyxia, stress, death, and dehydration. General anesthesia itself has a risk of cataractogenesis.

In order to understand the relationship between intraocular temperature changes and anesthesia, the ocular temperatures were measured during exposure with and without anesthesia. As described in the results, intraocular temperatures were higher in the group with systemic anesthesia than in the group without anesthesia (Fig. 8). The cooling effect of blood circulation on

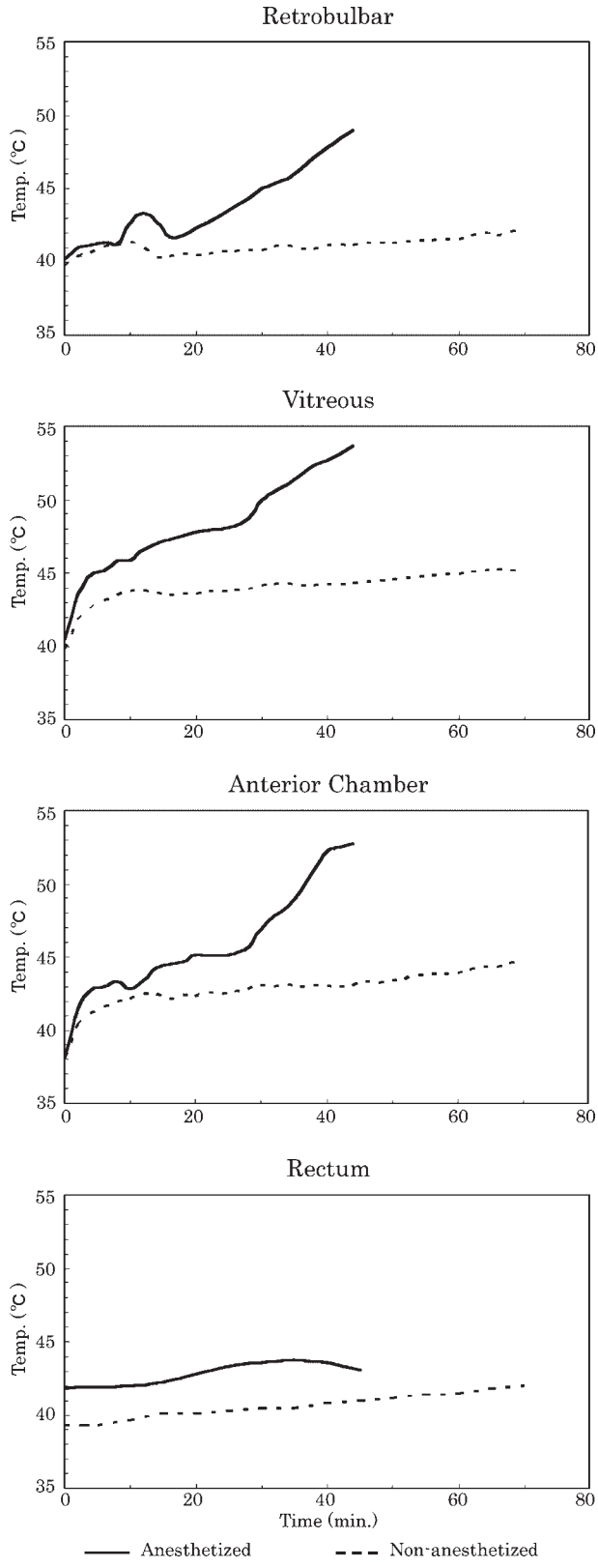

Fig. 8. Temperature changing pattern during exposure with or without anesthesia.

the eyeball may be disturbed by general anesthesia, although the authors still do not know the extent to which it is disturbed. Daily et al. [1950] has already pointed out the importance of the blood circulation: ''blood circulation in the vascular tunics adjacent to the aqueous and vitreous efficiently carries away a large part of the heat produced in these media by exposure of microwave.''

The relationship between ocular temperature and blood flow in anesthetized rabbits was explained by Carpenter et al. [1977]: ''if the temperature at the posterior pole of the lens in an anesthetized rabbit is measured prior to and during microwave irradiation, it may be found to rise perhaps 5 °C in the course of a 15-min exposure. If a lethal dose of anesthetic is then injected intravenously, the heart will stop beating, whereupon the intraocular temperature will rapidly rise another 10 °C, thus indicating that the vascular system is capable of handling at least two-thirds of the thermal stress which radiation imposes upon the eye.''

Based on the authors' own studies up to now and the previous investigations by Guy et al. [1975] and Saito et al. [1998], we consider that the threshold level which induces organic changes in ocular tissues such as the cornea and lens, would be lower when calculated under experimental conditions with general anesthesia than without general anesthesia. This conclusion is consistent with the thermal mechanism for microwave induced cataract. The exposure must be sufficiently intense to cause the temperature in the lens to reach 41 °C [Kramar, 1975]. In our study, we found much higher temperatures in the eyes of anesthetized rabbits than in the nonanesthetized rabbits.

The results gained from this study may yield useful information for future studies in this field.

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