


Ocular Effects of Exposure to 40, 75, and 95 GHz Millimeter Waves

Masami Kojima^{1,2,3}  · Yukihiisa Suzuki⁴ ·
Kensuke Sasaki⁵ · Masao Taki⁴ · Kanako Wake⁵ ·
Soichi Watanabe⁵ · Maya Mizuno⁵ · Takafumi Tasaki⁶ ·
Hiroshi Sasaki^{1,2}

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Abstract The objective of this study was to develop a model of ocular damage induced by 40, 75, and 95 GHz continuous millimeter waves (MMW), thereby allowing assessment of the clinical course of ocular damage resulting from exposure to thermal damage-inducing MMW. This study also examined the dependence of ocular damage on incident power density. Pigmented rabbit eyes were exposed to 40, 75, and 95 GHz MMW from a spot-focus-type lens antenna. Slight ocular damage was observed 10 min after MMW exposure, including reduced cornea thickness and reduced transparency. Diffuse fluorescein staining around the pupillary area indicated corneal epithelial injury. Slit-lamp examination 1 day after MMW exposure revealed a round area of opacity, accompanied by fluorescence staining, in the central pupillary zone. Corneal edema, indicative of corneal stromal damage, peaked 1 day after MMW exposure, with thickness gradually subsiding to normal. Three days after exposure, ocular conditions had almost normalized, though corneal thickness was slightly greater than that before exposure. The 50% probability of ocular damage (DD_{50}) was in the order $40 > 95 \approx 75$ GHz at the same incident power densities.

✉ Masami Kojima
m-kojima@kanazawa-med.ac.jp

¹ Division of Vision Research for Environmental Health, Medical Research Institute, Kanazawa Medical University, Kahoku, Japan

² Department of Ophthalmology, Kanazawa Medical University, Kahoku, Japan

³ School of Nursing, Kanazawa Medical University, 1-1 Daigaku, Uchinada, Kahoku, Ishikawa 920-0293, Japan

⁴ Department of Electrical Engineering and Computer Science, Graduate School of Systems Design, Tokyo Metropolitan University, Tokyo, Japan

⁵ National Institute of Information and Communications Technology, Tokyo, Japan

⁶ Division of Protein Regulation Research, Medical Research Institute, Kanazawa Medical University, Kahoku, Japan

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1 Introduction

Millimeter wave (MMW) technologies have come into widespread use in daily life, including in high-speed wireless communications, sensing, high-resolution radar imaging, spectroscopy, and automobile collision prevention systems. For example, Wireless Gigabit (WiGig) products, which operate at frequencies in 60 GHz band, are now commercially available, with additional MMW frequency bands expected to be used in the fifth generation wireless communication technologies [1–3]. Industrial development of 60 GHz technology and user expectations have increased concomitantly. However, increased public exposure to MMW has heightened the need to evaluate their health effects.

Several *in vivo* studies in experimental animals have evaluated the specific effects of MMW [4–6]. Frequency-specific thresholds for ocular damage were observed at 35 and 107 GHz. Exposure to 35 GHz MMW was associated with corneal damage, including high levels of corneal epithelial injury, persisting for almost 2 days, whereas exposure to 107 GHz was associated with transient injury to the corneal stroma, albeit more powerful in inducing immediate corneal stromal damage [4]. Under pulse wave conditions, the thresholds for corneal injury, corneal edema, and corneal epithelial defect were found to be 7.5 J/cm² for 35 GHz and 5.0 J/cm² for 94 GHz [5], suggesting that different frequencies have different ocular effects. These earlier studies employed a circular horn antenna [4, 6] or an open-ended waveguide [5]. Because their exposure methodology and experimental animals differed, the results of these studies cannot be directly compared. Similarly, we reported that different antennas caused different ocular effects [7].

To examine the clinical course of MMW-induced ocular damage with a high degree of reproducibility, we developed a model of acute ocular injury using high dose 60 GHz MMW in rabbit eyes [7]. The objective of this study was to develop models of ocular damage induced by 40, 75, and 95 GHz MMW, allowing us to evaluate the clinical course of thermal damage-induced ocular injury. We also assessed the dependence of ocular damage on incident power density, as well as the frequency characteristics of the ocular damage in rabbit eyes exposed to 40, 75, and 95 GHz MMW.

2 Materials and Methods

2.1 Exposure System

The *in vivo* exposure system has been previously described in detail [8]. Therefore, configuration of the exposure system is only briefly described here. Figure 1 depicts a block diagram of the system which comprises power sources, i.e., a signal generator (75 and 95 GHz) or a signal generator and amplifier (40 GHz), directional couplers, power sensors, and a power meter (E4417A, Agilent Technologies). Power sensors A and B, shown in Fig. 1, are used to measure incident power to the antenna and reflected power from the antenna, respectively, via directional couplers. A spot-focus-type lens antenna, i.e., a conical horn

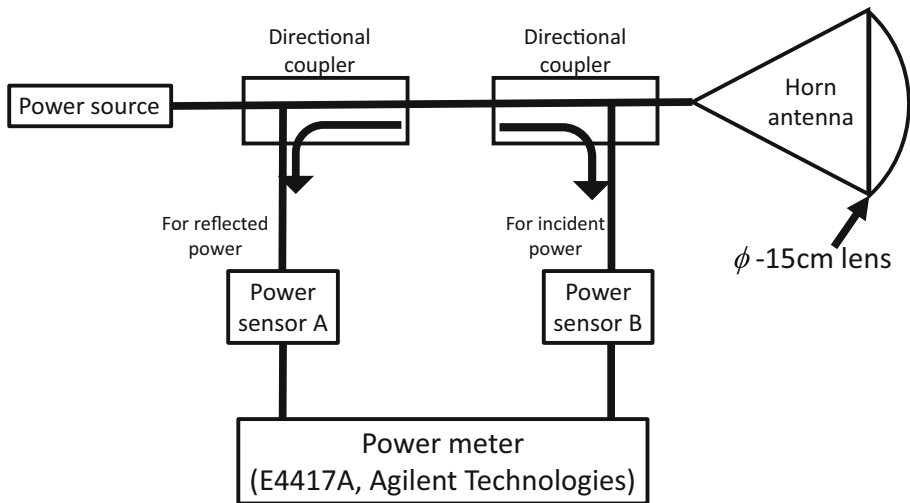


Fig. 1 Block diagram of the exposure system

antenna with a ϕ -15-cm lens, was used to ensure localization to the eye. By using this equipment, exposure of the skin, i.e., upper and lower eyelids surrounding the eye tissue, to MMW can be avoided preventing burns; facial burns are a limitation in results of MMW exposure studies due to variation in individual values of ocular damage [7]. The level of exposure was calculated as the spatially averaged incident power density over a circular region of 13 mm in diameter, the average size of the corneal region in Dutch-belted rabbits. The special profiles of incident power density radiating from the antenna aperture were measured using open-ended waveguide probes [8].

2.2 Experimental Animals

All animal experiments were conducted in accordance with the animal study guidelines of Kanazawa Medical University (Kahoku, Japan) and the ARVO (Association for Research in Vision and Ophthalmology) statement for the use of animals in ophthalmic and vision research [9].

One hundred and thirty male Dutch-belted pigmented rabbits (12–14 weeks old, 1.9–2.2 kg) were purchased from Sankyo Labo Service Co., Inc. (Toyama, Japan) and kept with unrestricted access to food and water. At baseline, all rabbit eyes were examined using a SL-130 slit-lamp microscope (Zeiss, Tokyo, Japan) to ensure absence of abnormalities in the anterior segment, and each eye was photographed.

Each rabbit was injected intramuscularly (IM) with a solution containing 0.8–1.0 mg/kg of medetomidine hydrochloride (Domitor, Nippon Zenyaku Kogyo Co., Ltd., Fukushima, Japan) to induce general anesthesia, and immobilized in an acrylic rabbit restrainer, specially constructed for studies of exposure to MMW [7]. Immediately before MMW exposure, 2% lidocaine hydrochloride topical anesthetic (Xylocaine 2%; AstraZeneca, Osaka, Japan) was administered to each eye. The upper and lower eyelids were held open with tape. Because anesthesia suppressed blinking, saline drops, pre-warmed to 35–37 °C, were administered to the eyes as necessary to prevent damage to corneal epithelial cells resulting from corneal desiccation.

Following each ocular examination, all rabbits were administered topical ofloxacin ointment (Tarivid; Santen Pharmaceutical Co., Ltd., Osaka, Japan) to prevent secondary infection. Temperature and humidity during exposure were maintained at 24 ± 2 °C and $60 \pm 10\%$, respectively, using an air conditioner and dehumidifier. Anesthesia was reversed with 0.8–1.0 mg/kg IM atipamezole hydrochloride (Antisedan, Nippon Zenyaku Kogyo Co., Ltd., Fukushima, Japan) to help the rabbits' recovery.

2.3 MMW Exposure

The center of the corneal surface of each rabbit's right eye was positioned 135 mm from the antenna aperture and on the line of maximum radiation of the antenna [7, 8]. The exposure point was set using red and green laser pointers on a target [10], and the right eye of 105 rabbits was exposed to continuous MMW of 10–600 mW/cm² (40 GHz), 50–300 mW/cm² (75 GHz), or 50–300 mW/cm² (95 GHz) for 6 min. The left eye of each rabbit was unexposed and regarded as a control eye.

To assess the ocular effects of exposure to MMW for 30 min, the right eye of another set of 21 rabbits was exposed to 75 GHz (10–300 mW/cm²) MMW, and the left eye of each of these rabbits was treated as non-exposed control eyes. All other experimental conditions were identical to those in rabbit eyes exposed to MMW for 6 min.

In order to assess the effects of sham exposure for 30 min or exposure to very low intensity infrared (IR) irradiation, another set of four rabbits was used. The right eye of each of these was sham exposure which involved the power supply of all exposure systems set to the ON state, but the signal generator did not feed the system with the (MMW) signal. The left eye of each of these was exposed with a 60-W desk lamp, such that the corneal surface temperature reached about 38 °C (IR exposure). Ocular conditions were assessed prior to exposure and 10 min and 1 day after exposure. Other experimental conditions were identical to those in rabbit eyes exposed to MMW for 6 min.

2.4 Corneal Surface Temperature

Corneal surface temperatures were recorded in MMW and IR exposed eyes at 5 s prior to exposure and at 5 s before the end of MMW exposure using a thermography camera (R300, NEC Avio, Tokyo, Japan). The same measurements were taken in control and sham exposure eyes.

2.5 Examination of Ocular Injury

The anterior segment was evaluated before IR and MMW exposure, and at 10 min, and 1, 2, and 3 days after exposure. Corneal epithelial damage was observed by slit-lamp microscopy using a modified method involving fluorescein staining of damaged corneal epithelial cells [4]. Briefly, rabbit eyes were gently washed with saline, and fluorescein solution (0.05%, 25 μ l) was instilled into the cul-de-sac with a micropipette. After a single blink, excess fluorescein was washed out with saline, and images of the anterior segment were recorded with a slit-lamp microscope, following excitation with blue light and monitoring with green light using appropriate filters (excitation light cutting filter), corneal cross-sectional thickness was measured and recorded by optical coherence tomography (OCT, Zeiss model 5000, Tokyo, Japan), and corneal opacity was assessed using a slit-lamp microscope.

2.6 Categorization of Corneal Epithelial Injury

Corneal epithelial injury was defined as a round area of epithelial injury in the central pupillary zone of exposed eyes, with no similar injury observed in unexposed eyes. Other types of corneal epithelial injury, such as desiccation of the cornea (i.e., dry eye) and mechanical damage, were excluded.

2.7 Data Analysis

The probability of corneal damage at 1 day after exposure depending on the power densities to different frequencies of MMW was evaluated by maximum likelihood estimation with probit analysis [11]. Morphological changes in the cornea were assessed by slit-lamp microscopy, including fluorescein staining, and optical coherence tomography. Ocular disorders, including corneal epithelial disorders, corneal opacity, and corneal edema, were determined by observation at 1 day after exposure. The dose-response relationship between corneal injury and range of power density at each frequency was evaluated by fitting with a cumulative lognormal distribution function for probit analysis using R Ver 3.3.3 software [12]. The MMW power density indicating the probability of eye damage was defined as damage dose (DD) and was derived from the best-fit probit function.

3 Results

Representative eye injuries from exposure with 200 mW/cm^2 at 75 GHz for 6 min are shown in Fig. 2. Slight ocular damage observed 10 min after MMW exposure included reduced corneal transparency around the pupillary area (Fig. 2d), reduced corneal thickness (Fig. 2e), and corneal epithelial damage as indicated by diffuse fluorescein staining around the pupillary area (Fig. 2f). Slit-lamp examination at 1 day after MMW exposure revealed a round area of corneal opacity in the central area of the pupil (Fig. 2g) and a round area of fluorescein staining (corneal epithelial defect, Fig. 2i) at the same place. Corneal edema, indicative of corneal stromal damage, peaked at 1 day after MMW exposure, with thickness gradually subsiding (Fig. 2h, k, and n) almost reaching that before exposure (Fig. 2b).

Tables 1, 2, and 3 summarize the effects of exposure to 95, 75, and 40 GHz MMW, respectively. Corneal surface temperature was highest in eyes exposed to 75 GHz MMW, followed by those exposed to 95 GHz, then those exposed to 40 GHz, in that order for the same incident power densities. Under the exposure condition of 95 GHz, 100 mW/cm^2 , for 6 min exposure, the corneal surface temperature reached an average of $37.0 \pm 3.3 \text{ }^\circ\text{C}$. Corneal epithelial damage was observed only in one rabbit at 1 day after exposure (Table 1). Corneal surface temperature reached $40.2 \pm 0.5 \text{ }^\circ\text{C}$ even under the same exposure condition (100 mW/cm^2 for 6 min exposure) at 75 GHz, corneal epithelial damage and corneal edema were observed in only one rabbit at 1 day after exposure (Table 2). The effect of 40 GHz exposure (100 mW/cm^2 , 6 min exposure) was almost the same as that of 95 GHz exposure, the corneal surface temperature was $37.1 \pm 2.7 \text{ }^\circ\text{C}$, and corneal epithelium damage was observed in only one rabbit (Table 3). Corneal surface temperature rises due to MMW exposure varied with frequency.

The extent of ocular damage and clinical course were similar in eyes exposed to high doses of 40 and 75 GHz MMW for 6 min. That is, mitosis and damage to the corneal epithelium

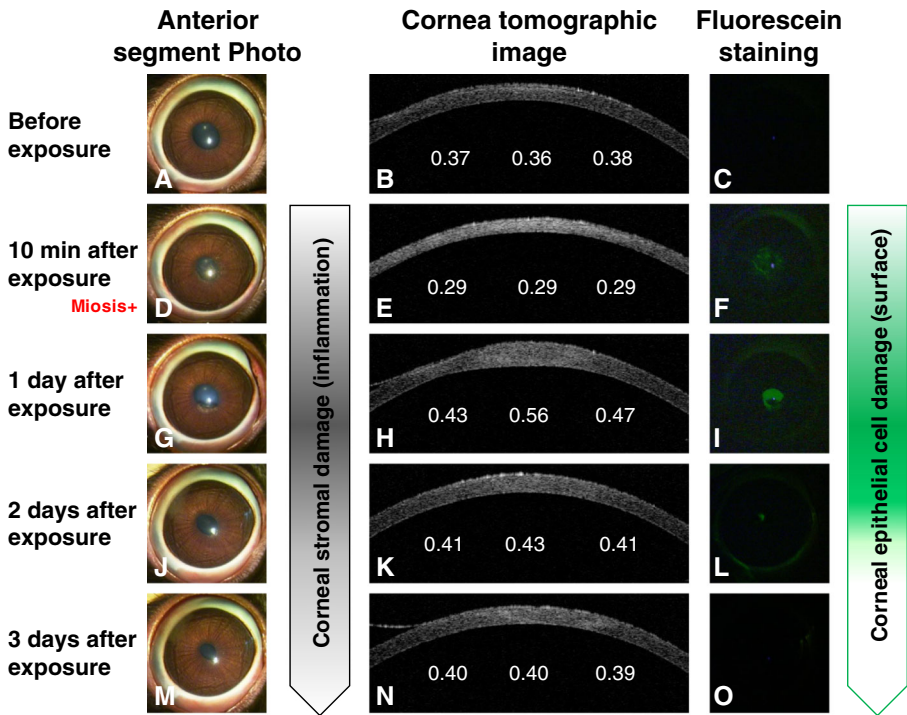


Fig. 2 Representative examples of eyes with corneal damage and their clinical courses following exposure of eyes to 75 GHz MMW at 200 mW/cm² for 6 min. The numbers indicate corneal thickness in millimeters. **a** Anterior segment photo, **b** Corneal tomographic image, and **c** fluorescein staining at before exposure condition. **d, e,** and **f** At 10 min after exposure. **g, h,** and **i** At 1 day after exposure. **j, k,** and **l** At 2 days after exposure. **m, n,** and **o** At 3 days after exposure





were observed immediately after irradiation with either 500–600 mW/cm² at 40 GHz (data not shown) or 300 mW/cm² at 75 GHz. The level of ocular damage, however, was milder in the eyes exposed to 300 mW/cm² at 95 GHz exposure, with mitosis and prominent corneal epithelial damage rarely observed immediately after exposure in these eyes.

Damage to both the corneal stroma (corneal opacity) and corneal epithelium was observed at 1 day after MMW exposure. At 3 days, corneal opacity was observed in all exposed eyes,

Table 1 Summary of the results of exposure of rabbit eyes to 95 GHz MMW. Damage + (n/N) indicates damage was observed in n of N exposed eyes



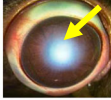
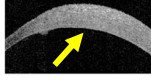
95 GHz One day after exposure	Corneal surface temperature (°C)	Corneal epithelium damage	Corneal opaque	Corneal edema
300 mW/cm ² _6 min	46.5±1.3	Damage+ (3/3)	Damage+ (2/3)	Damage+ (1/3)
200 mW/cm ² _6 min	43.7±1.7	Damage+ (11/13)	Damage+ (5/13)	Damage+ (6/13)
100 mW/cm ² _6 min	37.0±3.3	Damage+ (1/9)	Damage+ (0/9)	Damage+ (0/9)
50 mW/cm ² _6 min	34.1±2.3	No damage (0/4)	No damage (0/4)	No damage (0/4)

Table 2 Summary of the results of exposure of rabbit eyes to 75 GHz MMW. Damage + (n/N) indicates damage was observed in n of N exposed eyes

75 GHz One day after exposure	Corneal surface temperature) 	Corneal epithelium damage 	Corneal opaque 	Corneal edema 
300 mW/cm ² _6 min	50.7±1.9	Damage+ (3/3)	Damage+ (3/3)	Damage+ (3/3)
200 mW/cm ² _6 min	43.8±4.9	Damage+ (14/15)	Damage+ (13/15)	Damage+ (13/15)
150 mW/cm ² _6 min	43.1±1.9	Damage+ (3/6)	Damage+ (3/6)	Damage+ (3/6)
100 mW/cm ² _6 min	40.2±0.5	Damage+ (1/12)	Damage– (0/12)	Damage– (1/12)
50 mW/cm ² _6 min	37.6±1.5	Damage– (0/7)	Damage– (0/7)	Damage– (0/7)
300 mW/cm ² _30 min	52.7±2.5	Damage+ (5/5)	Damage+ (5/5)	Damage+ (5/5)
200 mW/cm ² _30 min	49.9±1.5	Damage+ (4/4)	Damage+ (4/4)	Damage+ (4/4)
100 mW/cm ² _30 min	42.7±1.8	Damage+ (3/4)	Damage+ (3/4)	Damage+ (3/4)
50 mW/cm ² _30 min	37.1±0.8	Damage+ (5/5)	Damage+ (1/5)	Damage+ (1/5)
10 mW/cm ² _30 min	33.7±1.0	No damage (0/3)	No damage (0/3)	No damage (0/3)

with ciliary injection peaking in some, although these symptoms gradually improved. Damage to corneal epithelial cells peaked at 1 day after exposure, gradually improving over the next 1–2 days. The most severe damage to the corneal stroma was observed at 3 days after exposure. These levels of ocular damage and clinical course observed in eyes exposed to 40 and 75 GHz MMW were similar to those reported for 60 GHz MMW [7].

Table 3 Summary of the results of exposure of rabbit eyes to 40 GHz MMW. Damage + (n/N) indicates damage was observed in n of N exposed eyes

40 GHz After 1 day Exposure	Corneal surface temperature (°C) 	Corneal epithelium damage 	Corneal opaque 	Corneal edema 
400 mW/cm ² _6 min	43.9±3.6	Damage + (6/8)	Damage + (5/8)	Damage + (5/8)
300 mW/cm ² _6 min	41.3±1.3	Damage + (5/6)	Damage + (1/6)	Damage + (1/6)
200 mW/cm ² _6 min	41.3±1.5	Damage+ (2/4)	No damage (0/4)	No damage (0/4)
100 mW/cm ² _6 min	37.1±2.7	Damage+(1/7)	No damage (0/7)	No damage (1/7)
50 mW/cm ² _6 min	33.6±1.8	No damage (0/8)	No damage (0/8)	No damage (0/8)

Although exposure to 40, 75, and 95 GHz at 50 mW/cm² for 6 min did not induce ocular disorder in any eye, corneal epithelial damage was observed in all five eyes exposed to 75 GHz MMW at 50 mW/cm² for 30 min. In addition, one of these five eyes also showed corneal edema and opacity indicating damage to the corneal stroma (Table 2). Exposure to 75 GHz MMW at 50 mW/cm² for 30 min resulted in a corneal surface temperature of 37.1 ± 0.8 °C, similar to rabbit body temperature. In contrast, none of the unexposed left eyes (control) showed any indication of eye damage.

Figure 3 shows representative experimental results of MMW sham exposure to right eyes and simultaneous IR exposure with a 60-W desk lamp to left eyes for 30 min. Exposure to sham exposure increased corneal surface temperature by 1.4 °C, from 32.5 to 33.9 °C, whereas IR exposure increased corneal surface temperature by 5.1 °C, from 32.7 to 37.8 °C, which is almost the same as the body temperature of these rabbits. Corneal thickness at 10 min after sham and IR exposure was reduced to 0.21 and 0.24 mm, respectively (Fig. 3g, l). Sham-exposed eyes were negative for fluorescein staining, but damage to corneal epithelial cells was observed in IR-exposed eyes. One day later, the sham-exposed eyes appeared normal, although their corneas were slightly thinner than normal (Fig. 3m, n, and o). In contrast, IR-exposed eyes at 1 day after exposure showed corneal epithelial damage accompanied by corneal edema (Fig. 3q, r).

The association between ocular damage and the power density at different MMW frequencies was assessed by determining the probability of corneal damage at 1 day after exposure by maximum likelihood estimation (MLE) with probit analysis (Fig. 4). The markers plotted in each graph denote the dependence of probability of eye damage relative to the number of eyes exposed to the power density (dose) following actual MMW exposure. Table 4 and Fig. 5 show the 10, 50, and 90% probability of ocular damage DD 10% (DD₁₀), DD 50% (DD₅₀), and DD 90% (DD₉₀), as determined by MLE, following exposure to 40, 75, and 95 GHz

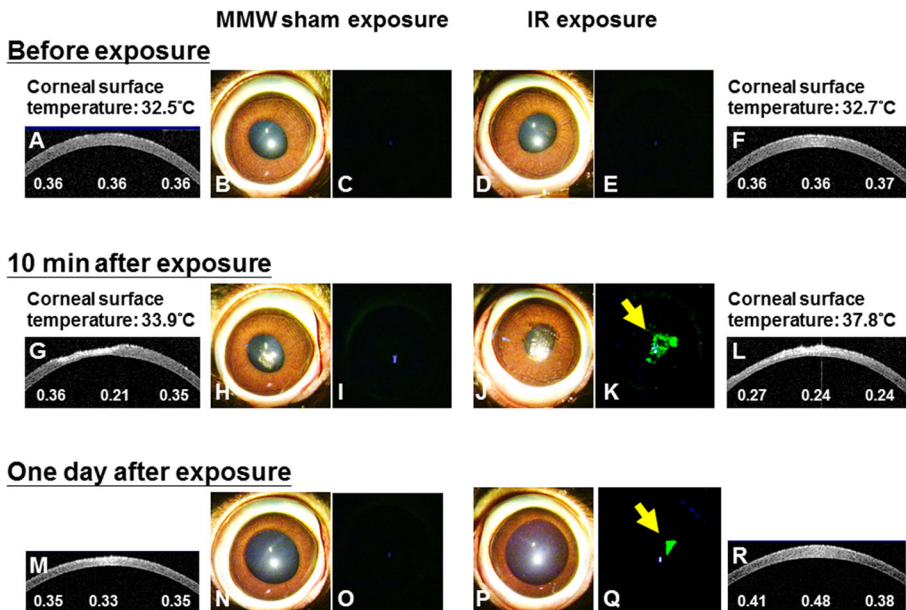


Fig. 3 Representative corneal damage to eyes exposed to MMW sham and IR irradiation with a 60-W desk lamp for 30 min

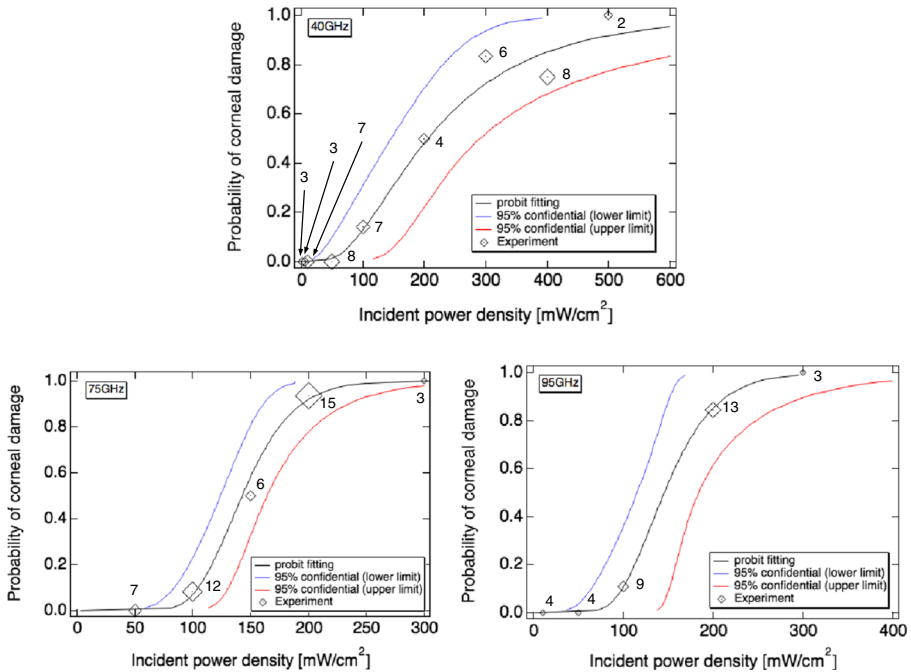


Fig. 4 Results of maximum likelihood estimation with probit analysis for exposure to 40, 75, and 95 GHz MMW. The markers in each graph denote the dependence of the probability of damaged eyes relative to the number of eyes exposed to the indicated power density (dose). The number of rabbit eyes at each power density corresponds to the size of the diamond-shaped markers. The blue and red lines indicate the lower and upper limits on 95% confidence intervals, respectively

MMW. The 50% probability of ocular damage (DD_{50}) was in the order $40 (206 \text{ mW/cm}^2) > 95 (146 \text{ mW/cm}^2) \approx 75 \text{ GHz} (143 \text{ mW/cm}^2)$ at the same incident power densities.

4 Discussion

4.1 Comparison Between our Methodology and that of Previous Studies

The main purpose of this study was to develop an appropriate rabbit model of thermally induced ocular damage using different frequencies of MMW (40, 75, and 95 GHz). Ocular

Table 4 Power densities for DD_{10} (DD₁₀), dose level to cause ocular damage with 10% probability, DD_{50} (DD₅₀), dose level to cause ocular damage with 50% probability and DD_{90} (DD₉₀>) dose level to cause ocular damage with 90% probability estimated from MLE results for exposure to 40, 75, and 95 GHz MMW

Frequency	Power density for DD_{10} [mW/cm ²]		Power density for DD_{50} [mW/cm ²]		Power density for DD_{90} [mW/cm ²]	
40 GHz	211	+ 88.1	317	+ 63.5	476	+ 183
		- 62.2		- 52.9		- 132
75 GHz	110	+ 50.5	163	+ 40.3	241	+ 114
		- 34.6		- 32.3		- 77.4
95 GHz	99.4	+ 80.8	224	+ 108	505	+ 748
		- 44.6		- 72.8		- 314

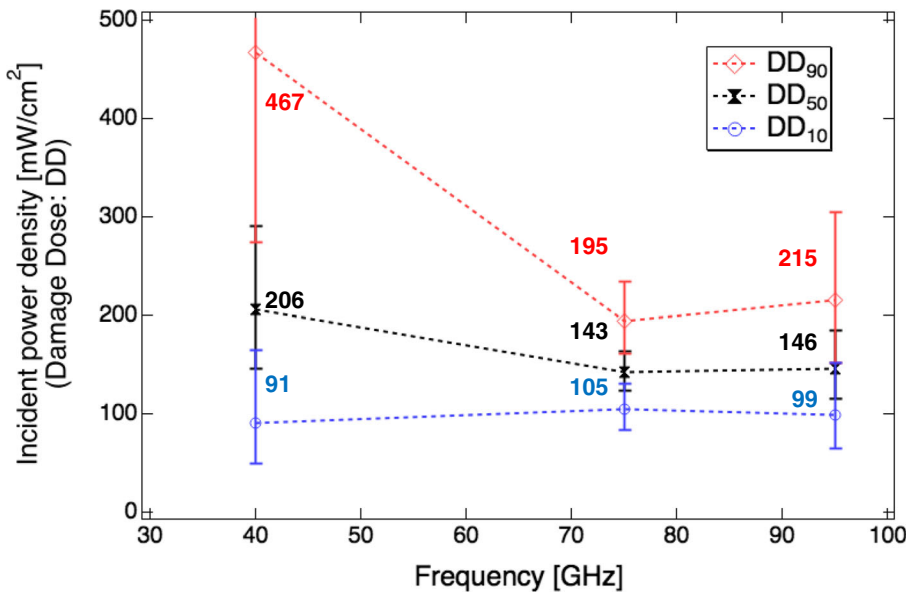


Fig. 5 DD 10% (DD₁₀), dose level to cause ocular damage with 10% probability, DD 50% (DD₅₀), dose level to cause ocular damage with 50% probability and DD 90% (DD₉₀) dose level to cause ocular damage with 90% probability estimated from results of MLE for exposure to 40, 75, and 95 GHz MMW. Error bars indicate 95% confidence intervals for each marker

damage, including damage to the corneal epithelium, corneal edema, and corneal opacity, resulting from exposure to high intensity MMW differed somewhat by frequency, but was generally similar.

Rosenthal et al. [4] classified corneal disorders caused by MMW exposure into “superficial and deep keratitis.” They also point out that surface keratitis will heal within 24 h and deep keratitis will be “persistent keratitis and leucoma (permanent scar in the stroma)” [4].

Heat generated by MMW energy is absorbed in the cornea, resulting in thermal damage of the cornea. The initial step of corneal disorder, occurring 10 min after exposure to MMW, included thinning of the cornea (corneal desiccation) due to thermal disturbance and partial dropout of corneal epithelial cells, as shown by diffuse staining with fluorescent dye. These findings seem to be surface keratitis described by Rosenthal et al. [4]. Corneal injury at 1 day after exposure was characterized by circular fluorescence staining, indicating a defect in the corneal epithelium, and confirmed by slit-lamp microscopy.

Damage to the corneal epithelium can be repaired by the proliferation [13] and migration [14] of cells in the basal layer. A study of a mechanically induced corneal epithelial disorder in rabbit eyes of diameter 6 mm, reported that this disorder was repaired within 48 h [15]. Similarly, we found that fluorescein staining disappeared about 2 days after MMW exposure.

Corneal edema seen after MMW exposure convexified to the corneal epithelium side, whereas corneal edema due to corneal endothelial damage protruded on the corneal endothelial side. Corneal edema or opacity is thought to be due to the entry of water into the corneal stroma from the site of the corneal epithelium defect caused by thermally induced cell death. Taken together, these findings indicate that this corneal disorder resulted primarily from corneal epithelial cell death induced by MMW exposure, whereas corneal edema and corneal opacity were secondary findings to corneal epithelial cell death. These are the reasons we used

corneal epithelial disorder in the present study to determine the end point of ocular disorder by MMW exposure.

4.2 Effects of Penetration Depth of MMW

We found that the degree of ocular disorder differed depending on the MMW frequency. This difference was likely due, at least in part, to differences in penetration depth. The corneal penetration depth of MMW by frequency difference was estimated by calculation [8] using measurements of dielectric properties [16]. These estimates found that the depths of corneal penetration in eyes exposed to 40, 75, and 95 GHz, were 0.57, 0.36, and 0.32 mm, respectively.

Normal rabbit corneal thickness is around 0.36–0.38 mm (OCT-measured data of Dutch rabbit). The corneal penetration depth of 75 and 95 GHz MMW was roughly comparable to the corneal thickness of these rabbits, but penetration of MMW at 40 GHz reached the anterior chamber whereas that of 75 and 95 GHz remained within the cornea of these rabbits. Sasaki et al. reported that the temperature of the rabbit cornea rises with increase in frequency in a simulation experiment using the same exposure equipment under the same exposure conditions [8] as the present experiment. One of the causes of the difference in penetration depth between 75 and 95 GHz in the simulation result of Sasaki et al. [8] and in the results of our animal experiments is considered to be the tear film. Sasaki's numerical model of the rabbit cornea was represented as homogeneous tissue since 90% of cornea is occupied by the stromal layer, and no tear film was considered. The tear film layer (thickness range, 1.9–5.1 μm) covering the surface of the cornea has roles such as maintaining eyeball moisture, lubrication in blinking, smoothing the corneal surface to maintain a clear view, and protection of the ocular surface [17]. The lipid layer constituting the tear film layer is very thin about 100 nm [18], but it acts as a "seal" to prevent evaporation of water from the ocular surface [17]. Although the tear film layer including the lipid layer is very thin, its importance is evident since its absence accompanied damage to the corneal surface (Fig. 3g) in the 30-min sham exposure experiment suppressing blinking of rabbits. Simulation experiments including a tear film layer in a cornea model are urgently needed.

Under conditions of much higher frequency exposure such as 95 GHz, heat absorbed by the cornea is not only transported into the inner part of the eye by aqueous humor convection, but effectively dissipated to the outside of the eye by transpiration. As described above, since the state of the tear film involves transpiration from the cornea, it is necessary to consider the state of the tear film and the transpiration of heat energy from the cornea. In addition, analysis of the transpiration of the heat to outside of the cornea is necessary to understand the heat transportation dynamics driven by higher frequency exposure, especially when penetration depth is less than corneal thickness.

4.3 Effects of Blinking

In this study, rabbits were prevented from blinking by fixing the eyelids with tape. Irradiation of the eyelids with MMW resulted in eyelid closure due to inflammation of eyelid skin, completely suppressing the effect of MMW exposure on the eye itself [7]. Moreover, the temperature on the corneal surface was increased for about 1 s by blinking, but gradually decreased thereafter, in normal physiological conditions [19]. In contrast, high frequency energy of 10–300 GHz was absorbed by the skin surface and the surface of the eyeballs

[20]. MMW-induced increase in corneal surface temperature to above body temperature may result in a blinking response to reduce corneal surface temperature.

Based on Japanese guidelines for time of exposure to radio waves [21], we set the average MMW exposure time at 6 min. Blinking intervals of rabbits have been reported to range widely, including 5.22 min [22], 6.3 min [23], 7 min [24], and 20 min [25]. Thus, eyelid retention for 6 min was unlikely to induce severe stress in rabbits. In contrast, blinking intervals of human eyes are much shorter, ranging from 3 to 10 s and including 3–4 s [26], 7.01 s [22], and 10 s [25]. Therefore, even if humans are exposed to the same MMW dose (such as 75 GHz 30 min exposure or sham+IR for 30 min exposure), humans are considered to be at less risk than rabbits.

4.4 Risks of Long-term Exposure

Ocular damage was more serious in rabbit eyes exposed to MMW for 30 min than for 6 min. Corneal surface temperatures during exposure to 75 GHz at 50 mW/cm² for 6 and 30 min were 37.6 ± 1.5 °C and 37.1 ± 0.8 °C, respectively. The mean corneal surface temperatures of normal and anesthetized Dutch rabbits have been found to be 34.67 ± 0.77 °C, (range, 32.07 to 37.00 °C) and 34.53 ± 1.08 °C (range, 30.19 to 36.71 °C) [27]. Because normal rabbit body temperature is 38.3 °C [28], the corneal surface temperature during MMW exposure to 75 GHz at 50 mW/cm² is comparable to body temperature. We sought to determine whether the corneal epithelial damage observed in rabbits exposed to 50 mW/cm² MMW for 30 min was due to MMW or to higher temperatures induced by exposure to a thermal source such as unintentional IR exposure. Because we did not observe any ocular disorder in unexposed control eyes during exposure to MMW for 30 min, we assessed the effects of sham exposure or exposure to very low intensity IR irradiation. We found no evidence of corneal epithelial damage after sham exposure for 30 min, although some eyes showed corneal desiccation. In contrast, corneal epithelial damage was induced by thermal exposure (IR exposure) around body temperature under conditions of corneal dryness, indicating that corneal disorders resulted from the increase in corneal surface temperature to about body temperature and were not unique to MMW (such as general hyperthermia). It is an important finding that corneal epithelial damage is induced by MMW exposure, accompanying very strong pain, although it is cured within 1–2 days after injury. Since humans blink more frequently than rabbits, exposure to these levels of MMW is unlikely to induce corneal epithelial damage in humans.

5 Conclusion

We created rabbit models of ocular disorder by exposure to 40, 75, and 95 GHz MMW. In assessing the relationship between the degree of ocular disorder and incident power density of these three frequencies, we found that ocular damage induced by exposure to 40, 75, and 95 GHz was essentially the same, with no characteristic specific to each frequency. We also found that corneal surface temperature during exposure was increased in the order 40 < 95 < 75 GHz, but there was no relationship between degree of ocular damage and eye surface temperature. In addition, we performed probit analyses by using experimental data and estimated probabilities for incidence of ocular damage depending on the power density. DD₅₀, defined as dose level to cause ocular damage with 50% probability, was in the order 40 GHz (206 mW/cm²) > 95 GHz (146 mW/cm²) ≈ 75 GHz (143 mW/cm²). At the same

incident power density, the degree of ocular damage was greater in the eyes exposed for 30 min than for 6 min. These findings suggested that damage to the corneal epithelium was not induced by corneal dryness alone, but by exposure of dried corneas to MMW-induced heat to above body temperature.

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Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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