IRE TRANSACTIONS ON MEDICAL ELECTRONICS

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# Opacities in the Lens of the Eye Experimentally Induced by Exposure to Microwave Radiation\*

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Summary-Lens opacities result from exposure of the rabbit eye to 2450-mc continuous wave radiation. Threshold for a single damaging exposure is determined by power density and duration. Opacities may also result as a cumulative effect of repeated subthreshold exposures. Intraocular temperature increases during irradiation, the extent and rate of increase being related to power density. Inasmuch as a particular temperature critical for opacity induction cannot be identified, it is suggested that the intraocular thermal response may be coincident with, rather than the cause of, induction of opacities. Lens damage may result from irradiation at power levels not sufficient to cause discomfort to nonanesthetized animals. Pulsed radiation with high peak intensities appears to be more potent in inducing lens opacities than continuous wave radiation of equal average power. Since ocular temperature is related to average rather than to peak power, these findings further suggest the possibility of a nonthermal biological effect of microwave radiation.

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## INTRODUCTION

PACITIES in the crystalline lens of the eye resulting from experimental exposure to microwave.... radiation were first reported in the dog [1]. Independently and in the same year, similar observations were made on the eye of the rabbit [2]. In both instances, the RF energy was emitted as continuous wave at a frequency of 2450 mc. These initial observations on the ocular effect of this frequency have since been confirmed for the dog eye [3] [4] and for the rabbit eye [5]-[10]. Also in the rabbit, lens opacities caused by exposure of the eye to continuous wave radiation at 3000 mc have been reported [11].

Similar effects have been described when pulsed instead of continuous wave radiation has been employed. Frequencies of 10,000 mc [12], 2800 mc [13], and 2450 mc [8], [10] have been used. All three pulsed frequencies caused cataracts in the irradiated eyes.

Negative results with respect to the effect of microwave radiation on the lens have also been reported. No damage was noted after exposure of the dog eye to 2450 mc con-

tinuous wave radiation for 20 minutes [14]. Dogs whose whole bodies were exposed to 2800 mc pulsed wave radiation for periods up to 6 hours did not develop cataracts, nor did rabbits after whole body irradiation for an hour [15]. Rabbits were subjected to repeated whole body continuous wave irradiation at a frequency of 468 mc and in doses which were near the lethal level, but no cataracts developed within the following 6 weeks. Employing continuous wave at a frequency of 200 mc, guinea pigs, dog and sheep were irradiated [17]. The whole body exposures ranged from 30 semiweekly one hour periods in the dog to 60 daily 2-hour periods in the guinea pig. In no case did a lens opacity develop.

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The pertinent data presented by these various investigators is summarized in Table I, from which the following general conclusions may be drawn:

a) Lens opacities (cataracts) have occurred in experimental animals following exposure of the eye to either continuous or pulsed wave radiation and at frequencies of 2450, 2800, 3000 and 10,000 mc. No ocular effects have been reported from exposures to the longer wavelengths of 400 and 200 mc radiation.

b) With but one exception, opacities resulted when the RF energy was directed particularly to the eye. In no case

did a lens opacity occur following experimental whole body irradiation.

c) If the attempt is made to relate ocular effects to power densities and duration of exposure, it appears either that there is no correlation between power density and the occurrence or nonoccurrence of cataracts or that the data on power densities are not valid for comparison. The latter conclusion is probably the more tenable one, for in some instances the figures refer to incident power and in others to absorbed power. In some cases, power levels were calculated or estimated. In others they were measured, but the measuring techniques differed widely.

Although not included in Table I, many of the reports [2], [4], [7], [8], [14], [18] presented data with respect to intraocular temperature changes induced by microwave irradiation. In all cases, there was an elevation of ocular temperature during irradiation, with increases ranging from 4° to 16°C recorded in the vitreous body directly behind the lens. These observations appear to substantiate the generally held view that the damaging effects of microwave radiation on biologic material are due entirely to the production of heat, the lens of the eye being particularly susceptible because of its location near the body surface and its inefficiency in heat dissipation, due chiefly to its lack of

Authors	Fre- quency	Power density	Conditions of Irradiation	Animal Subject	Ocular Effect
	.	(mw/cm²)	Eye: 5 minutes	Rabbit	Cataract
Richardson, Duane et al.	10,000	PW	-,	Rabbit	Cataract
Belova and Gordon	3000	110 CW	Eye: 60 minutes, 1 to 7 times; 10 minutes daily for 6 weeks		Negativ
Howland and Michaelson	2800	165 PW	Whole body: 40 minutes		Negativ
	2800	100 PW	Whole body: 60 minutes		Negativ
	2800	165 PW	Whole body: 2 hours		Negativ
	2800	100 PW	Whole body: 4-6 hours	L/OB	
	2800	200 PW	Eye: 60 minutes	Rabbit	Catarao
Biddle and Clark	1	2001 W	Eye: 15 minutes and 3 12 minutes every other day	Rabbit	Catara
Richardson, Duane et al.	2450	r Cw	-	Dog	Catara
	2450	? CW	Eye: 2 to 10 daily irradiations	Rabbit	Catara
Daily, Wakim et al.	24.50	> CW	Eye: 10-30 minutes per day	Rabbit	Cataro
	2430			Dog	Catara
Salisbury et al.	2450	3000 (?)	Eye: 10 minutes	Ŭ	NT
	0.00	2 CW	Eye: 20 minutes	Dog	Negati
Osborne and Frederick	2450	r cn		Rabbit	Catara
	2450	290 CW	Eve: 90 minutes	Rabbit	Catar
Williams et al.	24.50	590 CW	Eye: 5 minutes	Nation	Cutur
	2130				]
Carpenter, Biddle and				Rabbit	Catar
Van Ummersen	2450	400 CW	Eye: 31 minutes Eye: 1 hour daily ×15	Rabbit	Catar
	2450	80 CW	Eye: 1 hour	Rabbit	Catar
	2450	80 PW			
Cogan, Fricker et al.		60 CW	Whole body: 20 minutes daily ×10	Rabbit	Nega Nega
	468	60 CW	1 111 1. Ladar 30 minutes weekly X3 LO /	Rabbit	Nega
	468	60 CW	1 Whats body: 15 minutes semi-weekly AIV	Rabbit	Nega
	385	30 CW		Rabbit	Inega
	385	JUCH		Guinea pig	Nega
Osborne and Addington	200	480 CW	Whole body: daily; 1 hour ×74 exposures	Guinea pig	
	200	230 CW	I INLAL DODING TOURS AUT CADOSULO	Dog	Nega
	200	220 CW			Nega
	200	220 CW	Whole body: 1 nour semi-weekly xoo Whole body: 45 minutes 3 times per week for 32 hour total	Succh	1

TABLE 1 Ocular Effects of Microwave Energy

blood vessels. This general view has been well stated by Ely and Goldman [18]. After reviewing the reports of various investigators, a temperature of 45°C was suggested [19] as the threshold temperature beyond which damage may result in the human eye.

Several investigators [1], [2], [4], [5], [11] have reported cataracts induced by multiple exposures to microwave radiation, thereby raising the possibility of a cumulative effect of RF energy on the eye. Unfortunately, in no case was there evidence that a single one of the exposures was below the cataractogenic threshold dose and hence was not by itself sufficient to cause formation of an opacity. Indeed, only one group of authors [7] established time and power thresholds for the production of lens opacities, and this group did not subsequently investigate the effect of repeated subthreshold doses of radiation. Multiple exposures at the lower frequencies of 200 and 400 mc had no apparent effect. In the cases reported, the whole body was irradiated and the animals were free to move about or were continually rotated.

In summary then, microwave radiation at certain frequencies, either continuous or pulsed, causes a rise in intraocular temperature and the formation of opacities in the lens. Whether the former is the cause of the latter or the two are separate and coincidental effects has not been established. Neither has it been shown whether there is a difference between the effects of pulsed and of continuous wave radiation when the field intensities are equal. Nor is it known whether repeated episodes of microwave radiation can be cumulative in their effects upon the eye. It therefore seemed worthwhile to undertake a thorough study of these questions.

## Methods

We have used the rabbit, New Zealand White strain, as our experimental subject, chiefly because much previous work on the effects of radiated energy on the eye has been performed on this animal. In addition, the rabbit eye is approximately three-fourths the diameter of the human eye and rabbit body temperature is only 1.2°C higher than human body temperature. Anesthesia was by sodium Nembutal administered intravenously.

Our microwave power source, made by the Raytheon Company, operates at a frequency of 2450 megacycles, with a wave length of 12.2 cm. Based on the Raytheon Model CMD4 Microtherm, the instrument was modified for our requirements by the Raytheon Company so that its power can be emitted as continuous wave or pulsed wave. When pulsed, duty cycles can be varied from 0.5 per cent to 66 per cent. Pulse width can be varied between 50  $\mu$ sec and 2000  $\mu$ sec and the pulse repetition rate between 140 and 2200 per second. Essentially the same instrument is now available from the Raytheon Company as its power generator Model KV 104(NB)X2. The output is 85 watts.

A directional coupler in the coaxial cable to the antenna leads to a microwave power meter and permits monitoring of the power. The antenna is a Microtherm Director "C", a corner reflector type. Irradiations are carried out in an anechoic chamber,  $36 \times 34 \times 20$  inches, lined with microwave absorbent material. Only the head of the rabbit is exposed to the RF field, with the corneal surface of the right eye positioned opposite the dipole crossover of the antenna and 2 inches from the surface of the plastic housing covering it. Following irradiation, the eyes are examined regularly by ophthalmoscope and slit lamp microscope.

Power density measurements are made calorimetrically in the anechoic chamber, using a saline filled plastic sphere of known volume and profile area placed in the position of the rabbit eye. Measured thus, the maximal output of our generator gives a power density of 400 mw/cm<sup>2</sup> at the distance of the eye from the antenna. We are not satisfied that these are exact measurements. Indeed, we would hesitate to claim that they represent anything more than reproducible equivalents of absorbed power at the position of the eye. We are developing methods of instrumentation which we hope will provide more accurate measurements.

Temperatures within the eye during irradiation are measured by a thermistor-thermometer bridge and recorded on a strip-chart recorder. The shielded hypodermic needle thermistor probes are 22 or 24 gauge and can be inserted in the eye without damage to it or loss of vitreous.

### EXPERIMENTAL FINDINGS

## Time and Power Thresholds for Induction of Lens Opacities by Single Irradiation

A total of 136 rabbits were exposed to single doses of continuous wave radiation at various power levels and for different periods of time. The results are summarized in Fig. 1, in which each circle represents one or more experiments. The open circles represent exposures which did not effect the transparency of the lens. The blackened circles represent exposures which caused the formation of lens opacities identifiable by ophthalmoscopic or slit lamp examination of the eye. The lens of the left control eye remained clear.

The opacities were quite uniformly situated in the posterior subcapsular cortex of the lens and first appeared within 1 to 6 days after irradiation, the average latent period being  $3\frac{1}{2}$  days. The degree of opacification varied with the intensity and duration of the exposure, from clusters of granules or small vacuoles on or about the posterior suture to frank circumscribed or diffuse opacities involving extensive areas of the posterior cortex.

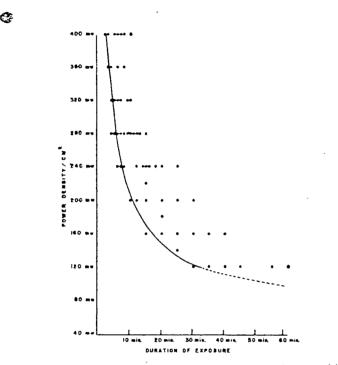
Certain ocular reactions were noted immediately after irradiation and likewise varied in degree according to the power and duration of the exposure. They included hyperemia of iris and limbal vessels, pupillary constriction, swelling and chemosis of bulbar and palpebral conjunctivae, and vitreous floaters and filaments. At power levels of 280 mw/cm<sup>2</sup> or less, these effects were usually transient and of minor severity.

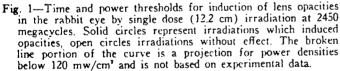
The threshold curve for cataractogenic exposures shown

in Fig. 1 gives the minimal exposure period at each power level which will cause a recognizable opacity to develop. It is similar in shape to that shown by Williams *et al.* [7] but our values are considerably lower. This may merely reflect the different techniques employed for measuring power density or it may be the result of differences in the manner of irradiation.

## Introocular Thermal Effects

Changes in intraocular temperature during irradiation were measured in 34 eyes and at 9 different power levels. A 22-gauge hypodermic needle probe was inserted in the eye of the anesthetized animal with its tip positioned in the





vitreous body directly behind the posterior pole of the lens but not in contact with the lens capsule. The temperatures recorded are shown in Fig. 2. The higher the power, the more rapidly does the temperature rise and the higher the level it reaches before it tends to flatten out.

## Cumulative Effects of Repeated Subthreshold Irradiation of the Eye

With the establishment of thresholds for induction of opacities by single exposures, we were in a position to test the effect of repeated exposures of duration less than the minimal required to cause an opacity. Fifty-one such experiments have been performed thus far. They are summarized in Table II.

We had found that at a power level of  $280 \text{ mw/cm}^2$  the minimal duration of an irradiation which would cause a lens opacity was 5 minutes. We therefore irradiated eyes for periods of only 4 minutes but repeated the exposure at

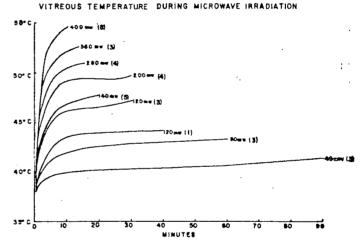


Fig. 2—Temperature changes in the vitreous body of the eye during irradiation at various power densities. Numbers in parentheses represent the number of experiments on which each curve is based.

TABLE II

CUMULATIVE EFFECT OF REPEATED SUBTHRESHOLD PERIODS OF EXPOSURE OF THE EYE TO MICROWAVE RADIATION (2450 MC.)

Power Threshold Density Period of (mw/cm <sup>1</sup> ) Exposure		Duration of	Tota	Effect in Number				
	Each Exposure - Period	i day	2 days	4 days	7 days	14 days	of Experiments	
280	5 minutes	4 minutes	4			2 or 3	3	Opacity (4 in 7) Opacity (3 in 7) Opacity (3 in 8)
280	5 minutes	3 minutes	5		3	. 5	,	Opacity (5 in 5) Opacity (5 in 5) Negative (5 in 5)
120	35 minutes	25 minutes	5	-				Opacity (5 in 5)
120	35 minutes	30 minutes		3				Opacity (4 in 4)
80	?	60 minutes	15	-				Opacity (3 in 3)
40	?	60 minutes	15	-				Negative (2 in 2)

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daily intervals for a total of 4 exposures. Of the 8 animals thus irradiated, 4 developed marked cataracts and 4 showed only slight effects. When 4-minute irradiations were carried out at weekly intervals in 7 animals, extensive cataracts developed in 2 cases after 2 exposures, minimal changes were noted in 3 lenses after 4 exposures, and in 2 cases there was no effect. When the interval between the 4minute exposures was increased to 2 weeks, opacities developed in 3 of the 8 cases after three exposures.

When the eye was irradiated for only 3 minutes, lens opacities developed after 5 such exposures given daily or after 3 exposures given at 4-day intervals. When the interval between exposures was increased to 1 week, then 5 successive weekly irradiations failed to have an effect on the lens.

These results suggest that the cataractogenic effect of microwave radiation involves initiation of a chain of events in the lens, the visible and end result of which is an opacity, and that this chain of events must be initiated by an adequate power density acting for a sufficient duration of time if it is to progress to the development of an opacity. If either the power density or the duration of the irradiation are below a certain threshold value, then the damage done to the lens is not irreparable and recovery can occur, provided sufficient time elapses before a subsequent similar episode. In the experiments described above, it appears that the interval necessary for recovery after damage done by a 3-minute exposure must be greater than 4 days but need not be longer than a week.

Inasmuch as it has been quite generally assumed that the biologic effect of RF radiation is solely the result of heat generated in the tissues, it is of interest to examine the intraocular temperature changes in these experiments. At the 280 mw/cm<sup>2</sup> power level, the shortest single exposure period which will cause a lens opacity is 5 minutes, at which time the temperature of the vitreous body at the posterior pole of the lens has reached 49.3°C. At the end of a 3-minute exposure period, however, this temperature is only 47.2°C. The 3-minute irradiation, if repeated at 4-day intervals, causes a lens opacity to develop, but if it is repeated only at weekly intervals, then there is no effect. One may therefore attribute cataracts to the thermal effect of microwave radiation only by assuming that the lower temperature associated with a subthreshold exposure may be cataractogenic if it occurs with sufficient frequency.

A cumulative thermal effect becomes even less probable in the light of certain other experiments cited in Table II. The minimal single period of irradiation necessary to induce lens opacities at 120 mw/cm<sup>2</sup> is 35 minutes. We therefore irradiated eyes at this power level for a period of 25 minutes each day for 5 successive days and for 3 periods of 30 minutes every other day. Lens opacities developed in every one of 9 cases.

In a rabbit under sodium Nembutal anesthesia, the vitreous temperature at the end of 30 minutes of irradiation at this power level is 44°C., approximately 5 degrees above normal body temperature. This amount of temperature elevation in the eye appears not sufficient even to cause discomfort to the animal, for irradiation at this power level can be performed without anesthesia, and the animals seem content to sit quietly before the antenna.

With the power reduced to  $80 \text{ mw/cm}^2$ , we irradiated eyes for an hour daily for 15 consecutive days. In 3 cases so far completed, frank opacities developed in each case. We have not yet been able to determine how long a single exposure period must be to induce an opacity at this power level but we do know that a single 1-hour exposure is not adequate. We suspect that a cumulative effect may result from fewer than 15 daily exposures but we have yet to establish what the minimal effective number is. It may be significant that in 2 eyes, scattered small punctate opacities first appeared in the vicinity of the suture after 10 irradiations and that development of the opacity progressed steadily in the ensuing 5 days.

In an anesthetized animal, 1 hour of irradiation at this power level raises the temperature of the vitreous body to 42.8°C, only 4 degrees above body temperature. If the cataracts formed under such conditions constitute a thermal effect of the radiation, then it must be a thermal effect which depends upon neither a critical temperature nor even a very appreciable elevation of temperature in the eye.

## Pulsed Wave Irradiation of the Eye

When the emitted power is pulsed, the eye can be exposed to rapidly repeated peaks of relatively high energy while the average power remains low during the irradiation period. Inasmuch as thermal flux is related to average power, it thus becomes possible to subject the eye at one and the same time to high peak power and low thermal flux. The effect can then be compared with effects of a) continuous wave irradiation of equal duration and of intensity equal to the average power of the pulsed wave radiation, and b) continuous wave irradiation of intensity equal to the peak power and duration equal to the ON time of the pulsed wave irradiation. With our equipment, the same magnetron tube supplies the power for all three conditions of irradiation.

In the initial experiments employing pulsed microwave, the right eyes of 18 animals were irradiated for 20 minutes each at an average power density of 140 mw/cm<sup>2</sup>, with a 50 per cent duty cycle affording peak power of 280 mw/ cm<sup>3</sup>. In terms of peak power, this is the equivalent of 10 minutes of continuous wave radiation at 280 mw/cm<sup>8</sup> power density, which is well above the threshold dose for cataract induction. In terms of thermal flux, it is the equivalent of continuous wave irradiation at a power density of 140 mw/cm<sup>2</sup> for 20 minutes, which is 5 minutes less than the minimal time required to cause development of a lens opacity.

The experiments did not yield clear-cut results in the sense that they were uniformly negative or that lens opacities developed in every instance. Opacities were formed

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in 10 of the 18 experiments; 4 of them were classified as minimal cataracts and 6 as extensive. With a 25 per cent duty cycle, so that the peak power was 560 mw/cm<sup>2</sup>, cataracts resulted in 2 of 4 experiments. We did not note any effect from varying the pulse width and the pulse repetition  $\nu$ rate within the same duty cycle.

Similar results occurred when 15 more animals were irradiated, with the average power densities ranging from 120 mw/cm<sup>2</sup> down to 40 mw/cm<sup>2</sup> and with accompanying peak powers of 400 mw/cm<sup>2</sup> up to 800 mw/cm<sup>2</sup>. Cataracts developed in 8 of the 15 eyes.

In more than half of the 37 experiments with pulsed wave radiation then, lens opacities resulted from exposure periods of significantly shorter duration than those required for induction of opacities by continuous wave radiation of used in the comparison, it may also be noted that with pulsed wave radiation, the vitreous temperature did not rise as high as it did during
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When eyes were subjected to pulsed wave radiation having an average power density of 80 mw/cm<sup>2</sup> and peak power of 400 mw/cm<sup>2</sup>, an irradiation period of 45 minutes was ineffective. After 60 minutes of such irradiation, however, cataracts developed in each of 4 experiments. At the end of a 60-minute irradiation period, the temperature of the vitreous body in an anesthetized animal was 42.8°C, a rise of only 4 degrees above normal body temperature. The same temperature was likewise reached after 60 minutes of continuous wave irradiation at the same power density, but in no case did this intraocular temperature cause development of a cataract. Indeed, it has already been noted here unat unis dose of continuous wave radiation must be re- [13] D. K. Biddle and L. A. Clark, Jr., unpublished data. peated daily for at least 10 days to cause cataract develop-  $\psi$  [14] S. L. Osborne and J. N. Frederick, "Microwave r ment.

These experiments lead us to question whether the cataractogenic effect of microwave radiation is entirely a  $\mu$ thermal effect. We also feel that consideration should be given to the role of peak power as a possible factor in the induction of lens opacities when the eye is subjected to pulsed microwave radiation. We are pursuing this particular question further. Its possible significance relative to the established RF radiation hazard level of 0.01-watts/cm.<sup>2</sup> average power density is apparent.

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