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A STUDY OF THE PRODUCTION OF CHORIORETINAL LESIONS BY THERMAL RADIATION

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FOREWORD

This investigation was accomplished by personnel of the Life Sciences Division of Technology, Inc., San Antonio, Tex., under contract No. AF 41(609)-2906, task No. 630103 and program element 6.16.46.01.D, project 5710, subtask 03.003, and was partially funded by the Defense Atomic Support Agency, during the period 15 October 1965 to 15 March 1966. The paper was submitted for publication on 28 September 1966.

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The experiments reported herein were conducted according to the "Principles of Laboratory Animal Care" established by the National Society for Medical Research.

This report has been reviewed and is approved.

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ABSTRACT

Chorioretinal burns have been systematically produced in pigmented rabbits unde carefully controlled laboratory conditions. Lesions were produced by high-intensit light flashes ranging in duration from 165 μsec. to 250 msec. and with image diameter which ranged from 1.0 to 0.11 mm. From these measurements, relationships were obtained between exposure duration and threshold irradiance for the production of "5-minute" minimal lesions.

A STUDY OF THE PRODUCTION OF CHORIORETINAL LESIONS BY THERMAL RADIATION

I. INTRODUCTION

The production of chorioretinal burns has been of interest for a number of years, particularly since the advent of nuclear weapons. The problem is so involved that it has not yet yielded to a theoretic approach. Progress has been made in this direction, but the prediction of chorioretinal burns still depends primarily on threshold data collected in the laboratory by using rabbits as subjects. In view of the importance of laboratory threshold data to the prediction problem, it was imperative that more complete and extensive data be obtained. Acquisition of more reliable and complete threshold data was the objective of this study.

Threshold data were obtained on the production of 5-minute minimal retinal lesions in rabbits for image sizes of 1.0, 0.54, 0.27, 0.20, and 0.11 mm. with exposure times ranging from 165 μsec. to 250 msec. Thermal energy, primarily in the visible, was generated with a Meyer-Schwickerath photo coagulator, which had been modified for pulsed operation under a previous contract (1, 2).

The criteria used to define a 5-minute minimal retinal lesion were as follows: (1) appearance of an area of disturbance with a grey or whitish center within 5 minutes after the end of exposure; and (2) nonappearance of a similar lesion within 5 minutes at an irradiance approximately 5% to 10% lower.

The irradiance level associated with the production of a minimal lesion was arbitrarily taken as the average of the lowest irradiance that produced a lesion as described, and the highest value of irradiance that would not produce such a lesion—where the difference between the two levels was required to be less than 10% of the value of the higher irradiance.

II. EQUIPMENT

The basic instrument used in this study was a Meyer-Schwickerath light coagulator manufactured by the Carl Zeiss Company. For the purpose of studying chorioretinal burns, this machine was modified as follows: (a) A Keeler ophthalmoscope with a pop-up mirror replaced the standard pinhole-mirror; (b) a KG-3 phosphate glass filter was added to the optical system to reduce the infrared energy in the beam; (c) one of the beam-size apertures was changed from 0.8 mm. (4.5° light cone) to 0.2 mm. (1° light cone); (d) the maximum opening of the iris was increased in order to obtain a 200-to-1 intensity control of the beam in 72 graded steps; (e) the lamp holder was modified to permit use of an Osram 2,500-w. xenon lamp; and (f) an auxiliary light control unit was added for accurate and automatic control of the length of the light pulse. Figure 1 shows the modified machine with its auxiliary equipment, and figure 2 shows the optical system in schematic.

Light pulses of specified durations were obtained by controlling the power applied to the lamp. To accomplish this, a solid-state switch was used to connect the xenon lamp to a source of power, either a set of aircraft batteries or a capacitor bank. With the batteries, pulses could be obtained with durations of

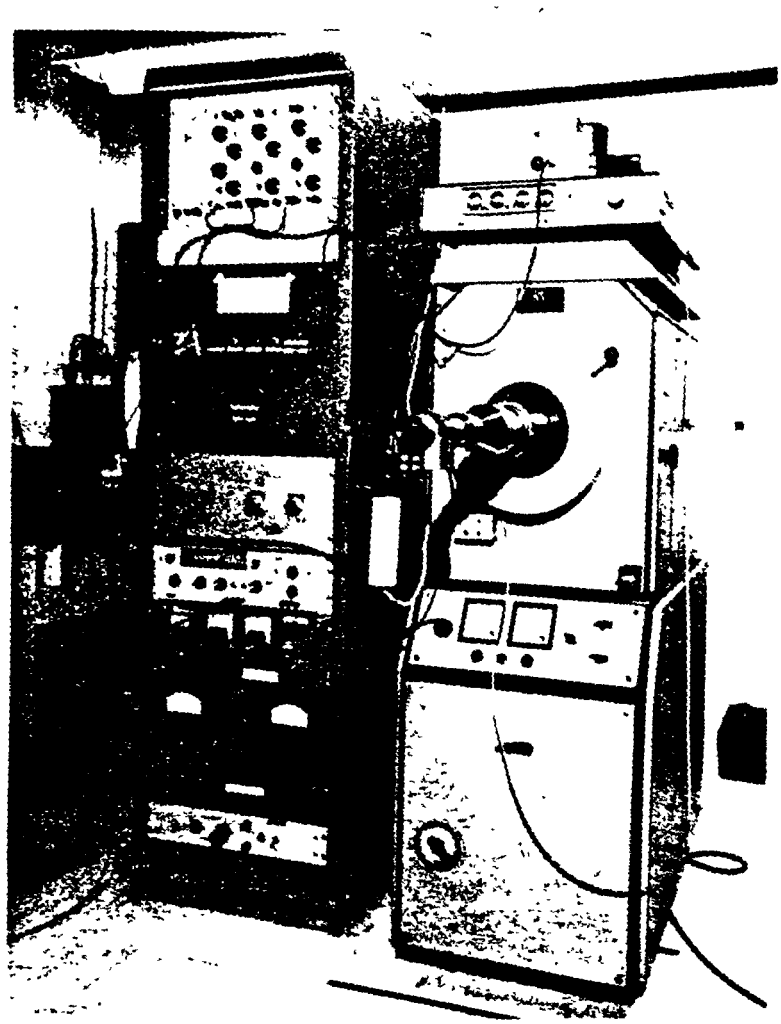

FIGURE 1

Modified Zeiss photo coagulator with auxiliary equipment.

2 msec. to 10 sec. For shorter pulses, 165 μsec. to 1 msec., the capacitor bank was used in place of the batteries. Current through the lamp was approximately 200 a. for battery operation and 2,000 a. for capacitor operation.

Measurements of the total irradiance and the spectral irradiance were made. Total irradiance measurements were made with a calibrated Eppley thermopile. Spectral measurements were made, in 10 mμ bandwidths, using a Jarrell-Ash Ebert monochromator and a National Bureau of Standards calibrated 1,000-w. lamp (3). The measured spectral distributions are shown in figures 3 and 4 with total energy, between 400 and 1,100 mμ, normalized to the energy radiated by a 5,800° black body in the same wavelength region.

The results of the integrated intensity measurements agreed with the values obtained from integration of the spectral distributions within 5%. It is seen from these figures that the spectrum shifts toward shorter wavelengths at higher currents and that the spectrum without the KG-3 filter may be considered as a rough approximation of the spectrum of a 5,800° black body.

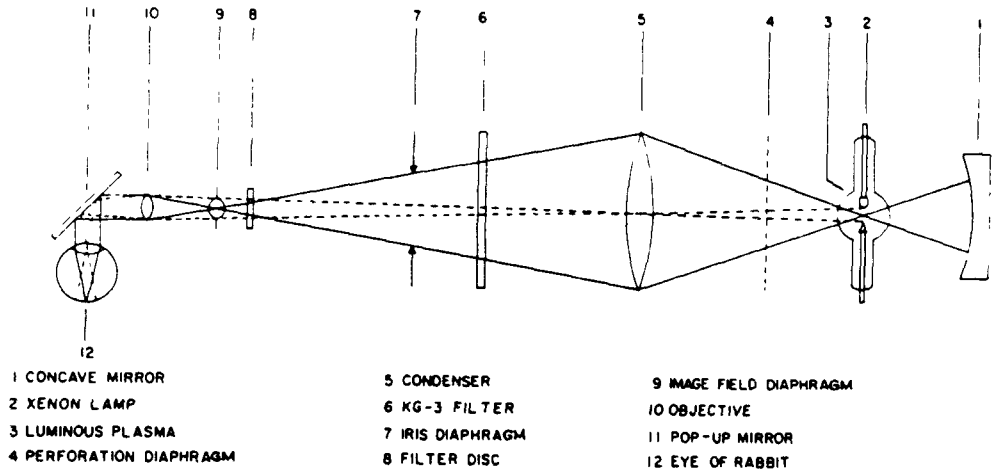

FIGURE 2
Optical beam director.

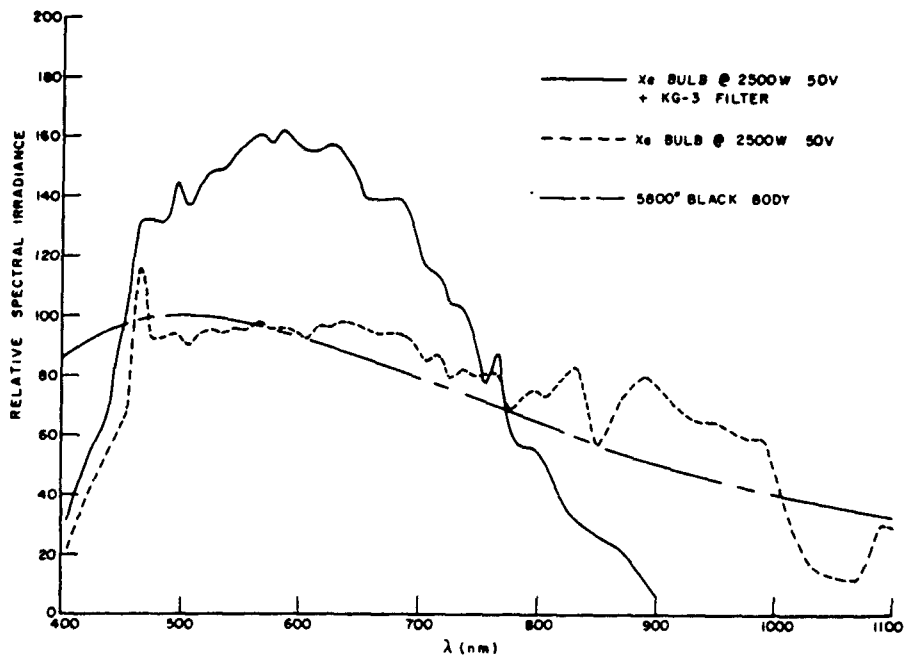

FIGURE 3
Spectral distributions of Xe bulb at 50 v. with and without KG-3 filter.

III. EXPERIMENTAL PROCEDURES

Air Force eye specialists established a baseline for all rabbits, and only rabbits with medium homogeneous pigmentation of the fundus and uniform unclouded clear media were used.

In preparation for exposure, hair was shaved from around the eyes of the animals; the animals were tranquilized with 2 cc. of Demerol, I.M.; and their pupils were dilated with 1% cyclopentolate hydrochloride ophthalmic solution. After a pre-exposure examination with an AO giantscope, the animal was

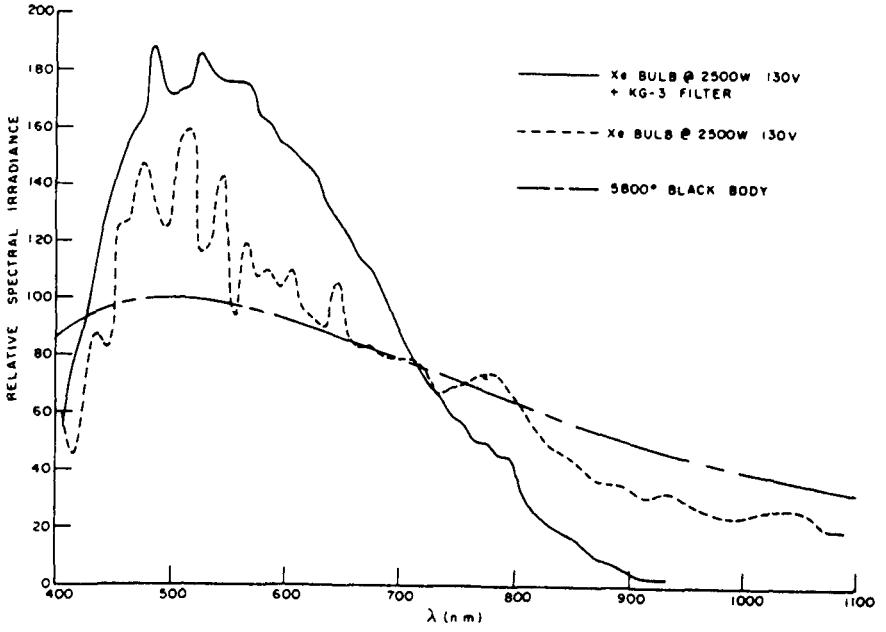

FIGURE 4

Spectral distributions of Xe bulb at 130 v. with and without KG-3 filter.

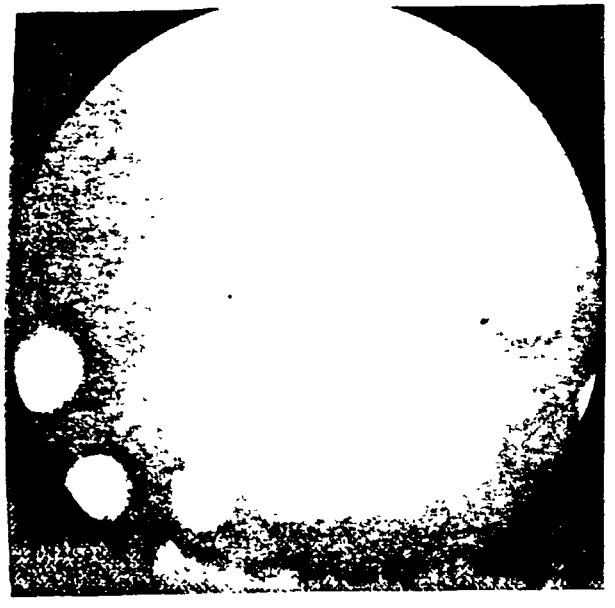

FIGURE 5

Fundus photograph of burns placed in horizontal row.

positioned in front of the photo coagulator shown in figure 1.

In making exposures, a marker burn was first placed on the fundus using an irradiance approximately twice that expected to produce a minimal burn for the particular image size concerned. This burn was placed in the central region of the fundus, about 5 mm. below the medullated nerve fibers, and served as a reference for subsequent exposures. The flash duration desired for the first test exposure was then set into the electronic pulse control unit; an irradiance level was selected that would produce a burn; and an exposure was made at a position located with respect to the marker burn. Immediately following exposure, the fundus was examined with the AO giantscope or the Keeler ophthalmoscope attached to the beam director. After determining that a burn had been produced, the rabbit's head was turned slightly to bring an adjacent area of the fundus into view; the iris diaphragm was reset to decrease the irradiance; and another exposure was made. This process was continued, with exposures placed in a horizontal row, until the irradiance level for the production of a 5-minute minimal burn was identified (fig. 5). This procedure was repeated for

different exposure durations, different image sizes, and different subjects, until approximately ten (or more) values were obtained at each of the combinations of image size and exposure duration selected for investigation. Ordinarily, a sufficient number of exposures could be placed in a single eye to establish several points on a curve of threshold irradiance versus time; however, the number of exposures actually placed in one eye depended on the image size.

The procedure of placing exposures in a horizontal row was adopted after inconsistencies were observed in the results obtained from placing exposures in a circle around the marker burn. The rather large variations observed in circling the marker burn were attributed to variations in the distribution of pigment. It was found that the irradiance required to produce a minimal burn at the 12 o'clock position was generally about 50% higher than that required to produce a minimal burn at the 6 o'clock position (a position farther from the medullated fibers). Variations in the horizontal direction were found to be much smaller. The dependence of threshold irradiance on retinal position was taken into account (averaged) by establishing threshold irradiances with exposures placed in horizontal rows and by systematically varying the positions of rows in the subjects.

IV. RESULTS AND DISCUSSION

Values of individual threshold irradiances for various image sizes are given in tables I through V. Average threshold irradiance, $\overline{H}_r$, standard deviation, and average retinal exposure, $\overline{Q}_r$, are also given. These results are summarized in table VI.

Figure 6 presents the average measured threshold irradiances along curves of "best fit" obtained through consideration of the entire set of data. To obtain these "best fit" curves, average values of threshold irradiance were graphed versus burn diameter for a fixed value of the exposure time. Smooth curves were fitted to these points by eye. Values of $\overline{H}_r$ corresponding to the exposure times actually employed were then taken from these curves and used to determine the curves which best fit the equation

$$\overline{H}_r = At^B + C$$

where A, B, and C are constants and t is expressed in seconds. The constants were determined for each curve by a machine program using Newton's iterative process and are given in table VII. From figure 6 it is seen that the burn data can be approximated reasonably well by equations of this form for times greater than approximately 100 μsec. The method used to generate these expressions rules out their use for times less than about 100 μsec. On the other hand, it is believed that some credence can be attached to values computed for relatively long exposures—e.g., exposures longer than 1 sec. In this scheme, the value for C has special significance in that it represents the lowest value of $\overline{H}_r$ that is capable of producing a burn for a given image size, regardless of exposure duration.

Figure 7 presents values of $\overline{Q}_r$ as a function of exposure time since it has been found that in many instances this presentation facilitates the solution of prediction problems.

It is known that a 5-minute minimal lesion does not represent the threshold of permanent injury since visible lesions have been observed to develop several hours after exposure and result from exposures at significantly lower irradiances. This situation is under investigation, and efforts are being made to relate the production of these late developing lesions to the production of 5-minute minimal lesions.

TABLE I

*Retinal irradiance ($\overline{H}_r$) for production of 5-minute minimal burns in rabbits**
(1.0 mm. image diameter—6° light cone from Zeiss coagulator)

Rabbit No.	Exposure time (msec.)						
	250	100	40	10	1	0.4	0.165
	(cal./cm.²-sec.)						
G-79	4.80		10.5		242		
Q-15	5.00	7.73			211		
N-03	5.40	9.88			211		
L-78	6.11	8.45			176		
Q-21	5.32	8.99		41.7		328	
Q-39	4.38	7.40		32.6		302	1,010
Q-43	5.78	9.52		33.6		324	590
S-96	5.27	8.66		36.5		374	
T-16	5.37	8.81	15.4	39.6		367	
T-18	4.76	8.05		37.7		287	797
Av. $\overline{H}_r$	5.22	8.61	13.0	37.0	210	330	799
S.D. for $\overline{H}_r$	.51	.81	3.47	3.48	26.9	34.6	210
Av. $\overline{Q}_r$	1.31	.86	.52	.37	.21	.13	.13

*Using Xe arc light source filtered with a 1.5 mm. KG-3 (phosphate glass) filter.

TABLE II

*Retinal irradiance ($\overline{H}_r$) for production of 5-minute minimal burns in rabbits**
(0.54 mm. image diameter—1.5° light cone)

Rabbit No.	Exposure time (msec.)						
	250	100	40	10	1	0.4	0.165
	(cal./cm.²-sec.)						
G-79	8.43		15.8		306		
P-97	5.78	5.78	12.0	27.9	179	482	
Q-15	7.73	10.6		52.9	220		
N-03	7.16	12.2			219		
L-78	9.70	12.4					
Q-21	7.60	10.5		49.6		454	
Q-39	6.25	8.66					869
Q-43	8.12	12.0		47.3		380	760
S-96	7.40	10.9		57.0		483	
T-16	6.36	9.97	19.6	58.0		506	
T-18	8.05	11.9		58.9		313	
Av. $\overline{H}_r$	7.51	10.5	15.8	50.2	231	436	815
S.D. for $\overline{H}_r$	1.11	2.02	3.8	10.8	46.4	74.6	77.1
Av. $\overline{Q}_r$	1.88	1.05	.63	.50	.23	.17	.13

*Using Xe arc light source filtered with a 1.5 mm. KG-3 (phosphate glass) filter.

TABLE III

*Retinal irradiance ($\overline{H}_r$) for production of 5-minute minimal burns in rabbits**
(0.27 mm. image diameter—1.5° light cone)

Rabbit No.	Exposure time (msec.)						
	250	100	40	10	1	0.4	0.165
	(cal./cm.²-sec.)						
G-79	12.1	18.2	28.9	70.8	357	979	
G-79	13.9				363		
P-97	6.9	9.5	18.2	41.7	190	564	
Q-15	16.7	21.4			220		
N-03	22.0	29.0	54.8		534		
Q-21	15.0	16.6		55.6		429	792
Q-39	13.7	16.2	25.4	46.9		292	603
Q-43	18.2	23.1	27.5	41.8		502	
Q-43		21.8					
S-96	20.2	26.8	30.0	63.2		376	
T-16	21.5	24.6	34.1	71.9		473	
T-18	16.9	19.8	25.1	44.1		268	603
K-37		22.8				520	
M-10	21.3		30.6	63.2		537	
Q-23			36.0	76.1		593	952
Q-27	22.7	24.7					
Q-17		29.2	39.3	55.7			
Q-47		31.0					
Q-51		37.8					
Av. $\overline{H}_r$	17.0	23.3	31.9	57.4	333	503	738
S.D. for $\overline{H}_r$	4.65	6.74	9.54	12.6	137	190.3	168.5
Av. $\overline{Q}_r$	4.25	2.33	1.28	.57	.33	.20	.12

*Using Xe arc light source filtered with a 1.5 mm. KG-3 (phosphate glass) filter.

TABLE IV

*Retinal irradiance ($\overline{H}_r$) for production of 5-minute minimal burns in rabbits**
(0.20 mm. image diameter—1.0° light cone)

Rabbit No.	Exposure time (msec.)						
	250	100	40	10	1	0.4	0.165
	(cal./cm.²-sec.)						
G-79	31.4		41.0		697		
P-97	15.0	18.2	25.5	70.0	211		
Q-15	65.0	49.0			239		
Q-21	23.5	30.3		74.3		808	
Q-21						676	
Q-39	25.4	28.5	39.1	64.8		365	670
Q-43	21.8	27.5	30.9	48.4		584	
S-96	30.0	33.6	45.4	99.7		820	
T-16	27.4	34.1	41.4	91.7		753	
T-18	22.4	22.4	31.2	79.1		831	1,090
Av. $\overline{H}_r$	29.1	30.5	36.4	75.4	382	691	880
S.D. for $\overline{H}_r$	13.5	9.22	7.19	17.0	273	169	297
Av. $\overline{Q}_r$	7.28	3.05	1.46	.75	.38	.28	.15

*Using Xe arc light source filtered with a 1.5 mm. KG-3 (phosphate glass) filter.

TABLE V

*Retinal irradiance ($\bar{H}_r$) for production of 5-minute minimal burns in rabbits**
(0.11 mm. image diameter—0.5° light cone)

Rabbit No.	Exposure time (msec.)							
	250	100	40	10	4	1	0.4	0.165
	(cal./cm.²-sec.)							
G-79	65.2		102					
P-97	69.9	80.2	75.7					
P-97			130					
Q-21	103	150		181				
Q-21	54.6	76.0						
Q-39	69.1	74.1	89.0	177			1,160	
Q-43	58.3	67.5	87.0	173			1,150	
S-96	83.6	94.3	190					
T-16	91.7	108	155					
T-18	79.1	109	216	376				
Q-93		117	131	230	431	726		
Q-93		89.0	119	222	447	619	1,010	
R-03	59.1	89.6	117	230	411	740	1,110	
R-03	50.1	63.4	84.8	209	423	490	883	1,030
R-17	62.5	82.3	105	217	472	586	985	1,150
R-17	77.9	92.7	142	275	438	690	1,240	1,330
R-31	126	149	201	343		666	1,110	1,240
R-31	97.5						1,280	1,280
W-007								1,610
W-007	116							1,610
Av. $\bar{H}_r$	79.0	96.1	130	239	437	685	1,100	1,320
S.D. for $\bar{H}_r$	22.48	26.42	43.94	66.54	21.14	138.1	125.8	219.6
Av. $\bar{Q}_r$	19.8	9.61	5.20	2.39	1.75	.685	.440	.191

*Using Xe arc light source filtered with a 1.5 mm. KG-3 (phosphate glass) filter.

TABLE VI

Average retinal irradiance ($\bar{H}_r$) for production of 5-minute minimal burns in rabbits

Image diameter (mm.)	Exposure time (msec.)						
	0.165	0.4	1	10	40	100	250
	(cal./cm.²-sec.)						
1.0	799 (3)*	330 (6)	210 (4)	37.0 (6)	13.0 (2)	8.61 (9)	5.22 (10)
0.54	815 (2)	436 (7)	231 (5)	50.2 (7)	15.8 (3)	10.5 (9)	7.51 (10)
0.27	738 (3)	503 (8)	333 (5)	57.4 (8)	31.9 (8)	23.3 (11)	17.1 (11)
0.20	880 (2)	691 (7)	382 (3)	75.4 (7)	36.4 (7)	30.5 (8)	29.1 (9)
0.11	1,320 (7)	1,100 (9)	685 (7)	239 (11)	130 (15)	96.1 (15)	79.0 (16)

*The numbers in parentheses give the number of animals used in obtaining the average retinal irradiance listed.

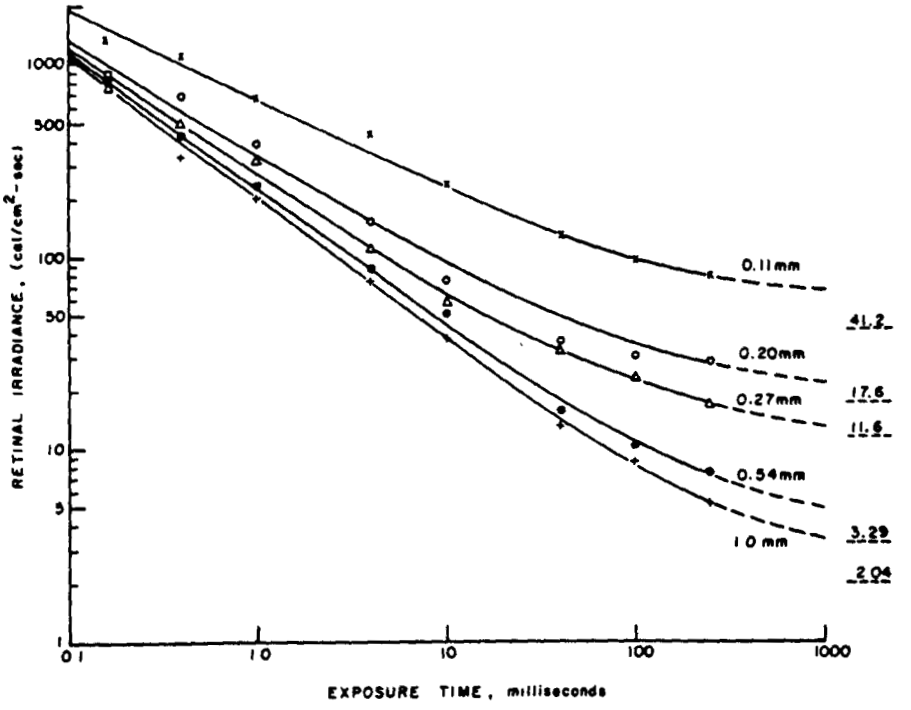

FIGURE 6

Average threshold irradiance ($\overline{H}_r$) versus time for five image sizes. Figures at right represent asymptotic values (C in equation under "Results and Discussion").

TABLE VII

Calculated constants for the equations for threshold retinal irradiance vs. time

Burn size (mm.)	A (cal./cm.^{2}-sec.$^{B+1}$)	B	C (cal./cm.^{2}-sec.)
0.11	17.5	−0.511	41.18
0.20	4.17	−0.626	17.60
0.27	2.28	−0.683	11.62
0.54	1.41	−0.730	3:29
1.00	1.11	−0.750	2.04

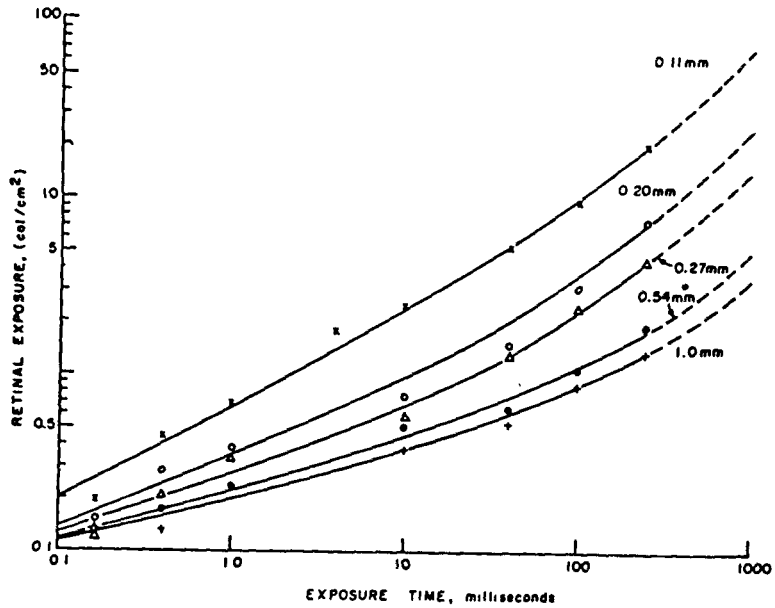

FIGURE 7

$\overline{Q}_r$ versus time for five image sizes.

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3. Bessey, R. L., and R. G. Allen, Jr. Calibration of Zeiss photo coagulator. Technical report, Technology, Inc., San Antonio, Tex., July 1966.

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13 ABSTRACT

Chorioretinal burns have been systematically produced in pigmented rabbits under carefully controlled laboratory conditions. Lesions were produced by high-intensity light flashes ranging in duration from 165 μsec. to 250 msec. and with image diameters which ranged from 1.0 to 0.11 mm. From these measurements, relationships were obtained between exposure duration and threshold irradiance for the production of "5-minute" minimal lesions.

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