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Ocular Effects of Laser Radiation

Part I

from the

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Introduction:

Although this paper is confined primarily to the biological effects of laser radiation on the mammalian retina the results should be applicable to other organs and other tissues. The physiological implications for the eye of laser beams have been discussed by Solon (1), (2); the production of ocular lesions by ruby lasers has been described by Zaret (3), (4), and, more recently, by Ham (5) and Geeraets (6). For convenience, retinal lesions produced by lasers will be discussed under 3 separate types of operation, steady state operation, normal pulsed operation, and Q-switched operation. Before proceeding to a detailed discussion of laser effects, it will be helpful to summarize some of the data about retinal damage as produced by more conventional sources in order to provide a background which can be extended to high power densities and short exposure times.

Background Information:

Previous researches from these laboratories on the production of mild or minimal lesions to the retina by means of relatively short time exposures to white light sources (nuclear fireballs, high density carbon arc, xenon arc under continuous and pulsed operation) provide a wealth of data which are applicable to the assessment

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of ocular hazards from laser radiation. For example, Ham et al. [7] have discussed the effects of pulse shape, exposure time, dose rate, radiation dose, and image size on the production of minimal lesions in the rabbit retina. Other experiments have furnished data on transmission and scattering in the ocular media [8], the absorption and scattering of light in the retina and choroid [9], [10], the effect of blood flow in the choroid on the conduction of heat [11], the pathological and histological characteristics of mild retinal lesions [12], the effects of thermal conduction on enzyme activity [12], [13], and the effects of thermal injury on retinal proteins [14]. Most of these data insofar as applicable to laser radiation are summarized in a publication [15], which also discusses the effect of spectral quality on retinal damage and describes an optical system whereby laser exposures of known size can be placed on the retina.

Pertinent data on power density, exposure time and image size for the production of extremely mild lesions in the rabbit retina are illustrated in Figure I, a log-log plot of power density in watts/cm^2 vs exposure time in seconds. The curve of best fit by regression analysis for all available data from several hundred milliseconds down to 175 microseconds for a single image diameter of 0.8 mm is the straight line shown in Figure I. Most of the data for exposure times greater than 15 milliseconds (ms) come from early experiments on rabbits, utilizing a high density carbon arc as a source [7]. The maximum power density obtainable on the rabbit retina with this source was approximately 300 watts/cm^2. For exposure times less than 15 ms or for image sizes 0.2 mm or less in diameter it was not possible at this power density to produce an observable lesion on the rabbit retina. Exposure times in the range 15 ms down to 175 microseconds (μs) were obtained subsequently either by using a Zeiss light coagulator [16] operating under steady state conditions or by means of an electronically pulsed xenon source [17]. Exposure times for laser pulses from ruby under normal pumping conditions range from

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approximately 1 ms down to 200 μs, thus overlapping the data obtained from white light sources at the short exposure times. To the best of the authors' knowledge, no data for mild lesions in the rabbit retina are available between approximately 200 μs and the nanosecond (ns) region which corresponds to laser pulses produced by Q-switching techniques. This region (200 μs to 25 ns) is being investigated currently by the authors, using a Kerr cell as an optical shutter.

An examination of Figure I reveals some interesting features. Since the slope of the log-log plot of power density, ϕ, vs exposure time, t, is less than 45° (it is 33.2°) reciprocity is not indicated for this particular biological endpoint, namely mild injury to the rabbit retina. Stating it another way, halving the exposure time does not double the power density required to produce a typically mild lesion. On the contrary, the power density increases by less than the reciprocal of the exposure time, thus defining a radiation dose, $D = \phi t$, which decreases with a decrease in exposure time. These data indicate no appreciable change in slope over an extensive range of exposure times, from several hundred milliseconds down to 175 microseconds. Another feature is that radiation dose depends to some extent on image size for the longer exposure times. This is illustrated in Figure I by plotting some of the data points for image diameters of 1.0 mm (circles) and 0.52 mm (crosses) at the longer exposure times. For short exposures below 1 ms the data do not indicate an appreciable relationship between image size and radiation dose. More interesting is the observation that mild lesions produced by laser pulses (200 μs) require approximately the same radiation dose (0.85 J/cm^2) as those produced by the more conventional white light sources. Finally, the dotted portion of the curve represents an extrapolation to the nanosecond region where some data obtained recently for Q-switched pulses from ruby lasers have been plotted. The fact that these data points for Q-switched pulses seem to fall near the extrapolated portion of the curve is not regarded as significant by the authors since in what follows it will be seen that both the physical phenomena

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accompanying Q-switched pulses and the nature of the lesions produced in the retina by these pulses differ from those produced at lower power densities and longer exposure times.

Experimental Apparatus:

The optical system used to produce lesions of known size on the rabbit retina by means of laser pulses has been described in a previous publication [15]. A block diagram of the apparatus with associated electronic equipment is given in Figure II. The complete optical system, including laser head is mounted rigidly on a maneuverable optical bench which has 5 degrees of freedom (3 of translation and 2 of rotation), thus providing the ophthalmologist with a flexible system for the production of lesions on the retina. A Keeler ophthalmoscope ("Practitioner") is attached to the exposure end of the optical system. This instrument has been modified by the insertion of a reticle which is projected on the retina. The instrument is mounted in such a manner that the projected reticle is always coaxial with the laser beam.

The laser head contains a ruby cylinder*, 3" x 1/4", with ground outside diameter, the faces optically flat and parallel but uncoated, optic axis cut at 90° to cylinder axis. Pumping is accomplished by 8 EG&G FX-100 lamps, connected separately into 2 sets of 4 lamps in series, each set being discharged separately but simultaneously by a high voltage trigger. The lamps are spaced at 45° around the ruby, close but not touching; a cylindrical aluminum reflector surrounds the lamps. Air cooling has been used until recently but the latest design employs a liquid cooled head in which a $CuSO_4$ solution can be circulated within a glass tube surrounding the ruby. The pumping circuit can store as much as 800 joules of energy and is matched to the lamp by means of a conventional pulse forming and impedance matching network.

* A Nd-glass cylinder of identical dimensions can be substituted for the ruby in the laser head.

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The input energy is reproducible to within 0.2 percent by means of an electronically controlled servo mechanical charging system. The pulse forming and impedance matching network has been included to lengthen the life of the lamps and increase the pumping efficiency. A Q-switched pulse approximately 30 ns in exposure time can be seen on the tail end of the pumping pulse shown in Figure III.

Provisions for both normal and Q-switched operation are included in the design of the laser head.* Q-switching is accomplished by rotating a totally internal reflecting (TIR) prism at 13,200 rpm; an optically flat dielectric reflector of either 95% or 60% reflectivity is used to complete the optical path which has a total length of 19 cm. A clamp with micrometer screw adjustment allows the rotating prism to be fixed parallel to the ruby face for normal laser operation.

Pulse outputs are displayed on a Tektronix 585 oscilloscope, using a fast photodiode (International Telephone and Telegraph FW 4000). A sample of approximately one percent of the beam is taken with a beam splitter, and is conducted to the photodiode by means of a light pipe. The system has a rise time of less than 4 ns, and is calibrated using a cone radiometer.[15] A 30 ns delay in the vertical amplifier of the oscilloscope facilitates internal triggering and observation (visual or photographic) of the trace of the entire pulse. This system allows a permanent record to be made of the pulse duration and energy for each exposure of the rabbit retina. However, it is not a convenient method for normal laser pulses which extend over hundreds of microseconds and contain a large number of individual spikes. Under these conditions it is more convenient to integrate the photodiode output by charging a condenser and recording the voltage rise by means of a Keithley electrometer feeding into an x-y recorder. This is the method of choice for monitoring both normal

*Martin Orlando furnished the design for normal and Q-switched operation under a contract with the Office of the Surgeon General, U. S. Army.

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and Q-switched pulses.

Although attenuation of the laser beam in the optical system is not negligible, the power density impinging on the rabbit eye is sufficient to produce severe biological damage; all exposures for mild damage to the rabbit retina require the introduction of neutral filters in the radiation beam.

The sequence of events leading to an exposure of the rabbit retina is under the control of the experimenter (ophthalmologist). Referring to the block diagram in Figure II, the following sequence is for Q-switched exposures: Depression of a foot pedal starts the high speed motor, rotating the TIR; when the ophthalmologist has selected the exposure site he depresses a button on the shank of the ophthalmoscope; this interposes a mirror between his eye and the laser beam, reflecting the beam into the rabbit eye; the mirror at the end of its travel closes a microswitch which actuates the opening of a camera shutter controlling exposures to the polaroid camera; when this shutter has opened completely the pumping circuit is triggered, initiating the laser pulse. The photodiode triggers the oscilloscope sweep and a picture of the pulse trace is registered on the polaroid camera at the same instant that the rabbit retina is exposed.

Steady State Laser Hazard

At the present state of development the power output from the CW or steady state operation of gas lasers (He-Ne) and semi-conductor diodes (GaAs), etc. rarely exceeds one watt. Under normal conditions the output beam may be extremely monochromatic and parallel. The hazard to the eye consists primarily in viewing a CW laser beam over extended periods of time, seconds or even minutes. The problem is essentially one of a steady state temperature equilibrium on the retina of the observer.

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Jones and Montan [18] have discussed the eye risk for continuous exposure to a CW laser such as the He-Ne gas device. Assuming that the retina of the human eye will tolerate a 1°C temperature rise for considerable periods of time without sustaining irreversible damage they have calculated that 10^{-6} watts is a safe power level for the retina even when the energy input is considered to be confined to a 10 micron (μ) diameter of the retina. Although most [19] estimates of the minimum light spread on the fundus after corrections for aberrations, diffraction, etc. are greater than 10 μ, this seems to be a reasonable assumption in view of the lack of experimental data. An underestimate of image size provides a factor of safety insofar as the energy density is concerned but it should be pointed out also that experiments on rabbits using relatively long pulses (100 - 250 ms) indicate that the minimum dose for mild injury varies with the diameter of the irradiated image [7]. It was found that the smaller the image size the larger the radiation dose required to produce mild injury. This can be attributed to the fact that the rate of energy dissipation by conduction from the irradiated image to the surrounding unirradiated tissue increases in proportion to the temperature gradient which, in turn, is an inverse function of the image diameter. Thus, the assumption of an image diameter of 10 μ, while overestimating the energy density may also overestimate the rate of energy dissipation from the irradiated image, so that the two factors tend to oppose each other. Actually, 10^{-6} watts incident on a 10μ diameter produces a power density of 1.27 watts/cm^2 on the retina. Experiments conducted by the authors [7] demonstrated that 300 watts/cm^2 focussed on a 200μ diameter of the rabbit retina for several seconds failed to produce an ophthalmoscopically visible lesion. A power density of 1.33 watts/cm^2 on the human retina for limited exposure times should not produce irreversible effects according to present information.

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Thermal damage to the retinal proteins is probably the limiting factor in considering the hazard of CW lasers. Nevertheless, it seems wise to keep in mind the possible effects upon the proteins of the crystalline lens. Continued exposures at intervals over an extended period of time could result conceivably in damage to the lens proteins with consequent opacification. The clinical use of laser beams to coagulate the retina is too recent to rule out completely the development of long term effects. It should not be assumed that the eye can accept with impunity low levels of laser radiation over an indefinite period of time. In this laboratory continuous exposure over 48 hours of an enzyme solution to a one milliwatt beam of unfocussed radiation from a He-Ne laser failed to produce significant deactivation of the enzyme in question. While comforting this evidence is not conclusive.

The Ocular Hazard from Normal Laser Pulses

The inevitable trend of laser technology toward higher output energies and greater power densities has increased the ocular hazard in the laboratory and in the field. Ruby and Nd-glass pulse trains containing more than 100 joules are commonplace, so that even diffuse reflectance from surrounding objects may prove hazardous to the eye. Before safety criteria can be established on a scientific basis it is necessary to define carefully the minimum radiation dose and exposure time which can be tolerated by the human eye without undergoing irreversible biological damage. Fortunately, some background information on safe exposure levels to the eye is available from the previously mentioned research on the retinal burn hazard from nuclear weapons. Clinical experience has shown that the rabbit retina provides a valid and useful model for estimating safe levels of human exposure.

Exposures were made with a 4.5° divergent cone of laser radiation striking the rabbit cornea to produce a beam diameter on the retina of approximately 0.8 mm. The

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rabbit pupil was dilated to approximately 8 mm before the experiment. Energy and time duration were measured accurately for each pulse by methods explained above. Standard operational procedure on each rabbit involved placing initially a moderately severe lesion on the retina, then attenuating subsequent exposures by means of calibrated filters until the lesion was no longer visible 5 minutes after exposure. Thus, a series of lesions, decreasing in severity until they were no longer visible were placed on a portion of the rabbit fundus which had been chosen carefully for uniformity of pigmentation. "Hot spots" in the laser beam and lack of uniform fundus pigmentation were major sources of error in determining an empirical "threshold".

The data points plotted in Figure I for monochromatic laser pulses 200 μs in duration are markedly similar to the "threshold" data for pulsed white light sources with the xenon lamp. Within experimental accuracy a radiation dose of approximately 0.85 J/cm^2 delivered in 200 μs produces a mild lesion on the rabbit retina. Histological examination of minimal lesions, whether produced by monochromatic ruby radiation or by the pulsed xenon lamp, fails to disclose any marked biological differences in the nature of the lesions. Thus, both physical and biological data indicate that the nature of the damage is similar.

The Ocular Hazard from Q-switched Laser Pulses

The distinguishing feature for biological damage from Q-switched pulses is the rate of energy delivery or power density in $watts/cm^2$. Normal laser pulses, while energetic, require an appreciable time for delivery, from several hundred microseconds to several milliseconds. Q-switched pulses, on the other hand, may contain less energy but the pulse duration is orders of magnitude less than for normal laser pulses. Power densities for Q-switched laser pulses range from

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1 to 100 megawatts/cm^2 and can even extend into the gigawatt/cm^2 range for special devices. Time duration for Q-switched pulses range from about 5 to 100 nanoseconds. In Figure IV, a ruby Q-switched pulse of approximately 30 ns is shown.

Procedures for determining power density and pulse time for Q-switched radiation exposures of the rabbit retina are identical with those outlined in the last section for normal laser action. There seem to be two outstanding experimental features which distinguish a minimal Q-switched lesion from all others: (1) the radiation dose (0.07 J/cm^2) required to produce an observable lesion on the rabbit retina in 30 ns is lower by more than a factor of 10 from that needed to produce minimal damage at 200 μs. (2) the clinical appearance and histologic evidence indicate that the minimal Q-switched lesion on the rabbit retina differs materially from minimal lesions produced at the relatively low power density levels encountered for normal laser pulses. Specifically, it is found that the relatively mild Q-switched lesion is accompanied by choroidal hemorrhages extending into the subretinal space [6]. A similar clinical or histological picture is not observed for minimal exposure to normal laser pulses and xenon lamp pulses of relatively low power density.

Thermal Injury as a Model for Radiation Damage to the Retina

Henriques [20] has proposed an explanation of thermal injury to biological systems in terms of rate process theory. This is a statistical mechanical approach to irreversible damage at the molecular level, based on chemical kinetics as a function of time-temperature history. The application of rate process theory to thermal injury demands, among other things, a knowledge of the time-temperature history of the exposed biological system; to acquire this knowledge, it becomes necessary to either calculate the time-temperature history in the irradiated system in terms of a mathematical model (differential equation of heat flow, for example) or to measure experimentally the temperature as a function of space and time. Both approaches have been tried

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(21), (22), (23), (24). Davis [25] has discussed the measurement of transient temperatures in biological systems and commented critically on the difficulties involved. Another and perhaps more practical approach to the determination of time vs temperature in biological systems involves the use of electrical analogues to simulate the irradiation program [26]. Whatever the approach, a knowledge of the time- temperature history for a biological system is necessary before chemical kinetics can be employed in a model to describe thermal damage at the molecular level.

Most of these approaches towards solving the time-temperature history require a physical model which will provide a reasonable approximation to the biological system under investigation. In the case of the mammalian retina, enough data has accumulated to construct a crude model. It has been demonstrated by histochemical staining techniques [12] that minimal lesions in the rabbit fundus involve primarily the pigment epithelium and the adjacent structural layers, including the outer retinal layers which contain the visual receptors.

In 24 human eyes, absorption and scattering data indicate that for the ruby laser wavelength (694.3 mμ) about 10 per cent of the radiation is absorbed or scattered in the ocular media (OM), while absorption and/or scattering in the PE varies from 15 to 40 per cent depending on the individual; absorption and/or scattering in the choroid varies from 10 to 80 per cent. Maximum absorption in the PE would represent the most hazardous case. Accordingly, it seems reasonable to assume that 40 per cent of the ruby radiation incident on the PE is absorbed in a thickness of 10 microns while the remaining 60 per cent is absorbed in the 100 - 150 micron thickness of the choroid. Absorption of radiation takes place primarily in the melanin granules dispersed within the single cell layer of the PE, and within the pigmented choroidal cells. The size and dispersion of these pigment granules varies widely among individuals, and the distribution of the

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pigmented cells is much more irregular in the choroid. Vascularization of the choroid provides an additional source of absorption.

Taking the above factors into account and considering the thermal properties of water as a first approximation to those of ocular tissue, a crude model of the ocular fundus is illustrated in Figure V. According to this model, significant absorption of radiant energy begins at the PE where 40 per cent is absorbed exponentially in passing through a 10μ thickness, and the remaining 60 per cent is absorbed exponentially in the choroid. The assumption of exponential absorption in PE and choroid implies a uniform but different concentration of absorbing material (melanin granules) in each structure. In view of the wide variation in both distribution and size of pigment material among individuals this assumption seems warranted.

Several features of this crude model are worthy of discussion. During the early stages of exposure the temperature gradient will be approximately the same on both sides of the PE. Since the choroid absorbs simultaneously with the PE, the temperature gradient between the interface of the PE and choroid will vary with exposure time, being large during the initial stages of exposure but gradually diminishing as the choroid continues to absorb energy and the PE conducts more energy into the choroid. This model does not include thermal dissipation by choroidal blood flow because the latter is slow in comparison to thermal conduction. The fact that damage is first seen in the PE and in the outer layers of the retina seems reasonable when it is considered that: (1) the energy density and thereby the temperature will be highest in the PE; (2) The outer retina contains highly developed and sensitive biological structures and substances.

A maximum temperature in the PE can be estimated by completely neglecting thermal conduction and considering the PE as a pill box having a thickness of 10μ , filled with a molecular substance dissolved in water which will absorb 40 per cent of the radiant energy incident on its surface. This simplified model, for all its crudity, can

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help in delineating the problem. For example, a radiation dose of 0.85 J/cm^2 delivered in 200 μs by a normal laser pulse produces minimal damage to the rabbit retina. A calculation of the maximum temperature rise under these conditions yields 81°C above ambient. The same calculation for a radiation dose of 0.07 J/cm^2 delivered in 30 nanoseconds, the conditions for minimal damage to the rabbit retina from a ruby Q-switched pulse, yields only a rise of 6.7°C above ambient. The model seems reasonable for the 200 μs laser pulse when it is remembered that the maximum temperature above ambient in the PE is considerably below 81°C because of heat conduction to the surrounding environment. On the other hand a rise of only 6.7°C in the PE does not seem compatible with the ophthalmoscopically visible lesion which appears soon after exposure to the Q-switched pulse.

Temperatures vs time at the center of the PE for square wave inputs of radiant energy of various durations in the microsecond region are shown in Figure VI. These curves are taken from the unpublished data of Schmidt [26] using an electrical analog which reduces the study of transient retinal temperatures to the recording of voltages vs time in a resistance-capacitance network constructed to simulate heat conduction within the ocular fundus. The physical model upon which this analog is based assumes a PE which is 10μ in thickness and composed of a substance having the thermal properties of water and capable of absorbing uniformly throughout its volume a normally incident power density of 4.18 $watts/cm^2$. The straight line in Figure VI represents the rise in temperature within a PE which is completely insulated, i. e. no conduction. For square wave or constant energy inputs up to 25 μs in duration, conduction plays no part in determining the final temperature of the PE; for constant energy inputs beyond 25 μs in duration conduction begins to play an increasingly important role in determining the peak temperature attained by the PE. The curves illustrated in Fig. VI and similar ones derived by analog techniques for longer exposure times can be used to estimate

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the maximum temperature attained in the PE. The results are shown in Table I in which maximum temperatures for various exposure times are listed. The radiation doses listed in column 2 were taken from the log-log plot of Figure I for image diameters of 0.8 mm. The simultaneous absorption of radiant energy in the choroid has been taken into account in calculating these maximum temperatures in the PE.

Discussion:

The Conventional Thermal Injury Model for Exposure Times of 200 μs or Greater

Reference to the last column of Table I shows that retinal lesions produced by exposure to Q-switched laser pulses cannot be discussed in terms of the model developed above for the examination of retinal lesions resulting from exposures to lower power densities. Further discussion of Q-switched phenomena is postponed until the more conventionally produced lesions have been examined in terms of the thermal model previously developed.

The estimates of maximum temperature above ambient in the PE (column 4, Table I) may be subject to considerable error, due to the assumptions implicit in the model, and should be regarded as approximations probably to within 20 per cent. However, the uniformity of maximum temperatures in the PE over a wide range of power densities and exposure times cannot be ignored. A plateau or threshold effect seems evident. The hypothesis of an "all or none" phenomenon for thermal injury at a particular temperature can be discarded immediately in view of the experiments of Geeraets [12], who has shown by histochemical techniques that enzyme damage extends well into the outer retina as well as radially into the unirradiated PE where the maximum temperatures attained during an exposure are considerably lower than at the center of the PE. A practical explanation may be that a temperature close to or perhaps at 100°C in the PE is required to coagulate retinal tissue to the point where the relative reflectance of light from the PE can be distinguished by ophthalmoscopic observation. The fact that this maximum temperature is

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relatively invariant over the range of power densities and exposure times shown in Table I can be taken as excellent evidence for the uniformity and reproducibility of the biological endpoint chosen to define a minimal retinal lesion. It should be emphasized again that the criterion of the appearance of an ophthalmoscopically visible lesion within 5 minutes after radiant exposure is, at best, a crude method for determining a practical "threshold" which can be used to define ocular safety.

Vos [21] suggested after an analysis of the earlier data of the authors that steam production might account for the lesions observed in the rabbit retina. Undoubtedly, this explanation has validity for the more severe lesions of the rabbit retina, but it does not hold for the mild lesions described by Geeraets [12] or those illustrated in Figure I of this report. Although temperatures in the PE above ambient could easily attain the steam point and still be within the estimated accuracy according to the model used in this paper, the experimental evidence indicates that the radiant exposures are terminated before the generation of steam produces a gross disarrangement of the structure of the outer retina. Possibly, the observed plateau in temperature is due to the conversion of energy to the latent heat of vaporization of water. In all events, the constant slope in Figure I for minimal observed lesions over an extensive range of power densities and exposure times suggests that the biological endpoint chosen as a criterion remains approximately constant. This may represent a maximum temperature in the PE needed to coagulate tissue to the point where relative reflectance from the ocular fundus can be used to define a retinal lesion.

These calculations of an approximate temperature plateau in the PE for the observation of a minimal retinal lesion do not invalidate rate process theory as a possible model for thermal damage at the molecular level. The minimal lesion reported here and illustrated in Figure I is a gross estimate of "overkill" which should not be used to test the validity of rate process theory. For the longer radiant exposures,

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there is a tendency for the maximum temperature in the PE to decrease. This is an indication that lower temperatures in the PE, if maintained over a sufficient time, can account for the same degree of retinal damage. More refined experiments are needed to test the effect of time-temperature history on macromolecules of biologic interest. Thermal denaturation of retinal proteins by the techniques available to molecular biology are currently under investigation.

Solutions of the differential equation of heat flow for particular boundary conditions conforming to those for radiation exposures of the mammalian retina have been provided by Schmidt and Vos*. [27] Temperatures in the PE as a function of time and space coordinates have been calculated on the assumption that the ocular fundus may be treated as a substance having the thermal properties of water. The radiation incident normally to the surface of the PE is considered to be absorbed uniformly throughout a finite depth. For the case of an infinitely large retinal image (infinite plane) the solution in terms of time and depth can be obtained by analytical integration. The more pertinent solution for finite retinal images has been obtained by numerical integration using a digital computer. In Figure VII, temperature rise in the PE per unit of incident radiation absorbed is plotted logarithmically against time for square parallelepipedons having dimensions of 632 and 20 microns on a side respectively. The temperature at the center of the PE continues to rise even after an exposure time of 100 ms for the larger image while it levels off at approximately 200 μs for the smaller image. For a given radiation input the temperature in the PE reaches saturation quickly and at a much lower value for the small image as compared to the large image.

Heat conduction at the borders of the image begins to have an appreciable effect on the temperature at the center of the PE after a time $t \approx Z^2/4K$ where Z is the half thickness of the PE (assuming that the thickness of the PE is considerably less than

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the dimensions of the square image) and K is the thermal diffusivity (taken as about 1.4×10^{-3} cm^2/sec for water). Taking Z as 5 μ for the PE, heat dissipation at the borders of the PE will become appreciable after approximately 40 μs. Thus, for the first 40 μs the temperature at the center of the PE will rise almost linearly with time. Referring back to Figure VI, it can be seen that the electrical analog predicts about the same behavior. During the next phase, the temperature in the PE will rise as the square root of t; in this phase heat dissipated from both faces of the PE affects appreciably the temperature at the center but heat from the borders of the parallelepipedon does not have time to affect the temperature at the center of the PE. Finally, heat dissipation by conduction at the image borders will have an appreciable effect on the temperature at the center of the 20 micron image in approximately 180 μs and for the 632 micron image in approximately 200 ms. At this time, $t \approx X^2/4K$, where X is the half width of the image, saturation effects become noticeable and the temperature at the center of the PE tends toward a maximum value. From this point on heat is dissipated as fast as it is generated and the temperature of the PE remains constant.

This type of behavior accounts quite well for the increase in thermal dose with decrease in image size needed for minimal thermal injury at the long exposure times represented by the circles and crosses in Figure I. It also demonstrates for a given steady state input of energy that both the magnitude of the equilibrium temperature attained at the center of the PE and the time taken to attain this equilibrium are strong functions of the image size. It would take approximately 1 ms to attain temperature equilibrium in the human retina when viewing a He-Ne CW laser beam which produced an image having a diameter of 20 microns. For small images on the retina, temperature equilibrium is attained so rapidly that it seems doubtful whether blood flow in the choroid could be effective in determining the final temperature.

The authors are of the opinion that mild retinal lesions produced by both laser sources and white light sources for exposure times ranging from 175 microseconds to steady state conditions can be attributed to thermal damage in the PE and the regions

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immediately adjacent to the PE, especially the outer layers of the retina. The gross phenomena associated with the production of these thermal lesions can be explained adequately in terms of the differential equation of heat flow, as applied to relatively crude physical models which approximate conditions in the ocular fundus during radiation exposure. For retinal lesions produced by high power densities and short exposure times (Q-switched pulses) the concept of thermal injury to the retina as outlined above is not considered adequate to explain either the physical phenomena or the biological effects.

Retinal Lesions Produced by Q-Switched Laser Beams

As mentioned previously the retinal lesions resulting from exposure to Q-switched laser beams cannot be explained in terms of conventional thermal injury. Heat flow from the irradiated image to the surrounding tissue is completely negligible during a pulse of 30 nanoseconds. The effective distance over which heat flow can take place within a given time may be estimated by solving $X = (4Kt)^{1/2}$, using 1.4×10^{-3} cm^2/sec as the thermal diffusivity of water and substituting 3×10^{-8} sec for t. The effective radius for heat flow in 30 ns is approximately 0.13 microns, a radius which would be comparable to the size of the melanin granules dispersed within the cells of the PE. This suggests that the absorbing volume within the PE during a 30 ns pulse might be confined to the immediate region surrounding the pigment granules. Under these circumstances temperatures within this region would be expected to reach very high values since electronic absorption of photons within the absorbing medium (presumably melanin in a polymerized form) would be effectively instantaneous for the purposes of this discussion, and the quantum mechanical exchange from electronic energy states to vibrational and rotational energy states (usually in aqueous media by the so-called mechanism of internal conversion) would be very rapid also.

How this relatively instantaneous deposition of energy within a restricted volume may be dissipated is a matter for future research. There is experimental evidence to

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indicate that an appreciable amount of energy is radiated according to the Stefan-Boltzmann law (σT^4)* and also via shock waves induced in the media by the intense temperature gradients [28]. Other mechanisms involving two photon processes and non-linear effects are not excluded. After exposure of the rabbit retina to relatively high power densities a plume of dark material can be seen ophthalmoscopically in the vitreous. This may be similar to the vaporization observed when a blackened surface is irradiated with a focussed laser pulse; also, thermionic emission has been reported from metal surfaces irradiated with focussed Q-switched beams [29]. It has been pointed out that electric field intensities within such a focussed beam are sufficient to ionize a dielectric substance and produce a plasma [30].

Exploration of power densities and exposure times in the interval represented by the extrapolated portion of Figure I should be helpful in determining experimentally what types of energy transfer become predominant for sub-microsecond exposures. Application of the classical equation of heat flow has already indicated that conduction phenomena should become unimportant for pulses of 40 μs or less. The authors postulate that other mechanisms of energy transfer (acoustic waves, σT^4 radiation, ionic emission, non-linear effects, etc.) become important as the power density increases from kilowatts/cm^2 to megawatts/cm^2. A study of this region of transition will facilitate the understanding of the physical phenomena involved in the production of retinal lesions by Q-switched laser beams. Meanwhile, experimental observation indicates that for exposures to power densities between 2 and 3 megawatts/cm^2, the rabbit retina undergoes irreversible damage of a nature which cannot be interpreted in terms of conventional thermal injury.

*The authors have irradiated the enucleated rabbit eye with ruby Q-switched pulses well above the power density needed to produce minimal damage to the retina and observed the light scattered from the retina through a trephined hole in the sclera by means of a photomultiplier placed well to the side of the transmitted laser beam. Scattered light reaching the photomultiplier passed through a filter having an optical density of 4 for wavelength 694.3 mμ. Photomultiplier response indicated a light pulse of several μs in duration.

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Conclusions

1) There is a fundamental difference in the physical phenomena and biological consequences accompanying exposure of the mammalian retina to high power density beams (megawatts/cm^2 from Q-switched lasers) as compared to moderate power density beams (kilowatts/cm^2 from normal laser pulses and pulsed xenon lamps.)

2) A radiation dose of approximately 0.07 J/cm^2 produces irreversible damage to the rabbit retina from a Q-switched ruby laser (exposure time 30 ns) whereas approximately 0.85 J/cm^2 is needed to produce ophthalmoscopic visible damage from a laser pulse lasting for 200 μs or longer.

3) No definite physical or biological differences between ruby laser pulses and pulsed white light cources of comparable power density have been detected for minimal damage to the rabbit retina. Both types of exposure can be explained adequately in terms of thermal injury using a simplified physical model and the classical law of heat conduction.

4) Ophthalmoscopically visible damage to the rabbit retina for exposure times ranging from 200 μs to 20 ms require a remarkably uniform temperature in the PE which is estimated to be close to 100°C.

5) For steady state exposure to a laser beam the maximum temperature and time taken to attain equilibrium depends primarily on the retinal image size. For an image whose diameter is 20 microns, equilibrium is attained in approximately 10 milliseconds. This time is too short to allow significant cooling from blood flow in the choroid.

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TABLE I

Maximum temperatures in the PE for different exposure times as estimated on the basis of the crude model illustrated in Figure V. An electrical analog has been used to take account of heat conduction in the model.

Exposure Time in μs	Radiation Dose in J/cm^2	Max. Temp.* in PE, neglecting conduction	Max. Temp.* in PE, correcting for conduction
0.030	.07	6.7	6.7
200.0	.85	81	52.8
500.0	1.10	105	50.5
1000.0	1.38	132	55.0
2000.0	1.72	165	53.5
5000.0	2.41	230	49.3
10000.0	3.07	294	47.3
20000.0	3.90	373	46.8

*Temperatures are °C above ambient.

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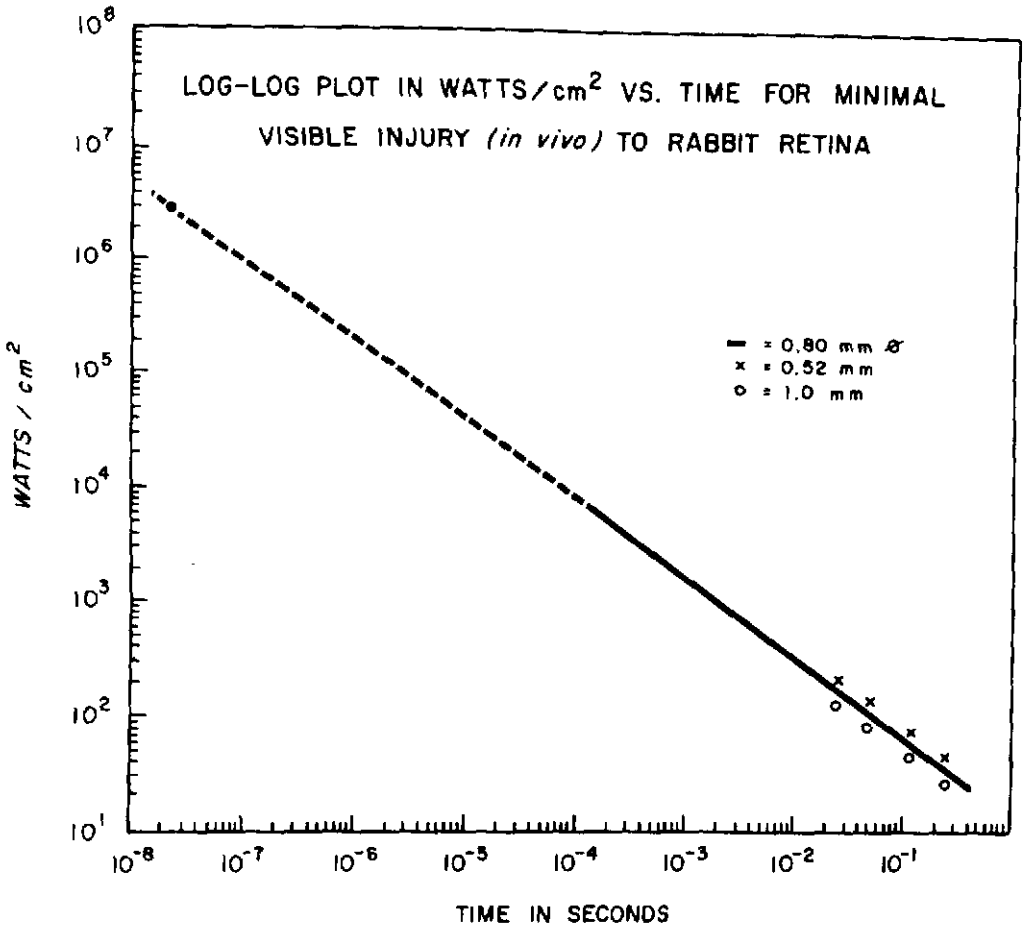

Figure I Log-log plot of power density in watts/cm^2 vs exposure time in seconds for the production of very mild lesions in the rabbit retina. The straight line represents data for retinal image diameters of 0.8 mm. Some data points for image diameters of 1.0 mm (circles) and 0.54 (crosses) are plotted for the longer exposure times. The data point at the extrapolated end of the curve represents a Q-switched pulse.

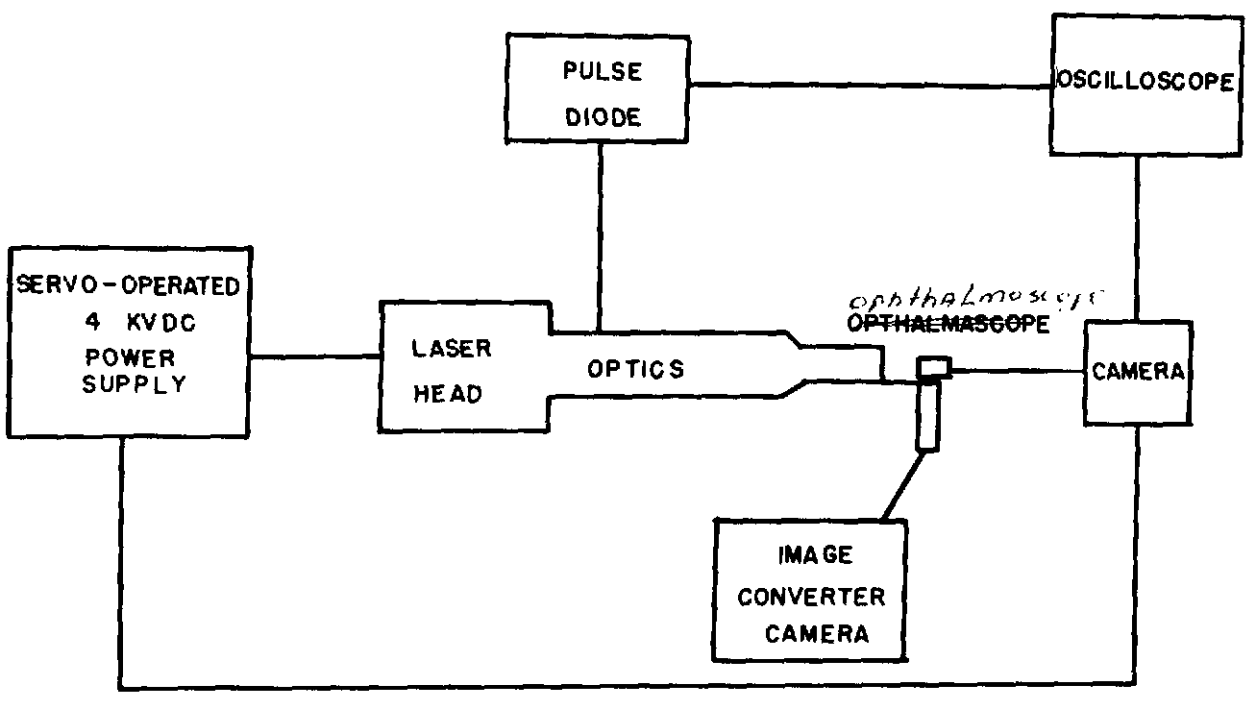

Figure II Block diagram illustrating schematically the relationship between the laser optical system and associated equipment.

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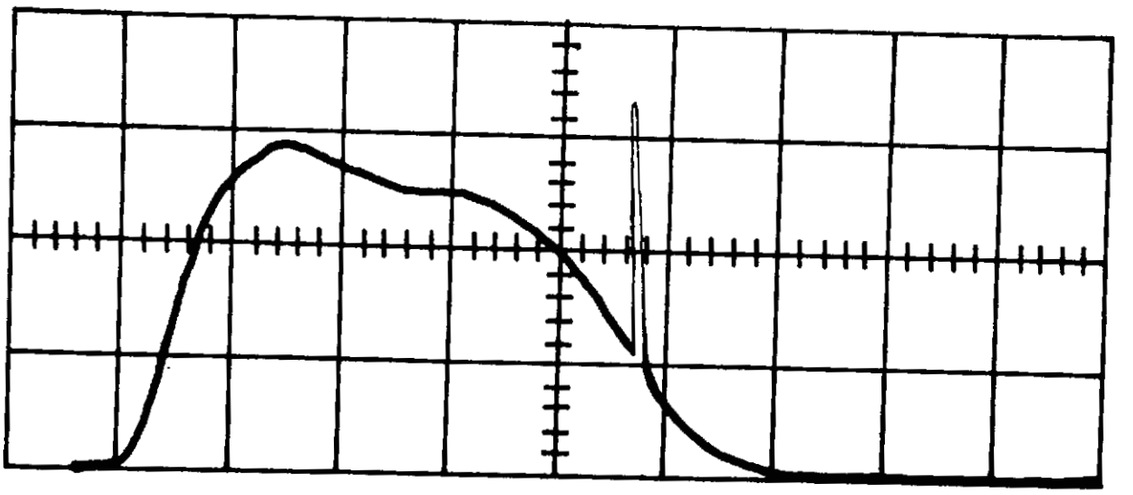

Figure III Oscilloscope trace of pumping pulse produced by pulse forming network. A Q-switched pulse of approximately 30 ns duration can be seen on the last part of the trace. Time scale 50 μs/cm.

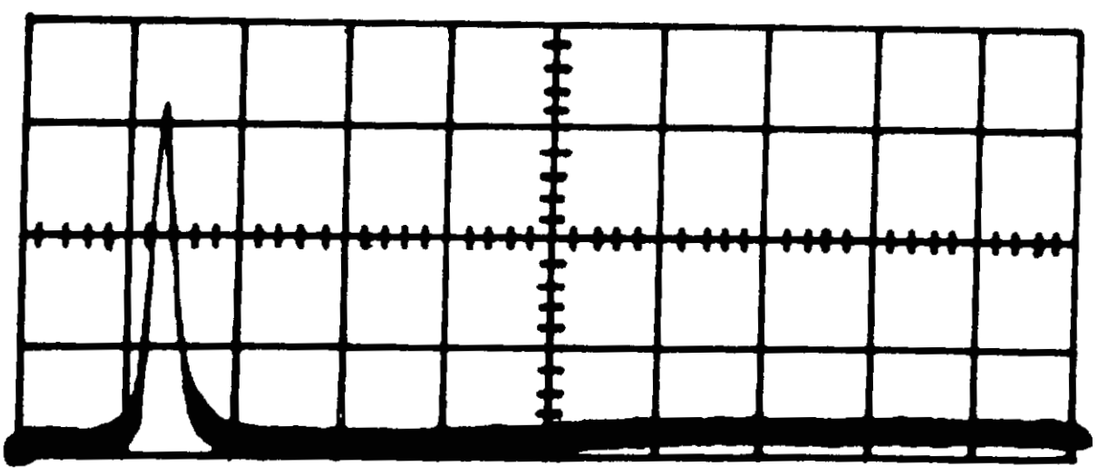

Figure IV Q-switched trace of typical ruby pulse lasting approximately 30 ns. Time scale 50 ns/cm.

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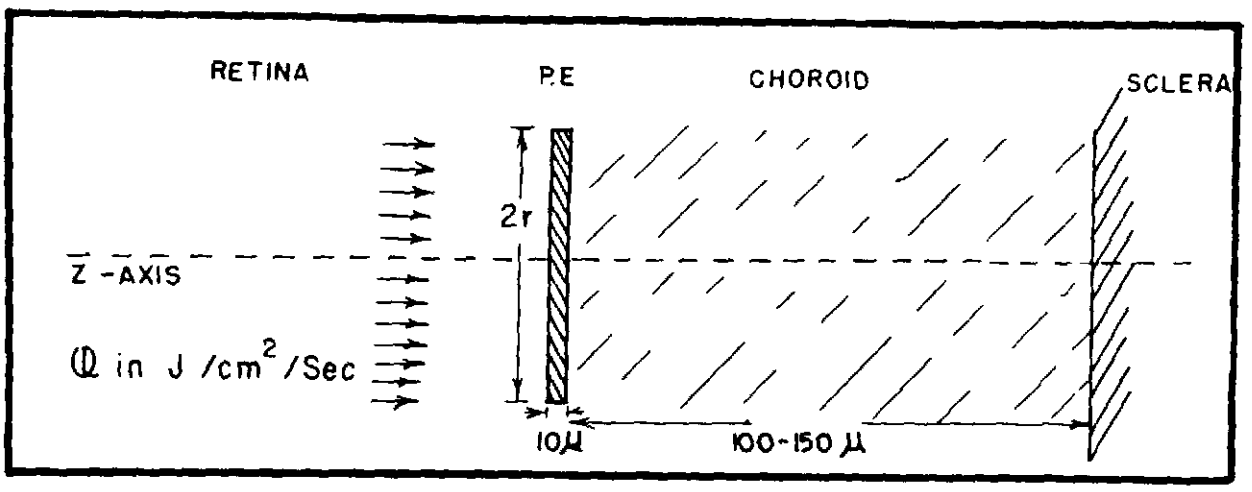

Figure V Schematic diagram of crude physical model of ocular fundus.

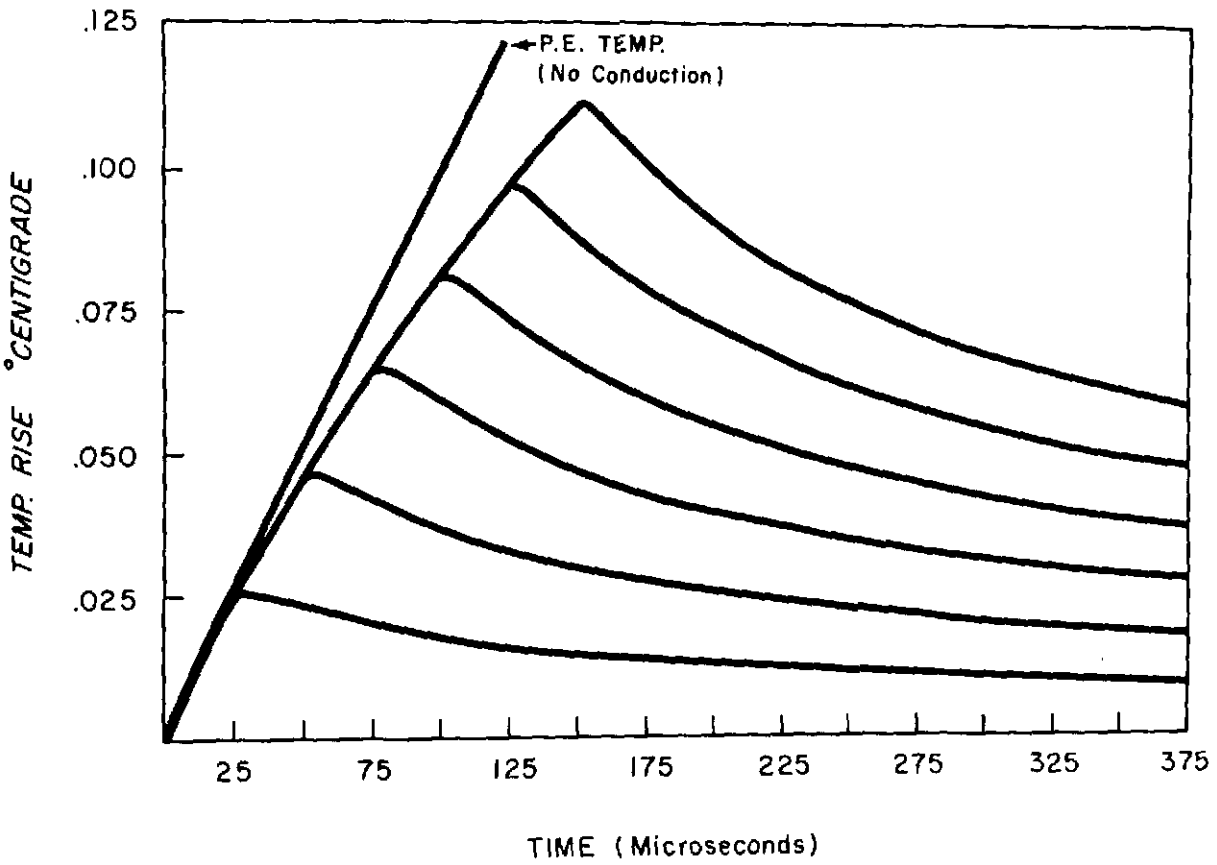

Figure VI Temperature in °C vs time in microseconds at the center of the PE for square wave inputs of radiant energy of various durations. Curves are based upon the uniform absorption of 4.18 J/cm^2/sec in PE.

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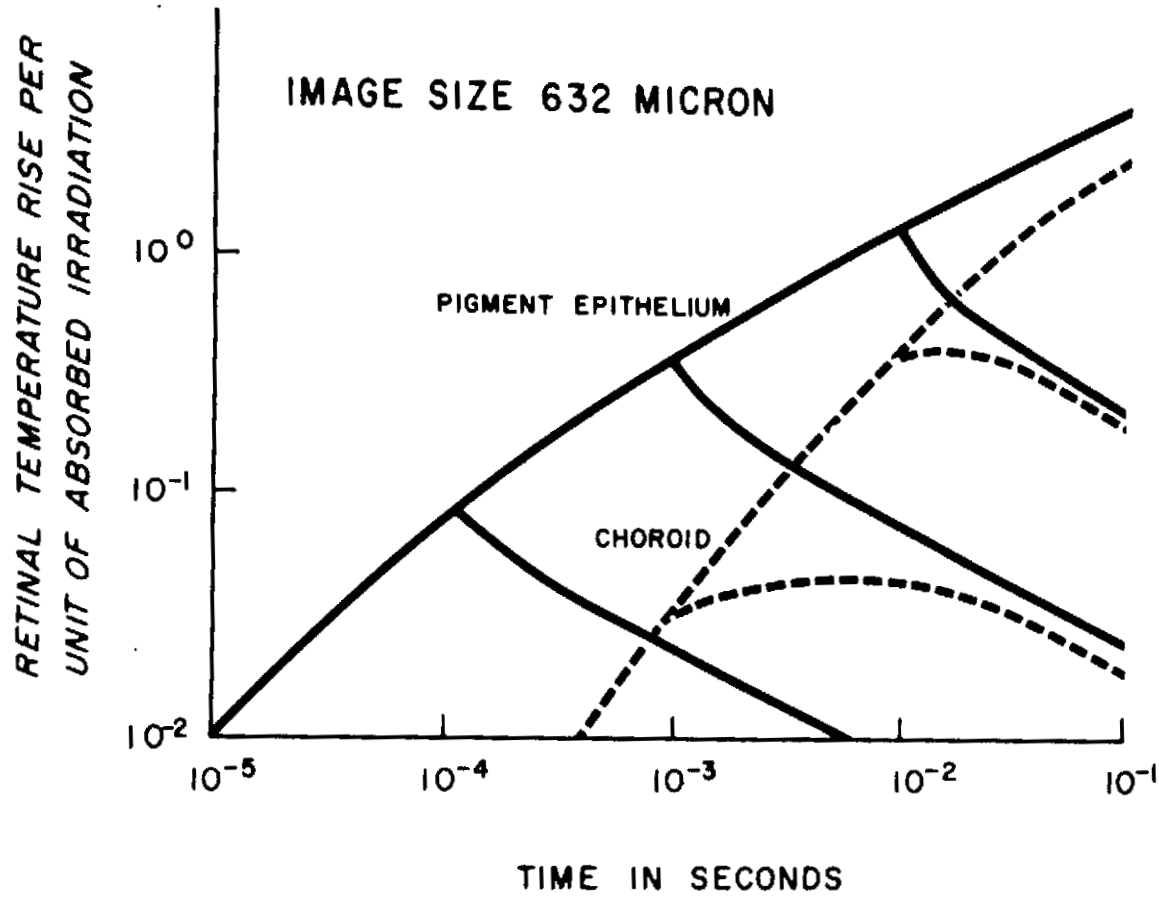

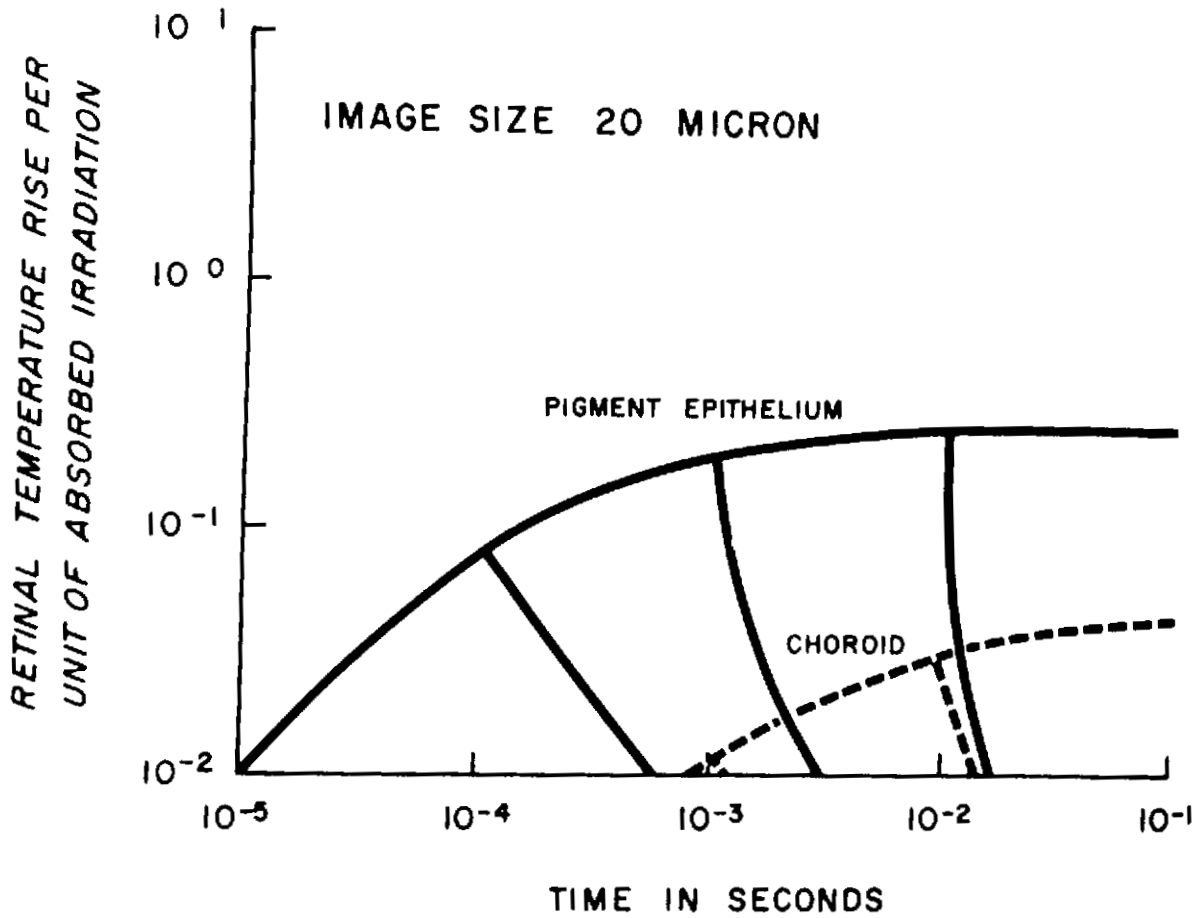

Figure VII A log-log plot of temperature rise in the PE per unit of absorbed radiation vs time in seconds for square parallelepipedons of 632 and 20 microns on a side. Taken from the data of Schmidt and Vos.

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