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Second Order PRA Model for Ocular Laser Damage

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ABSTRACT

Dose-response curves characterize the variability of damage thresholds within the population under consideration. In probabilistic risk analysis (PRA) for laser injury, a log-normal cumulative distribution is usually used as dose-response curve to calculate the probability for injury as function of radiant exposure. However, experimental uncertainty as well as a different variability within the group under consideration can influence the shape of the dose-response curve.

Previously, to our knowledge, dose response curves were used in PRA for laser injury without considering uncertainties. We have developed a second order probabilistic risk analysis model, which accounts for uncertainties of the dose response curve by defining distributions for the slope and ED-50 values of the dose response curve and using Monte-Carlo simulation.

1. INTRODUCTION

NASA, ESA and other space agencies plan to deploy space based laser (lidars) for measurement of atmospheric properties and these may represent an ocular hazard to people on the surface of the earth[1]. The risk of an eye injury depends on a range of parameters such as the energy per pulse, wavelength, beam divergence, space craft orbit, atmospheric conditions, properties of telescopes and other viewing aids, and the viewing behaviour of potentially exposed people.

A probabilistic risk model has been developed to quantitatively model the risk for ocular injuries due to laser beams being emitted from satellite based lidars. A fully probabilistic approach including uncertainties and variability distributions of model parameters was followed to determine the occurrence rate for exposure to the laser beam for relevant population groups, to calculate the ocular radiation exposure level with atmospheric scintillation effects included, and then predict the frequency distribution of an ocular injury from a space borne lidar.

In this paper we describe the part of the risk model that characterises the probability that ocular injury occurs for a given energy that is incident on the eye. For the first time, such a model accounts for the uncertainty and variability of the model parameters ‘ED-50’ and ‘slope’ by defining not point values but distributions which are propagated through the model with Monte Carlo simulation to produce a distribution of the probability for ocular injury per exposure.

2. NATURE AND SEVERITY OF INJURY

A quantitative risk analysis needs to include a characterisation and specification of the nature and severity of the injury for which the probability or frequency is characterised. The basic “negative consequence” of concern in laser risk analysis is *loss of vision*.

The risk model described here is based on experimental animal laser threshold data. The endpoint in typical laser threshold studies is the minimal visible lesion, MVL, which can be described as a just barely detectable lesion by visual inspection with an ophthalmoscope or similar instrument. Since retinal injuries are usually the main concern and also represent the most challenges in terms of a quantitative risk model, retinal injuries are discussed in more detail in the following. The severity of the injury depends not only on the level of the ocular exposure, but also on the location of the lesion, as a lesion in the fovea can result in serious vision loss, but may even go unnoticed if located in the periphery of the retina. This is because high visual acuity exists only within the most central part of the retina, referred to as the fovea centralis, or simply, "fovea". The visual acuity (visual resolution) of the eye steadily decreases with increasing angle away from the fovea. Therefore, even a relatively small injury to the fovea can result in a significant loss of high-acuity vision; whereas, a small lesion of the paramacular area might not even be noticed by the injured person for the case of MVL. A lesion in the peripheral retina that produces a large haemorrhage, could greatly impede normal vision because the blood flows in front of the retina thus preventing light from reaching the photoreceptors. However, after a few days, when the blood is absorbed and when scars form and when the lesion is not in the central part of the retina, recovery of visual function is usually good[2,3,4,5,6]. Even for foveal lesions, some level of recovery of visual acuity over time has been observed and animal studies indicate that minimum spot foveal MVLs result in relatively small visual acuity losses[7]. Wolfe[8] recommended a system of grading of acute retinal injuries where the above types of lesions were graded from I to IV, with subgrades which characterise the difference between a foveal lesion or a lesion outside of the fovea. The grading scheme is reproduced in Tab. 1.

Tab. 1 Grading scheme for acute retinal injuries as proposed by Wolfe[8] for military applications.

Grade	Ophthalmoscopic finding	Range of visual (Snellen) acuity in early phase after injury	
		Subgrade A (extrafoveal)	Subgrade B (foveal)
I	Retinal edema	20/15 to 20/25	20/30 to 20/200
II	Retinal necrosis	20/15 to 20/40	20/40 to 20/400
III	Subretinal and /or intraretinal hemorrhage	20/15 to 20/50	20/100 to 20/400
IV	Vitreous hemorrhage and /or full-thickness retinal hole	20/15 to finger counting or worse	20/100 to finger counting or worse

It is pointed out that the grading scheme as proposed by Wolfe applies rather to the short term impact of ocular damage to the performance of a soldier in a battle field rather than long term impact on vision – for instance for a haemorrhage and retinal hole in the periphery, immediately after the exposure, vision is impaired by blood, which however is absorbed after a few days and the long term visual impact can be much less serious than a non-haemorrhagic lesion in the macula or fovea.

Of more relevance for risk assessment of laser injury is a scoring system proposed by Marshall[9]. According to this system, numbers are assigned to different locations on the retina which are intended to give some indication as to the degree of visual debility such lesions would produce, i.e. the number characterise the "visual impairment potential" of a given lesion. Marshall also introduces a different set of scores for the case of non-haemorrhagic vs. haemorrhagic lesions. For instance, a lesion in the paramacula region scores 20. Interestingly, "strikes" on the head of the optic nerve have a very low score of 5, as exposure rarely causes damage of any significance, because relatively little of the energy is actually absorbed in the nerve mass. However, a suprathreshold lesion between the fovea and the optic nerve head, which has the potential to disrupt the neuronal connection between the fovea and the optic nerve, is scored relatively high, between 60 and 80. Exposure of the fovea scores 100.

The lidar risk model as discussed here was set up to characterise the probability for the development of a MVL as the type of injury. In terms of level of energy and types of injuries, beyond the MVL, further grades or severity levels of injury are not differentiated in the model. For instance, the laser parameters for a hypothetical lidar mission could be such that exposure with a 40 cm telescope would just produce a MVL, but exposure with a larger telescope can produce a haemorrhage. Both types of lesions would be counted as "injury" without further specification or interpretation of the severity of the injury. Haemorrhagic blood is absorbed in a few days and the location of the injury is more important in terms of the degree of vision loss than the depth and extent of the affected tissues. Also, the experimental data for other types of lesions than the MVL is extremely limited and associated uncertainties are very large[10, 11].

In terms of severity of the injury, the location of the (minimal) injury on the retina could be graded from "complete loss of central visual acuity" to "possibly unnoticed lesion in the outer periphery, practically no vision loss". However, from a public health standpoint of view, any retinal injury is to be avoided. Therefore, the location of the lesion is not specifically modelled. This constitutes a somewhat conservative, worst-case approach, since for the case that the lidar satellite is not intentionally viewed, exposure of the periphery of the retina, for which vision loss might be on a negligible level, is much more likely than exposure to the fovea or macula: the apparent FOV of high quality wide angle eyepieces can be larger than 80°, the apparent FOV of simple eyepieces is usually not less than 45°. This is considerably larger than the angles subtended by the fovea (and it should be noted that the probability relates to the ratio of the solid angle, and hence to the square of the ratios of the angles as given).

3. PROBABILISTIC MODEL BASICS

3.1 Dose-Response Curve

In such laser injury threshold experiments, a number of exposures are delivered to the eye or the skin for a given laser wavelength, pulse duration and spot size at the target site (for instance the retina) while varying the energy per pulse or the cw laser power. After each exposure, the exposed site is examined to see whether or not it develops a detectable lesion (an injury). In simplified terms, the threshold for damage is that level of exposure where exposures above the threshold leads to an injury (or more generally to some defined effect), and exposure to below that value does not induce an injury. As the exposed site is either damaged or potentially otherwise altered, one site can only be exposed once with a given pulse energy or power, and therefore a range of sites per animal and also a number of animals have to be exposed to determine the threshold. Generally it is found that there is not a sharply defined threshold exposure value below which no injuries occur and above which all exposures lead to damage. Rather, when a number of exposures are performed with a certain given exposure level, it is found that some of the exposures lead

to lesions, while others do not result in a lesion. By dividing the number of exposures where a lesion was detected with the total number of exposures for the given exposure level, a percentage figure for the 'response' is calculated for each exposure level (the 'dose'). Such a response percentage number is determined for a range of discrete exposure levels (but always with the same wavelength, exposure duration and spot size) thereby constituting a dose-response curve. The spread of threshold values characterizes the spread of sensitivities for the different exposure sites and animals, as well as some level of uncertainty[12]. The percentage axis of the dose-response curve can be transformed into probability units of 'probits' after a statistical analysis developed for toxicology [13, 14] which makes a straight line out of the curve shown in Fig. 1, and therefore the dose-response plot is also often called 'probit plot'. The exposure dose at which 50 % of the exposures lead to a lesion is called 'Effective Dose 50 %' or ED-50. The ED-50 is generally chosen and referenced as representative point of the dose-response curve and is also referred to as the 'threshold', even though there is a finite probability for damage at exposure energies somewhat below the ED-50.

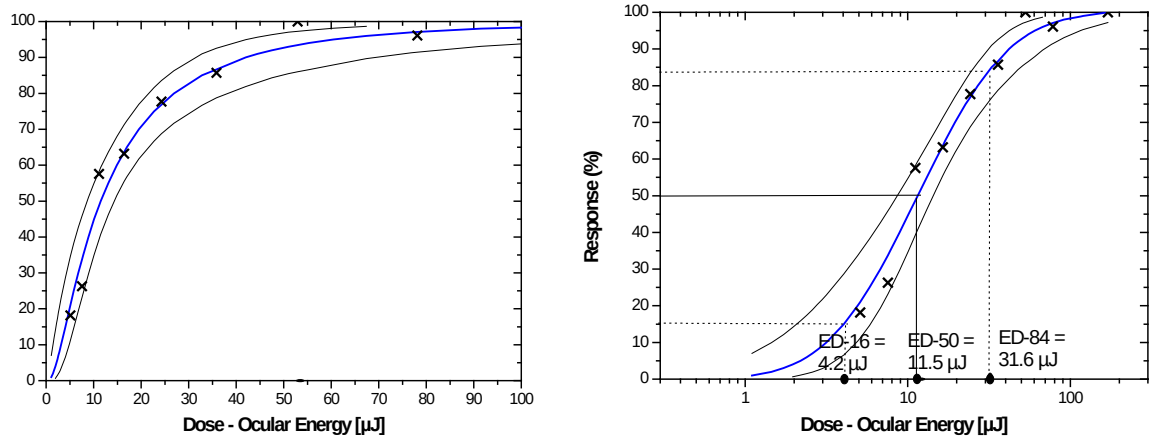

Fig. 1 Dose-response curves as obtained from 191 exposures of rhesus monkey retinas to 850 nm, 180 ns laser radiation (private communication J. Lund). The data points (x) are derived by binning of the experimental data into energy intervals and by plotting the resulting relative frequency data for the response between 0 and 100 %. For instance, if 12 exposures were to fall in a given energy interval or bin, of which 4 showed a response, the relative frequency for response for this bin is 33 %. The thinner lines are the result of a regression with 95 % confidence intervals, where a log-normal cumulative distribution is assumed.

The formula for the cumulative log-normal distribution is given by

$$P(OE) = \frac{1}{\ln(S)\cdot\sqrt{2\pi}}\cdot\int_0^{OE}\frac{1}{x}\cdot\exp\left[-\frac{\left(\ln(x)-\ln(ED50)\right)^2}{2\cdot\ln(S)^2}\right]dx = 0.5+0.5\cdot erf\left(\frac{\ln(OE)-\ln(ED50)}{\sqrt{2}\cdot\ln(S)}\right) \quad (1)$$

where OE is the ocular energy (dose), *erf* is the error function, which is tabulated for instance in Abramowitz and Stegun[15], and is also incorporated in many modern mathematical software packages. ED50 is the median dose, i.e., the dose at which 50 % of the exposures result in a response (a detectable lesion). Correspondingly, the dose at which 16 % and 84 % of the exposures result in detected lesions are referred to as ED16 and ED84 respectively. S is the slope, defined as

$$S = \frac{ED84}{ED50} = \frac{ED50}{ED16} \quad (2)$$

When the dose-response curve is obtained from a number of exposures to animals in an experiment, the response scale is defined as relative frequency, i.e. total number of exposures producing an effect with a given dose, divided by observed lesions. When a log-normal distribution is fitted to the data, this function can be interpreted as characterising the probability that an exposed individual will have a threshold less than the dose under consideration, i.e. will suffer an injury for a given dose.

The dose-response curve describes an observed distribution that has a spread whose range might be due to two sources of dispersion. One is solely due to variability, and the distribution gives the probability that an individual will have their threshold lower than the dose under consideration. Thus the probability is in respect to what damage threshold the exposed individual and exposed site has. Each individual or site has a given specific sharp threshold, and each time the threshold is exceeded, injury occurs. For this pure sense of variability, for each exposure to a given individual and a given site with a given (known) threshold dose, there is no randomness in the response. The dose-response curve in the sense of biological variability represents the fraction of the

population where a given dose produces a lesion, hence in this sense, the term "frequency of response" is more appropriate than the term "probability of response". For instance if the frequency of response, calculated from the dose-response curve, is 10^{-4}, this means that it is expected that in a population of 10 000 there is one individual who has a threshold lower than the respective dose. An interpretation of the ordinate as probability is possible, in the sense of the probability that exposure occurs to an individual who has an individual threshold lower than the dose under consideration. It is pointed out that this interpretation is substantially different than considering the formation of each lesion for a given threshold as stochastic, in the sense of the probability that a thrown dice shows 6. When a dose-response curve is used in the mathematical sense without considering the background of biological variability, it might be erroneously interpreted to characterise a stochastic probability in the sense of "let's throw a coin, does a lesion develop or not". Rather, once the threshold for the specific site and individual and the exposure level is known, the formation of a lesion can be even considered in a deterministic way, at least for non-ultrashort pulses.

Besides this interindividual variability, there is another source of variation, which arises because some laser injuries might be induced by stochastic mechanisms. For example, in cases of exposure to ultrashort pulses where the development of optical breakdown might play a role, the probability has the sense of an uncertainty for damage to develop for each exposure of a given individual. Thus, for each specific member of the population and for a given exposure level and site, there is a certain stochastic probability that an injury will occur, like flipping a coin for each exposure.

One main source of an increased spread of the observed distribution is the uncertainty associated with the experimental techniques, including systematic errors. These experimental uncertainties are discussed in more detail by Sliney et al[12]. The dose-response curve, as discussed in previous sections, describes the variability of the sensitivity within the population. Such a curve can also be used in quantitative risk analysis, where usually a log-normal cumulative distribution is used, and the parameters to be specified for the model are the ED50 and the slope S.

3.2 Experimental Human Data

Animal experiments give ED50 values that are generally lower than those for the few studies where human volunteers were exposed. In particular, Ren-yuan[16] reported for experiments on human Chinese retinas for 150 µs 1.06 µm radiation a factor 1.8 higher for human vs. grey rabbit and a factor 6 for human vs. rhesus monkey. Vassiliadis[17] reported a factor for human vs. rhesus monkey of about 3 for 100 ms 488 nm radiation, a factor greater than 10 for 200 µs 694 nm, a factor of greater 3 for 20 ns 694 nm, and a factor of greater 10 for 30 ns 1.06 µm radiation (the experimental data for humans are rather limited and were not sufficient to perform a probit analysis). Gabel[18] compared ED50 values of chinchilla rabbits to those obtained from human volunteers and obtained a factor of 4 for 488/514 nm 20 ms radiation. In summary, it seems that the higher ED50 values obtained for human exposure, depending on the experimental protocol used to determine the animal dose-response curves, either provide a safety margin or compensate for less sensitive experimental animal protocols. Generally, rhesus monkeys provide a good model for human exposure. However in terms of variability and uncertainty of the variability, i.e. uncertainty of the ED50 and slope and of the shape of the dose-response curve for small probabilities, additional sources of uncertainty, such as varying spot sizes due to focussing errors, need to be considered.

3.3 Relation of MPE to ED50

Obviously the ED50 cannot be considered as a safety threshold, as it is defined as the dose at which 50 % of the exposures lead to injuries. The MPEs are based on the ED50, and consideration of the slope and other factors, and are set at some level below the ED50 so that there is no realistic chance of injury at the MPE. The ratio of ED50 and the MPE is called safety factor. Following Sliney et al.[12], for retinal limits, this factor is most often taken as one order of magnitude, and based upon:

- the level of uncertainty in the data,
- a review of the experimental details and examination of sources of potential error,
- the differences between animals and humans,
- the level of understanding of the injury mechanism and
- the knowledge of biological sequelae.

The slope of the probit plot is also considered in recognising the overall uncertainty and quality of the experimental data, but it does not reflect all of the above factors. In addition to experimental uncertainties, the committees of experts adjust the MPE values to minimise complexity and do not attempt to mimic every spectral and temporal variation in threshold. In terms of dependence on the wavelength and the pulse duration, the MPEs when compared to the biological data, i.e. the respective ED50 values, often are simplifications (for instance

constant sections) and do not follow the detailed dependencies of the ED50. Correspondingly, the safety factor also varies over considerable ranges from less than 10 to several orders of magnitude.

The lidar risk model is directly based on experimental data of ED50 and slope but considers systematic errors and uncertainties of these values.

4. LIMITATIONS OF PROBABILISTIC MODELLING

4.1 Grouping of Individual Dose-Response Curves

Experimental slope values for "surface" laser injury such as to the cornea or the skin, are usually about[19,20] 1.1. Such a slope would characterise a distribution where 68 % of the distribution lies within a dose range of approximately ± 10 % around the median point, the ED50. Since the deposited energy, and hence the exposure dose, necessary to produce a given temperature rise depends directly on the absorption, biological variability of the absorption will also result in variability of the threshold, and this is reflected in the dose-response curve. For retinal exposure, the biological variability of the absorption within one macula for the smallest image spot size is of the order of[21] ± 5 % to ± 20 %, which would correspond to a dose-response curve slope of about 1.05 to 1.2.

As discussed in Sliney et al.[12], refractive errors during experiments with anaesthetized animals introduce an additional spread of the threshold data, as retinal spots that are larger than intended result in an erroneously high threshold. For the situation of an awake human, where refractive errors are usually corrected and where the eye "automatically" attempts to produce a focussed image, i.e. a minimal spot, only the dose-response curve for the minimal spot size appropriately characterises the risk for exposure to a collimated laser beam. When the experimental dose-response curve is biased by animals with refractive errors, the resulting ED50 and slope values need to be reduced correspondingly. In this sense, when applied to the human case, the influence of the variation of the experimental animal's refraction needs to be treated as bias or uncertainty, not as biological variability.

4.2 Correlation of ED50 and Slope for Pooled Data

Whenever data are pooled from a group of animals where the intra-individual variability is small but there is some inter-individual variability, the overall dose-response curve will have a larger slope S (i.e., the dose response curve is shallower) and a higher ED50 value as would be applicable for the most sensitive individual. Also the log-normal dose-response curve as implied in probit analysis of data might not be the appropriate distribution to characterise the frequency of response, especially for doses outside the region of the single multiplicative standard deviation, i.e. outside the dose range ED16 to ED84. Systematic errors such as from refractive errors of the experimental animal can be factored into the model for by reducing both the ED50 and the slope.

4.3 Small Probabilities

In the field of quantitative risk analysis and management, acceptable risk levels are often of the order of 10^{-6} per exposure or less, and scenarios are often evaluated where a larger number of people may be exposed. As a result, probabilities of injury often need to be calculated for doses far below the ED50.
The simulation of the pooling of experimental data showed that for the case of a small intra-individual variability but a certain inter-individual variability in a given population, it is not appropriate to extend the (shallow) log-normal dose-response curve to doses lower than about the ED10. However, even for the case where there is little experimental uncertainty and individual variability, or if the overall dose-response curve is corrected by reduction of the slope and correspondingly the ED50, the uncertainty associated with the lower-dose part of the dose-response curve is substantial. The dose-response curve cannot be determined experimentally for such low probability values and in practice cannot be determined, as tens of thousands of weak exposures would be needed (compare the "megamouse experiment"[14]). Finney[13] states that "…very extreme probits, say outside the range of 2.5 to 7.5, carry little weight, and may almost be disregarded unless many more subjects were used…" Probit values of 2.5 and 7.5 correspond to probabilities of about 1 % and 99 %, respectively. It has to be kept in mind that the log-normal dose-response curve describes the biological variation of the sensitivity of different individuals and of different locations of exposures for one individual (for instance different regions of the retina). Applying log-normal dose-response curves down to ever decreasing doses would imply that laser radiation of any level could cause injury, i.e. in a small but finite fraction of the population, be it 1 in a billion or less. However, for the case of thermal damage, simple biophysical reasoning shows that energy levels which do not result in a temperature increase of more than, say, 1 °C, cannot produce an ocular injury. If they did, the temperature elevation of 1 °C typical in a mild fever would cause blindness.

Following biophysical reasoning, for thermally induced damage, there will be a lower cut-off energy, below which injury is not possible, not even for the most sensitive individual. Also for acute photochemical damage, there is a minimum dose which is necessary to produce a lesion. For PRA, this could be modelled by truncating

the dose-response curve at a certain dose, i.e. setting the dose-response curve to zero below a certain ocular energy or exposure value. At present, the knowledge about this lowest possible dose is not sufficient to define such a truncated dose-response curve, but one could model the cut-off point with a probability distribution and perform Monte-Carlo simulation. However, in the PRA model discussed here, this was not done, as the application of steep slopes results in a marked decrease of the probability for damage for very small dose values, in effect similar to a cut-off. For instance, for a slope of 1.1, the calculated probability for the dose value of one 5^{th} of the ED50 is $5 \cdot 10^{-64}$ and for the dose of one 10^{th} of the ED50 could not be calculated with the mathematical software available, but is less than 10^{-100} (see Tab. 2). Considering that the dose-response curve in the sense of biological variability represents the fraction of the population where a given dose produces a lesion, probability numbers less than the reciprocal of the world population do not make sense.

Tab. 2 Sample values for the log-normal cumulative distribution for a list of slopes, for dose values of a factor 10 and 5, respectively, below the ED50.

slope	Probability for one 10^{th} of ED50	Probability for one 5^{th} of ED50
1.1	< 1E-100	5E-64
1.15	5E-61	7E-31
1.2	9E-37	6E-19
1.25	3E-25	3E-13
1.3	9E-19	4E-10
1.4	4E-12	9E-07
1.6	5E-07	3E-04
1.8	5E-05	3E-03
2	5E-04	1E-02

5. SECOND ORDER RISK MODEL

A quantitative risk model was developed to predict the probability for ocular injury upon exposure to pulsed laser radiation. The ocular damage model is based on log-normal dose-response curves, and uncertainties associated with the parameters of the dose-response curve, i.e. the ED50 and the slope, are modelled by sampling these values from probability distributions and calculating the probability of response for a given laser ocular energy for each sample. A PRA model, where the uncertainty and variability are modelled separately, is termed second order[22].

The probability distributions for the ED50 parameter, with wavelength and pulse duration dependence, where applicable, are derived from values as reported for rhesus monkeys, and for the corneal damage thresholds for rabbits. For retinal injury, the potential bias of the reported dose-response curve due to experimental uncertainties, such as focussing errors, were considered by using the lowest reported ED50 values as an upper border of the range of ED50 values, and setting the lower range of ED50 values a factor of 2 below the upper border. The slope S is set to vary between a value of 1.05 and 1.4, in correlation with the range of ED50 values, i.e. for the lowest ED50 value a slope of 1.05 is chosen and for the largest ED50 value, a slope of 1.4 is chosen. The distributions of ED50 and slope values are taken as uniform, i.e. with equal probability between the lower and upper possible values. The slope of the retinal dose-response curve for doses below about ED10 should be set to steep values, for instance of the order of 1.05 to 1.2. In the model the range of 1.05 to 1.4 is generally used for the dose-response curve, thereby somewhat overestimating the risk for the case of exposure to small doses. However, for the scenario of space based lasers, the exposure level of the naked eye at the earth surface is usually well below the ED50, and only for exposure with (large) telescopes, is energy sufficiently collected to cause ocular injury collected. The probability for exposure with a telescope with a relatively small field-of-view is quite small. The overall probability for ocular injury during a given mission is dominated by the probability of exposure with that type of telescope, which has the smallest diameter that results in a high probability of ocular damage (close to 1). For this kind of scenario, the overall risk numbers are not sensitive to the shape of the dose-response curve towards the low dose range. This part of the dose-response curve might, however, become relevant for a scenario where a large number of people is exposed to laser radiation and the exposure level with the naked eye is in a range closer to the lower range boundary of the ED50.

5.1 Format and Interpretation of Results

The uncertainty of the ED50 and slope is simulated with the Monte Carlo technique, where random numbers are calculated for a given distribution of possible values so that the relative frequency of the calculated values correspond to the respective probability distribution. These lists of values for the parameters of the model are

used to calculate the output parameter, such as the probability for ocular damage for a given ocular energy. A histogram of the values for the end result represents the distribution of values for the output parameter under consideration. The general scheme is visualised in Fig. 2, starting with the log-normal dose-response curve with a certain slope and ED50, where for a given ocular energy value, a single value for the probability for response can be identified (Fig. 2 (a)). For instance, a value of 0.78 for an ocular energy of 8 µJ. This is the level to which probabilistic models for ocular laser injury previously have been taken. When the parameters ED50 and slope are treated as uncertain, corresponding probability density distributions are defined (Fig. 2 (b)), which vary the ED50 and slope, and thereby the shape and location of the dose-response curve in a given range (Fig. 2 (c)). When the probability for ocular damage is to be determined for the ocular energy E_0, then instead of a single point for the probability for ocular damage, a frequency distribution for the probability for ocular damage is found (Fig. 2 (d)), representing the cumulative distribution of dose-response curves over the range of probability for ocular damage values, for a given ocular energy.

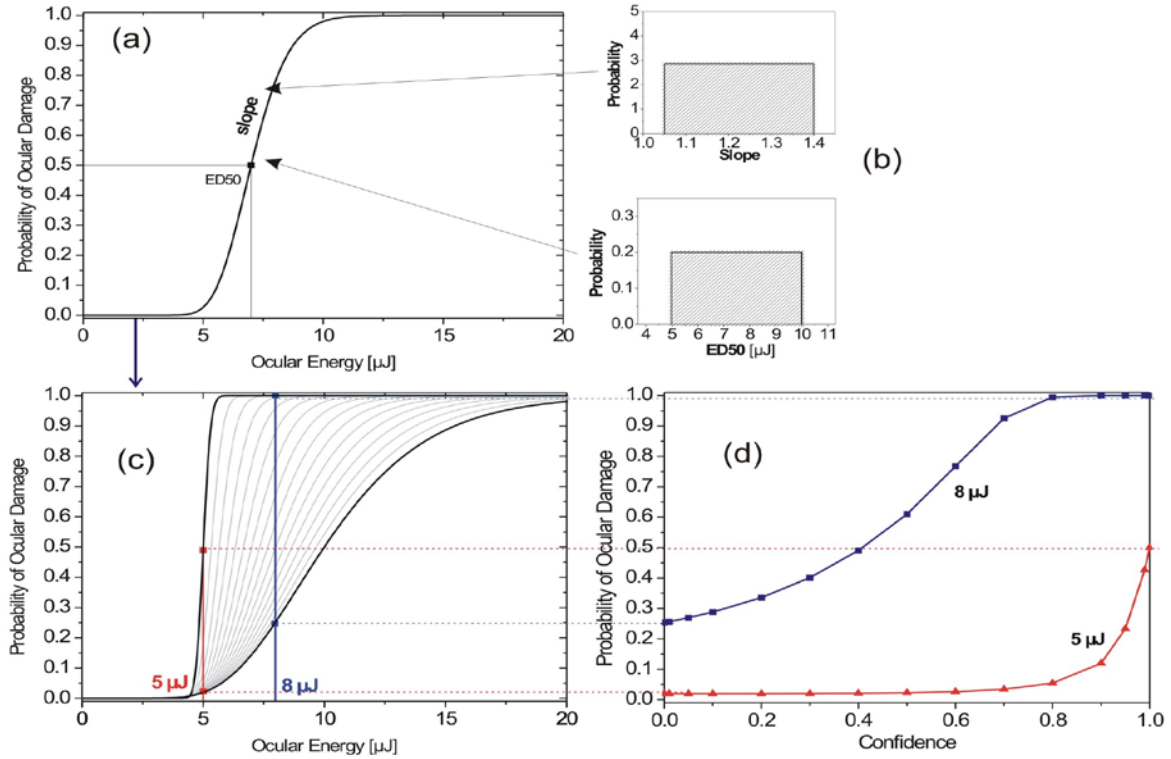

Fig. 2 Schematic overview of the calculation of a distribution characterising the probability for ocular damage given an exposure to a certain energy (a), and given a certain uncertainty of the shape parameters ED50 and slope S (b). The arbitrary values of 5 µJ and 8 µJ are taken as examples for the ocular energy for which the distribution of the probability for ocular injury values is plotted in (d).

By simulating the possible range of values for ED50 and slope, the single point value for the probability for ocular damage for a given energy (Fig. 2 (a)) is replaced by a distribution (Fig. 2 (d)). The result of the probabilistic analysis with uncertainty, Fig. 2 (d), is usually flipped regarding the axis and plotted with the confidence level on the ordinate and the risk figure, i.e. the probability for ocular damage, on the abscissa, as shown in Fig. 3 for a range of ocular energies. For the example shown in Fig. 3, a variation of ED50 between 5 µJ and 10 µJ and a variation of the slope between 1.05 and 1.4 for ocular energies between 0.5 µJ and 10 µJ was simulated. These values apply for instance to an exposure to radiation with a wavelength of about 900 nm and pulse durations between about 10 ns to 50 µs radiation with a minimal retinal spot diameter.

For plots resulting from the modelling of uncertainty, as shown in Fig. 3, the ordinate can be interpreted as the "confidence level" for the probability of ocular damage for a given ocular dose. The confidence level can best be explained by an example: in Fig. 3, with a confidence level of 95 % (the 95 % quantile), the probability for ocular damage, given exposure, to 5 µJ, is less than or equal 0.23, or 23 %. In other words, there is a 5 % chance (100 % minus 95 %) that the probability for ocular damage is larger than 23 %.

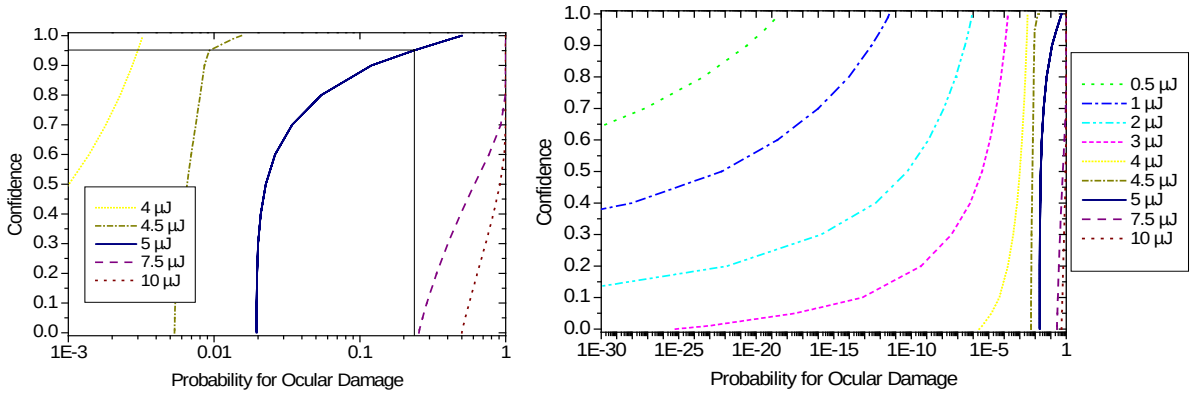

Fig. 3 Probability distributions for the probability of receiving ocular injury for a range of ocular energies (for a given wavelength and pulse duration). The right plot includes ocular energies well below the range of ED50, while the left plot covers a smaller range of probability values.

The level of confidence which is used to determine the value on the ordinate is usually a choice by the risk management. The higher the required level of confidence, the higher the calculated risk numbers become. For instance, if the choice for the level of confidence is 95 %, then one can be 95 % confident, that the probability for ocular damage is less than or equal 25 % (and there is 5 % probability that that the probability for ocular damage is larger than 25 %). The 95 % quantile is often used for environmental studies and other risk analysis studies where uncertainty is modelled[23]. The European Space Agency defines a representative quantity of the distribution, called "potentiality" (Pot), as the logarithmic mean between the 95 % quantile (q95) and the 50 % quantile (q50).

$$Pot = 10^{\frac{\log(q95)+\log(q50)}{2}} \qquad (3)$$

The intention for the definition of this quantity is to account for both the tail of the distribution towards higher risk numbers as well as the median of the distribution. The model as developed calculates the full set of quantiles, and it is the choice of the user which quantile is used to derive a risk number.
As expected, when exposure to doses within the modelled range of ED50 is considered, the probabilities at the 95 % quantile are high, but decrease for ocular energies which are below the lower border of the range of ED50s. For instance, in Fig. 3, for 1 µJ (a factor 5 below the lower boundary of the ED50 range and a factor 10 below the upper boundary of the ED50 range) the probability for ocular damage at the 99th quantile is less than 10^{-11}. It should be noted (and can be seen in Fig. 3) that the distributions for ocular energies below the ED50 range do not have an upper tail towards higher risk values, i.e. the risk hardly increases for levels of confidence above the 95th quantile, and one can have a confidence level of 100 % that the probability for ocular damage is less than or equal to instance 10^{-11} for the ocular energy of 1 µJ.

The above calculations where obtained for a given specified (single point) value for the ocular energy. In the model as developed for exposure from space based lasers, the ocular energy varies for instance due to scintillation, which is stochastic effect, but there is also variability within the population regarding optical transmittance of the instrument, or varying atmospheric transmittance. For such a case of uncertainty and variability of the ocular energy, the resulting probability distributions for ocular damage might show a shallower tail towards higher risk numbers.

6. CONCLUSIONS

A review of published threshold data and a consideration of systematic errors shows that there is considerable uncertainty associated with the values for a given wavelength, pulse duration and spot diameter. A PRA model for ocular injury was developed based on log-normal dose response curves to describe the variability of the thresholds within the population, however, the model parameters ED50 and slope where reduced in respect to the range of identified data to correct for systematic errors. This correction results in an increase of the probability for ocular injury for energies around the ED50 and above but in a drastic increase of the probability for low energies. For a quantitative risk model, the uncertainty associated to the model parameters need to be accounted for by Monte Carlo simulation, resulting in a second order PRA model.

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