Lowered threshold energy for femtosecond laser induced optical breakdown in a water based eye model by aberration correction with adaptive optics

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Abstract: In femtosecond laser ophthalmic surgery tissue dissection is achieved by photodisruption based on laser induced optical breakdown. In order to minimize collateral damage to the eye laser surgery systems should be optimized towards the lowest possible energy threshold for photodisruption. However, optical aberrations of the eye and the laser system distort the irradiance distribution from an ideal profile which causes a rise in breakdown threshold energy even if great care is taken to minimize the aberrations of the system during design and alignment. In this study we used a water chamber with an achromatic focusing lens and a scattering sample as eye model and determined breakdown threshold in single pulse plasma transmission loss measurements. Due to aberrations, the precise lower limit for breakdown threshold irradiance in water is still unknown. Here we show that the threshold energy can be substantially reduced when using adaptive optics to improve the irradiance distribution by spatial beam shaping. We found that for initial aberrations with a root-mean-square wave front error of only one third of the wavelength the threshold energy can still be reduced by a factor of three if the aberrations are corrected to the diffraction limit by adaptive optics. The transmitted pulse energy is reduced by 17% at twice the threshold. Furthermore, the gas bubble motions after breakdown for pulse trains at 5 kilohertz repetition rate show a more transverse direction in the corrected case compared to the more spherical distribution without correction. Our results demonstrate how both applied and transmitted pulse energy could be reduced during ophthalmic surgery when correcting for aberrations. As a consequence, the risk of retinal damage by transmitted energy and the extent of collateral damage to the focal volume could be minimized accordingly when using adaptive optics in fs-laser surgery.

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rate for multiphoton ionization which scales with $I^k$, where $I$ is the irradiance and $k$ is the and tunnel ionization [7]. The rate of nonlinear photoionization is likewise composed of the and corresponding Keldysh parameters around 1 is composed of both multiphoton ionization numbers of photons required for multiphoton ionization, and the rate for tunnel ionization which scales with $I^{1/2}$ [7]. For a diffraction limited irra diance distribution the overall electron density is therefore restricted to a small volume within the focal region [7]. In the presence of aberrations however, the plasma is not primarily formed in part of the focal volume but is can be quite large [3]. Theses aberrations originate mainly from the light passage through distort ing ocular media, especially the cornea and the crystalline lens, but can additionally be introduction depending on the application. For example, an oblique passage of the laser beam realizable as aberrations distort the wave front [2]. These aberrations can originate from numerous sources beginning at the laser system, to the optical pulse delivery system including focusing optics and contact glass plates, to the treated eye itself.

While a large extent of the system aberrations can already be minimized during optical design and alignment, the variation in aberration structure and image quality of human eyes can be quite large [3]. Theses aberrations originate mainly from the light passage through distorting ocular media, especially the cornea and the crystalline lens, but can additionally be introduced depending on the application. For example, an oblique passage of the laser beam through the ocular media during microsurgery in the ocular periphery can contribute to the overall aberrations [4].

During ophthalmic surgery large numerical apertures are advantageous because the threshold irradiance for optical breakdown can already be surpassed at lower pulse energies (considering laser powers below the critical power for self-focusing) [5]. Generally, less applied energy reduces the risk of damage to the retina by transmitted energy. However, in typical eyes the highest numerical aperture at the largest pupil diameter also implies the highest aberrations and the worst point spread function [6]. An ideal eye limited only by diffraction shows the smallest spot size or point spread function on the retina for the largest diameter of the pupil, which is 7-8 mm for a dilated eye (or less for older eyes), whereas the best result in typical eyes afflicted with aberrations can be accomplished for a pupil diameter of 2-3 mm [6]. The distorted irradiance distribution causes higher breakdown threshold pulse energies and also influences the site, form, and length of the plasma for nanosecond laser pulses [4].

Any tissue modification by shock wave and cavitation bubble processes or low-density plasma effects originates from locations where a critical electron density of the plasma is exceeded. The plasma is created by photoionization and avalanche ionization, whereas photoionization at irradiances in the range of $10^{13}$ W/cm$^2$ as required for optical breakdown and corresponding Keldysh parameters around 1 is composed of both multiphoton ionization and tunnel ionization [7]. The rate of nonlinear photoionization is likewise composed of the rate for multiphoton ionization which scales with $I^k$, where I is the irradiance and k is the number of photons required for multiphoton ionization, and the rate for tunnel ionization which scales with $I^{1/2}$ [7]. For a diffraction limited irradiance distribution the overall electron density is therefore restricted to a small volume within the focal region [7]. In the presence of aberrations however, the plasma is not primarily formed in part of the focal volume but is distributed according to the distorted point spread function [4]. This reduces the precision of optical breakdown, increases the required pulse energy, and also increases the amount of transmitted pulse energy with a generally higher risk of damage imposed on the retina [4].

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The required higher electrical field amplitude additionally increases the influence of competing nonlinear side effects to the optical breakdown such as self-focusing [8,9].

The considered influences of aberrations on LIOB and their consequences for retinal safety during ophthalmic surgery show the requirement for aberration correction. Additionally, in investigation of optical breakdown an aberration correction could enhance the understanding of the physical processes. A diffraction limited focus would eliminate one factor deteriorating the fundamental determination of the breakdown threshold in e.g. water which is an established medium for modeling eye tissue [10,11].

In vision science, where images of or stimuli to the retina also suffer from poor quality due to aberrations, adaptive optics (AO) is an established method for aberration correction to a diffraction limited point spread function [6,12–15]. Ophthalmic surgery and investigation of optical breakdown could benefit from developments in this field by combining adaptive optics for ophthalmic applications with a femtosecond laser surgery system. Benefits could also arise from femtosecond laser micromachining where spatial beam shaping with adaptive optics to e.g. top-hat or doughnut shapes enables customized material modifications [16].

The purpose of this study was to show a decrease in threshold energy for optical breakdown when correcting for aberrations with adaptive optics. We investigated the influence of aberrations from the laser system, the optical pulse delivery system, and a model eye on the optical breakdown in comparison to the diffraction limited beam. The investigation required the development of an optical system which combines adaptive optics for ophthalmic applications with a femtosecond laser system for ophthalmic surgery and investigation of optical breakdown in general. As a prerequisite the system needs to enable both the correction of aberrations and the detection of optical breakdown in a water based eye model which provides analogy to applications in ophthalmology.

For detection of optical breakdown experimental criteria include plasma luminescence, cavitation bubble formation, and transmission loss [7]. The determination of transmitted energy not only enables the detection of optical breakdown but also allows for conclusions regarding retinal safety considerations [17–20]. In case of LIOB, part of the incident energy is absorbed during plasma generation or is reflected or scattered at the plasma which causes a loss in transmitted energy. If less light is transmitted due to LIOB the potential risk of damage to the retina is reduced which is why this approach to LIOB detection was chosen for the present work.

Video imaging of the focal site was intended as a visual addition to LIOB detection by determination of transmitted energy. Imaging of femtosecond LIOB is typically aimed at either the plasma development itself or at the induced processes following LIOB, such as cavitation bubble formation and residual gas bubbles in liquids and soft tissues, or permanent material alterations due to photochemical, plasma-mediated accumulative thermal, or thermoelastic effects in tissues and solids. Due to their short duration with timescales in the femtosecond regime optical probing techniques (pump-probes scheme) are required to visualize plasma development [21]. For observation of cavitation bubble processes which last microseconds [22,23] e.g. time-resolved photography is necessary while gas bubbles show much longer life times and are visible in video sequences. Visualization in this study is therefore focused on video imaging of long-lasting gas bubbles, specifically the influence of aberrations on the threshold for gas bubble generation and on the dynamics of gas bubble motion.

A previous report by Vogel et al. [4] investigated the influence of aberrations on nanosecond LIOB by introducing additional wave front distortions of up to 18.5 λ with a resulting increase in breakdown threshold and plasma transmission. Our approach differs from that described in [4] in that we investigate the influence of aberrations on femtosecond LIOB not by introducing additional aberrations but by correcting any present aberrations including these which conventionally cannot be influenced, e.g. in the subject eye.
2. Methods

The experimental procedure for lowering the threshold energy for optical breakdown involves several different techniques. The basis for our investigation was the development of an optical system which combines an adaptive optics wave front correction with the delivery of femtosecond laser pulses from the source to the site of optical breakdown. To create an analogy to ophthalmic applications, a model eye was designed to allow for both aberration correction and detection of optical breakdown. Optical breakdown was verified by comparison of transmitted pulse energy to energy incident at the model eye. In the case of optical breakdown part of the pulse energy is absorbed or reflected at the plasma. Additionally, video images were acquired from the focal site where gas bubbles are generated in water.

2.1 Adaptive optics femtosecond laser instrument

The experimental setup of our adaptive optics femtosecond laser instrument (AOFL) is depicted in Fig. 1. The adaptive optics main components are a 1280 micro lenses Hartmann-Shack-sensor (HASO-32, Imagine Eyes, Orsay, France) and a 52-actuator electromagnetic deformable membrane mirror (mirao 52-e, Imagine Eyes, Orsay, France). The femtosecond laser (Spitfire Pro, Newport Spectra-Physics GmbH, Darmstadt, Germany) provides pulses for both aberration measurement and optical breakdown generation with a central wavelength of 795 nm and pulse length of 120 fs.

For aberration measurement, the pulses propagate twice through the system in a double-pass configuration. In the first pass, the pulses proceed into the model eye where they are focused on a scattering sample representing the retina. The backscattered light from the focus spot is considered a point light source which is used for aberration measurement. In the second pass, this backscattered light passes through the model eye where its aberrations are imprinted on the wave front. These aberrations are measured at the Hartmann-Shack-sensor to then numerically reconstruct the wave front. This allows for computation of commands to...
deform the surface of the deformable mirror in closed-loop operation such that it corrects for the wave front aberrations.

For optical breakdown generation the scattering sample is removed and the laser pulses are focused in water. Here, the laser pulses only have a single pass through the system but they share a common pass with the measurement light. Therefore the amount of non-common path errors is reduced and no additional chromatic aberrations are introduced. The shape of the deformable mirror surface, which in the measurement case enables a flat wave front at the sensor, provokes an initial rise in aberration as the wave front is pre-imprinted with the inverse of the model eye’s aberrations. After passing through the aberrated model eye media, however, the laser pulses come to a diffraction limited spot on the model retina.

The optical design further comprises two afocal telescopes which provide optical conjugation between the deformable mirror, the micro lenses of the Hartmann-Shack-sensor, and the pupil of the model eye. This ensures minimized fluctuations in signal intensity when the mirror surface is deformed. The telescopes also provide magnification such that the different apertures of sensor and actuator match a 7.3 mm pupil of the eye. The system entrance pupil diameter is then defined by the aperture of the Hartmann-Shack-sensor. Here, a telescope is used instead of an iris to adjust the laser output beam diameter to the entrance pupil in order to avoid diffraction which would compromise the irradiance distribution of the laser pulses for optical breakdown.

The telescopes are composed of lenses in order to avoid aberrations due to off-axis use of spherical mirrors and to reduce the complexity of the system. The drawback of using lenses is that even with an anti-reflection coating they show reflections which are several orders of magnitude larger than the reflections from the retina [24] and that femtosecond laser pulses show dispersion when passing through glass. To minimize the reflections there are three basic approaches [25]: The lenses can be used off-axis or tilted in the first pass so that the reflections do not reach the sensor. An iris can be placed in the focal point of the telescope to screen any off-axis reflection. And the signal can be separated from the reflection by using a quarter wave plate in front of the eye in combination with a polarizing beam splitter in front of the sensor. The double pass of light through the quarter wave plate causes the signal to have the orthogonal polarization to the reflections of the optics and the signal polarization can then be selected at the polarizing beam splitter. We incorporated the latter two approaches in our system. LIOB threshold energy is unaffected by changes in polarization [26]. The half wave plate before the beam splitter determines the pulse energy coupled into the system. The amount of dispersion was minimized by using achromatic lenses.

2.2 Model eye

An established method for investigation of optical breakdown in ocular tissue is the application of focused laser pulses in water as soft biological tissues contain a high amount of water (98% for vitreous body) and show a similar behavior during optical breakdown regarding breakdown threshold energy [10] even if photodisruption dynamics may differ [27]. Therefore our model eye for both adaptive optics aberration correction and investigation of optical breakdown is based on water. The schematic setup of the model eye is depicted in Fig. 2. The femtosecond laser pulses from the AOFL instrument are focused into a water chamber by an achromatic lens with 45 mm focal length in air which models the cumulative refractive power of the cornea and crystalline lens of the human eye. The lens is in water contact because air-glass-water interfaces of cuvettes generate a high amount of aberrations which additionally show a dependence on the cuvette-lens distance. As adaptive optics aberration correction relies on a signal of back scattered light from the focus the eye model cannot be based on water alone but needs a sample to model the scattering properties of the retina. Therefore, a polytetrafluoroethylene (PTFE) sample was placed in the focus for aberration correction (Fig. 2a). For optical breakdown generation the PTFE sample was removed and LIOB threshold was detected by transmission decrease (Fig. 2b).
During optical breakdown threshold measurements the deformable mirror was assigned the static surface deformation determined in the precedent closed-loop aberration correction. As with this method only static aberrations are corrected for during LIOB measurements, the amount of dynamic aberrations was determined over a period of 90 minutes for both the flat mirror surface (AO off) and the static deformed mirror surface after closed-loop aberration correction (AO on).

### 2.3 Optical breakdown threshold measurement

Optical breakdown threshold measurement was performed by detecting a decrease in transmitted energy due to absorption or reflection at the plasma [19]. The experimental setup is depicted in Fig. 3 (side view). The incident pulse energy was measured with a photodiode (PD10, Ophir Optronics, Jerusalem, Israel) in front of the model eye and compared to the transmitted pulse energy behind the water chamber. For each pulse energy value in the range from 0.4 µJ to 8.0 µJ 100 single pulses where applied with no more than 2 Hz to allow for a complete decay of the preceding event. The pulses were focused with an achromatic lens with 58 mm focal length in water and a numerical aperture of $NA = 0.08$, respectively. Transmission was defined as the ratio of transmitted to incident pulse energy $T = E_t/E_{in}$. Each energy value was computed as the mean of 100 single energy values. The measurement error for both incident energy $E_{in}$ and transmitted energy $E_t$ and their ratio is given by the standard deviation $\sigma$, the latter by $\sigma(E_t/E_{in}) = [(\sigma(E_t)/E_{in})^2 + (E_t\sigma(E_{in})/E_{in})^2]^{1/2}$.

Additionally, a camera (WAT-902H2 Ultimate, Watec Co., Ltd., Tsuruoka, Japan) with a macro objective (105 mm, Sigma, Aizu, Japan) was utilized to image the focal area from
For the camera images, pulse trains at 5 kHz were applied to use subsequent pulses to illuminate the preceding event, specifically by scattering and reflection at the gas bubbles generated in water. At this repetition rate only gas bubbles with life times above 200 µs can be detected. Furthermore, size and position of the gas bubble at the time of the subsequent pulse define whether the light is reflected in direction of the camera or remains undetected. For gas bubbles with size above the camera resolution (11 µm) a secondary white light source illuminated the focal area from above and allowed for detection of the bubbles via their shadow.

Image sequences of 200 frames for each energy value (corresponding to 4000 laser pulses) were acquired and analyzed with the image processing program ImageJ (National Institutes of Health, http://rsb.info.nih.gov/ij/). During analysis, the number of frames in which scattering from the focal site or from the surrounding gas bubbles occurred was quantified using the following image processing steps. First, the time series of images was converted into an image stack. The resulting image stack was resliced into orthogonal views. The orthogonal frame at the focus location provided a time profile of intensity levels. Levels above a distinct background level were counted as scattering events. Stray light from small particles drifting in the water was excluded by their low intensity. A sigmoidal curve was fitted to the data to allow for identification of 10%, 50%, and 90% probability range for a scattering event. Data is presented as ratio of observed frames with scattering events to total number of frames. An example for a frame with scattering event is shown in Fig. 8a and without scattering event in Fig. 8b. Furthermore, z-projections of each set of frames provided the maximum and minimum intensity of the events in the focal area. Maximum intensity allowed for the determination of any single illuminated event and minimum intensity portrays the gas bubbles via their shadow.

For both transmission measurement and camera images two cases were compared. The first case relates to a system which was well aligned using a Hartmann-Shack-sensor to ensure an optimized wave front after each element. Still, this case is referred to as the aberrated case because no adaptive optics correction was applied and therefore the aberrations from the model eye are present. The deformable mirror in this case is flat. The second case relates to a system after adaptive optics closed-loop correction and is referred to as corrected case.

3. Results

3.1 Adaptive optics

The adaptive optics system performance was analyzed for the model eye with the PTFE sample as a reflector. The result of the wave front measurement with the Hartmann-Shack-sensor and closed-loop aberration correction is given in Fig. 4 showing the reconstructed wave front before (left) and after (right) adaptive optics correction.

![Fig. 4. Aberration correction of model eye to diffraction limited wave front: eye model aberrations with 0.263 µm rms wave front error (left), wave front after adaptive optics closed-loop correction with 0.030 µm rms error (right).]
The aberrations of the model eye show a root-mean-square (rms) wave front error of 0.263 µm corresponding to λ/3 which is composed of 89% of high-order aberrations, therefore with a low amount of defocus and astigmatism. After adaptive optics correction the rms wave front error was reduced to 0.030 µm corresponding to a diffraction limited wave front. The corresponding point spread functions (PSF) are given in Fig. 5. The PSF of the corrected wave front (left) resembles the PSF of an ideal wave front (right) with only a negligible increase in diameter. The PSF of the aberrated wave front shows a substantial deviation from both the corrected and the ideal case with an increased spread of the intensity over a larger, non-uniform area. Corresponding Strehl ratios are 0.96 for the corrected case and 0.18 for the aberrated case.

The temporal variation of the dynamic aberrations is shown in Fig. 6 for a flat mirror surface (AO off) and a static deformed mirror surface (AO on). Please note that “AO on” does not refer to an active closed-loop operation but to a locked deformable mirror after closed-loop correction. The standard deviation of the wave front rms error is 6 nm for the flat mirror and 3 nm for the static deformed mirror.

3.2 Optical breakdown threshold measurement – single pulse transmission

The optical breakdown threshold measurement results for single pulse transmission are given in Fig. 7. The transmission of 120-fs laser pulses is given as a function of incident pulse energy for minimized aberrations with an rms wave front error of λ/3 (aberrated) and for aberrations corrected to the diffraction limit (corrected). Below the threshold energy both curves show a constant transmission of about 90%. At the threshold energy the curves show a drop and the transmission is reduced for higher pulse energies. The curve for the aberrated
wave front shows a smaller decline. The threshold energy is determined to be 3.4 µJ in the aberrated case and 1.1 µJ in the corrected case. This corresponds to a reduction in threshold energy by a factor of 3.1 when correcting for aberrations. Furthermore, the transmitted pulse energy above the threshold energy is reduced in the corrected case, e.g. at twice the threshold energy of the aberrated case the transmitted pulse energy is reduced by 17% when correcting for aberrations. Considering a diffraction limited focal spot, a beam waist radius of 4 µm was calculated using a NA = 0.08. At the threshold pulse energy of 1.1 µJ, the threshold radiant exposure is 2.2 J/cm² and the threshold irradiance is $1.8 \times 10^{13}$ W/cm². For the aberrated case, the Strehl ratio was used to estimate a threshold radiant exposure of 1.3 J/cm² and a threshold irradiance of $1.1 \times 10^{13}$ W/cm².

![Graph](image)

Fig. 7. Transmission of 120-fs laser pulses through water for adaptive optics aberration correction to the diffraction limit (diamonds •) and for conventionally minimized aberrations with $\lambda/3$ rms wave front error of model eye (crosses ×). The optical breakdown threshold energy was reduced by a factor of about three from 3.4 µJ in the aberrated case to 1.1 µJ in the corrected case. The transmitted energy above threshold is also reduced by aberration correction.

### 3.3 Optical breakdown threshold measurement – pulse trains

Figure 8 shows representative sample images of the focal site during application of pulse trains with and without adaptive optics correction for two different pulse energies. At 1.1 µJ pulse energy an adaptive optics correction enables intense reflection at the focus and the generation of small gas bubbles surrounding the bright center from preceding events (Fig. 8a). The same pulse energy does not suffice to create a visible effect for conventionally minimized aberrations with $\lambda/3$ rms wave front error of the model eye (Fig. 8b). At doubled pulse energy of 2.2 µJ the events in the AO corrected case show an increased extend with a larger size of the reflection at the focus and gas bubbles with increased dimensions which move an increased distance away from the focus (Fig. 8c). The extent of events at this pulse energy without adaptive optics correction is reduced with a small size reflection at the focus and small gas bubbles with less velocity (Fig. 8d).

The number of video frames which show scattering events from the focal site and from the surrounding gas bubbles is given in Fig. 9. The pulse energy with 50% probability for a scattering event was determined to be 1.1 µJ in the corrected case with diffraction limited wave front and 2.3 µJ in the aberrated case with $\lambda/3$ rms wave front error of the model eye.
The slope of the sigmoidal curve fitted to the data around threshold is much higher for the corrected than for the aberrated case and the 10%-90% probability range is reduced.

Fig. 8. Focal site of 120-fs laser pulse trains at 5 kHz in water. (a) Adaptive optics aberration correction enables generation of gas bubbles at 1.1 µJ pulse energy which in (b) is not sufficient pulse energy to create a visible effect for conventionally minimized aberrations. (c) Increased extent of gas bubble generation with adaptive optics correction at twice the pulse energy (2.2 µJ) which in (d) only enables a process with little extent for conventionally minimized aberrations. Laser incident from below.

Fig. 9. Scattering from the focal site and from surrounding gas bubbles for pulse trains at 5 kHz in water for adaptive optics aberration correction to the diffraction limit (diamonds *) and for conventionally minimized aberrations with λ/3 rms wave front error of model eye (crosses ×). Dotted lines indicate 10%- , 50%- , and 90%-event probability.

Depending on the state of focus aberration the gas bubble clouds show differences in extend and form which become more pronounced with higher energies. The development is shown in Fig. 10 as maximum intensity for the aberrated case (top row) and the corrected case (bottom row). All reflection events are shown as projection over 200 frames. In the aberrated
case the lateral extend of the process dynamics is much less pronounced than the axial extent. With rising pulse energy, the reflection events are increasingly spread along the optical axis. In the corrected case the lateral extent of the process dynamics is much more pronounced than the axial extent and reflection events are increasingly spread perpendicular to the optical axis with rising pulse energy. Both cases show a shift in focal position towards the laser incidence with rising pulse energy. Also, white light continuum generation is observed in both cases.

Figure 10. Maximum intensity: Process dynamics for conventionally minimized aberrations (top row) show little transverse extent but increasing axial expansion for high pulse energies. For aberration correction to the diffraction limit (bottom row), reflection events show an increased expansion perpendicular to the optical axis. Laser incident from below.

Figure 11 shows the development of process dynamics with rising pulse energy as minimum intensity for the aberrated case (top row) and the corrected case (bottom row). All reflection

Fig. 11. Minimum intensity: Gas bubble motion for conventionally minimized aberrations (top row) is restricted to a shorter path length than for aberration correction to the diffraction limit (bottom row) where longer pathways with predominant transverse direction are shown. Multiple bright points which always show reflection as e.g. for 7.02 µJ develop along the optical axis. Laser incident from below.
events and gas bubble shadows are shown as projection over 200 frames. In the aberrated case the gas bubble motion is restricted to a shorter path length and the direction is distributed equally around central bright points. With rising pulse energy, multiple bright centers develop which are distributed over an extended axial distance and e.g. for 7.02 µJ three major positions can be distinguished from which three rows of gas bubbles rise successively to the surface. In the corrected case, the gas bubble motion is directed mostly perpendicular to the optical axis and shows an increased path length. The multiple bright centers which develop along the optical axis for higher pulse energies are spread over a shorter distance than in the aberrated case.

4. Discussion

Our results confirm that the threshold energy for femtosecond laser induced optical breakdown and the transmitted energy are reduced when using adaptive optics to correct for wave front aberrations.

To investigate the influence of aberrations on optical breakdown threshold pulse energy we developed an adaptive optics femtosecond laser instrument which enables both the correction of aberrations and the detection of optical breakdown in a water based eye model. We found that a well corrected system and a model eye with minimized aberrations still show mostly high-order aberrations in the range of $\lambda/3$ which significantly influence the optical breakdown process.

4.1 Lowered threshold energy – single pulse transmission

In single pulse transmission measurements, the difference in threshold pulse energy for LIOB by a factor of three as compared to a diffraction limited wave front suggests that aberrations increase the focal volume and, thus, the pulse energy required for LIOB. It was found that an adaptive optics aberration correction reduces the threshold energy. The increased decline of the curve in the diffraction limited case indicates a sharper defined threshold when correcting for aberrations (cf. Fig. 7). With the application of a diffraction limited wave front it was possible to minimize one factor during optical breakdown generation which contributes to a raise in threshold energy. Next to aberrations, other distortive side effects such as self-focusing influence the plasma formation during optical breakdown generation. At focusing conditions with numerical apertures $NA \leq 0.9$ [28], which is generally the case in ophthalmic applications especially in the posterior eye segment, the pulse peak power required for optical breakdown is higher than the critical power for self-focusing [8,29], therefore self-focusing is present. At a NA of 0.08, self-focusing is expected to occur which was additionally confirmed by observation of white light continuum generation. The investigations presented here are aimed at ophthalmic applications accepting the consequences of low numerical apertures. However, the AOFL instrument could also be applied for high numerical apertures thus minimizing more side effects during optical breakdown next to aberrations.

The reduction in transmitted energy above threshold indicates that absorption during plasma generation is improved by spatial shaping of the irradiance distribution. The irradiance in the focal volume is distributed according to the point spread function (PSF). In the diffraction limited case only the central part of the PSF surpasses the irradiance threshold for LIOB. In the presence of aberrations the laser pulse power is spread over a larger area which requires a raised total irradiance to still surpass the threshold, especially since the absorption in water is nonlinear. Local peaks (or hot spots) in the irradiance can cause plasma formation before the breakdown threshold is surpassed in the entire focal volume [4]. Therefore, only a reduced fraction of the incident energy is absorbed in presence of aberrations as compared to a raised absorption for a diffraction limited focal shape. In the presence of dynamic aberrations, such as fluctuations in air or water, laser power in the local peaks could arbitrarily be increased or decreased. At irradiances close to threshold a small increase would cause LIOB generation whereas a small decrease would disable LIOB. This could explain the less sharp threshold in the presence of aberrations.
4.2 Comparison of experimental threshold data

When comparing experimental threshold values for LIOB in water, numerous values for threshold pulse energy, radiant exposure, or irradiance are available which depend on parameters such as wavelength, pulse duration, and numerical aperture, and which are additionally influenced by side-effects such as self-focusing and aberrations. An overview can be found e.g. in [7]. Best agreement in experimental parameters with respect to pulse duration and wavelength was found in [30], however, Schaffer et al. assumed the presence of spherical aberrations. The comparison of their values for radiant exposure of 5.64 J/cm² and irradiance of 5.64·10¹³ W/cm² with our values of 2.2 J/cm² for radiant exposure and 1.8·10¹³ W/cm² reveals lower threshold values in the present work. This reduction suggests that aberrations increase the pulse energy required for LIOB and decrease the volume with sufficient electron density for LIOB according to the PSF and that an adaptive optics aberration correction reduces the threshold energy. The threshold values presented here are presumably closer to the lower limit for LIOB in water even though self-focusing is present.

4.3 Lowered threshold energy – pulse trains

The difference in pulse energy with 50% probability for a scattering event as shown for pulse trains confirms the evidence from single pulse transmission measurements that adaptive optics aberration correction reduces the threshold energy. For a diffraction limited wave front the two measurement methods show good agreement, as both the threshold determined for single pulses and the threshold for pulse trains are at a pulse energy of 1.1 µJ. However, a difference in threshold was found for the aberrated wave front, where the threshold is at 3.4 µJ for single pulses and at 2.3 µJ for pulse trains. The increased slope of the sigmoidal curve in the corrected case indicates a sharper threshold when correcting for aberrations.

The reduction in threshold in the aberrated case for pulse trains as compared to single pulses is contrary to the anticipation based on the detection method. As the detection relies on reflections from the focal site and the generation of gas bubbles, the threshold determination is restricted to LIOB events that create a gas bubble (or several gas bubbles [31]) with life time above 200 µs which have not moved out of the laser beam path by the time of the next pulse(s) and to reflections in direction of the camera. Additionally, any reflected or refracted pulses will less likely create a LIOB. With less detected and less created LIOB events the threshold was expected to show an increase instead of a decrease. However, despite the unexpected threshold for pulse trains in the aberrated case, an improvement when correcting for aberrations was still shown. Future studies using time-resolved photography to determine optical breakdown with the creation of a cavitation bubble as criterion for threshold or using pump-probe experiments to investigate the plasma generation and consecutive effects could clarify the influence of aberrations on train pulses and determine a more reliable threshold value.

4.4 Long-lasting gas bubbles in LIOB processes

In an attempt to explain the reduction in threshold energy for pulse trains as compared to single pulses the existence of long-lasting gas bubbles at lower pulse energies could be attributed to low-density plasma effects well below the threshold for photodisruption. Note that – following the definition by Vogel et al. [7] – laser-induced optical breakdown describes the plasma generation by photoionization and the consequent avalanche cascade and therefore comprises both low-density plasma and photodisruption. The regimes are typically distinguished by onset of cavitation bubble generation as criterion for photodisruption which is associated with a specific electron density of the generated plasma (10¹⁸-10²¹ cm⁻³). The generation of gas bubbles can occur in both regimes. As described by Vogel et al. [7] gas bubbles with lifetimes of the order of a few seconds can arise in the low-density plasma regime for pulse trains in the MHz range due to accumulative effects from chemical dissociation of biomolecules into volatile, non-condensable fragments by free-electron chemical and photochemical bond breaking and plasma-mediated accumulative thermal
effects. The main driving force in bubble generation here is boiling and decomposition of biomolecules which may be supported by thermoelastic forces [7]. In the kHz regime, bubble formation starts at photodisruption threshold with thermoelastic stress-induced formation of minute transient cavitation bubbles which also result in gas bubbles, but these typically show a much shorter lifetime and size unless the pulse energy is increased well above threshold. However, at low numerical apertures in the presence of self-focusing Tse et al. [32] reported on long-lasting residual bubble generation at 3.8 kHz where size, lifetime, and dissolution dynamics of the bubbles depend on laser pulse fluence, total number of pulses delivered, and pulse repetition rate in water with low concentration of gelatin. The generation of a gas bubble can result either from crossing of the kinetic spinodal limit which is associated with a sharply defined threshold [33,34] or at reduced and less sharp threshold from the generation of inhomogeneous nuclei after disintegration of molecules below the superheat limit defined by the kinetic spinodal limit [7,35]. Here, tensile stress can reduce the vaporization energy [7,36] and gas bubble generation is supported by rectified diffusion in oscillating transient bubbles [7,37]. For pulse trains in the kHz regime with an aberrated wave front the gas bubble generation could be caused by inhomogeneous nuclei that follow the distribution of the hot spots in the irradiance and therefore only require a pulse energy below the threshold of single pulses. This is supported by the less sharp threshold. For single pulses the temporal pulse separation could be too long to enable accumulative low-density plasma effects. In the corrected case the processes are confined to a smaller volume in the focus where the sharper threshold could explain the agreement of threshold pulse energy for both pulse trains and single pulses (cf. Figs. 7 and 9).

4.5 Dynamics of long-lasting gas bubbles

The more pronounced lateral extend of the process dynamics perpendicular to the optical axis with increased path length and velocity suggests that the conversion of pulse energy into anisotropic or directional mechanical or kinetic energy is improved when correcting for aberrations. The further discussion of the process dynamics follows a phenomenological approach. For a supported conclusion regarding breakdown dynamics an observation with increased spatial and temporal resolution such as time-resolved photography or pump-probe experiments is required.

The distribution of multiple focus points axially allows for two possible conclusions. First, a filament could be formed with alternating self-focusing and plasma-defocussing causing the gas bubble generation in multiple focus points. The shift in focal position towards the laser incidence with rising pulse energy could support the presence of self-focusing but could also be attributed to moving breakdown according to the irradiance distribution. Second, the multiple locations of present gas bubbles could be caused by trapping of the low-index gas bubbles in a self-focused laser beam as observed by Ye et al. [38]. In the trapping procedure the bubble acts as a negative lens and refraction of the laser beam results in a force on the bubble towards the laser incidence and away from the focus. Ye et al. created a balance of the buoyant and the radiant pressure forces due to the laser incidence from below. For increased pulse energies the trapping of multiple bubbles at stable positions along the optical axis was observed. In the present work with a horizontal laser incidence the buoyant force will eventually draw the bubble out of the laser beam towards the surface, therefore the trapping cannot be stable. However, the subsequently generated gas bubbles could refill the void positions. This assumption is supported by the observed rise of rows of bubbles from multiple positions to the surface. This behavior was not observed in the corrected case which could be attributed to the improved conversion of pulse to kinetic energy [4,18].

A possible cause for the perpendicular orientation of the gas bubble motion could be the shape of the focal volume which in the diffraction limited case has an approximately ellipsoidal shape [39]. In general, plasma generation and cavitation bubble accordingly follow this ellipsoidal shape [18]. The major current during collapse of an elongated bubble is directed along the optical axis with two counter-propagating jets which collide in the center [40] and could then force the gas bubble to the lateral side. In the aberrated case the irregular
irradiance distribution with hot spots would cause a more random orientation of the current with a more random distribution of gas bubbles which could explain the observed more isotropic distribution.

4.6 Consequences for ophthalmic fs-laser surgery

The presented results allow for deducing several conclusions regarding ophthalmic fs-laser surgery. First, the lowered LIOB threshold pulse energy when correcting for aberrations suggests that the risk of retinal damage could be minimized because of the lowered incident energy. Less incident energy generally reduces the risk of retinal damage because both the total amount of possibly transmitted energy is limited and the extent of collateral damage to the focal volume is decreased. Second, the decrease in transmitted energy in the case of aberration correction as compared to the not corrected case for the same incident energy indicates an additional potential reduction in risk of retinal damage. As an increased fraction of the incident energy is absorbed during LIOB less energy can reach the retina. Third, the more transverse direction of the gas bubbles when using adaptive optics could be advantageous when performing surgery in close proximity to a sensitive interface such as the retina (provided that the dynamics in water relate to the dynamics in viscoelastic ophthalmic media). As the gas bubbles move mostly sideways they would not impact the retina which could also improve retinal safety. This advantage of aberration correction for fs-laser surgery also applies for other sensitive interfaces such as the lens capsule or Bowman’s membrane in the cornea.

The importance of aberrations and their influence on both LIOB and ophthalmic surgery has been stressed by many authors before. Fankhauser et al. acknowledged the advantages of fs-lasers over ps- and ns-lasers especially for potential vitreo-retinal surgery but they were convinced that aberrations form an insurmountable obstacle [41]. Based on their own investigation on the influence of aberrations on LIOB Vogel et al. concluded that minimizing aberrations is essential for clinical laser applications [4]. With the present work we are confident that the obstacle posed by aberrations can be overcome by using adaptive optics, which is especially beneficial for individual eye aberrations, and that an important step towards fs-vitreo-retinal surgery has been made.

5. Conclusion

Our AOFL instrument enables femtosecond LIOB in water with reduced threshold pulse energy and reduced transmitted pulse energy after wave front aberration correction. The spatial confinement with adaptive optics raises the irradiance at constant pulse energy. Less pulse energy is required to surpass the threshold irradiance for LIOB. Ophthalmic surgery could benefit from this development as the risk of retinal damage is reduced with both lowered applied and transmitted energy. A major advantage of the presented method is the ability to correct any present aberrations including these which conventionally cannot be influenced, e.g. in the subject eye or caused by an oblique passage of the laser through ocular media.

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