Effects of polarization, plasma and thermal initiation pathway on irradiance threshold of laser induced optical breakdown

Corso di Laurea Magistrale in Ingegneria Biomedica

Master of Science Thesis

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~ Confidential ~

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Declaration of the Master Thesis

I warrant that the thesis is my original work and that I have not received outside assistance. Only the sources cited have been used in this draft. Parts that are direct quotes or paraphrased are identified as such.

Eindhoven, ______________________________

Date

____________________________

Signature
All’Amore tra Mamma e Papá,
che non è mutato quando ha trovato mutamento.

Ho visto entrare una donna
con gli occhi bendati
e nelle mani teneva
tutti i miei desideri.
Lei mi porta lontano la mente,
nel gradino più stretto del cielo.

{ Le Orme }
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The development of laser based skin rejuvenation techniques has significantly increased in recent years. However, the presently available ablative and non-ablative methods for skin rejuvenation typically balance between efficacy, safety, social downtime and pain perception [1]. Highly effective ablative techniques are characterized by long recovery time and significant risk profile whereas the non-ablative methods, safer due to the ability to create dermis thermal damage without affecting epidermis, show limited efficient clinical results. To overcome the existing trade off, Philips Research has recently developed a novel minimally invasive laser technology for wrinkle reduction using a form of laser induced breakdown (LIB), i.e. laser induced optical breakdown (LIOB).

LIB is the partial or complete ionization of a solid, liquid or gas through absorption of thermal or electromagnetic energy generated by a laser source. Laser-induced breakdown (LIB) takes two different forms: laser-induced optical breakdown (LIOB) and laser induced thermal breakdown (LITB). LIB can occur by pure multiphoton ionization, by avalanche (cascade) ionization or a combination of the two. For both the mechanisms the initial phase is the creation of free electrons in the focal volume. Depending on medium purity two generation processes of seed electrons can be distinguished. In case of pure medium, the seed electrons come from ionization of a few molecules through multi-photon absorption. Several photons together containing enough energy to ionize the molecule must be simultaneously absorbed and the breakdown produced is LIOB. In case of impure medium these seed electrons come from ionization of impurities by thermal excitation. In other words, by heating of linear absorbing chromophores in the target these seed electrons are produced by thermionic emission and LITB occurs.

LIOB has attracted great interest in recent years due to its numerous applications in medicine and biology, while LITB has received less attention. The principles of LIOB have been exploited for applications regarding ophthalmic microsurgery, stone fragmentation, angioplasty, and, recently, skin rejuvenation. When LIOB is generated inside the skin, a grid of lesions appears within the dermis that induces new collagen formation without affecting the epidermis, resulting in reduction of wrinkles and fine lines [2]. Subsurface laser skin ablation through LIOB requires high irradiance in the order of $10^{13}$ W/cm$^2$ [3]. Beside the safety related advantages, reducing the irradiance required to create breakdown may allow reaching deeper layer of the skin, hence improving the efficacy of the treatment. In this work of thesis, three possible solutions have been provided to achieve the lowering of the irradiance threshold: the use of a properly polarized input beam, the exploitation of the LITB action mechanisms for the initial generation of seed electrons, and the combined use of the laser source with an external plasma source.
First of all we demonstrated the dependence of the irradiance threshold on the polarization state of the laser beam used, in order to consequently establish the polarization state giving a larger focal spot and a lower irradiance. We investigated the effects of polarization and apodization on laser induced optical breakdown (LIOB) irradiance threshold on liquid media resembling the optical properties of biological tissues relevant for LIOB based skin rejuvenation applications. Using a skin rejuvenation device recently developed by Philips, we measured the breakdown threshold obtained for linearly and radially polarized light under different apodization conditions. We proved that the irradiance threshold required to create LIOB in liquid media of different optical properties is lower for radial polarization due to a larger focal spot provided by it.

We proved the possibility to lower the irradiance threshold when the thermal pathway for the generation of seed electrons typical of LITB is induced in absorbing media. We calculated LIOB and LITB irradiance thresholds on transparent and absorbing aqueous media treated with the home built prototype device developed by Philips. We demonstrated a transition from laser-induced optical breakdown to laser-induced thermal breakdown as the absorption coefficient of the medium is increased. We observed also that irradiance threshold for optical breakdown, after correction for the path length dependent absorption losses in the medium, is nearly unaffected by the variation in the absorption properties of the medium, whereas irradiance threshold for thermal breakdown decreases with the increase in the absorption properties of the medium. Moreover we demonstrated that the irradiance threshold for LITB is always lower than LIOB threshold. Results obtained are the experimental confirmation of two of the most significant benefits of employing LITB in skin rejuvenation applications: (i) the selectivity of LITB for the target chromophore and the surrounding tissue as the process is dependent on the absorption properties of the target; (ii) the less demanding laser pulse parameters required for the LITB process as a result of the lower intensity threshold.

Also, we demonstrated the feasibility of lowering the intensity threshold for LIOB by providing seed free electrons in the focal volume of the tightly focused ultra-short laser pulses using an additional plasma source. Experiments were performed to confirm the proof of principle using a skin rejuvenation prototype developed by Philips Research in combination with a commercially available plasma device, kINPen®09. We proved that with a partial or weak ionization providing at least one seed electron in the focal volume, a 70% reduction of the irradiance threshold can be achieved.

Lowering the irradiance threshold with the above described methods may allow creating deeper lesions inside the skin and can lead to precise and well-localized tissue effects with less risk of collateral damage, thereby improving safety and efficacy of treatment. Furthermore the laser pulse parameters required for the LIOB process become significantly less demanding and this will result in better availability of laser sources with less critical requirements. Any laser energy reduction will have an exponential benefit on the price of the laser source, which is the main driver for cost of the entire system for devices based on LIOB.
Chapter 1
Introduction

Beauty is only skin deep, but it is only the skin you see
- Fifteenth century proverb

1.1. Introduction

The development of laser based skin rejuvenation techniques has significantly increased in recent years. In spite of the technological developments in the skin rejuvenation techniques throughout the years, no revolutionary approach has been introduced that is capable of accurately defining the balance between efficacy, safety, social downtime and pain perception [1]. The ablative techniques provide significant results but the post-treatment care required is substantial and the incidence of side effects is relatively high. On the other hand the non-ablative methods are safer and social downtime is shorter but the clinical efficacy is limited compared to ablative treatment.

Philips Research has recently developed a novel minimally invasive laser technology for wrinkle reduction using laser induced optical breakdown (LIOB). When LIOB is generated, a grid of lesions appears within the dermis that induces new collagen formation without affecting the epidermis, resulting in reduction of wrinkles and fine lines [2].

1.2. Research goal

LIOB requires high intensities in the order of $10^{13}$ W/cm$^2$ [3]. The initiation of optical breakdown through multi-photon ionization involves the generation of one or more seed electrons by absorption of multiple photons having same polarization in the focal volume [4]. Multiple scattering and tissue birefringence results in depolarization of light and this effect accumulates as a function of focusing depth inside the skin. Therefore skin needs to be exposed to high laser intensities to create sufficient number of photons with same polarization in order to exceed the breakdown threshold. The pulse parameters and the focusing conditions that are used for creating optical breakdown are very critical and tight focusing is required. Reducing the irradiance threshold required to create breakdown is very important, especially for aspects regarding laser safety and treatment efficacy. Lowering the irradiance threshold may let deeper layers of tissue to be targeted with less risks of collateral damage.

The aim of this work of thesis is to find an effective method to lower the irradiance threshold for laser induced optical breakdown. Here we investigated three potential solutions: (i) use of radially polarized light and influence of size of focal spot, (ii) thermionic emission of seed electrons (thermal
initiation pathway) for creating optical breakdown, and (iii) presence of free electrons in the focal volume provided by an external plasma source.

1.3. Research method

To create laser induced optical breakdown the skin rejuvenation prototype developed by Philips Research was used. This device provides high power laser pulses at a wavelength of 1064 nm. Performances of radial and linear polarization were analyzed in terms of irradiance threshold, conducting experiments on distilled water and diffuse media. The beam waist for linear and radial polarization for different apodization conditions was experimentally measured through the knife edge technique and the results were compared with numerical simulations. We investigated also the scrambling of polarization in the focus by means of the numerical simulations.

We experimentally measured the irradiance threshold for another form of laser induced breakdown, laser induced thermal breakdown (LITB), and we analyzed its dependence on the properties of the medium by conducting experiments in transparent and absorbing media resembling the optical properties of skin.

To demonstrate the reduction of the irradiance threshold for LIOB in plasma environment we used the same skin rejuvenation prototype described above in combination with a commercially available plasma device, kINPen®09. The plasma source created partial ionization of the medium and provided the free electron environment in the focal volume to initiate the breakdown process.

1.4. Structure of the thesis

The layout of the thesis is as follows.

In Chapter 2 the theoretical background underlying the content of thesis is given. First, mathematical aspects of light polarization are described. Then, a short description of the skin anatomy and its interaction with light is presented. An overview of different skin rejuvenation treatments is provided. Then the skin rejuvenation prototype developed by Philips is introduced. Principles of laser induced optical (LIOB) and thermal breakdown (LITB) are consequently explained. Then the mechanisms of plasma formation and some examples of cold plasma sources are described. Examples of laser devices for biomedical applications conclude the chapter.

In Chapter 3 the effects of polarization and apodization for LIOB threshold are investigated. The experimental measurements of the focal spot for linearly and radially polarized light through the knife edge technique are described. Results of numerical simulations are compared with experimental results and available literature. Finally the study of the scrambling of polarization in the focus by means of numerical simulations is presented.
In Chapter 4 the investigation of the irradiance threshold for LIOB and LITB in transparent and absorbing aqueous media resembling the skin optical properties is performed.

In Chapter 5 the effective solution for the reduction of the irradiance threshold for subsurface laser skin ablation through LIOB in plasma environment is presented.

In Chapter 6 the summary of the thesis and the outlook for future research are presented.
Chapter 2

Background Information

Boswell: Then, Sir, what is poetry?
Johnson: Why, Sir, it is much easier to say what it is not. We all know what light is; but it is not easy to tell what it is.
-Boswell’s Life of Johnson

2.1 Introduction

In this chapter, the theoretical background of the thesis is provided. First, principles of polarization of light and a brief description of homogeneous and spatially variable states of polarization are given. Then general description of the anatomy of the skin and its optical properties is presented; the skin rejuvenation methods available nowadays are then described. Particular attention is given to a novel minimally invasive technique developed by Philips based on the principles of laser induced optical breakdown. Then basic principles of plasma formation are explained and an overview of the mechanism of generation of cold plasma is provided. Examples of laser and plasma based biomedical applications conclude the chapter.

2.2 Polarization of light

Light consists of spatio-temporal electric (E) and magnetic fields (B). These fields are vectors, and their directions are perpendicular to each other and to the direction of propagation of light. Because the fields propagate together and maintain a constant phase difference (90°) with one another, it is usually sufficient to describe the wave with either the electric vector or the magnetic vector. Conventionally it is chosen the electric vector, largely because the interaction of matter with the electric field is stronger than that with the magnetic field ([5],[6]).

Polarization is a property of waves that describes the orientation of the electric field. When the vector direction is predictable light is called polarized; in any other case, light is defined partially polarized or unpolarized. To define the different states of polarization, the theory of the propagation of electromagnetic waves must be introduced. Briefly, any electromagnetic field may be resolved into an infinity of monochromatic fields of angular frequency $\omega$, of which any can be split up into an infinity of plane waves of $k$ wave vector [7]. The Fourier’s integral theory translates this concept in the following equation for the electric induction field $D(r,t)$:
\[ D(r,t) = \int \int D(k,w)e^{-i(\omega t - kr)} \, dk \]  

(2.1)

\( D(r,t) \) is the most significant field in crystalline media optics. All the other components of the electromagnetic field can be deduced from \( D(r,t) \) thanks to the Maxwell’s equations. In order to study the polarization of light it is then sufficient to consider only one of the monochromatic plane waves mentioned above. The electric field, for a propagation along the \( z \)-axis, can be described by its main components \( x \) and \( y \), defined as follows:

\[ E_{x,y}(z,t) = E_{xo,yo}(z,t)e^{-i(\omega t + kz)} + c.c \]  

(2.2)

where \( E_{xo} \) and \( E_{yo} \) are the amplitudes and \( k \) is the wave number (modulus of the wave vector \( k \)).

If \( E_x \) and \( E_y \) oscillate in phase, that is \( E_{xo}(z,t) = \alpha E_{yo}(z,t) \), with \( \alpha \) being a real constant, formula (2.2) represents the electric field of a linearly polarized plane wave. The wave is called linearly polarized because the observer sees the oscillating vector tracing out a straight line in the \( XY \) plane. If \( E_{xo}(z,t) \) or \( E_{yo}(z,t) \) are equal to 0, the wave is referred to as linearly polarized along the \( Y \) direction or the \( X \) direction respectively.

If there is a phase shift between \( E_x \) and \( E_y \), that is \( E_{xo}(z,t) = \pm i E_{yo}(z,t) \) where \( i \) is the imaginary unit, the wave is said to have circular polarization because the end of the vector \( E \) traces out a circle. Circularly polarized waves can be left or right-handed. If \( E_{xo}(z,t) = i E_{yo}(z,t) \) the electric field vector is tracing out a circle in a clockwise direction and the light is referred to as left-handed circularly polarized. If \( E_{xo}(z,t) = -i E_{yo}(z,t) \) the end of the electric field vector traces out a circle in a counterclockwise direction and the light is right-handed circularly polarized.

**FIG. 2.1.** Linearly and circularly polarized light
Linear and circular states of polarization are particular cases of the most general fully polarized homogeneous state of polarization that is elliptical polarization. In that case $E_{x_0}(z, t) = \alpha E_{y_0}(z, t)$, with $\alpha$ being a generic complex number, and for an observer facing the wave source the end of the vector $E$ is tracing out an ellipse [7].

For all the polarization states described above the direction of the electric field is the same in every position throughout the beam; therefore linear, circular are elliptical polarization are called spatially uniform polarization states. In recent years there has been growing attention towards spatially variable states of polarization. In particular laser beams with cylindrical symmetry polarization have been studied because of the unique properties of the electric field in the focal region. By decomposition of a generalized cylindrical vector beam two new states of polarization can be defined: radial polarization and azimuthal polarization. A clear and intuitive definition of the wave polarization states is based on the definition of the polarization orientation, calculated as follows:

$$\psi(\theta) = P\theta + \psi_0 \quad (2.3)$$

The integer $P$ is the polarization order number (a topological charge) that represents the number of polarization rotations per roundtrip ($\theta=0...2\pi$), and $\psi_0$ is the initial polarization for $\theta = 0$. For instance $P=0$ fields represents linearly polarized light with orientation $\psi_0$. Radial and azimuthal polarizations are given for $P$ equal to 1 and $\psi_0$ equal to 0 and $2\pi$ respectively (fig.2.3)
2.3 Skin rejuvenation

2.3.1 Skin anatomy

The skin covers the entire external surface of the human body and it is the principal site of interaction with the surrounding world. It serves as a protective barrier that prevents internal tissues from exposure to trauma, ultraviolet (UV) radiation, temperature extremes, toxins, and bacteria. Other important functions include sensory perception, immunologic surveillance, thermoregulation, and control of insensible fluid loss. The skin is made up of the following layers: epidermis, dermis and subcutaneous fat layer or “subcutis” (Fig. 2.4).
The epidermis is the outer layer of the skin and is average thickness is 100 μm. It is composed by a stratum corneum (or “horny layer”, mostly characterized by dead cells) and four underlying layers: stratum lucidum, granulosum, spinosum and basale (Fig.2.5).

The second layer of the skin is the dermis, tightly connected to the epidermis through a thin sheet of fibers constituting the basement membrane. The dermis contains the structural elements of the skin, the connective tissue, and can be from 1 to 4 mm thick. Two main areas can be identified: a superficial area adjacent to the epidermis, called papillary region, and a deep ticker area known as the reticular region. The papillary dermis is characterized by a network of thin (0.3-3 μm diameter) collagen fibers and elastic fibers (10-12 μm diameter), embedded in lose connective tissue and a highly developed microcirculation composed of arterioles, capillaries and venules. The reticular dermis is composed predominantly of dense bundles of thick (10-40 μm diameter) collagen fibers arranged parallel to the skin’s surface, elastic fibers and fibroblasts surrounded by an amorphous mix of water, electrolytes, plasma proteins and polysaccharides. Collagen is made by fibroblast and it is the main protein of connective tissue. Collagen consists of inter-woven fibrils of globular tropocollagen sub-units that spontaneously arrange themselves by numerous hydrogen and covalent bonds. Thanks to its great tensile strength, collagen is responsible for skin strength. Other properties of the skin, such as turgor and elasticity are given by glycosaminoglycans and elastin fibers respectively.

The deepest layer of skin is the subcutis (or “hypodermis), which can be from 1 to 6 mm thick depending on the body site. The subcutis, consisting of a network of collagen, elastin and fat cells, helps conserve the body's heat and protects the body from injury by acting as a "shock absorber."
2.3.2 Skin aging and wrinkle formation

The more dramatic effects of skin aging are seen in the dermis, which is thought to be mainly responsible for skin mechanical properties. In young skin, fibrillar collagen is highly organized. It forms a spread meshwork of rope-like small and thin bundles of tightly packed fibers in the papillary dermis, whereas in the reticular dermis it is more spaced with thicker bundles. Fibroblasts attached to collagen fibers via integrins are highly aligned with the collagen network and stretch it; in return, they are maintained in a tensed state. This well-organized collagenous structure has extraordinary properties in terms of resiliency and stiffness, together with a characteristic tensed aspect.

During chronological aging, dermal content in collagen is diminished, bundle becomes thinner and collagen meshwork tends to disappear. Therefore interactions between fibroblasts and collagen are reduced leading to randomly collapsed fibroblasts (Fig. 2.6). These changes in the scaffolding of skin cause skin to wrinkle and sag [8].

![Fig. 2.6. Histological feature of skin from young (left) and old (right) individuals. With aging fibroblasts oriented in the plane of thick fiber bundles are replaced by round and oblong interstitial cells randomly disposed between disorganized fibers.](image)

2.3.3 Light skin propagation

In laser skin therapy the knowledge of absorbing and scattering properties of the treated area is essential for the purpose of predicting a successful treatment.

Absorption is mainly caused by water molecules (in the IR region) or proteins, hemoglobin and melanin (in the UV and visible range). These absorbing molecules are termed as chromophores. When an incident electromagnetic wave is absorbed by a medium there is a decrease in the intensity expressed through the Lambert-Beer’s Law:

\[ I(x) = I_0 e^{-\mu_a x} \]  

(2.4)

where \( I_0 \) indicates the incident light intensity, \( I(x) \) the light intensity at a distance \( x \) inside the medium and \( \mu_a \) the absorption coefficient. The absorption spectrum of human skin is presented below (Fig.2.7).
FIG. 2.7. Absorption coefficient of the main constituents of the skin

Scattering in skin starts when the light interacts with single fibrils and more complex structure made by interlacement of them, called scattering centers. This phenomenon can be caused primarily by variation in polarizability, which can be characterized by variations of the optical index of refraction. This mismatch may be largely a function of shape, size and distribution of skin constituents and, in particular, of dermis constituents such as collagen, lipids, water, cells and their organelles. The epidermal scattering, which is affected by melanin granules and keratinocyte and melanocyte nuclei, is indeed sufficiently close to that of dermis and sufficiently thin to be not critical. The optical scattering properties of the dermis can be characterized by the scattering coefficient ($\mu_s$), or sometimes by the reduced scattering coefficient ($\mu_s'$), related to each other by the following formula:

$$\mu_s' = \mu_s (1 - g) \quad (2.5)$$

where $g$ is the anisotropy factor defined as the mean of the cosine of the scattering angle $\Theta$:

$$g = <\cos(\theta)> \quad (2.6)$$

Depending on the value of $g$, it is possible to identify the scattering direction: purely forward scattering for $g = 1$ and purely backward scattering for $g = -1$. Among the two layers of the dermis – papillary and reticular – the former is highly backscattering because of the small size of the collagen
fibers (diameter of an order of magnitude less than visible light wavelength). Contrariwise within the latter, the large size of collagen fiber bundles causes highly forward-directed scattering. The average scattering properties of skin are defined by the scattering properties of the reticular dermis because of its relatively big thickness (up to 4 mm) and typical values of $g$ are in the range of 0.7 - 0.95 [9].

\[ \mu' = \mu_a + \mu'_s \] (2.7)

As can be seen in Fig. 2.7 and Fig. 2.8, in a wavelength range of 600-1300 nm both absorption and scattering are low. Therefore this region, refer to as optical or therapeutic window, is used for imaging and treatment of the skin.

2.3.4 Light skin interactions

The laser-tissue interactions depend on the opto-thermal properties of tissue in combination with the characteristics of the laser source and in general they can be grouped as follows: photochemical interactions, photothermal (vaporization and coagulation) interactions, plasma induced ablation, photoablation and photodisruption (Fig. 2.9). The characteristic energy density (dashed lines of Fig. 2.9) varies over 15 orders of magnitude, ranging from approximately 1 mJ/mm$^2$ to 1 J/mm$^2$ and a single parameter distinguishes and primarily controls these processes: the duration of laser exposure, which is mainly identical with the interaction time itself [10]. The time scale can be roughly divided into five sections: continuous wave or exposure times $> 1$ s for photochemical interactions, 1 min down to 1 μs
for thermal interactions, 1 μs down to 1 ns for photoablation, and < 1 ns for plasma induced ablation and photodisruptive. The difference between the latter two is attributed to different energy densities, besides the fact that one is based exclusively on ionization whereas the other is primarily a mechanical effect. Thermal effects for instance may play also an important role when ultrashort laser pulses (< 100 ps) at high repetition rates are applied (10-20 Hz), adding up to a measurable increase in the temperature of the tissue treated.

**FIG.2.9.** Laser tissue interactions showing influence of exposure time and power density (double logarithmic map).

In the following part physical principles and possible applications of the mechanisms interesting for the purpose of our study, i.e. photothermal interactions and plasma induced ablation, are briefly presented.

In photothermal interactions, absorbed photons are converted into heat. The local increase in temperature is the most significant influencing factor and the effects of heating can be seen as denaturation and coagulation (T > 60°C), which can proceed to necrosis and vaporization (T>100°C), resulting in tissue ablation and carbonization (Fig.2.10).
The heat generated within the target can be confined to that target by the appropriate selection of pulse duration. This is related to the thermal relaxation time of the target, defined as the intrinsic cooling time taken for the target to dissipate half of the incident thermal energy [10], [11]. If the laser pulse duration is equal to or less than the thermal relaxation time of the target, then thermal diffusion to adjacent tissue will be reduced. The thermal relaxation time can be calculated as follows:

$$\tau = \frac{1}{4\alpha}d_{eff}^2 = \frac{1}{4\alpha\mu_{eff}}$$ (2.8)

The thermal diffusivity of the tissue is approximately \( \alpha = 0.106 \, mm^2 \, s^{-1} \), which is very similar to that of water (\( \alpha_{water} = 0.15 \, mm^2 \, s^{-1} \)) of which most of the tissue is composed. \( \mu_{eff} \) is the effective attenuation coefficient (equivalent to the molar extinction coefficient) and \( d_{eff} \) is the depth of penetration at which the intensity has fallen by \( 1/e \), equal to \( \mu_{eff}^{-1} \). The thermal relaxation time is primarily related to the physical size of the target: the larger the target, the longer the thermal relaxation time, as it possible to see in Tab.2.1, where the thermal relaxation times of the main skin chromophores are presented.

<table>
<thead>
<tr>
<th>Chromophore</th>
<th>Size (μm)</th>
<th>Thermal relaxation time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melanosome</td>
<td>0.5-1</td>
<td>1 μs</td>
</tr>
<tr>
<td>Erythrocyte</td>
<td>7</td>
<td>1 μs</td>
</tr>
<tr>
<td>Blood vessel</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>100 μs</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>1 ms</td>
</tr>
<tr>
<td></td>
<td>100</td>
<td>1 ms</td>
</tr>
<tr>
<td></td>
<td>200</td>
<td>20 ms</td>
</tr>
</tbody>
</table>

TAB.2.1. Thermal relaxation times of the main skin chromophores
Plasma induced ablation is obtained when the power densities exceed $10^{11}$ W/cm$^2$ in solids and fluids, or $10^{14}$ W/cm$^2$ in air [10]. Once the critical irradiance threshold is surpassed a phenomenon called breakdown occurs. The critical threshold can be defined also in terms of electric field strength $E$, related to the local power density $I$ by the basic electrodynamic equation:

$$I(r, z, t) = \frac{1}{2} \varepsilon_0 c E^2$$  \hspace{2cm} (2.9)

For power density of $10^{11}$ W/cm$^2$, the corresponding electric field amounts to approximately $10^7$ V/cm. This value is comparable to the average atomic or intramolecular Coulomb electric fields, thus providing the necessary condition for plasma ionization. The physical principles of breakdown and plasma formation have been extensively investigated in the past [12],[13],[14]. Further details will be explained in sec. 2.4 and 2.5.

2.3.5 Laser based skin rejuvenation methods

Laser and light based skin rejuvenation techniques has rapidly evolved over the last few decades from ablative to non ablative and more recently towards fractional resurfacing techniques (Fig.2.11).

The golden standard for laser resurfacing is based on ablative lasers such as CO$_2$ and Er:YAG. The ablation of the superficial layers of the skin is followed by the stimulation of new collagen growth in the dermis. New collagen replaces the disorganized collagen/elastin connective tissue matrix associated with wrinkled or photodamaged skin in the upper dermis. Since CO$_2$ and Er:YAG laser wavelengths target water as chromophore, these methods ablate the full epidermis before reaching the target papillary dermis. As a consequence a thin layer of heat-denatured dermal tissue remains. During the repair processes this heat damaged layer releases mediators which induce formation of the new and improved collagen matrix with an improved aesthetic appearance [1]. Despite the high efficacy of these ablative techniques, the significant risk of side effects and the prolonged postoperative recovery period associated with them prompted the development of alternative solutions.
Non ablative techniques exploit the principles of selective photothermolysis (SP) to injure the dermis leaving intact the epidermis. SP has become a widely used approach for the selective photocoagulation of blood vessels and pigmented cells [15]. The goal is indeed to deliver heat to the target in a time (pulse duration of the laser pulses) shorter than the time required for the heat to diffuse (thermal relaxation time) from the target to surrounding tissues such that heat remains confined to the target. Moreover superficial skin cooling is applied to avoid thermal damage in the epidermis.

Non ablative lasers can be classified into 3 main groups: infrared lasers (1064-nm neodymium yttrium aluminium garnet, Nd:YAG); visible pulsed lasers (or vascular lasers KTP and PDL), alone or in conjunction with the Nd:YAG laser; and intense pulsed light (IPL) sources. Among them, the Nd:YAG laser (at 1320 nm with a pulse duration of 200 μs) has the highest efficacy in terms of rhytides and scars improvement and induction of neocollagenesis.

More recently a new skin rejuvenation technique has been developed, called fractional photothermolysis (FP), based on linear absorption of optical energy by the skin constituents. In order to increase the ratio of damage between the dermis and epidermis, the optical energy is focused into the dermis at the desired depth and arrays of microscopic thermal wounds, called microscopic treatment zones (MTZs), are created.

To overcome the limitations of the skin resurfacing techniques described above, Philips developed non-invasive laser technologies for skin rejuvenation based on laser induced optical breakdown (LIOB) and laser induced thermal breakdown (LITB). The physical principles of these methods are fundamentally different from the methods previously discussed. LIOB relies on a non-linear absorption process while the above mentioned techniques are based on linear absorption processes. By tightly focusing near-infrared laser pulses, a grid of intradermal lesions is created and the epidermis is preserved (Fig.2.13).
LITB starts with a linear absorption followed by a non-linear absorption process. Isolated lesions are created only at the selected skin chromophores having high absorption coefficients at the specific laser wavelength (Fig 2.14). For instance targeting melanin, that in the epidermis can cause a mottled or uneven skin tone, re-epithelialization is induced and a better skin tone is achieved. Tissue surrounding the damaged zone is virtually unaffected due to the high selectivity of the treatment, leading to a shorter healing time and downtime associated with this technique [18].
2.4 Laser Induced Breakdown

Dielectric breakdown is the partial or complete ionization of a solid, liquid or gas through absorption of thermal or electromagnetic energy. The gas of charged particles resulting after the ionization process is called “plasma”, which constitutes the fourth state of matter. Plasmas could occur in nature through thermal breakdown or electrostatic breakdown. In thermal breakdown, high temperatures cause the vaporization and ionization of the ordinary matter. In electrostatic or dc breakdown the production of plasma is due to electron cascade ionization in a strong static field. If the intense electromagnetic field is generated by a laser, the breakdown is called laser induced breakdown. Laser-induced breakdown (LIB), like naturally produced plasmas, takes two different forms: laser-induced optical breakdown and laser induced thermal breakdown. These mechanisms are discussed in details in the following sections.

In breakdown by cascade ionization seed electrons come from ionization of impurities by thermal excitation (thermionic emission by heating of linear absorbing chromophores in the target) in case of impure medium or by ionization of a few molecules through multi-photon absorption in case of pure medium.

In multi-photon absorption, free electrons are created by simultaneous absorption of several photons by a molecule, together containing enough energy to ionize the molecule. A variable number of photons with same polarization state and with total energy (Nh_υ) exceeding the ionization potential of the investigated medium is required to produce an energetic electron.

![Diagram](image_url)

**FIG.2.15**: Initiation of ionization with subsequent electron avalanche [10].

Once a free electron exists in the medium, it can absorbs photons in a non-resonant process called “inverse Bremsstrahlung absorption” in the course of collisions with heavy charged particles, i.e. ions or atomic nuclei. During absorption, energy and momentum must be conserved so a third particle
(ion/atom) is involved in the process as well. The free electron gains kinetic energy during the absorption of the photon and after a sequence of $K$ inverse Bremsstrahlung events, the kinetic energy exceeds the band gap energy $\Delta E$. From that point on, the electron can produce another free electron through impact ionization and form two free electrons with low kinetic energies. The recurring sequence of inverse bremsstrahlung absorption events and impact ionization leads to an avalanche growth in the number of free electrons if the irradiance is high enough to overcome the losses of free electrons through diffusion out of the focal volume and through recombination [12]. During each collision a fraction of the kinetic electron energy proportional to the ratio of the electron and ion masses is transferred to the ion. Therefore the energy gain through inverse bremsstrahlung must be more rapid than the energy loss through collisions with heavy particles to sustain the electron avalanche growth.

2.4.1 Laser induced optical breakdown (LIOB)

Laser induced optical breakdown (LIOB) is a non-linear absorption process leading to plasma formation at locations where the threshold irradiance for breakdown is surpassed [12]. There are different mechanisms that can lead to LIOB: multiphoton absorption, cascade ionization (or avalanche ionization) or a combination of the two. The initial phase, for all of them, is the creation of free electrons in the focal volume and the minimum amount required is the medium nonspecific value of $10^{18}$-$10^{20}$ cm$^{-3}$.

Pulse duration and impurity presence are two of the main factors that influences the breakdown process. We can identify in particular three regimes, as shown in Tab.2.2.

<table>
<thead>
<tr>
<th>Pulsewidth</th>
<th>Pure Media</th>
<th>Impure media</th>
</tr>
</thead>
</table>
| **Long**   | 1. Ionization of impurities  
2. Cascade Ionization |               |
| **Intermediate** | 1. Multiphoton absorption  
2. Cascade Ionization |               |
| **Short**  | Multiphoton absorption      |               |

**Tab.2.2.** Mechanisms of LIOB for different pulsewidths

For long pulsewidth, cascade ionization is the dominating mechanism. In pure media, however, multi-photon ionization is needed for the creation of seed electrons. For intermediate pulsewidth multi-photon initiation dominates any contribution of seed electrons from impurities. Breakdown in both pure and impure media is by multi-photon initiated avalanche ionization. For short pulsewidth multi-photon ionization is the dominant mechanism, because the field is not present in the focal volume long enough to achieve an electron cascade. Each atom is independently ionized by the field, so neither particle-
particle interactions nor seed electrons are necessary. To summarize, decreasing the pulse duration (towards picoseconds and femtoseconds pulses) the multiphoton process becomes more important. This aspect can be justified also in terms of intensity dependence of cascade and multiphoton ionization rates. When electron losses are neglected, the cascade ionization rate is proportional to the light laser intensity, \( n_{\text{casc}} \propto I \). The multiphoton ionization rate \( n_{\text{mp}} \) is proportional to \( I^k \), where \( I \) is the intensity of the laser beam and \( k \) is the number of photons required for the ionization. With decreasing pulse duration, \( I \) must increase for breakdown to occur and multiphoton ionization, which has the strongest intensity dependence, becomes ever more important.

### 2.4.1.1 LIOB in aqueous media

The occurrence of electric breakdown in liquids has become of interest only in recent years in connection with medical applications of lasers such as for ophthalmic microsurgery, stone fragmentation and angioplasty [12]. This has raised an interest in gaining a better understanding of plasma formation in liquids which for many years received less attention than plasma formation in solids and gases.

Whereas the optical breakdown in gases leads to the generation of free electrons and ions, in condensed matter electrons are either bound to a particular molecule or they are “quasi free” if they have sufficient kinetic energy to be able to move without being captured by local potential energy barriers. Transitions between bound and quasi free states are equivalent of ionization of molecules in gases. From now on, for simplicity, we will use even in case of LIOB in aqueous media the terms “free electrons” and “ionization”, as abbreviations for quasi free electrons and excitation into the conduction band respectively.

![Diagram of LIOB in aqueous media](image)

**FIG. 2.16.** LIOB in aqueous media. Formation of quasi free electrons by multiphoton ionization and consequent avalanche ionization
Plasma absorbs optical radiation much more strongly than ordinary matter. The dense plasma created can thus be rapidly heated by inverse bremsstrahlung absorption while the laser pulse remains in the focal volume. Bremsstrahlung emission from free electrons and emission from electron-ion recombination combine to produce a visible “flash”, i.e. broadband plasma emission from the UV to the IR. The combined effect of high temperatures and pressures can lead to plasma expansion at supersonic velocities and to the creation of a shock wave together with a characteristic acoustic signature [12].

When nanosecond and picosecond pulses are employed, the plasma luminescence serves as experimental breakdown criterion. The standard theoretical definition of breakdown is in this case a free electron density of \(10^{19-20}\) cm\(^{-3}\). With shorter laser pulses (<10 ps), there is no plasma luminescence in the visible region of the spectrum and breakdown is experimentally detected by observing the cavitation bubbles formed in the liquid [12],[14].

### 2.4.2 Laser induced thermal breakdown (LITB)

Laser induced thermal breakdown refers to the damage inflicted in an absorbing medium by an intense laser field. The seed electrons are generated by the linearly absorbing chromophore (melanin, blood) in skin. The chromophore absorbs energy from the laser beam and quickly converts it into heat, increasing the probability of thermally liberating an electron. These free electrons gain energy from the laser field to ionize further atoms in collision (impact ionization) and repetition of this process leads to rapid multiplication of free electrons (avalanche ionization) with the resultant formation of a plasma and thereby surpassing the threshold for breakdown. In short, LITB starts with linear absorption of energy (linear absorption) and later proceeds to non-linear absorption via avalanche ionization [3],[18].

### 2.4.3 Comparison between LIOB and LITB

LITB occurs for long exposures to continuous wave (cw) or repetitively pulsed laser sources at high average power. It is encountered primarily in materials which have a fairly high linear absorption coefficient; i.e. those which are opaque at the laser wavelength. The (relatively) slow absorption of energy from the laser produces heating of the medium, followed by melting, vaporization, and collisional ionization. Contrariwise LIOB occurs primarily for short pulse exposures in the microsecond to femtosecond time regime, where short pulse interaction times do not allow breakdown by linear absorption or direct heating. In this regime, the high peak powers and irradiances characteristic of short pulses produce plasma formation through processes such as formation of an electron cascade and direct ionization of the medium by multiphoton absorption [3].

Optical breakdown does not differentiate between the target chromophore and the surrounding tissue as the process is independent of the absorption properties of the target. The process is therefore non-selective for the target chromophore and the surrounding tissue. In the case of thermal breakdown the effect will occur only at the locations where chromophores are present. The main differences between LIOB and LITB in terms of type of absorption, mechanisms involved, criteria to choose the laser
operating wavelength, and penetration depth are listed in Tab2.3. Benefits of both the processes are also presented [18].

<table>
<thead>
<tr>
<th></th>
<th><strong>LIOB</strong></th>
<th><strong>LITB</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type</strong></td>
<td>Non-linear absorption</td>
<td>1. Linear absorption of light</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2. Generation of seed electrons</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3. Non-linear absorption</td>
</tr>
<tr>
<td><strong>Wavelength</strong></td>
<td>Minimal absorption</td>
<td>Peak absorption</td>
</tr>
<tr>
<td><strong>Steps</strong></td>
<td>1. Plasma</td>
<td>1. Temperature rise</td>
</tr>
<tr>
<td></td>
<td>2. Photon absorption by plasma</td>
<td>2. Plasma</td>
</tr>
<tr>
<td></td>
<td>3. Breakdown</td>
<td>3. Photon absorption by plasma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4. Breakdown</td>
</tr>
<tr>
<td><strong>Ionization</strong></td>
<td>a. Multi-photon ionization</td>
<td>1. Thermal ionization</td>
</tr>
<tr>
<td></td>
<td>b. Avalanche ionization</td>
<td>2. Impact/Avalanche ionization</td>
</tr>
<tr>
<td></td>
<td>c. Multi-photon initiated</td>
<td></td>
</tr>
<tr>
<td></td>
<td>avalanche ionization</td>
<td></td>
</tr>
<tr>
<td><strong>Penetration</strong></td>
<td>High</td>
<td>Medium</td>
</tr>
<tr>
<td><strong>depth</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Benefits</strong></td>
<td>✓ Independent of wavelength</td>
<td>✓ Wavelength dependent</td>
</tr>
<tr>
<td></td>
<td>✓ Single wavelength</td>
<td>✓ Multiple wavelengths for different targets</td>
</tr>
<tr>
<td></td>
<td>✓ Localized lesions and also for homogenous media</td>
<td>✓ Localized lesions</td>
</tr>
<tr>
<td></td>
<td>✓ Feedback required</td>
<td>✓ Automated feedback</td>
</tr>
</tbody>
</table>

**TAB.2.3.** Comparison of laser induced optical breakdown and laser induced thermal breakdown.

### 2.5 The fourth state of matter: plasma

The plasma state occurs when matter is in the form of a charged mixture of positive ions and negative electrons after an ionization process. In all plasmas supported by electric field, electrons receive the external energy faster than the much heavier ions.

In non-thermal plasma, cooling of ions and uncharged molecules is more effective than energy transfer from electrons and the gas remains at low temperature. For this reason non-thermal plasma is also called non equilibrium plasma or “cold plasma”. In a thermal plasma (or “hot plasma”), on the other hand, energy flux from electrons to heavy particles equilibrates the energy flux from heavy particles to the environment only when temperature of heavy particles becomes almost equal to the electron
Moreover, a difference in terms of ionization exists between thermal and non thermal plasma. In general hot plasma is nearly fully ionized, while in cold plasma only a small fraction (for example 1%) of the gas molecules is ionized.

2.5.1 Generation mechanisms of cold plasma

To generate artificial cold plasmas operating at atmospheric pressure for both direct and indirect treatments, three types of plasma sources are applicable: barrier discharges (BDs), plasma jets and corona discharges. So far, activities were focused on the first two types of plasma sources.

BDs are characterized by the presence of at least one isolating layer in the discharge gap. The classical configuration is the so called volume BD (VBD), where one or two electrodes with an isolating layer form the discharge gap. The VBD enables mainly direct treatment of the object to be treated, i.e., the object with stray capacity is the second electrode. Since the local current is limited by the capacity of the discharge configuration, a painless treatment is possible.

Special configurations of the BD are the surface discharge and the coplanar discharge. In a surface barrier discharge (SBD), both electrodes are in direct contact with the isolator and the plasma is formed around the electrodes on the isolator surface. In the case of coplanar discharge (CBD), both electrodes are embedded in the dielectric and the plasma is generated at the isolator surface. All the discharge types described enable also indirect treatment of wounds, skin area, or other objects because they are not a distinct part of the discharge configuration.

Plasma sources that use a barrier-like approach produce plasmas that are either geometrically confined to the area between the electrodes or contained within a chamber or containment enclosure. Although this is very useful in several applications, there are cases where it is more desirable if the plasma is launched outside an area not bound by anything. Plasma jets or plumes fill exactly such a niche [21]. For this reason, together with aspects related to practical manageability, atmospheric pressure plasma jets are the ones of highest interest for skin treatment applications. Its tool-like, small size and light weight plasma generation unit indeed allows fast and almost arbitrary 3D movements. The contracted and comparably cold plasmas allow focused small-spot treatments, even of small size objects, as well as large-scale treatments by moving the jet over a selected area by applying blower nozzles [23].

Briefly, plasma jets consist of a gas nozzle applied with one or two electrodes. The plasma is generated inside the nozzle and transported to the object to be treated by a gas flow. There are numerous plasma jets available and described in literature [20],[21],[22],[23]. They mainly differ in electrode configuration, type of gas, and frequency of applied voltage. In general, one must distinguish between remote plasma jets (i.e., the plasma is potential free and consists of relaxing and recombining active species from inside the nozzle) and active plasma jets (i.e., the expanding plasma contains free and high energetic electrons). In the latter case, the substrate must be considered as a second or third electrode, i.e., the plasma is not potential free [23].

Possible mechanisms responsible for the production of atmospheric plasma jets remain largely unknown, even if the fundamental principle of the mechanism could be found in the so called streamer theory. The conditions necessary for streamer propagation are (a) that sufficient high energy photons
must be created in the initial electron avalanche to ionize some of the gas atoms or molecules present, (b) that these photons must be absorbed to produce ions in adequate proximity to the streamer tip, and (c) that the space-charge field at the rear of the avalanche tip shall be great enough to give adequate secondary avalanches in the enhanced field [22].

2.6 Biomedical applications

2.6.1 Laser plasma medicine

In the last decades laser induced breakdown has become a prime area of scientific and technological interest for researchers in the fields of biomedical engineering and medicine. High peak powers delivered with nanosecond and sub-nanosecond laser pulses, combined with the strong focusing of the eye, can produce irradiances at the retina and in the vitreous humor which are sufficient to cause LIB [12]. Nowadays, ophthalmic procedures based on laser plasmas produced by LIB are: (i) holes puncturing in capsulotomies and iridotomies, and (ii) cutting of collagen strands which form within the vitreous humor [24]. Other areas of laser medicine in which plasma plays a central role are urology and gastroenterology, cardiology and vascular surgery, dermatology and esthetic surgery.

Laser lithotripsy uses the shock waves provoked by optical breakdown to fragment large stones that form in the biliary apparatus and the urogenital system. The plasma is initiated by absorption of optical energy and subsequent conversion to heat by the stone, until vaporization or desorption creates enough free electrons for cascade ionization to be initiated. Once the plasma is formed, laser energy continues to be coupled into the plasma. The expansion and the confinement of the plasma, together with the high temperatures and pressures developed in the surrounding medium, causes a shock wave intense enough to fragment the stone [24].

Laser angioplasty is another plasma mediated approach for the treatment of atherosclerosis. Atherosclerosis is a pathological condition in which, due to the accumulation of cholesterol and triglycerides in the arterial blood vessels, atherosclerotic plaques develop and compromise the blood flow, causing death by ischemia or infarction [25]. By means of microsecond-long pulses of visible radiation, the laser source can preferentially ablate calcified plaque in comparison with normal artery. Even in this ablative process, formation of plasma is involved, with mechanical fracture and removal of particulate material. Other examples of biomedical application that makes use of optical breakdown (optical and thermal) are the novel breakthrough methods developed by Philips for skin rejuvenation which have already been presented in par. 2.3.5.

2.6.2 Plasma skin resurfacing

Some of the earlier applications of plasma in skin treatments relied mainly on the thermal effects of plasma. Heat and high temperature, together with the capability of hot plasma to penetrate into the
skin, have been exploited in the past for the treatment of wrinkles, superficial skin lesions common on sun-exposed areas, and actinic keratosis.

The non-thermal plasma treatments in living tissues can be fit into two major categories: direct and indirect. In direct plasma treatment, living tissues or organs are considered as one of the plasma electrodes and some current may flow in the form of either a small conduction current, displacement current, or both. Therefore a flux of active uncharged atoms and molecules ((O₃), NO, OH radicals, etc.) as well as ultraviolet (UV) radiation could reach the surface of the living tissue. To avoid any thermal effects or electrical stimulation of the tissue, conduction current should be limited. In contrast, in indirect plasma treatments uncharged atoms and molecules generated in plasma are typically delivered to the surface via flow of gas through a plasma region; as a consequence, small, if any, flux of charges reaches the tissue surface [27],[28].

Plasma skin regeneration (PSR) is a novel method of resurfacing that uses plasma energy to create a thermal effect on the skin. PSR is not chromophore dependent and does not vaporize the tissue, but leaves a layer of intact, desiccated epidermis that acts as a natural biologic dressing and promotes wound healing and rapid recovery [28].
The portrait PSR system from Rhytec is currently the only commercially available gas plasma resurfacing system to date. An ultrahigh frequency radiofrequency generator excites a tuned resonator and imparts energy to nitrogen gas molecules flowing through the hand-piece resulting in their ionization (Fig. 2.17). Nitrogen is chosen to produce the plasma because of its unique properties as an inert diatomic molecule, which locks up energy in a predictable manner when excited. The Nitrogen source purges oxygen from the skin surface, thereby minimizing the risk of unpredictable hot spots, charring and scar formation. The plasma is directed through a quartz nozzle out of the tip of the hand-piece and onto the skin with no RF energy being transferred to the patient [27],[28]. The effect of PSR plasma on the skin architecture is characterized by two zones of treatment: a zone of thermal damage (ZTD), wherein the cells are rendered non-viable, and a zone of thermal modification (ZTM), wherein the cells are thermally modified, yet remain viable (Fig. 2.18).

![FIG.2.18. The two zones of effect of Portrait plasma skin regeneration (Rhytech) device on the skin: the ZTD (purple) and the ZTM (red)](image)

This process exhibits a very low thermal time constant so it is virtually instantaneous. Each pulse of plasma energy is released onto the target in a Gaussian distribution and produces uniform tissue heating. Adjustment of the RF power and RF pulse width by the generator enables control of tissue effects by altering the amount of energy contained in the plasma pulse. At high energy settings, temperatures averaging 60°C are achieved in the dermis to a depth of approximately 500 μm. This leads to an immediate tissue contraction accomplished via thermal denaturation of dermal collagen, followed by neo-collagenesis and, consequently, skin rejuvenation.

Notwithstanding the deep thermal effects of PSR act in a unique fashion and the balance between efficacy and safety of this technique reaches satisfying levels, some disadvantages emerge during the use of this device on patients, i.e. an immediate and energy-dependent erythema, edema, and de-epithelialization with minimal charring. Moreover, several contraindications to PSR must be considered, i.e. pregnancy, predisposition to developing keloids, darker skin types (Fitzpatrick types V and VI), patients with skin barrier defects, inflammatory skin conditions, and active infections.
Chapter 3

Investigation of the focal spot and the irradiance threshold for linearly and radially polarized light

Measure a thousand times and cut once
- Old Turkish proverb

* This chapter has been published as: Babu Varghese, Simona Turco, Valentina Bonito, Rieko Verhagen, “Effects of polarization and apodization on laser induced optical breakdown threshold”, Optics Express, 21 (15), 18304-18310 (2013).

3.1. Introduction

When laser induced optical breakdown is created in-vivo in human tissue, lowering the incident irradiance required to create breakdown is very important, especially for reducing the risk profile and for increasing treatment efficacy. The irradiance threshold required for LIOB is a function of both medium characteristics (ionization energy, impurity level) and beam characteristics (wavelength, pulsewidth, beam diameter at focus).

In this chapter we investigate the influence of polarization and apodization on laser induced optical breakdown threshold in transparent and diffuse media using linearly and radially polarized light. We measure the focal spot size for linearly and radially polarized light and for different apodization conditions using the knife-edge technique. Results obtained are compared with numerical simulations.

The layout of the chapter is as follows. First the apodization function is explained and the effects of employing an annular illumination are described; the home built prototype for the generation of LIOB is presented; then the knife edge set up for the measurements of the beam waist is described; the results of the pulse energies for LIOB, the focal spots for linear and radial polarization and the irradiance thresholds are shown and discussed; finally the scrambling of polarization in the focus is analyzed by means of numerical simulations; a discussion about the benefits of radial polarization over linear polarization and vice versa concludes the chapter.

3.2 Apodization

An apodization function is used in general to change the input intensity profile of an optical system, with the intent to tailor the system to certain properties. One of the most common apodization function used in optic is annular illumination, created thanks to the blocking of the central part of the beam. In this way only of the rays at the periphery of the beam waist are able to pass. Since the outermost rays
are the ones that experience the highest bending especially when they propagates through high NA lens, the net effects of employing annular illumination is to enhance the longitudinal component in the focus and to yield a longer focal depth and a lower focal spot, on the expense of decreasing efficiency. In Fig.3.1 it is shown the effect of clear and annular illumination when the input beam is radially polarized.

![Schematic sketch of the focusing of a radially polarized beam in case of clear (left) and annular (right) aperture. The red and blue arrows indicate the longitudinal and the transverse electric fields, respectively. The sum of the transverse and the longitudinal components gives the total intensity profile (black line).](image)

### 3.3 Materials and methods

#### 3.3.1 Demonstration of feasibility in skin rejuvenation device

The experimental setup used for the optical breakdown threshold measurements comprises a pulsed laser source, beam shaping optics and mirrors to guide the laser beam via an articulated arm to an aspheric focusing lens (NA = 0.67, f = 2.84 mm, AR: 1050-1620 nm) (Fig.3.2). The laser source is a flash lamp pumped SLM TEM00 Nd:YAG laser which delivers 200 ps laser pulses of 1064 nm. The pulse energy is less than 1 mJ and it was controlled using a polarization beam splitter and a half lambda wave-plate [29]. To create annular illumination, we introduced in the beam path glass slides with a dark spot of diameter 1 and 2 mm. The size of apodization masks is expressed in terms of NA ratio as it follows:

$$\text{NA ratio} = \frac{N_{\text{A_min}}}{N_{\text{A_max}}}$$

where $N_{A_{\text{min}}}$ is defined as the NA of the inner annulus of the apodization mask, while $N_{A_{\text{max}}}$ is the NA of the objective lens. $N_{A}$ ratio=0 corresponds to the condition of clear aperture, without the glass slides. $N_{A}$ ratio=0.3 and 0.6 correspond to mask diameter of 1 mm and 2 mm respectively.
Radially polarized light was created using a commercially available radial polarization converter (ARCOptix, Switzerland) well described in ref [30]. Briefly, the main components of the radial polarizer are: (i) a retarder cell, (ii) a polarization rotator and (iii) a nematic liquid crystal cell (θ-cell) (Fig.3.3).

The laser power was initially set below threshold and was then increased until a visible flash and an audible sound were detected, which testify that LIOB had occurred. Optical breakdown was created in distilled water (sample 1) and scattering phantoms made by water suspensions of Polystyrene
microspheres (Polysciences, Inc) [29]. The particles diameter is 0.75 μm (anisotropy factor, g=0.85), which is in the size range of scattering structures found in human tissue. The reduced scattering coefficients ($\mu_s'$) obtained for the two samples are 5.3 cm$^{-1}$ (sample 2) and 7.1 cm$^{-1}$ (sample 3), based on scattering cross sections following from Mie theory calculations.

After measuring the pulse energy for LIOB in case of linear and radial polarization for different apodization conditions, we measured the beam waist in air for both the states of polarization in case of annular and clear aperture. The knife edge method used to pursue this goal will be described in the following section.

### 3.3.2 Knife edge method

The setup comprises a sliding blade, two photodiodes, an oscilloscope, two motorized stages, and a computer. The sliding blade was moved by two orthogonally-oriented stages actuated by two motors with nanometer accuracy. The motors were controlled by the computer via a LABView program which allows scanning the focal area in the $x$ and $z$ direction. For a given $z$ position, the blade was moved in the $x$ direction and the transmitted intensity was acquired. Scanning on $z$ direction allowed finding the minimum beam waist which corresponds to the beam waist at focus. For the scanning of the focal area, the step sizes along $x$ and $z$ direction were set to 0.15 μm and 0.3 μm respectively.

The two avalanche photodiodes (InGaAs APD110C by Thorlabs, 950 - 1650 nm), both connected to the oscilloscope, were employed for different purposes. One photodiode was used to measure the photocurrent change as a function of knife-edge position and it generated a feedback signal depending on the transmitted intensity to the oscilloscope. The other photodiode was used as the reference signal to the oscilloscope for background noise reduction. The recorded signal was post-processed for calculating the beam waist using LabVIEW (Fig.3.4).

![FIG.3.4. Knife edge technique](image-url)
3.4 Results and analysis

3.4.1 Demonstration of feasibility in skin rejuvenation device: pulse energy measurements

The pulse energy corresponding to optical breakdown threshold measured in distilled water and diffuse media using linearly and radially polarized light is shown in Fig.3.5. The error bars indicate the standard deviation of three measurements. As expected, the pulse energy required to create breakdown increases with the increasing scattering properties of the medium, regardless of the incident polarization state. Indeed, due to the higher scattering and absorption of the scattering medium, a lower number of photons reach the focus, and, as a result, higher incident energy is required.

Moreover we observe that higher incident power is required for radial polarization than for linear polarization, while it is comparable in sample 3 for higher NA ratios. The higher incident power required to create breakdown with radially polarized light could be the consequence of a larger focal spot for radially polarized light. To verify this aspect, we measured the beam waist for linear and radial polarization through the knife edge technique.

![Graph showing pulse energy as a function of reduced scattering coefficient](image)

FIG.3.5. Pulse energy corresponding to optical breakdown threshold as a function of reduced scattering coefficient for linearly and radially polarized light (NA ratio=0, 0.3 and 0.6).
3.4.2 Knife edge measurements

The focal spots obtained for linearly and radially polarized light in case are shown in Tab.3.1.

<table>
<thead>
<tr>
<th>Polarization</th>
<th>$\frac{NA_{\text{min}}}{NA_{\text{max}}} = 0$</th>
<th>$\frac{NA_{\text{min}}}{NA_{\text{max}}} = 0.3$</th>
<th>$\frac{NA_{\text{min}}}{NA_{\text{max}}} = 0.6$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Linear</td>
<td>Exp 3.31 Sim 1.51 Ref[32] 0.89</td>
<td>Exp 4.27 Sim 1.32 Ref[32] x</td>
<td>Exp 5.37 Sim 4.16 Ref[32] x</td>
</tr>
</tbody>
</table>

TAB.3.1. Spot size for linearly and radially polarized beam for different values of NA ratios (experimentally measured with the knife edge technique, numerically simulated, and found in literature).

The accuracy of the measurements is well exemplified by (i) the good fitting obtained for all the beam profiles and (ii) by the good overlapping between the experimental beam profiles and the simulated ones, as shown in Fig.3.6 and Fig.3.7 (for sake of simplicity, we show only the beam profiles in case of clear aperture for linear and radial polarization).

![BEAM PROFILE _ Linear Polarization, Clear Aperture](image-url)

**FIG.3.6.** Experimental and simulated Beam profiles for linearly polarized beam in case of clear aperture.
FIG. 3.7. Experimental and simulated Beam profiles for radially polarized beam in case of clear aperture.

As expected, radially polarized light gives always a larger focal spot, for all apodization conditions for the experimental settings used in the set-up (NA=0.67). While the superiority of radially polarized light for some specific choice of annular illumination and high NA was extensively demonstrated numerically and experimentally in the past [33], it turns out that radially polarized light is not always the best choice. Indeed, for spot size reduction applications the advantage of radially polarized light over the linearly polarized light becomes evident only for specific combinations of aperture illumination and NA. For other cases, it seems that radially polarized light is actually inferior in terms of spot size. In ref [32] it has been shown that for NA<0.7 radially polarized light gives always a larger focal spot over the linearly polarized light.

Let us consider now the effect of the apodization on the reduction of the focal spot for each state of polarization. In case of linearly polarized light, there is a slight increase of the focal spot with the increasing of the mask diameter. Contrariwise in case of radially polarized light the focal spot slightly decreases as the mask diameter increases.

From a theoretical point of view, the net effect of an apodization mask is to enhance the longitudinal component of the electric field in the focus, as explained in Sec.3.2. For clear aperture illumination, there is a significant contribution from plane waves that are barely tilted, which have a small longitudinal field component compared with their transverse field component. When blocking the inner section of the aperture only rays with relatively high bent angle can reach the focal plane and the portion of the longitudinal component relative to the portion of the transverse component is increased. The larger the inner opaque annulus the stronger the longitudinal component will be. For spot size
reduction applications the longitudinal component is desirable for radial polarization illumination, whereas it is detrimental for linearly polarized light, as will be explained in detail in Sec.3.3.3. We thus conclude that the introduction of the apodization mask in order to reduce the spot size is (slightly) effective only in case of radially polarized light. In any case it is interesting to underline that there is no annular aperture that gives tighter spot for the radial polarization over the linear one. Our results perfectly match previous works found in literature. In ref [32] for instance it is demonstrated that, for (relatively) low values of NA (NA<0.7) (i) there are no benefits employing an apodization mask in case of homogeneous states of polarization and that (ii) radial polarization gives always a larger focal spot, even when an apodization mask is used.

3.4.3 Demonstration of feasibility in skin rejuvenation device: irradiance thresholds calculations

The performances of the two states of polarization were analyzed also in terms of irradiance threshold (Fig.3.8). To calculate the irradiance threshold, the measured pulse energy was normalized by laser pulse width and the experimentally calculated spot size.

![Irradiance corresponding to optical breakdown threshold as a function of reduced scattering coefficient for linearly and radially polarized light (NA ratio=0, 0.3 and 0.6)](image)

Fig.3.8. Irradiance corresponding to optical breakdown threshold as a function of reduced scattering coefficient for linearly and radially polarized light (NA ratio=0, 0.3 and 0.6)
We found that radially polarized light yields a lower irradiance threshold in all samples. Furthermore, looking at the ratio of the irradiance required to create breakdown with linear over radial polarization $\frac{I_{th}^{lin}}{I_{th}^{rad}}$, a dependence on the scattering coefficient of the medium is demonstrated. The irradiance ratio is 1.4 in water ($\mu'_s = 0 \text{ cm}^{-1}$), 1.9 in sample 2 ($\mu'_s = 5.3 \text{ cm}^{-1}$), and 2.3 in sample 3 ($\mu'_s = 7.1 \text{ cm}^{-1}$). The ratio increases with the increasing of the scattering properties of the medium because of the path length dependent scattering losses of the photons as it propagates through the medium. This implies that when radially polarized light propagates through diffuse media like skin, the depolarization of photons resulting from multiple scattering is weak compared to linearly polarized light.

3.4.4 Investigation of the electric field and the scrambling of polarization in the focus

We investigated how the focusing lens affects the structure of the electric field in the focus for $NA_{max} = 0.67$ and for $NA$ ratio=0, 0.3 and 0.6. Numerical simulations were performed in MATLAB based on the analytic solution of the diffraction integral described at any point $P (r, \theta, \varphi)$ in the image space for linearly [33] and radially [34] polarized input beam. Annular illumination, represented by an apodizing filter constituted by a circular shading mask (mask diameter =0, 1 mm and 2 mm), was simulated multiplying $P (r, \theta, \varphi)$ by the following function:

$$T(\theta) = \begin{cases} 
0 & 0 \leq \theta \leq \alpha_{min} \\
1 & \alpha_{min} \leq \theta \leq \alpha
\end{cases}$$ (3.2)

Here, the angles $\alpha_{min}$ and $\alpha$ are the angles corresponding to the mask diameter (d) and the clear aperture diameter of the objective lens (D), as shown in Fig.3.9.

Fig.3.9. Schematic of a collimated Gaussian beam going through an annular mask.
In case of clear and annular aperture the components of the electric field in the focus act in a similar fashion, as it possible to see from a comparison between Fig.3.10, Fig.3.11 and Fig.3.12. The transverse component of the linearly polarized beam has a circular intensity distribution located at the center of the focal region, the orthogonal-transverse component shows a four leaf clover intensity distribution, and the longitudinal component is calculated to have an intensity distribution shaped as two off-axis lobes. When a radially polarized beam is employed, the transverse component is shaped as a ring around the focus, while the longitudinal component is a circle centered in the focus and the orthogonal transverse field is identically zero. These results can be regarded as a quantitative confirmation of one of the most peculiar properties of radially polarized light, which is to exhibit a very strong electric field along the optical axis.

**FIG.3.10.** Intensity distributions of transverse, orthogonal transverse and longitudinal focal fields, for linearly (Top) polarized (along the x direction) and radially (Bottom) polarized beam (NA = 0.67, NAmin/NAmax = 0, water as focusing medium n=1.33).
FIG. 3.11. Intensity distributions of transverse, orthogonal transverse and longitudinal focal fields, for linearly (Top) polarized (along the x direction) and radially (Bottom) polarized beam (NA = 0.67, NAmmin/NAmmax = 0.3, water as focusing medium n=1.33).

FIG. 3.12. Intensity distributions of transverse, orthogonal transverse and longitudinal focal fields, for linearly (Top) polarized (along the x direction) and radially (Bottom) polarized beam (NA = 0.67, NAmmin/NAmmax = 0.6, water as focusing medium n=1.33).
In terms of reduction of the focal spot, the transverse and longitudinal component work differently for radial and linear polarization. For a linearly polarized beam the narrow-peak intensity distribution of transverse field component is responsible for the reduction of the focal spot, while the two off-axis lobes of longitudinal component enlarges the focal spot. The situation is different for radially polarized light. The narrow peak profile of the longitudinal component and the ring shaped distribution of the transverse component are indeed both advantageous for the reduction of the focal spot. It is also fundamental to underline that the dominance of the longitudinal component over the transverse component or vice versa is highly dependent on the value of the NA. When the NA is set to low or medium value, as in our case, the focal field intensity profile shrinks weakly along every direction and the longitudinal component is set to low values. Therefore the detrimental contribution of the longitudinal component for linearly polarized light is still negligible and linearly polarized light gives a smaller focal spot compared to radially polarized light. This is in accordance with the knife edge measurements and the numerical simulations of the focal spot reported in Tab.3.1.

It is well known that the propagation of polarized light through biological tissue causes the polarization status of photons to change due to tissue birefringence and tissue scattering. The polarization state of light after a single scattering event depends on the scatterer, direction of scatter, and incident polarization state. Because each scattering event can modify the incident polarization state differently, the scrambling effect of single scattering events accumulates, until finally the polarization state is completely random, i.e. uncorrelated with the incident polarization state. With respect to this, the effect of the scrambling of polarization in the focus should be carefully considered.

Therefore we analyzed the polarization of the wave front in the focal plane in case of NA=0.67 with and without annular aperture. The appearance of an orthogonal-transverse component causes the partial rotation of the electric field vector, hence the scrambling of the state of polarization at certain locations in the focal volume. For a linearly polarized input beam, the contribution of the orthogonal-transverse component can be always considered negligible when integrated over the whole focal plane, but there are single locations at which its amplitude is not negligible and causes the rotation of the electric field. This effect is even more worsened when an annular illumination is employed. Contrariwise for a radially polarized beam the polarization in the focus is always oriented along the radial direction and its orientation depends only on the azimuthal angle, in exactly the same manner as the input beam. Therefore a radially polarized beam holds the additional property of maintaining the polarization pattern in the focus, regardless of the focusing conditions. The scrambling of polarization suffered by linear polarization with high focusing conditions here demonstrated could be used as an explanation for the comparable power and irradiance threshold obtained for sample 3 for high NA ratios.

Previous studies on the propagation of polarized light through scattering media have shown that linearly polarized light depolarizes quicker or slower than circularly polarized light depending on the medium properties (type, size and concentration of scattering particles) ([36], [37]). Most tissues, like the skin, have a preferential scattering in the forward direction with a scattering anisotropy (g) between 0.7 and 0.9 [38]. Here we demonstrated that radially polarized light performs better than linearly polarized light while propagating through tissue phantoms in scattering phantoms with an anisotropy factor g=0.85.
3.5 Conclusions

In this chapter we analyzed the effects of polarization and apodization on laser induced optical breakdown threshold using linearly and radially polarized light. The pulse energy for optical breakdown was experimentally measured for different conditions of polarization and apodization in transparent and scattering phantoms. Using the knife edge technique, we measured the beam waist for linearly and radially polarized light in air and we demonstrated that the former has a larger focal spot, independently from the apodization conditions. To calculate the irradiance thresholds for all the samples the pulse energy of all the samples were normalized by the focal spots experimentally measured. We showed that in terms of irradiance threshold, radially polarized light lowers the irradiance threshold in three samples of different scattering properties. The obtained results demonstrate dependence of MPA processes on input polarization and on the coherence of the laser light and also suggest that the degree of coherence in the focus is higher for radially polarized light than for linearly polarized light.

To summarize, different benefits could be obtained for different applications while using linearly and radially polarized light for optical breakdown. Linearly polarized light is attractive in terms of better availability of laser sources with less critical requirements on pulse energy and in reducing the cost price of ultra-short lasers and laser based skin treatment devices. Radially polarized light performs better in terms of creating optical breakdown with lower irradiance threshold. Lower irradiance threshold may allow deeper layers of tissue to be reached, resulting in higher efficacy of treatment and since a lower power is delivered over the same target area, the risks of collateral damage can also be reduced. This has important implications for optical breakdown based biological applications where desired photomechanical effects can be obtained with lower irradiance.
Chapter 4

Experimental investigation of irradiance threshold for LIOB and LITB

Theory is when you know everything and nothing works.
Practice is when everything works but no one knows why

– Albert Einstein

4.1. Introduction

Laser-induced breakdown (LIB) takes two different forms: laser-induced optical breakdown (LIOB) and laser-induced thermal breakdown (LITB) [12],[3]. The definition of the irradiance threshold for breakdown is very important, especially for aspects regarding laser safety and treatment efficacy. Laser induced optical breakdown threshold and its dependence on medium characteristics (ionization energy, impurity level) and beam characteristics (wavelength, pulse width, beam diameter at focus) has been the subject of several theoretical as well as experimental studies.

In this chapter, we investigate the LIOB and LITB irradiance thresholds on transparent and absorbing aqueous media and we demonstrate the transition from laser-induced optical breakdown to laser-induced thermal breakdown as the absorption coefficient of the medium is increased. The samples are chosen so as to resemble skin optical properties and experiments are performed using a skin rejuvenation prototype developed by Philips Research. We observe that the irradiance threshold for optical breakdown, after correction for the path length dependent absorption losses in the medium, is nearly unaffected by the variation in the absorption properties of the medium. Furthermore, whereas thermal breakdown is occurring for samples with relatively higher absorption properties. Moreover we demonstrate that the LITB irradiance threshold decreases with the increasing of the absorption properties of the medium and is lower than the LIOB irradiance threshold for higher absorbing samples.

The layout of the chapter is as follows. First LIOB and LITB mechanism are further explained. Then the home-built prototype of the LIOB based skin rejuvenation device developed by Philips is described; subsequently the set up for the estimation of the absorption properties of the samples is introduced; finally energy and irradiance thresholds obtained for optical breakdown and thermal breakdown are presented and analyzed.
4.1.1 Laser induced optical and thermal breakdown

LITB occurs primarily in materials which have a fairly high linear absorption coefficient; i.e. those which are opaque at the laser wavelength, through thermal initiation pathway. LITB starts with a linear absorption of light for generating seed electrons through multiphoton ionization, followed by a nonlinear absorption process. Contrariwise LIOB is a nonlinear absorption event unaffected by the absorption coefficient of the medium, except for the path length dependent absorption losses in the medium. In both cases, the triggering phase for plasma formation is the creation of free electrons.

In transparent dielectrics, free electron generation by the incident light relies primarily on LIOB mechanisms: multiphoton ionization, cascade ionization or a combination of the two, as already explained in detail in Sec.2.4.1. However, once energy carried by the primary free electrons is thermalized, thermal emission of free electrons comes into play as a secondary process.

For materials with a high absorption coefficients, heating of the material in the laser focus results in temperature rise and thermionic emission of free electrons. The additional energy levels associated with the absorption process can facilitate the generation of seed electrons for cascade ionization by multiphoton ionization. Moreover, if the thermal emission of free electrons provides seed electrons at a lower irradiance than what would be required for multiphoton ionization, LITB can be considered as the dominant process occurring in the medium. This will be the case primarily for intermediate and long pulsewidths. Indeed with increasing pulse duration, the absorption process provides not just seed electrons but also an even larger fraction of free electrons contributing to breakdown [39].

From the above, it is clear that consideration of thermal ionization is necessary to obtain a consistent picture of the evolution of free electron density contributing to breakdown in transparent and absorbing media. In [41] the influence of linear absorption on optical breakdown in transparent media was for the first time considered. Extension of the numerical model of LIOB to include thermal electron emission was also evaluated. However, to the best of our knowledge, laser induced thermal breakdown as an independent process was not analyzed in any of the previously published models of laser induced breakdown. Most of the attention to date has been focused just on LIOB and in particular on LIOB in aqueous media. An empirical justification for it is that the optical breakdown thresholds in water and in transparent tissues such as cornea were found to be very similar for laser wavelengths exhibiting small linear absorption in those tissues [24]. However, for laser wavelengths that are highly absorbed in tissues, the dynamics of laser induced breakdown will totally change. For instance experimental investigation of LIB threshold on skin carried out in recent years demonstrate that for UV wavelengths, for which the biomolecules of the skin are highly absorbing, plasma formation threshold could be even 6 times higher than the ablation threshold, which indicates once again that plasma formation must be supported by linear absorption [41],[42]. The interaction of linear and nonlinear absorption is relevant also for near and mid IR wavelengths because they are well absorbed in that case by water.

To summarize it would be desirable to include the influence of linear absorption on the breakdown process for biological tissues or, in other words, investigate laser induced thermal breakdown formation in absorbing media. Moreover using only water samples for modeling skin properties, as done by all the researchers to date, is an unrealistic approximation that does not take into
account the fact that even though biological cells and soft tissues consist largely of water, their content of biomolecules and chromophores also influence the dynamics of laser induced breakdown. Therefore also a careful preparation of well calibrated phantoms with optical properties resembling the skin properties should be considered.

In the following section, we describe first how the skin phantoms were obtained and then how their optical properties were measured.

4.2. Materials and Methods

4.2.1 Measurement of optical properties

Laser induced optical and thermal breakdown were created in transparent and absorbing media. As transparent medium we used distilled water (1064 nm: $\mu_a = 0.2$ cm$^{-1}$). As absorbing medium we chose the well-known India Ink by Talens. The optical properties of India ink have been previously studied at visible wavelengths [38].

Starting from a buffer sample made by distilled water and India Ink, dilutions were made to obtain samples with volume fraction of ink ranging from 0.5% to 100% (Tab. 4.1). The optical properties of the samples were experimentally measured using the optical setup schematically shown in Fig. 4.1.

![Fig. 4.1: Schematic of the experimental setup used for optical properties measurement](image)

The setup comprises a laser source (flash lamp pumped SLM TEM00 Nd:YAG laser) emitting at a wavelength of 1064 nm, and a 100 μm thick cuvette containing the sample. A power meter was used to measure the incident ($P_{in}$) and the transmitted power ($P_{out}$) before and after the cuvette respectively. Based on Lambert Beer’s law the ratio between the incident and transmitted power is equal to:
\[
\frac{P}{P_0} = e^{-\mu'_t x}
\]  

(4.1)

where \(x\) is the distance traveled inside the medium and \(\mu'_t\) is the total attenuation coefficient, which can be expressed as:

\[
\mu'_t = \mu_a + \mu_s
\]  

(4.2)

Here, \(\mu_a\) and \(\mu_s\) are the absorption coefficient and the reduced scattering coefficient of the medium, respectively. For the samples chosen the total attenuation coefficient \(\mu'_t\) is equal to the absorption coefficient \(\mu_a\) due to the absence of the scattering process.

4.2.2 Experimental demonstration of laser induced optical and thermal breakdown

The proof of principle was demonstrated employing a home-built prototype of the skin rejuvenation device developed by Philips, schematically depicted in Fig.4.2. The prototype device consists of a base station, an articulated arm, a treatment hand piece and a computer. The base station houses an optical system, a cooling system and electronics. The optical system comprises a pulsed laser source, beam shaping optics and mirrors to guide the laser beam to the hand piece via the articulated arm. The laser source is a flash lamp pumped SLM TEM00 Nd:YAG laser which delivers light pulses of 1064 nm with pulse energies in excess of 0.15 mJ at a pulsewidth of 200 ps. To focus the beam into the liquid samples we used an aspheric lens (NA = 0.67, \(f = 2.84\) mm, AR: 1050-1620 nm). Laser induced breakdown in the samples was created at three different focusing depths, i.e. 130 \(\mu\)m, 148 \(\mu\)m and 170 \(\mu\)m.

The power was initially set below threshold; the cuvette was then moved towards the objective to get LIOB at the desired distance; finally the power was increased again until a visible flash and an audible sound were detected inside the cuvette at the focusing distance desired, which testify that laser induced breakdown had occurred. Measurements were repeated for each path length and for each sample three times.
4.3. Results and Analysis

4.3.1 Measurement of optical properties

The optical properties of the samples were measured with the set up depicted in Fig.4.1. The results obtained are plotted in Fig.4.3.
4.3.2 Experimental investigation of irradiance thresholds for LIOB and LITB

The breakdown threshold pulse energy measured in the samples made by distilled water and different percentage of ink is shown in Fig.4.4. The error bars indicate the standard deviation of three measurements. For each value of the absorption coefficient, the pulse energy was measured positioning the cuvette at three different focusing depths (130 µm, 148 µm and 170 µm), as shown in Fig.4.2.

As expected, the qualitative trend of the pulse energy as a function of the absorption properties is the same for all the focusing depths investigated. For low values of the absorption coefficients ($\mu_a = [0.5 - 11.32] \text{ cm}^{-1}$) pulse energy required to create breakdown increases with the increasing of absorption properties of the medium. For $\mu_a = [11.32 \text{ cm}^{-1} - 172.08] \text{ cm}^{-1}$ the energy threshold is almost constant. From a theoretical point of view, this could be explained with the occurring of optical breakdown, which is by definition a process virtually unaffected by the absorption properties of the medium, as explained in Sec.4.1.1. Finally, for the highest values of the absorption coefficient ($\mu > 172.08 \text{ cm}^{-1}$), the dependence on the absorption coefficient is detected again, as demonstrated by the decreasing of the energy threshold with the increase of the absorption coefficient. This means that, when the absorption properties of the medium become significant, there is a transition from LIOB to
LITB. LITB indeed occurs primarily in materials which have a fairly high linear absorption coefficient, and shows a strong dependence on the properties of the medium.

Another aspect that should be underlined is that the energy pulse required for thermal breakdown is always lower than the LIOB energy threshold. The additional energy levels associated with the absorption process can facilitate the generation of seed electrons. Therefore the thermal emission of free electrons provides seed electrons at a lower pulse energy than what would be required for LIOB and LITB can be considered as the dominant process occurring in the medium. To date, to the best of our knowledge, the dominance of LITB process has been demonstrated only for intermediate and long pulsewidths [39]. Here we successfully proved for the first time the possibility to create LITB even at lower values of pulsewidth (range of ps).

After measuring the pulse energy to induce LIOB and LITB in the medium, we calculated, for each focusing depth, the irradiance threshold in the focus normalizing the pulse energy measured by the laser pulsewidth and the focal area. The focal area was approximated to a circle of radius 3.3 µm (beam waist experimentally measured through the knife edge technique). Results are shown in Fig.4.5.

![LIOB irradiance threshold](Fig.4.5: LIOB irradiance threshold in the focus (solid lines) and at the cuvette interface (points) as a function of the absorption properties of the medium for different focusing depths.)

When the irradiances are taken into account, a new interesting aspect emerges. For highest values of the absorption coefficients and higher focusing depths, the irradiance threshold measured for all the focusing depths is not sufficient to let breakdown happen ($I_{\text{calculated}} < 10^{10}$ W/cm$^2$, $I_{\text{Critic}} = 10^{11-13}$)
W/cm²). From a logical point of view this means that the breakdown is not occurring in the focus but at a different location in the medium. To further demonstrate this hypothesis, we calculated the irradiance thresholds at the interface sample-cuvette and we compared them to the irradiances in the focus previously calculated. The irradiance thresholds at the interface were obtained normalizing the pulse energy measured by the area at the interface. To calculate the area at the interface we considered the geometry of a Gaussian beam propagating in free space, for which the spot size (radius) \( w(z) \) is expressed as follows:

\[
w(z) = w_0 \sqrt{1 + \left( \frac{z}{z_r} \right)^2}
\]

(4.3)

where \( w_0 \) is the beam waist, \( z \) is the absolute distance between the focus and the inner interface of the cuvette, and \( z_r \) is called the Rayleigh range and it’s equal to:

\[
z_r = \frac{\pi w_0^2}{\lambda}
\]

(4.4)

where \( \lambda \) is the wavelength of the laser beam (1064 nm).

For high values of the absorption coefficient the irradiance threshold at the interface is higher than the irradiance required in the focus (Fig.4.5), meaning that the breakdown is occurring at the interface, due to a process called “surface breakdown”. As it is possible to see from Fig.4.6, as the absorption coefficient increases two phenomena can be detected: (i) the decreasing of the irradiance peak at the focus, and, in parallel, (ii) the appearance of a new irradiance peak at the interface, which is first lower, then comparable and finally higher than the irradiance peak in the focus.

Theoretically speaking, surface breakdown can be classified in surface optical surface breakdown and thermal surface breakdown. Trying to define which form of surface breakdown is taking place in our experiments is quite controversial. The lower value of the irradiance threshold reached in this case (~10^11 W/cm², 2 orders of magnitude less than the threshold for LIOB in the focus) is typical of LITB with respect to what explained before. However, the independence of the irradiance threshold on the absorption properties of the medium for surface breakdown needs further investigation.

To summarize, looking at the energy and the irradiance threshold of Fig.4.4 and Fig.4.5 three regions can be identified with the increasing of the absorption coefficient: (i) the LIOB constant region, where the critical irradiance threshold for breakdown is independent on the absorption properties of the medium and the breakdown occurs through multiphoton initiated cascade ionization; (ii) the LITB region where the breakdown occurs through cascade ionization initiated by thermionic emission; (iii) the surface breakdown region for which the irradiance threshold is virtually unaffected by the absorption properties of the samples.
Fig. 4.6: Variation of the LIOB irradiance threshold and at the cuvette interface as a function of the absorption properties of the medium for a fixed focusing depth (130 µm).

4.4. Conclusions

In this chapter we investigated LIOB and LITB threshold on transparent and absorbing liquid media, the former being similar to the aqueous content of the eye and cells, and the latter resembling the optical properties of tissues like the skin. We carried out experiments on water samples and phantoms having relevant skin absorption properties using a home-built prototype of the skin rejuvenation device developed by Philips. We compared the results of LIOB and LITB in terms of energies and irradiances required. We demonstrated that optical breakdown, after correction for the path length dependent absorption losses in the medium, is nearly unaffected by the variation in the absorption properties whereas thermal breakdown highly depends on them. In particular we showed that the irradiance threshold as a function of the absorption coefficient is constant and decreasing for LIOB and LITB respectively. Moreover we demonstrated that a lower irradiance threshold can be achieved when LITB is created, compared to the case of LIOB. This has important implications when LITB is applied on human tissue, especially regarding laser safety and treatment efficacy.
Chapter 5

Reduction of irradiance threshold for laser induced optical breakdown in an external plasma environment

We haven’t the money so we’ve got to think
- Lord Rutherford

5.1 Introduction

Subsurface laser skin ablation through laser induced optical breakdown (LIOB) requires high intensities in the order of $10^{13}$ W/cm$^2$. The initiation of optical breakdown through multi-photon ionization involves generation of one or more seed electrons by absorption of multiple photons having same polarization in the focal volume. However, multiple scattering and tissue birefringence results in depolarization of light and this effect accumulates as a function of focusing depth inside the skin. Therefore skin needs to be exposed to high laser intensities to create sufficient number of photons with same polarization in order to exceed the threshold for creating these seed free electrons.

In this chapter, we demonstrate the feasibility of lowering the intensity threshold for LIOB by providing seed free electrons in the focal volume of the tightly focused ultra-short laser pulses using an additional plasma source. Experiments were performed to confirm the proof of principle using a skin rejuvenation prototype developed by Philips Research in combination with a commercially available plasma device, kINPen®09.

The layout of the chapter is as follows. First, basic principles of laser induced breakdown in presence of an additional plasma source are explained; then the optical setup is described; finally, the results obtained are presented and analyzed.

5.1.1 Laser induced optical breakdown in an external plasma source

Laser induced optical breakdown is a non-linear absorption process leading to plasma formation at locations where the threshold irradiance for breakdown is surpassed [12]. The mechanisms that can lead to LIOB are cascade ionization, multi-photon absorption or a combination of the two. In both cases, the first step is the generation of free electrons in the focal volume. In breakdown by cascade ionization, seed electrons come from ionization of impurities by thermal excitation in case of impure medium, or by
ionization of a few molecules through multi-photon absorption in case of pure medium. In multi-photon absorption, free electrons are created by simultaneous absorption of a multiple number of photons with same polarization state and with total energy $(N\nu)$ exceeding the ionization potential of the investigated medium. In case of LIOB in aqueous media, for instance, six to twelve photons ($\lambda=1064$ nm) exceeding the ionization potential of water ($\Delta\approx$6.5-12.5 eV) are required (Fig.5.1)[43]. The generation of the seed electron requires significant thresholds ($I_{th1}$), typically 100-1000 times higher than the ones of subsequent cascade ionization ($I_{th2}$), and both intensity requirements contributes eventually to the overall high threshold intensity necessary for creating the LIOB event (Fig.5.1).

![Generation of seed electron by multi-photon absorption](image)

Here we propose a method to reduce the intensity threshold for LIOB process by creating a free electron environment using an external plasma source. In general, plasma state occurs when matter is in the form of a charged mixture of positive ions and negative electrons after an ionization process. Plasma is sometimes referred to as being "hot" if it is nearly fully ionized, or "cold" if only a small fraction (for example 1%) of the gas molecules is ionized. For the purposes of our study partial or weak ionization that can provide at least one seed electron in the focal volume is sufficient to lower the intensity threshold.

**5.2 Materials and Methods**

The proof of principle for lowering of optical breakdown threshold in an external plasma environment was demonstrated using the experimental setup schematically depicted in Fig.5.2. The experimental setup consists of a home-built LIOB based skin rejuvenation prototype device recently developed by Philips and a cold plasma source positioned such that partial or weak ionization occurs in the focal volume. To change the intensity of the laser beam, a polarizer was positioned after the second mirror of the setup.
5.2.1 LIpOB based skin rejuvenation device

Experiments were carried out using a home-built skin rejuvenation prototype device consisting of a base station, an articulated arm, a treatment hand piece and a computer. The base station houses an optical system, a cooling system and electronics. The optical system comprises a pulsed laser source, beam shaping optics and mirrors to guide the laser beam to the hand piece via the articulated arm. The laser source is a flash lamp pumped SLM TEM00 Nd:YAG laser which delivers sub-nanosecond light pulses of 1064 nm, and a pulse energy in excess of 0.15 mJ. The hand piece consists of a focusing system that focuses the laser beam to a tight focal spot (Φ < 10 μm).

5.2.2 Atmospheric pressure cold plasma device

To generate plasma in proximity of the laser beam we used a commercially available plasma device (kINPen® 09 by NeoPlas Tools) that fulfills European directive 2004/108/EG and German Standards EN 61000-6-1~4 (Fig.5.3). This device works under atmospheric pressure generating cold plasma for the treatment of temperature-sensitive surface. It is composed of a DC power supply unit (system power: 8-10 W at 230 V, 50/60 Hz) and a hand held device for the generation of plasma (dimensions: length = 170 mm, diameter = 20 mm, weight = 170 g). The gases (compressed air/Argon) are fed to the electrode head at an inlet pressure of 1.5 bar [22].
In the electrode head a high-frequency (HF) voltage (1.1 MHz, 2–6 kV$_{pp}$) is applied to a pin-type electrode (1 mm diameter) mounted in the center of a quartz capillary (inner diameter 1.6 mm). In the continuous working mode the plasma is generated from the top of the centered electrode and expands to the surrounding air outside the nozzle (Fig. 5.3). The visible plasma jet length is dependent on power input: adjusting the voltage in the range [0-10] V, the jet length can be varied between 0 mm (absence of plasma at 0 V) and 15 mm. At maximal input DC power of 3.5 W to the hand-held unit, the ignited plasma jet has a length of up to 12 mm and free electron density is in the range of $[10^{12}-10^{14}]$ cm$^{-3}$. The jet diameter is between 1 and 2 mm, depending on the kind of gas and gas flow [22]. To obtain the typical blue-violet plasma jet, the gas flow rate must be greater than 0.6 L/min and the power supply switched on.

We measured the intensity threshold for creating optical breakdown in air. The power was initially set below threshold and was then increased until a barely visible flash and a scarcely hearable sound were detected, which corresponds to the LIOB threshold. The energy of the laser beam was varied without changing the beam profile by means of the rotatable polarizer. Afterwards, the argon feeding was opened and the probe of the Kinpen device was carefully positioned close to the objective until an enhancing in the spot light and in the sound was detected. The energy threshold in presence of argon was measured at three different values of argon flow rate, (3, 5.4, 7.5) L/min. For each value of argon flow, we then measured the energy threshold in presence of plasma plume, after switching on the power supply of the Kinpen device. To verify also a possible dependence on voltage, for each value of argon flow we recorded the energy threshold at 2 V, 4 V and 6 V. In all the steps, the measurements were repeated three times and the average and the standard deviation were calculated.
5.3 Results and analysis

We measured the energy thresholds for optical breakdown in argon with and without plasma. To calculate the irradiance threshold we normalized the energy recorded by the focal area (beam waist 3.3 μm) and the pulsewidth (200 ps). The irradiance thresholds obtained are shown in Fig.4 for different values of argon flow rates (3, 5.4, 7.5) L/min and applied r.f. voltages (2, 4, 6) V. Our experimental results demonstrate a 70% reduction in optical breakdown threshold in the active jet plasma environment compared to the case of argon gas without ionization.

Let us consider now the differences between the irradiance thresholds calculated just in case of plasma environment and, in particular, the dependence on the voltage applied for a fixed flow rate. In case of argon pumped at 3 L/min, there is an increase of the threshold with the increasing of the applied voltage. For highest values of flow rate (5.4 L/min and 7 L/min), a specific trend cannot be identified, even if in both the cases the minimum irradiance is in correspondence of an intermediate value of voltage (4 V). However the differences between the maximum and the minimum value of irradiance for a certain flow rate at different voltages are not so significant, meaning that the voltage applied for the generation of the plasma plume doesn’t influence the irradiance threshold for optical breakdown.

If we consider the dependence on the flow rate for a fixed applied voltage, the possibility to identify a common trend that could include all the values measured is difficult as well. If we exclude the
case of plasma generated with 2V at an argon flow of 3 L/min, there is a decrease of the energy threshold with the increasing of the flow rate. Even in this case, anyhow, the differences between maximum and minimum thresholds detected are negligible.

In this chapter, we have demonstrated 70% reduction in irradiance threshold for laser induced optical breakdown when an active plasma environment is provided in the focal volume of tightly focused ultra-short laser pulses. The first ionization potential of argon is 1500 kJ/mol corresponding to ~ 15.76 eV and that of air is 1402.3 kJ/mol corresponding to 14.6 eV. Due to these high ionization potentials, the probability to generate seed electrons is extremely low and reduction in irradiance threshold is expected when the plasma source is providing free electron environment in the focal volume.

When a certain voltage is applied, the ionization of argon starts and an enhancement in the LIOB event (in terms of intensity of sound and frequency of the flickering green spot) occurs due to the presence of free electrons in the focal volume. From a logical point of view, for a fixed value of the flow rate, we should expect a decrease of the energy threshold with the increasing of the applied voltage, contrary to the results of Fig 5.4. With a higher applied voltage indeed, the production rate of free electron increases due to an enhancement of the ionization process.

To initiate cascade ionization there must be at least one seed electron in the focal volume Vf. Therefore, if we assume a constant number No_min of initial electrons (No_min=1), the minimum value of the initial free electron density can be deduced from No_min through:

$$n_{o min} = \frac{N_{o min}}{V_f}$$  (5.1)

The focal volume Vf is approximated by a cylinder with diameter d and length l:

$$d = 2w_0$$  (5.2)

$$l = \frac{\pi w_0^2}{\lambda}$$  (5.3)

where w_0 is the Gaussian waist radius (~1.5 μm) [12]. The minimum starting density required is then $n_{o min} = 21.3 \times 10^9$ cm$^{-3}$, which is lower than the estimated electron density for the plasma device ($n_{kinpen} = 10^{12}-10^{14}$ cm$^{-3}$), based on the specifications of the device. This is in agreement with our observation that the reduction in the irradiance threshold do not depend on the voltage applied for ionization.

Based on the rate equation, the time variation of the electron density $\frac{dp}{dt}$ is a function of electron generation through multiphoton absorption $\frac{dp}{dt}_{mp}$ and cascade ionization $n_{casc}$, where $n_{casc}$ is the probability per unit time that a free electron will have an ionizing collision with a bound electron, the diffusion of the electrons out of the focal volume $-g$ and attachment to neutral molecules (or trapping in localized potential wells), and the electron-ion recombination losses $-r_{rec}p^2$. Here the effects of electron losses due to trapping and recombination can be neglected. As the flow rate is increased, the concentration of free electrons in the focal volume is probably high because of lower probability for recombination and increased concentration of argon molecules present for ionization by
laser pulse. These two factors can contribute to the avalanche ionization phase of the optical breakdown process and thereby leading to reduction in irradiance threshold.

In general, lowering the irradiance threshold with the above described method may allow creating deeper lesions inside the skin and can lead to precise and well-localized tissue effects with less risk of collateral damage, thereby improving safety and efficacy of treatment. Furthermore the laser pulse parameters required for the LIOB process become significantly less demanding and this will result in better availability of laser sources with less critical requirements. Any laser energy reduction will have an exponential benefit of cost impact on the price of the laser source, which is the main driver for cost of the entire system for devices based on LIOB.

However, further research is required to demonstrate the advantages of the proposed method for skin treatment. These include investigation of penetration of plasma into skin, embodiments for combining plasma with laser pulses for treatment. Plasma is known to penetrate into the skin and commercial devices are already available for skin treatment applications, e.g. Plasma Portrait from Rhytec. In this hot plasma device, at high energy settings temperatures averaging 60°C are achieved in the dermis to a depth of approximately 500 μm (Fig. 5.5)[28].

Recent reports show developments of miniaturized cold plasma flashlights (Fig.5.6) driven by a 12 V battery that doesn’t require any external generator or wall power and external gas feed or handling system [45]. The temperature reached by the plume of plasma is between 20-23 °C, which is very close to room temperature and therefore prevents any damage to the skin. The device itself is fitted with resistor to stop it heating up and making it safe to touch. The device can be easily made and costs less than $100 to produce.
5.4 Conclusions

To summarize, in this chapter we demonstrated 70% reduction in the irradiance threshold for laser induced optical breakdown by providing seed free electrons in the focal volume of the tightly focused ultra-short laser pulses using an external plasma source. The experiments were performed by combining a optical breakdown based skin treatment prototype device with a commercially available plasma source. The use of an external plasma source and the consequent threshold lowering obtained may allow a reduction in terms of risk of collateral damage and, consequently, an improvement in terms of safety and efficacy of the treatment and cost production.
Chapter 6
Summary and Outlook

The future is like a corridor into which we can see only by the light coming from behind
— Edward Weyer Jr.

In this chapter, summary of results and conclusions are given and the outlook for future developments is presented.

6.1 Conclusions

The medical laser market for skin rejuvenation and wrinkle removal is increasing significantly in the last decades. The spectrum of skin resurfacing techniques ranges from ablative to non-ablative, and more recently to fractional resurfacing. These methods differ in technology, efficacy of treatment, patient discomfort, side effects and social downtime. Nowadays demand is strong for safety and effectiveness of the treatments to selectively bolster the tissue and mitigate all the undesired visible changes. To respond to this challenge and to overcome the limitations of all the existing technologies, Philips recently developed a novel minimally invasive skin rejuvenation method based on laser induced optical breakdown (LIOB). With this approach, new collagen production and skin remodeling are induced, with little or no healing time and less patient discomfort.

LIOB requires high irradiance thresholds to occur. Lowering the irradiance threshold is very important for aspects regarding the safety and efficacy of the treatment: deeper layers of tissue may be targeted and the risks of collateral damage would be significantly reduced. In this work of thesis we provide three solutions to lower the irradiance threshold of the LIOB based skin rejuvenation prototype by Philips: (i) use of radially polarized light to get a larger focal spot and, consequently, a lower irradiance threshold, (ii) generation of thermionic emission of seed electrons (thermal initiation pathway) to facilitate the avalanche process leading to optical breakdown, (iii) reduction of the pulse energy through generation of seed electrons in the focal volume by using an external plasma source.

In Chapter 2 the theoretical background underlying the content of thesis is given. First, basic principles of light polarization are described. Then, a short description of skin anatomy and its interaction with light is presented. Then, the skin rejuvenation methods and technologies available nowadays are investigated. The novel minimally invasive skin rejuvenation technique recently developed by Philips and based on laser induced optical breakdown (LIOB) is introduced. Then a detailed explanation of the theoretical principles behind LIOB and another form of laser induced breakdown, i.e laser induced thermal breakdown (LITB), is provided.
Then the ionization process underlying plasma formation is described and an overview of the mechanisms of generation of cold plasma is presented. Examples of laser and plasma based biomedical devices conclude the chapter.

In Chapter 3 the investigation of the energy threshold for optical breakdown in scattering and absorbing media is described. Then the experimental investigation of the focal spot for linearly and radially polarized light in case of clear and annular aperture is performed. The beam waist is measured through the knife edge technique and a larger focal spot is demonstrated for radial polarization, independently from the apodization conditions. The experimental results are then further confirmed by comparing them with available literature and with numerical simulations developed in a previous work.

Moreover it is shown that high NA focusing of homogenous states of polarization, e.g. linearly polarized light, results in scrambling of polarization, while radially polarized light theoretically maintains the polarization in the focus. To investigate the influence of polarization and apodization on irradiance threshold for LIOB, the energy thresholds measured for scattering and absorbing media are normalized by the focal spots measured through the knife edge technique. Our results show that radially polarized light gives a lower irradiance threshold relative to linearly polarized light. This has important implications for skin rejuvenation, because it may allow deeper layer of tissue to be reached with less risk of collateral damage, thereby improving safety and efficacy of the treatment.

In Chapter 4 the irradiance threshold for LIOB and LITB in transparent and absorbing aqueous media is investigated. The samples are chosen so as to resemble skin optical properties and experiments are performed using a skin rejuvenation prototype developed by Philips Research. The transition from laser-induced optical breakdown to laser-induced thermal breakdown as the absorption properties of the medium increase is demonstrated. Moreover it is shown that irradiance threshold for optical breakdown, after correction for the path length dependent absorption losses in the medium, is nearly unaffected by the variation in the absorption properties of the medium. Contrariwise the irradiance threshold for LITB decreases with the increasing of the absorption properties of the medium. It is also demonstrated that the LITB threshold is always lower than the LIOB threshold. This has important implications when LITB is applied on human tissue, especially regarding laser safety and treatment efficacy.

In Chapter 5 an alternative effective solution for the reduction of the irradiance threshold for subsurface laser skin ablation through laser induced optical breakdown (LIOB) is presented. We demonstrate that by providing seed free electrons in the focal volume of the laser objective using an additional plasma source, a 70% reduction of the irradiance threshold is obtained. Experiments are performed using a skin rejuvenation prototype developed by Philips Research in combination with a commercially available plasma device, kINPen®09.
6.2 Outlook

Despite the clarity of the benefits in terms of safety and efficacy of laser based skin treatments when a lower the irradiance threshold is used, an extensive study of all the possible solutions to achieve this goal still needs to be done. The results of this research project offer several promising directions for further investigation of some of them.

The influence of polarization on the irradiance threshold for multiphoton absorption processes has been studied with linear and radial polarization. The presented results suggest that great improvements can be obtained exploiting the properties of radially polarized light. As far as the LIOB based skin rejuvenation technique is concerned, in-vivo experiments are required to assess the potential advantages of employing radially polarized light for optimization of the technique. For instance measurements of the maximum depth at which LIOB can be created in vivo are needed, and the potential improvements in efficacy of treatment need to be verified.

The mechanisms underlying the surface breakdown are not yet well-understood. From our investigation of the irradiance threshold for absorbing media it emerges that for large linear absorption coefficients, the breakdown process resembles plasma formation at target surface more than breakdown in a bulk medium. This could be due to a diminishing of the optical penetration with respect to the focal length. Our results suggest that seed electrons produced during surface breakdown are available at a breakdown threshold typical of LITB (and lower than the one required for LIOB), meaning that surface thermal breakdown is occurring. On the other hand, an unexpected independence of the irradiance threshold from the absorption properties of the medium is detected. Therefore further investigation is required to fully characterize the process.

In laser skin therapy the knowledge of absorbing and scattering properties of the treated area is essential for the purpose of predicting a successful treatment. The investigation of the irradiance threshold for LIOB and LITB presented in Sec.4.3.1 is limited to the use of transparent and absorbing aqueous media. To characterize the influence of the scattering properties of the medium on the irradiance threshold the optical setup presented in Sec.4.2.2. is currently being modified and experiments will soon be started. The schematic of the final setup is shown in Fig.6.1. Layers of non-absorbing scatters for the used wavelength will be prepared and positioned before at the interface of the cuvette containing the absorbing medium. Moreover, to completely define the dependence of the irradiance threshold in case of LIOB and LITB, samples with different degrees of scattering will be tested. Results obtained from these experiments could be a valuable demonstration of the expected less affection of LITB to scatters, compared to the case of LIOB process.
FIG. 6.1. Set up for the investigation of LIOB and LITB threshold in absorbing and scattering samples

LITB primarily occurs for intermediate and long pulsewidths, where long pulse interaction times do allow breakdown by linear absorption or direct heating of the medium. An investigation of the thermal breakdown process for a pulsewidths in the nanosecond regime could reveal fundamental aspects of LITB that still need to be discovered. Experimental investigation of the irradiance threshold for breakdown in presence of a nanosecond laser source will soon be started.

LIOB by multiphoton initiated cascade ionization occurs when multiple photons exceeding the ionization potential of the investigated medium are absorbed. The irradiance threshold guiding the process is therefore highly dependent on the ionization energy of the medium considered. With respect to this, with the addition to the medium of substances with a very low ionization energy a lowering of the irradiance threshold could be achieved. The use of biocompatible substances would be preferred in order to consequently perform in-vivo experiments on different types of human skin.
Appendix

The numerical simulations presented in chapter 3 were carried out in MATLAB. We wrote the following code to calculate the focal spot for linearly and radially polarized light in case of clear and annular aperture and to obtain the graphs of the beam profiles for both the states of polarization.

**LINEAR POLARIZATION**

```matlab
load ke_lin

%Zoom on interesting part
x_r = ke_lin(:,1);
I_r = ke_lin(:,2);

x_r= x_r(200:500);
I_r = I_r(200:500);

%Baseline removal, normalization
bs = mean(I_r(end-60:end));
I_bs=I_r -bs;
Amp = mean(I_bs(1:60));
I_n = I_bs/Amp;

%Central point and x shift
ind_center = find(I_n<=0.5);
ind_center=ind_center(1);
x_n = (x_r-x_r(ind_center))*10^3; %microns
figure, plot(x_n,I_n,'o');

%Smoothed knife-edge profile
fit_lin_ke = fit(x_n,I_n,'smoothingspline','normalize','on','SmoothingParam',0.9995);
I_sm = fit_lin_ke(x_n);

%Derivative of smoothed profile
x_lin = x_n(1:end-1);
prof_lin_0 = -diff(I_sm);

%After derivative, the profile has some zero values to be removed
figure, plot(x_lin, prof_lin_0,'o')

%Zero removal
indices = find(prof_lin_0~=0);
x_focus_lin = x_lin(indices);
prof_focus_lin = prof_lin_0(indices);
prof_focus_lin = prof_focus_lin/max(prof_focus_lin);
fit_lin_prof=fit(x_focus_lin,
    prof_focus_lin,'smoothingspline','normalize','on','SmoothingParam',0.9995);
x_focus_lin = resample(x_focus_lin,10,1);
```

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% Beam waist calculation (1/e2 and FWHM)
prof_focus_lin = fit_lin_prof(x_focus_lin);

x_focus_lin = x_focus_lin(5:end-5);
prof_focus_lin = prof_focus_lin(5:end-5)

ind_1e2= find(prof_focus_lin>=0.135);
bound_1e2_1 = x_focus_lin2(ind_1e2(1));
bound_1e2_2 = x_focus_lin2(ind_1e2(end));

beam_waist_1e2= bound_1e2_2 - bound_1e2_1;

ind_fwhm= find(prof_focus_lin>=0.5);
bound_fwhm_1 = x_focus_lin(ind_fwhm(1));
bound_fwhm_2 = x_focus_lin(ind_fwhm(end));

beam_waist_fwhm= bound_fwhm_2 - bound_fwhm_1;

% Plot
figure, plot(x_focus_lin, prof_focus_lin, 'ko')
hold on
plot(x_focus_lin,ones(size(x_focus_lin))*0.135,'r')
plot(x_focus_lin,ones(size(x_focus_lin))*0.5)
line([bound_1e2_1,bound_1e2_1],[0,0.2],'Color','r')
line([bound_1e2_2,bound_1e2_2],[0,0.2],'Color','r')
line([bound_fwhm_1,bound_fwhm_1],[0,0.5]),
line([bound_fwhm_2,bound_fwhm_2],[0,0.5])
axis([-5 5 -0.1 1.1])

disp('beam waist 1/e2 def: '), disp(beam_waist_1e2);
disp('beam waist fwhm def: '), disp(beam_waist_fwhm);

============================================================================

RADIAL POLARIZATION

% Zero removal from smoothed profile
load ke_rad_sm
load x_rad_exp
load fitted_rad_prof
load x_rad_0
load prof_rad_0
load fitted_rad_sm

% Smoothed profile
figure, plot(x_rad_0,prof_rad_0, 'o')
hold, plot(x_rad_exp,ke_rad_sm,'r','linewidth',1.5)
axis([-8 8 -0.1 1.1])

% Derivative of smoothed profile
prof_focus_rad_zero = -diff(ke_rad_sm);
x_rad = x_rad_exp(1:end-1);

%After derivative, the profile has some zero values to be removed
figure, plot(x_rad, prof_focus_rad_zero,'o')

%Zero removal
indices = find(prof_focus_rad_zero~=0);
x_focus_rad = x_rad(indices);
prof_focus_rad = prof_focus_rad_zero(indices);

x_focus_rad = resample(x_focus_rad,10,1);

%Beam waist calculation (1/e2 and FWHM)
prof_focus_rad = fitted_rad_prof(x_focus_rad);
x_focus_rad = x_focus_rad(5:end-5);
prof_focus_rad = prof_focus_rad(5:end-5);
prof_focus_rad = prof_focus_rad/max(prof_focus_rad); %normalization
ind_1e2 = find(prof_focus_rad>=0.135);
bound_1e2_1 = x_focus_rad(ind_1e2(1));
bound_1e2_2 = x_focus_rad(ind_1e2(end));

beam_waist_1e2 = bound_1e2_2-bound_1e2_1;

ind_fwhm = find(prof_focus_rad>=0.5);
bound_fwhm_1 = x_focus_rad(ind_fwhm(1));
bound_fwhm_2 = x_focus_rad(ind_fwhm(end));

beam_waist_fwhm = bound_fwhm_2-bound_fwhm_1;

%Plot
figure, plot(x_focus_rad, prof_focus_rad,'ko')
hold on
plot(x_focus_rad,ones(size(x_focus_rad))*0.135,'r')
plot(x_focus_rad,ones(size(x_focus_rad))*0.5)
line([bound_1e2_1,bound_1e2_1],[0,0.2],'Color','r')
line([bound_1e2_2,bound_1e2_2],[0,0.2],'Color','r')
line([bound_fwhm_1,bound_fwhm_1],[0,0.5])
line([bound_fwhm_2,bound_fwhm_2],[0,0.5])
axis([-5 5 -0.1 1.1])

disp('beam waist 1/e2 def: '), disp(beam_waist_1e2);
disp('beam waist fwhm def: '), disp(beam_waist_fwhm);
6. S. Huard, “Polarization of light”, John Wiley & Sons Ltd, Ch1, (1997)


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