LASER APPLICATIONS IN BIO-MEDICAL FIELD

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Abstract

In this topic are described the main parameters controlling the laser-biological matter interactions. They will be illustrated the laser properties and the physical concepts at the base of the coherent light emission. In particular they will be discussed the role of the laser intensity, wavelength, duration of the laser pulse, mechanisms of photon energy transfer to bio-medical materials, and many bio-medical and bio -engineering applications. A close examination will concern the classification of the physical laser-matter interaction mechanisms like photochemical, photothermal, photoablation and electromechanical. Certain uses in diagnostics, therapeutic applications in Cardiology, Dentistry, Ophthalmology, deposition of biocompatible thin films and laser welding will be reported. Significant advantages of the laser over conventional techniques, will be discussed.

INTRODUCTION

The importance of knowledge of the mechanisms governing the operation of laser requires the submission of aspects of physics that are the basis for the study of the laser-matter interaction . An important parameter for the study of the effects of macroscopic and microscopic interaction with the matter and that characterizing the laser light is represented by the intensity, which is defined as the ratio of the emitted beam power and the unit of irradiated area. It is possible to distinguish the laser intensity in high ($>10^{16}$ W/cm^2), medium ($\sim 10^{10}$ W/cm^2) and low ($<10^6$ W/cm^2). The latter in particular are used in medicine for diagnostic use, those intermediate for surgical use and those of high power mainly for research purposes. The capacity to concentrate in a tiny solid angle an enormous power makes the laser does lend itself to a large number of applications. The peculiarities of laser (high directionality and high spatial and temporal accuracy, an excellent haemostatic effect, reduction of pain and post-operative complications) make them a valuable and indispensable tool for the care and intervention on some of the pathologies otherwise not curable. The wavelength plays a fundamental role in the laser-matter interaction as it is inherent in the value of the absorption coefficient and in its reverse, or rather in the depths of absorption of the laser light. Also the duration of the laser pulse, associated with high or low energies, ensures a localized beam deposition with less or higher energy.

STRUCTURAL MODEL

To understand the idea of the laser operation one should consider the atomic theory which is based on phenomena such as absorption, spontaneous emission and stimulated emission [1].

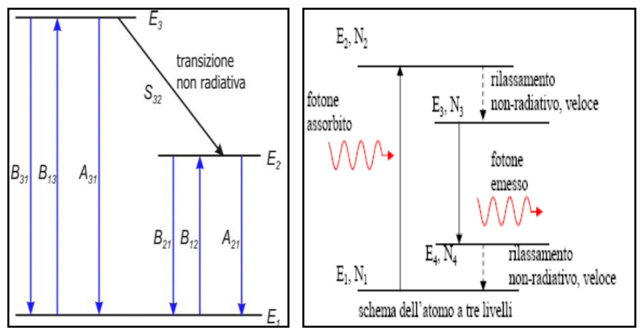

Fig.1: A laser scheme at three (a) and four (b) levels.

In a pattern of amplification at three levels, through a pumping operation is done by using another laser, a lamp or electrical discharges, a radiation forcing, induces an absorption process that brings the electrons from the ground state to the excited state. The electrons, will remain at this level for a time of about 10^{-8} sec and then, will make a non radiative transition in a metastable level. Remain at this level for about 10^{-3} sec, a sufficiently long time because a photon emitted during a process of spontaneous emission, interacts with one of the electrons that are in the metastable level and, through a process of stimulated emission, optical amplification is produced with a laser effect. The first laser, built in 1960 by T. Maiman, a Rubino laser, presented a diagram of this type [2]. The energy of photons emitted was 1.8 eV and fell in the visible spectrum. A four layer structure, allows to reach threshold for the as a consequence of the faster population inversion. In this case, the photon is emitted during the relaxation between E_3 and E_4, where E_4 is a higher level than the fundamental and therefore much less populated. The condition of population inversion is reached, with much lower energy costs. The Nd: YAG laser has a pattern with four levels. It consists in a crystal of Y_3 Al_5 O_{12} doped with Nd and the energy of the photons emitted falls in the infrared region. The laser stores energy in a cavity between two mirrors. The geometry of the resonators can be confocal, semifocal and, most widely used, with two flat parallel mirrors, a resonator known as Fabry-Perot. Between the two mirrors is an “active medium” within which, due to the stimulated emission process, the optical amplification effect occurs. Photons produced by stimulated emission cross more times the active medium, increasing the intensity of the stimulated emission. Photons off the optic axis are lost and do not contribute to the amplification of the stimulated emission. The resonant cavity selects the wavelength of the laser emission. Within the cavity only the wavelengths for which the distance between the two mirrors, L, is an integer multiple of half wavelengths (L = N/2) can oscillate. The first mirror is fully reflective while the second is partially reflective and 1-2% of it, is crossed by laser light arisen in the cavity. Pumping through an "active medium” provides electrons in order to be invested by the source to generate laser radiation. The nature of the active medium may be solid state (Nd, ruby, titanium-sapphire, glass, semiconductor, ...), liquid (dye laser dyes, organic liquids, ...) or gas (He-Ne, Ar, CO_2, excimer, ...). The pumping compensates exactly the spontaneous decay from the upper laser level. It is possible to distinguish the laser systems depending on four modes of operation between them:

- Continuous Emission: the emission takes place continuously with a relatively low power which does not change in time. The emission can be interrupted manually, or it is possible to install electronic control mechanisms capable to switch off the emission of the laser beam for a given time (minimum of 0.01 sec) (i.e. carbon dioxide laser).
- Pulsed Emission: the emitted pulses are short and powerful. The duration and power of the peak pulses are fixed parameters and specific for each device; the frequency may be controlled by the operator (i.e., gas lasers).
- Giant-pulses (Q-Switching): through the use of electro-optical systems placed in the cavities, which act as controlled shutters, it is possible to reach high peaks of power and short pulses with ns duration. In this case the laser intensity can reach values higher than 10^{10} W/cm^2 (i.e. Nd: YAG laser).
- Tied-in modes (Mode Locking): through phase modulators into cavities it will be possible to force the modes of oscillation by amplifying only those who have a certain phase relationship. It is possible to reach peak power higher those obtained in Q-Switching mode and short pulses of ps; the intensity can reach values even higher than 10^{20} W/cm^2 (i.e. titanium Sapphire laser).

APPLICATIONS

To describe the use of lasers in the bio-medical field should be considered the interaction between radiation and biological tissues. Indeed, it is important to know the type of interaction induced by the laser radiation and where this process takes place within the tissue, in order to be able to circumscribe the effects to the volume to be treated. A system to classify the interaction between laser and biological tissues is the use of so-called "medical laser interaction map", so as that reported in Fig. 2, which classifies the type of interactions depending on the intensity and duration of exposure to radiation. The diagonal lines indicate irradiations with constant fluence (J/cm^2) [3]. At equal flow of energy supplied, by changing the exposure time and wavelength (λ) of the laser radiation there will be four types of interactions of different nature:

• Photochemical interaction
• Photothermal interaction
• Photoablative interaction
• Electromechanical interaction.

These interactions will be examined later, discussing about biomedical field, as a demonstration of several laser applications. In the medical field it exploits the properties of the various biological tissues to absorb selectively the energy carried by the beam emitted by the laser, leaving intact the other surrounding tissues. The use of laser requires thus a major change in operations compared to conventional instruments used in medicine. It works not in contact with the tissue and in any case the action of the contact, does not depend on pressure. From the optical point of view the biological tissues, even if structurally complex, in a first approach can be considered as isotropic and homogeneous medium in which the propagation of the laser pulse (pulsed or continuous) can be described by fundamental properties such as reflection, absorption and scattering [4].

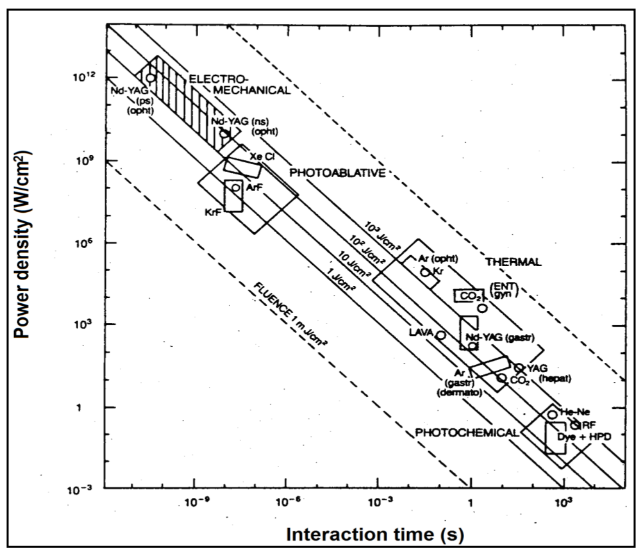

Fig. 2: Medical laser interaction map.

When a laser beam strikes perpendicularly on the surface of the tissue, as a consequence of the jump of refractive index between air and tissue, a small fraction of the radiation is reflected back. The remaining fraction is propagated into the tissue and undergoes absorption and scattering processes. In fact, the light impinging on the material interacts mainly with its electrons and produces ponderomotive forces effects. If electrons are linked are not put in motion and do not respond to the variation of the electromagnetic field. The radiation is not absorbed and the material that absorbs little is defined to be almost transparent. If the electrons are spread, an oscillating current is induced and electrons following the incident electromagnetic field, electron-electron interactions occur and ionization effects take place. The absorption of light energy, and the transformation of the light into heat, is indispensable for a tissue reaction occurs. The optical response of the tissue is given by the Beer-Lambert law, which describes in general the exponential decrease of light intensity (power per unit surface) E(z) as a function of the material depth z due to the absorption and scattering processes:

$$E(z) = (1-r)F_{sc}E_0 \exp\left(-\mu_{eff}\, z\right) \qquad (1)$$

where E (z) is the beam intensity attenuation in the tissue (W/m^2) at z depth; E_0 is the incident irradiance (W/m^2); r is the Fresnel reflection coefficient for unpolarized light, which is about 2 % for the normal light in the interspace air-tissue; F_{sc} takes account of the scattering phenomena; z is the penetration into the tissue; $\mu_{eff} = \mu_a + \mu_s$ is the effective absorption coefficient which takes account of absorption and scattering of the tissue at the used wavelength λ, as reported in Fig. 3.

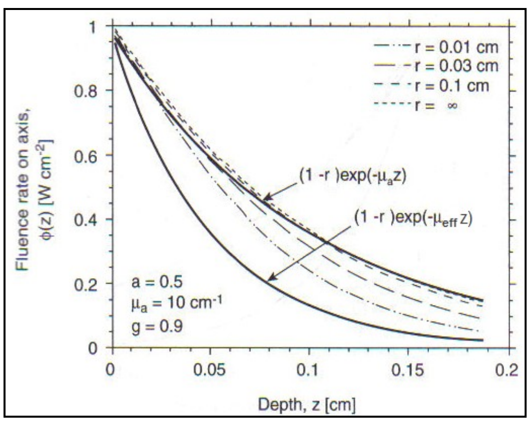

Fig.3: Optical response in the tissue vs. depth

May be beneficial to consider the way that on average the radiation travels before being absorbed, or rather the depth of penetration of the radiation (or thickness or length of extinction), defined as the depth at which the intensity of collimated beam is attenuated by a factor 1 / e (37%). It is expressed as a function of the absorption coefficient at μ_a ($\mu_{eff} = \mu_a + \mu_s$) of the tissue at λ wavelength:

$$L = 1/\mu_a \qquad (L = 1/\mu_{eff}) \qquad (2)$$

Tessuto	λ [nm]	μ_a [cm^{-1}]	μ_{eff} [cm^{-1}]	L [μm]	L_{eff} [μm]
Smalto	1053	<1.0	6.7	>10000	1490
Dentina	1053	4	56	2500	180
Osso	1064	0.5	13.4	20000	746
Cute	633	2.7	39	3700	256
Sangue	960	2.8	65	3570	154
Fegato	1064	0.3	11.6	33000	860

Table I: Absorption coefficients and penetration depth for different tissues measured at different wavelengths.

The effects of diffusion tend to reduce the actual penetration of the light in the tissue. The Table I contains absorption coefficients and penetration depth of the laser light for different tissues at different wavelengths [5, 6].
The absorption of optical radiation from the biological material is the most important process for surgical-therapeutic and diagnostic applications. Chemical species that participate to the absorption of light in tissue are several and their effect changes greatly with the wavelength of the radiation, as reported in Fig. 4.

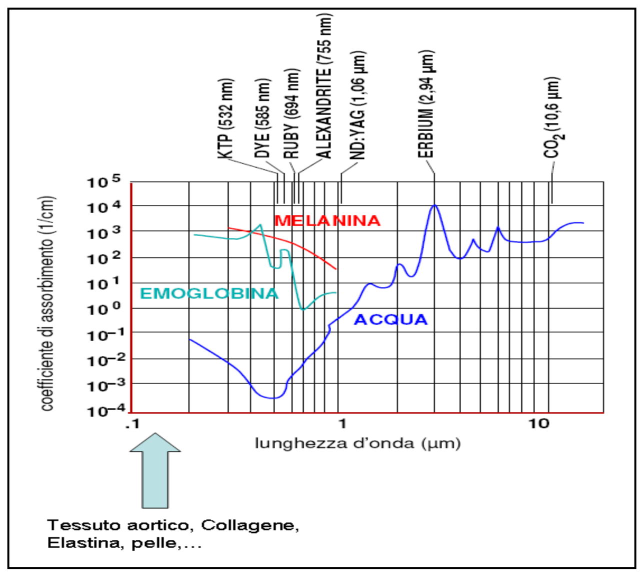

Fig.4: Absorption coefficient of water and of some chromophores for bio-medical interest as a function of the wavelength.

The absorption coefficient depends on the type and amount of chromophores present in the tissue [7]. The chromophores are molecules which confer a certain colour to a substance and which absorb a specific wavelength; their composition, which changes depending on the type of tissue, determines the response of the tissue to the laser radiation at a particular wavelength. Water is the chromophore present in greater quantities in biological tissues, and it is

practically transparent to visible light, while it is strongly absorbing in the infrared. Between biological tissues, those that can be considered highly transparent in the visible are the cornea and the intraocular lens.
Organic compounds such as proteins, lipids and DNA ,in part, absorb in the visible, but giving rise to important phenomena of light scattering; for their stimulation is exploited then normally high ultraviolet absorption of organic molecular bonds. The absorption at wavelengths in the visible is mainly due to specific pigments of the tissue, such as hemoglobin in red blood cells and rhodopsin in the retina. For this reason the main macroscopic effects for radiation below 500 nm are due to the breaking of molecular bonds and responsible for the generation of ablations cold; for radiation above 500 nm there is the production of roto-vibrational motions of the molecules, and then generation of heat.

LASER—TISSUE INTERACTIONS

Now we describe the main four laser-tissue interactions, which are used in medicine. In the following the lasers used and the most important medical applications will be presented. The interactions are based on the absorption of radiation by the water contained in the tissues, by hemoglobin in the blood and pigments or chromophores normally (or externally administered) present in some tissues.
- The photochemical interaction: occurs when the energy of photons is greater than that of chemical energy bond, typically greater than about 5 eV; occurs at very low levels of intensity or irradiance ($I \sim 1\ W/cm^2$)) and for high exposure times (duration time greater than a second). The field of action is that of ultraviolet radiation that generates chemical fragmentation effects. If the energy density deposited is very high it is possible to achieve an ablation with high spatial control (KrF laser, ArF). In this case the contours of the spots are well-defined for absence of thermal spreads. The energy absorbed in the tissue is used for structural modifications of the molecules existing, in fact the reaction:

$$h\nu + A + B \rightarrow (AB)^* \qquad (3)$$

represents the photo-induced formation of the excited molecule AB as a result of the absorption of the photon by part of the molecule A or B. An application example of this process is represented by PUVA therapy (Psoralen UltraVioletA Therapy) regarding the treatment of psoriasis or other skin diseases. In these cases, the psoralen molecules bind with thymine (pyrimidine base of DNA) by forming monofunctional adducts. Subsequently, the laser irradiation also leads to the formation of bifunctional adducts or crosslinks in DNA that induces genotoxic effects. When the deposited energy density is low, fluorescence and phosphorescence effects can be obtained. This technique is useful for the diagnostic type of treatments as for example in the use of optical marker to distinguish on a sick part tissue from a healthy one (example hematoporphyrin). The energy absorbed in the tissue is used for the production of new substances as a result of chemical reactions triggered by laser radiation. In this case, the light energy is used to excite a particular chromophore (molecules which confer a particular color to a substance and which absorb a specific wavelength) which gives rise to a complex biological process whose final products may have therapeutic relevance: the molecule acts with energy transfer functions, after having undergone a photoexcitation. A chromophore able to produce photoinduced reactions in molecules which themselves do not absorb light in the same spectral region is said photosensitizer. An example is the photodynamic reaction (PDT) involves the molecule which absorbs the photon (photosensitizer) and an oxygen molecule. The advantage of this therapy lies in the very low thermal damage to healthy tissue and in the low risk of perforation of hollow organs. Biomedical techniques which allow to diagnose cancer of the larynx, esophagus and bladder, they can see the differentiations of the tissues, and their metabolic activities, which allow a precise diagnosis of the disease may consist in the analysis of the fluorescence spectrum and acquiring of the fluorescence image of the organ.
In Fig.5 (a) it is possible to observe some examples of diagnostics based on the fluorescence of different tissues as a function of the wavelength emitted by them when they are hit by UV light.

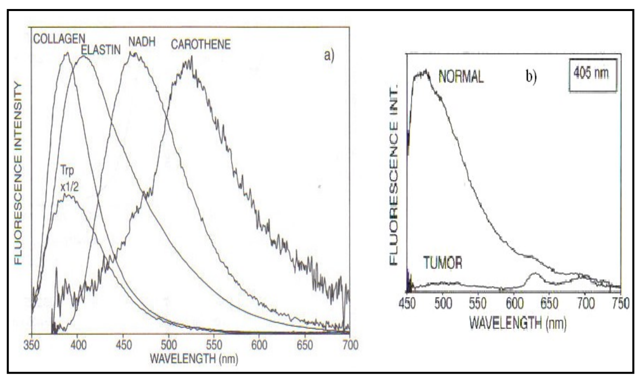

Fig.5: Fluorescence spectrum emitted from different tissues irradiated with UV light (a) and tumor tissues of the bladder (b).

Fig.5 (b) shows the fluorescence spectrum in the case of a papillary tumour of the bladder in which it is injected Photofrin 48 hours before the investigation, with a dose of 0.35 mg / kg of body weight. Irradiating healthy tissue and the tumour with radiation of 405 nm wavelength, it is possible to observe a very strong reduction of fluorescence in the blue-green with respect to the healthy tissue. However, the limit of this technique lies in the fact that the data on the fluorescence are "on time" and do not allow to see the area tumour in its extension (especially in large tumours).
- The photothermal interactions: occurs when the energy of a photon is lower than the binding energy and by using

infrared lasers, such as Nd: YAG or CO_2 lasers, for power densities above 100 W/cm^2, or by irradiation with pulsed lasers of durations up to microseconds (laser pulse duration between 1 ms and 5 sec). In infrared and visible ranges these interactions produce thermal effects on the irradiated tissues. At a microscopic level the photothermal processes are represented by the two stages of the reaction:

$$h\nu + A \rightarrow A^*;\ A^* + M(E) \rightarrow A + M(E+\Delta E) \qquad (4)$$

that is due to the absorption of a photon (IR) by a chromophore present in the tissue, which brings it into an excited state rotovibrational, and the subsequent de-excitation for inelastic collision with the surrounding molecules M, which increases the own kinetic energy or thermal energy. Once the laser light is absorbed, the consequent rapid thermalization that takes place for non-radiative decay induces a local temperature increase. The effects of temperature can cause a different degree of damage as a function of irradiation time, as reported in the scheme of Fig. 6. For temperatures below 50 °C the thermal damage involves heating and hyperthermia, and healthy tissue) up to 45 °C with a consequent necrosis of the tissue itself.

At temperatures between 50° and 100° C occurs the denaturation of the biomolecules and their aggregates (proteins, collagen, lipids, hemoglobin) or irreversible coagulation of proteins. A high heating causes an irreversible deformation of these structures and losing of protein function. The denatured cellular material is so absorbed by the body and replaced with scar tissue. These processes of photocoagulation are used for example in eye surgery for the reduction of retinal detachments, and in dermatology for the treatment of vascular lesions by using continuous Argon laser (λ = 488 and 514,5 nm).

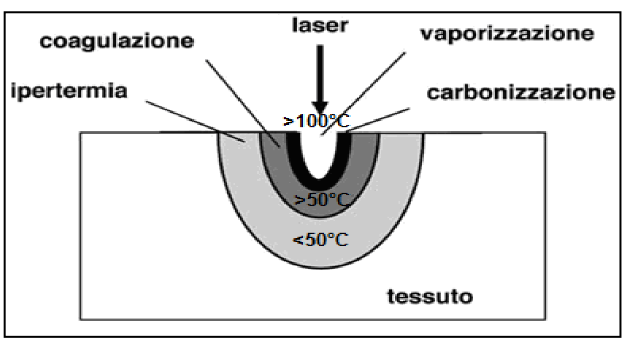

Fig.6: Scheme of the thermal interaction in biological tissue for different temperatures.

When the temperature of the tissue reaches about 100 °C the water constituting most of the soft tissues, vaporizes, dehydrating the tissue. When the water present in the tissue is completely evaporated, the tissue temperature rapidly increases up to about 300 °C and the tissue burns. In this case the vaporization together with the carbonization gives rise to the decomposition of the constituents tissue. It is possible to control the temperature rise limiting thermal damages to the predetermined target and to minimize the spread of heat to adjacent tissue [8].

Fig. 6 shows a scheme of the thermal interaction in biological tissues for different temperatures.

- The fotoablative interactions: occurs when the intensity and wavelength laser exceed certain threshold values that allow the removal of layers of material from the irradiated target; requires high power density (10^7-10^{10} W/cm^2) and pulse durations ranging typically from 10 to 100 ns. Many biomolecules absorb strongly in the UV band (200-320 nm) and in the visible band (400-600 nm); such strong absorptions involve a localized molecular dissociation that can be accompanied by thermal effects or not, effects of evaporation and ionization with the formation of plasma and removal of material from the target. The photoablation process is therefore in the photodissociation of macromolecules in photoproducts repulsive:

$$h\nu + AB \rightarrow (AB)^* \rightarrow A + B^* \qquad (5)$$

and the transfer of energy to atomic and molecular species that are emitted at high speed from the irradiated target. In the photoablation process the residual energy not used to break molecular bonds in the photoproducts remains in the form of translational kinetic energy. This behavior explains the instant high-speed ejection of photoproducts from the area irradiated by the laser beam. Similar effects may also be obtained by visible lasers with intensity of the order of 10^{10} W/cm^2.The process of photoablation is related to the product of laser intensity by the square of the wavelength according to the equation [9]:

$$I\,\lambda^2 \qquad (6)$$

The pattern of interaction is the following: pulses laser are focused on the tissue with an intensity greater than about 10^8 W/cm^2; the radiation is strongly absorbed by the molecules, for example by protein, starches and peptides, until to depths of penetration of the order of 1 µm. It follows a high excitation of macromolecules with the formation of photodissocitation in repulsive photoproducts; finally an expulsion of photo products at supersonic speed without tissue necrosis or thermal effects are produced in the case of UV band. The removal of atoms, molecules, clusters from the tissue, through laser irradiation, is described by the curves of the ablation rate, which represent the removal rate as a function of the used laser fluence.

The ablation threshold represents the minimum level of radiation above which is produced the removal of tissue and below which substantially is induced only fluorescence effect and heating, without any ablative effect. This parameter is important for the analysis of the ablation process, and it is generally expressed by the laser fluence threshold (J/cm^2).

- The electro-mechanical interactions: takes place when the laser pulses of high intensity, greater than about 10^{10} W/cm^2 impinging the material that absorbs them. Ionization effects are induced; they generate a plasma which causes cavitation effects that can be summarized in photomechanical effects with creation of shock waves, with high pressures, P_M. Such schock wave pressures are higher than the tensile strength of many materials, according to the relation that expresses the plasma pulse pressure in units of Mbar [10]:

$$P_M = 12{,}3\left(\frac{I_L}{10^{14}}\right)^{\frac{2}{3}} \lambda^{-\frac{2}{3}} \left(\frac{A}{2Z}\right)^{\frac{1}{3}} \qquad (7)$$

where I_L is the intensity of the pulse laser, λ the wavelength of the laser photons, A the atomic weight and Z the atomic number of the irradiated target. In the case of lasers working in the framework of "long pulse", with pulses of tens or hundreds of nano-seconds, it is possible to obtain effects of ablation with acceptable spatial resolution, high ablation yield and high coefficients of crushing of the target. However, in this case the shock waves propagates in all directions starting from the laser spot until large distances with respect to the size of the spot. In the case of the scheme "short pulse", with short pulses in the region of the pico-seconds or even of femto-seconds, there is no propagation of heat, the diffusion length is negligible and the ablative effects are located in the spot area and in the penetration depth of the light laser. In this case the control of the grinding process becomes more controllable and target-based on calcium compounds, as may be gallstones and kidney stones, can vaporize easily without a detrimental impact on neighboring tissues (Endoscopic Lithotripsy). In the field of urology Holmium laser (λ = 2100 nm) free energy by thin rigid or flexible optical fibres, which may act in liquid media, reaching endoscopically the kidney stone and proceed to lithotripsy to break them without any surgical incision. A typical example of Holmium lithotripsy is reported in Fig.7.

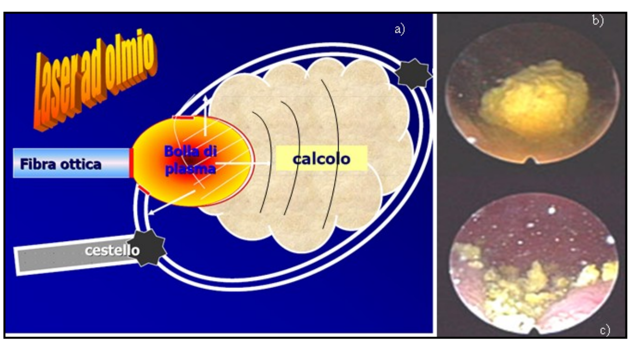

Fig 7: Endoscopic Lithotripsy in urological field (a); kidney stone (b); crushing of the kidney stone (c).

FOTOABLATIVE APPLICATIONS

Cardiology: In cardiovascular field the laser is used primarily to treat problems caused by the formation of plaques due to the accumulation of lipids and other substances within the arteries.

Transmyocardical Percutaneous Revascularization come channel through which bood can flow towards areas of the heart previously little drizzle, as schematized in Fig.8 (a). Transmyocardical Laser Revascularization (TMLR) is a more invasive technique Fig.8(b) because is necessary to make a small incision in the left chest but also more effective in creating channels and provides for the creation of channels in the left ventricle through the fiber that carries light from a CO_2 laser, in order to increase the flow of blood within the heart [4].

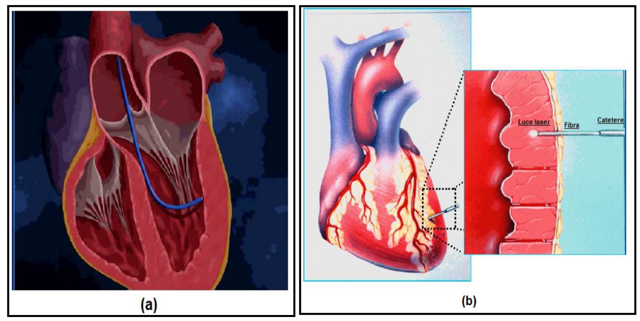

Fig 9: Transmyocardical Percutaneous Revascularization (PTMR) (a); Transmyocardical Laser Revascularization (TMLR) (b).

Pulse Laser Deposition (PLD) of biocompatible thin films and laser treatments: By means of PLD (Pulse Laser Deposition) is possible to deposit biocompatible thin films in prosthesis to facilitate the engagement and the use in the biological environment. Generally, the coatings are made with ceramic materials, glass-ceramics or metals, graphite or polymers, while the materials used to make protein devices can be metals, polymers, ceramics, silicon, titanium and composite materials. Even changing the physical and chemical properties of materials, such as hardness, wettability, chemical reactivity, wear resistance, optical properties, morphology, mechanical resistance, modellability can be controlled with high power lasers suitable for the purposes. Usually the treatment takes place under vacuum and are controlled by the intensity and wavelength of the used light. The experimental set-up of the PLD is schematized in Fig.9(a). It consists of a vacuum chamber at the center of which there is the irradiated target biomaterial. The pulse laser (e.i. excimer, XeCl, KrF, Ruby, Nd: YAG laser operating at the second harmonic (532 nm) with pulse duration from 9 to 20 ns, a maximum pulse energy of 100 mJ-1 J and in repetition rate mode of 1-30 Hz is focused through a lens, on a plate whirling often, chosen from biocompatible material. The vacuum in the chamber typically reaches at least 10^{-6} mbar. The target is ablated at the wavelength of the laser that causes a rapid release of vapors, clusters and micro-grains, which form a plasma emitting particles at high speed towards a nearby substrate to be coated in the form of thin film. The substrates are positioned in front of the plate at a distance of about 30 cm and at different angles, from 0° up to 60°, with respect to the normal to the target surface. The diameter of the laser spot measured generally ranges from about 1 to 20 mm^2, depending on the laser used.

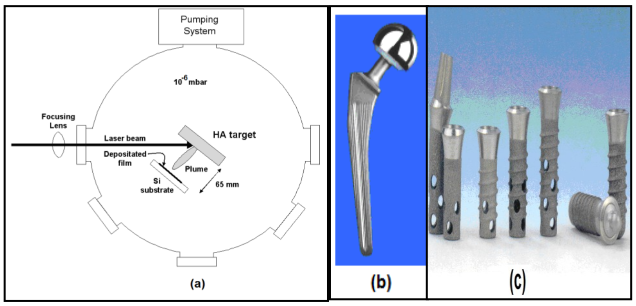

Fig. 9: Experimental set-up of the PLD (a); orthopedic prostheses(b); dental equipment (c).

In order to improve the adhesiveness between the film and the substrate, the latter is kept at a temperature between 300° and 800° C. The photodeposited films are often not uniform in thickness and can be compact or highly porous, very adherent to the substrate, with high osteoconduction and osseointegration. The conditions of photodeposition may change greatly depending on the nature of the biocompatible material that should be deposited and on the type of substrate on which to deposit [6]. Examples of biocompatible materials used in orthopedic prostheses and dental implants are Titanium, often present as oxide TiO_2, and Hydroxyapatite, HA - $Ca_{10}(PO_4)_3(OH)_2$, because they have a high capacity to be recognized and accepted from bone tissue and from other biological tissues and thus to be perfectly osteocompatible. The HA is present in high concentration (~ 70%) in cortical bone and tooth enamel (~ 98%). Fig. 9 shows an example of titanium hip prosthesis (b) and dental implant (c), covered by a thin PLD-HA film, to be anchored to the human bone tissues. Seeking to improve the quality of the deposits should be complied with certain conditions: high thick (100-300 mm); high microcrystallinity, high granulometry, and high porosity, high adhesion to the substrate, high mechanical strength, low content of other phases of Ca-P; low content of contaminants, in order to avoid that trigger processes of solubility of the material with the consequent re-absorption in the biological environment, inflammation or necrosis of tissues and the detachment of the prosthesis.

Of course the type of the oxide surface (HA, TiO_2, bioglass) on the implanted material, in particular, its porosity and thickness affects the absorption of proteins which follow the cell growth and then the osseointegration efficiency. By PLD it is possible to induce nitridations, oxidations and carbonizations processes that reduce the reactivity of the biomaterial inserted as prosthesis inside the human body.

Particularly interesting appears the case of polymer treatments by laser in order to improve their compatibility and functionality. For example, with laser irradiation it is possible to induce surface modifications in Teflon (PTFE) until to make it hydrophilic according to his characteristic hydrophobic. Laser irradiation through a metal mesh mask can be employed also to produce PTFE microfilters which are very useful to filter biological liquids. PTFE micrometric filters have been realized by lasers in micro-catheters for the drainage of cerebral-spinal liquid in children with peculiar pathologies. By way Fig.10(a) shows a typical micro-filter from 20 microns in size of mesh made on a Teflon catheter for drainage of the cerebrospinal fluid in the case of Hydrocephalous pathology, a condition in which there is an accumulation of cerebrospinal fluid in the children brain ventricles [11].

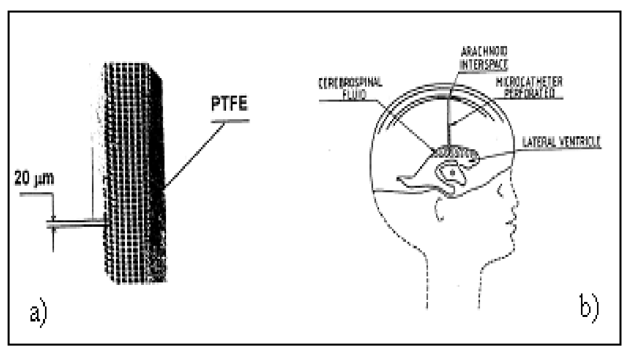

Fig. 10: Example of PTFE microfilters for drainage of cerebral-spinal liquid.

Laser treatments may change the refractive index of many polymers, such as PMMA, in order to adjust the power of convergence of artificial crystalline lens of the eye, can be realized polymer with special surface roughness, hardness and geometries.

Dentistry: The Erbium Cromo laser (Erbium, Chromium: Yttrium, Scandium Gallium Garnet) belongs to the middle infrared and interacts with water and hydroxyapatite: is employed in dentistry, having been specifically designed to handle both soft tissue and hard tissues. This laser works in pulsed mode, pulse duration of 140 s, 20 Hz repetition rate and 300 mJ of pulse energy, and transport fiber from 600 m in diameter. Feature of this laser is to hold the fiber in position on the target and to have a spray air-water supplemented with varying proportions from 0 to 100, such that the water not only removes debris from the ablation site and acts as a cooling agent, but also determines the ablation of tissues for hydrokinetic effect by means of microexplosions of the water itself. In Fig. 11(a) were compared the absorption coefficients of water, hydroxyapatite (HA) and the dentin as a function of the wavelength of the laser Er, Cr: YSGG, Nd: YAG and CO2. At the wavelength of the laser Er, Cr: YSGG (2,78 mm) we can see the peaks due to the resonant absorption of water, dentine and HA.

This result is due to high absorption coefficient and the use

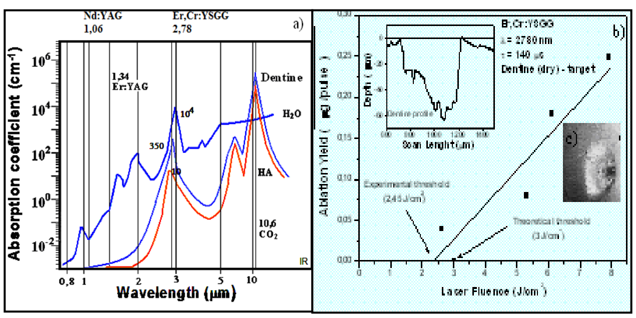

Fig.11: Absorption peak in water, dentin, and hydroxyapatite (HA) vs. wavelength (a); laser ablation as a function of fluence (b); SEM image of the channel in an enamel dentine product by laser (c).

of water-air-integrated spray to the laser provide high values of ablation yields. In fact, the ablation yield for lasers as Er, Cr: YSGG and for a laser fluence of 10 J/cm^2 was evaluated approximately of 0,35 mg/ pulse [12]. By way of example Fig 11(b) shows a test curve of laser ablation Er, Cr: YSGG. The ablation threshold below which there is no removal of molecules of hydroxyapatite, the main constituent of dental hard tissue, is equal to 2.45 J/cm^2, and the ablation yield, experimentally measured from Torrisi [12], is about 0.2 g/ pulse at the fluence of 6 J/ cm^2.The insert of Fig 11(b) shows a SEM picture of the channel created by laser irradiation in a tooth.

Ophthalmology: The excimer laser acts on the corneal tissue without heating it by evaporating the damage, thus allowing to shape the front surface of the cornea (the main component of Dioptre eye) thereby changing its refractive power. In practice "print" the lens directly on the cornea, thus correcting all refractive defects such as myopia, hypermetropia and astigmatism. The excimer laser (ArF: 193 nm) is characterized by a beam of energy of 180 mJ with a Gaussian energy profile, which operates in single mode or repetition rate of 30 Hz, whose radiation is almost totally absorbed by the corneal tissue [13]. Each pulse, the duration of about 15 nsec, doesn't cut the cells and doesn't burn it, but, by vaporization, removes on average a quarter of a micrometer of the corneal tissue exposed to radiation, leaving the tissue surface smooth and free of roughness. The operation is designed to reshape the curvature of the cornea, which is the natural lens of the eye and it is more superficial. In the case of a myopic eye one acts on the flattening of the cornea, so as to make the eye more divergent and also to ensure that the images of the most distant objects are formed on the retina. In the case of hypermetropia one acts on the cornea by increasing the curvature. Finally for the astigmatic eye tends to make the curvature of the cornea more spherical and homogeneous [13]. The two most common techniques in refractive surgery are PRK (PhotoRefrattive Keratectomy) and LASIK (LAser in SItu Keratomileusis). The intervention of PRK is carried out under topical anesthesia, after which it removes the surface layer of the cornea, the epithelium, then the front corneal stoma, which will reform in the days following the operation, to expose the underlying layer laser action. Then with a trend to Flying spot of the beam leaser it is possible to reshape the cornea correcting defects, as reported in Fig.12(a). After the operation is applied on the cornea a contact lens in order to limit the postoperative pain and facilitate re-epithelialization.

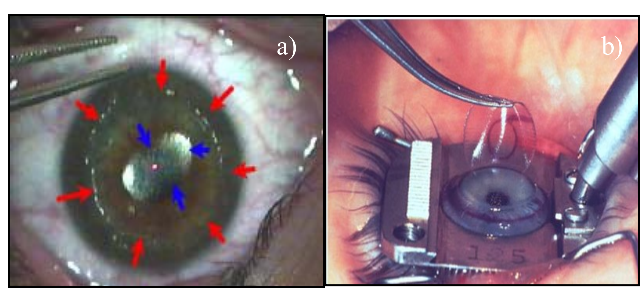

Fig. 12: PRK (a) e LASIK(b).

LASIK is an operation where ablation occurs in the deeper layers of the cornea after lifting a portion of the cornea surface (it is therefore necessary that the corneal thickness has a value sufficient to create such a flap). It is placed on the eye a surgical high precision instrument (microkeratome), and it is made to slide from right to left or top to bottom to obtain a flap of the cornea (often 140-180 microns). This layer is then raised and opened as if it were the page of a book Fig.12(b). The corneal tissue exposed is treated with the excimer laser. After treatment, the "page of the book, i.e. the corneal flap is repositioned without sutures.

A new frontier in refractive surgery is the femtosecond (10^{-15} s) pulsed laser (solid-state laser), ultra-fast, which emits a radiation of wavelength in the infrared with spots of the size of a few microns and short duration, less than the laser excimer. The femtosecond laser is characterized

not only for extremely short light pulses, are also very intense and powerful. Regardless of the type of material employed, the incredible power of the femtosecond laser, it evaporates almost instantly almost without a trace [14, 16]. The action of the femtosecond laser (also called femtolaser or intralaser) determines a very precise treatment with the maximum safety related to the action non-mechanical engraving and by the very high reproducibility of the results. The mechanism governing the operation of the femtosecond laser is to send pulses laser managed by a computer in the context of the corneal stoma, with adjustable accuracy and reproducibility ascertained in accordance with the programming. The software is very versatile and allows to choose the energy delivered and the distance between the spots in order to optimize the penetration in the various layers of the corneal stoma. The design of the cut can be obtained by the succession of vertical cuts and resections laminated with variable angle of incidence between them. The laser pulse gives rise to the formation of cavitation bubbles in the context of the corneal collagen thus determining the separation of the blades themselves. The effect of photodestruction occurs only in the focal point, i.e. in the area where is been cut the corneal tissue. The tissue outside the defined area remains unchanged. A full cut in the cornea, without the use of blades with a pre-programmed diameter and depth, is obtained by placing thousands of these pulses laser next to each other creating a macroscopic effect. To create the flap, the spot laser moves back and forth through the eye, and the bubbles are connected to form a corneal flap. After, the beam of femtolaser follows a program pattern along the circumference of the flap, while the thickness is gradually reduced. The perfect regularity of the flap allows a soft and very accurate self-closing. The corneal flap can be lifted with a precision instrument and replaced on the original position as reported in Fig.13 (a). Fig. 13 (b) shows a magnified view of the alignment of the flap.

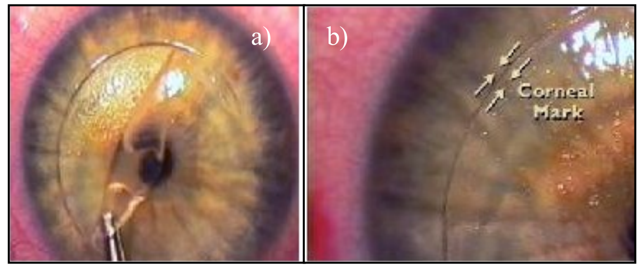

Fig. 13: Lifting the corneal flap (a); alignment of the flap (b).

Laser welding of polymeric materials: The technique known as the "Visible Through Transmission Laser Welding", TTVLW determinates to allow the welding surfaces and accurately without the inconvenience of the production of debris and waste. Generally the laser welding is realized by irradiating the polymer with a pulsed laser beam of light in the visible range (but also infrared radiations can be used). Normally the joint is composed of two polymer surfaces: one transparent to the laser wavelength and another highly absorbent. The formation of the welding takes place by absorption of energy at the Interface Between the two surfaces. The TTVLW process involves localized heating at the interface of two pieces of plastic that will be joined. This method produces strong and hermetically sealed welds with low thermal and mechanical stress, without particulates. Only some materials and combinations of materials are suitable for transmission laser welding, but many thermoplastic polymers can be jointed by laser sources, such as polyethylene, polyethylene terephthalate, polymethylmethacrylate and acrylonitrile butadiene styrene [17,18]. There are various methods to make the plastic able to absorb the laser energy, such as the use of nanostructures embedded in the polymer which have high absorption at the used laser wavelength. Additives such as carbon nanotubes (CNTs) and nanostructures of Fe_2O_3, for example, can be used to color with black or red, respectively, the polymer sample and to increase the visible laser absorption in the first sample layers [19]. Laser welding of polymers is getting off an alternative to conventional technologies. Examples of application can be found, amongst others, in the medical devices, automotive, electronics, human care and house hold devices industries [20]. In particular, in medical devices the laser welding could be use to produce filters, micro fluidic devices, medical packaging (blood bags), catheters and prostheses. The inset of Fig.14(a) shows a scheme of polymer welding. Different laser sources are commonly employed for the welding of polymers, such as continuous CO_2 high-power infrared lasers at 9.4 and 10.6 mm wavelengths, diode lasers and Nd:Yag lasers. Results showed are achieved employed to irradiate polymers in air by using 3 ns pulsed Nd:Yag lasers at the fundamental and second harmonic, in a single pulse or at 10 Hz repetition rate and at a laser intensity of about 8×10^8W/cm^2 with a maximum pulse energy of 150 mJ. Different physical and mechanical analyses were employed in order to characterize the properties of the single polymers before the welding and the joint obtained just after the welding process. The polymeric transmission curve of the visible light (532 nm) experimentally obtained as a function of the polymer kind and thickness is reported in Fig. 14a for the transparent UHMWPE and for the Fe_2O_3 nanostructures embedded in the polyethylene.

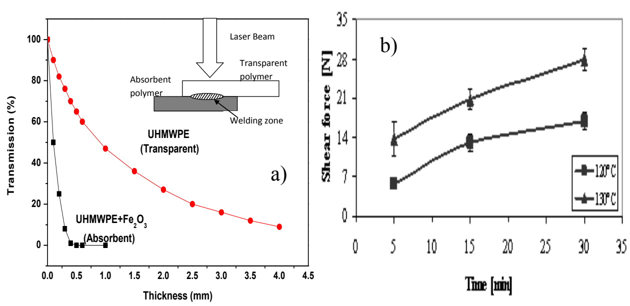

Fig. 14: Experimental transmission curves vs thickness of the investigated polymeric materials (a) and shear force in thermal joint (b).

Measurements of reflectance and scattering in the transparent polymers have permitted to evidence that these two contributions are negligible compared to the transmitted pulse energy. In fact, the surface reflectivity and scattering in 1mm^2 of transparent PE were of the order of 5–10% of the total laser pulse energy. Using high laser intensity, the measured absorption coefficient value depends on the laser pulse energy, probably due to the nonlinear absorption effects, like multiple photon absorption. The typical results obtained in the different polyethylene films are reported in Fig.14 (a). In the experimental conditions of 150 mJ/28 mm^2, the absorption coefficient value, measured by the experimental transmission decay curve, is 6.1 cm^{-1} in the transparent UHMWPE, while the absorption coefficient value is 380cm^{-1} in the absorbent PE-Fe_2O_3 (1%). The absorption coefficients were experimentally calculated by the Lambert-Beer law. Shear stress tests of joints were performed in order to know their mechanical resistance. These samples were put in the oven for different time (5 – 15 – 30 minutes) and a pressure of about 1 kPa was applied above the joint area. Results highlighted that the shear force depends on the temperature reaches to make the joint. In fact, as it is possible to see in the Fig.14 (b), the shear force is lower at 120°C than at 130°C. But in every case, the obtained values are more lower (30 N - about an order of magnitude) than the values obtained performing a laser joint (115 N). This last result is very important since it highlights that the laser welding represents a better solution to make joint in terms of high efficiency and mechanical resistance.

CONCLUSIONS

A focused laser beam can be suitably used as an engraver of biological tissues with very small dimensions, comparable with the wavelength. This possibility has opened many perspectives in the field of microelectronics, in the mechanical precision in the welding industry and medicine. In general we can say that these applications are a direct consequence of the special characteristics of the laser light discussed above.

In the field of bio-medicine a laser can be used as a scalpel allowing to carry out precise micro-surgery also in regions difficult to access, thanks to the use, for example, of optical fibers for the transport of the beam. In fact, in addition to superficial lesions, can therefore also be treated lesions accessible by techniques of laparoscopy or endoscopy, for example, in thoracic surgery, gynecology, urology, neurosurgery. The main application of laser technology in ophthalmology, and in particular in the anterior segment of the eye, is located in the field of corneal surgery and cataract. The femtosecond laser allows to obtain both vertical and transverse cuts corneal of extreme precision. They are used in refractive surgery to create the LASIK flap in the surface, but especially in corneal transplant surgery. It has recently been developed the femtosecond laser for cataract surgery.

Lasers are also essential tools in bio-engineering disciplines, allowing films to be made and catheters that are interesting applications in micro-perforated drainage of fluids: an example is the production of catheters in the pathology of hydrocephalus microperforated. Further developments have taken place also in the field of fabrication of using the technique of plasma spray with which it is possible to coat with the film of biocompatible material orthopedic prostheses or dental implants.

Must also remember the importance of the laser welding in medical devices to produce filters, medical packaging, catheters and prostheses. The basic physics, combined with knowledge of chemistry, biology and medicine, now enables us to better control the use of such radiation in order to be able to significantly improve the quality of life of every living being.

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