PENETRATION AND OPTIMIZATION OF LASER RADIATION IN SELECTIVE HEATING OF BIOTISSUE

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Abstract

The laws which manage the penetration of a laser beam in tissues have direct connection with the mechanism of biological impact of the laser. The temperature is the main parameter in the interaction between a laser beam and a tissue. In order to predict the thermal reaction in tissues, it is necessary to make a model of the distribution of temperature values within them. Usually, in biological tissues not only one but rather a few thermal effects occur and all of them depend on the parameters of the laser.

Keywords: lasers, biomedical technologies, selective heating of biotissues.

1. INTRODUCTION

There is a tendency in modern biotechnology and physiology which is related to the experimental and theoretical research of the processes of heat transfer within tissues, organs and the organism as a whole. The biological tissue is specific physical medium with complex organization and the study of the processes of heat-transferring is one of the primary problems (Alytshuler, Smirnov, Pushkareva 2004, s.151-154; Petrova, 2019c, pp. 346-353; Terziev, Petkova - Georgieva, 2019g, pp. 515-524).

The laws which manage the penetration of a laser beam in tissues have direct connection with the mechanism of biological impact of the laser. One of the reasons why the laser beam penetrates to a limited depth is the absorption of the beam which is the first link in a chain of changes which happen as a consequence of the irradiation of the organism. The depth of laser penetration in biological tissues is crucial in practical respect, that is, the depth is one of the major factors for determining the upper bound for clinical application of lasers.

The absorption is not the only process which leads to decreasing the power of a laser beam passing through biotissues. Simultaneous to the absorption of the radiation, other physical processes also happen, more specifically – the reflection of the beam from a surface between two media, the refraction of the beam when passing through the boundary, which separates two optically heterogeneous media, the diffraction of the beam caused by particles in the tissue and others. That is why one can talk about a complete decrease is the power of the beam which due to the combined contributions of absorption, losses as a result of other phenomena and the actual absorption of the radiation by the biotissues. When absorption occurs, a medium can be characterized with two parameters: absorbing ability and absorption depth. Absorbing ability is defined as the ratio between the energy which is absorbed by a medium to the energy which is emitted and which falls on the surface of the medium. This ratio is always less than 1 since the radiation only partially go through the medium. Absorption depth characterizes the spatial distribution of the absorbed energy in a medium. In the simplest example (exponential attenuation of the beam in a substance) the absorption depth is equal to the distance which corresponds to a 2,718 times decrease in the power of the initial radiation. The inverse value of the absorption depth is called absorption coefficient. It is measured in sm^{-1}. If concurrently with the absorption, diffraction of the beam is also observed, the distance, to which the beam reaches, decreases multiple times due to the compound effects of these processes. This distance is called attenuation depth or penetration depth and it's inverse value – attenuation coefficient is also measured in sm^{-1}.

In theoretical examination of the question about the absorption of laser radiation by biotissues, for simplification of the problem, one can assume that the laser radiation is a plane wave which falls on the surface of an object and the attenuation coefficient is the same for all the treated parts and it does not depend on the intensity of the beam. In this case the energy (power) of the beam would decrease exponentially with the increase of depth. The distribution of energy can be expressed with the following formula:

(1) $$P = P_0 \exp$$

where P is the power of the beam at certain depth, P_0 – the power of the beam falling on the surface of the tissue

In real situation, however, while irradiating biotissues, this simple relationship between the thickness of the tissue layer and the amount of absorbed energy does not hold true, i.e. because of differences in the attenuation coefficient of different parts of the irradiated tissue. The attenuation coefficient of melanin granules in eye's retina is 1000 times larger than the coefficient of the surrounding tissue and therefore the stronger irradiation. Bearing in mind that the absorption of a beam is a molecular process, which, eventually, depends on the concentration of radiation-absorbing molecules, the amount of absorption at cellular and subcellular level can greatly differ from organ to organ. Finally, absorption is a function of the wavelength, thus the attenuation coefficient varies in a wide range for lasers emitting light in different regions of the spectrum.

The impact of a laser on the organism is determined by emission parameters (power and emitted energy over a unit of the irradiated surface, laser's wavelength, impulse duration, frequency of the impulse repetition) but also by the irradiation time, the area of the irradiated surface, the localization of the impact and the physio-anatomical characteristics of the irradiated object (Alytshuler, Smirnov, Pushkareva 2004, s.151-154; Smirnov, Pushkareva, Surgutskaya, 2003, s. 37-40; Petrova, Petrov, 2018a, pp. 213-228; Terziev, Petkova - Georgieva,2019h, pp. 525-533).

Depending on the specifications of the technological procedure, the process of working with laser equipment can potentially lead to exposure of the staff to reflected and diffracted radiation. The energy of laser radiation which is beamed over the biological object (tissue, organ) can undergo different transformations and trigger organic changes in the irradiated tissue (primary effects) and unspecific changes which have functional characteristics (secondary effects).

The biological effects which arise out of the interaction between the laser beam and the organism depend on the energy exposure or the emitted energy, the wavelength, the impulse duration, the frequency of impulse repetition, the irradiated area and the biological and physical-chemical characteristics of the irradiated tissues and organs. The thermal effects of impulse lasers with high intensity have specific peculiarities. Under the action of radiation from an impulse laser, a faster heating of the target structures in biotissues can be observed. If the emission happens in a form of unrestricted generation, then for a duration of the impulse (in confines of $1ms$) the thermal energy causes a thermal burn.

As a result of a rapid heating of a structure to a high temperature, a quick rise in the pressure of the irradiated tissue takes place, which leads to mechanical destruction of the tissue. Said it this way, laser radiation leads to a combination of thermal and mechanical impacts (Petrova, Petrov, 2019d, pp. 29-40; Atanasov, 2019a, 248-269).

2. OPTIMIZATION OF THE LASER RADIATION PERIMETERS

Biotissues are multicomponent material which mainly consists of proteins (collagen), fats, minerals and water. Each of these ingredients has a different absorption coefficient α and thermal conductivity k. The principal specification of soft biotissues concludes in that their structure contains a high percentage of water ($\approx 60-80\%$). In the process of laser treatment of a tissue, it is obligatory that the impact is carried out with maximum efficiency and simultaneously any unwanted damage on the surrounding tissue must be avoided. For this purpose, one must adjust the parameters of laser treatment and to introduce criteria for optimization. An overview of the criteria for optimizing the parameters of laser radiation for treatment of superficial blood vessels would be made.

The optical radiation which falls on a living tissue, particularly on the skin, affects its components in a different way. The central principle of photobiology is based on that light acts on a biological object only if it absorbs light. The main components of the skin which absorb light are water, melanin and hemoglobin. Those compounds are the chromophores of the skin. The absorption spectrum of these compounds is different.

The transformation of laser energy in heat is accomplished only if the radiation is absorbed. Consequently, if a part of the skin contains chromophore which absorbs particular wavelength and the surrounding areas lack this chromophore, then only the part containing the chromophore would be heated. As a result, three zones are formed: a zone of maximal thermal effect, where the chief part of the radiation is absorbed (evaporation, carbonization); a zone of thermal impact which is caused by a small portion of the radiation which penetrates deeper in the tissue (coagulation, dehydration); a zone of thermal effect which is generated by the heat transfer from a warmer to a colder zone (bio-stimulating reaction). The size of the third zone is determined by the power of radiation, thermal conductivity of tissues and the time needed for thermal relaxation of the tissue. With the decrease in radiation power, the zone where the tissue is destroyed (the first zone) shrinks while the zone of bio-stimulation (third zone) increases. The degree to which a chosen area is being heated by laser radiation is defined by the radiation power, whereas the degree of heating (and the degree of thermal damage) of border area will depend not only on the power and the period of impact of the laser impulse but also on the thermal conductivity and the time for thermal relaxation of the tissue. If the radiation power is increased and the impulse duration is decreased, the border zone could be contracted and consequently prevent from thermal damage (burning) the nearby skin. For accelerating the heat transfer from skin, various substances, permeable for laser beams and possessing high thermal conductivity, are being utilized – ice pieces, gels and artificial sapphire. In this way, by selecting the radiation wavelength, the power and the duration of the impulse, it is possible to treat any structural component of the skin so that it is ultimately the least harmful procedure when it comes to the neighboring tissue. Such an impacted is called selective laser coagulation. This treatment method is based on the conception of selective photothermolysis, introduced for the first time by R. Anderson and J. Parrish from the Harvard University in 1981. Different chromophores have different absorption spectra, thus, for treatment of vessels pathologies, radiation with wavelength which is maximally absorbed by hemoglobin and minimally from melanin is used. The power and the duration of the impact is chosen in order not to harm the tissue which surrounds the vessel and to achieve a high selectivity of the impact.

For the aim to establish a safety impact on certain structural components of the skin, in accordance with the conception of selective photothermolysis, it is required that:

The wavelength of emitted light is fine-tuned so that it falls in an infinitesimal region around or better right at the pitch of absorption of the chromophore in the impacted object;

The impulse duration is shorter or equal to the time necessary for thermal relaxation of the object;

The radiation power should be adequate for achieving the desired effect but should not exceed some fixed boundaries.

The point of selective photothermolysis is to ensure a continuous thermal impact on the area while the neighboring tissue remains intact. To fulfil this conditions, it is essential that the duration of the impulse – t is shorter than the thermal relaxation time (TRT) of the structure. When the condition $t << TRT$ is met, the heat released inside an object, due to absorption, does not leave the structure until its complete destruction. This approach provides selective destruction (see below) of tissue with minimal energy consumption.

Using such a short-lived impulse is, however, inapplicable when the object is inhomogeneous and one of its fractions partially or totally does not absorb the radiation, meanwhile, the other fractions have high absorption properties. For describing such problems, the extended theory of photothermolysis is utilized. The basic principles of the extended theory of selective photothermolysis are:

The wavelength of a laser beam should be selected in such a way that a maximal contrast between the absorption coefficient of the pigmented area and the absorption coefficient of the surrounding tissue is observed. This postulate is identical with the classical theory of photothermolysis;

Padiation power should be limited in order to prevent losses of absorption abilities of the pigmented zones but also should be sufficient for reaching a temperature of the pigmented region above a certain value when it begins to destroy;

The impulse duration should be less than or equal to the thermal destruction time. The thermal destruction time is the time needed for irreversible damaging of the target without affecting the nearby tissue. The thermal destruction time could be significantly longer than the thermal relaxation time of the whole object.

The power and the format of laser radiation impulses are of a great importance for a successful treatment in contrast to the classical theory of selective photothermolysis where only the power density of radiation is substantial.

The extended theory of selective photothermolysis presumes a significantly longer treatment time than the classical theory. In dermatology this creates an additional possibility for a parallel cooling of the epidermis.

For a safe impact it is necessary to make an optimal choice for the radiation parameters such as radiation wavelength, impact energy and impulse duration. For this purpose, two criteria are introduced which determine the degree of selectivity and efficiency of treatment.

For example, let consider the impact on a blood vessel in human skin. The criterion for the degree of heating selectivity means that the aim, which in this case is a blood vessel, should be affected and simultaneously the surrounding tissue should remain intact. This criterion characterizes the safety of the impact. The main risk for the patient is overheating of the epidermis which is caused by the absorption of radiation from melanin. Then, the selectivity criterion should compare the temperature change of the impacted object (i.e. a blood vessel) and the bottom layer (basal layer) since it contains melanocytes which produce and secrete big amounts of melanin. In case of radiation which is strongly absorbed by water, the comparison should be made between the blood vessel and the surface of the skin. In the simplest instance, if the change in temperature of the medium happens only in positive direction, this criterion can be defined as (Stoev, Zaharieva, Mutkov, 2019e, pp 454-457; Terziev, Bogdanova, Kanev, Georgiev, Simeonov, 2019i; pp. 391-397):

(2) $$SR = \frac{\Delta T_{t\arg}}{\Delta T_{bas}}$$

where $\Delta T_{t\arg}$ and ΔT_{bas} are the temperature changes in the target object (blood vessel) and the basal layer respectively. Apparently, this value is dimensionless quantity which reflects the corresponding overheating of the blood vessel. For quantitative evaluation it is essential to determine the critical value of SR This could be carried out if one knows the critical temperatures at which thermal destruction and coagulation occur in the observed objects. These values could be obtained by analyzing Arrhenius' integral. The denaturation temperature of the walls of a blood vessel is around $80^{\circ}C$ with an impulse duration less than $1ms$. If the duration is increased to a few seconds, the value of T_{cr} decreases to around $50-60^{\circ}C$ (Stoev, Zaharieva, Borodzhieva, 2019f, pp 458-461; Ninov, Atanasov, 2019b, pp. 101-108). If the duration is in the boundaries between $10-20ms$, the denaturation temperature is about $72^{\circ}C$. Then, following the laws of selective heating of a blood vessel, its wall should be heated up to $72^{\circ}C$, whereas the temperature of the bottom layer should not exceed $66^{\circ}C$. From this originates the requirement of the relative overheating of a blood vessel to be: $SR > 1{,}2$. Equation (2) is also appropriate for estimation of the degree of selectivity when heating various multicomponent objects, multilayered structures and so on. In these cases, it is necessary to pick two control components – one would be selectively heated compared to the other.

The efficiency criterion is used in order to minimize the consumed energy and concurrently to achieve the desired effect. This means that one can choose the energy of the impact needed to heat an object to a fixed temperature. This property is called efficiency of the impact and characterize the change of temperature in the object based on the value of the density of energy or the density of radiation power:

(3) $$AE = \frac{\Delta T_{t\arg}}{\Delta E_0} \text{ or } AE = \frac{\Delta T_{t\arg}}{F_0}$$

where ΔE_0 is the energy density of the falling beam and F_0 – the power density. The efficiency of the impact is measured in $\left[\frac{K}{J/cm^2}\right]$ when dealing with an impulse source or $\left[\frac{K}{W/cm^2}\right]$ in case of continuous source.

The criterion for optimization depends on the wavelength. This correlation could be altered when altering the parameters of an object such as the type of the blood vessel, its depth, size, skin type or the parameters of the procedure such as the size of the object, impact duration and others.

By utilizing the initial data, presented in Table 1, one can select parameters like impulse regime for biological tissue treatment, duration of the impulse, duration of the interruptions between the impulses, density of the radiation power. The number of impulses should not be less than 5 since the temperature fluctuations during the whole procedure, in this case, are between $34-38^{\circ}C$. Simultaneously, calculations for treatment with a continuous laser beam are made by choosing the power density value so that the temperature of the tissue do not exceed $42^{\circ}C$. The period of treatment for both impulse and continuous laser beams is the same.

Table 1. Parameters of impulse radiation

№	Wavelength, [nm]	Impact duration, [s]
1	632,8	250
2	810	200
3	578	250
4	1000	200
5	1200	120

Determination of the mechanisms and exact critical characteristics of the field of ultrashort laser impulses in their impact on biological objects is of a considerable significance when it comes to their innumerable practical and scientific applications in the biotechnologies and medicine.

3. DISCUSSION

The morphological diversity of tissues determines the different ways that light passes through them. The size of cells, their structural elements and the connective tissue are in the range between tens nanometers to hundreds micrometers. It should be noted that, when laser radiation is applied on the skin, damage in the biological tissues occur which cannot be explained with the standard melting mechanism. The difference can be explained with the multiphoton excitement of electrons which happens in a period of time which is equal to the duration of the impulse when the energy is directly transferred to the atomic subsystem. In this case, the water molecules serve a transmission link which absorbs the energy from laser radiation and excites the vibrational regimes of collagen which have relaxation period of around 3 In various temperature ranges, the biological tissue can undergo different chemical and structural changes. If the temperature is between 40 and, no irreversible damage of the tissue is expected (only when the heating is long enough, could enzymes be activated and changes in the membrane occur which, eventually, result in cell's death). Heating of tissues up to temperatures around is used in clinical practice for local thermotherapy (Govedarski et al. 2013; Genadiev et al. 2015; Kirilova – Doneva et al. 2015a; Kirilova-Doneva et al 2016; Tsonkova, 2018b; Tsonkova, 2014).

4. CONCLUSION

The wavelength and power of the laser radiation are adjusted in accordance to the size of the tumor and the absorption spectrum of the pathological tissue. All types of laser thermo-treatments require careful determination of the laser radiation dose, availability of reliable data for the optical and thermal parameters of biotissues and utilization of techniques for control of these parameters. Often, the therapeutical effect of laser radiation is related to the high degree of coherence or polarization. The multiphoton excitement of biomolecules could be achieved with extra short laser impulses which have low energy but high pitch power (Terziev, Petkova- Georgieva, 2019j-p).

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