Quantum Electronics **47** (10) 935–941 (2017) ©2017 Kvantovaya Elektronika and Turpion Ltd

LASER MEDICINE https://doi.org/10.1070/QEL16384

Laser-induced modification of structure and shape of cartilage in otolaryngology and orthopaedics*

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Abstract. **We present the results of basic research in laser modification of tissues in otolaryngology (correcting the shape of nasal septum and larynx cartilages), cosmetology (correcting ear and nose shape), orthopaedics and spinal surgery (treatment of diseases of spine disc and joints). The physical processes and mechanisms of laser-induced relaxation of stresses and regeneration of tissues are considered. New results of studies in this fast-developing field of laser surgery are presented, in particular, the results of laser correction of costal cartilage shape in the process of making implants for the treatment of larynx stenosis and controlled regeneration of the hyaline articular cartilage.**

Keywords: *laser, optoacoustics, cartilage, intervertebral disc, arthritis, laser regeneration, laser relaxation of stresses.*

1. Introduction

The first and most widespread applications of lasers in surgery are related to laser ablation and coagulation of tissues [1]. The nondestructing modification of the tissue structure is a relatively new branch of medical physics and begins to be used for the treatment of widespread diseases, such as the nasal septum deviation, the intervertebral disc injury and the osteoarthritis. The laser method of cartilage shape correction is free of the drawbacks of the traditional surgical operation and can be used for the treatment of trachea and larynx stenosis, for correcting the shape of the ear auricle and nose wings.

The process of laser-induced stress relaxation leads to the controlled modification of the cartilage shape. For wide application of this method in the clinical practice, particularly, for making cartilage implants, it is necessary to carry out the studies aimed at the determination of optimal regimes of laser irradiation of the cartilages, ensuring the long-term stability of the new shape and preventing the undesired damage of the intercellular matrix. It is also necessary to develop reliable methods of control and diagnostics, as well as experimental instrumentation for controlling the processes of laser modification of the cartilage shape.

More than 70% of the Earth adult population suffer from the diseases of the spine disc cartilages [2]. The traditional methods, both therapeutic and surgical, are aimed mainly at the elimination of the acute symptoms of the disease or at the replacement of a destructed intervertebral disc [3]. At present, the laser reconstruction of the intervertebral discs is successfully used in clinical practice [4, 5]. The application of the laser regeneration technology to the articular cartilage is an urgent problem. In spite of the intense development of new conservative and surgical methods of arthritis and arthrosis treatment, this social problem is far from the final solution [6]. In particular, it is known that the large surface defects of the articular cartilage caused by a trauma never heal over by themselves. The degenerative injuries of the articular cartilage (osteoarthrosis) are even more widespread and intractable. The major difficulty in solving this problem is related to the low level of metabolism in the mature cartilage tissue and the low proliferation activity of chondrocytes. However, the number of efficient methods providing the slowing-down of the degenerative process or the restoration of the cartilage structures lost in the course of pathological process is still small. The most promising approaches in this field are the genic therapy, the introduction of growth factors into the injured tissue, the transplantation of autological chondrocytes or mesenchymal stem cells, as well as the combination of the latter with bioactive scaffolds [7, 8].

One of the results of the studies of laser thermoplastics of the ear cartilage is the discovery of laser-induced tissue regeneration processes under moderate laser heating [9]. It was found that the laser impact leads to the proliferation of chondrocytes, regeneration and growth of the hyaline-type cartilage. As a result of interdisciplinary studies, the new approach was proposed, namely, the controlled modification of the fine structure and the stress field in tissues by means of the nondestructing laser irradiation that allows the cartilage shape to be corrected and induces the reparative response of the injured or degraded tissue [10].

In the present paper, we consider the physical and chemical processes underlying a number of novel laser applications in medicine, namely, in otolaryngology (correcting the shape

*Presented at the Fundamentals of Laser Assisted Micro- and Nanotechnologies (FLAMN-2016) International Symposium (Pushkin, Leningrad oblast, 27 June to 1 July 2016).

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Received 24 March 2017; revision received 10 August 2017
Kvantovaya Elektronika **47** (10) 935–941 (2017)
Translated by V.L. Derbov

of nasal septum and larynx cartilages [11–14]), cosmetology (correcting ear and nose shape [13, 15, 16]), orthopaedics and spinal surgery (treatment of diseases of spine disc and joints [17–19]).

2. Laser impact on the cartilage mechanical properties

The results of the study of the cartilage tissue mechanical properties demonstrate the following.

1. Under the laser heating of a cartilage to 70 °C, a short-term decrease in the elasticity modulus occurs, which makes it possible to change the shape of the cartilage sample [20]. After the cartilage cooling and the restoration of the initial content of water, the mechanical properties of the cartilage tissue restore to the initial condition [21]. Thus, the process of laser deformation of cartilage does not worsen its strength properties.

2. The temperature dependence of the internal friction under the laser heating and oscillations of the cartilage plate has a maximum near 70 °C, the magnitude and the position of the maximum agreeing well with the appropriate parameters of the phase transition of the cartilage water from the 'bound' state into the 'free' one [22].

The pulsed or repetitively pulsed laser heating of cartilage causes the formation of an acoustic wave [opto-acoustic (OA) effect], which propagates through the cartilage tissue and can be detected by means of acoustic detectors both in the domain of laser impact and beyond this domain. By detecting the OA signal one can obtain important information about the condition and properties of the tissue (e.g., the presence of a certain pathology), as well as about the processes of the tissue interaction with the laser radiation. The OA diagnostics of the cartilage tissue under the laser heating was carried out with the purpose of creating a control system with feedback, required for precise dosing of laser radiation in the process of achieving the necessary conditions for irreversible relaxation of stresses in the cartilage [23]. Under laser irradiation of cartilage, the amplitude and the phase of the OA signal change with increasing temperature. Simultaneously, the damping of the signal increases. The character of the acoustic response also changes and becomes exponential at the end of irradiation, when the transition from the elastic state to the plastic one occurs. The signal shape of an individual OA response reflects the specific features of thermoelastic relaxation of stresses in the near-surface layer having thickness $\sim 1/\alpha$ (α is the effective absorption coefficient of the cartilage tissue at the wavelength of laser radiation).

3. Optical processes in the cartilage under the laser impact

The change in the internal structure and the mechanical properties of a tissue is accompanied by the change in its optical properties. To study these changes we performed the experiments, in which the cartilage of the nasal septum was mechanically bent, and the region of maximal stress was irradiated by a holmium laser with a wavelength of 2.09 μm [24]. In the process of irradiation, the temperature was measured inside the cartilage plate, as well as the dynamics of mechanical properties and the coefficient of the laser radiation transmission. The relaxation of stresses began when the temperature reached 70 °C. In this case, the intensity of transmitted radiation became minimal.

The experiments on measuring the intensity of light backscattered by the laser-irradiated cartilage demonstrated direct correlation of the stress relaxation processes (or cartilage shape change) with the light backscattering. The peak of the integral intensity of the backscattered probe radiation coincided in time with the beginning of stress relaxation. The measurement data for the spatial distribution of the scattered laser radiation intensity, passed through the sample, were used to study the dynamics of the tissue structural changes in the process of laser irradiation. This approach allowed the experimental determination of the denaturation thresholds for the cartilage tissue and the cornea as functions of the laser radiation wavelength. Using the light scattering method, the energy thresholds of the structural changes under the heating of cartilage by free-electron laser radiation having a wavelength varied in the range from 2.2 to 8.5 μm [25] were determined. In the experiment using a multichannel analyser, the angular distributions of the diode laser radiation intensity (λ = 630 nm) passed through the 1.3-mm-thick samples of nasal septum cartilage of a pig, heated by the radiation from a free-electron laser, were recorded. Using the method of IR Fourier spectroscopy the kinetics of water thermodiffusion in cartilage was studied in detail [26].

The time dependence of light scattering in the cartilage of a nasal septum and eye cornea were determined in order to estimate the kinetics of structural changes as a function of the wavelength and energy density of laser radiation [27]. The results show that the threshold of the structural changes for the cornea is slightly lower than for the cartilage, but depends on the wavelengths for both tissues. The threshold value of the structural changes is inversely proportional to the absorption coefficient for many wavelengths; however, for the absorption lines of water near λ = 3 and 6 μm (for which the absorption coefficient is too high) the threshold of structural changes is determined by the tissue heating kinetics.

To monitor the dynamics of the visible radiation scattering in the process of laser heating of the tissue of the intervertebral disc (IVD) nucleus pulposus, the optical scheme with a single fibre was chosen, which allows the delivery of both the working and the probe laser radiation into the tissue through the created channel [17]. For performing experiments, a multifunctional optical adapter was designed and fabricated, using which the probe radiation is delivered into the zone of laser heating of the tissue, and the diagnostic radiation (DR) is collected and transported to the detector. The IVD was irradiated through an optical fibre by a repetitively pulsed erbium laser. As a probe, the radiation of a laser diode with a wavelength of 532 nm was exploited.

For some combinations of the tissue condition (in particular, in the presence of degenerative changes) and the heating conditions, gas bubbles formed in the tissue in the course of laser heating can merge into a larger bubble with the size comparable with the optical fibre diameter. In the case of periodic heating and cooling the bubble smoothly changes its size, giving rise to the characteristic variation of the DR signal, practically repeating the behaviour of the temperature curve (Fig. 1). The appearance of such a bubble in the clinical conditions can lead to undesired consequences, in particular, to the change in the specified temperature regime of the laser procedure. The studies of backscattering dynamics in the nucleus pulposus under laser heating, performed using a single-fibre optical scheme, have shown the possibility of monitoring the tissue condition in the zone of action.

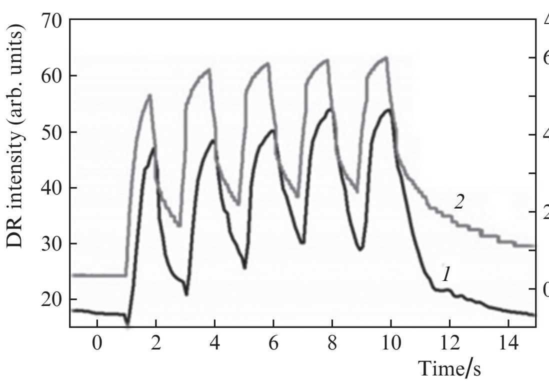

Figure 1. (*1*) Time dependences of the DR intensity, reflected from the walls of a gas bubble and (*2*) difference T between the maximal temperature and the initial one. The irradiation conditions were as follows: the radiation wavelength 1.56 μm, the power 1 W, the pulse duration 1 s, the pulse repetition rate 0.5 Hz, the fibre diameter 600 nm.

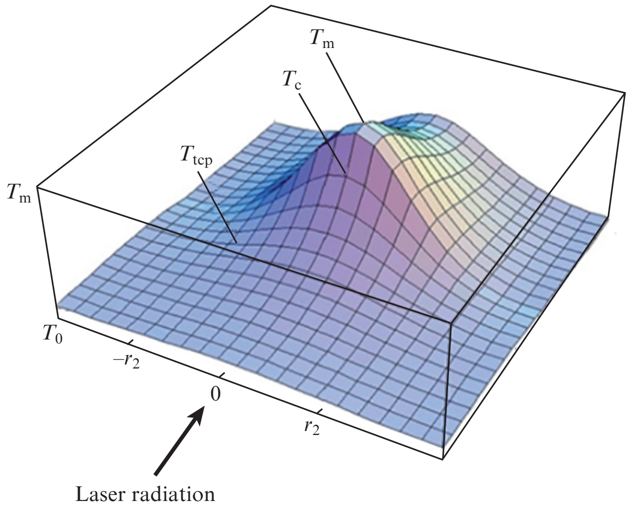

Figure 2. Characteristic temperature distribution under laser irradiation of cartilage; r_2 is the radius of the sapphire contactor tip, T_0 is the initial temperature.

4. Thermal processes in a cartilage under the laser impact

For theoretical modelling of the stress relaxation process in the laser-irradiated cartilage tissue, a few theoretical models have been proposed [9, 28, 29]: the models describing the temperature field in the cartilage under conditions close to the real procedure of laser correction of the nasal septum shape, with allowance for the multilayer structure comprising the cartilage, the mucous tunic, the sapphire tip of the special contactor instrument, at the face of which two thermocouples are mounted at the place of contact with the tissue; the model of thermal stresses in the cartilage tissue; and the model describing the dynamics of stress relaxation as a diffusion-limited process of relative displacement of the structural components of the cartilage matrix.

The calculations of the temperature profile allow the following conclusions:

1. The maximal temperature T_m is reached in the depth of the cartilage at some distance h from the surface rather than on the irradiated surface itself (Fig. 2). This is due to the heat losses at the irradiated surface, caused by water evaporation (in model experiments without the contactor) and with the heat outflow into the sapphire tip of the contactor in the situation of a real operation of laser correction of the nasal septum shape. That is why the control of the process of the tissue laser heating by measuring the surface temperature alone cannot provide adequate information about the heating level and the structural changes in the volume of the cartilage.

2. The power, exposure time and spatial distribution of the laser radiation intensity are the basic parameters affecting the relation between the temperature T_{tcp} measured by the thermocouple, the maximal temperature T_m characterising the heating efficiency and the temperature T_c in the centre of the irradiated spot. The latter ensures the absence of damage of the nasal septum mucous tunic, i.e., the safety of the procedure.

An important result of the theoretical modelling of the thermal stresses that arise under the laser impact is the possibility to predict the conditions of their relaxation. For the first time it was shown that the conditions of plastic deformation in cartilage tissues correspond to the Mises criterion known in material science, and the temperatures 65 °C – 75 °C of stress relaxation calculated using this criterion are in good agreement with the experimentally found temperatures, at which the plastic relaxation of the cartilage tissue begins [9].

5. Mechanisms of the controlled shape change in the cartilage tissue

It was proved that the main mechanism (or, at least, the first stage) of the laser-induced stress relaxation in cartilages is the transition of water from the bound state into the free one [20, 28, 30], accompanied by the following processes:

I. The local mineralisation of the biological tissue at the expense of neutralisation of anion groups of proteoglycans by the Na^+ and Ca^+ ions without any changes in the structure of collagen and proteoglycans [20]. It was shown that an increase in the local NaCl and $CaCO_3$ concentration accelerates the process of mechanical stress relaxation in the cartilage [31].

II. The local depolymerisation of proteoglycan aggregates under the short-time laser heating to 70 °C followed by the formation of new proteoglycan structure in the cartilage matrix [20, 28].

III. The short-time rupture of the bonds between the collagen and proteoglycan subsystems leading to a decrease in stresses in the cartilage and some changes in the spatial structure of proteoglycans [32]. The experimental results can be explained by the existence of relatively solid regions (domains) separated by weaker interfacial layers in the cartilage matrix. The destruction (melting) of these layers makes the domains mobile with respect to each other. This mechanism is related to small energy expenditures and cannot provide the long-term stability of the cartilage shape.

IV. The formation of micropores in the cartilage matrix. The pore formation and the related formation of new interfaces between phases is one of the known stress relaxation mechanisms in crystalline materials. In the papers devoted to the laser impact on biological tissues this mechanism was first detected in the process of cartilage laser irradiation [9, 33]. The experimental data on the formation of micropores in the cartilage matrix were obtained using atomic force microscopy, optical coherence tomography and structured illumination microscopy [20, 28, 33, 34]. The mean size of the pores observed in a healthy articular cartilage amounts to 12–15 nm [20], and the laser impact allows the width of the size distribution of pores to be measured from 50 to 300 nm [33].

V. The polygonisation, i.e., the structural change in the chondrone organisation under the nondestructing laser action [32]. The alignment of chondrones leads to the reduction of the elastic energy of the system and can be implemented under the moderate tissue heating without denaturation of the cartilage matrix.

VI. The new mechanism of stress relaxation, namely, the formation of stable gas bubbles that hamper the process of returning the polarised water molecules, removed by the laser heating, to their initial positions and stabilise the cartilage shape, changed by the mechanical deformation [33].

6. Role of mechanical stresses

Under the laser impact on biological tissues, the mechanical effects can play an essential role in both the destruction and the regeneration processes. It is known that the cells of a biological tissue are sensitive to the external mechanical pressures: the mechanical stresses in some range of their amplitudes facilitate the activation of regenerative processes, and the greater stresses lead to the deceleration of cell activity and cell death [35]. As to the process of laser-stimulated regeneration of biological tissues, for which it is important to provide the specified regime of repetitively pulsed heating and mechanical stress, the problem of pressure determination is of primary importance for the monitoring and optimisation of the laser impact.

In Refs [17, 23] the OA method was applied to the pressure recording in the acoustic wave arising under the interaction of laser pulses with the irradiated medium. The study of acoustic waves was carried out in hydrogels (close to tissues in their mechanical properties) placed in a closed volume and compressed between two glass plates. In the process of irradiation, the temperature and the acoustic signal were recorded. Figure 3 presents the results of measuring the pressure in the hydrogel heated by repetitively pulsed radiation of the erbium-doped fibre laser. It is seen that the steady-state regime of stabilised pressure oscillations is implemented after the action of a few laser pulses.

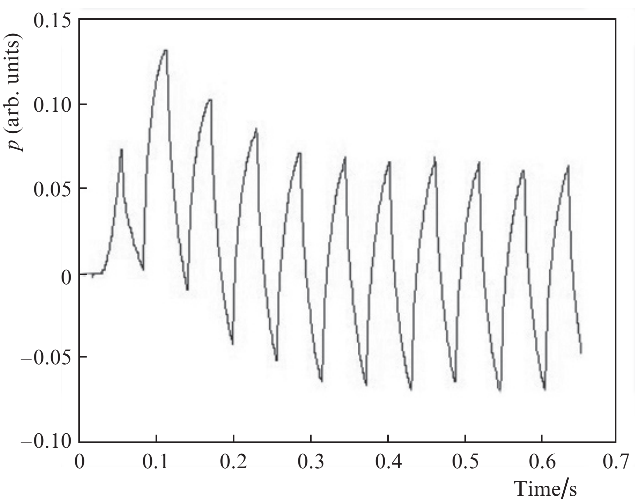

Figure 3. Time dependence of the pressure p in the hydrogel in the process of pulsed laser heating.

To determine the region of the acoustic wave localisation and the pressure distribution, the compression of the medium was visualised using a shadow camera (Fig. 4). The frame-by-frame shadowgraphs indicated the presence of gas bubbles and the localisation of the pressure wave inside the region of the radiation absorption rather than its propagation far beyond the laser beam.

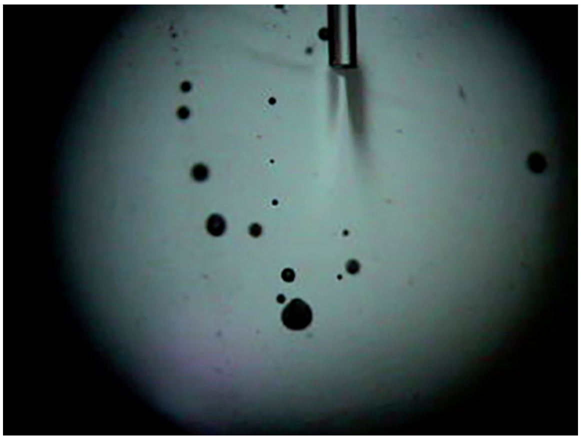

Figure 4. Shadowgraph of the laser impact on the tissue-like hydrogel.

7. Mechanisms of laser regeneration of biological tissues

Regeneration is a natural response of biological tissues of living organisms to practically any external damaging impact. However, the rate of the reparative processes and the type of the produced tissue depend on the characteristics of the external action. Two types of regeneration are distinguished. The substitutional regeneration (the replacement of the tissue or organ defect with the connective tissue, often accompanied with fibrous scar formation) is a quick response of the system to a sufficiently strong external impact, and the cellular one (based on the proliferation of the existing cells) is a relatively slow process leading to the growth of highly organised tissue.

It is known that the chondrocytes are sensitive to the external conditions, particularly, the temperature and the mechanical stress [35]. The laser radiation modulated in space and time causes the repetitively pulsed heating, leading to the nonuniform thermal expansion and the formation of a pulsed nonuniform mechanical stress field, which can actively affect the function of chondrocytes, facilitating their proliferation and biosynthetic activity.

In Refs [33, 36] the formation of pores smaller than 1 μm in the immediate vicinity of the hyaline cartilage cells after the nonablative impact of laser radiation was demonstrated for the first time. In this case, no significant structural changes in the cartilage tissue were observed. The micro- and nanopores formed in the cartilage play an important role in the improvement of its nutrition and the stimulation of regeneration process after the laser impact.

8. Cartilage implant fabrication for the treatment of larynx stenosis

The potentialities of laser correction of the cartilage shape are not exhausted by the technologies of correcting the shape of nasal septum and auricle. The larynx stenosis is a hard disease related to the breath and nutrition malfunction because of the larynx cartilage injury and the formation of scaring zone in this region [37]. As a rule, the stenosis development leads to the partial removal of the trachea and the necessity of closing the resulting defect with an implant. The installation of an implant made of artificial material is related to the essential risk of the disease recurrence in the tissue regions adjacent to the implant. At the same time, due to the particular geometry of the larynx cartilage that has the shape of a semiring with the radius depending on the specific physiological features of each individual patient, the choice of a suitable donor implant is difficult. Making the cartilage implants by mere cutting a sample of the required shape from the available donor cartilage material is also not very promising because of a significant risk of residual stresses left in such an implant, which can lead to poor predictability of its behaviour after the implantation into the trachea.

A new technology of larynx and trachea stenosis treatment was proposed, based on using implants in the form of the plates of costal cartilage preliminarily shaped as semirings by laser processing [14]. It was shown that the shape of the costal cartilage could be modified using lasers the wavelengths 0.98, 1.56 and 1.68 μm depending on the thickness of the used sample [14, 38]. The fabrication of implants about 3 mm thick for closing the trachea defect was implemented using the erbium-doped fibre laser (λ = 1.56 μm) equipped with a contactor having the sapphire tip 3 mm in diameter. The procedure included the preliminary fixation of cartilage plates using the special ring-shaped holders, the laser irradiation and the immersion into the physiologic medium until they acquire the stable bended shape (Fig. 5).

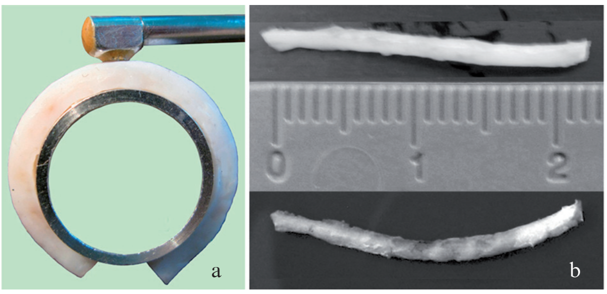

Figure 5. (a) Ring-shaped holder of the costal cartilage in the process of its shape modification under the impact of the laser contactor and (b) the costal cartilage of a rabbit before (top) and after (bottom) the laser-induced shape change.

The optimal regimes of the laser impact were found that allow the achievement of the required curvature of the costal cartilage without essential violation of its structure. The safety control of the used regimes was implemented using the differential scanning calorimetry and detecting the degree of collagen destruction in the cartilage, which appeared to be within the measurement error under the chosen regimes of the laser action [14]. The stability of the cartilages implanted to rabbits was studied during three months. It was shown that under the conditions of the physiological medium the new shape of the cartilage is stable and does not undergo any changes with time. In the present paper, the effect of nonlinearity of thermomechanical properties of the cartilage tissue was revealed, which consists in the different degree of cartilage plate curvature change under its double-side sequential irradiation. When first the inner surface and then the outer surface of the cartilage semiring was irradiated, the resulting curvature radius always appeared smaller than for the irradiation in the inverse order. This property of the cartilage tissue should be taken into account in the planning of geometrical parameters of laser-modified implants. The first operation of the trachea defect closing with a laser-modified cartilage auto-implant was performed in the Clinic of ENT diseases at the M.I. Sechenov First Moscow State Medical University and demonstrated the stable positive result.

9. Laser regeneration in orthopaedics

9.1. Measurement of cartilage electric conductivity

The studies of the electric conductivity of the IVD nucleus pulposus under the thermomechanical impact of repetitively pulsed radiation were performed using the erbium-doped fibre laser with a radiation wavelength of 1.56 μm [39]. The measurements of the tissue conductivity kinetics were carried out at the alternative-current frequency of 100 Hz by means of electrodes, coaxial with the optical fibre delivering the laser radiation to the irradiated tissue. To visualise the structural changes occurring in the tissue under laser irradiation simultaneously with the measurement of electric conductivity, the digital video recording using the shadow method was also performed. The measurements of the IVD tissue conductivity under the repetitively pulsed laser impact have shown that depending on the exposure duration both reversible and irreversible changes in the electric conductivity can occur in the tissue.

The displacement of the tissue with respect to the interelectrode gap causes the redistribution of free ions of the interstitial fluid and increases the contribution of these ions into the tissue conductivity. Moreover, the tissue denaturation can give rise to the additional contribution of the bound counter-ions into its conductivity. All these factors increase the conductivity in the domain of the laser action [39]. The cyclic displacements of the tissue modulate the magnitude of the conduction current in the interelectrode gap, which can be used as an indicator of the tissue mechanical condition. The dynamics of the tissue mechanical vibrations is determined by the variation of the current amplitude, and the concentration of the conductivity ions in the coagulation bag depends on its mean value.

The purposeful study of nonablative laser effect on the rabbit IVD revealed irradiation regimes that induce clearly expressed regeneration processes, namely, the proliferation of the chondrocytes of the annulus fibrosis and the nucleus pulposus, as well as the metaplasia of the inner layers of this annulus fibrosis and the damaged nucleus into the transit fibrous-hyaline or typically hyaline cartilage. The controlled nonablative laser action allows the restoration of the natural ability of the cartilage to regenerate. By means of the optical, thermal and mechanical effect of laser radiation, the cartilage cells are activated. This allows the growth of the hyaline cartilage in the destroyed IVD [40].

9.2. Modelling the diseases of the articular cartilage and subsequent laser regeneration

In the in vivo experiments simulating the regenerative processes in a damaged articular cartilage, the regimes of laser irradiation were chosen to provide a thermomechanical impact on the tissue. For irradiation we used a semiconductor laser with a radiation wavelength of 1.45 μm (the absorption depth in the cartilages amounting to 0.4 mm). This wavelength was chosen to eliminate a noticeable laser effect on the bone tissue underlying the articular cartilage and to avoid the reparative process triggering, related to the activation of the bone and marrow cells. In the process of laser action the temperature variation, monitored using a thermal imager, did not exceed 10 °C. The spatial inhomogeneity of the intensity distribution of the laser radiation produced the temperature gradients of the order of 100 °C cm^{-1}, and its temporal modulation gave rise to the thermomechanical effect with the frequency 0.5–1.0 Hz. In two months after the laser procedure the irradiated samples of the tissue and the control ones were subjected to the histological investigation. The results have shown that the laser-induced regeneration of the cartilage tissue surface defects occurs at the expense of the cells of the cartilage itself rather than the cells of the bone tissue, marrow, or fibroblasts present in the synovial fluid. The size of the visible defect is reduced due to its filling with the regenerated cartilage tissue from the edges towards the centre. It is important to note that the regeneration of the surface defect is implemented via the growth of the hyaline cartilage. The results of laser regeneration of the articular cartilages in animals have shown the promising potentialities of applying the nondestructing laser radiation, modulated in space and time, for the treatment of traumatic defects and degenerative diseases of the articular cartilage.

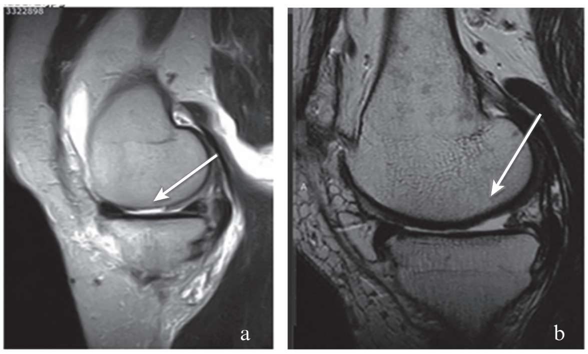

Figure 6. (a) Defect of the femoral condyle of the 3rd degree (according to the international classification) having the size 11.0–11.5 mm and (b) the same joint after laser irradiation. The cartilage surface became smoother, an increase in its thickness by 1–2 mm is observed.

Later the described technology was successfully applied to the treatment of human joints. The irradiation of degenerative knee joints of the patients aged from 35 to 72 was performed with the laser radiation having a wavelength of 1.56 μm. The magnetic resonance tomography of the joints was carried out before the laser impact and in six months after it (Fig. 6). For the studied group of patients the results of the study have shown the regeneration of the cartilage tissue by 1–2 mm on average during the observation time. For 90% of the patients the results have demonstrated essential reduction of the pain syndrome and improved functionality of the joint.

10. Conclusions

A new branch of medical physics, laser modification of cartilages, is developed. The experimental studies of physical, chemical and biological processes that occur under the laser change in the cartilage shape and laser regeneration of the articular cartilages are carried out. The region of optimal regimes of the laser impact is determined. The physical grounds of the new medical technology of correcting the cartilage shape in the process of implant manufacturing are developed, the indications and contraindications for their application in otolaryngology are determined. The physical and chemical grounds of the laser regeneration of cartilage tissues are developed, the growth of hyaline cartilage as a result of the nondestructing laser radiation is demonstrated and explained. The prospects of application of laser regeneration in the orthopaedics are shown.

References

1. Azadgoli B., Baker R.Y. *Annals of Translational Medicine*, **4** (23), 452 (2016).
2. Rubin D. *Neurol. Clin.*, **25** (2), 353 (2007).
3. Hansson T.H., Hansson E.K. *Spine*, **25**, 3055 (2000).
4. Baskov A.V. *J. Spine*, **4**, 210 (2015).
5. Sobol E. *Proc. Light-Activated Tissue Regeneration and Therapy Conf.* (New York: Springer, 2008) pp 259–266.
6. Reginster J.Y. *Rheumatology*, **41** (1), 3 (2002).
7. Peck Y. *Sci. Rep.*, **5**, 16225 (2015).
8. Makris E.A. *Nat. Rev. Rheumatol.*, **11**, 21 (2015).
9. Sobol E.N., Milner T.E., Shekhter A.B., Baum O.I., Guller A.E., Ignatieva N.Y., Omelchenko A.I., Zakharkina O.L. *Laser Phys. Lett.*, **4** (7), 488 (2007).
10. Sobol' E.N., Baum O.I., Omel'chenko A.I., Sviridov A.P., Vorobyova N.N., Zakharkina O.L., Soshnikova Yu.M., Yuzhakov A.V., Shcherbakov E.M., Shekhter A.B., Guller A.E., Bol'shunov A.V., Baskov A.V., Svistushkin V.M., in: *Sovremennye lazerno-informatsionnye tekhnologii* (Modern Laser Information Technologies) (Moscow: Interkontakt Nauka, 2015) pp 567–614.
11. Rothholtz V.S., Wong B.J.F., in *Lasers in Dermatology and Medicine* (New York: Springer, 2011) pp 495–521.
12. Bourolias C., Hajiioannou J., Sobol E., Velegrakis G., Helidonis E. *Head & Face Medicine*, **4**, 15 (2008).
13. Ovchinnikov Y., Sobol E., Svistushkin V., Shekhter A., Bagratashvili V., Sviridov A. *Arch. Facial. Plast. Surg.*, **4** (3), 180 (2002).
14. Baum O.I., Soshnikova Y.M., Sobol E.N. *Lasers Surg. Med.*, **43**, 511 (2011).
15. Omel'chenko A.I., Sobol' E.N., Sviridov A.P., Harding S. *Quantum Electron.*, **30** (11), 1031 (2000) [*Kvantovaya Elektron.*, **30** (11), 1031 (2000)].
16. Leclère F.M., Mordon S., Trelles M.A., in *Biomedical Optics in Otorhinolaryngology* (New York: Springer, 2016) pp 203–212.
17. Sobol E., Zakharkina O., Baskov A., Shekhter A., Borschenko I., Guller A., Baskov V., Omelchenko A., Sviridov A. *Laser Phys.*, **19** (4), 825 (2009).
18. Sobol E., Baum O., Shekhter A., et al. *J. Biomed. Opt.*, **16** (8), 080902 (2011). DOI: 10.1117/1.3614565 (2011).
19. Baltzer A.W.A., Stosch D., Seidel F., Ostapczuk M.S. *Z. Rheumatol*. DOI: 10.1007/s00393-017-0309-1 (2017).
20. Sobol E., Sviridov A., Omelchenko A., Bagratashvili V. *Biotechnol. Genet. Eng. Rev.*, **17**, 553 (2000).
21. Zemek A.J., Protsenko D.E., Wong B.J.F. *Lasers Surg. Med.*, **44** (7), 572 (2012).
22. Omel'chenko A.I., Sobol' E.N., Bagratashvili V.N., Sviridov A.P., Dmitriev A.K., Bagratashvili N.V. *Perspektivnye materialy*, **7** (3), 56 (1999).
23. Omelchenko A.I., Sobol E.N., Bagratashvili V.N., Karabutov A.A. *Laser Phys.*, **16** (12), 1681 (2006).
24. Sviridov A., Sobol E., Jones N., Lowe J. *Lasers Med. Sci.*, **13** (1), 73 (1998).
25. Sobol E.N., Sviridov A.P., Kitai M.S., Gilligan J.M., Tolk N.H., Edwards G.S. *Proc. SPIE*, **3601**, 122 (1999).
26. Bagratashvili V.N., Sobol E.N., Sviridov A.P., Popov V.K., Omel'chenko A.I., Howdle S.M. *J. Biomech.*, **30**, 813 (1997).
27. Sobol E.N., Sviridov A.P., Kitai M.S., Gilligan J.M., Tolk N.H., Edwards G.S. *J. Biomed. Opt.*, **8** (2), 216 (2003).

28. Bagratashvili V.N., Sobol' E.N., Shekhter A.B. *Lazernaya inzheneriya khryashchei* (Laser Engineering of Cartilages) (Moscow: Fizmatlit, 2006).
29. Shnirel'man A.I., Sobol E.N., Bagratashvili V.N. *Laser Phys.*, **14** (3), 1 (2004).
30. Chae Y., Protsenko D., Lavernia E.J., Wong B.J.F. *J. Therm. Anal. Calorim.*, **95** (3), 937 (2009).
31. June R.K., Mejia K.L., Barone J.R., Fyhrie D.P. *Osteoarthritis Cartilage*, **17** (5), 669 (2009).
32. Ignatieva N., Zakharkina O., Leroy G., Sobol E., Vorobieva N., Mordon S. *Laser Phys. Lett.*, **4** (10), 749 (2007).
33. Sobol E., Baum O., Shekhter A., Wachsmann-Hogiu S., Shnirelman A., Alexandrovskaya Yu., Sadovskyy I., Vinokur V. *J. Biomed. Opt.*, **22** (9), 091515 (2017).
34. Majda D., Bhattarai A., Riikonen J., Napruszewska B.D., Zimowska M., Michalik-Zym A., Töyräs J., Lehto V.-P. *Microporous Mesoporous Mater.*, **241**, 238 (2017).
35. Natenstedt J., Kok A.C., Dankelman J., Tuijthof G.J. *J. Exp. Orthopaed.*, **2** (1), 15 (2015). DOI: 10.1186/s40634-015-0029-x.
36. Soshnikova Yu.M., Baum O.I., Shcherbakov E.M., Omelchenko A.I., Shekhter A.B., Lunin V.V., Sobol E.N. *Lasers Surg. Med.*, **47** (3), 243 (2015).
37. Shields T.W., Lo Cicero J., Reed C.E., Feins R.H. *General Thoracicsurgery* (Lippincott: Williams & Wilkins, 2009).
38. Sviridov A.P., Zakharkina O.L., Ignatieva N.Y., Vorobieva N.N., Bagratashvili N.V., Plyakin V.A., Kulik I.O., Sarukhanyan O.O., Minaev V.P., Lunin V.V., Bagratashvili V.N. *Lasers Surg. Med.*, **46** (4), 302 (2014).
39. Omel'chenko A.I., Sobol' E.N. *Quantum Electron.*, **39** (3), 279 (2009) [*Kvantovaya elektronika*, **39** (3), 279 (2009)].
40. Sobol E., Shekhter A., Baskov A., in *Lasers for Medical Applications: Diagnostics, Therapy and Surgery* (Cambridge, UK: Woodhead Publishing, Series in Electronic and Optical Materials, 2013) Ch. 37, pp 621 – 656.