

Laser Engineering of Spine Discs

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Abstract—The laser engineering of intervertebral discs is one of the branch of medical physics aimed at the development of minimally invasive laser medical techniques based on the effect of the controlled (time- and space-modulated) laser radiation on the structure and the field of mechanical stress of biological tissues. A new method for the laser engineering of the intervertebral discs and the differences of this approach from the existing physical methods of medical treatment are considered. The newly formed tissues of animals and humans are histologically studied. Possible regeneration processes are discussed. A control system that provides for the treatment efficiency and safety is developed. The new laser medical equipment that is designed for the laser engineering of intervertebral discs is described, and the corresponding results of the clinical application are presented.

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1. INTRODUCTION

Aged cartilage tissue loses its regeneration ability. The regeneration of damaged cartilages remains an unsolved problem owing to an extremely low rate of reparative processes. However, the topicality of this problem is related to the widely spread spinal osteochondrosis (degenerative disease of the discs) and the osteoarthritis of joints [1, 2]. It has been demonstrated in the experiments with auricle cartilages [3] that relatively soft (nonablative) regimes of laser irradiation induce the proliferation of chondrocytes, the regeneration of perichondrium, and the cartilage formation. The experiments on various irradiation regimes of rabbit joints using Ho:glass and Er:glass fiber lasers [4] have shown that the hard radiation causes the destruction of the cartilage plate to the subchondral bone plate, which results in the growth of the granulation tissue. This tissue is partially transformed into the chondroid tissue and the fibrocartilage that replace the damaged hyaline cartilage. In the case of the soft (nonablative) regimes of the laser irradiation, the dystrophically modified cartilage tissue exhibits the proliferation of chondrocytes presumably from the reserve of the undifferentiated cells of the hyaline cartilage. This type of the regeneration is substantially more developed for the soft regimes (in comparison with the hard regimes), which indicates the specific regeneration activity of the nonablative laser radiation. The targeted analysis of various regimes of the laser irradiation of the intervertebral discs (IVDs) of rabbits has yielded the nonablative laser action that induces developed regeneration processes: the proliferation of chondrocytes of the annulus fibro-

sus (AF) and nucleus pulposus (NP) and the metaplasia of the AF inner layers and the damaged NP into the transient fibrous–hyaline or the typical hyaline cartilage. The experimental results have been used to develop a new branch of the modern spinal surgery—the laser reconstruction of discs (LRD), which is successfully employed in clinical practice [5–11].

The controlled nonablative laser irradiation makes it possible to restore the regeneration ability of cartilage. The optical, thermal, and mechanical action of the time- and space-modulated laser radiation activates the malfunctioning cartilage cells. This activation enables one to grow normal cartilage in the damaged IVD.

In this work, we consider the LRD method and the differences of this approach from the alternative physical methods of the medical treatment of IVD, present the histological analysis of the newly formed tissues of experimental animals and humans, discuss the possible regeneration processes, develop a control system that provides the efficiency and safety of the process, and present the new laser medical equipment for the LRD and the corresponding results of clinical applications.

2. FUNDAMENTALS OF THE LRD TECHNOLOGY AND THE COMPARISON OF THIS METHOD WITH ALTERNATIVE PHYSICAL METHODS OF THE IVD MEDICAL TREATMENT

The osteochondrosis is a spinal disease that is accompanied by various pathological processes in the spinal structures. The IVD degeneration is the main

pathological process. The disc disruption is clinically manifested as the pain syndrome. The reason for the pain syndrome is alterations in the anatomical, morphological, and biochemical state of the disc. The pathological vascular and nociceptive nerve ingrowth in the degenerative disc, and the entrapment of the fragments of the damaged NP in the annular tears maintain the inflammation inside the disc and provide the morphological substrate for pain. The successful treatment of the permanent pain syndrome of the patient suffering from the osteochondrosis necessitates a modification in the inner state of the disc cartilage. The LRD method is based on the regeneration of the cartilage tissue under the nondestructive laser irradiation. The medical effect is owing to the creation of the spatio-temporal nonuniformities of temperature and mechanical stress in the biological tissue when the tissue is heated by the repetitively pulsed laser radiation. The defects of the disc tissue are replaced by the newly formed hyaline cartilage in the IVD from two to six months after the local laser irradiation. The disc and, in particular, the region of the pain generator are morphologically modified. The clinical study indicate a relatively high efficiency of the LRD in the treatment of the permanent discogenic pain syndrome. Twelve months after the procedure, 86% of patients exhibit a positive effect of the laser treatment that is manifested as a reduction of the pain syndrome, a decrease in the rate of the attacks of pain, the refusal of anaesthetics, etc. The visualization of the discs proves the morphological modifications. The post-LRD discography yields the disappearance of the annular tears, and the NMR tomography shows the appearance of a new dense tissue. The LRD method is employed as a puncture procedure and in combination with the open discectomy when the removal of the hernial fragment is followed by the LRD at the last stage of the operation which substantially diminishes the hernia recurrence probability.

Thus, the LRD is a new effective and safe approach in the treatment of the IVD degeneration among the methods of the minimally invasive spinal surgery.

The conventional treatment of the spinal osteochondrosis involves both conservative and surgical procedures. The minimally invasive methods [12, 13] have gathered much recent interest, since they make it possible to avoid negative consequences of the surgery and provide for a relatively low traumaticity, the absence of general anesthesia, and a significant reduction of the recovery period. The puncture methods for the physical action [14], in particular, heating [15] of the IVD tissues have been developed in the framework of this approach. The IVD decompression can be characterized as the patriarch of the intradisc therapy. This approach is aimed at a decrease in the intradisc pressure owing to a partial removal of NP using either mechanical technique or chemical agents or the laser, or RF [16–18] evaporation of the tissue. The creation of cavities (or several channels) in the disk could have led to a decrease in the pressure and, hence, a decrease in the

painful stimulation of the disk and the nervous roots. However, the NP tissue remains degenerative after the procedures and the IVD height decreases by 5–7%. Such modifications cause a decrease in the strength of the disk and its stability against compressions, the further degeneration, and development of the AF circumferential tears [19].

The intradiscal electrothermal therapy (IDET) is another puncture method for the treatment of the discogenic pains [20]. In accordance with the author's concept, the local heating of the rare part of the AF must inactivate the pathological nerves and cause the denaturation of the AF collagen for the tear welding. However, the experimental results from [21, 22] do not prove the positive effects. In spite of the positive initial results on the IDET treatment of the degenerative IVD diseases, significant postoperative complications [23] minimize the efficiency and the randomized control trials indicate either zero or insignificant advantage of this procedure in comparison with placebo [24].

In comparison with the above methods, the LRD involves a moderate laser action on the IVD, which is not accompanied by the destruction or partial removal of the disc, does not lead to the necrosis of the disc tissues, and does not damage the nerve and vessel spinal structures in the vicinity of the disk. Thus, the LRD method is based on the activation of the regeneration processes in the IVD tissues, which makes it possible to eliminate the reasons for the disease and to reach the long-term positive effect.

3. LASER-INDUCED GROWTH OF NEW TISSUE IN IVDs

The results obtained in the *in vivo* experiments [5, 8] and in clinics [9, 11] demonstrate the formation of new cartilage tissue of the fibrous–hyaline and hyaline types in the IVDs under the laser irradiation of NP. In addition, a part of the irradiated discs exhibit the formation of the bone or bone-like tissue that contains specific cells (osteocytes) and the mineral component of the matrix [6, 25].

Fifteen skeletal-mature Chinchilla rabbits were used in the *in vivo* experiments on the remodeling of the IVD tissue in the presence of the nondestructive laser irradiation. We studied 90 lumbar discs: 60 discs were laser-irradiated, 15 discs served as placebo, and 15 discs were used for control. The radiation of the Er:glass fiber laser with a wavelength of 1.56 μm was delivered to the center of the IVD NP using a quartz optical fiber with a diameter of 400 μm and the puncture needle. The laser irradiation regimes were chosen based on the preliminary temperature measurements. We used the following ranges of the parameters: pulse duration, 10–2000 μs ; repetition rate, 0.3–2.0 Hz; and pulse energy, 0.03–3.50 J. For the animals, the experiments were terminated 4, 30, and 90 days after the operation. The lumbar discs were extracted for the histological analysis

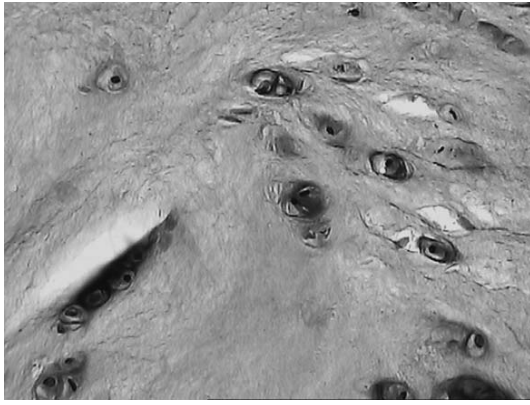


Fig. 1. NP. Transient fibrous–hyaline cartilage tissue with a tendency towards the domination of the hyaline-type cartilage structure (H&E staining, a magnification of 400).

and the electron microscopy. The features of the regeneration process in the IVD are observable four days after the laser irradiation. The most developed features are observed at the AF inner layer at the periphery of the necrosis regions. The appearance of large chondrocytes with the hyperchromic nucleus and the vacuolized cytoplasm indicates the synthesis of the matrix components. Note also the formation of small (two-to-three-cell) isogenous groups (clones). Glycosaminoglycans are accumulated around the active chondroblasts and the clones. The largest amount of the regenerating cells is formed around small necrosis foci.

At long times of the disc extraction, we observe the regeneration features in the AF inner layer and in the NP. Note a significant increase in the number of the active large chondrocytes surrounded by lacunas. They synthesize the matrix components, so that the number of collagen fibrils with a typical periodicity and the fine-grain proteoglycans (PGs) increases around such cells. Two-to-three-cell and multicell isogenous groups are frequently observed. The newly formed tissue exhibits the mixed features of the fibrous and hyaline cartilage: the chondrocytes are similar to the cells of the hyaline cartilage with respect to the ultrastructure but the structure of the extracellular matrix contains the regions with a random distribution of thin collagen fibers (as in the hyaline cartilage) and the regions with identically oriented thick collagen fibers (as in the fibrous cartilage). We call such a tissue the fibrous–hyaline cartilage. In addition, the AF inner layer, the regions in the vicinity of the locking plates, and the NP contain the areas of a typical hyaline cartilage with the homogeneous (in light microscopy) matrix structure that includes thin randomly oriented collagen fibrils and the cells surrounded by lacunas (Fig. 1).

The necrosis foci disappear in the NP tissue owing to the growth of the proliferating cells from the AF inner layer, the end-plates plates, and the resident low-differentiated NP cells. The tissue is replaced by the

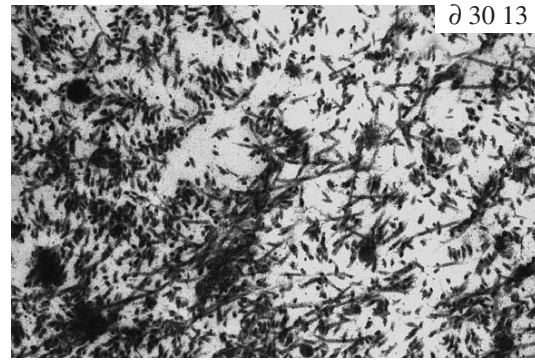


Fig. 2. The TEM image (with a magnification of 30000) of the randomly located thin collagen fibrils and multiple PG granules.

fibrous–hyaline and hyaline cartilages. Gradually, the clusters in the NP vanish and the matrix becomes denser and acquires the fibrillar or grain structure. The NP structure becomes mosaic. The volume and spatial relations of various structural fragments and the significance of the regeneration features depend on the laser-irradiation regime and the localization of the irradiation spot.

Owing to a unique occasion, we studied the IVD tissues of the patient who had the LRD operation. Three years after the operation, the patient got the disc trauma and underwent the microdiscectomy, which made it possible to perform the histological analysis of the disc tissue obtained in the second operation.

For the histological analysis and electron microscopy, we use a fragment of the earlier irradiated disc (i.e., a fragment of the newly formed tissue), which contains the modified fibrous cartilage and large tissue fragments with an extremely large amount of the isogenous groups of chondrocytes (both small (three-to-four cells) and large (up to 50 cells)). At certain fragments, the isogenous groups are close to each other. Note that, in the vicinity of the isogenous groups (especially, large), we observe the homogeneous (rather than fibrous) matrix as in the case of the hyaline cartilage. This matrix is enriched with PGs, which are observable owing to the metachromasia upon the toluidine blue staining. Sometimes, the matrix merges to large zones. This fact indicates the enhanced synthesis of PGs by the chondrocytes of the isogenous groups. The semithin sections and the electron-microscopy data show that large multicell isogenous groups consists of smaller groups. Most chondrocytes of the isogenous group exhibit a developed granular endoplasmic reticulum and the Golgi complex. This fact indicates the cell activity (the synthesis of collagen and PGs). The TEM images (Fig. 2) show that, in these areas, the matrix consists of a network of randomly interlaced thin collagen fibrils with a diameter of about 30 nm and the floccular material. Thus, the observed structure is simi-



Fig. 3. The structure of the region on the left-hand side is close to the structure of the hyaline cartilage (chondrocytes in lacunas and the homogeneous basophilic matrix) (H&E staining, a magnification of 400).

lar to the structure of the matrix of the hyaline cartilage. The cells have moderately active cytoplasm and lacunas. The earlier irradiated area also contains the fragments of various sizes whose structure is similar to the structure of the hyaline cartilage: the homogeneous matrix is enriched with PGs. The cell shapes in the lacunas are the same as in the hyaline cartilage. Such areas can be classified as the transient fibrous–hyaline cartilage (Fig. 3), which was observed in the experiments with rabbits in the irradiated fragments of the IVD.

Thus, the histological analysis proves the formation of the cartilage tissue of the hyaline or the fibrous–hyaline types in the area irradiated with the space- and time-modulated radiation.

4. MECHANISMS OF THE LASER REGENERATION OF BIOLOGICAL TISSUES

The regeneration is a natural response of a biological tissue to any external damage. However, the rate of the reparative processes and the corresponding results (the type of the newly formed tissue) depend on the characteristics of the external action. Below, we discuss the existing concepts of the laser-induced regeneration of biological tissues with respect to the regeneration of the hyaline cartilage.

(i) One of the possible regeneration processes is unspecific with respect to the laser radiation and is typical of the damage of any tissue. It is known that the cell damage can cause a reparative response of the system. The reparative effect of the cell disintegration products is related to a significant release of enzymes, mediators (including cytokines and chemokines), cytoplasmic and nuclear proteins, and the corresponding disintegration products (low-molecular peptides and aminoacids), phospholipids, and nucleotides from the dying or survival cells. Many of the released substances repre-

sent signal molecules for the induction of regeneration [26, 27]. Note a concept of the self-regulatory growth of the connective tissue [28, 29] based on the feedback that involves the catabolism and synthesis of collagen: the products of the collagen disintegration (polypeptides and aminoacids) serve as the signals for the fibroblast proliferation and the collagen production. In this case, the area and depth of the tissue damage are not directly correlated with the reparative activity. Moreover, the regeneration is impeded in large damaged areas (wounds, infarcts, burns, etc.) owing to an increase in the content of toxic disintegration products (wound hormones).

This effect is especially important for the cartilage tissue, since the tissue breakdown products remain unextracted for a long time due to the absence of vessels. Apparently, this can be a reason for a weaker regeneration in the cartilage under the hard laser irradiation in comparison with the case of the soft (nonablative) regimes. The morphological analysis at the light and ultrastructure levels indicates necrobiotic modifications of chondrocytes, swelling and disintegration of the matrix macromolecular complexes, and occasional micronecrosis foci in the case of the soft regimes over first several days after the irradiation. Undoubtedly, such modifications can be a source of signal products of a relatively weak destruction of cells and collagen that induce the fibroblast proliferation and the tissue regeneration. With regard to a certain thermal softening of the matrix, such products can penetrate in relatively distant areas of the cartilage tissue.

(ii) The comparison of the reparative processes after the damage of the joint cartilages of rabbits using a Nd:YAG laser with a power of 10–30 W, 1 Hz and a repetition rate of 10–60 W, 1 Hz and a cauterodyne can be found in [30]. In the case of the electroresection, broad edges of the necrotic modifications of the hyaline cartilage increase with time. Six weeks after any laser damage, the fibrocartilage growth is observed, and, twelve weeks after the laser irradiation, the chondrocyte proliferation is supplemented with the defect replacement by the fibrocartilage. These facts indicate a more active role of the laser radiation in the induction of regeneration in comparison with alternative damages.

(iii) It is known that chondrocytes are sensitive to external conditions (in particular, temperature and mechanical stress). The spatially and temporally modulated laser radiation causes a repetitively pulsed heating, which leads to a nonuniform thermal expansion and the nonuniform oscillating field of mechanical stress. These effects can influence the chondrocyte functions and provide their proliferation and the biosynthetic activity. In addition, the repetitively pulsed laser irradiation results in a periodic displacement of the intratissular water and the dissolved ions. At certain frequencies, such a displacement leads to a local increase in the concentration of the Ca ions. An

increase in the Ca ions concentration in the cytoplasm of chondrocytes and the pericellular matrix can be an important factor that influences the cell metabolism and the tissue regeneration.

(iv) In the experiments from [31], we have been the first to demonstrate the formation of pores with a size of about 1 μm in the hyaline cartilage after the nonablative laser irradiation. Note the absence of significant structural modifications of the cartilage tissue. Undoubtedly, the micro- and nanopores formed in the IVD cartilage can play an important role in the improvement of nutrition and the stimulation of the regeneration process after the laser irradiation.

(v) The modulated laser radiation causes a nonuniform nonstationary heating, which can lead to a structural modification of the intercellular matrix of the cartilage, in particular, the relaxation of mechanical stress owing to the polygonization of the chondron system [32].

The generated mechanical stresses and their relaxation can lead to a periodic reorientation of the electric dipole moment in the structure of the cartilage matrix. Identically oriented dipoles form certain clusters (domains) that are separated by boundary regions with randomly oriented domains. Torsional (orientational) oscillations of the identically oriented dipoles give rise to the torsional (orientational) waves [33], which can stimulate the chondrocytes and can facilitate the regeneration.

5. DEVELOPMENT OF THE CONTROL DIAGNOSTIC SYSTEM

5.1. Measurements of the IVD Tissue Conductivity

The measurements of the electric potential were used in [34, 35] to estimate the composition and state of the cartilage tissue. An array that measures the potential distribution related to the displacement of the intraarticular liquid is employed for the evaluation of the cartilage state [35]. The dc measurements were unstable owing to the polarization of electrodes. In addition, such a method is hardly compatible with a system that delivers the laser radiation. The electromechanical spectroscopy of the cartilage [34] enables one to analyze only the surface conductivity of the tissue. In this work, we consider the ac measurements of the local conductivity in the bulk of the tissue in the course of the laser irradiation of the animal (cow) IVD obtained from a slaughterhouse. The samples were stored in saline at a temperature of 2–4°C over no more than 48 h and were irradiated via an optical fiber with a diameter of 400 μm . A repetitively pulsed fiber laser with a radiation wavelength of 1.56 μm had the power ranging from 0.5 to 1.5 W, the pulse duration ranging from 100 ms to 2 s, and the pulse repetition rate ranging from 10 to 0.33 Hz.

The measurements of the conductivity of the IVD NP tissue were performed using specific electrodes, a

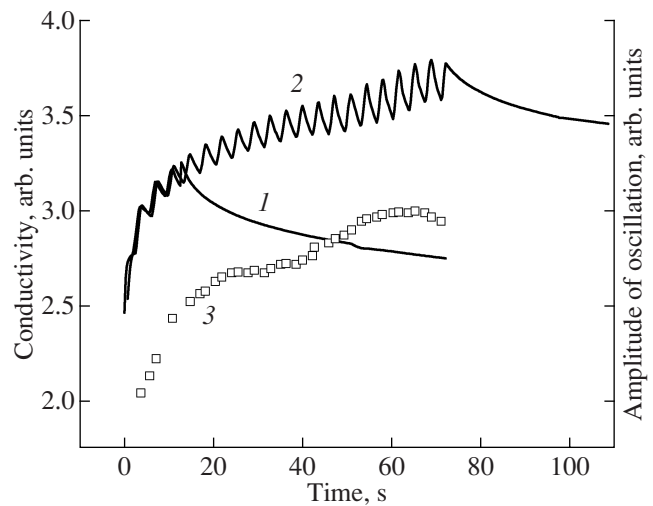


Fig. 4. Variations in the conductivity of the NP tissue under the action of laser pulses with a duration of 1 s, a repetition rate of 0.33 Hz, and a mean power of 1.2 W: (1) the laser action is terminated after five laser pulses, (2) long-term (70 s) laser action, and (3) dynamics of the amplitude of the conductivity oscillations.

puncture needle, and a computer system for the data acquisition and processing. The samples were strung at the needle, so that the electrodes were completely immersed in the tissue. An ac sine-shaped voltage was generated by a DAC incorporated in a National Instruments MIO-16E board. The current signal passing through the tissue sample was measured using an ADC. At the laser-irradiation spot, the tissue temperature was measured by a thermocouple placed at the end of the optical fiber. To establish a correlation between the electrical signals and the structural changes in the irradiated tissue, we supplement the conductivity measurements with the filming of the tissue by a Sony DCR-TRV 40E digital camera. The dependences of the NP-tissue conductivity on the amplitude and frequency of the ac current yield a low-frequency component that is sensitive to the laser-induced variations in the structure and state of the tissue. The action of five laser pulses with a duration of 1 s and a repetition rate of 0.5 Hz leads to an increase in the conductivity almost proportional to the number of pulses (curve 1 in Fig. 4). In this case, the conductivity returns to the initial level 10 s after the termination of the laser irradiation. In the case of the repeated irradiation of the same area, the conductivity curve is identical to curve 1 at the initial stages. Then (for an irradiation time of 30 s), the conductivity growth becomes slower, and, for an irradiation time of 50 s, the growth rate increases (curve 2 in Fig. 4). The amplitude of the conductivity pulses increases during 20 s and, then, exhibits stabilization with an increase in the mean level (curve 2 in Fig. 4). When the laser irradiation is terminated after 75 s, the conductivity of the tissue does not return to the initial level (curve 2 in

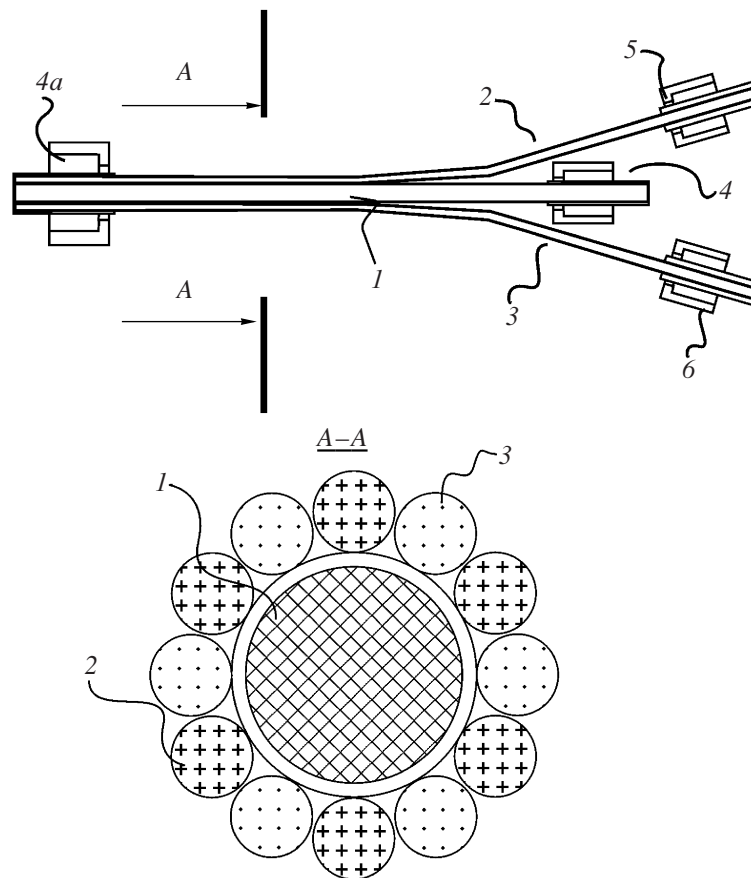


Fig. 5. Scheme of the optical adapter: (1) central optical fiber with a diameter of 300 μm that delivers the laser radiation, (2) and (3) peripheral optical fibers with a diameter of 150 μm that collect the DR and incouple the probe radiation to the power fiber, and (4–6) optical connectors.

Fig. 4). The growth rate of the mean conductivity decreases after 10 s of the laser irradiation and reaches a level of 30% of the initial value. After 50 s of the laser irradiation, the growth rate increases and remains increasing to the moment of the laser switch-off. In this case, a variation in the conductivity is about 40% of the initial value. Such variations in the conductivity are qualitatively reproduced in the measurements on different discs of the same animal (seven discs). The conductivity increases by 20–40% when the discs are irradiated three times using the laser radiation with a pulse duration of 1 s, a repetition rate of 0.5 Hz, and a mean power of 1.5 W. The analysis of the state of the irradiated tissue shows that the tissue is periodically displaced from the heated area at the rate of the radiation pulses. Note also a periodic increase in the tissue temperature with a maximum value of no greater than 50–55°C.

Thus, the measurements of the conductivity of the IVD tissue in the presence of the repetitively pulsed laser irradiation yield reversible and irreversible variations in the conductivity for various irradiation regimes. The periodic displacements of the tissue and the tissue

liquid induced by the temperature gradients modulate the conduction current in the interelectrode space. This effect can be used to characterize the state of the tissue. The modulation of the amplitude of the current is related to the dynamics of the mechanical oscillations (curve 3) whereas the mean value characterizes the concentration of the conduction ions in the tissue.

The experimental results yield a correlation between the modifications in the NP-tissue structure and the conductivity of the tissue. Thus, the ac measurements of the local conductivity in the bulk of the tissue can be used in the development of the control diagnostic system for the laser reconstruction of IVDs.

5.2. Development of the Control System Based on an Optical Signal

The analysis of the optical properties of cartilages and the dynamics of such properties in the course of the laser heating make it possible to characterize the laser-induced modifications of the inner structure of the cartilage [36, 37]. The laser heating of the cartilage is accompanied by the modification of the tissue matrix

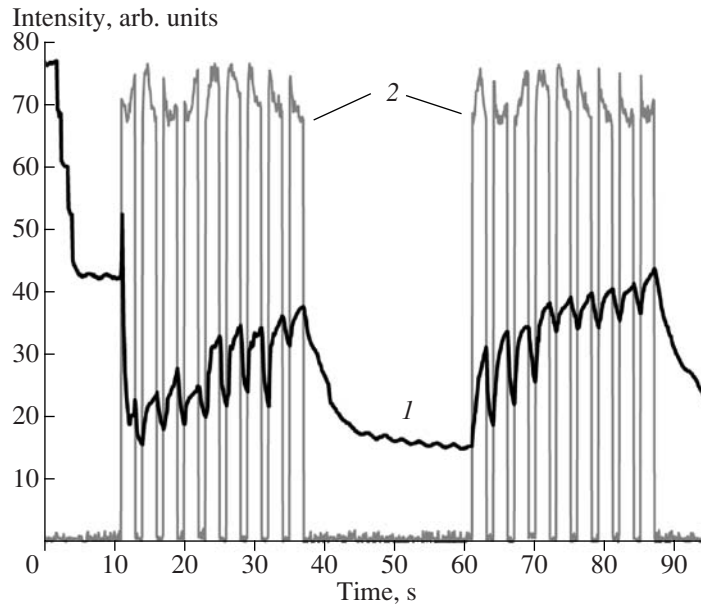


Fig. 6. (1) DR dynamics and (2) variations in the power of the IR laser upon the laser irradiation of the NP tissue.

and, hence, variations in the light scattering. A decrease in the transmittance owing to the scattering was measured in [38] in the experiments on the laser reshaping of cartilages. Wong [39] studied the light-scattering kinetics in the cartilage tissue heated by the radiation of a Nd:YAG laser with a wavelength of 1320 nm. When the temperature increases, the light-scattering signal, first, increases, reaches the maximum level, and, then, decreases. Similar dynamics of the light scattering (an increase changed by a decrease in the intensity) was observed in the experiments on the heating of the hyaline cartilage by the laser radiation with wavelengths of 970 and 1560 nm [40].

To monitor the light-scattering dynamics in the visible range in the course of the laser heating of the IVD NP tissue, one must choose an optical system that can be easily integrated in the scheme of the LRD procedure. The procedure involves a single puncture of the IVD AF using a needle and the delivery of the working and probe laser radiation through the channel to the NP. In this case, the reflected (backscattered) radiation is collected by the same optical fiber. The optical scheme with a single fiber was used in [41, 42] for the measurement of the optical properties of biotissues. In addition to simplicity, such a scheme exhibits an advantage that lies in the fact that the diagnostic radiation (DR) is collected from a relatively small local area comparable with the heated area [43]. This fact makes it possible to monitor the dynamics of the state of the tissue at the maximum temperature. In clinical practice, such an approach enables one to eliminate undesired (with respect to efficiency and safety) effects.

For the experiments, we have developed and created a multifunctional optical adapter (Fig. 5), which makes

it possible to deliver the probe radiation to the area of the laser heating, to collect the DR, and to deliver the DR to the sensor. The adapter consists of the central optical fiber (1) with a diameter of 300 μm , which is connected to the output optical fiber of the laser via optical coupler (4). At the other end, 12 peripheral optical fibers (2 and 3) with a diameter of 150 μm are placed in parallel to and around optical fiber (1) in a certain order (Fig. 1). An optical fiber whose distal end is in the direct contact with the tissue is connected to connector (4a). A system of optical fibers (3) can be used to deliver the probe radiation to the working fiber. Thus, the probe radiation reaches the distal end of the working optical fiber and the DR is fed to the system of fibers (2 and 3) at connector (4a). At the exit, these fibers form bundles (5) and (6), respectively. The DR from bundle (5) is delivered to the intensity sensor.

The optical adapter was placed in the LRD setup whose hardware and software make it possible to record and image the DR signal. The radiation of a laser diode with a wavelength of 532 nm and a maximum power of 2 mW is used in the setup as the probe radiation. The DR dynamics was studied in the ex vivo experiments on the laser irradiation of the sheep IVD. The spinal fragments (L1–S1) were extracted 2 h post mortem, muscles and ligaments were removed, and the samples were placed in a saline container. The tissues were stored at the temperature ranging from +2 to +4°C over no more than 48 h. An optical fiber with a diameter of 600 μm was introduced to the IVD NP area through an 18 G puncture needle. For this purpose, we performed the AF puncture in the ventral–lateral part of the disc. For the laser irradiation, we use a fiber laser with a radiation wavelength of 1.56 μm . Under the laser irradiation, we employ the remote measurements of the tis-

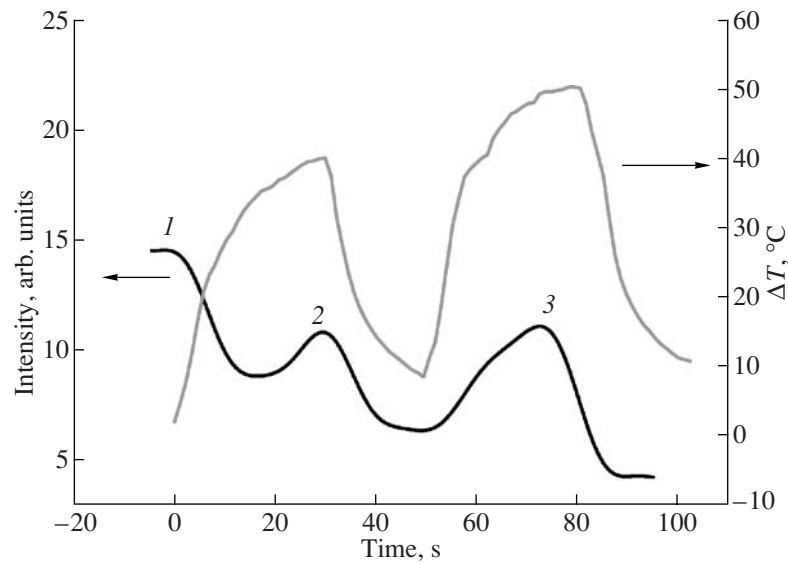


Fig. 7. Envelopes of variations in DR and the maximum temperature of the tissue measured using the IR camera in the course of irradiation.

sue temperature using an IRTIS 2000 IR camera with a frame rate of 70 Hz.

Figure 6 demonstrates the typical dynamics of the DR signal. Figure 7 shows the envelopes of the DR signal and the maximum tissue temperature measured using the IR camera for the laser irradiation at a power of 1.5 W, a repetition rate of 0.33 Hz, and a pulse duration of 2 s.

The diversity of the DR dynamics is related to the features of the NP tissue. With respect to the structure, the NP represents a strongly hydrated gel of the polysaccharide nature that contains randomly oriented fibers of the type-II collagen. The main component (80%) of the

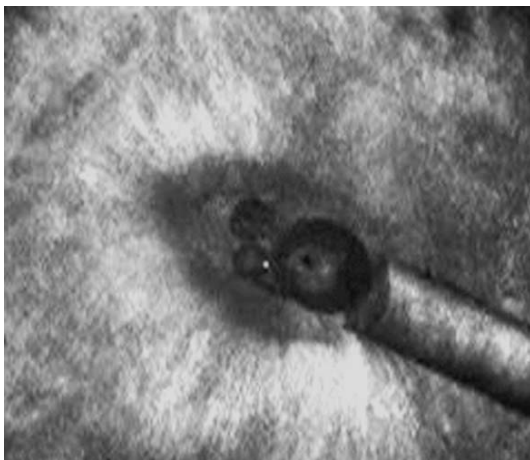


Fig. 8. Microphotograph of a large bubble that emerges in the vicinity of the optical fiber tip with a diameter of 400 μm during the laser heating.

healthy NP is water, which can easily move inside the loose isotropic matrix. The hydraulic permeability of the tissue is only $(0.67 \pm 0.09) \times 10^{-15} \text{ m}^4/\text{N s}$ [44]. From the biomechanical point of view, the NP can be classified as liquid or solid [45]. The optical properties of this tissue are poorly characterized.

Several factors can affect the DR signal. At the initial stage of the tissue heating, the DR intensity decreases by 30–50% of the initial level (region 1 in Fig. 7). Such a behavior can be owing to the formation of a negative thermal lens that was observed in hydrated biotissues in the presence of the nonuniform and non-stationary temperature field [46]. The simultaneous microvideo recording shows an increase in the intensity of the probe radiation scattered by angles of about 90° .

The temperature field that is varied in the course of the laser heating and the subsequent cooling determines the pressure distribution inside the tissue. The development of local pressures gives rise to directional water flows (from the heated area to the neighboring areas with lower temperatures) and the deformation of the collagen-fiber network. An increase in the scattering signal (region 2 in Fig. 7) can be related to the escape of water from the irradiated area and to the shrinkage and compression of the solid component of the matrix. The dynamics of the scattering coefficient is sensitive to the thermal denaturation of the tissue. At a temperature about 65°C , the NP tissue is denatured and the DR further increases (region 3 in Fig. 7).

A pressure gradient resulting from the irradiation of the NP tissue can lead to the generation of gas microbubbles close to fiber tip and the motion of these microbubbles in the presence of the stress field. Oscillations and complicated motions of the microbubbles cause sharp variations in the DR.

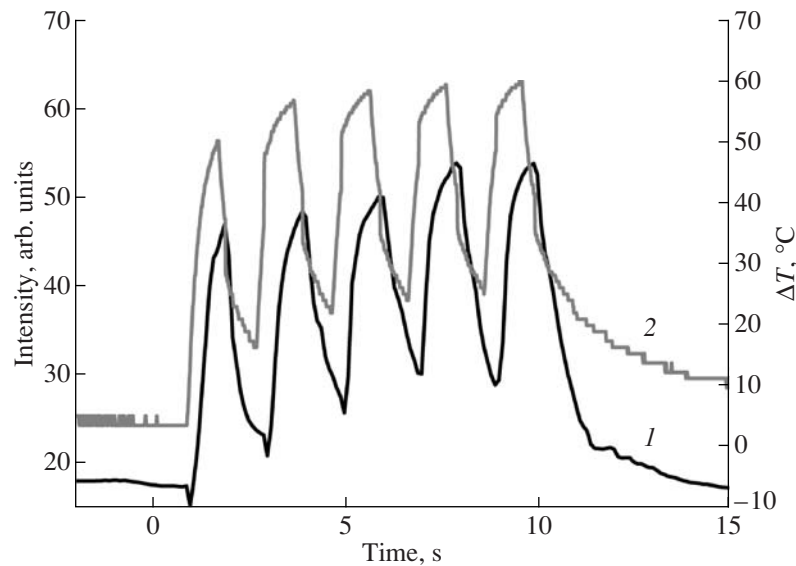


Fig. 9. Dynamics of (1) the DR intensity reflected from a large bubble and (2) the maximum temperature for the laser irradiation of the NP tissue at a power of 1.7 W, a pulse duration of 2 s, and a repetition rate of 0.33 Hz.

At certain combinations of the state of the NP tissue (in particular, at the degenerative modifications) and the heating conditions, the microbubbles can grow and merge to a relatively large bubble whose size is comparable with the diameter of the fiber tip (Fig. 8). Under clinical conditions, the formation of such a bubble can lead to undesired effects, in particular, the disconnection of tissues and changing in the given temperature regime of the laser treatment.

Under the conditions for the periodic heating and cooling of the tissue, the bubble size exhibits gradual variations, which lead to characteristic variations in the DR signal. Figure 9 (curve 1) demonstrates the dynamics of the DR intensity that corresponds to a variation in the curvature of the convex bubble surface that reflects light. This curve is similar to the temperature curve (curve 2 in Fig. 9).

The measurements of the backscattering in the NP tissue in the presence of the laser heating in the optical scheme with a single fiber that delivers and collects the probe radiation and delivers the working IR radiation show that the state of biotissue in the irradiation area can be monitored. The experimental results indicate that the scheme is promising for the control and safety system of the LRD procedure.

6. EQUIPMENT FOR THE LASER RECONSTRUCTION OF DISKS

Specific equipment (LRD-702 Laser Disc Reconstructor) has been developed for the LRD procedure (Fig. 10). The apparatus consists of (i) an Er:glass fiber laser with a radiation wavelength of 1.56 μm , (ii) a fiber-optic instrument for the beam delivery to the irradiation spot and the contact irradiation of NP, and

(iii) a feedback control system for the biotissue monitoring in the irradiated spot and the automatic termination of the irradiation in the case of abnormal operation, which provides the efficiency and safety of the laser procedure. The device is equipped with a computer system whose software allows the data input for a patient, the selection and modification of the working regimes, the control and monitoring of the laser irradiation, and the documentation and recording on external data car-



Fig. 10. Photograph of the LRD-702 laser reconstructor of the discs.

riers. The feedback control system is based on the analysis of the visible DR that is reflected from the irradiated tissue. A variation in the DR intensity is related to a local modification of the NP tissue upon the thermo-mechanical action of the modulated IR laser radiation.

The clinical tests of the device were performed at the First Central Clinical Hospital of the OAO RZhD and the Moscow Medical Center for Vertebrology and Orthopedics. In 2001–2007, more than 300 laser operations were carried out for the treatment of the degenerative spinal diseases and the prophylactics of the IVD hernia recurrence. The clinical observations indicate that 86% of the patients suffering from the chronic discogenic pain syndrome exhibit developed statistically significant differences between the life-quality indices and the pain intensities prior to and after (one half of a year) the LRD procedure.

CONCLUSIONS

The laser reconstruction of IVDs is a new approach in the minimally invasive treatment of spinal diseases related to traumatic or degenerative modifications of IVDs. A relatively high efficiency of the method has been demonstrated in clinics for more than 300 patients. In spite of the absence of a comprehensive interpretation of the laser regeneration, a sufficiently large amount of data indicates that the optical, thermal, and mechanical action of the space- and time-modulated laser radiation activates the cartilage tissue cells (chondrocytes) that proliferate and produce the hyaline cartilage. Several cartilage diseases are related to the poor nutrition of cells. The nutrition depends on the water exchange owing to the absence of blood vessels in cartilage. The experiments on animals demonstrate the therapeutic laser action that leads to the formation of new pores with a size of less than 1 μm in the cartilage matrix. Such micro- and nanopores facilitate the water circulation in the cartilage and provide the cell metabolism. The simultaneous activation of the cells and the improvement of the metabolism cause the long-term therapeutic effect.

Note the importance of the local character of the LRD procedure. The locality of the regeneration is related to the locality of the thermomechanical action upon the IVD tissues. The analysis of the NP structure, the spatial distribution of temperature in the cartilage, and the dynamics of the temperature under the repetitively pulsed laser irradiation of the IVD tissues indicates that the regeneration region is expanded by no greater than 1 mm relative to the irradiation spot. Outside the irradiation spot, we observe a sharp decrease in the tissue temperature and the temperature oscillations whose amplitude determines the efficiency of the mechanical action upon the cartilage cells. Several parameters of the laser irradiation (sizes and localization of the irradiation spots, the laser wavelength and intensity, and the pulse duration and repetition rate) must be thoroughly optimized to provide for the needed

rate of the tissue regeneration and the simultaneous control of the regeneration area. Such an optimization in the experiments on animals made it possible to determine the conditions for the regeneration of the hyaline cartilage in the LRD operations.

The method for the laser treatment of spinal diseases has been registered by the Federal Service on Surveillance in Healthcare and Social Development of Russian Federation (registration certificate FS-2006/025). The LRD-702 laser medical device that contains a fiber laser, a disposable fiber-optic instrument, and a feedback control system and provides for the safety of the laser procedure has been developed and constructed.

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