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Application of solid-state lasers in the ultraviolet range in refractive surgery of the cornea. Literature review.

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A B S T R A C T

In the survey there are some facts about solid-state ultraviolet laser plant generating radiation wavelength λ=210 and λ=213 nanometers. The results of the researches proving the safety of this kind of radiation for different eye structures are outlined. The advantages of this length wave radiation and the possibilities of its application to make photorefractive operations are also mentioned.

Key words: solid-state ultraviolet laser, characteristic,clinical trials

Since the beginning of the 80s of the last century, an active study of the effect of laser radiation on biological tissues has begun. The ability of laser radiation to change the curvature of the anterior surface of the cornea by the method of photoablation was established experimentally. Optimal in many respects (reliability, availability, durability, stability of the parameters of radiated energy) were gas excimer lasers used at that time in the defense and electronic industries. The wavelength λ = 193 nm, generated by the excimer ArF laser, proved to be maximally safe for eye structures due to the small penetration depth (2 ± 3 μm) and complete corneal collagen absorption [1, 6]. In addition, short-pulse radiation from excimer lasers (EL) does not cause clinically significant thermal damage to the corneal tissue, induces extremely low levels of DNA damage, and therefore does not have a mutagenic and carcinogenic effect [7, 16, 23].

To date, ArF-excimer lasers occupy a leading position in refractive surgery. All their advantages are thoroughly studied and used. Perfection of excimers proceeds along the path of increasing the frequency of pulse generation, optimization of the forming scheme based on the principle of a "flying spot", increasing the frequency of the video surveillance system ("eye tracking"), improving the quality of operations and facilitating the work of the surgeon. Nevertheless, the search continues for other types of laser radiation, similarly affecting the cornea, but reducing or eliminating the inconvenience caused by the technical features of the structure and work of the EL. In particular, one of the problems of EL operation is the need for constant filling of the device with a gas mixture and the presence of toxic fluorine in the gas mixture. In addition, the lack of radiation with a wavelength λ = 193 nm is its high absorption by oxygen molecules and water vapor. As a result of the reaction with oxygen, ozone is formed, which, in turn, also absorbs ultraviolet, which leads to the screening of laser energy.

It is also known the effect of air humidity and degree of hydration of the cornea on the effectiveness of ablation [14]. Each ophthalmic surgeon performing refractive surgery knows that the hyperhydrated stroma of the cornea reduces the ablation force, and surgery on a too dry cornea can lead to hypereffect. A good example is the situation when, as a result of excessive fluid accumulation at the flap leg (during LASIK and Epi-LASIK), as a result of uneven ablation, induced irregular astigmatism occurs. This causes the need for constant monitoring of the microclimate operating, conducting calibration tests, as well as visual control of the degree and uniformity of hydration of the cornea. Proceeding from the foregoing, attempts to find a more "convenient" source of laser radiation are justified, relevant and represent a wide field of activity for theoretical and practical ophthalmology.

Thus, as an alternative to radiation with a wavelength of λ = 193 nm, the Medilex excimer laser ophthalmic device (MNTK "Eye Microsurgery" named after Academician SN Fedorov together with the Institute of Laser Physics of the SB RAS) was developed, which makes it possible to use refractive operations the wavelength λ = 193 and λ = 223 nm [7, 10]. The source of radiation with a wavelength λ = 223 nm is an excimer KrCl laser. At the end of the last century, the US developed the Novatec LightBlade 2 ™ solid-state ultraviolet laser, generating radiation with a wavelength of λ = 210 nm. Speaking about this setup, V.V. Kurenkov [9] notes the unprofitability of solid-state lasers due to the rapid failure of a laser nonlinear crystal and the laboriousness of its replacement.

Nevertheless, about 5 years ago representatives of the next generation of solid-state lasers appeared: the Pulzar Z1 (CustomVis) diode Nd: YAG laser with a wavelength of λ = 213 nm and a diode λ = 210 nm LaserSoft laser (Katana Technologies). The results obtained with their use allow us to speak about the safe and qualitative impact on the cornea. Solving the issue of radiation safety with a wavelength greater than λ = 193 nm, it is necessary to clarify its penetrating ability in the eye tissue. According to A.M. Razhev [7] and Kh. P. Takhchidi with co-authors. [10], UV radiation in the region up to λ = 230 nm is completely absorbed by the cornea and does not penetrate into the inner parts of the eye (Fig. 1). This is confirmed by the results of the studies of Dair G. with co-authors [13]. L.I. Balashevich [2] indicates the ability of the cornea to fully absorb radiation in an even wider spectrum - up to λ = 280 nm. Therefore, radiation with wavelength λ = 210, λ = 213 and even λ = 223 nm is absolutely safe for deep structures of the eyeball.

As for the direct effect of radiation in the spectrum of λ = 193 - 223 nm on the cornea, a number of studies indicate its minimal damaging effect. In particular, Paul P. Saarloos, Jennifer Rodger [23] in vivo examined cornea of rabbits after ablation with excimer (λ = 193 nm) and solid-state lasers (λ = 213 nm). Thermal damage was assessed by light microscopy. With the help of autoradiography, unplanned DNA synthesis was estimated, reflecting the degree of DNA damage in each cell. The studies did not show any difference in the tested parameters between radiation with λ = 193 nm and λ = 213 nm. The absence of damaging thermal action was confirmed: the results obtained indicate a minimum of undesirable cicatricial changes in the corneal tissue and its good healing. It was also found that both wavelengths induce comparatively low levels of DNA damage (in both cases, unplanned DNA synthesis was detected in less than 4% of the corneal cells), and therefore did not cause significant mutations or oncogenic tissue degeneration. An insignificant level of influence of laser radiation with λ = 193 nm is explained by the presence of cytoplasmic membrane components shielding the cell nucleus from this wavelength. Thus, the dose of photons reaching the DNA of the cells is limited. The authors suggest that this same mechanism protects the cell from radiation with a wavelength λ = 213 nm.

In the work of N. S. Tsiklis with co-authors [20] data on the timing of regeneration of subepithelial neural plexuses after PRK and LASIK using a solid-state laser are fully comparable to those after EL operations. In turn, A.M. Razhev with co-authors and H. P. Tahchidi with co-authors conducted a comparative assessment of the clinical efficacy and safety of exposure to human cornea radiation with wavelengths λ = 193 and λ = 223 nm [7, 10]. In the course of the study, not only the same clinical efficacy of both wavelengths was corrected in the correction of myopia, but also the absence of significant changes in the level of biochemical parameters of the lacrimal fluid before and after photoregulation of the cornea (antibodies to native DNA antigens, lactoferrin, circulating immune complexes). The results of laboratory studies allow us to conclude that radiation with wavelength λ = 193 and λ = 223 nm does not cause the development of destructive inflammatory processes in the human cornea and the activation of immune response.

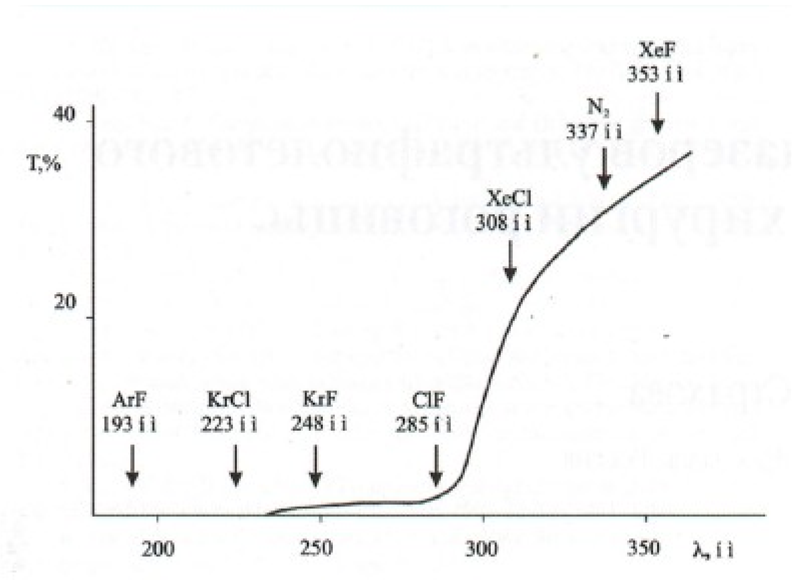

Figure 1. Transmission of radiation (thickness 0.6 mm) in the UV region of the spectrum

S.V. Kostenev [8] carried out a comparative evaluation of temperature changes on the surface of the donor cornea during the ablation process with two Medilux lasers with wavelengths λ = 193 and λ = 223 nm. As a result of the measurements, it was found that when the radiation with a wavelength λ = 193 nm is exposed, the corneal temperature rises an average of 11 ° C, while exposure to radiation with a wavelength of 223 nm is 5.2 ° C.

Some authors note two important advantages of the wavelength λ = 223 nm [7, 8, 10]. Firstly, it is possible to work on a wet operating field, since the water absorption coefficient for λ = 223 nm is much lower than for λ = 193 nm. Secondly, the decrease in the energy density necessary for ablation of corneal tissue (compared to λ = 193 nm), as well as the absence of the effect of "boiling" of the liquid on the surface of the cornea, which ensures its less traumatic and heated. In addition, a high accuracy of corneal profile changes was observed with the formation of smooth ablation surfaces [13, 19].

In works [22], N. S. Tsiklis with co-authors the effect of radiation from a solid-state laser (λ = 213 nm) on the state of the corneal endothelium was studied. The density of endothelial cells was analyzed before the operation and within 12 months after the operation using the PRK technique with myopia of medium degree on excimer and solid-state lasers. There were no significant differences of this parameter in these two groups at the appropriate time of observation, which also confirms the absence of damaging effect on the cornea of radiation with λ = 213 nm.

The same group of authors [21] carried out a comparative histopathological study of rabbit corneas after PRK performed on excimer and solid laser platforms. In both groups, immediately after surgery, smooth ablative surfaces were obtained without edema and changes in the corneal stroma. A month later, a significant number of activated keratocytes with insignificant vacuolation were recorded in the epistromal sections. In deeper layers of stroma, keratocytes and extracellular matrix retained a normal structure. The authors consider the state of the endothelial layer as a critical parameter determining the degree of safety of the procedure, which remained stably intact and unchanged throughout the follow-up period (12 months). During this period, there was no evidence of corneal mutagenesis in both groups. Nevertheless, some histological differences were recorded during the postoperative restoration of the cornea in each of the groups. But, since the histomorphological picture of the cornea after its complete restoration was similar in both groups, the authors consider these differences to be insignificant and do not affect the final visual result of the operation. If we talk about the influence of an acoustic wave on the cornea, then N. S. Tsiklis with co-authors. note that a decrease in the diameter of the beam in a solid-state laser minimizes the mechanical stress of the cornea during ablation [15].

All of the above indicates the safety of radiation with wavelength λ = 213 nm for the cornea and internal structures of the eye and the possibility of using this type of radiation for photorefractive operations. To date, experience has been accumulated and the results of observations of the condition of the eyes of patients operated with a solid-state laser Pulzar Z1 (CustomVis), sufficient to assess not only the safety, but also the quality of the performed interventions. The system works in more than 20 centers in Europe and Asia. The possibilities of this installation, indications for the operation, the advantages of the laser are actively used. Stable clinical results were obtained with correction of irregular astigmatism [11], myopia of mild and moderate degree, myopic astigmatism [4, 5, 17, 20]. At the 25th Congress of the European Society of Cataract and Refractive Surgeons, Dr. E. Rosen reported on the possibility of correcting high degree myopia, hypermetropia, presbyopia [3]. All authors note the high accuracy of the laser, the possibility of forming a smooth ablative profile of the cornea, the minimum damaging thermal and mechanical effect on the cornea.

Speaking about the advantages of a solid-state laser, one should return to the question of hydration of the cornea. We mentioned that the hydration of the cornea, the presence of a liquid layer on its surface, the increased humidity of the air operating factors that significantly affect the ablation force when working at a wavelength λ = 193 nm. The conducted studies showed that, firstly, the wavelength λ = 213 nm is closest to the maximum absorption of corneal collagen, and secondly, it is weakly absorbed by water, physiological saline and balanced saline (BSS). G. T. Dair with co-authors [12] revealed a significant difference in the absorption coefficients of these solutions and in the depth of penetration for radiation with wavelength λ = 193 and λ = 213 nm. It is established that radiation with λ = 213 nm is extremely poorly absorbed by 0.9% sodium chloride solution and balanced saline solution, while for radiation with λ = 193 nm these fluids are strong absorbents. The conclusions made by G. T. Dair with co-authors, are also supported by the results obtained by Hale and Querry (Table 1) [18]. Thus, the absorption coefficient of physiological solution (0.9% NaCl) for radiation with a wavelength λ = 193 nm is 1600 times greater than that for radiation with wavelength λ = 213 nm. These data allow us to consider the wavelength λ = 213 nm as more convenient, since during the refractive operation, strict monitoring of the amount of fluid on the cornea and the degree of its hydration is not required.

Table 1. Absorption coefficient (α) and penetration depth for different solutions (data Hale and Querry)

Solution	193 nm		213 nm	
	α, cm^{1-}	Depth penetration	α, cm1-	Depth penetration
BSS	140	72	6.9	1450
0.9% NaCl	81	123	0.05	$2.0x10^5$
H2O	0.12	$8.3x10^4$	0.04	$2.5x10^5$

Thus, radiation with a wavelength λ = 213 nm is effective for performing photorefractive operations, allowing to accurately obtain a given profile and a smooth ablation surface, to operate on a "wet" operating field. In addition, this radiation is safe, does not provoke the development of mutagenic and carcinogenic processes in the tissues of the eye, and also minimizes the thermal and mechanical effects on the cornea.

Our clinic has experience of operation, maintenance, as well as design and development of refractive laser systems. Since 1997, we have been working on the NIDEK EC-5000 excimer laser system. Since 2003, for the laser refractive operations, we use the excimer laser unit "OLIMP ™ -2000" (registration certificate FS-022b2004 / 2138-05, certificate of conformity No. ROSC RU IMO 2. B13160), created on the basis of our clinic together with the Yaroslavl state Medical Academy and Rostov Optical and Mechanical Plant. Similar installations successfully work in 7 cities of Russia; they carried out more than 20 000 operations. In 2007, we began work on the development of the domestic solid-state scanning refractive laser system "UL-02/213 OLIMP ™ -2000 ", and in March 2008 we started the resource testing of a prototype of a plant operating on the basis of a solid-state laser emitter with a wavelength λ = 213 nm. In December 2009, as part of clinical trials, we operated on the first patients. Working UV radiation with wavelength λ = 213 nm, used for ablation of corneal tissue during refractive surgery, is obtained by nonlinear conversion of the fundamental frequency λ = 1064 nm to the frequency of the second frequency (λ = 532 nm), third (λ = 355 nm) and fifth (λ = 213 nm) of the harmonics. The fundamental frequency is generated by the stimulated emission of the active element, an neodymium-doped Alumitrite garnet, when the Xenon lamp is pumped by radiation.

The forming system of the installation operates on the principle of a scanning spot at a frequency of 100 Hz. The device has an original uninertial system of active tracking in the visible spectrum and advanced software that allows to carry out in addition to classical personalized ablation by keratotopogram.

Our two-year tests already allow us to talk about the high technical resource of working crystals that have not been replaced during the entire period of the study. It should be noted that the replacement of the crystal is not a complicated manipulation and does not take much time. The solid-state laser is compact enough, does not need gas filling and purging of the optical path with nitrogen, does not require any special preparation for the beginning of work. The time to enter the operating mode is 7 - 10 minutes - the time needed to stabilize the temperature in the cooling circuit. A unique feature of the solid-state laser system is the high stability of the energy parameters, so the installation does not require calibration energy tests during the operational day, irrespective of the operating time and air humidity in the operating room. The pulse energy necessary to perform ablation of the cornea in a solid-state laser is much less - 0.9 mJ (compared to 1.6 mJ in an excimer laser), which provides a lower energy and mechanical load on the cornea.

Technical and clinical trials have demonstrated the possibility of ablation of the cornea in a given volume, irrespective of the degree of hydration and moistening of the surface of the cornea. In addition, the UV beam with λ = 213 nm, passing through the optical path, does not lose energy due to absorption by oxygen and water vapor, ozone does not form, which provides UV energy of a certain amount to the surface of the cornea without losses, regardless of the air humidity in operating and installation time. The correspondence of the preset ablation parameters actually made during the operation provides an accurate simulation of the expected, optically correct surface and curvature of the cornea.

The results of our studies of the new domestic solid-state refractive system UL-02/213 "OLIMP ™ -2000", using UV radiation with wavelength λ = 213 nm, confirmed the positive qualities of this radiation and solid-state technology proper, known to us only from foreign scientific publications . Such advantages of a solid-state laser as stability and accuracy of work, time savings, simplification and safety of maintenance, compactness and, importantly, reduction of operating costs, give us grounds for continuing work on the introduction of this laser installation into clinical practice.

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