LASERS IN RESEARCH AND THERAPY: DISCOVERIES THROUGHOUT THE YEARS

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In low-level laser therapy research there has been a clear division of physicists studying the laser itself and some specific cellular function in vitro, photobiologists studying cellular and molecular effects or medical doctors studying clinical effects. Effects of laser light have been under dispute ranging from ineffective to dangerous, cytotoxic, mutagenic, carcinogenic and proliferative effects. For years medical field based their reserve on lack of studies, poor studies, lack of evidence or no results. This has largely been due to the fact that quite a number of studies had been carried out in clinics with minimal funding, rendering double blind studies near impossible.

With the development of better and cheaper equipment cellular effects of laser and light became a popular topic of research. Clinical results gave encouraging reasons for further studies at the cellular and molecular level. This paper attempts to give a chronological review of notable studies in the use of low level lasers and light in the treatment of numerous medical conditions, focusing on the developing use of low level laser in the treatment of neurological diseases.

Keywords: *low-level laser radiation, research, therapy, neurololgical diseases, review.*

Endre Mester started his laser research in 1965. In 1974 he founded the Laser Research Center at Semmelweis, and continued working there for the remainder of his life. He is credited with the discovery of the biological effects of low power lasers [1] and he is believed to be only the fourth physician publishing in the area of laser medicine and surgery the first medical application having been reported by Goldman in 1963 [2, 3] and in cardiovascular surgery McGuff first used a Ruby-Laser in 1963 for the experimental ablation of atherosclerotic plaques [4].

In 1971, Mester began treating patients with non-healing skin ulcers, while using Low Intensity Laser Irradiation [5]. His two sons continued his work after his death in 1984.

Effects of laser light were under dispute ranging from ineffective to dangerous, cytotoxic, mutagenic, carcinogenic and proliferative effects. For years medical field based their reserve on lack of studies, poor studies, lack of evidence or no results even though at the same time ultrasound equipment with only a fraction of research in comparison to laser, was widely accepted both in diagnostic use as well as effective in treating pain.

In 1984 Abergel demonstrated that helium-neon (He-Ne) and gallium-arsenide (Ga-As), were shown to stimulate collagen production in human skin fibroblast cultures, suggesting that these lasers could be used for enhancement of wound healing processes [6, 7] and corroborating Mesters results. This triggered various studies in wound healing and treatment methods in dermatological conditions (Fig. 1).

In 1983 Gamaleya, Shishko, and Yanis published new data about mammalian cells photosensitivity and laser biostimulation commenting on the stimulative effects of light in general as well as polarized light [8]. In the same year a comparative study of laser acupuncture vs needle acupuncture and electroacupuncture in the treatment of autoimmune thyroid diseases was begun by Mäkelä & Mäkelä [9]. Results became available in 1987 when 3000 patients had been treated. Needle arm was discontinued after 40 patients due to poor results. Electroacupuncture arm was discontinued after 100 patients due to results, although better than needle acupuncture, were still not at the level of laser acupuncture. Electric current and laser were combined in 1984 after which 2800 patients were treated with combined electrolaser. This result of superior effect by the combination of laser light and electric current was based on the hypothesis that light, through changing cAMP and calcium levels, regulates the electrical potential of the cell thus emphasizing the effect of electric current and vice versa [10].This hypothesis was proved and improved upon later by Klebanov in 1998 [11].

In 1988 Fedoseyeva, Smolyaninova, Karu, and Zelenin began their long series of in vitro tests on the effects of He-Ne laser on lymphocyte chromatin changes, activation of transcription in lymphocytes and long and short-term responses of human lymphocytes to laser irradiation [12]. These studies continued later with infrared ranges and with pulsed lasers, comparing effects of frequencies.

At the same time Meyers, Joyce, and Cohan studied the effects of low-power He-Ne laser radiation on human lymphocyte cultures [13] and Inoue, Nishioka, and Hukuda published results on altered lymphocyte proliferation by low dosage laser irradiation [14]. The results of these experiments triggered a cascade of further studies on lymphocytes and immune responses, shortly followed by further studies on effects on blood cells in general, the immunological effects on intravenous blood irradiation, which had been discontinued for years.

Extracorporeal blood irradiation had been used in the early 1900 in the treatment of inflammation but was mostly discontinued after the discovery and development of antibiotics. Light mediated vasodilation was first described in 1968 by Furchgott, in his nitric oxide research that lead to his receipt of a Nobel Prize thirty years later in 1998 [15]. Later studies conducted by other researchers confirmed and extended Furchgott's early work, and demonstrated the ability of light to influence the localized production or release of NO, and to stimulate vasodilation through the effect NO on cGMP. In 1978 Mishalkin began his studies on intravenous laser irradiation with Helium-Neon laser [16] and in 1989 a congress was held in Kiev with the main topic being IV laser irradiation and the immunomodifying effects of laser light on blood cells. At this time Rochkind [17] began his studies on stimulative effects of laser light on nerve cells. Later it was found that the same vasodilatory effect was achieved also by using transdermal laser irradiation (Fig. 2).

In 1988 Passarella radiated isolated liver mitochondria with a He-Ne laser finding that it enhanced ATP-ADP metabolism, increased content of ATP, increased the electric potential across inner membranes and pH in matrix, as well as small changes in the matrix configuration [18].

By early 1990's low power lasers became more affordable and more stable bringing a boom of physiological studies by Gamaleya [19], Stranadko [20], Kaplan [21], Korochkin [22], Oshiiro [23], Karu [24]. In 1995 Porozov, Brill, Kiritchuk published their results on the influence of He-Ne laser on frog heart [25].

Laser-tissue interaction research took a huge leap forward after 1994 when the first semiconductor laser that can simultaneously emit light at multiple widely separated wavelengths – the quantum cascade (QC) laser – was invented at Bell Labs by Faist, Capasso, Sivco, Sirtori, Hutchinson and Cho. The development of semiconductor lasers decreased the price of laser equipment and made them more available for researchers, giving also a wider range of possible wavelengths for study.

Up until then, most common lasers used in the studies were the Helium-Neon laser with wavelength at 632.8 nm and the GaAlAs diode laser with a variety of wavelengths from 720 to 904 nm.

Mainstream of studies concentrated on penetration and absorption with great concern for safety as well. Lasers were mainly used for wound healing, pain and circulation. Continuous discussion on methodology and dosage prevailed.

At the beginning of the 1900 after the discovery of photodynamic effects, von Tappeiner and colleagues went on to perform the first PDT trial in patients with skin carcinoma using the photosensitizer, eosin [26, 27]. Out of 6 patients with a facial basal cell carcinoma, treated with a 1% eosin solution and a long-term exposure either to sunlight or to arc-lamp light, 4 patients showed total tumour resolution and a relapse-free period of 12 months. In 1948, Figge et al showed on laboratory animals that porphyrins exhibit a preferential affinity to rapidly dividing cells, including malignant, embryonic, and regenerative cells, and because of this, they proposed that porphyrins should be used in the treatment of cancer [28].

Subsequently many scientific authors have repeated the observation that cancerous cells naturally accumulate porphyrins and have characterized a number of mechanisms to explain it. Much later, in 1978, Dougherty and co-workers clinically tested PDT again [29]. They published striking results in which they treated 113 cutaneous or subcutaneous malignant tumors and observed a total or partial resolution of 111 tumors.

A new photosensitizer was derived from haematoporphyrin in 1990 by Mironov and coworkers in Moscow [30]. Photogem was approved by the Ministry of Health of Russia and tested clinically from February 1992 to 1996 by Stranadko and Kaplan, among others (Fig. 3).

By the mid 1990's research turned more toward cellular effects with mainstream of studies still concentrating on lymphocytes with Klebanov studying the effect of He-Ne laser on free radical mechanisms and the functional potential and priming of leucocytes [31] (Fig. 4). Later Klebanov and Vladimirov studied the effect of low intensity laser light in the red range on macrophage superoxide dismutase activity [32]. By this time various researchers had begun their studies on laser irradiation effects on cytochrome c oxidase function. Absorption spectra obtained for cytochrome c oxidase in different oxidation states were recorded and found to be very similar to the action spectra for biological responses to light. Therefore, it was proposed that cytochrome c oxidase (Cox) is the primary photoacceptor for the red-NIR range in mammalian cells.

In 1997 at the congress 'Problems of Laser Medicine' Rochkind [33, 34] presented his studies on use of laser in nerve regeneration after traumatic injury. By this time research versified to various cell functions and physiological reactions due to laser irradiation but due to varying dose requirements of different wavelengths results seemed baffling. It was not until the early 2000's when it became generally accepted that dosage was not the only determining factor of laser effects. Wavelength and frequency of pulsed laser became an interest of wider study. Wavelengths in the 600-700 nm range were considered best for treating superficial tissue, and wavelengths between 780 and 950 nm for deeper-seated tissues, due to longer optical penetration distances through tissue. Some reports regarded the pulse structure as an important factor in low-level laser effect; for instance Ueda and Shimizu in 2001 found better effects using 1 or 2 Hz pulses than 8 Hz or CW 830 nm laser on rat bone cells, but the underlying mechanism for this effect remained unclear [35].

Infrared laser was studied extensively in circulation due to its previously noted dilatory effect and penetration. It was also noted that specific pathogenic structures, such as atherosclerotic plaque, showed also positive conformational changes (Fig. 5).

Up to the mid 1990's there were two mainstreams of hypotheses on the action mechanism of laser light. First hypothesis was based on the idea of a specific action of coherent (laser) radiation on human and animal tissues, biological structures as a whole, water structure, haemoglobin, etc. The second hypothesis considered the photochemical action of light, including the radiation of lasers, LEDs, and other sources of visible and near infrared light. Karu concentrated at this time on the "singlet oxygen" hypothesis, according to which the light-absorbing molecules such as porphyrins and flavoproteins can be changed, for example, in the respiratory chain of mitochondria into derivatives possessing the properties of photosensitizers. Under the action of light, these compounds evolve singlet oxygen that can stimulate, in turn, such processes as the synthesis of RNA and DNA [36, 37]. Torinuki in 1980 [38] and Tatsuta in 1984 [39] had found corroboration of this idea in the fact that the spectra of activation of the synthesis of those compounds in HeLa cell cultures contained peaks that could be ascribed to porphyrins and flavin compounds.

The second hypothesis of laser light action on the oxidation-reduction properties of electron carriers was suggested in 1988 by Karu [40]. The excitation in cytochrome-oxidase complex of such chromophores as CuA, CuB, or hemes a (a3) influences the oxidation-reduction state of these centers and, consequently, the electron transfer rate in the molecule.

A study from Pastore in 2000 examined the effect of He-Ne laser illumination (632.8 nm) on the purified cytochrome c oxidase enzyme, and found increased oxidation of cytochrome c and increased electron transfer [41]. Artyukhov and colleagues found also in 2000 increased enzyme activity of catalase after He-Ne laser illumination [42].

In 2001 Oron published several papers on the effect of laser in the regeneration processes in the skeletal muscle, heart muscle and bone following trauma or ischemic injury [43, 44, 45] (Fig. 6). He and his research team continue to this day to explore the cellular mechanisms associated with the biostimulatory effects of the low energy lasers and, in particular, the mechanism associated with the beneficial effects of laser irradiation on cell survival under ischemic conditions and angiogenesis both in skeletal and cardiac muscle. They have studied extensively the expression of proteins of the heat-shock family in the ischemic heart and skeletal muscles. These studies showed that the laser stimulated cells migrate from the bone marrow to the remote organ (ischemic heart) in the rat infracted heart model and cause a reduction of 77% in the scarring post myocardial infarction. This novel phenomenon in stem cell biology is currently investigated also in other organs like, for example, the ischemic kidney.

After the development of powerful LEDs, one of the most topical and widely discussed issues in the low-level-laser clinical community became whether the coherence and monochromatic nature of laser radiation have additional benefits, as compared with more broad-band light from a conventional light source or LED with the same center wavelength and intensity. Samoilova had been studying the biomodulating effects of polarized light since the early 1990's [46, 47, 48] and Lubart at the same time also studying white light and its effects on sperm cells and later on the adipose derived stem cells [49, 50]. Two aspects of this problem became topics of discussion: the coherence of light itself and the coherence of the interaction of light with matter (biomolecules, tissues). The latter interaction produces the phenomenon known as laser speckle, which was postulated to play a role in the photobiomodulation interaction with cells and subcellular organelles. Discussions continue because of the difficulty to design an experiment to directly compare coherent laser light with non-coherent non-laser light. This is due to the fact that laser light is monochromatic with a bandwidth of 1 nm or less, and it is very difficult to generate light from any other source (even an LED) that has a bandwidth narrower than 10-20 nm, therefore it will be uncertain if observed differences are due to coher-

ent versus non-coherent light, or due to monochromatic versus narrow bandwidth light.

By the turn of the century cytokine and adipokine research had amassed compelling results in the effect of cytokines in a wide array of diseases and cellular function to give reason to investigate effects of light and laser on cytokines. There is no dearth of reports measuring circulating cytokines and their association with disease severity.

Several adipokines, such as IL-1α and TNFα, are already known for their pro-inflammatory role in the atherosclerotic processes. Among many substances, Leptin, although initially described as a naturally occurring suppressor of appetite, has been found to function primarily as a mediator of cytokine-induced inflammation and immune functions. Adiponectin is an anti-inflammatory adipokine inhibiting macrophage functions. Resistin increases insulin resistance in muscle and liver tissue but also induces chemokines and vascular adhesion molecules.

In 1993 Funk [52] showed that He-Ne laser irradiation decreased concentrations of interleukin-1 alpha (IL-1 alpha), tumor necrosis factor-alpha (TNF-alpha), interleukin-2 (IL-2), and interferon-gamma (IFN-gamma) in supernatants of cultures of human peripheral blood mononuclear cells (PBMC) with increased cytokine concentrations after irradiation of 18.9 J/cm^2 and decreased concentrations after irradiation of 37.8 J/cm^2. 1997 Schwartz [53] showed the effect of low-energy laser irradiation on cytokine secretion from skeletal muscle cells and the involvement of calcium in the process (Fig. 7). He argued that the transient increase in calcium permeability regulated cytokine release. Inoue and Ishimura showed in 2001 that low-power ND-YAG laser irradiation of synovial fluids decreased IL-1 and TNF-alpha levels without seeing any effect in calcium permeability. This demonstrated that different mechanisms regulate cytokine release under varying conditions.

It has now become quite clear that the effect of light cannot be attributed to any single mechanism or parameter. Even by examining the varying effects of cytokines alone it has become evident that in order to understand the possible effects of light and laser in the organism it is vital to understand the complex cellular mechanism and the biochemical effects ofeven small changes in cell metabolism, cell-membrane potential, and the thousands of chemicals, molecules, proteins or transmitters which are affected by changes in the cell environment and in turn causing further changes in cell and tissue function.

Throughout the 1980's and 1990's our own laser research was mainly clinical concentrating on diabetes, neurological diseases and thyroid diseases. At the turn of the century results in diabetes treatments gave reason to believe that low-level-laser treatment had diverse systemic effects, including tissue regeneration by stem cell regulation. Type 1 diabetics who had extensive damage to their pancreas, developed to a stage where they could manage for several months without external insulin. This result can not be explained by decrease of insulin resistance alone, since both insulin levels and C-peptide levels normalized. This brought about the studies on stem cell activation and homing. 2000 and 2004 Gasparyan, Brill and Mäkelä [55] (Fig. 8) published in vitro results on the influence of low-level laser radiation on migration of stem cells. Results showed that laser light irradiation could activate stem cell migration in vitro. The results were more reliable in the case of combined application of light and SDF-1α. The results gave ground to consider that stem cell reactions to light irradiation can be one of the key factors of light therapy. Studies continued on to test if the laser light irradiation in vivo was able to make homing of transplanted stem cells to the area of damage more efficient, to check the influence of laser light on the mobilization rate of stem cells from bone marrow and to investigate if laser light can enhance functional abilities of stem cells. At this point several research groups began their studies on the effect of laser light on different aspects of stem cell activation, homing and proliferation in different cell cultures, and later in vivo. 2009 Trimmer et al [56] published their results on the neuroprotective effect or transcranial laser irradiation, repeating experimentally on rats, procedures that had been carried out clinically by Kaplan in 2000 and presented by Kaplan and Mäkelä in 2006 in Laser Florence [57] (Fig. 9).

The apparent neuroprotective effect of near-infrared light applied transcranially gave reason to continue further studies of application of lasers in neurology. Electrolaser acupuncture had been used extensively since the mid 1980's in the treatment of Parkinson's, Alzheimer's, MS, ALS and Huntington's disease with good results. Clinical results led to the studies on the effect of different wavelengths on neurone growth and recovery, showing that in autoimmune neurological diseases 405-458 nm were especially effective in neurological recovery. Several substrates were found to be involved, among them the amino acid arginine, heparansulphateagrin, Vitamin D, calcium regulating mechanisms, and several hormones, including prolactin. By this time 1265 neurological patients had been treated by this method consisting of 220 patients with multiple sclerosis, 164 with amyotrophic lateral sclerosis, 420 with neuropathy, 672 with neuralgia, 186 with Alzheimer, 370 with infarct/hemiplegia, 220 with

Parkinson's, 5 with Huntington's and 81 accidental paraplegic/quadriplegic patients [58].

One feature common autoimmune neurological diseases is insulin-degrading enzyme (IDE) which is a Zn^{2+}-metalloprotease. It is involved in the clearance of insulin and amyloid-beta. Loss-of-function mutations of IDE in rodents cause glucose intolerance and cerebral accumulation of amyloid-beta, whereas enhanced IDE activity effectively reduces brain amyloid-beta. Two substrates of IDE, amyloid beta-protein A{beta} and insulin, are critically important in the pathogenesis of Alzheimer's Dementia, Parkinson's disease and type 2 diabetes mellitus, respectively. Insulin degrading enzyme (IDE) is expressed in the brain and may play an important role there in the degradation of the amyloid beta peptide A{beta} [59]. A{beta} has been shown to decrease PI3 kinase activity, which would decrease IDE levels and in turn increase A{beta} levels, thus creating a vicious cycle. Therefore, stimulating the insulin signalling and increasing PI3 kinase activity would break this cycle and reduce the accumulation of A{beta}.

Shen et al [60] report structures of human IDE in complex with four substrates (insulin B chain, amyloid-beta peptide (1–40), amylin and glucagon). The amino- and carboxy-terminal domains of IDE (IDE-N and IDE-C, respectively) form an enclosed cage just large enough to encapsulate insulin. Extensive contacts between IDE-N and IDE-C keep the degradation chamber of IDE inaccessible to substrates. Repositioning of the IDE domains enables substrate access to the catalytic cavity. IDE uses size and charge distribution of the substrate-binding cavity selectively to entrap structurally diverse polypeptides. The enclosed substrate undergoes conformational changes to form beta-sheets with two discrete regions of IDE for its degradation.

Kleifeld et al [61] and Auld [62] have shown that zinc metalloproteinase has several absorption maxima, not only in the far infrared also in the visible areas of red, near infrared and blue.

It is possible that due to deficiency of IDE, glucose-induced dysregulation of the p35/CDK5 pathway is a pathophysiological mechanism involved in the ß-cell dysfunction and the predisposition to apoptotic cell death associated with the progression of type 2 diabetes. The correction of this dysregulation by the use of light of specific wavelengths can also halt or reverse the progress of the disease as is seen in the clinical results.

Another important neural growth regulator is Agrin, a heparansulphate. Release of Agrin is required for the maintenance of normal function of neurons and muscle cells. Agrin plays a key role in synaptic differentiation (Fig. 10). Agrin also induces acetylcholine receptor phosphorylation and mediates acetylcholine receptor clustering by interacting with muscle-bound heparin-binding growth factors such as HB-GAM.

Significant increases in total Agrin mRNA are observed upon treatment with NGF. NGF induces the production of transcripts encoding isoforms with high aggregating activity and neuronal tissue distribution and together with calcium ion potentiates the effects of agrin.

Expression of NGF is positively influenced by Glutamate mediated neuronal activity, Vitamin D3, Phorbol 12-myristate- 13- acetate, TNF-alpha, PDGF (Platelet derived growth factor), TGF-Beta (Transforming growth factor), Interleukin 1 and Interleukin 6 which all have been found to be regulated by varying doses of light.

Some of the main regulating mechanisms in neural function and growth are Agrin, IDE and CDK5 and the release and functional changes in them by light may explain these variable results in previous laser experiments.

Many studies have shown that cytochrome b561 shows intrinsic tissuespecific expression. This has led to the hypothesis that cytochrome b561 would be a basic feature of all peptidergic and adrenergic tissues. In mammals other than humans, immunological studies have shown that it is present in splenic-nerve terminals and posterior and anterior hypophysis [63]; in many areas of the brain (64); in blood vessels, retina, enteric-nerve fibres, and atrial heart [65]; and in thyroid parafollicular cells [66].

Cytochrome b561 has specific activation and absorption spectra at wavelengths between 556- 570 nm with highest peak at 561 nm. This, considering the various actions of cytochrome b561 would give biochemical support to the clinical results on the immunological and neurological effects of light in the green spectra.

Several researchers have found laser light to strongly regulate the release of PDGF, EGF, FGF and TGF. Even though these have been studied in consideration of wound healing, it is known that they are also regulators of oligodendrocyte function. Earlier consideration of the neurological effects of transcranial laser irradiation being mainly due to changes in circulation and oxygen delivery could now be reconsidered.

Oligodendroglia arise during development from oligodendrocyte precursor cells, which can be identified by their expression of a number of antigens, including the ganglioside GD3, the NG2 chondroitin sulfate proteoglycan, and the platelet-derived growth factor-alpha receptor subunit PDGF-alphaR.

In the presence of epidermal growth factor (EGF)

and/or fibroblast growth factor (FGF), cultured subventricular zone SVZ progenitors self-renew and upon removal of growth factors can generate neurons, astrocytes, and oligodendrocytes [67]. In vivo, epidermal growth factor (EGF), fibroblast growth factor (FGF2), or TGFα infusions result in a dramatic enlargement of the subventricular zone (SVZ) and increased migration of progenitor cells into the surrounding brain parenchyma [68]. Hou et al [69] showed the modulatory effect of low level 635 nm diode laser light on endothelial growth factor (VEGF) and nerve growth factor (NGF). 0.5 J/cm^2 was found to be an optimal energy density [69]. Safavi et al [70] studied the effect of He-Ne laser (632.8 nm) on Interleukin 1 (IL-1), tumor necrotic factor-alpha (TNF-alpha), and interferon-gamma (IFN-gamma), platelet-derived growth factor (PDGF), transforming growth factor-beta, (TGF-beta) and blood-derived fibroblast growth factor (bFGF). (Fig. 11) Several studies have concentrated on direct irradiation of the regenerating nerve. Taking into consideration, however, all these above mentioned studies, it became quite obvious that systemic irradiation would have greater effect on the total regenerative properties of laser and light on neurological trauma as well as autoimmune neurological diseases. Taking into consideration the various biochemical and physiological changes occurring in autoimmune neurological diseases, lasers and light can be utilized in various ways to deter progress of disease and to augment general condition and functional capability of patient.

Looking back on low-level laser therapy research there has been a clear division of physicists studying the laser itself and some specific cellular function in vitro, photobiologists studying cellular and molecular effects, medical doctors studying clinical effects. For low-level laser use to develop further in the future with better understanding, research needs to combine all these fields with a thorough understanding of the biochemistry and genetics of the living cell and future studies need to utilize research methods, which can recognize systemic effects.

Future will also hopefully incorporate laser and light more in combined use with medications or nutritive therapy regulating immuno-endocrinological functions, preventive medicine, and further development of homecare units for diabetics, autoimmune neurologic patients, trauma rehabilitation and first aid.

For low-level laser therapy to be thoroughly accepted in general medicine, it is unfortunately necessary to change the way of thinking of the medical field. Laser and light have such a widely varying systemic effect that the doctor must be prepared to delve deep into the medical problem of the patient and be able to evaluate the condition and need for repair at cellular function level.

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ЛАЗЕРЫ В ИССЛЕДОВАНИЯХ И ТЕРАПИИ: ОТКРЫТИЯ НА ПРОТЯЖЕНИИ МНОГИХ ЛЕТ

Ану Макела

В работах по исследованию эффектов низкоинтенсивного лазерного облучения прослеживается четкое разделение интересов физиков, изучающих воздействие лазерного света на некоторые клеточные функции in vitro, фотобиологов, изучающих клеточные и молекулярные эффекты лазерного облучения, и врачей, изучающих клинические эффекты лазерной терапии. Различные исследователи выявили разнообразные эффекты лазерного воздействия, включая положительные эффекты, отрицательные эффекты (цитотоксические, мутагенные, канцерогенные, пролиферативные эффекты), а также отсутствие каких-либо специфических эффектов лазерного воздействия. Это в большой степени связано с тем фактом, что значительная часть исследований была проведена в клиниках с ограниченными ресурсами, из-за чего проведение испытаний с применением двойного слепого контроля было практически невозможно.

Исследование клеточных эффектов лазера и света становится популярной тематикой после появления усовершенствованного и более дешёвого оборудования. Обнадеживающие клинические результаты способствовали проведению исследований на клеточном и молекулярном уровне. В данной работе сделана попытка представить хронологический обзор некоторых значительных исследований по применению низкоинтенсивных лазеров и света в лечении различных патологий, и, особенно, при лечении неврологических заболеваний.

Ключевые слова: *низкоинтенсивное лазерное излучение, исследования, терапия, неврологические заболевания, обзор.*

ЛАЗЕРИ У ДОСЛІДЖЕННЯХ ТА ТЕРАПІЇ: ВІДКРИТТЯ ПРОТЯГОМ БАГАТЬОХ РОКІВ

Ану Макела

У роботах з дослідження ефектів низькоінтенсивного лазерного опромінення простежується чіткий поділ інтересів фізиків, що вивчають вплив лазерного світла на деякі клітинні функції in vitro, фотобіологів, що вивчають клітинні та молекулярні ефекти лазерного опромінення і лікарів, які вивчають клінічні ефекти лазерної терапії. Різні дослідники виявили різноманітні ефекти лазерної дії, включаючи позитивні ефекти, негативні ефекти (цитотоксичні, мутагенні, канцерогенні, проліферативні ефекти), а також відсутність будь-яких специфічних ефектів лазерної дії . Це у великій мірі пов'язано з тим фактом, що значна частина досліджень була проведена в клініках з обмеженими ресурсами, через що проведення випробувань із застосуванням подвійного сліпого контролю було практично неможливо.

Дослідження клітинних ефектів лазера і світла стає популярною тематикою після появи вдосконаленого і більш дешевого обладнання. Обнадійливі клінічні результати сприяли проведенню досліджень на клітинному і молекулярному рівнях. У даній роботі зроблена спроба представити хронологічний огляд деяких значних досліджень щодо застосування низькоінтенсивних лазерів і світла в лікуванні різних патологій, і, особливо, при лікуванні неврологічних захворювань.

Ключові слова: *низькоінтенсивне лазерне випромінювання, дослідження, терапія, неврологічні захворювання, огляд.*