

BIOMEDICAL APPLICATIONS OF EXIMER LASERS

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ABSTRACT

The use of lasers in medicine and biology has demonstrated its interest through innovative advanced technologies such as laser microdissection and /or photoablation which at different levels of expression enable understanding of the physiological mechanisms in the evolution of a disease. Lasers have achieved a prominent position in medical application and offer unique advantages for medical diagnosis, therapeutic treatments and internal surgeries in most medical disciplines including dermatology, dentistry, neurosurgery, eye surgery, cancer surgery, urology, gastroenterology etc. because of their ability to deliver high precision treatments, whilst remaining minimally invasive. Thus Laser-based therapies and diagnostic methods represent an area of huge future potential. Research efforts and continuous improvements over recent years have resulted in excimer lasers becoming the tool of choice for many applications in medical sciences. Excimer lasers, which are pulsed gas lasers operating with a special mixture of noble gases and halogens, emit laser radiation in the UV and VUV spectra, at discrete wavelengths between 351 nm and 157 nm, have shown promise in dermatology, angioplasty, biliary laser lithotripsy, ophthalmology and orthopedics. The principal advantage of excimer lasers is that they are capable of producing a very small, precise spot at a very low (UV) wavelength. Excimer lasers are excellent for removing excess material through laser ablation due to the fact that they are able to precisely destroy material with little to no thermal buildup. In the present review, applications of excimer lasers in biomedical sciences particularly in dermatology, ophthalmology, angioplasty, orthopaedics, lithotripsy, dentistry, medical implants have been presented and recent studies carried out have been reviewed. Laser-associated micro dissection offers a rapid, precise method of isolating and removing targeted cells or groups of cells from complex biological tissues which may be helpful in understanding physiological mechanisms on the level of a specific cell population and even on the level of the single cell in disease conditions. Multidisciplinary research studies on the interaction of laser with biological tissue at molecular level using biotechnological tools will enhance the therapeutic potential of laser technology in diagnosis and treatment of chronic complex diseases especially cancer, genetic disorders, neurodegenerative disorders, multidrug resistance tuberculosis, autoimmune diseases, HIV etc. and it may also be useful in designing new and innovative strategies in drug delivery and image-guided surgery.

Keywords: Excimer Lasers, Laser-tissue Interaction, Bio-medical Applications: Dermatology, Ophthalmology, Angioplasty, Lithotripsy, Orthopaedics, Dentistry, Biomedical Implants/ Materials/ Devices

INTRODUCTION

Laser : Light Amplified Stimulated Emission Radiation, unlike a standard light beam, is a source of monochromatic, coherent and unidirectional light. Over the past 50 years, scientific research and innovations made revolution in laser and led to the development

of many new varieties of laser becoming an integral part of human life with multiple numerous applications from medicine to manufacturing, from communication to measurement and from research and analysis to entertainment. The first working laser was demonstrated on 16 May 1960 by Theodore Maiman at Hughes Research Laboratory. Since

then the laser was being applied in medical procedure. In December 1961, a ruby laser was used to destroy an eye tumour at Columbia Presbyterian Hospital. Today lasers have achieved a prominent position in medical application and offer unique advantages for medical diagnosis, therapeutic treatments and internal surgeries in most medical disciplines including dermatology, dentistry, neurosurgery, eye surgery, cancer surgery, urology, gastroenterology etc. because of their ability to deliver high precision treatments, whilst remaining minimally invasive. Thus Laser-based therapies and diagnostic methods represent an area of huge future potential. Different types of laser like Nd:YAG laser, CO₂ laser, KTP laser, Ho: YAG laser, diode lasers, excimer lasers etc. are currently being used for various medical applications. In the present review, different applications of excimer lasers in various disciplines of medical sciences have been addressed. The main medical application is the use of excimer lasers at 193 nm in ophthalmology for vision-correction systems. A total of about 10,000 lasers are currently operating worldwide. The theoretical basis for the laser was established in 1917, when Einstein postulated the theoretical concept of stimulated emission.^[1] The first excimer laser was built in 1971 by Basow, 54 years later.^[2]

Excimer lasers are pulsed gas lasers operating with a special mixture of noble gases and Halogens. They emit laser radiation in the UV and VUV spectra, at discrete wavelengths between 351 nm and 157 nm. The most commonly used excimer lasers are krypton fluoride (KrF, 248 nm), argon fluoride (ArF, 193 nm), xenon chloride (XeCl, 308 nm), xenon fluoride (XeF, 351 nm). Research efforts and continuous improvements over recent years have resulted in excimer lasers becoming the tool of choice for many applications in medical sciences. Excimer lasers have shown promise in angioplasty, biliary laser lithotripsy, ophthalmology and orthopedics. It is heartening to emphasize that the first laser eye surgery using an excimer laser was performed in 1987, by ophthalmologist Steven Trokel. Today millions undergo eye surgery every year which is a path breaking achievement in eye surgery. Another medical application where excimer

lasers are being used is dermatology for treating a variety of dermatological conditions including psoriasis, vitiligo, atopic dermatitis, alopecia areata and leukoderma.

EXCIMER LASER AND LASER – TISSUE INTERACTION

The term “excimer” is a shortened form of “excited dimer”, which describes a molecule formed from two identical noble gas atoms. These atoms will only bond with each other in an excited state. The term “excimer” was later expanded to include all combinations of rare gases and halides. Therefore, in laser physics, all rare-gas halides and similar molecules are excimers, which are not really dimers. Nowadays excimer lasers are the dominant UV source in many applications. Using an excimer laser is the easiest way to generate photons in the deep ultraviolet. Although it is possible to generate radiation below 350 nm with solid-state lasers using non-linear optical effects, tremendous effort is involved in this process. A frequency-tripled Nd-YAG laser, for example, emits at 355 nm, but to generate photons in the deeper UV the processes become more and more inefficient. If output power is needed, solid-state lasers are definitely no match for excimer lasers. Due to their complex technology, the first excimer lasers were very sensitive devices. However, this has changed dramatically. As a result of effective improvement over the last 15 years, excimer lasers have now become fully competitive with other commercially used laser systems. Excimer lasers are pulsed gas lasers operating with a special mixture of noble gases and halogens. They emit laser radiation in the UV and VUV spectra, at discrete wavelengths between 351 nm and 157 nm. Continuous improvements over recent years have resulted in excimer lasers becoming the tool of choice for many applications. The excimer lasers produce ultraviolet light which due to its short wavelength allows for high-precision imaging. Different excimer laser transitions have been used to generate light pulses at various wavelengths between 126 nm and about 660 nm. The most commonly used excimer lasers are krypton fluoride (KrF, 248 nm), argon fluoride (ArF, 193 nm), xenon chloride (XeCl, 308 nm), xenon fluoride (XeF, 351 nm). Laser action in an excimer molecule

occurs because it has a bound excited state, but a repulsive ground state which is due to the fact that noble gases like xenon (Xe) and krypton (Kr) do not usually form compound. These noble gases in excited state can form temporarily bound molecules with themselves or with halogens like fluorine and chlorine. This bound state is the upper laser level in the case of excimer laser level. The excited compound can give up its excess energy by undergoing spontaneous or stimulated emission, resulting in a strongly repulsive ground state molecule which very quickly dissociates back into two unbound atoms. Since the excimer molecule returns to the unexcited ground state and separates into atoms, the population inversion condition is achieved the moment excited state is created, since the population of ground level is nil.

Excimer lasers are powerful ultraviolet lasers which use a mixture of noble gases and halogens as a gain medium. All lasers consist of three components: a pump (energy source), a gain (or laser) medium, and an optical resonator. The pump provides energy which is amplified by the gain medium. This energy is eventually converted into light and is reflected through the optical resonator which then emits the final output beam.

Like most gas lasers, excimer laser power is provided by an electrical current source. The laser medium is a tube filled with three different types of gases:

- A noble gas (argon, krypton, or xenon)
- A halogen gas (fluorine, chlorine, or bromine)
- A buffer gas (typically neon or helium)

Excimer lasers rely on the interaction between the noble gas and the halogen gas to produce a high-powered beam. The current source pumps the gas medium using very short, high voltage pulses transmitted through metal electrodes; the pulse excites the gas atoms and causes them to fuse together into atomic pairs called dimers. For example, pumping an argon fluoride (ArF) laser causes asymmetric molecules of ArF to form. Excimers only remain bound in an excited state, so that following the pulsed electrical discharge the atoms separate once

again. While active, though, the excimers emit a burst of electromagnetic radiation before quickly dissociating into separate gases. This rapid dissociation prevents molecular reabsorption of the emitted radiation, making it possible to achieve high gain using a relatively small concentration of excimers. The radiation is then reflected by mirrors placed at both ends of the gas tube (representing the optical resonator) until the beam is emitted via the front mirror.

Laser actions are governed according to the discovery of Einstein that light does not consist of continuous waves or small particles but it exists as bundles of wave energy called photons.^[3]

The type of interaction of laser with tissue that occurs depends on various factors such as the properties of laser system (wavelength, energy pulsed / continuous mode of emission), local blood circulation, the optical properties of the tissues, and the immune response of the patient.^[4,5] Further such type of interaction involves different effects like photo thermal effect, mechanical effect, photo chemical effect, tissue-welding effect. The understanding of interaction of laser with tissue involving different components viz protein, water, fat, melanin, hemoglobin etc. has led to numerous medical applications. Laser-tissue interaction involves scattering, absorption, heat generation and such properties could be harnessed for different applications. Time of interaction of the laser beam and intensity of the beam play critical role in defining the application of laser in humans subjects. These parameters need to be selected accordingly for a given purpose. The scattering properties of tissue could themselves be of diagnostic interest. Many spectrometric techniques like Laser Doppler Perfusion, Optical Coherence Tomography, Raman Scattering Spectroscopy etc. are based on scattering and have played significant role in designing the laser of diagnostic purpose. In excimer laser ablation, which involves ultraviolet laser action based on a medium of noble gas halides, the mechanism of tissue cutting by the 193 nm excimer laser is non-thermal and involves direct breakage of covalent bonds. Another characteristic of ultraviolet radiation is its high tissue absorption coefficient leading to shallow

penetration independent of water content. The combination of pulsed delivery, limited tissue penetration and non-thermal mechanism of tissue interaction seems to be ideally suited to extremely precise layer by layer ablation and make excimer lasers with diverse medical applications.

BIOMEDICAL APPLICATIONS

The effective utilization of lasers in medical sciences arises in many situations due to the unique aspects of laser light. The advantageous characteristic of lasers is due the ability to deliver high energy at precise wavelengths to minimize invasive damage. The technology of optical fibers facilitates precise delivery of very high energy to small regions of the tissues. Absorption of light by the target tissue and the depth of penetration are both wavelength dependant and thus several kinds of lasers have been developed for medical and therapeutic applications. The various kinds of lasers commonly used in many medical applications are CO₂ lasers, Argon ion lasers, Nd: YAG lasers, KTP-532 lasers, Pulse-dye lasers, Alexanderite lasers,

Ho: YAG lasers, Er: YAG lasers, Diode lasers, Excimer lasers. The largest application of Excimer lasers for medical use is in refractive laser surgery. As an ophthalmological tool, excimer laser has been widely used for photoablation process. The precision of excimer laser and, more important, the lack of damage to surrounding tissue, are instrumental for correction of refractive errors or optical problems of the eye, including nearsightedness, farsightedness, and astigmatism. Excimer laser light is typically absorbed in less than a nanometer of tissue. By means of intense excimer pulses, the surface of the human cornea is reshaped to change its refractive power and thus to correct for short or long sightedness.

Another medical application where excimer lasers are being used is dermatology for treating a variety of dermatological conditions including psoriasis, vitiligo, atopic dermatitis, alopecia areata and leukoderma. The biomedical applications of excimer lasers in various disease conditions are discussed below.

Dermatology

The use of excimer laser in dermatology has been considered more effective as compared to conventional phototherapy and photochemotherapy because of the lower cumulative UV-dose involved, the shorter time frame required for treatment and the option of targeting individual lesions without affecting the surrounding healthy skin. Grema and Raulin have reviewed the application of excimer laser in various skin diseases such as psoriasis vulgaris, vitiligo and atopic eczema and it has been found very useful in these skin diseases. The excimer laser has also been found effective in case studies ranging from post-operative hypopigmentation to acne vulgaris and from alopecia areata to parapsoriasis en plaque.^[6] UVB phototherapy has been found effective for the treatment of psoriasis. It has been observed that for patients with localized plaque-type lesions, 308-nm excimer laser phototherapy offers rapidly delivered, targeted, high UVB doses, while sparing adjacent healthy skin. Studies have been conducted to compare the advantages and disadvantages of the 308-nm xenon chloride (XeCl) UVB excimer laser with non targeted broadband UVB (BB-UVB), narrowband UVB (NB-UVB), and psoralen plus UVA (PUVA) phototherapies and it has been proposed that excimer laser exclusively treats diseased skin with better response rates, split-body trials revealed no differences.^[7] Narrowband UVB (311 nm) phototherapy is a well-established, widely used and highly efficient treatment for psoriasis which is a chronic, genetically determined inflammatory disease, characterized by an immunomediated pathogenesis, but a big disadvantage of this therapy is that large areas of unaffected skin are also irradiated along with the psoriatic lesions. Keeping in view of this disadvantage studies have been conducted to evaluate a 308-nm excimer laser and a 308-nm excimer lamp in comparison with 311-nm narrowband UVB in the treatment of patch psoriasis by using two different dose-increase schemes and the results of the study revealed that both 308-nm light sources can clear patch psoriasis in a similar manner to standard phototherapy, with the advantage of the ability to treat exclusively the affected skin and with a reduced cumulative dose, thus perhaps

reducing the long-term risk of carcinogenicity.^[8]

Recently Mehraban and Feily have reviewed the efficacy of 308nm xenon-chloride excimer laser in treatment of dermatological disorders and found that 308-nm excimer laser has currently a verified efficacy in treating skin conditions such as vitiligo, psoriasis, atopic dermatitis, alopecia areata, allergic rhinitis, folliculitis, granuloma annulare, lichen planus, mycosis fungoides, palmoplantar pustulosis, pityriasis alba, CD30+ lympho proliferative disorder, leukoderma, prurigo nodularis, localized scleroderma and genital lichen sclerosis.^[9]

Park et al has reviewed the application of monochromatic excimer light (MEL) in dermatology which has been found effective for the treatment of vitiligo. The specific 308-nm radiation wavelength is delivered in a targeted form by the xenon-chloride excimer laser and is also available in an incoherent form that is commonly referred to as the excimer lamp. MEL administered by both laser and lamp has shown efficacy superior to NB-UVB for the treatment of vitiligo and induces more changes at the cellular level than conventional UVB modalities. The excimer laser has been found effective in adults and children with vitiligo in all skin types as monotherapy or in combination with other established vitiligo therapeutics.^[10] Studies have been conducted to analyze the efficacy of the 308 nm excimer light in psoriasis, palmoplantar pustulosis, vitiligo, mycosis fungoides and alopecia areata and to examine potential new indications in patients and the results of the study confirm the use of monochromatic excimer light as a valid choice for the treatment of psoriasis, vitiligo, and mycosis fungoides and it has also been observed that monochromatic excimer light produces a therapeutic response in prurigo nodularis, localized scleroderma, genital lichen sclerosis, and granuloma annulare on the assessment of clinical response using photos, biopsies and specific clinical scores.^[11] John et al studied the response of 308nm Excimer Laser to facial Vitiligo and the results of the study revealed encouraging response in the treatment of male patients with Fitzpatrick skin types IV to VI undergoing combination treatment utilizing excimer laser with

calcipotriene.^[12] It is interesting to note that the 308nm excimer laser is a newer treatment option that can yield impressive results in an abbreviated time frame.^[10] Nicolaidou et al^[10] reviewed the use of excimer laser and demonstrated that 15 to 50 percent of patients achieved greater than 75-percent repigmentation. Notably, excimer laser treatment periods were 15 weeks or less in the overwhelming majority of the studies analyzed.^[10] Additionally, there has been some evidence that excimer laser treatment causes faster, more complete repigmentation in patients with higher Fitzpatrick skin types.^[13,14,15] Passeron et al has conducted the studies to compare the efficacy of combined tacrolimus and 308-nm excimer laser therapy vs 308-nm excimer laser monotherapy in treating vitiligo and the studies revealed that the combination treatment of 0.1% tacrolimus ointment plus the 308-nm excimer laser is superior to 308-nm excimer laser monotherapy for the treatment of UV-resistant vitiliginous lesions. Further the results of the study also confirm the efficacy and the good tolerance of the 308-nm excimer laser in monotherapy for treating localized vitiligo but this treatment regimen should be proposed only for UV-sensitive areas.^[16] A prospective clinical study has been conducted in patients with vitiliginous patches to investigate the clinical efficacy, safety, and psychosocial impact after treating vitiligo with the 308-nm excimer laser and the results of the study indicate that the treatment of vitiligo using the 308-nm excimer laser is effective and safe and improves psychosocial quality of life. It has also been observed that lesion location, duration of disease, and treatment duration are factors affecting the clinical and psychological outcome.^[17] Hofer et al has conducted the study to determine the optimal frequency of 308-nm excimer laser therapy for vitiligo and observed that 308-nm excimer laser therapy is effective against vitiligo. Although repigmentation occurs fastest with 3x weekly treatment, the ultimate repigmentation initiation seems to depend entirely on the total number of treatments, not their frequency. On the basis of the results of the study it has also been argued that treatment periods of more than 12 weeks may be necessary to obtain a satisfactory clinical repigmentation, particularly when vitiligo lesions

are treated only 1x or 2x compared with 3x weekly.^[18] Alhawaish et al has reviewed the effectiveness of 380-nm excimer laser in the treatment of vitiligo based on the available studies and case series and found that the excimer laser most likely constitutes the treatment of choice for localized vitiligo as compared to other treatment modalities and its efficacy can be further improved in combination with other therapies such as corticosteroids, pimecrolimus, or tacrolimus.^[19] Bronfenbrenner et al has studied the efficacy of 308nm excimer laser in treatment of Granuloma Annulare Granuloma annulare (GA) which is a relatively common disorder with a female predominance that usually presents as 1 to 5cm skin-colored or erythematous annular plaques with peripheral papules and a 73-year-old woman with a long-standing history of GA presented to the dermatology clinic complaining of gradual worsening of her condition was treated with the excimer laser and this case of generalized GA treated with the excimer laser resulted in resolution of lesions that had been refractory to other therapies.^[20]

Goldinger et al in their study indicated that monochromatic phototherapies such as 311-nm narrowband ultraviolet B therapy and 308-nm xenon chloride excimer laser have been found an effective and safe therapeutic option in children and adult patients with vitiligo and the addition of topically applied calcipotriol to phototherapy may increase its effectiveness. The results of the study showed that the addition of calcipotriol ointment to 308-nm xenon chloride excimer laser phototherapy does not significantly enhance its efficacy and small additive effects must be investigated in a larger trial.^[21] Low dose excimer 308 nm laser has been studied for its effectiveness in treatment of lichen planopilaris (LPP) which is a difficult to treat, chronic, inflammatory autoimmune disease targeting the hair follicle that eventually leads to permanent irreversible scarring alopecia and commonly affects adult women on the central scalp with multifocal patches, perifollicular erythema, hyperkeratosis, and subjective complaints like pruritus or pain. The results of the study have shown that for chronic inflammation UV-B excimer laser treatment might also be effective in LPP, since it has proven

beneficial for certain inflammatory skin disorders that are mediated by lymphocytes and are responsive to psoralen plus UV-A therapy.^[22] Tejaswi et al reviewed the studies describing excimer laser treatment protocol with particular attention to dosage determination, dose adjustment, dose fluency, number of treatments, and maintenance with an aim to characterize treatment parameters for 308 nm excimer laser phototherapy and found that the 308 nm excimer laser is an effective therapy for psoriasis regardless of the method used to determine initial dosage, dose fluency, or number of treatments. As its usage as a targeted monotherapy increases, future trials should consider evaluating and modifying these parameters to determine the most optimal management of localized psoriasis. They have observed^[22] that there is no consensus for a single excimer laser therapy protocol and as a result, patient preferences should continue to be an important consideration for phototherapy regimen planning.^[23] Besides above studies, several other studies have been conducted to evaluate the therapeutic efficacy of 308 nm excimer laser in treatment of alopecia areata (AA) and psoriasis and it has been effective in the treatment of these skin disorders.^[24-32] It has been shown that 193 nm excimer laser irradiation has potential to cleanly and effectively ablate a vascular tissue with minimal thermal damage to surrounding adjacent structures and the 193 nm excimer laser has been used to remove guinea pig epidermis *in vivo*. The results of the study indicate that the epidermis can be totally ablated with thermal damage extending only superficially into the dermis and this technique may be applicable to the removal of benign epidermal lesions.^[33,97] Gattu et al has reviewed the studies of the 308-nm excimer laser in the treatment of psoriasis vulgaris, palmoplantar psoriasis, and psoriasis of the scalp. The XeCl excimer emits a 308-nm wavelength beam of light that is monochromatic and coherent which allow selectivity when used as phototherapy against a psoriatic lesion while sparing healthy surrounding tissue.^[34] Clinical studies have been conducted to evaluate the therapeutic efficacy and safety of a 308-nm excimer laser for the treatment of scalp and palmoplantar psoriasis and the results of the study revealed that the

308-nm excimer laser is an effective, safe, easy, and relatively quicker method for the treatment of psoriasis at difficult to treat sites, with good results in a somewhat short time.^[35] An open level pilot study has been conducted to assess the efficacy of combination therapy using 308-nm excimer laser, clobetasol propionate spray and calcitriol ointment for the treatment of moderate to severe generalized psoriasis and the results of the study revealed that excimer laser therapy combined with an optimized topical regimen that includes clobetasol spray followed by calcitriol ointment appears to be an effective treatment for moderate to severe generalized psoriasis that avoids the risk of serious internal side effects associated with many systemic agents.^[36] Han et al conducted studies to evaluate the efficacy and safety of 308-nm monochromatic excimer light (MEL) in the treatment of psoriasis vulgaris and palmoplantar psoriasis and found that the MEL therapy is well tolerated with a low incidence of side effects, which included pruritus, erythema and blister formation. The results of the study revealed that the 308-nm MEL can be utilized as an effective and safe treatment modality for patients with mild-to-moderate psoriasis vulgaris and palmoplantar psoriasis.^[37] Kawada has reviewed the efficacy of light sources targeted phototherapy which include broad-band UVB, narrow-band UVB, 308-nm excimer laser and light, 307-nm excimer light and 312-nm flat-type fluorescent lamp for the treatment of psoriasis.^[38] 308 nm excimer laser has been found effective for the treatment of Atopic dermatitis (AD) which is a chronic, inflammatory skin disease affecting 3% of adults and 20% of children.^[39]

Ophthalmology

Argon fluoride excimer lasers operating at a wavelength of 193 nm are being used extensively throughout the world for both photorefractive (PRK) and phototherapeutic (PTK) keratectomies. Study has been conducted to assess the visual outcome of excimer laser photorefractive keratectomy (LPK) and laser in situ keratomileusis (LASIK) for the correction of moderate and high myopia in where the LASIK technique included a nasally based, 150 microns thick, 8.0 x 9.0 mm diameter, truncated, disc-shaped corneal flap created with

a microkeratome and the ablation of the stroma with a 193-nanometer ArF excimer laser and the photorefractive keratectomy technique included mechanical removal of the epithelium and ablation of the stroma with a 193-nanometer ArF excimer laser. The results of the study revealed that LASIK was more effective than photorefractive keratectomy in higher myopes. It was also observed that LASIK created less corneal haze and the refraction was more stable with LASIK in the correction of high myopia and its predictability was found three times that of PRK.^[40] The argon fluoride excimer laser emits radiation in the far ultraviolet part of the electromagnetic spectrum (193 nm). Each photon has high individual energy. Research studies have shown that exposure of tissues with peak absorption around 193 nm results in removal of surface layers (photoablation) with extremely high precision and minimal damage to non-irradiated areas and this precision is confirmed in a series of experiments on cadaver eyes and the treatment of eyes with anterior corneal disease and found that multiple zone excimer laser superficial keratectomy is considered the treatment of choice for rough, painful corneal surfaces. Where good visual potential exists, ablation of a single axial zone is recommended and results in improved visual acuity and reduction of glare.^[41] In addition to above studies, several studies have been conducted to assess the effectiveness of excimer laser in surgery of cornea and correction of astigmatism and excimer laser has been found useful.^[42-51] Studies have been conducted to evaluate epithelial wound healing and visual outcome of excimer laser photorefractive keratectomy (PRK) performed on high myopic eyes with contact lens intolerance due to dry eye and the results of the study have revealed that PRK is effective for patients with high myopia and contact lense intolerance due to dry eye.^[52] Taylor et al conducted the studies to assess the safety and efficacy of excimer laser treatment of myopic astigmatism and to compare this with the excimer laser treatment of myopia where a VISX Twenty/Twenty excimer laser was used to perform either photo astigmatic refractive keratectomy or photorefractive keratectomy and the results of the study revealed that excimer laser surgery offers an

effective option in the treatment of myopic astigmatism.^[53]In another study a series of 122 eyes with band keratopathy was treated by excimer laser phototherapeutic keratectomy (PTK), with a mean follow up of over 12.3 months (range 3 to 60 months) which revealed that excimer laser PTK is a safe and effective outpatient treatment for band keratopathy.^[54]Laser intrastromal keratomileusis (LASIK) has been found an evolving technique enabling high degrees of myopia and myopic astigmatism to be corrected. Clinical studies have shown that for the correction of high myopia and myopic astigmatism, LASIK results in less postoperative pain and relatively little subepithelial haze compared with high myopic photorefractive keratectomy. Furthermore, a stable refraction and reasonably predictable outcome occurs much earlier and high myopia up to -37.0 D can also be corrected.^[55] In a comparative study of excimer laser ablation of the cornea and crystalline lens using 193 nm and 248 nm radiation, it has been found that threshold fluence for corneal and lens ablation was higher at 248 nm than at 193 nm, conforming that the excimer laser is effective in producing well controlled ablation of the crystalline lens *in vitro*, with effects parallel to those seen in the cornea.^[56]The 193 nm excimer laser has generated much interest as a rapidly developing new technology for the correction of refractive errors. Previously published reports have demonstrated the efficacy of excimer laser photorefractive and phototherapeutic keratectomy in the treatment of low myopia, high myopia, and corneal scars. Photorefractive keratectomy using the 193-nm excimer laser appears to be a safe, effective treatment for the reduction of low, moderate, and high myopia. The results are more predictable in low and moderate myopia, than in higher degrees of myopia.^[57-64]

Angioplasty

Excimer Laser Angioplasty has become now a days a powerful tool for treating heart disease. It has been found that other laser types are too hot for delicate coronary surgery and could damage tissue, cause blood vessel spasms, or create blood clots. The excimer is a 'cool' laser that uses ultraviolet light energy to operate at

65° C, a temperature human tissue can tolerate. Laser angioplasty is a procedure where a thin fiber-optic catheter is inserted into an artery in the leg and threaded to a blockage in a coronary artery. A tiny optical assembly diffuses the laser strand into a small cone-shaped laser beam as it is emitted from the catheter. The non-thermal laser vaporizes blockages in the artery without damaging delicate tissue. The procedure can be performed in a non-surgical setting using a local anesthetic. The hospital stay is minimal, and there is less post-operative pain, discomfort, and risk to the patient. Developed by Advanced Interventional Systems, Inc., the Dwyer 200+ excimer laser angioplasty system vaporizes the buildup of fatty deposits - called plaque - in the arteries. It is safer than coronary bypass operations and offers wider utility than balloon angioplasty. In clinical trials the success rate in opening blocked coronary arteries was shown to be 85 percent, with fewer complications than in balloon angioplasty. In January 1992, the system received Food and Drug Administration approval for treatment of coronary disease. *Excimer laser-facilitated coronary angioplasty has been found clinically beneficial in treating heart disease as reported by many research workers. This technology has great use in tubular, diffuse, calcified, total, subtotal, and ostial lesions.* In addition to these advantages, the photoablative properties of excimer lasers result in precise atheroablation, including calcium, without harmful thermal injury.^[65-71]The studies conducted on the feasibility and safety of excimer laser angioplasty in selective patients with complicated acute myocardial infarction have revealed that application of excimer laser coronary angioplasty is feasible and safe in patients with acute myocardial infarction who either fail to respond to thrombolytics or have contraindications to these agents and intracoronary thrombus at the target lesion can be successfully dissolved with this wavelength laser energy without adverse effect on the procedure results.^[72]In a clinical multicentric trial study conducted to evaluate safety and efficacy of excimer laser angioplasty in patients with acute myocardial infarction (AMI) with thrombus-laden lesions, 95% device success, 97% angiographic success, and 91% overall procedural success rate were

recorded.^[73]Mintz et al studied the mechanisms of excimer laser coronary angioplasty (ELCA) in human coronary arteries *in vivo* selecting to treat 202 lesions in 190 patients and it was found that ELCA increased lumen CSA by both atheroablation and vessel expansion without calcium ablation and superficial fibrocalcific deposits developed a characteristic fragmented appearance which support both photoablation and forced vessel expansion as mechanisms of lumen enlargement and plaque dissection after ELCA.^[74]In a clinical study conducted to evaluate the efficacy and safety of percutaneous coronary excimer laser angioplasty in patients with coronary artery disease it has been observed that coronary excimer laser angioplasty for ablation of obstructive lesions is feasible and safe in patients with stable angina.^[75]

Lithotripsy

Weiqiang et al studied the use of a XeCl (308 nm) excimer laser in fragmentation of biliary stones and found that sixty biliary calculi pigment (n=40) and cholesterol (n=20) were fragmented *in vitro*. The results of the study indicate that the 308 nm excimer laser may be effective as a laser lithotripter with low threshold and good efficiency for biliary stone fragmentation.^[76] A study has been conducted where a long pulse XeCl excimer laser (200 ns) has been used to induce fragmentation of human urinary stone and artificial model during *in vitro* experiments and it has been found that total fragmentation was always successfully achieved, requiring a variable number of pulses (10-100) depending on the pulse energy and the hardness of the sample.^[77] Gundlach et al. conducted an *in vitro* study to evaluate the application of a laser beam for the fragmentation of salivary stones where optimal fragmentation was achieved using a pulsed excimer laser with a pulse width of 60 ns and a wave-length of 308 or 351 nm and a new "sialoendoscope" technique was developed. Laser lithotripsy of salivary stones with endoscopic monitoring represents a novel method that permits treatment on an outpatient basis under local anaesthesia.^[78]

Orthopaedics

Landsman et al has reviewed the applications of various kinds of lasers including

excimer lasers in podiatric and orthopedic surgery.^[79]The excimer lasers have been found very useful in orthopaedic surgery. It has been shown useful to provide forth edenucing of cartilage from bone due to its having an irradiation range approximately the same as cartilage's absorption pattern. This would allow for the ablation of cartilage with minute amounts of peripheral necrosis or structural change of the adjacent bone. The excimer laser has been found to be of great benefit compared with with the CO₂ and Nd-YAG lasers for fibrocartilage ablation.^[80-84] Glossop et al has reviewed clinical and laboratory experience with the 308 nm XeCl excimer laser in arthroscopy and found that this ultra violet laser is extremely proficient for debridement of degenerate articular cartilage and meniscus. Preliminary *in vitro* and *in vivo* studies were performed to investigate the character of laser-irradiated articular cartilage and to search for evidence of regeneration and the results of autoradiographic and histologic studies showed no evidence of cartilage regeneration.^[85] Beke et al has conducted studies to demonstrate high-resolution photocross-linking of biodegradable poly(propylene fumarate) (PPF) and diethyl fumarate (DEF) using UV excimer laser photocuring at 308 nm in a human osteosarcoma (HOS) cell line where cell adhesion and viability have been demonstrated showing that the produced scaffolds are suitable for assisting bone cell attachment and proliferation. Preliminary cell tests have proved that PPF : DEF scaffolds produced by excimer laser photocuring are biocompatible and are promising candidates to be applied in tissue engineering and regenerative medicine.^[86] An *in vivo* study has been conducted to see the effect of excimer laser (xenon chloride ultraviolet, 308-nm) irradiation on degenerate rabbit articular cartilage where adult rabbits with mechanically induced degenerative arthritis of one knee were used as experimental model and the results of the study revealed that in the laser-irradiated group initially there was macroscopic and microscopic smoothing of the fibrillated surface while in the control group there was no improvement in the macroscopic or microscopic appearance of the articular surface and by 6 weeks the surface had begun to show the

reappearance of fibrillation.^[87] Andreas has studied the application of various lasers including excimer lasers in orthopaedic surgery and found them clinically useful for meniscal cutting and ablation, lateral retinacular release, release of posttraumatic fibrosis, chondroplasty, synovectomy, debridement, labral tear ablation in a shoulder, subacromial decompression, rotator cuff debridement, tissue tightening (collagen shrinking), ankle impingement decompression and debridement, and percutaneous nucleotomy. The results of the study with laser tissue-photoagglutination and tissue welding may make it possible to repair torn meniscus by tissue welding with laser energy.^[88]

Dentistry

One of the milestones in technological advancements in dentistry is the use of lasers which have been found to provide more efficient, more comfortable and more predictable outcomes for the patient. Cutting in soft tissue, hard dental material ablation, caries removal and root canal therapy are only a few examples of dental laser uses. Excimer Lasers in dentistry are normally used for hard tissue ablation/ dental caries removal. Argon fluoride / Xenon fluoride lasers are used. They have a wave length from 193nm to 308nm. It has been shown that all the excimer lasers and especially the argon fluoride excimer laser at 193 nm are characterized by its nonthermal photoablation interaction with polymers^[89,90]. Pini et al studied the application of excimer lasers in dentistry for the treatment of dental root canals and the results of the study revealed that high-energy ultraviolet (UV) radiation emitted by an XeCl excimer laser (308 nm) and delivered through suitable optical fibers can be used to remove residual organic tissue from the canals.^[91] A study has been conducted to see the effect of ArF excimer laser on human enamel where human enamel surface was irradiated with ArF excimer laser and examined under light microscopy and scanning electron microscopy (SEM) and the influence of the laser irradiation was confined to the irradiated area only with no visible heat damage to the surroundings. The results of the study revealed that excimer laser may be applied in a controlled and defined manner for tooth enamel treatments in dentistry.^[92] Joseph et al

has studied the use of short pulse ArF excimer laser to ablation of dentin and enamel with emphasis on the effect of laser pulse repetition rates (PRR) and fluence levels on the efficiency of the ablation process and on the average thermal response of ablated surfaces. The results of the study showed that ablation of dentin was found to be considerably more efficient than the ablation of enamel and depends exponentially on the laser fluence and also tissue ablation rates were found to be comparable to or better than other nanosecond lasers and left smooth surfaces, free of thermal damage. With the application of short pulse ArF excimer laser the ablated surfaces appear to be very smooth, highly polished and glossy looking as if they were subjected to thermal melting.^[93]

Biomedical Implants/Materials / Devices

Laser surface texturing can be used to produce well defined micro-grooves on biomedical materials such as Ti-6Al-4V. Such micro-grooves can be optimized to improve the integration with surrounding tissue. Research studies have demonstrated that excimer lasers or large area masking techniques, grooves produced with Nd:YVO₄ has potential to exhibit improved roughness parameters and to reduce heat-affected zones. Further, processing parameters have also been established for the fabrication of micro-groove geometries on flat geometries having relevance to biomedical implants and devices.^[94] Studies conducted by Waugh and Lawrence^[95] to see the wettability and osteoblast cell response modulation through UV laser processing of nylon 6,6 have revealed that the laser-induced modifications have given rise to modulated osteoblast cell response in terms of cell proliferation and differentiation and laser surface treatment holds a large potential to be widely employed within regenerative medicine as laser surface treatment offers a unique means of varying biomimetic properties to determine generic parameters to predict cell responses.^[95] Segmented polyurethane (SPU) films with round micropores have been prepared and a quantitative assay method of endothelial cell (EC) migration through micropores of and growth on microprocessed SPU films as an *in vitro* model of transmural endothelialization in

open-cell-structured small-diameter vascular grafts has been developed using excimer laser which have great relevance in medicine and biology.^[96] A micropatterned microporous segmented polyurethane film (20×12 mm in size, 30 μm thick) with four regions was prepared by excimer laser microprocessing to provide an *in vivo* model of transmural tissue ingrowth in an open cell-structured scaffold specially designed for cardiovascular tissue engineering which has great clinical relevance in medicine.^[98]

Pyrenedecanoic acid and pyrene lecithin are optical probes well suited to investigate lipid bilayer membranes. The method is based on the determination of the formation of excited dimers or excimers. Applications of the excimer-forming probes have been reviewed and they have great relevance in biomedical research particularly in understanding phase separation phenomena and lipid-protein interactions in biological system.^[99]

A microprocessing method has been developed to prepare microporous polymer films by an excimer laser ablation technique, which may enable the fabrication of functional biomedical devices such as advanced artificial organs having relevance in medicine.^[100] The sheltered transfer and immobilization of rabbit anti-human antiserum immunoglobulin G (IgG) by matrix-assisted pulsed laser evaporation (MAPLE) have been studied and it has been found that IgG transfer and immobilization onto substrates are improved by addition of lipid to MAPLE solutions.^[101] Simulated body fluid (SBF) has been used as a screening method in determining the bioactivity of numerous biomaterials. Owing to insufficient surface properties of polymers it has been seen to be of great advantage to modify the surfaces of these materials to allow the polymer to become more biomimetic. Waugh and Lawrence has conducted the studies on the enhancement of biomimetic apatite coatings by means of KrF excimer laser surface treatment of nylon 6,6 and the results of the study suggest that through excimer laser surface treatment osteoblast cell adhesion and proliferation can be enhanced.^[102]

DISCUSSION

Lasers are concentrated beams of

electromagnetic radiation (light) travelling in a particular direction. The defining properties of laser light are that the light waves are coherent (all travelling in harmony with one another) and that they are usually of one wavelength, or colour. By harnessing these properties in a device that reflects light back and forth through a special material, it is possible to generate an amplified light source, or laser. Such light can be concentrated in time and space to create truly extreme conditions, or be used to provide exquisite imaging and analysis capability across a wide range of applications. The type of interaction of laser with tissue that occurs depends on various factors such as the properties of laser system (wavelength, energy pulsed / continuous mode of emission), local blood circulation, the optical properties of the tissues, and the immune response of the patient.^[4,5] Further such type of interaction involves different effects like photo thermal effect, mechanical effect, photo chemical effect, tissue-welding effect. The understanding of interaction of laser with tissue involving different components viz protein, water, fat, melanin, hemoglobin etc. has led to numerous medical applications. Laser-tissue interaction involves scattering, absorption, heat generation and such properties could be harnessed for different applications. Time of interaction of the laser beam and intensity of the beam play critical role in defining the application of laser in biomedical field. In the medical field, lasers are diagnostic and therapeutic instruments that offer a whole range of solutions. The laser which enables for greater surgical precision is less invasive and promotes healing time or cure. This technique is generally much less traumatic than traditional surgical techniques. The first use of lasers in medicine was to damage the retina to understand ocular injury due to accidental exposure.^[103] Since the first ruby laser, several devices have been improved placing ophthalmology at the forefront of medical specialties using this technology. The laser has also many applications in the field of biology. Researchers take the technology to its limits by playing on two main parameters, the short laser pulses-to the femtosecond, and energy beams. Since then, pulsed lasers have become increasingly popular for their ability to ablate

biological tissue. For patient diagnosis and experimental studies, biological tissue can be either analyzed under a microscope after immuno-histostaining or crushed for further molecular analysis. Laser-Assisted microdissection (LAM) provides a valuable link between these two approaches. It gives new insights into cellular mechanisms, genetic disorders, tumor biomarker identification patient-tailored therapy. The development of light-absorbing nanoparticles that are nontoxic to biological tissue has provided further potential for a more targeted delivery of heat with minimal damage to healthy tissue. At an appropriate wavelength, exposure of a nanoparticle to a laser can trigger a photothermal effect in the particle whereby electronic oscillations at the particle surface are converted to heat.^[104] The applications of laser technology in biology and medicine have been found great therapeutic potential in treatment of variety of disease conditions such as angiomas in children and infants; spider naevi, treatment of rosacea, psoriasis, aesthetic treatment of superficial veins of the skin, acne, rosacea, warts, birthmarks; ablation of hard dental tissues without the risk of micro- and macro-fractures, ablation of the epithelium on the non-pigmented skin of the eyelid in preparation for melanocyte transplantation in the treatment of segmental eyelid vitiligo, in the treatment of superficial pigmented lesions, pregnancy mask (melasma), dermatitis ocher, some pigmentation related to drugs, certain types of scarring or ulcers etc.^[105] The advantages of laser in ophthalmology have been well demonstrated particularly in the treatment of myopia and cataract where they enable patients with visual impairment to regain a clear vision and forget the stress of wearing glasses or contact lenses.^[106] In the field of dermatology, it has great potential in treatment of vascular lesions such as angiomas, telangiectasias, spider naevi, treatment of pigmented lesions (brown spots, naevus of ota, freckles) and tattoo or hair removal targeting the melanin stored in the hair follicles in order to destroy the hair matrix to enable permanent hair removal.^[107] Further, laser surgery has the advantage of reducing the risk of infection and it promotes healing. It is used in cosmetic surgery to erase cellulite and superficial wrinkles. Often less

invasive than conventional surgery, laser surgery is however not without risks.^[108] Lasers can also be used in dentistry (gum care and treatment of tooth decay) and phlebology (treatment of Varicose veins)).^[109,110] Lasers have achieved a prominent position in medical application and offer unique advantages for medical diagnosis, therapeutic treatments and internal surgeries in most medical disciplines including dermatology, dentistry, neurosurgery, eye surgery, cancer surgery, urology, gastroenterology etc. because of their ability to deliver high precision treatments, whilst remaining minimally invasive. Thus Laser-based therapies and diagnostic methods represent an area of huge future potential. Different types of laser like Nd : YAG laser, CO₂ laser, KTP laser, Ho : YAG laser, diode lasers, excimer lasers etc. are currently being used for various medical applications. Excimer lasers, which are pulsed gas lasers operating with a special mixture of noble gases and halogens, emit laser radiation in the UV and VUV spectra, at discrete wavelengths between 351 nm and 157 nm. The most commonly used excimer lasers are krypton fluoride (KrF, 248 nm), argon fluoride (ArF, 193 nm), xenon chloride (XeCl, 308 nm), xenon fluoride (XeF, 351 nm). The principal advantage of excimer lasers is that they are capable of producing a very small, precise spot at a very low (UV) wavelength. Excimer lasers are excellent for removing excess material through laser ablation due to the fact that they are able to precisely destroy material with little to no thermal buildup. This contrasts with carbon dioxide lasers, which rely heavily on thermal buildup to “boil off” material during ablation. Research efforts over recent years have resulted in excimer lasers becoming the tool of choice for many applications in medical sciences. Excimer lasers have shown promise in angioplasty, biliary laser lithotripsy, ophthalmology and orthopedics. Another medical application where excimer lasers are being used is dermatology for treating a variety of dermatological conditions including psoriasis, vitiligo, atopic dermatitis, alopecia areata and leukoderma. In the present review, applications of excimer lasers in biomedical sciences particularly in dermatology, ophthalmology, angioplasty, orthopaedics, lithotripsy, dentistry, medical implants have been

presented and recent studies carried out have been reviewed. The largest application of excimer lasers for medical use is in refractive laser surgery. As an ophthalmological tool, excimer laser has been widely used for photoablation process. The precision of excimer laser and, more important, the lack of damage to surrounding tissue, are instrumental for correction of refractive errors or optical problems of the eye, including nearsightedness, farsightedness, and astigmatism. Excimer laser light is typically absorbed in less than a nanometer of tissue. By means of intense excimer pulses, the surface of the human cornea is reshaped to change its refractive power and thus to correct for short or long sightedness. Another medical application where excimer lasers are being used is dermatology for treating a variety of dermatological conditions including psoriasis, vitiligo, atopic dermatitis, alopecia areata and leukoderma. Excimer lasers are very powerful UV sources.^[111] and they can also emit nanosecond pulses, with average output powers between a few watts and hundreds of watts. Typical wavelengths of excimer lasers are between 157 and 351 nm. The 308-nm excimer laser and a related 308-nm excimer lamp have been approved to treat psoriasis and vitiligo.^[112] Recently Gupta et al has reviewed the effects of UV radiation on wound healing which is a very complex process involving multiple tissue types influenced by local as well as systemic components^[113] where the effects of UV irradiation on skin cells *in vitro*, UV-induced damage and its repair, potential effects of UV irradiation for treatment of microbial infected wounds, especially those caused by antibiotic-resistant pathogens, effects of UV irradiation on wound healing, UV phototherapy for dermatological and other disorders, novel UV light sources to improve selective penetration and reduce the side effects have been discussed with an aim to provide nontoxic, minimally invasive and economically feasible technology for improving wound healing.^[114] Laser interaction with biological system is a very complex phenomena involving various factors having multiple therapeutic potential in disease conditions. These are photochemical, biostimulation - stimulatory effects of laser on biochemical and molecular processes that

normally occur in tissues such as healing and repair, photodynamic therapy inducing reactions in tissues for the treatment of pathologic conditions, tissue fluorescence useful as a diagnostic method to detect light reactive substance in tissue, photo thermal interactions useful for photoablation to remove tissue by vaporization and super heating of tissue fluids, coagulation, and hemostasis; photopyrolysis; photo disruption - breaking apart of structures by laser light; photoacoustic interaction-involving removal of tissue with shock wave generation, photoelectrical interaction including photoplasmolysis which describes how tissue is removed through the formation of electrically charged ions and particles that exist in a semi gaseous high energy state; photocoagulation: laser heats the tissues to 60⁰ C for a limited time leading to coagulation of the tissues with minimal alteration in the appearance of tissue structure. As a result of these proteins enzymes cytokines and other bioactive molecules get denatured. It has been demonstrated that high power lasers are used for surgical purposes and low power lasers are used to promote tissue regeneration. UV irradiation may cause both beneficial and damaging effects, which depend on wavelength, radiant exposure, and UV sources. Laser is a device producing a very intense and very narrow (collimated) beam of electromagnetic radiation in the wavelength range 180 nm to 1 mm and its important properties are monochromaticity (narrow wavelength range), directionality (high collimation) and coherence (propagation in same phase) and laser light is not an ionizing type of radiation. Interaction of laser with the body is generally at the surface. The eye and the skin are critical organs for laser radiation exposure, and the resultant effects vary depending on the type of laser (frequency or wavelength of the radiation) and beam energy output. Laser radiation of the proper wavelength and energy may be focused by the lens of the eye onto the retina causing severe damage. If laser radiation is of high enough energy, skin burns may also result if extremities or other body parts are placed in the laser beam. Therefore judicious application of laser technology may be beneficial in disease conditions. It should be used in a manner such

that the side effects would be minimized.

Although laser technology including excimer laser has made great progress in diagnosis and treatment of variety of complex diseases and its use has now been well-demonstrated in ophthalmologic and dermatologic treatments, and surgery, this technology has enormous scope in medicine and biology and could be explored towards the development of targeted therapy for complex chronic diseases. In the field of medicine, the energy delivered by the laser, whose intensity can be modulated, can cut, destroy or alter the cellular or extracellular structure of biological tissue. This unique property of laser opens a vast scope in the field of medicine. Further the ability of laser applications in reducing the risk of infection and promoting healing may deliver better therapeutic protocol in treatment of chronic diseases such as localized infectious diseases, especially those caused by antibiotic-resistant pathogens. Recent research studies have shown the potential of laser in destroying cancer cells which opens a path breaking approach in the treatment of dreadful disease cancer. However, high power lasers have been found to act indiscriminately and thus destroy cancer cells but also the surrounding tissue. Laser-associated micro dissection offers a rapid, precise method of isolating and removing targeted cells or groups of cells from complex biological tissues which may be helpful in understanding physiological mechanisms on the level of a specific cell population and even on the level of the single cell in disease conditions. Multidisciplinary research studies on the interaction of laser with biological tissue at molecular level using biotechnological tools will enhance the therapeutic potential of laser technology in diagnosis and treatment of chronic complex diseases especially cancer, genetic disorders, neurodegenerative disorders, multidrug resistance tuberculosis, autoimmune diseases, HIV etc. and it may also be useful in designing new and innovative strategies in drug delivery and image-guided surgery.

REFERENCES

1. Y. P. Raizer, Gas Discharge Physics, Springer-Verlag, Berlin (1991).
2. M. von Dadelszen and D. E. Rothe, IEEE Trans. On Plasma Science **19**, p.3s29ff (1991).
3. Einstein, A. Zur Quanten Theorie der Strahlung. Phys Zeit 1917; 18: 121 domized study. J Endourol 1999; 12: 575-80
4. Mulvaney, W.P. and Beck C. W. The laser beam in urology, J Urol, 1968;99: 112-5
5. Van Hillegersberg, R. Fundamental of laser surgery, Eur J Surg 1997; 163: 3-11
6. Grema H, Raulin C. The excimer laser in dermatology and aesthetic medicine. Hautarzt. 2004 Jan; 55(1):48-57. PMID:14749862 [PubMed - indexed for MEDLINE]
7. Mudigonda T, Dabade TS, West CE, Feldman SR. Therapeutic modalities for localized psoriasis: 308-nm UVB excimer laser versus non targeted phototherapy. Cutis. 2012 Sep; 90(3):149- 54 . PMID:23094316 [PubMed - indexed for MEDLINE]
8. Köllner K, Wimmershoff MB, Hintz C, Landthaler M, Hohenleutner U. Comparison of the 308-nm excimer laser and a 308-nm excimer lamp with 311-nm narrow band ultraviolet B in the treatment of psoriasis. Br J Dermatol. 2005 Apr; 152(4):750-4. PMID:15840108 [PubMed - indexed for MEDLINE]
9. Shadi Mehraban and Amir Feily .308nm Excimer Laser in Dermatology. J Lasers Med Sci. 2014 Winter; 5(1): 8–12 [PMCID: PMC4290518]
10. Park KK, Liao W, Murase JE . A review of monochromatic excimer light in vitiligo . Br J Dermatol. 2012 Sep; 167 (3):468-78. doi: 10.1111/j.1365-2133.2012.11008.x. Epub 2012 Aug 8. PMID: 22524428 [PubMed - indexed for MEDLINE]
11. Nisticò SP, Saraceno R, Schipani C, Costanzo A, Chimenti S. Different applications of monochromatic excimer light in skin diseases. . Photomed Laser Surg. 2009 Aug; 27(4):647-54. doi: 10.1089/pho.2008.2317. MID: 19563242 [PubMed - indexed for MEDLINE]
12. John A. Mouzakis, Stephanie Liu and George Cohen. Rapid Response of Facial Vitiligo to 308nm Excimer Laser and Topical Calcipotriene. Rapid Response of Facial Vitiligo to 308nm Excimer Laser and Topical Calcipotriene . J Clin Aesthet Dermatol. 2011 Jun; 4(6): 41–44. PMCID: PMC3140900]
13. Nicolaidou E, Antoniou C, Stratigos A, Katsambas AD. Narrowband ultraviolet B phototherapy and 308-nm excimer laser in the treatment of vitiligo: a review. J Am Acad Dermatol. 2009; 60(3):470–477.[PubMed]
14. Kawalek AZ, Spencer JM, Phelps RG. Combined excimer laser and topical tacrolimus for the treatment of vitiligo: a pilot study. Dermatol Surg. 2004; 30(2 Pt 1):130–135. [PubMed]

15. Goldinger SM, Dummer R, Schmid P, et al. Combination of 308-nm xenon chloride excimer laser and topical calcipotriol in vitiligo. *J Eur Acad Dermatol Venereol*. 2007;21(4):504–508. [PubMed]]
16. Passeron T, Ostovari N, Zakaria W, Fontas E, Larrouy JC, Lacour JP, Ortonne JP. Topical tacrolimus and the 308-nm excimer laser: a synergistic combination for the treatment of vitiligo. *Arch Dermatol*. 2004 Sep; 140(9):1065-9. PMID: 15381545 [PubMed - indexed for MEDLINE]
17. Al-Shobaili H A , Correlation of clinical efficacy and psychosocial impact on vitiligo patients by excimer laser treatment. *Ann Saudi Med*. 2014 Mar-Apr;34(2):115-21. doi: 10.5144/0256-4947.2014.115. PMID: 24894779 [PubMed]
18. Hofer A, Hassan AS, Legat FJ, Kerl H, Wolf P. Optimal weekly frequency of 308-nm excimer laser treatment in vitiligo patients. *Br J Dermatol*. 2005 May; 152(5): 981-5. PMID: 15888156 [PubMed - indexed for MEDLINE]
19. Alhowsaish AK, Dietrich N, Onder M, Fritz K. Effectiveness of a 308-nm excimer laser in treatment of vitiligo: a review. *Lasers Med Sci*. 2013 May; 28(3):1035-41. doi: 10.1007/s10103-012-1185-1. Epub 2012 Aug 15. PMID: 22892613 [PubMed - indexed for MEDLINE]
20. Roman Bronfenbrener, Jennifer Ragi and Sandy Milgraum. Granuloma Annulare Treated with Excimer Laser. *J Clin Aesthet Dermatol*. 2012 Nov; 5(11): 43–45]
21. Goldinger SM, Dummer R, Schmid P, Burg G, Seifert B, Läubli S. Combination of 308-nm xenon chloride excimer laser and topical calcipotriol in vitiligo. *J Eur Acad Dermatol Venereol*. 2007 Apr;21(4):504-8. PMID: 17373978 [PubMed - indexed for MEDLINE]
22. Alexander A. Navarini, Antonios G. A. Kolios, Bettina M. Prinz-Vavricka, Susanne Haug, Ralph M. Trüb. Low-Dose Excimer 308-nm Laser for Treatment of Lichen Planopilaris. *Arch Dermatol*. 2011; 147(11):1325-1326. doi:10.1001/archdermatol.2011.335.]
23. Tejaswi Mudigonda, Tushar S. Dabade, Steven R. Feldman . A Review of Protocols for 308 nm Excimer Laser Phototherapy in Psoriasis. *J Drugs Dermatol*. 2012; 11(1):92-97]
24. Al-Mutari N (2009). 308-nm Excimer laser for the treatment of alopecia areata in children. *Pediatr Dermatol* **26**:547–550
25. Al-Mutari N (2007). 308-nm Laser for the treatment of alopecia areata. *Dermatol Surg* **33**:1483–1487
26. Asawanonda P, Anderson RR, Chang Y et al. (2000). 308-nm Excimer laser for the treatment of psoriasis: a dose–response study. *Arch Dermatol* **136**:619–624 | Article | PubMed | ISI |
27. Bónis B, Kemény L, Dobozy A et al. (1997). 308 nm Excimer laser for psoriasis (letter). *Lancet* **350**:1522
28. Coven TR, Burack LH, Gilleaudeau R et al. (1997). Narrowband UV-B produces superior clinical and histopathological resolution of moderate-to-severe psoriasis in patients compared with broadband UV-B. *Arch Dermatol* **133**:1514-1522 | Article | PubMed | ISI | CAS |
29. Feldman SR, Mellen BG, Housman TN et al. (2002). Efficacy of 308 nm excimer laser for treatment of psoriasis: results of a multicentric study. *J Am Acad Dermatol* **46**:900–906 | Article | PubMed | ISI |
30. Gundogan C, Greve B, Raulin C (2004). Treatment of alopecia areata with the 308 nm xenon chloride excimer laser: case report of two successful treatments with the excimer laser. *Lasers Surg Med* **34**:86–90
- 31.. Novak Z, Bonis B, Baltas E et al. (2002) .Xenon chloride ultraviolet B laser is more effective in treating psoriasis and in inducing T cell apoptosis than narrow-band ultraviolet B. *J Photochem Photobiol B* **67**:32–38 | Article | PubMed | CAS |
- 32.. Raulin C, Gundogan C, Greve B et al. (2005). Excimer laser therapy of alopecia areata—side-by-side evaluation of a representative area. *J Dtsch Dermatol Ges* **3**:524–526]
33. Joseph G Morelli, Abdul-Ghani Kibbi, James Boll and Oon Tian Tan . 193 nm Excimer Laser Selective Ablation of In Vivo Guinea Pig Epidermis .*Journal of Investigative Dermatology* (1988) 91, 532–535; doi:10.1111/1523-1747.ep12476881]
34. S. attu, R M Rashid, Jashin J Wu. 308-nm excimer laser in psoriasis vulgaris, scalp psoriasis, and palmoplantar psoriasis. *Journal of the European Academy of Dermatology and Venereology (Impact Factor: 3.11).09/2008; 23(1):36-41. DOI: 10.1111/j.1468-3083.2008.02942.x]*
35. Nawaf Al-Mutairi , Ahmad Al-Haddad. Targeted phototherapy using 308 nm XeCl monochromatic excimer laser for psoriasis at difficult to treat sites. *Lasers in Medical Science* . 09/2012; 28(4). DOI: 10.1007/s10103-012-1210-4] Source: PubMed
36. Ethan Levin ,Maya Debbaneh ,Mona Malakouti,Gabrielle Brown, Eva Wang ,Rishu Gupta. Supraerythemogenic excimer laser in combination with clobetasol spray and calcitriol ointment for the treatment of generalized plaque psoriasis: Interim results of an open label pilot study. *Journal of Dermatological Treatment* , 02/2014; DOI: 10.3109/09546634.2013.860210, Source : PubMed]
37. Ling Han, Ally-Khan Somani, Qiong Huang, Xu

- Fang, Yi Jin, Lei-Hong Xiang , Zhi- Zhong Zheng. Photodermatology Photoimmunology and Photomedicine . 11/2008; 24(5):231-6. DOI : 10.1111/j. 1600-0781.2008.00364. Source: PubMed]
38. Akira Kawada.Evolution of targeted phototherapy for psoriasis. Expert Review of Dermatology 01/2014; 8(6). DOI: 10.1586/17469872.2013.856685]
39. Jillian W. Wong, Tien V. Nguyen, Kelly K. Park and John Y.M. Koo. The use of 308 Nm Excimer Laser for the treatment of atopic dermatitis .The Dermatologist, Volume 20 - Issue 7 - July 2012]
40. Pallikaris IG, Siganos DS. Excimer laser in situ keratomileusis and photorefractive keratectomy for correction of high myopia. Journal of Refractive and Corneal Surgery 1994, 10(5):498-510]
41. D. Gartry, M. Kerr Muir, and J. Marshall . Excimer laser treatment of corneal surface pathology: a laboratory and clinical study. Br J Ophthalmol. 1991 May; 75(5): 258–269.PMCID: PMC1042351]
42. Trokel SL, Srinivasan R, Braren B. Excimer laser surgery of the cornea. *Am J Ophthalmol*. 1983 Dec;96(6):710–715. [PubMed]
43. Marshall J, Trokel S, Rothery S, Schubert H. An ultrastructural study of corneal incisions induced by an excimer laser at 193 nm. *Ophthalmology*. 1985 Jun;92(6):749–758. [PubMed]
44. Puliafito CA, Steinert RF, Deutsch TF, Hillenkamp F, Dehm EJ, Adler CM. Excimer laser ablation of the cornea and lens. Experimental studies. *Ophthalmology*. 1985 Jun;92(6):741–748. [PubMed]
45. Marshall J, Trokel S, Rothery S, Krueger RR. A comparative study of corneal incisions induced by diamond and steel knives and two ultraviolet radiations from an excimer laser. *Br J Ophthalmol*. 1986 Jul;70(7):482–501. [PMC free article] [PubMed]
46. Seiler T, Bende T, Wollensak J, Trokel S. Excimer laser keratectomy for correction of astigmatism. *Am J Ophthalmol*. 1988 Feb 15;105(2):117–124. [PubMed]
47. Munnerlyn CR, Koons SJ, Marshall J. Photorefractive keratectomy: a technique for laser refractive surgery. *J Cataract Refract Surg*. 1988 Jan;14(1):46–52. [PubMed]
48. Tuft SJ, Zabel RW, Marshall J. Corneal repair following keratectomy. A comparison between conventional surgery and laser photoablation. *Invest Ophthalmol Vis Sci*. 1989 Aug;30(8):1769–1777.[PubMed]
49. Tuft SJ, Zabel RW, Marshall J. Corneal repair following keratectomy. A comparison between conventional surgery and laser photoablation. *Invest Ophthalmol Vis Sci*. 1989 Aug;30(8):1769–1777.[PubMed]
50. Kerr-Muir MG, Trokel SL, Marshall J, Rothery S. Ultrastructural comparison of conventional surgical and argon fluoride excimer laser keratectomy. *Am J Ophthalmol*. 1987 Mar 15;103(3 Pt 2):448–453. [PubMed]
51. Taylor DM, L'Esperance FA, Jr, Del Pero RA, Roberts AD, Gigstad JE, Klintworth G, Martin CA, Warner J. Human excimer laser lamellar keratectomy. A clinical study. *Ophthalmology*. 1989 May;96(5):654–664. [PubMed]]
52. I. Toda, Y. Yagi, S. Hata, S. Itoh, and K. Tsubota. Excimer laser photorefractive keratectomy for patients with contact lens intolerance caused by dry eye. *Br J Ophthalmol*. 1996 Jul; 80(7): 604–609. PMID: PMC505553
53. Taylor HR, Guest CS, Kelly P, Alpina NA . Comparison of excimer laser treatment of astigmatism and myopia. The Excimer Laser and Research Group. *Arch Ophthalmol*. 1993 Dec; 111(12):1621-6]
54. D P O'Brart, D S Gartry, C P Lohmann, A L Patmore, M G Kerr Muir, and J Marshall. Treatment of band keratopathy by excimer laser phototherapeutic keratectomy: surgical techniques and long term follow up. *Br J Ophthalmol*. 1993 Nov; 77(11): 702–708 PMID: PMC504628
- 55.. P Condon, M Mulhern, T Fulcher, A Foley-Nolan, and M O'Keefe. Laser intrastromal keratomileusis for high myopia and myopic astigmatism. *Br J Ophthalmol*. 1997 Mar; 81(3): 199–206]
56. Puliafito CA, Steinert RF, Deutsch TF, Hillenkamp F, Dehm EJ, Adler CM. Excimer laser ablation of the cornea and lens. Experimental studies. *Ophthalmology*. 1985 Jun ; 92(6):741-8. PMID: 4034169 [PubMed - indexed for MEDLINE]
57. Richard L. Lindstrom, David R Hardten and Paul J. Dougherty. Excimer Laser Photorefractive Keratectomy for myopia: A Single Surgeon Best-Case Analysis. *TR. AM. OPHTH. Soc. vol. XCII, 1994]*
58. Sher NA, Bowers RA, Zabel RW, et al: Clinical use of the 193-nm excimer laser in the treatment of corneal scars. *Arch Ophthalmol* 1991; 109:491-498.
59. Sher NA, Chen V, Bowers RA, et al: The use of the 193-nm excimer laser for myopic photorefractive keratectomy in sighted eyes: A multicenter study. *Arch Ophthalmol* 1991;109:1525-1530.
60. Zabel RW, Sher NA, Ostrov CS, et al: Myopic excimer laser keratectomy: A preliminary report. *Refract Co-neal Surg* 1990;6:329-334.
61. Sher NA, Barak M, Daya S, et al: Excimer laser photorefractive keratectomy in high myopia: A multicenter study. *Arch Ophthalmol* 1992; 110:935-943.

62. Stark WJ, Chamon W, Kamp MT, et al: Clinical follow up of 193-nm ArF excimer laser photokeratectomy. *Ophthalmology* 1992; 99:805-812.
63. Gartry DS, Kerr Muir MG, Marsall J: Excimer laser photorefractive keratectomy: 18-month follow-up. *Ophthalmology* 1992; 99:1209-1219.
64. Talley AR, Hardten DR, Sher NA, et al: The use of the 193-nm excimer laser for photorefractive keratectomy in low to moderate myopia: One year results. *Am J Ophthalmol* In press.
65. Bittl JA, Sanborn TA. *Excimer laser-facilitated coronary angioplasty: relative risk analysis of acute and follow-up results in 200 patients. Circulation.1992;86 :71-80.*
66. Bittl JA, Sanborn TA, Tchong JE, Siegel RM, Ellis SG *Clinical success, complications and restenosis rates with excimer laser coronary angioplasty. Am J Cardiol. 1992;70:1533-1539.*
67. Cook SL, Eigler NL, Shefer A, Goldenberg T, Forrester JS, Litvack F. *Percutaneous excimer laser coronary angioplasty of lesions not ideal for balloon angioplasty. Circulation. 1991;84:632-643.*
68. Grundfest WS, Litvack F, Forrester JS, Goldenberg T, Swan HJC, Morgenstern L, Fishbein M, McDermid IS, Rider DM, Pacala TJ, Laudenslager JB. *Laser ablation of human atherosclerotic plaque without adjacent tissue injury. J Am Coll Cardiol. 1985;5:929-933.*
- 69.- Litvack F, Grundfest WS, Segalowitz J, Papaioannou T, Goldenberg T, Laudenslager J, Hestrin L, Forrester J, Eigler NS, Cook SA. *Interventional cardiovascular therapy by laser and thermal angioplasty. Circulation. 1990; 81(suppl IV):IV-109-IV-116.*
70. Litvack F, Grundfest WS, Papaioannou T, Mohr FW, Jakubowski AT, Forrester JS. *Role of laser and thermal ablation devices in the treatment of vascular diseases. Am J Cardiol. 1988;61: 81G-86G*
71. Shelton ME, Hoxworth B, Shelton JA, Virmani R, Friesinger GC. *A new model to study quantitative effects of laser angioplasty on human atherosclerotic plaque. J Am Coll Cardiol. 1986;7: 909-915.*
72. Topaz O, Shah R, Mohanty PK, McQueen RA, Janin Y, Bernardo NL. *Application of excimer laser angioplasty in acute myocardial infarction . Lasers Surg Med. 2001; 29(2):185-92] PMID: 11553909 [PubMed - indexed for MEDLINE]*
73. On Topaz, Douglas Ebersole, Tony Das, Edwin L Alderman, Hooman adyoon, Kishor Vora, John D Baker, David Hilton, Johannes B Dahm, *Excimer laser angioplasty in acute myocardial infarction (the CARMEL multicenter trial) The American Journal of Cardiology, Vol. 93, Issue 6, 15 March 2004 , 694-701*
74. Gary S. Mintz, Julie A. Kovach, Saturnino P. Javier, Augusto D. Pichard, Kenneth M. Kent, Jeffrey J. Popma, Lowell F. Salter, Martin B. Leon, *Mechanisms of Lumen Enlargement After Excimer Laser Coronary Angioplasty An Intravascular Ultrasound Study. Circulation.1995; 92: 3408-3414doi: 10.1161/01.CIR.92.12.3408*
75. KR Karsch, KK Haase, W Voelker, A Baumbach, M Mauser and L Seipel. *Percutaneous Coronary Excimer Laser Angioplasty in Patients With Stable and Unstable Angina Pectoris- Acute Results and Incidence of Restenosis During 6-Month Follow-up . Circulation 1990, 81:1849-1859*
76. Weiqiang Shi, Thanassis Papaioannou, Leon Daykhovskiy Sandor G Vari, Warren S. Grundfest. . *Fragmentation of biliary stones with a 308 nm excimer laser, Lasers in Surgery and Medicine .01/1990; 10(3):284-290.OI: 10.1002/lsm.1900100309 Source: PubMed]*
77. George Benaim , Stefano Mattioli ,M. Cremona, Roberto Pini, Renzo Salimbeni, Matteo Vannini, Maria-Angela Franceschini *In-vitro tests of excimer laser lithotripsy in urinary stones. Proc. SPIE 1643, Laser Surgery: Advanced Characterization, Therapeutics, and Systems III, 73 (June 1, 1992); doi:10.1117/12.137327*
78. Gundlach P, Scherer H, Hopf J, Leege N, Müller G, Hirst L, Scholz C. *Endoscopic-controlled laser lithotripsy of salivary calculi. In vitro studies and initial clinical use. HNO. 1990 Jul; 38(7):247-50] PMID: 2394601 [PubMed - indexed for MEDLINE]*
79. MarkJ.Landsman, JohnE. Mancuso,StevenP. Abramow, *Laser's use in bone andsurgery. Laser Surgery Volume 9, Number 3 July 1992, 72 1- 37.*
80. BorovoyM, ZirkinRM, ElsonL, et al:*Healingoflaser-induced defectsofarticularcartilage: Preliminary studies.J Foot Surg 28:95-99,1989*
81. Bruhn EW, Hunter JG, etal:*TheErbium-YAG laser as a surgical tool. LasersSurg MedSuppl2:22-23,1990*
82. BucheliM, PapaioannouT, FishbeinM, etal:*Excimer laser ablation of fibrocartilage. An in vitroand-invivostudy. Lasers Surg Med11:271-279,1991s*
83. CallahanDJ,DennisJ;*Osseous healing after CO2 laserosteotomy.FootAnkle 11:146-151,1990*
84. CecereWL,LiebowC:*Laser Causes Greater Growth Factor Release than Scalpel. LasersSurg MedSuppl2:22,1990*
85. Glossop ND, Jackson RW, Koort HJ, Reed SC, Randle JA. *The excimer laser in orthopaedics. Clin Orthop Relat Res. 1995 Jan; (310):72-81.] PMID: 7641463 [PubMed - indexed for MEDLINE]*

86. S. Beke, F. Anjum, H. Tsushima, L. Ceseracciu, E. Chieregatti, A. Diaspro, A. Athanassiou, and F. Brandi , Towards excimer-laser-based stereolithography: a rapid process to fabricate rigid biodegradable photopolymer scaffolds. *J R Soc Interface*. 2012 Nov 7; 9(76): 3017–3026.
87. Stephen C. Reed , Robert W. Jackson ,Neil Glossop, John Randle , An in vivo study of the effect of excimer laser irradiation on degenerate rabbit articular cartilage. *The Journal of Arthroscopic and Related Surgery*, February 1994, Volume 10, Issue 1, Pages 78–84
88. Andreas B. Imhoff, The use of lasers in orthopaedic surgery. *Operative Techniques in Orthopaedics*, July 1995 , Volume 5, Issue 3, Pages 192–203
89. Srinivasan R, Mayne-Banton V. Self-developing photoetching of poly (ethylene terephthalate) films by far ultraviolet excimer laser radiation. *Appl Phys Lett* 1982; 41:576
90. Srinivasan R, Leigh WJ. Ablative photodecomposition: Action of far-ultraviolet (193nm) laser radiation on poly-(ethylene terephthalate) films. *J Am Chem Soc* 1982; 104:6784
91. Pini R, Salimbeni R, Vannini M, Barone R, Clauser C. Laser dentistry: A new application of excimer laser in root canal therapy. *Lasers Surg Med* 1989; 9:358-361.
92. Osnat Feuerstein, Daniel Palanker, Amihay Fuxbrunner, Aaron Lewis and Dan Deutsch, Effect of the ArF Excimer Laser on Human Enamel *Lasers in Surgery and Medicine* 12:471277 (1992)
93. Joseph Neev, Lih-Huei L. Liaw, Dan V. Raney, Jack T. Fujishige, Peter D. Ho and Michael W. Berns. Selectivity, efficiency, and surface characteristics of hard dental tissues ablated with ArF pulsed excimer lasers. *Lasers in Surgery and Medicine*, Volume 11, Issue 6, pages 499–510, 1991
94. A.Y. Fasasi, S. Mwenifumbo, N. Rahbar, J. Chen, M. Li, A.C. Beye C.B. Arnold, W.O. Soboyejo, Nano-second UV laser processed micro-grooves on Ti6Al4V for biomedical applications. *Materials Science and Engineering C* 29 (2009) 5–13
95. D.G. Waugh, J. Lawrence . Wettability and osteoblast cell response modulation through UV laser processing of nylon 6,6. *Applied Surface Science* , Volume 257, Issue 21, 15 August 2011, Pages 8798–8812
96. Takehisa Matsuda and Yasuhide Nakayama, Surface microarchitectural design in biomedical applications: *In vitro* transmurial endothelialization on microporous segmented polyurethane films fabricated using an excimer laser. *Journal of Biomedical Materials Research*, Volume 31, Issue 2, pages 235–242, June 1996
97. Morelli, J, Tan, OT, Kibbi, A, Farinelli, W, Parrish, JA: Ultraviolet excimer laser ablation: Effects of wavelength and repetition rate on the in vivo guinea pig skin. *J Invest Dermatol* 1987 88: 769–773 [PubMed]
98. Yasuhide Nakayama, Shogo Nishi, Hatsue Ishibashi-Ueda and Takehisa Matsuda . Surface microarchitectural design in biomedical applications: *In vivo* analysis of tissue in growth in excimer laser-directed micropored Scaffold for cardiovascular tissue engineering *Journal of Biomedical Materials Research*, Volume 51, Issue 3, pages 520–528, 5 September 2000
99. H. J. Galla, W. Hartmann. Excimer-forming lipids in membrane research. *Chemistry and Physics of Lipids* Volume 27, Issue 3, October 1980, Pages 199–219
100. Yasuhide Nakayama and Takehisa Matsuda . Surface microarchitectural design in biomedical applications: Preparation of microporous polymer surfaces by an excimer laser ablation technique. *Journal of Biomedical Materials Research*, Volume 29, Issue 10, pages 1295– 1301, October 1995
101. Felix Sima, Emanuel Axente, Carmen Ristoscu, Ion N. Mihailescu , Taras V. Kononenko, Ilya A. Nagovitsin , Galina Chudinova, Vitaly I. Konov, Marcela Socol, Ionut Enculescu, Livia E. Sima and Stefana M. Petrescu . Tailoring immobilization of immunoglobulin by excimer laser for biosensor applications. *Journal of Biomedical Materials Research Part A* Volume 96A, Issue 2, pages 384–394, February 2011
102. Waugh, David and Lawrence, Jonathan (2011). *The enhancement of biomimetic apatite coatings by means of KrF excimer laser surface treatment of nylon 6,6*. *Lasers in Engineering*, 21 (1&2). pp. 95-114
103. Zaret, M.M., Breinin, G.M., Schmidt, H., Ripps, H., Siegel, I.M. and Solon, L.R. (1961) *Science*, **134**, 1525-1526. <http://dx.doi.org/10.1126/science.134.3489.1525>
104. Avedisian, C.T., Cavicchi, R.E., McEuen, P.L. and Zhou, X. (2009) *Annals of the New York Academy of Sciences*, **1161**, 62-73. <http://dx.doi.org/10.1111/j.1749-6632.2009.04090.x>
105. Legres, L.G., Chamot, C., Varna, M. and Janin, A. (2014) The Laser Technology: New Trends in Biology and Medicine. *Journal of Modern Physics*, **5**, 267-279. <http://dx.doi.org/10.4236/jmp.2014.55037>
106. Moo-Young, G.A. (1985) *Western Journal of Medicine*, **143**, 745-750
107. Anderson, R.R. (2013) *Journal of Investigative Dermatology*, **133**, E21-E23.
108. Herd, R. (1996) *JAMA Dermatology*, **132**, 1262-1262. <http://dx.doi.org/10.1001/archderm.>

- 1996.03890340128035
109. Lehnert, M.W. (1996) *Northwest Dentistry*, **75**, 17-22
110. Fan, C.M. and Rox-Anderson, R. (2008) *Phlebology*, **23**, 206-213. <http://dx.doi.org/10.1258/phleb.2008.008049>
111. Basting D. Marowsky G. Excimer Laser Technology. Berlin, Germany: Springer/Praxis; 2005
112. Le Duff F. Fontas E. Giaccherio D. Sillard L. Lacour JP. Ortonne JP. Passeron T. 308-nm excimer lamp vs. 308-nm excimer laser for treating vitiligo: a randomized study. *Br J Dermatol*. 2010; 163:188. [PubMed]
113. Singer AJ. Clark RA. Cutaneous wound healing. *N Engl J Med*. 1999;341:738. [PubMed]
114. Ultraviolet Radiation in Wound Care: Sterilization and Stimulation. Asheesh Gupta, Pinar Avci, Tianhong Dai, Ying-Ying Huang, and Michael R. Hamblin, *ADVANCES IN WOUND CARE*, *Adv Wound Care* (New Rochelle). 2013 Oct; 2(8): 422– 437. doi: 10.1089/wound.2012.0366