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REVIEW

Excimer Lasers in Refractive Surgery

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ABSTRACT

Introduction: In the field of ophthalmology, laser technology is used in many basic and clinical disciplines and specialities. It has played an important role in promoting the development of ophthalmology. **Aim:** This article is designed to review the evolution of laser technology in refractive surgeries in ophthalmology, mainly focusing on the characteristics of the excimer laser applied in corneal refractive surgery. **Methods:** This article was performed based on a literature review and Internet search through scientific databases such as PubMed, Scopus, Web of Science and Google Scholar. **Result:** The literature on excimer laser technology addresses the technical and physical aspects of excimer lasers including types, characteristics and commercially available lasers on the market. **Conclusion:** The conclusion on this forum aims to help understand the benefits of excimer laser use in ophthalmology, with focus on correction of refractive errors.

Keywords: Excimer laser, corneal refractive surgery, ablation profile, laser pulse.

1. INTRODUCTION

In the field of ophthalmology, laser technology is used in many basic and clinical disciplines and specialities. It has played an important role in promoting the development of ophthalmology. Advancements in technology have allowed improvements in the surgical safety, efficacy, speed and versatility of the laser, especially in corneal refractive surgery. Because of the increasing numbers of applications in ophthalmology and their successful implementations, ophthalmic use of laser technology is expected to continue flourishing. (1)

2. HISTORICAL FACTS

Invention of the Excimer Laser

Three researchers at the IBM ® Thomas J. Watson Research Center in Yorktown, New York (Samuel Blum, Rangaswamy Srinivasan and James J. Wynne) had been exploring new ways to use the excimer laser that had been recently acquired by their laser physics and chemistry group. Blum was an expert in materials science; Srinivasan was a photochemist with 21 US patents to his name; and Wynne was a physicist, who was the manager of the group at IBM. The excimer laser uses reactive gases, such as chlorine and fluorine, mixed with inert gases, such as argon, krypton and xenon. When electrically excited, the gas mixture emits energetic pulses of ultraviolet light, which can make very precise, minute changes to irradiated material, such as polymers.

In the year 1987, Stephen Trokel, MD first used the Excimer Laser on the cornea. Dr. Steven Trokel introduced Photorefractive Keratectomy (PRK). He also patented the Excimer laser for vision correction and performed the first laser surgery on a patient's eyes in 1987. Upon learning of the IBM work, ophthalmologist Stephen Trokel, affiliated with Columbia Presbyterian Medical Center in New York City, came to the Watson Research Center in the summer of 1983 to collaborate on experiments with Srinivasan and researcher Bodil Braren. Trokel, Srinivasan, and Braren wrote a paper introducing the idea of using the laser to reshape or sculpt the cornea (the clear covering on the front of the eye) in order to correct refractive errors, such as myopia or hyperopia. Their paper, published in a major ophthalmology journal in December 1983, launched a worldwide program of research to develop excimer laser-based refractive surgery. New York City ophthalmologist, Steven Trokel made the connection to the cornea and performed the first laser surgery on a patient's eyes in 1987. The next ten years were spent perfecting the equipment and the techniques used in laser eye surgery. In 1996, the first Excimer laser for ophthalmic refractive use was approved in the United States (2).

Excimer laser principle of work

The excimer laser is based on the combination of two gases: a noble gas and halogen. Both of these are generally stable in their normal low-energy state. When a high-voltage electrical discharge is delivered into the laser cavity containing these gases, the gases combine to form a higher energy excited-gas state compound. The term "excimer" is derived from a contraction of "excited dimer". On the dissociation of this high-energy compound, a photon of energy is released that corresponds to the bond energy of the noble gas-halogen molecule (3, 4). This wavelength of light energy is amplified in the laser system, resulting in the production of a discrete high energy pulse of laser energy. The specific wavelength of an excimer laser depends on the composition of the gases used in the laser system. Excimer laser systems in current clinical use rely on argon and fluorine gases. The argon-fluorine excimer lasers emit energy at a wavelength of 193 nm. This wavelength falls in the UV-C range of the light spectrum. In contrast, the krypton-fluoride excimer laser used in early laboratory studies emits a wavelength of 248 nm (5, 6). Laser energy at 193 nm is very well absorbed by the proteins, glycosaminoglycans and nucleic acids comprising the cornea because of its sufficient photon energy (6.4 eV) and precision (only penetrating the superficial layer; 0.3 μm). The tissue-ablation depth is positively correlated with the logarithm of laser density; 1-J/cm^2 energy can ablate approximately 1-μm of corneal tissue. Since 193 nm photon is of higher energy than the molecular bond strength of these compounds, absorption of the laser energy results in breaking of the bounds. The resulting molecular fragments are ejected from the surface of the cornea at supersonic speeds (7-9).

The goal is to reshape the cornea so that rays of light that enter the eye are focused clearly onto the retina. It is important to understand that the excimer laser does not cut tissue like a scalpel; rather it ablates or removes tissue from the corneal surface. The ablated material appears as an effluent plume that upon analysis has been shown to consist of a variety of high-molecular-weight hydrocarbons (9). There is a concern about the potential for mutagenesis or carcinogenesis with any laser radiation, especially in the ultraviolet light spectrum. Studies have been done showing that the 193 nm excimer laser is neither mutagenic nor carcinogenic (10, 11). This may be in part a result of shielding of the nucleus by the cell's cytoplasm. Several attributes of the argon-fluoride excimer laser ablation make it particularly appropriate for corneal sculpting. The laser energy is well absorbed near the corneal surface and, thus, should have few deep direct or secondary mechanical (shock-wave) effects on the corneal tissue. The ablation process is rapid, and excess energy is ejected with the effluent plume (11). There is minimal thermal damage to the surrounding tissue. Because of these qualities, as a cold laser, the 193 nm excimer laser can be used to meticulously reshape large areas of the corneal surface while minimizing damage to remaining tissue (12).

The excimer laser technique is qualitatively different from refractive surgical techniques such as radial or astigmatic keratotomy, which achieves corneal reshaping through biomechanical changes mediated through thin knife incisions.

3. AIM

This article is designed to review the evolution of laser technology in refractive surgeries in ophthalmology, mainly focusing on the characteristics of the excimer laser applied in corneal refractive surgery.

4. METHODS

The relevant articles were searched from online data sources including PubMed, Scopus, Web of Science and Google Scholar.

5. RESULTS

The retrieved articles were reviewed by the authors and the results are presented along with the relevant discussion.

5.1. TYPES OF EXCIMER LASERS

The first generation excimer lasers were "broad beam lasers" or "full beam lasers" that created less uniform surface profiles than the newer generations. Full beam enables faster treatment (for given frequency) and is less sensitive for decentration, but homogenizes slower, gives irregular treatment of the surface and has more expressed thermal effect. It is needed to use masks for achievement of desired treatment form, and it is not possible to perform custom treatments (12).

Newer-generation of excimer lasers use scanning beams or flying spots, with smaller spot sizes and more efficient eye trackers. Systems for scanning slit delivery act like flying spot systems and it exceed some limitations of full beam systems, but maintained the speed of the treatment and low decentration sensitivity. System uses additional diaphragm between full beam and the eye, which flows through hexagonal beam of a smaller diameter (10 mm x 1 mm) to the eye, and improves homogeneity of the beam. Ablation masks rotate, enabling performance in different directions (12).

Flying spot systems convert laser beam in small round spot (between 0.6 and 2.0 mm). System uses only central most homogenic part of the beam, and beam direction is controlled by a mirror with rotation function.

CHARACTERISTICS	WAVELIGHT EX500	SCHWIND AM-ARIS 1050	MEL 90	STAR S4 IR (VISX)	TECHNOLAS TENEO 317 M2	NIDEK Quest/EC-5000 CX III
Ablation type	„Flying spot"	„Flying spot"	„Flying spot"	Adjustable spot size	„Flying spot"	„Scanning slit"
Beam profile	Ultra-thin Gaussian profile	Super Gaussian Profile	Gaussian Profile	Gaussian Profile	Truncated Gaussian profile	Gaussian Profile
Spot size (mm)	0,68	0,54	0,7	0,65-6,5	1	1
Pulse frequency	500	1050	250/500	10-20	500	100
Eye tracker implying rate (Hz)	1050	1050	1050	60	1740	200/1000
Characteristics of eye tracking system	6D tracking system	7D tracking system	Registration of pupil edge and limbus	3D tracking system	6D tracking system	6D tracking system

Table 1. Display of basic characteristics of excimer lasers available on the market

Ablation of targeted tissue is performed by repeated delivery of high number of pulses, in which every pulse removes only small area of tissue. Very high frequency is needed to shorten the treatment period, especially if the spots are very small. Also, spots need to be distributed precisely to avoid thermal effect. During that time eye tracking system is obligatory, because it is very sensitive to decentration. Energy profile of every spot is Gaussian and enables smooth areas of ablation, and the distance between two aiming spots is half of a beam size so the regular ablation can be provided. Main advantage of these systems is possibility of treatments high levels of irregularities. The smaller the spot, the treatment option of irregularities is higher (12).

Although excimer machines from different manufacturers converge in technology, individual lasers differ in laser ablation algorithm, eye-tracking technology, frequency of laser ablation, corneal thickness ablated, duration of treatment, and physical design.

5.2. PULSE DURATION

Pulse arises during highest instability of excited dimer (half-time break up from 9 to 23 ns) and lasts 10 to 20 ns. The shorter the pulses, the less influence of thermal effect is on the nearby tissues (12).

5.3. PULSE FREQUENCY

Frequency of pulses (number of pulses emitted in a second) varies from 10 to 1050 Hz depending on laser model. The higher the frequency – treatment is faster, but the thermal effect is higher, so the cooling of the treated tissue is ensured by using different algorithms. Optimal laser frequency with full beam is from 10 to 50 Hz, while with flying beam lasers it goes up to 1050 Hz, and the speed depends on success of algorithm for positioning sequent pulse strikes (12).

5.4. PULSE ENERGY

Energy that the pulse is delivering varies from 10 to 250 mJ depending on the laser. Difference in pulse energy can be up to 10%. During typical refractive procedure variation on the depth of tissue penetration is ±0,1% (which corresponds to 0,1 D) so it is negligible in clinical practice (12).

5.5. CONSTANT ENERGY OF RADIATION ON MEASURED AREA

Step of photoablation on the corneal surface of 193 nm wavelength is 50 mJ/cm2. Below this step photoablation is irregular and incomplete. Every pulse with constant energy of radiation above minimal step precisely removes certain amount of corneal tissue. Amount of tissue that pulse removes is increasing linearly with energy increase up to the values of 600 mJ/cm2. After that value, increase of radiation energy is not increasing the amount of tissue removed by pulse. Constant radiation energy depends on the type of laser, and goes from 160 i 250 mJ/cm2 (12).

5.6. DEGREE OF ABLATION

Degree of ablation goes from 0,25 to 0,6 μm by pulse hit, and is typical for every laser. Many factors have influence on ablation degree. Every histological layer of the cornea has different ablation degree (ablation of epithelium is faster than stromal ablation, while stromal ablation is 30% faster of Bowman's membrane ablation). Scaring slows down the ablation, while dehy-

Figure 1. Wavelight Allegretto Eye-Q 400 Hz laser platform

Figure 2. Schwind Amaris 750S laser platform

dration of the tissue accelerates it (12).

Conventional laser refractive surgery platforms are capable of correcting lower-order aberrations, such as hyperopia, myopia, and astigmatism. Higher-order aberrations (HOAs) such as coma, spherical aberration and trefoil are induced by, and remain uncorrected in traditional laser in situ keratomileusis (LASIK) surgery (13, 14). The HOAs call for more advanced optical measurements and more sophisticated laser algorithms. These laser algorithms are found in wavefront (WF) based treatments, which have been shown to diminish induced HOAs compared to traditional LASIK, and increase predictability of visual outcomes (13-23).

5.7. COMMERCIALLY AVAILABLE EXCIMER LASERS

Wavelight Allegretto is a flying-spot excimer laser, with a pulse repetition rate from 200 to 500 Hz depending on the laser model, with two galvanometric scanners for positioning laser pulses. The beam is a small-spot, <0.95 mm in diameter, with a Gaussian energy distribution. It has a short treatment time of 2 seconds per diopter. The system has an infrared high-speed camera operating at 400 Hz to track the patient's eye movements that either compensates for changes in eye position or interrupts the treatment if the eye moves outside a present predetermined range. The tracker has automatic pupil cantering and an integrated cross-line projector for alignment of the head and eye position, with a "NeuroTracker" for cyclotorsion control for the wavefront-optimized algorithm. Its eye-tracker system and laser trigger are synchronized. Its optimized ablation profile is designed to maintain a more natural corneal shape by adjusting for the asphericity of the cornea based on the anterior curvature readings (providing more treatment to the periphery than centrally), and minimizing the amount of spherical aberration induced during surgery (24, 25). The laser also features the ability to perform custom treatments (topography guided). The company supplies a nomogram chart, which recommends a standardized reduction in treatment for high degrees of myopia and cylinder. For low myopia, an increase in treatment is recommended instead (Table 1).

Schwind Amaris is a flying-spot excimer laser with a pulse repetition rate of 500 to 1050 Hz depending on the laser model and produces a beam size of 0.54 mm Full-Widthat-Half-Maximum (FWHM) with a super Gaussian ablative spot profile. It has a short treatment time of less than 2 seconds per diopter. Inside the software package the laser is able to perform aspheric and custom (topography and ocular guided) treatments. Its aspheric ("Aberration-FreeTM") ablation algorithm is designed to maintain the preoperative levels of ocular higher-order aberrations (26-29).

Aspheric aberration neutral (30) (Aberration-FreeTM (31) profiles are not based on the Munnerlyn proposed profiles, (32) and go beyond that by adding some aspheric characteristics to balance the induction of spherical aberration (prolateness optimization). The profile is aspherical-based, including a multidynamic aspherical transition zone, aberration and focus shift compensation due to tissue removal, pseudo-matrix based spot positioning, enhanced compensation for the loss of efficiency, and intelligent thermal effect control; all based on theoretical equations validated with ablation models and clinical evaluations.

Depending on the planned refractive correction, approximately 80% of the corneal ablation is performed with a high fluence level (>400 mJ/cm^2) and this leads to a considerable reduction in time spent treating the cornea. Fine correction is performed for the remaining 20% of the treatment using a low fluence level (<200 mJ/cm^2), aimed to reduce the amount ablated per pulse and smooth out the ablated stromal bed. The laser features a six-dimensional 1050 Hz infrared eye tracker with simultaneous limbus, pupil, iris recognition, and cyclotorsion tracking integrated in the laser delivery process (Table 1).

Mel (Carl Zeiss Meditec AG, Jena, Germany) – available in two laser models (Mel 80 and Mel 90–250 Hz, 500 Hz). Laser has Gaussian profile of laser beam with aiming spot of 0,7 mm. Overheating of corneal surface is controlled with nonrandomized arrangement of aiming spots, and atmosphere and homogenization of ejected gases over cornea is controlled with specially designed extension. On 500 Hz model eye tracker system works in infrared spectrum on a frequency of 1050 Hz, and registers limbus of cornea and edge of a pupil. Both models are equipped with software for custom treatments (33) (Table 1).

Star (Abbot Medical Optics, Santa Ana, California, USA) – Star S2, Star S3, Star S4 and Star S41R as newest model which beam has adjustable size of aiming spot that variates from 0,65 to 6,5 mm. Laser works on a frequency of 10/20 Hz, and has incorporated 3D iris recognition eye tracking system with speed of 60 Hz. Software program of the laser enables custom treatments also (34, 35) (Table 1).

Technolas 217z (Bausch & Lomb, Rochester, New York, USA) – Technolas 217z, Teneo 317 M2 are lasers that work with speed of 100 Hz with laser beam of truncated Gaussian profile and size of aiming spot of 2 mm. Thermal damage of corneal surface is controlled with overlapping form of aiming spots. Technolas 217z has 6D eye tracking system incorporated founded on iris recognition, and compensates movements on x/y/z axis, static and dynamic cyclotorsion, and iris movements. Software program besides custom treatments enables treatment of presbyopia with "Supracor" method (36-38). Newest model Teneo 317 M2 is flying spot laser capable of creating complex and customized treatments for all refractive errors and presbyopia. It works with speed of 500Hz, size of aiming spot of 1 mm and eye tracking system at frequency of 1,740Hz (39).

Nidex Quest/EC-5000 CX III (Nidek CO Ltd, Gamagori, Japan) – is "scanning slit laser" which cuboid beam is divided into six equal aiming spots with 1 mm size Gaussian profile. Laser works on 100 Hz frequency and has incorporated 6D eye tracking system, speed of 1 kHz. Software program enables custom ablations (40) (Table 1).

6. CONCLUSION

The review article concludes that modern excimer laser refractive surgery is an exciting field of medicine that provides ophthalmologists with a tool to lessen or eliminate patients' dependence on glasses and contact lenses. The field is a dynamic one with the introduction of newer, more advanced technology and surgical techniques at a rapid pace. These advances should enable refractive surgeons to treat patients with higher levels of nearsightedness, astigmatism, and hyperopia in the near future. The technology of excimer lasers has become so excellent and safe that it has been approved by the US military for use in soldiers, navy pilots, and in NASA astronaut candidates (41).

Quality of life studies have demonstrated that it has transformed and improved the quality of life of millions of people (42).

- **Author's contribution:** Ajla Pidro gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. Each author had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.
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