Are nanotechnology and robotics alternatives for therapeutic and theragnostic ophthalmic applications technologies for eye care services

Patricia Durán Ospina[1,2,*]

[1]*Fundación Universitaria del Área Andina Seccional Pereira, Research Group, Visual Health, Colombia*

[2]*Microbiologist, Universidad de los Andes, Colombia*

Abstract: *Objective*: To identify new technological advances in biotechnology, nanotechnology and robotics and their application in diagnosis and therapeutics for visual health.

Methodology: The systematic review was made in Journal of Engineering, Journal of Biomedical Nanotechnology, NIH Public Access, Investigative Ophthalmology & Visual Science, Intechweb open access journal and books, among others for a total review of 43 articles and 6 books. The databases used were: NLM Catalogue, (NCBI), Scirus, CiteSeer and open access (Intechopen, Hindawi) with the advances in nanotechnology, artificial vision and robotics applied to visual health.

Results: Retina implants, ocular memristors, ocular electrodes and chips, digital cameras and smart phone applications for low vision patients are some of the new alternatives in technology for the diagnosis based on biotechnology and nanotechnology and on the several years of job of interdisciplinary and multidisciplinary researchers of different fields to make innovation useful for visual impairment, ocular microbiology and molecular immunodiagnostics. The FDA recently approved the retina implants and this opened a new field to allow converting light signals into electrical signals. On the other hand, in the field of pharmacology, ocular nano-carrier molecules for sustained release of drugs and other devices to vitrectomies are some of the significant health advance studies for the future in visual health. Additionally, in the field of contact lenses and artificial corneas: biopolymers for biosensors have been developed for early detection of keratoconus and systemic diseases.

Conclusions: Nanotechnology, biotechnology, robotics and bio-molecular biology are emerging and convergent sciences that when applied to visual sciences will be helpful for the patients, and are an increase in papers on innovation of this field, involving a multidisciplinary team requiring new divulgation in the role and performance of the visual health professionals of the future. To know and divulgate these new technologies is important for continued joint efforts around global education, and to create a database with new keywords, in order to know who and where these innovations are improving around the world, to planning researcher mobility and to include these new valuable technologies in the curriculum of visual health and get the patient safe.

Keywords: Nanotechnology, Memristors, Nanopolymer, Nancocarrier, artificial vision, biosensors, Retinal implants, Ophthalmology, Visual Sciences, theragnostic, contact lenses, ocular biopolymers.

INTRODUCTION

Emerging and converging technologies are terms used interchangeably to indicate the emergence and convergence of new technologies [1] with demonstrated potential as disruptive technologies. Among them are: nanotechnology, biotechnology, information technology and communication, cognitive science, robotics, and artificial intelligence that have been launched as innovative products that promise to improve the quality of life and vision of patients with ocular compromised or low vision impairment. Some acronyms for these are:

NBIC: Nanotechnology, Biotechnology, Information technology and Cognitive science.

GNR: Genetics, Nanotechnology and Robotics.

GRIN: Genetic, Robotic, Information, and Nanotechnology.

BANG: Bits, Atoms, Neurons and Genes.

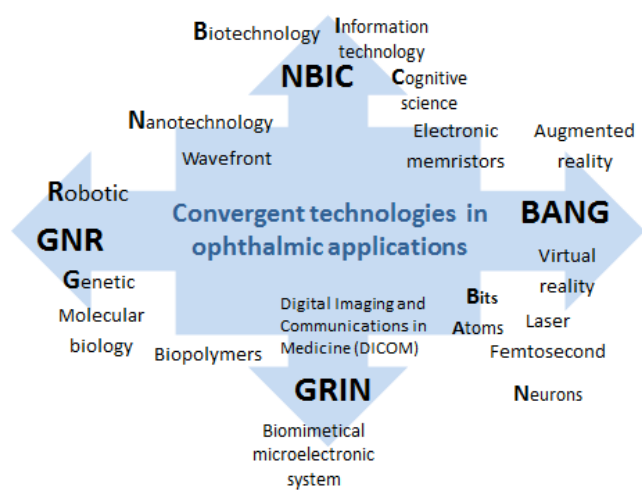

Figure 1: Map of "Convergent technologies" operated systems for ophthalmic applications: Now to the future.

*Address correspondence to this author at the Fundación Universitaria del Área Andina Seccional Pereira, Research Group, Visual Health, Colombia; E-mail: pduran@funandi.edu.co

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In the map of emergent technologies the nanotechnology, biotechnology, information technology and cognitive sciences (NBIC) leave open many sciences to come and help with these innovations and it requires visionary observers and researchers, in a transdisciplinary researching process, to create new alternatives in the prevention of blindness or diagnosis of ocular pathologies on time. In Ophthalmic surgery: wavefront, lasers femtosecond, and surgical instruments form part of these technologies, and more recently with the introduction of retina implants (Argus II), artificial corneas, and new molecular rapid tests for detection of ocular infections, diagnosis and therapeutics required team groups working as “global interactive researchers communities” of several research groups in a complex equipment and multiple labs trying to resolve blindness, improve surgical ophthalmic techniques, drug innovations and try to prevent harmful microorganisms in ocular infections, and improve new surgical techniques, among others.

Some indicators of these worldwide ophthalmic innovations are: applications to improve low vision, the creation of retinal implants, the application of biopolymers for creating artificial corneas, memristors: electronic devices for low vision and prosthesis for the retina among others. The implementation of mathematical models and the simulation of virtual reality systems, electronic devices known as MEMs (micro-electromechanical systems) based on models of augmented reality, are now possible. For some time, what was once considered as science fiction for bionic eyes, electronic implants are becoming more a reality and the technology must respond to specific visual disorders and impairments to restore vision. The challenge for institutions and researchers is to join groups around the world as a “collaborative investigation of groups that research global visual health” and work together within different disciplines. For ten or more years joint efforts and resources, revised university curricula, inclusion of masters and doctorates including those sciences that only a few years ago were reserved for biomedical or electronic engineers, but that today require ongoing communication between eye care professionals and other sciences such as electronic engineering, robotics and mechatronics to ensure that the devices meet the visual needs of the population. This article is a review of the products for innovative eye care coming to the market based on nanotechnology, robotics for visual health between now and the near future. The first studies of Nanotechnology were included by the Feynman physics at the annual meeting of the American Physical Society at the California Institute of Technology [2].

For many years, science has provided invaluable tools in eye care by creating diagnostic equipment (physics: interferometry, ultrasound, laser), and in chemistry and biotechnology advances (ophthalmic products for treatment and diagnosis, contact lens biopolymers, rapid diagnostic test based PCR). Recently, new advances in gene therapy, nanotechnology, retina implants and robotic surgery are entering ophthalmology surgery to restore low vision and to design rapid tests for molecular diagnosis of ocular diseases by means of molecular biology.

METHODOLOGY

A total of 89 articles were reviewed from 42 journals of Ophthalmology, Nanomedicine, Biotechnology, Ocular Therapy and Robotics. The databases used were: NLM Catalogue, (NCBI), Scirus, CiteSeer and open access (Intechopen, Hindawi) and the keywords were then selected: Nanotechnology, Memristors, Nanopolymers, Nanocarrier, biosensors, Retinal implants, ophthalmology, Chitosan, contact lenses, ocular biopolymers, theragnostic. Citations extracted from Software End Note V5. To control bias, the inclusion criteria for articles on Journals and Books were selected from Ophthalmics application including convergent technologies: 46 completed the inclusion requirements and six books were reviewed.

RESULTS

After the systematic review, the most relevant ophthalmic applications of the convergent technologies found were:

- Retina implants
- Drug delivery, nanocarriers, dendrimers for ophthalmic therapy
- Information technology and cognitive science.
- Intelligent contact lenses
- Theragnostic and rapid test diagnostics for detection of microorganisms and dry eye
- Stem cells
- Haptic and robotics for ophthalmology surgery and therapeutics

Some of the ophthalmic applications on those fields are listed on Table **1**.

Table 1: Review of Ophthalmic Applications of Emerging and Converging Technologies

TECHNOLOGIES	PRINCIPLE	OPHTHALMIC APPLICATION
Nanotechnology		
Nanoshells	Is a type of nanoparticles consisting of a dielectric core which is covered by a thin metallic shell. Involve a particle called plasmon which is a collective excitation or quantum plasma oscillation where the electrons simultaneously oscillate with respect to all the ions.	Drug delivery, ocular dispositive against microbe colonization Contact lens cases, Intraocular lenses
Nanotubes	Tubes at nanoscale (10-9mm) created by laser ablation creating "nanoarrays" to electrical transport mechanical properties.	Carbone nanotubes for ocular prosthesis Drug delivery Nanorecovers Ophthalmic and contact lenses
Memrtistors	Nanotransistors, nanotechnologic devices that allow ultrafast flash and "smart" memories. Memristors are electrical circuit, joining the resistor, the capacitor, and the inductor, that exhibit unique properties at the nanoscale. MEMS: micro-electro-mechanical systems.	Artificial retinas. Biomimetic model of outer plexiform layer. Neuro-ophthalmolgy. Replace tissues. Stimulate retina´s cells. Ocular diseases and therapeutic (theragnosis)
Nanocarriers Nanomicelles	Nanocarriers as a colloidal particulate systems with size ranging between 10 - 1000 nm such as of poly (D,L-lactic acid, PLA NPs), Nanomicelles as a nanomolecular aggregates with hydrophilic polar part and a nonpolar hydrophobic 50 nanometers in diameter, which allowed staying longer in the body and transporting protein and going through physiological channels that do not allow premature degradation in the body and provide longer lasting effects	Diagnosis, treatment and monitoring of various diseases. Enhance absorption of the ophthalmic drugs into a selected tissue, control the pharmacokinetic and drug tissue distribution profile and improve the intracellular penetration
Biotechnology / Molecular Biology		
Biopolymers	Biomaterial ensambled with steam cells and organical compounds	Bionsensors to detect ocular diseases Artificial Corneas Artificial Vítreo Intelligent contact lenses Ophthalmic drugs
Biosensors	Consists of two components: a bioreceptor and a transducer. Is a biomolecule that recognizes the target whereas the transducer converts the recognition event into a measurable signal. The uniqueness of a biosensor is that the two components are integrated into one single sensor	Detect ocular diseases, glaucoma, Intelligent contact lenses, detect photoreceptor degeneration, Rapid test for ophthalmic diagnosis
Stem cells	Biological cells found in all multicellular organisms, that can divide by mitosis and differentiate into diverse specialized cell types and can self-renew to produce more stem cells	Ocular tissue regeneration Corneal transplants Retina cell therapy Control Blindness
Information technology/Robotics		
Robotic	Is the branch of technology in relation with the design, application, construction and application of robots	Surgical instruments Ophthalmic haptics
Informatics Technologies (IT)	Is the application of computers and telecommunications equipment to store, retrieve, transmit and manipulate data	Tele-ophthalmology, Smartphone applications for low vision, integration to retina camera and diagnosis exams
3 D model and simulation software	Are graphics that use a three-dimensional representation of geometric data is stored in the computer for the purposes of performing calculations and rendering 2D images.	Design of surgical trainers for acquisition of ophthalmic skills, prototypes for future ophthalmic innovations
Cognitive sciences		
Cognitive sciences	Interdisciplinary study of mind and intelligence, embracing philosophy, psychology, artificial intelligence, neuroscience, linguistics, and anthropology	Visual cognitive neurosciences Artificial Intelligent Vision rehabilitation Low vision

Retina Implants

In France, at lab LIS-CEA, Saclay, retinal implants have been studied based on diamond nanomaterials and nanoparticles. The capabilities of many digital electronic devices and computer employees who respond to Moore's Law (processing speed, memory capacity, number of pixels) used in digital technology evolves towards the development of memristors (memory transistors, transistors that once inspired the creation of the cardiac pacemaker), which are nanotechnological devices that create intelligent flash. Since 1971 the concept introduced by Leon O. Chua has been developed as a model of neural networks, which are a biomimetic model of the retina that could even deliver 3D signals [3].

The introduction of microchips with silicon, known as a ”wafer”, was an open minded project to develop a biological and electronic device, as functional circuits that interact with living cells, it is the promise for now and the future [4]. Researchers are building tiny three-dimensional models of human organs that can be used for treatment, as well as replace costly and time-consuming animal studies that currently hamper drug development. Also, the Micro-electromechanical systems (MEMs) allow developed tests by providing increasing complexity for cell culture without having to use a whole tissue [5]. These biomimetic microsystems can replicate the functions of the organic structure and replace the functions of a complete tissue, and this is so useful to replicate mechanical and biochemical functions of blood and tissue as a nano-lab on a chip. Recently, these microsystems can be used to verify pharmacological effects of drugs, by replacing the animal model and just use tissue tests [6].

For more than ten years, physicians have been working with an interdisciplinary research group on the project: Second Sight's Argus II. A retinal prosthesis developed by Second Sight, Inc., with funding from the National Eye Institute, was recently recognized by the United States Patent and Trademark Office (USPTO), by the FDA in 2012 in the U.S.A. and by the European Union. It consists of a camera that captures images through implanted electrodes that stimulate cells in the retina, producing light in the field of vision of the patient, This camera mounted on a pair of eyeglasses wirelessly (it now has 60 electrodes with the hope for 1500), with a microelectrode array consisting of 200 μm diameter disc electrodes, an inductive coil link used to transmit power and data to the internal portion of the implant, an external belt worn with a video processing unit (VPU) and a miniature camera mounted on a pair of glasses which act as photodiodes sensitive to light, so that the chip is more sensitive, the video camera captures a portion of the visual field and relays the information to the VPU. The VPU digitizes the signal in real-time, applies a series of image processing filters, down-samples the image to a 6×10 pixelated grid, and creates a series of stimulus pulses based on pixel brightness values and look-up tables customized for each subject. The system is implanted in the retina and permits recognition of simple objects, track movement

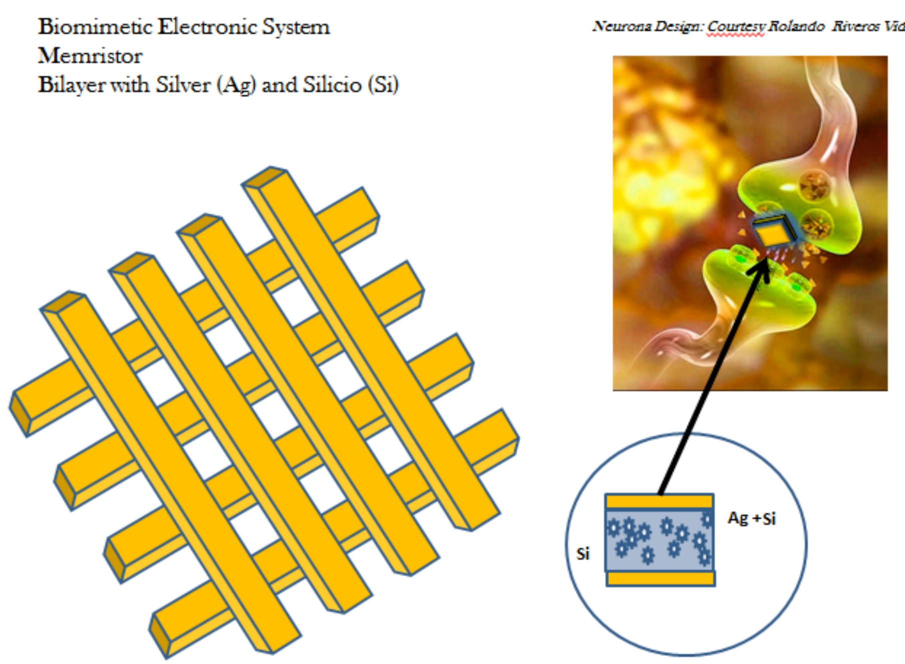

Figure 2: Schematic model of a memristor.

and objects while walking. In the U.S.A. 28 subjects with light perception vision that received the implant were monitored and evaluated. Multiple blind subjects fitted with the Argus II system consistently identified letters and words using the device, indicating reproducible spatial resolution [7].

Drug Delivery, Nanocarrier, Dendrimers for Ophthalmic Therapy

Other developments at the level of visual health pharmacology is the finding of nanocarriers for drug delivery. Among the most recent findings include:

Nanomicells

Nanomolecular aggregates with hydrophilic polar part and a nonpolar hydrophobic 50 nanometers in diameter, which allowed staying longer in the body and transporting protein and going through physiological channels that do not allow premature degradation in the body and provide longer lasting effects. As an example, the chitosan nanomicells are used for ocular drug delivery [8].

Nanocarriers

For topical preparation nanocarriers of poly (D,L-lactic acid, PLA NPs), those nanoparticles with 5-fluorouracil permits that for the small dimension and shape of nanoparticles, can penetrate the vitreous humor in the same way, there is not significant interaction between mucin and PLA NPs. Another carbohydrate acting as a nanocarrier is the introduction of non-polymeric permeabilizers in the permeation of acyclovir across excised rabbit cornea. The use of this with acyclovir contributes to solve problems with its solubility in tear fluid at the physiological pH of 7.4. As soon as the instillation is made, the physiological pH of the tear fluid is restored [9].

Dendrimers

Macromolecules of high stability to transport drugs which have recently been proposed as vectors for gene delivery, contrast agents for molecular imaging and nanocarriers.

Nanoparticles

As polymer spheres are nano-capsules or devices that allow the drugs to be surrounded by a single layer or be nano-matrices to prevent fungal growth or microorganisms such as nano-coatings [10], [11]. Most are made from metal ions like silver and are used to reduce biofilm and adherence of microorganism to contact lens cases.

Carbon Nanotubes

Cylindrical structures composed of layers of graphite or carbon material rolled and function as bioactive peptides, proteins, nucleic acids or drugs that release their load in the target cells. Being low toxicity molecules enables controlled drug release [12].

Polymer Conjugates

Systems for delivering drugs that fall into two major subgroups, polymer-protein conjugates or polymer-drug, which are formed by polyglutamic acids, polysaccharides, polyethylene and allow to only act in the target cell [13,14].

Theragnostic

The term theragnostic test is herein defined as a molecular test that is integrated in the drug development process so as to guide patient selection and drug treatment protocols. It is based on subtle genotypic or phenotypic variations, including nucleotide or amino acid substitutions at the level of DNA, RNA or protein. In ophthalmology it has been useful for oxidative stress treatment, measurement of intraocular pressure and treatment of new vessels, prevent scarring after glaucoma surgery and retinal degenerative diseases [15].

Some progress of these new technologies in ocular pharmacology include cyclosporine [16], the CF-101, A-3 oral receptor adenosine agonists, corticoids with iontophoresis EGP-437, low doses of bromfenac among others, an LFA-1 antagonist and anti-inflammatory secretagogue for corneal hydration, and the introduction of chitosan, a linear polysaccharide composed for β-(1-4)-linked D-glucosamine and N-acetyl-D-glucosamine and made by treating shrimp and other crustaceans shells with alkali sodium hydroxide [17-21].

Information Technology and Cognitive Science

The advances in digital images, interferometry and ultrasounds, permits now a better differential diagnosis and let *in vivo* to observe ocular malfunction. One of those examples are optical coherence tomography (OCT) and ultrasound biomicroscopy (UBM) which have enhanced the surgeon's ability to localize pathology both pre- and intra-operatively. Simultaneously, the approved femtosecond laser devices have been optimized for wound construction, capsulorhexis creation, and nucleus breakdown during cataract surgery. New utilities and the integration of a robotic system with OCT have been proposed for vitreoretinal surgery, and the addition of laser technology would facilitate automation of surgery to treat cataracts.

Intelligent Contact Lenses

To prevent biofilm adherence, silver nano-film has been developed of one cleaning solution preserved with alexidine. The cases and containers will be protected with silver nanofilm in order to prevent the adherence and colonization of microorganisms. Special studies will be developed with fungus sp. and not just bacteria; because the fungus keratitis is more aggressive at the corneal stromal in contact lenses users. Researchers in this fiel, also recognize that the original Fusarium keratitis epidemic of past years remain unclear [22]. Also, mixed infections may occur in contact case lenses between bacteria and fungus and infect post-keratoplasties transplants [23].

Other applications have been in contact lenses, with the implementation of diagnostic sensors to measure the corneal curvature changes caused by changes in intraocular pressure *via* two antennas with wireless communication and integrated electronic circuits compatible with biopolymers, the great challenge is the integration of special circuits that are not toxic to the ocular surface. Nowadays, LEDs aluminum gallium arsenide are toxic materials which cannot therefore be used for this purpose, additionally, these polymers must be fully transparent [24].

Recently, one of the most recognized ophthalmological research groups joined together in the project Prosthetic Replacement of the Ocular Surface Ecosystem (PROSE). Treatment in the Boston Foundation for sight prosthetic devices, PROSE consists of a transparent domo made of RGP contact lens material that permits oxygen to reach the cornea and fit under the eyelids and rest on the sclera vaulting the damaged cornea and creating a new smooth optical surface that protects the eye from the environment and blink trauma. As a liquid reservoir inside the domo, they are filled with sterile saline that remains in the devices. PROSE creates a new transparent, smooth optical surface over the irregular, damaged or diseased cornea, expanding the artificial tear reservoir that provides constant lubrication while maintaining it necessary for the treatment of several ocular dysfunction as dry eye, limbal stem cell deficiency (aniridia, Steven Johnson, thermal injury, conjunctivitis) [22].

In Switzerland, the Triggerfish® sensor is a soft single-use contact lens with embedded strain gauges to measure fluctuations in IOP at the junction between the cornea and sclera. Also embedded are the telemetric chip and micro-loop antenna for wireless reception of power and data output. The signal sent from the micro-antenna is directly correlated to changing IOP (Sensimed 2010).

Effective monitoring involves wearing the Triggerfish® system for up to 24 hours during which the patient carries out normal activities, including sleep. The system comprises the contact lens sensor, a flexible adhesive antenna which fits around the eye, and a recorder which is connected to the antenna *via* a thin, flexible data cable. At the conclusion of 24 hours, data is uploaded wirelessly *via* Bluetooth connectivity to a practitioner's computer for assessment [25].

Everyday more and more scientific literature reports that the future of "smart contact lenses" show a lot of varieties for detection of diabetes and communication options in the most attractive advances [26].

Rapid Diagnosis Test for Detection of Microorganisms and Dry Eye (Theragnosis)

For rapid diagnosis of adenoviral conjunctivitis with direct sampling microfiltration, similar to a pregnancy test, using incorporated colorimetric: blue control line is negative, and a red test line is positive for adenoviral particles (AdenoPlus, Rapid Pathogen Screening Inc.), which detects the most common cause of viral and validation and gold standard tests are on research with 128 patients. The procedure consists of the collected results with the test adenoviral and requires just 10 minutes to obtain results. It will be so helpful for differential diagnosis "in situ" in primary ocular care, because epidemiological of ECK, (epidemic keratoconjunctivitis) is a frequent misdiagnosis with allergy or bacterial conjunctivitis and will be a good alternative for adequate treatment [27].

In other important efforts to detect dry eye "in situ", another rapid test is being developed by the same researchers (InflammaDry, Rapid Pathogen Screening Inc.) to detect matrix metalloproteinase 9 (MMP9), a biomarker of inflammation expressed in dry eyes. He said it is important to detect the condition for patient comfort, for preventing ocular morbidity, and for other management decisions.

To test InflammaDry, researchers enrolled 143 patients aged 18 years or older with clinical signs and symptoms of dry eyes and 63 healthy control individuals. All were assessed and determined to have dry eyes or to be healthy using the Ocular Surface Disease Index. Also it detects MMP9 in 10 minutes greater than40 ng/mL. Previous studies have shown that the severity of dry eye correlates well with the level of MMP9 in the tears. [28].

Stem Cells

The theragnosis based on subtle genotypic or phenotypic variations, including nucleotide or amino acid substitutions at the level of DNA, RNA or protein is oxidative stress treatment, measurement of intraocular pressure and treatment of new vessels, prevent scarring after glaucoma surgery and retinal degenerative diseases. And on a molecular basis, stem cells also contribute to therapy in glaucoma and other applications. The human adipose tissue is a source of multipotent stem cells. Preparations of lipo-aspirates cells can differentiate into osteogenic, adipogenic, muogenic, neurogenic as mesenchymal stem cells. The orbital adipose stem cell population are starting to study derived embryological from neural crest cells, versus adipose tissue throughout the body which is generally mesodermal in origin. The eyelid, therefore, provides a unique place to compare orbital stem cells (nasal fat pad) with fat more similar to systemic adipose tissue (central fat pads). Mesenchymal stem cells transplanted into the vitreous body in a rodent model of glaucoma showed considerable capacity to protect retinal ganglion cell degeneration. This did not require any differentiation or integration of the transplanted stem cells. Similar results including RGC neuro-protection have been demonstrated in models of retinal ischemia. As a cell replacement therapy for glaucoma; stem cells face a much tougher set of hurdles. Optimal cellular integration may be limited by immune reactivity, response to injury, or factors found in development but missing in the adult microenvironment.

Stem cell replacement for ophthalmic of ganglion cells integrate with their presynaptic cells in the retina to receive visual information, and project their axons down the optic nerve and properly wire up with their targets in the lateral geniculate nucleus of the thalamus and other regions of the brain [29, 30].

Haptics and Robotics for Ophthalmic Surgery and Therapy

Recently the effect of “Nano surgeries” in the vitreous, robots consist of the introduction of biological fluids as MEMS: Micro-electro-mechanical systems that do not require a replaceable total vitreous and are less invasive, and only require monitoring with another chamber.

But at the same time new surgical instruments must be developed and patented to be appropriate for the insertion of these required micro and nano insertions. Researchers of Society of Photo-optical Instrumentation Engineers (SPIE) have presented an ophthalmic instrument for innovative analyses of the eye microcirculation. The developed system employs a laser source to perform the DWS (diffusing-wave-spectroscopy) analysis of the light intensity back diffused by the ocular fundus structures, thus allowing a noninvasive detection of changes and modulations of both optical and dynamical properties of blood flow. The reported preliminary experimental results recorded in-vivo on rabbits' ocular fundus, demonstrate the ability of the system to detect nano-micro-aggregates carried by the blood flow in the ocular fundus.

The Da Vinci Project, which incorporates robotic surgery, has already begun work on robotic surgery in ophthalmology. The California group Jules Stein Eye Institute at the University of California and the Center for Advanced Surgical and Interventional Technology, recently published advances in ophthalmic surgery. In Colombia, several institutions already exist with Da Vinci, so it would be interesting to train health professionals in these new technologies to improve the quality of life of patients. The U.S. Food and Drug Administration approved the Implantable Miniature Telescope (IMT), which works like the telephoto lens of a camera in 2010 [32, 33].

For less standardized procedures, such as vitreoretinal surgery, robotic augmentation could ultimately increase efficiency, amplify scale to allow performance of otherwise difficult tasks (e.g. sub retinal delivery of medication or stem cells), decrease complication rates by reducing tremor and increasing precision, and permit tele-surgical care in remote locations. Several obstacles remain before robotic surgery will become a clinical reality in ophthalmology. High cost, a steep learning curve, and patient trust all present individual challenges. The surgical procedure involves removing the eye's natural lens, as with cataract surgery, and replacing the lens with the IMT.

DISCUSSION

Eye health must turn our attention to new developments in order to take pause and review classrooms to include physical theories in the teaching curricula, for example, physics memristors, nano-devices, and augmented reality in order to wake up the future eye care professionals, and to give visual health research groups more transdisciplinary scenarios and less segmented. To describe the biological sciences as "nanos", create new languages such as the nano-polymer for visual health as alternatives for patients with visual difficulties. As visual health researchers we should include in our search engine: augmented reality for the blind, visual tele-rehabilitation, diagnostic applications in molecular biology and visual applications, optical coherence tomography, nano-polymers, among others, to be eyeopeners to multidisciplinary research projects in ophthalmology.

How to incorporate this technology in our country? First with high-level academic training in doctorates, have the possibility to make strategic monitoring to see which devices are effective, or that is required in our environment according to the visual needs of the country and try to make innovations that will meet those needs. State investment is required, partnerships with universities and private companies to implement, build and test these findings, as we break the learning technology segmented gaps, isolated research and build partnerships among universities with high-tech experts in institutes in these countries. Although the items for transfer in science and technology have improved, alliances between transnational research groups should be a priority to bridge the gaps. Elsewhere on curriculum flexibility, to be able to include some internships between biomedical engineers, electronic engineers and to support programs of Faculties of eyecare with different elective disciplinary programs, to expand our horizons with electronics engineers or to allow a master's level training to share experiences, or encourage the development of collaborative working groups, is another way for research groups from the Universities to open doors to training and curricular flexibility to improve quality of life and safety of patients requiring eye treatments or diagnostic advantage of new technologies in the population.

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