VISUAL IMPLANTS IN END STAGE OCULAR DISEASES

ESSAY

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المغروسات البصرية وعلاج أمراض العين المتأخرة

رسالة

توطئة للحصول على درجة الماجستير في

طب وجراحة العيون

مقدمـــة من

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LIST OF ABBREVIATIONS

AOS	**:**	Accessory Optic System
ARMD	**:**	Age-Related Macular Degeneration
CNS	**:**	Central Nervous System
DC	**:**	Direct Current
DTN	**:**	The Dorsal Terminal Nucleus
EEPs	**:**	Electrically Evoked Potentials
EPs	**:**	Electrical Potentials
ERS	**:**	Epiretinal Stimulation
FAZ	**:**	Foveal Avascular Zone
IPL	**:**	Inner Plexiform Layer
LGN	**:**	Lateral Geniculate Nucleus
LTN	**:**	The Lateral Terminal Nucleus
mC	**:**	milliCoulombs
MTN	**:**	The Medial Terminal Nucleus
nC	**:**	nanoCoulombs
NOT	**:**	Nucleus of the Optic Tract
OCT	**:**	Optical Coherence Tomography
OKAN	**:**	Optokinetic After-Nystagmus
OKN	**:**	Optokinetic Nystagmus
OPL	**:**	Outer Plexiform Layer
PFCL	**:**	Perfluorodecaline
PMMA	**:**	Polymethyl-Metacrylate
RGC	**:**	Retinal Ganglion Cells
RP	**:**	Retinitis Pigmentosa
RPE	**:**	Retinal Pigment Epithelium
SC	**:**	Superior Colliculus
SRS	**:**	Subretinal Stimulation
STS	**:**	Suprachoroidal-Transretinal Stimulation
VI	**:**	Primary Visual Cortex

ABSTRACT

Artificial vision uses electrical stimulation to drive neurons of the visual system, which are depleted from their natural input. Usually, electrical stimulation is provided in such concepts by implants consisting of an array of stimulating electrodes and electronic components, e.g., for pulse generation. Two main concepts evolved, **one** is that the optic path of the eye is still used to transmit visual information. In the **second** concept, visual information is obtained by a camera system. This information is then further processed depending on the level of the visual system where the stimulation is intended.

Key Words:

Artificial vision-visual implants-phosphens.

INTRODUCTION

The idea of replacing a dysfunctional or missing body part with prosthesis is perhaps as old as the history of humankind; yet, it still continues to be a fascinating theme. While early prostheses were limited to external organs (e.g. wooden legs), the twentieth century witnessed the implantation of numerous devices inside the human body, some of which have since become routine surgical procedures. For external prostheses, both proper fitting and functionality are needed to make a device acceptable for use; however, internally implanted prostheses have additional challenges, and the implantation of intelligent devices which interact with surrounding tissues is even more difficult ***(Ameri et al, 2007).***

As scientists began to understand electricity and apply it to living things, this knowledge improved understanding of human body systems and eased human suffering .in the nineteenth century, Galvani and Voletrra performed experiments demonstrating that both muscles and the auditory system responded to electrical stimuli. Those reports demonstrated that the human body is an electrical system and that electricity may have therapeutic uses. Electrical stimulation continuous to find valid therapeutic application in the human body. However therapeutic electrical stimulation to treat disease is not the same as electrical stimulation to replace lost function, and the two should not be confused ***(Weiland and Humsyun, 2003)***

Historically, several methods of supplementing remaining functional vision had been pursued via interventions at several points along the visual pathway, including the retina, optic nerve, and occipital cortex.The concept of electronically stimulating the nervous system to create artificial vision was first introduced in 1929 when Foerster et al observed that electrical stimulation of the visual cortex caused his subject to detect a spot of light (phosphene) they demonstrating that the spatial psychophysical location of this phosphene depended on the location of the electrical stimulation point over the cortex ***(Foerster, et al, 1929).***

The first serious effort of establishing an electrical artificial vision system was undertaken in the 1960s by *Giles Brindley*. *Brindley's* implantation of an 80 electrode device on to the visual cortex of a blind patient revealed the possibilities of electrical stimulation to restore vision and the barriers to implantation of a suitable device. Brindley pioneering work had influencing all subsequent major effort in the area of electronic visual prosthesis .in the past 50 years exponential advances in our understanding of electronics, physiology, and medicine have enabled the development of implantable micro electronic system that overcome the shortcoming of *Brindley's* large immobile visual stimulator ***(Brindley, 1965).***

Many cases of intractable vision loss arise from selective photoreceptor degeneration. Retinitis pigmentosa (RP), for example, causes the loss of up to 95% of the photoreceptor layer, but spares up to 80% of the inner nuclear layer and 30%of the ganglion cell layer ***(M.S.Humayun et al, 1999)***. Similarly, patients with age-related macular degeneration (AMD) can lose up to 70% of photoreceptors with no loss of other retinal cell types ***(S.Y.Kim et al, 2002).***

Until now, there is no known successful medical treatment to cure the tissue and renew the visual faculty ***(E. Zrenner et al, 2002).*** Thus, a visual prosthesis is used to bypass the damaged neural tissue using electrical stimulation to artificially deliver visual information to surviving retina. The different concepts apply electrical signals to the visual cortex ***(W.H Dobelle et al, 2000)***, the optic nerve ***(C.Verrart et al, 1998)*** or to the retinal tissue ***(H.G. Graf et al.2007).***

AIM OF THE WORK

To review the efficacy and safety of microelectronic visual implants in diseases that potentially benefit from the application of retinal implants as hereditary pigmentary degeneration (retinitis pigmentosa) and acquired macular diseases as age related macular degeneration.

ANATOMY OF THE RETINA

The retina remains the best studied part of the human brain. Embryologically part of the central nervous system but readily accessible to examination, it can be investigated with relative ease by both scientists and clinicians ***(Duke-Elder et al, 1963)***. Moreover, an estimated 80% of all sensory information in humans is thought to be of retinal origin, indicating the importance of retinal function for the ability to interact with the outside world ***(Sharma, Ehinger, et al, 2003).***

I. Topographic Organization of the Retina:

The retina proper is a thin, delicate layer of nervous tissue that has a surface area of about 266 mm. the major landmarks of the retina are the optic disc, the retinal blood vessels ,the area centralis with the fovea and foveola, the peripheral retina (which includes the equator)and the ora serrata . the retina is thickest near the optic disc ,where it measures 0.56mm. It becomes thinner towards the periphery, the thickness reducing to 0.18mm at the equator and to 0.1 mm at the ora serrata ***(Ogden, 1989).***

The optic disc

In the normal human eye the optic disc is a circular to slightly oval structure that measures approximately 1.5 mm in diameter. Centrally it contains a depression which is known as the physiological cup ; however, the size and shape of this excavation depends on several factors such as the course of the optic nerve through its canal, the amount of glial and connective tissues ,the remenants of the hyaloid vessels and the anatomical arrangement of the retinal and choroidal vessels ***(Born et al,1997***).

Area centralis:-

The adult *posterior pole* (anatomic macula or area centralis) is about 4.5–6 mm in diameter, centered on the fovea, and located between the superior and inferior temporal arcades. The *macula* (anatomic fovea centralis) is located approximately 3 mm temporal to the optic disc and is about 1.5 mm, or one disc size, in diameter (***Kincaid, M.C., et al, 1999).***

The fovea:

The most central part of the macula, the *fovea* (anatomic foveola), is formed by a central, circa 0.35 mm wide depression and represents the retinal region of greatest visual acuity ***(Oyster et al, 1999)***. The foveola has the highest density of cone photoreceptors (199,000/mm2), which are narrowed and elongated in this location to maximize light detection further ***(Curcio, C.A. et al, 1990)***. Because of its special histological organization, the posterior pole is subdivided into four concentric regions: the perifovea, the parafovea, the foveal slope, and the foveola ***(Provis, J.M.et al, 2005).***

The foveola itself is created in two opposing tissue migrations: the slow peripheral displacement of the inner nuclear and ganglion cells, while red and green cone photoreceptors in the surrounding outer retina migrate towards the foveola ***(Hendrickson, A.E., 1993).*** As a result of these migrations, the fovea thins and forms a central depression, the foveola. The foveola is populated by cone photoreceptors and Müller cells only. Rods are excluded from the foveolar depression, so are blue cones, all ganglion and inner retinal cells, blood vessels, and other glial cells ***(Provis, J.M.et al,2005).***

Ganglion axons from the temporal retina do not cross the fovea, but arc around the fovea.The central 500 mm of the fovea contains no retinal capillaries (the *foveal avascular zone [FAZ]*, making the fovea dependent on blood supply from the choriocapillaris ***(Provis, J.M.et al,2005).***

The functional consequence of this extreme specialization of foveal organization is that, though maximal central visual acuity can be generated in a very small area of the entire retina under photopic conditions, visual acuity is already halved at 1° eccentricity, quartered at 5° eccentricity, and is brought to less than 10% outside the temporal arcades, while the rod-free foveola is functionally blind under extreme scotopic conditions (***Oyster, C, 1999).***

<u>The peripheral retina:</u>

Comprises the remaining retina outside the temporal retinal arteries. Anatomically, the peripheral retina possesses only one layer of ganglion cells. The ampullae of the vortex veins lie just posterior to the equator, while the long posterior ciliary arteries and nerves mark the horizontal meridian. The *ora serrata* delineates the anterior termination of the sensory retina and the beginning of the pars plana of the ciliarybody ***(Hendrickson, A.E. et al, 1994).***