**The Bionic Eye: A Review of How Close we are to Replacing the Human Eye.**

Khadija S. Shahid, OD, FAAO, Ben Szirth, PhD

A. Visual Pathway
    a. 130 million Photoreceptors (PR)
    b. Horizontal, Bipolar, and Amacrine Cells
    c. 1.2 Million Ganglion Cells (GC).
    d. Lateral Geniculate Nucleus (LGN)
    e. Optic Radiations, Visual cortex (V1)

B. Visual Prosthetic Target Sites
    a. Retina
        i. Retinitis pigmentosa (RP), Age-related macular degeneration (AMD)
        ii. Retinal Target Site: GC and PR (epiretinal and subretinal space)
    b. Optic Nerve
    c. LGN/Visual Cortex
        i. TBI, Hemi vision and wartime injuries (30% of all casualties are head and neck)

C. Three Physiologic Principles of Visual Prosthetic:
    a. (1) Electric currents can substitute light photons in producing visual sensations (phosphene).
    b. (2) Most etiologies of blindness leave upstream structure intact.
        i. Up to 30% of retinal GC in RP patients can survive, even after several years of blindness.
    c. (3) Retinotopic organization of target neural structure: the retinal map is not lost when a subject loses sight.

D. Simulating Prosthetic Vision
    a. Limitations
        i. Vision, perception of phosphenes, visual comprehension.
        ii. Visual gaps, visual scene.
        iii. Multiple phosphenes, stimulating sites, uneven phosphene, limited contrast.
    b. Some essential features:
        i. Currents & waveforms
        ii. Encapsulation
        iii. Biocompatibility
        iv. Protection from stimulation
    c. Non essential, desired features

i. Data and power transmission
ii. Stimulus delivery
iii. Publishing specificities

d. Factors to consider
i. What is required for the subject to perform everyday tasks?
ii. What is required for 'depicting' a visual scene?
iii. What is required for adaptation/ optimum use of prosthetic vision
iv. Overloading patient with electronic information?

E. Human trial results to date
a. No standardized assessments exist
b. Subjects can recognize simple characters, objects and patterns.
c. Subjects can manipulate a high contrast environment.

F. Specific Task Requirements (ADL's)
a. Navigation: US National Research Council of Blind Pedestrian Needs (1996)
i. > 30 degrees VF would be ideal
b. Reading: Normal is >200 wpm.
c. Face recognition: larger phosphene lattice.
d. Smooth pursuit, tracking.

G. Review of existing Visual Prosthetic Systems
a. Overall results of all system trials
i. (1) Patients with implants have a crude level of visual perception
ii. (2) Problems with implants include availability of a power source, surgical complications, and long term viability;
iii. (3) No visual prosthesis has yet restored vision
b. Most prosthetic systems have similar system requirements:
i. Camera: to capture and digitize image information.
ii. Image processing: to reduce noise.
iii. Transmitter & receiver: to link the camera + image processor to stimulator + electrode array.
iv. Stimulator & electrodes: for stimulation or recording brain activity

H. Visual Prosthetic Systems by Target Site
a. Cortical and Intra Cortical
i. $18^{th}$ century – 1960's (Epicortical).

1. Otfrid Foerster, MD
2. Brindley & Lewin
3. Excessive electrode currents, irritated meninges and pain

ii. Intracortical stimulation: Localized, smaller electrodes, lower currents and less pain followed.

1. Artificial Vision System, Dobelle, described a cortical visual prosthesis system implanted for over 20 years.
2. The subject has a visual acuity of approximately 20/1200.
3. The Neuroprosthesis Program, NIH Bak et al.
4. Schmidt et al, 1996
5. The Utah Electrode Array (UAE), Richard Normann, University of Utah
6. The Cortical Implant for the Blind (CORTIVIS) 2001, Edwardo Fernandez, et al.
7. Intracortical visual prosthesis (Illinois Institute of Technology), Philip R Troy et al

b. Optic Nerve System

i. Veraart et al. Blind, RP subject.

ii. OPTIVIP, 2000-2004, Spiral-Cuff Electrode

c. Hybrid Retinal System

i. Micro-electrode and mechanical system

d. Subretinal System: between the RPE and PR

i. 1956, Australia

ii. Artificial Silicon Retinal (ASR), Optobionics. Chow et al.

1. No true, direct effect, possible retinal cell rescue effect, see Pardue et al.2005
2. Retinal Implant GmbH. Gekeler et al., 2007, and Dr. E. Zrenner

e. Epiretinal System: between vitreous and Internal Limiting Membrane (ILM), close to the GC.

i. Learning Retinal Implant, IIP-Technologies GmbH. Feucht et al., 2005

ii. Walter et al., 2005. Epi retinal stimulation of a cat.**Error! Bookmark not defined.**

iii. Rizzo and Wyatt, Harvard Medical School.

iv. EPI-RET, Gerding et al. 2007 (German research group, EPIRET 2 grant, German Ministry for Education and Research)

v. Intraocular Retinal Prosthesis (IRP): Dr. Mark Humayun, Doheny Eye Institute of USC, Second Sight Medical Products, Dept. of Energy National Laboratories.

1. Camera mounted on eye glasses (image capture) → Visual Processing Unit (translate image into pixilated form, then controlled patterns of electrical pulses) → Magnetic

Coils implanted in the temporal skull (transmits electrical pulses to the eye vial trans scleral wire) → Inductive link telemetry system → 16 platinum microelectrode array (sends impulses to viable inner retinal neurons) placed temporal to macula.

I. Visual Prosthetic System Comparisons: Advantages and Disadvantages

J. Intra Cortical Advantages

   f. Skull protection

   g. Long-term studies

   h. NOT limited to outer retina or optic nerve disease

K. Intra Cortical Disadvantages

   a. Lack of preliminary processing by the visual system

   i. Complex, individual visual cortex map

   j. Convoluted cortical anatomy

   k. Neurosurgery risks, seizures

L. Optic Nerve Implant Advantages

   a. Decreased surgical complications

   b. Not limited to outer retinal disease

   c. The entire VF is represented in one small area, (optic nerve)

M. Optic Nerve Implant Disadvantages

   a. Neurosurgery risks. Infection from external wires.

   b. Possible interruption of blood flow to the ON

   c. Requires functional ON pathway

   d. Retinotopic distribution

      i. challenges with retinotopic distribution of optic nerve.

   e. Complex electrode array

N. Retinal Implant Advantages

   a. Decreased surgical risk

   b. Less electrical stimulation: Proximal location

   c. Retinotopic organization preserved.

   d. Retinal and cortical signal processing.

   e. Neuronal plasticity? Could the retinotopic map reconfigure?

O. Retinal Implant Disadvantages

   a. Requires an intact visual pathway distal to the PR

b. Retinotopic organization
c. Retinal surgery risks
d. Encapsulation of the device.

P. Hybrid Implant Advantages
a. Artificial connection between CNS and Neural surface.
b. Electrode-neuron stability: firm cultured attachment prior to implantation

Q. Hybrid Implant Disadvantages
a. No long-term studies
b. Difficulty guiding axonal growth
c. No prototype

R. Subretinal Implant Advantages
a. Greater spatial resolution potential (positioned closer to retinal nerve cells)
b. Does not require mechanical fixation
i. Vacuum seal (forces between the neurosensory retina and RPE) created by RPE pumps.
c. Subjects can still utilize eye movements

B. Subretinal Implant Disadvantages
a. Nutrient block
b. External cables or electronics
c. Additional surgical risk of subretinal bleeding.
d. Requires intact optical media

B. Epiretinal Implant Advantages
a. Decreased risk of heat generation (position proximal to vitreous-- heat dissipation)
b. External camera, process and optimize signals
c. Slight decreased retinal surgical risk implanting and ex-planting
d. Does not require intact optical media
e. Long-term studies, survival of implant.

C. Disadvantages: Epiretinal Implant
a. Eye movements: stress of constant, normal ocular saccades (~17,000/ day) can destabilize implant.
b. Secure fixation of the implant on the retina.
c. Requires a higher electrical current than subretinal implant
i. Implants are being developed to generate their own electrical currents on stimulation
d. External image processor.

e. Adherence- cellular proliferation.

f. Retinotopic organization

D. Future Projects and Research

a. Concept: Neuronal/ brain plasticity may compensate for implant signal deficiencies, as seen in cochlear implant ("filling in the blank').

b. Transretinal stimulation

i. Transcleral, intrascleral, or suprachoroidal electrodes

1. Tokuda et al., 2007. Sclera pocket multichip for suprachoroidal transretinal stimulation.

c. Biocompatible carbon nanotubes (retinal prostheses)

i. Wang et al., 2006. Neural interfaces w. carbon nanotube pillars utilized as microelectrodes.

d. Implants with photosensitive dyes to generate impulses

e. Neurotransmitters to stimulate neurons via neural prostheses.

i. Peterman et al., 2004.

f. Other novel ideas

i. Palanker et al., 2005: optoelectronic system with theoretically increased pixilated densities.

Suggested readings


1. Alteheld N, Roessler G, Walter P. **Towards the bionic eye--the retina implant: surgical, opthalmological and histopathological perspectives.** Acta Neurochir Suppl. 2007;97(Pt 2):487-93.
2. Ameri H, Ratanapakorn T, Ufer S, Eckhardt H, Humayun MS, Weiland JD. **Toward a wide-field retinal prosthesis.** J Neural Eng. 2009 Jun;6(3):035002. Epub 2009 May 20.
3. Chader GJ, Weiland J, Humayun MS. **Artificial vision: needs, functioning, and testing of a retinal electronic prosthesis.** Prog Brain Res. 2009;175:317-32.
4. Chen SC, Hallum LE, Lovell NH, Suaning GJ. **Visual acuity measurement of prosthetic vision: a virtual-reality simulation study.** J Neural Eng. 2005 Mar;2(1):S135-45. Epub 2005 Feb 22.
5. Chen SC, Suaning GJ, Morley JW, Lovell NH. **Simulating prosthetic vision: I. Visual models of phosphenes.** Vision Res. 2009 Jun;49(12):1493-506.
6. Chen SC, Suaning GJ, Morley JW, Lovell NH. **Simulating prosthetic vision: II. Measuring functional capacity. Vision Res. 2009 Sep;49(19):2329-43.**
7. Cohen ED. **Safety and effectiveness considerations for clinical studies of visual prosthetic devices.** J Neural Eng. 2007 Mar;4(1):S124-9. Epub 2007 Feb 26.
8. Cohen ED. **Prosthetic interfaces with the visual system: biological issues.**J Neural Eng. 2007 Jun;4(2):R14-31. Epub 2007 Mar 14.
9. Cottaris NP, Elfar SD. **How the retinal network reacts to epiretinal stimulation to form the prosthetic visual input to the cortex.** J Neural Eng. 2005 Mar;2(1):S74-90. Epub 2005 Feb 22
10. Dowling J. **Artificial human vision.** Expert Rev Med Devices. 2005 Jan;2(1):73-85.
11. Gerding H. **A new approach towards a minimal invasive retina implant.** J Neural Eng. 2007 Mar;4(1):S30-7. Epub 2007 Feb 20.

12. Hossain P, Seetho IW, Browning AC, Amoaku WM. **Artificial means for restoring vision.** BMJ. 2005 Jan 1;330(7481):30-3.
13. Ifukube T. **Artificial organs: recent progress in artificial hearing and vision.** J Artif Organs. 2009;12(1):8-10. Epub 2009 Mar 29
14. Javaheri M, Hahn DS, Lakhanpal RR, Weiland JD, Humayun MS. **Retinal prostheses for the blind.** Ann Acad Med Singapore. 2006 Mar;35(3):137-44.
15. Hallum LE, Dagnelie G, Suaning GJ, Lovell NH. **Simulating auditory and visual sensorineural prostheses: a comparative review.** J Neural Eng. 2007 Mar;4(1):S58-71. Epub 2007 Feb 20.
16. Hallum LE, Suaning GJ, Taubman DS, Lovell NH.**Simulated prosthetic visual fixation, saccade, and smooth pursuit.** Vision Res. 2005 Mar;45(6):775-88.
17. Lane SS, Kuppermann BD, Fine IH, Hamill MB, Gordon JF, Chuck RS, Hoffman RS, Packer M, Koch DD. **A prospective multicenter clinical trial to evaluate the safety and effectiveness of the implantable miniature telescope.**Am J Ophthalmol. 2004 Jun;137(6):993-1001.
18. Lepri BP. **Is acuity enough? Other considerations in clinical investigations of visual prostheses.** J Neural Eng. 2009 Jun;6(3):035003. Epub 2009 May 20.
19. Mokwa W. **An implantable microsystem as a vision prosthesis.** Med Device Technol. 2007 Oct;18(6):20, 22-3.
20. Normann RA, Greger B, House P, Romero SF, Pelayo F, Fernandez E. **Toward the development of a cortically based visual neuroprosthesis.** J Neural Eng. 2009 Jun;6(3):035001. Epub 2009 May 20.
21. Park RI.**The bionic eye: retinal prostheses.** Int Ophthalmol Clin. 2004 Fall;44(4):139-54.
22. Pérez Fornos A, Sommerhalder J, Pittard A, Safran AB, Pelizzone M. **Simulation of artificial vision: IV. Visual information required to achieve simple pointing and manipulation tasks.** Vision Res. 2008 Jul;48(16):1705-18. Epub 2008 Jun 24.
23. Primo SA. **Implantable miniature telescope: lessons learned.** Optometry. 2010 Feb;81(2):86-93.
24. Rizzo JF, O'Malley ER, Hessburg PC. **The eye and the chip 2008.** J Neural Eng. 2009 Jun;6(3):030201. Epub 2009 May 20.
25. Sakaguchi H, Kamei M, Fujikado T, Yonezawa E, Ozawa M, Cecilia-Gonzalez C, Ustariz-Gonzalez O, Quiroz-Mercado H, Tano Y. **Artificial vision by direct optic nerve electrode (AV-DONE) implantation in a blind patient with retinitis pigmentosa.** J Artif Organs. 2009;12(3):206-9. Epub 2009 Sep 19.
26. Suaning GJ, Lovell NH, Schindhelm K, Coroneo MT. The bionic eye (electronic visual prosthesis): a review. Aust N Z J Ophthalmol. 1998 Aug;26(3):195-202. Review.
27. Stingl K, Greppmaier U, Wilhelm B, Zrenner E. **Subretinal visual implants.** Klin Monbl Augenheilkd. 2010 Dec;227(12):940-5. Epub 2010 Dec 14. *Article in German*
28. Tehovnik EJ, Slocum WM, Smirnakis SM, Tolias AS. **Microstimulation of visual cortex to restore vision.** Prog Brain Res. 2009;175:347-75.
29. Van Rheede JJ, Kennard C, Hicks SL. **Simulating prosthetic vision: Optimizing the information content of a limited visual display.** J Vis. 2010 Dec 29;10(14). pii: 32. doi: 10.1167/10.14.32. Print 2010.
30. Wickelgren I. **Biomedical engineering. A vision for the blind.** Science. 2006 May 26;312(5777):1124-6.