Digital Electro-Optical Surgical Platform for Retina Surgery as a Replacement of Operational Microscopes

- Adiel Barak, MD
- Amir Manor, MD
- Ron Schneider
- Abraham Zeitouny, PhD
- Anat Loewenstein, MD

OBJECTIVE Evaluate the use of Elbit's digital electro-optical systems for generating detailed high quality video imaging during surgery, and thus improving the surgeons visualization, performance and outcome.

PURPOSE Elbit LTD Head Mounted Systems (EHMS) are produced for aviation incorporating tracking, processing and display information to the user. Our aim was to study the key system parameters of an adapted system developed for visualization of vitreo-retinal surgeries. EHMS incorporates software that process and display stereoscopic high resolution cameras video for vitreo-retinal surgery.

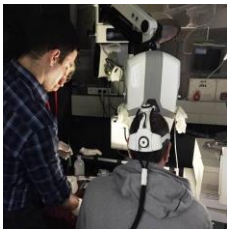
METHODS Enucleated bovine eyes were included in the primary part of the examination, followed by 5 patients, candidates for extraction of silicone oil from the vitreous cavity. The primary examination was carried out with the use of electro-optical system for visualization, while using an existing vitrectomy system to perform the surgical procedure itself. During the operation the system's key parameters were refined to enhance performance related to surgery visualization, functionality, surgery set up time, and ergonomics (strain on the surgeon's neck/head and fatigue).

RESULTS Good visualization of the posterior chamber was achieved using the electro-optical system in bovine enucleated eyes. Digital image manipulation allowed control of image rotation, lighting parameters and digital zooming for optimal visualization of both the retina and vitreous cavity. Following the success of the ex-vivo experiments,

human experiments will be carried out at the Tel Aviv Medical Center during February and March 2016. The results will be presented in detail during the meeting demonstrating functionality, shortened surgery setup time, less fatigue and ergonomic advantages.

CONCLUSION Elbit's digital electro-optical system that incorporates a unique head worn device, sterescopic cameras and software is capable of generating high quality detailed imagery for vitreo-retinal surgery and significantly improves the surgeon's visualization and enhances surgical performance.

TAKE HOME MESSAGE Superior visualization wearing a head mounted device can replace the need for operational microscopes in vitreo-retinal surgery



HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board

Thermal Profile of a Novel Hypersonic Vitrector (HV)

- Victor Hugo Gonzalez, MD

OBJECTIVE To report the results of thermal measurements using a new prototype Hypersonic Vitrector (HV) in cadaver porcine eyes during vitrectomy.

PURPOSE Temperature profile measurements at key locations in the cadaver porcine eye during vitrectomy are indicative of heat generation by active medical instruments. This data will demonstrate the thermal profiles from the HV around the Entry Site Alignment system, the retina and posterior capsular bag to be within specific safety boundaries.

METHODS This laboratory study used calibrated micro thermocouples (Omega HYP1-30-1/2-T-G-60-SMPW-M & Omega HYP2-21-1-1/2-T-G-48-OSTW-M) and a FLIR camera (FLIR A-Series SC325) to collect data and images. A 23 gauge posterior vitrectomy procedure is performed on cadaver porcine eyes with the HV device. Temperatures in the vicinity of various regions of the needle shaft in or near the eye were measured at six different drive (stroke) levels on three different hand pieces. Temperature was recorded during continuous operation of the HV or until a maximum temperature was reached. Where relevant, images were recorded using a FLIR camera.

RESULTS All data was collected and analyzed. Examples are attached in the graphical representations. A correlation between temperature and system settings was observed with lower amplitudes and On/Off cycles yielding lower temperatures. All measured temperatures were below typical body temperatures and well within recognized safe operating limits. The highest temperature was recorded on the outside port of the ESA at the Valve - HV shaft interface. The ESA insulated the scleral tissue effectively.

CONCLUSION The 23 gauge HV did not generate high levels of heat during vitrectomy surgical maneuvers in a cadaver porcine eye. **Graphics: Image 1.** FLIR temperature profile of a 23Ga ESA with active HV

TAKE HOME MESSAGE The new vitrectomy does not produce unacceptable heat and allows for vintage LOCF.

Engineered Biopolymer Thin-Films for Extended Intravitreal Drug Delivery: Preclinical Feasibility Studies

- Robert B. Bhisitkul, MD, PhD
- Kevin D. Lance, PhD
- Daniel A. Bernards, PhD, PhD
- Natalie Ciaccio, PhD, PhD
- Kazuhito Yamada, Master
- Sri Mudumba, PhD, PhD
- Tejal A. Desai, PhD

OBJECTIVE To describe preclinical development of a novel drug device technology for small molecule and biologic therapies.

PURPOSE Extended intravitreal drug delivery for retinal diseases offers to reduce treatment burden, improve outcomes with available agents, and enable novel therapeutic approaches. The aim is to test the feasibility of engineered thin-film biopolymer devices adapted for intraocular delivery of rapamycin (0.9 kD) and ranibizumab (48 kD) by i*n vitro* pharmacokinetics and *in vivo* performance in rabbit eyes.

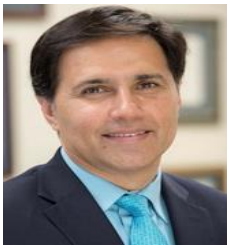
METHODS Flexible bilaminar disc devices (6 and 10 mm diameter) were constructed from polycaprolactone (PCL) films spin-cast on zinc oxide templates to generate nano-porous membranes (20 mm thickness), and polyethylene glycol additives for micro-porous membranes (4-70 mm thicknesses). Reservoirs of pelleted rapamycin and lyophilized FITC-ranibizumab were encapsulated by heat sealing. *In vitro* drug elution was quantified in controlled PBS fluid chambers with fluorometry, high-pressure liquid chromatography (HPLC), and UV spectrophotometry. In New Zealand White rabbits, devices were implanted in the vitreous for *in vivo* studies, with mass spectrometry or size exclusion chromatography used to measure drug concentrations.

RESULTS Rapamycin devices with micro-porous and unfeatured membranes showed linear release over 5 weeks *in vitro* at 1 mg to 0.6 mg per day, dependent on film thickness (4-66 mm). In rabbit eyes, mean rapamycin concentration at 16 weeks (n=5) was 5.2 ng/ml in the vitreous and 206 ng/ml in retina-choroid. Nano-porous ranibizumab devices showed biphasic release rates *in vitro* over 4 months (1.8 mg/day through week 5; 0.6 mg/day week 10 to 16; n=17). In rabbit eyes (n=13), *in vivo* ranibizumab concentrations in the vitreous averaged 0.96 mg/ml over 12 weeks. Residual payload extrapolated to 25 weeks for drug depletion. At 6 weeks *in vivo*, ranibizumab showed 93% stability, reduced to 52% at week 20. Ocular toxicity related to the device was not seen on serial clinical exams over 12-16 weeks for both devices. Complications related to implantation surgery included post-operative conjunctival injection and iatrogenic cataract, and intra-operative vitreous hemorrhage.

CONCLUSION Intraocular drug release from thin film biopolymer devices was seen at therapeutically sufficient levels for at least 4 months, with acceptable ocular tolerance. Pore architecture could be engineered for both the small molecule rapamycin and the biologic ranibizumab. Drug stability and linear release pharmacokinetics require further refinement.

TAKE HOME MESSAGE In preclinical studies, nano-engineered thin film polymer devices offer promise in the sustained delivery of small molecules and biologics for ocular therapies.

Argus I vs Argus II: A Comparison of Two Epiretinal Prostheses



- Mark S. Humayun, MD, PhD
- Lan Yue
- Jessy Dorn, PhD
- Uday Patel, PhD
- Hassan Aziz
- Lisa C. Olmos de Koo, MD, MBA
- James Weiland, PhD

OBJECTIVE Our objective was to study the visual responses of the only subject to date in the world that is implanted with the Argus I in one eye and the Argus II in the fellow eye.

PURPOSE The Argus I retinal implant, containing an array of 16 electrodes, was compared with an Argus II implant containing 60 electrodes. A subject previously implanted with Argus I received surgical implantation of Argus II in the fellow eye. This subject with both implants offers a unique opportunity to study the visual responses of the same subject to both devices.

METHODS The subject, who had no light perception in the right eye and bare light perception in the left eye due to advanced RP, was surgically implanted with Argus I in the right eye in 2004, followed by periodic tests of the implant performance for a decade. In 2015, the subject received Argus II in the left eye and has since been undergoing periodic testing. The subject's visual function was assessed by computer-based tests with high-contrast stimuli, static or moving, presented on a touch screen. Standardized assessments including square localization (SL), direction of motion (DOM) and grating visual acuity (GVA) were all conducted under monocular stimulation.

RESULTS Electrically elicited phosphenes were present after implantation of Argus I and Argus II. Mean error in SL performance was 198 pixels with Argus I vs 140 pixels with

Argus II. Subject's performance in DOM was not significantly better than baseline with Argus I vs being significantly improved ($p<<0.05$) with Argus II. The GVA remained worse than logMAR2.9 with Argus I vs being able to achieve logMAR 2.2±0.2 with Argus II.

CONCLUSION Our data, albeit preliminary, suggest that Argus II exhibits potential to restore vision of superior spatial resolution than Argus I or baseline. Further research is needed to better understand the improvements that Argus II might provide over Argus I.

TAKE HOME MESSAGE Our data suggest that Argus II exhibits potential to restore vision of superior spatial resolution. Changes of the Argus II-restored visual function over time will be monitored in future studies.

HUMAN RESEARCH This study involves human research.
IRB Approval Status: Approved by institutional review board