significant using the t-test at a level less than 0.05. This change when it occurred did so at one-half hour or later. On the basis of that experience, it is felt that the pressure measurements in this study are valid in that they were taken immediately after use of topical anesthetic and there was no time lapse which would allow an increased penetration of pilocarpine.

Discussion. Using the two mean values, the Ocusert with a mean value of 19.9 mm. Hg compared to pilocarpine at 20.7 mm. Hg would appear to be comparable. Statistical testing of the change in the intraocular pressure from the control period to the treatment period shows significance. In this study, the patients preferred the Ocusert to drops. The Ocusert tended to lodge in the upper outer quadrant and in the lower cul-de-sac immediately beneath the cornea. In general, the patients were more comfortable if the Ocusert were in the upper outer quadrant. Most patients found they could maneuver the Ocusert with their finger through a closed lid to a position where it was easy to remove or where it was comfortable. A number of patients reported that an Ocusert had fallen out during sleep but they simply washed it off and replaced it or put in a new Ocusert. In using this pilocarpine Ocusert system there is the precaution that, if a pressure is measured with applanation immediately after use of topical anesthetic and repeated again within a half an hour to an hour, a pressure drop could be due to the greater penetration of pilocarpine.

In the twelve months the authors have been studying the pilocarpine Ocusert, we have seen no untoward side effects or infections. We are both objectively and subjectively impressed that this treatment modality shows promise in the treatment of glaucoma.


Key words: glaucoma, Ocusert, pilocarpine, pressure response.

References

Intraocular pressure measurement with instrumented contact lenses. M. E. Greene and B. G. Gilman.

Flush-fitting, silastic gel contact lenses instrumented with strain gauges have been used to measure changes in the meridional angle of the corneoscleral function of a rabbit due to variation in intraocular pressure. Output from these strain gauges appears to be well defined and the sufficient magnitude to drive a miniature telemetry package which could be used to continuously monitor intraocular pressure without changing the pressure level due to the measurement itself.

Although there are several instruments currently available which can measure intraocular pressure reasonably accurately, all of them depend on applanation, indentation, or deformation of the ocular globe to determine the intraocular pressure. Continued and repeated use of these instruments will eventually induce changes in the very parameters which are being measured and thus generate inherent errors. A possible exception may be the new Non-Contact Tonometer manufactured by the American Optical Company. There is some limited data1 which indicate no change in measured intraocular pressure with repeated use. However, this instrument requires clinical utilization and could not be used to continuously monitor intraocular pressure during normal living and working conditions.

Our method of monitoring intraocular pressure change is to observe the deformation in the angle where the cornea joins the sclera. The structure of the eye suggests that this area may vary more with changes in intraocular pressure than any other. We have used distensibility data for rabbit cornea and sclera2 to estimate changes in the corneoscleral angle due to intraocular pressure variations. Typically, the theoretically predicted change in angle is about 0.020 to 0.016 radians per millimeter of mercury for intraocular pressures over the range of 10 to 45 mm. Hg, respectively. Measurement of angular deflections of this magnitude using strain-gauge techniques are well within the current state-of-the-art.

The eventual goal of this project is to measure intraocular pressure in a continuous manner with strain gauges mounted in a properly fitted hydrogel contact lens so as not to deform the eye in any manner. Absolute pressure-level signals, as well as diurnal variations and behavior
under stress conditions which would all be useful in detecting and treating glaucoma, would be telemetered from the lens to the laboratory where variations would be recorded. The purpose of this present work is to develop the methods to accomplish this and to demonstrate the functionality of the lens system.

White rabbits weighing approximately 2.9 kilograms were used as the subjects of this investigation. Since it is important to position the strain gauges exactly over the corneoscleral junction to obtain maximum output, both eyes of the rabbits were carefully fitted with soft lenses using scleral contact lens molding techniques previously developed for human patients.\(^3\) A flush-fitting soft silastic contact lens with strain-gauge transducers imbedded in it was fabricated and used to measure intraocular pressure variations.

Prior to the molding procedure, the rabbit was placed in a simple wooden restraining hutch and each eye was locally anesthetized with 2 drops of 0.5 per cent proparacaine hydrochloride administered about 3 minutes apart. After installation of 1 drop of sterile mineral oil, a menispheric plastic-fitting shell with a radius slightly larger than the cornea\(^1\) was inserted in the eye and the lids allowed to close over it and hold it in place. The exact shape of each eye was then obtained by injection molding using Ophthalmic Moldite eye impression material (Obrig Laboratories, Inc., Sarasota, Fla.).

While the eye mold was still moist, it was filled with a dental casting compound such as Castone which had previously been mixed and vibrated to eliminate any air bubbles. In approximately 2 hours the mold was removed and the hardened cast of the eye examined, cleaned, and marked. A thin (approximately 0.001 inch) deformable plastic membrane (commercially available Brownin' Bag) was then tightly stretched over it to provide fitting clearance.

This cast served as the male half of the mold which was used to produce the soft contact lens. The female half of the lens mold was made of Teflon and was a concave hemisphere of the same radius of curvature as the original fitting shell which was larger than the cornea but smaller than the sclera. It also had small holes drilled in it at the position of the corneoscleral junction as determined from the eye cast. Blunt hypodermic needles were inserted through these holes and connected to a vacuum pump to hold the pre-wired strain gauges by suction in the proper position while the lens was being molded around them.

The lenses used in this experiment were made from Dow Corning Medical Grade Polydimethylsiloxane (MSA4-4092) catalyzed with stannous octowate (Catalyst M) to form a two-package RTV material. After the catalyst was added and mixed the compound was desiccated for about 3 minutes to get rid of all air bubbles and then slowly poured into the female Teflon mold where the strain gauges were already in place. The male eye cast was then oriented over the mold so that the strain-gauge wires came out opposing the temporal canthus. This cast was lowered with a jack screw table until the scleral portion of the eye mold just touched the outside edge of the concave lens mold. The lens was allowed to set at room temperature for about 2 hours until it was fully cured. It was then carefully removed from the two mold halves and the excess material trimmed off.

Operation of the instrumented silastic lens was tested by connecting the gauge leads to a wheatstone bridge circuit in a manual balancing (Baldwin SR-4 Model K) strain indicator and

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Fig. 1. Photograph of the two contact lenses and transducer elements used. Lens with foil transducer is shown on the left and semiconductor lens on the right.

Fig. 2. Variation of contact lens strain output signal with change in intraocular pressure using a Bean foil transducer (gauge factor \(\approx 1.85\)) in the left eye of rabbit No. 1.

The female half of the lens mold was made of Teflon and was a concave hemisphere of the same radius of curvature as the original fitting shell which was larger than the cornea but smaller than the sclera. It also had small holes drilled in it at the position of the corneoscleral junction as determined from the eye cast. Blunt hypodermic needles were inserted through these holes and connected to a vacuum pump to hold the pre-wired strain gauges by suction in the proper position while the lens was being molded around them.

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Operation of the instrumented silastic lens was tested by connecting the gauge leads to a wheatstone bridge circuit in a manual balancing (Baldwin SR-4 Model K) strain indicator and
then placing the lens on the rabbit’s eye. Application of gentle finger pressure on the scleral part of the eye as far as possible from the contact lens produced a momentary unbalance of the bridge which disappeared when the finger was taken off the eye and the pressure released.

Quantitative data were obtained by changing the pressure in the eye via direct cannulation of the posterior chamber of the eye. The rabbits were anesthetized with approximately 30 mg. per kilogram of sodium pentobarbital injected through an ear vein. The eye cannulas used were 18- to 23-gauge hypodermic needles. These were connected via a U-tube manometer to a reservoir filled with sterile physiologic saline solution.

After the cannula was installed and the lens placed in position on the eye, the gauges were allowed to stabilize for temperature effects for 10 to 15 minutes with a pressure of about 20 mm. Hg in the eye as set by the reservoir and read from the U-tube manometer. After stabilization was achieved, the pressure in the eye was increased by specified increments (usually 10 cm. of H$_2$O) and the strain output from the gauges recorded by balancing the wheatstone bridge circuit.

Three types of strain gauges with resistances from 330 to 960 $\Omega$ were used in different lenses on rabbits. Fig. 1 is a photograph showing two lenses and strain-gauge elements. The Constantan (W. J. Bean, Inc., Detroit, Mich.) foil-gauge data are shown in Fig. 2 and the semiconductor-gauge data are shown in Figs. 3, 4, and 5. Each figure shows data that were taken during one test trial. As can be seen, the semiconductor gauge systems produced substantially more output than the foil gauges for any given pressure change. Furthermore, the Pixie (Endevco Corporation, Pasadena, Calif.) semiconductor gauges (Figs. 3 and 4) appeared quite linear over the entire experimental range of intraocular pressure (20
to 57 mm. Hg). The foil gauge, however, appeared to stabilize quicker after each pressure change and showed much less tendency to drift. Data with the Pixie semiconductor gauges were obtained with both increasing and decreasing pressure changes. The cannulas used during the foil and the Whittaker (Celesco Industries, Canoga Park, Calif.) microsensor semiconductor gauge tests became clogged with vitreous humor when the pressure in the eye was decreased so that no data were obtained in the decreasing pressure direction with these gauges.

A comparison between similar sensors can be seen in Figs. 3 and 4. Both of these figures were taken with Pixie semiconductor gauges but on different rabbits and, consequently, with different contact lenses. The slope of the curve in Fig. 3 is 35 μ inches per inch per millimeter of mercury and the slope of the corresponding curve in Fig. 4 is 38 μ inches per inch per millimeter of mercury. Since no attempt was made to match the two systems, this result appears quite good. With careful matching of the sensors, this difference (3 μ inches per inch per millimeter of mercury) should be reduced even further.

Over all, these preliminary data support the assertion that strain gauges mounted in soft contact lenses can measure changes in intraocular pressure by sensing the deformation of the meridional juncture between the cornea and sclera. Furthermore, the output of the Pixie semiconductor gauges is linear over the range of 20 to 57 mm. Hg with a slope of about 0.08 Ω per millimeter of mercury. This change appears to be quite sufficient for use with a miniature telemetry package completely contained in a hydrophilic hydrogel contact lens for continuous, noninvasive, long duration monitoring of intraocular pressure.


Key words: Intraocular pressure, tonometry, contact lens, transducer, instrumentation, glaucoma, corneoscleral junction.

REFERENCES

Adenine arabinoside effect on experimental idoxuridine-resistant herpes simplex infection. ANTHONY B. NESBURN, CHRISTINE ROBINSON, AND RANDOLPH DICKINSON.

Topical application of idoxuridine (IDU) is presently a standard treatment for epithelial herpes simplex keratitis in man. While IDU therapy is usually satisfactory, clinically resistant keratitis has been encountered. In most instances, the actual basis of these IDU treatment failures is never determined. On occasion, viral isolates from such cases have proved to be biochemically resistant to IDU. An important attribute for any new antiviral drug would be its ability to successfully manage cases in which IDU failed clinically, including those in which the infecting virus was biochemically resistant to IDU.

Adenine arabinoside (ARA-A), a new antiviral agent being actively investigated, has demonstrated its efficacy in suppressing both experimental1-3 and previously untreated human herpetic keratitis. In addition we, and others, have found ARA-A effective in instances where IDU therapy was clinically unsuccessful. In one case where ARA-A appeared to be efficacious and IDU failed, the virus isolated was actually biochemically resistant to IDU.

This study was performed to determine, under controlled experimental conditions, whether ARA-A is effective against the herpes simplex virus (HSV) exhibiting biochemical resistance to IDU. Stable, highly IDU-resistant virus strains were produced by growing McKrae-strain HSV in the presence of increasing concentrations of IDU. Strain I was produced in our laboratory, and Strain II was supplied by Dr. Herbert E. Kaufman. Strain II was used for in vivo studies. In vitro studies were carried out with both strains and no significant difference was demonstrated between them.

In vitro drug sensitivity studies and all titrations were performed using micro-testing plates (Falcon). Virus and drug dilutions were applied simultaneously to primary rabbit kidney cells after aspirating the microplate wells. Four wells were used for each dilution and the experiments done in duplicate. Appropriate cell, virus, and drug controls were included. Following a 16 hour adsorption, the wells were aspirated and refilled with fresh medium containing experimental drug. The wells were read “blind” every day for seven days and were considered negative only if viral cytopathology was completely suppressed. Virus titers, calculated by the Karber method, were expressed as the TCID₅₀ per cent end point.

In tissue culture, McKrae-stained HSV production was suppressed significantly by 40 μg per milliliter or by 100 μg per milliliter of either

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