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PROJECT ADMINISTRATION DATA SHEET

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Project No. E-23-631 — DATE 9/2/82

Project Director: Dr. Raymond P. Vito US — School/~~Unit~~: ESM

Sponsor: DHHS, Public Health Service, National Eye Institute

Type Agreement: Grant No. 1 R03 EY04514-01

Award Period: From 7/1/82 To ~~6/30/83~~ ~~12-31-83~~ 10/30/84 (Performance) ~~9/30/83~~ 9/30/84 (Reports)

Sponsor Amount: $17,770 — Contracted through: GTRC/GIT

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Title: Basic Studies of the Biomechanics of the Cornea

ADMINISTRATIVE DATA — OCA Contact: Faith G. Costello x4820

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Defense Priority Rating: n/a

Security Classification: n/a

RESTRICTIONS

See Attached NIH Supplemental Information Sheet for Additional Requirements.

Travel: Foreign travel must have prior approval – Contact OCA in each case. Domestic travel requires sponsor approval where total will exceed greater of $500 or 125% of approved proposal budget category.

Equipment: Title vests with GIT

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GEORGIA INSTITUTE OF TECHNOLOGY OFFICE OF CONTRACT ADMINISTRATION

SPONSORED PROJECT TERMINATION/CLOSEOUT SHEET

2
5K,646

Date 10-1-87

Project No. E-23-631 School/~~XXX~~ ESM

Includes Subproject No.(s) N/A

Project Director(s) Dr. Raymond Vito GIT

Sponsor DHHS, Public Health Service, National Eye Institute

Title Basic Studies of the Biomechanics of the Cornea

Effective Completion Date: 6-30-84 (Performance) 9-30-84 (Reports)

Grant/Contract Closeout Actions Remaining:

- [X] None
- [ ] Final Invoice or Final Fiscal Report
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FORM OCA 69.285

Basic Studies of the Biomechanics of the Cornea

FINAL REPORT
(Grant # RO3 EY04514-01)

submitted to

Small Grant Program for Pilot Study
National Eye Institute
Washington, DC

by

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SUMMARY

The cornea accounts for about 70% of the refractive power of the eye. As a result, several clinical procedures have been developed to exploit the refractive power of the cornea in order to correct visual abnormalities. For example, radial keratotomy, the surgical placement of radial slits on the cornea, flattens the central cornea and can correct myopia. Such clinical procedures are becoming common practice. However, the biomechanical factors which determine pre and post surgical corneal shape are not well understood. There are several reasons for this. We note especially the complex structure of the cornea, the experimental difficulties in measuring corneal shape and mechanical properties, the difficulties of developing a mechanical model of the cornea and corneal healing. For these reasons, clinical approaches to refractive surgery are based on experience and the outcome is uncertain. Our investigations to date have focused on the determinants of corneal shape. During the grant period, we have made crude measurements of corneal mechanical properties using strips of cornea and have investigated the Moire fringe technique for measuring corneal shape. More recently, we have constructed a simplified finite element model of the cornea, especially as altered by RK surgery, assuming linear elastic, isotropic behavior. We are currently extending this work toward the goals of understanding the factors that account for corneal shape and of creating a more realistic mechanical model of the cornea capable of predicting qualitatively the results of refractive surgery.

BACKROUND

The cornea accounts for about 70% of the refractive power of the eye. Therefore, the corneal shape, especially as affected by various clinical procedures, is a subject of current interest. It is interesting to note that surgical attempts to modify corneal refraction are over a century old. Early German ophthalmic surgeons performed corneal incisions and applied heat to the cornea to try to change its shape, all unsucessfully.

There are three clinical areas of ophthalmology where problems with corneal shape are apparent:

1) There is intense interest in kerato-refractive surgery, typically for treating myopia, but including other refractive errors as well. (Sato, et al 1953, Fyodorov, 1980, Barraquer, 1964, Sanders, et al 1985). With 25% of the American population myopic, and at least 11 million individuals between 2.00 and 8.00 diopters of myopia, surgical attempts to change corneal shape to treat this myopia represent a substantial public health problem.

2) Increasing numbers of cataract operations are being done every year in America, and the most frequent complication of cataract surgery now seems to be corneal astigmatism, since the operation itself is technically successful in most instances.

3) Corneal transplant surgery is also achieving a high degree of technical success, at least 75% of grafts remained clear in most series. The most frequent long complication of corneal transplantation is now astigmatism as well.

The central role of biomechanics in determining corneal shape cannot be denied. This is especially true in surgical techniques such as radial keratotomy. In spite of this, there has been little contribution from the mechanical sciences to understanding the biomechanical factors affecting corneal shape.

This is due to a number of factors not the least of which is the lack of stress-strain-time (constitutive) law for the intact cornea. Such a law is of fundamental importance (Fung, 1981) in biomechanics.

In addition, the layers of the cornea that are most important in determining corneal shape have not been identified. Intuitively, many researchers think that Bowman's layer should be the primary shape determining portion of the cornea, since it is an a-cellular dense feltwork of fine fibrils that seems to have no elastic properties, and since corneal swelling takes place by way of posterior protrusion because of the elasticity of Descemet's membrane, the anterior surface remaining less deformed.

RESULTS

Studies of the mechanical properties of the cornea are motivated by the well accepted principle in solid mechanics that experimental data from relatively simple tests can be used to generate a stress-strain-time (constitutive) law of general validity (Fung, 1965). For example engineers use data from constant strain rate and other simple tests on structural materials such as steel to develop constitutive laws of general validity. These general laws are then used with the theory of solid mechanics to determine stresses and deformation (shape) for complex structures such as bridges.

We are aware of the problems inherent in the mechanical testing of strips of corneal tissue; specifically, the fact that the structure is most likely altered by cutting and mounting the specimens. The strips themselves are also not homogeneous i.e., the contributions of Bowman's layer, Descemet's membrane, and the corneal stroma to the results are unknown. The few previous studies of the mechanical properties of corneal strips (e.g., Nyquest, (1967)) are difficult to relate to the growing literature on tissue mechanics. Accordingly, Vito et al (1981,2) undertook a preliminary study of the mechanical properties of human corneal strips (see Attachments). The results indicate that the cornea behaves as a nonlinear viscoelastic material. Specifically, the stress-strain curves in constant strain rate tests are exponential in nature and relatively strain rate insensitive. Stress relaxation effects were also found to be significant.

Although the individual contributions of the Bowman's layer, Descemet's membrane, and the stroma are unknown, it does appear that the cornea behaves very much like other soft tissues. Hence, it may be that the considerable literature on constitutive equations for soft tissues (e.g., Fung, 1973) may be relevant to corneal biomechanics.

Results using the Moire technique were discouraging. It was necessary to coat the surface of the cornea in order to increase its reflectivity. Thus the technique is limited to in-vitro studies; a major limitation. Attached are representative results taken from the M.S. thesis of S. Kirshner. Another thesis, that of S. Deng, was also completed during the grant period.

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ATTACHMENTS

THE ELASTIC AND VISCOELASTIC PROPERTIES OF THE HUMAN CORNEA

R. P. Vito, S. B. Kirschner, J.P. Frazier, D.L. Vawter,
Georgia Institute of Technology*
and G. Waring, B. McCarey
Emory University**

Introduction

Altering the corneal shape by surgical or thermal means offers hope for the correction of visual disorders like myopia, aphakia after cataract surgery, and astigmatism after corneal transplantation (Barraquer et al., 1980). A variety of surgical approaches now exist: circumferential relaxing incisions or wedge resections, radial incisions and removing slices for cornea for turning on a cryolathe with subsequent reattachment to the cornea, and focal heating of the cornea.

Mechanical models of the cornea are emerging which may be used to predict the results of these techniques. Of fundimental importance to the construction of such models are the mechanical properties of the tissue.

There is little data on the mechanical properties of the cornea. This paper is a systematic study of the elastic and viscoelastic properties of human corneal strips.

Experiment

Experiments were conducted on ten corneas using microprocessor controlled instrumentation described elsewhere (Vito et.al. 1980). Specimens were loaded at a constant strain rate either to a fixed stress or to a fixed strain. Peak stresses of 0.5, 0.75, and 1.0 x 10^6 dynes/cm^2 or peak strains of 6%, 8%, and 10% were used. In each case, strain rates of 0.01, 0.05, and 0.10 sec^{-1} were used.

In the relaxation tests, the specimens were preconditioned, subjected to a quick stretch and allowed to relax.

Results

A representative plot of loading curves for strain rates of 0.01 and 0.10 sec^{-1} is shown in Figure (1). Note the apparent strain rate independence of the results as well as the exponential shape of the curve.

Figure (2) shows the stress relaxation (mean $\pm$ one standard deviation) for all experiments.

Conclusion

These results indicate that the cornea is mechanically similar to other soft tissues. Hence, it may be possible to use the results from the literature of soft tissues (Fung 1973) to formulate a constitutive law for the cornea; the first step in constructing a mechanical model of the cornea.

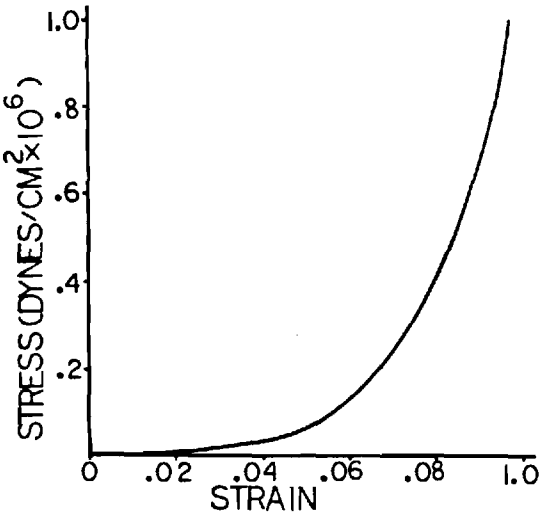

Figure 1. Stress-strain curves for loading at 0.1 and 0.01 sec^{-1}. Curves are coincident.

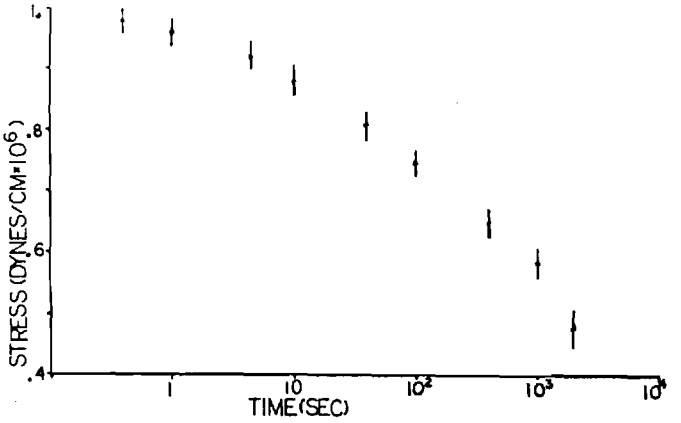

Figure 2. Stress relaxation results.

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** Dept. of Opthalmology, Atlanta,Ga. 30322

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COMPARATIVE STUDY OF THE BIOMECHANICAL PROPERTIES OF CORNEAL STRIPS. Albert S. Leveille, M.D., Raymond P. Vito, Ph.D., Don Vawter, Ph.D., George O. Waring, III, M.D., Emory University, Atlanta, Georgia.

Biomechanical models of the cornea are becoming increasingly important to help predict the results of keratorefractive surgery. The construction of such models depends on measurement of the basic mechanical properties of the cornea. We have studied the uniaxial mechanical properties of strips of 10 human corneas using microprocessor-based instrumentation especially developed for the mechanical testing of soft tissues.

Results of the constant strain rate test show the cornea to be viscoelastic with loading and unloading curves which are exponential and relatively strain rate independent. Stress relaxation over 3 hours was approximately 15%. These results indicate that the cornea is mechanically similar to other soft tissues. Therefore, it may be possible to use results obtained on other soft tissues to formulate a constitutive law for the cornea.

We will report results of comparative experiments on rabbit, cat, monkey, and human cornea strips and will point out differences among these animals that might affect their use as models in keratorefractive surgery. We will also report results of stress-strain experiments on partial thickness human corneal strips to detect the differences between the anterior portion that contains Bowman's layer and the posterior portion that contains Descemet's membrane.

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RELIABILITY OF MEASUREMENTS USED IN EVALUATION OF REFRACTIVE SURGERY IN THE ADULT RHESUS MONKEY. P. Asbell, A. Safir, G. Kissling, M. Ostrick, and T. Yamaguchi. LSU Eye Center, LSU School of Medicine, New Orleans, LA

Refractive measurements in animals, most frequently monkeys, are crucial to the evaluation of refractive surgery. The reliability of such data can be determined only by replicate measurements. Two independent observers performed keratometry, retinoscopy, and pachymetry on 24 adult rhesus monkey eyes, and repeated these examinations 6 to 18 times, using identical procedures, within one month (2 day minimum-- 21 day maximum). The variability between examiners for the same procedure and for each examiner on different occasions, and the expected average findings were determined. No significant inter-observer differences were found ($P > 0.25$ for any procedure). The means and standard deviations were: keratometry, 53.73 D (1.51); amount of cylinder as measured by keratometry, 0.80 D (0.84); retinoscopy spherical equivalent, +0.29 D (0.90); cylinder by retinoscopy, 0.46 D (0.41); optical pachymetry, 0.49 mm (0.04); and ultrasound pachymetry, 0.43 mm (0.007). Variability in endothelial cell and corneascope photographs was also seen.

It is therefore predictable that any two measurements made on the same eye have a 50% probability of differing by: 0.43 D for keratometry, 0.37 D for retinoscopy spherical equivalent, and 0.03 mm for optical pachymetry. We have applied these results to observations in monkeys post radial keratotomy. [Supported in part by USPHS grants EY03635, EY05496, and EY02377 from the National Eye Institute.]

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ALLOPLASTIC EPIKERATOPHAKIA IN MONKEYS. Marguerite B. McDonald, Miles Friedlander, Steven Koenig and Herbert E. Kaufman. LSU Eye Center, LSU School of Medicine, New Orleans, LA

Intracorneal plastic lenses are being widely investigated as a means of correcting aphakic infants requiring more than 15 D of correction at the corneal plane. Presently, it is difficult to create human tissue lenticules of greater than 15 D with acceptably large optical zones. Thirty-one monkeys underwent 5 types of implantation surgery using high plus Duragel lenses: 1) plus power human lyophilized epikeratophakia grafts were placed over the Duragel lenses on the recipient corneas; 2) plano human lyophilized epikeratophakia grafts were placed over the Duragel lenses on the recipient corneas; 3) Duragel lenses were implanted secondarily under healed epikeratophakia grafts; 4) Duragel lenses were placed in intrastromal pockets; and 5) fresh microkeratome-cut plano human "cap" grafts were placed over Duragel lenses on the recipient corneas. Several methods were tolerated well; alloplastic implants have provided optically clear results for more than 7 months, with corrections as high as 33 D, combining the power of the alloplastic material and the superimposed donor cornea.

[Supported in part by USPHS grants EY03635, EY07073, and EY02377 from the National Eye Institute, an award (G-705) from Fight for Sight, Inc., New York, N.Y.]

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EPIKERATOPHAKIA GRAFT FOR ASTIGMATISM CONTROL IN KERATOCONUS. Theodore P. Werblin and J. Elliott Blaydes, The Blaydes Foundation, Bluefield and Herbert E. Kaufman, LSU Eye Center, New Orleans.

Epikeratophakia is a new form of refractive corneal surgery which has several potential clinical applications. Currently, clinical studies are ongoing in several institutions looking at the correction of keratoconus with plano lamellar epikeratophakia grafts. Patients with keratoconus generally have several refractive abnormalities--myopia, regular astigmatism and irregular astigmatism. The epikeratophakia grafts eliminate the irregular astigmatism but leave significant amounts of both regular astigmatism and myopia. Experimental studies were undertaken on non-human primate eyes to see if one could control regular astigmatism by altering the shape of the epikeratophakia grafts. In one example, a graft shaped in an elipse with major and minor axis of 8 and 6 mm was sutured into a 7 mm recipient bed (47.0 D spherical). After complete healing and suture removal three months postoperative, 15.2 D of astigmatism was induced (40.8 x 56.0 D @ 143). In an attempt to demonstrate the reversibility of the induced cylinder, the wound along the steep meridian was opened and this resulted in a 90% loss of cylinder (49.5 x 51.0 D @ 143). This technique has been used clinically to eliminate some of the residual astigmatism after epikeratophakia lamellar surgery. (Supported in part by USPHS grant EY03636 from the National Eye Institute).

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ENDOTHELIAL CELL COUNTS FOLLOWING EPIKERATOPHAKIA. Robert B. Guss, Penny A. Asbell, Richard A. Berkowitz, and Herbert E. Kaufman. LSU Eye Center, LSU School of Medicine, New Orleans, LA.

Epikeratophakia is a form of refrsctive surgery for the correction of aphakia in which a piece of donor corneal tissue is shaped to a specific dioptric power on a cryolathe and sutured onto the recipient cornea. Specular microscopy was employed to study the endothelium of eight randomly-chosen aphakic patients who underwent such surgery. The average postoperative period was sixteen months, with a range of twelve to eighteen months. Average corneal thickness increased from 0.52 mm + 0.01 mm to 0.88 mm + 0.04 mm with the addition of the onlay graft. Preoperative endothelial cell counts were low, measuring 1450 per mm^2 + 218, and did not differ significantly from postoperative cell counts (average 1438 per mm^2 + 222) ($p > .9$). Despite a nearly 60% increase in corneal thickness and low endothelial cell counts, no corneal edema was seen in any of these patients. We conclude that epikeratophakia is well-tolerated by the cornea, and can be performed on eyes that have already undergone substantial trauma to the endothelium. [Supported in part by USPHS grants EY02377, EY05496, and EY07073 from the National Eye Institute, and an unrestricted grant from Research to Prevent Blindness, Inc., New York, N.Y.]

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ASSESSMENT OF CORNEAL STRENGTH POST RADIAL KERATOTOMY IN RABBIT EYES Nazareth E. Darakjian, M.D., Anthony Marchese, Ph.D.

Radial keratotomy was performed on 25 rabbits. Operated eyes showed a mean increase in hyperopia of 2.5 diopters at the end of six months compared to controls (Presented at A.R.V.O. 1980)

About 9-12 months after surgery, the eyes were enucleated. A 22 gauge I.V. catheter was put through the sclera at the equator. The intraocular pressure was raised by injecting water into the globe with a syringe. A pressure gauge was attached to the syringe to monitor the intraocular pressure. It was noted that the sclera always ruptured first when the pressure reached 60 psi and the rupture site never involved the site of entry of the catheter. In order to raise the pressure of the cornea even more, the cannulated eyes were placed in SUPERGEL alginate powder (used for dental impressions) mixed with the appropriate amount of water. When the alginate hardened, it provided support for the sclera and limbus but most of the corneal surface was left open. By this method the pressure on the endothelial side of the cornea could be raised up to 110 psi. It was noted that the corneas that had radial keratotomy as well as unoperated eyes that served as controls could withstand intraocular pressures of up to 110 psi without rupture. However, corneas that suffered perforations at the time of surgery did burst at a mean pressure of 90 psi. The rupture occured along the radial keratotomy scars in these cases.

Conclusion: Rabbit corneas after radial keratotomy can withstand a sudden rise in intraocular pressure that is enough to rupture the sclera. This is true even when the cornea was perforated at the time of surgery. However, these corneas have a tendency to rupture more easily than the non-perforated corneas.

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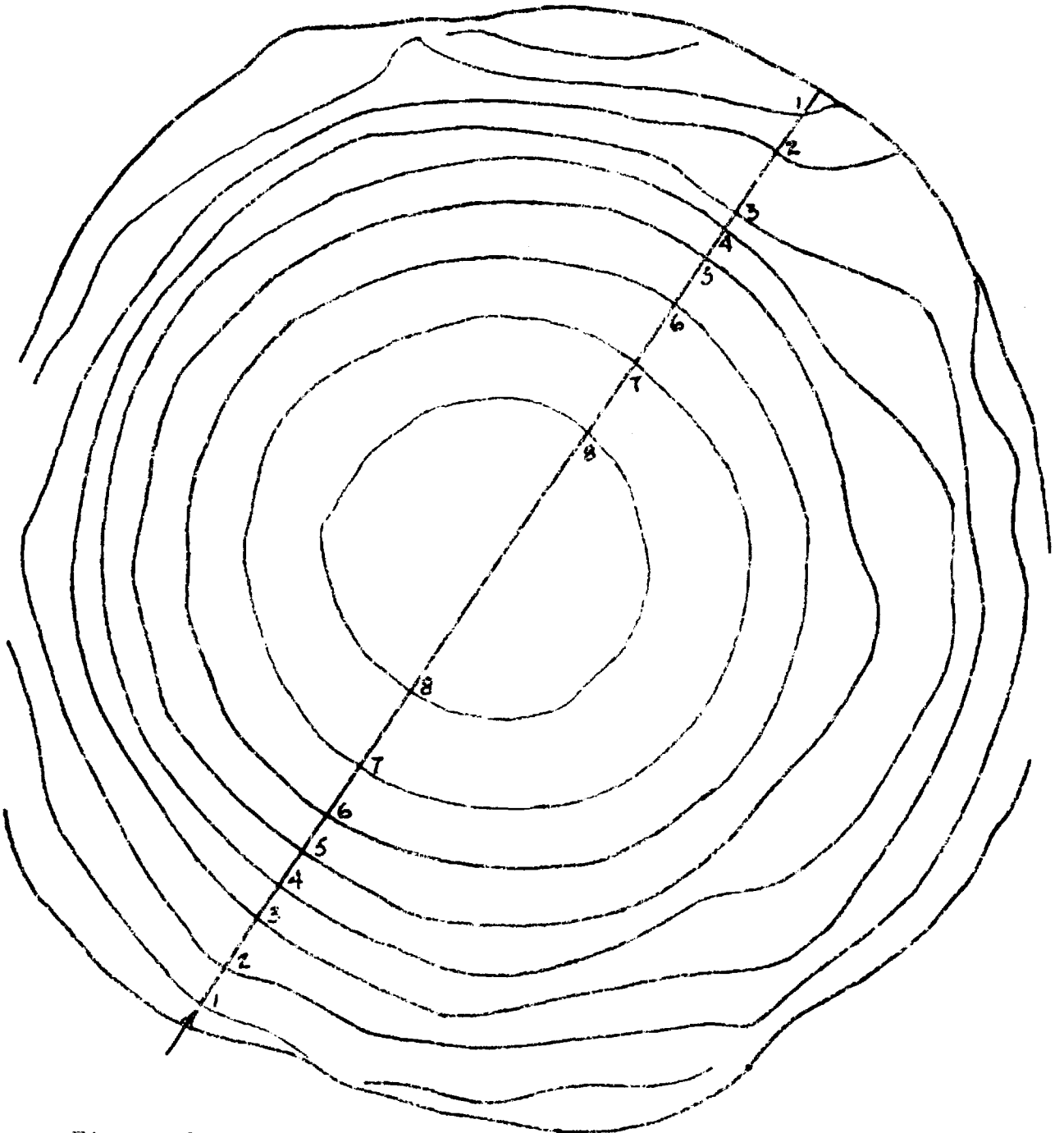

Figure 27: Sample Eye A: 50 mm Hg

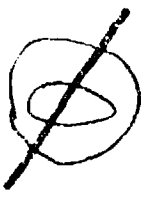

Figure 27

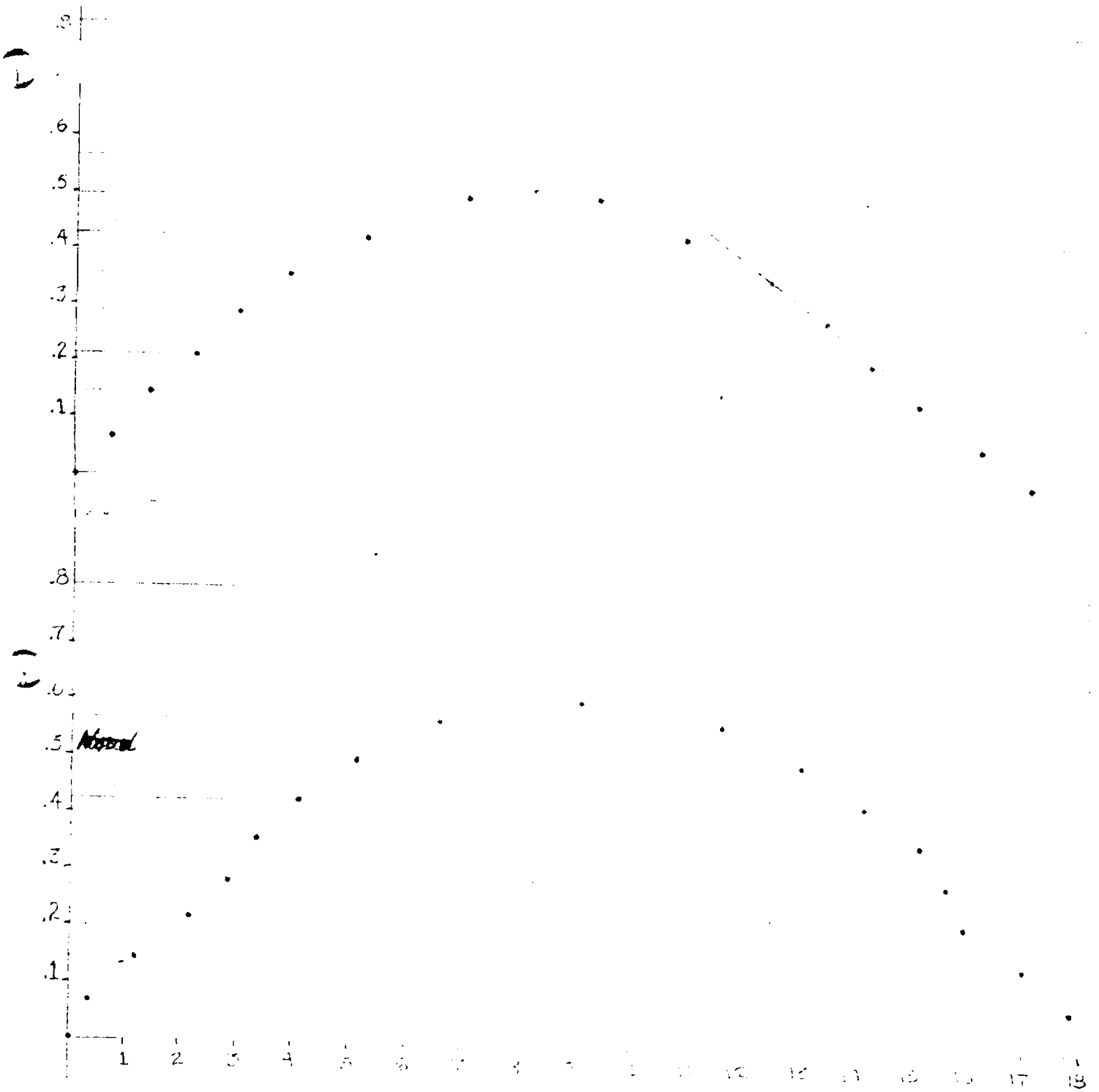

Figure 33: Profiles: Sample eye A 20 mm Hg.
50 mm Hg.

Figure 33