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Evaluation of negative pressure transfer through tissue in a benchtop cornea and eyelid model

Nathan Chu, Enrico Brambilla, Paul Yoo and Tanner J. Ferguson

Abstract

Purpose: A new glaucoma treatment device, known as the multi-pressure dial (MPD), has been introduced, which offers a novel approach to IOP reduction by delivering negative pressure to the periocular region. Clinical studies have demonstrated the IOP-lowering effect of the MPD via direct measurements using pneumatonometry. It remains unclear whether the eyelids, when closed, affect the transmission of negative pressure and subsequently affect IOP reduction. This study aimed to evaluate whether the transfer of negative pressure and subsequent decrease in IOP are altered by the presence of synthetic eyelid tissue.

Methods: A model with 13 different configurations controlling for eyelid material type, presence of slit/opening, and eyelid–cornea contact was employed. The slit modification was employed to mimic the physiologic separation that exists between the eyelids. Baseline IOP within an eye model was set at various levels ranging from 10 to 30 mmHg with applied negative pressure settings of 10, 15, and 20 mmHg utilized at each baseline IOP. The percentage of vacuum transfer was calculated by comparing baseline IOP to resultant IOP measurements following application of vacuum to the system.

Results: In the open configuration (without eyelid tissue), the mean % vacuum transfer was 98.7%. The sealed, full-contact configurations exhibited values of 97.4%, 98.8%, and 97.2%. The slit configurations, which closely mimic the physiologic eyelid, demonstrated a mean % vacuum transfer of 98.7% across all settings.

Conclusions: The impact of eyelid tissue on transfer of negative pressure can be isolated and evaluated. The presence of eyelid tissue has an insignificant impact on the transfer of negative pressure, and the IOP reduction achievable with the MPD would not be altered with the eyelids closed.

Keywords: glaucoma treatment, MPD, multi-pressure dial, multi-pressure glaucoma management, normal-tension glaucoma, open-angle glaucoma

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Introduction

Glaucoma is a major cause of irreversible blindness worldwide.[1,2] Intraocular pressure (IOP) remains the most significant risk factor for glaucoma, and conventional treatment options target the reduction of IOP.[3] The current treatment options include topical medications, lasers, and surgeries. The glaucoma treatment space has undergone notable innovation and expansion over the last decade, including the introduction and integration of minimally invasive glaucoma surgery (MIGS),[4–6] a growing space of surgical options defined by ab-interno, minimally traumatic approaches with an emphasis on safety. However, the current array of glaucoma treatment options does not include a non-drug, non-laser, or non-surgical option.

A novel glaucoma treatment device has recently been introduced known as the multi-pressure dial

Correspondence to:
Tanner J. Ferguson
Cole Eye Institute, Cleveland Clinic, 9500 Euclid Ave., Mail code: i-13, Cleveland, OH 44195, USA
tannerferg@gmail.com

Nathan Chu
Enrico Brambilla
Paul Yoo
Equinox Ophthalmic, Inc., Newport Beach, CA, USA

(MPD).[7,8] The MPD (Equinox Ophthalmic, Inc., Newport Beach, CA, USA) includes a pair of goggles with separately enclosed periorbital regions with each eye individually connected to a regulated vacuum system. The vacuum or negative pressure is modulated by a programmable pump with software that allows target negative pressure settings to be set for each eye. Once a secure seal is obtained and the programmed negative pressure is activated, a corresponding, instantaneous reduction in IOP is achieved.[9]

The MPD modulates the atmospheric pressure immediately anterior and external to the patient's eye in an enclosed environment. Prior work in healthy subjects has demonstrated the titratable IOP-lowering capability of the device at various negative pressure test settings.[10] However, it remains unclear whether the eyelids, when closed, affect the IOP-lowering mechanism created by the localized negative pressure microenvironment. Transmission of negative pressure through a closed eyelid would enable patients to use the therapy while sleeping. The goal of this study was to explore whether the transmission of negative pressure and subsequent reduction in IOP is affected or mitigated by the presence of eyelid tissue. To investigate, an eye model that incorporates the mechanical properties of the eyelid was created to evaluate the transfer of vacuum.

Figure 1. The multi-pressure dial, which includes the goggles connected to a pressure-modulating pump.

Methods

Study materials

The following materials are used for this study:

Cast silicone eyelid model
Cast silicone cornea model
Equinox multi-pressure dial
Deltran® II 3 cc pressure transducer
Extech™ HD755 Differential Pressure Manometer
Atrion PN 2530 syringe
Test fixture
  Tissue mounting plate
  Vacuum chamber

Study design

The MPD (Figure 1) reduces IOP via alteration of the atmospheric pressure immediately external to the patient or subject's eye. The IOP-lowering effect of the device has been established in patients with their eyes open and the negative pressure is applied directly to the cornea. However, it remains unclear whether the IOP-lowering mechanism of the device is altered with a subject's eyelids closed. This study created a model to simulate the mechanical properties of the eyelids with different configurations to explore whether the application of negative pressure and the subsequent IOP reduction are affected by the transmission of negative pressure through tissue (e.g. eyelids).

The model created was similar to the perfusion organ culture model previously described by Bahler and colleagues[11] but replaces the human anterior segment with a cast silicone cornea, and the fluid column and perfusion pump are replaced with a fluid-filled syringe and pressure transducer (Figure 2). The cast silicone cornea consists of a cast silicone dome to simulate a cornea that was mounted on the fixture. The eyelid tissue was created using either cast silicone or SynDaver® artificial tissue. The eyelids created using SynDaver artificial tissue were molded and formed to the same shape as those using cast silicone. Each eyelid was modified based on anatomical scans to match the mean thickness of an eyelid.[12] As this article did not include any human/animal subjects or cadaver tissue, this study did not require approval from an Ethics Committee or Institutional Review Board (IRB).

Model description and justification

The eye is a control volume with pressure characterized by inflow and outflow of aqueous humor.

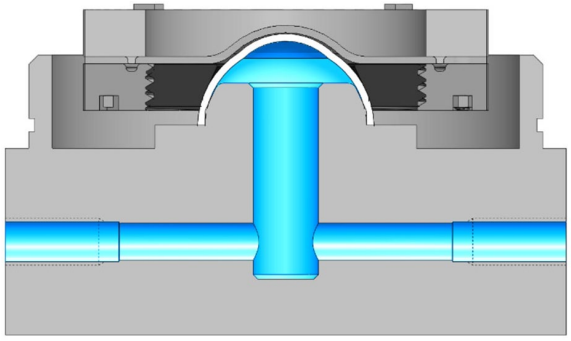

Figure 2. Cast silicone cornea with expanded volume of fluid beneath the eye demonstrating the fluid path of the fixture.

The Goldman equation describes the relationship between facility of outflow of aqueous humor and IOP as follows:

$$P_o = \frac{F}{C} + P_V$$

where P_o is the IOP, F is the rate of aqueous formation (inflow), C is the facility (opposite of resistance to flow), and P_V is the episcleral venous pressure (0 for this model).

The model used in this study utilizes a preset IOP, removing the flow elements from the equation and eliminating the pump and fluid column from the setup (used in the human anterior segment model previously described). It also expands the pressure term into a pressure differential, and applies a general loss term L. Thus, under vacuum, P_o is defined as follows:

$$P_o = P_I + P_{amb} + L$$

where P_I is the preset IOP, P_{amb} is the vacuum applied, and L is the general loss term comprising various energy losses due to deformation of cornea and tissue.

The results of this test are represented by a percentage, determined using the following formula:

$$Vacuum\ Transferred\,(\%) = \frac{(P_I - P_o)}{P_{amb}}$$

where P_{amb} is the vacuum chamber pressure and $P_I - P_o$ is the vacuum transferred to the fluid system.

Table 1. Primary variables included in the study.

Configuration	Tissue	Contact type
Open	Silicone, 18A	No Contact
Sealed	Silicone, 40A	Full Contact
Slit	Synthetic Tissue, SynDaver, 2N	

The main variables include the comparison between open, sealed, and slit configurations, as well as mechanical properties of the tissue and the eyelid–cornea contact control.

The model included several configurations to investigate the transfer of vacuum to the system (Table 1). For each configuration, the following variables were modified: eyelid material type, slit, and eyelid–cornea contact. For the eyelid model, 40A silicone, 18A silicone, and 2N SynDaver artificial tissue were used. To simulate the separation that exists between the eyelids and the cornea, a slit modification was created by creating a slit in the silicone/formed artificial tissue. Without the slit modification, the configuration was simply denoted 'sealed'. The final variable in the model was eyelid–cornea contact control. The contact control served to modulate the contact between the underside of the synthetic tissue and the surface of the cornea. In the non-contact format, there is no contact between the eyelid and the cornea, which allows for a compressible layer of air to exist between the eyelid and the cornea. In the full-contact format, the eyelid is in complete contact with the cornea; no compressible layer of air exists between the surfaces. Eyelid–cornea contact control was achieved by threading a tissue retaining plate to accommodate an eyelid retaining ring; the eyelid was sandwiched between a threaded portion and clamp and the assembly was raised/lowered relative to the cornea by rotating the assembly on the mount (Figure 3). Water droplets were placed in between the cornea and the tissue to simulate a fluid layer between the two layers, to lubricate the surfaces and to monitor contact. This is depicted and labeled accordingly in Figure 4. For eyelid–cornea contact control, the 'no contact' configuration includes the simulated eyelid mounted onto the eyelid retaining ring, but using the guidance of the fluid layer between the two layers and the absence of droplet formation as visualized through the tissue, the simulated eyelid maintains no contact with the underlying cornea. The 'full-contact' configuration was created by threading the assembly onto the fixture clockwise

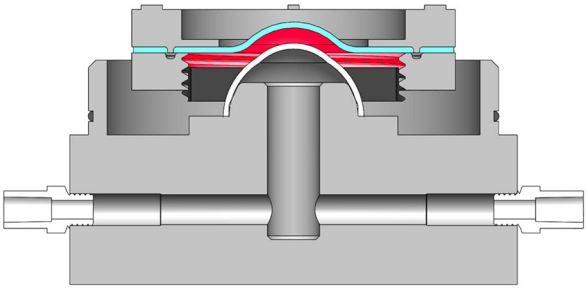

Figure 3. The air-filled intermediate space (red) between the eyelid (teal) and the cornea (white) in the model. In this study, the non-contact configuration allowed an intermediate, air-filled chamber to exist between the eyelids that accounted for the significant reduction in vacuum transfer with these configurations.

until no air bubbles were visible to ensure 100% contact between the layers.

The complete structure of the model employed in this study is illustrated in Figure 5. After the components are assembled onto the fixture (e.g. transducer, syringe, silicone cornea/eyelid), a vacuum chamber is placed over the entire setup and the MPD device is installed with a manometer at the vacuum port.

Procedure sequence

The procedure sequence is as follows:

1. The pressure transducer was zeroed against air using a calibrated differential pressure manometer;
2. All of the components were installed onto the fixture;
3. System was filled with fluid and purged of air using the syringe;
4. Vacuum was programmed to prespecified negative pressure;
5. Stopcock between syringe and fluid system was opened;
6. Syringe was adjusted until system achieves the target IOP; stopcock is closed;
7. Vacuum (negative pressure) applied and released briefly to 'settle' the system;
8. Initial IOP is recorded;
9. Vacuum applied to the system; final IOP recorded;
10. Vacuum released;
11. Final IOP after vacuum chamber returns to baseline value is observed; if IOP deviates more than 0.3 mmHg from initial value, steps 3–10 are repeated.
12. Steps 1–11 were repeated for each test configuration.

At each configuration, the target baseline IOP was set to 10, 15, 20, 25, and 30 mmHg. The negative pressure (vacuum) was applied at −10, −15, and −20 for each target initial IOP. For example, −10 mmHg was applied for the baseline target IOP of 10, 15, 20, 25, and 30 mmHg and this was repeated with −15 and −20 mmHg, which yielded 15 data points for each configuration. To compare the percentage of vacuum transferred at each setting, the recorded vacuum value was obtained for each application. The resultant IOP with vacuum applied was recorded and used to calculate the transferred vacuum value by subtracting the resultant IOP from the initial IOP setting. After the transferred vacuum value was calculated, this was divided by the recorded vacuum value to calculate the percentage of vacuum transferred for each vacuum application. An example of this was calculated as demonstrated below:

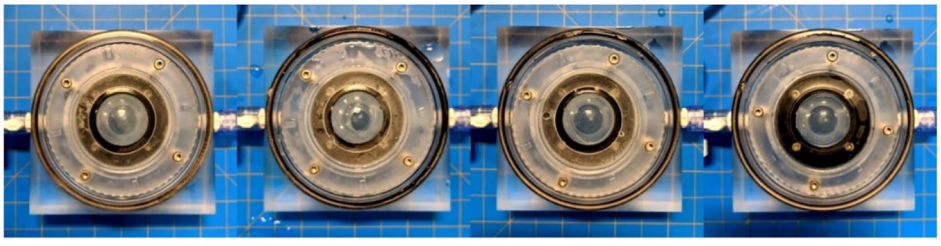

Figure 4. Contact-area control is depicted in this series of four images. Wet spot forms at the point of contact (image 2) and increases in size as the assembly is rotated close to the cornea (image 3) until complete contact is achieved and no bubbles are present on the surface (image 4).

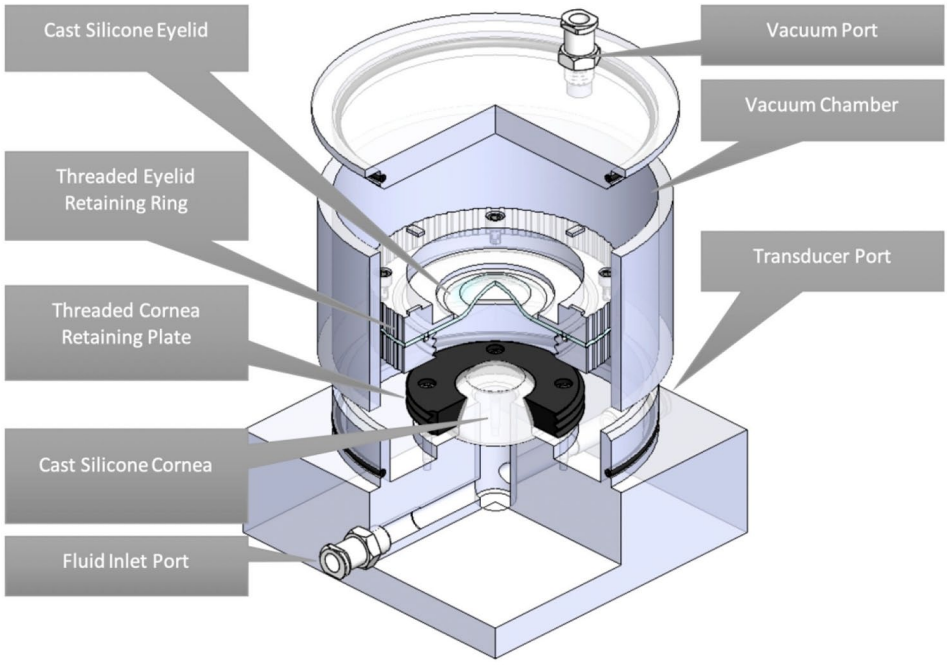

Figure 5. The complete model and all of the components.
Each component is labeled in the figure.

Sample

Target baseline IOP: 10 mmHg
Measured baseline IOP: 10.1 mmHg
Target vacuum setting: −10 mmHg
Measured vacuum setting: −9.8 mmHg

Measured IOP (with vacuum application): 0.4 mmHg
Vacuum transferred: (10.1 mmHg – 0.4 mmHg) = 9.7 mmHg

% Vacuum transferred: (9.7 mmHg) / (9.8 mmHg) = 99%

Results

To establish a baseline and to verify the percentage transfer of vacuum from the vacuum through fluid, a baseline test was performed without the silicone cornea. This process was conducted for three preset pressures and three vacuum settings (−10, −15, and −20 mmHg). In this baseline test, the mean % vacuum transferred was 99.7%, which indicates there is close to 100% transfer in the model without a membrane between the air and the fluid and established that any observed mitigation of pressure transfer can be attributed to layers of material between the vacuum and the fluid.

Thirteen different configurations were tested controlling for eyelid type, slit, and eyelid–cornea contact control. The first configuration was open and thus was not controlled for contact, slit, and the artificial eyelid tissue was absent. The mean % vacuum transferred with the open configuration was 98.7%. The sealed (no slit), non-contact configuration demonstrated the largest mitigation of mean % vacuum transfer, and this was consistent across synthetic eyelids of various material properties (40A, 18A, 2N). The mean % vacuum transfer with the 40A, 18A, and 2N eyelid tissue was 90.3%, 90.8%, and 81.5%, respectively. In comparison, the sealed (no slit), full-contact configurations (configs 2, 6, 10) exhibited minimal reduction in vacuum transfer with a collective mean % transfer value of 97.8% across all tissue types. The results for all 13 configurations are shown in Table 2.

The slit configurations, with or without contact control, demonstrated minimal reduction in vacuum transfer with all tissue types. With the 40A silicone eyelid, the mean % vacuum transfer was 98.5% and 98.6% with and without contact, respectively. With the 18A silicone, the values were

Table 2. Variables in all 13 configurations evaluated in this study.

Configuration overview													
Configuration	1	2	3	4	5	6	7	8	9	10	11	12	13
Eyelid durometer	None	40	40	40	40	18	18	18	18	2N	2N	2N	2N
Slit	N/A	No	No	Yes	Yes	No	No	Yes	Yes	No	No	Yes	Yes
Contact	N/A	Full	None	Full	None	Full	None	Full	None	Full	None	Full	None
Average % transferred	98.7	97.4	90.3	98.5	98.6	98.8	90.8	98.7	98.7	97.2	81.5	98.9	98.8

The first configuration was open and thus was not controlled for contact, slit, and the artificial eyelid tissue was absent. Of note, the cornea durometer was the same for all configurations (45).

98.7% for both contact and non-contact configurations. With the 2N tissue, the mean % transfer values were similar with 98.9% with full contact and 98.8% without contact. These numbers demonstrate that with the slit configurations, regardless of eyelid–cornea control, a mean % vacuum transfer of more than 98.5% was observed at all settings.

Of note, configuration 11 (demonstrated in Table 1) had the lowest mean % vacuum transfer at 81.5%. In this configuration, the SynDaver 2N tissue was difficult to manipulate and contact with the retaining plate could not be effectively controlled. To accommodate the tissue and correctly conduct the testing, a taller tissue retaining ring had to be installed. Due to the larger tissue retaining ring, this permits a larger intermediate, air-filled chamber which likely accounts for the substantial decrease in % vacuum transfer.

Discussion

The MPD, a novel device currently under investigation, decreases IOP by modulation of atmospheric pressure in a localized, enclosed microenvironment immediately anterior and external to the patient's eye. With prior work[10,13] establishing the IOP-lowering benefit of the device with direct application of negative pressure (e.g. patient awake with eyelids open) to the cornea, this study aimed to investigate with a model whether a mitigation in negative pressure application occurs when applied through tissue (e.g. closed eyelids). This study has meaningful implications as the MPD may prove to be most beneficial or useful while a patient is sleeping and application of negative pressure would occur through a closed eyelid.

The outcome of this model produced meaningful results that improve the understanding of vacuum transfer with tissue in place. The sealed, non-contact configurations demonstrated the most significant mitigation of vacuum transfer, regardless of eyelid tissue type. However, it is important to recognize the non-contact configuration allows an intermediate, air-filled chamber to exist between the eyelids that accounts for the significant reduction in vacuum transfer. The evidence for this is clear when comparing between sealed, non-contact and sealed, full-contact configurations and recognizing the restoration of vacuum transfer percentage to values greater than 97% with the full-contact configuration. Furthermore, not only is a large, intermediate air-filled space between the cornea and the eyelid physiologically inaccurate, it also prohibits the

ability to evaluate the contribution of the eyelid tissue to the transfer of negative pressure.

Overall, the results demonstrate that by controlling the contact between the surfaces, the contribution of the eyelid to transfer of negative pressure can be isolated and evaluated. The results of this study also suggest that the mechanical properties (e.g. rigidity) of the eyelid do not contribute to the loss of vacuum transfer given that there was no meaningful difference in vacuum transfer among the three tissue types (18A, 40A, 2N). Furthermore, while the sealed, full-contact configuration provides meaningful data from a modeling standpoint, a closed eyelid still exposes regions of corneal tissue and thus, the sealed, full-contact configuration is an incomplete representation of a closed eyelid and cornea. From a physiologic standpoint, the slit, full-contact configuration likely provides the most accurate model as the slit represents the small separation that exists between the eyelids when a human has their eyelids closed.

Due to the slit, full-contact configuration being the most physiologically accurate model, it is helpful to look at the data from those configurations of the model to anticipate how the MPD negative pressure application would behave with a subject and their eyelids closed. In the open configuration, where the eyelid tissue is absent and the vacuum is directly applied to the cornea, the mean % vacuum transferred was 98.7%. In comparison, with the slit, full-contact configuration, the mean % vacuum transferred for each eyelid tissue variation was 98.7%, 98.9%, and 98.5%, or collectively a mean of 98.7%. Given the lack of difference regardless of tissue type, these values suggest any mitigation of vacuum transfer due to the eyelid is negligible.

This study and model have limitations. This study employed a model to understand the impact of tissue on negative pressure transfer but it remains unclear how this translates to performance in human subjects. A human anterior segment has unique and complex biomechanical properties that contribute to differential responses of IOP reduction. Thus, additional loss or mitigation of the vacuum transferred would be expected in a human anterior segment model. However, the primary goal of this study was to employ a model to study whether the presence of tissue between the cornea and the application of vacuum would affect the transfer of vacuum. While the physics employed in this model were simple, the results improve the understanding of vacuum transfer through tissue. Moreover, the results encourage use and investigation of the MPD under conditions with a closed eyelid (e.g. sleeping) in human subjects.

Conclusion

The impact of the eyelid tissue on vacuum transfer can be isolated and evaluated. The results of this model suggest that the eyelids' impact on the transfer of negative pressure is insignificant and the IOP reduction achieved with the MPD may not be altered with the eyelids closed.

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All authors had complete access to the study data and assume full responsibility for the integrity of the data and the accuracy of the data analysis. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published. The authors are grateful to the study participants for their participation in this study.

Conflict of interest statement

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Mr Chu, Mr Brambilla, and Dr Yoo are employees of Equinox Ophthalmic, Inc.; Dr Ferguson is a consultant of Equinox Ophthalmic, Inc.

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ORCID iD

Tanner J. Ferguson https://orcid.org/0000-0002-7754-0465

Data availability

The data set collected and analyzed for this study is available from the corresponding author based on reasonable request.

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