

Comparison of Aqueous Outflow Facility Measurement by Pneumatography and Digital Schiøtz Tonography

Arash Kazemi,¹ Jay W. McLaren,¹ Shuai-Chun Lin,¹ Carol B. Toris,^{2,3} Vikas Gulati,³ Sayoko E. Moroi,⁴ and Arthur J. Sit¹

¹Department of Ophthalmology, Mayo Clinic, Rochester, Minnesota, United States

²Department of Ophthalmology and Visual Sciences, Case Western Reserve University, Cleveland, Ohio, United States

³Department of Ophthalmology and Visual Sciences, University of Nebraska Medical Center, Omaha, Nebraska, United States

⁴Department of Ophthalmology and Visual Sciences, University of Michigan, Ann Arbor, Michigan, United States

Correspondence: Arthur J. Sit, Department of Ophthalmology, Mayo Clinic, 200 1st Street SW, Rochester, MN 55905, USA; sit.arthur@mayo.edu.

Submitted: September 14, 2016

Accepted: October 24, 2016

Citation: Kazemi A, McLaren JW, Lin S-C, et al. Comparison of aqueous outflow facility measurement by pneumatography and digital Schiøtz tonography. *Invest Ophthalmol Vis Sci.* 2017;58:204–210. DOI:10.1167/iov.16-20754

PURPOSE. It is not known if outflow facilities measured by pneumatography and Schiøtz tonography are interchangeable. In this study we compared outflow facility measured by pneumatography to outflow facility measured by digital Schiøtz tonography.

METHODS. Fifty-six eyes from 28 healthy participants, ages 41 to 68 years, were included. Intraocular pressure (IOP) was measured in the sitting and supine positions with a pneumatometer. With the subject in the supine position, IOP was recorded for 2 minutes by using a pneumatometer with a 10-g weight and for 4 minutes by using a custom digital Schiøtz tonometer. Outflow facility was determined from the changes in pressure and intraocular volume and a standard assumed ocular rigidity coefficient for each instrument, respectively, and by using an ocular rigidity coefficient calculated by measuring pressure without and with a weight added to the pneumatometer tip.

RESULTS. The outflow facility was 0.29 ± 0.09 $\mu\text{L}/\text{min}/\text{mm Hg}$ by Schiøtz tonography and 0.24 ± 0.08 $\mu\text{L}/\text{min}/\text{mm Hg}$ by pneumatography ($P < 0.001$) when using the standard assumed constant ocular rigidity coefficient. Mean calculated ocular rigidity coefficient was 0.028 ± 0.01 μL^{-1} , and outflow facility determined by using this coefficient was 0.23 ± 0.08 $\mu\text{L}/\text{min}/\text{mm Hg}$ by Schiøtz tonography and 0.21 ± 0.07 $\mu\text{L}/\text{min}/\text{mm Hg}$ by pneumatography ($P = 0.003$). Outflow facilities measured by the two devices were correlated when the ocular rigidity was assumed ($r = 0.60$, $P < 0.001$) or calculated ($r = 0.70$, $P < 0.001$).

CONCLUSIONS. Outflow facilities measured by pneumatography were correlated with those measured by Schiøtz tonography, but Schiøtz tonography reported approximately 10% to 20% higher facilities when using the standard method. When ocular rigidity was determined for each eye, differences were smaller. Measurements from these devices cannot be compared directly.

Keywords: aqueous outflow facility, tonography, ocular rigidity, tonometry

Aqueous humor is formed by the ciliary processes, flows through the pupil and anterior chamber, and exits the eye at the anterior chamber angle. It returns to the venous system primarily through the trabecular or conventional pathway, but also exits by the uveoscleral or unconventional route.^{1,2} The ease of aqueous humor outflow through the conventional path is usually expressed as outflow facility in microliters per minute per millimeter of Hg pressure difference ($\mu\text{L}/\text{min}/\text{mm Hg}$).³ Impairment of aqueous humor outflow, which decreases outflow facility, elevates IOP and is a central tenet of pathophysiology and treatment of ocular hypertension and glaucoma.^{4,5} Although outflow facility is not routinely measured to diagnose glaucoma, it is used as a research tool to study physiological properties of the eye, and mechanisms of action of glaucoma medications and surgery.^{1,6,7}

Outflow facility links the aqueous humor flow rate, Q , and intraocular pressure, IOP , as described by the modified Goldmann equation:

$$Q = C(IOP - P_c) + U \quad (1)$$

where C is the conventional outflow facility, P_c is the episcleral venous pressure, and U is the unconventional outflow.⁸ Outflow facility, aqueous humor flow rate, and intraocular and episcleral venous pressures can be measured directly, while unconventional outflow is calculated from Equation 1.

Outflow facility has been measured noninvasively by tonography, a method that determines the volume of fluid that leaves the eye in response to a known pressure elevation. Pressure is increased by applying to the cornea a weighted tonometer, such as the electronic Schiøtz tonometer originally described by Grant,⁹ or the pneumatometer introduced by Langham et al.¹⁰ The force from the tonometer probe deforms the cornea and increases IOP. The increased IOP drives aqueous humor through the trabecular meshwork at a faster flow rate than at steady state as determined by outflow facility. The induced pressure change and the volume of aqueous humor loss during the 2 to 4 minutes that the tonometer is applied to the eye are used to estimate outflow facility. The volume of fluid loss is estimated from the pressures at the beginning and the end of tonography.





FIGURE 1. Pneumatometer and its probe, which has a flat tip with an external diameter of 5.3 mm. The weight on the probe is used only for tonography.

Electronic Schiøtz tonography was the standard method for measuring outflow facility for many years but this instrument is no longer commercially available. It indents the cornea with a weighted plunger and the depth of indentation can be directly related to intraocular pressure. Volumes that correspond to the degree of indentation have been estimated by Friedenwald¹¹ from geometric considerations and a coefficient of ocular rigidity. The pneumatometer is commercially available and can be adapted for tonography with the addition of a weight to the measurement tip. Similar to the Friedenwald tables for Schiøtz tonography, Langham et al.¹⁰ have developed tables that relate pressure to volume and used them to determine outflow facility with the pneumatometer. Outflow facility measured by pneumatography has been compared to that of Schiøtz in several studies.^{6,12,13} However, it is not known if outflow facilities measured by these two instruments are interchangeable. In this study we compared outflow facility measured by pneumatography to outflow facility measured by digital Schiøtz tonography.

METHODS

Study Subjects

Twenty-eight healthy participants were recruited from employees and patients of Mayo Clinic, or local area residents as part of a multicenter clinical trial (NCT01677507). Each participant underwent a general health interview and comprehensive ophthalmologic examination including visual acuity, IOP with pneumatometry, gonioscopy, slit-lamp biomicroscopy, and funduscopy. Subjects were excluded if they had a history or evidence of ocular pathology, intraocular surgery or trauma, laser treatment, narrow angles, or glaucoma. Each subject gave informed consent to participate after discussion of the nature and possible risks of the study. This study was approved by the Institutional Review Board at Mayo Clinic and followed the tenets of the Declaration of Helsinki.

Measurements

Intraocular Pressure. Baseline IOP was measured in both eyes in the sitting position by using a pneumatometer (Model 30 Classic; Medtronic Solan, Jacksonville, FL, USA). The subject was placed in a supine position and after 5 minutes, IOP was remeasured (P_0). Calibration of the tonometer was verified according to the manufacturer's instruction and the tip was cleaned before each set of measurement. Topical proparacaine 0.5% was instilled before each IOP measurement and tonography. The right eye was always measured first.

Outflow Facility by Pneumatography. Outflow facility was measured by using a pneumatometer with a tonography option. The subjects were placed in a supine position. Subjects were then asked to breathe normally and fixate on a target on the ceiling approximately 2 m from their eyes during the procedure. The eyelids were gently retracted by the examiner's fingers without applying additional pressure on the globe. The corneas were anesthetized by instilling



FIGURE 2. Paper tracing by pneumatography.

proparacaine 0.5% topically. The pneumatometer probe (tip diameter of 5.3 mm) with an added 10-g weight (Fig. 1) was placed on the center of the cornea and held perpendicularly to the corneal surface. Intraocular pressure was recorded for 2 minutes and the probe was removed from the eye. The right eye was always measured before the left eye.

Each 2-minute pressure tracing was printed by the pneumatometer (Fig. 2), scanned, and digitized by using CurveSnap 1.1 (Fig. 3; <http://xoofee.com/2012/12/curvesnap/>). A second-order polynomial line was fitted to the pressure curve by least-squares regression and the IOP at the beginning (P_1) and end of the interval (P_2), while the eye was exposed to the weighted probe, was determined from the value of the line at 0 and 2 minutes. The outflow facility coefficient, C , was determined by using Grant's formula⁹:

$$C = \frac{\Delta V_s + \Delta V_c}{\left[\frac{P_2 - P_1}{2} - (P_0 + P_c)\right]t} \tag{2}$$

where ΔV_s is the intraocular volume change from relaxation of tension in the sclera and corresponding to the pressure change during tonography, ΔV_c is the change in intraocular volume by corneal indentation, P_0 is pressure in the supine position, P_c is a correction of the steady-state pressure, and t is the duration of the contact, typically 2 or 4 minutes. Langham et al.¹⁰ have estimated that P_c is equal to -4 mm Hg because of an assumed indentation effect by the pneumatometer, while Friedenwald¹¹ has estimated a value of 1.25 mm Hg to account for episcleral venous pressure change during Schiøtz tonography, based on the measurement made by Linner.¹⁴

The relationship between pressure and indentation volume is based on the value of ocular rigidity for each instrument. A constant value for ocular rigidity is implicit in the tables by Langham et al.¹⁰ for pneumatography ($0.0126 \mu\text{L}^{-1}$) and Friedenwald¹¹ for the Schiøtz tonometer ($0.0215 \mu\text{L}^{-1}$). In

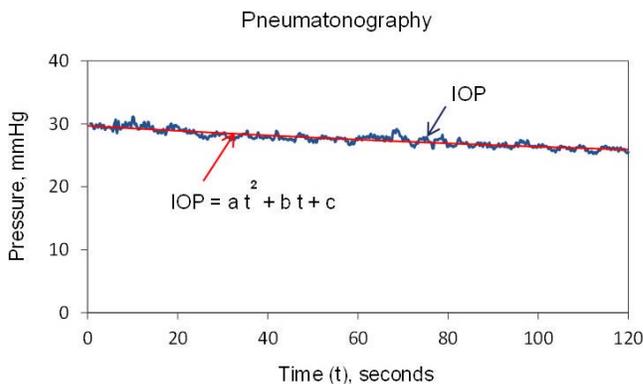


FIGURE 3. Digitized pressures by pneumatography. A second-order polynomial was fitted to IOP, and outflow facility was calculated by using IOP determined from the fitted curve at 0 and 2 minutes. a , b , c : constants of second-order polynomial.



FIGURE 4. Custom digital Schiøtz tonographer and its probe, which has a plunger with a concave tip and an external diameter of 10 mm.

addition, we calculated the ocular rigidity coefficient (K) from measurements of pressure without and with the weight added to the pneumatometer probe and by using the equation of Friedenwald¹¹:

$$K = \frac{\text{Log}P_1 - \text{Log}P_0}{V_1 - V_0} \quad (3)$$

where V_1 and V_0 are the volumes indented in the eye by the tonometer when the pressure was P_1 and P_0 , respectively. For pneumatography, these volumes were extracted from data tabulated by Langham et al.¹⁰

Outflow Facility by Custom Digital Schiøtz Tonography. Outflow facility was also measured 45 minutes after pneumatography by using a digital Schiøtz tonographer designed by the Mayo Clinic Division of Engineering.¹⁵ This tonographer probe had a plunger with a concave tip and an external diameter of 10 mm (Fig. 4). The subjects were placed in the supine position for 5 minutes and fixated on a target on the ceiling, approximately 2 m in front of their eyes. The corneas were anesthetized by instilling proparacaine 0.5% topically, and the probe with a 5.5-g weight was placed on the center of cornea and held perpendicularly for 4 minutes. The right eye was always tested first followed by the left eye. A second-order polynomial was fitted to pressures recorded by the tonographer (Fig. 5) and outflow facility was determined from pressure on the fitted curve at 0 and 4 minutes by using Equation 2. The change in corneal indentation volume (ΔV_c) was estimated from the 1955 tables by Friedenwald,¹⁶ and P_c was set to 1.25 mm Hg on the basis of the measurements made by Linner.¹⁴ The change in scleral distension volume (ΔV_s) was determined by using the standard tables introduced by Friedenwald,^{11,16} which assumes a normal ocular rigidity coefficient ($0.0215 \mu\text{L}^{-1}$), and by using the ocular rigidity coefficient estimated by our measurements with pneumatometry.

Statistical Analysis

The difference in outflow facility between instruments and significance of correlations between instruments were exam-

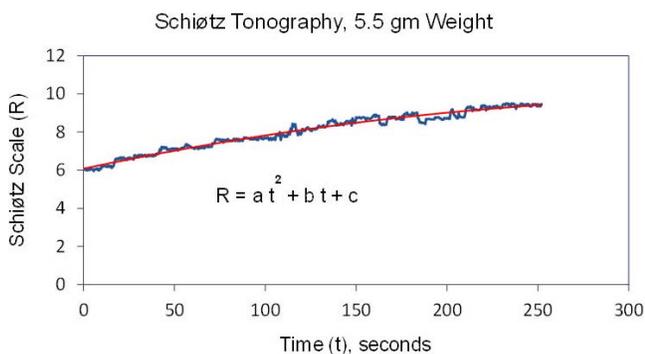


FIGURE 5. Outflow facility from Schiøtz tonography. A second-order polynomial was fitted to IOP, and outflow facility was calculated by using IOP determined from the fitted curve at 0 and 4 minutes. a , b , c : constants of second-order polynomial.

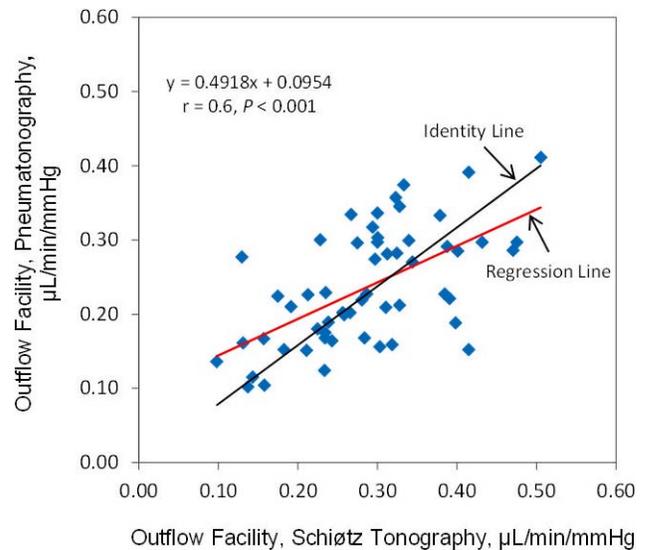


FIGURE 6. Correlation of outflow facility measured by pneumatography and Schiøtz tonography with assumed ocular rigidity coefficient.

ined by using generalized estimating equation models to account for possible correlation between fellow eyes. Relationships between instruments were illustrated by Pearson correlation. Limits of agreement between measurements were defined as the mean difference \pm 2 standard deviations (SDs) of the difference (Bland and Altman).¹⁷ All statistical tests were two sided and were calculated by using SPSS statistical software (version 21.0; SPSS, Inc., Chicago, IL, USA). Differences were considered significant if P was less than 0.05.

RESULTS

Fifty-six eyes from 28 healthy participants (6 males and 22 females; 27 Caucasians and 1 African American), ages 41 to 68 years (51 ± 8 years, mean \pm SD) were included in the study.

The mean outflow facility was $0.29 \pm 0.09 \mu\text{L}/\text{min}/\text{mm Hg}$ (\pm SD) by Schiøtz tonography and $0.24 \pm 0.08 \mu\text{L}/\text{min}/\text{mm Hg}$ by pneumatography ($P < 0.001$) when using the assumed ocular rigidity coefficient for each device (Table). Outflow facilities by the two devices were correlated ($r = 0.6$, $P < 0.001$) (Fig. 6). The mean difference between instruments was $0.05 \pm 0.08 \mu\text{L}/\text{min}/\text{mm Hg}$ and limits of agreement ranged from -0.1 to $0.21 \mu\text{L}/\text{min}/\text{mm Hg}$ (Fig. 7).

The mean calculated ocular rigidity coefficient was $0.028 \pm 0.01 \mu\text{L}^{-1}$ (\pm SD, $n = 56$ eyes). When the same calculated ocular rigidity coefficient was used to calculate outflow facility for both Schiøtz tonography and pneumatography, the mean outflow facility was $0.23 \pm 0.08 \mu\text{L}/\text{min}/\text{mm Hg}$ by Schiøtz tonography and $0.21 \pm 0.07 \mu\text{L}/\text{min}/\text{mm Hg}$ by pneumatography ($P = 0.003$). There was a strong correlation between outflow facility calculated by the two devices ($r = 0.7$, $P < 0.001$) (Fig. 8). The mean difference between instruments was $0.02 \pm 0.06 \mu\text{L}/\text{min}/\text{mm Hg}$ and limits of agreement ranged from -0.09 to $0.14 \mu\text{L}/\text{min}/\text{mm Hg}$ (Fig. 9).

DISCUSSION

With tonography, we calculate the outflow facility of aqueous humor from the volume of aqueous humor forced out of the eye by a transiently elevated pressure. The pressure is increased by placing a weighted tonometer probe on the cornea, and the volume of fluid loss is estimated from the

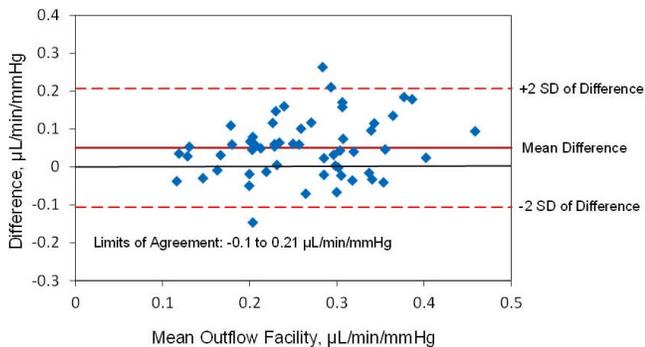


FIGURE 7. Limits of agreement, outflow facility measured by pneumatonography and Schiötz tonography with assumed ocular rigidity coefficient.

change in pressure from the beginning to the end of application of the weighted probe. The pressure change is recorded through the tonometer, but the volume change must be estimated from the indentation volume of the tonometer during contact with the eye and the change in ocular volume associated with the reduced pressure during tonography. However, differences in the way that indentation volume is calculated, along with the subsequent calculation of ocular rigidity, may result in slightly different values for outflow facility from the two devices.

The two tonographers used here both measure IOP but the approach to deriving the change in volume from pressure is somewhat different between instruments. The indentation volume from the Schiötz tonometer has been tabulated and is based on geometric considerations of the probe plunger as it indents the cornea.¹¹ The indentation volume is directly related to the height of the plunger below the probe contact position on the cornea, and this is directly related to the measured pressure. These relationships are unique for each weight added to the plunger and have been tabulated for direct conversion to outflow facility.^{11,16} The pneumatonometer does not have a plunger and the indentation volume is associated with the indentation of the entire probe, and because there is not a way to measure the indentation of the probe directly, this relationship has been determined empirically and published by

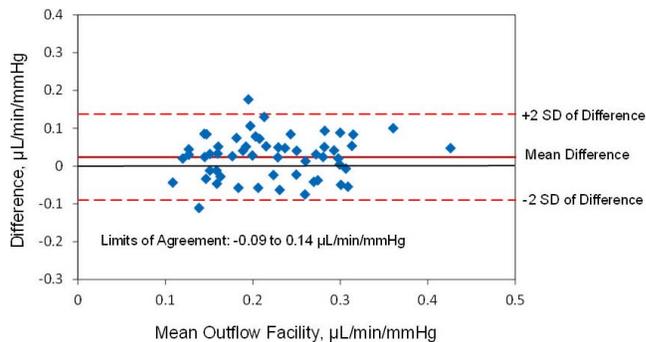


FIGURE 9. Limits of agreement, outflow facility measured by pneumatonography and Schiötz tonography with calculated ocular rigidity coefficient.

Langham et al.¹⁰ However, the derivation of this relationship for the pneumatonometer has not been explicitly described.

The relationship between volume and pressure for both instruments is dependent on the ocular rigidity coefficient, a parameter determined by the resistance that the eye exerts against distending forces and described by Equation 3.¹¹ This relationship is implicit in the calculation of outflow facility, and the most commonly used pressure-volume relationship for the calculation of ocular rigidity has been the equation of Friedenwald.¹¹ Friedenwald found a mean value of $0.0215 \mu\text{L}^{-1}$ as derived from measurements on cadaveric human eyes and this has been used in the calibration data for conversion of Schiötz tonometer scale readings to IOP measurements in millimeters of Hg, as well as tables for estimation of ocular volume change (microliters). Since the Schiötz scale is based on the assumption that the eye has an average normal rigidity, large deviations in rigidity from the average normal eye will result in erroneous estimates of IOP or outflow facility.¹⁸ Clearly, accuracy of the outflow facility estimates from each device is dependent on the accuracy of the calibration data,¹⁹ but it is unclear if either the Schiötz or pneumatonography calibration data are superior to the other in accuracy.

Another potential difference between the two devices is the reported difference in the pressure-volume relationship of living eyes compared with enucleated eyes.¹⁰ Several studies have concluded that the ocular rigidity of enucleated eyes is higher than that in living human eyes. The difference may be related to lack of active choroidal blood flow that leads to smaller volume of displaced fluid and postmortem changes in enucleated eyes.^{10,20-22} While the ocular rigidity coefficient in Friedenwald's tables for Schiötz tonography was calculated based on enucleated eyes, the assumed ocular rigidity coefficient for pneumatonography in Langham's tables was developed based on living eyes.

Measurement of ocular rigidity in living human eyes has been reported previously, based on injection of small volumes of saline solution into the anterior chamber and measurement of the resulting pressure change with a transducer.^{23,24} This method has been reported by Prijot and Weekers,²⁵ Prijot,²⁶ Ytteborg,^{20,21,27,28} and Eisenlohr et al.²² More recently, Pallikaris et al.²³ calculated the ocular rigidity coefficient as the slope of the line fitted by linear regression, to the pressure-volume relationship as measured during cataract surgery. The mean ocular rigidity coefficient was $0.0126 \mu\text{L}^{-1}$ with their method. Karyotakis et al.²⁹ and Dastiridou et al.^{5,30} used the same manometric method and fitted an exponential curve to the pressure-volume relationship over a range of IOP from 15 to 40 mm Hg. The mean ocular rigidity coefficients were $0.028 \mu\text{L}^{-1}$ and $0.022 \mu\text{L}^{-1}$ respectively. This variability in directly measured ocular rigidity coefficient in different study popula-

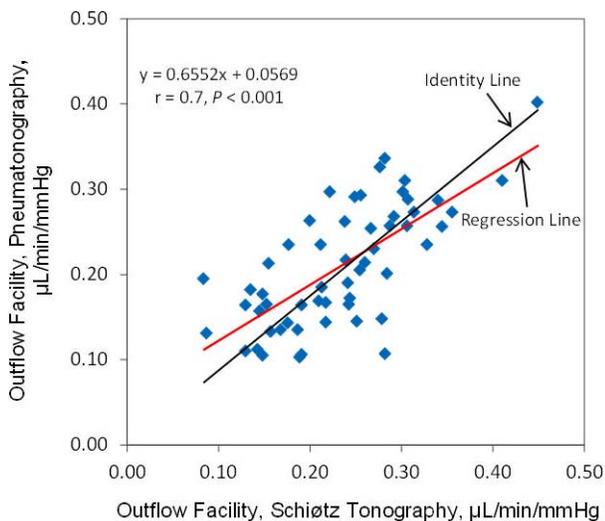


FIGURE 8. Correlation of outflow facility measured by pneumatonography and Schiötz tonography with calculated ocular rigidity coefficient.

TABLE. Outflow Facility Measurements by Pneumatography and Schiøtz Tonography

	Assumed Ocular Rigidity Coefficient		Calculated Ocular Rigidity Coefficient	
	Pneumatography	Schiøtz Tonography	Pneumatography	Schiøtz Tonography
Ocular rigidity coefficient, μL^{-1}	0.0126	0.0215	0.028 \pm 0.01	
Outflow facility, mean \pm SD, $\mu\text{L}/\text{min}/\text{mm Hg}$	0.24 \pm 0.08	0.29 \pm 0.09	0.21 \pm 0.07	0.23 \pm 0.08
<i>P</i> value	<0.001*		0.003*	
Correlation, <i>r</i>	0.60 (<i>P</i> < 0.001)*		0.70 (<i>P</i> < 0.001)*	

Outflow facility determined by using assumed and calculated ocular rigidity coefficients by pneumatography and Schiøtz tonography in 56 eyes of 28 participants. The assumed ocular rigidities were from the literature and have typically been used to calculate outflow facility. The calculated ocular rigidities were determined in each eye according to Equation 3.

* Generalized estimating equation models.

tions suggests that assumption of a constant value may not be ideal for calculation of outflow facility.

Because the Friedenwald and Langham tables assume a constant (normal) ocular rigidity coefficient, calculation of outflow facility can be different on eyes with high or low ocular rigidity. We accounted for these differences by calculating the ocular rigidity coefficient for each eye from IOP measured by using a pneumatometer without and with a 10-g weight added to the tonometer probe, based on the Friedenwald's equation (Equation 3),¹¹ and by using Langham's tables for determining ocular volume change.¹⁰ Notably, our mean ocular rigidity coefficient, $0.028 \pm 0.01 \mu\text{L}^{-1}$, was higher than both assumed values. One possible reason is that we assumed that the ocular displacement volume was zero when the probe was not weighted on the initial supine measurement (P_0). However, the inherent weight of the tonometer probe would have indented the cornea slightly, and this would have somewhat reduced the volume change used to determine the ocular rigidity coefficient. This coefficient therefore may have been slightly overestimated. Although our estimate was somewhat higher than that reported for living eyes by Friedenwald¹¹ ($0.021 \mu\text{L}^{-1}$) and Dastiridou et al.^{5,30} ($0.022 \mu\text{L}^{-1}$), it was similar to that of Karyotakis et al. ($0.028 \mu\text{L}^{-1}$),²⁹ who used a manometric technique to determine the ocular rigidity coefficient.

The effect of the ocular rigidity coefficient on outflow facility was apparent from the results of our study. When we used the traditional assumed constant ocular rigidity coefficients, the outflow facilities calculated by pneumatometry were significantly lower than those by Schiøtz tonography. However, when we calculated *K*, based on Friedenwald's equation and the estimated indentation volumes from Langham et al.,¹⁰ our estimate of outflow facility by pneumatography was much closer to that by Schiøtz tonography.

Another potential error in the outflow facility calculation is in the measurement of the initial unweighted supine IOP (P_0). The ocular volume parameters vary with pressure, and an error of a few millimeters of Hg in P_0 can cause large errors in the outflow facility coefficient. This may be particularly important for the Schiøtz tonometer, since it cannot measure P_0 directly (because a weight is a necessary component of the device) and consequently, values of P_0 are determined by using an average value of the ocular rigidity coefficient. Several studies have reported that current Schiøtz readings based on Friedenwald's 1955 calibration scale¹⁶ are in error. Friedenwald used applanation tonometry on seated patients as a means of checking the indentation calibration scale, based on the assumption that the mean IOP of normal eyes increased by 1 mm Hg upon lying down, owing to an identical pressure increment in the episcleral vein.³¹ However, subsequent studies³²⁻³⁹ report that this postural effect exceeds 1 mm Hg and is between 1.8 and 5 mm Hg. These studies suggest that

the Schiøtz values may be significantly low, with the Schiøtz calibration in error by as much as 3 to 5 mm Hg.

In contrast to Schiøtz tonometry, pneumatometry can measure initial unweighted supine IOP (P_0) directly without the need to use the ocular rigidity relationship. Langham et al.¹⁰ report that pneumatometry measurements are 2.6 ± 0.26 mm Hg greater than Goldmann applanation tonometry measurements from normal and glaucomatous eyes in the sitting position. They state that this difference is caused by a slight corneal indentation by the pneumatometer. Measurements in the supine position increases an additional 1 mm Hg owing to the weight of the piston when the tonometer is held vertically. Hence, for pneumatography, Langham et al.¹⁰ suggest the addition of a correction factor of -4 mm Hg to the P_0 in Equation 2.

The outflow facility estimated by pneumatometry with default ocular rigidity in our study subjects ($0.24 \pm 0.08 \mu\text{L}/\text{min}/\text{mm Hg}$) was close to that estimated by others. Langham et al.¹⁰ report an outflow facility of $0.28 \pm 0.01 \mu\text{L}/\text{min}/\text{mm Hg}$ by 4-minute pneumatography, which is not significantly different from $0.29 \pm 0.01 \mu\text{L}/\text{min}/\text{mm Hg}$ by 2-minute pneumatography. They conclude that the 2-minute tonography could be used as a standard for pneumatography. Liu et al.⁴⁰ report $0.23 \pm 0.05 \mu\text{L}/\text{min}/\text{mm Hg}$ for normal subjects aged 37 to 74 years and in another study Toris et al.⁴¹ obtained $0.25 \pm 0.11 \mu\text{L}/\text{min}/\text{mm Hg}$ for subjects aged 21 to 30 years and $0.20 \pm 0.09 \mu\text{L}/\text{min}/\text{mm Hg}$ for subjects aged 60 to 79 years. The difference between age groups is not significant.

Our outflow facility measured by digital Schiøtz tonography ($0.29 \pm 0.09 \mu\text{L}/\text{min}/\text{mm Hg}$) with assumed constant ocular rigidity was also similar to measurements of others by the same method. Grant^{9,19} reports values of $0.23 \mu\text{L}/\text{min}/\text{mm Hg}$ and $0.24 \mu\text{L}/\text{min}/\text{mm Hg}$ for outflow facility by tonography in normal human living eyes, and Becker⁴² reports a mean value of $0.28 \pm 0.05 \mu\text{L}/\text{min}/\text{mm Hg}$ in his study on 909 normal eyes. Selvadurai et al.,¹⁵ Nau et al.,⁴³ and Sit et al.⁴⁴ recently performed several studies on normal subjects. They report an outflow facility of $0.28 \pm 0.09 \mu\text{L}/\text{min}/\text{mm Hg}$ in one study, and in two separate studies report $0.28 \pm 0.09 \mu\text{L}/\text{min}/\text{mm Hg}$ in younger group (age 30-45 years) and $0.23 \pm 0.06 \mu\text{L}/\text{min}/\text{mm Hg}$ in older subjects (age 47-76 years).

Other investigators compared Schiøtz tonography to pneumatography in the same subjects and found that the two methods produce similar mean outflow facilities, although outflow facility measured by pneumatography shows more variability. Feghali et al.¹² found no significant difference in outflow facility between methods on 13 normal subjects and 3 glaucoma patients ($0.24 \pm 0.11 \mu\text{L}/\text{min}/\text{mm Hg}$ with pneumatography and $0.22 \pm 0.07 \mu\text{L}/\text{min}/\text{mm Hg}$ with Schiøtz tonography). However, both intersubject and interobserver variabilities were significantly higher with pneumatography. Wheeler et al.⁶ estimate a mean outflow facility of $0.22 \pm 0.09 \mu\text{L}/\text{min}/\text{mm Hg}$ and $0.23 \pm 0.07 \mu\text{L}/\text{min}/\text{mm Hg}$

with pneumatography and Schiøtz tonography, respectively, in eight normal subjects. Although these mean outflow facilities are not significantly different, pneumatography had high standard deviation and poor reproducibility. The study is limited by a small sample size. Lim et al.¹³ studied 30 subjects and found a mean of tonographic outflow facility of 0.23 ± 0.09 $\mu\text{L}/\text{min}/\text{mm Hg}$ and 0.22 ± 0.08 $\mu\text{L}/\text{min}/\text{mm Hg}$ with Schiøtz and 2-minute pneumatography, respectively, for right eye and 0.26 ± 0.07 $\mu\text{L}/\text{min}/\text{mm Hg}$ and 0.20 ± 0.08 $\mu\text{L}/\text{min}/\text{mm Hg}$ with Schiøtz and 2-minute pneumatography, respectively, for left eye.

The higher variability of outflow facilities by pneumatography may be associated with a greater mobility of the smaller probe tip, which is flat and can slide across the cornea. This tip design could allow more transmission of eye and hand movements to the transducer and cause variable indentation and transient changes in IOP. In contrast, the tip of the Schiøtz tonometer is concave, has larger diameter, and rests more steadily on the cornea. The greater mechanical stability of this design may result in less variability of IOP than with pneumatography.

It is not completely clear why our study found a difference between Schiøtz tonography and pneumatography, while previous investigators did not. Smaller sample size in previous studies may be one of the reasons. One significant difference in the analysis methods was the use of data extraction by fitting of a second-order polynomial to the data in our study. It is possible that this technique accentuates differences by eliminating the temptation to manually smooth a paper tonography tracing. Further research is required to determine if the differences in outflow facility between the two devices persist in other populations, such as glaucoma patients.

SUMMARY

Outflow facilities measured by using the pneumatography are correlated with those measured by Schiøtz tonography, but Schiøtz tonography reports approximately 10% to 20% higher facilities. Consequently, the measurements from these devices cannot be directly compared to determine differences in outflow facility, and the devices cannot be used interchangeably. Differences in shape, size, and weight of the two tonographer tips, method of IOP measurement, and using different calibration tables may be responsible for the differences in outflow facility measurement. When the ocular rigidity coefficient for each eye was calculated and the same value used for both instruments, outflow facilities were much closer between methods. Each method has several advantages and disadvantages, and which method is more accurate cannot be determined from our noninvasive study. Each of the methods appears to provide reasonable estimates of outflow facility, and while the indicated values are not identical, they are tightly correlated. Therefore, the instruments cannot be used interchangeably, but either is a reasonable choice for assessing differences in outflow facilities in human subjects.

Acknowledgments

This study was presented in part at the annual meeting of the Association for Research in Vision and Ophthalmology (ARVO), Denver, Colorado, United States, May 2015.

Supported by National Institutes of Health (NIH) EY022124 (SEM), NIH EY007003 (University of Michigan National Eye Institute Core Grant), and unrestricted departmental grants from Research to Prevent Blindness, New York, New York, United States (Mayo Clinic and University of Michigan). AJS is a recipient of a Schaub

Special Scholar Award from Research to Prevent Blindness. VG has received funding from NEI-K23EY023266.

Disclosure: **A. Kazemi**, None; **J.W. McLaren**, None; **S.-C. Lin**, None; **C.B. Toris**, None; **V. Gulati**, None; **S.E. Moroi**, None; **A.J. Sit**, None

References

1. Johnstone MA. Aqueous humor outflow system overview. In: Stamper RL, Lieberman MF, Drake MV, eds. *Becker-Shaffer's Diagnosis and Therapy of the Glaucomas*. Edinburgh, UK: Mosby Elsevier; 2009:25-46.
2. Johnson M, McLaren JW, Overby DR. Unconventional aqueous humor outflow: a review [published online ahead of print February 2, 2016]. *Exp Eye Res*. doi:10.1016/j.exer.2016.01.017.
3. Becker B, Friedenwald JS. Clinical aqueous outflow. *AMA Arch Ophthalmol*. 1953;50:557-571.
4. Grant WM. Clinical measurements of aqueous outflow. *AMA Arch Ophthalmol*. 1951;46:113-131.
5. Dastiridou AI, Tsironi EE, Tsilimbaris MK, et al. Ocular rigidity, outflow facility, ocular pulse amplitude, and pulsatile ocular blood flow in open-angle glaucoma: a manometric study. *Invest Ophthalmol Vis Sci*. 2013;54:4571-4577.
6. Wheeler NC, Lee DA, Cheng Q, Ross WF, Hadjiaghai L. Reproducibility of intraocular pressure and outflow facility measured by pneumatic tonography and Schiøtz tonography. *J Ocul Pharmacol Ther*. 1998;14:5-13.
7. Cameron D, Finlay ET, Jackson CR. Tonometry and tonography in the diagnosis of chronic simple glaucoma. *Br J Ophthalmol*. 1971;55:738-741.
8. Goldmann H. The aqueous veins and the Poiseuille law [in German]. *Ophthalmologica*. 1949;118:496-519.
9. Grant WM. Tonographic method for measuring the facility and rate of aqueous flow in human eyes. *Arch Ophthalmol*. 1950;44:204-214.
10. Langham ME, Leydhecker W, Krieglstein G, Waller W. Pneumatographic studies on normal and glaucomatous eyes. *Adv Ophthalmol*. 1976;32:108-133.
11. Friedenwald JS. Contribution to the theory and practice of tonometry. *Am J Ophthalmol*. 1937;20:985-1024.
12. Feghali JG, Azar DT, Kaufman PL. Comparative aqueous outflow facility measurements by pneumatography and Schiøtz tonography. *Invest Ophthalmol Vis Sci*. 1986;27:1776-1780.
13. Lim KS, Nau CB, O'Byrne MM, et al. Mechanism of action of bimatoprost, latanoprost, and travoprost in healthy subjects: a crossover study. *Ophthalmology*. 2008;115:790-795.e794.
14. Linner E. Further studies of the episcleral venous pressure in glaucoma. *Am J Ophthalmol*. 1956;41:646-651.
15. Selvadurai D, Hodge D, Sit AJ. Aqueous humor outflow facility by tonography does not change with body position. *Invest Ophthalmol Vis Sci*. 2010;51:1453-1457.
16. Friedenwald JS. Tonometer calibration: an attempt to remove discrepancies found in the 1954 calibration scale for Schiøtz tonometers. *Trans Am Acad Ophthalmol Otolaryngol*. 1957; 61:108-122.
17. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986;1:307-310.
18. Friedenwald JS. Clinical significance of ocular rigidity in relation to the tonometric measurement. *Trans Am Acad Ophthalmol Otolaryngol*. 1949;53:262-264.
19. Grant WM. Clinical tonography. *Trans Am Acad Ophthalmol Otolaryngol*. 1951;55:774-781.
20. Ytteborg J. The role of intraocular blood volume in rigidity measurements on human eyes. *Acta Ophthalmol (Copenh)*. 1960;38:410-436.

21. Ytteborg J. Influence of bulbar compression on rigidity coefficient of human eyes, in vivo and enucleated. *Acta Ophthalmol (Copenh)*. 1960;38:562-577.
22. Eisenlohr JE, Langham ME, Maumenee AE. Manometric studies of the pressure-volume relationship in living and enucleated eyes of individual human subjects. *Br J Ophthalmol*. 1962;46:536-548.
23. Pallikaris IG, Kymionis GD, Ginis HS, Kounis GA, Tsilimbaris MK. Ocular rigidity in living human eyes. *Invest Ophthalmol Vis Sci*. 2005;46:409-414.
24. Detorakis ET, Pallikaris IG. Ocular rigidity: biomechanical role, in vivo measurements and clinical significance. *Clin Exp Ophthalmol*. 2013;41:73-81.
25. Prijot E, Weekers R. Contribution to the study of the rigidity of the normal human eye [in French]. *Ophthalmologica*. 1959;138:1-9.
26. Prijot E. Contribution to the study of tonometry and tonography in ophthalmology [in French]. *Doc Ophthalmol*. 1961;15:1-225.
27. Ytteborg J. The effect of intraocular pressure on rigidity coefficient in the human eye. *Acta Ophthalmol (Copenh)*. 1960;38:548-561.
28. Ytteborg J. Further investigations of factors influencing size of rigidity coefficient. *Acta Ophthalmol (Copenh)*. 1960;38:643-657.
29. Karyotakis NG, Ginis HS, Dastiridou AI, Tsilimbaris MK, Pallikaris IG. Manometric measurement of the outflow facility in the living human eye and its dependence on intraocular pressure. *Acta Ophthalmol (Copenh)*. 2015;93:e343-e348.
30. Dastiridou AI, Ginis HS, De Brouwere D, Tsilimbaris MK, Pallikaris IG. Ocular rigidity, ocular pulse amplitude, and pulsatile ocular blood flow: the effect of intraocular pressure. *Invest Ophthalmol Vis Sci*. 2009;50:5718-5722.
31. Linner E, Rickenbach C, Werner H. Comparative measurements of the pressure in the aqueous veins and the conjunctival veins using different methods. *Acta Ophthalmol (Copenh)*. 1950;28:469-478.
32. Armaly MF, Salamoun SG. Schiøtz and applanation tonometry. *Arch Ophthalmol*. 1963;70:603-609.
33. Galin MA, Mc IJ, Magruder GB. Influence of position on intraocular pressure. *Am J Ophthalmol*. 1963;55:720-723.
34. Schwartz JT, Dell'Osso GG. Comparison of Goldmann and Schiøtz tonometry in a community. *Arch Ophthalmol*. 1966;75:788-795.
35. Langham ME, McCarthy E. A rapid pneumatic applanation tonometer: comparative findings and evaluation. *Arch Ophthalmol*. 1968;79:389-399.
36. Roberts W, Rogers JW. Postural effects on pressure and ocular rigidity measurements. *Am J Ophthalmol*. 1964;57:111-118.
37. Hetland-Eriksen J. On tonometry—5: the pressure of glaucomatous eyes measured in the sitting and the lying positions by means of the Goldmann applanation tonometer. *Acta Ophthalmol (Copenh)*. 1966;44:515-521.
38. Hetland-Eriksen J. On tonometry—6: comparative tonometry with the Goldmann applanation tonometer and the Schiøtz tonometer in the lying position. *Acta Ophthalmol (Copenh)*. 1966;44:522-538.
39. Anderson DR, Grant WM. Re-evaluation of the Schiøtz tonometer calibration. *Invest Ophthalmol*. 1970;9:430-446.
40. Liu H, Fan S, Gulati V, et al. Aqueous humor dynamics during the day and night in healthy mature volunteers. *Arch Ophthalmol*. 2011;129:269-275.
41. Toris CB, Yablonski ME, Wang YL, Camras CB. Aqueous humor dynamics in the aging human eye. *Am J Ophthalmol*. 1999;127:407-412.
42. Becker B. Tonography in the diagnosis of simple (open angle) glaucoma. *Trans Am Acad Ophthalmol Otolaryngol*. 1961;65:156-162.
43. Nau CB, Malihi M, McLaren JW, Hodge DO, Sit AJ. Circadian variation of aqueous humor dynamics in older healthy adults. *Invest Ophthalmol Vis Sci*. 2013;54:7623-7629.
44. Sit AJ, Nau CB, McLaren JW, Johnson DH, Hodge D. Circadian variation of aqueous dynamics in young healthy adults. *Invest Ophthalmol Vis Sci*. 2008;49:1473-1479.