Variation in Schlemm’s Canal Diameter and Location by Ultrasound Biomicroscopy

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Purpose: To measure variations in diameter and location of Schlemm’s canal in vivo by ultrasound biomicroscopy.
Design: Prospective, single-institution, consecutive case series.
Participants: Ninety-four patients with and without glaucoma.
Methods: Under topical anesthesia, an 80-MHz iUltrasound probe (iScience Interventional, Inc., Menlo Park, CA) placed at the 12-o’clock position was used to measure the canal’s diameter and its distance from both the anatomic limbus (corneoscleral junction) and the angle (the base of the canal and the angle of iris insertion).

Main Outcome Measures: Diameter and location of the canal were measured relative to gender, age, intraocular pressure, race, diagnosis, previous glaucoma surgery, pachymetry, refraction, lens type, axial length, and keratometry.
Results: The average canal diameter was 121 μm (±45 μm). The canal diameter in hyperopes was larger than the canal diameter in myopes (180±69 μm vs. 122±45 μm; P<0.001). The diameter of Schlemm’s canal was smaller in patients with previous glaucoma surgery compared with patients without glaucoma surgery (98±20 μm vs. 125±4 μm; P<0.01). The mean distance between the angle and Schlemm’s canal was found to be smaller in hyperopes than in myopes (281 vs. 335 μm; P = 0.03). The location of the canal in black patients compared with white patients was found to be more posterior from the limbus (659±92 μm vs. 624±73 μm; P = 0.05). Similarly, canal location in patients with corneal thickness of more than 555 μm was found to be more posterior to the limbus (702 vs. 625 μm; P<0.01) compared with those with thinner corneas.

Conclusions: When measured in vivo with ultrasound biomicroscopy, Schlemm’s canal diameter was significantly smaller (121 μm) than demonstrated in previous histopathologic studies.

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Schlemm’s canal is a circumferential channel that runs parallel to the limbus. The canal is lined with a single layer of vascular-derived endothelial cells and transports 2 to 3 μl per minute of aqueous humor from the anterior chamber to the venous plexus.1,2 In previous electron microscopic examinations of banked eyes, the canal was measured at 190 to 350 μm in cross-sectional diameter.3 The anatomic features of the Schlemm’s canal are increasingly important with the advent of new techniques such as canaloplasty (iScience Interventional, Menlo Park, CA), trabeculotomy ab interno performed with the Trabectome (NeoMedix Corporation, Tustin, CA), and iStent implantation (Glaukos Corporation, Laguna Hills, CA).

Previously, measurements of diameter and location of the canal have been possible only in postmortem eyes using microscopy. Recent developments in high-frequency ultrasound technology allow for direct visualization of the canal in vivo. To date, there are no studies discussing variations in the anatomic features of Schlemm’s canal as measured by ultrasound techniques. iUltrasound (iScience Interventional, Inc.) is a new imaging system that allows for examination of the canal in vivo.

Patients and Methods

A prospective study was performed at the Tulane Medical Center with the approval of the Tulane University Institutional Review Board. Methods described below adhere to the tenets of the Declaration of Helsinki. Each participant signed a standardized informed consent approved by the Institutional Review Board.

Ninety-four consecutive patients met the enrollment criteria and were included in the study (54 females, 40 males). Patients aged 18 years or more, with no previous history of trauma or of previous canal surgery were deemed eligible. A single, randomly selected eye from each patient was studied. The study was performed on patients before pupillary dilation. Each patient had a comprehensive ophthalmologic examination, including slit-lamp biomicroscopy, intraocular pressure by Goldmann applanation tonometry, refraction, keratometry, and axial length. The latter 2 values were obtained using the IOLMaster (Carl Zeiss Meditec, Inc., Dublin, CA). Pachymetry was added as part of the protocol during the course of the study and was performed on only 33 patients (66 eyes). The age, gender, race, number of glaucoma medications, number and type of previous glaucoma surgeries, and lens type for each eye were entered into a confidential computer database.

For consistency, the same experienced technician (MSM) identified and measured the Schlemm’s canal diameter and location for each eye using the iUltrasound imaging system. The iUltrasound features an 80-MHz transducer frequency with an axial resolution of 25 μm and a lateral resolution of 50 μm. For this study, the system’s electronic resolution and caliper positioning limit was 10 μm. The imaging window measured 4.0×3.5 mm. Tissue penetration depth was approximately 2 mm. The scan angle was 10.5°. The scan rate was 7 frames per second, a speed that greatly reduces...
motion artifact caused by hand movements. The iUltrasound’s self-contained probe was placed directly on the eye for imaging. To test the accuracy of the iUltrasound caliper measurements, a phantom created with string targets spaced 0.125 mm apart was imaged and measured. Measurements were performed at the center and the lateral ends of the imaging field. Measurements yielded an average variation coefficient of 3.8% across the full width (4 mm) of the imaging field. Interoperator variance was determined by obtaining a set of 10 images of the target phantom and having 5 reviewers obtain 5 different measurements of each image. The intraoperator and interoperator standard deviation measured 10 μm, and the interoperator reproducibility variance was 11 μm. Thus, the imaging system’s caliper measurement provided a high level of precision under conditions of high imaging contrast and resolution.

Topical anesthesia was obtained using proparacaine 0.5% drops. Canal diameter and location were measured in each eye at the 12-o’clock position using the iUltrasound transducer with a low-viscosity gel to aid in transduction. As soon as an accurate, artifact-free image was obtained from each eye (Fig 1), the caliper function was used to measure the distance from the anatomic limbus inferiorly to the roof of Schlemm’s canal. The anatomic limbus was identified as the intersection of lower attenuated corneal tissue and hyperdense scleral tissue. The distance from the angle was determined by measuring between the base of the canal and the angle of iris insertion. Finally, the diameter of the canal was measured directly along its y-axis (major diameter) using the caliper function (Fig 2). In eyes previously treated surgically for glaucoma at the 12-o’clock position, canal measurements were performed in the adjacent area within 1 to 2 clock hours. Eyes were organized by diagnostic categories, including: healthy, ocular hypertension (intraocular pressure ≥21 mmHg with no optic nerve or visual field changes secondary to elevated intraocular pressure). Refractive error was defined as myopia (–1 diopter [D] or less) or hyperopia (+1 D or more). Thick cornea was defined as pachymetry >555 μm.

Statistical Analysis

One eye (right or left) of each of the 94 patients was selected randomly for analysis using a Uniform (0,1) random number generator in SPSS (SPSS, Inc., Chicago, IL). The Student t test was applied to compare continuous (normally distributed) variables between subgroups, with the Pearson correlation coefficient (r) used to measure association. Differences in binary proportions were assessed by the Fisher exact test and the chi-square test was used for categorical variables such as race. Multiple linear regression and analysis of covariance were used to determine variables independently correlated with Schlemm’s canal diameter and location and to control for possible confounders.4 Statistical analysis was performed using the SPSS software package version 16.0 (SPSS, Inc., Chicago, IL). Two-tailed values of P<0.05 were considered statistically significant.

Results

A total of 94 patients were studied with random selection resulting in 49 right eyes and 45 left eyes for analysis. Mean patient age was 49±20 years (range, 22–91 years). Mean canal diameter for all eyes in this study was 121±45 μm (range, 60–300 μm). Schlemm’s canal was located 322±95 μm from the angle (range, 100–630 μm) and 640±80 μm from the limbus (range, 400–850 μm).

Table 1 presents a comparison of Schlemm’s canal diameter, location from angle, and location from limbus in relation to 8

Figure 1. Example of Schlemm’s canal as visualized by the iUltrasound Imaging System (iScience Interventional, Menlo Park, CA).
patient characteristics. Age, gender, intraocular pressure, lens type, axial length, and a diagnosis of glaucoma or ocular hypertension were not found to be significant predictors of Schlemm’s canal diameter or location (all $P > 0.10$).

Blacks and Hispanics were found to have canals in a more posterior location as measured from the limbus when compared with whites and Asians ($P = 0.05$). Twelve of the 94 patients had prior glaucoma surgery (trabeculectomy). The mean canal diameter was significantly smaller in the surgery group compared with those without surgery ($98 \pm 20 \mu m$ vs. $125 \pm 47 \mu m; P < 0.01$).

Patients with corneal pachymetry of less than $555 \mu m$ were associated with canals located more proximal to the limbus compared with those with pachymetry of more than $555 \mu m$ ($625 \pm 85 \mu m$ vs. $702 \pm 61 \mu m; P < 0.01$). The scatterplot of pachymetry versus canal location from the limbus is shown in Figure 3 and depicts a moderate positive correlation ($r = 0.47; P = 0.008$). Analysis of covariance indicated that pachymetry values were correlated significantly with location from the limbus independent of intraocular pressure ($F$ test, $7.60; P = 0.01$).

Hyperopes had larger canal diameters compared with myopes ($180 \pm 69 \mu m$ vs. $122 \pm 45 \mu m; P < 0.01$). The mean distance between the canal and the angle was smaller in hyperopes compared with myopes ($281 \pm 46 \mu m$ vs. $342 \pm 100 \mu m; P = 0.03$). Multivariate analysis was performed to compare canal diameter, canal location based on distances from the angle and from the limbus, average $K$, and axial length in patients with myopia and those with hyperopia based on refraction data. Canal diameter was found to be significantly smaller ($P < 0.01$) and the location from the angle was greater ($P = 0.02$) in patients with myopia compared with those with hyperopia.

**Discussion**

The current study explores the diameter and location of Schlemm’s canal as measured by high-frequency ultrasound in patients with and without glaucoma. The major finding of the study is that the diameter of the canal measured in vivo is much smaller than reported canal diameter measured in banked eyes. These previous studies used light and electron microscopy on enucleated human eyes and showed canal diameter ranging between 180 and 350 $\mu m$. The resolving power of light and electron microscopy is superior to ultrasound biomicroscopy; thus, measurement variations based on resolving power are expected, especially in a narrow canal. Differences in measurements also may be related to specimen preparation and fixation conditions (immersion vs. perfusion) for microscopy as well as the partial apposition of the canal walls that occurs in vivo. The canal diameter measured in vivo may reflect the canal’s functional size more accurately because of partial collapse of the canal secondary to physiologic conditions. It is also possible that hand motion may influence in vivo measurements because a handheld transducer is positioned over the area to be mea-

![Figure 2. iUltraSound Imaging System image showing Schlemm's canal in relation to surrounding anatomic features. The caliper application on the iUltraSound Imaging System (iScience Interventional, Menlo Park, CA) was used to measure distance from the anatomic limbus to the roof of Schlemm's canal. The distance from the base of Schlemm's canal to the angle of insertion was measured to obtain the distance from the angle. The diameter of Schlemm's canal was measured as the maximum linear dimension.](image-url)
surgery eyes versus 276/H9262 between 30 and 60 mmHg.

in the canal size in patients with intraocular pressures be-
do not know if there would have been significant differences
mmHg; average, 14.8/H11006 4.9 mmHg) and canal diameter. We
Age (yrs)

sure correlates with smaller canal diameter in glaucoma
previously published in vivo measurements of Schlemm’s
tissues and may affect the reading. The system operators are
sured and any excess pressure on the eye may distort the
tissues and may affect the reading. The system operators are
trained to recognize and avoid creating this type of artifact
underperfusion of these structures. In the current study,
similar results were seen in postfiltration surgery eyes com-
pared with those without any surgery.

In a study of 38 eyes by immediate perfusion-fixation and
immersion-fixation by light microscopy, Ainsworth and
Lee8 described a significant decrease in the anteroposterior
width of Schlemm’s canal with age. McMenamin et al9
reported an increased frequency of narrow canals in older
eyes (light and electron microscopy). They also reported
significant areas of normal morphologic features even in the
oldest eyes. Although filtration function and Schlemm’s
canal histologic features may be influenced by age, the
current study indicates no significant variation in canal
diameter or location. Because we measured the canal only at
the 12-o’clock position, it is possible that we missed areas
of narrowing elsewhere in the canal.

Significant differences in the canal diameter based on
refractive error (myopes>hyperopes) and the posterior loca-
tion of canals in black persons compared with white
persons and those with thicker corneas have not been re-
ported previously. The significance of these findings pre-
sently is unknown. However, this information may be helpful
to the surgeon trying to locate the canal during surgery.

The limitations of this study include the following: mea-
surements were performed only at the 12-o’clock location
in each patient, and other quadrants were not analyzed in
this preliminary study. The same operator performed all
iUltrasound measurements. Subjects younger than 18 years
were not included. No patient with very high intraocular
pressure (>30 mmHg) was included in the present study.
The preliminary study findings with regard to variations in
canal diameter associated with refractive error and prior

glaucoma surgery, and variations in canal location relative
to refractive error, corneal thickness, and race need to be
verified in a larger study with adequate sample size.

Table 1. Measurements of Diameter and Location of Schlemm’s
Canal Based on Ultrasound Biomicroscopy (N = 94 Patients)

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of Patients</th>
<th>Schlemm Canal Diameter</th>
<th>Location from Angle</th>
<th>Location from Limbus</th>
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</thead>
<tbody>
<tr>
<td>Age (yrs)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥40</td>
<td>37</td>
<td>120±7</td>
<td>334±9</td>
<td>645±73</td>
</tr>
<tr>
<td>&gt;40</td>
<td>57</td>
<td>122±6</td>
<td>314±9</td>
<td>636±84</td>
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<tr>
<td>P value</td>
<td>0.79</td>
<td>0.33</td>
<td>0.58</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>54</td>
<td>128±50</td>
<td>329±106</td>
<td>633±85</td>
</tr>
<tr>
<td>Male</td>
<td>40</td>
<td>113±37</td>
<td>313±77</td>
<td>648±71</td>
</tr>
<tr>
<td>P value</td>
<td>0.12</td>
<td>0.43</td>
<td>0.36</td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>47</td>
<td>117±44</td>
<td>338±104</td>
<td>624±73</td>
</tr>
<tr>
<td>Black</td>
<td>34</td>
<td>128±52</td>
<td>314±87</td>
<td>659±92*</td>
</tr>
<tr>
<td>Asian</td>
<td>8</td>
<td>124±39</td>
<td>268±56</td>
<td>626±43</td>
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<tr>
<td>Hispanic</td>
<td>5</td>
<td>110±32</td>
<td>308±83</td>
<td>680±68</td>
</tr>
<tr>
<td>P value</td>
<td>0.72</td>
<td>0.24</td>
<td>0.05*</td>
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</tr>
<tr>
<td>Refractive error</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Myope</td>
<td>44</td>
<td>127±45</td>
<td>342±100</td>
<td>638±89</td>
</tr>
<tr>
<td>Hyperope</td>
<td>6</td>
<td>180±69</td>
<td>281±46</td>
<td>613±53</td>
</tr>
<tr>
<td>Plano</td>
<td>44</td>
<td>113±37</td>
<td>309±91</td>
<td>649±72</td>
</tr>
<tr>
<td>P value</td>
<td>&lt;0.01*</td>
<td>0.03*</td>
<td>0.52</td>
<td></td>
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<tr>
<td>Lens</td>
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<td></td>
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</tr>
<tr>
<td>Phakic</td>
<td>75</td>
<td>123±46</td>
<td>318±84</td>
<td>640±80</td>
</tr>
<tr>
<td>PSK</td>
<td>19</td>
<td>116±43</td>
<td>339±130</td>
<td>636±80</td>
</tr>
<tr>
<td>P value</td>
<td>0.57</td>
<td>0.38</td>
<td>0.83</td>
<td></td>
</tr>
<tr>
<td>IOP (mmHg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤21</td>
<td>88</td>
<td>121±47</td>
<td>322±96</td>
<td>641±81</td>
</tr>
<tr>
<td>&gt;21</td>
<td>6</td>
<td>125±34</td>
<td>323±89</td>
<td>618±60</td>
</tr>
<tr>
<td>P value</td>
<td>0.84</td>
<td>0.97</td>
<td>0.50</td>
<td></td>
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<tr>
<td>Pachymetry (μm)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤555</td>
<td>15</td>
<td>106±36</td>
<td>287±66</td>
<td>625±85</td>
</tr>
<tr>
<td>&gt;555</td>
<td>18</td>
<td>124±48</td>
<td>263±84</td>
<td>702±61</td>
</tr>
<tr>
<td>P value</td>
<td>0.23</td>
<td>0.39</td>
<td>&lt;0.01*</td>
<td></td>
</tr>
</tbody>
</table>

IOP = intraocular pressure; PSK = pseudophakic eye; SD = standard
deviation.
Data are presented as mean±SD in micrometers.
*Statistically significant (see text for details).

Figure 3. Scatterplot illustrating a significant moderate positive correla-
tion between corneal thickness and Schlemm’s canal location from the
limbus. The linear regression equation is: y = 0.85x+200 μm (solid line),
where y is the predicted location of Schlemm’s canal from the limbus in
micrometers and x denotes corneal thickness in micrometers. The dashed
lines represent the 95% confidence interval as determined by least-squares
regression analysis.
In conclusion, in this study, Schlemm’s canal diameter and location were measured successfully in vivo using high-frequency ultrasound and found the in vivo canal diameter to be significantly smaller than prior in vitro measurements.

References


Footnotes and Financial Disclosures

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Melinda S. Mayfield - Employee - iScience Interventional, Inc. (at the time of the study)
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