Central Corneal Thickness in the Ocular Hypertension Treatment Study (OHTS)

James D. Brandt, M.D.
Mae O. Gordon, Ph.D.
Michael A. Kass, M.D.

for the
OHTS Investigators Group
The OHTS is a prospective, randomized, multi-center trial designed to determine whether the medical lowering of IOP in patients with ocular hypertension is safe and effective in delaying or preventing the development of primary open-angle glaucoma.

In the OHTS, patients are randomly assigned to medical treatment or close observation.
Entry Criteria

- Age 40 - 80
- Normal VF’s
- Normal Optic Discs
- Untreated IOP:
  - 24 - 32 mmHg in qualifying eye
  - 21 - 32 in fellow eye

OHTS Demographics

- Enrollment complete in 10/96
- 1,636 subjects at 23 clinical centers
- 409 (25%) African-American
Corneal Thickness & IOP

- Goldmann applanation assumes a corneal thickness (CT) of 500 µM
- Argus (1995) demonstrated that CT was greater in ocular hypertensives than in either normals or POAG patients
- Herndon (1997) measured CT in 184 eyes:
  - 561 ± 26 µM among normals
  - 554 ± 22 µM among POAG patients
  - 606 ± 41 µM among ocular hypertensives (p<0.001)
Aims of Present Study

- Describe the corneal thickness of the subjects enrolled in the OHTS
- Determine if corneal thickness is related to:
  - Race
  - IOP
  - Age
  - Gender
  - Medical status (e.g., diabetes, hypertension)
Methods

- Matching ultrasonic pachymeters provided to each clinical center
- 5 measurements of central corneal thickness from each eye
- Data transmitted to OHTS Coordinating Center (St. Louis)

DGH-500 Pachette™
Methods

Quality Control

- Repeat measurements required for inter-eye difference $\geq 40 \, \mu M$
- Repeat measurements in 63 subjects at one site (UC Davis) to determine test-retest reliability

Data Analysis

- One eye randomly chosen from each subject
- SAS v6.0
  - T-test and Pearson correlations
  - Multivariate general linear analysis
Results

- 1,099 (69%) of OHTS subjects have undergone corneal thickness measurements as of 8/30/2000

- High data quality
  - 0.9% with inter-eye difference ≥40 µM
  - (Repeat) - (initial measurement) = 11.0 ± 13.7 µM

- 1,094 measurements available for analysis
## Results

<table>
<thead>
<tr>
<th></th>
<th>African-American</th>
<th>Others</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>N = 85</td>
<td>N = 375</td>
<td>N = 460</td>
</tr>
<tr>
<td></td>
<td>548.2 ± 42.4 µM</td>
<td>574.1 ± 36.8 µM</td>
<td>569.3 ± 39.2 µM</td>
</tr>
<tr>
<td>Female</td>
<td>N = 188</td>
<td>N = 446</td>
<td>N = 634</td>
</tr>
<tr>
<td></td>
<td>557.3 ± 38.6 µM</td>
<td>582.0 ± 36.0 µM</td>
<td>574.7 ± 38.7 µM</td>
</tr>
<tr>
<td>All</td>
<td>N = 273</td>
<td>N = 821</td>
<td>N = 1,094</td>
</tr>
<tr>
<td></td>
<td>554.5 ± 40.0 µM</td>
<td>578 ± 37.0 µM</td>
<td>572.4 ± 39.0 µM</td>
</tr>
</tbody>
</table>

Difference between African-American and ‘Others’ subjects

p<0.0001
Distribution of Corneal Thickness
(all OHTS subjects)

Corneal thickness (µM)

- <=500: 3%
- 501-525: 8%
- 526-550: 19%
- 551-575: 24%
- 576-600: 23%
- 601-625: 15%
- >625: 8%
Corneal Thickness by Race

Corneal thickness (µM)

Other
African American
Corneal Thickness vs. Baseline IOP

<table>
<thead>
<tr>
<th></th>
<th>&lt;=24</th>
<th>25-27</th>
<th>28-30</th>
<th>&gt;30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Af-Am</td>
<td>120</td>
<td>89</td>
<td>47</td>
<td>17</td>
</tr>
<tr>
<td>Oth</td>
<td>353</td>
<td>301</td>
<td>130</td>
<td>37</td>
</tr>
<tr>
<td>N</td>
<td>583.9</td>
<td>573.6</td>
<td>591</td>
<td>555.8</td>
</tr>
<tr>
<td>Median</td>
<td>605.6</td>
<td>602</td>
<td>603.6</td>
<td>594.4</td>
</tr>
<tr>
<td>75 %tile</td>
<td>553</td>
<td>556.6</td>
<td>552.4</td>
<td>533.2</td>
</tr>
<tr>
<td>25 %tile</td>
<td>534.5</td>
<td>516.6</td>
<td>527</td>
<td>518.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Other Relationships

- Baseline refraction (N = 1,090)
  - $r = -0.09$, $p = 0.0018$

- Gender
  - Female $574.7 \pm 38.7$ µM; Male $569.3 \pm 39.2$ µM ($p = 0.02$)

- Diabetes
  - Diabetic (N = 117): $580.2 \pm 42.0$ µM
  - Non-diabetic (N = 974): $571.5 \pm 38.5$ µM ($p = 0.02$)

- Age at time of measurement
  - $r = -0.16$, $p < 0.001$
Multivariate Analysis

- The multivariate model included race, gender, age at testing, baseline refraction, baseline IOP, baseline medical history and the interaction of race with gender, systemic hypertension and diabetes.

- Significant relationships
  - Race ($p < 0.001$)
  - Age ($p < 0.0001$)
  - Gender ($p = 0.014$)
  - Diabetes ($p = 0.0016$)

- Baseline refraction, Baseline IOP, systemic hypertension and the racial interactions were not statistically significant in the multivariate model.
What is “Normal” Corneal Thickness?

- A recent meta-analysis* of the corneal thickness literature found that mean corneal thickness of ‘normal’ eyes is 534 µM
  - 530 µM for optical pachometry
  - 544 µM for ultrasonic pachymetry

- Our study demonstrates that subjects in the OHTS have increased corneal thickness (572.4 ± 39 µM)

* Doughty & Zaman (2000)
Survey of Ophthalmology 44:367-408
Race and Corneal Thickness

- Most previous studies of corneal thickness have been performed in racially homogeneous populations.
- Foster (1998) found thinner corneas (495 µM) in a Mongolian population.
- Our study demonstrates that African-American OHTS subjects have thinner corneas than their ‘others’ counterparts.
Correcting IOP for Corneal Thickness

- Ehlers (1975) cannulated 29 eyes undergoing cataract surgery
  - 5 mmHg/70 µM

- Doughty & Zaman (2000) meta-analysis
  - 2.5 mmHg/50 µM

- Whitacre (1993) and the Rotterdam Eye Study (1997)
  - 2.0 mmHg/100 µM
Baseline IOP

- Unadjusted

% of Subjects

Baseline IOP Distribution

Baseline IOP vs. mmHg

Baseline IOP Graph

Baseline IOP Scatter Plot

Baseline IOP Line Graph

Baseline IOP Area Graph
“Corrected” IOP

- Unadjusted
- Whitacre
“Corrected” IOP

- Unadjusted
- Whitacre
- Doughty
- Ehlers
Clinical Significance

- 45% of ‘others’ had a ‘corrected’ IOP < 21 mmHg
- 27.5% of African-American subjects had a ‘corrected’ IOP < 21 mmHg
- If we choose an arbitrary cutoff of 600 µM, above which corneal thickness affects applanation IOP measurement to a clinically significant degree, then:
  - 28% of ‘Others’ had corneal thickness > 600 µM
  - 12% of African Americans had corneal thickness > 600 µM
Conclusions

- OHTS subjects have thicker corneas than ‘normal’ subjects.
- African-American OHTS subjects have thinner corneas than their ‘others’ counterparts.
- Corneal thickness must be considered in the development of any risk model for ocular hypertensive patients.
OHTS Clinical Centers

- Bascom Palmer Eye Institute
- Baylor Eye Clinic
- Charles R. Drew University
- Devers Eye Institute
- Emory University Eye Center
- Eye Associates of Washington, DC
- Eye Consultants of Atlanta
- Eye Doctors of Washington
- Eye Physicians and Surgeons of Atlanta
- Glaucoma Care Center
- Great Lakes Ophthalmology
- Henry Ford Hospitals
- Johns Hopkins University
- Jules Stein Eye Institute, UCLA
- Kellogg Eye Center
- Kresge Eye Institute
- Krieger Eye Institute
- Maryland Center for Eye Care
- Mayo Clinic/Foundation
- New York Eye & Ear Infirmary
- Ohio State University
- Salus University
- Scheie Eye Institute
- University of California, Davis
- University of California, San Diego
- University of California, San Francisco
- University of Louisville
- University Suburban Health Center
- Washington Eye Physicians & Surgeons
- Washington University, St. Louis
OHTS Resource Centers

Study Chairman’s Office
&
Coordinating Center
Washington University
St. Louis, MO

Optic Disc Reading Center
Bascom Palmer Eye Institute
University of Miami
Miami, FL

Visual Field Reading Center
University of California, Davis
Sacramento, CA