Corneal hysteresis measured with the Ocular Response Analyzer® in normal and glaucomatous eyes

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ABSTRACT.
Purpose: To identify differences in corneal hysteresis (CH) and central corneal thickness (CCT) between healthy and glaucomatous patients.
Methods: Retrospective observational study. One hundred and thirty-three eyes of 75 healthy and 58 glaucomatous patients were included. CH was measured in each patient using Ocular Response Analyzer. CCT was determined by ultrasonic pachymetry. For each patient, one eye was randomly selected. We used a Student t-test to search for significant differences between the different groups (p<0.05).
Results: In healthy and glaucomatous eyes, mean CH values were 10.46 ± 1.6 and 8.77 ± 1.4 mm Hg, respectively. Mean CCT values were 560.2 ± 36.3 and 535.3 ± 42.7 μm, respectively. CH and CCT were significantly lower in glaucomatous eyes than in normal eyes, (p<0.05).
Discussion: In our series, CH was lower in glaucomatous than in normal eyes. The relationship between glaucoma, IOP, and ocular structures may not be confined to the consideration of CCT. A low CH value could be responsible for under-estimation of IOP. CH could also be a risk factor for glaucoma, independent of IOP. Further studies are needed to support these hypotheses.
Conclusion: In our investigation, CCT and CH were significantly lower in glaucomatous eyes than in healthy eyes.

Key words: central corneal thickness – corneal biomechanics – glaucoma – hysteresis

Introduction
Elevated intraocular pressure (IOP) is an important risk factor for glaucoma; the reduction of IOP in subjects with ocular hypertension (OHT) has been proven to reduce the incidence of conversion to glaucoma (Gordon et al. 2002). The Goldmann applanation tonometer (GAT), which is frequently used to measure IOP, operates on the basis of the Imbert–Fick law (W = P × A), where W is the force to applanate, P is IOP, and A is the area planaplated. This law assumes that the cornea is an infinitely thin, perfectly flexible membrane. This assumption is flawed, however, because the cornea is not perfectly thin and infinitely flexible, and nor are all corneas similar in their elastic and mechanical characteristics. Therefore, the force required to applanate the cornea depends not only on IOP, but also on corneal rigidity, which itself depends on corneal thickness, curvature, hydration, composition and viscoelastic properties. Other components also play a role in the accurate measurement of IOP, including the subject’s race and refractive surgery status (laser in situ keratomileusis [LASIK], photorefractive keratectomy [PKR]), and the presence of corneal pathology (keratoconus, Fuchs’ dystrophy, scars). The influence of central corneal thickness (CCT) on IOP values measured with GAT has been demonstrated (Ehlers et al. 1975; Whitacre et al. 1993; Wolfs et al. 1997) and is now taken into account in the interpretation of IOP measurements. Several studies have already shown a significant correlation between a thin CCT and the severity of glaucomatous neuropathy (Herndon et al. 2004; Jonas et al. 2005; Congdon et al. 2006; Kniewest et al. 2006; Papadia et al. 2007). Moreover, according to the Ocular Hypertension Treatment
Study (OHTS), a thin CCT may be an independent risk factor for the development and progression of glaucoma in patients with OHT (Gordon et al. 2002).

Until recently, corneal biomechanical properties could not be measured in vivo. The Ocular Response Analyzer® (ORA) (Reichert Ophthalmic Instruments, Inc., Buffalo, NY, USA) is a new, non-invasive device that analyses corneal biomechanical properties simply and rapidly (Luce 2005). The ORA allows IOP measurements and can estimate corneal hysteresis (CH) and rigidity.

Elasticity refers to how a material deforms in response to an external stress. The stress-strain relationship can be plotted graphically; an elastic material is one that regains its original form in a completely reversible displacement direction along the stress–strain pathway when the imposed stress is removed. Hysteresis refers to the energy lost during the stress–strain cycle. Viscous materials flow when an external shear stress is applied, but, unlike materials with elastic properties, they do not regain their original shape when the stress is removed. Collagen is viscoelastic and therefore exhibits hysteresis (Kotecha 2007).

The ORA uses a quick calibrated air puff that causes the cornea to move inward, past applanation and into a state of slight concavity. The cornea then recovers its normal configuration, passing through a second applanation state. An electro- optic detector system indirectly evaluates the corneal curvature in the central 3 mm during the 20 milliseconds of measurements and detects the two applanation moments when there is a spike of luminous intensity. Thus, the device measures two applanation pressures, P1 and P2, and then provides:

(1) the mean of the two measured pressures (P1 and P2) to give an IOP measurement correlated to IOP measured with GAT (IOPG), and
(2) the difference between the two pressures (P1 and P2) to give a measurement of CH.

This new parameter is very important in any assessment of corneal biomechanical properties (Luce 2005).

We sought to identify differences in CH and CCT between normal and glaucomatous patients.

Materials and Methods

We conducted a retrospective study including patients referred to our hospital between December 2005 and May 2007. All procedures conformed to the tenets of the Declaration of Helsinki. Based on their ophthalmological status and history, two groups of patients were constituted.

Normal control subjects

Normal control subjects were patients with no remarkable medical or ocular history who sought refractive or cataract surgery. All patients underwent a full eye examination including review of medical history, slit-lamp biomicroscopy and dilated fundoscopic examination. The ORA was used to record the CH and IOPG in both eyes of each patient. Patients with familial or personal history of glaucoma, IOPG > 20 mmHg or abnormal cup : disc ratios were excluded from the study. All subjects underwent corneal topography (Orbscan®; Bausch & Lomb, Inc., Rochester, NY, USA) and subjects with previously undetected keratoconus or suspected forme fruste keratoconus were also excluded.

Glaucomatous patients

All glaucomatous patients had a confirmed white-on-white automated 24-2 or 30-2 Humphrey typically glaucomatous visual field defect. All patients also had a history of OHT and were therefore treated with antiglaucoma eyedrops. Patients with normal tension, pigmentary, inflammatory and aphakic glaucoma and patients who had undergone glaucoma surgery were excluded from the study. Patients with angle-closure glaucoma were also excluded, except for those with a combined mechanism.

Ocular Response Analyzer® measurements were performed in all patients during a medical ophthalmological examination carried out by trained physicians. All patients gave their oral consent to undergo ORA measurement. Unreliable measurements (atypical signals) were excluded. Four measures of the CH were saved and averaged at each examination. During the same examination, GAT IOP and ultrasonic CCT were measured in all patients.

In glaucoma subjects with glaucoma in only one eye, that eye was selected for statistical analysis. In all other subjects (glaucoma subjects with glaucoma in both eyes and control subjects), one eye was randomly selected for statistical analysis. All statistical tests were performed on computer (excel; Microsoft Corp., Seattle, WA, USA). A Student’s t (p < 0.05) was used to search for significant differences in CH and CCT between the groups.

Results

Table 1 summarizes baseline characteristics, CCT, CH and IOPG in normal and glaucoma patients. The study included a total of 133 eyes of 133 patients, of whom 75 subjects served as normal controls and 58 had glaucoma. Fifty-one patients (87.9%) had open-angle glaucoma and seven (12.1%) had angle-closure glaucoma with suspected combined mechanism. Mean CH values in healthy and glaucomatous eyes were, respectively, 10.46 ± 1.6 mmHg and 8.77 ± 1.4 mmHg. Mean CCT values were, respectively, 560.2 ± 36.3 μm and 535.3 ± 42.7 μm. Both CH and CCT were significantly lower in glaucomatous eyes than in normal eyes (p < 0.05). There was no statistically significant correlation between age and CH in the control group (r = −0.149, p > 0.05), nor in the glaucoma group (r = −0.078, p > 0.05). Moderate correlations were found between CCT and CH in both the control

| Table 1. Baseline characteristics, central corneal thickness (CCT), corneal hysteresis (CH), and intraocular pressure measured with the ORA (IOPG) in normal (n = 75) and glaucoma (n = 58) subjects. Values are means ± standard deviation (SD). |
|---------------|----------------|----------------|----------------|
|               | Normal subjects | Glaucoma subjects | t-test p-value |
| Age, years    | Mean ± SD (range) | Mean ± SD (range) |               |
| 61.44 ± 10.9 (45–85) | 65.68 ± 13.9 (37–93) | 0.06 |
| CCT, μm       | 560.2 ± 36.3 (483–657) | 535.3 ± 42.7 (435–654) | 0.001 |
| CH, mmHg      | 10.46 ± 1.6 (7.1–14.9) | 8.77 ± 1.4 (5.0–11.3) | < 0.0001 |
| IOPG, mmHg    | 15.9 ± 2.6 (10.3–19.9) | 17.1 ± 5.1 (7.3–29.8) | 0.09 |
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Discussion
In this study, CH, like CCT, was signifi-
cantly lower in glaucoma patients
than in control subjects. Congdon
et al. (2006) postulated that lower CH
might be associated with a progressive
field worsening. The relationship
between glaucoma, IOP and ocular
structures may therefore not be con-
fined to the consideration of CCT.

Intraocular pressure is underesti-
mated in patients with thin CCT
(Thelers et al. 1975). Similarly, a low
CH value may be responsible for the
underestimation of IOP when mea-
sured with GAT. Some epidemiologi-
cal studies have found a systematic
bias in IOP measurements in certain
races. As Foster et al. (2000) were
unable to identify any association
between measurement error and cor-
neal thickness, corneal curvature,
anterior chamber depth or axial
length, this bias may reflect differ-
ces in corneal biomechanics. These, in
turn, may be explained by differences
in the composition of ocular struc-
tures. Thus, the 'elastic responses' of
eyes with the same CCT might differ.

According to Copt et al. (1999),
overestimation of IOP in normal sub-
jects who have thick corneas may lead
to a misdiagnosis of OHT, and, if
IOP were to be corrected for CCT,
many patients with OHT might be
reclassified as normal. We may also
assume that correcting IOP values
according to CH might change a
patient's diagnosis. Indeed, we found
a moderate, but significant, correla-
tion between IOPG and CH in glau-
coma patients. However, this
correlation was not significant in
healthy patients.

It is also possible that CCT and CH
each correspond to risk factors for
glaucoma, independent of IOP. Eyes
with lower CH and/or thinner than
normal CCT might exhibit structural
weakness. Some researchers have
already found a lower CCT in normal-
tension glaucoma (NTG) eyes than in
open-angle glaucoma eyes (Copt et al.
1999). Corneal hysteresis represents a
dynamic resistance component of the
cornea (Congdon et al. 2006). More
distensible ocular structures may be associated with the progression
of glaucomatous lesions and, according
to this hypothesis, the biomechanical
status of the cornea may reflect weak-
ness of the lamina cribrosa. Indeed,
Bochmann et al. (2008) compared CH
measurements in glaucoma patients
and patients with acquired pit of the
optic nerve head (APON). The latter
condition predominantly occurs in
NTG and is associated with a higher
risk of progressive optic disc changes
(Ugurlu et al. 1998). They found that
CH was significantly lower in APON
than in glaucoma patients (Bochmann
et al. 2008). This finding also suggests
that a lower CH could be a marker for
a possible susceptibility of the optic
der to glaucomatous damage.

Given that chronic OHT is respon-
sible for lesions on the optic nerve
head, it may also lead to alterations in
corneal structure, with subsequent
reductions in CH and CCT. Indeed,
Weizer et al. (2006) showed that CCT
diminishes after a mean follow-up of
8 years, and this reduction was more
pronounced in glaucomatous patients
than in healthy subjects. However,
the exact link between this reduction
and glaucomatous lesions has not been
explained. Other parameters, such as
age, may also influence CCT values.
Indeed, several studies have shown a
reduction of CCT with age (Foster
et al. 1998; Nemesure et al. 2003;
Kotecha et al. 2006; Moreno-
Montanes et al. 2008). According
to Ortiz et al. (2007), CH also dimin-
ishes with age, which suggests that the
elastic properties of the cornea alter
with age. In our series, we found no corre-
lation between CH and age in normal
and glaucoma subjects. In agreement
with our results, Kirwan et al. (2006)
found that CH in children was similar
to that reported in adults.

In our series, CH was lower in glau-
comatous than in normal eyes and
several hypotheses can be used to
explain these results. However,
because of our selection criteria,
our groups were not matched for parame-
ters other than age. Therefore, other
factors may have affected the CH val-
ues in both groups. The majority of
our glaucoma patients had been tak-
ing glaucoma medications, including
prostaglandins, for a significant length
of time. There is a chance that this
may have affected their corneal bio-
 mechanical properties. Prospective
studies should be carried out to con-
firm this hypothesis.

It is known that CH varies with
CCT, such that a cornea with a thicker
CCT will have a greater CH (Kotecha
et al. 2006); this may suggest that the
differences in CH between our groups
may be partly explained by differences
in IOP and CCT. In our series, mean
IOP was 15.9 mmHg in the normal
group and 17.1 mmHg in the glaucoma
group. The difference between the two
groups was not statistically significant
(p = 0.09). Plus, even though we
found a moderate correlation between
CH and IOPG in the glaucoma group,
there was no correlation in the control
group. Central corneal thickness was
higher in the normal group than the
glaucoma group and we found a corre-
lation between CH and CCT in the
normal and glaucoma groups. (Kirwan
& O'Keefe (2007) also found a moder-
ately strong correlation between CH and
CCT.

Our analyses of CH and CCT were
made at a single time-point; however,
the values of both parameters can
change with time. Therefore, it would
be interesting to perform a prospective
study with longer follow-up.

Conclusions
The present study simply compared
corneal biomechanical findings in a
glaucoma and a control group. Fur-
ther prospective longitudinal studies
are required to confirm this results
and to analyse the usefulness of CH
measurements in clinical practice in
order to allow for better interpretation
of IOP values and earlier administra-
tion of medical treatment.

References
Bochmann F, Ang GS & Azuara-Blanco A
(2008): Lower corneal hysteresis in glau-
coma patients with acquired pit of the
optic nerve (APON). Graefes Arch Clin
Congdon NG, Broman AT, Bandeen-Roche
K, Grover D & Quigley HA (2006): Cen-
tral corneal thickness and corneal hysteresis
associated with glaucoma damage. Am J

References
Bochmann F, Ang GS & Azuara-Blanco A
(2008): Lower corneal hysteresis in glau-
coma patients with acquired pit of the
optic nerve (APON). Graefes Arch Clin
Congdon NG, Broman AT, Bandeen-Roche
K, Grover D & Quigley HA (2006): Cen-
tral corneal thickness and corneal hysteresis
associated with glaucoma damage. Am J


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