



Queensland University of Technology
Brisbane Australia

This may be the author's version of a work that was submitted/accepted for publication in the following source:

[Read, Scott & Collins, Michael](#)

(2011)

Intraocular Pressure in Keratoconus.

Acta Ophthalmologica, 89(4), pp. 358-364.

This file was downloaded from: <https://eprints.qut.edu.au/30361/>

© Consult author(s) regarding copyright matters

This work is covered by copyright. Unless the document is being made available under a Creative Commons Licence, you must assume that re-use is limited to personal use and that permission from the copyright owner must be obtained for all other uses. If the document is available under a Creative Commons License (or other specified license) then refer to the Licence for details of permitted re-use. It is a condition of access that users recognise and abide by the legal requirements associated with these rights. If you believe that this work infringes copyright please provide details by email to qut.copyright@qut.edu.au

Notice: *Please note that this document may not be the Version of Record (i.e. published version) of the work. Author manuscript versions (as Submitted for peer review or as Accepted for publication after peer review) can be identified by an absence of publisher branding and/or typeset appearance. If there is any doubt, please refer to the published source.*

<https://doi.org/10.1111/j.1755-3768.2009.01690.x>

Acta Ophthalmologica

Intraocular pressure in keratoconus

Journal:	<i>Acta Ophthalmologica</i>
Manuscript ID:	ACTA-09-02-0094.R2
Manuscript Type:	Original Article
Date Submitted by the Author:	18-May-2009
Complete List of Authors:	Read, Scott; Queensland University of Technology, School of Optometry Collins, Michael; Queensland University of Technology, School of Optometry
Keywords:	Keratoconus, Intraocular pressure, Dynamic contour tonometry, Corneal topography, Corneal thickness.

1
2
3 **Intraocular pressure in keratoconus**
4
5
6

7 Scott A Read (PhD)

8
9 Michael J Collins (PhD)

10
11
12 Contact Lens and Visual Optics Laboratory

13 School of Optometry

14
15 Queensland University of Technology

16
17
18 Room B556, O Block, Victoria Park Road, Kelvin Grove 4059

19
20 Brisbane, Queensland, Australia

21
22 Phone: 617 3864 5739, Fax: 617 3864 5665

23
24 Email: sa.read@qut.edu.au
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Date: 18/05/2009

Abstract:

Aims: To investigate IOP measurements with the dynamic contour tonometer (DCT) and non contact tonometer (NCT) in subjects with keratoconus.

Methods: Twenty keratoconic subjects and 20 age-matched control subjects had IOP measurements taken using DCT and NCT instruments. Central and off-centre measures were taken with the DCT in order to highlight any systematic errors associated with corneal biomechanical factors. Measures of anterior and posterior corneal topography and thickness were also taken for each subject.

Results: No significant difference was found between the central and off-centre DCT IOP readings for the keratoconics and age-matched controls ($p>0.05$). The average DCT IOP for the keratoconics was 14.2 ± 1.4 mmHg and for the age-matched controls was 14.2 ± 1.6 mmHg. However, the average NCT readings differed significantly ($p<0.001$) between the keratoconics (9.2 ± 1.5 mmHg) and age-matched controls (12.9 ± 2.4 mmHg). DCT IOP showed no significant ($p>0.05$) correlation with the severity of keratoconus, as determined through measures of corneal topography and thickness. NCT IOP was correlated significantly with certain measures of corneal curvature and thickness in the keratoconic population. The difference between DCT and NCT IOP was strongly correlated with measures of corneal topography and thickness, with differences increasing for more advanced keratoconus.

Conclusions: The measurements from the DCT do not appear to be dependent upon corneal factors, unlike the NCT. The presence or severity of keratoconus was not correlated with DCT IOP values.

Keywords: Keratoconus, intraocular pressure, dynamic contour tonometry, corneal topography, corneal thickness.

Introduction:

Keratoconus is a non-inflammatory, usually bilateral (although often asymmetric) corneal condition known to result in substantial alterations in the shape, thickness and biomechanical properties of the cornea (Edmund 1989; Rabinowitz 1998; Luce 2005; Hayes et al. 2007; Shah et al. 2007; Touboul et al. 2008). The corneal changes associated with keratoconus, may potentially lead to difficulties in the accurate determination of intraocular pressure (IOP) in these patients, as tonometric devices based upon the applanation principle, are known to be affected by altered corneal parameters (Whiteacre & Stein 1993; Damji et al. 2003; Liu & Roberts 2005).

Previous studies investigating IOP in keratoconus using applanation tonometric techniques have highlighted the potential inaccuracies of these measures in keratoconus, and typically note patients with keratoconus to exhibit lower than normal IOP (Brooks et al. 1984; Swann & Waldron 1986; Edmonds 1993; Goodman et al. 1996; Böhm et al. 1997; Patel & McLaughlin 1999; Browning et al. 2004). The majority of these studies suggest the IOP levels found in keratoconic subjects are falsely low, due to errors associated with applanation tonometry in measuring corneas with altered biomechanical properties.

The Pascal Dynamic Contour Tonometer (DCT) (Ziemer Ophthalmic Systems, Port, Switzerland) is a newly introduced contact instrument for measuring IOP. The DCT is based upon the principle of contour matching, and theoretically measures IOP independently of corneal thickness and biomechanical properties

1
2
3 (Kanngiesser et al. 2005). Recent clinical studies of normal subjects indicate that
4
5 IOP measures from the DCT are relatively unaffected by corneal properties
6
7
8 (Kaufmann et al. 2004; Kanngiesser et al. 2005; Kotecha et al. 2005; Ku et al.
9
10 2006; Schneider & Grehn 2006). The DCT might therefore be expected to
11
12 provide a more accurate reflection of IOP in keratoconic patients. A number of
13
14 recent studies have investigated IOP with the DCT in keratoconus patients
15
16
17 (Barreto et al. 2006; Ozbek et al. 2006; Meyenberg et al. 2008; Mollan et al.
18
19 2008; Papastergiou et al. 2008; Schädle et al. 2008). These studies have
20
21 reported the DCT to give higher IOP readings than applanation tonometry.
22
23
24 However, some investigators have suggested that the DCT may be influenced to
25
26 some degree by corneal biomechanical properties in eyes with irregular corneas
27
28
29 (Barreto et al. 2006; Meyenberg et al. 2008).
30
31

32
33
34 In this study, we investigated IOP measures using the DCT instrument in
35
36 subjects with keratoconus and an age-matched control population, using a
37
38 protocol utilizing both central and off-centre IOP readings (designed to highlight
39
40 any dependence of the technique upon corneal factors). We compared these IOP
41
42 readings with those from an applanation tonometer (a non-contact tonometer). In
43
44 order to examine the potential relative dependence of IOP measures upon
45
46 corneal factors, each subject also underwent a comprehensive series of corneal
47
48
49 topographical and biometric measures.
50
51
52
53
54
55
56
57
58
59
60

Materials and methods:

Twenty subjects previously diagnosed with keratoconus, and 20 age-matched control subjects participated in this study. The mean age of the two populations of subjects was 32 ± 6 years and 30 ± 5 years for the keratoconics and controls respectively. Both populations consisted of 10 male and 10 female subjects. No subject reported a history of any ocular pathology (apart from keratoconus), including glaucoma or ocular hypertension. Six of the keratoconic subjects wore rigid gas permeable (RGP) contact lenses on a full-time basis, and 7 of the normal subjects were soft contact lens wearers. Each subject underwent an initial ophthalmic examination to ensure good ocular health and to determine their refractive status. We excluded any eyes that exhibited significant corneal scarring, of greater than grade 1 according to the grading scale of McMahon et al. (2006).

Measurements were performed on the right eye only for the normal population, but for the keratoconic subjects, measurements were performed on both eyes and data from the most advanced keratoconic eye was used in all analyses. One keratoconic subject had a history of penetrating keratoplasty to one eye, and another exhibited substantial (grade 2) corneal scarring in one eye only, and so their fellow eye was used. To ensure that diurnal variations in IOP and corneal thickness had minimal confounding effects on our results, all measurements were collected between 10am and 4pm and at least 2 hours after subjects woke (Read et al 2008). Approval from the university human research ethics

1
2
3 committee was obtained prior to commencement of the study and all subjects
4
5 were treated in accordance with the declaration of Helsinki.
6
7
8
9

10 A series of four anterior corneal topography readings using the Medmont E300
11 videokeratoscope (Medmont Pty. Ltd., Victoria, Australia) and five measurements
12 of corneal thickness and posterior corneal topography using the Pentacam HR
13 rotating Scheimpflug camera (Oculus Inc, Wetzlar Germany) were taken for each
14 subject. For one keratoconic subject, reliable, well focussed measurements with
15 the Medmont E300 were unable to be captured due to anatomical factors, and
16 therefore videokeratographic measurements were obtained with the Keratron
17 videokeratoscope (EyeQuip Division, Alliance Medical Marketing, Jacksonville,
18 FL).
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33

34 Following the collection of corneal data, measurements of IOP were carried out
35 using the Canon Tx-F Full Auto Non-Contact Tonometer (Canon USA Inc, Lake
36 Success, NY, USA), and the Pascal DCT (Ziemer Ophthalmic Systems, Port,
37 Switzerland). The Canon TX-F Full Auto Tonometer is a non-contact "air-puff"
38 tonometer based on the applanation principle. Non-contact tonometers estimate
39 IOP by determining the force required for a pulse of air to applanate a known
40 area of the cornea (Grolman 1972). The DCT is an electronic contact tonometer
41 that works on the principle of contour matching and has been described in detail
42 elsewhere (Kanngiesser et al 2005). The instrument has a concave tip (with a
43 diameter of 7 mm and radius of curvature of 10.5 mm), that makes contact with
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 the corneal surface. Once the cornea conforms to the shape of the tip, (i.e. when
4
5 contour matching between the cornea and instrument occurs), a small piezo-
6
7
8 resistive sensor (of diameter 1.2 mm) built into the centre of the instrument's tip
9
10 provides a direct measurement of IOP.
11

12
13
14
15 For each subject, three NCT IOP measurements and four valid DCT measures
16
17 (i.e. with a quality score of 3 or better) were taken, with the DCT measures
18
19 always performed last. Two DCT measures were captured with the instrument
20
21 contacting the central cornea, and two were captured with the instrument (angled
22
23 at $\sim 15^\circ$) contacting the temporal non-central cornea, with central and off-centre
24
25 measures alternated in sequence. We limited the number of DCT measures at
26
27 each corneal location to 2 in order to reduce any changes in IOP due to repeated
28
29 corneal contact (Johannesson et al 2008). For one subject, reliable off-centre
30
31 DCT measures were unable to be collected due to a narrow palpebral aperture,
32
33 therefore only their central measurements were used in analysis. Based upon
34
35 analysis of each subject's corneal data along the horizontal meridian, we
36
37 estimated that the DCT sensor tip came in contact with the cornea at a point
38
39 approximately 2 mm temporal to centre for the off-centre IOP measures.
40
41
42
43
44
45
46
47

48 **Statistical analysis:**

49
50 Following data collection, the raw corneal topography and thickness data from
51
52 the instruments were analysed using customised software to calculate average
53
54 maps for each subject. The mean and steepest axial curvature (anterior and
55
56
57
58
59
60

1
2
3 posterior) was calculated over the central 4mm for each subject. The average
4
5 anterior corneal height maps were analysed to determine the wave aberrations of
6
7 the anterior corneal surface for a 4 mm pupil. The higher order RMS (HO RMS)
8
9 was then derived from the corneal wavefront for each subject. Each subject's
10
11 corneal thickness maps were also analysed to determine the central corneal
12
13 thickness (CCT), and the minimum corneal thickness (MinCT), as well as the
14
15 average corneal thickness over the central 4 mm and the thickness at a point
16
17 2mm temporal from map centre (i.e. the approximate point of corneal contact for
18
19 the off-centre DCT measures). The percentage increase in corneal thickness
20
21 from the thinnest corneal point to the averaged peripheral corneal thickness (i.e.
22
23 for a ring of data of 8mm diameter concentric to this point) was also recorded
24
25 from the Pentacam instrument.
26
27
28
29
30
31
32
33

34 Five different parameters describing anterior corneal curvature, aberrations and
35
36 thickness were used to determine which of the two eyes of the keratoconic
37
38 subjects was the most advanced. These parameters were: mean and steepest
39
40 anterior axial curvature, anterior corneal HO RMS, minimum corneal thickness
41
42 and percentage increase in corneal thickness. The eye showing the steepest,
43
44 most highly aberrated, thinnest cornea of the two eyes of each subject was
45
46 deemed to be the most advanced.
47
48
49
50
51
52

53 For each subject, the mean IOP readings from the NCT (IOP_{NCT}), and from the
54
55 central (IOP_{DCT-C}) and off-centre DCT (IOP_{DCT-OC}) measures were calculated. An
56
57
58
59
60

1
2
3 average DCT IOP ($IOP_{DCT-AVE}$) was calculated for each subject based on the
4 mean of the (four) central and off-centre DCT IOP measures. The mean
5
6
7
8 difference between $IOP_{DCT-AVE}$ and IOP_{NCT} was also calculated ($IOP_{DCT-NCT}$).
9
10

11
12 The Kolmogorov-Smirnov test revealed that the data for each of the corneal and
13 IOP measures from the two populations of subjects did not differ significantly
14
15 from a normal distribution and therefore parametric statistical methods were used
16
17 throughout. Two-tailed independent sample t-tests were used to investigate for
18
19 significant differences between the two populations of subjects in terms of both
20
21 IOP and corneal parameters. Two-tailed paired t-tests were used to investigate
22
23 for significant differences between the tonometric techniques used. To
24
25 investigate for any significant dependence of the IOP measures on corneal
26
27 parameters in our keratoconic subjects, correlation analysis was carried out for
28
29 each of the measured corneal parameters and the IOP measures from each
30
31 instrument.
32
33
34
35
36
37
38
39
40
41
42
43

44 **Results:**

45
46 The mean IOP measures for the central (IOP_{DCT-C}) and off-centre (IOP_{DCT-OC})
47
48 DCT and from the NCT (IOP_{NCT}) for the keratoconic and age-matched control
49
50 populations are shown in Figure 1. The mean IOP_{DCT-C} was 14.3 ± 1.4 mmHg for
51
52 the keratoconic subjects and 14.2 ± 1.7 mmHg for the age-matched control
53
54 subjects. The mean IOP_{DCT-OC} was 14.1 ± 4.4 mmHg and 14.3 ± 1.6 mmHg for
55
56
57
58
59
60

1
2
3 the keratoconic and age matched control populations respectively and was not
4 significantly different to IOP_{DCT-C} for either population ($p = 0.09$ for the
5 keratoconics and $p = 0.29$ for the age matched controls). No significant difference
6 was found in the mean IOP as measured with the DCT ($IOP_{DCT-AVE}$) between the
7 keratoconic and age-matched control populations ($p = 0.885$).
8
9
10
11
12
13
14
15
16

17 The mean IOP_{NCT} was 9.2 ± 1.5 mmHg for the keratoconic subjects and $12.9 \pm$
18 2.4 mmHg for the age-matched controls, which represents a highly statistically
19 significant difference between the two populations ($p < 0.0001$). The IOP_{NCT} was
20 significantly different to the $IOP_{DCT-AVE}$ for both the age-matched controls (p
21 $= 0.001$) and the keratoconics ($p < 0.0001$). The mean difference between the
22 $IOP_{DCT-AVE}$ and IOP_{NCT} measures was 1.4 ± 1.6 mmHg for the age matched
23 controls and 5.0 ± 1.5 mmHg for the keratoconic subjects.
24
25
26
27
28
29
30
31
32
33
34
35

36 An overview of the parameters describing the anterior and posterior corneal
37 curvature and corneal thickness from the keratoconic and control populations is
38 displayed in Table 1. As expected, the keratoconic subjects exhibited
39 significantly ($p < 0.001$ for all parameters) steeper anterior corneas, steeper
40 posterior corneas, thinner central corneas, a greater percentage increase in
41 corneal thickness between the thinnest point and peripheral corneal regions and
42 larger magnitude of anterior corneal aberrations than the control subjects.
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 We investigated the association between each of the IOP measures (IOP_{NCT} ,
4 $IOP_{DCT-AVE}$, IOP_{DCT-C} , IOP_{DCT-OC} , and $IOP_{DCT-NCT}$) and the corneal topography and
5 thickness data for the population of keratoconic subjects. Table 2 exhibits an
6 overview of this correlation analysis. None of the DCT measures (i.e. neither
7 IOP_{DCT-C} , IOP_{DCT-OC} or $IOP_{DCT-AVE}$) showed any significant correlation with any of
8 the corneal topography or thickness measures for the keratoconic subjects.
9
10 However, the IOP_{NCT} measures did exhibit a significant correlation with certain
11 corneal parameters, such as the average ($r^2 = 0.20$) and steepest ($r^2 = 0.39$)
12 anterior corneal curvature, average posterior corneal curvature ($r^2 = 0.25$) and
13 percentage increase in thickness ($r^2 = 0.22$). These correlations indicate that
14 steeper central anterior and posterior corneas, and larger differences between
15 the central and peripheral corneal thickness values (i.e. corneal changes
16 associated with more advanced keratoconus), are associated with lower IOP_{NCT}
17 readings. The difference between the $IOP_{DCT-AVE}$ and IOP_{NCT} measures (IOP_{DCT-}
18 NCT) showed a significant correlation with the majority of parameters describing
19 the topography and thickness of the cornea, with r^2 values ranging from 0.19 to
20 0.55. This indicates that steeper, thinner, more highly aberrated corneas were
21 associated with a greater difference between $IOP_{DCT-AVE}$ and IOP_{NCT} (i.e. the
22 more advanced the keratoconus, the greater the difference between DCT and
23 NCT IOP measures). Figure 2 illustrates the relationship between $IOP_{DCT-NCT}$
24 and parameters describing the anterior and posterior corneal curvature and
25 thickness.
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Discussion:

In our current study, no significant difference was found between the DCT IOP measures of our age-matched control and keratoconic subjects, and these measures were also not significantly correlated with any measures of corneal shape or thickness. Furthermore, no systematic differences were found between the DCT IOP measures taken from the central and off-centre corneal regions in either the keratoconic or age-matched control populations. As the off-centre measures represent IOP estimates where the instrument is contacting a thicker, flatter region of the cornea, systematic errors in the DCT measures should manifest as differences between these central and off-centre IOP measures.

This suggests that the DCT instrument is not being substantially influenced by the altered corneal biomechanics of keratoconus, and is performing reliably for IOP measures in these patients. The fact that valid central and off-centre DCT measures were able to be collected for both our keratoconic and control populations confirms that contour matching at the DCT sensor can occur for a wide range of corneal curvatures.

Our findings are in general agreement with previous studies of IOP with the DCT in keratoconus (Barreto et al. 2006; Ozbek et al. 2006; Meyenberg et al. 2008; Mollan et al. 2008; Papastergiou et al. 2008; Schädle et al. 2008). The majority of these recent studies have also reported differences between DCT and applanation tonometry readings of similar magnitude, and no significant association between DCT IOP and corneal thickness or curvature measures in

1
2
3 keratoconic eyes. These studies have primarily reported upon associations
4
5 between IOP and central corneal thickness and anterior keratometric curvature
6
7 readings. In our current study, we derived a comprehensive range of parameters
8
9 describing the thickness (central, peripheral thickness measures and estimates
10
11 of thickness progression), and shape of the cornea (curvature of both the anterior
12
13 and posterior cornea and corneal aberrations), and found no significant
14
15 association between DCT IOP and any of these parameters. This further
16
17 supports the contention that the DCT is providing IOP measures that are largely
18
19 independent of corneal factors in keratoconus.
20
21
22
23
24
25
26

27 In contrast to the DCT IOP measures, the NCT measures do appear to be
28
29 significantly influenced by certain corneal factors in keratoconus. The NCT may
30
31 have substantially underestimated the IOP in our keratoconic subjects, in
32
33 comparison to both age-matched controls as well as to measures with the DCT
34
35 instrument. This potential underestimation of IOP with the NCT increased with
36
37 more advanced keratoconic corneal topographical changes. We found an
38
39 average difference between NCT and DCT, of 5 mmHg in our population of
40
41 keratoconic subjects, (with a maximum difference of 8 mmHg) which is
42
43 substantial and could significantly influence a patients' clinical management.
44
45
46 Previous studies have also reported lower than normal IOP readings with the
47
48 NCT instrument in keratoconic patients (Swann & Waldron 1986; Edmonds 1993;
49
50 Papastergiou et al. 2008).
51
52
53
54
55
56
57
58
59
60

1
2
3 The NCT measures in our keratoconic subjects were also significantly correlated
4 with a number of corneal parameters. The majority of these significant
5 associations were with corneal parameters describing the shape of the cornea,
6 with lower IOP readings being associated with steeper corneal shapes. In
7 normal subjects, steeper corneal curvatures can lead to an overestimation of IOP
8 with applanation tonometers (Whiteacre and Stein 1993; Fukuoka et al 2008).
9

10
11 The reason for our finding of a lower IOP being associated with a steeper corneal
12 curvature is therefore unlikely to be a direct influence of corneal curvature on the
13 tonometry measures, and is more likely due to an association between steeper
14 corneas and more advanced keratoconic corneal changes (i.e. altered corneal
15 structural characteristics and biomechanics). Other recent studies (Papastergiou
16 et al 2008; Meyenberg et al 2008) have not found a significant association
17 between applanation IOP measures and keratometric corneal curvature readings
18 in keratoconic subjects. In our current study, the most significant association
19 was found between NCT IOP and the steepest corneal curvature (across the
20 central 4 mm), a corneal characteristic that may not have been detected through
21 analysis of keratometric curvature readings due to the substantial asymmetric
22 corneal topographical characteristics typically found in the keratoconic cornea.
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45

46
47
48 In our keratoconic subjects, no significant association was found between CCT
49 and NCT IOP. NCT measures in normal subjects (Eysteinnsson et al 2002, Tonnu
50 et al. 2005; Pelit et al. 2009) and subjects with glaucoma and ocular hypertension
51 (Erdurmus et al. 2008) have previously been found to be influenced by corneal
52
53
54
55
56
57
58
59
60

1
2
3 parameters such as CCT (with thicker corneas typically found to be associated
4 with higher IOPs). Papastergiou et al (2008) recently investigated NCT IOP
5 readings in keratoconus and did find a significant association between CCT and
6 IOP. However, the relationship between IOP and CCT was noted to be weaker
7 in their keratoconic subjects compared to normal eyes, with a relatively small
8 amount of the variance in IOP accounted for by CCT. The findings of a reduced
9 association between CCT and NCT IOP by Papastergiou et al, and no significant
10 correlation in our current study suggests that corneal characteristics aside from
11 the central corneal thickness may also have an influence on applanation IOP
12 readings in keratoconus (e.g. corneal biomechanical characteristics). Liu &
13 Roberts (2005) suggested that corneal biomechanical factors potentially have a
14 much larger influence on applanation tonometry than corneal thickness. It
15 therefore appears that there is not a simple direct relationship between central
16 corneal thickness and corneal structural and biomechanical changes in
17 keratoconus as evidenced by the fact that associations between corneal
18 biomechanical measures such as corneal hysteresis typically exhibit only
19 relatively weak associations with corneal thickness in keratoconus (Shah et al
20 2007).

21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48 An interesting finding from our current study was the significant correlations
49 found between $IOP_{DCT-NCT}$ and the measures of corneal thickness and
50 topography in our keratoconic population. The difference in IOP readings
51 between the DCT and NCT appears to provide a relatively strong correlation with
52
53
54
55
56
57
58
59
60

1
2
3 a wide range of measures describing the severity of keratoconus. Previous
4 studies of both normal (Tonnu et al. 2005; Pelit et al. 2009) and keratoconic
5 subjects (Edmonds 1993; Papastergiou et al. 2008) have found IOP measures
6 with NCT appear to be influenced by corneal parameters to a greater degree
7 than other tonometers. We postulate that because NCT's IOP measures appear
8 to be relatively dependant upon corneal biomechanical factors, and DCT
9 measures appear to be relatively independent of these factors, the difference
10 between the readings from the two instruments may therefore be providing a
11 measure of the cornea's biomechanical properties. Hence the $IOP_{DCT-NCT}$
12 exhibited strong correlations with a number of measures of the severity of
13 keratoconus, which is known to lead to changes in corneal biomechanics
14 (Edmund 1989; Luce 2005; Shah et al. 2007; Touboul et al. 2008). There has
15 been considerable recent interest in the ophthalmic community in identifying
16 corneas that are biomechanically compromised, and therefore at risk of
17 developing keratoconus or iatrogenic keratoectasia following laser refractive
18 surgery (Pallikaris et al. 2001; Randleman et al. 2003; Rad et al. 2004; Klein et
19 al. 2006; Rabinowitz 2006). Whilst further study is required, if $IOP_{DCT-NCT}$ is
20 providing a metric of corneal biomechanics, it may prove useful as a screening
21 tool to identify corneas that are biomechanically weaker and hence at risk of
22 developing ectatic changes.
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49

50
51
52 The accurate determination of IOP is of particular clinical importance in the
53 diagnosis and monitoring of glaucoma (Brandt et al. 2001; Boland & Quigley
54
55
56
57
58
59
60

1
2
3 2007). In subjects with substantially altered corneal characteristics such as
4
5 keratoconus, errors with traditional tonometric techniques could therefore
6
7 potentially lead to difficulties in the accurate diagnosis of glaucoma in these
8
9 patients. We found that the DCT instrument appears to be providing reliable
10
11 measures of IOP in patients with keratoconus that do not appear to be influenced
12
13 by altered corneal biomechanics. We found no significant relationship between
14
15 IOP as measured with the DCT and the severity of keratoconus. The difference
16
17 in IOP readings between the DCT and NCT appears to correlate strongly with a
18
19 number of parameters describing the severity of keratoconus. This difference in
20
21 measures may therefore be providing a useful estimation of corneal
22
23 biomechanical properties.
24
25
26
27
28
29
30
31

32 **Acknowledgements:**

33
34 This work was supported by a Queensland University of Technology, Institute of
35
36 Health and Biomedical Innovation early career research grant. The assistance of
37
38 Keratoconus Association Australia with subject recruitment is also gratefully
39
40 acknowledged.
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

References:

Barreto J, Babic M, Vessani RM & Susanna R (2006): Dynamic contour tonometry and goldman applanation tonometry in eyes with keratoconus. *Clinics* **61**: 511-514.

Böhm A, Kohlhaas M, Lerche R-C, Bischoff B & Richard G (1997): The effects of changed biomechanical parameters on measurements of intraocular pressure in keratoconus patients. *Ophthalmologie* **94**: 771-774.

Boland MV & Quigley HA (2007): Risk factors and open-angle glaucoma: Classification and application. *J Glaucoma* **16**: 406-418.

Brandt JD, Beiser JA, Kass MA, Gordon MO & The Ocular Hypertension Treatment Study Group (2001): Central corneal thickness in the ocular hypertension treatment study. *Ophthalmology* **108**: 1779-1788.

Brooks AMV, Robertson IF & Mahoney A-M (1984). Ocular rigidity and intraocular pressure in keratoconus. *Aust J Ophthalmol* **12**: 317-324.

Browning AC, Bhan A, Rotchford AP, Shah S & Dua HS (2004): The effect of corneal thickness on intraocular pressure measurement in patients with corneal pathology. *Br J Ophthalmol* **88**: 1395-1399.

1
2
3 Damji KF, Muni RH & Munger RM (2003): Influence of corneal variables on
4 accuracy of intraocular pressure measurement. *J Glaucoma* **12**: 69-80.
5
6
7

8
9
10 Edmonds CR (1993): Accuracy of IOP measurement in keratoconus. *ICLC* **20**:
11 29-30.
12
13

14
15
16
17 Edmund C (1989): Corneal topography and elasticity in normal and keratoconic
18 eyes. *Acta Ophthalmol Suppl* **193**: 1-36.
19
20
21

22
23
24 Erdurmus M, Totan Y, Hepsen IF & Yagci R (2008): Comparison of dynamic
25 contour tonometry and noncontact tonometry in ocular hypertension and
26 glaucoma. *Eye*. Advance online publication 8 February 2008.
27
28
29
30

31 Doi:10.1038/eye.2008.3
32
33
34
35

36 Eysteinnsson T, Jonasson F, Sasaki H, Arnarsson A, Sverrisson T, Sasaki K,
37 Stefansson E & the Reykjavik Eye Study Group (2002): Central corneal
38 thickness, radius of the corneal curvature and intraocular pressure in normal
39 subjects using non-contact techniques: Reykjavik eye study. *Acta Ophthalmol.*
40
41
42
43
44
45
46 **80**:11-15.
47
48
49

50 Fukuoka S, Aihara M, Iwase A & Araie M (2008): Intraocular pressure in an
51 ophthalmologically normal Japanese population. *Acta Ophthalmol.* **86**:434-439.
52
53
54
55
56
57
58
59
60

1
2
3 Goodman WT, Mathers WD, Munden PM, Ossoinig KC & Daley TE (1996): A
4 study of aqueous humor dynamics in keratoconus. *Exp Eye Res* **62**: 95-99.
5
6
7

8
9
10 Grolman B (1972): A new tonometer system. *Am J Optom Arch Am Acad*
11 *Optom.* **49**:646-660.
12
13
14

15
16
17 Hayes S, Boote C, Tuft SJ, Quantock AJ & Meek KM (2007): A study of corneal
18 thickness, shape and collagen organisation in keratoconus using
19 videokeratography and X-ray scattering techniques. *Exp Eye Res* **84**: 423-434.
20
21
22
23
24

25
26
27 Johannesson G, Hallberg P, Eklund A, Linden C. Pascal, ICare and Goldmann
28 applanation tonometry – a comparative study. *Acta Ophthalmologica.* 2008; **86**:
29 614-621.
30
31
32
33

34
35
36 Kanngiesser HE, Kniestedt C & Robert YCA (2005): Dynamic contour
37 tonometry. Presentation of a new tonometer. *J Glaucoma* **14**: 344-350.
38
39
40
41

42
43 Kaufmann C, Bachmann LM & Thiel MA (2004): Comparison of dynamic contour
44 tonometry with goldmann applanation tonometry. *Invest Ophthalmol Vis Sci* **45**:
45 3118-3121.
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Klein SR, Epstein RJ, Randleman B & Stulting RD (2006): Corneal ectasia after
4 laser in situ keratomileusis in patients without apparent preoperative risk factors.
5
6 Cornea **25**: 388-403.
7
8

9
10
11
12 Kotecha A, White ET, Shewry JM & Garway-Heath DF (2005): The relative
13 effects of corneal thickness and age on Goldmann applanation tonometry and
14
15 dynamic contour tonometry. Br J Ophthalmol **89**: 1572-1575.
16
17
18

19
20
21
22 Ku JYF, Danesh-Meyer HV, Craig JP, Gamble GD & McGhee CNJ (2006):
23
24 Comparison of intraocular pressure measured by Pascal dynamic contour
25
26 tonometry and Goldmann applanation tonometry. Eye **20**: 191-198.
27
28
29

30
31
32 Liu J & Roberts CJ (2005): Influence of corneal biomechanical properties on
33
34 intraocular pressure measurement. Quantitative analysis. J Cataract Refract
35
36 Surg **31**: 146-155.
37
38
39

40
41 Luce DA (2005): Determining in vivo biomechanical properties of the cornea with
42
43 an ocular response analyzer. J Cataract Refract Surg **31**: 156-62.
44
45
46

47
48 McMahon TT, Szczotka-Flynn L, Barr JT, Anderson RJ, Slaughter ME, Lass JH
49
50 et al. (2006): A new method for grading the severity of keratoconus. The
51
52 keratoconus severity score (KSS). Cornea **25**: 794-800.
53
54
55

1
2
3 Meyenberg A, Iliev ME, Eschmann R & Frueh BE (2008): Dynamic contour
4 tonometry in keratoconus and postkeratoplasty eyes. *Cornea* **27**: 305-310.
5
6
7

8
9
10 Mollan SP, Wolffsohn JS, Nessim M, Laiquzzaman M, Sivakumar S, Hartley S et
11 al. (2008): Accuracy of Goldmann, Ocular response analyser, Pascal and
12 Tonopen XL tonometry in keratoconis and normal eyes. *Br J Ophthalmol* **92**:
13 1661–1665
14
15
16
17
18
19

20
21
22 Ozbek Z, Cohen EJ, Hammersmith KM & Rapuano CJ (2006): Dynamic contour
23 tonometry. A new way to assess intraocular pressure in ectatic corneas.
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For Peer Review

Cornea **25**: 890-894.

31
32 Pallikaris IG, Kymionis GD & Astyrakakis NI (2001): Corneal ectasia induced by
33 laser in situ keratomileusis. *J Cataract Refract Surg* **27**: 1796-1802.
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

38
39 Papastergiou GI, Kozobolis V & Siganos DS (2008): Assessment of the Pascal
40 dynamic contour tonometer in measuring intraocular pressure in keratoconic
41 eyes. *J Glaucoma* **17**: 484-488.
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

48
49 Patel S & McLaughlin JM (1999): Effects of central corneal thickness on
50 measurement of intra-ocular pressure in keratoconus and post-keratoplasty.
51
52
53
54
55
56
57
58
59
60

Ophthal Physiol Opt **19**: 236-241.

1
2
3 Pelit A, Altan-Yaycioglu R, Pelit A & Akova YA (2009): Effect of corneal
4 thickness on intraocular pressure measurements with the Pascal dynamic
5 contour, Canon TX-10 non-contact and Goldmann applanation tonometers in
6 healthy subjects. Clin Exp Optom **92**: 14-18.
7
8
9

10
11
12
13
14
15 Rabinowitz YS (1998): Keratoconus. Surv Ophthalmol **42**: 297-319.
16
17

18
19
20 Rabinowitz YS (2006): Ectasia after laser in situ keratomileusis. Curr Opin
21 Ophthalmol **17**: 421-426.
22
23
24

25
26
27 Rad AS, Jabbarvand M & Saifi N (2004): Progressive keratectasia after laser in
28 situ keratomileusis. J Refract Surg **20**: S718-S722.
29
30
31

32
33
34 Randleman JB, Russell B, Ward MA, Thompson KP & Stulting RD (2003): Risk
35 factors and prognosis for corneal ectasia after LASIK. Ophthalmology **110**: 267-
36 275.
37
38
39

40
41
42
43 Read SA, Collins MJ & Iskander DRI (2008): Diurnal variation of axial length,
44 intraocular pressure, and anterior eye biometrics. Invest Ophthalmol Vis Sci **49**:
45 2911–2918.
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

1
2
3 Schädle N, Unterlauff JD, Klink T & Geerling G (2008): Evaluation of dynamic
4 contour tonometry in keratoconus. *Ophthalmologe*. Published online Aug 2
5
6 2008; doi: 10.1007/s00347-008-1812-1.
7
8
9

10
11
12 Schneider E & Grehn F (2006): Intraocular pressure measurement – comparison
13 of dynamic contour tonometry and Goldmann applanation tonometry. *J*
14
15 *Glaucoma* **15**: 2-6.
16
17
18
19

20
21
22 Shah S, Laiquzzaman M, Bhojwani R, Mantry S & Cunliffe I (2007): Assessment
23 of the biomechanical properties of the cornea with the ocular response analyzer
24 in normal and keratoconic eyes. *Invest Ophthalmol Vis Sci* **48**: 3026-3031.
25
26
27
28
29

30
31 Swann PG & Waldron HE (1986): Keratoconus: The clinical spectrum. *J Am*
32
33 *Optom Assoc* **57**: 204-209.
34
35
36
37

38
39 Tonnu P-A, T Ho, T Newson, A El Sheikh, K Sharma, E White, et al. (2005): The
40 influence of central corneal thickness and age on intraocular pressure measured
41 by pneumotonometry, noncontact tonometry, the Tono-Pen XL, and Goldmann
42 applanation tonometry. *Br J Ophthalmol* **89**: 851–854.
43
44
45
46
47
48

49
50 Touboul D, Roberts C, Kerautret J, Garra C, Maurice-Tison S, Saubusse E et al
51 (2008): Correlations between corneal hysteresis, intraocular pressure, and
52 corneal central pachymetry. *J Cataract Refract Surg* **34**: 616-622.
53
54
55
56
57
58
59
60

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Whiteacre MM & Stein R (1993): Sources of error with use of Goldmann-type tonometers. *Surv Ophthalmol* **38**: 1-30.

For Peer Review

Figure Legends:

Figure 1: Mean IOP with the NCT and DCT instruments from the keratoconic and age-matched control subjects. The difference between the keratoconic and control subjects was non-significant for DCT measures ($p=0.885$) but was highly significant for NCT measures ($p<0.0001$).

For Peer Review

1
2
3 Figure 2: The relationship between the difference in IOP measures from the
4 DCT and NCT ($IOP_{DCT-NCT}$) and measures of anterior corneal topography
5 (steepest axial curvature within the central 4mm), posterior corneal topography
6 (steepest axial curvature within the central 4mm) and corneal thickness (thinnest
7 corneal thickness) in the keratoconic population.
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

For Peer Review

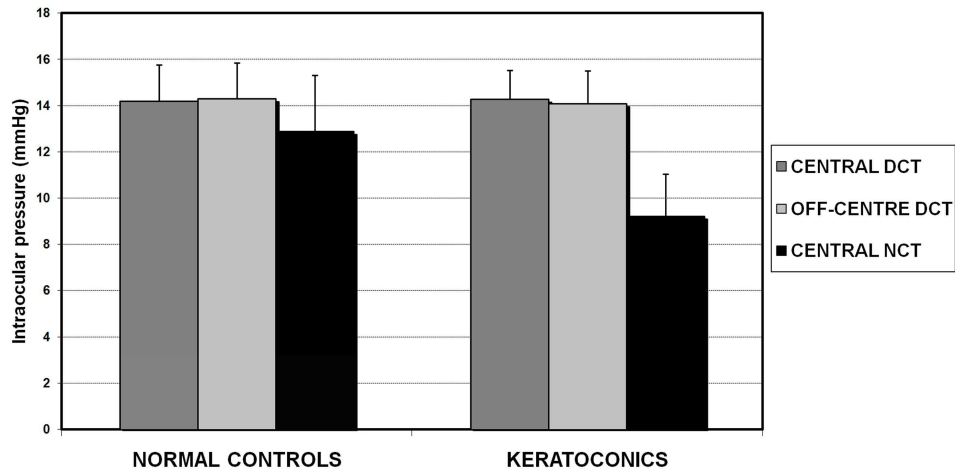


Figure 1: Mean IOP with the NCT and DCT instruments from the keratoconic and age-matched control subjects. The difference between the keratoconic and control subjects was non-significant for DCT measures ($p=0.885$) but was highly significant for NCT measures ($p<0.0001$)

130x67mm (600 x 600 DPI)

Peer Review

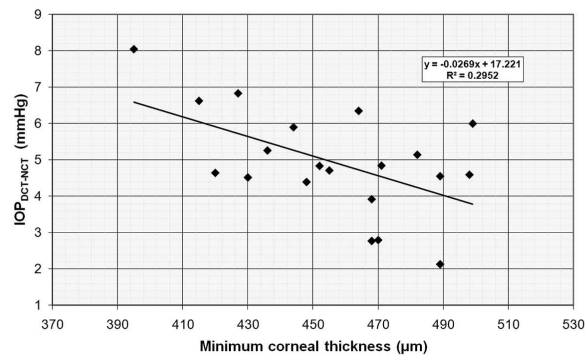
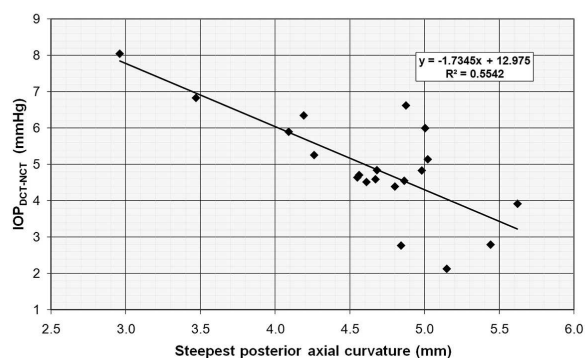
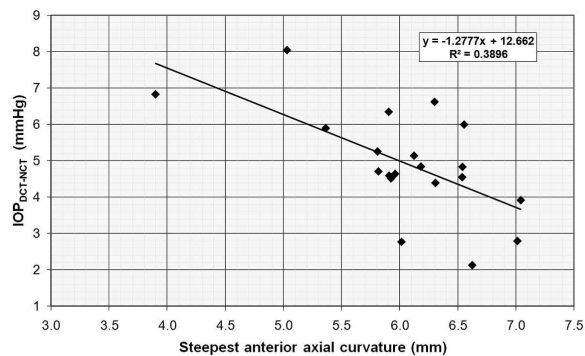


Figure 2: The relationship between the difference in IOP measures from the DCT and NCT (IOP_{DCT-NCT}) and measures of anterior corneal topography (steepest axial curvature within the central 4mm), posterior corneal topography (steepest axial curvature within the central 4mm) and corneal thickness (thinnest corneal thickness) in the keratoconic population.
116x203mm (600 x 600 DPI)

1
2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
21
22
23
24
25
26
27
28
29
30
31
32
33
34
35
36
37
38
39
40
41
42
43
44
45
46
47
48
49
50
51
52
53
54
55
56
57
58
59
60

Table 1: Average corneal topography and thickness parameters for the keratoconic and age-matched control populations. Axial curvature, average CT and HO RMS parameters calculated across a 4 mm corneal diameter. P-values are derived from independent sample t-tests comparing mean keratoconic parameter to mean age-matched normal parameter.

Corneal parameter	Mean \pm SD		P-value
	Keratoconic subjects (n = 20)	Age-matched control subjects (n = 20)	
Average anterior axial curvature (mm) [*]	7.04 \pm 0.56	7.83 \pm 0.23	P < 0.001 for all parameters
Steepest anterior axial curvature (mm)	6.04 \pm 0.70	7.63 \pm 0.26	
Anterior Corneal HO RMS (μ m) [*]	1.34 \pm 0.64	0.10 \pm 0.03	
Average posterior axial curvature (mm) [†]	5.61 \pm 0.56	6.55 \pm 0.23	
Steepest posterior axial curvature (mm) [†]	4.63 \pm 0.62	6.13 \pm 0.27	
CCT (μ m) [†]	473 \pm 25	529 \pm 33	
Min CT (μ m) [†]	456 \pm 29	527 \pm 33	
Average CT (μ m) [†]	493 \pm 23	539 \pm 33	
Temporal CT (2.0mm) (μ m) [†]	500 \pm 28	541 \pm 34	
% Thickness increase (8mm) [†]	47.93 \pm 11.80	28.40 \pm 3.96	

^{*}Parameter derived from data from Medmont E300 videokeratoscope

[†]Parameter derived from data from Pentacam HR rotating Scheimpflug camera

Table 2: Overview of correlation analysis exploring association between IOP measures and corneal topographical and thickness parameters for the keratoconic population. Pearson's correlation coefficient (r) and significance displayed for the correlation between each corneal parameter.

Corneal parameter		IOP MEASURE		
		IOP _{DCT_AVE}	IOP _{NCT}	IOP _{DCT-NCT}
Average anterior axial curvature (mm) [*]	r (p-value)	-0.179 (0.449)	0.447 (0.048)	-0.617 (0.004)
Steepest anterior axial curvature (mm) [*]	r (p-value)	-0.233 (0.323)	0.624 (0.003)	-0.624 (0.003)
Anterior Corneal HO RMS (μm)	r (p-value)	0.156 (0.512)	-0.358 (0.122)	0.505 (0.023)
Average posterior axial curvature (mm) [†]	r (p-value)	-0.221 (0.349)	0.502 (0.024)	-0.712 (0.0004)
Steepest posterior axial curvature (mm) [†]	r (p-value)	-0.359 (0.120)	0.404 (0.078)	-0.744 (0.0002)
CCT (μm) [†]	r (p-value)	-0.339 (0.144)	0.116 (0.627)	-0.438 (0.05)
Min CT (μm) [†]	r (p-value)	-0.344 (0.138)	0.216 (0.360)	-0.543 (0.013)
Average CT (4mm) (μm) [†]	r (p-value)	-0.25 (0.287)	-0.012 (0.476)	-0.226 (0.338)
Temporal CT (2.0mm) (μm) [†]	r (p-value)	-0.326 (0.16)	-0.138 (0.563)	-0.174 (0.464)
% Thickness increase (8mm) [†]	r (p-value)	0.235 (0.319)	-0.474 (0.035)	0.697 (0.001)

*Parameter derived from data from Medmont E300 videokeratoscope

†Parameter derived from data from Pentacam HR rotating Scheimpflug camera