

# A comparison of rebound and applanation tonometry in children with and without primary congenital glaucoma



## Authors:

Hester Kruger<sup>1</sup>   
Naseer Ally<sup>1,2</sup>   
Natasha Naidu<sup>1</sup>   
Ismail Mayet<sup>1</sup>

## Affiliations:

<sup>1</sup>Department of Neurosciences, Faculty of Ophthalmology, University of the Witwatersrand, Johannesburg, South Africa

<sup>2</sup>Department of Neurosciences, Faculty of Ophthalmology, Manchester Royal Eye Hospital, Manchester, United Kingdom

## Corresponding author:

Hester Kruger,  
hettie.kruger@gmail.com

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**Background:** Intraocular pressure (IOP) measurement should be accurate in a paediatric population with primary congenital glaucoma (PCG).

**Aim:** This study aims to investigate the difference between the change in IOP measurements using rebound tonometry (RBT) and handheld applanation tonometry (AT) (Perkins applanation tonometer [PAT]) in patients with and without PCG.

**Setting:** Johannesburg, South Africa.

**Methods:** Measurements were taken under anaesthesia, using RBT and AT at 0 min, 5 min and 10 mins after induction and prior to intubation. Corneal pachymetry and corneal diameters were measured.

**Results:** Sixty-five children were included, 19 with PCG and 46 without PCG. The mean age (standard deviation [s.d.]) was 3.2 (2.25) years and 4.8 (2.4) years, respectively. The overall mean difference in IOP between RBT and PAT across both PCG and non-PCG groups was found to be 4.92 mmHg (95% confidence interval [CI]: 2.80 – 7.03)  $p < 0.001$ , with RBT having higher readings. This difference was greater in the PCG group, with the IOP difference of 9.05 mmHg (95% CI: 2.6 – 15.5)  $p = 0.004$ . Mean corneal pachymetry (s.d.) was 585.6 (81.48)  $\mu\text{m}$  in the PCG group and 518.31 (39.9)  $\mu\text{m}$  in the non-PCG group. Univariate analysis showed that IOP was significantly related to corneal pachymetry, with a 11 mmHg increase in IOP for every 100  $\mu\text{m}$  change in corneal thickness for measurements done with RBT ( $p < 0.001$ ), compared to 4 mmHg using PAT ( $p = 0.008$ ).

**Conclusion:** Intraocular pressure measurements done with RBT in children with and without PCG were overestimated compared to PAT.

**Contribution:** This difference was more pronounced in PCG patients. In addition, IOP was significantly related to corneal thickness.

**Keywords:** intraocular pressure; applanation tonometry; rebound tonometry; primary congenital glaucoma; paediatric ophthalmology; tonometry; glaucoma; corneal pachymetry.

## Introduction

Primary congenital glaucoma is a developmental glaucoma that accounts for most of the primary paediatric glaucoma.<sup>1</sup> The incidence varies with ethnicity, with the highest incidence occurring in Slovakia and Saudi Arabia reported at 1 in 1250 and 1500 live births, respectively.<sup>2</sup> Prevalence rates are lower for other parts of Europe, North America and Australian populations, ranging from 1:10 000 to 1:38 000.<sup>3,4,5</sup> Sub-Saharan African studies report PCG to account for up to 4% of all new glaucoma cases.<sup>6</sup> In South Africa, glaucoma contributes to 6.7% of childhood blindness.<sup>7</sup>

Raised intraocular pressure (IOP) is a modifiable risk factor in glaucoma.<sup>1</sup> Handheld applanation tonometers, like the Perkins applanation tonometer (PAT), are frequently used in paediatric patients but often require general anaesthesia.

Commonly used anaesthetic agents like Sevoflurane and propofol, have an IOP lowering effect,<sup>8,9</sup> while ketamine raises IOP with doses above 4 mg/kg.<sup>10</sup> Additionally manipulation of the airway may further cause fluctuations in IOP.<sup>11</sup>

Rebound tonometry (RBT) offers the advantage over applanation tonometry (AT) in that it does not require any topical anaesthesia and needs less patient co-operation making it a good adjunct

to in-office IOP measurement in awake children.<sup>12</sup> The reliability, however, still needs to be established in the paediatric population.

Some previous studies comparing RBT to AT in paediatric patients with PCG have found that RBT overestimates IOP compared to AT,<sup>13,14,15,16</sup> while others<sup>17</sup> found RBT to be comparable. There is, therefore, clinical equipoise regarding whether there is a significant difference between RBT and AT when comparing PCG eyes to non-PCG eyes under general anaesthesia without the potential effect of the volatile agents. We also do not know if this difference is more pronounced in PCG patients compared to non-PCG patients.

This study therefore aimed to assess the difference between RBT and handheld AT in paediatric patients with PCG compared to healthy controls when undergoing examination under anaesthesia (EUA). The role of possible predicting factors of IOP in study participants, including corneal pachymetry, corneal diameter, and age was also investigated.

## Materials and methods

This single centre, non-interventional, prospective study included patients diagnosed with PCG undergoing EUA and a control group undergoing routine unilateral ophthalmological procedures under anaesthesia. The study was conducted at St John Eye Hospital, Johannesburg, South Africa. The hospital is affiliated to the University of the Witwatersrand.

Inclusion criteria included patients 10 years and younger. The study group included PCG group patients undergoing routine EUA. The control group included paediatric patients undergoing routine unilateral ophthalmological procedures. These included lens washouts, chalazion and molluscum contagiosum excision and eyelid surgery.

Exclusion criteria included the presence of any corneal disease not related to PCG and secondary causes of glaucoma.

One eye per study patient was included. Where both eyes qualified as a study eye, a computer-based randomisation sequence was used to determine which eye should be included.

Anaesthesia was standardised and based on the Chris Hani Baragwanath Academic Hospital's anaesthetic department protocol, recommended by Van Der Walt et al.<sup>18</sup> This protocol, consisted of sevoflurane gas induction limited to 6% until placement of an intravenous cannula and given via a mask, followed by a ketamine bolus of 2 mg/kg and a titrated ketamine infusion of no more than 4 mg/kg. Topical oxybuprocaine 0.4% drops and sodium fluorescein staining were placed on the ocular surface.

Intraocular pressure measurements were recorded first with rebound (RBT) followed by applanation (PAT) tonometry. The measurements were conducted as the sevoflurane gas

was switched off and repeated 5 min and 10 min later. All measurements were done prior to intubation.

During measurements, children were placed in the supine position, with the head turned to the opposite side of the study eye for both tonometers. Rebound tonometry using the Icare® TA01i (Icare, Tiolat Oy Helsinki, Finland) was performed prior to measuring IOP with PAT (Perkins, Clement-Clarke, Haag-Streit, Harlow, United Kingdom) at each specified time interval. The average of two measurements using RBT and one measurement from PAT was captured. A single study investigator (H.K.) performed all measurements.

Corneal pachymetry was measured using the Ocuscan® RxP (Alcon Laboratories, California, United States) pachymeter. Horizontal and vertical corneal diameters were measured using a calliper, under view of a microscope.

A sample size of 82 patients was calculated using Satterthwaite's *t*-test with 80% power to detect a difference of at least 2 mmHg between the means of the differences between AT and RBT in the PCG and non-PCG groups. Unequal variances were assumed. We added a small margin for error and got a final sample size of 90 patients, with 45 patients in each group. Because of the rarity of PCG patients attending the hospital, the required number of PCG patients was not reached. However, upon interim analysis, the results were found to be significant, and the decision was made to stop recruitment.

Data were collected and stored on an electronic database, using Research Electronic Data Capture (REDCap®).<sup>19,20</sup> Results were analysed using Stata (version 16.1).

Categorical data were presented as a number or mean  $\pm$  standard deviation (s.d.).

A paired *t*-test was used to assess the differences between RBT and PAT at the specified time intervals. A two-sample *t*-test was used to derive the differences between the two instruments in the PCG and non PCG group.

Evaluation of the concordance between RBT and PAT in the PCG and non PCG group was done using Lin's concordance correlation coefficient. To analyse possible predictive factors between groups, univariate and multivariate linear mixed effects models were used.

## Ethical considerations

Ethical clearance to conduct this study was obtained from the University of the Witwatersrand, Johannesburg, Human Research Ethics Committee (No. R14/49). The study protocol followed the principles of the declaration of Helsinki. Written informed consent was obtained from all parents. Written informed medical assent was obtained from patients 7 years and older.

## Results

### Demographics

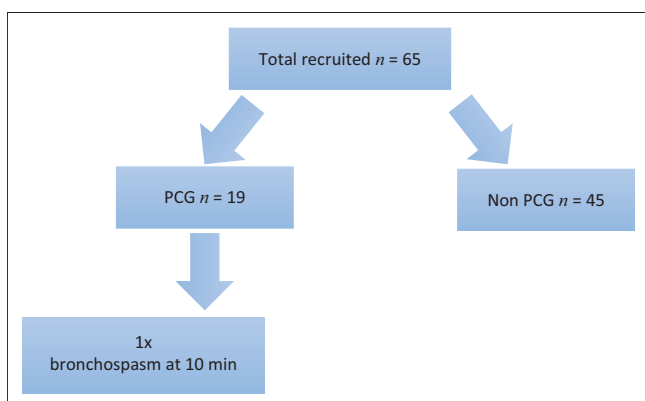
A total of 65 eyes of 65 children were included in the study, 19 with PCG and 46 patients without PCG. One patient developed bronchospasm during measurements, accounting for the missing data point at 10 min (see Figure 1). Thirty-two patients were male (58.2%) and 23 (41.8%) were female. In the PCG group, 13 patients (68%) were male. The mean age (s.d.) in years in the PCG group and the non-PCG group was 3.12 (2.27) and 4.85 (2.42), respectively (see Table 1).

### Mean intraocular pressure

The overall mean (s.d.) IOP obtained was higher with RBT, measuring 20.92 (13.79) mmHg, compared to PAT measuring 16.00 (8.40) mmHg. In the PCG group, the mean IOP measured with RBT and PAT at 10 min was 36 (17.07) mmHg and 25.06 (10.29) mmHg, respectively. In the non-PCG group, IOP was 14.71 (4.20) mmHg and 12.38 (3.47) mmHg using RBT and PAT at 10 min, respectively (see Figure 2).

### Mean intraocular pressure difference between rebound tonometry and Perkins appplanation tonometer

Analysis of the overall IOP differences between RBT and PAT, regardless of patient group, was statistically significant at each time interval. Rebound tonometry overestimated IOP by 4.37 mmHg (95% confidence interval [CI]: 2.52 – 6.21) ( $p < 0.001$ ), 4.52 mmHg (95% CI: 2.91 – 6.13) ( $p < 0.001$ ) and 4.71 mmHg (95% CI: 2.80– 7.03) ( $p < 0.001$ ), at 0 min, 5 min and 10 min, respectively (see Table 2).



PCG, primary congenital glaucoma.

**FIGURE 1:** Outline of patient recruitment.

**TABLE 1:** Patient demographics.

Groups	Patients enrolled (n)	Male	Female	Mean age ± s.d. (years)
PCG	19	13	6	3.12 ± 2.27
Non PCG	46	26	20	4.85 ± 2.42
<b>Total</b>	<b>65</b>	<b>39</b>	<b>26</b>	<b>3.83 ± 2.49</b>

PCG, primary congenital glaucoma; s.d., standard deviation.

### Mean intraocular pressure difference between rebound tonometry and Perkins appplanation tonometer between groups

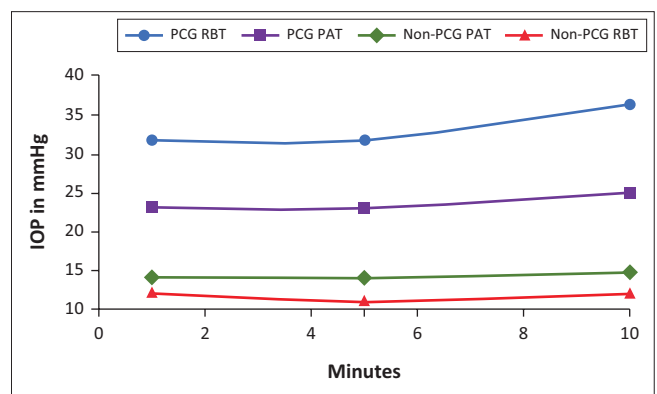
Between the PCG and non PCG groups, RBT overestimated IOP significantly at all time intervals. The mean IOP difference for both groups measured 6.17 mmHg (95% CI: 0.19 – 12.14) ( $p = 0.02$ ), 6.10 mmHg (95% CI: 1.36 – 10.84) ( $p = 0.007$ ) and 9.05 mmHg (95% CI: 2.60 – 15.5) ( $p = 0.004$ ) at 0 min, 5 min and 10 min, respectively.

### Mean intraocular pressure difference between rebound tonometry and Perkins appplanation tonometer in primary congenital glaucoma vs non-primary congenital glaucoma

The study data showed that the IOP difference between RBT and PAT was more discordant in the PCG group, and that these differences were larger with time, with a difference of 8.71 mmHg (95% LOA: 15.49 – 32.91)  $p < 0.001$ , 8.81 mmHg (95% LOA: 10.13 – 27.76) and 11.38 mmHg (95% LOA: 13.71 – 36.56) at 0 min, 5 min and 10 min, respectively.

Mean horizontal corneal diameter (s.d.) was 13.95 (1.24) mm in the PCG group, compared to 11.09 (0.32) mm in the non-PCG group (Figure 3).

Mean corneal central corneal thickness (CCT) (s.d.) was 585.6 (81.48)  $\mu\text{m}$  in the PCG group and 518.31 (39.9)  $\mu\text{m}$  in the non-PCG group. Corneal pachymetry significantly influenced IOP measurements during univariate and multivariate analysis. Our data showed that for every 100  $\mu\text{m}$  increase in corneal pachymetry, IOP will increase by 11  $\mu\text{mHg}$  ( $p < 0.001$ ) for measurements conducted with RBT, compared to



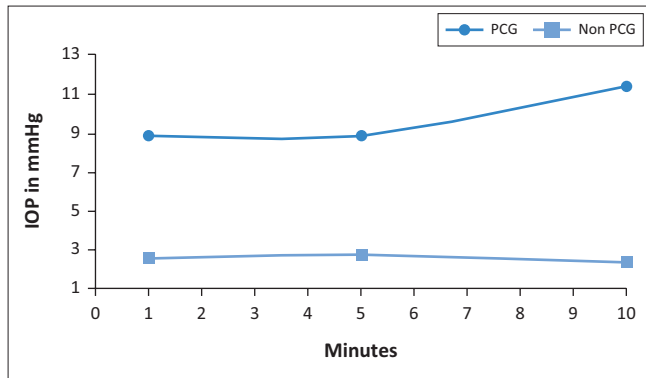
PCG, primary congenital glaucoma; RBT, rebound tonometry; PAT, Perkins appplanation tonometer; IOP, intraocular pressure.

**FIGURE 2:** Mean intraocular pressure for rebound tonometry and Perkins appplanation tonometer for primary congenital glaucoma and non-primary congenital glaucoma patients at 0 min, 5 min and 10 min after Sevoflurane gas was switched off.

**TABLE 2:** Overall difference between rebound tonometry and Perkins appplanation tonometer.

Time interval	Number of patients (n)	Mean IOP difference (mmHg)	95% confidence interval	p
0 min	65	4.37	2.52–6.21	$p < 0.001$
5 min	65	4.52	2.91–6.13	$p < 0.001$
10 min	64	4.71	2.80–7.03	$p < 0.001$

RBT, rebound tonometry; PAT, Perkins appplanation tonometer; IOP, Intraocular pressure.



PCG, primary congenital glaucoma; RBT, rebound tonometry; PAT, Perkins applanation tonometer; IOP, Intraocular pressure.

**FIGURE 3:** Overall difference between rebound tonometry and Perkins applanation tonometer in primary congenital glaucoma vs non-primary congenital glaucoma at 0 min, 5 min and 10 min after Sevoflurane gas was switched off.

**TABLE 3:** Multivariate linear mixed effects analysis.

Group	Parameter	Coefficient	Standard deviation	p-value
PAT	Pachymetry	0.01	-0.01–0.03	0.293
	Age	-0.04	-0.008–0.09	0.1
	Gender	0.48	-2.38–3.35	0.74
RBT	Pachymetry	0.05	0.01–0.09	<0.01
	Age	-0.09	-0.007–0.16	0.03
	Gender	-1.78	-6.31–2.75	0.44

RBT, rebound tonometry; PAT, Perkins applanation tonometer.

4 mmHg ( $p = 0.002$ ) for measurements conducted with PAT during univariate analysis. Multivariate analysis showed that pachymetry had a significant effect on measurements done with RBT but not with measurements done with PAT. Gender did not influence IOP measurements (see Table 3).

## Discussion

The aim of this study was to compare the IOP difference between RBT and AT among two groups, with and without PCG. This study findings showed that RBT significantly overestimated IOP in both PCG and non PCG children. This IOP difference between RBT and PAT was more pronounced in the PCG group when compared to the non-PCG group. To our knowledge, this is the first study to report such a large difference between RBT and AT in PCG children.

Previous literature has reported RBT to overestimate IOP in children with<sup>13,14,15,16</sup> and without glaucoma.<sup>12,21</sup> This study data correlate with these findings, regardless of the clinical group. The reason for the discrepancy between RBT and AT is not clear. Corneal thickness<sup>16</sup> and corneal biomechanics<sup>22</sup> have been reported to influence IOP measurements; however, the difference between the mechanism of the two tonometers should also be kept in mind. While AT is based on the Imbert-Fick principle,<sup>1</sup> determining the force needed to flatten an area of central cornea, RBT calculates IOP from the rate of deceleration of a probe after it hits the cornea.<sup>12</sup>

In the study analysis, the difference in IOP between RBT and AT was most pronounced in the PCG group. Strzalkowska et al.<sup>13</sup> reported a mean IOP difference between RBT and AT of 6.0 mmHg  $\pm$  6.1 mmHg in their study investigating the

optimal timing of measuring IOP in children with and without PCG undergoing anaesthesia.

In a larger study consisting of 194 eyes of 105 children with glaucoma, Angmo et al.<sup>23</sup> showed a mean difference between PAT and RBT of 2.34 mmHg in the subgroup of patients with corneal scarring.

Martinez de la Casa et al.<sup>16</sup> found the mean IOP difference between RBT and PAT to be 3.1 mmHg  $\pm$  4.0 mmHg,  $p < 0.001$ ) in awake children with a mean age of 8.8 years  $\pm$  2.9 years. This is in comparison to our study, where the children were younger with a mean age of 3.83 years  $\pm$  2.49 years. During this study analysis, age was not a significant predictor of IOP; however, our study included patients with advanced disease, which could account for the larger difference measured between devices.

Other authors<sup>14,17,24</sup> have reported differences in IOP between RBT and AT of less than 1 mmHg. In a Spanish study, Perez-Garcia et al.<sup>24</sup> found a mean difference in IOP of 0.98 mmHg ( $p = 0.47$ ) when comparing RBT and AT in PCG patients. Esmael et al.<sup>14</sup> also found that RBT was more likely to overestimate IOP when IOP is greater than 15 mmHg, the difference between devices being 0.59 mmHg  $\pm$  2.60 mmHg. Although the trend towards RBT overestimating IOP is similar, our study showed markedly higher IOP differences between devices. This can perhaps relate to the advanced cases of PCG that presents to our centre, along with our anaesthetic protocol that controls for confounding factors influencing IOP, such as anaesthetic drugs. In addition, our results showed an increase in IOP difference with time possibly because of the effect of sevoflurane wearing off, along with the change in corneal biomechanics in buphthalmic eyes.

Corneal thickness in our study population showed that PCG patients had thicker corneas compared to the control group. This can be explained by PCG patients presenting with corneal oedema. In addition, corneal pachymetry in the non PCG group was thinner than average. Taking into account the fact that our patient population were all of African descent, our findings correlate with a previous studies<sup>25,26</sup> that found thinner corneal thickness measurements in African patients, compared to Caucasian patients.

During our analysis, corneal pachymetry was found to be a significant predictor of IOP on univariate analysis. Our results revealed that for every 100  $\mu$ m increase in corneal pachymetry, IOP will increase by 11 mmHg ( $p < 0.001$ ) for RBT compared to PAT of 4 mmHg ( $p = 0.002$ ).

The literature is divided on the role of CCT and IOP. Morales-Fernandez et al.<sup>22</sup> did not find an association between IOP and CCT in their study, which compared corneal biomechanical properties in patients with and without PCG during their multivariate analysis. This was attributed to corneal hysteresis and corneal resistance factor being more sensitive predictors of IOP compared to pachymetry alone. However, Perez-Garcia et al.<sup>24</sup> found a significant correlation between IOP and corneal pachymetry, using linear regression

in healthy children. This finding was not observed in children with PCG. This can be explained by the differences in corneal changes that take place because of PCG, including corneal oedema, Haab's striae, multiple prior surgeries and topical medications used. In addition, our analysis revealed that age and gender had no influence on IOP.

Limitations of the study included the limited number of PCG patients at the centre. The initial calculated sample size of 45 patients was not obtained for the PCG group. Despite this, statistical significance was still reached because of the marked difference in IOP recorded between tonometers.

Although a single operator performed all measurements, the operator was not masked to the device nor the underlying condition of the study participant. This would not affect the reading with reference to RBT, but the operator can influence the reading of the PAT.

## Conclusion

Intraocular pressure measurements conducted with RBT in children with and without PCG were overestimated compared to handheld Perkins applanation tonometry. This difference was more pronounced in PCG patients compared to non-PCG patients. In addition, IOP was significantly related to corneal thickness. Based on this study's results, we can recommend that care should be taken when measuring IOP with RBT in children with PCG, as PAT is more likely to give an accurate IOP.

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## Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

## Authors' contributions

H.K., N.A., N.N. and I.M. contributed to the manuscript equally: H.K.: writing of original draft, investigations, editing. N.A.: formal analysis, supervision, review and editing. N.N.: supervision, review and editing. I.M.: conceptualisation, methodology, supervision, review and editing.

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## Data availability

Data are kept on a password protected data base (REDCap) and access to the data base can be obtained from the corresponding author, H.K. (kruger@gmail.com).

## Disclaimer

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