Comparison of handheld rebound tonometry with Goldmann applanation tonometry in children with glaucoma: a cohort study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-001788
Article Type:	Research
Date Submitted by the Author:	25-Jul-2012
Complete List of Authors:	Dahlmann-Noor, Annegret; NIHR Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, Paediatric Ophthalmology Bunce, Catey; Moorfields Eye Hospital NHS Foundation Trust, Research and Development Puertas, Renata; Moorfields Eye Hospital, Glaucoma Tabasa-Lim, Shenille; Moorfields Eye Hospital, Paediatric Ophthalmology El-Karmouty, Ahmed; Moorfields Eye Hospital, Glaucoma Kadhim, Mustafa; Moorfields Eye Hospital, Glaucoma Wride, Nicholas; Moorfields Eye Hospital, Glaucoma Lewis, Amanda; Moorfields Eye Hospital, Glaucoma Grosvenor, Dawn; Moorfields Eye Hospital, Glaucoma Rai, Poornima; Moorfields Eye Hospital, Glaucoma Papadopoulos, Maria; Moorfields Eye Hospital, Glaucoma brookes, john; Moorfields Eye Hospital, Glaucoma Khaw, Peng; NIHR Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, Glaucoma
Primary Subject Heading:	Ophthalmology
Secondary Subject Heading:	Paediatrics, Evidence based practice
Keywords:	Paediatric ophthalmology < OPHTHALMOLOGY, Community child health < PAEDIATRICS, Glaucoma < OPHTHALMOLOGY

SCHOLARONE™ Manuscripts

Handheld rebound tonometry in children with glaucoma

Authors

Annegret Hella Dahlmann-Noor

Renata Puertas

Shenille Tabasa-Lim

Ahmed El-Karmouty

Mustafa Kadhim

Nicholas Wride

Amanda Lewis

Dawn Grosvenor

Poornima Rai

Maria Papadopoulos

John Brookes

Catey Bunce

Peng Tee Khaw

Corresponding author: Annegret Dahlmann-Noor, Moorfields Eye Hospital, 162 City Road, London EC1V 2PD; annegret.dahlmann-noor@moorfields.nhs.uk

Funding statement:

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Acknowledgements:

The authors are grateful for the support from Fight for Sight and the Helen Hamlyn Trust. The research took place at the National Institute for Health Research (NIHR) Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Competing Interests Statement:

None of the authors have competing interests to declare.

Contributorship Statement:

AHDN and CB designed the trial and prepared the manuscript. AHDN, RP, STL, AE, PR, MK, NW, AL, DG, MP, JB and PTK facilitated recruitment, obtained informed consent, acquired data and completed case report forms. AHDN entered data onto the electronic database. CB analysed the data. All authors reviewed the manuscript.

Abstract

Objective: To test agreement of two methods to measure intraocular pressure (IOP): rebound tonometry (RBT) and gold standard Goldmann applanation (GAT) tonometry in children with glaucoma

Design: observational prospective cohort study

Setting: tertiary paediatric glaucoma clinic at a single centre

Participants: 102 children with glaucoma, mean (SD) age 11.85 (3.17), of whom 53 were male

Primary and secondary outcome measures: intraocular pressure, central corneal thickness, child preference for measurement method

Results: Limits of agreement for intra- and interobserver were respectively (-2.71, 2.98) mmHg and (-5.75, 5.97) mmHg. RBT frequently gave higher readings than GAT and the magnitude of disagreement depended on the level of IOP being assessed. Differences of 10mmHg were not uncommon. RBT was the preferred method for 70% of children.

Conclusions: There is poor agreement between RBT and GAT in children with glaucoma. RBT frequently and significantly overestimates IOP. However, “normal” RBT readings are likely to be accurate and may spare children an EUA. High RBT readings should prompt the practitioner to use another standard method of IOP measurement if possible, or consider the RBT measurement in the context of clinical findings before referring the child to a specialist clinic or considering EUA.

Background/Introduction

Glaucoma is a potentially blinding condition. Raised intraocular pressure (IOP) is an important risk factor for the development and progression of optic nerve damage in glaucoma, and is the target of both medical and surgical treatment. There are no published figures on how many children have an IOP test per year, but both community optometrists and hospital clinics regularly perform IOP measurement as part of a comprehensive eye examination. For all practitioners IOP measurements in young children are challenging . The current gold standard measurement technique is Goldmann applanation tonometry (GAT) on a slit lamp, or handheld Perkins applanation tonometry (PAT) during an examination under anaesthesia (EUA).

GAT requires the instillation of topical anaesthetics and a high degree of co-operation from the child. Frequently children are unable to suppress the natural reflex of moving backward or closing their eyes. This leads to repeated attempts being made at obtaining a reading, prolonged examination times and distress to children and families.

In 2005 a new device to measure intraocular pressure became available, the iCare® rebound tonometer (RBT). Its main advantage over other instruments is that no topical anaesthesia is required. In addition, it is a hand-held device, which children may perceive as less intimidating and allows examiners to move “with the child” when required.

The RBT acquires six readings in quick succession by propelling a fine sensor tip less than 2mm in diameter against the central cornea from the instrument base held at a distance of 4-8mm from the surface of the eye. [1] [2] After contact, the probe bounces back; the higher the IOP the faster the rebound. Measurements are taken within 0.1 seconds. The force impacting on the cornea is minimal and does usually not even trigger the highly sensitive blink reflex. The instrument display then shows the average of the six readings and whether the standard deviation (SD) is low, medium or high.

Since its introduction, RBT has become very popular and is now being used in many children’s eye services and by many community-based optometrists. Two surveys of tonometry practice in children (Table 1 and reference [3]) indicate that for most paediatric ophthalmologists in the UK, RBT has become the preferred method to measure IOP in children. Whilst the device is considered easy to use, many users report that RBT measurements tend to be higher than GAT measurements (Table 1).

Data comparing RBT performance with GAT in children with glaucoma are scarce and limited to one study only. [4] Studies which have compared RBT with non-contact tonometry and tonopen in healthy children indicate good intra- and interobserver reliability and good agreement. [5] [6] [7] In children with glaucoma good agreement has been reported with both PAT [8] and GAT, [4] although RBT measurements are consistently higher than PAT or GAT readings.

In adults with healthy eyes, glaucoma or ocular hypertension, papers have reported good agreement between the RBT and GAT, albeit with systematically higher measurements on RBT. [9] [10] [11] [12] [13] [14] [15]

Accuracy of RBT may be affected by levels of IOP [8] [16] and central corneal thickness (CCT), [7] [13] [14] it might not be CCT alone but rather other corneal properties (hysteresis and resistance) that affect IOP measurement. [17] These parameters are not routinely assessed in clinics and impossible to assess in young children.

We carried out the present study to evaluate the accuracy and reliability of RBT in children with glaucoma as compared to GAT. Secondary objectives were to investigate the influence of IOP and CCT, and to determine children's preference for RBT or GAT.

Methods

Patients

We recruited children and teenagers between the age of 5 and 19 years with an established diagnosis of primary or secondary glaucoma, attending our tertiary paediatric glaucoma service at Moorfields Eye Hospital. The study was approved by the local research ethics committee. All parents/guardians gave written informed consent and children were invited to give assent.

The sample size was determined by recommendations for Bland-Altman analysis. [18]

Protocol

Three observers took the measurements required for this study. Observer 1 measured the IOP in one eye by RBT. In children with glaucoma in both eyes, readings were taken from the right eye. In children with glaucoma only in the left eye, readings were taken from the left eye. Observer 1 recorded two consecutive averageRBT readings from six measurements and the SD indicated by the device.

One repeat average RBT measurement was obtained by a second observer and recorded separately.

Following instillation of a drop of proxymethacaine, observer 2 recorded CCT on ultrasound pachymetry.

The third observer recorded IOP on GAT and asked the child which instrument they preferred.

All data were recorded on a Case Report Form which also recorded the child's diagnosis and ethnic background. At the end of the study, data were entered into a computerised database.

Data analysis

Summary statistics were produced for demographic factors and for IOP readings made by each observer and method (Tables 2 and 3). Repeat readings made by observer 1 using RBT were used to estimate intraobserver agreement using the Bland-Altmann limits of agreement method. [18] The same method was used to determine interobserver agreement, analysing RBT reading 1 from observer 1 and the RBT reading obtained by observer 2. Agreement between RBT and GAT was analysed based on reading 1 from observer 1 and GAT recorded by observer 3. A histogram for CCT was plotted in two age bands (under and over 10 years of age). Child preference for either device was summarised by descriptive statistical methods.

Results

Demographics

We carried out the study between 1/1/2009 and 31/3/2010. We enrolled n=102 children with a confirmed diagnosis of glaucoma. Age ranged from 4.9 to 19 years (mean 11.85, SD 3.17 years). 53 boys and 49 girls took part (Table 2). In 85 children the right eye was the study eye, and in n=17 children the left eye.

Analysis of first RBT reading by observer 1

One hundred and two datasets were analysed. Data were missing for 3 subjects. In 16 participants the variability reading on the RBT was high. Nineteen sets of data were therefore excluded from analysis.

Analysis of second RBT reading by observer 1

There were nine missing values, and 11 children with high SD scores. Cross-tabulation of the first and second reading by observer 1 showed that readings were missing on both occasions for three children, and missing only on the second occasion for six children. Six children had high SD scores on both measurements.

Analysis of RBT reading by observer 2

Data was missing on 38 children. This was due to the trial being run within a busy tertiary centre clinic, with observers not always able to complete this part of the examination.

Excluding RBT data with high variability readings, we were left with 83 measurements by observer 1 (reading 1), 82 measurements by observer 1 (reading 2), and 50 measurements by observer 2.

Analysis of GAT data

GAT readings were missing in 12 datasets. Most of these children had complex ocular pathology (corneal graft n=1, microphthalmos/sunken socket n=1, nystagmus n=1, microcornea n=1, congenital glaucoma and multiple surgery n=1, Sturge Weber syndrome n=1). One child was very anxious and difficult to examine. Two children were glaucoma suspects, and in three cases no comment was available explaining missing GAT.

Analysis of IOP readings by RBT and GAT

The mean RBT reading 1 (SD) by observer 1 was 21.1mmHg (8.19), RBT reading 2 by observer 1 was 21.9 mmHg (8.94), observer 2 RBT was 21.14 mmHg (8.41), and GAT was 18mmHg (6.45).

Reproducibility of RBT readings: intra- and inter-observer variability

Data were available for 74 children who had two readings by observer 1. The mean difference between the readings was 0.135 (SD 1.45). A t-test revealed no evidence of systematic bias between reading 1 and reading 2 ((73 df)=0.7987, p=0.427).

The distribution of the differences appeared symmetric. The Bland Altman plot showed no systematic relationship between the average measure and the difference, and limits of agreement were computed as (-2.71, 2.98) mmHg (Fig. 1A).

First RBT reading by observer 1 and RBT reading by observer 2 were available for 45 cases. The mean difference between readings was 0.11 mmHg (2.99). A t-test revealed no evidence of systematic bias between observers (t(44)=0.25, p=0.8).

Again, the data appeared symmetric. The Bland-Altman plot showed no systematic relationship, limits of agreement were (-5.75, 5.97) mmHg (Fig. 1B).

Agreement between GAT and RBT

We used data from first RBT reading by observer 1. These and GAT data were available for 74 children. The mean difference was -3.3 mmHg (5.3). A t-test showed evidence of systematic bias (t(73)=-5.41, p<0.001). The Bland Altman plot also showed evidence of a relationship between the magnitude of the difference between methods and the magnitude of the measurement, with smaller differences being seen with lower measurements. This would imply that limits of agreement cannot be simply produced.
Stratifying data at 21 mmHg allows production of LOA. These are -2.35+/-1.96*3.19 for readings less than 21mmHg, and -5.52+/-1.96*7.94 for readings greater than 21mmHg.

Based on these analyses, agreement between the two methods appears poor and not clinically acceptable.

As demonstrated by the graph (Fig 1C), RBT frequently gave higher readings than GAT. Differences of 10mmHg were not uncommon.

Pachymetry data

Pachymetry measurements were obtained in n=83 children, of whom 67 had IOP measurements taken by both RBT and GAT. As expected for the study population we found a high prevalence of increased pachymetry values (Fig 1D). Defining the “normal range” as 460-650um, two readings were below the normal range (452, 456 um), and 13 readings were above the normal range; of these, seven participants had both RBT and GAT measurements.

Pachymetry and RBT readings

Disagreement between GAT and RBT readings was greater with higher pachymetry readings, p=0.003.

Patient preference

Eleven children preferred GAT, 70 preferred RBT, and 21 gave no preference.

Discussion

The main finding of the present study is that the agreement of RBT and GAT appears poor in children with glaucoma. Since previous studies have largely concluded that there is good agreement between RBT and applanation tonometry, this observation was a surprise.
We believe that this discrepancy may in part be due to the fact that many studies have considered correlation rather than agreement. It is quite possible for methods to correlate well, but to disagree by amounts that are of real clinical relevance. Our data provide strong evidence of a linear association between measures made by GAT and RBT - but linear association is not the same as agreement, which is why Bland and Altman advocated the Limits of Agreement method. [18]

The present study is the second to compare RBT and GAT in children with glaucoma. The only other study into RBT in this population also included children with suspected glaucoma, excluded readings from children who were nervous or squeezing during the RBT measurement, and repeated RBT readings until a measurement with minimal variability was obtained, or three readings had been taken. [4] Whilst this guaranteed the vast majority of readings had either minimal or low variability, this approach means that the operator manually reduced device errors – an approach often not possible in a busy clinic setting. The results of this study are comparable to those presented in our work: the authors report that RBT were higher than GAT readings in 75%, and within +/- 3mmHg of GAT in 63%. [4] Our view is that disagreements of greater than 3 mm Hg are of concern if they can impact on the management of the child.

The only other study exploring the use of RBT in children with glaucoma compared it with Perkins applanation tonometry (PAT). [8] The authors performed RBT and PAT in random order, which means that RBT measurements were performed after administration of topical anaesthesia. According to the manufacturer's manual topical anaesthesia may reduce the RBT reading. [19] [20] Again, the authors repeated RBT measurements when the variability indicator was high or IOP > 19mmHg with medium standard variation, excluding readings with erroneous device performance. The authors found greater disagreement with higher IOP measurements, yet did not provide limits of agreement stratified by IOP, or present regression-based limits of agreement. Interestingly, the graphs show that RBT measurements were consistently higher – up to 17mmHg, which is consistent with our findings. Both PAT and RBT readings were higher in cases of increased corneal thickness, another finding that agrees with our report.
Other paediatric studies of RBT are limited to healthy children, and none used GAT as comparator. [5] [6] [21]

Difference in study population is likely to be a contributory factor explaining why agreement between RBT and GAT was significantly poorer in our study than in others. Comparisons with GAT have been conducted in adults with glaucoma, but excluding significant other pathologies such as astigmatism, microphthalmos, buphthalmos, dry eyes, nystagmus. [13] [11] [15] [22] Results in studies with mixed populations (adults with glaucoma/ocular hypertension and healthy adults) also reported good GAT/RBT agreement. [12] [16] [23]
However, all studies except two used topical anaesthesia before RBT. Interestingly, the two studies who did not use topical anaesthesia found significant differences between GAT and RBT, with RBT overestimating IOP by 1 to 15mmHg. [15] [16]

Three studies performed on healthy adults without topical anaesthesia reported good agreement between RBT and GAT, [9] [24] [10] whilst three others reported significant differences in some cases. [14] [25] [17] The main limitation of these studies might be the inclusion of "normal" eyes with normal IOP only. Findings from this population cannot be generalised to subjects with raised IOP.

Sequence of tests may also explain differences in findings. Applanation tonometry, especially repeated measurements, can progressively lower IOP by a mechanism know as “aqueous massage”. [26] [16] [12] Our study design avoided this effect by obtaining RBT before GAT measurements. Studies that obtained GAT before RBT or conducted tests in random order [8] [11] [13] [22] [23] may have induced IOP lowering, thereby erroneously obtaining lower RBT readings.

Similar to other groups [8] [13] [16] [22] we found increased disagreement between RBT and GAT with higher CCT values. However, we found that even in children with pachymetry readings of 581um, disagreements could be greater than 10 mmHg.

Our study confirms reports [5] [6] [21] that the hand-held RBT has high acceptability in children. Since we started this work in 2008, it has become widely available and popular in many community optometric practices and hospital eye units in the UK (Table 1). [3] Seventy percent of the children enrolled in this study had a clear preference for the new device which does not require instillation of anaesthetic eye drops and no prolonged sitting in an uncomfortable position.

On the basis of previously published reports and our own work, we would recommend the use of the RBT in children, but advise practitioners to be cautious in the interpretation of findings, particularly in children with thicker corneas. It is reassuring that measurement discrepancies tend to reflect a systematic over-reading by the RBT: “normal” values obtained by this method are likely correct, and the IOP is unlikely to be high. This in turn can re-assure examiners and spare children the need for other IOP measurement methods and even examinations under anaesthesia. High RBT readings, on the other side, should not automatically trigger a trip to the operating theatre, but should prompt the examiner to seek confirmation of IOP level by another established technique.

Legends

Table 1. Survey of current paediatric tonometry practice in the UK. Using an electronic mailing list, we contacted 144 of paediatric ophthalmologists in the UK. The survey ran for 10 days, from February 2 to 16, 2012, and collected 36 replies.

Table 2. Demographic details of study participants.

Table 3: Agreement (inter observer, Intra observer and with GAT) for RBT

Fig. 1. Tonometry and pachymetry results. A: Intraobserver agreement of RBT measurements. B: Interobserver agreement of RBT measurements. C: Agreement between RBT and GAT measurements. D: Distribution of corneal thickness as determined by pachymetry.

Tables and Figures

In which setting do you work and measure IOP in children?	Teaching hospital District general hospital Community clinic	55.6% 47.2% 5.6%
Do you run a specialist paediatric glaucoma service?	Yes No	19.4% 80.6%
In how many children do you measure the IOP per month?	Less than 5 Between 5 and 20 More than 20	25% 44.4% 30.6%
What is your preferred method to measure IOP in children?	**RBT** Goldmann/Perkins applanation Tonopen Air puff	**77.8%** 44.4% 5.6% 5.6%
If you are using a RBT, how easy do you find it to use?	**Very easy** Moderately easy Not at all easy Not applicable	**60%** 25.7% 2.9% 11.4%
In your experience, are RBT readings accurate as compared to Goldmann applanation tonometry readings?	As accurate as Goldmann **RBT tend to be higher than GAT readings** RBT tend to be lower than GAT readings	22.7% **72.7%** 4.5%

Table 1. Survey of current paediatric tonometry practice in the UK. Using an electronic mailing list, we contacted 144 of paediatric ophthalmologists in the UK. The survey ran for 10 days, from February 2 to 16, 2012, and collected 36 replies.

Sex	Male:female (n	53 :49
Age (Years)	Mean (SD)	11.85 (3.17)
Laterality	Right:left	85:17
Ethnicity	Caucasian	57
	Mixed	19
	Asian or Asian British	1
	Carribbean/African/Any other Black background	8
	Other ethnic groups (incl. Chinese)	11
	Not stated or not recorded	6
Pachymetry	Median (IQR)*	581 (537, 622)

* IQR : interquartile range, 19 children had no pachymetry readings

Table 2: Demographic factors of the children under investigation

	Mean difference	SD difference	LOA
Intra observer (n = 74)	0.13	1.46	(-2.71, 2.98)
Inter-observer (n = 45)	0.11	2.99	(-5.75, 5.97)
ICare-GAT (n = 74)	-3.34	5.31	< 21 mmHg : (-8.60, 3.90)
			>=21 mmHg : (-21.08, 10.04)

Table 3: Agreement (inter observer, Intra observer and with GAT) for RBT

References

1. Kontiola AI, Goldblum D, Mittag T, et al. The induction/impact tonometer: a new instrument to measure intraocular pressure in the rat. *Experimental eye research* 2001;**73**(6):781-5

2. Kontiola A, Puska P. Measuring intraocular pressure with the Pulsair 3000 and Rebound tonometers in elderly patients without an anesthetic. *Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie* 2004;**242**(1):3-7

3. Chan WH, Lloyd IC, Ashworth JL, et al. Measurement of intraocular pressure in children in the UK. *Eye (London, England)* 2012;**25**(1):119-20

4. Flemmons MS, Hsiao YC, Dzau J, et al. Icare rebound tonometry in children with known and suspected glaucoma. *J Aapos* 2011;**15**(2):153-7

5. Kageyama M, Hirooka K, Baba T, et al. Comparison of ICare rebound tonometer with noncontact tonometer in healthy children. *Journal of glaucoma* 2011;**20**(1):63-6

6. Sahin A, Basmak H, Niyaz L, et al. Reproducibility and tolerability of the ICare rebound tonometer in school children. *Journal of glaucoma* 2007;**16**(2):185-8

7. Sahin A, Basmak H, Yildirim N. The influence of central corneal thickness and corneal curvature on intraocular pressure measured by tono-pen and rebound tonometer in children. *Journal of glaucoma* 2008;**17**(1):57-61

8. Martinez-de-la-Casa JM, Garcia-Feijoo J, Saenz-Frances F, et al. Comparison of rebound tonometer and Goldmann handheld applanation tonometer in congenital glaucoma. *Journal of glaucoma* 2009;**18**(1):49-52

9. Fernandes P, Diaz-Rey JA, Queiros A, et al. Comparison of the ICare rebound tonometer with the Goldmann tonometer in a normal population. *Ophthalmic Physiol Opt* 2005;**25**(5):436-40

10. Davies LN, Bartlett H, Mallen EA, et al. Clinical evaluation of rebound tonometer. *Acta ophthalmologica Scandinavica* 2006;**84**(2):206-9

11. Brusini P, Salvetat ML, Zeppieri M, et al. Comparison of ICare tonometer with Goldmann applanation tonometer in glaucoma patients. *Journal of glaucoma* 2006;**15**(3):213-7

12. Nakamura M, Darhad U, Tatsumi Y, et al. Agreement of rebound tonometer in measuring intraocular pressure with three types of applanation tonometers. *American journal of ophthalmology* 2006;**142**(2):332-4

13. Sahin A, Niyaz L, Yildirim N. Comparison of the rebound tonometer with the Goldmann applanation tonometer in glaucoma patients. *Clinical & experimental ophthalmology* 2007;**35**(4):335-9

14. Pakrou N, Gray T, Mills R, et al. Clinical comparison of the Icare tonometer and Goldmann applanation tonometry. *Journal of glaucoma* 2008;**17**(1):43-7

15. Rehnman JB, Martin L. Comparison of rebound and applanation tonometry in the management of patients treated for glaucoma or ocular hypertension. *Ophthalmic Physiol Opt* 2008;**28**(4):382-6

16. Munkwitz S, Elkarmouty A, Hoffmann EM, et al. Comparison of the iCare rebound tonometer and the Goldmann applanation tonometer over a wide IOP range. *Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie* 2008;**246**(6):875-9

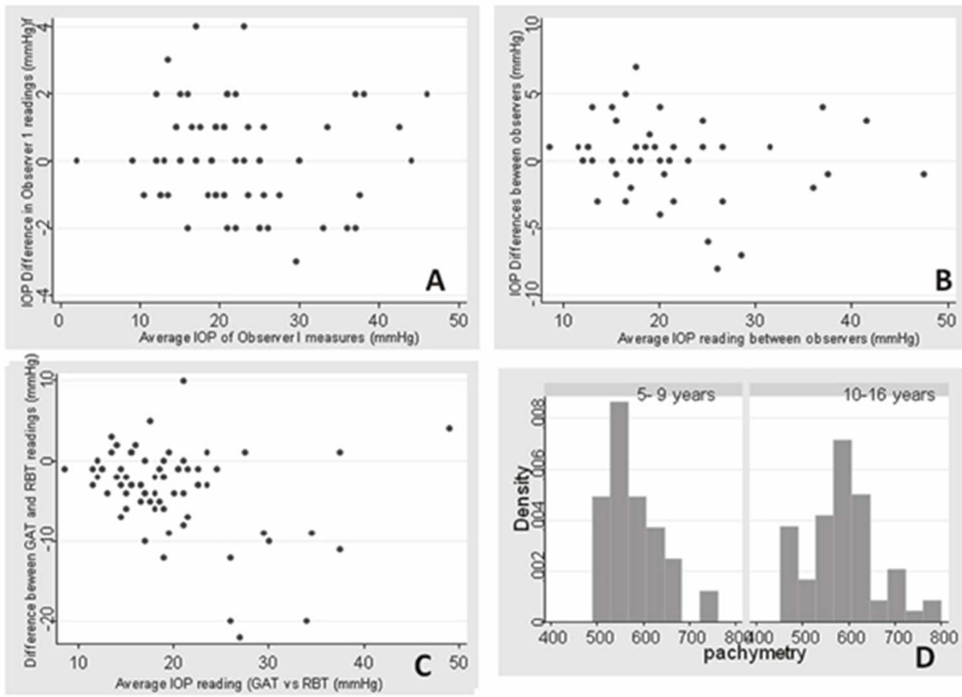
17. Chui WS, Lam A, Chen D, et al. The influence of corneal properties on rebound tonometry. *Ophthalmology* 2008;**115**(1):80-4

18. Bland JM, Altman DG. Applying the right statistics: analyses of measurement studies. *Ultrasound Obstet Gynecol* 2003;**22**(1):85-93

19. Tiolat. *iCare Tonometer: User's and Maintenance Manual*. Helsinki.

20. Baudouin C, Gastaud P. Influence of topical anesthesia on tonometric values of intraocular pressure. *Ophthalmologica. Journal international d'ophtalmologie. International journal of ophthalmology* 1994;**208**(6):309-13

21. Lundvall A, Svedberg H, Chen E. Application of the ICare rebound tonometer in healthy infants. *Journal of glaucoma* 2011;**20**(1):7-9
22. Martinez-de-la-Casa JM, Garcia-Feijoo J, Vico E, et al. Effect of corneal thickness on dynamic contour, rebound, and goldmann tonometry. *Ophthalmology* 2006;**113**(12):2156-62
23. van der Jagt LH, Jansonius NM. Three portable tonometers, the TGDc-01, the ICARE and the Tonopen XL, compared with each other and with Goldmann applanation tonometry*. *Ophthalmic Physiol Opt* 2005;**25**(5):429-35
24. Jorge J, Fernandes P, Queiros A, et al. Comparison of the IOPen and iCare rebound tonometers with the Goldmann tonometer in a normal population. *Ophthalmic Physiol Opt*;**30**(1):108-12
25. Poostchi A, Mitchell R, Nicholas S, et al. The iCare rebound tonometer: comparisons with Goldmann tonometry, and influence of central corneal thickness. *Clinical & experimental ophthalmology* 2009;**37**(7):687-91
26. Krakau CE, Wilke K. On repeated tonometry. *Acta Ophthalmol (Copenh)* 1971;**49**(4):611-4



50x36mm (300 x 300 DPI)

Comparison of handheld rebound tonometry with Goldmann applanation tonometry in children with glaucoma: a cohort study

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-001788.R1
Article Type:	Research
Date Submitted by the Author:	11-Nov-2012

Complete List of Authors:	Dahlmann-Noor, Annegret; NIHR Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, Paediatric Ophthalmology Bunce, Catey; Moorfields Eye Hospital NHS Foundation Trust, Research and Development Puertas, Renata; Moorfields Eye Hospital, Glaucoma Tabasa-Lim, Shenille; Moorfields Eye Hospital, Paediatric Ophthalmology El-Karmouty, Ahmed; Moorfields Eye Hospital, Glaucoma Kadhim, Mustafa; Moorfields Eye Hospital, Glaucoma Wride, Nicholas; Moorfields Eye Hospital, Glaucoma Lewis, Amanda; Moorfields Eye Hospital, Glaucoma Grosvenor, Dawn; Moorfields Eye Hospital, Glaucoma Rai, Poornima; Moorfields Eye Hospital, Glaucoma Papadopoulos, Maria; Moorfields Eye Hospital, Glaucoma brookes, john; Moorfields Eye Hospital, Glaucoma Khaw, Peng; NIHR Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology, Glaucoma

Primary Subject Heading:	Ophthalmology
Secondary Subject Heading:	Paediatrics, Evidence based practice
Keywords:	Paediatric ophthalmology < OPHTHALMOLOGY, Community child health < PAEDIATRICS, Glaucoma < OPHTHALMOLOGY

Handheld rebound tonometry in children with glaucoma

Authors

Annegret Hella Dahlmann-Noor

Renata Puertas

Shenille Tabasa-Lim

Ahmed El-Karmouty

Mustafa Kadhim

Nicholas Wride

Amanda Lewis

Dawn Grosvenor

Poornima Rai

Maria Papadopoulos

John Brookes

Catey Bunce

Peng Tee Khaw

Corresponding author: Annegret Dahlmann-Noor, Moorfields Eye Hospital, 162 City Road, London EC1V 2PD; annegret.dahlmann-noor@moorfields.nhs.uk

Funding statement:

This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Acknowledgements:

The authors are grateful for the support from Fight for Sight and the Helen Hamlyn Trust. The research took place at the National Institute for Health Research (NIHR) Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Competing Interests Statement:

None of the authors have competing interests to declare.

Contributorship Statement:

AHDN and CB designed the trial and prepared the manuscript. AHDN, RP, STL, AE, PR, MK, NW, AL, DG, MP, JB and PTK facilitated recruitment, obtained informed consent, acquired data and completed case report forms. AHDN entered data onto the electronic database. CB analysed the data. All authors reviewed the manuscript.

Abstract

Objective: To test agreement of two methods to measure intraocular pressure (IOP): rebound tonometry (RBT) and gold standard Goldmann applanation (GAT) tonometry in children with glaucoma

Design: observational prospective cohort study

Setting: tertiary paediatric glaucoma clinic at a single centre

Participants: 102 individuals attending a paediatric glaucoma clinic, mean (SD) age 11.85 (3.17), of whom 53 were male

Interventions: n/a

Primary and secondary outcome measures: intraocular pressure, central corneal thickness, child preference for measurement method

Results: Limits of agreement for intra- and interobserver were respectively (-2.71, 2.98) mmHg and (-5.75, 5.97) mmHg. RBT frequently gave higher readings than GAT and the magnitude of disagreement depended on the level of IOP being assessed. Differences of 10mmHg were not uncommon. RBT was the preferred method for 70% of children.

Conclusions: There is poor agreement between RBT and GAT in children with glaucoma. RBT frequently and significantly overestimates IOP. However, “normal” RBT readings are likely to be accurate and may spare children an examination under anaesthesia (EUA). High RBT readings should prompt the practitioner to use another standard method of IOP measurement if possible, or consider the RBT measurement in the context of clinical findings before referring the child to a specialist clinic or considering EUA.

Trial registration: n/a

Article Summary

Article focus

- Measuring intraocular pressure (IOP) is critical in diagnosis and monitoring of glaucoma, and is often difficult in children.
- Rebound tonometry (RBT) may be more child-friendly than other tonometry methods.
- Agreement between RBT and reference standard Goldmann applanation tonometry (GAT) in children and young people attending glaucoma clinics has not been sufficiently evaluated.

Key messages

- Agreement between RBT and GAT is poor in children and young people with glaucoma; RBT frequently and significantly overestimates IOP.
- "Normal" RBT readings are likely to be accurate and may spare children an examination under anaesthesia.
- High RBT readings should prompt the practitioner to use another standard method of IOP measurement, if possible.

Strengths and limitations of this study

- This study focuses on a cohort of children and young people attending a paediatric glaucoma clinic, a population in whom accurate tonometry is required for correct diagnosis and management.
- Statistical analysis is based on the limits of agreement method rather than correlation.

Background/Introduction

Glaucoma is a potentially blinding condition. Raised intraocular pressure (IOP) is an important risk factor for the development and progression of optic nerve damage in glaucoma, and is the target of both medical and surgical treatment. There are no published figures on how many children have an IOP test per year, but both community optometrists and hospital clinics regularly perform IOP measurement as part of a comprehensive eye examination. For all practitioners IOP measurements in young children are challenging . The current reference standard for tonometry is the Goldmann applanation tonometer (GAT, ISO 8612) mounted on a slit lamp. The Perkins tonometer (PAT), as the hand-held version of GAT, is a suitable reference standard for IOP measurements for patients in the supine position, and hence for children during an examination under anaesthesia (EUA). Another commonly used handheld tonometer is the Reichert Tono-Pen[R], but for comparison of diagnostic test accuracy, we opted for the reference standard devices.

GAT requires the instillation of topical anaesthetics and a high degree of co-operation from the child. Frequently children are unable to suppress the natural reflex of moving backward or closing their eyes. This leads to repeated attempts being made at obtaining a reading, prolonged examination times and distress to children and families.

In 2005 a new device to measure intraocular pressure became available, the iCare® rebound tonometer (RBT). Its main advantage over other instruments is that no topical anaesthesia is required. In addition, it is a hand-held device, which children may perceive as less intimidating and allows examiners to move “with the child” when required.

The RBT acquires six readings in quick succession by propelling a fine sensor tip less than 2mm in diameter against the central cornea from the instrument base held at a distance of 4-8mm from the surface of the eye. [1] [2] After contact, the probe bounces back; the higher the IOP the faster the rebound. Measurements are taken within 0.1 seconds. The force impacting on the cornea is minimal and does usually not even trigger the highly sensitive blink reflex. The instrument display then shows the average of the six readings and whether the standard deviation (SD) is low, medium or high.

Since its introduction, RBT has become very popular and is now being used in many children’s eye services and by many community-based optometrists. Two surveys of tonometry practice in children (Table 1 and reference [3]) indicate that for most paediatric ophthalmologists in the UK, RBT has become the preferred method to measure IOP in children. Whilst the device is considered easy to use, many users report that RBT measurements tend to be higher than GAT measurements (Table 1).

Data comparing RBT performance with GAT in children with glaucoma are scarce and limited to one study only. [4] Studies which have compared RBT with non-contact tonometry and tonopen in healthy children indicate good intra- and interobserver reliability and good agreement. [5] [6] [7] In children with glaucoma good agreement has been reported with both PAT [8] and GAT, [4] although RBT measurements are consistently higher than PAT or GAT readings.

In adults with healthy eyes, glaucoma or ocular hypertension, papers have reported good agreement between the RBT and GAT, albeit with systematically higher measurements on RBT. [9] [10] [11] [12] [13] [14] [15]

Accuracy of RBT may be affected by levels of IOP, [8] [16] central corneal thickness (CCT) [7] [13] [14] and other corneal properties such as hysteresis and resistance. [17] The latter parameters are not routinely assessed in clinics and impossible to assess in young children.

We carried out the present study to evaluate the accuracy and reliability of RBT in children with glaucoma as compared to GAT. Secondary objectives were to investigate the influence of CCT on IOP measurements by RBT, and to determine children's preference for RBT or GAT.

Methods

Patients

We recruited consecutive subjects attending our tertiary paediatric glaucoma service at Moorfields Eye Hospital. The study was approved by the local research ethics committee. All parents/guardians gave written informed consent and children were invited to give assent.

The sample size was determined by recommendations for Bland-Altman analysis. [18]

Protocol

Three observers took the measurements required for this study. Observer 1 measured the IOP in one eye by RBT. In children with glaucoma in both eyes, readings were taken from the right eye. In children with glaucoma only in the left eye, readings were taken from the left eye. Observer 1 recorded two consecutive averageRBT readings from six measurements and the SD indicated by the device.

One repeat average RBT measurement was obtained by a second observer and recorded separately. Following instillation of a drop of proxymethacaine, observer 2 recorded CCT on ultrasound pachymetry.

The third observer recorded IOP on GAT and asked the child which instrument they preferred.

All data were recorded on a Case Report Form which also recorded the child's diagnosis and ethnic background. At the end of the study, data were entered into a computerised database.

Data analysis

Summary statistics were produced for demographic factors and for IOP readings made by each observer and method (Tables 2 and 3). Repeat readings made by observer 1 using RBT were used to estimate intraobserver agreement using the Bland-Altmann limits of agreement method. [18] The same method was used to determine interobserver agreement, analysing RBT reading 1 from observer 1 and the RBT reading obtained by observer 2. Agreement between RBT and GAT was analysed based on reading 1 from observer 1 and GAT recorded by observer 3. A histogram for CCT was plotted in two age bands (under and over 10 years of age). Child preference for either device was summarised by descriptive statistical methods.

Results

Demographics

We carried out the study between 1/1/2009 and 31/3/2010. We enrolled n=102 children with a confirmed diagnosis of glaucoma. Age ranged from 4.9 to 19 years (mean 11.85, SD 3.17 years). 53

boys and 49 girls took part (Table 2). In 85 children the right eye was the study eye, and in n=17 children the left eye.

Analysis of first RBT reading by observer 1

One hundred and two datasets were analysed. Data were missing for 3 subjects. The RBT automatically indicates a higher than normal standard deviation of the acquired measurements by displaying a flashing "P" or a line in the "Up" position following the measurement. These are indicators of poor reliability, and the manufacturer recommends repeating the measurement. We excluded 16 participants in whom measurements displayed these poor reliability parameters. Nineteen sets of data were therefore excluded from analysis.

Analysis of second RBT reading by observer 1

There were nine missing values, and 11 children with poor reliability scores. Cross-tabulation of the first and second reading by observer 1 showed that readings were missing on both occasions for three children, and missing only on the second occasion for six children. Six children had poor reliability indicators on both measurements.

Analysis of RBT reading by observer 2

Data was missing on 38 children. This was due to the trial being run within a busy tertiary centre clinic, with observers not always able to complete this part of the examination.

Excluding RBT data with poor reliability indicators, we were left with 83 measurements by observer 1 (reading 1), 82 measurements by observer 1 (reading 2), and 50 measurements by observer 2.

Analysis of GAT data

GAT readings were missing in 12 datasets. Most of these children had complex ocular pathology (corneal graft n=1, microphthalmos/sunken socket n=1, nystagmus n=1, microcornea n=1, congenital glaucoma and multiple surgery n=1, Sturge Weber syndrome n=1). One child was very anxious and difficult to examine. Two children were glaucoma suspects, and in three cases no comment was available explaining missing GAT.

Analysis of IOP readings by RBT and GAT

The mean RBT reading 1 (SD) by observer 1 was 21.1mmHg (8.19), RBT reading 2 by observer 1 was 21.9 mmHg (8.94), observer 2 RBT was 21.14 mmHg (8.41), and GAT was 18mmHg (6.45).

Reproducibility of RBT readings: intra- and inter-observer variability

Data were available for 74 children who had two readings by observer 1. The mean difference between the readings was 0.135 (SD 1.45). A t-test revealed no evidence of systematic bias between reading 1 and reading 2 ((73 df)=0.7987, p=0.427).

The distribution of the differences appeared symmetric. The Bland Altman plot showed no systematic relationship between the average measure and the difference, and limits of agreement were computed as (-2.71, 2.98) mmHg (Fig. 1A).

First RBT reading by observer 1 and RBT reading by observer 2 were available for 45 cases. The mean difference between readings was 0.11 mmHg (2.99). A t-test revealed no evidence of systematic bias between observers (t(44)=0.25, p=0.8).

Again, the data appeared symmetric. The Bland-Altman plot showed no systematic relationship, limits of agreement were (-5.75, 5.97) mmHg (Fig. 1B).

Agreement between GAT and RBT

We used data from first RBT reading by observer 1. These and GAT data were available for 74 children. The mean difference was -3.3 mmHg (5.3). A t-test showed evidence of systematic bias ($t(73)=-5.41$, $p<0.001$). The Bland Altman plot also showed evidence of a relationship between the magnitude of the difference between methods and the magnitude of the measurement, with smaller differences being seen with lower measurements. This would imply that limits of agreement cannot be simply produced. Stratifying data at 21 mmHg removed evidence of bias and limits of agreement were then computed as (-8.6, 3.9) mmHg for for readings less than 21mmHg, and (-21.08, 10.04) mmHg for readings greater than 21mmHg.

Based on these analyses, agreement between the two methods appears poor and not clinically acceptable.

As demonstrated by the graph (Fig 1C), RBT frequently gave higher readings than GAT. Differences of 10mmHg were not uncommon.

Pachymetry data

Pachymetry measurements were obtained in n=83 children, of whom 67 had IOP measurements taken by both RBT and GAT (Fig 1D). Defining the "normal range" as 460-650um, two readings were below the normal range (452, 456 um), and 13 readings were above the normal range; of these, seven participants had both RBT and GAT measurements. Of the 13 children with CCT greater than 650um, one had corneal clouding/oedema and enlarged cornea, and in two children "multiple previous glaucoma interventions" were recorded. None of these children had nystagmus, aphakic glaucoma, aniridia or anterior segment dysgenesis syndromes, or other confounding corneal abnormalities.

Pachymetry and RBT readings

Disagreement between GAT and RBT readings was greater with higher pachymetry readings, p=0.003.

Patient preference

Eleven children preferred GAT, 70 preferred RBT, and 21 gave no preference.

Discussion

The main finding of the present study is that the agreement of RBT and GAT appears poor in children with glaucoma. Since previous studies have largely concluded that there is good agreement between RBT and applanation tonometry, this observation was a surprise.
We believe that this discrepancy may in part be due to the fact that many studies have considered correlation rather than agreement. It is quite possible for methods to correlate well, but to disagree by amounts that are of real clinical relevance. Our data provide strong evidence of a linear association between measures made by GAT and RBT - but linear association is not the same as agreement, which is why Bland and Altman advocated the Limits of Agreement method. [18]

The present study is the second to compare RBT and GAT in children with glaucoma. The only other study into RBT in this population also included children with suspected glaucoma, excluded readings from children who were nervous or squeezing during the RBT measurement, and repeated RBT readings until a measurement with minimal variability was obtained, or three readings had been taken. [4] Whilst this guaranteed the vast majority of readings had either minimal or low variability, this approach means that the operator manually reduced device errors. The results of this study are comparable to those presented in our work: the authors report that RBT were higher than GAT readings in 75%, and within +/- 3mmHg of GAT in 63%. [4] Our view is that disagreements of greater than 3 mm Hg are of concern if they can impact on the management of the child.

The only other study exploring the use of RBT in children with glaucoma compared it with Perkins applanation tonometry (PAT). [8] The authors performed RBT and PAT in random order, which means that RBT measurements were performed after administration of topical anaesthesia. According to the manufacturer's manual topical anaesthesia may reduce the RBT reading. [19] [20] Again, the authors repeated RBT measurements when the variability indicator was high or IOP > 19mmHg with medium standard variation, excluding readings with erroneous device performance. The authors found greater disagreement with higher IOP measurements, yet did not provide limits of agreement stratified by IOP, or present regression-based limits of agreement. Interestingly, the graphs show that RBT measurements were consistently higher – up to 17mmHg, which is consistent with our findings. Both PAT and RBT readings were higher in cases of increased corneal thickness, another finding that agrees with our report.
Other paediatric studies of RBT are limited to healthy children, and none used GAT as comparator. [5] [6] [21]

Difference in study population is likely to be a contributory factor explaining why agreement between RBT and GAT was significantly poorer in our study than in others. Comparisons with GAT have been conducted in adults with glaucoma, but excluding significant other pathologies such as astigmatism, microphthalmos, buphthalmos, dry eyes, nystagmus. [13] [11] [15] [22] Results in studies with mixed populations (adults with glaucoma/ocular hypertension and healthy adults) also reported good GAT/RBT agreement. [12] [16] [23]
However, all studies except two used topical anaesthesia before RBT. Interestingly, the two studies who did not use topical anaesthesia found significant differences between GAT and RBT, with RBT overestimating IOP by 1 to 15mmHg. [15] [16]

Three studies performed on healthy adults without topical anaesthesia reported good agreement between RBT and GAT, [9] [24] [10] whilst three others reported significant differences in some cases. [14] [25] [17] The main limitation of these studies might be the inclusion of "normal" eyes with normal IOP only. Findings from this population cannot be generalised to subjects with raised IOP.

Sequence of tests may also explain differences in findings. Applanation tonometry, especially repeated measurements, can progressively lower IOP by a mechanism know as "aqueous massage". [26] [16] [12] Our study design avoided this effect by obtaining RBT before GAT measurements. Studies that obtained GAT before RBT or conducted tests in random order [8] [11] [13] [22] [23] may have induced IOP lowering, thereby erroneously obtaining lower RBT readings.

Similar to other groups [8] [13] [16] [22] we found increased disagreement (ie larger discrepancies In IOP measures between RBT and GAT with higher CCT values. However, we found that even in children with pachymetry readings of 581um, disagreements could be greater than 10 mmHg.

Our study confirms reports [5] [6] [21] that the hand-held RBT has high acceptability in children. Since we started this work in 2008, it has become widely available and popular in many community optometric practices and hospital eye units in the UK (Table 1). [3] Seventy percent of the children enrolled in this study had a clear preference for the new device which does not require instillation of anaesthetic eye drops and no prolonged sitting in an uncomfortable position.

On the basis of previously published reports and our own work, we would recommend the use of the RBT in children, but advise practitioners to be cautious in the interpretation of findings, particularly in children with thicker corneas. It is reassuring that measurement discrepancies tend to reflect a systematic over-reading by the RBT: "normal" values obtained by this method are likely correct, and the IOP is unlikely to be high. This in turn can re-assure examiners and spare children the need for other IOP measurement methods and even examinations under anaesthesia. High RBT readings, on the other side, should not automatically trigger a trip to the operating theatre, but should prompt the examiner to seek confirmation of IOP level by another established technique.

Legends

Table 1. Survey of current paediatric tonometry practice in the UK. Using an electronic mailing list, we contacted 144 of paediatric ophthalmologists in the UK. The survey ran for 10 days, from February 2 to 16, 2012, and collected 36 replies.

Table 2. Demographic details of study participants.

Table 3: Agreement (inter observer, Intra observer and with GAT) for RBT

Fig. 1. Tonometry and pachymetry results. A: Intraobserver agreement of RBT measurements. B: Interobserver agreement of RBT measurements. C: Agreement between RBT and GAT measurements. D: Distribution of corneal thickness as determined by pachymetry. In healthy children of age5-9 years, mean (SD) CCT has been reported as 566 (48) um, and in children over the age of 10 years, 554 (35) um. [27]

Tables and Figures

In which setting do you work and measure IOP in children?	Teaching hospital District general hospital Community clinic	55.6% 47.2% 5.6%
Do you run a specialist paediatric glaucoma service?	Yes No	19.4% 80.6%
In how many children do you measure the IOP per month?	Less than 5 Between 5 and 20 More than 20	25% 44.4% 30.6%
What is your preferred method to measure IOP in children?	**RBT** Goldmann/Perkins applanation Tonopen Air puff	**77.8%** 44.4% 5.6% 5.6%
If you are using a RBT, how easy do you find it to use?	**Very easy** Moderately easy Not at all easy Not applicable	**60%** 25.7% 2.9% 11.4%
In your experience, are RBT readings accurate as compared to Goldmann applanation tonometry readings?	As accurate as Goldmann **RBT tend to be higher than GAT readings** RBT tend to be lower than GAT readings	22.7% **72.7%** 4.5%

Table 1. Survey of current paediatric tonometry practice in the UK. Using an electronic mailing list, we contacted 144 of paediatric ophthalmologists in the UK. The survey ran for 10 days, from February 2 to 16, 2012, and collected 36 replies.

Sex	Male:female (n	53 :49
Age (Years)	Mean (SD)	11.85 (3.17)
Laterality	Right:left	85:17
Ethnicity	Caucasian	57
	Mixed	19
	Asian or Asian British	1
	Carribbean/African/Any other Black background	8
	Other ethnic groups (incl. Chinese)	11
	Not stated or not recorded	6
Pachymetry	Median (IQR)*	581 (537, 622)

* IQR : interquartile range, 19 children had no pachymetry readings

Table 2: Demographic factors of the children under investigation

	Mean difference	SD difference	LOA
Intra observer (n = 74)	0.13	1.46	(-2.71, 2.98)
Inter-observer (n = 45)	0.11	2.99	(-5.75, 5.97)
ICare-GAT (n = 74)	-3.34	5.31	< 21 mmHg : (-8.60, 3.90)
			>=21 mmHg : (-21.08, 10.04)

Table 3: Agreement (inter observer, Intra observer and with GAT) for RBT

References

1. Kontiola AI, Goldblum D, Mittag T, et al. The induction/impact tonometer: a new instrument to measure intraocular pressure in the rat. *Experimental eye research* 2001;**73**(6):781-5

2. Kontiola A, Puska P. Measuring intraocular pressure with the Pulsair 3000 and Rebound tonometers in elderly patients without an anesthetic. *Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie* 2004;**242**(1):3-7

3. Chan WH, Lloyd IC, Ashworth JL, et al. Measurement of intraocular pressure in children in the UK. *Eye (London, England)* 2012;**25**(1):119-20

4. Flemmons MS, Hsiao YC, Dzau J, et al. Icare rebound tonometry in children with known and suspected glaucoma. *J Aapos* 2011;**15**(2):153-7

5. Kageyama M, Hirooka K, Baba T, et al. Comparison of ICare rebound tonometer with noncontact tonometer in healthy children. *Journal of glaucoma* 2011;**20**(1):63-6

6. Sahin A, Basmak H, Niyaz L, et al. Reproducibility and tolerability of the ICare rebound tonometer in school children. *Journal of glaucoma* 2007;**16**(2):185-8

7. Sahin A, Basmak H, Yildirim N. The influence of central corneal thickness and corneal curvature on intraocular pressure measured by tono-pen and rebound tonometer in children. *Journal of glaucoma* 2008;**17**(1):57-61

8. Martinez-de-la-Casa JM, Garcia-Feijoo J, Saenz-Frances F, et al. Comparison of rebound tonometer and Goldmann handheld applanation tonometer in congenital glaucoma. *Journal of glaucoma* 2009;**18**(1):49-52

9. Fernandes P, Diaz-Rey JA, Queiros A, et al. Comparison of the ICare rebound tonometer with the Goldmann tonometer in a normal population. *Ophthalmic Physiol Opt* 2005;**25**(5):436-40

10. Davies LN, Bartlett H, Mallen EA, et al. Clinical evaluation of rebound tonometer. *Acta ophthalmologica Scandinavica* 2006;**84**(2):206-9

11. Brusini P, Salvetat ML, Zeppieri M, et al. Comparison of ICare tonometer with Goldmann applanation tonometer in glaucoma patients. *Journal of glaucoma* 2006;**15**(3):213-7

12. Nakamura M, Darhad U, Tatsumi Y, et al. Agreement of rebound tonometer in measuring intraocular pressure with three types of applanation tonometers. *American journal of ophthalmology* 2006;**142**(2):332-4

13. Sahin A, Niyaz L, Yildirim N. Comparison of the rebound tonometer with the Goldmann applanation tonometer in glaucoma patients. *Clinical & experimental ophthalmology* 2007;**35**(4):335-9

14. Pakrou N, Gray T, Mills R, et al. Clinical comparison of the Icare tonometer and Goldmann applanation tonometry. *Journal of glaucoma* 2008;**17**(1):43-7

15. Rehnman JB, Martin L. Comparison of rebound and applanation tonometry in the management of patients treated for glaucoma or ocular hypertension. *Ophthalmic Physiol Opt* 2008;**28**(4):382-6

16. Munkwitz S, Elkarmouty A, Hoffmann EM, et al. Comparison of the iCare rebound tonometer and the Goldmann applanation tonometer over a wide IOP range. *Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie* 2008;**246**(6):875-9

17. Chui WS, Lam A, Chen D, et al. The influence of corneal properties on rebound tonometry. *Ophthalmology* 2008;**115**(1):80-4

18. Altman DG. Method comparison studies. In: Practical Statistics for medical research. Chapman & Hall/CRC, 1991, Chapter 14, p 396-403

19. Tiolat. *iCare Tonometer: User's and Maintenance Manual*. Helsinki.

20. Baudouin C, Gastaud P. Influence of topical anesthesia on tonometric values of intraocular pressure. *Ophthalmologica. Journal international d'ophtalmologie. International journal of ophthalmology* 1994;**208**(6):309-13

21. Lundvall A, Svedberg H, Chen E. Application of the ICare rebound tonometer in healthy infants. *Journal of glaucoma* 2011;**20**(1):7-9
22. Martinez-de-la-Casa JM, Garcia-Feijoo J, Vico E, et al. Effect of corneal thickness on dynamic contour, rebound, and goldmann tonometry. *Ophthalmology* 2006;**113**(12):2156-62
23. van der Jagt LH, Jansonius NM. Three portable tonometers, the TGDc-01, the ICARE and the Tonopen XL, compared with each other and with Goldmann applanation tonometry*. *Ophthalmic Physiol Opt* 2005;**25**(5):429-35
24. Jorge J, Fernandes P, Queiros A, et al. Comparison of the IOPen and iCare rebound tonometers with the Goldmann tonometer in a normal population. *Ophthalmic Physiol Opt*;**30**(1):108-12
25. Poostchi A, Mitchell R, Nicholas S, et al. The iCare rebound tonometer: comparisons with Goldmann tonometry, and influence of central corneal thickness. *Clinical & experimental ophthalmology* 2009;**37**(7):687-91
26. Krakau CE, Wilke K. On repeated tonometry. *Acta Ophthalmol (Copenh)* 1971;**49**(4):611-4
27. Hussein MA, Paysse EA, Bell NP, et al. Corneal thickness in children. *American journal of ophthalmology* 2004;**138**(5):744-8

Handheld rebound tonometry in children with glaucoma

Authors
Annegret Hella Dahlmann-Noor
Renata Puertas
Shenille Tabasa-Lim
Ahmed El-Karmouty
Mustafa Kadhim
Nicholas Wride
Amanda Lewis
Dawn Grosvenor
Poornima Rai
Maria Papadopoulos
John Brookes
Catey Bunce
Peng Tee Khaw

Corresponding author: Annegret Dahlmann-Noor, Moorfields Eye Hospital, 162 City Road, London EC1V 2PD; annegret.dahlmann-noor@moorfields.nhs.uk

Funding statement:
This research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors.

Acknowledgements:
The authors are grateful for the support from Fight for Sight and the Helen Hamlyn Trust. The research took place at the National Institute for Health Research (NIHR) Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Competing Interests Statement:
None of the authors have competing interests to declare.

Contributorship Statement:
AHDN and CB designed the trial and prepared the manuscript. AHDN, RP, STL, AE, PR, MK, NW, AL, DG, MP, JB and PTK facilitated recruitment, obtained informed consent, acquired data and completed case report forms. AHDN entered data onto the electronic database. CB analysed the data. All authors reviewed the manuscript.

Abstract

Background: Glaucoma is a blinding condition. Raised intraocular pressure (IOP) damages the optic nerve, is the treatment target, and needs to be measured regularly. Goldmann tonometry (GAT) is difficult in children, as it requires topical anaesthesia which can cause ocular irritation. Rebound tonometry (RBT) does not require topical anaesthesia and may be more child-friendly than other tests. RBT is becoming the method of choice for community optometrists and paediatric ophthalmologists. However, studies comparing agreement between RBT and GAT in children are rare. Accuracy can be affected by level of IOP and central corneal thickness (CCT), both of which are often abnormal in children with glaucoma.

Methods: We evaluated the agreement between IOP measurements obtained by RBT and GAT in subjects attending a paediatric glaucoma clinic. children with glaucoma age 5-16 years. We analysed data with the Bland-Altman limits of agreement method (LOA). We recorded CCT and child preference for either method.

Results: 102 children, mean (SD) age 11.85 (3.17) years were enrolled, of whom 53 were male. Limits of agreement for intra- and interobserver were respectively (-2.71, 2.98) mmHg and (-5.75, 5.97) mmHg. RBT frequently gave higher readings than GAT and the magnitude of disagreement depended on the level of IOP being assessed. Differences of 10mmHg were not uncommon. RBT was the preferred method for 70% of children.

Conclusions: There is poor agreement between RBT and GAT in children with glaucoma. RBT frequently and significantly overestimates IOP. However, "normal" RBT readings are likely to be accurate and may spare children an EUA. High RBT readings should prompt the practitioner to use another standard method of IOP measurement if possible, or consider the RBT measurement in the context of clinical findings before referring the child to a specialist clinic or considering EUA.

Article Summary

Article focus

- Measuring intraocular pressure (IOP) is critical in diagnosis and monitoring of glaucoma, and is often difficult in children.
- Rebound tonometry (RBT) may be more child-friendly than other tonometry methods.
- Agreement between RBT and reference standard Goldmann applanation tonometry (GAT) in children and young people attending glaucoma clinics has not been sufficiently evaluated.

Key messages

- Agreement between RBT and GAT is poor in children and young people with glaucoma; RBT frequently and significantly overestimates IOP.
- "Normal" RBT readings are likely to be accurate and may spare children an examination under anaesthesia.
- High RBT readings should prompt the practitioner to use another standard method of IOP measurement, if possible.

Strengths and limitations of this study

- This study focuses on a cohort of children and young people attending a paediatric glaucoma clinic, a population in whom accurate tonometry is required for correct diagnosis and management.
- Statistical analysis is based on the limits of agreement method rather than correlation.

Formatted: Font: +Body (Calibri), 11 pt

Formatted: List Paragraph, Bulleted + Level: 1 + Aligned at: 0.27" + Indent at: 0.52"

Formatted: Font: +Body (Calibri), 11 pt

Formatted: List Paragraph, Bulleted + Level: 1 + Aligned at: 0.27" + Indent at: 0.52"

Formatted: Font: +Body (Calibri), 11 pt

Formatted: List Paragraph, Bulleted + Level: 1 + Aligned at: 0.25" + Indent at: 0.5"

Formatted: Font: +Body (Calibri)

Background/Introduction

Glaucoma is a potentially blinding condition. Raised intraocular pressure (IOP) is an important risk factor for the development and progression of optic nerve damage in glaucoma, and is the target of both medical and surgical treatment. There are no published figures on how many children have an IOP test per year, but both community optometrists and hospital clinics regularly perform IOP measurement as part of a comprehensive eye examination. For all practitioners IOP measurements in young children are challenging . The current reference standard for tonometry is the Goldmann applanation tonometer (GAT, ISO 8612) mounted on a slit lamp. The Perkins tonometer (PAT), as the hand-held version of GAT, is a suitable reference standard for IOP measurements for patients in the supine position, and hence for children during an examination under anaesthesia (EUA). Another commonly used handheld tonometer is the Reichert Tono-Pen^{R}, but for comparison of diagnostic test accuracy, we opted for the reference standard devices. ~~The current gold standard measurement technique is Goldmann applanation tonometry (GAT) on a slit lamp, or handheld Perkins applanation tonometry (PAT) during an examination under anaesthesia (EUA).~~

GAT requires the instillation of topical anaesthetics and a high degree of co-operation from the child. Frequently children are unable to suppress the natural reflex of moving backward or closing their eyes. This leads to repeated attempts being made at obtaining a reading, prolonged examination times and distress to children and families.

In 2005 a new device to measure intraocular pressure became available, the iCare® rebound tonometer (RBT). Its main advantage over other instruments is that no topical anaesthesia is required. In addition, it is a hand-held device, which children may perceive as less intimidating and allows examiners to move "with the child" when required.

The RBT acquires six readings in quick succession by propelling a fine sensor tip less than 2mm in diameter against the central cornea from the instrument base held at a distance of 4-8mm from the surface of the eye. [1] [2] After contact, the probe bounces back; the higher the IOP the faster the rebound. Measurements are taken within 0.1 seconds. The force impacting on the cornea is minimal and does usually not even trigger the highly sensitive blink reflex. The instrument display then shows the average of the six readings and whether the standard deviation (SD) is low, medium or high.

Since its introduction, RBT has become very popular and is now being used in many children's eye services and by many community-based optometrists. Two surveys of tonometry practice in children (Table 1 and reference [3]) indicate that for most paediatric ophthalmologists in the UK, RBT has become the preferred method to measure IOP in children. Whilst the device is considered easy to use, many users report that RBT measurements tend to be higher than GAT measurements (Table 1).

Data comparing RBT performance with GAT in children with glaucoma are scarce and limited to one study only. [4] Studies which have compared RBT with non-contact tonometry and tonopen in healthy children indicate good intra- and interobserver reliability and good agreement. [5] [6] [7] In children with glaucoma good agreement has been reported with both PAT [8] and GAT, [4] although RBT measurements are consistently higher than PAT or GAT readings.

In adults with healthy eyes, glaucoma or ocular hypertension, papers have reported good agreement between the RBT and GAT, albeit with systematically higher measurements on RBT. [9] [10] [11] [12] [13] [14] [15]

Accuracy of RBT may be affected by levels of IOP, [8] [16] ~~and~~ central corneal thickness (CCT)~~,~~ [7] [13] [14] and ~~it might not be CCT alone but rather~~ other corneal properties such as ~~(~~hysteresis and resistance~~) that affect IOP measurement~~. [17] The latter~~se~~ parameters are not routinely assessed in clinics and impossible to assess in young children.

We carried out the present study to evaluate the accuracy and reliability of RBT in children with glaucoma as compared to GAT. Secondary objectives were to investigate the influence of CCT on IOP ~~and CCT~~measurements by RBT, and to determine children's preference for RBT or GAT.

Methods

Patients

We recruited consecutive subjects ~~children and teenagers between the age of 5 and 19 years with an established diagnosis of primary or secondary glaucoma,~~ attending our tertiary paediatric glaucoma service at Moorfields Eye Hospital. The study was approved by the local research ethics committee. All parents/guardians gave written informed consent and children were invited to give assent. The sample size was determined by recommendations for Bland-Altman analysis. [18]

Protocol

Three observers took the measurements required for this study. Observer 1 measured the IOP in one eye by RBT. In children with glaucoma in both eyes, readings were taken from the right eye. In children with glaucoma only in the left eye, readings were taken from the left eye. Observer 1 recorded two consecutive averageRBT readings from six measurements and the SD indicated by the device.

One repeat average RBT measurement was obtained by a second observer and recorded separately. Following instillation of a drop of proxymethacaine, observer 2 recorded CCT on ultrasound pachymetry.

The third observer recorded IOP on GAT and asked the child which instrument they preferred.

All data were recorded on a Case Report Form which also recorded the child's diagnosis and ethnic background. At the end of the study, data were entered into a computerised database.

Data analysis

Summary statistics were produced for demographic factors and for IOP readings made by each observer and method (Tables 2 and 3). Repeat readings made by observer 1 using RBT were used to estimate intraobserver agreement using the Bland-Altmann limits of agreement method. [18] The same method was used to determine interobserver agreement, analysing RBT reading 1 from observer 1 and the RBT reading obtained by observer 2. Agreement between RBT and GAT was analysed based on reading 1 from observer 1 and GAT recorded by observer 3. A histogram for CCT was plotted in two age bands (under and over 10 years of age). Child preference for either device was summarised by descriptive statistical methods.

Results

Demographics

We carried out the study between 1/1/2009 and 31/3/2010. We enrolled n=102 children with a confirmed diagnosis of glaucoma. Age ranged from 4.9 to 19 years (mean 11.85, SD 3.17 years). 53 boys and 49 girls took part (Table 2). In 85 children the right eye was the study eye, and in n=17 children the left eye.

Analysis of first RBT reading by observer 1

One hundred and two datasets were analysed. Data were missing for 3 subjects. The RBT automatically indicates a higher than normal standard deviation of the acquired measurements by displaying a flashing "P" or a line in the "Up" position following the measurement. These are indicators of poor reliability, and the manufacturer recommends repeating the measurement. We excluded ~~In~~ 16 participants ~~the variability reading on the RBT was high~~in whom measurements displayed these poor reliability parameters. Nineteen sets of data were therefore excluded from analysis.

Analysis of second RBT reading by observer 1

There were nine missing values, and 11 children with ~~high SD scores~~poor reliability scores. Cross-tabulation of the first and second reading by observer 1 showed that readings were missing on both occasions for three children, and missing only on the second occasion for six children. Six children had high SD scorespoor reliability indicators on both measurements.

Analysis of RBT reading by observer 2

Data was missing on 38 children. This was due to the trial being run within a busy tertiary centre clinic, with observers not always able to complete this part of the examination.

Excluding RBT data with high variability readingspoor reliability indicators, we were left with 83 measurements by observer 1 (reading 1), 82 measurements by observer 1 (reading 2), and 50 measurements by observer 2.

Analysis of GAT data

GAT readings were missing in 12 datasets. Most of these children had complex ocular pathology (corneal graft n=1, microphthalmos/sunken socket n=1, nystagmus n=1, microcornea n=1, congenital glaucoma and multiple surgery n=1, Sturge Weber syndrome n=1). One child was very anxious and difficult to examine. Two children were glaucoma suspects, and in three cases no comment was available explaining missing GAT.

Analysis of IOP readings by RBT and GAT

The mean RBT reading 1 (SD) by observer 1 was 21.1mmHg (8.19), RBT reading 2 by observer 1 was 21.9 mmHg (8.94), observer 2 RBT was 21.14 mmHg (8.41), and GAT was 18mmHg (6.45).

Reproducibility of RBT readings: intra- and inter-observer variability

Data were available for 74 children who had two readings by observer 1. The mean difference between the readings was 0.135 (SD 1.45). A t-test revealed no evidence of systematic bias between reading 1 and reading 2 ((73 df)=0.7987, p=0.427).

The distribution of the differences appeared symmetric. The Bland Altman plot showed no systematic relationship between the average measure and the difference, and limits of agreement were computed as (-2.71, 2.98) mmHg (Fig. 1A).

First RBT reading by observer 1 and RBT reading by observer 2 were available for 45 cases. The mean difference between readings was 0.11 mmHg (2.99). A t-test revealed no evidence of systematic bias between observers (t(44)=0.25, p=0.8).

Again, the data appeared symmetric. The Bland-Altman plot showed no systematic relationship, limits of agreement were (-5.75, 5.97) mmHg (Fig. 1B).

Agreement between GAT and RBT

We used data from first RBT reading by observer 1. These and GAT data were available for 74 children. The mean difference was -3.3 mmHg (5.3). A t-test showed evidence of systematic bias (t(73)=-5.41, p<0.001). The Bland Altman plot also showed evidence of a relationship between the magnitude of the difference between methods and the magnitude of the measurement, with smaller differences being seen with lower measurements. This would imply that limits of agreement cannot be simply produced. Stratifying data at 21 mmHg removed evidence of bias and limits of agreement were then computed as (-8.6, 3.9) mmHg for Stratifying data at 21 mmHg allows production of limits of agreement (LOA). These are -2.35+/-1.96*3.19 for readings less than 21mmHg, and -5.52+/-1.96*7.94(-21.08, 10.04) mmHg for readings greater than 21mmHg.

Based on these analyses, agreement between the two methods appears poor and not clinically acceptable.

As demonstrated by the graph (Fig 1C), RBT frequently gave higher readings than GAT. Differences of 10mmHg were not uncommon.

Pachymetry data

Pachymetry measurements were obtained in n=83 children, of whom 67 had IOP measurements taken by both RBT and GAT. As expected for the study population we found a high prevalence of increased pachymetry values (Fig 1D). Defining the "normal range" as 460-650um, two readings were below the normal range (452, 456 um), and 13 readings were above the normal range; of these, seven participants had both RBT and GAT measurements. Of the 13 children with CCT greater than -> 650um, one had corneal clouding/oedema and enlarged cornea, and in two children "multiple previous glaucoma interventions" were recorded. None of these children had nystagmus, aphakic glaucoma, aniridia or anterior segment dysgenesis syndromes, or other confounding corneal abnormalities.

Pachymetry and RBT readings

Disagreement between GAT and RBT readings was greater with higher pachymetry readings, p=0.003.

Patient preference

Eleven children preferred GAT, 70 preferred RBT, and 21 gave no preference.

Discussion

The main finding of the present study is that the agreement of RBT and GAT appears poor in children with glaucoma. Since previous studies have largely concluded that there is good agreement between RBT and applanation tonometry, this observation was a surprise.

We believe that this discrepancy may in part be due to the fact that many studies have considered correlation rather than agreement. It is quite possible for methods to correlate well, but to disagree by amounts that are of real clinical relevance. Our data provide strong evidence of a linear association between measures made by GAT and RBT - but linear association is not the same as agreement, which is why Bland and Altman advocated the Limits of Agreement method. [18]

The present study is the second to compare RBT and GAT in children with glaucoma. The only other study into RBT in this population also included children with suspected glaucoma, excluded readings from children who were nervous or squeezing during the RBT measurement, and repeated RBT readings until a measurement with minimal variability was obtained, or three readings had been taken. [4] Whilst this guaranteed the vast majority of readings had either minimal or low variability, this approach means that the operator manually reduced device errors ~~– an approach often not possible in a busy clinic setting~~. The results of this study are comparable to those presented in our work: the authors report that RBT were higher than GAT readings in 75%, and within +/- 3mmHg of GAT in 63%. [4] Our view is that disagreements of greater than 3 mm Hg are of concern if they can impact on the management of the child.

The only other study exploring the use of RBT in children with glaucoma compared it with Perkins applanation tonometry (PAT). [8] The authors performed RBT and PAT in random order, which means that RBT measurements were performed after administration of topical anaesthesia. According to the manufacturer's manual topical anaesthesia may reduce the RBT reading. [19] [20] Again, the authors repeated RBT measurements when the variability indicator was high or IOP > 19mmHg with medium standard variation, excluding readings with erroneous device performance. The authors found greater disagreement with higher IOP measurements, yet did not provide limits of agreement stratified by IOP, or present regression-based limits of agreement. Interestingly, the graphs show that RBT measurements were consistently higher – up to 17mmHg, which is consistent with our findings. Both PAT and RBT readings were higher in cases of increased corneal thickness, another finding that agrees with our report.

Other paediatric studies of RBT are limited to healthy children, and none used GAT as comparator. [5] [6] [21]

Difference in study population is likely to be a contributory factor explaining why agreement between RBT and GAT was significantly poorer in our study than in others. Comparisons with GAT have been conducted in adults with glaucoma, but excluding significant other pathologies such as astigmatism, microphthalmos, buphthalmos, dry eyes, nystagmus. [13] ~~-~~[11] [15] [22] Results in studies with mixed populations (adults with glaucoma/ocular hypertension and healthy adults) also reported good GAT/RBT agreement. [12] [16] [23]

However, all studies except two used topical anaesthesia before RBT. Interestingly, the two studies who did not use topical anaesthesia found significant differences between GAT and RBT, with RBT overestimating IOP by 1 to 15mmHg. [15] [16]

Three studies performed on healthy adults without topical anaesthesia reported good agreement between RBT and GAT, [9] [24] [10] whilst three others reported significant differences in some cases. [14] [25] [17] The main limitation of these studies might be the inclusion of "normal" eyes with normal IOP only. Findings from this population cannot be generalised to subjects with raised IOP.

Sequence of tests may also explain differences in findings. Applanation tonometry, especially repeated measurements, can progressively lower IOP by a mechanism know as “aqueous massage”. [26] [16] [12] Our study design avoided this effect by obtaining RBT before GAT measurements. Studies that obtained GAT before RBT or conducted tests in random order [8] [11] [13] [22] [23] may have induced IOP lowering, thereby erroneously obtaining lower RBT readings.

Similar to other groups [8] [13] [16] [22] we found increased disagreement (ie larger discrepancies In IOP measures between RBT and GAT with higher CCT values. However, we found that even in children with pachymetry readings of 581um, disagreements could be greater than 10 mmHg.

Our study confirms reports [5] [6] [21] that the hand-held RBT has high acceptability in children. Since we started this work in 2008, it has become widely available and popular in many community optometric practices and hospital eye units in the UK (Table 1). [3] Seventy percent of the children enrolled in this study had a clear preference for the new device which does not require instillation of anaesthetic eye drops and no prolonged sitting in an uncomfortable position.

On the basis of previously published reports and our own work, we would recommend the use of the RBT in children, but advise practitioners to be cautious in the interpretation of findings, particularly in children with thicker corneas. It is reassuring that measurement discrepancies tend to reflect a systematic over-reading by the RBT: “normal” values obtained by this method are likely correct, and the IOP is unlikely to be high. This in turn can re-assure examiners and spare children the need for other IOP measurement methods and even examinations under anaesthesia. High RBT readings, on the other side, should not automatically trigger a trip to the operating theatre, but should prompt the examiner to seek confirmation of IOP level by another established technique.

Legends

Table 1. Survey of current paediatric tonometry practice in the UK. Using an electronic mailing list, we contacted 144 of paediatric ophthalmologists in the UK. The survey ran for 10 days, from February 2 to 16, 2012, and collected 36 replies.

Table 2. Demographic details of study participants.

Table 3: Agreement (inter observer, Intra observer and with GAT) for RBT

Fig. 1. Tonometry and pachymetry results. A: Intraobserver agreement of RBT measurements. B: Interobserver agreement of RBT measurements. C: Agreement between RBT and GAT measurements. D: Distribution of corneal thickness as determined by pachymetry. In healthy children of age5-9 years, mean (SD) CCT has been reported as 566 (48) um, and in children over the age of 10 years, 554 (35) um. [27]

Tables and Figures

In which setting do you work and measure IOP in children?	Teaching hospital District general hospital Community clinic	55.6% 47.2% 5.6%
Do you run a specialist paediatric glaucoma service?	Yes No	19.4% 80.6%
In how many children do you measure the IOP per month?	Less than 5 Between 5 and 20 More than 20	25% 44.4% 30.6%
What is your preferred method to measure IOP in children?	**RBT** Goldmann/Perkins applanation Tonopen Air puff	**77.8%** 44.4% 5.6% 5.6%
If you are using a RBT, how easy do you find it to use?	**Very easy** Moderately easy Not at all easy Not applicable	**60%** 25.7% 2.9% 11.4%
In your experience, are RBT readings accurate as compared to Goldmann applanation tonometry readings?	As accurate as Goldmann **RBT tend to be higher than GAT readings** RBT tend to be lower than GAT readings	22.7% **72.7%** 4.5%

Table 1. Survey of current paediatric tonometry practice in the UK. Using an electronic mailing list, we contacted 144 of paediatric ophthalmologists in the UK. The survey ran for 10 days, from February 2 to 16, 2012, and collected 36 replies.

Sex	Male:female (n	53 :49
Age (Years)	Mean (SD)	11.85 (3.17)
Laterality	Right:left	85:17
Ethnicity	Caucasian	57
	Mixed	19
	Asian or Asian British	1
	Carribbean/African/Any other Black background	8
	Other ethnic groups (incl. Chinese)	11
	Not stated or not recorded	6
Pachymetry	Median (IQR)*	581 (537, 622)

* IQR : interquartile range, 19 children had no pachymetry readings

Table 2: Demographic factors of the children under investigation

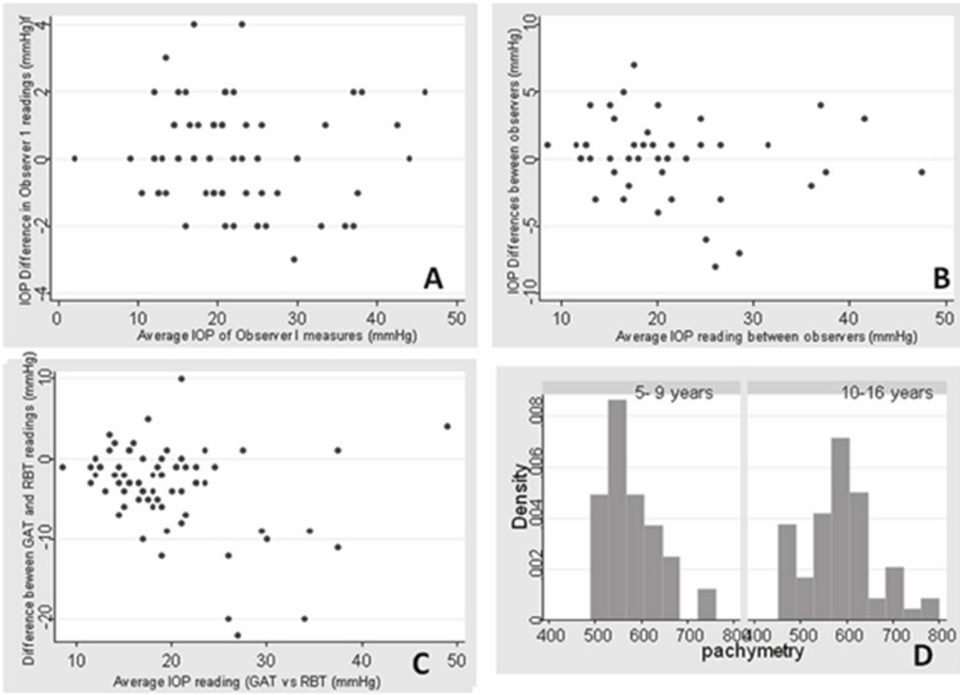
	Mean difference	SD difference	LOA
Intra observer (n = 74)	0.13	1.46	(-2.71, 2.98)
Inter-observer (n = 45)	0.11	2.99	(-5.75, 5.97)
ICare-GAT (n = 74)	-3.34	5.31	< 21 mmHg : (-8.60, 3.90)
			>=21 mmHg : (-21.08, 10.04)

Table 3: Agreement (inter observer, Intra observer and with GAT) for RBT

References

1. Kontiola AI, Goldblum D, Mittag T, et al. The induction/impact tonometer: a new instrument to measure intraocular pressure in the rat. *Experimental eye research* 2001;**73**(6):781-5
2. Kontiola A, Puska P. Measuring intraocular pressure with the Pulsair 3000 and Rebound tonometers in elderly patients without an anesthetic. *Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie* 2004;**242**(1):3-7
3. Chan WH, Lloyd IC, Ashworth JL, et al. Measurement of intraocular pressure in children in the UK. *Eye (London, England)* 2012;**25**(1):119-20
4. Flemmons MS, Hsiao YC, Dzau J, et al. Icare rebound tonometry in children with known and suspected glaucoma. *J Aapos* 2011;**15**(2):153-7
5. Kageyama M, Hirooka K, Baba T, et al. Comparison of ICare rebound tonometer with noncontact tonometer in healthy children. *Journal of glaucoma* 2011;**20**(1):63-6
6. Sahin A, Basmak H, Niyaz L, et al. Reproducibility and tolerability of the ICare rebound tonometer in school children. *Journal of glaucoma* 2007;**16**(2):185-8
7. Sahin A, Basmak H, Yildirim N. The influence of central corneal thickness and corneal curvature on intraocular pressure measured by tono-pen and rebound tonometer in children. *Journal of glaucoma* 2008;**17**(1):57-61
8. Martinez-de-la-Casa JM, Garcia-Feijoo J, Saenz-Frances F, et al. Comparison of rebound tonometer and Goldmann handheld applanation tonometer in congenital glaucoma. *Journal of glaucoma* 2009;**18**(1):49-52
9. Fernandes P, Diaz-Rey JA, Queiros A, et al. Comparison of the ICare rebound tonometer with the Goldmann tonometer in a normal population. *Ophthalmic Physiol Opt* 2005;**25**(5):436-40
10. Davies LN, Bartlett H, Mallen EA, et al. Clinical evaluation of rebound tonometer. *Acta ophthalmologica Scandinavica* 2006;**84**(2):206-9
11. Brusini P, Salvetat ML, Zeppieri M, et al. Comparison of ICare tonometer with Goldmann applanation tonometer in glaucoma patients. *Journal of glaucoma* 2006;**15**(3):213-7
12. Nakamura M, Darhad U, Tatsumi Y, et al. Agreement of rebound tonometer in measuring intraocular pressure with three types of applanation tonometers. *American journal of ophthalmology* 2006;**142**(2):332-4
13. Sahin A, Niyaz L, Yildirim N. Comparison of the rebound tonometer with the Goldmann applanation tonometer in glaucoma patients. *Clinical & experimental ophthalmology* 2007;**35**(4):335-9
14. Pakrou N, Gray T, Mills R, et al. Clinical comparison of the Icare tonometer and Goldmann applanation tonometry. *Journal of glaucoma* 2008;**17**(1):43-7
15. Rehnman JB, Martin L. Comparison of rebound and applanation tonometry in the management of patients treated for glaucoma or ocular hypertension. *Ophthalmic Physiol Opt* 2008;**28**(4):382-6
16. Munkwitz S, Elkarmouty A, Hoffmann EM, et al. Comparison of the iCare rebound tonometer and the Goldmann applanation tonometer over a wide IOP range. *Graefe's archive for clinical and experimental ophthalmology = Albrecht von Graefes Archiv fur klinische und experimentelle Ophthalmologie* 2008;**246**(6):875-9
17. Chui WS, Lam A, Chen D, et al. The influence of corneal properties on rebound tonometry. *Ophthalmology* 2008;**115**(1):80-4
18. ~~Bland JM,~~ Altman DG. ~~Applying the right statistics: analyses of measurement~~Method comparison studies. In: Practical Statistics for medical research. Chapman & Hall/CRC, 1991, Chapter 14, p 396-403 ~~*Ultrasound Obstet Gynecol* 2003;**22**(1):85-93~~
19. Tiolat. *iCare Tonometer: User's and Maintenance Manual*. Helsinki.

20. Baudouin C, Gastaud P. Influence of topical anesthesia on tonometric values of intraocular pressure. *Ophthalmologica. Journal international d'ophtalmologie. International journal of ophthalmology* 1994;**208**(6):309-13
21. Lundvall A, Svedberg H, Chen E. Application of the ICare rebound tonometer in healthy infants. *Journal of glaucoma* 2011;**20**(1):7-9
22. Martinez-de-la-Casa JM, Garcia-Feijoo J, Vico E, et al. Effect of corneal thickness on dynamic contour, rebound, and goldmann tonometry. *Ophthalmology* 2006;**113**(12):2156-62
23. van der Jagt LH, Jansonius NM. Three portable tonometers, the TGDc-01, the ICARE and the Tonopen XL, compared with each other and with Goldmann applanation tonometry*. *Ophthalmic Physiol Opt* 2005;**25**(5):429-35
24. Jorge J, Fernandes P, Queiros A, et al. Comparison of the IOPen and iCare rebound tonometers with the Goldmann tonometer in a normal population. *Ophthalmic Physiol Opt*;**30**(1):108-12
25. Poostchi A, Mitchell R, Nicholas S, et al. The iCare rebound tonometer: comparisons with Goldmann tonometry, and influence of central corneal thickness. *Clinical & experimental ophthalmology* 2009;**37**(7):687-91
26. Krakau CE, Wilke K. On repeated tonometry. *Acta Ophthalmol (Copenh)* 1971;**49**(4):611-4
27. Hussein MA, Paysse EA, Bell NP, et al. Corneal thickness in children. *American journal of ophthalmology* 2004;**138**(5):744-8



50x36mm (300 x 300 DPI)