UPDATE IN TONOMETRY.
PHOSPHENE AND REBOUND TONOMETRIES,
SELF-TONOMETRY AND TECHNOLOGIES FOR THE FUTURE

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ABSTRACT
The Proview™ phosphene (eye-pressure) tonometer and the Rebound tonometer ICare® are relatively new devices basically different from the Goldmann applanation tonometry (GAT). Both technologies will be presented in this review with respect to their principle, their technique, their advantages and limits, as well as their accuracy, the IOP measurements agreement with GAT, and the influence of central corneal thickness on the reliability of these measurements. Because the current data base for the interpretation of glaucoma disease course and its management are still relatively small, the development of a continuous, accurate, reliable and harmless monitoring of IOP over 24 hours is strongly desirable in the future. Approaches for self-tonometry and devices such as smart contact lenses which can take the IOP from the corneal surface have been developed with this goal. The future will probably confirm whether telemetric IOP monitoring with an implantable active microsystem allows a reliable IOP monitoring or not. In any case, active implants will open new and important perspectives in the diagnosis and the treatment of glaucomatous optic neuropathy.

RÉSUMÉ
Actualités en tonométrie. tonométrie par phosphène, tonométrie a rebond, autocontrôle de la pression intra-oculaire et technologies du futur.

Le tonomètre Proview™ à phosphène (par pression oculaire) et le tonomètre ICare® dynamique à rebond sont des tonomètres récents dont les principes de mesure sont différents de celui du tonomètre à aplanation de Goldmann. Leur principe physique, leur technique de mesure, leurs avantages et limites respectifs sont repris dans cette revue. Leur précision, la corrélation des mesures obtenues avec celles de l’aplanomètre de Goldmann et l’influence de l’épaisseur cornéenne centrale sur la précision de ces mesures sont également analysées à la lumière des données de la littérature.

Le suivi clinique d’un patient glaucomateux et l’adaptation de son traitement ne reposent encore que sur une quantité assez restreinte de renseignements. Il serait donc très souhaitable que l’on parvienne à développer à terme un dispositif d’enregistrement continu de la PIO, qui puisse être à la fois précis, fiable et doué d’une excellente innocuité. Plusieurs méthodes d’autocontrôle de la PIO et différents dispositifs basés en particulier sur l’adaptation de lentilles de contact permettant d’enregistrer la PIO à partir de la surface cornéenne ont été développés dans ce but. L’avenir confirmera peut-être si les récentes technologies basées sur l’implantation d’un microsystème actif dans l’œil permettent d’obtenir un enregistrement à distance fiable et précis de la PIO. Dans l’affirmative, les microcapteurs de PIO ouvrent d’importantes perspectives dans le diagnostic et le traitement de la neuropathie glaucomateuse.

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Intraocular pressure (IOP) measurement is one of the key parameters to diagnose, to follow-up glaucoma, as well as to assess the response to treatment in routine clinical practice. New tonometers that appear to be less or non affected by central corneal thickness compared with Goldmann Applanation Tonometry (GAT) have been developed to have a more accurate reading of the true IOP in the past few years (17).

Outsiders among the different currently available tonometers, the ProviewTM phosphene and the Rebound tonometers are relatively recent devices that are based on quite different physical principles than those of the GAT, the Pascal Dynamic Contour tonometer (DCT) and the Ocular Response Analyzer (ORA). Both devices are potentially designed for self-tonometry.

PROVIEW PHOSPHENE TONOMETER

The Proview™ eye-pressure phosphene tonometer (PPT) (Bausch & Lomb Inc. Tampa, FL, USA) is a psychophysical technique to evaluate IOP based on the entoptic phenomenon of pressure phosphenes (4,15, 27). Recognized by Aristotle in ancient Greece, and later by Purkinje and Helmholtz, phosphenes are sensations of light, that are elicited by nonphotic stimuli such as mechanical pressure, electricity, or x-rays. The application of mechanical pressure to the superonasal portion of the eye (where a phosphene can be stimulated most rapidly through half-closed eyelids) creates a self-perceptible pressure phosphene in the inferotemporal outer visual field which is usually the final area to become affected by glaucomatous damage. The phosphene elicited by the PPT is relatively easy to be perceived and looks similar to a solar eclipse with a dark central circle surrounded by a brighter ring. The bipolar cells in the retina, or parts of the rods and cones situated anterior to the external limiting membrane, are thought to be responsible for this phenomenon (27). As been suggested by Fresco, the threshold pressure for creating a phosphene may provide an indication of the level of IOP (15).
Approved by the FDA, the Proview™ phosphene tonometer is a pencil-shaped spring compression device calibrated in millimetres of mercury and consisting of a probe with a flat applicator of the same diameter (3.06 mm) as the area applanated by the Goldmann tonometer. It is applied to a partially closed eyelid without topical anaesthetic. The scale runs from 8 to 40 in 2-mm Hg increments. Practically, the patient is asked to look down and out. The examiner places the tip of the device on the superior nasal portion of the patient’s eyelid. The pressure is slowly increased until the patient indicates that she/he perceives a well-formed pressure phosphene in inferotemporal visual field. As soon the patient has detected the phosphene, the tonometer is removed from the eyelid. The pressure is read from the scale on the side of the device (15, 27) (Figures 1, 2).

The Proview™ method has some advantages over the Goldmann method. It is relatively simple to use, inherent safe, portable and relatively easy to perform, without extensive training. It does not require anaesthetic drops, fluoresceine, or expensive equipment. As it does not need contact with the cornea, it may be useful for patients with corneal abnormalities that may interfere with or preclude accurate IOP measurements (e.g. prior penetrating keratoplasty, corneal edema, corneal scarring, marked astigmatism, and prior refractive surgery) (15, 37). By not applanating the cornea, the Proview™ may also circumvent inaccuracies related to central corneal thickness (15).

The Proview™ has been proven to be a valuable and accurate tool for patients to monitor their IOP at home, in the range of 9 to 25 mmHg (4, 27). With the exception of patients with very advanced glaucomatous disease, the ability to see phosphene could be correlated with the severity of glaucoma (6,40).

The PPT could also provide a good alternative method for the IOP assessment in post-LASIK patients (6,39).

Unfortunately, the accuracy of the tonometer and even more, the assumption that phosphene generation threshold correlates with the IOP, has been strongly questioned (7, 8,18, 30, 40, 41). In an evaluation of the PTT device including 100 healthy volunteers and glaucomatous patients, Alvarez concluded that, even despite of reproducible results, the PTT was not reliable as an indicator of IOP (1). Intraclass correlations of IOP values obtained with the GAT and the Proview™ were not strong. The sensitivity to detect high IOPs was low while the agreement between GAT and the Proview™ readings ranged from 2.4 mmHg to 2.8 mm H. Furthermore, the 95% confidence interval could be 10.3 mmHg below to 15.2 mm Hg above GAT readings. The sensitivity of the Proview™ technique to detect patients with high IOP appeared to concern only less than 20% of these patients (1). Most of the IOP values obtained with the Proview™ were significantly lower than those measured with GAT (31). Variations of the corneal thickness did not contribute to these differences. Up to one third of patients could not perceive a pressure phosphene using this device (7). Finally, the position of probe application can influence the measurements taken
using the Proview (18)

In conclusion, the Proview™ may have a potential role in self-monitoring of IOP and represents an advance in the area of self-tonometry (30, 39, 43). However, the current Proview™ device has numerous limitations. These include the absence of correlation between PPT and GAT, the high subjectivity of the measurement, the impossibility for a significant proportion of patients to perceive the pressure phosphene and the fact that IOP measurement within the target IOP might give patients a false sense of security and influence their compliance (31, 33).

Appropriate position of the instrument is very important (17, 44). Corneal characteristics do theoretically not influence the measurements but scleral characteristics potentially do it. Further clinical investigation and refinements of the instrument are hence crucial before a reliable application could be considered in glaucomatous patients.

REBOUND DYNAMIC TONOMETRY

The Rebound tonometry (RBT), also called induction-impact tonometry, has been used primarily as a research tool to measure IOP in rodent and mice models of glaucoma because of the small size of its probe (9, 22). Based on the same physical principle as the earlier vibration tonometer introduced by Krakau, RBT is a dynamic tonometry that contacts the cornea with a probe and detects the motion as the probe collides with the eye and bounces back. The motion parameters of the probe vary according to eye pressure and are used to calculate IOP. In other words, the probe deceleration is less at low than at high IOP levels, and consequently the higher the IOP, the shorter is the duration of the impact (19-21, 25). In animals, this method has been proven to be easy to use, precise, reproducible and well correlated with manometric IOP readings (9, 19-23, 49). The ICare® tonometer has been recently marketed both for routine laboratory and veterinary use.

The dynamic rebound method has also led to the marketing of a handheld tonometer for humans, named the ICare® (ICare; Tiolat Oy, Helsinki, Finland). It is an assembly of two coaxial coils to a probe shaft that bounce a magnetized probe off the cornea and detect the deceleration of the probe caused by the eye. Of all the variables linked to the probe’s movement, the reverse of the probe’s deceleration speed seems to correlate best with the IOP level (19).

The probes are disposable. Their tip has a 1-mm-diameter plastic cover to minimize corneal damage and microbiological contamination. Practically the tip of the probe must be aligned perpendicular to the cornea apex, 4-8 mm away from the corneal surface. Six consecutive readings are taken with the same probe and averaged with rejection of poor quality measurements (Figures 3, 4).

Compared to other methods, The ICare® tonometer has several advantages: it is small, light-
weight, and portable. A slitlamp is not required; it is easy to use; IOP is taken in a very short time with the patient in a comfortable sitting position; an anaesthetic or sedation is not required.

Based on measurements performed with the ICare® and The Pulsair 3000 tonometer in 131 residents of two Finnish nursing homes, Kontiola had concluded that tonometry with the ICare® was a rapid and well-tolerated procedure, and that IOP readings of the two tonometers were within ±1 mmHg in 53% of the measurements and within 2 mmHg in 72% of the measurements (23).

A summary of the clinical evaluation of the ICare® in the literature is presented on table 1 (5, 10, 11, 14, 34, 38). Briefly, the intra- and inter-observer variability of IOP measurements was close to those of GAT. The ICare® IOP readings appeared to be reproducible, well correlated with those of GAT, although they were consistently higher than GAT measurements. Importantly, the 95% confidence intervals of the differences in measurements made with the two devices were clinically relevant in the majority of the studies.

Finally both GAT and RBT are similarly affected by changes in CCT (5, 11, 38). As the CCT got thicker, the ICare could overestimate GAT considerably (38).

To conclude on dynamic rebound tonometry, the ICare® appears to offer reproducible IOP measurements. Learning curve is of short duration. It can be easily and very briefly applied. The fact that the probe should be in the horizontal plane limits the procedure. Readings 1 to 2 mmHg higher than those provided by conventional tonometry can be expected, although in some cases, the difference could even exceed 7 mmHg. Due to these relatively large limits of agreement between the ICare® and Goldmann, the instrument cannot be used for a routine clinical glaucoma practice. It may be useful in the screening of ocular hypertension when a standard applanation tonometry is not available or impossible.

In any case, measured IOP must be considered at the light of the CCT values and even more of the individual corneal viscoelastic properties. Its potential advantages in paediatric, geriatric and home care have to be further evaluated. Specially, the validity of the device as a home tonometer by a second person must be further evaluated.

### OTHER SELF-TONOMETERS

Large fluctuations in diurnal IOP have been shown to be a significant and independent risk factor for glaucoma progression (2). In fact the role of the IOP in the pathogenesis of glaucoma is still not exactly defined and is often difficult to assess in an individual patient. Because it is performed under very artificial conditions in the office or in the hospital, tonometry provides with only a fleeting glimpse of IOP. The sufficiency of a given treatment is judged on very sparse IOP data. Short- and long-term IOP fluctuations in glaucoma patients or glau-
coma suspects are too often neglected. This situation could be dramatically improved by knowing the continuous IOP profile of an individual. Such a system is especially desirable for people who are not able to visit the ophthalmologist very frequently.

Clearly, the development of a continuous, accurate, reliable and harmless monitoring of IOP over 24 hours, as has been achieved in 24-hour profiles of blood pressure, would allow to better evaluate the full IOP range of a patient and improve his/her management.

For this purpose, self-tonometry could be established as an important diagnostic tool in the early diagnosis and follow-up of glaucoma. Ideally, a self-tonometer must be safe and easy to use. It must yield reliable results and comply with the legal standards for tonometer calibration. The advantages of self-tonometry are multiple. They include lower costs, a potentially better compliance by an active patient, the absence of dependence on the slitlamp, the possibility to measure IOP in the horizontal plane and to detect IOP peaks without hospitalization at times outside of normal office hours. The influence exerted by the examiner’s expectations can be also theoretically excluded.

The concept and the application of self-tonometry is more than 25-years old. The earlier self-tonometer for home use was designed by Zeimer (51). Developed by Draeger several years later, the Ocuton S hand-held applanation tonometer has been initially used in aeronautic medicine during the German Spacelab D2 mission in 1991 (12, 24, 33, 46). Other devices such as the Pulsair-Keeler non-contact tonometer and the Tono-Pen have been almost simultaneously manufactured for home tonometry (3, 26).

All these different devices have been proven to be relatively accurate, reproducible and well to reasonably correlated with GAT (13, 16, 45, 51). However in 2006, self-tonometry has still many potential pitfalls and limitations.

- Most of the devices are based on corneal applanation. As such, they can induce corneal abrasions and require a topical anaesthetic with per contra, a possible abuse of local anaesthetics. In this field, the expansion of non-contact tonometers would be very beneficial for home use in the future (3).

- The procedure itself is often difficult, constraining and requires an extensive training. A significant proportion of patients have difficulty and/or impossibility to applanate their own cornea and obtain reliable results (42). They often need a second person to help them. Moreover, three to five on average repeated measurements have been proven to be necessary at each timepoint of the day (42).

- Self-tonometers are generally only applicable during a short period of time. Some of them are fully automated applanation tonometers but they are relatively expensive (13).

- The instrument’s readings might be influenced in different ways by the diurnal changes of corneal thickness (24).

- Finally, the possible detrimental influence on compliance if patients know that their IOP is “normal” has to be considered (50).

For these different reasons, further technical and methodological refinements are required before the current devices can be considered as effective as the Goldmann tonometer for routine clinical use.

TECHNOLOGIES FOR THE FUTURE

With the considerable progress that has been made in miniaturizing microelectronic components embedded in biocompatible materials and in reducing the energy consumption of such systems, active sensors have recently been developed to allow a continuous long-term IOP monitoring (47). The goals of the ideal option monitor are multiple.

- It has to measure the pressure where it acts, i.e inside the eye.
- It measures the pressure without any examiner bias;
- It does no need any battery or wires;
- It provides a reading system outside the eye with IOP data;
- It is fast enough to correlate IOP data with the heart cycle;
- It measures IOP continuously or any time cycles chosen;
- It does not impact the daily life activity of patients;
- It is accurate over a long time;
- It is harmful and allows feedback signals to modify treatment if needed (48).

The current devices are of two types.

1. The external device consists in a pressure sensing contact lens with an embedded micro strain gauge designed to measure changes in corneal curvature arising from IOP variations. IOP measurements are taken from the corneal surface. Although a prototype of this device has been successfully tested in porcine eyes, it does not match with all the ideal monitor options (28).

2. The internal device allows a telemetric IOP monitoring with an implantable active microsystem. The sensor system should be integrated into an intraocular lens and inserted during a cataract procedure through a relatively small incision, or through a scleral incision onto the choroidal surface. This system has the advantage that the IOP measurements are independent of the ocular surface or rigidity. Its working principle has been established. It has been shown that it works over a long period of time and, more importantly that both the device and the energy transfer were safe to the eye (48). This implanted telemetric system for IOP recording could be especially useful for eyes after reconstruction of the anterior segment, e.g., after keratoplasty, keratoprosthesis, or other procedures.

However further improvements have to be made with respect to its stability and the hermetic sealing of the electronic subsystems, before the device could be implanted in humans. Moreover, the considerable overflow of the registered data is still one of the major limitations of the system.

The results of the research project with this implant which had started in 2003 and named the IOPS Research Project (intraocular Pressure Sensor) will be presented in a near future. If it will reveal successful, this implant could be the first system available in ophthalmology to make homecare and telemedicine possible. In the current state and with a very short experience, it has been suggested that self-tonometry with telemedicine could be a cost effective technique enabling the early diagnosis of pathologically increased IOP (35). Science fiction does not stop at this stage. Why not imagine other types of pressure sensors that would allow to record IOP just in front of the optic nerve where glaucomatous damage develops?

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