Original Investigation

An Implantable Intraocular Pressure Transducer
Initial Safety Outcomes

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IMPORTANCE To our knowledge, this is a report of the first implantation of a wireless intraocular pressure transducer (WIT) in a human eye.

OBJECTIVE To report preliminary safety data on the WIT.

DESIGN, SETTING, AND PARTICIPANT In an institutional setting, a patient with open-angle glaucoma consented to be the recipient of the WIT in one eye in an interventional study design.

INTERVENTIONS The WIT was implanted into the ciliary sulcus following extracapsular cataract extraction and "in the bag" intraocular lens implantation. The patient was monitored postoperatively for 18 months.

MAIN OUTCOMES AND MEASURES Any adverse events.

RESULTS There were no complications noted during the WIT insertion or postoperatively. No persistent intraocular inflammation, pigment dispersion, or angle narrowing was noted.

CONCLUSIONS AND RELEVANCE The WIT was well tolerated in the eye and no overt signs of toxicity or other adverse events were noted. This may allow the constant monitoring of intraocular pressure in the future.

JAMA Ophthalmol. doi:10.1001/jamaophthalmol.2014.1739
Published online June 26, 2014.

Video at jamaophthalmology.com

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Intraocular pressure (IOP) remains, to date, one of the most important factors to monitor disease progression in glaucoma. It is still unclear whether short-term and long-term IOP fluctuation is associated with an increased rate of glaucoma progression.[1-5] Currently available technology only permits isolated IOP recordings during scheduled visits to the eye care provider and often fails to detect the true peak and trough of the IOP diurnal curve as well as the long-term IOP trend.[6]

A device that can enable a patient to self-monitor IOP on demand or at preset intervals can conceivably capture enough data points to enable the physician to construct a true diurnal and nocturnal curve as well as long-term IOP trend. If such a device can be safely implanted within the eye, it can also overcome some or most of the limitations of the commonly used indentation tonometry techniques. These largely rely on factors such as corneal biomechanics, curvature, and thickness for registration of IOP.

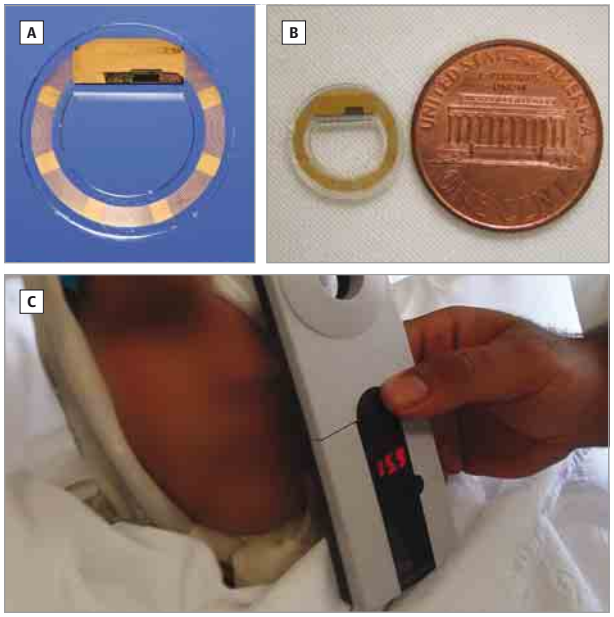
A recent study[7] evaluated a novel wireless IOP transducer (WIT) (Implandata Ophthalmic Products GmbH). The device exhibited favorable biocompatibility in rabbit eyes as well as concordance with IOP measured by manometry. There were no signs of intraocular toxicity or inflammation throughout the 25-month study period. The present study describes our experience with the first implantation of the WIT within the human eye and the 18-month safety and IOP data.

Methods

Wireless Intraocular Transducer

The WIT integrates pressure sensors, temperature sensor, identification encoder, analog-to-digital encoder, and telemetry unit into a single microelectromechanical system application-specific integrated circuit.[7] This digital ultraminiature system uses complementary metal oxide semiconductor technology for its electronic components. The electronic components are either biocompatible or inert. The application-specific integrated circuit is attached to a circular microcoil antenna made of gold, and both of these components are hermetically encapsulated in platinum-cured silicone. This biocompatible silicone material makes up the entire surface of the implant. The implant itself is designed to remain in vivo indefinitely. The outside diameter of the transponder disc is 11.3 mm, the inside diameter is 7 mm, its thickness is 0.9 mm,

Figure 1. View of the Wireless Intraocular Pressure Transducer (WIT) Showing the Ring-Shaped Device Consisting of 2 Parts: an Application-Specific Integrated Circuit Chip and a Microcoil Antenna



A, The device is encapsulated in silicone and has an 11.3-mm outer diameter and a 7-mm inner diameter. B, A view of the WIT showing its relative size alongside a US cent. C, The external reading device is held no farther than 5 cm from the transducer. It allows intraocular pressure (IOP) measurement by radiofrequency and displays an IOP reading representing the average of 10 to 20 IOP measurements.

and its weight is 0.1 g (**Figure 1**A and B). The metal (gold) and polyimide structure that forms the radio frequency coil required for energy supply to the implant is extremely thin (0.9 mm) and ductile and can be folded for implantation; the encapsulation material that covers the implant is very flexible and can be folded without delamination from the structure. The silicone chip where the actual sensor module resides is rigid and does not need to be folded for implantation.

The IOP is measured by an array of capacitive pressure sensors. These sensors, in a simplistic model, can be visualized as being composed of 2 parallel plates: a thin flexible membrane that is indented by the IOP and a thicker rigid base. When the cell membrane is mechanically deflected by pressure changes, the capacity of the cell changes in accordance with the change in distance between the "plates." This results in an analog signal that is proportional to the absolute pressure within the eye. The membrane, being indented by the IOP, changes the distance between itself and the rigid base, resulting in a capacitance change. The capacitive pressure sensor is integrated with an inductor to form an inductor capacitor resonant circuit. The magnitude of the capacitance change is measured digitally and transmitted externally by radiofrequency. As stated above, the IOP is then tracked by the external reader unit (Figure 1C), which is electromagnetically coupled with the sensor by bringing the reader in proximity with the sensor and pressing a button on the reader unit.[7]

The implant does not require a battery. It is electrically passive until powered externally by the proprietary reader device. It derives the necessary power via electromagnetic inductive coupling to an external magnetic field generator housed in an external reader unit. The reader unit is battery powered and resembles a television remote control in its current design. The same reader unit picks up the digital data relayed by the transponder unit and subsequently displays the IOP values on its light-emitting diode display. The reader and the transponder unit need to be brought into close proximity of each other (within 5 cm) before a button is pressed on the reader to activate the electromagnetic coupling sequence (Figure 1C). The device is capable of providing 10 IOP samples per second. In normal operation, to obtain an IOP reading, 10 subsequently acquired samples are averaged. A "continuous mode" can be activated acquiring a reading every 5 minutes. It is also possible to acquire subsequent samples for longer periods of time (eg, 100 seconds) in a so-called online mode.

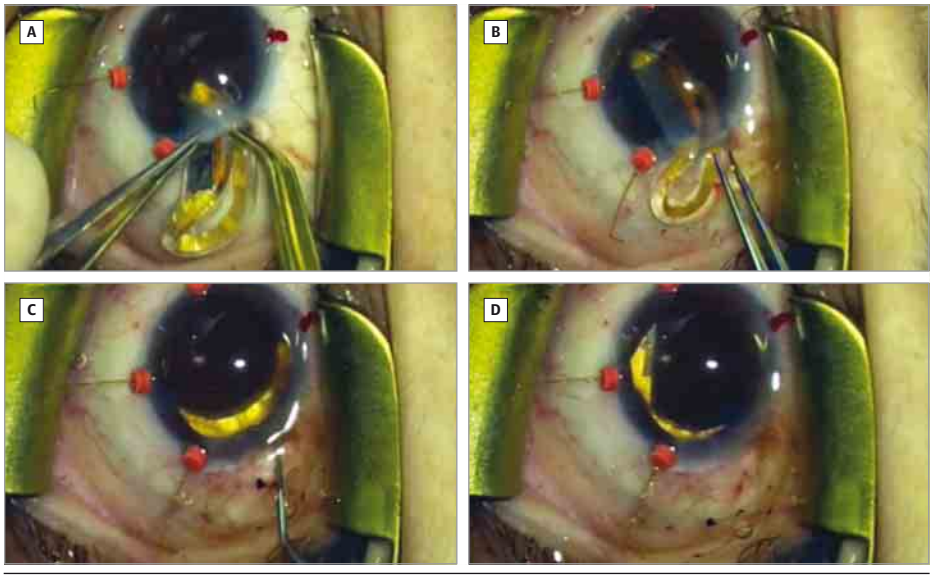
All of the data are digitally transmitted from the implantable device to the external reader via the telemetric link and stored in the memory module of the reader. The current configuration of the reader allows for storage of up to 3000 IOP values, which can be enhanced by installing additional memory modules, if needed. The storage capacity of the reader can be replenished by downloading the data to a computer. An optional 3G wireless module can also be connected to the reader, which can be set to automatically transmit all measured data to a cloud-based server, making the data instantly available to the eye care provider.

Surgical Technique

A woman in her 60s with history of primary open-angle glaucoma and cataract was selected to be the recipient of the WIT concurrent with cataract extraction and intraocular lens implantation. The benefits, alternatives, and risks of the procedure were discussed with the patient. The specific benefit to this particular patient was her difficulty to return for frequent visits on a long-term basis to monitor her glaucoma because she lived in a remote area. If successful, the WIT would allow the woman to obtain measurements at home and send the reader for data download with members of her family when they travel to the hospital area. Assurance was obtained that she would adhere to the follow-up visits specified in the research protocol. The protocol was approved by the investigational review board of the Lebanese American University, Beirut, Lebanon, and a written informed consent form was signed by the patient. The surgical procedure as well as the office visits were performed at the Beirut Eye Specialist Hospital, Beirut, Lebanon. The patient received no financial compensation.

The patient had a history of primary open-angle glaucoma and cataract diagnosed 5 months prior to the procedure. Her maximal IOP measured at presentation was 39 mm Hg in the eye that underwent the operation. Her visual field did not show significant visual loss. Prior to the procedure, her best-corrected visual acuity was 20/200. Examination showed a clear cornea, an open angle by gonioscopy, and a 3+ nuclear sclerotic cataract. Her other eye showed a 1+ nuclear sclerotic cataract with a best-corrected visual acuity of 20/50. The retinal examination was within normal limits. Optic nerve exami-

Figure 2. Surgical Implantation of the Wireless Intraocular Pressure Transducer (WIT) in the Ciliary Sulcus



The pupil was stretched with iris hooks, the cataract was extracted and an intraocular lens placed in the capsular bag. The main wound was enlarged to accommodate the placement of the WIT. The WIT antenna is folded between a pair of curved forceps (A) and placed directly in the sulcus space while it is unfolding (B). It is then manipulated into place while ensuring that the sensor side of the WIT faces the cornea (C and D).

nation showed a cup-disc ratio of approximately 0.6 with a temporal sloped rim in both eyes. Treatment was started with topical dorzolamide hydrochloride plus timolol maleate ophthalmic solution (Cosopt; Merck) at presentation. Her IOP was measured in the mid-teens in the study eye at the last 2 visits before surgery.

Phacoemulsification was performed through a 3.0-mm incision located at the 12-o'clock position. Iris hooks were placed during the procedure because of poor dilation. The cataract extraction was uncomplicated. A plate haptic intraocular lens (Rayner Superflex 620H; Rayner) was placed in the capsular bag. The WIT was then folded with forceps (**Video** and **Figure 2**) and inserted in the anterior chamber after enlarging the incision to approximately 5 mm. The first attempt was not successful because the folded WIT was prematurely released in the iris plane and attempts to slide it into the sulcus space were not successful. This necessitated transecting the antenna coil in one location with scissors (Vannas) and extracting it through the main wound by dialing it out while holding it with generic forceps. A second attempt resulted in successful unfolding of another device directly in the sulcus space. The sensor side was facing the cornea as intended. The iris hooks were removed and the pupil constricted after removal of viscoelastic and placement of acetylcholine chloride intraocular solution (Miochol-E; Bausch & Lomb Inc).

The patient was monitored postoperatively at various times (1 day; 2, 3, 6, 12, 23, 27, 31, 36, 52, and 76 weeks). Visual acuity, slitlamp biomicroscopy, and dilated fundus examination were performed at all visits. Gonioscopy was performed at the 1-week, 36-week, and 76-week visits. Three IOP measurements with Goldmann applanation tonometry (GAT) and the WIT were obtained at every visit. The GAT measurements were obtained first to avoid influencing the examiner. The WIT measurements were then obtained by the patient as instructed.

Results

Postoperative recovery was longer than expected after cataract extraction. This was most likely the result of the additional manipulation needed with iris hooks and the WIT implantation. There was initial corneal edema as well as mild iritis that resolved within the first month. Ultrasonic pachymetry was not obtained, because the level of edema noted on clinical examination was mild. The uncorrected visual acuity during the first month was 20/70. No intraocular inflammation was noted after the surgery. Best spectacle-corrected visual acuity was 20/60 at 6 weeks postoperatively and moderate posterior capsular opacification was noted. A YAG capsulotomy was performed. There was no significant improvement in vision noted. Ocular coherence tomography of the macula (3D OCT-2000; Topcon) obtained at week 23 showed the absence of edema or other abnormalities. The lessened acuity was attributed to a small capsulotomy, necessitating enlargement with additional laser treatment. This improved the patient's vision to 20/25 with a manifest refraction of +0.25 + 0.50 × 005. Gonioscopy at 36 weeks revealed an open drainage angle with 1 clock hour of peripheral anterior synechiae at the surgical site. Subsequent visits until the last follow-up visit at 76 weeks postoperatively did not reveal new findings.

Intraocular pressure measurements were collected during office visits. A minimum of 3 IOP measurements were obtained at all visits by GAT and by the WIT. The **Table** shows all measurements taken with the WIT and GAT at various postoperative office visits. The IOP indicated for each visit is the mean of measurements obtained at that particular visit. The overall mean of IOP at office visits was 18.8 mm Hg for GAT and 19.4 mm Hg for the WIT. Latanoprost (Xalatan; Pfizer) was added at week 31 to treat elevated IOP (25 mm Hg by GAT). It

Table. IOP Data Collected at Various Office Visits Comparing the WIT and GAT

Time of Visit	Mean IOP, mmHg[a]		Difference
	WIT	GAT	
Day 1	30.8	30.0	0.8
Week			
1	21.1	21.0	0.1
2	24.6	21.0	3.6
3	21.1	20.0	1.1
6	16.7	14.0	2.7
12	18.8	16.0	2.8
31	31.5	25.0	6.5
36	9.6	12.0	−2.4
52	8.1	12.5	−4.4
76	12.2	16.7	−4.5
No. of measurements	10	10	
Mean (SD)	19.4 (8.1)	18.8 (5.7)	
Median	19.9	18.3	

Abbreviations: GAT, Goldmann applanation tonometry; IOP, intraocular pressure; WIT, wireless IOP transducer.

[a] At least 3 measurements per device were collected at each visit.

was stopped at week 36 (IOP 12 mm Hg by GAT). The reason for this transient rise in IOP was not clear.

To test preliminary concordance of the 2 sets of measurements, we performed the Brown-Forsythe test of equality of variances.[8] For each group, we computed the median value and then subtracted this value from each IOP measurement. We then performed a one-way analysis of variance using the absolute value of this transformed response. The Brown-Forsythe test produced a *P* value of .32. This is well above the .05 significance level, indicating the absence of a significant difference in group variance. This demonstrates good concordance between the measurements collected using the WIT and GAT.

Discussion

Telemetric IOP assessment through an intraocular device provides several distinct advantages when compared with the standard applanation tonometry. It allows true estimation of IOP, independent of corneal biomechanics. It even makes it possible to record IOP in eyes implanted with a keratoprosthesis. It enables self-monitoring of IOP by the patient and allows for increased frequency at which such measurements can be obtained. These abilities may provide significant insight into the role of IOP fluctuation in glaucoma progression.

An intraocular device allowing telemetric IOP measurements should have as many of the following properties as possible: be safe and biocompatible, exhibit long-term stability in accuracy and reproducibility, measure IOP as frequently as possible, be independent of ocular health and/or corneal thickness and curvature, be directly correlated with currently validated IOP measurement devices, and be user-friendly to allow self-measurements by the patient. The WIT seems to have many of the above characteristics.

The WIT is designed to be placed in the sulcus space, either concurrent with or after cataract extraction. There are several risks associated with such an implantation. Anterior iris displacement with subsequent peripheral anterior synechiae as well as angle narrowing may occur. Iris chafing leading to pigmentary glaucoma is another risk. Intraocular fibrosis around the transducer may occur, leading to impingement on the surrounding ocular structures as well as device malfunction. Our patient was monitored for all of the listed possibilities. The drainage angle did not exhibit any narrowing and there was no evidence of pigment dispersion. There was no sign of intraocular inflammation or fibrosis 1 year after implantation of the WIT. The device seems to be biocompatible in the human eye, confirming data collected during the animal studies.[7] Although no pigment dispersion was noted in this patient, it remains to be seen whether this would occur with other types of intraocular lenses that may be thicker than the plate device used in this case. A thinner version of the WIT is currently in production to minimize this risk. Studies in a larger number of eyes are needed to confirm these preliminary findings. Other diagnostic studies would also be beneficial, such as anterior-segment ocular coherence tomography, as well as long-term endothelial cell counts. Both modalities were not available at the site of the present study.

The concordance between the WIT and GAT over the course of this study was satisfactory and statistically significant. This was seen at low and high IOP values. Nevertheless, this is a relatively small number of measurements and the degree of concordance will have to be validated by future studies encompassing a larger number of data points. Data from animal experiments have shown an unexplained downward drift in IOP measurements.[7] This did not occur in ex vivo experiments or in our patient. It may also be interesting to see how the GAT measurements compare with other modalities of IOP measurements, such as rebound tonometry, especially when corneal thickness is taken into consideration.

De Smedt and colleagues[9] have studied a contact lens–like telemetric IOP sensor allowing IOP measurements over a 24-hour period. Participants had a significant, but reversible, drop in visual acuity while wearing the device and a nonsignificant trend toward decreasing comfort with increased wear time. The authors postulated that offering sensors with different radii may help to alleviate these drawbacks. Limitations of the contact lens–like technology compared with the WIT include the inability to measure the IOP over several days or months. The measurements are inferred from corneal curvature rather than actual eye tension. The accuracy of the contact lens–like device may be influenced by factors such as the fit of the contact lens onto the cornea, corneal abnormalities, and edema. Changes in the pressure of the eyelids on the cornea both during the day (due to eye movements and eyelid movements) and night (change in tonus in different stages of sleep) may also affect the measurements of the contact lens–like device.

Conclusions

The present study provides an initial favorable indication concerning the safety and biocompatibility of an implantable IOP-measuring device. The study demonstrates that the WIT is able to obtain data that seem to have initial good concordance with GAT. Further development and study of this technology may allow better understanding of the role of IOP fluctuation in glaucoma progression.

ARTICLE INFORMATION

Submitted for Publication: December 9, 2013; final revision received March 1, 2014; accepted March 4, 2014.

Published Online: June 26, 2014. doi:10.1001/jamaophthalmol.2014.1739.

Author Contributions: Dr Melki had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Study concept and design: Melki, Todani.
Acquisition, analysis, or interpretation of data: All authors.
Drafting of the manuscript: Melki, Todani.
Critical revision of the manuscript for important intellectual content: Todani, Cherfan.
Obtained funding: Melki.
Administrative, technical, or material support: All authors.
Study supervision: Melki Cherfan.

Conflict of Interest Disclosures: None reported.

Funding/Support: Implandata Ophthalmic Products GmbH provided the device at no charge.

Role of the Sponsor: Implandata Ophthalmic Products GmbH had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Additional Contributions: Statistical analysis was conducted by Amy Driscoll, MA, who received no financial compensation for her services.

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