tvst

Cornea & External Disease

Ex Vivo Evaluation of a Pressure-Sensitive Device to Aid Big Bubble Intrastromal Dissection in Deep Anterior Lamellar Keratoplasty

Alfonso Iovieno[1,2], Luigi Fontana[2], Marco Coassin[2,3], Dario Bovio[4], and Caterina Salito[4]

[1] Department of Ophthalmology and Visual Sciences, University of British Columbia, Vancouver, British Columbia, Canada
[2] IRCCS Azienda Ospedaliero-Universitaria di Bologna, Italy
[3] Department of Ophthalmology, University Campus Bio-medico, Rome, Italy
[4] Biocubica Biomedical Engineering, Milan, Italy

Correspondence: Alfonso Iovieno, Department of Ophthalmology and Visual Sciences, University of British Columbia, 2550 Willow Street V5Z3N9 Vancouver, BC, Canada. e-mail: alfonsoiovieno@hotmail.com

Received: June 13, 2022
Accepted: November 10, 2022
Published: December 29, 2022

Keywords: DALK; big bubble; medical device; keratoplasty

Citation: Iovieno A, Fontana L, Coassin M, Bovio D, Salito C. Ex vivo evaluation of a pressure-sensitive device to aid big bubble intrastromal dissection in deep anterior lamellar keratoplasty. Transl Vis Sci Technol. 2022;11(12):17, https://doi.org/10.1167/tvst.11.12.17

Purpose: To develop and perform ex vivo testing for a device designed for semiquantitative determination of intracorneal dissection depth during big bubble (BB) deep anterior lamellar keratoplasty.

Methods: A prototype device connected to a syringe and cannula was designed to determine depth of intrastromal placement based on air rebound pressure emitted by a software controlled generator. Ex vivo testing of the device was conducted on human corneas mounted on an artificial anterior chamber in three experiments: (1) cannula purposely introduced at different depths measured with anterior segment optical coherence tomography, (2) cannula introduced as per the BB technique, and (3) simulation of the BB technique guided by the device.

Results: A positive pressure differential and successful BB were observed only when the cannula was positioned within 150 microns from the endothelial plane. In all successful BB cases (21/40), a repeatable increase in tissue rebound pressure was detected, which was not recorded in unsuccessful cases. The device was able to signal to the surgeon correct placement of the cannula (successful BB) in 16 of 17 cases and incorrect placement of the cannula (unsuccessful BB) in 8 of 8 cases (94.1% sensitivity, 100% specificity).

Conclusions: In our ex vivo model, this novel medical device could reliably signal cannula positioning in the deep stroma for effective pneumatic dissection and possibly aid technical execution of BB deep anterior lamellar keratoplasty.

Translational Relevance: A medical device that standardizes big bubble deep anterior lamellar keratoplasty could increase the overall success rate of the surgical procedure and aid popularization of deep anterior lamellar keratoplasty.

Introduction

Deep anterior lamellar keratoplasty (DALK) is a surgical technique that aims at selectively replacing diseased corneal stroma, thereby leaving the recipient unaffected endothelium in place.[1,2] It is the surgical technique of choice for corneal transplantation in corneal stromal diseases, including keratoconus, corneal dystrophies, and corneal scarring limited to the stromal layer. Several techniques for performing DALK have been developed over the years.[2] The collective purpose of any DALK technique is to complete a total or subtotal uniform stromal excision. At present, successful execution of DALK is largely left to surgeon's experience. The "big bubble" (BB) technique proposed by Anwar and Teichman[3] is arguably the most popular surgical approach to DALK and is based on the forceful injection of air in the deep stroma inducing a cleavage at the level of the predescemetic or descemetic layer.[4] Formation of the BB is ultimately secondary to placement of the cannula for air injection

translational vision science & technology

in the deep stromal layers.[5,6] Consequently, the technique requires a steep learning curve and is characterized by a reported BB success rate not exceeding 80%, even in the most experienced hands.[7,8]

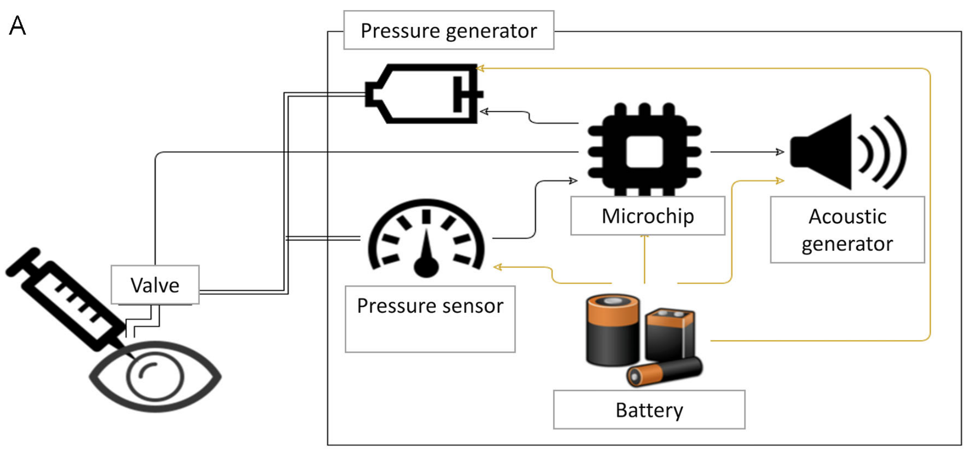
In the effort to standardize dissection in DALK and increase the BB success rate, we have developed and tested in an ex vivo setting a simple pressure-sensitive medical device to aid correct placement of the air injection cannula.

Methods

Description of the Device and Experimental Setup

The device consists of a battery-operated air pressure generator that produces high frequency micropumps of filtered air continuously into a disposable sterile inextensible tubing system. The opposite end of the tubing is connected to a disposable sterile three -way valve situated between a Luer Lock syringe and a DALK cannula of choice. The valve switch is connected to the syringe plunger and allows the surgeon to close off the system while injecting air for BB formation (Figs. 1A, B). The constant flow of small quantities of air generates a certain value of pressure within the system (Supplemental Movie). The pressure is continuously measured by a pressure sensor and a microchip for signal recording and processing. Delta P or pressure variation (ΔP) (in mm Hg) is defined as the differential in internal pressure measured between the point of final placement of the cannula before BB injection and the time of first introduction of the cannula within the stroma. A ΔP of zero is equivalent to constant pressure within the system, whereas

A



B

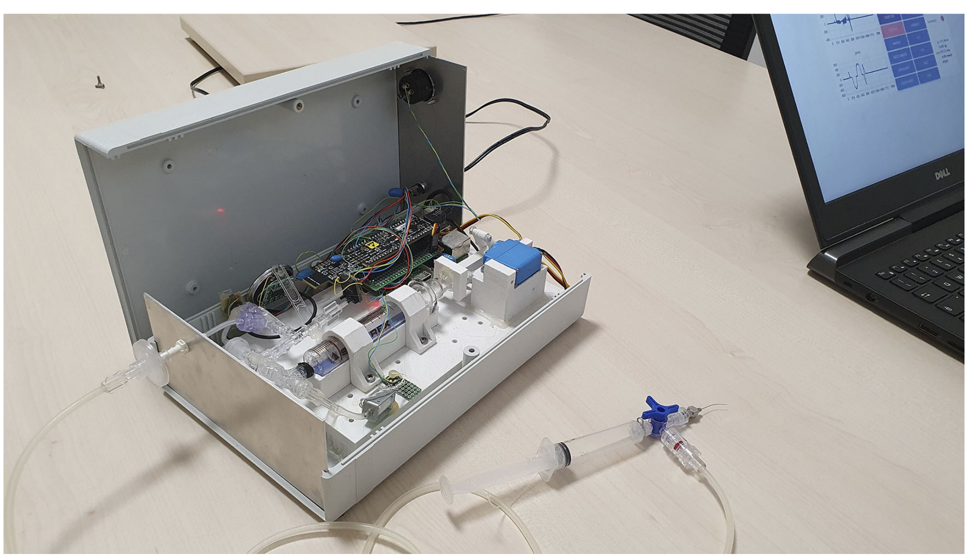


Figure 1. Schematic of the components of the device (A). Prototype used for the study experiments (B). box open to show components.

a negative or positive ΔP corresponds with a decrease or increase in the system internal pressure, respectively. Correct positioning of the cannula within the stroma for successful BB injection may be signaled to the surgeon via an acoustic generator.

Human donor corneoscleral rims deemed unsuitable for transplantation (Emilia Romagna Eye Bank, Bologna, Italy) were mounted on an artificial anterior chamber (Barron artificial anterior chamber, Katena). The duration of storage for all corneas was less than 10 days. The pressure within the artificial anterior chamber was evaluated qualitatively by digital palpation and set to mimic physiologic values. A partial thickness 8 mm trephination was performed with a set depth of 400 µm (Moria One trephine, Moria, Antony, France). A 27G reusable DALK cannula (Moria, Antony, France) connected to a 5-mL Luer Lock syringe and to the device by inextensible tubing was then introduced in the depth of the trephination and slowly advanced intrastromally toward the center. Continuous measurements with the device were obtained during cannula insertion. The ΔP is reported as median, and mean ± standard deviation. Three sets of experiments were conducted: (1) definition of signal corresponding with the depth of cannula placement, (2) definition of signal corresponding with successful BB dissection, and (3) ex vivo simulation of BB dissection guided by the device.

Definition of Signal Corresponding With the Depth of Cannula Placement

The operator purposely introduced the cannula at different depths within the cornea (superficial and deep stroma). The cannula was then withdrawn and the corneas were analyzed with anterior segment optical coherence tomography (Topcon Maestro #D OCT-1, Topcon, Japan) to image and measure the intrastromal depth (expressed as distance from the inner surface of the cornea in micrometers). Measurements corresponding with different intrastromal depths of the cannula were analyzed. After OCT imaging, the cannula was reintroduced in the previously formed track and air injection for BB formation was attempted.

Definition of Signal Corresponding With Successful BB Dissection

The purpose of this experiment was to determine whether the instrument could record a signal corresponding with successful BB formation. The operator attempted correct positioning of the cannula in the deep stroma to obtain a successful BB dissection. Measurements corresponding with successful versus unsuccessful BB were analyzed.

Ex Vivo Simulation of BB Dissection Guided by the Device

Based on the signal defined by experiment 2, we sought to verify the accuracy of the device in predicting BB formation. In this set of experiments, the operator tried to replicate ex vivo a successful BB dissection. Before injecting air, the ΔP recoding was analyzed and the operator was informed of correct or incorrect positioning of the cannula. At that point, the operator would attempt air injection for BB dissection. Sensitivity and specificity of the test were calculated.

Statistical Analyses

Statistical analysis was performed using SigmaStat version 12.5 (Systat Software, San Jose, CA). The Mann–Whitney rank-sum test was performed to assess differences of ΔP in case of successful BB dissection and when a BB was not obtained. Pearson correlation analysis was performed to compare values of ΔP and the depth of cannula placement. A P value of less than 0.05 was considered statistically significant.

Results

Definition of Signal Corresponding With the Depth of Cannula Placement

Eight corneoscleral rims were used in this experiment. BB dissection was achieved in three of eight cases. Superficial placement of the cannula and consequent failed BB produced a null or negative ΔP (Supplementary Table S1, Fig. 2). Deeper placement of the cannula and consequent successful BB dissection yielded a positive ΔP (Supplementary Table S1, Fig. 2). More negative values of ΔP corresponded with a more superficial placement of the cannula; conversely, higher positive values of ΔP marked a deeper placement of the cannula ($P < 0.0001$, $r = -0.85$) (Supplementary Table 1, Fig. 3).

Definition of Signal Corresponding With Successful BB Dissection

Forty donor corneoscleral rims were used in the experiment. BB formation was achieved in 21 corneas and failed in 19 corneas. In case of successful BB dissection, a positive ΔP within the system was detected (median, 4.4 mm Hg; mean, 6.3 ± 4.46 mm Hg) (Figs. 4A, C); when a BB was not obtained, a null or negative ΔP within the system was observed (median, −0.03 mm Hg; mean, −0.29 ± 1.56 mm Hg) (Figs. 4B, C) ($P < 0.001$).

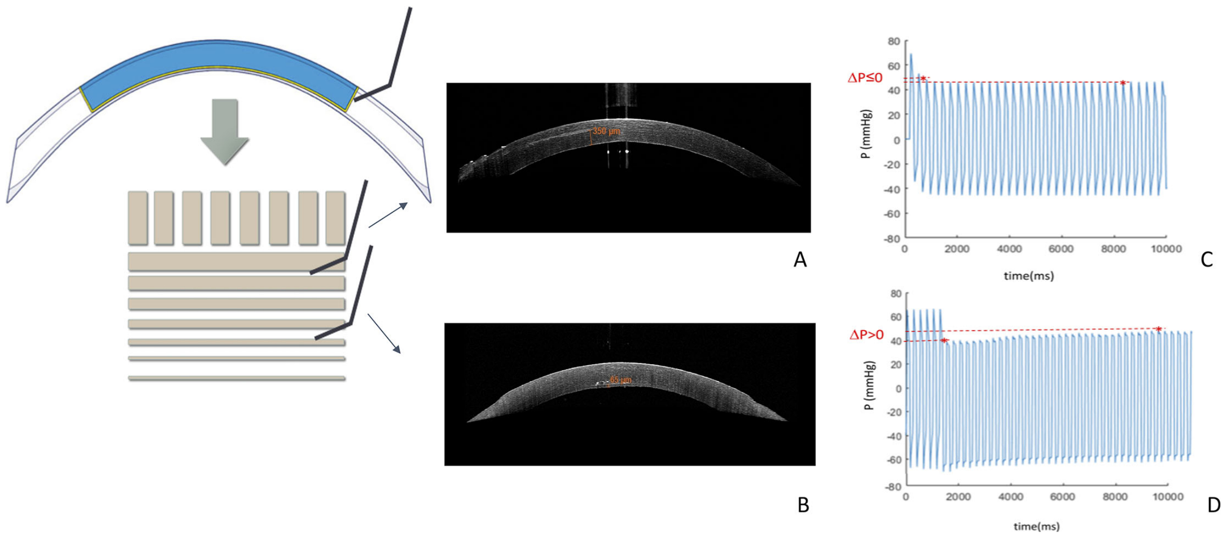


Figure 2. Positioning of the cannula at different stromal depths generates different signals. OCT image of the track created by cannula insertion in the superficial (A) and deep stroma (B) and corresponding signal detected by the device (C, D). Red asterisks and dotted lines in C and D correspond with the pressure within the system at the moment of the cannula first entry in the stroma (left asterisk) and immediately before BB injection (right asterisk). Delta P or ΔP (in mm Hg) was calculated as the differential in internal pressure measured between the point of final placement of the cannula before BB injection (asterisk to the right) and the time of first introduction of the cannula within the stroma (asterisk to the left). A ΔP of zero is equivalent to constant pressure within the system, whereas a negative or positive ΔP correspond with a decrease or increase in the system internal pressure, respectively.

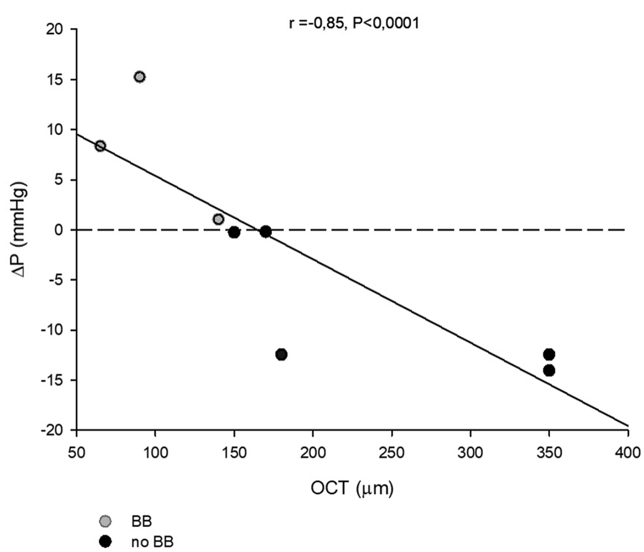


Figure 3. **The** ΔP signal corresponding to different depths of intrastromal placement of the cannula in relationship to BB success. The *x* axis reports distance from the endothelial surface of the cornea (in µm).

Ex Vivo Simulation of BB Dissection Guided by the Device

Twenty-five donor corneoscleral rims were used in this set of experiments. Successful BB formation was obtained in 17 corneas and failed in 8 corneas. In 16 of 17 successful BBs, the device signaled to the surgeon correct placement of the cannula for BB formation. Conversely, in 1 of the 17 cases a BB formed despite the device signaling an incorrect position of the cannula. In addition, the device signaled incorrect positioning of the cannula for BB formation in 8 of 8 cases of unsuccessful BB. Consequently, the device was able to signal correct placement of the cannula with 94.1% sensitivity and 100% specificity.

Discussion

Corneal stromal diseases represent a significant cause of morbidity worldwide and one of the leading indications for keratoplasty. Among them, keratoconus is characterized by corneal ectasia resulting in irregular astigmatism and often causing loss of correctible visual acuity. Although the number of keratoplasty recipients for keratoconus has been decreasing over the years, secondary in part to corneal cross-linking and improved contact lens models, keratoconus remains one of the principal corneal diseases treated with keratoplasty, following only endothelial decompensation and repeat grafting.[9–13]

DALK has been established as the procedure of choice for the surgical treatment of corneal stromal diseases. There is a consistent body of previous

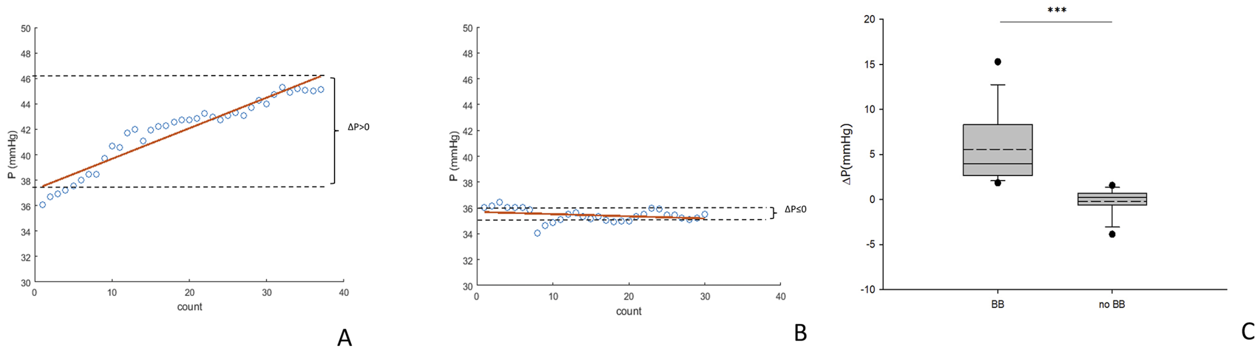


Figure 4. (A, B) Datapoints (labeled as "counts" on the *x* axis) corresponding with sequential measurements of the system internal pressure (P) in a case of successful BB (A) and unsuccessful BB (B). In the successful BB case (A), there is a gradual increase of pressure within the system (positive ΔP). In the unsuccessful BB case (B), the pressure within the system remains fairly constant and slowly declines at the moment of BB injection (flat or negative ΔP). (C) Box-and-whiskers plot comparing ΔP of successful (n = 21) vs unsuccessful (n = 19) BB dissections (***$P < 0.001$). Bars correspond with minimum (0) and maximum (100) percentiles, dotted line in the box corresponds with the median, and the solid line in the box corresponds with the mean. Dots correspond with outliers (for the BB box: 1845 and 15,278; for no BB box: −3874 and 1557).

literature which shows that DALK produces visual outcomes and postoperative astigmatism that are similar to penetrating keratoplasty, but with a lower rejection rate, increased survival, and decreased endothelial cell decay.[14–20] In addition, DALK does not alter corneal biomechanical properties, whereas an overall reduction in corneal hysteresis and resistance factor is observed after penetrating keratoplasty.[21] Last, the cost-effectiveness ratio, as outlined in Singaporean and Dutch corneal transplant registry analyses, would also favor DALK over penetrating keratoplasty.[22,23]

Despite proven superiority to penetrating keratoplasty for the treatment of corneal stromal diseases, the adoption of DALK has been somewhat suboptimal worldwide. In the 2019 EBAA Statistical Report, donor corneas used for anterior lamellar keratoplasty procedures accounted for 2.5% of domestic use.[13] This occurred despite corneal ectasias and thinning being the sixth most common surgical indication for keratoplasty in the United States overall. Consequently, 14% of penetrating keratoplasties in the United States are performed for corneal ectasia and thinning, thereby indicating gross underuse of DALK procedures. To paraphrase the 2019 EBAA statistical report, "The number of anterior lamellar keratoplasty … has been essentially flat over the last 8 years."[13] The reasons behind DALK's lack of popularity are multifactorial. Among them, the intrinsic difficulty of the surgical procedure and the long learning curve, often requiring prolonged unaccounted surgical time, seem to play a pivotal role. Popular DALK surgical techniques can be broadly divided into two categories: the ones in which cleavage of predescemetic or descemetic layer is obtained by injection of a foreign substance (e.g., air, saline solution, or ophthalmic viscoelastic material) and the ones where the deeper portion of the stroma is reached by manual layer-by-layer dissection.[2] The depth of placement of the injection cannula within the corneal stroma or depth of manual stromal dissection are largely based on personal surgical experience. Although surgeon's experience seems to affect outcomes minimally in academic settings, a definitive learning curve in single surgeon series with a decreased incidence of intraoperative complications over time has been reported.[24–26] Only referral centers performing high numbers of keratoplasties often have sufficient critical mass of surgical volume to overcome the DALK learning curve and ultimately achieve reproducible results.

In an effort to decrease intraoperator variability, standardize the surgical technique, and ultimately aid popularization of DALK we sought to conceive an inexpensive, simple, and versatile surgical device that may aid successful BB dissection. Our device does not require sterilization and uses disposable components (tubing and valve) that can be adapted to any DALK cannula of choice. Obtaining a consistent BB dissection could significantly decrease the overall surgical time and benefit efficiency in the operating room. Moreover, for surgeons needing to perform manual dissection DALK, the depth reached by the air cannula with this device could also be used a starting point to initiate manual dissection at the appropriate depth and rapidly reach the predescemetic or descemetic layer.

The depth of stromal insertion of the cannula for effective BB that could be extrapolated from our OCT experiment was roughly 150 μm from the endothelial side, which is in keeping with what was observed in previous studies.[5,6]

The device captured a positive pressure differential when the BB was achieved versus a flat or negative pressure differential in unsuccessful cases. We have hypothesized that the reason behind these observations may lie in the amount of stromal tissue present above the DALK cannula. For a successful pneumatic dissection, the DALK cannula has to be positioned within the deeper layers of the stroma. In these cases, the remaining stroma may act as a hinged flap, producing a valve mechanism that is responsible for air entrapment in the system and consequent pressure increase. In contrast, a superficial placement of the cannula may not result in external compression by the overlying stroma therefore allowing air escape and creating a flat or negative pressure differential (Fig. 2A). As a corollary to this observation, one could also postulate that not only the deep placement of the cannula is paramount in effective BB dissection, but also avoiding backtracking of air through a leaky path when the injection is performed, which is also a common observation in DALK surgery.

Another possible explanation could be that corneal stroma, because of its spongy macrostructure, would accommodate the small volume of air generated by the continuous air injection of the device, thereby not causing a pressure rise within the system.[27] Conversely, the predescemetic or descemetic layer would be less compliant and penetrable to air and produce a better sealing of the system, with a consequent increase in pressure and a positive pressure differential.

In an ex vivo setting, this device was able to signal to the surgeon correct intrastromal placement of the cannula corresponding with successful BB 94.1% of the time, which is superior to the success rate of BB dissection reported in the literature. The feedback from the device was given to the surgeon once intrastromal insertion of the cannula was completed. In an in vivo setting, we postulate that the surgeon would withdraw the cannula in case of negative signal from the device and attempt intrastromal introduction from a different point.

Presently, the only technological aid to assist cannula placement for BB dissection is offered by intraoperative anterior segment OCT (iAS-OCT). iAS-OCT produces real-time imaging of the anterior segment that could be of great help in guiding accurate placement of the cannula in BB DALK.[28–31] iAS-OCT can also guide manual dissection in DALK and contribute to early recognition and treatment of complications.[32,33] The repeatability, sensitivity, and specificity of iAS-OCT in BB-DALK have never been investigated. To date, this technology comes at a high cost, to the point that the cost effectiveness of iAS-OCT devices remains a challenge. In addition, real time imaging is often not coaxial with microscope focusing, requiring the surgeon to look away from the surgical field for an inconvenient additional focusing step. Last, DALK cannulae produce OCT shadowing, which decreases the quality of the imaging of the stromal bed under the cannula.[28] One of the advantages of our device would definitely be the lower cost of the machinery and consumables. The device signals the point of optimal penetration depth via an acoustic signal and does not require the surgeon to stop looking through the microscope binoculars at any point.

Newer, technologically advanced approaches based on evolution of OCT technology are under investigation. Shin et al.[34] showed promising results ex vivo and in a rabbit model using a custom-made 26G cannula with integrated M-mode swept source OCT in the tip. In addition, robotic fully automated or semiautomated needle insertion guided by volumetric OCT has been developed.[35] Robotic insertion and OCT-integrated cannulae have also been used in combination.[36] These cutting-edge technological approaches are presently still in early development.

In conclusion, this study proposes a simple prototypical pressure-based device that could indirectly measure depth of cannula placement in DALK by providing an acoustic signal to the surgeon once the deeper corneal stroma has been reached. The device could increase the success rate of DALK and flatten the learning curve for inexperienced surgeons. In addition, it may represent an inexpensive alternative to iAS-OCT. Future studies to further simulate surgical scenarios are in the pipeline. Additionally, we are planning a multicenter clinical trial in which the device would be used by surgeons with different levels of surgical experience with DALK.

Acknowledgments

Funded by a competitive grant awarded by the Italian Ophthalmological Society in conjunction with Fondazione Cottino for translational research in Ophthalmology ("Premio Applico" 2017).

Disclosure: **A. Iovieno**, None; **L. Fontana**, None; **M. Coassin**, None; **D. Bovio**, None; **C. Salito**, None

References

1. Luengo-Gimeno F, Tan DT, Mehta JS. Evolution of deep anterior lamellar keratoplasty (DALK). *Ocul Surf*. 2011;9(2):98–110.

2. Fontana L, Iovieno A. Techniques of anterior lamellar keratoplasty. In: Krachmer JH, Mannis M, Holland EJ, eds. *Cornea*, 3rd ed. Philadelphia, PA: Lippincott, Williams, & Wilkins; 2016:1361–1365.
3. Anwar M, Teichmann KD. Big-bubble technique to bare Descemet's membrane in anterior lamellar keratoplasty. *J Cataract Refract Surg*. 2002;28(3):398–403.
4. Dua HS, Faraj LA, Kenawy MB, et al. Dynamics of BB formation in deep anterior lamellar keratoplasty by the big bubble technique: in vitro studies. *Acta Ophthalmol*. 2018;96(1):69–76.
5. Pasricha ND, Shieh C, Carrasco-Zevallos OM, et al. Needle depth and big-bubble success in deep anterior lamellar keratoplasty: an ex vivo microscope-integrated OCT study. *Cornea*. 2016;35(11):1471–1477.
6. Scorcia V, Busin M, Lucisano A, et al. Anterior segment optical coherence tomography-guided big-bubble technique. *Ophthalmology*. 2013;120(3):471–476.
7. Feizi S, Daryabari SH, Najdi D, et al. Big-bubble deep anterior lamellar keratoplasty using central vs peripheral air injection: a clinical trial. *Eur J Ophthalmol*. 2016;26(4):297–302.
8. Li J, Chen W, Zhao Z, et al. Factors affecting formation of type-1 and type-2 big bubble during deep anterior lamellar keratoplasty. *Curr Eye Res*. 2019;44(7):701–706.
9. Gain P, Jullienne R, He Z, et al. Global survey of corneal transplantation and eye banking. *JAMA Ophthalmol*. 2016;134(2):167–173.
10. Flockerzi E, Maier P, Böhringer D, et al. Trends in corneal transplantation from 2001 to 2016 in Germany: a report of the DOG–Section Cornea and its Keratoplasty Registry. *Am J Ophthalmol*. 2018;188:91–98.
11. Williams KA, Keane MC, Coffey NE, Jones VJ, Mills RAD, Coster DJ. The Australian Corneal Graft Registry 2018 Report. Bedford Park, SA: The Australian Corneal Graft Registry; 2018:319.
12. Sklar JC, Wendel C, Zhang A, et al. Did collagen cross-linking reduce the requirement for corneal transplantation in keratoconus? The Canadian experience. *Cornea*. 2019;38(11):1390–1394.
13. 2021 Eye Bank Association of America (EBAA) Statistical Report. Washington, DC; Restore Sight; 2021.
14. Romano V, Iovieno A, Parente G, et al. Long-term clinical outcomes of deep anterior lamellar keratoplasty in patients with keratoconus. *Am J Ophthalmol*. 2015;159:505–511.
15. Keane M, Coster D, Ziaei M, et al. Deep anterior lamellar keratoplasty versus penetrating keratoplasty for treating keratoconus. *Cochrane Database Syst Rev*. 2014(7):CD009700.
16. Cheng YYY, Visser N, Schouten JS, et al. Endothelial cell loss and visual outcome of deep anterior lamellar keratoplasty versus penetrating keratoplasty: a randomized multicenter clinical trial. *Ophthalmology*. 2011;118(2):302–309.
17. Sharma N, Kandar AK, Singh Titiyal J. Stromal rejection after big bubble deep anterior lamellar keratoplasty: Case series and review of literature. *Eye Contact Lens*. 2013;39(2):194–198.
18. Borderie VM, Sandali O, Bullet J, et al. Long-term results of deep anterior lamellar versus penetrating keratoplasty. *Ophthalmology*. 2012;119(2):249–255.
19. Chen G, Tzekov R, Li W, et al. Deep anterior lamellar keratoplasty versus penetrating keratoplasty: A meta-analysis of randomized controlled trials. *Cornea*. 2016;35(2):169–174.
20. Henein C, Nanavaty MA. Systematic review comparing penetrating keratoplasty and deep anterior lamellar keratoplasty for management of keratoconus. *Contact Lens Anterior Eye*. 2017;40(1):3–14.
21. Jiang MS, Zhu JY, Li X, et al. Corneal biomechanical properties after penetrating keratoplasty or deep anterior lamellar keratoplasty using the ocular response analyzer: a meta-analysis. *Cornea*. 2017;36(3):310–316.
22. Van Den Biggelaar FJHM, Cheng YYY, Nuijts RMMA, et al. Economic evaluation of deep anterior lamellar keratoplasty versus penetrating keratoplasty in the Netherlands. *Am J Ophthalmol*. 2011;151:449–459.
23. Koo TS, Finkelstein E, Tan D, et al. Incremental cost-utility analysis of deep anterior lamellar keratoplasty compared with penetrating keratoplasty for the treatment of keratoconus. *Am J Ophthalmol*. 2011;152(1):40–47.
24. Kasbekar SA, Jones MNA, Ahmad S, et al. Corneal transplant surgery for keratoconus and the effect of surgeon experience on deep anterior lamellar keratoplasty outcomes. *Am J Ophthalmol*. 2014;158(6):1239–1246.
25. Smadja D, Colin J, Krueger RR, et al. Outcomes of deep anterior lamellar keratoplasty for keratoconus: learning curve and advantages of the big bubble technique. *Cornea*. 2012;31(8):859–863.
26. Gadhvi KA, Romano V, Fernández-Vega Cueto L, et al. Deep anterior lamellar keratoplasty for keratoconus: multisurgeon results. *Am J Ophthalmol*. 2019;201:54–62.

27. Iovieno A, Yeung SN, Nahum Y, et al. Polarimetric interferometry for assessment of corneal stromal lamellae orientation. *Cornea*. 2016;35(4):519–522.
28. Myerscough J, Friehmann A, Busin M, et al. Successful visualization of a big bubble during deep anterior lamellar keratoplasty using intraoperative OCT. *Ophthalmology*. 2019;126(7):1062.
29. De Benito-Llopis L, Mehta JS, Angunawela RI, et al. Intraoperative anterior segment optical coherence tomography: a novel assessment tool during deep anterior lamellar keratoplasty. *Am J Ophthalmol*. 2014;157(2):334–341.
30. Siebelmann S, Steven P, Cursiefen C. Intraoperative optische Kohärenztomografie bei der tiefen anterioren lamellären Keratoplastik. *Klin Monbl Augenheilkd*. 2016;233(6):717–721.
31. Liu YC, Wittwer V V., Yusoff NZBM, et al. Intraoperative optical coherence tomography-guided femtosecond laser-assisted deep anterior lamellar keratoplasty. *Cornea*. 2019;38(5):648–653.
32. Chaniyara MH, Bafna R, Urkude J, et al. Rescuing the host Descemet's membrane in full-thickness traumatic wound dehiscence in deep anterior lamellar keratoplasty: intraoperative optical coherence tomography (iOCT)-guided technique. *BMJ Case Rep*. 2017;2017: bcr2017221495.
33. Sharma N, Aron N, Kakkar P, et al. Continuous intraoperative OCT guided management of post-deep anterior lamellar keratoplasty Descemet's membrane detachment. *Saudi J Ophthalmol*. 2016; 30(2):133–136.
34. Shin S, Bae JK, Ahn Y, et al. Lamellar keratoplasty using position-guided surgical needle and M-mode optical coherence tomography. *J Biomed Opt*. 2017;22(12):1–7.
35. Draelos M, Tang G, Keller B, et al. Optical coherence tomography guided robotic needle insertion for deep anterior lamellar keratoplasty. *IEEE Trans Biomed Eng*. 2020;67(7):2073–2083.
36. Guo S, Kang JU, Sarfaraz NR, et al. Demonstration of optical coherence tomography guided big bubble technique for deep anterior lamellar keratoplasty (DALK). *Sensors (Switzerland)*. 2020;20(2):428.

Supplementary Material

Supplementary Movie. Video of the device in action. Generation of signal is started and the pressure-generator is activated.