Outcomes of Air Injection Within 2 mm Inside a Deep Trephination for Deep Anterior Lamellar Keratoplasty in Eyes With Keratoconus

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• PURPOSE: To evaluate the outcomes of a new technique for deep anterior lamellar keratoplasty (DALK) employing the injection of air up to 2 mm inside a deep trephination (intended within 100 µm from the endothelial surface) obtained with a guarded trephine set by means of anterior segment optical coherence tomography (AS OCT).
• DESIGN: Retrospective, noncomparative, interventional case series.
• METHODS: The success rate and learning curve of pneumatic dissection in one clinical practice were analyzed in nonscarred keratoconic eyes undergoing a standardized DALK including 9-mm trephination intended to a depth within 100 µm from the endothelial surface, based on the thinnest AS OCT measurement at this site; and injection of air through a cannula advanced 1–2 mm centripetally from the bottom of the trephination. Surgical parameters, success rate of pneumatic dissection, and complications were recorded.
• RESULTS: Eighty-eight eyes of 88 patients were included in the study. Pneumatic dissection succeeded in 75 of 88 eyes (85%). No significant correlation could be found between number of cases performed and success rate for this surgeon. Complications included loss of suction (n = 2, 2.3%) and perforation (n = 4, 4.6%). Conversion to penetrating keratoplasty was necessary in 1 case (1.1%).
• CONCLUSION: Setting an adjustable trephine to a depth within 100 µm from the endothelial surface eliminates the need for reaching the central cornea for successful pneumatic dissection and substantially flattens the learning curve of DALK, while achieving a constant success rate above 80% and minimizing complications. (Am J Ophthalmol 2016;164:6–13. © 2016 by Elsevier Inc. All rights reserved.)

Since its introduction in 2002, pneumatic dissection leading to the formation of the so-called “big bubble” has emerged as the most popular surgical technique employed for deep anterior lamellar keratoplasty (DALK). However, as shown by the 2014 annual report of the American Eye Bank Association, to date this procedure is performed only in a small percentage of those eyes for which it is indicated. Until now, most techniques have involved a trephination within the anterior two thirds of the stroma; the centripetal advancement of a needle/cannula into the center of the cornea, trying to reach the deep stroma; and finally the injection of air. Surgeons have done so under the assumption that, in order to maximize the success rate of pneumatic dissection, before injecting air the needle/cannula should reach the central cornea as close as possible to the posterior corneal surface. Recently, it has been confirmed that the rate of big bubble formation exceeds 90% when the needle/cannula reaches a depth within 100 µm from the internal corneal surface.

The challenge with this approach is to reach the central cornea at the proper depth with a safe and reproducible technique. Even the use of pachymetric values as reference to guide the surgical procedure has not added substantial advantages. As shown in Figure 1 (Top), setting the trephine/blade to target the thinnest central measurement still obliges the surgeons to advance the needle/cannula from a relatively superficial peripheral level all the way into the thinner central cornea, still following the surgeon’s intraoperative judgment.

To truly standardize DALK, we combined anterior segment optical coherence tomography (AS OCT) technology with the use of a trephine with predetermined and measurable blade advancement for the development of a new surgical approach. The technique is based on the assumption that it is also possible to achieve a big bubble by injection of air into the deep stroma in the peripheral cornea. If this is proven true, there would be no need for the cannula/needle to reach the center of the cornea, thus eliminating the subjectively guided part of the procedure. The technique consists of 3 main steps: exact measurement of corneal thickness at the site of trephination; calibration of the trephine to stop the blade advancement within 100 µm from the thinnest pachymetric value obtained at the site of trephination; and injection of air after minimal (1–2 mm)
centripetal introduction of a dedicated cannula into the stroma. We report herein the success rate of pneumatic dissection using this technique, the complication rate, and the learning curve observed for 1 surgeon with this technique in a series of consecutive nonscarred keratoconic eyes.

METHODS

WE REVIEWED THE CHARTS OF ALL PATIENTS WITH nonscarred keratoconus who had undergone pneumatic dissection for DALK from the initial use of this procedure from September 1, 2013 to July 31, 2015. Eyes with scarred keratoconus were excluded in an attempt at eliminating factors possibly affecting the success of pneumatic dissection, as well as optimizing the homogeneity of the study population. All eyes had been operated on by the same surgeon (M.B.) at Villa Igea Hospital in Forlì (Italy). The study followed the tenets of the 1964 Declaration of Helsinki and was approved by the local ethics committee (Comitato Etico Ospedali Privati Forlì); a detailed informed consent had been provided by all patients.

Data collected included preoperative corneal thickness measured by AS OCT (Casia; Tomey, Tokyo, Japan) over the entire cornea, surgical parameters (depth of trephination, cannula advancement, amount of air injected), success or failure of pneumatic dissection, and all complications.

Data were analyzed with the Minitab, version 16 (Minitab Inc, State College, Pennsylvania, USA). Pearson correlation was used to analyze the relationship between the number of surgeries performed and the overall success rate. A $P$ value of $<.05$ was considered statistically significant.

- **SURGICAL PROCEDURE:** In all patients anesthesia and akinesia were obtained with a peribulbar injection of 8–10 cc of ropivacaine (0.75% solution). To reach the intended depth, a suction trephine (Moria, Antony, France) with a predetermined block of the measurable blade advancement (Figure 2) was centered on the geometric center of the cornea. The measurable blade advancement can be regulated precisely only in 50-µm steps, so the trephine was set to a depth between 0 and 50 µm from the thinnest AS OCT measurement at the site of trephination (9 mm in diameter).

A temporal paracentesis was performed to soften the eye and a small air bubble was injected into the anterior chamber. Then, a blunt Fogla probe (Bausch & Lomb Storz Ophthalmics, Irvine, USA) was inserted at the base of the trephination (Figure 3, Top left) and advanced up to 1 mm into the stroma, tangentially to the corneal posterior.
surface, with the purpose of maintaining the depth reached with the trephination (Figure 3, Top right).

The probe was then exchanged for a 27 gauge Fogla cannula (Bausch & Lomb Storz Ophthalmics), which was slowly advanced, following the track obtained with the probe, up to 1 additional millimeter into the cornea (Figure 3, Bottom left) and air was gently and progressively forced into the stroma until a bubble was obtained (Figure 3, Bottom right).

DALK was then completed in all eyes according to a technique presented as a video in 2013 at the Annual Meeting of the American Academy of Ophthalmology, including baring the bubble floor only in the central 6 mm of the cornea and transplanting an anterior lamella cut by microkeratome-assisted dissection. When pneumatic dissection failed, including in the 2 cases of incomplete trephination due to loss of suction, the procedure was completed in the same way, but baring of the central 6 mm was obtained by manual dissection.

When trephination (n = 2) or cannula advancement (n = 1) caused a perforation, pneumatic dissection was attempted at a site about 3 mm away from the perforation, succeeding in creating a big bubble and allowing uneventful completion of the procedure. In the remaining case, after a macroperforation occurred during hand dissection, the procedure was converted into a 2-piece mushroom keratoplasty according to the technique described in the past.8,9

RESULTS

EIGHTY-EIGHT EYES OF 88 PATIENTS WERE IDENTIFIED. THE mean age at the time of surgery was 32.3 ± 10.4 years. There were 50 male and 38 female patients.

The average peripheral corneal thickness was 602.3 ± 46.7 μm. The intended depth of trephination (setting of the trephine block) was 500 μm in 52 eyes and 550 μm in 36 eyes (ie, 520.4 ± 24.7 μm on average). The total advancement of the cannula centripetally never exceeded 2 mm. The amount of air injected varied between 1 and 5 cc.

Intraoperative complications occurred in 6 eyes (6.8%) and included loss of suction during trephination in 2 eyes (2.3%); perforation during trephination in 2 eyes (2.3%); perforation during cannula advancement in 1 eye (1.1%); and perforation during hand dissection after failed pneumatic dissection in 1 eye (1.1%). Two of these cases could be continued as planned with successful bubble formation; in the 4 remaining cases the procedure was completed by hand dissection (n = 3, 3.4%) or converted into a mushroom keratoplasty (n = 1, 1.1%).

The overall success rate of pneumatic dissection was 85.2% (75 of 88 eyes). In all cases of successful pneumatic dissection, the bubble obtained was clinically classified as type 1, according to Dua and associates’ description.10 If eyes with complications related to trephination (n = 4) are excluded, pneumatic dissection was achieved in
88.0% (74 of 84 eyes). As shown in Figure 4, the success rate for the initial 10 cases was 80% and did not differ substantially in the following cases. An insignificant and inverse correlation was found between the number of cases and the overall success rate ($r = -0.67, P = .22$).

Postoperatively, double chamber formation was seen in 2 cases and was managed successfully by filling the anterior chamber with air through the surgical side entry. Incomplete re-epithelialization leading to peripheral superficial stromal melting was seen in 1 case, which was treated successfully with conservative therapy.

**DISCUSSION**

ALTHOUGH DALK ELIMINATES ENDOThelial REJECTION while yielding visual and refractive results substantially equal to those obtained with penetrating keratoplasty (PK), eye bank statistics show that the procedure has not yet gained popularity. The main reason for this is generally considered to be the difficulty of consistently achieving pneumatic dissection of the Descemet membrane involved in the big-bubble procedure, which has emerged as the technique of choice for DALK. In particular, the intraoperative identification of the proper location at which air has to be injected remains the main challenge. Most experts say that air must be injected into the corneal stroma only when the surgeon “feels” a reduced resistance to the advancement of the cannula/needle into the stroma, assuming that this “feeling” corresponds to reaching a level deep enough to “guarantee” the success of pneumatic dissection. To develop this “feeling” and therefore master the procedure, a steep learning curve is the rule, thus discouraging even experienced corneal surgeons from facing the challenges of DALK.

Attempts at finding a standardized technique that does not rely on surgeon “feel” for the air injection location try to use ultrasonic thickness measurements as a guide for cannula insertion. However, some of the reports do not specify how and where corneal thickness was measured, or which thickness was used as a reference target. In addition, with ultrasound (US) pachymetry, it is difficult to determine the precise location of the measurement on the cornea. This is even more important in keratoconic eyes, as corneal thickness may vary substantially owing to the presence of central/paracentral ectatic areas next to more normal peripheral cornea.

Ghanem and associates and Knutsson and associates made an incision next to a partial-thickness trephination, setting a calibrated diamond knife to 90% and 100%, respectively, of the thinnest value of corneal thickness, as measured by US pachymetry and AS OCT, minus 20 μm; then, they advanced a cannula from the bottom of the incision to the center of the cornea, with the purpose of reaching the proper location for air injection, and obtained a very high success rate of bubble formation (80%–90%).

This use of central or paracentral pachymetric values as reference for pneumatic dissection does not overcome the problem of standardization. As Figure 1 (Top) illustrates, the overall thinnest pachymetric value, precisely measured by AS OCT in the paracentral cornea, corresponds to a rather superficial level in the peripheral cornea. As a result, the cannula/needle must be advanced into depth for a quite long track and still relies on subjective judgment.

More recently, Riss and associates used Scheimpflug technology to map corneal thickness and set the intended depth of trephination to 90% of the thinnest pachymetric value at that site; however, the following surgical steps did not differ from those of conventional DALK and

![Figure 4](image-url)
<table>
<thead>
<tr>
<th>Authors</th>
<th>Pachymetry Method</th>
<th>Site of Pachymetry</th>
<th>Trephination Depth</th>
<th>Trephine</th>
<th>Bubble Formation</th>
<th>Perforation Rate</th>
<th>Conversion to PK</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anwar et al, 2002</td>
<td>Not specified</td>
<td>Not specified</td>
<td>60%–80%</td>
<td>Calibrated guided trephine system</td>
<td>80–90%</td>
<td>9%</td>
<td>0.5%</td>
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<td>Fontana et al, 2007</td>
<td>U/S (Altair, Optikon 2000, Rome, Italy)</td>
<td>Central and cone apex</td>
<td>400 μm</td>
<td>Hanna (Moria, Paris, France)</td>
<td>64%</td>
<td>13%</td>
<td>4%</td>
</tr>
<tr>
<td>Feizi et al, 2010</td>
<td>Not specified</td>
<td>Not specified</td>
<td>80%</td>
<td>Hessburg-Barron suction trephine</td>
<td>81.7%</td>
<td>4%</td>
<td>2.4%</td>
</tr>
<tr>
<td>Sarricola et al, 2010</td>
<td>Not specified</td>
<td>Not specified</td>
<td>400 μm</td>
<td>Hessburg-Barron (Kataen Products, Naples, Italy)</td>
<td>77%</td>
<td>11%</td>
<td>1%</td>
</tr>
<tr>
<td>Jhanji et al, 2010</td>
<td>U/S (Sonogage, Inc, Cleveland, Ohio, USA)</td>
<td>Not specified</td>
<td>60%–80%</td>
<td>Hessburg-Barron (JedMed Instrument Co, St Louis, Missouri, USA)</td>
<td>77%</td>
<td>20%</td>
<td>23%</td>
</tr>
<tr>
<td>Arslan et al, 2011</td>
<td>Not specified</td>
<td>Not specified</td>
<td>Not specified</td>
<td>Not specified</td>
<td>79%</td>
<td>10.1%</td>
<td>8.8%</td>
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<td>Riss et al, 2012</td>
<td>Pentacam (Oculus, Wetzlar, Germany)</td>
<td>Intended position of trephination</td>
<td>90%</td>
<td>Hessburg-Barron (Katena, Denville, New Jersey, USA)</td>
<td>80%</td>
<td>11.9%</td>
<td>16%</td>
</tr>
<tr>
<td>Smadja et al, 2012</td>
<td>AS OCT, Visante (Carl Zeiss Medical, Jena, Germany)</td>
<td>Not specified</td>
<td>80%</td>
<td>Hessburg-Barron (Katena, Denville, New Jersey, USA)</td>
<td>72.7%</td>
<td>31.8%</td>
<td>27.3%</td>
</tr>
<tr>
<td>Ghanem et al, 2012</td>
<td>Intraoperative U/S (AccuPachVI, Accutome, Malvern, Pennsylvania, USA)</td>
<td>0.8 mm inside the trephination groove</td>
<td>60%–70%</td>
<td>Hessburg-Barron (Katena, Denville, New Jersey, USA)</td>
<td>88%</td>
<td>11.0%</td>
<td>4.5%</td>
</tr>
<tr>
<td>Knutsson et al, 2015</td>
<td>U/S (Pacline; Optikon, Rome, Italy) and AS OCT, Visante (Carl Zeiss Medical, Jena, Germany)</td>
<td>Central and peripheral</td>
<td>70%</td>
<td>Hanna (Moria, Paris, France)</td>
<td>77%</td>
<td>10%</td>
<td>10%</td>
</tr>
</tbody>
</table>

AS OCT = anterior segment optical coherence tomography; PK = penetrating keratoplasty; U/S = ultrasound.
pneumatic dissection was attempted only after the cannula had been advanced up to the center of the cornea. DALK was complicated by perforation in 13 of 42 eyes (30.1%), with a rather unacceptable conversion rate to PK of 16%.

The Table summarizes the variables in the surgical technique employed to date by various surgeons performing DALK, showing a striking lack of detail about pachymetry in most series.

In an attempt at developing a different approach to the challenges of DALK, we have assumed that the success rate of pneumatic dissection relates to the depth at which air is injected but is independent of the peripheral, central, or paracentral location of the injection. Following this rationale, we have tested the feasibility of inserting the cannula at a depth within 100 μm from the endothelial surface, but limiting its advancement to less than 2 mm from the base of the trephination (Figure 1, Bottom).

To do so, we have first evaluated the peripheral corneal thickness by means of AS OCT and chosen the thinnest measurement obtained at the trephination site. Then we used a trephine with an adjustable block of the blade advancement, set to create an incision within 100 μm from the pachymetric reference value.

Finally, at the base of the trephination, the cannula was advanced centripetally in the same plane of dissection just 1–2 mm, with the only purpose of sealing the track and avoiding air reflux when injecting (Figure 1, Bottom; and Figure 3). The short distance of the insertion and the reduced resistance created by the paracentesis allowed the residual bed to “give in” as the cannula was pushed forward and were instrumental in minimizing the risk of perforation (1 of 88 cases =1.1%). This should add to the appeal of the technique, especially to inexperienced surgeons. Moreover, in the only case of perforation in our series, which occurred during the advancement of the cannula, successful pneumatic dissection was still possible after reinserting the cannula, 3 mm away from the site of perforation.

The main new evidence obtained from this study is that successful pneumatic dissection can be obtained in a very high percentage of cases with injection of air far from the central cornea, indicating that it is the depth of injection rather than the site of injection (ie, center or periphery of the cornea) that determines success. This represents very important information, especially for surgeons in training, who can thus avoid the most challenging maneuver of DALK (ie, reaching the deep corneal layers when advancing the cannula/needle up to the central cornea).

The rate of successful bubble formation obtained with a peripheral, deep injection compares favorably with those reported with the conventional DALK approach, especially considering that it was obtained with a single injection. Most of all, the high rate of successful pneumatic dissection was obtained in the absence of a learning curve,
thus offering a substantial and unique advantage over the
techniques employed to date.\textsuperscript{13,14,15}

The second major advantage of our approach concerns its
safety. No new complications were seen with our tech-
nique; also, perforation during trephination has been
-described in the past, especially for more decentered cones,
even when shallow trephination was intended.\textsuperscript{15}

Trephination caused a perforation in 2 eyes of our se-
ries, both with a thinnest peripheral pachymetric value
between 600 μm and 610 μm. In both cases the blade
advancement was set at 550 μm, thus intending to reach
a depth of 50–60 μm from the endothelial surface. We
noticed that in the other 8 eyes with thinnest peripheral
pachymetric value within the same interval, no perfora-
tion occurred despite the same depth of intended trephi-
nation (550 μm). Several sources of error or wrong
surgical maneuvers could have caused or contributed to
the occurrence of perforation. The 9-mm trephination
may have not precisely coincided with the 9-mm circle
of pachymetric analysis, thus cutting through a more cen-
tral and thinner part of the peripheral cornea; in addition,
it must be considered that the AS OCT pachymetric map
is supposed to show 8 measurements at the 9-mm circle,
but some of them may not be obtained owing to anatomical
obstacles, such as deep orbits or partial eyelid closure
(Figure 5); moreover, pachymetric values in between the
standard 8 ones may vary substantially from them.
Other sources of error may relate to surgical maneuvers:
turning the spokes to advance the blade may cause inad-
ventent movements of the blade block and therefore affect
the depth of trephination; also, pressure on the trephine
may push the blade against the residual stroma and create
an incision deeper than the intended one. Therefore, to
minimize the risk of perforation in eyes with peripheral
thickness of 600–610 μm, it may be advisable to set the
intended depth of trephination at an intermediate value,
between 500 μm and 550 μm.

The combination of an overall extremely low rate of
perforation (4 of 88 eyes = 4.5%) with an even lower rate of conversion to PK (1 of 88 eyes = 1.1%) is
superior to that described in previous studies.\textsuperscript{1,4,6,7,13–17}
In addition, the perforations that occurred during
trephination or the minimal advancement of the cannula
were still compatible with successful pneumatic dissection.

The fact that no bubble of type 2 was obtained in our series
adds to the appeal of the technique, since the type 2 bubbles
can easily break during the subsequent surgical steps while
not yielding better visual results.\textsuperscript{16} The absence of type 2
bubbles may be due to the very deep trephination, blocking
the air from spreading from the site of injection back through
the thin residual bed connecting it with the outer periphery
of the cornea, where type 2 bubbles originate.

Our new approach could also improve the success of big-
bubble DALK in eyes with centrally scarred stroma, such as
after infections. In these eyes, starting the insertion of the
cannula/needle at a stromal level below that of the scar
should be easier than trying to penetrate from more super-
ficial layers through the scarred tissue, to come to the required
depth.\textsuperscript{19} In addition, since the depth of trephination and
insertion of the cannula are possible without direct visual-
ization, it should be easier to achieve pneumatic dissec-
tion in eyes with corneal opacification.

In conclusion, we believe that as long as DALK continues
to be a surgical technique based on subjective feelings, it is
doomed to be confined to the hands of few surgeons. Instead,
a standardized technique, such as the one we have proposed,
will make DALK performable also by less experienced
corneal surgeons, thus substantially increasing the number
of procedures performed worldwide and making its advan-
tages available for a much larger number of patients.

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REFERENCES


