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Double-Docking Technique for Femtosecond Laser-Assisted Deep Anterior Lamellar Keratoplasty: A Retrospective Consecutive Case Series Study of Advanced Keratoconus

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Purpose: The aim of this study was to report the clinical outcomes and prognosis of femtosecond laser (FSL)-assisted double-docking deep anterior lamellar keratoplasty (DD-DALK) for advanced keratoconus (AK).

Methods: Records of consecutive patients with keratoconus who underwent FSL-assisted DALK (DD-DALK) were reviewed.

Results: We analyzed 37 eyes from 37 patients who underwent DD-DALK. Sixty-eight percent of eyes had a successful big-bubble formation and 27% had a manual dissection to achieve the DALK deep dissection. Stromal scarring was associated with not achieving a big bubble. Intraoperative conversion to penetrating keratoplasty was conducted in 2 cases (5%). The best-corrected visual acuity improved from a median (± interquartile range) of 1.55 ±0.25 logMAR preoperatively to 0.2 ±0.2 logMAR ($P < 0.0001$). The median postoperative spherical equivalent was −5.75 ±2.75 D with a median astigmatism of −3.5 ±1.3 D. BCVA, SE, and astigmatism were not statistically different between patients who underwent DD-DALK and patients who underwent manual DALK. Stromal scarring was associated with big-bubble (BB) formation failure ($P = 0.003$). All patients with failed BB requiring manual dissection had anterior stromal scarring.

Conclusions: DD-DALK is safe and reproducible. The success rate of BB formation is hampered by stromal scarring.

Key Words: double-docking technique, deep anterior lamellar keratoplasty, femtosecond laser, keratoconus, corneal scar, big bubble

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Deep anterior lamellar keratoplasty (DALK) is a surgical technique used to treat corneal stromal disorders, such as keratoconus. DALK has several advantages over penetrating keratoplasty (PK), especially for the limited rate of rejection.[1,2] The big-bubble (BB) technique was described by Anwar and Teichmann[3] to dissociate Descemet membrane from the posterior stroma during DALK. Although this technique allows optimal vision recovery, the BB technique is associated with a steep learning curve. The depth of air injection (~100 μm above the endothelial layer[4]) was associated with a favorable outcome for BB formation. However, the insertion of a cannula or a needle close to Descemet membrane presents a risk of perforation, which frequently requires conversion to penetrating keratoplasty (PK). To improve the reproducibility of DALK, a femtosecond laser (FSL) was used for the precision of the incisions.[5–18] We previously described a technique using FSL and intraoperative OCT to assist surgeons during surgery.[5] This technique was coined as the double-docking technique for FSL-assisted DALK (DD-DALK). FSL with intraoperative OCT enables the first lamellar resection to be performed under direct visual control (first docking), limiting the risk of corneal perforation that could occur when using a manual trephine. This lamellar resection also allows the needle or cannula to be positioned close to Descemet membrane, a prerequisite for successful BB formation.[4] After BB formation, a second docking was performed to cut the residual irregular posterior stroma with the FSL, which was subsequently removed using forceps. This second docking to remove the residual stroma minimizes surgical dissection, thereby improving the learning curve for this difficult technique. In this study, we present the results of DD-DALK in patients with advanced keratoconus and the predictive factors associated with BB formation.

MATERIAL AND METHODS

This was a retrospective study of patients with consecutive keratoconus who underwent femtosecond laser-assisted deep

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anterior lamellar keratoplasty by a single surgeon (EEG) in the ophthalmology department of the Adolphe de Rothschild Foundation Hospital (Paris, France). The research was approved by the Rothschild Foundation Hospital Review Board (IRB 00012801) under the study number CE_20210323_10_DGT. The surgical technique was described previously[5] (Video 1, http://links.lww.com/ICO/B546). In brief, surgeries were performed under general anesthesia. After a first docking under the Victus FSL platform (Bausch + Lomb, Bridgewater, NJ), a lamellar cut and vertical single-plane side cuts were made. The diameter of this lamellar cut was set at 8 mm and its depth chosen to obtain a residual stromal bed of less than 150 μm. After the stromal lamella was resected, a 30-gauge needle or a Fontana cannula was inserted in the residual stroma to pneumodissect Descemet membrane. The needle was always inserted in the stroma at equidistance between the central cornea and the edge of the first flap. After big-bubble (BB) formation, a second docking is made under the FSL platform and a cylindrical vertical stromal cut is made in the residual stromal bed, before its resection and corneal graft placement and suture. In case of BB formation failure, a manual dissection of the posterior stroma was performed using Gabison Scissors (Moria, France). The surgeries were performed by a single surgeon.

For each patient, the following information was collected: age, sex, staging of the keratoconus according to the Krumeich classification,[19] and preoperative and postoperative best-corrected visual acuity (BCVA). Visual acuity was converted to logMAR values. The corneal thickness at the thinnest point (TP) and maximum keratometry (Kmax) were acquired using a Pentacam HR topographer (Oculus, Germany). The depth of stromal hyperreflectivity (stromal scar) was measured using images acquired with Visante OCT (Carl Zeiss, Dublin, CA). For this purpose, calipers were placed at the back of the stromal hyperreflectivity, and the distance from the corneal surface to the back of the hyperreflectivity was measured and was related to the thinnest corneal thickness to obtain a ratio (Sc/TP) that aimed to estimate the relative position of the stromal scar. Values of the Sc/TP ratio range from 0 to 1; values close to 0 tend to represent anterior stromal scars, whereas as the value of the ratio increases, the stromal scar becomes more posterior. During surgery, we collected the following information: depth of the first lamellar cut and success of BB formation.

Statistics. Quantitative data were reported as median and first and third quartiles or interquartile range and compared using a nonparametric Mann–Whitney test. Receiver operating characteristic (ROC) curve analyses were performed to evaluate the prognostic value of risk factors. The area under ROC curve (AUC) was calculated for each variable. Qualitative data were compared using the Fisher exact test. A P value <0.05 was considered statistically significant. Statistical analyses were performed using GraphPad Prism 8 (GraphPad Software, La Jolla, CA).

RESULTS

Thirty-seven consecutive DD-DALK procedures performed in 37 patients were included in the study. Patient characteristics are summarized in Table 1. All patients had stage 3 or 4 keratoconus (Krumeich classification). Among them, 3 had a history of crosslinking and 25 had an anterior stromal scar without a history of hydrops.

Overall, DALK was achieved in 95% (n = 35/37). The first docking and anterior stromal lamellar resections were completed in all cases. Pneumodissection of DM from the residual stroma allowing complete BB formation was successful in 25 patients (68%; BB+ group), with a type I BB in 23 cases and a type II BB in 2 cases.[20] A manual dissection had to be performed in 12 patients (32%; BB group) after failed large bubble formation using the Melles technique with a residual stromal of approximately 50 μm (limit of the reproducibility of the Visant OCT).[13] Two macroperforations occurred in the manual dissection group (failed BB), which required conversion to full-thickness keratoplasty, and no microperforation occurred during the surgeries. The second docking and removal of the residual posterior stroma were achieved in all patients for whom we obtained BB formation. No perforation occurred during the FSL-assisted cut in either the first or second phase of dissection, and no perforation occurred either with the needle during the air injection step. Median preoperative and

TABLE 1. Patients Characteristics

	N = 37
Sex (Male/Female)	17 M/20F
Age (yr)	33 (25; 38)
Preoperative BCVA (logMar)	1.55 (1.08; 1.80)
Thinnest corneal thickness (μm)*	325 (293; 363)
Kmax (D)	66.7 (60.6; 71.8)
Keratoconus stage 4**	34
Keratoconus stage 3**	3
Stromal scar	25
Follow-up* (mo)	10 (5; 22)

*median (Q1; Q3);
**according to the Krumeich classification; BCVA: best-corrected visual acuity; F: female; Kmax: keratometry at the steepest point; M: male.

TABLE 2. Predictive Factors of Successful Big-Bubble Formation During FSL-Assisted DALK

	Successful BB (BB+; n = 25)	Failed BB (BB-; n = 12)	*P*
Age* (yr)	34 ±15	30 ± 14	NS
Sex (M/F)	10/15	7/5	NS
Preoperative Kmax* (D)	65.5 ±11.3	67.6 ± 14.2	NS
Thinnest corneal thickness* (μm)	343 ±76	297 ±88	0.01
Residual stromal bed thickness* (μm)	142 ±28	134 ± 22	NS
Stromal scar	52%	100%	0.003
Stromal scar depth* (μm)	98 ±44	228 ± 97	<0.0001
Sc/TP ratio*	0.29 ±0.19	0.94 ± 0.41	<0.0001

*median ±interquartile range; BB: big bubble; Sc/TP: stromal scar depth over the thinnest point; Kmax: keratometry at the steepest point; NS: not significant.

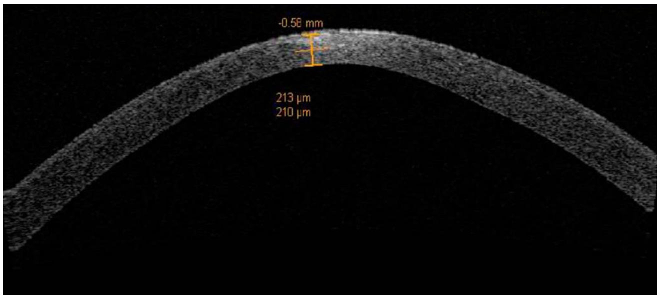

FIGURE 1. Assessment of stromal scar depth on corneal OCT images. (The full color version of this figure is available at www.corneajrnl.com.)

postoperative best-corrected visual acuity (BCVA) were 1.4 ±0.8 and 0.3 ±0.35 (P <0.0001) in the successful BB group and 1.65 ±0.4 and 0.2 ±0.35 (P <0.0001) in the group where BB failed. The preoperative and postoperative BCVA values did not differ significantly between the 2 groups. The median follow-up duration was 10 months (±20 months). The median postoperative sphere, cylinder, and spherical equivalent were −3.1 ±4.3, −4.1 ± 4.3, and −5.6 ± 4.4 in the successful BB group and −5.0 ± 4.9, −3.6 ±4.6, and −6.4 ± 5.9 in the group where BB failed, with no significant statistical difference between the 2 groups. No complications related to the use of FSL were observed.

As the first femtosecond cut always allows the injection of air in the last 100 µm of the posterior stroma, we next determined the other predictive factors associated with the realization of a successful BB (Table 2). Corneal stromal thickness and the presence of stromal scarring, which are related to the keratoconus stage, were associated with BB failure. DALK using the BB technique was successful in all patients without stromal scarring (n = 12), although it was also achieved in some patients with stromal scarring (n = 13). Importantly, all patients who underwent manual dissection after failed big-bubble formation had stromal scars (Table 2). Using this technique, we were able to reproducibly perform air injection below the requisite 100 µm and therefore to further characterize other factors influencing the big-bubble formation rate [4].

Preoperative corneal OCT images (Fig. 1) were also analyzed to further assess the influence of the stromal scar and its relative thickness within the stroma on the success rate of BB formation. The values of the thinnest point, the depth of the stromal scar, and the stromal scar/thinnest point ratio (Sc/TP) are given in Table 2 and represented in Figure 2A–C. Successful BB formation was systematically achieved in the group in which the stromal scar was more superficial, while a deeper stromal scar required manual dissection (Table 2, Fig. 2B; $P < 0.0001$). Stromal scarring located deeper than 159 µm was associated with a risk of failed BB formation (Fig. 2B and D). The calculated Sc/TP ratio (Fig. 2C) corroborates our previous finding that successful BB formation was observed in the group with a lower Sc/TP ratio (P <0.0001). The prognostic value of this ratio was studied using an ROC curve (Fig. 2E; AUROC = 0.997).

DISCUSSION

FSL-assisted DD-DALK was safe, with a high rate of success (68% complete procedure, 27% successful manual DALK completion, ie, an overall DALK success of 95%), a low perforation rate, and a low rate of intraoperative conversion to PK. This is in line with the results of Gadhvi et al,[7] who compared the success rate of FSL-assisted DALK with that of conventional DALK. Conversely, Salouti et al[13]

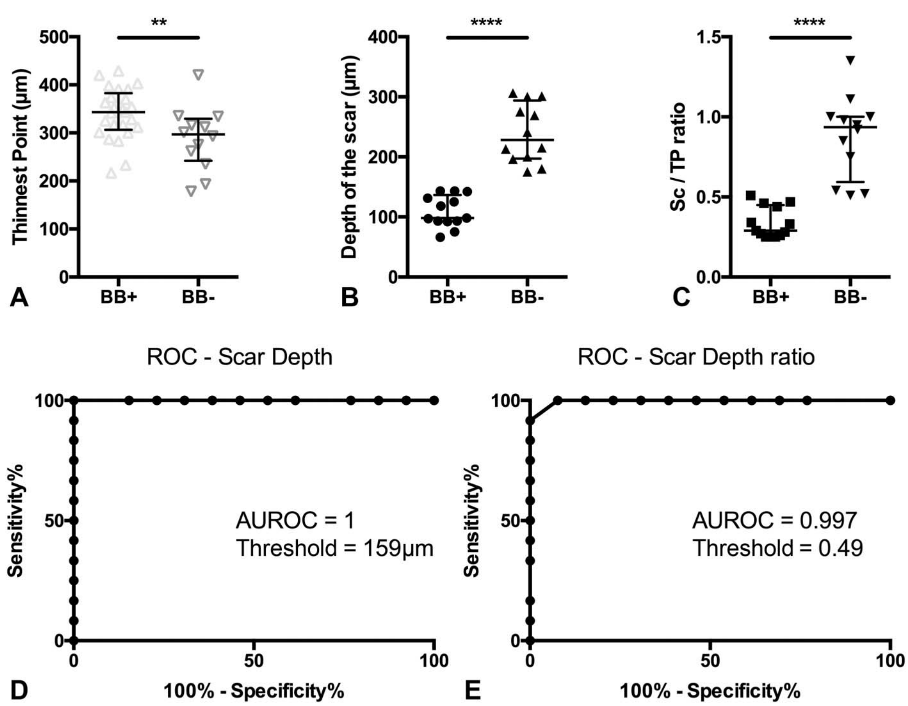

FIGURE 2. Corneal thickness and position of the stromal scar as predictive factors for successful BB formation. Diagram representing the corneal thickness at the thinnest point (A), the depth of the stromal scar (B), the ratio of the depth of the stromal scar over the thinnest corneal thickness (C), and the receiving operating characteristic (ROC) curves related to B (D) and C (E). Median and interquartile range are represented. AUROC: area under receiver operating characteristics curve; BB+: successful big-bubble formation; BB-: failed big-bubble formation; ROC: receiver operating characteristics; Sc: stromal scar; TP: thinnest point. Mann–Whitney test; **: P <0.01; ****: P <0.0001.

reported a very low conversion rate without a significant difference between FSL-assisted and conventional DALK.

In our study, BB formation was achieved in 68% of cases, which is in the range of the rates reported in the literature (53%–88%).[4,21–24] The aim of FSL-assisted DALK is to improve its reproducibility and facilitate BB formation and to minimize the subsequent surgical steps of residual posterior stromal removal. The use of FSL with intraoperative OCT enabled us to perform the anterior lamellar cut under direct visual control, which eased the positioning of the needle in the residual stroma close to Descemet membrane (first docking). However, despite the precision of the FSL cut, BB formation was not achieved in 12 patients, suggesting that other preoperative factors may influence the success rate of BB formation.

It has been suggested that maximum keratometry, central corneal thickness, surgeon skills, sex of the recipient, and trephining size influence the success rate.[24–29] In our study, BB formation failed in only a subpopulation of patients with deep anterior stromal scarring. Little is known about the realization of the BB technique in eyes with keratoconus and stromal scarring.[30] In cases of extreme corneal thinning, stromal predescemetic reorganization associated with stromal scarring strengthens the corneal stroma and may cause BB failure.[31]

Ozmen et al studied the effect of anterior stromal scarring on the success rate of DALK with the BB technique in 38 patients with keratoconus. They reported that 91% of patients successfully underwent DALK, while large bubbles were obtained in 63.2% of the procedures. They reported that the ratio of "depth of the stromal scar to the thinnest point" was significantly different between eyes with and without DALK failure due to perforation. According to their study, a threshold of 53% for an Sc/TP predicted Descemet membrane perforations with good sensitivity and specificity (100% and 62%, respectively).[30] Borderie et al[32] also suggested that deep stromal scars are associated with failure to obtain type 1 BB. The surgical technique used (DD-DALK) in our study, which consistently allowed an air injection of less than 100 μm from Descemet membrane, confirmed that an anterior stromal scar with an Sc/TP greater than 49% seems to predict big-bubble failure and thus the requirement of manual dissection. The depth of the deepest stromal scar measured with Visant anterior segment OCT was compared with the thinnest point of the keratoconus. Although new generation anterior segment OCT could have improved the measurement accuracy, all data collected were performed using the same technique to be able to compare the results of this retrospective consecutive case series.

Unlike Feizi et al[24] who have shown that a large trephination size was associated with an increase in the probability of achieving BB formation, our trephination size was standardized and did not represent a variable for the BB formation rate. In regard to the corneal thickness, our study is in accord with Michieletto et al[29] who suggested that a corneal thickness below 250 μm was associated with a risk of failed BB formation. Indeed, our failed BB group had a lower corneal thickness than the successful BB group. This feature may be associated with the stage of keratoconus and probability of developing deep stromal scarring.

Our study shows that DD-DALK is a reproducible technique in patients with keratoconus with an Sc/TP below 49% because deep stromal scars hamper BB formation and completion of the double-docking procedure. All surgeries were performed by a single surgeon (EEG). Although the success rate is similar to the commonly reported rate with the conventional DALK technique, the DD-DALK allows an easy access to the residual posterior stroma and Descemet membrane minimizing the dissection steps and therefore the learning curve of this challenging technique. Although femtosecond lasers do have the potential to make this difficult technique more successful with a single deep laser cut without the need for further stromal dissection, this would result in interface irregularities and poor visual recovery due to the irregularity of these thin and deformed corneas and due to the increased irregularities created by the laser when increasing the depth of the surgical plan. Although this femtosecond laser-assisted BB technique allows to bypass these difficulties and to improve its learning curve, it does raise the question of cost effectiveness of this expensive laser technology.

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