CASE REPORT

Femtosecond laser–assisted intrastromal corneal lenticule implantation for treatment of advanced keratoconus in a child's eye

Edna Motta Almodin, MD, MSc, Paulo Ferrara, MD, Flavia Motta Almodin Camin, MD, Juliana Motta Almodin Colallilo, MD

We present a case of a 12-year-old male patient who received a femtosecond laser-assisted intrastromal implantation of a donor corneal lenticule for the treatment of advanced keratoconus. Initially, the uncorrected distance visual acuity (UDVA) in the left eye was counting fingers (CF) and cycloplegic refraction was $-18.50 - 4.50 \times 85 = 20/400$. Preoperative corneal topography demonstrated a curvature of 65.90 \times 62/57.17 \times 152. Twelve months after lenticule implantation, the cornea was completely clear and the thickness changed from 245 µm

eratoconus is a progressive noninflammatory disorder that results in the thinning of the corneal stroma, irregular astigmatism, myopia, and corneal protrusion.^{1,2} Because correction with spectacles might be limited by the progressive nature of the corneal irregularity, the use of rigid contact lenses is usually required.

Difficulties with adaptation, discomfort, and sometimes intolerance, might prevent patients from wearing contact lenses,³ and surgical procedures might have to be considered. In the past 2 decades, new surgical techniques for the treatment of keratoconus, such as the implantation of intrastromal corneal ring segments (ICRS)⁴⁻⁷ and corneal crosslinking (CXL) with riboflavin and ultraviolet (UV) light,^{8–14} have been developed to improve visual performance and to prevent further keratoconus progression. However, in very thin corneas under 400 μm , both ICRS and CXL are contraindicated.^{7,15} New developments in CXL techniques, in particular with the use of hypoosmolar riboflavin solution, have been made to expand its use to corneas with less than 400 µm.^{12,16} However, in cases of corneas showing severe thinning and steepening, the efficacy and safety of these procedures have yet to be demonstrated.¹³

Stabilizing the cornea and halting keratoconus progression might be an important strategy to preserve visual to 639 μ m. The UDVA was CF at 2 m and refraction was $-12.25 - 2.50 \times 180 = 20/30$, whereas topography demonstrated a curvature of 61.44 \times 52/59.28 \times 142. The results showed that the procedure was successful in thickening and flattening the cornea. It is expected that penetrating or deep anterior lamellar keratoplasty, if required, could be postponed to a more suitable age.

JCRS Online Case Reports 2018; 6:25-29 © 2018 ASCRS and ESCRS.

acuity while simultaneously postponing or even preventing the inherent complications of corneal transplantation.^{17,18} In cases of children and young patients, the situation is complicated by the fact that a full-thickness corneal transplant has demonstrated a high incidence of rejection,¹⁹ the prognosis of penetrating keratoplasty (PKP) is limited, and results in children are not as good as they are in adults.20,21

We present a case of a 12-year-old patient with an extremely thin cornea who had a femtosecond laserassisted intrastromal implantation of a donor corneal lenticule to thicken and flatten the cornea so that PKP or deep anterior lamellar keratoplasty (DALK) could be postponed to a more suitable age.

CASE REPORT

A 12-year-old white boy with extremely poor visual acuity in both eyes was referred to our clinic for advanced keratoconus treatment. At the initial clinical examination, the UDVA in the left eye was counting fingers (CF) and cycloplegic refraction was $-18.50 - 4.50 \times 85 = 20/400$. The preoperative corneal topography (TMS-4, Tomey Corp.) showed a curvature of 65.90 \times $62/57.17 \times 152$ (Figure 1), whereas tomography (Allegro Oculyzer, Wavelight GmbH) demonstrated a curvature of 62.00 imes $56.4/57.50 \times 146.4$ (Figure 2). Central pachymetry (Allegro

25

Submitted: December 11, 2017 | Final revision submitted: January 11, 2018 | Accepted: January 19, 2018

From the Provisão Hospital de Olhos de Maringá, Maringá, Paraná, Brazil.

Mr. Antonio Carlos Correa reviewed and translated the text into English.

Corresponding author: Edna M. Almodin, MD, MSc, Provisão Hospital de Olhos de Maringá, R. Silva Jardim, 359, 86010-390 - Maringá - PR, Brasil. E-mail: ealmodin@ gmail.com.

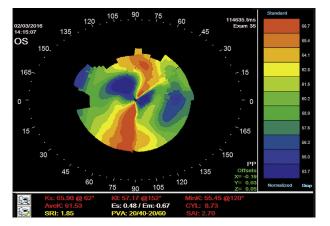


Figure 1. Preoperative topography of the cornea in the left eye.

Oculyzer, Wavelight GmbH) measured 245 μ m (231 μ m in its thinnest part). Specular microscopy (Heron, Wavetek Vision Systems, Inc.) revealed 2620 cells/mm,² and biomicroscopy demonstrated leucoma in the lower paracentral Descemet membrane.

Tests with a fluorocarbon contact lens, piggyback with gelatinous lens, scleral lens, and a semi-scleral lens resulted in lens intolerance. The very thin cornea contraindicated the implantation of ICRS or the application of CXL. Penetrating keratoplasty would incur a high risk for complications, especially at this patient's very young age. Thus, a femtosecond laser–assisted intrastromal implantation of a corneal lenticule obtained from a donor cornea was performed in an attempt to thicken and flatten the cornea.

Donor Corneal Lenticule Preparation

The donor cornea was placed in a Barron artificial chamber (Medical Mix), deepithelialized with a number 15 blade, and submitted to crosslinking (IROC Innocross AG) with the application of riboflavin (Mediocross) every 5 minutes for 30 minutes, followed by application of riboflavin every 5 minutes under UV light for another 30 minutes. Then, the cornea was stored in a flask with Optsol-GS (Bausch & Lomb, Inc.) until the moment of surgery.

On surgery day (48 hours after CXL), the donor cornea was placed in the artificial chamber of a femtosecond laser (Femto LDV Z8 Ziemer Ophthalmic Systems AG). The equipment was programmed to perform a lamellar cut at a depth of 110 μ m, followed by a second cut at a depth of 400 μ m from the surface of the cornea. A cut 6.0 mm in diameter was then performed perpendicular to the surface of the cornea. This process resulted in a corneal lenticule measuring 290 μ m thick \times 6.0 mm in diameter.

Lenticule Implantation

Once the lenticule was ready for implantation, a 9.0 mm diameter pocket centered in the optical zone, 150 μ m deep, together with a 5.0 mm incision at 12 hours, and another 2.0 mm incision at 6 hours were performed with the femtosecond laser (Figure 3). A spatula was inserted into the pocket to create the necessary space for the introduction of the lenticule. The lenticule was then introduced into the pocket through the 5.0 mm incision with the aid of a spatula. The 2.0 mm incision on the opposite side was used to aid lenticule manipulation during its introduction. After the surgical procedure was finished, the antibiotic moxifloxacin (Vigamox) and an occlusive dressing were applied.

Twenty-four hours after the surgery, the slitlamp evaluation (biomicroscopy) showed that the lenticule was well positioned and centered. The eye presented a 4 + corneal edema. Pachymetry showed a central corneal thickness (CCT) of 880 μ m.

One-week postoperatively, corneal edema had reduced to 3+, pachymetry showed that the CCT was 870 μ m, whereas optical coherence tomography (OCT) (Cirrus 5000, Carl Zeiss

Meditec AG) showed a thickness of 916 μ m. The UDVA was CF at 1.5 m. Topography demonstrated a curvature of 58.00 \times 170/ 54.92 \times 80 and tomography showed a curvature of 61.02 \times 63/ 57.07 \times 153.

At the 1-month follow-up, some corneal edema (1+) was still present. Pachymetry showed a CCT of 720 μ m (OCT = 800 μ m). The UDVA was CF at 2 m. Topography demonstrated a curvature of 59.93 \times 52/56.43 \times 142, and tomography showed a curvature of 62.00 \times 53/59.8 \times 143.

At the 3-month follow-up, biometry demonstrated a clear cornea, and pachymetry showed a CCT of 677 μ m (OCT = 771 μ m). The UDVA was CF at 2 m. Refraction was -12.00 $-5.50 \times 105 = 20/60$. Topography demonstrated a curvature of 61.38 \times 59/60.42 \times 149, and tomography showed a curvature of 63.2 \times 48/58.1 \times 138.

At the 6-month follow-up, pachymetry showed a CCT of 671 μm (OCT = 742 μm). The UDVA was CF at 2 m. Refraction was -12.25 -2.50 -180 = 20/30. Topography demonstrated a curvature of $61.82 \times 55/60.02 \times 145$, and tomography showed a curvature of $62.6 \times 54/58.3 \times 144$. The fundus examination was within normal limits for high myopia.

Twelve months after lenticule implantation, the CCT was 639 μm (OCT = 698 μm). The UDVA was CF at 2 m. Refraction was -12.25 -2.50×180 = 20/30. Topography demonstrated a curvature of 61.44 \times 52/59.28 \times 142 (Figure 4), and tomography showed a curvature of 62.90 \times 70.9/59.20 \times 160.9 (Figure 5). Figure 6 shows the progressive incorporation of the lenticule in the cornea of the left eye.

DISCUSSION

This is a delicate case of an adolescent boy who developed severe social dysfunction because of his extremely poor visual acuity caused by advanced keratoconus. He refused to communicate with anyone other than his mother, which reflected in his school performance and lack of socialization with other children. Waiting until the patient reached adulthood to increase his chances of a successful corneal transplant was unacceptable. Thus, a new approach was attempted to, at least, thicken and flatten the cornea and postpone the need for corneal transplantation until he reached adulthood.

A previous study used an isolated Bowman layer graft implanted in mid-stroma to strengthen and flatten the cornea of advanced keratoconus in a series of patients. The results reported by the authors showed a low risk for complications with a high success rate.²² Following the same rationale in the present study, a layer of corneal stroma was obtained from a donor cornea to increase the chances of cornea stabilization. Before implantation, the donor cornea was submitted to UV crosslinking to strengthen the stromal collagenous corneal matrix and to eliminate keratocytes. Because the final lenticule was basically composed of acellular tissue, the risk for allographic rejection was minimal.

Donor lenticule preparation and the corneal pocket in the receiving eye were performed with the femtosecond laser. With the introduction of the femtosecond laser several refractive procedures have become safer and more precise without the loss of corneal tissue.²³ Among the advantages of the femtosecond laser are small incisions with minimal invasiveness, excellent accuracy, predictable improvement of refractive outcomes, decreased suture-induced surgical astigmatism, and low risk for infection.²⁴

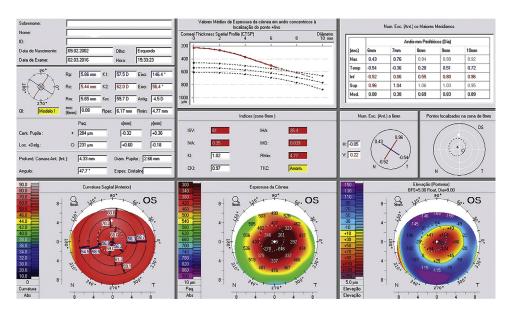


Figure 2. Preoperative tomography of the cornea in the left eye.

Previous animal studies have already demonstrated that femtosecond laser autogenous²⁵ and allogenic^{24,26} intrastromal implantation of lenticules obtained with the small-incision lenticule extraction technique are safe and feasible. In those studies, the lenticule was shown to thrive and integrate within the recipient stroma. In the present study, although a boundary between the lenticule and the adjacent stroma can be seen (Figure 6), no serious postoperative complications such as infection, haze, or diffuse lamellar keratitis were observed.

The regular follow-ups conducted after the procedure demonstrated that postoperative edema subsided and the cornea eventually became totally clear. In addition, pachymetry demonstrated that the cornea in the central optic zone increased from 290 μ m to 639 μ m 12 months later. Although visual acuity was still CF without correction, refraction showed $-12.25 - 2.50 \times 180 = 20/30$. To improve the quality of the patient's visual acuity, the adaptation of a contact lens in the left eye will be attempted.

Some corrected distance visual acuity (CDVA) improvement after the intrastromal implantation of a donor lenticule was a possibility. Previously, van Dijk et al.²² also reported that 4 of the 22 eyes treated with the transplantation of a mid-stromal isolated Bowman layer demonstrated an objective reduction in CDVA. The authors attributed such a result to the decreased irregularity of the corneal curvature after the procedure, improving optical image quality despite the low visual acuity. However, the marked CDVA improvement observed in the present study was an unexpected and surprising outcome. It was probably because of the regularization of corneal astigmatism, which reduced from 8.73 diopters (D) preoperatively to 2.16 D at 12 months postoperatively. Among the possible explanations for this decrease would be the precise centering of the lenticule inside the cornea provided by the femtosecond laser, or even the fact the donor cornea was hardened by the crosslinking treatment previously to its transplantation. Nonetheless, further clinical studies are necessary to ascertain the reasons for the marked CDVA improvement observed and whether this could become a predictable outcome.

After thickening and flattening the patient's cornea in the left eye, we opted for a more conservative approach. The

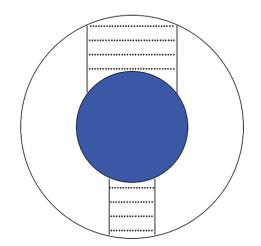


Figure 3. Femtosecond intrastromal pocket preparation.

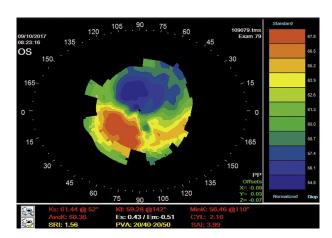
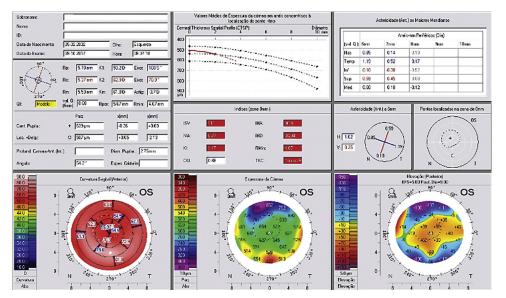
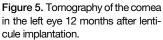


Figure 4. Topography of the cornea in the left eye 12 months after lenticule implantation.





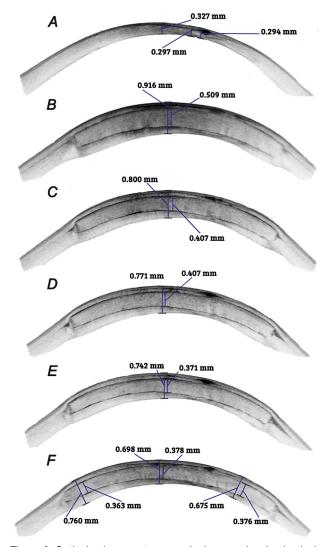


Figure 6. Optical coherence tomography images showing lenticule incorporation over time into the cornea in the left eye. *A*: Preoperative. *B*: One-week postoperatively. *C*: One-month postoperatively. *D*: Three-months postoperatively. *E*: Six-months postoperatively. *F*: Twelve-months postoperatively.

patient will be followed regularly and, in case cornea curvature in the left eye shows signs of progressive ectasia, the application of CXL might be conducted in the future. Nonetheless, It is expected that PKP or DALK, if required, might be postponed to a more suitable age.

REFERENCES

- Jhanji V, Sharma N, Vajpayee RB. Management of keratoconus: current scenario. Br J Ophthalmol 2011; 95:1044–1050
- Rabinowitz YS. Keratoconus. Surv Ophthalmol 1998; 42:297–319. Available at: http://www.keratoconus.com/resources/Major+Review-Keratoconus.pdf. Accessed February 12, 2018
- Bilgin LK, Yölmaz Ş, Araz B, Yüksel SB, Sezen T. 30 years of contact lens prescribing for keratoconic patients in Turkey. Cont Lens Anterior Eye 2009; 32:16–21. Available at: http://www.contactlensjournal.com/article /S1367-0484(08)00107-0/pdf. Accessed February 12, 2018
- Hamdi IM. Preliminary results of intrastromal corneal ring segment implantation to treat moderate to severe keratoconus. J Cataract Refract Surg 2011; 37:1125–1132
- Barbara R, Barbara A, Naftali M. Depth evaluation of intended vs actual intacs intrastromal ring segments using optical coherence tomography. Eye 2016; 30:102–110. Available at: https://www.ncbi.nlm.nih.gov/pmc/art icles/PMC4709544/pdf/eye2015202a.pdf. Accessed February 12, 2018
- Liu X-L, Li P-H, Fournie P, Malecaze F. Investigation of the efficiency of intrastromal ring segments with cross-linking using different sequence and timing for keratoconus. Int J Ophthalmol 2015; 8:703–708. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4539624/pdf/ijo-08-04-7 03.pdf. Accessed February 12, 2018
- Lago MA, Rupérez MJ, Monserrat C, Martónez-Martónez F, Martónez-Sanchis S, Larra E, Dóez-Ajenjo MA, Peris-Martónez C. Patient-specific simulation of the intrastromal ring segment implantation in corneas with keratoconus. J Mech Behav Biomed Mater 2015; 51:260–268
- Elbaz U, Shen C, Lichtinger A, Zauberman NA, Goldich Y, Ziai S, Rootman DS. Accelerated versus standard corneal collagen crosslinking combined with same day phototherapeutic keratectomy and single intrastromal implantation for keratoconus. Br J Ophthalmol 2015; 99:155–159
- Schuerch K, Tappeiner C, Frueh BE. Analysis of pseudoprogression after corneal cross-linking in children with progressive keratoconus. Acta Ophthalmol 2016; 94:e592–e599. Available at: http://onlinelibrary.wiley.com /doi/10.1111/aos.13060/epdf. Accessed February 12, 2018
- Viswanathan D, Kumar NL, Males JJ. Outcome of corneal collagen crosslinking for progressive keratoconus in paediatric patients. Biomed Res Int 2014; article ID140461. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles /PMC4071785/pdf/BMRI2014-140461.pdf. Accessed February 12, 2018
- Arora R, Jain P, Goyal JL, Gupta D. Comparative analysis of refractive and topographic changes in early and advanced keratoconic eyes undergoing corneal collagen crosslinking. Cornea 2013; 32:1359–1364

- Sloot F, Soeters N, van der Valk R, Tahzib NG. Effective corneal collagen crosslinking in advanced cases of progressive keratoconus. J Cataract Refract Surg 2013; 39:1141–1145
- 13. Ivarsen A, Hjortdal J. Collagen cross-linking for advanced progressive keratoconus. Comea 2013; 32:903–906
- 14. Arora R, Gupta D, Goyal JL, Jain P. Results of corneal collagen cross-linking in pediatric patients. J Refract Surg 2012; 28:759–762
- Chan E, Snibson GR. Current status of corneal collagen cross-linking for keratoconus: a review. Clin Exp Optom 2013; 96:155–164. Available at: http://onlinelibrary.wiley.com/doi/10.1111/cxo.12020/pdf. Accessed February 12, 2018
- Raiskup F, Spoerl E. Corneal cross-linking with hypo-osmolar riboflavin solution in thin keratoconic corneas. Am J Ophthalmol 2011; 152:28–32
- Niziol LM, Musch DC, Gillespie BW, Marcotte LM, Sugar A. Long-term outcomes in patients who received a corneal graft for keratoconus between 1980 and 1986. Am J Ophthalmol 2013; 155:213–219.e3
- Alvarez de Toledo J, de la Paz MF, Barraquer RI, Barraquer J. Long-term progression of astigmatism after penetrating keratoplasty for keratoconus; evidence of late recurrence. Cornea 2003; 22:317–323
- Gupta PC, Ram J. Results of deep anterior lamellar keratoplasty for advanced keratoconus in children less than 18 years [letter]. Am J Ophthalmol 2016; 167:97; reply by R Arora, P Jain, P Jain, A Manudhane, J Goyal, 97–98. Available at: http://www.ajo.com/article/S0002-9394(16)30186-6 /pdf. Accessed February 12, 2018
- O'Hara MA, Mannis MJ. Pediatric penetrating keratoplasty. Int Ophthalmol Clin 2013; 53 (2):59–70
- Huang C, O'Hara M, Mannis MJ. Primary pediatric keratoplasty: indications and outcomes. Cornea 2009; 28:1003–1008
- van Dijk K, Liarakos VS, Parker J, Ham L, Lie JT, Groeneveld-van Beek EA, Melles GRJ. Bowman layer transplantation to reduce and stabilize progressive, advanced keratoconus. Ophthalmology 2015; 122:909–917

- 23. Vestergaard A, Ivarsen A, Asp S. Hjortdal JØ. Femtosecond (FS) laser vision correction procedure for moderate to high myopia: a prospective study of ReLEx[®] flex, and comparison with a retrospective study of FS-laser in situ keratomileusis. Acta Ophthalmol 2013; 91:355–362. Available at: http://onlinelibrary.wiley.com/doi/10.1111/j.1755-3768.2012.02406.x/pdf. Accessed February 12, 2018
- Zhao J, Shen Y, Tian M, Sun L, Zhao Y, Zhang X, Zhou X. Corneal lenticule allotransplantation after femtosecond laser small incision lenticule extraction in rabbits. Cornea 2017; 36:222–228
- Liu H, Zhu W, Jiang AC, Sprecher AJ, Zhou X. Femtosecond laser lenticule transplantation in rabbit cornea: experimental study. J Refract Surg 2012; 28:907–911
- 26. Liu R, Zhao J, Xu Y, Li M, Niu L, Liu H, Sun L, Chu R, Zhou X. Femtosecond laser-assisted corneal small incision allogeneic intrastromal lenticule implantation in monkeys: A pilot study. Invest Ophthalmol Vis Sci 2015; 56:3715–3720. Available at: http://iovs.arvojournals.org/article.aspx?arti cleid=2319736. Accessed February 12, 2018

Disclosures: None of the authors has a financial or proprietary interest in any material or method mentioned.



First author: Edna Motta Almodin, MD, MSc

Provisão Hospital de Olhos de Maringá, Maringá, Paraná, Brazil