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Tectonic keratoplasty using small incision lenticule extraction-extracted intrastromal lenticule for corneal lesions

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Abstract

Objective: This study investigated an alternative approach for obtaining donor corneas for keratoplasty that can be used in nations with high corneal demand and high costs for treatment of non-healing ulcers or lesions.

Methods: Eighteen patients (18 eyes) who underwent tectonic keratoplasty using small incision refractive lenticule extraction (SMILE)-extracted lenticule were included. Data were recorded regarding age, corneal status, corneal lesion location and size, preoperative and postoperative visual acuity, lenticule layer, and additional medical history.

Results: Corneal thinning and corneal perforation in 13 and 5 patients, respectively, were treated with tectonic keratoplasty using SMILE-extracted lenticule. After tectonic keratoplasty, globe integrity was maintained in 16 of the 18 patients. The mean decimal visual acuity improved from 0.2555±0.3326 preoperatively to 0.3303±0.3487 at the final follow-up. Visual acuity improvement was greater in patients with corneal perforation than in patients with corneal thinning. In addition, visual acuity was most improved in patients with infratemporal lesions.

Conclusion: Tectonic keratoplasty using SMILE-extracted lenticule is a comparatively safe, effective, and reliable alternative approach for the treatment of corneal lesions.

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Keywords
Cornea transplantation, corneal lesions, small incision refractive lenticule extraction, lenticule, corneal perforation, corneal thinning, visual acuity, tectonic keratoplasty

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Introduction

Corneal lesions, such as corneal thinning and perforation, are sight-threatening complications of corneal diseases.[1] Urgent surgical intervention is therefore necessary to preserve the anatomic integrity of the eyeball and prevent disastrous complications such as retinal detachment, secondary glaucoma, endophthalmitis, and panuveitis.[2] Thus far, corneal gluing, bandage contact lens, amniotic membrane transplantation, and conjunctival flap can be used as temporary treatments for corneal lesions.[3,4] However, the long-term outcomes of bandage contact lens, multilayered amniotic membrane transplantation, and conjunctival flaps are unsatisfactory. Furthermore, for most patients with corneal lesions, corneal transplantation is the sole treatment option currently available.[5,6] However, a shortage of donor corneas is an important limiting factor in corneal transplantation, especially in developing countries such as China, where the graft demand is very high.[7] Small incision refractive lenticule extraction (SMILE) is a femtosecond laser technique used for the correction of myopia and myopic astigmatism; this technique uses the VisuMax FS laser system (Carl Zeiss Meditec, Jena, Germany) to extract intrastromal corneal lenticule.[8] In this study, we used intrastromal lenticule extracted with the SMILE procedure as corneal patch graft in tectonic keratoplasty for the treatment of corneal thinning and perforation.

Methods

Patients

This study protocol was approved by the Institutional Ethics Committee of the First Hospital of Jilin University and was performed in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained from all patients prior to participation in this study. This non-comparative retrospective study included patients who were diagnosed with corneal lesions (corneal thinning or corneal perforation) secondary to ocular pathology (e.g., corneal ulcer, recurrent pterygium, blepharokeratoconjunctivitis, limbal dermoid, exposure keratitis, and/or pseudopterygium) and who underwent tectonic keratoplasty using SMILE-extracted lenticule in the Department of Ophthalmology of the First Hospital of Jilin University, Changchun, China from March 2017 to October 2018. Patients with very large corneal lesions, bilateral ocular defects requiring intervention, and/or prior cornea transplantation were excluded from the study. From the medical charts of eligible patients, data were recorded regarding age, sex, diagnosis, corneal status, corneal lesion location and size, preoperative and postoperative visual acuity (VA), lenticule layer used for transplantation, surgical procedure, and additional medical history. VA was recorded using the decimal system. The corneal

lesion size and location were determined by slit-lamp examination or anterior segment optical coherence tomography (Visante OCT, Carl Zeiss Meditec). Corneal perforation was assessed by slit-lamp examination or by Seidel test with fluorescein staining. All lenticule donors who underwent the SMILE procedure had provided written informed consent for donation. All donors were healthy individuals and ranged in age from 16 to 35 years. The donor inclusion criteria were myopic spherical refractive error of -6 to -10 diopters; astigmatism <-0.5 diopters; negative serological findings for infectious disease; no malignancy, ocular disease, or ocular infection; and no systemic disease.

Surgical procedure

Under retrobulbar block, the initial surgical procedure was performed; debridement was performed in patients with corneal ulcer, while excision was performed in patients with dermoid or recurrent pterygium. The size of the corneal lesion was then measured using a caliper. SMILE lenticule, extracted using a VisuMax Femtosecond laser, was placed in the area with lesion. In patients who received single-layer lenticules, size 10-0 nylon cardinal sutures (synthetic, monofilament, and non-absorbable; Ethicon, San Lorenzo, Puerto Rico) were placed at 12 o'clock and 6 o'clock, immediately followed by cardinal sutures at 3 o'clock and 9 o'clock. Subsequently, the remaining sutures were placed. In patients who received double-layer lenticules, the single lenticule pieces were trimmed to the size of the lesion and then sutured using three interrupted 10-0 nylon sutures at 1 o'clock, 4 o'clock, and 9 o'clock. A second lenticule piece was placed over the sutured lenticule and both lenticules were sutured together with interrupted 10-0 nylon sutures.

Postoperative treatment and evaluation

Postoperatively, patients were prescribed topical 0.3% ofloxacin (Allergan, Irvine, CA, USA) four times per day for 2 months, as well as topical steroids (1% prednisolone, Allergan) four times per day for 1 month. After 1 month, steroid treatment was gradually tapered to twice per day, then maintained at that dosage for 6 months. There were no steroid-related complications. Artificial tear eye drops were also prescribed. Patients with blepharokeratoconjunctivitis were advised to scrub the eyelid with tea tree oil, maintain lid hygiene, and use warm compression daily. In addition, antibiotic eye ointment (0.3% ofloxacin eye ointment: Santen, Japan) was administered to all patients, twice daily for the first month. In patients with fungal keratitis, topical antifungal drugs (5% natamycin; Alcon, Fort Worth, TX, USA) were used. Patients were examined postoperatively on days 1, 2, 4, 7, 14, and 21; they were then examined once per month for 6 months. Slit-lamp microscopy was used to assess the healing of the cornea on first postoperative day. The following assessments were performed at each follow-up visit, beginning on postoperative day 7: best-corrected decimal VA, slit-lamp microscopy, and anterior segment optical coherence tomography. All complications were recorded. Surgical success was defined as recovery of corneal thinning or perforation and survival of the corneal grafts.

Statistical analysis

All statistical analyses were conducted using PASW Statistics for Windows, version 18.0 (SPSS Inc., Chicago, IL, USA). Quantitative data were expressed as mean $\pm$ standard deviation and qualitative data were expressed as number (percentage). Because there were fewer than 40 patients,

the comparisons among patients were performed using Fisher's exact test. $P < 0.05$ was considered statistically significant.

Results

We evaluated 18 patients with various corneal lesions who underwent tectonic keratoplasty using SMILE-extracted lenticule. After application of inclusion and exclusion criteria, all 18 patients were included in the analysis. Tables 1 and 2 describe the characteristics of the included patients. Notably, in two patients (11.1%), the surgical outcome was poor; re-implantation of the lenticule was performed in one patient with exposure keratitis and conjunctival flap surgery was performed in a patient

Table 1. Summary of patient demographic and clinical characteristics.

Characteristic	
Sex, M/F (n [%])	10/8 (55.6%/44.4%)
Age, years (mean ± standard deviation [range])	46.2±25.2 (7–82)
Prior medical history, yes/no (n [%])	6/12 (33.3%/66.7%)
Occupation	
Farmer (n [%])	7 (38.9%)
Student (n [%])	6 (33.3%)
Other (n [%])	5 (27.8%)
Affected eye, left/right (n [%])	7/11 (38.9%/61.1%)
Predisposing pathology	
Corneal ulcer (n [%])	11 (61.1%)
BKC (n [%])	2 (11.1%)
Limbal dermoid (n [%])	2 (11.1%)
Recurrent pterygium (n [%])	1 (5.6%)
Exposure keratitis (n [%])	1 (5.6%)
Pseudopterygium (n [%])	1 (5.6%)
Corneal status	
Thin (n [%])	13 (72.2%)
Perforated (n [%])	5 (27.8%)
Lesion location	
Infratemporal (n [%])	8 (44.4%)
Central (n [%])	6 (33.3%)
Nasal (n [%])	2 (11.1%)
Supratemporal (n [%])	1 (5.6%)
Infranasal (n [%])	1 (5.6%)
Lesion size	
<3 mm × 3 mm (n [%])	4 (22.2%)
≥ 3 mm × 3 mm (n [%])	14 (77.8%)
Preoperative visual acuity, decimal (mean ± standard deviation [range])	0.2555±0.3326 (light perception–1.00)
Postoperative visual acuity, decimal (mean ± standard deviation [range])	0.3303±0.3487 (light perception–1.00)
Graft lenticule layer	
Single (n [%])	11 (61.1%)
Double (n [%])	7 (38.9%)
Postoperative visual acuity outcome, unchanged/improved (n [%])	11/7 (61.1%/38.9%)

Abbreviations: M, male; F, female; BKC, blepharokeratoconjunctivitis.

Table 2. Detailed patient demographic and clinical characteristics.

Age/eye/sex	Diagnosis	Symptoms	Corneal status	Lesion location	Lesion size (mm)	Preoperative VA (decimal)	Postoperative VA (decimal)	Lenticule layer	Follow-up period (months)	Medical history	Occupation
66/L/M	Recurrent pterygium	FB sensation	Thinning	IF	3 × 3	0.8	0.8	Single	16	No	Other
82/L/F	CU	Iris prolapse	Perforation	IF	4 × 3	HM	0.1	Single	12	No	Other
77/L/M	CU	Redness	Thinning	Central	5 × 5	LP	LP	Single	14	DM	Farmer
19/R/F	Limbal dermoid	FB sensation	Thinning	IF	2 × 3	0.25	0.5	Single	14	No	Student
41/R/M	Exposure keratitis	FB sensation	Thinning	Central	5 × 4	0.01	0.01	Single	12	Brain tumor	Other
41/R/M	CU	Redness	Thinning	Central	5 × 4	HM	HM	Single	18	No	Farmer
50/L/F	CU	Iris prolapse	Perforation	IF	5 × 4	HM	0.1	Single	12	HTN, RA	Farmer
18/R/M	BKC	Iris prolapse	Perforation	IF	2 × 2	0.2	0.3	Single	12	No	Student
22/R/M	Mooren CU	Redness	Thinning	ST	3 × 4	0.5	0.5	Double	14	No	Student
65/R/M	CU	Redness	Thinning	IF	4 × 4	0.4	0.5	Double	13	No	Farmer
69/L/F	CU	Redness	Thinning	Central	3 × 4	0.01	0.01	Double	13	No	Farmer
66/R/F	CU	Redness	Thinning	IF	5 × 5	0.01	0.01	Double	12	RA	Farmer
7/R/F	Pseudopterygium	FB sensation	Thinning	IN	4 × 4	0.5	0.8	Double	11	Keratoconus	Student
61/R/M	CU	Redness	Thinning	Central	3 × 4	LP	LP	Single	11	No	Farmer
76/L/M	CU	Iris prolapse	Perforation	Nasal	3 × 2	0.8	0.8	Double	10	DM, HTN	Other
14/R/M	Limbal dermoid	FB sensation	Thinning	IN	3 × 3	1	1	Single	10	No	Student
44/L/F	CU	Redness	Thinning	Central	4 × 5	0.01	0.01	Single	9	No	Other
14/R/F	BKC	Iris prolapse	Perforation	IF	2 × 2	0.1	0.5	Double	19	No	Student

Abbreviations: M, male; F, female; L, left; R, right; IF, infratemporal; IN, infranasal; DM, diabetes mellitus; HTN, hypertension; RA, rheumatoid arthritis; CU, corneal ulcer; BKC, blepharokeratoconjunctivitis; HM, hand motion; LP, light perception; VA, visual acuity.

with corneal ulcer to seal the perforation and preserve the anatomical structure of eyeball.

Stratification on the basis of postoperative VA outcome revealed that there were no significant differences in age, sex, affected eye, predisposing pathology, lesion size, lenticule layer, follow-up period, or occupation. However, corneal status and lesion location significantly differed on the basis of postoperative VA outcome ($P < 0.05$). VA improvement was greater in patients with corneal perforation than in patients with corneal thinning. In addition, VA was most improved in patients with infratemporal lesions (Table 3).

Stratification on the basis of corneal status revealed no differences in age, sex, affected eye, predisposing pathology, lesion location, lenticule layer, or follow-up period. However, there was a significant difference in lesion size on the basis of corneal status ($P < 0.05$). Corneal perforation was more common in patients with lesion size $< 3\,\text{mm} \times 3\,\text{mm}$, whereas corneal thinning was more common in patients with lesion size $\geq 3\,\text{mm} \times 3\,\text{mm}$ (Table 4).

Discussion

Corneal thinning involves a reduction in the total thickness of the cornea, which may lead to perforation in severe cases.[9] Corneal perforation is an ophthalmic emergency that requires immediate intervention. In addition to the risk of permanent loss of vision, these lesions may reduce patients' quality of life. The etiology of corneal perforation can be traumatic (e.g., penetrating trauma or burns) or non-traumatic (e.g., corneal infections [bacterial, viral, or fungal] or autoimmune keratitis).[1,10–12] If left untreated, corneal thinning can result in perforation, which involves various complications including severe loss of anterior segment anatomical integrity, as well as endophthalmitis, panuveitis, secondary glaucoma, and irreversible vision loss.[2] Hence, timely diagnosis and proper intervention is needed to prevent these complications. Numerous treatment options are available based on the size and location of the lesion.[4,13] However, for patients with unresponsive lesions and for patients with large perforations, keratoplasty is the only treatment option.[14] Although keratoplasty is an effective and safe surgical approach for the treatment of corneal lesions, it has a few limitations in developing nations including lack of access to an eye bank, high cost of donor cornea, severe shortage of corneal tissue, lack of trained ophthalmologist/eye care providers, and patient resistance to transplantation.[15,16] Of these limitations, the severe shortage of corneal tissue is the primary barrier in developing nations.

In this study, we performed tectonic keratoplasty using SMILE-extracted lenticule in patients with corneal lesions. The aim of tectonic keratoplasty using SMILE-extracted lenticule is to restore eyeball integrity and facilitate visual rehabilitation. The procedure was successful for 16 of 18 patients in the initial attempt; of the remaining two patients, one underwent re-implantation of the lenticule and one underwent conjunctival grafting. Furthermore, we observed that the eyeball integrity was restored in all patients who underwent the tectonic keratoplasty procedure. No adverse effects were observed during the follow-up period, such as infection, graft melting, or graft rejection. We concluded that this procedure is effective for preservation of the anatomical eyeball structure. Our findings are consistent with those of Wu et al.,[17] who reported the use of SMILE lenticule as a patch graft in six patients with corneal ulcer perforation; notably, they suggested that the application of SMILE-extracted lenticule may be a reliable and efficient surgical alternative for closure of corneal perforation, as well as

Table 3. Comparisons between patients based on postoperative visual acuity outcome.

Variable	Improved VA	Unchanged VA	*P*
Sex			
Male	2	8	0.145
Female	5	3	
Age			
<60 years	5	5	0.367
≥60 years	2	6	
Occupation			
Farmer	2	5	
Student	4	2	0.280
Other	1	4	
Affected eye			
Left	2	5	0.637
Right	5	6	
Predisposing pathology			
Corneal ulcer	3	8	0.332
Other	4	3	
Corneal status			
Thinning	3	10	0.047
Perforation	4	1	
Lesion location			
Infratemporal	6	2	0.010
Central	0	6	
Other	1	3	
Lesion size (mm)			
<3 mm × 3 mm	3	1	0.245
≥3 mm × 3 mm	4	10	
Lenticule layer			
Single	4	7	1.000
Double	3	4	
Follow-up period (months)			
≤12	4	6	1.000
>12	3	5	

Abbreviation: VA, visual acuity.

for maintenance of the anatomical eyeball structure.

Based on our findings, we recommend single-layer lenticule for patients with superficial lesions, as well as those with uncomplicated lesions; we recommend double-layer lenticule for patients with deep, large, and complicated corneal lesions. In this study, we observed that mean best-corrected VA was improved after the procedure, which indicates that tectonic keratoplasty using SMILE-extracted lenticule is effective for visual recovery. Similarly, Jiang et al.[18] observed improved VA in 22 eyes with corneal ulcer and perforation that underwent tectonic keratoplasty using SMILE-extracted lenticule; they also suggested that this approach could be used for treatment of inflammation.

In our study, the extracted lenticule was sutured using interrupted 10-0 nylon sutures; this approach was advantageous

Table 4. Comparisons between patients based on corneal status.

Variable	Corneal thinning	Corneal perforation	*P*
Sex			
Male	8	2	0.608
Female	5	3	
Age			
$<$ 60 years	7	3	1.000
$\geq$ 60 years	6	2	
Affected eye			
Left	4	3	0.326
Right	9	2	
Predisposing pathology			
Corneal ulcer	8	3	1.000
Other	5	2	
Lesion location			
Infratemporal	4	4	0.119
Central	6	0	
Other	3	1	
Lesion size (mm)			
$<$3 mm $\times$ 3 mm	1	3	0.044
$\geq$3 mm $\times$ 3 mm	12	2	
Lenticule layer			
Single	8	3	1.000
Double	5	2	
Follow-up period (months)			
$\leq$12	6	4	0.314
$>$12	7	1	

in that it reduced the risks of corneal epithelial erosion, recurrent graft loss, granulomatous keratitis, and Tenon's cyst, all of which are common complications associated with the use of fibrin glue for grafting.[19] The major limitations of this study were its small sample size and short follow-up period. Hence, a larger prospective study with long-term follow-up is needed to confirm our findings.

In conclusion, tectonic keratoplasty using SMILE-extracted lenticule is a comparatively safe, effective, and reliable alterative approach for the treatment of corneal lesions. In addition to maintaining the anatomical eyeball integrity and facilitating visual rehabilitation, it is functionally and cosmetically effective. Furthermore, this technique can be used in emergency conditions, and can resolve the problems of donor shortage and high cost of donor cornea in developing nations.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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