Article

Discovery Medicine 2026; 38(210): 2201–2209
https://doi.org/10.24976/Discov.Med.202638210.172

The Corneal Wound Healing Process Following Limbal Relaxation Incision in Rabbits

Miaoying Zhang[1,*], Xianling Luo[1]

[1]Department of Ophthalmology, Fuyang Campus of Zhejiang Provincial People's Hospital (The First People's Hospital of Fuyang), 311400 Hangzhou, Zhejiang, China

*Correspondence: Zmy37487703@163.com (Miaoying Zhang)

Submitted: 5 March 2026 Revised: 15 May 2026 Accepted: 29 May 2026 Published: 23 July 2026

Background: Through animal experiments, the effects of Limbal relaxation incision (LRI) on corneal healing were preliminarily observed, aiming to explore the process of corneal limbal wound healing.

Methods: A rabbit LRI surgical model was established and dynamically observed until 90 days after the operation. The haze scoring system and a modified Draize eye irritation test were used to quantify corneal opacity and irritation responses. Corneal epithelial integrity and dry eye disease were evaluated using fluorescein sodium staining. Hematoxylin and eosin (HE) staining was applied to observe the pathological changes in corneal tissue. Immunofluorescence staining was used to detect the expression of the proliferation marker Ki-67 in epithelial cells and the myofibroblast marker α-smooth muscle actin (α-SMA).

Results: At 7 days postoperatively, the cornea showed opacity, dilation, epithelial defect and inflammatory responses. Ki-67 expression, a marker of epithelial cell proliferation, peaked at 7 days after the surgery and then gradually decreased. The activation of myofibroblasts α-SMA peaked at 30 days after the surgery, accompanied by corneal stroma thickening. From 30 to 60 days after the surgery, corneal opacity, inflammatory responses, dry eye syndrome and epithelial damage gradually improved. By 90 days after the surgery, corneal transparency was largely restored, vascular congestion was no longer evident, and the tissue architecture nearly returned to normal. The expression of α-SMA declined to a low level.

Conclusion: LRI triggered a wound healing response, resulting in significant recovery of corneal transparency, epithelial integrity, and stromal structure. This indicates that although the limbal dissection incision induces corneal injury, the wound-healing process eventually occurs with relatively mild long-term fibrosis. The results of this study will provide a theoretical basis for a deeper understanding of corneal healing after LRI surgery and contribute to the treatment of residual astigmatism after clinical cataract surgery.

Keywords: limbal relaxation incision; rabbit; corneal; wound healing; Ki-67; α-SMA

Introduction

The cornea, as the outermost transparent tissue of the eye, is exposed to the external environment and is easily susceptible to damage [1]. Corneal wound healing is an important clinical issue due to the high incidence of corneal injuries and the growing use of refractive surgical procedures [2]. As the primary refractive medium of the eye, the structural integrity of the cornea is the foundation for maintaining visual function. Limbal relaxation incision (LRI) is a refractive surgical technique used to correct low-degree corneal astigmatism. It involves the creation of an arc-shaped incision along the steep axis of corneal astigmatism, thereby locally relaxing the corneal tension. LRI has been shown to be an effective method for correcting low-degree astigmatism [3]. However, the impact of LRI on corneal healing remains to be clarified.

Normal wound healing is a dynamic process that maintains the integrity and health of the corneal epithelial surface, thereby preserving corneal transparency and vision. Cell proliferation and migration are crucial processes in the repair of corneal epithelial damage [4]. When the cornea is injured, the quiescent corneal cells in the wound stroma undergo apoptosis, while nearby corneal cells are activated. The activated corneal cells begin to proliferate and transform into fibroblasts, which then migrate toward the injured area [5]. Once the cells reach the wound edge, they expand in the stroma and differentiate into myofibroblasts [6]. Myofibroblasts populate the wound in a woven, interconnected network pattern and express α-smooth muscle actin (α-SMA) filaments, promoting wound contraction [7,8]. However, excessive and uneven contraction may change corneal curvature, causing irregular astigmatism. Even when the scar lies outside the pupillary area, vision can be impaired due to image distortion [9]. In addition, abnormal corneal wound healing, particularly excessive scar formation and the persistence of myofibroblasts, is a major cause of corneal opacity and vision loss [10]. Therefore, it is essential to explore the impact of LRI on corneal wound healing.

To clarify the corneal wound-healing process of the rabbit after LRI surgery, we established a rabbit LRI model to dynamically observe the healing process of the corneal epithelium and stroma after LRI surgery. The results of this study will provide a theoretical basis for a deeper understanding of post-LRI healing biology and contribute to the treatment of clinical ophthalmic diseases.

Materials and Methods

Animals

Twenty-four healthy adult New Zealand white rabbits of the same breed and age, weighing 2.0–2.5 kg, regardless of sex, were provided by the Animal Experimentation Center of Zhejiang Chinese Medical University. The negative control (NC) group was defined as the animals that did not receive any treatment before surgery. At 7 days, 30 days, 60 days, and 90 days, 3 rabbits were sacrificed to obtain fresh tissues, while the remaining 12 rabbits were subjected to eye observations. This research was conducted in strict accordance with the recommendations outlined in the National Institutes of Health Guide for the Care and Use of Laboratory Animals. This research was reviewed by the animal management and ethics committee. All experimental processes complied with the principles of animal protection, animal welfare and ethics, and the relevant regulations on experimental animal welfare and ethics of laboratory animals. All the experimental protocols of this study were approved by the Experimental Animal Management and Ethics Committee of Zhejiang University of Chinese Medicine (Approval Number: IACUC-202503-19).

Rabbit LRI Model Surgery

Preoperative inhalation of isoflurane (cat. R510-22, RWD Company, Shenzhen, China) for general anesthesia in 24 rabbits, with an induction concentration of 5% and maintenance concentration of 3%, using an anesthesia machine (cat.R500, RWD Company, Shenzhen, China). After the initiation of surgery, the conjunctival sac was rinsed with saline, and surface anesthesia was performed using 2 drops of alcaine (hydrochloride) eye drops (cat. H20160133, 15 mL:75 mg, s.a. ALCON-COUVREUR n.v.). Under the microscope, corneal incisions with a depth of 80–90% of the corneal depth and an arc length of 90 degrees were made at the nasal and temporal canthus regions of the small pupil.

Specific operative steps of LRIs [11]: After placing the eyelid speculum, the conjunctival sac was irrigated with normal saline. A corneal positioning ring and corneal marking pen were used to mark the required locations and incision arc length for limbal relaxing incisions at the nasal and temporal corneal limbus. The depth of the corneal depth-setting knife was adjusted, the eyeball was stabilized with forceps, and an arcuate corneal incision was made along the marked guide. The incision was located within the peripheral corneal vascular arcade. After completion of the arcuate incision, the corneal wound was irrigated with normal saline. Diclofenac ophthalmic ointment (cat.H10960176, Shenyang Xingqi Pharmaceutical Co., Ltd) was applied into the conjunctival sac. After the operation, antibiotic eye drops were administered 3 times a day for 7 consecutive days to prevent infection.

Regular Images

Photographs of 12 rabbits were taken at 7, 30, 60, and 90 days after the LRI procedure. After surface anesthesia, the eyelid speculum was used to open the eyelids, and hand-held slit-lamp photography was performed under standardized illumination to examine the overall appearance of the cornea, conjunctiva, and sclera. Imaging parameters: 16× magnification, crack width 0–9 mm, crack height 1, 3, 5, and 10 mm, light spot 0.1, 1, 3, 5, 10 mm, lamp arm rotation angle adjustable from –30° to +30°. The filter consisted of a heat-insulating, light-blocking sheet without red light and a cobalt blue filter.

Haze Grading

The degree of corneal opacity was graded using a slit-lamp biomicroscope [12]: 0, completely transparent cornea; 0.5, mild corneal haze; 1, mild corneal haze, not affecting the observation of iris texture; 2, mild corneal haze, affecting the observation of iris texture; 3, moderate corneal haze, significantly affecting the observation of iris texture; 4, severe corneal haze, making it impossible to view the iris texture.

Draize Ocular Irritation Study

After performing LRI on the 12 rabbits, an adapted Draize test was used to assess irritation [13]. Cornea (0–4): 0, no opacity; 1, diffuse opacity, iris clearly visible; 2, semi-transparent areas easily discernible, iris unclear; 3, grayish-white semi-transparent areas, iris details unclear, pupil size barely visible; 4, corneal opacity, iris unrecognizable. Iris (0–2): 0, normal; 1, wrinkles noticeably deepened, congestion, swelling, pupil still reacts to light; 2, bleeding/visible necrosis, no light reaction (or one of these). Conjunctiva (0–3): 0, normal blood vessels; 1, blood vessels congested, bright red; 2, blood vessels congested, dark red, vessels hard to distinguish; 3, diffuse congestion, purplish-red.

Fluorescein Sodium Staining

Staining was performed by adding 1% sodium fluorescein (cat. 518478, Solarbio) for one drop to the corneal area of the rabbit's eye. The extent of staining was then assessed by slit-lamp photography of the rabbit's cornea under cobalt blue light.

Hematoxylin and eosin (HE) Staining

After the rabbits were euthanized by intravenous injection of 1% pentobarbital sodium (150 mg/kg, cat.11715,

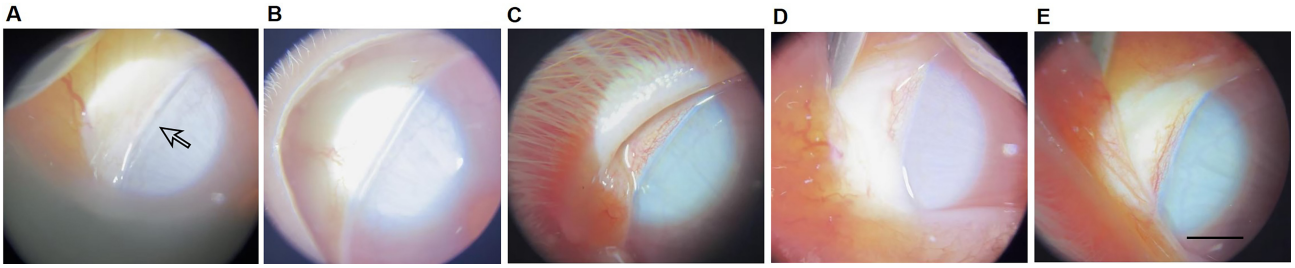

Fig. 1. The routine images of corneal wound healing after LRI surgery. (A) right after surgery, (B) 7 days, (C) 30 days, (D) 60 days, (E) 90 days. Note: The arrow indicates the corneal incision. Scale bar: 3 mm.

MilliporeSigma, Shanghai, China), the ocular tissues were collected. The collected ocular tissues were fixed in neutral formalin solution for 24 hours and dehydrated in ethanol. After embedding in paraffin, 4 µm paraffin sections (HM 355S, Epredia Experimental Equipment Manufacturing Co., Ltd.) were prepared. Rabbit tissue sections were baked in an oven at 60 °C for 2 hours. The sections were deparaffinized in Xylene I and II for 15 minutes each and rehydrated through a graded ethanol series (absolute ethanol I and II for 10 minutes each, 95% ethanol, 80% ethanol, and 70% ethanol for 2 minutes each), followed by rinsing in tap water for 1 minute. The sections were then stained with hematoxylin for 5 minutes, followed by rinsing with tap water for 1 minute. The sections were blued with 0.5% dilute ammonia water for 20 seconds, rinsed with tap water for 3 minutes, stained with 0.5% eosin solution for 2 minutes, rinsed with tap water for 1 minute, and then dehydrated with graded ethanol (80% and 95% for 30 seconds each, absolute ethanol I and II for 2 minutes each), and cleaned in Xylene I and Xylene II for 5 minutes. Finally, the sections were mounted with neutral balsam. Images were captured using a digital slide microscope (OLYMPUS, VS120).

Immunofluorescence Staining

Immunofluorescence staining was performed to detect Ki-67 (cat. 27309-1-AP, dilution ratio: 1:100, Proteintech Biotechnology Co., LTD, Wuhan, China) and α-SMA (cat. M0851, dilution ratio: 1:200, Dako, Glostrup, Denmark), which are markers of corneal epithelial cells and myofibroblasts, respectively. Rabbit corneal sections were air-dried by baking at 60 °C for 2 hours, deparaffinized in water, and washed in distilled water for 2 minutes. High-pressure antigen retrieval was performed, followed by washing with phosphate buffer solution (PBS, cat. ZLI-9062, Jiachen Chemical Co., Ltd.) for 5 minutes $\times$ 3 times. Primary antibodies for α-SMA and Ki-67 were applied and incubated at 4 °C overnight. The following day, the sections were warmed to 37 °C, incubated for 60 minutes, washed with PBS for 5 minutes $\times$ 3 times, and then secondary fluorescent antibodies (cat. CSM1003, dilution ratio: 1:1000, Celnovte Biotechnology, Rockville, Maryland, USA) were added and incubated at 37 °C for 30 minutes. After washing with PBS for 5 minutes $\times$ 3 times, the sections were mounted with a DAPI-containing mounting medium. The tissue samples were observed under a fluorescence microscope (Eclipse 80i, Nikon, Japan).

Statistical Analysis

Statistical analysis of the positive cells in each corneal sample was performed using GraphPad Prism 8.0 software (GraphPad Software Inc., San Diego, CA, USA). ImageJ (version 1.8.0, National Institutes of Health, Bethesda, MD, USA) was used to analyze the immunofluorescence images. Categorical variables were analyzed using the Friedman test. Independent sample *T*-tests were used to compare differences with negative control groups. A p value less than 0.05 was considered statistically significant.

Results

Observation of Wound Healing After LRI Surgery

Images capturing the wound healing process were taken. Fig. 1A shows the postoperative image. One week after surgery, the cornea was hazy and ectatic (Fig. 1B). 30 days post-surgery, the cornea remained ectatic (Fig. 1C). Two months post-surgery, although there was still some congestion and dilation, the corneal wound gradually shrank and healed (Fig. 1D). Three months post-surgery, the cornea showed no haze, vascular congestion, or dilation (Fig. 1E).

Haze Examination After LRI Surgery

Table 1 summarizes the results of grading corneal opacity using a slit-lamp microscope and grading system. The analysis was performed for each eye of 12 rabbits. The results show that 7 days post-surgery, the cornea exhibited mild opacity, which slightly affected the observation of iris texture. At 30 days and 60 days post-surgery, the cornea gradually became more transparent, with fewer cases of corneal opacity. By 90 days post-surgery, complete restoration of corneal transparency was observed in all rabbits.

Table 1. Corneal opacity grading results.

	0	0.5	1	2	3	4	χ^2	p value
7 days	0	0	14	10	0	0		
30 days	5	0	13	6	0	0		
60 days	20	0	4	0	0	0		
90 days	24	0	0	0	0	0		
							61.737	$p < 0.01$

Eye Irritation Situation

The modified Draize test was used in 12 rabbits as the model animals to assess the irritation potential of LRI (Table 2). The results showed that at 7 days postoperatively, obvious abnormal conditions were observed, including diffuse corneal opacity, blurred iris details, and bright red vascular congestion. At 30 and 60 days after surgery, the cornea gradually recovered, with an increasing number of cases showing no opacity and no congestion. By 90 days postoperatively, all rabbits exhibited clear corneas with normal vasculature.

Table 2. Draize eye irritation test.

	7 days	30 days	60 days	90 days	
Cornea (0–4)					
0	1	5	20	24	
1	13	13	4	0	
2	10	6	0	0	
3	0	0	0	0	
4	0	0	0	0	
χ^2					60.130
p value					$p < 0.01$
Iris (0–2)					
0	24	24	24	24	
1	0	0	0	0	
2	0	0	0	0	
Conjunctiva (0–3)					
0	9	9	10	24	
1	15	15	14	0	
2	0	0	0	0	
3	0	0	0	0	
χ^2					42.261
p value					$p < 0.01$

Corneal Dry Eye Condition

To investigate the effect of LRI on corneal dry eye, fluorescein sodium staining was performed on the corneas of rabbits undergoing the relaxing incision procedure. Corneal dry eye conditions were recorded preoperatively and at 7, 30, 60, and 90 days postoperatively. The results in Fig. 2 showed that the normal, intact corneal epithelium showed slight staining preoperatively, indicating that the rabbits might have mild dry eye. Compared to preoperative conditions, there was green fluorescein retention in the corneal epithelium at 7 days postoperatively, indicating a more severe degree of corneal dry eye. At 30, 60 and 90 days postoperatively, the area of fluorescein retention in the corneal epithelium gradually decreased, and the dry eye conditions gradually improved.

HE Staining of Corneal Tissue After LRI Surgery

HE staining pathological examination showed in Fig. 3 that the LRI wound contained more cells compared to the normal cornea. The epithelial cells of the wound exhibited a multilayered morphology at 7 and 30 days postoperatively, accompanied by significant corneal thickening. Additionally, the subepithelial extracellular matrix in the wound was more abundant at 7 and 30 days than at 60 and 90 days post-surgery. At 60 and 90 days after surgery, the corneal structure in the wound area was thinner than at 7 and 30 days, with fewer dead cells and a more intact structure in the stromal matrix.

The Effect of LRI on the Proliferation of Corneal Epithelial Cells

To investigate the effect of LRI on the corneal epithelial injury repair process in rabbits, Ki-67 was chosen as a marker for epithelial cell proliferation, and immunofluorescence staining was performed on the rabbit corneal epithelium. The results in Fig. 4 showed that, compared with the preoperative control group, the number of Ki-67-positive cells peaked at 7 days post-surgery. At 30, 60, and 90 days after the surgery, the number of positive cells gradually decreased, and the integrity of the corneal epithelium was gradually restored.

The Influence of LRI on Corneal Myofibroblasts

To investigate the effect of LRI on corneal myofibroblast formation in rabbits, α-SMA was chosen as a marker for myofibroblasts, and immunofluorescence staining was performed on rabbit corneal tissue. The results in Fig. 5 showed that, preoperatively, corneal stromal cells in healthy, uninjured corneas were quiescent and did not express α-SMA. α-SMA, a marker of myofibroblasts, is typically expressed during tissue repair and fibrosis. At 7 days post-surgery, the number of α-SMA-positive cells significantly increased and peaked at 30 days. At 60 and 90 days postoperatively, the number of α-SMA-positive cells gradually declined.

Discussion

This study systematically explored the effect of LRI on the corneal wound healing process in rabbits through a series of observations and tests. The results showed that after LRI, the cornea underwent a typical, dynamic wound healing process, characterized by early inflammatory responses, epithelial repair, proliferation and activation of stromal cells, followed by subsequent tissue remodeling

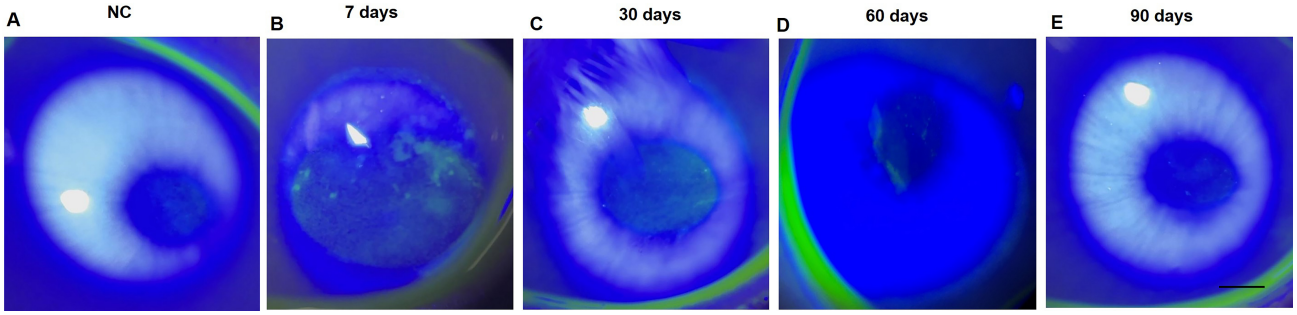

Fig. 2. Corneal dry eye status after LRI. (A) Preoperative corneal sodium fluorescein staining. (B–E) Sodium fluorescein staining of rabbit corneas at different time points after LRI to assess the corneal dry eye conditions. NC, negative control group. Scale bar: 3 mm.

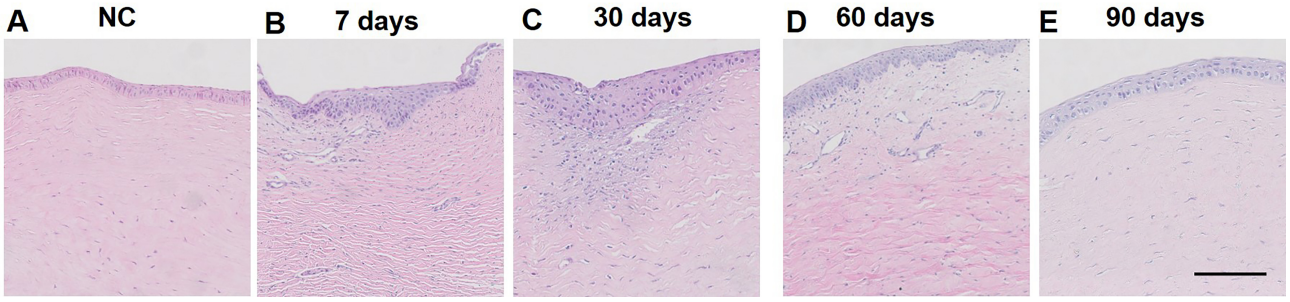

Fig. 3. HE staining of corneal wounds after LRI surgery. (A) Preoperative corneal section. (B–E) HE staining of the wounds at different postoperative time points. NC, negative control group. Scale bar: 100 µm.

and restoration of transparency. The overall healing cycle lasted approximately 3 months.

LRI can lead to corneal nerve damage and sensory impairment [14]. This study evaluated the corneal opacity and ocular irritation using haze scoring and the Draize ocular irritation test [13]. The results showed that early after LRI (1 week to 1 month), the cornea exhibited opacity, dilation, and vascular congestion, which are typical manifestations of the acute phase response after corneal injury, associated with inflammatory cell infiltration, tissue edema, and neovascularization [15]. Subsequently, these signs gradually diminished over 2 to 3 months, with restoration of corneal transparency and structure. Guo *et al*. [16] found that, compared to normal individuals, mild dry eye was associated with a few fluorescein staining spots on the cornea, moderate dry eye with an increased number of spots (5–30 spots), and severe dry eye with more than 30 spots. In this study, corneal fluorescein sodium staining was maximal at 7 days post-LRI, and gradually decreased from 30 to 90 days postoperatively. This suggests that LRI impairs the stability of the tear film, leading to corneal fluorescein staining, with gradual recovery over time. Previous research has reported that after phacoemulsification with a clear corneal incision, harmful changes in all parameters of corneal sensitivity were immediately detected, and corneal sensitivity did not return to preoperative levels until 3 months postsurgery [17], consistent with the corneal recovery time in this study.

The histopathological results (HE staining) in this study further confirmed the above process. Early postsurgery (1 week and 1 month), there was an increase in cell numbers at the wound site, epithelial thickening, and stromal disorganization, corresponding to the clinical stages of opacity and edema. At 2–3 months post-surgery, corneal architecture became thinner and more intact, with a reduction in cell death, suggesting the completion of the tissue remodeling phase and restoration of transparency. The findings of Li *et al*. [18] are consistent with this study, with epithelial proliferation and subepithelial accumulation of fibroblasts observed at 14 and 21 days, and a decrease in fibroblasts in the wound area after three months.

Corneal injury damages the epithelium. Ki-67 is a well-recognized proliferative marker in the process of corneal epithelial regeneration [19]. We investigated Ki-67 immunohistochemical staining in injured and healing corneas, and the results showed that at 7 days post-surgery, the corneal wound exhibited a large number of Ki-67-positive basal cells, indicating that it promoted epithelial reformation. The proliferative activity of corneal epithelial cells peaked at 1 week post-surgery, which may represent a compensatory proliferative response to epithelial injury aimed at accelerating coverage of the defected area. Subsequently, proliferative activity continuously decreased and returned to normal levels by 3 months, coinciding with the completion of epithelial repair. This suggests that epithelial repair involves not only cell migration but also an active yet

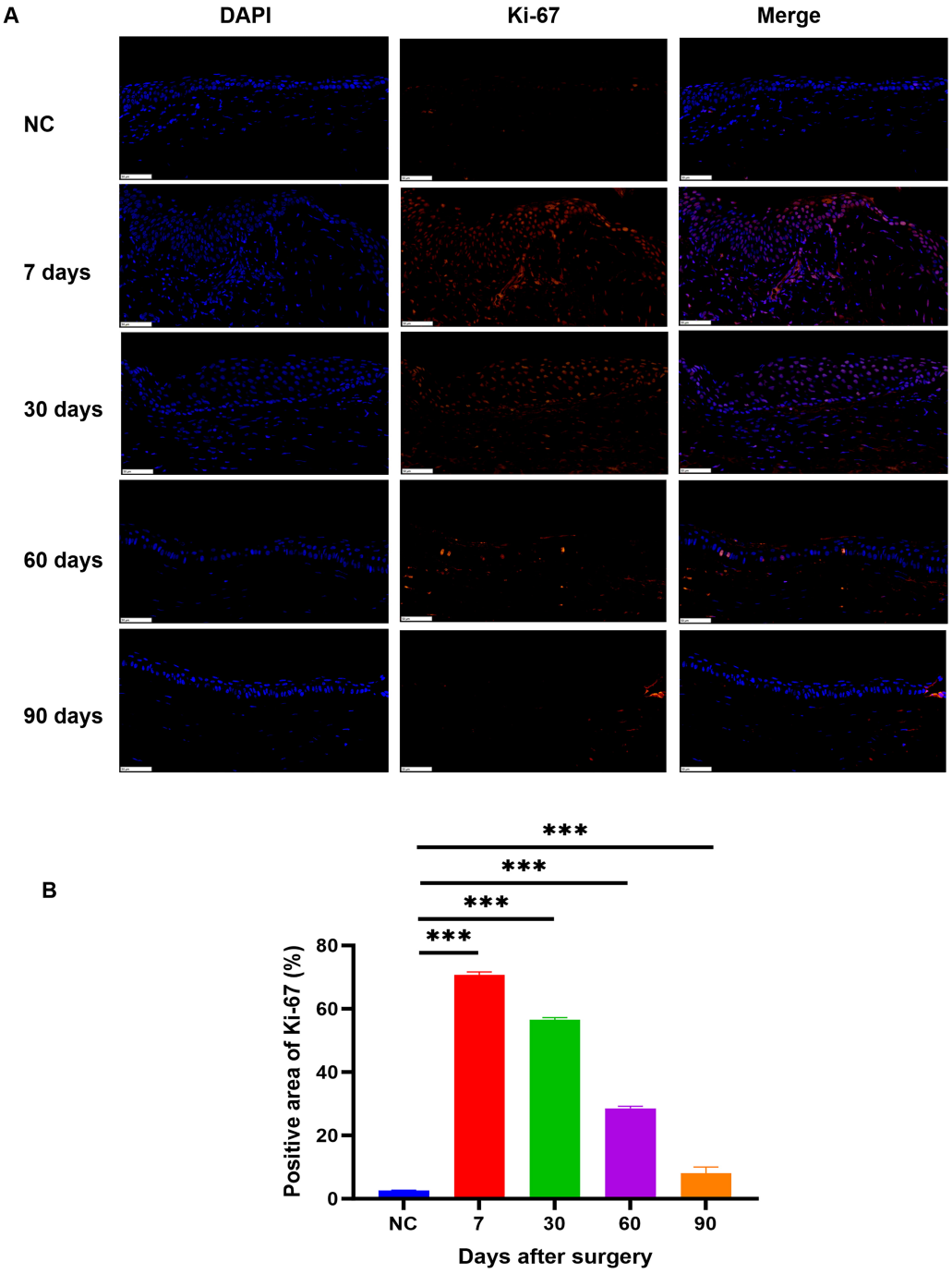

Fig. 4. Expression of Ki-67 in corneal epithelial cell proliferation after LRI surgery. (A) Immunofluorescence analysis of Ki-67 expression in corneal tissues at different times after LRI. (B) Statistical analysis of the number of Ki-67 immunofluorescence-positive cells. (n = 3). *** represents the p value < 0.001 compared with the NC group. NC, negative control group. Scale bar: 50 µm.

controlled proliferative phase. Li *et al.* [20] and Samivel *et al.* [21] also confirmed that when the cornea is injured, Ki-67 levels are upregulated, inducing basal cell proliferation and epithelial formation.

Corneal injury damages the basement membrane. Under stimulation, fibroblasts migrate to the damaged area and differentiate into myofibroblasts, which participate in the restoration of tissue integrity by secreting α-SMA [22]. The appearance of α-SMA-positive myofibroblasts is a key event in the wound healing and fibrosis process [23,24]. This study found that myofibroblasts began to significantly increase at 7 days post-surgery, with a peak in α-SMA expression at 30 days after LRI. In contrast, Li *et al.* [18] indicated that the peak of α-SMA expression after simple interrupted suture (SIS) and horizontal mattress suture (HMS) occurred around 21 days post-surgery. This difference re-

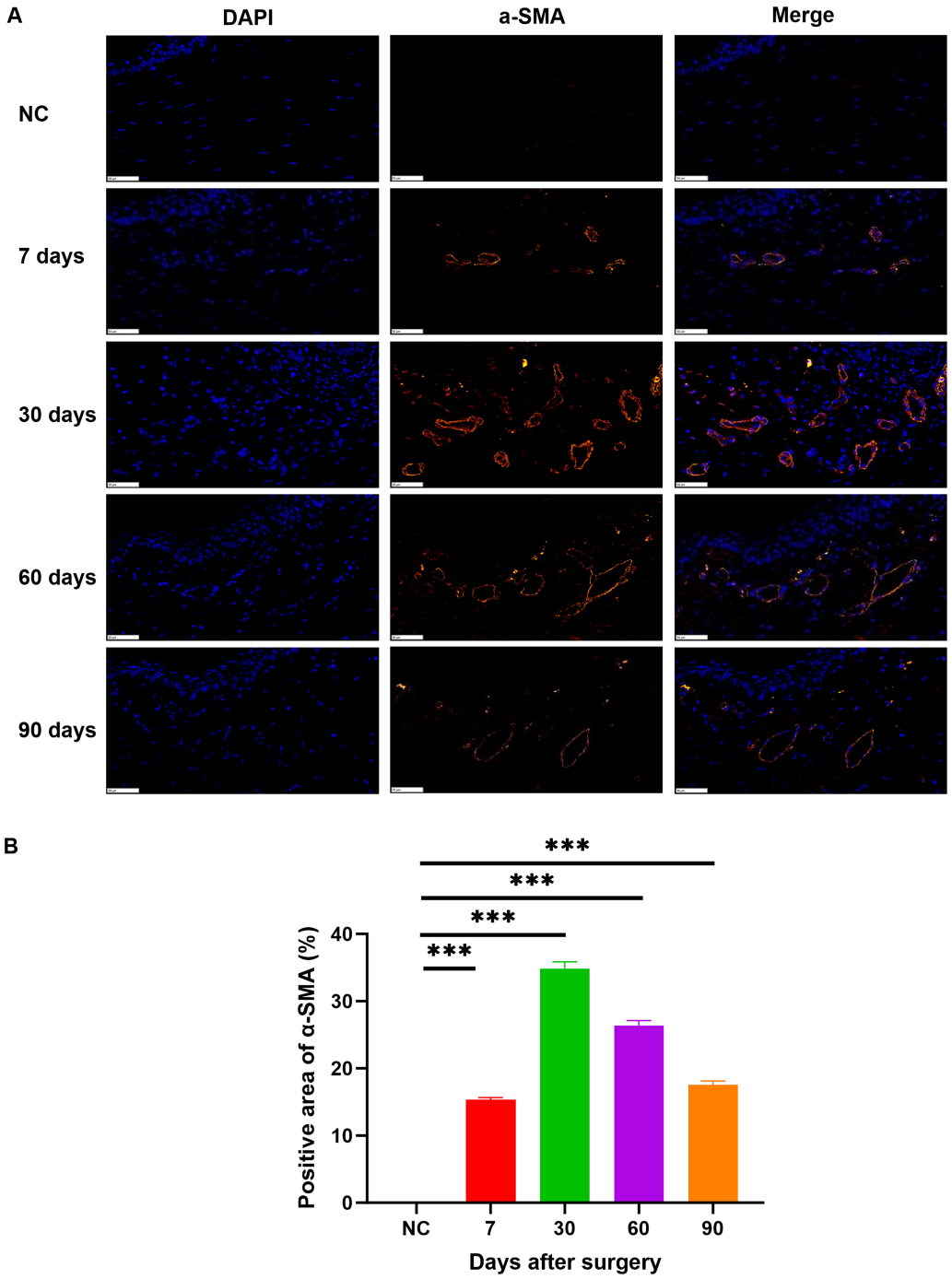

Fig. 5. Expression of α-SMA in corneal wounds after LRI surgery. (A) Immunofluorescence analysis of α-SMA expression in corneal tissues at different times after LRI. (B) Statistical analysis of the number of α-SMA immunofluorescence-positive cells. (n = 3). Note: *** represents the p value < 0.001 compared with the NC group. NC, negative control group. Scale bar: 50 µm.

veals the effects of different surgical methods on wound healing biology. From the perspective of healing dynamics, it is possible that the tight approximation of the sutured wound edges leads to a rapid and relatively synchronized initiation of the repair process, including inflammation, proliferation, and remodeling. In contrast, the LRI incision remains open and requires gradual filling with granulation tissue from the stroma, followed by epithelial migration over the wound surface. This process is relatively delayed and prolonged. The core task of myofibroblasts is not only "closure" but also the continuous generation of contractile force to achieve the desired and precise corneal shape change. This "purposeful contraction" may require a longer time to reach maximum activation. At 2 to 3 months post-surgery, the number of α-SMA-positive cells gradually decreased, which is consistent with the resolution

of corneal opacity and completion of structural remodeling. These findings suggest that the healing process has smoothly transitioned from the proliferation/fibrosis phase to the remodeling phase, which is the key cellular basis for the cornea's restoration of transparency.

This study has some limitations. In the study, a healthy rabbit model was adopted, which cannot recapitulate the clinical conditions of patients undergoing cataract surgery or those with existing dry eye disease. Moreover, the study lacks functional visual indicators, such as corneal topography and corneal thickness, precluding correlation analysis with histological changes.

Conclusion

In summary, LRI, as a corneal surgery, initiates a controllable wound healing response sequence. In the early stages, it is characterized by inflammatory responses, delayed epithelial repair, and the transformation of fibroblasts into myofibroblasts, which may lead to temporary corneal opacity and structural changes. However, the cornea has a strong ability to repair and remodel itself. Within 3 months post-surgery, through complete epithelial regeneration, reversal of the myofibroblast phenotype, and orderly stromal remodeling, the cornea ultimately achieves restoration of both structure and transparency. This study provides a detailed description of the cellular and histological changes during this dynamic process, and the findings will offer a theoretical basis for a deeper understanding of post-LRI healing biology and contribute to the treatment of clinical ophthalmic diseases.

Availability of Data and Materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Author Contributions

MYZ designed the study; XLL collected and analyzed the data. MYZ wrote the first draft. Both authors contributed to critical revision of the manuscript for important intellectual content. Both authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

All the experimental protocols of this study were approved by the Experimental Animal Management and Ethics Committee of Zhejiang University of Chinese Medicine (Approval Number: IACUC-202503-19). All procedures complied with the ARRIVE Guidelines 2.0.

Acknowledgment

Not applicable.

Funding

This study is supported by Hangzhou Medical and Health Science and Technology Project (No. B20240562).

Conflict of Interest

The authors declare no conflict of interest.

References

[1] Mohan RR, Kempuraj D, D'Souza S, Ghosh A. Corneal stromal repair and regeneration. Progress in Retinal and Eye Research. 2022; 91: 101090. https://doi.org/10.1016/j.preteyeres.2022.101090.

[2] Fortingo N, Melnyk S, Sutton SH, Watsky MA, Bollag WB. Innate Immune System Activation, Inflammation and Corneal Wound Healing. International Journal of Molecular Sciences. 2022; 23: 14933. https://doi.org/10.3390/ijms232314933.

[3] Matossian C. Impact of Thermal Pulsation Treatment on Astigmatism Management and Outcomes in Meibomian Gland Dysfunction Patients Undergoing Cataract Surgery. Clinical Ophthalmology (Auckland, N.Z.). 2020; 14: 2283–2289. https://doi.org/10.2147/OPTH.S263046.

[4] Saghizadeh M, Kramerov AA, Svendsen CN, Ljubimov AV. Concise Review: Stem Cells for Corneal Wound Healing. Stem Cells (Dayton, Ohio). 2017; 35: 2105–2114. https://doi.org/10.1002/stem.2667.

[5] Wilson SE. Corneal wound healing. Experimental Eye Research. 2020; 197: 108089. https://doi.org/10.1016/j.exer.2020.108089.

[6] de Oliveira RC, Wilson SE. Fibrocytes, Wound Healing, and Corneal Fibrosis. Investigative Ophthalmology & Visual Science. 2020; 61: 28. https://doi.org/10.1167/iovs.61.2.28.

[7] Shinde AV, Humeres C, Frangogiannis NG. The role of α-smooth muscle actin in fibroblast-mediated matrix contraction and remodeling. Biochimica et Biophysica Acta. Molecular Basis of Disease. 2017; 1863: 298–309. https://doi.org/10.1016/j.bbadis.2016.11.006.

[8] Shu DY, Lovicu FJ. Myofibroblast transdifferentiation: The dark force in ocular wound healing and fibrosis. Progress in Retinal and Eye Research. 2017; 60: 44–65. https://doi.org/10.1016/j.preteyeres.2017.08.001.

[9] McKay TB, Hutcheon AEK, Zieske JD, Ciolino JB. Extracellular Vesicles Secreted by Corneal Epithelial Cells Promote Myofibroblast Differentiation. Cells. 2020; 9: 1080. https://doi.org/10.3390/cells9051080.

[10] Joung C, Noh H, Jung J, Song HY, Bae H, Pahk K, *et al*. A Novel CD147 Inhibitor, SP-8356, Attenuates Pathological Fibrosis in Alkali-Burned Rat Cornea. International Journal of Molecular Sciences. 2020; 21: 2990. https://doi.org/10.3390/ijms21082990.

[11] Hu X, Qi J, Cheng K, He W, Du Y, Zhang K, *et al*. Efficacy of image-guided accurate limbal relaxing incisions for astigmatism correction during cataract surgery. Advances in Ophthalmology Practice and Research. 2025; 5: 212–219. https://doi.org/10.1016/j.aopr.2025.06.001.

[12] Fantes FE, Hanna KD, Waring GO, III, Pouliquen Y, Thompson KP, Savoldelli M. Wound Healing After Excimer Laser Keratomileusis (Photorefractive Keratectomy) in Monkeys. Archives of Ophthalmology. 1990; 108: 665–75.

[13] Badran MM, Alomrani AH, Almomen A, Bin Jardan YA, Abou El Ela AES. Novel Metoprolol-Loaded Chitosan-Coated Deformable Liposomes in Thermosensitive In Situ Gels for the Management of Glaucoma: A Repurposing Approach. Gels (Basel, Switzerland). 2022; 8: 635. https://doi.org/10.3390/gels8100635.

[14] Wang H, Yu X, Li Y, Sun L, Liu M, Zhang X, *et al*. Tissue Damage on Ocular Surface After Combined Phacoemulsification with Limbal Relaxing Incision Compared with Standard Phacoemulsification. Clinical Ophthalmology (Auckland, N.Z.). 2025; 19: 2743–2750. https://doi.org/10.2147/OPTH.S534006.

[15] Kumar R, Tripathi R, Sinha NR, Mohan RR. RNA-Seq Analysis Unraveling Novel Genes and Pathways Influencing Corneal Wound Healing. Investigative Ophthalmology & Visual Science. 2024; 65: 13. https://doi.org/10.1167/iovs.65.11.13.

[16] Guo M, Huang B, Jia X, Liu B. Utilizing Corneal Fluorescein and Conjunctival Lissamine Green Staining Combined with in vivo Confocal Microscopy for Grading the Severity of Dry Eye Disease. Clinical Ophthalmology (Auckland, N.Z.). 2025; 19: 807–817. https://doi.org/10.2147/OPTH.S498893.

[17] Khanal S, Tomlinson A, Esakowitz L, Bhatt P, Jones D, Nabili S, *et al*. Changes in corneal sensitivity and tear physiology after phacoemulsification. Ophthalmic & Physiological Optics: the Journal of the British College of Ophthalmic Opticians (Optometrists). 2008; 28: 127–134. https://doi.org/10.1111/j.1475-1313.2008.00539.x.

[18] Li Y, Chen HJ, Zhang H, Wu JG, Hu YT, Ma ZZ. Effects of different sutures on fibrosis and wound healing in a rabbit model of corneal wounds. Experimental and Therapeutic Medicine. 2016; 12: 2827–2834. https://doi.org/10.3892/etm.2016.3703.

[19] Li H, Peng H, Ma B, Sun X, Zhang L, Chen B. DJ-1 Promotes Diabetic Corneal Epithelial Wound Healing by Attenuating Hyperglycemia-Induced Oxidative Stress Through Inhibiting PTEN. Investigative Ophthalmology & Visual Science. 2025; 66: 20. https://doi.org/10.1167/iovs.66.9.20.

[20] Li L, Wang H, Pang S, Wang L, Fan Z, Ma C, *et al*. rhFGF-21 accelerates corneal epithelial wound healing through the attenuation of oxidative stress and inflammatory mediators in diabetic mice. The Journal of Biological Chemistry. 2023; 299: 105127. https://doi.org/10.1016/j.jbc.2023.105127.

[21] Samivel R, Alanazi MA, Khan AA, Masmali AM, Alanazi SA, Almubrad T, *et al*. Therapeutic efficacy of BSA formulated hydrogels in corneal wound healing and epithelial cell regeneration: an ex vivo study. Scientific Reports. 2025; 15: 19956. https://doi.org/10.1038/s41598-025-04408-3.

[22] Meng N, Wu J, Chen J, Luo Y, Xu L, Li X. Basement membrane regeneration and TGF-β1 expression in rabbits with corneal perforating injury. Molecular Vision. 2023; 29: 58–67.

[23] Putra A, Alif I, Hamra N, Santosa O, Kustiyah AR, Muhar AM, *et al*. MSC-released TGF-β regulate α-SMA expression of myofibroblast during wound healing. Journal of Stem Cells & Regenerative Medicine. 2020; 16: 73–79. https://doi.org/10.46582/jsrm.1602011.

[24] Wang P, Zhao Y, Wang J, Wu Z, Sui B, Mao X, *et al*. Dephosphorylation of Caveolin-1 Controls C-X-C Motif Chemokine Ligand 10 Secretion in Mesenchymal Stem Cells to Regulate the Process of Wound Healing. Frontiers in Cell and Developmental Biology. 2021; 9: 725630. https://doi.org/10.3389/fcell.2021.725630.