

**Case Series**

Open Access, Volume 3

**Evaluating plasma assisted noninvasive surgery (PANIS) as a new method for pterygium removal; a clinical case series****Farhad Nejat<sup>1\*</sup>; Khosrow Jadidi<sup>2</sup>; Shiva Bagheri<sup>1</sup>; Shima Eghtedari<sup>1</sup>; Nazanin Sadat Nabavi<sup>1</sup>; Mohsen Ghiasi<sup>2</sup>**<sup>1</sup>Vision Health Research Center, Semnan University of Medical Science, Semnan, Iran.<sup>2</sup>Department of Cellular and Molecular Biology, Faculty of Advanced Science and Technology, Tehran Medical Sciences, Islamic Azad University, Tehran, Iran.**\*Corresponding Author: Farhad Nejat**

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Received: Dec 24, 2021

Accepted: Mar 31, 2022

Published: Apr 07, 2022

Archived: www.jcimcr.org

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DOI: www.doi.org/10.52768/2766-7820/1782

**Abstract****Purpose:** The present study aimed to evaluate the outcomes of a new technique for pterygium surgery using a plasma-based method.**Methods:** A clinical case series study was carried out in 6 patients. Six eyes with grade 2 or 3 of primary pterygium were operated. The pterygium head was detached from the corneal surface. Then, the free conjunctival edges were attached near the limbus using the plasma spots [generated by Plexr device (GMV, Rocca Priora, RM, Italy)]. Refractive Error (RE), Visual Acuity (VA), Intraocular Pressure (IOP), Contrast Sensitivity (CS), Corneal Fluorescein Staining (CFS), Tear Meniscus Height (TMH), High Order Aberrations (HOA), and Ocular Surface Disorder Index (OSDI) were measured before the operation, one week after the operation, as well as one, three, and six months post-surgery. Slit-lamp images were taken before surgery and six months after that.**Results:** No intraoperative and postoperative complications were observed. Mild degrees of pain, tearing, foreign body sensation, and irritation was reported during the first week after surgery. No significant change was found in IOP, CS, and TMH parameters during the 6-month follow-up. A slight improvement was measured in CFS and HOA after surgery. Compare to before surgery, RE, VA, and OSDI improved after pterygium removal. The follow-up examinations revealed pterygium recurrence in 2 eyes.**Conclusion:** Our results showed that plasma-assisted noninvasive surgery can provide a simple, fast, and effective technique for pterygium removal with no suture or glue. Although, considering the two observed recurrences in this study, we decided to modify the surgical method in the subsequent studies.**Keywords:** pterygium; treatment; plasma; noninvasive surgery; case series.**Abbreviations:** PANIS: Plasma-Assisted Noninvasive Surgery; RE: Refractive Error; VA: Visual Acuity; IOP: Intraocular Pressure; CS: Contrast Sensitivity; CFS: Corneal Fluorescein Staining; TMH: Tear Meniscus Height; HOA: High Order Aberrations; OSDI: Ocular Surface Disorder Index; UV: Ultraviolet; AMT: Amniotic Membrane Transplantation; ALTP: Atmospheric Low-Temperature Plasma; NEI: National Eye Institute/Industry.

## Introduction

The pterygium is described as a prevalent degenerative ocular surface disorder which a wing-like fibrovascular tissue of the bulbar conjunctiva growth on the cornea [1,2]. Different researches reported a prevalence rate of pterygium varying from 1.2% to approximately 50% in various populations around the world. The highest prevalence has been observed in countries closer to the equator [3-6]. The most important risk factor in pterygium pathology is long-term exposure to Ultraviolet (UV) radiation [7,8]. However, aging, hereditary factors such as the p53 gene, cholesterol metabolism modification, tear film abnormalities, low humidity, inflammatory mediators, and smoking are other potential risk factors [1,9-13].

In general, the primary approaches for managing the early-stage pterygium include prevention of UV light using protective eyewear, using lubricator eye drops, and a short course of topical steroids [14]. Additionally, surgical intervention has a considerable indication in cases with reduced vision secondary to either proximity to visual axis or induced astigmatism, restriction of ocular motility, frequent inflammation, chronic symptoms of irritation, and cosmetic concerns [15]. Over the years, various surgical techniques have been tested for pterygium treatment, including bare sclera excision, primary conjunctival closure, conjunctival (or limbal conjunctival) autograft, conjunctival rotational flap, and Amniotic Membrane Transplantation (AMT). It is note worthy that the risk of recurrence is a main concern after the surgical excision [16]. Many studies have assessed the effective factors on this condition and have reported that the age (< 50 years), clinical appearance of pterygium, surgical technique, chronic inflammation, and graft attachment type are frequent risk factors correlating to the recurrence [17-19].

Recently, the plasma medicine has played a significant role in achieving a minimally invasive treatment of living cells and tissues [20,21]. Plasma is known as the fourth state of matter, and the potential of Atmospheric Low-Temperature Plasma (ALTP) for inactivation of various microorganism and material sterilization has been addressed repeatedly. Also, ALTP has applications in many other medical fields including dermatology, dentistry, ophthalmology, and cancer therapy were declared in several studies [22-24]. For example, in two studies on animal models conducted by Nejat et.al, the histopathological changes of the ocular surface were evaluated after one and six months of ALTP exposure. Their results showed that ALTP can be safe for applying to the ocular surface [25,26]. In the other study, concentrations of candidate cytokines as well as duration of inflammation after conjunctival exposure of ALTP were assessed [27]. In the following, this team investigated the outcomes of three plasma-based approaches for treating conjunctival cysts [28], conjunctivochalasis [29], pinguecula [30], and benign conjunctival nevus [31] using the Plexr device (GMV, Rocca Priora, RM, Italy). They reported ALTP application as a simple and effective method without serious complications for treating ocular surface disorders.

In the current study, a new technique of sutureless and glueless pterygium excision using Plasma-Assisted Noninvasive Surgery (PANIS) has been described in six patients.

## Materials and methods

The ethics committee of Semnan University of Medical Sciences approved the protocol of this study (IR.SEMUMS.REC.1397.198). Each patient completed an informed written consent form before surgery. This study was performed in adherence to the tenets of the Declaration of Helsinki.

Six eyes (1 OD/ 5 OS) of six patients (3 males, 3 females) with a mean age of 54 years attending the Vision Health Research Center in Tehran, Iran were enrolled in the study. Four patients had grade three and two patients had grade two of primary pterygium, according to the extent of corneal involvement [32] (Table 1). Patients with the recurrence of pterygium and who had any ocular or systemic disease that may affect visual acuity were excluded from this study.

**Table 1:** Grading of pterygium.

Pterygium grading	Extension
Grade 1	between limbus and a point midway between limbus and pupillary margin.
Grade 2	head of the pterygium present between a point midway between limbus and pupillary margin and pupillary margin.
Grade 3	crossing pupillary margin.

Before surgery, all candidates underwent slit lamp and fundus examination. Refractive Error (RE), Uncorrected Visual Acuity (UCVA), the Best-Corrected Visual Acuity (BCVA), Intraocular Pressure (IOP), Contrast Sensitivity (CS), Tear Meniscus Height (TMH), Corneal Fluorescein Staining (CFS), Total High Order Aberrations (HOA), and Ocular Surface Disease Index (OSDI) were measured for each subject.

Measuring the CS was performed using the Mars letter contrast sensitivity test (Mars Perceptrix, Chappaqua, New York, USA), and the logarithm of contrast sensitivity score was recorded as the lowest contrast numeral prior to two wrongly recognized numerals. Where, score 2 represented the normal contrast sensitivity, and scores <2 and  $\geq 1.5$  indicated a poor contrast sensitivity. Scores <1.5 and  $\geq 1$  were considered as visual impairment. Scores of less than 1 were considered as signifying the visual disability.

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All of these values were reevaluated one week, and one, three, and six months after the pterygium removal. Slit-lamp images were only taken before the treatment and six months after surgery.

## Surgical procedure

The surgical procedure was carried out under local anesthe-

sia using 0.5% tetracaine (Sina Darou, Tehran, Iran) in the operating room, with 5-minute intervals between the three drops.

For surgery, at first, the scalpel blade was inserted through the conjunctiva, the pterygium was excised near the limbus and the head of the pterygium was detached from the corneal surface. Then, the remnant attachments were shaved and removed with a knife, and the corneal surface polished. Next, the involved tenon tissue was cautiously dissected off the normal conjunctiva. After that, the patient's free conjunctival edges were fused near the limbic margin using the plasma spots (see the additional file 1). For this purpose, the white handpiece (Vpp = 500 V, Power = 0.7 W, and Frequency = 75 kHz) (Table 2) of the plexr device was used. The plexr is a cordless microsurgical handheld device that ionizes the air between the handpiece tip and the target tissue by producing a suitable potential difference. The energy is moved to the superficial layer of the tissue where sublimates the plasma-exposed areas. The energy is not straightly transported from the device to the deeper or close tissues [35].

**Table 2:** Technical features of the Plexr device.

Parameter	Values
Working gas	Air
Power supply	Docking station = 24 V Handpieces: Embedded inductive charger = 5 V
<b>Handpieces:</b>	
Max output	≤ 2 W
Max working voltage	≤ 1,3 kVPP
Output frequency	(70-80) kHz
<b>Handpiece types:</b>	
White	V peak to peak = 500 V, Power = 0.7 W, Frequency = 75 kHz
Green	V peak to peak = 600 V, Power = 2 W, Frequency = 75 kHz
Red	V peak to peak = 700V, Power = 2W, Frequency = 75 kHz
Maximum absorbed power (Docking station)	120 W
Applicator electrode	Stainless steel sterile disposable needle
Risk classification of the device	IIb (Medium-high risk)

After surgery, a combination of antibiotic and corticosteroid eye ointment was applied to the patient's eye and the eye was closed gently with the eye pad.

All patients were prescribed ciprofloxacin 0.3% (Sina Darou, Tehran, Iran) every four hours for one week and betamethasone 0.1% (Sina Darou, Tehran, Iran) every four hours for one week which thentapered over four weeks. All surgeries were performed by the same surgeon (F.N.).

All eyes were followed up within the first week and then at months 1,3, and 6 postoperatively.

## Results

The characteristics of the patients are summarized in Table 3. There were no intraoperative and postoperative complications in patients within the 6-month follow-up. In all patients, the major postoperative complaints included mild degrees of pain, irritation, foreign body sensation, and tearing during the first week.

As expected, visual acuity parameters (UCVA and BCVA) improved after the surgery and RE went down considerably. During the 6-month follow-up, no significant changes were observed in the CS, TMH, and IOP after treatment compared to before it. The total HOA parameter slightly declined after the surgery. In almost all cases, CFS showed a moderate improvement during 6 months. As presented in Table 3, in all patients, the OSDI score significantly dropped after the pterygium excision. Recurrence including regrowth of fibrovascular pterygium-like tissue crossing the limbus onto the cornea [36] was observed in two eyes (33%) after 6 months. The preoperative and postoperative slit-lamp photos of two eyes after pterygium treatment can be observed in Figures 1-4.

## Discussion

Pterygium stays a significant health care subject matter globally and several techniques have been tested for its treatment [37]. Bare sclera and primary conjunctival closure are the two old, simple, and quick surgical techniques for treating pterygium. In the bare sclera method, the pterygium is excised and its site is left open, whereas, in the primary conjunctival closure, the conjunctiva is closed over the scleral bed by suturing it together. These methods are not currently preferred because of their high reported rates of recurrence ranging from 38% to 88% and 45% to 70%, respectively [15,37-39]. Another pterygium removal method is the conjunctival limbal autograft, which includes applying an autograft from limbal tissue and near by conjunctiva to cover the scleral bed where the pterygium was excised. The recurrence rate reported following this method is 2% to 20% [37,40-42]. The conjunctival rotational flap is another surgical procedure for treating pterygium. In this method, after the pterygium excision, a conjunctival flap is harvested from the conjunctiva, and then, the flap is rotated near the limbus and sutured to the bare sclera [43,44]. The recurrence rate of this method has been reported to be from 13% to 33% [45, 46]. AMT is another relatively common method. In this technique, a piece of amniotic membrane is used to cover the bare sclera (with the recurrence rate between 14.5% and 27.3%) [47,48].

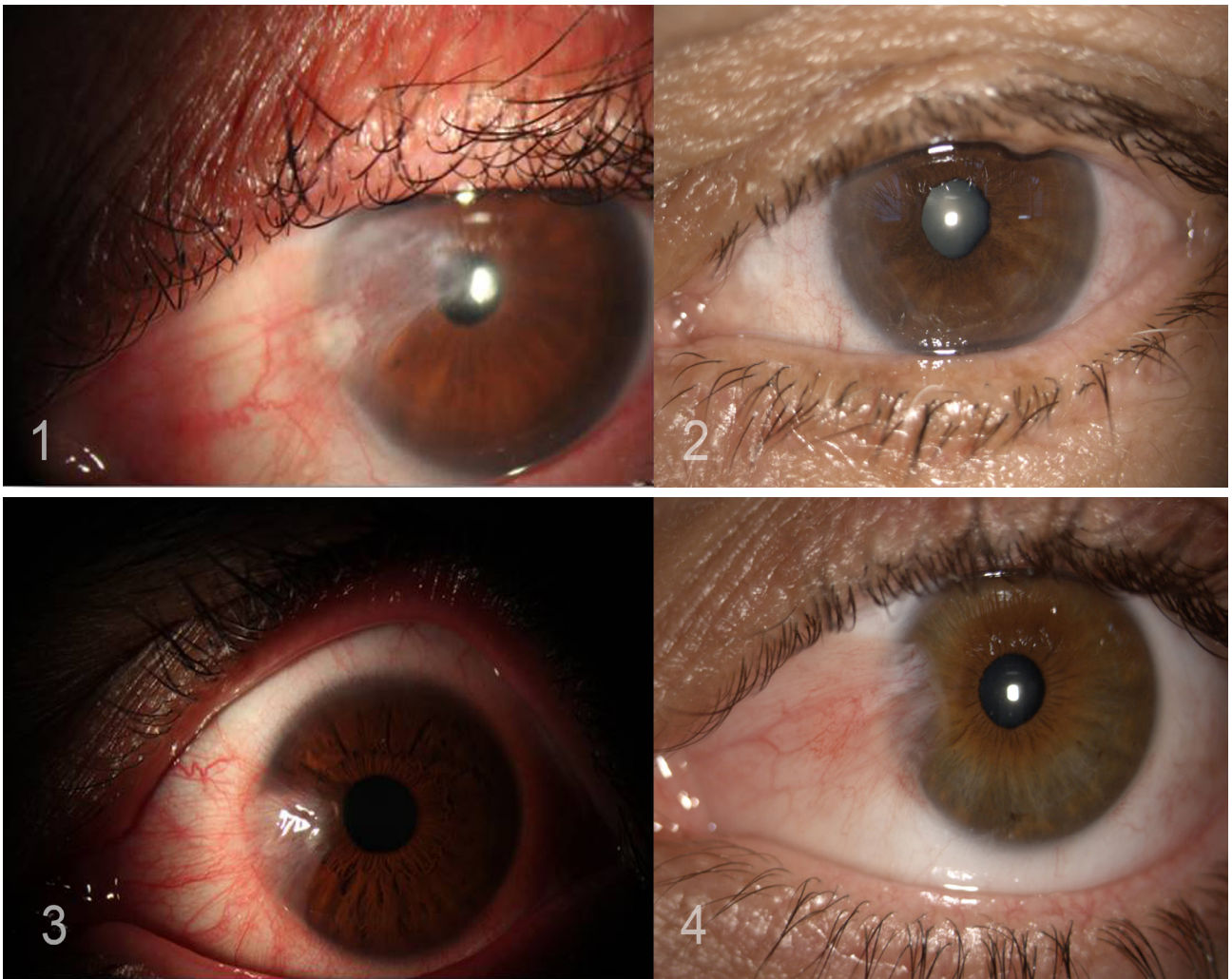
As mentioned, after pterygium removal, having a low recurrence and complication rate is the most concern of surgeons. In a relevant review, the post-surgery recurrence risk has been described to be multifactorial. It is thought that postoperative inflammation can contribute to pterygium recurrence [49,50]. Subsequently, to reduce the pterygium recurrence rate, it has been recommended that combine the surgical procedures with the adjunctive agents such as mitomycin C, 5-Fluorouracil,  $\beta$ -irradiation, and anti-vascular endothelial growth factor [15,48,51].

A study conducted by Suzuki et al. [52] has reported that nylon or silk sutures in the bulbar conjunctiva can cause conjunctival inflammation. As well, patient discomfort, Dellen formation, or dehiscence due to suture application have been observed [53,54].

Some studies have suggested to use a biologic adhesive such as fibrin glue instead of suture in order to decrease the recurrence rate [55-57]. Whereas, some other studies have reported no variation in recurrence [58,59]. Shorter procedure time and fewer postoperative complications have been other benefits mentioned for fibrin glue in pterygium surgery. Although, the higher cost and potential of infection are the problems associated with fibrin glue [60-63]. Autologous blood is another al-

**Table 3:** The ocular parameters which were assessed during the six-month follow-up.

Case 1: Male (60 y old), the patient 's right eye with grade 3 of pterygium											
Follow-up	UCVA (Decimal)	RE			BCVA (Decimal)	I-care Mm Hg	TMH (mm)	CFS	CS	OSDI	Total HOA
pre	0.2	-5	-5	170	0.5	15	0.2	1/2 inferior	0.64	54.16	2.054
1 week	0.4	-2	-1	170	0.7	15	0.2	1/3 inferior	1.2	10	0.87
1 month	0.4	-1.5	-0.75	170	0/7	12	0.4	1/3 inferior	1.2	2.2	0.83
3 months	0.4	-2.5	-1	175	0/8	12	0.2	1/3 inferior	1.08	10.41	1.361
6 months	0.5	-2	-1	170	1	16	0.2	1/4 inferior	1.16	8.33	0.545
Case 2: Female (65 y old): The patient's left eye with grade 3 of pterygium											
wpre	0.1	-1	-3	180	0.1	12	0.2	1/2 inferior	1.08	46.87	0.098
1 week	0.2	-0/5	-3	10	0.3	12	0.35	1/2 inferior	1.12	37.5	0.062
1 month	0.2	-1	-2	180	0.7	11	0.1	1/3 inferior	1.12	37.5	0.076
3 months	0.2	-0/75	-2/75	180	0.6	12	0.2	1/3 inferior	1.12	22.72	0.073
6 months	0.3	-1	-2	180	0.7	11	0.2	1/3 inferior	1.12	22.72	0.074
Case 3: Female (50 y old): Thepatient's left eye with grade 2 of pterygium											
pre	0.3	-1	-3.5	160	0.8	12	0.3	1/4 inferior	1.76	50	0.432
1 week	0.6	-0.75	-2	170	0.9	14	0.15	1/4 inferior	1.68	30	0.34
1 month	0.6	-0.25	-1.75	150	1	15	0.2	0	1.68	25	0.256
3 months	0.7	-0.5	-1.5	160	1	13	0.15	0	1.76	14/57	0.137
6 months	0.8	-0.5	-1.5	160	1	15	0.2	0	1.76	12/5	0.263
Case 4: Female (63 y old): Thepatient's left eye with grade 3 of pterygium											
pre	0.2	-1	-5.5	180	0.5	13	0.2	1/3 inferior	1.08	62.5	0.756
1 week	0.3	-1	-4	175	0.5	11	0.2	1/3 inferior	1.2	52.77	0.682
1 month	0.3	-2	-2.5	180	0.5	10	0.1	1/3 inferior	1.32	44.44	0.667
3 months	0.5	-1	-2.5	5	0.6	11	0.2	1/3 inferior	1.28	33.33	0.326
6 months	0.6	-1	-2	5	0.7	10	0.15	1/3 inferior	1.32	25	0.348
Case 5: Male (45 y old): The patient's left eye with grade 3 of pterygium											
pre	0	-1.5	-4	180	0.8	18	0.2	1/3 inferior	1.64	20.83	1.769
1 week	0/4	-1/5	-2	170	0.9	15	0.1	1/3inferior	1.64	6.81	0.49
1 month	0/2	-1.5	-0/75	170	1	16	0.3	1/3 inferior	1.72	12.5	0.614
3 months	0/6	-1	-1	180	1	12	0.3	1/4inferior	1.72	7.5	0.284
6 months	0/6	-1	-0/5	180	1	10	0.2	0	1.76	7.5	0.483
Case 6: Male (45 y old): The patient's left eye with grade 2 of pterygium											
pre	0.4	-1	-3.5	150	0.7	17	0.2	1/3 inferior	1.8	41	0.098
1 week	0.6	-0.5	-1.5	160	0.9	15	0.2	1/4 inferior	1.88	33.33	0.062
1 month	0.6	0	-1.5	160	1	11	0.1	1/4 inferior	1.8	18.18	0.076
3 months	0.8	0	-1.25	160	1	12	0.1	0	1.76	20	0.073
6 months	1	0	-0.5	160	1	17	0/2	0	1.76	18	0.074



**Figure 1-4:** Pterygium removal using the plexr device. After the pterygium excision, the plasma spots were used for attaching the free conjunctival edges near the limbus. 1) Before surgery, and 2) after surgery of an eye without pterygium recurrence. 3) Before surgery, and 4) after surgery of an eye with pterygium recurrence. In this case, six months after the pterygium surgery fibrovascular tissue crossed the limbus onto the cornea.

ternative to fibrin glue which costs less. The results from studies evaluating the autologous blood are controversial. Some studies have shown that the recurrence rate of autologous blood is similar to sutures or fibrin glue. However, the adhesion time of autologous blood is longer than that of the fibrin glue [64-66].

Given the potential of ALTP in the treatment of ocular surface disorders, in the present study, we proposed a novel technique for removal of the pterygium using PANIS, which is a simple, minimally invasive, short learning curve, and low-cost method. In this method, we used the fusion property of plasma spots to attach the free edges of the conjunctiva to the limbus. Our results showed that the application of ALTP instead of suture or glue is an effective and fast alternative method. This method was the first experience of using PANIS for pterygium treatment and had no significant postoperative complication. But two pterygium recurrences occurred. Following these findings, we modified the pterygium surgical method. In a study conducted by our team, the results of pterygium removal surgery with AMT and PANIS method were reported in 4 cases. No recurrence was found during the six months of follow-up [67].

The small number of samples and the short follow-up duration were the limitation of this study. Therefore, studies with more patients and long-term follow-up periods are recommended.

## Conclusion

According to our results, the PANIS method can be a simple, fast, and effective technique for pterygium removal. However, considering the two recurrences observed in this study, we decided to modify the surgical method and in later studies to try PANIS with conjunctival autograft, AMT, and rotational flap methods.

## Declarations

**Acknowledgments:** We thank the participants in this case series in helping us introduce a novel approach to treating pterygium.

**Funding:** The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

**Competing interests:** The authors have no relevant financial or non-financial interests to disclose.

**Author contributions:** Conceptualization, methodology, formal analysis and investigation, funding acquisition, supervision: [Farhad Nejat]; methodology, conceptualization, formal analysis and investigation: [Khosrow Jadidi]; conceptualization, formal analysis and investigation, writing-original draft preparation:

ration, review and editing, resources: [Shiva Bagheri]; conceptualization, formal analysis and investigation, writing-original draft preparation, review and editing: [Shima Eghtedari] conceptualization, writing-original draft preparation, writing-review and editing: [Nazanin-Sadat Nabavi]; conceptualization, writing - review and editing [Mohsen Ghiasi].

**Ethics approval:** This study was performed in adherence to the tenets of the Declaration of Helsinki. The Ethics Committee of Semnan University of Medical Sciences approved the study protocol.

**Consent to participate:** Informed consent was obtained from all individual participants included in the study.

**Data availability:** The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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