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Use of automated central lamellar superficial keratectomy in the treatment of chronic pigmentary superficial keratitis in dogs

[*Uso da ceratectomia superficial lamelar central automatizada no tratamento das ceratites superficiais pigmentares crônicas em cães*]

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ABSTRACT

Pigmentary superficial keratitis (PSK) is a chronic corneal disorder with different causes, which may include immune-mediated diseases and reactions to ultraviolet rays. This study aimed to evaluate the use of automated central lamellar superficial keratectomy (ACLSK) in the treatment of chronic pigmentary superficial keratitis (CPSK) in dogs. We enrolled 24 animals with CPSK and loss of visual function even after clinical treatment with preserved post-corneal transparent media, and the potential for recovery of visual function after surgical treatment. The microkeratome was positioned on the eye surface, and the central corneal lamellae were obtained after translation. With ACSLC, 21 animals (87.5%) recovered their visual function. In 3 animals (12.5%), the formation of granuloma and posterior central leukoma in the cornea compromised the transparency of the visual axis. This study concludes that ACLSK is a viable surgical alternative for the restoration of visual function in dogs with severe PSK, thus improving their quality of life. The short execution time of this procedure reduces the costs and anesthetic risks.

Keywords: cornea, surgical mechanization, pigmentary keratitis

RESUMO

A ceratite pigmentar superficial (CPS) é uma doença crônica da córnea, com diferentes causas, que podem incluir doenças imunomediadas e reação aos raios ultravioleta. Este estudo teve como objetivo avaliar a utilização da ceratectomia superficial lamelar central automatizada (CSLCA) no tratamento da ceratite superficial pigmentar crônica (CSPC) em cães. Vinte e quatro animais incluídos apresentaram CSPC e perda da função visual mesmo após o tratamento clínico, porém mantiveram os meios transparentes pós-córnea preservados e o potencial de recuperação da função visual após o tratamento cirúrgico. O microcerátomo foi posicionado na superfície do olho e, após o término de sua translação, foram obtidas as lamelas centrais da córnea. Com a CSLCA, 21 animais (87,5%) recuperaram a função visual. Em três animais (12,5%), a formação de granuloma e leucoma central posterior na córnea comprometeu a transparência do eixo visual. Este estudo conclui que a CSLCA é uma alternativa cirúrgica viável para o restabelecimento da função visual em cães com CPS grave, melhorando, assim, sua qualidade de vida. Seu curto tempo de execução proporciona redução de custos e de riscos anestésicos.

Palavras-chave: córnea, mecanização cirúrgica, ceratites pigmentares

INTRODUCTION

Corneal diseases can be etiologically classified as either non-inflammatory or inflammatory (Ledbetter and Gilger, 2013). Chronic irritation of the cornea can lead to the development of pigmentary keratitis. In dogs of any breed, corneal pigmentation can be a non-specific response to chronic keratitis. However, some brachycephalic breeds (Pug, Shih Tzu, Lhasa Apso, and Pekingese) are likely to develop corneal pigmentation more quickly. Corneal pigmentation

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results from the migration of perilimbal melanocytes through neoformed vessels to the corneal surface and the consequent deposition of melanin granules in the corneal epithelial cells (Bellhorn and Henkind, 1966; Mccracken and Klintworth, 1976). Pigmentary keratitis is often a multifactorial condition (Whitley, 1991). Chronic superficial keratitis (CSK) is a progressive, bilateral, inflammatory disease with great potential to cause blindness in dogs.

Clinical treatment aims to remove the stimulus, in the sense of preventing or delaying the progression of pigmentation; however, as noted in practice, pigmentation cannot recede. Clinically, the treatment consists of immunomodulation, protection against ultraviolet rays, and the use of topical corticosteroids. Immunomodulators such as cyclosporins and, more recently, tacrolimus and pimecrolimus, have also been used with some frequency in the treatment of pigmentary keratitis (Slatter *et al*, 2008). Ultraviolet light-blocking soft contact lenses were evaluated for the treatment of dogs with CSK (Denk *et al*., 2011).

In brachycephalic breeds, a combination of surgical procedures, which generally include removal of the aberrant dermis in the medial canthus and correction of the entropion of the lower and lateral medial eyelid or medial canthoplasty, are often used to prevent disease progression (Yi *et al.*, 2006). For severe cases in which central corneal pigmentation results in blindness, superficial keratectomy may be necessary, but recurrence should be expected, thus requiring a new keratectomy (Gilger *et al.*, 2007).

The current standard surgical treatment involves superficial lamellar keratectomy performed manually, which has the following disadvantages: long surgical time, inability to standardize the coverslip, and uncontrolled corneal depth, which can generate irregularities and, consequently, refractive aberrations and risks of eye perforations, in addition to the need for the surgeon's experience. Advances in ophthalmology have allowed the development of equipment used to produce corneal lamellae of programmed thickness and diameter and, predominantly, for correction of refractive disorders in humans.

This technique involves the superficial removal of a corneal lamella in an automated manner. Mechanization promotes a reduction in surgical time, anesthetic risk, and other complications that exist in the manual technique. By promoting the removal of a homogeneous corneal lamella, the technique decreases Descemet's membrane exposure, corneal perforation, and loss of vision.

In humans, superficial lamellar keratectomy using an automated microkeratome is described as an alternative surgical treatment for the removal of severe corneal scars that affect vision, whether they originate from eye diseases or from complications of other surgical procedures (Rasheed and Rabinowitz, 1999; Victor *et al.*, 2006). The complications described in this technique in humans include corneal perforations and refractive aberrations (Crews *et al.*, 1994; Sugar, 1996). The aim of this study was to evaluate the use of superficial keratectomy automated lamellar central in the treatment of chronic pigmented superficial keratitis in dogs.

MATERIAL AND METHODS

This study is based on a retrospective study that analyzed data obtained from the routine of a veterinary service. Therefore, this study was not submitted to CEUA. Twenty-four dogs from routine veterinary service were selected. The selection criteria adopted for this study included dogs with pigmentary keratitis and vision loss. The dogs underwent a general physical examination, as suggested by Feitosa (2014), and an ophthalmological examination, which included analysis of the corneal surface and, when there was sufficient corneal transparency, of the anterior segment (anterior chamber, iris, and lens), with the aid of a slit lamp biomicroscope (SL 15 - Kowa®, Japan).

The evaluation of the posterior segment of the eye: vitreous chamber, retina, and optic nerve, when there was corneal transparency, was performed using direct (Panoptic, Welch Allyn®, USA) and indirect (Welch Allyn® -USA) ophthalmoscopes. Intraocular pressure was measured using an applanation tonometer (Tono-Pen Vet; Reichert®, USA). To examine the intraocular structures, especially the transparent post-corneal media (aqueous, crystalline, and vitreous humor), ocular ultrasound A/B Scan 10 mHz (Sonomed® E-Z Scan B5500 + - USA) was performed.

The inclusion criteria were set as dogs that presented chronic pigmentary superficial keratitis (CPSK), with loss of visual function, even after clinical treatment, but who still preserved the transparent post-corneal media, and who were considered fit and thus had the potential to recover visual function after surgical treatment. Animals with comorbidities that would interfere with the final result, such as cataracts, severe vitreous degeneration, retinal detachment, and optic nerve excavation, were excluded.

As a pre-anesthetic medication, morphine sulfate (Cristália Prod. Quím. Farm. Ltda., Itapira, Brazil) was used at a dose of 0.2 mg / kg IM. After 20 min, a cephalic vein puncture (BD AngiocathTM 22GAx1.00 IN - Becton, Dickinson Ind. Cir. Ltda., Juiz de Fora, Brazil) was performed for intraoperative fluid therapy with Ringer's solution with sodium lactate (5mL/kg/H).

Anesthetic induction was then performed using propofol (Cristália Prod. Quím. Farm. Ltda., Itapira, Brazil) (3 mg/kg IV), and tracheal intubation was performed after the loss of laryngeal reflexes (endotracheal tube with Solidor® cuff - Medico Int. Trading Co. Ltd., Tianjin PR, China) in the prone position and connected to an anesthetic circuit with or without rebreathing (Anesthesia Apparatus Set KT - 15 K. Takaoka Ind. E Com. Ltda., São Paulo, Brazil), according to the size of the animals.

The animals were maintained on spontaneous ventilation. Anesthetic maintenance was performed using isofluorane and, after reaching the desired anesthetic plan, peribulbar block was performed with a combination of 2% lidocaine hydrochloride (Hipolabor Farmacêutica LTDA, Sabará, Minas Gerais, Brazil) and bupivacaine hydrochloride 0,5% (Hypofarma - Instituto de Hypodermia e Farmácia Ltda., Ribeirão das Neves, Minas Gerais, Brazil) in the proportion of 1mL: 1mL.

Immediately after the blockade, one drop of anesthetic eye drops with 1% tetracaine hydrochloride and 0.1% phenylephrine hydrochloride (AllerganTM) was applied. After 5 min of topical anesthetic application, antisepsis was performed with 5% topical povidone-iodine solution (Farmax-Distribuidora Amaral LTDA, Divinópolis, MG), and the ocular surface and periocular region were washed with gauze soaked in this solution.

Subsequently, the surgical field was applied, and the surgical procedure was started. The Masyk® microkeratome, Loktal®, used to perform the procedure, consists of a control unit (Fig. 1) equipped with two footswitches (one suction ring driver and another microheader head advance and return controller) (Fig. 2), handpiece with a 9.5mm diameter suction ring, head with blade and support (oscillator) (Fig. 3), motor, and vacuum tube.

Figure 1. MASYK® LOKTAL® microkeratome control unit. Connection points for the suction system (red arrow), the power supply system for the handpiece (yellow arrow) and the pedals (blue arrow). Source: personal archive.

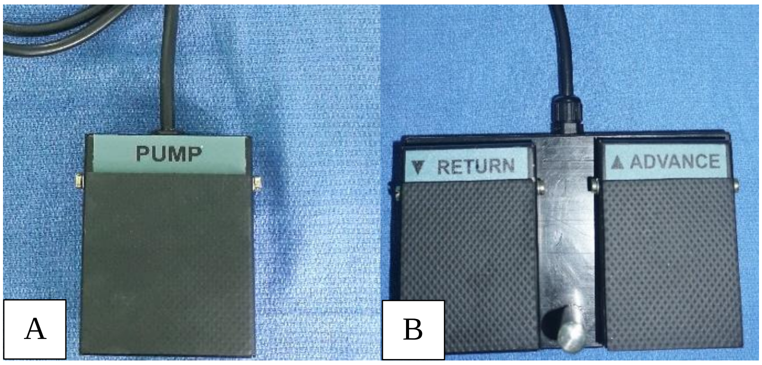


Figure 2. Footswitch components of the MASYK® LOKTAL® microkeratome connected to the control unit. A: The suction system trigger pedal to be connected to the suction ring (pump); B: The microkeratome head advance pedal (advance) and microceratome head return controller (return). Source: personal archive.

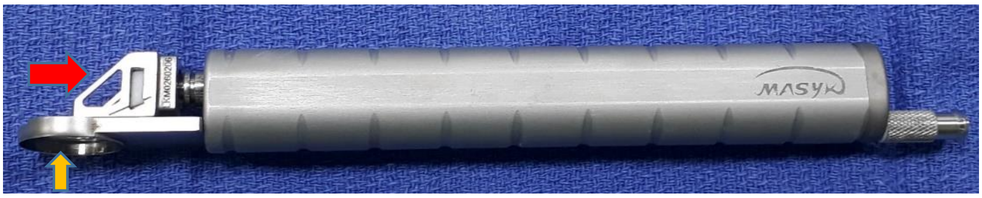


Figure 3. Handpiece component of the MASYK® LOKTAL® microkeratome; Red arrow: head with blade and oscillating support; Yellow arrow: suction ring. Source: personal archive.

The animals were placed in the prone position. The eyes were kept open with the aid of a Barraquer blepharostat (3cm). Eye centralization was achieved using a peribulbar block. After preparing the surgical field and placing the blepharostat, the suction ring of the Masik® microkeratome, Loktal® was positioned over the eyeball to ensure that the entire extension of the ring was in contact with the corneal surface. By compressing the suction ring lightly on the cornea, the vacuum system actuator footswitch (pump) was pressed so that the suction ring was attached to the surface of the eyeball (Fig. 4).

Figure 4. MASYK® LOKTAL® microkeratome handpiece positioned on the surface of the eyeball, ensuring that the suction ring remains attached to the corneal surface. Source: personal archive.

Once the ring adhered to the cornea, the advance footswitch was pressed to promote the advancement of the microkeratome head, where the cutting blade is inserted, towards the distal end of the suction ring, thus covering the entire corneal surface. The head of the microkeratome took 3.5 s to travel this path and, at the end of this time, the corneal lamella was produced (Fig. 5 A and B).

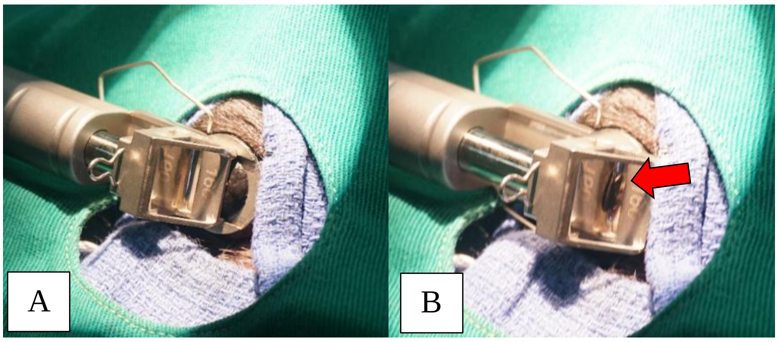
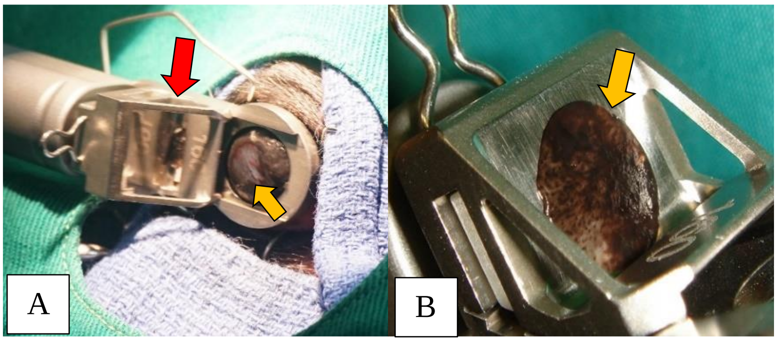


Figure 5.A and B: Head of the MASYK® LOKTAL® microkeratome sliding anteriorly over the surface of the eyeball of a dog undergoing automated central lamellar superficial keratectomy to obtain the corneal lamella (red arrow). Source: personal archive.

After the translation, the return footswitch was pressed, which promoted the return of the microceratome head, triggering the microceratome head, after another 3.5 s, to return to its original position, acquiring the corneal lamella on its surface. (Fig. 6 A and B).



C

Figure 6.A and B: Head of the MASYK® LOKTAL® microkeratome returns back to its original position (red arrow) with the corneal lamella accommodated on its surface (yellow arrow). C: Please scan the QR Code to watch the video demonstrating the automated central lamellar superficial keratectomy procedure. NOTE: To use the QR Code, the free application compatible with the operating system of the mobile device can be used. Source: personal archive.

The advance and return times of the blade to its original point were 7s. Some animals still showed pigmentation in the cornea after the first cut, making it necessary to make one or two more cuts until corneal transparency could be achieved. In the immediate postoperative period, the analgesic tramadol hydrochloride (Laboratorio Teuto Brasileiro S/A, Anápolis-GO) was administered at a dose of 2mg/kg.

The eyes submitted to the procedure underwent topical postoperative treatment: cyclopegic eye drops based on atropine 1%, were administered at 1 drop BID for 7 days and broad-spectrum antibiotic eye drops based on gatifloxacin 0.3%, 1 drop TID were given for 15 days; and systemic treatment with opioid analgesics based on tramadol hydrochloride (Laboratorio Teuto Brasileiro S/A, Anápolis-GO), 2 mg/kg, BID was provided for 5 days.

After anesthetic recovery, the animals were subjected to a complete ophthalmic evaluation to assess their visual capacity.

The first evaluation was performed after the immediate anesthetic recovery. The second evaluation was performed 7 days after the procedure. The third procedure was performed 15 days after the procedure, the fourth, 30 days after the procedure, and the fifth, 1 year after the surgical procedure.

Subsequently, evaluations were carried out every year, with the same environment and the same order of the tests.

The postoperative evaluation time ranged from 15 to 8 years. Corneal transparency restitution was evaluated using a slit lamp biomicroscope, with which the anterior chamber, iris, and lens were visualized and evaluated through the transparent cornea. Direct and indirect ophthalmoscopes were also used to visualize and evaluate the retina and optic nerves.

RESULTS AND DISCUSSION

In the period from September 2011 to July 2019, 24 animals with pigmentary keratitis from routine veterinary service were included in this study. The age of the animals ranged from 2 to 13 years (mean - 7 and a half years). Of the subjects, 16 (66.7%) were male and eight (33.3%) were female. Fifteen animals (62%) were of the Pug breed, 4 (17%) were of the Shih Tzu breed, 4 (17%) were of the German Shepherd breed, and 1 (4%) was of the Pekingese breed (Table 1).

Table 1. Distribution of dogs from the veterinary routine selected to perform automated central lamellar superficial keratectomy according to race, age, sex and the primary cause of pigmentary keratitis

Animals	Breed	Age	Gender	Primary cause
1	Pug	2 yo	Female	Entropion, Dysticiasis
2	Pug	9 yo	Female	Entropion, Palpebral conjunctival neoplasia
3	Pug	4 yo	Male	Entropion, Dysticiasis, Lagophthalmos, Pannus
4	Shih tzu	7 yo	Male	Pannus
5	German Shepherd	10 yo	Female	Pannus
6	German Shepherd	9 yo	Male	Pannus
7	German Shepherd	9 yo	Female	Pannus
8	Shih tzu	5 yo	Male	Palpebral conjunctival neoplasia
9	Pug	5 yo	Male	Entropion
10	German Sheperd	6 yo	Female	Pannus
11	Shih tzu	13 yo	Male	Entropion, Lagophthalmos
12	Pug	4 yo	Male	Entropion, Lagophthalmos
13	Pug	8 yo	Female	Entropion, Dysticiasis, Trichiasis
14	Pug	10 yo	Male	Entropion, Lagophthalmos
15	Pekingese	10 yo	Male	Entropion, Lagophthalmos, Trichiasis, Distiquíase
16	Shih tzu	9 yo	Male	Entropion, Dysticiasis
17	Pug	2 yo	Male	Entropion
18	Pug	13 yo	Male	Entropion, Dysticiasis
19	Pug	6 yo	Female	Entropion
20	Pug	6 yo	Male	Entropion
21	Pug	5 yo	Male	Entropion, Dysticiasis
22	Pug	6 yo	Male	Entropion
23	Pug	7 yo	Female	Entropion
24	Pug	8 yo	Male	Entropion, Lagophthalmos

Slit lamp biomicroscopy examination revealed the complete loss of corneal transparency and the inability to evaluate the anterior segment of the eye (anterior chamber, iris, pupil, and lens), and therefore the loss of vision, in all submitted eyes. for the surgical procedure in this study, as described by Whitley (1991) (Fig. 7). Therefore, direct and indirect ophthalmoscopy were not possible. The intraocular pressure measured in all eyes of the animals included in this study was within the reference range (10–25 mmHg).

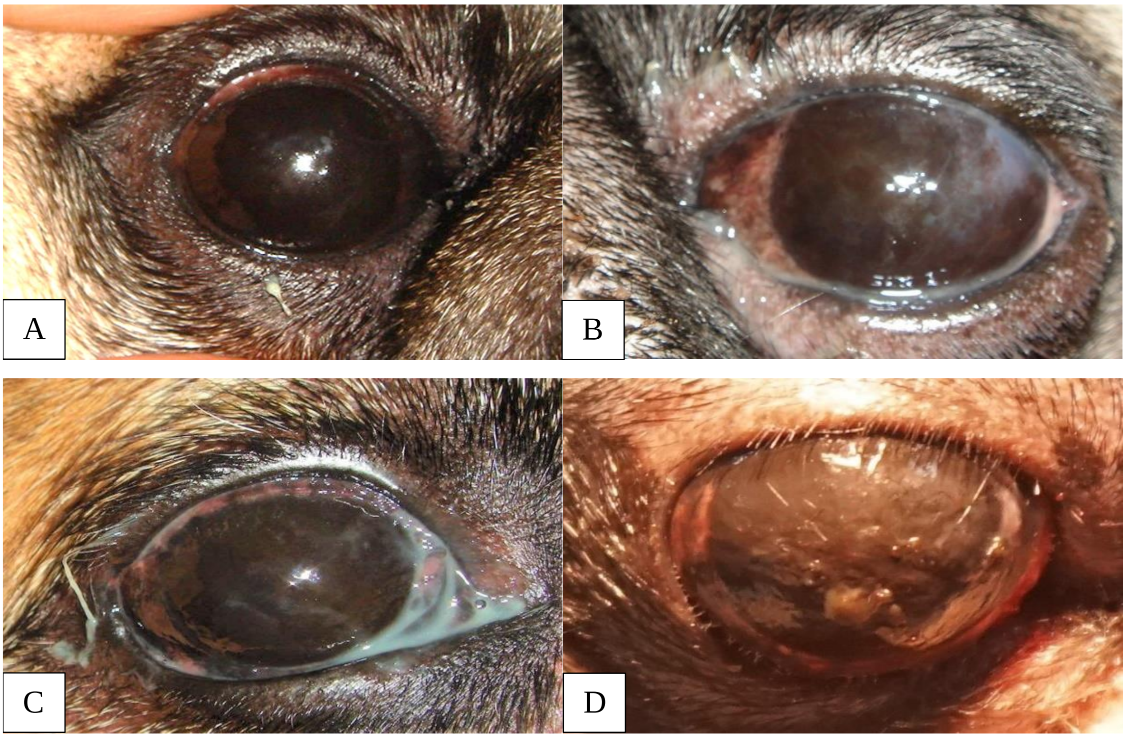


Figure 7. Eyes of 4 dogs selected for automated central lamellar superficial keratectomy. All corneas were completely covered with pigment (melanin). The impregnation with melanin totally compromised the corneal transparency, with no light passing through, making it impossible to visualize or perform biomicroscopic exam the inside of the affected eye. A: presence of pigment in the central region of the cornea. B: pigmentation covering the entire corneal surface and the presence of mucopurulent secretion. C: central region of the cornea covered with pigment, presence of mucopurulent secretion and conjunctival hyperemia. D: cornea completely covered with pigment and showing thickening in the central region. Source: personal archive.

Ocular ultrasonography revealed that all animals maintained the transparent post-corneal media preserved, and therefore had the potential to recover visual function after the proposed surgical treatment. Rasheed *et al.* (1999) described that, in humans, automated lamellar keratectomy can be used to excise corneal scars that compromise vision, and this technique can produce a relatively smooth anterior corneal surface with good optical properties.

When performed in the traditional method, through manual dissection, it can result in an irregular corneal surface, determining severe refraction aberration, and may even be necessary for a lamellar transplant to restore the corneal topography and, thus, the visual function. In veterinary medicine, Shieh *et al.* (1992) described that superficial keratectomy is most performed using traditional microsurgical instruments; however, it can also be performed using ablation with carbon dioxide or excimer laser.

This is the first study to use an automated surgical technique for the treatment of pigmentary keratitis in dogs. The use of the automated microkeratome to perform central lamellar superficial keratectomy in this study provided the following advantages: the acquisition of complete corneal lamellae without perforations, a result similar to that obtained by Victor *et al.* (2006), in humans, as well as obtaining a regular corneal surface with good optical properties, a result similar to that obtained by Rasheed *et al.* (1999) in humans.

As described by Crews *et al.* (1994), in humans, automated lamellar keratectomy is a relatively new and rapidly expanding area of keratorefractive surgery, and this procedure is generally reserved for individuals with high myopia. When not performed correctly, it can have undesirable effects on the quality of vision, such as loss of visual acuity, similar to in humans. Sugar (1996) reported that perforation of the cornea occurs at a rate of up to 3 per 1,000 patients undergoing these procedures, highlighting the importance of meticulous attention to details of assembly and use of the instrument.

In this study, there were no complications during the use of the microkeratome, such as exposure to Descemet's membrane, perforation of the cornea, or loss of visual acuity, contrary to the results obtained by Crews *et al.* (1994) and Sugar (1996), in humans. This result may be related to the fact that the canine cornea is thicker than the human cornea. Using the automated technique, the time of surgery varied between 7 seconds, in the animals that had the affected eye submitted to only one cut (Fig. 8), and 21 seconds in the animals subjected to more than one cut in the affected eye.

According to the author's experience, lamellar keratectomy performed manually can last, on average, 30 minutes, which allows us to conclude that, with the reduction in the time of surgery, there was a reduction in both the anesthetic risk, related to the time of exposure to anesthetic agents, as well as the anesthetic cost, during automated keratectomy. In three (12%) animals, two cuts were made in one eye, while in two (8%) animals, three cuts were made in one eye.

In these cases, the need for subsequent cuts was determined by verifying the presence of pigment in the corneal layer below that which had been removed (Fig. 9). According to Gelatt *et al.* (2013), as the stroma of the cornea may not completely regenerate, the number of superficial keratectomies that can be performed in the same location is limited to two or three, depending on the depth of the tissue removed during each procedure. In dogs, the thickness of a normal cornea can vary from 409 to 784 µm (Wilkie and Whittaker, 1997), and in each cut made through automated keratectomy, a lamella of 160 µm in thickness was produced. Since the corneas submitted to the procedure were thicker than normal, it was possible to safely make subsequent cuts until the cornea was completely transparent.

Considering that corneal thickness can be accurately measured using ultrasound or applanation pachymetry, this can be an important resource to be used, both pre- and postoperatively, to increase the safety of the procedure.

In this study, 21 dogs (87.5%) showed recovery of visual function in the immediate postoperative period, and this function was preserved throughout the period in which they were evaluated (Fig. 10), demonstrating that the automated technique is a useful alternative reproducible therapy and produces satisfactory results in recovering the animal's vision and quality of life.

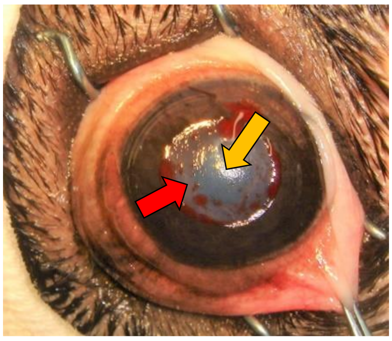


Figure 8. Aspect of a dog's eye undergoing automated central lamellar superficial keratectomy in which one cut was sufficient to restore corneal transparency. At the end of the cut, it is possible to see the iris (red arrow) and the pupillary orifice (yellow arrow). Source: personal archi.

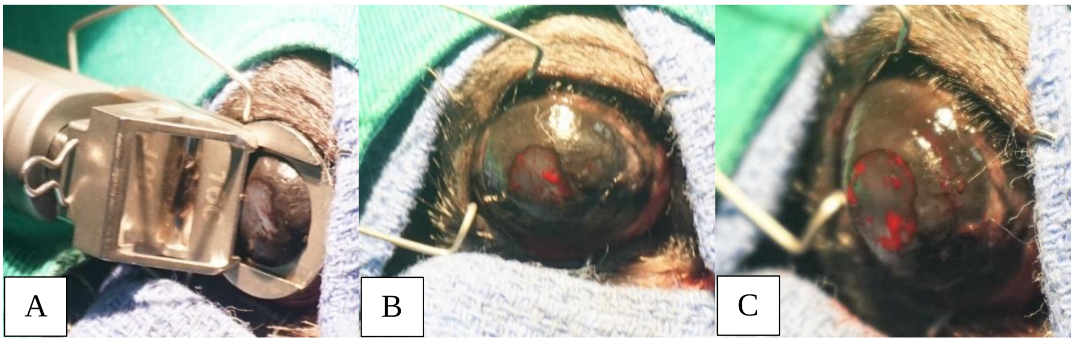


Figure 9. Aspect of the eye of a dog undergoing automated central lamellar superficial keratectomy in which two cuts were necessary for the corneal transparency to be restored. At the end of the first cut (A, B and C), it was found that there was still the presence of pigmentation in the cornea, preventing visualization of the inside of the eye. Source: personal archive.

According to the author's experience, when compared to the manual technique, used for surgical treatment of other corneal disorders, such as corneal degeneration by deposit, automated keratectomy proved to be advantageous with respect to the quality of the incision; regularity of the corneal surface, producing a result similar to that of corneal scar removal surgery, obtained by Rasheed and Rabinowitz (1999). In humans, the quality of the obtained lamellae, reduced surgery time, and shorter learning curve on the part of the surgeon.

The primary drawback of the technique proposed in this study is the cost of equipment and supplies to carry it out. However, the search for excellent veterinary medicine and the professional's zeal for the patient justify such investments. Of the 24 animals submitted to the procedure, 3 (12.5%) showed vision recovery in the immediate postoperative period; however, they manifested complications from the evaluation performed 15 days after the procedure.

Slit lamp biomicroscopy examination revealed the formation of scar granuloma and posterior leukoma in the central region of the cornea, compromising the transparency of the cornea in its visual axis; therefore, direct and indirect ophthalmoscopy cannot be performed (Fig. 11).

In these animals, after the first cut, a greater number of blood vessels and deeper layers of the corneal tissue were verified, which may have influenced the expected result. As described by Lee *et al.* (1998), stromal corneal vascularization is a non-specific response to injury or inflammation, and the presence of blood vessels within the corneal tissue is always a pathological change.

Vascularization is a normal component of the repair response after injury to various tissues; however, in the cornea, this process results in broken corneal architecture, opacity, and reduced vision. Thus, the presence of a greater number of blood vessels and different layers of the cornea could explain the healing response observed in these three cases.

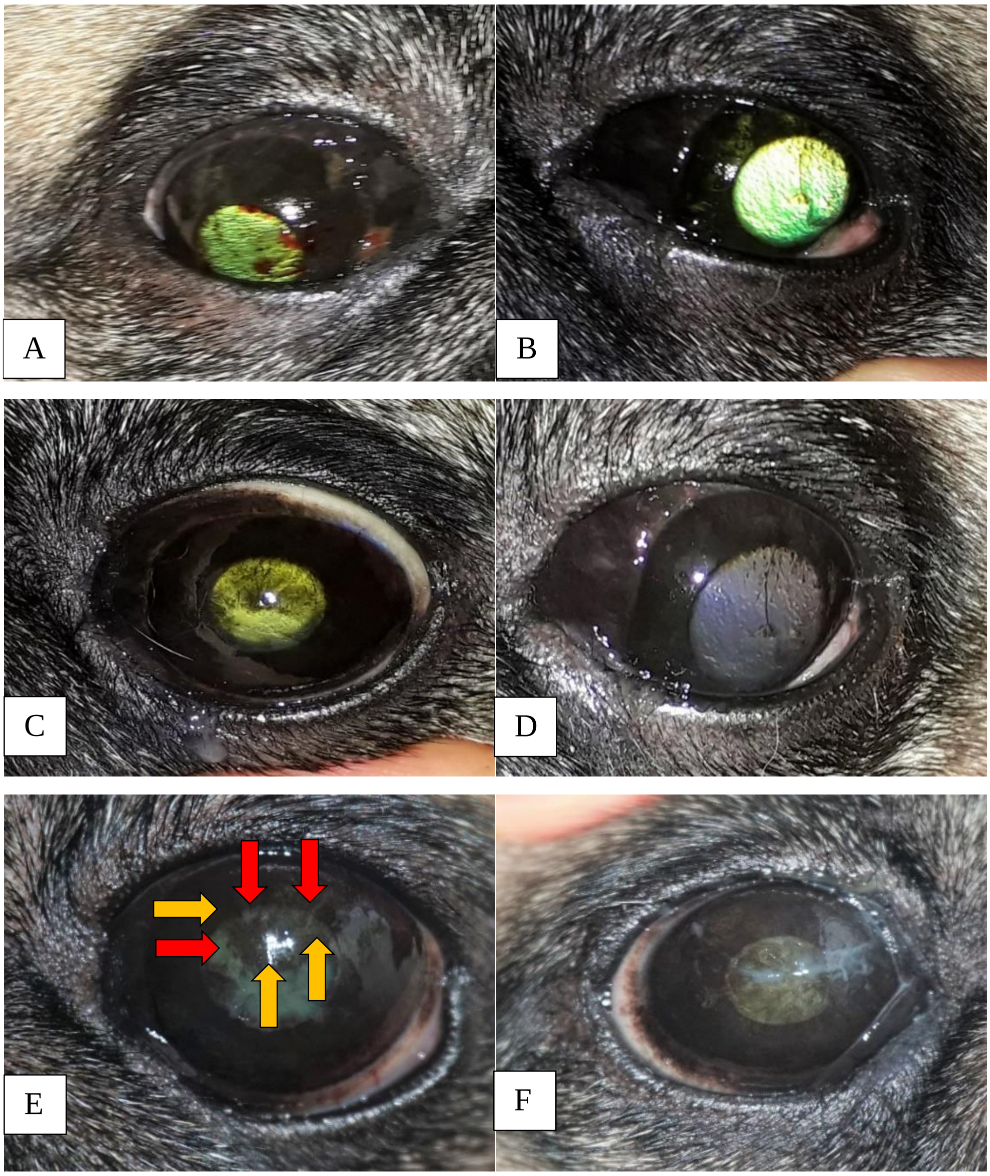


Figure 10. Postoperative evaluation of 6 dogs submitted to the automated central lamellar keratectomy procedure. A: Immediately postoperative. B: 7-day postoperative, free visual axis allowing visualization of the fundus. C: 4 months postoperative, transparency maintained with clear visualization of the fundus. There is a subtle area of repigmentation on the pupillary axis. D: 8 months postoperative, visual axis totally transparent and without repigmentation. E: After 1 year and 6 months, the central region of the cornea (visual axis) presents edema (yellow arrow) and areas of repigmentation (red arrow), however, without determining visual impairment. F: 2 years after the operation, the corneal transparency allows the visualization of the fundus reflex through the pupil. There is a subtle deposit of pigment on the surface, however, without loss of transparency. Source: personal archive.

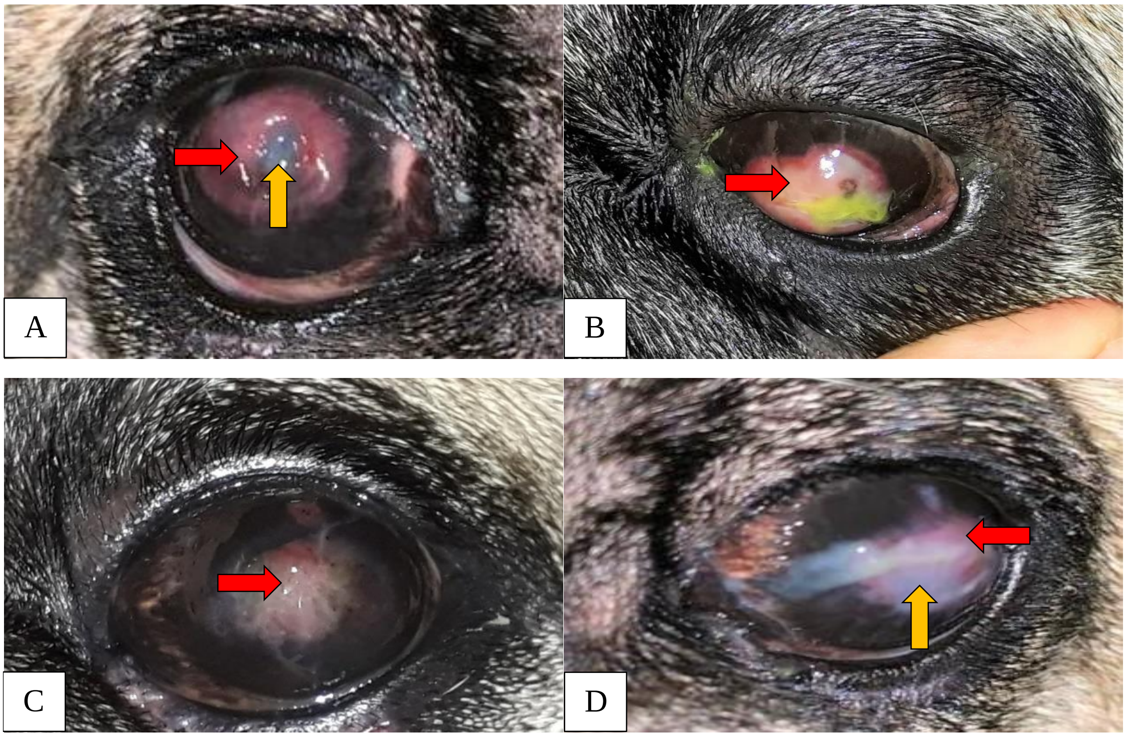


Figure 11. Postoperative evaluation of 3 dogs submitted to the automated central lamellar keratectomy procedure. A: 15 days postoperative. Granuloma formed in the peripheral region where the lamella was removed (red arrow) and severe edema in the central corneal area (yellow arrow). B: 21-day postoperative period. Formation of intense scar granuloma on the corneal surface, totally compromising its transparency (red arrow). C: 30 days postoperative. Granuloma formed on the visual axis compromising corneal transparency, and, consequently, the animal's vision. D: 2 months postoperative. Intense edema (yellow arrow) and granuloma (red arrow) on the cornea. Source: personal archive.

CONCLUSIONS

Automated central lamellar superficial keratectomy proved to be effective at allowing the recovery of visual function in dogs previously blinded due to severe corneal melanosis. This technique can be performed in a short time, reducing anesthetic costs and risks. When used, the technique avoids complications such as irregularities and corneal perforations.

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