Patient demographics, and outcome of striate keratotomy versus diamond burr debridement for treatment of spontaneous chronic corneal epithelial defects in dogs in South Africa

by

Dr Brent Sirrals

BSc Veterinary Biology, BVSc Honours

Student number: 23090759

https://orcid.org/0000-0002-4930-473X

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Supervisor: Dr A.D. Goodhead

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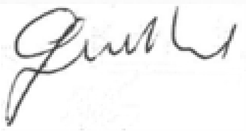
Signature of supervisor: 

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Faculty of Veterinary Science
Research Ethics Committee

09 March 2023

LETTER OF APPROVAL

Ethics Reference No	**REC010-23**
Protocol Title	**Spontaneous chronic corneal epithelial defects, analysis of canine cases presented to specialist referral practices in South Africa**
Principal Investigator	**Dr B Sirrals**
Supervisors	**Dr AD Goodhead**

Dear Dr B Sirrals,

We are pleased to inform you that your submission conforms to the requirements of the Faculty of Veterinary Sciences Research Ethics committee.

Please note the following about your ethics approval:

1. Please use your reference number (REC010-23) on any documents or correspondence with the Research Ethics Committee regarding your research.
2. Please note that the Research Ethics Committee may ask further questions, seek additional information, require further modification, monitor the conduct of your research, or suspend or withdraw ethics approval.
3. Please note that ethical approval is granted for the duration of the research as stipulated in the original application (for Post graduate studies e.g. Honours studies: 1 year, Masters studies: two years, and PhD studies: three years) and should be extended when the approval period lapses.
4. The digital archiving of data is a requirement of the University of Pretoria. The data should be accessible in the event of an enquiry or further analysis of the data.

Ethics approval is subject to the following:

1. The ethics approval is conditional on the research being conducted as stipulated by the details of all documents submitted to the Committee. In the event that a further need arises to change who the investigators are, the methods or any other aspect, such changes must be submitted as an Amendment for approval by the Committee.
2. Note: All FVS animal research applications for ethical clearance will be automatically rerouted to the Animal Ethics committee (AEC) once the applications meet the requirements for FVS ethical clearance. As such, all FVS REC applications for ethical clearance related to human health research will be automatically rerouted to the Health Sciences Research Ethics Committee, and all FVS applications involving a questionnaire will be automatically rerouted to the Humanities Research Ethics Committee. Also take note that, should the study involve questionnaires aimed at UP staff or students, permission must also be obtained from the relevant Dean and the UP Survey Committee. Research may not proceed until all approvals are granted.

APPROVED

We wish you the best with your research.

Yours sincerely

MOosthuizen

PROF M. OOSTHUIZEN
Chairperson: Research Ethics Committee

100 YEARS

Room 6-6, Arnold Theiler Building
University of Pretoria, Faculty of Veterinary Science
Private Bag X04, Onderstepoort, 0110, South Africa
Tel +27 (0)12 529 8390
Email marie.watson-kriek@up.ac.za
www.up.ac.za

Faculty of Veterinary Science
Fakulteit Veeartsenykunde
Lefapha la Disaense tša Bongakadiruiwa

Abstract

Background: Spontaneous chronic corneal epithelial defects (SCCED) are a common finding in canine patients referred for non-healing corneal ulceration. Various names have been used for this condition historically. The classic lesion and history include an axial or paraxial, superficial, corneal epithelial ulcer, that is non-responsive to topical therapy and is recurrent in nature. The lesions are not infected and not associated with any physical cause preventing healing. Pathology is well described, and various topical and surgical treatments have been used to treat SCCED lesions. Patient demographics for referral cases treated at a specialist veterinary ophthalmology hospital in South Africa, and the surgical outcome between striate keratotomy (SK) and diamond burr debridement (DBD) are reported in this study.

Methods: Clinical records for dogs that presented with SCCED lesions over a five-year period between 1st January 2019 and 31 December 2023 were retrospectively evaluated. The patients were included if they were positively diagnosed with a SCCED lesion and underwent either a SK or DBD surgery. Year of surgery, patient demographics, intra-ocular pressure (IOP), Schirmers tear test (STT), laterality, surgeon, surgical procedures, follow-up surgeries and fluorescein stain results were manually evaluated. Results were captured in *Excel* and statistical analysis was performed in "*R*". Patients were excluded if they had confounding pathology that may have affected healing post-operatively.

Results: 441 unique surgeries were identified for SCCED lesions and after exclusions were applied a total of 288 surgeries were included in the results. 240 dogs and 274 eyes made up these cases. French Bulldogs, Staffordshire Bull Terriers, Boxer dogs, and Labrador Retrievers were the most common breeds (54.1%) presented for SCCED lesions. Male dogs (58.0%) were over-represented. The average age of the dogs were 8.3 years, and the average body weight was 19.3 kg. Affected and unaffected eyes had a mean IOP of 17.12 mmHg and 17.41 mmHg respectively. Affected and unaffected eyes had a mean STT of 25.59 mm/min and 22.49 mm/min respectively. The STT of affected eyes was significantly raised compared to unaffected eyes. The most reported clinical signs at initial presentation were keratitis, blepharospasm, lacrimation, and corneal oedema. Left or right eyes were equally likely to be affected. The contralateral eye was subsequently affected in 7.6% of dogs during the study period. Bilateral SCCED lesions were diagnosed in 10.4% of the dogs, and 4.9% of the eyes required a second follow-up surgery. The surgical outcome, between day 10-14 post-operatively, were not significantly different for SK and DBD. Both SK and DBD resulted in surgical success in 87.6% and 85.1% of eyes respectively. The main predictive variables for surgical procedure outcome were increased lacrimation at the initial examination and repeated follow-up surgeries for a single eye.

KEYWORDS

Canine, dog, SCCED, corneal ulcer, diamond burr, striate keratotomy, Algerbrush

Acknowledgements

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I would also like to extend my gratitude to the staff at The Johannesburg Animal Eye Hospital for their assistance and overall support during the last three years.

A special thank you to Dr John Grewar for his assistance with the statistical analysis.

This research has been presented as a poster presentation at the 39th World Veterinary Association Congress in Cape Town, South Africa, 16-19 April 2024.

Dedications

To my wife, Lyndi, for your ongoing support, love, and encouragement!

"A soul mate's purpose is to shake you up, tear apart your ego a little bit, show you your obstacles and addictions, break your heart open so new light can get in, make you so desperate and out of control that you have to transform your life, then introduce you to your spiritual master."

- Elizabeth Gilbert, Eat, Pray, Love

To my son, Liam, may your future hold many bold adventures!

"The joy of discovery is the single most important thing in life!"

- Unknown

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List of Abbreviations

CN	Cranial nerve
D	Day
DBD	Diamond burr debridement
dPLR	Direct pupil light response
CI	Confidence interval
cPLR	Consensual pupil light response
CV	Coefficient of variance
IOP	Intra ocular pressure
IQR	Inter quartile range
JAEH	Johannesburg Animal Eye Hospital
Max	Maximum
Min	Minimum
Med	Median
mmHg	millimetre Mercury
nm	Nanometre
µm	Micrometre
OD	Oculus Dextra
OS	Oculus Sinistra
OU	Oculus Uterque
PLR	Pupil light response
RSA/SA	Republic of South Africa / South Africa
SAVC	South African Veterinary Council
SCCED	Spontaneous chronic corneal epithelial defect
SCL	Soft contact lens
SD	Standard deviation
SEM	Scanning electron microscopy
SK	Striate keratotomy
SP	Substance P
STT	Schirmer tear test
TEL	Third eyelid

TEM Transmission electron microscopy

Glossary

Afferent	Conducting inwards or towards the central nervous system.
Akinesia	Anaesthesia of an anatomical structure which result in the inability to perform voluntary movement.
Blepharospasm	Reflex eyelid blinking or eyelid movement that can't be controlled.
Confocal	Having a common focus point.
Contralateral	Belonging to or occurring on the opposite side of the body.
Co-pivotal	Two or shaft pivoting on a central point.
Efferent	Conducting outwards, or away from the central nervous system.
Enophthalmos	Abnormal retraction of the globe or sunken eyes.
Epiphora	Excessive tearing or watery eye.
Microplicae	Specialized surface structure of epithelial cells of wet surface tissue, with plasmalemmal folds.
Microvilli	Microscopic cellular membrane protrusions that increase the surface area for diffusion and minimize any increase in volume.
Multivariate	Type of data involving a number of statistical variables
Ipsilateral	Belonging to or occurring on the same side of the body.
Isocentric	All beams have a central focus point.
Photopic	Bright light.
Scotopic	Dim light.
Specular reflection	Mirror-like reflection of waves, such as light, from a surface.
Stoic	Enduring pain or hardship without expressing feeling or complaint.
Univariate	A type of data which consists of observations on only a single characteristic or attribute.

Chapter 1: Introduction

Spontaneous chronic corneal epithelial defect (SCCED) is a common presenting complaint in canine patients referred for non-healing corneal ulceration. Various names have been used for this condition historically, these include indolent ulcer, indolent erosion, canine recurrent erosion, Boxer ulcer, recurrent epithelial erosion, persistent corneal erosion, nonhealing erosion, idiopathic persistent corneal erosion. (Bentley, 2005)

The classic lesion and history include an axial or paraxial, superficial, corneal epithelial ulcer, that is non-responsive to topical therapy and is recurrent in nature. The lesion is not infected and is not associated with any physical cause preventing healing. Clinically the lesion is surrounded by a region of loose epithelium. (Murphy et al., 2001) Although a physical cause may be an initiating factor, this generally goes unnoticed by the pet owner.

Fluorescein staining of the lesion is the diagnostic method of choice, with careful examination of the periocular structures to rule out confounding pathology.

This recurrent nature of SCCED lesions is particularly frustrating to both pet owners and veterinarians alike. Typically, weeks may go by before a general veterinarian may develop a suspicion that the dog has a SCCED lesion. Most superficial corneal ulcers are treated conservatively at first, and only after recurrence is determined are cases referred for a second opinion to a veterinary ophthalmologist. A tendency experienced in South Africa is that some general veterinarians may attempt cotton tip debridement, but most veterinarians do not have the adequate experience or magnification equipment to perform more invasive procedures. And many cases are referred to the Johannesburg Animal Eye Hospital (JAEH) for a second opinion. At the time of this study the JAEH was the only specialist veterinary ophthalmology hospital servicing the greater part of South Africa (SA).

Historically, because of the high success rate, striate keratotomy (SK) was the treatment of choice for canines, presented for a second opinion to the JAEH, if conservative medical therapy and topical debridement with a cotton tip applicator was unsuccessful for SCCED lesions. There are inherent risks to performing a SK, and it is routinely done under general anaesthetic at the JAEH. Thermal cautery and lamellar keratectomy are more invasive compared to SK and are not preferred. Diamond burr debridement (DBD) has been described as an alternative to SK. It is a procedure that does not routinely require general anaesthetic, has fewer inherent risks, and has a high rate of success. DBD has been offered as a treatment option at the JAEH since 2014.

To the author's knowledge there are no published research papers about SCCED lesions or patient demographics from Southern Africa. The main aim of this study was to present an overview of the patient demographics for SCCED lesions in canines that are referred for specialist ophthalmology opinion in South Africa. The second aim was to compare the outcome of two surgical interventions often used to treat SCCED lesions in canines in South Africa.

The following chapter will provide an overview to completing an ophthalmic examination and discuss relevant corneal anatomy. These are important to understand as subtle lesions may be missed easily, or more importantly, treatment approach to each case is based largely on the periocular and corneal abnormalities detected. Chapter 3 will then further build on this and provide an overview of SCCED lesions and treatment options.

Chapter 2: Literature review: Ophthalmic examination and corneal anatomy

2.1: Ophthalmic examination and vision assessment

A complete ophthalmic examination includes the following steps and is covered in detail in ophthalmic textbooks. (Gelatt, 2020) (Maggs et al., 2013) (Martin et al., 2019) It is briefly discussed here to illustrate the procedures performed routinely on cases presented for a second opinion.

- History & Field vision assessment: A complete medical history should be obtained from the client. Common observations made by a client may include the following, decreased vision or blindness, ocular discharge, any colour changes, and signs of pain. In the normal "field setting" a crude assessment of vision can only discern severe deficiencies or suspected complete loss of vision. In general, an owner would notice some form of visual deficit with complete blindness but not always with partial visual loss in a known environment. For SCCED patients, the history may include ocular pain and an ocular discharge.
- General Ocular Exam
    - Ophthalmic exam in ambient light from a distance - General observation and assessment for ocular or periocular lesions using no instruments or physically touching the animal. Special attention must be given to conformation, signs of pain, globe size and position, discharge, and the eyelids. Patients with SCCED lesions may present with typical signs of ophthalmic pain; blepharospasm, epiphora, third eyelid protrusion and enophthalmos. The specular reflection (Purkinje image) of the corneal surface can be observed with normal room light. It is a crude method to judge the optical smoothness of the corneal surface and pre-corneal tear film. This may show a slight distortion if a SCCED lesion is present.
- Restraint
    - For ease of examination an experienced handler may assist to gently hold the patient's body and head. This is best done on a raised examination table with the patient's eyes at a comfortable height for the examiner. Fractious and aggressive animals may require additional restraint, the use of a muzzle or sedation to allow examination. Akinesia is not required in canine patients, but topical anaesthesia may be necessary if severe pain is present. This will provide relief from blepharospasm, and third eyelid prolapse. Oxybuprocaine (*Novasin Wander, Novartis South Africa*) is commonly used by the investigator.
- Vision assessment and neuro-ophthalmic exam
    - Maze test - A maze test may be performed by having the animal walk in an unfamiliar environment, with obstacles placed on the floor, and observing the animal's movement in the environment. It can also be completed after placing an eye patch over one eye at a time to assess individual eye function. A maze test should be performed in photopic and scotopic conditions.
    - Tracking response - A tracking response can be done with cotton balls tossed within the patient's field of vision. A positive response is eye or head movement acknowledging the object and following the object's path of flight.
    - Visual placing response - The animal's body is supported with the legs hanging free. The animal is presented towards a raised flat surface but without allowing the feet or legs to touch it. A normal response in a visual animal is to lift its feet and attempt to place them on the surface. This is not a sensitive test and may be influenced by anxiety, pain, and other factors.
    - Menace response - A menacing gesture made towards the eye may be used to elicit a blink reflex or closure of the eyelids in the ipsilateral eye. This is a learned protective response and will be one of the first tests to evaluate individual eyes of an animal. The menace response may be present from 3-4 weeks of age but is generally only reliable after 12 weeks

of age. (Lavely, 2006) The response tests the function of the retina and optic nerve (CNII) as part of the afferent pathway and the palpebral branch of the facial nerve (CNVII) as part of the efferent pathway. Globe retraction may be seen and is affected by the abducens nerve (CNVI). If a menace response is absent, a palpebral or corneal reflex should be elicited to see if the animal is able to blink and to rule out facial nerve paralysis. A menace response may still be present if partial vision is present or in severe loss of visual acuity. False positive results may be elicited if the patient feels any air movement or touching of the facial hairs. False negative results, vague or inconsistent responses may be seen in anxious, depressed, and stoic animals.

- Pupillary light reflex (PLR) - Pupil size should be noted, in photopic and scotopic conditions, before any stimulation takes place. A PLR is performed by shining a bright, focal light at one eye and observing the pupil response in the ipsilateral and contralateral eye. Finoff-transilluminator (*3.5 V Halogen Fiber Optic Transilluminator, Welch Allyn*) or otoscope without the reusable specula (*Pneumatic otoscope, Welch Allyn*) lights are suitable options. Constriction of the ipsilateral pupil (direct [dPLR]) and constriction of the contralateral (indirect/consensual [cPLR]) pupil is a normal response. The retina, optic nerve (CNII), optic chiasm, optic tract, Edinger-Westphal nucleus, midbrain, oculomotor nerve (CNIII) (parasympathetic fibres) and iris are assessed with this reflex. It is suggested that this test is performed in a darkened environment. The pupillomotor fibres branch off the optic tract before the visual fibres and a PLR may be seen with cortical blindness. Normal PLR responses are present from the time the retina is mature in dogs. This is around 28 days post-partum. (Lavely, 2006)
- Dazzle reflex - A bright light, Finoff-transilluminator (*3.5 V Halogen Fiber Optic Transilluminator, Welch Allyn*), is quickly shone into one eye at a time from a close distance. A normal response is closure of the eyelids and retraction of the globe in the ipsilateral eye. The dazzle reflex tests similar pathways as the menace response but instead, it is a subcortical reflex in the brain. It may be present from birth in carnivores.
- Palpebral reflex and corneal reflex - This can be elicited by gently touching the skin around the palpebral opening with your finger, or touching the cornea itself, by using a cotton tip applicator. This is usually done if the menace and dazzle responses are suspected to be absent. By performing these you confirm innervation of the ocular muscles responsible for blinking of the eyelids via the following pathway: Palpebral nerve/corneal nerve, trigeminal nerve, brainstem, and facial nerve. Corneal sensitivity (corneal touch threshold) may be evaluated in a quantitative manner by using a Cochet-Bonnet aesthesiometer.
- Vestibulo-Ocular Reflex - The animal's head is moved vertically and horizontally while the body is held stationary. A normal response is for the eyes to fixate and maintain the last eye direction. Slow eye movement will be seen in an opposite direction to the head movement. As the head is moved further (through vestibular system input) a quick eye movement in the direction of head movement may be seen. The eye movement will stop when head movement stops. The eyes must move in unison. This indirectly assesses cranial nerves II, IV & VI innervating the extra-ocular muscles and cranial nerve VIII & the medial longitudinal fasciculus. These nerves coordinate eye movement. Blind animals will show a physiological nystagmus due to vestibular system input.

- Close examination of the adnexa, globe, anterior segment, lens and vitreous using a slit-lamp biomicroscope. The handheld slit-lamp is commonly used in veterinary medicine and allows a magnified and three-dimensional image with the convenience of being mobile. The slit-lamp is a combination instrument, it is a binocular microscope together with a source of illumination. The instrument is co-pivotal, confocal and isocentric. With this specific model (*Keeler PSL Classic, Keeler UK*) the light source pivots. The light source can be adjusted by a series of filters and diaphragms and results in a diffuse or focused beam, different intensities of light, shape, orientation, and colour of the light beam. The eye structures are examined using various settings on the slit-lamp to identify pathology and to create a three-dimensional mental image of the eye.

- Posterior segment examination using direct and indirect ophthalmoscopy.
    - Obscurement of a tapetal reflex and the deeper fundic structures is suggestive of a non-neurological/obstructive cause of vision loss. A fundic examination to assess the vitreous, retina, retinal vasculature and optic nerve head is done to complete the vision assessment.
    - Direct ophthalmoscopy is performed by using a handheld power source with a built-in light source (*Coaxial Ophthalmoscope, Welch Allyn*). Light is reflected via a mirror or prism into the patient's eye and then reflects via a lens to the examiner's eye. A series of lenses can be adjusted to focus on various depths. The direct ophthalmoscope also allows light intensity, shape, and colour adjustment. It allows a magnified image of the fundus being examined but only a small field of view is possible. The patient may be examined at an arm's length distance (distant direct ophthalmoscopy) or close-up (<10 cm) (close direct ophthalmoscopy).
    - Indirect ophthalmoscopy is performed by having a focal light source close to the examiner's eyes and a 20-diopter handheld magnifying lens (*Indirect Viewing Lens Veterinary, Welch Allyn*) close to the patient's eye. This allows for a safe working distance and for a larger field of view of the fundus at a comparatively lower magnification in comparison to direct ophthalmoscopy. The image generated is inverted and reversed. Binocular (*Vantage Plus LED Indirect Ophthalmoscope, Keeler UK*) or monocular indirect systems are available. Binocular systems allow for depth perception of lesions and surrounding tissues.
- Diagnostic procedures
    - Schirmer Tear test (STT) - This is a quantitative measurement of the aqueous component of the tear film. A standardized strip of Whatman no. 41 filter paper, 5x35 mm, with a rounded tip and a notch 5 mm from the end is used. A commercially available strip (*Schirmer Tear Test, MSD Animal Health*) has 1 mm increments and a blue dye at the 5 mm point, this allows easier visualization of moisture uptake into the paper strip. It is advised to bend the tip at the notch, with the strip in the packaging. Remove from the packaging without handling the tip to avoid contamination with oils which could influence readings. The strip is then placed in the fornix of the lateral half of the lower eyelid and the reading is taken after 60 seconds.
    - Intraocular pressure (IOP) measurement - IOP is measured directly with manometry, but this method is invasive. Alternatively, it can be measured indirectly in various ways. Digital, indentation, applanation and rebound tonometry are common indirect methods. Rebound tonometry (*TonoVet, iCare*) is easy, cost effective and efficient to perform. The principles are that a small probe is electromagnetically propelled to the cornea, from a defined distance. It contacts the cornea and rebounds back towards the instrument. The instrument assesses the characteristics of the probe deceleration and return time. A value, measured in mmHg, is then displayed on the instrument. TonoVet rebound tonometry has been compared to direct manometry and found to deliver accurate results in various species.
    - Fluorescein dye test - Fluorescein is available commercially (*Haag-Streit Diagnostics*) as a 2 % solution in pipettes or impregnated strips. It is a water soluble weak dibasic acid. Sodium fluorescein appears orange - yellow in colour in acid environments but in alkaline environments, such as the tear film, it is fluorescent green (520nm) with blue light (490 nm) exposure. The most common use is to detect corneal epithelial defects or ulceration. After application to the eye surface the eyelids should be allowed to blink and excess dye should be rinsed from the eye with saline. Fluorescein is hydrophilic and lipophobic and does not penetrate intact corneal epithelium. It will adhere to the corneal stroma but not to Descemet's membrane. Alternative observations or tests with fluorescein are to detect conjunctival epithelial defects, assess for qualitative tear film abnormalities via the tear film

break up time, observe for aqueous humour leakage via a Seidel's test and to assess patency of the nasolacrimal ducts via a Jones' test.

2.2: Normal canine corneal anatomy

The canine cornea, together with the sclera, is part of the fibrous tunic of the globe. The sclera is covered by a thin layer of conjunctival tissue and fibrous connective tissue called Tenon's capsule. The sclera, conjunctiva and Tenon's capsule join at the limbus and transition into corneal tissue. The cornea is composed of various layers. From outermost centrally, in the dog (*Canis familiaris*), they are the epithelium, stroma, Descemet's membrane and the endothelium. The cornea possesses essential properties. It is transparent and devoid of vascular tissue. It both transmits and refracts light passing through it. Nutrition is supplied by the limbal vasculature, pre-corneal tear film and aqueous humor. (Gelatt, 2020; Maggs et al., 2013; Martin et al., 2019)

Corneal epithelial cells and its basement membrane are the outermost physical layer. Histologically the epithelial cells are stratified, squamous, non-keratinized cells. The basal cells (innermost) are elongated and situated on the epithelial basement membrane. Moving towards the surface, the next layers are polyhedral wing cells and then transition to non-keratinized squamous epithelial cells (outermost). Together they make up 5-11 cell layers in total. The surface epithelial cells have microplicae and microvilli in close association with the glycocalyx layer of the pre-corneal tear film of which it is dependent on for nutrient supply. (Gelatt, 2020; Maggs et al., 2013; Martin et al., 2019)

The anterior corneal basement membrane is situated deep to the epithelial layer. It consists of an intricate network of nano-meter sized fibres with pores and elevations. (Abrams et al., 2002; Evans et al., 2013) The basement membrane is actively secreted by the basal epithelial cells and consists of type IV collagen fibrils, heparin sulphate, laminin and fibronectin. (Levin et al., 2011) The basement membrane is a scaffold for cell movement and attachment. (Levin et al., 2011)

The basal epithelial cells are connected horizontally between each other with desmosomes. Basally, they are connected to the basal lamina and anterior stroma through an anchoring complex. This complex consists of hemidesmosomes, type VII collagen anchoring fibrils and deeper anchoring plaques. (Levin et al., 2011) The anchoring fibrils extend into the upper stroma, branch among the collagen fibrils and attach to anchoring plaques of the corneal stroma. (Bentley, 2005)

With normal cell turnover and wound healing the basal epithelial cells' hemidesmosomes disassemble and reassemble to allow migration and proliferation of the basal epithelial cells. With large wounds new basement membrane is secreted by the basal epithelial cells. (Abrams et al., 2002) Epithelial cell turnover is estimated to be between 7-10 days. (Levin et al., 2011) Most of the cell mitosis is confined to the basal epithelial cells. (Gelatt, 2020)

Stromal tissue consists of organized collagen fibrils and interspersed cells. The fibrils are uniform in size, highly organized and arranged in different lamellae. Interspersed between the lamellae and fibrils are fibrocytes, called keratocytes. (Evans et al., 2013) Most of the corneal thickness is composed out of stromal tissue.

The basement membrane of the endothelial cells is called Descemet's membrane. It is acellular and thicker than the anterior basement membrane and has some elasticity. It is composed of different collagen fibrils. (Gelatt, 2020) Descemet's membrane thickens with age due to being continuously secreted by the endothelial cells. (Maggs et al., 2013)

The innermost layer of the canine cornea is the endothelial cell layer. It is a single layer of flattened cells, these cells are postmitotic in adult canines, with limited to no ability for replication. (Maggs et al., 2013) A main function of the endothelial cells is to actively pump ions out of the stromal tissue into the aqueous humor. This induces a state of relative dehydration in the corneal stroma and is essential to maintain corneal clarity. (Levin et al., 2011)

Chapter 3: Literature review: SCCED lesions and treatment options

3.1: Superficial chronic corneal epithelial defects (SCCED)

The typical presentation is a middle-aged dog with a non-healing superficial corneal ulcer, but dogs of any age may be affected. These are uncomplicated lesions that have not healed in over 7-14 days. Ophthalmic examination will exclude underlying causes for delayed wound healing, such as mechanical irritation, foreign bodies, infection, abnormalities of the tear film, exposure of the cornea or corneal oedema related pathology. (Bentley, 2005; Murphy et al., 2001; Whitley and Hamor, 2020)

The characteristic lesion is a superficial corneal ulcer staining brightly with fluorescein, surrounded by a ring of loose epithelium which stains less intensely. The lesion does not include stromal loss and mild corneal oedema is typically confined to the central erosion. Variable amounts of vascularization may be present, depending on the chronicity (**Figures 3.1 & 3.2**). (Bentley, 2005; Maggs, 2018; Whitley and Hamor, 2020)

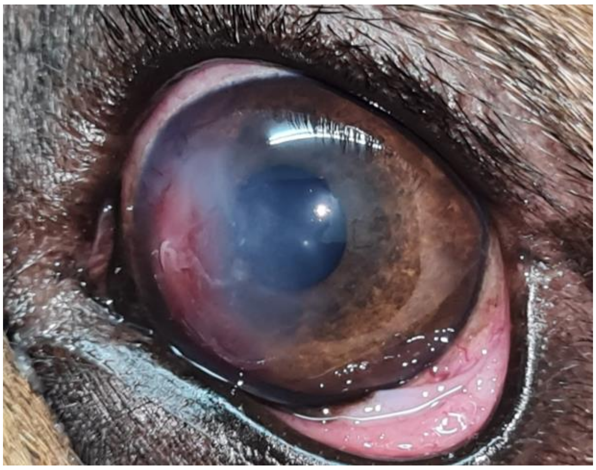

Figure 3.1: Typical SCCED lesion. This image illustrates the subtle superficial lesion with indistinct margins of loose epithelium and mild localized corneal oedema. Superficial vascularization extends off the medal limbus towards the lesion. (Photo: B. Sirrals)

Figure 3.2: Fluorescein staining of the SCCED lesion in Figure 3.1. This image shows the indistinct staining of the border or "halo" surrounding the central SCCED lesion. In contrast to this image, superficial lesions without surrounding loose epithelium will have a crisp edge to the stained area. (Photo: B. Sirrals)

SCCED lesions do not result in loss of vision unless a concurrent complication develops. Ocular discharge type and character change may be noted. A superficial corneal lesion may present with an increase in lacrimation and epiphora. (Bentley, 2005) Ocular colour changes may include corneal oedema seen as a light blue grey to white discolouration if a superficial corneal lesion is present. (Bentley, 2005) The cornea may also develop vascularization and show red discolouration in severe chronic cases, but this is variable. (Bentley, 2005) Pain is commonly seen and blepharospasm, third eyelid prolapse and rubbing of the eye may be noted. (Bentley, 2005) Miosis may be present but may not be commonly observed by the client.

Basal cell, basement membrane abnormalities and decreased hemidesmosomes have been described in SCCED lesions. (Bentley et al., 2001; Gelatt and Samuelson, 1982) Morphological abnormalities described by Bently *et al*. included: poor stromal attachment of adjacent epithelium, with dysmaturation of the epithelium, and varied epithelial thickness. In the stroma fibroplasia, vascularization and leukocyte infiltration was described. Immunohistochemistry revealed a lack of basement membrane or adhesion complexes, or basement membrane with small discontinuous segments. Laminin, collagen IV, and collagen VII were usually either not present or present only in short, discontinuous segments on the surface of the erosion. Furthermore, electron microscopy was used to confirm the lack of basement membrane. (Bentley et al., 2001)

Corneal stromal samples revealed the formation of an acellular hyalinized zone superficially, of 4.4 micrometre thickness. These findings were not associated with basement membrane or anterior stromal dystrophies. (Bentley et al., 2001) Leukocyte (neutrophils & lymphocytes) infiltration were typical in the area under the lesion. (Bentley et al., 2001)

Nerve fibre abnormalities included an abnormal dense plexus of substance P and calcitonin gene-related peptide immunoreactive nerve fibres in the stroma surrounding SCCED lesions. (Murphy et al., 2001) Elevated substance P levels were detected in the epithelium but not in the tears of dogs with SCCED lesions. In this same study Boxers, Golden Retrievers and Keeshonds were overrepresented. (Murphy et al., 2001)

3.2: Treatment options for SCCED

A large number and variety of medical treatments have been described and may include serum, tetracycline, oral tetracycline, substance P, epidermal growth factor, aminocaproic acid, combinations of antibiotic/chondroitin sulphate and glycosaminoglycans. (Bentley, 2005; Wu et al., 2018)

Topical treatment with substance P (SP) resulted in an improvement in patient comfort level, decrease in blepharospasm, decreased pawing at the affected eye and an increase in the patient's activity level. SP treatment was effective in 70-75% of cases. (Murphy et al., 2001)

Limitations of studies reporting topical medications have been mentioned to include the fact that various of these have included topical debridement with a cotton-tip as part of the procedure process. The other concerns are that the studies included small case numbers without randomization. Not all medications are commercially available or require frequent application, which may be difficult for pet owners to comply with. (Whitley and Hamor, 2020)

A review article covered treatment options that include some form of intervention and the expected outcome: cotton-tip debridement alone (overall success rate 50%), cotton tip debridement & contact lens (58%), cotton-tip debridement & third eyelid flap (64%), diamond burr debridement or grid/striate keratotomy (80-87%), anterior stromal puncture (68-88%), thermal cautery (up to 100%), and lastly lamellar keratectomy (100%). (Bentley, 2005)

Thermal cautery may have a variable outcome. 100% success was reported in a study by Bentley and Murphy, the case numbers were low in this study. (Bentley and Murphy, 2004) A recent article that had more case numbers reported successful healing in only 65.1% of eyes at 15.4 days post-operatively. 22.7% of eyes required a second procedure. (Landrevie et al., 2023)

Striate keratotomy is a well excepted surgical treatment option. Various reports states that this can safely be performed in a conscious patient under topical anaesthesia. Our experience is that this may increase the risk for complications, especially if performed by inexperienced surgeons. By using a technique that punctures the anterior stroma it produces anterior stromal adhesions and increases extracellular matrix components that promotes epithelial adhesion. (Bentley et al., 2001) Some variations of the technique exist but in general debridement of loose epithelium is first performed with a cotton-tip. Then a 25-gauge needle can be grasped with a needle holder such that only the very tip of the needle is exposed. This is then used to make a cross-hatched grid (0.5-1.0 mm apart) of superficial incisions over the ulcerated area, it should puncture the superficial anterior stroma (5-10%), and extending slightly into the normal epithelium past the ulcerated area (2-3mm). (Whitley and Hamor, 2020; Wu et al., 2018) The procedure can safely be repeated at 1 to 2-week intervals until the lesion has healed.

Published data for treatment success as measured by a negative fluorescein stain at Day (D) 14 for a single SK procedure is approximately 80-87%. (Bentley, 2005; Gelatt, 2020; Moore, 2003). With the average healing time between 9.3-13.4 days. (Moore, 2003)

Diamond burr debridement is regarded as a safe and easy procedure to perform. The effect of DBD was demonstrated to be safe. Based on histology, it did not remove corneal stromal tissue past the epithelial basement membrane level. Significantly more basement membrane material was removed with longer application time. (Da Silva et al., 2011) Micro-erosions in the basement membrane are created with DBD, which affects assembly of new epithelial adhesion complexes. This, together with fibrosis and extracellular matrix protein expression changes, may then subsequently promote epithelial healing. (Da Silva et al., 2011) DBD will also affect the superficial stromal hyaline acellular zone, causing significant thinning and even complete removal. (Dawson et al., 2017) These reports establish the framework for using DBD to treat SCCED lesions in dogs. Performing a DBD is fairly easy and well described. (Gosling et al., 2013; Wu et al., 2018) A battery-operated Algerbrush unit (*Algerbrush II, Alger Equipment*) is used with a 2.5 or 3.5 fine or medium grit burr. The unit rotates the burr which is then slowly and continuously passed over the ulcer site. A combination of circular, vertical, and horizontal movement may be applied for a few minutes. This action removes the loose epithelium until a stable epithelial edge is achieved. The burrs must be steam sterilized between patients. The advantages of a DBD include ease of use and reduced training time, cost effective, simple to perform, less corneal scarring, effective at removal of epithelium and basement membrane material, and minimal refractive error changes. (Gosling et al., 2013)

Published data for treatment success as measured by a negative fluorescein stain for single DBD procedure is approximately 82% at D13. (Nevile et al., 2016) Another study reported 70% success by D7 and 92.5% by D15.5. (Gosling et al., 2013) Hung *et. al*. recently reported a 73.9% success rate with one treatment of DBD. 17.0% required additional treatment and 4.7% of eye developed complications. (Hung et al., 2020) Another report found no significant difference in healing outcome between DBD (77.4%) and DBD + SK (77.3%) with average healing time 13.3 and 15.4 days respectively. This report stated a higher complication rate of 13.3%. (Wu et al., 2018)

Chapter 4: Approach to SCCED cases in South Africa

Descriptions of the techniques used in South Africa

Historically, because of the high success rate, a striate keratotomy (SK) was the treatment of choice in canines presented for a second opinion in South Africa at the JAEH, if conservative medical therapy and topical debridement with a cotton tip applicator was unsuccessful for SCCED lesions. The success rate after performing a SK has however never been measured in a scientific approach to date in South Africa.

There are inherent risks in performing a SK, such as deep stromal laceration, perforation of the globe, inability to adequately debride loose epithelial tissue, and inability to perform adequate striations. The risk for perforation and deep stromal lacerations are the main concerns for inexperienced surgeons when performing this procedure. Certain breeds of dogs with an aggressive nature or anxious demeanour would also require a form of anaesthesia. As a rule, the specialists in South Africa have always opted to have the dogs under anaesthesia before performing a SK. Thermal cautery and lamellar keratectomy are generally more invasive procedures compared to SK & DBD.

Striate keratotomy technique used: Patients are anaesthetised. Meloxicam (*Petcam, Ascendis Animal Health*), morphine (*Morphine sulphate, Fresenius Kabi*) and diazepam (*Valium, Roche*) are used as pre-medication and induction is performed with propofol (*Fresenius Propoven, Fresenius Kabi*). Patients are intubated and sevoflurane (*Sojourn, SL Safeline Pharmaceuticals*) is used as an inhalation agent for the duration of the procedure. Patients are placed in a dorso-lateral position with the affected eye facing up towards the surgeon. The surgeon sits at the edge of the table on the side of the head. The eye is aseptically prepared with dilute 0.5% povidone iodine solution (1:20 dilution) (*Povidone Iodine Solution, B Braun Medical*) followed by a gentle saline rinse. An eyelid speculum is used to keep the eyelids open. Under an operating microscope, the loose corneal epithelium is debrided, first with a dry cotton-tip and then with a nr. 15 scalpel blade. The blade is dragged at a slight angle across the cornea allowing the loose epithelium to be sloughed off. A 27-gauge needle, with a slightly bent tip, is used to perform the cuts on the anterior surface of the cornea. The bevelled edge of the needle is used to perform the cutting and not the tip (**Figure 4.1**). This is done "free hand" under high magnification to ensure superficial anterior stromal penetration. Two series of multiple parallel cuts are made perpendicular to each other and an average total of 50-200 cuts are made, depending on the size of the eye and the lesion. The eye is rinsed with saline solution throughout the duration of the procedure. On conclusion, a soft contact lens (SCL) (*0.00 power factor, PureVision, Bausch & Lombe*) is placed on the cornea.

An Elizabethan collar (*Buster*) is placed to help limit self-trauma post-operatively. The patient is then allowed to recover from anaesthesia, under supervision of a veterinary nurse. The patient is discharged with a topical antibiotic eye drops (*Exocin, Allergan*) prescribed 4x/day in the affected eye, topical preservative free morphine (*Morphine sulphate, Fresenius Kabi*) 4x/day in the affected eye, 15 minutes after the antibiotic eye drops, for 2-3 days only to control pain, and oral non-steroidal anti-inflammatory medication (*Petcam, Ascendis Animal Health*) 1x/day orally, for 3-5 days.

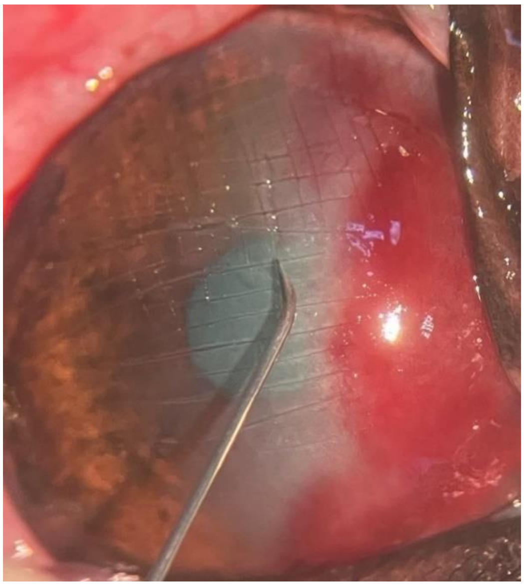

Figure 4.1: Striate keratotomy being performed with the bevel edge of a 27-gauge needle. (Photo: B. Sirrals)

Diamond burr debridement technique used: Topical anaesthesia (*Novasin Wander, Novartis*) is instilled 5 minutes prior to intra-venous sedation with butorphanol (*Dolorex, MSD Animal Health*). Topical anaesthesia may be applied repeatedly as required. Once the patient is calm and compliant it is placed in lateral recumbency with the affected eye facing up. The eye is aseptically prepared with dilute 0.5% povidone iodine solution (1:20 dilution) (*Povidone Iodine Solution, B Braun Medical*) followed by a gentle saline rinse. An eyelid speculum is used to keep the eyelids open. Under an operating microscope the loose non-adherent epithelium is gently debrided with a dry cotton-tip. Further debridement is then performed with a handheld, battery operated, motorized device (*Algerbrush II, Alger Equipment*) using a sterilized, 3.5 mm, medium grit, burr tip attachment for approximately 2 minutes. The eye is rinsed with saline solution and a soft contact lens (*0.00 power factor, PureVision, Bausch & Lombe*) is placed on the cornea.

Post operative care is the same as for a SK surgery. An Elizabethan collar (*Buster*) is placed to help limit self-trauma post-operatively. The patient is then allowed to recover from sedation, under supervision of a veterinary nurse. The patient is discharged with a topical antibiotic eye drops (*Exocin, Allergan*) prescribed 4x/day in the affected eye, topical preservative free morphine (*Morphine sulphate, Fresenius Kabi*) 4x/day in the affected eye, 15 minutes after the antibiotic eye drops, for 2-3 days only to control pain, and oral non-steroidal anti-inflammatory medication (*Petcam, Ascendis Animal Health*) 1x/day orally, for 3-5 days.

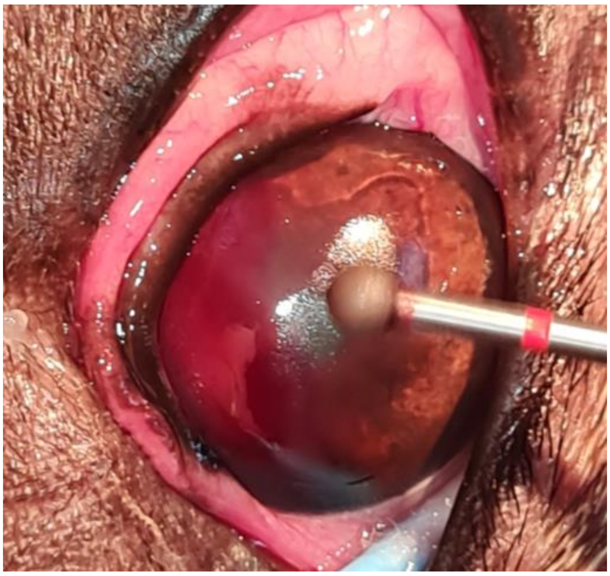

Figure 4.2: Diamond burr debridement with an Algerbrush II device. (Photo: B. Sirrals)

Figure 4.3: Placement of a soft contact lens on the cornea. (Photos: B. Sirrals)

For both procedures post-operative examination advised is between 10-14 days. During this visit, slit-lamp biomicroscopy and fluorescein stain examinations are performed. The soft contact lens is removed if it is still present at the follow-up examination.

All the examinations and procedures are performed by South African Veterinary Council (SAVC) recognized specialist veterinary ophthalmologists and/or ophthalmology residents working under specialist supervision at the JAEH.

Chapter 5: Motivation for the study

5.1: Problem statement

To the author's knowledge no published data exists about patient demographics and outcome of treatments performed for SCCED lesions in canine patients in South Africa referred to a specialist veterinary ophthalmology practice.

5.2: Aim

The main aim of this study was to present an overview of patient demographics referred for a second opinion for SCCED lesions in canines in South Africa.

The second aim was to compare the outcome of two surgical interventions often used to treat SCCED lesions in canines in South Africa at a specialist veterinary ophthalmology referral practice.

The influence of breed, sex, surgeon, laterality, age, weight, year of surgery, IOP, STT, and other relevant variables, on the procedure outcome, was evaluated.

5.3: Objectives

To describe the patient population characteristics of canines presented for a second opinion for non-healing spontaneous chronic corneal epithelial defects over a five-year period at a specialist veterinary ophthalmology referral practice in South Africa.

To critically evaluate the outcome of two surgical interventions commonly used to treat non-healing spontaneous chronic corneal epithelial defects, over a five-year period, at a specialist veterinary ophthalmology referral practice in South Africa.

5.4: Benefits arising from the study

SCCED lesions are a commonly diagnosed condition causing ophthalmic pain and discomfort and which frequently needs surgical intervention for treatment purposes. Further to this, the recurrent nature of the lesions causes frustration for the pet owner and general veterinarian treating the pet. The information will assist veterinary practitioners to recognize the typical patient and clinical presentation for SCCED lesions in canines, in South Africa, and serve as a guide to easily diagnose a SCCED lesion.

The study will aid South African veterinarians to make recommendations to their clients with regards to specific treatment options available at a referral hospital and the expected outcome.

5.5: Hypothesis

H_1: Striate keratotomy surgery for SCCED lesions is more likely or less likely to stain fluorescein negative at 10-14 days post-operatively compared to SCCED lesions treated with diamond-burr debridement.

H_0: Striate keratotomy surgery for SCCED lesions is equally likely to stain fluorescein negative at 10-14 days post-operatively compared to SCCED lesions treated with diamond-burr debridement.

Chapter 6: Materials and methods

6.1: Study Population

The study population was selected from digital clinical records from the largest private specialist veterinary ophthalmology practice in South Africa, The Johannesburg Animal Eye Hospital. At the time of this study, this clinic was the only specialist veterinary ophthalmology referral practice servicing the greater part of South Africa's inland. Cases that presented during the five-year period, 1st January 2019 to 31st December 2023, were included in the study. Canine patients (*Canis familiaris*) are the species of interest. Cases must have presented with the history of a chronic superficial corneal ulcer or ulcers that failed to resolve through normal wound-healing processes and had the typical clinical presentation for SCCED lesions, identified with slit-lamp biomicroscopy, and no other physical or physiological cause that would have prevented healing. Positive fluorescein staining of the SCCED lesion, at the initial examination, was required too.

Exclusion will apply to cases with missing ophthalmic examination information specific to the lesion identified, no follow-up examinations, patients with confounding ocular pathology that may potentially influence corneal healing.

6.2: Study design

This was a retrospective case-controlled study using clinical records from a specialist veterinary ophthalmology referral practice in South Africa. Clinical records between 1st January 2019 and 31st December 2023 were screened for patients that presented for, or were referred for, a non-healing corneal ulcer. Cases that received a full ophthalmic examination, matched the diagnosis of spontaneous chronic corneal epithelial defect with positive fluorescein staining, and were treated with either a striate keratotomy or diamond-burr debridement were identified. Case data were evaluated by the author for completeness and follow-up examinations between 5-60 days post-operatively. Cases that did not receive an ophthalmic examination were excluded. Cases that were not presented for a post-operative examination were excluded from the data set. Cases with confounding ocular pathology that could have influenced the procedure outcome were excluded from the data set.

6.3: Study procedures

Avimark® practice software was used to collect patient data. The "Who got" function was used with the following search terms: "SCCED", "STRIATE KERATOTOMY", "ALGERBRUSH", "SOFT CONTACT LENS" or "SCL".

Records identified with the above search terms were restricted to the period 01/01/2019 - 31/12/2023. During this period both treatment options were available to the patients. Selection of the appropriate treatment was done by the attending clinician at the time of the consultation with the pet owner.

Records were exported to *Microsoft Excel*. The data sets generated were consolidated into one complete data set. Duplicate records for the same patient/surgery were removed from the complete data set. The final complete data set contains the *Avimark* unique "patient number". This was used to access an individual patient's chronological history data.

The original examination reports were manually screened for criteria that would exclude the patient from the data set. Individual patient's chronological history data on *Avimark* were further screened for relevant variables, and manually added to the complete data set.

The total number of dogs and the various breeds that presented to the hospital during the same period 01/01/2019 - 31/12/2023 were identified from the *Avimark* practice software with the search term "CON1". This represents the patients presented to the hospital for the first time with a new condition.

Thus, is it representative for the number of dogs per breed examined by the veterinarians at the referral hospital. This list will be compared to the list of breeds presented for SCCED lesions.

The complete data set was used for statistical analysis in "*R*". (Wickham et al., 2023)

6.4: Study observations

Descriptive component of the study:

Procedure performed (SK or DBD),

Age, breed, weight, and sex,

Laterality, contralateral eye, repeat procedure, bilateral procedure,

Surgeon that performed the procedure,

Year in which the procedure was performed,

Clinical signs at the time of presentation,

Intra-ocular pressure, and

Schirmer tear test.

Analytic component of the study:

Independent variables:

Age, breed, sex, weight, laterality,

Striate keratotomy surgery (SK),

Diamond burr debridement (DBD),

Schirmer tear test value (mm/minute),

Intra-ocular pressure (mmHg),

Time to follow-up examination/Day of examination post-operatively,

Surgeon,

Year of surgery,

Subsequent SCCED in the same eye or contralateral eye during the study period,

Bilateral SCCED lesions at initial examination, and

Number of days post-operatively F1 (first fluorescein examination) was performed.

Dependent Variables:

Fluorescein stain results at the first post-operative examination (F1) between day 10-14 post operatively.

6.5: Data analysis and statistical planning

Data analysis was performed with the assistance of Dr John Grewar (Specialist Veterinary Epidemiologist and Extra-ordinary lecturer, Department of Production Animal Studies, Faculty of Veterinary Science, University of Pretoria) using "*R*".

The dataset comprises a retrospective data dump from practice software with validation and direct input by the investigator.

The primary dependent variable relates to the response to treatment, making use of fluorescein stain results (positive or negative) at post-operative examination. This outcome is binary.

The primary independent variables of interest relates to the surgical intervention (i.e. treatment choice) and were either striate keratotomy surgery (SK) or diamond burr debridement (DBD). Other variables that may influence outcome include age, breed, sex, eye laterality, previous episodes of corneal ulceration, Schirmer tear test values at presentation, intra-ocular pressure at presentation, time to follow-up examination, year of surgery and surgeon. Clinical signs present, specifically the presence of pain, lacrimation and blepharospasm at presentation, and other pathology identified at presentation, specifically the presence of corneal oedema and corneal vascularization are included. Year of surgery has been included to account for change in surgeon skill and/or surgical approach preference. In combination with the surgeon variable (see below in multivariate analysis) this assists in dealing with potential temporal and surgical approach bias.

Exploratory data analysis included the univariate analysis of continuous parameters' central tendency and spread using means, median, range, variance, standard deviation, and shape for those independent variables that are continuous. T-tests are most appropriate for evaluating differences between surgical approaches with visualisation by boxplots.

For categorical independent variables logistic regression was used to evaluate potential significance on outcome, both with and without the inclusion of the surgical choice. Depending on the final model choice, variables with significance at $p > 0.2$ were excluded from multivariate analysis.

A further bias that was included in the review was one of case selection bias where it was considered that more severe cases may bias surgical approach selection. This bias was explored in the univariate analysis where the clinical score will be assessed against the surgical approach taken. If there is a reasonable possibility of association between clinical presentation and surgical approach, then the clinical severity variable will be included in the multivariate analysis to account for this.

Finally, a mixed effects logistic regression model was employed to evaluate final association between surgical approach and outcome. The random effect will include the surgeon and patient (as patients may have multiple interventions). Fixed effects are those variables discussed above. Variables were either further excluded using forward and backwards exclusion or all variables included if a lasso regression is employed.

The data set included 288 surgeries.

Published data for treatment success as measured by a negative fluorescein stain at D14 for single SK procedure is approximately 80-87%. (Bentley, 2005; Gelatt, 2020; Moore, 2003). With the average healing time between 9.3-13.4 days. (Moore, 2003)

Published data for treatment success as measured by a negative fluorescein stain at D14 for single DBD procedure is approximately 82% at D13. (Nevile et al., 2016) Another study reported 70% success by D7 and 92.5% by D15.5. (Gosling et al., 2013)

6.6 Experimental site and facilities

Study site: Johannesburg Animal Eye Hospital, 44 Kingfisher drive, Fourways, South Africa. GPS coordinates: 26°01'41"S 28°00'20"E.

Motivation for the study site includes a large data collection, accurate records, reliable diagnosis, high post-operative follow-up examination rate, and examination were performed by a SAVC registered specialist veterinary ophthalmologist or ophthalmology resident under supervision.

6.7 Experimental animals

Dogs (*Canis familiaris*) presented for non-healing superficial corneal epithelial ulceration and positively diagnosed with fluorescein staining for a spontaneous chronic corneal epithelial defect at examination. The patients were surgically treated with either a striate keratotomy or diamond burr debridement procedure and presented post-operatively for at least one follow-up examination between 10-14 days after the surgical procedure.

6.8 Experimental staff

Researchers:	Primary investigator	Dr Brent Sirrals
	Supervisor	Dr Antony Goodhead
	Statistical analysis	Dr John Grewar
	Assistants	JHB Animal Eye Hospital practice staff

6.9 Deviations

Certain case records did not include all the data points – the outcome of surgical intervention in the final data set were assessed on an individual basis by the primary researcher, statistician, and supervisor.

Any other deviations were recorded, or the case excluded from the final data set.

6.10 Record management

Data collected from *Avimark* were transferred to *Microsoft Excel* on a personal computer. The personal computer was backed-up in real time to *Microsoft OneDrive* over an internet connection.

A copy of the data was stored in the University of Pretoria Research Data Repository according to the University of Pretoria guidelines upon conclusion of the study.

Chapter 7: Results: Descriptive

Dataset

Search terms for "SCL", "SOFT CONTACT LENS", "STRIATE KERATOTOMY", "ALGERBRUSH" and "SCCED" on the *Avimark* practice management software identified 441 unique surgical cases during the period from 1 January 2019 until 31 December 2023. After exclusions were removed a final total of 288 ocular surgeries were included. These were 223 striate keratotomies (77.4%) and 65 diamond burr debridement (22.6%) surgeries.

149 right eyes (51.7%) and 139 left eyes (48.3%) were operated on. This included surgeries on the contra-lateral eye of a single patient (22 cases) (7.6%) and repeat follow-up surgeries on individual eyes (14 cases) (4.9%). 15 patients (5.2%) presented for bilateral SCCED at the initial examination. The total number of dogs operated on were 240 patients, and a total number of 274 eyes were operated on.

Exclusions.

Exclusions included the presence of the following conditions or findings: No follow-up examinations, ectopic cilia, distichiasis, entropion, keratoconjunctivitis sicca, corneal endothelial dystrophy oedema, trauma, unrelated uveitis, glaucoma, corneal degeneration, corneal dystrophy, periorbital pathology, exophthalmos, intra-capsular lens extraction, diabetes insipidus, trans-corneal lens reduction surgery, corneal cross-linking, invasive surgery by the general practice clinician before presentation to a specialist veterinary ophthalmologist, and ocular nodosa.

Breed distribution.

There was a total of 39 different dog breeds that presented for SCCED lesions during the study period which were included in the results. The 10 most common breeds presented for SCCED lesions are listed in descending order in **Table 7.1**. A total of 8283 dogs and 213 different breeds presented to the hospital during the study period for new conditions. The 20 most common dog breeds presented to the hospital during the study period are listed in descending order in **Table 7.2**.

Table 7.1: The 10 most common dog breeds presented for SCCED lesions during the study period.

French Bulldog	48	16.3%
Staffordshire Bull Terrier	36	12.5%
Boxer	28	9.7%
Labrador Retriever	23	8.0%
Yorkshire Terrier	22	7.6%
Crossbreed	21	7.3%
Boston Terrier	15	5.2%
Jack Russell Terrier	12	4.2%
English Bulldog	9	3.1%
Shih Tzu	7	2.4%

Table 7.2: The 20 most common dog breeds presented to the JAEH during the study period.

Jack Russell Terrier	622	7.5%
Crossbreed	606	7.3%
Pekingese	565	6.8%
Yorkshire Terrier	520	6.2%
Dachshund	505	6.1%
Boston Terrier	372	4.5%

English Bulldog	331	4.0%
Labrador Retriever	263	3.2%
French Bulldog	256	3.1%
Maltese Poodle	218	2.6%
Pug	207	2.5%
Beagle	150	1.8%
German Shepherd Dog	141	1.7%
Border Collie	130	1.6%
Rottweiler	126	1.5%
Golden Retriever	120	1.4%
Shih Tzu	118	1.4%
Cocker Spaniel	112	1.4%
Chihuahua	107	1.2%
Min. Schnauzer	102	1.2%

Patient sex distribution.

Sex of the patients were recorded, male dogs included 167 patients (58.0%) and female dogs 121 patients (42.0%) (**Table 7.3**). The neuter status of the patients was not recorded accurately in the patient records, and this was not included in the analysis. Based on a Chi-squared test and using a 50:50 expected distribution the male dogs were overrepresented ($p<0.05$).

Table 7.3: Sex distribution for dogs presented for SCCED lesions.

Female	121	42.0%
Male	167	58.0%

Weight range distribution.

Body weights ranged from 2.0-72.0 kg (**Figure 7.1**). Mean body weight was 19.3 kg, (Median 15.3 kg; SD 12.9 kg; IQR 16.1; CV 0.7).

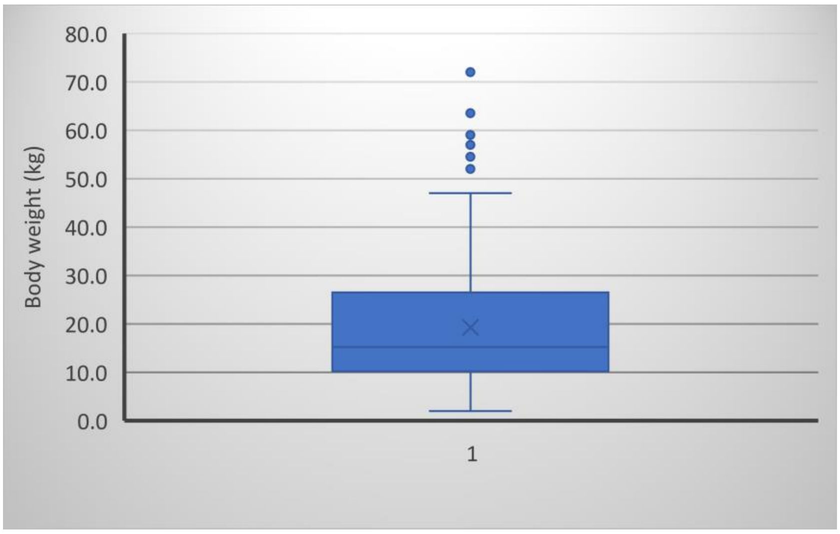

Figure 7.1: Body weight distribution.

Age distribution

The mean age for dogs presenting with a SCCED lesion was 8.3 years (100.2 months) (SD 33.7). The youngest patient was 7 months old, and the oldest patient was 16.9 years old (203 months). (Median 96 months; SD 33.7 months; IQR 16.1; CV 0.3).

Surgeons

The study included procedures performed by four surgeons. The surgeons were captured as 1, 2, 3 and 4. Surgeon 1 performed a total of 69 surgeries (24.0%) (49 x SK & 20 x DBD). Surgeon 2 performed 110 surgeries (38.2%) (94 x SK & 16 x DBD). Surgeon 3 performed 26 surgeries (9.0%) (24 x SK & 2x DBD). Surgeon 4 performed 83 surgeries (28.8%) (57 x SK & 27 x DBD).

Soft contact lens

The SCL was present at the follow-up examination in 75 cases (26.0%) and lost in 213 cases (74.0%).

Intra-Ocular Pressure

Intra-ocular pressures were collected for 263 right eyes and 252 left eyes. The mean estimate IOP for right eyes (OD) was 17.19 mmHg (SD 4.68; Min 5.0; Median 16.0; Max 35.0; IQR 6.0; CV 0.27) (95% CI: 16.63 - 17.76). The mean estimate IOP for left eyes (OS) was 16.65 mmHg (SD 4.64; Min 5.0; Median 16.0; Max 46.0; IQR 5.0; CV 0.28) (95% CI: 16.07 - 17.22).

These measurements were recorded in the final data sheet under "affected" (eyes with the SCCED lesion) or "unaffected" (normal eye, no SCCED lesion). Data were limited to data that contains both affected and unaffected eye descriptors with IOP values for both eyes. Any data points that included procedures that were performed under the repeat, duplicate of contralateral classes were excluded. This left a total of 202 cases (**Figure 7.5**).

For affected eyes the range was between 5-35 mmHg, and the mean estimate IOP was 17.12 mmHg, (95% CI: 16.45-17.78) (Median 17.00; SD 4.79; IQR 6.00; CV 0.28).

For unaffected eyes the range was between 5-46 mmHg, and the mean estimate IOP was 17.41 mmHg, (95% CI: 16.73-18.09) (Median 17; SD 4.9, IQR 6.00; CV 0.28).

An evaluation of the comparison between the affected and unaffected eyes showed a mean of the differences of -0.29 with a *p*-value of 0.35.

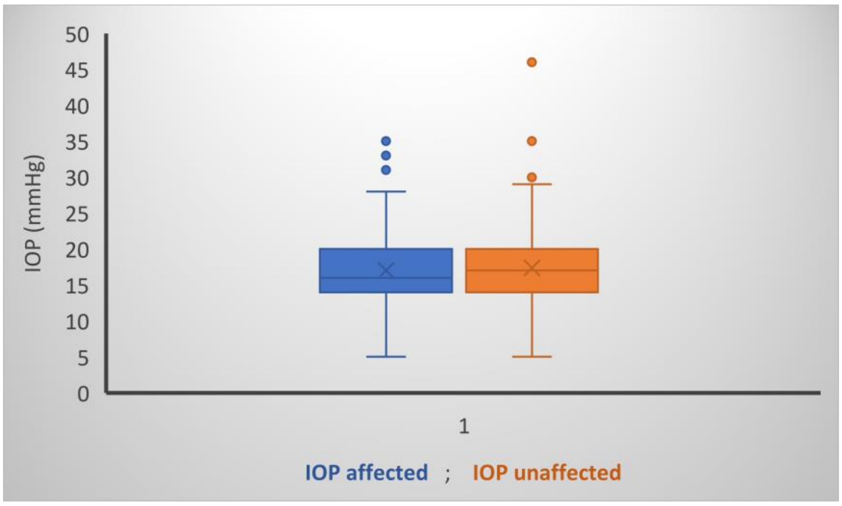

Figure 7.2: IOP distribution in affected and unaffected eyes.

Schirmer Tear Test

Schirmer tear test measurements were collected for 179 right eyes and 176 left eyes. The mean estimate STT for right eyes (OD) was 24.65 mm/min (95% CI: 23.91 - 25.39) (SD 5.00; Min 5.0; Median 25.0; Max 37.0; IQR 6.0; CV 0.20). The mean estimate STT for left eyes (OS) was 24.12 mm/min (95% CI: 23.37 - 24.87) (SD 5.02; Min 6.0; Median 25.0; Max 35.0; IQR 7.0; CV 0.21).

The measurements were recorded in the final data sheet under "affected" (eyes with the SCCED lesion) or "unaffected" (normal eye, no SCCED lesion). Data were limited to data that contains both affected and unaffected eye descriptors with STT values for both eyes. Any data points that included procedures that were performed under the repeat, duplicate of contralateral classes were excluded. This left a total of 140 cases (**Figure 7.6**).

For affected eyes the range was between 5.0-37.0 mm/min, and the mean STT was 25.59 mm/min, (95% CI: 24.76 - 26.41) (Median 26.00; SD 4.92; IQR 5.00; CV 0.19).

For unaffected eyes the range was between 6-33 mm/min, and the mean STT was 23.1 mm/min, (95% CI: 21.62 - 23.36) (Median 23.00; SD 5.20; IQR 6.25; CV 0.23).

An evaluation of the comparison between the affected and unaffected eye showed a mean of the differences of 3.09 with a *p*-value of 0.

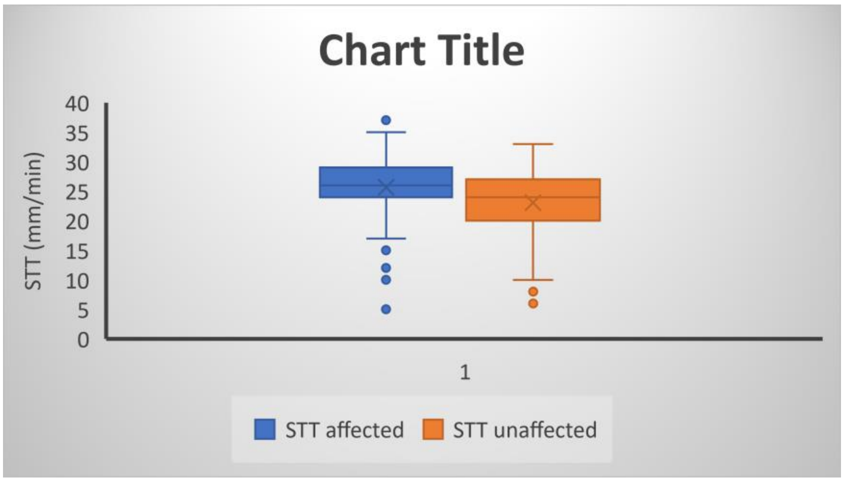

Figure 7.3: STT distribution in affected and unaffected eyes.

Lesions

Ocular lesions were manually recorded for each patient based on the clinical records at the initial presentation for SCCED. The most reported lesion was keratitis which would range from mild limbal neovascularization to locally extensive corneal vascularization. Blepharospasm and lacrimation were also a frequent presenting clinical finding. Localized corneal oedema at the SCCED lesion was the fourth most reported pathology. **Table 7.4** below presents the lesions and the number of times it was reported on an affected eye basis. An upset plot (**Figure 7.7**), to represent clinical sign associations, was generated in "*R*".

Table 7.4: Total count of ocular lesions and clinical signs reported for affected eyes.

keratitis	99
spasm	77
lacrimation	67

oedema	40
glaucoma	4
granulation	4
hyperaemia	3
dystrophy	2
pigmentary keratitis	1
uveitis	1
pigmentary keratitis	1
degeneration	1
miosis	1
TEL protrusion	1
scarring	1

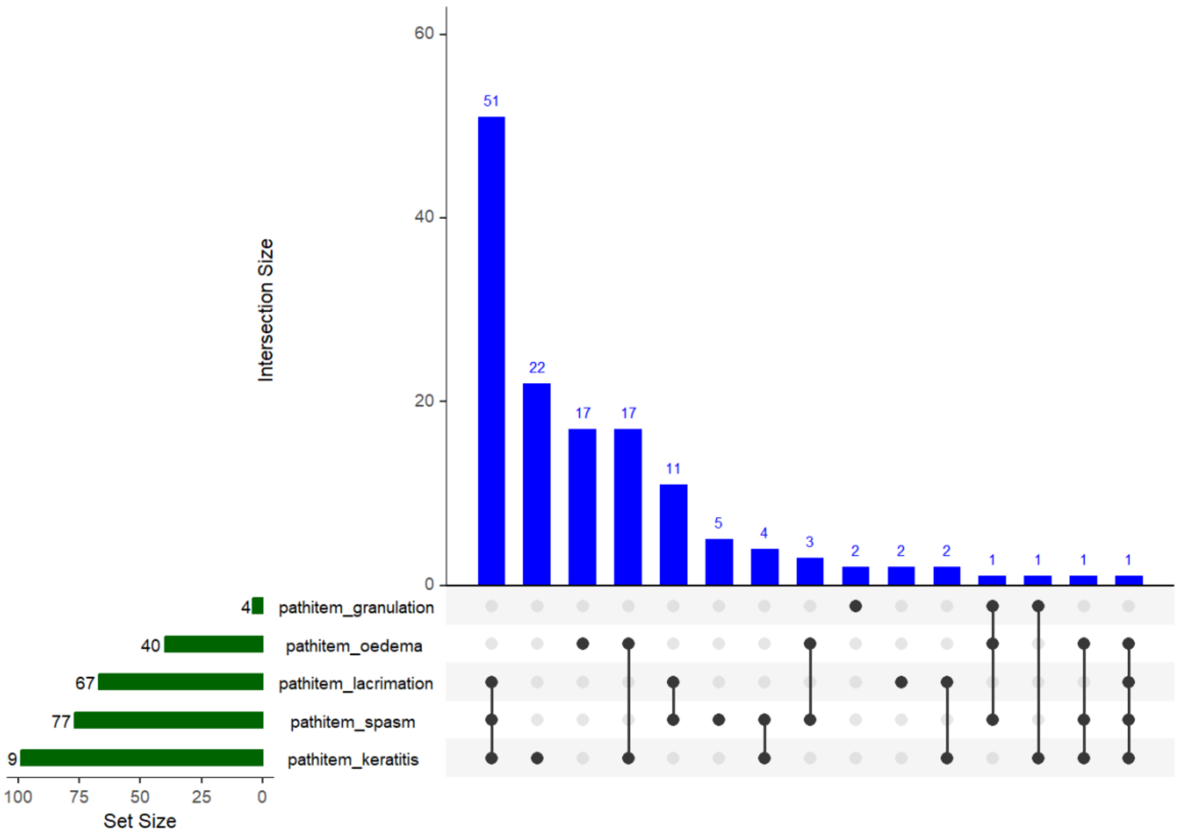

Figure 7.4: Upset plot (using R) of clinical signs described at the initial diagnosis of SCCED lesions.

Surgical outcome (F1 results)

The first post operative fluorescein stain results were available for 288 surgeries. This includes repeat procedures in the same ipsilateral affected eyes. For all SK surgeries (223 cases) the F1 results were as follows: 189 surgeries were negative (84.8%) and 34 were positive (15.2%). For all DBD surgeries (65 cases) the F1 results were as follows: 55 surgeries were negative (84.6%) and 10 were positive (15.4%). The day of presentation for F1 ranged between 5-28 days post-operatively, with an average presentation at day 12.8 post-operatively (Median day 13).

For our hypothesis testing we wanted to restrict the follow up period for F1 presentation to between days 10-14 post-operatively. This influenced the total number of procedures included in the analysis and only 170 SK and 47 DBD procedures presented for a follow-examination during this specific period. SK findings were 149 negatives (87.6%) & 21 positive (12.4%) between day 10-14 post operatively. DBD findings for the same period post-operatively are 40 negative (85.1%) and 7 positive (14.9%).

Further evaluating the individual surgeons for each procedure during the same 10-14 days post-operative period may provide indication of the influence this had on the results and the findings are as follows (**Table 7.5**): Surgeon 1 performed 33 SK procedures with the outcome 26 cases negative (78.8%) and 7 cases positive (21.2%). Surgeon 1 performed 14 DBD procedures with the outcome being 12 negative (85.7%) and 2 cases (14.3%) being positive.

Surgeon 2 performed 74 SK procedures with the outcome 70 cases negative (94.6%) and 4 cases positive (5.4%). Surgeon 2 performed 10 DBD procedures with the outcome being 9 negative (90.0%) and 1 case (1.0%) being positive.

Surgeon 3 performed 16 SK procedures with the outcome 15 cases negative (93.8%) and 1 case positive (6.3%). Surgeon 3 performed a single DBD procedure with the outcome being negative (100%).

Surgeon 4 performed 47 SK procedures with the outcome 38 cases negative (80.9%) and 9 cases positive (19.1%). Surgeon 4 performed 22 DBD procedures with the outcome being 18 negative (81.8%) and 4 cases (18.2%) being positive.

Table 7.5: Percentages of successful procedure outcomes per surgeon.

Surgeon	SK	DBD
1	78.8%	85.7%
2	94.6%	90.0%
3	93.8%	100%
4	80.9%	81.8%

Year of surgery

The year in which the surgeries were performed made part of the final analysis. (**Table 7.5**). More surgeries were performed in the latter years (55.6%) compared to the first three years of the study period (44.4%).

Table 7.6: Year of surgery and the count of procedures performed in each year.

2019	21	7.3%
2020	49	17.0%
2021	58	20.1%
2022	76	26.4%
2023	84	29.2%

Chapter 8: Results: Univariate Data Analysis

In this section are the results of the univariate analysis using logistic regression. Logistic regression is a powerful statistical method used to model the relationship between a binary outcome variable (outcome_0 where surgical success is 1 and failure is zero) and one or more predictor variables. For univariate purposes each parameter is input as a single predictor. By fitting logistic regression models to each predictor variable individually, we assessed their individual associations with the outcome variable. It's important to note that in this analysis, the intercept represents the estimated log odds and odds of the outcome for the first alphabetical category of each predictor variable. Therefore, while the intercept is included in the results table, its *p*-value is not considered in the interpretation. Instead, our focus was on the *p*-values of the predictor variable classes against that of the intercept which indicate their individual significance in predicting the outcome variable. The results are summarized in the figures below (**Figures 8.1, 8.2 & 8.3**), providing insights into the impact of each predictor on the likelihood of the outcome, along with measures of statistical significance. Variables considered worth retaining with a *p*-value of 0.2 or less are labelled as such.

ModelVariable	VariableCoefficient	Estimate	StdError	ZValue	PValue	Odds	retain
proc	(Intercept)	1.7429693	0.4097037	4.2542189	0.0000210	5.7142857	NA
proc	procsk	0.2652447	0.4738855	0.5597233	0.5756682	1.3037500	no
laterality	(Intercept)	2.2560650	0.3168673	7.1199049	0.0000000	9.5454541	NA
laterality	lateralityos	-0.5978370	0.4181024	-1.4298815	0.1527510	0.5500000	yes
contralateral	(Intercept)	1.8951951	0.2103376	9.0102554	0.0000000	6.6538462	NA
contralateral	contralateralTRUE	0.8773937	1.0520058	0.8340198	0.4042698	2.4046243	no
repeater	(Intercept)	2.0368819	0.2170256	9.3854470	0.0000000	7.6666667	NA
repeater	repeaterTRUE	-1.5260563	0.7618618	-2.0030619	0.0451707	0.2173913	yes
bilateral	(Intercept)	2.0329215	0.2267279	8.9663508	0.0000000	7.6363636	NA
bilateral	bilateralTRUE	-0.5978370	0.5468313	-1.0932750	0.2742731	0.5500000	no
surgeon	(Intercept)	1.4403616	0.3707113	3.8853993	0.0001022	4.2222222	NA
surgeon	surgeon2	1.3196484	0.5916761	2.2303562	0.0257238	3.7421053	yes
surgeon	surgeon3	1.3322271	1.0954000	1.2162015	0.2239082	3.7894737	no
surgeon	surgeon4	0.1000835	0.4884848	0.2048855	0.8376616	1.1052632	no
breed	(Intercept)	19.5660685	7604.2356640	0.0025730	0.9979470	314366018.0352674	NA
breed	breedaustralian shepherd	-0.0000000	13170.9223391	-0.0000000	1.0000000	1.0000000	no
breed	breedbeagle	-0.0000000	10754.0130731	-0.0000000	1.0000000	1.0000000	no
breed	breedboerboel	-0.0000000	10754.0130726	-0.0000000	1.0000000	1.0000000	no
breed	breedborder collie	-0.0000000	10754.0130940	-0.0000000	1.0000000	1.0000000	no
breed	breedboston terrier	-17.3688440	7604.2357371	-0.0022841	0.9981776	0.0000000	no
breed	breedboxer	-17.5736384	7604.2356889	-0.0023110	0.9981561	0.0000000	no
breed	breedbull mastiff	-0.0000000	13170.9222976	-0.0000000	1.0000000	1.0000000	no
breed	breedbull terrier	-0.0000000	13170.9222977	-0.0000000	1.0000000	1.0000000	no
breed	breedbulldog	-17.7743091	7604.2357407	-0.0023374	0.9981350	0.0000000	no
breed	breedchihuahua	-0.0000000	10754.0130948	-0.0000000	1.0000000	1.0000000	no
breed	breedcorgi	-18.4674562	7604.2357517	-0.0024286	0.9980623	0.0000000	no
breed	breedcrossbreed	-17.8920921	7604.2356900	-0.0023529	0.9981227	0.0000000	no
breed	breeddachshund	-0.0000000	10754.0130729	-0.0000000	1.0000000	1.0000000	no

Figure 8.1: Univariate analysis results.

ModelVariable	VariableCoefficient	Estimate	StdError	ZValue	PValue	Odds	retain
breed	breeddalmation	-39.1321370	13170.9223300	-0.0029711	0.9976294	0.0000000	no
breed	breedfrench bulldog	-18.7010711	7604.2356757	-0.0024593	0.9980378	0.0000000	no
breed	breedgerman shepherd	-0.0000000	13170.9223314	-0.0000000	1.0000000	1.0000000	no
breed	breedgreat dane	-0.0000000	13170.9223379	-0.0000000	1.0000000	1.0000000	no
breed	breedhusky	-0.0000000	8997.4529209	-0.0000000	1.0000000	1.0000000	no
breed	breedjack russell terrier	-17.4866270	7604.2357380	-0.0022996	0.9981652	0.0000000	no
breed	breedlabrador	-17.4260024	7604.2357008	-0.0022916	0.9981716	0.0000000	no
breed	breedlhaso apso	-0.0000000	13170.9223387	-0.0000000	1.0000000	1.0000000	no
breed	breedmaltese	-0.0000000	8780.6149589	-0.0000000	1.0000000	1.0000000	no
breed	breedmin pin	-18.8729213	7604.2357626	-0.0024819	0.9980197	0.0000000	no
breed	breedmin poodle	-0.0000000	9313.2485516	-0.0000000	1.0000000	1.0000000	no
breed	breedmin schnauzer	-0.0000000	10754.0130700	-0.0000000	1.0000000	1.0000000	no
breed	breedmorkie	-0.0000000	13170.9222975	-0.0000000	1.0000000	1.0000000	no
breed	breedpomeranian	-0.0000000	9817.0259288	-0.0000000	1.0000000	1.0000000	no
breed	breedpug	-0.0000000	9313.2485627	-0.0000000	1.0000000	1.0000000	no
breed	breedridgeback	-0.0000000	13170.9222974	-0.0000000	1.0000000	1.0000000	no
breed	breedrottweiler	-0.0000000	13170.9223048	-0.0000000	1.0000000	1.0000000	no
breed	breedshih tzu	-0.0000000	8622.3927286	-0.0000000	1.0000000	1.0000000	no
breed	breedst bernard	-0.0000000	13170.9223080	-0.0000000	1.0000000	1.0000000	no
breed	breedstaffie	-17.2146933	7604.2357000	-0.0022638	0.9981937	0.0000000	no
breed	breedwire haired terrier	-0.0000000	13170.9222980	-0.0000000	1.0000000	1.0000000	no
breed	breedyorkshire terrier	-18.1797742	7604.2356914	-0.0023907	0.9980925	0.0000000	no
sex	(Intercept)	2.0918641	0.3351707	6.2411894	0.0000000	8.1000000	NA
sex	sexm	-0.2429462	0.4247613	-0.5719594	0.5673495	0.7843137	no
weight	(Intercept)	1.6079551	0.3997867	4.0220322	0.0000577	4.9925914	NA
weight	weight	0.0224971	0.0193387	1.1633198	0.2446998	1.0227521	no
year_surgey	(Intercept)	827.8346005	385.0016010	2.1502108	0.0315385	Inf	NA
year_surgey	year_surgey	-0.4085049	0.1904118	-2.1453761	0.0319228	0.6646432	yes
age_surgery	(Intercept)	1.4207194	0.6556787	2.1667922	0.0302507	4.1400978	NA
age_surgery	age_surgery	0.0051231	0.0063944	0.8011910	0.4230211	1.0051363	no
iop_affected	(Intercept)	0.2434745	0.9554987	0.2548140	0.7988668	1.2756737	NA
iop_affected	iop_affected	0.1107196	0.0608014	1.8210043	0.0686062	1.1170816	yes
stt_affected	(Intercept)	3.1269787	1.7427556	1.7942727	0.0727697	22.8049748	NA
stt_affected	stt_affected	-0.0439544	0.0647885	-0.6784292	0.4974996	0.9569976	no

Figure 8.2: Univariate analysis results continued (1).

ModelVariable	VariableCoefficient	Estimate	StdError	ZValue	PValue	Odds	retain
outcome1_SCL	(Intercept)	1.7548549	0.2258253	7.7708523	0.0000000	5.7826087	NA
outcome1_SCL	outcome1_SCLTRUE	0.8842024	0.5646702	1.5658740	0.1173781	2.4210526	yes
pathitem_congestion	(Intercept)	1.9406051	0.2058062	9.4292846	0.0000000	6.9629630	NA
pathitem_congestion	pathitem_congestionTRUE	12.6254627	882.7433991	0.0143025	0.9885886	304206.6988713	no
pathitem_degeneration	(Intercept)	1.9459101	0.2057370	9.4582413	0.0000000	7.0000000	NA
pathitem_dystrophy	(Intercept)	1.9352718	0.2058753	9.4002143	0.0000000	6.9259259	NA
pathitem_dystrophy	pathitem_dystrophyTRUE	13.6307965	1029.1214851	0.0132451	0.9894323	831341.9637627	no
pathitem_glaucoma	(Intercept)	1.9299098	0.2059451	9.3709920	0.0000000	6.8888889	NA
pathitem_glaucoma	pathitem_glaucomaTRUE	14.6361586	1385.3778051	0.0105647	0.9915707	2271971.7276747	no
pathitem_granulation	(Intercept)	1.9352718	0.2058753	9.4002143	0.0000000	6.9259259	NA
pathitem_granulation	pathitem_granulationTRUE	13.6307965	1029.1214850	0.0132451	0.9894323	831341.9636495	no
pathitem_hyperaemia	(Intercept)	1.9730121	0.2093051	9.4264899	0.0000000	7.1923077	NA
pathitem_hyperaemia	pathitem_hyperaemiaTRUE	-1.2798649	1.2425007	-1.0300717	0.3029763	0.2780749	no
pathitem_keratitis	(Intercept)	2.0949457	0.2649307	7.9075243	0.0000000	8.1250000	NA
pathitem_keratitis	pathitem_keratitisTRUE	-0.4153036	0.4219556	-0.9842353	0.3249998	0.6601399	no
pathitem_lacrimation	(Intercept)	2.2643639	0.2626661	8.6206918	0.0000000	9.6250000	NA
pathitem_lacrimation	pathitem_lacrimationTRUE	-1.1069111	0.4341359	-2.5496877	0.0107819	0.3305785	yes
pathitem_miosis	(Intercept)	1.9406051	0.2058062	9.4292846	0.0000000	6.9629630	NA
pathitem_miosis	pathitem_miosisTRUE	12.6254627	882.7433991	0.0143025	0.9885886	304206.6988715	no
pathitem_oedema	(Intercept)	1.9965539	0.2272147	8.7870806	0.0000000	7.3636364	NA
pathitem_oedema	pathitem_oedemaTRUE	-0.3101549	0.5372742	-0.5772749	0.5637537	0.7333333	no
pathitem_pigmentary_keratitis	(Intercept)	1.9406051	0.2058062	9.4292846	0.0000000	6.9629630	NA
pathitem_pigmentary_keratitis	pathitem_pigmentary_keratitisTRUE	12.6254627	882.7433992	0.0143025	0.9885886	304206.6988898	no
pathitem_scarring	(Intercept)	1.9406051	0.2058062	9.4292846	0.0000000	6.9629630	NA
pathitem_scarring	pathitem_scarringTRUE	12.6254627	882.7433992	0.0143025	0.9885886	304206.6988900	no
pathitem_spasm	(Intercept)	2.1503933	0.2562538	8.3916554	0.0000000	8.5882352	NA
pathitem_spasm	pathitem_spasmTRUE	-0.6917782	0.4346513	-1.5915705	0.1114812	0.5006849	yes
pathitem_tel_protrusion	(Intercept)	1.9406051	0.2058062	9.4292846	0.0000000	6.9629630	NA
pathitem_tel_protrusion	pathitem_tel_protrusionTRUE	12.6254627	882.7433991	0.0143025	0.9885886	304206.6988710	no
pathitem_uveitis	(Intercept)	1.9406051	0.2058062	9.4292846	0.0000000	6.9629630	NA
pathitem_uveitis	pathitem_uveitisTRUE	12.6254627	882.7433991	0.0143025	0.9885886	304206.6988710	no

Figure 8.3: Univariate analysis results continued (2).

The following predictor variables were retained for multivariate analysis: lateralityos, repeater, surgeon2, surgeon3, surgeon4, year_surgery, IOP_affected, outcome1_SCL, pathitem_lacrimation, pathitem_spasm and procsk.

Chapter 9: Results: Multivariate data analysis

In this section are the results of the first of two multivariate analysis using logistic regression. Building upon the findings of the univariate analysis, selected predictor variables were those that individually showed significance at a threshold of $p <= 0.2$. Additionally, we explicitly included the type of surgery performed (proc) as it was the primary focus of the research, despite it not individually reaching statistical significance. By incorporating these predictor variables into a single model, the aim is to explore the combined effect of multiple factors on the likelihood of the outcome variable. The results are summarized in the figures below (**Figures 9.1 & 9.2**), providing insights into the adjusted associations between each predictor variable and the outcome, while controlling for other covariates in the model. This analysis allows us to identify the key factors influencing the outcome of interest. It's important to note that the repeater variable became singular due to missing data in the IOP_affected variable, resulting in only FALSE values of repeater being observed.

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	-175.5	628	-0.2794	0.7799
lateralityos	-0.1179	0.5512	-0.214	0.8306
surgeon2	0.7477	0.8397	0.8904	0.3733
surgeon3	0.7027	1.262	0.5569	0.5776
surgeon4	0.04301	0.6896	0.06237	0.9503
year_surgey	0.08666	0.3106	0.279	0.7802
iop_affected	0.1354	0.06756	2.004	0.04509
outcome1_SCLTRUE	0.4576	0.6486	0.7054	0.4805
pathitem_lacrimationTRUE	-2.84	1.485	-1.912	0.05586
pathitem_spasmTRUE	1.736	1.51	1.149	0.2504
procsk	0.1137	0.6266	0.1814	0.8561

Figure 9.1: Summary of the full multivariate model preceding backwards elimination.

	OddsRatios
(Intercept)	6.326e-77
lateralityos	0.8888
repeaterTRUE	NA
surgeon2	2.112
surgeon3	2.019
surgeon4	1.044
year_surgey	1.091
iop_affected	1.145
outcome1_SCLTRUE	1.58
pathitem_lacrimationTRUE	0.05841
pathitem_spasmTRUE	5.674
procsk	1.12

Figure 9.2: Summary of the full multivariate model preceding backwards elimination continued (1).

For completeness' sake a backwards selection approach was employed to refine the model and identify the most influential predictor variables. Beginning with the full model containing all potential predictor variables, variables are removed that do not significantly contribute to the model's predictive power, based on a stepwise elimination process. This approach streamlines the model by keeping only the most relevant predictors, while discarding those that do not add significant explanatory value. The results of the backwards selection process are presented in the figures below (**Figures 9.3 & 9.4**), showing the final set of predictor variables retained in the model and their respective contributions to predicting the outcome variable.

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	0.431	1.006	0.4287	0.6682
iop_affected	0.1249	0.06448	1.937	0.05273
pathitem_lacrimationTRUE	-1.34	0.5399	-2.482	0.01308

Figure 9.3: Summary of the full multivariate model post backwards elimination.

	OddsRatios
(Intercept)	1.539
iop_affected	1.133
pathitem_lacrimationTRUE	0.2619

Figure 9.4: Summary of the full multivariate model post backwards elimination continued (1).

Chapter 10: Results: Multivariate data analysis - excluding missing parameter IOP_affected

This section is the same as above except the variable IOP_affected was removed as it had substantial missing data that impacted other variables. It is important to note that IOP_affected was a variable that seems important in the final outcome, so this section should be treated with restraint. The results are presented in the figures below (**Figures 10.1, 10.2, 10.3 & 10.4**)

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	-190.3	553.2	-0.3441	0.7308
lateralityos	-0.6927	0.4509	-1.536	0.1245
repeaterTRUE	-1.574	0.8809	-1.787	0.07401
surgeon2	1.356	0.7296	1.858	0.06315
surgeon3	1.761	1.339	1.315	0.1884
surgeon4	0.3955	0.5305	0.7456	0.4559
year_surgey	0.09506	0.2735	0.3475	0.7282
outcome1_SCLTRUE	0.8448	0.6062	1.394	0.1635
pathitem_lacrimationTRUE	-2.311	1.088	-2.124	0.03365
pathitem_spasmTRUE	1.422	1.13	1.259	0.208
procsk	-0.05445	0.5255	-0.1036	0.9175

Figure 10.1: Summary of the full multivariate model preceding backwards elimination – excluding missing parameter IOP_affected.

	OddsRatios
(Intercept)	2.223e-83
lateralityos	0.5002
repeaterTRUE	0.2073
surgeon2	3.879
surgeon3	5.821
surgeon4	1.485
year_surgey	1.1
outcome1_SCLTRUE	2.327
pathitem_lacrimationTRUE	0.0992
pathitem_spasmTRUE	4.146
procsk	0.947

Figure 10.2: Summary of the full multivariate model preceding backwards elimination – excluding missing parameter IOP_affected continued (1).

	Estimate	Std. Error	z value	Pr(>|z|)
(Intercept)	2.205	0.299	7.374	1.656e-13
repeaterTRUE	-1.723	0.798	-2.16	0.03079
outcome1_SCLTRUE	0.8132	0.5753	1.414	0.1575
pathitem_lacrimationTRUE	-1.145	0.4474	-2.559	0.01049

Figure 10.3: Summary of the full multivariate model post backwards elimination – excluding missing parameter IOP_affected.

	OddsRatios
(Intercept)	9.068
repeaterTRUE	0.1784
outcome1_SCLTRUE	2.255
pathitem_lacrimationTRUE	0.3182

Figure 10.4: Summary of the full multivariate model post backwards elimination – excluding missing parameter IOP_affected continued (1).

Chapter 11: Discussions

SCCED in South Africa

The typical SCCED lesion included in this study were similar to the description by previous authors, a corneal epithelial defect in the interpalpebral region, central or paracentral cornea, which stain brightly with fluorescein and was surrounded by a ring of less intense staining loose epithelium. It was recurrent in nature, failed to heal with conservative treatment, and there were no confounding pathology preventing healing to take place. (Murphy et al., 2001) Lesions were diagnosed during ophthalmic examination using slit-lamp biomicroscopy and fluorescein staining.

Morphological, light microscopy, transmission and scanning electron microscopy, and immunohistochemistry findings of SCCED lesions were discussed above (Chapter3). (Abrams et al., 2002; Bentley et al., 2001; Murphy et al., 2001) None of the cases in our study underwent lamellar keratectomy or had histopathological analysis performed.

Bacterial culture and sensitivity testing were also not performed on the patients in our study. SCCED lesions are by nature not infected and thus this was not clinically relevant. Recent evidence suggest that we may need to rethink this notion and that some ulcers (19%) are culture-positive but this may not influence outcome. (Levitt et al., 2020) It may however be seen as “good practice” if a patient has been treated with some form of antibacterial therapy before presentation to a referral clinic and should be considered to make appropriate choices with regards to antibacterial use. Our clinic’s use of topical antibacterial medication is based on historic experience and data on file for infected corneal ulcers. Bacterial culture and sensitivity are commonly used at the JAEH when stromal tissue is affected.

The JAEH sees referral and first opinion cases. Most of the SCCED lesions presented to this clinic were recurrent and non-healing in nature and were present for some time before presentation to a specialist ophthalmologist. The cases that had some form of intervention performed before presentation were excluded from our analysis. This commonly include cotton-tip debridement by the referring clinician. In some rare cases the referring clinician also attempted a striate keratotomy procedure. This was mostly disastrous to the cornea and some form of rescue therapy was required in these cases, such as corneal cross-linking or additional medical therapy to assist healing. Our initial data sheet included 441 SCCED cases that presented for referral during our study period. Thus, a large proportion of cases referred to us were excluded from our analysis. A study done in England and using data from 110 primary-care practices estimated a 0.8% incidence of corneal ulceration in dogs presented for examination. (O’Neill et al., 2017) Thus, 1 out of 125 dogs presented for consultation was for a corneal ulcer. This number was not only SCCED lesions but included various types of corneal ulceration. It does however highlight the fact that a SCCED lesion remains an important differential to be able to diagnose!

At the time the JAEH was also the only specialist veterinary ophthalmology referral centre in the greater part of South Africa and some clients would present their pets directly to us. If these cases met the criteria for SCCED lesions, and had no other exclusions, they were included in our data sheet.

The period that the SCCED lesion was present before referral or direct presentation to us was not captured accurately in the clinical notes. Thus, it could not be used for our analysis. In general, this was typically anything from a few days to weeks. In some cases, it may even be a few months (up to 15 weeks) before presentation to a specialist. (Gosling et al., 2013) Landrevie reported a mean progression time of 33.5 ± 23 days before referral. (Landrevie et al., 2023) An extended progression may affect clinical signs at presentation and particularly the amount of keratitis or granulation tissue present. Thus, future studies should endeavour to include this parameter.

As mentioned above, the historic surgery of choice has been to perform a striate keratotomy when a patient was referred for a SCCED lesion. Diamond burr debridement was introduced into JAEH in 2014 and has been used as a secondary option for SCCED lesion treatment. The choice of procedure was largely based on the discussion that the attending clinician had with the client about their pet and the options available. The main motivation for SK was that it was seen as a more successful treatment compared to DBD during these discussions. DBD was offered as a more cost-effective treatment option, and safer for geriatric patients or patients that may be too compromised to undergo general anaesthesia. This may introduce selection bias in a retrospective study. Clinical scoring of the presenting signs at examination can be used to evaluate bias for procedure selection (discussed in section 6.5), but due to missing information in the clinical records, this could not be performed in this study.

A motivation to perform this study was to scientifically evaluate the two treatment options available to dogs with SCCED lesions in South Africa, which were referred to a specialist ophthalmology hospital. Both options were available at the time of the study, both options were used regularly since 2014, and the clinicians were adept at performing both procedures.

Dataset

The dataset was extensive and as mentioned 441 surgeries were performed during the study period. After exclusions were applied the total number of surgeries included were only 288. This was still a significant number that could be used for statistical evaluation. The number of DBD procedures were however much less compared to SK surgeries performed and a prospective study may eliminate this discrepancy by using randomization to equal the number of procedures between SK and DBD. This should be considered if future studies are to be performed.

A multivariate analysis with logistic regression was chosen as the best model to evaluate a binary dependent variable and multiple predictor variables that can be a mix of numerical, nominal, and ordinal variables. One of the benefits for using this model is that the assumption of the predictors does not have to be normally distributed or linearly related. A univariate analysis preceding the multivariate model helps to discard predictors with minimal influence and simplify the model without decreasing the predictive value. (Hazra and Gogtay, 2017) A backwards selection approach was employed to refine the model and identify the most influential predictor variables. This approach streamlines the model by keeping only the most relevant predictors, while discarding those that do not add significant explanatory value.

Ethics

The study underwent ethical scrutiny through the University of Pretoria's ethical committee and was approved to be completed. This was a retrospective study and as such only clinical records were evaluated. For a prospective study to be completed animal ethics evaluation would be a requirement too, as per the University of Pretoria's regulations.

Exclusions

Several exclusions were applied to this study. These are mentioned above (Chapter 7). The main exclusions were concurrent pathology that may have influenced healing or potentially related to the cause of the corneal ulcerations, such as ectopic cilia. Some exclusions were unrelated to SCCED lesions, but which also required a DBD procedure, or which had previous invasive surgery performed. To limit exclusions a prospective case controlled randomized study may be used.

Breeds

The ten most common breeds presented for SCCED lesions in this study are listed above (**Table 7.1**). The five most common breeds made up a significant number of the cases in this study (54.1%). These included French Bulldogs, Staffordshire Bullterriers, Boxers, Labrador Retrievers and Yorkshire Terriers. Only Yorkshire Terriers are included in the five most common dog breeds seen at the JAEH during the same study period. This is most likely due to the popularity of this breed in South Africa, especially in urban areas.

An analysis of the risk for certain breeds to present with a SCCED lesion was not completed as this was not relevant to the hypothesis. Only the surgical outcome using breed as a predictor variable was evaluated. Based on the univariate analysis (**Figure 8.1 & 8.2**), none of the breeds had a significant effect (p<0.2) on the outcome of the procedure performed.

The breeds in this study were similar to other breeds previously reported. Boxers, Golden Retrievers and Keeshond were overrepresented in a study by Murphy *et al*. (Murphy et al., 2001) Brachycephalic breeds reported in a recent study consisted of French Bulldogs (30.3%), Boxers (12.5%), English Bulldogs (4.5%), and Cavalier King Charles spaniels (4.5%). They were also overrepresented in this study. (Landrevie et al., 2023) Labrador Retrievers has also been reported to be commonly affected. (Gosling et al., 2013; Wu et al., 2018) Boxers were over-represented and more likely to develop SCCED lesions in the contralateral eye in another report. (Hung et al., 2020)

Patient sex

Male dogs accounted for 58.0% of the patients presented for SCCED lesions included in this study and females only 42.0% (**Table 7.3**). Male dogs were overrepresented in this study (p<0.05). However, patient sex did not have a significant effect on the surgical outcome of the procedures used to treat SCCED lesions in this study and was excluded as a predictor variable for surgical outcome based on the univariate analysis (p>0.2) (**Figure 8.2**).

The sex distribution varies in published studies. Some reports have no sex predisposition. (Gosling et al., 2013; Landrevie et al., 2023; Murphy et al., 2001) While others may point to a predisposition. (Wu et al., 2018)

Body weight

Average body weight for dogs presented for SCCED lesions included in this study was 19.3kg (**Figure 7.1**). This is likely to relate to the common breeds in this study, which were medium to large breed dogs. It had no significant effect on the surgical outcome of the procedures used to treat SCCED lesions in this study and the univariate analysis excluded it as a predictor variable (p>0.2) (**Figure 8.2**).

Patient age

Mean age of the dogs presented for SCCED lesions included in this study was 8.3 years. It had no effect on the surgical outcome of the procedures used to treat SCCED lesions in this study and the univariate analysis excluded it as a predictor variable (p>0.2) **(Figure 8.2**).

Age range in this study was similar to reports published previously, which seems to be middle aged dogs. (Bentley, 2005) Median age was 9 years in a study by Murphy et al. (Murphy et al., 2001) A recent study on 89 eyes reported the mean age of the patients as 8.78 years. (Landrevie et al., 2023) Gosling *et al* reported a mean age of 8.9 years. (Gosling et al., 2013) 8.7 year were reported in another study comparing DBD and DBS+SK. (Wu et al., 2018)

Surgeon

Surgeons 2 and 3 are ophthalmology specialists with over ten years of experience and together they performed 47.2% of the procedures in this study. Surgeons 1 and 4 were ophthalmology residents during the study period, with one to three years of experience. Surgeons 1 and 4 together performed 52.2% of the procedures during the study period.

Successful outcome between days 10-14 post operatively expressed as a percentage illustrates the effect of experience on outcome. Surgeon 2 and 3 each had a relatively higher successful outcome for both SK (94.6% & 93.8%) and DBD (90.0% & 100%) compared to surgeon 1 and 4 for both SK (78.8% & 80.9%) and DBD (85.7% & 81.8%) (**Table 7.5**).

Including the year as a predictor in the multivariate analysis (excluding missing parameter IOP_affected) highlighted the fact that the odds ratio for a successful outcome for either procedure was 1.1 as the years progressed (**Figure 10.1 & 10.2**). This indicates that as the surgeons gained more experience the outcome was positively influenced. Mild temporal bias. Even though the *p*-value for this was ultimately not significant ($p>0.05$) in the univariate analysis (**Figure 8.2**) and multivariate analysis (**Figures 9.1 & 10.1**), it should be considered when training new residents. If an inexperienced surgeon is to perform the procedure it is advised to have an experienced surgeon guide the less experienced surgeon.

Using each surgeon as a predictor variable for surgical outcome they were deemed not significant by the univariate analysis (**Figure 8.1**), with a $p>0.2$. Even though the univariate analysis excluded surgeon as a predictor variable it was still included in the multivariate analysis for further assessment (**Figure 9.1 & 9.2**). Odds ratios for surgeons 2, 3 and 4 were 2.112, 2.019 and 1.044 respectively. The *p*-values were relatively high with $p>0.2$ for all surgeons and thus the surgeon did not have a significant effect on procedure outcome.

The final interpretation is that the individual surgeons did not have a significant effect on the outcome of the procedure performed, but both the experienced surgeons had a slightly higher percentage of successful outcomes for both SK and DBD compared to the inexperienced surgeons.

Lesions

Bentley *et al* provides a concise overview of clinical lesions that may be observed in dogs with SCCED lesions in their review article. Ocular discharge type and character change may be noted. A superficial corneal lesion may present with an increase in lacrimation and epiphora. Ocular colour changes may include corneal oedema seen as a light blue grey to white discolouration if a superficial corneal lesion is present. The cornea may also develop vascularization and show red discolouration in severe chronic cases, but this is variable. Pain is commonly seen and blepharospasm, third eyelid prolapse and rubbing of the eye may be noted. Miosis may be present but may not be commonly observed by the client. (Bentley, 2005)

Several clinical lesions were identified during examination at the initial presentation for SCCED lesions in this study (**Table 7.4**). The most common of these were some form of keratitis (99 cases), blepharospasm (77 cases), an increase in lacrimation (67 cases) and localized corneal oedema (40 cases). The upset plot (**Figure 7.4**) gives an idea of the association of the lesions reported. Keratitis, blepharospasm and lacrimation were reported together in 51 cases.

Keratitis was the most common finding in patients in this study (34.4%). This was similar to the study by Murphy *et al* which found vascularization in 56% of cases. In their study they reported that vascularization were more common in lesions located near the periphery. (Murphy et al., 2001). This is most likely related to the pathogenesis of corneal vascularization. (Whitley and Hamor, 2020) The univariate analysis (**Figure 8.3**) excluded it as a predictor variable of surgical outcome ($p>0.2$). The term keratitis was used in this study if any form of corneal neovascularization or stromal vascularization were reported in the clinical examination record. Lesion location or severity scoring was not accurately reported for keratitis, and thus it was excluded in the final data sheet. Granulation tissue development at the site of the lesion was reported separately. Granulation tissue development would be related to a more chronic SCCED lesion and was reported in only 4 cases. Any change in nature of the vascularization or granulation tissue between the initial examination and the post-operative follow-up examination were not taken into consideration for this study. From experience, vascularization may however develop during the healing period and is only addressed with medical intervention if it assessed as moderate to severe at the follow-up examinations.

Blepharospasm and an increase in lacrimation were reported in 26.7% and 23.3% of cases respectively. These symptoms are likely to be related because corneal sensation drives both responses. Blepharospasm and lacrimation were identified as potential predictive variables in the univariate analysis ($p<0.2$) (**Figure 8.3**). Further evaluation of blepharospasm in the multivariate analysis (**Figure 9.3 & 9.4**) and multivariate analysis excluding IOP_affected (**Figure 10.1 & 10.2**) were completed. But backwards elimination excluded it as a predictive variable for procedure outcome. Multivariate analysis (**Figures 9.1-9.4**) for lacrimation revealed it as a negative predictive variable of surgical procedure outcome ($p=0.056$). After backwards selection was applied it revealed an increased risk and Odds Ratio of 0.2619. Multivariate analysis excluding missing IOP_affected (**Figures 10.1-10.4**) also indicated an increased risk of negatively affecting the surgical outcome of the procedure ($p<0.05$). With an Odds Ratio of 0.3182 after backwards selection was applied. Thus, the conclusion is that a clinical examination finding of increased lacrimation at the initial presentation for SCCED lesions in this study was as a negative predictor variable for surgical outcome.

Some degree of localized corneal oedema was reported in 13.9% of the SCCED cases in this study (**Table 7.4**). Corneal oedema develops after the epithelial barrier is disrupted and the stromal tissue exposed. This is usually mild if encountered with only a superficial epithelial ulcer. Corneal oedema may be worsened if an ulcer extends into the stromal tissue or if there is significant anterior uveitis present. The univariate analysis (**Figure 8.3**) excluded oedema as a predictive variable for surgical procedure outcome ($p>0.2$).

The study design that was used may introduce bias for the number of lesions reported. Some clinicians may be very thorough and descriptive with regards to the clinical presentation, size, shape, location, and severity of lesions. Whereas another clinician may merely state the main clinical findings. A prospective study design, and limiting the examinations to fewer clinicians, will eliminate this variability, lessening the chance for bias in the final analysis.

A small number of lesions, reported in individual cases, were also part of the exclusion list. These specific cases, included in the study, were deemed incidental, and not contributing to the SCCED lesion pathology or interfering with healing, and was clearly stated as such in the attending clinician’s examination report at the time. These included four cases of glaucoma, two cases with mild corneal dystrophy, one case with mild uveitis, one case with mild corneal degeneration, and one case with mild corneal scarring.

Intra-ocular pressure

Mean IOP measurements in affected eyes were 17.12 mmHg and 17.41 mmHg in unaffected eyes (**Figure 7.2**). The mean of the differences was -0.29 and the descriptive evaluation revealed no significant difference for the IOP between affected and unaffected eyes ($p>0.05$). The univariate analysis found that IOP of affected eyes may be a potential predictive variable for procedure outcome ($p<0.2$) (**Figure 8.2**). This was further evaluated in the multivariate analysis (**Figures 9.1-9.4**). Multivariate analysis with backwards elimination revealed that IOP in affected eyes may potentially serve as a predictive variable for procedure outcome (p=0.053). However, the risk (Odds Ratio 1.133) was low after backwards elimination is applied.

The presence of anterior uveitis may affect the IOP of a globe. We also know that corneal ulceration may be a cause of anterior uveitis. Thus, it is advised to pay close attention and perform a detailed examination in patients with SCCED lesions to confirm the presence of anterior uveitis and manage this accordingly. There was significant missing data for IOP measurements in the clinical notes on *Avimark*. The clinicians may also not have mentioned mild anterior uveitis signs in their clinical notes. It was recorded only once under lesions (**Table 7.4**). The nature of this study may thus result in bias and for the final multivariate analysis the IOP in affected eyes were excluded. This can be addressed in prospective studies as it may be a variable to consider.

Schirmer tear test

Mean STT readings in affected eyes in this study population was 25.7 mm/min and unaffected eyes were 23.1 mm/min (**Figure 7.3**). The mean of the difference (3.09) between affected and unaffected eyes in this study was significant (p<0.05). Yet, in this study the STT was excluded as a predictive variable for procedure outcome in the univariate analysis (p>0.2) (**Figure 8.2**). This was an interesting finding because increased lacrimation was determined to be a significant predictive variable. Based on this, future prospective studies would need to look closely at the relationship between increased lacrimation as a clinical finding and STT measurements in eyes affected with a SCCED lesion.

Murphy *et al* found a mean STT in affected eyes of 21.2 mm/min and unaffected eyes of 17.9 mm/min and the affected eyes were also significantly different. (Murphy et al., 2001)

Soft contact lens

At the post-operative follow examination the presence of the SCL was noted in only 26.0% of cases. Nevertheless, the univariate analysis identified it as a predictive variable (p<0.2) for procedure outcome (**Figure 8.3**). The multivariate analysis excluding missing parameter IOP_affected with backwards selection retained SCL presence at the follow-up examination as a positive predictive variable for procedure outcome in this trial, with an Odds Ratio of 2.255. (**Figure 10.3 & 10.4**). The p-value was however high (p>0.05) and ultimately it should not be regarded as a significant predictive variable in this study.

The practical implication of this finding only serves as an observation. Why may you ask? Because the observation of SCL retention, or loss, is only made by the veterinarian at the follow-up examination. It comes after a choice about treatment/intervention has already been made. What is not evident in this study either, is when the contact lens was lost during the follow-up period. It may have been within hours after surgery, or minutes before the follow-up examination, as the pet owner does not always observe or report the loss of the SCL.

It is however suggested as a valuable part of the treatment for SCCED lesions in dogs, because it may shield migrating epithelial cells from abrasion, support more rapid cellular migration, and improve patient comfort post-operatively. (Gosling et al., 2013; Spertus et al., 2017) Placement of a SCL after cotton-tip debridement compared to cotton-tip debridement alone may result in increased healing response for SCCED lesions. (Bentley, 2005) SCL was not a significant variable in another study. (Wu et al., 2018) The JAEH surgeons routinely place a SCL after both a SK and DBD procedures based on the expected improved healing of SCCED lesions post-operatively and improved patient comfort.

Retention of the SCL was reported as good (95%) by Gosling *et al*. (Gosling et al., 2013) In this study the SCL variable is likely to suffer from bias due to under reporting in the clinical examination notes at the follow-up examinations. A limitation of retrospective data. A well designed randomized prospective study comparing SCL placement to non-placement under similar conditions as this study, with ongoing confirmation of SCL retention during the post-operative period, would be required to evaluate the true effect on procedure outcome.

Laterality, repeat surgeries, collateral, or bilateral surgeries.

Subsequent surgery on a collateral eye of a patient during the study period and bilateral surgery performed on the same day were excluded as predictive variables based on the univariate analysis ($p>0.2$) (**Figure 8.1**).

Univariate analysis of laterality identified OS as a potential predictive variable for surgical procedure outcome ($p<0.2$) (**Figure 8.1**). Multivariate analysis with backwards selection ultimately excluded it as a significant predictive variable for procedure outcome (**Figure 9.3 & 9.4**).

Follow-up procedures on a single eye (repeat) was found to be a significant negative predictive variable for procedure outcome. Both univariate analysis, and multivariate analysis (excluding missing parameter IOP_affected) with backwards selection retained "repeat" as a predictive variable ($p<0.05$) (**Figures 8.1, 10.3 & 10.4**). The Odds Ratio was 0.1784.

A large study including 249 cases reported bilateral cases as 4.4%, and contralateral cases of 10.6%. (Hung et al., 2020) These were both less and more respectively compared to this study (bilateral 10.4 % and contralateral 7.6%).

Surgical procedure

Comparing the surgical outcome after performing a SK or DBD was one of our main aims for this study. Univariate analysis indicated that it is unlikely to be a predictive variable for surgical outcome based on a $p>0.2$ (**Figure 8.1**). But because it was the main variable under investigation it was retained for the multivariate analysis component. Here it was found to be not significant ($p>0.05$) in both parts of the multivariate analyses that were performed (with and without missing parameter IOP_affected) (**Figures 9.1, 9.2, 10.1 & 10.2**). Backwards selection for each variable confirmed that procedure type was ultimately not significant as a predictive variable for procedure outcome.

These results reflect published literature in which either procedure has a relatively high success rate as treatment options for SCCED lesions in dogs. (Wu et al., 2018) In her review about SCCED lesions Bentley mentions both DBD and SK as effective treatment options. (Bentley, 2005)

Predictor variables retained

The only two variables that were found to be significant as a predictor for procedure outcome were the presence of increased lacrimation at initial examination and the need for a follow-up surgery (repeat) in a single eye.

Increased lacrimation (epiphora) detected at the initial examination was a significant negative predictive variable for the surgical outcome. Odds Ratio 0.3182. ($p<0.05$).

A repeat surgery in a single eye was found to be a significant negative predictive variable for the surgical outcome. Odds Ratio 0.1784. ($p<0.05$).

Study limitations

Various comments were made under the above headings and relevant sections. In general, retrospective studies will always suffer from missing data points, inaccurate medical records, procedure selection bias, and temporal bias. In this study the number of DBD procedures where less than SK procedures. Time period for the progression of the lesion, lesion grading, and SCL loss where not accurately recorded in the clinical notes. Another important aspect is post-operative complications, although rare, these where not consistently recorded and could not be evaluated. However, the main aim of this study did not focus on complication rate, and it was not relevant to the hypothesis. Selection bias (for procedure) is another aspect which could not be evaluated based on missing lesion grading data.

To address these limitations a prospective case-controlled randomized study is advised. The alternative is to evaluate each procedure (SK or DBD) individually for outcome and complications.

Chapter 12: Summary

Spontaneous chronic corneal epithelial defects are a common presenting complaint in canine patients referred for non-healing corneal ulceration. The classic lesion and history include an axial or paraxial, superficial, corneal epithelial ulcer, that is non-responsive to topical therapy and is recurrent in nature. The lesions are not infected and are not associated with any physical cause preventing healing. Clinically the lesion is surrounded by a region of loose epithelium. Pathogenesis of SCCED lesions is not fully understood but morphological and functional abnormalities present in the cornea, discussed under section 3.1, prevents normal healing of the epithelial defect.

Various topical and surgical treatments have been described. Treatment options that include some form of intervention include cotton-tip debridement, cotton tip debridement & placement of a soft contact lens, cotton-tip debridement & third eyelid flap, diamond burr debridement, grid/striate keratotomy, anterior stromal puncture, thermal cautery, and lastly, lamellar keratectomy.

The main aim of this study was to present an overview of the patient demographics for SCCED cases in canines that are referred for specialist ophthalmology opinion in South Africa. The second aim was to compare the outcome of two surgical interventions often used to treat SCCED in canines in South Africa.

441 unique surgical cases during the period from 1 January 2019 until 31 December 2023 were identified in JAEH clinical records. After exclusions were removed a final total of 288 ocular surgeries were included in the results. These were 223 striate keratotomies and 65 diamond burr debridement procedures. 149 were right eyes and 139 were left eyes. This included surgeries on the contra-lateral eye of a single patient (22 cases) and repeated surgeries of a single eye (14 cases). 15 patients presented for bilateral SCCED lesions at the initial examination. The total number of dogs operated on were 241 patients, and a total number of 274 eyes were operated on. Laterality, surgery on a contra-lateral eye or bilateral surgeries did not affect the surgical procedure outcome. However, a repeat surgery in a single eye was a significant negative predictive variable for the surgical outcome ($p<0.05$).

A total of 39 different dog breeds were included in the results. French Bulldogs, Staffordshire Bull Terriers, Boxer dogs, and Labrador Retrievers were the most common breeds presented for SCCED lesions. Together they represented 54.1% of the cases. French Bulldogs, as a group, had a lower total negative fluorescein stain percentage between 10-14 days post-operatively, but statistical analysis concluded that the breed of dog did not have a significant effect on the surgical procedure outcome. It is reasonable to assume that the breed conformation, being brachycephalic, may play some role in why French Bulldogs were commonly affected and showed some degree of delayed healing.

Male dogs were over-represented ($p<0.05$) and constituted 58.0% of the patients surgically treated for SCCED. Female dogs were the remaining 42.0% of cases. Neuter status could not be evaluated due to missing parameters. The average age of the patients was 8.3 years old, and the average body weight was 19.3 kg. Age, sex, and body weight did not affect the surgical procedure outcome.

The most common clinical signs reported were keratitis, blepharospasm, an increase in lacrimation and localized corneal oedema. Increased lacrimation (epiphora) detected at the initial examination was a significant negative predictive variable for the surgical outcome ($p<0.05$).

Intra-ocular pressure measurements were collected in 263 right eyes and 252 left eyes. For eyes affected with SCCED the mean IOP was 17.12 mmHg. For unaffected eyes the mean IOP was 17.41 mmHg. IOP values were not significantly different between affected and unaffected eyes ($p>0.1$). A lower IOP in affected eyes was suggestive of being a predictive variable ($p<0.1$) for surgical procedure outcome but there were large numbers of missing data for this field. It was excluded in the final multivariate analysis because of the missing data.

Schirmer tear test measurements were collected for 179 right eyes and 176 left eyes. For eyes affected with SCCED the mean STT was 25.59 mm/min. For unaffected eyes the mean STT was 22.49 mm/min. STT values were significantly different between affected and unaffected eyes ($p<0.05$). STT itself was not a significant predictive variable for surgical procedure outcome ($p>0.1$), but an increase in lacrimation detected during examination was a significant predictive variable. This is somewhat contrasting, and it is suggested that future prospective studies evaluate this in more detail.

The first post operative fluorescein stain results (F1) were available for 288 surgeries. A negative fluorescein stain result indicated surgical success and a positive stain result a surgical failure. The day of presentation for F1 ranged between 5-28 days post-operatively, with an average presentation at day 12.8 post-operatively. For our hypothesis testing we restricted the follow up period for F1 presentation to between days 10-14 post-operatively. This influenced the total number of procedures included in the final analysis. SK findings were 148 negative cases (87.6%) & 21 positive cases (12.4%) between day 10-14 post operatively. DBD findings for the same period post-operatively are 40 negative cases (85.1%) and 7 positive cases (14.9%). Univariate ($p=0.58$), multivariate ($p=0.86$), and multivariate analysis excluding missing IOP_affected data ($p=0.92$) concluded that the type of procedure, be it SK or DBD, did not significantly affect the outcome of the surgical procedure.

The soft contact lens placed post-operatively was only retained until the follow-up examination in 26.0% of cases. By far most patients (74.0%) would lose the contact lens before re-examination. SCL retention was a slight positive predictive variable for surgical procedure outcome, but this was not significant ($p>0.1$) in the final multivariate analysis with backwards selection. It is also highly likely to suffer from bias due to under reporting.

The surgeries were performed by four individual surgeons in this study and the effect of the surgeon on the procedure outcome was evaluated in both the univariate and multivariate models. The surgeon effect was ultimately determined as non-significant ($p>0.05$). However, surgeon 2 had a reasonably low *p*-value ($p<0.05$) in the univariate analysis and $p=0.063$ before backwards selection was applied in the multivariate analysis. Taking this information together with the higher percentage of F1 negative results compared to the inexperienced surgeons (1 and 4), it is reasonable to assume that a surgeon with experience may potentially have a better surgical outcome. It is an important observation and should be considered when training inexperienced surgeons to perform both SK and DBD procedures. Our recommendation is that training should be extensive and include cadaver surgeries before operating on live patients. Future studies on SCCED surgeries should also take note of surgeon experience when reporting results.

Chapter 13: Final conclusions

The main aim of the study was to describe patient demographics for SCCED lesions presented to a specialist veterinary ophthalmology referral hospital in South Africa. In summary, French Bulldogs, Staffordshire Bull Terriers, Boxer dogs, and Labrador Retrievers were the most common breeds (54.1%) presented for SCCED surgery. Male dogs were over-represented in this study and represented 58.0% of the cases. The average age of the dogs were 8.3 years, and the average body weight was 19.3 kg. Affected and unaffected eyes had a mean IOP of 17.12 mmHg and 17.41 mmHg respectively. Affected and unaffected eyes had a mean STT of 25.59 mm/min and 22.49 mm/min respectively. The STT of affected eyes was significantly raised compared to unaffected eyes. The most reported clinical signs at initial presentation were keratitis, blepharospasm, lacrimation, and corneal oedema. Left or right eyes were equally likely to be affected. The contralateral eye was subsequently affected in 7.6% of cases during the study period. Bilateral SCCED lesions were diagnosed in 10.4% of cases, and 4.9% of cases required a second follow-up surgery. The main predictive variables for surgical procedure outcome were increased lacrimation at the initial examination and repeated follow-up surgeries for a single eye. Increased lacrimation (epiphora) detected at the initial examination had a final Odds Ratio of 0.3182. ($p<0.05$). A repeat surgery in a single eye had a final Odds Ratio of 0.1784. ($p<0.05$).

The second aim of this study was to compare the surgical procedure outcome between striate keratotomy and diamond burr debridement for SCCED lesions in canines at the JAEH. Our hypothesis was the following: Striate keratotomy surgery for SCCED lesions is more likely or less likely to stain fluorescein negative at 10-14 days post-operatively compared to SCCED lesions treated with diamond-burr debridement. Our finding in this study was that fluorescein stain results were not significantly different between SK and DBD. Our hypothesis is thus rejected, and the null hypothesis is assumed based on these results. Striate keratotomy surgery for SCCED lesions is equally likely to stain fluorescein negative at 10-14 days post-operatively compared to SCCED lesions treated with diamond-burr debridement.

Declaration of conflict of interest

The primary researcher is an employee at the Johannesburg Animal Eye Hospital.

The supervisor is the owner and principal veterinarian at the Johannesburg Animal Eye Hospital.

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Appendix list

A) Data capture sheet.

Sirrals_UP_Data Capture Sheet & Ophthalmic Examination Record: Case nr:

Date: Patient EID number: Breed: Sex: Age:

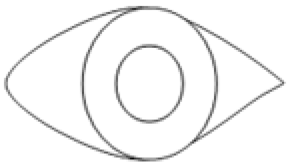
History & General observations:

Weight: D0: D45: D120: Final live mass: Other:

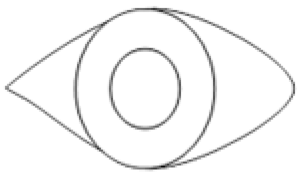
Warm carcass mass: Cold carcass mass: Dressing percentage:

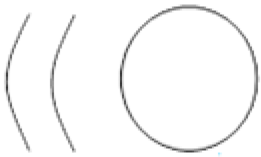
	Photopic	Scotopic		R	L		R	L		R	L	
Obstacle course			Menace response			Red light			STT			mm/min
Tracking response			Dazzle reflex			Blue light			Flourescein			
Placing reflex			Palpebral reflex			Direct PLR			Tear BUT			sec
			Corneal reflex			Indirect PLR			IOP			mmHg

RIGHT EYE **LEFT EYE**

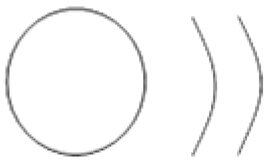


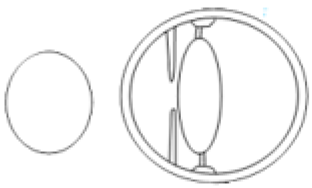
	WNL	ORBIT/GLOBE	WNL	
	WNL	EYELIDS	WNL	
	WNL	CONJUNCTIVA	WNL	
	WNL	THIRD EYELID	WNL	
	WNL	SCLERA	WNL	
	WNL	NL DUCTS	WNL	
	WNL	IRIS	WNL	



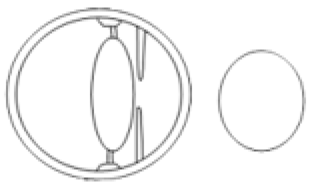


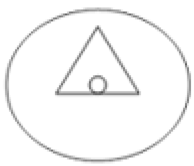
	WNL	CORNEA	WNL	



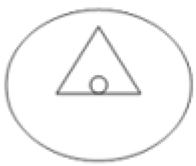


	WNL	ANT CHAMBER	WNL	
	WNL	LENS	WNL	
	WNL	VITREOUS	WNL	





	WNL	RETINA	WNL	



Notes:

Vision assessment: Visual ☐ Blind: OD ☐ OS ☐

Pain assessment: Free ☐ Mild pain ☐ Moderate pain ☐ Severe pain ☐

Signs of pain detected:

B) Informed Consent form

B) Informed Consent form

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

DEPARTMENT OF COMPANION ANIMAL CLINICAL STUDIES

FACULTY OF VETERINARY SCIENCE

UNIVERSITY OF PRETORIA

1. To be completed by the researcher:

Project title: Spontaneous chronic corneal epithelial defects, analysis of canine cases presented to specialist referral practices in South Africa.

Name of researcher: Dr Brent Sirrals; BSc, BVSc (Hons) Ophthalmology resident; brent@animaleyehospital.co.za Tel: 076 413 1221

Purpose of the research project: Observations made and recorded in this study will add to the current knowledge of ocular pathology seen in dogs. The information may lead to increased awareness of a condition commonly seen causing ophthalmic pain and discomfort and which frequently needs surgical intervention for treatment purposes. The information will assist veterinary practitioners to recognize the typical patient and clinical presentation for SCCED lesions in canines, in South Africa. The study will aid South African veterinarians to make recommendations to their clients with regards to specific treatment options available, their potential complications and expected outcome.

Information usage: Data gathered will be used as part of the fulfilment of Master of Veterinary Medicine degree purposes for Dr Brent Sirrals. Data may be published in peer-reviews journals and presented at relevant congresses or meetings. **No personal data relating to the patient, client, facility and their intellectual property will be shared or made public.**

Detailed procedures to be performed: Access to clinical records to collect data on surgical procedures performed and the outcome or complications arising from the procedure.

Risk(s) involved in the specified procedures: There are no direct risks associated with this study.

Identification of records to be used: Avimark patient identifier.

Unmistakeable distinguishing description of the animals to be used: No live animals – clinical records of *Canis familiaris*, a small to medium sized land roaming carnivore.

To be completed by the owner of the clinical records, or person duly authorized to sign on his/her behalf:

Name of the owner / authorized manager Johannesburg and Cape Animal Eye Hospital:

Dr Antony Goodhead

Have you received detailed information regarding the proposed study? YES NO

Have all the risks involved in the procedures been explained to you and do you fully understand these risks? YES NO

Do you grant full consent for the procedures to be performed? YES NO

2. The undersigned parties further agree that no compensation will be payable to the animal's owner or anybody else and that all research associated costs will be covered by the researcher(s).
3. The undersigned parties further agree that this form would serve to fully indemnify the University of Pretoria and the undersigned researcher(s) against any future claims resulting from the specified procedure by or on behalf of the animal's owner.
4. The undersigned parties further agree that no material of any kind including data and research findings, obtained, or resulting from the procedure, would be passed on to any third party or used for any purpose other than that specified in this form, except with the written consent of the undersigned owner of the animal.

Signature Researcher

Signature owner / authorized manager

Signature Witness

02/03/2023.
Date

C) Research ethics certificate

UNIVERSITEIT VAN PRETORIA
UNIVERSITY OF PRETORIA
YUNIBESITHI YA PRETORIA

Faculty of Veterinary Science
Research Ethics Committee

09 March 2023

LETTER OF APPROVAL

Ethics Reference No	**REC010-23**
Protocol Title	**Spontaneous chronic corneal epithelial defects, analysis of canine cases presented to specialist referral practices in South Africa**
Principal Investigator	**Dr B Sirrals**
Supervisors	**Dr AD Goodhead**

Dear Dr B Sirrals,

We are pleased to inform you that your submission conforms to the requirements of the Faculty of Veterinary Sciences Research Ethics committee.

Please note the following about your ethics approval:

1. Please use your reference number (REC010-23) on any documents or correspondence with the Research Ethics Committee regarding your research.
2. Please note that the Research Ethics Committee may ask further questions, seek additional information, require further modification, monitor the conduct of your research, or suspend or withdraw ethics approval.
3. Please note that ethical approval is granted for the duration of the research as stipulated in the original application (for Post graduate studies e.g. Honours studies: 1 year, Masters studies: two years, and PhD studies: three years) and should be extended when the approval period lapses.
4. The digital archiving of data is a requirement of the University of Pretoria. The data should be accessible in the event of an enquiry or further analysis of the data.

Ethics approval is subject to the following:

1. The ethics approval is conditional on the research being conducted as stipulated by the details of all documents submitted to the Committee. In the event that a further need arises to change who the investigators are, the methods or any other aspect, such changes must be submitted as an Amendment for approval by the Committee.
2. Note: All FVS animal research applications for ethical clearance will be automatically rerouted to the Animal Ethics committee (AEC) once the applications meet the requirements for FVS ethical clearance. As such, all FVS REC applications for ethical clearance related to human health research will be automatically rerouted to the Health Sciences Research Ethics Committee, and all FVS applications involving a questionnaire will be automatically rerouted to the Humanities Research Ethics Committee. Also take note that, should the study involve questionnaires aimed at UP staff or students, permission must also be obtained from the relevant Dean and the UP Survey Committee. Research may not proceed until all approvals are granted.

APPROVED

We wish you the best with your research.

Yours sincerely

PROF M. OOSTHUIZEN
Chairperson: Research Ethics Committee

100 YEARS

Room 8-8, Arnold Theiler Building
University of Pretoria, Faculty of Veterinary Science
Private Bag X04, Onderstepoort, 0110, South Africa
Tel +27 (0)12 529 8390
Email marie.watson-kriek@up.ac.za
www.up.ac.za

Faculty of Veterinary Science
Fakulteit Veeartsenykunde
Lefapha la Disaense tša Bongakadiruiwa

D) Informed consent to treatment form (example)

Johannesburg Animal Eye Hospital [JAEH]

44 Kingfisher Drive Fourways, Tel: 011 465 1237 / Fax: 011 465 2916

INFORMED CONSENT TO TREATMENT

DIABETIC	
STARVED	
CLIENT CONTACTED P/O	
DISCHARGE TIME	
OTHERS:	

CLIENT DETAILS	*Please check your particulars and change where necessary*		
Owner/Legal Agent:	**<title> <first-name> <client>**		**(<number>)**
Address:	**<address> , <city> , <zip>**		
Tel.No. Home:	**<phone>**	Tel. No. Work:	**<business>**
Cell:	**<cell-phone>**	ID Number	_______________
E-mail:	**<e-mail>**		
PATIENT DETAILS	*Please check your pet's details and change where necessary*		
Pet's Name:	**<animal>**	Sex:	**<sex-name>**
Breed:	**<breed>**	Age:	**<age-name>**
Weight:	**<weight> <measure>**		

Preliminary Diagnosis / Treatment:

____

Estimate of costs for treatment:

____

**Please note: We always endeavour to keep costs within the estimate. However, costs are dependent on many variables, including the progression of the disease. It is sometimes impossible to predict these factors at the time of admission. If you are not available and the circumstances require an immediate decision, then treatment will be continued in the best interests of the patient and costs charged to your account. Estimates do not include follow-up consultations and treatments.*

1. I, the undersigned, an adult major, hereby authorize the veterinarians and staff of this veterinary facility to perform any reasonable treatment/anaesthesia and surgery they may deem necessary, including further or alternative measures as may be necessary during the course of the surgery and/or treatment of my animal.
2. I acknowledge that a quote cannot be provided, and that I have been provided with an **estimate** for an average procedure, but the **final cost may vary** substantially and be significantly higher than discussed because of the particular factors that may be encountered as the procedure unfolds. I agree to settle the final bill in full upon request or discharge, whichever is earlier.
3. I undertake to keep in daily contact to enable the staff to inform me of progress, costs incurred and additional treatment involved.
4. I acknowledge that I am indebted to the above practice for veterinary treatment, service rendered and expenses incurred therewith and hereby render myself responsible for all costs, telephone calls and legal expenses, as between attorney and own client including collection charges that may be incurred in the recovery of the outstanding amount.
5. I recognize that there is some degree of risk attached to any medical or surgical procedure or treatment. I have discussed any concerns I may have with the veterinarian. I hereby absolve the veterinarians, staff and this facility from all actions arising directly or indirectly for the treatment/anaesthetic/surgery.
6. While the veterinarians at this facility provide diagnosis, treatment and prognosis to the best of their ability, economic constraints prevent these from being made with all the necessary information available. Consequently, the vets will not be liable for any consequences arising from incorrect diagnosis, treatment or prognosis.
7. I am aware that this veterinary facility does not provide 24 hours per day monitoring of patients.
   I wish to have my pet monitored at night at Fourways Veterinary Hospital [FVH] After Hours facility. FVH will collect my pet and provide the afterhours service and return my pet to JAEH the following morning and I accept that FVH will be wholly responsible for my animal from leaving JAEH to return to JAEH. The estimated cost will range from **R1000-R1400** or more if high care is required.

   I accept ☐ or decline this service ☐

8. I hereby authorize the veterinarians and staff of this veterinary facility, using their own transport, to transport my pet between clinics or to a specialist or to any other facility as may be required. I hereby absolve the veterinarians, staff and this facility from all actions, arising directly or indirectly from the transport of my pet.
9. I have arranged appropriate insurance cover for any loss or damages of whatsoever nature that may arise from this; alternatively, I accept that I self-insure for any such loss or damages.
10. I am aware that depending on the availability of veterinarians at JAEH, surgery may be performed by a different veterinarian to the one seen during the initial consultation. This may include a veterinary ophthalmology resident. DR ______________________________
11. I am aware that the surgery may be performed by a surgical intern and that the costs and implications have been explained to me.
12. This facility will not provide any opinions, reports, certificates, comments, recordings or copies of clinical notes to any person for any purpose, under any circumstances.
13. In the event of any grievance or dispute with this veterinary facility or its veterinarians, I undertake to enter into and complete the VDA's free Alternate Dispute Resolution process, before resorting to any other action or remedy.
14. I understand that Pre-Anaesthetic blood screening is strongly recommended for all animals over 7 years old and those where anaesthesia is a concern. These assist in testing the animal's ability to excrete anaesthetic and shows up liver, kidney and blood abnormalities. It is painless and involves drawing of blood. I want this screening test to be carried out on my pet.

    (Additional Cost about R1225). Yes ☐ No ☐
15. Is your pet insured? ☐ Insurance Company: Petsure / Medipet / One Plan / Dot sure / Other:
16. I acknowledge: That this facility is not party to my arrangement with my pet insurer and that no obligations whatsoever are placed on this facility. This facility will not deal with or provide information to the pet insurer. I am solely responsible for payment of veterinary fees to this facility and I hereby absolve this facility from all actions, arising directly or indirectly from my pet insurance arrangement.
17. List any allergies or known drug reactions: ______________________________
18. List any co-morbidities: ______________________________
19. Medical data and photos of the patient may be used, anonymously, for research purposes and in lectures, medical journals, and in social media.

I confirm that I am aware that the account is to be settled in full at the time of discharge from hospital and I acknowledge that I have read these conditions and hold myself bound thereto.

Date: ________________ Signed: ______________________________

Witness: ______________________________