
UNIVERSIDADE DE LISBOA

Faculdade de Medicina Veterinária

# OCULAR BRACHYCEPHALIC SYNDROME

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DISSERTAÇÃO DE MESTRADO INTEGRADO EM MEDICINA VETERINÁRIA

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**ABSTRACT**

**OCULAR BRACHYCEPHALIC SYNDROME**

Background: Brachycephalic breeds are well known to have anatomical skull changes that are responsible, directly or indirectly, for ocular alterations, known as ocular brachycephalic syndrome. The most common diseases include entropion, distichiasis, trichiasis, keratoconjunctivitis sicca, ectopic cilia and corneal ulceration. When not treated, they lead to permanent damage, causing a decrease of the dogs' vision acuity and compromise their wellbeing.

Purpose: This prospective study aims to describe a sample of brachycephalic dogs concerning their breed, age, gender, clinical signs, ocular alterations, medical and surgical treatment and their outcomes, to better characterize the disease complex ocular brachycephalic syndrome.

Materials & Methods: The studied population consisted of 47 brachycephalic dogs. The clinical approach included an ophthalmological examination, including assessment of ocular reflexes and responses, Schirmer tear test, tonometry, biomicroscopy and fundoscopy. Originated data was organized in a database using Microsoft Office Excel 2007® and statistical analysis was performed using descriptive statistics with the software IBM SPSS Statistics 20®.

Results: The population in study was composed of 49% females and 51% males, including 45% French Bulldogs, 34% Pugs, 7% English Bulldogs, 4% Boston Terriers, 4% Bullmastiffs, 2% Boxers, 2% Shar-Peis and 2% Shih-Tzus, with an age range between 4 months and 12 years old. The most frequent clinical signs were blepharospasm in 28% of the animals, conjunctivitis in 26%, ocular discharge in 19%, and epiphora in 15% of the cases.

The most frequent ocular abnormalities were macroblepharon in 75%, entropion in 45%, corneal ulcers in 40%, corneal pigmentation in 28%, corneal opacity in 23% and distichiasis in 21% of the studied animals. There was a higher incidence of corneal pigmentation in Pugs (62%) and corneal opacity in French Bulldogs (82%). The surgical techniques more frequently used were medial canthoplasty in 28% and electroepilation in 11% of the cases, with a good recovery and without post-operative complications. Medical treatment was indicated in cases of superficial ulcers, management of keratoconjunctivitis sicca and during surgical recovery.

Conclusions: This study allowed the perception of the incidence of ocular alterations related to the brachycephalic conformation. Some differences between breeds were noted, including a higher incidence of corneal pigmentation in Pugs and corneal opacity in French Bulldogs, which suggests that some brachycephalic breeds may be predisposed to certain ocular abnormalities. The percentage of secondary problems such as ulcers was high, which highlights the importance of a regular ophthalmological check-up, so that an early diagnosis of the primary disorders can be achieved, avoiding the development of secondary alterations and allowing for the institution of an adequate treatment.

Key-words: Ocular Brachycephalic Syndrome; entropion; corneal ulcers; distichiasis

**RESUMO**

**SÍNDROME OCULAR BRAQUICEFÁLICO**

Introdução: As raças braquicefálicas são conhecidas por apresentarem modificações anatómicas que são responsáveis, diretamente ou indiretamente, por doenças oculares que formam a síndrome ocular braquicefálico. As alterações mais comuns incluem entrópion, distiquíase, triquíase, queratoconjuntivite seca e úlceras. Quando não são corrigidas, podem comprometer a acuidade visual destes cães, e também o seu bem-estar.

Objetivo: Este estudo prospetivo tem como objetivo descrever uma amostra de cães braquicefálicos relativamente à sua raça, idade, género, sinais clínicos, alterações oculares, tratamento médico, cirúrgico e os seus resultados, para melhor caracterizar a síndrome ocular.

Materiais e Métodos: A população em estudo consistiu em 47 cães braquicefálicos. A abordagem clínica consistiu na realização de um exame oftalmológico e a determinação dos reflexos e respostas oculares, teste de Schirmer, tonometria, biomicroscopia e fundoscopia. Os dados resultantes foram organizados numa base de dados recorrendo a Microsoft Office Excel 2007® e a análise estatística foi realizada com o software IBM SPSS Statistics 20®.

Resultados: a população estudada foi composta por 49% fêmeas e 51% machos, incluindo 45 % Bulldogs Franceses, 34% Pugs, 7% Bulldogs Ingleses, 4% Boston Terriers, 4% Bullmastiffs, 2% Boxers, 2% Shar-Peis e 2% Shih Tzus, com idades compreendida entre os 4 meses e os 12 anos. Os sinais clínicos mais frequentes foram blefarospasmo em 28%, conjuntivite em 26%, corrimento ocular em 19% e epífora em 15% dos casos. Após um exame oftalmológico que incluiu a determinação dos reflexos e respostas oculares, e uma inspeção mais detalhada com um oftalmoscópio, alguns exames complementares foram realizados.

As alterações oculares mais frequentes foram macrobléfaro em 75%, entrópion em 45%, úlceras da córnea em 40%, pigmentação da córnea em 28%, opacidade da córnea em 23% e distiquíase em 21% dos animais. A incidência de pigmentação corneal em Pugs (62%) e opacidade corneal em Bulldogues Franceses (82%) foi elevada. As técnicas cirúrgicas mais frequentes foram a cantoplastia medial em 28% e eletroepilação em 11% dos casos, com uma boa recuperação e sem complicações pós-cirúrgicas. O tratamento médico foi indicado em casos de úlceras superficiais, queratoconjuntivite seca e durante a recuperação pós-cirúrgica.

Conclusões: O estudo permitiu a perceção da incidência de alterações oculares relacionadas com a conformação braquicefálica. Algumas diferenças entre raças foram notadas, e a maior incidência de pigmentação em Pugs e opacidade corneal em Bulldogues Franceses sugere que algumas raças poderão estar predispostas a certas alterações oculares. A percentagem de problemas secundários, como úlceras da córnea, foi elevada, evidenciando a importância da realização de um exame oftalmológico regularmente, para que se diagnostiquem precocemente as alterações primárias. Deste modo não se desenvolvem problemas secundários e torna-se possível a instituição de um tratamento adequado atempadamente.

Palavras-chave: Síndrome Ocular Braquicefálico; entrópion; úlceras da córnea; distiquíase

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**ABBREVIATIONS**

BOAS: Brachycephalic Obstructive Airway Syndrome
CsA: Cyclosporine A
IOP: Intra-Ocular Pressure
KCS: Keratoconjunctivitis sicca
Mm: milimiter
Mm/min: milimeter per minute
OBS: Ocular Brachycephalic Syndrome
NMP: Nictitating Membrane Prolapse
STT: Schirmer Tear Test

## I. TRAINEESHIP REPORT

I did my traineeship in Tierklinik- Universität Leipzig from 15th January until 31th May, with a duration of 792 hours.

Every morning, all the hospital workers gathered together at 7:30 AM to discuss the new cases that entered the night before and to discuss the working plan for the present day. Once a week there was always a doctor that presented a case, and that asked questions about it to the students. Almost every department also had a Journal Club, in which one or two articles chosen by the doctors were presented mostly by trainees and students. There was a second meeting at 3:15 PM to pass the new interned cases to the employees that worked on the afternoon and to take a glimpse of the next day's working plan.

The trainees worked one weekend per month, and the routine tasks- making clinical exams of the interned patients, preparing and giving medication- were divided between the trainees, last year students, and working students, under the veterinarian surgeon's supervision. There were no planned appointments on weekends, but all help was needed in emergency appointments and surgeries. In the end of the day, the following doctors and students arrived and there was a passing of the cases.

I started the rotation in Otorhinolaryngology and stayed there for two weeks. This hospital is well known for its Brachycephalic Airway Syndrome's correcting surgery, receiving dozens of animals each week. I've also seen several endoscopies for diagnosis of other diseases and surgical procedures, such as foreign body removals and nasal tumours exeresis.

The next rotation was in Diagnostic Imaging, for a month, in which I did x-rays and ultrasounds, interpreted CT's and had the opportunity to observe many MRI's.

The third department I stayed at was Internal Medicine, for another month. I saw many appointments and started some others myself, helped in treating hospitalized patients and discussed other cases. When there was some free time, the veterinarian surgeons called the trainees and students to discuss a theme of our or their choice. During that time, I've also spent some time in the Ophthalmology, Dermatology and Cardiology departments.

After that, I stayed in the Anaesthesiology department. I learned a lot about anaesthetics and other drugs, helped with the process of anesthetising the animals, and then controlled the anaesthesia during diagnostic exams or the surgery and taking care of the patient during the post-surgical period.

Two weeks later, I stayed at the Surgery department for a month. I watched and even helped many times in surgical procedures, whether it was soft tissue surgery, orthopaedics, ophthalmologic or dental surgery.

Next, I did a straight week of 12-hour night shifts, and the work required was similar to the one performed on weekends

My traineeship ended up in Neurology, in which I stayed for the last week. I watched referral appointments, interpreted MRI's and helped during surgeries. Once more, when possible, the doctors gave the students and trainees complete explanations about neurological mechanisms and diseases. The day ended with a meeting of the Neurological team to present new cases from the present day to the remaining colleagues.

# II. BIBLIOGRAPHIC REVIEW

## 1 Introduction

The brachycephalic breeds are spread around the world and their popularity is growing. That can be verified on the daily life of small animal veterinarians, as the number of these patients is increasing. Their personalities, wrinkly faces and appealing large eyes have turned them into popular pets. This popularity is thought to exist because humans find the large and round eyes, as well as the round face very appealing (Packer & Tivers, 2015b).

Pedigree dogs are artificially selected for extreme aesthetics dictated by formal breed standards, and breed-related disorders as a result are diverse. The pressure of selection applied over the last decades, trying to meet breed standards, developed therefore dramatic changes to the brachycephalic breeds' skull shapes (Appelboam, 2016). The foreshortening of the facial skeleton represents one of those changes and is a discrete mutation that has been selected in many popular flat-faced dogs (Packer, Hendricks, Tivers & Bum, 2015a).

Therefore, the concern by veterinarians has also increased. According to well-recognized entities such as the Federation of European Companion Animal Veterinary Associations (FECAVA), the World Small Animal Veterinary Association (WSAVA) and the Danish Small Animal Veterinary Association (DSAVA), the selection for extreme facial morphology leads to dog health and welfare problems (Feng, Mconnell, O'Hara, Chai & Spadafori, 2017). This brachycephaly acts like a risk factor for owning severe morbidities, like neurological, gastrointestinal and ear related abnormalities (Harvey & Haar, 2016). There are also in these breeds two easily recognized syndromes: Brachycephalic Airway Obstructive Syndrome and Brachycephalic Ocular Syndrome. The last one is not so well-known, but small facial alterations can have as consequences complications that put these dogs' vision at risk.

### 1.1 Anatomical and physiological considerations

The brachycephalic breeds are known to have a wider and disproportionately shorter skull, comparing to the mesocephalic and dolichocephalic ones. Some of their marked features include a short nose and maxilla, and a flat muzzle (McNabb, 2017).

The appearance of the eye is also a little different, as it is influenced by the size of the ocular globe, depth of the orbit and shape and length of the palpebral fissure. The orbits are characterized for being shallow and the palpebral fissures are large, in opposite to dolichocephalic dogs. That results in a quite prominent ocular globe, although it should belong within the orbit, centrally positioned and be freely mobile. These two last features are possible because of the existence of the extraocular muscles. The sympathetic innervation is responsible for an anterior position of the ocular globe, by maintaining a positive tone within the orbit and, as well as the retractor bulbi muscles, that help in its retraction.

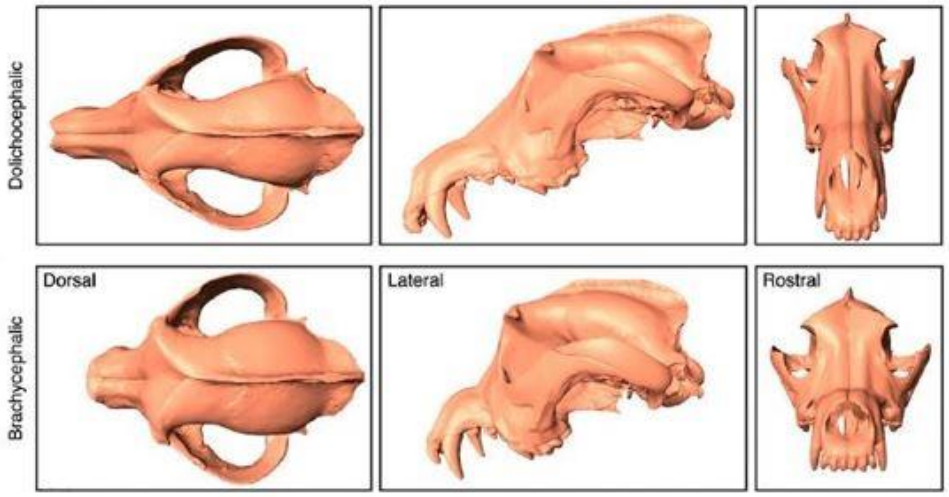


Figure 1 - Comparison between dolichocephalic and brachycephalic skulls. The orbits are wider and shallower on the second example (Adapted from and with authorization of Schoenebeck & Ostrander, 2013)

The characteristics responsible for the prominence of the ocular globe are multifactorial inherited and can predispose to conjunctivitis, keratitis or even ocular proptosis, an ocular emergency (Townsend, Bedford & Jones, 2009). If not treated rapidly, the prognosis for the vision capacity is guarded to poor and, according to Spiess & Pot (2014), only 20% of these cases gain some of their functional vision back. This prognosis can be predicted through the presence or absence of the pupillary light reflex and the degree of ocular damage (Townsend et al*.,* 2009). The protrusion of the ocular globe is also responsible for alterations in the adjacent structures, including orbital cellulitis and extraocular myositis (Spiess et. Al, 2014)

The eyelids are very important to protect the ocular globe, because they maintain the physiologic thickness of the tear film, spread it on the ocular surface, help the movement of the tears within and to the nasolacrimal system and remove some particles from the cornea and conjunctiva. They consist of a superior, inferior and nictitans and contain the meibomian glands (Gum & Mackay, 2013). These sebaceous glands are responsible for secreting the outer, oily layer of the preocular tear film. The third eyelid, or nictitans membrane, protects the cornea and the conjunctiva by moving over the cornea when the ocular globe is retracted and contains also one or more accessory glands that produce the aqueous part of the preocular tear film. Usually, the blinking movement allows the eyelids to move freely and fully across the

corneal surface, but not in short-muzzled dogs (Cook, Peiffer & Landis, 2009). They blink less frequently and incompletely, a condition called lagophtalmos, because of their decreased corneal sensitivity and exophthalmos. This condition is responsible for an evaporation of the tear film and constant drying of the central cornea, which can turn into ulcerative keratitis (Appelboam, 2016).

The nasolacrimal duct's goal is to drain tears from the ocular surface to the nasal passages and its length is variable among brachycephalic, mesocephalic and dolicocephalic dogs. The first ones present often very short ducts, leading to a drainage of the tears into the pharynx. Tear volume is mostly drained through the inferior puncta and canaliculi and it flows ventrally according to gravity pressure, and it's pulled into the canaliculi when the eyelids close. About fifty percent of the dogs have a second opening in the oral mucosa of the central hard palate, behind the incisors at the level of canine teeth (Grahn & Sandmeyer, 2014).

A scleral exposure can be associated with the more prominent eyes, although it hasn't been enough studied yet if its severity can act be a predisposition to eye disorders (Packer et al, 2015).

The genetic background plays an important role. Many genes have been already identified and correlated with some of the brachycephalic dogs' ocular diseases. They are described in the table below.

| Gene | Disease | Breeds |
|---|---|---|
| BEST1 (VMD2) | Canine multifocal retinopathy type 1 | American Bulldog<br>Bullmastiff<br>English Bulldog<br>French Bulldog |
| CTSD | Neuronal ceroid lipofuscinosis | American Bulldog |
| FAM83H | Curly Coat Dry Eye | CKCS |
| HSF4-1 | Hereditary Cataract | Boston Terrier<br>French Bulldog |
| PRCD | Progressive Rod Cone Degeneration | Bolonka Zwetna |
| rhodopsin | Dominant Progressive Retinal Atrophy | Bullmastiff |

Table 1 - Known genes mutations in brachycephalic breeds (Adapted from Chadieu & Guandalini, 2013).

This means that genetic testing is a possibility to identify these genes and avoid the affected dogs from breeding, preventing their transmission to the following generations.

## 1.2 Clinical findings

A sign of ocular problems that can be detected by the owners is ocular discharge. It varies from a simple tear overflow, epiphora, to an intense mucopurulent discharge. An epiphora-induced staining is commonly noticed, and it is responsible sometimes for a dermatitis ventrally to the eye (Plummer, 2015). It usually locates at the medial canthus and develops secondary to alterations of the nasolacrimal duct system or to an excessive production of tears, for example lacrimation because of ocular pain (Grahn et al., 2014). An excessive lacrimation can be detected by the clinician, when performing a Schirmer tear test and its causes are hair-related, involving an irritation of the ocular surface. Some of these examples are trichiasis, caruncular trichiasis, distichiasis, ectopic cilia, entropion and excessive nasal fold (Peterson-Jones & Stanley, 2009). The nasolacrimal duct may present congenital lesions, acquired blockage or occlusion of the nasolacrimal system, not permitting an accurate flow of the tear-film. In some brachycephalic dogs, the lower medial canthal entropion can displace and obstruct the lacrimal punctum inward, by rolling the medial eyelid margin to the cornea. (Hartley, 2013). Ocular discharge, whether purulent or not, and conjunctivitis, may also develop after a nasolacrimal sac inflammation, dacryocystitis.

The clinical findings may be divided into two sections: diseases related to conformation, or breed-related conditions, and known or suspected inherited disease problems, whether with a congenital or juvenile/adult onset. Most of the inherited ocular diseases are not congenital, with the first clinical findings appearing in young to middle-aged dogs, after they become sexually mature. This fact may have as a result an undesired transmission of the abnormal trait to their offspring (Davidson, 2009).

Diseases related to conformation include exposure keratopathy, keratitis pigmentosa, corneal erosion and ulceration.

The cornea is physiologically transparent, so that it transmits light freely. The loss of transparency of the cornea is the first sign of a corneal disease and influences the dogs' vision capability. Superficial pigmentary keratitis is especially present in exophthalmic breeds and consists of a corneal response to a chronic and repeated irritation. This irritation may be caused by all the abnormalities above described, alterations of the tear film quality or quantity, by leaving parts of the cornea uncovered and lagophtalmos, for the same reason (Townsend et al., 2009). In brachycephalic dogs, it is usually a pigmentary or epithelial dystrophy. Superficial corneal pigmentation is a result of the migration of melanin deposition from the corneal epithelium or corneal stroma to the superficial cornea, after the irritation or chronic inflammation. The melanotic cells originate from the limbal conjunctiva and its deposition is made via neovascularization, although it can also be deposited by fibroblasts and macrophages (Ledbetter & Gilger, 2013). A study by Labelle, Dresseer, Hamor, Allender and Disney (2013) reported a very high incidence of corneal pigmentation in Chinese Pugs.

There are some conditions that make the brachycephalic dogs' cornea more susceptible to suffer injuries, whether acute, like ocular trauma, or chronic. Some of them have already been approached, such as the anatomical features that make the ocular globe more exposed, but also cilia and tear film abnormalities (Townsend et al., 2009).

An exposure keratopathy can happen when such features are responsible for corneal damage. The severity of the damage varies and can go from discrete punctate erosions to gross ulceration, with a possibility for infection and perforation. Other important fact to be considered is the variation of corneal sensitivity, that is not the same in different areas of the cornea and in different dog's skull types. Brachycephalic conformation has been associated with reduced number of corneal nerve endings, when comparing with other skull types (Barret, Scagliotti, Merideth, Jackson & Alarcon, 1991).

The known or suspected inherited ocular problems play a big role in this syndrome by itself, although they can predispose dogs to develop some other breed-related diseases, as seen ahead. They are trichiasis, caruncular trichiasis, distichiasis, ectopic cilia, entropion, excessive nasal fold, decreased corneal sensitivity, corneal dystrophies, prolapse of the nictitating membrane, keratoconjunctivitis sicca, hereditary cataracts and progressive retinal atrophy.

Trichiasis is a condition in which normally positioned but abnormally directed hairs irritate the ocular globe, conjunctiva, or both. It can lead to corneal damage when in direct contact with this structure, and the chronic corneal irritation causes not only extra lacrimation, but also pain, blepharospasm and mucopurulent conjunctival discharge. Its location is commonly in the nasal folds, the upper eyelid, or a combination with entropion in the same area (Stades & Woerdt, 2013).

Caruncular hairs arise from the caruncle at the medial canthus and are usually short, soft and point outwards. When growing excessively, they irritate the ocular globe and lead possibly to medial pigmentary keratitis or ulcers (Renwick & Petersen-Jones, 2009). This happens specially in some breeds, such as Pekingese, Shih Tzu and Lhasa Apso. In extreme cases, these hairs can grow up to 10-15 mm (Stades et al., 2013).

The presence of single or multiple hairs arising from the free lid margin is known as distichiasis. In these cases there is one, two or more hairs that arise from the meibomian duct openings. Unless they have a thick appeareance, the majority of dogs with this problem don't show many signs of irritation. If so, corneal damage and accompanying pain can be detected (Renwick et al., 2009). Altough this condition is considered to have an inherited origin, the mode of transmission is not known until today. Some of the brachycephalic breeds with a particular predisposition are Cavalier King Charles Spaniels, Boxer, English Bulldog, Shih Tzu and Pekingese (Stades et al., 2013).

Ectopic cilia arise also from follicles adjacent or within the meibomian glands, are usually located centrally in the upper eyelid and single in number. The differences between it and distichia is that ectopic cilia emerge trough the palpebral conjunctiva several milimiters from

the eyelid margin and that this situation is less frequent. In fact, many dogs suffer from both problems at the same time, what may lead the veterinary surgeon to presume that the distichia are responsible for the clinical manifestations. However, the degree of discomfort and corneal change for distichia is smaller when comparing to ectopic cilia (Petersen-Jones, 2002a).

Entropion is defined by Stades et al. (2013, p.843) as "the inversion of all or part of the margin of the eyelid such that the outer skin contacts the conjunctival or corneal surface, or both". The degree of entropion depends on how many degrees the eyelid margin is tilted. If the margin is turned inward by about 45 degrees, it is mild. If about 90 degrees, it is considered moderate. In the most extreme case, when the margin is tilted by about 180 degrees, it is a severe entropion. This condition may affect any lid and it's classified in terms of its location as lateral, angular, medial or total. In the brachycephalic dogs, a medial canthal entropion is the most seen one (McNabb, 2017). Multiple factors have the capability of influencing an entropion. Some of these are conformation of the skull, orbital anatomy, length of the lid fissure, gender, and the extensiveness of facial skin folds around the ocular area. Most of the cases are due to a hereditary defect, although its genetic basis is not well known. Secondary clinical findings to the chronic irritation caused by the inverted position of the lid, other than epiphora, can occur, like blepharospasm, mucopurulent discharge and conjunctival hyperaemia. When affecting the corneal site, oedema, neovascularization, granulation, pigmentation, and even ulceration can develop. From the trigeminal irritation and the patient's pain, results a lacrimal overproduction, enophthalmos, loss of support of the eyelid margin and consequently, a worsening of the entropion (Stades & Woerdt, 2014).

Figure 2 - 2-year-old Rottweiller with a lateral canthal entropion (Photograph kindly given by Prof. Esmeralda Delgado).

Another important conformational characteristic frequently seen in the more extreme brachycephalic breeds is a nasal fold, that is not proportioned to the facial skeleton, and

consequently forced into wrinkles. Nasal fold trichiasis happens when the medial canthal hairs of the nasal fold rub against the cornea (Packer et al., 2015a). As a result, a chronic low-grade superficial keratitis or ulcers may develop (Townsend et al., 2009).

Corneal sensitivity was shown to be lowest centrally and greatest peripherally (Crispin, 2002a). The ophthalmic branch of the trigeminal nerve is responsible for the corneal sensory innervation. The nerves located at the corneal periphery are myelinated, and the myelin disapears as they enter into the central area, which can explain that difference in sensitivity. When it comes to the skull types, it is greatest in dolicocephalic dogs, and lowest in the brachycephalic ones (Barret et al, 1991). Therefore, they are more likely to suffer damages, like corneal ulcers. In fact, a study made by Nationwide (2017) showed that it is three to four times more likely for brachycephalic dogs to injure their corneas, than the other dogs.

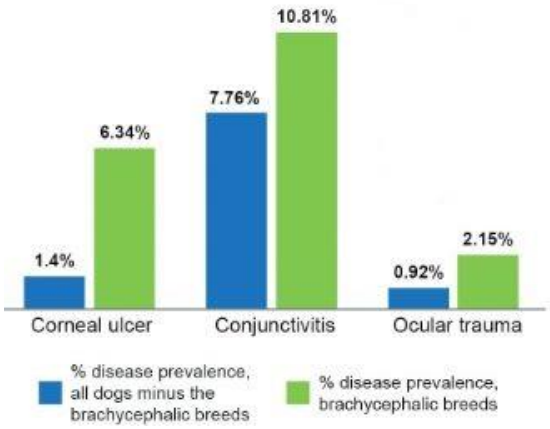


Chart 1 - Prevalence of eye disorders in brachycephalic and non brachycephalic breeds in UK. Notice the difference between them regarding corneal ulcers (Adapted from Nationwide, 2017).

As seen above, conjunctivitis has also an increased risk on these breeds. Once more, the anatomical differences play its role as well as some alterations with the potential of causing chronic irritation of the conjunctiva, such as entropion, ectopic cilia, trichiasis and distichiasis (Heirich, 2015).

Corneal dystrophies are primary and bilateral inherited conditions of the cornea that are not related with corneal inflammation or systemic diseases. The presentation is mostly grey, white or silver opacities in the central or paracentral cornea, and the corneal epithelium, stroma or endothelium might be involved (Ledbetter & Gilger, 2013). They are inherited in some breeds and, depending on its cause, are divided into Corneal Lipid Dystrophy, Corneal Epithelial Dystrophy and Corneal Endothelial Dystrophy. The first one refers to an accumulation of cholesterol and triglyceride deposits in the superficial corneal stroma, affecting the vision, and the more predisposed breed is the Cavalier King Charles Spaniel. The second one has its origin in a recurrent corneal erosion, because of a a defect within the epithelial columnar cells and their basement membrane in the cornea. It is normally a bilateral condition, in the Boxer

and from 6 or 7 years of age onwards. The third one is a bilateral condition, more common in the Boston Terrier, due to a degeneration of the corneal endothelium and the clinical sign is a persistent corneal oedema (Bedford, 2010).

Prolapse of the gland of the nictitating membrane, or “cherry eye”, can also be commonly encountered in short-muzzled dogs. According to Hendrix (2013), it is an inherited developmental disorder. The glandular prolapse happens as a result of a defective connective tissue development and glandular laxity in predisposed breeds, such as English Bulldog and Shih Tzu. A study showed that this alteration is more usual in dogs younger than one year old, and unilaterally (Mazzucchelli, Vaillant, Wéverberg, Arnold-Tavernier, Honegger, Payen & Chahory, 2012). Whether the prolapse is parcial or total, the presentation is a protrusion of a smooth and pink to red tissue from the posterior surface of one or both third eyelids. Some consequent symptoms are conjunctivitis, a decrease in lacrimal function, ocular discharge, and possibly secondary ulcerative keratitis, inflammation or bacterial infection, if not treated in a short amount of time (Esson, 2015).

The tear film irregularity that is usually diagnosed in such cases, is a tear film deficiency. Keratoconjunctivitis sicca, or Dry Eye Syndrome, can develop because of that deficiency, or excessive tear evaporation. There is a predisposition for some breeds, including Cavalier King Charles, English Bulldog, Pug, Shih Tzu and Lhasa Apso (McNabb, 2017). In any of these cases, a green to yellow discharge with a thick consistency is common (Crispin, 2002b). However, many of the clinical signs of KCS can vary according to gravity and to the onset of the illness. On the one hand, a lacklustre appearance of the cornea, superficial keratitis and conjunctivitis, blepharospasm, corneal ulceration and pain are quite common in an acute KCS. On the other hand, corneal vascularization and pigmentation and xerosis, keratinization of the ocular surface as a result of extreme dryness, are present in a chronic KCS. Severe pain is not frequently present in the chronic onset of the disorder, as the corneal nerves may be damaged and insensitive (Petersen-Jones et al., 2009). When not rapidly treated, secondary periocular dermatitis and secondary bacterial conjunctivitis are possible (Giuliano, 2013).

Hereditary cataracts are a quite common disease among breeds like Boston Terrier and Cavalier King Charles Spaniel. Some other brachycephalic breeds may also be involved, but in a smaller degree, like the French Bulldog, Pekingese, Pug, Lhasa Apso and Shih Tzu (Bedford, 2010). The inherited cataracts can be classified as congenital or juvenile, between 2 and 5 years old. The presentation of Boston Terriers, Cavalier King Charles Spaniels and English Bulldogs is mostly congenital, and the form of transmission is autosomal recessive in the first two breeds, meaning that the parents of a certain dog do not develop cataract as puppies, they are only carriers (Gelatt & Mackay, 2005). It is always a bilateral condition, and the progression is quite fast. However, 90% of the early onset cataracts are detectable in 8 to 12 weeks old puppies, which translates the importance of an early screening of the disease (Mellersh, Graves, Mclaughlin, Ennis, Pettitt, Vaudin & Barnett, 2007).

Progressive Retinal Atrophy is also, according to Bedford (2010), a possibility in small brachycephalic breeds. It is a bilateral degeneration of the neurosensory retina that happens when the rod photoreceptors fail to develop normally or degenerate prematurely. There is a gradual loss of vision and the ultimate result is invariably total blindness (Mclellan, 2002). Until today, there are more than 100 breeds reported with cases of this type of retinal degeneration, including Boston Terrier, Cavalier King Charles Spaniel, Maltese and Shih-Tzu (Comittee, 2015). Most of them are cases of autosomal recessive mutations, in contrast to English Bulldog and Bullmastiff, that are associated with autosomal dominants ones. This means that the transmission of PRA is much easier and likely to happen in the two previous indicated breeds (Narfstram & Petersen-Jones, 2013).

### 1.3 Diagnosis

The essence of ophthalmology is, as well as the other departments of veterinary medicine, diagnosis, which depends on a careful clinical observation and interpretation. At ophthalmological appointments, a diagnosis is often complete at the time of examination, knowing that the most obvious clinical sign may not be primary, but secondary.

No matter what the dog's complaint is, the veterinary surgeon should always perform some basic ophthalmological tests and exams, and then proceed to the more specific ones.

After collecting the animal's history, a distance examination is made to assess the ocular globe's position, size and movement, and to observe whether discharge, asymmetries, PMN or fold abnormalities are present. Then, a visual test with a cotton ball should be made to assess the dog's visual capacity as well as a neuro-ophthalmologic testing. Some of the tests and exams included in a neuro-ophthalmologic assessment are dazzle reflex, menace response, pupillary light reflex, corneal reflex, palpebral reflex and vestibulo-ocular reflex (Featherstone & Heinrich, 2014). Some of them may be altered physiologically in brachycephalic dogs, misleading the veterinarian clinician into a wrong diagnosis.

The palpebral reflex is tested by lightly touching the medial and lateral canthi, resulting in eyelid closure. If some brachycephalic typical alterations can be found, like exophthalmos and lagophtalmos, the reflex may be interpreted as a false-negative result (Featherstone & Heinrich, 2013). When proceeding to the corneal reflex, it should be present that many of the breeds presented in this study are associated with the already discussed decrease in the corneal sensation and the dog's response may be toned down (Crispin, 2002b).

At this point in the examination, or even before part of the neuro-ophthalmological assessment, tear production should be measured by using the Schirmer Tear Test (STT). This avoids having a momentarily tear production increase because of over manipulation of the eyelids or eye and before the administration of topical agents (Featherstone & Heinrich, 2013). The purpose to this strip-test is to quantify the aqueous component of the tear film, and it can be performed in

all patients with external ocular disorders. However, it has no clinical relevance if it is performed when the dog has a visible deep ulcer or if this structure was penetrated. In such cases, it is more reliable to measure the tear production once the cornea has healed. The STT measures the basal and reflex tearing, as it is performed in an unanaesthetised eye (Crispin, 2002). A normal tear production would have a result between 15 mm/min and 25 mm/min. If the value is lower than 10 mm/min, there is an indication of a deficit in aqueous tear production, or dry eye. The most part of clinical cases with KCS are associated with values smaller than 5 mm/min (Featherstone & Heinrich, 2013). The values between 10 and 15 are considered by some authors, including Crispin (2002) to be borderline, being possible at this point to have already visible manifestations of dry eye.

Next comes a more minacious observation of the ocular surface in a darkened room and using a slit-lamp biomicroscope. Here, several ocular structures can be appreciated with high magnification, such as adnexa, cornea, anterior chamber, lens, iris and pupil. This is the moment when many of the breed-related disorders can be identified, like the cilia-related ones. Some of the corneal alterations can also be seen, thus the fluorescein test represents the gold-standard test for it.

Full fundic evaluation is usually not necessary on a daily basis. The more relevant alteration that can be found on the fundoscopy, is a mottled pigmentation of the non-tapetal fundus, that can be found in cases of PRA (Narfstram & Ekesten, 1999).

The Intra-Ocular Pressure (IOP) is then quantitatively evaluated throughout tonometry, which is a great tool to diagnose cases of uveitis, a disease that may happen secondarily to the OBS. The IOP can physiologically be increased if the animal is not quiet or firmly restrained during measurement and be decreased in older animals (Mould, 2002).

Topical sodium fluorescein is a water-soluble weak dibasic acid constantly used in ophthalmological appointments, especially in animals with the OBS, and it is used with two purposes. The first purpose is to identify corneal ulceration, conjunctival epithelial defects, aqueous humor leakage (Seidel test), and qualitative tear film alterations. Being the corneal ulceration very likely to happen in brachycephalic breeds, this is a very important test. When an animal suffers from corneal ulceration, the cornea gets a stain of fluorescein at the injured site. That event happens because of this substance's properties. Fluorescein is highly hydrophilic and lipophilic, and that makes it adhere and be absorbed by any exposed stroma. However, it does not work in the Descemet's membrane. The second purpose is to test the whole mechanism of tear drainage, allowing the veterinary surgeon to determine not only the anatomic, but also the physiologic patency of the nasolacrimal system. This is called the Jones test and is usually, however, not very clinically advantageous in these types of dogs, as many reasons can be found for a false-negative result (Featherstone et al., 2014). That can be explained by a study that discovered that approximately 40% of dogs have an additional communication between the duct and the ventral nasal meatus at the level of the canine tooth

root (Michel, 1995). Moreover, many authors claim that brachycephalic breeds have abnormal tear drainage into the caudal nasal cavity and then into the nasopharynx (Grahn & Sandmeyer, 2014; Ollivier, 2007; Kern, 1986). It is possible, but not easy, to see fluorescein dye in the oropharynx or on the tongue (Binder & Herring, 2010).

Methods like ultrasound and electroretinography are key when diagnosing and characterizing cataracts. The ERG allows the assessment of retinal activity and the ultrasound is relevant to search for secondary lens luxation and retinal displacement (Cook et al., 2009).

The ERG may have also abnormal records in dogs that suffer from PRA, as the waves that correspond to the flicker response have usually a lower amplitude or may even be inexistent (Aguirre, 1978).

Nowadays there are DNA-based tests available that allow to genotype an animal for a specific hereditary disease before the onset of the clinical signs. They are accurate, specific for the DNA variation that they are being tested for and detect carriers of recessive conditions. Although they are not routinely made, they can be a valuable tool in preventing the appearing of more dogs affected with the hereditary disease and to eradicate the mutant allele from the population.

Eye examinations are therefore very important to preserve the patient's ocular health. The ECVO committee recommends an ophthalmic examination once a year for the breeding dogs, starting before the reproduction period, and three times in a life-time for the remaining dogs, starting at the age of 1 year old (Chadieu & Guandalini, 2013).

## 1.4 Treatment

### 1.4.1 Medical treatment

After the cause of the ulcer is identified and removed, the extension and severity of the lesion should be determined, and the right treatment applied. Uncomplicated superficial ulcers may resolve with topical antibiotic three to four times a day to avoid secondary bacterial infection. Some of the options are oxytetracycline, erythromycin and other ophthalmic preparations. A mydriatic agent, like 1% atropine or tropicamide is advised once or twice daily to control the ciliar muscle spasm and to decrease the discomfort related with secondary uveitis. This problem should resolve within 2 to 6 days. If not, the case should be re-evaluated for a hidden cause or contributing factor. Surgical treatment should be considered if the ulcer does not respond to medical therapy in 2 weeks (Ledbetter et al., 2013).

The great majority of patients with KCS can be successfully managed medically, with surgery being only indicated in cases that are refractory to medical therapy. The drugs that take part of the KCS's treatment are lacrimostimulants, lacrimomimetics, mucinolytics, antibiotics and anti-inflammatories. The lacrimostimulants consist in drugs that improve tear secretion and include cholinergic drugs, like pilocarpine, and immunomodulatign agents, such as tacrolimus and Cyclosporine A (CsA). Having the most of KCS cases an immune-mediated cause, the

CsA has been the primary treatment for KCS in decades. The tear replacement therapy is very important and should be adapted to each animal's requirements, being a desirable frequency of administration on the affected eye every 2 to 6 hours (Lewin, 2014). Many ophthalmic solutions are available nowadays with different compositions and concentrations, but with the same goal. However, it is important not to use these drugs as a replacement treatment, but as a supplemental one (Grahn et al., 2014). A broad-spectrum topical antibiotic is useful in cases where a secondary bacterial infection is present, 2 to 4 times a day. The concomitant administration of a corticosteroid must be avoided in KCS due to the potential risk of corneal ulceration (Lewin, 2014). The mucinolytic-anticollagenase agents are advantageous in removing mucoid debris and copious exudates that might be present. The most common one is a 5-10% solution of acetylcysteine 2 to 4 times a day. The anticollagenase properties of this drug may also aid in the prevention of enzymatic degradation of surface ocular tissues. The anti-inflammatory drugs may help improving the clinical signs of KCS, including conjunctivitis, alleviate discomfort and reduce some corneal opacities. In addition to other effects, CsA reduces the corneal inflammatory infiltrates and is safe to use when any corneal ulcer is present (Grahn et al., 2014). If the medical approach isn't successful, surgical interventions should be considered, although they are quite limited.

The treatment of pigmentary keratitis is essentially through the delay of the progression of the pigmentation and the correction of the initiating cause. The initiating cause needs frequently a surgical approach. Removal of abnormal lashes and excess of nasal fold, medial canthoplasty and correction of entropion are examples of procedures that may prevent disease progression (Yi, Park & Jeong, 2006). The use of beta radiation by strontium-90β plesiotherapy or cryotherapy has been suggested, but with an unknown success rate (Gilger et al., 2007). Topical CsA, tear-substituting eye drops and corticosteroids are commonly prescribed in these cases (Townsend et al., 2009). These drugs have got an unknown clinical efficacy, although some studies have demonstrated effectiveness in treatment of chronic superficial keratitis and its associated corneal pigmentation (Nell, Walde, & Billich, 2005; Williams, Hoey & Smitherman, 1995). A study in humans demonstrated aswell the capacity of CsA to inhibit cell proliferation and melanogenisis in cultured human melanocytes (Lee & Kang, 2003).
Unfortunately, there is so far any treatment proven to be effective to alter the progression of PRA, or reverse some of its ocular changes. However, an antioxidant supplementation may have beneficial effects on retinal cell health, preserving the remaining cone function, and slow the progression of the disease. A study by Wang, Hernandez, Moore, Jackson & Narfström (2016) showed a positive correlation between antioxidant suplementation, specially vitamin C and E, and the improvement of visual function in healthy dogs. Similar studies in humans with retinal diseases have shown positive outcomes, but further research is required to evaluate this possibility in dogs with PRA.

### 1.4.2 Surgical treatment

A severe lagophtalmos and consequent ocular disease can be solved by using a surgical procedure known as medial canthoplasty. The goals are the reduction of palpebral fissure, upper and lower eyelids' length, eversion of the medial inferior entropion, functional relief of the nasolacrimal system's obstruction and removal of the hairy medial caruncle. Moreover, by increasing the ocular globe's coverage, the blink mechanism may be improved, the tear better distributed across the ocular surface, and the risk of proptosis is reduced (Bedford, 2010). The technique creates a permanent union of both eyelids, which reduces the area of the ocular surface exposed to the environment and the frictional irritation that may lead to keratitis and the subsequent pigmentation (Gellat & Whitley, 2011). In giant breeds, this technique has a variation as a result of a weak lateral canthus. A different surgical correction, lateral canthoplasty, is used to stabilize the lateral canthus and to diminish the eye's exposure (Sahr, Clasen & Steinmetz, 2013).

The lid situation with giant breeds is fundamentally different from the brachycephalic dogs and requires one other surgical approach. The main starting point for the surgical intervention is not the medial canthus, like the short-headed breeds, but the lateral canthus. The lateral canthus is often weak and moved to a more ventral position. The surgical approaches are many and have therefore besides a lid-shortening goal, a stabilization one.

When the medial canthoplasty is not able to correct the entropion by itself, a Hotz-Celsus technique can be applied. The goal here is to excise skin in a way that allows the eversion of the entropic area of the eyelid margin. It is important to estimate prior to the surgery how many soft tissues should be removed in a way that not only solves the problem but also avoids the formation of an iatrogenic ectropion.

The definitive treatments for trichiasis, distichiasis, ectopic cilia and caruncle hair are through electroepilation and cryoepilation, two non-invasive techniques. These are quite effective in maintaining the eyelid function, as they do not interfere with the eyelid margin and normally do not cause scarring (Westermeyer & Hendrix, 2012).

The excess of nasal fold can easily be solved by a resection of that excessive area, the permanent method to prevent trichiasis. Special attention should be given during the pre-surgical evaluation to ensure that equal portions of both nasal folds are excised to maintain facial symmetry (Gellat et al., 2011).

The surgical approach to a prolapse of the nictitans membrane includes a reposition of the prolapsed tissue. The excision of this area should be avoided as much as possible, as the function of the gland is important for a normal tear production. The most appropriate technique is the Morgan pocket technique. The surgeon should be careful not to leave knots on the bulbar surface of the third eyelid (Andrew, 2014).

Some corneal lesions including indolent ulcers and corneal dystrophies, if accompanied by a high visual deficit, can be treated by a surgical procedure called superficial keratectomy. The surgeon should previously determine the depth of the lesion, as a conjunctival pedicle flap or amniotic membrane graft is needed when the lesion is deeper than one half of the corneal thickness, in order to protect the cornea, help prevent perforation and help healing. This technique consists in an epithelial debridement of the lesion site with the help of multiple dry cotton-tipped applicators, corneal diamond burrs, excimer laser spatulas and scalpel blades (Ledbetter et al., 2013).

According to Giuliano (2013), dogs with KCS may benefit from a partial permanent tarsorrhaphy, and medial or lateral canthoplasty, to conceive a greater corneal protection and maximize the conservation of existing tears. Only the animals with persistent absolute KCS after several weeks of the medical treatment have indication for a parotid duct transposition (Rhodes, Heinrich, Featherstone, Braus, Manning, Cripps & Renwick, 2011). Its logic relies on the physiologic similarity between saliva and tear film, including osmolarity and pH. The parotid duct is transposed in a way that the papilla is sutured in the ventral conjunctival fornix and allows a better lubrification of the eye, through the use of saliva instead of the missing tears (Gelatt et al., 2013).

Surgical removal of pigmentary keratitis is possible if the inciting cause has been corrected. However, a recurrence of the pigment often happens as well as corneal scarring, limiting the success of the procedure (Gilger et al., 2007).

The only current treatment for cataracts is the surgical removal. The techniques have evolved throughout the years and they are each time less invasive. Many authors consider the phacoemulsification the gold-standard procedure to resolve cataracts (Petersen-Jones, 2002b).

# III. PROSPECTIVE STUDY

## 1 Objectives

This study aims to study the incidence of ocular alterations related to the brachycephalic conformation.

It also aims to highlight the different predisposition of certain brachycephalic breeds to certain ocular abnormalities.

It also intends to evaluate the importance of a regular ophthalmological check-up, so that an early diagnosis of the primary disorders can be achieved, avoiding the development of secondary alterations and allowing the institution of an adequate treatment.

## 2 Material and Methods

Dogs with ophthalmological complaints, presented to the Leipzig's University Animal Hospital, Germany, from January 2018 to May 2018, were examined by the veterinarians that belong to the Ophthalmology department. A detailed examination of the selected 47 dogs of different ages, sexes and breeds was performed.

The studied parameters included the dogs' iatrotopic stimulus, age, breed, ocular abnormalities, ophthalmological complementary exams, surgeries and their outcomes, whether they were new or follow-up cases or had concomitant BOAS.

About 83% of the above described animals were examined for the first time, and the remaining ones were previously diagnosed and went to follow-up appointments.

The ophthalmological exams performed were different and adapted to each case, but a complete and basic ophthalmological examination was performed each time. Neuro-ophthalmological evaluation consisted of the cotton ball test, dazzle test, menace response, and palpebral, corneal and pupillary light reflexes. Depending on the complaints, a complete ophthalmological examination including Schirmer tear test, tonometry, biomicroscopy and fundoscopy were performed. Whenever necessary, complementary exams such as electroretinography, ocular ultrassound, fluorescein test, Jones test and measurement of the arterial blood pressure were performed.

The animals that filled the inclusion criteria, belonging to a brachycephalic breed, were included in the study and originated data that was organized in a database using Microsoft Office Excel 2007® and its statistical analysis was performed using descriptive statistics with the software IBM SPSS Statistics 20®.

# 3 Results

## 3.1. Studied population

The population consists in 24 males, 4 of them neutered, and 23 females, 8 of them spayed. The breeds included could be classified as brachycephalic in terms of skull shape and they were Boston Terrier (n=2), Boxer (n=1), Bullmastiff (n=2), English Bulldog (n=3), French Bulldog (n=21), Pug (n=16), Shar-Pei (n=1) and Shih-Tzu (n=1). Their mean age was 5,0 ± 3,1 years.

Out of the 47 animals included in the study, 1 Boston Terrier, 4 French Bulldogs, 2 Pugs and the Shih-Tzu were already being followed in the Ophthalmology Department and went to control appointments. The rest of the animals, 83%, went to a first appointment throughout the study time.

About 30% of the dogs went to Otorhinolaryngologic appointments and were then transferred by the corresponding veterinarian to the Ophthalmology Department, and the remaining 70% went to an ophthalmological appointment by their tutors' initiative. These 30%, represented only by French Bulldogs and Pugs, were diagnosed with Brachycephalic Obstructive Airway Syndrome. Some of the ocular surgeries were performed in the same surgery time as the BOAS correction.

## 3.2. Iatrotopic stimulus

The main complaints that made these 70% dogs' tutors to take them to the Leipzig's Animal Hospital were blepharospasm, epiphora, conjunctivitis and ocular discharge, whether thick or purulent. Less common clinical signs were also considered. Therefore, each dog presented at least one of these signs and its graphical distribution can be visualized below.

Ocular discharge was present in more than half of the studied sub-population, 22 out of 34 dogs, being the most common clinical iatrotopic stimulus. It was reported as the only stimulus in 10 of them and as in combination with other stimuluses in the remaining 12 dogs.

The "red eye", or conjunctivitis, was also a quite common sign referred by the pets' tutors and affected 12 out of 34 animals, about a third of them. Out of these, only 1 had it as the only iatrotopic stimulus.

Epiphora and blepharospasm were reported, respectively, 3 and 2 times as being the main cause of the ophthalmological appointment. When considering the combination with other clinical signs, they were reported in 7 and 11 dogs out of the 34 considered for this studied parameter.

The least common clinical signs were trauma, palpebral mass and reduced visual acuity.

However, most of the tutors mentioned a combination of more than two of these signs when collecting the clinical history, concerning 12 animals of the considered sub-population.

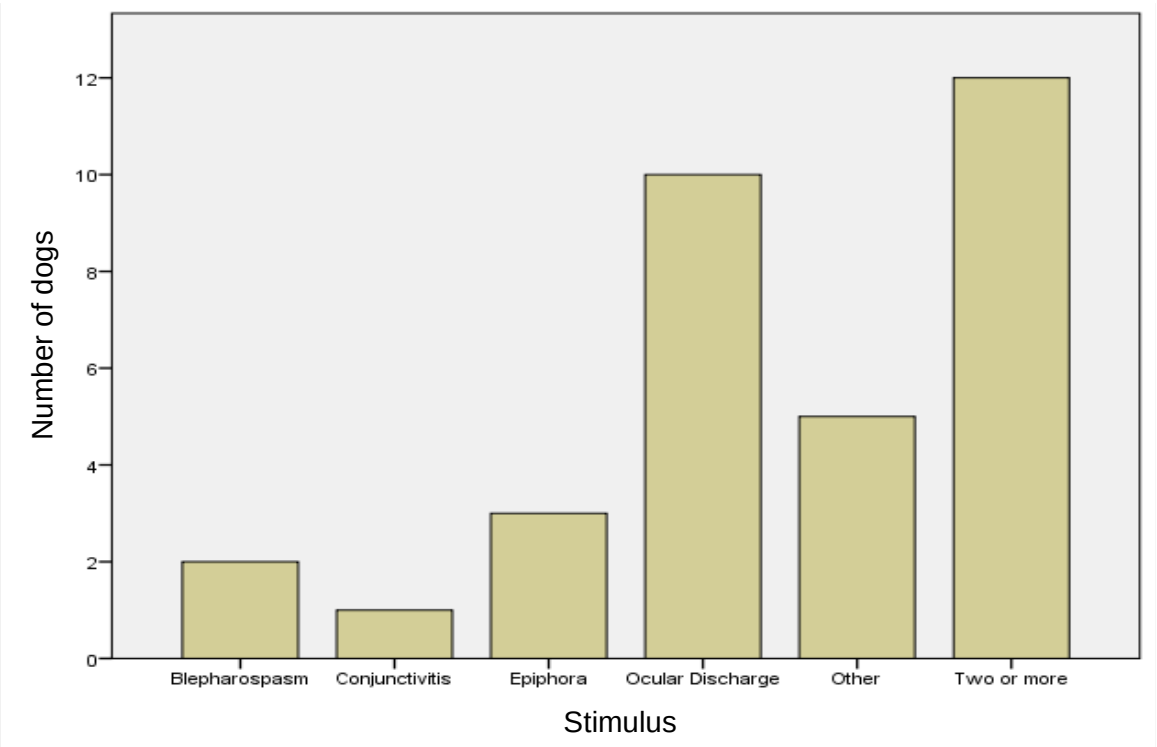


Chart 2 - Iatrotopic Stimulus

### 3.3. Clinical signs

The ocular alterations were found in different location within the ocular globe and its annexes, including eyelid, hair/cilia, conjunctiva, cornea, sclera, nictitating membrane, iris, lens, retina, anterior and vitreous chamber, and retrobulbar space.

- **Eyelids**

The eyelid defects were mostly cases of macroblepharon and tumours.

Macroblepharon was very common among almost all the population (35/47), affecting almost three quarters of the population, and there were two extreme cases in French Bulldogs. Three cases of palpebral tumours were registered (3/47), all in French Bulldogs older than the mean age of this study. One of them was diagnosed as an adenoma, but the remaining two lacked a definitive diagnose.

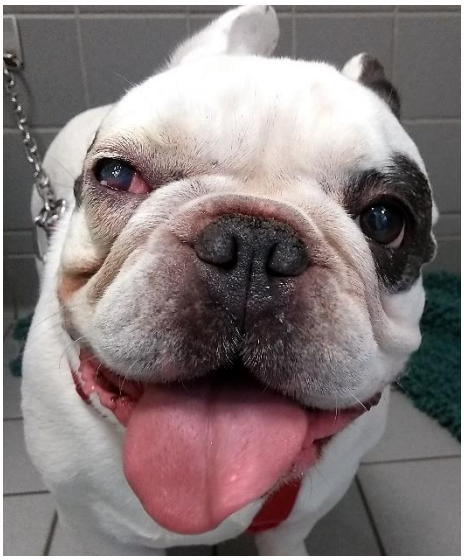

Fig. 03: A seven-year-old French Bulldog with a corneal ulcer caused by distichiasis and a mass on the inferior eyelid in the right eye (Original picture).

- **Hair/ciliar changes**

The hair/ciliar alterations were significant and included entropion, an excessive nasal fold, ectopic cilia, trichiasis and distichiasis. Among these, entropion was the most frequent problem (21/47), with an incidence of 45%. Not only that, but it affected every breed in this study, excluding the Boxer, and was especially recurrent in Pugs, which represent almost half of the affected dogs. The entropion's location was always medial and bilateral. In three cases- a Boxer, a Shar Pei and an English Bulldog- the entropion affected not only the inferior eyelid, but also the superior one.

Distichiasis was the second most important ciliar disorder (10/47), with an incidence of about 21%, affecting three Pugs, one Bullmastiff, one English Bulldog, four French Bulldogs and one Boston Terrier. A gender predisposition was not noticed.

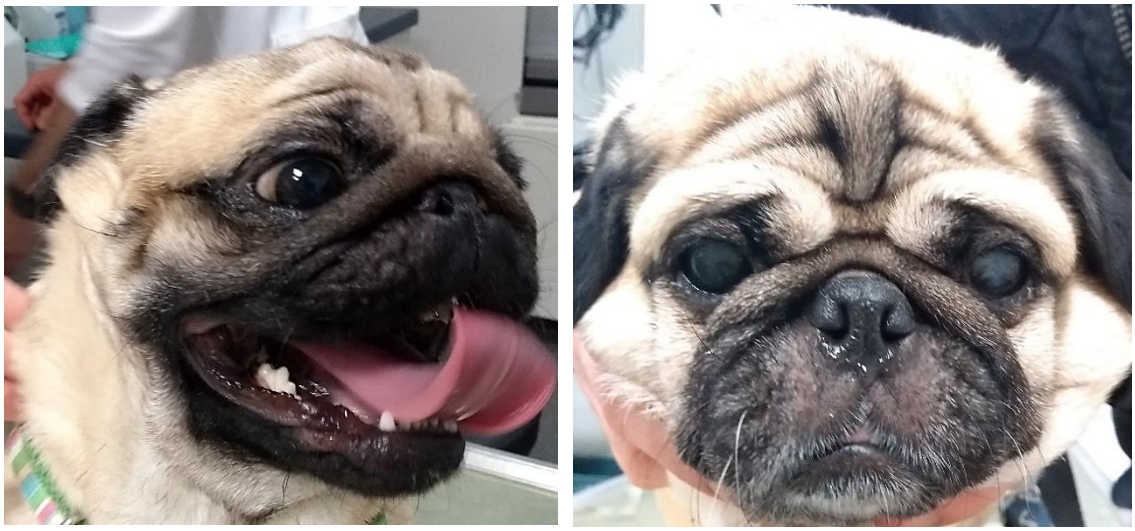

Fig. 04: One male and one female Pug showing an excessive nasal fold. Notice its proximity to the eye surface (Original picture).

Concerning trichiasis, this disorder was present bilaterally in the Shih-Tzu breed representatives and one Bullmastiff (2/47), and the caruncular type (3/47) committed two Pugs and one English Bulldog.

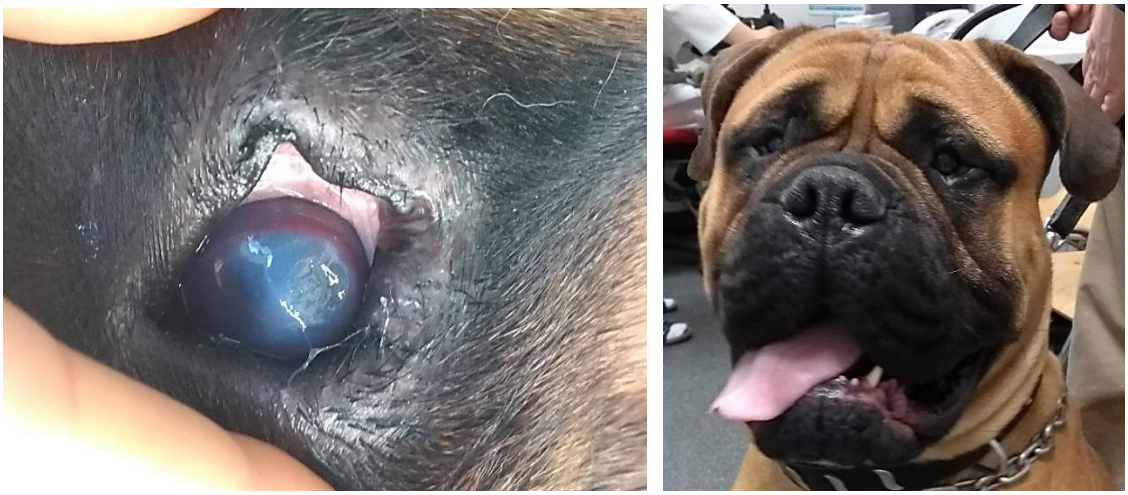

Fig. 05: A two-year-old BM with trichiasis, which lead to a corneal ulcer. Corneal oedema and neovascularization around the lesion can be seen in the first picture, and the second one shows the typical “diamond eye” appearance of the eyelid fissure (Original picture).

An excess of the nasal fold was seen in three Pugs (3/47) and ectopic cilia were only found in one eye of a Boston Terrier (1/47).

- **Cornea**

The corneal events were quite commonly present and include ulcers, erosion (3/47), oedema, degeneration, pigmentation and opacity. Corneal ulcers (19/47) affected only French Bulldogs, Bullmastiffs and Pugs, with an incidence of 57%, 100% and 31%, respectively. Three French Bulldogs were the severe cases, as one of them had ulcers bilaterally and two other cases involved a commitment of 80% of the corneal surface. The ulcers of the Bullmastiffs were only classified as unilateral and superficial. Two of the Pugs had also unilateral and deep ulcers, each one affecting about three quarters of the cornea, and one of them had also a concomitant erosion in the contralateral eye. Two other Pugs showed this condition bilaterally. In contrast, erosion had little relevance (3/47), being present only in the described Pug, in the Shar Pei dog and in one French Bulldog.

Fig. 06: A ten-year-old female French Bulldog with a corneal ulcer on the left eye, caused by a traumatic event (Original picture).

Corneal pigmentation (13/47) and opacity (11/47) could be noticed in many cases, although neither one nor the other was present in some of the breeds included in the study, like Boxer, Bullmastiff and English Bulldog. Corneal pigmentation had an incidence of 24% and was present in half of the breeds included in the study, and the great majority of the cases were related to Pugs (8/47). The remaining affected breeds were French Bulldog, Shih Tzu and Shar Pei. The percentage of affected Pugs was 38% and French Bulldogs was 14% and the gender distribution was irrelevant.

On the other hand, corneal opacity had an incidence of 21% and affected mainly French Bulldogs (9/47), but one case was registered in Pugs and Boston Terriers. Moreover, out of

these 9 cases, 8 of them are female French Bulldog and only one is a male. When looking to the French Bulldog breed as a whole, the incidence of this ocular alteration was 38%.
Corneal oedema (1/47) and degeneration (1/47) had, in opposition, a very low frequency.

- **Sclera**

The scleral alterations had little relevance, as there were only two animals with abnormalities, a case of scleral pigmentation (1/47) and another case diagnosed with episcleritis (1/47).

- **Nictitating membrane**

The prolapse of the gland of the nictitating membrane was only seen in two cases (2/47), unilaterally in one Boston Terrier and bilaterally in one French Bulldog. They were both 5 months old.

- **Iris**

The iris also revealed few problems, because there were only two registered cases of alterations in this ocular structure (2/47). The dogs were both Pugs and one had a sand type pattern in the iris, and the other one had iris's discoria.

- **Lens**

Concerning the lens, two French Bulldogs showed lens subluxation and inflammation (2/47), and the Shih-Tzu with 13 years old had nuclear sclerosis (1/47). This last animal had more abnormalities in other ocular structures, such as asteroid hyalosis in the vitreous chamber, and presence of blood inside the anterior chamber. The anterior chamber abnormalities' (2/47) included not only the presence of blood in it, but also opacity of the same structure (1/47), shown by an English Bulldog. There were also two cases of cataracts in Pugs (2/47) with the ages of 2 and 7 years old, respectively. The older Pug suffered also of lens's atrophy in the right eye.

- **Miscellaneous**

About 17% (8/47) of the population suffered from some conditions that were only seen once throughout this study. These included a retrobulbar process (1/47) leading to exophthalmos, panuveitis (1/47), pannus (1/47), asteroid hyalosis (1/47), corneal oedema (1/47), corneal fat degeneration (1/47), nuclear sclerosis (1/47) and blockage of the lacrimal duct (1/47).

### 3.4. Ophthalmological tests

Concerning STT values, seven of the animals had values below the normal range. From these, three of them had values between 10-14 mm Hg considered low and four of them were severe cases of keratconjunctivitis sicca, with STT values varying between 0-10 mmHg. This exam in particular, in addition to the remaining clinical signs, allowed the diagnosis of six animals with KCS.

Tonometry values were also valuable to help in the diagnosis of ophthalmic diseases. Five of the patients (5/47) had results outside the reference range, from which three values were below and two were above it. The first ones were 9 mmHg, 5 mmHg and 10 mmHg, values compatible with uveitis, and the high ones were 56 mmHg and 57 mmHg, values compatible with glaucoma.

### 3.5. Complementary exams

Fluorescein test was the most performed complementary exam, used in nine cases of suspected corneal ulcers (9/47).

Ocular Ultrasound and Jones test was used in the same amount of cases, three (3/47). The first exam detected two lens alterations and another change in the vitreous chamber. The second one was evaluated in a French Bulldog case and in two other Pug cases, which were all negative. Electroretinography was performed with a lower frequency in two cases, and the result was in both within the reference range.

The least required complementary exam was measurement of the arterial blood pressure (1/47). It diagnosed a severe hypertension, as the value for systolic arterial pressure was 250 mmHg.

### 3.6. Treatment

#### 3.6.1. Medical Treatment

Superficial ulcers were systematically treated with topical drugs that involved a combination of atropine SID, lubricating eye drops with 1.8-2 mg/ml of hyaluronic acid 3-6x/day and gentamicin 5x/day, with the concomitant use of an Elizabethan collar. Regarding dogs with deep and severe ulcers, they were medicated with a topical antibiotic, such as ofloxacin 5x/day, atropine BID, lubricating eye drops with 1 mg/ml of hyaluronic acid 3x/day and a systemic antibiotic, such as cephalexin for 10 days, and then received a surgical resolution that involved a placement of a conjunctival flap. If a surgical treatment was not intended, a conservative medical approach was considered and included the same drugs as in the superficial ones, but

with a higher frequency of administration, and a placement of a contact lens in the injured eye until cure was achieved.

### 3.6.2. Surgery

When it comes to surgery, more than half of the study population had indication to do some type of ocular surgery. The surgical procedure most frequently recommended was medial canthoplasty, with thirteen indications to do so (13/47). However, surgery was only performed in seven of the referred cases.

When considering only the surgical indication, it was only advised in two breeds, French Bulldogs and Pugs. The first breed presented three cases with indications for this surgical procedure, and the second one showed ten of the same.

On the other hand, lateral canthoplasty was the least seen procedure, having just one case in one Bullmastiff. Electroepilation was the second most performed surgical treatment, being advised five times, in one Bullmastiff, one Boston Terrier, two French Bulldogs and only one Pug.

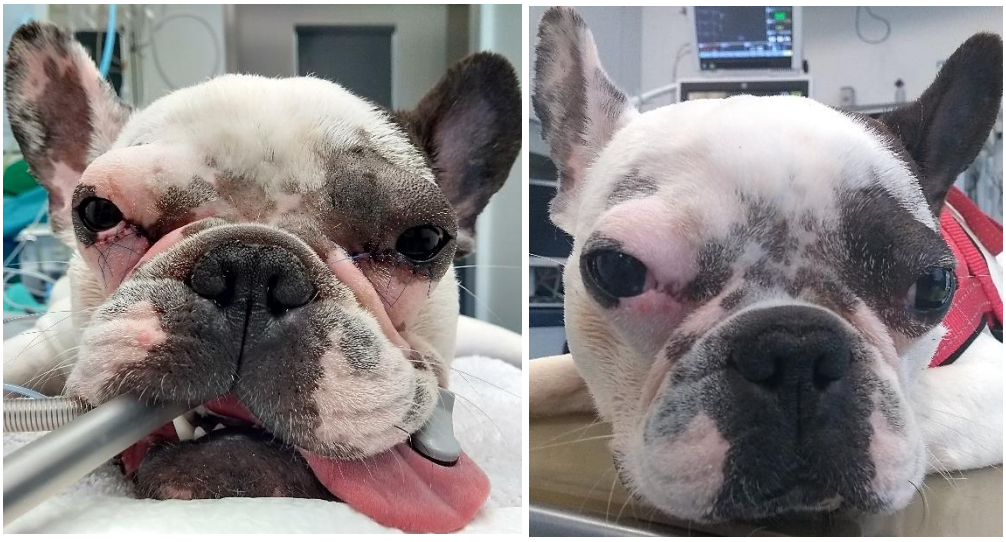

Fig. 07: A one-year-old male French Bulldog after MCP technique and fifteen days later after stitches' removal (Original picture).

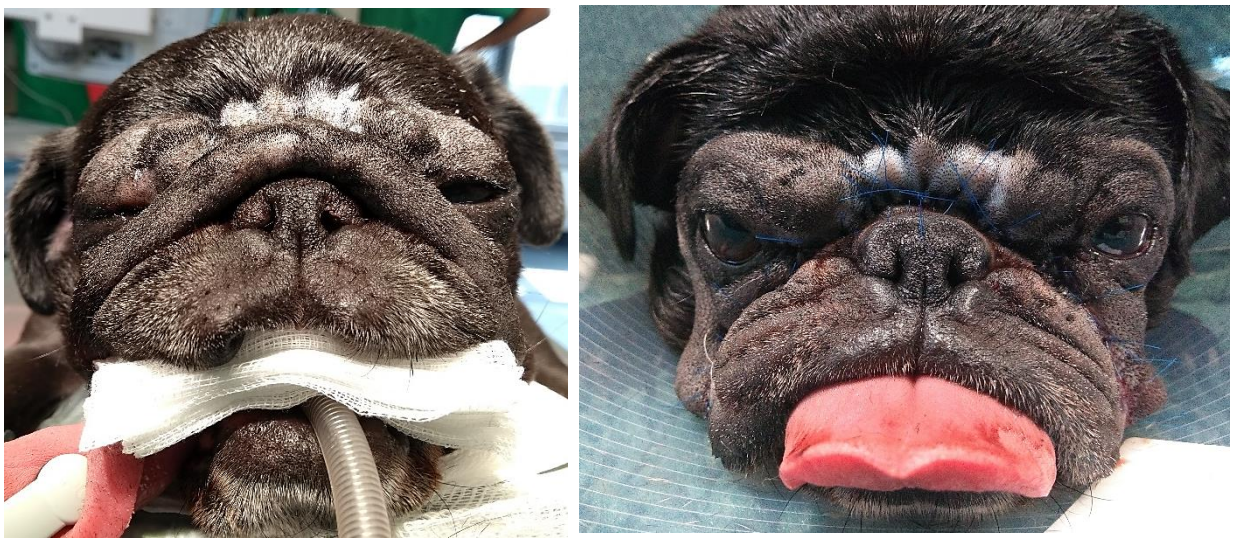

Fig. 08: A six-year-old female Pug before and after MCP and resection of the excessive nasal fold (Original picture).

Fig. 09: The same BM before and after the correction of trichiasis, using the LCP technique (Original picture).

Conjunctival flap, Abrasio cornea and the Hotz-Celsus technique were performed in the same number of cases (3/47), three, although there was also another indication for that last technique in the Shar Pei. These surgeries were performed in different breeds, except for the Hotz-Celsus technique that was only necessary in Pugs.

Replacement of the gland of the nictitating membrane was achieved in both cases of prolapse (2/47) and supplementary resection of nasal fold was necessary in two Pug dogs (2/47).

## 4. Discussion

### 4.1. Studied population

Due to the actual tendency in terms of breed predilection, the study population is mainly formed by French Bulldogs and Pugs. That constitutes a major limitation when comparing the same ocular abnormality within the same breed and between a large and a low representative breed. With that said, such comparisons will be made, knowing that the certainty of some conclusions would require further investigation.

The fact that more than 80% of the population went to the ophthalmological appointment for the first time during the study time can be justified by the late onset of very noticeable clinical signs in some diseases, and by the quick correction and recovery of many situations that form the OBS. Moreover, in the OBS, the surgery is sometimes the treatment itself, and the time between the surgery and post-surgical control is quite scarce. Other contributing factor is that, if the case is a reference and is not severe, the follow up can be made whether at the hospital or at the usual pet's clinic, as the tutor desires.

Knowing that almost one third of the dogs was consulted after the recommendation from an otorhinolaryngologic veterinarian to do so, is another indication that the clinical signs can pass unnoticed by their owners, and that many of them may be not informed of the importance of ocular alterations commonly found in brachycephalic breeds.

Many of the French Bulldogs and Pugs have been already diagnosed with BOAS, showing that their skull conformation brings repercussions in different ways. When needing both BOAS and OBS surgical correction, they were made in the same surgical time in order to avoid unnecessary anaesthesia. That leaves us an idea that many tutors don't notice any alterations on their pet's eyes, since they are many times discrete, which may delay the diagnosis and treatment and worsen the ocular condition.

### 4.2. Iatrotopic stimulus

The study of this topic highlighted some interesting facts. All of the frequent iatrotropic stimulus were within of what has been already described by many authors about this syndrome. The clinical signs described many times by the tutors and being the reason for the appointment were, by decrease in incidence, blepharospasm, epiphora and ocular discharge. Discharge was present in 21 % of the population and was mostly described as thick and only a third as purulent, which can be related with KCS (Lewin, 2014) (Petersen-Jones et al, 2009).

Most of the dogs presented a combination of two or more clinical signs instead of just one, which is relatable to many ocular diseases. For instance, in the presence of hair or ciliar changes such as entropion, ectropion, trichiasis and distichiasis, and due to the chronical

trauma of the eye surface it is expected for the dog to show epiphora, ocular discharge and conjunctivitis (Stades, 2013). Moreover, blepharospasm may also be present due to the discomfort associated with the ocular pain.

Conjunctivitis was also a relatively frequent problem, because it was present in 25% of the dogs. Having an immense number of problems that could be possibly behind it, the predisposition is always dependent from the primary disorder. Once again, the extended eye exposure plays its role in terms of raising the probability of ocular trauma (Townsend et al, 2009).

Considering that the clinical signs were commonly the same in dogs with different problems, they are not pathognomonic signs. For example, a dog with KCS and another with a traumatic corneal ulcer may show both ocular discharge, conjunctivitis and blepharospasm (Lewin, 2014) (Ledbetter et al, 2013). This emphasizes the value of a careful and complete ophthalmologic evaluation in order to determine the cause of the problem.

### 4.3. Clinical signs

- **Eyelids**

Concerning eyelid clinical alterations, macroblepahron was seen across the population, as it is directly related to the brachycephalic dogs' skull features. This characteristic is very important, because it predisposes dogs to ocular trauma.

There were few cases of palpebral neoplasms and they affected only French Bulldogs. However, this condition is not described by many authors as having an inheritance component (Committe, 2017) (Committe, 2015) (Gough et al, 2004).

The definitive diagnose was only possible in one case, and the histopathologic result came as a sebaceous adenoma. The benign neoplasms outnumber the malignant ones by a ratio of 3:1, and the sebaceous adenoma is, by far, the most common one (Stades et al., 2013). The remaining dogs were not submitted to a histopathological exam, as one of them went back to the referral clinic overseas, and the other one had more severe problems, such as partial facial paralysis and corneal ulcer, that required priority treatment.

- **Hair/ciliar changes**

The hair/ciliar related disorders played a significant role. The most frequent abnormality within all the study was entropion. About 45% of the population was affected by it and the Boxer represented the only breed without this ocular alteration, whereas at least one element of each the remaining breeds suffered from it. In all the cases, it was bilateral and medially, and there were three cases of both upper and lower eyelids being affected- a Bullmastiff, an English Bulldog and a Shar Pei. Being the Shar Pei breed only represented by one patient in this study, this was more frequent in the Pug, with 69% of incidence in this breed, followed by the English

Bulldog, with 66%, Boston Terrier and Bullmastiff, with 50%, and the French Bulldog, with a lower incidence of 19%. The gender incidence within the two most common breeds in the study corresponded to 25% females and 75% males in the French Bulldog. The same parameter presented 64% females and 36% males in Pugs. Thus, it is unexpected for this alteration to be directly influenced by gender. One interesting fact is that there was only one case of ulcer and ectopic cilia, one case of concomitant trichiasis and three cases of associated entropion. That indicates, once again, that the main cause attributed to all the other ulcers was more likely due to unknown trauma, rather than the presence of those disorders. This supposition is supported by a study by Amol (2016), that recorded an incidence of almost 87% ulcerated eyes due to trauma and 13% of ulcerated eyes that with a primary cause of ectopic cilia. Nevertheless, the same author did not find a correlation between corneal ulcers and distichiasis, and with trichiasis, whereas we found such events (Amol, 2016). This finding supports partially studies of Packer et al. (2015a), because they described this correlation. However, these authors claimed that dogs with nasal folds were five times more likely to develop corneal ulcers. This disparity points towards the small size of our study population, or even to the existence of additional and undetermined factors.

The second most common hair-related disorder was distichiasis. The gender distribution was not meaningful except perhaps for the French Bulldogs, with three males and one female having distichiasis. There were few bilateral cases of distichia, and they were a male Pug and a neutered French Bulldog female.

Ectopic cilia and trichiasis are two conditions that only happened once during this time, the first one in one Boston Terrier and the second one bilaterally and in the Shih Tzu.

The excess of nasal folds was only registered three times as being responsible for causing ocular alterations, and surprisingly, they were all Pugs, although there are other breeds described to normally have some degree of nasal fold, such as Bulldogs (The Kennel Club, 2012).

The hair alteration seen the fewer was haired carunculas, an abnormality that affected only one English Bulldog and two Pugs.

- **Cornea**

Corneal ulcers were the second most common alteration in this study. They were present in 30.4 % of the study population and only in Bullmastiffs, French Bulldogs and Pugs. Their mean age was 1.71, 5.46 and 5.6 years old, respectively. Except for the Bullmastiffs, that are not largely represented, it is interesting that the French Bulldogs' and Pugs' age for this event was very similar. However, the mean age does not seem to be in agreement with some previous studies. Moore (2003) registered a mean age for this event at 8.2 years, whereas as a more recent study by Ramani, Ahirwars, Shafiuzama & Nagarajan (2012) reported a mean age somewhere between 3 months and 3 years.

When it comes to the general gender distribution, a slight difference between males and females was noticed, 52.6 % and 47.4 %, respectively. These results are also very similar to the ones described by the first mentioned author. However, when looking closely to each breed, the distribution was slightly more uneven in one of them. The proportion in Pugs was 4 females to 1 male. There was only one register of bilateral ulcers, in a male French Bulldog, which goes against the study from Ramani et al (2012), that reported more bilateral ulcers than the unilateral ones. Some of the most severe cases included a male Pug, with a corneal erosion in the left eye and a deep ulcer in the right eye, and two female Pugs with a deep ulcer. The most severe case was, however, a female French Bulldog with a corneal perforation that resulted in a prolapse of the iris. The erosion was the only corneal alteration in two cases, bilaterally in a female French Bulldog, and unilaterally in the Shar Pei. When analysing the unilateral ulcers, they were present 10 times on the left eye and 8 times on the right eye, and the distribution within French Bulldogs and Pugs was also quite alike, not showing a side-presentation predisposition. Such fact leads to a suspicion of ocular trauma as the primary cause of these corneal ulcers.

Two other corneal alterations were also important, such as the opacity and corneal pigmentation. The corneal pigmentation affected four breeds and its incidence was more than double in Pugs. That can indicate that this breed was predisposed to this clinical presentation. However, no gender predisposition was noticeable. On the other hand, the corneal opacity was typical for the French Bulldog breed. 38% of the all the French Bulldogs had it and there are some differences in terms of male and female proportion. Therefore, the hypothesis that there might exist a gender predisposition should not be discarded.

- **Nictitating membrane**

The prolapse of the NM was seen two times, both in dogs with 5 months old. Their age is congruent to the findings of the retrospective study of Mazzuchelli et al (2012), that reported that the prolapse was much more frequent with dogs with a maximum age of one year old.

- **Miscellaneous**

Some less frequent abnormalities registered during the present study were cataracts and iris's disorders. Both cases of cataracts were found in Pugs, which is concordant to some authors that considered an important inheritance component between this breed and cataracts, especially in dogs between 1 and 4 years old (Committe, 2015) (Chaudieu & Chahory, 2013). One of them is within this range, but the other is seven years old. However, it should be taken in consideration that this is only the age at the time of the diagnosis, while the age of onset remains unknown. This means that this disease cannot be attributed with certainty to inheritance or to age consequences.

Different conditions were only registered once throughout this study that are not directly involved in the OBS. Some examples include the presence of a foreign body in the anterior chamber, a retrobulbar process, a case of fat corneal degeneration and other of scleral pigmentation.

Many clinical signs described by Gough and Thomas (2004) as being predisposed in the studied breeds were not reported, due to the size of our study population and to the fact that they are not all equally frequent.

### 4.4. Ophthalmological tests and complementary exams

The alteration of the visual reflexes or responses happened four times. One menace response was attenuated in a French Bulldog, but the dog had severe cataracts, what would explain that weakened response. Another French Bulldog presented with acute loss of vision showing all the ocular reflexes and responses negative, except for the palpebral reflex, possibly due to a lesion on the optic chiasma. One senior English Bulldog had also all reflexes and responses negative but he suffered from glaucoma in both eyes, secondary to panuveitis. Chronic glaucoma is responsible for many ocular alterations, from which cataracts, optic disc and optic nerve degeneration and thickening of the cornea due to corneal oedema are possibilities and also justifies the negative response to those tests (Plummer, Regnier & Gellat, 2014). The last one was the Shih Tzu, over 12 years of age, without menace response and maze reflex. These can be attributed to other existing problems, such as hyphaemia, lens nuclear sclerosis and asteroid hyalosis. These are all abnormalities that diminish the entrance of light through the eye, and also decrease the cortex's capacity of processing images and, consequently, producing an adequate response against it, justifying the negative menace response. On the other hand, a hypertensive retinopathy was diagnosed and since the retina is involved in the sensory, or afferent, pathway of the pupillary light reflex, a negative response is expected (Bjerkâs, Ekesten, Narfstrom & Grahn, 2009).

Concerning the Schirmer tear-test, twelve of the patients showed a value within the normal range and three were between the border-line values. The remaining had values below 10 mm Hg, revealing four diagnoses of KCS. The most severe case was seen in a French Bulldog, with a unilateral STT value of 0 mm/min.

Tonometry was measured with a rebound tonometer and allowed the diagnosis of glaucoma in two cases. One of them was already mentioned above, which was the English Bulldog with panuveitis, with concomitant *ablatio retinae*, or retinal detachment, leading to a secondary increase of IOP (Gellat, Brooks & Kallberg, 2007). Although not so frequently, this condition is also described by Bjerkâs et al. (2009) with having a hereditary predisposition in brachycephalic breeds. The other one was a French Bulldog with a deep corneal ulcer, presumably due to the very high IOP value, of 56 mmHg. On the other side, the IOP was below the reference value in three cases. The reasons behind it were exophthalmos in the Boxer, the

presence of an auto-immune disease in a French Bulldog and a possible measuring error in a Pug, since the values were 13 mmHg and 14 mmHg, close to the normal range, and there was no apparent reason for a low value.

In terms of complementary exams. the fluorescein test was the most frequently used and enabled the diagnose of 47% of all the corneal ulcers. The remaining 53% animals had corneal ulcers that were so evident that didn't need the staining test to be confirmed.

Ocular ultrasound was useful to assess the lens's and chambers' status. For instance, the Shih Tzu that suffered from nuclear sclerosis and the Pug with a severe lens's atrophy, what can be justified with her age. Both were almost 13 and 7 years old, respectively, and since these abnormalities are age related, these are the most probable causes. The anterior and vitreous chambers showed very few alterations.

In two blind dogs that showed a positive pupillary reflex, both with cataracts, an ERG was performed to locate the vision loss's primary cause and, therefore, differentiate blindness due to retinal disease from vision loss due to diseases of the cerebral cortex or optic nerve. This result, in addition to the other normal ophthalmological tests including ocular ultrasound, suggested that the vision loss could be purely attributed to the cataracts, with no other detectable lesions. Concerning the second case, further diagnostic tests should be performed, such as magnetic resonance imaging or computed tomography, cerebrospinal fluid analysis and search of systemic inflammatory or neoplastic diseases (Plummer, 2016).

The arterial pressure measurement was performed in one patient and it presented a high importance to validate the definitive diagnose in the Shih Tzu with hypertensive retinopathy, which had already been demonstrated by other authors (Bjerkâs et al., 2014).

## 4.5. Treatment

### 4.5.1. Medical treatment

Regarding differences between the medical treatment for superficial and deep ulcers, the concentration of hyaluronic acid is almost half in the pharmacological formulation advised for the last ones. That can be justified because the formulation's viscosity is proportional to the concentration of this active principle. Since the management of deep ulcers is more intense in terms of frequency when comparing to the superficial ones, namely the atropine administration, a more fluid presentation is advantageous to ensure that the remaining drugs are properly administered and absorbed (Williams, Middleton, Fattahian & Moridpour, 2012).

Topical antibiotic is also not the same in both cases. Gentamicin is used in the superficial ulcers and belongs to the aminoglycosides group. On the other hand, ofloxacin is chosen to treat deep ulcers and is part of the quinolones group. Since ofloxacin maintains a minimal inhibitory concentration more prolonged in time, it is associated with a better bactericide effect and, therefore, there are less chances of the development of secondary bacterial infections

(Williams, Zolezio & Tang-Liu, 1990). A more powerful bactericidal effect is very important in cases of deep ulcers due to a bigger disruption of the epithelial layers of the cornea (Ledbetter, 2013).

### 4.5.2. Surgery

The most frequent surgical procedure was medial canthoplasty. Seven surgeries were performed, and six other cases had indication to do so, but their tutors decided not to move on with it for multiple reasons. There is only one registered case of lateral canthoplasty, since this is not a typical approach for the brachycephalic dogs.

The excess of nasal folds was surgically solved with its removal in two cases. The third registered case didn't need the same surgery because it was submitted to medial canthoplasty, which has itself the potential to straighten the skin below the lower eyelid, and to cover the part of the eye previously exposed to the nasal fold trauma, solving several problems at once.

The conjunctival flap technique was performed in three cases for the resolution of deep ulcers, and the corneal abrasion with the Alger Brush® (Rumex; Clearwater, Philadelphia, United States of America) solved other three superficial ulcers.

Only three out of twenty-one cases of the entropion went through a Hotz-Celsus technique. The reasons behind it included often the dog owners' personal or economic motives. However, in some cases where the degree of entropion was not so severe and that required a medial canthoplasty as well, this last technique allowed by itself to unfold the curled margin of the entropion. Other animals had some other complications or health problems that required priority in treatment.

All the previously described techniques were successfully applied, and any secondary problems were detected during the dogs' recovery.

## 5. Conclusion

Ocular Brachycephalic Syndrome is part of the complex Brachycephalic Syndrome, from which takes also part the usually known Obstructive Airway Syndrome. Both include different diseases caused by anatomical alterations in these dogs' oculofacial skull region.

Understanding the morphological modifications in the brachycephalic breeds and being alert to clinical signs is, therefore, essential. Some of the most frequent clinical signs are directly related to the morphological component itself, like entropion and trichiasis. Others are secondarily acquired, including corneal ulcers and corneal dystrophies. Although the size of the population was not ideal, some discovered findings supported some authors' conclusions, while being opposite to other authors' results. These discrepancies illustrate to not only the need of making further studies, but also to the fact that the clinical appearance of the Brachycephalic Syndrome might be different overtime because of the higher selection of brachycephalic dogs with more extreme skull features.

A basic ophthalmological examination allows a quick assessment of the patients' visual acuity and even indicates sometimes a possible localization of the problem. When having doubts, a more complete ophthamological examination, includind shirmer tear test, tonometry and biomicroscopy, as well as fundoscopy are very valuable in confirming many abnormalities, such as corneal ulcers, KCS and cataracts.

Many of the primary abnormalities can be solved with surgery and the rate of success is very high, and the recovery does not usually bring any issues. Despite their good prognosis, these animals may still develop other ocular diseases in the future, since their morphological features, such as exoftalmia, remain the same. When it comes to the secondary developed problems, the prognosis is most of the times depending on how long the primary cause has been present.

Alerting the tutors to the higher susceptibility of having this Syndrome in these breeds plays a big role. Properly informed tutors enable an earlier detection of the Syndrome and, consequently, help improving the veterinarian's chances of success when treating it. Moreover, a basic ophthalmological examination should be performed in routine appointments, particularly when it refers to dogs with more extreme features. Not only some abnormalities are discrete and may pass unnoticed at first sight, but also many of them affect dogs at a very young age, which compromises their vision on a long term and affects their wellbeing.

Our results emphasise the need for a better clarification of pet owners of dogs from brachycephalic breeds due to the very high incidence of respiratory and ocular problems, and breeders should avoid whenever possible breeding the individuals that present with the most intense phenotypic characteristics.

This study allowed the perception of the incidence of ocular alterations related to the brachycephalic conformation. Some differences between breeds were suggested, including a higher incidence of corneal pigmentation in Pugs and corneal opacity in French Bulldogs,

which suggests that some brachycephalic breeds may be predisposed to certain ocular abnormalities. However, and since there are limitations when it comes to the size of the studied sample, further studies with larger samples should be taken in consideration, so that results can be statistically more significant.

The percentage of secondary problems, like ulcers, was high, which alerts to the importance of a regular ophthalmological check-up, so that an early diagnosis of the primary disorders can be achieved, avoiding the development of secondary alterations and allowing for the institution of an adequate treatment.

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## V. ANNEXES

**Annex 01**: Characterization of the study population

| Animal | Breed | Age (years) | Gender | New case | BOAS |
|---|---|---|---|---|---|
| **1** | BT | 6.67 | CF | | |
| **2** | BT | 0.42 | F | ✓ | |
| **3** | Boxer | 11 | CF | ✓ | |
| **4** | EB | 3,5 | M | ✓ | |
| **5** | EB | 9,25 | M | ✓ | |
| **6** | EB | 7,25 | CF | ✓ | |
| **7** | BM | 1,83 | M | ✓ | |
| **8** | BM | 1,58 | M | ✓ | |
| **9** | FB | 2,83 | F | | |
| **10** | FB | 2,25 | M | ✓ | ✓ |
| **11** | FB | 10 | F | ✓ | |
| **12** | FB | 5,58 | F | ✓ | |
| **13** | FB | 4,17 | M | | |
| **14** | FB | 4,5 | M | ✓ | |
| **15** | FB | 7,58 | M | | |
| **16** | FB | 9,33 | CF | ✓ | |
| **17** | FB | 1,92 | CM | ✓ | ✓ |
| **18** | FB | 3 | M | ✓ | ✓ |
| **19** | FB | 4,75 | M | ✓ | ✓ |
| **20** | FB | 1,08 | M | ✓ | |
| **21** | FB | 1,17 | M | ✓ | |
| **22** | FB | 5,5 | F | ✓ | |
| **23** | FB | 5,42 | CM | ✓ | |
| **24** | FB | 1,5 | M | ✓ | |
| **25** | FB | 0,42 | F | ✓ | |
| **26** | FB | 8,25 | CM | | |
| **27** | FB | 6,75 | M | ✓ | |
| **28** | FB | 5,75 | F | ✓ | ✓ |
| **29** | FB | 8,75 | F | ✓ | |
| **30** | Pug | 5 | CM | ✓ | ✓ |
| **31** | Pug | 2,33 | M | ✓ | ✓ |
| **32** | Pug | 3,75 | M | ✓ | ✓ |
| **33** | Pug | 7 | F | ✓ | |
| **34** | Pug | 2,17 | F | ✓ | |
| **35** | Pug | 2,58 | CF | ✓ | |
| **36** | Pug | 8,42 | M | ✓ | |
| **37** | Pug | 5,83 | F | | |
| **38** | Pug | 4 | F | ✓ | ✓ |
| **39** | Pug | 2,75 | F | ✓ | ✓ |
| **40** | Pug | 8,17 | CF | ✓ | ✓ |
| **41** | Pug | 3,58 | F | ✓ | |
| **42** | Pug | 1,92 | M | ✓ | ✓ |
| **43** | Pug | 3,08 | M | ✓ | ✓ |
| **44** | Pug | 8,67 | F | | |

(continuation)

| | | | | | |
|---|---|---|---|---|---|
| **45** | Pug | 8,67 | CF | ✓ | ✓ |
| **46** | Shar-Pei | 0,5 | M | ✓ | |
| **47** | Shih-Tzu | 12,67 | CF | | |

BT- Boston Terrier; EB- English Bulldog; BM- Bullmastiff; FB- French Bulldog; CF- Castrated female; F- Female; M- Male; CM- Castrated male

**Annex 02**: Clinical signs

| Animal | Blefarospasm | CT | Cataracts | Conjunctivitis | Corneal Opacity | Corneal Ulcer | Distichiasis | Ectopic Cilia | Entropion | Epiphora | Erosion | KCS | Macroblepharon | Nasal Fold | NMP | Palpebral Mass | KP | Trichiasis |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1** | ✓ | | | | ✓ | | | ✓ | | | | | | | | | | |
| **2** | | | | ✓ | | | ✓ | | ✓ | | | | ✓ | | ✓ | | | |
| **3** | | | | ✓ | | | | | | ✓ | | | | | | | | |
| **4** | | ✓ | | | | | | | | | | | ✓ | | | | | |
| **5** | | | | ✓ | | | | | | | | | | | | | | |
| **6** | | | | | | | ✓ | | ✓ | | | ✓ | ✓ | | | | | |
| **7** | ✓ | | | | | ✓ | ✓ | | | | | | ✓ | | | | | |
| **8** | ✓ | | | ✓ | | ✓ | | | ✓ | ✓ | | | ✓ | | | | | |
| **9** | | | | ✓ | | | | | | | | | | | | | | |
| **10** | | | | | | | | | ✓ | | | | ✓ | | | | | |
| **11** | ✓ | | | | | ✓ | | | | | | | ✓ | | | | ✓ | |
| **12** | | | | | | ✓ | | | | | | | | | | | | |
| **13** | | | | | | ✓ | | | | | | | ✓ | | | | | |
| **14** | ✓ | | | ✓ | | ✓ | ✓ | | | | | | | | | | | |
| **15** | ✓ | | | ✓ | ✓ | ✓ | | | | | | ✓ | ✓ | | | | | |
| **16** | ✓ | | | | | ✓ | | | | | | | | | | | | |
| **17** | ✓ | | | ✓ | ✓ | ✓ | | | | | | | | | | | | |
| **18** | | | | | | | | | ✓ | | | | ✓ | | | | | |
| **19** | | | | | ✓ | | | | ✓ | | | | ✓ | | | | | |
| **20** | | | | | ✓ | | | | | | | | ✓ | | | | ✓ | |
| **21** | | | | ✓ | ✓ | | | | | | | | ✓ | | | | | |
| **22** | | | | | | ✓ | | | | | | | ✓ | | | | | |
| **23** | | | | | | | | | | ✓ | | | ✓ | | | | | |
| **24** | ✓ | | | | ✓ | ✓ | | | | | | | ✓ | | | | | |

(continuation)

| Animal | Blefarospasm | CT | Cataracts | Conjunctivitis | Corneal Opacity | Corneal Ulcer | Distichiasis | Ectopic Cilia | Entropion | Epiphora | Erosion | KCS | Macroblepharon | Nasal Fold | NMP | Palpebral Mass | KP | Trichiasis |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **25** | | | | | ✓ | ✓ | | | | | | | ✓ | | ✓ | | | |
| **26** | | | | ✓ | ✓ | ✓ | ✓ | | | ✓ | | | | | | ✓ | | |
| **27** | ✓ | | | | ✓ | ✓ | ✓ | | | ✓ | | | ✓ | | | ✓ | | |
| **28** | | | | ✓ | | | ✓ | | ✓ | | | ✓ | ✓ | | | ✓ | | |
| **29** | ✓ | | | | | | | | | | | ✓ | | | | | ✓ | |
| **30** | | ✓ | | | | | | | ✓ | | | | ✓ | | | | | |
| **31** | | ✓ | | | | | | | ✓ | | | | ✓ | | | | ✓ | |
| **32** | | | | | | | | | ✓ | | | | ✓ | | | | ✓ | |
| **33** | | | ✓ | | | | | | | | | | ✓ | | | | | |
| **34** | | | ✓ | | | | ✓ | | ✓ | | | | ✓ | | | | ✓ | |
| **35** | | | | | | | | | ✓ | | | | ✓ | | | | | |
| **36** | | | | | | | | | ✓ | | | | ✓ | | | | ✓ | |
| **37** | | | | | | | | | ✓ | | | | ✓ | ✓ | | | ✓ | |
| **38** | | | | | | ✓ | | | | | | ✓ | ✓ | | | | | |
| **39** | | | | | | | | | ✓ | | | | ✓ | | | | ✓ | |
| **40** | | | | | | | | | ✓ | | | | ✓ | ✓ | | | ✓ | |
| **41** | | | | | | ✓ | | | ✓ | | | | ✓ | | | | | |
| **42** | | | | | ✓ | | | | | | | ✓ | ✓ | ✓ | | | | |
| **43** | ✓ | | | | | ✓ | ✓ | | | | ✓ | | ✓ | | | | | |
| **44** | ✓ | | | | | ✓ | | | | | | | ✓ | | | | | |
| **45** | | | | | | ✓ | ✓ | | ✓ | | | | ✓ | | | | ✓ | |
| **46** | ✓ | | | ✓ | | | | | ✓ | ✓ | ✓ | | | | | | ✓ | |
| **47** | | | | | | | | | ✓ | ✓ | | | | | | | ✓ | ✓ |

CT- Caruncular trichiasis; KCS: Keratoconjunctivitis sicca; NMP- Nictitating membrane prolapse; KP- Keratitis pigmentosa

**Annex 03**: Complementary exams results

| Animal | Arterial Pressure | Electroretinography | Fluorescein | Jones I | Schirmer Test | Tonometry | Ultrassound |
|---|---|---|---|---|---|---|---|
| 1 | | | | | ✓ | | |
| 2 | | | | | | | |
| 3 | | | | | | ✓ | |
| 4 | | | | | ✓ | | |
| 5 | | | | | | ✓ | |
| 6 | | | | | ✓ | | |
| 7 | | | | | | | |
| 8 | | | | | | | |
| 9 | | | | | | ✓ | |
| 10 | | | | ✓ | ✓ | | |
| 11 | | | | | | ✓ | ✓ |
| 12 | | | | | | | |
| 13 | | | | | | | |
| 14 | | | ✓ | | ✓ | | |
| 15 | | | ✓ | | ✓ | ✓ | |
| 16 | | | | | ✓ | | |
| 17 | | | ✓ | | | | |
| 18 | | | | | | | |
| 19 | | | | | | | |
| 20 | | | | | | | |
| 21 | | | | | | | |
| 22 | | | | | | | |
| 23 | | ✓ | | | | ✓ | |
| 24 | | | ✓ | | | | |
| 25 | | | | | | | |
| 26 | | | ✓ | | ✓ | | |
| 27 | | | | | | | |
| 28 | | | | | ✓ | | |
| 29 | | | | | ✓ | ✓ | |
| 30 | | | | | | | |
| 31 | | | | | | ✓ | |
| 32 | | | | | ✓ | | |
| 33 | | ✓ | | | | ✓ | ✓ |
| 34 | | | | | ✓ | | |
| 35 | | | | | | | |
| 36 | | | | | ✓ | | |
| 37 | | | | | | ✓ | |
| 38 | | | ✓ | | ✓ | | |
| 39 | | | | ✓ | | | |
| 40 | | | | | ✓ | | |
| 41 | | | | | ✓ | | |
| 42 | | | | ✓ | ✓ | | |

(continuation)

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **43** | | | | | | | |
| **44** | | | ✓ | | | | |
| **45** | | | ✓ | | ✓ | | |
| **46** | | | ✓ | | ✓ | | |
| **47** | ✓ | | | | | ✓ | ✓ |

**Annex 04**: Surgery results

| Animal | Abrasio Cornea | CPM | Conjunctival Flap | Electroepilation | Hotz-Celsus | LCP | Nasal Fold Resection | FNM |
|---|---|---|---|---|---|---|---|---|
| 1 | | | | ✓ | | | | |
| 2 | | | | | | | | ✓ |
| 3 | | | | | | | | |
| 4 | | | | | | | | |
| 5 | | | | | | | | |
| 6 | | | | | | | | |
| 7 | | | | ✓ | | ✓ | | |
| 8 | ✓ | | | | | | | |
| 9 | | | | | | | | |
| 10 | | | | | | | | |
| 11 | | | | | | | | |
| 12 | | | ✓ | | | | | |
| 13 | | | ✓ | | | | | |
| 14 | | | | | | | | |
| 15 | | | | | | | | |
| 16 | ✓ | | | | | | | |
| 17 | | | | | | | | |
| 18 | | ✓ | | | | | | |
| 19 | | | | | | | | |
| 20 | | ✓ | | | | | | |
| 21 | | ✓ | | | | | | |
| 22 | | | | | | | | |
| 23 | | | | | | | | |
| 24 | | | | | | | | |

(continuation)

| Animal | Abrasio Cornea | MCP | Conjunctival Flap | Electroepilation | Hotz-Celsus | LCP | Nasal Fold Resection | FNM |
|---|---|---|---|---|---|---|---|---|
| 25 | | | | | | | | ✓ |
| 26 | | | | | | | | |
| 27 | | | | ✓ | | | | |
| 28 | ✓ | | | ✓ | | | | |
| 29 | | | | | | | | |
| 30 | | | | | | | | |
| 31 | | ✓ | | | ✓ | | | |
| 32 | | ✓ | | | ✓ | | | |
| 33 | | | | | | | | |
| 34 | | ✓ | | | | | | |
| 35 | | | | | | | | |
| 36 | | ✓ | | | | | | |
| 37 | | ✓ | | | | | ✓ | |
| 38 | | ✓ | | | | | | |
| 39 | | | | | | | | |
| 40 | | ✓ | | | ✓ | | ✓ | |
| 41 | | | | | | | | |
| 42 | | ✓ | | | | | | |
| 43 | | | | ✓ | | | | |
| 44 | | ✓ | ✓ | | | | | |
| 45 | | ✓ | | | | | | |
| 46 | | | | | ✓ | | | |
| 47 | | | | | | | | |

MCP- Medial canthoplasty; LCP- Lateral canthoplasty; FNM- Fixation of the nictitating membrane

**Annex 05**: Predisposed ocular diseases (Adapted from Gough & Thomas, 2004)

| Disease \ Breed | Boxer | Bull Mastiff | Bulldog (English) | French Bulldog | Pekingese | Pug | Shar-pei | Shitzu | Boston terrier |
|---|---|---|---|---|---|---|---|---|---|
| Entropion | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | |
| Ectropion | ✓ | ✓ | | | | | | | |
| Prolapse of the gland of the nictitating membrane | ✓ | | ✓ | | | | ✓ | | ✓ |
| Distichiasis | ✓ | ✓ | | ✓ | ✓ | ✓ | | ✓ | |
| Refractory corneal ulceration | ✓ | | ✓ | | ✓ | ✓ | | ✓ | ✓ |
| Corneal dystrophy | ✓ | | | | | | | | ✓ |
| Canine anterior uveal melanoma | ✓ | | | | | | | | |
| Macropalpebral fissure resulting in combined entropion–ectropion | | ✓ | ✓ | | | | | | |
| Persistent pupillary membranes (PPM) | | ✓ | | | | | | | |
| Glaucoma | | ? | | | | | ✓ | | |
| Multifocal retinal dysplasia | | ✓ | ✓ | | | | | | |
| Keratoconjunctivitis sicca | | | ✓ | | ✓ | ✓ | | ✓ | ✓ |
| Cataract | | | | ✓ | ✓ | | ✓ | | ✓ |
| Geographic retinal dysplasia | | | | | | | | | |
| Generalised progressive retinal atrophy | | | | | ✓ | | | | |
| Multiple ocular defects | | | | | | | | | |
| Trichiasis | | | ✓ | ✓ | | | | | ✓ |
| Pigmentary keratitis | | | | | | ✓ | | ✓ | ✓ |
| Iris cysts | | | | | | | | | ✓ |

(continuation)

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| **Vitreal syneresis** | | | | | | | | ✓ | ✓ |
| **Nasal fold trichiasis** | | | | | ✓ | | | | |
| **Caruncular trichiasis** | | | | | ✓ | ✓ | | ✓ | |
| **Proptosis** | | | | | ✓ | ✓ | | ✓ | |
| **Micropapilla** | | | | | | | | ✓ | |
| **Optic nerve hypoplasia** | | | | | | | | ✓ | |
| **Primary lens luxation** | | | | | | | ✓ | | |
| **Fibrosing esotropia** | | | | | | | ✓ | | |
| **Anterior uveal melanoma** | ✓ | | | | | | | | |

**Annex 06**: Poster presented at the *Centre for Interdisciplinary Research in Animal Health* (CIISA) Congress, in 16 and 17 de November de 2018

# OCULAR BRACHYCEPHALIC SYNDROME


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## 2. PURPOSE

The conformational alterations of the skull are responsible, many times, for trauma, exposure keratopathy, keratitis pigmentosa, corneal erosion and ulceration.
There are also known or suspected inherited ocular problems that include trichiasis, distichiasis, ectopic cilia, entropion, excessive nasal folds, decreased corneal sensitivity, corneal dystrophies, prolapse of the nictitating membrane, keratoconjunctivitis sicca (KCS), hereditary cataracts and progressive retinal atrophy[3].

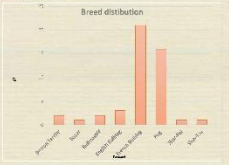
Medical treatment should be considered in superficial ulcers and KCS[3,4]. Other conditions, such as pigmentary keratitis, may be managed by a surgical approach of the initiating cause.

The surgical correction of lagophtalmos is trough a medial canthoplasty (MCP), or lateral canthoplasty (LCP) in giant breeds[5].
The definitive treatment for trichiasis, distichiasis, ectopic cilia and caruncle hair are through electroepilation and cryoepilation and the excess of nasal fold can easily be solved by a resection of that area[6].
The surgical approach to a prolapse of the nictitans membrane includes a reposition of the prolapsed tissue[7]. Indolent ulcers and corneal dystrophies can be treated by using a superficial keratectomy[3].

The aim of this study is to characterize and classify ocular alterations in our studied population of brachycephalic dogs and to evaluate the impact of these ocular changes in different brachycephalic breeds.

## 3. MATERIAL AND METHODS

47 brachycephalic dogs were presented to the Leipzig's University Animal Hospital, Germany, from January 2018 to May 2018, were examined the Ophthalmology department. The population consists of 24 males, 4 of them neutered, and 23 females, 8 of them spayed. Their mean age is 5,0 ± 3,1 years and the breed distribution is as follows:




A basic ophthalmological examination was performed and complementary exams such as Schirmer tear test, electroretinography, ocular echography, fluorescein test, Jones I, tonometry, and measurement of the arterial pressure were also considered.

The animals that went through surgery were followed-up to assess its outcomes.

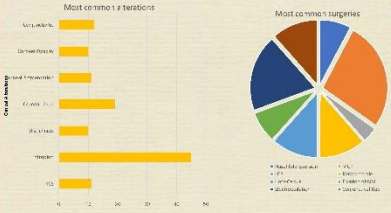

Fig. 1 and 2: FB after a MCP and 2 weeks later, after the removal of the stitches

## 1.INTRODUCTION

The pressure of selection applied continuously over the last decades, trying to meet breed standards, has led to dramatic changes in the brachycephalic breeds skulls' shapes.
There are in these breeds two syndromes: Brachycephalic Obstructive Airway Syndrome (BOAS) and Brachycephalic Ocular Syndrome. The last one is not so well-known, but some small facial alterations can develop several complications that put these dogs' vision at risk.

## 4. RESULTS

Both clinical alterations and surgeries are represented:




None of the corneal alterations were present in breeds like Boxer, Bullmastiff and English Bulldog. On the other side, corneal ulcers were only seen in French Bulldogs, Bullmastiffs and Pugs. The last two breeds showed some severe cases, and the biggest incidence intra-breed was in FB, with 57% of affected dogs. Entropion was present in every breed except for the Boxer, and affected 11 out of 16 Pugs,.


Fig. 3 and 4: Before and after MCP and nasal fold resection in a Pug

## 5. DISCUSSION

Macroblepharon was, by far, the most common alteration, and affected all of the breeds. But that did not happen with the rest of the diseases. For example, corneal pigmentation was present in 14% of FB, and 38%, more than double, of Pugs. That can indicate that this abnormality could be predisposed in such breed. Other particularities are corneal opacity that, typical in the FB, as 38% of them had it, and eyelid tumours, all of them in in this breed, which may have the same meaning. In terms of gender distribution, corneal opacity incidence was different according to sex, being the incidence in males of 13% and in females of 54%.

One interesting fact is that there are only three cases of corneal ulcers also with concomitant entropion. Entropion was, in fact, massively present in breeds such as Pug, EB, BT, and BM between $^1/_2$ and $^2/_3$.

However, the incidence in FB was less than one quarter. These two facts indicate that the main cause of the ulcers was not the presence of entropion, but instead trauma or KCS.

Not all of the animals with surgical indication went through surgery, whether for health reasons, their owners' personal reasons, or because some other ocular surgeries allowed the correction of other problems. Sometimes a MCP is enough for an entropion to stop causing trouble. However, all of the dogs that went through surgery showed improvement.

Some data about the correlation with BOAS was also relevant. Almost half of the French Bulldogs and two thirds of the Pugs, which represents 30% of the total study population, were former diagnosed with Brachycephalic Airway Obstructive Syndrome. Moreover, most of them were transferred by the vets from the Otorhinolaryngology department to the Ophthalmology one. That means that the ocular alterations are frequently missed by the owners, leading to a possible compromising of their pet's vision acuity.

## 6. CONCLUSIONS

The study population was mainly formed by French Bulldogs and Pugs, which constitutes a limitation to this study. However, it showed that ocular abnormalities are quite common and some breeds seem to be predisposed to certain diseases, such as corneal pigmentation in Pugs, corneal opacity and palpebral tumours in FB.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