Veterinary Ophthalmology

WILEY

ORIGINAL REPORT

Measurement of the Retention Time of Two Different Carbomer-Based Ophthalmic Gels With and Without Hyaluronic Acid in Anesthetized Dogs Using Ultrahigh-Resolution Optical Coherence Tomography

Bertrand Michaud[1] | Inès Desquiens[1] | Sophie Amiriantz[2]

[1]Clinique Vétérinaire Anima-Vet, Saint-Genis-Pouilly, France | [2]Dômes Pharma, Pont-du-Château, France

Correspondence: Bertrand Michaud (dr.michaud@anima-vet.fr)

Received: 17 May 2025 | **Revised:** 16 October 2025 | **Accepted:** 23 October 2025

Keywords: carbomer | dog | eye | hyaluronate | lubricant | OCT | tear film thickness

ABSTRACT

Purpose: To evaluate the stability of two ophthalmic gels—one containing carbomer alone (Ocry-gel), and the other combining carbomer with sodium hyaluronate (Eye Lube Pro)—on the corneal surface of anesthetized dogs, using spectral-domain optical coherence tomography (SD-OCT) to quantify Central Tear Film Thickness (CTFT) over time.

Materials and Methods: Twenty healthy dogs undergoing general anesthesia for non-ocular routine procedures were included in a randomized controlled study. Each dog received Ocry-gel in one eye and Eye Lube Pro in the contralateral eye, according to a randomization protocol. CTFT was measured with ultrahigh-resolution anterior segment SD-OCT before (T0) and after (T1) administration of 200 μL of each gel, then at 10, 15, 20, 25, 30, 35, 40, 45, 50, and 60 min. CTFT evolution was analyzed by two-way repeated-measures ANOVA with normality testing and non-parametric correction when required.

Results: CTFT profiles significantly differed between formulations. Eye Lube Pro exhibited more sustained thickness than Ocry-gel. After 60 min, CTFT remained measurable in 14/20 dogs for Eye Lube Pro versus 2/20 for Ocry-gel. Statistical analysis confirmed significantly higher CTFT for Eye Lube Pro at most time points ($p < 0.001$). No significant influence of sex, age, or brachycephalic phenotype was observed.

Conclusions: Addition of sodium hyaluronate to a carbomer-based gel significantly prolongs pre-corneal retention time in anesthetized dogs. These results suggest that selecting the protective gel should consider anesthesia duration or guide adjustment of administration frequency.

1 | Introduction

In veterinary ophthalmology, ensuring the stability and retention of ocular medications is crucial for the effective treatment of various eye conditions in canines [1]. Carbomer, a synthetic high-molecular-weight polymer, is widely used in ophthalmic formulations due to its high viscosity, prolonged retention time on the ocular surface and its ability to retain water [2]. These characteristics make it an attractive candidate for treating dry eye conditions or to prevent anesthesia-induced dry eye during surgical procedures by providing sustained lubrication and protection to the ocular surface [3]. Previous studies have demonstrated the efficacy of carbomer-based eye drops in reducing symptoms and improving ocular surface health in human patients with dry eye syndrome [4, 5]. These studies highlight the potential benefits of carbomer in increasing the volume of

the tear film and reducing cellular damage caused by osmotic stress and friction from eyelid movements [5, 6]. Additionally, carbomer formulations have been compared to other lubricants, such as sodium hyaluronate, with findings indicating varying degrees of effectiveness and patient comfort [7, 8]. The purpose of this study was to evaluate the stability and retention time of two carbomer-based ophthalmic formulations, one of which also contains sodium hyaluronate, on the ocular surface of anesthetized dogs. By using advanced imaging techniques such as ultrahigh-resolution optical coherence tomography, we aim to gain insights into how these formulations behave in the unique physiological environment of the canine eye [9]. This research will contribute to optimizing corneal protection protocols and improving the management of ocular conditions in veterinary practice.

2 | Materials and Methods

Twenty dogs (11 males and 9 females; mean age 69.0 ± 51.2 months; median: 64 months), of various breeds (Table 1), were included in the study. All were anesthetized to undergo scheduled surgical procedures, including mass removal ($n = 7$; 35%), sterilization ($n = 10$; 50%), and wound repair ($n = 3$; 15%).

Client-owned dogs presented for non-ophthalmic procedures under general anesthesia were included if they had a normal complete ophthalmic examination and a Schirmer Tear Test (STT) ≥ 15 mm/min. Dogs were excluded if they had active ocular disease, a history of ocular surgery, systemic conditions likely to affect the ocular surface, or if they had received topical or systemic medications within the previous 2 weeks.

This randomized controlled study adhered to the Association for Research in Vision and Ophthalmology Statement for the Use of Animals in Ophthalmic and Visual Research and was approved by the Ethics Committee on the Use of Animals of the School of Veterinary Medicine and Agronomy (VetAgroSup). The owners provided informed consent for this study.

TABLE 1 | Distribution of dog breeds included in the study, sorted by frequency.

Breed	Number of dogs (*n*)	Percentage (%)
Labrador Retriever	6	30%
Cavalier King Charles Spaniel	4	20%
French Bulldog	3	15%
Golden Retriever	2	10%
Dachshund	2	10%
Border Collie	1	5%
Shih Tzu	1	5%
Boxer	1	5%
Total	20	100%

Two ophthalmic gels were tested: a 0.2% carbomer-based gel (Ocry-gel, Dômes Pharma, Lempdes, France), and a 0.45% carbomer and 0.3% linear hyaluronic acid-based gel (Eye Lube Pro, Dômes Pharma Inc., Salt Lake City, UT, USA). Each dog received one formulation in each eye. The assignment of gels to the right or left eye was randomized. Dogs were anesthetized using a standard protocol to minimize movement and discomfort. All animals were anesthetized using the same standardized protocol: intravenous injection of medetomidine (2 μg/kg), butorphanol (0.1 mg/kg) and ketamine (1 mg/kg) and maintained with isoflurane (1%) in oxygen until the end of measurements. All procedures were performed in a controlled environment at 22°C–23°C with relative humidity between 45% and 55%.

Following the patients were anesthetized, 200 μL of each gel was instilled into the lower fornix of the respective eye. The eyelids were closed and opened manually three times to ensure full coverage of the ocular surfaces. An eye speculum and conjunctival forceps were placed to hold the eye open and centered. A vacuum mattress could be used to stabilize the head in cases of instability or to minimize movements related to the ongoing surgical procedure. Video S1 illustrates the method used to instill the ophthalmic gel in a dog positioned in dorsal recumbency during surgery. The method used to perform the OCT examination in dorsal or sternal recumbency was identical, except that the conjunctival forceps were hanging by gravity in dogs positioned dorsally, whereas it was taped to the head in sternal recumbency.

Ultrahigh-resolution anterior segment spectral domain OCT (Solix, Optovue Inc., Fremont, CA, USA) was used to measure central tear film thickness (CTFT) and evaluate gel retention. CTFT was measured as the distance, at the center of the pupil, from corneal epithelium to the external level of the eye gel at each time point after instillation. The lower limit of quantitation of the CTFT with the OCT was 5 μm.

OCT images were taken before (T0) and immediately after instillation for the first evaluation (T1), then 10 min after (T10) and thereafter every 5 min for 40 min (T10–T50); a final image was taken 60 min after instillation (T60). Figure 1 provides a composite visualization of sequential OCT tomograms acquired from both eyes of a representative subject at each imaging timepoint.

All OCT measurements were performed concomitantly with the scheduled surgical procedures, with animals positioned either in dorsal (Figure 2) or ventral recumbency (Figure 3) depending on the type of intervention. In cases where the surgical procedure lasted less than 60 min, anesthesia was maintained with 1% isoflurane in the same position until all timepoint measurements were completed.

All animals underwent a standardized ophthalmic examination 48 h post-intervention (D2) to assess for potential complications; no corneal lesions, epithelial defects, or treatment-related reactions were observed in any subject.

Data were analyzed using a two-way repeated-measures ANOVA to assess differences in CTFT over time between the

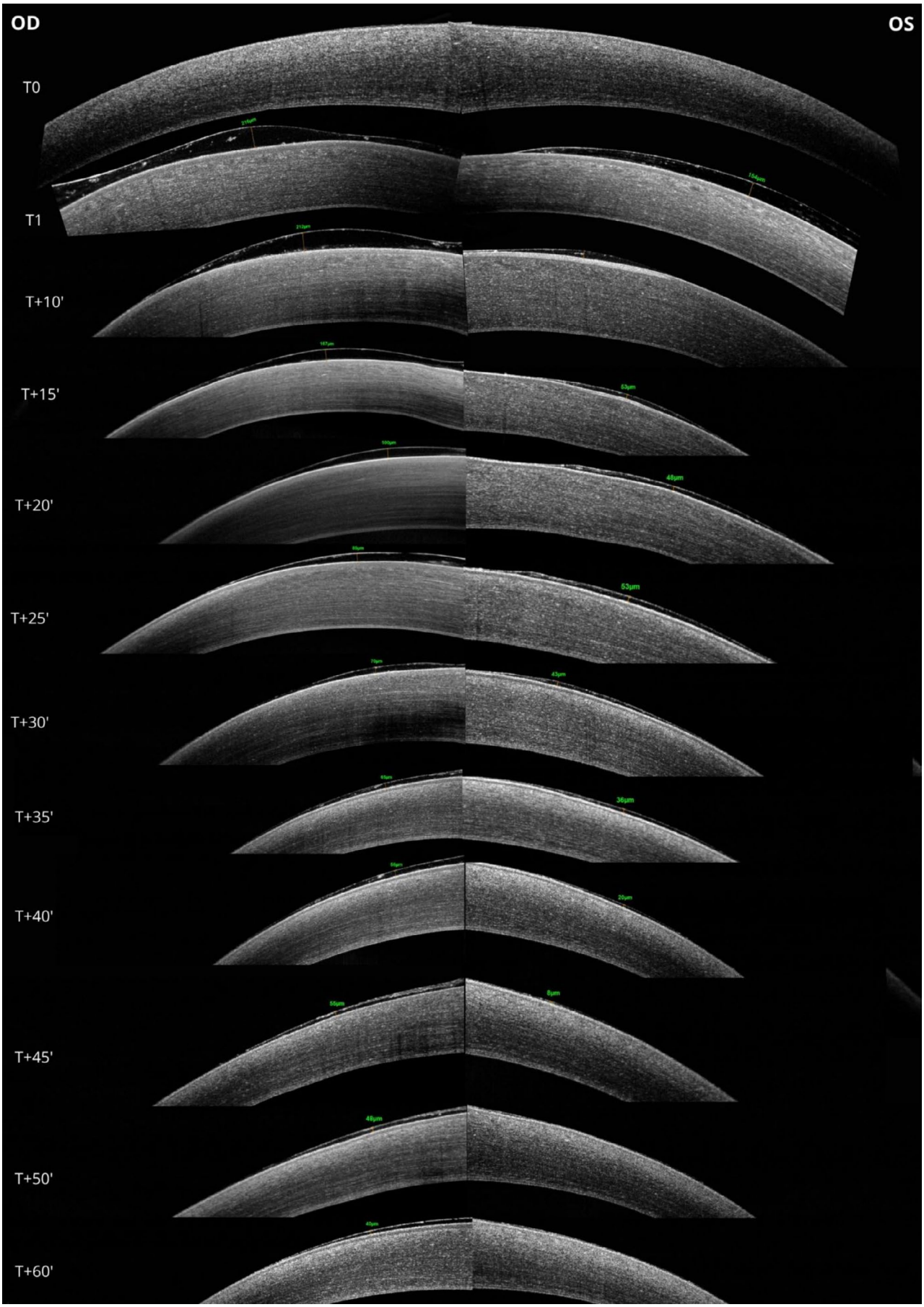

FIGURE 1 | Legend on next page.

FIGURE 1 | Sequential OCT tomograms of a dog having participated in the study (OD:Eye Lube Pro; OS: Ocry-gel) at each imaging timepoint, illustrating tear film thickness evolution over 60 min.

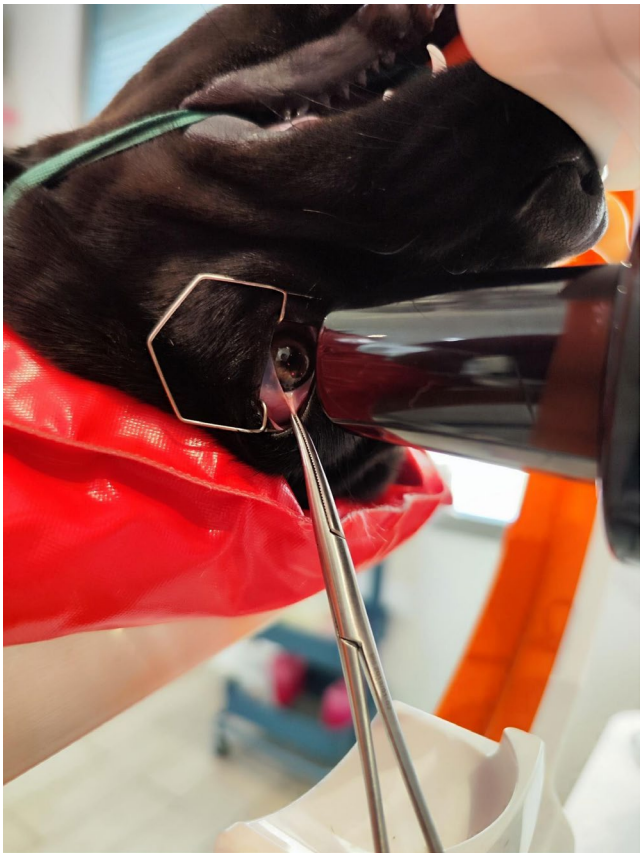

FIGURE 2 | Dog positioned in dorsal recumbency under general anesthesia during OCT imaging.

FIGURE 3 | Dog positioned in ventral recumbency under general anesthesia during OCT imaging.

two formulations. Normal distribution of variables was verified using the Shapiro–Wilk test. When assumptions of normality were not met, the non-parametric Wilcoxon signed-rank test was applied. A p-value < 0.05 was considered statistically significant. The primary outcome was the duration of corneal retention of each formulation, as indicated by the CTFT measurements over time. Secondary outcomes included the potential influence of sex, age, and brachycephalic morphology on gel stability, which were evaluated using Fisher's test.

3 | Results

All 20 dogs enrolled completed the study protocol, and OCT measurements were successfully obtained at all scheduled time points.

The temporal profile of CTFT differed markedly between the two lubricants. As illustrated in Figure 4 and Table 2, the CTFT decreased rapidly following Ocry-gel instillation, with a mean value dropping below 20 μm by 30 min and approaching the lower limit of quantification thereafter. In contrast, Eye Lube Pro exhibited a slower and more sustained elimination, with measurable thickness maintained in the majority of eyes up to the 60-min mark. At the 60-min timepoint, a marked difference in gel retention was observed between the two ophthalmic formulations. The mean central tear film thickness (CTFT) for Eyelub Pro was 32.8 ± 20.1 μm, whereas for Ocrygel it was only 3.2 ± 3.9 μm. This difference was statistically significant ($p < 0.000001$).

To further illustrate interindividual variability and group differences, Figure 5 presents the distribution of CTFT values at each time point using box-and-whisker plots. These plots highlight the more consistent persistence of Eye Lube Pro over time, with higher median values and narrower interquartile ranges compared to Ocry-gel, especially beyond the 30-min mark. Additionally, Figure 6 displays the number of dogs with detectable CTFT over time, emphasizing the prolonged ocular surface retention of Eye Lube Pro as evidenced by a flatter clearance curve compared to the faster decline observed with Ocry-gel. At the 60-min timepoint, visible gel was still present in 17 out of 20 dogs for Eye Lube Pro, whereas only 2 dogs retained a measurable tear film with Ocrygel.

Group mean curves ± standard deviation (SD) showed a statistically significant difference in CTFT values at multiple time points (Figure 4), favoring Eye Lube Pro. Given that CTFT was still detectable 60 min after instillation in several cases, defining a "mean retention time" was deemed inappropriate. Instead, the evolution of CTFT over time was analyzed as a repeated-measures profile. No statistically significant differences were found within the Eye Lube Pro group when stratified by sex ($p = 0.87$), age class (< 64 vs. ≥ 64 months; $p = 0.51$), or brachycephalic conformation ($p = 0.11$). These findings suggest that the longer persistence of Eye Lube Pro was consistent across interindividual differences.

Although not part of the initial study objectives, a post hoc analysis compared the influence of body position on CTFT

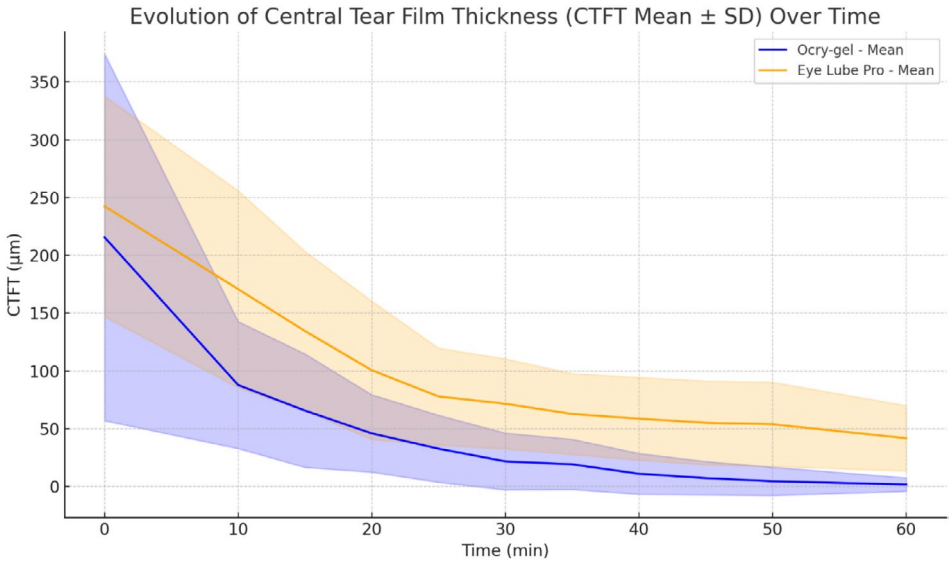

FIGURE 4 | Temporal evolution of Central Tear Film Thickness (CTFT) following corneal application of Ocry-gel and Eye Lube Pro in anesthetized dogs, as measured by spectral-domain optical coherence tomography (SD-OCT). Each point represents the mean CTFT (μm) at a given time point post-application. Shaded areas correspond to ± one standard deviation. Ocry-gel (blue) demonstrated a rapid decline in CTFT, with levels close to the lower limit of quantitation reached before 45 min. Eye Lube Pro (orange) showed a more sustained pre-corneal presence, with measurable CTFT maintained in several eyes after 60 min.

TABLE 2 | Mean ± SD central tear film thickness (CTFT, in μm) measured at each time point (0–60 min) following instillation of two different carbomer-based ophthalmic gels (Ocry-gel and Eye Lube Pro) in anesthetized canine eyes.

Time (min)	Ocry-gel	Eye lube pro
T0	220.4 ± 161.3	240.2 ± 93.1
T10	87.8 ± 54.9	169.7 ± 83.6
T15	65.7 ± 49.1	133.1 ± 66
T20	46 ± 33.5	100.6 ± 59.8
T25	31.4 ± 29.9	77.8 ± 41.8
T30	21.7 ± 24.6	71.6 ± 38.9
T35	19.2 ± 21.7	60.5 ± 34.3
T40	11 ± 17.7	58.4 ± 36.2
T45	7.2 ± 14.4	54.5 ± 37.1
T50	4.6 ± 12.3	53.9 ± 36.4
T60	1.7 ± 5.8	41.8 ± 28.3

measurements. Fifteen dogs were examined in dorsal recumbency and five in sternal recumbency. No statistically significant difference was observed between the two groups, indicating that recumbency did not affect gel retention time.

4 | Discussion

To our knowledge, this is the first study in veterinary medicine to compare two ophthalmic gel formulations in dogs by evaluating the evolution of Central Tear Film Thickness (CTFT) over time using spectral-domain optical coherence tomography (SD-OCT). This methodology, previously applied in humans to assess tear film clearance noninvasively [9], provides a quantitative approach to compare lubricant persistence over time on the ocular surface. Our findings demonstrate a significantly longer ocular surface retention for the carbomer–hyaluronate combination (Eye Lube Pro) compared to carbomer alone (Ocry-gel). After 60 min, CTFT remained measurable in 70% of eyes having received Eye Lube Pro versus only 10% with Ocry-gel. These results are consistent with data obtained using fluorophotometry in dogs [10], which demonstrated that viscous formulations such as gels persist significantly longer on the ocular surface than aqueous solutions. The enhanced performance of Eye Lube Pro likely stems from the viscoelastic, mucoadhesive, and hydrophilic properties of hyaluronic acid (HA), which are well established in both human and veterinary ophthalmology [4–6]. HA increases residence time through strong water retention, pseudoplastic behavior, and adherence to the ocular mucins. These properties are further enhanced when HA is cross-linked, as shown in experimental studies using fluorescent tracking in dogs [8], rabbits, and rodents [11, 12]. In our study, the HA used in Eye Lube Pro was linear; however, its combination with carbomer—a high molecular weight polymer with mucoadhesive and water-retaining properties—may produce a synergistic effect [5, 6, 8]. This approach has already been supported in human clinical studies, where formulations combining HA with carbomer provided better symptom relief and tear film stability than carbomer alone [6]. Our protocol was directly adapted from the study by Gagliano et al. [9], using repeated SD-OCT measurements to assess CTFT centrally over time. As noted in their work, when CTFT drops below ~5 μm, the reflectivity of the interface diminishes, possibly leading to underestimation of lubricant persistence at later timepoints [9]. However, in our model, general anesthesia limited lacrimal stimulation and blinking, reducing interindividual variability and improving measurement repeatability [3]. The use of SD-OCT to assess the anterior segment in veterinary species has been validated

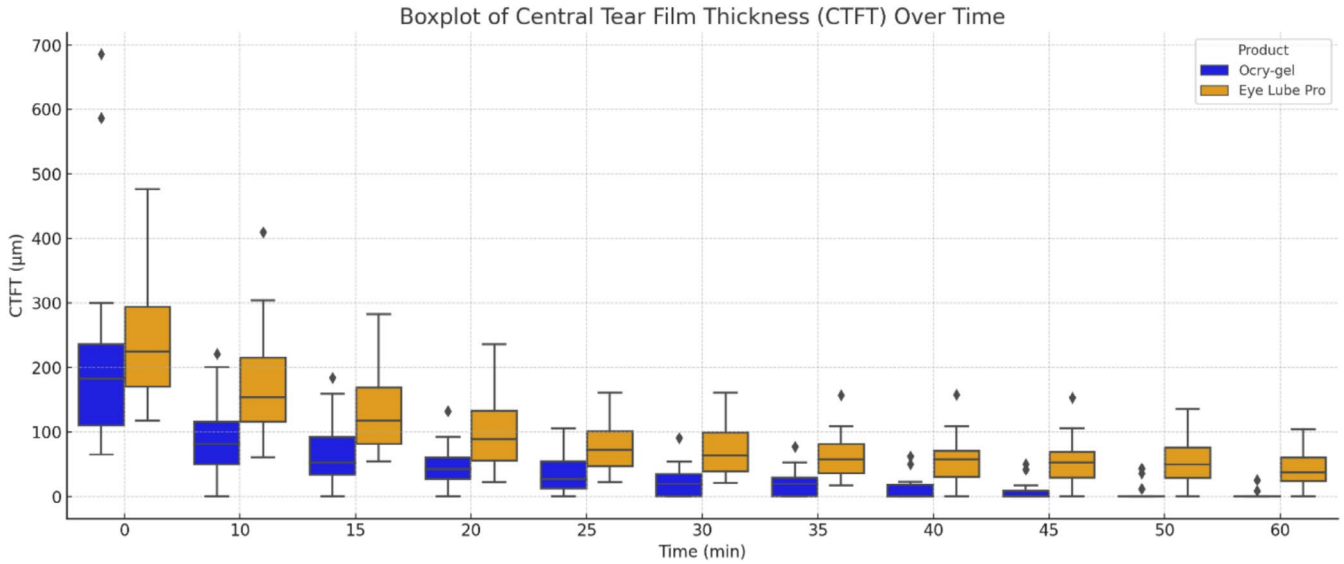

FIGURE 5 | Boxplot distribution of Central Tear Film Thickness (CTFT) over time following instillation of Ocry-gel (blue) and Eye Lube Pro (orange) in anesthetized dogs. CTFT was measured using spectral-domain OCT at multiple time points post-application. Each box represents the interquartile range (IQR) with the median (horizontal bar), and whiskers indicate variability outside the upper and lower quartiles. Ocry-gel demonstrated a rapid decline in CTFT values over time, with most eyes reaching the lower limit of quantitation before 45 min. In contrast, Eye Lube Pro maintained higher and more consistent CTFT levels throughout the 60-min follow-up period, reflecting greater pre-corneal stability.

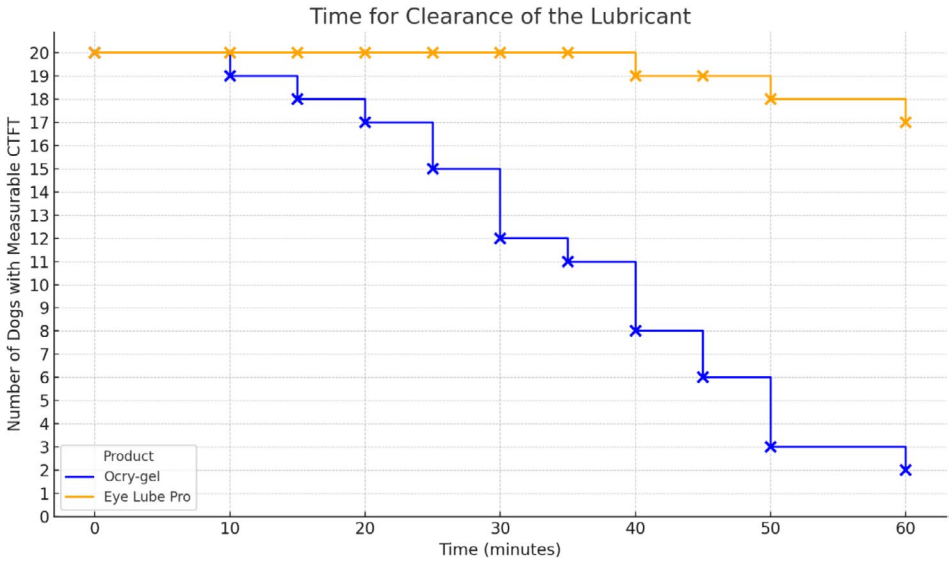

FIGURE 6 | Time-dependent clearance of the two ophthalmic lubricants as assessed by spectral-domain optical coherence tomography (SD-OCT). The graph shows the number of eyes with a measurable Central Tear Film Thickness (CTFT > 0 µm) at each time point following instillation of Ocry-gel (blue) and Eye Lube Pro (orange). Data are represented as stepwise curves to reflect the discrete loss of detectable product over time. Eye Lube Pro exhibited a slower clearance profile, with 14 out of 20 eyes still showing a measurable pre-corneal layer after 60 min, compared to only 2 with Ocry-gel.

in dogs [3], and comparable anterior segment analyses have also been conducted in rabbits [13], cats [14], and rabbits again using Scheimpflug imaging [13]. These confirm the relevance of central optical metrics as indicators of ocular surface changes in veterinary ophthalmology. Beyond conventional gels, recent experimental formulations—including bioinspired hydrogels, nanoparticles coated with HA, and in situ gelling drug delivery platforms [13]—have also shown improved retention and ocular surface coverage. Such strategies aim to extend tear film stability, reduce dosing frequency, and improve patient comfort, and may benefit from assessment using the type of time-resolved OCT-based kinetic model we describe. Limitations of our study include the moderate sample size and heterogeneity in breed, age, and skull morphology. Nonetheless, this reflects clinical reality in veterinary ophthalmology, increasing external validity [1]. As observed in earlier studies on lubricant efficacy in KCS [6], neither age, sex, nor brachycephalic phenotype significantly influenced CTFT profiles, reinforcing the interpretation that formulation properties themselves drive ocular persistence.

Another limitation of this study is that the two formulations differed not only by the presence of hyaluronic acid, but also by their

carbomer concentration (0.2% in Ocry-gel versus 0.45% in Eye Lube Pro). This difference in polymer content may itself influence viscosity and ocular surface retention, making it difficult to attribute the observed effect solely to the addition of hyaluronic acid.

An additional limitation of the study is that the standardized ophthalmic examination was performed only at 48 h post-surgery. While this timeframe allowed for the detection of persistent or clinically relevant adverse effects, it cannot exclude the possibility that transient corneal erosions or minor lesions occurring immediately after gel instillation may have already healed and thus remained undetected.

In conclusion, our results support the use of carbomer–HA combinations such as Eye Lube Pro for prolonged ocular surface protection in dogs and validate OCT-based CTFT kinetics as a robust framework for future comparative lubricant studies in veterinary species.

5 | Conclusion

This study provides first-time evidence that spectral-domain OCT can be used to objectively monitor and compare the CTFT profiles of tear substitute gels in dogs. The addition of sodium hyaluronate to a carbomer-based formulation significantly improves precorneal retention under controlled experimental conditions. These results support the use of dual-polymer gels like Eye Lube Pro in clinical settings requiring sustained ocular surface protection. Further studies should expand this approach to other species, more diverse formulations, and disease contexts such as keratoconjunctivitis sicca.

Acknowledgments

The authors thank the team at AnimaVet and the participating dog owners. We also thank Dômes Pharma for supporting the study design and statistical analysis, without influence over the data collection, interpretation, or writing process. AI Use Statement: Artificial intelligence was used during manuscript preparation solely for grammar and language editing. All scientific content and analysis were created by the authors.

Ethics Statement

All procedures involving animals were approved by the Animal Ethics Committee of VetAgro Sup, Lyon, France (approval number: 2456). The research complied with Directive 2010/63/EU and ARVO guidelines.

Consent

Written informed consent was obtained from all dog owners prior to inclusion.

Conflicts of Interest

Dômes Pharma contributed to the study design, statistical analysis and manuscript reviewing but had no role in data collection, interpretation, or drafting. No financial compensation was received.

Data Availability Statement

The data that support the findings of this study are openly available in Table – Stability Study OcryGel vs EyelubPro at http://www.doi.org/10.6084/m9.figshare.29093348.

References

1. L. Bedos, R. A. Allbaugh, M. Roy, M. A. Kubai, and L. Sebbag, "Precorneal Retention Time of Ocular Lubricants Measured With Fluorophotometry in Healthy Dogs," *Veterinary Ophthalmology* 26, no. Suppl 1 (2023): 81–88.

2. M. E. Johnson, P. J. Murphy, and M. Boulton, "Carbomer and Sodium Hyaluronate Eyedrops for Moderate Dry Eye Treatment," *Optometry and Vision Science* 85, no. 8 (2008): 750–757.

3. H. Wolfel, C. Lucca, C. E. Plummer, G. Ben-Shlomo, and G. E. Moore, "Canine Central Corneal Thickness Measurements via Pentacam-HR Optical Tomography," *Veterinary Ophthalmology* 21, no. 4 (2017): 362–370.

4. D. L. Williams, "Optimising Tear Replacement Rheology in Canine Keratoconjunctivitis Sicca," *Eye* 32, no. 1 (2018): 195–199.

5. C. Gard, C. Cassagnes, S. Muller, C. Navarro, and B. Jahier, "Evaluation of a Preservative-Free, Cross-Linked Sodium Hyaluronate-Based Solution, Lacri+, in Dogs With Dry Eye: A Pilot Trial," *Irish Veterinary Journal* 76 (2023): 30.

6. K. Marner, P. M. Møller, M. Dillon, and E. Rask-Pedersen, "Viscous Carbomer Eye Drops in Patients With Dry Eyes: Efficacy and Safety. A Randomized, Open, Cross-Over, Multicentre Study," *Acta Ophthalmologica Scandinavica* 74, no. 3 (1996): 249–252.

7. S. Atzet, F. Montiani-Ferreira, D. J. Haeussler, E. K. Behan, and A. Fankhauser, "Fluorometric Evaluation of Cross-Linked vs Linear Hyaluronic Acid Eye Lubricants," in *ACVO Conference Proceedings*, vol. 170 (Palm Springs, CA, 2022).

8. M. H. Chan, C. L. Tseng, W. H. Huang, and C. T. Lin, "Assessment of Gelatin-Epigallocatechin Gallate Nanoparticles With Hyaluronic Acid Coating for Treating Dry Eye Associated Keratopathy in Rats," *Journal of Veterinary Medical Science* 87, no. 4 (2025): 364–376.

9. C. Gagliano, V. Papa, R. Amato, G. Malaguarnera, and T. Avitabile, "Measurement of the Retention Time of Different Ophthalmic Formulations With Ultrahigh-Resolution Optical Coherence Tomography," *Current Eye Research* 42, no. 12 (2017): 1714–1719.

10. L. Andrade Ramos, C. V. Seullner Brandão, C. G. Arce, et al., "Dual-Scheimpflug-Placido-Disc Corneal Analysis in Cats," *Veterinary Ophthalmology* 25, no. 5 (2022): 360–366.

11. F. Li Puma, S. Picciolini, G. Rossi, et al., "Iridocorneal Angle Assessment of Companion Rabbits Using Gonioscopy, Spectral-Domain Optical Coherence Tomography, High-Resolution Ultrasound, and Pentacam HR Imaging," *Veterinary Ophthalmology* 22, no. 6 (2019): 834–841.

12. H. Yüksel, F. M. Türkcü, S. Ari, et al., "Anterior Segment Parameters of Rabbits With Rotating Scheimpflug Camera," *Veterinary Ophthalmology* 18, no. 3 (2015): 210–213.

13. J. Li, Y. Zhang, C. Wu, et al., "A Bioinspired Synthetic Soft Hydrogel for the Treatment of Dry Eye," *Bioactive Materials* 14 (2022): 312–324.

14. D. Santillo, S. Arpaia, C. Toschi, M. C. Marchesi, and P. L. Dodi, "The Effect of Periocular Fatty Acids and 0.15% Hyaluronate Eye Drops Application on Keratoconjunctivitis Sicca in Dogs: An Exploratory Study," *Veterinary Ophthalmology* 26, no. 3 (2023): 199–208.

Supporting Information

Additional supporting information can be found online in the Supporting Information section. **Video S1:** Instillation technique of the ophthalmic gel in a dog positioned in dorsal recumbency during surgery.