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ORIGINAL INVESTIGATION

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Contouring in the optic plane improves the accuracy of computed tomography-based segmentation of the optic pathway

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Abstract

Canine optic pathway structures are often contoured on CT images, despite the difficulty of visualizing the optic pathway with CT using standard planes. The purpose of this prospective, analytical, diagnostic accuracy study was to examine the accuracy of optic pathway contouring by veterinary radiation oncologists (ROs) before and after training on optic plane contouring. Optic pathway contours used as the gold standard for comparison were created based on expert consensus from registered CT and MRI for eight dogs. Twenty-one ROs contoured the optic pathway on CT using their preferred method, and again following atlas and video training demonstrating contouring on the optic plane. The Dice similarity coefficient (DSC) was used to assess contour accuracy. A multilevel mixed model with random effects to account for repeated measures was used to examine DSC differences. The median DSC (5th and 95th percentile) before and after training was 0.31 (0.06, 0.48) and 0.41 (0.18, 0.53), respectively. The mean DSC was significantly higher after training compared with before training (mean difference = 0.10; 95% CI, 0.08–0.12; $P < 0.001$) across all observers and patients. DSC values were comparable to those reported (0.4–0.5) for segmentation of the optic chiasm and nerves in human patients. Contour accuracy improved after training but remained low, potentially due to the small optic pathway volumes. When registered CT-MRI images are not available, our study supports routine addition of an optic plane with specific window settings to improve segmentation accuracy in mesaticephalic dogs ≥11 kg.

KEYWORDS
cross-sectional imaging, radiation oncology, veterinary

1 | INTRODUCTION

Dose constraints for the optic nerves and optic chiasm (also known as the optic pathway) applied during radiation treatment planning impact radiation plan evaluation and quality for dogs with head tumors. Radiation therapy planning for the head is often based on CT alone despite the difficulty in visualizing the canine optic pathway with CT imaging using standard transverse, reconstructed sagittal, and dorsal planes. Optic pathway delineation is usually performed based on other anatomical landmarks when visualization of the optic pathway

ABBREVIATIONS: DSC, Dice similarity coefficient; PDF, portable document format; RO, radiation oncologist; TPS, treatment planning system.

itself is not possible, introducing uncertainty in the accuracy of the contours. With stereotactic radiation prescriptions becoming more frequently implemented in the canine head region,[1–6] the accuracy of optic pathway contours is critical to prevent optic neuritis and to ensure the preservation of patient vision, particularly as recommended dose constraints for the optic pathway are considerably lower than dose constraints when conventional fractionation is used.[7–9] For example, while for a 30-fraction conventional protocol, less than 0.5cc of the optic pathway should receive a total dose equal to or greater than 44 Gy, the recommended volume constraint for the human optic pathway for a 3-fraction stereotactic protocol is that less than 0.2cc of optic pathway receives a total dose equal to or greater than 15.3 Gy.[9]

Contouring guidelines could potentially improve consistency and accuracy. To date, there is little guidance published regarding optic pathway delineation for veterinary patients. There is one published guideline for contouring the feline optic pathway from the transverse view utilizing both CT and MRI.[10] Several studies have focused on the identification of the optic pathway using advanced imaging in the dog.[11–13] However, to the best of the authors' knowledge, there have been no studies that describe a method for contouring the canine optic pathway.

Modern contouring software allows for viewing images at any angle, enabling visualization of features commonly obscured in the standard planes. The use of nonstandard planes opens the possibility of visualizing the optic nerves from the globe to the opening of the optic canals when the viewing angle is set to a dorsal oblique plane parallel to the optic nerves, henceforth referred to as the optic plane, and an appropriate window width and level is selected. The purpose of this study was to examine the accuracy of optic pathway contouring by board-certified veterinary radiation oncologists before and after training guidelines were provided for canine optic pathway contouring using an optic plane. The study hypothesis was that optic pathway contouring accuracy would increase after training on optic plane contouring.

2 | MATERIALS AND METHODS

2.1 | Selection and description of subjects

This prospective, analytical, diagnostic accuracy study was approved by the University of Saskatchewan Institutional Behavioral Ethics Review Board (BEH-2406) and the Animal Research Ethics Board (AUP-20200114). Eight client-owned dogs were recruited for study participation. Inclusion criteria included canine patients referred for radiation therapy and weight >5 kg. Dogs with a disease process in the region of the optic pathway were excluded. The final inclusion/exclusion decisions were made by a board–certified veterinary radiation oncologist (M.M., ACVR [RO]).

Each dog underwent pre-and post-contrast CT and MRI under the same anesthetic event; imaging was acquired between November 2020 and October 2021. All dogs were immobilized in sternal recumbency for imaging using a vacuum fixation cushion (SecureVac, Bionix Radiation Therapy, Toledo, OH), a thermoplastic neck cushion (Klarity Moldable AccuCushion, Klarity Medical Products, Newark, OH), and a custom acrylic maxillary plate with a vinyl bite block (VP Mix Putty, Henry Schein Inc., Melville, NY). A thermoplastic head mask covered the head (Green Profile Frame Extended Head Mask, Klarity Medical Products) and was attached, along with the maxillary plate, to an acrylic baseplate (Klarity MultiFix AIO Baseplate, Klarity Medical Products). A 64-slice CT scanner (Discovery MIDR, GE Medical Systems, Waukesha, WI) was used to acquire images for contouring. Scanning parameters included 120 kVp, 150–500 mA, tube rotation time 0.7 s, and 512 × 512 matrix dimensions. Iohexol (Omnipaque, 350 mgI/mL, GE Healthcare, Chicago, IL) at 2 mL/kg was administered intravenously three minutes prior to acquisition of postcontrast images. Reconstruction algorithms included soft tissue and bone window levels at a slice thickness of 1.25 mm. A 1.5 Tesla MR unit (Siemens Symphony, Siemens, Oakville, ON, Canada) was used to acquire fat-saturated T2-weighted (TR 3000–4000 ms, TE 75 ms) sequences in the optic plane.

The CT and MR images were registered in a treatment planning system (TPS) (Eclipse version 13.6, Varian Medical Systems, Palo Alto, CA) and the optimal window level and width for soft tissue or full window reconstruction that distinguished the optic nerve from surrounding soft tissue were determined (Figure 1). Consensus (gold standard) contours of the optic pathway were developed by one veterinary radiation oncologist (M.M.), two veterinary ophthalmologists (L.S, DVS(O); S.O., ACVO), one veterinary radiologist (E.R., ACVR), and one dual-boarded veterinary radiologist and radiation oncologist (L.G., ACVR, ACVR [RO]). Separate contours were created for the left and right optic nerves as well as the optic chiasm.

2.2 | Data recording and analysis

Email invitations to participate were sent to 114 board-certified veterinary radiation oncologists. Thirty-six agreed to participate in the study and provided informed consent. Each participant was assigned a random two-digit identifying number that was used to link contours with participants, and only the resident (E.W.) had access to this information. Contouring was performed in two phases (before and after the provision of an optic pathway contouring training guide). After phase one contouring was completed, a short, anonymous questionnaire (SurveyMonkey, San Mateo, CA) was sent to all participants that completed the contours with the purpose of describing the participating population. The participants were asked five questions: how frequently they contour the optic pathway based on CT imaging in their clinical practice, what plane(s) of CT imaging they use to contour the optic pathway, and the percentage of time they use those plane(s), whether the TPS used for the study prevented them from performing any of their normal contouring practices, what type of practice they primarily work at, and whether they had additional comments on the study (with the option to add comments).

Participants were supplied with remote access credentials to connect via Microsoft Remote Desktop (Microsoft Corporation, Redmond, WA) to the same treatment planning system used to create the con-

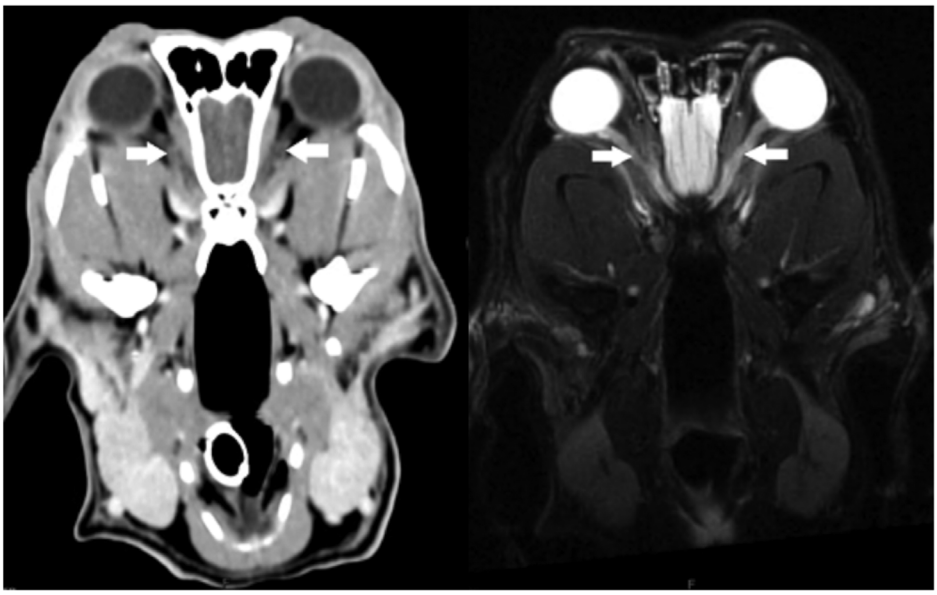

FIGURE 1 Dorsal oblique CT (left) and fat-saturated T2-weighted MR (right) images showing the optic nerves (arrows) of a dog. The angles of the images were chosen to coincide with the extracranial path of the optic nerves. The CT window level of 40, and window width of 150, were selected to optimize the visualization of the optic apparatus.

TABLE 1 List of steps for contouring the optic pathway.

1. Use a window level of 40 and a window width of 150 (corresponding to an upper grey level of 115 and a lower grey level of −35).
2. Rotate the sagittal view until the hard palate of the dog is approximately 35–45 degrees off the vertical axis.
3. Use the dorsal plane window, now the optic plane, to make slight adjustments to the viewing angle to maximize the length of the visible nerve.
4. Contour the optic nerves from the caudal globe to the opening of the optic canal.
5. Use the transverse view and bone windowing to extend the optic nerve contours caudally through the optic canal to the level at which the presphenoid bone between the two canals begins to recede.
6. Starting on the next slice caudally, switch back to a window level of 40 and a window width of 150 and contour the region of slightly decreased density as optic chiasm for two to three slices.

sensus contours. All CT image sets were anonymized, and a structure set was created for each participant containing three empty structures (Optic Nerve L, Optic Nerve R, Optic Chiasm). Access to the remote system was managed through a Google Sheets document (Google, Inc., Mountain View, CA) in 4 or 8 h blocks, each separated by 1 h to allow time for structure sets to be backed up and changed out between participants. All participants independently contoured the optic pathway in all dogs using their preferred method using the supplied structures. The structure sets were associated with a post-contrast soft tissue CT reconstruction and with an available registered bone reconstruction dataset.

To reduce recall bias, participants waited at least three weeks before beginning phase two. Scheduling was done as in phase one. Participants were instructed to follow a specific contouring sequence, utilizing the optic plane, described in a portable document format (PDF) training atlas. The resident (E.W.) developed the contouring sequence described in the training atlas under the supervision of a veterinary radiation oncologist (M.M.). The supervision involved direct contact as well as independent work by the resident with review and feedback from the radiation oncologist. The steps described in the training atlas are presented in Table 1. To supplement the training atlas, an optional 4 min video demonstrating the method was also created by the resident (E.W.) and provided to study participants.

The training atlas instructed participants to contour using a preset window level of 40 and a window width of 150 (corresponding to an upper gray level of 115 and a lower gray level of −35 on a soft tissue reconstruction, and then to rotate the dorsal plane view to a dorsal oblique angle coinciding with the extracranial path of the optic nerves (i.e., the optic plane). This was achieved by rotating the sagittal view until the hard palate of the dog was approximately 35°–45°off the vertical axis, then scrolling through the dorsal oblique (optic) plane until the maximum extracranial length of optic nerves could be visualized (Figure 1).

The participants were then instructed to contour the extracranial portion of the optic nerves using the optic plane from the caudal globe to the opening of the optic canal, using a brush size of 3–4 mm in diameter.

After completion of extracranial contouring, the participants were directed to switch to the transverse view and use a bone window to extend the contours through the optic canal to the level at which the

presphenoid bone between the two optic canals initially recedes. Participants were then instructed to scroll to the next caudal slice, switch back to a window level of 40 and width of 150, and contour the region of slightly decreased density as optic chiasm for 3–4 mm caudally, which corresponded to two to three slices based on the slice thickness used in the datasets.

A modified PDF training atlas (https://hdl.handle.net/10388/14383) and a 7 min video (https://hdl.handle.net/10388/14377) were developed by the resident (E.W.) and a radiation oncologist (M.M.) after data collection was completed to demonstrate the contouring method tested in this study; these were similar to the materials provided to the participants but did not include study-specific information and provided more detail on optic chiasm contouring to address participant variation in chiasm definition.

2.3 | Statistical analysis

All analysis was completed with commercially available software (STATA/SE version 17 for Windows, StataCorp, College Station, TX) under the supervision of an analytic epidemiologist (S.P.). For each image set, the TPS was used by a radiation oncology resident (E.W.) to measure the Dice similarity coefficient (DSC) between each observer's optic pathway contour and the expert consensus contour. The median, range, and 5th and 95th percentiles were calculated for the DSC before and after the training atlas intervention. A multilevel mixed model with random effects to account for repeated measures on patients and by observers was used to examine the difference in the DSC before and after the training atlas intervention; predicted mean differences between pre-and post-training were reported with 95% confidence intervals. The Kruskal–Wallis test was used to assess the association between dog weight category ($>$ or $\leq$ the median weight) and the DSC for optic pathway contours. *P*-values ≤ 0.05 were considered significant.

3 | RESULTS

The median age and weight of the study dogs were 12.6 years (range, 11–15.3 years) and 23.5 kg (range, 11–53 kg), respectively. There were two neutered males, five spayed females, and one intact female. Breeds included mixed (n = 4), Dachshund (n = 1), Queensland Blue Heeler (n = 1), Border Collie (n = 1), and Newfoundland (n = 1). Dogs were referred for treatment of an oral melanoma (n = 6) or nasal adenocarcinoma (n = 2). One dog was brachycephalic and seven were mesaticephalic. The median volume of the dogs' optic pathway contours reached by expert consensus was 1.25 cm^3 (range, 0.7–3 cm^3).

Of the 36 veterinary radiation oncologists who consented to participate in the study, 28 completed the first phase of contouring on all eight dogs, and 21 completed the second phase of contouring. Participants who failed to complete both phases of contouring were excluded from the analysis (n = 7).

During the first phase of contouring, registration errors between the soft tissue and bone CT reconstructions were noted in three dogs. The errors were small (maximum of 0.8 mm translational and 0.1° rotation) and likely secondary to the innate movement of the dog between successive scans that could not be accounted for in the TPS autoregistration. After the registration errors were corrected, all participants were given the opportunity to review their contours for accuracy. One participant was unable to review their contours before the start of phase two, therefore the contours of that participant for these three dogs were excluded from the analysis. It was also found that for one dog, the soft tissue reconstruction provided to participants was pre-contrast. By the time this was noticed, the raw CT data had been deleted and it was not possible to generate a new reconstruction, so no correction was made.

Ninety-six percent (27/28) of respondents completed the online questionnaire. Participants who did not complete phase two contours were included in the questionnaire results because the survey was anonymous, preventing the identification and removal of participants who did not complete phase two. Responses to the questionnaire are presented in Table 2. Of the six respondents who indicated that the TPS used for the study prevented them from using their normal contouring practices, five commented that the transverse plane resolution did not allow for a small enough brush size, and one did not provide an explanation. General comments on the study included more detailed information about optic nerve contouring at the participants' practice (n = 4).

The median DSC for the first phase of contouring, prior to standardized optic pathway training, was 0.31 (5th and 95th percentile, 0.06, 0.48). Phase two median DSC was 0.41 (5th and 95th percentile, 0.18, 0.53).

The mean DSC for the optic pathway contours was significantly higher after training than before training (mean difference = 0.10; 95% CI, 0.08–0.12; $P < 0.001$) on average across all observers and patients. Dogs weighing $\leq$23.5 kg had a median DSC of 0.33 (5th and 95th percentile 0.1, 0.5), which was significantly ($P < 0.001$) lower than the median DSC of 0.41 (5th and 95th percentile 0.08, 0.53) for dogs weighing $>$23.5 kg. Body weight and consensus optic pathway volume were highly correlated (0.93).

4 | DISCUSSION

The findings of the study supported our study hypothesis: manual segmentation of the canine optic pathway was significantly improved following the implementation of specific training guidelines for the use of the optic plane and window settings to optimize optic nerve and chiasm visualization in a popular, commercially available TPS (Eclipse). This is the first study to evaluate a training method to address potential inaccuracies in the optic pathway contours that are used in radiation treatment planning for canine patients.

Although the optimal setting for individual systems may vary, a window level of 40 and a window width of 150 were found to provide the most contrast between soft tissue and the optic nerves on the TPS

TABLE 2 Optic pathway contouring practices of members of the American College of Veterinary Radiology (subspecialty radiation oncology) (n = 27 respondents).

Variable		N	%
Which statement best describes how frequently, on average, contouring of the optic pathway on CT is part of your clinical practice?	≥1 CT optic pathway contouring per day	2	7
	<1 CT per day, ≥1 CT optic pathway contouring per week	8	30
	<1 CT per week, ≥1 CT optic pathway contouring per month	6	22
	<1 CT optic pathway contouring per month	5	19
	Never contour optic pathway on CT images	6	22
Which plane(s) of CT imaging do you use for contouring the optic pathway?[a]	Transverse (axial)	24	96
	Dorsal (frontal)	22	88
	Sagittal	17	68
	Other	8	29
For approximately what percentage of optic pathway contouring do you use those CT plane(s)?[b]	Transverse (axial)		68
	Dorsal (frontal)		22
	Sagittal		6
	Other		4
Did the study treatment planning software prevent you from performing any of your normal contouring practices?	Yes	6	22
	No	21	78
At what type of practice do you primarily work?	Academia	18	67
	Private practice	8	30
	Other	1	4

[a]Twenty-five participants answered this question.
[b]The percentage of time the plane was used across all participants.

used for the current study. It is important to note that the window level setting must be applied to the standard or soft-tissue reconstructions. Modifications to the image data from other reconstruction algorithms remove image data in this viewing region that impairs visualization of the optic nerves.

The total number of slices to contour will vary based on slice thickness and transverse window size. A CT slice thickness greater than 1.5 mm is not recommended for contouring small-volume organs at risk, such as the optic nerves.[14] For the current study, in which a 1.25 mm slice thickness was used, six to ten slices in the optic plane were sufficient to contour the extracranial optic nerves for most dogs. While contouring in the optic plane, some bleed-through of the contours to slices before and after the contoured slice will occur. This is presumably due to the non-spherical shape of the voxels making up the three-dimensional representation of the dog. Additionally, the contours will become very small for one to three slices after switching back to the transverse view at the caudal end of the contour. This is due to the rounded end of the contour as it is translated back to a transverse view. Delineating the optic nerves can therefore be challenging in this plane and contours should be evaluated in all planes prior to approval. For example, small contours on the cranial or caudal ends of the transverse structure sections should be expanded to ensure they are at least 3 to 4 mm after switching from the optic plane.

The accuracy of CT-based contours remained low after training. The DSC values in our study were comparable to those reported for manual and automatic segmentation of the optic chiasm and nerves in human patients (DSC, 0.4–0.5).[15] In that study, contours were compared between eight physicians and two autosegmentation methods for 20 human patients in which the eyes, optic pathway, and brainstem were contoured.[15] The low DSC score was explained by the small volume and tubular shape of the optic pathway. Because the DSC compares the overlap of true positive (the voxels included in both contours), to the true negative and false negative (the voxels contoured by only one contour), then if for both a large structure and a small structure the same number of voxels fall into the true or false negative category, the resulting ratio between positive and negative will be smaller and result in a lower DSC for the smaller structure. Our finding of lower accuracy in smaller dogs is consistent with the supposition that smaller volumes reduce DSC values.

There are additional factors that may have negatively affected post-training accuracy. Monitor quality could not be controlled for, and the use of low-quality monitors may have impacted the results. If a participant contoured on a low-quality laptop screen using bony landmarks for contouring the optic pathway, the image quality may not have been sufficient to visualize subtle attenuation changes between the optic nerves and soft tissue. Minimum contouring brush sizes available in the TPS of 3 mm (n = 2), 4 mm (n = 3), or 5 mm (n = 1) for some dogs could have resulted in inferior contours in either phase due to the increased difficulty in contouring smaller volumes. This limitation was presumably due to a combination of the small patient size and

increased dimensions of the transverse window of the image. Notably, six participants stated that they never contour the optic pathway on CT, and one stated that they had done no contouring during the prior 2 years, therefore a lack of contouring experience could also have contributed to reduced accuracy in each phase of the study. However, we do not know if these six participants completed both phases of contouring due to the anonymous nature of the questionnaire. The training method could have also negatively impacted phase two accuracy. The instructions may have been unclear or difficult to understand, and it is also possible that participants failed to use the training atlas and video as instructed.

Even though participants contoured three separate structures, we elected to present results for the entire optic pathway (combined optic nerves and chiasm) because a small number of participants mislabeled the left and right optic nerves and there was a subset of participants that contoured the optic nerves within the optic canal as chiasm in phase one (n = 6). Although the participants were instructed in the training atlas to define the structure within the optic canal as optic nerve, some participants continued to contour chiasm into the optic canal in phase two (n = 3). The instructions for contouring the optic chiasm in the training atlas were developed to be consistent with the published anatomical description, which states that the chiasm is caudal to the optic canal at the rostroventral floor of the middle cranial fossa, where the fibers from the left and right optic nerve cross.[16] Combining all structures into a single contour eliminated participant variability for when the optic nerves ended and the chiasm began.

Accurate contouring of each portion of the optic pathway separately can aid in treatment planning; if one eye must be in or near the high-dose planning region to adequately treat a tumor, it may be possible to spare vision in the contralateral eye. In such an instance, it would be important to avoid exceeding the tolerance dose in one optic nerve and the chiasm, thus supporting a need to separate left and right structures.

The recommended brush size of this study of 3–4 mm closely matches the previously reported measurement methodology. One previous study reported a mean diameter of 3.7 mm for the optic nerve sheath for a group of 10 dogs with a mean weight of 17.0 kg, comprised of crossbreeds (n = 5), beagles (n = 4), and a Labrador retriever.[12] That study utilized a dorsal oblique (optic plane) MRI scanning angle and distinguished between the optic nerve and optic nerve sheath. The current study chose not to distinguish between optic nerve and optic nerve sheath because it is not possible to make that distinction in CT imaging.

Based on our review of the literature, there is no other published study investigating the accuracy of contours drawn on nonstandard viewing planes. Prior recommendations have been to draw contours on the transverse view, with Scoccianti et al. (2015) recommending observation of positioning in the dorsal and sagittal views to verify the location of the contours.[10,17]

This study demonstrates that it is possible to reliably distinguish nerves from surrounding soft tissue when using appropriate windowing and viewing angle. It may be possible to apply this technique to nerves near other sites to more accurately apply constraints when planning other anatomic regions.

Future studies investigating alternative contouring methods may benefit from a live hands-on training session so that participants can ask questions and receive feedback. Multiple presentation formats may improve support for multiple learning styles and ensure compliance with the recommended technique. Additional research could also be performed to investigate optic nerve movements over successive anesthetic events. Costa et al.[18] found that the anesthetic protocol can affect globe position and Drolet et al.[19] uncovered ultrasonographic evidence that optic nerve sheath diameter is impacted by anesthesia. Research into optic nerve movement could result in the recommendation for an expansion of delineation to allow for movement and improve optic tract avoidance.

Contours created in the optic plane often translate to contours in the transverse plane that are not smooth, but this may depend on the TPS and user. The impact on the TPS of this characteristic was not explored, however, it is presumably dependent on the implementation of the dose calculation algorithm and readers who create contours in the optic plane should contact the software development team for their TPS for guidance on the need to smooth contours in the transverse or other planes for organs at risk.

One important limitation of this study is the inclusion of only one brachycephalic dog. The recruitment period available for this study was limited, and only one brachycephalic dog presented for radiation during the period. Consequently, results from this study may not be applicable to brachycephalic dogs. The brachycephalic dog in this study had the lowest average scores from both phases, however, it was also the smallest dog by weight. Another limitation was the limited MRI sequences available for the expert reference contours. To meet imaging time constraints at the study institution, some cases only had the optic plane T2 fat saturation sequence covering the optic pathway.

The use of MRI for optic pathway contouring is expected to provide the highest accuracy, especially with small dogs. However, when CT alone is used, our study supports the routine use of an optic plane contouring method as described, with a window level of 40 and a window width of 150 to improve segmentation accuracy.

AUTHOR CONTRIBUTIONS

Category 1

(a) Conception and Design: Walther, Mayer
(b) Acquisition of Data: Walther
(c) Analysis and Interpretation of Data: Walther, Griffin, Randall, Sandmeyer, Osinchuk, Sukut, Hansen, Keyerleber, Lawrence, Parker, Mayer

Category 2

(a) Drafting the Article: Walther, Mayer
(b) Revising Article for Intellectual Content: Walther, Griffin, Randall, Sandmeyer, Osinchuk, Sukut, Hansen, Keyerleber, Lawrence, Parker, Mayer

Category 3

(a) Final Approval of the Completed Article: Walther, Griffin, Randall, Sandmeyer, Osinchuk, Sukut, Hansen, Keyerleber, Lawrence, Parker, Mayer

Category 4

(a) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: Walther, Griffin, Randall, Sandmeyer, Osinchuk, Sukut, Hansen, Keyerleber, Lawrence, Parker, Mayer

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest. PetCure Oncology played no role in determining the content for this paper.

PREVIOUS PRESENTATION OR PUBLICATION DISCLOSURE

The findings of this study were presented at the 2022 ACVR annual scientific meeting.

REPORTING CHECKLIST DISCLOSURE

No EQUATOR network or other reporting checklist was used.

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