COMPARISON OF COMPUTED TOMOGRAPHY AND MYELOGRAPHY TO A REFERENCE STANDARD OF COMPUTED TOMOGRAPHIC MYELOGRAPHY IN THE EVALUATION OF DOGS WITH INTERVERTEBRAL DISC DISEASE

By

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COMPARISON OF COMPUTED TOMOGRAPHY AND MYELOGRAPHY TO A REFERNCE STANDARD OF COMPUTED TOMOGRAPHIC MYELOGRAPHY IN THE EVALUATION OF DOGS WITH INTERVERTEBRAL DISC DISEASE

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CHAPTER I

INTRODUCTION

Hansen type I intervertebral disc disease is a common cause of acute canine myelopathy. Myelography has been the standard diagnostic used for localization and lateralization of Hansen type I extrusions for many years. With the growing popularity and availability of computed tomography (CT) and magnetic resonance imaging (MRI), many surgeons and neurologists now use these cross-sectional imaging techniques as the sole diagnostic tool for surgical planning. All imaging techniques have inherent limitations and limited comparative studies exist to guide clinicians regarding which techniques have superior accuracy[1-5]. The accuracy of CT and myelography has been found to be similar when compared to surgical findings in chondrodystrophic dogs with intervertebral disc disease[1-3]. However, the use of surgical findings as a reference standard has been questioned due to a high degree of bias and limited ability to circumferentially inspect the spinal canal when performing a hemilaminectomy[6]. A prospective comparison of CT, nonselective angiographic CT, myelographic CT, and myelography in dogs with various myelopathies found that CT myelography had the highest accuracy when compared to surgical findings[5]. This study found poor accuracy of CT and nonselective angiographic CT unless intervertebral disc material was mineralized or neoplasms caused bony lysis. The purpose of the following study was to prospectively compare the diagnostic accuracy of CT and myelography to a reference standard of CT myelography in evaluating chondrodystrophic dogs with intervertebral disc extrusions. Our null hypothesis was that there would be no difference in the diagnostic accuracy.

CHAPTER II

MATERIALS AND METHODS

Chondrodystrophic dogs that were presented with acute onset myelopathy were prospectively recruited to the study with owner consent. None of the dogs had a history of trauma. The study protocol was approved by the Institutional Animal Care and Use Committee.

All dogs received a complete neurologic examination by either a veterinary surgical resident or board certified veterinary surgeon. After a pre-anesthetic complete blood count and serum biochemistry panel were performed, anesthetic protocols were chosen by the anesthesiologist to meet specific patient needs. Following anesthetic induction, CT of the spine was performed using a four slice CT scanner[a]. Dogs were scanned from the base of the skull through the fourth thoracic vertebra when neurologic examination suggested a C1-5 or C6-T2 myelopathy. Dogs were scanned from the tenth thoracic through the fifth lumbar vertebra when neurologic examination suggested a T3-L3 myelopathy. Dogs were scanned from the second lumbar vertebra through the sacrum when neurologic examination suggested a L4-S3 myelopathy. Dogs weighing less than 20 kg were scanned using helical acquisition with the following parameters: 200 mA, 120 KVp, 2.5 mm slice thickness, 0.8 pitch, no gantry tilt, and reconstructions with 1.25 mm thickness and 0.625 mm intervals. Dogs weighing greater than 20 kg were scanned using helical acquisition with the following parameters: 100 mA, 120 KVp, 5 mm slice thickness, 0.8 pitch, no gantry tilt, and reconstructions with 2.5 mm thickness and 2.5 mm intervals. Following the initial acquisition, an intravenous contrast bolus of 240 mgI/ml iohexol[b] was administered at a dose of 2ml/kg and the CT scan was repeated one minute after administration. A myelogram was then performed by a veterinary surgical resident or board certified veterinary radiologist. Lumbar puncture of the subarachnoid space was used for all dogs at either L4/5 or L5/6, and the dose of intrathecal contrast used was 0.4ml/kg of 240 mgI/ml iohexol. Lateral, ventrodorsal, right and left oblique images were obtained for all dogs. The images were acquired using direct digital radiography[c]. An additional CT scan was then performed using the same parameters as the initial CT. Hemilaminectomy was performed using the guidance of the CT myelogram for side and site of the lesion. All dogs had confirmed Hansen type I intervertebral disc disease at surgery. Postoperative care was individualized to the needs of the patient.

All imaging studies were anonymized and three blinded reviewers (two board certified veterinary radiologists and one board certified veterinary surgeon) were asked to evaluate the studies for the following: presence of a lesion, type of lesion, confidence in assessment, longitudinal location of lesion, and lateralization of lesion. The type of lesion could be classified as intramedullary, extramedullary, intradural, or lesion present/cannot categorize. A confidence score was assigned to each study consisting of one the four following categories: A) lesion absent/no further imaging recommended, B) presence or absence of lesion unclear/further imaging recommended, C) lesion present /further imaging recommended, and D) lesion present/no further imaging recommended. The lateralization of the lesion was classified as left, right, or midline. The reviewers were asked to classify the lateralization of the lesion based on the surgical approach that would allow the most complete removal of extradural material. Reviewers were asked to utilize bone, soft tissue, and brain algorithms when assessing CT imaging. Reviewers were asked to view myelograms in both normal and inverted grey scale formats using digital software. The designated reference standard for the study was CT myelogram. Any CT myelographic study that lacked 100% agreement between readers was reassessed by the readers as a group to achieve a consensus. This consensus was then used as the reference standard. Myelograms and CT scans were then compared to the reference standard for accuracy. Accuracy was divided into localization, lateralization, and overall accuracy. Overall accuracy was defined as a study that was accurate for both localization and lateralization. When lesions were classified as midline with the reference standard, myelogram and CT classifications of right, left, and midline were all accepted as accurate. However, when lesions were classified as right or left with the reference standard, myelogram and CT classifications of midline were considered inaccurate. When multiple lesions were present, the study was only considered accurate if all lesions in the study were accurate when compared to the reference standard. Significance was set at $p<0.05$.

CHAPTER III

RESULTS

Thirty three dogs were included in the study. Breeds represented were Dachshund (n=21), Beagle (n=2), Shih Tzu (n=2), Toy Poodle (n=2), mixed breed (n=2), and one each of the following: Basset Hound, Affenpinscher, Springer Spaniel, and Miniature Schnauzer. The mean age was 5.8 years (range 2-13.3 years). Fifteen dogs were male, eleven of which were castrated. Eighteen dogs were female, none of which were spayed.

Twenty three dogs were non-ambulatory at the time of admission and three of these patients had lost deep pain perception. The remaining 10 cases were able to weakly ambulate at the time of admission. Neurologic examination suggested a C1-C5 myelopathy in two patients and a T3-L3 myelopathy in the remaining 31 patients.

The lateralization, localization, and overall accuracy of myelogram and CT are shown in Figure 1. The lateralization accuracy was 59% for myelography and 88% for CT. These values were significantly different ($p<0.0001$). The longitudinal localization accuracy was 69% for myelography and 86% for CT. These values were significantly different ($p=0.0039$). The overall accuracy was 48% for myelography and 84% for CT. These values were significantly different ($p<0.0001$).

The accuracy of myelography and CT by confidence score is shown in Table 1. The myelographic lateralization, localization, and overall accuracies were significantly different between confidence scores ($p<0.001$, $p=0.0041$, $p<0.0001$). The CT lateralization, localization, and overall accuracies were significantly different between confidence scores ($p<0.001$, $p<0.001$, $p<0.001$).

The accuracy of myelography and CT by reader is shown in Table 2. The myelographic lateralization, localization, and overall accuracies were not significantly different between readers ($p=0.0789$, $p=0.8287$, $p=0.1435$). The CT lateralization, localization, and overall accuracies were not significantly different between readers ($p=0.7524$, $p=0.9202$, $p=0.7422$).

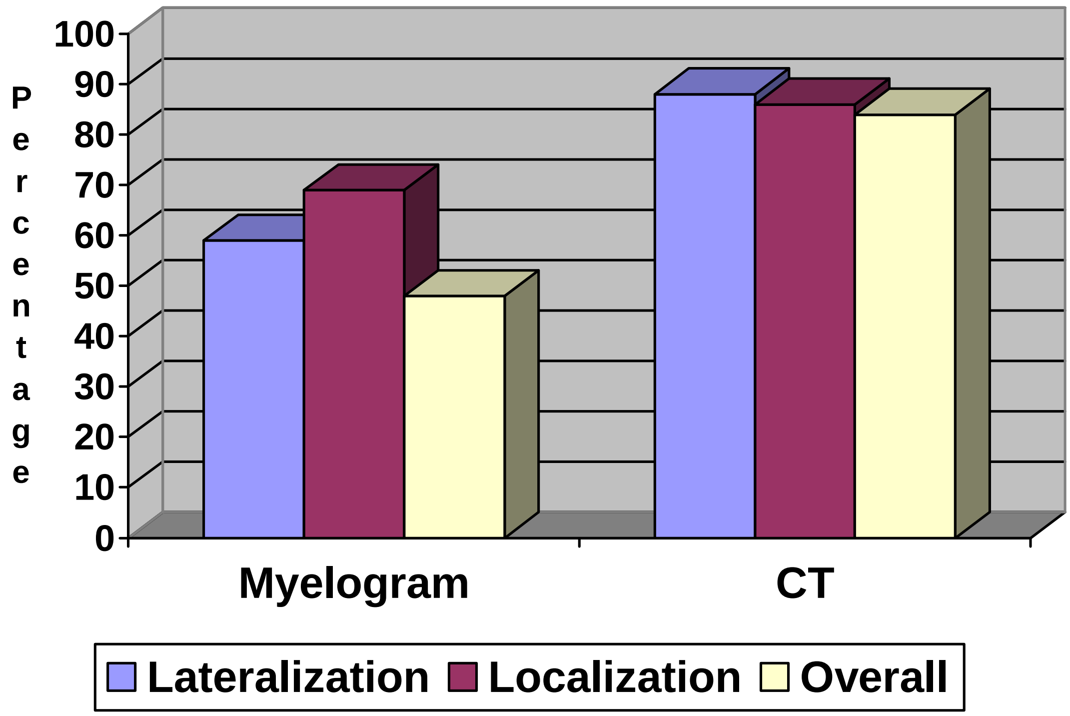
Table 1: Accuracy of Techniques by Confidence Score

Conf. Score	Myelogram lateralization	Myelogram localization	Myelogram overall	CT lateralization	CT localization	CT overall
B	n/a	n/a	n/a	44%	44%	44%
C	44%	65%	34%	69%	62%	62%
D	94%	85%	82%	96%	95%	92%

Table 2: Accuracy of Techniques by Reader

Reader	Myelogram lateralization	Myelogram localization	Myelogram overall	CT lateralization	CT localization	CT overall
1	73%	73%	61%	88%	85%	82%
2	58%	67%	48%	85%	85%	82%
3	45%	67%	36%	91%	88%	88%

Figure 1:Myelogram & CT Accuracy



CHAPTER IV

DISCUSSION

Computed tomography was significantly more accurate than myelography in identifying the lateralization and localization of extradural compression caused by intervertebral disc extrusions in chondrodystrophic dogs when compared to a reference standard of CT myelography. Computed tomography also demonstrated less variation than myelography among reviewers and a greater percentage of CT studies were assessed with high confidence scores than myelography.

It is very important to view these findings in light of the study population. Nonchondrodystrophic dogs were not included in this study due to the recent findings of a comparable study by Dennison et al[5]. In that study, a broad patient population was recruited with roughly equal chondrodystrophic and nonchondrodystrophic representation (54% and 46% respectively). CT was found to be ineffective at diagnosing conditions that did not involve mineralization of extradural material or lysis of bone. The sensitivity of conventional CT was 66% and the sensitivity of nonselective angiographic CT was 53% in that study when considering all disease processes. Only 39% of conventional CT and 35% of nonselective angiographic CT studies were accurate with regard to lesion characterization, lateralization, and localization. The myelographic sensitivity in that study was 79% for detecting lesions. Only 63% of myelographic studies were accurate with regard to characterization, lateralization, and localization of all lesions. Based on the findings of Dennison et al[5], we do not believe CT represents a good diagnostic screening tool for nonchondrodystrophic dogs. However, all mineralized disc extrusions in that study were detected and all were accurate in lateralization and localization. Other studies[2-3] have demonstrated the accuracy of CT in chondrodystrophic dogs when compared to a reference standard of surgical findings. Hecht et al[2] found an accuracy of 87% for conventional CT and 85% for helical CT for localization and lateralization of disc extrusions in chondrodystrophic dogs. Olby et al[3] found CT to be 90% accurate for the localization and 96% accurate for the lateralization of disc extrusions in chondrodystrophic dogs. In contrast, one retrospective study[4] concluded that CT may be ineffective in localizing disc extrusions in chondrodystrophic dogs because compressive disc material was detected on CT myelograms and not detected on initial CT in 4/11 studies. However, viewers were only allowed to assess CT with a bone algorithm which markedly limits the capability of CT to detect extradural material unless it is highly mineralized. Based on the findings of the above mentioned references, we believe CT represents an excellent initial diagnostic imaging technique for chondrodystrophic dogs with acute myelopathies.

The predominant difference of our study with previous studies is the use of CT myelography as the reference standard. All previous veterinary studies have used surgical findings as a reference standard. Use of this reference standard introduces a high level of bias. Surgeons are aware of the imaging findings in these studies and use the findings to guide their surgical approach. This obviously does not allow an independent surgical assessment as the reference standard. Another limitation is the limited circumferential view of the spinal canal when performing hemilaminectomy. It may be difficult to truly detect which side of the spinal canal contains the majority of extruded material due to this limited view. If no disc material is found upon entering the spinal canal and the spinal cord is deviated towards the surgeon, the surgeon will likely consider the imaging assessment incorrect. However, if the spinal cord is not deviated towards the surgeon and extruded material is retrieved, the preexisting bias may affect the assessment of whether more material was present on the operated or non-operated side. Many veterinary studies assign agreement between the imaging findings and surgery findings based solely on whether the surgeon is able to retrieve disc material but we believe this criterion to be biased and potentially inaccurate as demonstrated in figures 2 and 3. Gross necropsy findings would be the most accurate way to determine the true extent and location of extruded intervertebral disc nuclear material but is obviously impossible in the clinical scenario. Magnetic resonance imaging is the gold standard imaging technique for neurologic disease in general and therefore likely represents the best imaging reference standard for diagnosing type I intervertebral disc rupture in dogs. The authors acknowledge the superiority of MRI; however availability and, depending on the magnet strength, slow acquisition times, are practical considerations which must be taken into account. We chose CT myelography as the reference standard in this study for two reasons: to avoid the limitations and bias of relying on surgical findings alone and the lack of availability of MRI in our hospital. Multiple studies have suggested myelography is highly accurate for detecting the lateralization and localization of intervertebral disc extrusions[2, 7-10]. Oblique myelographic images have been shown to increase the accuracy of detecting the lateralization of extradural disc material[9-10]. Bos et al described “paradoxical contrast obstruction” on the ventrodorsal myelographic view whereby extradural material was found on the side with the shorter contrast gap 83% of the time[8]. Our study conflicts with these previous reports and found the accuracy of myelography to be poor. We believe the reason for the difference in our study from previous studies is best explained by the difference in the reference standard used (surgical findings versus CT myelography)..

It is unknown what the impact would have been with sole reliance on myelography in the patients of this study. The surgeon would have approached the side opposite the majority of disc material in 41% of patients and approached the wrong location in 31% of patients. It is unknown how much extruded disc material must be removed from the spinal canal to achieve successful outcomes in clinical patients. The inflammatory nature of extruded disc material has been demonstrated suggesting complete removal of disc material is warranted[11-15]. It is also unknown how much impact a surgical approach to the incorrect side has in the clinical patient. When extruded material is ventrolateral and nonadherent to surrounding structures, it may be possible to retrieve the material from the opposite side. However, this would require more manipulation of the spinal cord. Material that is adhered to the spinal cord or truly contralateral to the side of the surgical approach would likely require approaching the opposite side for complete removal. A bilateral approach can potentially increase patient morbidity and spinal instability[16-17].

There was greater variation between readers for myelographic accuracy than CT; however, this difference was not statistically significant. The lack of statistical significance likely represents a type II error. There was a 28% variation between the least and most accurate reader for myelographic lateralization compared to a 6% variation for CT lateralization. There was a 25% variation between the least and most accurate reader for overall myelographic accuracy compared to a 6% variation for overall CT accuracy. These findings suggest that the diagnostic accuracy of myelography may be more user dependent than CT.

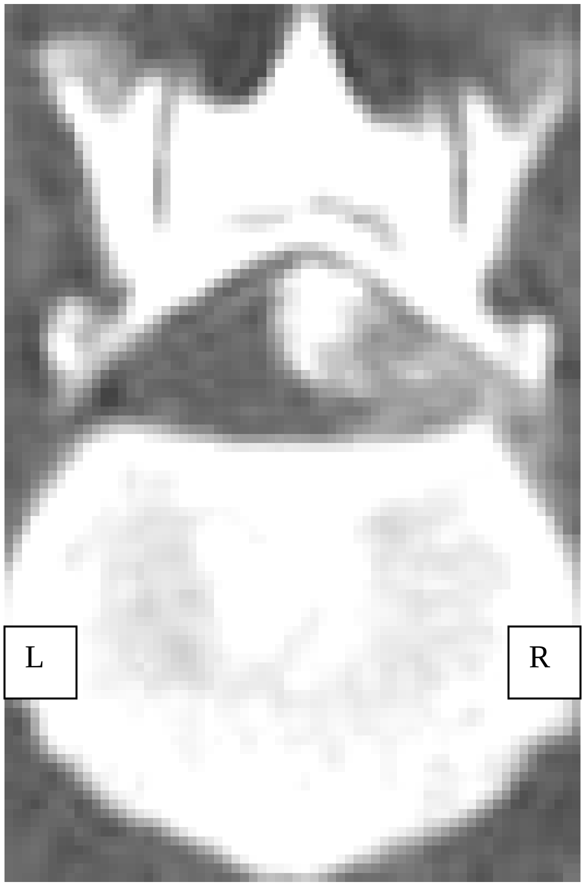
The technique accuracy demonstrated a significant increase as the confidence scores increased for both myelography and CT. This is an intuitive finding with clinical application. Confidence score C demonstrated confidence in the presence of a lesion but not in the exact location to guide the surgeon. Confidence score D demonstrated both confidence in the presence of the lesion as well as its precise location. The overall myelographic accuracy increased 48% and the overall CT accuracy increased 30% between scores C and D. The clinical application of this finding is that both techniques can yield high accuracy when confidence in the assessment is high. However, when the precise location of the lesion is not clear and doubt exists, further imaging should be pursued if possible to increase the accuracy for surgical planning. The readers chose confidence score D for 78% of the CT studies, but only chose confidence score D for 33% of the myelograms. Therefore, while both techniques can yield high confidence, CT represents a better choice as the initial diagnostic in chondrodystrophic dogs because it will yield high confidence more frequently.

Chondrodystrophic dogs that have an acute disc extrusion concurrent with other historical extrusions represent a limitation of CT. If multiple lesions are displacing the spinal cord and appear compressive, it is not possible to determine which lesion is responsible for the current neurologic episode. Neurologic examination (perispinal pain or panniculus) may be helpful if the lesions are spread apart by multiple vertebral segments. Myelography or CT myelography in these patients demonstrates the presence or absence of subarachnoid space to guide the surgeon to the causative disc extrusion. Magnetic resonance imaging would demonstrate spinal cord parenchymal changes and would also demonstrate the causative lesion.

The authors acknowledge several study limitations. It is likely that MRI would have represented a better reference standard than CT myelography. However, the authors believe that CT myelography represents an acceptable reference standard when MRI is not readily available. The CT scans did not include the entire region of neurolocalization and therefore other concurrent disease cannot be ruled out in the study population. CT scans were started at the tenth thoracic vertebra due to the paucity of disc extrusions that occur cranial to this location. The strength of the intercapital ligament cranial to the tenth thoracic vertebra is believed to be responsible for the limited frequency of disc rupture and extrusion of nuclear material into the spinal canal. Several previous authors have also excluded the cranial thoracic spine in CT scans[2-3].

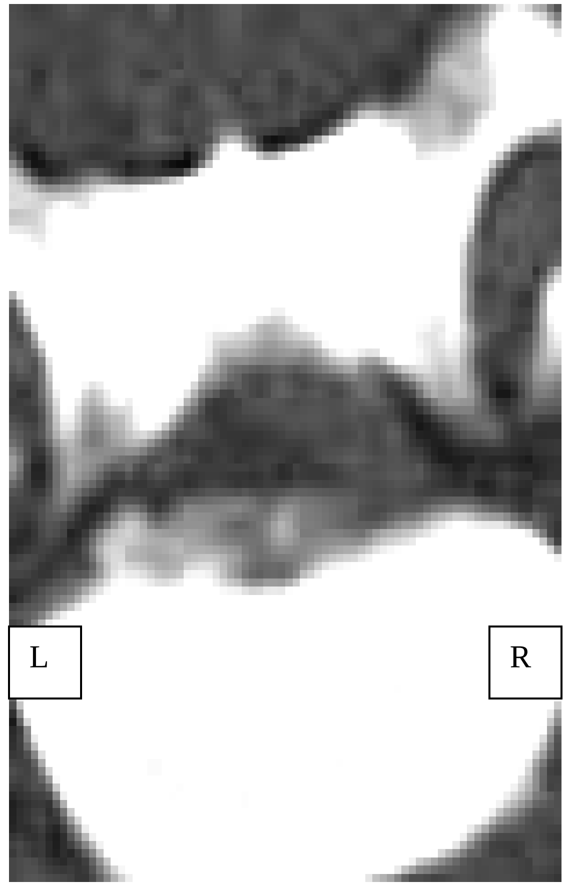
In conclusion, CT had significantly greater lateralizing, localizing, and overall accuracy than myelography when compared to CT myelography in chondrodystrophic patients with intervertebral disc extrusions. When confidence in the assessment of the imaging technique is not high, further imaging should be pursued if possible. The authors believe that future comparative studies of myelography and CT should use MRI or CT myelography as a reference standard due to decreased bias and the ability to circumferentially localize extruded disc material.

Figure 2



Axial CT image representing a scenario in which surgical approach from the left would be obviously incorrect to the surgeon.

Figure 3



Axial CT image representing a scenario in which surgical approach from the left may not be obviously incorrect to the surgeon due to retrieval of disc material ventrally. However, a large amount of material is also present on the right side of the cord.

REFERENCES

1. Israel SK, Levine JM, Kerwin SC, et al. The relative sensitivity of computed tomography and myelography for identification of thoracolumbar intervertebral disk herniations in dogs. Vet Radiol Ultrasound 2009; 50: 247-252.

2. Hecht S, Thomas WB, Mariono-Henry K, et al. Myelography vs. computed tomography in the evaluation of acute thoracolumbar intervertebral disc extrusion in chondrodystrophic dogs. Vet Radiol Ultrasound 2009; 50: 353-359.

3. Olby NJ, Munana KR, Sharp NJH, et al. A comparison of computed tomography and myelography in the diagnosis of acute intervertebral disc disease in dogs. Proc ACVIM 1999; 17: 705.

4. Shimizu J, Yamada K, Mochida K, et al. Comparison of the diagnosis of intervertebral disc herniation in dogs by CT before and after contrast enhancement of the subarachnoid space. Vet Rec 2009; 165: 200-202.

5. Dennison SE, Drees R, Rylander H, et al. Evaluation of different computed tomography techniques and myelography for the diagnosis of acute canine myelopathy. Vet Radiol Ultrasound 2010; 51: 254-258

6. Schulz KS, Walker M, Moon M, et al. Correlation of clinical, radiographic, and surgical localization of intervertebral disc extrusion in small-breed dogs: a prospective study of 50 cases. Vet Surg 1998; 27: 105-111.

7. Kirberger RM, Roos CJ, Lubbe AM. The radiological diagnosis of thoracolumbar disc disease in the dachshund. Vet Radiol Ultrasound 1992; 33: 255-261.

8. Bos AS, Brisson BA, Holmberg DL. Use of the ventrodorsal myelographic view to predict lateralization of extruded disk material in small-breed dogs with thoracolumbar intervertebral disk extrusion: 104 cases (2004-2005). J Am Vet Med Assoc 2007; 230: 1860-1865.

9. Gibbons SE, Macias C, De Stefani A. The value of oblique versus ventrodorsal myelographic views for lesion lateralisation in canine thoracolumbar disc disease. J Small Anim Practice 2006; 47: 658-662.

10. Tanaka H, Nakayama M, Takase K. Usefulness of myelography with multiple views in diagnosis of circumferential location of disc material in dogs with thoracolumbar intervertebral disc herniation. J Vet Med Sci 2004; 66 (7): 827-833.

11. Royal AB, Chigerwe M, Coates JR, et al. Cytologic and histopathologic evaluation of extruded canine degenerate discs. Vet Surg 2009; 38 (7): 798-802.

12. Habtemariam A, Virri J, Gronblad M, et al. Inflammatory cells in full-thickness annulus injury in pigs. An experimental disc herniation animal model. Spine (Phila Pa 1976) 1998; 23 (5): 524-529.

13. Olmarker K, Blomquist J, Stromberg J, et al. Inflammatogenic properties of nucleus pulposus. Spine (Phila Pa 1976) 1995; 20 (6): 665-669.

14. McCarron RF, Wimpee MW, Hudkins PG, et al. The inflammatory effect of nucleus pulposus. A possible element in the pathogenesis of low-back pain. Spine (Phila Pa 1976) 1987; 12 (8): 760-764.

15. Nygaard OP, Mellgren SI, Osterud B. The inflammatory properties of contained and noncontained lumbar disc herniation. Spine (Phila Pa 1976) 1997; 22 (21): 2484-2488.

16. Corse MR, Renberg WC, Friis EA. In vitro evaluation of biomechanical effects of multiple hemilaminectomies on the canine lumbar vertebral column. Am J Vet Res 2003; 64 (9): 1139-45.

17. Smith GK, Walter MC. Spinal decompressive procedures and dorsal compartment injuries: comparative biomechanical study in canine cadavers. Am J Vet Res 1988; 49 (2): 266-73.

APPENDICES

a. GE Lightspeed Plus, General Electric Healthcare, Milwaukee, WI.

b. Omnipaque, GE Healthcare Inc., Princeton, NJ.

c. Eklin Medical Systems Inc., Santa Clara, CA.

VITA

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Candidate for the Degree of

Master of Science

Thesis: COMPARISON OF COMPUTED TOMOGRAPHY AND MYELOGRAPHY TO A REFERENCE STANDARD OF COMPUTED TOMOGRAPHIC MYELOGRAPHY IN THE EVALUATION OF DOGS WITH INTERVERTEBRAL DISC DISEASE

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Title of Study: COMPARISON OF COMPUTED TOMOGRAPHY AND MYELOGRAPHY TO A REFERNCE STANDARD OF COMPUTED TOMOGRAPHIC MYELOGRAPHY IN THE EVALUATION OF DOGS WITH INTERVERTEBRAL DISC DISEASE

Pages in Study: 19 Candidate for the Degree of Master of Science

Major Field: Veterinary Biomedical Science

Scope and Method of Study: Prospective blinded comparative study

Findings and Conclusions:

Objective: To compare the accuracy of myelography and CT to a reference standard of CT myelography in chondrodystrophic dogs with intervertebral disc extrusions.

Study design: Prospective blinded comparative study

Animals: Chondrodystrophic dogs with acute canine myelopathy due to intervertebral disc extrusions (n=33).

Methods: Dogs received CT, myelography, and CT myelography to diagnose and localize intervertebral disc extrusions. The accuracy of CT and myelography was compared to CT myelography for lateralization, localization, and overall accuracy. Confidence in the assessment of each study was scored by the readers.

Results: The lateralizing, localizing, and overall accuracy of CT was 88%, 86%, and 84% respectively. The lateralizing, localizing, and overall accuracy of myelography was 59%, 69%, and 48% respectively. The accuracies of all three categories were significantly different between myelography and CT. Significant differences were found between confidence scores for both myelography and CT. Poor accuracy was obtained except for studies with the highest confidence score.

Conclusions: CT is a more accurate imaging technique than myelography for diagnosing chondrodystrophic disc extrusions when using a reference standard of CT myelography. However, both techniques can yield high accuracy when the reader is confident in their assessment. Further imaging should be pursued when confidence in the localization is not high.

ADVISER’S APPROVAL: Mark Rochat