Influence of chondrodystrophy on intervertebral disc mineralization and vertebral geometry in the Nova Scotia Duck Tolling Retriever

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INTRODUCTION

Chondrodystrophy is a genetic disorder where the presence of one or more copies of the fibroblast growth factor 4 (*FGF4*) retrogene on chromosome 12 (CFA12) are apparent (1). Chondrodystrophy results in shortened limbs and inappropriate calcification of intervertebral discs contributing to intervertebral disc disease (IVDD) while also increasing susceptibility to disc herniation (1,2,3). The Nova Scotia Duck Tolling Retriever (NSDTR) breed has been used to study *FGF4* on CFA12 because NSDTRs may have 0, 1, or 2 copies of *FGF4* on CFA12 while appearing to be free of other mutations influencing skeletal development. The purpose of the geometrical analysis of several vertebrae is to determine whether chondrodystrophy impacts vertebral geometry, just as it impacts the growth of long bones. The analysis of disc mineralization is to determine whether the presence of 1 or 2 copies of *FGF4* on CFA 12 leads to multifocal disc mineralization.

STUDY DESIGN

The NSDTR breed was selected due to their distinct genetic status, size, and availability. 22 NSDTRs underwent CT scans of their spines for evaluation.

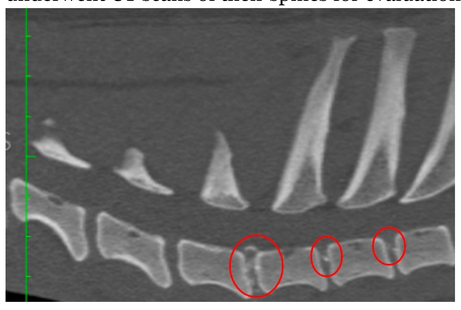

Figure 1. Sagittal view of CT scan demonstrating a herniated mineralized disc at C7-T1 and mineralized discs at T1-2 and T2-3 on medical visualization software (Horos 3.0, Brooklyn, NY).

3 vertebrae and all intervertebral discs were isolated from the CT scans and geometric parameters were captured using medical visualization, segmentation, and analysis software (Mimics 23.0 and 3-Matic 17.0, Materialise, Plymouth, MI).

The effects of the genetic status on geometric parameters were statistically analyzed.

Animals

Client-owned animals were enrolled. The research protocol was IACUC-approved. Clients signed an informed consent.

- 7 wildtypes (0 copies of *FGF4* on CFA12)
- 8 heterozygotes (1 copy of *FGF4* on CFA12)
- 7 mutants (2 copies of *FGF4* on CFA12)

METHODS

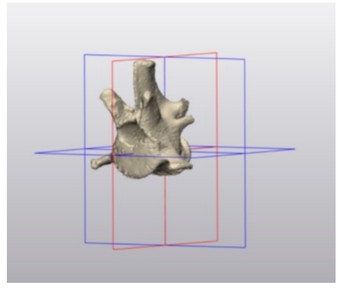

Figure 2. A reconstructed first lumbar vertebra is shown. The transverse, sagittal, and frontal planes of that vertebra are also shown. These 3 planes form a Cartesian coordinate system used to measure vertebral size and geometry.

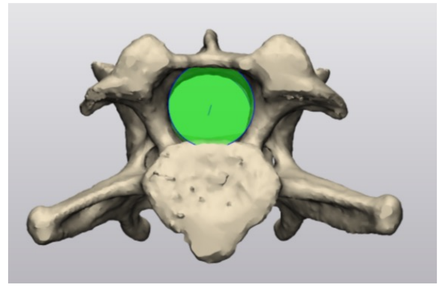

Figure 3. C3 vertebra with best fit elliptical cylinder to measure canal height and width.

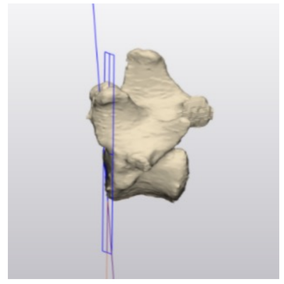

Figure 4. T13 vertebra with frontal plane and measured cranial endplate angulation.

CT scans were imported and segmented to visualize the spine in 3D (Mimics 23.0, Materialise, Plymouth, MI). The third cervical (C3), thirteenth thoracic (T13), and first lumbar (L1) vertebrae were isolated from the rest of the spine via medical segmentation software. These vertebrae were selected because they belong to separate spine segments and are at sites of high intervertebral mobility. After mineralized discs were identified on medical visualization software (Horos 3.0, Brooklyn, MI), they were isolated from disc spaces via medical segmentation software. 3D models of vertebrae were analyzed using Computer Aided Design (CAD) software (3-Matic 17.0, Materialise, Plymouth, MI).

A Cartesian coordinate system was developed that allowed standardization of measurements to ensure parameters were collected at the same location within the same plane of view each time (Figure 2). Three perpendicular planes were oriented on the vertebrae: sagittal, transverse, and frontal planes. Geometric parameters measured included vertebral volume, canal height, canal width, canal length, vertebral body length, vertebral body width, endplate angulation, dorsal spinous process height, transverse processes length, and spinal body curvature (Figures 3-4). Mineralized discs underwent analysis via CAD software evaluating volume, surface area, disc density, and sphericity.

RESULTS

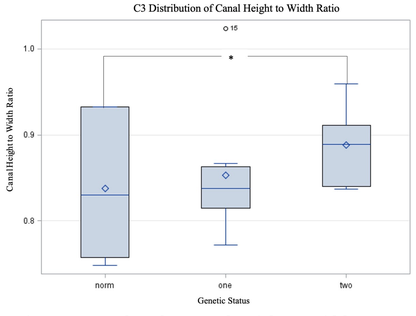

Figure 5. Box plot of C3 Canal Height to Width Ratio

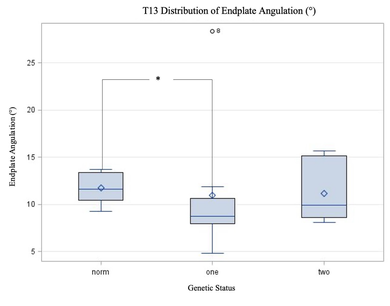

Figure 6. Box plot of T13 Endplate Angulation

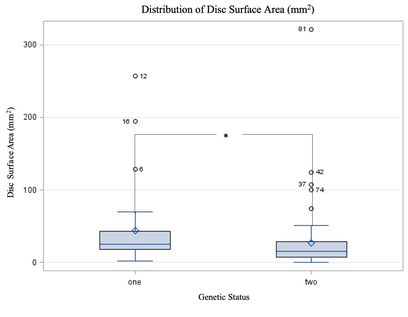

Figure 7. Box plot of Disc Surface Area

For C3, the canal height to width ratio was larger for 2 copies (0.86) of the *FGF4* retrogene compared to no copies (0.83) ($p=.033$). The effect on size was a modest difference. For T13 vertebrae, endplate angulation was lower in dogs with 1 *FGF4* copy (8°) than no copy (12°) ($p=.008$). The effect on size was a modest difference. Statistical trends ($.05 < p < .10$) were seen in C3 canal height, C3 transverse process length, and T13 endplate angulation.

Dogs with no *FGF4* copy on CFA12 had no mineralized intervertebral discs. Genetic status influenced mineralization where the mean disc number of dogs with 1 copy of *FGF4* was 4 discs (SD, 3; median, 3.5) and with 2 copies was 11 discs (SD, 5; median, 11). Disc volume, disc surface area, and disc sphericity differed for various spinal segments (cervical, thoracic, lumbar, sacral/caudal). For disc surface area, dogs with one copy of *FGF4* (43 mm²) were larger in surface area than those with two copies (27 mm²) ($p=.048$). Other geometric parameters did not differ statistically among the 3 dog groups.

SUMMARY

Differences in canal geometry and endplate angulation were identified which can contribute to the overall appearance, gait, and mechanical properties in chondrodystrophic dogs. Clear differences in IVD mineralization among dog groups were confirmed.

CONCLUSIONS & FUTURE DIRECTIONS

Computer aided design (CAD) software is a powerful method to analyze geometric variation in both long and short bones. 3D analysis of the canine spine with the use of CAD software is state of the art because there are currently no published 3D analytical methods of the canine spine or qualitative analysis of canine disc mineralization. Specific changes in angulation will be corrected with the changes in angulation detected in the radius of dogs with 0, 1, or 2 *FGF4* copies on CFA12. These correlations will enhance our understanding of the impact of *FGF4* on endochondral and intramembranous ossification. These discoveries open the door to analyze further spinal and canal geometry in this skeletal disease and other skeletal diseases. These early findings will be reviewed and discussed with neurosurgeons.

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UCDAVIS VETERINARY MEDICINE
JD Wheat Veterinary Orthopedic Laboratory

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