Evaluation of Total Disc Arthroplasty: A Canine Model

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Abstract

The study reported here was designed to examine the biomechanical and histopathologic properties of total disc arthroplasty (TDA) using a canine model. Thirty-seven dogs were divided into 3 groups (intact spine, fusion, TDA) and sacrificed either at study commencement or at 3 months. Results showed progressive fusion from 0 to 3 months in the fusion group. The TDA group maintained motion throughout this period. No neurologic complications were noted in either group. These results establish the canine as a model for future studies of TDA.

Total disc arthroplasty (TDA) is increasingly being used as an alternative to arthrodesis for the treatment of spine discogenic pathology.[1-5] In the 1950s, interest arose in replacing the degenerated parts of the spine with a motion-sparing alternative.[1] This interest led to the design of the total disc prosthesis. Since then, many different models have been designed.[6-12] It was not until the 1980s that TDA was considered to be a viable form of therapy for the degenerative spine.[2,13-16] The goal with implant design is to allow almost "normal" mobility while retaining many of the properties of the native intervertebral disc.[17] Two different classes of implants have evolved: total disc prosthesis and nucleus pulposus replacement.[2] The total disc prosthesis has been put into practice much more.[3,8,10,18-21] In Europe, many of these devices are routinely implanted into humans; in the United States, they are still in the clinical trial phase. So far, only one disc (LINK Charité III, DePuy Spine, Johnson & Johnson, Raynham, Mass) has been approved by the US Food and Drug Administration for commercial use in the United States.[3]

Thorough review of the literature reveals few studies of spine disc replacement implants using animal models.[7,10,22-25] To our knowledge, there are no studies of total mechanical disc replacement using the canine spine as an animal model. Other models that have been used to study TDA include human cadavers,[7] baboons,[7,9,24] and sheep.[10,26] Our objective in the present study was to use a canine model to compare the biomechanical and histopathologic features of TDA with those of lumbar spine arthrodesis. The ultimate goal was to validate the canine model as a biomechanical model in the study of TDA. The findings may also lead to future studies of complications from TDA use,[21] ultimately providing insight into revision surgery strategies.

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Materials and Methods

Animal Research Permission

Adult dogs were obtained from Marshall Farms USA (North Rose, NY). The investigation was reviewed and approved by the Animal Studies Committee at Washington University School of Medicine for the proper care and handling of laboratory animals.

Implants

The disc arthroplasty implant consisted of 2 polished cobalt-chrome endplates (Minco Group, 3HBFM, Dayton, Ohio). The articulations of the endplates were sutured together with a No. 2 FiberWire suture (Arthrex, Naples, Fla) through holes within the prosthesis. The implant is semiconstrained in the flexion/extension/lateral bending planes and unconstrained with regard to axial rotation. Three-millimeter screws were used to secure the implant into predrilled 2.5-mm holes in the vertebral bodies. The fusion model had a titanium cervical plate (Orthotec/REO Spine Line Zenith Plate System, Beverly Hills, Calif).

Animal Model and Treatment Groups

Thirty-seven adult large-breed dogs were divided into 3 groups (intact spine, fusion, TDA) and sacrificed either at study commencement (0-month groups) or at 3 months (3-month groups). All animals were obtained from other stud-

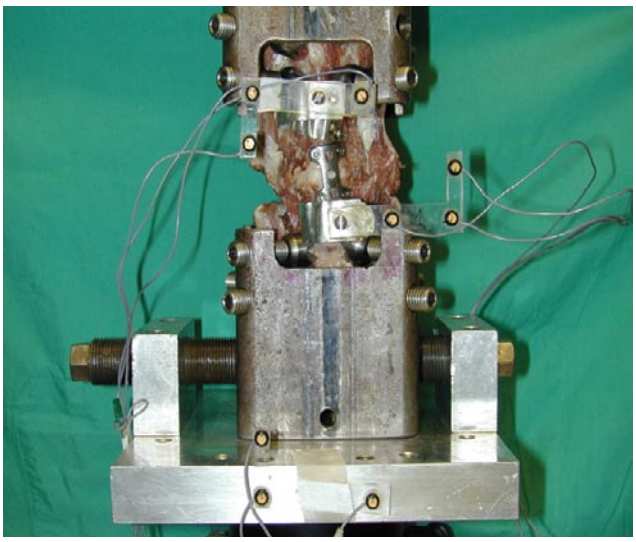

Figure 1. Instron multiaxial materials testing machine (Instron Structural Testing Systems, Norwood, Mass).

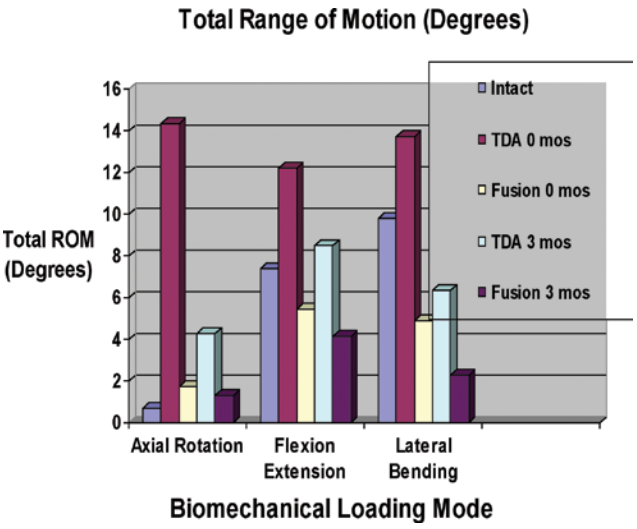

Figure 2. Total range of motion.

ies in the laboratory. No animals were sacrificed uniquely for spine explantation. Thus, the number of animals within each group was not uniform. The L2–L6 lumbar spine segment was harvested at the beginning of the study for the 0-month groups. Biomechanical testing was conducted in vitro, after removal of the lumbar spine segment and implantation of devices when applicable. The 3-month groups underwent in vivo implantation of devices (plate or TDA) and were sacrificed at 3 months. The L2–L6 lumbar spine segment was then harvested from the dogs, and ex vivo biomechanical testing was conducted.

Surgical Technique

Animals that underwent time-0 analysis were sacrificed at study commencement. For the 0-month fusion group, polymethylmethacrylate (PMMA) and a plate were placed across L5–L6 after in vitro discectomy (vs iliac crest bone graft). The rest of this section applies only to animals that underwent plate/TDA implantation and then sacrifice at 3 months.

Anesthesia. Before induction, animals were sedated with midazolam 0.4 to 1.3 mg/kg IM/IV and atropine 0.13 mg/kg IM. General anesthesia was induced with 2.5% sodium thiopental 5 to 10 mg/kg IV titrated to effect. The animals were then intubated with a 7.0- to 7.5-mm high-low pressure cuff endotracheal tube. Isoflurane 2.5% to 3% in an air–oxygen mixture of 40% to 60% was used to maintain anesthesia. A rumen tube was passed for gas decompression. Mechanical ventilation was initiated and maintained at 10 mL/kg tidal volume and at rates of 8 to 10 mL/kg/min. Crystalloids were given at a rate of 1 mL/kg/h.

Surgical Implantation. An anterior abdominal approach was used with animals in a supine position. A longitudinal incision was made to expose the L5–L6 spinal segment. Dissection was then carried down to the midline. Viscera or blood vessels were then retracted to expose the spinal column. The L5–L6 disc space was identified, and an incision was made in the anterior longitudinal ligament. The disc was then removed with a pituitary rongeur. A Caspar retractor was used to open the disc space further, and the adjacent endplate cartilage was removed with a high-speed burr under continuous irrigation to prevent thermal-related osteonecrosis. For the fusion group, the iliac crest was exposed using blunt dissection. The anterior iliac crest structural corticocancellous bone graft was harvested from the crest after subperiosteal dissection. Hemostasis was facilitated at the crest harvest site using bone wax and gel foam. Structural cortical cancellous autograft was placed into the evacuated decorticated intervertebral disc. The plate was placed across the affected disc space. Four bone screws were applied to maintain plate position. The TDA group had surgery performed with an exposure similar to the arthrodesis procedure and animals in a supine position. The implant was placed into the evacuated disc space, and 2 screws were placed to secure the prosthesis in appropriate position. After the procedure, vessels and viscera were allowed to return to their anatomical position, and the abdominal wound was closed in layers using 1-0 polyglycolic acid suture material. The subcutaneous tissue was loosely reapproximated, and suture was used for the skin. After surgery, the animals were returned to their cages and housed singly with at least daily observation by veterinary technicians for any sign of disease or other medical problems. Animals were given injections of buprenorphine 0.006 mg/kg IM every 12 hours for 96 hours and as needed thereafter.

Biomechanical Flexibility Testing

Biomechanical analysis of range of motion (ROM) was conducted using an Instron multiaxial materials testing machine with dedicated Labview data acquisition systems (Instron Structural Testing Systems, Norwood, Mass; Figure 1). For the 0-month groups, in vitro testing was conducted immediately after harvest of the L2–L6

Table I. Total Range of Motion

Group	Axial Rotation	Flexion-Extension	Lateral Bending
Intact (n = 11)	0.69° ± 0.33°	7.41° ± 1.84° [c]	9.78° ± 1.84° [e]
TDA 0 month (n = 3)	14.35° ± 5.10° [a]	12.19° ± 1.55° [a]	13.67° ± 2.10° [a]
Fusion 0 month (n = 6)	1.74° ± 0.40°	5.47° ± 1.88°	4.93° ± 1.49° [f]
TDA 3 months (n = 7)	4.28° ± 1.19° [b]	8.57° ± 3.41° [d]	6.34° ± 2.67° [f]
Fusion 3 months (n = 10)	1.31° ± 0.62°	4.13° ± 1.32°	2.25° ± 1.20°

Abbreviation: TDA, total disc arthroplasty.
[a] $P<.05$ vs all other groups. [b] $P<.05$ vs intact and fusion. [c] $P<.05$ vs fusion 3 months. [d] $P<.05$ vs all fusion. [e] $P<.05$ vs fusion and TDA 3 months. [f] $P<.05$ vs fusion 3 months.

Table II. Neutral-Zone Range of Motion

Group	Axial Rotation	Flexion-Extension	Lateral Bending
Intact (n = 11)	0.10° ± 0.51°	3.03° ± 1.17° [b]	4.40° ± 1.69° [c]
TDA 0 month (n = 3)	7.99° ± 5.37° [a]	6.58° ± 1.5° [a]	6.03° ± 0.91° [a]
Fusion 0 month (n = 6)	0.44° ± 0.14°	1.59° ± 0.68°	1.29° ± 0.58°
TDA 3 months (n = 7)	1.63° ± 0.89°	4.47° ± 2.52°	1.71° ± 1.22°
Fusion 3 months (n = 10)	0.34° ± 0.15°	1.74° ± 0.99°	0.73° ± 0.59°

Abbreviation: TDA, total disc arthroplasty.
[a] $P<.05$ vs all other groups. [b] $P<.05$ vs fusion 3 months. [c] $P<.05$ vs all fusion and TDA 3 months.

Table III. Radiographic Analysis of Total Disc Arthroplasty at 3 Months

Grade	Features	N = 7
I	Implant intact with no screw or body radiolucency	0
II	Implant intact with presence of screw and/or body radiolucency	7
III	Implant loose with gross screw and body radiolucency	0

lumbar spine segment and device implantation when applicable. For the 3-month groups, animals were euthanized with an overdose of sodium pentobarbital 100 mg/kg IV, and then L2–L6 vertebrae were removed intact. The specimens were cleaned of all soft tissue, with care taken to preserve any fibrous tissue at the operative level and to leave the ligamentous and osseous structures intact. The implant sites were evaluated grossly to determine the adequacy of healing and mobility. The L2 and L6 vertebrae were securely embedded in potting material using crossed transfixing pins. Reflective markers were attached to each vertebra to allow a motion-analysis system to separately capture the motion of each vertebral body. Each specimen then underwent nondestructive axial compression (200 N), flexion (2.5 Nm), extension (2.5 Nm), and torsion (2.5 Nm with a 100-N axial load). Loads were applied in sawtooth wave, ramping from 0 to peak and back to 0 over a 10-second interval. Five load cycles were applied to allow for conditioning of the specimen. Crosshead and load cell data were acquired over all loading cycles at a frequency of 2 Hz. Stiffness, total ROM, and neutral-zone ROM were measured in each loading direction (axial rotation, flexion-extension, lateral bending).

Histopathologic Analysis

After biomechanical analysis, the operative motion segments were sectioned in the midsagittal plane using a Beuhler Isomet saw (Buehler, Ontario, Canada). Histologic preparation of the sections included dehydration in 100% ethanol, staining with Villanueva osteochrome bone stain, undecalcified solution processing, and embedding in PMMA. The EXAKT Microgrinding Device (Exakt Technologies, Oklahoma City, Okla) was used to cut the embedded specimens 250 to 300 µm thick and grind and polished them to 75 µm. Faxitron radiography was used to obtain microradiographs of the slide-mounted specimens. Slides were placed 12 in from the beam and exposed for 2 minutes using a technique of 45 kVp and 3 mA while in direct contact with the single-emulsion high-resolution graphics arts film. The high-resolution microradiographs were used for histomorphometric quantification of the trabecular bone area at the implant–bone interface using a BioQuant Image Analysis System (BioQuant, Nashville, Tenn).

Data and Statistical Analysis

At the L5–L6 level, intervertebral ROM was calculated as the sum of the neutral and elastic zones (NZ + EZ = ROM); it represents peak total ROM at the third load-

Table IV. Radiographic Analysis of Fusion at 3 Months

Grade	Features	N = 10
I	Full interbody radiodensity	0
II	Partial interbody radiodensity	2
III	No interbody radiodensity, implant intact	8
IV	No interbody radiodensity, implant loose	0

Table V. Histologic Analysis of Total Disc Arthroplasty at 3 Months

Grade	Features	N = 7
I	Bone around screws with no osseous bridging across implant body	1
II	Mild lucency around screws with no osseous bridging across implant body	6
III	Moderate lucency around screws with no osseous bridging across implant body	0
IV	Gross lucency around screws with grossly loose implant	0

Table VI. Histologic Analysis of Fusion at 3 Months

Grade	Features	N = 10
I	Full interbody consolidation with complete osseous bridging	0
II	Partial interbody consolidation with >50% osseous bridging	2
III	Partial interbody consolidation with <50% osseous bridging	8
IV	No consolidation with failure/loosening	0

ing cycle. Expressed degrees of rotation in axial rotation, flexion-extension, and lateral bending are in accord with the conceptual framework of Panjabi.[26] Statistical analysis included descriptives and repeated-measures analysis of variance (ANOVA), with the Student-Newman-Keuls test for group-to-group comparisons. For comparisons, statistical significance was set at $P<.05$.

Results

All dogs were neurologically intact with normal gait and no evidence of infection before sacrifice. Biomechanical results from testing total ROM at 0 month showed significantly more motion in axial rotation, flexion-extension, and lateral bending in the TDA group relative to the intact and fusion groups ($P<.05$). TDA spines were significantly less mobile at 3 months relative to 0 month ($P<.05$). Nevertheless, compared with the fusion groups, the TDA groups still had more ROM in both flexion-extension and lateral bending at 3 months ($P<.05$). Of note, compared with intact spines, TDA spines had more motion only in axial rotation ($P<.05$) but were less mobile in lateral bending ($P<.05$) at 3 months. Fusion spines had less motion than intact spines only in lateral bending at 0 month ($P<.05$) and in both flexion-extension and lateral bending at 3 months ($P<.05$). Finally, the fusion group progressively had less lateral bending from 0 month to 3 months (Table I, Figure 2).

Neutral-zone ROM showed that the TDA 0-month group differed from all other groups in all axes ($P<.05$). However, the TDA 3-month group had motion comparable to that of the intact spine, except in lateral bending, with the intact spine being more mobile ($P<.05$). The other significant finding is that, compared with intact spines, fusion spines had less motion in flexion-extension and lateral bending at 3 months ($P<.05$). This finding is similar to those for total ROM ($P<.05$) (Table II, Figure 3).

X-rays showed variable degrees of incorporation of both devices into their respective groups (Figures 4-7). Tables III and IV show the schemes used to analyze x-rays at 3 months. All 8 dogs in the 3-month TDA group showed grade II incorporation of the implant. In the 3-month fusion group, 8 dogs had grade III incorporation, and 2 had grade II.

Histologic results showed fusion and TDA implants in good position. Use of anterior plating as a means to achieve fusion was successful, according to histology (Figure 8). Osseous bridging across L5–L6 suggested fusion. The TDA implant (Figure 9) was well incorporated into bone, with no evidence of loosening at 3 months. Overall, histopathologic interpretation of the slide-mounted undecalcified specimens indicated no evidence of significant pathologic changes in the tissues of any treatment specimens. In all artificial disc replacements, there was no prosthetic endplate migration or evidence of particulate wear debris. For all undecalcified tissues, tissue architecture underwent pathologic assessment; there was no debris or any signs of foreign-body giant cell/granuloma inflammatory reactions, degenerative changes, or autolysis.

The grading scheme presented on Tables V and VI provides more specific analysis of each of the specimens at 3 months. In the TDA group, 1 dog had grade I incorporation, and 6 had grade II; in the fusion group, 2 had grade II, and 8 had grade III.

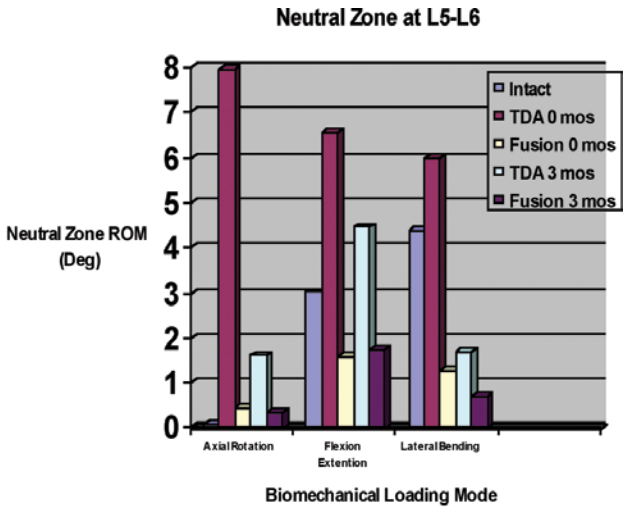

Figure 3. Neutral-zone range of motion.

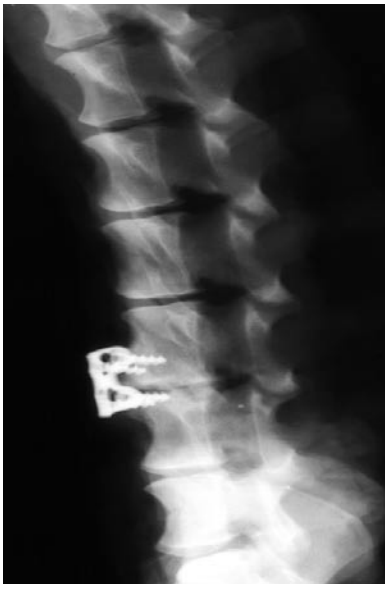

Figure 5. Lateral x-ray of fusion.

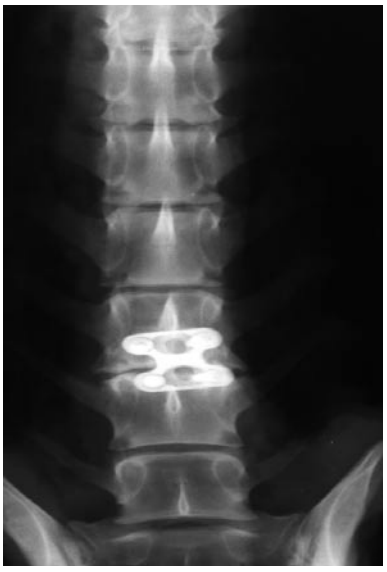

Figure 4. Antero-posterior x-ray of fusion.

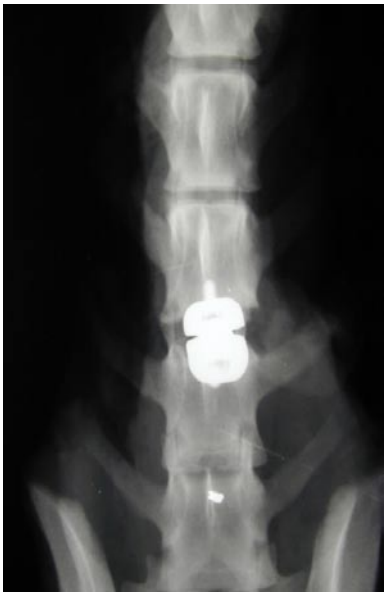

Figure 6. Antero-posterior x-ray of total disc arthroplasty.

Discussion

TDA studies have used cadaveric spines from humans and other animals.[7-10,24,26-28] The human cadaveric spine is difficult and expensive to obtain when larger amounts of data must be obtained for a more comprehensive biomechanical study. Humans were not used as controls in the present study because the objective was to introduce the canine as a feasible, practical, standalone model to study TDA and its potential complications. Baboons have been used in several TDA studies,[7,9,24] but the costs involved in obtaining and maintaining these primates are prohibitive for extensive biomechanical studies.[29] A canine model offers a more affordable alternative to investigate TDA and its potential complications. The purpose of the present study was to use a canine model to evaluate TDA features.

Our study results showed that, compared with the intact group, the 0-month TDA group had significantly more ROM in every plane analyzed. By 3 months, however, the TDA group was more mobile than the intact spine only in axial rotation. The intact spine actually had more motion than the 3-month TDA spine in lateral bending. This result was found for both total ROM and neutral-zone ROM. The TDA implant design probably accounts for these findings. The implant is semiconstrained and thus does not limit axial rotation while limiting lateral bending. Although the increased motion found with TDA at time 0 may be considered "hypermobile," the animals did not suffer any untoward outcomes. Furthermore, their spines stabilized over the course of the study, allowing for potential use of the animals in other experimental investigations at the 3-month time frame. Comparison of the 0- and 3-month TDA groups showed significant diminution in motion over the course of the study. The initial increased motion can be accounted for by the disc approach, which involved dissection of the annulus and many of the surrounding, stabilizing soft-tissue structures.

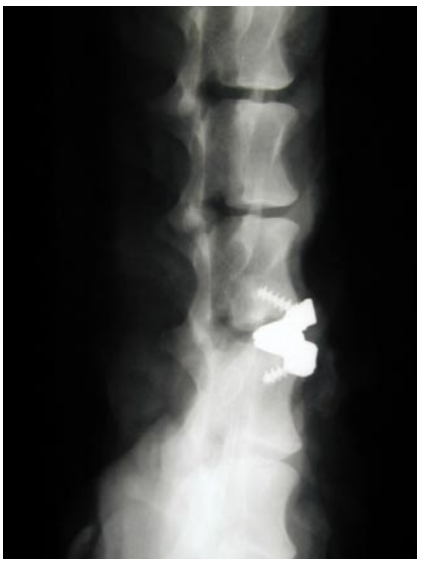

Figure 7. Lateral x-ray of total disc arthroplasty in this study.

Figure 8. Fused spine at 3 months. Take note of the remodeling across the disc space demonstrated by the presence of cancellous bone. This is indicative of the fusion process. Stability of the construct is intimated by lack of osteolysis around the screw threads.

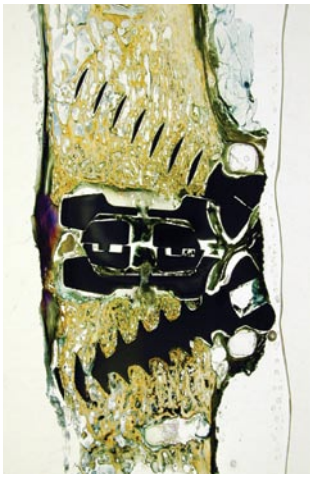

Figure 9. Total disc arthroplasty at 3 months. The implant occupies the entire disc space, thus maximizing control of motion. The presence of cancellous bone around the screws suggests a stable construct.

Comparison of the TDA and fusion groups showed clear preservation of motion in the TDA groups at all time points. The 3-month TDA group differed significantly from the 0- and 3-month fusion groups in axial rotation and from the 3-month fusion group in flexion-extension and lateral bending. Cunningham and colleagues[8] used Bagby and Kuslich (BAK) cages and screws to produce similar differentiation in motion between their arthroplasty and arthrodesis groups using human cadavers. We were able to produce statistically significant results using PMMA (0-month fusion) or iliac crest autograft (3-month fusion) and an anterior plate.

Comparison of the intact spine and fusion groups showed the fusion group's significantly diminished ROM progressing from 0 to 3 months. The only measure of motion in which the fusion group did not differ from the intact spine group at 3 months was axial rotation. A similar trend of decreasing movement was found in a comparison of the 2 fusion groups from 0 to 3 months. These results imply that the autograft progressively incorporated into the adjacent vertebral endplates over the duration of the study and again demonstrate that the technique used for arthrodesis was effective in accomplishing its stated goal. The extent of fusion occurring by study end was encouraging but limited, as the study period was only 3 months. We believe that more fusion would be observed over a longer period.

Radiographic and histologic data show relatively stable incorporation of the TDA and fusion implants. Although neither implant showed full incorporation over this 3-month study, a full biomechanical analysis could be performed. Better incorporation might be facilitated by performing such an analysis later, at 6 or 9 months, for example. Using a porous-coated or hydroxyapatite-impregnated body for the arthroplasty may also facilitate quicker incorporation. Nonetheless, the model presented here is still valid in its current form.

In this study, the canines (all mongrel dogs) varied somewhat in weight. The techniques used for TDA and fusion were consistently applied to all animals. We believe that the effect of weight differences on results was not significant. Nevertheless, as our objective was to introduce the canine model as a viable model for studying TDA, other investigators should be able to negate any potential confounding factors by making appropriate modifications to our techniques.

This discussion would not be complete without reviewing the issue of applying quadruped-based TDA study results to humans. Past criticisms have included dimensional differences in anatomy as well as the horizontal orientation of the quadruped spine. Smit[29] examined the spinal loads in standing, walking, and running quadrupeds and argued that the muscle and ligament tensile forces that control posture result in an inherent axial compression of the spine. This theory is supported by analysis showing a predominant cranial-to-caudal orientation of trabecular structure in a goat vertebra. Another argument against use of bipeds would be the (already mentioned) prohibitive costs associated with doing research on these animals. Canines are much more practical for these studies.

Conclusions

The biomechanical, radiographic, and histopathologic data from this study demonstrated that the canine lumbar spine can be used as a model for TDA research. We anticipate the potential of this model in studies of material safety, wear debris, subsidence, polyethylene extrusion, infection, and other potential complications from TDA use. The canine model can thus be used to test disc arthroplasty with reasonable results with respect to motion preservation.

Authors' Disclosure Statement and Ackowledgment

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This study was conducted at the Department of Orthopaedic Surgery, Washington University School of Medicine, St. Louis, Missouri.

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