Original Article

Lumbar Scoliosis Induction in Juvenile Dogs by Three-dimensional Modulation of Spinal Growth Using Nickel-Titanium Coil Springs

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Abstract

Background: Current treatments for scoliosis have some defects and complications. To study spinal deformities and test novel scoliosis treatments, many animal models of scoliosis have been developed. These models applied a single load to the spine and could not precisely modulate the spinal growth in different dimensions. In this study, we applied posterior tethering in various directions with the application of nickel-titanium (NT) coil springs in dog's spine to modulate spinal growth in the coronal, sagittal, and transverse planes and create a scoliosis model possess curves that mimic adolescent idiopathic scoliosis (AIS) three dimensionally.

Methods: Scoliosis was surgically induced in eight 8-week-old female dogs (weight: 1.95–2.30 kg) using bone screws and NT coil springs. The deformity was induced through the placement of posterior NT coil springs that tethered the spine by bone screw fixation. All dogs were monitored with serial radiographs to document changes in deformities.

Results: All experimental animals developed scoliotic curves convex to the left in the lumbar segment. The mean coronal Cobb angle was 18.0° immediately postoperatively and 54.5° at 22 weeks. The mean lordosis increased from 6.2° postoperatively to 35.0° at final follow-up. Apical axial rotation increased from 4.5° postoperatively to 31.2° at 22 weeks.

Conclusions: With the application of NT springs in dogs that allowed posterior tethering in various directions, lumbar spinal deformity was achieved in three planes: coronal, sagittal, and transverse planes. Notably, the lumbar spine in surgically treated dogs developed lordoscoliosis with obvious rotation and the curves mimic AIS three dimensionally well. This method allows lumbar scoliosis to develop without deep dissection of muscle and maintains the essential anatomical elements along the spinal curve. Moreover, the spinal growth modulation technique could yield information that would provide a basis for developing novel early-stage treatments for children with scoliosis.

Key words: Asymmetric Load; Growth Modulation; Nonfusion; Scoliosis Model

INTRODUCTION

Current treatment options for scoliosis are not ideal and many approaches have limitations and complications. Bracing is the only nonoperative treatment, but this approach only stops the progression of spinal curvature in a growing child and does not typically reduce the degree of curve that is already present.[1] Moreover, most bracing regimens require that braces should be worn 23 h a day, which can cause skin irritation and discomfort.

Severe scoliosis cases require surgery to correct the spinal deformity. The spinal fusions provide better deformity correction, but render the patient with reduced mobile segments postoperatively and set the stage for future sagittal plane issues in late adulthood. Thus, spinal fusion is not the ideal treatment for lumbar scoliosis.

Access this article online

Quick Response Code:	
	Website: www.cmj.org
	DOI: 10.4103/0366-6999.213910

For many years, fusionless surgery has been used to treat infantile and juvenile idiopathic scoliosis. More than 45 years ago, Roaf attempted to modulate spine growth by

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Received: 15-06-2017 **Edited by:** Yuan-Yuan Ji
How to cite this article: Zhang HY, Li QY, Wu ZH, Zhao Y, Qiu GX. Lumbar Scoliosis Induction in Juvenile Dogs by Three-dimensional Modulation of Spinal Growth Using Nickel-Titanium Coil Springs. Chin Med J 2017;130:2579-84.

ablating convex epiphyseal cartilage and adjacent discs at the vertebra near the apex of the curve.[2] Currently, growing rod surgery is the main fusionless technique used to treat scoliosis. Although the approach produces acceptable results,[3-6] there are some complications associated with this approach,[7,8] and it often requires final fusion surgery.

Previous studies indicate that the asymmetric load from an erect posture plays an important role in the development of scoliosis,[9-12] and several experiments have demonstrated that mechanical factors contribute to the progression of scoliosis.[13-16] To study spinal deformity and test novel scoliosis treatments, many animal models of scoliosis have been developed in the recent years. Most of these models used mechanical tethering techniques to create an asymmetric load. Tethering techniques are considered to be the most reliable approaches for generating animal models of spinal deformity;[17-21] however, there are some limitations. The growth of each single segment cannot be modulated separately, and the spinal curve then progresses slowly. Moreover, scoliosis is characterized by a three-dimensional spinal deformity.[22] A single tethering was hard to address deformities in the three dimensions simultaneously.

The bone growth depends on the amount of growth plate compression. Our previous study[23] demonstrated that nickel-titanium (NT) coil springs could be used to modulate spinal growth through the application of asymmetric compression to the vertebral growth plate, but it only applied a single spring load to the lumbar spine and could not modulate the spinal growth in different dimensions. The purpose of this study was to develop a scoliosis model by modulating spinal growth in the coronal, sagittal, and transverse planes using NT coil springs.

METHODS

Ethical approval

All experiments were conducted in accordance with regulations from the Care and Use of Laboratory Animals and were approved by the Ethical Committee of the Peking Union Medical College Hospital.

Experimental animals

Eight female mongrel dogs (age: 8 weeks; weight: 1.95–2.30 kg) were obtained from the experimental animal center of Peking Union Medical College Hospital. The 8-week-old female dogs were newly weaned and retained sufficient growth potential for the duration of the study.

Nickel-titanium coil springs and bone screws

NT coil springs (TOMY International Inc., Japan) with a free length of 3.0 mm were selected for the study [Figure 1]. Heavy springs (load: 200 g) with superelastic properties allowing for soft, stabilized, and sustainable tension were used. According to the manufacturer's information on NT coil spring weight ranges, 200 g of spring tension could be maintained 4.0 mm to 15 mm from the spring.

Figure 1: The nickel-titanium coil spring.

The bone screws are self-drilling (Titanium Alloy, Xiji Inc., China) and had lengths of 20 mm or 30 mm [Figure 2]. The thread length accounted for 80% (20 mm screws) or 50% (30 mm screws) of the total length, and the screw diameters were 1.5 mm and 2.0 mm in the threaded and nonthreaded portions, respectively.

Surgical protocol

After preoperative placement of a fentanyl patch (12 h preoperative), dogs were sedated with propofol (5–10 mg/kg), intubated, and then maintained on Zoletil (5–10 $mg \cdot kg^{-1} \cdot h^{-1}$) and Forane® (minimum alveolar concentration, 1.5%). Lidocaine mucilage was used to facilitate intubation. Peri-operative prophylactic antibiotics were also given. Cephalexin (30 mg/kg) was given intravenously on induction, and intramuscular injections (20 $mg \cdot kg^{-1} \cdot d^{-1}$) were given for 3 days after surgery.

Dogs were placed in a prone position on a grounding pad, and the lumbar region was shaved, followed by sterile prep and draping. A midline posterior skin incision from T13 to the L6 level was used to gain access to the subcutaneous lipoid space, and the space was then enlarged to the right side by blunt dissection. The left vertebral pedicles (L2–L4), right vertebral pedicles (L1–L5), and right transverse processes (L1–L5) were identified by C-arm fluoroscopy and marked with 25-gauge needles (0.7 mm diameter, 38 mm length; Becton Dickinson, S.A., Spain). The needles were then drilled into the vertebral bodies from the vertebral pedicles or the roots of the right transverse processes. After removal of the needles, bone screws (20 mm screws for vertebral pedicles and 30 mm screws for transverse processes) were fixed into the resulting holes in the vertebral bodies such that the screw heads were on the muscle surface [Figure 3]. The NT coil springs were secured to the screws using a stainless steel ligature (Xihubiom Inc., China). Posteroanterior and lateral radiographs of the spine taken immediately after the operation showed the pattern of tethering using NT coil springs [Figure 4]. The right lateral longitudinally tethered springs modulated spinal growth in the coronal plane to create scoliosis, the posterior longitudinally tethered springs connecting right pedicle screws applied loads

Figure 2: The bone screw.

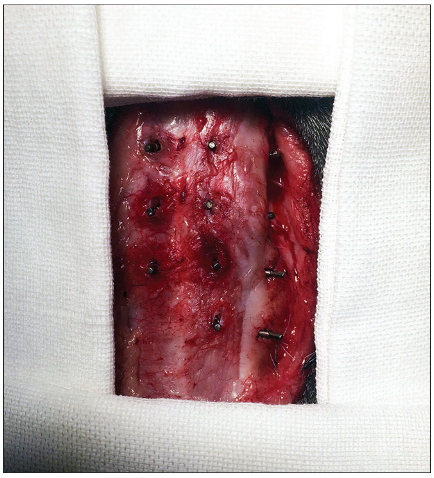

Figure 3: Fixation of bone screws into vertebral bodies through the muscle.

Figure 4: Posteroanterior and lateral radiographs of the spine immediately after surgery.

to modulate spinal growth mainly in the sagittal plane to create lordosis, whereas the diagonal springs provided torques to L2-L4 to create axial rotation. Wound closure proceeded through absorbable sutures. Postoperative analgesia was provided through proper dosing of fentanyl patches.

Postoperative follow-up

Dogs were observed for up to 22 weeks, and posteroanterior and lateral radiographs were taken at postoperative weeks 0, 1, 2, and then at 5-week intervals to document the progression of the deformity [Table 1 and Figures 4-7]. At the end of week 22, the dogs were more than 7 months old and had passed through the growth spurt of puberty whereupon the spinal deformity progression gradually ceased.[23,24] Axial rotation was measured using a computed tomography (CT) scanner (GE Discovery CT 750 HD) at weeks 0 and 22 after the operation [Figure 8]. Dogs were sedated before radiographic acquisition to ensure that standardized films were obtained.

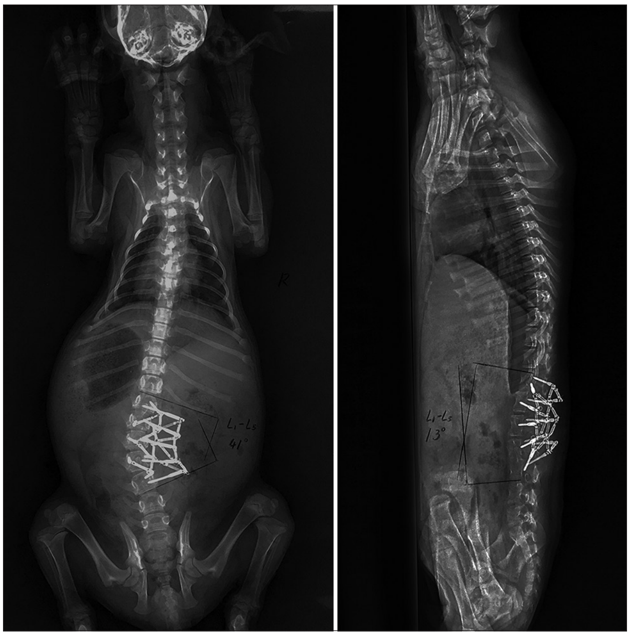

Figure 5: Posteroanterior and lateral radiographs of the spine two weeks after surgery.

Statistical analysis

Statistical analysis was performed with SPSS software version 19.0 for Windows (SPSS Inc , Chicago, IL, USA). Progression of the deformity between radiographic data acquisition points was shown as mean ± standard deviation (SD) and evaluated using Student's *t*-test, with a level of significance set as $P < 0.05$.

RESULTS

Preoperative radiographs of all dogs confirmed that none had preexisting scoliosis. Of the eight dogs that were enrolled in this study, two had NT coil spring fracture and were excluded before the study completion. Of the remaining six experimental animals, no dogs developed postoperative complications or neurological deficits, and all postoperative dogs could move freely within 1 week of surgery.

Table 1: Postoperative degrees of spine deformity (L1–L5) of postoperative dogs (°)

Spine deformity	Postoperative time			
	0 week	1st week	2nd week	7th week
Scoliosis	18.0 ± 2.6 (15.0–22.0)	41.3 ± 3.2 (36.0–45.0)	51.3 ± 5.0 (43.0–57.0)	54.0 ± 4.2 (49.0–59.0)
Lordosis	6.2 ± 1.2 (5.0–8.0)	14.5 ± 2.4 (11.0–18.0)	20.2 ± 3.6 (15.0–25.0)	30.5 ± 4.2 (24.0–36.0)
Rotation	4.5 ± 1.0 (3.0–6.0)	–	–	–

Spine deformity	Postoperative time		
	12th week	17th week	22nd week
Scoliosis	54.3 ± 3.9 (50.0–60.0)	54.8 ± 3.7 (50.0–59.0)	54.5 ± 3.7 (50.0–59.0)
Lordosis	34.2 ± 2.9 (30.0–38.0)	34.8 ± 2.6 (31.0–39.0)	35.0 ± 2.8 (31.0–39.0)
Rotation	–	–	31.2 ± 3.8 (26.0–36.0)

n=6. Data were expressed as mean±SD (range). SD: Standard deviation.

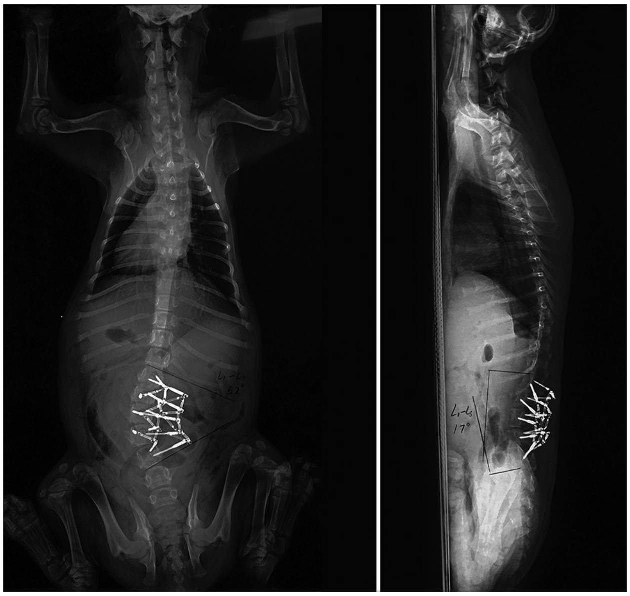

Figure 6: Posteroanterior and lateral radiographs of the spine 7 weeks after surgery.

All the six dogs with spring-tethered lumbar spines developed a progressive structural lordoscoliotic deformity associated with axial rotation of the vertebral body during the 22-week observation period [Figure 9].

The average initial coronal Cobb angle was 18.0 ± 2.6° (range: 15.0–22.0°) immediately after the operation, which progressed to 54.5 ± 3.7° on an average (range: 50.0–59.0°) over 22 weeks. The average progression of 36.5 ± 1.6° (range: 34.0–38.0°) was statistically significant ($t = -54.4$, $P < 0.001$). The degrees of scoliosis were not statistically significantly altered between 7 and 22 weeks after the operation (week 7 vs. 22, $t = -1.5$, $P = 0.203$). In the sagittal plane, the average initial lordosis progressed from 6.2 ± 1.2° (range: 5.0–8.0°) immediately after surgery to 35.0 ± 2.8° on an average (range: 31.0–39.0°) at the final follow-up. The progression of 28.8 ± 1.9° (range: 26.0–32.0°) in the sagittal plane was found to be statistically significant ($t = -36.4$, $P < 0.001$). The degrees of lordosis were not statistically significantly altered between 17 and 22 weeks after the operation (week 17 vs. 22, $t = -0.5$, $P = 0.611$). The average initial axial rotation measured by CT scan was 4.5 ± 1.0° (range: 3.0–6.0°) immediately after the operation and progressed to 31.2 ± 3.8° (range: 26.0–36.0°) on an average by the end of the observation period [Figure 8]. The average progression of 26.7 ± 4.1° (range: 22.0–31.0°) was statistically significant ($t = -16.0$, $P < 0.001$).

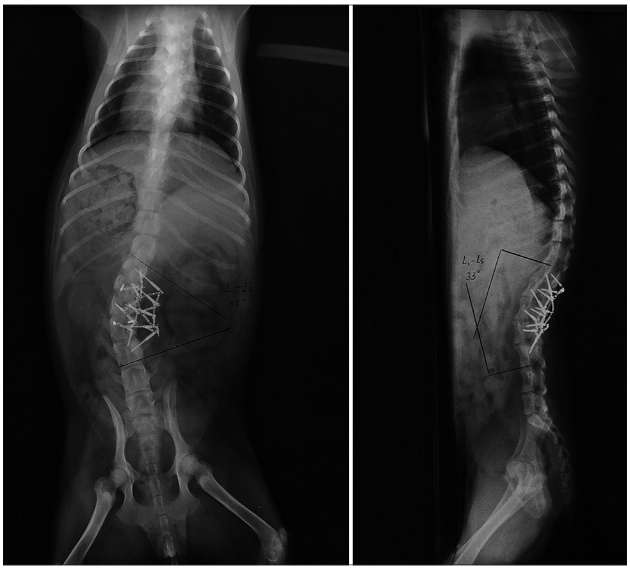

Figure 7: Posteroanterior and lateral radiographs of the spine 22 weeks after surgery.

DISCUSSION

The asymmetric load is known to play an important role in the development of scoliosis. The pathological compression inhibits vertebral growth on one side of the spine while reduced compression accelerates the longitudinal vertebral growth of the other side of the spine.[25] In earlier animal models of scoliosis, the mechanism by which scoliosis is formed involved tethering techniques (rigid and flexible) to fix the longitudinal length of the torso. As such, subsequent development of the deformity depended on the growth potential of the animal, and scoliosis models were not as severe as human patients. Our study established a lumbar segment scoliosis model in immature dogs that creates progressive, structural, idiopathic-type, marked lordoscoliotic curve convex to the left with axial rotation of the apical vertebral body. The curve progression of previous tethering models depends on the growth potential. Long tethering periods are required for the development of curves, which consume the majority of the animals' rapid growth period. Our study establishes a dog model for progressive lumbar scoliosis in a short amount of time. Our previous study demonstrated that the scoliosis model could maintain stable scoliotic curves after spring removal as the animals approached sexual maturity.[23] We found that the deformity progressed rapidly in the early stages after spring implant surgery, partly because of the better flexibility of the spine in dogs at an early age and partly because of the rapid growth during this time. Moreover, the tension of the NT coil springs remained basically unchanged as the dogs aged. Thus, the ratio of the spring tension to animal body weight dropped with age and the same tension had less of an influence on spinal growth of older and bigger dogs.

Scoliosis is a three-dimensional spinal deformity. Classical tethering models can only apply a force to the spine in one direction, which makes modulating spinal growth simultaneously in three dimensions challenging. Moreover, it is hard to control which segment is going to be the apex of the curve. In our study, we applied multiple NT coil springs to tether each segment of the lumbar spine. The posterior longitudinally tethered springs applied loads to modulate spinal growth mainly in the sagittal plane, whereas lateral longitudinally tethered springs modulated spinal growth in the coronal plane, and diagonal springs provided torque to create axial rotation. Thus, the three-dimensional, fusionless modulation of spinal growth described in this study represents advancement over previous tethering techniques, and the curve shape of this model is more similar to scoliosis observed in patients [Figure 9]. Moreover, the growth of each lumbar segment was modulated by NT coil springs separately, so we could determine the apex level of the curve in this model.

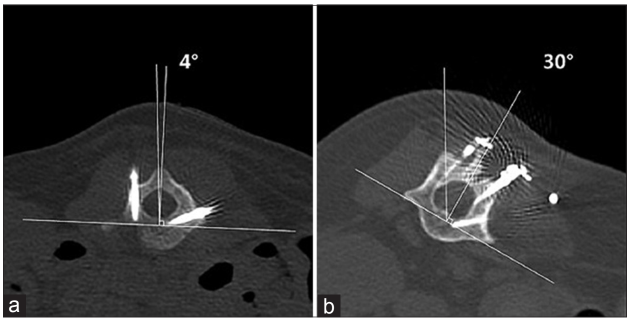

Figure 8: Computed tomography images of initial axial rotation (a) and final axial rotation (b) after surgery.

Each scoliosis patient is unique, and the condition may vary in shape and size. Some spine deformities are predominated by scoliosis, while others have kyphosis or rotatory deformities. As such, although the single tethering technique can create a spinal scoliosis deformity, precisely modulating spinal growth to mimic a scoliosis deformity through a single tether is difficult. The NT coil springs have five specifications ranging from 25 g to 200 g (ultralight: 25 g; extra light: 50 g; light: 100 g; medium: 150 g; and heavy: 200 g). To achieve the favorable experimental results of this study, we selected the heavy NT (200 g) coil springs. Since mechanical overloading can produce tissue trauma and accelerate disc degeneration,[26] we calculated the torque of the NT coil springs applied to the lumbar spine to ensure that the pressure at the concave side of the vertebral discs was no more than half the animal's body weight. Therefore, the loading of the NT coil springs should prevent damage to the vertebral disc. Furthermore, a combination of springs having different tensions could be used to create different three-dimensional curve shapes. For creating spinal deformities in which scoliosis predominates, an orthopedic scheme could involve heavy NT coil springs to modulate spinal growth in the coronal plane and medium or light NT coil springs to modulate spinal growth in the sagittal and transverse planes. Similarly, we can use springs that can impose larger forces to create kyphosis-based spinal deformities in the sagittal plane or rotation-based spinal deformities in the transverse plane. Each spinal experimental segment can be fixed with bone screws, and thus the vertebral growth at different spinal levels could be modulated by applying springs with different tensions. The technique developed from this preliminary study could be used to create different scoliosis shapes based on different experimental requirements.

Nowadays, lumbar scoliosis (including idiopathic and congenital scoliosis) is difficult to treat in the clinic. Bracing treatment is not effective for lumbar scoliosis because this region does not have ribs through which corrective forces can be transferred, and spinal fusion surgery renders the patient with reduced mobile segments postoperatively and sets the

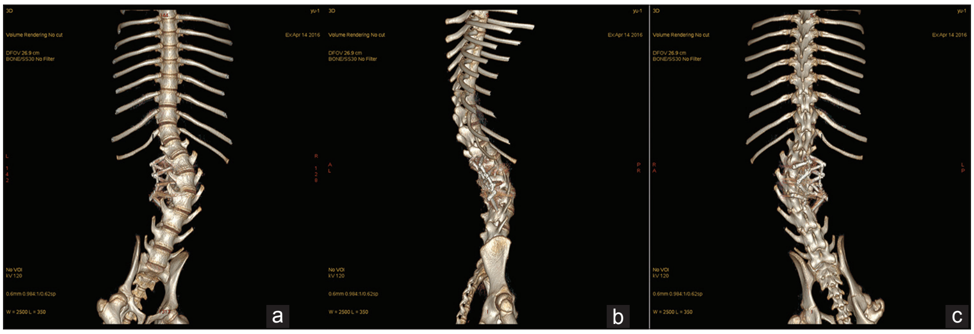

Figure 9: Computed tomography scan with three-dimensional reconstruction of the spinal deformity. The front view (a), the side view (b), and the back view (c) of the reconstructed spinal deformity.

stage for future sagittal plane issues in late adulthood. This study describes an excellent model for lumbar scoliosis, and the method in this study maintains the essential elements along the curve. The screw-setting technique in our study is borrowed from mini-invasive percutaneous pedicle screw fixation, which avoids deep dissection of muscle [Figure 3], maintains essential elements along the spinal curve, and allows for faster recovery. Indeed, all the dogs in this study could move freely within 1 week of surgery, suggesting that the tethering technique in this study is a minimally invasive method to create scoliosis.

Although the positive results of this animal model of scoliosis were notable, several problems need to be resolved. The NT coil spring tension was suitable for the demands of this study, but the spring strength was insufficient. Of the eight dogs that were enrolled in this study, two had NT coil spring fracture. The NT coil springs used in this study were originally designed for orthodontic applications, so the NT springs would likely need to be completely redesigned for use in spine in order to meet the strength requirements of orthopedic procedures. Furthermore, we must determine the optimal NT coil spring tension that would allow spinal growth modulation but avoid tissue trauma or acceleration of disc degeneration.

Current nonfusion treatments (e.g., growing rod technique) for adolescent idiopathic scoliosis have achieved acceptable results.[3] However, the growing-rod surgery often involves complications,[7,8] and many patients treated with this approach require final fusion surgery. NT coil springs are commonly and successfully used in orthodontics, but they have not yet been used for scoliosis treatment. Despite the limitations that need to be addressed, the spinal growth modulation technique involving NT springs described in this study could yield information that would provide a basis for developing novel early-stage treatments for children with scoliosis.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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