Neurocentral Synchrondrosis Screws to Create and Correct Experimental Deformity

A Pilot Study

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Abstract

Background Unilateral pedicle screw epiphysiodesis of the neurocentral synchondrosis (NCS) can produce asymmetric growth of the synchondrosis to create scoliosis in an immature animal model.

Questions/purposes We asked whether a preexisting experimentally created scoliosis could be limited and corrected by modulating the growth of the faster-growing NCS by a similar method.

Methods Nine 1-month-old pigs were assigned to each of three groups: (1) a sham group in which three animals received a sham operation but without a pedicle screw fixation; (2) an experimental group with double right pedicle screws placed across the NCS from T7 to T14 (scoliosis-untreated); and (3) an experimental group treated in the same way except a second set of double pedicle screws was placed in the left pedicles 6 weeks after the screws were placed on the right (scoliosis-treated). All animals were euthanized at 17 weeks, and radiographs and axial CT images of the spine were obtained.

Results A scoliotic curve was not seen in any of the animals in the sham group, in three of three in the scoliosis-untreated group with an average of 34°, and in three of

three in the scoliosis-treated group with an average of 20°. In comparison to the scoliosis-untreated group, the second set of pedicle screws produced a 41% correction of the scoliosis.

Conclusions We found the pedicle screw inhibited the overgrowth of the NCS to prevent further curve progression and obtained some correction of the deformity. The NCS screw epiphysiodesis can create and reverse scoliosis in an immature pig model.

Introduction

The neurocentral synchondrosis (NCS) is a bipolar growth cartilage in the vertebra located bilaterally at the junction of the pedicle and the vertebral body [9, 15–17, 19]. It is considered important for vertebral growth in the transverse plane [3, 4, 6, 14, 20]. NCS growth asymmetry can produce an axial deformity, which may result in three-dimensional deformity of the spine (scoliosis) [1, 5, 10, 12, 13]. We previously demonstrated a unilateral pedicle screw fixation, which traverses the NCS in an immature pig model, produced NCS epiphysiodesis on the operative side resulting in scoliosis with the convexity on the side of the screw fixation resulting from continued growth of the unaffected side [18]. Thus, if scoliosis can be created in a straight spine using the screw NCS epiphysiodesis unilaterally, it is logical to assume a preexisting deformity can be treated by modulating the growth of the faster-growing NCS on the contralateral side by a similar method.

We therefore determined whether (1) the unilateral pedicle screw NCS inhibition would create a scoliosis in a straight immature growing spine; (2) the contralateral staged NCS screw placement would limit or correct this scoliosis; (3) the NCS screw would inhibit the transverse

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Each author certifies that his or her institution has approved the animal protocol for this investigation and that all investigations were conducted in conformity with ethical principles of research.

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growth of the vertebra to produce shortening of the pedicle and result in the vertebral rotation toward the screw side; (4) the NCS screw would disturb the spinal canal growth resulting in the iatrogenic spinal stenosis; and (5) the NCS screw would arrest longitudinal growth of the spine.

Material and Methods

In a pilot study, we tested the pedicle screw NCS epiphyseodesis to create and reverse a scoliosis in nine 1-month-old pigs. The right pedicle NCS screws were placed at eight thoracic levels to produce a right thoracic scoliosis in six animals. At 6 weeks postoperatively, three of six animals were treated to correct the deformity by a second set of NCS screws placed in the left pedicle at the same thoracic levels. The animals were followed up for 17 weeks and plain radiographs and axial CT images were performed to analyze the scoliosis development and the screw NCS inhibition of the vertebral growth. Three sham animals were treated by unilateral paraspinal muscle exposure only without NCS screw fixation to test whether the muscle denervation would produce a scoliotic deformity. This study was approved by the Institutional Animal Care and Use Committee.

All animals (5–8 kg) underwent general anesthesia with 6 mg/kg Telazol (Fort Dodge Animal Health, Fort Dodge, IA) administered intramuscularly. All received antibiotics preoperatively (35 mg/kg cephazolin intravenously) and postoperatively (3 mg/kg ceftiofur intramuscularly twice a day for 3 days). The animals were placed in the prone position and a standard posterior midline incision was made to expose the spinous processes from T7 to T14. The right paraspinal muscles were dissected superficial to the periosteum at the level of the lamina and exposed to the tip of the transverse processes unilaterally. The ligament of the transverse process-costal facet was identified without injuring the adjacent spinal facet joints. The operation then proceeded according to whether the animal had been randomly assigned to the sham, scoliosis-untreated, or scoliosis-treated group.

For the sham group (three animals), after soft tissue dissection of the paraspinal muscles, the incision was left open for 60 minutes, the estimated time necessary to place pedicle screws in the treatment groups.

For the scoliosis-untreated group (three animals), the animals underwent double pedicle screw fixation of the right pedicles from T7 to T14. We selected double screw insertion based on our previous study in which single screw insertion failed to produce scoliosis in two of three animals [18]. The starting point for the pedicle screws was identified with use of anatomic landmarks on the posterior elements of the spine and was confirmed with fluoroscopy.

The landmark for the cephalad-caudal starting point was on the medial edge of the ligament of the transverse process-costal facet, and the medial-lateral starting point was the lateral margin of the superior facet joint (Fig. 1). Within each pedicle, two screws were placed so the starting point for the first pedicle screw was on the superior margin of the pedicle and the starting point for the second screw was just inferior to the first one. The orientation of the two screws was parallel in the sagittal plane and directed 35° to 40° from the perpendicular in the axial plane. Intraosseous pedicle penetration was confirmed with use of a ball-tipped probe to palpate five pedicle walls and to determine pedicle depth. The pedicle was then tapped with a 2.5-mm-diameter tap, after which a 3.5-mm cortical screw (Synthes, Paoli, PA) of appropriate length (usually 20–22 mm) was placed.

For the scoliosis-treated group (three animals), in the scoliosis-untreated animals, a second set of double pedicle screws was placed in the left pedicles from T7 to T14 6 weeks after the screws were placed on the right.

After screw placement, the soft tissues were closed in layers with use of absorbable suture. AP and lateral radiographs of the entire spine were made immediately after the surgery in all animals.

Analgesics (1.5 mg/kg flunixin meglumine) were administered intramuscularly twice a day for 3 days postoperatively. No postoperative immobilization was used. The animals were radiographed to assess the curve in the coronal and sagittal planes at 2-week intervals for the first

Fig. 1 This photograph shows the starting points for the pedicle neurocentral synchondrosis (NCS) screw insertion. A is the 10th rib, B is the ligament of the transverse process-costal facet, C is the superior facet of the T10, and D is the lamina of the T10. The starting points for the NCS screw is on the medial edge of the ligament of the transverse process-costal facet and just the lateral margin of the superior facet joint.

6 weeks postoperatively and at 10 and 17 weeks postoperatively. All animals survived without neurologic complications and remained normal and healthy for 17 weeks. All pedicle screws crossed the location of the NCS in the instrumented animals. All animals were euthanized with pentobarbital sodium and phenytoin sodium (90 mg/kg intravenously) at 17 weeks, and the entire spine (T1 to lumbar vertebra 5), including the ribs, was harvested.

CT scans with three-dimensional reconstruction of the thoracic spine were performed (Philips Medical System, Bothell, WA) with a 32-cm field of view, a scanning power of 200 mA, 120 kV, and a 0.67-mm slice thickness. The inclination of the vertebrae was adjusted to ensure all transverse images were parallel to the superior margin of the vertebra and symmetrically across both pedicles.

Assessment of fusion over the operatively treated levels (T7 through T14) was performed by visual inspection, manual palpation, and evaluation of the radiographs and three-dimensional reconstructed CT images by two independent observers (HZ, DS).

One of us (HZ) measured the following parameters on either radiographs or CT images using the Synapse analysis system (Fujifilm Medical System, USA, Inc, Stamford, CT): (1) coronal Cobb angle: On the AP radiographs, the vertebrae with the greatest amount of tilt were selected as the cephalad and caudal end vertebrae. Lines were drawn perpendicular to the end plate of the vertebrae. The angle subtended by these lines was the coronal Cobb angle; (2) anterior-pedicle zone-posterior (APP) length: This was measured in the midtransverse CT image from T7 to T14 (Fig. 2); (3) apical vertebral axial rotation: This was measured in the midtransverse CT image of the apical vertebrae (Fig. 3); (4) spinal canal area: The total and two hemicanal areas were measured in the midtransverse CT image from T7 to T14 (Fig. 2); (5) thoracic height: On the AP radiographs, the thoracic height was the perpendicular distance between the midpoint of the superior margin of T1 and the midpoint of the inferior margin of T15. The thoracic height was measured on the immediate and the 17-week postoperative radiographs. The increase in the thoracic height in 17 weeks and thoracic growth rate (mm/day) were calculated; (6) instrumented-vertebrae height: On the lateral radiographs, the height of the instrumented and sham vertebrae was measured on the midportion of the vertebra immediately and at 17 weeks postoperatively. The increase in the vertebra height during the 17-week and the vertebra growth rate (mm/day) were calculated; (7) screw orientation: On the axial CT image, each pedicle screw position was evaluated to determine whether the screw crossed the NCS.

Paired *t* tests were used to determine differences between the left and right side with respect to the APP

Fig. 2 Axial CT image of a vertebra in the sham group showing the measurement of anterior-pedicle zone-posterior (APP) length and spinal canal area. Line 1 was drawn through the right posterior element of the vertebra, and Line 2 was drawn through the left posterior element. B is the midpoint of the right neurocentral synchondrosis (NCS). C is the midpoint of the width of the right pedicle. Line 3 was drawn through Points B and C. A is the point along Line 3 that intersects the anterior margin of the vertebral body. P is the point at which Line 3 intersects Line 1. The line between A and P is the length of the right anterior-pedicle zone-posterior, and the line between A1 and P1 is the length of the left anterior-pedicle zone-posterior. Line 5 was drawn between the anterior aspect of the midpart of the vertebral body and the spinous process. D is the right hemicanal area and D1 is the left hemicanal area. D and D1 is the total spinal canal area.

length and hemicanal area in each group. The parameters, including the total spinal canal area, vertebral rotation, thoracic height, and the height of instrumented vertebrae, were compared among the three groups with use of one-way analysis of variance and Tukey multiple comparison methods.

Results

At 17-week followup, three of three animals in the scoliosis-untreated group had scoliosis with an average Cobb measurement of 34.3° (Table 1). All curves were located at the operated levels with the convexity toward the screw side (Fig. 4A–F).

In the scoliosis-treated group, an average 33.3° scoliosis was created in all animals at 6 weeks postoperatively (Table 1). After the second NCS screw placement on the contralateral side, the scoliosis was limited and the curve

decreased to 20.3° at the 17 weeks postoperatively (Fig. 5A–G).

In the sham group (Table 1), all three animals had a right thoracic scoliosis with an average of 16° at 2 weeks postoperatively, but by 6 weeks, only one of three animals had a curve, and no scoliosis was seen after 10 weeks postoperatively (Fig. 6A–F).

The NCS screw arrested the vertebral growth in the transverse plane to produce shortening of the pedicle and to result in vertebral rotation toward the screw side (Table 2). In the scoliosis-untreated group (Fig. 7), the

Fig. 3 Axial CT image of a vertebra in the scoliosis-untreated group showing the measurement of the vertebral axial rotation. Line 1 was drawn perpendicular to the base of the CT table. Line 2 was drawn between the anterior aspect of the midpart of the vertebral body and the spinous process. Angle A, subtended by Lines 1 and 2, is the vertebral axial rotation angle. The vertebra is axially rotated toward the screw side by 24° .

APP length on the screw-insertion side was 12% shorter ($p < 0.001$) than on the nonscrew side. The vertebral axial rotation occurred toward the screw-insertion side with an average of $23.8^\circ \pm 2.6^\circ$. In the scoliosis-treated group (Fig. 8), compared with the sham group, the first- and second-insertion screws resulted in 12% ($p < 0.001$) and 9% ($p = 0.002$) shortening of the APP length, respectively. The vertebral rotation was toward the first screw-insertion side with an average of $16^\circ \pm 3.6^\circ$, which was smaller ($p < 0.001$) than the scoliosis-untreated group. There were no differences in the APP length between the left (intact) and right (sham operation) side in the sham group (Fig. 2). No vertebral rotation was found in the sham animals.

The NCS screw disturbed the spinal canal growth resulting in the spinal stenosis. The mean total spinal canal area was $113.3 \pm 14.4 \text{ mm}^2$ in the sham group, $104.5 \pm 12.4 \text{ mm}^2$ in the scoliosis-untreated group, and $96.5 \pm 10 \text{ mm}^2$ in the scoliosis-treated group. The total spinal canal area in the sham group was 8% and 15% greater ($p < 0.001$) than the area in the scoliosis-untreated and treated groups, respectively. No difference was seen between the scoliosis-untreated and treated groups.

The NCS screw narrowed the hemicanal area on the screw-insertion side (Table 2). In the scoliosis-untreated group, the hemicanal area on the screw-insertion side was 42% narrower ($p < 0.001$) than the area on the nonscrew side. In the scoliosis-treated group, compared with the sham group, the first- and second-insertion screws resulted in 21% and 10% narrowing ($p < 0.001$) of the hemicanal area, respectively. There were no differences in the hemicanal area between the left (intact) and right (sham operation) sides in the sham group.

The NCS screw did not arrest the longitudinal growth of the spine. At the time of euthanasia, the mean increase in

Table 1. Coronal Cobb angle (degrees)

Group	Animal number	Immediately postoperative	2 weeks postoper	4 weeks postopera	6 weeks postoperatively	10 weeks postoperatively	17 weeks postoperatively
Sham	1	0	18	8	0	0	0
	2	0	7	0	0	0	0
	3	0	23	20	16	0	0
	Average	0	16	9.3	5.3	0	0
Scoliosis untreated	1	0	45	45	36	40	42
	2	0	46	43	40	26	30
	3	0	30	31	35	23	29
	Average	0	40.3	39.7	37	29.7	34.3
Scoliosis treated	1	0	48	47	32	19	14
	2	0	47	47	40	27	25
	3	0	37	35	28	24	22
	Average	0	44	43	33.3	23.3	20.3

Fig. 4A–F AP radiographs showing a scoliosis-untreated case. (A) Immediate postoperative radiograph showing no coronal curve. A 45°, 45°, 36°, 40°, and 42° scoliotic curve with convexity on the

right (screw insertion) side at 2 (B), 4 (C), 6 (D), 10 (E), and 17 (F) weeks postoperatively, respectively.

Fig. 5A–G AP radiographs showing a scoliosis-treated case. (A) Immediate postoperative radiograph showing no coronal curve. A 48° and 47° scoliotic curve with convexity on the right (first screw insertion) side at 2 (B) and 4 (C) weeks postoperatively, respectively. (D) A 32° scoliotic curve at the 6 weeks postoperatively.

(E) Immediately postoperatively (second set of neurocentral synchondrosis [NCS] screw placement) with 28° curve. A 19° and 14° scoliotic curve with the convexity on the right (first screw insertion) side at 10 (F) and 17 (G) weeks postoperatively, respectively.

Fig. 6A–F AP radiographs showing a sham case. (A) Immediate postoperative radiograph showing no coronal curve. (B) An 18° scoliotic curve with convexity on the right (sham operation) side at

2 weeks postoperatively. (C) An 8° scoliotic curve at 4 weeks postoperatively. No curve at 6 (D), 10 (E), and 17 (F) weeks postoperatively.

Table 2. Anterior pedicle zone posterior length and hemicanal area

Group	Anterior-pedicle zone-posterior length (mm)			Hemicanal area (mm ²)		
	Left*	Right [†]	Paired t	Left [‡]	Right [§]	Paired t
Sham	27.9 ± 1.4	27.9 ± 1.5	NS	55.4 ± 8.0	57.1 ± 8.0	NS
Scoliosis untreated	27.6 ± 2.8	24.3 ± 2.6	<0.0001	65.3 ± 8.4	37.6 ± 9.3	<0.0001
Scoliosis treated	25.4 ± 3.2	24.5 ± 2.5	NS	50.0 ± 5.4	45.0 ± 9.7	0.02

* $p = 0.002$, sham and untreated > treated group; [†] $p < 0.0001$, sham > untreated and treated group; [‡] $p < 0.0001$, untreated > sham > treated group; [§] $p < 0.0001$, sham > treated > untreated group; NS = nonsignificant

Fig. 7 Axial CT image of a vertebra in the scoliosis-untreated group. The vertebra is axially rotated to the screw side. The left (concave, untreated) anterior-pedicle zone-posterior length (APP1) is greater than the right (convex, screw insertion) APP. The left hemicanal area (D1) is greater than the right hemicanal area (D).

Fig. 8 Axial CT image of a vertebra in the scoliosis-treated group. The vertebra is slightly rotated to the first screw-insertion side. The left (concave, second screw insertion) anterior-pedicle zone-posterior length (APP1) is slightly greater than the right (convex, first screw insertion) APP. The left hemicanal area (D1) is similar to the right hemicanal area (D).

the length of the thoracic spine was similar in the three groups: 15.2 ± 3.7 cm (growth rate, 1.28 mm/day) in the sham group, 16 ± 2 cm (growth rate, 1.34 mm/day) in the

scoliosis-untreated group, and 14.1 ± 2.6 cm (growth rate, 1.18 mm/day) in the scoliosis-treated group.

The NCS screw did not inhibit the longitudinal growth of the instrumented vertebrae. The mean increase in the height of the vertebra in the region of T7 to T14 was similar in the three groups: 11.8 ± 3.4 mm (growth rate, 0.099 mm/day) in the sham group, 12.2 ± 2.6 mm (growth rate, 0.103 mm/day) in the scoliosis-untreated group, and 13.1 ± 1.7 mm (growth rate, 0.110 mm/day) in the scoliosis-treated group.

No evidence of fusion over the operative levels was detected by direct visualization. The manual palpation test demonstrated the spine mobility at the operatively treated levels was similar among the three groups. No fusions could be seen on the radiographs, CT images, and three-dimensional CT (Fig. 9A–C).

Discussion

NCS is a growth plate in the spine and contributes to the growth of both the vertebral body and the posterior arch. One would presume an asymmetric disturbance of the NCS would result in relative excess growth on the unaffected side and lead to both a coronal and axial plane deformity. If scoliosis can be created in a straight spine by inhibiting the NCS growth unilaterally, it is logical to assume that this deformity can be limited by modulating the growth of the faster-growing NCS on the contralateral side by a similar method. In a pilot study, we asked whether (1) the unilateral screw NCS inhibition would create a scoliosis in a straight immature growing spine; (2) the contralateral staged NCS screw placement would limit or correct this scoliosis; (3) the NCS screw would inhibit the transverse growth of the vertebra to produce shortening of the pedicle and result in the vertebral rotation toward the screw side; (4) the NCS screw would disturb the spinal canal growth resulting in the iatrogenic spinal stenosis; and (5) the NCS screw would arrest longitudinal growth of the spine.

Our study is subject to certain limitations. First, the number of animals is small. Although this study is a continuation of our work and the results are consistent, we

Fig. 9A–C Three-dimensional CT images showing no fusion on the operative region in the sham (A), scoliosis-untreated (B), and scoliosis-treated (C) groups.

believe more animals for each group would be better to demonstrate our goals. Second, the 17-week followup is relatively short; however, the rapid growth seen in the pigs between 4 weeks and 21 weeks parallels roughly the growth seen in children between the infantile and early juvenile periods in which the NCS is actively open [19].

The unilateral NCS screw over thoracic segments successfully created scoliosis in every animal at the 17-week followup. All curves and the apex of the deformity were located at the operated levels with the convexity on the screw-insertion side. The contralateral staged NCS screw placement inhibited the overgrowth of the NCS to prevent further curve progression obtaining some correction of the deformity. Our observations suggest the NCS screw epiphysiodesis can create and reverse the scoliosis in an immature pig model.

NCS is histologically a bipolar growth plate with two directly opposed series of cell columns, which is responsible for growth both anterior toward the vertebral body and posterior toward the pedicle [16]. Under normal conditions, the symmetric growth of the right and left NCS results in the synchronized growth of the pedicle and vertebra bilaterally without deformity [11, 19]. NCS growth asymmetry may produce unequal pedicle and vertebra growth leading to vertebral rotation and lateral curvature of the spine [7, 8]. The present study demonstrated unilateral NCS screw epiphysiodesis disturbed the growth of the ipsilateral pedicle and hemivertebra in the transverse plane to produce shortening of the pedicle-vertebra (APP) length and result in relative overgrowth on the opposite APP, which induced vertebral axial rotation toward the operative side and produced scoliosis with the convexity on the screw-insertion side. Therefore, the asymmetry of the APP

length would be an important pathoanatomic feature of scoliosis.

The contralateral staged NCS screw arrested the overgrowing APP to prevent the vertebrae from continually rotating toward the convexity, which limited further curve progression and obtained some correction of the deformity. Our results showed the second set of NCS screws produced 33% reduction of the apical vertebral rotation and 41% correction of the scoliosis.

One previous study suggests injury to the NCS or application of compressive forces across the NCS results in iatrogenic spinal stenosis in an animal model [2]. Using a histomorphometric analysis in an 8-week-old pig model, Zhang and Sucato demonstrated unilateral pedicle NCS screws do not lead to narrowing of the total spinal canal area [18]. In the current study, using younger age (4-week-old) animals and measurement of the axial CT images, we reported either unilateral or bilateral pedicle NCS screws disturbed the spinal canal growth resulting in narrowing of the hemicanal area on the epiphysiodesis side. Although the exact age is unknown in humans, the current study and the data from others would suggest strongly that pedicle screws when in use with younger animals may present a greater risk for creating spinal canal stenosis.

The current study suggests the pedicle NCS screw does not arrest longitudinal growth of the spine and could be a fusionless technique. Pedicle screw epiphysiodesis of the faster-growing (concave) NCS in early-onset scoliosis thus has the potential to prevent further curve progression and improve the deformity with continued growth. This growth modulation strategy would be especially useful in young patients with scoliosis in whom formal arthrodesis of the spine results in a short trunk and limits lung development

and ultimately has a detrimental effect on pulmonary function.

Pedicle screw epiphysiodesis of the NCS through a posterior approach is an open procedure requiring paraspinous muscle exposure and may cause denervation to produce a scoliotic deformity. The sham animals in this study showed a scoliosis averaging 16° at 2 weeks postoperatively. However, the curvature declined to 5° at 6 weeks and, consequently, disappeared at 10 weeks postoperatively. The presumed denervation may modify the dynamic internal equilibrium of the spine to induce deformity, which then recovers over time. This muscle-effect curvature was seen only at the early stages postoperatively.

Based on our preliminary findings, we conclude a pre-existing experimentally created scoliosis can be limited and corrected by modulating the growth of the faster-growing NCS using contralateral staged pedicle NCS screw placement. The NCS screw epiphysiodesis can create and reverse the scoliosis in an immature pig model. Further studies are necessary to clarify why (1) the unilateral NCS screw rapidly produced scoliosis in the first 2 weeks postoperatively, which was nonprogressive; and (2) the second set of NCS screws corrected the deformity although the first set of screws was still in place.

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