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BIOMECHANICS

Biomechanics of Spinal Hemiepiphysiodesis for Fusionless Scoliosis Treatment Using Titanium Implant

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Study Design. *In vitro* study of the effect of hemiepiphyseal implant on biomechanical properties of porcine thoracic motion segments.

Objective. Determine whether implantation of a titanium clip-screw construct alters spine biomechanical properties.

Summary of Background Data. Growth modification is under investigation as a treatment of early adolescent idiopathic scoliosis. Biomechanical property changes due to device implantation are essential to characterize immediate postoperative treatment effects.

Methods. *In vitro* biomechanical tests were conducted on 18 thoracic functional spinal units. Specimens were tested before and after implantation of a clip-screw construct in lateral bending, flexion-extension, or axial rotation (n = 6 per loading direction). Pure moments were applied, and range of motion, stiffness, and neutral zone were measured. Axial translations were determined bilaterally.

Results. Implantation of the clip-screw construct decreased range of motion in lateral bending by 19% ($P < 0.0003$), flexion-extension by 11% ($P < 0.04$), and axial rotation by 8%. Mean stiffness in lateral bending toward and away from the treated side increased by 20% ($P < 0.007$) and 33%, respectively. In flexion and extension, mean stiffness increased by 10% and 16%, respectively. Treatment decreased the neutral zone in lateral bending toward and away from the instrumented side by 30% ($P < 0.0003$) and 47% ($P < 0.02$), respectively. In flexion and extension, neutral zone decreased by 20% ($P < 0.04$) and 26% ($P < 0.007$), respectively. In axial rotation toward and away from the treated side, mean neutral zone decreased by 22% ($P < 0.04$) and 7%, respectively. Range of axial translation decreased on the ipsilateral side by 49% ($P < 0.001$) and increased on the contralateral side by 17%.

Conclusion. Implantation of a titanium clip-screw construct decreased range of motion by less than one-fifth, increased stiffness by one-third or less, and decreased the neutral zone by less than one-half. Range of axial translation decreased on the instrumented side and increased contralaterally. This study suggests that most of the flexibility of the spine is preserved in the immediate postoperative period after implantation of the spinal hemiepiphyseal construct.

Key words: spinal hemiepiphysiodesis, biomechanics, thoracic, growth modulation, titanium, fusionless, scoliosis treatment, nonfusion scoliosis surgery, innovative technique, vertebral growth, clip-screw construct, biomechanical properties, porcine model.

Level of Evidence: N/A

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The device that is the subject of this manuscript is being evaluated as part of an ongoing FDA-approved investigational protocol (IDE) for patients who are skeletally immature and who have a diagnosis of idiopathic scoliosis with a single main thoracic curve Cobb angle 25° to 40° and Lenke type 1A or 1B.

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Growth modification is a successful technique for correction of lower limb deformities, as well as one of the least invasive surgical procedures in pediatric orthopedics. Staple and screw-plate hemiepiphysiodesis are established methods of treating limb angular deformities. Similarly, harnessing growth either to prevent spine deformity progression or to correct an existing spine deformity might obviate some spinal fusions. Asymmetrical compression on epiphyseal plates as an cause for scoliosis progression was hypothesized as early as the 19th century.[1]

Unlike long-bone physes, the vertebral growth plates are contiguous with the disc. Therefore, any spine growth modification method that effectively applies compression must also decrease intervertebral joint motion. Maintaining sufficient motion is important to the viability of disc cartilage and joints. Because these implants would be expected to be in place for a minimum of 2 years and, perhaps permanently, short- and long-term loss of motion must be considered.

Preliminary studies have shown that implants are capable of creating spine curves in growing animal models.[2–4] In preclinical studies, an average curve of 20° occurred by 8 weeks in otherwise normal immature porcine spines, using 6 mid-thoracic stainless steel implants.[4] Based in part on a knee staple design, implant blades were designed with a divergent internal angle to induce initial compression on the treated side.[5] Histomorphometry showed that the height of the growth plate hypertrophic zone was reduced near the implant whereas the height close to the opposite cortex was nearly that of controls.[6] This effect is similar to that described for growth-modulating knee staples[7] and experimental tail models.[8,9]

Toward the goal of a clinical trial for patients with early adolescent idiopathic scoliosis, changes were made to the implant materials and design for safety, manufacturability, mechanical performance, and improvements in surgical technique. A titanium clip-screw construct was tested in a preclinical model. Spine curves were induced within 2 months in a growing domestic porcine model.[10] Curvatures at 8 weeks increased by 10° (SD = 4.5°) compared with immediate postoperative values ($P < 0.005$). The implants did not break, loosen, migrate, or plow in this growing animal model. *Ex vivo*, fatigue testing to 10 million cycles was performed. Subsequently, a prospective clinical safety study of the implant was conducted (institutional review board approved, FDA IDE [investigational device exemption]; clinicaltrials.gov no. NCT01465295).[11]

Preliminary biomechanical studies on the stainless steel implants indicated a large reduction in range of motion (ROM) in lateral bending[12] and small changes to compressive load-displacement behavior with stress shielding of peak dynamic stresses of 20%.[13] No study has yet reported any biomechanical changes due to the construct of the clinical study. Therefore, the purpose of this study was to determine the immediate postoperative biomechanical changes due to implantation of a titanium clip-screw construct for spinal hemiepiphysiodesis. The hypotheses were that ROM and neutral zone would decrease and stiffness increase in lateral bending, flexion-extension, and axial rotation. In addition, axial translations were determined bilaterally as an estimate of disc displacements during lateral bending.

MATERIALS AND METHODS

In vitro biomechanical tests were conducted on 10 thoracic spines harvested from skeletally immature domestic swine (age, 2–4 mo; body weight, ≈40 kg). The muscles and ribs were removed and intervertebral discs, posterior ligaments, and spinous processes were preserved. The spines were divided into 18 functional spinal units consisting of 2 vertebrae, disc, and ligaments. Specimens from the upper (T4–T5), middle (T7–T8), and lower (T10–T11) regions were assigned to 1 of 3 loading modes, using a blocked design to yield 2 specimens per thoracic level and 6 specimens per loading mode (n = 6). Vertebrae were fixed in fiberglass-reinforced polyester resin (Bondo; 3M, St. Paul, MN) in stainless steel fittings.

Specimens were tested before and after insertion of a titanium clip-screw construct (Figure 1). The device was placed so that the blades spanned the intervertebral disc and growth plates, with the posterior edge set just anterior to the costovertebral articulation. The specimen was retained in the apparatus during implantation to maintain its initial position. Specimens were tested in lateral bending, flexion-extension, or axial rotation. Moments up to ±4 N·m were applied using a materials test system (Instron 4465; Instron, Norwood, MA) with control and acquisition software (TestWorks 4; MTS, Eden Prairie, MN). Loads were measured using a load cell (5000 N) and converted to moments using the pulley diameter. The custom apparatus consisted of an aluminum frame with low-friction pulleys connected to a sliding loading ring by means of double-braided cable (ultrahigh-molecular-weight polyethylene, 1.8-mm diameter, Spectra; New England Ropes, Fall River, MA). The system was designed on the basis of previous reports,[14–16] with modifications to allow for continuous cycling through the ROM (Figure 2). By moving the crosshead, cable tension was applied to the loading ring to apply moments to the cephalad vertebra. Five cycles were

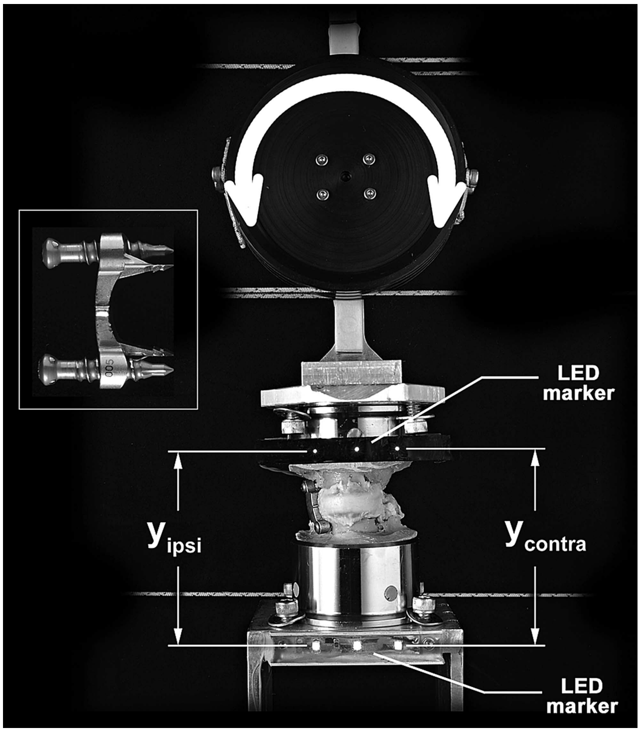

Figure 1. Specimen instrumented with titanium clip-screw construct (inset) mounted in test fixture, anterior view. Motion of materials test system crosshead generates tensile load in cables (horizontal lines), which is converted into an applied moment through the sliding ring (disc marked with curved arrow, top-center). Note that y_{ipsi} and y_{contra} are the distances between the cephalad and caudad markers in the initial position, with the specimen under no load. Changes in y from the initial position are the axial translations (d_y).

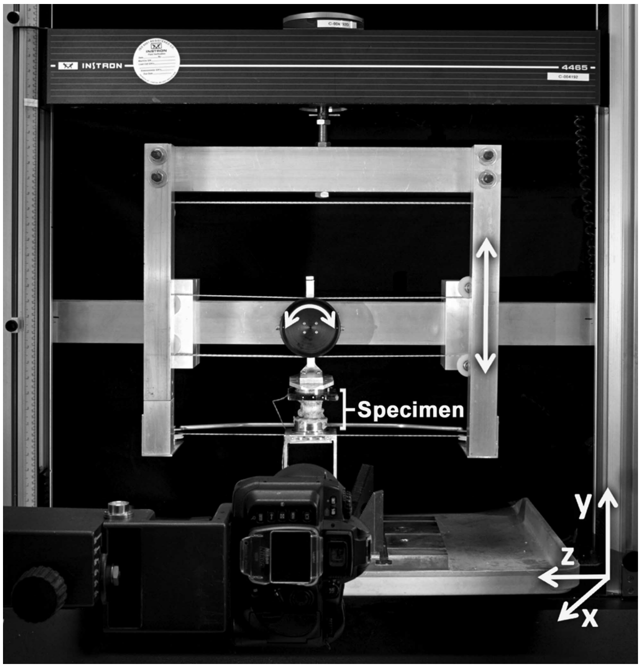

Figure 2. Biomechanical test assembly with specimen (center) oriented for lateral bending test. Central, inverted U-shaped structure moves with the crosshead, whereas the longer horizontal bar remains fixed to the load frame uprights. For flexion-extension, the specimen was rotated 90° about the longitudinal (*y*) axis. For axial rotation, the specimen was oriented such that the caudad vertebra was toward the camera and the anterior aspect up.

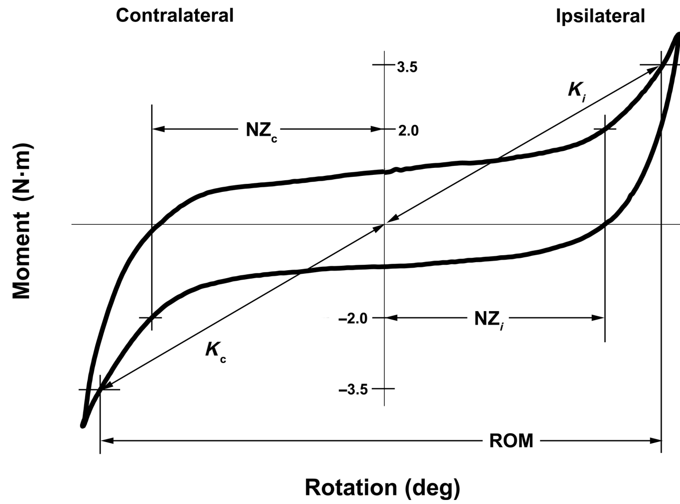

Figure 3. Sample moment-rotation curve with calculated biomechanical properties, for lateral bending toward (ipsilateral) and away (contralateral) from the instrumented side. Range of motion describes the physiological extent of motion and can be divided into a low-stiffness neutral zone and a high-stiffness zone. The low-stiffness region allows spinal movements near the neutral position with minimal effort. The high-stiffness region prevents damaging motion beyond the limit of physiological motion. Stiffness, as defined as the slope of the overall moment-rotation curve, indicates the average internal resistance to motion over the entire range of motion. *K* indicates stiffness; NZ, neutral zone; ROM, range of motion.

applied, and the fourth cycle was analyzed. Crosshead cycling frequency was 0.05 Hz. Sampling frequency for load and position was 24 Hz.

Vertebral position and orientation were determined from 3 LEDs rigidly attached to each vertebral body at locations ipsilateral, central, and contralateral to the implant, using high-definition video (Nikon D7000; Nikon, Tokyo, Japan) with Tokina AT-X Pro Macro 100 F2.8 D lens (Tokina, Tokyo, Japan). Marker positions were determined using a published computer program[17] (MATLAB; MathWorks, Inc., Natick, MA). Applied bending moments and vertebral rotations were calculated using a custom program (MATLAB).

Biomechanical properties determined from the moment-rotation curves (Figure 3) were ROM, stiffness, and neutral zone. ROM describes the physiological extent of motion and is divided into regions of low and high stiffness. The low-stiffness neutral zone indicates the range around the neutral position that requires minimal energy for joint motion. The high-stiffness region resists damaging motion beyond the physiological motion limit. Stiffness, defined as the slope of the overall moment-rotation curve, indicates the resistance to motion over the entire ROM. Specifically, ROM was defined as the side-to-side rotation between ±3.5 N·m, stiffness as the slope of the moment-rotation curve from 0 to 3.5 N·m for each direction and sense, and neutral zone as the rotation from 0 to 2.0 N·m for each direction and sense. Bending sense was defined as rotation of the cephalad vertebra toward (ipsilateral) or away from (contralateral) the instrumented side. In addition, as an estimate of the range of disc displacement during lateral bending, axial translation (d_y) was measured on the left and right sides as the difference between cephalad and caudad marker displacements. The range of axial translation was the total translation between ±3.5 N·m.

Statistical differences were determined by analysis of variance using a mixed model (SAS version 9.3; SAS Institute, Inc., Cary, NC) ($\alpha = 0.05$). Differences between control and instrumented conditions were evaluated separately for each loading direction and sense. The 2 factors were animal (spine 1–10) and treatment (before and after instrumentation). The hypotheses were that the outcome variables would decrease (ROM, neutral zone, d_y) or increase (stiffness) between control and treated conditions, so 1-tail tests were used. When significant differences were found in the overall model, the Bonferroni correction was applied. For ROM, the significance level to test for differences was 0.017 (0.05/3) to account for 3 loading directions. For stiffness and neutral zone, the significance level was 0.0083 (0.05/6) to account for loading direction and sense. For d_y, the significance level was 0.025 (0.05/2) to account for the left and right sides.

RESULTS

Implantation decreased the mean ROM and neutral zone and increased mean stiffness (Figures 4–7). The largest changes were in lateral bending. Range of axial translation decreased on the side ipsilateral to the implant and increased on the contralateral side (Figure 8).

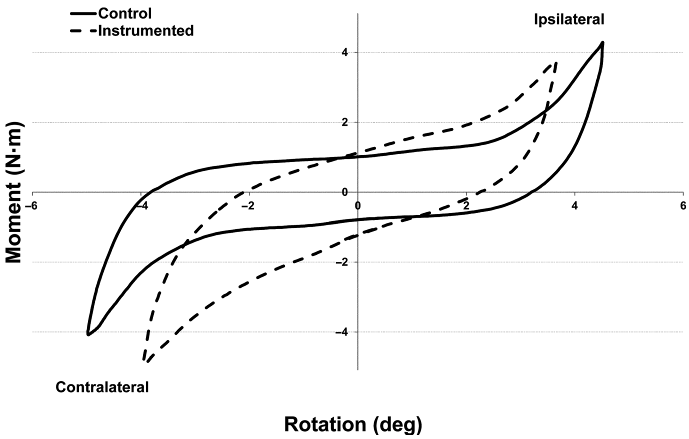

Figure 4. Typical moment-rotation curves, fourth cycle, lateral bending, before (control) and after (instrumented) implant placement, toward (ipsilateral) and away from (contralateral) the instrumented side.

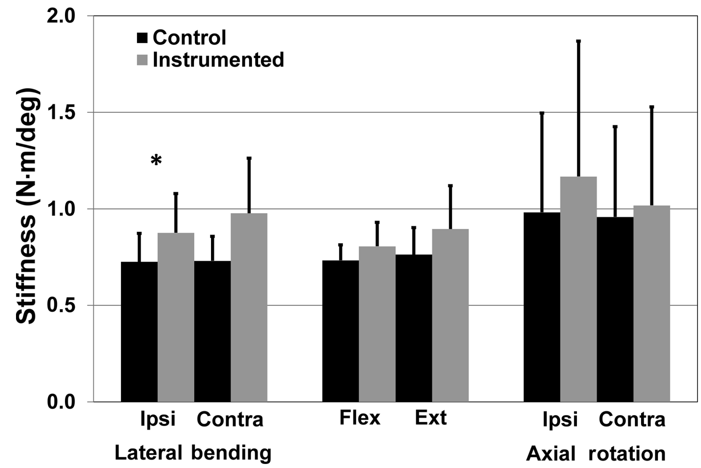

Figure 6. Stiffness before (control) and after instrumentation in lateral bending, flexion-extension, and axial rotation, for movement toward (Ipsi) and away from (Contra) the instrumented side (* $P < 0.007$). Contra indicates contralateral; Ext, extension; Flex, flexion; Ipsi, ipsilateral.

Before instrumentation, ROMs, as mean (SD), in lateral bending, flexion-extension, and axial rotation were 10.0° (SD = 2.1°), 9.5° (SD = 1.2°), and 9.0° (SD = 4.5°), respectively. After instrumentation, these values were 8.1° (SD = 2.5°), 8.6° (SD = 1.8°), and 8.4° (SD = 4.7°). Mean paired ROM decreased for each direction by 19% ($P < 0.0003$), 11% ($P < 0.04$), and 8%, respectively (Figure 5).

Stiffness of control specimens was symmetric for motion toward and away from the implant side. In lateral bending, stiffness values before instrumentation were 0.73 (SD = 0.15) N·m/deg and 0.73 (SD = 0.13) N·m/deg moving toward ipsilateral and contralateral sides, respectively. In flexion-extension, these values were 0.73 (SD = 0.08) N·m/deg and 0.76 (SD = 0.14) N·m/deg, and in axial rotation, these values were 0.98 (SD = 0.51) N·m/deg and 0.96 (SD = 0.47) N·m/deg. After implant insertion, stiffness values in lateral bending moving toward and away from the implant were 0.88 (SD = 0.20) N·m/deg and 0.98 (SD = 0.29) N·m/deg, respectively. In flexion-extension, these values were 0.81 (SD = 0.12) N·m/deg and 0.90 (SD = 0.22) N·m/deg, and in axial rotation, these values were 1.17 (SD = 0.70) N·m/deg and 1.02 (SD = 0.51) N·m/deg. Mean stiffness values increased compared with paired pretreatment control for each direction and sense. For lateral bending, increases moving toward sides ipsilateral and contralateral to the implant were 20% ($P < 0.007$) and 33%, respectively. For flexion-extension, these values were 10% and 16%, and for axial rotation, 15% and 6%, respectively (Figure 6).

Neutral zones for control specimens were symmetric for motions toward ipsilateral and contralateral sides. In lateral bending, neutral zones before instrumentation were 3.8° (SD = 0.93°) and 3.8° (SD = 0.98°) moving toward and away

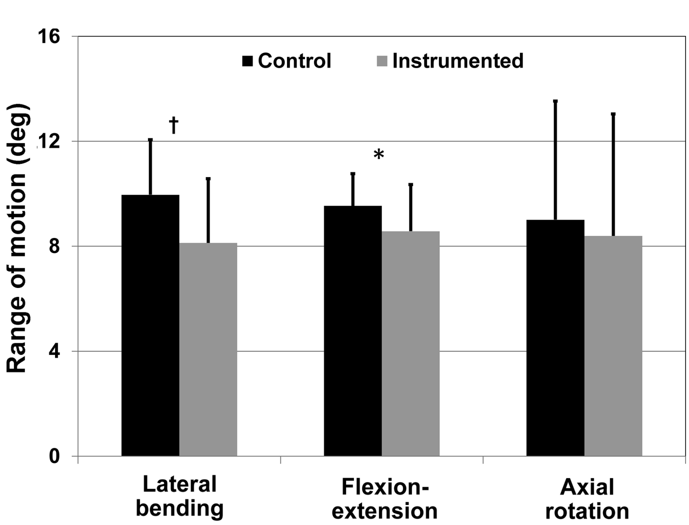

Figure 5. Range of motion before (control) and after instrumentation in lateral bending, flexion-extension, and axial rotation (* $P < 0.04$; † $P < 0.0003$).

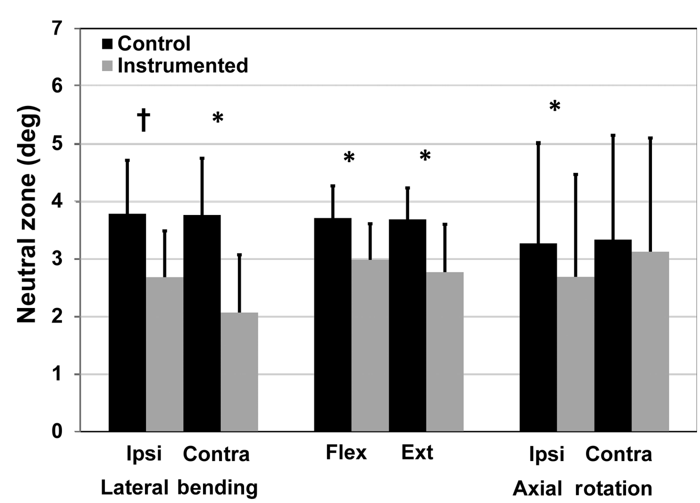

Figure 7. Neutral zone before (control) and after instrumentation in lateral bending, flexion-extension, and axial rotation, for movement toward (Ipsi) and away from (Contra) the instrumented side (* $P < 0.04$; † $P < 0.0003$). The reduction in neutral zone in lateral bending, in particular, indicates that implant insertion significantly reduced the laxity of the intervertebral joint through the neutral position. Contra indicates contralateral; Ext, extension; Flex, flexion; Ipsi, ipsilateral.

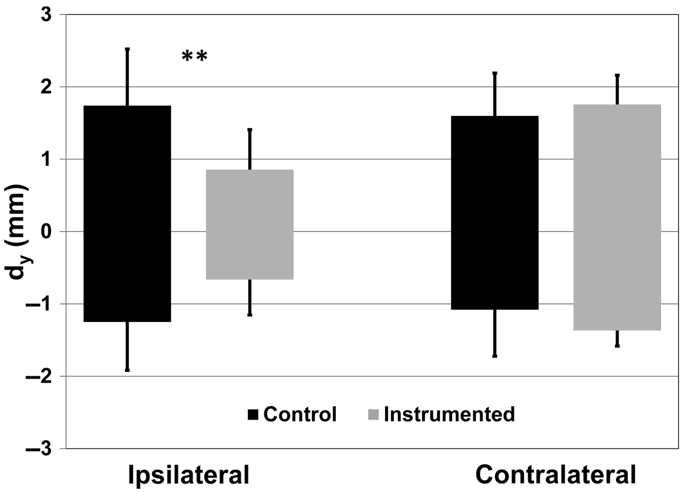

Figure 8. Axial translation before (control) and after instrumentation on the instrumented side (ipsilateral) and on the side contralateral to the instrumented side, during lateral bending. Positive values indicate distraction of the corresponding side of the motion segment, and negative values indicate compression. The total length of each bar is the range of axial translation (*$P < 0.001$).

from the implant, respectively. In flexion-extension, these values were 3.7° (SD = 0.56°) and 3.7° (SD = 0.55), and in axial rotation, 3.3° (SD = 1.8°) and 3.3° (SD = 1.8°). After instrumentation, neutral zones in lateral bending moving toward and away from the implant were 2.7° (SD = 0.80°) and 2.1° (SD = 1.0°). In flexion-extension, these values were 3.0° (SD = 0.62°) and 2.8° (SD = 0.83°), respectively, and in axial rotation, 2.7° (SD = 1.8°) and 3.1° (SD = 2.0°). Mean neutral zone decreased for each direction and sense compared with pretreatment controls. For lateral bending toward ipsilateral and contralateral sides, neutral zone reductions were 30% ($P < 0.0003$) and 47% ($P < 0.02$), respectively. For flexion-extension, these values were 20% ($P < 0.04$) and 26% ($P < 0.007$), and for axial rotation, 22% ($P < 0.04$) and 7% (Figure 7), respectively.

Range of axial translation in lateral bending decreased on the side ipsilateral to the implant and increased on the contralateral side after instrumentation compared with pretreatment controls (Figure 8). On the ipsilateral side, range of d_y decreased by 49% ($P < 0.001$), from 3.0 (SD = 0.77) mm to 1.5 (SD = 1.1) mm, for control and instrumented conditions, respectively, whereas on the contralateral side, mean range of d_y increased by 17%, from 2.7 (SD = 0.38) mm to 3.1 (SD = 0.41) mm.

DISCUSSION

A titanium spinal hemiepiphyseal implant designed for growth modulation, when applied to a spine motion segment, decreased the ROM and neutral zone and increased the stiffness in lateral bending, flexion-extension, and axial rotation compared with pretreatment controls. Reductions in ROM were less than 20%, below levels reported for fusion-promoting instrumentation.[18] These results indicated that most of the spine flexibility was retained in the immediate postoperative period, consistent with an *in vivo* study.[19] The greatest reduction was in the neutral zone. Axial translations remained measurable on the contralateral and ipsilateral sides in lateral bending, with side-to-side differences indicating a translation of the axis of rotation toward the ipsilateral side. The primary source of motion after instrumentation was elastic deformation of the titanium clip bridge. In addition, bone-implant interface motion was observed for large ranges of loading. However, no clip back-out or radiolucency around blades has been noted in any *in vivo* study to date.

Some retained motion is required in this type of growth modification surgery for deformity to maintain disc viability. If disc health is not maintained in the long term, patients may later need a spinal fusion, which would defeat the original purpose. Motion segment flexibility was conferred in part by features of the titanium clip-screw construct that were different from those of the previous stainless steel implant. Titanium has higher fatigue strength and fracture toughness, a lower bending modulus that allows for greater load sharing with the bone and the disc, creates fewer imaging artifacts, and allows the use of magnetic resonance imaging. The titanium screws are preloaded into the clip, have cancellous threads, are shorter, and contain locking and anti–back-out features. Eliminated from the current design were a cannulated screw in the clip body used to connect to the insertion tool and a guide-wire that had been used to center the implant over the disc.[4]

Limitations include that *in vitro* tests are most applicable to the immediate postoperative period. Changes would be expected to increase with postoperative time. Other limitations include differences between simulated and physiological loading conditions, porcine and human anatomy, and normal and scoliotic spines. Porcine vertebral bodies are more triangular in transverse section than those present in human, with no part of the lateral aspect parallel to the sagittal plane, so the construct was placed at an angle more oblique than that in humans. The plane of maximum reduction in motion would be expected to be in the plane of the implant. Biomechanical properties of quadruped and human spines have differences,[20] but changes between control and treated specimens within a species would be expected to be lower than property differences between species. Axial translations were measured lateral to the edges of the vertebrae and the disc and outside of the clip blades and likely overestimate the magnitude of motion at the implant site or the disc.

Comparisons with prior biomechanical studies indicated that changes due to the titanium construct are within reported ranges, although direct comparisons are limited by differences in test methods and outcome variable definitions. Preliminary studies on the stainless steel construct indicated a larger reduction in ROM in lateral bending[12] and smaller changes to compressive load-displacement behavior and stress shielding.[13] Changes in biomechanical properties in the current study were less than those in the preliminary study, with differences attributed primarily to the lower stiffness of the titanium implant than that of the stainless steel construct. Biomechanical studies at the immediate postoperative time have been reported for related devices, including shape memory alloy (SMA) staples[21–24] and tether systems.[24] Differences in pullout strength between shape memory staples and a tether system have been reported,[23] although without consideration of differences in expected physiological forces on each. It has been conjectured that using a tether may confer greater flexibility to the spine than that by other device types after fixation across multiple levels using bicortical screws.[23–27] In tests using SMA staples at multiple segments, lateral placement of a 4-prong design reduced ROM in lateral bending by about 15%, greater than that in flexion-extension and axial rotation.[21] In tests comparing SMA staples with a polymer tether construct,[24] the largest percent reductions in ROM, using reported group mean differences and as expressed as change from control divided by control, were 66% in lateral bending for the tether and 60% in axial rotation for the SMA staple. Compared with the titanium construct of the current study, the forces and moments applied to the spine might be expected to differ significantly. Tether systems that link together multiple motion segments tend to concentrate loads at the end of the construct and so have greater potential for screw plough or pullout. Differences at the bone-implant interface would be expected between the titanium clip-screw construct and the SMA staple due to the thinner and convergently angled blades of the SMA design and the motion of those blades during the phase change. These factors would be expected to affect the magnitude and distribution of static and dynamic stresses on vertebral growth plates differentially.

Direct comparisons among these related devices, however, are not yet possible because of differences in test methods and outcome variable definitions. For spine biomechanical testing in general, flexibility, stiffness, and hybrid test protocols have been described.[28–32] ROM measurements have been shown to be repeatable between laboratories with systems that applied moments similarly.[33] Some types of systems may allow for less biased comparisons between treatment conditions than others.[30–32,34] Compared with robotic 6-axis test machines[35–38] and cable-driven systems,[15,28,39,40] the test assembly of the current study was relatively simple and inexpensive, did not prescribe the locations of the axes of rotation, and applied moments symmetrically across the ROM.[41,42]

CONCLUSION

Spinal hemiepiphysiodesis with a titanium clip-screw construct decreased ROM by less than 20% compared with pretreatment controls. Results indicate that most of the mobility of the spine is retained, at least in the immediate postoperative time period. The amount of motion needed to maintain disc health is not yet well known. However, combined with prospective clinical trial results, understanding biomechanical changes due to this, and any, proposed spine growth modification method is necessary to balance the competing requirements of treatment efficacy and disc health maintenance.

➢ Key Points

- ❑ Implantation of a titanium clip-screw construct for spine growth modification reduced ROM by less than 20% in lateral bending, flexion-extension, and axial rotation.
- ❑ The construct increased stiffness by less than one-third in each direction.
- ❑ The largest changes in biomechanical properties occurred in the neutral zone due largely to linearization of the moment-rotation relationship.
- ❑ All joint motions remained measurable and dynamic.
- ❑ A titanium clip-screw construct restricted motion but not to levels of fusion promoting instrumentation.

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