INTERNATIONAL JOURNAL of SPINE SURGERY

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Int J Spine Surg 2017, 11 (3)
doi: https://doi.org/10.14444/4020
https://www.ijssurgery.com/content/11/3/20

Integrated Fixation Cage Loosening Under Fatigue Loading

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Abstract

Background

Screw loosening is a well-known adverse event in traditional spinal fusion instrumentation. This phenomenon may hinder segmental stability of the spine leading to bony non-union. In recent years numerous lumbar integrated fixation cages (IFC) have been introduced that offer a low profile alternative to a standard cage with an anterior plate (AP+C). The fixation approach for IFCs is different than a traditional anterior approach; therefore, it is unclear whether IFCs may loosen from the surrounding bone over time. The purpose of this study was to quantify screw loosening of IFC devices compared to AP+C implants under fatigue loading using micro-CT and image processing techniques.

Methods

L2-3 and L4-5 functional spinal units (FSUs) were obtained from nine human lumbar spines. These FSUs were then reconstructed with either AP+C or IFC implants designed to attach to vertebral bodies using four screws (two top and two bottom for AP+C; two medial and two lateral for IFC). The reconstructed specimens were fatigued in flexion-extension load of ±3 Nm at 1Hz for first 5,000 cycles and it was increased to ±5 Nm until 20,000 cycles. After removing screws to prevent image artifact, micro-CT scans were performed on all FSUs post-fatigue. These images were post-processed to calculate three-dimensional volumes around screw holes created due to damage at the screw-implant interface.

Results

IFC screws had significantly greater ($p=0.008$) screw hole volumes compared to AP+C screws after fatigue testing. This increased screw hole volume for IFC devices was mainly due to loosening in medial screws. Medial screws had significantly greater ($p<0.003$) screw hole volumes compared to lateral IFC screws and all AP+C screws. There was no difference ($p>0.888$) between the screw hole volumes of lateral IFC, top AP+C, and bottom AP+C screws.

Conclusions

This study elucidated screw-loosening mechanisms in integrated fixation cages under simulated physiological loading. In particular, spatial differences in fixation was observed for IFC screws across the vertebra where medial screws loosened at a greater frequency compared to lateral screws post-fatigue. This novel technique may also be used to quantitatively investigate screw fixation post-fatigue testing in a variety of spinal devices.

BIOMECHANICS
KEYWORDS: MICRO-CT, INTEGRATED FIXATION CAGE, ANTERIOR PLATE, CADAVER, FATIGUE, SCREW LOOSENING, IMAGE PROCESSING
VOLUME 11 ISSUE 3 DOI: 10.14444/4020
PAGES 160 - 166

Introduction

Anterior lumbar interbody fusion (ALIF) is a common spinal fusion procedure to treat degenerative disc disease, spondylolisthesis, spinal deformity, or pseudoarthrosis.[1,2] This procedure often involves inserting an intervertebral body fusion device (cage) into the disc space and further stabilizing the motion segment with supplemental fixation such as spinal anterior plates and pedicle screws. These fixation systems have been widely used to improve fusion rates and help patients return to ambulatory status sooner.[3,4] Although ALIF procedures have good clinical outcomes, previous studies reported screw loosening in 8-18% of patients.[5-9] Dynamic loading prior to fusion has been thought to cause loosening and in severe cases may lead to bony non-union.

Evaluations of loosening at the screw-bone interface have been primarily based on two-dimensional X-rays or low-dose computed tomography (CT) scans.[10-13] One of the studies assessed screw loosening in human patients by qualitative observations of radiolucent zones surrounding implanted screws.[13] This study also performed pullout testing in sheep vertebrae and found that screws with radiolucent zones possessed decreased pullout forces compared to those without radiolucency. Another study assessed screw loosening using semi-quantitative scoring based on tightness of the screw in canine vertebrae during extraction.[10] The results indicated that 36% of screws were considered loose after implanted for 9 months. Other biomechanical studies provided functional measures of screw loosening such as changes in the stiffness or pullout force post-fatigue.[11,13] Histological methods have also been used to provide an assessment of radiolucent zones and bone contact area around the screw threads.[12,14] However, histology only allows for two-dimensional visualization and semi-quantitative measures of damage at the bone-implant interface.

Although previous studies have used semi-quantitative or two-dimensional techniques to understand damage at the screw-bone interface, the use of quantitative, three-dimensional methods to investigate bone damage created at the screw-bone interface has not been reported. Micro-CT is a powerful system that can provide high resolution images to quantify changes in bone around the implant. Developing a micro-CT based method to assess whether device designs damage bone surrounding the implant may aid in reducing screw loosening observed clinically. In particular, integrated fixation cages (IFC) are different than traditional cages as fixation is typically achieved through screws inserted at different angles through the vertebral endplate. However, there is no long term data in literature documenting clinical performance of these IFC devices, particularly at the bone-implant interface where screw loosening may occur over time. Previous biomechanical studies of IFC devices have largely focused on quasi-static testing methodologies.[15-17] Fatigue testing is advantageous compared to quasi-static testing as it provides a more realistic assessment of device loosening by simulating post-operative dynamic loading. Therefore, the objective of this study was to quantify three-dimensional bone damage created by spinal screws used in IFCs and anterior plates under fatigue loading.

Materials and Methods

Specimen Preparation and Mechanical Testing

Nine fresh-frozen human cadaver spines, seven male and two female (mean age: 74 ± 8 years), were procured from accredited tissue banks (National Disease Research Interchange and Maryland State Anatomy Board). Each specimen was radiographically screened to exclude osteolysis, fractures, or other abnormalities. Dual-energy X-ray absorptiometry (DEXA, Hologic, Bedford, MA, USA) was used to assess bone mineral density (BMD) for these nine specimens. Lumbar (L1-4) BMD and T-scores were 0.93 ± 0.17 g/cm^2 and -1.0 ± 1.6, respectively (Table 1). Post DEXA scans, specimens were sectioned into L2-3 and L4-5 functional spinal units (FSUs) and prepared for device implantations.

Anterior plate (AP) and IFC devices were designed incorporating common features of commercially available implants. Anterior plates and screws were manufactured from titanium 6Al-4V alloy and IFC devices were fabricated from PEEK-OPTIMA® (Invibio, Lancashire, UK). This anterior plate was attached to the vertebral body using 4 bone screws, two top screws and two bottom screws (Figure 1A). The

Table 1. Demographic and Lumbar DEXA information for each Cadaver.

Specimen	Sex	Age	T-Score	BMD (g/cm^2)
1	M	69	1.2	1.176
2	M	72	1.5	1.206
3	M	61	-2.1	0.813
4	M	71	0.1	1.053
5	M	85	-1.1	0.923
6	M	81	-1.6	0.865
7	M	70	-1.8	0.841
8	F	70	-2.4	0.782
9	F	83	-2.9	0.724

DOI: 10.14444/4020

IFC design also used 4 bone screws to attach to the vertebral body using two medial and two lateral screws (Figure 1B). Screws used in both AP and IFC implants had dimensions (5.5 mm outer diameter and threaded length of 25 mm) representative of those commonly employed in both lumbar APs and IFCs.

Implantations for IFC constructs was alternated between L2-3 and L4-5 FSUs with AP+C constructs placed in the complementary FSU. Implant size for each FSU was selected based on the intervertebral disc height, lordosis, anterior-posterior, and lateral vertebral endplate measurements obtained from micro-computed tomography (micro-CT, Scanco Medical, Basserdorf, Switzerland) images and radiographs. A board certified spine surgeon performed anterior discectomy and inserted the appropriate sized cage into the disc space of FSU. Prior to insertion of screws, consistent pilot holes (3.5 mm in diameter and 18 mm in length) were drilled into the bone for both construct types. For AP+C constructs, the plate was attached to the anterior cortex of the vertebral body using bone screws. For IFC constructs, screws were inserted through the cage into the vertebral endplates. Prior to fatigue testing, flexion-extension range of motion (ROM) to +/- 7.5 N-m was similar (p=0.94) between AP+C (2.5° ± 1.4°) and IFC (2.6° ± 1.7°) groups, providing confidence that load transfer to the fixation screws would be similar between implant groups. Implanted specimens were fatigued initially in flexion-extension (FE) loading to ±3 Nm at 1 Hz for the first 5,000 cycles and then increased to ±5 Nm until 20,000 cycles. Testing was conducted in ambient conditions with specimens wrapped in saline-soaked gauze and sprayed regularly with phosphate buffered saline to maintain specimen hydration during testing. This loading protocol is similar to previously reported studies.[18-21]

Screw loosening analysis

After fatigue testing, screws were carefully removed to prevent metal artifacts during micro-CT imaging of the FSUs. All FSUs were imaged in transverse plane at 51 µm voxel resolution (slice thickness of 51 µm), which was sufficient to quantify screw loosening created from fatigue testing. Digital Imaging and Communications in Medicine (DICOM) files obtained from micro-CT scans were imported into Mimics (Materialise, Leuven, Belgium). A global threshold was applied to segment all four screw hole regions from trabecular bone and marrow space for each FSU. After thresholding, each individual screw hole was further processed with segmentation tools (e.g. draw, erase, and local thresholding) applied to image slices in order to accurately capture the morphology of each screw hole. Finally, a 3D representation of each screw hole was created and quantified for IFC and AP+C constructs (Figure 2). Initial screw hole volume (SHV) prior to fatigue testing was obtained using CAD drawings (Solidworks, Dassault Systèmes, Waltham, MA, USA). The post-fatigue SHV was then divided by the initial volume to obtain the amount of loosening (Normalized SHV) from mechanical testing.

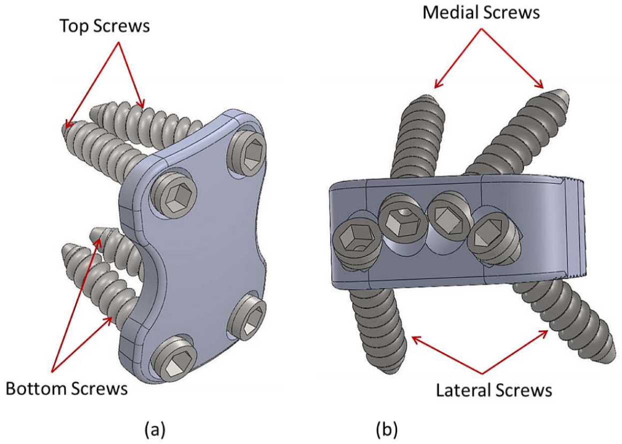


Fig. 1. (a) Anterior plate and (b) Integrated fixation cage designs used for the fatigue testing.

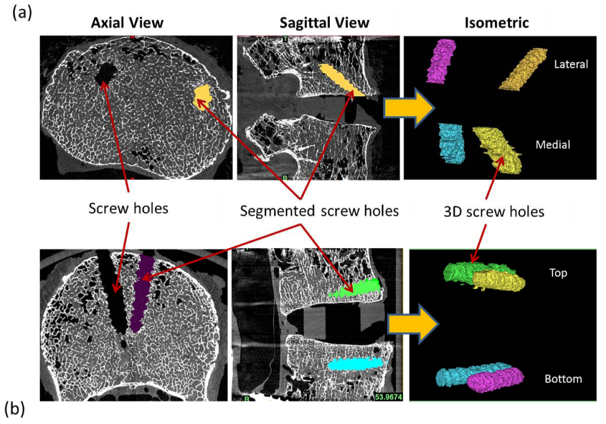


Fig. 2. Steps involved in creating three dimensional (3D) volumes of screw holes from post-fatigue micro-CT images of (a) Integrated fixation cage and (b) Anterior plate constructs.

DOI: 10.14444/4020

Since removal of screws post-fatigue testing may artificially increase SHV, the effects of screw insertion and removal on SHV was analyzed on a separate set of FSUs. AP+C and IFC constructs and screws were implanted and immediately removed (i.e. no fatigue testing performed). These FSUs were then imaged using micro-CT and the same image processing was conducted to quantify the impact of screw removal on calculated SHVs from fatigue samples.

Statistical Analysis

Normalized SHV for each FSU (average of all four screws) was compared between AP+C and IFC constructs using a paired t-test. In addition, to understand how loosening occurred spatially, normalized SHVs were compared between medial IFC screws, lateral IFC screws, top AP+C screws, and bottom AP+C screws using a one-way analysis of variance (Minitab, State College, PA). To accomplish this, the two medial screws within each IFC construct were averaged (medial-IFC). Similar procedure was followed for lateral IFC screws (lateral-IFC), top AP+C screws (top-AP+C), and bottom AP+C screws (bottom-AP+C). All values were reported as mean ± standard deviation with significance set as $p \leq 0.05$. Linear regression analysis was performed between normalized screw hole volume and BMD for both constructs. To perform these regressions, L2 and L3 BMD values were averaged; whereas, only L4 vertebral BMD values were used to represent the L4-5 FSU since L5 BMD values are not available for DEXA scans.

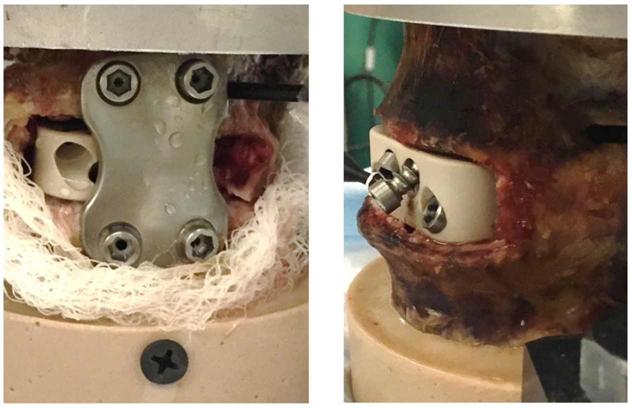
Results

Visual inspection and tactile feel of tightness during screw removal was performed post-fatigue testing. Top and bottom AP+C screws loosened in 7/9 specimens; however, none of these screws backed out from plate (Figure 3A). In IFC constructs, medial screws loosened in 6/9 specimens and screw back out was observed in five of those donors (Figure 3B). In two cases, screws backed out by over 8 mm. Lateral screws in IFCs only loosened in one specimen. Regardless of construct type, screw loosening resulted in noticeable lift-off of vertebral endplates from the cage during fatigue testing.

IFC screws had significantly greater ($p=0.008$) normalized SHV compared to AP+C screws (1.34 ± 0.16 mm^3/mm^3 vs. 1.16 ± 0.12 mm^3/mm^3, respectively, Figure 4) after fatigue testing. Spatial comparisons revealed that the medial IFC screws (1.47 ± 0.30 mm^3/mm^3) had significantly greater ($p<0.003$) normalized SHV compared to lateral IFC (1.21 ± 0.17 mm^3/mm^3), top AP+C (1.15 ± 0.16 mm^3/mm^3), and bottom AP+C (1.17 ± 0.12 mm^3/mm^3) screws (Figure 5). There were no differences ($p>0.888$) in normalized SHVs between lateral IFC, top AP+C, and bottom AP+C screws. Screw insertion and immediate removal from cadaver specimens resulted in normalized SHVs of 1.06 ± 0.09 mm^3/mm^3 for IFC screws and 1.07 ± 0.03 mm^3/mm^3 for that of AP+C screws. As expected, cadavers with low BMD values had greater loosening; however, this correlation was weak ($18\% \leq R^2 \leq 33\%$, $p \geq 0.109$, Figure 6) for both AP+C and IFC. In addition, significant correlations between BMD and IFC medial, IFC lateral, AP+C top, or AP+C bottom SHVs were not observed ($p \geq 0.183$, data not shown).

Discussion

The dynamic *in vivo* environment presents challenges to stability of spinal constructs, particularly at the bone-implant interface where screw loosening may occur over time. Therefore, there is a need to develop methods that can assess the potential for different device designs to damage the surrounding bone. In this study, we developed a novel method



(a) (b)

Fig. 3. Optical images of (a) anterior plate and cage and (b) integrated fixation cage (IFC) constructs after fatigue testing. Medial screw back out is visible in the IFC construct.

DOI: 10.14444/4020

that incorporated high resolution micro-CT scanning

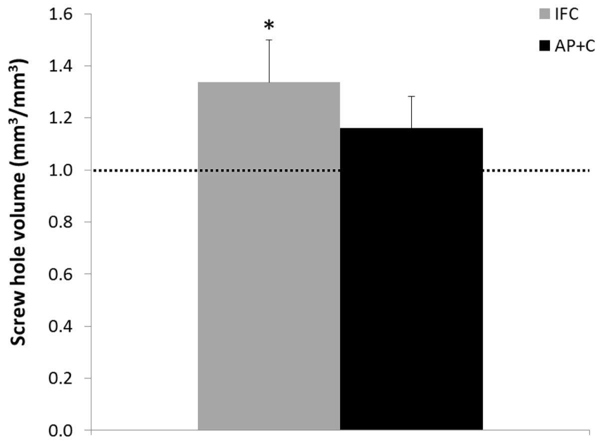


Fig. 4. Mean and standard deviations of normalized screw hole volumes for IFC and AP+C constructs. Dotted line represents no change in screw hole volume post-fatigue testing. * indicates significantly greater screw loosening than AP+C (p=0.008).

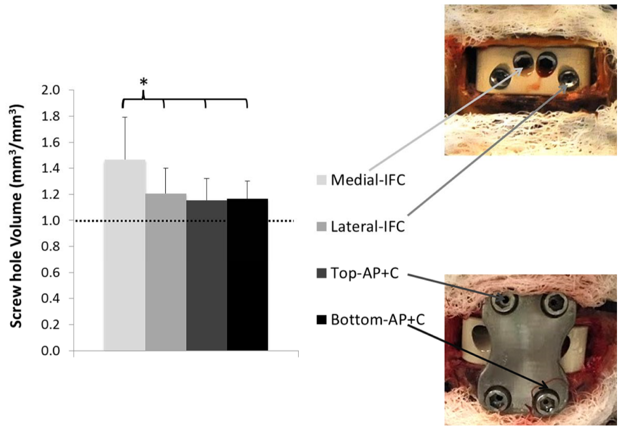


Fig. 5. Mean and standard deviations of normalized screw hole volumes for medial and lateral screws of IFC and top and bottom screws of AP+C. Dotted line represents no change in screw hole volume post-fatigue testing. *Indicates significantly greater screw loosening (p<0.003).

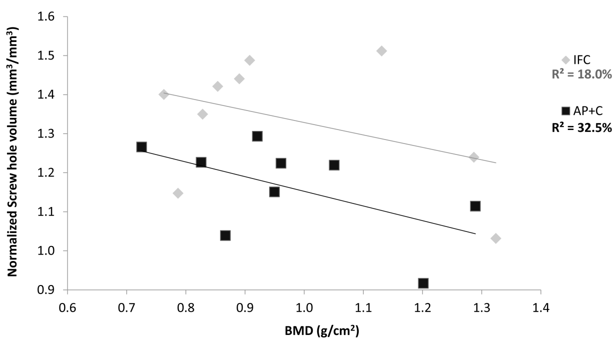


Fig. 6. Screw loosening after fatigue testing vs. BMD for IFC and AP+C constructs. Linear regression values yielded 18-33% R-squared values (p≥0.11).

with image processing techniques to quantify damage of vertebral bone created by screws during fatigue testing. Using this technique, we compared traditional spine fixation (AP+C) to a more recent fixation approach (IFC). The results demonstrated that medial IFC screws created more damage in surrounding bone than lateral IFC and AP+C screws. Although medial IFC screws loosened more than AP+C screws, FE ROM post fatigue testing indicated that there was no difference (p=0.54) between AP+C (5.8° ± 3.6°) and IFC (4.9° ± 2.8°) groups. We suspect that lateral screws, which had similar loosening to AP+C screws, provided the necessary fixation strength for IFC constructs in order to maintain similar stability with AP+C constructs up to 20,000 cycles. With further fatigue testing, the lateral screws may loosen more quickly than the AP+C screws as they have to bear more of the bending moment. However, longer duration fatigue testing is needed to confirm this hypothesis.

The increased loosening of medial screws may be explained by the heterogeneity of trabecular bone within a vertebral body. Hulme and colleagues found reduced trabecular bone volume fraction, trabecular thickness, and trabecular number in center of cadaver vertebra compared to the peripheral regions.[22] In addition, these authors found that the endplate's outer ring (ring apophysis) was significantly thicker than its central region. Taken together, these data suggest that screws inserted laterally into areas of the vertebra that have thicker endplates and better trabecular microstructure may provide superior fixation than screws placed more centrally. The inherent heterogeneity in human vertebral trabecular bone and endplates should be considered when designing implants for fixation to the vertebral body.

Although the technique presented in this study provides improvements to current two-dimensional methods such as histology and radiography, there are limitations that must be considered when using this procedure to quantify damage at the bone-implant interface. In order to measure screw hole volume, we needed to remove screws to prevent metal artifacts during micro-CT scans. Removal of screws may artificially increase the hole volume. Our study found that screw removal increased hole volume less than

10% and was similar for AP+C or IFC constructs. Therefore, this technique may not provide sufficient sensitivity if attempting to detect very small changes in screw hole volume. Future studies will allow for implants to remain within the bone during micro-CT scans and investigate the ability of metal artifact reduction methods to clearly visualize the bone-implant interface. In addition, it is important to note that this method provides a measure of damage to bone surrounding the implant. Although this metric is related to loss of fixation, mechanical testing (e.g. spine range of motion) should also be performed when possible to get a functional measure of fixation strength.

Conclusions

This study found that integrated fixation cage screws created greater vertebral bone damage compared to anterior plate with standard cage screws. The use of high resolution micro-CT scanning and image processing techniques improves on existing radiographic techniques to quantitatively assess damage created from loosening of implants. This method can be used in future cadaveric studies to investigate screw performance in a variety of spinal devices.

References

1. Benli ÍT, Kaya A, Uruç V, Akalin S. Minimum 5-year follow-up surgical results of post-traumatic thoracic and lumbar kyphosis treated with anterior instrumentation: comparison of anterior plate and dual rod systems. *Spine.* 2007;32(9):986-994.
2. Gerber M, Crawford NR, Chamberlain RH, Fifield MS, LeHuec JC, Dickman CA. Biomechanical assessment of anterior lumbar interbody fusion with an anterior lumbosacral fixation screw-plate: comparison to stand-alone anterior lumbar interbody fusion and anterior lumbar interbody fusion with pedicle screws in an unstable human cadaver model. *Spine.* 2006;31(7):762-768.
3. Lim TH, An HS, Hasegwa T, McGrady L, Hasanoglu KY, Wilson CR. Prediction of fatigue screw loosening in anterior spinal fixation using dual energy x-ray absorptiometry. *Spine.* 1995;20(23):2565-2568.
4. Schleicher P, Gerlach R, Schär B, Cain CM, Achatz W, Pflugmacher R, et al: Biomechanical comparison of two different concepts for stand alone anterior lumbar interbody fusion. *European Spine Journal*. 2008;17(12):1757-65.
5. Eldin M, Mohamed M, Ali AM. Lumbar transpedicular implant failure: A clinical and surgical challenge and its radiological assessment. *Asian spine journal*. 2014;8(3):281-297.
6. Louis R. Fusion of the lumbar and sacral spine by internal fixation with screw plates. *Clinical orthopaedics and Related research*. 1986;203:18-33.
7. Pihlajamäki H, Myllynen P, Böstman O. Complications of transpedicular lumbosacral fixation for non-traumatic disorders. *Journal of Bone & Joint Surgery, British Volume*. 1997;79(2):183-189.
8. Thalgott JS, LaRocca HE, Aebi M, Dwyer AP, Razza BE. Reconstruction of the lumbar spine using AO DCP plate internal fixation. *Spine*. 1989;14(1):91-95.
9. Yamagata M, Kitahara H, Minami S, Takahashi K, Isobe K, Moriya H, et al: Mechanical stability of the pedicle screw fixation systems for the lumbar spine. *Spine*. 1992;17:51-54.
10. Dalenberg DD, Asher MA, Robinson RG, Jayaraman G. The effect of a stiff spinal implant and its loosening on bone mineral content in canines. *Spine*. 1993;18(13):1862-1866.
11. Lu WW, Zhu Q, Holmes AD, Luk KD, Zhong S, Leong CY. Loosening of sacral screw fixation under in vitro fatigue loading. *Journal of Orthopaedic Research*. 2000;18(5):808-814.
12. Lyons AS, Foley K, Bonin H, Lange E, Turner AS, Beck M, et al: Hydroxyapatite Surface Augmentation Improves Pedicle Screw Osseointegration for Posterior Dynamic Fixation Systems. In Proceedings of 54th *Orthopaedic Research Society*. 2008;San Francisco, CA, USA.
13. Sanden B, Olerud C, Petren-Mallmin M, Johansson C, Larsson S. The significance of radiolucent zones surrounding pedicle screws. Definition of screw loosening in spinal instrumentation. *Journal of Bone & Joint Surgery, British Volume*. 2004;86(3):457-461.
14. Wan S, Lei W, Wu Z, Liu D, Gao M, Fu S. Biomechanical and histological evaluation of an expandable pedicle screw in osteoporotic spine in sheep. *Eu-*

ropean Spine Journal*. 2010;19(12):2122-2129.
15. Cain CM, Schleicher P, Gerlach R, Pflugmacher R, Scholz M, Kandziora F. A new stand-alone anterior lumbar interbody fusion device: biomechanical comparison with established fixation techniques. *Spine*. 2005;30(23):2631-2636.
16. Kornblum MB, Turner AW, Cornwall GB, Zatushevsky MA, Phillips FM. Biomechanical evaluation of stand-alone lumbar polyether-ether-ketone interbody cage with integrated screws. *The Spine Journal*. 2013;13(1):77-84.
17. Nagaraja S, Palepu V, Peck JH, Helgeson MD. Impact of screw location and endplate preparation on pullout strength for anterior plates and integrated fixation cages. *The Spine Journal*. 2015;15(11):2425-2432.
18. Hitchon PW, Goel VK, Rogge TN, Torner JC, Dooris AP, Drake JS, et al: In vitro biomechanical analysis of three anterior thoracolumbar implants. *Journal of Neurosurgery: Spine*. 2000;93(2):252-258.
19. Vadapalli S, Robon M, Biyani A, Sairyo K, Khandha A, Goel VK. Effect of lumbar interbody cage geometry on construct stability: a cadaveric study. *Spine*. 2006;31(19):2189-2194.
20. Freeman AL, Camisa WJ, Buttermann GR, Malcolm JR. Flexibility and fatigue evaluation of oblique as compared with anterior lumbar interbody cages with integrated endplate fixation. *Journal of Neurosurgery: Spine*. 2016;24(1):54-9.
21. Palepu V, Peck JH, Simon DD, Helgeson MD, Nagaraja S. Biomechanical evaluation of an integrated fixation cage during fatigue loading: a human cadaver study. *Journal of Neurosurgery: Spine*. 2017 Apr;26(4):524-31.
22. Hulme P, Boyd S, Ferguson S. Regional variation in vertebral bone morphology and its contribution to vertebral fracture strength. *Bone*. 2007;41(6):946-957.

Disclosures & COI

The authors report no relevant financial disclosures or conflicts of interest.

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Published 28 June 2017.