Influence of cage design on interbody fusion in a sheep cervical spine model

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Object. The purpose of this study was to compare the characteristics of interbody fusion achieved using an autologous tricortical iliac crest bone graft with those of a cylinder- and a box-design cage in a sheep cervical spine model. This study was designed to determine whether there are differences between three interbody fusion procedures in: 1) ability to preserve postoperative distraction; 2) biomechanical stability; and 3) histological characteristics of intervertebral bone matrix formation.

Methods. Twenty-four sheep underwent C3–4 discectomy and fusion in which the following were used: Group 1, autologous tricortical iliac crest bone graft (eight sheep); Group 2, titanium cylinder-design cage filled with autologous iliac crest bone graft (eight sheep); and Group 3, titanium box-design cage filled with autologous iliac crest graft (eight sheep). Radiography was performed pre- and postoperatively and after 1, 2, 4, 8, and 12 weeks. At the same time points, disc space height, intervertebral angle, and lordosis angle were measured. After 12 weeks, the sheep were killed, and fusion sites were evaluated by obtaining functional radiographs in flexion and extension. Quantitative computed tomography scans were acquired to assess bone mineral density, bone mineral content, and bone callus volume. Biomechanical testing was performed in flexion, extension, axial rotation, and lateral bending. Stiffness, range of motion, neutral zone, and elastic zone were determined. Histomorphological and histomorphometric analyses were performed, and polychrome sequential labeling was used to determine the time frame of new bone formation.

Over a 12-week period significantly higher values for disc space height and intervertebral angle were shown in cage-treated sheep than in those that received bone graft. Functional radiographic assessment revealed significantly lower residual flexion–extension movement in sheep with the cylinder cage–fixed spines than in those that received bone graft group. The cylinder-design cages showed significantly higher values for bone mineral content, bone callus content, and stiffness in axial rotation and lateral bending than the other cages or grafts. Histomorphometric evaluation and polychrome sequential labeling showed a more progressed bone matrix formation in the cylindrical cage group than in both other groups.

Conclusions. Compared with the tricortical bone graft, both cages showed significantly better distractive properties. The cylindrical cage demonstrated a significantly higher biomechanical stiffness and an accelerated interbody fusion compared with the box-design cage and the tricortical bone graft. The differences in bone matrix formation within both cages were the result of the significantly lower stress shielding on the bone graft by the cylinder-design cage.

KEY WORDS • cervical spine • interbody cage • spinal fusion • sheep

Anterior decompression and interbody fusion are a widely accepted surgical treatment for patients with cervical spondylosis. Until now, tricortical iliac crest bone graft has been the gold standard, although it is associated with a high rate of donor-site morbidity.

Additional problems such as pseudarthrosis, graft collapse–induced kyphotic deformity, and graft extrusion have led to a rapid increase in the use of cervical spine interbody fusion cages as an adjunct to arthrodesis. Although experimental data are lacking.

Several interbody construct designs have been developed. According to Weiner and Fraser cage designs can be subdivided into three groups: screw (horizontal cylinder), box, or cylinder (vertical ring) designs.

Devices used for interbody stabilization must ensure good primary stability. Cages have been specially designed to provide immediate strong anterior column support. This effect has already been proven in several bio-

Abbreviations used in this paper: BCV = bone callus volume; BMC = bone mineral content; BMD = bone mineral density; CT = computerized tomography; DSH = disc space height; EZ = elastic zone; IVA = intervertebral angle; LA = lordotic angle; NZ = neutral zone; ROI = region of interest; ROM = range of motion; SD = standard deviation; 2D = two-dimensional.
mechanical in vitro studies in which all cage designs were evaluated. In particular, in vitro biomechanical fixation properties of screw-design cages have been evaluated extensively. Only scarce data, however, are available concerning comparative evaluation of different cage designs. Recently, Oxland, et al., compared a box- and a cylinder-design cage in a biomechanical clinical in vitro study and found no differences between the two cages. In contrast, Mittmeier, et al., found fundamental differences among box-, screw- and cylinder-design cages in a sheep cervical spine model. They demonstrated that cylinder-design and box-design cages were able to control extension and bending more effectively than screw-design cages.

Additionally, interbody cages have been developed to provide interspace structural stability during bone fusion. Cages should retain interbody distraction and should be resistant to subsidence into the adjacent vertebrae to foster a biological environment that guarantees the desired quality of osseous fusion. This can only be evaluated, however, by performing in vivo investigations. The structural stability of screw-design cages has already been proven by authors of some in vivo studies, who have shown that these cages preserved interbody distraction more effectively than autologous tricortical iliac crest bone graft. Experimental in vivo data for cylinder- or box-design cages, however, are not available. Additionally, no information is available concerning comparative experimental in vivo evaluation of different cage designs.

Therefore, the purpose of this study was to compare a developing interbody fusion fostered by an autologous tricortical iliac crest bone graft with those of a cylinder- and a box-design cage in a sheep cervical spine interbody fusion model. This study was designed to determine whether there were differences, at a given early time point, in a developing fusion mass between the three interbody fusion techniques with regard to: 1) ability to preserve postoperative distraction; 2) biomechanical stability; and 3) histological characteristics of intervertebral bone matrix formation.

Materials and Methods

Study Design

Twenty-five (2-year-old) adult female merino sheep underwent C3–4 discectomy and fusion; one animal was lost to follow up. The remaining 24 sheep were randomly assigned to the following groups: Group 1, autologous tricortical iliac crest graft (eight sheep); Group 2, cylinder-design titanium cage filled with autologous cancellous iliac crest bone graft (eight sheep); and Group 3, box-design titanium cage filled with autologous cancellous iliac crest graft (eight sheep).

The sheep were evaluated prospectively for 12 weeks, after which they were killed and underwent radiographic, biomechanical, and histological evaluations. All animal-related experimental work was approved by local authorities.

Surgical Technique and Postoperative Care

All sheep received 2 g amoxicillin intravenously before surgery. Surgery was performed after induction of general endotracheal anesthesia (0.5 g thiopental-natrium and 0.1 mg fentanyl citrate). For maintenance of anesthesia, inhalational isoflurane and intravenous dosages of 0.2 mg fentanyl/dihydrogencitrate were applied. The anterior part of the neck and the left iliac crest was prepared in a sterile fashion, and a left anterolateral approach to the cervical spine was undertaken through a longitudinal skin incision. The longus colli muscle was incised in the midline, and the intervertebral C3–4 disc was exposed. After a Caspar device was used to distract the motion segments, anterior C3–4 discectomy was performed. The endplates were shaved using a 2-mm high-speed diamond drill down to bleeding bone, resulting in an excision of 1 mm of each endplate. No attempt was made to excise the posterior longitudinal ligament or expose the spinal canal. For interbody stabilization, titanium cylinder-design cages (Group 2, Harms cage; width 14 mm, depth 14 mm, and cage volume 0.1 cm³) or box-design cages (Group 3, SynCage-C; width 15 mm, depth 13 mm, and cage volume 0.26 cm³) of appropriate height (mean height 8 mm for both groups) were used. Prior to insertion, cages were filled with autologous cancellous bone grafts. In Group 1 a tricortical autologous bone graft (mean height 8 mm, mean depth 14 mm, and 11 mm average width) was taken from the left iliac crest. Prior to insertion the volumes of the cages filled with autologous bone or the volumes of the bone grafts were determined using water displacement technique (Archimedes principle). The tricortical bone graft was inserted press-fit into the intervertebral space with the cortical shape of the graft anterior (Robinson technique). Finally, the wound was irrigated with saline, and the longus colli muscle was closed using a running suture. The subcutaneous tissue and skin were reaproximated using interrupted sutures, and a soft bandage was applied to the neck.

After surgery, the sheep were observed until fully recovered from anesthesia. They received two 0.5-g doses of metamizol-natrium per day for 5 days intramuscularly. Clinical examination was performed daily for the first 10 days and weekly thereafter. The sheep were allowed ad libitum activity for the remainder of the experiment. Fluorochrome sequential labeling was performed at 3, 6, and 9 weeks postoperatively (oxalatecalciclin [25 mg/kg intravenously] at 3 weeks, calcein green [15 mg/kg intravenously] at 6 weeks, and xylene orange [90 mg/kg intravenously] at 9 weeks). Twelve weeks after surgery, after induction of anesthesia (0.5 g thiopental-natrium and 0.1 mg fentanyl/dihydrogencitrate) the sheep were killed by an intravenous injection of potassium chloride. The complete cervical spine, including parts of the occiput and T-1, was excised and cleaned from the surrounding tissue.

Radiographic Evaluation

To allow for comparable radiographic evaluation, special fixation devices for the sheep cervical spine were developed. The reproducibility of the positioning of the sheep cervical spine in this fixation device was investigated by repeated measurements. Prior to surgery, one sheep in each group was selected randomly to undergo radiography, and 10 lateral and 10 anteroposterior digital radiographs were obtained. After each radiograph was acquired, the sheep was removed from the fixation device, turned around, and then repositioned in the fixation device. Thus, the complete series of linear and angular measurements was performed on each radiograph.

Lateral and anteroposterior digital radiographs were acquired pre- and postoperatively and after 1, 2, 4, 8, and 12 weeks. During the same time periods anterior, middle, and posterior intervertebral DSH, IVA, and LA of the C3–4 motion segment were measured on lateral radiographs (Fig. 1). The mean intervertebral DSH was calculated from anterior, middle and posterior DSH measurements (anterior + middle + posterior DSH/3). After 12 weeks, bone fusion was categorized using the following parameters: A) no bone fusion; B) maximum intervertebral gap of more than 5 mm; C) maximum intervertebral gap of less than 5 mm; and D) complete bone fusion. The maximum intervertebral gap in the craniocaudal direction was measured directly on lateral x-ray films by using a ruler. All radiographic measurements were evaluated by three independent observers.

Functional Radiographic Analysis

After sacrifice fusion sites were evaluated using lateral digital functional radiographic scans in flexion and extension (Fig. 2). For this purpose, T-1 was rigidly fixed with a Steinmann pin while a 60-N load was applied through C-1 by using a newton meter. Flex-
ion–extension differences in IVA and LA were calculated. All functional radiographic measurements were evaluated by three independent observers.

Quantitative CT Analysis

After the sheep were killed, quantitative CT scanning was performed using a scanner. Axial cuts with 1-mm slice thickness were made parallel to the intervertebral disc space. Bone mineral density measurements of the bone callus have been described in detail earlier.\footnote{18} Measurements were calibrated with a six-point BMD phantom and were performed using software designed specifically for the scanner. Bone callus volume was measured using an image analyzing system. Bone mineral content was calculated from BMD and BCV measurements (BMC = BCV / H1). After 12 weeks bone fusion was categorized on sagittal and coronal 2D CT reconstructions by using the aforementioned parameters. The maximum intervertebral gap in the craniocaudal direction was measured directly on midsagittal 2D CT reconstructions by using the specifically designed scanner software. All CT measurements were evaluated by three independent observers.

Biomechanical Analysis

After the sheep were killed, the specimens were biomechanically tested in a nonconstrained testing apparatus by using a nondestructive flexibility method previously described.\footnote{16,18} Pure bending moments were applied to the C3–4 motion segments by using a system of cables and pulleys to induce flexion, extension, and left and right lateral bending, and left and right axial rotation. Tension was applied to the cables with a uniaxial testing machine. Three-dimensional displacement of each motion segment was measured using an optical measurement system. Triangular markers with three diodes were attached to the vertebral bodies of C-3 and C-4. Marker positions were detected using two cameras and recorded using a computerized motion analysis system. Angular displacement of the upper vertebra (C-3) in relation to the lower vertebra (C-4) was calculated from marker position by using custom-made computer software. The experimental error associated with this method was \( \pm 0.1\% \).\footnote{16,18}

The vertebrae were mounted in pots by using polymethylmethacrylate. The lower pot was rigidly attached to the base of the testing apparatus. This test setup resulted in a compressive preload of 25 N because of the weight of the upper fixation pot, which represents the mean weight of the head of the sheep. Moments were applied in a quasi-static manner in increments of 1 Nm to a maximum of 6 Nm. Specimens were preconditioned with three cycles of 6-Nm load with a velocity of 1.2 mm/second of the transverse bar. The fourth cycle was measured.

The mean apparent stiffness values in the EZ were calculated from the corresponding load-displacement curves. Range of motion, NZ, and EZ were determined.

Histomorphological, Histomorphometric, and Fluorochrome Analyses

All C3–4 motion segments were harvested at 12 weeks for histological examination of the bone. The motion segments had been fixed for 7 days in 10% normal buffered formaldehyde followed by dehydration in ascending concentrations of ethanol and embedded without being decalcified, in polymethylmethacrylate.

For histomorphological and histomorphometric analyses longitudinal sections in the sagittal plane were cut at 6 \( \mu \)m by using a microtome and a 40\( ^\circ \) stainless-steel knife. The residual parts of the cages were then removed, and the following stains were used: safranin O/lightgreen, Safranin O/van Kossa, astrablue, and Masson–Goldner. Masson–Goldner staining was used for histomorphological analysis. Histomorphological analysis included evaluation of bone fusion according to the A through D parameters previously defined. The maximum intervertebral gap in craniocaudal direction was measured directly on midsagittal sections.

Histomorphometric parameters were measured on the residual stainings using a Leica microscope and the image analyzing system. Parameters were measured at a magnification of \( \times 1.6 \). The sagittal diameter distance of C-3 and the mean preoperative DSH were determined to define the size of the ROI for histomorphometric evaluation (Fig. 3). The complete intervertebral fusion area was included in this ROI. The following structural indices were calculated in the ROI: bone volume/total volume, cartilage volume/total volume, and mineralized cartilage volume/cartilage volume.
For fluorochrome analysis, longitudinal sections in the parasagittal plane were cut at 400 μm with a precise macrogrinding machine. These slices were then ground to a thickness of 80 μm by using a precise microgrinding machine. Fluorochrome markers were analyzed under appropriate lighting conditions by using a Leica microscope and an image analyzing system. Parameters were measured at a magnification of ×1.6.

Fluorochrome analysis of intervertebral fusion areas has previously been described in detail. The first appearance of the marker served to indicate formation of new bone matrix. The presence or absence of each marker around or within the cage or the bone graft, respectively, was used to determine the relative time frame of new bone formation.

Sources of Equipment

We obtained the Harms cages from Motech GmbH (Schwenningen, Germany) and the SynCage-3 implants from Synthes GmbH (Bochum, Germany). The radiography unit (Mobilett Plus), the quantitative CT scanner (Somatom plus 4), and scanner software (Sienet MagicView VA 30A) were purchased from Siemens AG (Erlangen, Germany). We acquired the x-ray film (CR 24X30) from Fuji (Kleve, Germany). The macro- and microgrinding machines were manufactured by Fa. Exact (Norderstedt, Germany). The device for measuring Newtons was obtained from Inha GmbH (Berlin, Germany). The imaging analysis system (model KS 400) used to measure BCV was produced by Zeiss GmbH (Oberkochen, Germany).

We acquired the uniaxial testing machine (model 1456) from Zwick GmbH (Ulm, Germany). The optical measurement system, the three-diode triangular markers, and the computerized motion analysis system (PC-Reflex) were purchased from Qualysis (Sävebalden, Sweden). We acquired the polymethylmethacrylate (Technovit 3040) and the methacrylate (Technovit 9100) from Heraeus Kulzer GmbH (Wehrheim/Ts, Germany). The SPSS software was obtained from SPSS (Chicago, IL).

Statistical Analysis

Comparison of data was performed using one-way analysis of variance for independent samples followed by Tukey post-hoc analysis for multiple comparison procedures in which Bonferroni correction was used for multiple measurements. Intraobserver variability for radiographic, functional radiographic evaluation and CT measurements was determined using k statistics. The A through D scores previously described (see Radiographic Evaluation) used to categorize semiquantitative bone fusion on plain radiographs, CT scans, and histological stainings; however, no statistical evaluation of this score was performed. Statistically significant differences were defined at a 95% confidence level. The values are given as mean ± standard deviation. The SPSS software supported statistical evaluation.

Results

Failure Parameters and Complications

One sheep died of an anesthesia-related complication on Day 0. This animal was excluded from the study and replaced by another animal.

In Group 1, one sheep developed a hematoma at the donor site of the iliac crest graft. In group 3, one sheep developed wound healing problems at the donor site. Both
complications resolved without further difficulty under provision of conservative treatment.

**Volume of the Implants**

The volume of the implants was evaluated prior to insertion using water-displacement technique. The mean volume of the autologous tricortical iliac crest bone graft was 1.3 ± 0.1 cm³. The mean volumes of the autologous iliac crest graft–filled cylinder- and box-design cages were 1.52 ± 0.1 and 1.5 ± 0.1 cm³, respectively.

**Fig. 4.** Radiographic analyses. **Upper:** Mean DSH of the different groups throughout the observation period. *p < 0.05 compared with the bone graft. **p < 0.05 compared with the bone graft and the cylinder-design cage. **Center:** Mean IVA of the different groups throughout the observation period. *p < 0.05 compared with the bone graft. **p < 0.05 compared with the bone graft and the cylinder-design cage. **Lower:** Mean LA of the different groups throughout the observation period. *p < 0.05 compared with the bone graft.
Radiographic Results

We conducted repeated measurements to determine the reproducibility of the positioning of the cervical spines in the fixation devices for radiographic evaluation. The reproducibility of the mean DSH and IVA was high, showing a maximum difference on 10 radiographs of 0.8 mm (approximately 10% of total value) and 1.5° (approximately 10% of total value), respectively. The reproducibility of the LA, however, was moderate showing a maximum difference on 10 radiographs of 4° (approximately 60% of total value).

Intraobserver agreement for radiographic measurements was good, showing \( \kappa \) values ranging from 0.76 to 0.92.

With regard to preoperative baseline values of all radiographic parameters, there were no intergroup differences. At 8 and 12 weeks both cage-fitted groups showed significantly higher values for mean DSH than Group 1 (\( p < 0.05 \); Fig. 4 upper). At 1 week mean DSH values for the box-design cage were significantly higher than those for the cylinder-design cage and the tricortical iliac crest bone graft (\( p < 0.05 \)); however, no differences were found in DSH between the two cage types during the experimental period. At 2, 4, 8, and 12 weeks both cage-treated groups (Groups 2 and 3) showed significantly higher values for IVA (\( p < 0.05 \); Fig. 4 center) compared with the autologous tricortical iliac crest graft–treated group (Group 1). During the experimental period, no significant differences in IVA were found between the cage groups, except for at the 2-week time point, at which the box-design cage showed a significantly higher IVA than the cylinder-design cage (\( p < 0.05 \)). At 1, 4, 8, and 12 weeks the box-design cage (Group 3) showed significantly higher values for LA (\( p < 0.05 \); Fig. 4 lower) compared with the autologous iliac crest graft group (Group 1) and the cylinder-design cage group (Group 2).

After 12 weeks, bone fusion was evaluated radiographically scans (Fig. 5). In the cage groups (Groups 2 and 3), a slightly more advanced interbody fusion was found compared with that in Group 1 (Table 1).

Functional Radiographic Results

Intraobserver agreement with regard to functional radiographic measurements was excellent, showing \( \kappa \) values ranging from 0.84 to 0.96.

Flexion–extension differences in LA were not significantly different between Groups 2 and 3 (Table 2); however, functional radiographic assessment revealed significantly lower residual flexion–extension movement in the cylinder-design cage group (Group 2) than in the tricortical iliac crest graft group (Group 1) (\( p < 0.05 \)).

Quantitative CT Results

Intraobserver agreement for CT measurements was excellent, showing \( \kappa \) values ranging from 0.82 to 0.92.

After 12 weeks, there were no significant differences for BMD between the tricortical iliac crest graft group (Group 1) and both cage groups. In the cylinder-design
Influence of cage design on interbody fusion

Histomorphometric Results

The results of histomorphometric analysis are summarized in Table 7. No significant differences in sagittal diameter distance (baseline) were determined among all groups. Compared with the bone graft group and the box-design cage group histomorphometric parameters showed significantly more advanced bone formation (bone volume/total volume) in the cylinder-design cage group (p < 0.05). The bone graft–stabilized group showed significantly higher histomorphometric values in cartilage volume/total volume and mineralized cartilage volume/total volume than both cage groups (p < 0.05).

Fluorochrome Analysis Results

The results of fluorochrome analysis are summarized in Table 8. In spines stabilized with both cage types earlier new bone formation was exhibited both within and around the cages compared with those stabilized with the bone graft group at all time points. Compared with the box-design cage, the cylinder-design cage showed a greater amount of new bone formation both within and around the cages at 6 and 9 weeks.

Discussion

The objective of this study was to compare characteristics of interbody fusion among an autologous tricortical iliac crest bone graft, a cylinder-design cage, and a box-design cage in a sheep cervical spine interbody fusion model. This study was designed to determine whether there were differences among the three interbody fusion materials with regard to: 1) the ability to preserve postoperative distraction; 2) biomechanical stability; and 3) histological characteristics of intervertebral bone matrix formation.

Distractive Properties

The authors of several clinical studies have demonstrated that tricortical iliac crest graft–assisted interbody fusion induced decreases in DSH during the postoperative period.8,10,20 The findings in these clinical investigations are in agreement with the experimental results in our study, with regard to a significant decrease in DSH in the bone graft group. Interbody cages have been specially developed in the quest to provide interspace structural stability during bone fusion. Cages should retain interbody distraction and should be resistant to subsidence into the adjacent vertebrae to guarantee the desired quality of fu-
Currently, however, subsidence of cages has only been investigated in one animal experimental in vivo study. Sandhu, et al., demonstrated in a sheep model that screw-design cages preserved interbody distraction more effectively than an autologous iliac crest bone graft. Experimental in vivo data for cylinder- or box-design cages are not currently available. Analysis of the data in the present study demonstrated that, at the time of surgery, both cages and the tricortical iliac crest graft were able to distract intervertebral spaces beyond their baseline measurements to nearly the same values. In all conditions, however, significant subsidence developed beyond normal DSH values during the 12-week observation period. Whereas the loss of DSH of the cages resulted from subsidence into the subchondral bone of the adjacent vertebral bodies, the loss of the intervertebral space in the tricortical iliac crest graft group resulted mainly from gradual graft collapse. Both cages were able to decrease the loss of DSH significantly compared with the tricortical iliac crest graft. Although the box-design cage showed significantly less subsidence after 2 weeks, both cages demonstrated similar DSH values at final measurements.

### Biomechanical Properties

In this in vivo experiment the tricortical iliac crest bone graft has shown significantly less biomechanical stiffness in bending and rotation and a higher ROM in rotation than the cylinder-design cage. These in vivo results are in accordance with those reported in several in vitro studies; a higher biomechanical stiffness was demonstrated for the cylinder-design cage used in this study than for a bone graft. In a previous biomechanical in vitro study reported by Mittlmeier, et al., the authors found that a significantly higher biomechanical stiffness was associated with the box-design cage than with the tricortical bone graft. In contrast to the findings of Mittlmeier, et al., we found no significant biomechanical difference between the box-design cage and the bone graft after 12 weeks in vivo. Additionally, we found a higher biomechanical stiffness in rotation and bending and a lower ROM in rotation for the cylinder-design cage than for the box-design cage. These in vivo results are also in crucial contrast to in vitro results obtained by our own working group. In our previous in vitro studies, we demonstrated significantly higher stiffness for the box-design cage than for the cylinder-design cage. The differences between biomechanical in vitro and in vivo results may be a result of the “biological qualities”

| Table 3: Summary of quantitative CT data for BMD, BMC, and BCV after 12 weeks |
|-----------------|-----------------|-----------------|-----------------|-----------------|
|                  | Group 1         | Group 2         | Group 3         |
| BMD (g/cm³)     | 0.58 ± 0.04     | 0.55 ± 0.05     | 0.58 ± 0.07     |
| (0.56–0.64)      | (0.52–0.59)      | (0.52–0.59)      |
| BMC (g)         | 2.3 ± 1.0       | 3.2 ± 0.3†‡     | 2.2 ± 0.3       |
| (1.7–3.1)       | (2.8–3.7)       | (1.8–3.6)       |
| BCV (cm³)       | 4.0 ± 1.0*      | 5.4 ± 1.4*†‡    | 3.8 ± 0.3*      |
| (3.8–5.1)       | (3.8–6.3)       | (3.0–4.4)       |

* Initial bone graft volumes of the iliac crest graft, the cylinder cage, and box cage were 1.3, 1.5, and 1.52 cm³, respectively.
† p < 0.05 compared with Group 1.
‡ p < 0.05 compared with Group 3.

| Table 4: Summary of fusion results observed on 2D CT reconstructions after 12 weeks |
|-----------------|-----------------|-----------------|-----------------|
| Fusion Parameter (score) | Group 1 | Group 2 | Group 3 |
| A                | 0              | 0              | 0              |
| B                | 5              | 4              | 6              |
| C                | 3              | 3              | 2              |
| D                | 0              | 1              | 0              |

Fig. 6. Computerized tomography analysis. After 12 weeks, interbody fusion was evaluated on axial CT scans obtained parallel to the intervertebral space.
Influence of cage design on interbody fusion

of different cage designs in vivo, suggesting that currently available biomechanical in vitro tests are not highly predictive of the in vivo performance of any interbody fusion cage. The predictive value of biomechanical in vitro tests for the in vivo performance of spinal implants has also been questioned by other authors.6,22,26,32,36

Histological Characteristics

Histomorphometric analysis demonstrated the presence of significantly higher intervertebral bone volume in the cylinder-design cage group than in the bone graft group. Additionally, significantly higher values for bone matrix formation were found in the cylinder design-group than in the box-design group. There are some possible explanations for these findings.

The limited biomechanical properties of the tricortical iliac crest bone graft resulted in a compression and sometimes fragmentation of the graft, which was followed by extensive osteoclastic activity and finally graft resorption. In contrast, because the bone grafts packed inside the cages have a biomechanically protected and, consequently, biologically improved environment for fusion,37 a more stable interbody fusion mass develops, especially in the cylinder-design cage group.

The initial biomechanical in vivo stability of the cage combined with the graft composite is nearly exclusively a result of the biomechanical properties of the cage.15,26 Only secondarily, the interbody fusion mass arising from the incorporated bone graft contributes to biomechanical stability.15 With the biomechanical in vitro results of both cages in mind,26 the significantly greater biomechanical stability in the cylinder cage–fixed group compared with the box cage–fixed group in vivo was an effect of an accelerated interbody fusion in the former. Biomechanical loads in vivo consist of shear and compression. Whereas shear loads promote bone matrix formation, compressive loads do not.37,38 In contrast to the bone graft, the cage mainly functions as a protector against compressive loads.

Therefore, this cage-related factor contributed to the more stable interbody fusion mass in the cylinder-design cage group compared with the bone graft group.

The ideal biological environment for bone fusion is achieved by optimum grafting techniques and the maximum filling of the intervertebral space with graft material.37 As cage volume increases, however, graft volume

![Fig. 7. Bar graph demonstrating results of biomechanical stiffness of the different groups for the different test modes.](image)

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**TABLE 5**

Summary of biomechanical results after 12 weeks*

<table>
<thead>
<tr>
<th>Test mode (degrees)</th>
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<th>Group 3</th>
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<td>EZ</td>
<td>2.7 ± 1.8</td>
<td>1.6 ± 0.9</td>
<td>2.3 ± 0.7</td>
</tr>
<tr>
<td>right bending</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROM</td>
<td>4.5 ± 2.4</td>
<td>4.2 ± 2.2</td>
<td>5.6 ± 2.2</td>
</tr>
<tr>
<td>NZ</td>
<td>1.5 ± 1.5</td>
<td>1.2 ± 1.2</td>
<td>1.9 ± 1.0</td>
</tr>
<tr>
<td>EZ</td>
<td>3.0 ± 1.3</td>
<td>3.0 ± 1.9</td>
<td>3.7 ± 1.8</td>
</tr>
<tr>
<td>left bending</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ROM</td>
<td>4.6 ± 2.2</td>
<td>4.1 ± 2.1</td>
<td>5.6 ± 2.2</td>
</tr>
<tr>
<td>NZ</td>
<td>1.7 ± 1.6</td>
<td>1.3 ± 1.2</td>
<td>2.0 ± 1.3</td>
</tr>
<tr>
<td>EZ</td>
<td>2.9 ± 0.7</td>
<td>2.8 ± 1.9</td>
<td>3.6 ± 1.8</td>
</tr>
</tbody>
</table>

* All values are presented in degrees.
† p < 0.05 compared with Group 1.
‡ p < 0.05 compared with Group 3.
decreases. Therefore, biologically, the ideal cage would be the one with the smallest cage volume that will provide adequate mechanical stability, because this cage will allow for the maximum filling of the intervertebral space with graft material. Although both cages in this study were of similar volumes when filled with bone grafts (cylinder-design cage: 1.52 cm³; box-design cage: 1.50 cm³), the volume of the isolated cages was substantially different (cylinder-design cage: 0.1 cm³; box-design cage: 0.26 cm³). Therefore, a higher bone graft volume was incorporated in the cylinder-design cage, which potentially contributed to the more stable intervertebral fusion mass in this group.

Kanayama, et al., in an in vitro study, showed that the cage design has a significant influence on the loads of a graft within a cage. They demonstrated that a larger contiguous pore is important to decrease the stress-shielding effect on a graft within an interbody fusion device. The authors assumed that the lower the stress-shielding effect on a graft, the greater the possibility for interbody fusion. Finally, they wrote that “it remains unclear whether the stress-shielding environment influences the bone quality of the developing interbody fusion mass” in vivo. The incorporation and remodeling of a bone graft within an interbody cage has been investigated in several animal experiments. Brantigan, et al., placed carbon cage implants in a goat model and found a complete incorporation of the autograft and continuous trabecular bridging within the cage. Cunningham, et al., and Zdeblick, et al., investigated the efficacy of a screw-design cage in a sheep model. They found no significant difference in bone quality of the interbody fusion mass between the autologous bone-packed screw-design cage and the tricortical iliac crest graft during a short-term postoperative observation period. In the present study we evaluated bone matrix formation within both cages. A significantly higher interbody bone volume and an accelerated interbody fusion on polychrome sequential labeling was shown in the cylinder-design cages than in the box-design cage. Therefore, it can be assumed that whereas both cage designs were able to provide an adequate biological environment for interbody fusion, the cylinder-design cage was more effective than the box-design cage. Comparing both cages, a significantly larger contiguous pore was obvious in the cylinder-design cage (Fig. 5). Therefore, based on the results reported by Kanayama, et al., the cylinder-design cage apparently has a significant lower stress-shielding effect on the incorporated bone graft than the box-design cage.

TABLE 6
Summary of fusion results determined by histomorphological analysis after 12 weeks

<table>
<thead>
<tr>
<th>Fusion Parameter</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>score</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>B</td>
<td>5</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>C</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>D</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
</tbody>
</table>

Fig. 8. Histomorphological analysis. After 12 weeks, interbody fusion was evaluated histomorphologically and histomorphometrically. Safranin-O/v. Kossa staining, original magnification (M) × 1.6.

TABLE 7
Summary of histomorphometric results obtained after 12 weeks*

<table>
<thead>
<tr>
<th>Index</th>
<th>Group 1</th>
<th>Group 2</th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>baseline SDD (mm)</td>
<td>26.2 ± 1.0</td>
<td>25.5 ± 1.1</td>
<td>26.1 ± 0.8</td>
</tr>
<tr>
<td>(25.0–28.3)</td>
<td>(24.6–27.8)</td>
<td>(25.2–28.0)</td>
<td></td>
</tr>
<tr>
<td>BV/TN (%)</td>
<td>31.4 ± 3.9</td>
<td>45.5 ± 6.7†‡</td>
<td>31.6 ± 3.8</td>
</tr>
<tr>
<td>(24.8–39.0)</td>
<td>(38.5–61.3)</td>
<td>(20.5–42.3)</td>
<td></td>
</tr>
<tr>
<td>CV/TN (%)</td>
<td>10.1 ± 2.8</td>
<td>4.6 ± 2.7†</td>
<td>4.2 ± 1.1†</td>
</tr>
<tr>
<td>(1.0–22.1)</td>
<td>(0.8–9.4)</td>
<td>(2.8–6.4)</td>
<td></td>
</tr>
<tr>
<td>mCV/CV (%)</td>
<td>5.5 ± 2.0</td>
<td>2.8 ± 1.3†</td>
<td>3.2 ± 1.4†</td>
</tr>
<tr>
<td>(0.6–9.4)</td>
<td>(0.2–7.6)</td>
<td>(1.0–5.1)</td>
<td></td>
</tr>
</tbody>
</table>

* Initial graft volumes of the iliac crest graft, the cylinder cage, and box cage were filled 1.3, 1.5, and 1.52 cm³, respectively. Abbreviations: BV/TN = bone volume/total volume; CV/TN = cartilage volume/total volume; mCV/CV = mineralized CV/TN; SDD = sagittal diameter distance. †p < 0.05 compared with Group 1. ‡p < 0.05 compared with Group 3.
Influence of cage design on interbody fusion

TABLE 8
Summary of results of fluorochrome analysis after 12 weeks*

<table>
<thead>
<tr>
<th>Index</th>
<th>Group 1</th>
<th></th>
<th>Group 2</th>
<th></th>
<th>Group 3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Adjacent</td>
<td>W/in</td>
<td>Adjacent</td>
<td>W/in</td>
<td>Adjacent</td>
</tr>
<tr>
<td>3 wks</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>6 wks</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>9 wks</td>
<td>1</td>
<td>0</td>
<td>4</td>
<td>6</td>
<td>4</td>
</tr>
</tbody>
</table>

* Depicted are the number of fusion sites (of the different groups at different time points) in which the fluorochrome marker was present adjacent to or within the cage or bone graft, respectively.

In conclusion, the significantly lower stress-shielding effect of the bone graft within the cylinder-design cage might be the most important cause of the significantly higher interbody fusion mass found in this cage design.

Conclusions

Compared with the tricortical bone graft, both cage designs were associated with significantly better distracting properties. A significantly greater biomechanical stiffness in rotation and bending and an accelerated interbody fusion was associated with cylinder-design cages than the box-design cage and the tricortical bone graft. The differences in bone matrix formation within both cages were mainly a result of the significantly lower stress-shielding effect of the bone graft within the cylinder-design cage. Further investigations are necessary to determine quantitatively the small borderline between biomechanically protected environment of the graft within a cage that accelerates interbody fusion and the stress shielding of a graft within the cage that inhibits interbody fusion.

References

31. Pinzen T, Caspar W, Matthias D, et al: [Primary stability of 2 PLIF (posterior lumbar interbody fusion) - a biomechanical in


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