Eur Spine J (2003) 12 : 216–223
DOI 10.1007/s00586-002-0471-1

ORIGINAL ARTICLE

T. R. Blattert
G. Delling
A. Weckbach

Evaluation of an injectable calcium phosphate cement as an autograft substitute for transpedicular lumbar interbody fusion: a controlled, prospective study in the sheep model

Received: 5 June 2002
Accepted: 8 June 2002
Published online: 29 October 2002

This study was carried out at the Trauma and Reconstructive Surgery Unit, Würzburg University Hospital.
The biomaterials were provided by Stryker Howmedica-Osteonics, Mahwah, New Jersey. No financial support was granted.

T.R. Blattert (✉) · A. Weckbach
Trauma and Reconstructive Surgery,
Würzburg University Hospital,
Josef-Schneider-Str. 2,
97080 Würzburg, Germany
e-mail:
blattert@chirurgie.uni-wuerzburg.de,
Tel.: +49-931-20131253,
Fax: +49-931-20131253

G. Delling
Department of Bone Pathology,
Hamburg-Eppendorf University Hospital,
Hamburg, Germany

Abstract Anteroposterior procedures for lumbar interbody fusion usually combine posterior instrumentation with anterior techniques that achieve primary stability for compressive loading: tricortical strut-graft, anterior plating systems, or cages. In comparison to transpedicular lumbar interbody fusion (TLIF), these methods bear the burden of the additional anterior approach. TLIF with autograft, in contrast, does not prove to be clinically sufficient because of its lack of primary compressive stability. In a sheep model, we therefore developed a TLIF method providing primary stability for axial loading. In 24 sheep, L4–L6 were instrumented posteriorly. An endoscopically assisted L4/L5 TLIF procedure was performed via a bilateral approach. In 12 sheep, the defect was filled with an injectable calcium phosphate cement. After setting, this cement gains a stability against axial loading comparable to healthy vertebrae. Another 12 sheep were treated with autograft. The animals were killed at 8 weeks and evaluated by radiologic (plain X-ray, computed tomography), histologic and histomorphometric analysis, and fluorochrome labeling. Only ten autograft sheep were available for evaluation. Radiologically and histologically, TLIF with calcium phosphate led to a 2/12 fusion rate compared to autograft (1/10 fused) (P=0.70). Semiquantitative radiologic and histologic scoring did not reveal significant differences (P=0.88). In 4/12 calcium phosphate sheep, excessive resorption was responsible for local aseptic inflammation. The findings of this study show that calcium phosphate cement is not superior to autograft, despite enabling primary stability against compressive loading. Biointegration of the osteoconductive cement does not occur fast enough, and shear forces cause early cement fracture, subsequent fragmentation, and gross resorption with the possibility of severe inflammation.

Keywords Burst fracture · Calcium phosphate · Hydroxyapatite · Transpedicular lumbar interbody fusion (TLIF) · Sheep model

Introduction

Discogenic disease as well as injuries of the lumbar spine (i.e. spondylolisthesis, low back pain, burst fractures, etc.) may cause gross degeneration or destruction of intervertebral discs. For the affected functional spinal units, this will result in a highly unstable situation for axial loading. Therefore, the attempt to achieve solid lumbar fusion is the first option amongst therapeutic choices.

Interbody fusion techniques have been developed to provide immediate fixation of the unstable functional spinal unit while maintaining the load-bearing capacity of the spine. If successfully performed, they preserve the sagittal plane alignment even after the removal of the posterior instrumentation device [8, 30]. Over the course of

time, spinal surgeons have introduced a variety of different approaches and techniques for interbody fusion. Each has specific advantages, as well as inherent disadvantages, pitfalls, and shortcomings. However, none have so far been able to gain general acceptance as the "gold standard" [12, 14, 21, 22].

Methods for achieving interbody fusion can either use anterior or posterior approaches, or the combination of both, resulting in anteroposterior pathways. Anterior augmentation may consist of tricortical auto- and allograft struts, anterior plating systems, or cages. Anteroposterior methods usually combine these anterior techniques with a posterior instrumentation device (e.g. internal fixator etc.). In comparison to posterior techniques, these methods bear the burden of the morbidity factors associated with the anterior approach to the spine [6, 9, 16, 22, 25].

Of posterior interbody fusion techniques, the transpedicular path to the intervertebral space proves to be minimally invasive, safe, and uniformly applicable throughout the lumbar spine, when compared to the technically more demanding transforaminal approach and the posterior approach, which cannot be performed at levels above L3 due to the potential damage to the cauda equina and conus medullaris [15]. Transpedicular lumbar interbody fusion (TLIF) was first described by Daniaux [7]. Originally, it combined posterior pedicle instrumentation with transpedicular inter- and intravertebral cancellous autografting. However, this technique failed in clinical trials, since it did not prove to permanently restore the sagittal alignment, but featured a rather uniform loss of correction after removal of the internal fixator [18, 27, 31]. A hypothesis for this phenomenon is that autograft lacks primary compressive stability within the interbody site. This insufficient stability prohibits proper bony integration and solid interbody fusion [5, 13].

Therefore, combining the advantageous transpedicular approach with an autograft substitute that guarantees primary stability for axial loading might pose a solution to the problem. In addition, refraining from the use of an autograft avoids its specific morbidity and limitations [1, 2, 11, 19, 28, 35]. For this very purpose, we designed a controlled prospective preclinical study and evaluated an injectable calcium phosphate cement against autograft in the lumbar spine of 24 sheep.

Materials and methods

The sheep used for this study were adult female Merino sheep, with a mean age of 14±5 months and a mean body weight of 57± 3 kg. The experimental protocol was approved by the Institutional Animal Care and Use Committee of the Regional Government Authority of Subfranconia, Germany.

Animal model and surgical technique

The standardized human surgical technique for TLIF was applied because of the proportional anatomical similarity of human and sheep spine [32, 33]. All sheep were premedicated with 1.3 cc of xylazine I.M. Anesthesia was induced by 10 cc of thiopental I.V. and maintained by intubation inhalation during surgery with halothane. The sheep were placed into a prone position and then underwent a dorsal median approach with bilateral fascia incision from L4 to L6. The back muscles were moved laterally. The small vertebral joints of L4 to L6 were exposed. Every subsequent stage of the operation was performed under intermittent fluoroscopic control. A bisegmental pedicle instrumentation from L4 to L6 was performed using a titanium internal fixator of the Universal Spine System (USS) (Synthes, Umkirch, Germany). Subsequently, bilateral transpedicular canals were created, reaching posteriorly from L5 to the intervertebral space of L4/L5 by means of a 6.0-mm oscillating reamer. Using sharp spoons and rongeurs, the nucleus pulposus was extracted and both neighboring endplates were decorticated. To ensure proper removal of the disc tissue and a sufficient amount of decortication, the latter surgical step was performed under transpedicular endoscopic assistance through one of the canals. Both canals were used alternately for the instruments or the use of the endoscope, thus enabling full optical control of the entire procedure. The appropriate disc replacement material was then inserted transpedicularly into the cavity using a funnel and a plunger. Finally, the wound was sutured over subfascial and subcutaneous drains.

The 24 animals were divided into two groups of 12, and in each group one of the following materials was implanted:

1. Autologous bone graft (autograft group): cancellous bone chips harvested from the left posterior iliac crest at the time of TLIF surgery.
2. Calcium phosphate (CP group): 5.0 cc of a biphasic, synthetic, two-component (powder and liquid $NaPO_4$ solution) di-/tetracalcium phosphate cement (BoneSource, Stryker Howmedica-Osteonics, Mahwah, New Jersey). Under in vitro conditions, this injectable cement sets after 7 min, gaining a compressive strength of 25.6±3.7 MPa by 24 h, and is fully converted to hydroxyapatite via crystallization within 24 h. It has a porous microstructure (porosity 5.9–10.3% of the total volume) that guarantees the cement's osteoconductive property.

Containment of the transferred materials and prevention of spinal canal intrusion was guaranteed by an entirely intact anulus fibrosus surrounding the closed space, which was accessible only through the transpedicular canals.

After a postoperative conventional biplanar radiograph, the animals were held in separate pens for 2 days for postoperative monitoring and recovery. They were bearing full weight immediately post anesthesia. Postoperative pain control was performed with anticipatory I.M. analgesic injection. The drains were removed by day 2 post surgery, after documentation of the interstitial fluid volume loss. The animals were then transferred into another pen, where they stayed until day 14, when the stitches were removed. From then on, the animals were kept in an open air enclosure for the remainder of the study.

In addition to daily clinical monitoring during the postoperative healing process, vital fluorochrome staining was performed by I.V. infusion of 90 mg/cc xylenol orange (1.0 cc per kg body weight; Sigma-Aldrich, Taufkirchen, Germany) at 2 weeks, 30 mg/cc calcein green (0.33 cc per kg body weight; Synopharm, Barsbüttel, Germany) at 4 weeks, and doxycycline yellow (2 g per animal; Hexal, Holzkirchen, Germany) at 6 weeks [24, 26, 29]. The animals of each group were killed under deep sedation at 8 weeks postoperative, and the L3/L7 segment was explanted. The following examinations were performed: conventional biplanar X-ray imaging, high-resolution contact-radiography, computed tomography (CT) imaging, and histologic assessment (including histomorphologic and macromorphometric evaluation, and analysis of fluorochrome labeling).

Table 1 Definition of histological parameters

Parameter	Definition	Value
Intervertebral fusion	Bilateral bridging	2
	Unilateral bridging	1
	No bridging	0
Presence of cartilage	No cartilage	2
	Cartilage in some areas of the intervertebral space	1
	Cartilage throughout the intervertebral space	0
Presence of inflammatory reactions	No signs of inflammatory reaction	1
	Local inflammatory reaction	0

Radiographic analysis

Anteroposterior and lateral radiographs (Opti 150/40/73 C-100L, Siemens, Munich, Germany) of each spine were obtained at 0 and 8 weeks. CT scans (Somatom Plus4, Siemens, Forchheim, Germany) with 2-mm sections were performed at 8 weeks in the axial plane, with subsequent reconstruction in the coronal and sagittal planes. High-resolution contact-radiographs (Faxitron X-Ray Corp., Wheeling, Illinois) were obtained of the histologic sections in the coronal plane. Two examiners blinded to the treatment groups assessed the degree of interbody fusion at 8 weeks. A four-point grading scale ranging from 0 (no bone formation) to 3 (bilateral bridging) was used. Fusion was assumed when both investigators agreed for all three radiographic techniques utilized. A successful fusion was indicated by the presence of continuous bridging from endplate to endplate for conventional radiographs and high-resolution contact-radiographs. CT fusion was noted by the presence of continuous bridging in three subsequent sections in either plane.

Histologic examination

All ex vivo lumbar spines were fixed in neutral buffered formalin. The specimens were then transected in four contiguous coronal sections within the area of the vertebral body, with a separation gap of 4 mm. Each section was macrophotographed, multi-stained (toluidine blue, Goldner´s trichrome, Berlin blue (iron detection), and Movat´s silvering), and prepared for undecalcified sectioning. After embedding in polymethylmethacrylate (PMMA), the specimens were sectioned at a thickness of 15 µm and ground-polished. Two investigators examined all sections.

Histology was assessed with both qualitative and quantitative techniques:

1. Descriptive and semiquantitative histomorphologic analysis was performed to evaluate structural and cellular findings. The degree of intervertebral bridging, the presence and amount of cartilage formation in the intervertebral area, and the presence of local inflammatory reactions were scored using a multipoint grading scale (Table 1).
2. Quantitative macromorphometric analysis was performed by evaluation of macrophotographs. The amount of decortication of the lower endplate of L4 was measured along with the intrusion height of the graft material.
3. Fluorochrome-stained ground-polished coronal transections were used for qualitative analysis of trichrome fluorescence labeling under ultraviolet filters.

Statistics

Average values are presented as mean±standard deviation. For radiologic and histologic evaluation, groups were compared with each other using the Wilcoxon test. A significance level of $P<0.05$ was chosen. All statistical tests were performed using statistical software (SAS Institute Inc., Cary, North Carolina).

Results

Complications and clinical assessment

Two animals from the autograft group were not available for assessment. The first two surgeries resulted in early euthanasia due to immediate postoperative hemiplegia from spinal cord injury. Medial placement of the pedicle screws caused these injuries. This complication did not occur again after a more laterally situated entrance point into the transpedicular canal was defined. Thus, 10 sheep were available for assessment in the autograft group and 12 sheep in the CP group.

Clinically, all of the remaining 22 animals tolerated the surgical procedure well, with an increase in body weight (59±4 kg) after 8 weeks. The volumes of interstitial fluid lost to drainage were 45±30 cc (subcutaneous), 205±80 cc (subfascial), and 50±30 cc (iliac crest of the autograft group). Four sheep featured less agility than the others. They all belonged to the CP group, and all suffered from local aseptic inflammatory reactions. Microbiological examination was negative for infection upon sacrifice of these animals.

Radiographic analysis

Of the ten sheep in the autograft group, only one had fused unilaterally from endplate to endplate. Four animals showed signs of new bone formation partially filling the intervertebral space, but with no bony bridging. The remaining five sheep did not show signs of bone formation within the intervertebral space. In seven animals, remnants of the cancellous bone graft were seen. No signs of osteolysis were seen.

Two of the 12 CP sheep had fused, one bilaterally (Fig. 1), the other one unilaterally. Four animals showed signs of new bone formation, but without continuous bridging of the intervertebral space. The remaining six sheep did not show any intervertebral bone formation. The intravertebral part of the cement was intact, with no signs of resorption. In contrast, the intervertebral part of the cement exhibited a horizontal crack. This was a consistent finding in the CP sheep. In the two cases of interbody fusion, the crack was bridged. In the remaining ten animals, there was further fracturing of the cement at multiple locations with gross fragmentation and resorption of the hydroxyapatite leaving big clefts in the formerly solid structure.

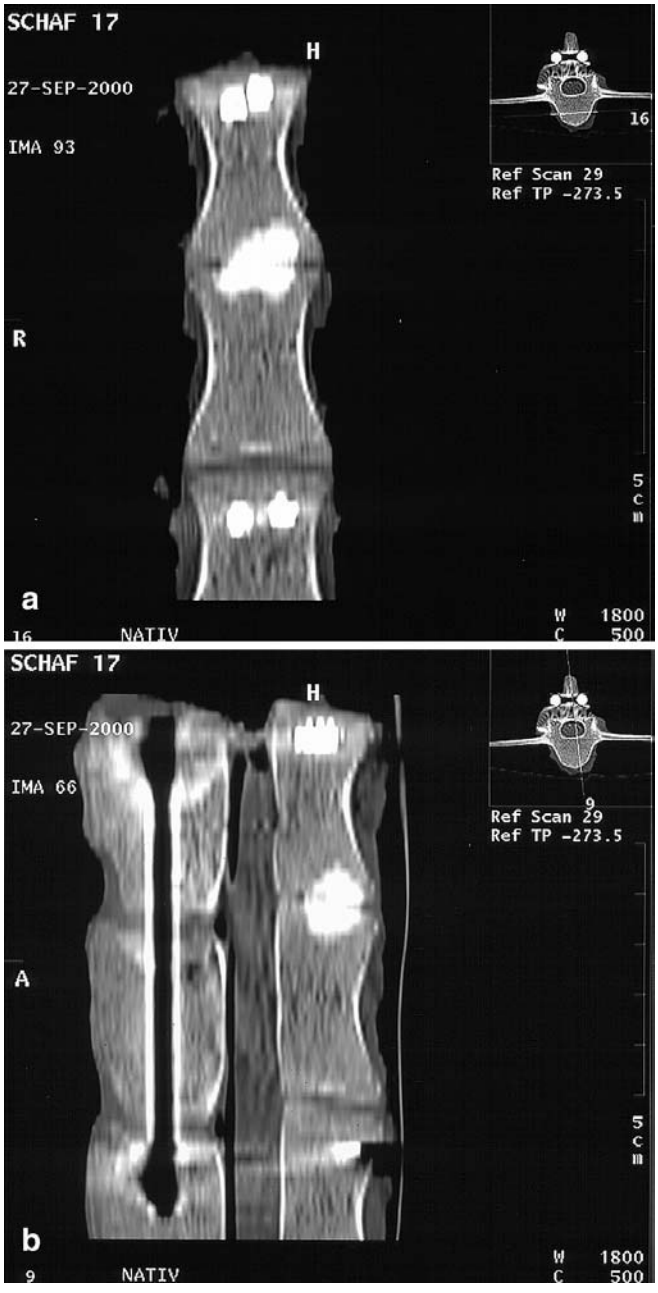

Fig. 1a, b Computed tomography reconstructions of L4–L6 segments from the calcium phosphate (CP) group. **a** Coronal plane, **b** sagittal plane. The images depict one of two cases from the CP group with interbody fusion at the time of sacrifice, 8 weeks post surgery

Additionally, in four cases there was considerable osteolysis of adjacent vertebrae.

Intervertebral fusion rates by radiographic (and histologic) evaluation for both groups are summarized in Table 2. The degree of radiographic intervertebral bridging as assessed by the four-point grading scale is presented in Table 3.

Table 2 Intervertebral fusion rates in radiographic and histologic evaluation after 8 weeks

Trial group	Intervertebral fusion rate	Significance[a]
Autograft	1/10	P=0.6981
Calcium phosphate	2/12	

[a] The P-value was derived using the Wilcoxon test

Table 3 Radiographic score[a] after 8 weeks

Trial group	Mean value	Standard deviation	Significance[b]
Autograft	0.60	0.66	P=0.8848
Calcium phosphate	0.75	0.92	

[a] Score index: 0 = no bone formation, 1 = non-bridging bone formation, 2 = unilateral bridging, 3 = bilateral bridging
[b] The P-value was derived using the Wilcoxon test

Histologic examination

Histologic examinations confirmed the radiographic findings in the autograft group: nine of ten sheep were not fused. The intervertebral defects were filled with metaplastic chondral tissue accompanied by isolated fibroblasts and remnants of the autograft (Fig. 2 a). A few calcified islands could be seen, but only in the intravertebral parts of the defects and corresponding to an osseous integration process of the original autograft. One sheep showed interbody fusion with a contiguous unilateral bridge of trabecular bone. No signs of local inflammatory reactions were seen in the autograft group.

The CP group featured a more divergent histologic appearance. Of twelve sheep, ten were not fused, thus confirming the radiographic examinations. Macrophotographs and ground-polished sections consistently showed one or more cracks in the former cement mass. The cracks were running horizontally through the intervertebral space. The cement in these areas was multi-fragmented and grossly resorbed. Only small remnants of hydroxyapatite were left as scattered islands. The majority of the intervertebral space was filled by fibrous tissue combined with fibrocartilage in most sheep. In contrast, those parts of the cement lying in the intravertebral areas were still solid masses, with little sign of resorption or cracking in eight sheep (Fig. 2b). At higher magnification, in some areas of the bone-cement interface, there was a little ossification with a few osteoblasts. However, in most areas there were layers of intervening fibrous tissue. Four sheep showed signs of a chronic aseptic inflammatory response with fragmentation of the entire hydroxyapatite mass and osteolysis of one or both adjacent vertebral bodies (Fig. 3). Cytologic evaluation of these specimens revealed many inflammatory cells and cement particles engulfed by macrophages. The two CP sheep that were fused showed a crack in the

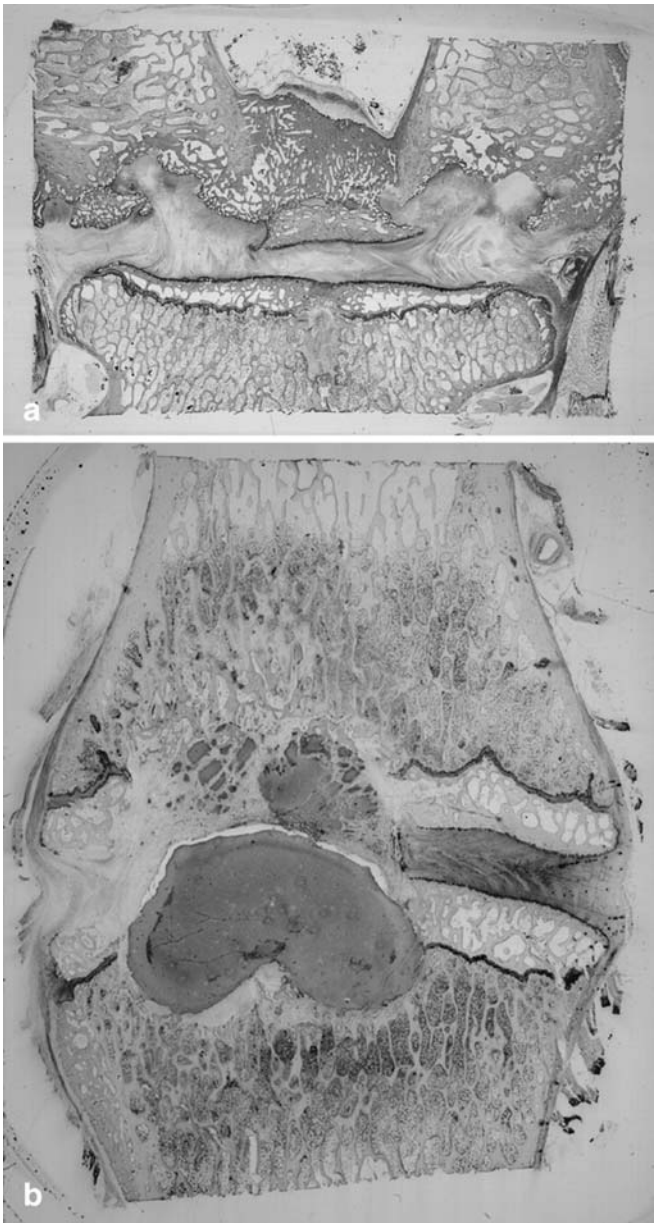

Fig. 2a, b Ground-polished coronal L4/L5 transections, 15 µm thick. **a** Representative image from the autograft group, showing no interbody fusion. The defect is filled with metaplastic chondral tissue. **b** Characteristic image of the CP group, showing no interbody fusion. Note the fragmentation of the cement mass in the interbody region. The defect is filled with fibrous tissue and there are no signs of new bone formation

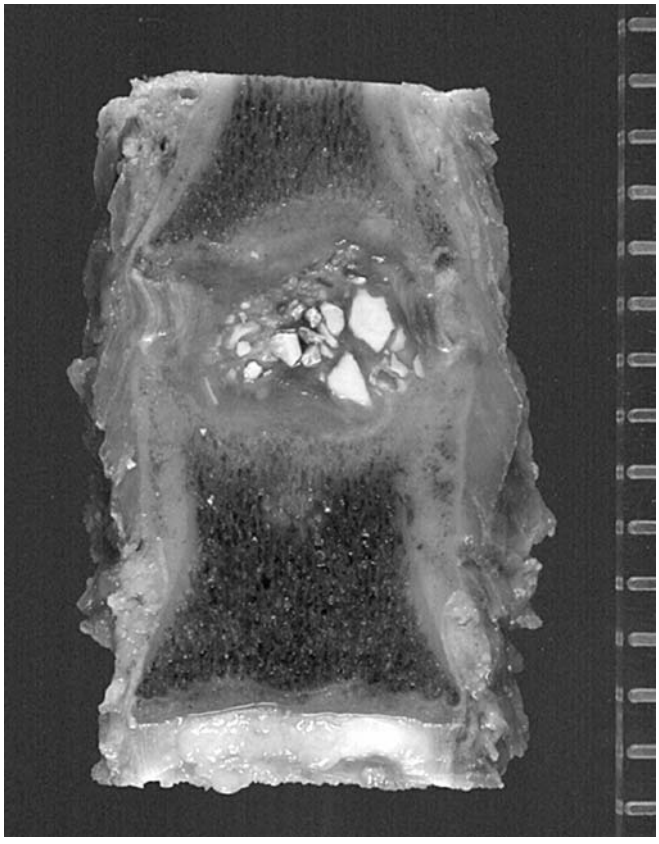

Fig. 3 Macrophotograph of a coronal L4/L5 transection from the CP group. Gross fragmentation and massive resorption of the hydroxyapatite mass with severe local inflammation and osteolysis of both adjacent vertebrae is noted, with no interbody fusion. Microbiological testing was negative for infection

Table 4 Histologic score[a] after 8 weeks

Trial group	Mean value	Standard deviation	Significance[b]
Autograft	1.20	0.60	P=0.7947
Calcium phosphate	1.30	1.55	

[a] Score index: see Table 1
[b] The P-value was derived using the Wilcoxon test

area of the disc similar to the non-fused, but without subsequent fragmentation and gross resorption. In these two sheep, the crack was bridged with newly formed bone and bridging was unilateral in one case and bilateral in the other.

Intervertebral fusion rates by histologic and radiographic evaluation are summarized in Table 2. Score results of the histologic parameters evaluated are shown in Table 4.

Quantitative macromorphometric analysis revealed sufficient decortication of the lower L4 endplate in all sheep. The average intrusion height of the graft material was 13.7±2.7% in the autograft group and 14.3±6.6% in the CP group. Upon comparison, no statistically significant difference was detected (P=0.7402).

Analysis of fluorochrome labeling showed consistently for both groups the three different fluorochrome bands in the L4 and L5 vertebrae. This corresponded to an early alteration of cancellous bone at the time of surgery, along

with an immediate remodeling response. The areas of newly formed bone in the interbody region of all three animals fused showed only deposits of calcein and doxycycline at 4 and 6 weeks. Thus, the time of interbody bone formation can be dated at between the 2nd and 4th week post surgery.

Discussion

The transpedicular pathway is advantageous in many respects. It enables 360° fusion with a single posterior approach when combined with a posterior fixation device. The advantages are less morbidity, less time, lower resource consumption, and higher cost-effectiveness, which surpass both the anterior and combined anteroposterior methods [6, 9, 12, 14, 15, 16, 21, 22, 25]. Of the latter, neither technique has gained status as the "gold standard" at this time, for a variety of reasons: Tricortical strutgrafts have the potential to dislocate, collapse, or fracture, consequently preventing spinal fusion [3, 10]. This is aggravated by the risk of infection transmission and immunologic rejection in the case of allograft struts [20]. In anterior plating systems, screw fixation in the cancellous bone of lumbar vertebral bodies very often will not provide sufficient biomechanical stability [3, 25]. This is especially true for osteoporotic bone in the elderly. For interbody cages, secondary dislocation has been shown to occur [23]. In cases of unsuccessful periprosthetic interbody fusion, long-term mechanical stability of the cage will determine the outcome and limit its clinical indications, especially in younger patients [17]. Furthermore, the results of spinal statics and function are not available in the case of long-term exposure to foreign-body presence.

The TLIF procedure was originally described nearly two decades ago [7], and it has been proven to fail clinically. The procedure suffers from a long-term loss of correction and does not permanently restore the sagittal profile of the spine [18, 27, 31]. In vivo experimentation to account for this is missing, although virtual computer simulations have implicated technical shortcomings in the surgical procedure. Insufficient removal of the disc and decortication of the endplates will result, as interbody manipulations are controlled in a "blind" and indirect fashion by use of a fluoroscope. Thus, the implanted autograft will not gain access to needed vascularity, resulting in graft necrosis [34]. A technique that has never been described before is our introduction of transpedicular endoscopic access to the entire interbody site. This provides verification of sufficient extraction of the disc and decortication of the endplates. Interestingly, even with this major technical improvement of surgical accuracy, our autograft interbody fusion rate was only 1/10. Nine animals featured gross metaplastic chondral transformation of the autograft histologically. A similar situation is known to develop in hypertrophic non-unions of fractured long bones with insufficient biomechanical stability. We conclude that autograft failure in TLIF is due to insufficient primary axial loading stability, based upon our preclinical data and clinical experience [5, 13, 31].

Any type of bone substitution material might pose a solution to this problem, as long as it guarantees sufficient compressive strength. The material must be injectable to be applied via the transpedicular canals. No experimental study at this time has investigated this idea of biomechanical improvement of the original autograft version of the TLIF procedure. In a limited prospective clinical trial, however, the authors have demonstrated that the use of an injectable calcium phosphate containing bone cement (Norian SRS) was not superior to autograft in long-term radiologic outcome [4]. The current study utilized an injectable calcium phosphate cement that crystallizes to hydroxyapatite in an isothermic reaction (i.e. no temperature hazard to neighboring neural tissues). This cement provides compressive strength comparable to that of healthy lumbar vertebrae. However, the fusion rate with this biomaterial did not exceed 2/12. Upon radiologic and histologic evaluation 8 weeks post surgery, the originally solid mass of cement underwent multiple fracturing, fragmentation and gross resorption. Although featuring enough primary strength against axial compression, the hydroxyapatite obviously was not able to withstand the additional lateral bending and axial rotational motions that occur in the interbody region [32]. These shear forces initially caused the cement to fracture and, upon further mobilization of the animals, resulted in subsequent and gradual fragmentation. (This effect could not be observed in stress-shielded intravertebral regions, where the cement remained solid.) Gross resorption will occur as soon as fragments are small enough for macrophage clearance. In 4/12 cases in the CP group, these resorption phenomena caused a cellular response excessive enough to result in severe local inflammation.

In summary, using this calcium phosphate cement may show good results in some sheep (two sheep fused in the CP group), whereas others will end up in a deleterious situation (four sheep with inflammatory reactions and instability of the functional spinal unit). Prediction of outcome proves to be very uncertain for the CP group. In conclusion, reliable interbody fusion with an osteoconductive biomaterial demands an injectable device with more biomechanical properties than mere compressive strength. It must withstand considerable shear forces as well. To our knowledge, no such material is currently available.

A limitation in the study design is that we did not randomly assign the sheep to one of the groups. Surgery was performed on the autograft group first, followed by the CP group. An argument can be made that the learning curve in the surgical technique may have introduced an outcome bias. However, macromorphometric data on the accuracy of decortication of the endplates and the intru-

sion height of the graft material did not reveal any statistically significant difference between the two groups. The quality of the individual surgical procedure did not change over the course of the study.

Caution is expressed with respect to replicating these experiments in humans during clinical trials. At the L4/L5 level, both axial rotation and lateral bending ranges of motion are higher in humans than in sheep [32]. Therefore, shear forces that occur upon mobilization might also be higher in humans. As a consequence, subsequent fragmentation and resorption of the hydroxyapatite along with cases of chronic aseptic inflammation processes might even be more pronounced in humans than in sheep.

Conclusions

The following conclusions can be drawn from the findings of this study:

1. In the TLIF procedure, reason for failure of the autograft is its lack of primary stability against axial loading forces, causing chondral transformation of the autograft. This effect is comparable to the development of hypertrophic non-unions of long-bone shaft-fractures after insufficient stabilization.
2. Calcium phosphate cement is not superior to autograft, despite offering primary stability against compressive loading. The process of biointegration of the osteoconductive cement does not proceed fast enough to make use of its primary axial stability to enhance interbody fusion. Consequently, shear forces cause early fracture of the cement and subsequent fragmentation along with gross resorption, initiating severe inflammatory reactions in 4/12 cases.
3. Two theoretical options exist to bring the TLIF procedure to a final success. Either the calcium phosphate cement must be altered to gain improved biomechanical properties enabling it to withstand both compressive and shear forces, or an osteoinductive *momentum* must be introduced to accelerate the process of biointegration of the cement, thus preventing it from early fragmentation.

Acknowledgements The authors wish to thank the following individuals for their technical support: M. Anetseder, M. Fein, W. Geise, S. Pantzner, A. Pierce, K. Reali, A. Reichert, C. Schuhmacher, A. Thiede, K. Ulrichs, H. Vogt.

References

1. Arrington ED, Smith WJ, Chambers HG, Bucknell AL, Davino NA (1996) Complications of iliac crest bone graft harvesting. Clin Orthop 329:300–309
2. Banwart JC, Asher MA, Hassanein RS (1995) Iliac crest bone graft harvest donor site morbidity. Spine 20:1055–1060
3. Beisse R, Potulski M, Ufer B, Bühren V (1999) Thorakoskopische Behandlung von Frakturen der Brust- und Lendenwirbelsäule. Operationstechnik und Frühergebnisse von 100 Fällen. Arthroskopie 12:92–97
4. Blattert TR, van Seil B, Wagner R, Weckbach A (2001) Ventrale Abstützung von Frakturen der thorakolumbalen Wirbelsäule durch thorakoskopische Applikation eines Calciumphosphatzementes (Abstract). Proceedings of the 118th Conference of the German Society of Surgery, Munich, p 31
5. Blattert TR, Delling G, Weckbach A (2002) Pedikuloskopisch assistierte transpedikuläre Spongiosaplastik zur interkorporellen Fusion an der lumbalen Wirbelsäule. Eine tierexperimentelle Untersuchung am Schafsmodell. Unfallchirurg 105:680–687
6. Christensen FB, Bunger CE (1997) Retrograde ejaculation after retroperitoneal lower lumbar interbody fusion. Int Orthop 21:176–180
7. Daniaux H (1986) Transpedikuläre Reposition und Spongiosaplastik bei Wirbelkörperbrüchen der unteren Brust- und Lendenwirbelsäule. Unfallchirurg 89:197–213
8. Evans JH (1985) Biomechanics of lumbar fusion. Clin Orthop 193:38–46
9. Faciszewski T, Winter RB, Lonstein JE, Denis F, Johnson L (1995) The surgical and medical perioperative complications of anterior spinal fusion surgery in the thoracic and lumbar spine in adults. A review of 1223 procedures. Spine 20:1592–1599
10. Feil J, Wörsdörfer O (1992) Ventrale Stabilisierung im Bereich der Brust- und Lendenwirbelsäule. Chirurg 63: 856–865
11. Fernyhough JC, Schimandle JJ, Weigel MC, Edwards CC, Levine AM (1992) Chronic donor site pain complicating bone graft harvesting from the posterior iliac crest for spinal fusion. Spine 17:1474–1480
12. Fraser RD (1995) Interbody, posterior, and combined lumbar fusions. Spine 20:167S-177S
13. Fuller DA, Stevenson S, Emery SE (1996) The effects of internal fixation on calcium carbonate. Ceramic anterior spinal fusion in dogs. Spine 21:2131–2136
14. Hacker RJ (1997) Comparison of interbody fusion approaches for disabling low back pain. Spine 22:660–665
15. Humphreys SC, Hodges SD, Patwardhan AG, Eck JC, Murphy RB, Covington LA (2001) Comparison of posterior and transforaminal approaches to lumbar interbody fusion. Spine 26:567–571
16. Isiklar ZU, Lindsey RW, Coburn M (1996) Ureteral injury after anterior lumbar interbody fusion: A case report. Spine 21:2379–2382
17. Jost B, Cripton PA, Lund T, Oxland TR, Lippuner K, Jaeger Ph, Nolte LP (1998) Compressive strength of interbody cages in the lumbar spine: the effect of cage shape, posterior instrumentation and bone density. Eur Spine J 7: 132–141
18. Knop C, Blauth M, Bastian L, Lange U, Becker T, Tscherne H (1997) Frakturen der thorakolumbalen Wirbelsäule – Spätergebnisse nach dorsaler Instrumentierung und ihre Konsequenzen. Unfallchirurg 100:630–639
19. Kurz LT, Garfin SR, Booth RE Jr (1989) Harvesting autogenous iliac bone grafts. A review of complications and techniques. Spine 14:1324–1331
20. Liljenqvist U, O'Brien JP, Renton P (1998) Simultaneous combined anterior and posterior lumbar fusion with femoral cortical allograft. Eur Spine J 7:125–131
21. Lin PM (1985) Posterior lumbar interbody fusion technique: complications and pitfalls. Clin Orthop 193:16–19

22. Loguidice VA, Johnson RG, Guyer RD, Stith WJ, Ohnmeiss DD (1988) Anterior lumbar interbody fusion. Spine 13:366–369
23. McAfee PC (1999) Interbody fusion cages in reconstructive operations on the spine. J Bone Joint Surg Am 81: 859–880
24. Milch RA, Rall DP, Tobie JE, Albrecht JM, Trivers G (1958) Fluorescence of tetracycline antibiotics in bone. J Bone Joint Surg Am 40:897–910
25. Potulski M, Beisse R, Bühren V (1999) Die thorakoskopisch gesteuerte Behandlung der "vorderen Säule". Technik und Ergebnisse. Orthopäde 28: 723–730
26. Rahn BA, Perren SM (1971) Xylenol orange, a fluorochrome useful in polychrome sequential labeling of calcifying tissues. Stain Technol 46:125–129
27. Speth MJGM, Cumhur Oner F, Kadic MAC, Klerk LWL, Verbout AJ (1995) Recurrent kyphosis after posterior stabilization of thoracolumbar fractures. Acta Orthop Scand 66:406–410
28. Summers BN, Eissenstein SM (1989) Donor-site pain from the ilium: a complication of lumbar spine fusion. J Bone Joint Surg Am 71:677–680
29. Sun TC, Mori S, Roper J, Brown C, Hooser T, Burr DB (1992) Do different fluorochrome labels give equivalent histomorphometric information? Bone 13:443–446
30. Voor MJ, Mehta S, Wang M, Zhang YM, Mahan J, Johnson JR (1998) Biomechanical evaluation of posterior and anterior lumbar interbody fusion techniques. J Spinal Disord 11:328–334
31. Weckbach A, Vogel S (1997) Einfluß der transpedikulären intercorporellen Spongiosaplastik auf den Korrekturverlust nach alleiniger dorsaler Instrumentierung thoracolumbaler Wirbelsäulenverletzungen. Hefte Unfallchirurg 268: 205–208
32. Wilke H-J, Kettler A, Claes LE (1997) Are sheep spines a valid biomechanical model for human spines? Spine 20: 2365–2374
33. Wilke H-J, Kettler A, Wenger KH, Claes LE (1997) Anatomy of the sheep spine and its comparison to the human spine. Anat Rec 247:542–555
34. Winkler H, Fischer M, Keßler T, Fernandez F, Köpke J (1999) Korrekturverlust und Einheilungsverhalten transpedikulärer Spongiosaplastiken bei der Behandlung thorakolumbaler Wirbelfrakturen. Trauma Berufskrankh 1:294–301
35. Younger EM, Chapman MW (1989) Morbidity at bone graft donor sites. J Orthop Trauma 3:192–195