

Trabecular Bone Remodeling after Lateral Lumbar Interbody Fusion: Indirect Findings for Stress Transmission between Vertebrae after Spinal Fusion Surgery

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Abstract:

Introduction: After posterior lumbar interbody fusion (PLIF), trabecular bone remodeling (TBR) occurs in the vertebral body. This study aimed to investigate whether imaging findings obtained with PLIF are applicable to lateral lumbar interbody fusion (LLIF).

Methods: A total of 53 cases who underwent one- or two-level LLIF with polyether ether ketone cage and posterior spinal fixation/fusion (PSF) were retrospectively included in this study. TBR, vertebral endplate cyst (VEC), facet union, and pseudarthrosis were investigated on computed tomography (CT) images at 3 months, 1 year, and 2 years postoperatively. Of the 53 patients, 36 (68%) who underwent CT examination at approximately 5 years postoperatively were subanalyzed.

Results: TBR was commonly observed anterior to the cage on CT sagittal images. The TBR-positive rate was 21%, 67%, and 73% at 3 months, 1 year, and 2 years postoperatively, respectively. The 3-month TBR-positive segments showed significantly less VEC (0% vs. 29%, $P=0.029$) at 1 year postoperatively. The 1-year TBR-positive segments showed a significantly higher facet union rate (83% vs. 57%, $P=0.019$) and less pseudarthrosis (0% vs. 13%, $P=0.041$) at 2 years postoperatively. At 5 years postoperatively, 50% of the 2-year TBR-positive segments turned negative with solid intervertebral bony fusion.

Conclusions: TBR-positive segments had significantly lower future VEC positivity, higher future facet union rates, and lower future pseudarthrosis rates. In LLIF-PSF, TBR suggests the establishment of intervertebral stability and allows consideration of intervertebral biomechanics.

Keywords:

lateral lumbar interbody fusion, osseointegration, trabecular bone remodeling, vertebral endplate cyst, polyether ether ketone

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Introduction

With increased intervertebral stability after lumbar fusion surgery, imaging changes occur not only at the interface between the interbody cages and vertebral endplates but also within the vertebral trabecular bone. Although there is a lack of histological evidence, these changes are thought to be trabecular bone remodeling (TBR)¹⁾ of the vertebral body. It has been suggested that TBR results from stresses on the vertebral endplates being concentrated in the interbody cages in the posterior lumbar interbody fusion (PLIF) segment.

This is partially consistent with the results of finite element models^{2,3)}. Since the intervertebral discs are no longer present, the stress exerted in the PLIF segment is primarily carried by the cages. The stress is concentrated in the small cage-endplate contact area because the contact area is much smaller than the entire vertebral endplate area. Therefore, new bone trabeculae are needed to accommodate the load and remodeling is assumed to occur.

Various lumbar fusion approaches using interbody cages have been developed^{4,5)}. Among them, lateral lumbar interbody fusion (LLIF), which is called lateral access spine sur-

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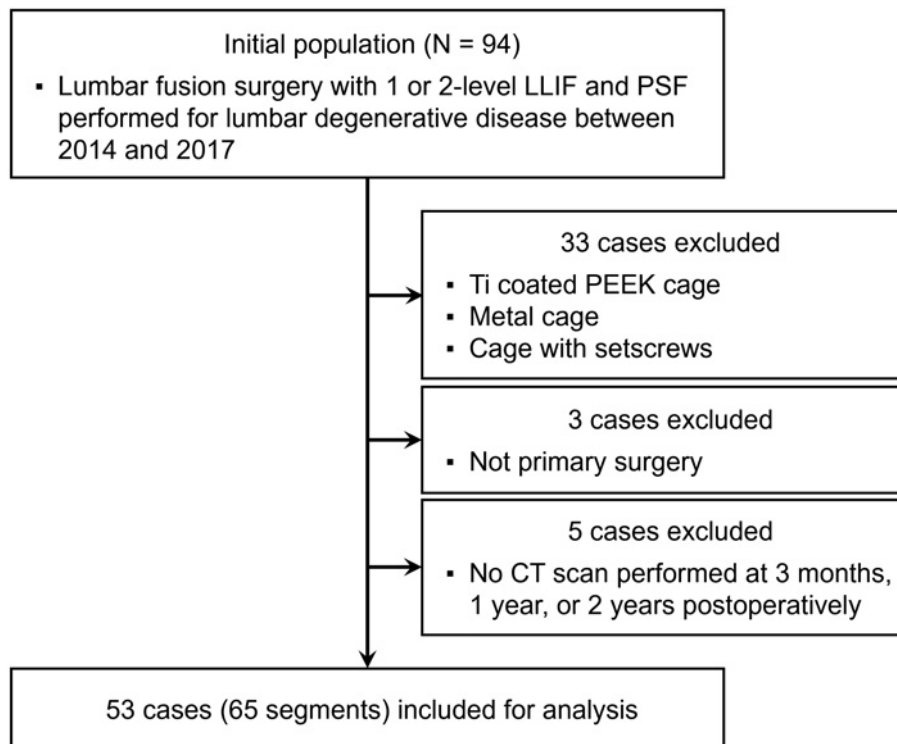


Figure 1. Case selection flowchart.

LLIF, lateral lumbar interbody fusion; PSF, posterior spinal fixation/fusion; Ti, titanium; PEEK, polyether ether ketone; CT, computed tomography

gery, is a minimally invasive approach. From a spinal interbody fusion surgery perspective, LLIF allows for the placement of extremely large interbody cages compared with conventional procedures such as PLIF. Unlike PLIF cages, the transverse diameter of LLIF cages is equivalent to that of vertebral endplates⁶. Although the anteroposterior diameter of LLIF cages is smaller than that of typical PLIF cages, the huge transverse diameter maximizes the contact area between the LLIF cage and vertebral endplates, resulting in completely different mechanical properties from those of PLIF.

The different design of LLIF cages from that of PLIF cages may affect the cage-vertebral bone interaction. However, it remains unclear whether the imaging findings obtained in PLIF are equally applicable to LLIF. The biological responses of vertebral endplates and trabecular bone in contact with a load-stressed interbody cage would be universal, and similar responses would occur in LLIF as in PLIF. In contrast, the completely different cage geometries may cause the responses to exhibit different characteristics in terms of the site and timing of their appearance. Thus, understanding these characteristics will lead to a deeper understanding of the biomechanics of lumbar interbody fusion. Therefore, this study aimed to investigate the imaging findings of cases who underwent lumbar fusion with LLIF and posterior spinal fixation/fusion (PSF) up to 2 years postoperatively to determine whether the imaging findings obtained in PLIF are equally applicable to LLIF. Furthermore, a subanalysis was performed approximately 5 years postopera-

tively on segments with imaging findings to examine the association with intervertebral bony fusion.

Materials and Methods

Patient population

The Institutional Review Board of the authors' affiliated institutions approved this study. Informed consent was obtained from all patients. Data from 94 consecutive cases who underwent one- or two-level lateral-posterior combined spine surgery with LLIF-PSF for lumbar degenerative disease (not including vertebral fracture) between 2014 and 2017 were retrospectively reviewed. The exclusion criteria were as follows: cases with titanium-coated polyether ether ketone (Ti-PEEK) cages, metal cages, or cages with setscrews, cases that were not primary surgeries, and cases that did not undergo postoperative computed tomography (CT) evaluation. A total of 53 patients were included in the final analysis. Their mean age was 68.5 ± 8.2 years, and 22 of the 53 patients were women (Fig. 1).

Surgical procedure

All surgeries were performed under general anesthesia. First, LLIF was performed in the standard fashion with the patients in the lateral position. One interbody cage (CoRoent XL PEEK, NuVasive, San Diego, CA, USA; Clydesdale PEEK, Medtronic, Memphis, MN, USA) per segment was used in all cases. The anteroposterior width of the cage was

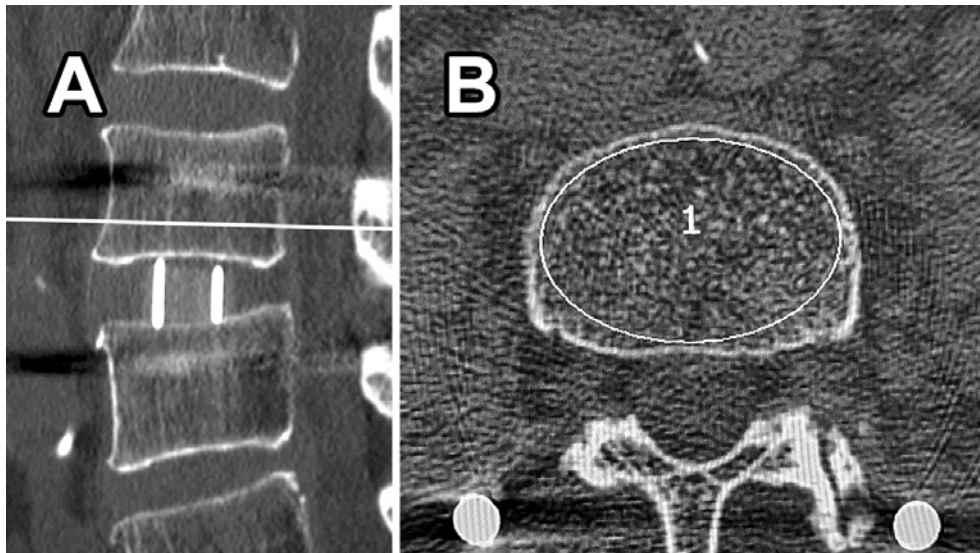


Figure 2. Measurement of vertebral CT values.

Since PS halos were inevitable in the caudal vertebrae, an oval region of interest (ellipse in B) was set up on the axial image at the midpoint between the PS and endplate of the cephalic vertebra (line in A).

CT, computed tomography; PS, pedicle screw

18 mm. The cage was filled with bone allografts. The cage was 8-12 mm high and 45-55 mm wide as determined by intraoperative trial manipulation. The cage lordosis angle was 6° (Clydesdale) or 10° (CoRoent XL). PSF was then performed in the prone position. Bilateral pedicle screw (PS)-rod system was used in all cases. PSF with percutaneous PSs (PPSs) was performed in patients who lacked symptoms while at rest. PSF with laminectomy for decompression was performed in patients with lower extremity numbness or pain symptoms even at rest or bowel bladder symptoms. No facetectomy or osteotomy was performed to correct the spinal alignment. All patients wore a hard corset for 3 months postoperatively.

Variables

Data, such as patients' age, sex, body mass index, comorbidities, preoperative bone mineral density (T-score of the proximal femur measured using dual-energy X-ray absorptiometry [Prodigy, GE Healthcare, Chicago, IL, USA]), and the Japanese Orthopaedic Association (JOA) score⁷⁾, were analyzed. The JOA score ranges from 0 to 29 points, with higher scores indicating better patient condition. Three subjective symptoms are scored from 0 to 9; three clinical signs from 0 to 6; seven activities of daily living from 0 to 14; and urinary bladder function from -6 to 0.

Radiological evaluations were performed preoperatively, postoperatively, and at 3 months, 1 year, and 2 years postoperatively. Furthermore, patients who underwent radiological evaluations at 4-6 years postoperatively were included in the midterm subanalysis. The local angle (measured from the rostral endplate of the upper vertebra to the caudal endplate of the lower vertebra) was measured on the standing lateral images, and the range of motion (ROM) was calculated

from forward- and backward-bending radiographs.

CT images were obtained using standard methods at our institution, and multiplanar reconstruction (MPR) images were produced. TBR was identified on coronal or sagittal CT-MPR images by comparison with the immediate postoperative images. A previous report¹⁾ revealed that TBR involved relatively thick, tilted trabeculae inside the vertebra that were not shown on the normal (immediate postoperative) images. In addition, since vertebral endplate cyst (VEC)^{8,9)} appears in unstable interbodies, VEC formation was used as an imaging reference that contrasted with osseointegration. The appearance of VEC that was not present on previous imaging or an enlargement of VEC was defined as VEC-positive. Cage subsidence was defined as cage migration of more than 2 mm into the vertebral endplate in any part of the cage compared with previous imaging studies. No progression of subsidence after previous imaging was defined as negative. Notably, there was no cage dropout from the intervertebral space in our series. Clear zone around PS (CZPS) was defined as a translucent zone of 2 mm or greater width around the PS. CZPS was expressed as the number of PSs per segment that met the definition (0-4).

Vertebral CT values (Hounsfield unit (HU)) were measured using axial images as previously reported¹⁰⁾, but on the cephalad vertebra to avoid halation artifact due to PS (Fig. 2). TBR was included in this measurement plane. CT values were presented as percentages of the postoperative measurements as 100%.

Vertebral bridging was defined as a segment demonstrating bone formation bridging the outer surface of the vertebrae¹¹⁾. Facet union was defined as the fusion of facet gaps on CT axial images¹¹⁾. Pseudarthrosis was diagnosed by the presence of any of the following findings: local ROM

Table 1. Patient Demographics.

	N=53
Age, year	68.5±8.2
Sex, female	22 (42%)
BMI, kg/m ²	23.4±2.9
Smoking	14 (26%)
T-score, hip	-0.9±1.2
PTH use	5 (9%)
Diabetes	13 (25%)
Number of LLIF	
1	40 (75%)
2	13 (25%)
LLIF level	
L4-5	30 (57%)
L3-5	13 (25%)
L3-4	7 (13%)
L2-3	3 (6%)
Op time, min	156.2±59.5
EBL, mL	102.9±199.9
Cage	
CoRoent XL	33 (62%)
Clydesdale	20 (38%)
Cage angle (N=65)	
10°	42 (65%)
6°	23 (35%)
Cage height (N=65)	
<10 mm	22 (33%)
10 mm	34 (52%)
>10 mm	9 (15%)
PPS	46 (87%)
JOA score	
Preop	14.6±2.2
2 years postop	25.9±3.2

BMI, body mass index; PTH, parathyroid hormone; LLIF, lateral lumbar interbody fusion; EBL, estimated blood loss; PPS, percutaneous pedicle screw; JOA, The Japanese Orthopaedic Association

greater than 5¹²), CZPS of 4, or intervertebral vacuum phenomenon on CT. Notably, there was no pseudarthrosis that required revision surgery.

Statistical analysis

Data were presented as mean±standard deviation for continuous variables and numbers and percentages for categorical variables. All statistical analyses were performed using R software version 4.3.1 (The R Foundation, Vienna, Austria; <http://www.R-project.org>). Continuous and categorical variables were compared using the Wilcoxon rank-sum and Fisher’s exact tests, respectively. The intra- and interrater reliability of the TBR judgments were assessed using the Kappa coefficient. A P value of <0.05 was considered statistically significant.

Results

Table 1 shows the demographic characteristics of the patients. LLIF-PSF surgery was performed on one or two consecutive segments (L3-5). CoRoent XL was used in 33 cases (62%), and Clydesdale was used in 20 cases (38%). PSF with PPS was performed in 46 (87%) cases.

The Kappa coefficients were 0.846 and 0.682 for the intra- and interrater reliability of the TBR judgments, respectively. After LLIF-PSF, TBR was observed mainly anterior to the cage on CT-MPR sagittal images (Fig. 3). The CT imaging data at 3 months, 1 year, and 2 years postoperatively for each segment were classified according to the presence or absence of TBR at 3 months and 1 year postoperatively. Fifteen segments (23%) were TBR-positive at 3 months postoperatively (Table 2). The 3-month TBR-positive segments showed no significant differences in VEC, subsidence, and CZPS. However, the 3-month TBR-positive segments showed a significantly higher TBR-positive rate (100% vs. 54%, *P*=0.001) and less VEC (0% vs. 30%, *P*=0.014) at 1 year postoperatively. A total of 42 segments

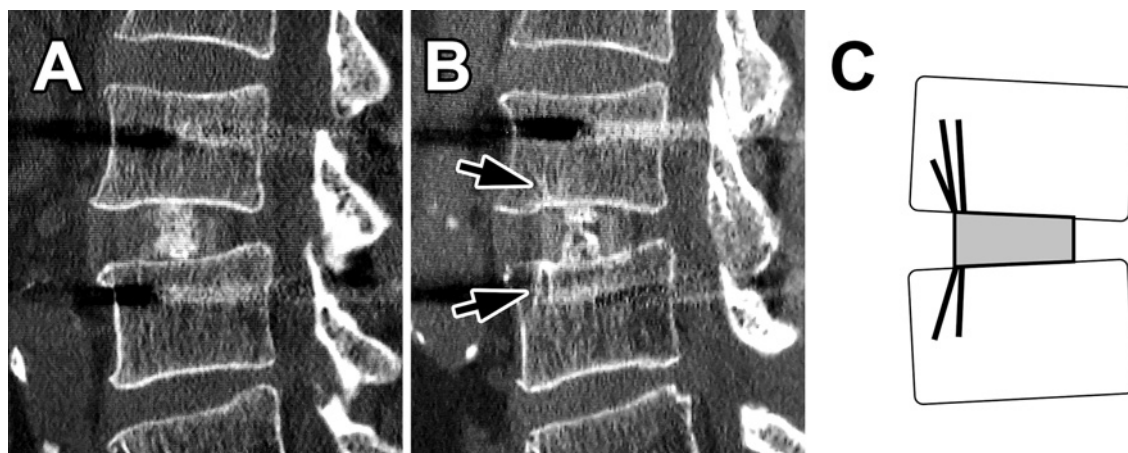


Figure 3. TBR observed after LLIF-PSF.

(A) Postoperatively. (B) 1 year postoperatively. TBR (black arrow). (C) Schematic of TBR. Newly developed trabeculae bordering the LLIF cage that were not present postoperatively.

TBR, trabecular bone remodeling; LLIF, lateral lumbar interbody fusion; PSF, posterior spinal fixation/fusion

Table 2. Imaging Findings at 3 Months and 1 Year Postoperatively Based on 3-month TBR.

	3 months postop			1 year postop		
	3-month TBR (+) N=15	3-month TBR (-) N=50	P-value	3-month TBR (+) N=15	3-month TBR (-) N=50	P-value
TBR	15 (100%)	0 (0%)	–	15 (100%)	27 (54%)	0.001
VEC	1 (7%)	10 (20%)	0.43	0 (0%)	15 (30%)	0.014
Subsidence	2 (15%)	5 (10%)	0.62	0 (0%)	13 (26%)	0.029
CZPS			0.55			>0.99
0	14 (93%)	48 (96%)		13 (87%)	40 (80%)	
1	0 (0%)	1 (2%)		0 (0%)	2 (4%)	
2	1 (7%)	1 (2%)		2 (13%)	7 (14%)	
3	0 (0%)	0 (0%)		0 (0%)	1 (2%)	
4	0 (0%)	0 (0%)		0 (0%)	0 (0%)	
Vertebral %HU	102.3±23.2	106.4±29.3	0.58	94.3±24.1	109.4±36.5	0.070
Bridging				1 (7%)	4 (8%)	>0.99
Facet union				3 (23%)	18 (35%)	0.52
ROM 5°≤				1 (8%)	1 (2%)	>0.99
Vacuum				0 (0%)	0 (0%)	–
Pseudarthrosis				0 (0%)	1 (2%)	>0.99

TBR, trabecular bone remodeling; VEC, vertebral endplate cyst; CZPS, clear zone around pedicle screw; HU, Hounsfield unit; ROM, range of motion

Table 3. Imaging Findings at 1 and 2 Years Postoperatively Based on 1-year TBR.

	1 year postop			2 years postop		
	1-year TBR (+) N=42	1-year TBR (-) N=23	P-value	1-year TBR (+) N=42	1-year TBR (-) N=23	P-value
TBR	42 (100%)	0 (0%)	–	39 (93%)	2 (9%)	<0.001
VEC	6 (14%)	9 (35%)	0.10	0 (0%)	3 (13%)	0.041
Subsidence	4 (10%)	8 (35%)	0.019	0 (0%)	2 (9%)	0.12
CZPS			0.003			0.014
0	39 (93%)	14 (61%)		39 (93%)	15 (65%)	
1	0 (0%)	2 (9%)		1 (2%)	2 (9%)	
2	3 (7%)	6 (26%)		2 (5%)	5 (22%)	
3	0 (0%)	1 (4%)		0 (0%)	0 (0%)	
4	0 (0%)	0 (0%)		0 (0%)	1 (4%)	
Vertebral %HU	98.8±27.0	118.9±42.7	0.049	92.8±23.9	111.4±46.2	0.082
Bridging	3 (7%)	2 (9%)	>0.99	9 (21%)	6 (26%)	0.67
Facet union	14 (33%)	7 (30%)	0.81	35 (83%)	13 (57%)	0.019
ROM 5°≤	0 (0%)	1 (4%)	0.35	0 (0%)	1 (4%)	0.35
Vacuum	0 (0%)	0 (0%)	–	0 (0%)	2 (9%)	0.12
Pseudarthrosis	0 (0%)	1 (4%)	0.35	0 (0%)	3 (13%)	0.041

TBR, trabecular bone remodeling; VEC, vertebral endplate cyst; CZPS, clear zone around pedicle screw; HU, Hounsfield unit; ROM, range of motion

(67%) were TBR-positive at 1 year postoperatively (Table 3). The 1-year TBR-positive segments showed significantly less subsidence (10% vs. 35%, $P=0.019$) and smaller CZPS (CZPS 0: 93% vs. 61%, $P=0.003$). In addition, the 1-year TBR-positive segments showed significantly less VEC (0% vs. 13%, $P=0.041$), smaller CZPS (CZPS 0: 93% vs. 65%, $P=0.014$), higher facet union rate (83% vs. 57%, $P=0.019$), and less pseudoarthrosis (0% vs. 13%, $P=0.041$) at 2 years postoperatively. A sensitivity analysis made by Examinees 1 and 2 independently was performed using the TBR determi-

nation, presenting similar results for pseudoarthrosis (Table S1).

The vertebral CT values showed a significantly greater increase in HU in the 1-year TBR-negative segments. Otherwise, there were no significant differences, with CT values consistently higher in the TBR-negative segments than in the TBR-positive segments. There were no significant differences in the incidence of intervertebral bridging in any period.

Fig. 4 shows a representative case. Three months postop-

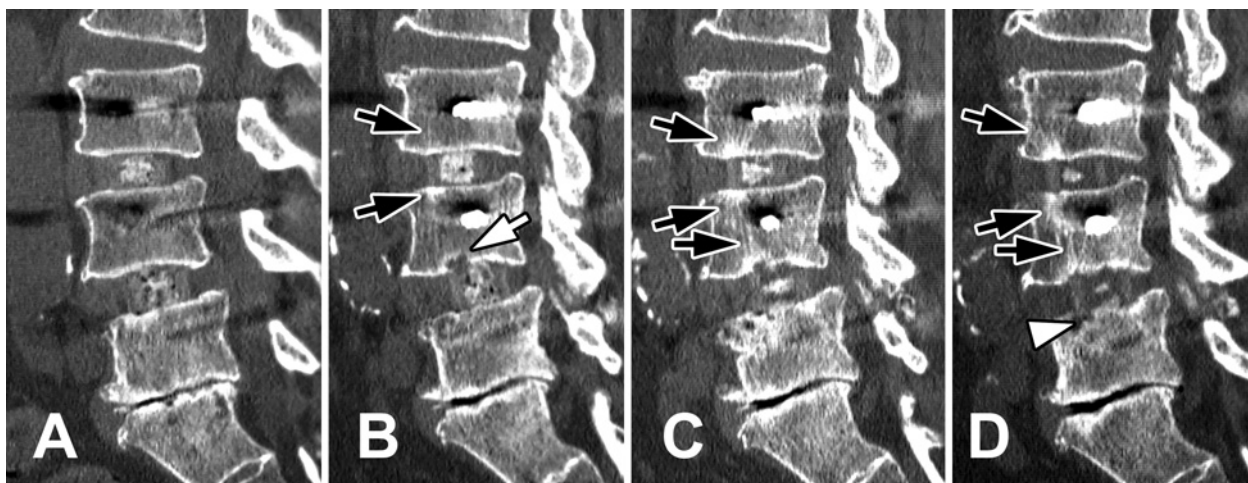


Figure 4. TBR and VEC observed after LLIF-PSF. (A) Postoperatively. (B) 3 months postoperatively. The L3-4 segment was TBR-positive (black arrow), and the L4-5 segment was VEC-positive (white arrow). (C) 1 year postoperatively. TBR (black arrow) was clear at the L3-4 segment. Although VEC was present at the L4-5 segment, TBR (black arrow) was also present. (D) 2 years postoperatively. TBR (black arrow) at both segments was maintained, and the cage at the L4-5 segment was subsided (white arrowhead). TBR, trabecular bone remodeling; VEC, vertebral endplate cyst; LLIF, lateral lumbar interbody fusion; PSF, posterior spinal fixation/fusion

Table 4. Imaging Findings at 5 Years for 2-year TBR-positive Segments (N=26).

	5-year TBR (+) N=13	5-year TBR (-) N=13	P-value
VEC	0 (0%)	0 (0%)	-
Subsidence	0 (0%)	0 (0%)	-
CZPS			>0.99
0	12 (92%)	13 (100%)	
2	1 (18%)	0 (0%)	
Vertebral %HU	101.2±38.7	85.5±26.9	0.24
Bridging	6 (46%)	12 (92%)	0.030
Facet union	13 (100%)	13 (100%)	>0.99
ROM 5°≤	0 (0%)	0 (0%)	-
Vacuum	0 (0%)	0 (0%)	-
Pseudarthrosis	0 (0%)	0 (0%)	-

TBR, trabecular bone remodeling; VEC, vertebral endplate cyst; CZPS, clear zone around pedicle screw; HU, Hounsfield unit; ROM, range of motion

eratively, the L3-4 segment was TBR-positive, and the L4-5 segment was VEC-positive. One year postoperatively, a clear TBR was observed at the L3-4 segment. In addition, the L4-5 segment was not only VEC-positive but also TBR-positive. Two years postoperatively, although both segments remained TBR-positive, the cage at the L4-5 segment had subsided.

A total of 36 patients (68%) who underwent radiological evaluation 4-6 years (mean 5.0 years) postoperatively were included in the subanalysis to assess the midterm course. Of the 26 segments that were 2-year TBR-positive, 13 (50%) were still TBR-positive and 13 (50%) were TBR-negative, respectively, at 5 years postoperatively. Segments that changed to TBR-negative at 5 years postoperatively exhib-

ited significantly more intervertebral bridging (92% vs. 46%, $P=0.030$) (Table 4 and Fig. 5).

Discussion

In this study, the characteristics of TBR were investigated in cases who underwent lumbar fusion with LLIF-PSF using PEEK cages. TBR associated with LLIF cages was commonly observed anterior to the cage on CT-MPR sagittal images. The TBR-positive rate increased to 21%, 67%, and 73% at 3 months, 1 year, and 2 years postoperatively, respectively. In addition, TBR-positive segments had significantly lower future VEC positivity, higher future facet union rates, and lower future pseudarthrosis rates. TBR may be as useful in LLIF as in PLIF for estimating the fate of interbody fusion.

Consistent with a previous study on PLIF¹⁾, intervertebral stability and osseointegration after lumbar fusion with LLIF-PSF not only were significantly more in the TBR-positive segment but also did not cause problems such as cage subsidence. Furthermore, the 3-month TBR-positive rate for LLIF using PEEK cages was 21%. In contrast, the 3-month TBR-positive rate for “PLIF” using Ti-PEEK cages was 4.5%¹⁾. From a biomaterial perspective, Ti-PEEK is expected to have higher biocompatibility by improving the biologically inert properties of PEEK. Therefore, the osseointegration of PEEK may be inferior to that of Ti-PEEK. Nevertheless, LLIF with PEEK cages had a higher early TBR-positive rate than “PLIF” with Ti-PEEK cages. Therefore, TBR suggests established intervertebral stability in LLIF-PSF and indicates that LLIF-PSF may have superior early fixation to PLIF.

Unlike in PLIF, TBR in LLIF segments was evident on the sagittal CT image and not on the coronal CT image. In

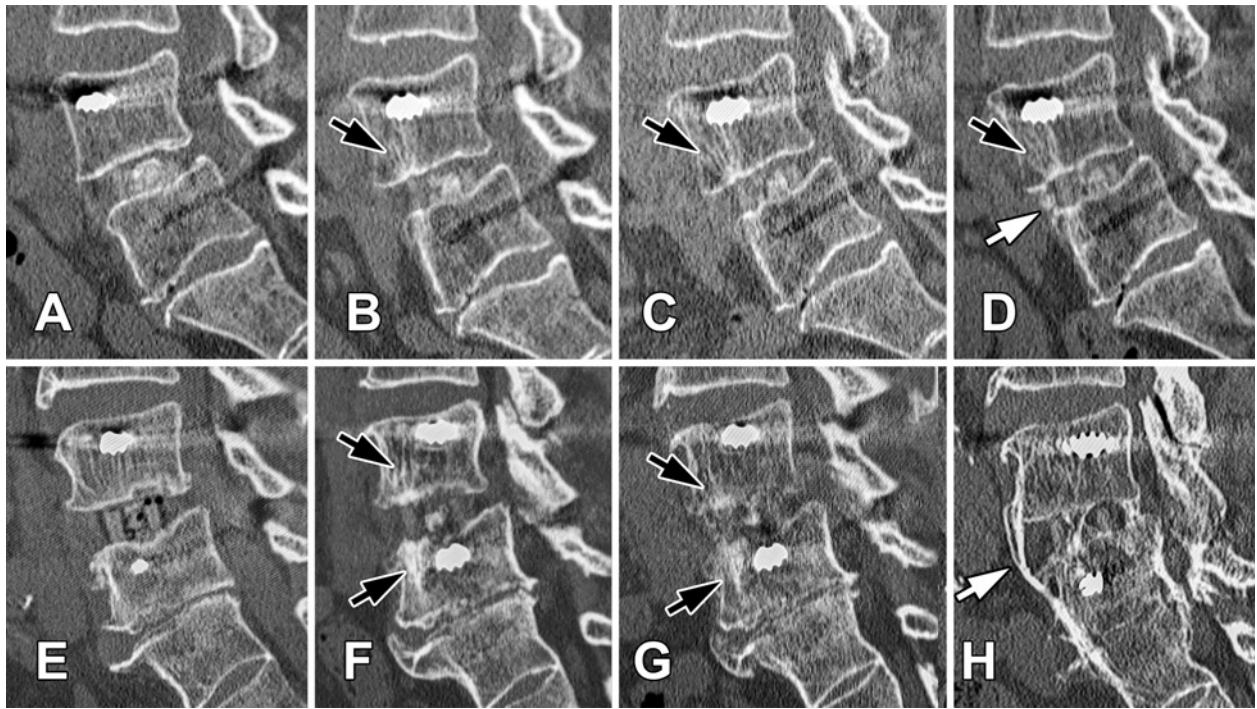


Figure 5. TBR changes after 5 years.

(A) Postoperatively. (B) 1 year postoperatively. (C) 2 years postoperatively. The segment was TBR-positive (black arrow). (D) 5 years postoperatively. Vertebral bridging was not yet solid (white arrow), and TBR (black arrow) was still present. (E) Postoperatively. (F) 1 year postoperatively. (G) 2 years postoperatively. The segment was TBR-positive (black arrow). (H) 5 years postoperatively. Solid vertebral bridging (white arrow) was complete, and TBR was no longer present.

TBR, trabecular bone remodelling

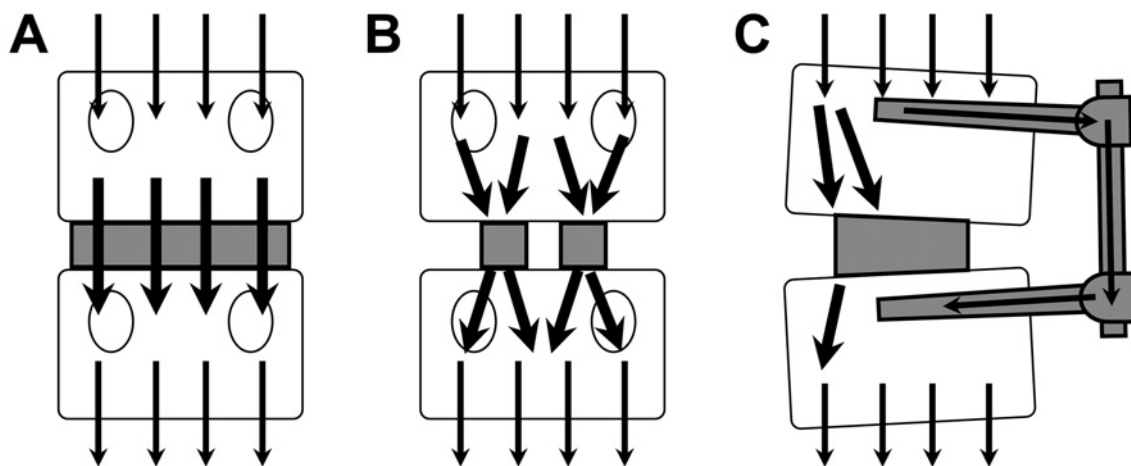


Figure 6. Stress transmission around LLIF and PLIF cages.

(A) LLIF cage in the coronal plane. (B) PLIF cages in the coronal plane. (C) LLIF cage and posterior instrumentation in the sagittal plane. Stress transmission is indicated by arrows.

LLIF, lateral lumbar interbody fusion; PLIF, posterior lumbar interbody fusion

PLIF, the stress transmission between the vertebrae is believed to be concentrated on the narrow contact surface between the vertebral endplate and PLIF cages (typically around 10 mm wide; Fig. 6B), resulting in remodeling of the trabeculae to accommodate the stress concentration^{1,13}. TBR represents a “concentrated path of stress transmission” within the vertebral body. Thus, TBR would probably not be

observed without stress concentration. Since LLIF cages are almost as wide as the vertebral endplates^{6,14}, stresses passing through the intervertebral bodies are evenly transmitted to the cage in the coronal plane so that they are not concentrated in limited areas (Fig. 6A). This might explain blurriness of the TBR finding in the LLIF segments on the coronal image. This is also suggested by the fact that PLIF-like

TBR can be observed in coronal images at corresponding locations where stress concentrations occur between the endplate and cage (Fig. S1). In contrast, the LLIF cage antero-posterior width (18 mm) was narrower than the vertebral endplate anteroposterior width in the sagittal plane. This might have caused stress concentration, and TBR could be observed in the sagittal plane. Therefore, TBR observed in the LLIF segment is essentially the same as that observed in the PLIF segment.

However, TBR in LLIF segments observed in the sagittal plane was commonly present anteriorly. This observation is heterogeneous compared with the symmetrical TBR observed in PLIF segments^{1,13}. However, based on the figure exemplified in the finite element analysis report¹⁵⁻¹⁸, the stresses received by the vertebral endplates after LLIF are more dominant on the anterior side than on the dorsal side. This might be due to stress dispersion caused by the posterior column (e.g., facet joints)^{19,20}. In addition, since all cases in our series underwent PSF with a bilateral PS-rod system, load stresses were distributed to the posterior instrumentation (Fig. 6C)²¹. This may have further reduced the stresses received by the spinal mid-column. Thus, the vertebrae-cage stress transmission was predominantly anterior. Therefore, TBR, which represents the path of stress concentration, was anterior to the LLIF cage.

Since TBR has only been studied up to 1 year postoperatively^{1,13}, another question was how TBR changes when intervertebral bony fusion is completed and stresses are dispersed over a longer period of time. Interestingly, half of the 2-year TBR disappeared at 5 years postoperatively, and the imaging parameter associated with the disappearance of TBR was intervertebral bridging, i.e., solid intervertebral bony fusion. Presumably, completed fusion frees intervertebral stress transmission from the “narrow pathway” through the cage. This result would be reflected in bone remodeling, and the TBR created as a result of limited stress transmission would disappear. Therefore, in LLIF-PSF, TBR up to 2 years postoperatively may indicate intervertebral osseointegration, and the subsequent disappearance of TBR may represent complete intervertebral integration.

Previous radiological evaluations using CT images after lumbar interbody fusion are based on observations of the vertebral endplate boundary surface in contact with the cage, not only for bone fusion evaluation^{22,23} but also for risk findings for pseudarthrosis such as VEC formation^{8,9}. However, TBR is distinct from previous evaluations, focusing on the fact that the cage-vertebral body interaction affects the vertebral trabecular bone and causes modification of the bone structure. Furthermore, TBR suggests that the biomechanical response of the bone to the cage emerges at the point where cage-vertebral endplate stress transmission is maximized. In other words, TBR is an indicator for determining that a stable stress concentration occurs at the vertebral endplate and an established path of stress transmission is forming within the vertebra. Furthermore, this property implies that TBR can be a tool to indirectly understand the biomechanics in

the segments after spinal fusion surgery.

No quantitative method has been established for TBR evaluation, and evaluation can be subjective²⁴. Therefore, the possibility of measuring vertebral CT values to determine TBR was investigated. Intuitively, the vertebral body CT values were expected to increase with TBR. In addition, the axial image shows areas of high CT values that may reflect TBR (Fig. S2). However, there was no significant difference in CT values between segments with and without TBR. CT values were higher in the TBR-negative segments than in the TBR-positive segments. This might be due to the fact that CT value heterogeneity may occur within the vertebral body, with CT values increasing at TBR localization, whereas other vertebral trabecular bones may atrophy due to stress shielding. This hypothesis aligns with the expectation that TBR results from a narrow concentration of stress transmission¹ but require fairly precise measurements for demonstration. Thus, a method to quantitatively evaluate TBR remains unknown.

Paradoxically, the significance of imaging for determining achievement of mechanical stability of the segment at 3 months or 1 year after LLIF-PSF surgery should be reconsidered. Achieving bony fusion is one of the goals of lumbar fusion²⁵. Furthermore, surgeons must evaluate the poor mechanical stability of the segments to take remedial measures as early as possible to prevent the unfavorable outcomes following pseudoarthrosis. VEC, an excellent pseudoarthrosis risk assessment, might be suitable for this purpose. However, VEC cannot directly predict osseointegration and requires repeated CT evaluation to observe cyst expansion or contraction. In contrast, TBR directly predicts good progress. Therefore, patients can skip subsequent CT surveillance after TBR confirmation. Furthermore, TBR is an imaging finding that complements VEC and can provide another perspective on the osseointegration that cannot be determined by VEC only¹. Thus, TBR diversifies the means of imaging assessment of the mechanical stability of the postoperative segment.

This study had some limitations. First, the number of cases was relatively small. Second, the cage material was standardized to PEEK, but shape of the cage was not. Although cage material affects TBR in PLIF, the effect remains unknown as this study was limited to PEEK. In addition, PPS was not used for PSF in some cases. However, PSF without PPS was intended for central decompression, and no osteotomy was performed for spinal realignment. Third, there may be potential for error in the judgment of imaging findings. Fourth, there is no histological evidence to support our interpretation of the TBR observations. TBR may be a finding of endplate injury and subsequent compression of the cancellous bone below the endplate. However, TBR showed dynamic appearance and disappearance with the progression and establishment of intervertebral fusion, indicating TBR to be a biological response to stress transmission between the bone and implant. Therefore, despite these limitations, this study provided insight into the

interpretation of imaging results sufficient to consider vertebral cage biomechanics after LLIF.

This study investigated the characteristics of TBR in LLIF-PSF using PEEK cages. TBR associated with LLIF cages was commonly observed anterior to the cage on CT-MPR sagittal images. TBR-positive segments had significantly lower future VEC positivity, higher future facet union rates, and lower future pseudarthrosis rates than TBR-negative segments. Furthermore, 50% of the 2-year TBR-positive segments turned negative at 5 years with solid intervertebral bony fusion, representing a change in stress transmission. In LLIF-PSF, TBR serves as an indicator of the establishment of intervertebral stability along with an important finding to consider in intervertebral biomechanics.

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Author Contributions: N.S. designed the study; S. Ito, J.O., R.O., I.Y., Y. Miyairi, Y. Morita, M.T., H.T., K.M., and K.O. collected the data; N.S. and H.N. wrote the manuscript; and T.K. and S. Imagama supervised the project.

Ethical Approval: The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Institutional Review Board of Konan Kosei Hospital, Konan, Japan (2019-006 (0339)).

Informed Consent: Informed consent was obtained from all patients involved in the study.

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