

## Volumetric change in interbody bone graft after posterior lumbar interbody fusion (PLIF): a prospective study

Zenya Ito · Shiro Imagama · Tokumi Kanemura · Kotaro Satake · Kei Ando · Kazuyoshi Kobayashi · Ryuichi Shinjo · Hideki Yagi · Tetsuro Hida · Kenyu Ito · Yoshimoto Ishikawa · Mikito Tsushima · Akiyuki Matsumoto · Hany El Zahlawy · Hidetoshi Yamaguchi · Yukihiro Matsuyama · Naoki Ishiguro

Received: 3 December 2012/Revised: 6 June 2014/Accepted: 7 June 2014/Published online: 19 June 2014  
© Springer-Verlag Berlin Heidelberg 2014

### Abstract

**Purpose** The purpose of this study is to quantify the change in the volume of the interbody bone graft after the PLIF and monitor the change over time for subsequent analysis.

**Methods** The 114 cases were selected as the subjects of this study. The observation period was for 5 years following the surgery. The volume of the bone graft in the interbody space was calculated by summing up the cross-sectional area of the bone graft on each axial image multiplied by the height (2 mm) (the volume of the two cages was excluded). The volume ratio (%) = (bone graft volume)/(total volume of the interbody space – cage volume) was used for the purpose of evaluation.

**Results** The volumetric change of the bone graft was 51 % (3 months), 53 % (6 months), 54 % (1 year), 55 % (2 years), 59 % (3 years), 62 % (4 years), and 72 % (5 years), indicating a continued increase up to the 5-year mark. In particular, a significant increase was observed from the second year as compared with the previous years'

result. Additionally, the volumetric increase from the second year to the fifth year was significantly higher than that before the second year.

**Conclusions** The post-PLIF volumes of interbody bone grafts exhibited increases particularly from the second to fifth years after the procedure. Even the elderly and those with poor bone qualities can expect to have volumetric increases over time. Sufficient interbody space should be secured for accommodating bone grafts by intraoperative reduction, wherever possible.

**Keywords** Volumetric change · Posterior lumbar interbody fusion · Interbody bone graft · A prospective study

### Introduction

With sound union following PLIF, the interbody bone graft goes through the process of: (1) increasing continuity between the adjacent vertebral endplates and the bone graft; (2) remodeling to form cancellous bone; and (3) an increase in volume of bone union. If this process does not occur as desired, the result is delayed union or pseudarthrosis. Generally, the patient is diagnosed of delayed union with absence of normal bone union by 1 year after surgery and as pseudarthrosis if normal bone union has not occurred by 2 years postoperatively. This definition suggests that from 2 years on following surgery, hardly any sound union or a substantial increase in the volume of the interbody bone graft can be expected. However, numerous cases have been reported where volume of the interbody bone graft increased even beyond 2 years linking the vertebral bodies. Tokuhashi et al. [1] reported bone union in 42 % of patients 2 years beyond

---

Z. Ito · S. Imagama (✉) · K. Ando · K. Kobayashi · R. Shinjo · H. Yagi · T. Hida · K. Ito · Y. Ishikawa · M. Tsushima · A. Matsumoto · H. El Zahlawy · N. Ishiguro  
Department of Orthopedic Surgery, Nagoya University School of Medicine, 65 Tsurumai Shyowa-ward, Nagoya 466-8550, Aichi, Japan  
e-mail: si1222@b-star.jp

Z. Ito  
e-mail: z.ito@nifty.com

T. Kanemura · K. Satake · H. Yamaguchi  
Department of Orthopedic Surgery, Konan Kosei Hospital, Konan, Japan

Y. Matsuyama  
Department of Orthopedic Surgery, Hamamatsu Medical University School of Medicine, Hamamatsu, Japan

the PLIF procedure. In our previous study, 74 % of the cases formed bony bridges around the cages by 2 years after surgery and in the remaining 23 %, excluding cases with pseudarthrosis, bony bridges developed more than 2 years later [2]. There have been occasional reports on bone union following PLIFs, focusing on continuity within the bone graft and the rates of remodeling/bone union [3–8]. No reports exist, however, that closely examine the volume increases in bone union over time or more precisely evaluate the volumetric changes in the bone graft sites where ossein is insufficient in supply as with old patients and local bone grafting. The purpose of this study is to quantify the change in volume of the interbody bone graft after PLIF and monitor that change over time for subsequent analysis.

## Methods

### Subjects

Patients who performed PLIF from April 2003 to July 2006 at our institution were registered in this study. The inclusion criteria were unresponsiveness to conservative treatment for at least 6 months, intervertebral rotation of 15° or more at the morbidity site in dynamic views and 5° or more of posterior aspects of adjoining endplates spreading in position of maximum flexion, and cases requiring single level fusion. 114 cases (65 males and 49 females with an average age of 59.7) met the above criteria for this study.

The cases included 13 with lumbar disc herniation (8 recurrent cases), 67 with degenerative spondylolisthesis, and 34 with lumbar canal stenosis. Iliac autografts were used in 55 cases (the odd numbered ID group) and local bone grafts were used in 59 cases (the even numbered ID group). The levels operated upon consisted of 13 cases

(11 %) at L3/4, 87 cases (76 %) at L4/5, and 14 cases (12 %) at L5/S.

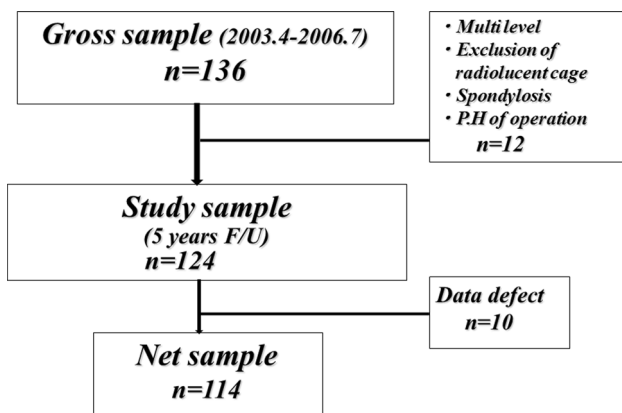
The follow-up period was up to 5 years after surgery. Factors believed to affect bone union and bone volume change, such as smoking, body mass index, and employment situation were noted. Patients with previous spinal surgery (other than recurrent disc cases), lumbar spondylolysis, infection, spinal tumors, and lesions were excluded (Fig. 1).

### Surgical technique employed

Two surgeons belonging to the institution performed all the PLIFs using the same technique. To minimize instability in adjacent vertebral bodies, only the lower two-thirds of the laminae and the spinous process was removed, thus maintaining continuity of the remaining spinous process with the one above through the supraspinous ligament. Titanium screws and rods were used for fixation. Fusion bed was prepared by curetting the intervertebral disc and the cartilaginous endplates. Either the harvested iliac bone or local bone from the removed vertebral arch was packed into the forward and side regions of the interbody space after preparation by chipping using a bone mill. Two carbon fiber cages filled with bone grafts were then inserted into the space. No bone substitutes were used to increase the bulk of the bone grafts.

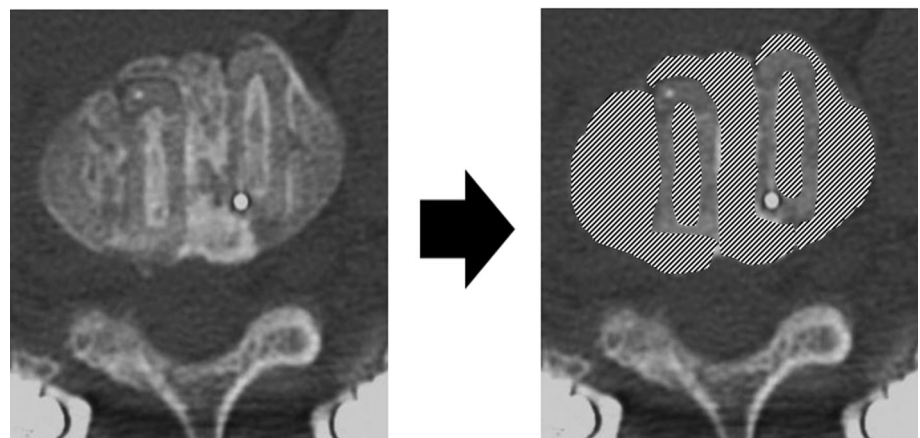
### Image evaluation and evaluation items

CT images of the fused interbody space were taken with 2 mm slice thickness. The volume of the bone graft in the space was calculated by summing up the cross-sectional area of the graft on each axial image multiplied by the height (2 mm) (the volume of the two cages was excluded) (Fig. 2) The volume ratio (%) = (bone graft volume)/(total volume of the interbody space – cage volume) was used for purpose of evaluation. Third person not involved in the treatment performed blind evaluation of the images. Additionally, a computer software for area calculation (Scion Image®) was used to check the measurements for the cross-sectional areas of the bone graft. The change in the volume of the interbody bone graft over time (1 month, 3 months, 6 months, 1 year, 2 years, 3 years, 4 years, and 5 years) was evaluated. Other items evaluated included differences in volume changes by age (below 65 years old vs. at least 65 years old), smoking history (present and past smokers vs. non-smokers), bone graft type (iliac bone vs. local bone), amount of bone graft (less than 50 vs. 50 % or more), postoperative intervertebral disc height (less than 10 vs. 10 mm or more), postoperative slip percentage (less than 10 vs. 10 % or more), and fixation level (L3/4 vs. L4/5 vs. L5/S).

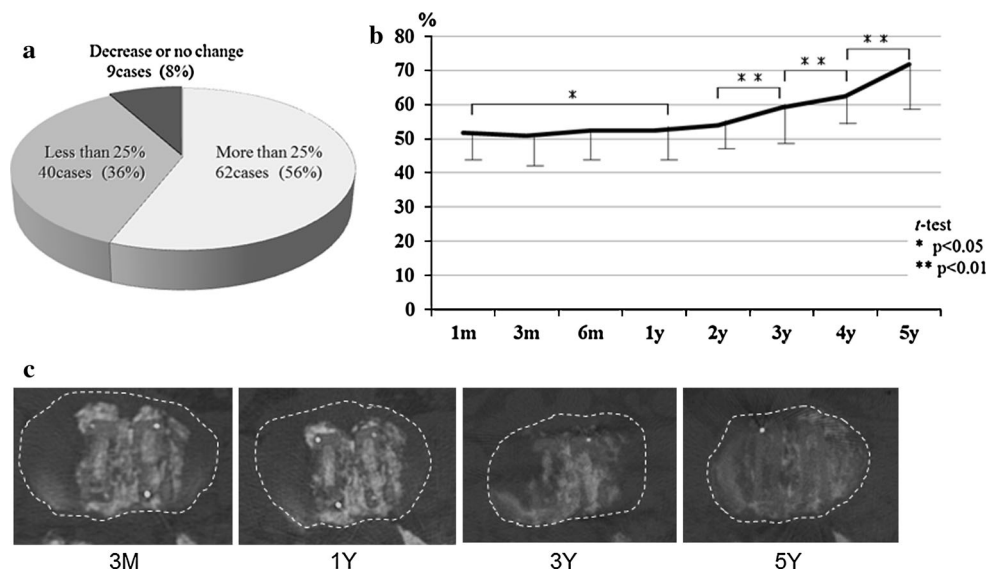


**Fig. 1** Flowchart of subjects

**Fig. 2** Method of calculating bone graft volume. The volume of the bone graft in the interbody space was calculated by summing up the cross-sectional area of the bone graft on each axial image multiplied by the height (2 mm) (the volume of the 2 cages was excluded). A third person who was not involved in the treatment (radiologist) quantified the bone densities in CT scan for determining whether or not the particular bone was a graft



**Fig. 3 a** Volumetric change at final follow-up. **b** Volumetric change over time. **c** Time course of volumetric change for a case



**Analysis**

Paired *t* test and analysis of covariance (ANCOVA) were used for statistical analysis.

**Results**

Bone union was observed in 111 out of the 114 cases at final examination with three confirmed cases (2.6 %) of

pseudarthrosis. Among those 111 cases, on comparing the volume of the interbody bone graft at final examination and that calculated immediately after surgery 9 cases (8 %) showed reduction or no change, 40 cases (36 %) showed increases of less than 25 %, and 62 cases (56 %) revealed increases of at least 25 % (Fig. 3a).

The volume ratio of the bone graft in sequential follow-ups was 51 % (3 months), 53 % (6 months), 54 % (1 year), 55 % (2 years), 59 % (3 years), 62 % (4 years), and 72 % (5 years), indicating a continued increase up to 5 years. In particular, a significant increase was observed from the second year on as compared with the result from the previous years. The volumetric increase from the second year to the fifth year was significantly higher than that before the second year (the rate of increase: 4 % during 1 month–2 years, 17 % during 2–5 years). ( $p < 0.05$ ) (Fig. 3b).

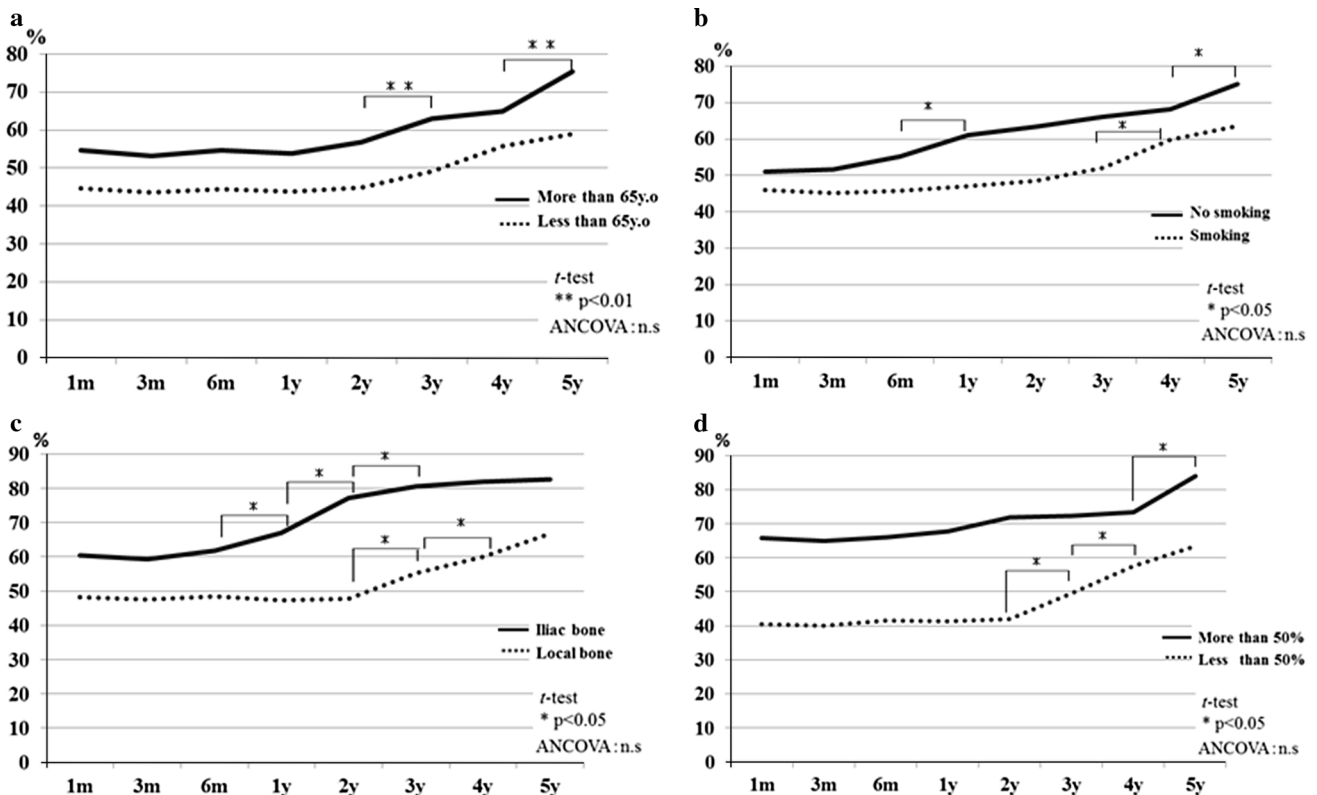
The volumetric comparisons by age, smoking history, bone graft type, bone graft amount, and postoperative intervertebral disc height likewise indicate increases up to the fifth year in both groups with no significant differences (analyzed by ANCOVA) between each groups in terms of volume change over time and volume at final examination. Conversely, on comparison between different bone graft types, significant volumetric increases were observed in the

iliac bone group from the sixth month and from the second year for the local bone group, showing an earlier volumetric increase in the former group. Furthermore, a significantly greater increase in volume was observed from the second year for the group with less than 10 % of slippage when compared to the other group ( $p < 0.05$ ).

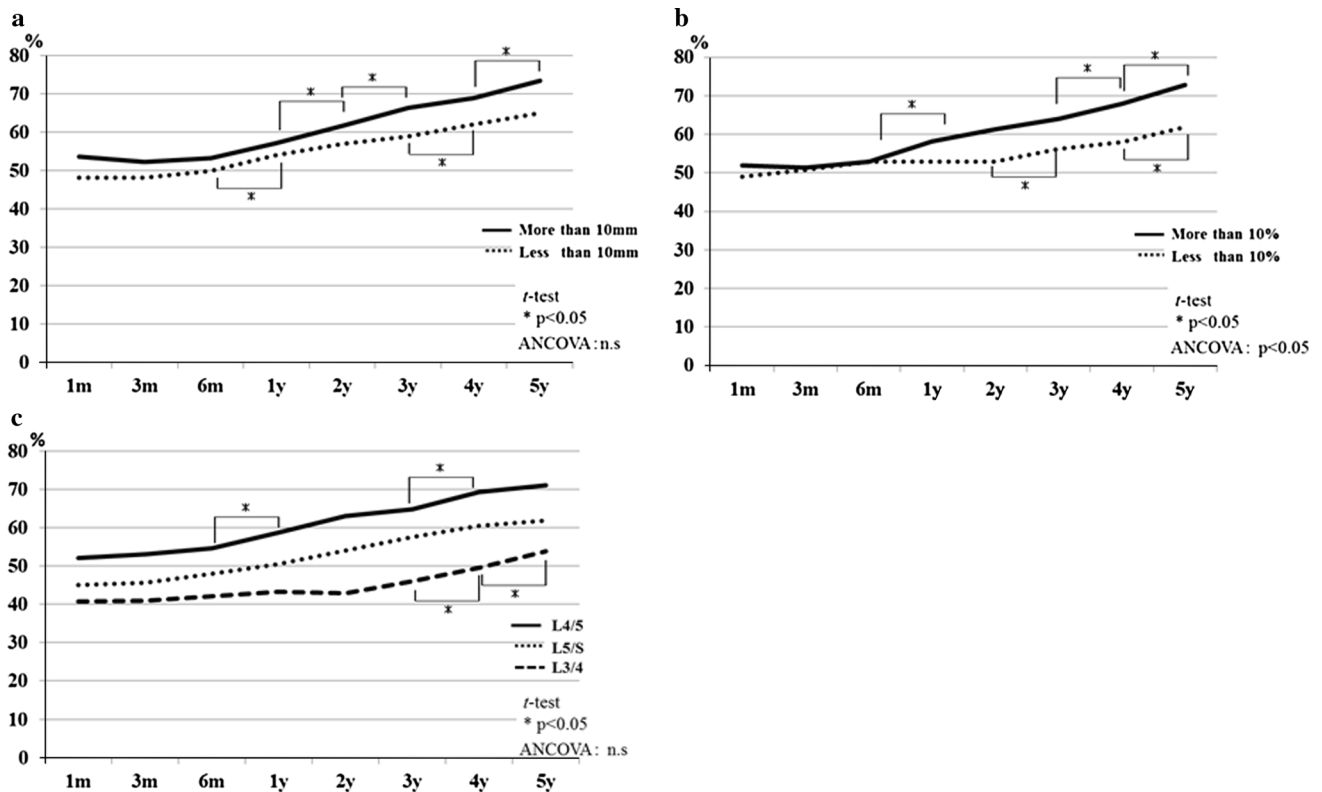
No significant difference emerged in volumetric increase among the different fusion levels. The final examination, however, revealed a significant volumetric difference between the L4/5 (73 %) and L3/4 (54 %) ( $p < 0.05$ ) (Figs. 4a–d, 5a–c).

**Discussion**

Since Cloward first reported on the PLIF technique, numerous research studies have been conducted and reports published on various aspects of bone union, including the rate of bone union, iliac bone and local bone as sources of bone graft, and grafting of exogenous bone, ceramics, demineralized bone matrix, rhBMP-2, rhBMP-7, and cultured stem cells [9–19]. In view of absence of reports on volumetric change over time, we performed a detailed evaluation of the volumetric change in the interbody bone graft taking into account the age, smoking history, bone



**Fig. 4** Volumetric change over time. **a** 65 years old vs. at least 65 years old, **b** history of smoking (present and past smokers vs. non-smokers), **c** iliac bone vs. local bone grafting, **d** bone graft amount (less than 50 vs. 50 % or higher)



**Fig. 5** **a** Postoperative intervertebral disc height (10 mm or more vs. less than 10 mm); **b** postoperative slip percentage (less than 10 vs. 10 % or higher); **c** fixation level (L3/4 vs. L4/5 vs. L5/S)

graft type among other parameters. This study is the first to focus on such.

According to the results of this study, the post-PLIF increase in the interbody bone graft volume from second year to fifth year was significantly greater than that of before second year (the rate of increase 1 month–2 years: 4 %, 2–5 years: 17 %) ( $p < 0.05$ ). Furthermore, substantially the same volumetric change was observed despite differences in bone quality, amount of bone graft, and pre/postoperative differences in bone union environment. However, the volumetric increase was particularly poor among the group with a postoperative slip of 10 % or more. The volumetric increase is thought to be insufficient in cases with significant postoperative slippage because of the insufficient bone grafting space behind the cages. And end-plate sclerosis with reduced perfusion was one of the causes of the significant volume change. Accordingly, sufficient interbody space should be secured for accommodating bone grafts by intraoperative reduction, whenever possible.

Among other reports, Kim et al. [7] reported that fusion masses were formed around the cages in 10 % of patients who performed PLIF 6 months after the surgery and 35 % of the cases in 12 months. In the study we conducted in the past, interbody bony bridges were observed in 9.5 % of the cases in 6 months and 46 % in 12 months, and 74 % in 24 months

after the procedure [2]. The above are mostly all reporting on the volumetric change in the interbody bone graft over time and no other qualitative evaluations are available.

As for iliac bone grafting, numerous cases of complications at its harvest sites have been reported (1–39 % of complications according to various publications) [20–23]. Accordingly, it would be preferable and beneficial to the patient to avoid harvesting of iliac bone whenever possible. In this study, a volumetric increase was observed in the iliac bone group as well as the local bone group with no significant difference recognized in volume at the final follow-up. However, the iliac bone group exhibited an earlier volumetric increase. One might argue that earlier bone union achieved by iliac bone would facilitate earlier rehabilitation and return to society as compared with the use of local bone. In addition, the local bone is of poor quality in many patients and is of limited volume, which necessitates special attention on selection of bone for grafting. Although various reports have associated smoking with pseudarthrosis [24–28], both the smoking and non-smoking groups exhibited similar volumetric increases.

The shortcomings of this study are that it dealt only with single level fusions and that no volumetric change was evaluated in pseudarthrosis cases. In this study, three cases of pseudarthrosis were excluded from our evaluation.

According to general diagnostic criteria, pseudarthrosis is identified in the absence of bone union in 2 years after the surgery. As reported by Tokuehashi et al. [1], however, there have been documented cases of bone union occurring even after 2 years. Additionally, in view of the results of this study, it is advisable to carry out follow-up over a sustained period of time after the initial 2-year period, irrespective of the age or the type of bone graft. The above suggests that determining bone union from pseudarthrosis may not be conclusive in just 2 years.

## Conclusion

The post-PLIF volumes of interbody bone grafts exhibited increases particularly from the second to fifth years after the procedure. Even the elderly and those with poor bone qualities can expect to have volumetric increases over time. Sufficient interbody space should be secured for accommodating bone grafts by intraoperative reduction, wherever possible.

**Conflict of interest** None.

## References

1. Tokuehashi Y, Matsuzaki H, Oda H, Uei H (2008) Clinical course and significance of the clear zone around the pedicle screws in the lumbar degenerative disease. *Spine* 33(8):903–908
2. Ito Z, Matsuyama Y, Sakai Y, Imagama S, Wakao N, Ando K, Hirano K, Tauchi R, Muramoto A, Matsui H, Matsumoto T, Kanemura T, Yoshida G, Ishikawa Y, Ishiguro N (2010) Bone union rate with autologous iliac bone versus local bone graft in posterior lumbar interbody fusion. *Spine* 35(21):E1101–E1105
3. rantigan JW, Steffee AD, Lewis ML et al (2000) Lumbar interbody fusion using the Brantigan I/F cage for posterior lumbar interbody fusion and the variable pedicle screw placement system: two-year results from a Food and Drug Administration investigational device exemption clinical trial. *Spine* 25:1437–1446
4. Agazzi S, Reverdin A, May D (1999) Posterior lumbar interbody fusion with cages: an independent review of 71 cases. *J Neurosurg* 91:186–192
5. Christensen FB, Hansen ES, Eiskjaer SP et al (2002) Circumferential lumbar spinal fusion with Brantigan cage versus posterolateral fusion with titanium Cotrel–Dubouset instrumentation: a prospective, randomized clinical study of 146 patients. *Spine* 27:2674–2683
6. Hashimoto T, Shigenobu K, Kanayama M et al (2002) Clinical results of single-level posterior lumbar interbody fusion using the Brantigan I/F carbon cage filled with a mixture of local morselized bone and bioactive ceramic granules. *Spine* 27:258–262
7. Su KK, Ki YT, Lee JC (2005) Radiological changes in the bone fusion site after posterior lumbar interbody fusion using carbon cages impacted with laminar bone chips: follow-up study over more than 4 years. *Spine* 30:655–660
8. Diedrich O, Perlick L, Schmitt O et al (2001) Radiographic characteristics on conventional radiographs after posterior lumbar interbody fusion: comparative study between radiotranslucent and radiopaque cages. *J Spinal Disord* 14:522–532
9. An HS, Lynch K, Toth J (1995) Prospective comparison of autograft vs. allograft for adult posterolateral lumbar spine fusion: differences among freeze-dried, frozen, and mixed grafts. *J Spinal Disord* 8:131–135
10. Le Huec JC, Lesprit E, Delavigne C et al (1997) Tri-calcium phosphate ceramics and allografts as bone substitutes for spinal fusion in idiopathic scoliosis: comparative clinical results at four years. *Acta Orthop Belg* 63:202–211
11. Frenkel SR, Moskovich R, Spivak J et al (1993) Demineralized bone matrix. Enhancement of spinal fusion. *Spine* 18:1634–1639
12. Holliger EH, Trawick RH, Boden SD et al (1996) Morphology of the lumbar intertransverse process fusion mass in the rabbit model: a comparison between two bone graft materials-rhBMP-2 and autograft. *J Spinal Disord* 9:125–128
13. Tay BK, Le AX, Heilman M et al (1998) Use of a collagen-hydroxyapatite matrix in spinal fusion. A rabbit model. *Spine* 23:2276–2281
14. Miura Y, Imagama S, Yoda M et al (2003) Is local bone viable as a source of bone graft in posterior lumbar interbody fusion? *Spine* 28:2386–2389
15. Ito Z, Imagama S, Kanemura T et al (2013) Bone union rate with autologous iliac bone versus local bone graft in posterior lumbar interbody fusion (PLIF): a multicenter study. *Eur Spine J* 22(5):1158–1163
16. Thaler M, Lechner R, Gstottner M et al (2013) The use of beta-tricalcium phosphate and bone marrow aspirate as a bone graft substitute in posterior lumbar interbody fusion. *Eur Spine J* 22(5):1173–1182
17. Kim H, Lee CK, Yeom JS et al (2012) The efficacy of porous hydroxyapatite bone chip as an extender of local bone graft in posterior lumbar interbody fusion. *Eur Spine J* 21(7):1324–1330
18. Mura PP, Costaglioli M, Piredda M et al (2011) TLIF for symptomatic disc degeneration: a retrospective study of 100 patients. *Eur Spine J* 20 Suppl 1:S57–S60
19. Nakashima H, Yukawa Y, Ito K et al (2011) Extension CT scan: its suitability for assessing fusion after posterior lumbar interbody fusion. *Eur Spine J* 20(9):1496–1502
20. Younger EM, Chapman MW (1989) Morbidity at bone graft donor sites. *J Orthop Trauma* 3:192–195
21. Keller EE, Triplett WW (1987) Iliac bone grafting: review of 160 consecutive cases. *J Oral Maxillofac Surg* 45:11–14
22. Summers BN, Eisenstein SM (1989) Donor site pain from the ilium: a complication of lumbar spine fusion. *J Bone Joint Surg Br* 71:677–680
23. Robertson PA, Wray AC (2001) Natural history of posterior iliac crest bone graft donation for spinal surgery: a prospective analysis of morbidity. *Spine* 26:1473–1476
24. Brown CW, Orme TJ, Richardson HD (1986) The rate of pseudarthrosis (surgical nonunion) in patients who are smokers and patients who are nonsmokers: a comparison study. *Spine* 11(9):942–943
25. Daftari TK, Whitesides TE Jr, Heller JG, Goodrich AC, McCarey BE, Hutton WC (1994) Nicotine on the revascularization of bone graft. An experimental study in rabbits. *Spine* 19(8):904–911
26. Silcox DH 3rd, Daftari T, Boden SD, Schimandle JH, Hutton WC, Whitesides TE Jr (1995) Effect of nicotine on spinal fusion. *Spine* 20(14):1549–1553
27. Theiss SM, Boden SD, Hair G, Titus L, Morone MA, Ugbo J (2000) The effect of nicotine on gene expression during spine fusion. *Spine* 25(20):2588–2594
28. Glassman SD, Anagnost SC, Parker A, Burke D, Johnson JR, Dimar JR (2000) The effect of cigarette smoking and smoking cessation on spinal fusion. *Spine* 25(20):2608–2615