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# Clinical Use of a New Nano-Hydroxyapatite/Polyamide66 Composite Artificial Lamina in Spinal Decompression Surgery: More Than 4 Years' Follow-Up

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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**Background:** Long-term follow-up results showed that epidural scar formation and adhesion after laminectomy always affected the outcomes of repeat operations. The establishment of a barrier between scar tissue and dura was effective in preventing epidural scar formation.

**Material/Methods:** A nano-hydroxyapatite/polyamide66 (n-HA/PA66) artificial lamina was designed and fabricated and used to cover the opened spinal canal in patients who received laminectomy. The visual analogue scale (VAS) and Japanese Orthopedic Association (JOA) Scores, X-ray, computed tomography, and magnetic resonance imaging results were periodically recorded and evaluated.

**Results:** All patients were followed up for 4–7 years, with an average period of 5.2 years. The clinical symptoms improved significantly after surgery, as the JOA scores were significantly improved after the operation and maintained to last follow-up when compared with preoperative ones ($P<0.05$). The vertebral canal became noticeably enlarged, from 16.7±4.7 mm to 32.9±2.2 mm, after surgery and well maintained to 32.1±1.8 mm. The lumbar lordosis was well maintained after surgery. No rupture, absorption, or dislodgement of the n-HA/PA66 lamina was found. MRI showed the spinal canal had the correct morphology, with no stenosis, no obvious scar formation, and no nerve roots or epidural sac compression.

**Conclusions:** The artificial lamina is a reasonable choice for prevention of epidural scar formation after laminectomy, in spite of the results from a small sample of cases.

**MeSH Keywords:** Clinical Trial • Laminectomy • Prostheses and Implants

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## Background

Total laminectomy and semi-laminectomy have been performed as routine surgical procedures for many spinal problems, especially in degenerated disc diseases. These procedures can effectively expand the vertebral canal and decompress the spinal cord. However, long-term follow-up results showed that these procedures could lead to epidural scar adhesion. Ross et al. [1] found that patients with extensive peridural fibrosis were 3.2 times more likely to experience recurrent radicular pain than those with less scarring. The epidural scar may not cause serious clinical symptoms, but it can affect the outcomes of repeat operations for recurrent herniation or stenosis, as it may lead to complications such as dural tearing, excessive bleeding, and nerve root injury. Therefore, the success rate of reoperation is low, possibly 30% to 35%, whereas 15% to 20% of patients reported worsening of symptoms [2]. Postsurgical peridural scar formation is an inevitable nonspecific inflammatory process of wound healing [3]. After laminectomy, a series of pathological processes, including fibrous connective tissue proliferation, inflammation, and granulation tissue development, occur that can cause the formation of scar tissue. Then, the inflammatory cells interact with repair cells instantly and eventually form the laminal membrane, which presses the nerve roots and causes a barrier effect to both nutrition and nerve conduction in the back of the dural sac [4]. In 1990, Songer [5] first proposed the three-dimensional fibrosis formation theory, which holds that fibrosis formation results from musculus sacrospinalis injury, with damage to the fiber layer and longitudinal ligaments. Furthermore, the fibrous tissue envelops the nerve root and worsens the problem.

To reduce and prevent the formation of epidural scars, many clinical and experimental studies have been carried out. The establishment of a barrier between scar tissue and dura is an effective way to prevent scar adhesions [6]. Both biodegradable and non-biodegradable materials have been used to fabricate the barrier; however, few results were satisfactory. To the best of our knowledge, there has been no clinical study using an artificial biomaterial lamina as a barrier for vertebral canal reconstruction after laminectomy surgeries. The aim of the present study was to develop a new biomaterial artificial lamina and to assess its long-term clinical effects in prevention of epidural scar formation after total laminectomy.

## Material and Methods

### Study design and patients

This retrospective study of patient series was designed to assess the long-term effect of an artificial lamina for prevention of peridural scar formation after laminectomy. From January 2003 to December 2005, 20 patients underwent n-HA/PA66 artificial lamina implantation after laminectomy of lumbar spine at the same department. All the surgery was done by the same senior surgeon. The clinical data of the patients were collected and analyzed anonymously to verify the preventive effect of the n-HA/PA66 artificial lamina on peridural scar formation.

This study was approved by the Institutional Review Board of the First Affiliated Hospital of Chongqing Medical University, and all aspects of the study complied with the Declaration of Helsinki. All patients signed an informed consent form before entry into the trial. Patients with tumor or infection, metabolic diseases, and those who had undergone prior laminectomy were excluded. Patients who were lost to follow-up were also excluded from the study.

### Preparation of the n-HA/PA66 composite artificial lamina

An n-HA/PA66 artificial lamina was designed and manufactured jointly by our department and the Sichuan Guona Corporation of Science and Technology and was approved for clinical use in 2005 by the State Drug and Food Administration of China. The n-HA/PA66 composite was developed with a bioactive ceramic, n-HA, and an organic polymer, PA, to mimic natural bone. The n-HA/PA66 material was molded into the hump shape of the lumber spinal lamina. Eight different scales were designed with 20–35 mm width, 10.6–12.4 mm height, and 4 mm thickness. The appearance of the n-HA/PA66 artificial lamina is shown in Figure 1.

### Surgical procedure

The operation was performed with the patient in the prone position under general anesthesia. A midline skin incision was made to expose the spinous processes, lamina, facets, and transverse processes at the involved levels. The pedicle screws were implanted by free-hand method under C-arm radiography confirmation. Total laminectomy was performed for decompressing the nerve elements. Discectomy was performed and the autograft and cage were implanted for interbody fusion. Then, an n-HA/PA66 artificial lamina of appropriate size was used to cover the opened spinal canal, and titanium rods were placed to fix the artificial lamina. If the artificial lamina was not stable enough, an extra suturing fixation was performed. Excised cancellous bone granules were grafted on the edge of both sides of the artificial lamia for bony fusion. After flushing the operation field, the incision was closed after placing a drainage tube. The drainage tube was removed after 24~48 h, and 14 days later we removed the sutures. After 3 days, patients gradually began to move about protected by a rigid lumbar brace.





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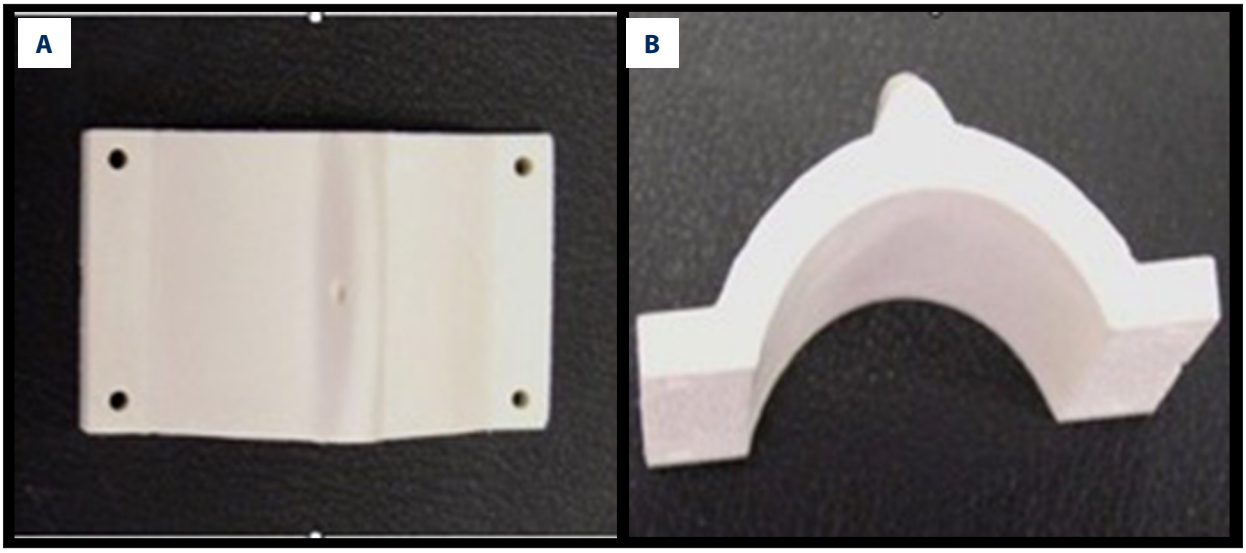


**Figure 1.** The appearance of artificial vertebral lamina of n-HA/PA66 composites (front view and profile view).

### Outcome assessments

Patients were followed up at postoperative months 3, 6, and 12 and then every year thereafter. X-ray films and computed tomography (CT) or magnetic resonance imaging (MRI) were performed for each patient periodically. The clinical outcomes were assessed by Japanese Orthopaedic Association (JOA) scores for the lumbar spine, which included subjective symptoms, clinical signs, restricted daily activities, and bladder function. X-rays and CT were used to evaluate the spine alignment, location of artificial lamina, spinal canal morphology, and bone bonding between the artificial material and natural bone. The lumbar lordosis was defined as the Cobb angle between the superior endplate of 12$^{th}$ thoracic vertebra and sacrum and measured on X-ray film. The size of the vertebral canal was defined as the distance between the posterior margin of the vertebral body to the root of spinal process and measured on axial CT through the section crossing both sides of the pedicle. MRI was used to assess adhesion and repression of scar tissue on the dura and the nerve root. The adhesion and repression were defined as the high signal of CSF disappeared and lower signal of scar intruded into the posterior spinal canal on MRI.

### Statistical analyses

The Statistical Package for the Social Sciences version 17.0 (SPSS, Chicago, IL, USA) was used to analyze all statistical data. Data were recorded as means and standard deviations and checked for Gaussian distribution using the Kolmogorov-Smirnov test. According to the data distribution, the independent-samples *t* test or one-way analysis of variance was used to evaluate the difference between the preoperative and postoperative after comparison. Statistical significance was determined at *p* value less than 0.5.

**Table 1.** Demographic data of patients.

| Factors | Value |
|---|---|
| Male/Female | 10/7 |
| Age of years (mean) | 41–73 (57.9) |
| Clinical presentation | |
| Lumbar spondylosis | 6 |
| Lumbar herniation combined stenosis | 9 |
| Lumbar fracture | 2 |
| Laminectomy segments | |
| L2 | 1 |
| L3 | 3 |
| L4 | 5 |
| L5 | 3 |
| L4 and L5 | 5 |
| Surgery duration in minutes (mean) | 185.6 |
| Blood loss in milliliter (mean) | 301.2 |
| Admitted days (mean) | 15.5 |

## Results

This retrospective study followed 17consecutively enrolled patients, as 3 patients who were lost to or refused the last follow-up were excluded. Among the 17 patients, there were 10 males and 7 females, aged 41~73 years, with a mean age of 57.9 years. All patients chiefly complained of a long history of low back pain with radiating leg pain: lumbar spondylosis with spinal canal stenosis in 6 cases, lumbar disc herniation with





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**Table 2.** Clinical outcome and radiologic data (n=17, $\bar{\chi}$±s).

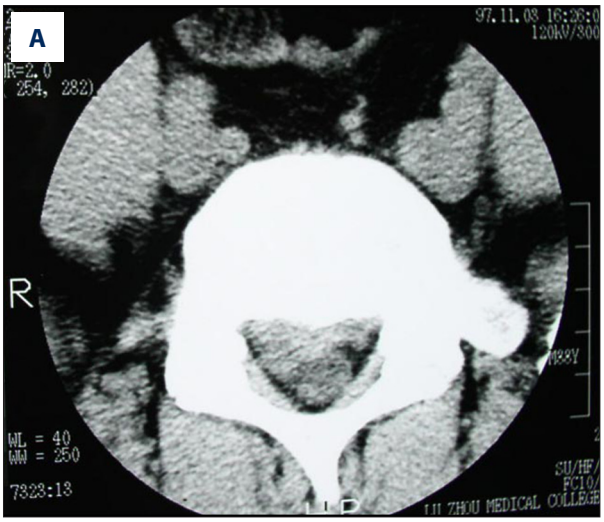
| Factors | Preoperative | Postoperative | Last follow-up |
|---|---|---|---|
| VAS | 5.9±1.4 | 2.4±0.7* | 1.8±0.7# |
| JOA | 16.7±2.7 | 25.8±1.6* | 27.5±1.3# |
| VCD | 16.7±4.7 | 32.9±2.2* | 32.1±1.8# |
| LL(–) | 43.4±4.8 | 44.7±4.6* | 44.8±4.2# |

VAS – visual analogue scale; JOA – Japanese Orthopedic Association; VCD – vertebral canal diameter; LL – lumber lordosis. * Compare to preoperative, p<0.05; # compare to postoperative, p>0.05.

spinal canal stenosis in 9 cases, and lumbar vertebral fracture with spinal canal stenosis in 2 cases. All patients had undergone total laminectomy and the opened spinal canal was covered and reconstructed with the n-HA/PA66 artificial lamia, including 1-segment spinal canal reconstruction in 12 patients and 2-segment reconstruction in 5 patients. The duration of surgery was 145–285 min, with a mean of 185.6 min. The average blood loss was 301.2 ml, and ranged from 220 to 470 ml. No postoperative neurological complication or incision infection was noted (Table 1).

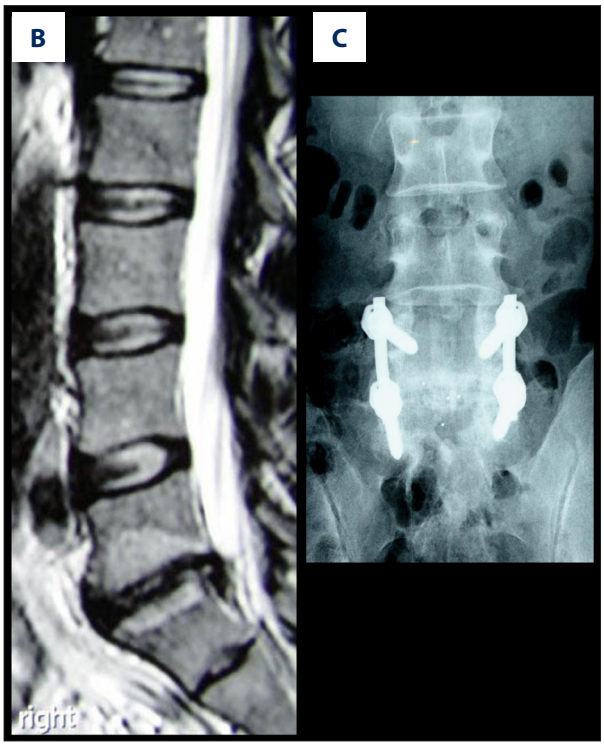
All patients were followed up for 4–7 years, with an average of 5.2 years. Their clinical outcomes were evaluated by JOA scores, as shown in Table 2. The difference between the preoperative and postoperative JOA scores in subjective symptoms, physical signs, daily activity restriction, and bladder function was statistically significant. At the last follow-up, the JOA scores improved and were significantly higher than the preoperative ones. These results show that clinical symptoms improved significantly after surgery.

Radiologically, the mean preoperative lumbar lordosis was 43.4±4.8 mm compared with a mean postoperative lordosis of 44.7±4.6 mm, and the difference was not statistically significant.




At the last follow-up, the lumbar lordosis was well-maintained to 44.8±4.2 mm. The vertebral canal was clearly enlarged after surgery, with a sagittal diameter of 16.7±4.7 mm before the operation and 32.9±2.2 mm after the operation, and was well-maintained at 32.1±1.8 mm at the last follow-up.

At the time of last follow-up, the internal fixation was in good position upon X-ray examination, without screw loosening or breakage. The three-dimensional CT scan showed the artificial vertebral lamina completely covered the posterior part of vertebral canal, with a bony contact with the recipient bone, without any shape change or rejection reaction. We found no rupture, absorption, or dislodgement of the n-HA/PA66 lamina. MRI showed the spinal canal had correct morphology, with no stenosis, no obvious scar formation, and no nerve root or dural sac compression. The pictures of a typical case are shown in Figure 2.





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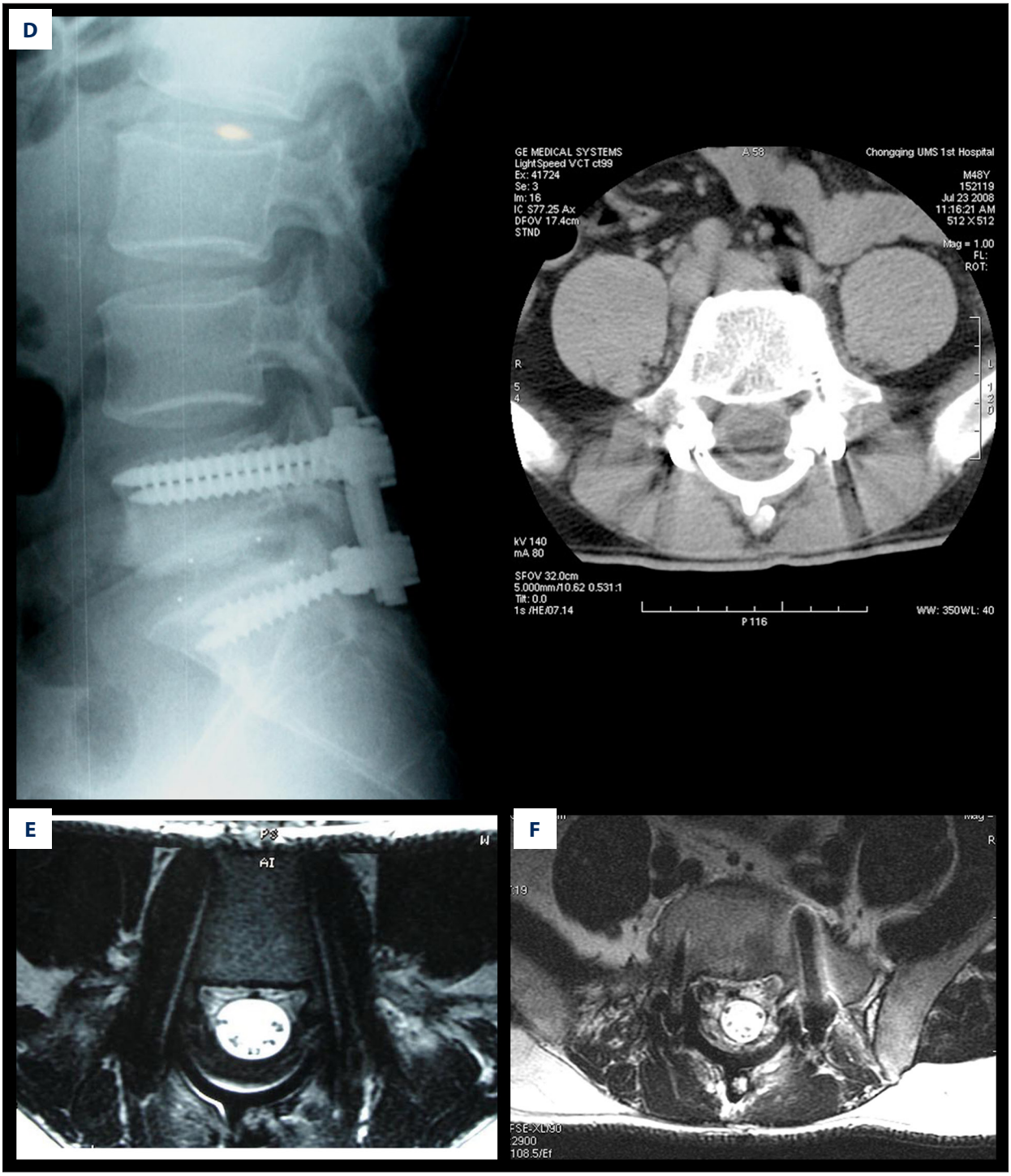


**Figure 2.** (**A, B**) The CT and MRI of pre-op showed the lumbar disc herniation compressing the nerve root on right side. (**C, D**) The postoperative X-ray films showed the internal fixation was in good position with a good spinal alignment. (**E**) The postoperative CT and MRI of post-op showed the lumbar vertebral canal had good morphology and was covered by the n-HA/PA66 artificial lamina. (**F, G**) The postoperative axial MRI of post-op and follow-up at 5 years showed no epidural scar formation and no compression of the nerve root.





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## Discussion

LaRocca [4] first proposed the laminectomy membrane theory of epidural scar formation, in which the scar grows into the vertebral canal as the repair of the injured musculus sacrospinalis. Songer [7] proposed the three-dimensional theory, as they considered that the musculus sacrospinalis damage, fiber ring, and longitudinal ligament injury were the common sources of epidural scar formation. Nakano [8] found that damage to the nerve-blood barrier caused changes in vascular permeability, which was the most important cause of cauda equina adhesion. They proposed that the trauma caused by lamina excision induces the tight junction between endothelial cells to become loose, which increases vascular permeability in cauda equina nerve roots through a series of pathological changes, causing nerve adhesion.

According to the theory, establishment of a barrier between posterior injured tissues and the dura is an effective way to prevent scar formation and adhesion. Many materials have been employed as mechanical barriers between the dura and the scar tissue in an attempt to prevent or limit scar tissue formation, such as gelatin sponge, biophysical barriers, autogenous soft tissue, or bone grafts, but the clinical effect was not very promising [9,10]. Many artificial laminae fabricated from biomaterial have been tested in animal studies, with promising results [11,12]. Until now, however, no study has documented the results of a biomaterial artificial lamina in clinical use. The aim of this study, therefore, was to develop a new biomaterial artificial lamina and assess its long-term clinical effect for prevention of epidural scar formation after total laminectomy. According to our study, the n-HA/PA66 lamina effectively prevented the epidural scar formation and maintained the morphology of the vertebral canal as a barrier between the musculus sacrospinalis and dura. The effect persisted to the last follow-up, as the n-HA/PA66 composite lamina is not absorbable and could be a barrier lasting for the rest of the patient's life.

The n-HA/PA66 composite is a bioactive material made of nano-hydroxyapatite (n-HA) and polyamide (PA), made possible by the unique structure of nano-apatite crystals and collagen matrix in natural bone. The mechanical test demonstrated the composite possessed similar mechanical properties to the cortical bone, in particular, compression and bending strength and elastic modulus [13]. The n-HA/PA66 composite exhibited excellent biocompatibility and osteogenesis *in vivo* [14]. The n-HA/PA66 composite strut has successfully been used for reconstruction and fusion of the cervical spine after cervical corpectomy in patients with cervical myelopathy [15–17].

In our patient series, all of the bony vertebral canal was completely reconstructed and maintained even after several years from the CT scanning. The dural sac was fully expanded without any nerve root compression or epidural scar formation, as assessed with MR imaging. These results show that the artificial lamina acted as an effective barrier to prevent epidural scar formation. Although n-HA/PA66 is a bioactive material [14], the bony union between the host bone and the artificial lamina was not detected. We assumed that the smaller area of contact surface and cortex-cortex contact between the host bone and artificial lamina discouraged bone ingrowth. However, the pedicle screws and rods held the artificial lamina in the right position and never failed unless there was loosening of the internal fixation. It is encouraging that no displacement or dislodgment of the artificial lamina occurred and intervertebral fusion was achieved in all patients.

## Conclusions

The study has many limitations in spite of its favorable results. Firstly, this was a retrospective study of a small sample of cases, and a large-scale prospective study is needed. Secondly, there were no control cases in the series, as we cannot advocate the n-HA/PA66 lamina is better than other materials. However, the results of our study are still encouraging, showing that the artificial lamina is a promising method for vertebral canal reconstruction to prevent epidural scar formation.

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**Conflict of interest**

None.





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