

PEEK-OPTIMA™ HA Enhanced: The Latest Material Development for Interbody Fusion

Ovine Cervical Fusion Study Finds Performance Advantages
with PEEK-OPTIMA HA Enhanced Polymer.¹

Introduction

For more than a decade, PEEK-OPTIMA™ Natural, the first medical grade unfilled PEEK from Invibio Biomaterial Solutions™, has been utilized in spinal fusion surgeries, predominantly in the form of load-bearing cages. Today, PEEK is the most popular biomaterial for interbody fusion, accounting for 69% of devices in 2013.² Clinical studies continue to suggest that PEEK-OPTIMA performs as well as, or better than, equivalent interbody fusion devices made of metals or bone, while providing some distinct clinical advantages over competing biomaterials, including high fusion rate, lower incidence of subsidence and lack of donor site morbidity.³⁻⁵

The introduction of PEEK-OPTIMA™ HA Enhanced heralds the next evolutionary step in the development of high performance materials for interbody fusion devices. The properties that have made PEEK-OPTIMA Natural one of the leading interbody fusion biomaterials for over 15 years; modulus similar to cortical bone, radiolucency, biocompatibility and processing adaptability, are maintained with PEEK-OPTIMA HA Enhanced.

Hydroxyapatite (HA) is the main inorganic constituent of bone. The synthetic form of HA in PEEK-OPTIMA HA Enhanced has a chemical and crystal structure similar to that found in bone, and is fully incorporated into the PEEK-OPTIMA matrix, making it available on all surfaces of a finished device. Over the years, the osteoconductive properties of HA and its ability to promote bidirectional bone healing have been demonstrated experimentally as well as in clinical studies.⁶⁻⁹ Both naturally occurring and synthetic forms of HA have been successfully applied as a bone void filler and as a coating for orthopedic and dental implants to ensure fixation, without obvious material-related bio-incompatibility reactions.¹⁰⁻¹⁴

Invibio has previously demonstrated that PEEK-OPTIMA HA Enhanced leads to increased bone apposition (approximately 75% direct bone contact) compared with PEEK-OPTIMA Natural in a bone defect sheep model, as early as 4 weeks following implantation.¹⁵ Using fluorochrome labels, the study also demonstrated that bone was deposited at the surface of PEEK-OPTIMA HA Enhanced as early as 10 days following implantation.

Now, Invibio has commissioned an independent study to compare outcomes between interbody fusion devices composed of PEEK-OPTIMA HA Enhanced, PEEK-OPTIMA Natural and allograft bone. Results from this ovine cervical fusion study, carried out at the Surgical & Orthopaedic Research Laboratories (SORL) at the University of New South Wales (UNSW) under the direction of Professor Bill Walsh, indicate that PEEK-OPTIMA HA Enhanced may provide advantages in mechanical performance, new bone formation and quality of new bone bridging.

Methods

Under a UNSW Animal Care and Ethics Committee approved study protocol, 25 fully mature female sheep (*Ovis Aries*) underwent surgery at two non-adjacent cervical spinal levels (C2-C3 and C4-C5). Sheep were randomly assigned to 3 test groups: PEEK-OPTIMA HA Enhanced v. Allograft, PEEK-OPTIMA Natural v. Allograft, or PEEK-OPTIMA HA Enhanced v. PEEK-OPTIMA Natural. Eighteen of the animals were used in the in vivo portion of the study (6 animals each at 6*, 12 and 26 weeks). The remaining 6 animals were used for time zero biomechanical testing and as a source of ovine bone to prepare implants for the allograft group.

Implants and Allograft Preparation

All implants were of identical design, with outer dimensions of 14 x 11 x 7mm and a central graft cavity. Both PEEK-OPTIMA Natural and PEEK-OPTIMA HA Enhanced devices were steam sterilized by SORL prior to surgery.

Cortical allograft implants were prepared by SORL from the harvested metatarsals of the animals used for time zero biomechanical testing. Cortical allografts were cut into spacers with dimensions approximate to the PEEK devices. The devices were washed in 70% ethanol prior to air drying, gamma irradiated (25 kGy) on dry ice, and then stored frozen prior to implantation. Allograft implants were radiographed prior to use to confirm that no cracks or damage had occurred during preparation.

Surgical Procedure

Anterior cervical discectomies were performed and the disc spaces were prepared using a high-speed burr to decorticate the endplates of the operative level, allowing for as complete and intimate contact of the interbody device with bone as possible. Locally harvested bone was saturated with autogenous bone marrow aspirate (BMA) and used to fill the central cavity of the interbody fusion devices (Figure 1). The prepared devices were inserted and supplemental anterior plate fixation was applied. Post-operative radiographs were taken in the lateral plane to confirm implant placement. Fluorochrome bone labels were administered at intervals during the 6, 12 and 26 week implantation periods to provide a dynamic view of new bone formation over time at the treated levels.

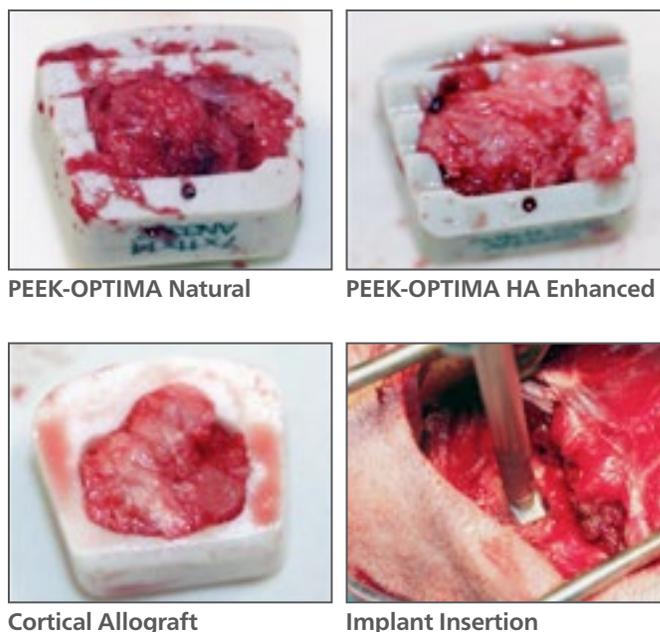


Figure 1. Cervical spacers used in the study (all filled with local autograft bone), and implantation of a PEEK-OPTIMA HA Enhanced interbody fusion device.

* An additional animal was added to the 6 week group (PEEK-OPTIMA Natural v. Allograft)

Methods

Radiographs

Radiographs were obtained at the time of sacrifice at 6, 12 and 26 weeks in the anteroposterior and lateral planes in order to assess device integrity and the progression of spinal fusion. Faxitron radiographs were also taken following harvest of the spines and graded in a blinded fashion on a scale of 0-3 for new bone formation (0 = none detected, and 3 = extensive, multiple, coalescing foci) and quality of new bone bridging (0 = no bridging by new bone, and 3 = extensive bridging in > 70% of the vertebral body interface).

Micro computed tomography (μ CT)

Micro Computed tomography (μ CT) was performed on the operated levels using an Inveon Scanner (Siemens, USA). Three dimensional models were reconstructed and examined in the axial, sagittal, and coronal planes. Fusion was graded in a similar manner to the radiographs and were further assessed and graded for amount of direct bone-implant contact on a scale of 0-3 (0 = no contact by new bone, 3 = extensive contact at > 70% of the interface).

Biomechanical Testing

In vitro phase

Cervical spine segments (C2-C5) were harvested from 6 animals and pure moments were applied to the entire construct in flexion-extension, lateral bending, and axial rotation for the intact spine and after placement of the device and plate. Motion segments for C2-3 and C4-5 were monitored during testing to determine relative displacement of each of the levels, providing time zero control data prior to fusion.

In vivo phase (6 and 12 weeks only)

Immediately following explant and radiographic evaluation, cervical spine segments (C2-C5) were harvested and biomechanically tested to determine relative displacement of each of the fused and unfused segments. All tests were performed with the instrumentation in place. Flexion-extension, lateral bending, and axial rotation values were reported for each animal and compared to non-operated controls.

Mechanical testing was not performed at the 26 week time point due to concern that testing displaced the devices and potentially compromised the histology at the device-implant interface.

Histology and Histological Assessment

All samples were fixed in phosphate buffered formalin, embedded in PMMA and stained using methylene blue and basic fuchsin. Sections were evaluated for fibrotic tissue response (0 = no fibrotic tissue at the vertebral body interface, 3 = fibrotic tissue at > 70% of the vertebral body interface) and inflammatory response (0 = no response, 3 = severe response). The histology was also evaluated with respect to new bone formation, quality of new bone bridging and direct bone-implant contact in the same grading manner as for the radiographs and μ CT. Finally, residual graft in the graft space was graded from 0-3 (0 = none detected, 3 = extensive multiple foci remaining).

The local effects of implantation of PEEK-OPTIMA Natural and PEEK-OPTIMA HA Enhanced devices were evaluated at 12 and 26 weeks following the principles of ISO 10993-6:2007 (Biological evaluation of medical devices – Part 6: Tests for local effects after implantation).

Results

The biocompatibility of PEEK-OPTIMA HA Enhanced was supported in this large animal cervical fusion study following histological evaluation according to the principles of ISO 10993 Part 6. Neither implant material elicited a notable inflammatory response, and the devices were well tolerated. Both PEEK-OPTIMA Natural and PEEK-OPTIMA HA Enhanced devices remained structurally intact throughout the implantation periods and no failures were observed. In contrast, there was significant osteoclast-mediated resorption of the allograft implants, and fracture of the devices was evident, as early as the 6 week time point (Figure 2). In total 6/13 (46%) allograft implants fractured during the implantation period.

Biomechanically, range of motion (flexion-extension, lateral bending, and axial rotation) was progressively reduced at each successive time point for all groups, indicating fusion progression, although no biomechanical differences were noted between the groups.

Both new bone formation and the quality of new bone bridging improved over time in the PEEK-OPTIMA Natural and PEEK-OPTIMA HA Enhanced groups based on grading of Faxitron radiographs, but no significant difference between the groups was noted. Micro CT analysis provided a more detailed evaluation of the operated levels and allowed differentiation between the materials. Figure 3 provides an overview of the fusion progression over time for the different devices and highlights the significant resorption of the allograft implants.

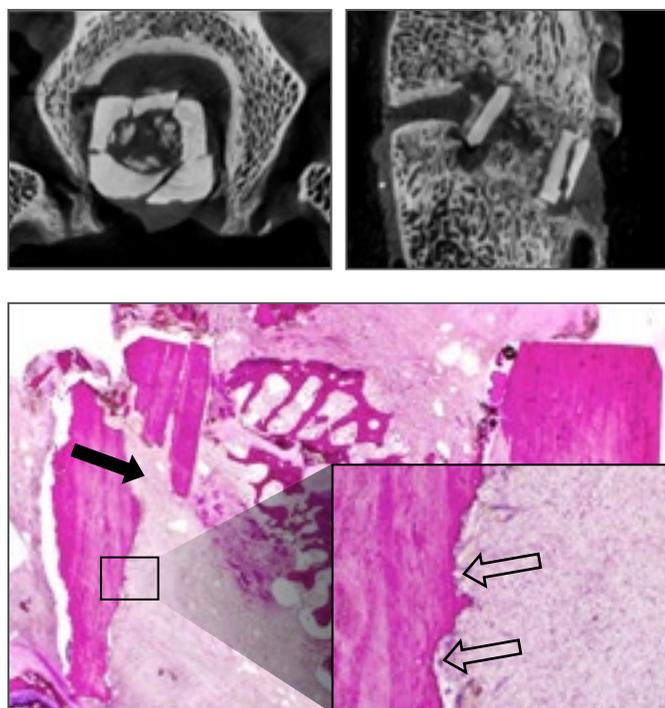


Figure 2
 TOP: Micro CT analysis reveals fracture of an allograft device in the 6 week implantation group.
 BOTTOM: Fracture of an allograft device in the 6 week group is evident (arrow), together with an uneven surface formed by osteoclast activity (inset open arrows).

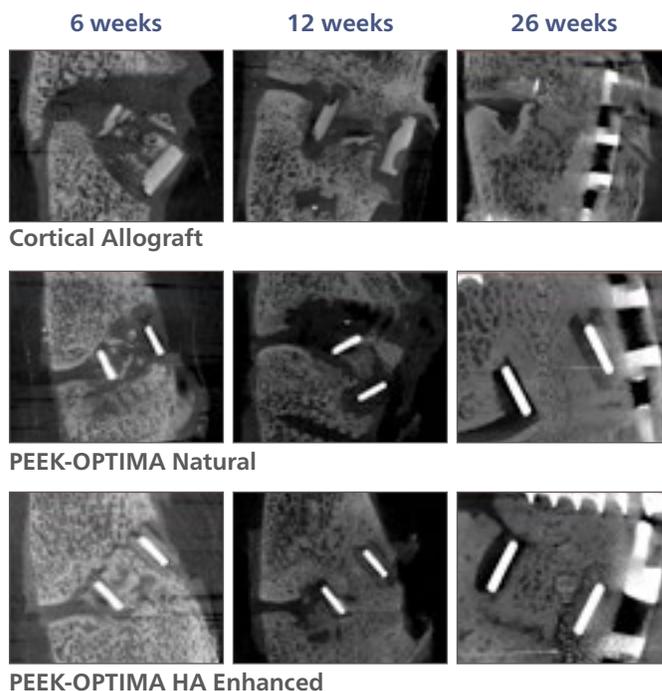


Figure 3. A micro CT comparison between allograft, PEEK-OPTIMA Natural and PEEK-OPTIMA HA Enhanced demonstrates the status of the graft material inside the devices versus time.

Results (cont.)

At the 6 week time point, μ CT analysis demonstrated that new bone formation was greater with the PEEK-OPTIMA HA Enhanced devices compared with PEEK-OPTIMA Natural, although no statistical significance could be reached due to the small sample size (Figure 4). The allograft devices were biologically active at 6 weeks, showing a high degree of new bone formation and incorporation into the surrounding bone. This was countered however, by the high degree of resorption and mechanical instability leading to fracture, as discussed previously. The quality of new bone bridging also appeared to be superior in the PEEK-OPTIMA HA Enhanced group compared with PEEK-OPTIMA Natural, at both the 6 and 12 week time points (Figure 5).

Quality of New Bone Bridging

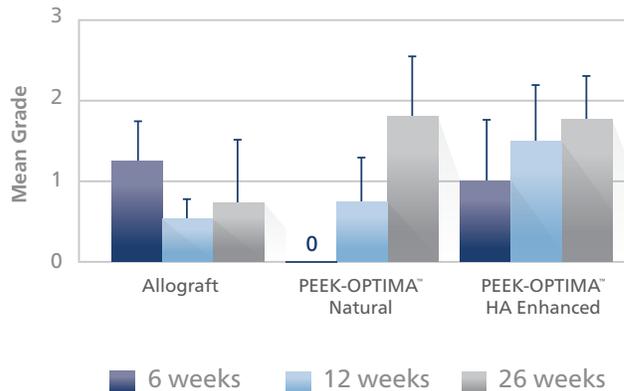


Figure 5. Micro CT analysis of the quality of new bone formation bridging in the fusion, as well as the device surfaces.

New Bone Formation

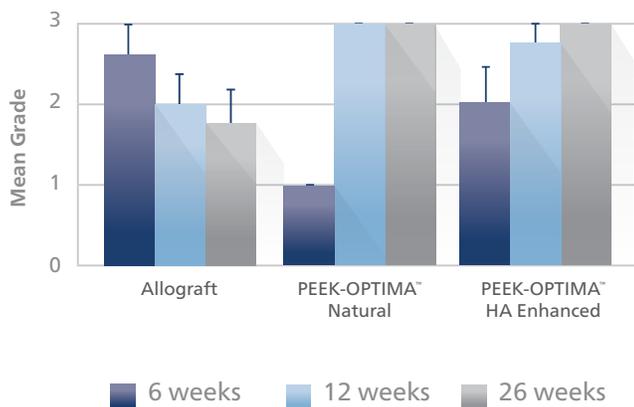


Figure 4. Micro CT analysis of new bone formation in the fusion as well as the device surface.

Results (cont.)

Finally, there was a trend towards greater direct bone contact with the PEEK-OPTIMA HA Enhanced devices compared with PEEK-OPTIMA Natural, and this was more evident at the early time points (Figure 6). Where the interbody implant was opposed to remnant intervertebral disc material, there was limited fibrous response, but no evidence of bone growth. Further, it was not possible to discern clear differences between PEEK-OPTIMA Natural and PEEK-OPTIMA HA Enhanced in terms of bone-implant contact, specifically at the endplates.

Histologically, the local bone inside the PEEK-OPTIMA HA Enhanced devices appeared to be more robust at 6 and 12 weeks compared to the local bone inside the PEEK-OPTIMA Natural devices at the same time points. These differences were less evident at 26 weeks, but remained suggestive of a superior result for graft in the PEEK-OPTIMA HA Enhanced devices compared to PEEK-OPTIMA Natural (Figure 7).

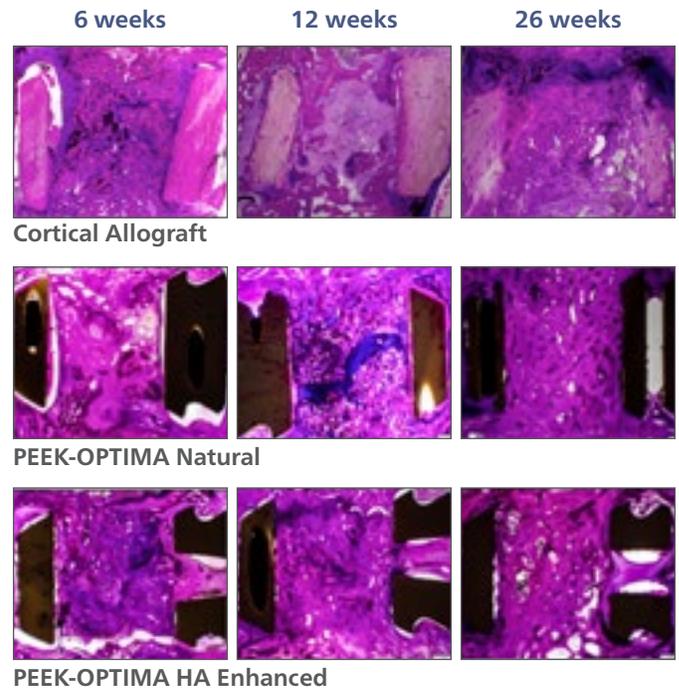


Figure 7. Histological comparison between allograft, PEEK-OPTIMA Natural and PEEK-OPTIMA HA Enhanced demonstrates the status of the graft material inside the devices over time.

Bone-Implant Contact

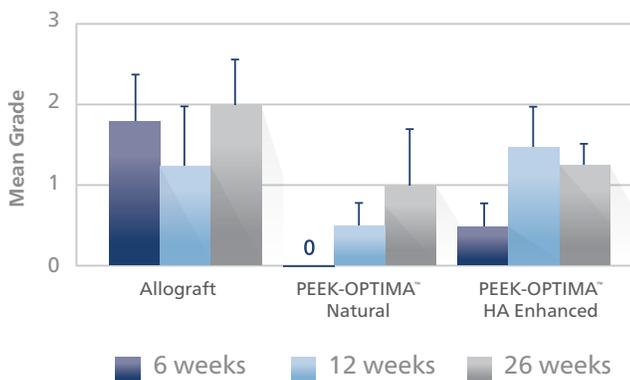


Figure 6. Micro CT analysis of direct bone-implant contact.

Discussion

Histological comparison between allograft, PEEK-OPTIMA Natural and PEEK-OPTIMA HA Enhanced demonstrates the status of the graft material inside the devices over time. This cervical interbody fusion model represents a complex and challenging setting for the evaluation of new materials. The previous long bone study commissioned by Invibio was the first step in demonstrating the potential of PEEK-OPTIMA HA Enhanced in enhancing bone ongrowth, and providing a more favourable local environment for bone compared with PEEK-OPTIMA Natural.¹⁵ The long bone model is different in that there is no movement between the bone and the implant surface, and the implants are not under load. In contrast, the cervical fusion model is a more demanding and dynamic environment, with implants under load and motion between the vertebral bodies and the device endplates. The current study builds on the findings of the long bone model, in which enhanced bone ongrowth was demonstrated, and supports the

notion that PEEK-OPTIMA HA Enhanced provides a more favourable environment than PEEK-OPTIMA Natural or allograft bone in a cervical fusion setting, providing an osteoconductive surface throughout the device for:

- ▶ **Superior mechanical performance**

PEEK-OPTIMA HA Enhanced devices outperformed allograft, with fracture of allograft devices in 6/13 (46%) instances.

- ▶ **Greater new bone formation**

PEEK-OPTIMA HA Enhanced resulted in greater new bone formation at 6 weeks compared with PEEK-OPTIMA Natural.

- ▶ **Higher quality of new bone bridging**

PEEK-OPTIMA HA Enhanced resulted in a higher quality of new bone bridging at 6 and 12 weeks compared with PEEK-OPTIMA Natural.

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