PEEK-OPTIMA® Ultra-Reinforced Polymer: A New Solution for Fracture Fixation

In vivo Healing Study & Biocompatibility Data
Introduction

PEEK-OPTIMA® Ultra-Reinforced*, from Invibio Biomaterial Solutions, is a continuous carbon fiber-reinforced composite material manufactured from PEEK-OPTIMA polymer that demonstrates high strength and stiffness properties. PEEK-OPTIMA Ultra-Reinforced is generating interest among surgeons as an alternative biomaterial to titanium and stainless steel metals for medical device applications such as trauma plates and nails as it has a modulus of elasticity closer to cortical bone.¹ Combined with its mechanical properties the material also offers advantages in terms of increased visibility of the fracture site during surgery and throughout the healing process, higher fatigue life² increasing the window of opportunity for healing and low weight. As the material can provide a metal free solution it reduces concerns around cold welding, metal sensitivity and shielding of tissue during oncologic treatment.

Carbon fiber reinforced PEEK-OPTIMA has been successfully used clinically in orthopaedic applications for more than 10 years and its biocompatibility is well established.²⁻⁹ PEEK-OPTIMA Ultra-Reinforced has been used clinically within CE marked devices and FDA approved medical implants since 2005.¹⁰

In support of this we have assessed the potential biological response to the material and also the efficacy of the resulting implants. This paper focuses on these aspects providing a glimpse into the data Invibio have gathered in collaboration with AccelLab (Boisbriand, Quebec) to support the efficacy of PEEK-OPTIMA Ultra-Reinforced implants¹ and also the assessment of its biocompatibility in alignment with the requirements of ISO10993.

Figure 1. PEEK-OPTIMA Ultra-Reinforced continuous fiber composite manufactured from PEEK-OPTIMA polymer and PAN based carbon fiber.

* Previously known as ENDOLIGN®
The aim of this study was to assess the efficacy of a PEEK-OPTIMA Ultra-Reinforced intramedullary nail in an osteotomy model. The model was based on that used by Bottlang et al.\(^1\) to demonstrate the benefits of far cortical locking technology and involved a 3 mm osteotomy gap with immediate weight bearing following fixation. Stainless steel nails were used as the control. Twelve animals were used within the study with two early losses to follow-up (one from each test group) due to reasons unrelated to the implants.

Animals were monitored over a 12 week time period and the healing of the fracture was assessed by CT and X-ray at 2, 4, 6, 9 and 12 weeks with a focus on evaluating callus formation and bridging of the osteotomy site.

The callus formation was evaluated and quantified using radiograph and indicated a trend towards greater callus formation within the PEEK-OPTIMA Ultra-Reinforced group. This trend was observed throughout the study period, but there was a more pronounced effect at the earlier time points. Callus formation was shown to be 158\% of that in the control article at 2 weeks, 67\% at 4, 33\% at 9 weeks and 24\% at 12 weeks these differences were not shown to be statistically significant, with \( p \) values of 0.09, 0.08, 0.10, 0.20, respectively. Representative images depicting the callus formation observed at weeks 4 and 12 in an animal implanted with PEEK-OPTIMA Ultra-Reinforced are shown in figure 2.

Further to the increased callus formation at the earlier time points, an improvement in bridging of the osteotomy site was observed at the 12 week time period, with bridging being observed on radiographs of 100\% of animals (5 of 5) implanted with the PEEK-OPTIMA Ultra-Reinforced constructs in contrast to only 60\% within the stainless steel group (3 of 5).

Figure 2. Callus formation observed by radiograph for animal D84-10 implanted with a PEEK-OPTIMA Ultra-Reinforced nail at week 4 (left) and week 12 (right).
ISO 10993-6: Bone Implantation Study\textsuperscript{12}

The purpose of the study was to evaluate the local effects of PEEK-OPTIMA Ultra-Reinforced when implanted in the femoral bone of rabbits after 26 weeks. The lateral mid-shaft femurs of five male New Zealand rabbits were exposed and three unicortical circular defects were created in each femur. The defect holes were spaced at least 1 cm apart from one another. Test implants composed of PEEK-OPTIMA Ultra-Reinforced were implanted into the three defects in the right femur of each rabbit. Control implants composed of high density polyethylene were implanted into the defects in the left femur of these same rabbits. At 26 weeks, the animals were sacrificed and the responses to the PEEK-OPTIMA Ultra-Reinforced implant compared to the control implant. The femurs implanted with the PEEK-OPTIMA Ultra-Reinforced implants (figure 3) showed no adverse local effects or tissue irritation compared to the control (figure 4).

Figure 3. Images showing tissue response to PEEK-OPTIMA Ultra-Reinforced implants (test articles) 26 weeks after implantation.

Figure 4. Images showing tissue response to high density polyethylene implants (control articles) 26 weeks after implantation.
Further Biocompatibility Testing

**Muscle Implantation Study**
A sample of PEEK-OPTIMA Ultra-Reinforced composite rod was implanted into rabbit muscle tissue and the surrounding tissue was evaluated after 7 days. In this study, there was no evidence of any significant macroscopic reactions when compared with the polyethylene negative control.

**ISO 10993-5: Cytotoxicity**
The PEEK-OPTIMA Ultra-Reinforced sample was extracted in a 1.5% dimethyl sulfoxide (DMSO) solution in complete cell culture medium (DMEM-FBS) at 37°C +/-2°C for 7 days. The 1.5% DMSO solution was incubated for 7 days under the same conditions as a negative control and dimercaptosuccinic acid (DMSA) was used as a positive control. As expected, the sample was non-cytotoxic.

**USP Intracutaneous Toxicity**
Samples of PEEK-OPTIMA Ultra-Reinforced composite rod were extracted in 0.9% sodium chloride solution, alcohol in saline, polyethylene glycol and sesame oil. These extracts were evaluated, and under the conditions of the study, there was no evidence of irritation or toxicity.

**ISO 10993-10: Maximum Sensitization**
A test article of PEEK-OPTIMA Ultra-Reinforced composite rod was extracted in 0.9% sodium chloride solution and in sesame oil, and the extracts were evaluated for induced sensitization. Under the conditions of the study, there was no evidence of delayed sensitization.

**ISO 10993-11: Systemic Toxicity**
A sample of the PEEK-OPTIMA Ultra-Reinforced composite rod was extracted in 0.9% sodium chloride solution, alcohol in saline, polyethylene glycol and sesame oil, and the extracts were evaluated for systemic toxicity according to the ISO guidelines. There was no evidence of systemic toxicity from the extracts evaluated.

**ISO 10993-12, ISO 10993-18: Characterization of Organic Leachables**
Extraction was carried out in a 5% Ethanol/water mixture for 7 days at 37°C, and in tert-butyl methyl ether for 24 hours at 37°C. The organic substances released were characterized by GC-MS and quantified by GC-FID. In both solvents the amount of organic substances released was below the limit of detection of the instruments of 1μg/cm².
Conclusions

PEEK-OPTIMA Ultra-Reinforced is a continuous carbon fiber-reinforced composite manufactured from PEEK-OPTIMA polymer and PAN-based carbon fiber which can be used to produce implants to support osteosynthesis in the form of fracture fixation plates (as depicted in figure 5) and intramedullary nails.

An in vivo ovine tibial osteotomy study has been carried out and it has shown the efficacy of the product in supporting fracture healing. The biocompatibility of the material has been established in accordance with ISO 10993.

Figure 5: Distal femoral plate composed of PEEK-OPTIMA Ultra-Reinforced.
References

1. Data on file at Invibio.
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