

PRE-CLINICAL BIOCOMPATIBILITY TESTING OF THE M6 ARTIFICIAL DISC

Introduction

Arthroplasty is an alternative to fusion for the treatment of symptomatic disc disease that provides the ability to preserve motion. The Spinal Kinetics M6[®]-C and M6[®]-L are advanced generation artificial cervical and lumbar intervertebral discs designed to replicate the anatomic structure and biomechanical performance of the natural disc. The novel design of the M6 allows for a controlled range of motion in all 6 degrees of freedom and incorporates a viscoelastic polymer core which serves as an artificial nucleus, UHMWPE fibers which serve as an artificial annulus and titanium endplates. The biocompatibility of any motion-preserving implant must be addressed. All materials used in the M6-C and M6-L have an extensive history of use in medical device implants and have a proven track record of biocompatibility. Three studies were performed to confirm the biocompatibility of the M6 over the projected life of the implant. A caprine implant study was performed to assess biological response as well as the potential for wear debris generation. A rabbit debris study was performed to assess biologic response to a worst case debris mass. All materials were also subjected to a full battery of biocompatibility testing.

Methods

Caprine model:

Device implantations were conducted in a caprine model to evaluate the local and systemic responses to any particulate debris generated by the implant (Figure 1).

- 20 devices implanted in the cervical spines of 14 goats
- 3, 6, and 12 month time points
- **Gross Evaluation:** At sacrifice, gross evaluations of major organ systems, spleen, liver, peri-prosthetic tissues, regional draining lymph nodes, and the functional spinal unit (FSU) containing the implant and spinal cord were performed
- **Histologic samples:** Samples of the liver, spleen, kidney, cervical and submandibular lymph nodes, FSU, spinal cord, and tissue adjacent, cranial and caudal to the implant were obtained for histologic examination
- **Histologic examination:** Samples were assessed for particulate traceable to the M6 and for inflammatory response per ISO 10993 and ASTM F981 standard guidelines



Figure 1: Spinal Kinetics' M6-C implanted in the goat.

Rabbit Study:

A worst case wear debris implantation study was conducted in a rabbit model to evaluate the local and systemic biologic response, including toxicity, associated with particulate debris that might be generated by M6 wear debris.

- Wear debris injected percutaneously into the epidural space of 54 rabbits (Figure 2; 9 groups, n=6 per group):
 - High dose, low dose and control groups
 - 2, 3, and 6 month time points
- Wear debris profile:
 - All device materials were included
 - 20mg low dose, 40mg high dose which constitutes a worst case for quantity (equivalent to 511 mg in a 90 lb human, which is a conservative estimate of minimum patient weight¹);
 - Particle size range 0.26 – 175 µm, a worst case relative to that observed in kinematic wear (see *Wear Debris Analysis of the M6-C Artificial Cervical Disc* and *Wear Debris Analysis of the M6-L Artificial Lumbar Disc*).
- **Histologic samples:** Complete spinal segments and samples of the brain, heart, lungs, liver, spleen, thymus, kidneys, adrenal glands, lymph nodes (mesenteric, submandibular, thoracic), and gonads were obtained for histologic examination
- **Histologic Examination:** Samples were assessed for clinical and general inflammatory response

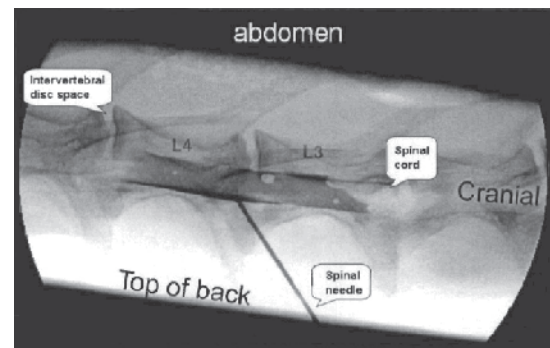


Figure 2: Example of epidural injection procedure used in the rabbit study.

Biocompatibility test battery:

- All materials used in the M6-C and M6-L have an established biocompatibility track record and have been widely implanted for at least 15 years without adverse reactions
- Testing was performed on all device materials in accordance with ISO 10993, "Biological Evaluation of Medical Devices Part I: Evaluation and Testing"
- Testing included cytotoxicity; sensitization; irritation/ intracutaneous reactivity; systemic toxicity; genotoxicity; carcinogenicity; and pyrogen testing

Results

Caprine study:

- A minimal amount of particulate was observed in proximity to the implant, resulting in negligible inflammatory response (Figure 3).
- Histological assessment indicated no adverse effects or foreign body responses due to the implant.
 - No acute inflammation
 - No systemic toxicity
 - No debris migration to distant organs

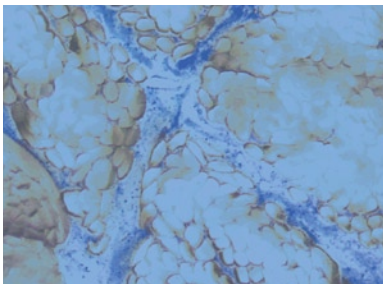


Figure 3: Histologic slide from the caprine study showing the UHMWPE fibers surrounded by serum with no evidence of inflammation or vascularity.

Rabbit study:

- As expected, histological assessment indicated the presence of particles in the general region of the injection site, along with some expected macrophages, giant cells, and occasional lymphocytes (Figure 4, Figure 5).
 - No systemic particulate observed
 - No acute inflammation
 - No evidence of bone resorption
 - No neurotoxicity, systemic toxicity, or local effects

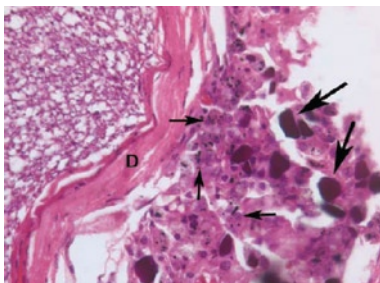


Figure 4: Histologic slide from the rabbit study showing macrophages (small arrows) and metal particles (large arrows) in proximity to the implantation site (D= dura).

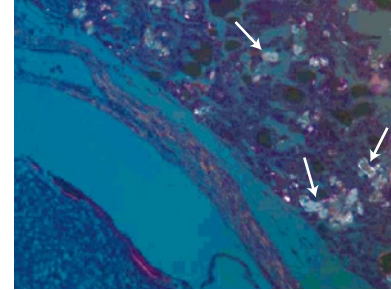


Figure 5: Image of histologic slide from the rabbit study taken under polarized light to emphasize the polymer particles (arrows).

Biocompatibility test battery:

- The M6 passed all aspects of the test battery. All tests demonstrated that the device is biocompatible for its intended use as a permanent implant with tissue/bone contact.

Discussion

The goat study demonstrated that the M6 had an acceptable biologic response, with little particulate observed and negligible inflammatory response. Analysis of adjacent tissue, lymph nodes and distant organs demonstrated no evidence of wear debris generation or debris migration in this model. The rabbit study confirmed this in a worst case scenario: histological assessment indicated no significant clinical or general inflammatory response. Based on the clinical and histologic findings, the potential wear debris associated with the device is considered safe and does not present any concerns regarding clinical use of the device. The ISO 10993 testing further confirmed that all the materials and processes used to manufacture the M6 are biocompatible.

Conclusion

All biomaterials were found to be biocompatible per ISO 10993 as well as through device implantation and worst case debris implantation studies.

1. Ogden CL, Fryar CD, Carroll MD, et al (2004). "Mean Body Weight, Height, and Body Mass Index, United States 1960-2002" In: [CDC: Advance Data](#), 347.