Osseointegration and Biocompatibility Evaluation of Silicon Nitride Composite Using
Ovine Distal Femoral Epiphyseal Insertion and Rabbit Paravertebral Muscle Implantation Models

Michel Assad¹, Bryan J. McEntire², Sandra Iacampo¹, Yannick Trudel¹, B. Sonny Bal²
¹AccelLAB Inc., Boisbriand, QC, Canada; ²Amedica Corporation, Salt Lake City, UT, USA
BMcEntire@amedica.com

INTRODUCTION: Silicon nitride (Si₃N₄) is a non-oxide bioceramic material that was originally developed in the early 1980s. In addition to its strength, stability and appealing imaging properties such as partial radiolucency, the surface chemistry of Si₃N₄ is hypothesized to be conducive to osteogenesis, have anti-infective properties, and to increase bone-to-implant contact, resulting in improved osseointegration [1,2]. Because of this unique combination of material properties, Si₃N₄ can be used for spinal fusion implants and is being considered for bearing components in prosthetic hip and knee joints. In this development program, an osseointegration study evaluated the ingrowth capability of Si₃N₄ materials implanted into the femoral condyles of skeletally mature sheep compared to similar titanium controls. A concurrent ectopic bone formation study was designed to evaluate the heterotopic bone formation potential of a particularly bioactive form of porous Si₃N₄ compared to titanium alloy implants in non-osseous sites, utilizing implantation in rabbit paravertebral muscles.

METHODS: In the first study, eight (8) skeletally mature female sheep (Dorset Rideau Arcott Hybrids) were used in order to evaluate two types of porous metallic dowels (N₃-annealed Si₃N₄ vs. Ti-6Al-4V cylindrical implants; n=8 samples per test and control group; 11.2-mm Ø × 24.13-mm L; 72% circular central porosity; 25% circular area corresponding to solid shell) were inserted in a press-fit fashion, bilaterally into ovine femoral medial condyles following defect creations. The specific objective was to quantify bone ingrowth and remodeling phenomena using histomorphometry and histopathology following four (4) weeks (28 ± 2 days) and twelve (12) weeks (84 ± 3 days) of implantation. In the second study, the osteoinductivity potential of the corresponding biomaterials cylindrical implants (discs, 6-mm Ø × 3-mm thickness) were implanted bilaterally in four (4) paravertebral muscle pouches of two (2) New Zealand White rabbits for a period of eight (8) weeks (56 ± 3 days) of implantation. The specific objectives were to evaluate ectopic bone formation (if any) and other local effects using histomorphology and histopathology analysis at 8 weeks (56 days ± 3 days) post-implantation. All surgical procedures and animal husbandry adhered to protocols approved by the Institutional Animal Care and Use Committee of an AAALAC-certified preclinical testing facility. Upon receipt and before use in this study, all animals were held for environmental acclimation for at least seven (7) days. All cages and enclosures conformed to standards set forth in the NIH Guide for Care and Use of Laboratory Animals.

RESULTS: The Si₃N₄ condylar implant showed good osteoconductivity and histomorphometry results (Fig. 1). The mean maximal linear penetration of new bone formation within the implant was higher in the Si₃N₄ test articles than in the porous Ti controls at both 4 and 12 weeks. The muscle implantation study revealed that implants made of porous Si₃N₄ and titanium alloy (controls) exhibited excellent safety and biocompatibility as evidenced by the mild tissue reaction without obvious adverse effects. Ectopic bone formation/osteoinductivity was not seen around the paravertebral devices or within the pores of the devices. Nevertheless, good neovascularization, characterized by minimal focal capillary proliferation or groups of 4 to 7 capillaries, was observed in the fibrous connective tissue/fibrosis around the device and within the device pores. Neovascularization scores were similar in both groups.

DISCUSSION: A new non-oxide ceramic material, silicon nitride (Si₃N₄), has demonstrated favorable osteoconductivity in this study. Unlike synthetic apatites, it has the strength and stability to be used in structural applications. It has yet to be effectively evaluated as to its osteoinductive behavior although it is believed that the surface chemistry of Si₃N₄ may also be conducive to osteogenesis. These two studies have contributed to evaluate a particularly active form of Si₃N₄ in terms of its ability to conduct and generate new bone formation within its porous structure.

SIGNIFICANCE/CLINICAL RELEVANCE: Novel Si₃N₄ composites, unlike synthetic apatites, are considered to have the strength, stability as well as partial radiolucency to be used in structural applications. Their porous core allows for osteoconduction, resulting in improved osseointegration, which may contribute to reduce the need for bone grafting.


IMAGES:

Figure 1. Si₃N₄ implant cross-section view under (a) high-resolution radiography and (b) micro-computed tomography. Light microscopy view of Exakt-microground longitudinal Si₃N₄ sections of: (c) rabbit paravertebral muscular tissue integration at 8 weeks postop (H&E, 10x) and (d) osseointegration after 12 weeks in an ovine medial condyle (Goldner’s Trichrome, 10x) showing pores colonized with mineralized bone.