A Collagen-Anorganic Bone Composite for Bone Repair: Part II: *In Vivo* Study in a Rabbit Radius Defect Model

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Introduction: The collagen-anorganic bone composite (OssiMend™) was engineered by Collagen Matrix, Inc., Franklin Lakes, NJ. Characterization of the device is presented in Part I. Characteristics of the device are shown in Table 1. We present here the use of this device in combination with autologous bone marrow for repair of critical size defects in a rabbit radius model.

Table 1. Physical Characteristics of OssiMend

Composition (mineral:collagen):	50:50 (w/w)
Pore size:	100 – 500 μm
Hydrothermal stability of collagen:	61.7 ± 1.3 °C
Absorption capacity:	21.9 ± 0.6 ml/g
Domain/crystal size of mineral:	29 nm

Methods / Surgery: Bilateral surgeries were performed on 6mo NZW rabbits with 6wk intervals between the surgeries. The area of the greater trochanter of the femur was shaved and disinfected. Femurs were palpated and 0.5 ml marrow aspirated with sterile 18g needles. OssiMend™ was soaked with the marrow. Critical size defects (1.5cm) were created in the diaphyses of the radii to hold the implants. Partly calcified interosseus membranes between radii and ulnae were intersected at defect sites. Osteotomies were performed with a rongeur and a 1.5cm bone segment was removed. Periosteum covering bone ends was removed and the bone marrow saturated implants placed in the defects. Implants were sutured at both ends to the periosteum. Muscle and skin were closed. Defects (6) were repaired with OssiMend™ and 3 empty defects (ED) were used as controls. Rabbits survived for 6 and 12wks.

Radiography: At 6 and 12wks post-surgery, rabbits were sacrificed and subjected to radiographic examination.

Histology: Following radiography, specimens were processed for histology (H&E, trichrome) with standard tissue preparation techniques. Key parameters were scored histologically (0 = none; 1+ = minimal; 2+ = moderate and 3+ = extensive): residual implant, new bone formation, bone union, and host tissue response (vascularization, inflammation and necrosis).

Results / Discussion: Radiographs at 6 and 12 weeks (Figure 1) and histology (Figure 2) show progressively more dense bone over time with formation of cortical bone. OssiMend™ showed significantly greater new bone formation than ED (Figure 3). This *in vivo* study demonstrated that OssiMend™ in combination with autologous bone marrow successfully repaired critical size defects in the rabbit radius. The implant achieved axial regeneration of radius-like bone and synostosis. It is known from the literature that at this critical defect size there is a 10% probability for self-regeneration. No ED rabbits showed self-regeneration at 6wks and 1/3 ED rabbits showed self-regeneration at 12wks, indicating that the probability of self-regeneration in this study is consistent with the literature.

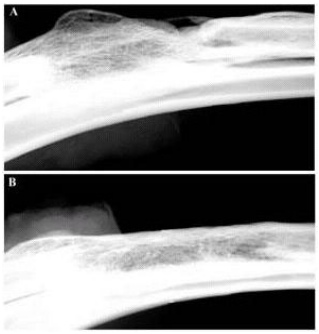

Figure 1: Radiographs at 6 (A) and 12 (B) weeks

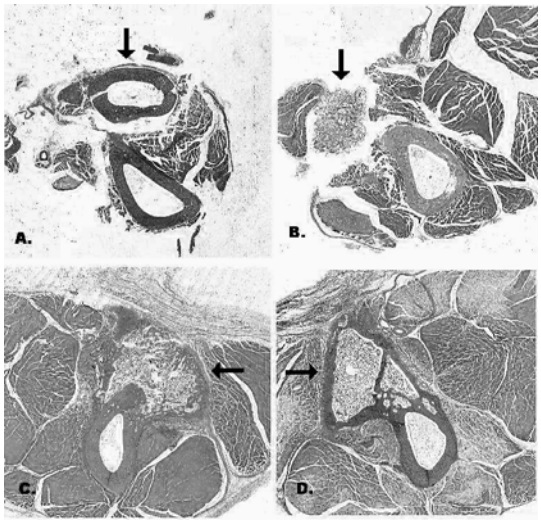

Figure 2: Histology of radius (→): A) Intact radius, no defect, B) OssiMend™ at day 0, C) OssiMend™/new bone at 6 weeks, D) OssiMend™/new bone at 12 weeks

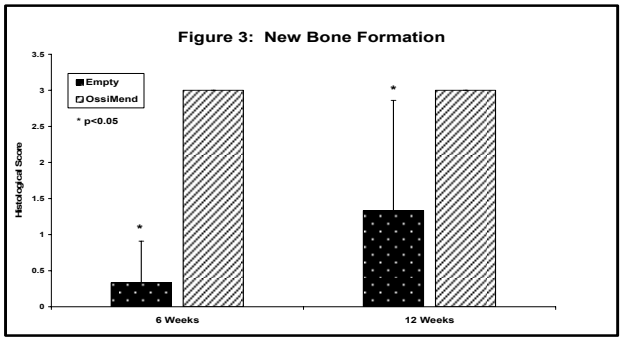

Figure 3: New bone formation at 6 and 12 weeks

Conclusion: Complete new bone formation at all 12 implanted sites provides confidence that OssiMend™ is a suitable resorbable bone growth guiding device for clinical application when used in combination with autologous bone marrow for bone defect repair. It has potential use in bone tumor resection, segmental defects, areas of traumatic bone loss and spinal reconstruction.