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A paradigm for the development and evaluation of novel implant topologies for bone fixation: In vivo evaluation

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ABSTRACT

While contemporary prosthetic devices restore some function to individuals who have lost a limb, there are efforts to develop bio-integrated prostheses to improve functionality. A critical step in advancing this technology will be to securely attach the device to remnant bone. To investigate mechanisms for establishing robust implant fixation in bone while undergoing loading, we previously used a topology optimization scheme to develop optimized orthopedic implants and then fabricated selected designs from titanium (Ti)-alloy with selective laser sintering (SLS) technology. In the present study, we examined how implant architecture and mechanical stimulation influence osseointegration within an in vivo environment. To do this, we evaluated three implant designs (two optimized and one non-optimized) using a unique in vivo model that applied cyclic, tension/compression loads to the implants. Eighteen (six per implant design) adult male canines had implants surgically placed in their proximal, tibial metaphyses. Experimental duration was 12 weeks; daily loading (peak load of $\pm$22 N for 1000 cycles) was applied to one of each animal's bilateral implants for the latter six weeks. Following harvest, osseointegration was assessed by non-destructive mechanical testing, micro-computed tomography (microCT) and back-scatter scanning electron microscopy (SEM). Data revealed that implant loading enhanced osseointegration by significantly increasing construct stiffness, peri-implant trabecular morphology, and percentages of interface connectivity and bone ingrowth. While this experiment did not demonstrate a clear advantage associated with the optimized implant designs, osseointegration was found to be significantly influenced by aspects of implant architecture.

1. Introduction

One strategy to improve prosthetic limb functionality is engineering implantable, bio-integrated devices. A critical aspect in implementing this technology is anchoring the system to remnant bone, which ensures secure fixation under various loading conditions and offers mechanical stability for connections with neural or muscle tissue.

Currently, a small number of amputees use osseointegrated prosthetic limbs, which are generally anchored with an intramedullary stem (Branemark et al., 2001; Hagberg and Branemark, 2009). Complications with these devices have yet to be adequately addressed (Hagberg and Branemark, 2009; Sensinger et al., 2009). One issue is resorption of structurally-critical bone, which may result from infection (Tillander et al., 2010), stress shielding (Tomaszewski et al., 2010; Xu and Robinson, 2008) or both. Furthermore, these devices are only available to amputees with sufficient bone to anchor the intramedullary implant (Branemark et al., 2001; Hagberg and Branemark, 2009). Despite these concerns, little data exists to design alternative implant structures.

Previously, we coupled topology optimization with a finite element (FE) model to develop novel implants that promote secure fixation (Kang et al., 2012). We found optimal structures by distributing limited implant material within a design domain. The FE model comprised a cylindrical design domain surrounded by trabecular bone, and loading consisted of uni-axial forces. The optimization objective minimized compliance of the bone-implant system, which is analogous to minimizing interface deformation. Two designs were fabricated from medical-grade Ti-alloy (Ti-6Al-4V) using selective laser sintering (SLS), a solid freeform fabrication (SFF) technique. Thus, we

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demonstrated part of a design strategy where optimized implants were developed and then rapidly fabricated.

Evaluating implants within a biological environment is critical to our design strategy. Since functional bone-implant systems undergo daily loading, this requires application of direct, in vivo loads to the implant. Additionally, mechanical loading affects osseointegration (Guldberg et al., 1997a; Leucht et al., 2007; Willie et al., 2010). The cellular processes of mechano-regulated bone adaptation occur locally (Parfitt, 2002); therefore, aspects of implant architecture can influence adaptive changes. Ultimately, peri-implant bone adaptation will affect performance.

The purpose of this study was to (1) develop an in vivo system that applies controlled, cyclic loads to implants embedded in trabecular bone and (2) use this system to evaluate effects of implant architecture on osseointegration.

2. Materials and methods

2.1. In vivo implant system

The in vivo system consisted of the implant in trabecular bone, a percutaneous housing column, a pneumatic actuator that generated tension/compression loads and a control unit with real-time display (Fig. 1). The implant and housing column, placed in the medial, proximal metaphysis of canine tibiae, were aligned perpendicular to the bone's long axis. Prior to loading, co-axial threads were used to simultaneously attach the actuator to the implant and housing column. Implant loads were applied through a connecting rod attached to a diaphragm inside the actuator. Air pressure changes from a pneumatic hose placed positive/negative pressures on the diaphragm, creating compression/tension forces on the implant. A computerized controller and gating mechanism generated cyclic loading (trapezoidal waveform) by alternately exposing the hose to positive and negative air pressures stored within two cylinders (Suppl. Fig. 1). A vacuum-compressor maintained cylinder pressures (model P251, Gast Manufacturing Inc., Benton Harbor, MI); bleed valves controlled air pressures/force magnitudes. Real-time load display was achieved with a calibrated strain gage on the actuator's connecting rod, amplifier and oscilloscope (model 123 Industrial ScopeMeter, Fluke Corp., Everett, WA). Following loading, the actuator was removed, and the housing column was covered with a cap.

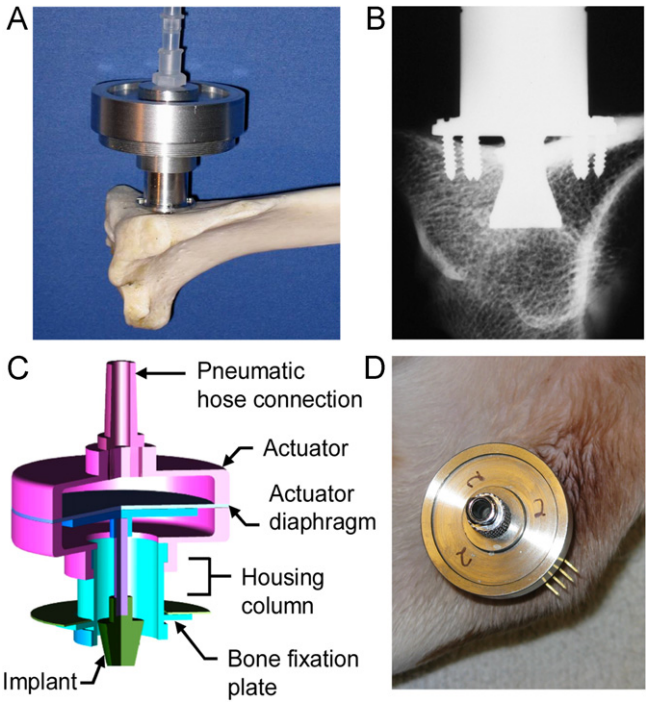

Fig. 1. (A and B) Loading systems were placed in proximal, medial canine tibiae with the implants embedded in trabecular bone. (C and D) These systems consisted of the implant, a percutaneous housing column and a removable pneumatic actuator.

2.2. Surgical implantation

At surgery, animals were pre-medicated with buprenorphine (0.01–0.02 mg/kg), acepromazine (0.05 mg/kg) and glycopyrollate (0.01 mg/kg) administered intramuscularly. An intravenous catheter was placed and thiopental sodium (17–35 mg/kg) was given until anesthetic induction. Following intubation, anesthesia was maintained with isoflurane. Under sterile conditions, an incision over the anterior-medial surface of the proximal tibia exposed the sub-periosteal bone. The bone was machined flat with a custom instrument for placing the housing column, which was attached with eight self-tapping stainless steel screws (size 00 × 3/16″ or 00 × 1/4″, JI Morris Co., Southbridge, MA). The housing column then served as a guide for drilling a 6.4 mm diameter hole using a square end mill (series 5–3 flute with 1/4″ cutting dia., SGS Tool Co., Munroe Falls, OH); implants were interference fitted into trabecular bone. Soft tissue was closed around the housing column, and bupivicaine (1 mg/kg) was administered subcutaneously. Oral antibiotic (cephalexin 30 mg/kg twice daily) and anti-inflammatory analgesic (carprofen 2–4 mg/kg once daily) were administered the first post-operative week. For the experimental duration, percutaneous housing columns were routinely cleaned with dilute chlorhexidine. Animals were housed individually with unrestricted cage activity; E-collars prevented oral contact with implant sites.

2.3. Experimental design

To examine the influence of implant architecture on osseointegration, two optimized titanium (Ti)-alloy implants were fabricated for in vivo analysis (Fig. 2) (Kang et al., 2012). Both were based upon the same global topology optimization scheme; the objective was to minimize compliance of the bone-implant system, thus minimizing interface deformation. One of the designs had a solid structure derived directly from the global layout of the topology optimization; the other had a porous structure created by converting the design domain into a hierarchical scaffold (Kang et al., 2010). The scaffold was generated by using the layout of the solid design to map low and high porosity microstructure sub-units optimized to be both stiff and permeable (Kang et al., 2012). The low and high density microstructures had porosities of 63% and 33%, respectively; the implant's overall porosity was 50%. The size of the microstructures within the implant was established to generate pores ranging between 300 and 960 μm. This range of pore sizes enabled accurate production of the scaffold using SLS technology (Synergeering Group, Farmington Hills, MI), which was utilized for fabricating both optimized implants. A third design, representing a non-optimized control, was also included in this study. This implant had a machined Ti-alloy cylinder with a porous coating formed by sintering a double-layer of commercially pure (CP) Ti beads 420–590 μm in diameter (Orchid Coating, Southfield, MI) (Guldberg et al., 1997a). This bead coating had a mean pore size of 160 μm and porosity of 32%. Overall dimensions of all implants were 6.4 mm diameter by 12.7 mm length.

Eighteen skeletally-mature, male purpose-bred beagles (13.3–15.5 months of age and 11.0–12.6 kg at surgery, Covance Research Products, Inc., Kalamazoo, MI) were entered into the study. The same implant design was placed bilaterally in each animal with each design assigned to six animals. Three groups of six animals entered the experiment during a three month period; within groups, each design was assigned randomly to two animals.

Experimental duration for each animal was twelve weeks. Prior to implant loading, there was a six week post-operative healing period for neo-bone formation,

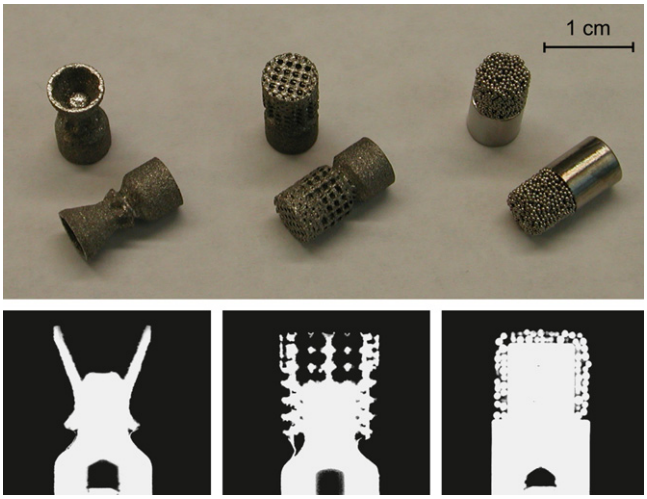

Fig. 2. Three implants were fabricated for in vivo analysis: a solid optimized, a porous optimized and a non-optimized porous cylinder.