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Optimal internal fixation of anatomically shaped synthetic bone grafts for massive segmental defects of long bones

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ABSTRACT

Background: Large segmental bone defects following tumor resection, high-energy civilian trauma, and military blast injuries present significant clinical challenges. Tissue engineering strategies using scaffolds are being considered as a treatment, but there is little research into optimal fixation of such scaffolds.
Methods: Twelve fresh-frozen paired cadaveric legs were utilized to simulate a critical sized intercalary defect in the tibia. Poly-ε-caprolactone and hydroxyapatite composite scaffolds 5 cm in length with a geometry representative of the mid-diaphysis of an adult human tibia were fabricated, inserted into a tibial mid-diaphyseal intercalary defect, and fixed with a 14-hole large fragment plate. Optimal screw fixation comparing non-locking and locking screws was tested in axial compression, bending, and torsion in a non-destructive manner. A cyclic torsional test to failure under torque control was then performed.
Findings: Biomechanical testing showed no significant difference for bending or axial stiffness with non-locking vs. locking fixation. Torsional stiffness was significantly higher ($P = 0.002$) with the scaffold present for both non-locking and locking compared to the scaffold absent. In testing to failure, angular rotation was greater for the non-locking compared to locking constructs at each torque level up to 40 N-m ($P < 0.05$). The locking constructs survived a significantly higher number of loading cycles before reaching clinical failure at 30 degrees of angular rotation ($P < 0.02$).
Interpretation: The presence of the scaffold increased the torsional stiffness of the construct. Locking fixation resulted in a stronger construct with increased cycles to failure compared to non-locking fixation.

1. Introduction

Massive skeletal defects of the tibia following high-energy civilian and military trauma or extensive resection of tumors remain a therapeutic challenge. Large bony defects occur in a small minority (0.4%) of fractures overall, but are common (11.4%) in open fractures (Keating et al., 2005). In the tibia, defects greater than 2 cm are unlikely to heal without additional bone grafting and defects greater than 5–6 cm are difficult to manage with autologous bone graft alone (Keating et al., 2005; Aho et al., 2013; May et al., 1989). A number of surgical techniques exist to address these larger defects but require multiple procedures and significant morbidity with a high rate of complications.

Segmental allografts have been advocated to reconstruct defects after tumor resection and trauma but have a non-union rate as high as 17.3% and fracture rate of 17.7% (Hornicek et al., 2001; Sorger et al., 2001). Distraction osteogenesis has been shown to be effective but also requires multiple procedures, an extended period of protected weight bearing with a bulky external fixator, and carries a re-fracture rate of 5% and amputation rate of 2.9% (Papakostidis et al., 2013). It also loses effectiveness for defects larger than 6–8 cm (Papakostidis et al., 2013; Rigal et al., 2012). Vascularized free fibula grafting is a viable option as well but requires specialized surgical skill as well as significant donor site morbidity (Han et al., 1992; Myeroff and Archdeacon, 2011). More recently, a staged procedure with placement of a poly(methyl methacrylate) spacer to induce an osteogenic membrane followed by autogenous bone grafting has been advocated and shown to be effective for defects up to 20 cm (Aho et al., 2013; Karger et al., 2012; Taylor et al., 2012).

While effective, these techniques all require multiple procedures and carry significant donor site morbidity for bone grafting (Myeroff and Archdeacon, 2011). Tissue engineering has emerged as a promising approach for addressing large bony defects. The triad of tissue engineering has been proposed as a scaffold to provide structural stability as well as a platform for delivery of osteogenic growth factors and/or cells (Nie et al., 2012). Scaffolds are now able to be designed with the correct

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micro- and macroarchitecture for bony ingrowth and vascularization with promising results in animal studies (Lee et al., 2009, 2010; Alhadlaq and Mao, 2005; Oest et al., 2007; Amorosa et al., 2013). The load-bearing capacity of the bone scaffold-fixation construct in human patients is an important factor in order to guide post-operative rehabilitation. However, most of previous studies focused on bone regeneration rather than the weight-bearing capacity of the bone scaffold-fixation construct.

Plate and screw fixation is commonly used for forearm bone fractures. For femur and tibia, intramedullary nailing is a common choice of internal fixation. For the humerus, both plate and screws and intramedullary nailing are used. However, for skeletal defects following resection of malignant tumors, intramedullary nailing is not conceptually preferred due to a theoretical concern of spreading tumors into the proximal and distal host bone and soft tissues during nail introduction and reaming.

In the present study, we examined the load-bearing capacity and optimal internal fixation of a bone/poly-ε-caprolactone-hydroxyapatite (PCL-HA) composite scaffold/plate construct that was anatomically fabricated in order to match the 5 cm segmental defect in the human tibia. We compared the non-locking versus the locking plate and screw constructs because one of the future indications for biocompatible and biomechanically competent scaffolds will be massive defects following tumor surgeries. Numerous biomechanical studies have demonstrated the mechanical superiority of locking fixation in a fracture model, but none have focused on fixation of the bone scaffolds (Fulkerson et al., 2006; Davis et al., 2012; Will et al., 2011). We hypothesized that the locking plate fixation provides more stable internal fixation under cyclic axial, bending, and torsional loading. The study is clinically relevant in that it will guide treating surgeons with respect to internal fixation and guide post-operative regimens for the patients with massive intercalary skeletal defects treated with bone scaffolds.

2. Materials and methods

2.1. Fabrication of intercalary tibia scaffolds

The anatomical morphology of a native cadaver adult human tibia was acquired from computed tomography scans on a clinical machine (SIEMENS/Biograph 40, Malvern PA, USA) and manipulated using computer-aided design software for 3D modeling (Mimics, Materialise Co., USA). A 5 cm mid-shaft anatomically correct model of the tibia was designed. A composite polymer scaffold was fabricated using layer-by-layer deposition with a 3D printing system (Bioplotter, EnvisionTec, Berlin, Germany). The composite consisted of 90 wt% poly-ε-carpolactone (PCL) and 10 wt% hydroxyapatite (HA) (Sigma, St. Louis, MO, USA). PCL-HA composite was molten in the chamber at 120 °C and dispensed through an 18 Ga needle to create interlaid strands and interconnected micro-channels (diameter 400 μm). Gaps between strands were 0.5 mm, and the porosity was 35%. Each layer was dispensed with a 0.9 mm height. We selected this PCL-HA composite in accordance with previous findings of cell adhesion and osteochondral histogenesis using the same material (Lee et al., 2009).

2.2. Implantation of structural scaffolds into the intercalary defect of the tibia

Twelve fresh-frozen cadaveric limbs from six individuals (6 pairs, average age 75, range 72–78, 4 males, 2 females) were utilized in this study. An antero-lateral incision was made and the lateral aspect of the tibia was exposed sharply. The surrounding soft tissue and fibula were maintained and a 5 cm section of the tibia was removed from the diaphysis. A 14-hole 4.5 mm broad, 260 mm large fragment locking compression plate from Synthes (Paoli, PA) was placed provisionally with bone clamps. The scaffold was provisionally placed with suture augment around the plate. The plate was fixed with five 5.0 mm diameter locking screws superior and inferior to the scaffold. Two 4.5 mm diameter cortical screws were placed into the scaffold to secure it. All screws bridged both cortices. The plate was contoured slightly at the distal end to conform to the distal tibia surface. All soft tissue was removed for biomechanical testing.

2.3. Biomechanical testing

The tibial plateau was cut to create a square end that was placed within a 10.2 cm square fiberglass tube. Orthogonal Steadman pins were passed through the tube and bone and the entire construct filled with poly(methyl methacrylate). A metal plate with a spherical depression and a steel ball was placed on top of the fiberglass tube when axial compression was applied and the tibia was loaded via a flat platen. When torsion loading was applied, the plate and ball were removed and square clamp was lowered around the fiberglass tube that allowed for axial motion while preventing any slippage in rotation. The distal end of the tibia was potted in the same manner as the proximal end except a 5.1 cm square polycarbonate tube was used and placed within a square clamp rigidly connected to the biaxial load cell. Torsional loading was applied at the proximal end of the tibia (Fig. 1).

Loading was applied with a MTS 858 Bionix (MTS Eden Prairie, MN, USA) testing system. Axial loading was applied via a series of increasing sinusoidal loads from a baseline of 50 N to a peak load of 400 N, 500 N, 600 N, and 700 N, respectively. At each step, the load was applied in a sinusoidal fashion for 50 cycles at a rate of 2 Hz. Data were collected at a rate of 10 Hz. Three-point bending loads were applied to the middle of the plate also via a series of increasing sinusoidal loads from a baseline of 50 N to a peak load of 200 N, 250 N, 300 N, and 350 N in the same manner as was done for the axial loading. Bending supports were placed 27.9 cm apart for all specimens. Mid-span displacements were recorded with a MTS Model 632.03 extensometer. Finally, a sequence of increasing sinusoidal torsional moments of +/−3, +/−6, and +/−9 N-m was applied for 20 sinusoidal cycles at a rate of 0.5 Hz. This testing protocol was adapted from well-established, clinically relevant, previously validated testing models (Dennis et al., 2000, 2001; Fulkerson et al., 2006; Choi et al., 2010). The loading sequence was randomized for each pair but was the same for each leg of a pair. Following sub-failure testing with the scaffold in place, the scaffold was removed and the same series of tests repeated without the scaffold. The order of scaffold / no scaffold was not randomized because the main intent of the study was to determine the stiffness of the construct with the scaffold in place. Specimens were then loaded to failure in torsion with the scaffold absent. A sequence of increasing sinusoidal torsional moments of +/−10, +/−15, +/−20, +/−25, +/−30, +/−35, +/−40, and +/−45 N-m was applied at 0.5 Hz for 25 cycles at each level of torsional loading and allowed to continue indefinitely at the +/−45 N-m level until failure.

2.4. Statistical analysis

Separate statistical analyses were performed for the non-destructive and failure testing. Two-way repeated measures ANOVAs (SAS, Cary, NC) were performed for non-destructive testing. Factors were fixation type (locking, non-locking screws) and scaffold condition (scaffold present, scaffold absent). Axial stiffness, bending stiffness, and torsional stiffness were the measured parameters. Two-way repeated measures were also performed for failure testing with the factors of fixation type (locking, non-locking screws) and torsional load (+/−10, +/−15, +/−20, +/−25, +/−30, +/−35, +/−40, and +/−45 N-m). Student–Newman-Keuls multiple comparisons tests were used to discern differences between loading levels. Statistical significance was taken as $P < 0.05$.