New Intramedullary-fixation Technique For Long Bone Fragility Fractures Using Bioabsorbable Materials
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Introduction: The number of hip fractures in Japan for 2010 exceeded 150,000. Metallic implants such as locked plating or intramedullary nailing can stantaneously strengthen a weakened long bone metaphyses, however, they sometimes cause cutout because the bone strength is much less than that of the metallic implants in severely osteoporotic patients. We therefore developed a new technique (intramedullary-fixation with biodegradable materials, IFBM) to instantaneously strengthen a severely weakened long bone metaphyses using a poly(L-lactic acid) (PLLA) woven tube, a nonwoven polyhydroxyalkanoates (PHA) fibermat, and injectable calcium phosphate cement (CPC). The goal of this work is to evaluate the feasibility of IFBM in both mechanical testing and animal experiment models.

Methods: Intramedullary-fixation with biodegradable materials (IFBM) The procedure for IFBM begins with reaming the intramedullary cavity and inserting a PLLA woven tube into the cavity, followed by injection of CPC paste both inside and outside the PLLA woven tube using a syringe. However, massive CPC paste leakage from the fracture site appeared likely to inhibit bone union, so we used a nonwoven PHA fibermat to prevent CPC leakage. The 3-hydroxybutyrate (3HB) and 4-hydroxybutyrate (4HB) copolymers (Poly (P) (3HB-co-4HB)) used in the PHA fibermat in this work demonstrate properties of both strength and flexibility. The nonwoven PHA fibermat can prevent CPC leakage. Therefore, when we injected the CPC paste inside and outside the PLLA woven tube, the nonwoven PHA fibermat could be expanded until it fitted itself to the cavity(Figure).

Preparation of a nonwoven PHA fibermat Polyhydroxyalkanoates (PHA) represent a complex class of biopolymers consisting of various hydroxyalkanoic acids. They are synthesized by microorganisms. PHA exhibits biodegradable, biocompatible and elastomeric properties once extracted from the cells. Polymerization of 4HB with other hydroxyl acids such as 3HB can produce elastomeric compositions at moderate 4HB contents (15%-35%), and relatively hard rigid polyesters at lower 4HB contents. 3HB and 4HB copolymer (P(3HB-co-4HB)) at 18% HB content as a CPC leakage prevention tool were used in our work. The nonwoven PHA fibermat showed excellent expandability, so that it is not fractured easily even when the CPC paste would be injected to expand it.

Mechanical testing Five profile specimens were tested for each sample composition. The PLLA woven tube was wrapped by the nonwoven PHA fibermat, and it was inserted into two acrylic pipes placed longitudinally as group 1. Just after kneading, the CPC paste was injected inside and outside the PLLA woven tube. After 10 min, a three-point bending test was performed. For group 2, the nonwoven PHA fibermat was inserted into acrylic pipes. Then the CPC paste was injected into nonwoven PHA fibermat. In group 3, the CPC paste was injected into acrylic pipes. The maximum flexural strength and fracture energy were calculated. Data from multiple groups were compared using a one-way analysis of variance (ANOVA). Experimental animal model of osteoporosis Eight, 8-month-old, female New Zealand White rabbits were used. Experimental rabbit models of osteoporosis were made by performing bilateral ovariectomy followed by intramuscular steroid injection for 4 weeks. Then, the eight rabbits were randomly allocated into two experimental groups. Group 1 was a combination-use group (PLLA woven tube + CPC + nonwoven PHA fibermat). Group 3 was a control group (CPC alone). Postoperative lesions were evaluated with the use of Soft X-ray at weeks 1, 4, 8, 12 and 20. The rabbits in group 1 (PLLA + CPC + PHA) were sacrificed at week 20, and a 15 mm segment of the metaphyseal portion of the femur was removed for histological examination.

Results: Mechanical testing The mean maximum flexural strength values at 10 min immediately following the CPC injection in group 1 (PLLA + CPC + PHA; 2.71 ± 0.66 MPa) was significantly higher (p < 0.001) than the values of group 2 (CPC + PHA; 0.79 ± 0.23 MPa) and group 3 (CPC alone; 0.52 ± 0.24 MPa).

The average fracture energy at 10 min following the CPC injection in group 1 (PLLA + CPC + PHA; 1210 ± 334 J/m²) were significantly higher (p <0.001) than both the group 2 values (CPC + PHA; 19.4 ± 6.4 J/m²) and the group 3 (CPC alone; 5.5 ± 5.7 J/m²).
The average modulus of bending elasticity in group 1 was 179 ± 89 MPa (zone-1) and 18.2 ± 8.7 MPa (zone-2). The average modulus of bending elasticity in groups 2 and 3 was 183 ± 64 MPa and 223 ± 69 MPa, respectively. **Animal experiments** Soft X-ray photographs revealed that there were no re-fractures over the entire postoperative period in group 1 (PLLA + CPC + PHA), whereas three of four rabbits had re-fractures at postoperative week-1 in group 3 (CPC alone). All rabbits in group 1 achieved bony union in 8 weeks (Figure). There were no postoperative infections in group 1. **Histologic examination** (H&E) at week-20 in group 1 (PLLA + CPC + PHA) indicated that a PHA fibermat layer surrounded the CPC. It indicated that the PHA fibermat prevented the CPC leakage. A mild inflammation and neovascularization was observed with surrounding granulation tissue in the PHA fibermat layer.

**Discussion**: Mechanical testing has clearly shown that the combination of the PLLA woven tube with CPC improved the apparent mechanical properties, to include a significant increase of the fracture energy and the maximum flexural strength. It should be emphasized that the average fracture energy for the IFBM group (PLLA + CPC + PHA) was 60 to 200 times greater than that of the other groups (CPC + PHA, or CPC only). The animal experiment using a rabbit femur incomplete fracture model revealed that no rabbit in a combination treatment group (PLLA + CPC + PHA) fractured even under full weight bearing, whereas three of four rabbits in a control group (CPC only) completely fractured within the first postoperative week.

**Significance**: The present work demonstrated the superior usefulness of IBM in treating metaphyseal insufficiency fractures even in locations exposed to high bending and torsional stresses like the distal femur. The combination of three biomaterials with different physical and biological properties is preferable because it is safer and more biocompatible than the metal implants.

**Acknowledgments**

**References**