

Treatment of high-energy tibial shaft fractures with internal fixation and early prophylactic NovaBone grafting

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Objective: To evaluate the safety and efficacy of early NovaBone grafting in accelerating healing of high-energy tibial shaft fractures.

Methods: In a prospective, randomized, controlled study 78 patients with open or closed tibial shaft fractures were treated with reamed interlocking nails, combined with NovaBone grafting. Forty patients were randomly assigned to the experimental group (with NovaBone grafting at fracture site), and 38 to the control group (without NovaBone grafting).

Results: All patients were followed up for an average of 8 months (range 6–18 months). The average fracture healing time was 12 weeks (range 8–16 weeks) in the experimental group, and 19 weeks (range 12–36 weeks) in the control group ($P < 0.01$). No delayed union or nonunion was found in the experimental group, but four cases (10.5%) in the control group were found to heal spontaneously between 7 and 8 months. When the data were analyzed at week 12 and week 26 according to the criteria of Johner and Wruhs, 88% and 100% of the cases in the experimental group were rated as excellent and good respectively, but in the control group, 50% and 89% were rated as excellent and good respectively, these being significant differences ($P < 0.05$).

Conclusion: Internal fixation supplemented with early prophylactic NovaBone grafting of high-energy tibial shaft fractures is a safe and effective treatment which accelerates fracture healing.

Key words: Bone substitutes; Fracture healing; Tibial fractures; Treatment outcome

Introduction

High-energy tibial shaft fractures have long been known to require a long healing time and to have high rates of nonunion^{1,2}. Despite advances in surgical techniques and fixation, treatment of this type of fracture continues to be associated with high rates of delayed union and nonunion^{2,3}. The prevalence of delayed union of tibial shaft fractures reported in the orthopaedic literature ranges from 16% to 60% for mild, and from 43% to 100% for severe, fractures^{3–6}. Therefore, it is important to stimulate fracture healing and decrease the rate of nonunion^{7–9} for high-energy tibial shaft fractures. NovaBone (NovaBone Products, LLC/US Biomaterials Corporation, FL, USA), based on 45S5 Bioglass, invented by Hench *et al.* in 1971^{10–13}, is a new type of synthetic material, and has already been confirmed to expedite fracture

healing and repair of osseous defects. We used early prophylactic NovaBone grafting at the fracture sites combined with reamed interlocking nails for treating high-energy tibial shaft fractures from March 2004 to October 2006. The purpose of this study was to evaluate the safety and efficacy of NovaBone grafting in accelerating healing of high-energy tibial shaft fractures.

Materials and methods

Seventy-eight patients with acute tibial shaft fractures were examined and treated on the protocol at our institution: 47 males and 31 females, with a mean age of 40.5 years (range, 17–78 years). Forty-eight fractures resulted from traffic accidents, 19 from tumbling, 6 from crushing and 5 from other causes. Twenty-eight of the 78 patients (36%) had multiple system injuries. There were 52 closed fractures and 26 open fractures, and all patients had either a type I or type II wound according to the classification of Gustilo and Anderson¹⁴. Type III fractures were not included because of severe wound contamination. The fractures were further classified according to the

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AO-system (Arbeitsgemeinschaft für Osteosynthesefragen or Association for the Study of Internal Fixation)¹⁵. By fracture location, 17 cases were in the proximal third, 30 in the middle third, and 31 in the distal third. The degree of the fractures was classified as Group A (8 cases, 10%), B (49 cases, 63%), and C (21 cases, 27%). Forty-two of 78 (54%) fractures were 50% to 99% displaced, 36 fractures (46%) were 100% or more displaced. All cases were associated with fibular fractures. Fifty-three fractures were fixed with the Russel-Taylor nailing system (Smith & Nephew Richards, Memphis, TN, USA), and 25 fractures with the Orthofix nailing system (Orthofix Srl, Verona, Italy).

All patients were randomly assigned with randomization tables. Forty patients were assigned to the experimental group and received NovaBone grafting at the fracture sites, while the control group of 38 patients were treated without NovaBone grafting.

Graft material

NovaBone grafting material, supplied to the surgeon as a sterile kit containing 6.3 g of particulates (Fig. 1), has proven to be an effective graft material for oral and maxillofacial bone augmentation^{10–13}. The success of NovaBone is partly due to the bioactivity of the material resulting from its composition (45% SiO₂, 24.5% CaO, 24.5% Na₂O and 6% P₂O₅). After implantation into the fracture site, the surface of the NovaBone responds very quickly to tissue fluids and releases a substantial concentration of soluble silicon, as well as soluble calcium and phosphorus, which may be responsible for its osteogenic effects. It is proposed that the soluble silicon activates stem

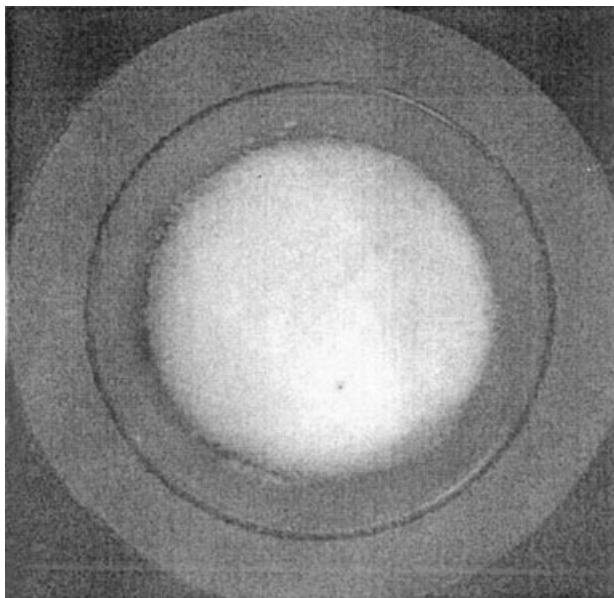


Figure 1 NovaBone particulates(90 to 710 μm).

cells that produce transforming growth factor- β (TGF- β), which is reversibly adsorbed and desorbed in the hydrated silica–calcium–phosphate gel layer formed on the surface. The TGF- β stimulates differentiation and subsequent growth of bone cells in contact with the NovaBone particles, leading to rapid bone formation. The size of NovaBone particles ranges from 90 to 710 μm . It has been shown that this wide range of particle size is optimal for osseous regeneration.

Operative technique

After cardiovascular and respiratory stabilization, all patients with open fractures were immediately taken to the operating room for irrigation, debridement, wound closure and stabilization with reamed interlocking nails. All closed fractures were fixed with reamed interlocking nails within four weeks of injury.

During surgery, a limited longitudinal incision over the anterior border of the fracture site was made, and reduction maintained from the time the nail crossed the fracture site until final seating in the distal fragment. The starting point was made with an awl, then the nail was inserted with reaming in an antegrade manner by hyperflexing the knee. Distal and proximal interlocking was performed with a nail-mounted guide without fluoroscopy. For both closed and open fractures, we placed one or two kits of NovaBone in the fracture site of each patient at the time of wound closure in the experimental group. No fibular fixation was performed in this series.

Patients with static locked nails were kept non-weight-bearing on ambulation for 4 to 6 weeks postoperatively. These patients were allowed protected weight-bearing ambulation with crutches once a fracture callus was radiographically visible, which usually occurred 8 to 14 weeks after surgery.

Statistical analysis

The chi square test was performed for overall efficacy and pairwise comparisons. We considered differences significant when $P < 0.05$.

Results

All patients were followed up until fractures healed. The final results were evaluated based on Johner and Wruhs criteria¹⁵. The time for fracture union was defined as the period between surgery and weight-bearing without external support together with a radiographically healed fracture. Delayed union was considered to have occurred if radiographs failed to show fracture consolidation by the end of the sixth month. Nonunion was defined by the presence of pain at the fracture site without radiographic

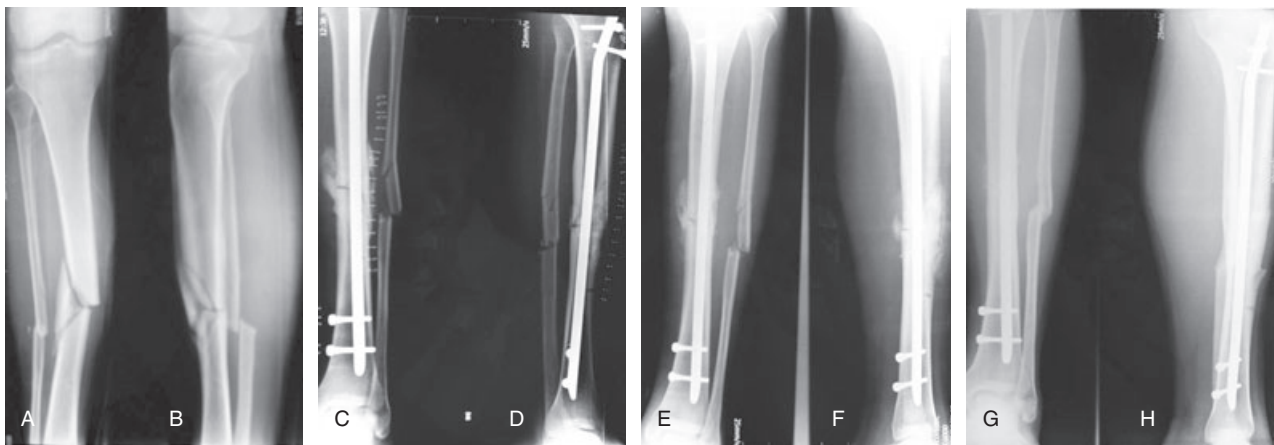


Figure 2 A 36-year-old man with an open tibial fracture (Gustilo type II, AO type B2) resulting from a car accident, treated by open reduction and stabilization with interlocking nail. NovaBone was added to the fracture site. (A, B) Preoperative radiographs. (C, D) Radiographs obtained postoperatively, NovaBone had been added to the fracture site. (E, F) Radiographs at 6 weeks' follow-up showing a large amount of NovaBone has been degraded and replaced by callus. (G, H) Radiographs at 12 weeks' follow-up showing complete healing.

evidence of healing 9 months after nail fixation. Once the radiopaque NovaBone particles were no longer visible, determination of fracture healing was made by an independent radiologist who was blind in respect to the treatment group.

All patients were followed up for 6–18 months, (average 8 months). The average healing time in the experimental group was 12 weeks (range, 8–16 weeks; Fig. 2). Radiographs showed that most of the NovaBone was degraded and replaced by callus by 6–8 weeks after surgery, and by 8–10 weeks there was a large amount of callus. In contrast, the average healing time in the control group was 19 weeks (range, 12–36 weeks; Fig. 3). The difference in fracture healing time between the two groups was statistically significant ($P < 0.01$). In the experimental group, no delayed union or nonunion was found. However, in the control group, four fractures (10.5%) healed spontaneously

between 7 and 8 months. No deep infection, re-fracture, postoperative compartment syndrome, neurological defects or broken nail occurred in either of the groups. According to the criteria of Johner and Wruhs¹⁵, by the 12th week 35 cases (88%) were rated as excellent or good in the experimental group and 19 (50%) in the control group, which was a statistically significant difference (Table 1, $P < 0.05$). By week 26, there were 40 (100%) excellent and good cases in the experimental group, and 34 (89%) in the control group, also a significant difference (Table 2, $P < 0.05$). The four cases with fair results in the control group were attributable to delayed union.

Discussion

The traditional role for bone grafting in treating tibial shaft fractures has been in cases with established delayed

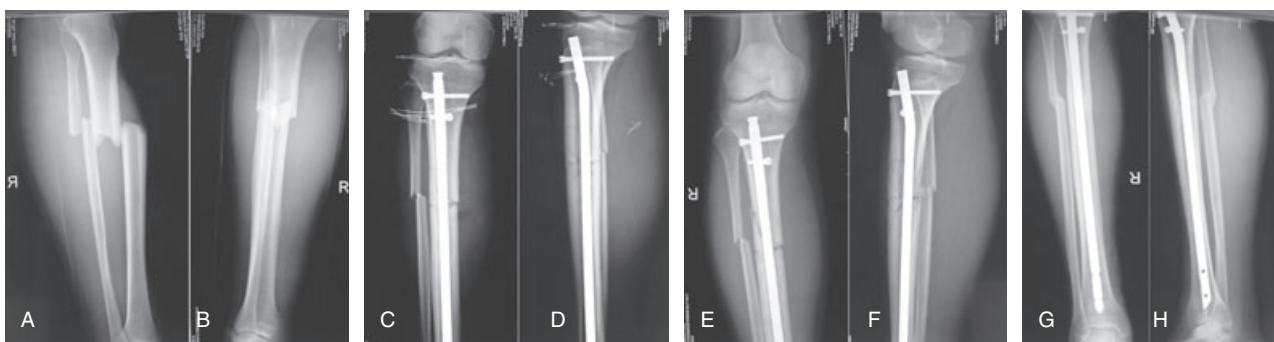


Figure 3 (A–H) A 30-year-old man with an open tibial fracture (Gustilo type II, AO type A) resulting from a car accident, treated by open reduction and stabilization with interlocking nail (without NovaBone grafting). (A, B) Preoperative radiographs. (C, D) Radiographs obtained postoperatively. (E, F) Follow-up radiographs at 8 weeks showing no callus at fracture site. (G, H) Radiographs at 8 months' follow-up showing complete healing.

Table 1 Clinical results of NovaBone grafting and non-grafting at 12 weeks follow-up

Rating*	Experimental group (40 cases)	Control group (38 cases)	χ^2 -value	P-value
Excellent	24 (60%)	13 (34%)	10.961	<0.05
Good	11 (28%)	6 (16%)		
Fair	5 (12%)	19 (50%)	—	—
Poor	0	0	—	—

*Rated according to the criteria of Johner and Wruhs¹⁵.

union or nonunion. Because the natural history of high-energy tibial shaft fractures is delayed union or nonunion, and secondary interventions to treat delayed union or nonunion are associated with high rates of patient morbidity and reduced quality of life, some authors have recommended early prophylactic bone grafting^{7,8,16}. It is not a new idea. In 1961, Charnley first recommended prophylactic bone grafting of tibial shaft fractures to reduce the total time of disability⁸. He stated that the most common error in the treatment of tibial shaft fractures was excessively long postponement of bone grafting. He believed that the likelihood of delayed union could be predicted. However, his new idea was not accepted until the 1980s. Behrens *et al.* reported a statistically significant decrease in healing time for severe open tibial fractures in which bone grafting was used within 30 days of injury¹⁶. In the Blick series (1989), there was a reduction in healing time of almost 12 weeks compared with a matched historical control group of tibial fractures that did not receive early bone grafting⁷.

Previously, autogenous bone was regularly used as a bone graft material. However, autogenous bone graft has certain limitations. Occasionally, the autogenous bone available for grafting is of poor quality (osteoporotic) or limited quantity. Moreover, obtaining an autogenous graft may entail serious morbidity at the donor site and an increase in the operative time of twenty minutes or more. In order to overcome these problems, various bone graft substitutes have been developed for early bone graft¹⁷. One bone graft substitute is collagen–calcium phosphate ceramic. Chapman *et al.* evaluated the safety and efficacy of this bone graft substitute as compared to autogenous bone graft for treating fractures of long bones in humans, and found no significant differences between the two groups with respect to rates of union or functional measures¹⁸. Another bone graft substitute is recombinant human bone morphogenetic protein-2 (rhBMP-2). Govender *et al.* treated acute tibial fractures with rhBMP-2, and fracture healing was significantly faster⁹. Based on this clinical research, he pointed out that the goal of initial

fracture treatment should be to increase the likelihood of union, and so reduce the risk and cost of secondary procedures.

Recently, a synthetic material 45S5 Bioglass (NovaBone) has been used extensively as a bone graft substitute^{10–13}. In the experiments of Oonishi *et al.*¹³, the authors discovered that by 2 weeks after Bioglass implantation, almost all of the surrounding particles had formed new bone and extended to the center of the defect, and by 3–6 weeks after implantation, the newly formed bone tissue within the particles had continued to increase, and dense new bone trabeculae had completely surrounded the layers of Bioglass particles. After 12 weeks, most of the Bioglass particles had been absorbed and all glass particles were connected by bone bridges.

In the current clinical study, our findings are consistent with the results of Oonishi *et al.*¹³, which indicated that NovaBone, as early prophylactic graft material, is effective and safe in the treatment of high-energy tibial shaft fractures. We found a reduction in healing time of almost 7 weeks compared with a control group that did not receive early NovaBone grafting (12 vs. 19 weeks). Although the two groups were not matched for age, mechanism of injury, initial displacement, injury severity or comminution, none of these factors was found to affect fracture healing significantly in the present series. Because of random selection, there is no reason to believe that the failure to match for these factors in the protocol introduced any bias into the study.

The exact clinical role for a synthetic bone graft material such as the one that we studied remains to be defined. Autogenous graft has three overlapping clinical roles: (i) it can provide immediate structural support; (ii) it can provide an osteoconductive scaffold for the filling of a defect; and (iii) it can provide an osteogenic stimulus from both cells and growth factors. The synthetic graft material that we have used as a particulate form is unable to play the first of these roles (immediate structural support), however, it functions well as an osteoconductive gap-filling material, and attracts osteoprogenitor cells and

Table 2 Clinical results of NovaBone grafting and non-grafting at 26 weeks follow-up

Rating*	Experimental group (40 cases)	Control group (38 cases)	χ^2 -value	P-value
Excellent	30 (75%)	20 (52%)	4.438	<0.05
Good	10 (25%)	14 (37%)		
Fair	0	4 (11%)	—	—
Poor	0	0	—	—

*Rated according to the criteria of Johner and Wruhs¹⁵.

osteoblasts to the graft material, which provides an osteogenic stimulus.

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