MULTICENTER NONUNION CLINICAL INVESTIGATION OF THE DONJOY® OL1000 BONE GROWTH STIMULATOR

The Clinical Investigation

Introduction

The purpose of this study was to investigate the use of the DONJOY® OL1000 Bone Growth Stimulator for 30 minutes per day in the treatment of established nonunions acquired secondary to trauma, excluding vertebrae and all flat bones, where the nonunion gap was less than one-half the width of the bone to be treated. For purposes of the clinical investigation, a nonunion was considered to be established when a minimum of nine months had elapsed since injury and the fracture site showed no visibly progressive signs of healing for a minimum of three months.

Seventeen investigators/institutions participated in the clinical investigation (see table below for study participants). A total of 112 subjects were enrolled in the investigation between June 26, 1989 and January 4, 1991. In four subjects, two distinct nonunion sites were treated concurrently, therefore accounting for 116 treated fractures.

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Inclusion Criteria

In order to be eligible for participation in the study, a patient must have had the following:

- a nonunion acquired secondary to trauma;
- no clinical or radiographic evidence of union at least nine months after the injury;
- no surgical intervention within the three months prior to enrollment;
- no radiographic evidence of healing within at least three months prior to enrollment as determined by an independent review panel composed of two orthopaedic surgeons and one musculoskeletal radiologist;
- radiographic evidence of skeletal maturity or at least 18 years of age.

Exclusion Criteria

Patients were excluded from participation in the study if:

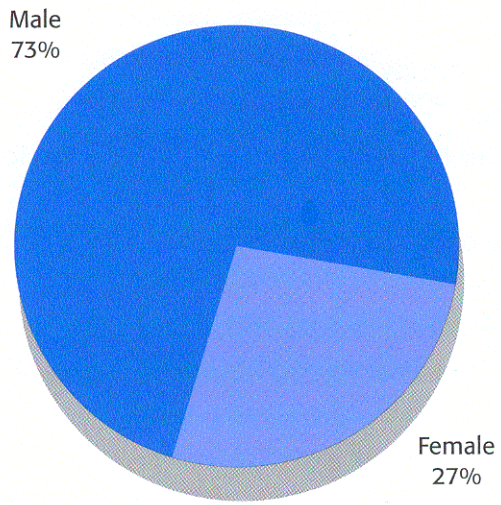
- written informed consent was not provided;
- a fracture gap greater than half the diameter of the bone existed in the bone to be treated;
- the fracture involved a vertebrae, flat bone or was a pathological fracture;
- a congenital or true synovial pseudarthrosis existed at the fracture site;
- the nonunion was due to a failed fusion of spine, skull or joint;
- there was a concurrent pregnancy (patient treatment was immediately discontinued if pregnancy occurred during participation in the study);
- the patient had a demand type pacemaker in proximity to the treatment site. This would include fractures of the upper extremities (hand, wrist, arm). Further screening by the attending cardiologist was recommended (such as with an electrocardiogram).

Criteria for Measuring Safety and Effectiveness

Toxicological studies on isolated cells, as well as on animals, were performed to evaluate the safety of combined static and dynamic magnetic fields. The studies showed that there were no significant adverse findings which could be associated with chronic exposure to the combined static and dynamic magnetic fields. Further, *in vitro* and *in vivo* studies were conducted to determine whether the application of these magnetic fields in animal models would stimulate bone healing and other related biological responses. The studies found that a combined static and dynamic magnetic field like the one produced by the OL1000 had a statistically significant stimulatory effect on bone healing. Other *in vitro* studies conducted on chick embryo femurs indicated a significant effect on bone development from the treatment of the combined magnetic fields.

Demographics

112 Patients 116 Fractures



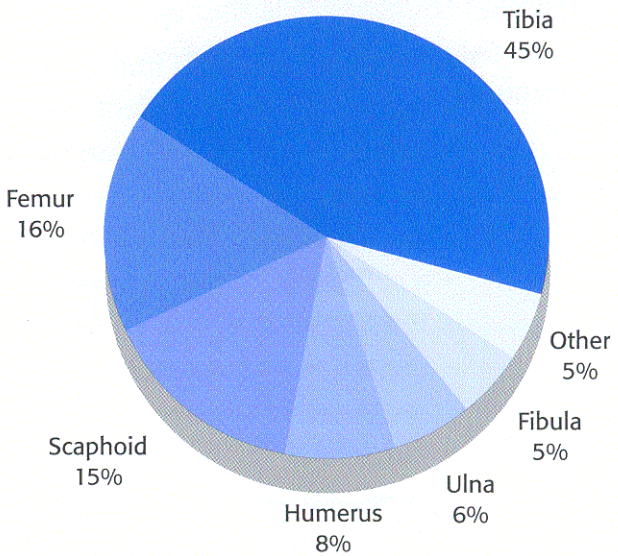
AGE

- **Mean = 38.2 years**
- **Range = 17.1 – 77.9 years**

WEIGHT

- **Mean = 175.5 pounds**
- **Range = 99.0 – 315.0 pounds**

Bones – 11 different bones were represented in the 116 fractures.



Tibia	**52**
Femur	**19**
Scaphoid	**17**
Humerus	**9**
Ulna	**7**
Fibula	**6**
Other	**6**
Malleolus	2
Radius	1
Metacarpal	1
Capitate	1
Metatarsal	1

Patients' History

Original Injury

- 47 Fractures (40.9%) had a low energy trauma
- 68 Fractures (59.1%) had a high energy trauma
- 1 Fracture history was unavailable

Time Since Original Injury

- Mean = 29.3 months
- Range = 8.5 to 256.0 months
- 64 patients had fractures less than two years post injury

Fracture Classification

- 48 Fractures (41.4%) were open
- 68 Fractures (58.6%) were closed

Fracture Configuration

- 51 Fractures (44.0%) were transverse
- 34 Fractures (29.3%) were oblique
- 22 Fractures (19.0%) were comminuted
- 7 Fractures (6.0%) were spiral
- 2 Fractures (1.7%) other

Displacement

- 53 Fractures (45.7%) were displaced
- 63 Fractures (54.3%) were non-displaced

Bone Location Effected

- 18 Fractures (15.5%) were in the proximal third
- 47 Fractures (40.5%) were in the mid third
- 44 Fractures (37.9%) were in the distal third

Fracture Gap Ratio

- Mean = 0.22 (SD = 0.14)
- Range = 0 to 0.82

Prior Surgical Procedures

- Mean = 2.5
- Range = 0 to 11
- 81.9% had 1 or more
- 18.1% had none
- Plating & Intramedullary Rod Placement 72 Fractures
- Bone Grafting 51 Fractures
- Debridement 49 Fractures
- External Fixation 33 Fractures

Healed Criteria

- Clinically no pain or motion at the fracture site.
- Three or more cortices bridged on radiograph.
- Final outcome verified by an independent review panel composed of two orthopaedic surgeons and one musculoskeletal radiologist.

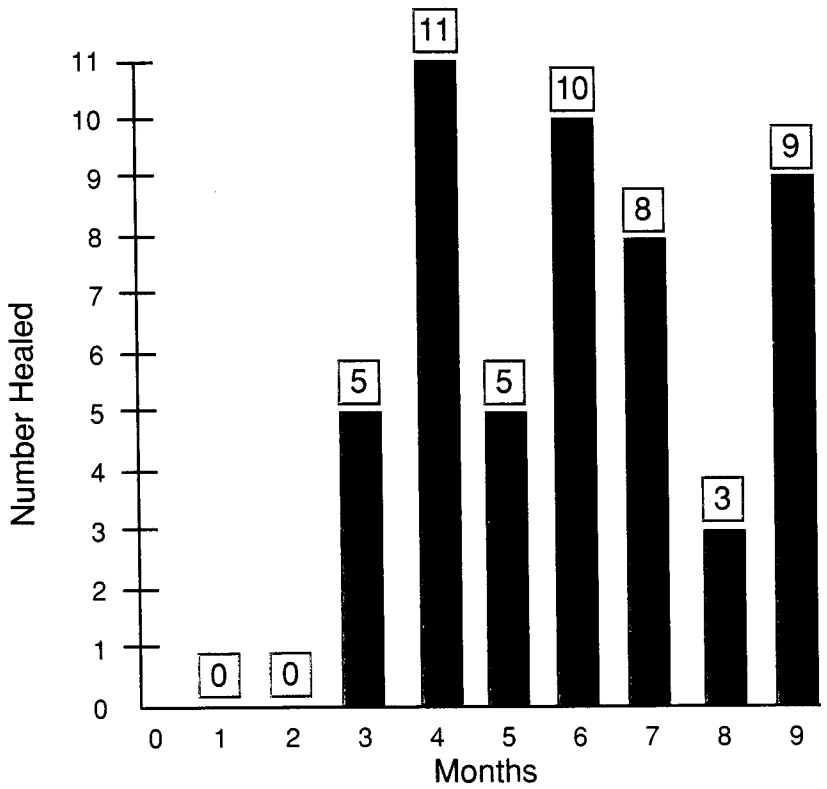
Results

Of the 112 patients who participated in the study, 48 (51 fractures) healed, 32 (33 fractures) did not heal, and 32 (32 fractures) did not complete their treatment. The study was closely monitored to assure patient compliance with monthly follow-ups.

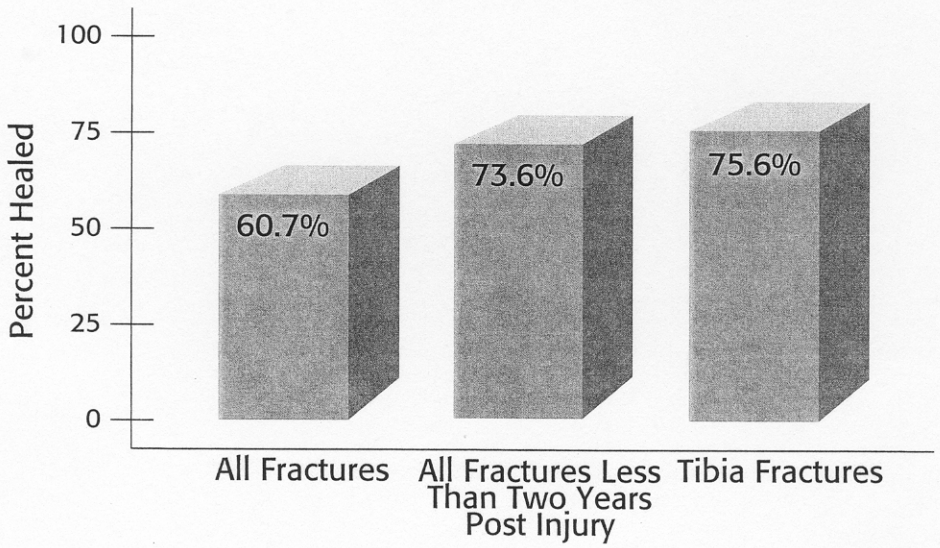
Thirty-two patients did not complete their treatment for the following reasons: 16 voluntarily withdrew; 5 were reported to be noncompliant; 8 withdrew due to study protocol violations; 1 was hospitalized for a pre-existing medical condition; 1 was incarcerated; and 1 geographically relocated and was unable to continue the study. Only 2 patients in this group subsequently had an amputation.

Of the 80 patients (84 fractures) with established nonunions who completed the treatment in this study, 48 (51 fractures) healed and 32 (33 fractures) did not heal. A nonunion was determined to be healed if three or more cortices were bridging the fracture gap based on radiographic assessment by an independent review panel, no motion was seen clinically at the fracture site, and no pain was associated with the fracture. Pain was assessed at rest, with the application of stress, and upon weightbearing (if applicable) at the nonunion site.

Average healed time: 6.0 months



NONUNION STUDY RESULTS



Conclusion

The overall success rate of 60.7% is clinically significant, given that no significant morbidity occurred with this device as compared to the morbidity and mortality associated with surgical intervention. In addition, it must be noted that many of the nonunions in this study were destined to undergo one or more additional surgical interventions, possible amputations, along with continuing disability and pain.

The results of the *in vitro* and *in vivo* nonclinical toxicological studies conducted with the OL1000 support its safety. The data obtained from the nonclinical *in vivo* studies further demonstrated the potential effectiveness of the OL1000 in humans. The findings from the multicenter clinical investigation provided assurance of the safety and effectiveness of the OL1000.

Of the 48 patients (51 fractures) with an established nonunion who completed the treatment and healed, **100% of the fractures were still healed 3 months post-treatment.**