

# Basic Research on a Cylindrical Implant Made of Shape-Memory Alloy for the Treatment of Long Bone Fracture

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**Abstract:** The internal fixing materials made from shape-memory alloys (SMAs) have recently been reported for long bone fracture. We present a new internal fixation technique using a cylindrical SMAs implant in a rat femoral fracture healing. The implant was designed in a shape to circumferentially fix the fractured bone using resilient SMA claws. To evaluate the fixing ability of the implant, three-point bending and rotation tests were performed. Fifteen female Wister rats were treated surgically as an experimental model. All rats were killed at 16 weeks postoperatively, and the radiological and histological evaluations were performed. In biomechanical test, the good fixation ability of the implant was demonstrated. In animal model, no cases of postoperative infection or death were encountered and postoperative gait was stable in all cases. Radiological examination at 16 weeks postoperatively demonstrated the implant firmly fixed to the fractured part, endosteal healing, and no callus formation in all cases. In Histological evaluation, bone union in all cases was characterized by endochondral ossification from within the medullary cavity. In conclusion, our cylindrical SMA implant provided good fixation in biomechanical tests, and achieved bone union in all 15 rats. If a larger size is designed in the future, our implant will be a clinically applicable, useful fixing material for fracture of the human long bones.

**Keywords:** Bone fusion, experimental study, fracture, implants, internal fixation, shape-memory alloys.

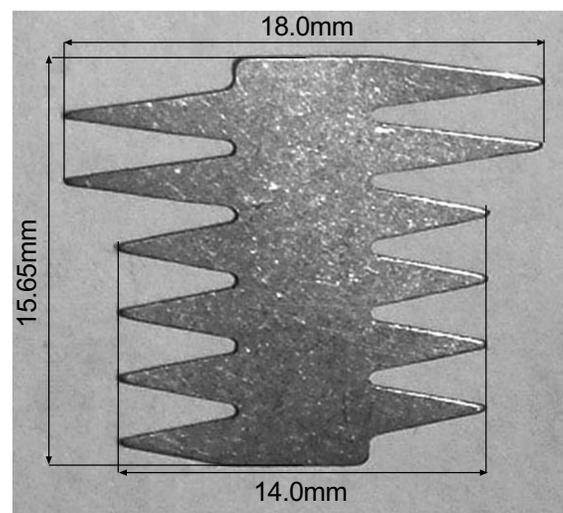
## INTRODUCTION

Shape-memory alloys (SMAs), or metals with both shape-memory and superelastic properties, are clinically applied in various surgical areas, including orthopedic surgery [1-8]. In 2003, we reported a method using superelastic SMA wires as intramedullary nails in the treatment of pathological fracture of a human femur due to metastatic bone tumors. However, if superelastic SMA wires are used as intramedullary nails in the treatment of normal traumatic fracture, the SMA nails cannot be extracted even after bone union is achieved, remaining in the body over a long period and raising concerns about nickel toxicity. We have thus developed a cylindrical SMA implant as an internal fixing material for fractures that combines three concepts: 1) a simple method based on the shape-memory effect of SMA; 2) removability after bone union; and 3) good fixation with potential clinical application. More specifically, the implant is designed in a shape like the existing Mennen plate, to circumferentially fix the fractured bone using resilient SMA claws.

We report herein the profile of this SMA implant and the results of biomechanical tests and an experiment in a rat fracture model, and discuss current problems and future tasks for the implant.

## METHODS

In the preparation of an implant for rat femurs, casting the implant with SMA is impossible, as the rat femur is too small. We therefore cut out an SMA shape (proximal width, 18 mm; distal width, 14 mm; length, 15.65 mm) with 6 pairs of alternating claws from 0.3-mm-thick forged Ti-Ni (Ti, 44.2 wt%; Ni, 55.8 wt%) plate material (Fig. 1), and



**Fig. (1).** SMA plate: We cut out an SMA shape (proximal width, 18 mm; distal width, 14 mm; length, 15.65 mm) with 6 pairs of alternating claws from 0.3-mm-thick plate material.

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prepared an implant that could circumferentially fix a rat femur according to the following procedure. First, the SMA piece was annealed at 500°C for 30 min, barrel-polished and inserted into a mold while being rolled up in hot water at 100 °C to form a cylinder. The cylinder was then quenched at 420 °C for 10 min to acquire a shape-memory effect of extending in ice water at about 0 °C and recovering the cylindrical shape at rat body temperature (about 36 °C) (Fig. 2). After removal from the mold and washing with acid, the SMA shape was sterilized with ethylene oxide at 60 °C for 15 min. Phase transformation temperatures were set at -3.6 °C for transformation starting temperature (Ms), 0.5 °C for transformation final temperature (Mf), 17.5 °C for adverse transformation starting temperature (As) and 30.0 °C for adverse transformation final temperature (Af). This cylindrical SMA implant is changed from first extended shape to final closed one for 10 minutes at about 36 °C (Fig. 2).

*In vitro* and *in vivo* analysis was performed in this study. One was biomechanical testing of construct using extracted rat femurs. The other was *in vivo* study for 16 weeks.

### Biomechanical Tests

To evaluate the fixing ability of the implant, three-point bending and rotation tests were performed using rat femurs at expected rat body temperatures, i.e., at room temperatures

of 37-39°C. To obtain test materials, unfractured left femurs were extracted from euthanized rats. Test materials were carefully separated from soft tissues such as muscles, and fixed in resin to the respective test jigs.

### Three-Point Bending Test

A tabletop-type universal testing machine (Little Senstar®; Tokyo Testing Machine, Tokyo, Japan) was used for 3-point bending tests (Fig. 3). With the power point placed in the middle of the femoral shaft, tests were performed with a gauge length of 40 mm and crosshead speed at 0.2 mm/min. Maximum displacement was defined at a point when a normal femur was macroscopically fractured or the implant was obviously dislodged from the bone. Two test models were prepared: a normal rat femur (normal model); and rat femur transversely fractured in the middle of the shaft and then fixed with the cylindrical SMA implant (implant-fixed model). These models were individually tested, and the load (bending force) at maximum displacement was measured.

The normal model developed a fracture with a load of 300 N·mm at a displacement of 2.7 mm, whereas the implant-fixed model showed no implant dislodgement or dislocation of the fractured part even at maximum displacement (Fig. 4). Moreover, the load applied at maximum displacement was 300 N·mm on the normal

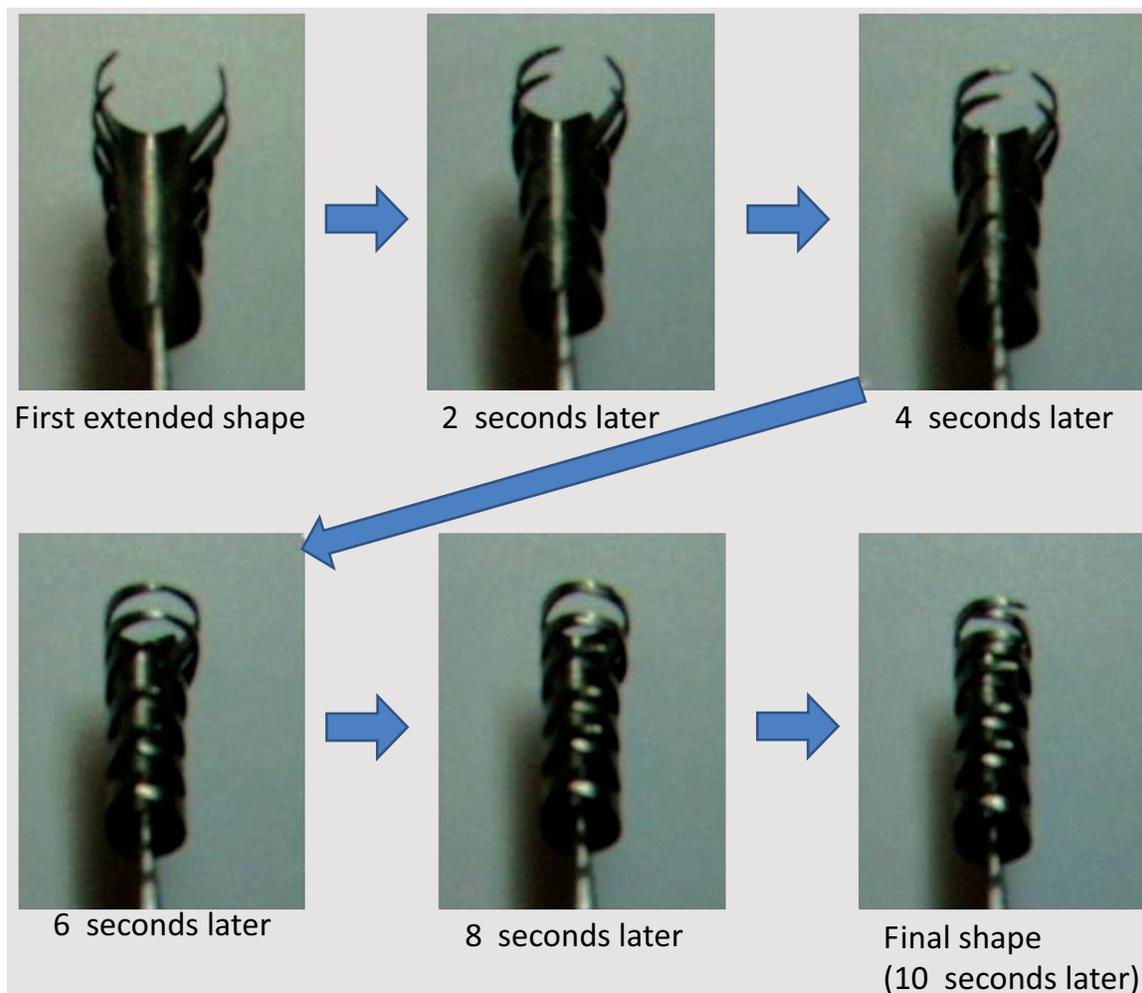
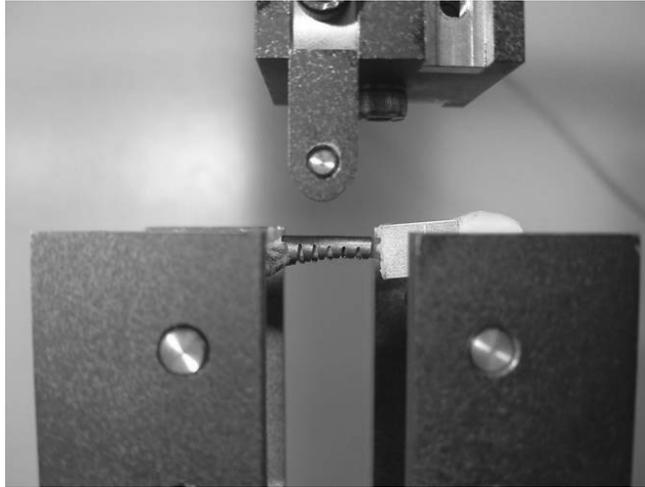
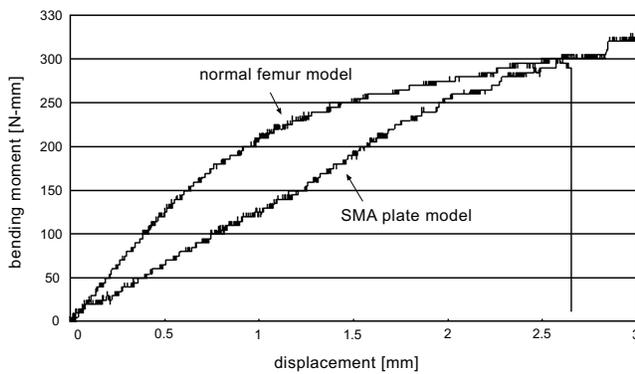


Fig. (2). Shape memory effect of the cylindrical implant.

model, and 290 N·mm on the implant-fixed model, demonstrating that the implant-fixed model could endure shearing stress large enough to cause fracture in a normal femur.



**Fig. (3).** Three-point bending test machine: SMA implant-fixed model was installed in an examination machine.

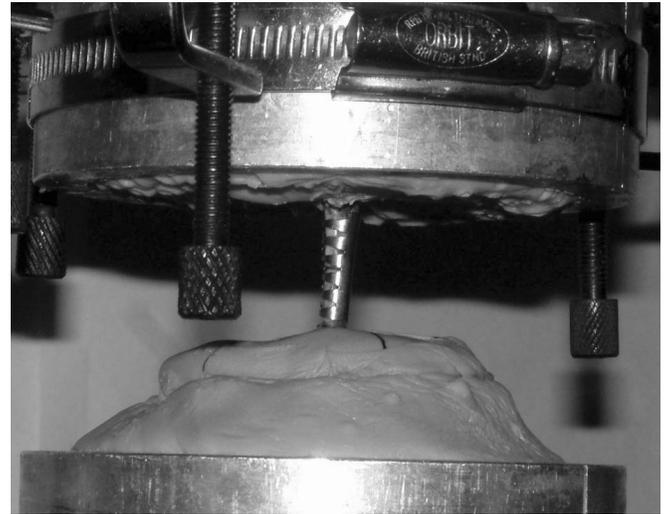


**Fig. (4).** Result of three-point bending test.

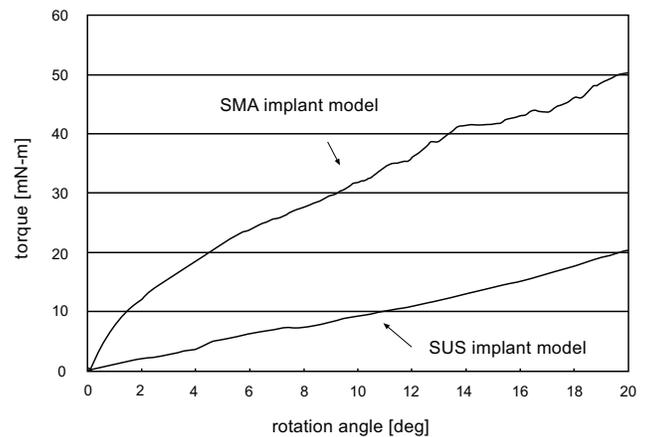
### Rotation Test

An autograph (AG-G; Shimadzu, Kyoto, Japan) was used for rotation tests (Fig. 5). To evaluate SMA-derived fixation against rotating stress, a stainless-steel implant (SUS implant) was prepared in the same configuration as the SMA implant described above. Two rat femur models, one transversely fractured in the middle of the shaft and then covered with the SMA implant, and the other forcibly attached with the claws of the SUS implant using pliers, were prepared to compare fixing ability against rotating stress between the two types of implants. These models were tested using a gauge length of 20 mm, crosshead speed at 7.2°/min, and a maximum rotating angle of 20°, and torque (bending moment) against the rotating angle was measured. In addition, torsion stiffness at maximum rotating angle was calculated according to a report by White *et al.*, and compared between models.

The SMA implant model was able to endure a larger torque than the SUS implant model at the same rotating angle (Fig. 6). Furthermore, torsion stiffness at maximum rotating angle was 2.5 mN·m/degree on the SMA implant model, and 1.1 mN·m/degree on the SUS implant model, indicating superior fixing ability of the SMA implant.



**Fig. (5).** Rotation test machine: SMA implant-fixed model was installed in an examination machine.



**Fig. (6).** Result of rotation test.

### In Vivo Analysis

#### Methods

Fifteen female Wister rats (mean age, 11.4 weeks; range, 11-12 weeks; mean body weight, 244.0 g; range, 234-267 g) were used as an experimental model. Following the introduction of inhalation anesthesia (diethyl ether), all rats were intraperitoneally anesthetized with 5 mg/100 g of pentobarbital sodium. After shaving the hair from the right thigh and disinfecting with povidone-iodine, surgery was performed with the animal in the left lateral decubitus position. A fracture model was prepared by linearly incising the skin for about 3 cm along the axis of the right femur, incising the fascia of the tensor fascia lata muscle, conservatively peeling the muscle away from the entire circumference of the right femur, and cutting the femur in the middle of the shaft using a T-saw (Medtronic Sophomor Daneck, Tokyo, Japan). A cylindrical SMA implant was allowed to extend in sterilized saline at 0 °C, then was applied to the manually reset femur to fix the fractured part using the shape-memory effect. Finally, the implant was covered with the muscle, and the fascia and skin were sutured to complete the operation. The awakened rats were allowed to freely exercise in a cage until being euthanized at

16 weeks old. Right femur were extracted and fixed in 5% formalin. Three end points were designated: length of the operation; radiological evaluation at 16 weeks postoperatively; and histological findings. The experiment was performed with the approval of the ethics committee at Mie University Faculty of Medicine.

#### Length of the Operation

To evaluate the simplicity of surgical techniques, the time required for setting the bone with the SMA implant was measured as the time from creation of the femoral fracture to fixation with the implant.

#### Radiological Evaluation

Plain radiography (front and lateral views) of the femur was performed following euthanasia at 16 weeks postoperatively. Radiographs were examined by two independent investigators for any dislodgment or malalignment of the implant. Any malalignment with an angle  $\geq 5^\circ$  between axes of the proximal and distal parts of the femur was regarded as abnormal.

#### Histological Evaluation

The femur with the implant was fixed in 5% formalin. After completion of fixation, the femur was embedded in resin and cut in half along the length of the implant using a refine cutter. The two halves of the femur were separated from the implant, decalcified in 5% formalin, and embedded in paraffin. Then, 30- $\mu\text{m}$  sections of femoral tissue were prepared and stained using hematoxylin and eosin and safranin-O. In histological observations, any continuity of the bone cortex was regarded as an indication of bone adhesion, and periosteal thickness was measured at three femoral points (Fig. 7) for the purpose of statistical comparison. Statistical analyses were conducted using Student's *t* test at the 5% significance level.

### RESULTS

Mean time required for setting the bone with the SMA implant was 92 s (range, 35-124 s). No cases of postoperative infection or death were encountered and postoperative gait was stable in all cases. Radiological examination at 16 weeks postoperatively demonstrated the implant firmly fixed to the fractured part with no obvious dislodgment, malalignment or loose plate in all cases (Fig. 8a, b). No cases were regarded as abnormal by both investigators. Histological observation revealed that all cases

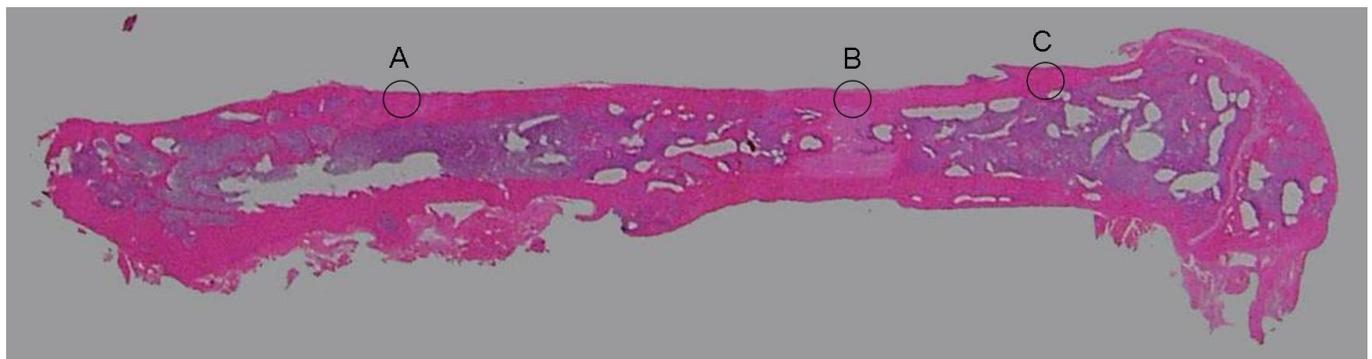
showed cross-linkage in the fractured part, indicating successful bone union. Bone union in these cases was characterized by endochondral ossification from within the medullary cavity, as well as membranous ossification localized to the subperiosteal region near the fractured part. The fractured part displayed proliferation of osteoblasts and chondrocytes, along with neovascularization, and conversion of these cells into osteocytes (Fig. 9). Chondrocytes, stained in red by safranin-O, were detected around osteocytes (Fig. 10). Measurement of the periosteal thickness showed no significant differences between regions covered and not covered by the implant (Table 1).

### DISCUSSION

SMA's have gradually become common as materials in internal fixing implants for fractures such as bone-setting plates, intramedullary nails and staples [1-4]. Musialek *et al.* described the usefulness of SMA implants based on favorable clinical results from the use of SMA clamps in 64 patients with small bone fractures [3]. Da *et al.* reported satisfactory bone union achieved using interlocking intramedullary SMA nails for tibial and femoral fractures [2]. Previously reported SMA materials for internal fixing of fractures have mostly been designed as nails, wires, clamps or staples, and few reports have described cylindrical implants such as the one we have developed. Our cylindrical implant provides SMA-derived persistent resilience, ensuring good fixation even if shearing stress is applied to the plate. As demonstrated in the present study, our implant only requires basic surgical techniques and can achieve relatively good bone fusion, and is thus highly expected to prove clinically applicable.

Periosteal stripping was considered as a potential risk factor of non-union due to insufficient blood supply [9]. Minimally invasive plate like locking plate was recommended in the surgical treatment of femur fracture recently [10]. SMA has the same advantage to fix the fracture rigidly without periosteal stripping as locking plate. Additionally, setting the bone with SMA implant only required 92 seconds in this study. Shortening operation time means low infection rate, less tissue damage and blood loss.

Before conducting the present study, we were concerned that continuous compression due to the persistent resilience of the SMA implant might adversely affect the bone, particularly the periosteum. Measurement of periosteal



**Fig. (7).** Histological longitudinal section through the rat femur at 16 weeks postoperatively (magnification  $\times 1$ , hematoxylin and eosin staining): A, region proximal to implant; B, near the fractured part; C, region distal to implant.

thickness at two points not covered by the implant (i.e., proximal and distal regions of the femur) and one point immediately below the implant showed no significant differences. However, healing of the fracture was mostly achieved by endochondral ossification from within the medullary cavity, and involved little membranous ossification localized to the subperiosteal region near the fractured part. This suggests the possibility that the SMA-derived resilience or the circumferentially covering implant might adversely affect the periosteum.

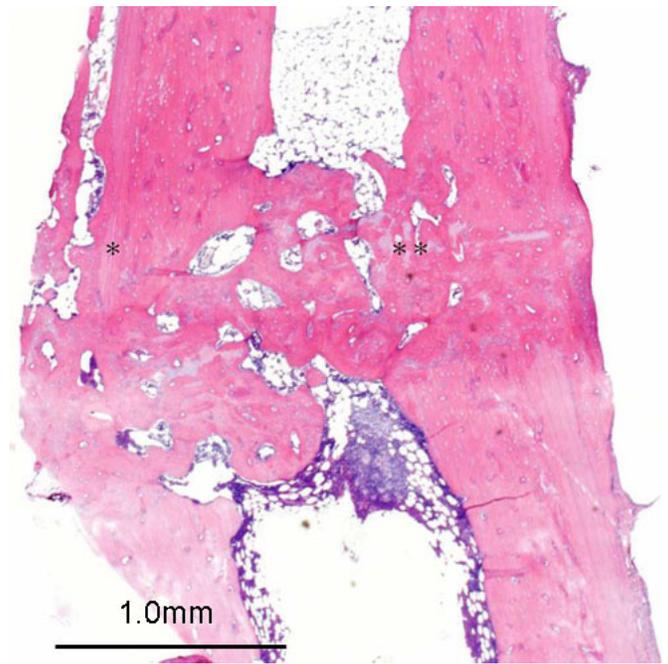
(a)



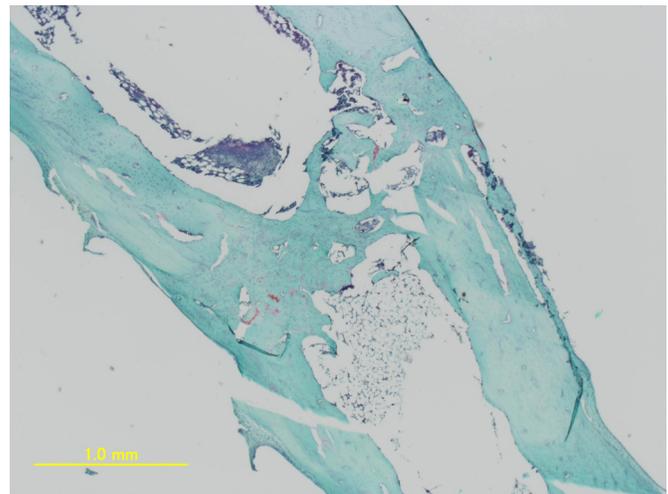
(b)



**Fig. (8).** Plain radiography of the rat femur at 16 weeks postoperatively: anteroposterior view (a) and lateral view (b).



**Fig. (9).** Histological longitudinal section through the rat femur at 16 weeks postoperatively (magnification  $\times 40$ , hematoxylin and eosin staining): membranous ossification in the subperiosteal region(\*) and the primary fusion from endochondral ossification which were displayed proliferation of osteoblasts, chondrocytes and neovascularization (\*\*).



**Fig. (10).** Histological longitudinal section through the rat femur at 16 weeks postoperatively (magnification  $\times 20$ , safranin-O staining): Chondrocytes which were stained in red were detected around fractured part.

**Table 1. Periosteal Thickness**

Region	A	B	C
Periosteal Thickness ( $\mu\text{m}$ )	221 $\pm$ 35	180 $\pm$ 40	205 $\pm$ 26

Statistical differences were not showed among three regions.

There are some prospective concerns regarding the toxicity of Ni contained in the SMA, including carcinogenesis [11,12], toxicity in bronchitis or dermatitis [13], and adverse effects on bone modeling [14]. Wever *et*

*al.* [15] reviewed cytotoxic, allergic and genotoxic activities of Ti-Ni alloy, and concluded that Ti-Ni alloy was safe for surgical use. However, absolute risk of Ti-Ni alloy is not well-known, and therefore, Ti-Ni alloy implants are thought to be removed as soon as possible after bone union.

Limitations of our study included: 1) short follow-up extending only to the 16 weeks postoperatively; 2) a relative lack of bone union in the osteosynthesis process with our implant. Regarding the first point, endochondral ossification was histologically observed at 16 weeks postoperatively, indicating that conversion of chondrocytes into osteocytes was incomplete, and suggesting the necessity of a longer follow-up. As for the second point, since we expect that an implant not circumferentially covering the fractured part will facilitate bone union, improvement of the implant configuration represents one of our tasks for the future. In view of the potential clinical applications, we also admit the necessity of evaluating the implant in an experiment with larger animals than rats.

### CONCLUSION

Our cylindrical SMA implant provided good fixation in biomechanical tests, only required basic surgical techniques, and achieved bone union in all 15 rats. If a larger size is designed in the future, our implant will be a clinically applicable, useful fixing material for fracture of the human long bones.

### ACKNOWLEDGEMENT

Declared none.

### CONFLICT OF INTERESTS

The authors declare no conflict of interest. The manuscript submitted does not contain information about medical device(s)/drug(s). No funds were received in support of this work. No benefits in any form have been or will be received from a commercial party related directly to the subject of this manuscript.

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