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Comparison of the bone modeling effects caused by curved and straight nickel–titanium intramedullary nails

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Nitinol (NiTi) shape memory metal alloy makes it possible to prepare functional implants. A curved intramedullary NiTi nail has been shown to cause bending of the bone, bone thickening, increase in cortical area, and reduction in bone longitudinal growth. The purpose of the present study was to find out whether these changes are caused by the bending force of the curved nail or by the intramedullary nailing itself. Pre-shaped intramedullary NiTi nails were implanted in the cooled martensitic form into the medullary cavity of the right femur in 12 rats, where they started to restore their austenitic form, causing a bending force. Straight nails were used as controls in another 12 rats. After 12 weeks, the operated femurs were compared with their non-operated contralateral counterparts and the differences were compared between the groups. Anteroposterior radiographs demonstrated bone bowing only in the curved nail group. Retardation of longitudinal growth was observed in both groups, showing that the growth effect seems to be due to the intramedullary nailing itself. Increase in bone cross-sectional area and cortical thickness were found in both groups. However, this increase was more evident with the curved nail, indicating that the bending force of the functional nail seems to induce these changes.

1. Introduction

Nitinol (NiTi) is a promising implant material, whose biocompatibility has been shown to be good [1–6]. Because of its shape memory property, NiTi makes it possible to prepare functional implants which are activated at body temperature. Recently, functional NiTi rods have been experimentally studied for their ability to correct scoliosis [7, 8].

In this study, we fabricated a functional intramedullary nail that was used to apply controlled bending force to bone. Cooling down to the martensitic phase enables insertion of the shaped nail into the medullary cavity. At body temperature, the nail begins to regain its original shape, causing a bending force inside the bone. Bone has been shown to have an ability to respond to mechanical forces and to gradually change its external geometry and internal structure, a phenomenon called bone modeling [9–15]. In our preliminary study, we showed that bone modeling can be controlled using a curved intramedullary NiTi nail [16]. In addition to the bowing of bone, thickening of bone and increase in the cortical cross-sectional area (CSA) and cortical thickness (CtTh) were observed. Reduction in bone longitudinal growth and changes in cortical bone mineral density (BMD) were also observed. The purpose of the present study was to find out if these changes are caused by the bending force effected by the curved nail or if they are due to the intramedullary nailing itself.

2. Materials and methods

2.1. Implants

We fabricated a set of pre-shaped intramedullary NiTi nails (length 25 mm, thickness 1.3 mm) with a curvature radius of 25 mm and a set of straight intramedullary NiTi nails (length 25 mm, thickness 1.4 mm). The material used was NiTi (55.7% Ni and 44.3% Ti by weight) melted in a vacuum high-frequency furnace. To fabricate a wire of 1.3 mm in diameter, the ingot was hot-rolled followed by cold drawing accompanied by intermediate

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annealing. The initial round pieces for implants of curvature radii of 25 mm were made by constraining the wires in special mandrels while annealing at 450 °C. After surface finishing, the ultimate intramedullary nails 25 mm in length and 1.3 mm in thickness were cut. The chemical compound and the technological itinerary of the alloy resulted in implants that could be deformed at about 0 °C (fully martensitic state) and that restored their initial shape at about 25–30 °C (fully austenitic state). The implants were finally degreased with 70% ethanol, washed in an ultrasonic vibrobath, and autoclaved (30 min, 121 °C).

2.2. Animals

Twenty-four male Sprague Dawley/MOL rats (Laboratory Animal Center, University of Oulu, Finland) were utilized as an animal model and randomized into two groups, each consisting of 12 rats. Their ages ranged between 11 and 12 weeks. The mean weight ($\pm$ SD) was 384 ± 28 g in the study group and 392 ± 24 g in the control group. The animals were housed in groups of 4–6 in Macrolon IV polycarbonate cages in a thermostatically controlled room at 20 ± 1 °C with a relative humidity of $50 \pm 10\%$. The room was artificially illuminated with 12 h of light and 12 h of darkness. Aspen chips (Fintapway, Finland) were used as bedding. Pelleted rat feed (SDS R3 (E), Special Diet Services Ltd., Great Britain) and tap water were available *ad libitum*. The animal tests were performed after approval by the ethical committee of the University of Oulu. All aspects of animal care complied with the Animal Welfare Act and the recommendations of the NIH-PHS Guide for the Care and Use of Laboratory animals.

2.3. Surgical procedure

The animals were unilaterally operated for intramedullary nailing as previously described [16]. Briefly, the rats were anesthetized and the nails were surgically implanted into the medullary canal of the right femur via medial parapatellar arthrotomy and lateral dislocation of the patella. The medullary canal was approached distally via a hole drilled through the intercondylar notch and reamed carefully using an 18-gauge needle with rotating motion. All nails and all instruments used during the implantation were submerged in sterile iced saline to reach and maintain the martensitic form of NiTi throughout the implantation process. The nails were allowed to settle in an incidental position. The patella was relocated, the extensor mechanism was reconstructed, and the wound was closed in layers using resorbable sutures (Vicryl®, Ethicon, Inc., Somerville, New Jersey). The limb was checked for normal post-operative motion of the knee joint. Buprenorphin 0.3 mg/kg s.c. (Temgesic® 0.3 mg/ml, Reckitt & Colman Pharmaceuticals, Inc, Richmond, England) was used as a postoperative analgesic. The rats were allowed to move freely in their cages after the operation with no external support and were observed daily for activity and weight bearing on the operated limb. The rats were killed using carbon dioxide at 12 weeks after the implantation. All femurs with implants were dissected, as were also the contralateral femurs. The bones were fixed in 10% buffered formalin. The lengths of both the operated and the control bones were measured using a digital vernier caliper. The mean of three measurements was used in the calculations.

2.4. Radiography

Standard plain radiographs of the dissected bones were taken in anteroposterior (AP) and lateral projections. The radiographs were digitized on a light table with a ccd camera (Dage MTI 72E, Dage-MTI, Inc., Michigan City, IN, USA) using a Micro Nikkor 55 mm objective (Nikon, Tokyo, Japan). The angle between the distal articular surface and the long axis of the femur (a line drawn from the intercondylar space to the end of trochanter major) was measured from AP radiographs using a digital image analysis system MCID M4 with the software version 3.0, rev. 1.1 (Imaging Research, Inc., Brock University, St. Catharines, Canada). The mean of three measurements was used in the calculations. The main bending direction of the nail was visually observed from the radiographs, and the main direction in the AP radiographs was considered the positive angle.

2.5. pQCT densitometry

After radiography, the nails were removed for 3D densitometry by excavating the necessary amount of bone around the distal end of the femur to expose the tip of the nail and to allow the nail to be grasped with forceps and pulled out. The bones with implants and all the instruments were submerged in iced saline to reach the martensitic state of NiTi before removal of the nail. The whole femur was scanned with a peripheral quantitative computed tomography (pQCT) system, Stratec XCT 960A, with the software version 5.20 (Norland Stratec Medizintechnik GmbH, Birkenfeld, Germany). The bone was inserted with the anterior surface upwards into a plastic tube adapter for measurement. Forty consecutive cross-sections with a slice distance of 1 mm and voxel size of $0.148 \times 0.148 \times 1.25\,\text{mm}^3$ were measured, adjusting the first scan line at the distal end of the femur. The maximum axial scanning length of the pQCT device is only 30 mm. Therefore, the sample adapter was axially moved after 20 cross-sections, to enable all the 40 scans. Total cross-sectional area (Tot A), CSA, CtTh and cortical BMD were measured by using an attenuation threshold of $0.93\,\text{cm}^{-1}$ to define cortical bone.

2.6. Statistics

Statistical analysis was done by using the SPSS software, ver. 10.07 (SPSS Inc., Chicago, IL, USA). The differences between the nailed femur and the control femur of each rat were calculated for all parameters. The mean differences in femoral length and articular surface angle were calculated. The mean differences in Tot A, CSA, CtTh and BMD were calculated both slice by slice and for the average difference of all slices from the diaphysis of the femur. Slices number 1–6 from the distal end were excluded from statistical analysis because of the defect due to nail removal. The caput of the femur was also excluded, having the next slice to the caput to be the last slice included. To compensate for the differences in bone size between the nailed and the control bones, 25 anatomically equal slices, starting from the distal and proximal ends of the diaphysis, were defined for statistical analysis. The differences between the operated and contralateral femurs were tested versus zero by one-sample t-test, to evaluate the statistical significance of all changes. These differences were also used in compairment between the two groups. The independent samples t-test was used here to evaluate the statistical significance. Values $p < 0.05$ were considered significant.

3. Results

No rats died during the experimental period. No adverse effects were seen after the arthrotomies. Significant retardation of longitudinal growth was observed after the insertion of both curved and straight nails compared to the contralateral normal femurs (Table I). Femoral length decreased by an average of 4.5% in the curved nail group ($p < 0.001$) and by 5.1% in the straight nail group ($p < 0.001$). There were no significant differences between the two groups. The rats in the curved nail group weighed less by an average of 21 g at the end of the study compared to the straight nail group ($p = 0.021$) (Table I).

3.1. Radiography

The AP radiographs demonstrated significant bowing in the femurs with a curved nail, as indicated by the angle between the distal articular surface and the long axis of the femur averaging 3.3° ($p = 0.026$) (Table I). The straight nails showed a 1.1-degree bending of the bone in the direction opposite to that in the study group compared to the contralateral normal femur, but the result was not significant (Table I). In some of the cases, there was also some posterior bending of the nail in lateral radiographs. The bending of bones into this direction was not measured, however, because most cases involved no bending of the nail into this direction at all, although turning of the nail inside the femoral cavity over time might be possible.

3.2. pQCT densitometry

Quantitative densitometry showed a statistically significant overall increase in Tot A, CSA, and CtTh in the femurs nailed with bent nails compared to their non-operated contralateral counterpairs, when calculated from the whole set of slices (Table I). These changes were most obvious in the mid-diaphyseal area. The femurs with a straight nail also showed some increase in Tot A, CSA, and CtTh, but these changes were smaller and only significant in the midmost diaphyseal slices, with no significant change in the means of the whole set of slices. Only minor changes in overall BMD were observed in both groups. However, there was a statistically significant increase in BMD in most distal slices in both groups and a slight overall increase in the BMD of the bones operated with straight nails (Table I). The changes in CSA, CtTh and BMD measured slice by slice along the diaphyseal axis are shown in Fig. 1.

4. Discussion

Previously, we have found that bone modeling can be controlled using a functional intramedullary NiTi nail [16]. Here, we found similar bone bowing in femurs with curved nails. As expected, the straight nails showed no significant bowing of the bone. This confirms that the bending force caused by the nail rather than the factors associated with intramedullary nailing itself induces this bone modeling effect. The average bowing in this study was 3.3°, while in the earlier study it was 6.7°. There was remarkable individual variation in the bowing angle between the rats. This is partly because of the different positions of the nail inside the femoral cavity, which produces variable forces in the AP plane, in which the radiographs were taken. As in the previous study, there was a trend towards more bending when the nail crossed the epiphyseal plate, while the nails inserted deeper into the medullary cavity caused less bowing of the bone. In this study, most of the nails were inserted deep into the medullary cavity, thus producing less bending. The nails used here were also 1 mm shorter than those in the previous study, producing less bending force.

In our previous study, significant retardation of longitudinal growth in the femur operated with a curved intramedullary nail was observed [16]. It remained unclear if this effect was induced by the bending force caused by the curved nail or the nailing itself. In the current study, significant retardation of longitudinal growth was observed with both curved and

TABLE I The effect of a 12-week treatment with a curved or straight intramedullary NiTi nail on rat femur. The differences between the operated and contralateral femurs are given for femoral length, articular surface angle and densitometry parameters. The increase of Tot A, CSA, CtTh, and cortical BMD as an average of the whole set of 25 pQCT scans along the femoral diaphysis. The operated femur compared to the contralateral femur

	Curved nail	p	Straight nail	p
N	12		12	
Weight gain (g)	96 ± 21		117 ± 22	
Femur length	− 4.5%	< 0.001	− 5.1%	< 0.001
Articular surface angle (degrees)	− 3.3	0.026	1.1	N.S.
Densitometry				
Tot A	5.4%	($p = 0.001$)	3.5%	($p = 0.326$)
CSA	8.5%	($p < 0.001$)	5.6%	($p = 0.067$)
CtTh	6.7%	($p < 0.001$)	4.6%	($p = 0.062$)
BMD	0.4%	($p = 0.245$)	1.1%	($p = 0.016$)

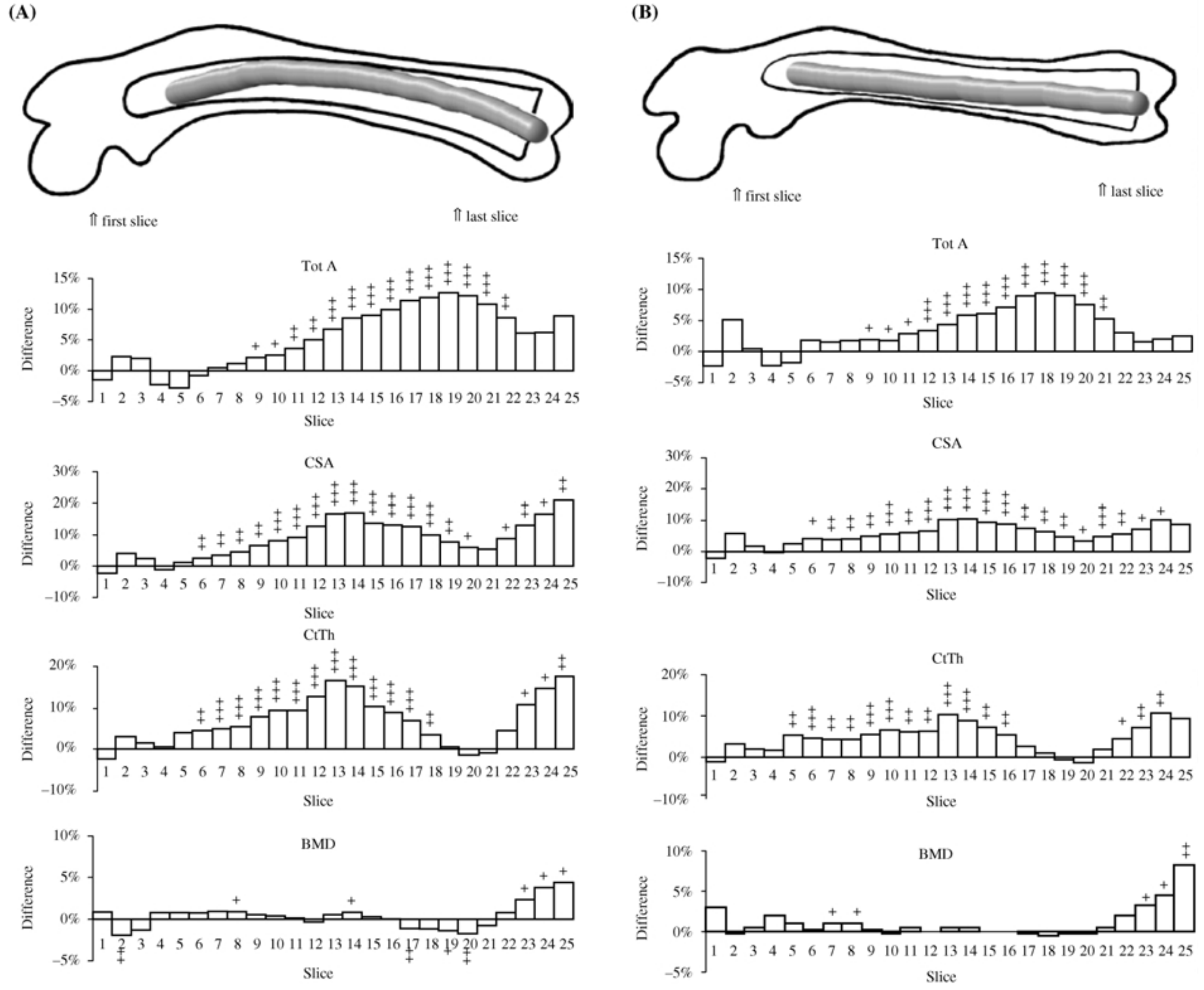

Figure 1 Percentage differences in mean Tot A, mean CSA, CtTh, and BMD as measured from 25 pQCT scans along the femoral diaphysis. (A) The femur operated with a functional intramedullary NiTi nail compared to the contralateral non-operated femur ($N = 12$). (B) The femur operated with a straight intramedullary NiTi nail compared to the contralateral femur ($N = 12$). $+p < 0.05$, $++p < 0.01$, $+++p < 0.001$.

straight nails. This indicates that the growth effect seems to be due to the intramedullary nailing itself rather than the bending force. This effect might be caused by some damage in the epiphyseal growth plate during nailing. In a prior study with 1.8–2.0 mm thick steel pin intramedullary fixation with nailing from the distal to the proximal direction, growth retardation was also observed [17]. In another study, where the nail was implanted from a proximal to a distal direction, with the nail entering the bone via the trochanteric groove, no differences in bone length were seen [18].

The increases in bone cross-sectional area and cortical thickness, which was also seen in the previous study [16], were present in both the curved and the straight nail groups of this study. However, this increase was more clearly seen with the curved nail, indicating that the bending force of the functional nail seems to primarily induce these changes. Stress shielding, i.e. the implant taking over part of the load that would normally be carried by the bone [13, 19–21], can be presumed to be present in femurs nailed with both curved and straight nails. In our preliminary study, BMD showed a statistically significant decrease in the proximal slices and an increase at the distal end. In the present study, a significant increase in BMD was observed in the distal end of the diaphysis in both groups, but the changes were smaller than in the previous study. According to the present results, it seems that only minor changes in BMD were seen after intramedullary nailing with a NiTi intramedullary nail. The reason might be that Niti has an elastic modulus closer to that of bone than any other metal, which decreases the stress shielding effect compared to the other implant metals [22–24].

The geometry of bone is the result of functional adaptation to normal physiological loads [9, 10]. It has been shown that bone also adapts to externally applied forces [11–15]. This process is called adaptive bone modeling [25–27]. Experiments suggest that adaptive bone modeling is sensitive to dynamic but not to static strain changes, the latter producing an effect similar to disuse [12, 28, 29]. As the leg was not immobilized, the normal weight-bearing activity by the rat also produced a dynamic strain in both groups [30–32]. The curved nail caused a static strain inside the rat femur, which was not present in the femurs nailed with straight nails [19–21, 26, 27]. Presumably, the final adaptive bone modeling reaction seen with curved nails was due to the combined effect of an osteogenic response to the static strain and stress shielding caused by the nail, and the dynamic strain caused by weight bearing.

In future studies, the effect of the nailing direction should be studied. Proximal to distal nailing would spare the growth plate and presumably solve the growth retardation problem observed here. The possibility of using a functional NiTi nail to straighten a deformed bone caused by a fracture or osteogenesis imperfecta in the future is a tempting idea, as it would save the patient from large cortical osteotomies with a cast, internal fixation, or external fixation [33–36].

As a conclusion, bone bowing was observed after intramedullary nailing with a curved functional NiTi nail. Both curved and straight nails caused similar retardation of growth. The bending force of the curved nail resulted in more evident bone thickening and increase in cortical area of the femur.

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