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Introduction

Osteoporosis is a chronic systemic metabolic disease[1-3]. It is caused by a hormone imbalance that breaks down more bone faster than it is created. This reduces the volume of bone in the tibial compartment and its strength. In the United States, 54% of people over 50 years of age have osteoporosis or osteopenia[3]. Loss of bone quality and volume leads to bone fractures that are often treated with orthopedic implants. Securing and stabilizing load-bearing implants is difficult in osteoporotic patients, leading to more pain and revision surgeries.

This article by Kang et al. explores the influence of titanium nanotubes on the biology of osteoporotic bone through cell culture studies and an ovariectomized (OVX) rat model[2]. The removal of the female hormones (ovaries) mimics the post-menopausal state in humans, leading to the loss of bone volume and strength. The authors utilize titanium nanotubes to create a tunable size range of nanotubes[2,5]. The varying sizes of nanotubes demonstrate specific biologic influences on osteoblasts, osteoclast formation, and bone formation around implants[2,4-6].

Methods

Female rats were ovariectomized (OVX model) at six months, either representing the osteoporosis scenario, or received a mock surgery (control model) and allowed to recover for one month. Titanium implants, 0.8 mm diameter pins with machine finished control, and 90 nm nanotube surfaces, were implanted into the upper tibial compartment of the knee. The opposite knee was left alone as a control for bone loss. After two months post-implantation, the rats were sacrificed and tibias were imaged with micro-CT scans. Scans collected information on trabeculae parameters including mean connectivity density (Conn. D) and trabecular numbers (Tb. N).

Results

Control animal micro-CT imaging shows the baseline level of bone that should be in the upper tibial compartment containing cancellous bone compared to the OVX model, Figure 1A. The OVX model shows significant bone loss without any implant. The micro-CT cross section of titanium control shows bone loss relative to the nanotube surface at two months post-implantation in an OVX model, Figure 1B. The nanotube surface has significantly more connective density and trabecular thickness, Figure 1C. The control and nanotube surfaces have similar number of trabeculae. There is more non-boney space in the trabecular bone surrounding the control surface in the tibial compartment. Histology shows more collagen surrounding the nanotube implants, Figure 1D.

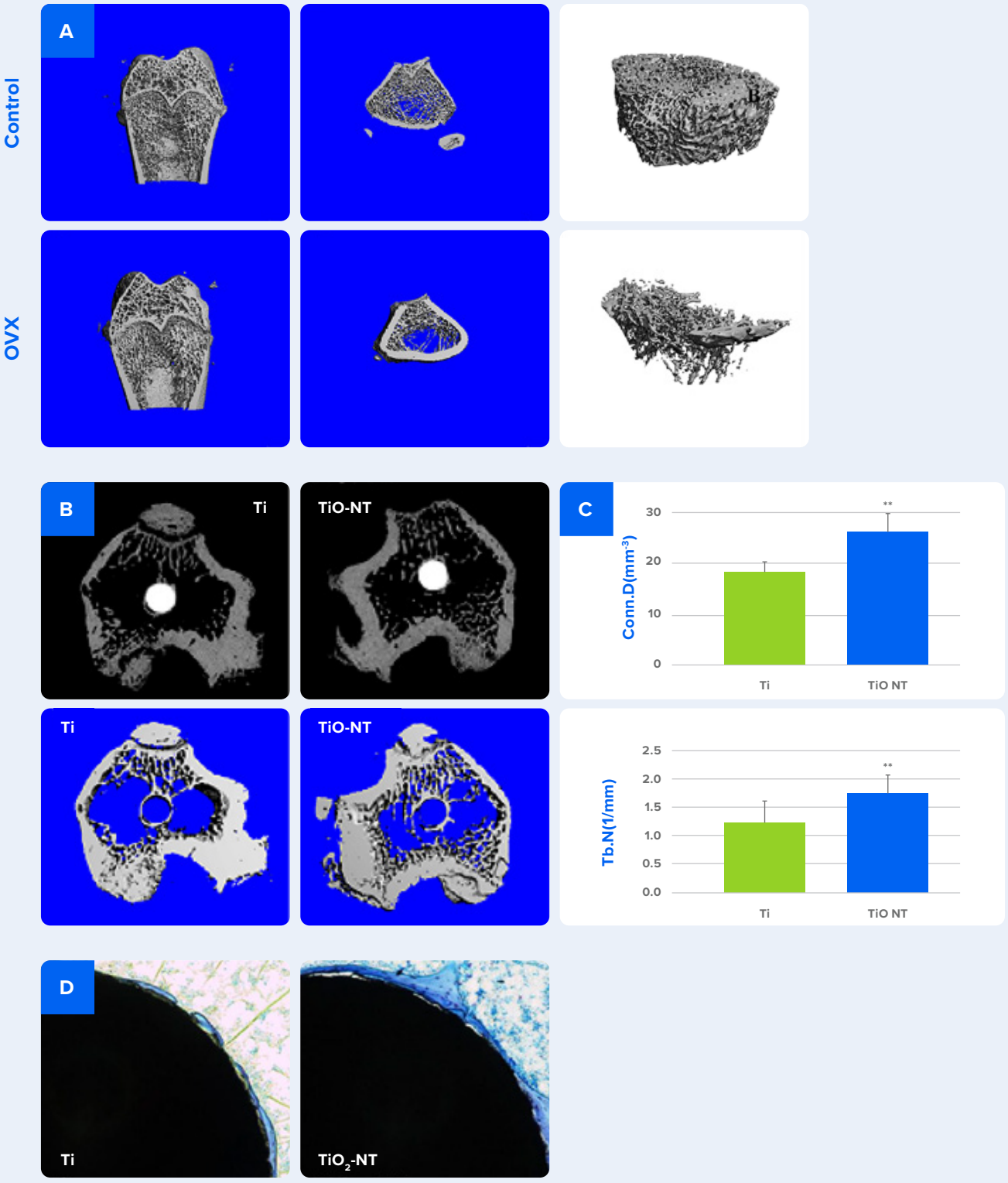

*Figure 1: TiO2-NTs affect ovariectomy-induced bone loss. (A) To evaluate whether the OVX model succeeded, micro-CT scanning was performed, and the 3D images of OVX rats or Control rats are shown. (B) Ti implants and TiO2-NT (90 nm) implants were implanted in the tibias of OVX rats and fed for two months. Animals were sacrificed and the tibia were subjected to micro-CT scans. (C) Micro-CT images were quantified for parameters including the mean connectivity density (Conn. D) and trabecular numbers (Tb. N) using the software built into the micro-CT. (D) Hard tissue slicing and staining were performed for histomorphometry analysis. NS, no statistical significance. **P < 0.01. Data are presented as means. (Modified from Kang et al. 2022[2])*

Discussion

Nanotubes in a size range from 60 to 100 nm have shown positive immune, vascular, stem cell, osteoblast, and overall osteointegration results in multiple studies[2,4-7]. The implant surface only contacts a small fraction of the tibial compartment, but a retention of dense bone volume was observed in the entire compartment, Figure 1B. This indicates that it is not just physical contact with the nanotubes but the release of soluble growth factors such as vascular endothelial growth factor (VEGF) and bone morphogenetic protein (BMP) that can recruit vascular tissue and encourage more bone formation[2,6,7].

Also covered in this publication, but not covered here, is the ability of the nanotube surface to inhibit osteoclast formation and maturation. Osteoclasts form to digest and resorb bone that is damaged or needs replacement. The bone resorption by osteoclasts can be inhibited by 90 nm nanotubes. New bone formation in osteoporosis can be pushed towards bone formation with the incorporation of titanium nanotubes on the surface of implants. Preventing bone loss by osteoclasts, retaining bone volume, and encouraging bone growth with nanotube induced responses, has enormous implications for orthopedic device use in the physical restoration of patients with osteopenia or osteoporosis.

Conclusion

Nanotube surfaces present a new, durable, and non-pharmaceutical option to help osteoporosis patients recover when orthopedic implants become necessary to restore patient's health, mobility, and quality of life. The technology offered to the orthopedic community with the nanoVIS Ti™ Surface Technology has the potential to redefine how orthopaedic osteoporosis and osteopenia patients are treated.

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