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Authors:

David Detwiler, PhD
Sabrina Huang, PhD
Alan Kraft, BSNE
Kreigh Williams, BS

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Background

Osteoporosis is a chronic systemic metabolic disease[1-3]. It is caused by a hormone imbalance that breaks down 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 aged 50 years and older 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, longer recoveries, and more revision surgeries.

Kang et al. explored the influence of titanium nanotubes on the osteoporotic bone through 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. This paper compared titanium implants with and without nanotube surfaces in the OVX-induced rat model to evaluate the potential of nanotube surfaces for improving implant osteogenesis under osteoporotic conditions.

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. The OVX model rats were divided into two groups receiving either titanium implants or titanium implants with 90 nm nanotube surfaces. These 0.8 mm diameter pins were implanted into the upper tibial compartment, while the opposite knee was left alone as a control for bone loss. 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 showed the baseline level of cancellous bone in the upper tibial compartment compared to the OVX model, as shown in Figure 1A. The OVX model demonstrated significant bone loss without any implant. The micro-CT cross section of the control titanium implant showed bone loss relative to the nanotube surface at two months post-implantation in an OVX model, as shown in Figure 1B. The nanotube surface demonstrated significantly greater connective density and trabecular numbers than the control titanium implant, as shown in Figure 1C. Histology showed more collagen accumulation surrounding the nanotube implants compared to the controls, as shown in Figure 1D.

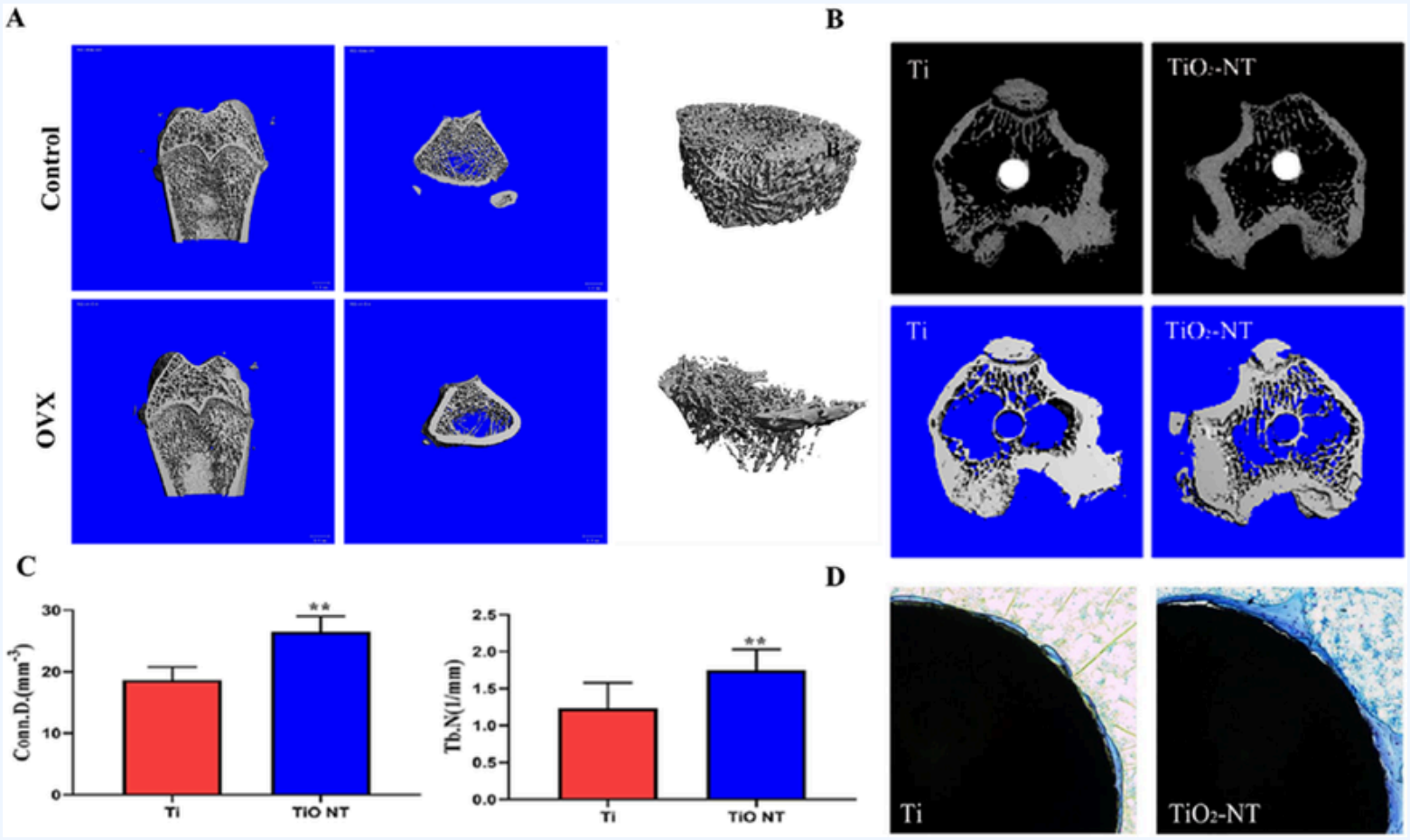

Figure 1: TiO2-NTs affect ovariectomy-induced bone loss. (A) To evaluate whether the OVX model succeeded, micro-CT scanning was performed, and the 3D images of OVX rats or Control rats are shown. (B) Ti implants and TiO2-NT (90 nm) implants were implanted in the tibias of OVX rats and fed for two months. 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. **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]. As shown in Figure 1B, the implant surface contacted only a small fraction of the tibial compartment, but a retention of dense bone volume was observed in the entire compartment. 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 discussed in the original publication, but not covered in this paper, 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 patients with osteoporosis when orthopedic implants become necessary to restore a patient's health, mobility, and quality of life. In this paper, an OVX rat model was used to evaluate the osteogenic performance of titanium surfaces under osteoporotic conditions. Results showed that the titanium nanotube surface enhanced osteogenesis compared to the control titanium surface.

References

1. Codrea, C. I. et al. Advances in Osteoporotic Bone Tissue Engineering. J Clin Med **10**, doi:10.3390/jcm10020253 (2021).

2. Kang, H. et al. Titania-Nanotube-Coated Titanium Substrates Promote Osteogenesis and Suppress Osteoclastogenesis via Integrin αvβ3. ACS Appl Bio Mater **5**, 5832-5843, doi:10.1021/acsabm.2c00811 (2022).

3. Wright, N. C. et al. The recent prevalence of osteoporosis and low bone mass in the United States based on bone mineral density at the femoral neck or lumbar spine. J Bone Miner Res **29**, 2520-2526, doi:10.1002/jbmr.2269 (2014).

4. Oh, S. et al. Stem cell fate dictated solely by altered nanotube dimension. Proc Natl Acad Sci U S A **106**, 2130-2135, doi:10.1073/pnas.0813200106 (2009).

5. Ding, X. et al. The effects of hierarchical micro/nanosurfaces decorated with TiO2 nanotubes on the bioactivity of titanium implants in vitro and in vivo. International Journal of Nanomedicine **10**, 19 (2015).

6. Yu, W. P. et al. Titanium dioxide nanotubes promote M2 polarization by inhibiting macrophage glycolysis and ultimately accelerate endothelialization. ImmunInflamm Dis **9**, 746-757, doi:10.1002/iid3.429 (2021).

7. Khosravi, N., Maeda, A., DaCosta, R. S. & Davies, J. E. Nanosurfaces modulate the mechanism of peri-implant endosseous healing by regulating neovascular morphogenesis. Commun Biol **1**, 72, doi:10.1038/s42003-018-0074-y (2018).