



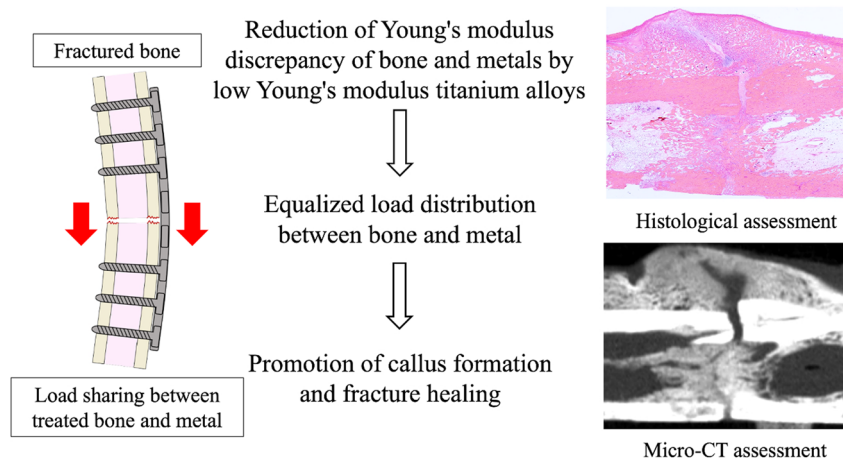
Advances in titanium alloys and orthopedic implants: new titanium alloys and future research directions

Yu Mori¹ · Naoko Mori²

Received: 8 April 2024 / Accepted: 19 August 2024 / Published online: 30 September 2024
© Zhejiang University Press 2024

Graphic abstract

Schema for fracture healing promotion by titanium alloys with low Young's modulus



Dear Editor,

We read with great interest the article by Tan et al. titled “Accelerated fracture healing by osteogenic Ti45Nb implants through the PI3K–Akt signaling pathway” [1]. This research thoroughly examines the bone-forming capabilities of the Ti45Nb alloy. The *in vitro* studies revealed that the Ti45Nb alloy enhances the osteogenic differentiation of MC3T3-E1 cells more effectively than Ti6Al4V alloy controls, showing no noticeable cytotoxic effects. *In vivo* tests demonstrated that Ti45Nb alloy implants improved

fracture healing compared to the Ti6Al4V alloy, with its biological safety confirmed through histological assessments. Moreover, immunohistochemical staining indicated that the Ti45Nb alloy could enhance bone generation by activating the PI3K/Akt signaling pathway. Thus, the Ti45Nb alloy not only promotes bone formation and fracture healing but also emerges as a promising new orthopedic material.

Several reports highlight the clinical success of new titanium alloys in orthopedics. A new hip prosthesis using a TiNbSn alloy, which combines a low Young's modulus (40 GPa) with high strength and biocompatibility, has shown good clinical results. This alloy eliminates the stress imbalance between the cortical bone and the hip stem, thereby reducing stress shielding [2]. Preclinical studies in animal models, particularly rabbits, have demonstrated the utility of TiNbSn alloy as a fracture treatment material, outperforming intramedullary nails or plates made of Ti6Al4V alloy [3, 4]. In a tibia fracture model using TiNbSn alloy intramedullary nails in mice, there was enhanced expression of Runx2,

✉ Yu Mori
yu-mori@med.tohoku.ac.jp

Naoko Mori
naokomori7127@gmail.com

¹ Department of Orthopaedic Surgery, Tohoku University Graduate School of Medicine, Sendai 980-8574, Japan

² Department of Radiology, Akita University Graduate School of Medicine, Akita 010-8543, Japan

attributed to low Young's modulus of the TiNbSn alloy, which equalizes the load-sharing between bone and metal [5]. Although Young's modulus of the Ti45Nb alloy used in this study was not precisely described, it was anticipated to be lower than that of the Ti6Al4V alloy, potentially promoting bone formation by dispersing stress more effectively between bone and metal. If Nb, as the authors suggested, enhances fracture healing through the upregulation of the PI3K-Akt signaling pathway, then Nb-containing titanium alloys could be useful as orthopedic implants.

The accelerated fracture healing effect of the Ti45Nb alloy demonstrated in this study warrants further detailed investigation, particularly with fracture treatment plates, to assess the alloy's overall utility. Given the importance of strength and corrosion resistance in orthopedic implants, along with their bone osseointegration properties, it is expected that research on these important factors will be developed.

Author contributions YM and NM performed the literature research and wrote the manuscript. Both authors have read and approved the final submitted manuscript.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The animal experimental protocol was reviewed and approved by the animal studies committee of our institution.

References

1. Tan J, Li JX, Ran ZY et al (2023) Accelerated fracture healing by osteogenic Ti45Nb implants through the PI3K-Akt signaling pathway. *Bio-Des Manuf* 6(6):718–734. <https://doi.org/10.1007/s42242-023-00250-6>
2. Chiba D, Yamada N, Mori Y et al (2021) Mid-term results of a new femoral prosthesis using Ti–Nb–Sn alloy with low Young's modulus. *BMC Musculoskelet Disord* 22:987. <https://doi.org/10.1186/s12891-021-04879-1>
3. Kogure A, Mori Y, Tanaka H et al (2019) Effects of elastic intramedullary nails composed of low Young's modulus Ti–Nb–Sn alloy on healing of tibial osteotomies in rabbits. *J Biomed Mater Res B Appl Biomater* 107:700–707. <https://doi.org/10.1002/jbm.b.34163>
4. Ito K, Mori Y, Kamimura M et al (2022) Beta-type TiNbSn alloy plates with low Young modulus accelerates osteosynthesis in rabbit tibiae. *Clin Orthop Relat Res* 480:1817–1832. <https://doi.org/10.1097/CORR.0000000000002240>
5. Mori Y, Fujisawa H, Kamimura M et al (2021) Acceleration of fracture healing in mouse tibiae using intramedullary nails composed of beta-type TiNbSn alloy with low Young's modulus. *Tohoku J Exp Med* 255:135–142. <https://doi.org/10.1620/tjem.255.135>