LETTER TO THE EDITOR

Revisiting Scaffold Design Paradigms: From Modulus Matching to Strain Optimization

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Dear Editor

I read with great interest the recent article by Qin et al. introducing a two-stage metamaterial scaffold (TMS) that decouples strength and modulus, achieving an effective stiffness of only 13 MPa while retaining sufficient load-bearing capacity.[1] By enabling >2 % callus strain *in vivo*, the TMS activated mechanosensitive calcium channels and HIF-1α signaling, thereby enhancing both osteogenesis and angiogenesis. This work challenges the conventional "modulus-matching" paradigm by highlighting mechanical strain as a key driver of bone regeneration.

While the compressive behavior of the TMS is well-characterized, two critical aspects require further clarification. First, many skeletal sites are subject to complex tensile and shear forces, which bone scaffolds must withstand to maintain functionality in physiological conditions; however, the performance of TMS under such loading modes remains unexplored.[2] Second, long-term *in vivo* studies are essential to evaluate fatigue resistance, remodeling dynamics, and potential late-stage stress shielding.[3] Previous reports have shown that functionally graded designs can improve fatigue life by up to 30%.[4] In addition, patient-specific finite element (FE) modeling could further optimize strain-targeted scaffold designs by predicting callus strain distribution under realistic physiological loading, as demonstrated in fibular healing studies where case-specific FE models incorporating anatomical geometry significantly improved the accuracy of strain and stress distribution predictions.[5]

By addressing these points, the TMS approach could be better positioned for translational success. Overall, this study represents a significant step toward strain-optimized scaffold design and provides a valuable foundation for next-generation orthopedic implants.

Keywords Metamaterial, Scaffold, orthopedic implants

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