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Mechanical stimulation of tendon tissue engineered constructs: effects on construct stiffness, repair biomechanics, and their correlation

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Abstract: The objective of this study was to determine how in vitro mechanical stimulation of tissue engineered constructs affects their stiffness and modulus in culture and tendon repair biomechanics 12 weeks after surgical implantation. Using six female adult New Zealand White rabbits, autogenous tissue engineered constructs were created by seeding mesenchymal stem cells (0.1x10(6) cellsml) in collagen gel (2.6 mgml) and combining both with a collagen sponge. Employing a novel experimental design strategy, four constructs from each animal were mechanically stimulated (one 1 Hz cycle every 5 min to 2.4% peak strain for 8 hday for 2 weeks) while the other four remained unstretched during the 2 week culture period. At the end of incubation, three of the mechanically stimulated (S) and three of the nonstimulated (NS) constructs from each animal were assigned for in vitro mechanical testing while the other two autogenous constructs were implanted into bilateral full-thickness, full-length defects created in the central third of rabbit patellar tendons (PTs). No significant differences were found in the in vitro linear stiffnesses between the S (0.15+/-0.1 Nmm) and NS constructs (0.08+/-0.02 Nmm; mean+/-SD). However, in vitro mechanical stimulation significantly increased the structural and material properties of the repair tissue, including a 14% increase in maximum force (p=0.01), a 50% increase in linear stiffness (p=0.001), and 23-41% increases in maximum stress and modulus (p=0.01). The S repairs achieved 65%, 80%, 60%, and 40% of normal central PT maximum force, linear stiffness, maximum stress, and linear modulus, respectively. The results for the S constructs exceed values obtained previously by our group using the same animal and defect model, and to our knowledge, this is the first study to show the benefits of in vitro mechanical stimulation on tendon repair biomechanics. In addition, the linear stiffnesses for the construct and repair were positively correlated (r=0.56) as were their linear moduli (r=0.68). Such in vitro predictors of in vivo outcome hold the potential to speed the development of tissue engineered products by reducing the time and costs of in vivo studies.