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Abstract

A Stem Cell-Laden 3D-Printed Scaffold Enriched with an Anti-Fibrotic Drug Improves Healing of Urethral Lesions in a Rabbit Experimental Model

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Abstract

Background and Aim: Difficulties in treating complex urethral strictures have forced us to look for innovative modern technologies to create alternative solutions for the urethral fibrotic process. Having experience in 3D bioprinting and following recent publications we have designed a personalized artificial urethral tissue and evaluated it in a rabbit experimental model. The aim of our study was to prove the advantage of cell laden artificial tissue loaded with antifibrotic drug in repressing the fibrotic process.

Method: Biocompatible materials, hydrogels and thermopolymers were chosen to compose the scaffold. Employing free different 3D printing technologies, these materials were used to manufacture a structure akin to urethral tissue. Adult stem cells isolated from various tissues were evaluated for their proliferation potential and differentiation. Antifibrotic medication was added expecting reduced fibrosis postoperatively. Action of antifibrotic drug was evaluated *in vitro* by measuring the levels of myofibroblast markers - αSMA and latent TGFβ (LTGFB) using the Western blot method. Four different prototypes of bioprinted tissue were created and tested in rabbit experimental model *in vivo*.

Results: different source cells showed different expression of cell markers CD44, CD45 and CD90 measured by flow cytometry. According this expression, two different stem cells sources were chosen to form multilayer transitional epithelium and smooth muscle tissue layers in 3D printed scaffolds. Antifibrotic drug was tested *in vitro*, and the optimal concentration, which demonstrated suppressive action to αSMA protein expression was chosen. Composition of scaffolds was gradually improved optimising tensile strength and sutureability. 20 New Zealand white rabbits were used to test artificial scaffold *in vivo*. Urethrograms showed advantage of cell-laden scaffold. Histologically intensive inflammatory infiltration was found in cell absent scaffolds and multilayer

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urothelium formation and less intensive fibrosis was confirmed in stem cells and with antifibrotic drug enriched scaffolds.
Conclusion: 3D bioprinting methodology is optimal for producing artificial tissue, able to add stem cells and medications into its composition. Adult stem cells are optimal choice for urethral tissue formation. Cell-laden and antifibrotic drug enriched scaffolds show best results in rabbit experimental model *in vivo*.
Keywords: *3D Printed, Artificial tissue, Scaffold, Urethral stem-cells*