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# Immediate production of a tubular dense collagen construct with bioinspired mechanical properties

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ABSTRACT

The intrinsic complexity of tissues and organs demands tissue engineering approaches that extend beyond planar constructs currently in clinical use. However, the engineering of cylindrical or tubular tissue constructs with a hollow lumen presents significant challenges arising from geometrical and architectural considerations required to tailor biomaterials for tissue and organ repair. Type I collagen is an ideal scaffolding material due to its outstanding biocompatibility and high processability. However, the highly hydrated nature of collagen hydrogels results in their lack of mechanical properties and instability, as well as extensive cell-mediated contraction, which must be overcome to achieve process control. Herein, tubular dense collagen constructs (TDCCs) were produced simply and rapidly (in less than 1 h) by circumferentially wrapping plastically compressed dense collagen gel sheets around a cylindrical support. The effects of collagen source, i.e. rat-tail tendon and bovine dermis-derived acid solubilized collagen, and concentration on TDCC properties were investigated through morphological, mechanical and chemical characterizations. Both tensile strength and apparent modulus correlated strongly with physiologically relevant collagen gel fibrillar densities. The clinical potential of TDCC as a tubular tissue substitute was demonstrated mechanically, through circumferential tensile properties, theoretical burst pressure, which ranged from 1225 to 1574 mm Hg, compliance values of between 8.3% to 14.2% per 100 mm Hg and suture retention strength in the range of 116–151 grams-force, which were compatible with surgical procedures. Moreover, NIH/3T3 fibroblast viability and uniform distribution within the construct wall were confirmed up to day 7 in culture. TDCCs with fibrillar densities equivalent to native tissues can be readily engineered in various dimensions with tunable morphological and mechanical properties, which can be easily handled for use as tissue models and adapted to clinical needs.



## 1. Introduction

Tissue engineering approaches are primarily applied in clinical settings for planar tissues because of their relatively low complexity and simple geometry [1]. To extend the utility of engineered tissues for regenerative medicine and to circumvent challenges associated with allotransplantation [2], the development of biocompatible and mechanically relevant tubular tissue constructs would potentially provide improved solutions for the repair of gastrointestinal, urinary, vascular and respiratory systems. In particular, the regeneration of tubular tissues involves sequential steps beginning with the reproducible production of a biodegradable scaffold based on well-characterized materials and moving towards scaffold seeding with a population of committed cells, which is readily available and easily expanded [3]. Furthermore, the potential clinical success of a tissue engineered tubular construct is represented by a combination of cost- and time-effectiveness along with long-term functionality.

Several approaches have been considered for the development of tubular constructs with tissue-like properties including biodegradable polymers, decellularized tissues and cell-based extracellular matrix (ECM) production. Biodegradable synthetic polymers (e.g. poly α-hydroxy acids) have been extensively investigated as they are mechanically and structurally tunable, yet the therapeutic application of these constructs is limited by inflammatory host responses [4–6]. Decellularized cadaveric trachea has been clinically implanted, after seeding the scaffold with autologous stem cells [7]. However, limited donor availability, the need for extensive material processing and the detrimental effects of residual biological material in vivo significantly impact the broad clinical use of this methodology [8]. Furthermore, a cell-assembled tissue model has been used to generate completely biological vascular grafts with mechanical and structural features comparable to natural tissues [9,10]. Nevertheless, variation in cell function and extended time in culture increase production costs and reduce immediate clinical use [11]. Further tissue engineering approaches have been

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