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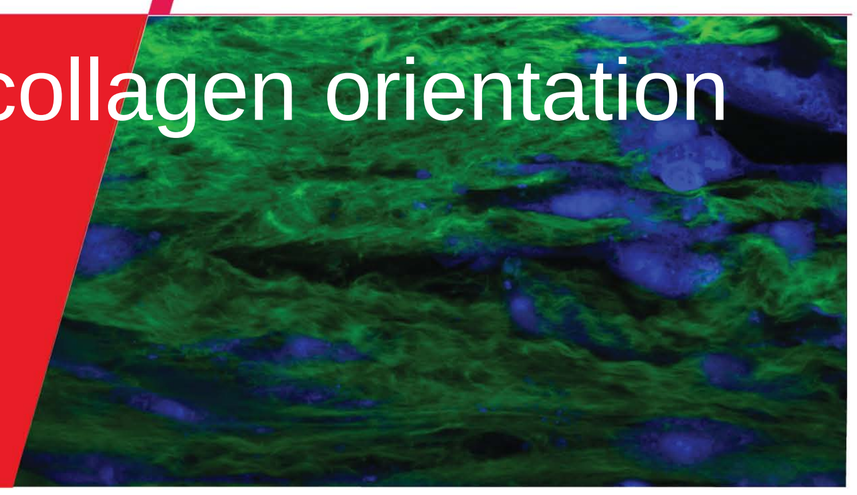

Introduction

Loading protocols in tissue engineering (TE) aim to improve the deposition of a properly organized collagen network. Cells synthesize the collagen fibers and develop traction forces that play an important role in the fiber alignment. These forces are particularly important in static loading protocols, where no other external force is applied.

Objective: The goal of this study is to investigate the role of cellular traction forces in collagen remodeling of TE constructs developed under static loading conditions.

Methods

The theory of Driessen et al. [1] is extended to include cell stress. The total stress is split in an isotropic matrix part and an anisotropic fiber part.

$$\sigma = \hat{\tau} + \frac{3}{4\pi}\int_S \left(\phi_f \varphi_f + \sigma_c\right)\vec{e}_f\vec{e}_f dS \qquad (1)$$

where $\hat{\boldsymbol{\tau}}$ represents the matrix stress. Φ_f is the collagen fiber content, φ_f is the fiber stress and $\boldsymbol{\sigma_c}$ is the cell stress, both acting only in the direction of the fiber $\vec{e_f}$. The isotropic matrix stress is modeled as a compressible Neo-Hookean material. The collagen constitutive behavior is described by an exponential law. The constitutive behavior of the cells is described by the theory of Desphande et al. [2]. The cell stress is given by a Hill-like equation and is dependent on the isochoric extension/shortening of the fiber and fiber content η.

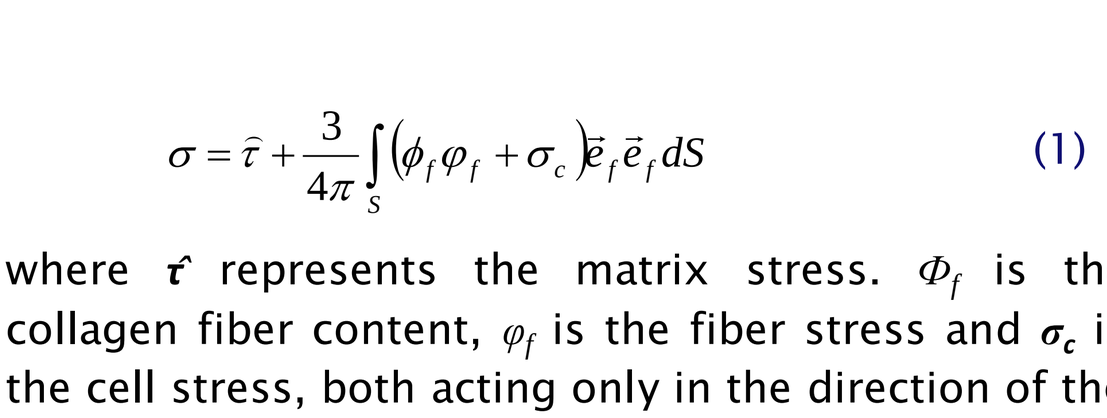

Figure 1. Compaction in width (A) and stress generation (B) of the TE strips obtained experimentally [3] (red) and numerically (blue).

The formation and dissociation of the cell α-actin stress-fibers η is modeled by a first-order kinematic scheme and assumed equal to the collagen content

Results

A 3D finite element model (FEM) is derived. The model is validated using experimental results where TE strips are developed under uniaxial static conditioning [3] (Fig. 1). The model is then utilized to predict experimental results in TE small diameter vessels developed under the same conditions (Fig. 2). The TE vessels are allowed to compact in length to a final value of λ_z=0.88

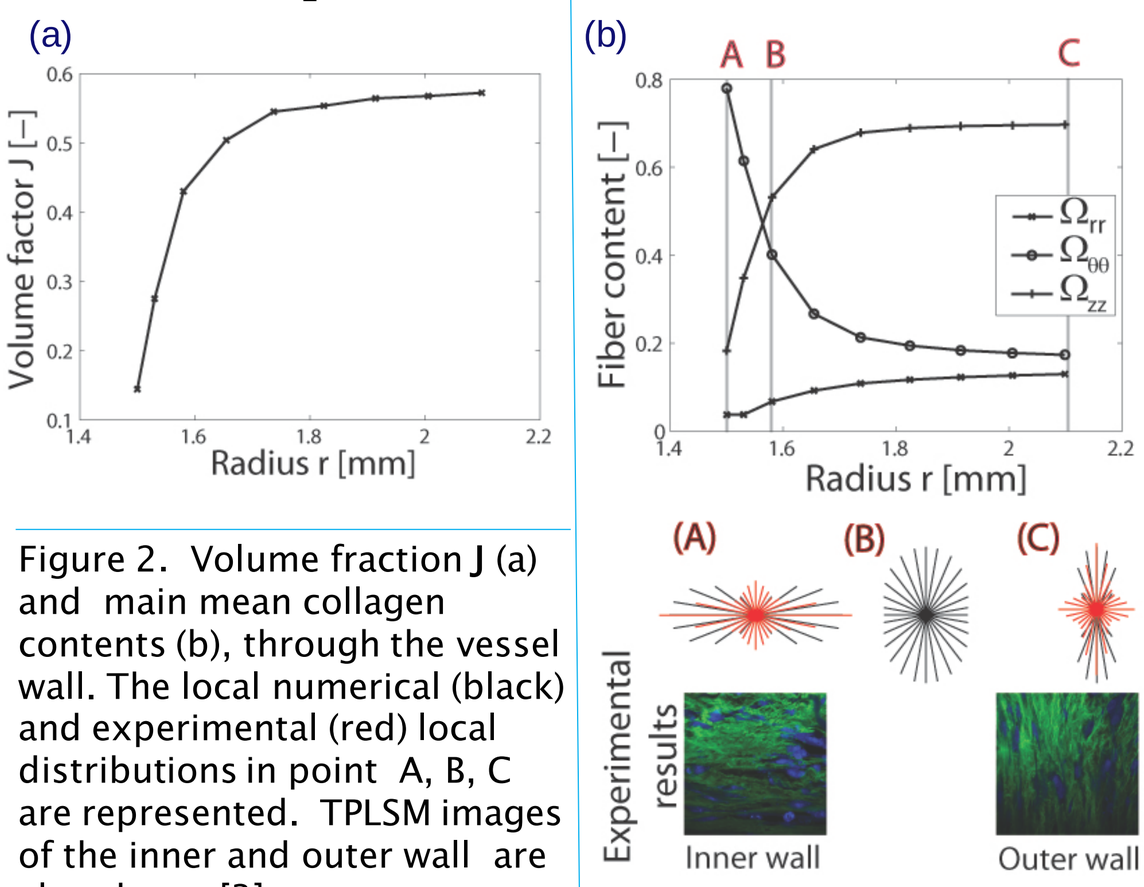

Figure 2. Volume fraction J (a) and main mean collagen contents (b), through the vessel wall. The local numerical (black) and experimental (red) local distributions in point A, B, C are represented. TPLSM images of the inner and outer wall are also shown [3].

The numerical framework predicts a compaction of 56% of the initial width comparable to the 60% obtained experimentally [3]. The volume fraction J is lower near the lumen and increases through the outer side of the vessel. The model also outcomes a collagen orientation comparable to experimental results: circumferential near the lumen and longitudinal along the outer wall [3].

Discussion

The model successfully predicts the collagen fiber orientation obtained in TE small diameter vessels developed under static loading conditions. Thus cellular traction is an important component in collagen remodeling.
Therefore, the model may be a valuable factor in the improvement of loading protocols for TE.

Driessen, N.J.B.. *et al. Biomech. Model. Mechanobiol. (2008)* [1]
Deshpande V.S. *et al. Proc. R. Soc., London, A (2007)* [2]
Van Vlimmeren, M.A.A. *et al.*, Tissue Eng. Part C: Methods (2011) [3]
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