Modelling collagen fiber architecture in Tissue Engineered small vessels
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Introduction
Numerical models can assist in studying the highly coupled interplay between mechanical loading, collagen modelling and tissue compaction. In this study, a structural constitutive framework is introduced that relates the collagen fiber architecture to the cell mechanical behaviour. In its turn, the cell mechanics is related to the local mechanical conditions within the tissue. To demonstrate its capabilities, the model is applied to study the collagen orientation of the TE constructs developed under either static or dynamic conditions.

Method
Experimental method
Small diameter blood vessels constructs were obtained as described by Stekelenburg et al. [1].

The tubular constructs were slid over a silicone tubing, mounted in a sterile bioreactor and fixed by sutures (Fig 1). The constructs were then cultured under static or dynamic loading conditions in the bioreactor for 4 weeks.

Afterwards, the fiber distribution along the vessel wall was obtained by two-photon microscopy (TP-LSM).

Numerical method
The tissue is modelled as a compressible fiber reinforced material and the Cauchy stress is written as

\[
\sigma = \tilde{\tau} + \tilde{\tau}_c + \sum_{i=1}^{N_c} \sum_{j=1}^{N_f} \phi_f \tilde{\tau}_f (\phi_f \tilde{\tau}_f - \tilde{\varepsilon}_f \varepsilon_f^2 \lambda \gamma)\]

with \( \tilde{\tau} \) the isotropic compressible matrix stress, \( \tilde{\tau}_c \) the cell stress-fibres stress, the \( \phi_f \) fiber volume fraction, \( \phi_f \) the fiber stress and \( \tilde{\varepsilon}_f \) the fiber direction in the deformed configuration. For the cell stress-fibres stress, a model developed by Deshpande et al. [2] is used. They consider that the mechanical response of the cell stress-fibres comprises three coupled phenomena:

- An activation signal triggering actin filament formation given by

\[
C = \exp \left( \frac{t_0}{\beta} \right)
\]

were \( \beta \) is the decay constant of the signal and \( t_0 \) is the time measured from the instance of the application of the first signal.

- A fiber formation rate dependent on the activation signal, coupled with a dissociation rate affected by the tension,

\[
\eta(\omega, \gamma) = \left( 1 - \frac{\sigma}{\sigma_0} \right) \frac{C k_f}{\beta} - \left( 1 - \frac{\sigma}{\sigma_0} \right) \frac{\eta(\omega, \gamma)}{\beta} k_b
\]

were \( \sigma \) is the stress-fiber stress, \( \sigma_0 \) the corresponding isometric stress, \( k_f \) and \( k_b \) are dimensionless constants governing the rate of formation and dissociation of the cell stress-fibres, and \( \omega \) and \( \gamma \) are the angles of the stress-fibers with respect to the axis of the vessel.

- A stress in the stress-fiber dependent on the extension/shortening of the fibres \( \lambda_i \). This relation is given by a Hill-like equation.

The previous stress-fibres stresses contribute to the total contractile response of the stress-fibers as an active response. To this active stress is added a passive elastic response described as a compressible neo-Hookean material.

Finally, the cell stress-fiber distribution is assumed to be equivalent to the collagen fiber distribution \( \phi_f(\omega, \gamma) = \eta(\omega, \gamma) \)

Result analysis
The predicted angular fiber distributions for the vessel wall are presented and compared to the experimental results. An example for the collagen fiber distribution of TE vessels cultured under static conditions is presented in Fig 2.