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FIBROBLAST-CONTROLLED ANEURYSM GROWTH IN A HUMAN CEREBRAL ARTERY

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ABSTRACT

Aneurysms are abnormal dilatations of arteries, and these lesions are found almost exclusively in humans. Saccular cerebral aneurysms occur most frequently in the Circle of Willis, which is a circuit of arteries supplying the brain with blood. Only a few percent of these lesions actually rupture, but once rupture occurs the consequences are severe, often with often lethal outcome. In order to be able to model the constitutive behaviour of an aneurysm, the structural features of the aneurysm wall need to be determined. Knowledge of the etiology of the aneurysm may here provide important insights. Therefore, in this communication, a theoretical model of the growth of a saccular cerebral aneurysm, based on fibroblast-controlled collagen turnover, is presented. The model is an extension of the one proposed by Kroon and Holzapfel [1,2].

It is assumed that the development of the aneurysm is accompanied by a loss of intima and media, and that collagen fibres alone provide load-bearing capacity to the remaining adventitia and the developing aneurysm wall. The continuous turnover of collagen is the driving mechanism in the growth of the aneurysm, and degradation, and production of collagen is accomplished by fibroblasts (cf. Alberts et al. [3]). The aneurysm is modelled as an axisymmetric multi-layered membrane, exposed to an inflation pressure (cf. Fried [4]). The fibres and fibroblasts within a specific layer are perfectly aligned in a specific orientation angle. Fibroblasts are responsible for the collagen production, and the stretch of the aneurysm wall, caused by the pulsating blood pressure, is assumed to govern the proliferation and collagen production rate fibroblasts. The mass production rate $\dot{m}_i$ of collagen fibres in layer i is expressed according to

$$\dot{m}_i(t) = n_i \beta_0 C_i^{\alpha}, \tag{1}$$

where β_0 and α are material constants, n_i is the current number of fibroblasts per unit reference volume, and C_i characterizes the stretching of fibroblasts in layer i. In addition, the change in fibroblast concentration is taken to be

$$\dot{n}_i(t) = \gamma n_i (C_i - C_{th}) \cdot H(C_i - C_{th}), \tag{2}$$

where γ is a material parameter, and C_{th} is a threshold value.

The constitutive response of layer *i* in the aneurysm wall is characterized by a time-dependent strain-energy function

$$\Psi_i(t) = \int_{-\infty}^{t} g(t, t_{\mathrm{dp}})\, \dot{m}_i(t_{\mathrm{dp}})\, \psi_{\mathrm{fib}}(t, t_{\mathrm{dp}})\, \mathrm{d}t_{\mathrm{dp}} , \tag{3}$$

where ψ_{fib} is the strain energy per unit mass stored in the collagen fibres (cf. Humphrey and Rajagopal [5]). Eq. (3) integrates the contribution to the strain energy from fibres deposited through the history of the aneurysm growth. The continuous turnover of collagen is accounted for by the *g* function in Eq. (3), which is equal to 1 for $t_{\mathrm{dp}} \in [t - t_{\mathrm{lf}}, t]$ and 0 otherwise. The life-time of the collagen fibres is denoted by t_{lf}.

The model is able to predict physiologically reasonable shapes and growth rates of the aneurysm (see Fig. 1), and the predicted wall stress agrees well with experimental observations. Figure 1 shows an evolving aneurysm at different time stages. The double lines in Fig. 1 indicate the deformed states at diastole and systole, respectively.

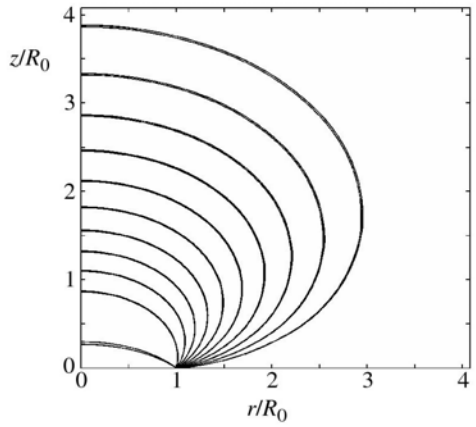

Figure 1. Example of an evolving aneurysm: normalized coordinates are used where *r* and *z* denote cylindrical coordinates and R_0 is a reference radius.

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