Ultrasonic monitoring of the decellularization process of porcine corneal stroma

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ABSTRACT

Nowadays, they are multiple pathologies that may damage several organs of the human organism, being the transplant of the affected organ mostly the unique available therapy. This highlights two mayor concerns, together with the huge cost of this process: the missing donators and the possibility of reject of the transplanted organ. Recent works describe the advances in the substitutive organ therapy [1, 2, 3], based on the development of the so-called bio-artificial organs (decellularized organs of human or animal origin), that benefit of their extracellular matrix, and whose cells are substituted through a re-cellularization process via primary cells that show ability to differentiate themselves in their interior. To standardize and optimize the process, it is necessary to control most of the parameters that may vary its effectiveness. We propose to monitor the changes that may suffer the matrix during the decellularization process using mechanical and optical parameters. To ensure the viability of this protocol, a bioreactor has been designed.

The proposed methodology consists of three elements: An (1) experimental setup based on ultrasound-cornea interactions is monitored in real-time, a (2) model that simulates the ultrasound-cornea interactions is numerically solved by the transfer matrix formalism, and a (3) model-based inverse problem [4] is used to reconstruct the evolution of the relevant mechanical parameters during the decellularization process. A low-frequency ultrasonic setup was manufactured for real-time measurements of mechanical and geometrical properties of the cornea, as depicted in Fig. 1 The experimental system is idealized by a mathematical model of the propagation and interaction of the ultrasonic waves with all the parts of the system until they are received by the sensor. This mathematical approach is approximated by a semi-analytical model of the wave interactions within multilayered materials, based on the transfer matrix formalism [5, 6]. According to Lee *et al.* [7], the parameters (p) that characterize the decellularization process are found by a search algorithm that minimizes the cost functional f, by means of a least-square estimation of the residual energy,

$$(\hat{p}) = \arg\min_{p} f(p) \tag{1}$$

where f characterizes the discrepancy between the experimental and numerically predicted signals. Genetic algorithms [8] are applied to minimize equation (1), and provide the inverse problem optimal solution.

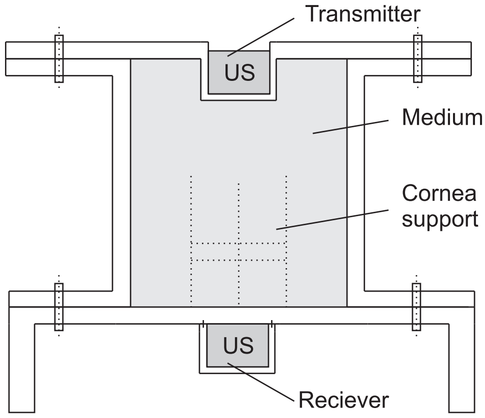

Figure 1: Simplified squeme of the bioreactor

A numerical method to determine the mechanical parameters associated to a decellularization process has been developed by combining an inverse problem, applying genetic algorithms to minimize a cost functional, and using a semi-analytical modeling of the interaction between ultrasonic waves and cornea. The evolution of the relevant reconstructed mechanical parameters during the decellularization process shows its viability.

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