Matching Endothelial Cell and Vascular Substitute Dimensions with Tailored Biodegradable Air-Spun Nanofibrous Scaffold

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Introduction

The absence of neo-endothelium coverage on the intimal surface of small-diameter vascular substitutes is known to be one cause of failure upon implantation of these prostheses in humans [1]. As coating with proteins does not improve the endothelialization capability of textile prostheses, it was sought to replace this protein layer with a poly(lactic acid) (PLA) nanofiber mesh scaffold obtained by an innovative air spinning system. The ultimate goal of this fine-tuned interface between blood and textile threads is to provide an adequate scaffold for endothelial cells to proliferate as monolayer [2].

PLA is an aliphatic biodegradable polyester currently used for tissue engineering applications. This FDA approved polymer material is biocompatible, easy to form, and consequently, widely used in medical procedures. Thanks to its inherent biodegradability, it is expected that this synthetic scaffold will be gradually replaced by the natural extracellular matrix.

In this context, the aim of the present study is to optimize the air spinning process and understand PLA nanofiber scaffold biodegradation mechanism for a sustainable vascular replacement solution.

Material and Methods

Optimization of the air spinning process as a function of spinning parameters through multivariate statistical analysis has been performed to control and finely tune scaffold morphology. Then, two commercial PLAs have been air-spun and afforded to degrade in air and physiologic serum (PS) during 90 days, with materials characterization performed every 15 days. On one hand, quantitative measurements of the number of polymer end-chains, which allows determining PLA molecular weight, has been performed using classical ^{1}H-NMR spectroscopy every 15 days. In addition, the utilization of homonuclear decoupled ^{1}H-NMR spectroscopy allowed studying the stereosequence evolution during the degradation process. On the other hand, the polymer crystallinity evolution has been highlighted by modulated differential scanning calorimetry (MDSC) and X-Ray Diffraction (XRD).

Results

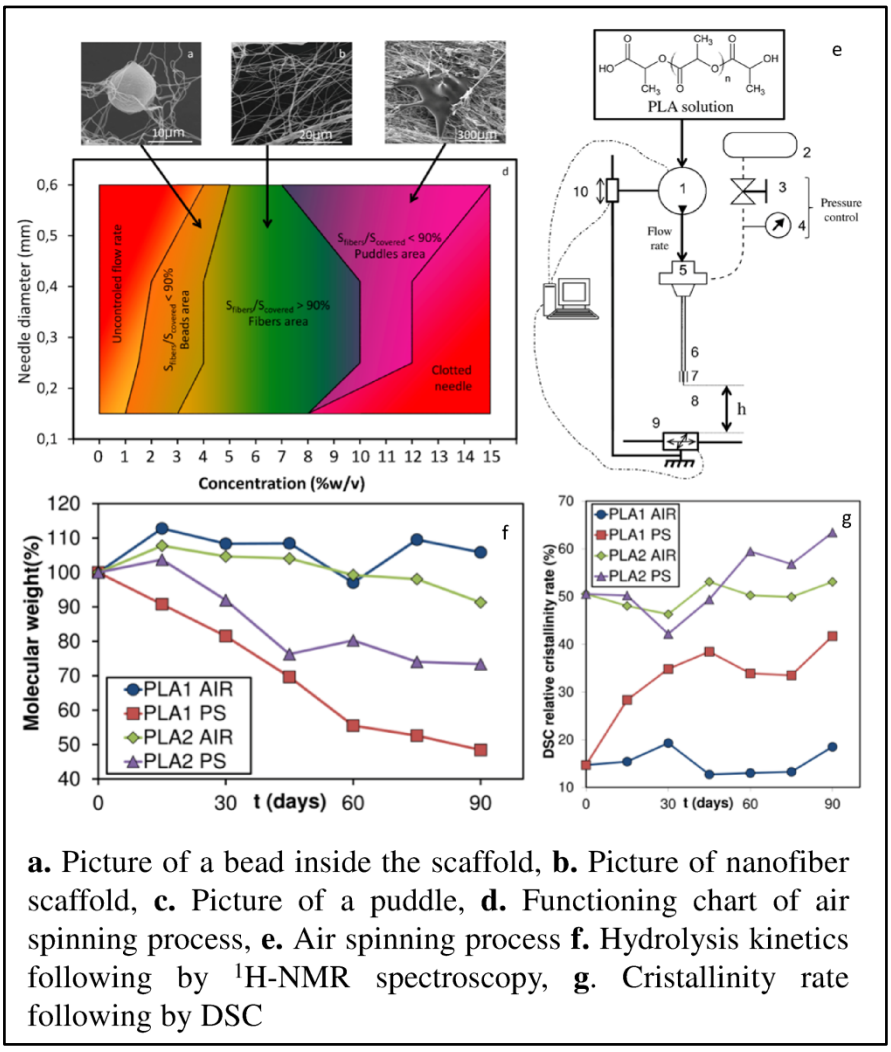
Tailored air-spinning parameters ranges have been established by a SEM pictures (figure a-c) analyses for producing nanofibers with appropriate morphology and mechanical properties. Figure d exhibits the concentration as a function of needle diameter where the most appropriate surface is represented by the fiber area (surface recovered by nanofibers > 90%).

In addition, a multivariate statistical analysis allowed determining the significance of air spinning parameters (figure e) on the nanofiber diameter.

NMR data have shown that the two investigated PLAs displayed different degradation rates (figure f) despite having very similar average initial molecular weights. Using homonuclear

decoupled NMR, it was evidenced that PLA hydrolysis partly related to this polymer L/D stereosequence ratio [3].

Finally, DSC experiments allowed putting in evidence the role of PLA crystallinity on the degradation mechanism (figure g).



a. Picture of a bead inside the scaffold, **b.** Picture of nanofiber scaffold, **c.** Picture of a puddle, **d.** Functioning chart of air spinning process, **e.** Air spinning process **f.** Hydrolysis kinetics following by ^{1}H-NMR spectroscopy, **g**. Cristallinity rate following by DSC

Discussion

Optimization of air-spinning process has led to a better understanding of fiber formation and allowed producing uniform and reproducible nanofiber scaffolds with a global understanding of PLA degradation. Indeed, the PLA stereochemistry, its composition and its crystalline state play a key role in this polymer biodegradation kinetics. The results already obtained in this study constitute key elements for developing a PLA scaffold with tailored degradation behavior. Once optimized, this time-dependent biodegradable construct will be tested using cell cultures in dynamic conditions that mimic physiological, biological and mechanical environments found in human arteries.

Reference

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