NEAR-FIELD ELECTROSPINNING OF POLYDIOXANONE TISSUE REGENERATION TEMPLATES

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Introduction

The ideal biodegradable, biomaterial-based regeneration template should be engineered to mimic the extracellular matrix (ECM) of native tissues to coordinate the cellular response and ultimately guide *in situ* regeneration. Electrospinning is a popular method to artificially recreate the ECM, and by reducing the process's working distance to a few millimeters, the method of near-field electrospinning (NFES) was devised[1]. NFES allows for the "direct writing" of fibers; thus, adding another dimension of tissue template specificity and tailorability. Specifically, mechanical properties, pore size, and fiber orientation can be tightly controlled to bring about desired cellular responses. With this project, we demonstrated NFES devices designed around two commercial 3D printers for the creation of highly precise tissue regeneration templates.

Materials and Methods

A preliminary NFES apparatus was designed around a MakerFarm Prusa i3v 3D printer based on the work of Fattahi et al[2]. The stock filament extruder was replaced with a custom 3D printed adapter to accommodate a NE-300 Just Infusion™ syringe pump. Fibers could be directly written onto a flat collector and sequential stacked to create 3D, fibrous constructs. The polymer polydioxanone (PDO) was chosen as a candidate material due to its superior inflammatory response, mechanical properties, and *in vivo* degradation rate of 6-8 weeks. PDO solutions were made at varying concentrations in 1,1,1,3,3,3-hexafluoro-2-propanol. Template sheets were created by sequentially writing parallel fibers with a 90° rotational offset after each layer. The effect of polymer concentration on fiber size was evaluated by varying PDO concentration from 140 to 220 mg/mL in increments of 20 mg/mL. The remaining processing parameters of air gap, applied voltage, translational velocity, polymer flow rate, and needle gauge were held constant at 1.8 mm, -1.3 kV, 30 mm/s, 15 µL/hr, and 23, respectively. Scaffolds were imaged with a Nova Nano 650 FEG scanning electron microscope, and fiber diameters were measured via Fibraquant v1.3.149. Data were analysed non-parametrically by Kruskal-Wallis test with Dunn's multiple comparison in Prism 7.

Subsequently, a successor apparatus was constructed around a MakerFarm Pegasus 12" 3D printer with a Legato 130 syringe pump (KD Scientific) to create regeneration templates with more complex 3D geometries. The Pegasus 3D printer was integrated with a rotating cylindrical mandrel driven by a stepper motor (Applied Motion Products). This platform allowed for a fiber to be written onto a cylindrical collector with a wind angle as the resultant vector between the translational 3D printer and rotational mandrel. Cylindrical templates were created by translating the 3D printer at a velocity of 70.7 mm/s and rotating the mandrel at an outer surface velocity of 70.7 mm/s, producing a 45° wind angle from the center axis with a resultant velocity of 100 mm/s. Air gap was held constant at 1.8 mm, applied voltage at +1.4 kV, polymer concentration at 120 mg/mL, flow rate at 25 µL/hr, and a needle gauge of 26.

Results and Discussion

As early stage preliminary data, the direct writing of PDO fibers resulted in orderly sheet templates with tailored fiber sizes (FIG. 1 A, B). The template's average fiber diameter significantly increased from 4.1 ± 1.1 to 8.0 ± 2.1 µm over the PDO concentration range of 140 - 220 mg/mL ($p < 0.05$) (FIG. 2). The addition of a rotational collecting surface resulted in the creation of complex cylindrical templates with an average wind angle of 46.9° ± 6.9°, fiber sizes of 2.0 ± 1.1 µm and pores sizes of 17.7 ± 7.7µm (FIG. 3 A, B).

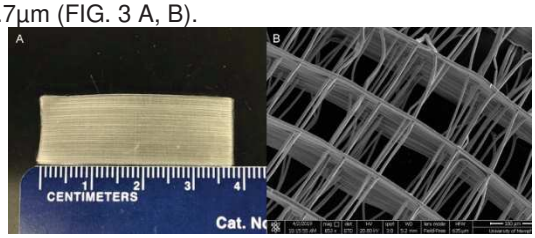

FIG. 1. A. Sheet template.; B. SEM of sheet template with fiber diameter of 4.9 ± 1.5 µm and pore size of 116 ± 34 µm. SEM scale bar 100 µm.

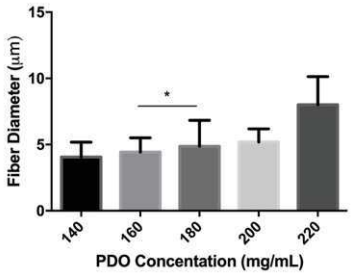

FIG. 2. Fiber diameter as a function of PDO concentration (n=5). All comparisons significant ($p < 0.05$) except *.

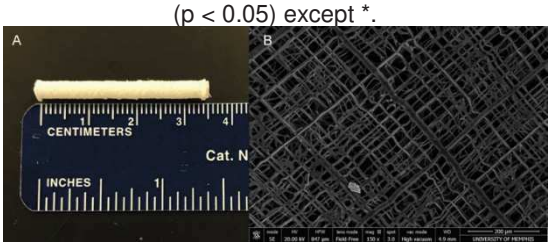

FIG. 3. A. Cylindrical tissue regeneration template; B SEM of cylindrical template with fiber diameter of 2.3 ± 1.3 µm and pore size of 19.8 ± 10.8 µm. SEM scale bar 200 µm.

Conclusions

We have demonstrated that NFES of PDO is a viable technique to precisely create multiple types of 3D, fibrous tissue regeneration templates. The creation of seamless templates has numerous biomedical applications in fields such as vascular, neural, gastrointestinal, and urinary tissue engineering.

Future Work

The mechanical properties of these templates will be evaluated as a function of processing properties and design geometry. Furthermore, these materials interactions with the innate immune system, most notably the neutrophil, will be characterized.

Acknowledgments

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References

[1] Sun et al. Nano Lett. 2006. 6. 839-842
[2] Fattahi et al. Adv Healthc Mater. 2017