Mater. Res. Soc. Symp. Proc. Vol. 1094 © 2008 Materials Research Society 1094-DD06-02

Versatile Core-Sheath Biofibers using Coaxial Electrospinning

Daewoo Han[1], Steven T. Boyce[2], and Andrew J. Steckl[1]
[1]Department of Electrical and Computer Engineering, University of Cincinnati, Cincinnati, OH, 45221
[2]Department of Surgery, University of Cincinnati, Cincinnati, OH, 45267

ABSTRACT

We have investigated coaxial electrospinning to produce core-sheath fibers for tissue engineering. We have successfully produced core-sheath structured fibers of poly(ε-caprolactone) (PCL) and gelatin using the coaxial electrospinning technique. The core-sheath scaffold exhibits better mechanical properties compared to gelatin scaffold. We have characterized the resulting core and core-sheath fiber diameters and the scaffold porosity, etc.

INTRODUCTION

Electrospinning is a versatile technique for the production of nanofibers of many natural and synthetic materials. This includes biopolymers (DNA[1], gelatin[2]), liquid crystalline polymers (polyaramid)[3], textile fiber polymers (nylon)[4], electrically conducting polymers (polyaniline)[5], etc. Electrospinning uses a high electric field to extract a liquid jet of polymer solution from the liquid reservoir. Sufficient distance between nozzle and substrate is required in order to fully evaporate the solvent. The highly charged liquid jet experiences bending and stretching effects due to charge repulsion and, in the process, becomes continuously thinner. During bending and whipping, the volatile solvent is thoroughly evaporated and the solidified nanofibers are collected on the conducting substrate. Advantages of electrospinning are the ability to control: (a) the fiber diameter from micrometer to nanometer dimensions; (b) the various fiber compositions; (c) the spatial alignment of multiple fibers. Electrospinning can produce non-woven fiber mats with exceptional surface to volume ratios and with pores which penetrate the entire mat.

However, the resulting scaffolds of either natural or synthetic polymers display certain limitations. Natural polymers, such as gelatin and collagen, have very good biocompatibility for cell adhesion and proliferation, but their mechanical strength is not sufficient to support the scaffold during healing process. On the other hand, synthetic polymers, such as PCL, have very good mechanical properties but the therapeutic effectiveness is not as good as that of natural polymers. Therefore, there is a need to develop a novel structure to overcome these limits for tissue engineered scaffolds. The core-sheath structure is an excellent candidate to solve this problem. We have utilized synthetic polymers for the core to take advantage of their mechanical strength and biomaterials for the sheath, such as gelatin, to keep very good biocompatibility of the scaffold. This core-sheath structure enables many possibilities to develop and improve tissue scaffolds for wound healing. To make core-sheath structured fiber, coaxial electrospinning is the most attractive method due to its simplicity and versatility. Coaxial electrospinning was first demonstrated by Sun et al.[6] Xia et al. used coaxial electrospinning to produce TiO_2 hollow nanofibers with controllable dimensions.[7] Mead et al. produced core-sheath electrospun fibers using polymer blends.[8] Recently, Zhang et al. reported coaxial electrospinning research for tissue

engineering applications.[9] In coaxial electrospinning, two different polymer solutions are used to make a core-sheath (or a hollow) structure. To be successful in coaxial electrospinning, the selection of materials and solvents, field strength and the balance between E-field strength and feeding rates of solutions are critical.

EXPERIMENT

Our coaxial electrospinning setup and coaxial nozzle are shown in Figure 1. It consists of plastic syringe with 18g blunt needle, LabView™ controlled two NE-1000 syringe pumps purchased from New Era Pump Systems, a Glassman PS/EL30R01.5 high voltage supply, temperature and humidity monitor from Fisher, motic2300 CCD camera and plastic cage.

PCL (Mw=80,000) and gelatin type B (225g bloom) were purchased from Sigma Aldrich and 2,2,2-Trifluoroethanol (TFE) solvent (99.8% purity) was purchased from Acros Organics. The core solution was prepared as 11wt% of PCL in TFE solvent. The gelatin solution for the sheath was prepared as 11wt% of gelatin into the mixture of 80wt% of TFE and 20wt% of DI water. Adding DI water gives a better core-sheath structure profile because PCL cannot be dissolved in water. Both solutions were delivered at the same flow rate of 0.40mL/hr by each assigned syringe pump. Total amount of dispensed solution from both syringe pumps was 1400µl. A voltage of 18kV was used during coaxial electrospinning and the distance between coaxial nozzle and metal plate was fixed at 25cm.

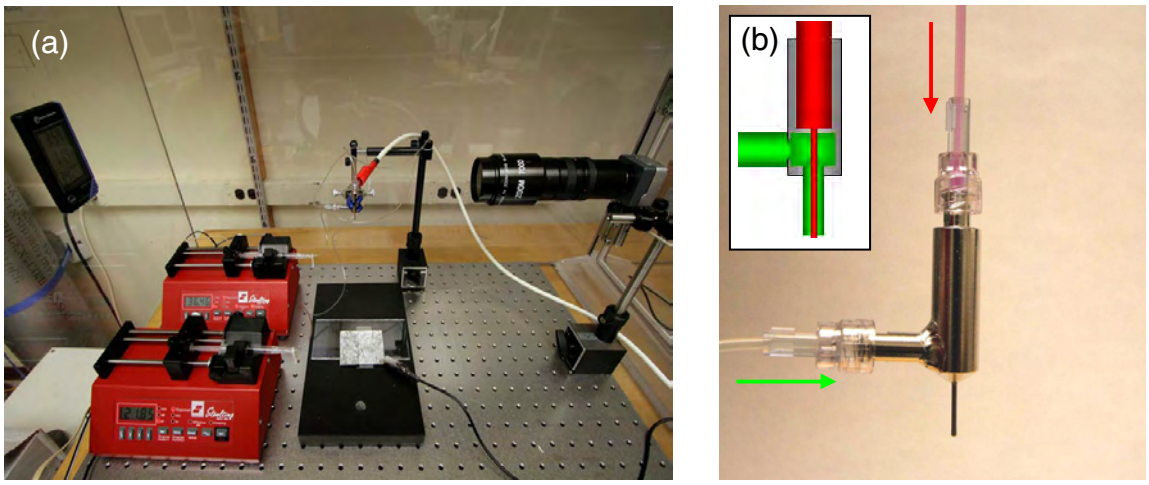

Fig. 1 Electrospinning setup: (a) experimental setup; (b) coaxial nozzle.

For comparison purposes, we have also produced gelatin-only and PCL-only electrospun scaffolds. Gelatin scaffolds have been electrospun using 12wt% gelatin in 90% TFE and 10% DI water solvent at the condition of 25cm gap distance, 11kV applied bias and 0.8mL/hr feeding rate. PCL scaffolds have been electrospun using 12wt% PCL in TFE solvent in condition of 20cm gap distance, 11kV applied bias and the feeding rate of 2.0mL/hr.

We have measured the mechanical properties of both dry and wet samples because wet scaffolds are normally used for cell culture growth. To make a wet scaffold, electrospun scaffolds were first dried in a nitrogen purged desiccator for 24 hours, and then chemically crosslinked using 7mM 1-ethly-3-3-dimethylaminopropylcarbodiimide hydrochloride (EDC) in

pure ethanol for 24 hours, disinfected in 70% ethanol and 30% water for 24 hours and, finally, rinsed twice with phosphate buffer solution (PBS) for 24 hours.[10] EDC crosslinking should have almost no effect on PCL fibers. However, gelatin scaffold in wet condition cannot be handled without crosslinking. The difference in mechanical properties observed between dry and wet conditions can be due to differences in thickness and temperature between samples, and to calibration differences of the two tensile test equipments which were used.

The dimension of electrospun scaffold was 5cm by 5cm. The overall scaffold was then cut into four dog bone shaped samples for mechanical tensile test. The dog bone shape gives better test results because the samples are broken in the middle range of the gauge. We prepared 6~7 samples per each case, controlled fiber diameters within 1~2μm range and scaffold thickness about 300μm at dry status for all cases. Also, considering the concentration of material and the dispensed volume of solution, the same amount of solutes was electrospun for all cases. The thickness was measured using a digital caliper. The dimension of the gauge is 3mm width by 13~15mm length.

We have investigated the core-sheath structure of coaxially electrospun fibers using various methods such as fluorescence microscopy, scanning electron microscopy (SEM) and transmission electron microscopy (TEM). Mechanical properties of scaffolds have been examined using TestResources 100R series tensile testers with either 10N or 500N load cell.

DISCUSSION

We have successfully produced core-sheath structure using coaxial electrospining. SEM images in Fig. 2(a) and (b) show that coaxially electrospun fibers have core-sheath structure. Using fluorescence microscopy this core-sheath structure is also observed, as shown in Fig. 2(c). Red fluorescence dyes were added to core solution. We have occasionally observed the electrospun fibers without core. These non-core fibers were made by the separation of core and sheath solutions. When the coaxial electrospinning condition is not adequate, such as excess electrical field strength and polymerization of solution at the end of nozzle, two separate liquid jets are ejected from each core and sheath solutions. More obviously, TEM images in Fig. 3 show us the core-sheath structure and give us their diameters. Resulting core-sheath and core diameters are 1-2μm and 0.5-1μm respectively. In TEM observations, we could get high contrast difference between core and sheath because the density of PCL (1.15g/mL) is higher than 1.01g/mL of gelatin density. Fewer electrons are transmitted through the PCL core.

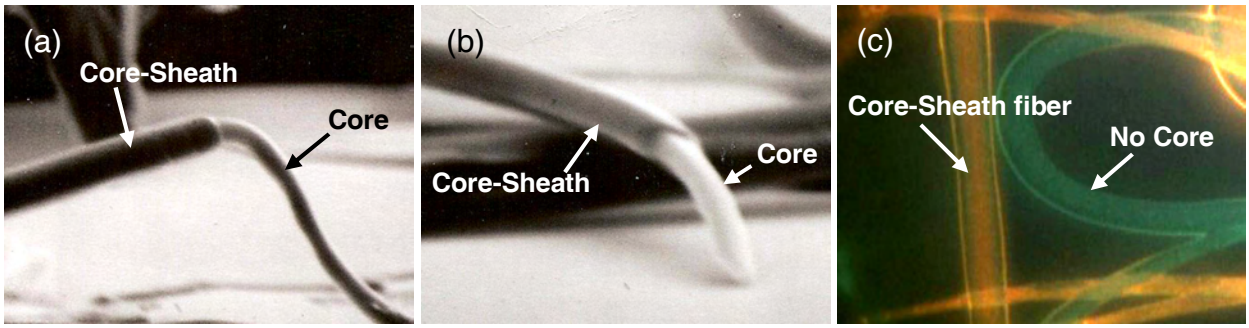

Fig. 2 Core-sheath structured fiber produced by coaxial electrospinning: (a), (b) SEM; (c) fluorescence microscopy

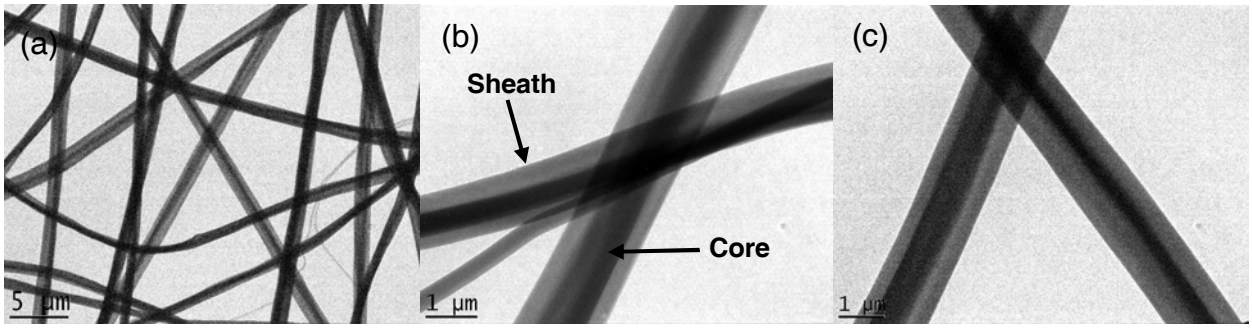

Fig. 3 TEM images of coaxially electrospun core-sheath fibers.

We have characterized the mechanical properties of conventionally and coaxially electrospun scaffolds. This includes gelatin-only, PCL-only and coaxially electrospun PCL/gelatin scaffolds. For more accurate mechanical tensile test, we have controlled fiber diameters within 1~2μm range as shown in Fig. 4 and scaffold thickness about 300μm for all cases. Our typical scaffolds have a density of ~0.25g/cm^3 and a porosity of 75~80% using following equation (1)[11]:

$$\text{Porosity} = \left(1 - \frac{scaffold\ \ density(g/cm^3)}{bulk\ \ density(g/cm^3)}\right) \times 100\% \qquad (1)$$

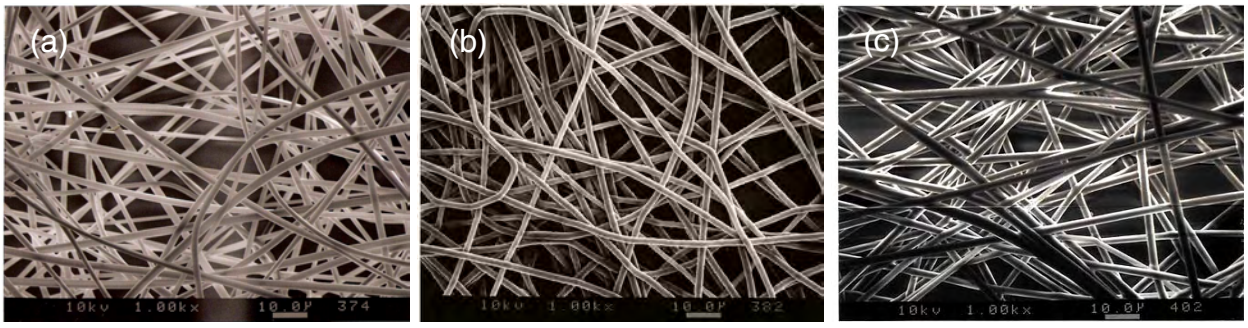

Fig. 4 Electrospun fibers that have fiber diameter controlled within 1~2 μm: (a) gelatin-only; (b) PCL-only; (c) coaxial PCL/gelatin.

The results of mechanical testing are shown in Fig. 5. For dry samples, shown in Fig. 5(a), the mechanical properties represent a 200~300% improvement in ultimate tensile strength of coaxially electrospun scaffold vs. gelatin scaffold. The mechanical properties of PCL, however, appear better than that of coaxially electrospun scaffolds because the PCL core diameter of coaxially electrospun fiber is thinner than that of PCL-only fiber. Because the stiffness of gelatin is higher than PCL stiffness in dry condition, the stress of coaxial electrospun fiber is higher than that of PCL-only fiber in the beginning of the tensile test.

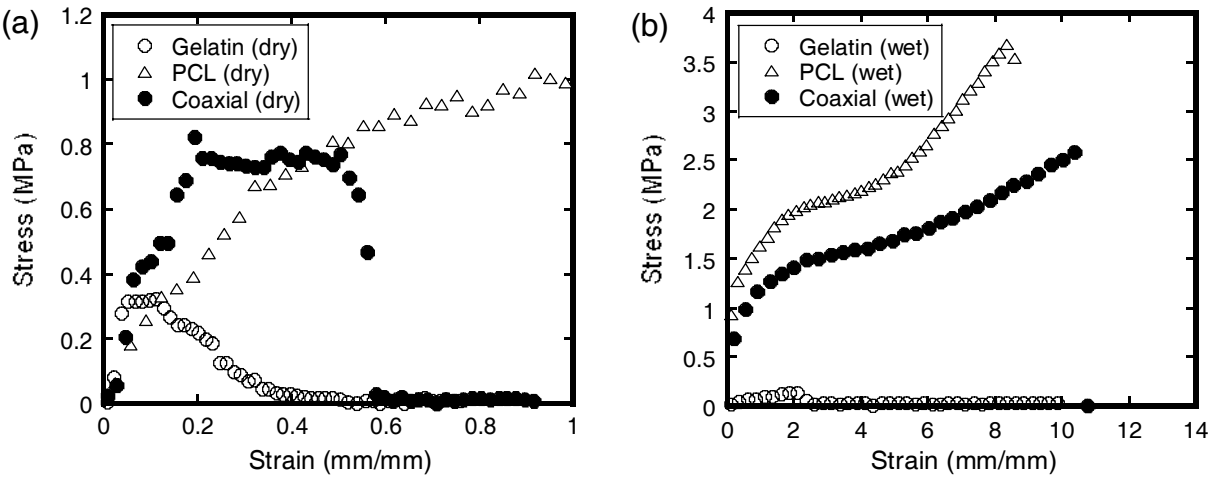

Fig. 5 Mechanical properties comparison of gelatin-only, PCL-only and coaxially electrospun PCL/gelatin scaffolds: (a) dry samples; (b) wet samples.

For wet samples shown in Figure 5(b), the coaxially electrospun scaffold shows maximum elongation property comparable to the PCL scaffold and its ultimate tensile strength was improved significantly vs. the gelatin scaffold. When the PCL core diameter is same with that of PCL-only fiber, their ultimate tensile strength will be similar. However, in dry condition, the tensile strength is not proportional to the portion of PCL core because the broken gelatin area acts as a crack in the core-sheath fiber. Even though we have successfully produced core-sheath fiber, their separation is not perfect yet. Some amount of interdiffusion between core and sheath can occur during electrospinning because materials have essentially the same solvent. As the core-sheath structured fiber has not been optimized yet, we are expecting better mechanical properties than current results after its optimization.

To fully demonstrate the versatility of coaxially electrospun scaffold for tissue engineering, cell culture experiments will be done in cooperation with Dr. Steven Boyce of the Shriners Burns Center and the Department of Surgery at the University of Cincinnati.

CONCLUSIONS

Our preliminary results show that core-sheath structured fibers can be successfully produced by coaxial electrospinning technique and indicate that the mechanical properties are superior to gelatin scaffolds. In wet status, coaxially electrospun scaffolds have shown comparable maximum elongation with PCL scaffolds.

ACKNOWLEDGMENTS

We appreciate Dr. David Butler and his students, Kirsten Kinneberg and Nat Dyment, of the Department of Biomedical Engineering for assistance with the mechanical characterization. D. H. is supported by a graduate assistantship from the Nanomedicine Center at the University of Cincinnati.

REFERENCES

[1] X. Fang and D. H. Reneker, *Journal of Macromolecular Science, Part B* **36** (2), 169 (1997).

[2] Y. Zhang, H. Ouyang, C. T. Lim, S. Ramakrishna and Z. M. Huang, *Journal of Biomedical Materials Research* **72B** (1), 156 (2005).

[3] D. H. Reneker and I. Chun, *Nanotechnology* **7** (3), 216 (1996).

[4] H. Fong, W. Liu, C. S. Wang and R. A. Vaia, *Polymer* **43** (3), 775 (2002).

[5] N. J. Pinto, Jr A. T. Johnson, A. G. MacDiarmid, C. H. Mueller, N. Theofylaktos, D. C. Robinson and F. A. Miranda, *Applied Physics Letters* **83** (20), 4244 (2003).

[6] Z. Sun, E. Zussman, A. L. Yarin, J. H. Wendorff and A. Greiner, *Advanced Materials* **15** (22), 1929 (2003).

[7] D. Li and Y. Xia, *Nano Letters* **4** (5), 933 (2004).

[8] M. Wei, B. Kang, C. Sung and J. Mead, *Macromolecular Materials and Engineering* **291** (11), 1307 (2006).

[9] Y. Zhang, Z. M. Huang, X. Xu, C. T. Lim and S. Ramakrishna, *Chemistry of Materials* **16** (18), 3406 (2004).

[10] H. M. Powell and S. T. Boyce, *Journal of Biomedical Materials Research Part A* **84A** (4), 1078 (2007).

[11] E. J. Chong, T. T. Phan, I. J. Lim, Y. Z. Zhang, B. H. Bay, S. Ramakrishna and C. T. Lim, *Acta Biomaterialia* **3** (3), 321 (2007).