Proceedings of the Canadian Society for Mechanical Engineering International Congress 2021
CSME Congress 2021
June 27-30, 2021, Charlottetown, PE, Canada

Sensitivity study for optimizing Electrospun Helix fibers production for Cardiac Scaffold

Ahmed AlAttar[1], Aleksander Czekanski[2]
[1]Mechanical Engineering, York University, Toronto, Canada
[2]Mechanical Engineering, York University, Toronto, Canada

Abstract— Cardiac tissue infraction is one of the leading factors to hospitalization or the cause of severe limitation in day-to-day activities. Due to the structure of the native cardiac tissue, depending on the native regeneration rate alone will not mitigate the damage incurred in the tissue. Naturally, research has shifted toward increasing the regeneration rate of the cardiac tissue. The regeneration rate can be amplified by utilizing Electrospun patches with seeded cardiac cells implanted on scared areas of the heart tissue. To increase the percentage of successful scaffold implantation the materials are carefully selected, and process parameters are varied to achieve the desired mechanical properties. Helical fibers are required to achieve the same stretch as the native cardiac tissue during expansion and contraction of the muscle. In this sensitivity study, the effect of various electrospinning parameters has been explored to optimize the production of helical fibers.

Keywords-Native Cardiac Tissue, Electrospun, Scaffold, Helix fibers,

I. INTRODUCTION

Heart failure impacts a significant number of people worldwide. With 5.8 million patients in the United States alone and 26 million more around the world, heart failure has been determined as the leading cause of hospitalization [1]. Furthermore, heart failure costs the global healthcare about $108 billion annually, estimated to be 1-2% of the global healthcare budget, with 28% of the spending in the United States and 7% in Europe [2]. Patients with heart failure suffer deteriorating quality of life, while evidence-based therapies have been able to slightly improve the decreasing rate of quality of life and treat symptoms. However, such efforts are not deemed enough for a stable quality of life [2].

The main function of the cardiac muscle is to provide a constant supply of blood to tissues and organs. On average the heart beats in the range of 100,000 beats in a day, totaling to 35 million beats in a year and 2.5 billion beats [3]. Furthermore, the Electrocardiogram (ECG) of a normal adult heart shows that pumping cycle lasts about 60 msec, where the pressure on the left ventricular cardiac tissue reaches the maximum of 16 kPa and regulating at 1 to 1.5 kPa afterwards [4, Sec. 8.3.1]. While the Cardiac muscle is known to be have a high adaptability rate to ensure the blood delivery, tissue infraction will lead to structural and biochemical changes of the muscle which in turn might suppress this ability and lead to progressive damage of the heart tissue with limited tissue recovery [3, pp. 7–12].

Heart muscle tissue is classified into three layers, endothelium, myocardium, and epicardium, with each layer serving a unique function [3], [4]. Endothelium layer is a thin layer inner layer of epithelial cells, that is in contact with blood. While myocardium is considered as the middle layer and epicardium being the outer layer of the heart wall. Myocardium being the most common type of muscle in the cardiac muscle, constituting about 95% of the muscle tissue and the main contributor of coordinated contraction action in the heart [4]. The contraction force generated by the myocardium is due to the structure of the layer [4]. Myocardium consists of specialized straited smooth muscle cells called cardiomyocytes [4].

Mimicking the native cardiac tissue structure or also known as the Extracellular matrix (ECM), has been proven in the literature to provide scaffold with relative mechanical properties [5], [6], [7]. Improving a scaffold's mechanical properties require to examine the ECM further. There are three main routes for cardiac tissue repair Cell entrapment, Cell sheet technology and 3D scaffolds, where their advantages and disadvantages outlined by Ruvinov et al. 2012, [3]. Moreover, there are various methods to manufacture 3D scaffold with Electrospinning gaining the most popularity due to the versatility of the setup and tremendous results [8] [9]. Feiner et al. 2019, stated that utilizing an aligned fiber scaffold would help achieve similar mechanical properties to the native heart tissue [10, pp. 688–689]. Moreover, Fleischer et al. 2013, suggested that a coiled Electrospun fibers would aid in the stretch of the scaffold and the contraction force generated [11].

Based on the literature the production of fully structured helical fibers using an Electrospinning technique is a major challenge [12]. The major conundrum is that electrospinning in nature produces randomized results. Meanwhile, Buckling is considered the main factor in producing helical fibers, buckling in generally is difficult to predict due to the numerous factors affecting the result. Han et al. 2007, derived a theoretical model to predict the buckling of the fibers in the electrospinning process, and determined that velocity of the fiber emitted, diameter of the needle, and viscosity of the solution where all crucial factors to the buckling of the fibers [13]. In this sensitivity study, the effects of various parameters have been examined on the buckling of the Electrospun fiber.

II. MATERIALS AND METHODS

A. Production of helical fibers and scaffolds

A polymer solution of Poly(3-caprolactone) (PCL) with an average M_n of 80,00 (Sigma-Aldrich) as the solute and, Dichloromethane (DCM) and Dimethylformamide (DMF) as the solvents was prepared. The solution was mixed with ratios 1:1 DCM: DMF with varying PCL concentrations of 15%, 17% and 19% w/v. To ensure optimal mixing of the solution, a magnetic stirrer mixed the solution for 12 hours, while being air sealed to prevent the evaporation of the volatile solvent, DCM. Subsequently the solution was placed into a syringe with a stainless steel 20 Gauge capillary and emitted using a syringe pump (New Era -300) at three different flowrates, 0.5ml/hr., 0.75ml/hr., and 1ml/hr. Furthermore, the positive terminal of a DC high voltage power supply was connected to the needle, with voltage of 17kV. Meanwhile, a grounded aluminum collector was placed at varying distance for every test starting from 10cm, 15cm, and 20cm from the needle tip, also known as tip to collector distance (TCD). The angle of collectors examined were 0°, 10° and 20° with TCD of 15cm. Refer to table 1 for a summary of the experiments conducted with the varying parameters.

B. Fiber Characterization

Fiber characterization have been performed using an optical microscope (Zeiss, Axio Imager M2) to examine each scaffold. Subsequently random fibers have been selected from each image captured from the microscope and analyzed using image processing software (ScopeImage 9.0). The average number of fibers characterized for every scaffold is 49.7. The fiber characterization has been divided into three segments: (i) Helix fibers, where the fibers have experienced complete buckling, (ii) partially buckled fibers, where fibers have experienced a varying degree of buckling, and (iii) Straight fibers, where the fibers are straight with no evidence of buckling.

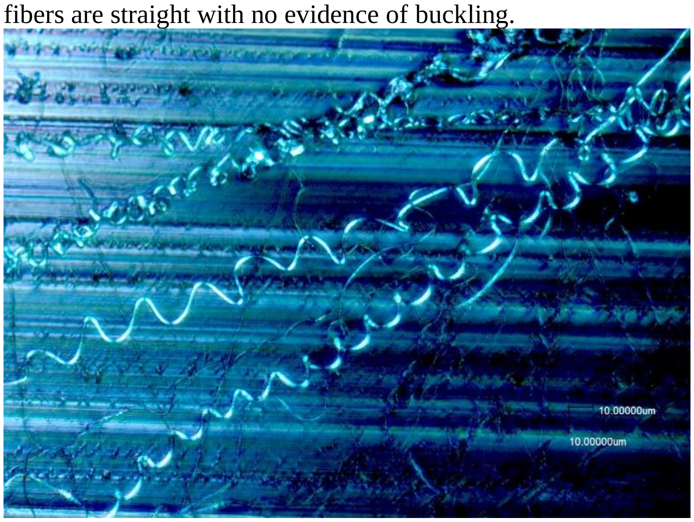

Figure 1 Helix fiber obtained from the following parameters: PCL concentration:15%, TCD:15cm, Flowrate:1ml/hr. and collector angle 0°

Natural Sciences and Engineering Research Council of Canada - *CREATE*

Figure 2 Helix fiber obtained from the following parameters: PCL concentration:15%, TCD:15cm, Flowrate:0.75ml/hr. and collector angle 0°

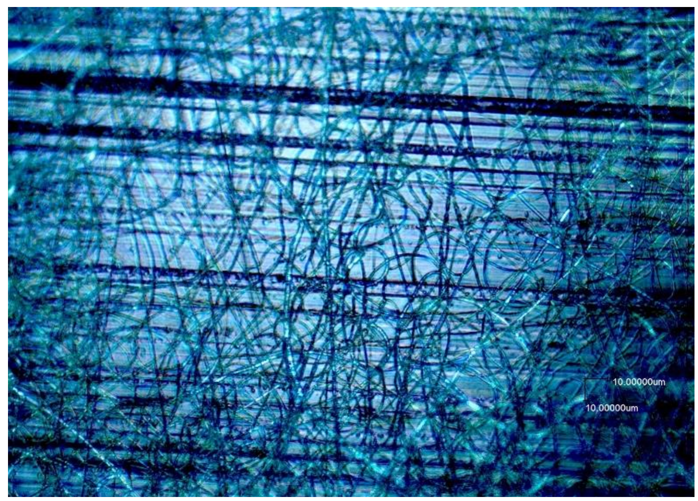

Figure 3 Straight fibers obtained from the following parameters: PCL concentration:19%, TCD:15cm, Flowrate: 0.5 ml/hr., and collector angle: 0°

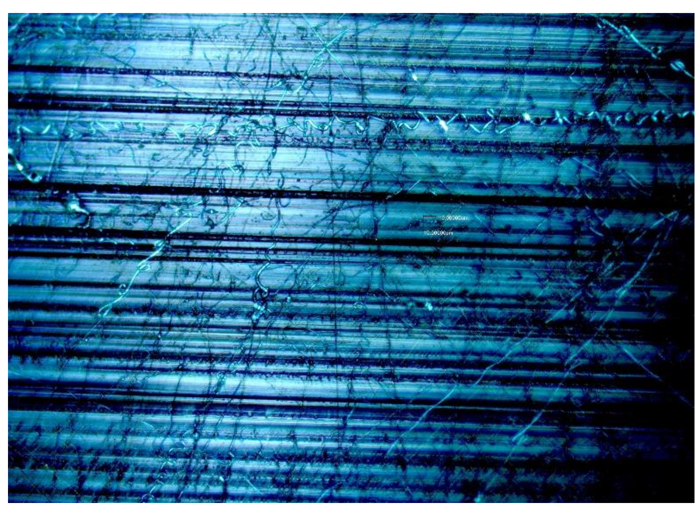

Figure 4 Partially buckled fibers obtained from the following parameters: PCL concentration:15%, TCD:15cm, Flowrate:1ml/hr., and collector angle: 0°

III. RESULTS AND DISCUSSION

A. *15% PCL concentration solution*

Utilizing 15% PCL concentration solution, the highest percentage of helix fibers produced in a scaffold were observed at 59.7% occurrence and was achieved using the following parameters: flowrate 1 ml/hr., TCD of 15cm and a flat collector. The average helical fiber diameter is higher than both the partially buckled and straight fibers. The average diameters of the fibers are 3.24μm, 1.97μm and 1.32μm for helical fiber, partially buckled and straight fibers, respectively. Furthermore, partially buckled fiber would also be considered as a positive catalyst due to a minor contribution of stretch in a scaffold. Fiber production percentages for the 15% PCL concentration solution are presented in Figure5, and average fiber diameters are presented in figure 6.

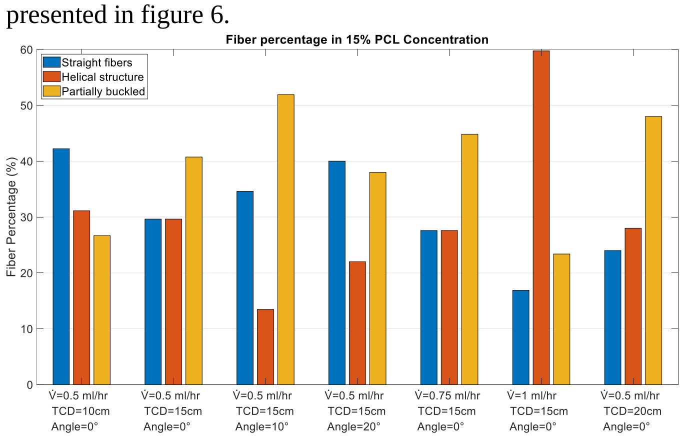

Figure 5 Percentage of fiber production obtained with 15% PCL concentration solution.

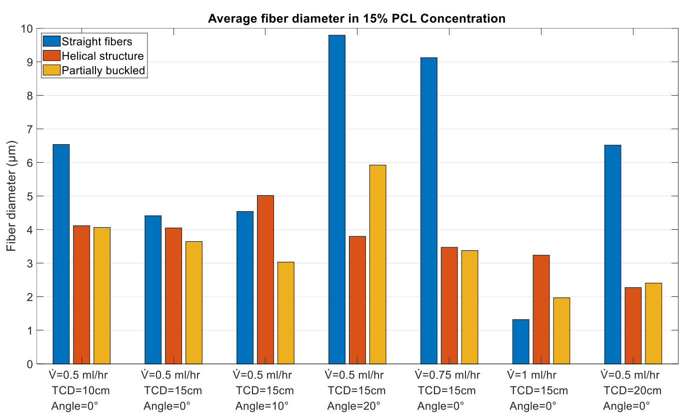

Figure 6 Average fiber diameter obtained using 15% PCL concentration solution.

B. *17% PCL concentration solution*

For the 17% PCL concentration solution for two parameters provided similar results of helical fiber production of about 44.9%, partially buckled fibers are 33.3% and straight fibers is 21.7%. The similar results were obtained at both the flowrate of 0.5 ml/hr., flat collector and a varying TDC of 10 cm and 15 cm for each experiment, respectively. However, a slight variation in fiber diameter was observed between both experiments. For the experiment with TDC of 10 cm the fiber diameters where 3.82μm, 2.88μm and 6μm for helical fiber, partially buckled, and straight fibers, respectively. However, for the experiment with TCD of 15 cm fiber diameter was 2.56 μm, 2.47 μm and 3.86 μm for helical fiber, partially buckled, and straight fibers, respectively.

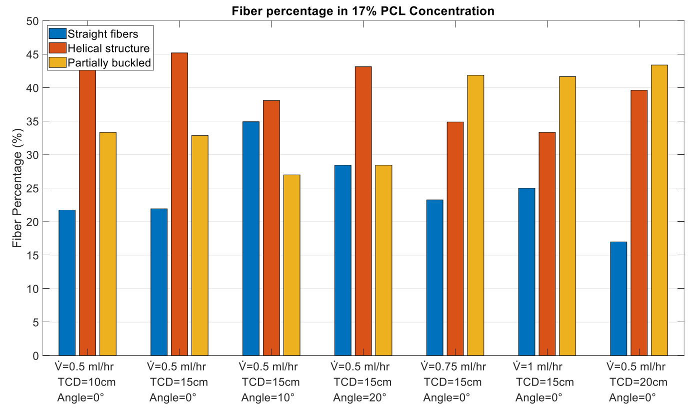

Figure 7 Percentage of fiber production obtained with 17% PCL concentration solution.

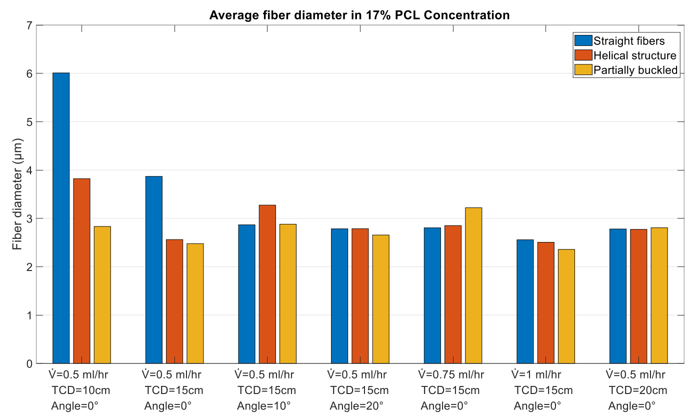

Figure 8 Average fiber diameter obtained using 17% PCL concentration solution.

C. *19% PCL concentration solution*

Meanwhile for 19% PCL concentration solution, the highest helical fiber production of about 51.5%, obtained with the following parameters of 0.5 ml/hr., TCD of 20cm and a flat collector. Diameters of helical, partially buckled, and straight fibers are 2.3μm, 2.10μm, and 1.79μm, respectively. While this higher PCL concentration solution resulted in large ratio of helical fiber production, utilizing this concentration provides a challenge due to the solution drying at the needle tip over an extended duration of time.

Another observation, this concentration obtained the highest percentage of straight fiber with a ratio of 82.35%, while is has the lowest production of helical fibers with percentage of 5.88% and 11.76% for partially buckled fibers, respectively. Moreover, the number of beads and beaded fibers increased significantly as the angle of the collector increased, and this observation is shared across all solution concentrations.

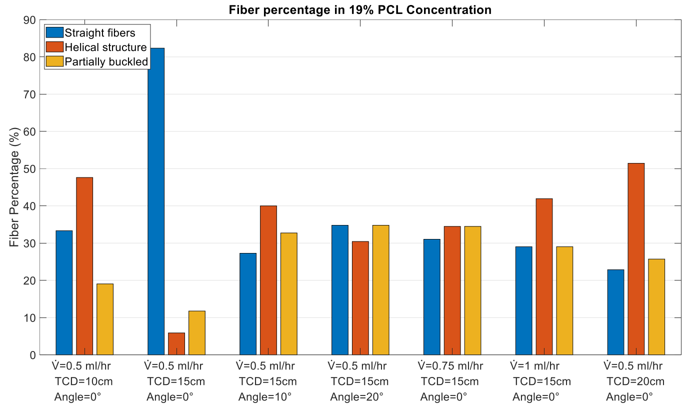

Figure 9 Percentage of fiber production obtained with 19% PCL concentration solution.

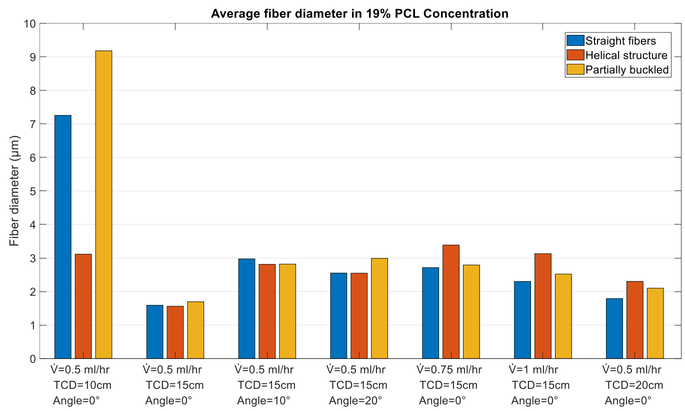

Figure 10 Average fiber diameter obtained using 19% PCL concentration solution.

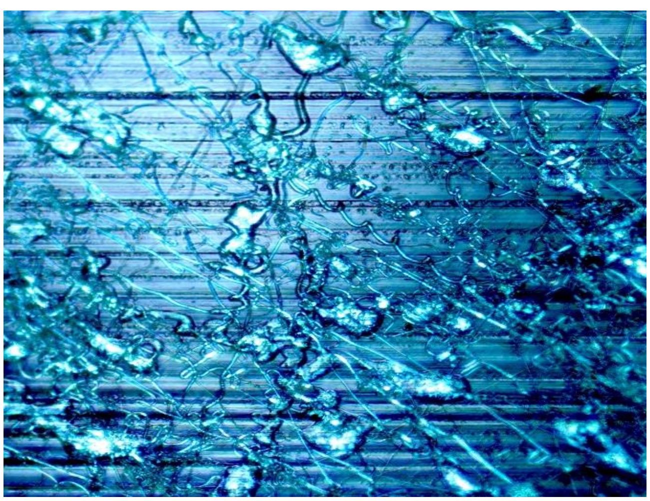

Figure 11 Beaded structures obtained due to collector angle of 10° in obtained using 15% PCL concentration solution.

IV. CONCLUSION

Fiber structure determines the mechanical properties of the scaffold and thus subsequently, influences scaffold longevity and human body immune response. The objective of obtaining helix fiber structure in the scaffold is to improve the scaffold stretchability. A more elastic scaffold that mimics the native tissue structure movement during contraction and expansion has higher percentage of cell survivability. In this sensitivity study, the parameter of the electrospinning process was varied to examine the optimal helix fiber production. Helix fibers are formed due to buckling of the fibers under their own weight, subsequently the fibers were classified into Helix structured, partially buckled and straight fibers. Partially structured fibers will contribute to the desired scaffold mechanical properties with a certain structural limitation. Based on this characterization each scaffold was scanned using an optical microscope to determine the optimum parameters for helical fiber production, and consequently analyzed using a software.

It was observed that 15% PCL concentration solution produced the highest percentage of helical structured fibers. While a solution with 17% concentration provided median result when compared to the solutions utilized in the experiment. Moreover, increasing the solution concentration to 19% PCL concentration, resulted more helical fibers present in the scaffold. However, the scaffold also presented an increase in the number of beaded structures. Utilizing an angled collector with higher solution concentration, did not provide any desired results. Scaffold obtained higher number of beaded structures when compared to scaffold produced with flat collectors.

Table 1 Summary of experiments performed with observations.

Flowrate	TCD	Angle	Results
15% PCL concentration solution			
0.5	10	0	Helical fibers were more present in the outskirts of the scaffold than center.
0.5	15	0	Helix fibers was equal to the straight fiber production.
0.5	15	10°	Larger production of partially buckled fiber, and beaded structures due to the angle.
0.5	15	20°	High number of beaded structure due to the angled collector.
0.75	15	0	Bead structures are higher when compared to other flat collector experiments.
1	15	0	Significantly high helix fiber production, with a higher presence on the outskirts of the scaffold.
0.5	20	0	Most the fiber are partially buckled.
17% PCL concentration solution			
0.5	10	0	Highest helical fiber production in this solution concentration, and the largest straight fiber diameter.
0.5	15	0	Close percentage of helix fibers as the previous experiment, however the straight fibers diameter is smaller.
0.5	15	10°	Fiber towards the top of the scaffold have a higher straight fiber concentration.
0.5	15	20°	High number of beaded structures spread out on the scaffold, with a high helix production toward the middle and the end of the scaffold.
0.75	15	0	Number of partially buckled fiber is higher than other parameters utilizing this concentration.
1	15	0	Number of partially buckled fiber is high, along with the smallest average fiber diameter in this concentration
0.5	20	0	Highest percentage of partially buckled fibers.
19% PCL concentration solution			
0.5	10	0	Considerably larger fiber diameter, specifically partially buckled fibers.
0.5	15	0	Noticeably smaller fiber diameter, with most of the fibers having a straight structure.
0.5	15	10°	Bead structures are present, however secondary to other solution concentrations.
0.5	15	20°	Bead structure are present in larger footprint.
0.75	15	0	Helix fiber structure is on average spread throughout the scaffold.
1	15	0	Helix fiber production increased slightly.
0.5	20	0	Highest helical fiber production using this solution concentration, with a slight decrease in fiber diameter.

V. REFRENCES

[1] J. Park and H. S. Suradi, "State-of-the-art Structural Interventions in Heart Failure," *Card. Fail. Rev.*, vol. 5, no. 3, pp. 147–154, Nov. 2019, doi: 10.15420/cfr.2019.12.2.

[2] J. H. Morris and L. Chen, "Exercise Training and Heart Failure: A Review of the Literature," *Card. Fail. Rev.*, vol. 5, no. 1, pp. 57–61, Feb. 2019, doi: 10.15420/cfr.2018.31.1.

[3] E. Ruvinov, Y. Sapir, and S. Cohen, "Cardiac Tissue Engineering: Principles, Materials, and Applications," *Synth. Lect. Tissue Eng.*, vol. 4, no. 1, pp. 1–200, Sep. 2012, doi: 10.2200/S00437ED1V01Y201207TIS009.

[4] D. R. Peterson and J. D. Bronzino, *Biomechanics: principles and applications*. Boca Raton: CRC Press, 2008.

[5] S. Fleischer, R. Feiner, and T. Dvir, "Cardiac tissue engineering: from matrix design to the engineering of bionic hearts," *Regen. Med.*, vol. 12, no. 3, pp. 275–284, Apr. 2017, doi: 10.2217/rme-2016-0150.

[6] N. F. Huang *et al.*, "Big bottlenecks in cardiovascular tissue engineering," *Commun. Biol.*, vol. 1, no. 1, Art. no. 1, Nov. 2018, doi: 10.1038/s42003-018-0202-8.

[7] M. Kitsara, O. Agbulut, D. Kontziampasis, Y. Chen, and P. Menasché, "Fibers for hearts: A critical review on electrospinning for cardiac tissue engineering," *Acta Biomater.*, vol. 48, pp. 20–40, Jan. 2017, doi: 10.1016/j.actbio.2016.11.014.

[8] J. An, J. E. M. Teoh, R. Suntornnond, and C. K. Chua, "Design and 3D Printing of Scaffolds and Tissues," *Engineering*, vol. 1, no. 2, pp. 261–268, Jun. 2015, doi: 10.15302/J-ENG-2015061.

[9] I. Jun, H.-S. Han, J. R. Edwards, and H. Jeon, "Electrospun Fibrous Scaffolds for Tissue Engineering: Viewpoints on Architecture and Fabrication," *Int. J. Mol. Sci.*, vol. 19, no. 3, Mar. 2018, doi: 10.3390/ijms19030745.

[10] R. Feiner, A. Shapira, and T. Dvir, "32 - Scaffolds for tissue engineering of functional cardiac muscle," in *Handbook of Tissue Engineering Scaffolds: Volume One*, M. Mozafari, F. Sefat, and A. Atala, Eds. Woodhead Publishing, 2019, pp. 685–703.

[11] S. Fleischer *et al.*, "Spring-like fibers for cardiac tissue engineering," *Biomaterials*, vol. 34, no. 34, pp. 8599–8606, Nov. 2013, doi: 10.1016/j.biomaterials.2013.07.054.

[12] P. E. S. Silva, F. V. de Abreu, and M. H. Godinho, "Shaping helical electrospun filaments: a review," *Soft Matter*, vol. 13, no. 38, pp. 6678–6688, Oct. 2017, doi: 10.1039/C7SM01280B.

[13] T. Han, D. H. Reneker, and A. L. Yarin, "Buckling of jets in electrospinning," *Polymer*, vol. 48, no. 20, pp. 6064–6076, Sep. 2007, doi: 10.1016/j.polymer.2007.08.002.