Cardiovascular Electrospinning

Prof. Steven S. Saliterman
Department of Biomedical Engineering, University of Minnesota
http://saliterman.umn.edu/

Review Article

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Review article

Fibers for hearts: A critical review on electrospinning for cardiac tissue engineering

Maria Kitsara[a,*], Onnik Agbulut[b], Dimitrios Kontziampasis[c], Yong Chen[d,e], Philippe Menasché[f,g,*]

[a] Institute de Microelectrònica de Barcelona, IMB-CNM (CSIC), Campus Universidad Autònoma de Barcelona, 08193 Bellaterra, Barcelona, Spain
[b] Sorbonne Universités, UPMC Univ Paris 06, Institut de Biologie Paris-Seine (IBPS), UMR CNRS 8256, Biological Adaptation and Ageing, 75005 Paris, France
[c] School of Chemical and Process Engineering, Engineering Department, University of Leeds, LS2 9JT Leeds, UK
[d] Ecole Normale Supérieure-PSL Research University, Sorbonne Universités, UPMC Univ Paris 06, UMR CNRS 8640, PASTEUR, 75005 Paris, France
[e] Institute for Integrated Cell-Material Science, Kyoto University, Kyoto 606-8507, Japan
[f] Université Sorbonne Paris Cité, Univ Paris Descartes; INSERM U970, 75015 Paris, France
[g] Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Department of Cardiovascular Surgery, 75015 Paris, France

General Considerations

- Mimicking the fibrillar structure of the extracellular matrix is important for scaffolds.
- Clinical trails to date with cardiac stem cells, cardiospheres and adipose-driven stroma cells are minimal, unlike skeletal myoblasts and bone marrow derived cells.
- There is a low rate of engraftment and high mortality of the transplanted cells into diseased hearts. (From cell leakage due to inflammation, ischemia and apoptosis.)
- Tissue engineering provides a 3D environment similar to endogenous cardiac tissue, ability to deliver stems cells, support structures, and growth factors.

Kitsara, M., O. Agbulut, D. Kontziampasis, Y. Chen, and P. Menasche. "Fibers for Hearts: A Critical Review on Electrospinning for Cardiac Tissue Engineering." *Acta Biomaterialia* 48 (Jan 2017): 20-40.

Electrospinning

- In electrospinning polymeric solution is fed through a thin needle opposite to a grounded collector and a high voltage is applied to form a jet of the solution that travels from the needle to the collector, where it is deposited in the form of dried nanofibers.
- Electrospinning of synthetic and natural fibers is easy and cost effective.
- Electrospun nanofiber matrices show morphological similarities to the natural ECM characterized by continuous fibers ranging from nano to micro scale, high surface-to-volume ratio, high porosity and variable pore size distribution.

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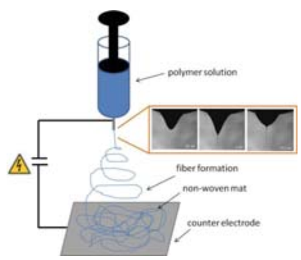
Typical Electrospinning Setup



Reneker, D.H.; Yarin, A.L. Electrospinning jets and polymer nanofibers. Polymer 2008, 49, 2387-2425.

Scaffold Considerations

- Natural vs synthetic materials.
- Mimicking the aligned pattern of fibrous cells (microenvironment).
- Recognition of Young's modulus for healthy and diseased tissue throughout the cardiac cycle.
- Conductivity (charge carriers).
- Biocompatibility and biodegradability.
  - Natural fibers may allow for better cell adhesion, differentiation, and proliferation, but have poorer mechanical properties. Their degradation products are less toxic and have a lower immune response.
- Replacing static seeding with dynamic, magnetic, vacuum, electrostatic, and centrifugal seeding.

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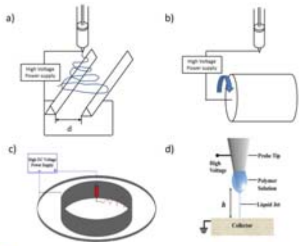
Inducing Fiber Alignment



(a) Parallel electrodes.
(b) Rotating collector.
(c) Rotating jet method,
(d) Near field electrospinning

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Sun, D.; Chang, C.; Li, S.; Lin, L. Near-field electrospinning. Nano Lett. 2006, 6, 839-842.

Natural Polymers for Electrospinning

- Collagen (type I, III)
  - Found in myocardial connective stroma.
  - Support H9c2 cardiomyoblasts culture.
- Fibrinogen (glycoprotein)
  - Ability to bind with high affinity to functional vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and a number of other cytokines.
- Chitosan (polysaccharide)
  - CM-fibroblast co-cultures resulted in polarized CM morphology and retained their morphology and function for long-term culture.
  - Fibroblast co-cultures demonstrated synchronized contractions involving large tissue-like cellular networks.

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- Elastin
  - Used as a composite when electrospun.
- Silk
  - Glue-like sericin protein which role is to hold fibers together, and a fibroin filament component.
  - Good mechanical properties.
  - hAECs and hCASMCs demonstrate an affinity for the electrospun silk fibroin/PEO blend.

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Synthetic Polymers for Electrospinning

- Poly(ε-caprolactone)-based scaffolds (PCL)
  - Widely used.
  - High stiffness and hydrophobicity do not provide significant cell attachment and proliferation in cardiac tissue engineering.
  - PCL/gelatin scaffolds promote cell attachment and alignment.
- Poly-(ι-lactide) (PLLA), polyglycolide (PGA) and the copolymer poly(lactide-co-glycolide) (PLGA).
  - PLLA scaffolds promoted better cell adhesion and mature cytoskeleton structure with well-defined periodic units in the contractile machinery (sarcomeres).
  - Co-spinning with gelatin and a-elastin lead to stable scaffolds in an aqueous environment without crosslinking.

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- Polyurethane (PU)
  - Construction of heart valves.
- Poly(ester urethane) ureas (PEUU)
- Poly(glycerol sebacate) (PGS)
- Poly(3-hydroxybutyrate) (PHB)

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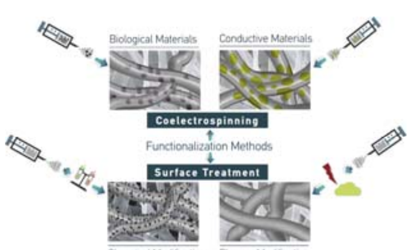
Surface Functionalization



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Summary

- Mimicking the fibrillar structure of the extracellular matrix is important for scaffolds.
- Electrospun nanofiber matrices show morphological similarities to the natural ECM characterized by continuous fibers ranging from nano to micro scale, high surface-to-volume ratio, high porosity and variable pore size distribution.
- Electrospinning of synthetic vs natural fibers, co-spinning and surface functionalization.
- Clinical trails to date with cardiac stem cells, cardiospheres and adipose-driven stroma cells are minimal.