

## Review Article

# Tubular electrospun scaffolds tested in vivo for tissue engineering

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## ABSTRACT

Tissue engineering has been widely used for its great variety of functions. It has been seen as a solution to satisfy the need for vascular substitutes like small diameter vessels, veins, and nerves. One of the most used methods is electrospinning, due to the fact that it allows the use of various polymers, sizes, mandrels and it can adjust the conditions to create personalized scaffolds. For the creation of scaffolds is fundamental to understand the advantages and disadvantages of each polymer, of this, will depend the biodegradability, biocompatibility, porosity, cellular adhesion, and cell proliferation as it is essential to mimic the extracellular matrix and provide structural support for the cells. The aim of this review was to investigate which materials are being used for the creation of tubular scaffolds by electrospinning. Here we selected only in vivo evaluation to demonstrate remodeling of the grafts into native-like tissues, in vitro evaluations had been excluded from this review. We analyze the conditions like speed, distance and voltage and the modifications like growth factors and combinations of natural and synthetic polymers that allow the authors to have a functional scaffold that will suit its purpose.

**Keywords:** Biomaterials, Dynamic collector, Dynamic electrospinning, Electrospinning, Tissue engineering, Tubular scaffold

## INTRODUCTION

Tissue engineering comes from the field of biomaterials and consists of combining scaffolds, cells and biologically active molecules to form functional tissues. The mission of this field is to create structures that re-establish or enhance tissues or damaged organs.<sup>1</sup> A scaffold is a material which will “provide the structural

support for the adhesion and/or cellular growth, that will favor posterior tissue development”.<sup>2</sup> Giving the necessary microenvironment for proliferation and cellular viability. The scaffold can be elaborated with a natural or synthetic polymer base, trying to mimic the extracellular matrix, that will enhance cell adhesion and migration, and if the environment is adequate it will form a new tissue.<sup>3</sup>

Many techniques have been adopted in the tissue engineering field for scaffold fabrication, among them, electrospinning.<sup>4</sup> Electrospinning is made by nanometric fibers of different polymers and solvents.

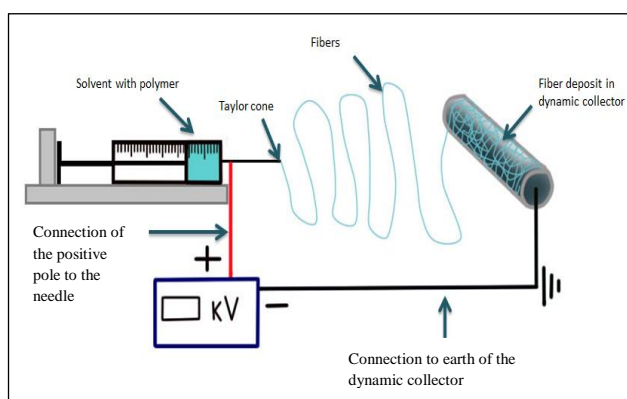
During the threading, the polymeric solution is electrospun by coaxial stretch by an electrical potential differential produced by a high voltage source, generally between 5-35Kv, which generates the electric field necessary to overcome the surface tension of the solution and thread the microfilaments towards a collector that can be flat or tubular.<sup>5</sup> This technique allows the production of tridimensional scaffolds made by micro-nanometric polymeric fibers, with similar properties from the ones that confirm the extracellular matrix, permitting cellular growth due to the microporous structure obtained.<sup>6-7</sup>

To begin the electrospinning process a biocompatible and biodegradable polymer is needed, such as polycaprolactone (PCL) or polylactic acid (PLA) dissolved in a solvent to produce a viscoelastic solution. This solution, in the presence of an electric field, may be considered as a dipole arrangement composed of positive and negative charges.<sup>8</sup>

The solvents are chosen in function of their dielectric constant, Table 1, from which the one that is capable of achieving greatest electrical conduction in the solution is selected. This solution will be injected through the capillary connected to the positive pole of the high voltage source; meanwhile, the simple or dynamic collector where the fibers deposit will be connected to earth from the same high voltage source (Figure 1).

**Table 1: Principal solvents used in electrospinning with its dielectric constant.**

Solvent	Dielectric constant	Solvent	Dielectric constant
Chloroform	4.8	Acetone	20.7
Ethanol	24.55	Dimetilformamide (DMF)	38.3
Water	79	1,1,1,3,3,3-Hexafluoro-2-propanolol (HFIP)	16.7
Distilled Water	80	Acetic acid	6.15
Methanol	32.6	Tetrahydrofurane (THF)	7.58
Hexafluoroisopropanolol (HFIP)	16.7	Formic acid	58
Trifluoroacetic acid (TFA)	8.55	Dimethylacetamide (DMAC)	37.8
Methylene chloride	10.7	Dichloromethane	9.1
2,2,2 Trifluoroethanol (TFE)	26.14	Dichloroethane	10.36



**Figure 1: Representation of the nanofiber creation by electrospinning to elaborate tubular scaffolds.**

Among the most used synthetic polymers for electrospinning, there are PCL and PLA. PCL is aliphatic, hydrophobic polyester of slow degradation, so it is usually used in scaffolds that must last long periods of time to allow recellularization. It is characterized by having low resistance to traction and high elongation it is

vastly porous which favors cellular infiltration, that enables excellent biocompatibility. PLA is a semicrystalline polymer of slow degradation, hydrolysis resistant; for its biocompatible properties, it does not create toxic or carcinogenic effects of local tissues.<sup>9</sup> Talking about its mechanical properties, it has good traction force and low elongation percentage, but as it is a hydrophobic material the degradation process takes longer than a year.<sup>10</sup>

## REVIEW OF LITERATURE

### Polycaprolactone

One of the applications of the scaffolds made by electrospinning is the vascular grafts, which use mainly PCL as its biomaterial. PCL is an excellent option because it shows good surgical and mechanical properties, rapid endothelialization and cell ingrowth.<sup>11,12</sup> When used in neovessels it has shown the development of neointima and endothelialization.<sup>13</sup> PCL has also been used for drug delivery.<sup>14</sup>

Mungai D et al, in 2013 made by electrospinning tubular scaffold of PCL with the purpose of comparing its effectiveness of small caliber vessels (<6mm) with respect to expanded polytetrafluoroethylene (ePTFE). They implanted the grafts in the aorta of 14 rats and observed that the PCL grafts show no stenosis and had more presence of vascular endothelium, while the 2 scaffolds of ePTFE had thrombi, they concluded that the PCL scaffolds have the potential to provide a better result in the revascularization of small caliber vessels.<sup>15</sup> For its slow degradation properties PCL enhances cellular adhesion, Jha BS and Cols in 2010 created electrospun scaffolds to use them as nerve regeneration guides. They implanted a sciatic nerve graft in three rats for seven weeks. The authors observed that the rats did not drag the affected limb, increased the movement of the knee and responded to painful stimuli. They also observed the presence of Schwann cells, parallel aligned to the regenerated tissue, indicating myelination.<sup>16</sup>

### ***Polycaprolactone and collagen***

One of the most combined polymers together with polycaprolactone is collagen. Bryan W et al, in 2008, used these materials to prove if the scaffold was up to cellular growth and whether or not it was able to endure physiological conditions. They did an aorto-iliac bypass of 4.54mm diameter in a rabbit, finding great adhesion and muscular and endothelial cell growth, as well as a high degree of permeability and structural integrity, the luminal diameter kept constant, as the 3D scaffold structure.<sup>17</sup> Wenwen Yu and Cols in 2014, made artificial nervous conduits by electrospinning, the scaffolds were made by collagen and polycaprolactone, which was improved by adding multi-walled carbon nanotubes (MWNT). The objective of their research was to see the mechanical behavior, biocompatibility, effectiveness, and toxicology of the MWNT-Col/PCL scaffold in vivo. They used 15 rat models, in which an 8mm long defect was created along the sciatic nerve. They concluded that MWNT improved the scaffold solubility, the hydrophilicity and it was able to endure the in vivo conditions. Finally, the authors concluded that the MWNT-Col/PCL scaffold promotes the neural regeneration and prevents muscular atrophy.<sup>18</sup>

Sampaziotis F et al, in 2017, created a new method to expand a spread epithelial biliary extrahepatic cells. They managed to aise extrahepatic cholangiocytes by mechanical dissociation, the cells preserved their functions and characteristic markers, and they call them "extrahepatic cholangiocyte organoids (ECOs). This team made a scaffold out of collagen, which was seeded with ECOs aiming to repair rats bile duct. As a control group, they used collagen scaffolds seeded with fibroblasts. The authors observed that the control scaffold presented liminal occlusion while the ones seeded with ECOS had biliary biomarkers, minimal apoptosis, stability and integrity of the new biliary epithelium, and there was no cholestasis or luminal occlusion. They concluded that the

use of ECOS may successfully rebuild the biliary duct, with the possibility using them on electrospun scaffolds.<sup>19</sup>

### ***Modified polycaprolactone***

As polycaprolactone is one of the most used polymers many authors have given themselves the task to combine it with other materials. Fukunishi et al, made a combination of polyglycolic acid (PGA) and poly (l-lactide-co-e-caprolactone) (PLCL) scaffolds for the creation of an inferior vena cava for a sheep, this lead to no cases of aneurysm formation or ectopic calcification, as effective graft mechanical properties.<sup>20</sup> Antonova LV et al, made a combination of natural polymer PHBV and synthetic PCL for the creation of small vessels. They saw that physico-mechanical properties of this materials together are poor, so they incorporated vascular endothelil factor (VEGH) to improve them.<sup>21</sup> Beigi et al, made a combination of PCL with Gel to create a 10mm schiatic nerve graft for rats, they saw that this materials can support axonal regeneration.<sup>22</sup> Zhou M et al, made a hybrid chitosan/PCL scaffold for a small diameter vascular graft, they saw endothelium regeneration, and the presence of collagen and elastin.<sup>23</sup> Cirillo V et al, made synthetic nerve conduits with PCL and gelatin, they saw that gelatin lead to uniform electrospun fiber size in vitro but in vivo the conduits were nos satisfactory because of its degradation kinetics.<sup>24</sup>

Lei Zhu et al, in 2017 made 1.5mm diameter scaffolds using polycaprolactone, they modified it with two peptide sequences: arginine-glycine-aspartic acid (RGD) and tyrosine-isoleucine-glycine-serine-arginine (YIGSR) with the aim of promoting the regeneration of rat sciatic nerve. The result was that the PCL-RGD/YIGSR had a better neurological functional recovery, increase in the number of motor and sensory neurons, increase in regeneration and axonal transport, with the improvement of muscle atrophy and increase in vascularization, in comparison with the only PCL group. This team concluded that PCL scaffolds may be improved by the use of RGD/YIGSR peptides.<sup>25</sup>

One of the possible modifications of the electrospinning technique is the fabrication of a layered scaffold, which can regulate degradation time and improve mechanical/biological properties. Chung J et al in 2014 made tubular scaffolds of three layers: internal and external layers made of polycaprolactone and a middle layer made of silk fibroin. The diameter of the scaffolds was 2.45mm, and they used 11 rats with esophageal circumferential lesions which were then fixed with the 3 layered scaffolds. They observed a full recovery of the esophageal lesions around the second week, like proliferation, adhesion and cellular infiltration.<sup>26</sup> Shiyu Cheng and Cols in 2017 made tubular scaffolds as carotid artery grafts for rabbits. They used PCL for is expanding and rapid degradation capacity, with poly (DL-Lactide-co-glycolide) (PLGA), which tends to shrink and degrade quicker. Knowing these properties, the authors decided to

combine and take advantage of their qualities and create a multi-layered Scaffold, using PCL for the middle layer and PLGA for the internal and external layers. This allowed them to regulate the tendency of expansion and shrinking of both materials, managing to make a structure capable of resisting degradation. They saw that the PCL-PLGA graft was free of obstruction, with a well-maintained lumen, abundant cellular growth, excellent cell proliferation and migration.<sup>27</sup>

### ***Polyurethane-urea and silk***

Soletti L and Cols in 2010 made tubular scaffolds of polyurethane urea (PEEU) of 1.3mm diameter for the replacement of abdominal aorta in rats, they made a comparison between scaffolds covered with a layer of no thrombogenic polymer (MPC) that favors less platelet adhesion, against polyurethane urea scaffolds alone. The result of the study demonstrates diminishment in platelet adhesion and muscle cells, an augmentation in permeability rates and absence of ischemic zones in the PEUU-MPC scaffold in comparison with the PEUU one.<sup>28</sup> Yahoua G et al, made tubular scaffolds to use them as vascular grafts in the abdominal aorta of rats. They used poly (ester urea) (PEU) and made two scaffolds with different wall thickness: scaffold A was 250µm and B de 350µm. Authors saw that scaffold A didn't show aneurismatic dilatation or stenosis but did show confluent endothelial cells that mimicked the native aorta, in comparison with scaffold B that presented occlusion at moth 12 and didn't have well-organized cells.<sup>29</sup> Park SY et al, in 2015 made 1.5mm diameter silk scaffolds as grafts for sciatic nerves in rats. They wanted to evaluate the mechanical properties and regenerative capacity of the silk graft. The surgical process of connecting the graft with the ends of the nerve was more successful in the silk scaffold than in the allograft, because the second one wasn't personalized resulting in incompatibility. The mechanical flexibility as the strength of the scaffolds was adequate to maintain the patency and mimic the sciatic nerve, favoring mayor axonal myelin regeneration. They concluded that silk scaffolds promote functional nerve regeneration.<sup>30</sup>

### ***Polyurethane***

Bergmeister H and Cols in 2011 made 1.5mm diameter scaffolds using polyurethane to study its characteristics using it as a small vessel vascular graft in rats. They didn't find the formation of clots, obstruction or intimal hyperplasia. Histologically they made the CD34+ test, where they observed cellular migration since week one that improved to week six.<sup>31</sup> Barreon M and Cols in 2017 made 2.5cm diameter scaffolds to use them as an esophageal prosthesis in a pig. They used polyurethane (PU) seeded with esophageal mucous cells from a pig. The objective of this study was to demonstrate if mucosal cells can be used to fulfill the optimal properties of a synthetic matrix. Macroscopically the aspect of the graft was similar to the native esophagus. With hematoxyline-

eosine they determine that the graft had an external layer of esqueletical muscle and adventive layer and formation of new tissue with the native esophageal layers. They determined that the polyurethane scaffold is able to achieve esophageal regeneration in an in vivo pig model.<sup>32</sup>

### ***Growth factors, bioactive molecules and drugs***

It is common to add growth factors, bioactive molecules and/or drugs to the electrospun scaffolds, such as the vascular endothelial growth factor (VEGF), which can regulate proliferation, migration, and survival of endothelial cells. Hydrophobin class I can enhance the hydrophobicity of polycaprolactone which helps cellular adhesion. Wang K and cols in 2017 made 2mm diameter scaffolds with PCL-VEGF-HGFI, with the aim of determining if adding these molecules to PCL can improve the endothelialization and vascular regeneration. They saw that only the PCL-VEGF-HGFI scaffold compared with the controls of the only PCL showed augmentation in capillary formation, the liberation of nitric oxide, endothelial formation, cellularization and smooth muscle cell regeneration. They concluded that this modified scaffold is excellent for vascular grafts.<sup>33</sup>

Kuihua Z et al, in 2013 made nerve guidance conduits (NGCs) by coaxial electrospinning using silk fibroin (SF), PLA and PCL. They wanted to prove if adding to the scaffold the nerve growth factor (NGF) could improve sciatic nerve regeneration in rats. They decided to do the coaxial electrospinning because this technique allows the fabrication of a core-shell graft that releases the drug in a controlled way. In the electrophysiological examination, they saw an improved speed restoration of the nerve and compound motor action potential in the group of SF/PLA/NGCs (group I) than in the SF/PLA/NGF NGCs (group II) indicating that functional recuperation of group II was superior. In the histological and electronic microscope, they proved that group II had better nervous regeneration in quantity and quality. They concluded that adding Nerve Growth Factor (NGF) to the scaffold improves nerve regeneration.<sup>34</sup>

Salehi M et al, in 2017 made neuronal guide scaffold for a defect in rat sciatic nerve. They created a graft of PLA multiwalled carbon nanotubes (MWCNTs), gelatin nanofibers (GNFs), coated with recombinant human erythropoietin loaded chitosan nanoparticles (rhEpo-CNPs) and Schwann cells (SC). The results showed that the liberation of EPO is beneficial for the recuperation of periphery nervous lesions, in the footprint test HPL and CMAP, in which nociception a muscular generation is tested. PLA/MWCNTs/GNFs/rhEpo-CNPs/SC and the autograph obtained better results, as in the weight loss test, where they evaluated muscle reinnervation. Histopathological findings proved that this group mimicked the most the native sciatic nerve. Authors concluded that the use of Swann cells and the release of rhEpo-CNPs has a high range of nervous recuperation.<sup>35</sup>

**Table 2: Tubular scaffolds made by electrospinning.**

Author	Scaffold measures	Material	Solvent	Conditions	Sterilization method	Organ	Expt. model
Wang K et al <sup>33</sup>	1.1cm ID: 2mm	PCL- VEGF-HGFI	Methanol and chloroform	Flow rate: 8ml/h, Voltage: 11kV, Distance: 17cm, Speed: 300rpm	Immersion in 75% (v/v) ethanol solution for 1h	Abdominal aorta	15 rats
Wang Z et al <sup>14</sup>	1cm ID: 2mm	PCL, Resveratrol	Methylene chloride and methanol	Flow rate: 8 mL/h Voltage: 11 kV Distance: 11 cm	Ethylene oxide	Abdominal aorta	5 rats
Chan AHP et al <sup>13</sup>	ID: 0.5mm	PCL	1,1,1,3,3,3-hexafluoro-2-propanol (HFIP)	Flow rate: 2 mL/hr Voltage: 20 kV Distance: 20 cm Speed: 500 rpm	Ethanol immersion 70% during 30 minutes	Carotid artery	48 mice
Fukunishi T et al <sup>20</sup>	1.5cm x 12mm	PGA/PLCL	Hexafluoroisopropanol (HFIP)	PGA Flow rate: 2.5 mL/h PCL Flow rate: 5.0 5mL/h Voltage: 25 kV Distance: 20 cm Speed: 30 rpm	Gamma radiation	Inferior cava vein	6 sheep
Zhu L et al <sup>25</sup>	15mm x 1.5mm	PCL-RGD/YIGSR	Mixture of methanol and chloroform	Flow rate: 5 mL/h Voltage: 12 kV Distance: 20 cm Speed: 100 rpm	-	Sciatic nerve	135 rats
Barron MR et al <sup>32</sup>	5cm x 2.54cm	PU	Hexafluoro-2-propanol HFIP	Flow rate: 5 ml/h Distance: 30 cm Speed: 100 rpm	-	Esophagus	1 pig
Salehi M et al <sup>35</sup>	10mm x ID: 1mm, ED: 3mm	PLA Gelatin	Acetic acid	Flow rate: 0.50 mL/h Voltage: 18-20 kV Distance: 15 cm	UV light in laminar flux during 60 minutes	Sciatic nerve	36 rats
Fotios S et al <sup>19</sup>	500µm x ED: 200-600µm	Collagen	-	-	70% ethanol immersion during 30 minutes	Biliary duct	Mice
Buscemi S et al <sup>5</sup>	1cm	PHEA PLA PCL	Water Dichloromethane	Flow rate: 1mL/h Voltage: 20-25 kv Distance: 10-20 cm Speed: 200rpm	Rinsed with double distilled water and vacuum dried	Biliary duct	10 rabbits
Larisa V et al <sup>21</sup>	10mm DI: 2mm	PHBV/ PCL PHBV/PCL/ VEGF	Chloroform	Flow rate: 0.3 mL/h Voltage: 20 kV, 22G needle	Ethylene oxide	Abdominal aorta	24 rats
Yaohua G et al <sup>29</sup>	2cm ID: 1mm	PEU	hexafluoroisopropanol (HFIP)	Flow rate: 1 mL/h Voltage: 10 kV Distance: 15 cm Speed: 100 rpm	Ethylene oxide	Abdominal aorta	5 mice
Park SY et al <sup>30</sup>	10mm ID: 1.65mm	Silk	Formic acid	Voltage: 10 kV Distance: 10 cm	-	Sciatic nerve	18 rats
Beigi M et al <sup>22</sup>	13mm ID: 1.29mm	PCL/GEL	hexafluoro-2-propanol (HFIP)	Flow rate: 1 mL/h Voltage: 12 kv	UV for 6 hours	Sciatic nerve	Rats
Yu W et al <sup>18</sup>	1-1.2cm ID: 1.2mm	MWNT-CO/PCL	1,1,1,3,3,3hexafluoro2propanol (HFIP)	Flow rate: 2ml/h Voltage: 16 kV Distance: 12 cm Speed: 500-600 rpm	UV for 2 hours	Sciatic nerve	15 rats
Zhou M et al <sup>23</sup>	50mm x 3mm	Chitosan/policaprolactone	Acetic acid	Flow rate: 25 µl/min Voltage: 3 kV Distance: 10cm Speed: 150 rpm	-	Carotid artery	6 dogs
Cirillo V et al <sup>24</sup>	7mm x 1.5mm	PCL PCL/GEL	PCL con chloroform PCL/Gelatin con HFIP	PCL, Flow rate: 0.5 mL/h Voltage: 20 kv Distance: 15 cm Speed: 50 rpm PCL/Gelatin: Flow rate: 0.5 mL/h Voltage: 13kV Distance: 8cm Speed: 50 rpm	70% ethanol immersion solution for 30 minutes	Sciatic nerve	16 rats

**Table 3: Tubular scaffolds made by electrospinning.**

Author	Scaffold measures	Material	Solvent	Conditions	Sterilization method	Organ	Experimental model
Mugnai D et al <sup>15</sup>	20 mm ID: 2 mm	PCL	CHCl3/EtOH	Flow rate: 12 mL/h Voltage: 20 kV Distance 20cm	Gamma radiation (25 kGy)	Aorta	14 mice
Huang C et al <sup>37</sup>	5 cm ID: 4 mm	PLLA-Heparin PLLA	TFE	PLLA Flow rate: 0.1 mL/h Heparin Flow rate: 0.8 mL/h Voltage: 18kV Distance: 15cm	-	Femoral aorta	8 dogs
Zhai W et al <sup>38</sup>	5 cm ID: 2.5-3.5 mm	P(LLA-CL) Heparin	TFE	Flow rate: 1.2 mL/h Voltage: 16 kV Distance: 15 cm Speed: 800 rpm	--	Femoral aorta	8 dogs
Zhang K et al <sup>34</sup>	15 mm x 1.40 mm	SF/ P(LLA-CL)	1,1,1,3,3,3-Hexafluoro-2-propanol (HFIP)	Flow rate 1: 0.10-0.20 mL/h Flow rate 2: 1.0-1.2mL/h Voltage: 10kV Speed 4000 rpm Distance: 12-15 cm	-	Sciatic nerve	36 rats
Wang S et al <sup>36</sup>	5-6 cm x 4 mm	P(LLA-CL)/ Heparin	TFE	External flow rate 0.8 mL/h Voltage: 18 kV Internal flow rate 1.0mL/h Distance: 15cm Speed: 250 rpm	Soak up in polypropylene sterilized tube	Femoral artery	20 dogs
Mrówczyński W et al <sup>11</sup>	5 cm x 4 mm	PCL	CHCl3/EtOH Chloroform	Flow rate: 12 ml/h Voltage: 20 kV Distance: 20 cm	Gamma radiation (25 kGy)	Carotid artery	11 pigs
Ye L et al <sup>12</sup>	4 cm x 2 mm	PCL Heparin	Chloroform	Flow rate: 5 mL/h Voltage: 20 kV	--	Femoral artery	2 dogs
Yu W et al <sup>18</sup>		Collagen/ PCL	1,1,1,3,3,3-Hexafluoro-2-propanol (HFP)	Flow rate: 2 ml/h Voltage: 16 kv Distance: 12 cm	--	Sciatic nerve	Rats
Bermeister H et al <sup>31</sup>	15 mm x 1.5 mm	Polyurethane	HFIP	Flow rate: 0.01 mL/m Voltage: 20 kV Distance: 90mm Speed: 200 rpm		Abdominal aorta	40 rats
Soletti L et al <sup>19</sup>	1 cm ID: 1.3 mm	PEUU	1,1,1,3,3,3-hexafluoroisopropanol (HFIP)	Flow rate :1 mL/h Voltage: 10kV Speed: 250 rpm	70% ethanol solution immersion for 24hours	Abdominal aorta	22 rats
Jha BS et al <sup>12</sup>	10-15 mm x 5-7 mm	PCL	TFE	Flow rate: 2-20 mL/h Voltage: 22kV	Immersion in 100% ethanol solution	Sciatic nerve	3 rats
Bryan WT et al <sup>13</sup>	4 cm ID: 4.75 mm	PCL/ Collagen	1,1,1,3,3,3-hexafluoro-2-propanol (HFP)	Flow rate: 3 mL/h Voltage: 20 kV Distance: 10 cm Speed: 1000 rpm	Ethylene oxide	Aortoiliac bypass	1 rabbit

### PLLA and heparin

Heparin is one of the most common antithrombotic methods used for the fabrication of scaffolds. Sheng Wang and cols in 2013 made scaffolds for the small vessel using of poly (l-lactide-co-e-caprolactone) P(LLA-CL) and heparin, they created 4 groups of study, two of P(LLA-CL) with and without endothelial cells and two of P(LLA-CL) and heparin with and without endothelial cells. They used them in the femoral artery of 20 dogs. They saw that using endothelial cells and heparin in the scaffold had an important improvement in patency compared to the other groups.<sup>36</sup> Chen Huang et al, made scaffolds of poly (l-lactide-co-e-caprolactone) (PLLA-CL) and heparin. They implanted the grafts in the femoral artery of dogs. They concluded that heparin is an easy and economical way to enhance in vivo patency.<sup>37</sup> Zhai W et al, also made grafts with P(LLA-CL) and heparin to use them in the femoral artery of dogs. As a control group, they used scaffolds made only by P(LLA-CL). They saw that using heparin improved the scaffold patency in short, medium and long-term.<sup>38</sup>

### DISCUSSION

In tissue engineering one of the most relevant topics is the creation of scaffolds that act as a structure for cellular adhesion and proliferation that will lead to the creation of a functional tissue. For this scaffold creation, electrospinning technique has demonstrated to have an important role because of its capacity of using different materials and conditions that will suit the purpose.<sup>2</sup>

In this article, we talk about the different materials used to create scaffolds, specifically tubular ones that can be used for small vessel replacement, nerves, veins, and even esophagus.

Polycaprolactone is one of the materials that have been more used; it has been widely used for small vessels showing low grades of stenosis and absence of thrombus. It has also been used for nerve regeneration and has shown the presence of Schwann cells as myelination.<sup>17</sup> In this technique is common to use different polymers and also to add other materials that will enhance cellular adhesion, such is the case of collagen, that favors better cellular adhesion, scaffold patency, and cellular regeneration.<sup>20</sup>

Apart from modifying the type of polymer, the size and wide of the scaffold can also be modified, been capable of creating three-layered scaffolds, each layer of different polymers that will degrade in different time and will help cellular infiltration.<sup>26</sup> Another benefice of this technique is the capacity of adding growth factors, bioactive molecules, and drugs, such as vascular endothelial growth factor which can regulate proliferation, migration, and survival of cells.

Because of the endless possibilities for the creation of tubular scaffolds by electrospinning we have created the following tables (Table 2, 3) in which we include the material, solvent, conditions such as flow rate, voltage, distance, speed, scaffold measures, sterilization method, organ created and the experimental model in which the scaffold was tested in vivo.

### CONCLUSION

Tissue engineering uses different techniques that help the regeneration or replacement of tissue and organs. Electrospinning is an excellent alternative due to the fact that it can be made with different polymers and solvents that help adjust the exact need of the tissue, it can be combined with growth factor or different molecules to personalize the needs and enhance the regeneration.

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