Electrospinning a Valved Arterial Conduit

Bilal Ahmad[1], Gareth Williams[1], Jane Ogilvie[2], Christopher Barnett[2], Pierre Pouponneau[3], Sebastien Perrot[3], Kyun Thibaut[4], Marilys Blanchy[5], Konstantin Sipos[5], Philippe Menasche[6], David Kalfa[6]

[1]UCL School of Pharmacy, UK; [2]Euram Ltd, UK; [3]Statice, France; [4]Cardio3 Biosciences, Belgium;
[5]Rescoll, France; [6]Assistance Publique - Hopitaux de Paris, France

1. BACKGROUND

Approximately 42% of infant mortality worldwide is related to congenital heart defects (prevalence: 8-12/1000 births). Over one third of these defects require the reconstruction of the right ventricular outflow tract (RVOT; Fig.1) by surgical procedures which currently use inert materials without any growth potential. Consequently, multiple reoperations are often required, with their attendant high risk of mortality and morbidity.

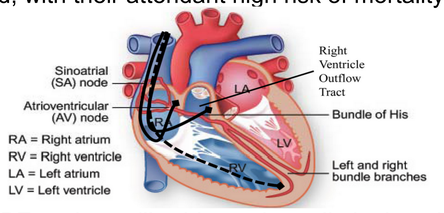

Figure 1. A schematic diagram illustrating the RVOT inside the human heart.

The TEH-TUBE project will address these limitations by electrospinning (ES) a novel bioresorbable biomaterial using a polymeric valved tube either seeded with autologous adipose tissue derived stem cells (ADSC) or functionalized by a peptidic sequence triggering homing of the host cells onto the scaffold to make it a living self-populated structure. The project aims to develop an innovative biomaterial for the treatment of congenital heart abnormalities in children and young adults. By creating a material whose growth will keep pace with that of the patient, this product should decrease the need for risky reoperative surgeries, improve patient quality of life, and ultimately have a positive impact on healthcare costs.

2.METHODS

In a typical experiment (Fig.2) the polymer solution is loaded into a syringe fitted with a metal needle tip, and a syringe pump used to expel liquid at a precisely-controlled rate towards a metal collector. A high voltage power supply is connected to the needle tip (usually +ve) and the collector (grounded) and used to apply a large (kV) potential difference between the two. There are a range of parameters which can be varied in this technique: the applied voltage, flow rate, polymer concentration, solvent, spinneret-to-collector distance, *etc*.

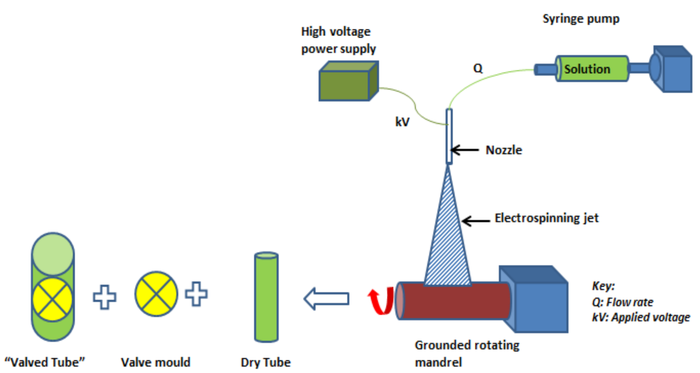

Figure 2. A schematic diagram illustrating the electrospinning setup.

This parametric optimisation process is critical in electrospinning a reproducible polymeric structures, and can be carried out to generate simple flat patches to more complex shapes such as those produced in this project. Fig. 3 illustrates the purpose built electrospinning instrument used to generate the polymeric tubes.

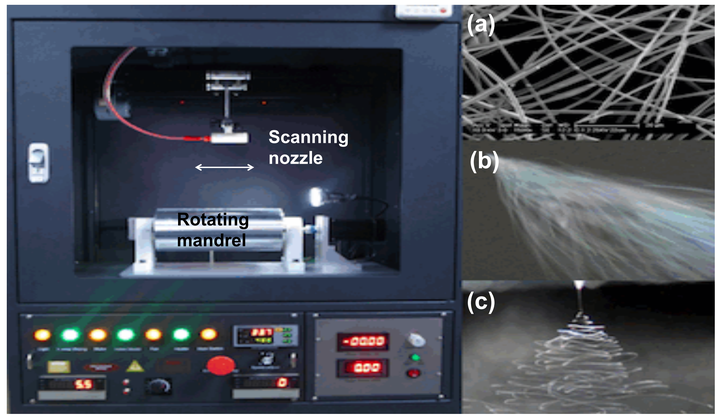

Figure 3. The electrospinning instrument used in this project. (a) Scanning electron microscopy image of the resultant fibres with high speed camera images (b) and (c) of the electrospun jet. Images courtesy of NaBond (www.nabond.com).

3. RESULT AND DISCUSSION

Our preliminary experiments revolved around optimising the preparation of polymer patches (Fig.4a) and concurrent *in vitro* studies. Initial results indicate good reproducibility and an encouraging cellular response to the electrospun patches. The next step was to translate the patch work on to our purpose built ES instrument with a rotating collector. This was successfully achieved and we were able to generate polymeric tubes with a highly anisotropic microstructure (Fig. 4b). This work led us to the concept of preparing a "valved tube" design (Fig. 4c), which is currently under investigation.

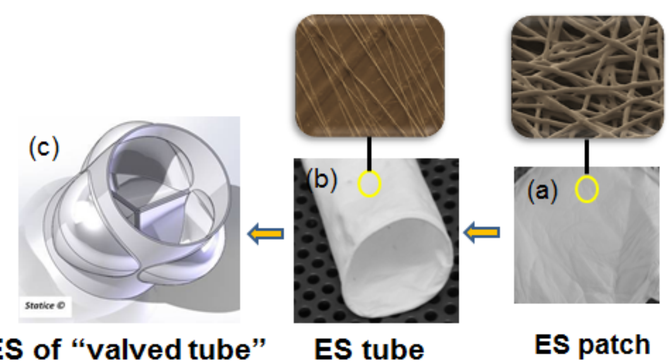

Figure 4. Scanning electron microscopy and digital images of (a) an ES patch and (b) an ES tube. (c) a CAD diagram of the "valved tube" design.

Several samples were subjected to a rigorous regime of mechanical properties testing. The results were then compared with the parameters of the native human artery and heart valve documented in the literature. The electrospun structures were tested under non-physiological conditions (*i.e.* at room temperature and under 50% humidity).

Table 1. Uniaxial tensile mechanical properties: Young's modulus (E), ultimate tensile strength (UTS), and strain (∈) at maximum stress of native heart valves and the electrospun patches and tubes. [A] denotes the thickness of the patch.

Sample	E (MPa)	UTS (MPa)	∈max (%)
[1]Native HV circumferential (wet)	15	2.6	22
[1]Native HV radial (wet)	2	0.4	30
[2]Native pulmonary artery (wet)	0.04	0.38	91
Dry Electrospun patches			
200 μm[A]	21 ± 7.3	3.3 ± 0.87	190 ± 88
150 μm[A]	18 ± 7.2	3.1 ± 0.22	220 ± 24
100μm[A]	2.2 ± 0.92	0.71 ± 0.12	53 ± 22
Dry Electrospun tube			
Perpendicular	22 ± 5.3	5.0 ± 0.50	61 ± 7.7
Longitudinal	10 ± 1.7	3.0 ± 0.40	210 ± 8.8

It can be seen that both electrospun patches and tubes possess mechanical properties that closely match the native heart valve; however, the non-physiological conditions employed during our mechanical testing are not fully indicative of their real potential. The higher modulus values in the electrospun tube can be attributed to the highly aligned fibre microstructure.

4.CONCLUSION

We were able to successfully electrospun a tube made from a medical grade polymer, and optimise the processing so that it possessed good mechanical properties. Further attempts at mimicking the native ECM using electrospinning are being made to make a "valved-tube" which behaves more elastically whilst maintaining sufficient strength during sustained biomechanical degradation.

5.REFERENCES

1.A. Balguid, M.P. Rubbens, A. Mol, R.A. Bank, A. Bogers, J.P. Van Kats, B. De Mol, F.P.T. Baaijens, C.V.C. Bouten. The role of collagen cross-links in biomechanical behavior of human aortic heart valve leaflets – relevance for tissue engineering. Tissue Eng., 13 (2007), pp. 1501–1511.
2.R. Sodian, S.P. Hoerstrup, J.S. Sperling, S. Daebritz, D.P. Martin, A.M. Moran, B.S. Kim, F.J. Schoen, J.P. Vacanti, J.E. Mayer. Early in vivo experience with tissue-engineered trileaflet heart valves. Circulation, 102 (2000), pp. 22–29

Supported by the European Union FP7 Grant Agreement 604049.