Vascular tissue engineering - from strong human vascular grafts towards an in-vivo porcine model

technische universiteit eindhoven

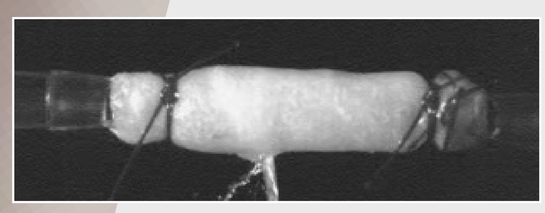
Vascular tissue engineering

From strong human vascular grafts towards an in-vivo porcine model

M. Stekelenburg, Rolf Pullens, Mark Post, F.P.T. Baaijens
Eindhoven University of Technology, Department of Biomedical Engineering

Introduction

Vascular tissue engineering represents a promising approach for the development of living small diameter blood vessels that can be used for replacement therapy. We recently succeeded in culturing strong human vascular grafts based on a fast-degrading polymer scaffold (PGA/P4HB) and fibrin gel. The resulting grafts demonstrated burst pressures of 900 mmHg after 4 weeks of in-vitro culture. A next step involves in-vivo implantation in a porcine model, this will further elucidate the potential of the engineered grafts.



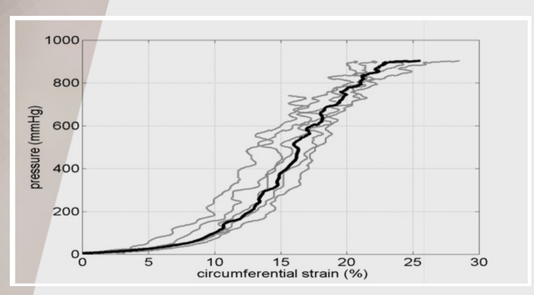


Figure 1: Human TE vascular graft possessing a burst pressure of 900mmHg

The first step in this study involves adapting the human tissue-engineering protocol to the use of porcine cells. This step is not trivial as it is known that cells from (young) animals behave differently compared to human cells from older donors, which were used to culture the human vascular grafts.

Materials&Methods

Myofibroblasts were harvested from human saphenous veins and porcine jugularis veins. Rectangular and tubular scaffolds were fabricated from PGA coated P4HB (Fig. 2) and seeded using fibrin gel as a cell carrier. In a first approach, human tissue strips were cultured for 4 weeks with 10% FBS while porcine tissue strips were cultured for 2 weeks with 5 % FBS. These porcine culture conditions were based on experience in our laboratories with the use of sheep cells.

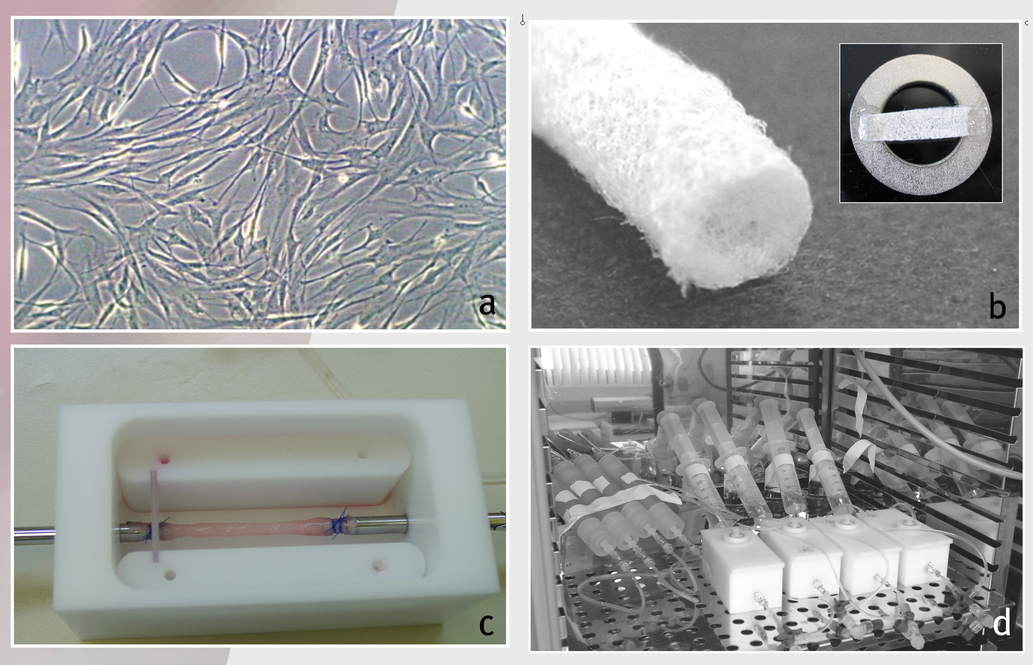


Figure 2: Vascular tissue engineering using myofibroblasts (a), a PGA/P4HB scaffold (b, tubular/rectangular) and a bioreactor set-up (c,d)

Results

Porcine venous myofibroblasts appeared to be much smaller than the human venous cells (Fig. 3). In addition, porcine cells proliferated much faster.

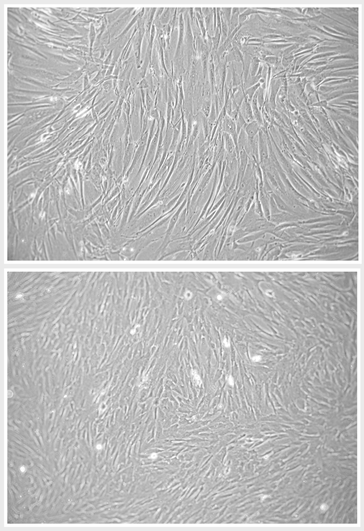
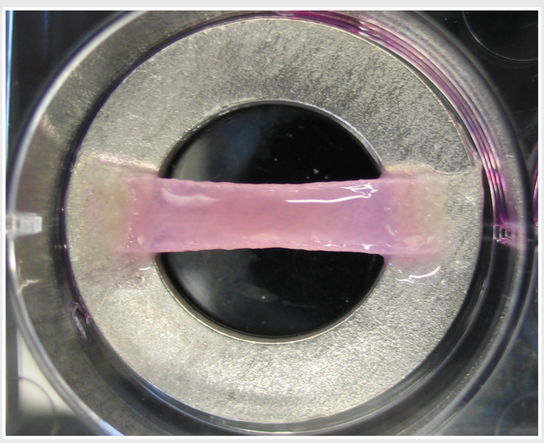


Figure 3: Human saphenous vein (top) and porcine jugularis vein (bottom) myofibrobasts .

Fig. 4 shows an example of a cultured tissue strip. No macroscopically differences could be observed between the human and porcine strips, both showing good tissue formation. Uniaxial tensile tests showed that the mechanical behavior of the porcine and human tissue strips were in the same range (Fig. 4), although the porcine strips were cultured for only 2 weeks and with 5% FBS.



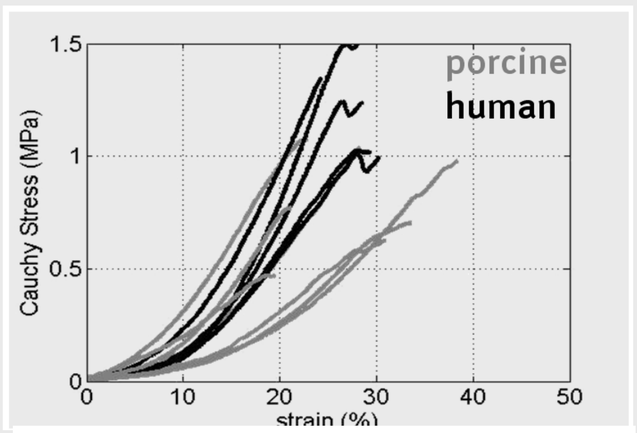
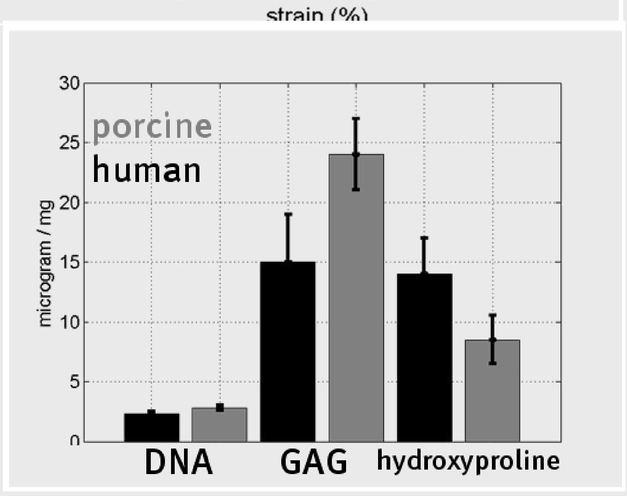


Figure 4: Example of a cultured tissue strip (left), stress-strain curves (top) and amounts of extracellular matrix (bottom) of human and porcine tissue strips.



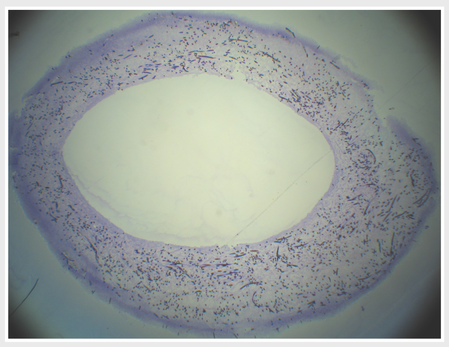


Figure 5: Toluidine blue staining of a statically cultured porcine vascular graft showing homogeneous tissue formation.

Conclusions

The culture of porcine tissue strips, displaying similar mechanical behavior as human strips, required a shorter culture time and less serum. In future experiments, porcine vascular grafts will be cultured under dynamic strain conditions. This will elucidate on the ideal culture conditions to obtain strong porcine vascular grafts that will be suitable for in-vivo studies.