Vascular tissue engineering : towards in-vivo implantation of porcine vascular grafts

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Vascular Tissue Engineering

Towards in-vivo implantation of porcine vascular grafts

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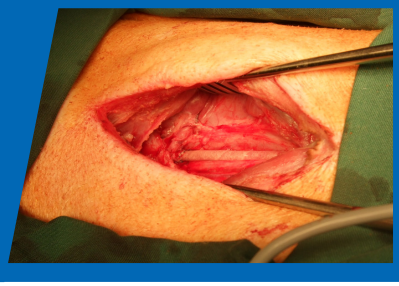


Introduction

The need for small diameter vascular grafts is large. These grafts are used in coronary and peripheral bypass grafting and as arterio-venous (AV) shunts in hemodialysis patients. Vascular tissue engineering represents a promising approach for the development of living small diameter blood vessels. In-vivo implantation of tissue-engineered vascular grafts in an animal model will elucidate the potential of these grafts. In the current study a protocol was developed to culture strong porcine grafts. In addition, a first feasibility experiment was performed which included in-vivo implantation as a interposition graft of the carotid artery in a porcine model.

Materials&methods

Myofibroblasts and endothelial cells (ECs) were harvested from porcine jugularis veins. Tubular and rectangular scaffolds were fabricated from PGA coated P4HB (Fig.1) and seeded using fibrin gel as a cell carrier.

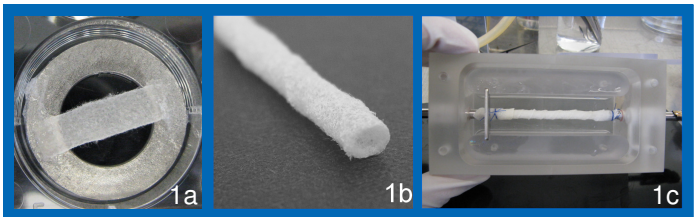


Fig. 1 *Rectangular and tubular scaffold for tissue culture*

Tissue strips were cultured to investigate the differences between culture protocols and between cells of different pigs. Tubular constructs were seeded and statically cultured to obtain vascular grafts. All constructs were seeded with $25*10^6$ cells/ml. After 4 weeks of culture, ECs were seeded on the inside of the grafts. In a first in-vivo feasibility study cells were isolated from 9 pigs. Grafts were implanted as an interposition graft of the carotid artery.

Results

Strips - Culturing tissue strips (Fig.2a) with cells of different pigs revealed that large differences can exist in tissue formation. Figure 3 shows representative stress strain curves and the corresponding hydroxyproline contents (as a measure of collagen) of 3-week cultured tissue strips with cells of 5 different pigs, illustrating the variance in tissue formation.

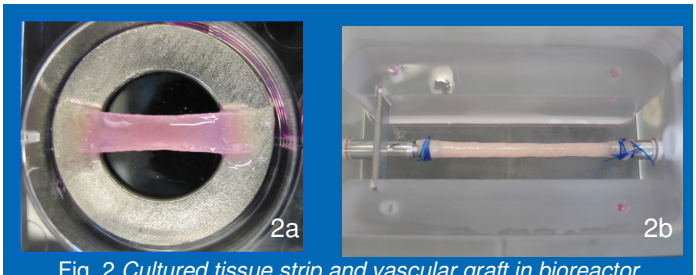
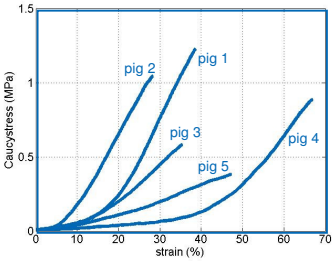


Fig. 2 *Cultured tissue strip and vascular graft in bioreactor*



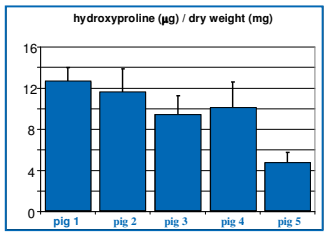


Fig. 3 Representative s*tress-strain curves and hydroxyproline content of tissue strips cultured with cells of 5 different pigs.*

Grafts - Culturing tubular constructs for 4 weeks in the bioreactor (Fig.1c) resulted in porcine grafts (Fig.2b) with estimated burst pressures between 400-1000mmHg. For each pig, 3 vascular grafts were cultured (Fig. 4). One graft was implanted as an interposition graft of the carotid artery (Fig.5), the other 2 served as controls. In case of 8 pigs it was possible to implant the graft. Angiograms and analyses of explants, 4 weeks after implantation, should reveal the post-implant performance of these grafts. Although not all data is yet available, it is already clear that axial suturability and EC seeding should be improved.

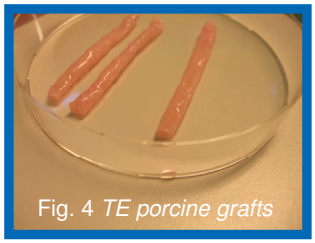


Fig. 4 *TE porcine grafts*

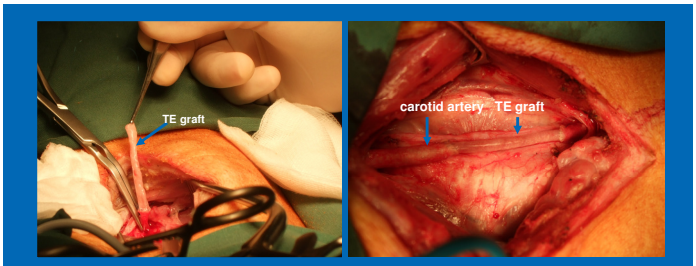


Fig. 5 *Implantation of tissue engineered graft*

Conclusions

Strong porcine vascular grafts were successfully cultured and implanted into pigs. The grafts exhibited burst pressures ranging from 400 to 1000mmHg, indicating a relative strong variability in tissue formation. Preliminary results of the in-vivo feasibility study showed that at least the suturability of the grafts and the seeding of endothelial cells should be improved.