First in vivo experiences with living, autologous TE heart valves implanted by minimally invasive replacement procedures

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First *In vivo* Experiences with Living, Autologous TE Heart Valves implanted by Minimally Invasive Replacement Procedures

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Introduction

Minimally invasive valve replacement procedures rapidly evolve as alternative treatment option for patients with valvular heart disease. Tissue engineered heart valves provide a living, autologous valve replacement with the capacity of regeneration and growth, that have shown functionality in chronic animal studies .[1]

Aim

The aim of this project was to study the feasibility of combining two promising novel technologies: minimally invasive valve replacement and tissue engineering.

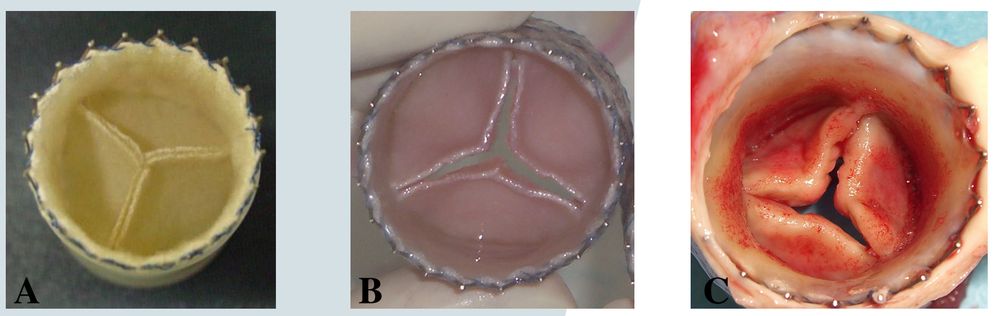

Figure 1: Stented PGA-P4HB scaffold before seeding (A) and TE heart valve before (B) and after (C) implantation.

Materials and methods

Trileaflet heart valves (n=8, Ø30mm) based on rapidly degrading polymer scaffolds (figure 1) and self-expandable stents were engineered from ovine vascular derived autologous cells.

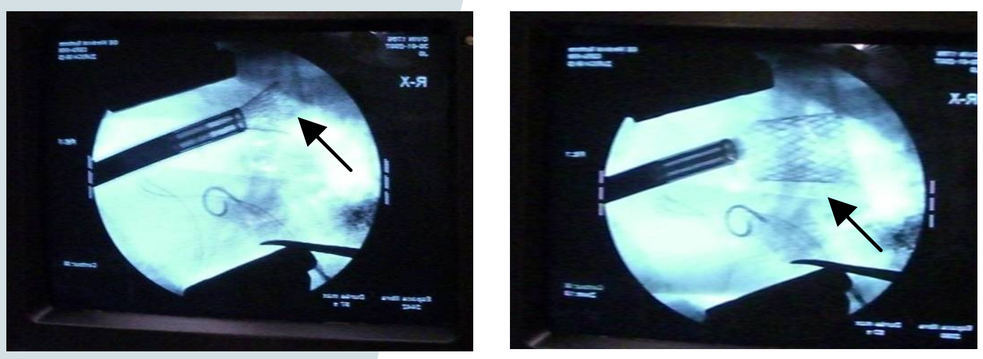

Figure 2: Minimally invasively delivery of the TE heart valve in the pulmonary artery of the sheep. Arrows indicate the stent, that unfolds, after release from the device, by the temperature of the bloodstream.

Valves were seeded with myofibroblasts and grown *in-vitro* for 10 days utilizing diastolic loading bioreactor systems.[2] Thereafter, valves were seeded with endothelail cells and cultured for 2 more days aplying only perfusion. The valves were crimped applying a newly developed introduction system (12mm, figure 3).

Four valves were delivered minimally invasively (mini-thoracotomy, trans-apical approach) in sheep replacing the native pulmonary valves (figure 2). Controls were analyzed directly after the crimping/delivery process for structural integrity. Post-operative follow-up comprised angiography and echocardiography. TE valves were explanted after 4 and 8 weeks. Neo-tissue analyses included histology (figure 4), SEM, ECM quantification and biomechanical testing.

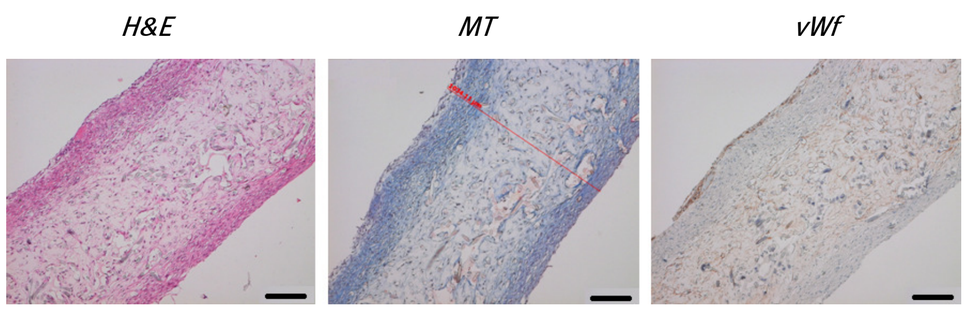

Figure 4: Typical results of H&E staining, Masson trichrome (MT) staining, and von Willebrand factor (vWf) staining of a control leaflet. Sufficient tissue formation is shown (left and middle) as well an endothelial layer on the outflow side of the leaflet (right). (Scalebars represent 200 µm.)

Results

TE heart valves showed preserved structural integrity after the crimping and delivery process. The minimally invasive procedure was successful in all implanted valves and adequate functionality was observed up to 8 weeks. Morphological analyses of the leaflets demonstrated a thickened, layered tissue formation (figure 5) comparable to previous animal studies.[2] The TE valve ring structures were integrated into the adjacent native tissue after 8 weeks.

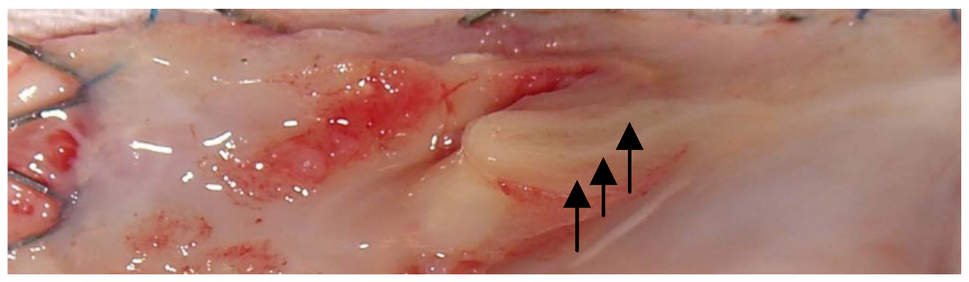

Figure 5: Macroscopic photo of explanted valve after 4 weeks. A thickened layered tissue formation on the leaflets is shown by arrows.

Discussion

This *in-vivo* study demonstrates for the first time the successful merging of the two promising heart valve technologies tissue engineering and minimally invasive replacement procedures. Although representing only a preliminary in vivo experience, process safety is shown and extended studies are initiated to assess long-term function.

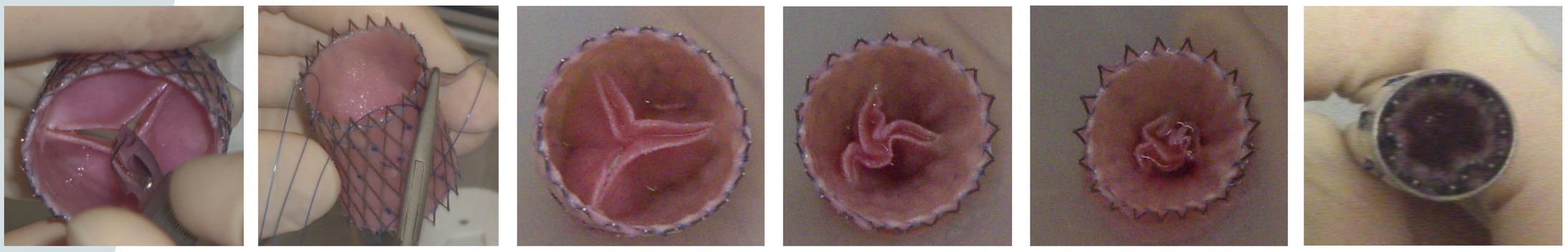

Figure 3: Above; Separation of the leaflets and crimping of the TE heart valve. Below; Insertion of the TE heart valve into the implantation device.

1) Sodian *et al., **Circulation 2000***
2) Mol *et al., **Annals of Biom. Engineering 2005***

/department of biomedical engineering