An elastic, biodegradable cardiac patch induces muscle regeneration with preserved cardiac function in a porcine myocardial infarction model

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Introduction: Regional implantation of an elastic biodegradable cardiac patch made from a polyester urethane urea (PEUU) [1] was recently shown to improve cardiac function and was associated with regenerated muscle bundles in a small animal myocardial infarction model [2]. The present pre-clinical study evaluated the effect of PEUU patch implantation on myocardial regeneration and cardiac functional contribution after infarction in the porcine model.

Methods: PEUU was synthesized from polycaprolactone diol and 1,4-diisocyanatobutane with chain extension by putrescine as previously reported [1], and processed into porous scaffolds with thermally induced phase separation [3]. Porcine left ventricle (LV) infarcts were created by catheter-based balloon occlusion for 90 min and reperfusion of the circumflex artery. Two weeks post-infarction, the infarcted LV was covered with a sutured 6 cm diam (800 um thick) PEUU porous patch (n=6). Infarction control animals had sham surgery (n=6). Echocardiography assessed cardiac function and explants were evaluated histologically.

Results: There was no mortality in peri-post-operative course of PEUU group. One animal in infarction control group died due to mediastinitis. At the time of explantation, the implanted PEUU showed no dehiscence and was integrated onto the host heart. (**Fig. 1a**) The LV wall in the PEUU group was significantly thicker than infarction controls ($p<0.05$, **Fig. 1b**). Histological assessment at 8 wks showed that the PEUU patch was largely resorbed and replaced with abundant myofibroblasts and that a substantial layer of immature muscle tissue was observed beneath the patched area. Immunohistochemically, these cells were positive for alpha-smooth muscle actin, alpha-sarcomeric actinin, and actin. In addition, the capillary density in the infarcted LV wall of the PEUU group was significantly higher than for infarction controls ($p<0.05$). After 8 wks, end-diastolic LV cavity area in infarction controls significantly increased, whereas the area for PEUU patched animals remained the same as pre-implantation, which was smaller the infarction control, $p<0.05$, **Fig. 2a**) The LV fractional area change trended higher in the PEUU group ($P=0.08$, ANOVA, **Fig. 2b**).

Conclusions: PEUU patch implantation prevented LV dilatation, preserved contractile function, and induced new muscle formation in the infarcted LV wall. LV wall thickness was maintained concurrent with stimulated angiogenesis. These data in a large animal pre-clinical model are consistent with our previous results in small animals and suggest that PEUU patch placement would be efficacious for cardiomyoplasty of the chronically infarcted LV wall by triggering cellular remodeling and contributing to preserved myocardial function.

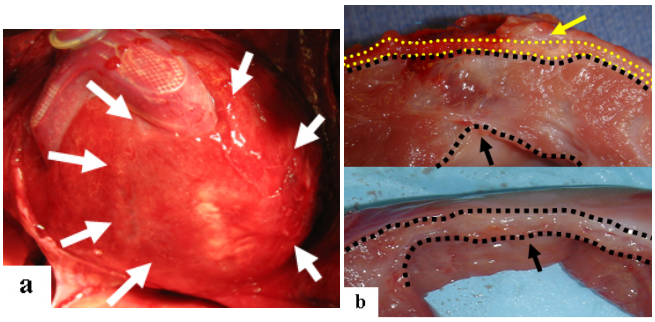

Fig. 1. Representative macroscopic of PEUU patched LV wall 8 wks post-implant (a), and the appearance of wall thickness in PEUU group (upper b) and infarction control (lower b). White arrows (a) indicate PEUU patch remnant, yellow dots (b) indicate PEUU patch and black dots (b) show LV wall thickness.

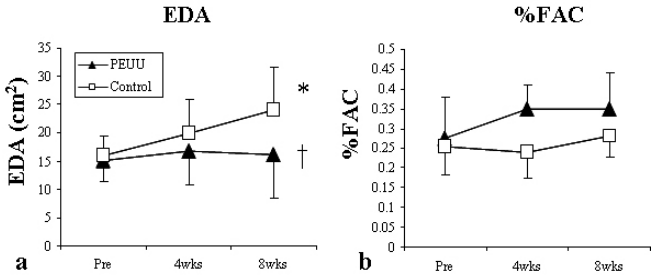

Fig. 2. Echocardiographic assessment of PEUU and infarction control group during the study period. EDA (end-diastolic area) is shown in (a), and %FAC (fractional area change) in (b).*$p<0.05$ vs. 0 wk within group; †$p<0.05$ between groups.

Acknowledgements & References
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