Human cardiac progenitor cell seeded-collagen patches for cell therapy applied to right ventricular dysfunction: Preliminary results in a large animal model

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Background: Cell therapy using intramyocardial injections of cardiac progenitors differentiated from human embryonic stem cells showed benefits on overloaded right ventricular (RV) tissue remodelling and arrhythmic susceptibility but this delivery mode failed to improve RV function. Our aim was to evaluate in a porcine model of overloaded RV dysfunction a new delivery mode of such therapy.

Methods: A combined overloaded RV dysfunction was obtained in piglets using a surgical procedure mimicking repaired tetralogy of Fallot. After 4 months, cell therapy was surgically administrated using 2 types of human NKX2.5+ cardiac progenitor cell-seeded collagen patches applied on the epicardium: QGel® and pressured-patches. Myocardial function was measured 1 month after transplantation by conductance catheter technique and echocardiography (standard and strain). The fate of progenitors was studied using antibodies directed against human Nkx2.5, human mitochondria, GFP, CD31, actinin and Islet1.

Results: All pigs survived without any complication. Pressured-patches allowed human progenitors to survive well and to migrate away from the epicardium while QGel® patches restricted the cell migration. Progenitors differentiated close to the epicardium toward the cardiac lineage as assessed actinin expression. NKX2.5+ cells within pressured-patches migrated between myocardial fibers. Only pressured-patches (N=3) tended to improve the contractility (Emax slope). By contrast, this parameter decreased in QGel® patches animals (N=2). Moreover, in 2 pressured-patch animals, standard echocardiographic functional parameters (FAC, TAPSE, s’wave) were maintained while 2D strain and strain rate values increased.

Conclusion: Cell therapy using seeded-patches was more conservative for engrafted cells than intramyocardial injections but only pressured-patches seemed to give benefits on overloaded RV function and contractility. These first promising results need to be checked at longer term.