A novel pulsatile platform for the *ex-vivo* evaluation of early remodelling events in human saphenous veins

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INTRODUCTION: After coronary artery bypass grafting (CABG), structural modifications of the human saphenous vein (hSV) wall lead to the lumen narrowing in response to the different hemodynamic conditions experienced: pulsatile pressure of 80-120 mmHg, pulsatile flow with mean flow rate of 250 ml/min, and elevated shear stress (1-7 Pa) [1]. Here we present a novel pulsatile platform conceived for mimicking the CABG surgery hemodynamic conditions and studying the hSV early remodeling events.

METHODS: A culture system (Fig.1A) was developed to stimulate vessel samples with CABG-like pressure/flow patterns, *i.e.* a sphygmoid-like pulsatile pressure in counter-phase with a pulsatile flow rate (Figure 1B). Six hSV samples were subjected to pulsatile stimulation for 7 days, and native hSV segments served as control. Dextran (3.5% w/v) was added to DMEM, to reach 3.07±0.07 cP viscosity. At the end of the conditioning period, hSVs were fixed and stained with Masson's trichrome and Weigert van Gieson stainings for morphological/morphometric evaluation. Immunofluorescence investigations (αSMA for labeling smooth muscle cells and CD31 and vWF for endothelial cells) were also performed.

RESULTS: *Ex vivo* experiments with hSVs revealed the ability of the CPD to mimic the complexity of the coronary hemodynamic environment with good fidelity in comparison with state-of-the-art devices. Morphometric analysis on Masson's trichrome stained sections (Fig.1C) revealed that both intima and media thickness were significantly decreased after 7 days of conditioning, resulting in significantly reduced wall thickness, but without affecting lumen perimeter. The media consisted mainly of SMCs, and on the luminal lining, most cells expressed CD31/vWF. There was a partial EC denudation.

DISCUSSION & CONCLUSIONS: Our novel platform enables prolonged ex vivo stimulation of hSVs segments with CABG-like hemodynamic conditions. Seven day conditioning resulted in thinning of both intima and media of the veins. Studies are currently ongoing in our Laboratories to correlate the hemodynamic changes to the activation of cellular and molecular pro-pathologic pathways involved in the SV graft disease.

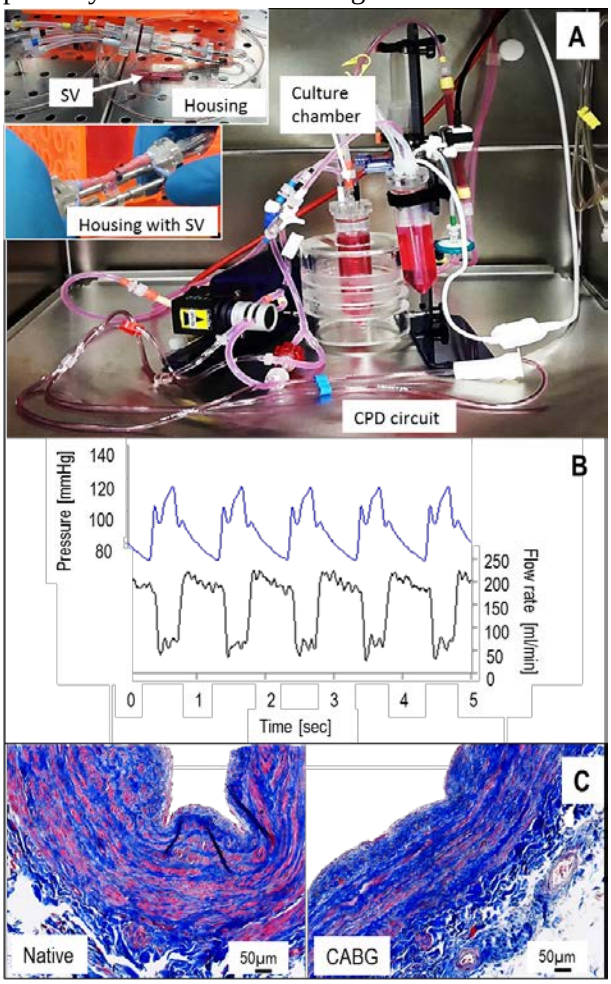

Fig. 1: Image of the CPD platform (A). Pressure and flow rate traces acquired during the experiments (B). Masson's trichrome sections before (Native) and after conditioning (CABG).

REFERENCES:[1]Piola et al., (2012) *Recent Pat Cardiovasc.***7** : 186–195.

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