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Promising surgical options for CABG with a new shelf-ready, synthetic, biodegradable, small-calibre vascular graft

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Nowadays most CABGs and peripheral revascularisation procedures are carried out on an urgent basis and therefore especially when autologous graft materials are diseased or have been used in previous surgeries, shelf-ready, alternative graft material is required. Despite intense research over many decades, no suitable clinical, shelf-ready, small calibre, synthetic graft is available.

We developed small diameter vascular grafts made of slow degradable poly(e-caprolactone) nanofibers obtained by electrospinning (Figure 1). The process was optimized by a factorial design approach that led to reproducible grafts with inner diameters of 2mm and 4mm, respectively. Fibre sizes, graft morphology, and the resulting tensile stress and tensile strain values were studied as a function of various parameters in order to obtain optimal vascular grafts for implantation after gamma sterilization. The influence of polymer concentration, solvent, needle-collector distance, applied voltage, flow rate, and spinning time has been studied. Consequently, an optimized vascular graft was implanted as an abdominal aortic or carotid substitute in more than 100 animals (rats and pigs) for periods up to two years (Figure 1). Our new synthetic, biodegradable small-calibre, nano-fibre electro-spun polycaprolactone graft shows no aneurysms, better patency, compliance and biocompatibility with faster endothelialisation, less intimal hyperplasia and calcification compared to the clinically used ePTFE graft after long-term implantation in the rat aorta (Figure 2). Despite degradation, our graft maintains good mechanical characteristics, growth potential, and tissue regeneration with specific cells, adequate angiogenesis and extra-cellular matrix formation (Figure 1-right panel: Morphological analysis of PLC grafts. (A) SEM image of the lumen of the PCL graft after explantation showing complete endothelialization. (B) Longitudinal section of the graft wall showing homogenous cellular infiltration giant cells on the periphery (arrows; HE staining, 100x magnification). (C) Immunohistochemistry anti CD31 labeling endothelial cells on the luminal side (200x magnification). (D) Elastin deposition in the neo-intimal layers is revealed in blue and collagen deposition is revealed in green by a Miller-Masson staining (200x magnification).

Thus, such a novel *in situ* tissue-engineered graft, using the body as bio-reactor, may become a better, cheaper and clinically widely applicable method for future cardiovascular applications.

In contrast, other tissue engineering methods have been used for the development of better vascular grafts such as cell sheet techniques or *in vitro* cell seeding with the possibility of using different autologous patient-derived or stem cells which are aimed at reconstituting the three basic layers of a vessel. The disadvantages of this method are the time, manpower and cost required to mature such a vascular graft in a bio-reactor. This approach has been shown to be scientifically successful. However, so far neither large-scale applications nor shelf-readiness are available.

Our graft could therefore cover this clinical need with the advantages of easy manufacturing in all shapes and sizes, sterilisation, storage and especially at an affordable price which would enable also patients in developing countries to profit from such revascularisation procedures. Additionally, the growing potential of our graft is given due to the fact that it degrades over time and the patient's own tissue regenerates a 'neo-vessel' in the appropriate size. Thus, such a novel *in situ* tissue engineered graft could become a future option for clinical applications such as coronary artery or peripheral bypass grafting.

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Figure 1

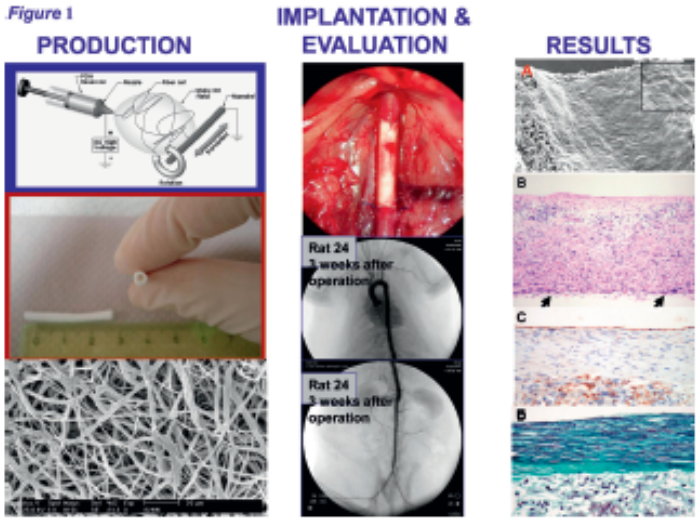

Figure 2

PCL vs. ePTFE grafts at 15 months

	PCL (n=8)	ePTFE (n=6)	P<
Patency (%)	100	67	ns
Endothelialization (%)	98	93	ns
Compliance (%)	8.2	5.7	0.01
Calcification (%)	7.0	15.8	0.04
Intimal Hyperplasia (µm)	47.2	62.2	0.09
Cellular Ingrowth (%)	31.4	11.3	0.001