P.2606

Vascular remodeling of a novel absorbable polymeric conduit in the ovine pulmonary circulation

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Background: Right ventricular outflow tract (RVOT) conduits in young patients with congenital heart disease degenerate and are unable to grow with the patient. As a consequence, many children undergo multiple surgeries as they age. Evidence is mounting that appropriately configured polymeric vascular grafts can undergo remodeling mediated by endogenous cells without the use of stem cells or animal-derived products. The new living tissues have structures resembling the arterial wall. In this study, we report the in vivo use of an entirely synthetic graft demonstrating endogenous tissue restoration (ETR) in an ovine model.

Methods: We developed and characterized the structure, mechanical properties, biocompatibility, and in vivo remodeling of a fully bioabsorbable polyester based on the self-complementary ureido-pyrimidinone (UPy) quadruple hydrogen-bonding motif. Electrospinning was used to process the polymer into a three dimensional porous graft. The graft was implanted as a pulmonary interposition graft in 9 adult sheep for up to one year.

Results: Angiography confirmed extended graft patency in all 9 animals. Stable diameters were found in 8 animals throughout follow-up. In one case an aneurysmal dilation was found after 10 weeks, which was traced back to a specific faulty polymer batch. Graft polymer resorption in vivo was uniform and mediated by transient macrophage infiltration. Histologic examination revealed that he remodeled graft structure had key features of a stable vascular wall. Burst pressures for all explants 8 weeks and beyond were above 500 mmHg and largely determined by newly formed tissue. Based on this preclinical work, a clinical first-in-man study was performed. A pulmonary arterial graft was successfully implanted in each 5 patients with congenital heart disease. No significant complications were observed at 12 months post-operative.

Conclusions: This study demonstrates experimental endogenous tissue restoration of a new bioabsorbable polymeric graft in sheep. These preclinical studies and limited first-in-man clinical studies suggest the potential of a fully synthetic bioabsorbable conduit in the pulmonary circulation to guide the restoration of a patient's natural tissue into a functional living vascular replacement.