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Influence of the fiber diameter and surface roughness of electrospun vascular grafts on blood activation

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ABSTRACT

Electrospun grafts have been widely investigated for vascular graft replacement due to their ease and compatibility with many natural and synthetic polymers. Here, the effect of the processing parameters on the scaffold's architecture and subsequent reactions of partially heparinized blood triggered by contacting these topographies were studied. Degrapol® (DP) and poly(lactic-co-glycolic acid) (PLGA) electrospun fibrous scaffolds were characterized with regard to fiber diameter, pore area and scaffold roughness. The study showed that electrospinning parameters greatly affect fiber diameter together with pore dimension and overall scaffold roughness. Coagulation cascade activation, early platelet adhesion and activation were analyzed after 2 h of exposure of blood to the biomaterials. While no differences were found between DP and PLGA with similar topographies, the blood reactions were observed to be dependent on the fiber diameter and scaffold roughness. Scaffolds composed of thin fibers (diameter <1 μm) triggered very low coagulation and almost no platelets adhered. On the other hand, scaffolds with a bigger fiber diameter (2–3 μm) triggered higher thrombin formation and more platelets adhered. The highest platelet adhesion and activations rates as well as coagulation cascade activation were found in blood incubated in contact with the scaffolds produced with the biggest fiber diameter (5 μm). These findings indicate that electrospun grafts with small fiber diameter (<1 μm) could perform better with reduced early thrombogenicity due to lower platelet adhesion and lower activation of platelets and coagulation cascade.

1. Introduction

In Europe, cardiovascular diseases (CVD) are responsible for about 50% of all mortality, causing about 4.3 million deaths per year [1], and in 2008 over 2.6% of the overall population in Europe was admitted to hospital for CVD [2]. The restriction of blood flow by arteriosclerosis thus represents a significant medical burden. If detected early, many obstructed blood vessels can be bypassed or replaced by vascular substitutes, including arterial autografts, polytetrafluoroethylene (ePTFE) and polyester grafts [3].

Autografts have been observed to be the most successful choice for the repair of small-diameter vascular grafts, with primary patency rates of 73%, compared to 47% for ePTFE and 54% for polyester grafts [4]. The main limitations of autologous grafts are their availability and donor site morbidity [3]. Therefore, tissue-engineered vascular grafts (TEVG) using autologous cells are promising alternatives. While large-diameter TEVG grafts regenerated successfully in humans with a five-year patency of about 90% [5], small-diameter vascular grafts (diameter <5 mm) are still a challenge [6]. Among the main reasons for graft failure of small-diameter grafts (anastomotic intimal hyperplasia, aneurysm formation, infection and progression of atherosclerotic disease), acute thrombogenicity of the graft is one of the most important [7–9].

Reduction of thrombogenicity is crucial for improving the graft success rate, and several strategies have been developed with partial success. The most studied graft surface modifications are the addition of anti-thrombotic factors, coating with cell-adhesive ligands to promote endothelialization and seeding with endothelial cells. However, the addition of soluble anti-thrombotic factors has a time-limited activity, which eventually stops when the whole drug supply is used up. Coating with cell-adhesive ligands and seeding with endothelial cells both aim at better endothelialization, which provides excellent anti-thrombogenic properties [10]. However, coating with cell-adhesive ligands is not specific to endothelial cells and also supports platelets and smooth muscle cells adhesion, leading to clotting and subsequent pseudointimal thickening [3]. Also, in vitro endothelialization cannot guarantee full

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