TARGETED DRUG DELIVERY IN ARTERIAL STENOSIS - ROLE OF HEMODYNAMICS

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Hemodynamics play a central role in cardiovascular targeted drug delivery systems. Sites of abnormal vascular narrowing (stenosis) exhibit unique flow features including an abnormally elevated level of shear stress as well re-circulating flows downstream of the narrowing. Here we study the deposition of particulate drug carries in models of arterial stenosis under defined hemodynamic conditions.

First, fluorescently tagged Poly (Lactic-co-Glycolic Acid) (PLGA) nano-particles functionalized with collagen targeting motifs have been fabricated. Then experiments in a microfluidic channels coated with collagen were performed to characterize the adhesion properties of the examined particles as a function of shear. Next, perfusion experiments on collagen coated millimeter sized vascular models of stenotic coronary arteries have been performed using a custom-built perfusion system capable of emulating pulsatile physiological flow. The particle deposition was monitored using time-lapse fluorescence microscopy at defined locations within the model. Our results show that particle size and coating density affect the deposition pattern within the stenosis and that there is correlation between the microfluidic results under defined shear stress and the deposition in the stenosis models. Altogether our results illustrate the key role of hemodynamics in designing cardiovascular nano-medicines.
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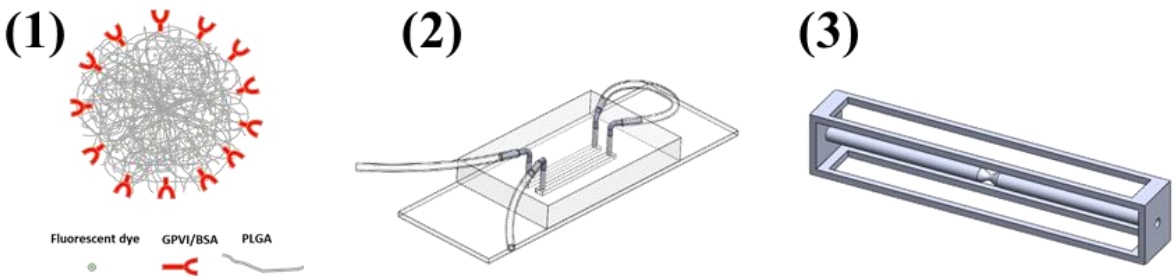

Figure 1 – Scheme representing the different stages of the study. (1) PLGA particle conjugated with collagen binding motifs (2) A CAD (computer aided design) model of microfluidic channels used to test particle adhesion to defined surfaces under constant flow (3) A stenosis CAD model showing the geometry of the model to study adhesion in a stenosis site.