# Modeling actively-targeted drug delivery in patient-specific coronary arteries to treat vulnerable plaques

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**Abstract**

The vast majority of heart attacks are caused by rupture of plaques with large cores of lipid and necrotic debris, so-called vulnerable plaques (VPs), which often do not create significant narrowing of the lumen. It has been postulated that the diseased arteries can be acutely treated with drugs delivered locally to rupture prone plaques in order to promote rapid plaque stabilization, and thereby preventing heart attacks. To that end, we built a comprehensive 3D computational tool-set to support the design and analysis of local drug delivery systems that utilize surface-functionalized nanoparticles (NPs) as drug carriers to treat vulnerable plaques.The methodology allows the investigation of NP transport through the blood stream, their adhesion onto and penetration into the vessel wall, and the subsequent release and propagation of the encapsulated drug through the arterial tissue in a patient-specific vasculature. These events are influenced significantly by the physical, chemical and biological properties of the particles including size, shape, surface chemistry, and targeting component (e.g., ligands) type and density; and also by physiological factors such as local wall shear stress and density of target receptors associated with the disease process. The goal is to optimally design these surface-functionalized nanoparticles in conjunction with patient specific attributes to ensure maximum endothelial-targeting efficiency and therapeutic efficacy in an individual patient.

In the first phase of the work, a Navier-stokes solver coupled to the scalar advection diffusion equation was utilized within the isogeometric analysis framework to simulate blood flow and particle transport within the artery [1]. To account for the number of particles adhering to the vessel wall, a special Robin type boundary condition was developed and validated *in vitro* using a parallel plate flow chamber (PPFC) apparatus. The influences of the vascular architecture, local wall shear rate, target receptor density, and

particle size on adhesion were analyzed. With the particle deposition on the vessel wall quantified as such, in the second phase of this work, a coupled drug and drug-encapsulated NP transport model was employed in conjunction with a bi-phasic mixed particle drug release model to quantify the time evolution of drug (released from the NPs ) concentration within the patient-specific coronary artery wall [2]. The diseased condition was simulated by placing an idealized vulnerable plaque model with a large lipid core and thin fibrous cap in the left circumflex branch. Results indicate that the particles accumulate preferentially to the VP region where the receptors over express themselves. Lipid core attracts the hydrophobic drug released from the NPs and retains it for a long period of time, which is encouraging from a therapeutic perspective.

Our computational framework can therefore help to personalize, thus optimize, therapeutic interventions by answering critical design questions such as, given a desired drug-tissue concentration in the targeted region, what would be the optimum NP delivery mechanism, NP shape, size and surface properties, and drug release rate, for maximum efficacy?

**Keywords:** patient-specific, vulnerable plaque, nanoparticle, isogeometric, drug delivery.

# References

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