Characterization of the Effects of Particle Shape and Blood Cells on Nanoparticle Delivery Efficiency

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Nanoparticulate systems have been widely used in diagnostic imaging and targeted therapeutic applications in recent years. One of the major challenges in nanomedicine is to improve particle selectivity and adhesion efficiency under complex vascular flow conditions. Most current studies on nanoparticle drug delivery considered a Newtonian fluid with suspending spherical nanoparticles. However, blood is a complex biological fluid composed of deformable cells, proteins, platelets, and plasma. For blood flow in capillary, arterioles and venules, the particulate nature of the blood need to be considered in the delivery process. Non-Newtonian effects such as the cell-free-layer and nanoparticle-cell interaction will largely influence both the dispersion and binding rates, thus impact targeted delivery efficacy. In addition, theoretical studies of nanoparticle deposition are typically focused on spherical particles. With the emergence of non-spherical nanoparticles in recent years, it is important to develop a predictive tool that can handle a variety of shapes and sizes of nanoparticles to identifiy suitable design under given vascular conditions. A 3D multiscale particle-cell hybrid model is developed to model nanoparticle transport, dispersion, and adhesion dynamics in blood suspension. The motion and deformation of red blood cell is captured through Immersed Finite Element method. The motions and bindings of individual nanoparticles of various shapes are tracked through Brownian adhesion dynamics and molecular ligand-receptor binding kinetics. Nanoparticle dispersion and binding coefficients are derived from the developed model under various rheology conditions. The influences of vascular flow rate, geometry, nanoparticle shape and size on nanoparticle distribution and delivery efficacy are characterized. Nanorods are found to have much higher adhesion probability that their spherical counter-parts. A non-uniform nanoparticle distribution profile with higher particle concentration near the vessel wall is observed. Such distribution leads to 50% higher particle binding rate compared to the case without RBC considered. The tumbling motion of RBCs in the core region of the capillary is found to enhance nanoparticle dispersion. The modeled binding results are validated through designed experiments in microfluidic devices. Results from this study contribute to the fundamental understanding and knowledge on how the particulate nature of blood and nanoparticle influences for nanoparticle delivery efficiency, which will provide mechanistic insights on the nanomedicine design for targeted drug delivery applications.