A Three-dimensionnal Mesoscopic Model of Thrombolysis

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Abstract

A clot, as observed in a stroke event is made of fibrin strands that are entangled, making a solid structure blocking partially or completely the blood flow in a brain artery. In addition to the fibrin network, the clots are made of other procoagulant factors such as platelets and von Willebrand Factor (vWF) as well as red blood cells (RBC).

Thrombosis is the result of the polymerization of the fibrinogen, transported by blood, into fibrin strands under the action of thrombin molecules. Thrombin is typically produced in case of body malfunction, such as injured endothelial cells, vessel walls exposed to low shear rate or hypoxia. In normal physiological conditions, the anti-thrombin that is naturally present in the blood can neutralize the thrombin and prevent from clot formation.

Fibrinolysis is the inverse process: it corresponds to the dissolution of the fibrin, which results eventually in the breakdown of the clot (or thrombolysis). The molecule able to cleave the fibrin strands is the plasmin, which is created when blood streamed plasminogen attaches to fibrin and meets tissue plasminogen activator (t-PA) molecule. Patients with a stroke event are often medicated by an injection of t-PA, however in many cases the treatment is unsuccessful and the reasons of the high variability in patients response remain unclear.

In this work we propose a three-dimensional mesoscopic approach to investigate the efficacy of the fibrinolytic procedure for different patient vessel geometries and physiological flow conditions. We adopted the Lattice Boltzmann and cellular automata frameworks to model the transport and the reactions of the most relevant bio-chemical compounds of the thrombolysis. Briefly, the

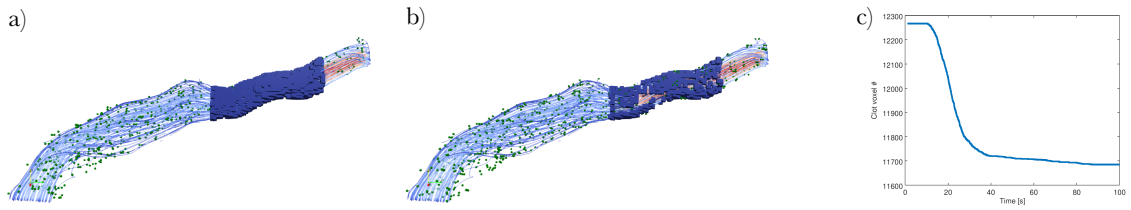

FIG. 1. Typical clot lysis by in real patient artery. a) Initial configuration. b) After 65% of clot dissolution. Clot voxels are in blue, lysing particles in green. The blood flow is represented by its stream lines showing low velocity (blue) before the clot and high velocity (red) after the clot. c) Lysis curve.

thrombolysis process is first abstracted as a two-particle system with the fibrin described as a static particle filling up voxels inside the vessel and a fictitious particle describing the combined effect of t-PA, plasminogen and PAI-1. We first show that this simplified model can qualitatively and quantitavely reproduce results obtained with a detailed one-dimensional macroscopic model of thrombolysis (four differential equations and one PDE). Then we tested the model in real artery geometry with different types of t-PA injection to test the response of the treatment under different flow conditions. Finally we simulated the lysis of clots with different compositions and spatial structures to test how the properties of the clot has an impact on the lysis efficacy.

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