Thromboembolism is one of the leading causes of morbidity and mortality worldwide, characterized by formation of obstructive intravascular clots (thrombi) and their mechanical breakages (embolism). A novel two-dimensional multi-phase computational model is introduced that describes active interactions between main components of the clot, including platelets and fibrin, to study the impact of various physiologically relevant blood shear flow conditions on deformation and embolization of a partially obstructive clot with variable permeability-dependent mechanisms. Simulations provide new insights into mechanisms underlying clot stability and embolization that cannot be studied experimentally at this time. In particular, model simulations, calibrated using experimental intravital imaging of an established arteriolar clot, show that flow-induced changes in size, shape and internal structure of the clot are largely determined by two shear-dependent mechanisms, reversible attachment of platelets to the exterior of the clot and removal of large clot pieces. Model simulations indicate that blood clots with higher permeability are more prone to embolization with enhanced disintegration under increasing shear rate. In contrast, less permeable clots are more resistant to rupture due to shear-rate dependent clot stiffening originating from enhanced platelet adhesion and aggregation. These results can be used in future to predict risk of thromboembolism based on the data about composition, permeability and deformability of a clot under specific local hemodynamic conditions.

Model Approach

Governing equations. Generalized Navier–Stokes equations coupled with the Cahn–Hilliard equations are used in our 2D-model to describe blood flow and deformation of a clot consisting of platelets and fibrin.

\[
\rho (\dot{u} + \nabla \cdot u) + \nabla \cdot \left( \frac{1}{2} \mu (\nabla u + (\nabla u)^T) \right) = -\nabla p + \rho f + F_{\text{ext}}
\]

\[
\frac{1}{\rho_0} \left( \frac{\partial c}{\partial t} + \nabla \cdot (c u) \right) = - \nabla \cdot (D \nabla c)
\]

Model Approach

Accounting for accumulation and detachment of free-floating platelets over the surface of the blood clot (rate function \(S_p\)).

\[
S_p = \frac{1}{1 + \left( \frac{\|D_{gt}\|}{D_{gt0}} \right)^{n_p}}
\]

Effect of clot permeability on clot deformation, fragmentation and flow dynamics. (a) Volume averaged deformation tensor norm as a function of clot shell permeability. The inset shows the evolution of the average deformation gradient tensor (DGT). (b) Relationship between the mean plasma velocity in the clot shell region and shell permeability (c,d) Spatial distribution of the shear force density induced by the flow over the clot with low and high shell permeability values at \(t = 0\). (e) Flow-induced deformations of blood clots at flow shear rate of 1000 s⁻¹ at 10 h.s. The black curve outlines the surface of the blood clot and its fragments. The red curve depicts the interface between the core and shell regions. The blue dot lines indicate initial interfaces.

Conclusions

- A multi-phase continuum model was developed to examine the mechanical behavior of blood clots under various physiologically relevant flow conditions and with varying clot permeability.
- Flow shear induces clot size reduction via two mechanisms, namely, formation and breakage of weak bonds between individual platelets and the surface of the clot, and (ii) tearing pieces off the clot.
- The degree of clot deformation varies nonlinearly with time and the clot becomes stiffer as its deformation increases in response to flow.
- The clot stiffness, associated with increased platelet density in the shell domain of the clot, reduces the degree of clot deformation.
- Clots with lower permeability are less deformable and less prone to shear-induced embolization.

References