COMPUTATIONAL MECHANICS 2021
36th conference with international participation
Srní
November 8 - 10, 2021

In-silico study of flow-mediated thrombosis in portal vein reconstructions

V. Dušková[a], A. Jonášová[a], S. Plánička[a], J. Vimmr[a]

[a] *Faculty of Applied Sciences, University of West Bohemia, Univerzitní 8, 301 00 Plzeň, Czech Republic*

Surgical treatment of advanced pancreatic cancer is often accompanied by removal and consequent replacement of adjacent portal vein segments infiltrated by tumour cells. In accordance with the general consensus in vascular surgery, harvested autografts are recognised as the best grafting material, which, unfortunately, is not always available or of adequate quality. Thus, finding a clinically reliable alternative to this type of grafts has become one of the main tasks within the medical community and as such led to various experimental and clinical studies. Notable in this regard is the recent experimental study by Pálek et al. [3] that explored the possible use of various allogeneic venous grafts in portal vein reconstructions of pig models, Fig. 1.

According to the observations made in the study, some types of implanted allografts showed susceptibility to thrombotic events resulting in graft occlusions and failures. Because the occurrence of these events could not be explained by technical errors of the performing surgeon, it was hypothesised that they are of hemodynamic origin and as such induced by the altered vessel geometry. Although the following computational analysis of the hemodynamic environment could explain some of the observed tendency to form blood clots [3], it showed that the problem is of much more complex origin than initially thought, thus, triggering the need for a more in-depth study.

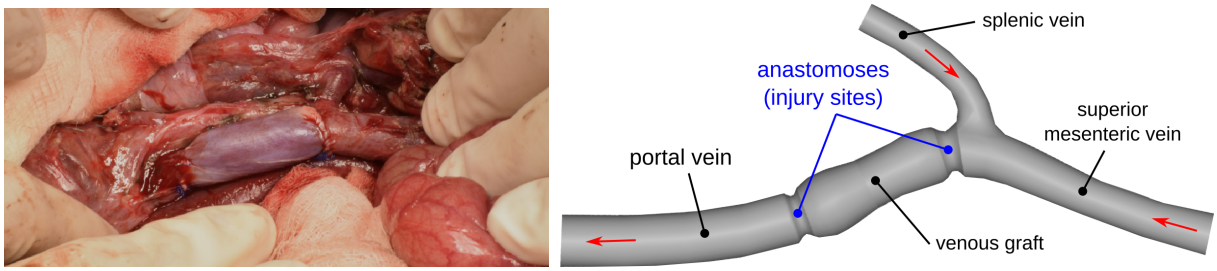

Fig. 1. Porcine portal vein reconstruction (*left*) and its computational counterpart (*right*)

The present work brings the first results of this study, whose aim was to provide an in-silico insight into the post-surgical development of intravascular thrombosis in portal vein reconstructions, particularly in relation to several key factors. These factors were selected to reflect the relationship between the blood clot growth and the direct and indirect stimuli such as the trigger level or injury extent. For the intended simulations of flow-mediated thrombosis, a special computational model was proposed in the form of three interlinked submodels (Fig. 2), each representing a process crucial for the in-vivo formation of a stable blood clot. In other words, compared to other similar studies, which were mainly limited to the modelling of the generally accepted blood clotting mechanism (haemocoagulation), the present mathematical model

also recognises the need for the formation of a platelet plug as a primary thrombus [2, 5] and introduces a moment-based submodel governing the polymerisation and cross-linking of fibrin monomers up to the formation of a secondary thrombus [1, 4]. Because of the overall model complexity and the need for a robust CFD solver to ensure the two-way interaction between the growing blood clot and portal haemodynamics, the proposed model of thrombosis was implemented and numerically solved in the Ansys Fluent software by means of user-defined functions (UDFs) written in the C programming language.

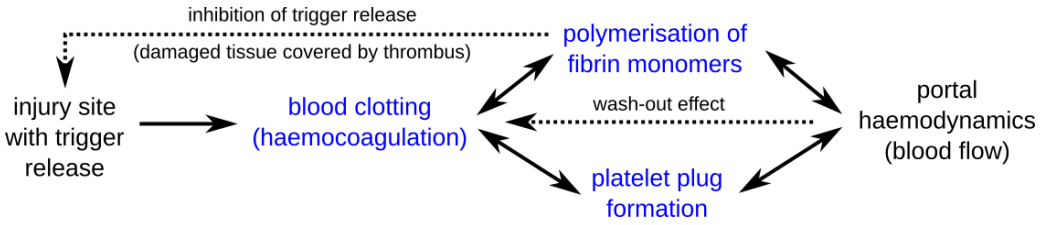

Fig. 2. Submodels of the thrombosis model (in blue) and their interaction with the vessel environment

The numerical results obtained for various scenarios (normal/elevated trigger levels, injury position etc.) allowed for several interesting observations. Particularly notable in this regard is the key role of platelets during the initial phase of clot formation, which is demonstrated by the results shown in Fig. 3. The left set of pictures corresponds to a thrombosis model without the inclusion of platelets (formation of a pure fibrin clot), whereas the right set was obtained for a complete model as listed in Fig. 2. Aside from the significantly dissimilar thrombus shapes in both scenarios, it should be pointed out that the presence of platelets, particularly the bound ones at injury sites, allowed for simulations of much higher blood flow velocity than when these blood cells were completely omitted (compare velocity ranges in Fig. 3). Note that this behaviour is in full agreement with experimental observations [2] due to the fact that high velocity haemodynamics tends to significantly dilute the concentration of activated coagulation

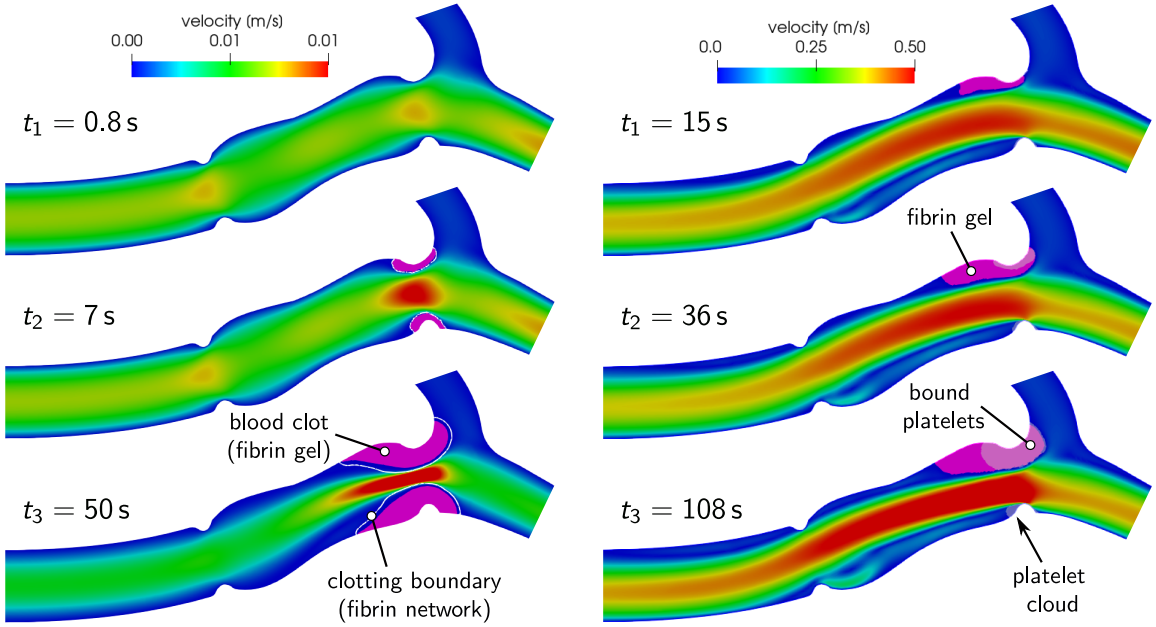

Fig. 3. Blood clot formation within the flow field of a portal vein reconstruction with the coagulation trigger located at the upstream anastomosis – (*left*) model without platelets, (*right*) complete model

factors (the so-called "wash-out effect"). In other words, the blood clotting mechanism requiring chemical species of certain concentration cannot be started properly, requiring so a drastic decrease in blood flow velocity in order to be able to observe the formation of a fibrin clot.

Acknowledgements

The study was supported by the European Regional Development Fund-Project "Application of Modern Technologies in Medicine and Industry" (No. CZ.02.1.01/0.0/0.0/17_048/0007280). Computational resources were supplied by the project "e-Infrastruktura CZ" (e-INFRA CZ ID:90140) supported by the Ministry of Education, Youth and Sports of the Czech Republic.

References

[1] Guria, G. T., Herrero, M. A., Zlobina, K. E., A mathematical model of blood coagulation induced by activation sources, Discrete & Continuous Dynamical Systems 25 (1) (2009) 175-194.

[2] Link, K. G., Sorrells, M. G., Danes, N. A., Neeves, K. B., Leiderman, K., Fogelson, A. L., A mathematical model of platelet aggregation in an extravascular injury under flow, Multiscale Modeling & Simulation 18 (4) (2020) 1489-1524.

[3] Pálek, R., Jonášová, A., Rosendorf, J., Mik, P., Bajcurová, K., Hošek, P., Moulisová, V., Eberlová, L., Haidingerová, L., Brzoň, O., Bednář, L., Kříž, T., Dolanský, M., Třreška, V., Tonar, Z., Vimmr, J., Liška, V., Allogeneic venous grafts of different origin used for portal vein reconstruction after pancreaticoduodenectomy – Experimental study, Anticancer Research 39 (12) (2019) 6603-6620.

[4] Rukhlenko, O. S., Dudchenko, O. A., Zlobina, K. E., Guria, G. T., Mathematical modeling of intravascular blood coagulation under wall shear stress, PLOS One 10 (7) (2015) No. e0134028. https://doi.org/10.1371/journal.pone.0134028

[5] Seo, J. H., Abd, T., George, R. T., Mittal, R. A coupled chemo-fluidic computational model for thrombogenesis in infarcted left ventricles, American Journal of Physiology-Heart and Circulatory Physiology 310 (11) (2016) H1567-H1582.