Blood Clot Contraction Depends Both on Clot Shape and Volume

Rafael R. Khismatullin[1], Shakhnoza M. Saliakhutdinova[1], Alina I. Khabirova[1], Rustem I. Litvinov[2], John W. Weisel[2]

[1]Department of Morphology and General Pathology, Institute of Fundamental Medicine and Biology, Kazan Federal University, Kazan, Russian Federation; [2]Department of Cell and Developmental Biology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania, USA

INTRODUCTION

Contraction/retraction of blood clots driven by activated platelets has important pathophysiological implications. It is unknown whether clot contraction depends on the clot geometry and size.

AIM

To determine how the volume and shape of blood clots affect their contraction.

METHOD

Thrombin-induced clots formed in citrated whole blood or platelet-rich plasma ranged 0.3-1.5 ml by volume in a cylinder, cuboid, or flat plastic vessel, pre-lubricated with a detergent to prevent fibrin sticking to the walls. The clots were allowed to contract at 37°C for 60 minutes and photographed every 5 minutes to quantify the rate and extent of clot shrinkage.

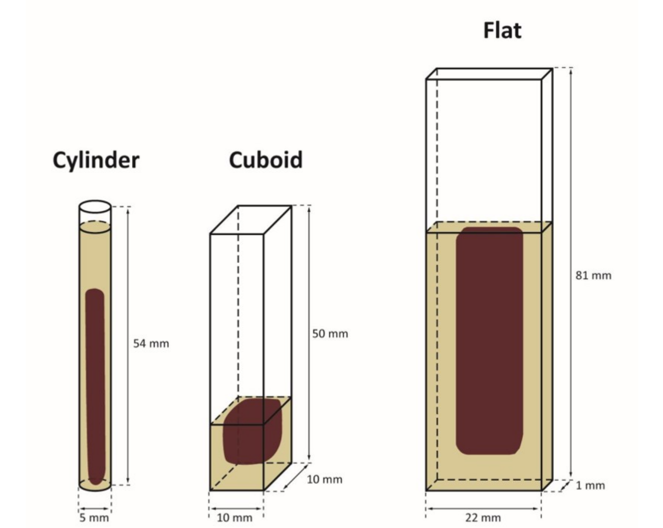

Figure 1. Schematic diagrams showing the types of vessels used to form whole blood or PRP clots of various shapes and size (exemplified with 1.5-ml whole blood clots after contraction).

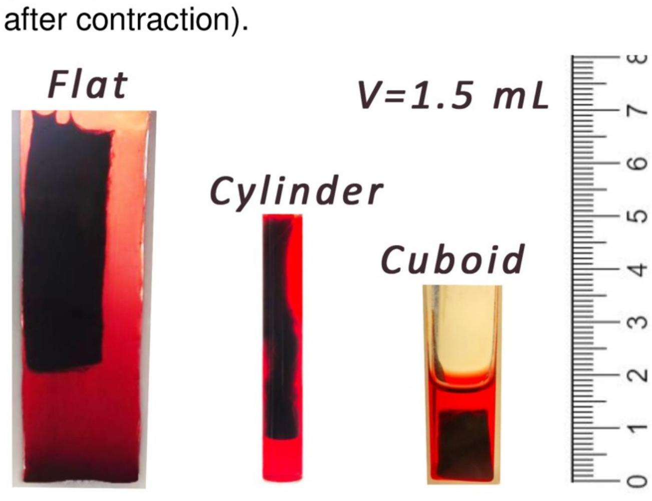

Figure 2. Macrophotographs of blood clots of the same initial volume but various shapes with different extents of contraction.

ACKNOWLEDGEMENTS

This study was supported by the Program for Strategic Academic Leadership at the Kazan Federal University (PRIORITY-2030).

CONTACT INFORMATION

Rafael R. Khismatullin
rafael.khismatullin@gmail.com

RESULTS

The contraction of whole blood clots varied depending on their shape and size. Blood clots with smaller volumes always contracted faster and more. At the same volumes studied, the cuboid clots contracted faster and stronger than the flat ones, while the compression of cylindrical clots was the slowest and weakest. In the cylindrical clots of various volumes, the order of the contraction rates was the following: small > medium > large. In cylindrical clots of various volumes but constant height, the smallest clot showed the highest extent of contraction. In the cylindrical clots of a constant volume (1.5 ml) and various diameters, the narrowest clots demonstrated somewhat delayed but the highest extent of contraction. Unlike in whole blood, in platelet-rich plasma clots, there was no difference in contraction between clots of various volumes and shapes studied, suggesting a role of erythrocytes. The observed differences may be due to varied compressibility and spatial redistribution of erythrocyte masses.

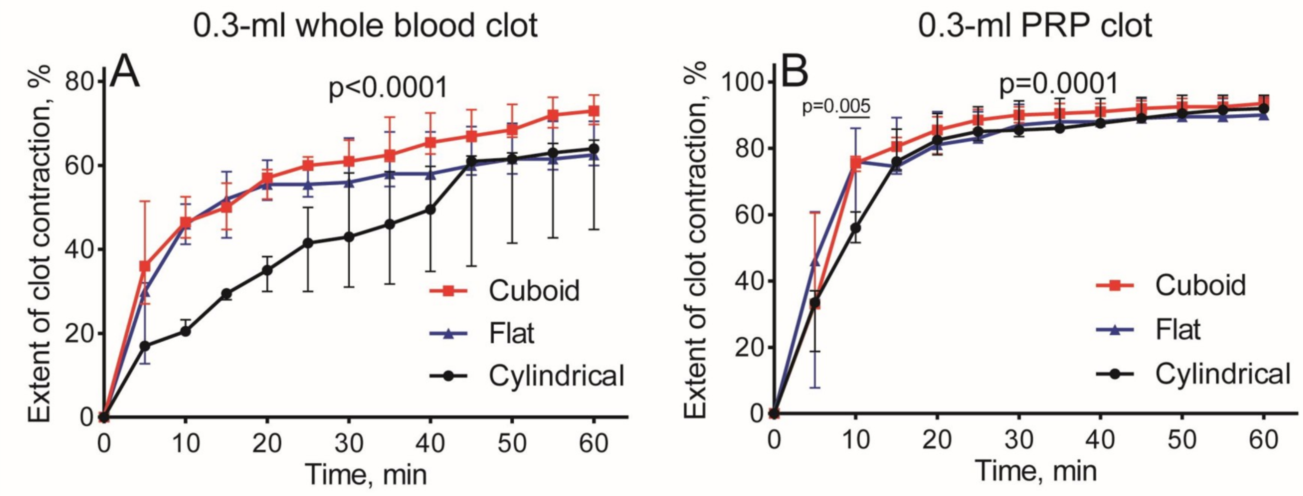

Figure 3. **The kinetics of contraction for clots of a fixed initial volume but different shapes (cuboid, flat, or cylindrical).** (**A**) 0.3-ml whole blood clots of the 3 different shapes (n=3); (**B**) 0.3-ml PRP clots of the same 3 different shapes (n=3). The p-values determined with the Friedman test reflect a significant difference between the entire kinetic curves (rates) for clots formed both in whole blood and PRP. To assess differences between the extents of contraction at each time point, one-way ANOVA test with Holm-Sidak's multiple comparisons test or Kruskal-Wallis test with Dunn's multiple comparisons test were used. **The rates and final extents of contraction of whole blood clots were significantly different in the following order: cuboid > flat ≥ cylindrical. Unlike in whole blood, in 0.3-ml PRP clots, there was no difference in the final extent of contraction, but there was a moderate yet significant variance in the rate of contraction at the early stage.**

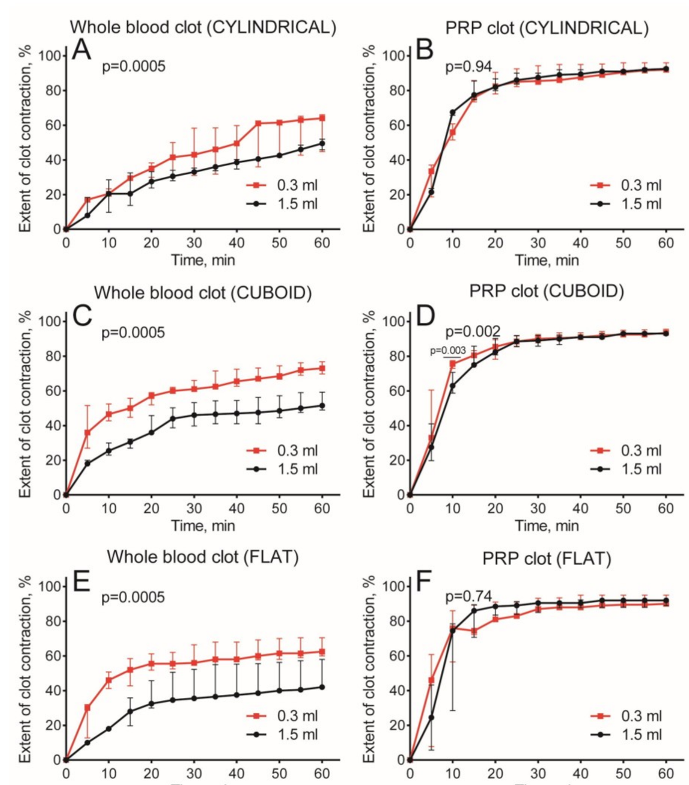

Figure 4. The kinetics of clot contraction for clots of the same shapes (cuboid, flat, or cylindrical) but various dimensions (0.3 ml and 1.5 ml initial volumes). (**A**) Cylindrical whole blood clots; (**B**) Cylindrical PRP clots; (**C**) Cuboid whole blood clots; (**D**) Cuboid PRP clots; (**E**) Flat whole blood clots; (**F**) Flat PRP clots. The p-values determined with Wilcoxon matched-pairs signed rank test reflect a difference between the entire kinetic curves (rates) for clots formed both in whole blood and PRP. To reveal differences between the extents of contraction at each time point, Mann-Whitney test or unpaired *t*-test were used. **The smaller (0.3 ml) blood clots always contracted faster and to a larger extent than the larger (1.5 ml) clots. In PRP clots, unlike in whole blood, there was no discernible difference in the rate and extent of contraction between cylindrical and flat clots of various initial volumes studied. In cuboid PRP clots, there was no difference between 0.3-ml and 1.5-ml clots in the final extent of contraction, but there was a deviation in the rate of contraction at the early stage. The rate and extent of contraction were always higher in PRP clots compared to whole blood clots.**

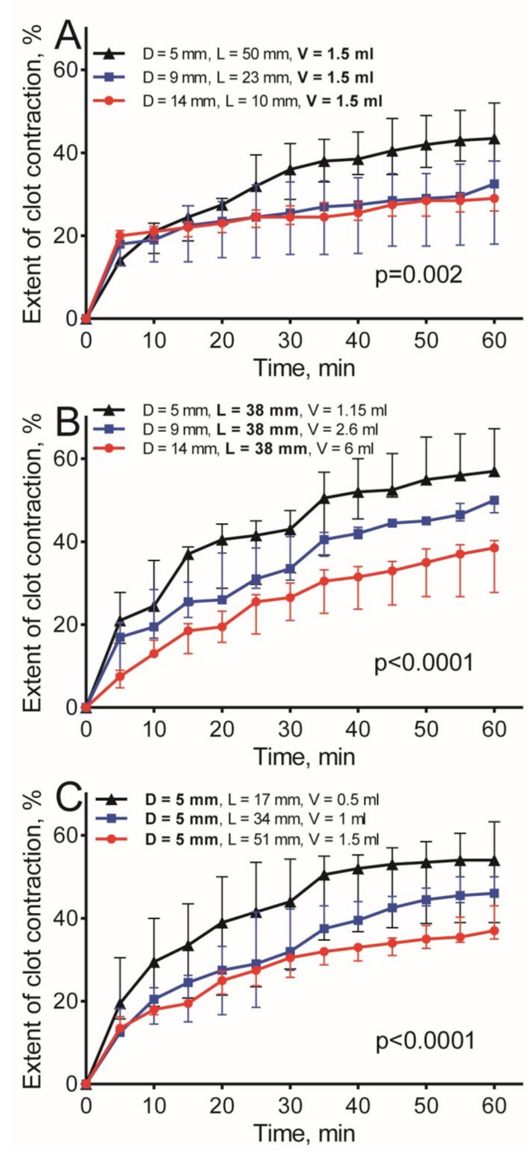

Figure 5. The kinetics of clot contraction for cylindrical clots of various diameters, lengths, and initial volumes formed in whole blood. (**A**) Various diameters (*D*) and corresponding lengths (*L*) but a constant initial volume (*V=1.5 ml*); (**B**) various diameters (*D*) and corresponding initial volumes (*V*) but a constant length (*L=38 mm*); (**C**) various lengths (*L*) and corresponding initial volumes (*V*) but a constant diameter (*D=5 mm*) (n=3 for each condition). The p-values determined with Friedman test reflect a difference between the entire kinetic curves (rates) of clot contraction. **All three variable parameters studied, namely a clot volume, length, and diameter, influence the rate and final extent of blood clot contraction.**

CONCLUSIONS

Contraction of blood clots depends on their size and shape, such that the smaller clots shrink faster and more and the cylindrical or flat clots contract weaker than the cuboid clots. These findings are physiologically relevant as intravascular thrombi have variable geometry and size.