

Analyzing the efficacy of antithrombotic treatments on platelets in patients with COVID-19 by optical frequency-division-multiplexed microscopy

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During the global pandemic COVID-19, COVID-19-induced thrombosis is found to be a crucial factor in the mortality from COVID-19^[1]. For the prevention of thrombosis, the World Health Organization (WHO) and the International Society of Thrombosis and Haemostasis (ISTH) recommend the prophylactic dose of antithrombotic drugs under suitable conditions^[2]. However, there is no appropriate tool to monitor and evaluate the effects of different antithrombotic treatments on platelets in COVID-19 patients to date. Here we present a new method to analyze the effects of antithrombotic treatments on platelets by optical frequency-division-multiplexed (FDM) microscopy on a microfluidic chip, shown in Fig. 1a, that enables high-throughput imaging of single platelets and platelet aggregates at the event rate of 100-300 events per second^[3]. Examples of bright-field images (67×67 pixels/image) are shown in Fig. 1b, which were obtained in the field of view of $53.6 \mu\text{m} \times 53.6 \mu\text{m}$ with a spatial resolution of $0.8 \mu\text{m}$ ^[3]. To conduct the intelligent classification of the images of platelets under different antithrombotic treatments, we carried out the morphology-based analysis of the platelets using a convolutional neural network (CNN) model. As shown in Fig. 1c, the confusion matrix of the CNN demonstrates the quantitative analysis of different treatments, where the average diagonal element value of 84% for the group of moderate patients with COVID-19 reveals that our method is able to differentiate antithrombotic treatments for patients with COVID-19. As morphological features of platelet aggregates possibly reflect the mechanisms of thrombosis formation in patients^[4], our work holds promise for evaluating different antithrombotic treatments not only for COVID-19 patients, but also for other patients with high risks of thrombosis.

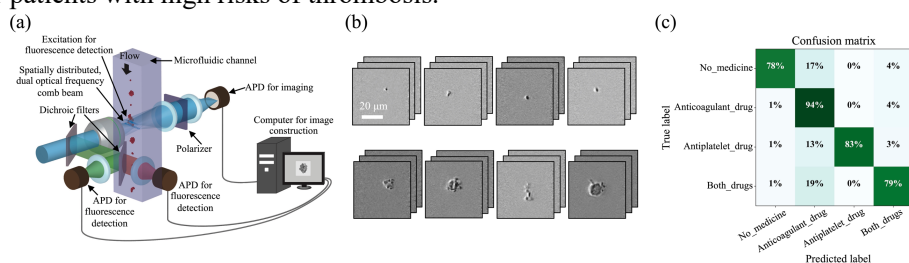


Figure 1. Experimental results. (a) Schematic of the setup. (b) Images of single platelets and platelet aggregates in blood samples of COVID-19 patients. (c) Confusion matrix of the CNN model trained with images taken from the group of moderate patients with COVID-19.

References

[1] Russell, P., et al. Nat Nanotechnol, 2022. doi.org/10.1038/s41565-022-01270-6. [2] Maldonado, E., Tao D., and Mackey K. J Gen Intern Med, 2020. **35**(9): p. 2698-2706. [3] Nishikawa, M., et al. Nat Commun, 2021. **12**(1): p. 7135. [4] Zhou, Y., et al. eLife, 2020; **9**:e52938.