T2MR® Platelet Analysis Enables Fast and Effective Diagnosis of Qualitative Platelet Disorders in Microliter Volumes of Whole Blood

INTRODUCTION

T2MR is a diagnostic technology that has a highly sensitive diagnostic technology with applications in direct from whole blood analysis including screening and hemostasis.

There is a need for a rapid, simple, platelet activity diagnostic with similar or improved performance related to the established standard, light transmission aggregometry (LTA).

Recent results highlight the need for a transfusion service to demonstrate sensitivity to anti-platelet medications and to predict clinical bleeding and thrombotic events.

For these purposes, we present new data characterizing the T2MR hemostasis methodology for the assessment of platelet-mediated clot formation in whole blood.

Our objectives were:

- Assess the ability of T2MR to discriminate platelet activity between donors with normal and impaired platelet function, defined by LTA.
- Compare the information learned by T2MR in LTA in patients with established or unexpected qualitative platelet defects (QPD).

The T2MR platform is available for research applications and broad hemostasis and coagulation studies on the T2MR® Instrument (T2 Biosystems, Inc.,

METHODS

T2MR Measurement of Hemostasis Parameters

- Water serves as a microscopic probe within changing micro environments (such as a coagulating blood sample).
- “Reconstructed” blood samples were generated using autologous RBCs, platelets and plasma. ADP was then added to the sample to activate platelets. Clotting was initiated with a formulation containing reptilase to generate fibrin mesh.
- The feasibility of T2MR to measure agonist specific platelet activity and inhibition in vivo was investigated by measuring platelet activity in response to arachidonic acid using T2MR and LTA after ingestion of 325 mg of aspirin over 3 days.
- T2MR demonstrated partial recovery of platelet activity 29 hours after ingestion of ASA. Using LTA, partial recovery was only evident at 78 hours (Fig. 4A). This demonstrates that T2MR, like LTA, can assess restoration of platelet activity measuring platelet activity in response to arachidonic acid using T2MR and LTA after ingestion of 325 mg of aspirin over 3 days.
- T2MR also successfully identified all known genetic or acquired function defects (N = 7), with exception of a single patient with Glanzmann’s thrombasthenia (Fig. 5).

CONCLUSIONS

These studies show that the T2MR device detects a range of clinically valuable parameters to provide rapid and accurate assessment of platelet activity. Further, the T2MR device provided highly accurate results when compared to gold standard methods (100% PPA and 99% NPA). In previous sessions, the T2MR device had predicted thrombotic events missed by established diagnostic methods. Clinical-quality measurements could impact patient management by providing rapid, comprehensive diagnosis at the point of care. Advantages to T2MR device include:

- High accuracy: T2MR detects residual 60% of whole blood and provides a quantitative measure of platelet activity consistent with the results of LTA using “standard” and “all samples” (100% PPA and 99% NPA).
- Rapid results: Turn-around times with T2MR are shorter than with LTA (20 minutes vs. 3 hours).
- Ease of use: T2MR measurements require no laboratory expertise, a simple wash and read measurement using whole blood.

High sensitivity using ADP and its antagonists to study platelet aggregation, T2MR showed dependence on P2Y1 signaling, suggesting the potential importance of evaluating platelet aggregation in whole blood.

T2MR detected “incomplete” recovery from aspirin earlier than LTA, supporting the suitability of T2MR in platelet function and potential applications in which assessment of even weak platelet activity levels is important, such as in thrombocytopenia.

These observations suggest that the ADP effects seen in T2MR are even more strongly dependent on both P2Y1 and P2Y12 signals than LTA. These results using T2MR are consistent with experiments using genetically engineered mice that have decreased or even thromboxane production (independently and equally) dependent on both P2Y1 and P2Y12. Whether this observation will be further more detailed.

Agonists with LTA in patients: High agreement with LTA in patients with known or suspected platelet defects (94% PPA, 79% NPA). These results demonstrated that T2MR is able to detect these defects with similar sensitivity and specificity to LTA, and therefore has promise as a clinically viable diagnostic to manage patients with platelet defect.

Patients with HIT: Using T2MR, the low intensity of platelet functionality was clearly evident with T2MR, which very accurately detected these defects with similar sensitivity and specificity to LTA, and therefore has promise as a clinically viable diagnostic to manage patients with platelet defect.

In conclusion, T2MR is a rapid, simple, platelet activity diagnostic that has been successfully implemented in transfusion centers including the T2 Biosystems Instrument and the T2bialyne panel. This study, T2MR’s core technology of the T2Biosystems, demonstrated rapid and accurate assessment of platelet function on a simple-to-use device. Taken together, the quantitative readout of T2MR in whole blood, close correlation with gold standard methods, and ability to discriminate between normal donors and patients with quantitative platelet defects indicate that T2MR has a potential impact on the diagnosis and management of patients with quantitative platelet defects.

REFERENCES


