Thrombosis Research 145 (2016) 3–11

Contents lists available at ScienceDirect

Thrombosis Research

journal homepage: www.elsevier.com/locate/thromres

Full Length Article

Dielectric permittivity change detects the process of blood coagulation: Comparative study of dielectric coagulometry with rotational thromboelastometry

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ARTICLE INFO

Article history:
Received 28 April 2016
Received in revised form 18 June 2016
Accepted 29 June 2016
Available online 30 June 2016

Keywords:
Coagulation
Dielectric blood coagulometry
Anticoagulant therapy

ABSTRACT

Background: Intravascular thrombus formation causes various cardiovascular diseases. To monitor coagulation is important for screening native status, prevention from bleeding and maintaining it within its therapeutic range. The prothrombin time and the activated partial thromboplastin time are widely used for assessment and recognized as the conventional methods. Prothrombin time methods employ enhancement of coagulation with thromboplastin. Since the laboratory data depend on the production lot and/or the manufacturer, the accurate methods are required for evaluation. Rotational thromboelastometry (ROTEM) is a method based on detection of the change in resistance to rotational movement during blood clotting, while dielectric blood coagulometry (DBCM) is a novel method for assessment of clotting by measuring the change of electrical permittivity. These methods are thus based on the technology for observation of different physical phenomena. The aim of this study was to compare parameters such as the clotting time obtained by ROTEM and DBCM to evaluate their clinical usefulness.

Methods and results: ROTEM and DBCM parameters were measured in 128 patients. The ROTEM clotting time showed a significant positive correlation with the DBCM coagulation time ($R = 0.707$, $p < 0.001$). Comparison of the DBCM coagulation time between patients with and without anticoagulant therapy (including novel oral anticoagulants) revealed a significant difference (43.8 ± 11.9 min in the anticoagulant group vs 29.4 ± 8.3 min in the control group, $p < 0.001$). Evaluation of coagulation was equivalent with DBCM and ROTEM.

Conclusions: The present study suggested that DBCM, a novel method for measuring blood clotting, could provide the detail assessment for the status of anticoagulant therapy.

1. Introduction

Intravascular thrombus formation is associated with various cardiovascular conditions, such as stroke, coronary artery disease, venous thromboembolism, atrial fibrillation, and prosthetic heart valves [1–5]. During the process of hemostasis after vascular injury, 1) aggregation of platelets occurs through binding to exposed subendothelial collagen, 2) release of tissue factor activates the coagulation cascades, and 3) activated thrombin promotes further platelet aggregation and catalyzes the conversion of fibrinogen into fibrin to reinforce the soft thrombus with a firm fibrin network that coats the complex of aggregated platelets and blood cells. While these hemostatic processes are crucial for maintaining the integrity of the high pressure circulatory system, excessive generation of thrombin triggered by continuous endothelial stimulation or inflammation can initiate pathologic thrombosis with dysregulation of hemostasis and the development of a hypercoagulable state. Although anticoagulants and antiplatelet agents are prescribed for prevention of thrombosis, these medications sometimes cause bleeding complications such as intracranial hemorrhage or gastrointestinal bleeding [6,7]. To monitor coagulation, the prothrombin time (PT) and the activated partial thromboplastin time (aPTT) are often used in clinical practice [8], however, these methods are not necessarily useful for assessing native coagulation status.

Rotational thromboelastography (TEG) and rotational thromboelastometry (ROTEM®, Tem International, Munich, Germany) have recently been proposed as methods for assessing the hemostatic status by estimating clot formation, clot dissolution kinetics, and clot strength from the response to a continuously applied rotational force. Both methods generate parameters based on the strength of thromboplastin in blood, and have mainly been adopted in the fields of surgery and anesthesiology

Abbreviations: ROTEM, rotational thromboelastometry; DBCM, dielectric blood coagulometry.

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http://dx.doi.org/10.1016/j.thromres.2016.06.030
0049-3848/

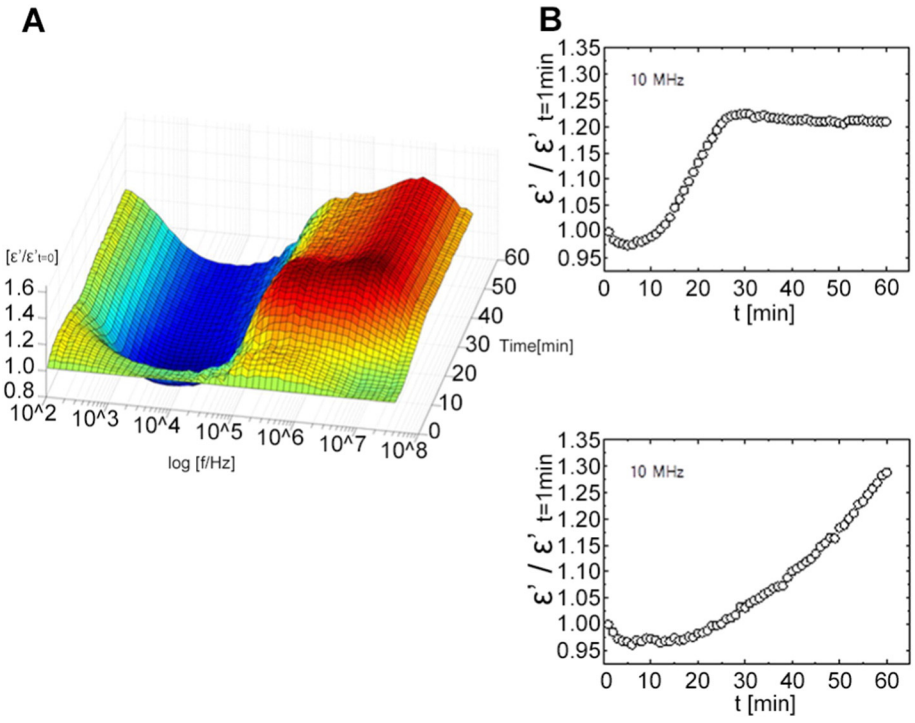

Fig. 1. DBCM data. (A) Example of a 3-dimensional dielectric spectrum obtained according to the standard protocol. The AC frequency (Hz), time (t), and change of dielectric permittivity ($\varepsilon'/\varepsilon'_{t=0}$) are shown on the x, y, and z axes. The color changes from blue at a lower permittivity to red at a higher permittivity. (B) Time course of the change in dielectric permittivity at 10 MHz. A subject without anticoagulant therapy is shown in the upper panel and one with anticoagulant therapy is shown in the lower panel. The vertical line indicates the peak time, showing the peak time is shifted to the right in the lower panel.

as point-of-care tests [9]. Previous reports have shown the usefulness of these methods for evaluating coagulation in patients with severe bleeding and acute or old venous thromboembolic events [9,10].

Hayashi et al. have proposed dielectric blood coagulometry (DBCM) as a new technique for estimating whole blood coagulability by measuring the change in the dielectric permittivity of a blood sample as it coagulates. Because alternating electric current around 10 MHz is very sensitive to the heterogeneity of the distribution and morphology of blood cells, the dielectric permittivity of whole blood gradually alters with clot formation, reflecting changes of the cells assembled in the clot [11,12]. In a previous study, the coagulation time obtained by DBCM showed a good correlation with the clotting time (CT) obtained by a rheological method, thus confirming that the changes of dielectric permittivity corresponded to the progression of coagulation. This method enables us to evaluate the physiological process of blood coagulation from a new perspective. In the present study, we examined the correlation of DBCM findings with conventional laboratory tests (PT and aPTT), and also with ROTEM, as well as the clinical usefulness of DBCM for monitoring anticoagulant therapy.

Table 1
Clinical characteristics of study patients.

	Control (n = 26)	Antiplatelet (n = 44)	Anticoagulation (n = 52)	Antiplatelet + anticoagulation (n = 6)
Male, n (%)	14 (54)	22 (50)	34 (65)	5 (83)
Age (mean ± SD)	58.7 ± 20	62.9 ± 18	68 ± 12	71 ± 8
Hypertension	14	27	28	3
Dyslipidemia	11	14	22	3
Diabetes mellitus	5	10	12	1
Chronic kidney disease	1	7	7	1
Current smoking	1	3	6	1
Old myocardial infarction	0	9	0	2
Atrial fibrillation	3	3	44	2
Low EF (LVEF < 35%)	1	3	2	1
Prior stroke	0	6	6	1
Prior DVT	1	0	3	0
Prior PCI/CABG	0	23	0	3
Prior valvular op.	0	1	7	1
History of malignancy	1	2	8	2
Aspirin	0	41	0	6
Clopidogrel	0	17	0	0
Ticlopidine	0	2	0	0
Warfarin	0	0	45	5
Dabigatran	0	0	5	1
Rivaroxaban	0	0	2	0

Abbreviations: LVEF = left ventricular ejection fraction, DVT = deep vein thrombosis, PCI = percutaneous coronary intervention, CABG = coronary artery bypass grafting.