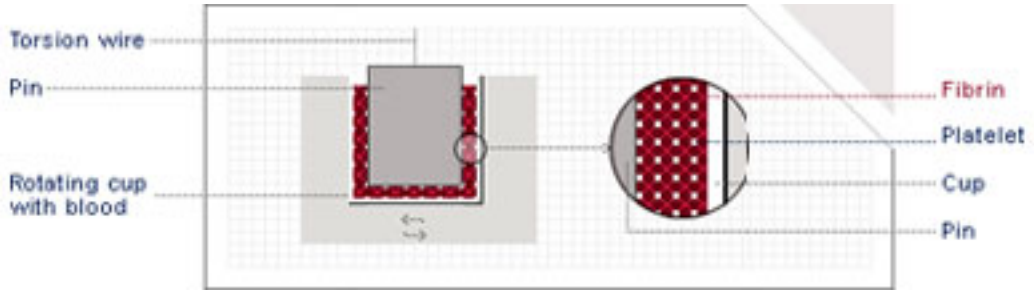
TEG
http://www.frca.co.uk/article.aspx?articleid=100103

Classical thromboelastometry is performed by filling a cuvette with native whole blood and lowering a pin suspended by a torsion wire into the sample. The cup is rotated through 4° 45' over 10 seconds with a 1 second rest period at each end. The torque of the cup is transmitted to the pin through the sample in the cup. The width of the tracing is proportional to the magnitude of the elastic shear modulus of the sample. Liquid blood has little or no torque so there will be no deflection even when the viscosity is high. As the blood clots and fibrin strands begin to form between the cup and the pin, the motion of the cup is transmitted to the pin.



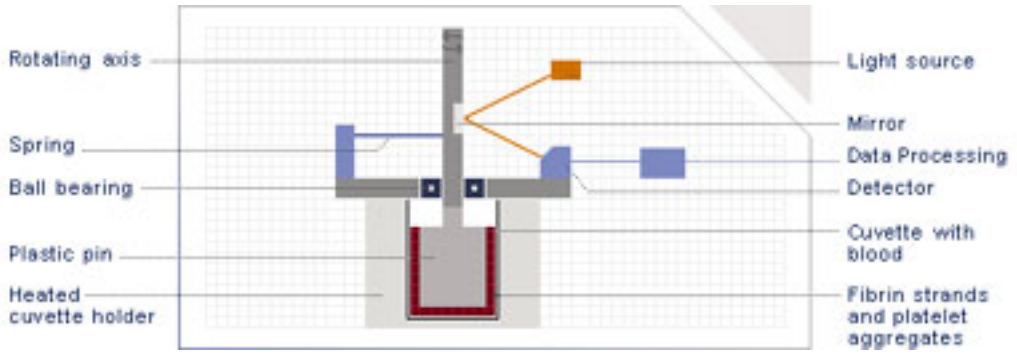
The pin is guided by a ball bearing ensuring that all movement is limited to rotation. The movement of the pin is detected by an optical detection system and is transmitted to and processed by a computer with specific software. Results obtained by thromboelastometry are dependent on the activity of the plasma coagulation system, platelet function, fibrinolysis and many factors which influence these interactions, including several drugs.

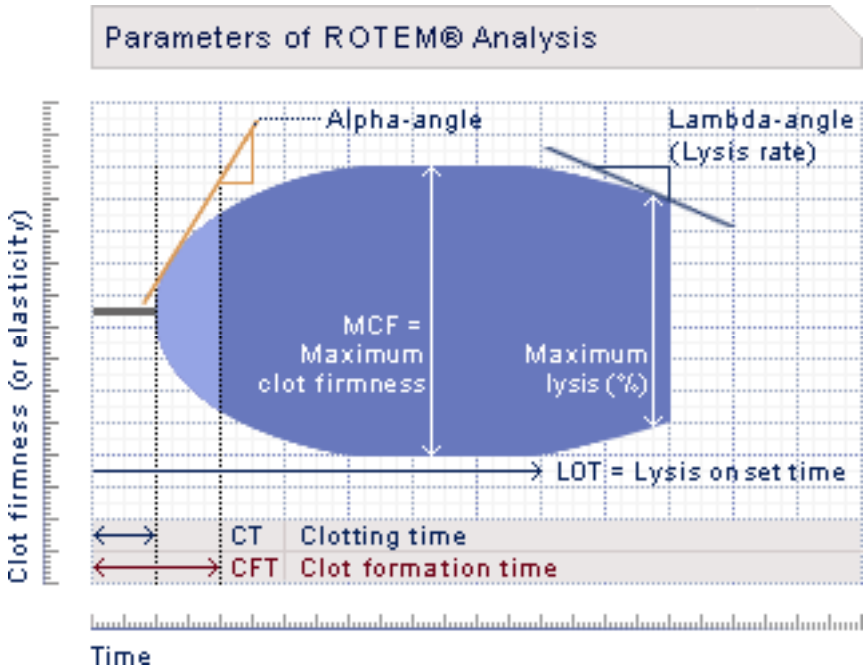
Many limitations of classical thromboelastometry are overcome by the innovative rotation thrombelastometry (ROTEM®). Data obtained with ROTEM® correlate well with classical thromboelastometry (Calatzis et. al, 1996).

In ROTEM®, the pin (sensor) is fixed onto the tip of a rotating shaft, which is guided by a high precision ball bearing system. The shaft

rotates back and forth (+/- 4.75 °; cycle time 10/min). It is connected with a spring for the measurement of elasticity. The exact position of the axis is detected by the reflection of light by a small mirror that is attached to the shaft.
The loss of the elasticity upon clotting of the sample leads to a change in the rotation of the shaft. This is detected by a CCD array and the data are analysed by a computer.

This opto-mechanical detection method provides a good protection against the impact of vibrations and mechanical shocks.





Clotting time (CT) or reaction time(R time)

The time from the start of the curve until it reaches 1 mm wide
This is the time taken to form fibrin. Prolonged with clotting factor deficiencies, anticoagulants and thrombocytopaenia.
Clot formation time (CFT) or K time

The time taken for the graph to widen from 1 mm to 20 mm. This is dependent on fibrinogen and platelets.
Maximum clot firmness (MCF)or maximum amplitude

This is the width of the curve at the widest point. This is affected by platelet function and number and fibrinogen.
Alpha angle

This is the angle measured between the midline of the tracing and a line drawn from the 1 mm point tangential to the curve.

The alpha value and CFT indicate the rate of increase of elastic shear modulus in the sample – i.e. how fast the clot structure is forming.

This is abnormal in the presence of clotting factor deficiencies, platelet dysfunction, thrombocytopenia and hypofibrinogenaemia.
Fibrinolysis

This is measured as a decrease in amplitude from the maximum. If there is a substantial decrease – i.e. more than 15% – then this is an indication of fibrinolysis taking place.
Advantages of thromboelastometry

- Real time production of a trace
- Heparinase modification allows the diagnosis of excess heparin as a cause of long R time.
- Fibrinolysis may be demonstrated by the lysis times at 30 and 60 minutes.
- A normal trace in a bleeding patient suggests a surgical source.
- Repeated tests can monitor the progress of intervention.

Cardiac surgery

Cardiac surgery has become an area, in which application of thrombelastometry has contributed significantly to an optimisation of therapy.

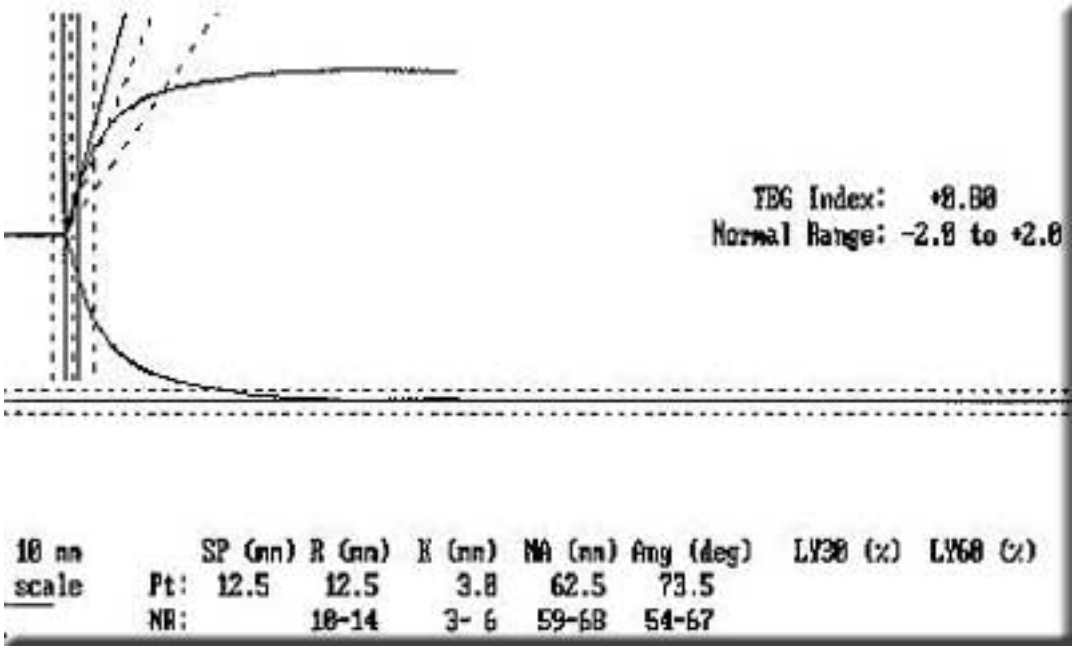
Except for surgical bleeding, the most often observed problems arise from:

the management of heparin dosage and of protamine chloride
hyperfibrinolysis
dilution
haemostasis disorders by plasma expanders and hypothermia
consumption of coagulation factors and platelets
activation of coagulation and hyperfibrinolysis
other drug effects

A differentiation of surgical bleeding from a true haemostasis disorder is important and influences therapeutic strategies. Thromboelastometry analysis is able to characterise the majority of relevant haemostasis disorders within a few minutes. This is not only a benefit for the outcome of the patient but also an economical advantage. Interventions can be made faster, and often with fewer blood products or other expensive therapies.

Bleeding disorders
Coagulation assays may sometimes generate results which do not reflect the clinical situation. Pathological prothrombin time or activated partial thromboplastin time results initiate additional tests which can often not be performed in the same location. This delays therapeutic decisions, may postpone surgery and increases costs. Thromboelastometry is sensitive for factor XIII and reflects any disturbances in fibrinogen polymerisation or the interaction between fibrinogen and platelets much better than clotting assays, and should be used in those cases.

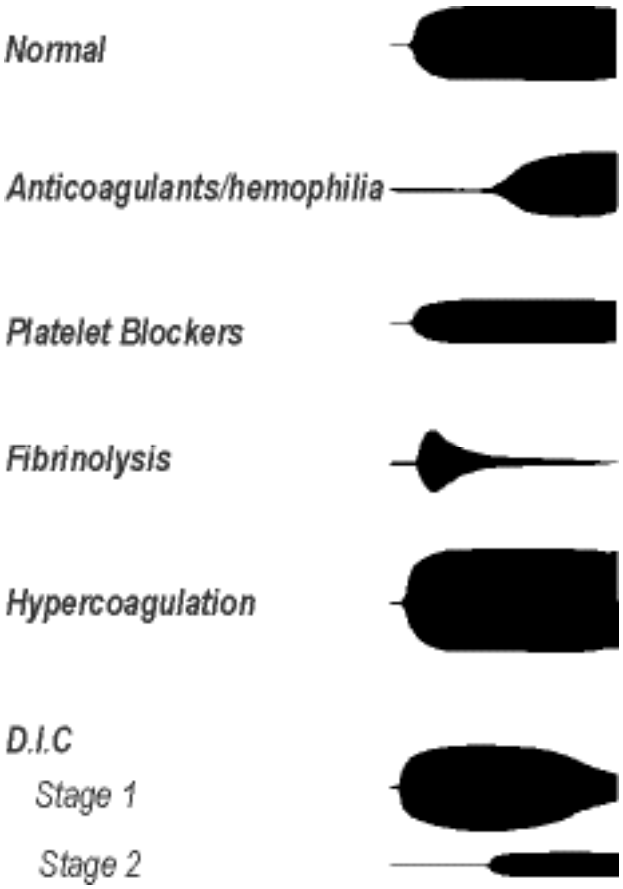
In some cases of haemophilia, especially with inhibitors, ROTEM® has been successfully used in order to manage substitution therapy with factor VIIa, which is difficult to manage with clotting assays. Also, for other cases of haemophilia, thromboelastometry may give a better picture on the clot stability than clotting tests, which are sometimes subject to interference by lupus anticoagulants.



Alterations of the normal thromboelastographic pattern can give information about:

The coagulation factor activation – R value
The coagulation factor amplification – k value and alpha angle
The platelet aggregation – maximal amplitude
Fibrinolysis – amplitude 60 minutes after maximum
Platelet adhesion to the collagen matrix is not assessed

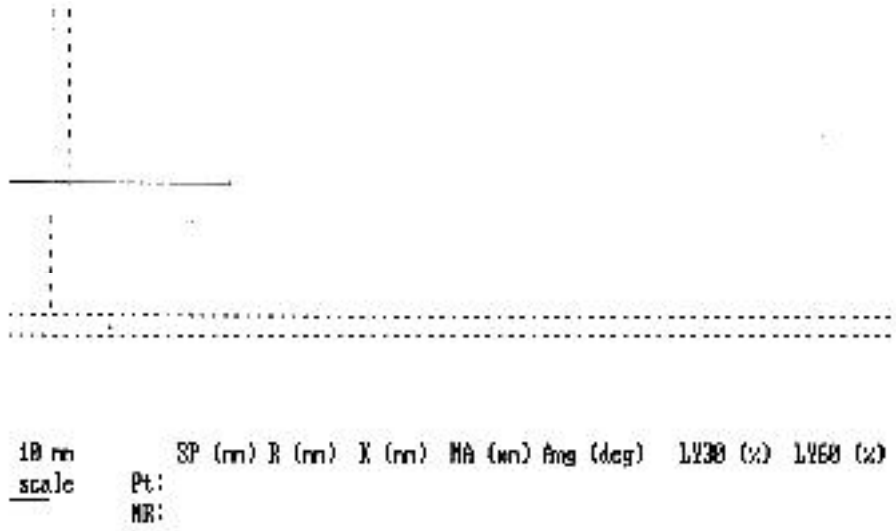
Overview



Examples of thromboelastometry

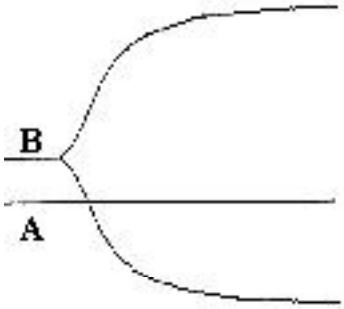
Example 1

No clot formation due to very low factor levels or a heparin effect.



Example 2

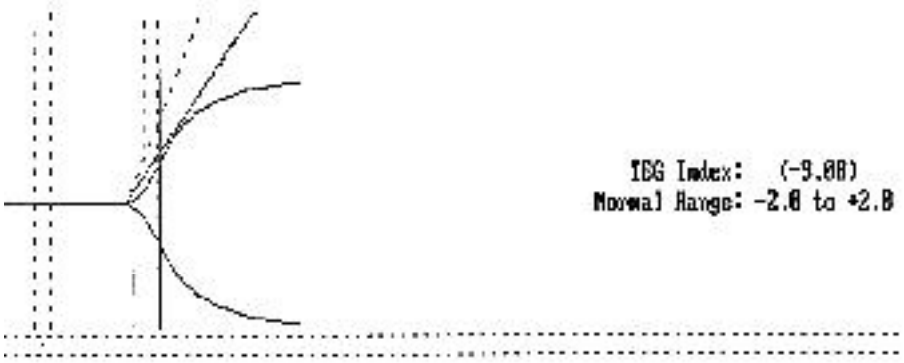
A: No coagulation at all – due to whole blood from a heparinised patient
B: Normal curve – due to whole blood after the addition of heparinase.



			SP (mm)	R (mm)	K (mm)	MA (mm)	Ang (deg)	LY30 (%)	LY60 (%)
10 mm scale	B	Pt:	14.5	16.0	5.5		59.0		
		NR:		10-14	3- 6		54-67		
	A	Pt:							
		NR:							

Example 3

Prolonged R value suggesting factor deficiency or possibly a minimal heparin effect.

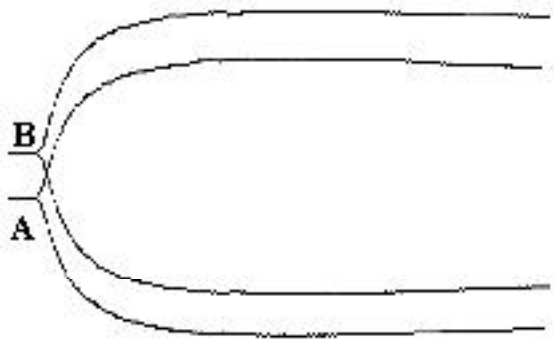


TEG Index: (-9.0B)
Normal Range: -2.0 to +2.0

		SP (mm)	R (mm)	K (mm)	MA (mm)	Ang (deg)	LY30 (%)	LY60 (%)
10 mm scale	Pt:	31.5	33.0	6.5	(53.5)	54.5		
	NR:		10-14	3- 6	59-68	54-67		

Example 4

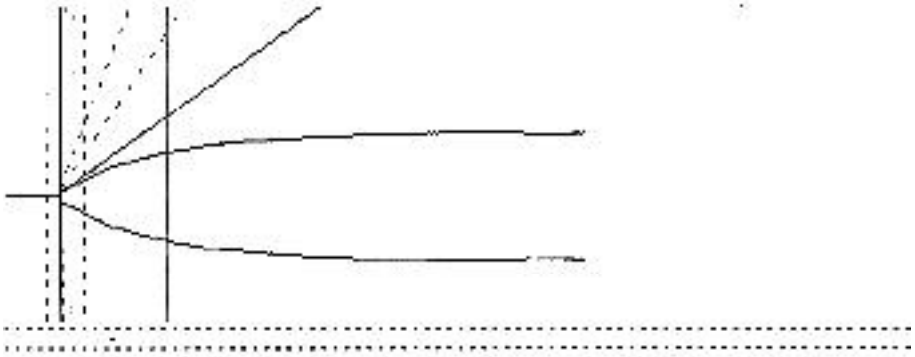
Normal coagulation profile with adequate reversal of heparin by protamine. This is confirmed by the second trace with heparinase added.



			SP (mm)	R (mm)	K (mm)	MA (mm)	Ang (deg)	LY30 (%)	LY60 (%)
10 mm scale	B	Pt:	6.5	7.5	3.0	63.0	70.0	1.0	
		NR:		10-14	3- 6	59-68	54-67		
	A	Pt:	6.5	7.5	3.0	61.5	69.5	1.5	
		NR:		10-14	3- 6	59-68	54-67		

Example 5

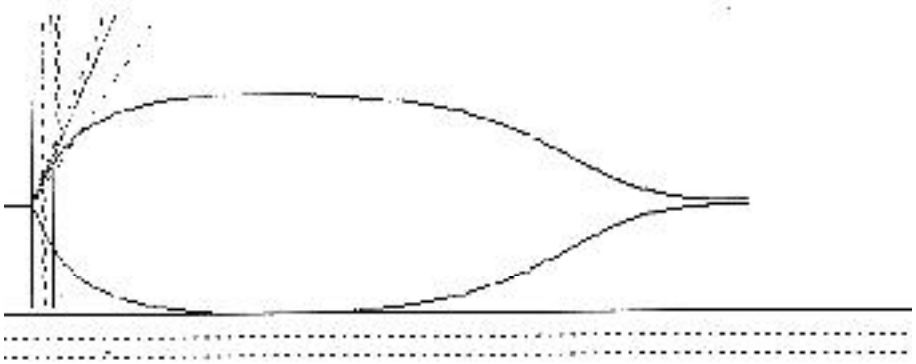
Small alpha angle and small maximal amplitude with weak clot formation. This may be due to thrombocytopenia or hypofibrinogenaemia.



		SP (mm)	R (mm)	K (mm)	MA (mm)	Ang (deg)	LY30 (%)	LY60 (%)
10 mm scale	Pt:	12.0	13.0	25.5		34.0		
	NR:		10-14	3- 6		54-67		

Example 6

Short R value, borderline maximal amplitude. There is significant clot lysis due to poor platelet function and fibrinolysis.



10 mm		SP (mm)	R (mm)	K (mm)	MA (mm)	Ang (deg)	LY30 (%)	LY60 (%)
scale	Pt:	7.0	7.5	5.8	49.8	64.0	6.5	
	NR:		10-14	3- 6	59-68	54-67		

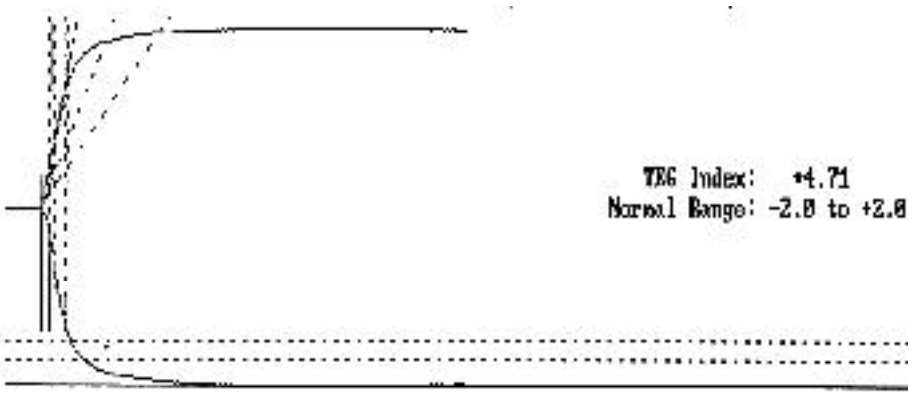
Example 7

Elongated R value, k value not readable, small alpha angle and small maximal amplitude. Due to technical error in thrombelastograph processing or severe coagulopathy.

10 mm		SP (mm)	R (mm)	K (mm)	MA (mm)	Ang (deg)	LY30 (%)	LY60 (%)
scale	Pt:	23.0	41.5		(2.5)	(3.8)		
	NR:		10-11		59-68	54-67		

Example 8

Short R value, short k value, large alpha angle and large maximal amplitude. No fibrinolysis evident, possibly due to aggressive replacement of factors, e.g. platelet rich plasma or chronic hypercoagulable states.



10 mm		SP (mm)	R (mm)	K (mm)	MA (mm)	Ang (deg)	LY30 (%)	LY60 (%)
scale	Pt:	8.0	8.5	2.0	79.5	78.0		
	NR:		10-14	3- 6	59-68	54-67		

Thrombelastography

Wenker O, Wojciechowski Z, Sheinbaum R, Zisman E: Thrombelastography. The Internet Journal of Anesthesiology 1997; Vol1 N3: http://www.ispub.com/journals/IJA/Vol1N3/teg.htm. Published July 1, 1997; Last Updated January 28, 1999.

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Introduction

Hazardous risks accompanying the transfusion of heterogenous blood products and increasing shortage of blood products led to further search for better techniques of coagulation monitoring. Because of the limitations of standard coagulation tests, other

techniques such as thrombelastography (TEG®) have been re-examined. TEG® was originally described by Hartert in 1948 (1). Continuous improvements of this technique over the decades made this test a valuable tool for the medical personnel interested in coagulation. The TEG® monitors hemostasis as a whole dynamic process instead of revealing information of isolated conventional coagulation screens (2). The TEG® measures the viscoelastic properties of blood as it is induced to clot under a low shear environment resembling sluggish venous flow. The patterns of changes in shear-elasticity enable the determination of the kinetics of clot formation and growth as well as the strength and stability of the formed clot. The strength and stability of the clot provides information about the ability of the clot to perform the work of hemostasis, while the kinetics determine the adequacy of quantitative factors available to clot formation.

Principles of Thrombelastography (Back to Quick Links)

The Computerized Thrombelastograph® Coagulation Analyzer (Haemoscope Corp. Skokie IL.) is a small instrument capable of running two samples simultaneously, easy to set up. It is connected to a computer (running the TEG® Analytical Software) through an A/D interface box . The coagulation profile is displayed on the screen as an outline of the Thrombelastograph® Coagulation Analyzer with the range of normal values displayed as dotted lines. The thromboelastogram is one of two clinically available viscoelastic tests that characterize formation and strength of the blood clot over time. The TEG® can measure in vitro the life of a clot, the time to initial clot formation, then evaluate a developing clot it's acceleration phase, strengthening and retraction. TEG® can also detect clot lysis. A sample of celite activated whole blood (0.36 ml) is placed into a prewarmed cuvette. A suspended piston is then lowered into the cuvette which moves in rotation of a 4.5 degree arc backwards and forwards. The normal clot goes quite fast through an acceleration and strengthening phase. The fiber strands which interact with activated platelets attach to the surface of the cuvette and the suspended piston. The clot forming in the cuvette transmits its movement onto the suspended piston. A "weak" clot stretches and therefore delays the arc movement of the piston, which is graphically expressed as a narrow thromboelastogram. A strong

clot in contrary will move the piston simultaneously and proportionally to the cuvettes movements, creating a thick thromboelastogram.

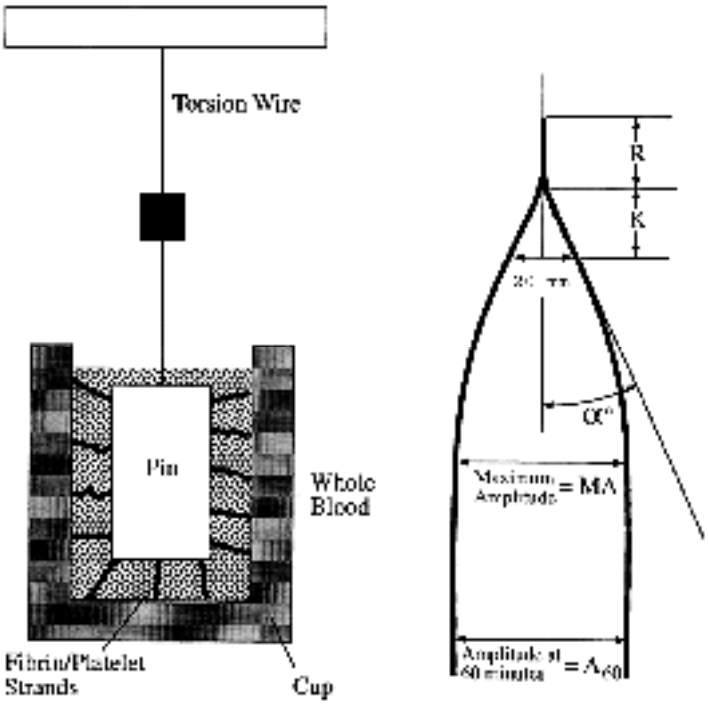

Figure 1: Principles of TEG®

bare_teg_0.jpg (10332 bytes)

published with permission of Eli Cohen, Ph.D., Haemoscope Corporation

The strength of a clot is graphically represented over time as a characteristic cigar shape figure. There are five parameters of the TEG® tracing: R, k, alpha angle, MA and MA60, which measure different stages of clot development.

R: is a period of time from initiation of the test to the initial fibrin formation.

k: is a measure of time from beginning of clot formation until the amplitude of thromboelastogram reaches 20 mm, and represents the dynamics of clot formation.

alpha angle: is an angle between the line in the middle of the TEG® tracing and the line tangential to the developing "body" of the TEG® tracing. The alpha angle represents the acceleration (kinetics) of fibrin build up and cross-linking.

MA - Maximum amplitude reflects strength of a clot which is dependent on number and function of platelets and its interaction with fibrin.

MA60: measures the rate of amplitude reduction 60 min. after MA and represents the stability of the clot.

Thromboelastographic evaluation of clot formation during heparinization (i.e., cardiopulmonary bypass) is now available. Recently, heparinase (an enzyme breaking heparin) has been introduced to the TEG® technology, allowing identification of abnormal coagulation in "heparinized" patients, prior to heparin reversal with protamine. This test may prove particularly useful during long pump runs, deep hypothermia, use of ventricular assist devices or complicated major vascular cases i.e.: repair of thoracoabdominal aneurysm. The test will also detect if more protamine is needed to fully reverse heparin.

Other reagents that may be added to the whole blood sample are antifibrinolytic agents such as Epsilon-Aminocaproic Acid, Tranexamic acid and Aprotinin. This will test their effectiveness in treatment of fibrinolysis.

Another modification of the TEG® will enable to determine the specific contribution of platelets and fibrinogen to the MA value of the TEG® tracing. Adding c7E3 Fab (REOPRO), a recently FDA approved monoclonal antibody which binds to the platelet GPIIb/IIIa receptors, to the TEG® sample will eliminate platelet function from the thromboelastogram (3). The MA will become a function of fibrinogen activity (MAR). Therefore subtraction of (MAR) from a whole blood MA (without REOPRO) (MAW), will result in determining specific contribution of platelets function to MA (MAP).

Discussion (Back to Quick Links)

The TEG® enables global assessment of hemostatic function. While other conventional tests stop with the formation of the first fibrin strands, the TEG® begins to evaluate clot formation at this point and collects data as clotting continues through to eventual clot lysis or retraction 2. Therefore, one single test produces information about several steps in the coagulation process. Unlike laboratory tests of hemostatic function which are measured in plasma, the TEG® measures clotting in whole blood and thus the interaction between fibrinogen, platelets and the protein coagulation cascade. Poor correlations are seen between most conventional coagulation tests and TEG® measurements (4) (5). The only significant correlation could be shown between the maximum amplitude MA of the TEG® and platelet aggregometry (6).

The modification of the TEG® through the addition of other substances such as heparinase or the monoclonal antibody fragment c7E3 (REOPRO) allow evaluation of heparin reversal with protamine or further differentation of coagulopathies. The heparinase-modified TEG®-assay proved to be more sensitive in detecting very low levels of heparin in patients undergoing cardiopulmonary bypass surgery compared to the activated clotting time (ACT) (7). Data gathered in the same study identified the presence of heparin before systemic heparinization or protamin reversal, and evaluated platelet-fibrinogen interaction in patients receiving systemic heparin. The use of heparinase-guided thrombelastography was as well described in the assessment of a parturient who had been anticoagulated with heparin for suspected thromboembolic disease (8). TEG®-controlled heparin reversal in this case resulted in safe performance of regional anesthesia. In pediatric patients undergoing open heart surgery, the TEG® was able to predict with 100% accuracy increased postoperative bleeding. The specificity of TEG® prediction of future bleeding was 73% (9).

On the other hand, standard coagulation tests in adult patients undergoing cardiopulmonary bypass could only explain 12% of the observed variation in blood loss (10). The TEG® seems therefore to be superior in the assessment of postoperative coagulopathies. This hypothesis correlates with the observation made by the authors of this article. Another study compared the usefulness of the TEG® in post-cardiopulmonary bypass coagulopathies (11).

Thrombelastography was a significantely better predictor (87% accuracy) of postoperative hemorrhage and need for reoperation than the activated clotting time ACT (30% accuracy) or coagulation profile (51% accuracy). Changes in transfusion therapy after institution of a blood management program based on TEG® in cardiac surgery patients resultet in a significantly lower incidence of overall transfusion (78.5% vs. 86.3%) during hospitalization and in total transfusion in the operating room (57.9% vs. 66.4%) (12). Mediastinal reexploration for hemorrhage was 5.7% before institution of TEG®-based coagulation monitoring and 1.5% in TEG®-monitored patients. The authors concluded that the use of TEG®-monitoring decreased the costs and potential risk for patients undergoing coronary artery bypass grafting surgery.

Summary (Back to Quick Links)

The usefulness of thrombelastography has been sufficiently documented in general surgery (13) (14) (15), cardiac surgery (10-12) (16), urology (17), in obstetric patients (18) (19) (20), in pediatric patients (21) (22), and in liver transplantation (23) (24). TEG® certainly takes an important place among the different coagulation tests. It is the only test measuring all dynamic steps of clot formation until eventual clot lysis or retraction. The cost-effectiveness of TEG® could be demonstrated in several studies. A comprehensive knowledge of the method is necessary in order to make appropriate decisions. Better management of coagulopathies will result in a decrease of donor exposure and the risks accompanying transfusion of heterogeneous blood products. The authors hope to provide a better understanding and an increase in popularity of the TEG® among health care providers.

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