THROMBOELASTOGRAPHY (TEG) AND ROTATIONAL THROMBOELASTOMETRY (ROTEM)

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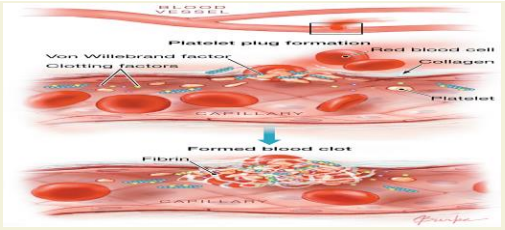
Objectives

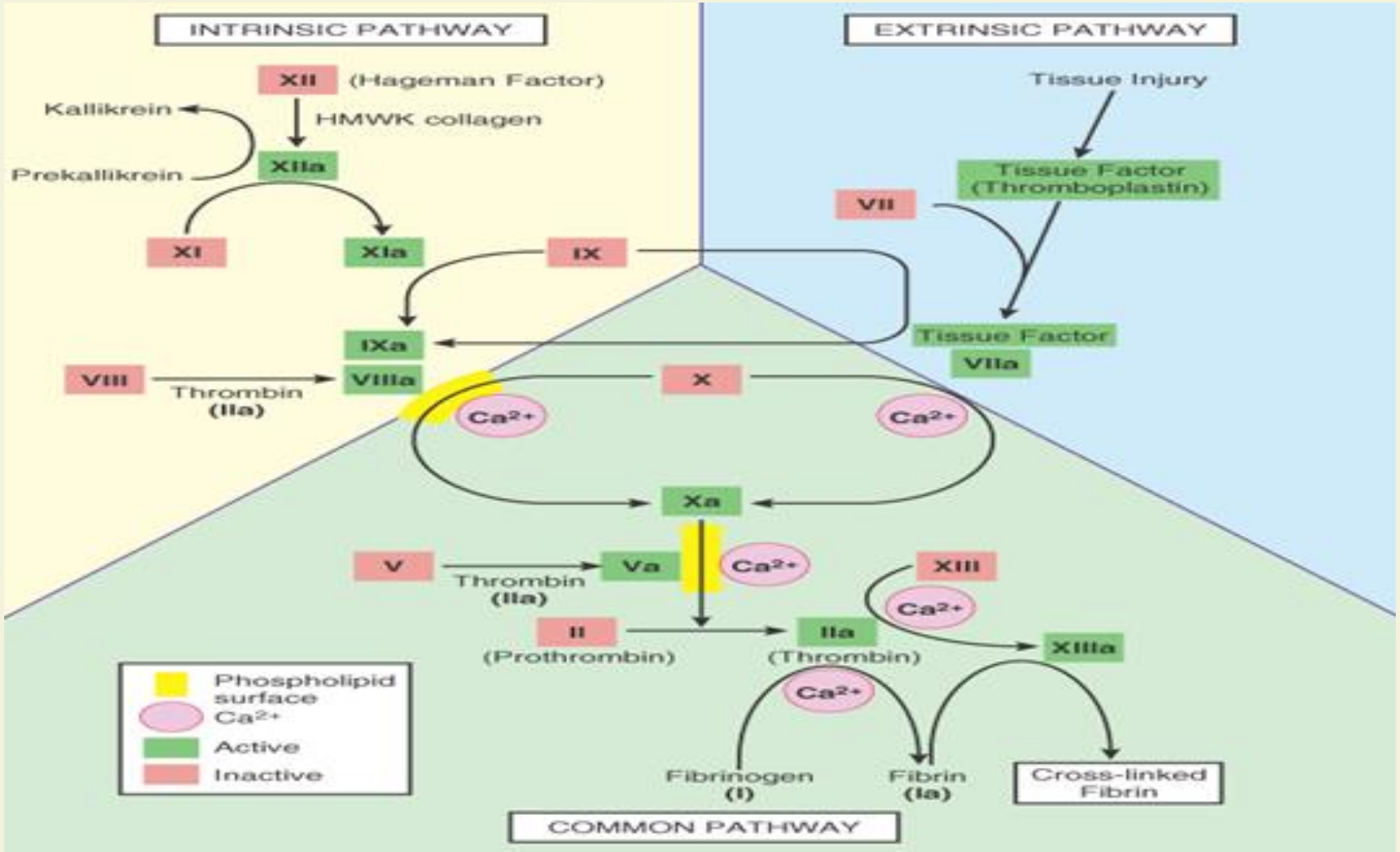
- Review coagulation cascade
- Review cell-based model of coagulation
- Limitations of conventional tests
- History of TEG and ROTEM
- Current research
- Differences between TEG and ROTEM
- ROTEM parameters and analysis
- Cardiac and liver case management
- Limitations of TEG and ROTEM

Hemostasis



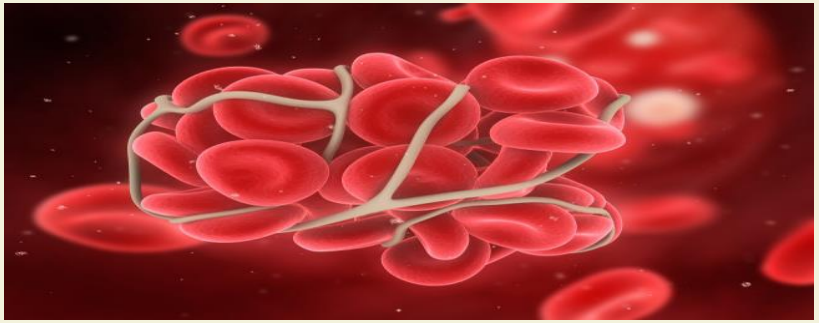
- Balance between bleeding and clotting
  - Procoagulants: I, II, III, IV, VII, VIII, VIIII, X, XI, XII
  - Anticoagulants: Protein C, Protein S, Antithrombin III
  - Cellular components: Platelets, Leukocytes, Red blood cells (RBC)
  - Fibrinolysis: Plasminogen, Plasmin
- Sequence of hemostasis:
  - Vasoconstriction, plt adhesion, plt aggregation, activation of coagulation factors, formation of fibrin, activation of fibrinolysis, clot lysis.

Coagulation Cascade



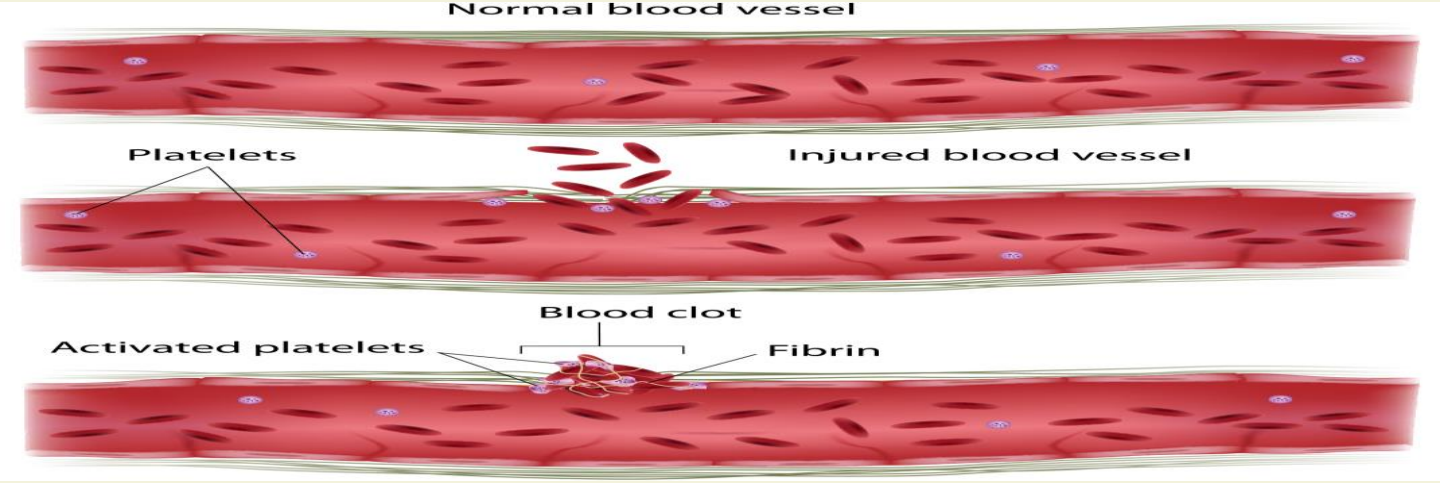
Cell- Based Model of Coagulation

- Three activation steps:
  - Initiation, Amplification, and Propagation
- Initiation
  - Triggered by injury to the endothelial surface.
  - Resting endothelium changes into an activated state.
  - Tissue factor is exposed and binds to factor VII.
  - Activated factor VII activates the intrinsic and common pathway to form thrombin and initiate clot formation.
  - Factors Xa and Va only create a small mount of thrombin.



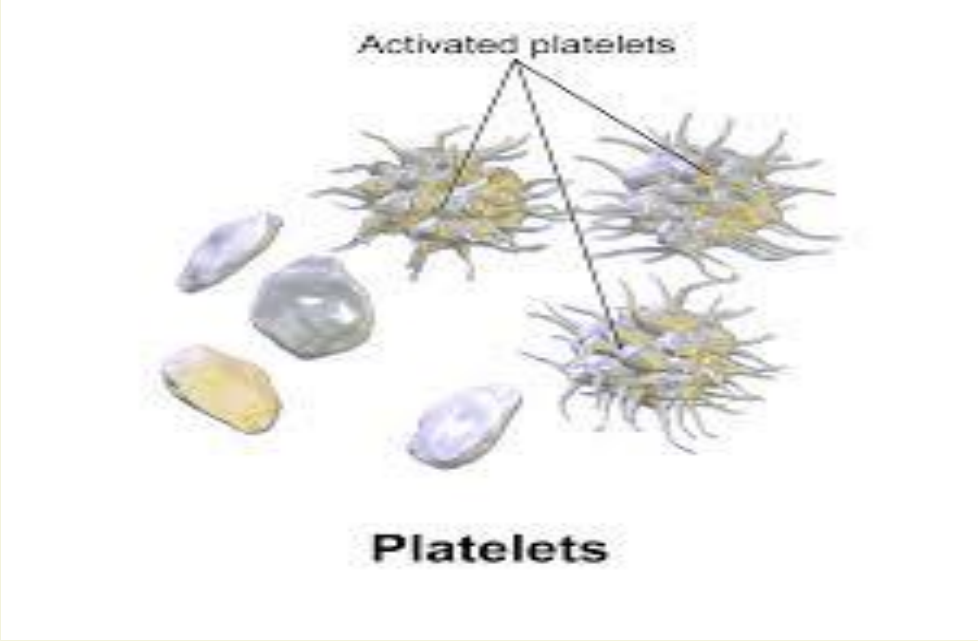
Cell- Based Model of Coagulation

- Amplification
  - Platelets adhere to the injury site.
  - Thrombin production greatly increases and activation and acceleration of clotting factors continue.
  - Von Willebrand factor stimulates platelet aggregation.
  - Expression of GpIIb-IIIa on platelet surface promotes further platelet aggregation.



Cell- Based Model of Coagulation

- Propagation
  - Coagulation factors are actively promoting coagulation and activating prothrombin.
  - Results in a large production of thrombin.



Limitations of Conventional Tests

- Prothrombin (PT), international normalized ratio (INR), and activated partial thromboplastin time (aPTT) do not represent the complexity of hemostasis in vivo.
  - They only provide information on clot initiation and do not reflect clot formation, fibrin polymerization, fibrinolysis, or factor XIIIa.
- Platelet count indicates bleeding risk but does not provide information regarding platelet functionality.
- Preanalytic variables must be taken into consideration.
  - Anticoagulants used in sample tubes.
  - Sample placed on ice.
- PT and aPTT testing is performed at 37°C and at a normal pH in the lab.
- Pre- surgical tests have limited value.
- Hemodilution and low platelet count influence test interpretation.

Introduction

- TEG and ROTEM are rapid point of care tests (POCT) that assess whole blood coagulation.
- They assist in identifying if the patient has normal hemostasis or is bleeding due to anticoagulant therapy or coagulopathy.
- They provide global and dynamic information regarding clot formation, stabilization, and degradation that reflects in vivo hemostasis.
- They provide information regarding platelet function and fibrinolysis.
- A graphical display of the viscoelastic changes of a clot as it develops and degrades is provided.

History of TEG and ROTEM

- Thromboelastography was developed in 1948 in Germany by Hartert.
- Helliege Thromboelastograph
- Its use in the United States was limited until the 1980's when the test became more practical, timely, and reproducible.
  - Computerized software
  - Disposable components
  - Tissue activators

History of TEG and ROTEM

- 1990s- Increasing popularity in cardiac surgery.
- 1993-TEG introduced into the market.
- 2000s- Increasing popularity in liver patients.
- 2003- ROTEM introduced into the market.

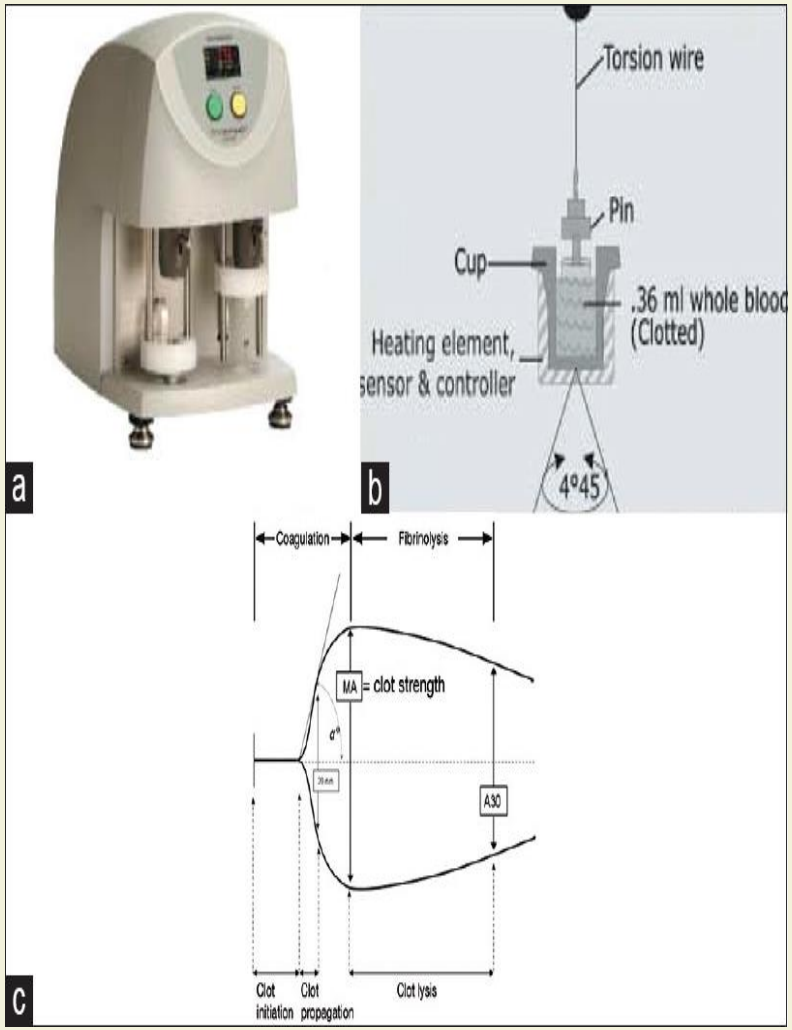
- Uses have been described in the settings of liver transplantation, obstetrics, trauma and cardiac surgery.

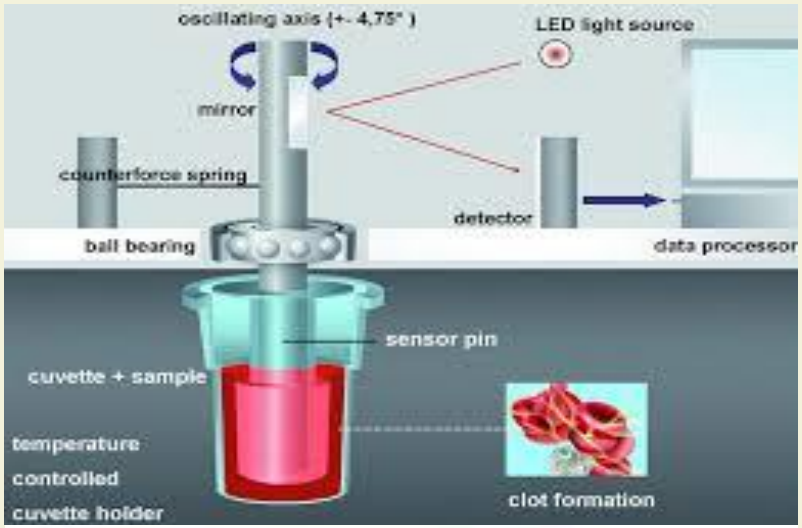
Literature supports that TEG and ROTEM are effective in guiding blood transfusion therapy and decrease the overall use of blood products.

Current Research

Research Article	Results
Levy et al., 2010	TEG & ROTEM are effective in guiding transfusion therapy and decreasing overall administration of blood products. Considered superior to conventional tests.
Sartorious, Waeber, Pavlovic, Frei, & Diaper, 2014	ROTEM is more helpful in predicting and treating clot formation abnormalities than conventional tests.
Weber et al., 2012	TEG & ROTEM are associated with decreased administration of blood products and improved clinical outcomes. Overall occurrence of adverse events were lower.
Sun, Jeleniowski, Zhao, Shen, Li,& Hammond, 2014	Use of TEG reduced the overall administration of platelets and FFP.
Ak et al., 2009	Use of TEG decreased the amount of blood product transfusion, decreased mediastinal chest tube drainage after 12 hours, and decreased use of tranexamic acid.
Spalding et al., 2007	Use of ROTEM decreased the amount of platelet, factor concentrates, aprotinin, and RBC transfusion. Overall cost savings of 40% in managing postoperative bleeding.

TEG vs ROTEM


a
Torsion wire
Pin
Cup
.36 ml whole blood
(Clotted)
Heating element,
sensor & controller
4°45'
b
Coagulation
Fibrinolysis
MA = clot strength
A30
Clot initiation
Clot propagation
Clot lysis
c

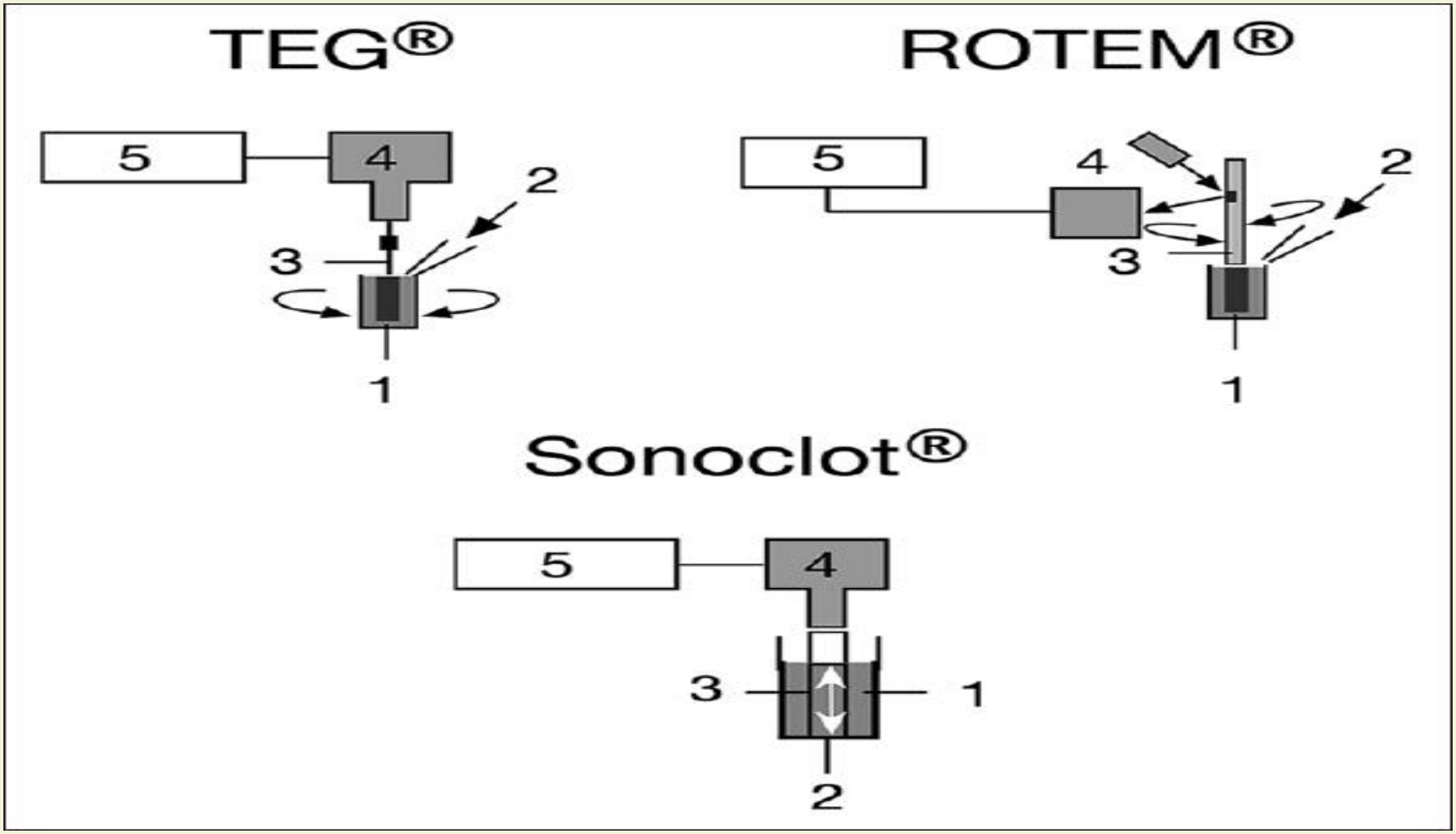

oscillating axis (+- 4,75°)
LED light source
mirror
counterforce spring
detector
ball bearing
data processor
sensor pin
cuvette + sample
temperature
controlled
cuvette holder
clot formation


ROTEM delta

Method

- Whole blood is added to a cuvette in a cup at 37°C and a pin is immersed.
  - The cup and pin are connected to a detector system.
  - The cup and pin move in relation to each other.
- Formation of a blood clot creates fibrin strands between the cup and pin.
- Data is obtained from the reflected light on a small mirror.
- A graphical representation is then created from the data.

TEG vs ROTEM



TEG vs ROTEM

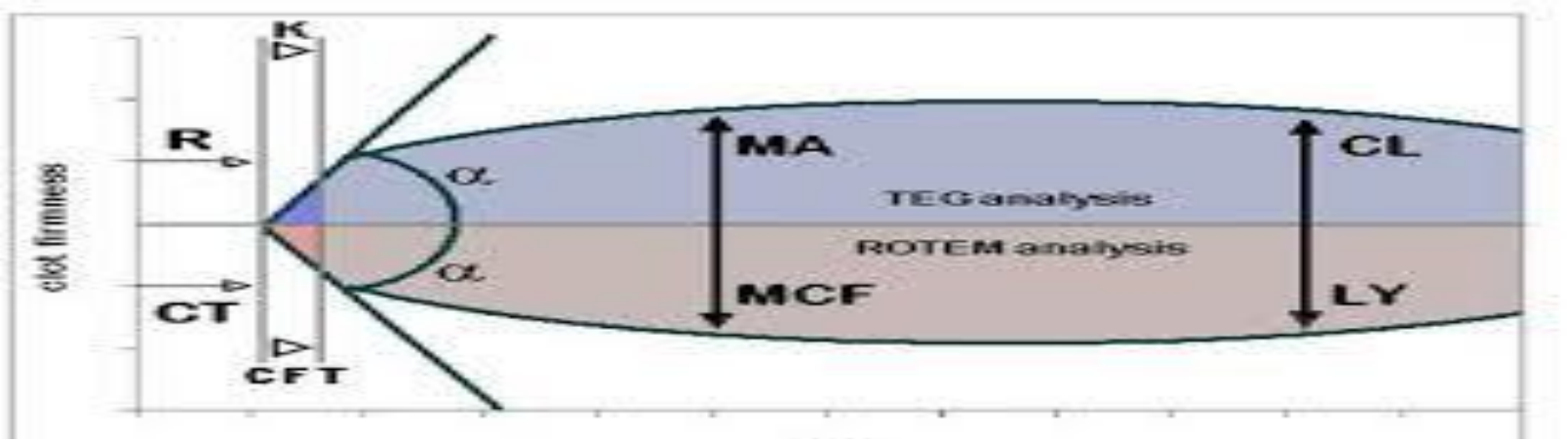


TABLE. TEG and ROTEM parameters and their meanings

TEG	ROTEM	Definition	Representative clotting process
R	CT	Time to 2 mm amplitude	Enzymatic clotting factor activation
K	CFT	Clot kinetics (time from 2 to 20 mm amplitude)	Thrombin's ability to cleave soluble fibrinogen
α	α	Slope between R and K	Rate of thrombin generation, which directly influences conversion of fibrinogen to fibrin
A (A30, A60)	A (A10, A15, A20, A25, A30)	Amplitude (at a fixed time)	Affected by fibrinogen, platelet (number and function) and factor XIII
MA	MCF	Maximal platelet-fibrin interaction via Gp IIb/IIIa receptors	
CL (Cl30, CL60)	LY (LY30, LY60)	% Of lysis at a certain time from MA	Antifibrinolytic activity such as plasminogen activation

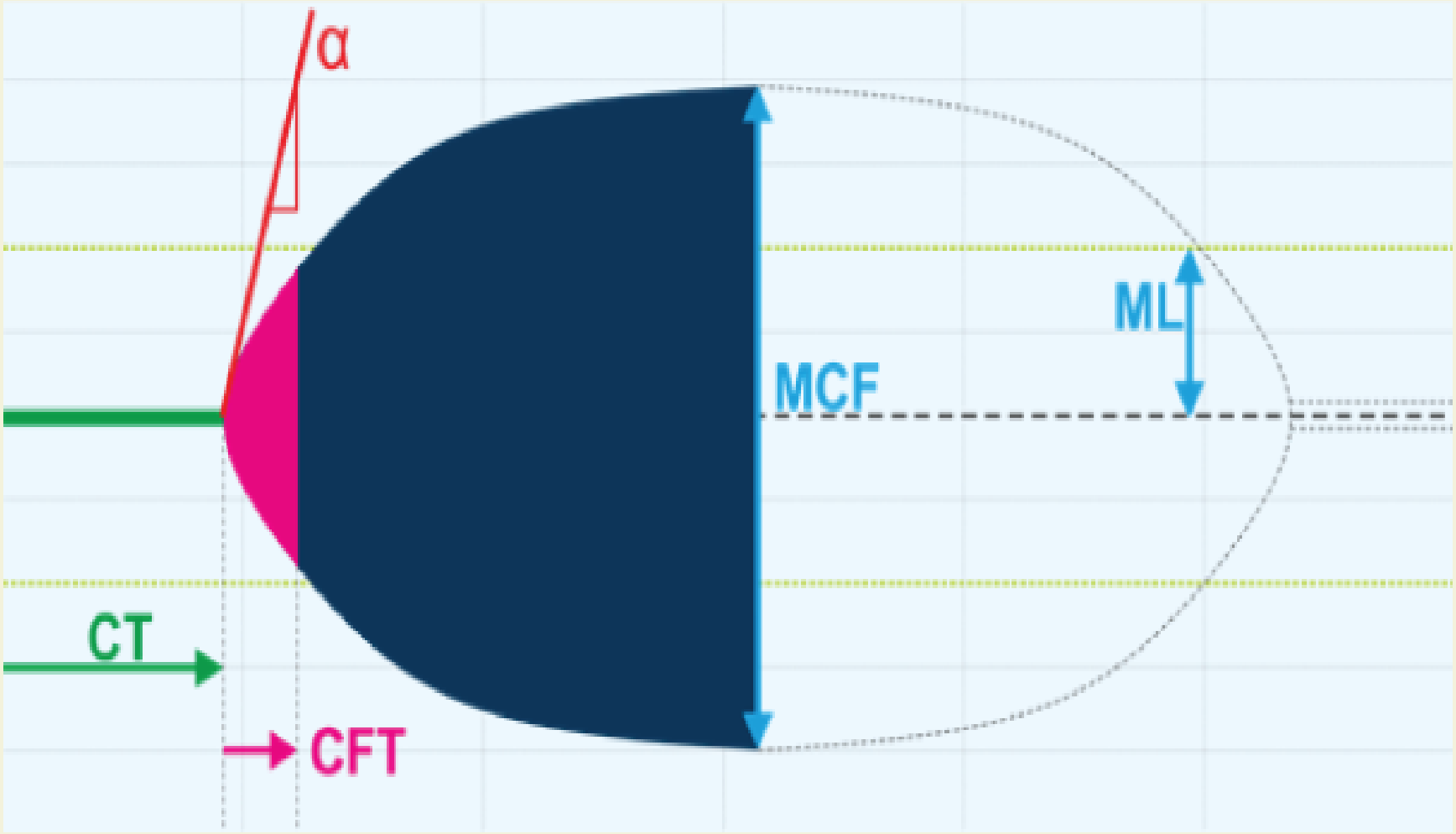
Abbreviations: α = alpha angle; A = amplitude; CFT = clot formation time; CL = clot lysis; CT = clotting time; Gp = glycoprotein; K = kinetics; LY = clot lysis; MA = maximum amplitude; MCF = maximum clot firmness; R = reaction time; ROTEM = rotational thromboelastometry (Tem International GmbH, Munich, Germany); TEG = thrombelastography (Hemoscope Corporation, Niles [IL], US)

(Yeung et al., 2014)

ROTEM Parameters

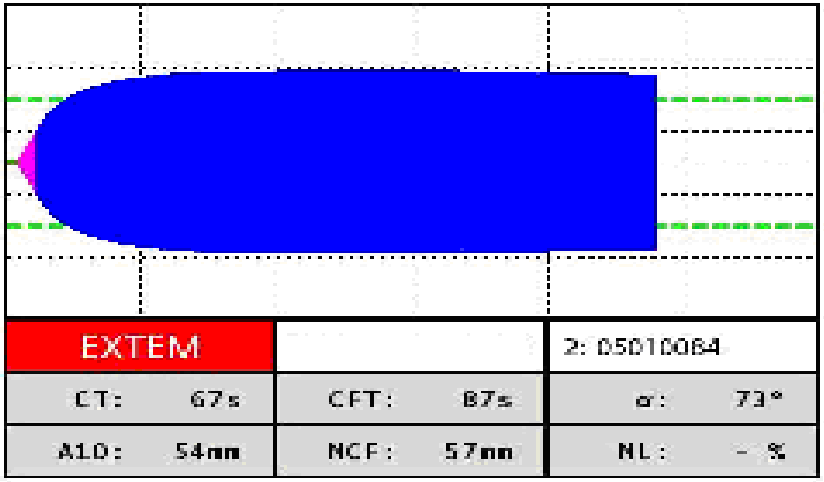
Parameter	Definition	Information
Clotting Time CT (sec)	Time from start of test until initiation of clotting. Time to reach 20 mm amplitude.	Speed of fibrin formation. Clotting factors and anti-coagulants affect CT.
Clot Formation Time CFT (sec)	Time from start of clotting until 20 mm amplitude.	Motion of clot formation. Affected by platelets, fibrinogen, and ability to polymerize.
Amplitude Time A10, A20, A30	Amplitude at a fixed time.	Influenced by platelets, fibrinogen, and factor XIII.
Maximum Clot Firmness MCF (mm)	Firmness of the clot. Maximum amplitude.	Affected by platelets, fibrinogen, factor XIII, and fibrinolysis.
Maximum Lysis ML (% of MCF)	Percent of clot firmness reduction in relation to MCF.	Abnormal ML at 30 minutes typically suggests fibrinolysis.

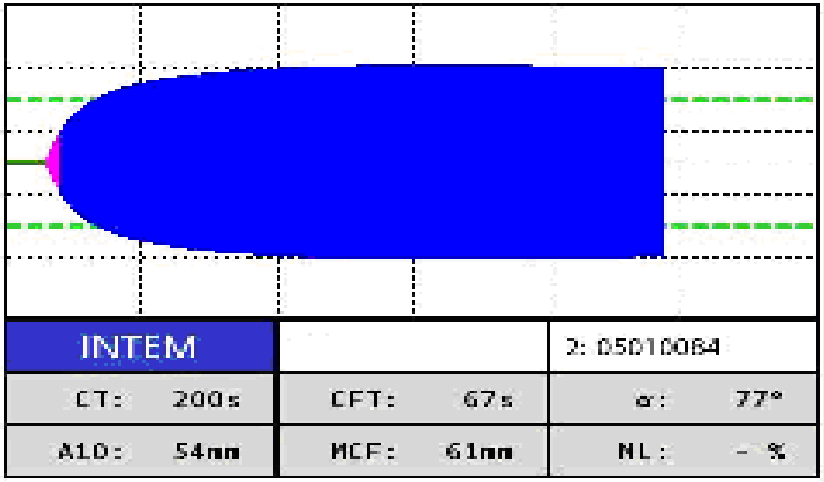
ROTEM Parameters

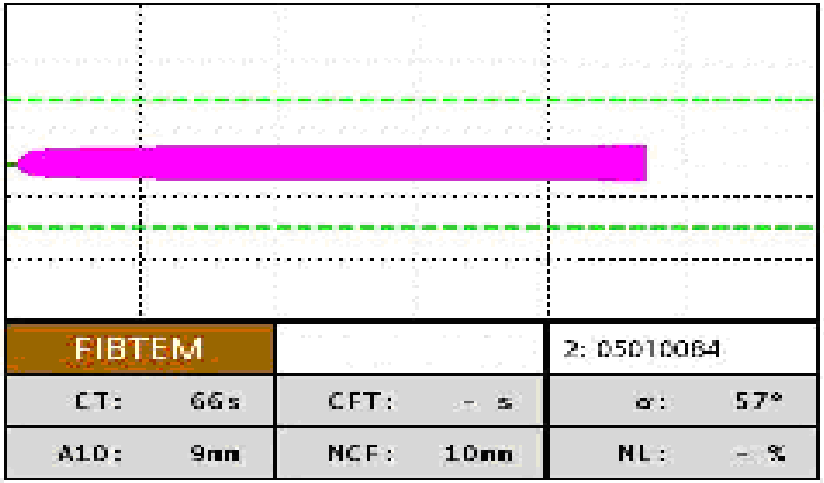


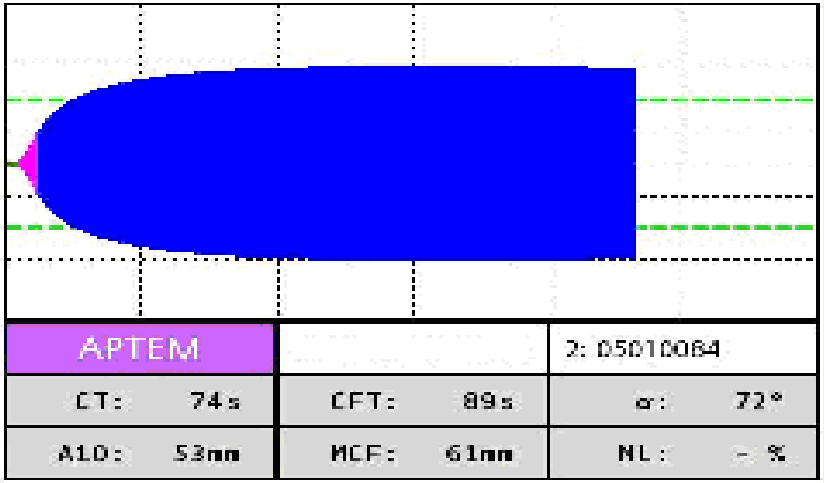
ROTEM ANALYSIS

Normal ROTEM





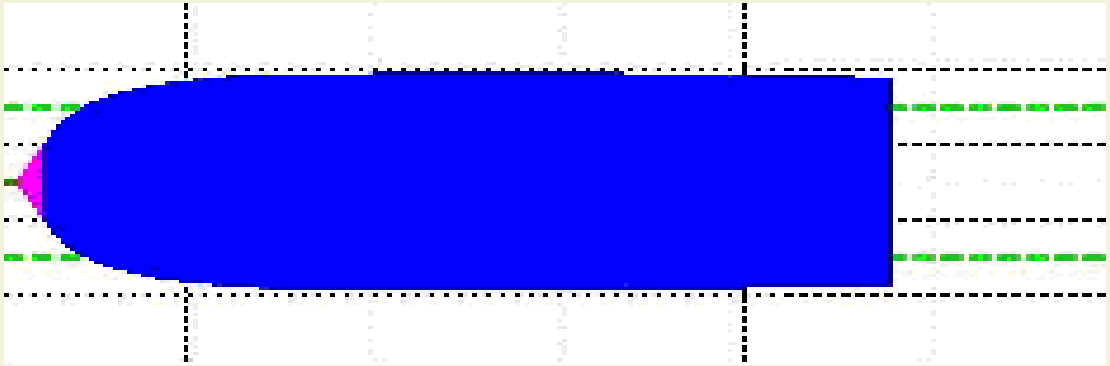




EXTEM

Extrinsic Pathway

- **CT**: Extrinsic/common factor deficiency
- **A10**(20): Predicted MCF
- **MCF**: Interaction of platelets, fibrin, and XIIIa
- **CFT**: Inadequate fibrin polymerization
- **Alpha angle**: Overall indication of hypo/hyper-coagulable state
- **LI30**: Reflects presence of premature clot lysis
- **ML**: % of clot lysis at any point through the test from point of highest amplitude

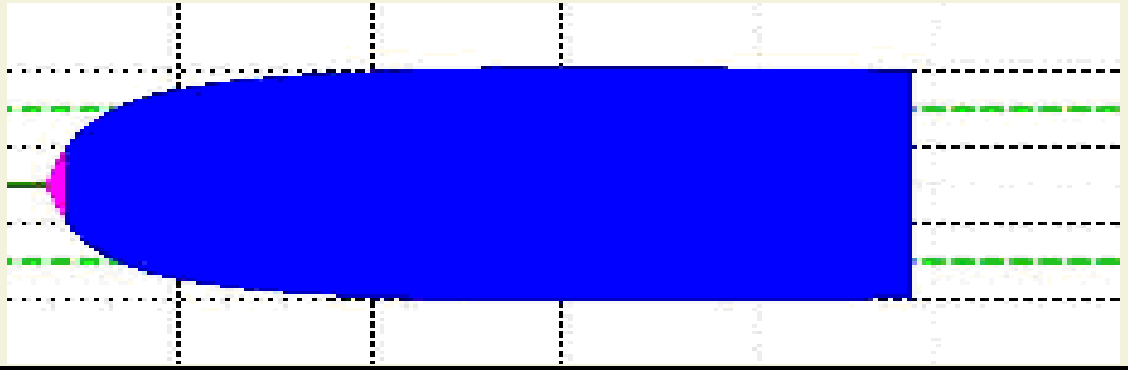


EXTEM		
CT: 43-82	CFT: 48-127	**α:** 65-80
A10: 40-60	MCF: 52-70	ML: : >15% in 1hr

INTEM

Intrinsic Pathway

- **CT**: Inadequate heparin reversal or intrinsic/common factor deficiency
- **A10**(20): Predicted MCF
- **MCF**: Interaction of platelets, fibrin, and XIIIa
- **CFT**: Inadequate fibrin polymerization
- **Alpha angle**: Overall indication of hypo/hyper-coagulable state
- **LI30**: Reflects presence of premature clot lysis
- **ML**: % of clot lysis at any point through the test from point of highest amplitude

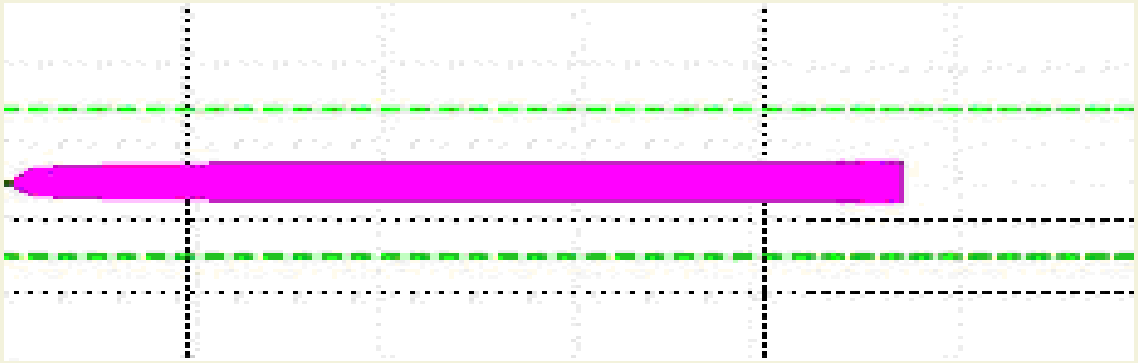


INTEM		
CT: 122-208	CFT: 44-110	**α:** 70-81
A10:40-60	MCF: 51-72	ML: >15% in 1hr.

FIBTEM

Fibrin(ogen) Contribution
(Extrinsic Pathway wo PLTs)

- **CT**: Consider factor deficiency
- **A10**(20): Predicted MCF
- **MCF**: Fibrin contribution to clot formation
- **CFT**: Inadequate fibrin polymerization
- **Alpha angle**: Overall indication of hypo/hyper-coagulable state
- **LI30**: Reflects presence of premature clot lysis
- **ML**: % of clot lysis at any point through the test from point of highest amplitude

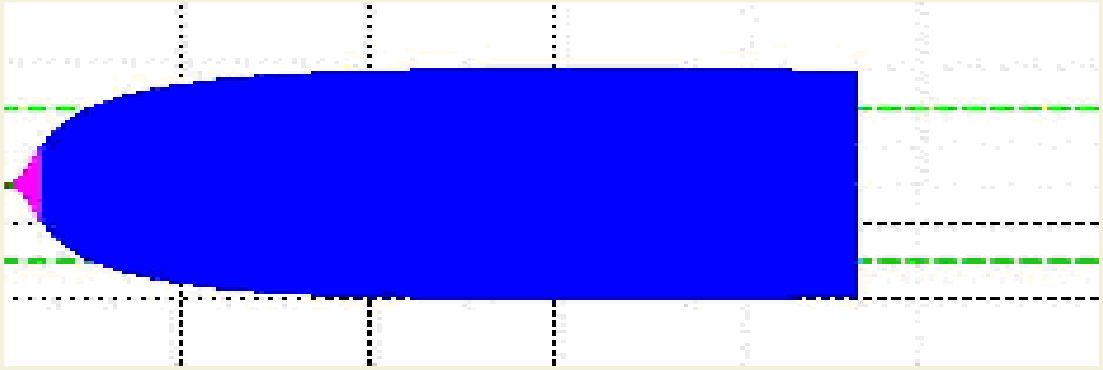


FIBTEM		
CT: Comp. to IN	CFT: Comp. to IN	**α:** Comp. to IN
A10: Comp. to IN	MCF: ***7-24***	ML: Comp. to IN

APTEM

Confirms hyper-fibrinolysis
(compared to EXTEM)

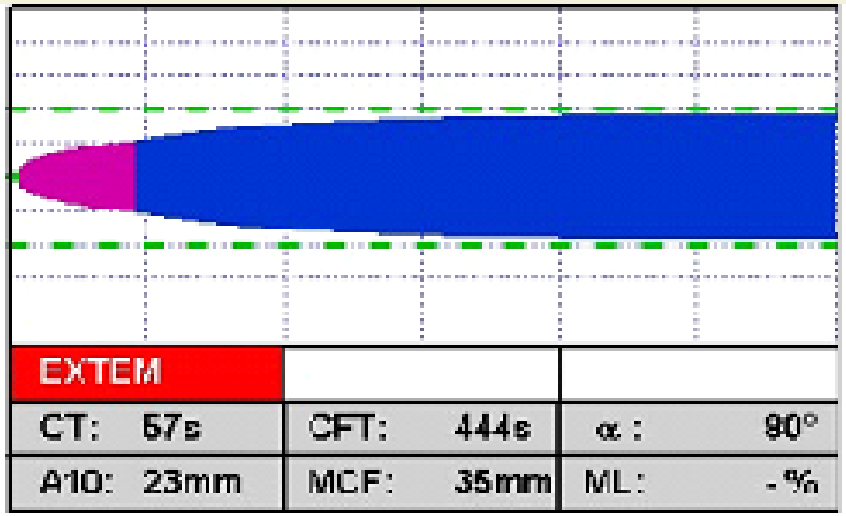
- **CT**: Consider factor deficiency
- **A10**(20): Predicted MCF
- **MCF**: Interaction of platelets, fibrin, and XIIIa
- **CFT**: Inadequate fibrin polymerization
- **Alpha angle**: Overall indication of hypo/hyper-coagulable state
- **LI30**: Reflects presence of premature clot lysis
- **ML**: % of clot lysis at any point through the test from point of highest amplitude

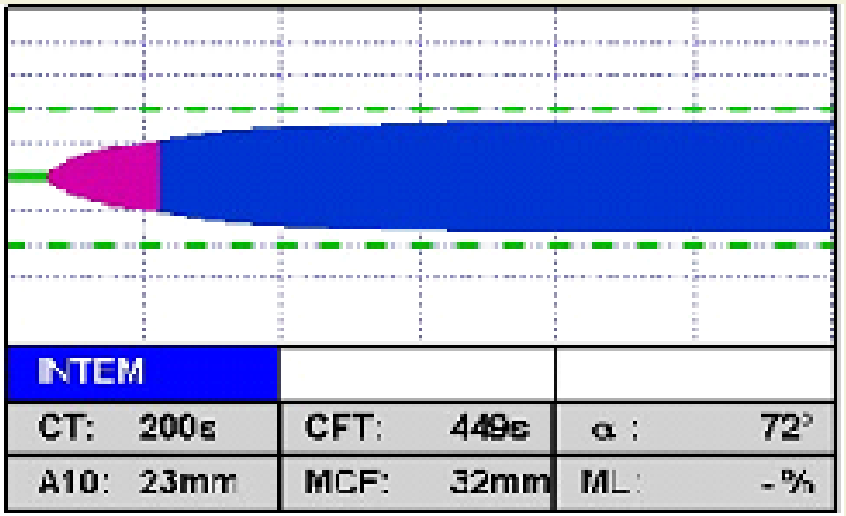


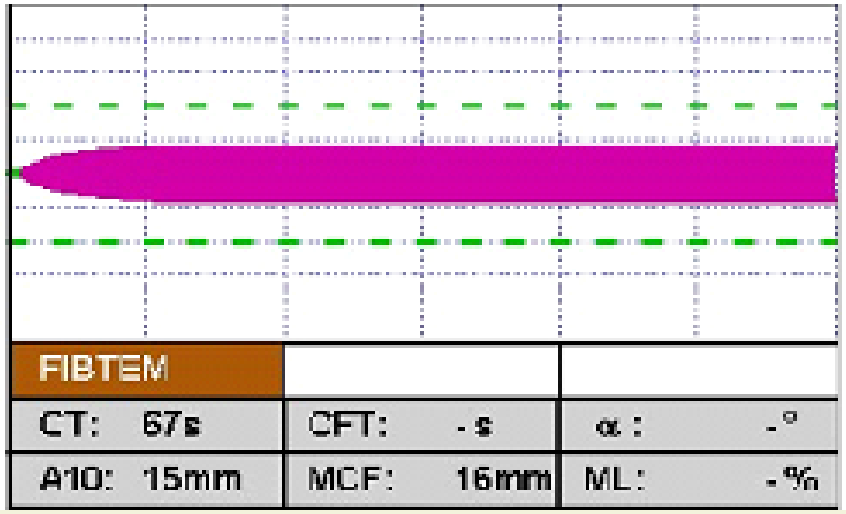
APTEM		
CT: Comp. to EX	CFT: Comp. to EX	**α:** Comp. to EX
A10: Comp. to EX	MCF: Comp. to EX	ML: Comp. to EX

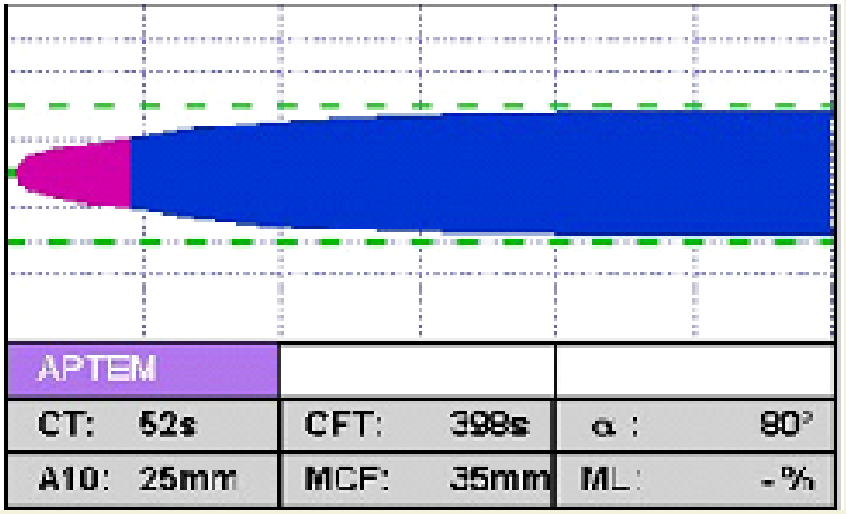
COAGULOPATHIES

Platelet Deficiency

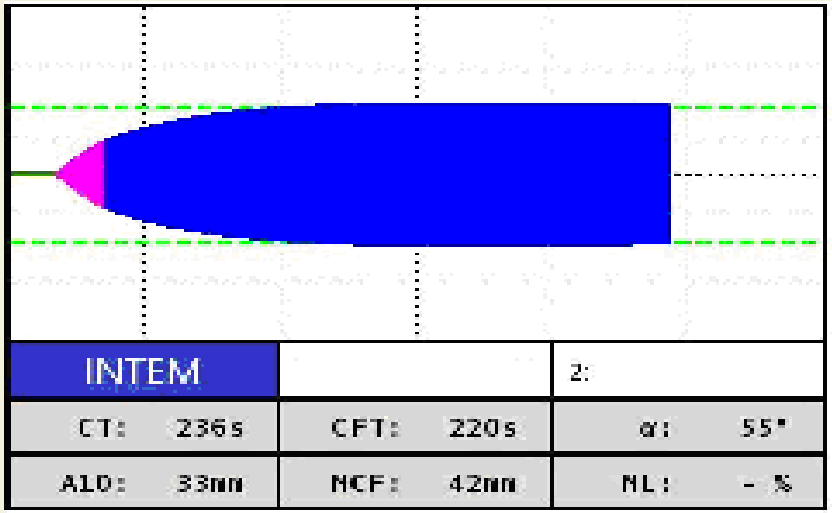


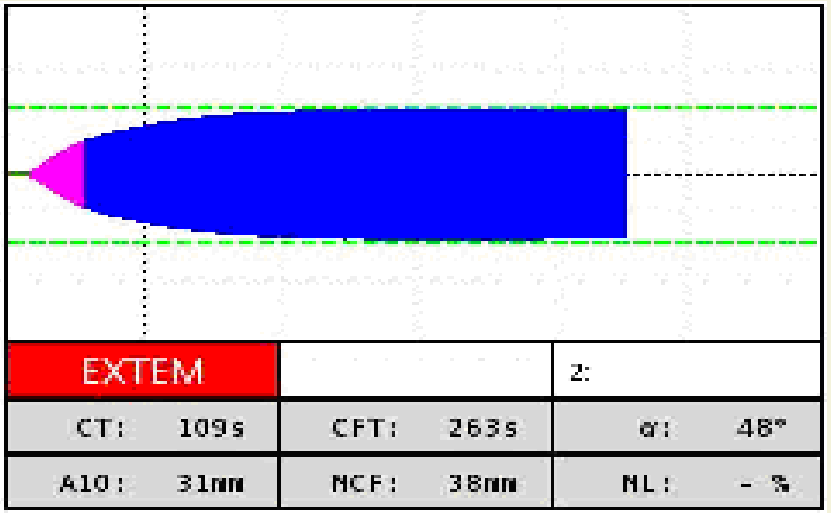


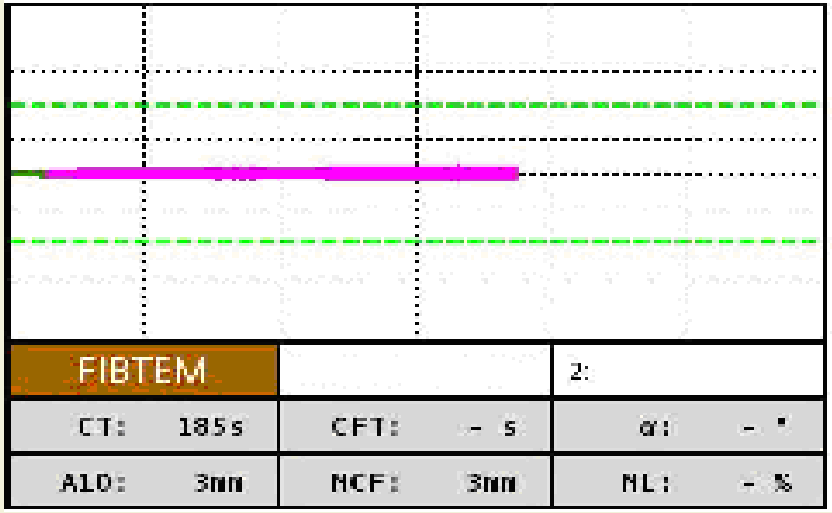


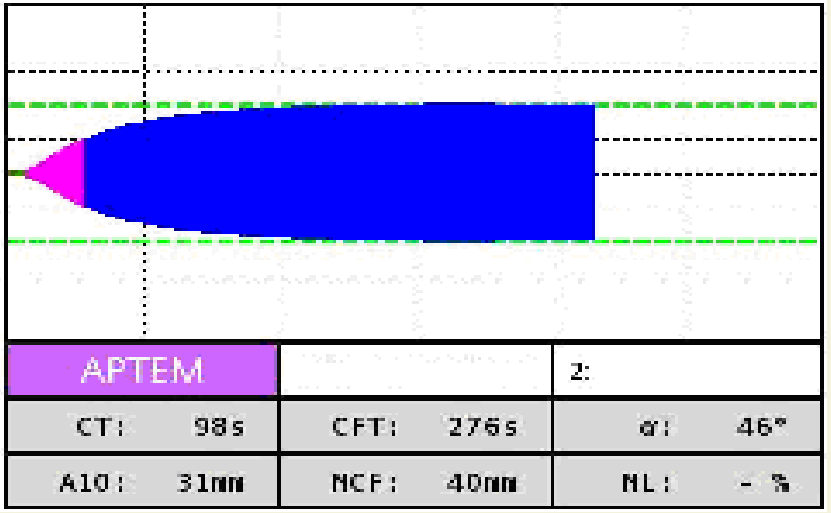


Fibrinogen Deficiency

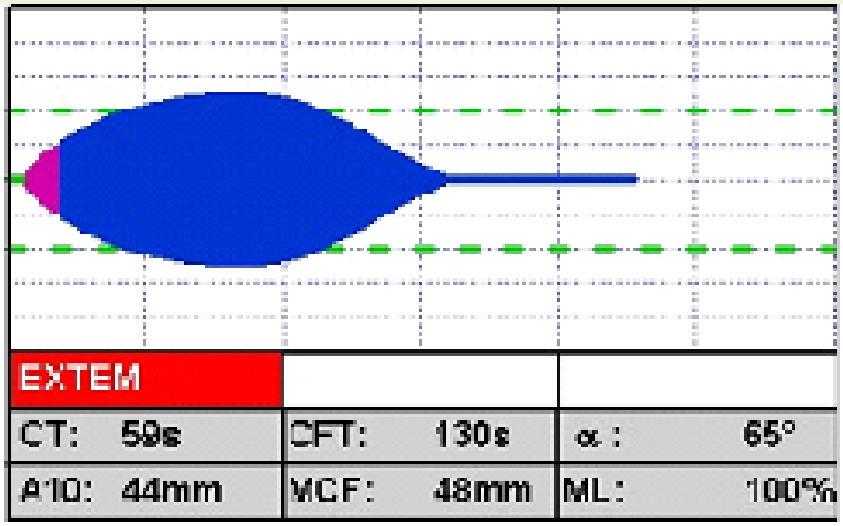


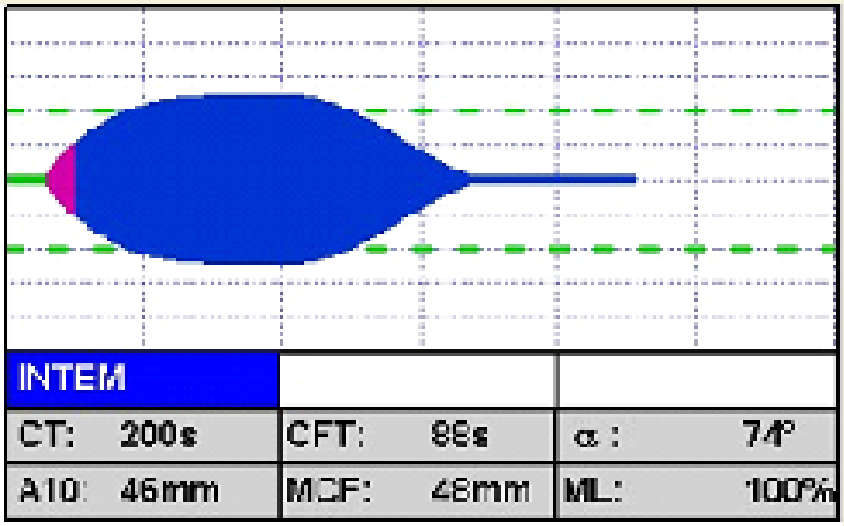


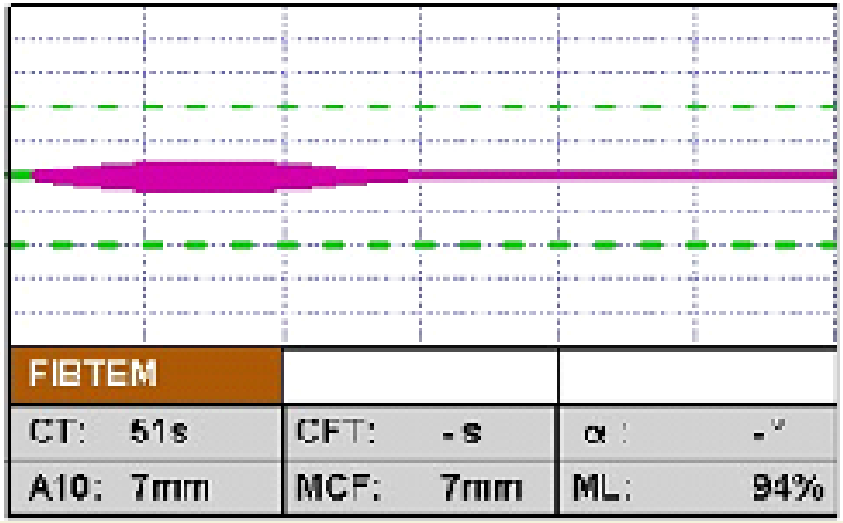


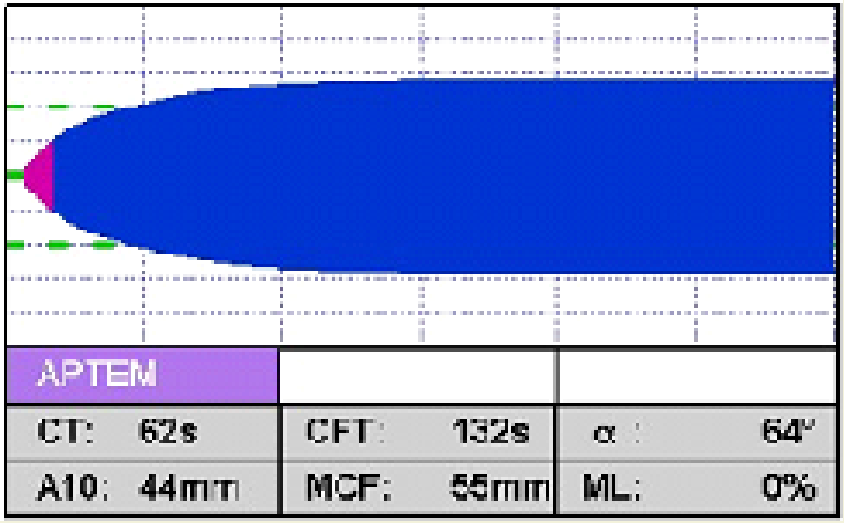


Hyperfibrinolysis

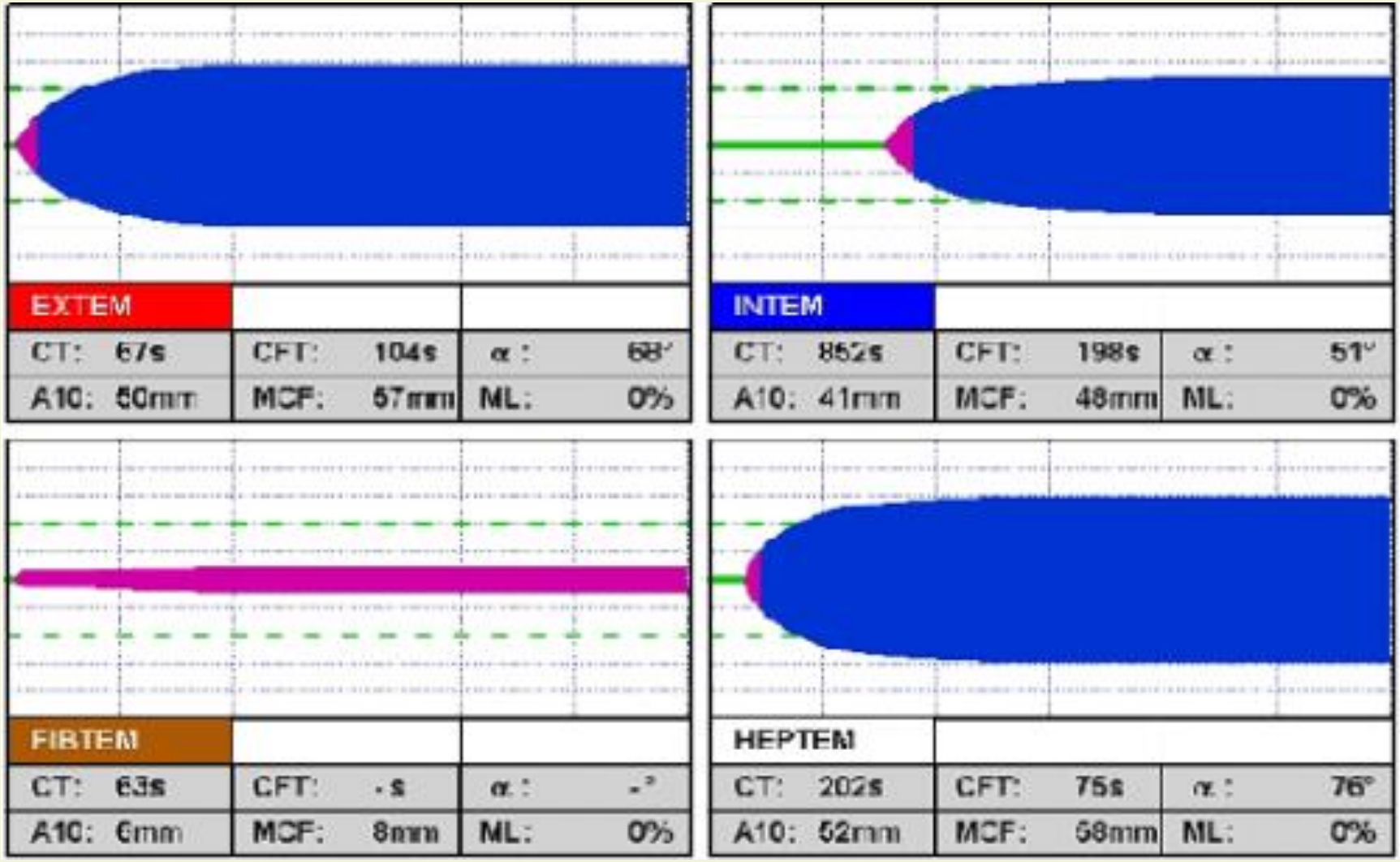


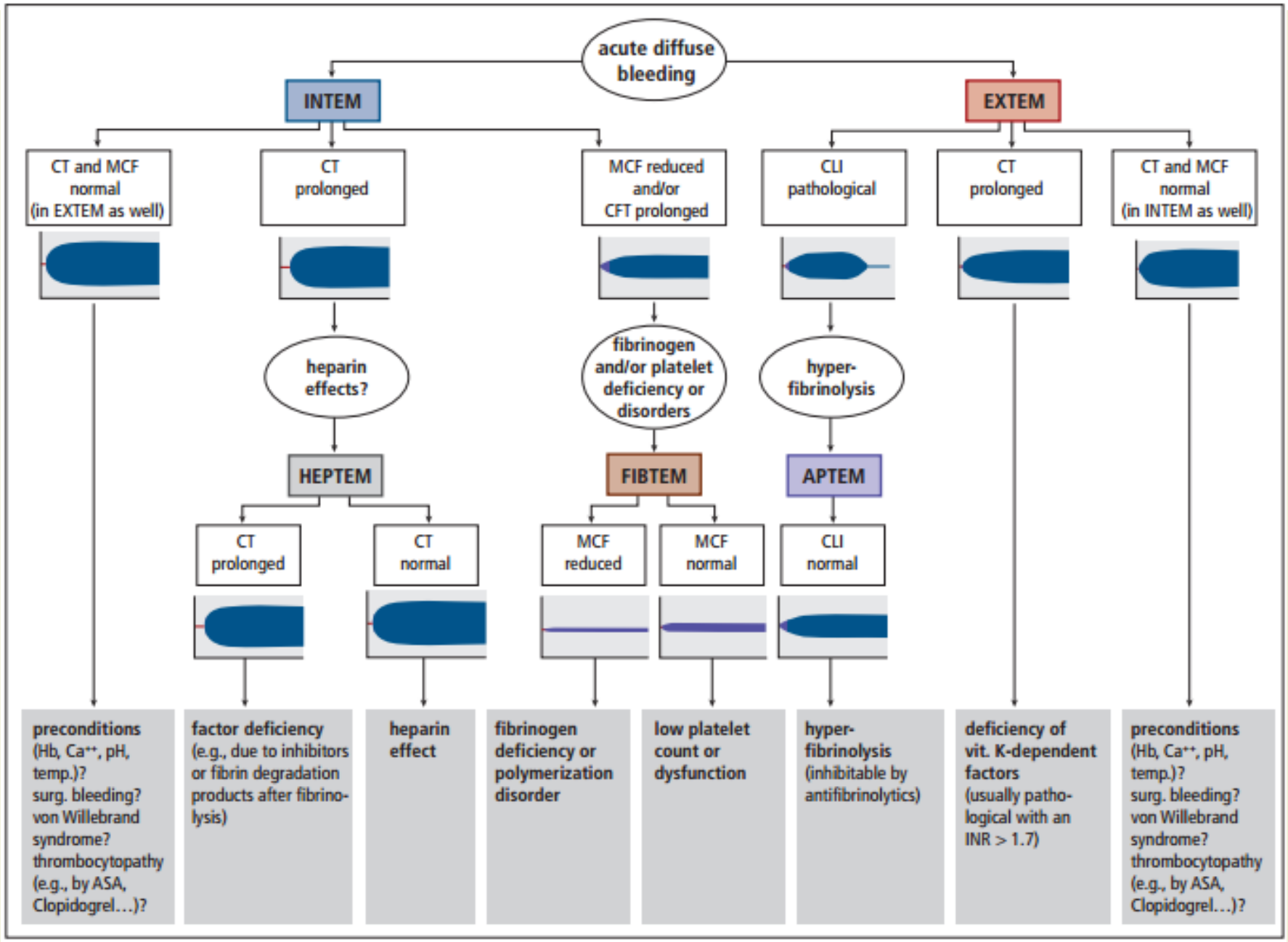






Heparin Influence





(Lier, Vorweg, Hanke, & Gorlinger, 2013)

Cardiac Case Management

- Baseline: INTEM, use HEPTEM if patient on heparin
  - PLT count and fibrinogen for interpretation
  - If patient is on warfarin or clopidogrel/aspirin
- 30 min before CPB* termination: HEPTEM
  - Prepare for post-op bleeding
  - MCF<50 mm, may need PLT or cryoprecipitate
  - MCF<40 mm, likely need both PLT and cryoprecipitate
- Post-protamine: INTEM/HEPTEM
  - If CT>240 s, consider protamine (✓HEPTEM) or FFP
  - MCF criteria as above

*for off-pump cases, HEPTEM before proximal anastomosis

(Azam, 2014)

Liver Transplant Case Management

- Baseline: INTEM
  - PT/INR, PLT count and fibrinogen for interpretation
  - If CT>240 s, consider to have FFP available
- At the end of anhepatic phase: INTEM
  - Prepare for post-reperfusion bleeding
  - MCF<50 mm, may need PLT or cryoprecipitate
  - MCF<40 mm, likely need both PLT and cryoprecipitate
- Post-reperfusion: INTEM/HEPTEM
  - If CT>240 s, consider heparin release from graft (HEPTEM) or FFP
  - MCF criteria as above

(Azam, 2014)

step		therapy
1.	stabilization of concomitant factors (prophylaxis and therapy)	• core temperature ≥ 34°C • pH ≥7.2 • ionised Ca^{++} ≥ 0.9 mmol/l
2.	substitution of oxygen carriers	**PRBC** (functionally: Hb 6[-8] g/dl, but haemostatically in active severe bleeding: Hct ≥ 30% or Hb ~ 10 g/dl [6.2 mmol/l]), resp.
3.	inhibition of potential (hyper)fibrinolysis (always before fibrinogen!)	**tranexamic acid** initial 2 g (25 mg/kg bw) for expected or proven hyperfibrinolysis: ML_{EXTEM} >15% anytime within 60 min
4.	substitution of coagulation factors (for ongoing, severe bleeding)	if **FFP**, then ≥ 30 ml/kg bw if CT_{EXTEM} < 80 s **and** CT_{HEPTEM} > 280 s (despite application of PCC and prior normalized $A10_{EXTEM}$ and $A10_{FIBTEM}$) **and fibrinogen** (2-)4(-6) g if $A10_{EXTEM}$ < 45 mm **and** $A10_{FIBTEM}$ < 15 mm **and PCC** initially 25 U/kg bw if CT_{EXTEM} > 80 s if necessary 1–2× **FXIII** 1250 U (15–20 U/kg bw) if $CLI60_{EXTEM}$ > 12% **and** $CLI60_{APTEM}$ > 10% **and** $CLI60_{XIII}$ < 10%
	and (suspecting thrombocytopathy) enhanced platelet adhesion + endothelial release of VWF and FVIII	**DDAVP (= desmopressin)** 0.3 µg/kg bw over 30 min if AUC-ASPI < 200 or AUC-ADP < 300 AU × min (Multiplate®)
5.	substitution of platelets for primary haemostasis	**platelets** if $A10_{EXTEM}$ < 45 mm **and** $A10_{FIBTEM}$ > 15 mm
6.	if necessity of a thrombin burst	**rFVIIa** initially 90 µg/kg bw on a case-by-case basis, if other therapeutic options fail, after consideration and correction of concomitant factors (if CT_{EXTEM} < 80 s **and** $A10_{EXTEM}$ > 50 mm **and** $A10_{FIBTEM}$ > 18 mm **and** Multiplate® ok **and** no surgical bleeding)
for ongoing, severe bleeding		no antithrombin substitution

(Lier, Vorweg, Hanke, & Gorlinger, 2013)

Limitations of ROTEM Analysis

- Does not detect anti-thrombotic drugs that impair platelet aggregation.
- Does not detect vWF or flow dependent platelet function.
- Low sensitivity to GP IIB-IIIa.
- Low sensitivity to oral anticoagulants.

Summary

- Research indicates that TEG and ROTEM are effective in guiding transfusion therapy.
- Decreases overall administration of blood products.
  - Better targeted therapy
- Rapid POCT that evaluates whole blood (vs plasma) and overall hemostatic status including fibrinolysis and platelet function.
- Real time graphical representation of coagulation status within 10 minutes.
- Research shows ROTEM is better able to predict and treat abnormalities in clot formation compared to conventional tests.

References

Ak, K., Isbir, C., Tetik, S., Atalan, N., Tekeli, A., Aljodi, M., & Arsan, S. (2009). Thromboelastography- based transfusion algorithm reduces blood product use after elective CABG: A prospective randomized study. *Journal of Cardiac Surgery*, 404-410. doi:10.1111/j. 1540-8191.2009.00840.x

Azam, M. (2014). ROTEM delta thromboelastometry. Powerpoint presentation. JLR medical group, Orlando, FL.

Ganter, M., & Hofer, C. (2008). Coagulation monitoring: Current techniques and clinical use of viscoelastoc point of care coagulation devices. *Anesthesia and Analgesia*, 1366-75. doi:10.1213/ane. 0b013e318168b367

Goerlinger, K. (2006). [Suplemental material]. *Hamostaseologie*, *26*, 64-76. Retrieved from http://www.schattauer.de/t3page/1214.html?manuscript=8536&L=1

Kashuk, J., Moore, E., Sawyer, M., Le, T., Johnson, J., Biffl, W., ... Stahel, P. (2010). Postinjury coagulopathy management. *Annals of Surgery*, *251*(4), 604-614. doi:10.1097/SLA.0b013e3181d3599c

References

Levy, J., Dutton, R., Hemphill, J., Shanders, A., Cooper, D., Paidas, M., ... Lawson, J. (2010). Multidisciplinary approach to the challenge of hemostasis. *International Anesthesia Research Society*, *110*(2), 354-364. http://dx.doi.org/10.1213/ANE.0b013e3181c84ba5

Moganasundram, S., Hunt, B., Sykes, K., Holton, F., Parmar, K., Durward, A., & Tibby, S. (2010). The relationship among thromboelastography, hemostatic variables, and bleeding after cardiopulmonary bypass surgery in children. *Anesthesia and Analgesia*, *110*, 995-1002. http://dx.doi.org/10.1213/00000539-200011000-00009

Romlin, B. S., Wahlander, H., Berggren, H., Synnergren, M., Baghaei, F., Nilsson, K., & Jeppsson, A. (2011). Intraoperative thromboelastometry is associated with reduced transfusion prevalence in pediatric cardiac surgery. *Anesthesia & Analgesia*, *112*(1), 30-36. http://dx.doi.org/DOI:10.1213/ANE.0b013e3181fe4674

Rotem. (2010). Results interpretation. *Rotem,* Retrieved from www.rotem-usa.com

References

Sartorious, D., Waeber, J., Pavlovic, G., Frei, A., & Diaper, J. (2014). Goal-Directed hemostatic therapy using the rotational thromboelastometry in patients requiring emergent cardiovascular surgery. *Annals of Cardiac Anesthesia*, 100-108. doi:10.4103/0971-9784.129829

Semon, G. (2013). Thormboelstography (teg) in trauma. Retrieved from http://www.surgicalcriticalcare.net/Guidelines/TEG%202013.pdf

Spalding, G., Hartrumpf, M., Sierig, T., Oesberg, N., Kirschke, C., & Albes, J. (2007). Cost reduction of perioperative coagulation management in cardiac surgery: value of bedside thrombelastography (ROTEM). *European Journal of Cardiothoracic Surgery*, *31*, 1052-1057. http://dx.doi.org/doi: 10.1016/j.ejcts.2007.02.022

Sun, W., Jeleniowski, K., Zhao, X., Shen, P., Li, D., & Hammond, J. (2014). Thromelastography (TEG)-based algorithm reduces blood product utilization in patients undergoing VAD implant. *Journal of Cardiac Surgery*, *29*(2), 238-243. doi:10.1111/jocs.12302

Weber, C., Gorlinger, K., Meininger, D., Herrmann, E., Bingold, T., Moritz, A., ... Zacharowski, K. (2012). A prospective, randomized clinical trial of efficacy in coagulopathic cardiac surgery patients. *Anesthesiology*, *117*(1), 531-547. http://dx.doi.org/10.1097/ALN.0b013e318264c644