



## Emerging Technologies in Coagulation Point of Care Testing (POCT)

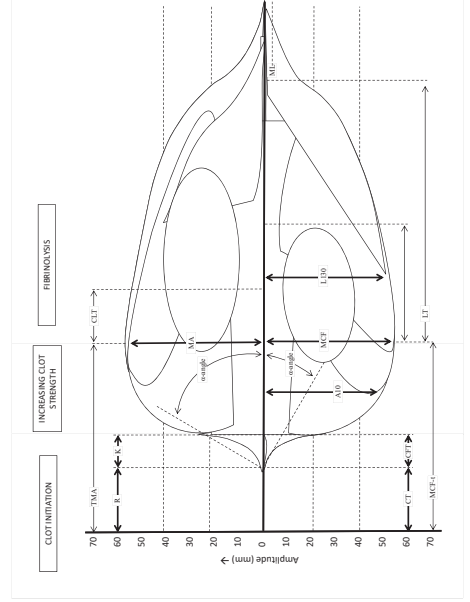


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### Viscoelastic POCT

#### Viscoelastic NPT

- Measure and graphically display the changes in viscoelastic properties of all stages of the developing and resolving clot (initial formation, clot rate, strength, stability and lysis) in one test
- Functional assays (reflect interaction of platelets with clotting factors)
  - TEG uses a mechanical detection system (a pin suspended in a blood sample with a torsion wire that is monitored for motion)
  - ROTEM uses an optical detection of the pin motion
  - *Sonoclot* measures changes in impedance to movement imposed by the developing clot
  - *HemoSonics* uses ultrasound to initiate and measure mechanical resonance in a clotting blood sample



## Disclosures

- Haemonetics**
- Consultant
  - Speaker
  - Advisory Council
- Stago**
- Speaker

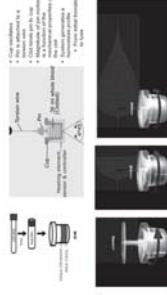
## Learning Objectives

- As a result of attending this session, participants will be able to:
- Understand how the VHA assays of hemostasis are used for assessment of patient's hemostatic status
  - Describe POCT available for assessment of platelet function along with limitations of each method
  - Describe POCT used for UFH monitoring along with benefits and pitfalls of each method
  - Recognize effect of direct oral anticoagulants DOAC on various POCT
  - Understand POCT usefulness in specific clinical settings

### Thrombelastography (TEG)



- ✓ TEG with heparinase
- ✓ Functional fibrinogen
- ✓ rTEG
- ✓ TEGPM

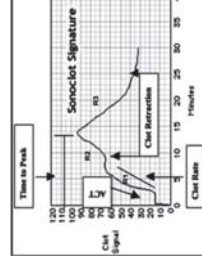


HAEMONETICS

### Thromboelastometry (ROTEM)



### Sonoclot



### HemoSonics



Stago Group acquires HemoSonics LLC



## Viscoelastic assays (VHA)

- Not even VHA provide information about the function of the entire hemostasis ( vWF, FXIII)
- VHA are performed at 37°C, and may not adequately assess coagulopathy of the patients with hyper or hypothermia
- Despite the similarity between the TEG and ROTEM measured variables, results produced by these instruments cannot be directly compared

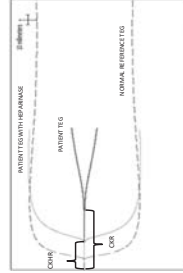
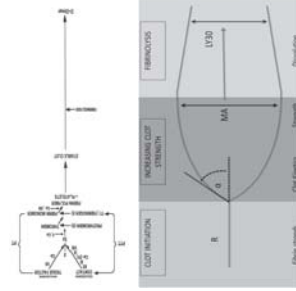
## Laboratory Monitoring of UFH Therapy: POC T

### Activated Clotting Time (ACT)<sup>Ref1</sup>

- Measures the clotting time of the whole blood activated by surface contact activator (celite, kaolin, glass)
- Values are **device-specific**, even if the same activator is used
- Celite ACT is significantly longer than kaolin ACT
- Kaolin ACT is less accurate in low intensity anticoagulation (<1U/ml)
- ACT following administration of heparin varies based on heparin-dependent (heparin responsiveness/resistance) and heparin-independent (hemodilution, hypothermia, platelet count, race) factors
- ACT is also affected by concomitant administration of other antithrombotic agents (abiximab, aprotinin (Celite-ACT))

### HMS Plus Hemostasis Management System (Previously Heparon<sup>®</sup> Jeri)

- Measures ACT in high-intensity anticoagulation and can also directly assess heparin concentration in samples
- Heparin dose-response (HDR) test is done to determine the patient's individual response to heparin



## POC Assessment of Platelet Function

- Multiplate
- TEGPM
- PFA 100
- Verify Now



## Heparin Management POC Systems

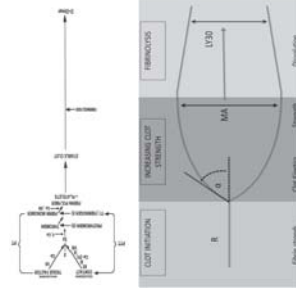


Device	Design	What does it measure	Available tests	Limitations
PFA-100	Mimics bleeding time	Test stops when platelet adhesion and aggregation occurs through Capillary (closure time)	Co/EPH test, Co/ADP test, P2Y12, receptor antagonists	Sensitive to platelet count and platelet reactivity. P2Y12, receptor antagonists
Multiplate	Impedance aggregometry caused by platelet aggregation	Measures the change in resistance after addition of a platelet activator during a 6-min period; changes in impedance are related to arbitrary aggregation units	Thrombin receptor, ADP, AA, and other less commonly used	Results depend on platelet count, potentially also on Hematocrit
Verify Now	Agglutination occurring between activated platelets and the fibrinogen-coated beads.	Agglutination causes the beads to fall out of suspension, thereby leading to an increase in light transmission through the suspension. The amount of agglutination is used to calculate the platelet reaction units	P2Y12 (P2Y12 receptor antagonist), aspirin test, Clopidogrel test, or aspirin/ASA test	Results depend on hematocrit, potentially also on platelet count. Studies in patients undergoing percutaneous coronary intervention or neurovascular stenting only
TEG PM	Uses thromboelastography to estimate platelet function	Maximum platelet activation produced by thrombin in a citrated blood sample with either aprotinin or aprotinin (TEG MAA) or samples anticoagulated with heparin to prevent thrombin generation	Platelet activation by either aprotinin or aprotinin (TEG MAA) or by adenosine diphosphate (TEG MMAP) (TEG MMAP)	Overestimation of ADP or AA inhibition when MAA is high

## Overview of main NPT devices used to measure ACT<sup>Ref1</sup>

Manufacturer	Device Signature, and Signature Elite	ACT Test	Reagent	Detection Method
International technology	Hemobron Jr. Signature, ACT and ACT-UR	Kaolin		Optical
	Hemobron Response	3 different ACT tests: PFG350, MACT, P24	Celite, kaolin in glass tube (if aprotinin is present), glass beads	Mechanical
	Hemobron Jr. Hemonox	Hemoxox CT	Proprietary lipidated recombinant-rabbit brain tissue factor	Mechanical
Medtronic	HMS PLUS	ACT-HR	Celite	Mechanical
	ACT PLUS	ACT-UR	Celite	Mechanical
Sienco	Sonolite	Aprotinin/Inhibitor-ACT (SIACI)	Celite + clay	Mechanical
Abbot Laboratories Instrumentation Laboratory	ISTAT	Celite-ACT, kaolin-ACT	Celite kaolin	Electrochemical
	GEM PCL	ACT, ACT-IR	Kaolin (for ACT), Celite + silica (for ACT-IR)	Optical
Helena Laboratories	Celsate	Celite-ACT	Celite	Photomechanical
	Acelyte XL, Acelyte Mini II	Celite-ACT, kaolin-ACT, glass-ACT, MAA-ACT	Celite, kaolin, glass, or a cocktail of Celite, kaolin and glass	2-Point, electromechanical

## TEG Analysis with Heparinase



## TEG Parameters

Parameter	Description
R	Reflects the time to initial fibrin formation. Relates to plasma clotting factor and inhibitor activity.
K	A measure of the speed to reach 20 mm amplitude.
α angle	A measure of the rapidity of fibrin build up and cross linking ( clot strengthening) - fibrinogen function
MA	A direct function of the maximum dynamic properties of fibrin and platelet bonding via fibrin. Represents maximum platelet function
G	A transformation of MA into dyn/cm2
CI	A linear combination of R, K, α, MA
LY30	Lysis 30 minutes after MA reached
EPL	

## DOAC's

- Direct Oral Anticoagulant Agents (DOACs)
- Target-Specific Oral Anticoagulants (TSOACs)

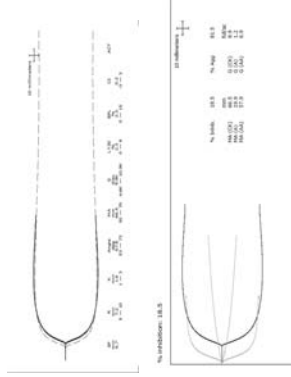
- Direct Thrombin Inhibitors (DTI)
- ❖ Dabigatran ( Pradaxa)
- ❖ Ximelagatran (Exanta, Exarta)

- Direct Xa Inhibitors
- ❖ Rivaroxaban ( Xarelto)
- ❖ Apixaban (Eliquis)
- ❖ Edoxaban (Lixiana)

## Point-of-Care Coagulation Tests Monitoring of Direct Oral Anticoagulants

- **Dabigatran**
  - TEG, ROTEM, ACT
- **Apixaban**
  - Available evidence from the literature points toward a low sensitivity of the POC tests for apixaban
- **Rivaroxaban**
  - Kaolin-activated TEG as well as ACT and INTEM do not show a linear increase of the CT with increasing Rivaroxaban dose
- **Edoxaban**
  - No clinical or preclinical data are available for edoxaban monitoring with POCs

### TEG PM 1 week later on Dabigatran x 2



Interpretation : Adequate anticoagulation



## Case



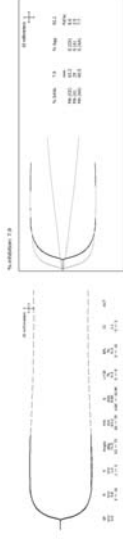
- 64 years old female status post traumatic brain injury (25 feet fall in an escalator).
- Fall occurred 30 minutes prior to the admission.
- Concurrent PT 15.9 s, PTT 41 s, hemoglobin 12.2 g/dL, platelet 156 x 103/u

## DOASENSE ( Urine Test)



## Case

- 52 years old male with CVA
- Negative Thrombophilia work up
- Placed on clinical trial Aspirin vs Dabigatran
- Develop 2<sup>nd</sup> stroke while on trial



Interpretation: Coagulation factor/s hypercoagulability, No Aspirin effect

## Point-of-Care Coagulation Monitoring in Trauma Patients

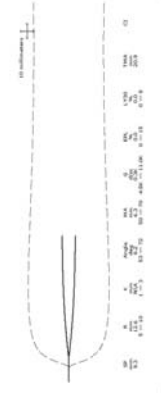
- Trauma is a major cause of death and disability all over the world
- Treatment may consist of blood product transfusion at a fixed ratio or in an individualized goal-directed way based on point-of-care (POC) and routine laboratory measurements

## Point-of-Care Coagulation Monitoring in Trauma Patients

- TEG/ROTEM
  - TEG-guided protocol was superior to a massive transfusion protocol with a fixed ratio strategy in patients with penetrating trauma receiving 10 units or more RBC (Ref 2)
- PT and aPTT: CoaguChek
  - The reliability of these POC devices was investigated in several studies, demonstrating a high correlation of POC results compared with the results of conventional assessment of INR and aPTT (Ref 3)
  - The CoaguChek is approved only to monitor the effect of vitamin K antagonists
  - In the era of direct oral anticoagulants also taken by trauma patients, the value of POC INR measurement is limited
- Platelet Function: Multiplate, ROTEM platelet, TEG platelet mapping, PFA100, VerifyNow



## Case : ESLD Patient who is Oozing (Liver Transplant)



TEG Interpretation:  
DIC (final stage)

GROUP	COMPONENT	DATA
PTT	PTI	63*
PROTIME W/INR	Fibrin Fibrinogen	40.7*
	INR	4.8*
COAG FACTOR ACTIVITY	Fibrinogen	27
COAG OTHER	Fibrinogen	<30*

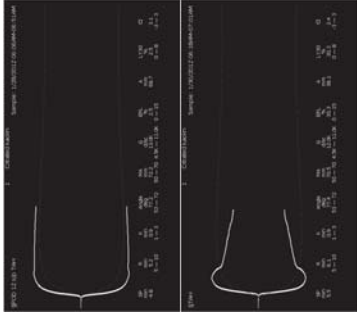


## Point-of-Care Coagulation Testing in Cardiac Surgery (Ref 4-6)

- **ACT**
  - To detect therapeutic effects of high-dose unfractionated heparin (typically 300–400 U/kg to reach ACT >400–480 seconds during CPB)
- **VHA (TEG/ROTEM/Sonoclot)**
  - The use of ROTEM and TEG has shown to reduce the transfusion of allogeneic blood products in cardiac surgery (ref)
- **Heparin Management System's (HIMS)**
  - Recent studies in pediatric and adult cardiac surgery demonstrated no improvement in postoperative hemostasis, bleeding volumes, or usage of allogeneic blood products (ref)
- **POC PT and aPTT**
  - Caution should be exercised in the interpretation of POC PT/aPTT results in the perioperative setting because of dynamic changes in multiple factors (ref)
- **POC fibrinogen**
  - Is a cartridge-based fibrinogen assay approved for clinical use in Japan
- **Plateletlet function assays**



Case : 39 yo female day 12 s/p TAH

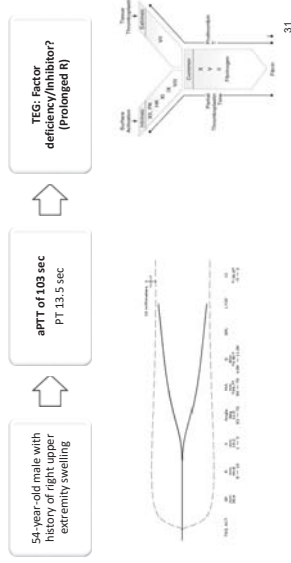


## Point-of-Care Testing in Acute Hemorrhagic and Thrombotic States

- PT 18 sec
- PTT 37 sec
- Plt 455 000
- Fibrinogen 608 mg/dl (>)
- WBC 42.9 (>)
- TEG: Combined Hypercoagulability
- PT 22.5 sec
- PTT 48 sec
- Plt 429 000
- Fibrinogen 536 mg/dl
- WBC 25.7
- TEG: II ry Fibrinolysis



Case : Call from ED (Friday PM)



## More History & Additional Work Up



Patient noted swelling and ecchymosis to humeral area 2 days ago.

No epistaxis or gingival bleeding. No other ecchymosis to other body parts.

Deficits trauma to his extremity.

Other: onset of diarrhea 6 months ago

No prior personal or family history of bleeding.

aPTT 98 sec (22-37 sec)

aPTT Immediate Mix- 49 sec

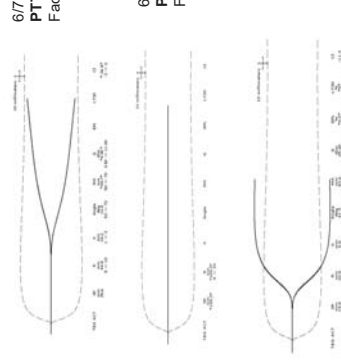
aPTT Incubated Mix- 81 sec

Factor VIII <2 % (50-150%)

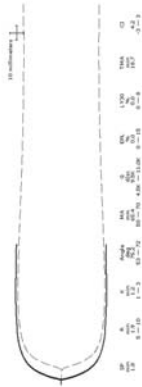
Factor VIII inhibitor 6.5 BU

Dx: Factor VIII Inhibitor (Acquired Hemophilia A)

## TEG Guided Management



Case : Renal Transplant, Clotting Intraoperatively



	Reference Range
ACA IgG	<10 GPL
PT II Gene Mut	Negative
PAI	<34 IU/mL

### Thrombophilia Panel



## References

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