Objectives

- Review POC coagulation systems
- Discuss coagulation management strategies in the operating room
- Understand ROTEM® assays, graph information and measured parameters
- Learn basic interpretation of TEMograms
Disclosures

• No disclosures or conflicts of interests
The Classic Coagulation Cascade
Hemostasis Tests: aPTT, PT

Cellular effects are not detected.

Low sensitivity:
- Fibrinogen
- Polymerization disorders

No sensitivity:
- F XIII function
- Fibrinolysis

Limited or no information about:
- Interactions
- Clot quality
Coagulation Inhibitors
Hemostasis Tests: Thromboelastography
TEG® and ROTEM® delta
Thromboelastography-Directed Transfusion in Cardiac Surgery: Impact on Postoperative Outcomes

Roberta E. Redfern, PhD, Kevin Fleming, CCP, Rebekah L. March, MPH, Nathan Bobulski, CCP, Michael Kuehne, PhD, PA-C, John T. Chen, PhD, and Michael Moront, MD

Departments of Research, Perfusion Services, and Cardiothoracic Surgery, ProMedica Toledo Hospital, Toledo; Department of Public Health and Preventive Medicine, University of Toledo, Toledo; and Department of Statistics and Mathematics, Bowling Green State University, Bowling Green, Ohio
Thromboelastography

- TEG, Prof. Helmut Hartert (1948)
- Viscoelastic test of hemostasis in whole blood
- Visual assessment of clot formation and subsequent lysis under low shear conditions (0.1/sec)
- Assesses the interactions of coagulation factors, inhibitors, red blood cells, platelets, and anticoagulants

Thromboelastogram / TEMogram
**ROTEM® Parameters**

CT (clotting time): time from start of measurement until initiation of clotting => initiation of clotting, thrombin formation, start of clot polymerization

Alpha (ct-angle - tangent to the TEMogram through the 2mm mark): CFT and ct-angle parameters denote the speed at which a solid clot forms => they are primarily influenced by platelet function, and, to a limited extent, by fibrinogen and coagulation factors.

CFT (clot formation time): time from initiation of clotting until a clot firmness of 20mm is detected => fibrin polymerization, stabilization of the clot with thrombocytes and F XIII

MCF (maximum clot firmness): firmness of the clot => increasing stabilization of the clot by the polymerized fibrin, thrombocytes as well as F XIII

A10 (amplitude 10 min after CT): has high correlation* $r^2 >0.94$ to MCF (maximum clot firmness)

LI (Lysis Index): The LI is a parameter representing the percentage of fibrinolysis at a determined time point. It correlates to the MCF as the percent clot remaining. For example, LI-30 describes the remaining clot firmness 30 minutes after CT.

ML (maximum lysis): reduction of the clot firmness after MCF in relation to MCF => stability of the clot (ML < 15%) or fibrinolysis (ML > 15% within 1h)

*Oelering et al., Fast Interpretation of Thromboelastometry in Non-Cardiac Surgery, ASA 2010 Annual Meeting, Oct 20, 2010 San Diego, Cal
Reading TEMogram

The graph demonstrates the change in amplitude (clot firmness) over a time period.

The greater the amplitude, the firmer the clot.

Time (results expressed in sec)

Amplitude in (mm)
The graph information or “TEMogram”

The graph and TEMogram provides colors and other visual markers to aid in the rapid assessment of the developing clot.

©2013 TEM Systems, Inc - Durham, NC
The graph information or "TEMogram"

By looking at the shape of the graph you can determine, for example, whether a clot is firm and stable, has premature lysis or is weak or fragile.

- Firm & Stable
- Unstable (early Lysis)
- Relatively Weak
**CT\textsubscript{IN, EX}** – onset of clot formation (sec)

Ref Value: 122 – 208 sec \(^{(1)}\)

Ref Value: 43 – 82 sec \(^{(1)}\)

Provides information about the patient’s ability to generate thrombin and information about the effects of heparin (INTEM) or pathway specific enzymatic factor (INTEM or EXTEM) deficiencies.
ROTEM® Parameters

**CFT\textsubscript{IN,EX}** - Influence of enzymatic coagulation factors and fibrin polymerization on the specific pathways

Ref. Range\(^{(1)}\) : 44 – 110 sec

Ref. Range\(^{(1)}\) : 48 – 127 sec

Consider this as a demonstration of the rate of clot propagation

©2013 TEM Systems, Inc - Durham, NC
ROTEM® Parameters

A10 – Amplitude 10 min after CT (mm)

A10 Ref Value: 40 – 60 mm\(^{(2-5)}\)

Provides an early and highly predictive assessment of clot firmness (platelets, fibrin activity and FXIIIa).

©2013 TEM Systems, Inc - Durham, NC
ROTEM® Parameters

MCF – Maximum Clot Firmness (mm)

A10 Ref Value: 40 - 60 mm\(^{(2-5)}\)
MCF Ref Value: 51 - 72 mm\(^{(1)}\)

Provides an early and highly predictive assessment of clot firmness (platelets, fibrin activity and FXIIIa).

**Easy to remember: “A10 plus 10 mm”**\(^{(3)}\)
ROTEM® Parameters

**ML – Maximum Lysis (% of clot lysis at T= (X))**

@ 20 min ML = 3% Lysis
@ 25 min ML = 40% Lysis
@ 30 min ML = 80% Lysis
@ 33 min ML = 100% Lysis

ML% > 15% within 60 minutes indicates premature clot lysis.

Also consider: In patients with severe trauma, an early ML > 3% can be associated with increased mortality\(^6\).
ROTEM Parameters

- CT – Thrombin burst
- \( \alpha \) and CFT – Soft plug kinetics
- A10/A20 and MCF – Firm plug kinetics
- ML – Clot Lysis
### ROTEM® delta Whole Blood Hemostasis Analyzer

<table>
<thead>
<tr>
<th>Test Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>INTEM</td>
<td>Mild intrinsic activation via Ellagic Acid; high heparin responsiveness; screening test</td>
</tr>
<tr>
<td>HEPTEM</td>
<td>Neutralization of heparin with Heparinase; compare to INTEM</td>
</tr>
<tr>
<td>EXTEM</td>
<td>Extrinsic activation via Tissue Factor; heparin insensitivity up to 4U; screening test</td>
</tr>
<tr>
<td>APTEM</td>
<td>Inhibition of fibrinolysis with Aprotinin; compare to EXTEM</td>
</tr>
<tr>
<td>FIBTEM</td>
<td>Inhibition of platelets with Cytochalasin D; measurement of fibrin contribution; compare to EXTEM</td>
</tr>
<tr>
<td>NATEM</td>
<td>Global recalcification test; endogenous hemostatic potential of the sample; sensitive to various anticoagulants; mostly used in research</td>
</tr>
</tbody>
</table>

Results from the ROTEM® delta should not be the sole basis for a patient diagnosis; ROTEM® delta results should be considered along with a clinical assessment of the patient’s condition and other coagulation laboratory tests.
ROTEM® Parameters

Ref Range: 7-24 mm

Maximum FIBTEM value can be predicted very accurately at A5. Normally there is only slight change (1-4 mm) from A5, A10, A20 and MCF.

©2013 TEM Systems, Inc - Durham, NC
Limitations of Current Methods in ROTEM® delta Analysis

- Low sensitivity to therapeutic concentrations of GP IIb/IIIa antagonists
- No sensitivity for aspirin or clopidogrel (Plavix®)
- No detection of vWF or flow-dependent platelet function aspects
- Low sensitivity to effects of oral anticoagulants
Receptors of Main Antiplatelet Agents

PAR1: PAR-1 receptor (protease-activated receptor 1)
ADP: adenosine diphosphate
P2Y12: P2Y12 receptor
PDE: phosphodiesterase
GPIIbIIIa: glycoprotein IIbIIIa
TXA2: thromboxane A2
TXA2R: thromboxane A2 receptor
ASA: acetyl salicylic acid
POC platelet function tests
ROTEM® delta
• 4 Channels
  viscoelastic tests

ROTEM® platelet
• 2 Channels
  impedance aggregometry
ROTEM® platelet

Uses Impedance Aggregometry to measure platelet function in whole blood

Single Use Reagents
- adp-tem®
  - e.g. for the detection of ADP receptor blockage (Clop tidogrel)
- ara-tem®
  - e.g. for the detection of cyclooxygenase inhibitors (Aspirin®)
- trap-tem®
  - e.g. for the detection of GP IIb/IIIa receptor antagonists (Abcimab)

Reaction curve

- MS (Ω·min)
- A6 (Ω)
- AUC (Ω·min)

SAMUEL AND JEAN FRANKEL CARDIOVASCULAR CENTER
Normal platelet function

Aspirin effect

Clopidogrel effect
Severe platelet dysfunction

GPIIbIIIa receptor antagonist

Severe thrombocytopenia

Dual antiplatelet therapy

Vorapaxar effect
ROTEM® delta Examples

EXTEM

INTEM

FIBTEM

APTEM

Normal Temograms

© 2012 TEM Systems, Inc - ROTEM® Durham, NC
ROTEM® delta Examples

Platelets or Fibrinogen

**EXTEM & INTEM**
- Normal CT
- Low amplitude

**FIBTEM**
- Low amplitude
- Suggests: Fibrinogen deficiency due to low amplitude of FIBTEM

**APTEM ≈ EXTEM**
- Suggests: no hyperfibrinolysis

© 2012 TEM Systems, Inc - ROTEM® Durham, NC

---

**EXTEM**
- 2006-12-15 13:50
- CT: 100s
- CFT: 263s
- θ: 48°
- A10: 31mm
- MCF: 34mm
- ML: - %

**INTEM**
- 2006-12-15 13:46
- CT: 226s
- CFT: 220s
- θ: 55°
- A10: 33mm
- MCF: 42mm
- ML: - %

**FIBTEM**
- 2006-12-15 13:50
- CT: 185s
- CFT: - s
- θ: - °
- A10: 31mm
- MCF: 34mm
- ML: - %

**APTEM**
- 2006-12-15 13:33
- CT: 98s
- CFT: 276s
- θ: 46°
- A10: 21mm
- MCF: 40mm
- ML: - %
ROTEM® delta Examples

FIBTEM
Low/borderline amplitude

HEPTEM
Normal CT and CFT
Confirms: heparin influence

INTEM
Prolonged CT
Consider: heparin influence

HEPTEM
Normal CT and CFT
Confirms: heparin influence

© 2012 TEM Systems, Inc - ROTEM® Durham, NC
ROTEM® delta Examples

© 2012 TEM Systems, Inc - ROTEM® Durham, NC
Case Study: Baseline

EXTEM

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CT</strong></td>
<td>86</td>
<td>[43 - 82]</td>
</tr>
<tr>
<td><strong>CFT</strong></td>
<td>76</td>
<td>[48 - 127]</td>
</tr>
<tr>
<td><strong>a</strong></td>
<td>74</td>
<td>[65 - 80]</td>
</tr>
<tr>
<td><strong>A10</strong></td>
<td>61</td>
<td>mm</td>
</tr>
<tr>
<td><strong>A20</strong></td>
<td></td>
<td>mn [50 - 70]</td>
</tr>
<tr>
<td><strong>MCF</strong></td>
<td>* 64</td>
<td>mn [52 - 70]</td>
</tr>
<tr>
<td><strong>ML</strong></td>
<td>* 0</td>
<td>%</td>
</tr>
</tbody>
</table>

INTEM

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CT</strong></td>
<td>176</td>
<td>[122 - 208]</td>
</tr>
<tr>
<td><strong>CFT</strong></td>
<td>65</td>
<td>[45 - 110]</td>
</tr>
<tr>
<td><strong>a</strong></td>
<td>77</td>
<td>[70 - 81]</td>
</tr>
<tr>
<td><strong>A10</strong></td>
<td>60</td>
<td>mn</td>
</tr>
<tr>
<td><strong>A20</strong></td>
<td></td>
<td>mn [51 - 72]</td>
</tr>
<tr>
<td><strong>MCF</strong></td>
<td>* 62</td>
<td>mn [51 - 72]</td>
</tr>
<tr>
<td><strong>ML</strong></td>
<td>* 0</td>
<td>%</td>
</tr>
</tbody>
</table>

FIBTEM

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CT</strong></td>
<td>61</td>
<td>s</td>
</tr>
<tr>
<td><strong>CFT</strong></td>
<td>252</td>
<td>s</td>
</tr>
<tr>
<td><strong>a</strong></td>
<td>64</td>
<td>*</td>
</tr>
<tr>
<td><strong>A10</strong></td>
<td>24</td>
<td>mn</td>
</tr>
<tr>
<td><strong>A20</strong></td>
<td></td>
<td>mn [7 - 24]</td>
</tr>
<tr>
<td><strong>MCF</strong></td>
<td>* 25</td>
<td>mn [7 - 24]</td>
</tr>
<tr>
<td><strong>ML</strong></td>
<td>* 0</td>
<td>%</td>
</tr>
</tbody>
</table>
Case Study: OB post partum

EXTEM

FIBTEM

INTEM
Case Study: Open AAA during XC
Case Study: Rewarming on CPB

---

**FIBTEM**

- **CT**: 50 s
- **CFT**: 65
- **A10**: 12 mm
- **A20**: 12 mm [7 - 24]
- **MCF**: 12 mm [7 - 24]
- **ML**: * 13%

---

**EXTEM**

- **CT**: 71 s [43 - 82]
- **CFT**: 438 s [48 - 127]
- **α**: 36 ° [65 - 80] ▼
- **A10**: 24 mm
- **A20**: 32 mm [50 - 70] ▼
- **MCF**: * 37 mm [52 - 70]
- **ML**: * 0 %
Case Study: Post-protamine
Case Study: Trauma, multiple injuries

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
<th>Range 1</th>
<th>Range 2</th>
<th>Notes</th>
</tr>
</thead>
</table>
| EXTEM | 296 s | 43 - 82 | ▲ | 10 30 40 50 min | pt in ptcu at mott, results s[...]
| INTEM | 394 s | 122 - 208 | ▲ | 10 30 40 50 min | pt in ptcu at mott, results s[...]
| FIBTEM | 2600 s | 7 - 24 | | 10 30 40 50 min | pt in ptcu at mott, results s[...]

- **EXTEM**
  - CT: 296 s [43 - 82] ▲
  - CFT: 888 s [48 - 127] ▲
  - A10: 16 mm [65 - 80] ▼
  - A20: 23 mm [50 - 70] ▼
  - MCF: * 28 mm [52 - 70]
  - ML: * 0 %

- **INTEM**
  - CT: 394 s [122 - 208] ▲
  - CFT: 888 s [45 - 110] ▲
  - A10: 23 mm [70 - 81] ▼
  - A20: 23 mm [51 - 72] ▼
  - MCF: * 28 mm [51 - 72]
  - ML: * 0 %

- **FIBTEM**
  - CT: *2600 s
  - CFT: *
  - A10: mm
  - A20: mm [7 - 24]
  - MCF: mm [7 - 24]
  - ML: %
Case Study: ICH in Patient with AF
Studies of PCC as Part of a Concentrate-based Approach to Managing Coagulopathy in Trauma or Perioperative Bleeding

From: Prothrombin Complex Concentrates in Trauma and Perioperative Bleeding
Anesthes. 2015;122(4):923-931. doi:10.1097/ALN.0000000000000608
Case Study: Liver transplant

EXTEM

INTEM

HEPTEM

FIBTEM
Case Study: Post-CPB (Bivalirudin)
Case Study: Post-CPB (Bivalirudin)
Case Study: Post-CPB (Bivalirudin)
Microvascular Bleeding

ROTEM + POC CBCP (Coulter) → All Normal → Surgical Exploration

EXTEM MCF

<48mm

FIBTEM MCF

<10mm

Cryo 2 5-packs

and

If EXTEM CT > 100 sec

FFP 10 ml/kg or PCC 25 IU/kg

and/or

Platelets <100 x 10^9/L

>10mm

Cryo 2 5-packs

and

DDAVP 0.3 mcg/kg

>48mm

FIBTEM MCF

<10mm

Platelets

<10mm

<100 sec

>10mm

<100 sec

>100 sec

Explore Surgical Bleeding

and/or

INTEM / HEPTEM APTEM

APTEM ML <15%

HEPTEM CT

<240 sec

Aminocaproic Acid 70 mg/kg

Protamine 50 mg

>240 sec

FFP 10 ml/kg or PCC 25 IU/kg

EXTEM CT

>15%

EXTEM ML >240 sec

INTEM CT

>240 sec

All Interventions Have To Be Approved by Surgery and Anesthesia Faculty

MCF, Maximum Clot Firmness
CT, Coagulation Time
PCC, Prothrombin Complex
FFP, Fresh-frozen Plasma
Cryo, Cryoprecipitate
DDAVP, Desmopressin
ML, Maximum Lysis

Adapted from:
- Journal of Cardiothoracic and Vascular Anesthesia, Vol 26, No 6 (December), 2012: pp1083-1093
- Transfusion Medicine Reviews, Vol 26, No 1 (January), 2012: pp1-13
- Journal of Cardiothoracic and Vascular Anesthesia, Vol 27, No 6 (December), 2013: pp 1181-1188
Questions?