Basics of Cardiovascular Surgery with Bypass: Monitoring acid base, oxygenation, and clotting status

*Evaluating Two Models for POC Blood Gas Testing

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Disclosures

- Receives consultation fees from Werfen (formerly IL)

Objectives for Talk

- Describe how acids and bases are produced
- Describe the Cardio Pulmonary (CP) Bypass process:
  - Physiologic and monitoring goals during CP Bypass
  - When to use hypothermia on patients
  - Describe blood gas interpretation during CPB: Whether to temp correct (pH-stat) or not temp correct (α-stat) results for patients in hypothermia.
- Evaluate different models of POC blood gas (etc) testing in the operating rooms for costs, test menu, and test volumes.
- Describe the coagulation parameters reported by Viscoelastic Testing systems (ROTEM, TEG, and Quantra).
- Evaluate the pluses and minuses of the new viscoelastic testing systems: Sigma, 6s, Quantra.

Where Does Acid Come From?

- ***Metabolic:***
  - Hypoxemic / Ischemic
    - May be related to pulmonary and/or cardiac function, blood flow, mitochondria
    - Blood lactate often a marker
  - High Anion Gap acidosis:
    - Related to lactate, ketoacids, ethanol, methanol, Tylenol, ethylene glycol, etc
  - Normal Anion Gap acidosis
    - GI loss of bicarbonate: diarrhea
    - Kidney: RTA: Increased loss of HCO_3 (PCT) or increased retention of H^+ (DCT):
    - Decreased aldosterone: promotes loss of Na^+ / gain of K^+ / H^+
  - ***Lab diagnosis:*** A decreased pH and HCO_3.

- ***Respiratory:***
  - Hypoventilation
    - May be from trauma, drugs, airway obstruction, etc
    - Depressed ventilation = Increased pCO_2
  - ***Lab diagnosis:*** A decreased pH and increased pCO_2.

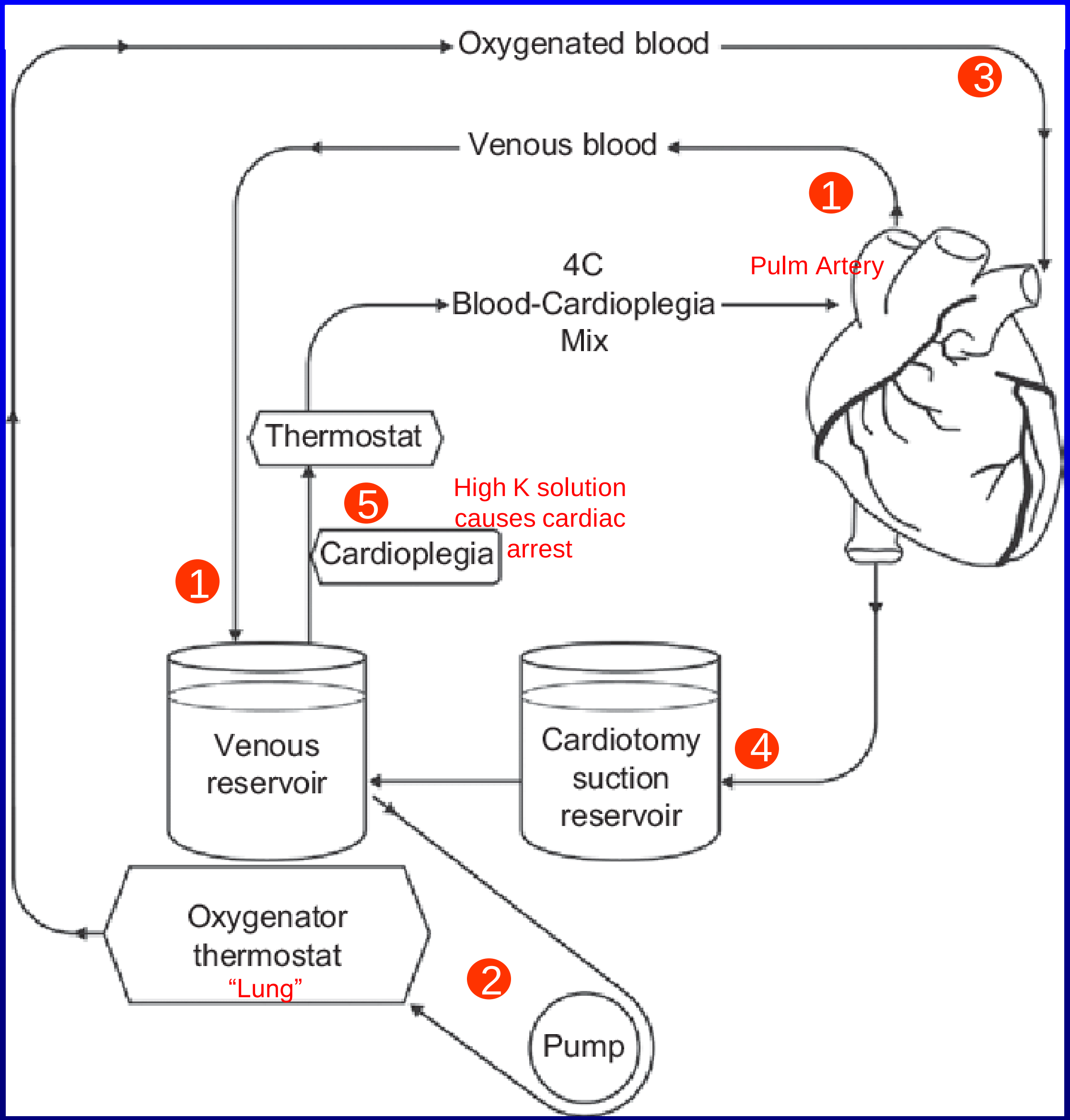
Where Does Alkali Come From?

- *Metabolic:*
  - Very little HCO_3 or other alkaline substances are produced by metabolism: Ammonia is produced, but it is 98% NH_4^+ and 2% NH_3.
  - Kidney: Gain of bicarbonate often related to Na^+ / K^+ / Cl^- movements:
    - Urinary loss of Cl^- can lead to increased retention of HCO_3
    - Increased aldosterone: Gain of Na^+ = loss of K^+ / H^+ and gain of HCO_3
  - GI absorption of HCO_3
    - Excess HCO_3 administration
  - Loss of acidic upper GI fluids: vomiting
  - *Lab diagnosis:* An increased pH and HCO_3.
- *Respiratory:*
  - Hyperventilation
    - May be from trauma, anxiety, sepsis, drugs, hormonal / pregnancy
    - Loss of CO_2 from excessive mechanical ventilation
- *Lab diagnosis:* An increased pH and decreased pCO_2.

Simplified Diagram of CPB Circuit and Components

PROCESSES IN THE CARDIOPULMONARY CIRCUIT

1) Blood from venous circulation is passed into a reservoir,
2) pumped through an oxygenator,
3) then reinfused distal to the heart.
4) Shed blood is aspirated to a reservoir, then into the venous reservoir.
5) Cardioplegia solution is added to the venous reservoir, cooled to 4oC, then reinfused to the heart via the cardioplegia line.



From Researchgate by Martin Besser

Processes in Cardiopulmonary Bypass

- Cannulae connect the patient to the CPB circuit.
- Heparin (3-4 U/mL is added to the priming solution.
  - To maintain desired hematocrit at 21-24%, external blood may be added to the circuit.
- Anticoagulation is monitored every 30-40 minutes.
  - Clotting is life threatening
- Hypothermia may be used when blood flow has to be paused:
  - A blood-free zone is needed for surgery: aortic, peds open-heart, et al.
- Acid-base management: α-stat or pH-stat?

Acid-Base, Oxygenation, Hb, Lytes, and Coagulation Goals in CPB Procedure

- Flow rate: 2.2 – 2.4 L/min/m^2 = ~ 4 – 5 L/min for most people.
- Mean Art Pressure: $\geq$ 65 mmHg
- Mixed Ven O_2 sat: > 75%
- Arterial pH: 7.35 – 7.45 (w/ α-stat and pH-stat?)
- Arterial pO_2: 150 – 250 mmHg
- Arterial pCO_2: 35 – 45 mmHg
- Hemoglobin > 7.5 g/dL; Hct > 22%
- Blood glucose < 180 mg/dL
- For K, Ca^{++}, Mg: Monitor every 30 min
  - Essentially keep normal
- Anticoagulation: ACT: 400 to 480 sec; Heparin > 4 U/mL

Cheung AT, Stafford-Smith M, Heath M. Management of CPB. UpTo Date Sept 2022

α-stat vs pH-stat During Hypothermic Surgery: Temperature Correct or Not?

- α-stat does not temp correct:
  - aims for pH of 7.40 and pCO_2 of 40 mmHg as measured at 37ºC (analyzer temp).
- pH-stat *does* temp correct:
  - aims for normal pH and pCO_2 as calculated for the patient's temperature.
  - CO_2 may be deliberately added to maintain pCO_2 of 40 mmHg = increased cerebral blood flow.
- Published reports conclude that:
  - α-stat control led to better neurological outcomes in adults.
  - 3 of 4 studies on pediatric patients concluded pH-stat control led to better outcomes.

Information Provided by Blood Lactate Measurements In Adult Cardiopulmonary Bypass (CABG) Surgery

Monitoring blood lactate evaluates the complex metabolic state of the patient recovering from cooling, hemodilution, anesthesia, vasoactive drugs, inflammation, coagulopathies, etc.

Principles of Evaluating an Elevated Lactate After Open-Heart Surgery

- If reperfusion is good, lactate should decline by 1-2 hours after surgery.
  - However, lactate declines slowly in some patients.
- If lactate remains elevated 1-2 hr after surgery:
  - Make sure cardiac output is good.
  - Make sure airways are clear and blood oxygenation is good.
  - Evaluate liver function
    - liver shutdown can diminish lactate removal.
  - Look for gut ischemia or peripheral ischemia.

Case: CABG Operation with Minor Complication on 67 yo male with recent Myocardial Infarction

Time	8:40	9:15	10:00	11:15	11:30	12:00	14:00
FI-O_2	0.40	0.40	0.70	0.70	0.21 (RA)	0.21	1.00
pO_2	108	101	210	280	180	45	120
%O_2 Hb	98.5	96.7	99.2	99.6	99.3	84.0	98.8
Hb	11.5	10.8	8.2	8.0	8.2	8.5	10.2
O_2 content	15.7	14.5	11.3	11.1	11.3	9.9	14.0
Lactate	1.2	0.9	1.5	2.5	3.8	4.6	2.5

Patient on pump

Rise in lactate immediately post-op is relatively normal.

For decreased pO_2 and increased lactate 30 minutes post-op: gave supplemental oxygen.

Evaluating Two Models of Point-of-Care Blood Gas/Electrolyte/Etc. Testing in Operating Room Areas

In 2013, Duke Medical Center Opened a Major Addition: the Duke Medical Pavilion

(Blood Gas Lab on 6^{th} Floor)

Duke Cancer Center at Left

Blood Gas POC Model #1

1 or 4 hand-held (HH) blood gas analyzers with single-use cartridges used in ORs, Cardiac Cath, etc:

- Used by perfusionists, CNAs, anesthesia technicians.
- Supplies, maintenance, and regulatory responsibilities under Clinical Laboratories.

Blood Gas POC Model #2

1 or 2 Hybrid blood gas analyzers (Hyb) with multi-use reagent packs used in cardiac/thoracic ORs, cardiac cath lab, clinical laboratories, etc:

- Used by perfusionists, anesthesia technicians, and cath lab personnel.
- Maintenance, quality control, and regulatory responsibility are under Clinical Laboratories.

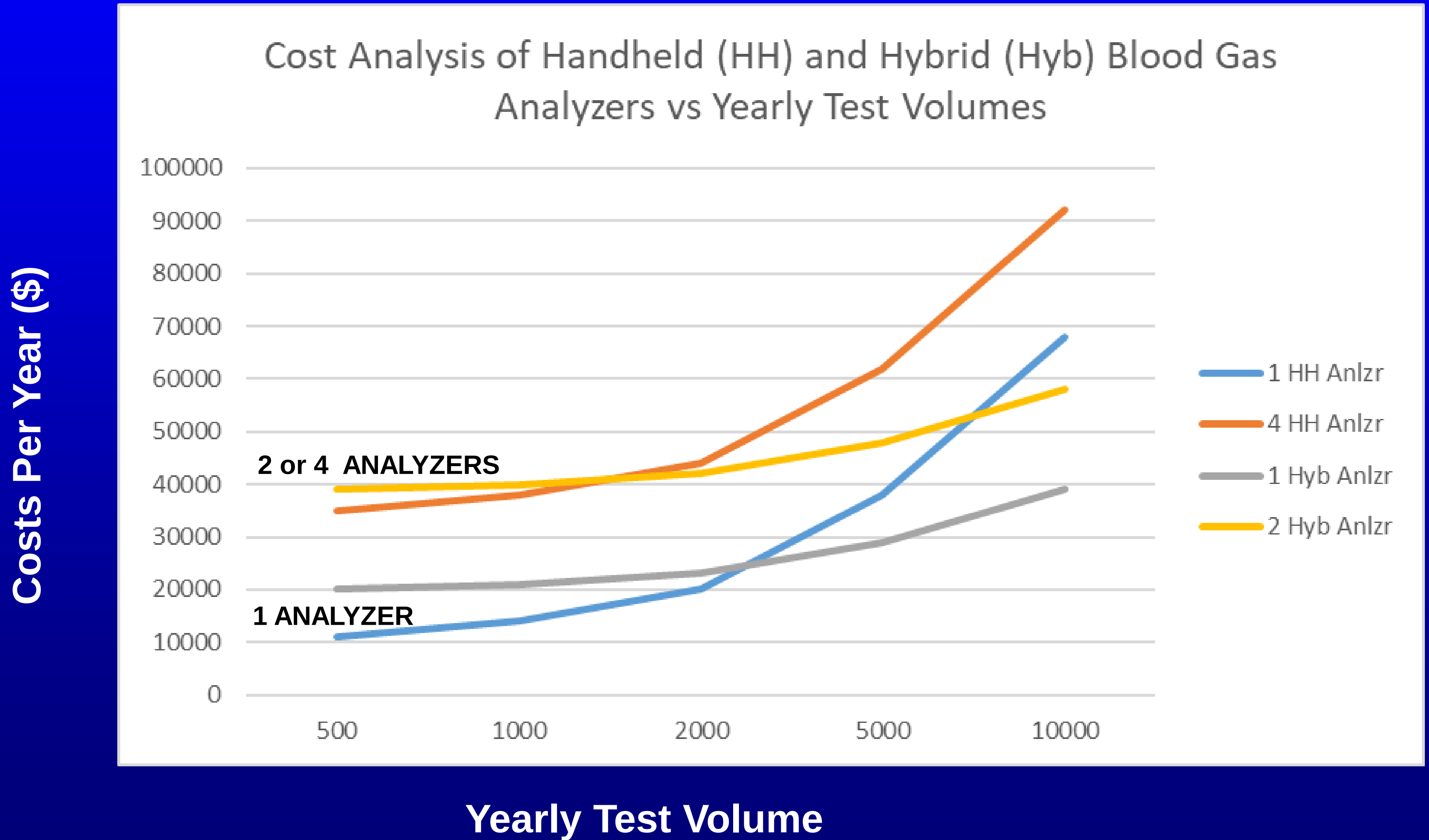
Disclaimer:

The following cost data are approximate costs based on quotes from manufacturers at different times and different test volumes.

Yearly Costs for Handheld (HH) and Hybrid (Hyb) POC Test Systems

	Costs for one HH analyzer ($)	Cost for 4 HH analyzers ($)	Costs for one Hyb analyzer ($)	Cost for 2 Hyb analyzers ($)
Analyzer cost	8,000	32,000	19,000	38,000
Cost per 1 test card (need 2?)	6.00	6.00	2.00	2.00
500 tests/y	11,000	35,000	20,000	39,000
1000 tests/y	14,000	38,000	21,000	40,000
2000 tests/y	20,000	44,000	23,000	42,000
5000 tests/y	38,000	62,000	29,000	48,000
10,000 tests/y	68,000	92,000	39,000	58,000
20,000 tests/y	128,000	152,000	59,000	78,000

Plots of Yearly Costs vs Test Volume for Handheld and Hybrid Analyzers



Pros/Cons of POC Model #1:
Hand-held Single-Use Cartridge System

- Advantages
  - Excellent portability
  - Wider variety of tests available; ie. ACT, TnI
  - Financially suited to lower volume settings
  - Very good accuracy and reliability
- Disadvantages
  - A complete critical care panel may require 2-3 cartridges (adds time and $/test)
  - Cooximetry parameters are not measured
  - Requires IQCP

Pros/Cons of POC Model #2:
Multiple-Test Reagent Pack System

- **Advantages**
  - Cost, throughput , and speed are well-suited for high test volume settings.
  - Complete BG/lytes/glu/lact /coox available with one analysis.
  - Excellent accuracy and potential agreement with laboratory results.
- **Disadvantages**
  - Very costly for low test volumes.
  - Changing reagent packs takes ~40 min.
  - Not portable.
  - May require IQCP

The Present and Future of Viscoelastic Testing: Potential for POC Testing

Rotem, TEG, and now Quantra

The TEG 5000 Analyzer (older analyzer)

(About 12 inches high)

TEG 5000:

Operational features:

- 2 test channels
- Automated testing system
- Liquid QC every 8 hours.
- Bar code scanner

ROTEM® Delta (older analyzer)

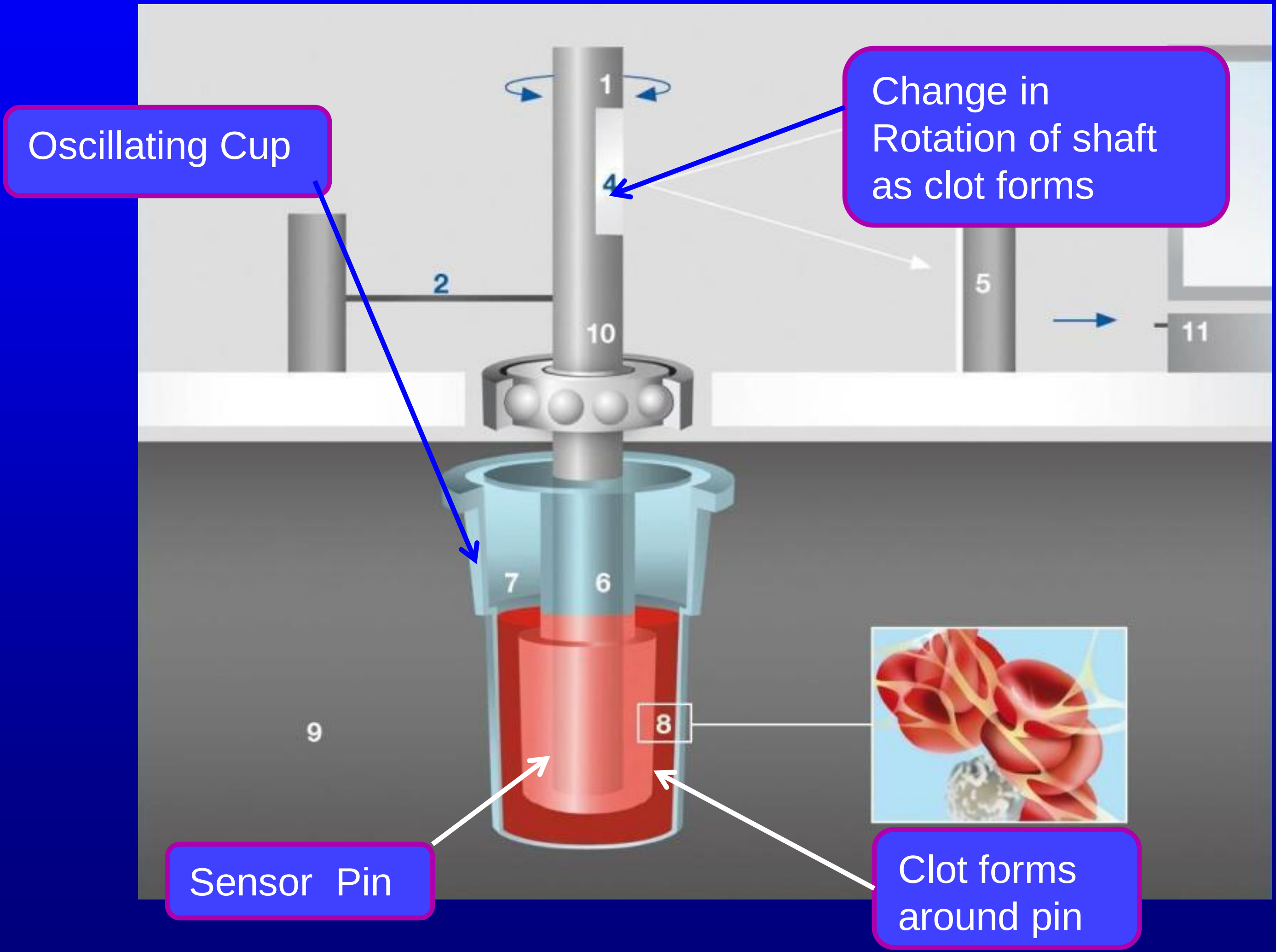
ROTEM® *Delta*

Operational features:

- 4 test channels
- Semi-automated system
- Touch screen monitor
- Weekly Liquid QC
- Bar code scanner

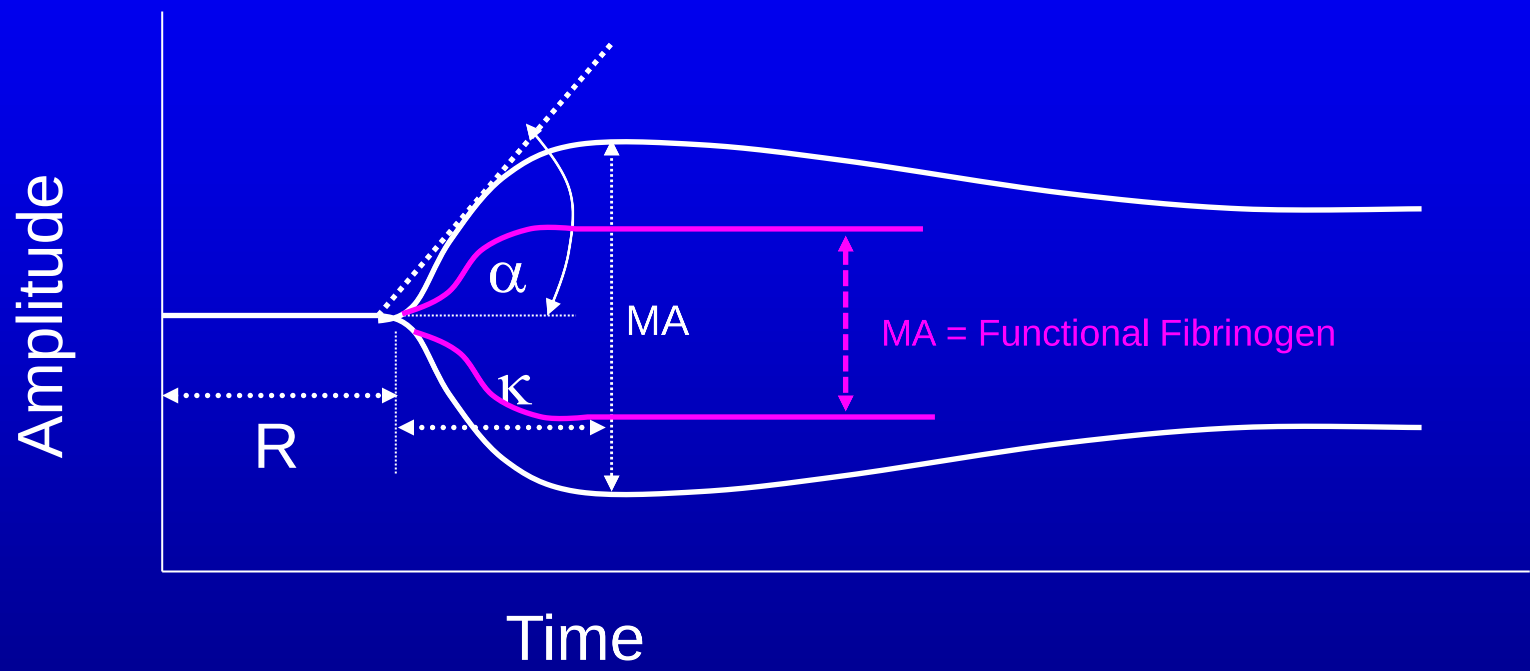
Concept of Oscillating Thromboelastography

(Similar for TEG and Rotem)



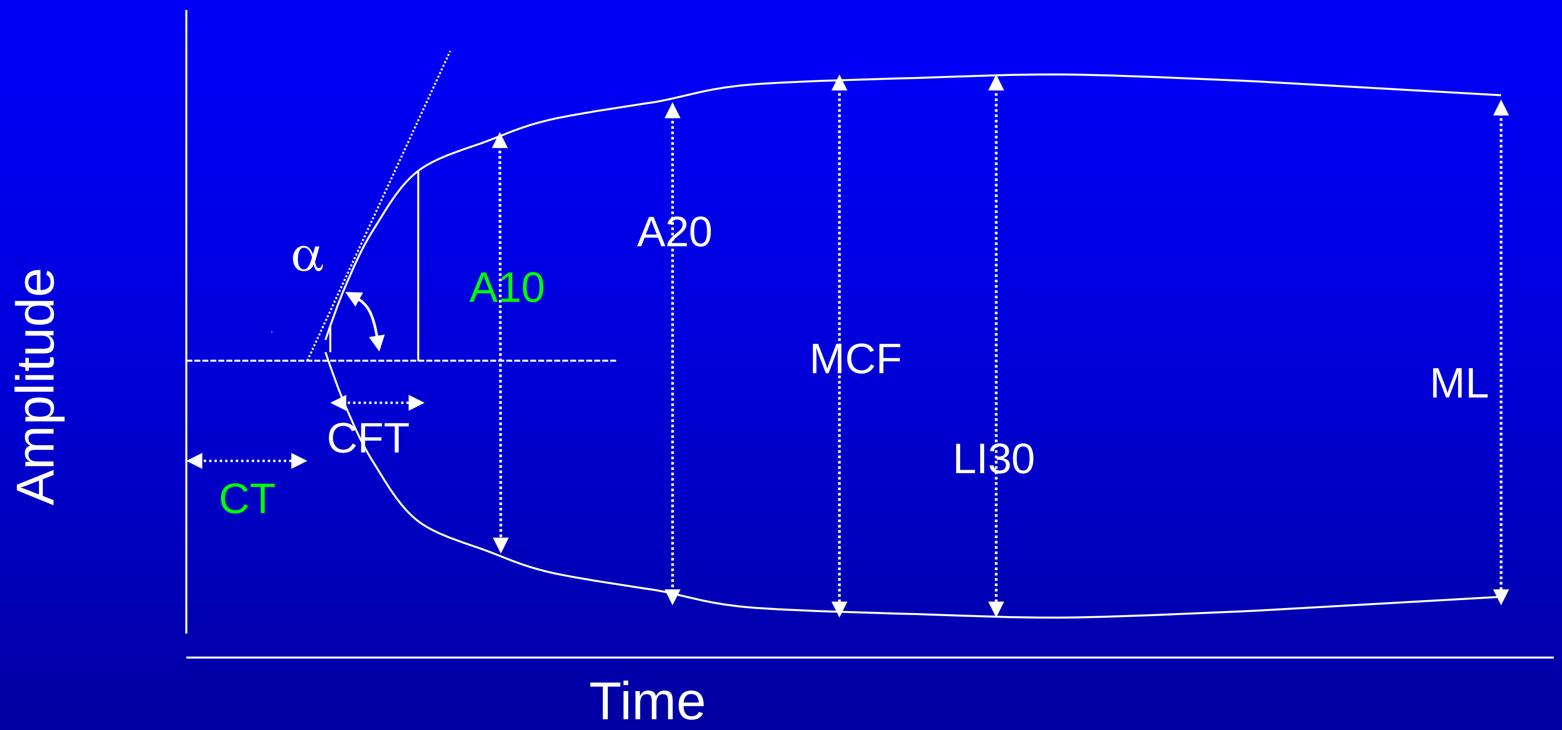
Provides information on clotting factors, and platelet and fibrinogen activities.

Adding Platelet-Inhibiting Reagent in TEG Gives a Functional Fibrinogen



The MA with platelet inhibitor added (plavix) is related to the fibrinogen activity.

Parameters in The ROTEM Delta Graph



CT time measures when the blood starts to coagulate (like an ACT).

CFT is the time between the 2mm and the 20 mm amplitudes

α-angle measures the speed of fibrin formation.

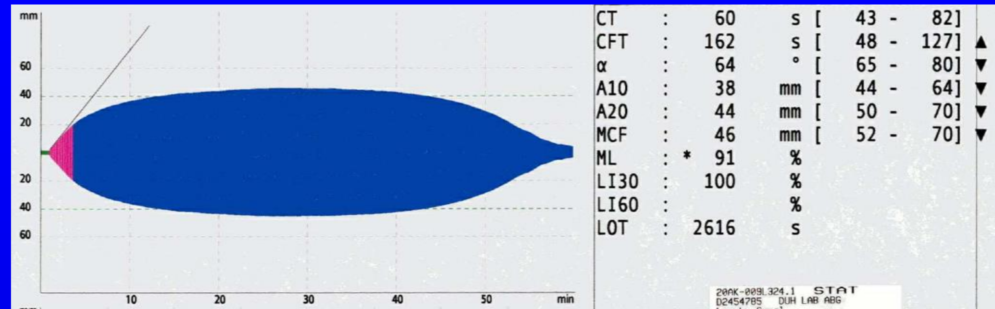
A10, A20, and MCF measure the clot strength at 10 min, 20 min, and maximal strength after the CT.

LI30 and ML measure the degree of fibrinolysis

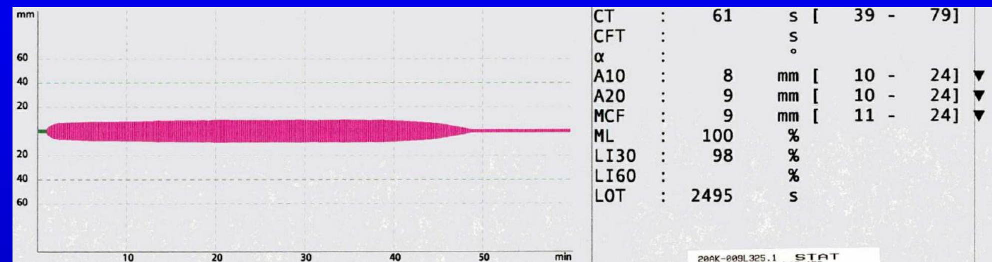
Rotem Case

67 yo F; Liver Txp

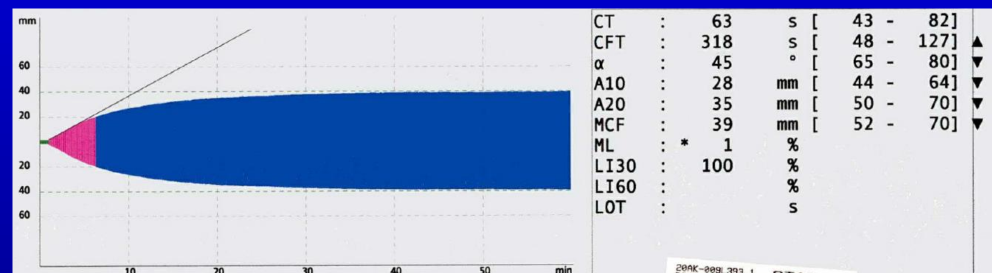
EXTEM



FIBTEM

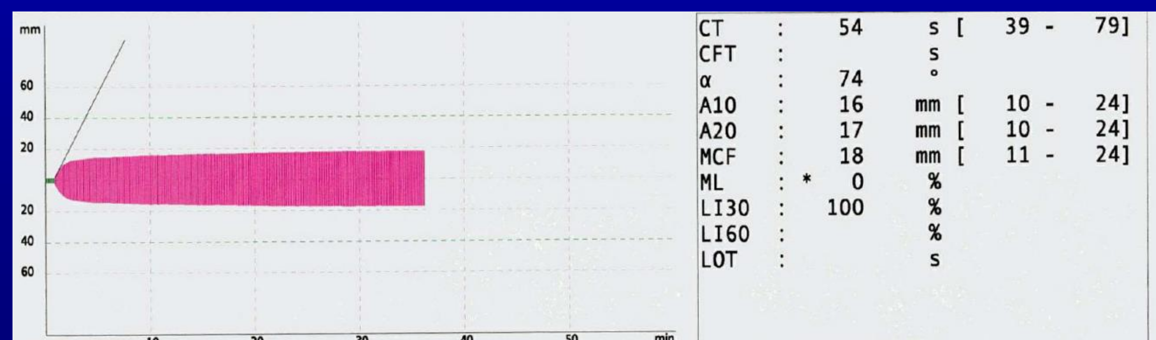


EXTEM



FIBTEM

FFP, Cryo, Plts given



The New Generation of Viscoelastic Testing: All are suited for POC Testing

- TEG 6s, ROTEM Sigma, Hemosonics Quantra:
  - All use a single 4-test cartridge:
    - Evaluates Intrinsic clot pathway: kaolin, elagic acid
    - Evaluates clotting if heparin removed: heparinase
    - Evaluates Extrinsic clot pathway: kaolin, tissue factor, etc
    - Evaluates fibrinogen activity: Uses platelet inhibitor:
      - Abciximab (Reopro) or cytochalasin D.
    - Some evaluate platelet contribution by subtraction:
      - Extrinsic - Fibrinogen

Measuring Technologies of New Generation VE Anayzers

- The TEG 6s and Hemosonics Quantra measure clot viscoelasticity and clot strength by exposing the sample to ultrasound vibrations:
  - Stronger clots have higher resonant frequencies
- The Rotem Sigma uses traditional mechanical resistance to oscillation as blood coagulates.

TEG 6s: Instrument and Cartridge

(10.5 inches high)

TEG 6s: Insertion of Cartridge and Application of Blood

The New ROTEM Sigma Analyzer:

4-Channel Cartridge Being Inserted
(25.5” high; 23” deep)

The New ROTEM Sigma Analyzer:

Tube with Citrated Blood Being Inserted

ROTEM Sigma With Graphs Displayed:

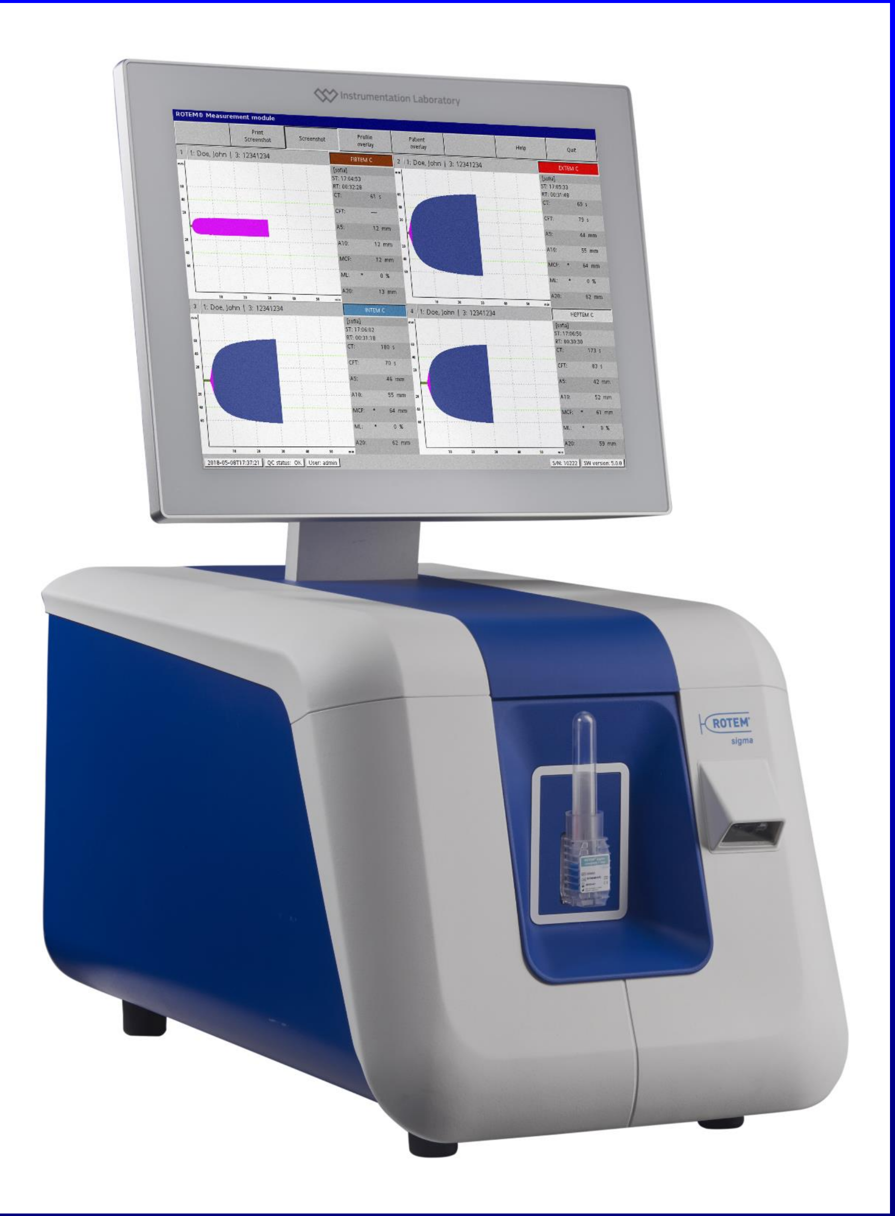
FIBTEM

EXTEM

INTEM

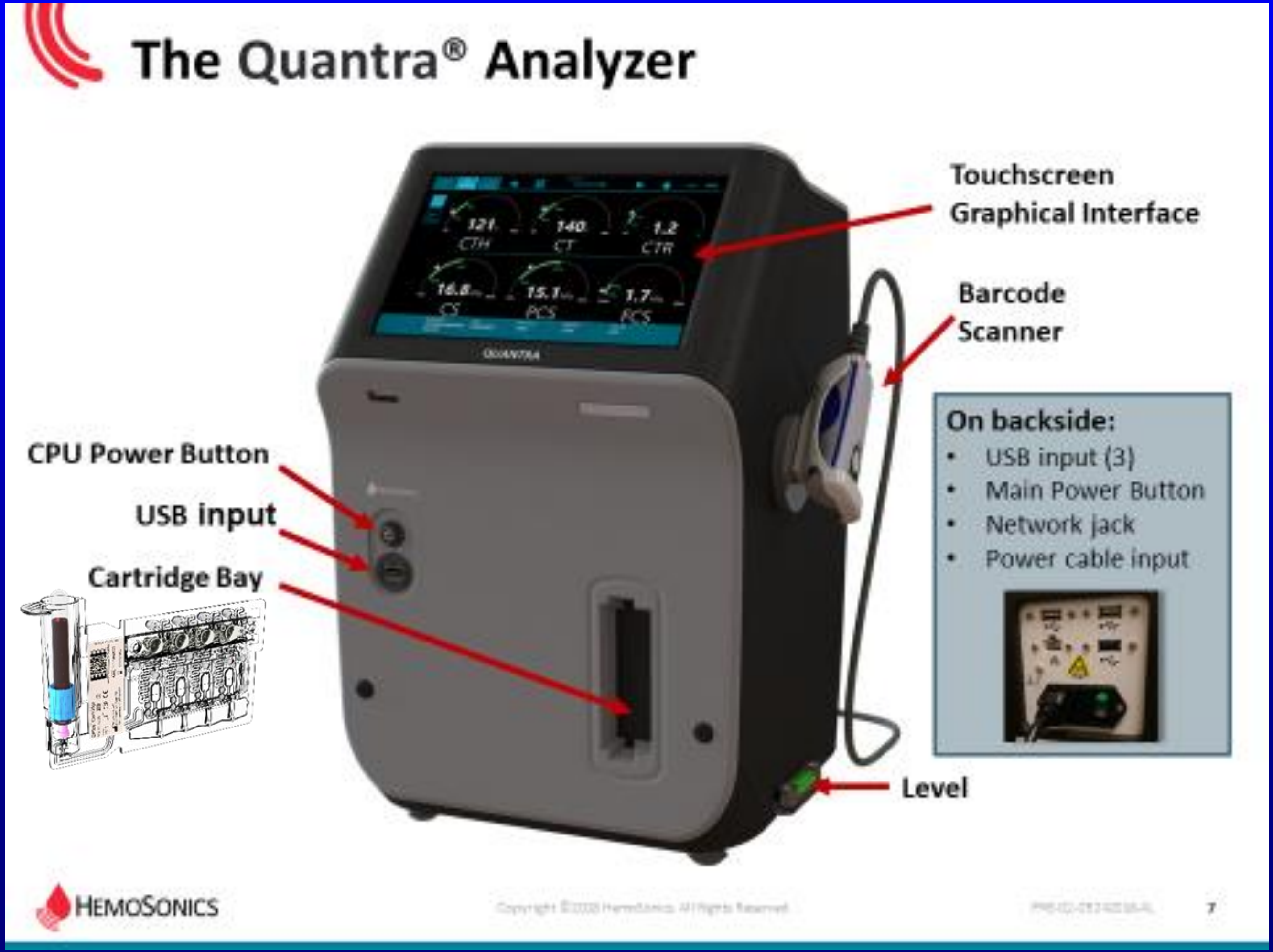
HEPTEM

(PLTEM calculated)

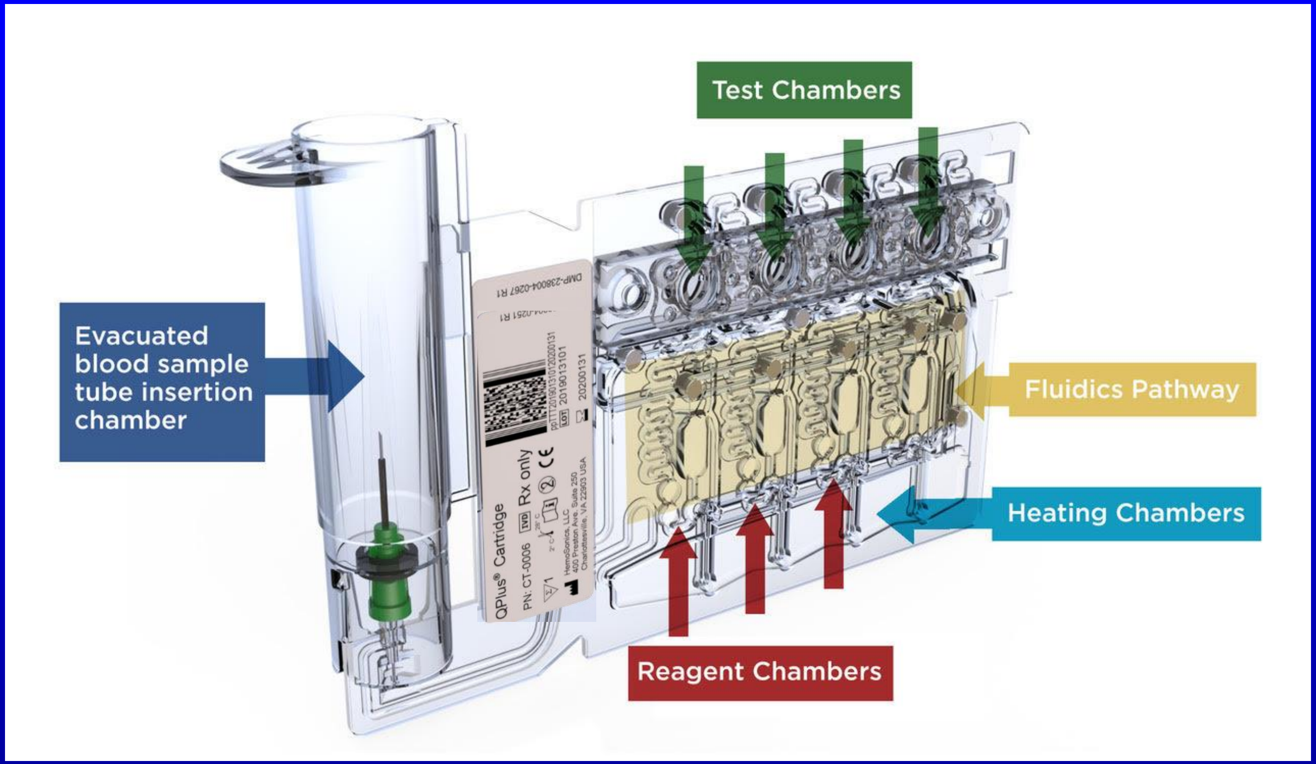


Hemosonics Quantra Analyzer and Cartridge

19.5 inches high



Quantra® QPlus® Cartridge

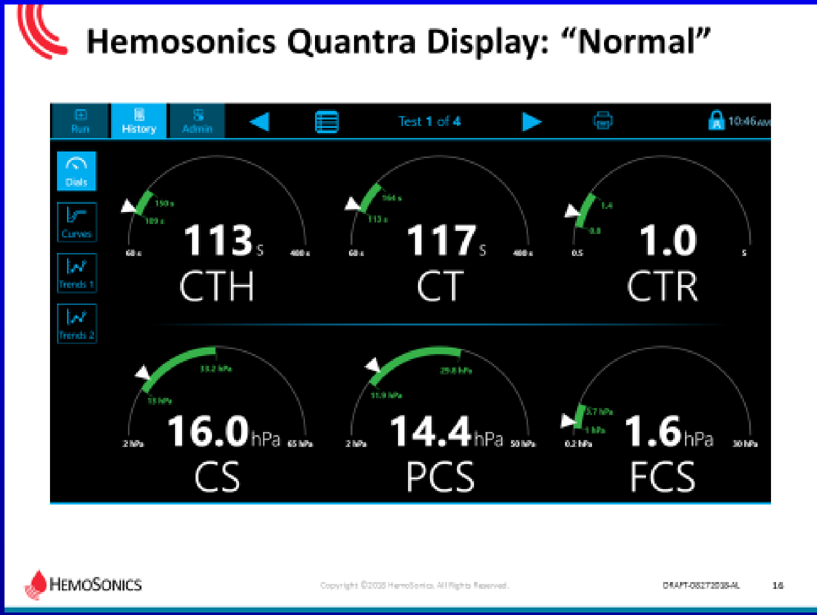


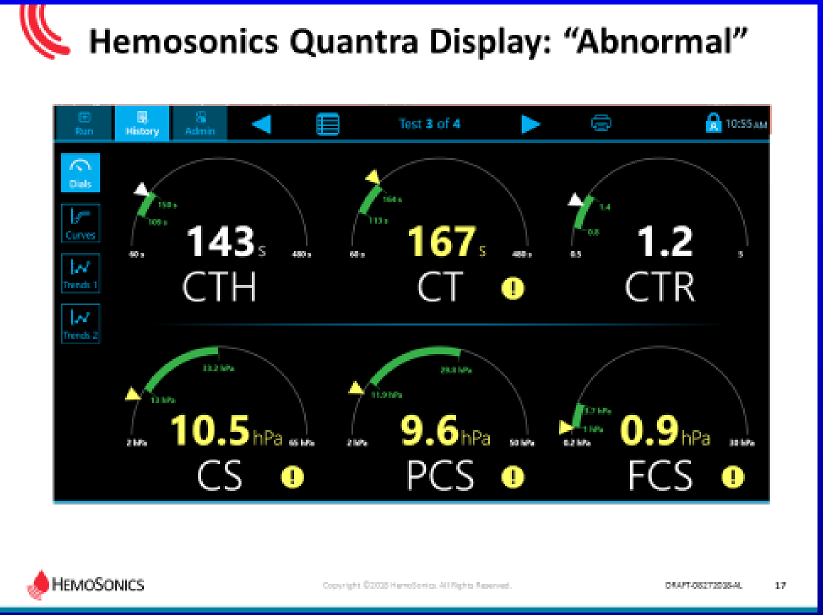
- Uses citrated blood
- No open tube blood transfer; Forms a closed system
- Not susceptible to external interferences
- Room temperature storage
- 4 tests run simultaneously. Results in 15 minutes

Quantra Parameters Displayed:
4 measured; 2 Calculated

Parameter	Definition (units)	ROTEM Similar	Measurement	Reagents
CT	Clot Time (sec)	INTEM CT	Clot time in citrated whole blood	Kaolin, calcium, buffers and stabilizers
CTH	Heparinase Clot Time (sec)	HEPTEM CT	Clot time in citrated whole blood with heparin neutralization	Kaolin, **heparinase**, calcium, buffers and stabilizers
CTR	Clot Time Ratio (CT/CTH)	Not comparable	Indicator of potential heparin influence in sample	Defined as the ratio of CT to CTH
CS	Clot Stiffness (hPa)	EXTEM A10	Stiffness of the whole blood clot	Thromboplastin, polybrene, calcium, buffers and stabilizers
PCS	Platelet Contribution to Clot stiffness (CS - FCS)	PLTEM A10 (EXTEM – FIBTEM)	Contribution of platelet activity to overall clot stiffness	Derived from the difference in clot stiffness values from CS and FCS
FCS	Fibrinogen Contribution to Clot stiffness (hPa)	FIBTEM A10	Contribution of fibrinogen to overall clot stiffness	Thromboplastin, polybrene, abciximab, calcium, buffers and stabilizers

Normal and Abnormal Result Displays for Quantra





Comparison of TEG, ROTEM, and Quantra

Activation	TEG 6S Global Hemostasis (GH) *and* GHL with Lysis (Trauma)	ROTEM Sigma*	Quantra System
Intrinsic Pathway	R time (Kaolin; min)	INTEM CT (elagic acid, Ca^{++}; sec)	CT:: Clot Time
	Kaolin R + Heparinase R (min)	HEPTEM: CT w/ heparinase (sec)	CTH: Clot Time with Heparinase
	N/A	N/A	CTR: Clot Time Ratio (CT/CTR)
Extrinsic Pathway	RapidTEG MA* (kaolin + tissue factor)	EXTEM A5/10/20: Tissue factor, Ca^{++}, polybrene (sec)	CS: Clot Stiffness
	Functional Fibrinogen MA (tissue factor + abxicimab; Reopro)	FIBTEM A10/A20: cytochalasin D (sec)	FCS: Fibrinogen Contribution (abxicimab)
	Platelet contribution (not calculated)	PLTEM: EXT – FIBTEM (not calculated)	PCS: Platelet Contribution (CS - FCS)
	LY30(%): only on Trauma cartridge	EXTEM ML/LI60 (%)	*Clot Stability to Lysis (CSL on QStat only)*

Comparison of TEG, ROTEM, and Quantra

	TEG 6s	ROTEM Sigma	Quantra
Height	10.5 inches	25.5 inches	19.5 inches
Blood volume required	Pipet ~340 uL of citrated blood	2.7 mL citrated blood tube (no pipetting)	Requires 2.7 mL citrated blood (no pipetting)
Time of analysis	15 min for first result; 25 min to final results. *(includes 12 min incubation)*	About 11 min to first result; 22 min for all results.	About 7 min to first result, 14 min for all results.
QC frequency	Generally similar recommendation for each lab to determine frequency: approximately every 2 weeks to 1 month. Can develop an IQCP to validate this.		

Will Viscoelastic Testing Go Point-of-Care?

- **These new VE analyzers and reagents have potential to make this true POC testing:**
  - ***But how many in Lab; how many at POC?***
- **However, all POC testing requires more instruments and laboratory oversight:**
  - ***Higher costs for instruments and reagents.***
  - ***Compliance with validation, QC, proficiency testing, competency testing, etc. are more challenging with POC testing.***

Factors That Promote Increase In POC Testing

- Test panel or menu provides useful information.
- Testing requires minimal additional effort:
  - Testing is rapid and convenient.
  - Test ordering, billing, and documentation automatic (connected to lab information system).
- Analyzer has reliable accuracy and precision:
  - Fewer preanalytical effects
  - No puzzling results to investigate
  - Results agree with laboratory results
- POC testing improves finances, outcomes, and/or satisfaction of users/patients.

Actual, Totally True Incident (Years Ago) in Our Point-of-Care Glucose Testing Program

- A lab person in the POCT program called a caregiver about a result being an "outlier" on a proficiency test sample.
- Caregiver heard this slightly differently and told their supervisor: "The lab said I was an 'out and out liar' on my [PT] result."
- Moral: Effective communication is a must in POC testing.