Basics of Cardiovascular Surgery with Bypass: Monitoring acid base, oxygenation, calcium, 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.
  - Describe when ionized Ca is monitored and administered.
- 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 (VE) Testing systems (ROTEM, TEG, and Quantra).
  - Evaluate the pluses and minuses of these new VE systems.

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.

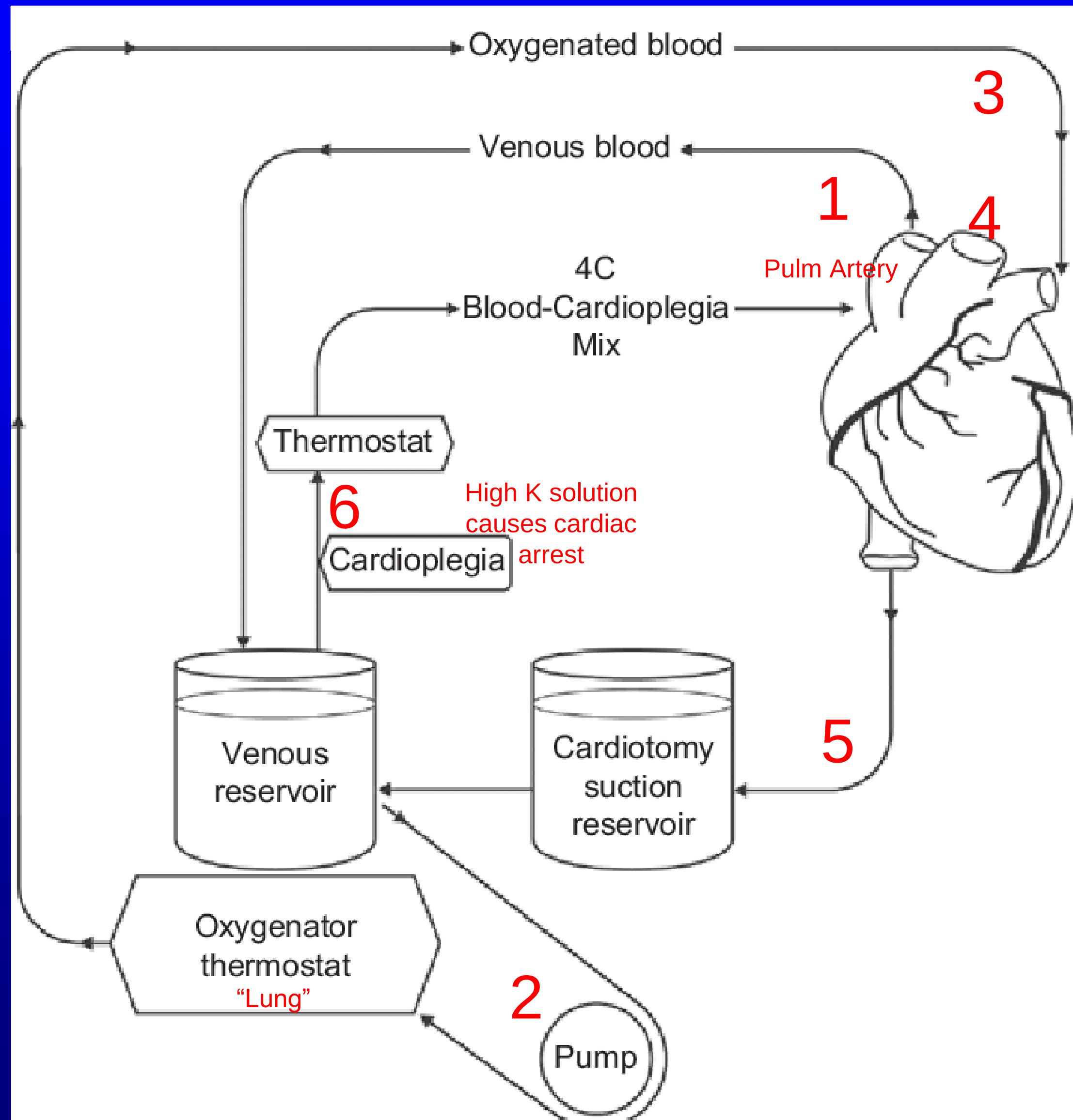
Where Does Alkali Come From?

- ***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, then
3) reinfused distal to the heart.
4) Aorta cross-clamped to isolate the heart for surgery.
5) Shed blood is aspirated to a reservoir, then into the venous reservoir.
6) 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 and cross-clamping 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 *p*CO_2 of 40 mmHg as measured at 37ºC (analyzer temp).
- pH-stat *does* temp correct:
  - aims for normal pH and *p*CO_2 as calculated for the patient's temperature.
  - CO_2 may be deliberately added to maintain *p*CO_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.

When to Supplement Ca During Cardiac Bypass Surgery*

- May be based on blood pressure:
    - During surgery: give if hypotensive.
    - When coming off bypass and removing cross clamps:
        - Avoid adding Ca^{++} if BP is adequate, because the possible cell injury during reperfusion is Ca^{++} mediated
        - However, there is scant or no *in vivo* data suggesting Ca supplementation is dangerous
- May be given empirically when coming off bypass:
    - Ca^{++} ions counteract the high [K+] in the heart following cardioplegia.
- Typically not based solely on ion Ca measurements

** From Ian Welsby, MD. Duke anesthesiologist*

Clinical Utility of Ionized Calcium Measurements With Cardiovascular Surgery

- **Ion Ca measurements are not useful for maintaining “normal” [Ca^{++}] in CV surgery patients.**
  - **Changes in perioperative [Ca++] were not associated with LV Ejection fraction.** *J Pers Med 2024; 14, 850.*
- **Ion Ca results do appear to have prognostic value in predicting prognosis:**
  - **Mild hypocalcemia 1-day post-CV surgery had worse short- and long-term prognosis: longer ICU stay; higher rate of kidney injury (AKI).** *Frontiers in Cardiovasc Medicine 2021; 8: 733528.*

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 6th 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.

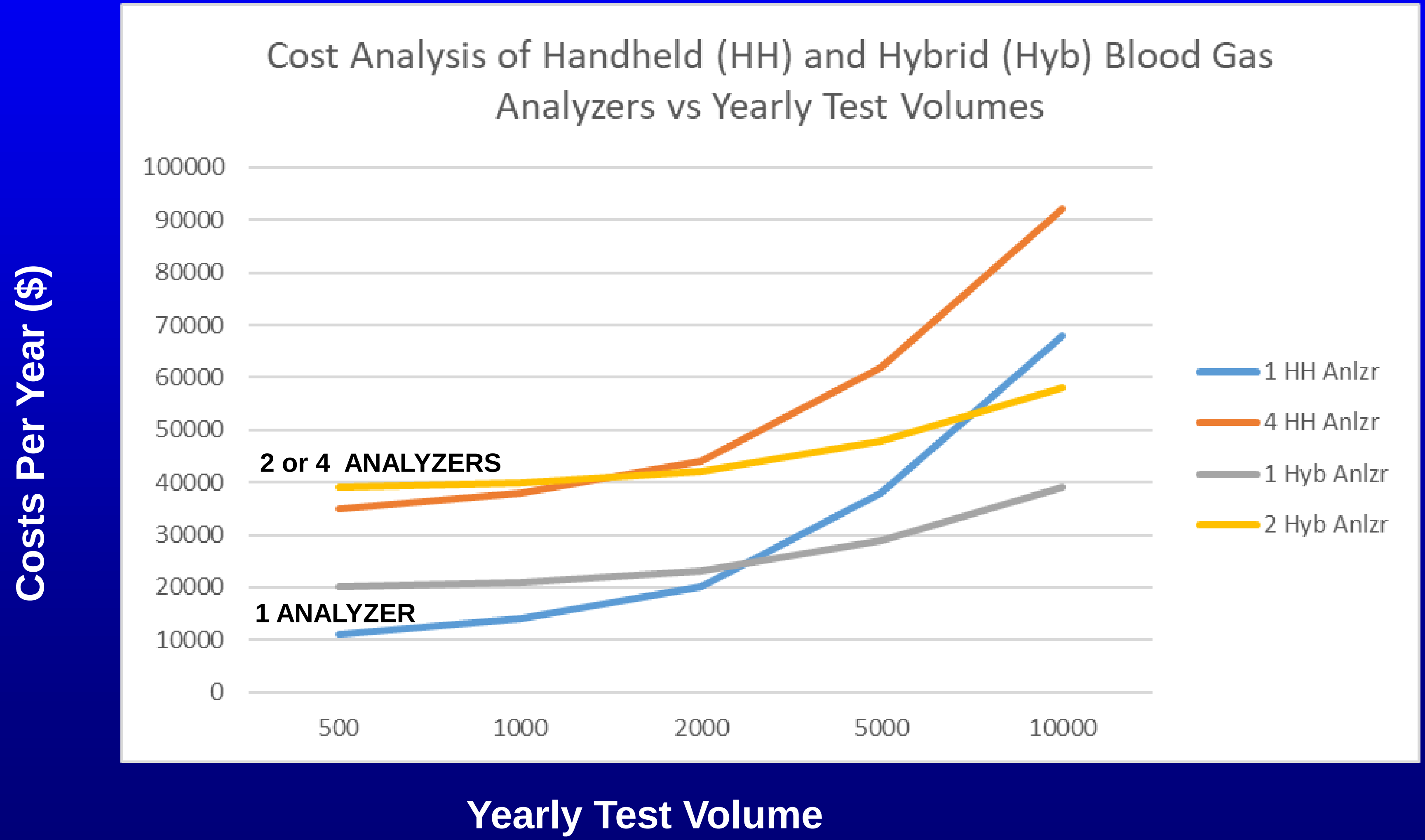
Disclaimer:

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

Repurposed Walnut Table

History:
1983: Original walnut table built in traditional style.
1998: Inherited mahogany table from Mother-in-Law.
1999: Banished walnut table to attic.
2023: Daughter wants nice dining table. Does not like traditional design of walnut table.
2023-24: Good daddy cuts apart original walnut table; repurposes walnut wood into modern design table here.

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)

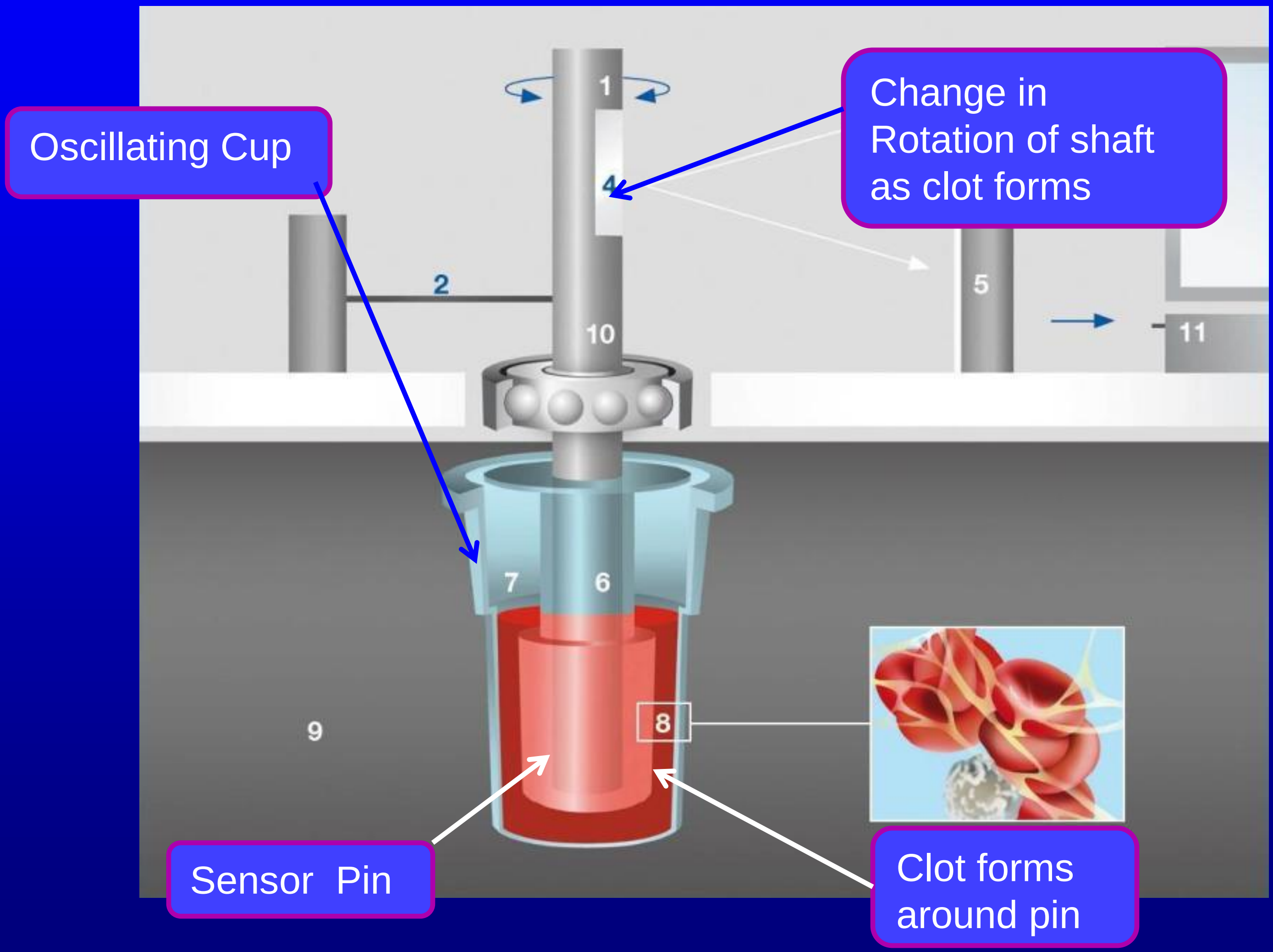
ROTEM® *Delta*

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, fibrinogen, and platelet activities.

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.

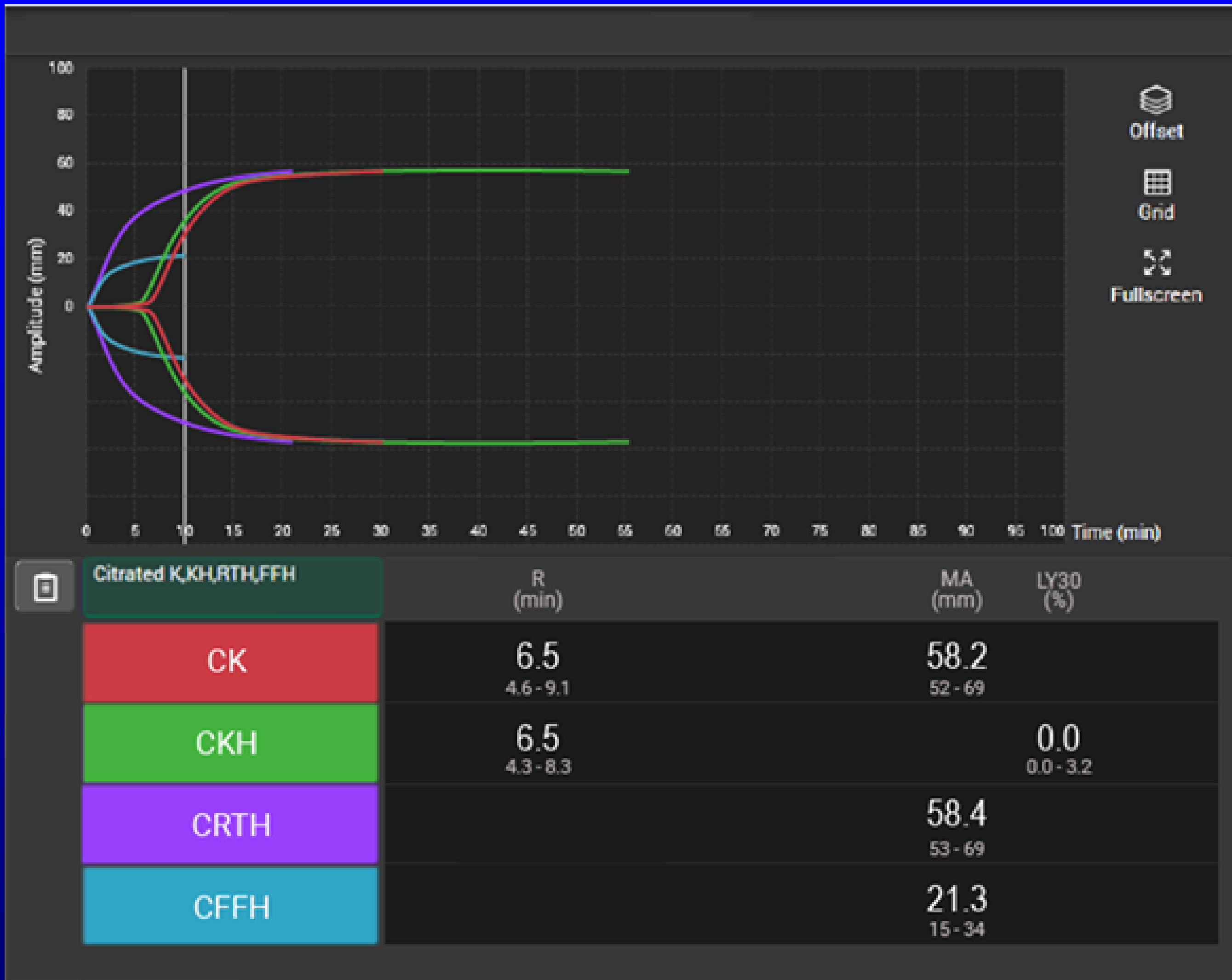
TEG 6s: Instrument and Cartridge

(10.5 inches high)

TEG 6s: Insertion of Cartridge and Application of Blood

Graph of Normal Blood on New TEG 6S HN Cartridge

(HN = Heparin Neutralized)



This blood has:

- No heparin: R times same for CK and CKH.
- Normal coagulation factors: Normal R time.
- Normal fibrinogen: Normal CFFH.
- No fibrinolysis (LY30 %)

CK = citrated Kaolin test.

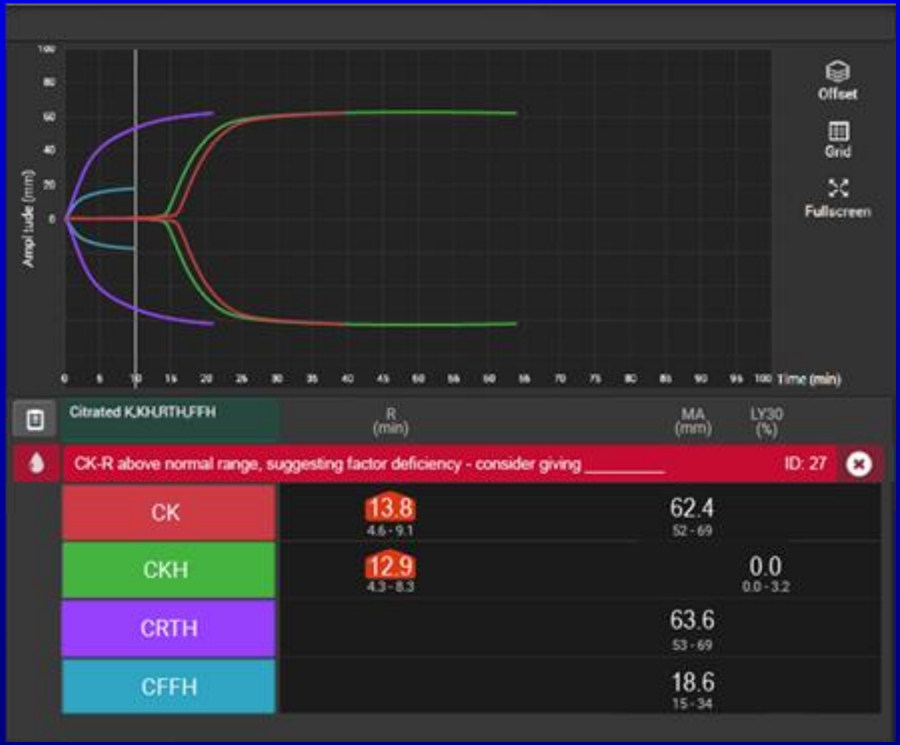
CKH = citrated Kaolin test w/ heparinase.

CRTH = citrated Rapid TEG w/ heparinase

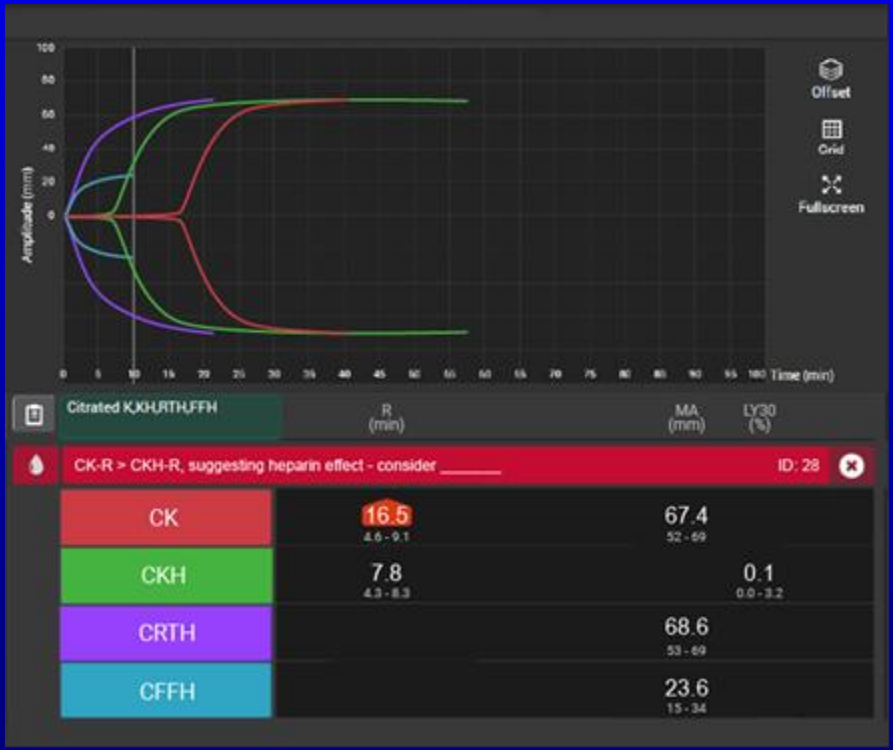
CFFH = citrated functional fibrinogen test.

Examples of Abnormal TEG Graphs

Example of blood with poor factor function and no heparin effect



Example of blood with high heparin level.



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

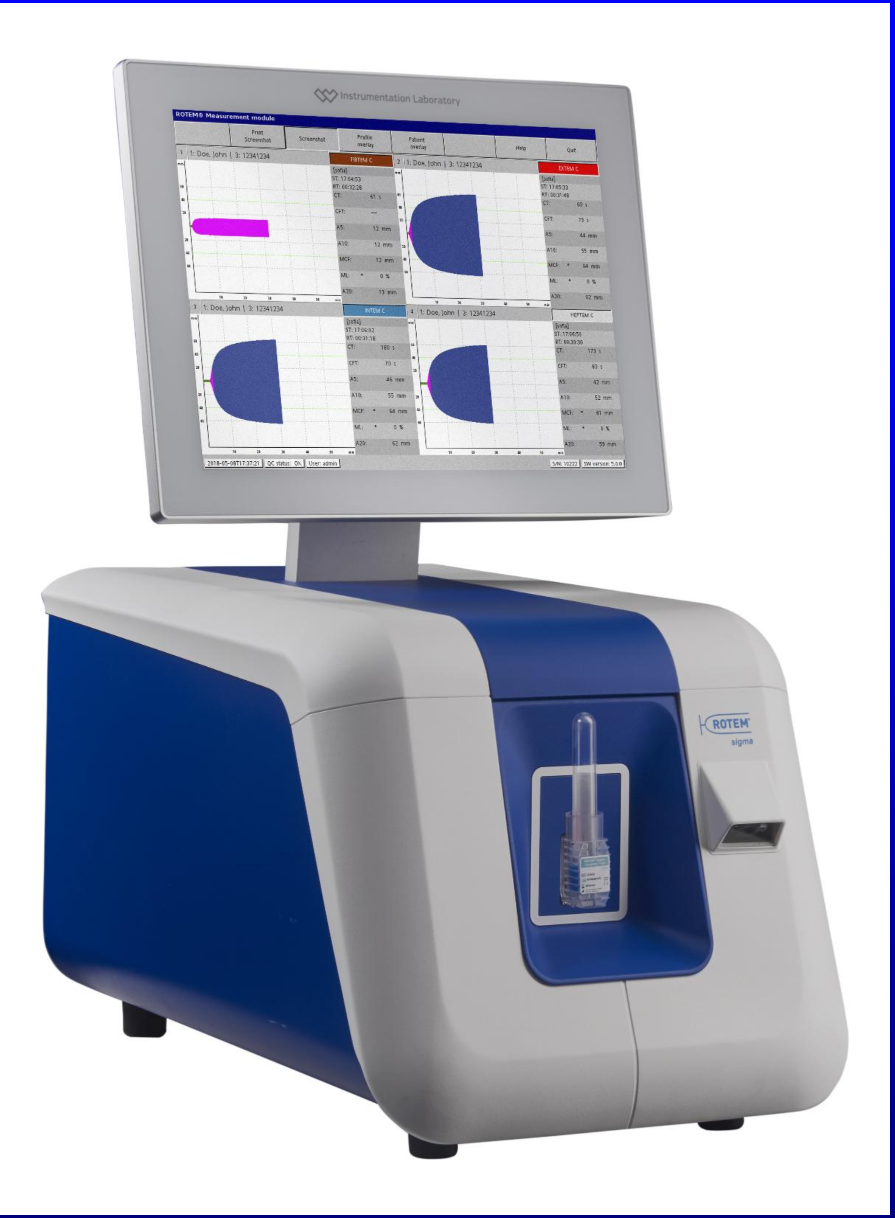
ROTEM Sigma With Graphs Displayed:

FIBTEM

EXTEM

INTEM

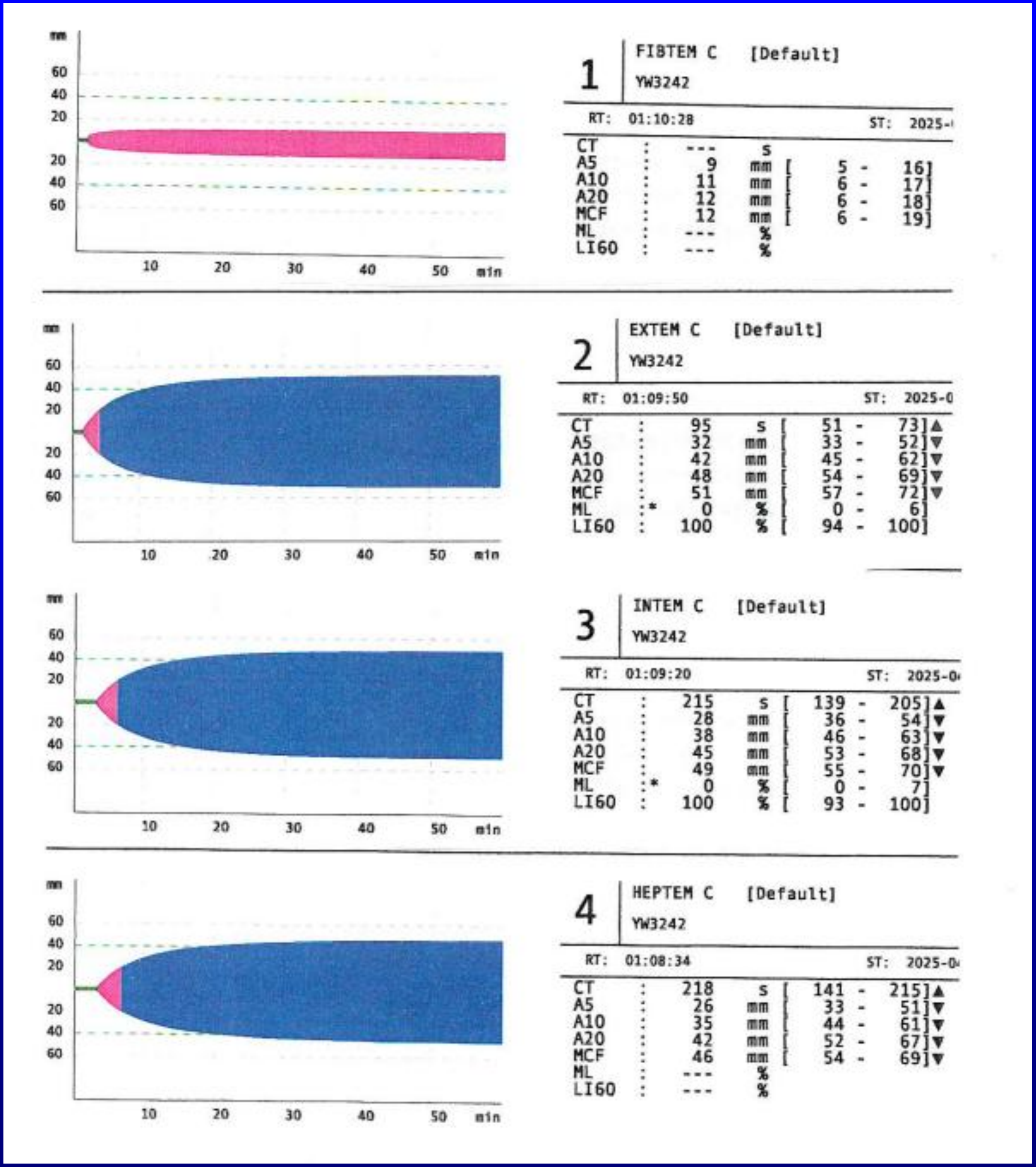
HEPTEM



Rotem Sigma Graphs

Interpretation:

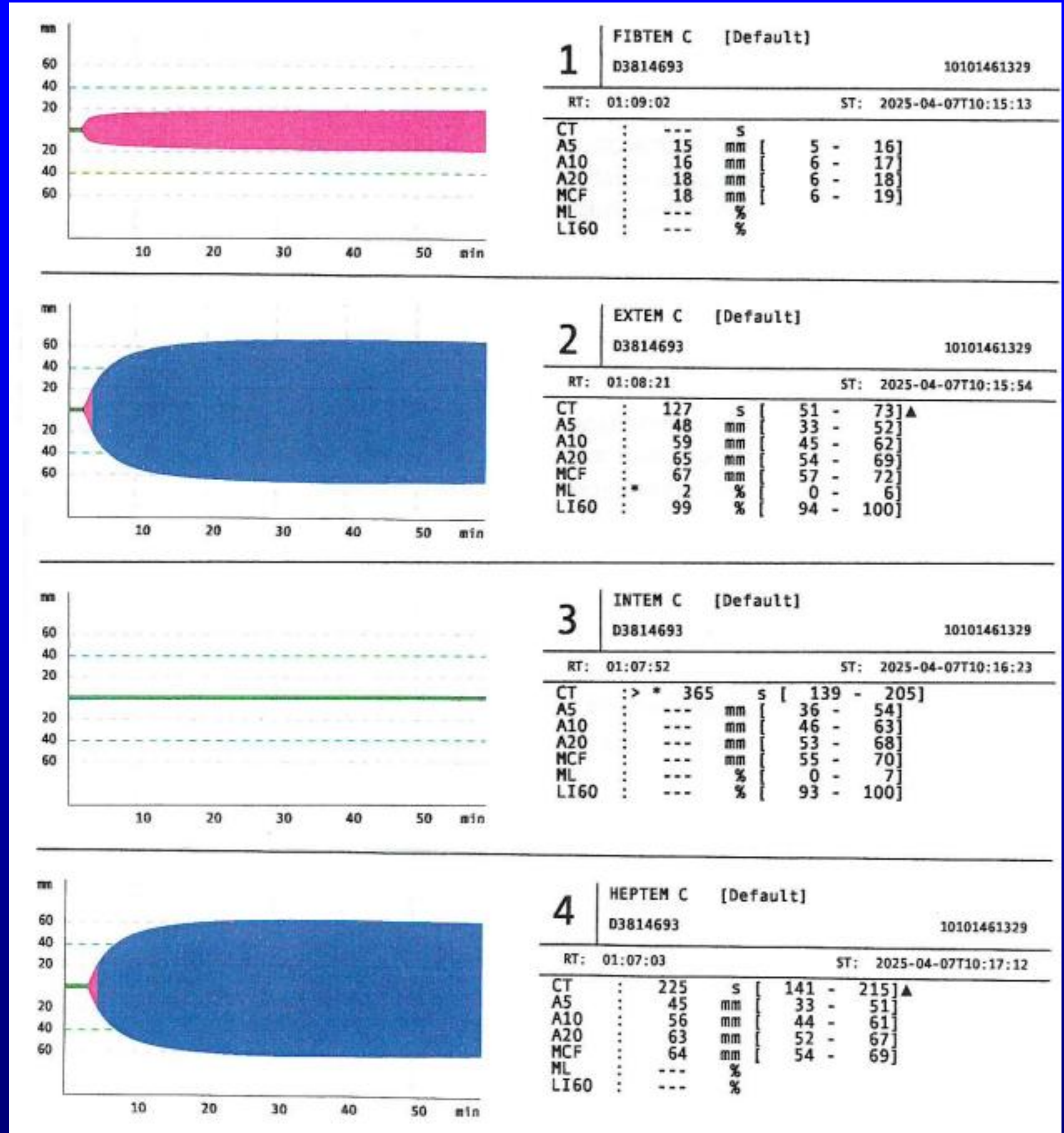
- **Adequate fibrinogen**
- **Slight factor deficiency:** *Prolonged CTs*
- **Low platelet activity?:** *Low EXTEM and INTEM A5s/A10s w/ Normal fibrinogen*



Rotem Sigma Graphs

Interpretation:

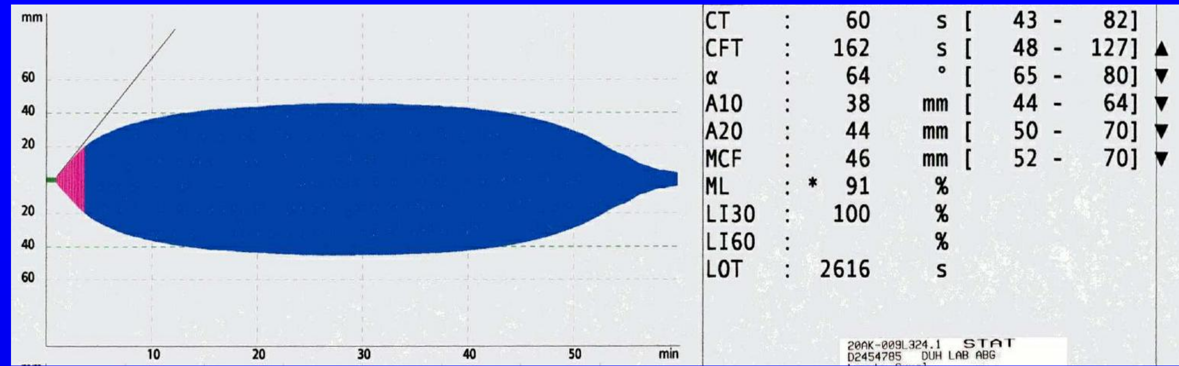
- **Normal fibrinogen**
- **Slightly weak clotting factors:** *prolonged CT*
- **Normal platelet activity**
- **Patient on heparin:** *Flat INTEM*



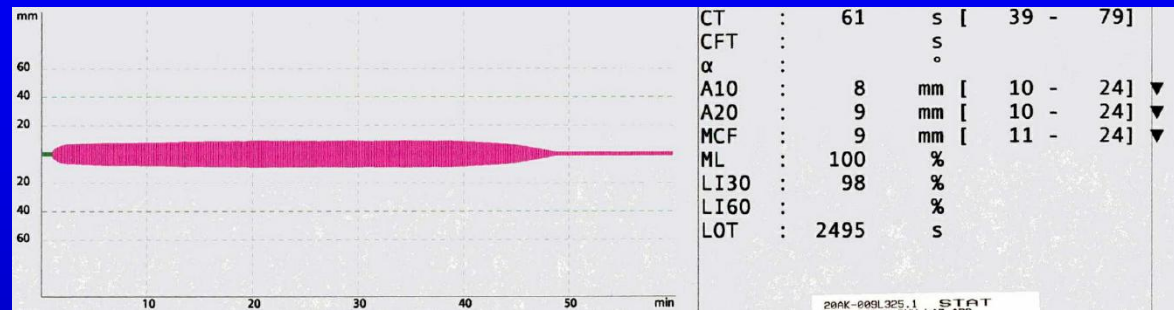
Rotem Case CL

67 yo F; Liver Txp

EXTEM at 12:30

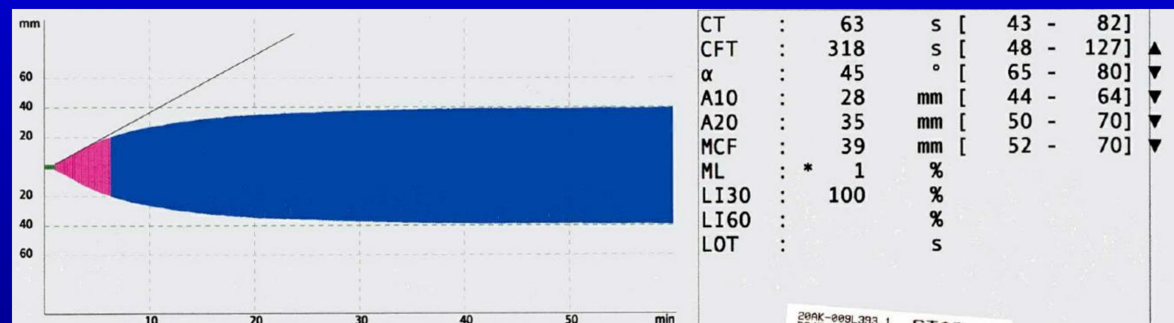


FIBTEM at 12:30



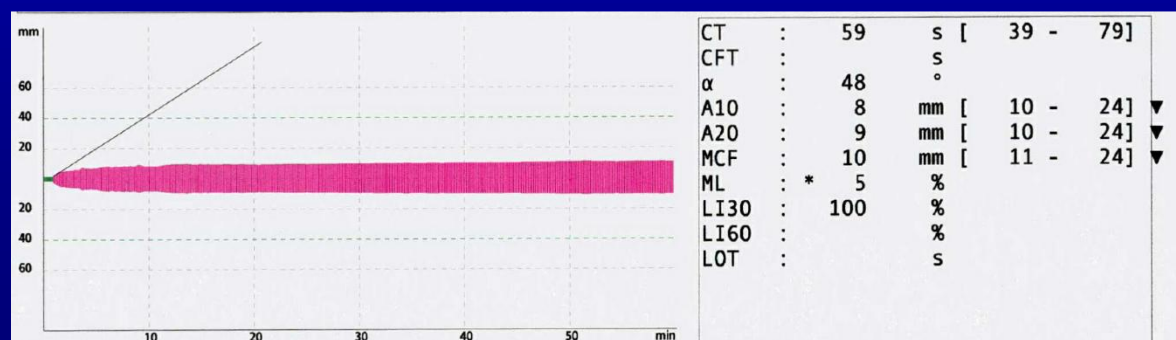
TxA given

EXTEM at 14:30



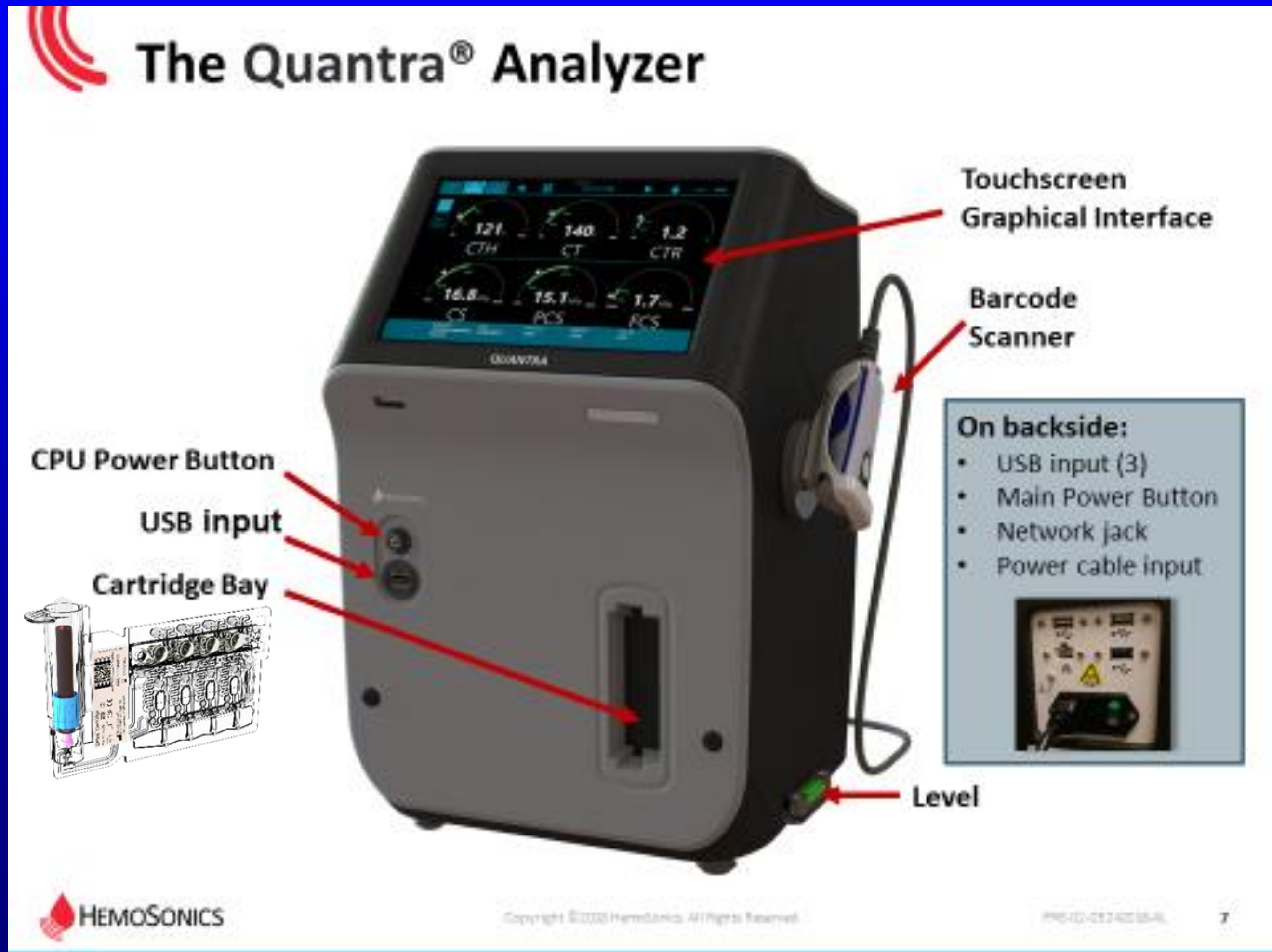
FFP, Cryo, Plts given

FIBTEM at 14:30

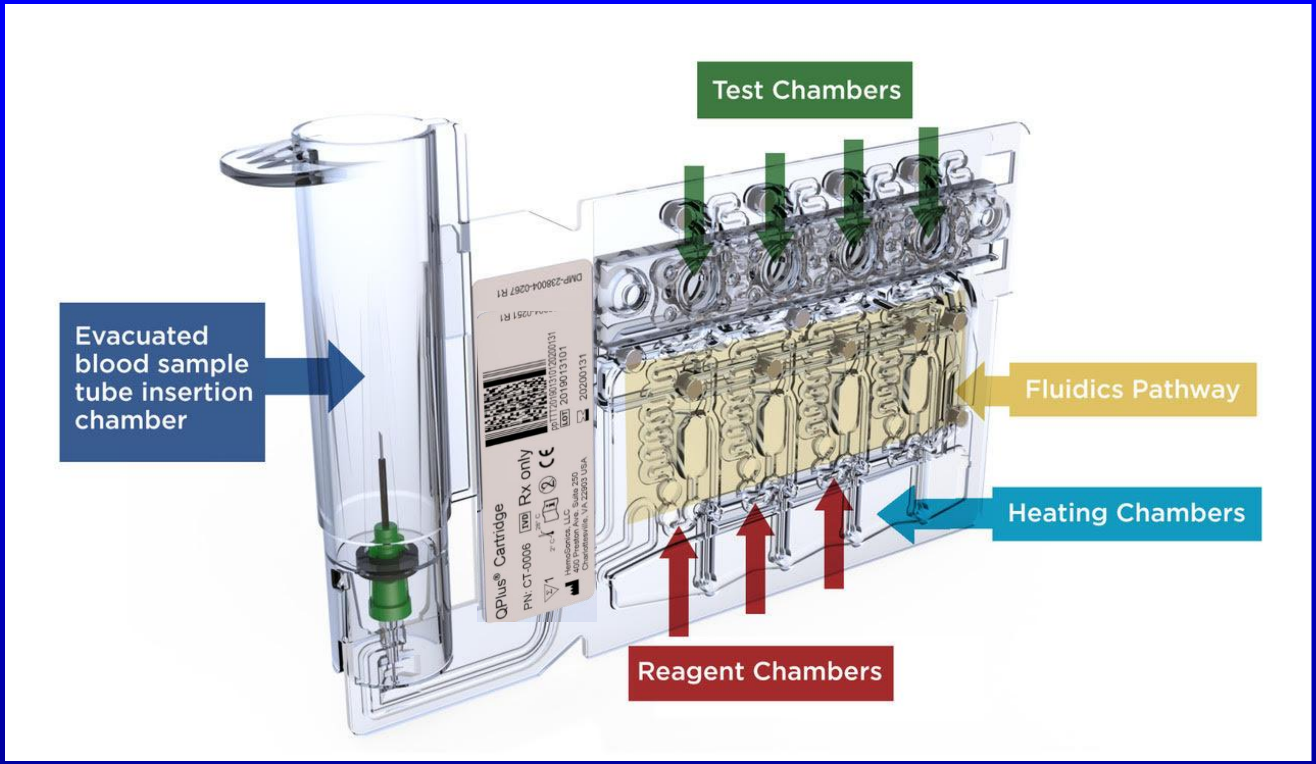


Hemosonics Quantra Analyzer and Cartridge

19.5 inches high

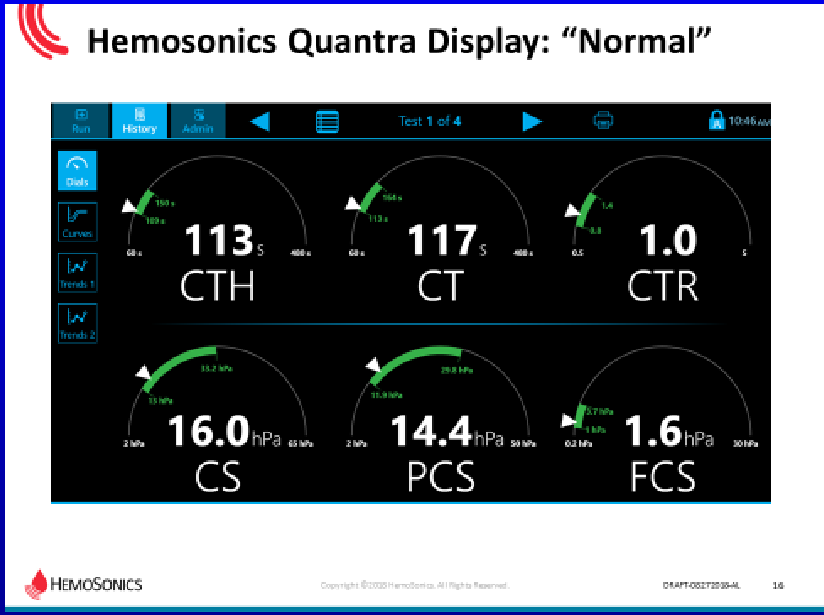


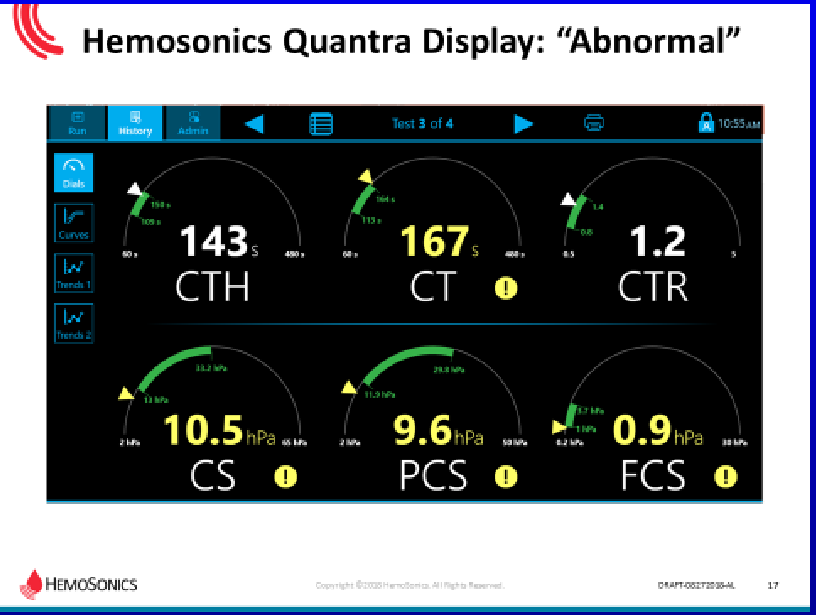
Quantra® QPlus® Cartridge



- 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

Normal and Abnormal Result Displays for Quantra





Comparison of TEG, ROTEM, and Quantra

Parameter Detected	TEG 6S Global Hemostasis (HN)	ROTEM Sigma*	Quantra System
Clotting Factors	R time (Kaolin; min)	INTEM/EXTEM CT (elagic acid, Ca^{++} (sec)	CT:: Clot Time
Clotting factors w/ heparin removed	Kaolin R + Heparinase R (min)	HEPTEM: CT w/ heparinase (sec)	CTH: Clot Time with Heparinase CTR: Clot Time Ratio (CT/CTR)
Overall clot strength	TEG MA (kaolin + tissue factor)	EXTEM A5/10/20: Tissue factor, Ca^{++}, polybrene (mm)	CS: Clot Stiffness
Fibrinogen activity (w/ platelet inhibitor	Functional Fibrinogen MA (tissue factor + abxicimab; Reopro)	FIBTEM A10/A20: cytochalasin D (mm)	FCS: Fibrinogen Contribution (abxicimab)
Platelet contribution?	Platelet contribution (not calculated)	PLTEM: EXT – FIBTEM (not calculated)	PCS: Platelet Contribution (CS - FCS)
Fibrinolysis	*LY30(%)*	EXTEM ML/LI60 (%)	*Clot Stability to Lysis (CSL)*

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.***
  - ***Wasted/lost cartridges: ~$90 each.***
  - ***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.

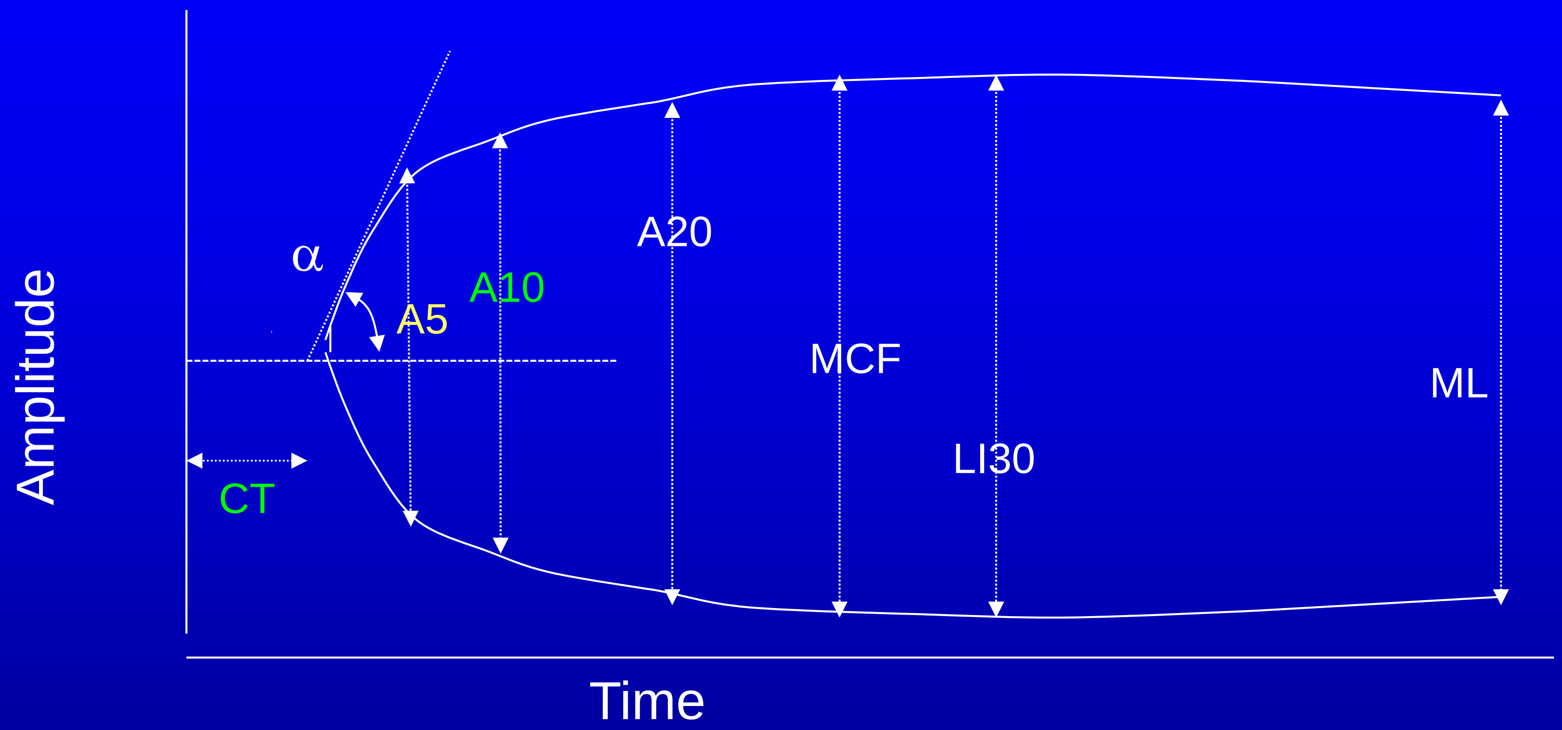
That’s All!

Now time for questions…

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

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