

Blood Gas Testing and Other Contemporary Issues in POCT in the Operating Room:

- *Evaluating POC Models for Blood Gas Testing**
- *Need Better POC Methods for PTH**
- *Monitoring Clotting Status in the Bleeding Patient**

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Disclosures

- Receive research support from Instrumentation Laboratory.
- Receive consultation fees from Roche Diagnostics, Becton-Dickenson, and Instrumentation Laboratory.

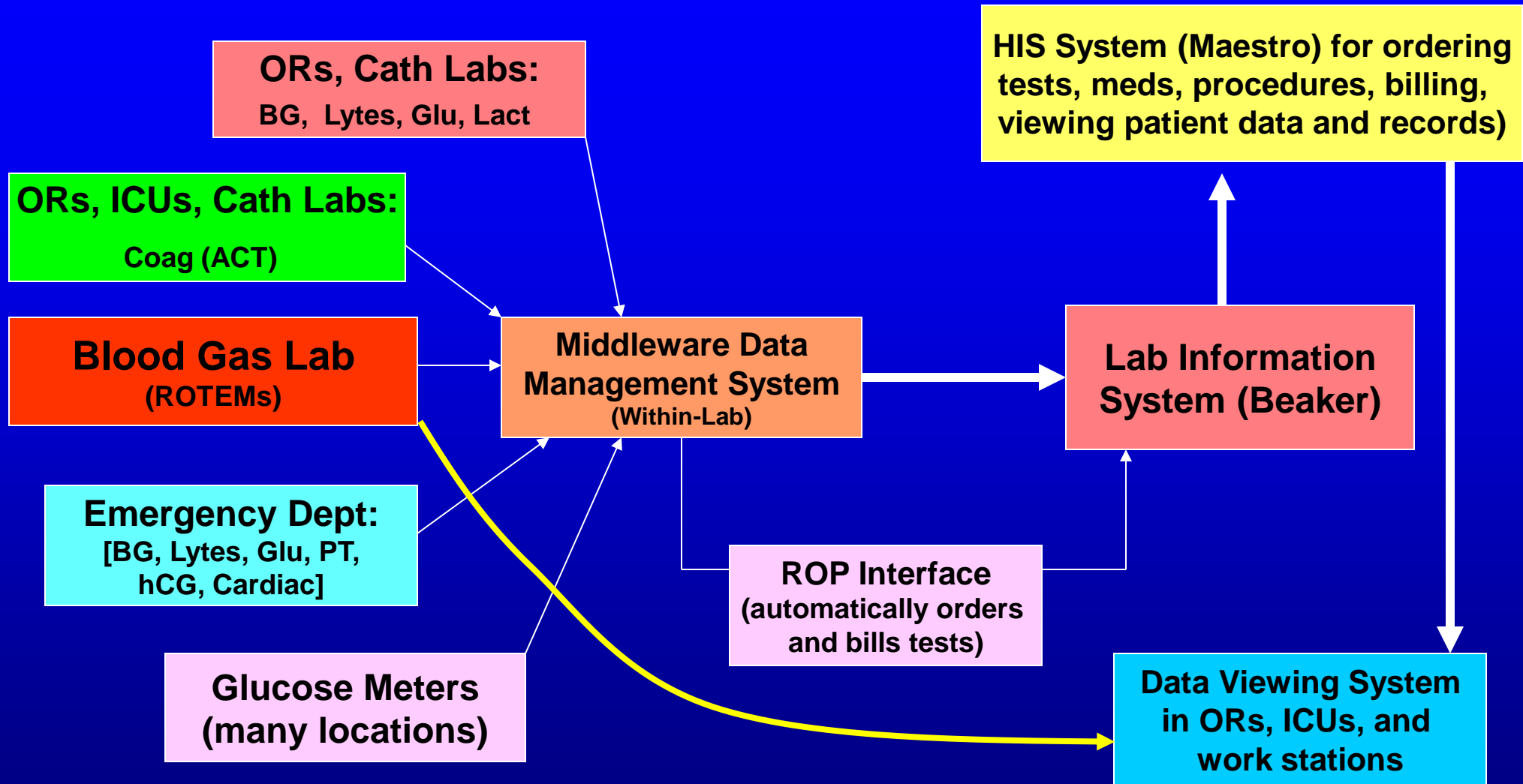
Objectives for Talk

- Evaluate different models of POC blood gas (etc) testing in the operating rooms for costs, test menu, and test volumes.
- Describe the need for intra-operative PTH measurements.
- Describe an ideal POC testing device for PTH measurements.
- Describe the operation and coagulation parameters reported by the ROTEM and TEG thromboelastography systems.
- Describe how ROTEM results guide therapy for bleeding during open-heart surgery.

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:**
 - No puzzling results to investigate
 - Results agree with laboratory results
- **POC testing improves finances, outcomes, and/or satisfaction of users/patients.**

Connectivity Is Key to POC Testing



**In 2013, Duke Medical Center Opened a
Major Addition: the Duke Medical Pavilion
(Blood Gas Lab on 6th Floor)
Duke Cancer Center at Left**



The Duke Medical Pavilion: A Major Addition to Duke Medical Center

- **In July 2013, the Duke Medical Pavilion opened.**
- **Many new operating rooms: all on an expanded 3rd floor connecting the older Duke North Hospital and the new Duke Medical Pavilion.**
- **The Blood Gas Lab moved from the 3rd floor Duke North Hospital to the 6th floor of the new Duke Medical Pavilion.**
 - **Lab now close to ICUs, but further from ORs.**
- **More POC testing would be needed.**

2013: New OR Locations and Estimated POC Blood Gas Test Volumes

Old Locations	New Locations	Old Test Volumes (Model 1a and 2a)	New Test Volumes (est) (Model 1b and 2b)
OR 6	OR 33	3600/yr	1500/yr
OR 7	OR 34	3600	600
OR 8	OR 35	3600	900
OR 9	OR 36	3600	900
OR 37	OR 37	5000	3000
	DMP OR 49	0	1200
	DMP OR 50	0	2400-3000
	DMP OR 51	0	900
	DMP OR 54	0	900
	DMP OR 55	0	2400-3000
	DMP OR 56	0	2400
	DMP OR 57	0	2400-3000
	Pediatric ORs	0	2400

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

Model 1 (a and b): Single-use cartridges in hand-held device.

Model 2 (a and b): Multi-use reagent packs in stationary device.

Blood Gas Single-Use POC Model (1a and 1b)

- **Blood gas analyzers with single-use cartridges used in operating rooms:**
 - Used by perfusionists, CNAs, and (if needed) anesthesia technicians.
 - Supplies, maintenance, and regulatory responsibilities under Clinical Laboratories.
- **Completed test is automatically ordered, billed, and archived in information system.**

Blood Gas Multi-Use POC Model #2a (1985-2013)

- **Blood gas analyzers with multi-use reagent packs used in 5 (very busy) cardiac/thoracic operating rooms and 1 peds cardiac cath lab:**
 - Used by perfusionists, anesthesia technicians, and cath lab personnel.
 - Maintenance, quality control, and regulatory responsibility are under Clinical Laboratories.
- **Completed test is automatically ordered, billed, and archived in information system.**

Blood Gas POC Model #2b (2014--)

- **Blood gas analyzers with multi-use reagent packs used in 14 cardiac/thoracic operating rooms and 1 peds cardiac cath lab:**
 - Used by perfusionists, anesthesia technicians, and cath personnel.
 - Maintenance, quality control, and regulatory responsibility are under Clinical Laboratories.
- **Completed test is automatically ordered, billed, and archived in information system.**

Disclaimer:

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

CVOR Blood Gas POC Model #1a

Blood Gas Analyzers with Single-Use Test Cartridge

Test Card Menu	Cost / Panel	Test Vol / yr	Yearly Cost (\$)	Average Cost/Test Menu*
pH, $p\text{CO}_2$, $p\text{O}_2$, Na, K, Ca_{ion} , calc tCO_2 , sO_2 , Hct/Hb	\$10.00	18,500	\$185,000	\$10.50*
pH, $p\text{CO}_2$, $p\text{O}_2$, lact, calc HCO_3 , sO_2	\$6.60	18,500	\$122,100	\$7.10*
Controls, Cals, etc			\$800	
6 instruments (yearly cost rate)			\$8,900	

* Includes cost/yr of analyzers, test cartridges, and controls.

POC Model #2a: 5 Blood Gas Analyzers with Multi-Use Packs (data from 2012)

Test Menu	Location	OR Test Vol / yr	Yearly Cost (\$)	Cost/ panel
OR Panel	OR 6	3600	\$18,000	\$5.00
"	OR 7	4100	"	\$4.40
"	OR 8	3200	"	\$5.63
"	OR 9	3000	"	\$6.00
"	OR 37	4000	"	\$4.50
	Peds Cath	600	"	\$30.00
TOTALS		18,500	\$108,000	\$5.85

OR Panel: pH, $p\text{CO}_2$, $p\text{O}_2$, Na, K, ion Ca, glucose, lactate, tot Hb, %O₂Hb, %COHb, %metHb

CVOR Blood Gas POC Model #1b

Blood Gas Analyzers with Single-Use Test Cartridge

Test Card Menu	Cost / Panel	Test Vol / yr	Yearly Cost (\$)	Average Cost/Test Menu*
pH, $p\text{CO}_2$, $p\text{O}_2$, Na, K, Ca_{ion} , calc tCO_2 , sO_2 , Hct/Hb	\$10.00	28,550	\$285,500	\$10.80*
pH, $p\text{CO}_2$, $p\text{O}_2$, lact, calc HCO_3 , sO_2	\$6.60	28,550	\$188,400	\$7.40*
Controls, Cals, etc			\$2,000	
14 instruments (yearly cost rate)			\$20,500	

* Includes cost/yr of analyzers, cartridges, and controls.

POC Model #2b: 14 Blood Gas Analyzers with Multi-Use Packs

Test Menu	Location	OR Test Vol / yr	Yearly Cost (\$)	Cost/ panel
OR Panel	OR 33	1400	\$18,000	\$12.85
“	OR 34	2000	“	
“	OR 35	600	“	
“	OR 36	320	“	\$56.25
“	OR 37	2650	“	
“	OR 49	980	“	\$18.37
“	OR 50	4100	“	\$4.40
“	OR 51	2500	“	
“	OR 53	1200	“	
“	OR 54	3100	“	\$5.80
“	OR 55	3000	“	
“	OR 56	3800	“	\$4.75
“	OR 57	550	“	
“	Peds OR #6	1750	“	
“	Peds Cath	600	“	\$30.00
TOTALS		28,550	\$270,000	mean = \$9.45

Summary of Relative Costs of POC Blood Gas/Lytes: *Models vs Test Volumes*

System	# Analyzers	Test Volume / Year	Average Cost / Test
#1a (single-use)	6	18,500	\$10.50
#1b (single-use)	15	28,550	\$10.80
#2a (multi-use)	6	18,500	\$5.85
#2b (multi-use)	15	28,550	\$9.45

Notes:

1. The test menus are distinctly different between the single-use and multi-use cartridges.
2. Assumed the cost per cartridge stayed the same for each test volume.

The Duke Clinical Pediatric Lab (CPED)

- **A very busy lab offering chemistry, hematology, urinalysis, drugs, fetal/maternal testing and phlebotomy.**
- **Located amidst the PICU, NICU, Newborn Nursery, L&D on 5th floor of the Duke North Hospital for over 30 years.**
- **Recently a Peds Cardiac ICU (PCICU) was moved to expanded space on 4th floor.**
 - **PCICU now needs POC testing.**
- **Also, the Neonatal ICU now wants POC testing.**
- **More challenges for POC vs Lab testing:**
 - **One multiple-use stationary analyzer vs a few “hand-held” analyzers.**
 - **Test menus needed?**

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

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

Pros/Cons of POC Models #2:

Multiple-Test Reagent Pack System

- Advantages

- Cost, throughput, speed, and ease of use 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.

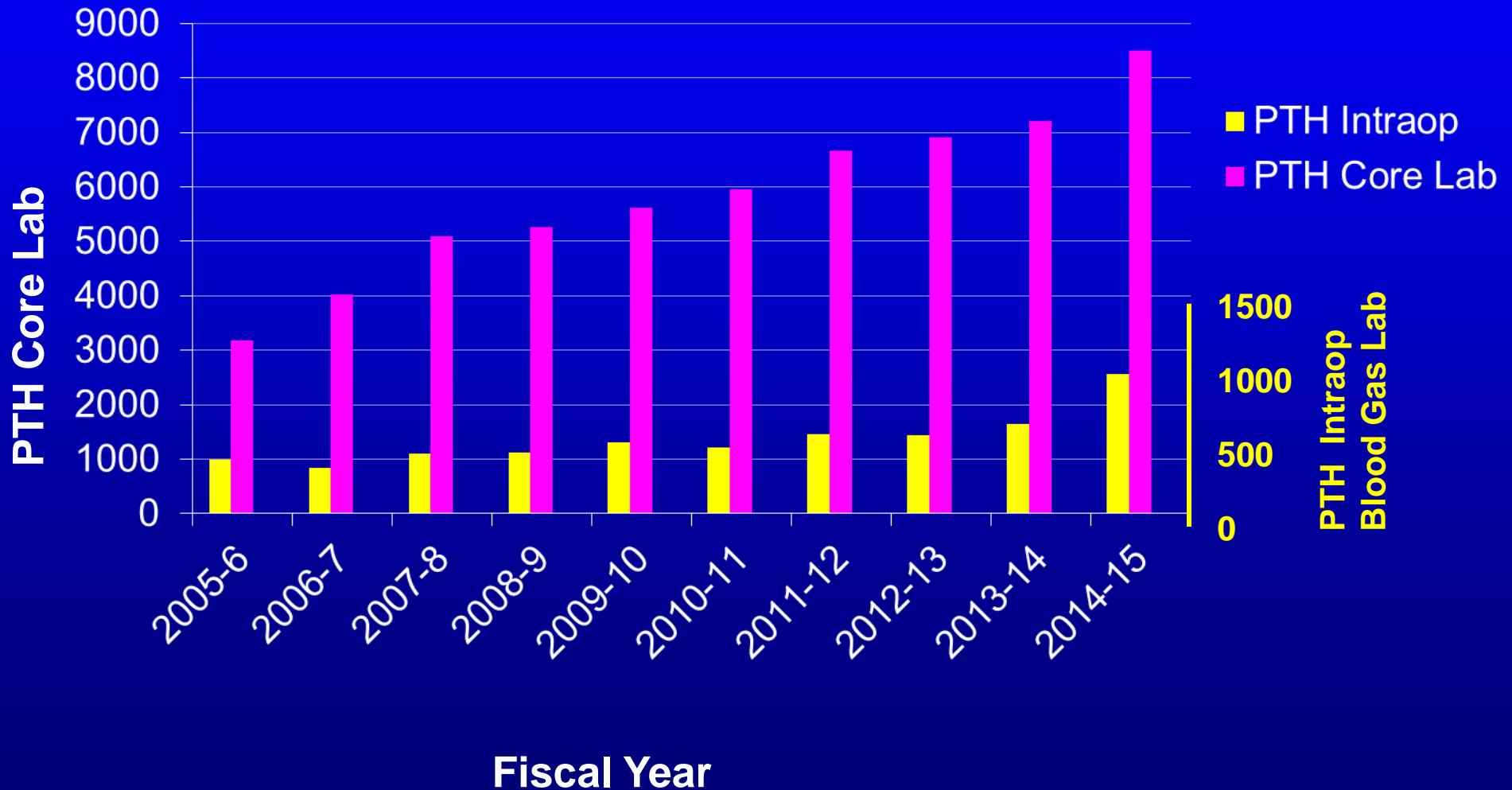
- Disadvantages

- Very costly for low test volumes.
- Changing reagent packs takes ~40 min.
- Not portable.
- ~~Requires IQCP~~ ☹️ May not require IQCP 😊

Opportunities for Improved Assay Devices for Intraoperative Parathyroid Hormone (ioPTH) Measurements

PTH Workload at Duke Med Center:

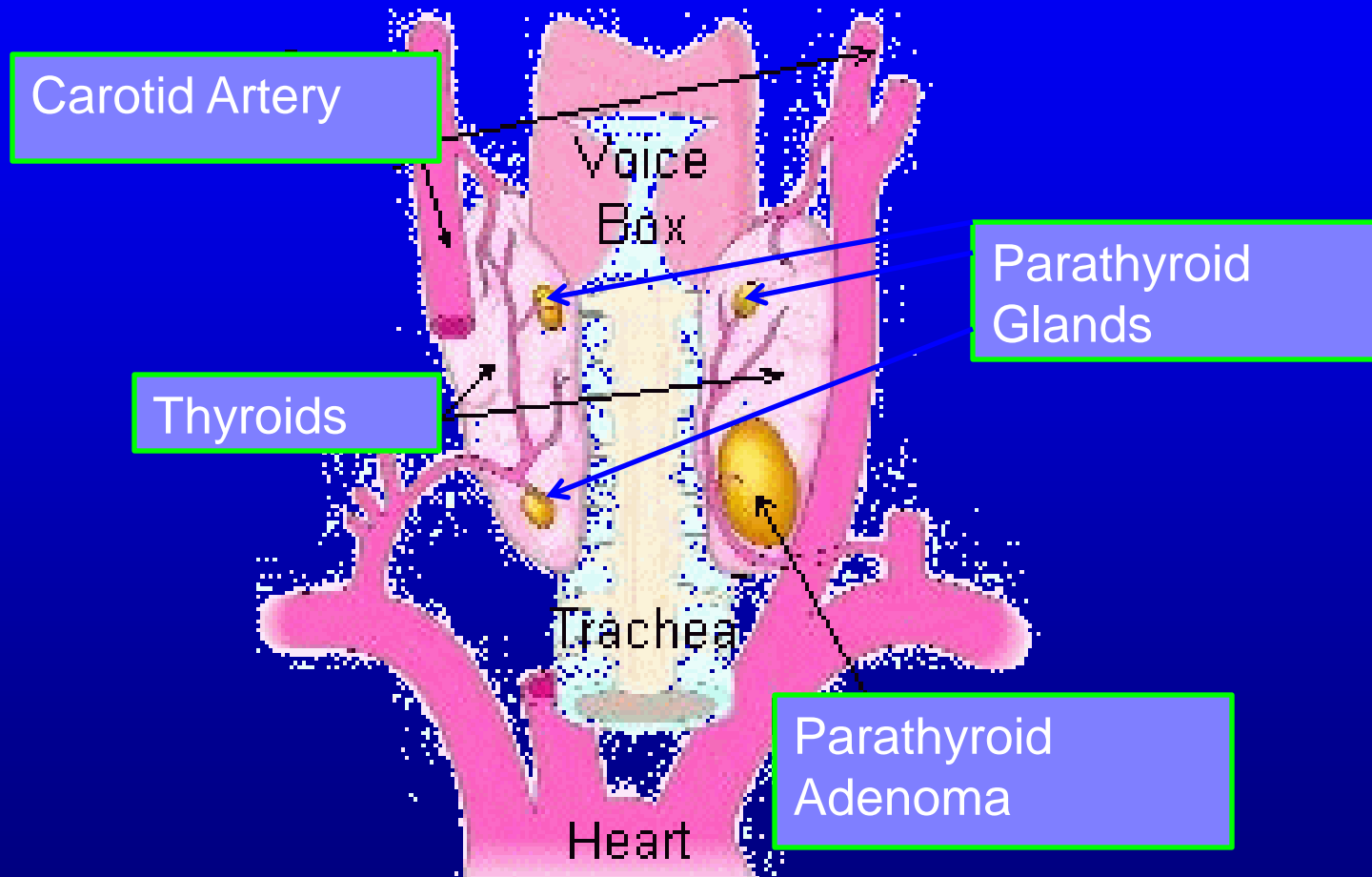
Core Lab and Intraop PTH



Facts about Surgery on the Parathyroid Glands

- The 4 parathyroid glands located behind the thyroid glands:
 - Each gland about the size of a grain of rice
 - Not related to thyroid glands in function
 - In ~90% of cases, only one PT gland is hyperactive.
- Types of hyperparathyroidism:
 - Primary HPTH due to parathyroid adenoma (a benign tumor)
 - Secondary HPTH due to renal disease.
- Surgery is the only treatment for hyperparathyroidism.

Rear-View Diagram of Parathyroid Glands in Relation to Thyroid Glands



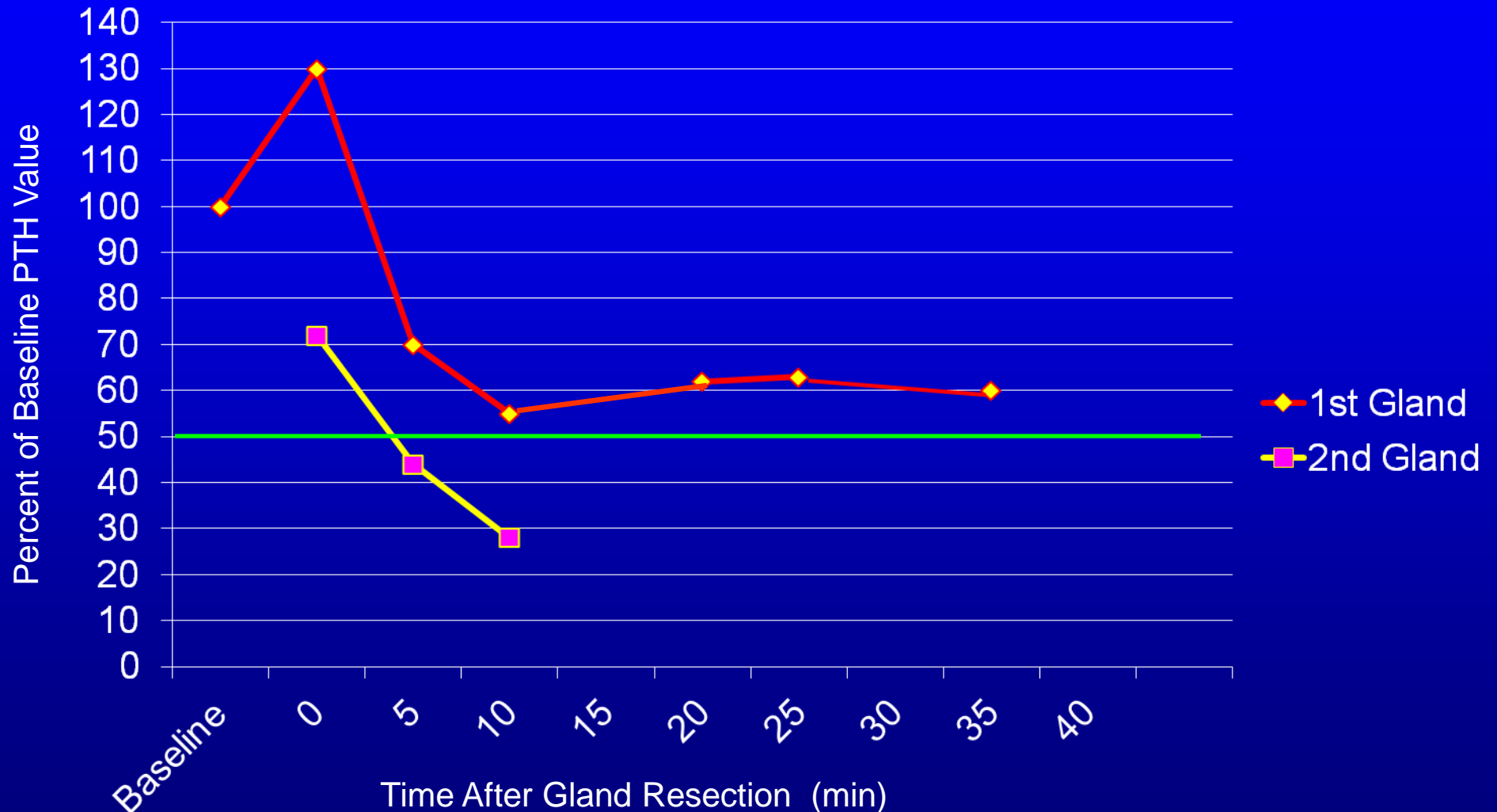
Challenges in Providing Rapid PTH Results During Surgery

- **Results needed as soon as possible:**
 - Best available TAT is still 10-11 min.
 - POC location is highly desirable.
- **Analyzer designed for main lab (not ideal for POC):**
 - Requires a medical technologist to operate.
 - Specimens must be centrifuged.
 - Medical technologist is at POC and cannot help with other workload.
 - Requires 1.5-2 hrs (in addition to testing time) to set-up and shut down analyzer.
- **Test volume is increasing..**

Using Intraoperative PTH Measurements

- Formerly, 4-5 PTH measurements were taken:
 - Two baseline levels: (1) at induction of anesthesia; (2) after parathyroid glands are isolated.
 - 5 min post resection of parathyroid gland.
 - 10 and 20 min post resection of gland.
- Interpretation:
 - PTH level at 10 min should be $\leq 50\%$ of the baseline value.
 - If not, wait a period of time then measure PTH again.
 - If level still not $\leq 50\%$ of baseline, the neck is explored further for other abnormal parathyroid glands.
- Current use: More PTH measurements taken, including some on minced tissue samplings.

Percent Change in Intraoperative PTH in Patient with Two Enlarged Glands



Benefits of Intraoperative PTH Testing

- **Helps identify multiple-gland disease that is present in approximately 12% of patients with primary hyperparathyroidism.**
- **Helps surgeon know that parathyroidectomy has been successfully completed:**
 - **Avoids having to tell the patient the next day that the operation did not cure the disease and they will need another operation.**

Sample Stability for PTH

- **PTH is not stable in blood circulation**
 - **½ life of 5-10 min.**
- **Depending on the assay, PTH is stable in serum/plasma for about 8 hours at RT.**
- **EDTA appears to stabilize PTH in plasma for 24 – 48 hours at RT.**

What Is Needed for an Intraoperative PTH Test System?

- Small and portable analyzer.
- Easy test setup after days of non-use.
- No water or plumbing needed.
- No reagent preparation.
- Analysis on whole blood:
 - Saves time AND you do not need a centrifuge.
- Results ASAP, but ideally in less than 10 min.
 - Bench-type analyzer(s) has very few desirable features, but assay takes about 11 min.

Reducing Transfusions in Cardiac OR by Thromboelastography: TEG and ROTEM

- Cardiac surgery accounts for about 1/3 of all intraoperative transfusions.
- Mortality correlates linearly with the number of transfused blood products.
- When to give RBCs, platelets, fresh frozen plasma (FFP), fibrinogen (as cryoprecipitate)?

Evaluating Need for Fibrinogen/Cryoprecipitate in OR

- When to give cryoprecipitate (fibrinogen)?
- Multiple problems with giving cryo:
 - *1 dose of cryo exposes recipient to 10 donors!*
 - Giving cryo empirically is often wasteful (\$\$).
 - *But not giving cryo when needed can cause major problems.*
 - Cryo has to be thawed to use (takes 20-30 min) and cannot be refrozen.
- A rapid WB fibrinogen assay would be very helpful.

Picture of the TEG Analyzer

(About 12 inches high)

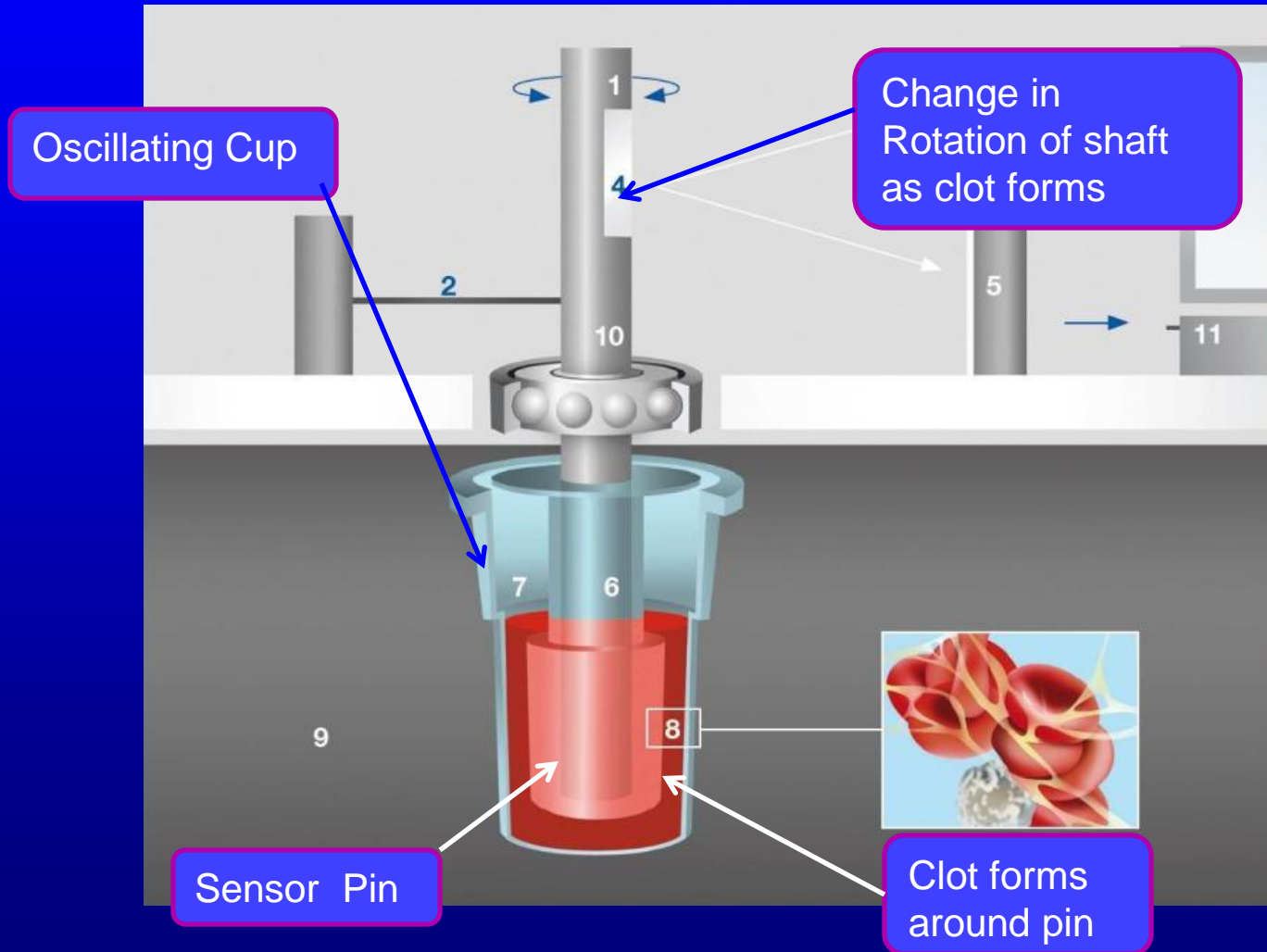


TEG Analyzer:

Operational features:

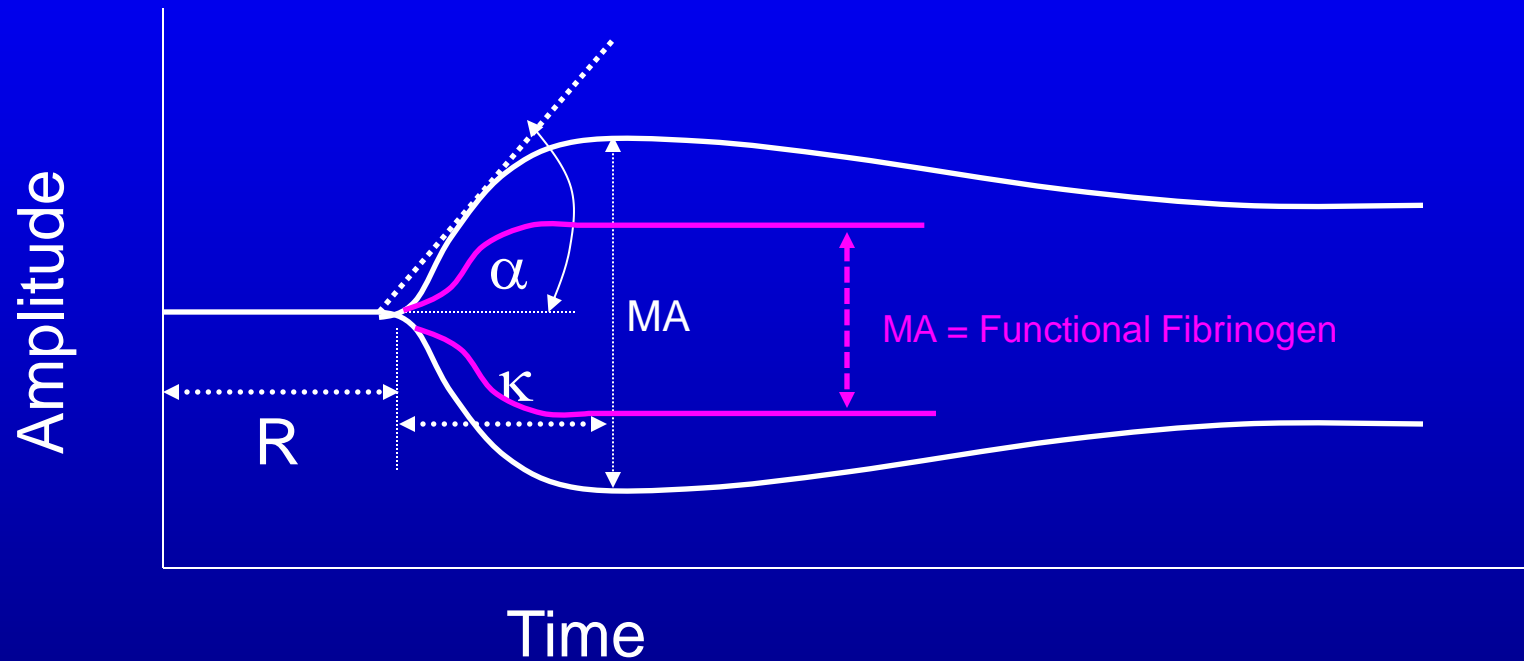
- 2 test channels
- Automated testing system
- Liquid QC every 8 hours.
- Bar code scanner

Concept of Oscillating Thromboelastography (TEG)



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

Adding Platelet-Inhibiting Reagent in Rotational Thromboelastometry Gives a Functional Fibrinogen



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

ROTEM® Thromboelastometry



ROTEM® *delta*

Operational features:

4 test channels

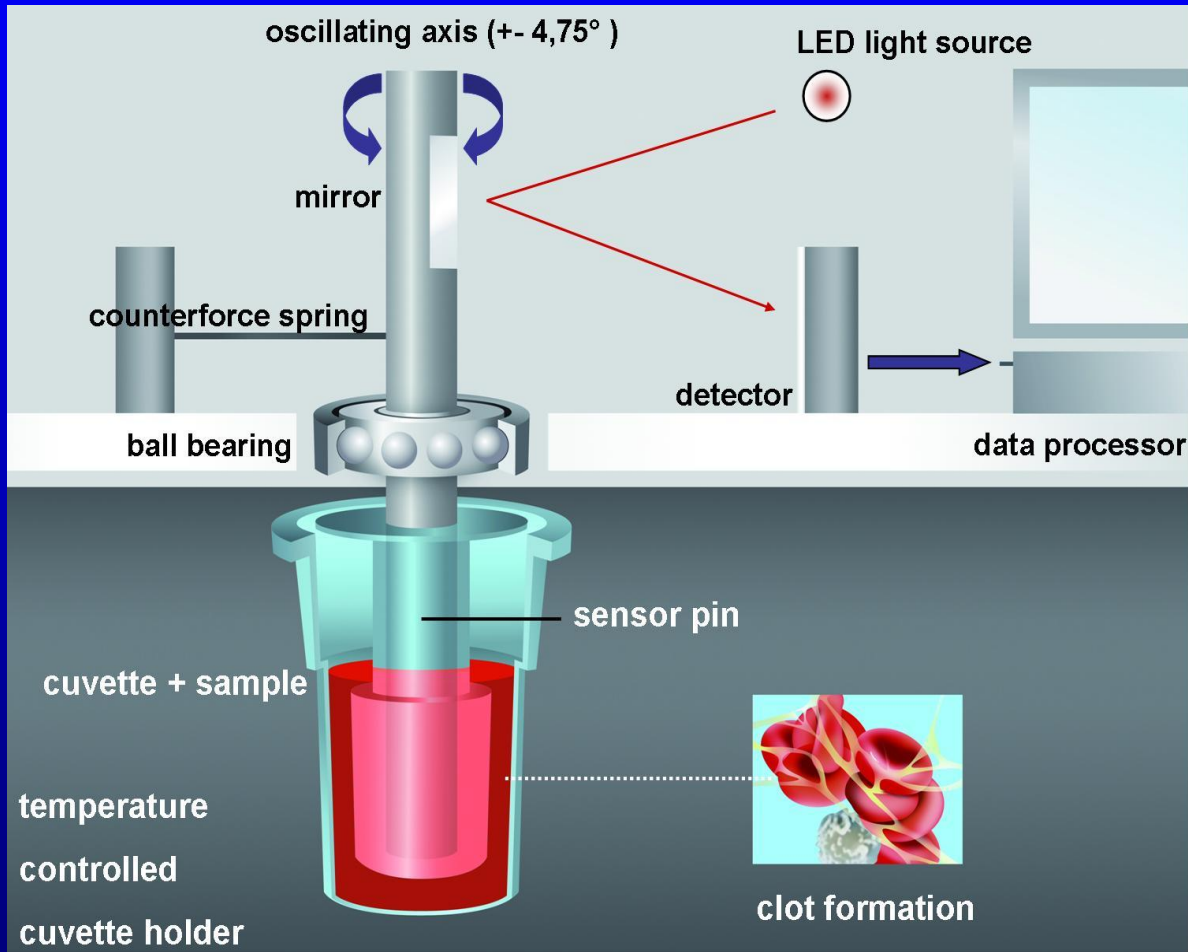
Automated testing system

Touch screen monitor

Weekly LQC

Bar code scanner

ROTEM® Thromboelastometry Design



ROTEM's shaft, spring, and ball bearing technology detects clot formation and uses an inverse function to display a tracing that resembles clot formation.

It is less susceptible to movement or vibrations that can affect other viscoelastic methods.

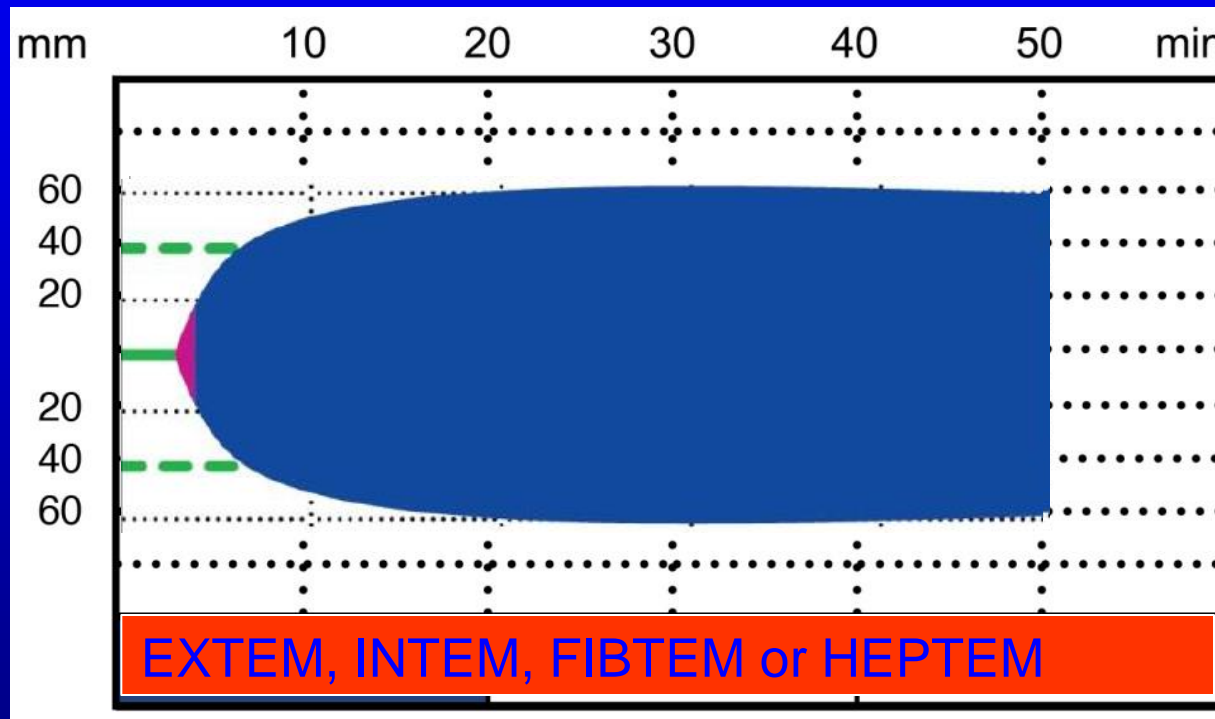
The ROTEM Graph:

Records the Change in Amplitude vs Time

Time (results in sec)



Amplitude
(in mm)



The greater
the
amplitude
the firmer
the clot

ROTEM® Assays

EXTEM – Extrinsic activation (via Tissue Factor)

FIBTEM – Detects fibrinogen activity by adding
Cytochalasin D to inhibit platelets.

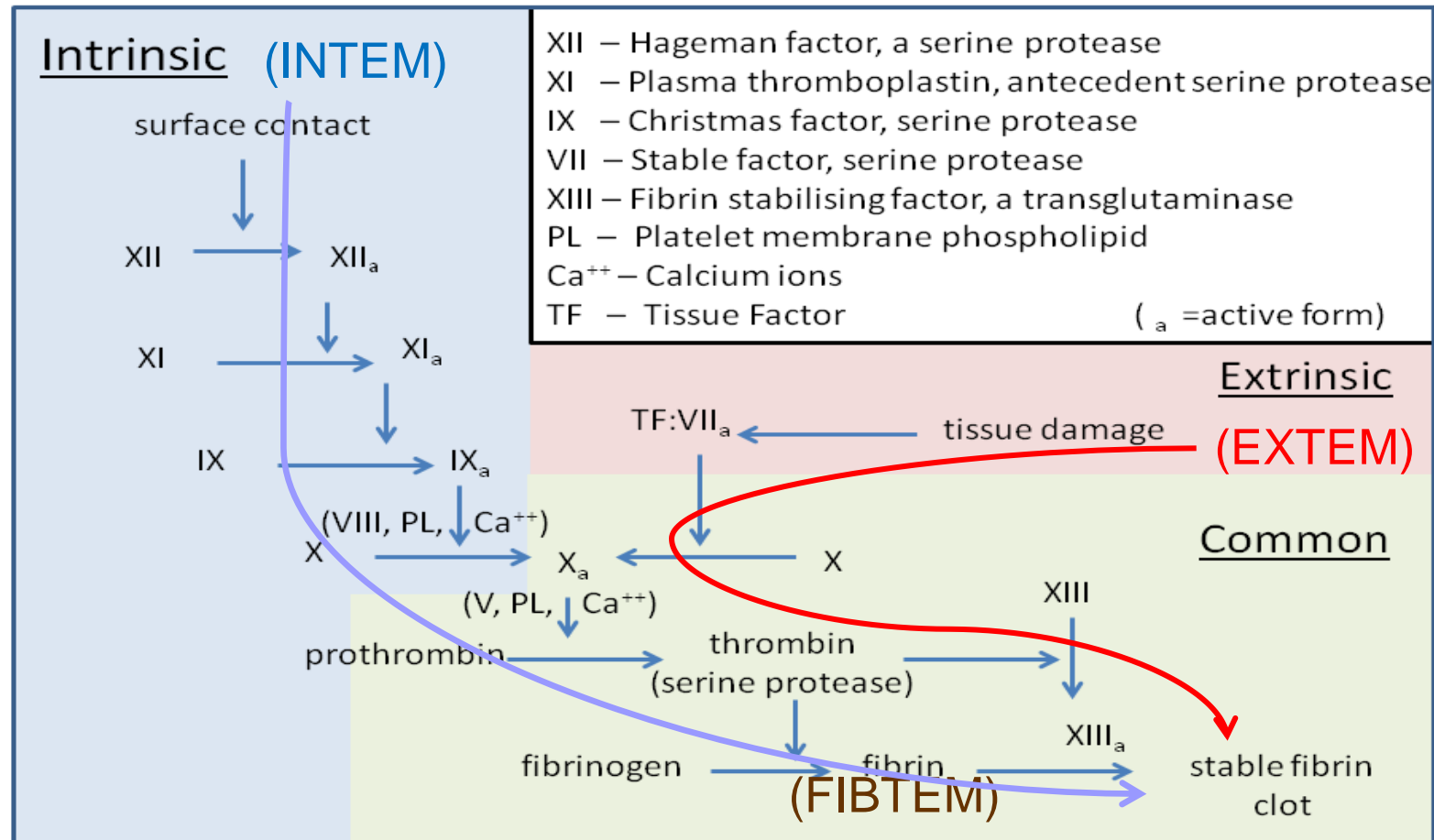
INTEM – Intrinsic activation (via Ellagic Acid)

HEPTEM – adds Heparinase to remove heparin
from sample.

APTEM – adds aprotinin to inhibit hyperfibrinolysis

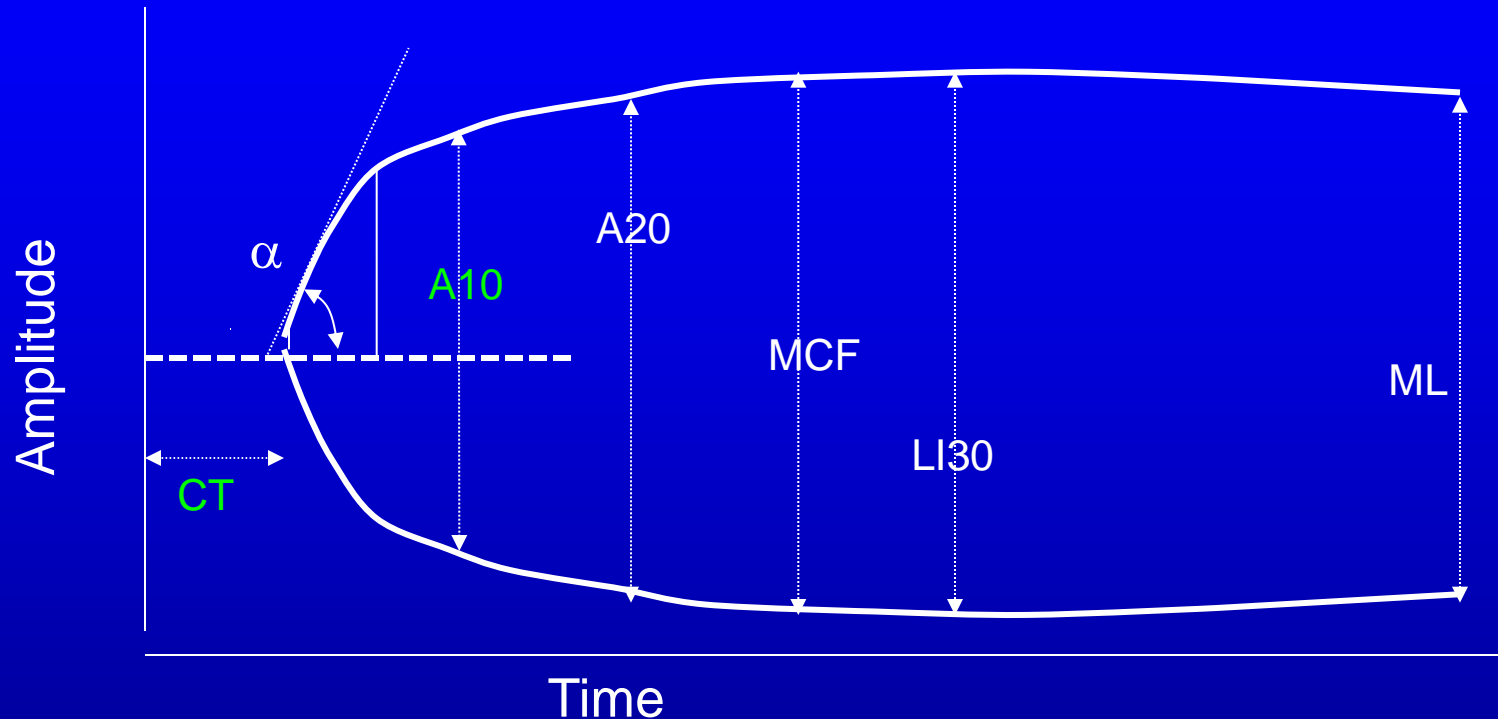
Coagulation Cascade Related to ROTEM Tests

The three pathways that makeup the classical blood coagulation pathway



Pallister CJ and Watson MS (2010). *Haematology*. Scion Publishing. pp. 336–347. [ISBN 1-904842-39-9](https://doi.org/10.1080/17445019.2010.504842).

Parameters in The ROTEM Graph



CT – start of clot formation (sec)

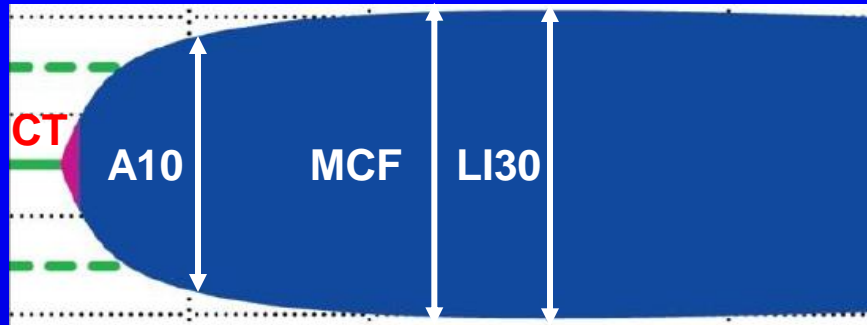
α –angle – tangent to the clotting curve at 2mm (deg °) – Related to fibrinogen activity

A10, A20, MCF (maximum clot firmness) – Amplitude (mm) at 10 min, 20 mins, or max.

LI30– Lysis Index (% of clot remaining 30 mins after CT)

ML – Maximum Lysis (% of lysis)

ROTEM Results and Clinical Interpretations



Parameter	Change	Suggested Clinical Interpretation
CT_{EXTEM}	Prolonged	Intrinsic factor deficiency (or influence of heparin)
CT_{INTEM}	Prolonged	Extrinsic factor deficiency.
$A10_{\text{EX}}$ (or MCF_{EX}) $A10_{\text{IN}}$ (or MCF_{IN})	Reduced	Poor clot firmness due to decreased: platelets, fibrinogen, and/or Clot Factors
$A10_{\text{FIBTEM}}$, MCF_{FIBTEM}	Reduced	Poor fibrin contribution to clot firmness.
$A10_{\text{EXTEM}} - A10_{\text{FIBTEM}}$	Reduced	Poor platelet contribution to clot firmness
LI30	>15%	Hyperfibrinolysis (RARE)

ROTEM Parameters Used in IntraOP and P-P Bleeding Algorithm: CT, A10 and ML:

If $CT_{EX} > 70$ sec: give FFP 10-15 mL/kg (or profilnin)

If $CT_{EX} > 80$ sec: Consider FFP, cryoppt, Platelet concentrate, and/or vit K (less urgent) to correct fibrinogen.

If $A10_{FIB} \leq 13$ mm: give 5 U cryoppt

If $A10_{FIB} \leq 10$ mm: give 10 U cryoppt

If $A10_{EX} < 45$ mm and $A10_{FIB} > 12$ mm: give platelets

If $ML_{IN,EX} \geq 15\%$: consider anti-fibrinolytics

Example: ROTEM EXTEM and FIBTEM suggest fibrinogen deficiency

Duke Univ Medical Center
Blood Gas Lab

ROTEM Analyser, Tem Innovations
3212

Name: [REDACTED]

TestID: EXTEM

PatID: [REDACTED]

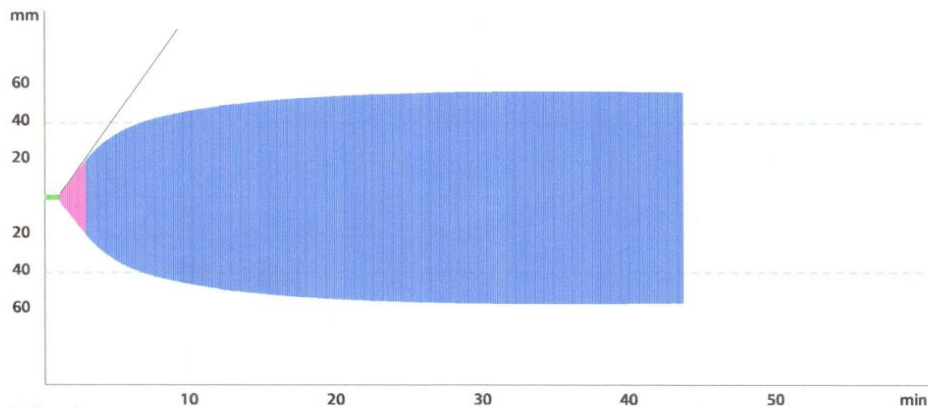
Comment: OR- [REDACTED]

SampleID: 1000 [REDACTED]

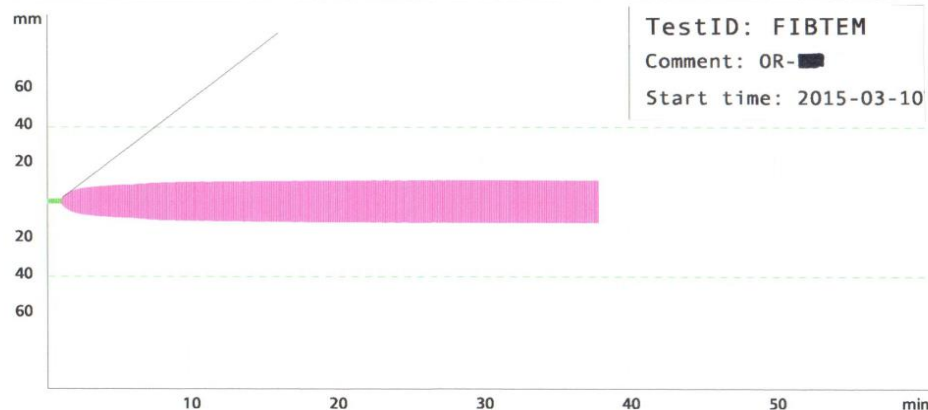
Date of birth: [REDACTED]

Start time: 2015-03-10 [REDACTED]

Run time: 00:43:42



CT	:	64	s	[40	-	85]
CFT	:	109	s	[40	-	115]
α	:	71	°	[65	-	80]
A10	:	48	mm	[44	-	64]
A20	:	55	mm	[50	-	70]
MCF	:	57	mm	[52	-	70]
LI30	:	100	%	[97	-	100]
LI60	:		%				
ML	:	*	1	%			
LOT	:		s				



TestID: FIBTEM

Comment: OR- [REDACTED]

Start time: 2015-03-10 [REDACTED]

CT	:	62	s				
CFT	:		s				
α	:	57	°				
A10	:	11	mm	[12	-	31]
A20	:	11	mm	[12	-	31]
MCF	:	11	mm	[12	-	31]
LI30	:	100	%				
LI60	:		%				
ML	:	*	0	%			
LOT	:		s				

Are Either TEG or ROTEM Suitable for POC Use?

- **Some hospitals have these at POC:**
 - But, we have them in the laboratory (5 ROTEMs)
 - These are very challenging to have at POC:
 - Both use reagent bottles and require multiple manual pipetting steps.
- **Usually needed at multiple ORs:**
 - Not portable
 - Relatively expensive.
- **Remote viewing at POC extremely helpful!**

Pipetting Steps in ROTEM Assays

EXTEM	FIBTEM	INTEM	HEPTEM
Pipet STARTEM reagent	Pipet EXTEM reagent	Pipet STARTEM reagent	Pipet INTEM reagent
Add air segment	Add reagent to sample cup	Add air segment	Add reagent to sample cup
Pipet EXTEM reagent	Pipet FIBTEM reagent	Pipet INTEM reagent	Pipet HEPTEM reagent
ALL ASSAYS: Add reagents to sample cup			
ALL ASSAYS: Pipet 300 uL blood to sample cup			
ALL ASSAYS: Mix and place onto pin to start test			

Comparison of TEG and ROTEM

TEG	ROTEM
All reagents in a cup. Simply pipet blood into cup and start analysis.	For each type of assay, requires 2 pipetting steps before pipetting blood into cup and mixing.
Takes 25-30 min for results (MA)	Provides valid A10 result in 10 min after CT.
Approved for native blood. Can use citrated blood, but that gives different results and must be validated by lab.	FDA approved for citrated blood. Not critical to start assay within 4-5 min after collection.
Typically used the heparinase cup to see clotting profile during CABG with heparinization.	Overall, INTEM, EXTEM, FIBTEM, and HEPTM give better clinical information.
QC every 8hr more expensive. Reagent test cups less expensive. Does not require IQCP 😊	Weekly external QC less expensive. Reagents for 4 tests more expensive. Requires IQCP ☹️

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.**