Blood Gas Testing and Other Contemporary Issues in POCT in the Operating Room: \*Evaluating Two 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
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- 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 or TEG 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 6<sup>th</sup> 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 3<sup>rd</sup> floor connecting the older Duke North Hospital and the new Duke Medical Pavilion.
- The Blood Gas Lab moved from the 3<sup>rd</sup> floor Duke North Hospital to the 6<sup>th</sup> 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	New Test Volumes
OR 33	OR 33	3600/yr	1500/yr
OR 34	OR 34	3600	600
OR 35	OR 35	3600	900
OR 36	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

## **Blood Gas POC Model #1**

- 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 POC Model #2a (1985-2013)**

- Blood gas analyzers with multi-use reagent packs used in 4 (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 #1** Blood Gas Analyzers with Single-Use Test Cartridge

Test Card Menu	Cost / Panel	Test Vol / yr	Yearly Cost (\$)	Average Cost/Test Menu*
pH, <i>p</i> CO <sub>2</sub> , <i>p</i> O <sub>2</sub> , Na, K, Ca <sub>ion</sub> , calc tCO <sub>2</sub> , sO <sub>2</sub> , Hct/Hb	\$10.10	14,430	\$145,743	\$10.66*
pH, $pCO_2$ , $pO_2$ , lact, calc HCO <sub>3</sub> , sO <sub>2</sub>	\$6.60	14,430	\$95,238	\$7.16*
Controls, Cals, etc			\$750	
5 instruments (yearly cost rate)			\$7,375	

\* 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
u	OR 7	4050	"	\$4.44
"	OR 8	3200	"	\$5.63
u	OR 9	2980	"	\$6.04
"	Peds Cath	600	"	\$30.00
TOTALS		14,430	\$90,000	\$6.24

OR Panel: pH,  $pCO_2$ ,  $pO_2$ , Na, K, ion Ca, glucose, lactate, tot Hb,  $%O_2Hb$ , %COHb, %metHb

### **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	1337	\$18,000	\$13.46
"	OR 35	614	"	
"	OR 36	326	"	\$55.20
"	OR 37	2632	"	
"	OR 49	980	"	\$18.37
"	OR 50	4122	"	\$4.37
"	OR 51	2454	"	
"	OR 53	1180	"	
"	OR 54	3072	"	\$5.85
"	OR 55	2986	"	
"	OR 56	3740	"	\$4.81
"	OR 57	555	"	
"	Peds OR #6	1711	"	
"	Peds Cath	592	"	\$30.41
"				
TOTALS		28,242	\$252,000	mean = \$8.92

### **CVOR Blood Gas POC Model #1** Blood Gas Analyzers with Single-Use Test Cartridge

Test Card Menu	Cost / Panel	Test Vol / yr	Yearly Cost (\$)	Average Cost/Test Menu*
pH, <i>p</i> CO <sub>2</sub> , <i>p</i> O <sub>2</sub> , Na, K, Ca <sub>ion</sub> , calc tCO <sub>2</sub> , sO <sub>2</sub> , Hct/Hb	\$10.10	28,242	\$285,244	\$10.90*
pH, <i>p</i> CO <sub>2</sub> , <i>p</i> O <sub>2</sub> , lact, <i>calc</i> HCO <sub>3</sub> , sO <sub>2</sub>	\$6.60	28,242	\$186,397	\$7.40*
Controls, Cals, etc			\$2,000	
14 instruments (yearly cost rate)			\$20,645	

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

### Relative Costs of Blood Gas/Lytes POC Models vs Test Volume

System	# Analyzers	Test Volume / Year	Average Cost / Test
#1 (single-use)	5	14,430	\$10.66
#1 (single-use)	14	28,242	\$10.90
#2 or #3 (multi-use)	5	14,430	\$6.24
#2 or #3 (multi-use)	14	28,242	\$8.92

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.

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

- Advantages
  - Excellent portability
  - Wider variety of tests available; ie. ACT, Tnl
  - 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 Models #2 and #3: 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.
  - Requires IQCP 😕

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

### PTH Workload at Duke Med Center: Core Lab and Intraop PTH



**Fiscal Year** 

## 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 parathryoid 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 ≤50% of the baseline value.
  - If not, wait a period of time then measure PTH again.
  - If level still not <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



Point of Care 2007; 6: 253-260

# 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  $-\frac{1}{2}$  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 refreeze cryoppt.
- 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.

# 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 manual pipetting steps.
- Usually needed at multiple ORs:
  - Not portable
  - Relatively expensive.
- Remote viewing at POC extremely helpful!

### The ROTEM Graph: Records the Change in Amplitude vs Time

#### Time (results in sec)



Amplitude (in mm)

## **Parameters in The ROTEM Graph**



#### Time

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

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

 $\alpha$ -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®** 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



## **ROTEM® Thromboelastometry – Measured Parameters**

- **CT** start of clot formation (sec) [need Factors via FFP]
- **CFT** clot propagation rate (sec)
- $\alpha$ -angle tangent to the clotting curve at 2mm (deg, °)
- A10, A20 Amplitude (mm) at 10 or 20 mins [need Platelets or Cryo?]
- MCF Maximum Clot Firmness (mm) [same as for A10]
- LI30– Lysis Index (% of clot remaining 30 mins after CT)
- ML Maximum Lysis (% of lysis) [need for anti-fibrinolytics]

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

- If CT<sub>EX</sub> > 70 sec: give FFP 10-15 mL/kg (or profilnin)
- If CT<sub>EX</sub> > 80 sec: Consider FFP, cryoppt, Platelet concentrate, and/or vit K (less urgent) to correct fibrinogen.
- If A10<sub>FIB</sub>  $\leq$  13 mm: give 5 U cryoppt
- If  $A10_{FIB} \le 10$  mm: give 10 U cryoppt
- If  $A10_{EX} < 45$  mm and  $A10_{FIB} > 12$  mm: give platelets

If ML <sub>IN,EX</sub> ≥ 15%: consider anti-fibrinolytics

### Example: ROTEM EXTEM and FIBTEM suggest fibrinogen deficiency



## **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 a 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 HEPTEM give better clinical information.
QC every 8hr more expensive. Reagent test cups less expensive.	Weekly external QC less expensive. Reagents for 4 tests more expensive.

### 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.