Wednesday, August 3, 2016

Poster Session: 9:30 AM - 5:00 PM

Point-of-Care Testing

B-241

Point of Care Glucose Testing - Five-Years Performance Review with an In-house Established Quality Assessment Framework

V. M. Lo. *Hong Kong Sanatorium and Hospital, Happy Valley, Hong Kong*

Introduction: In our hospital Chemical Pathology laboratory held key responsibility for the quality of point of care-glucose-testing (POC-G-T) service through the establishment of a well-designed quality management (QM) system. The QM system focused in management, technical, and quality assurance. Every three years, our laboratory participated in a well established assessment system delivered by National Association of Testing Authority (NATA) according to medical testing laboratory standard ISO 15189. Despite POCT had a quality standard ISO 22870, there was lacking a similar assessment system. Looked up PubMed as at 1 September 2015 there was insufficient publication reported assessment framework of a POCT QM system, neither was local hospital as an example

Method: In September 2015, after running the system for five years, we conducted a five-year performance review with an in-house established QM system assessment framework composing of five quantifiable quality indicators. They were categorized into two aspects, analytical and operator. In analytical aspect they were (1) RCPA QAP KPI score, (2) sigma metric , by (TEa-bias)/CVa , TEa was total error, CVa was analytical coefficient of variation (CV) of period collected low and high IQC imprecision and (3) analytical goal, by CVa/CVi, CVi was intra-individual biological variation. In operator aspect, they were (4) daily internal quality control repeat status, being interpreted as repeat frequency and reason of repeat, and (5) external quality assurance (EQA) performance, in terms of sample analysis failure rate. During the assessment process all stakeholders were involved, namely doctor, nurse, laboratory, biomedical engineering department, supplies department, laboratory information system department and vendor.

Results: Three biannual KPI scores indicated good performance. Sigma-metric ranged between 5.9 and 7.8 corresponded to error rate of 0.00050% and <0.00034% respectively. Analytical goal was achieved satisfactorily. EQA sample analysis failure rate declined from 10.0% to 0.9% in January 2015 and kept persistently low at <1.0% till July 2015. Daily IQC repeat status identified two deficiencies of sample application technique and sample verification compliance before analysis owning to lacking focus in the training program.

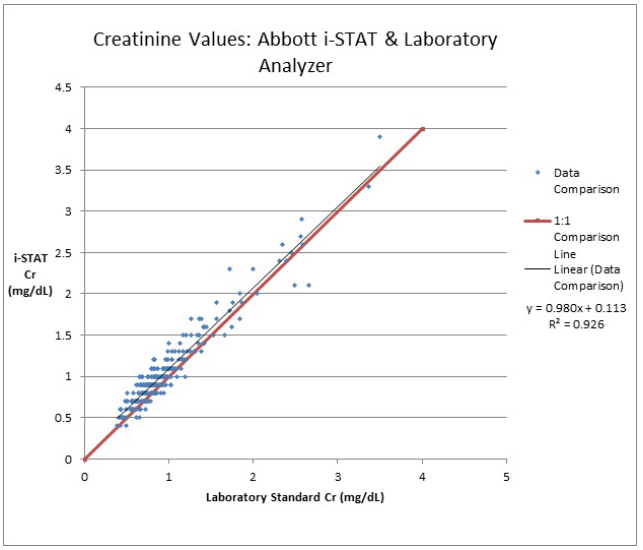
Conclusion: The outcome ascertained the five quantifiable quality indicators as a landmark for tangible assessment of the QM system and established reference points for another five years or shorter, such as annual, performance review.

B-242

Accuracy of i-STAT point-of-care creatinine measurements in outpatient chemotherapy patients: A direct comparison to laboratory based methods.

J. Mahlow, E. Reineks. *Cleveland Clinic, Cleveland, OH*

Background: Renal function is an important consideration in administration of chemotherapeutics that are either subject to renal excretion or nephrotoxic. The oncology service at our institution has transitioned to the Abbott i-STAT point-of-care (POC) device to determine kidney function in outpatients presenting for chemotherapy infusion. POC devices offer advantages in this setting by rapidly determining chemotherapy eligibility based on established cutoffs, guiding dosing, and reducing wait times associated with traditional laboratory testing. This investigation compared creatinine values obtained in the POC setting to samples submitted for standard laboratory analysis. Methods: A retrospective analysis of creatinine level was performed on POC and standard samples (N=540) collected from the same patient on the same calendar day over a 6 month period from April 2014 to September 2014. Respective samples were tested on the Abbott i-STAT CHEM8 cartridge and our core laboratory analyzer, Roche COBAS 8000. Results: The i-STAT results demonstrated a small but consistent positive bias in each of the 6 months of our investigation. When averaged over the entire six month period, i-STAT creatinine values were higher than the laboratory analyzer by 0.11 ± 0.04 mg/dL. Despite the positive bias, the two methods had an excellent linear relationship (slope = 0.980, R^2 = 0.926). When used for the calculation of glomerular filtration rate (GFR) these values result in an underestimation of 4-12%, depending on gender and absolute creatinine value. Conclusion: These findings suggest the i-STAT is an appropriate screening tool to identify patients with kidney dysfunction prior to chemotherapy infusion. However, calculations used in the dosing scheme of some chemotherapeutics rely directly on GFR and could result in sub-therapeutic dosing when POC creatinine concentrations are biased relative to laboratory results. The clinical impact of this potential dosing discrepancy may warrant further investigation.



B-243

Development of a new interface for POCT competency tracking

K. Halverson. *Children's of Minnesota, Minneapolis, MN*

OBJECTIVE: To accurately, efficiently and effectively track elements of competency for the point of care testing (POCT) department at a multi-site pediatric hospital system via electronic means.

INTRODUCTION: Per the Clinical Laboratory Improvement Act (CLIA), there are six elements of competency that must be included in assessing laboratory testing operators. Ensuring these elements are met and tracked year to year can be a daunting task. Children's of Minnesota has approximately 2200 operators trained to perform any number of the eleven different POC tests offered across over forty departments in seven physical locations. Manual tracking of competency is done by sorting operators by department and test type in TELCOR QML and then matching them up with lists of employees who have completed competency each year. These lists are two large spreadsheets generated from the e-learning software which manages the online tests of comprehension and from tracking Competency Fair attendance. Manually updating each operator takes on average 5 minutes per device type. Adding up all combinations of operators and POCT tests performed at Children's equates to thirty nine eight hour days of competency updating needed. Collaboration between Children's Human Resources Information Systems (HRIS) staff, POCT staff and POCT middleware vendor TELCOR to develop an interface providing the transfer of competency record data from HRIS to QML to track competencies would greatly simplify this process.

METHODOLGY: TELCOR QML is middleware software commonly used to transfer results from any POCT device to a hospital Lab Information System or directly to the Electronic Medical Record. Within QML, competency parameters can be set for each device type in use. Parameter options include the following: e-learning course records, patient tests, quality control tests, proficiency testing and/or linearity testing. When an operator meets all parameters set, they are automatically updated. A report created in Children's e-learning software, People Soft, is run each day looking for any staff that has successfully completed any POCT e-learning courses. This report is saved as a file in Children's network where QML knows to look for it. QML then automatically pulls that report and updates operator records within QML. In addition to course completion information, this report delivers information such as new hire additions, name changes, badge number changes, departmental changes and terminations.

RESULTS & CONCLUSION: The first production interface run resulted in the update of approximately 1500 operators. This occurred in a matter of seconds. This report run is scheduled on a daily basis and an alert occurs within QML if issues arise. The implementation of an e-learning interface drastically reduces the number of hours needed each year to update POCT competencies. It allows the POCT department to smoothly meet regulatory compliance for competency assessment tracking and it also eliminates the number of errors that occur with manual editing of competency updates and QML operator records each year. The time saved in the POCT department will be used to concentrate on other quality initiatives, instrumentation and regulatory compliance.

B-244

Low-density protein microarray method for detecting three antibodies associated with invasive fungal infections

F. Li. *Jingling Hospital, Nanjing, China*

Background: The frequency of invasive fungal infections (IFI) has risen dramatically in recent years. Early and accurate diagnosis of these infections is important for several reasons, including timely institution of antifungal therapy and to decrease the unnecessary use of toxic antifungal agents. The value of serological detection techniques are apparent, but they suffer from several disadvantages, mainly be time-consuming and inability to produce simultaneous results. Protein chip, a convenient technology, can be used to perform high through-put antibody detections and enable the monitoring of different antibodies simultaneously. **Methods:** A microarray was constructed using purified recombinant enolase (Eno) fructose-bisphosphate aldolase (Fba1) of *Candida*, and thioredoxin reductase (TR) of *Aspergillus fumigatus* as immobilized antigens. The issues about microarray construction and serum test such as loading concentration and loading buffer for tree antigens, antigen immobilized condition, blocking buffer, and testing dilution of patient's sera were optimized. The sensitivity, reproducibility and stability of the assay were investigated using the sera from patients with *Candida* and *Aspergillus* invasive infections and control subjects. **Results:** The following issues were selected for protein microarray assay: nitrocellulose filter was used as solid carrier, Tris-HCl as loading buffer, the loading concentrations for Eno, Fba1 and TR were 0.5mg/mL, 0.04mg/mL, 1.0mg/mL respectively, antigens were immobilized at damp thermosis for 2 hours, 5% skimmed milk powder in PBS was applied in blocking buffer, testing dilution of patient's sera was 1:10. In the invasive candidosis (IC) patients, the sensitivity, specificity were 67.6%, 96.5% for anti-Eno and 64.8%, 90.3% for anti-Fba1 antibodies, respectively. The combined detection of anti-Eno and anti-Fba1 gave a sensitivity of 81%. While in invasive aspergillomycosis (IA) patients, the sensitivity and specificity of detection were 71.4%, 98.2% for anti-TR antibody. **Conclusion:** A low-density protein microarray assay has been developed for detecting three antibodies against two fungi simultaneously. The results demonstrated that the method has potential value in the diagnosis of IC and IA

B-245

Operational outcomes and interchangeability of results with ABL90 Flex Plus and ABL90 Flex

R. Núñez, D. García, P. Oliver, P. Fernández-Calle, M. Alcaide, A. Buño. *Hospital Universitario La Paz, Madrid, Spain*

Background: One of the advantages of ABL90 Flex Plus blood gas analyzer is that up to 17 critical parameters can be determined from extremely small volume blood samples. This operational aspect is crucial for delivery rooms or neonatal intensive care units (NICU) and it should take into account for selecting a POCT device. Before using this new analyzer at any POCT setting, the comparability of results must be verified following guidelines recommendations

Methods: The frequency of "Aborted sample" and "Insufficient sample" errors were obtained by Aqure (Radiometer). 50 samples in syringes heparinized whole blood corresponding to randomly selected patients were used. After homogenization samples, blood gas samples were measured in both analyzers. Evaluation of results was performed following the EP09-A2 CLSI considering as reference method ABL90 Flex measurements. Linear regression was calculated for each parameter in order to estimate bias at the medical decision levels (www.westgard.com). The allowable bias was established according to biological variation criteria. Statistical analyses were performed using StatisPro™ (CLSI)

Results: When using ABL90 Flex Plus, the frequency of "Aborted sample" decreased from 5.9% to 3.6% and "Insufficient sample" from 3.2% to 2.2%.

Parameter (measurement interval)	Clinical decision levels	Estimated bias	Confidence interval 95%	Allowed bias	Allowed bias (%)
	7.25	0.0009	-0.0002 to 0.0019	0.0732	1.01
pH (7.053 - 7.500)	7.35	0.0025	0.0018 to 0.0031	0.0742	1.01
	7.5	0.0049	0.0033 to 0.0065	0.0758	1.01
	60.0	0.429	-1.73 to -1.19	5.82	9.7
PaO_2	80.0	0.600	-2.50 to -1.58	7.76	9.7
	90.0	0.726	-2.89 to -1.76	8.73	9.7
	100.0	0.863	-3.30 to -1.93	9.7	9.7
	35.0	0.141	-0.38 to 0.18	0.63	1.79
$PaCO_2$	45.0	0.090	-0.17 to 0.19	0.81	1.79
	55.0	0.111	-0.11 to 0.34	0.98	1.79
	4.5	0.077	-0.34 to -0.03	0.28	6.3
Hemoglobin	10.5	0.029	-0.40 to -0.28	0.66	6.3
	17	0.044	-0.60 to -0.42	1.07	6.3
	23.0	0.096	-0.86 to -0.48	1.45	6.3
	115.0	0.2129	-0.3 to 1.5	1.3	1.1
Sodium (114 - 151) mmol/L	135.0	0.45	0.2 to 0.7	1.5	1.1
	150.0	0.11	0.00 to 0.7	1.7	1.1
	3.00	0.027	-0.06 to 0.05	0.08	2.7
Potassium (2.6 - 7.7) mmol/L	5.80	0.032	-0.14 to -0.01	0.16	2.7
	7.00	0.054	-0.22 to 0.00	0.19	2.7
Chloride (87 - 118) mmo/L	90	0.17	-0.5 to 0.2	0.6	0.7
112	0.09	-0.5 to -0.1	0.8	0.7	
	0.65	0.0062	0.001 to 0.026	0.020	3.1
Ionized Calcium (0.6 - 1.3) mmol/L	1.00	0.0023	0.011 to 0.020	0.031	3.1
	1.30	0.0016	0.014 to 0.020	0.040	3.1
	45	0.59	-0.4 to 2.0	3.1	6.96
Glucose	120	0.44	4.4 to 6.2	8.4	6.96
	180	0.76	7.3 to 10.4	12.5	6.96
	2.00	0.02	-0.01 to 0.06	0.08	4
Lactate	4.00	-0.07	-0.10 to -0.04	0.16	4
	6.00	-0.16	-0.21 to -0.11	0.24	4

Conclusion: With ABL90 Flex Plus, more blood gas analysis results are obtained without sampling error. It could have a relevant clinical impact for avoiding new sample collections or reducing the timeframe to therapeutic intervention. ABL90 Flex Plus results are equivalent to ABL90 Flex. If more than one system is used to follow patients, it is also important to consider the relative bias that could be safely tolerated between methods at medical decision points.

B-246

A Preliminary, Multi-analyte Comparison Study of Whole Blood Point-of-care Testing (POCT) on the Piccolo analyzer in Our Ebola Biocontainment Unit Versus Plasma Testing on the Advia 1800 Chemistry Analyzer

M. N. B. Subia, D. V. Lai, S. A. Khan, A. Hardesty, P. Akl, K. E. Blick. *Un of OK Health Sci Ctr, Oklahoma City, OK*

Background: Generally, the goal of bedside POCT is *to expedite diagnosis and facilitate immediate evidence-based medical decisions that can potentially improve patient outcomes. However, more recently, in high risk infectious diseases like Ebola, POCT can be more easily be isolated in a biocontainment unit and therefore testing can be performed without the risk of Ebola exposure/contamination in the core laboratory. However, the menu of FDA approved tests for POCT devices is rather limited hence, when our infectious disease physicians requested liver function testing (LFTs) on our Ebola patients, the FDA-cleared Piccolo Xpress chemistry analyzer was selected because of the availability of 1) a whole blood comprehensive metabolic chemistry panel on a single-used reagent test "disc", 2) a test disc designed for LFTs, and 3) other important analytes such as lactate dehydrogenase(LDH), magnesium, and phosphorus. We assessed the general accuracy of nineteen whole blood chemistry*

Piccolo methods by comparing plasma chemistry results obtained on our Advia 1800 chemistry analyzer. **Methods:** Lithium-heparinized whole blood samples obtained from random patients were analyzed first on the Piccolo Xpress employing test specific reagent discs/cartridges for Liver Panel Plus, Basic Metabolic Panel Plus, and other analytes. Subsequently, samples were centrifuged and analyzed on the Advia. **Results:** Piccolo Advia comparison results are shown in the Figure. Patient means were comparable across the 19 analytes with no statistically significant difference observed (r^2=0.96; p=0.86). Good-to-excellent correlation was observed for the Piccolo Liver Panel Plus when compared to the Advia (r^2=0.94-1.00) except albumin (r^2=0.79). While most analytes showed acceptable correlation and regression line slopes, weak correlation was observed for chloride, LDH, sodium, TCO2, magnesium, potassium (r^{2-} 0.45-0.66). Between run precision on all Piccolo analytes was generally acceptable (CV%= 0.55-7.01). **Conclusion:** The Piccolo Xpress Chemistry Analyzer appears to show generally acceptable comparison performance for testing/screening purposes in our biocontainment unit.

Comparison data for various analytes on the Piccolo versus the ADVIA 1800

Analyte	N	Slope	Y intersection	R Square	SE	Piccolo mean	Advia 1800 mean
Albumin	14	0.88	0.11	0.79	0.38	3.70	4.06
Alkaline phospatase	14	0.68	6.94	1.00	1.97	193.14	274.29
ALT	14	0.86	1.01	1.00	3.61	45.36	51.29
AST	14	0.93	1.50	1.00	6.79	59.64	62.43
Total Bilirrubin	14	0.94	0.22	1.00	0.10	2.46	2.39
GGT	13	1.01	-2.43	1.00	4.64	103.77	105.31
Total protein	14	1.25	-1.8	0.94	0.26	7.29	7.30
Phosphorus	12	1.05	0.21	0.96	0.17	2.97	2.88
LDH	13	0.70	83.66	0.67	35.56	272.23	268.85
Magnesium	13	0.92	0.15	0.89	0.13	2.07	2.08
Calcium	12	0.90	0.93	0.91	0.19	9.08	9.04
Chloride	13	0.87	11.78	0.61	2.52	104.08	106.31
Creatinine	12	0.92	0.14	0.99	0.08	1.09	1.03
Glucose	13	1.00	1.50	0.99	5.37	115.23	116.62
Sodium	12	0.86	20.12	0.59	1.83	140.08	140.50
Total CO2	12	0.54	13.50	0.45	1.20	27.75	26.33
Blood urea nitrogen	13	1.02	-0.73	1.00	1.39	27.54	27.23
Potassium	12	0.83	0.81	0.80	0.15	4.23	4.12

B-247

Determination of Analytical Performance Characteristics of RAMP® Procalcitonin

J. F. Wilson, P. Francis, E. Williams, L. Canapi, S. Moran, A. Carter. *Response Biomedical Corp., Vancouver, BC, Canada*

Background: The RAMP® System is a lateral flow immunoassay platform that provides accurate and precise diagnostic information in minutes. RAMP Procalcitonin is a quantitative *in vitro* diagnostic test used with the RAMP System to measure levels of the prohormone procalcitonin (PCT) in human EDTA anticoagulated whole blood. PCT is a biomarker elevated in the blood of patients suffering from bacterial sepsis. Rapid detection of PCT aids in the early diagnosis and treatment of sepsis, leading to improved patient outcomes and reduced healthcare costs. The objective of these studies was to determine the analytical performance characteristics of RAMP Procalcitonin.

Methods: Detection limits, linearity, hook effect, repeatability, total precision, interference and cross-reactivity, and reference range (95th percentile) were determined for RAMP Procalcitonin according to methods outlined in CLSI guidelines, where applicable, using either plasma-based controls or EDTA whole blood samples.

Results: The limit of blank (LoB) and limit of detection (LoD) were determined to be 0.18 ng/mL and 0.36 ng/mL, respectively, using methods described in EP17-A. The 20% and 10% limits of quantitation (LoQ) were determined to be 1.28 ng/mL and 0.64 ng/mL, respectively, using total error estimates as described in EP17-A. Linearity analysis yielded a linear regression slope (95%CI) of 0.97 (0.93 to 1.02) and an R (95%CI) = 1.00 (0.99 to 1.00). No high dose hook effect was observed up to 2000 ng/mL.

Repeatability and within-laboratory precision were determined as per EP5-A3 by testing three levels of frozen plasma control materials in duplicate, twice per day for 20 days on three lots of RAMP Procalcitonin. Repeatability coefficients of variation (CVs) were 6.6 to 8.5% at 92.7 ng/mL, 8.0 to 9.0% at 2.72 ng/mL and 16.0 to 18.7% at 0.58 ng/mL. Within-laboratory precision CVs were 7.2 to 9.4%, 7.7 to 9.3% and 15.8 to 19.3% at the same concentrations. Simple precision was also determined for whole blood samples by testing 10 replicates of 3 blood samples in a single run on one lot of RAMP Procalcitonin tests. CVs in whole blood were 8.2% at 103.2 ng/mL, 6.8 % at 3.00 ng/mL and 14.1% at 0.75 ng/mL.

As per EP7-A2, no interference was observed for RAMP Procalcitonin as the result of hemoglobin (500 mg/dL), bilirubin (conjugated 40 mg/dL, unconjugated 40 mg/dL), triglycerides (3260 mg/dL), human serum albumin (2.4 g/dL) or 11 common pharmaceutical compounds. No statistically significant cross-reactivity was observed with calcitonin (5 ng/mL), katacalcin (10 ng/mL), α-CGRP (30 ng/mL) or β-CGRP (30 ng/mL).

The RAMP Procalcitonin reference range study was conducted at one site and included 125 apparently healthy subjects. The 95th percentile from these results was determined to be 0.36 ng/mL, using nonparametric analysis methods described in C28-A3C.

Conclusion: RAMP Procalcitonin demonstrated robust analytical performance for the quantification of procalcitonin, based on methods outlined in applicable CLSI guidelines.

B-248

Multivariable Statistical Techniques for the Acceptance of Several Glucose Meters. A Practical Example with AccuChek Inform II ®.

V. M. Genta[1], S. S. Church[2], M. Ferguson[1], J. Shea[1], L. Weyer[2], Y. Shen[1]. *[1]Sentara Virginia Beach General Hospital, Virginia Beach, VA, [2]Sentara Healthcare, Norfolk, VA*

Background: In Hospitals, several glucose meters are used for assessing the patient glycemia to direct insulin therapy at the bedside. To maintain a seamless operation, the values as obtained with a glucose meter should be interchangeable with those as determined with other glucose meters and the laboratory method. We describe the application of multivariable statistical techniques for acceptance of Accuchek Inform II ® glucose meters upon receipt from the manufacturer. Methods: Upon receipt, three AccuChek Inform II® (Roche) meters were compared to two meters in use. QC material (Level 1,2 lot # 50100531, Roche). Reagent strips (lot #474135, (Roche). Linearity material (lot #5010720, Roche). Five assays with level 1 and 2 control material were performed for five days. Three assays, for each value of the linearity material, were performed for each meter. Twelve patient specimens for each meter, with values between 40 and 550 mg/dL, were obtained in green top tubes (Becton-Dickinson) and assayed in parallel and within twenty minutes with AccuChek Inform II and the laboratory method (Cobas c501®, Roche). The data were transferred to Minitab® (Version 17, Minitab, Inc.) statistical software and analyzed with multivariable statistical techniques for equality of means variances, linearity and equality of regression lines and their graphic representations. Results: Precision study: The multivariable parallel box plots showed equality of means and variability (height of the boxes and whiskers) by day and meter. This was corroborated by the multiple comparisons of the means by day and instruments obtained with the GLM and Tuckey's multiple comparisons (Level 1: day F=0.7, P=0.6, meter F=0.4, P=0.8; Level 2: day F=0.8, P=0.5, meter F=0.3, P=0.9). Bonett's and Levene's statistical tests showed homogeneity of variance by day and meter for both levels of control (level 1: P=03, P=0.7; level 2: P=0.05, P=0.8). Linearity study: The weighted polynomial regression (y=-0.6+0.97x, Sy/x=0.35,) showed that the relationship was linear (Pure error test: F=1.1, P=0.3) and the meters regression lines were not statistically significantly different from each other (F=0.54, P=0.71). This was also visualized by the lowess regression model. Comparison with the laboratory method: The regression line obtained with the orthogonal model (y=2.4+0.96x) was similar to that obtained with the weighted least squares model (y=2.9+0.96x). Furthermore, the weighted polynomial model showed equality of regression lines for the meters (beta for meter not statistically significantly different from zero: F=0.76, P=0.56). The plot of the absolute and relative differences by the values, as obtained with the laboratory method, showed that all the differences were within the CLIA's criterion (target value ± 6 mg/dL, 10% greater). Conclusions: This practical example showed that multivariable statistical techniques offered straightforward numerical results and compelling, multidimensional graphics to evaluate the performance of new glucose meters for acceptance prior use for patient testing. Multivariable methods are more powerful and parsimonious than univariate methods for comparing the performance of several variables. However, they require intense numerical analysis. Consequently, the availability of statistical software, such as Minitab, was of critical importance for numerical and graphic analyses and the storage of their results.

B-249

Evaluation of four simplified protocols to verify the interchangeability of POCT blood gas patient results

A. Buño, J. Sanguino, D. García-Rodríguez, P. Oliver, M. Alcaide, P. Fernández-Calle. *salud madrid, Madrid, Spain*

Background:

When new equipment is introduced into a laboratory, verification of patients´ results interchangeability with the previous method is mandatory.This is especially difficult in complex POCT blood gas networks due to short stability of samples and multiple magnitudes and devices. Existing protocols (CLSI EP09, C54) are complex when facing these scenarios.

Aim:

To evaluate the performance of four simplified evaluation protocols to verify the interchangeability of blood gas patient results.

Methods:

CLSI EP09-A3 protocol results were considered as reference results. Comparison through bias estimation between results of ABL-90 and ABL-90 plus (Radiometer®) was performed (40 blood gas syringes randomly selected). pH, pO_2, pCO_2, sodium, potassium, chloride, glucose, lactate and hemoglobin were measured.

We designed four simplified protocols:

P1 (n:10): 1 day, 5 samples, two replicates/sample.

P2 (n:10):5 days, 1 sample, two replicates/sample.

P3 (n:18): 3 days, 3 samples/day, two replicates/sample.

P4 (n:9): 3 days, 3 samples/day, one replicate/sample.

Results of bias estimation (BE) were compared with those obtained from CLSI EP09-A3.Bias desirable biological variation specification was selected as criteria to determine the interchangeability of patient results at clinical decision levels

Results:

Table shows the bias estimation of CLSI EP09-A3 and the simplified protocols.

Magnitude (TEa %)	Clinical Decision levels	Allowable Bias	EP09-A3 BE(95%IC)	P1BE(95%IC)	P2BE(95%IC)	P3BE(95%IC)	P4BE(95%IC)
pH (<1.01%)	7.25	0.073	0.0009 (-0.0002to0.0019)	-0.0004 (-0.0042to0.0033)	0.0032 (-0.0048to0.0112)	0.0033 (0.0014to0.0051)	0.0053 (0.0022to0.0085)
	7.35	0.074	0.0025 (0.0018to0.0031)	0.0014 (-0.0014to0.0041)	0.0027 (-0.0013to0.0068)	0.0035 (0.0026to0.0045)	0.0068 (0.0053to0.0083)
	7.50	0.076	0.0049 (0.0033to0.0065)	0.0040 (-0.0021to0.0102)	0.0020 (-0.0029to0.0069)	0.0039 (0.0018to0.0061)	0.0089 (0.0057to0.0122)
pO_2 (<9.7%)	60	5.82	-1.46 (-1.73to-1.19)	-2.20 (-4.78to0.38)	-1.12 (-2.18to-0.07)	-0.86 (-1.31to-0.42)	1.13 (-0.83to3.09)
	80	7.76	-2.04 (-2.50to-1.58)	-3.08 (-6.57to0.40)	-1.63 (-3.36to0.10)	-0.88 (-1.64to-0.13)	2.17 (-1.68to6.02)
	90	8.73	-2.33 (-2.89to-1.76)	-3.52 (-7.72to0.67)	-1.89 (-4.10to0.33)	-0.90 (-1.84to0.05)	2.69 (-2.24to7.62)
	100	9.70	-2.61 (-3.30to-1.93)	-3.96 (-8.95to1.02)	-2.14 (-4.88to0.59)	-0.91 (-2.05to0.23)	3.21 (-2.83to9.24)
pCO_2 (<5.75%)	35.0	0.63	-0.10 (-0.38to0.18)	-0.07 (-1.07to0.92)	0.44 (-0.85to1.74)	-0.39 (-0.83to0.05)	-0.86 (-1.65to-0.07)
	45.0	0.81	0.01 (-0.17to0.19)	0.39 (-0.20to0.98)	0.54 (-0.89to1.96)	-0.40 (-0.83to0.03)	-1.12 (-1.74to-0.50)
	55.0	0.98	0.12 (-0.11to0.34)	0.85 (-0.04to1.74)	0.63 (-1.79to3.06)	-0.41 (-1.18to0.37)	-1.38 (-2.15to-0.60)
Hemoglobin (<6.3%)	4.5	0.28	-0.18 (-0.34to-0.03)	**-0.32*** (-1.31to0.67)	0.07 (-0.69to0.82)	-0.01 (-0.39to0.38)	**1.50*** (0.03to2.97)
	10.5	0.66	-0.34 (-0.40to-0.28)	-0.38 (-0.75to-0.02)	-0.25 (-0.59to0.08)	-0.30 (-0.47to-0.14)	0.29 (-0.34to0.91)
	17.0	1.07	-0.51 (-0.60to-0.42)	-0.45 (-1.07to0.18)	-0.60 (-0.93to-0.27)	-0.63 (-0.84to-0.42)	-1.03 (-1.39to-0.66)
	23.0	1.45	-0.67 (-0.86to-0.48)	-0.51 (-1.81to0.80)	-0.92 (-1.67to-0.17)	-0.93 (-1.37to-0.48)	**-2.24*** (-3.43to-1.04)
Sodium (<1.1%)	115	1.3	0.6 (-0.3to1.5)	**-6.1*** (-17.2to5.0)	**-4.0*** (-9.8to1.7)	**-3.8*** (-7.4to-0.1)	**3.7*** (-3.8to11.2)
	135	1.5	0.5 (0.2to0.7)	-1.1 (-3.7to1.5)	-0.6 (-2.1to0.8)	-0.6 (-1.6to0.5)	**1.7*** (-0.5to3.9)
	150	1.7	0.3 (0.0to0.7)	**2.7*** (-1.2to6.5)	**1.9*** (0.1to3.7)	**1.8*** (0.8to2.9)	0.2 (-1.7to2.1)
Potasium (<2.7%)	3.0	0.08	0.00 (-0.06to0.05)	-0.03 (-0.12to0.06)	0.07 (-1.01to1.14)	0.00 (-0.18to0.18)	**0.11*** (-0.12to0.35)
	5.8	0.16	-0.08 (-0.14to-0.01)	0.08 (-0.12to0.28)	**-0.24*** (-1.27to0.79)	-0.08 (-0.35to0.20)	**0.24*** (-0.20to0.68)
	7.0	0.19	-0.11 (-0.22to0.00)	0.13 (-0.19to0.45)	**-0.37*** (-2.26to1.52)	-0.11 (-0.56to0.34)	**0.29*** (-0.42to1.01)
Chloride (<0.7%)	90	0.6	-0.1 (-0.5to0.2)	**-0.8*** (-3.1to1.5)	-0.5 (-3.5to2.6)	-0.2 (-1.2to0.8)	0.2 (-0.7to1.2)
	112	0.8	-0.3 (-0.5to-0.1)	0.3 (-0.7to1.2)	-0.1 (-1.1to0.9)	-0.2 (-0.7to0.3)	-0.3 (-0.9to0.3)
Glucose (<6.96%)	45	3.1	0.8 (-0.4to2.0)	0.5 (-3.6to4.7)	0.7 (-1.5to2.9)	-0.5 (-2.1to1.1)	-0.5 (-2.3to1.2)
	120	8.4	5.3 (4.4to6.2)	4.7 (-1.4to10.8)	3.2 (1.6to4.8)	3.4 (2.3to4.4)	3.5 (2.3to4.6)
	180	12.5	8.9 (7.3to10.4)	8.1 (-4.4to20.6)	5.2 (3.3to7.2)	6.4 (5.0to7.9)	6.6 (5.2to8.1)
Lactate (<4.0%)	2.0	0.08	0.02 (-0.01to0.06)	-0.04 (-0.12to0.05)	-0.04 (-0.21to0.14)	0.00 (-0.07to0.07)	0.00 (-0.11to0.12)
	4.0	0.16	-0.07 (-0.10to-0.04)	-0.10 (-0.21to0.01)	-0.08 (-0.27to0.10)	-0.08 (-0.13to-0.03)	-0.03 (-0.10to0.04)
	6.0	0.24	-0.16 (-0.21to-0.11)	-0.17 (-0.38to0.04)	-0.13 (-0.53to0.27)	-0.16 (-0.26to-0.06)	-0.06 (-0.17to0.04)
False positive rate			Reference	3/9	2/9	1/9	3/9

(*BE higher than allowable bias)

False positive: Non interchangeable result of the simplified protocol when EP09-A3 result is interchangeable. False positive rate: non interchangeable magnitudes / number of magnitudes.

No false negative results were found. Protocol 3 showed the best agreement

Conclusion:

After the laboratory performs the whole verification protocol with the first analyzer, when facing a change in POCT blood gas network involving multiples devices, these simplified verification protocols could be used as a screening tool for the rest of devices.

When applying these protocols, if the expected bias is higher than allowable bias, it can constitute a trigger to initiate a more complete validation protocol

B-250

Comparison of Siemens DCA Vantage and Alere Afinion Point of Care Analyzers for Hemoglobin A1c Determination

G. R. Deobald, A. Wockenfus, N. Myhre, L. Donato, B. Karon. *Mayo Clinic, Rochester, MN*

Background: Point of Care (POC) A1c testing may improve compliance with diabetes monitoring guidelines and promote better glycemic control in diabetic patients. We compared assay performance characteristics and ease of use of two CLIA-Waived POC analyzers for hemoglobin A1c testing: the Siemens DCA Vantage (Siemens Healthcare, Erglangen, Germany) which utilizes a monoclonal antibody agglutination reaction and the Afinion S100 (Alere Inc., Waltham, Massachusetts, USA) which is a boronate affinity assay. The two CLIA-Waived analyzers were compared to our internal central laboratory reference method, BioRad Variant II Turbo Hemoglobin A1c assay (BioRad Laboratories, Hercules, California). **Methods:** Precision was determined by performing 4 replicates each of 2 levels (low, high) of commercially available quality control material for 5 days. To test accuracy we compared capillary whole blood A1c on both POC devices to reference A1c in a venous sample in 32 diabetic patients and in 21 non-diabetic laboratory volunteers. Usability features such as footprint, required maintenance and turnaround time were also compared for the two point of care methods. Statistical significance of differences in mean bias between devices was determined using unpaired t test.

Results: Precision studies yielded coefficients of variation (CVs) on the Afinion of 1.8% and 1.3% and 2.8% and 2.5% for DCA at low and high levels. . Among the 53 comparison samples spanning a reference A1c range of 4.6-10.0%, mean bias on the Afinion was -0.06 ± 0.17 while mean bias on the DCA was -0.17 ± 0.16 (p=0.0007). Compared to the DCA, the Afinion also had a smaller footprint, no required maintenance, and a faster turnaround time of 3 minutes on the Afinion compared to 6 minutes on DCA.

Conclusion: Both devices demonstrated acceptable precision, and all capillary samples on both DCA and Afinion were within 0.5% of the paired venous A1C reference value. The Afinion showed less systematic bias and better usability features compared to the DCA.

B-251

Detection of NT proBNP using fluorescent protein modified by streptavidin as a label in immunochromatographic assay

h. li[1], x. yin[1], d. sun[1], k. xia[2], c. kang[1], s. chu[1], p. zhang[1], h. wang[1], y. qiu[1]. *[1]Department of Laboratory Medicine, Nanfang Hospital, Southern Medical University, guangzhou, China, [2]Guangzhou Tebsun Dio-tech Development Co.,Ltd, guangzhou, China*

Background:

N-terminal pro-B-type natriuretic peptide (NT-proBNP) has been widely applied as a biomarker of cardiovascular disease and in particular a marker of heart failure. During the past decades, several analytical methods have been developed for the detection of serum levels of NT-proBNP, including radioimmunoassay (RIA), immunoradiometric assay (IRMA), the enzyme-linked immunosorbent assay (ELISA) and recently-developed electrochemiluminescence immunoassay (ECLIA). While ELISA needs more sample volume and a long detection time, RIA and IRMA have more radionuclide pollution problem and less automation, ECLIA characterized by high sensitivity, specificity and easily-operated automation, still needs high cost, laboratory-oriented large analytical instrument and increased waiting time. Therefore, investigating a novel, simple, rapid, sensitive and specific method to detect NT-proBNP at an early stage and to improve the treatment success has garnered considerable interest. Our objective was to investigate a novel, simple, rapid, sensitive and specific method to detect NT-proBNP at an early stage and to improve the treatment success has garnered considerable interest.

Methods:

Based on a sandwich-type immunoassay format, NT-proBNP in samples were captured by one monoclonal antibody labeled with fluorescent protein and "sandwiched" by another monoclonal antibody immobilized on the nitrocellulose membrane, the fluorescence and concentration of analytes were measured and then calculated by fluoroanalyzer. The linear range, analytical sensitivity, precision and accuracy of the immunochromatographic assay were evaluated. The feasibility of the assay for clinical application was investigated by analyzing 131 clinical serum samples from patients. And the results were compared with those detected by a commercial CLIA kit.

Results:

With the advantages of fluorescent protein, the immunochromatographic assay exhibited a wide linear range for NT-pro BNP from 200 pg ml^{-1} to 26000 pg ml^{-1}, with a detection limit of 46.89 pg ml^{-1} under optimal conditions. The precision and recovery of the immunoassay were demonstrated to be acceptable. Compared with chemiluminescence immunoassay (CLIA), 131 human serum samples were analyzed and the correlation coefficient of the developed immunoassay was 0.978.

Conclusion:

A novel fluorescent immunochromatographic method for detecting NT-pro BNP in human serum was successfully developed. The methold applied a fluorescent protein modified by streptavidin as a tracer to conjugate the biotin-labeled anti-NT-pro BNP antibody on the conjugation pad to facilitate the detection of NT-pro BNP in human serum samples. This assay platform revealed several advantages compared with conventional methods, such as higher sensitivity, higher efficiency, broader dynamic assay ranges and less consumption of reagents. And it also displayed good correlation with CLIA kit. Thus, this assay has significant promise to offer a new avenue for POCT of more future important biomarkers.

B-252

Clinical Evaluation of the Next Generation I-STAT® Point-of-Care Instrument using a Sodium Test* *Submission pending FDA review

K. Grasso[1], B. Wise[1], J. Rogers[1], D. Geiger[2], M. Fischer[3], S. Roth[4], M. Wayne[5]. *[1]Abbott Laboratories, Abbott Park, IL, [2]John T Mather Memorial Hospital, Port Jefferson, NY, [3]Pennsylvania State University Hershey Medical Center, Hershey, PA, [4]The Cleveland Clinic Foundation, Cleveland, OH, [5]PeaceHealth, Bellingham, WA*

Introduction: The next generation i-STAT is an *in-vitro* diagnostic instrument developed for Point-of-Care use with singleuse i-STAT cartridges to perform simultaneous quantitation of specific analytes in whole blood. A study was performed to evaluate the performance of the next generation i-STAT using the i-STAT sodium test. The study evaluated next generation i-STAT precision using the i-STAT sodium test and compared performance of the i-STAT sodium test on the next generation i-STAT to the i-STAT 1 wireless in a Point-of-Care setting. This was done using i-STAT E3+ cartridges. **Methods:** The clinical evaluation included multi-day precision, whole blood precision and method comparison using one lot of i-STAT E3+ cartridges. Multi-day and whole blood precision were completed at 3 sites. Multi-day precision was performed using aqueous solutions (i-STAT TriControls Calibration Verification Set) containing 5 levels of sodium. Each site tested the panel once daily for 5 days on 5 next generation i-STAT instruments. Whole blood precision testing was performed using venous whole blood samples representing low, normal and high sodium levels. At each site, each of 3 samples was tested 3 times on each of 7 next generation iSTAT instruments (for a total of 21 results per sample). Method comparison was performed at 4 sites. Testing was performed using whole blood samples prospectively collected or leftover from routine patient care. Duplicate testing and analysis of 174 samples was performed on both the next generation i-STAT and i-STAT 1 wireless. Two next generation i-STAT instruments and two iSTAT 1 wireless analyzers were used for this testing. **Results:** Multi-day imprecision (Total SD) for Sites 1, 2, and 3 ranged from 0.29 mmol/L to 0.65 mmol/L, 0.41mmol/L to 0.62 mmol/L, and 0.37 mmol/L to 0.53 mmol/L, respectively. Whole blood imprecision (Total SD) across all levels for Sites 1, 2, and 3 ranged from 0.00 mmol/L to 0.50 mmol/L, 0.36 mmol/L to 0.45 mmol/L, and 0.30 mmol/L to 0.51 mmol/L, respectively. Method Comparison analysis was performed for the measuring interval of 100-180 mmol/L. For all four sites combined, the slope for Passing-Bablok regression results was 1.0; correlation coefficients for the first replicate result of the next generation i-STAT vs. first replicate result of i-STAT 1 wireless, first replicate result of the next generation i-STAT vs. mean result of i-STAT 1 wireless, and the mean replicate result of the next generation i-STAT vs. mean result of i-STAT 1 wireless are 0.998, 0.999, and 0.999, respectively. The Estimated Bias and Estimated Percent Bias for Passing-Bablok regression at all 3 medical decision points (115 mmol/L, 135 mmol/L, and 150 mmol/L) for all sites combined are 0.00. **Conclusion:** Multi-day and whole blood precision results demonstrate acceptable precision on the next generation i-STAT. Method comparison results demonstrate acceptable correlation between the next generation i-STAT and the i-STAT 1 wireless for whole blood specimens. Overall the clinical evaluation of the next generation i-STAT using the sodium assay demonstrated equivalent performance between the next generation i-STAT and the iSTAT 1 wireless in a Point-of-Care (POC) setting. The study was funded by Abbott Laboratories.

B-253

Analytical and Clinical Evaluation of the NowDx Whole Blood Qualitative hCG Device

R. D. Nerenz, J. R. Bell, N. M. de Oca, J. Short, T. Mims, J. D. Moore, R. L. Humphries. *University of Kentucky, Lexington, KY*

Background: Point-of-Care (POC) urine qualitative hCG devices are frequently used to rapidly assess pregnancy status but these devices are susceptible to false negative results caused by elevated concentrations of hCG beta core fragment (hCGβcf) that are frequently encountered during normal pregnancy. In this study, we evaluate the analytical and clinical performance of the NowDx qualitative hCG device approved for use with capillary fingerstick whole blood, a specimen that does not contain hCGβcf.

Methods: hCG-negative heparinized whole blood was spiked with purified hCG to generate samples with known hCG concentrations and the resulting samples were used to evaluate device sensitivity, low-end reproducibility, high-dose hook effect, linearity, acceptable specimen volume, acceptable hematocrit range and lot-to-lot variation. Device results were interpreted by ten laboratory technologists with a range of experience with qualitative hCG testing. To confirm the hCG concentrations of the spiked whole blood specimens, quantitative hCG measurement was performed in plasma isolated from each specimen using the Roche Cobas e602. Device performance was also prospectively evaluated in 40 pregnant and 40 non-pregnant women aged 18-44 in a hospital-based clinic or an academic hospital emergency department. Capillary fingerstick whole blood hCG results were compared to urine qualitative (Beckman Coulter Icon 20) and plasma quantitative (Roche Cobas e602) hCG test results generated during the same clinic or hospital visit. IRB approval was obtained for this study.

Results: 100/100 device observations were positive when used to test a whole blood specimen containing a plasma hCG concentration of 18 IU/L and 18/20 were positive at 17 IU/L. 20/20 device observations were positive at 2.2 $x10^6$ IU/L, although test line intensity began to decrease

above 6.0 x 10^5 IU/L. 100% of device observations were positive over a range of 18 IU/L to 1.2 x 10^3 IU/L and from 2.5 x 10^4 IU/L to 2.2 $x10^6$ IU/L but three invalid results were observed in the intermediate range (2/20 invalid at 5.7 x 10^3 IU/L and 1/20 invalid at 1.2 x 10^4 IU/L) due to decreased control line intensity. 60/60 observations were positive at a specimen volume $\geq$ 30 µL but 1/60 was positive at a specimen volume $\leq$ 25 µL. 20/20 observations were positive at a hematocrit of 46.2% and 16/20 were positive at 50.3%. The non-positive observations were invalid due to the absence of a control line. In 40 pregnant and 40 non-pregnant prospectively recruited women aged 18-44, the NowDx device generated 100% agreement with urine qualitative and plasma quantitative test results.

Conclusions: The NowDx qualitative whole blood hCG device demonstrates acceptable performance for the determination of pregnancy status using capillary fingerstick specimens.

B-254

Moving a Point of Care Program from Vision to Action

H. Simon[1], M. Schmidt[1], P. Toupal[1], J. Joshua[2], M. Knutson[1], F. S. Apple[1], S. A. Love[1]. *[1]Hennepin County Medical Center, Point of Care Division, Department of Laboratory Medicine and Pathology, Minneapolis, MN, [2]Hennepin County Medical Center, Lean, Department of Performance Measurement & Improvement, Minneapolis, MN*

A Point of Care (POC) program has the unique opportunity to bridge the gaps that exist between the laboratory and nursing in a healthcare institution. There are many challenges that need to be overcome in order to have a quality POC program. Our objective was to demonstrate the usefulness of a visual management board (VMB) in overcoming barriers, empowering a POC program to address challenges collaboratively within an organization. We implemented a VMB that allowed us to prioritize POC specific challenges within the organizational goals. The VMB was

implemented in August of 2014 in the POC division as part of an organizational wide Lean management initiative. Goals were selected that aligned with the organizational scorecard. The priorities are categorized by focus areas such as: quality, patient experience, and employee engagement. The top 3 priorities are then displayed on the VMB in separate columns. It provides a visual display of the top level metrics, the problem analysis, and the quality metrics after improvements have been put in place. The organizational leadership rounds to the VMB to offer support and recognize accomplishments. We have found that the VMB has positively impacted patient safety, staff engagement, and leadership engagement. It allowed the problem solving process to be transparent and teachable within the department. First, POC was able to improve the utilization of scanning technology when identifying a patient for POC testing in the outpatient setting. A Pareto was used to analyze patient identification errors revealing that a majority of errors were caused by manual entry. Baseline metrics revealed that staff were using the scanning function only 8% of the time when identifying patients for POC glucose testing. An A3 problem solving tool revealed there was a lack of availability of a scannable barcode in the outpatient setting. The countermeasure required redesigning the patient visit label. Changes could not be implemented without understanding the unique needs of multiple departments. After implementation, scanning improved to 85.2% compliance. Second, we focused on improving critical glucose documentation by operators in the inpatient setting. This project is on its third A3 and there have been multiple countermeasures put in place. The baseline compliance was 12.1% in January 2015. The current compliance is 67.1%. A third A3 was completed and trending increased towards our scorecard goal of >90% compliance. Third, the POC team has worked together with nursing leadership and the electronic health record (EHR) team to develop countermeasures that will help staff be successful. Nursing leadership also developed an operator compliance policy in partnership with POC to standardize coaching and discipline. In conclusion, the implementation of a VMB in POC has fostered a collaborative environment and created more opportunities to build relationships across the organization. Each project has involved working with various disciplines and levels within the organization. It created a dynamic process improvement system that allowed the POC division to rapidly improve the overall quality of the POC testing program. The VMB gives an ongoing sense of purpose and drives the POC division's vision to action.

B-255

Development and Evaluation of The Transthyretin Assay for Point-of-Care Testing

D. Tokudome[1], T. Baba[1], H. Yoshida[1], K. Noma[2], M. Morimoto[2], T. Nobori[3]. *[1]NIPRO CORPORATION, Kusatsu, Japan, [2]Central Clinical Laboratories, Mie Univ. Hospital, Mie, Japan, [3]Oyamada Memorial Spa Hospital, Mie, Japan*

Background: The nutritional management for the elderly is getting more important than ever. The malnutrition results in the impairement of the immunity and the decreased muscle amount; as a result, it leads to the various problems such as the high morbidity from infectious diseases and the decline of the ADL. Therefore, the early detection of the malnutrition and the necessary medical intervention are important. Transthyretin (TTR), a rapid turnover protein (RTP) with a half-life of 2 days, is considered to be a sensitive indicator of the nutritional status. We have newly developed a rapid assay of TTR by immunochromatography using whole blood samples for the intended use at home or in clinic. In the prototype assay, the whole blood sample needed the two-step dilution which made the assay difficult to handle. To overcome this problem, we have made the device collecting a small amount (1uL) of blood followed by the one-step dilution and dispensing. In this paper, we report a performance of the sample collecting device and the TTR assay.

Methods: We first evaluated a quantity of whole blood by the sample collecting device. To characterize the analytical performance of the TTR assay, we evaluated the limit of Quantitation (LOQ), linearity, within-run precision, an effect of interfering substances, correlation with turbidimetry and nephelometry and comparison of blood collection sites. The fundamental assay performance was evaluated using control sera. For testing correlation, whole blood samples were measured by IC and the results were compared with measured levels of plasma samples by turbidimetry and those of serum samples by nephelometry. For the comparison of blood collection sites, we measured whole blood samples collected from antecubital vein, fingertip and earlobe in 10 healthy individuals.

Results: The precision of a quantity of blood collected by the device when measured 5 times was CV3.9% and average value was 1.26uL. The device shortened the sample preparing time to one third (the device: 24sec, the prototype method: 83sec). The LOQ of the TTR assay was 8.3mg/dL (CV≤10%). The linear range was 8.7mg/dL - 35.4 mg/dL, when the error of measured value is within +/-10%. The within-run precision of 10-time measurement of two sera with different concentration were CV6.1% and 8.6%, respectively, with an average value of 15.7mg/dL and 26.5mg/dL. Interference substances tested did not influence the measurement. The correlation between IC(y) and turbidimetry(x) was determined to be y=0.968x+0.883(R=0.958, n=43). The correlation between IC(y) and nephelometry(x) was determined to be y = 0.927x + 2.62 (r=0.935, n=64). There was no significant difference of measured values in each of the two groups by paired t-test (venous-earlobe p=0.108, venous -fingertip p=0.206, earlobe-fingertip p=0.781).

Conclusion: The sample collecting device made it possible to easily prepare the diluted sample. The TTR assay using the sample collecting device will be useful to evaluate the nutritional status of the elderly at home and in clinic and to monitor the effect of nutrition intervention.

B-256

Development of a novel immune-chromatographic assay for quantitative detection of NT-proBNP

Q. Zhang[1], M. Du[1], Y. Li[1], M. Chen[2], Y. Wan[3], Y. Cui[4]. *[1]Xi'an GoldMag Nanobiotech Co.,Ltd, Xi'an, China, [2]The first affiliated hospital of Xi'an Jiaotong University, Xi'an, China, [3]Providence college, Providence, RI, [4]Northwest University, Xi'an, China*

Background: Clinical data have revealed a strong association between the N- terminal pro-B-type natriuretic peptide (NT-proBNP) level and the mortality in patients with heart failure. Therefore, the NT-proBNP is recommended as a promising marker for the diagnosis of heart failure as well as acute coronary syndrome. While immuno-fluorescence quantity analysis is widely used to detect NT-proBNP, the result of this method can be stable for a quite short time after adding sample, which may result in the detection error. Here we have developed a new rapid and quantitative assay for the detection of NT-proBNP on the principle of lateral flow immunochromatography.

Methods: This new magnetic immuno-chromatographic assay device is set up based on sandwich format using both magnetic nanoparticles conjugated to anti NT-proBNP antibody and goat-anti rabbit IgG immobilized on the nitrocellulose membrane as probes to detect NT-proBNP for standards or sera of patients. The strip is comprised of a sample pad, two conjugate pads, NC membrane, and an absorbent pad. The concentration of NT-proBNP was calculated by the detection of magnetic intensity using the Magnetic Assay Reader (MAR). The detection can be completed within 20 minutes while it remains reliable for 40 minutes. Clinical tests for 200 of human sera sample were tested by our method and the comparison method of proBNP electrochemiluminescence (ECL) kits (Roche Diagnostics) simultaneously.

Results: This new method is able to differentiate concentrations of NT-proBNP from 0 to 8000 pg/ml with a correlation coefficient of R^2=0.9914, and the limit of detection (LOD) is 43 pg/ml. An attractive combination of a medically relevant LOD, high dose-response sensitivity and high reproducibility allows the analysis of both low and high concentration with this assay strip. For the group with 250 pg/ml, the intra-assay CV is 4.25% (run 1),5.00% (run 2),and 5.06% (run 3),respectively. The CV for inter-assay is 7.00%. For another group with 2000 pg/ml, the CV for intra-assay is 8.10% (run 1),8.50% (run 2),and 13.70% (run 3) and the inter-assay CV is 8.10%. According to the examination of specificity, there is no cross reaction in the presence of 10 ng/ml cTnI, 1ng/ml NT-proANP and 3.5 µg/ml BNP. No interference was observed when testing with icterus (bilirubin up to 0.2 mg/ml), hemolysis (hemoglobin up 10 mg/ml) and lipemia (triglycerides up to 200 µg/l). In the clinical tests of 200 human sera samples, comparison of our assay with Roches ECL kit yielded an equation of Y (Bland-Altman Plot) =0.9796X+60.87 (R2=0.9860). The comparison results also showed a bias offset of 28.98 pg/ml with 95% limits of agreement (bias and 2SD) from 6.056 to 72.74 pg/ml for NT-proBNP.

Conclusion: Through immuno-chromatographic assay using gold magnetic nanoparticles as a carrier, we have established a novel quantitative testing approach to measure NT-proBNP in serum. The results show that this novel and simple test is of high sensitivity and accuracy comparable an approved IVD. With a portable MAR Assay Development System that has been approved by US FDA, this new method could be widely used in point of care testing of NT-proBNP in the near future.

B-257

Development of an assay for measuring biochemical parameters in 65-µL fingertip blood samples collected at home

S. OSAWA[1], S. SUGIMOTO[1], Y. KUDO[2], K. TERASHIMA[3]. *[1]Leisure, Inc., Tokyo, Japan, [2]International University of Health and Welfare, Chiba, Japan, [3]Fujifilm Co., Kanagawa, Japan*

BACKGROUND

The prevention of lifestyle-related diseases is important for improving health and reducing medical costs in aged societies like Japan. Thus, we newly produced a test kit for performing health checkups based on 65-µL fingertip blood samples. The examinees collect the blood samples according to written instructions and isolate diluted plasma themselves. The samples are then mailed to a laboratory.

METHODS

1. The **DEMECAL kit**

The **DEMECAL kit** (Fujifilm, Japan) is composed of a tube, dilution buffer solution, a lancet, a blood-aspiration sponge, a cylinder with a blood cell separation filter, a cap, a swab, and a sticking plaster. The dilution buffer solution is composed of 4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid buffer and ethylenediaminetetraacetic acid dipotassium salt dihydrate (EDTA-2K).

2. Calculation of biochemical concentrations in diluted plasma

The plasma sample dilution ratio was measured by assessing the sodium level of each diluted sample using an enzymatic assay. The concentrations of each molecule in diluted plasma were then multiplied by the dilution ratio.

3. Measurement of sodium dilution

The dilution of plasma sodium was determined using an enzymatic rate assay involving β-galactosidase and *o*-nitrophenyl-*β*-galactopyranoside.

4. Instrument and measurement conditions

A JCA-BM6050 automated analyzer (JOEL Ltd., Japan) was used to obtain the biochemical measurements with commercially available reagents. The sample volume was greater than that of the original sample.

RESULTS

The sodium analysis exhibited good linearity from 0-25 mmol/L. The proportionality of the dilution rate of sodium was twenty fold admitted. The measurements were performed 20 times, and the mean co-efficient of variation (CV) at a dilution rate of 9.8-fold was 2.2%. To examine the within-run variation of the **DEMECAL kit**, 20 EDTA whole blood samples were analyzed as venous blood samples. The CV (%) of the examined parameters were as follows: aspartate aminotransferase (AST): 3.8, alanine aminotransferase (ALT): 2.6, gamma-glutamyl transferase (GGT): 2.3, total cholesterol: 2.3, high-density lipoprotein (HDL)-cholesterol: 2.4, low-density lipoprotein (LDL)-cholesterol: 2.3, triglycerides: 1.6, creatinine: 3.4, urea-nitrogen: 2.2, uric acid: 2.3, and glucose: 2.7. The correlations between the results obtained with the **DEMECAL kit** and venous plasma analysis were as follows: AST: 0.990, ALT: 0.998, GGT: 0.998, total cholesterol: 0.973, HDL-cholesterol: 0.987, LDL-cholesterol: 0.990, triglycerides: 0.999, urea-nitrogen: 0.993, creatinine: 0.966, uric acid: 0.994, and glucose: 0.994. The diluted plasma remained stable in three different temperature conditions (4°C, room temperature, and 37°C).

CONCLUSIONS

This measurement system can provide reliable clinical data about various molecules in diluted plasma derived from 65-µL samples of fingertip blood collected at home. The **DEMECAL kit** can be used to collect blood at distant locations, providing a suitable transport system is available, and hence, can contribute to nationwide healthcare provision. The **DEMECAL kit** can also be employed for other biochemical and immunity tests.

B-258

Basic Evaluation of a novel Glycohemoglobin Analyzer RC20 for POCT

E. Hamada, M. Maekawa. *Hamamatsu University School of Medicine, Hamamatsu, Japan*

Background: An HbA1c (glycohemoglobin) test can check the long-term control of blood glucose levels, and is essential to diagnose prediabetes or diabetes. Therefore, HbA1c can be hopefully checked in clinics and small-sized hospitals as well as large hospitals. Glycohemoglobin Analyzer RC20 (RapidColumn A1c) is a compact autoanalyzer based on HPLC and can be used for point of care testing (POCT). Here we evaluated analytical performance of the glycohemoglobin autonalyzer.

Methods: Rapid Column A1c and its dedicated reagents (Sekisui Medical Co., Ltd.) were compared with HLC-723 G9 (Tosoh Co.).

Results: The within-run precision (CV) examined by using patients' specimens was 0.4%, and between-run precision using HbA1c control (Sekisui, JCCRM411-3, Sysmex Co.) for 8 days (n=2) was 0.6 to 1.0%. The trueness examined by using JCCRM411-3 level 1 to 5 for triple assay was below 0.12% for the bias and -1.21 to 1.00% for the relative error. The relation between the two analyzers examined by using patients' specimens was 0.995 for the correlation efficient and y=0.971x + 0.10 for the regression line.

Conclusion: The basic performances of Glycohemoglobin Analyzer RC20 were satisfactory. We assessed the device useful for POCT. In addition, the device has some excellent properties, for example easy handling and maintenance, user friendliness, small sample volume (3 microL), short measuring time (3 min), comfortable reporting and search function. The excellent performance could lead to improved patient care in POCT.

B-259

Activated Clotting Time (ACT): Comparison of the Hemochron Signature Elite and the Abbott i-STAT

L. M. Evans[1], S. Gallo[1], J. J. Leo[2], B. M. Goldsmith[1]. *[1]Thomas Jefferson University Hospital, Philadelphia, PA, [2]Specialty Care, Inc, Nashville, TN*

Background: ACT is commonly used for heparin anticoagulation monitoring during procedures including cardiopulmonary bypass surgery, coronary angioplasty, and interventional radiology. To prevent thrombosis, moderate to high levels of heparin anticoagulation are required. The Hemochron Signature Elite (HSE, Accriva Diagnostics, formerly ITC, San Diego, CA) was implemented at TJUH as a replacement for the older model Hemochron Response (Accriva/ITC Model HRS.110, San Diego, CA). Operating room (OR) perfusionists reported irreproducible high results using HSE that could not be explained clinically. In consideration of use of i-STAT analyzers (Abbott Point of Care, Princeton, NJ) as an alternative to HSE, we performed a comparison of ACT results as analyzed by HSE and i-STAT (Abbott Point of Care, Princeton, NJ) analyzers.

Methods: A comparison of inter-device reproducibility of results for each method was performed using the same samples for both the HSE and i-STAT (22 OR patient specimens, sampled across all analyzers within a 10 sec interval), measured in duplicate across two separate analyzers for each method. Measuring ranges were: HSE-68-1005 sec; i-STAT-50-1000 sec. Linearities for HSE (Kaolin ACT+ cartridges) and i-STAT (ACT-K cartridges) analyzers were assessed by heparin dilution curves. Precision for each method was measured by repeat testing of controls. In the duplicates experiment, 10 additional specimens were excluded because HSE results exceeded the HSE measuring range.

Results: Precision for i-STAT controls (n=40) were 3.6% CV and 3.8% CV (91-169 sec and 406-754 sec, respectively) across devices. These were comparable to precision for HSE controls (n=120), which were 5.5% CV and 2.3% CV (110-196 sec and 284-504 sec, respectively). A heparin curve demonstrated acceptable linearity for the i-STAT ACT therapeutic range (units heparin/mL = x, heparin response (sec) = y, $R^2 = 0.9613$, y = 99.607x + 174.61, range = 107-748 sec) and also for the HSE ACT therapeutic range. A comparison of inter-analyzer reproducibility between HSE and i-STAT showed significant differences, however. Among 22 specimens, the average % difference from the mean for HSE results across two analyzers (4.6%; median ACT = 477 sec, range 91-757 sec) was significantly different ($p < 0.002$) from that for i-STAT results (1.8%; median ACT = 374 sec, range = 106-951 sec). Correlation of average results was $r^2 = 0.05881$, 0.946x + 35.5.

Conclusion: Both i-STAT (ACT-K cartridge) and Hemochron Signature Elite (Kaolin ACT+ cartridge) analyzers showed acceptable linearity, and there was reasonable correlation between ACT results from each. However, we found that the iSTAT ACT-K cartridge performed with better precision and cross-device reproducibility than the Hemochron Signature Elite (Kaolin ACT+ cartridges) for patient samples. The i-STAT was subsequently chosen for measurement of ACT in the OR.

B-260

Performance of Creatinine and Chloride on the epoc Analyzer

L. M. Evans, S. Gallo, S. K. Mardekian, B. M. Goldsmith. *Thomas Jefferson University Hospital, Philadelphia, PA*

Background: The epoc Blood Analysis System (Alere, Orlando, FL) performs blood gases, electrolytes, and metabolites using a Blood Gas Electrolyte and Metabolite

(BGEM) Test Card panel on 92 uL of whole blood. The BGEM test card uses potentiometric sensors to measure sodium, potassium, ionized calcium, pH, pCO2; amperometric sensors to measure pO2, glucose, and lactate; and a conductometric sensor to measure hematocrit. Results are available in 3-10 minutes, depending upon the time between calibration and patient testing. TJUH implemented the epoc in its ICUs in 2012 to provide Point of Care (POC) results. Alere recently added creatinine and chloride sensors to its BGEM cartridge. At the request of our Emergency Department, we evaluated creatinine and chloride on the epoc.

Methods: Precision and method comparisons were performed at our Center City (CC) and Methodist Hospital (MH) sites. Whole blood was collected from 40 CC patients and 24 MH patients. Inter- and intra-precision was performed on 3 levels of controls (Eurotrol, Burlington, MA). Comparison studies were performed on the RapidLab 800 (Radiometer, Brea, CA) at the CC site. Comparison studies were performed at the MH site on the GEM 3500 blood gas analyzer (Instrumentation Laboratories, Bedford, MA) and the Cobas 6000 (Roche, Indianapolis, IN) using plasma from concurrently drawn specimens.

Results: Intra-precision for creatinine on the epoc (n=20, 4 devices) was 6.6%CV, 2.1%CV, and 3.9%CV for Levels 1, 2, and 3, respectively, and 0.7%CV, 0.6%CV, and 0.5%CV, respectively for chloride. Inter-precision for creatinine (n=20, 4 devices over 5 days) was 3.9%CV, 2.0%CV, and 2.7%CV for Levels 1, 2, and 3, respectively and 1.1%CV, 0.5%CV and 0.5%CV, respectively for chloride. Method comparison for CC for creatinine (n=40) was: mean=1.636, median=1.135, r^2= 0.979, y=1.0343x+0.0317, and for chloride (n=40) mean=107.8, median=107.25, r^2=0.888, y=0.839x+17.634. Method comparison for MH for creatinine (n=24) was: mean=1.105, median=0.730, r^2=0.8944, y=1.1125x-0.1095, and for chloride (n=24) mean=103.667, median=104.000, r^2=0.8172, y=1.0275x+1.7272.

Conclusion: The epoc creatinine and chloride studies performed showed comparable results when compared to laboratory results and considered acceptable for implementation at those sites where epoc is currently in use.

B-261

The Stability of Color and Clarity in Urinalysis Quality Control Products

A. T. Schaeffer, M. Ban, M. Ghadessi. *Quantimetrix Corporation, Redondo Beach, CA*

Background: Color and clarity are important parameters in urinalysis. Changes in urine color can be caused by urine concentration, presence of blood, drugs, or ingestion of certain foods. The clarity of the urine is an important indicator of infection, but can also be affected by many other factors. This study was designed to determine whether clarity and color would remain stable in human urine preparations designed to act as quality control products for urinalysis.

Methods: : Human urine from multiple donors was combined and preserved using antibiotics to prevent microbial growth during the duration of the study. The combined urine was then split into two pools. The first pool was held without further modification and designated the normal pool. The second pool was further modified by the additions of reagents to produce a positive reaction on all the pads found on Siemens Multistix® 10SG reagent strips. This was designated the abnormal pool. The urine was then dispensed into either 15 mL glass tubes (dipper format) or 25 mL plastic bottles with a dropper tip (dropper format). The filled tubes and bottles were held at either 2-8 or 25°C. The Dipper tubes were dipped into 20 times using the Multistix 10SG. Color and clarity were determined using a Siemens Clinitek 500 analyzer. This study was repeated three times.

Results: Color and clarity were determined to be yellow and clear in both the normal and abnormal urine pools at the beginning of the study for both the dipper and dropper format. The pools remained yellow and clear for up to 18 months when stored at 2-8°C. They also remained unchanged for up to 48 days when stored at 25°C. It was found that 20 dips of the Multistix 10SG urinalysis strips into the dipper tubes did not change the color or clarity of either the normal or the abnormal pool, when using the dipsticks as per the manufacturer's instructions. The addition of the reagents to the abnormal pool including; protein, bilirubin and urobilinogen reactive compounds, and hemoglobin did not lead to detectable changes to the color or clarity of the material either initially or over time at either of the tested temperatures.

Conclusion: The results of this study demonstrate that color and clarity are stable in both the normal and abnormal pools of preserved human urine for up to 18 months when stored at refrigerated temperatures and up to 48 days when stored at room temperature. In addition, the color and clarity of the pooled urine placed in Dipper tubes is not affected by up to 20 dips using Multistix 10SG reagent strips. These results demonstrate that the color and clarity parameters can be incorporated into the quality plan of laboratories performing urinalysis using the Siemens Multistix 10SG strips and the Clinitek 500 reader.

B-262

Development of a Novel Quantum Dot-based Immunoassay for Point-of-Care Testing

R. Wu[1], S. Zhou[2], T. Chen[2], J. Li[1], H. Yuan[2], H. Shen[1], X. Chai[2], L. Li[1]. *[1]Henan University, Kaifeng, China, [2]Neptunus NanoBio-Med Co, Taizhou, China*

Background: There is a need for point-of-care testing (POCT) of common lateral flow immunoassays that can do all common diagnostic tests reliably, high sensitive, and low in cost (device and consumable cost). Here we have developed a novel quantum dot-based immunoassay for POCT. The tunable optical and physical properties of semiconductor quantum dots (QDs) based on their size and shape have attracted considerable interest for biological and medical applications. Due to QD's highly photoluminescent quantum yields and stability, it is potentially a good candidate to replace organic dye as new generation fluorescence labels and can be widely used in POCT.

Methods: Starting hydrophobic CdSe/ZnS core-shell QDs were prepared according to low-cost, green, phosphine-free method. Then, an amphiphilic oligomer was used to prepare water-soluble CdSe/ZnS QDs. Certain amount of oligomer and QDs was dispersed in chloroform and stirred for 1 h (room temperature, molar ratio of QDs/oligomer was 1:2) in a flask. After stirring, chloroform was gradually evaporated, and a clear solution of water-soluble QDs was obtained after the pH value of solution was kept between8-10. After the conjugation with selected antibodies by an EDC/NHS-mediated course, such QD-based photoluminescent probes was stored at 4degree before use. To prepare QD based-lateral flow immunoassays strips, selected antibody was dispensed onto a nitrocellulose membrane as a test line and the QD probes and selected antigen were dispensed onto a sample pad by using the XYZ Dispensing System (BioDotInc, Irvine, CA). The sample pad was treated with 10 mM sodium phosphate (pH 7.4) buffer, BSA (0.5%, w/v) and Triton-X100 (2%, w/v) and dried before the dispensation. The membrane and sample pad were then dried overnight at room temperature under 10% relative humidity condition. Then the membrane and sample pad were assembled and cut into strips with a width of 3 mm/strip by using the CM4000 Guillotine Cutter (BioDotInc, Irvine, CA). To perform the detection, different test solutions were added to the end of the sample pad. The QD fluorescence signal on the test line was observed by home-made photoluminescent detection device.

Results: Data analysis indicates that the QD-based lateral flow immunoassays have a CV <15%.The linearity fell in the range of 0-200 mg/L of C-reactive protein (CRP), and the analytical detection limit was 0.048 mg/l within 5 min. The mean recovery of the control was 102.63% in a working range. Through cross-reactivity, it can be out of interference of bilirubin, hemoglobin, lipoidaemia, rheumatoid factor. The QD-based lateral flow immunoassays correlated well with Tina-quant CRP (Latex) for quantification of CRP concentration (r = 0.956, N = 213).

Conclusion:The developed technology platform for QD-based lateral flow immunoassays is reliable with high sensitivity. It meets all the performance specifications of POCT. Hence, we believe it can be easily applied for low cost, sensitive, quantitative, and rapid detection of common diagnostics tests for infection diseases (such as CRP, Procalcitonin, HIV, Syphilis, Hepatitis, *etc*), tumor, and chronic cardiovascular/cerebrovascular diseases (like Myo, cTn, CKMB, AST, LDH, *etc*).

B-263

A Quantum Dot-based Fluorescence-linked Immunosorbent Assay for Rapid Disease Detection

Y. Lv[1], K. Feng[2], R. Wu[1], Q. Mao[2], J. Li[1], H. Yuan[2], H. Shen[1], X. Chai[2], L. Li[1]. *[1]Henan University, Kaifeng, China, [2]Neptunus NanoBio-Med Co, Taizhou, China*

Background: The conventional and widely used enzyme-linked immunosorbent assays (ELISA), due to fast and high-sensitive, were suitable *in vitro* diagnosis and a large number of samples screening. In this study, we have developed a novel quantum dots-labeled immunosorbent assay for rapid disease detection. Semiconductor quantum dots (QDs) have been successfully used in biological and medical research, with high luminescence and high resistance to photobleaching. Furthermore, the developed immunoassay has immense potential for the development of rapid and cost-effective *in vitro* diagnostic kits.

Method: The aqueous CdSe/ZnS QDs was conjugated with antibody to produce QDs-Ab probes using EDC and NHS as coupling reagents. Then, the QDs-Ab was purified by centrifugation and the product was stored at 4degree before use. The monoclonal antibody (mAb) was immobilized on a standard 96-well microplate by the following protocol: Primary antibody was diluted in 50mM carbonate-bicarbonate buffer (pH

9.6) and incubating 24h at 4degree. Then excess binding sites were blocked with BSA (0.5%, w/v) in 10mM PBS (pH 7.4) incubating overnight at 4 degree after removing excess coating antibody by washing three times with washing buffer(10mMPBS containing 0.05% Tween-20, PBST). Then different concentrations of antigen (Ag) were captured by the mAb immobilized on the microplate. At last the QDs labeled detection antibody is introduced to form a mAb-Ag-mAb sandwich complex. Within a certain range, the fluorescence intensity which can be read out using the SpectraMax i3 Multi-Mode microplate reader was enhanced gradually with the increase of antigen concentration.

Results: Through the optimization of reaction conditions, we established a new detection method *in vitro* with the reaction time regulated within 50min,which is shorter than the commercialization ELISA. The novel assay provides a linear analytical range, such as C-reactive protein (CRP) assay range of 0-400 ng/mL with a detection limit of 1.61 ng/mL and procalcitonin (PCT) assay range of 0-100 ng/mL with a detection limit of 0.09 ng/mL. The precision of the assay has been confirmed for low coefficient of variation (CV), less than 10% (intra-assay) and less than 15% (inter-assay), and together with recoveries of 85-105%. Through interferences and cross-reactivity, it can be out of interference of bilirubin, hemoglobin, lipoidaemia, and rheumatoid factor.

Conclusion: This developed analytical method meets all the needs of the rapid, sensitive, and high-throughput determination of inflammation factors (CRP and PCT). It has not only shortened the reaction time, but also simplified the operation steps, and more important, the detection sensitivity was greatly improved. This result indicates that the developed method can be applied to rapid disease detection effectively.

B-264

Clinical Equivalence of the VerifyNow PRUTest and P2Y12 - Target Values for Patients Treated with Thienopyridine Inhibitors

G. Garner, D. Britch, J. McDermed, M. Foster, F. M. LaDuca. *Accriva Diagnostics, San Diego, CA*

VerifyNow (VN) uses light transmission technology to measure platelet function in whole blood and the effectiveness of specific platelet inhibitors. The thienopyridine class of inhibitors including clopidogrel and prasugrel are used in acute coronary syndrome (ACS) to block the ADP platelet P2Y12 receptor, thus reducing platelet induced vascular obstruction. The native VN P2Y12 test has been used in large randomized trials, including GRAVITAS, which defined the P2Y12 value of 208 as an effective platelet inhibition for reducing thrombosis and ischemia. PRUTest (P2Y12 Reaction Units) is the next generation assay. This study was undertaken to demonstrate the equivalence of the two assays to ensure transference of the ACS trial information to the current PRUTest platform. Following an initial direct method comparison study, in which normal donors were evaluated showing equivalence of the PRU lower limit reference range (x = 183; 2.5 centile; 90%CI= 169-198, N=147) and P2Y12 (x = 180; 2.5 centile 90%CI=164-197, N=84), a survey of PRU values in an ACS platelet inhibited population was conducted. The table below demonstrates PRU mean values, SD, central 90% CI for untreated (N=231) and treated (N=101) patients with drug dosage shown for clopidogrel, prasugrel and aspirin, usually given in a dual antiplatelet regimen.

Parameter	No treatment	Clopidogrel	Prasugrel
N	231	71	30
Mean	297	160	98
SD	56	73	71
2.5th centile (90% CI)	186 (175-196)	12 (-11-37)	3.5*
97.5th centile (90% CI)	408 (398-419)	307 (283-330)	268*
Mean aspirin dose (SD)	NA	167 (117)	171 (120)
Mean P2Y12-RI dose (SD)	NA	79 (28)	13 (13)
*Calculated by non parametric percentile method (CLSI C28-A3). All others by "robust" method			

Summary: The P2Y12 receptor inhibitors clopidogrel and prasugrel inhibit platelet aggregation measureable as a statistically lower PRU range compared to that of the untreated ACS population. In the study population 19.0% of clopidogrel treated patients did not achieve a PRU value <200 PRU; which coincides with medical literature which cites 20-25% patients retain high residual platelet reactivity (HRPR) on clopidogrel ("clopidogrel resistance"). These patients are at a much higher risk of cardiovascular events, e.g., myocardial infarction and stroke and require more aggressive antiplatelet drug treatment. The VerifyNow PRUTest provides the means to identify and properly manage clopidogrel effectiveness.

B-265

Evaluation of the LABGEO PT10 point-of-care testing: Comparison between capillary whole blood and lithium heparin whole blood

J. Lim, G. Kwon, H. Kim. *Chungnam National University Hospital, Daejeon, Korea, Republic of*

Background: Point-of-care (POC) testing device has been widely used because of its rapid availability of results making diagnosis and management as early as possible. Collection of venous blood samples through venipuncture requires technical expertise of sample. However, capillary blood can dramatically reduce the difficulty of obtaining samples and allows the prompt testing results facilitating patient management even faster. In this study, by comparing the measurements in Samsung LABGEO PT10 using capillary blood with those using lithium heparin whole blood and in central laboratory using serum, we evaluated the usefulness of capillary blood in Samsung LABGEO PT10.

Method: A total of 51 patients and 18 healthy adults aged between 20 and 65 were enrolled. Capillary and venous blood samples were collected after informed consents were obtained. Venous blood samples were split into lithium heparin tube and serum separating tube. Measurements using capillary blood and lithium heparin whole blood were performed in LABGEO PT10. Venous samples in serum-separating tube were centrifuged and serum was used for measurement by Toshiba 2000FR NEO in central laboratory duplicate. Comparison of measurement results were as follows; 1) Measurements in LABGEO PT10 using capillary blood and lithium heparin whole blood, 2) Measurements in LABGEO PT10 using lithium heparin whole blood and in central laboratory using serum, and 3) Measurements in LABGEO PT10 using capillary blood and in central laboratory using serum.

Results: In comparison between measurements in LABGEO PT10 using capillary blood and lithium heparin whole blood, the slope ranged between 0.9289 and 1.0795, R^2 was over 0.95 except albumin, high density lipoprotein and total protein. Comparison between measurements in LABGEO PT10 using lithium heparin whole blood and in central laboratory using serum revealed that the slope ranged between 0.6255 and 1.1602 except alkaline

phosphatase, R^2 was over 0.95 for most of anlaytes. And in comparison between measurements in LABGEO PT10 using capillary blood and in central laboratory using serum, the slope ranged between 0.6433 and 1.1364 except alkaline phosphates, R^2 was over 0.95 for most of analytes. In Bland-Altman analysis, all measurements were within 95% limit of agreement.

Conclusion: Measurements in LABGEO PT10 using capillary blood was well correlated with those in LABGEO PT10 using lithium heparin whole blood and also with in central clinical laboratory using serum. In conclusion, capillary blood provides reliable measurements across a clinically relevant range and can be trustfully used in LABGEO PT10.

B-266

Use of the Piccolo XPress (Abaxis) as a point-of care analyser in an ebola setting

L. Florin, V. Stove. *University Hospital Ghent, Ghent, Belgium*

Introduction The Piccolo Xpress (Abaxis) is a CLIA-waived portable point-of-care analyser, able to perform multiple assays simultaneously on a single-use reagent disc, after the addition of 100 µL Li-heparin whole blood, plasma or serum. This device was placed in the laboratory of the Ghent University Hospital for testing of blood from suspected ebola patients. The aim of this study was to carry out a performance characterization of the AmLyte 13 reagent disc (albumin, ALT, amylase, ALST, total bilirubin, calcium, CK, creatinine, CRP, glucose, K, Na and blood urea nitrogen) on the Piccolo Xpress.

Methods Accuracy (n=10) was tested on 2 levels Abaxis Chemistry quality control material. Within-run and between-run imprecision were assessed with both quality control material (n=10) and 2 patient samples (n=6). Method comparison was performed on 70 whole blood Li-heparin samples (50 ICU patients, 20 healthy volunteers) against the routinely used core laboratory Cobas 8000 chemistry analyser (Roche Diagnosics) and the RP450 blood gas analyser (Siemens) for glucose, K and Na. Check of reference values was done on 20 healthy volunteers and lot-to-lot comparability was verified on 11 samples.

Results Imprecision and accuracy did not all fulfil Westgard acceptance criteria, with i.e. AST, ALT and creatinine suffering from high variability on patient samples (11%, 11% and 9% respectively) However, this variability was considered to be acceptable for the purpose of this device. Method comparison showed a good correlation to

both Cobas 8000 and RP450, with exception of sodium (correlation coefficient 0.80 compared to Cobas and 0.75 to blood gas analyser), which showed a high scattering of results on the Bland-Altman plot. A significant bias was observed (Piccolo vs Cobas) for both albumin (-17%; to be explained by differences in methodology) and amylase (-22%). Check of reference values was within criteria for all parameters, however very wide reference intervals were observed for both albumin (33 - 55 g/L) and sodium (128 - 145 g/L). Wilcoxon test for paired samples was performed for lot-to-lot comparability of the 13 different parameters and although statistically significant differences were observed for some assays, none were found to be clinically significant.

Conclusions The point-of-care Piccolo Xpress analyser of Abaxis is easy to use and demonstrates acceptable performance for the tested AmLyte 13 reagent disc. Significant differences were found for albumin and amylase compared to the core lab Cobas 8000 chemistry analyser, and hence, these results are not 'as such' interchangeable. Sodium results on the Piccolo show a high variability and are not reliable for routine practice. We conclude that the Piccolo Xpress is suitable for analysis of critical sera from suspected ebola patients in an urgent setting.

B-267

Development and Performance Evaluation of urinary soluble CD14 immunoassay on FREND system

K. Lee[1], C. Lee[1], S. Yoo[2], Y. Park[2], W. Kim[2], S. Han[1]. *[1]NanoEnTek, Seoul, Korea, Republic of, [2]Catholic University of Korea, Seoul, Korea, Republic of*

Background: FREND System is a portable FREND cartridge reader which is based on immunoassay technology capable of quantifying single or multiple analytes by measuring laser-induced fluorescence in a single-use disposable reagent cartridge. CD14 is a component of innate immune system which recognizes pathogen-associated molecular patterns such as LPS. Soluble CD14 (sCD14) is soluble form of CD14 and it either appears after shedding of membrane anchored CD14 (mCD14) or is directly secreted from intracellular vesicles. Recently, it has been reported that urinary sCD14 had a high predictive value for rheumatoid arthritis (RA) disease activity when combined with a conventional serum biomarker. We developed a fluorescence immunoassay (FREND uCD14) to measure the level of urinary sCD14 on the FREND System, which may serve as a valuable monitoring tool for RA patients. **Objective:** The objective of this study is to evaluate the analytical performance of FREND™ uCD14 assay. **Methods:** The imprecision, linearity, method comparison and detection limit of FREND uCD14 were evaluated according to CLSI guidelines EP05-A3, EP 06-A, EP 09-A3 and EP 17-A2. The FREND uCD14 assay is traceable to the calibrators prepared with the recombinant soluble CD14 (R&D systems 383-CD-050). For the method comparison, aliquots of urine samples over the measuring ranges were measured with FREND uCD14 assay on NanoEnTek FREND™ system. The comparative assay was Human CD14 DuoSet ELISA (DY383, R&D systems) on TECAN Infinite M200 Plate reader. For the clinical performance evaluation, urine samples were collected from the patients with written consent who visited St. Mary Hospital. Urine samples from RA patients were tethered to the disease activity score 28-joint assessment (DAS28) which is measurement values of the disease activity from RA patients. Additionally, 100 apparently healthy subjects were enrolled for establishing the reference interval. **Results:** The imprecision for urinary sCD14 assay produced coefficient of variation (CV) of <10% (range 5.8-9.9%) at concentrations of 51.23, 182.90 and 398.16 ng/mL. The AMR of the assays were 10 ~ 500 ng/mL with ordinary least squares regression fit of y=1.0255x - 2.1767 (r^2=0.9898). LoD was determined to be 6.077 ng/mL. In the method comparison studies with R&D Systems Human CD14 DuoSet ELISA, the correlation coefficient(r) was 0.9956 (95% CI= 0.9930 to 0.9972), and the slopes /intercepts were 1.015 (95% CI= 0.9868 to 1.0441)/-1.3493(95% CI= -4.5261 to 1.9733) by Passing-Bablock regression fit. **Conclusion:** Data indicates that the newly developed FREND uCD14 assay exhibits reliable analytical performance and can be useful as an easy-to-use urinary RA monitoring kit. Clinical studies for Receiver-Operating Characteristic (ROC) curve analysis and reference interval establishment will be conducted shortly. **Acknowledgements:** This work was supported by grants from the Korea Healthcare Technology R&D Project, Ministry for Health, Welfare and Family Affairs (No. HI14C3417).

B-268

A new one-step direct-sampling HIV antibody rapid test.

M. Tsang[1], J. K. Babra[1], T. Yang[1], F. Kreutz[2], C. McArthur[3], M. Souleymane[4], Q. Shi[1]. *[1]ZBx Corporation, Toronro, ON, Canada, [2]FK BioTec, Porto Alegre, Brazil, [3]University of Missouri, Kansas City, MO, [4]University of Cheikh Anta Diop, Dakar, Senegal*

Background: The human immunodeficiency viruses 1 & 2 are the retroviruses that cause acquired immunodeficiency syndrome (AIDS). There are a number of tests that are used to determine whether a person is infected with HIV. They include the HIV antibody test, P24 antigen test and PCR test for HIV RNA or DNA. HIV antibody tests are the most appropriate test for routine diagnoses of HIV infections. Most people develop detectable HIV antibodies within 6 to 12 weeks of infection. There are many commercially available HIV antibody tests intended for use either in the laboratory or rapid tests for use at the point-of-care. Most rapid tests are multi-step in their operation requiring, for example, the addition of a chasing buffer or a pre-run dilution in order to complete the test. Each step possibly contributes to operator error and additional labour costs. However, a rapid test that is single-step in operation and requires only a small volume of whole blood and without the need of a sample transfer device, is ideal for point-of-care as well as self-testing for HIV infection. The objective of this study is to demonstrate the clinical utility of a new one-step HIV antibody test.

Principle: The ADEXUS-Dx HIV-1/2 Antibody Test was developed using a direct sampling immunoassay technology for whole blood, plasma or serum. HIV -1/2 recombinant antigens were employed for the detection of both HIV-1 and HIV-2 antibodies. A small sample volume (35µL) is required to run the test and no extra buffer is needed. Capillary blood from a finger tip can be directly applied to the test without any transfer device. When the sample is sufficient to fill a built-in receiving channel, it flows into a dry porous test strip composed of a membrane array with gold conjugated HIV antigens. The appearance of one or two visible purplish-red band(s) at the test region indicates the sample contains a detectable level of HIV antibodies for HIV-1 and/or HIV-2.

Performance: The ADEXUS-Dx HIV-1/2 Antibody Test requires less than 40µL of sample and was completed in 15 minutes without any additional step. Testing with the WHO HIV Antibody Reference Panel confirmed that the test recognized HIV-1 subtype A, B, C, E, Group O antibodies as well as HIV-2 antibodies. Clinical studies of the ADEXUS-Dx HIV-1/2 Antibody Test were conducted in three different countries: Brazil, Cameroon and Senegal. A total of 937 clinical samples (442 positive and 495 negative) were tested. There was 100% agreement for HIV antibody positive samples and 99.8% agreement for HIV antibody negative samples. Testing of a characterized 15 member low titer panel showed 14 positive samples.

Conclusion: The ADEXUS-Dx HIV-1/2 Antibody Test is a true one-step rapid test with excellent sensitivity and specificity. It is suitable for use in the detection of HIV infection at the point-of-care and for self-testing.

B-269

Design and evaluation of a mobile nucleic acid amplification testing system in a hospital emergency setting

D. Shin, P. Athamanolap, L. Chen, J. Hardick, M. Lewis, Y. Hsieh, R. Rothman, C. A. Gaydos, T. Wang. *Johns Hopkins University, Baltimore, MD*

Nucleic acid amplification tests (NAAT) possess remarkable sensitivity and speed capable of producing actionable results in an hour or less. However, today's clinical environment based on batch processing of samples in centralized laboratories introduces delays on the order of days or more. We previously reported the development of a low-cost mobile nucleic acid analysis platform for streamlined analysis of vaginal swabs for chlamydia screening. Here, we report the development of a comprehensive mobile phone user interface and evaluation of our platform in hospital emergency rooms by naïve operators. The platform consists of three components: a disposable cartridge, a phone charger-powered handheld instrument and a mobile phone user interface. The cartridge is designed based on the principle of droplet magnetofluidics which enables integration of sample preparation with amplification without sophisticated fluidic manipulation. Each cartridge costs less than $2 to manufacture, which is an order of magnitude cheaper than currently available molecular POC tests. Fluorescent LAMP assay is implemented on the cartridge, yielding analytical sensitivity of 10^2~10^3 copies of gene targets and excellent specificity against a panel of vaginal flora and human genomic DNA. The phone charger-powered instrument coordinates thermal incubation and magnetic particle manipulation via microcontroller-driven thermoelectric module and a servomotor. Initial validation using a panel of 20 blinded

vaginal swabs from clinical sample archives was evaluated against the standard of care NAAT assay, yielding full agreement. In order to facilitate easy access to the POC platform, we developed a comprehensive user interface around a mobile phone app. The interface consists of three features including a tutorial module, data archive and a 1-click test routine capable of acquiring POC data in a digital format. The tutorial provides concise video instructions outlining platform design and operation for naïve operators. The entire platform workflow takes up to 72 minutes from start to finish for a first-time user, including 6 minutes of user tutorial, 60 minutes of incubation and minimal hands-on time. Samples tested to this date amplified within the first 40 minutes, suggesting a workflow that is capable of delivering results within an hour of collection. Patients visiting the emergency department at Johns Hopkins Hospital were recruited in a chlamydia POC study, where two sets of swabs were collected during pelvic examination. One set was analyzed using the gold standard Gen-Probe AC2 CT assay. The second set was aliquoted and evaluated using the POC NAAT platform deployed in the emergency room. The two results were in agreement for 30 out of 30 samples, demonstrating that the POC assay performance is comparable to the gold standard for the samples tested. Subsequently, the remaining aliquot of tested samples was evaluated by a research staff member at the emergency department, whose sole exposure to the POC platform was via training module embedded in the mobile phone app. A total of 13 samples were evaluated, with results in full agreement with the standard of care assay. This study illustrates the potential utility of nucleic acid tests that are both mobile and user-friendly in a clinical environment.

B-270

The Variance between Point-of-Care (POC) and Clinical Chemistry Laboratory Glucose Testing Results in Critically Ill Patients

S. Narla, J. Forcucci, C. Newman, J. Epps, Y. Zhu. *Medical University of South Carolina, Charleston, SC*

Background: It is desirable that the results of POC glucose testing are comparable to those measured by clinical chemistry laboratory method in all patients. FDA recently proposed guidelines states that the current glucose meters may not be used for critically ill patients as the accuracy of the results in this patuent population is unknown. The objective of this study is to determine if the currently used glucose meters meet the FDA new criteria in critically ill patients.

Methods: Glucose was measured by POC glucose meters (FreeStyle Precision Pro, Abbott) and clinical chemistry analyzers (ARCHTECT c16000, Abbott) with a difference in blood sample collection of ≤ 5 minutes. POC glucose tests were performed using finger stick or arterial/venous blood. Electronic medical records of these patients were accessed to determine if they fall under any one or more of the following categories: hypotension (BP < 90/60 mm Hg) and receiving vasopressors. The variances between POC test results versus clinical chemistry analyzers were calculated. Fisher's exact test was used for statistical analysis for the percentages of patients with the variance greater than 10% between testing and control groups as well as between finger stick and arterial/venous subgroup. P < 0.05 was considered statistically significant.

Results:

Control		**Vasopressor**				**Hypotension**			
Finger Stick (N=60)		Arterial/Venous (N=49)		**Finger Stick (N=54)**		Arterial/Venous (N=68)		Finger Stick (N=80)	
≤ 10%	> 10%	≤10%	> 10%	≤10%	> 10%	≤ 10%	> 10%	≤ 10%	> 10%
35 (58%)	25 (42%)	39 (80%)	10 (20%)	25 (46%)	29 (54%)	47 (69%)	21 (31%)	47 (59%)	33 (41%)

For finger stick, the p values for hypotension vs control and vasopressor vs control were 0.543 and 0.086, respectively. In the vasopressor and hypotension groups, the p values between arterial/venous and finger stick subgroups were 0.0006 and 0.2313, respectively.

Conclusion: The results of this preliminary study suggest that the current glucose meters do not meet the accuracy criteria proposed by the new FDA guidelines for both general and critically ill patients.

B-271

A Rapid Dilute and Shoot-Flow Injection Tandem Mass Spectrometric Method for Quantification of Phenobarbital in Urine

r. alagandula. *cleveland state university, cleveland, OH*

Background: In recent years, UDT (urine drug testing) is the mainstays for drug compliance monitoring/ abuse in pain management. Although, LC-MS/MS is considered as a gold standard for UDT, these methods are highly time consuming and require 2 separate LC-MS screening procedures, since most of the pain drugs are usually split into positive mode and negative mode panels, where majority of the drugs are positively ionized and only barbiturates and EtG (ethanol metabolite) ionize better in negative mode. Due to this, completely separate and time consuming LC-MS/MS runs were applied just to analyze two drugs, where approximately 50 positively ionizing drugs can be analyzed in the same time frame, utilizing different buffers, mobile phases and chromatography columns. In order to address this, we have developed a fast and robust tandem mass spectrometric method to analyze and quantify phenobarbital in urine in 2 minutes with a simple sample preparation: 10 times dilution with deionized water, with no chromatographic separation.

Methods: The samples were rapidly prepared by simple one step dilution of blank urine (mixture of 6 lots) spiked with phenobarbital followed by flow injection of sample to mass spectrometer using 5mM Ammonium acetate/70% Acetonitrile as a carrier solvent, without HPLC. Quantification and detection of phenobarbital was achieved via mass spectrometry analysis by electro-spray ionization triple-quadrupole mass spectrometry in multiple reaction monitoring mode employing a stable isotope-labeled internal standard (phenobarbital-d5). **Results:** The validated method was linear at the dynamic range of 5-200ng/ml with correlation coefficient > 0.9998. The coefficients of variation and relative errors for intra and inter assay at four QC levels (i.e., 5, 12.5, 45 and 160 ng/ml) were > 3.0% and > 5.0% respectively. The major advantages of our method are: (1) Simple dilution, as sample preparation, (2) FI-MS/MS analysis (no HPLC) of phenobarbital in urine with 2 minutes run time enabling much higher throughput.

Conclusion: The acquired results proved that this novel method is simple and robust, has the capacity to process 720 samples/day, and can lead to the transfer of existing methodologies to the newer robust platforms; application of this method can permit rapid screening of multiple pain drugs in urine with short sample preparation recommended for clinical UDT studies. Nevertheless, no change in the signal intensity or sensitivity was found even after 1200 injections proving that this method was robust.

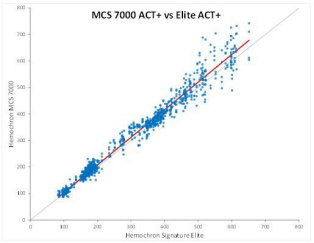
B-272

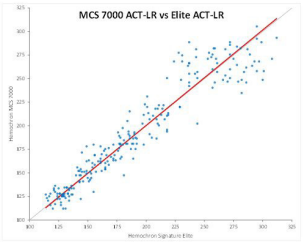
Validation of the Hemochron MCS 7000; A new Point of Care Coagulation Instrument for Heparin Anticoagulation Management

G. Garner, D. Miers, M. Foster, A. Mishra, F. M. LaDuca. *Accriva Diagnostics, San Diego, CA*

The Hemochron MCS 7000 (MCS) is the next generation Hemochron® point-of-care microcoagulation instrument capable of assessing heparin anticoagulation using either the ACT+ (high range therapy) or the ACT-LR (low range therapy). The clot detection method uses a high optical resolution camera for end point identification yielding improved precision and accuracy. The MCS system also uses unique bar coded ACT+ and ACT-LR test cuvettes results to ensure assay type identity with each test and cuvette expiration dating. Critical to the transition to the new system is ensuring comparable results with those obtained with the predicate Hemochron® Signature Elite (Elite) instrument. In a laboratory based validation protocol, donor blood samples were spiked with heparin and tested using ACT+ cuvettes (n = 794) and ACT-LR cuvettes (n = 227) on both the MCS and the Elite. Reference Range was identical in the two systems. Across the reportable range, the weighted Deming fit showed a correlation of $R^2 = 0.97$ and a slope 1.04 for ACT+ and a correlation of $R^2 = 0.91$ and a slope 1.01 for ACT-LR, demonstrating the clinical equivalence of results.

Summary: This validation demonstrated the equivalence of ACT results with the MCS and Elite ensuring consistency of clinical use and heparin management. The MCS expands the user capabilities of the Elite system, offering state-of-the-art graphical user interface (GUI) with a capacitive color touch screen, wireless communication (Wi-Fi & Bluetooth), POCT1A compliance to support network connectivity, a 2D bar code scanner, user replaceable battery, expanded database for test record storage, and QC lockout menu. An additional feature is a browser based configuration manager allowing broadcast system configuration to multiple instruments.





B-273

"Inconclusive qualitative pregnancy test, followed by quantitative pregnancy test of hcg with discrepancies between the values and the real clinical pregnancy status"

L. Velasquez, W. Furmaga. *UTHSCSA, San Antonio, TX*

Objectives: The aim for this study is to assess a false negative in pregnancy identification by the qualitative point of care (POC) devices, when compare to the human chorionic gonadotropin (hCG) quantitative assays and to the chart review. The POC device cut off for HCG concentration above which POC shows positive results is 10IU/dL. **Relevance:** Females at reproductive age are tested for a possible pregnancy before diagnostic or therapeutic procedures which might be contraindicated in the case of positive results. An accurate diagnosis of pregnancy should be pursued to avoid possible teratogenic effect or life treating complication causing by a missing ectopic pregnancy. **Methodology:** The POC *using Sure-Vue® Serum/Urine hCG-STAT* pregnancy test, is a rapid chromatographic immunoassay for qualitative detection of hCG utilizes mouse monoclonal anti alpha subunit-hCG and goat monoclonal anti beta subunit- hCG, using Sure-Vue® antibodies. The manufacture's instruction advises to evaluate the results of the test after 5-6 minutes. Because large number of ambiguous results had been detected, a pilot study was performed which showed discrepancy of the results between readings after 5 and 10 minutes of incubation. The sample with such discrepancy was resulted as an "inconclusive". Subsequently, 124 patients form the University Hospital at San Antonio with inconclusive results of a serum qualitative pregnancy test were reflexed to the HCG quantitative testing and for the chart review. **Validation:** The charts review confirmed viable pregnancies, complete or incomplete abortions in 18 of 124 females with inconclusive qualitative pregnancy test (viable pregnancies= 7; miscarriage=11). In addition, qualitative test showed low accuracy (86.2%) when compared with the gold standard (quantitative tests) since the reading at 5 minutes missed 17 patients who presented higher levels to the cut off (≥ 10 IU/dl). Due to the retrospective character of our study we couldn't assess an accurate relation between those 17 patients and their pregnancy status. **Conclusions:** Qualitative pregnancy test (read at 5 minutes) yield 124 negative results that switch to positive when read at 10 minutes, among which 18 females from this population were found to be pregnant (NPV=85.4%). 17 out of the 124 patients with inconclusive results have a positive quantitative test (hCG ≥10-31 mIU/dl). A common cause for false negatives results by qualitative test is the low accuracy of used devices when compared to the chemistry instrumentation. To improve a detection of the pregnancy in the female patients in the hospital settings, serum HCG quantitative testing should be offered, or detailed validation of qualitative POC device should be performed before the assay is offered to the patients. The cut off for positivity of such devices should be set at the level, which guarantees a maximal negative predictive value performance.

B-274

A Nano-Calorimeter Based Platform Technology for Enzyme-Linked Immunosorbant Assays

E. Kazura, B. Lubbers, I. Ges, J. Layer, R. Mernaugh, F. Baudenbacher. *Vanderbilt University, Nashville, TN*

Background: The next generation of point of care devices will measure a variety of biomarkers using a miniaturized, highly integrated, multiplexed platform technology, and will require only a minute amount of sample (<1 µl). At present labor-intensive sandwich-based enzyme-linked immunosorbant assays (ELISAs) are used in diagnostic settings to quantify antigens in human biological samples. Antigens are captured using antigen-specific antibodies and subsequently labelled with enzyme-conjugated antigen-specific antibodies. Substrates and/or chromogenic or fluorescent developers reactive with the enzyme are added to produce a detectable signal. Typically spectrophotometers or microtiter plate readers are used to quantify ELISA chromogenic or fluorescent signals, indicative of sample antigen or analyte concentration. We utilized an alternative strategy by detecting the heat generated either during direct binding or generated by an enzyme/substrate reaction using a micromachined calorimeter. The reaction volume is thermally insulated from the substrates using polymeric membranes. Heat is detected using thermocouples to produce an electronic signal, allowing the quantification of analyte concentration in nanoliter sample volumes. The platform technology was integrated into a capillary point of care format and a 64 calorimeter array for a laboratory based instrument.

Methods: Devices are fabricated using standard photolithographic methods on 3 inch silicon <100> wafers, with 500 nm low stress silicon nitride (SiN) coated on both sides. Rectangular windows are etched anisotropically through the wafer, then covered with a thin Su-8 polymer film. Titanium and bismuth thermopiles are deposited by e^- beam evaporation, and patterned by HF wet etch and ion milling, respectively. A second thin Su-8 membrane is applied to protect the thermopiles. Reactive ion etching removes the SiN layer under the window, suspending the calorimeter on thin, thermally-isolating rugged polymer membranes. The point of care device has two thermopiles connected as a differential calorimeter to reject common mode noise. For the calorimeter array, 8 thermopiles are connected in series for a sequential readout. Horse radish peroxidase or catalase is linked to antibodies as a secondary label. The heat generated in the reaction between the HRP/catalase and peroxidase is directly used to determine the concentration of enzyme bound to the calorimeter surface.

Results: The calorimeters consist of 27 junction bismuth/titanium thin film thermopiles with a total Seebeck coefficient of 2160 µV/K. The calorimeter has an energy resolution of 1.4±0.2 nJ/(Hz)$^{1/2}$ and a time constant of 100 ms at a sample volume on the order of 1 nL. We demonstrated the detection of sub-picogram amounts of catalase integrating the thermal signal over a time period of 100s. This translates well to quantification of clinically relevant concentrations of therapeutic antibodies in serum.

Conclusion: We have demonstrated the feasibility to utilize a Nano-Calorimeter based platform for enzyme-linked immunosorbant assays. The device can be used in a 64 array as well as a point of care format. This novel biosensor concept can be multiplexed and adapted to a large number of applications utilizing different strategies and reagents.

B-275

A rapid H-FABP test for qualitative measurement of H-FABP in serum, plasma and whole blood.

C. Xu[1], R. Keck[2], Q. Shi[1]. *[1]ZBx Corporation, Toronto, ON, Canada, [2]ZBx Corporation (CE representative), Rust, Germany*

Background: Human cardiac FABP ("**H-FABP**") is one of the most abundant proteins found in cardiomyocytes. H-FABP is mainly responsible for the transport of fatty acids. In the event of an acute myocardial infarction ("**AMI**"), the concentration of H-FABP in blood rises within 1-3 hours and returns to normal after 24 hours. Therefore, H-FABP is clinically useful as an early biomarker of AMI. According to industry literature, 99% of normal populations have an H-FABP level below 6 ng/mL. An increased level of FABP in circulation correlates with an increased risk of cardiac muscle damage. Early diagnosis is important because timely treatment of an AMI significantly improves the prognosis of a patient. An easy-to-use rapid test for the detection of H-FABP can facilitate an early diagnosis of an AMI. The objective of this study is to evaluate the performance of a new H-FABP rapid test.

Principle: The ADEXUS-Dx H-FABP Rapid Test ("**H-FABP Test**") is a solid phase immunochromatographic assay. The H-FABP Test uses a sandwich format to detect the presence of H-FABP above an established reference concentration in blood, plasma, and serum samples. The appearance of a purplish-red band in the test window indicates that the sample contains H-FABP above normal levels. The H-FABP Test has a unique feature of finger-stick, capillary whole blood sampling needing only 35 µl blood.

Performance: The H-FABP Test was negative to other forms of FABP, including liver-FABP, intestine-FABP, adipocyte-FABP, epidermal-FABP, ileal-FABP, brain-FABP. There is no hook effect at the highest H-FABP concentration present in patient serum (700 ng/ml). Sera containing human anti-mouse antibodies (HAMA) up to 327 ng/mL tested negative suggesting minimal interference by HAMA in a normal population based on the reference range for HAMA (0-188 ng/mL). The same test results were obtained for serum and plasma samples, the later of which were unaffected by anti-coagulants. A method comparison study between the H-FABP Test and the Randox quantitative assay showed the H-FABP Test cut-off was 6 ng/ml relative to Randox assay. The agreement between the two assays [for samples with H-FABP concentrations] is: 100% [below 1.5ng/mL]; 80% [1.5-3ng/mL]; 52% [3-12

ng/mL]; 73% [12-18 ng/mL]; and, 100% [above 18 ng/mL]. The discrepancies are likely due to the different antibodies used in the H-FABP Rapid Test and the Randox assay.

Conclusion: The H-FABP Test is a one-step rapid test with demonstrated specificity to cardiac FABP. It has a cut-off at 6 ng/ml based on comparison with the Randox assay, a generally acceptable clinical reference value for H-FABP. Therefore the H-FABP Rapid Test is a useful test for the early detection of AMI.

B-276

Correlation of HbA1c Measurements by Three Different Methodologies: Ion Exchange HPLC, Boronic Acid Affinity Reflectometry, and Monoclonal Antibody Agglutination

L. R. Moss[1], E. N. Gregory[2], J. A. Aloi[1], G. Pomper[1], S. H. Wong[1], J. Wofford[1]. *[1]Wake Forest School of Medicine, Winston-Salem, NC, [2]Wake Forest Baptist Medical Center, Winston-Salem, NC*

Background: Hemoglobin A1c (HbA1c) concentration is important in diagnosing diabetes mellitus and in monitoring glycemic control in these patients. HbA1c measurements are performed both in our outpatient clinics as point-of-care tests (POCT) as well as in our hospital's main laboratory. The aim of this study was to determine the HbA1c correlation among two POCT methods and the main laboratory. The outpatient clinics assessed the Alere Afinion AS100 (AF) POCT instrument (boronic acid affinity reflectometry) due to its faster turn-around-time (≈3 minutes) and on-board quality control checks. Capillary HbA1c concentrations from AF were correlated to the current Siemens DCA Vantage POCT (DCA) instrument (monoclonal antibody agglutination). In collaboration with physicians, an additional correlation study between the AF and the main laboratory's BioRad Variant II Turbo (BioRad) (ion exchange HPLC) was conducted on venous samples. **Methods:** Capillary blood from thirty-two patients was collected as part of routine care and assayed on both the AF and DCA according to manufacturer's recommendations. Venous blood was collected in EDTA tubes on nineteen of the thirty-two patients after consent was obtained and assayed on the AF and BioRad instruments according to the manufacturer's recommendations. The data were analyzed on EP Evaluator. **Results:** HbA1c measurements ranged from 4.5 – 14.6%. DCA and AF results of capillary blood samples were well correlated (y=1.043x-0.17, R^2=0.9858, n=32). BioRad and AF results also showed good correlation with the capillary (y=0.995x-0.01, R^2=0.9960, n=20) and venous blood (y=0.991x+0.14, R^2=0.9968, n=19). In comparison, the results of the BioRad venous blood and DCA capillary blood were not as highly correlated (y=0.929x+0.30, R^2=0.9950, n=20) because the 95% confidence interval of the slope (0.883-0.975) did not include 1.00. Additionally, results of AF capillary and venous samples were well correlated (y=1.012x-0.13, R^2=0.9985, n=20). **Conclusions:** Overall, the three methods for assaying HbA1c demonstrated good correlation with each other. Afinion AS100 is our chosen POCT instrument because its on-board quality control checks, faster turn-around-times, and acceptable correlation to the BioRad methodology of the main laboratory.

B-277

Eliminating i-STAT Invalid Patient and Operator Identification Errors: How Collaborating with Anesthesia Improved Point-of-Care Compliance

B. Lynn[1], L. Filipova[1], B. B. Suh-Lailam[2]. *[1]Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, [2]Ann & Robert H. Lurie Children's Hospital of Chicago/Northwestern University Feinberg School of Medicine, Chicago, IL*

Background: Point-of-care tests (POCTs) must meet specific accreditation standards, including patient identification (ID) requiring patient results to be in medical records, and operator ID requiring medical records to indicate the operator. A principal challenge with POCTs is enabling non-laboratory trained clinical staff to maintain compliance with accreditation standards. This was the case at our institution where i-STATs are widely used. We noticed high invalid patient and operator ID rates from the same location in the hospital, the operating room (OR): patient ID that did not match the electronic health records were being entered, hence patient results could not cross in to the medical records. Incorrect operator IDs were being entered in to the system, and consequently medical records were lacking the name of the operator. We hypothesize that these high invalid patient and operator ID error rates may be due to errors in manual entry. These are both operator-related errors so we decided to engage the operators. A review of our records showed that i-STAT operators in the OR included anesthesiologists, anesthesia techs and nurses.

Method: Quality improvement collaboration was established between point-of-care and anesthesia and tasked with: identifying the root cause of the high invalid patient and operator ID error rates and, implementing practical strategies that will eliminate these errors and bring the OR into compliance with accreditation standards. A previously unidentified group of operators was identified: residents. Every month, a new set of residents rotate in the OR. These residents perform the bulk of i-STAT testing and although they were trained by anesthesiologists this was not recorded. Also they were not assigned operators so were not recognized by the system when their IDs were scanned. Furthermore, we found that operators sometimes scanned a patient label that was not associated with the patient account number resulting in an invalid patient ID. To address these issues: (1) i-STAT training added to on-boarding process for OR residents where they are assigned operator IDs, (2) clinical educator ensures competency for all OR operators and, (3) education provided on the correct patient label to scan. Invalid patient and operator ID error rates (Number of invalid IDs per month/Total number of tests per month x 100) were determined over a 17 month period including 9 months before and 8 months after initiating the collaboration.

Results: Previous efforts by POC to decrease invalid patient ID error rate in the OR were partially successful, however it showed a slow increase from 14% to 62% over 8 months. After the POC team collaborated with anesthesia, invalid patient ID error rate decreased to 0% in 7 months. Similarly, previous efforts to decrease invalid operator ID error rate in the OR reduced it from 99% to 68% over 7 months. After collaboration with anesthesia, the operator ID error rate decreased to 0% in 7 months.

Conclusion: Engaging in quality improvement projects with clinical teams to improve communication, identify underlying problems, and collaborate to provide solutions, is an effective way of overcoming some of the challenges that plague point-of-care testing.

B-278

Clinical Significance of Accurate Total Hemoglobin Measurements in the Perioperative Setting

R. Caynak, K. Lima, N. Lambuth, F. Lara, N. Tran. *University of California, Davis, Davis, CA*

Background: Conductance-based techniques are often employed by point-of-care (POC) devices to determine total hemoglobin (tHb) in the perioperative settings. These techniques are low cost and convenient, however, only calculate tHb through the measurement of hematocrit and may be susceptible to hemodilution effects encountered in surgical settings. Inaccurate determination of tHb may result in inappropriate blood transfusions. *The objective of this study is to evaluate the clinical significance of POC calculated tHb versus measured tHb for intraoperative blood transfusion practices.*

Methods: We compared the clinical performance of a handheld POC analyzer to a central laboratory hematology analyzer (LH 750, Beckman Coulter, Brea, CA) serving as a reference method. The POC device (epoc, Alere, San Diego, CA) utilize conductance methods. Paired remnant whole blood specimens were obtained from adult (age ≥18 years) requiring cardiac surgery at risk for hemodilution, and tested on each analyzer. Patient chart review and physician arbitration was conducted to determine the potential clinical impact of each tHb result intraoperative transfusion decisions. Units of administered packed red blood cells (PRBC) were recorded. The paired t-test was used to compare the two devices.**Results:** Sixty unique patient samples were collected and used for paired comparisons. Mean (SD) tHb for the cohort was 9.5 (2.4) g/dL. Mean bias for the POC device versus the hematology analyzer was -1.4 (1.1) g/dL, P=0.011 (**Figure 1**). Ten patients received 12 potentially unnecessary units of PRBC based on POC results and case arbitration—resulting in $7,584 of additional costs ($632/PRBC).**Conclusion:** The POC analyzer exhibited a negative mean bias compared to reference methods. Conductance-based determination of tHb may have resulted in unnecessary blood transfusions and leading to excess cost. Further studies are needed to determine when conductance based measurements become unreliable such as in cases of hemodilution.

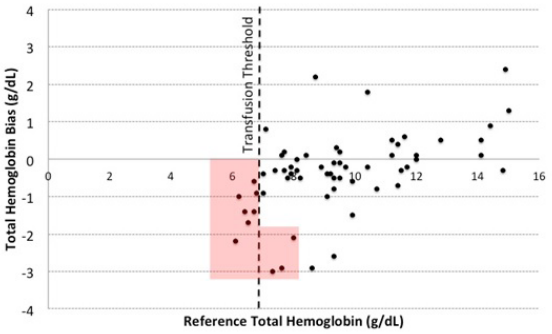


Figure 1. Bland-Altman Plot Comparing POC versus Lab Total Hemoglobin. The figure compares bias (POC – Lab) on the y-axis against reference total hemoglobin measurements. The vertical broken black line indicates the institutional transfusion threshold for total hemoglobin of 7 g/dL. Red zones indicate data points, which may have prompted unnecessary transfusions.

B-279

An Enzymatic Creatine Assay Based on a Single Reagent

O. Beeks. *Instrumentation Laboratories, Bedford, MA*

Objective

To develop a reliable method for the determination of creatine in aqueous and clinical samples.

Relevance

Creatine (Cr) is an essential metabolite synthesized naturally in the body by two amino acids, glycine and arginine. This chemical provides a base for ATP re-synthesis, allowing for continued muscle energy. To improve the performance, oral ingestion of creatine monohydrate is widely used by athletes. Although the majority of the ingested Cr is removed by the kidneys, the chronical effect on renal function with long-term Cr supplementation is of interest in the field of sports medicine.

An accurate and reproducible method is essential for measuring Cr in aqueous and clinical samples. Unlike Creatinine (Crea), there is no NIST traceable standard available for Cr. Furthering this challenge is the fact that there are only few Cr testing reagents available on the market. All of the commercialized reagents are either for research purposes only, or unfit for high throughput testing. Therefore, our primary goal is to develop both the standard and the reagent which can provide accurate Cr determination, which is also important for Crea assay development which contains both Cr and Crea.

Methodology

The proposed method is based on a single-part reagent via enzymatic conversion of Cr with colorimetric end-point detection at 547 nm. In contrast to commercialized microtiter plate assay kits, this method can be fully automated and easily adapted to any clinical chemistry analyzers with programmable parameter settings. Cr in clinical samples can be analyzed simultaneously with other commercially available assays, such as Crea, etc. To develop a robust and accurate method a total error of < 5% must be met. Listed below are the reagent, standard and instrument used in the development process.

Gravimetric Cr standard: freshly prepared, by dissolving creatine monohydrate in 1 mMole sodium hydroxide

Reagent: A mixture of creatinase, sarcosine oxidase, 4-aminoantipyrine and horseradish peroxidase

Instrument: Roche Cobas c311, via one available open channel (programmable parameters)

Sample volume: 30 uL

Reagent volume: 150 uL

Incubation time: 10 min

Results

We have shown performances as the following:

Linearity: 0.2–15mg/dL (R^2 >= 0.999)

Imprecision: 0.2% with-in run (n=12), 0.8% run-to-run (n=3 runs, n=36 samples total)

Inaccuracy: less than 2%

Recovery: ranging from 97-102% versus gravimetric

Interference: None from Crea, glucose, lactate and urea

Total error: 4% maximum

Recovery in serum samples: Three levels of serum creatine show correlation versus IDMS determined Cr

Cr assay= 1.2509*IDMS - 0.3079, R^2>0.999. CV% is 7.9% at the low level (0.5mg/dL) and 1.7% between levels 2-5mg/dL.

Conclusions

We have demonstrated that the Cr assay meets our specifications in aqueous and clinical samples.

References

1.Becque, M. Daniel, John D. Lochmann, and Donald R. Melrose. “Effects of oral creatine supplementation on muscular strength and body composition.”Medicine & Science in Sports & Exercise 32 (2000): 654-658.

2. Farquhar, William B., and Edward J. Zambraski. “Effects of creatine use on the athlete’s kidney.” Current sports medicine reports 1.2 (2002): 103-106.

B-280

Comparative analysis of lactate quantitation via the Radiometer ABL800 and point-of-care i-STAT and GEM4000 systems

C. Randall, R. R. Henriquez, S. M. Leal, D. Smith, K. Hrischuk, N. Korpi-Steiner. *University of North Carolina Hospitals, Chapel Hill, NC*

Background: Early identification of sepsis with rapid medical intervention improves patient outcomes and decreases sepsis-related mortality. The Surviving Sepsis Campaign (SSC) recommends lactate measurement within the first 3 h of sepsis suspicion and fluid resuscitation for patients exhibiting hypotension or lactate ≥ 4 mmol/L. Additional lactate testing within 6 h is recommended if the initial lactate is elevated to facilitate monitoring patient response to treatment when targeting normalization of lactate concentration. The Center for Medicare and Medicaid Services Severe Sepsis/Septic Shock Early Management Bundle (SEP-1) requires lactate testing within 6 h if the initial lactate is above a 2 mmol/L threshold. Point-of-care (POC) lactate testing is rapid and may aid in early diagnosis and management of sepsis patients. The aim of this study was to assess the analytical performance and overall concordance of lactate measurements using POC devices, i-STAT and GEM4000, as compared to lactate measurement using the Radiometer ABL800.

Methods: Lithium-heparin whole blood samples submitted to UNC hospitals during January 2016 for routine lactate measurement were quantified via the Radiometer ABL800 Series and assigned the reference method (Radiometer A/S, Bronshoj, Denmark). Residual samples (n=42) spanning threshold limits of 2 mmol/L and 4 mmol/L were selected for subsequent analysis using the i-STAT (CG4 cartridge, Abbott Diagnostics, Irving, TX) and GEM Premier 4000 (Instrumentation Laboratory, Bedford, MA). Linear regression, Bland-Altman, and concordance analyses were performed. Overall concordance was calculated as the percent of lactate values falling into the correct lactate category (i.e. below or above 2 mmol/L or 4 mmol/L) using each POC method compared to the Radiometer ABL800.

Results: Comparative analysis of lactate results yielded the regression equations: [i-STAT]= 0.98[ABL800]- 0.12, (r^2 = 0.99) and [GEM4000]= 0.95[ABL800]+ 0.11, (r^2 = 0.99). The mean (± standard deviation) bias in measured lactate concentration < 4 mmol/L using the i-STAT and GEM4000 compared to the Radiometer ABL800 was -0.15 ± 0.12 mmol/L and 0.03 ± 0.12 mmol/L, respectively. In analysis of high-range lactate (> 4 mmol/L), the i-STAT and GEM4000 demonstrated a mean bias of -0.28 ± 0.51 mmol/L and -0.29 ± 0.54 mmol/L compared to the Radiometer ABL800, respectively. The overall concordance of i-STAT and GEM4000 lactate measurements compared to the Radiometer ABL800 at a 2 mmol/L threshold was 90.5% and 92.9%, respectively; at a 4 mmol/L threshold both POC devices demonstrated 100% concordance.

Conclusion: The i-STAT and GEM4000 devices demonstrated excellent correlation with lactate measured by the Radiometer ABL800. Both POC methods exhibited minimal bias in lactate measurements < 4 mmol/L compared to the Radiometer ABL800 suggesting an acceptable alternative testing approach for initial patient assessment in clinical settings where lab testing is unavailable or has prolonged turnaround time. Discordance in lactate measurements between testing methodologies at a 2 mmol/L threshold will impact additional lactate testing required based on SEP-1 criteria. Both POC methods demonstrated a systematic negative proportional bias compared to the Radiometer ABL800 which may confound interpretation of high lactate concentrations (≥ 4 mmol/L) if serial measurements are performed using multiple methods.

B-281

Comparative study of Protein C-reactive Ultra sensitive assay in Point of Care

L. B. Faro, M. L. Garcia, N. Silva, P. V. F. Monteiro, K. Salviato, S. S. A. Baroni, S. E. M. Cruz. *DASA, São Paulo, Brazil*

Background: The C Reactive Protein (CRP) is an acute protein phase produced by the liver in response to factors released by macrophages and adipocytes during infections, tissue injuries, and acute inflammation. The CRP high concentration indicates an increased risk of myocardial infarction, cardiovascular acute syndromes prognosis, and it is strongly associated with cardiovascular disease adding predictive value for others cardiovascular disease and peripheral vascular markers. Previously, the CRP evaluation was reported as positive or negative, but currently, the circulate CRP is already quantified which support the clinical and therapeutic protocols. The AHA/CDC guideline referee that CRP measurement from intermediate values could alert the physician for the monitoring of the coronary disease. According with this risk stratification guideline, the CRP value above 10 mg/L, detected into 6 to 24 hours, after onset IAM symptoms; it is an indicative of recurrent cardiac events in a short time (30 days to 1 year). This study compared the results from CardioPhase® hsCRP assay in Point of Care Stratus® CS 200 Acute Care (Siemens Healthcare Diagnostics) and for RCRP assay in Dimension® RXL MAX (Siemens Healthcare Diagnostics) at Central Laboratory

Methods: We evaluated forty (40) plasma samples with Lithium Heparin. We used the CardioPhase hsCRP in POC - Stratus® CS 200 with Solid Phase Radial Partition Immunoassay Technology and Extended Range CRP assay with Dimension® RXL MAX system by Turbidimetric Immunoassay Technique. According to literature, for healthy individuals, expected values are under 3 mg/L (0.3 mg/dL) for both methodologies. Results were 100% concordant between the methods (n=40 samples - 75% of pathological samples (n=30) and 25% normal (n=10)). The Kappa coefficient was 1.00 and r = 0.989.

Results & Conclusion: The data showed a high concordance between Stratus® CS 200 (POC) and Dimension® RXL MAX (Central Laboratory), which suggest that Stratus® CS 200 is a point of care technology for quantitative determination of high sensitivity CRP simplifying the pre analytical process without compromise the quality of the patient care.

B-282

Analytical Evaluation of the Roche CARDIAC Troponin T Assay Performed on the POC Cobas® h232 Instrument

M. P. Rozmanc[1], D. C. C. Lin[2], E. Proctor[1], A. Wong[1], Z. McIntyre[1], M. Cheung[3], T. O'Brien[4], L. Fu[3], D. E. C. Cole[3]. *[1]Sunnybrook Health Sciences Centre, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]Sunnybrook Health Sciences Centre and University of Toronto, Toronto, ON, Canada, [4]Women's College Hospital and University of Toronto, Toronto, ON, Canada*

Background: Measurement of cardiac troponins is of central importance for the diagnosis of acute myocardial infarction (AMI). Point-of-care testing (POCT) devices for troponin measurement can produce rapid results and facilitate timely evaluation of patients with suspected AMI. The aim of this study was to evaluate the Roche CARDIAC T Quantitative assay (POC TropT) performed on the POC Cobas® h232 instrument.

Methods: Method comparison between the CARDIAC Troponin T assay on the POC Cobas® h232 and the Troponin T hs (high sensitivity) (cTnT-hs) assay on core facility Roche MODULAR® ANALYTICS E170 system was first evaluated by assaying 119 heparinized whole blood samples from patients with a wide range (6-3161 ng/L) of cTnT-hs values. Precision was assessed by measurement of two levels of liquid quality control materials (Roche CARDIAC) Control Troponin T) and patient samples at two different concentrations. After implementation, the assay was further validated with parallel testing of patient samples using the cTnT-hs assay.

Results: Comparison between the POC TropT and cTnT-hs methods in the quantitative range (100 to 2000 ng/L) yielded a linear correlation with a slope of 0.96, y-intercept of -10.7 ng/L and R^2-value of 0.96 (n=62). A mean negative bias of -29.6 ng/L (-6.6%) was observed. For POCT purposes, qualitative intervals of <50 ng/L are reported, yielding a false negative rate of 10%. For POCT samples reported in a qualitative range of 50-100 ng/L, a false positive rate of 12% and a false negative rate of 12% were observed. For imprecision, a CV of 8.6 - 10.8% was determined using quality control material across two different reagent lots and two different POCT instruments. Using two patient samples with mean concentrations of 147 ng/L and 271 ng/L, CV's of 15.1% and 13.4%, respectively, were observed. After implementation, 32 patient samples were tested by both POC TropT and core facility cTnT-hs. The resultant POCT values (<50 ng/L, n=29; and 50-100 ng/L, n=3) were all consistent with the cTnT-hs values.

Conclusions: The semi-quantitative CARDIAC Troponin T assay on the POC Cobas h232 instrument demonstrates acceptable imprecision in our hands and correlates well with the central laboratory cTnT-hs assay. Elevated results (>100 ng/L) identify high risk patients; however, negative results (<50 ng/L) cannot be used reliably to "rule out" cardiac ischemia. In addition, this assay cannot detect/monitor change in troponin levels when the concentration of troponin is <100 ng/L. In settings with no immediate access to central laboratory testing, this POC TropT assay might be used as an aid in the diagnosis of patients with suspected AMI, in conjunction with clinical pre-test probability assessments and electrocardiogram (EKG) findings.