COMPARISON BETWEEN FULLY AUTOMATED URINE COBAS 6500 AND SEMI-AUTOMATED URINE COBAS U 411 AT SUNMED

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ABSTRACT

Urine analysis is an essential component of patient assessment used in screening, diagnosis and monitoring of patients in healthcare setting. It is also most common performed tests in the clinical laboratory. However, the testing procedures used currently are labor intensive, time consuming and lacks of standardization. In this study, we evaluated fully automated urine analyzer named cobas 6500 series with our current system, semi-automated cobas u 411 for test strip analysis (chemistry) and KOVA cell chamber counting for microscopy of formed elements in the urine sample. Besides the comparison study done we also measure the productivity performance between these systems. Methods: A total of 225 urine specimens were analyzed for analytical performance; correlation for cobas u 701 and KOVA® cell chamber and verification of analytical sensitivity for RBC and WBC .Performance of TAT and productivity were measured as well. The results showed:

- For chemical testing u601 and Roche strip showed that all parameters met ± 1 block agreement except for specific gravity and bilirubin
- Cobas u 701 and KOVA cell microscopy met ±1 block agreement for RBC and WBC at 91% and 96% respectively.Besides crystal, mucus and yeast all parameters met the defined acceptance criteria.
- For u701 , LoB <1p/µl and LoD <5p/µl for both RBC and WBC were observed as manufacturer claimed
- Average run test/sample for C6500 and u411 is 1.48 minutes and 1.73 minutes respectively with productivity increased by 15%

Conclusions: Cobas 6500 is well correlated with u411 and KOVA chamber with some limitations. By using fully automated urine system can reduce non-value steps and increased efficiency by consolidation of urine work area. Standardization at all steps of the processes help to increase quality of results and optimize the workflow. Interfacing of results direct to Laboratory Information System (LIS) facilitates in less operator intervention and prevents transcription error. Thus, increased the productivity value and can release technician for other value works. Nevertheless, manual intervention and competent scientist is still required for some differentiation of casts and certain crystals.

BACKGROUND

In the current setup, for more than a decade, urinalysis in our lab is performed by using test strips at semi-automated system for chemistry parameters testing and as for manual urine sediment counting,Kova grid slides are used. The urine sediments particles such as red blood cell (RBC), white blood cells (WBC) and pathological particles will be identified and quantified by referring to value table provided and calculated into number of cells per µl. Current method at SunMed refer to Figure 1 and Figure 2.However it was observed the semi-automated system are very labor intensive, time consuming and lacking in standardization. Therefore it urged us to look into a more robust and automated solution such as Cobas 6500 series urine analyzer comprises of the u601 for urine chemistry and u701 automated for microscopy module. The u701 module has in-built microscope that captures and report on 15 different digital frames per sample. These systems are integrated by option and results can be linked to Laboratory Information System (LIS). New system refer to Figure 3. In this study, we evaluated fully automated Cobas 6500 series with our current semi-automated Cobas u 411 for test strip analysis (chemistry) and KOVA cell chamber counting for microscopy of formed elements in the urine sample. Besides the comparison study done we also measure the productivity performance between these systems.

Figure 1: Cobas u411

Figure 2: Kova slides with grid

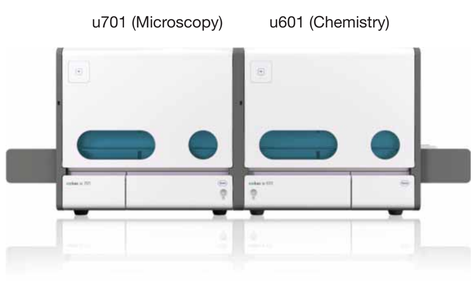


Figure 3: Cobas 6500

TEST METHOD AND MATERIALS

All the defined experiments performed here are according to following guidelines:

- CLSI EP05-A2 Evaluation of Precision of Quantitative Measurement Performance Methods for precision study
- CLSI EP09-A3 Measurement Procedure Comparison and bias Estimation using Patients' Samples for method comparison study
- CLSI EP 17-A2 Evaluation of Detection Capability for Clinical Laboratory Measurement Guidelines for LoD measurement
- The acceptance criteria was defined by manufacturer

1. Precision study for u601
   - Studies were performed by analyzing Biorad Liquichek Urinalysis Control multiple times.
   - This study was performed according to CLSI (Clinical and Laboratory Standards Institute) guidelines and manufacturer's (Roche Diagnostics) standard operating procedures.
   - 15 runs were measured each for level 1 and level 2 Biorad Liquichek Urinalysis Control on the same day for within-daily imprecsion study. For intermediate imprecision study, 1 run for each level was measured consecutively for 5 days.

2. Correlation studies:
   A total of 225 urine specimens were analysed for analytical performance; correlation for Cobas u 701 and KOVA® cell chamber and verification of analytical sensitivity for RBC and WBC were carried out. Following are the several correlation studies carried out between Cobas 6500 with U 411 and Kova chamber. The correlation studies include:
   - Between u601 with u411 chemistry parameters (Refer to Table 2)
   - Between u701 with kova slide (Refer to Table 3,4 and 5)
   - Correlation u601 versus u701(Refer to Table 6 and 7)

   Both the chemistry and the microscopy data were tabulated according to the result differences observed within a ± 1 block agreement.

3. Analytical study: Verification of Limit of Blank (LoB) and Limit of Detection (LoD)
   LoD is determined based on the LoB and the standard deviation of low concentration samples. The LoD corresponds to the lowest analyte concentration which can be detected (value above the LoB with a probability of 95%).The LoB and LoD were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2 requirements

4. Productivity
   - To determine productivity, the number of the test performed was multiplied by the Workload Unit (WLU) and then divided by the number of minutes worked.

$$\text{Productivity (\%)} = \frac{\text{Number of tests x WLU}}{\text{Number of techs x 480 minutes}}$$

   - Number of steps for urine analysis taken between current and automated 6500 was compared to determine non-value steps involved.

RESULT

1) Precision study for u601

	Biorad Liquidcheck L1				Biorad Liquidcheck L2			
Parameter	**No.of Measurement**	**Target Value**	**Exact Agreement (%)**	**Agreement within 2 adjacent conc. ranges (%)**	**No.of Measurement**	**Target Value**	**Exact Agreement (%)**	**Agreement within 2 adjacent conc. ranges (%)**
SG	5	1.013	60	100	5	1.022	80	100
pH	5	6	100	100	5	7	100	100
LEU	5	NEG	100	100	5	500µ/L	100	100
NIT	5	NEG	100	100	5	POS	100	100
PRO	5	NEG	100	100	5	POS	100	100
GLU	5	NORM	100	100	5	1000mg/L	100	100
KET	5	NEG	100	100	5	150mg/L	100	100
UBG	5	NORM	100	100	5	8mg/L	60	100
BIL	5	NEG	100	100	5	6mg/L	100	100
ERY	5	NEG	100	100	5	250µ/L	100	100
CLA	5	CLEAR	100	100	5	CLEAR	100	100
CLR	5	YELLOW	100	100	5	BROWN	100	100

Table 1: Repeatability for u601 on chemistry parameters

2) Correlation Studies
i. Between u601 with u411 chemistry test strips

Test Strip Parameter	Sensitivity (%)	Specificity (%)	±1 Block Agreement (%)	Best Fit Agreement (%)	Overall Agreement (%)	pH5-6 Agreement (%)	pH8-9 Agreement (%)	Acceptance
pH	100	100	NA	79	100	99.92	100.00	YES
LEU	87	95	100	87	92	NA	NA	YES
NIT	100	99	NA	99	99	NA	NA	YES
PRO	84	100	100	92	94	NA	NA	YES
GLU	100	99	100	96	99	NA	NA	YES
KET	92	99	100	95	98	NA	NA	YES
UBG	89	99	100	99	97	NA	NA	YES
BIL	53	97	100	92	92	NA	NA	YES
ERY	84	100	99	79	91	NA	NA	YES
SG	NA	NA	93	41	NA	NA	NA	YES

Table 2: Agreement between u601 with u411 for chemistry test strips

ii. Between u701 with kova slide

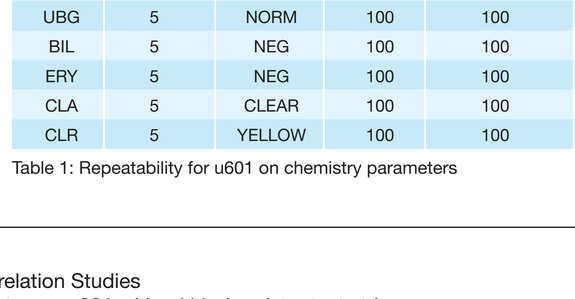


Table 3 : Regression analysis for RBC between u701 with Kova grid

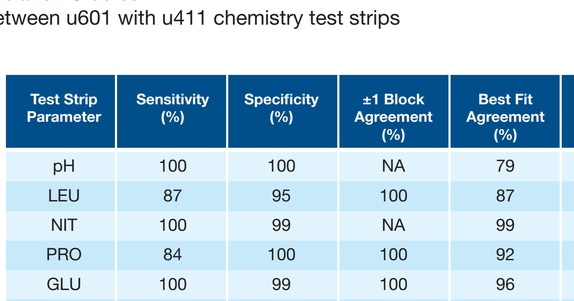


Table 4 : Regression analysis for WBC between u701 with Kova grid

Microscopy Parameters	Sensitivity (%)	Specificity (%)	Acceptance
Epithelial Cells (SEC & NEC)	85.71	83.75	YES
PAT	100	83	YES
BAC	80	75	YES
HYA	100	98	YES
CRY	43	99	NO*
MUC	68	75	NO*
SPRM	N/A	96	YES
YEA	50	96	NO*

*Failed by acceptance criteria

Table 5: Acceptance performance between u701 and Kova grid for sediment analysis

iii. Correlation u601 versus u701

			u601					
			neg	1+	2+	3+	4+	5+
			neg	10/µL	25/µL	50/µL	150/µL	250/µL
u701	neg	neg	61	16	6	2	3	
	1+	10/µL	4	4	8	1		
	2+	25/µL			3	1		1
	3+	50/µL		1			2	1
	4+	150/µL	1		1	1	2	2
	5+	250/µL						8
Test path	36	Test norm	61	Exact match	78	±1 block		112
Ref path	63	Ref norm	66	Total Data	129	Total Data		129
Sensitivity	**57**	**Specificity**	**92**	**Best fit (%)**	**60**	**± block agreement (%)**		**87**

			TP+TN	97
			Total Data	129
			Overall	**75**

Table 6: RBC agreement between u601 and u701

			u601					
			neg	1+	2+	3+		
			neg	25/µL	100/uL	500/µL		
u701	neg	neg	57	8				
	1+	25/µL	23	14	5	4		
	2+	100/µL		1	4	5		
	3+	500/µL				8		
Test path	41	Test norm	57	Exact match		83	±1 block	125
Ref path	49	Ref norm	80	Total Data		129	Total Data	129
Sensitivity	**84**	**Specificity**	**71**	**Best fit (%)**		60	**± block agreement (%)**	**97**

		TP+TN	98
		Total Data	129
		Overall	**76**

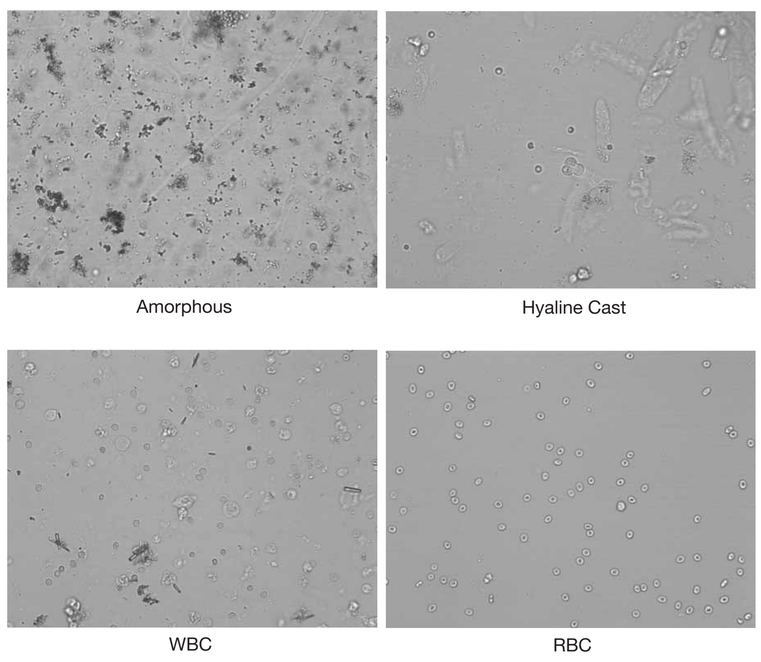
Table 7: WBC agreement between u601 and u701

3) Analytical study

Low conc. samples	
RBC/µL	WBC/µL
3.52	1.32
3.52	1.32
3.52	3.96
2.64	3.52
3.52	2.64
3.52	3.96
4.40	3.52
6.16	2.64
1.76	3.52
4.40	1.32
3.52	1.32
3.52	3.52
4.40	1.32
4.40	5.28
1.76	2.20
2.64	3.52
5.28	2.64
4.40	2.20
4.40	1.32
3.52	3.96
3.74	2.75
1.03	1.18
2.75	3.00
5.00	5.00

Table 8: Measurement of samples with lower concentration range for RBC and WBC

Cobas 6500 Digital images



4) Productivity

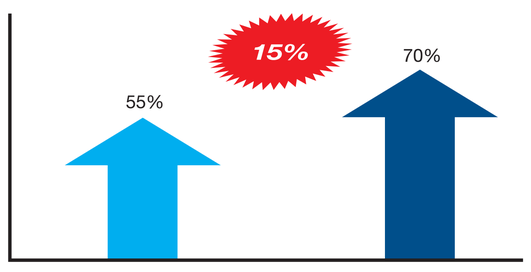


Figure 4: Productivity comparison between current method and automated urine systems

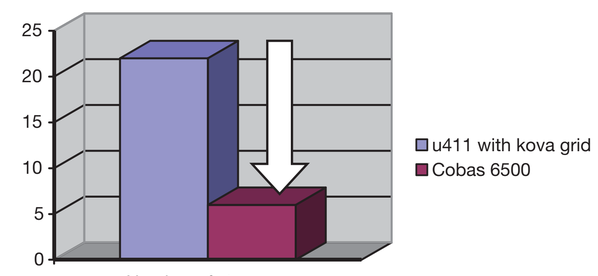
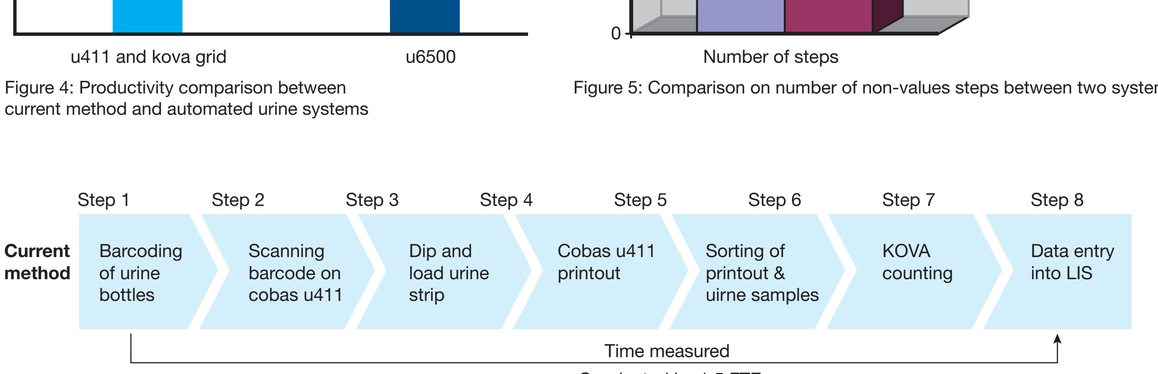


Figure 5: Comparison on number of non-values steps between two systems



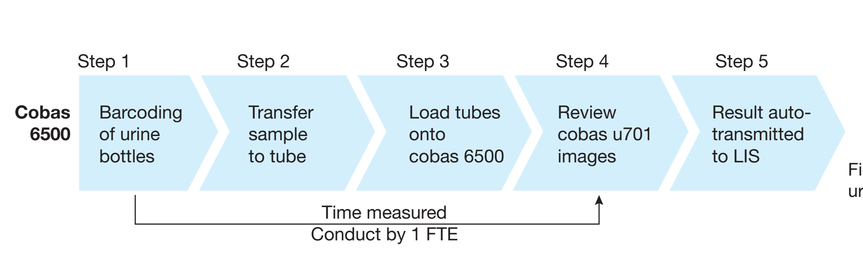


Figure 6: Comparison basic steps during urine analysis between two systems

Discussion

The precision study for u601, all parameters met 100% agreement in both the QC levels except for semi-quantitative parameters such as specific gravity (SG) and urobilingen (UBG).It was noted that these parameters had an agreement of less than 90% however it's still between 2 adjacent concentration ranges. This is due to the difference in the method of reading the strips between u601 and u411. For detail agreement data refer to Table 1.

Summary of correlation study between u 411 versus Cobas 6500 test strips is presented in table 2.However it was noted that the sensitivity for bilirubin and SG is low this is mainly due to insufficient positive sample obtained during the study. Whereas for Specific gravity the differences is noted due to the measurement method at u 601 and u 411 in which the SG is measured either by quantitatively or detecting ion concentration of urine using bromothymol blue on the test strip respectively. Therefore the best fit agreement was slightly lower however it was acceptable based on the ±1 Block Agreement.

These two parameters, WBC and RBC obtained good correlation between u701 and kova grid. RBC and WBC regression factor, R^2= 0.92 and R^2= 0.88 respectively as tabulated in Table 3 and 4.There would be a slight different for WBC between automated u701 and kova grid. The reason for the difference was due to operator counting technique in which would have resulted in missing counting area in Kova grid slide. However it was noted, linearity of RBCs and WBCs was excellent for both the method. Limitation of KOVA counting method, in differentiating the epithelial cells as either squamous cells (SEC) or nucleus (NEC) cells, determined us to combine SEC and NEC in this evaluation.In addition to that, CRY and YEA, met the defined acceptance criteria whereas for MUC the sensitivity met the acceptance criteria however the specificity was 5% short from the acceptance criteria as mentioned in Table 5.

Table 6 and Table 7 demonstrate the correlation of RBC and WBC agreement between u601 urine chemistry and u701 microscopy module.

The LoD were determined in accordance with the CLSI (Clinical and Laboratory Standards Institute) EP17-A2requirements. The calculated LoD for both RBC and WBC are less than manufacturer's claim on LoD (5 p/µL) thus accepted.

Besides having advantages in the result acceptability in terms of accuracy and reliability, of the fully automated system , we do observed a more lean work process with reduction of non-values steps and a substantial improvement of 15% in productivity as shown in Figure 4, 5 and 6.

CONCLUSION

Cobas 6500 is well correlated with u411 and KOVA chamber with some limitations. By using fully automated urine system can reduce non-value steps and increased efficiency by consolidation of urine work area. Standardization at all steps of the processes help to increase quality of results and optimize the workflow. Interfacing of results direct to Laboratory Information System (LIS) facilitates in less operator intervention and prevents transcription error. Besides having advantages in the result acceptability in terms of accuracy and reliability, of the fully automated system , we do observed a more lean work process with reduction of non-values steps and a substantial improvement of 15% in productivity. Nevertheless, manual intervention and competent scientist is still required for some differentiation of casts and certain crystals.

References
1. David TW, et al. AnalytcalPerfomance of the iQ200 Automated UrineMicroscopy Analyzer and Comparison with Manual Counts Using Fuchs_Rosenthal Cell Chambers. Am J ClinPathol. 2005; 123:290-295
2. Shayanfar et al. Automated urinalysis: first experience and a comparison between the Iris iQ200 urine microscopy system, the Sysmex UF-100 flow cytometer and manual microscopic particle counting. Clin Lab Med 2007;45(9):1251-1256.