Comparison of the iQ™200 Automated Urine Microscopy Analyzer automatic particle recognition performance to that of the 939UDx Urine Pathology System

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ABSTRACT

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Summary

Automatic particle recognition performance of the new iQ™200 Automated Urine Microscopy Analyzer was compared to that of the 939UDx Urine Pathology System (939UDx), which has represented the state-of-the-art flow imaging urinalysis technology, to determine the benefit this new instrument can provide in the clinical laboratory. ROC area for RBC, WBC, SQEP, Bacteria and Crystals exceeds 0.9 for both the iQ 200 and 939UDx. ROC area for SPRM and WBCC is greater than 0.9 for iQ 200 but between 0.7 and 0.9 for 939UDx. ROC area for Yeast and NSE is 0.889 and 0.866 for iQ 200 and 0.779 and 0.823 for 939UDx. ROC area for casts is between 0.75 and 0.874 for iQ 200, but between 0.5 and 0.7 for 939UDx.

Introduction

Automatic particle recognition performance of the iQ 200 and 939UDx were compared in a study of 457 specimens run in duplicate. Both the iQ 200 and 939UDx use digital imaging, while the iQ200 uses Auto Particle Recognition software (APR™) and the 939UDx uses Auto Analyte Recognition software (AAR) to classify urine constituents into 12 particle categories, and quantitatively report concentrations of: RBCs, WBCs, WBC Clumps (WBCC), Hyaline Casts, Pathological Casts, Squamous Epithelial Cells (SQEP), Non-squamous Epithelial Cells (NSE), Bacteria, Yeast, Crystals, Mucus and Sperm. Concentrations of each constituent, determined using images from each method unequivocally identified by experts, were compared to the concentrations determined by the APR and AAR software for the iQ 200 and the 939UDx, respectively. For each method, the Receiver Operating Characteristic (ROC) area of the auto-calculated result compared to the expert result was computed for each constituent. ROC area values of 0.5-0.7 indicate low diagnostic accuracy, values of 0.7-0.9 suggest limited clinical utility and values >0.9 indicate high global diagnostic accuracy (SWETS JA. Measuring the accuracy of diagnostic systems. Science 1988;240:1285-93).

Materials and Methods

Experiment Design: An iQ200 and a 939UDx each processed two aliquots from 457 specimens with normal levels of amorphous particulates. Specimen-by-specimen microscopic particle concentrations determined from expert identification of formed element images obtained from the iQ 200 were compared with those produced by the iQ 200 APR software, as were concentrations determined from expert identification of formed element images obtained from the 939UDx and those produced by the 939UDx AAR software, the reference method.

For each particle the ROC area of the APR/AAR-determined concentrations compared to the normal/abnormal state of the specimen established from expert identification of images from the same instrument was used to measure the efficacy of the APR/AAR for both the iQ 200 and the 939UDx. The ROC was computed using SPSS 11.0 Software (SPSS Inc., Chicago, IL, USA). Performance of the iQ 200 APR relative to the 939UDx AAR is determined by comparing each formed element ROC for the iQ 200 to the corresponding ROC for the 939UDx.

Individual formed element concentrations for the iQ 200 and 939UDx were based on the average concentrations for the two aliquots from each specimen. An individual formed element concentration is deemed normal if it falls within the NORMAL range defined in Table 1.

Table 1: Formed element concentrations/levels for comparing results from the iQ 200 Automated Urine to the reference system 939UDx Urine Pathology System operator edits.

FORMED ELEMENT UPPER LIMIT of NORMAL (ULN) VALUES (formed elements per microliter)			
FORMED ELEMENT	**TITLE**	**939UDx**	**iQ 200**
RBC	RBCs	16.5	16.5
WBC	WBCs	27.5	27.5
SQEP	Squamous Epithelial Cells	27.5	27.5
HYAL	Hyaline Casts	0.7	0.7
UNCC	(Unclassified) Pathologic Casts	0.3	0.3
BACT	Bacteria	59.0	6.8
BYST	Hyphae or Budding Yeast	11.0	11.0
NSE	Non-squamous Epithelial Cells	5.5	4.0
UNCX	Unclassified Crystals	27.5	13.6
SPRM	Spermatozoa	5.5	5.5
WBCC	White Cell Clumps	1.4	1.4

Receiver Operating Characteristic: A Receiver Operating Characteristic (ROC) graph plots sensitivity (ordinate) versus 1 – specificity (abscissa) as a function of the Upper Limit of Normal (ULN). Assuming that increasing values of particle concentration correspond to increasing abnormality, the ROC graph will have the following properties. For an ULN value of 0, the point on the ROC will be (1,1) corresponding to 100% sensitivity and 0% specificity. For an ULN value of infinity, the point on the ROC will be (0,0) corresponding to 0% sensitivity and 100% specificity. Any other (positive) ULN value will determine a sensitivity - specificity pair where each is in the range (0,1).

In general, if the ROC for one method uniformly dominates the ROC for another method then it will yield superior sensitivity and specificity at any operating point. Comparing the area under two ROCs is an accepted way to compare the potential sensitivity and specificity of two methods even though it does not guarantee that the one with greater area is uniformly dominant. In addition to the area, the standard error of the estimate and 95% confidence interval bounds are computed. This allows one to assess if the difference between two ROC areas is statistically significant. The asymptotic significance is the probability of observing an ROC area as great or greater than the estimated area when in fact the true area is 0.5 corresponding to a fair coin flip random choice between normal and abnormal.

Results

ROC area and statistical measures of the estimate for the iQ200 are compared to those for the 939UDx in Table 2.

Table 2: Comparison of formed element ROC area of iQ200 APR and 939UDx AAR showing greater ROC area for the iQ200 compared to the 939UDx.

Formed Element	Instrument	Area	Std. Error(a)	Asymptotic Sig.(b)	Asymptotic 95% Confidence Interval	
					Lower Bound	Upper Bound
RBC	iQ 200	.954	.010	.000	.935	.973
	939UDx	.933	.012	.000	.910	.955
WBC	iQ 200	.991	.003	.000	.984	.997
	939UDx	.968	.008	.000	.952	.984
SQEP	iQ 200	1.000	.000	.000	1.000	1.000
	939UDx	1.000	.000	.000	.999	1.001
HYAL	iQ 200	.874	.018	.000	.838	.909
	939UDx	.556	.119	.609	.322	.791
UNCC	iQ 200	.757	.025	.000	.708	.806
	939UDx	.673	.078	.013	.521	.825
BACT	iQ 200	.958	.010	.000	.939	.978
	939UDx	.943	.020	.000	.902	.983
BYST	iQ 200	.889	.032	.000	.826	.951
	939UDx	.779	.084	.000	.614	.943
NSE	iQ 200	.866	.034	.000	.800	.932
	939UDx	.823	.044	.000	.737	.909
UNCX	iQ 200	.945	.018	.000	.910	.981
	939UDx	.968	.017	.000	.934	1.002
SPRM	iQ 200	.970	.017	.000	.937	1.004
	939UDx	.719	.110	.024	.504	.935
WBCC	iQ 200	.941	.017	.000	.908	.974
	939UDx	.854	.074	.000	.710	.998

a Under the nonparametric assumption; b Null hypothesis: true area = 0.5

ROC area for RBC, WBC, SQEP, Bacteria and Crystals exceeds 0.9 for both the iQ200 and 939UDx. Both instruments exhibit statistically equivalent performance for these particles since the 95% confidence intervals for the two instruments overlap significantly. With ROC areas greater than 0.9, high global diagnostic accuracy of the APR/AAR methods is to be expected. Finally, the likelihood that the true area is 0.5 is zero since the asymptotic significance for these elements is zero.

ROC area for Sperm is 0.970 for iQ 200 but only 0.719 for 939UDx. This is a statistically significant difference since the 95% confidence intervals do not overlap. Thus, iQ200 has high global diagnostic accuracy for Sperm while the 939UDx AAR exhibits only limited clinical utility. ROC area for WBCC is 0.941 for iQ 200 but only 0.854 for 939UDx. The 95% confidence limits for the iQ 200 are 0.908 to 0.974 so that a value of 0.854 is outside this range. However, the 939UDx limits are 0.710 to 0.998 because of the relatively few WBCC detected by this method. Thus, while there is strong evidence that the iQ200 has high global diagnostic accuracy for WBCC, the evidence is weaker that 939UDx AAR exhibits only limited clinical utility. Finally, the likelihood that the true area is 0.5 is zero for both instruments since the asymptotic significance for these elements is zero. ROC area for Yeast is 0.889 for iQ200 and 0.779 for 939UDx. The 95% confidence limits for the iQ200 are 0.826 to 0.951 so that a value of 0.779 is outside this range. However, the 939UDx limits are 0.614 to 0.943. Thus, while APR and AAR nominally exhibit only limited clinical utility for both instruments for yeast, statistically iQ200 APR is closer to high global diagnostic accuracy than 939UDx AAR. ROC area for Non-squamous epithelial cells is 0.866 for iQ200 and 0.823 for 939UDx. The 95% confidence limits for the iQ200 are 0.800 to 0.932, while those for 939UDx are 0.707 to 0.909 so ROC area for both instruments are statistically equivalent, and in the limited clinical utility range. ROC area for hyaline casts is 0.874 for iQ200 but only 0.556 for 939UDx. This is a statistically significant difference since neither estimated ROC area falls within the 95% confidence interval of the other instrument. Thus, while the ROC for the iQ200 APR indicates possible limited clinical utility for the detection of hyaline casts, the 939UDx has low diagnostic accuracy. ROC area for Pathologic casts (UNCC) is 0.757 for iQ200 but only 0.673 for 939UDx. The 95% confidence limits for the iQ200 are 0.708 to 0.806 so that a value of 0.673 is outside this range. However, the 939UDx limits are 0.521 to 0.825 because of the relatively few UNCC detected by this method. Thus, while there is strong evidence that the iQ200 has limited clinical utility for UNCC, the evidence is weaker that 939UDx AAR exhibits low diagnostic accuracy. In general, we see that in all cases iQ 200 APR performance measured by ROC area is statistically equivalent to or better than 939UDx AAR performance. The iQ200 exhibits high or limited diagnostic accuracy for all 12 particles auto-classified, while the 939UDx AAR has low diagnostic accuracy for casts, both hyaline and pathologic.

Conclusions

iQ200 APR performance exceeds that of the 939UDx AAR thus providing improved urinalysis results in a smaller, faster, lower cost instrument.

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