



Performance Validation of HORIBA Medical Yumizen H2500 Blood Cell Counter, Analytical Component for HORIBA Evolutive Laboratory Organisation (HELO*) Solution, Compared to DXH 800

Gilles Bonicelli¹, Philippe Halfon¹, Cécile Chabert², Elise Darrambide², Jean-Remy Gougard², Franck Seguy³, Bruce H Davis³

¹Laboratoire Alphabio, Marseille, France, ²Clinical Quality Dept. and ³International Marketing, HORIBA Medical, Montpellier, France and ⁴Bruce H Davis MD, Inc, Clifton, Maine, USA⁵



Introduction :

HORIBA Medical has released a new laboratory automation system for hematology testing, the HORIBA Evolutive Laboratory Organization (HELO*) system, which includes a new high throughput blood cell counters that offers CBC/DIFF parameters, including routine nucleated RBC counts, fluorescence based reticulocyte analysis and optical extinction platelet counts and body fluid (BF) counting. Initial validation studies were performed to confirm performance specifications on precision, LOQ, linearity, precision and method comparisons to other blood counter models and microscopic leukocyte differential counts, which are reported here. The cell differential matrix is based on the patented HORIBA Double Hydrodynamic Sequential System «DHSS» flow cytometric design.

Throughout the performances evaluation, we were able to collect a large number of clinical cases that were the subject of a dedicated study.

Methods:

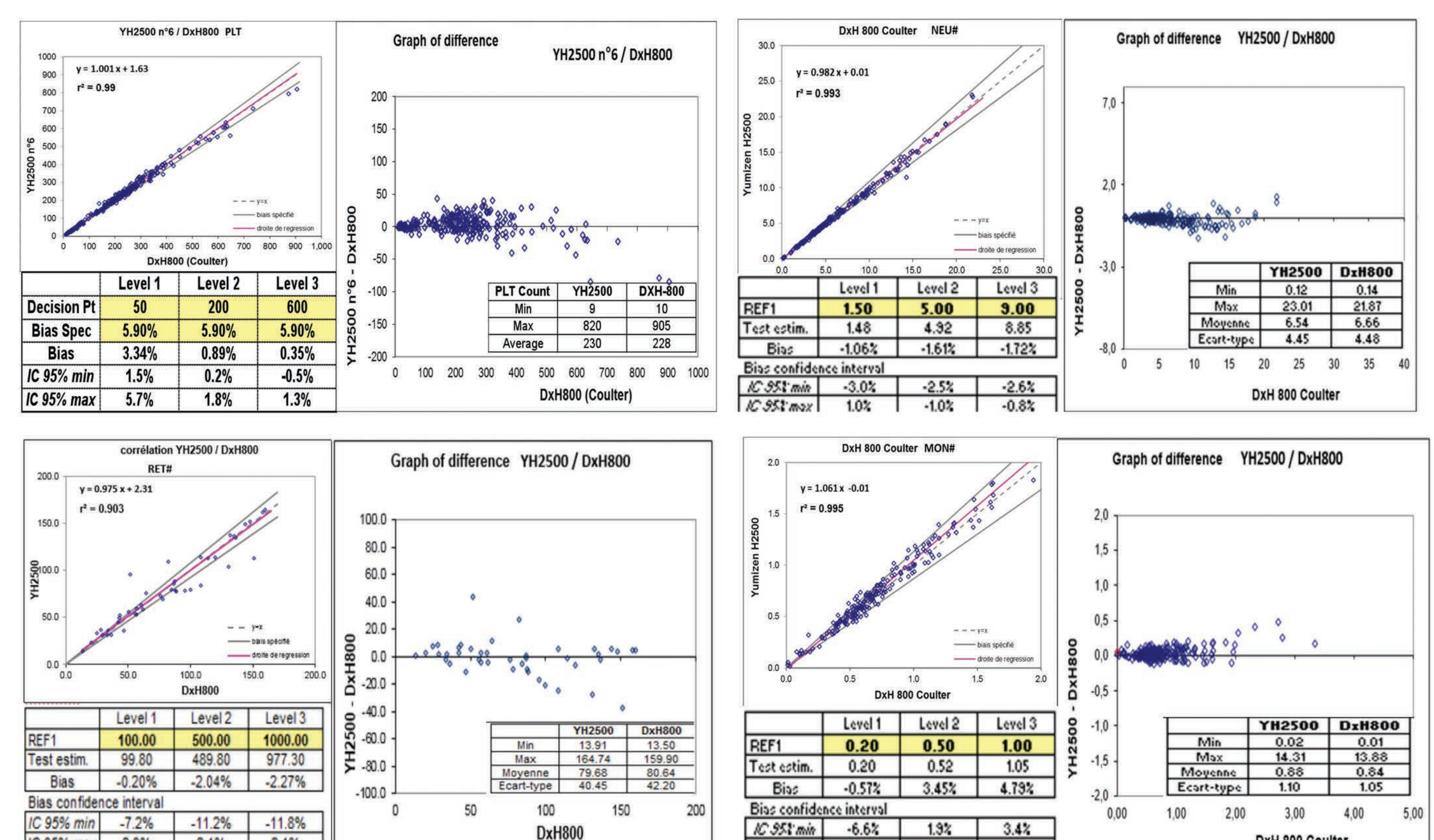
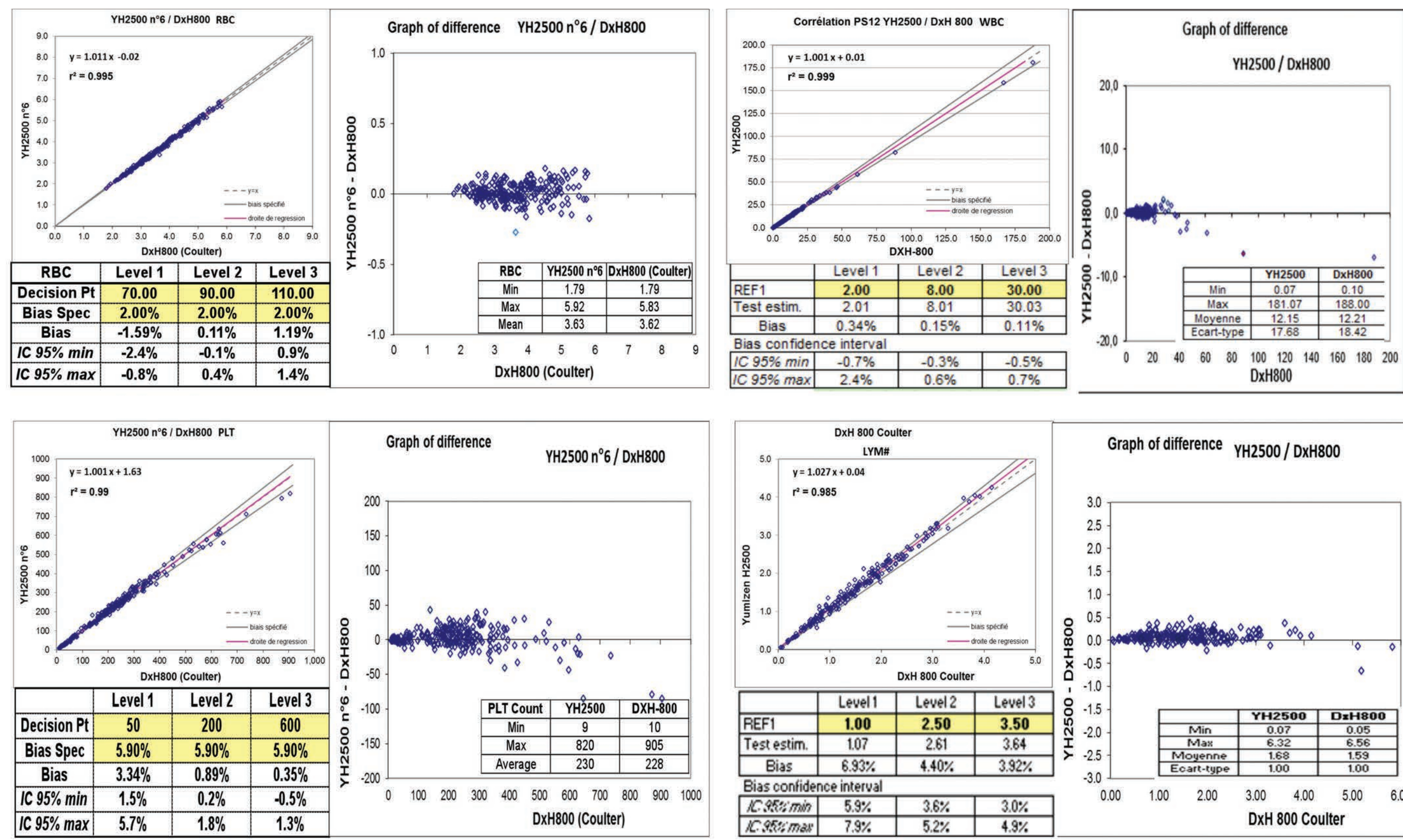
273 Fresh blood samples collected in K2 or K3 EDTA from patients and healthy controls were analyzed on a Yumizen H2500 instruments with Yumizen P8000 middleware for method comparison to Beckman Coulter DXH800 instruments. Method comparison and bias estimation were performed according to CLSI EP09-A3. Statistical analysis was performed using Passing Bablok regression fit with Pearson's and Bland Altman's difference plots. Precision, linearity and limit of detection were determined according to CLSI and ICSH guidelines.

Conclusions:

The Yumizen H2500 instrument is safe, as effective, and performs as well or better than the BCI DXH-800 for all the usual CBC/DIFF parameters. The novel optical extinction platelet count performs as well or better than impedance counts. Ergonomic features of the instrument were identified by the naive users as those functions and custom flag settings, designed to be done within the Yumizen P8000 middleware module. The body fluids analytical validation will have to be evaluated on a larger statistical series (Fig 6).

Results:

Precision in the low, normal and high ranges of all parameters was determined to be below the manufacturing specifications for CV, including WBC <2%, RBC <2%, HGB <1%, HCT <2%, PLT <5% (<10% below 30 x 10⁹/L). Linearity was confirmed for platelet counts between <10 – 5000 x 10⁹/L, for RBC counts 0.22 – 8.95 x 10¹²/L, for HGB 0.6 – 24.5 g/L, for HCT 1.8 – 69.7%, for WBC 0.3 – 406 x 10⁹/L and for reticulocytes 0.043 – 1.244 x 10⁹/L. The correlation of the DXH - 8000 and Yumizen H2500 models exceeded 0.98 for the parameters of WBC, HGB, HCT, and PLT count and exceeded 0.90 for MPV, RBC and reticulocytes with samples covering the full analytical measurement range. Platelet counts by impedance and optical extinction methods correlated at levels also >0.95.



Parameters	High target value	Low Target value
	Whole Blood	
WBC (10 ⁹ /L)	> 50	> 0.3 and < 3
RBC (10 ¹² /L)	> 6.2	> 0.5 and < 1.5
HB (g/L)	> 200	> 20 and < 50
RET (10 ⁹ /L)	> 300	< 30
PLT (10 ⁹ /L)	> 800	> 10 and < 30

Parameters	LoQ	LoQ Claimed	Linearity
WBC	0.1 x 10 ⁹ /µL	0.2 x 10 ⁹ µL	0.20 – 350 x 10 ⁹ /µL
RBC	0.22 x 10 ¹² /µL	0.22 x 10 ¹² µL	0.24 – 8.81 x 10 ¹² /µL
Hgb	0.6 g/dL	0.6 g/dL	0.6 – 24.5 g/dL
HCT	1.90%	2.00%	2.0 – 68.8 %
PLT-I	4 x 10 ⁷ /µL	6 x 10 ⁷ /µL	6 – 5019 x 10 ⁷ /µL
PLT-ox	12 x 10 ⁷ /µL	12 x 10 ⁷ /µL	12 – 3446 x 10 ⁷ /µL
RET%	0.30%	0.30%	0.3 – 35.8 %
RET#	0.01 x 10 ⁹ /µL	0.01 x 10 ⁹ µL	0.05 – 1.24 x 10 ⁹ /µL

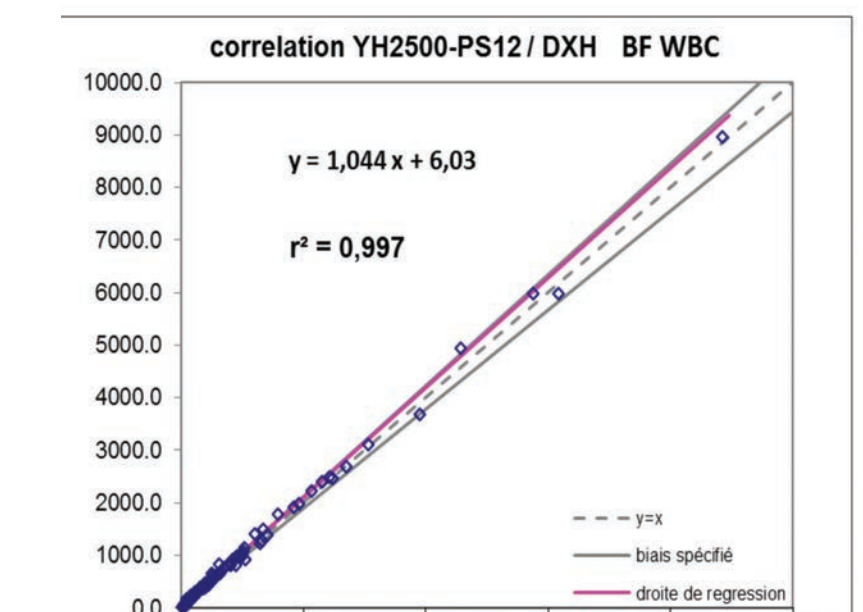


Table 1. carry-over specimen values determined for YH2500.

Table 2. Linearity and limits of quantification (LOQ) determined for YH2500.

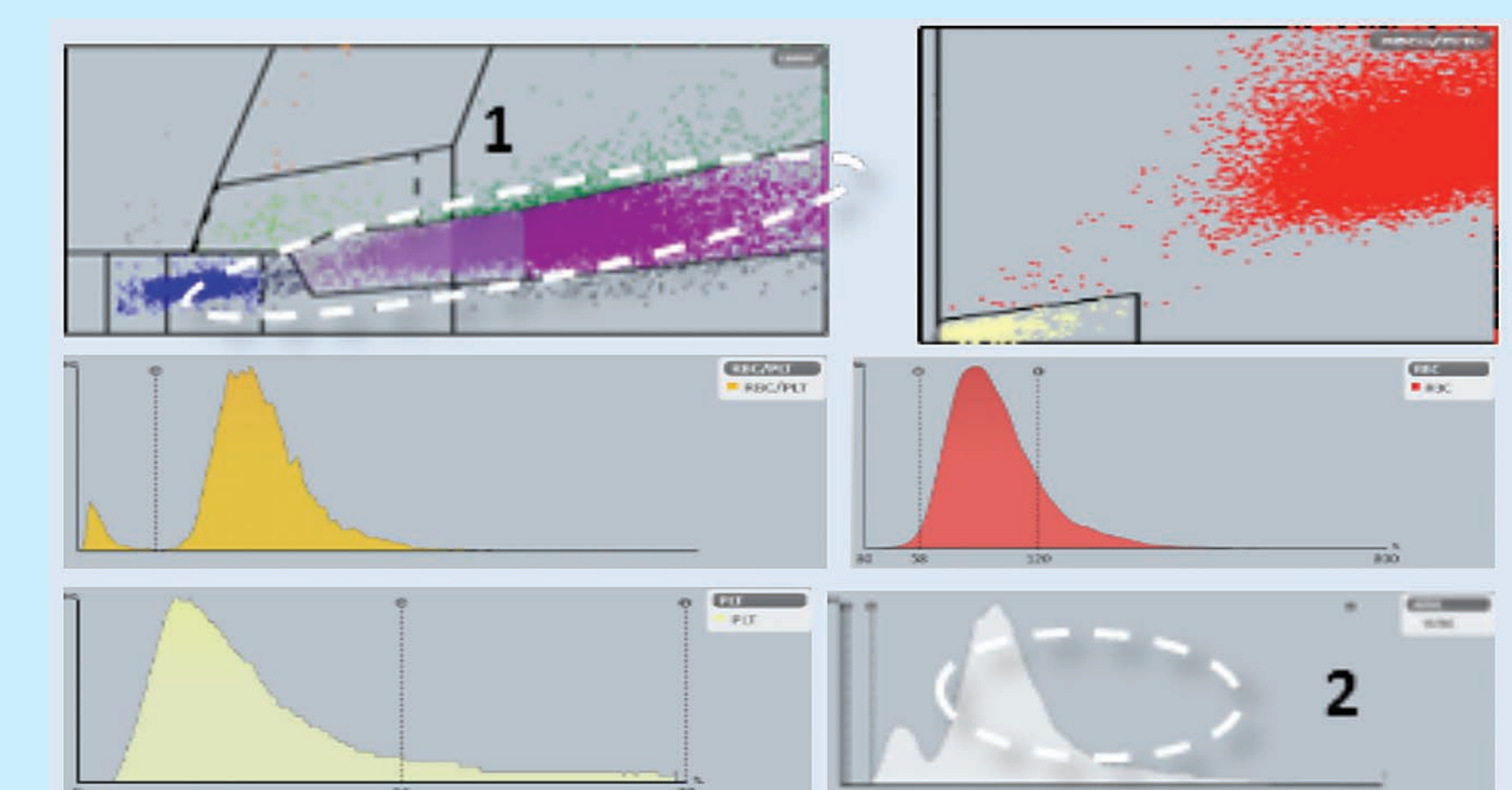
Fig 6 : Body Fluids Counts, Analysis of 123 various serous, CSF and synovial specimens

Clinical cases study:

is to assist all users to rapidly familiarize the laboratory scientists and physicians with the Yumizen H1500 and Yumizen H2500 data display. The key to optimal use of any cytometer or blood counter is the subtle use of details provided by careful review of the histograms and data matrix displays.

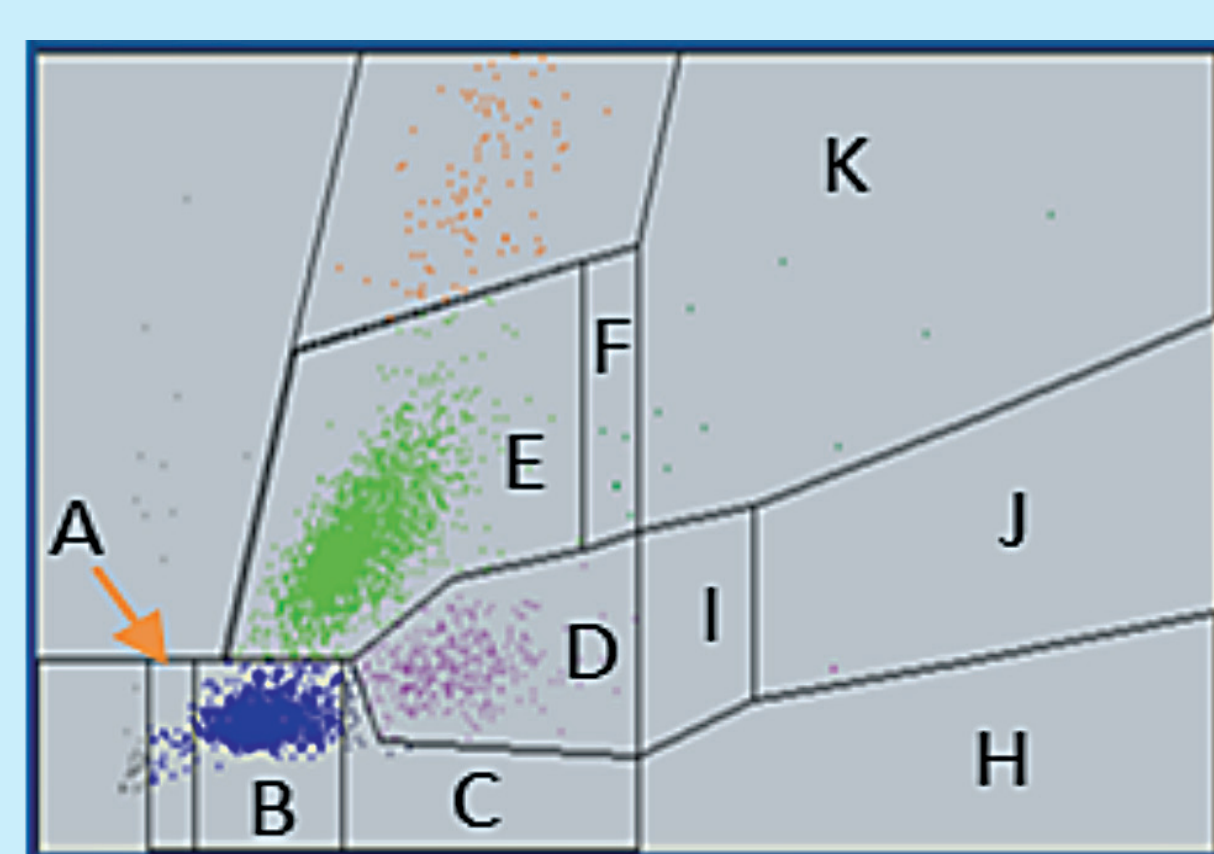
Pathology	Expected	Achieved
RBC Double population		
Patients transfused	5	5
Anemias		
Megaloblastic anemia	3	2
Thalassemia	6	6
Drepanocytose (Sickle cell disease)	3	1
Iron deficiency	10	10
Myelodysplasia	5	5
Erythroid blastemia (nRBCs presence)	3	3
Sideroblastic anemia	2	0
Polycythemia vera	3	2
Post-splenectomy state or body Howell Jolly	3	0
Samples with blood clots and platelet aggregates	5	5
Chronic Leukemia		
CLL	10	10
CML	5	2
CMML	2	1
Acute Leukemia		
ALL	4	2
AML	6	11
Platelet Disorders		
ITP - Purpura thrombopenic Idiopathic	3	1
TTP - Thrombotic Thrombocytopenic Purpura	2	1
Thrombocytosis	10	10
Myelodysplasia	5	5
Post-chemotherapy	14	15
Multiple myeloma	5	0
Multiple myeloma (plasmatic cells)	2	0
Reactive leucocytosis	10	10
Reactive lymphocytosis	5	5
Monocytose	3	3
Eosinophilia (>10% eosinophils)	5	4
Infections (viral, malaria, bacterial, HIV)	>=2	>2/1>2/2

Acute Myeloid leukemia M5



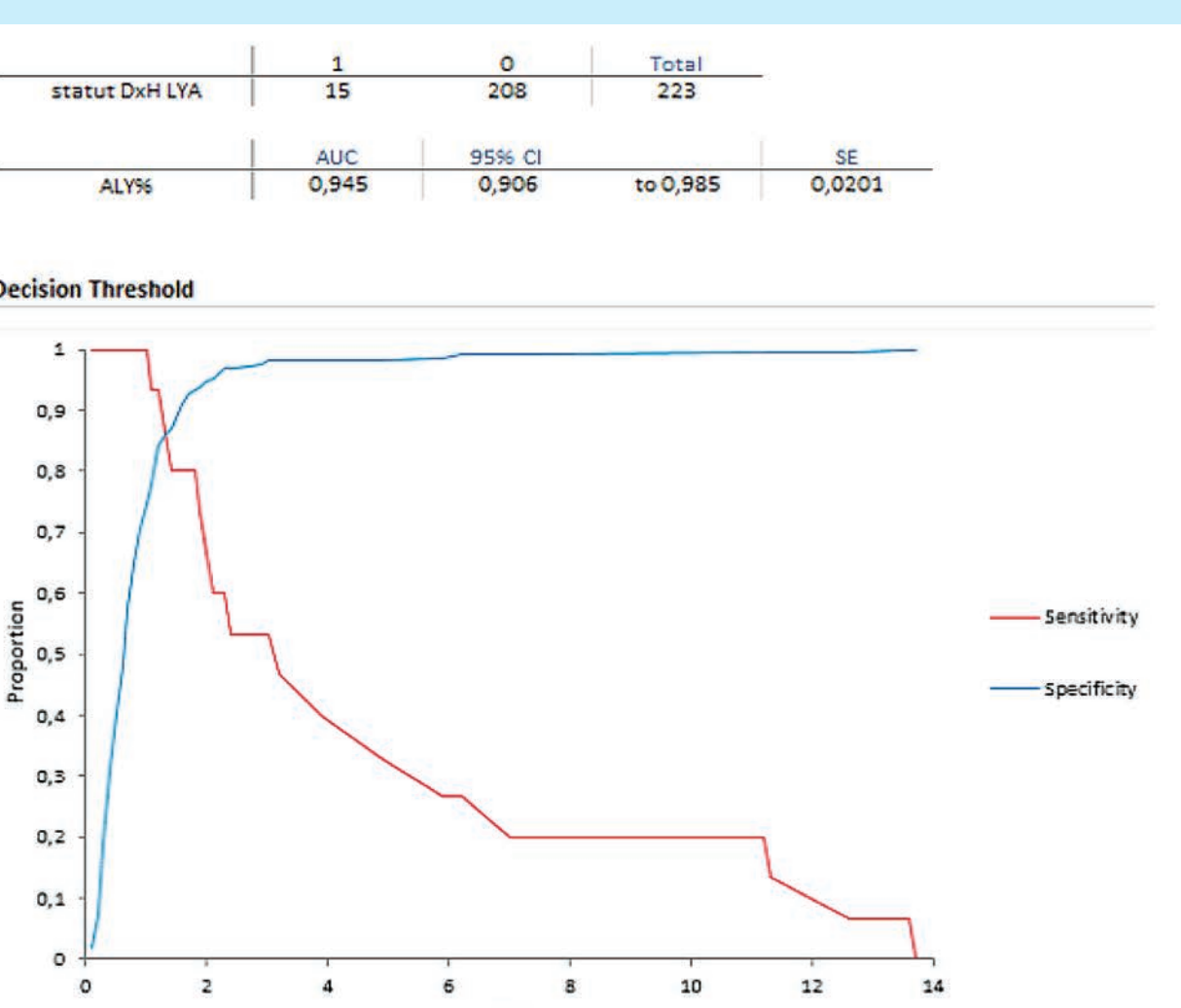
On the DIFF scattergram we observe the presence of immature monocytic population. The population is essentially composed of all step of monocytes maturation between the monoblasts, promonocytes and monocytes. The monoid population is perfectly defined in the DIFF scattergram in the dedicated area. We observe also the severe neutropenia. On the WBC histogram, we observe the important ratio of the monocyte cells versus the lymphocyte or granulocyte cells.

White cell matrix (left panel) for the cell differential counts for YH1500 and YH2500 display the populations of NRBC (A), Lymphocytes (B), "atypical" lymphocytes (C), monocytes (D), neutrophils (E) including "left-shifted" neutrophils (F), eosinophils (G), immature lymphocytes (H), immature monocytes (J) including "left-shifted" monocytes (I) and immature myeloid cells (K).



A threshold at 2% ALY on YUMIZEN H2500 provides 92 % of correlation with DxH relative sensitivity at 93% and relative specificity at 73%.

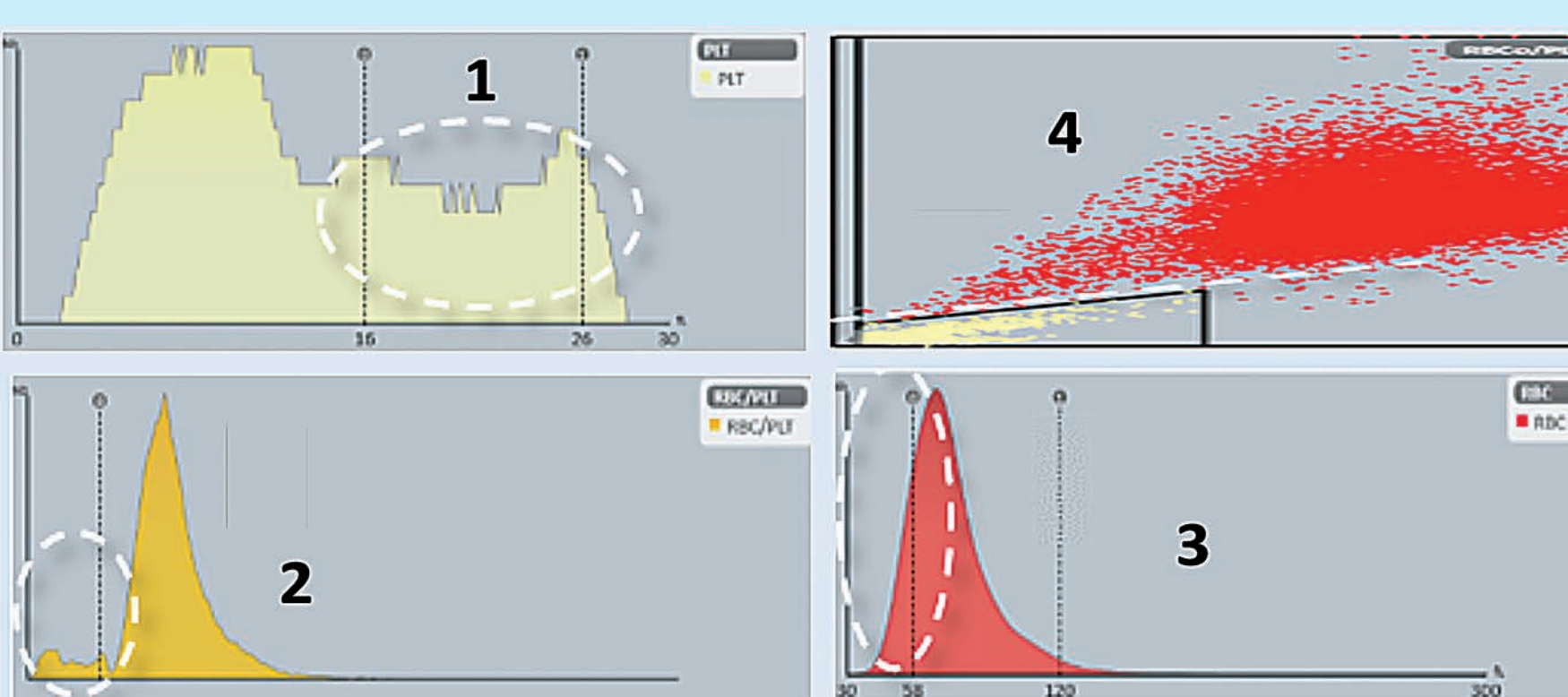
Statut DxH	Statut YH2500 LIC or ALY>2%		Total
	Neg YH2500	Pos YH2500	
Neg DxH800	167	36	203
Pos DxH800	5	15	20
Total	172	51	223



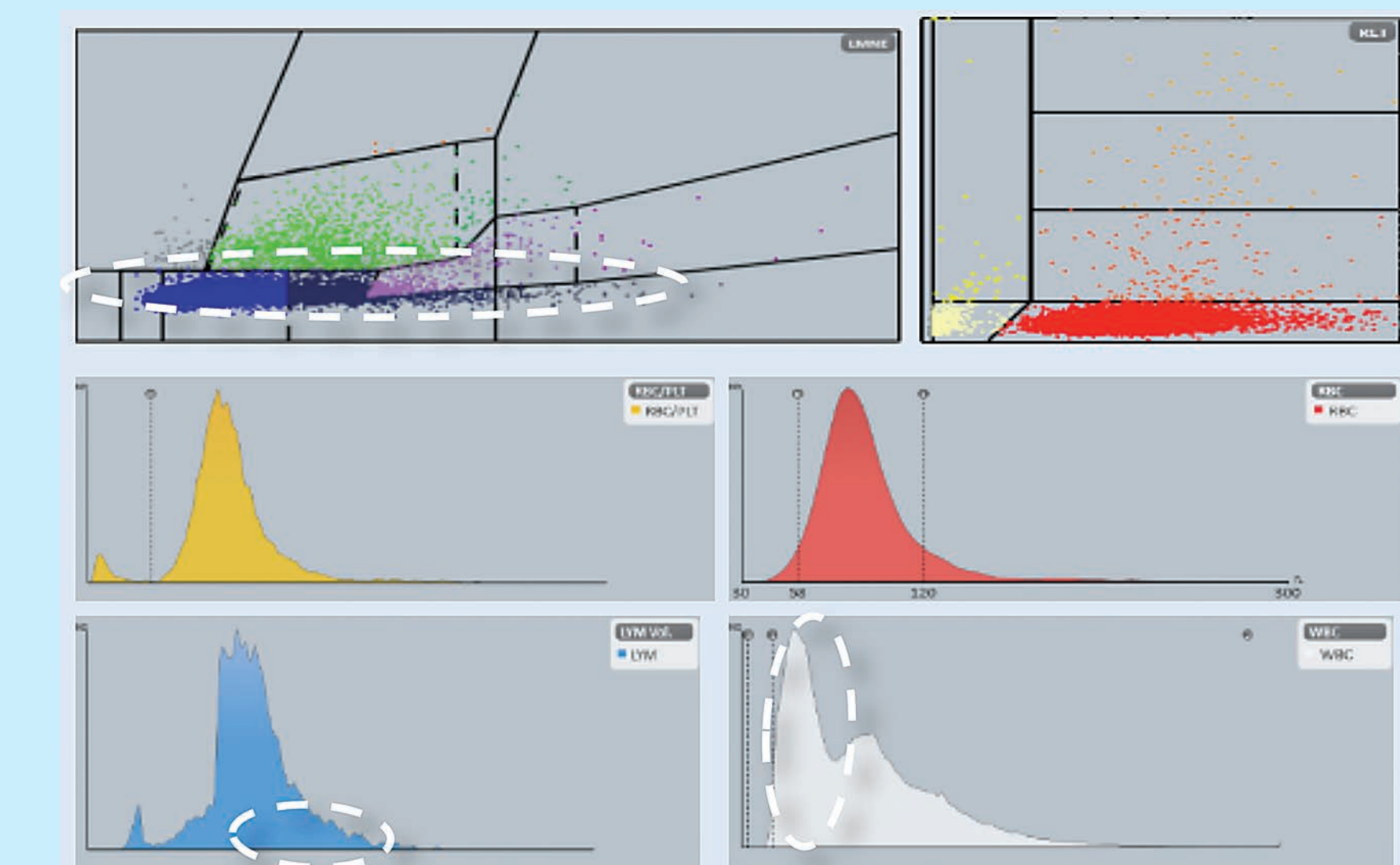
Cut-Off = 2%	Statut YH2500 (v)		Total
	Négatif YH2500	Positif YH2500	
Statut dxH	Négatif	Positif	
Négatif DxH	195	13	208
Positif DxH	4	11	15
Total	199	24	223

Overall agreement LYA% 92%

Interference RBC/PLT



1- On the PLT histogram, we observe no valley in the macroplatelets area. The MPV is artificially increased by the RBC interference.
 2- On the RBC/PLT histogram, we observe the valley between the both population and the bad position of the threshold in impedance. The impedance value of PLT is rejected and an automatic PLTOx is more correct.
 3- On the RBC histogram we observe the presence of microcytic population. Associated with low reticulocyte response, the hypoproliferative microcytic anemia is typical of hypothyroidism.
 4- On the PLTOx scattergram we observe the separation between the PLT population and the RBC population in the optical axe. The PLTOx value is correct.



1. On the DIFF scattergram we observe the presence of atypical lymphocytes and immature lymphocytic cells from the CLL.
 2. On the WBC histogram, we observe the ratio of the lymphocyte population is higher than the granulocyte population.
 3. On the Lymphocyte distribution histogram, we observe large cells on the right of the lymphocyte population which correspond to the large cells from the CLL. Results with smudges cells included in the lymphocyte population: NEU% 1.1, LYM% 98.7, MON% 0.2.