Evaluation of Laser Light Scattering Technology in Rapid Diagnosis of Urinary Tract Infections in Children

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ABSTRACT

Background and Aim: Urinalysis (UA) has been routinely used as a screening tool prior to microbial culture set-up in many labs. BacterioScan 216Dx instrument utilizes laser light scattering technology to detect bacterial growth in urine and results are available in 3 hrs. The aim of this study was to compare the performance of 216 DX and UA against culture as gold standard.

Methods: Clean-catch, unpreserved, either UA positive (leukocyte esterase > trace, or nitrite positive or white blood cells >5/hpf) or UA negative samples from children age <18 years were tested by 216Dx within 24 hours of sample collection. 'Presumptive positive' samples by 216Dx were further confirmed by MALDI-TOF. Sensitivity and specificity of 216Dx and UA was determined against urine culture.

Results: Total of 205 urine samples were included in this study, of which 48.0% (98/205) and 52.0% (107/205) were UA positive and negative, respectively. 77.0% of samples were collected from female and median age was 108 months. Overall sensitivity, specificity, positive and negative predictive value (PPV and NPV) of 216Dx and UA are shown in table. Of 27 true positive (TP) samples by 216Dx, 77.0% (21/27) were successfully identified by MALDI-TOF. There were total 96 samples identified as contamination/normal flora by culture. Among these, 63 samples (65.0%) were correctly detected as true negative (TN) by 216Dx vs 50 samples (53.1%) as TN by UA. Two false negative (FN) samples by 216Dx were *Klebsiella oxytoca* and *Staphylococcus epidermidis* (both >100 K). UA missed one *E. coli* positive sample (FN) (>100 K cfu/ml).

Conclusions: Although sensitivity of both 216Dx and UA is comparable, specificity of 216Dx was higher than UA. 216Dx can be used as an alternative screening tool to UA to rule out bacterial infection in children. Faster turn-around-time (3 hours) of 216Dx helps in rapid identification by MALDI-TOF has the potential to reduce unnecessary antibiotic use, improve patient-management and reduce health-care related cost.

Fig 1

A

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The 216Dx System for Bacterial UTI Detection

B

Fig 1A. The BacterioScan 216Dx instrument and disposable multi-cuvettes.
Fig 1B. The 216Dx operates by measuring forward-angle laser light-scattering of suspended particles in liquid samples, which is assessed kinetically as a gauge of microbial growth.

Methods

Sample Collection: Clean-catch, non-preserved urine samples obtained from children age 90 days to <18 years were included in this study and collected between March-April, 2018. Samples with blood or visibly turbid were excluded from study. All urine samples were stored and transported in refrigerated condition until testing within 24 hours.

Urinalysis: Urinalysis was done by using automated Siemens Clinitek Advantus Analyzer. Urine samples were considered UA positive if they met any of the following criteria: i) Leukocyte esterase>trace, ii) Nitrite positive, iii) White blood cells >5/hpf). UA positive samples were reflexed to culture. For the purpose of the study, UA negative samples were collected and culture was set up according to lab SOP following BacterioScan testing.

BacterioScan Assay: 360 µl of urine was mixed with 2.5 ml of tryptic soy broth (TSB; Remel) inside the detection cuvette. Multi-cuvettes were loaded directly onto the BacterioScan 216Dx device and continuously read for approximately 3 h. Results were provided as either 'presumptive positive' or 'presumptive negative' by the device.

MALDI-TOF Identification: After BacterioScan results, 'Presumptive positive' samples were transferred from cuvette into 2.0 ml tube, centrifuged for 5 min at 13,000 rpm. Supernatant was removed and pellet was used for direct MALDI-TOF identification (Bruker), according to lab SOP.
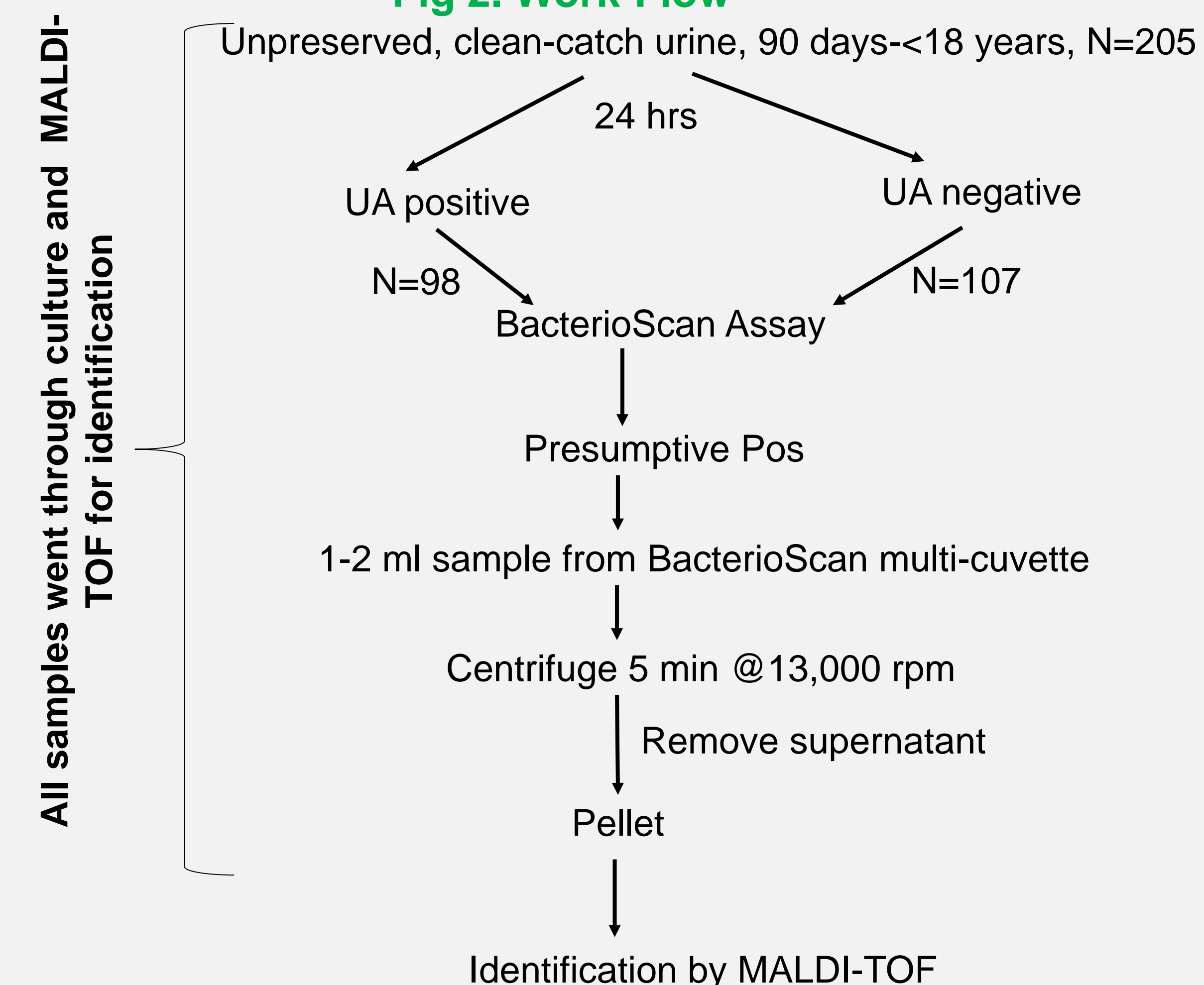
RESULTS

Fig 2. Work-Flow

All samples went through culture and MALDI-TOF for identification

Unpreserved, clean-catch urine, 90 days-<18 years, N=205
↓ 24 hrs
UA positive N=98 / UA negative N=107
↓
BacterioScan Assay
↓
Presumptive Pos
↓
1-2 ml sample from BacterioScan multi-cuvette
↓
Centrifuge 5 min @13,000 rpm
↓
Remove supernatant
↓
Pellet
↓
Identification by MALDI-TOF

Table 1. Comparative performance characteristics of BacterioScan and Urinalysis compared to reference method (urine culture)

Assay	TP	FP	TN	FN	%Sensitivity (95% CI)	%Specificity (95% CI)	%PPV (95% CI)	%NPV (95% CI)	Accuracy
216Dx	27	36	140	2*	93.1 (75.7-98.8)	79.5 (72.6.0-85.1)	42.8 (30.6-55.9)	98.6 (94.4-99.7)	81.0%
UA	28	70	106	1**	96.5 (80.3-99.8)	60.2 (52.5-67.4)	28.5 (20.1-38.7)	99.0 (94.1-99.9)	65.3%

K. oxytoca, S. epidermidis (Both >100K CFU/ml), ** *E. coli*, 100K CFU/ml)

Fig 3. Pathogens Distribution

Pos 14% / Neg 39% / Mixed 47%

87%

■ Neg ■ Mixed ■ Pos

■ E. coli ■ GBS ■ K. oxytoca ■ Staph epi ■ E. cloacae
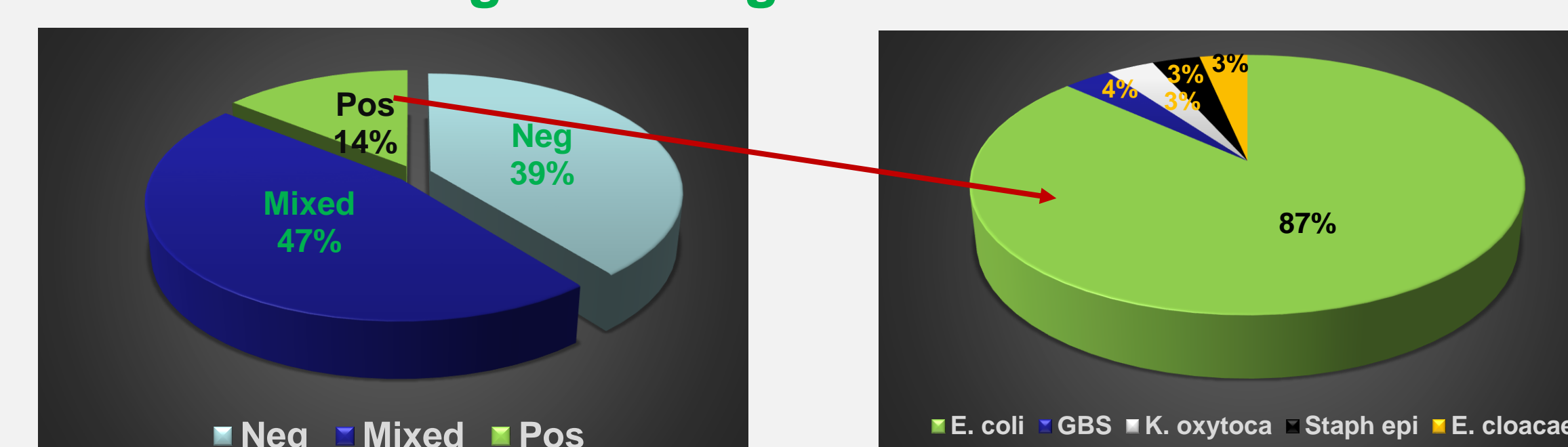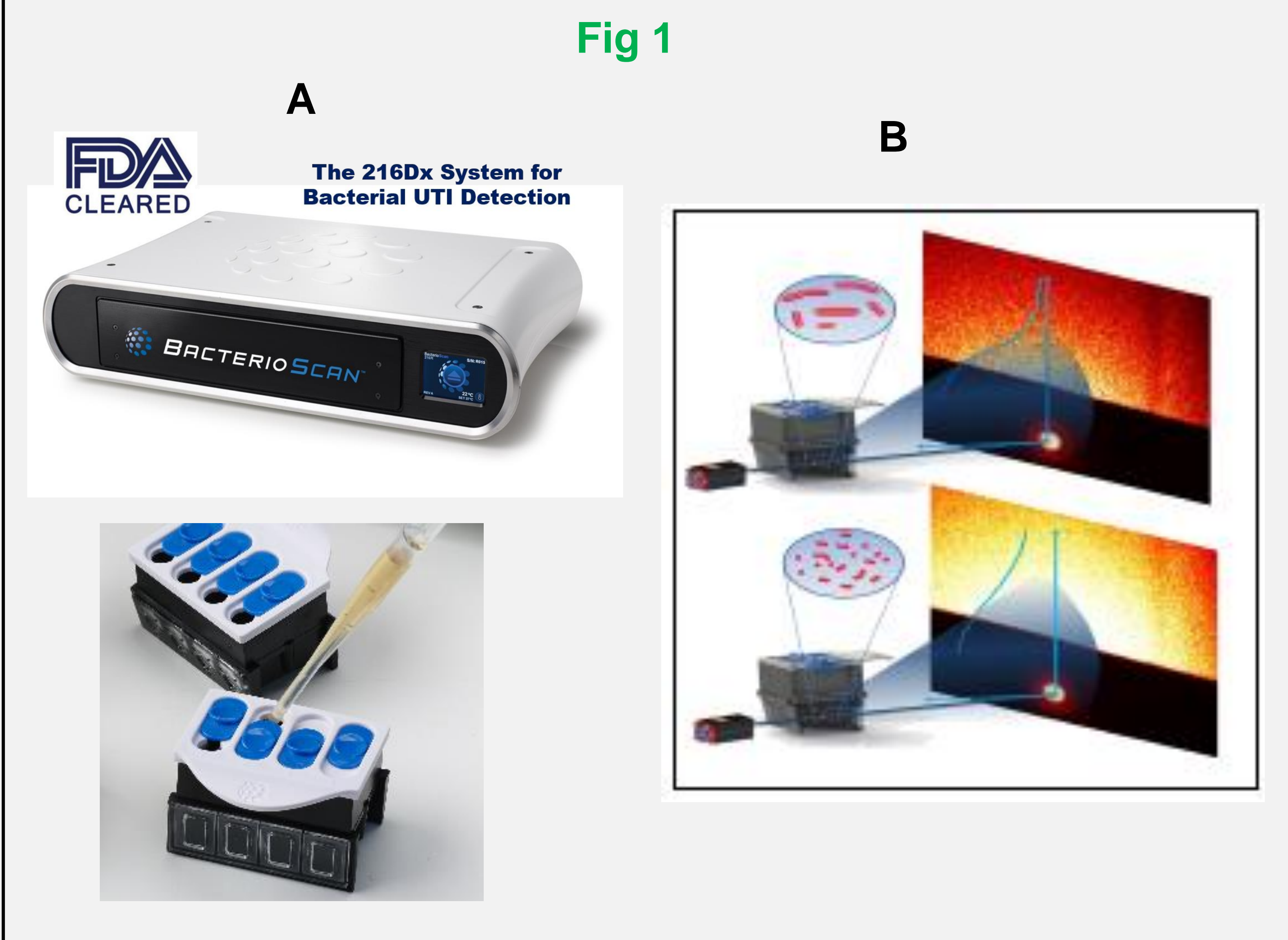
Table 2. BacterioScan and Urinalysis results for specimens with a positive urine culture (n=29)

Pathogens	<50K CFU/ml	50-99K CFU/ml	>100K CFU/ml	Bacterioscan negative samples (no. of CFU/ml)	UA negative samples (no. of CFU/ml)
E. coli	4	1	20	0	1 (>100K CFU/ml)
K. oxytoca	0	0	0	1 (>100K CFU/ml)	0
Staph epi	0	0	0	1 (>100 K CFU/ml)	0
E. Cloacae+S. aur	1	0	0	0	0
Total (% of Pos, n=205)	5 (17.0%)	1 (3.0%)	20 (69.0%)	2 (7.0%)	1 (3.0%)

Fig 4. Performance of BacterioScan and Urinalysis on detecting mixed flora/contamination

Fig 4A

P= <.0173 ■ Pos ■ Neg
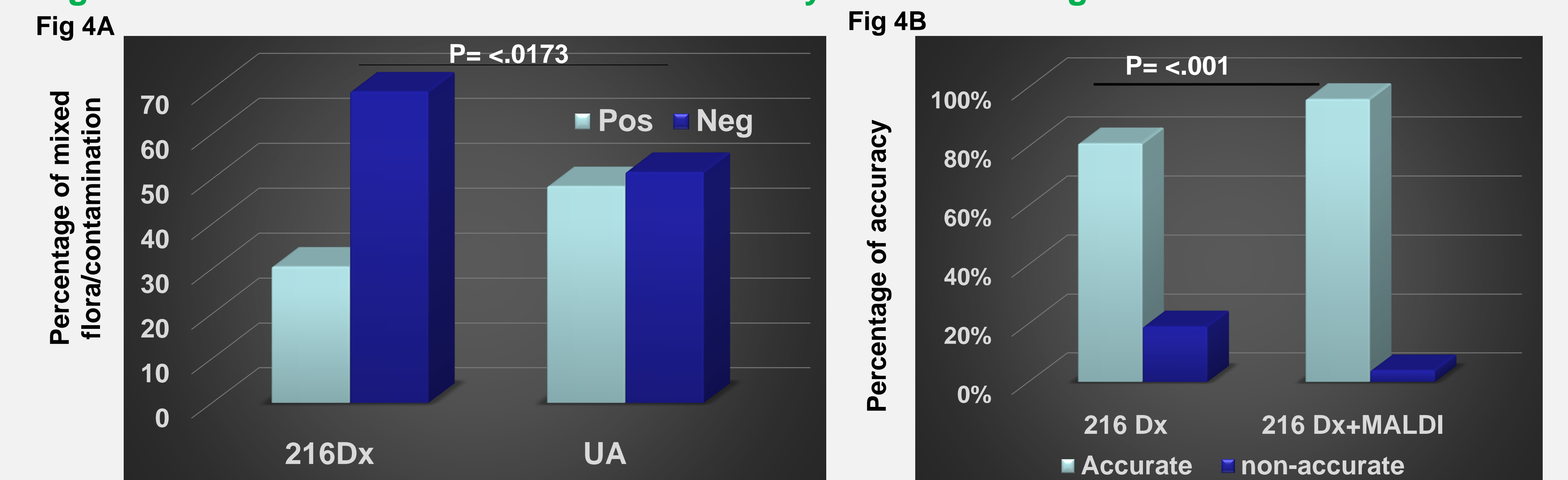
4A. BacterioScan significantly improved the early detection of common flora/contamination

Fig 4B

P= <.001 ■ Accurate ■ non-accurate

4B. When paired with MALDI-TOF, overall accuracy of BacterioScan was significantly improved.

Table 3. BacterioScan paired with MALDI-TOF enhances overall clinical performance

MALDI-TOF Results on All 216 Dx "Presumptive Pos' samples

	No growth (n=81)	Mixed Flora (n=46)	Not uropathogen (n=49)	Cx Pos (n=29)	Culture Pos, 216 Dx Pos — Accurate ID	No peaks	Culture Results — No growth	Mixed Flora	Not Uropathogens
216 Dx Pos	7 (9.0%)	17 (37.0%)	12 (24.0%)	27 (93.0%)	21 (77.0%)	6**	No peaks 100.0% (7/7)	No Peaks-100.0% (17/17)	No Peaks 100.0% (12/12)
216 Dx Neg	74 (91.0%)	29 (63.0%)	37 (76.0%)	2 (7.0%)	NA	NA	NA	NA	NA
UA Pos	24 (30.0%)	30 (65.0%)	16 (33.0%)	28 (96.0%)	NA	NA	NA	NA	NA
UA Neg	57 (70.0%)	16 (35.0%)	33 (67.0%)	1 (4.0%)	NA	NA	NA	NA	NA

**4/6 samples had ≤20K CFU/ml, 2/6 had >100K CFU/ml

SUMMARY AND CONCLUSIONS

➤ Although sensitivity is comparable, BacterioScan has higher specificity (79.5%) than urinalysis (60.2%) and can be used as an alternative screening tool to detect presence or absence of pathogens.

➤ Due to BacterioScan's high negative predicative value (98.6%), negative urine samples can be reliably screened out within 3 hours, thus reducing the urine culture work-up, its associated cost and unnecessary antibiotic use.

➤ BacterioScan more accurately detected mixed flora/contamination as true negative than urinalysis (65.0% vs 53.0%).

➤ When paired with MALDI-TOF, BacterioScan accurately (77.0%) identified the organism within 4 hours. Simultaneously, accuracy was increased to 96.0% compared to BacterioScan alone (81.0%).

➤ Overall, BacterioScan can potentially reduce the overall urine culture work-up turn-around time from 24-72 hours to 3-4 hours, resulting better patient management.