Utility of Laser Scattering Technology followed by Matrix Assisted Laser Desorption Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS) for Urinary Tract Infection (UTI) Screening and Identification

K. M. Riederer, L. B. Johnson, J. T. Fishbain
St. John Hospital & Medical Center, Detroit, MI

Introduction

Urine culture is often performed in high volume with many negative samples that require 18 – 24 hours for results. Screening urine samples for organism prior to culture may reduce this volume and provide more timely information. Current technology utilizing narrow angle forward laser scanning via the 216 Dx device (BacterioScan) is designed to flag urine samples with microbial growth characteristics at >10^6 CFU/ml as “likely positive” with a three hour result.

MALDI-TOF MS (Bruker) has dramatically improved the time required to identify common organisms. Direct identification from urine samples is feasible if organisms can be recovered in high enough number. The ability to reliably screen for the presence of organisms at quantities >10^4 CFU/ml and subsequently perform MALDI-TOF MS organism identification (ID) were explored in this pilot study. Methods to distinguish negative urine samples from potential positives and to rapidly identify organisms associated with urinary tract infection (UTI) are presented.

Results

• 224 samples were tested; 151 under phase 1 processing and 73 in phase 2.
• Urine cultures were positive (68; 30.4%), negative (91; 40.6%) or contaminated samples (65; 29%).
• BacterioScan screening results (Figure 1) were positive (124; 59.3%) or negative (85; 40.7%) with 15 discordant duplicate samples (10.2%).
• BacterioScan sensitivity, specificity, positive and negative predictive values were 95.5, 57.8, 51.6, and 96.5, respectively with culture as gold standard (Table 1).
• 44 Gram-negative pathogens had DS MALDI-TOF ID, score ≥1.99 at 3 hours (Table 2).
• Gram-positives had DS (6) or EX (4) identification score ≥1.99, or no reliable ID (4).
• Yeast were identified by MALDI-TOF EX score ≥1.99 (1) or no reliable ID (4).
• Culture negative false positives had no MALDI-TOF ID (22/23) and 1 K. pneumoniae.
• Contaminant culture false-positives failed no reliable ID (21), EX (8) or DS (8) MALDI-TOF ID, score ≥1.99. Four DS ID were after extended incubation.
• BacterioScan false negative screens (3) occurred with E. faecalis, M. morganii and S. mitis/oralis organisms (Figure 2).

Table 1: BacterioScan Screening Results Compared to Gold Standard Urine Culture

<table>
<thead>
<tr>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive Predictive Value</th>
<th>Negative Predictive Value</th>
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<td>95.5</td>
<td>57.8</td>
<td>51.6</td>
<td>96.5</td>
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| BacterioScan Positive (66) | 64 | 3 | 1 |
| BacterioScan Negative (65) | 23 | 60 | 6 |

Table 2: MALDI-TOF Organism Identification of BacterioScan Positive Cuvettes (Score value ≥ 1.99)

<table>
<thead>
<tr>
<th>Gram-Negative Organisms (45)</th>
<th>E. coli (30)</th>
<th>K. pneumoniae (5)</th>
<th>P. mirabilis (2)</th>
<th>E. aerogenes (1)</th>
<th>Mixed GN (6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-Positive Organisms (14)</td>
<td>E. faecalis (2)</td>
<td>E. faecalis (2)</td>
<td>Lactobacillus (2)</td>
<td>E. faecium (2)</td>
<td>Mixed GP (1)</td>
</tr>
<tr>
<td>Yeast</td>
<td>C. albican (1)</td>
<td>C. albican (1)</td>
<td>C. glabral (1)</td>
<td>No ID (2)</td>
<td></td>
</tr>
</tbody>
</table>

Bscan Positive/Culture Positive (64) | E. coli (1) |
Bscan Positive/Culture Negative (23) | K. pneumoniae (1) |
Bscan Positive/Contaminated (37) | C. glabral (1) | E. faecalis (30) | P. aerogenes (1) | M. morganii (1) | L. casei (1) | S. simulans (1) | P. stuartii (1) | S. anginosus (1) | Mixed GP (1) |

Figure 1: Growth curves of eight culture positive urines with duplicate BacterioScan positive screening, shown as solid and dashed lines.

Figure 2: Three culture positive urines did not yield BacterioScan positive results.

Conclusions

- Negative urines can be reliably screened out using the 216 Dx BacterioScan device to reduce unnecessary cultures.
- Most Gram-negative and Gram-positive organisms producing a BacterioScan positive screen result can be rapidly identified by MALDI-TOF direct smear.
- Many BacterioScan false positive screen results can be discriminated by lack of, or low score, MALDI-TOF identification.
- Urine culture remains necessary to determine if samples are polymicrobial or contaminated and to perform antimicrobial susceptibility testing.

Acknowledgements

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