Performance of the new Accelerate ID/AST System in highly resistant *Acinetobacter baumannii* bloodstream infection isolates, compared to routine laboratory testing

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OBJECTIVES: Identification (ID) and antimicrobial susceptibility testing (AST) of pathogenic bacteria significantly impact the selection of optimal antimicrobial therapy, and early results are crucial for the treatment of critically ill patients and in settings challenged by multi-resistant bacteria, such as intensive care units. Early AST is crucial for escalating antimicrobial treatment in critically ill patients when needed – but more importantly, early AST is also essential for fast de-escalation of the antimicrobial treatment, which is a key element of antimicrobial stewardship. The objective of this study was to evaluate the performance of the new Accelerate ID/AST System* (Accelerate Diagnostics, Inc.) that aims to deliver fast ID and AST results and compare those results to routine laboratory microbial characterization.

(*For Research Use Only. Not for use in diagnostic procedures.)

METHODS: Fifty *Acinetobacter baumannii* bloodstream isolates were pre-screened by broth microdilution (BMD) for minimum inhibitory concentrations (MICs) ≥16 mg/L for imipenem or meropenem. For each isolate, 10 to 100 colony forming units were spiked into blood culture bottles and incubated at routine conditions for 20-24 hours prior to analysis. Using a single pipetting step, 3.5 ml from the blood culture bottle was directly loaded onto a prototype of the fully automated Accelerate ID/AST System. The system automatically identified microbial cells using a broad panel of fluorescence *in situ* hybridization (FISH) probes in parallel channels. Due to the multiplexing capacity, the Accelerate ID/AST System has the potential to detect multiple species present in polymicrobial samples. Following a one hour pre-growth and automated dilution step, remaining sample was automatically split and immobilized in separate flowcells for AST testing. ID results drove antimicrobial selection for AST. Only a single concentration of each antimicrobial was used, and different antimicrobials were tested in separate flowcells. Automated microscopy captured time-lapse images of each flowcell which were used by the computer software to analyse growth rates and other characteristic features of each individual immobilized progenitor bacterial cell during growth. An algorithm converted the growth characteristics (growth rate, growth inhibition and other characteristics) of all bacteria present in a flowcell into a MIC value for each tested antimicrobial agent. Routine laboratory testing included MALDI-TOF species identification, VITEK 2 MIC determination, agar disk diffusion susceptibility testing and E-test MIC determination. Tested antimicrobial agents included meropenem, imipenem, piperacillin/tazobactam and ciprofloxacin. Standard CLSI frozen BMD was used as the gold standard.

Video 1. Accelerate ID/AST System† components.

† Study performed on a prototype of the final system shown here.

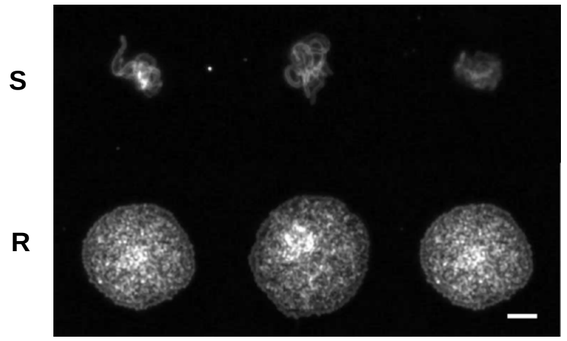
RESULTS: The overall ID agreement was 100%. For AST of the included antimicrobial agents, overall essential agreement (EA) was 98.8% and overall categorical agreement (CA) was 95.9% compared to routine laboratory testing. Compared to BMD, the Accelerate ID/AST System showed an overall EA of 99.4%, and an overall CA of 100% for the tested antimicrobial agents (Table 1). When Accelerate/Routine Laboratory discrepant results were resolved by BMD, Accelerate ID/AST was confirmed as correct in all cases. Accelerate ID/AST System ID results were obtained in one hour, and MIC results were obtained within five hours, with approximately 6 min. of total hands-on time including data management and a loading procedure consisting of a single pipetting step. Routine laboratory test results (agar disk diffusion susceptibility and VITEK 2 and E-test MICs) were available in 16+ hours, with more than two hours of hands-on time.

Table 1. Essential agreement (EA) and categorical agreement (CA) of the Accelerate ID/AST System with broth microdilution.

Antimicrobial	EA	CA‡	Errors‡
Meropenem	44/44 (100%)	44/44 (100%)	0
Imipenem	36/36 (100%)	36/36 (100%)	0
Piperacillin/ Tazobactam	43/44 (98%)	44/44 (100%)	0
Ciprofloxacin	45/45 (100%)	45/45 (100%)	0
TOTAL	**168/169 (99.4%)**	**169/169 (100%)**	**0**

‡ CLSI breakpoints

Video 2. Susceptible (S) and resistant (R) *Acinetobacter baumannii* progenitor cells growing into clones of daughter cells in 16 mg/L piperacillin/tazobactam from 0 to 4 hours. Susceptible clones show filamentation and lysing while resistant clones continue to grow. Scale bar at lower right is 10 µm.



CONCLUSION: The Accelerate ID/AST System performed very well on the highly resistant *Acinetobacter baumannii* isolates analysed in this study, with 100% correct identification. Regarding EA and CA, the Accelerate ID/AST System had excellent concordance with BMD (99.4% and 100% respectively) and compared very well with routine laboratory testing (98.8% and 95.9% respectively). Because of these promising results, a significantly faster time-to-result, and laboratory benefits including a short hands-on-time and an easy-to-use, fully automated workflow, the Accelerate ID/AST System may enable clinicians to adjust antimicrobial treatment earlier, thus maximizing clinical impact on patient management and outcomes. In addition, earlier availability of AST results may enable earlier de-escalation of antimicrobial treatment, thus meeting an essential requirement of antimicrobial stewardship.