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Evaluation of the LifeScale rapid antimicrobial susceptibility testing platform for positive blood cultures

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ABSTRACT

The emergence of drug-resistant microorganisms has increased the need for prompt and reliable antimicrobial susceptibility testing (AST). Rapid AST allows for quicker start of optimal therapy, which can improve patient outcomes and lower costs related to hospital stays. Currently, several platforms being developed deliver rapid AST results, however, rapid results may not improve patient care if they are not considered equivalent to standard results. Thus, the accuracy and reliability of results from rapid AST is of utmost importance. In this study, we assessed the performance of the new LifeScale rapid AST platform (Affinity Biosensors) that uses resonant mass measurements for calculation of antimicrobial susceptibility results.

Positive BACTEC blood-culture bottles collected from patients at the University of Utah Healthcare system were included if gram stain revealed only gram-negative rods (GNRs). Standard of care (SOC) AST results, as determined by a combination of routine BD Phoenix automated, Sensititre broth microdilution, and standard disk diffusion methods, were compared to results generated by directly testing positive blood culture broth on the LifeScale system. Minimum inhibitory concentrations (MICs) and susceptibility interpretations based on CLSI M100-32Ed were compared by microorganism and drug to calculate essential and categorical agreement for five species with pending claims on the LifeScale system: *E. coli* (N=33), *K. aerogenes* (N=1) *K. pneumoniae* (N=10), *K. oxytoca* (N=5), *P. aeruginosa* (N=11) and *A. radioresistens* (N=1); tested against 13 antibiotics: Amikacin, ampicillin, aztreonam, cefazolin, cefepime, ceftazidime, ertapenem, gentamicin, levofloxacin, meropenem, piperacillin/tazobactam, trimethoprim/sulfamethoxazole & ceftazidime/avibactam.

Overall, LifeScale results had an 95.1% essential agreement with the SOC results, and a 93.8% categorical agreement based on CLSI criteria. Of the 675 organism-drug combinations evaluated, agreement was high, with only 1 very major discrepancy, 8 major discrepancies and 37 minor discrepancies, of which 14 were within ±1 doubling dilution. Among discrepant results, LifeScale MICs averaged 1 dilution higher than SOC MICs, which may reduce the risk of false-susceptible interpretations.

The technology of the LifeScale is unique among other AST platforms as it measures bacterial cell mass and counts to generate MIC values for up to 14 antibiotics in 4 hrs. These results suggest this platform is able to deliver rapid, actionable results to guide antimicrobial therapy for patients with bacteremia.

METHODS

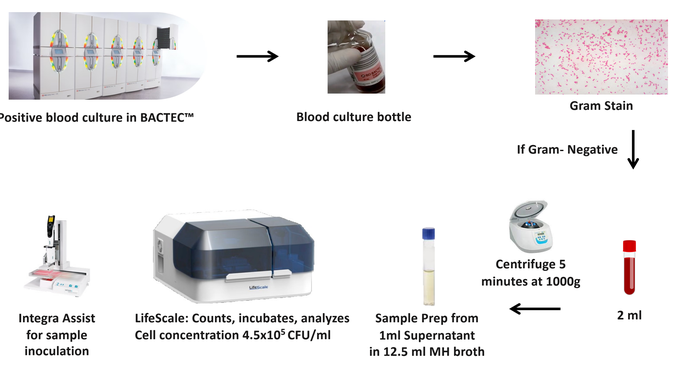


Table 1. LifeScale Antimicrobials Tested

E. coli & *Klebsiella* spp.	*P. aeruginosa*	*Acinetobacter* spp.
Amikacin	Amikacin	Amikacin
Ampicillin	Aztreonam	Aztreonam
Aztreonam	Cefepime	Cefepime
Cefazolin	Ceftazidime	Ceftazidime
Cefepime	Ceftazidime/Avibactam	Gentamicin
Ceftazidime	Gentamicin	Levofloxacin
Ertapenem	Levofloxacin	Meropenem
Gentamicin	Meropenem	Piperacillin/Tazobactam
Levofloxacin	Piperacillin/Tazobactam	Trimetho/Sulfa
Meropenem	Trimetho/Sulfa	
Piperacillin/Tazobactam		
Trimetho/Sulfa		
12 drugs	10 drugs	9 drugs
BD Phoenix™	Broth Microdilution	Broth Microdilution

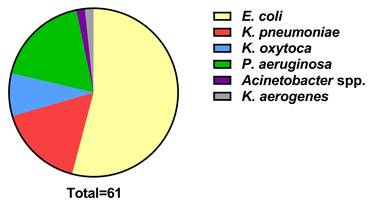
Table 1: Comparator method for each genus listed in the last row

RESULTS

Breakdown of microorganisms tested

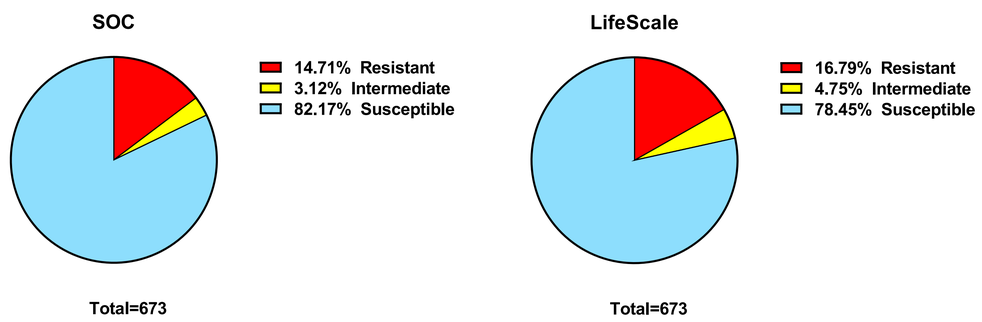
Table 2. Microorganisms Tested

Organism	N
Escherichia coli	33
Klebsiella aerogenes	1
Klebsiella pneumoniae	10
Klebsiella oxytoca	5
Pseudomonas aeruginosa	11
Acinetobacter radioresistens	1



Distribution of Microorganisms tested: Organisms were obtained directly from positive blood culture bottles submitted from the University of Utah Hospital. Upon reveal of gram-negative by gram stain, blood samples were eligible for testing.

LifeScale performance compared to Standard of Care (SOC) results



Higher percentage of non-susceptible interpretations in the LifeScale compared to the Standard of Care (SOC). Data comprises of all microorganisms and antibiotics tested for this study;2 tests were not considered for this data given that there are no interpretations for this antibiotic/ drug combination.

Table 3. Summary of LifeScale performance per microorganism vs Standard of care results
Legend**: VMD:** Comparator method resistant, evaluation method susceptible; **MD:** Comparator method susceptible, evaluation method resistant; **mD:** Intermediate by one method and resistant or susceptible by the other; **CA:** Agreement in interpretation (R, S or I); **EA:** Agreement in +/- 1-dilutions from standard of care method

	E. coli	*K. aerogenes*	*K. pneumoniae*	*K. oxytoca*	*P. aeruginosa*	*Acinetobacter* spp.
Number of isolates	33	1	10	5	11	1
Total Number of Tests	**394**	**10**	**115**	**54**	**93**	**9**
Very Major Discrepancy (VMD)	0	0	0	0	1	0
Major Discrepancy (MD)	3	0	0	0	5	0
Minor Discrepancy (mD)	19	0	10	2	6	0
Categorical Agreement	372	10	105	52	81	9
CA %	**94.4**	**100**	**91.3**	**96.3**	**87.1***	**100**
Essential Agreement	375	9	105	52	93	9
EA %	**95.1**	**90**	**91.3**	**96.3**	**100**	**100**

Table 3. **P. aeruginosa* discrepant results*:* 1 VMD with levofloxacin, 3 MD with cefepime, 1 MD ceftazidime & 1 MD ceftazidime/avibactam.

Table 4. Overall Agreements

Agreement	N of Tests	Percentage
Categorical	633	93.8
Essential	642	95.1

Table 5. Overall Discrepancies

Discrepancy	N of Tests	Percentage
VMD	1	1.01
MD	8	1.44
mD	37	5.6

Table 4 & 5: Agreements and discrepancies between LifeScale vs. Standard of care. The same definitions described in table 3 apply for tables 4 & 5. %VMD = N of VMD / Total Resistant isolates by SOC. %MD = N of MD / Total susceptible isolates by SOC. %mD = N of mD / total number of tests.

CONCLUSIONS

- LifeScale has demonstrated a respectable performance across the microorganisms/antibiotics tested with >90% CA and EA overall agreements. However, more isolates are required to fully assess its true performance.
- These results suggest that LifeScale can deliver rapid, actionable results to guide antimicrobial therapy for patients with bacteremia.
- Discrepant LifeScale MICs averaged 1 dilution higher than SOC MICs, which may reduce the risk of false-susceptible interpretations.
  - Discrepant results will be resolved using reference broth microdilution.

ACKNOWLEDGMENTS

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Overall, LifeScale results had an 92.7% essential agreement with the SOC results, and a 92.4% categorical agreement based on CLSI criteria. Of the 738 organism-drug combinations evaluated, agreement was high, with only 1 very major discrepancy, 8 major discrepancies and 48 minor discrepancies, of which 31 were within ±1 doubling dilution. Among discrepant results, LifeScale MICs averaged 1 dilution higher than SOC MICs, which may reduce the risk of false-susceptible interpretations.

The technology of the LifeScale is unique among other AST platforms as it measures bacterial cell mass and counts to generate MIC values for up to 14 antibiotics in 4 hrs. These results suggest this platform is able to deliver rapid, actionable results to guide antimicrobial therapy for patients with bacteremia.

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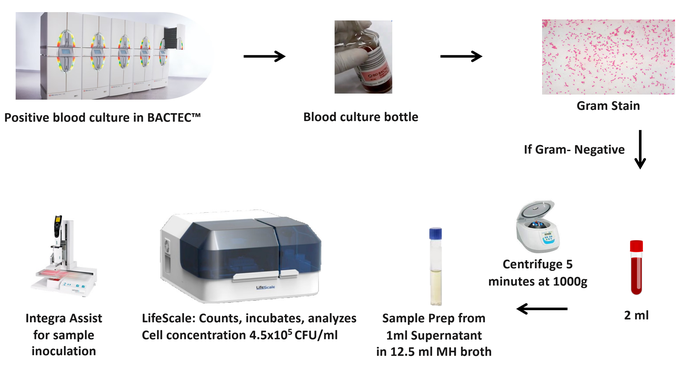

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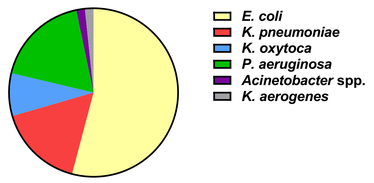

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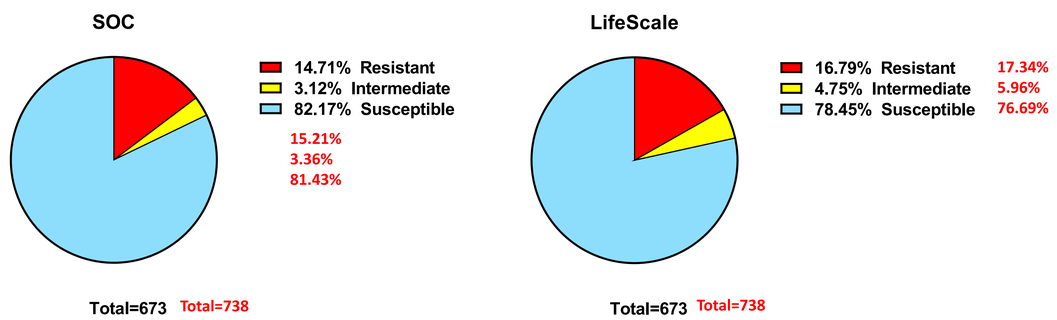

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	E. coli	*K. aerogenes*	*K. pneumoniae*	*K. oxytoca*	*P. aeruginosa*	*Acinetobacter* spp.
Number of isolates	35	1	12	5	12	1
Total Number of Tests	419	11	142	58	100	8
Very Major Discrepancy (VMD)	0	0	0	0	1	0
Major Discrepancy (MD)	5**	0	1	1	1	0
Minor Discrepancy (mD)	24	1	10	3	10	0
Categorical Agreement	390	10	131	54	89	8
CA %	93.3	90.9	92.3	93.1	88.1*	100
Essential Agreement	401	9	131	57	80	6
EA %	95.7	90	92.3	98.3	80	75

Table 3. **P. aeruginosa* discrepant results: 1 VMD with levofloxacin was resolved by broth microdilution, 1 MD with ceftazidime/avibactam was within ±1 doubling dilution;

*** E. coli* 5 major discrepant results: 2 MD with Cefazolin 1 was resolved by broth microdilution, 1 MD with Aztreonam, 2 MD with Piperacillin/Tazobactam remain to be tested by broth microdilution

Table 4. Overall Agreements

Agreement	N of Tests	Percentage
Categorical	682	92.4
Essential	684	92.7

Table 5. Overall Discrepancies

Discrepancy	N of Tests	Percentage
VMD	1	0.78
MD	8	1.41
mD	48	6.50

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