Reduced Time to Results for a Phenotypic MRSA Detection Assay for Use Directly from Positive Blood Cultures

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ACCELERATE DIAGNOSTICS

BACKGROUND

The Accelerate PhenoTest™ BC kit used with the Accelerate Pheno™ system (AXDX) produces identification (ID) results in approximately 2 hours, and phenotypic antimicrobial susceptibility testing (AST) results in approximately 7 hours directly from positive blood cultures (PBC). AST test panels are based on the organism ID, and include MRSA/MSSA detection for *Staphylococcus aureus*.

In this study, data from the AXDX FDA-registration trial was reanalyzed to determine if the time to report MRSA/MSSA could be reduced.

METHODS

Results were reported for the MRSA/MSSA phenotypic cefoxitin screen for 184 PBC containing *S. aureus* during the AXDX FDA-registration trial (Pancholi, *et al.*). The raw image data available from 177 of these runs were reanalyzed with the analysis algorithm at 4.5, 5.0, and 5.5 h after the start of the run, and sensitivity (SN), specificity (SP), positive predictive value (PPV) and negative predictive value (NPV) for MRSA detection were calculated at each time point.

RESULTS

SN and NPV for MRSA detection were 100% across all time points (Table 1). SP and PPV ranged from 97.6% to 99.0% for all time points 5.0 h or later. However, SP decreased to 73.7% and PPV to 86.0% at 4.5 hours after run start, due to the higher MRSA false-positive rate at this time point. Reportability also decreased as the algorithm was applied to increasingly earlier time points.

The algorithm is based on changes in clone brightness and size over time. Figure 1 shows a MRSA organism increasing in brightness and size over time. The MSSA with a false-positive result at 4.5 hours also shows an increase in brightness and size between 2.5 h and 4.5 h, but brightness and size decrease after 4.5 h. In contrast, the MSSA with true-negative results at 4.5 h shows an increase in brightness, but minimal increase in size between 2.5 h and 4.5 h compared to the other two organisms, and decreasing brightness and size after 4.5 h.

RESULTS

Table 1: Performance of cefoxitin screen for MRSA/MSSA at various time points after the start of the run.

Time After Run Start (h)	n	TP	TN	FP	FN	SN	SP	PPV	NPV
~7	177	92	84	1	0	100%	98.8%	98.9%	100%
5.5	176	92	83	1	0	100%	98.8%	98.9%	100%
5.0	174	92	80	2	0	100%	97.6%	97.9%	100%
4.5	149	92	42	15	0	100%	73.7%	86.0%	100%

Abbreviations: n=number; h=hours; TP=true positive; TN=true negative; FP=false positive; FN=false negative; SN=sensitivity; SP=specificity; PPV=positive predictive value; NPV=negative predictive value
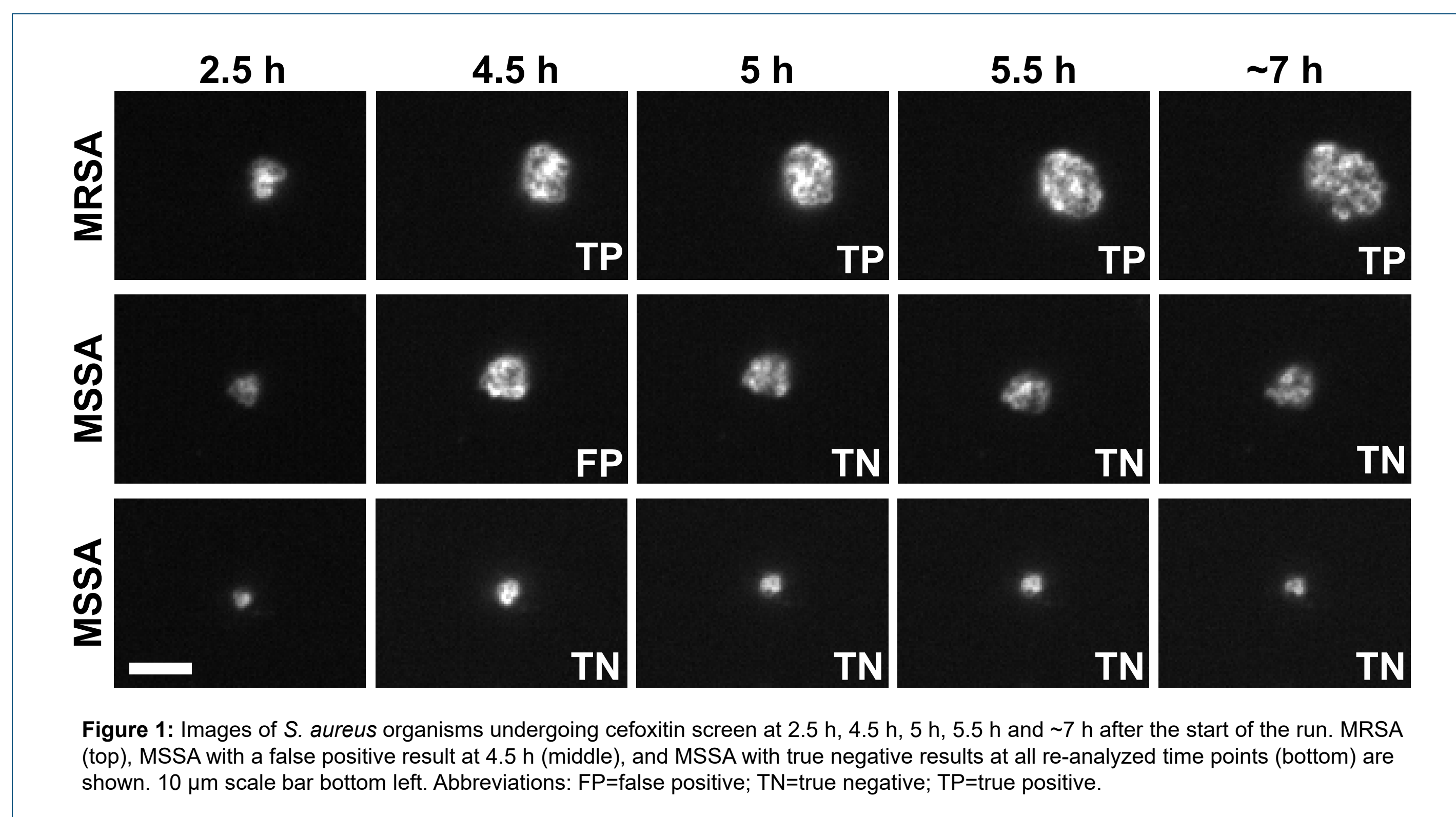
Figure 1: Images of *S. aureus* organisms undergoing cefoxitin screen at 2.5 h, 4.5 h, 5 h, 5.5 h and ~7 h after the start of the run. MRSA (top), MSSA with a false positive result at 4.5 h (middle), and MSSA with true negative results at all re-analyzed time points (bottom) are shown. 10 μm scale bar bottom left. Abbreviations: FP=false positive; TN=true negative; TP=true positive.

CONCLUSIONS

These data demonstrate the time to results for MRSA/MSSA detection with AXDX can be substantially reduced from approximately 7 h to less than 5.0 h, with minimal algorithm changes. Algorithm optimization is in development, to further reduce time to results and improve reportability and specificity at earlier time points.

REFERENCE

1) Pancholi P, Carroll KC, Buchan BW, *et al*. Multicenter Evaluation of the Accelerate PhenoTest BC Kit for Rapid Identification and Phenotypic Antimicrobial Susceptibility Testing Using Morphokinetic Cellular Analysis. *J Clin Microbiol* 2018; 56(4):e01329-17.